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Catalytic Enantioselective Three-Component Hetero-[4+2] Cycloaddition/Allylboration Approach to α-Hydroxyalkyl Pyrans: Scope, Limitations, and Mechanistic Proposal

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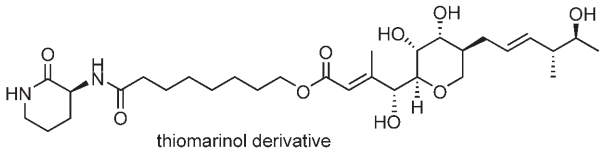
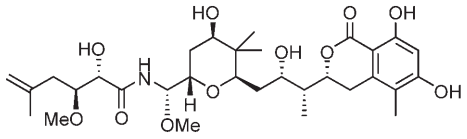
Abstract: This article describes the design and optimization of a catalytic enantioselective three-component hetero-[4+2] cycloaddition/allylboration reaction between 3-boronoacrolein, enol ethers, and aldehydes to afford α-hydroxyalkyl dihydropyrans. The key substrate, 3-boronoacrolein pinacolate (**2**) was found to be an exceptionally reactive heterodiene in the hetero-[4+2] cycloaddition catalyzed by Jacobsen's chiral Cr^{III} catalyst **1**. The scope and limitations of this process were thoroughly examined. The adduct of 3-boronoacrolein pinacolate and ethyl vinyl ether was obtained in high yield and with over 95% enantioselectivity. This cyclic α-chiral allylboronate adds to a very wide variety of aldehyde substrates, including unsaturated aldehydes and α-chiral aldehydes to give diastereomerically pure products. Acyclic 2-substituted enol ethers can be employed, in which case the catalyst promotes a kinetically selective reaction that favors *Z* enol ethers over the *E* isomers. Surprisingly, 3-boronoacrolein pinacolate was found to be a superior heterodiene than ethyl (*E*)-4-oxobutenoate, and a mechanistic interpretation based on a possible [5+2] transition state is proposed.

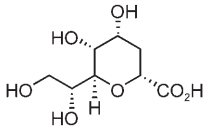
Keywords: asymmetric catalysis · boron · cycloaddition · enol ethers · pyrans

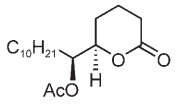
Introduction

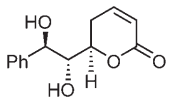
Myriad natural products contain substituted pyran units.[1] These substances display a broad range of biological properties, including antibiotic and anticancer activity. The pyran units embedded within these natural products present a very diverse range of substitution patterns. Consequently, there is significant interest in the development of new synthetic methods to access polysubstituted pyran derivatives in optically pure form.[2] In particular, α-hydroxyalkyl pyrans constitute one of the most common motifs amongst all the dif-











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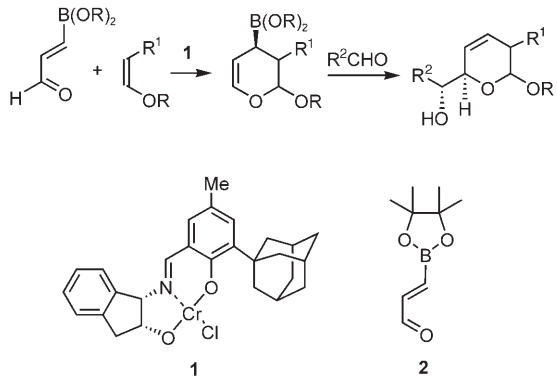
ferent structural varieties of pyrans found in nature. Notable examples include thiomarinol antibiotics[3] and the anticancer agent psymberin.[4]

Here, we report our joint efforts in the development and optimization of a three-component, catalytic enantioselective hetero-[4+2] cycloaddition/allylboration method to construct α-hydroxyalkylated dihydropyrans.[5] We envisioned that 3-boronoacrolein esters could be viable substrates in inverse electron demand hetero-[4+2] cycloadditions with enol ethers (Scheme 1). The known and stable unsaturated aldehyde **2** represented an ideal model heterodiene to test

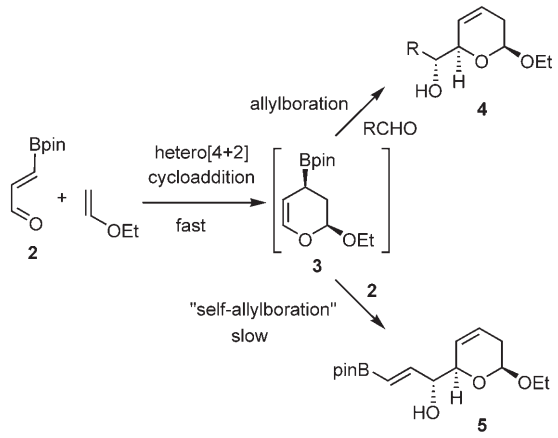


Scheme 1.

