

88-88.5 °C;  $[\alpha]_D +9.2^\circ$  (c 3.5,  $\text{CHCl}_3$ );  $^1\text{H NMR}$  (250 MHz,  $\text{CDCl}_3$ )  $\delta$  0.83 (s, 3 H), 0.98 (s, 3 H), 1.1-1.7 (m), 1.6 (m, 1 H), 2.25 (m, 1 H), 3.61 (ABX system,  $J_{AB} = 10$  Hz,  $J_{AX} = 9.1$  Hz,  $J_{BX} = 6.9$  Hz,  $\delta_A - \delta_B = 0.038$  ppm).

**Tosylate of *endo*-Camphanol (9).** A solution of *endo*-camphanol (8, 3.11 g) and tosyl chloride (4.05 g) in pyridine (9 mL) was left for 12 h at 4 °C. After addition of water, the tosylate 9 was extracted with ether and purified by chromatography of Florisil: mp 39-41 °C (Lit.<sup>28</sup> mp 48-48.5 °C);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 90 MHz)  $\delta$  0.81 (s, 3 H), 0.97 (s, 3 H), 2.17 (1 H), 2.42 (s, 3 H), 4.00 (d,  $J = 7.5$  Hz, 2 H), 7.28 (d,  $J = 7.5$  Hz, 2 H), 7.73 (d,  $J = 7.5$  Hz, 2 H).

**$[\alpha\text{-}^2\text{H}_2]$ Benzyl Camphyl Thioether (12).** A solution of sodium  $[\alpha\text{-}^2\text{H}_2]$ benzenemethanethiolate (14.5 mmol) and *endo*-camphanol tosylate (9, 4.1 g) in methanol (13 mL) and HMPT (4.8 mL) was refluxed for 20 h. After extraction with hexane, the thioether 12 was purified by chromatography on silica gel (150 g) and by HPLC (Lichroprep Si-60). The thioether 12 was obtained as an oil: (2.53 g;  $[\alpha]_D -16.6^\circ$  (c 4.7,  $\text{CHCl}_3$ ; for unlabeled product);  $^1\text{H NMR}$   $\delta$  0.80 (s, 3 H), 0.95 (s, 3 H), 1.24 (4 H), 1.56 (3 H), 1.74 (1 H), 2.25 (1 H), 2.40 (ABX,  $J_{AB} = 12$  Hz,  $J_{AX} = 9.6$  Hz,  $J_{BX} = 5.9$  Hz,  $\delta_A - \delta_B = 0.05$  ppm), 3.70 (s, 2 H, for the unlabeled compound 11), 7.3 (5 H). The deuterium content determined by mass spectroscopy was as follows:  $^2\text{H}_1$ , 2.6%;  $^2\text{H}_2$ ,

97.4%. The mass spectrum on the deuterated compound was as follows:  $m/e$  (relative intensity) 262 (80,  $\text{M}^+$ ), 169 (100), 137 (38), 136 (25). Anal. ( $\text{C}_{17}\text{H}_{24}\text{S}_{24}$ ) C, H.

**Elimination on  $[\alpha\text{-}^2\text{H}_2]$ Benzyl Camphyl Thioether (12).** A solution of  $[\alpha\text{-}^2\text{H}_2]$ benzyl camphyl thioether (12) (460 mg) and TMEDA (0.3 mL) in THF (50 mL) was treated at -20 °C with butyllithium (1 equiv) solution. After 0.5 h, the temperature was raised to 20 °C. After 6 h, cyclodecane (204 mg) was added as an internal standard, water was added, and extraction with pentane was performed, the aqueous phase being acidified. After the mixture was dried over sodium sulfate, the pentane was removed under reduced pressure. The benzyl mercaptan (150 mg) was separated by chromatography on silica gel and transformed into (*R*)-ethyl (benzylthio)phenylacetate (18) as described above. The yield of camphene (83%) was determined by GC with cyclodecane as a standard.

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## Theoretical Study of Borohydride Addition to Formaldehyde. A One-Step, Nonsynchronous Transition State

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Concerted and stepwise pathways for the reduction of  $\text{CH}_2\text{O}$  by  $\text{BH}_4^-$  have been investigated with ab initio calculations by using 3-21G and 6-31G\* basis sets. The transition structure for the one-step process is *not* the traditional [2 + 2] four-center structure involving BH bond breaking simultaneous with CH and BO bond making. Instead, it is best described as a  $\text{BH}_3$  transfer from the already formed CH bond to the oxygen. This transition state lies 30 kcal/mol above the reactants but 5 kcal/mol below the intermediates in the two-step path,  $\text{BH}_3 + \text{CH}_3\text{O}^-$ . When a single water molecule is hydrogen bonded to the formaldehyde oxygen, the calculated activation energy is only 9 kcal/mol. An OH substituent on boron and the presence of a counterion also reduce the barrier substantially.

