

# Formation of $\beta$ -Lactones through Lewis Acid-Promoted [2 + 2] Cycloaddition Reaction. A Theoretical Study

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**Abstract:** The formation of  $\beta$ -lactone through Lewis acid-promoted [2 + 2] cycloaddition is studied using semiempirical (AM1/RHF and AM1/CI) and *ab initio* (HF/6-31G\* and MP2/6-31G\*) calculations. After a preliminary semiempirical study of the BF<sub>3</sub>-catalyzed parent reaction through two distinct reaction paths, *ab initio* and/or semiempirical studies on solvent and Lewis acid (BH<sub>3</sub> and BF<sub>3</sub>) effects concentrate on the mechanism involving the prior formation of the C–C bond. At the HF/6-31G\* level of theory the introduction of BF<sub>3</sub> induces a reduction of the activation energy from 40.8 to 11.9 kcal/mol, and calculations performed with AM1/COSMO showed that the introduction of a solvent results in the formation of an earlier transition state. The case of BH<sub>3</sub> is somehow more complicated since the studied system induces, both at the semiempirical and *ab initio* levels, a hydride transfer leading to a very stable product.

## Introduction

The chemistry of  $\beta$ -lactone has advanced by leaps and bounds over the last 15 years.<sup>1</sup> One reason is the discovery of several natural  $\beta$ -lactones with very interesting biological activities.<sup>2</sup> This has therefore attracted much attention on the preparation of this moiety and, consequently, on its use as a synthetic intermediate. Among the preparation methods of  $\beta$ -lactones, the [2 + 2] cycloaddition reaction between a ketene and a carbonyl compound is a well established one. It was first reported by Staudinger at the beginning of the century<sup>3</sup> and was granted a second lease of life in 1975<sup>4</sup> when Zaitseva introduced the use of silylketenes and Lewis acids in such reactions. Since then, silylketenes have been widely used to prepare  $\beta$ -lactones; particularly, highly stereoselective examples<sup>5</sup> and natural products syntheses<sup>6</sup> were reported. However, the study of the mechanism of this reaction has attracted little experimental attention.<sup>7</sup> Theoretical studies, unlike those devoted to the

formation of cyclobutanones,<sup>8</sup> and more recently  $\beta$ -lactams,<sup>9</sup> by [2 + 2] cycloaddition reactions, are also rare.<sup>10</sup> As part of our interest in  $\beta$ -lactone and silylketene chemistry,<sup>1b,2,6</sup> we have also undertaken a theoretical study of the reaction. In our preliminary communication,<sup>11</sup> we reported results on the parent reaction. According to our semiempirical calculations, that were performed at the RHF level and with configuration interaction (C.I.), the formation of oxetanone **3**, from formaldehyde **1** and ketene **2**, can occur through two different paths (Scheme 1) (despite a careful search, no synchronous path was found): Mechanism A, which involves the preliminary formation of the C<sub>4</sub>–C<sub>5</sub> bond, is a concerted, but asynchronous, closed-shell mechanism. The approach between the two reactants is synperiplanar and the activation energy is of 38 kcal/mol (AM1/RHF). Mechanism B, which involves the preferential formation of the O<sub>3</sub>–C<sub>2</sub> bond, is a stepwise process with significant biradical character. The approach between the two reactants is antiperiplanar, and the activation energy is of 32 kcal/mol (AM1/C.I.).

Given the importance of Lewis acids in organic synthesis in general<sup>12</sup> and in this reaction in particular, we then decided to

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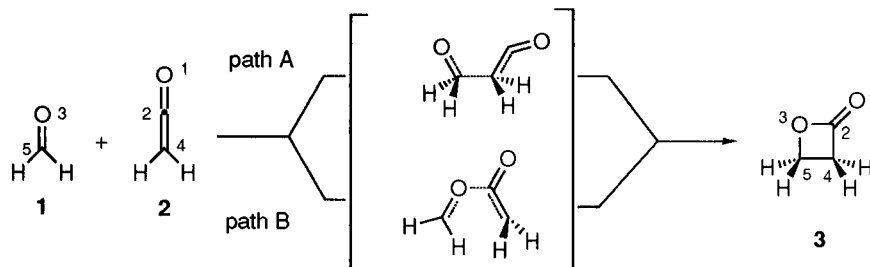
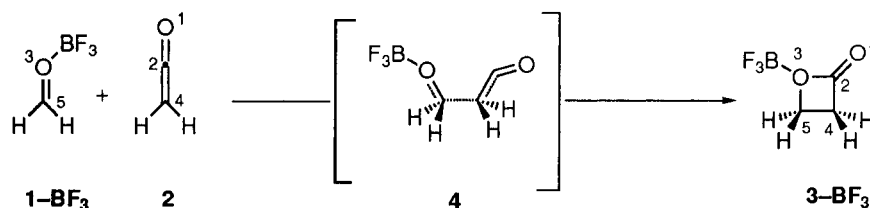
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**Scheme 1.** Two Reaction Paths toward  $\beta$ -lactone **3**: Mechanism A vs Mechanism B<sup>11</sup>**Scheme 2.** Formation of  $\beta$ -Lactone **3-BF<sub>3</sub>** through Mechanism A

