BH₃-Catalyzed Oligomerization of Ethyl Diazoacetate: The Role of *C*-Boron Enolates

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Abstract: In contrast to trialkyl boranes, the reaction of borane (BH₃) and ethyl diazoacetate (EDA) generates dimer, trimer, and oligomers of EDA. The products arise from double, triple, and multiple insertions of CHCO₂Et groups in B−C bonds. On the basis of NMR spectroscopic data, trapping experiments, and computational studies, a novel *C*-boron enolate has been identified as a key intermediate in this reaction. This *C*-boron enolate species is calculated to be 7.1 kcal/mol (gas phase) more stable than its isomeric *O*-boron enolate form. Both spectroscopic data and trapping results also reveal the formation of a doubly borylated enolate generated as a side product by a proton transfer between the *C*- and *O*-boron monoenolates.

Introduction

The reaction of organoboranes with diazo compounds is a valuable sp³−sp³ carbon−carbon bond forming method.[1] Examples include the homologation reaction of trialkylboranes with ethyl diazoacetate (EDA, **1**).[2] Scheme 1 illustrates the reaction of EDA **1** with tri-*n*-propylborane. Ethyl pentanoate is formed by a single insertion of the ethoxycarbonylmethylidene group (CHCO₂Et) with elimination of N₂.[2] This reaction stops after a single insertion; products from multiple carbon−carbon bond insertions were not observed.

The oligomerization of alkyl diazoacetates has been achieved by transition metal catalysts including Cu powder[3] and Pd complexes[4] resulting in the synthesis of low molecular weight poly(alkyl 2-ylidene-acetate) (viscous oil with degree of polymerization up to 100), while high molecular weight polymers with a number average molecular weight (M_n) up to 57 kDa were obtained when rhodium catalysts were employed.[5] Related polymer structures have been prepared by free radical polymerization of dialkyl fumarates, a rare example of polymerization of 1,2-disubstituted olefins.[6]

As part of our study of repetitive sp³−sp³ carbon−carbon bond forming reactions,[7] we had occasion to examine the reaction of EDA **1** with borane (BH₃, **2**). In contrast to trialkylboranes, we observed that the reaction gives a mixture of products, including oligomers derived from multiple ethoxycarbonylmethylidene group (CHCO₂Et) insertions. A mechanistic investigation was undertaken to elucidate the origin of oligomer formation. This study has led to the discovery of a novel *C*-boron enolate, which serves as the resting state for the reaction and provides insight to the repetitive sp³−sp³ carbon−carbon bond formation in the polymerization reaction of diazocarbonyl compounds.

Results

Reaction of Borane 2 and EDA 1. Based on earlier reports that trialkylboranes react with EDA **1** to give monohomologated products[2] and that borane **2** reacts with an excess of trimethylsilyl diazomethane to generate tris(trimethylsilylmethyl)borane (82% yield),[8] the reaction of BH₃ **2** and an excess of EDA **1** was anticipated to produce either ethyl acetate **3** or bis- or tris-(ethoxycarbonylmethyl)borane. However, upon reaction, a number of products were isolated that included dimer, trimer, and oligomers arising from multiple insertions of CHCO₂Et groups. The reaction is shown in Scheme 2. EDA **1** (3 equiv)

(1) (a) Hooz, J.; Linke, S. *J. Am. Chem. Soc.* **1968**, *90*, 5936. (b) Hooz, J.; Morrison, G. F. *Can. J. Chem*. **1970**, *48*, 868. (c) Hooz, J.; Gunn, D. M. *Chem. Commun.* **1969**, 139. (d) Hooz, J.; Gunn, D. M. *J. Am. Chem. Soc.* **1969**, *91*, 6195.
(2) (a) Pasto, D. J.; Wojtkwski, P. W. *Tetrahedron Lett.* **1970**, *11*, 215−218. (b) Hooz, J.; Linke, S. *J. Am. Chem. Soc.* **1968**, *90*, 6891−6892. (c) Hooz, J.; Gunn, D. M. *Tetrahedron Lett.* **1969**, 3455. (d) Paquette, L. A., Ed. *Encyclopedia of reagents for organic synthesis*; John Wiley & Sons: Chichester, England, 1995; Vol. 4, p 2419.
(3) Liu, L.; Song, Y.; Li, H. *Polym. Int.* **2002**, *51*, 1047.
(4) (a) Ihara, E.; Haida, N.; Iio, M.; Inoue, K. *Macromolecules* **2003**, *36*, 36. (b) Ihara, E.; Fujioka, M.; Haida, N.; Itoh, T.; Inoue, K. *Macromolecules* **2005**, *38*, 2101.
(5) Hetterscheid, D. G. H.; Hendriksen, C.; Dzik, W.; Jellema, E.; Bloemberg, T. G.; van Eck, E. R. H.; Smits, J. M. M.; Vacatello, M.; Castelli, V. V. A.; Segre, A.; Rowan, A. E.; Busico, V.; de Bruin, B. *J. Am. Chem. Soc.* **2006**, *128*, 9746−9752.
(6) (a) Otsu, Y.; Toyota, N. *J. Polym. Bull.* **1984**, *11*, 453−458. (b) Otsu, T.; Yasuhara, T.; Shiraishi, K.; Mori, S. *Polym. Bull.* **1984**, *12*, 449−456. (c) Otsu, T.; Shiraishi, K. *Macromolecules* **1985**, *18*, 1795−1796. (d) Otsu, T.; Shiraishi, K.; Matsumoto, A. *J. Polym. Sci., Part A: Polym. Chem.* **1993**, *31*, 885−890. (e) Toyoda, N.; Yoshida, M.; Otsu, T. *Polym. J.* **1983**, *15*, 255−260.
(7) (a) Shea, K. J.; Walker, J. W.; Zhu, H.; Paz, M.; Greaves, J. *J. Am. Chem. Soc.* **1997**, *119*, 9049−9050. (b) Shea, K. J.; Busch, B. B.; Paz, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 1391−1393. (c) Shea, K. J.; Lee, S. Y.; Busch, B. B. *J. Org. Chem.* **1998**, *63*, 5746−5747. (d) Shea, K. J.; Staiger, C. L.; Lee, S. Y. *Macromolecules* **1999**, *32*, 3157−3158. (e) Zhou, X.-Z.; Shea, K. J. *J. Am. Chem. Soc.* **2000**, *122*, 11515−11516. (f) Busch, B. B.; Paz, M. M.; Shea, K. J.; Staiger, C. L.; Stoddard, J. M.; Walker, J. R.; Zhou, X.-Z.; Zhu, H. *J. Am. Chem. Soc.* **2002**, *124*, 3636−3646. (g) Busch, B. B.; Staiger, C. L.; Stoddard, J. M.; Shea, K. J. *Macromolecules* **2002**, *35*, 8330−8337. (h) Wagner, C. E.; Kim, J.-S.; Shea, K. J. *J. Am. Chem. Soc.* **2003**, *125*, 12179−12195.
(8) Bai, J.; Shea, K. J. *Macromol. Rapid Commun.* **2006**, *27*, 1223−1228.

Scheme 1
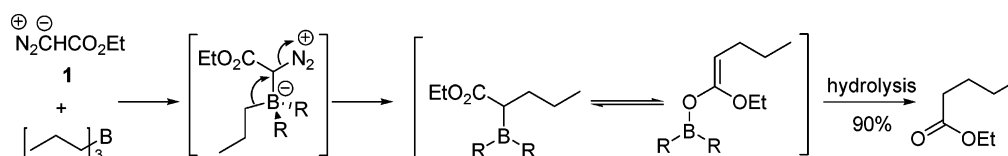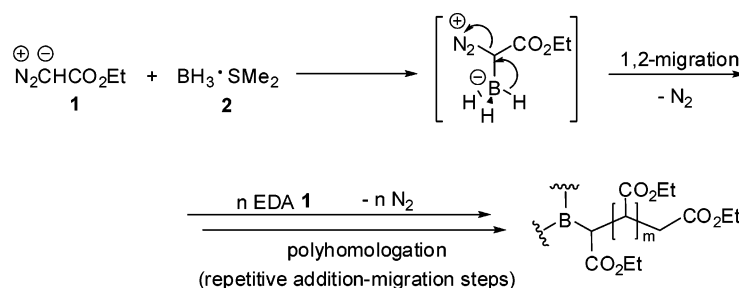

Scheme 2
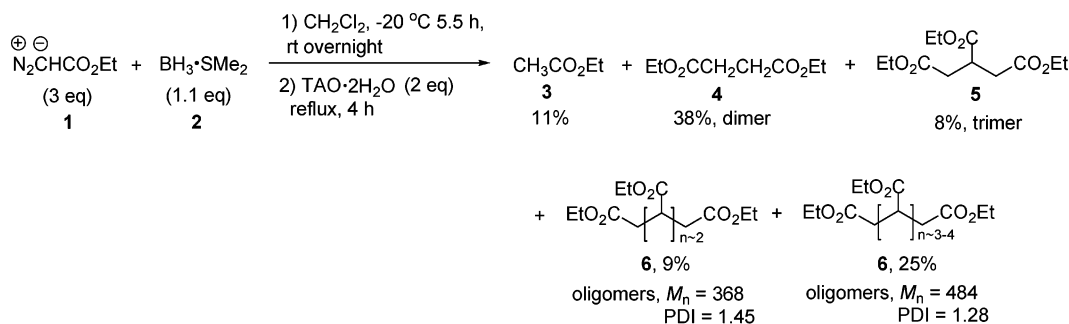
(Yield is based on EDA, and the overall yield is 91%.)