this idea.[6] At the outset, the reactivity of 3-boronoacrolein pinacolate (**2**) with ethyl vinyl ether was successfully explored in the presence of [Yb(fod)$_3$] (fod = 6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionate.[7] As in the carbocylic variant,[8] the intermediate cyclic allylboronate can be further reacted with an added aldehyde in a sequential fashion to provide α-hydroxyalkyl dihydropyrans as final products. The asymmetric version of this sequence, performed in the presence of Jacobsen's tridentate (Schiff base)chromium(III) complex **1**,[9] would constitute the first catalytic enantioselective approach to the compelling class of cyclic α-chiral allylboronates.[10] Furthermore, the realization that this three-component sequence could be performed as an operationally simple one-pot reaction adds significant value to this strategy. Indeed, multicomponent reactions are particularly attractive because of their intrinsic advantages of operational simplicity, step-economy, and high degree of convergence.[11] Recently, this one-pot three-component reaction was successfully applied to the enantioselective total syntheses of a number of natural products, namely, the mosquito oviposition pheromone (5*R*,6*S*)-6-acetoxy-5-hexadecanolide,[5a] goniodiol,[12] and a thiomarinol antibiotic.[13] This article presents a thorough study of the scope and limitations of this methodology for use in the synthesis of complex pyran-containing natural products.

Results and Discussion

Optimization of the hetero-[4+2] cycloaddition: Initially, our design of the hetero-[4+2] cycloaddition/allylboration strategy with diene **2** led to worries that the latter could undergo an undesired "self allylboration" with the intermediate allylboronate **3**, and give product **5** instead of the desired allylation product **4** from a second aldehyde (Scheme 2,

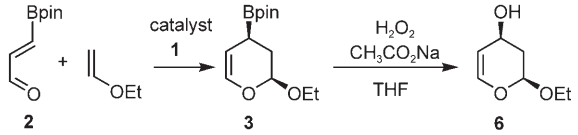


Scheme 2.

pin = pinacolate). To circumvent this potential problem, a fast cycloaddition step that would occur at a lower temperature than that required for the allylboration step was needed.

Initial optimization studies focused on both the conversion and enantioselectivity in the formation of cyclic allylboronate **3** by a hetero-Diels–Alder reaction between ethyl vinyl ether and 3-boronoacrolein pinacolate **2** catalyzed by chiral complex **1** (Table 1). The enantiomeric excess (*ee*)

Table 1. Optimization of the hetero-[4+2] reaction of **2** and ethyl vinyl ether catalyzed by **1**.[a]

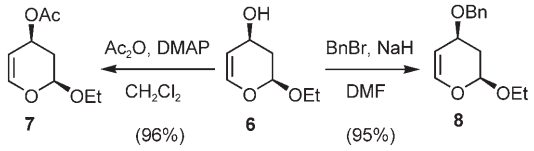


Entry	Catalyst loading [mol%][b]	Additive	conversion [%][c]	*ee* [%][d]
1[e]	5	BaO	100	< 50
2	5	BaO	100	95
3	5	4 Å m.s.	100	96
4	1	4 Å m.s.	100	96
5	0.5	4 Å m.s.	100	96
6	0.3	BaO	100	96

[a] pin = pinacolate, m.s. = molecular sieves. Conditions: distilled **2** (1 M, 2 mmol, 0.36 g), vinyl ethyl ether (1.9 mL), RT, 14 h. [b] Relative to **2**. [c] Measured by the integration of representative signals by ^{1}H NMR spectroscopy. [d] Measured by chiral HPLC (Chiralpak AD-RH column). [e] With nondistilled **2**.

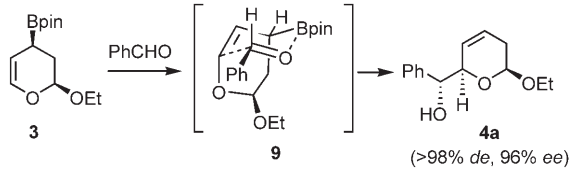
was measured for the corresponding secondary alcohol product **6** following oxidation/hydrolysis of the boronate substituent with retention of stereochemistry.[14] The *ee* can also be determined directly for the cycloadduct by GC analysis using a chiral stationary phase.

We quickly realized that the purity of the key substrate 3-boronoacrolein pinacolate (**2**) is crucial. When using heterodiene **2** prepared in two steps from 3,3-diethoxy-1-propyne with our recently described distillation-free procedure,[6] only a low *ee* could be obtained under the standard conditions[9] with 5 mol% of catalyst **1** and BaO as the dehydrating agent for 14 h in neat ethyl vinyl ether (entry 1). Although the ^{1}H NMR spectrum of substrate **2** purified by distillation showed no noticeable difference when compared with that of a sample obtained as before, the enantioselectivity was drastically improved (entry 2). The *ee* was equally high with molecular sieves instead of BaO as the dehydrating agent (entry 3). The stereoselective formation of product **6** indicates that the *endo* cycloadduct **3** had been formed as predicted.[9] We noted that the enantioselectivity was strongly dependent on the reaction temperature and to ensure a reproducibly high (>95%) enantioselectivity, it was crucial that the cycloaddition was carried out at or below 23°C. Our next goal was to reduce the catalyst loading (entries 4–6), and we were glad to observe that both conversion and *ee* remained very high with as low as 0.3 mol% of complex **1**. Further reduction of catalyst loading slowed down the cycloaddition and allowed competitive formation of significant amounts of side-product **5** from the allylboration between **3** and **2** (Scheme 2). In comparison with the loading values of 5–10 mol% previously reported for a wide range of α,β-unsaturated aldehydes,[9] this result suggests that 3-boronoacrolein pinacolate (**2**) is a particularly favorable heterodiene in this reaction. It is noteworthy to emphasize that it can also serve as a valuable surrogate for 3-acyloxylacroleins, which were reported to afford the synthetically useful 4-hydroxy dihydropyran derivative with lower selectivity (89% *ee*).[9] Here, intermediate **6** was isolated in a 81% yield and with 96% *ee* from the hetero-[4+2] cycloaddition/oxidation reaction of **2**. Routine transformations of the hydroxyl group of **6** led to other intermediates (e.g., **7** and **8**) that could be useful in allylic substitution chemistry (Scheme 3, DMAP = 4-dimethylaminopyridine).