study the effect of a Lewis acid on the reaction path. Although the association of Lewis acids with carbonyl compounds was studied from a theoretical point of view for many years,<sup>13</sup> their role in a dynamic process, i.e., along a reaction path, has only been tackled fairly recently.<sup>14</sup> Although  $\text{BH}_3$  is commonly used as a model Lewis acid in calculations,<sup>14a-h</sup> we thought that  $\text{BF}_3$ , which is less studied from a theoretical point of view<sup>14i</sup> but commonly used at the bench in many reactions including the studied one,<sup>4-6</sup> would be a better model.<sup>15</sup> While this work was in progress, Cossio *et al.* reported, in two important papers, *ab initio* calculations on catalyst ( $\text{BH}_3$ ), substituents, and solvent ( $\text{CH}_2\text{Cl}_2$ ) effects on the reaction between ketene (or chloro-ketene) and formaldehyde (or acetaldehyde).<sup>10c,d</sup> They showed that the introduction of  $\text{BH}_3$  induces a significant diminution of the activation energy of the reaction from 40.8 to 14.3 kcal/mol (HF/6-31G\*); in both cases, the reaction is concerted but with a stronger asynchronous character, in favor of the preliminary formation of the C-C bond, in the presence of  $\text{BH}_3$ . Solvent (dichloromethane) effect, calculated with the Onsager SCRF model, induced a diminution of the activation energy from 14.3 to 11.6 kcal/mol when calculated at the HF/6-31G\* level and from 3.1 to 1.1 kcal/mol when calculated at the MP2/6-31G\*. These papers prompted us to disclose our own results, based on *ab initio* and semiempirical calculations, on the Lewis acid-catalyzed reaction. *We discuss particularly the respective effect of  $\text{BH}_3$  and  $\text{BF}_3$  on the reaction path.*

**Methodology**

All calculations reported in this work were performed using either the semiempirical AM1 method (RHF/AM1 and AM1/CI)<sup>16</sup> available in the AMPAC program<sup>17</sup> or the GAUSSIAN 94<sup>18</sup> package with the 6-31G\* (HF/6-31G\* and MP2/6-31G\*) basis set. AM1/CI calculations were run with the following key words: OPEN (2,2) and C.I.=8. All transition states showed only one negative eigenvalue in their diagonalized force constant matrices. Along with *ab initio* studies, the AM1 method was chosen mainly for three reasons: (a) its reliability compared to *ab initio* calculations (at least for these systems), (b) the reasonably short calculation times which enabled us to perform IRC from every transition state we found, and (c) our desire to tackle, in the future, more complex structures, close to those involved in experimental work, a task which can only be achieved with a semiempirical method. Solvent effects were tackled at the semiempirical level (AM1) with the COSMO<sup>19</sup> option recently available in the AMPAC program. Finally, the simulated annealing,<sup>20</sup> available in the AMPAC program, provides a very efficient tool for a systematic multiple-minima search and enabled us to check all our semiempirical calculations.

**Results and Discussion**

**(1) The  $\text{BF}_3$ -Catalyzed Reaction between Ketene and Formaldehyde, Mechanism A vs Mechanism B: An AM1 Study.** As for the study of the uncatalyzed reaction,<sup>11</sup> we have studied the reaction path of both mechanisms A and B. In mechanism A, we have associated  $\text{BF}_3$  to formaldehyde **1**, inducing therefore an electrophilic activation of the aldehyde (Scheme 2 and Figure 1), while in mechanism B, we have associated  $\text{BF}_3$  to ketene **2** (Scheme 3 and Figure 2).