Scheme 3

was treated with borane **2** (1.1 equiv) in CH_2Cl_2 in a dry ice−ice bath ($\sim$ −20 °C). After 5.5 h, an aliquot was analyzed by ^{1}H NMR with bibenzyl as internal standard. The ratio of unreacted EDA **1** (N_2C*H*CO_2Et), bibenzyl (PhC*H*$_2$C*H*$_2$Ph), and newly generated ethyl acetate **3** (C*H*$_3CO_2$Et) was determined by integration of peaks at 4.72, 2.89, and 1.99 ppm, respectively. It was found that most of the EDA **1** was consumed, and the product from the monohomologation reaction, ethyl acetate **3**, was present in a yield of 11%. In addition, the proton signal of dimer (EtO_2CCH_2)$_2$ was observed as a singlet at 2.66 ppm, and formation of oligomers was seen from the broad multiplet of the −CO_2C*H*$_2$C*H*$_3$ groups. The reaction mixture was kept at room temperature overnight and then trimethylamine *N*-oxide (TAO·2H_2O, dihydrate, 2 equiv) was added, followed by heating at reflux for 4 h. Workup and flash chromatography afforded diethyl succinate (dimer, **4**, 38%),[9] triethyl 1,2,3-propanetricarboxylate (trimer, **5**, 8%),[9] and oligomers (**6**, 34%),[3−6] all arising from multiple sp^3−sp^3 carbon−carbon bond formations. It is clear that the major products of this reaction are dimer **4** and oligomers **6**, not the monohomologated ethyl acetate **3**.
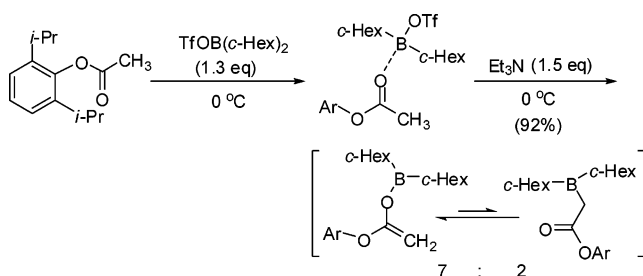
Five control experiments were conducted to gain some insight into this reaction. The first employed an excess of EDA **1** ($\sim$3 equiv) with triethylborane. After the same workup step, an aliquot of the crude reaction mixture was analyzed by GC/MS. The spectrum showed a single peak corresponding to ethyl

butyrate in 85% yield. This experiment verified the reported monohomologation reaction of EDA **1** and trialkylboranes.[2] The second control experiment was designed to establish if background decomposition reaction of EDA **1** contributed to the observed products. In the absence of borane **2**, after 18 h in CH_2Cl_2 at room temperature most of the EDA **1** remained, and only a small amount (<6%) of oil was found. The third control experiment concerned the possibility that trace boric acid in the reaction mixture, formed from the reaction of borane **2** with air and moisture, could be responsible for the observations. Borinic acid (1 equiv) was mixed with EDA **1** (3.8 equiv). It was found that most of EDA **1** remained unreacted, and only a small amount (<7%) of an uncharacterized oil was isolated. In addition, considering the reaction of borane **2** with moisture may generate a trace amount of $[BH_3X]^-[H]^+$, a fourth control experiment was performed to examine the possibility of $[BH_3X]^-$-$[H]^+$-initiated cationic decomposition/polymerization of EDA **1**.[10] Deionized water (10 mmol%) was added at the beginning of the reaction. Although $\sim$18% of brown oil was isolated from the reaction after the same reaction time and workup step, its ^{1}H NMR spectrum was quite different from that of oligomers **6**. It should be noted however that this does not rule out the

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(9) Pouchert, C. J. *The Aldrich Library of NMR Spectra*, 2nd ed.; Aldrich Chemical Co.: Milwaukee, WI, 1983. Spectra of diethyl succinate **4** and triethyl 1,2,3-propanetricarboxylate **5** were in accordance with the literature.

(10) Lewis acids catalyzed decomposition reaction of diazomethane to form polymethylene with high molecular weight. See: (a) Meerwein, H. *Angew. Chem.* **1948**, *A60*, 78. (b) Kantor, S. W.; Osthoff, R. C. *J. Am. Chem. Soc.* **1953**, *75*, 931. (c) Feltzin, J.; Restaino, A. J.; Mesrobian, R. B. *J. Am. Chem. Soc.* **1955**, *77*, 206−210. (d) Imoto, M.; Nakaya, T. *J. Macromol. Sci., Rev. Macromol. Chem.* **1972**, *C7*, 1−48. (e) Cowell, G. W.; Ledwith, A. *Quart. Rev.* **1970**, *24*, 119. (f) Mucha, M.; Wunderlich, B. *J. Polym. Sci., Polym. Phys. Ed.* **1974**, *12*, 1993.

Scheme 4

Figure 1. ^{1}H NMR spectrum of the *C*-boron enolate **8** derived from the reaction of borane **2** and EDA **1**.

possibility that the cationic polymerization could contribute to some of the products observed in the reaction of EDA **1** and borane **2**. The last control experiment used deionized water in the workup step in place of TAO·2H$_2$O. The reaction gave an identical product mixture of dimer **4** (41%), trimer **5** (9%), and oligomers **6** (27%). This indicates that the oxidizing reagent was not necessary for the workup.

Discussion

The reaction of borane **2** and EDA **1** produced dimer **4**, trimer **5**, and oligomers **6** in addition to ethyl acetate **3**. Products **4**, **5**, and **6** arise from double, triple, and multiple additions of CHCO$_2$Et groups. In order to elucidate the origin of these sp^3– sp^3 carbon–carbon bond formation products, a mechanistic investigation was undertaken. The reaction is complicated, but mechanistic insight into this system has been gained. Three separate facets of this reaction are considered below.

Mechanism 1: The Polyhomologation Reaction. Reaction of EDA **1** and borane **2** was believed to share some common features of the polyhomologation reaction, a polymerization reaction of ylides and diazoalkanes that has been used to construct a carbon backbone polymer *one carbon at a time*.[7] Within this framework, EDA **1** and Lewis acidic borane **2** are proposed to form a zwitterionic complex. This is followed by 1,2-migration of H (or carbon) with concurrent expulsion of N$_2$ to generate the homologated borane. Repetitive addition– migration steps would eventually give poly(ethoxycarbonylm- ethylidene) (Scheme 3). Besides polyhomologation, two other facets of this reaction that need to be considered are developed in the following sections.

Mechanism 2: Carbon vs Oxygen Boron Enolates. Boron enolates are important reagents in organic synthesis.[11] *C*-Boron enolates (α-borylcarbonyl compounds) have been proposed as the reactive intermediate in many transformations.[12] Direct evidence of *C*-boron enolates however is sparse as they are thought to be unstable toward isomerization to the *O*-boron isomer (vinyloxyboranes).[12,13] For example, attempted synthesis of α-boryl ketones by the reaction of α-diazo ketones with tripropylborane resulted in exclusive formation of the *O*-boron enolate.[12d] *Ab initio* molecular orbital calculations indicate that
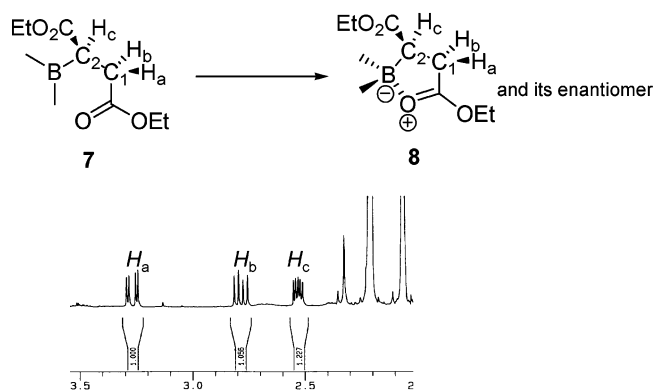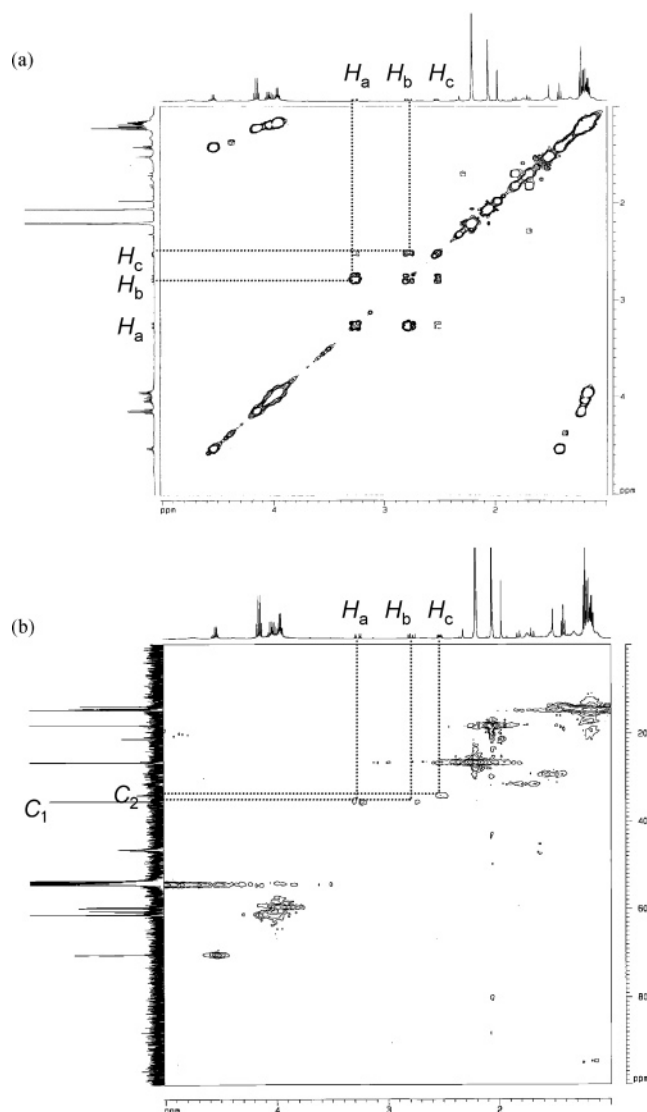

