

## Observation of an Unusually Large Inverse Secondary Deuterium Kinetic Isotope Effect for the Reaction of a Sterically Congested Olefin with Br<sub>2</sub>

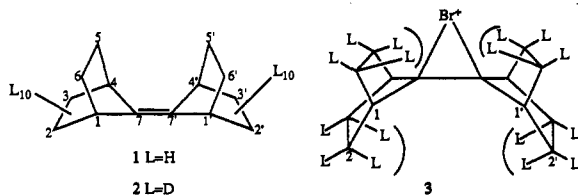
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Despite a limited number of reports,<sup>1,2</sup> the application of deuterium kinetic isotope effects<sup>3</sup> (DKIE) has proven valuable in the study of electrophilic bromination of olefins. These have mostly involved secondary  $\alpha$  DKIE studies of the bromination of stilbene,<sup>1a</sup> styrenes,<sup>1b</sup> and various deuterated cyclohexenes,<sup>2a</sup> although a primary DKIE has been reported for bromination of a sterically crowded olefin (tetraisobutylethylene) that gives a double-bond rearranged allylic bromide as the product.<sup>2b</sup>

7-Norbornylidene-7'-norbornane (**1**) has been reported to react with Br<sub>2</sub> to form the corresponding 7,7'-dibromide.<sup>4</sup> Clearly, **1** is incapable of forming a double-bond rearranged allylic bromide, nor can the perdeuterated analogue **2**<sup>5</sup> exhibit an  $\alpha$  DKIE for its reaction with Br<sub>2</sub>. Nevertheless, herein we report that this system



exhibits an unusually large inverse DKIE for the reaction with Br<sub>2</sub> in both HOAc and MeOH (e.g.,  $k(2/1) > 1$ ). This effect appears to be a consequence of the involvement of a pronounced steric DKIE on the partitioning of a reversibly formed bromonium ion (**3**).

Given in Tables 1 and 2 are the second-order rate constants for disappearance of Br<sub>2</sub> in the presence of olefins **1** and **2**<sup>5</sup> and added LiBr in HOAc and MeOH. Also in the tables are the percentages of the dibromide and bromosolvate products isolated from the reaction media as determined by GC mass spectrometry.<sup>6</sup> There are three main observations. First, the second-order rate constant for bromination ( $k_g$ ) in both solvents decreases markedly upon the addition of small quantities of LiBr. Second, in all cases, there is an inverse DKIE ( $k_g(2/1) > 1$ ). In HOAc, the DKIE becomes increasingly inverse as [LiBr] increases, going from 1.53 at zero added [Br<sup>-</sup>], to 2.75 at [Br<sup>-</sup>] = 0.05 M. In MeOH, the inverse DKIE is essentially constant at  $1.85 \pm 0.15$

**Table 1.** Second-Order Rate Constants for Bromination of **1** and **2** in HOAc, T = 25 °C,  $\mu = 0.1$  (LiClO<sub>4</sub>) and Product Distribution as a Function of [LiBr]<sup>a</sup>

[LiBr] (M)	$k_g$ (M <sup>-1</sup> s <sup>-1</sup> ) <sup>b</sup>		$k_g(2/1)$	% <sup>c</sup>	
	<b>1</b>	<b>2</b>		dibromide <sup>c</sup>	bromosolvate <sup>c</sup>
0	38.2	58.6	1.53		
0.01	2.07	3.33	1.61	38.6	61.4
0.03	0.27	0.54	2.00	62.4	37.6
0.05	0.092	0.253	2.75	82.6	17.4

<sup>a</sup> [Br<sub>2</sub>] =  $9 \times 10^{-5} - 1 \times 10^{-4}$  M; [ol]  $\approx 1 \times 10^{-3}$  M; followed at 410 nm. <sup>b</sup>  $k_g = k_{\text{obsd}}/[\text{ol}]$ ; see text. <sup>c</sup> Dibromide and bromoacetate percentages for bromination of **1** as determined by GC mass spectrometry.

**Table 2.** Second-Order Rate Constants for Bromination of **1** and **2** in MeOH, T = 25 °C,  $\mu = 0.3$  (LiClO<sub>4</sub>) and Product Percentages as a Function of Added [LiBr]<sup>a</sup>

[LiBr] (M)	$k_g$ (M <sup>-1</sup> s <sup>-1</sup> ) <sup>b</sup>		$k_g(2/1)$	% <sup>c</sup>	
	<b>1</b>	<b>2</b>		dibromide <sup>c</sup>	methoxybromide <sup>c</sup>
0.005	33.3				100
0.01	17.52	33.57	1.83		100
0.02	6.23	11.82	1.90		
0.03	3.28	5.98	1.98	7	93
0.04	1.85	3.12	1.68		

<sup>a</sup> [Br<sub>2</sub>] =  $9 \times 10^{-5} - 1 \times 10^{-4}$  M; [ol]  $\approx 1 \times 10^{-3}$  M; followed at 410 nm. <sup>b</sup>  $k_g = k_{\text{obsd}}/[\text{ol}]$ ; see text. <sup>c</sup> Dibromide and methoxybromide percentages for bromination of **1** as determined by GC mass spectrometry.

as a function of added [Br<sup>-</sup>]. Third, in HOAc, increasing [Br<sup>-</sup>] gives an increasing amount of dibromide product. In MeOH, dibromide is never a prominent product even at the highest [Br<sup>-</sup>]. We will deal with these observations in turn.