Scheme 3.

Optimization of the three-component process: Following optimization of the hetero-Diels–Alder reaction, the second step in the three-component sequence, the allylboration, was optimized by using benzaldehyde (Scheme 4, *de* = diastereomeric excess). To this end, hetero-Diels–Alder adduct **3** was isolated by distillation or by using a short column of silica gel. Allylboration reactions are usually carried out in noncoordinating solvents like dichloromethane and toluene. To our surprise, we found that the reactivity of allylboronate **3** was not attenuated when using ethyl vinyl ether as the solvent.[15] The addition occurs readily at a relatively low temperature (40°C) and affords α-hydroxybenzyl dihydropyran **4a** as a single diastereomer. This outcome is consistent with the expected Zimmerman–Traxler transition structure **9** involving *anti* coordination of the aldehyde to the boronyl group, which is positioned in a pseudo-axial orientation with respect to the pyran ring (Scheme 4). A measurement of the enantiomeric purity of **4a** confirmed that allylboronate **3** suffers no loss of stereochemical integrity in its additions to aldehydes. On a practical standpoint, we found that it was not necessary to purify intermediate **3** and eliminate residual catalyst **1** when used only in a 1 mol% loading. Thus, this hetero-[4+2] cycloaddition/allylboration sequence can be performed in a "one-pot" procedure from **2** by simple addition of the aldehyde after completion of the cycloaddition step. In contrast to recent reports describing the acceleration of allylborations by certain Lewis acids,[16] our control experiments showed that there is no metal-promoted acceleration nor any retardation effect in the additions of **3** when using catalyst **1**.

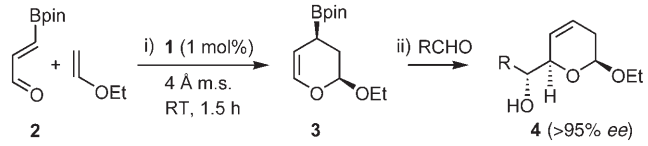


Scheme 4.

Scope of the carbonyl substrate: We first explored the generality of the allylboration with nonchiral aldehydes. As detailed in Table 2, suitable aldehyde substrates include aromatic and α,β-unsaturated aldehydes with different electronic characteristics, and aliphatic aldehydes including functionalized ones, such as TBDMSOCH$_2$CHO (entry 9, TBDMS = *tert*-butyl dimethylsilyl). All these different aldehydes afforded dihydropyran products **4a**–**4p** in high yields, and the adducts were obtained as pure diastereomers according to ^{1}H NMR spectroscopic analysis of crude isolates. The concentration of the allylboration reaction has an important impact. Provided the aldehyde is a liquid, it was found that unactivated aldehydes afford significantly higher yields with shorter reaction times when reactions were performed as neat mixtures. Importantly, reactions with electron-poor α,β-unsaturated aldehydes required a change of solvent to dichloromethane to avoid a competing hetero-[4+2] cycloaddition of these aldehydes with ethyl vinyl ether (e.g., entry 12).

The possibility of using functionalized α-chiral aldehydes is particularly attractive in the context of natural product synthesis. By using both enantiomers of aldehyde **10** as a model system, and pure isolated allylboronate (*S*)-**3**, we found that the additions are subject to a strong reagent control effect dominated by the α-chiral allylboronate **3** (Scheme 5, TBDPS = *tert*-butyl diphenylsilyl). The (*S*)-enan-

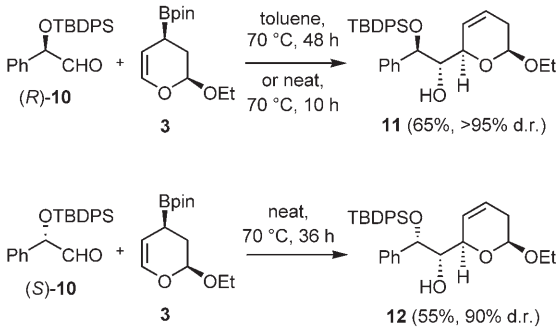
Table 2. Substrate scope for the catalytic enantioselective three-component hetero-[4+2] cycloaddition/allylboration reaction.[a]



2 3 4 (>95% *ee*)