Figure 2. (a) [^{1}H, ^{1}H] COSY, and (b) [^{1}H, ^{13}C] HMQC spectra of the *C*-boron enolate **8** derived from the reaction of EDA **1** and borane **2**.

the simple α-boryl aldehyde (H$_2$BCH$_2$CHO) is less stable than the isomeric *O*-boron enolate (CH$_2$=CHOBH$_2$) by 19.4 kcal/ mol (Table 2).[13] In 2002, the first spectroscopic characterization of *C*-boron enolates was achieved by Abiko and co-workers in their study of double aldol reactions of acetate esters.[14] They found that when 2,6-diisopropylphenyl acetate was treated with

(11) Kim, B. M.; Williams, S. F.; Masamune, S. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed; Pergamon: Oxford, 1991; Vol. 2, p 239.
(12) (a) Brown, H. C.; Rogic, M. M.; Rathke, M. W. *J. Am. Chem. Soc.* **1968**, *90*, 6218. (b) Brown, H. C.; Rogic, M. M.; Rathke, M. W.; Kabalka, G. W. *J. Am. Chem. Soc.* **1968**, *90*, 818. (c) Pasto, D. J.; Wojtkowski, P. W. *J. Org. Chem.* **1971**, *36*, 1790. (d) Mukaiyama, T.; Murakami, M.; Oriyame, T.; Yamaguchi, M. *Chem. Lett.* **1981**, 1193. (e) Ochiai, M.; Tuchioto, Y.; Higashiura, N. *Org. Lett.* **2004**, *6*, 1505−1508. (f) Bell, N. J.; Cox, A. J.; Cameron, N. R.; Evans, J. S. O.; Marder, T. B.; Duin, M. A.; Elsevier, C. J.; Baucherel, X.; Tulloch, A. A. D.; Tooze, R. P. *Chem. Commun.* **2004**, *16*, 1854−1855.
(13) Ibrahim, M. R.; Buhl, M.; Knab, R.; von Rague Schleyer, P. *J. Comput. Chem.* **1992**, *13*, 423.
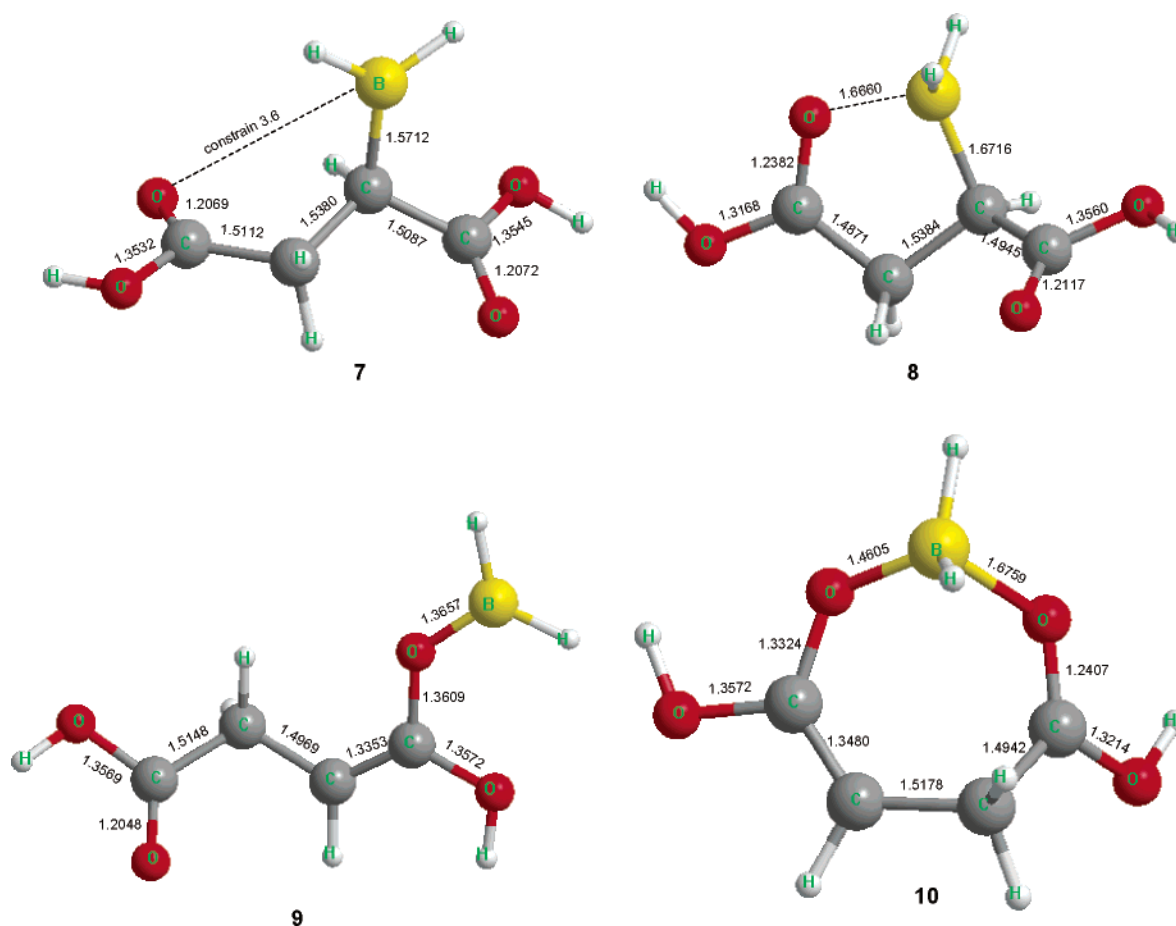
Figure 3. Structures of doubly homologated boron enolates **7**−**10** (optimized at the B3LYP/6-311++G** level of theory, bond distances in Å).

c-Hex$_2$BOTf (1.3 equiv) and triethylamine (1.5 equiv) in CDCl$_3$, boron enolates were formed as an equilibrating mixture of the *O*- and *C*-isomers in a 7:2 ratio at 0 °C (Scheme 4). Evidence for both intermediates was obtained by NMR spectroscopy. Steric factors were attributed to the similarity in energy between the *C*- and *O*-boron enolates. This is in striking contrast to the *C*- vs *O*-boron enolate calculated energy difference for acetaldehyde. This result is relevant to the present study since we are proposing a *C*-boron enolate in the borane-catalyzed oligomerization of EDA **1**.

NMR Spectroscopic Characterization of *C*-Boron Enolate 8. In an effort to establish the intermediate in the oligomerization of EDA **1** catalyzed by borane **2**, the reaction was monitored by NMR. EDA **1** (1.0 equiv) was mixed with 1.2 equiv of borane **2** in CD$_2$Cl$_2$ at −78 °C (0.22 M for EDA **1**, 0.25 M). After warming to room temperature for 1 h, the dominant species present in the ^{1}H NMR spectrum of the crude reaction mixture (Figure 1) was assigned to a *C*-boron enolate **8**. *This intermediate requires the addition of two HC(CO$_2$Et) groups to the borane.* In addition, the proton signal of ethyl acetate (EtO$_2$-CCH$_3$) was also observed as a singlet at 1.98 ppm, and formation of oligomers was noted by the broad multiplet of the −CO$_2$CH$_2$CH$_3$ groups. The enolate **8** comprised approximately 22% of the reaction mixture based upon the total amount of

EDA **1** in the reaction. This quantification was obtained by comparing the diagnostic peaks of enolate **8** with the total −OCH$_2$CH$_3$ signals as an internal standard. The proposed *C*-boron enolate structure was supported by two-dimensional NMR. Enolate **8** exhibited two doublet of doublets, one at 3.27 ppm (H_a) (J = 19.6, 5.3 Hz), the other at 2.78 ppm (H_b) (J = 19.8, 9.8 Hz), and a multiplet at 2.52 ppm (H_c) that could be attributed to coupling of the boron atom and/or the possible proton on the boron atom. These three protons were correlated in the [^{1}H, ^{1}H] COSY spectrum (Figure 2a). Protons H_a and H_b both correlated to the ^{13}C signal at 35.4 ppm (C_1), and proton H_c correlated to the signal at 33.2 ppm (C_2) in the [^{1}H, ^{13}C] HMQC spectrum (Figure 2b). Interestingly, it was noted that in the ^{13}C NMR spectrum an ester carbonyl group had a downfield chemical shift of 190.6 ppm, consistent with its coordination to the Lewis acidic boron center; in the ^{1}H NMR spectrum H_c was shifted upfield from H_a and H_b, which can be explained by the increased electron density of the boron center. Furthermore, the ^{11}B NMR spectrum showed a resonance at 11.7 ppm, characteristic of a tetra-coordinated organoboron species.[15] The spectroscopic signatures are consistent with a boron "onium-ate" complex which can form by donation of the *γ*-carbonyl lone pair into the empty *p* orbital of the boron atom.[16] This intermediate has a stable five-member ring geometry. The

(14) (a) Abiko, A.; Inoue, T.; Masamune, S. *J. Am. Chem. Soc.* **2002**, *124*, 10759−10764. (b) Furuno, H.; Inoue, T.; Abiko, A. *Tetrahedron* **2002**, *43*, 8297. (c) Abiko, A. *J. Synth. Org. Chem. Jpn.* **2003**, *61*, 24. (d) Abiko, A.; Inoue, T.; Furuno, H.; Schwalbe, H.; Fieres, C.; Masamune, S. *J. Am. Chem. Soc.* **2001**, *123*, 4605. (e) Abiko, A. *Acc. Chem. Res.* **2004**, *37*, 387−395.

