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Enolboration. 6. Dicyclohexyliodoborane, a Versatile Reagent for the Stereoselective Synthesis of Either *Z* or *E* Enolates from Representative Esters

by

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ABSTRACT

A smooth, rapid, quantitative and highly stereoselective synthesis of either *Z* or *E* enolates from representative esters has been achieved with dicyclohexyliodo-borane, Chx_2BI, in the presence of a suitable tertiary amine, such as triethylamine or *N,N*-diisopropylethylamine. A systematic investigation of the enolboration of ethyl propionate and ethyl phenylacetate, as model esters, by the various Chx_2BX and B-X-9-BBN reagents (X = OMs, I, and Br) established Chx_2BI as the preferred reagent in terms of yield and selectivity. Further study of representative esters (RCH_2COOR') with Chx_2BI established that both the steric requirements of the alkyl group (R) at the α-position and the alkoxy group (OR') play a significant role in controlling the enolate geometry. The steric requirements of the amine (R''_3N) also contribute considerably to the stereoselectivity of the reaction. The present study provides a simple procedure for the synthesis of *Z* or *E* enol borinates from representative esters (RCH_2COOR') using the combined stereodirecting effects of the alkyl (R) and the alkoxy (OR') groups. These enol borinates are highly reactive with aldehydes at temperatures as low as –78 °C and are exceptionally stereoselective even at 0 °C. In this exploratory study, the synthesis of stereoselective enolates from representative esters (RCH_2COOR') using Chx_2BI/R''_3N is discussed, with special emphasis on the effects of the steric requirements of R and OR' in controlling the enolate geometry.

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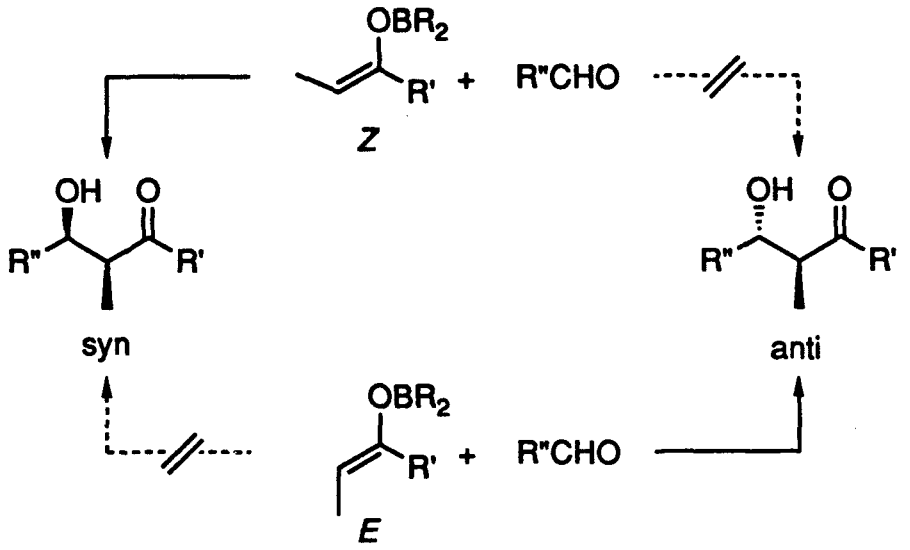
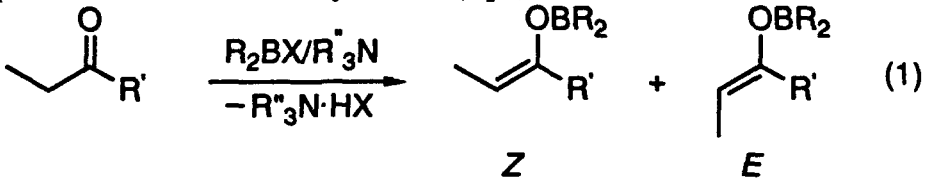
A smooth, rapid, quantitative and highly stereoselective synthesis of either *Z* or *E* enolates from representative esters has been achieved with dicyclohexyliodoborane, Chx_2BI, in the presence of a suitable tertiary amine, such as triethylamine or *N,N*-diisopropylethylamine. A systematic investigation of the enolboration of ethyl propionate and ethyl phenylacetate, as model esters, by the various Chx_2BX and B-X-9-BBN reagents (X = OMs, I, and Br) established Chx_2BI as the preferred reagent in terms of yield and selectivity. Further study of representative esters (RCH_2COOR') with Chx_2BI established that both the steric requirements of the alkyl group (R) at the α-position and the alkoxy group (OR') play a significant role in controlling the enolate geometry. The steric requirements of the amine (R''_3N) also contribute considerably to the stereoselectivity of the reaction. The present study provides a simple procedure for the synthesis of *Z* or *E* enol borinates from representative esters (RCH_2COOR') using the combined stereodirecting effects of the alkyl (R) and the alkoxy (OR') groups. These enol borinates are highly reactive with aldehydes at temperatures as low as –78 °C and are exceptionally stereoselective even at 0 °C. In this exploratory study, the synthesis of stereoselective enolates from representative esters (RCH_2COOR') using Chx_2BI/R''_3N is discussed, with special emphasis on the effects of the steric requirements of R and OR' in controlling the enolate geometry.