Not surprisingly,  $\text{BF}_3$  induces a significant reduction of the activation energy which falls to 14.2 kcal/mol (AM1/RHF). The reaction keeps, however, its zwitterionic character illustrated by a significant separation of net atomic charges on  $\text{C}_2$  and  $\text{O}_3$  (Table 1). Imaginary frequency of transition state **4a** was assumed to be  $-431.3 \text{ cm}^{-1}$ . Calculations performed with C.I. further confirmed the closed-shell nature of the reaction since

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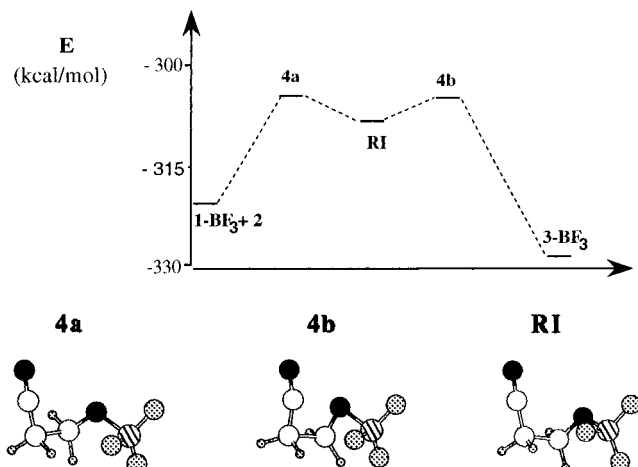
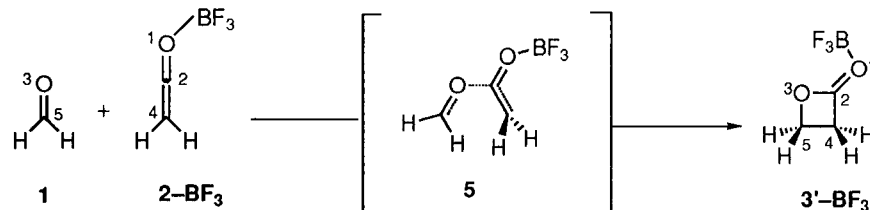
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**Scheme 3.** Formation of  $\beta$ -Lactone  $3'$ -BF<sub>3</sub> through Mechanism B

**Figure 1.** Formation of  $\beta$ -lactone  $3$ -BF<sub>3</sub> through mechanism A. Structures of transition states **4a** and **4b** and intermediate **RI** (AM1/RHF).

energy values for transition states **4a** (−307.6 kcal/mol) and **4b** (−307.1 kcal/mol) were very similar to those obtained at the RHF level (Table 1). Moreover, the contribution of the ground state configuration was calculated to be 99% for both **4a** and **4b**. Apart from the activation energy, the only other noticeable difference with the uncatalyzed reaction is the existence of a reaction intermediate **RI**. However both its geometry and energy value are very close to those found for the two transition states, **4a** and **4b**, of the reaction path (Table 1).

As for the uncatalyzed reaction, the BF<sub>3</sub>-promoted formation of the  $\beta$ -lactone through mechanism B is an open-shell process. All semiempirical calculations were therefore performed with C.I. The main point is that the introduction of the Lewis acid does not induce an important diminution of the activation energy of the reaction; indeed, it only diminishes from 32 to 24 kcal/mol. Aside from that, the mechanism remains a stepwise one, and the approach is still antiperiplanar. The first transition state **5a**, corresponding to the creation of the O<sub>3</sub>–C<sub>2</sub> bond, is the highest transition state; it is followed by **5b**, associated to the rotation around the new O<sub>3</sub>–C<sub>2</sub> bond, **5c**, and **5d** which leads to the product through a conrotatory electrocyclozation.

It appears from this study that the introduction of BF<sub>3</sub> has a much greater effect on the activation energy of mechanism A (from 38 to 14 kcal/mol) compared to this effect on mechanism B (from 32 to 24 kcal/mol). The fact that a polar mechanism should be more sensitive than a radical mechanism to the introduction of a Lewis acid seems reasonable; nevertheless, Lewis acid promoted radical reactions do exist.<sup>21</sup> As a result of this contrasted effect of BF<sub>3</sub>, mechanism A, involving a nucleophilic ketene attacking an activated electrophilic aldehyde, becomes the likeliest one. Moreover, the difference in

favour of mechanism A is probably even greater due to the well-known tendency of semiempirical methods to overestimate the stability of biradicals.<sup>22</sup> Finally, this finding is in good agreement with independent experimental results (diastereoselectivity of the reaction) of our own<sup>6b</sup> and of Romo<sup>23</sup> on silyl ketenes. We have therefore concentrated our study on solvent and Lewis acid effects on mechanism A (which is also the one that Cossio has studied in his *ab initio* study of the BH<sub>3</sub>-catalyzed reaction<sup>10c,d</sup>).