The reduction of ketones by metal hydrides is one of the most extensively used reactions in synthetic organic chemistry. Nonetheless, in spite of numerous studies spanning 3 decades and involving dozens of research groups, the mechanistic problems implicated in these reactions are not entirely resolved. Evidently, a fuller understanding of the reaction mechanism and its transition state is desirable not only for the satisfaction of intellectual curiosity but also from a synthetic viewpoint as it would allow more accurate prediction of regio- and stereoselectivities in reductions of carbonyl functions belonging to

a variety of chemical and biochemical systems. The nature of the transition state in metal hydride reductions has been a subject of speculation and controversy for more than a quarter of a century. In 1953, Barton<sup>1</sup> pointed out that the reduction of ketones in alicyclic series "in general affords the equatorial epimer if it is hindered or very hindered". At the same time, Cram and Greene<sup>2</sup> suggested that the approach of an attacking group would occur from the least hindered side of the carbonyl function. The variable stereochemical results led Dauben, Fonken, and Noyce<sup>3</sup> to formulation of the two fundamental concepts:

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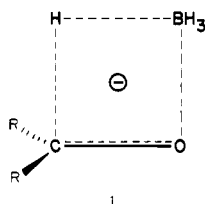
“steric approach control” and “product development control”.

The most commonly accepted interpretation of these concepts is as follows: for the reduction of hindered ketones the transition state is assumed to be reactant-like, and thus the product ratio reflects the ease of approach of the nucleophile to the carbonyl group. Alternately, in unhindered ketones the transition state geometry resembles the product and consequently the stereomeric transition state of lowest energy leads to the major product.

Many investigators objected to the idea of two vastly different transition states for fundamentally similar reactions and maintained the view that all metal hydride reductions<sup>4</sup> have a transition state resembling the reactants in geometry and that the reduction stereochemistry is determined by a combination of several factors such as steric interferences,<sup>5</sup> torsional strain,<sup>6</sup> electrostatic,<sup>7</sup> and antiperiplanar<sup>8</sup> effects in the transition state. On the other hand, certain workers have consistently supported the productlike transition state, at least for borohydride reductions.<sup>9</sup>

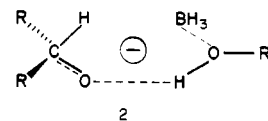
The stereochemical results may be rationalized in a variety of ways, but the origin of regio- and stereoselectivity cannot be completely understood unless one has a clear notion of the reaction mechanism and the geometry of the transition state.

On the basis of experimental results, three reaction mechanisms with quite different transition state geometries have been proposed for the borohydride reduction of ketones;<sup>4b</sup> still different mechanistic pictures were suggested for reductions with  $\text{LiAlH}_4$ .<sup>10</sup> The four-center mechanism 1<sup>11</sup> has been ruled out as a process forbidden



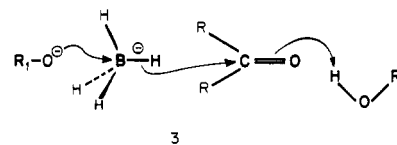
in terms of orbital symmetry<sup>12</sup> and, moreover, as incompatible with the experimental evidence.<sup>13a,b</sup> Wigfield and Gowland have demonstrated that such mechanism is not operative in borohydride reductions carried out in protic

solvents.<sup>13a</sup> However, there is no evidence that the four-center mechanism may not be implicated in borohydride reductions carried out in nonprotic solvents such as tetrahydrofuran or diglyme where the forming alkoxy group is the best receptor for  $\text{BH}_3$ . Moreover, it has been shown<sup>13c</sup> that these reactions are considerably accelerated by irradiation. An alternate cyclic mechanism, 2, which



involves a molecule of protic solvent<sup>14</sup> has also been eliminated by Wigfield<sup>15</sup> on the basis of kinetic results and by Gold<sup>16</sup> on the basis of hydrogen-exchange experiments.

The remaining proposal, “the linear mechanism”,<sup>17</sup> can of course assume a number of different variations depending on the solvent and the definition of the transition state geometry. An acyclic mechanism, 3, comprising



participation of two solvent molecules, is favoured by Wigfield<sup>15</sup> for borohydride reductions in hydroxylic solvents. On the other hand, Gold<sup>16</sup> suggests a two-step process in which  $\text{BH}_3$  is formed as a discrete species before forming a boron-oxygen bond.<sup>16</sup>

In conclusion, although the majority of experimentalists agree as to what the transition state for the borohydride reduction is *not*, there is no consensus as to what it is. A similar lack of accord concerning the nature of the transition state prevails among theoretical chemists.