Enol borinates are valuable intermediates in organic synthesis.[1] Evans has established that *Z* enol borinates give syn aldols and *E* enol borinates give anti aldols stereoselectively[3] (Scheme I). Similar studies of stereoselection have also been described by other groups.[2,4-8]

Scheme I



Mukaiyama developed a simple methodology[2] for the generation of enol borinates, involving the reaction of ketones with R_2BX reagents containing a powerful leaving group (X = OTf) in the presence of suitable tertiary amines (eq 1).



The nomenclature of the enol borinate (*Z* or *E*) is based on the simplified rule[1a] proposed by Evans. For the C-1 enolate substituents R' and OM, the highest priority designation is always assigned to the OM group, independent of the metal. The normal priority designations of substituents at C-2 are maintained. Thus, irrespective of the nature of the R' group (H, alkyl, aryl, *N,N*-dialkyl, *N,N*-diaryl, *O*-alkyl, *O*-aryl, *S*-alkyl and *S*-aryl), the enol borinate is designated *Z* when CH_3 and OBR_2 are cis and *E* when CH_3 and OBR_2 are trans (eq 1). This simplified rule has been widely adopted in this field.[2-8] The major advantage of this designation is the simple

relationship between the stereochemistry of the enolate intermediate and the aldol product. In all cases, *Z* enol borinates give syn aldols and *E* enol borinates give anti aldols.

Many R_2BX reagents (X = OTf, OMs, I, Br and Cl) have now been examined for the enolboration of ketones.[2-8] However, very little is known of reagents which can enolize esters, a very important class of carbonyl compounds. The widely used R_2BOTf and R_2BCl reagents are ineffective for the enolization of esters.[3,6b] However, thioesters are readily enolized by these reagents.[3,4b,d,6a]

The lack of simple and effective organoboron reagents for the enolization of esters encouraged us to explore new reagents. Only one reagent, R^*_2BBr, had been reported in the literature[9] until we communicated that Chx_2BI was a simple, successful reagent for the enolization of esters and tertiary amides.[10] The utility of the R^*_2BBr was also demonstrated only for the *tert*-butyl esters, a special class of sterically hindered esters, to obtain the corresponding *E* enol borinates.[9] A systematic study of the enolboration of esters with a range of representative structures was, therefore, considered highly desirable to achieve an understanding of the factors influencing the enolboration of a wide range of substrates.

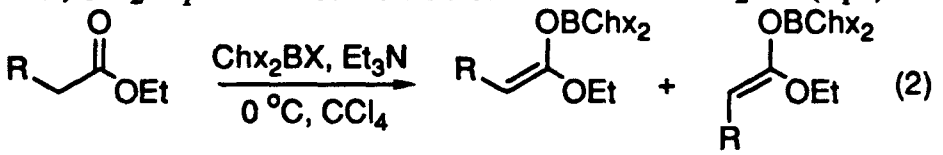
Results and Discussion

Since both dialkylboron triflate and chloride reagents could not enolize esters, Chx_2BX and B-X-9-BBN reagents with other leaving groups, such as mesylate, iodide and bromide, were examined using ethyl propionate, as a representative aliphatic ester, and ethyl phenylacetate, as a representative aromatic ester. From this study, Chx_2BI was selected as the most favorable reagent in terms of yield and selectivity. Representative esters (RCH_2COOR') of variable steric and/or electronic requirements of R (Me, Et, *i*-Pr, *t*-Bu and Ph) and OR' (OMe, OEt, O*i*-Pr, O*t*-Bu and OPh) were selected to achieve an understanding of their effects on the enolate geometry. Et_3N, a smaller amine, and *i*-Pr_2EtN, a bulkier amine, were employed to establish the effect of the amine on the enolate geometry.