**(2) BF<sub>3</sub>-Catalyzed Reaction between Ketene and Form-aldehyde (Mechanism A): An *ab Initio* Study and a Semiempirical (AM1/COSMO) Solvent Effect Study.** *Ab initio* calculations conducted at the HF/6-31G\* level for transition state **4a** confirmed the AM1/RHF calculations (Table 3). Indeed, the activation energy was found to be of 11.9 kcal/mol (AM1: 14.2 kcal/mol) and  $d_{O_3-C_2}$  to be of 2.978 Å (AM1: 2.825 Å). However,  $d_{C_4-C_5}$ , 2.016 Å instead of 1.720 Å (AM1), and the dihedral angle O<sub>3</sub>C<sub>5</sub>C<sub>4</sub>C<sub>2</sub>, 57.0° instead of 43.1° (AM1), are greater. Finally, the imaginary frequency of **4a** was calculated to be −314.1 cm<sup>−1</sup>. When calculated at the MP2/6-31G\* level, with optimization of the geometry, activation energy fell to 3.6 kcal/mol. Such a difference between HF and MP2 calculations is very similar to the one reported by Cossio in his study of the BH<sub>3</sub>-catalyzed reaction: 14.3 vs 3.1 kcal/mol.<sup>10c,d</sup>

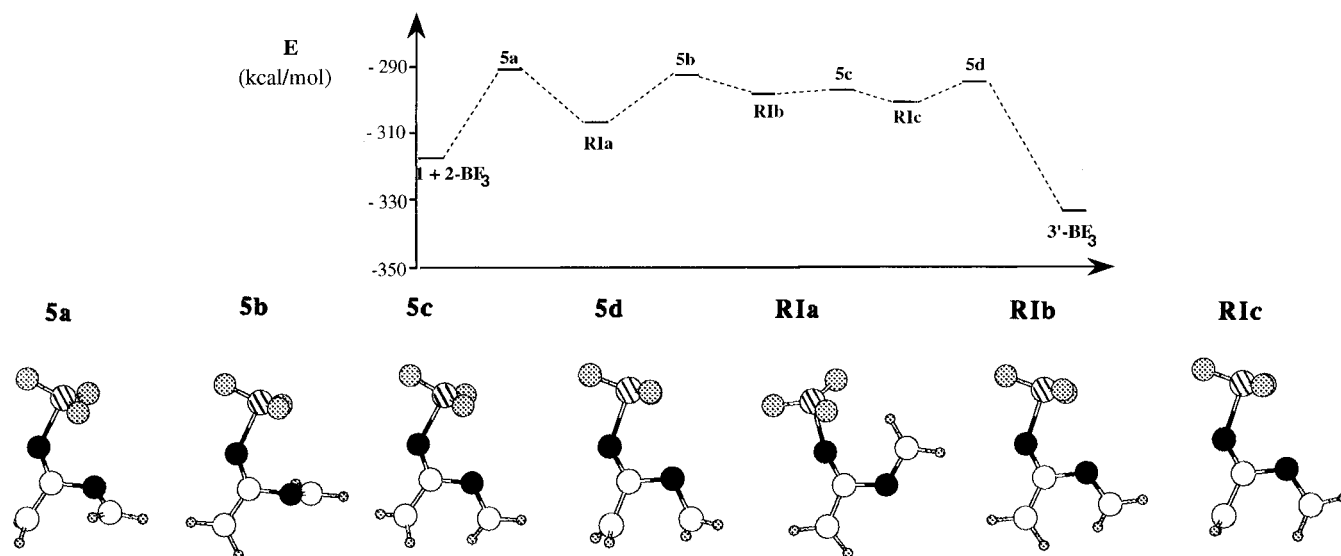
Solvent effects were calculated at the semiempirical (AM1) level of theory with the COSMO option which allows the analytic calculation of energy gradient and Hessian and is therefore very accurate for the geometry optimization of critical points.<sup>19</sup> It appears that in all three cases studied, diethyl ether, dichloromethane, and toluene, the activation energy is lower. Indeed, in each case transition state is earlier as indicated by the greater values for  $d_{C_4-C_5}$ ,  $d_{C_2-O_3}$ , and O<sub>3</sub>C<sub>5</sub>C<sub>4</sub>C<sub>2</sub>.

**(3) BH<sub>3</sub>-Catalyzed Reaction between Ketene and Form-aldehyde (Mechanism A).** AM1 calculations performed at the RHF level on mechanism A enabled us to localize and characterize transition state **6a**; its main parameters being  $E_a$  = 14.0 kcal/mol;  $d_{O_3C_2}$  = 2.87 Å;  $d_{C_4C_5}$  = 1.79 Å; O<sub>3</sub>C<sub>5</sub>C<sub>4</sub>C<sub>2</sub> = 56.8° (Table 5). It appears from net atomic charges on C<sub>2</sub> and O<sub>3</sub> that although the reaction keeps a zwitterionic character, it is less pronounced than with BF<sub>3</sub>. However, the I.R.C. never allowed us to connect **6a**, either directly or through reasonable intermediates, to the expected 2-oxetanone **3-BH<sub>3</sub>**. Indeed, after a little shoulder **6b** ( $\Delta H_f$  = −16.7 kcal/mol), the I.R.C. led to a very stable product **7a** ( $\Delta H_f$  = −100.4 kcal/mol) resulting from a hydride transfer from BH<sub>3</sub> to the pseudoacylium ion present in **6a** and **6b**. The same product **7e**, however, under a different conformation, could also be reached from oxetanone **3-BH<sub>3</sub>** through transition state **6c**. It is indeed possible to connect the two conformations of **7a** and **7e**, but the whole process cannot be considered as a coherent reaction path.