The stereochemistry of the reaction pathway for nucleophilic addition at a carbonyl group has been inferred from crystal structure data<sup>18</sup> and confirmed by quantum mechanical calculations of simple model systems.<sup>19</sup> The ab initio calculations for the addition of hydride anion to formaldehyde show that, within the bonding distance, as the importance of the orbital interactions increases, the angle of  $\text{H}\cdots\text{C}=\text{O}$  approaches  $110^\circ$  and the central ( $\text{sp}^2$  hybridized) carbon atom becomes tetrahedrally coordinated. This process is accompanied by a rapid drop in energy. There is no transition state. Borohydride reductions lack the simplicity of the hydride addition. By adopting a productlike transition state, Perlberger and Müller,<sup>20</sup> on the basis of molecular mechanics calculations, reproduced rates and isomer distribution ratios in borohydride reductions of 31 ketones studied. At the same time, Wipke and Gund,<sup>21</sup> using a reactant-like transition-state model with a torsion-corrected function, were also able to account for the stereoselectivities of a large number of reductions (both  $\text{NaBH}_4$  and  $\text{LiAlH}_4$ ) although they did

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Table I. Calculated Equilibrium Structures and Total Energies

structure	basis set	total energy, kcal/mol	geometry <sup>a</sup>	ref
H <sub>2</sub> CO ( <i>C</i> <sub>2v</sub> )	3-21G	-113.221 82	<i>R</i> (CO) = 1.207, <i>R</i> (CH) = 1.083, <HCO = 122.5	28
	6-31G*	-113.866 33	<i>R</i> (CO) = 1.184, <i>R</i> (CH) = 1.092, <HCO = 122.1	19, 29
H <sub>3</sub> CO <sup>-</sup> ( <i>C</i> <sub>3v</sub> )	3-21G	-113.724 80	<i>R</i> (CO) = 1.348, <i>R</i> (CH) = 1.134, <HCO = 117.3	
	6-31G*	-114.384 47	<i>R</i> (CO) = 1.312, <i>R</i> (CH) = 1.133, <HCO = 116.5	
BH <sub>3</sub> ( <i>D</i> <sub>3h</sub> )	3-21G	-26.237 30	<i>R</i> (BH) = 1.188	30
	6-31G*	-26.390 01	<i>R</i> (BH) = 1.188	
BH <sub>4</sub> <sup>-</sup> ( <i>T</i> <sub>d</sub> )	3-21G	-26.812 95	<i>R</i> (BH) = 1.241	31
	6-31G*	-26.965 10	<i>R</i> (BH) = 1.243	
CH <sub>3</sub> OBH <sub>3</sub> <sup>-</sup> ( <i>C</i> <sub>s</sub> , all staggered)	3-21G	-140.113 59	<i>R</i> (CO) = 1.408, <i>R</i> (BO) = 1.516, <COB = 115.9, <i>R</i> (CH <sub>1</sub> ) = 1.092, <i>R</i> (CH <sub>2</sub> ) = <i>R</i> (CH <sub>3</sub> ) = 1.094, <i>R</i> (BH <sub>1</sub> ) = 1.234, <i>R</i> (BH <sub>2</sub> ) = <i>R</i> (BH <sub>3</sub> ) = 1.251, <OCH <sub>1</sub> = 109.6, <OCH <sub>2</sub> = <OCH <sub>3</sub> = 112.9, <OBH <sub>4</sub> = 108.3, <OBH <sub>5</sub> = <OBH <sub>6</sub> = 111.5, <H <sub>2</sub> CH <sub>3</sub> = 106.2 <H <sub>3</sub> BH <sub>6</sub> = 107.3	
	6-31G*	-140.889 686	<i>b</i>	

<sup>a</sup> Distances (*R*) are in angstroms and angles in degrees. <sup>b</sup> 3-21G optimized geometry used.

not fare equally well in correlating rate factors.

Recently, Dewar and McKee<sup>22</sup> carried out the standard MNDO calculations for the reaction of borohydride with (1) formaldehyde and (2) methyl formate. The authors concluded that the reaction "takes place in two distinct steps, by an initial complete transfer of hydride to form a borane and an alkoxide ion"<sup>22</sup> followed by the formation of the boron-oxygen bond.<sup>22</sup>

In this paper we present a series of *ab initio* calculations carried out in order to examine equilibrium geometries and to search for the transition structures involved in the addition of borohydride anion to formaldehyde. We also report a preliminary study of the effects of a protic solvent on the course of the above reaction.

### Methods

*Ab initio* molecular orbital calculations were performed with the GAUSSIAN 80<sup>23</sup> series of programs on the Amdahl 470-V/6 at Wayne State University by using the 3-21G<sup>24</sup> and 6-31G\*<sup>25</sup> basis sets. Energies were calculated at the SCF level. Equilibrium geometries and transition structures were optimized by using a gradient procedure. Unless otherwise stated, the structures reported have been fully optimized within the indicated symmetry at the 3-21G basis. All two-heavy-atom molecules were also optimized at the 6-31G\* level, which contains *d* orbitals on all first-row atoms. For three-heavy-atom structures only single point calculations with the 6-31G\* basis were possible (performed at the 3-21G-optimized geometry).