Enolboration. Enolization was carried out in CCl_4 since this solvent permitted the direct recording of the ^1H NMR spectrum for the reaction mixture. ^1H NMR was employed to

determine the yield and the *Z/E* ratio of the enol borinate using both the well established internal standard method and the aldolization technique, respectively.[5-8,11] Enolization could also be carried out in other organic solvents, such as CH_2Cl_2, $CHCl_3$, toluene, pentane, and hexane. Wherever the subsequent aldolization was to be performed at –78 °C, the corresponding enolization was carried out in hexane.

Selection of the Best Reagent. A preliminary study with representative Chx_2BX and B_TX-9-BBN reagents (X = OMs, I, and Br) for the enolboration of ethyl propionate and ethyl phenylacetate revealed that both Chx_2BI and Chx_2BBr achieve the quantitative enolboration of esters. However, Chx_2BI proved to be more stereoselective than Chx_2BBr (eq 2).



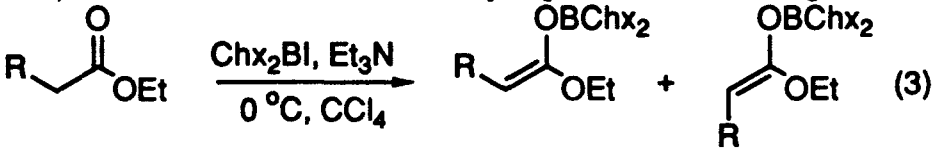
(2)

R	X	*Z* (%)	*E* (%)
Me	I	>97	<3
Me	Br	84	16
Ph	I	<3	>97
Ph	Br	7	93

The highly reactive Chx_2BI reagent generates *Z* enol borinate essentially exclusively from ethyl propionate and *E* enol borinate essentially exclusively from ethyl phenylacetate, while the corresponding bromide reagent yields a significantly larger amount of the other isomer. It is surprizing to note that the B-I-9-BBN reagent also failed to enolize esters. The stronger complexation between this smaller reagent and the amine used for the enolization may be responsible. Consequently, Chx_2BI was selected as the most favorable reagent for the stereoselective enolboration of esters.

Steric Requirements of R in RCH_2COOEt on the Enolate Geometry. The formation of *Z* enolate from ethyl propionate and *E* enolate from ethyl phenylacetate (eq 2) suggests a significant effect of the phenyl substituent at the α-position for the opposite *E* selectivity. To determine if this strong influence of the phenyl group is due to its steric or electronic effect and

to examine also the effect of the steric requirements of the alkyl group (R) at the α-position, a series of representative ethyl esters, RCH_2COOEt, with variable steric requirements of R (Me, Et, *i*-Pr and *t*-Bu) was selected for our further study (eq 3). The results are given in Table I.



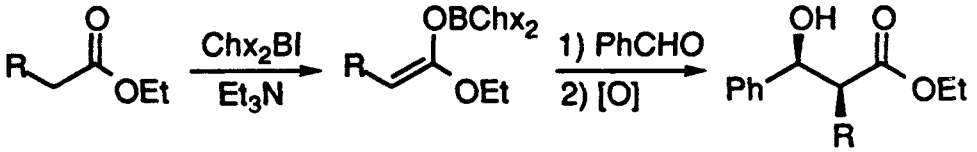
(3)

R = Me, Et, *i*-Pr, *t*-Bu *Z* *E*

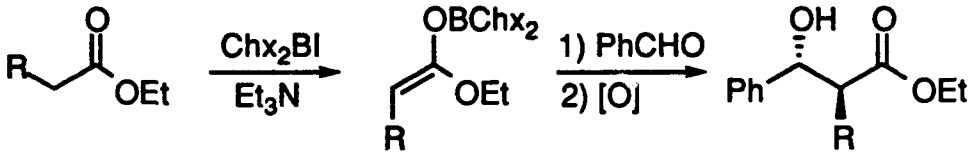
The results in Table I reveal a strong influence of the steric requirements of the R group on the enolate geometry. For example, when R = Me or Et, the smaller substituents, *Z* enolate is formed essentially exclusively. But when R = *i*-Pr or *t*-Bu, the more bulky substituents, the *E* enolate is obtained essentially exclusively. It is now possible to get either *Z* or *E* enolate merely by controlling the steric requirements of the α-substituent. This study, however, does not establish the precise nature of the influence of the phenyl substituent (steric or electronic) in favoring the formation of the *E* enolate geometry. Possibly, the extra stability of the trans enol borinate due in part to the effect of the extended conjugation.