Entry	Aldehyde [R]	*T* [°C]	*t* [h]	Product[b]	Yield [%][c]
1	C_6H_5	40	24	**4a**	82
2	4-NO_2-C_6H_4	25	24	**4b**	92
3	4-MeO-C_6H_4	45	24	**4c**	81
4	4-Cl-C_6H_4	40	24	**4d**	77
5	4-F-C_6H_4	40	24	**4e**	75
6	$PhCH_2$	45	24	**4f**	82
7	$PhCH_2CH_2$	45	24	**4g**	74
8	$(CH_3)_2CHCH_2$	45	24	**4h**	81
9	$TBDMSOCH_2$	45	24	**4i**	82
10	$C_{10}H_{21}$	45	24	**4j**	89
11[d]	$(CH_3)_2CH$	50	18	**4k**	78
12[e]	(*E*)-4-NO_2-C_6H_4CH=CH	45	24	**4l**	81
13[d]	(*E*)-CH_3CH=$(CH_3)C$	50	48	**4m**	76
14[d]	(*E*)-EtO_2CCH=$(CH_3)C$	25	24	**4n**	88
15[d]	CH_2=CH	25	24	**4o**	73
16[d]	$CH_3(CH_2)_4CC$	40	18	**4p**	86

[a] pin = pinacolate. Conditions: distilled **2** (1 M, 2 mmol, 0.36 g), vinyl ethyl ether (1.9 mL), with catalyst **1** (1 mol%), RT, 1.5 h, followed by the addition of the aldehyde (2.0 equiv) and reaction at the indicated temperature and time. [b] Diastereomerically pure. Retention of the absolute stereochemistry in the allylboration of **3** is assumed based on **4a** (see Experimental Section). [c] Unoptimized yields of products isolated after flash chromatography. [d] Ethyl vinyl ether was evaporated after step i), and step ii) was carried out without solvent. [e] Ethyl vinyl ether was evaporated after step i) and replaced with dichloromethane.

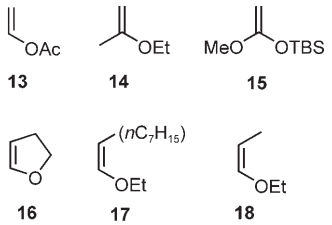


Scheme 5.

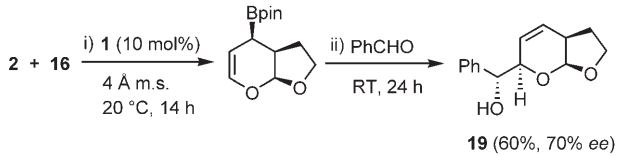
tiomer of **3** reacted with two equivalents of (*R*)-**10** in toluene at 70 °C for 48 h to give the diastereomerically pure adduct **11** in 78% yield. To decrease the time of the reaction and the amount of aldehyde, the reaction was also carried out without solvent. After ten hours at 70 °C and by using only one equivalent of **10**, compound **11** was obtained in 65% yield. The configurations of the four stereocentres were determined by X-ray crystallographic analysis, which is in agreement with Felkin–Anh selectivity.[17] The enantiomer (*S*)-**10** reacts much slower (36 h, 70 °C, neat, 55%) to form the major adduct **12** (90% *de*) with the same configuration at the newly formed center. The examples illustrated in Scheme 5 raise the possibility that an efficient kinetic resolution of racemic aldehydes could be possible. It is also worthy to note that, by using the same experimental conditions, the (*R*)- or (*S*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanal, $PhCH_2$-CH(NHBoc)-CHO, gave only untractable mixtures of products, probably due to the low reactivity of these aldehydes and their thermal decomposition in the allylation step.

Scope of the enol ether: A number of substituted derivatives were tested as dienophiles. Enol acetate **13** failed to react, confirming the need for an alkoxy substituent, as observed previously.[9] Likewise, 1-substituted enol ethers **14** and **15** did not provide the desired products of hetero-[4+2] cycloaddition.

One of the main appeals of this tandem reaction method is the possibility that 2-substituted enol ethers, such as cyclic derivatives, can be used. It is known, however, that 2-substituted enol

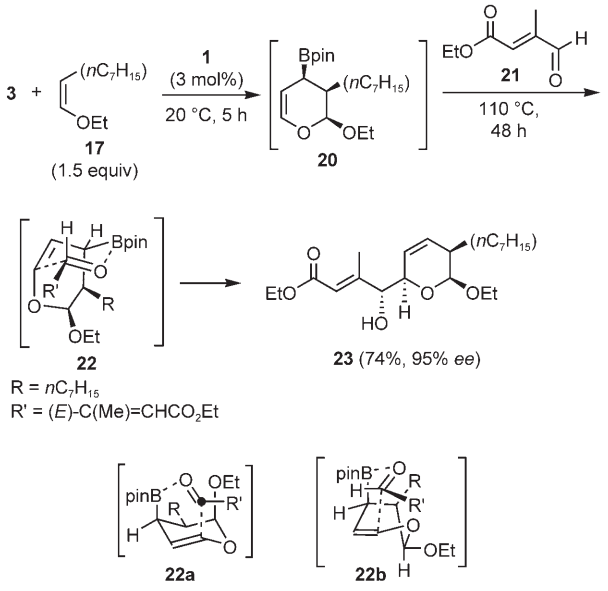


ethers are difficult substrates in inverse electron demand Diels–Alder (IEDDA) cycloadditions due to the added steric effect of the 2-substituent.[18] Our preliminary work with **3** highlighted its exceptional reactivity as a heterodiene,[5] which we hoped could overcome the low reactivity of a 2-substituted enol ether as a dienophilic partner. The resultant dihydropyrans would integrate a 5-substituent that would be difficult to install otherwise. In the event, all the cyclic enol ethers attempted were unsuccessful except for 2,3-dihydrofuran **16**. The structure of the resulting adduct **19** was determined by X-ray crystallographic analysis;[19] however, it was isolated with only about 70% *ee* (Scheme 6).