### Results and Discussion

The addition of borohydride to formaldehyde can in principle follow a number of different reaction pathways, as illustrated in Figure 1. The final product, CH<sub>3</sub>OBH<sub>3</sub><sup>-</sup>, can be reached via one-step addition (path 1), a two-step process with borane and methoxy anion as intermediates (path 2 and 3), or a three-step sequence involving hydride ion (paths 4, 5 and then 3). Due to the high energy of the hydride ion, the three-step route is undoubtedly the least favored. Using the semiempirical MNDO method, Dewar and McKee<sup>22</sup> have shown the two-step process to be the lowest energy pathway. Their detailed search did not yield

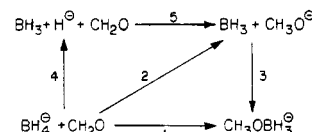
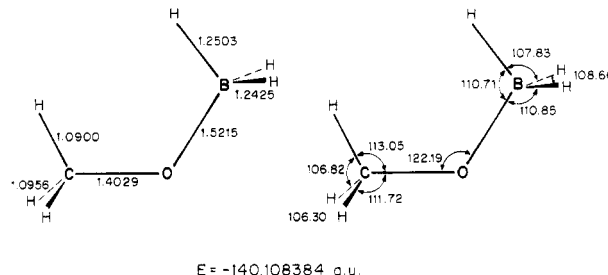


Figure 1. Possible reaction pathways for the addition of borohydride to formaldehyde, indicating one-, two-, and three-step mechanisms.

a transition structure for a one-step mechanism, despite precedents for a concerted transition state in [2 + 2] additions.<sup>26,27</sup> Calculated equilibrium geometries and total energies for the structures in Figure 1 are presented in Table I. The optimized geometries compare well with the experimental data and calculated values reported in literature.<sup>19,28-31</sup> The 3-21G-determined structures are nearly identical with the 6-31G\* results, with the exception of a ca. 0.03-Å shortening in the CO bond length. For the final product, CH<sub>3</sub>OBH<sub>3</sub><sup>-</sup>, the all-eclipsed conformation 4 and the all-staggered conformation 5 were calculated. The



latter was found to be more stable by 3.3 kcal/mol. Such a difference in energy between these two rotamers is small enough to assume free rotation about C-O and B-O bonds. Thus it is evident that internal rotation will not affect

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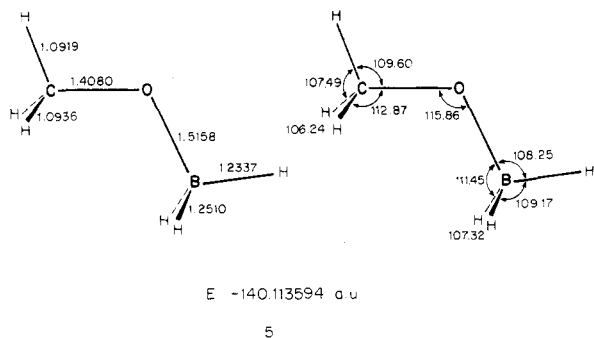
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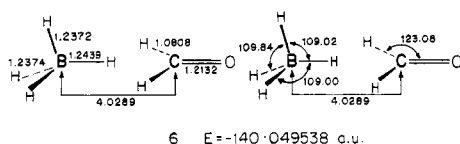
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significantly the energetics of the reaction path.

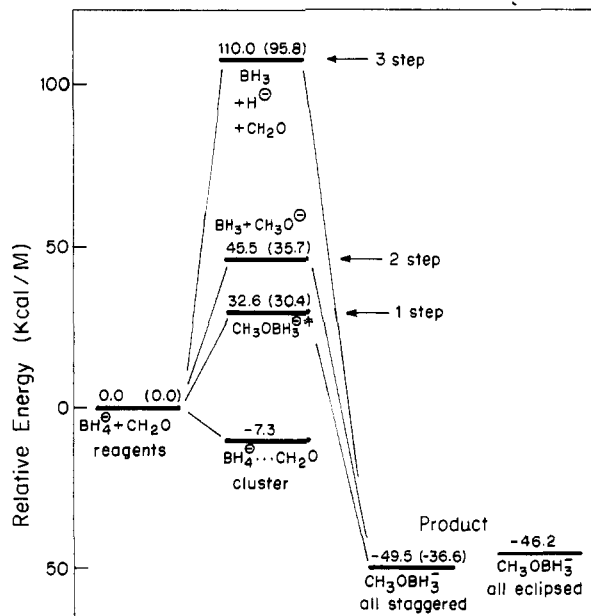
The energetics of the possible reaction mechanisms are displayed in Figure 2. The various theoretical calculations agree that the overall reaction is strongly exothermic (-28.0 kcal/mol, semiempirical MNDO; -49.5 kcal/mol, 3-21G, ab initio; -36.6 kcal/mol, 6-31G\*, ab initio). As suggested above, the three-step pathway is most unfavorable, requiring 110.0 kcal/mol at the 3-21G or 95.8 kcal/mol at the 6-31G\* level. The borane plus methoxide system is calculated with the 3-21G basis set to be 45.5 kcal/mol higher in energy than the borohydride plus formaldehyde system. A somewhat smaller difference of 35.7 kcal/mol is found with the more accurate 6-31G\* basis set. The ab initio results bracket the activation energy for the two-step process (40.8 kcal/mol) obtained by semiempirical MNDO calculations.<sup>22</sup> The determination of the barrier for the one-step mechanism requires a more detailed exploration of the full energy surface of  $\text{CH}_3\text{OBH}_3^-$  and is discussed below.