The results provide a simple procedure to obtain the syn or the anti aldol from representative ethyl esters by varying the steric and/or electronic requirements of the α-substituent (Scheme II).

Scheme II



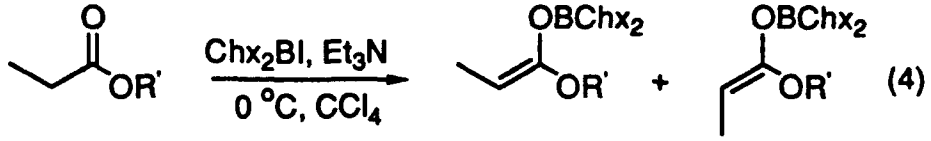
R = Me, Et *Z* syn (>97 %)



R = *i*-Pr, *t*-Bu, Ph *E* anti (>97 %)

Steric Requirements of OR' in EtCOOR' on the Enolate Geometry. The effect of the steric requirements of the carbonyl substituent (R' in EtCOR', EtCOOR', EtCOSR') in controlling the enolate geometry has been well established.[3-9] *E* enolates are provided essentially exclusively when R' = *t*-Bu. In the recent study of the enolization of esters with R^*_2BBr, various *tert*-butyl esters were selected to obtain the corresponding *E* enol borinates.[9] The sterically hindered aryloxy groups have also been used in the enolization of esters with LDA to achieve the synthesis of anti aldols.[12]

Even though there are a few reports indicating the effect of sterically hindered carbonyl substituents favoring the *E* enolate geometry, no systematic study has been reported to understand this important stereodirecting effect. Such an effect is especially valuable in the case of esters, since the synthesis of an ester with a suitable alkoxy group is usually quite easy by trans esterification. Accordingly, we undertook a detailed study of this valuable stereodirecting effect of the OR' group. Representative propionate esters with different OR' groups (OMe, OEt, O*i*-Pr, O*t*-Bu and OPh) of variable steric and/or electronic requirements were selected (eq 4) and the results are summarized in Table II.



OR' = OMe, OEt, O*i*-Pr, O*t*-Bu, OPh

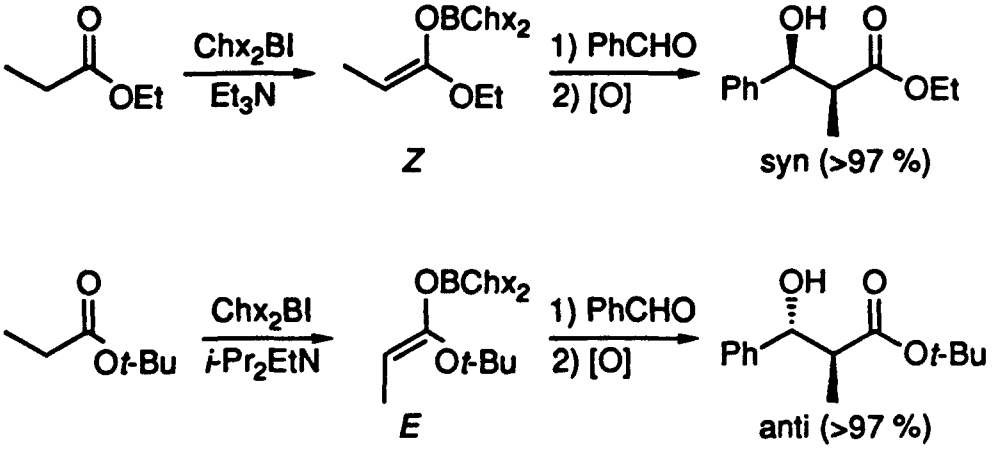
The results in Table II reveal the influence of the steric requirements of the OR' group in controlling the enolate geometry. As the steric requirements of the OR' group increases from OMe to O*t*-Bu, the amount of *E* enolate formed also increases. The propionate ester, with the smaller methoxy or ethoxy groups, gives essentially exclusive *Z* enolate, while that with the more bulky isopropoxy or *tert*-butoxy groups, gives a mixture of *Z* and *E* enolates. The effect of steric and/or electronic requirements of the phenyloxy group also contributes to the enolate geometry, providing *E* enolate predominantly in the enolboration of phenyl propionate.

Steric Requirements of Amine on the Enolate Geometry. It has been established in the enolboration of ketones with R_2BOTf[2,3,5a] and R_2BCl[5a,8] reagents that smaller amines favor the formation of *E* enolates and bulkier amines favor the formation of *Z* enolates. However, such data on the effect of the amine is not now known for the enolboration of esters.