It is well known<sup>7</sup> that the rates for bromination of olefins generally decrease in the presence of added [Br<sup>-</sup>]. This is due to the fact that an equilibrium,  $\text{Br}^- + \text{Br}_2 \rightleftharpoons \text{Br}_3^-$ , is instantaneously established, the net effect being to deplete the available free [Br<sub>2</sub>]. In HOAc and MeOH, the equilibrium constants ( $K_{\text{eq}}$ ) for this process are 92 and 177 M<sup>-1</sup>, respectively.<sup>7a,b</sup> Both Br<sub>2</sub> and Br<sub>3</sub><sup>-</sup> (or its kinetic equivalent) are brominating agents, and it can be shown<sup>7</sup> that the global rate constant for disappearance of Br<sub>2</sub> is

$$k_g = (k_{\text{Br}_2} + k_{\text{Br}_3^-} K_{\text{eq}} [\text{Br}^-]) / (1 + K_{\text{eq}} [\text{Br}^-]) \quad (1)$$

where  $k_g$  is the overall second-order rate constant for Br<sub>2</sub> disappearance (i.e., ( $k_{\text{obsd}}$ ) divided by [ol]). For most normal olefins, a plot of  $k_g(1 + K_{\text{eq}}[\text{Br}^-])$  vs  $K_{\text{eq}}[\text{Br}^-]$  yields a straight line, the intercept of which is  $k_{\text{Br}_2}$ , the rate constant for Br<sub>2</sub> reaction, and the slope of which is  $k_{\text{Br}_3^-}$ , the rate constant for the tribromide reaction.

Shown in Figure 1 are plots of the so-manipulated kinetic data for **1** and **2** in both solvents. The important feature of note is the marked downward curvature of the plots which asymptotically approach the  $x$ -axis. This sort of behavior has been reported in only two previous instances, those of bromination of 2-acetoxy-2-cholestene<sup>8</sup> and tri-*tert*-butylethylene,<sup>9</sup> and was interpreted as arising from a Br<sup>-</sup> promoted bromonium ion reversal (i.e., a common ion rate depression). By the same token, all of the observations made with **1** and **2** can be explained by a reaction involving a reversibly formed bromonium ion (**3**), where the rate-limiting step involves nucleophilic capture of the ion on carbon. MMX calculations<sup>10</sup> of the structure of bromonium ion **3** indicate that the C<sub>2</sub>, C<sub>2</sub>', C<sub>3</sub>, C<sub>3</sub>' *endo* hydrogens are separated by only 2.1 Å

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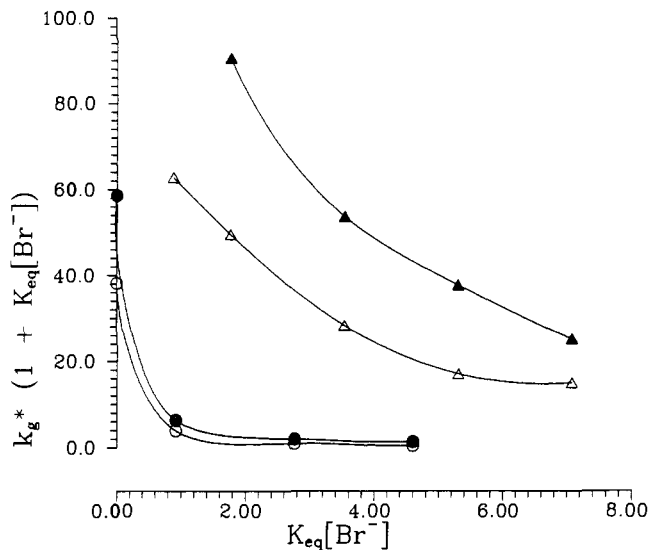
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(5) The procedure employed for synthesis of the perdeuterated material was analogous to that reported by Gassman and Pape (Gassman, P.; Pape, P. G. *J. Org. Chem.* **1964**, *29*, 160) for the synthesis of 7-norbornanone, except we employed deuterated precursors (LeBel, N. A.; Beirne, P. D.; Karger, E. R.; Powers, J. C.; Subramanian, P. M. *J. Am. Chem. Soc.* **1963**, *85*, 3199. MacKenzie, K. *J. Chem. Soc.* **1962**, 457), details to be published. The protium content of purified olefin **d**<sub>20</sub> (**2**) was analyzed by <sup>1</sup>H NMR using 0.0021 g of **2** and 1.0  $\mu$ L of CHCl<sub>3</sub> in 0.5 mL of CD<sub>2</sub>Cl<sub>2</sub>. The signals at  $\delta$  2.4 (bridgehead), 1.48 (*exo*), and 1.25 (*endo*) showed 6%, 8%, and 9.4% protium, respectively.