**Energy Surface for the  $\text{BH}_4^- + \text{CH}_2\text{O}$  Reaction.** In a study of hydride attack at formaldehyde, Bürgi, Lehn, and Wipff<sup>19</sup> have shown that at distances larger than 3 Å the hydride approaches the  $\text{CH}_2\text{O}$  molecule in the molecular plane, along the C-O axis. Borohydride follows the same line of maximum electrostatic attraction toward the carbonyl function, with a 9.3 kcal/mol minimum at a C...H distance of 2.785 Å (3-21G basis). The components of the  $\text{BH}_4^- \cdots \text{CH}_2\text{O}$  cluster, 6, show very little distortion from their monomer geometries.



At distances less than 3 Å, hydride ion approaches the carbon atom of the carbonyl group with an H-C-O angle of ca. 110°, and the energy of the systems drops constantly along the reaction path. A map of the analogous portion of the energy surface for borohydride addition to formaldehyde, at the semiempirical level, shows a steady increase in energy from  $\text{BH}_4^- + \text{CH}_2\text{O}$  to  $\text{BH}_3 + \text{CH}_3\text{O}^-$ . The reaction path for the hydride transfer is not specified.<sup>22</sup> Our ab initio calculations of several points on a linear synchronous transit pathway for hydride transfer ( $\text{B} \cdots \text{O}$  distance fixed at 3.4 Å) indicate also a monotonic increase in energy along this route.

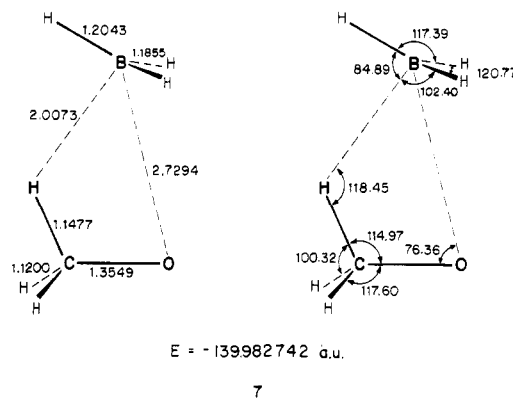
Since no steric strain should appear in the process of creating of the B-O link in  $\text{CH}_3\text{OBH}_3^-$  for the two-step mechanism, the formation of free  $\text{CH}_3\text{O}^-$  and  $\text{BH}_3$  constitutes the transition state for the borohydride reduction of formaldehyde. Nonetheless, there is an ample reason to expect the existence of a concerted transition structure. Williams, Maggiora, and Schowen<sup>26</sup> have shown that the formally analogous [2 + 2] (uncatalyzed) addition of water to formaldehyde proceeds exclusively through four-center



**Figure 2.** Energy diagram for the possible reaction pathways for borohydride addition to formaldehyde. Activation energies for the one-step, two-step, and three-step mechanisms are indicated for the 3-21G basis set. Values for the 6-31G\* basis set are given in parentheses.

transition state. A concerted transition structure has also been located for the addition of borane to acetone and ketene.<sup>22</sup> Alternately, it can be argued that infinitely separated  $\text{BH}_3$  and  $\text{CH}_3\text{O}^-$  cannot represent the lowest transition state, since attraction between electron-deficient  $\text{BH}_3$  and the anion will lower the energy when the two species are brought closer together.

Since previous studies indicated that a concerted transition structure for borohydride addition might be difficult to find, our search proceeded in two phases: a constrained optimization to delimit the region of the energy surface that might contain the desired transition structure and a full optimization to define precisely the geometry of the saddle point (7).