In the present study, it was observed that those amines which are smaller than Et_3N, such as pyridine, 2,6-lutidine, Me_2EtN, and Et_2MeN, coordinate strongly with Chx_2BI and cause the reagent to be totally ineffective for enolization, while those amines which are bulkier than *i*-Pr_2EtN, such as *i*-Pr_3N, give very poor yield. Therefore, only Et_3N and *i*-Pr_2EtN with the suitable steric requirements have been examined in the present study. Incidentally, these are the two amines established for the quantitative and stereoselective enolboration of ketones with Chx_2BCl[8] and are also widely used with triflate reagents.[2-4,9]

A comparison of the results obtained with Et_3N and *i*-Pr_2EtN in Tables I and II reveals the role of the steric requirements of the amine on the enolate geometry. Unlike the previous trend observed for ketones, an opposite trend was realized, with the smaller Et_3N favoring the formation of *Z* enolates and the bulkier *i*-Pr_2EtN favoring the formation of *E* enolates. These studies reveal the possibility of proceeding from the synthesis of the syn to the anti aldol from alkyl propionate esters using the combined stereodirecting effects of the alkoxy group and the amine (Scheme III).

Scheme III



A similar effect of Et_3N and *i*-Pr_2EtN favoring the opposite enolate geometry, resulting in the selective synthesis of either syn or anti aldols, has also been reported for the aldolization of enol borinates derived from oxazolidinone with *n*-Bu_2BOTf and aromatic aldehydes.[13]

Effect of Temperature on the Enolate Geometry. The results in Tables I and II suggest that good stereocontrol can be achieved when the enolization is carried out at 0 °C. A small amount of the other isomer is also obtained at 25 °C. To get a good kinetic aldol stereosolection, aldolization is usually carried out at –78 °C.[2-9] In the present study, however, the results obtained with the aldolizations at –78 °C and at 0 °C are essentially the same, except for ethyl propionate with Chx_2BI/*i*-Pr_2EtN. This clearly shows that the enol borinates derived from these esters using Chx_2BI are highly reactive and exceptionally stereospecific. The required ^1H NMR data for the benzaldehyde aldol products are contained in Table III.

The yields are essentially quantitative with Chx_2BI/Et_3N at 0 °C with all esters examined, except for the sterically hindered *tert*-butyl propionate. With *i*-Pr_2EtN, the yields are somewhat lower, as compared with Et_3N. However, better yields were obtained by carrying the reaction out at 25 °C. Under all the experimental conditions tried, very low yields were obtained from phenyl propionate. It may be due to the +I effect of OPh group making the α-proton less acidic for enolization. While the effect of steric and electronic requirements of the alkoxy group (OR') may affect the yield considerably, that of the alkyl group (R) does not.

Under the experimental conditions, no cleavage of esters was observed. Ether solvents were avoided in the present study since the R_2BI reagents are known to cleave such solvents. A ^{11}B NMR study of Chx_2BI (δ 83 ppm) in ether suggested a slow but definite cleavage of ether, even at 0° C. About 25% borinate (Chx_2BOEt, δ 51.04 ppm), a cleaved product, was observed after 0.5 h and 89% was observed after 4 h at 0 °C. However, a model enolboration of CH_3CH_2COOMe in diethyl ether using the reverse addtion, Chx_2BI to Et_3N in ether followed by the ester, achieved quantitative and stereoselective (>97%) syn aldol. A white solid, due to the complexation of Chx_2BI and Et_3N, was observed when Chx_2BI was added to Et_3N in ether at 0

°C which may be either unreactive or less reactive towards ether. However, when the ester was added, the enolization occured with the concurrent formation and precipitation of $Et_3N{\cdot}HI$. The solid $Et_3N{\cdot}HI$ was collected by centrifugation, washed with ether, dried and weighed. An essentially quantitative yield was obtained. Two more experiments were also carried out by adding one equivalent of $PhCH_2OCH_3$ and $CH_3CH_2OCH_2CH_3$ respectively to the reaction mixture in the enolboration of CH_3CH_2COOMe with Chx_2BI/Et_3N using the standard procedure. Stereoselective syn aldol (≥97%) was obtained quantitatively. These studies suggest that ether can be used as a solvent, if desired, using reverse addition, and that substrates with protecting ether groups may also be enolized successfully without cleaving the protecting groups.