(15) (a) Wrackmmeyer, B. *Nuclear Magnetic Resonance Spectroscopy of Boron Compounds Containing Two-, Three and Four-Coordinate Boron* in *Annual Reports on NMR Spectroscopy*; Webb, G. A., Ed.; Academic Press: San Diego, 1998; Vol. 20, p 139. (b) Dash, A. K.; Jordan, R. F. *Organometallics* **2002**, *5*, 777−779.

(16) Wittig, G. *Quart. Rev. (London)* **1966**, *20*, 191−210.

Table 1. Relative Energy of Isomers of the Doubly Homologated *C*-Boron Enolate **8** at the B3LYP/6-311++G** Level of Theory

isomer	relative energy (gas phase) + ZPE correction (kcal/mol)	relative energy (solvated) (kcal/mol)
7	10.5	15.0
8	0.0	0.0
9	7.1	12.8
10	6.5	9.7

remaining substituents on the boron atom of **8** could not be identified. However, we believe that it is highly unlikely they are both alkyl groups. We suspect that at the early stages of the reaction both are hydrogens. This point is based on the first control experiment with triethylborane and an excess of EDA **1**, a reaction that gives an unreactive intermediate after monohomologation. Since it is necessary to insert two EDA groups into borane to achieve this structure, the difference in reactivity of borane and trialkylborane can be attributed to the ability of the borane to undergo multiple insertions of EDA before eventually leading to an unreactive intermediate.

Computational Studies. Surprisingly, in our NMR spectroscopic study of the reaction of EDA **1** and BH₃ **2**, we did not observe the *O*-boron enolate **9**, which would arise from the tautomerization of *C*-boron enolate **7**. As mentioned earlier, simple boron enolates are believed to exist mainly in *O*-boron enolate form.[13] In order to corroborate and extend our experimental findings, modeling studies were undertaken on the *C*-boron enolate **7**, its isomeric *O*-boron enolate **9**, and their corresponding ester carbonyl group-stabilized structures (**8** and **10**) and ester ethoxy group-stabilized structures (**11** and **12**).
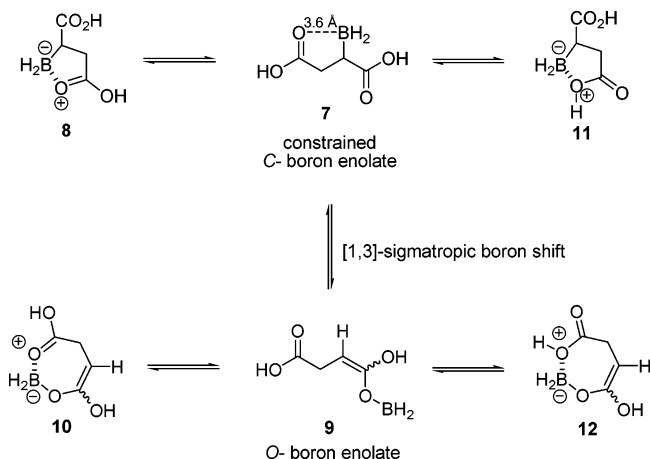
The constrained molecule (**7**), without the intramolecular B−O coordination, was included to represent the kinetic product from the 1,2-migration. In this study, ground-state conformations of the boron enolate species were first optimized by the semiempirical/PM3 method. The energy of conformation **11** and **12** was 10.8 and 9.0 kcal/mol higher than that of **8** and **10**, respectively, so structures **11** and **12** were eliminated from further consideration. Geometry optimization of structures **7**, **8**, **9**, and **10** were then carried out at the B3LYP/6-311++G** level of theory with ZPE correction. Inclusion of solvation energy (CH₂Cl₂) as single-point values was also obtained using the CPCM model. The geometry-optimized structures are shown in Figure 3, and their relative energies are summarized in Table

Table 2. Reference Energy Data Summary for the [1,3]-Sigmatropic Boron Shift

entry		activation barrier (kcal/mol)	relative energy of *O*-boron enolate (kcal/mol)
1	R₁, R₂, R₃ = H[a]	8.8	−19.4
2	R₁, R₂ = H, R₃ = Me[a]	10.9	−18.4
3	R₁ = −OAr, R₂ = H, R₃ = *c*-Hex		−2.81

[a] QCISD(T)/6-31+G*//MP2/6-31G*, corrected for the 6-31G* zero-point energies.
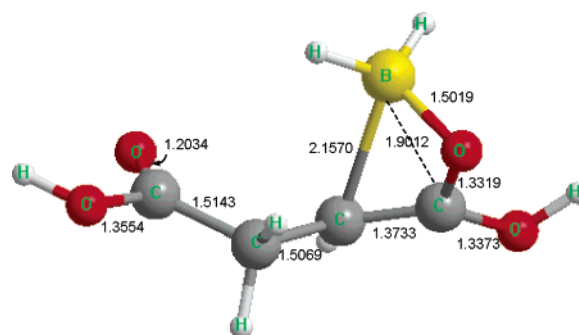
Figure 4. Transition state structure calculated for [1,3]-sigmatropic boron shift of *C*-boron enolate **7** to give *O*-boron enolate **9** isomer. Calculation is at the B3LYP/6-311++G** level of theory. Bond distances are in Å.

Table 3. Calculated Transition State Energies at B3LYP/6-311++G** Level of Theory for the [1,3]-Sigmatropic Boron Shift from the Constrained *C*-Boron Enolate **7** en Route to the Isomeric *O*-Boron Enolate **9**

	energy barrier E_{TS}[a] (kcal/mol)	energy difference ΔE[a] (kcal/mol)
unsolvated energy (+ZPE correction)	15.3	−3.4
solvated energy	15.7	−2.2

[a] The energy barrier E_{TS} was defined as E(transition state) − E(**7**), and the ΔE value was calculated from E(**7**) − E(**9**).

1 (absolute energies at different levels of theory are included in the Supporting Information). All calculations were conducted using the simplified structures that have −COOH groups instead of −COOEt ester groups and have hydrogen as the two substituents on the boron atom.

The intramolecularly coordinated *C*-boron enolate (**8**) was found to have the lowest ground state energy, and the *O*-boron enolate (**10**) was calculated to be the second lowest in energy ($\Delta E_{10-8} = 6.5$ kcal/mol (ZPE corrected); 9.7 kcal/mol (solvated)) at the B3LYP/6-311++G** level of theory (Table 1). The same ordering of stability of **8** and **10** was also found at the mPW1PW91/6-31+G* ($\Delta E_{10-8} = 7.4$ kcal/mol (gas phase)) and MP2/6-31+G* ($\Delta E_{10-8} = 8.5$ kcal/mol (gas phase)) levels

Scheme 5 [a]
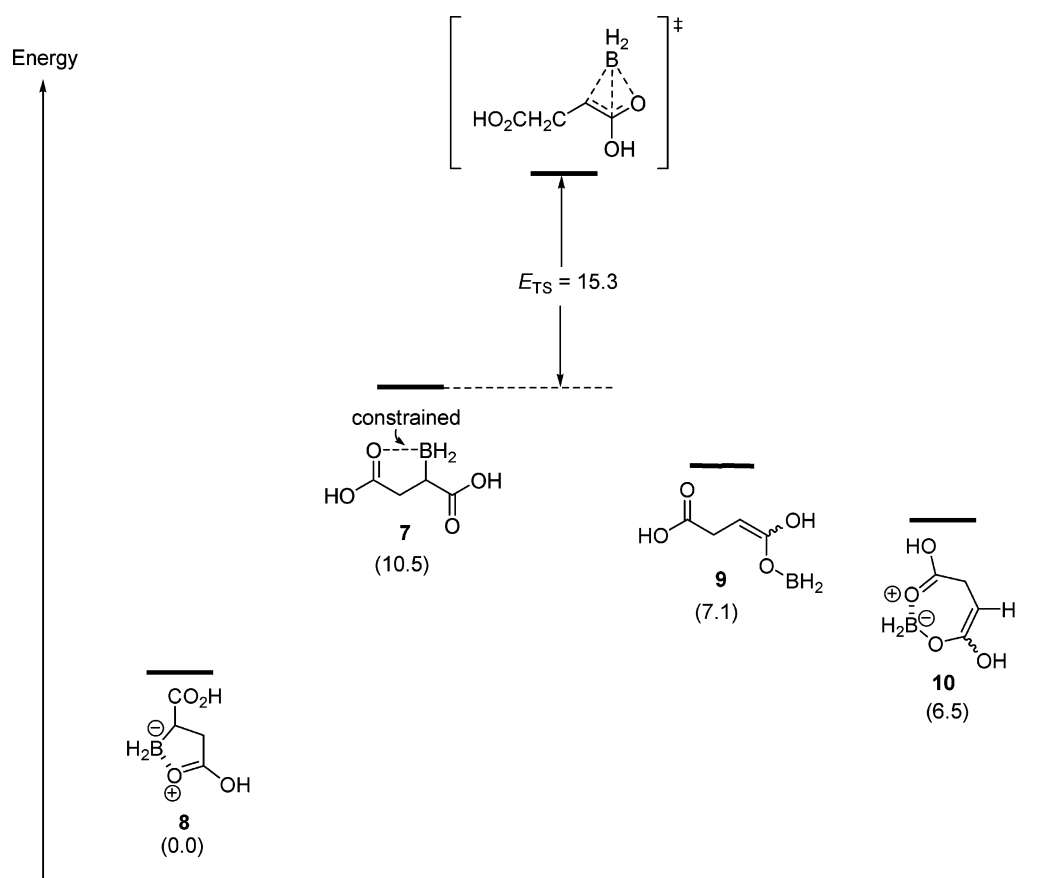
[a] Note: Relative Energies Are Shown in kcal/mol at B3LYP/6-311++G** Level of Theory + ZPE Correction.