The geometry of this transition structure 7 is far removed from the idealized four-center transition state in which CH and BO bond formation is synchronized with BH cleavage. The carbon atom is  $\text{sp}^3$  hybridized (the HCO angle is 114.97°), and the new CH bond is fully formed (1.148 Å), with the CO bond approaching the length of the carbon-oxygen link in the methoxyanion. The  $\text{BH}_3$  is nearly flat with the short B-H bonds and the plane of the molecule almost perpendicular to the direction of the breaking BH link. The former BH bond is almost completely broken (2.01 Å), but the new BO bond is not yet formed. In effect we have a loose asymmetric structure

Table II. Effect of Substituents and Solvent on Borohydride Reductions<sup>a</sup>

no.	reaction	$\Delta E$ , kcal/mol	
		3-21G basis	6-31G* basis
1	$\text{BH}_4^- + \text{H}_2\text{CO} \rightarrow \text{BH}_3 + \text{H}_3\text{CO}^-$	45.6	35.7
2	$\text{BH}_4^- + \text{HCOOH} \rightarrow \text{BH}_3 + \text{HOCHO}^-$	45.2	39.7 <sup>c</sup>
3	$\text{BH}_3\text{OH}^- + \text{H}_2\text{CO} \rightarrow \text{BH}_2\text{OH} + \text{CH}_3\text{O}^-$	20.5	12.4
4	$\text{BH}_4^- \cdot \text{H}_2\text{O} + \text{H}_2\text{CO} \rightarrow \text{BH}_3 \cdot \text{H}_2\text{O} + \text{H}_3\text{CO}^-$	30.6	39.7
5	$\text{BH}_4^- + \text{H}_2\text{CO} \cdot \text{H}_2\text{O} \rightarrow \text{BH}_3 + \text{H}_3\text{CO}^- \cdot \text{H}_2\text{O}$	19.7 <sup>b</sup>	16.6 <sup>c</sup>
6	$\text{BH}_4^- \cdot \text{H}_2\text{O} + \text{H}_2\text{CO} \cdot \text{H}_2\text{O} \rightarrow \text{BH}_3 \cdot \text{H}_2\text{O} + \text{CH}_3\text{O}^- \cdot \text{H}_2\text{O}$	4.7 <sup>d</sup>	20.6 <sup>c</sup>
7	$\text{BH}_4^- \cdot \text{Na}^+ + \text{H}_2\text{CO} \rightarrow \text{BH}_3 + \text{H}_3\text{CO}^- \cdot \text{Na}^+$	-1.2	
8	$\text{AlH}_4^- + \text{H}_2\text{CO} \rightarrow \text{AlH}_3 + \text{H}_3\text{CO}^-$	56.7	

<sup>a</sup> All molecules were fully optimized with both basis sets unless otherwise indicated. <sup>b</sup> Water frozen at 3-21G monomer geometry and hydrogen bond constrained to be linear. <sup>c</sup> 6-31G\* energies of the three heavy-atom molecules' computed 3-21G-optimized geometries. <sup>d</sup> From no. 4 and 5.

which may be described as the transfer of  $\text{BH}_3$  from the hydride to the oxygen atom. Indeed, according to the Mulliken overlap population, at this point the interaction of borane with H is already repulsive, while its interaction with oxygen is weakly attractive.

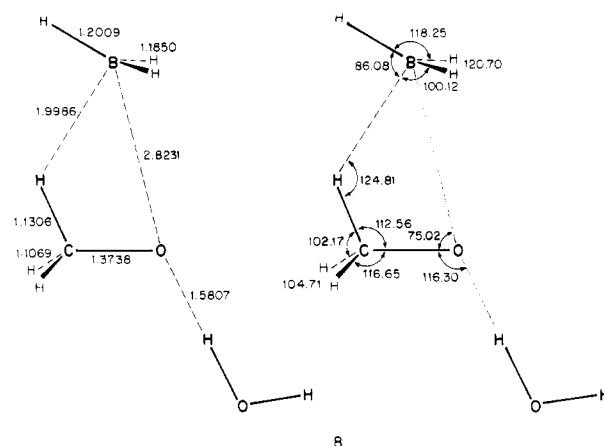
**Substituent Effects.** Although the one-step mechanism possesses the lowest energy transition state, it is useful to know the energy of the two-step process as it represents an upper limit for the barrier in borohydride addition. Since only the energy of equilibrium structures is required for the two-step mechanism, the consideration of upper limits for analogous reactions allows comparison of the trends in energy for such processes without the tedious search for transition states.

A survey of substituent and solvent effects on the energy of the two-step process are presented in Table II. For comparison, the  $\text{AlH}_4^-$  reduction is included. We should keep in mind that the comparison between model calculations in the gas phase and experimental results in solutions should be made very cautiously. The calculated activation energies for the two-step process for the borohydride addition to formaldehyde and formic acid (used as a model for methylformate) are nearly equal, which is in agreement with earlier semiempirical results obtained for formaldehyde and methyl formate.<sup>22</sup> Alkoxyborohydrides are more reactive than  $\text{BH}_4^-$ . This trend is reproduced by our calculations. The upper limit to the transition structure energy for  $\text{BH}_3\text{O}^-$  addition to formaldehyde (20.5 kcal/mol, 3-21G; 12.4 kcal/mol, 6-31G\*) is significantly lower than the calculated one step barrier for  $\text{BH}_4^-$  addition (32.6 kcal/mol, 3-21G; 30.4 kcal/mol, 6-31G\*). The decrease in the barrier height is due primarily to the stabilization of  $\text{BH}_2\text{OH}$  relative to  $\text{BH}_3$  by the donation of  $\pi$  electrons from the hydroxy substituent into the empty orbital of the boron atom.