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**Figure 2.** Formation of  $\beta$ -lactone  $3\text{'-BF}_3$  through mechanism B. Structures of transition states **5a–d** and intermediates **RIa–c** (AM1/C.I.).

**Table 1.** Main Parameters of the Critical Points Involved in the Formation of the  $\beta$ -Lactone  $3\text{-BF}_3$  through Mechanism A (AM1/RHF)<sup>a</sup>

critical points	$\Delta H_f$ (kcal/mol)	$E_a$ (kcal/mol)	$d_{\text{O}_3\text{C}_2}$ (Å)	$d_{\text{C}_4\text{C}_5}$ (Å)	$\text{O}_3\text{C}_5\text{C}_4\text{C}_2$ (d°)	$d_{\text{O}_3\text{B}}$ (Å)	$\text{BO}_3\text{C}_5\text{C}_4$ (d°)	$\partial\text{O}_3$	$\partial\text{C}_2$
<b>4a</b>	-305.3	14.2	2.825	1.720	43.1	1.690	81.7	-0.43	+0.42
<b>RI</b>	-307.8		2.592	1.585	29.3	1.588	66.2	-0.45	+0.48
<b>4b</b>	-306.9		2.348	1.602	23.0	1.618	136.2	-0.49	+0.48

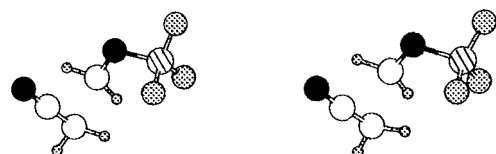
<sup>a</sup>  $\Delta H_f$ : heat of formation;  $E_a$ : activation energy;  $\delta$ : atomic charge.

**Table 2.** Main Parameters of the Critical Points Involved in the Formation of  $\beta$ -Lactone  $3\text{'-BF}_3$  through Mechanism B (AM1/C.I.)

critical points	$\Delta H_f$ (kcal/mol)	$E_a$ (kcal/mol)	$d_{\text{C}_2-\text{O}_3}$ (Å)	$d_{\text{C}_4-\text{C}_5}$ (Å)	$\text{C}_5\text{O}_3\text{C}_2\text{C}_4$ (d°)	$d_{\text{O}_1-\text{B}}$ (Å)	$\text{BO}_1\text{C}_2\text{O}_3$ (d°)	$\partial\text{C}_4$	$\partial\text{C}_5$
<b>1 + 2-BF<sub>3</sub></b>	-316.0		2.888	4.213	-174.8	1.929	79.9	-0.37	+0.15
<b>5a</b>	-292.0	24.0	1.393	3.044	-69.1	1.912	-8.9	-0.23	-0.21
<b>RIa</b>	-299.7		1.376	3.618	-176.9	1.939	53.0	-0.12	-0.17
<b>5b</b>	-293.3		1.398	3.198	89.2	1.906	10.2	-0.13	-0.22
<b>RIb</b>	-294.9		1.380	2.834	26.9	1.893	3.6	-0.15	-0.21
<b>5c</b>	-294.6		1.374	2.770	16.3	1.901	2.5	-0.20	-0.20
<b>RIc</b>	-295.3		1.372	2.765	2.5	1.905	1.5	-0.24	-0.21
<b>5d</b>	-294.3		1.370	2.512	9.1	1.895	2.6	-0.25	-0.16
<b>3'-BF<sub>3</sub></b>	-333.3		1.388	1.553	0.0	1.903	0.1	-0.20	-0.26

**Table 3.** Main Parameters of Transition State **4a** (AM1/RHF, HF/6-31G\*, MP2/6-31G\*)

<b>4a</b>	$E_a$ (kcal/mol)	$d_{\text{O}_3\text{C}_2}$ (Å)	$d_{\text{C}_4\text{C}_5}$ (Å)	$\text{O}_3\text{C}_5\text{C}_4\text{C}_2$ (d°)	$d_{\text{O}_3\text{B}}$ (Å)	$\text{BO}_3\text{C}_5\text{C}_4$ (d°)
<b>AM1/RHF</b>	14.2	2.825	1.720	43.1	1.690	81.7
<b>HF/6-31G*</b>	11.9	2.978	2.016	57.0	1.558	76.3
<b>MP2/6-31G*</b>	3.6	3.084	2.048	68.2	1.598	74.2