Scheme 6
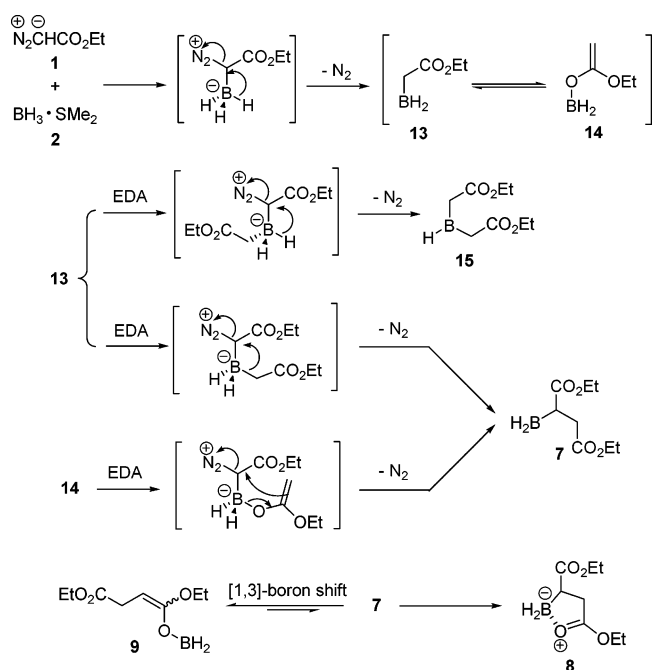
of theory. The calculated energies of **7**–**10** at all levels of theory are summarized in the Supporting Information. The optimized structure of *C*-boron enolate **8** contains a five-member ring geometry with the carbonyl oxygen atom lone pair coordinated to the boron center. This intramolecular coordination is consistent with what was proposed on the basis of NMR spectro-

scopic investigations. The calculated B_1–O_5 distance of enolate **8**, 1.6660 Å (see Figure 3), is significantly longer than that of an average covalent B–O bond (1.38 Å in methyl borate,[17] 1.47 Å in tetramethoxyborate[18]). It is also slightly longer than that of $B(C_6F_5)_3$ coordinated ketone (1.56 Å) and aldehyde (1.52 Å), and BF_3 coordinated aldehyde (1.53 Å),[19] while it is shorter than that of $BF_3\cdot OMe_2$ (1.75 Å),[20] and within the range of organoboron complexes that include the 1-borohomoadamantane–DMSO complex (B–O dative bond 1.668 Å).[7h] In summary, the calculated B_1–O_5 bond length of enolate **8** shows an interaction between the γ-carbonyl oxygen and the Lewis acidic boron center. This intramolecular dative binding contributes to the stabilization of the *C*-boron enolate **8**.

Following the finding that the *C*-boron enolate **8** is the lowest energy structure, we next studied the [1,3]boron shift, a mechanism by which a *C*-boron enolate rearranges to its isomeric *O*-boron enolate form. In a previous investigation, Schleyer and co-workers reported an *ab initio* study of the potential energy surface for the B–C to B–O barrier of a 1,3-boron shift in simple β-ketoboranes.[13] The data, summarized in entries 1 and 2 of Table 2, reveal that the isomerization of a *C*- to *O*-boron enolate is estimated to have an activation energy of ~10 kcal/mol. Recently Abiko and co-workers employed VT-NMR to

(17) Bauer, S. H.; Beach, J. V. *J. Am. Chem. Soc.* **1941**, *63*, 1394–1403.
(18) Abrahams, B. F.; Haywood, M. G.; Robson, R. *J. Am. Chem. Soc.* **2005**, *127*, 816–817.
(19) Ogoshi, S.; Yoshida, T.; Nishida, T.; Morita, M.; Kurosawa, H. *J. Am. Chem. Soc.* **2001**, *123*, 1944–1950.
(20) Iijima, K.; Yamada, T.; Shibata, S. *J. Mol. Struct.* **1981**, *77*, 271–276.

Table 4. Calculated Activation Energies (E_{TS}) of H vs Me 1,2-Migration in Borate Complexes at the B3LYP/6-311++G** Level of Theory + ZPE Correction

Complex						
E_{TS} (kcal/mol)	2.6	2.5	5.4	2.3	5.5	5.8

Table 5. Temperature Dependence of the Equilibrium between *E* and *Z* Isomers of the Doubly Borylated Enolate **28**

temp (°C)	5	10	15	20	25
28(*E*):**28**(*Z*)	3.0:1	1.7:1	~1:1	~1:1	~1:1

obtain the only experimental thermodynamic parameters for the 1,3-boron shift of enolate ArOC(O)CH$_2$B(*c*-Hex)$_2$ (entry 3 in Tale 2).[14]

The transition state calculations were carried out for the [1,3]-sigmatropic rearrangement from *C*-boron enolate **7** to *O*-boron enolate **9**. The calculated transition state structure is shown in Figure 4, and the energies are summarized in Table 3. It is interesting to point out that the calculated energy difference between the *C*- and *O*-boron enolates for esters is considerably less than that for aldehydes.

The *O*-boron enolate **9** was calculated to be more stable than the initial constrained *C*-boron enolate **7** by 3.4 kcal/mol. This is in line with previous calculated and experimental results (Table 2) indicating that the equilibrium between **7** and **9** lies to the right. However, enolate **7** is expected to readily form the stable *C*-boron enolate **8**. Once enolate **8** is generated, it must first dissociate to **7** and then rearrange to **9**. The calculated energy barrier for the [1,3]-boron shift from **7** en route to **9** is 15.3 kcal/mol. The overall process of **8** → **9** has an activation barrier of at least 25.8 kcal/mol. These calculations indicate that there would be a very slow interconversion between enolates **8** and **9** at room temperature.

The calculated values of ground state and transition state energies summarized above were used to graph the pathways and the relative energies for enolates **7** to **10** (Scheme 5). The computational results are consistent with the experimental observations.

Formation of *C*-Boron Enolate 8. A pathway to generate the *C*-boron enolate **8** is proposed in Scheme 6. Lewis acidic borane **2** reacts first with the nucleophilic EDA **1** to form a zwitterionic borate complex. Attempted detection of this complex in CD$_2$Cl$_2$ by low temperature ^{1}H and ^{11}B NMR experiments was not successful. It apparently undergoes loss of N$_2$ and rapid 1,2-H migration to afford *C*-boron enolate **13**. Compound **13**, the kinetic product from the 1,2-migration, can isomerize to the *O*-boron enolate **14** *via* a [1,3]-boron shift (E_{TS}
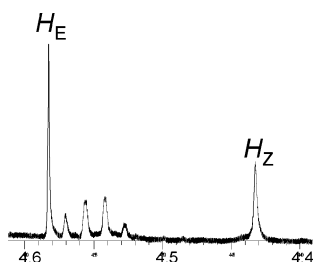

Figure 5. ^{1}H NMR spectrum of the doubly borylated enolate **28** derived from the reaction of borane **2** and EDA **1** at 15 °C.

= 13.7 kcal/mol, and ΔE = −0.5 kcal/mol calculated at the B3LYP/6-311++G** level of theory). It is expected that there is an equilibrium between the *C*-(**13**) and *O*-(**14**) boron enolates.

The enolate **13** can react with a second molecule of EDA **1** to form a zwitterionic complex, followed by either 1,2-migration of the CH$_2$CO$_2$Et group to generate enolate **7** or H migration to give compound **15**. Calculated energy barriers of those two pathways are shown in Table 4. The numbers do not change significantly with ZPE correction or with the inclusion of solvation (CH$_2$Cl$_2$). The calculations do not permit a distinction between the H and the alkyl group migration pathways. Both energy barriers are very low and may be dictated by the initial conformation of the zwitterionic complex. An alternative path, the reaction of the *O*-boron monoenolate **14** with EDA **1**, to afford enolate **7** must also be considered. We cannot at this point evaluate the importance of this pathway. Intermediate **7** would then collapse into the cyclic borane **8**, the "*resting*" species in the oligomerization.

Formation of Oligomers 6. A mechanism for the formation of poly(ethoxycarbonylmethylidene) oligomers **6** is proposed in Scheme 7. The resting intermediate, enolate **8**, generates the dimer product **4** upon workup.[12e,f] This intermediate can undergo an S$_N$2 reaction at boron with EDA **1**, to produce the triply homologated *C*-boron enolate **16** after expulsion of N$_2$. An alternate pathway to afford enolate **16** involves the reaction of *O*-boron enolate **9** with EDA **1**. By analogy with enolate **7**, enolate **16** can collapse to form the stabilized enolate **17** or isomerize to *O*-boron enolate **18**. Enolate **17**, a homologue of enolate **8**, could generate trimer **5** after hydrolysis. Repetitive addition−migration cycles afford oligomers **6**.