Scheme 6.

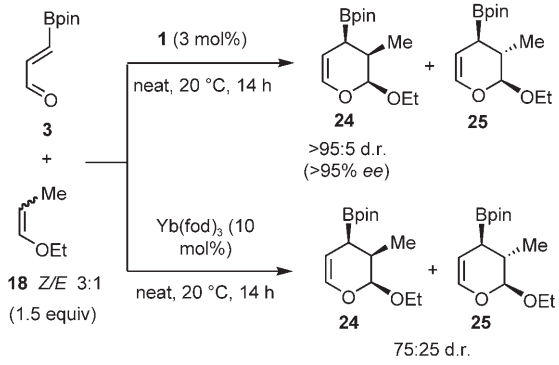
The reaction of acyclic 2-substituted enol ethers was also examined. These cycloadditions are further complicated by difficulties in making isomerically pure 2-substituted acyclic enol ethers. The model *Z*-configured enol ether **17**, synthesized according to a literature method,[20] was studied first in the [4+2] cycloaddition/allylboration process. The [4+2] cycloaddition reaction was indeed more difficult with such a 2-substituted enol ether (Scheme 7). Whereas, ethyl vinyl



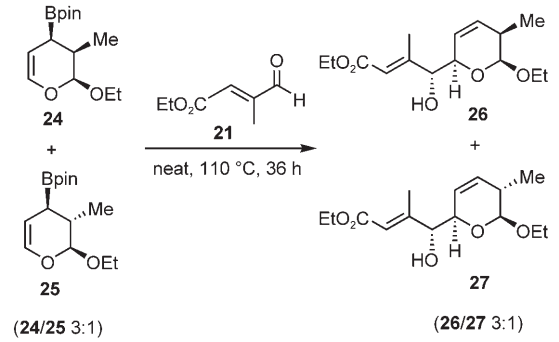
Scheme 7.

ether reacted with **3** in less than 2 h with 1 mol% of catalyst **1**,[5a] **17** required over 5 h with 3 mol% of **1** (neat, 20 °C). Nonetheless, the all-cis *endo* adduct **20** was cleanly formed as a single stereoisomer. To our surprise, it was the allylboration step that proved challenging. Whereas the adduct of ethyl vinyl ether reacted with various aldehydes at a temperature of 45 °C, an astonishing 110 °C was needed to produce **23** from **20** and aldehyde **21**. As a result, the tandem process could not be performed in "one-pot", and we found it necessary to remove catalyst **1** with a quick silica filtration to afford a clean allylboration product. In the putative allylboration transition state **22** leading to **23**, the ring may assume an unfavorable chair-like conformation (i.e., **22a**) with both pseudo-axial boronate and ethoxy substituents. Alternatively, a stereoelectronically viable boat-like conformation of type **22b** featuring a pseudo-equatorial ethoxy substituent may also be proposed. In both scenarios, it is possible that gauche interactions from the *n*-heptyl chain (R) further increase the barrier for conformational change, thus leading to a higher reaction temperature. The C4 and C5 stereochemistry can be explained in the same manner as for **3**.[5]

A case similar to that of **17** was recently exploited with success in the total synthesis of a thiomarinol antibiotic.[13] In the latter work, a (*Z*)-2-substituted enol ether was found to be more reactive than its *E* isomer. Reactions with a mixture of isomers only afforded products consistent with a kinetically selective cycloaddition of the *Z* isomer. Here, we have examined the origin of this preference by comparing the cycloaddition of a 3:1 mixture of (*Z*)-**18** and (*E*)-**18** under catalysis by **1** and a standard achiral catalyst, [Yb(fod)$_3$] (Scheme 8). The resulting cycloadducts **24** and **25** were characterized as their separable allylation products **26** and **27** (Scheme 9), and *endo*/*exo* stereochemistry was



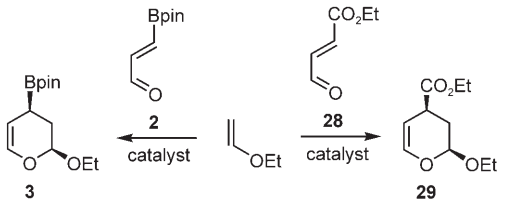
Scheme 8.