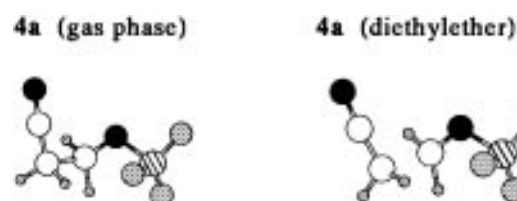


**4a (HF/6-31G\*)**

**4a (MP2/6-31G\*)**

**Figure 3.** Structures of transition state **4a** (HF/6-31G\* and MP2/6-31G\*).

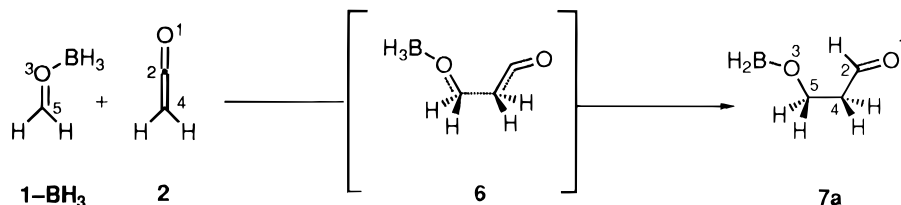
These results obtained in gas phase were confirmed when calculations were carried out with solvent effects. As in the case of  $\text{BF}_3$ , transition state **6a** is earlier, as shown by the greater values of  $d_{\text{C}_4-\text{C}_5}$  and  $d_{\text{O}_3-\text{C}_2}$ . Consequently, the activation energy of the reaction falls from 14.0 kcal/mol to 6.8 (diethyl ether) or 5.6 kcal/mol (dichloromethane). Finally, in both cases **6a** leads



**Figure 4.** Structures of transition state **4a**.

to the hydride transfer product **7a**; indeed, we were not able to find a pathway leading to the formation of a  $\beta$ -lactone.

Since AM1 calculations describe a completely different reaction path compared to the one obtained with  $\text{BF}_3$ , we decided to check this process by *ab initio* calculations conducted at the HF/6-31G\* level of theory. Starting from the AM1 geometry of **6a**, we found a very similar transition state **6a\*** (Table 7) which seems to be identical to the one described by Cossio *et al.*<sup>10c</sup> We then performed an IRC from **6a\***. On the one hand, it led to the reactants ( $E_a = 16.0$  kcal) but, on the other hand, only toward a hydride transfer product without reaching it, the energy gradient being then too low. However, the geometry of the point we were able to reach, **7\***, clearly indicates that transition state **6a\*** would not lead to the formation of  $\beta$ -lactone **3-BH<sub>3</sub>** but rather to a hydride transfer product as evidenced by AM1 calculations. Indeed, from **6a\*** to **7\***, the

**Scheme 4.** Formation of **7** from Formaldehyde **1** and Ketene **2** in the Presence of  $\text{BH}_3$ **Table 4.** Main Parameters of the Transition state **4a** Calculated in Gas Phase (AM1/RHF) and with Solvent Effects (AM1/COSMO)

<b>4a</b>	$E_a$ (kcal/mol)	$H_f$ (kcal/mol)	$d_{\text{O}_3\text{C}_2}$ (Å)	$d_{\text{C}_4\text{C}_5}$ (Å)	$\text{O}_3\text{C}_5\text{C}_4\text{C}_2$ ( $d^\circ$ )	$d_{\text{O}_3\text{B}}$ (Å)	$\text{BO}_3\text{C}_5\text{C}_4$ ( $d^\circ$ )	$\partial\text{O}_3$	$\partial\text{C}_2$
gas	14.2	-12.1	2.825	1.720	43.1	1.690	81.7	-0.43	+0.42
$\text{Et}_2\text{O}$	7.0	-11.3	3.060	1.967	70.8	1.662	87.2	-0.41	+0.47
$\text{CH}_2\text{Cl}_2$	6.8	-23.0	3.241	2.023	89.5	1.650	84.2	-0.40	+0.48
PhMe	9.0	-11.6	2.936	1.919	59.2	1.673	86.3	-0.41	+0.45