As previously discussed, the remaining two substituents on boron were not identified. Since trialkylboranes do not give oligomeric products when reacted with EDA **1**, we believe one or both must be hydrogen for it to be an active propagation species. Our calculations indicate that the 1,2-migration of H and Me groups have similar and very low activation energies, so, during oligomerization, there will be a competition between H and alkyl group migrations. Once a trialkylborane is formed, the product will have little reactivity toward EDA **1**. Since the alkyl group migration can happen at any stage of oligomerization, distributions of oligomers will be observed. This also explains the observation that even in the presence of a large excess (18 equiv) of EDA **1**, polymers of high molecular weight were not formed and substantial quantities of unreacted **1** remained.

Trapping Studies of Boron Enolate Intermediates with Benzaldehyde. *O*-Boron enolates react with aldehyde to give aldol products.[21] Recently, the reaction of *C*-boron enolates with
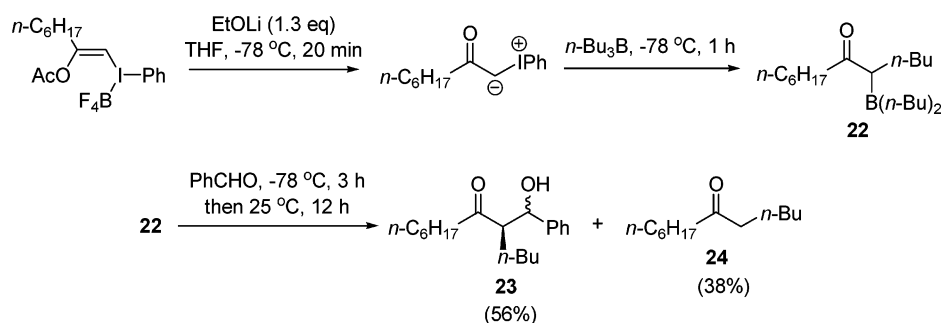
(21) (a) Mukaiyama, T.; Inoue, T. *Chem. Lett.* **1976**, 559. (b) Masamune, S.; Mori, S.; Horn, D. V.; Brooks, D. W. *Tetrahedron Lett.* **1979**, 967−968. (c) Mukaiyama, T.; Inomata, K.; Muraki, M. *J. Am. Chem. Soc.* **1973**, 967−968.
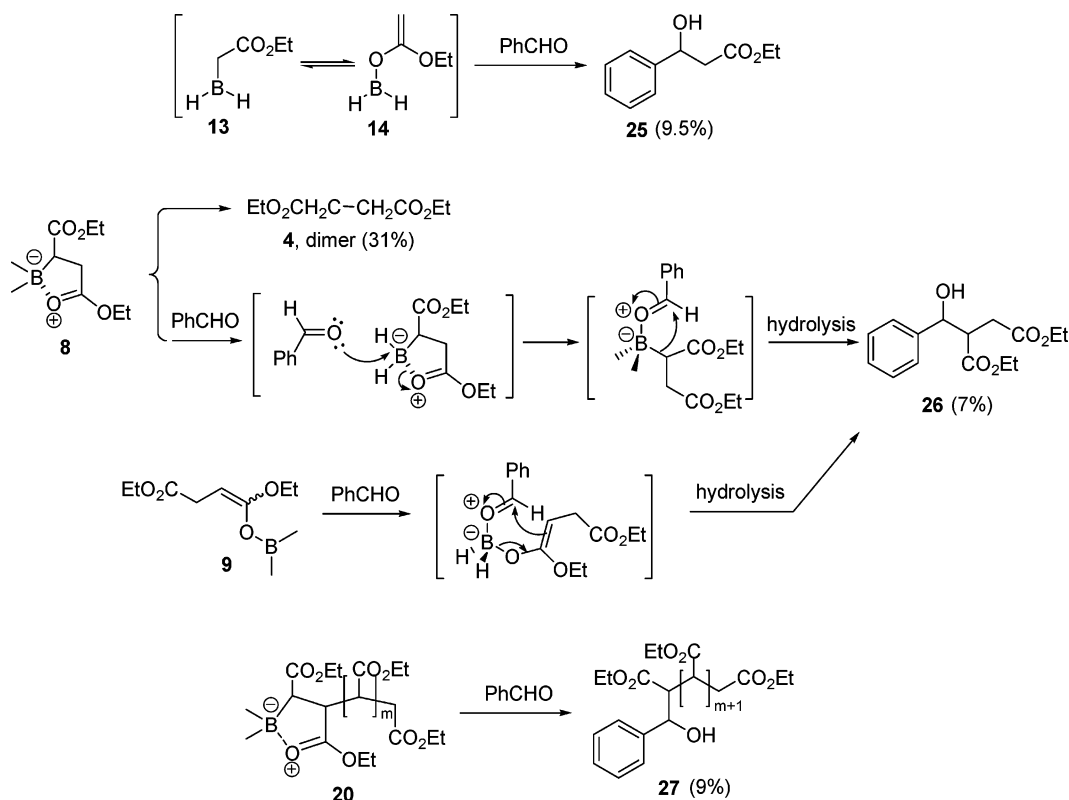
Scheme 7
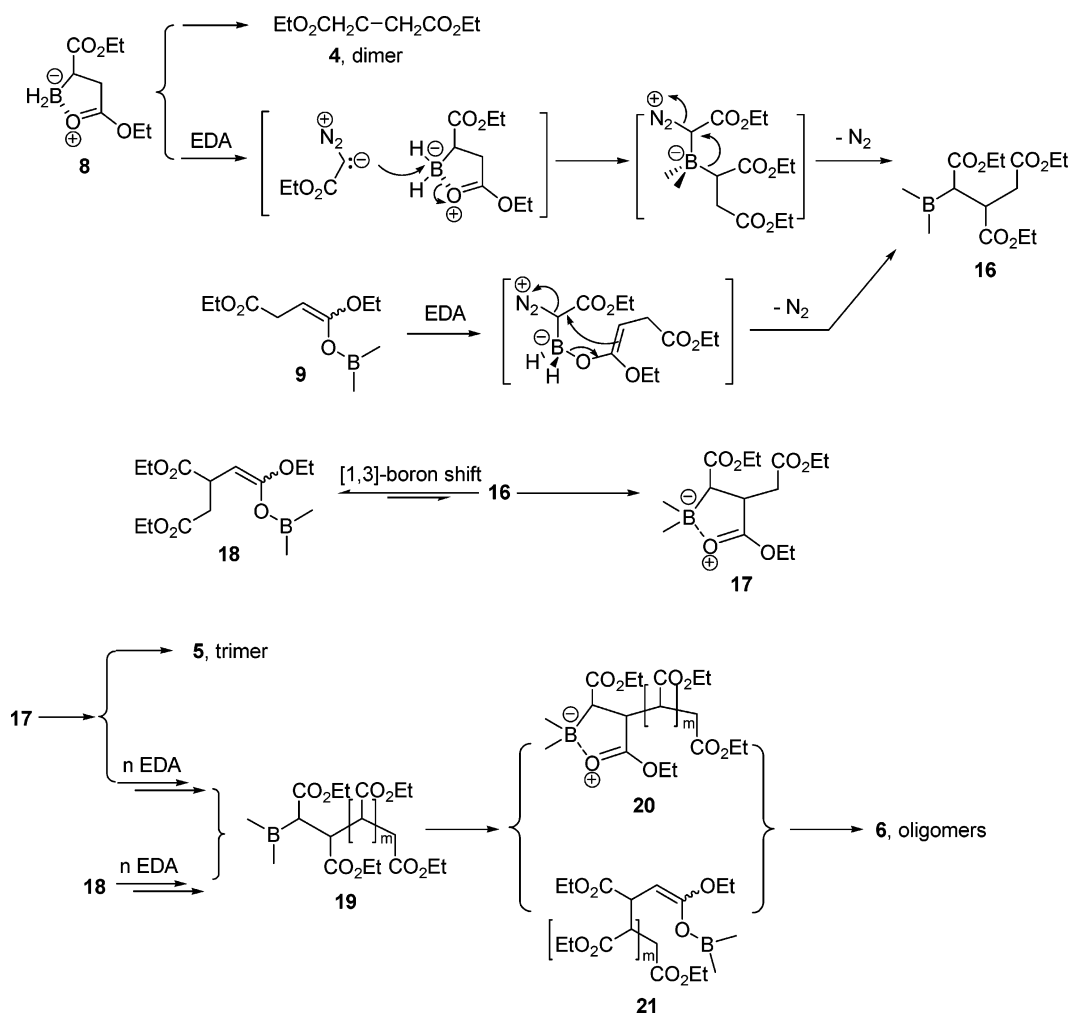
Scheme 8

benzaldehyde has been proposed by Ochicai and co-workers.[12e] As shown in Scheme 8, exposure of monocarbonyl iodonium ylide, generated from ester exchange of (*Z*)-(2-acetoxyvinyl)-λ^3-iodanes with EtOLi at −78 °C, to tri(*n*-butyl)boron was proposed to form α-boryl ketone **22**. It was also proposed that this α-boryl ketone **22** reacted with benzaldehyde at −78 °C to afford a mixture of aldol products **23** in 56% yield together with a ketone product **24** in 38% yield. As temperature increased, the yield of the aldol product **23** decreased while the yield of **24** increased, a result attributed to the low thermal stability of the *C*-boron enolate.