Scheme 9.

proven by NOE experiments. For the enantioselective variant catalyzed by **1** (Scheme 8), the *ee* of 96% was measured by chiral HPLC analysis of derivative **26**. As deduced from the outcome of the [Yb(fod)$_3$]-catalyzed reaction, which leads to no kinetic selectivity in the formation of adducts **24** and **25**, it appears that the huge catalyst **1** (the active catalyst is a water-bridged dimer)[9] provides steric control leading to a faster consumption of (*Z*)-2-substituted enol ethers.[21] This selectivity is particularly useful in view of the difficult preparation of isomerically pure, acyclic (*Z*)-2-substituted enol ethers.

Preliminary mechanistic investigations: To explore the influence of the boronate substituent on the reactivity of heterodiene **2**, a comparison with ethyl (*E*)-4-oxobutenoate (**28**) was conducted (Scheme 10). With both catalyst **1** and [Yb(fod)$_3$], the cycloaddition of **2** was significantly faster (Figure 1, shown for catalyst **1** only).



Scheme 10.

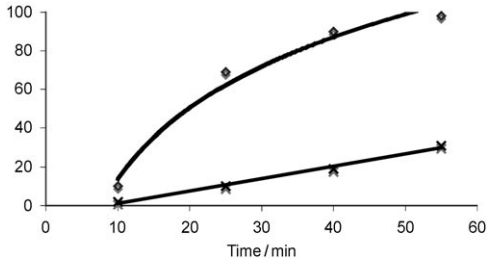
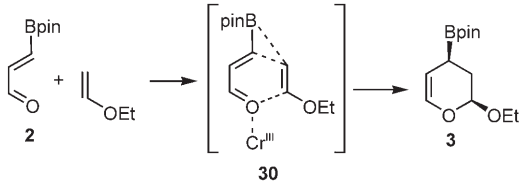


Figure 1. Comparative cycloaddition rates (conversion vs. time) between 3-boronoacrolein pinacolate (**2**, ◇) and ethyl (*E*)-4-oxobutenoate (**28**, ×) using catalyst **1** (Scheme 10).

As shown for chiral catalyst **1**, conversion to product **3** is significantly faster for 3-boronoacrolein pinacolate (**2**). An extrapolation of the data for diene **28** reveals a half-time conversion value approximately five times longer than that of **2**. It is well known that boronate substituents are much less electron-withdrawing than carboxyesters. For example, vinylboronates are much less reactive as dienophiles in normal electron demand Diels–Alder reactions than acrylates.[22] The electron-stabilizing effect of a boronyl group is thought to be comparable to that of a phenyl group.[23] The presence of a two-electron-three-atom center has been postulated in Singleton's [4+3] transition structure for the cycloadditions of vinylboranes or the dimerization of 1,3-dienyl-2-boronic esters.[24,25] The formation of reactant complexes where the nitrone oxygen is bound up to the boron atom (B··O interactions) has also been proposed in the 1,3-cycloaddition of nitrones to vinylboranes.[26] The superior reactivity of heterodiene **2** over **28** may therefore lie in the presence of a similar interaction between the boronyl group and the alkenyl moiety of the enol ether, thus suggesting a [5+2] process (i.e., transition structure **30**) rather than a common [4+2] Diels–Alder reaction mechanism (Scheme 11). Quantum mechanical calculations will be necessary to rationalize the experimental results and to confirm (partially or completely) this hypothesis.



Scheme 11.

Conclusion

This article described a useful study of the scope and limitations of the first catalytic enantioselective hetero-[4+2] cycloaddition/allylboration reaction. This multicomponent reaction process presents several appealing features. From the key substrate, 3-boronoacrolein pinacolate (**2**), the one-pot three-component reaction provides α-hydroxyalkyl dihydropyrans with very high enantio- and diastereoselectivity. The alkene functionality of these products can be further functionalized to increase the versatility of this tandem hetero-[4+2]cycloaddition/allylboration reaction. The key cycloaddition step occurs rapidly and efficiently with as little as 0.3 mol% of the chiral Cr^{III} catalyst. A wide variety of aldehyde substrates can be employed in the allylboration, including unsaturated aldehydes and α-chiral aldehydes. Acyclic 2-substituted enol ethers can be employed, in which case the catalyst promotes a kinetically selective reaction that favors *Z* enol ethers over the *E* isomers. Further extensions and applications of this powerful and practical process in the synthesis of complex natural products are underway.