**Table 5.** Main Parameters of the Critical Points Involved in the  $\text{BH}_3$ -Catalyzed Reaction between Formaldehyde **1** and Ketene **2** (AM1/RHF)

critical points	$\Delta H_f$ (kcal/mol)	$E_a$ (kcal/mol)	$d_{\text{O}_3\text{C}_2}$ (Å)	$d_{\text{C}_4\text{C}_5}$ (Å)	$\text{O}_3\text{C}_5\text{C}_4\text{C}_2$ ( $d^\circ$ )	$d_{\text{O}_3\text{B}}$ (Å)	$\text{BO}_3\text{C}_5\text{C}_4$ ( $d^\circ$ )	$\partial\text{O}_3$	$\partial\text{C}_2$
<b>1-BH<sub>3</sub> + 2</b>	-29.8		3.735	2.615					
<b>6a</b>	-15.8	14.0	2.873	1.792	56.8	1.594	71.8	-0.31	+0.41
<b>6b</b>	-16.7		2.834	1.625	57.0	1.550	68.2	-0.34	+0.44
<b>7a</b>	-100.4		2.928	1.516	61.9	1.341	105.4	-0.27	+0.18
<b>7b</b>	-99.3		3.483	1.529	117.4	1.342	98.1	-0.26	+0.18
<b>7c</b>	-100.2		3.728	1.524	168.4	1.341	105.6	-0.27	+0.18
<b>7d</b>	-99.1		3.560	1.519	-127.1	1.342	90.1	-0.26	+0.18
<b>7e</b>	-99.9		3.086	1.520	-76.9	1.341	107.3	-0.27	+0.18
<b>6c</b>	-20.1		1.940	1.543	4.2	1.589	83.4	-0.35	+0.45
<b>3-BH<sub>3</sub></b>	-39.9		1.439	1.548	-0.7	1.798		-0.23	+0.31

**Table 6.** Main Parameters of Transition State **6a** (Gas Phase, Diethyl Ether, and Dichloromethane) Calculated with AM1/COSMO

<b>6a</b>	$E_a$ (kcal/mol)	$d_{\text{O}_3\text{C}_2}$ (Å)	$d_{\text{C}_4\text{C}_5}$ (Å)	$\text{O}_3\text{C}_5\text{C}_4\text{C}_2$ ( $d^\circ$ )	$d_{\text{O}_3\text{B}}$ (Å)	$\text{BO}_3\text{C}_5\text{C}_4$ ( $d^\circ$ )	$\partial\text{O}_3$	$\partial\text{C}_2$
gas	14.0	2.873	1.792	56.8	1.590	71.8	-0.31	+0.41
$\text{Et}_2\text{O}$	6.8	2.924	2.000	51.0	1.580	79.3	-0.31	+0.48
$\text{CH}_2\text{Cl}_2$	5.6	2.943	1.962	47.7	1.569	82.1	-0.31	+0.49

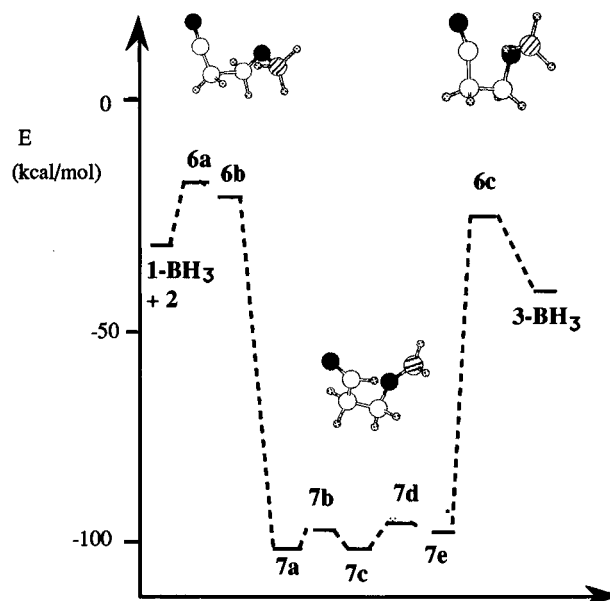
**Table 7.** Main Parameters of the Critical Points Involved in the  $\text{BH}_3$ -Catalyzed Reaction between Formaldehyde **1** and Ketene **2** (HF/6-31G\*)

critical points	total energy (au)	$E_a$ (kcal)	$d_{\text{BH}_3}$ (Å)	$d_{\text{C}_3\text{H}_3}$ (Å)	$\text{C}_5\text{C}_2\text{C}_6\text{O}_1$ ( $d^\circ$ )
<b>(1-BH<sub>3</sub> + 2)*</b>	-291.995 310		1.200	3.343	39.4
<b>6a*</b>	-291.969 864	16.0	1.235	2.625	37.6
<b>7*</b>	-292.073 708		1.990	1.155	26.3
<b>7a*</b>	-292.104 465		3.880	1.090	57.9