Conclusions

This is the first systematic, detailed study of the enolboration of esters. A preliminary investigation on the various Chx_2BX and B-X-9-BBN reagents (X = OMs, I, and Br) using ethyl propionate and ethyl phenylacetate established Chx_2BI as the best reagent in terms of yield and selectivity. A further study in the enolboration of representative esters, RCH_2COOR', with Chx_2BI reveals that the steric requirements of both R and OR' play a vital role in controlling the enolate geometry. A significant contribution from the steric requirements of amine was also observed. Unlike the trend observed for ketones, the esters showed the opposite trend, with the smaller Et_3N favoring the formation of *Z* enolates and the bulkier *i*-Pr_2EtN favoring the formation of *E* enolates. The present study leads to a simple procedure for the synthesis of essentially pure (>97%) *Z* or *E* enol borinates from representative esters, $RCHCOOOR'$, using the combined stereodirecting effects of the alkyl (R) and the alkoxy (OR') groups of the ester with a suitable amine. The remarkable reactivity, impressive stereoselectivity, ease of preparation and handling, and the greater stability combined to make Chx_2BI a highly versatile reagent for the stereoselective enolboration of esters.

Experimental Section

Materials. All glassware was thoroughly dried in an air oven, cooled and assembled under nitrogen for the experiments. Degassed, anhyd solvents, CH_2Cl_2, $CHCl_3$, CCl_4, toluene,

pentane, and hexane, were used in the present study. Et_3N and *i*-Pr_2EtN were distilled over CaH_2. Cyclohexene and all esters, except for isopropyl and *tert*-butyl propionate, were commercial products of the highest purity available. Borane-methyl sulfide (BMS), monobromoborane-methyl sulfide (MBBS) and 9-BBN were purchased from Aldrich and used as such for the reaction. The special experimental techniques used in handling air- and moisture-sensitive compounds have been described elsewhere.[14] All of the following experiments were conducted under a nitrogen atmosphere.

Synthesis of Various R_2BX (X = OMs, I and Br) reagents. The synthesis of various Chx_2BX and B-X-9-BBN reagents are described in our earlier paper.[7b] Only the synthesis of Chx_2BI, the preferred reagent for esters, is described below.

Synthesis of Chx_2BI reagent. A 250-mL two necked, round-bottom flask capped with rubber septums, a magnetic stirring bar, and a connecting tube attached to a mercury bubbler was kept at 0 °C and charged with Chx_2BH[6a] (26.7 g, 150.0 mmol) and CH_2Cl_2 (100 mL). Powdered iodine (19.1 g, 75.2 mmol), kept under a nitrogen atmosphere in a solid transfer tube attached to the side neck, was added in small installments with constant stirring. Hydrogen is evolved and should be safely vented. Addition of I_2 was repeated immediately after the previous addition had been consumed (disappearance of pink color). After adding all the I_2, the stirring was continued at 0 °C for 2 h and at 25 °C for 1 h. A pale pink color (due to the small excess of I_2) persists, which establishes completion of the reaction. Then the solvent was removed using a water aspirator (15–20 mm). Distillation of the concentrated mixture under vacuum yields pure, colorless Chx_2BI: bp 198–200 °C (1.25 mm); yield 80%; ^1H NMR ($CDCl_3$) 1.64–1.84 (10 H, m), 1.48–1.60 (2 H, m), 1.18–1.42 (10 H, m); ^{11}B NMR ($CDCl_3$) 84.52; ^{13}C NMR 42.29, 28.73, 26.65, 26.48.

Synthesis of Esters. Isopropyl and *tert*-butyl propionate esters were prepared from the commercially available propionyl chloride and the corresponding alcohol using the standard procedure. Distillation provided >99% GC pure isopropyl propionate (bp 108–109 °C) and *tert*-butyl propionate (bp 121 °C) and ^1H NMR spectra confirmed the structures.

Spectra. ^{1}H, ^{13}C, and ^{11}B NMR spectra were recorded on 300-MHz instrument and the chemical shift values are in δ (ppm) relative to TMS and $BF_3 \cdot OEt_2$ respectively.