Experimental Section

General information: Catalyst **1** was prepared according to Jacobsen's procedure.[9] 3-Boronoacrolein pinacolate **2** was prepared according to our previously published procedure and purified by Kugelrohr distillation (<0.5 mm Hg, 94%).[6] Toluene and CH_2Cl_2 were distilled from CaH_2. Ethyl vinyl ether was stirred over KOH for 30 min before distillation. All aldehydes were purified by Kugelrohr distillation prior to use. BaO (Acros) was used as supplied (90% tech powder). Powdered 4 Å molecular sieves (<5 micron, Aldrich) were dried in a vacuum oven (138°C) prior to use. Unless otherwise stated, all reagents were purchased from Aldrich and used as received. Analytical TLC was performed on Merck Silica Gel 60 F254 plates and were visualized with UV light and 1% $KMnO_4$ (aq). Deactivated silica-gel refers to silica-gel washed with triethylamine prior to use. NMR spectra were recorded on Varian INOVA-300, INOVA-400, or INOVA-500 MHz instruments. The residual solvent protons (^1H) or the solvent carbon (^{13}C) were used as internal standards. ^1H NMR spectroscopic data are presented as follows: chemical shift in ppm (δ) downfield from tetramethylsilane (multiplicity, coupling constant, integration). The following abbreviations are used in reporting ^1H NMR spectroscopic data: s, singlet; brs, broad singlet; d, doublet; t, triplet; q, quartet; dq, doublet of quartets; dd, doublet of doublets; m, mutiplet. HRMS were recorded on instruments from the University of Alberta mass spectrum service laboratory by using either EI or ES ionization techniques, or by using an MS/MS TOF instrument. IR spectra were obtained on a Nicolet Magna-IR 750 with frequencies expressed in cm^{-1}. Optical rotations were measured by using a 1 mL cell with a 1 dm length on a P.E. 241 polarimeter. Melting points were determined in a capillary tube by using Gallenkamp melting point apparatus and are uncorrected. Enantiomeric excesses (*ee*) of compounds **4d**–**4g** were determined by gas chromatography by using a Varian CP3380 GC unit equipped with a capillary chiral column Varian WCOT Fused Silica 25×0.25 mm coated CP Chirasil-dex CB DF=0.25. Other *ee*'s reported were obtained by chiral HPLC analysis as described in the procedures.

Synthesis of (2*S*,4*S*)-2-ethoxy-3,4-dihydro-2*H*-pyran-4-ol (6) (Table 1, method A): Compound **1** (9.60 mg, 0.020 mmol) and powdered 4 Å molecular sieves (300 mg) were added to a mixture of 3-boronoacrolein pinacolate **2** (364 mg, 2.00 mmol) and ethyl vinyl ether (1.90 mL, 20.0 mmol) in an oven dried 10 mL round-bottomed flask containing a stirbar. The reaction was stirred for 14 h at ambient temperature (23°C)

and was then filtered through celite and concentrated in vacuo to give crude **3**. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.22 (dd, J = 6.2, 2.1 Hz, 1H), 4.98 (dd, J = 3.8, 2.9 Hz, 1H), 4.82 (dd, J = 6.2, 4.4 Hz, 1H), 3.82 (dq, J = 9.7, 7.1 Hz, 1H), 3.56 (dq, J = 9.7, 7.1 Hz, 1H), 1.96–2.02 (m, 2H), 1.73–1.79 (m, 1H), 1.16–1.23 ppm (m, 15H).

The Diels–Alder cycloadduct **3** was dissolved in THF (10 mL) and cooled to 0 °C. An aqueous solution of NaOAc (3 M, 1.00 mL, 3.00 mmol) was then added dropwise and the temperature maintained below 5 °C. Hydrogen peroxide (0.610 mL, 6.55 mmol) was added and the mixture was stirred at 0 °C for 1 h. After this time, water (10 mL) was added and the aqueous layer was extracted with ether (2 × 30 mL). The ether layers were combined, washed with aqueous saturated solutions of NH_4Cl (15 mL) and NaCl (15 mL), then dried over anhydrous $MgSO_4$. Filtration and concentration in vacuo gave the crude product **6**, which was purified by flash-column chromatography (deactivated silica gel, pentane/ether 4:1) to provide **6** (234 mg, 81 %) as a clear oil. $[\alpha]_D^{23}$ = +136.0 (c = 1.0 in $CHCl_3$); IR (CH_2Cl_2, cast): $\tilde{\nu}$ = 3553, 3431, 1646, 1297 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.24 (d, J = 6.2 Hz, 1H), 5.22 (dd, J = 2.2, 2.2 Hz, 1H), 5.13–5.17 (m, 1H), 3.90- 3.95 (m, 1H), 3.80 (dq, J = 9.7, 7.1 Hz, 1H), 3.52 (dq, J = 9.7, 7.1 Hz, 1H), 3.04 (d, J = 11.2 Hz, 1H), 2.21–2.25 (m, 1H), 2.02 (ddd, J = 14.5, 5.0, 2.7 Hz, 1H), 1.21 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.8, 105.9, 96.6, 64.2, 58.6, 35.0, 15.2 ppm; HRMS (EI): m/z: calcd for $C_7H_{12}O_3$: 144.0786; found: 144.0783 $[M+Na]^+$; assay of enantiomeric excess: chiral HPLC analysis (Chiralpak AD-RH, 50 % isopropanol/water, 0.300 mL min^{-1}, 210.8 nm), t_R(major) = 8.60 min; t_R(minor) = 10.64 min): 96 % *ee*.