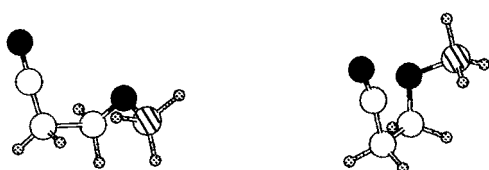
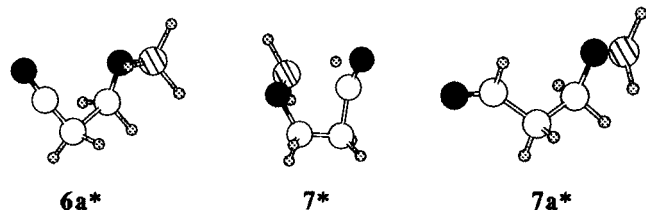
distance between the boron atom and one of its hydrogen atoms,  $\text{H}^{13}$ , increased from 1.235 to 1.990 Å, while in the same time the distance between the same hydrogen atom,  $\text{H}^{13}$ , and the central carbon atom of the ketene,  $\text{C}^5$ , reduced from 2.625 to 1.155 Å. Moreover, an energy minimization performed from **7\*** with a quadratic method led to a very stable product, **7a\***, resulting from the complete hydride transfer and with a geometry close to **7a** (AM1/RHF).<sup>24</sup> Finally, the thermodynamic of the process is very similar to the one calculated by semiempirical means (Table 5).

The reduction into alcohols of carbonyl compounds by  $\text{BH}_3$  is well-known<sup>25</sup> and has been investigated from an experimental point of view,<sup>26</sup> but, to the best of our knowledge, a reaction

(24) Despite careful search, we were not able to find another transition state, resulting from a rotation of  $\text{BH}_3$  around the  $\text{C}_5\text{-O}_3$  bond, that would be part of a different reaction path. When such a rotation was imposed in order to increase the distance between the hydrogen atoms of  $\text{BH}_3$  and  $\text{C}_2$  over 4 Å, the subsequent geometry optimization of such a structure led to the hydride transfer product and not to the expected  $\beta$ -lactone

**Figure 5.** Formation of **7a-e** from formaldehyde **1** and ketene **2** in the presence of  $\text{BH}_3$  or from  $3\text{-BH}_3$ . Structures of critical points involved in the process (AM1/RHF).

leading to the formation of a hydride transfer product, or any corresponding derivative, is unknown; just as is the formation of  $\beta$ -lactones through  $\text{BH}_3$ -promoted [2 + 2] cycloaddition. We therefore decided to perform a reaction between hexanal and

**6a (gas phase)**      **6a (diethylether)****Figure 6.** Structures of Transition State **6a**.**Figure 7.** Structures of critical points **6a\*** and **7a\*** and of **7\*** obtained by *ab initio* calculations (HF/6-31G\*).

*n*-hexyl(trimethylsilyl)ketene<sup>6b</sup> in the presence of BH<sub>3</sub>. However, and as could be expected from the literature,<sup>23</sup> the only product of a reaction was 1-hexanol (84% yield), the silylketene being mainly recovered unchanged. No traces of either a  $\beta$ -lactone or a hydride transfer derivative could be identified.

## Conclusion

We have studied the BF<sub>3</sub>-promoted [2 + 2] cycloaddition between ketene and formaldehyde through two different mechanisms:

–Mechanism A is a closed-shell, quasi-concerted but asynchronous process (priority to the C–C bond formation). The

approach of the reagents is synperiplanar, and the activation energy is of 14.2 kcal/mol (AM1/RHF) or 11.9 (HF/6-31G\*).

–Mechanism B is an open-shell stepwise process (priority to the O–C bond formation). The approach of the reagents is antiperiplanar, and the activation energy is of 24.0 kcal/mol (AM1/RHF).

BF<sub>3</sub> has a greater influence on the activation energy of mechanism A compared to mechanism B. Consequently, mechanism A, from unfavored in the uncatalyzed reaction (A *vs* B: 38 *vs* 32 kcal/mol),<sup>11</sup> becomes favored in the BF<sub>3</sub>-catalyzed one (A *vs* B: 14 *vs* 24 kcal/mol).

The case of BH<sub>3</sub> is somehow more complicated. Although a transition state close to the one obtained with BF<sub>3</sub> was found, it led (in an I.R.C. sense) to a stable product resulting from an hydride transfer from the boron to the pseudoacylium cation. No reasonable reaction path leading to the  $\beta$ -lactone moiety was found. Experiment could not reproduce that reaction but led to a more classical reduction of the carbonyl moiety into the corresponding alcohol. Despite the longer calculation times, it is therefore, at least from our point of view, better to use BF<sub>3</sub> rather than BH<sub>3</sub> as a model Lewis acid in this reaction.

Further studies, devoted to the influence, on the cycloaddition reaction, of substituents such as –SiH<sub>3</sub>, –Cl, and –CN on the ketene, and alkyl and alkoxyalkyl on the aldehyde, and on the reduction of carbonyl compounds by BH<sub>3</sub> are currently underway.<sup>27</sup>

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