Since *C*-boron enolates are proposed to be the dominant intermediates in the reaction of EDA **1** and BH₃ **2**, we attempted to trap them with benzaldehyde (Scheme 9). EDA **1** (3 equiv)

was mixed with 1 equiv of borane **2** in CH₂Cl₂ in a dry ice−ice bath. After 5.5 h, 1.5 equiv of benzaldehyde were added. The reaction mixture was warmed to room temperature slowly over 8 h. After workup and flash chromatography, aldol product **25**, ethyl 2-hydroxy-2-phenylacetate,[22] derived from the reaction of *C*- and *O*-boron enolates **13** and **14** with benzaldehyde, was isolated in 10% yield. Doubly homologated *C*-boron enolates **8** or **9** reacted with benzaldehyde to afford a mixture of aldol product, diethyl 2-(hydroxyphenylmethyl)succinate **26**[23] (7%) and dimer **4** (31%). Aldol products (**27**) of the oligomer enolates, i.e., **20** or **21**, were isolated in a yield of 9%.[24] The trapping reaction was also carried out at a higher (room temperature)

(22) Data obtained from ¹H NMR spectroscopy, MS, and GC/MS were consistent with the structure of the known compound, ethyl 2-hydroxy-2-phenylacetate.
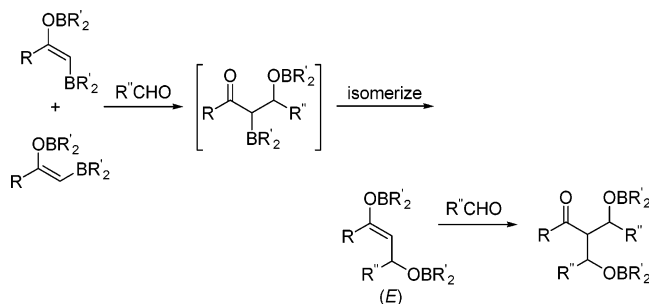
Scheme 9

Scheme 10
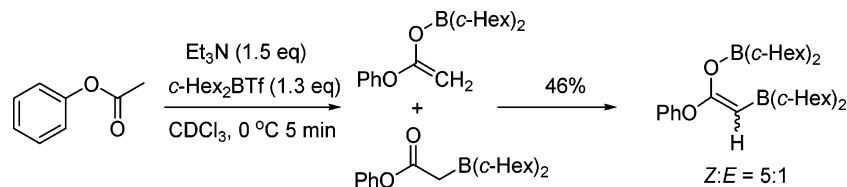
Scheme 11

and a lower (−78 °C) temperature, and the crude reaction mixture was analyzed by GC/MS and ¹H NMR. Consistent with the reported temperature effect of the aldol reaction of *C*-boron enolates,[14] the highest yield of aldol product **26** (16%) was

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(23) Mixture of isomers (1*R*,2*R*)/(1*R*,2*S*) = 2:1. Selected peaks of the mixture: ¹H NMR (500 MHz, CDCl₃) (1*R*,2*R*) δ 7.42−7.28 (m, 5H), 4.16 (d, *J* = 4.6 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 4.05 (q, *J* = 7.1 Hz, 2H), 3.19 (m, 1H), 2.73 (dd, *J* = 16.8, 9.4 Hz, 1H), 2.50 (dd, *J* = 16.8, 4.4, 1H), 1.28−1.12 (m, 6H); (1*R*,2*S*) δ 7.42−7.28 (m, 5H), 5.67 (d, *J* = 7.2 Hz, 1H), 4.31−4.20 (m, 4H), 3.32 (m, 1H), 3.00 (dd, *J* = 17.8, 8.9 Hz, 1H), 2.93 (dd, *J* = 17.8, 9.5 Hz, 1H), 1.37−1.25 (m, 6 H); [¹H, ¹H] COSY (1*R*,2*R*) 4.16−3.19, 3.19−2.73, 3.19−2.50, 2.73−2.50; (1*R*,2*S*) 5.67−3.32, 3.32−3.00, 3.32−2.93; ¹³C NMR (125 MHz, CDCl₃) (1*R*,2*R*) δ 173.45, 172.63, 141.25, 129.09, 128.02, 126.12, 73.61, 61.29, 60.93, 49.13, 31.25, 14.31, 14.29; (1*R*,2*S*) 174.40, 170.99, 138.29, 129.13, 125.63, 125.55, 82.48, 62.14, 48.95, 32.48, 14.32, 14.23.

observed at −78 °C, while the highest yield of dimer **4** (46%) was seen when the trapping reaction was carried out at room temperature.

These results confirm the presence of several important boron enolate intermediates proposed in the reaction of EDA and borane. The observation of product dimer is consistent with the initial accumulation of the stable *C*-boron enolate **8**, the proposed "*resting*" intermediate in the reaction mixture.

Mechanism 3. The Role of Doubly Borylated Enolates in the Reaction of EDA (1) and BH₃ (2). Doubly borylated enolates have been found to be a common side product in the reaction of carbonyl compounds such as acetate esters, acetic acid, dimethylacetamide, methoxyketone, and 3-acetyl-2-ox-azolidinone with *c*-Hex₂BOTf and triethylamine. An example is shown in Scheme 10.[14] In the enolboration reaction of phenyl acetate under *c*-Hex₂BOTF/Et₃N, doubly borylated enolates were generated *via* a proton-transfer process occurring between *O*- and *C*-boron monoenolates.

Doubly borylated enolates have been proposed to be the origin of double aldol products from a trapping experiment with aldehyde.[14] The proposed mechanism of formation involves reaction with 1 equiv of aldehyde to afford an α-boryl-β-

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(24) GPC (Gel Permeation Chromatography) data were obtained as a monomodel peak with M_n (number average molecular weight) = 412 and PDI (polydispersity index) = 1.16.
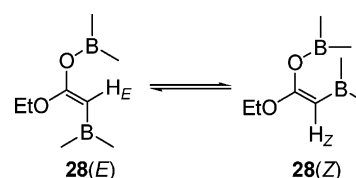
Scheme 12
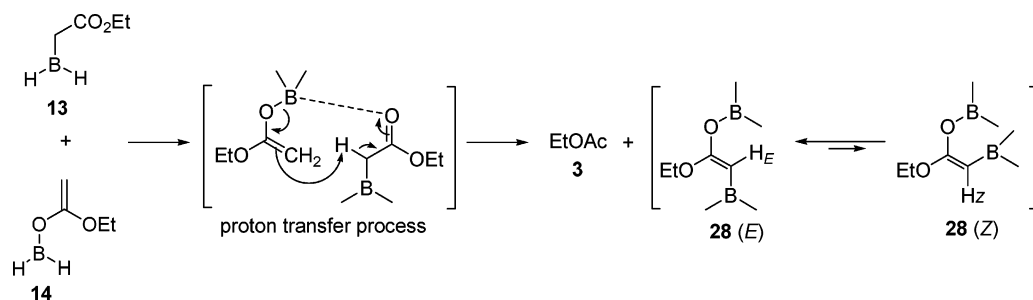
Scheme 13
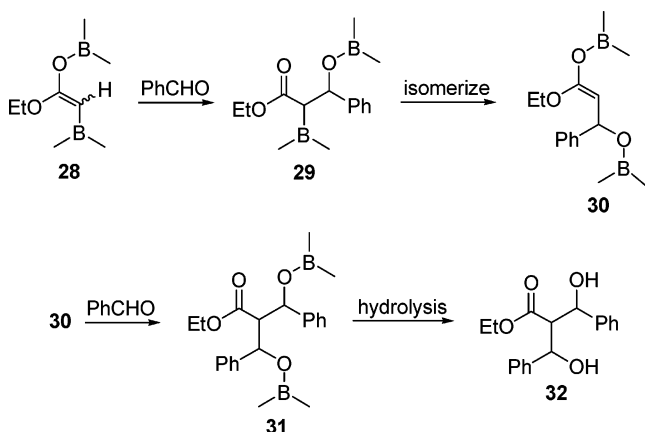
boryloxycarbonyl intermediate, which isomerizes to an *O*-boron enolate of *E* configuration. This then reacts with a second equivalent of aldehyde to give bis-aldol products (Scheme 11).

We were interested if related reactions might contribute to the chemistry of the reaction of borane **2** and EDA **1**. EDA **1** (7.6 equiv) was treated with borane **2** (1 equiv) in CD_2Cl_2 at -78 °C; ^{1}H NMR spectra were taken as the temperature of the reaction mixture increased from -20 °C to 25 °C in 5 °C increments. Two minor singlets were observed at 4.42 and 4.57 ppm, respectively (Figure 5). These two chemical shifts were consistent with the reported *Z* and *E* isomers (4.42 and 4.60 ppm) of doubly borylated enolates derived from the reaction of phenyl acetate with *c*-Hex$_2$BOTf/Et$_3$N.[14] It was also noted by Abiko and co-workers that, in the low-temperature enolization reaction of acetate esters with bulky ester groups, the config- uration of the initially formed doubly borylated enolate was the *E* configuration, and this product then isomerized to a *Z* isomer upon warming, indicating a facile interconversion between these two enolate isomers.[14] The slight kinetic preference for the *E* isomer was attributed to a lower steric hindrance compared to the *Z* isomer. Assuming a similar relative stability in the system
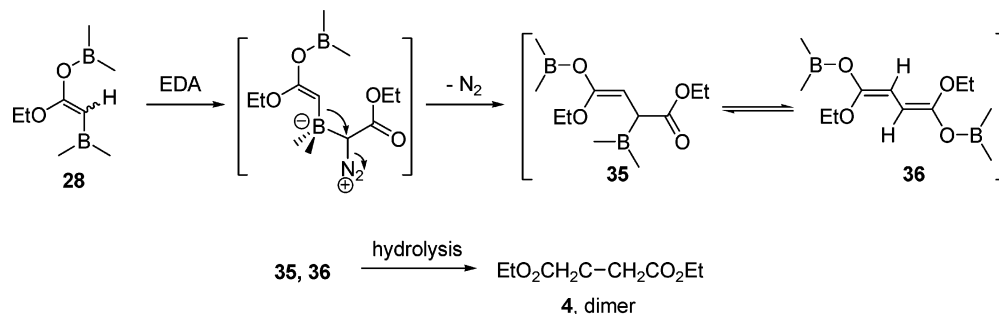
under investigation, we observed the intensity of the peak at 4.57 ppm decreased as the temperature increased (VT−NMR). We tentatively assign this peak to the *E* isomer of doubly borylated enolate **28** and the peak at 4.42 ppm to the *Z* isomer. The temperature-dependent ratio of the *E* and *Z* isomers is summarized in Table 5.