(6) GC–MS performed using a Varian Vista 6000 GC with a Hewlett-Packard HP5 30-m  $\times$  0.24-mm capillary column operating at 12 psi and attached to a VG 7070E low-resolution mass spectrometer. Percentages given on the basis of integrated GC areas.



**Figure 1.** Plot of  $k_g(1 + K_{eq}[Br^-])$  vs  $K_{eq}[Br^-]$  for the reaction of olefins **1** (open symbols) and **2** (closed symbols) with  $Br_2$  in HOAc (circles) and MeOH (triangles).  $T = 25^\circ C$ ,  $\mu = 0.1$  ( $LiClO_4$ ) and  $0.3$  ( $LiClO_4$ ). Lines drawn through the points are for visual aid only and are not fits to any equation.

$\text{\AA}$ , substantially less than the sum of their van der Waals radii ( $1.2 \text{\AA} \times 2$ ).<sup>11</sup> A similar crowding of the analogously positioned hydrogens is both calculated<sup>10</sup> and observed by X-ray diffraction<sup>12</sup> for the stable bromonium ion of adamantylideneadamantane ( $Ad=Ad$ ) and is cited as the source of the stability of the  $Ad=Ad$  bromonium ion toward nucleophilic capture.<sup>12,13</sup> By reasonable analogy, the steric crowding of the *endo* hydrogens in **3** must be present in the transition states leading to and from that ion: this compression retards nucleophilic capture of the ion, which accounts for the relatively slow bromination.<sup>13</sup> Added  $Br^-$  preferentially captures the bromonium ion on the relatively exposed  $Br^+$ , thereby depressing the reaction rate.

The large inverse DKIE observed for  $k_g(2/1)$  is, to our knowledge, unique and therefore worthy of further comment. Remote secondary DKIEs can result from any of three effects: hyperconjugative, inductive, and steric.<sup>3,14</sup> From the geometries of **1–3**, hyperconjugation-based DKIEs are not expected for the allylic C–L bonds. However, one must be mindful of small but cumulative inductive effects that might result from the substitution

(10) Calculated with the PCMODEL program (Serena Software, Box 3076, Bloomington, IN 47402-3076). The C– $Br^+$  force constants and parameters were chosen so as to duplicate the known geometry for the three-membered ring in the bromonium ion of adamantylideneadamantane.<sup>12</sup>

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of the 20 C–H bonds by the slightly more inductively donating C–D bonds. Nevertheless, even if we allow an inductive effect that contributes 1–2% per D/H substitution (which is probably an overestimation considering that 16 of these are  $\gamma$  substitutions<sup>13,14</sup>), this accounts for a predicted inverse DKIE of  $k_g(2/1) \leq 1.4$ . While an inductive effect of this magnitude cannot be ruled out with certainty, it cannot account for all of the observed inverse DKIE, nor can it account for the increasingly inverse value observed as a function of added  $[Br^-]$  in HOAc. Rather, we believe that whatever the electronic contributions are, they are superimposed upon an important steric component. Because the amplitudes of vibration of C–H bonds are greater than those of C–D bonds<sup>14c,15</sup> (i.e., the C–D bond is shorter and less sterically demanding), there is less compression of the *endo* C–L groups in the rate-limiting transition state for electrophilic addition to **2** than there is for **1**. This allows product-forming nucleophilic capture of the ion to proceed more rapidly with the  $d_{20}$  species, therefore contributing substantially to the observed  $k_g(2/1) > 1$ . In effect, the isotopic induced change in the steric effects alters the partitioning of the reversibly formed intermediate.

Finally, the fact that increasing  $[LiBr]$  in HOAc generates both more dibromide product and a larger inverse DKIE suggests that the transition state for  $Br^-$  capture on C is more sterically demanding than for HOAc capture. Product analyses indicate that in the more nucleophilic solvent MeOH,  $Br^-$  capture is never as important a process as MeOH capture of the carbons of bromonium ion, so the DKIE is relatively constant as a function of  $[Br^-]$ .

There are several examples of inverse steric DKIEs reported for processes involving such phenomena as inversions, rotations, or racemizations.<sup>15</sup> Inverse steric DKIEs on nucleophilic reactions have been reported,<sup>16,17</sup> but their magnitude is generally quite small and not readily interpretable. Insofar as we are aware, the large inverse DKIE for this system and its sensitivity to the nature of the capturing nucleophile is highly unusual.<sup>17</sup> We believe that the congested nature of **1** and **2** and particularly the strategic placement of the *endo* hydrogens relative to the double bond will make this system and its specifically deuterated analogues attractive for testing the steric demands of transition states for other reactions of, and leading to, the double bond.

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