**Solvent Effects.** Until now we have been considering the addition of an isolated borohydride molecule to an isolated molecule of formaldehyde as if the reaction were occurring in a gas phase. To investigate the catalytic influence of a protic solvent, we have examined the effect of a single water molecule on the addition reaction. The calculation results, listed in Table II, indicate that the interaction of water with boron lowers the two-step barrier to 30.6 kcal/mol (from 45.6 kcal/mol) at the 3-21G level. Such a drop in energy is somewhat misleading, since the 3-21G basis set overestimates the stability of the  $\text{BH}_3 \cdot \text{H}_2\text{O}$  complex.<sup>32</sup> Calculations at the 6-31G\* level indicate a net increase in the heights of the barrier for water-boron compound interactions. When a water molecule is hydrogen bonded to the oxygen atom of formaldehyde

molecule, the activation energy of the two-step process decreases dramatically (19.7 kcal/mol, 3-21G; 16.6 kcal/mol, 6-31G\*). This is due chiefly to the strong anionic hydrogen bond in the water-methoxide complex.

Since the energy value in Table II represents an upper limit to the transition-state energy, the effect of a water molecule hydrogen bonded to the oxygen atom in the transition structure was explored further. A full optimization at the 3-21G level<sup>33</sup> by starting from a previously calculated geometry for the transition structure 7, to which, in this case, a molecule of water was hydrogen bonded, yielded a transition structure, 8, with an activation energy

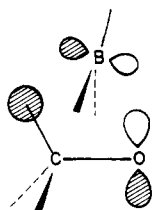


of only 9.1 kcal/mol. The principal difference between 8 and 7 is in the slightly larger CHB angle. However, the central carbon atom remains tetrahedrally coordinated. In effect, addition of a water molecule influences the geometry of the transition state only marginally but results in lowering the activation energy from 32.6 to 9.1 kcal/mol. The overall reaction is more exothermic than the noncatalyzed process (-63.5 vs. -40.5 kcal/mol) principally due to the stabilization of the  $\text{CH}_3\text{OBH}_3^-$  product by a hydrogen-bonded molecule of water. Thus the former highly unfavorable process becomes feasible upon addition of even one molecule of water. This conclusion is confirmed by gas-phase ICR studies of solvation effects on carbonyl substitution reactions, which have demonstrated that a single solvent molecule can dramatically decrease the energy of tetrahedral anionic intermediates.<sup>34</sup> Although interference of one molecule of water does not represent the whole stabilizing effect of the solvent, there is evidence

(32) Dill, J. D.; Schleyer, P. v. R.; Pople, J. A. *J. Am. Chem. Soc.* **1975**, *97*, 3402.

(33) The structure was fully optimized except for the  $\text{H}_2\text{O}$  geometry being frozen at the monomer geometry and the hydrogen bond being fixed linear. The structural parameters used for the  $\text{H}_2\text{O}$  molecule were as follows: H-O bond length, 0.9660 Å; HOH bond angle, 107.65°.

(34) Fukuda, E. K.; McIver, R. T., Jr. *J. Am. Chem. Soc.* **1979**, *101*, 2498.



**Figure 3.** Orbitals involved in a  $\text{BH}_3$  shift from the hydride to the oxygen atom.

that the interaction with one molecule of solvent reflects the major trend of the total solvent effect.<sup>35</sup>

It is important to point out here that the solvent can play another role than the simple stabilization effect. The reaction carried out in a hydroxylic solvent may follow an entirely different mechanistic route than the reaction in a nonprotic solvent. It has been suggested by Wigfield that the protic solvent may be involved in the mechanism in a complex fashion.<sup>13d</sup> He has shown<sup>13a</sup> that the neutral borane moiety does not transfer to the alkoxy group being formed but to the alkoxy anion originating from the solvent (see mechanism 3). Due to computational complexities and costs we have not considered such a system. As a result, our calculations including one solvent molecule cannot tell us much about the mechanism of the reaction in protic solvent but only show the net effect of such association on the heights of the energy barrier. On the other hand, our study may be relevant to the reactions occurring in nonprotic solvents, where the stabilizing factor is the counterion and where the alkoxy group being formed is the best receptor for  $\text{BH}_3$ .