Formation of Doubly Borylated Enolate 28. A suggested mechanism for the formation of doubly borylated enolate **28** involves a proton transfer between *C*- (**13**) and *O*- (**14**) boron monoenolates (Scheme 12). This mechanism assumes the intermediacy of enolates **13** and **14**, whose presence in the reaction mixture has already been proposed. This reaction must compete with reaction of a second molecule of EDA.

Aldol Reaction of Doubly Borylated Enolate 28. In order to support the proposed formation of doubly borylated enolate **28** in the reaction of borane **2** and EDA **1**, we carefully examined the products from benzaldehyde trapping. Based on Abiko's results shown in Scheme 11, we anticipated that the reaction of enolate **28** with benzaldehyde would proceed by reaction with the first equivalent of aldehyde to afford the *C*-boron enolate **29** intermediate, which subsequently isomerizes to an *O*-boron enolate **30** of *E* configuration (Scheme 13). This then can react with a second equivalent of aldehyde to give bis-aldol products **32** after hydrolysis.

In the event, EDA **1** (3 equiv) and borane **2** (1 equiv) in CH_2Cl_2 at -20 °C were allowed to react for 5.5 h, followed by the addition of 1.5 equiv of benzaldehyde. The reaction mixture was warmed to room temperature overnight. After workup and flash chromatography, bis-aldol product **32**, ethyl 3-hydroxy- 2-(hydroxy(phenyl)methyl)-3-phenylpropanoate, derived from
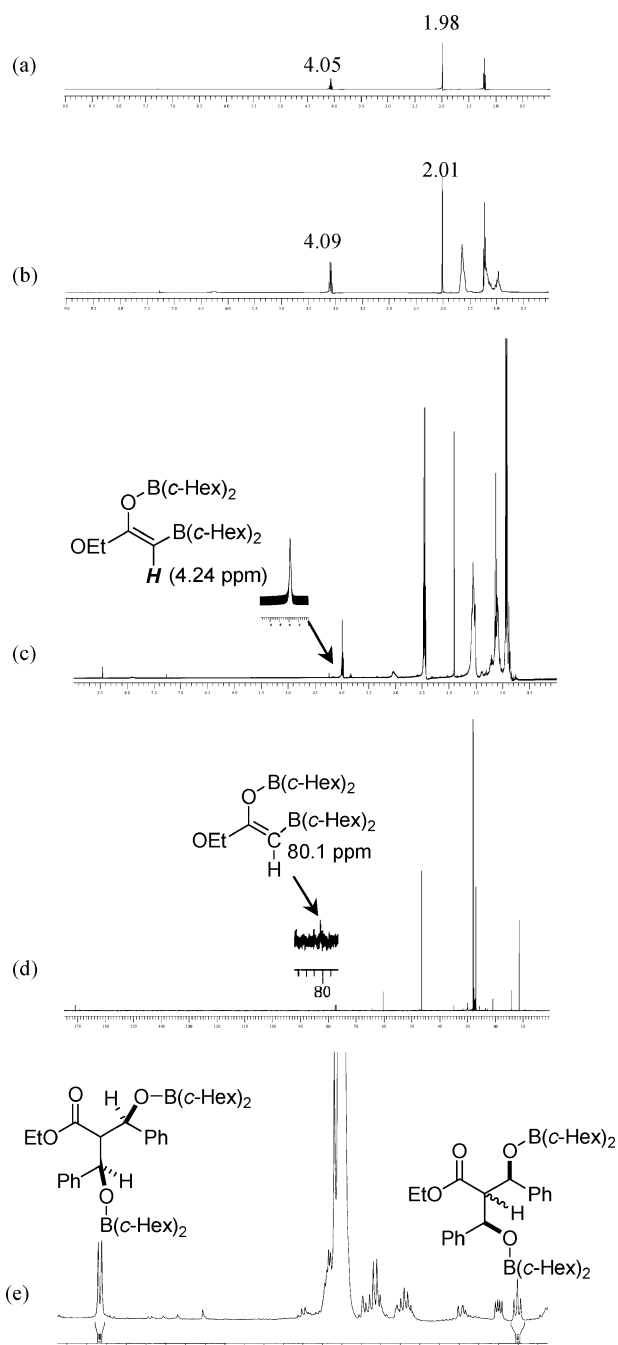
Scheme 14

Figure 6. (a) ^1H NMR of EtOAc; (b) ^1H NMR of EtOAc (1 equiv) + *c*-Hex₂BOTf (1 equiv); (c) ^1H NMR of EtOAc (1 equiv) + *c*-Hex₂BOTf (2 equiv) + Et₃N (3 equiv); (d) ^{13}C NMR of (c); (e) ^1H NMR of (c) + PhCHO (4 equiv).

the reaction of doubly borylated enolate **28** and benzaldehyde, was isolated in a yield of 1.5%.[25]

The identity of doubly borylated enolate **28** was established by comparison with an authentic sample (compound **34**) prepared by an independent route reported in ref 14a. EtOAc (1 equiv, Figure 6a) and *c*-Hex₂BOTf (1 equiv) were mixed in

CDCl₃ (0.67 M for EtOAc and 0.67 M for *c*-Hex₂BOTf) at room temperature, and the corresponding ^1H NMR spectrum showed a downfield chemical shift attributed to a complex formation (Figure 6b). Adding 3 equiv of Et₃N to the reaction mixture, followed by removal of an aliquot that was mixed with 1 equiv of *c*-Hex₂BOTf, generated the doubly borylated enolate **33** (Figure 6c and d). The [^1H, ^{13}C] HMQC spectrum demonstrated the presence of an alkene proton with a ^1H signal at 4.24 ppm, which was correlated to a ^{13}C signal at 80.1 ppm. Enolate **33** underwent the double aldol reaction with benzaldehyde to stereoselectively afford bis-aldol product **34** (Figure 6e).
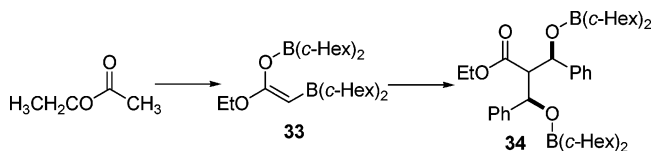

A ^1H NMR spectrum of the crude reaction mixture containing enolate **34** showed the characteristic signals of bis-aldol product **32**. This result adds additional support to the formation of doubly borylated enolate **28** in the reaction of EDA **1** and BH₃ **2**. It must be noted however that this is a very minor reaction pathway.

Formation of Oligomers 6. Doubly borylated enolate **28** could also contribute to the multiple products isolated from the reaction of EDA **1** and borane **2**. A possible mechanism is proposed in Scheme 14. The addition of EDA **1** to the Lewis acidic enolate **28** forms a borate complex. A subsequent 1,2-migration of an alkyl group with expulsion of N₂ would afford enolates **35** and **36**, which could hydrolyze to give dimer **4**. However, this reaction must be a very minor pathway.

Conclusions

BH₃ and trialkylborane (BR₃) have different chemical reactivities toward EDA. In the reaction of BH₃ with EDA, insertion of the second equivalent of EDA with concurrent alkyl group migration eventually produces a stabilized doubly homologated *C*-boron enolate **8**. This *C*-boron enolate intermediate is calculated to be 7.1 kcal/mol more stable than its corresponding *O*-boron enolate isomer **9**. Enolate **8** and its homologated species, *C*-boron enolates **17** and **20**, are proposed as the *resting* state for the intermediate in a novel oligomerization reaction of EDA.
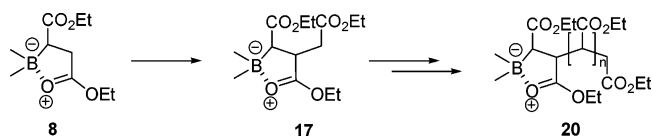
Evidence is also provided for the presence of doubly borylated enolate intermediates *E/Z*-**28**, which can also contribute to the formation of the observed products, but their role may be minor.

Supporting Information Available: Experimental details of enolate observation and computational modeling data. This material is available free of charge via the Internet at http://pubs.acs.org.

(25) Vieregge, H.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas Belg.* **1959**, *78*, 921–8. ^1H NMR (500 MHz, CDCl₃) δ 7.42–7.18 (m, 10H), 4.91 (d, *J* = 6.0 Hz, 2H), 4.02 (q, *J* = 7.1 Hz, 2H), 3.09 (t, *J* = 6.0 Hz, 1H), 0.95 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl₃) δ 173.0, 144.8, 128.7, 128.1, 126.0, 73.5, 61.2, 59.9, 14.0.