General Procedure for the Enolization of Esters with Chx_2BX Reagents (X = I and Br). To a stirred solution of Chx_2BX (5.15 mmol), and R''_3N (5.15 mmol) in CCl_4 (17.0 mL), kept at the required temperature (0 °C or 25 °C), the ester (5.00 mmol) was added dropwise. The enol borinate was generated rapidly with concurrent formation and precipitation of $R''_3N \cdot HX$. An internal standard, benzene (0.50 mL, 1.00 M in CCl_4, 0.50 mmol), was added for quantification of the enolate by ^{1}H NMR analysis, except in the cases of ethyl phenylacetate and phenyl propionate, where the aromatic ring was used as the standard. The reaction mixture was stirred at the enolization temperature for 2 h and then transferred into a centrifuge vial using a double-ended needle (18 gauge). Centrifugation resulted in the separation of the enol borinate solution from the precipitated $R''_3N \cdot HX$. In representative cases, the solid $R''_3N \cdot HX$ has been collected, washed, dried, and weighed. Essentially quantitative yields were obtained. The enol borinate solution was then transferred into an NMR tube using a double-ended needle. The ^{1}H NMR analysis gave the extent of enolization and the ^{11}B NMR (borinate region, usually broad, around 50–56 ppm) also confirmed the formation of enol borinates. The ^{1}H NMR data of the olefinic protons of the various ester enolates were reported in our earlier communication.[10]

General Procedure for the Aldolization (at 0 °C) of the Enolates, Generated with Chx_2BBr/Et_3N, with PhCHO. To a solution of enolate in CCl_4 generated from 5.00 mmol of the ester using Chx_2BBr/Et_3N as described above, PhCHO (5.00 mmol) was added dropwise at 0 °C and the reaction mixture was stirred for 2–3 h. Then 10 mL of methanol was added to dissolve the precipitated $Et_3N \cdot HBr$. To this homogeneous mixture at 0 °C, 1.70 mL of H_2O_2 (30%) was added dropwise. The resulting mixture was stirred at 25 °C for 3–4 h. The solvent and methanol were then removed by a water aspirator (15–20 mm) and the reaction mixture was extracted with ether, washed with water, and then dried over anhyd Na_2SO_4. The solvent was removed and the products were analyzed as such by ^{1}H NMR to determine the syn/anti ratio.

General Procedure for the Aldolization (at 0 °C) of the Enolates, Generated with $Chx_2BI/R"_3N$, with PhCHO. To a solution of enolate in CCl_4 generated from 5.00 mmol of the ester using $Chx_2BI/R"_3N$ as described above, PhCHO (5.00 mmol) was added dropwise at 0 °C and the reaction mixture was stirred for 2–3 h. Then 10 mL of methanol was added to dissolve the precipitated $R"_3N{\cdot}HI$. To this homogeneous mixture at 0 °C, 2.50 mL of H_2O_2 (30%) was added dropwise. Pink color was observed due to the formation of iodine. [Oxidation of the reaction mixtures containing the aldol borinates produced from the Chx_2BI requires excess H_2O_2 (2.50 mL in place of 1.70 mL used for Chx_2BBr). The excess hydrogen peroxide is necessary because the iodide, present as $R"_3N{\cdot}HI$, also gets oxidized to iodine]. The resulting mixture was stirred at 25 °C for 3–4 h. The solvent and methanol were then removed by a water aspirator (15–20 mm) and the reaction mixture was extracted with ether. The dark-colored ether solution containing iodine was washed with dilute sodium thiosulfate solution and then with water. The colorless ether solution was dried over anhyd Na_2SO_4, the solvent was evaporated and the products were analyzed as such by ^1H NMR to determine the syn/anti ratio.

General Procedure for the Aldolization (at –78 °C) of the Enolates, Generated with $Chx_2BI/R"_3N$, with PhCHO. To a solution of enolate in hexane generated from 5.00 mmol of the ester using $Chx_2BI/R"_3N$ as described above, PhCHO (5.00 mmol) was added dropwise at –78 °C. The reaction mixture was stirred at this temperature for 2–3 h and then allowed to warm slowly to room temperature overnight. Then 10 mL of methanol was added at 0 °C to dissolve the precipitated $R"_3N{\cdot}HI$. To this homogeneous mixture at 0 °C, 2.50 mL of H_2O_2 (30%) was added dropwise. The resulting mixture was stirred at 25 °C for 3–4 h. The solvent and methanol were then removed by a water aspirator (15–20 mm) and the reaction mixture was extracted with ether. The dark-colored ether solution was washed with dilute sodium thiosulfate solution and then with water. The colorless ether solution was dried over anhyd Na_2SO_4, the solvent was evaporated and the products were analyzed as such by ^1H NMR to determine the syn/anti ratio.