### Conclusion

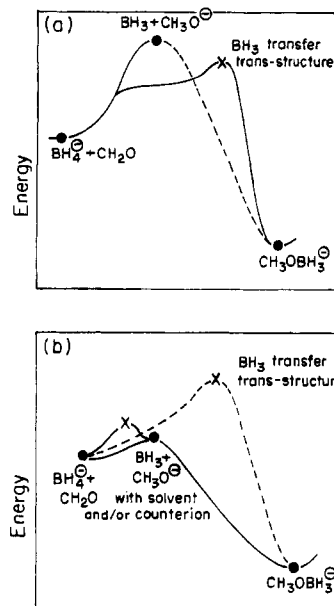
The results reported here demonstrate that borohydride addition to formaldehyde proceeds via a single-step mechanism with a nonsynchronous four-center transition state with a productlike geometry. The net reaction is exothermic; however, as the activation energy is high (32.1 kcal/mol), it is unlikely to occur. Upon the addition of a solvent molecule, the energy barrier is lowered by 20 kcal/mol, making the reaction quite feasible. The highly exothermic reaction with a productlike transition state is difficult to visualize in terms of the Hammond postulate.

We suggest that these apparent contradictions result from the fact that the observed reaction is actually a superposition of two reactions: (a) hydride transfer from  $\text{BH}_4^-$  to formaldehyde and (b) a  $\text{BH}_3$  shift from the hydride to the carbonyl oxygen atom.

The first reaction requires a large activation energy necessary to form the highly unfavorable tetrahedral intermediate. This process depends on the nature of the incipient nucleophile and it can be modified by the presence of a cation and/or solvent that is capable of stabilizing the intermediate being formed. Williams, Maggiora, and Schowen have reached a similar conclusion in studying addition of  $\text{H}_2\text{O}$ ,  $\text{NH}_3$ , and  $\text{OH}^-$  to formaldehyde.

The second reaction,  $\text{BH}_3$  transfer, is less sensitive to external perturbation around the alkoxyanion. This process is a [1,3]sigmatropic shift involving the HOMO of methoxy anion and the LUMO of borane. Formally, the transfer can occur with continuous conservation of bonding accompanied by inversion of configuration at the borane atom (Figure 3).

(35) It has been shown experimentally that one molecule of solvent may reproduce the major part of the total solvation effect. Bromilow, J.; Abboud, J. L. M.; Lebrilla, C. G.; Taft, R. W.; Scorrano, G.; Lucchini, V. *J. Am. Chem. Soc.* 1981, 103, 5448.



**Figure 4.** Proposed energy profiles for (a) uncatalyzed and (b) catalyzed borohydride addition to formaldehyde.

The calculated geometry of the transition structure suggests that 1,3-shift of  $\text{BH}_3$  occurs with retention of configuration. The inversion pathway may be disfavored by repulsive interactions between the CO bond and the two straddling BH bonds, preventing the  $\text{BH}_3$  from approaching close enough for good HOMO-LUMO overlap.

A superposition of the hydride-transfer and borane-shift pathways is illustrated in Figure 4. In the noncatalyzed case, the production of distinct  $\text{BH}_3$  and  $\text{CH}_3\text{O}^-$  species is too high in energy. Thus, a 1,3-shift of borane occurs before the molecules are fully separated. A single molecule of protic solvent lowers the borane-shift transition state, 8, as well as the energy of separated  $\text{BH}_3$  and  $\text{CH}_3\text{O}^-$  (Table II). Several molecules of water would lower the energy of the intermediates even further, perhaps below the 1,3-shift barrier (Figure 4b). In such a case, the  $\text{BH}_3$ -shift transition structure may no longer exist, since it would be unstable toward dissociation.

Depending on the nature of the solvent interaction, the hydride-transfer step may or may not involve a barrier.

The effect of a counterion is even stronger than the effect of a water molecule (Table II). A sodium ion stabilizes the intermediates (1–1.2 kcal/mol at the 3-21G level) with respect to the reactants. This model is in agreement with the experimental findings<sup>36</sup> showing a promotion of borohydride reduction in the presence of cation. Further calculations of the counterion and more extensive solvent effects on the geometry of the transition structure are necessary for a better understanding of the reaction.

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**Registry No.**  $\text{H}_2\text{CO}^-$ , 3315-60-4;  $\text{CH}_3\text{OBH}_3^-$ , 54809-85-7;  $\text{BH}_4^-$ , 16971-29-2;  $\text{H}_2\text{CO}$ , 50-00-0;  $\text{HCOOH}$ , 64-18-6;  $\text{BH}_3\text{OH}^-$ , 24492-48-6;  $\text{BH}_4^-\text{Na}^+$ , 16940-66-2;  $\text{AlH}_4^-$ , 19469-81-9.

(36) Pierre, J. L.; Handel, H. *Tetrahedron Lett.* 1977, 2317.