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Supplementary Material Available: ^{1}H, ^{11}B, ^{13}C NMR spectra of Chx_2BI, ^{11}B NMR study of Chx_2BI in diethyl ether, and ^{1}H NMR spectra of the benzaldehyde aldols of the representative ethyl esters, RCH_2COOEt, and propionate esters, CH_3CH_2COOR' (15 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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Table I. Effect of Steric Requirements of R on the Enolate Geometry in the Stereoselective Enolboration of Representative Ethyl Esters, RCH_2COOEt, with Chx_2BI/R''_3N[a,b]

ester	amine	temperature (°C) enol.	aldol.	yield[c,d] (%)	stereochemistry (%)[e] syn /[Z]	anti/[E]
$MeCH_2COOEt$	Et_3N	0	0	96	>97	<3
		0	–78	96	94	6
		25	25	97	88	12
$MeCH_2COOEt$	*i*-Pr_2EtN	0	0	70	>97	<3
		0	–78	65	43	57
		25	25	93	79	21
$EtCH_2COOEt$	Et_3N	0	0	95	95	5
i-$PrCH_2COOEt$	Et_3N	0	0	94	<3	>97
t-$BuCH_2COOEt$	Et_3N	0	0	84	<3	>97
$PhCH_2COOEt$	Et_3N	0	0	96	<3	>97
		0	–78	95	3	97
		25	25	97	10	90
$PhCH_2COOEt$	*i*-Pr_2EtN	0	0	95	<3	>97
		0	–78	95	12	88
		25	25	96	27	73

[a]Enolizations were carried out in CCl_4 and in hexane when the corresponding aldolizations were carried out at 0 °C (or at 25 °C) and at –78 °C respectively. [b]In cases where the spectrum shows only one major isomer, we have indicated the minor isomer to be <3% since such small peaks may be lost in the background. [c]Determined by ^1H NMR. [d]The yields were also confirmed by collecting and weighing the precipitated $R''_3N{\cdot}HI$. [e]Z/E ratio was determined on the basis of the syn/anti ratio of their corresponding benzaldehyde aldol products.

Table II. Effect of Steric Requirements of OR' on the Enolate Geometry in the Stereoselective Enolboration of Representative Propionate Esters, EtCOOR', with Chx_2BI/R''_3N[a]

ester	amine	temperature (°C) enol.	aldol.	yield (%)	stereochemistry (%) syn /[Z]	anti/[E]
EtCOOMe	Et_3N	0	0	97	>97	<3
	i-Pr_2EtN	0	0	75	>97	<3
EtCOOEt	Et_3N	0	0	96	>97	<3
	i-Pr_2EtN	0	0	70	>97	<3
EtCOO*i*-Pr	Et_3N	0	0	90	86	14
	i-Pr_2EtN	0	0	65	64	36
EtCOO*t*-Bu	Et_3N	0	0	60	59	41
		0	–78	57	51	49
		25	25	87	66	34
EtCOO*t*-Bu	*i*-Pr_2EtN	0	0	57	3	97
		0	–78	54	10	90
		25	25	74	19	81
EtCOOPh	Et_3N	0	0	36	25	75
		0	–78	35	25	75
		25	25	55	27	73
EtCOOPh	*i*-Pr_2EtN	0	0	32	69	31
		0	–78	33	71	29
		25	25	50	80	20

[a]Refer to footnotes *a-e* of Table I.

Table III. ^{1}H NMR Data of the Carbinol Protons of the Syn and Anti Aldols

	^{1}H NMR[a] (δ ppm)	
ester	syn	anti
$MeCH_2COOEt$	5.01 (d, J = 4.95 Hz)	4.72 (d, J = 8.67 Hz)
$EtCH_2COOEt$	4.91 (d, J = 5.76 Hz)	4.82 (d, J = 8.40 Hz)
i-$PrCH_2COOEt$[b]	4.97 (d, J = 6.63 Hz)	4.96 (d, J = 5.49 Hz)
t-$BuCH_2COOEt$[b]	4.98 (d, J = 10.17 Hz)	5.06 (d, J = 3.57 Hz)
$PhCH_2COOEt$	5.26 (d, J = 7.92 Hz)	5.15 (d, J = 9.27 Hz)
EtCOOMe	5.07 (d, J = 4.62 Hz)	4.73 (d, J = 8.55 Hz)
EtCOO*i*-Pr	5.04 (d, J = 4.62 Hz)	4.72 (d, J = 8.40 Hz)
EtCOO*t*-Bu	4.94 (d, J = 5.19 Hz)	4.71 (d, J = 8.85 Hz)
EtCOOPh	5.16 (d, J = 5.43 Hz)	4.88 (d, J = 8.73 Hz)

[a]Corresponds to the benzylic protons of the benzaldehyde aldol products.

[b]$J_{\alpha\beta}$ is larger for the syn aldol than for the corresponding anti aldol.[11]