(2*S*,4*S*)-2-Ethoxy-3,4-dihydro-2*H*-pyran-4-ol (Table 1, method B): Compound **1** (2.90 mg, 0.006 mmol) and powdered BaO (200 mg) were added to a mixture of 3-boronoacrolein pinacolate **2** (364 mg, 2.00 mmol) and ethyl vinyl ether (1.90 mL, 20.0 mmol) in an oven-dried round-bottomed flask (10 mL) containing a stirbar. The reaction was stirred for 14 h at ambient temperature, then filtered through celite and concentrated in vacuo to give crude **3**. An aqueous solution of NaOAc (3 M, 1.00 mL, 3.00 mmol) was then added dropwise to a precooled solution (0 °C) of the Diels–Alder cycloadduct **3** in THF (10 mL) and the temperature maintained below 5 °C. Hydrogen peroxide (0.610 mL, 6.55 mmol) was added and the mixture was stirred at 0 °C for 1 h. After this time, water (10 mL) was added and the aqueous layer was extracted with ether (2 × 30 mL). The ether layers were combined, washed with aqueous saturated solutions of NH_4Cl (15 mL) and NaCl (15.0 mL), then dried over anhydrous $MgSO_4$. Filtration and concentration in vacuo gave the crude product **6**, which was purified by flash-column chromatography (deactivated silica gel, pentane/ether 4:1) to provide **6** (234 mg, 81 %) as a clear oil. Assay of enantiomeric excess: chiral HPLC analysis (Chiralpak AD-RH, 50 % isopropanol/water, 0.300 mL min^{-1}, 210.8 nm), t_R(major) = 8.60 min; t_R(minor) = 10.64 min): 96 % *ee*.

(2*S*,4*S*)-2-Ethoxy-3,4-dihydro-2*H*-pyran-4-yl acetate (7): A solution of **6** (186 mg, 1.29 mmol), 2,6-lutidine (0.200 mL, 1.96 mmol), and DMAP (15.7 mg, 0.129 mmol) in dry CH_2Cl_2 (4 mL) was prepared in a round-bottomed flask (25 mL). The mixture was cooled to 0 °C and then acetic anhydride (0.120 mL, 1.29 mmol) was added by a syringe. The reaction mixture was stirred at 0 °C for 1 h and then further stirred at ambient temperature overnight. After this time, water (10 mL) and ether (30 mL) were added to the solution. The phases were separated and the aqueous layer was extracted with ether (3 × 20 mL). The combined organic layers were washed with an aqueous saturated solution of NaCl, dried over anhydrous $MgSO_4$, filtered, concentrated, and purified by flash-column chromatography (deactivated silica-gel, hexanes/ether 9:1) to provide **7** (233 mg, 96 %) as a colorless oil. $[\alpha]_D^{23}$ = +37.0 (c = 1.0 in $CHCl_3$); IR (CH_2Cl_2, cast): $\tilde{\nu}$ = 3071, 2929, 1730, 1650, 1244 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.42 (dd, J = 6.3, 1.0 Hz, 1H), 5.26–5.32 (m, 1H), 5.06 (dd, J = 5.2, 2.9 Hz, 1H), 4.96 (dd, J = 6.3, 4.9 Hz, 1H), 3.90 (dq, J = 9.7, 7.1 Hz, 1H), 3.58 (dq, J = 9.7, 7.1 Hz, 1H), 2.06–2.30 (m, 2H), 2.05 (s, 3H), 1.21 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.9, 144.2, 100.7, 96.6, 64.5, 62.7, 33.0, 21.3, 15.0 ppm; HRMS (EI): m/z: calcd for $C_9H_{14}O_4$: 186.0892; found: 186.0897.

(2*S*,4*S*)-2-Ethoxy-3,4-dihydro-2*H*-pyran-4-yl benzoate (8): NaH (95 %, 131 mg, 5.20 mmol) was added to a precooled (ice-water bath) solution of **6** (570 mg, 3.95 mmol) in DMF (10 mL). The mixture was stirred at 0 °C for 30 min and then benzyl bromide (0.570 mL, 4.80 mmol) was added dropwise. The reaction mixture was slowly warmed to ambient temperature and stirred overnight. After this time, the mixture was added to water (25 mL) and ether (50 mL), and the phases were separated. The aqueous layer was extracted with ether (2 × 30 mL), and the combined organic layers were washed with an aqueous saturated solution of NaCl, dried over anhydrous $MgSO_4$, concentrated, and then purified by flash-column chromatography (deactivated silica-gel, hexanes/ether 95:5) to provide **8** (878 mg, 95 %) as a colorless oil. $[\alpha]_D^{23}$ = +22.8 (c = 1.0 in $CHCl_3$); IR (CH_2Cl_2, cast): $\tilde{\nu}$ = 3064, 2976, 1646, 1229 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.10–7.20 (m, 5H), 6.30 (dd, J = 6.3, 1.3 Hz, 1H), 4.99 (dd, J = 7.7, 2.5 Hz, 1H), 4.92 (ddd, J = 6.3, 2.8, 1.0 Hz, 1H), 4.56 (d, J = 1.3 Hz, 2H), 4.15–4.20 (m, 1H), 3.88 (dq, J = 9.7, 7.1 Hz, 1H), 3.58 (dq, J = 9.7, 7.1 Hz, 1H), 2.22 (dddd, J = 13.3, 6.4, 2.5, 1.1 Hz, 1H), 2.05 (ddd, J = 13.3, 7.5, 7.5 Hz, 1H), 1.25 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.0, 138.6, 128.3, 127.6, 127.5, 102.8, 98.2, 69.7, 67.9, 64.5, 34.3, 15.1 ppm; HRMS (EI): m/z: calcd for $C_{14}H_{18}O_3$: 234.1256; found: 234.1258.

General synthesis of compounds 4 (Table 2), exemplified with 4a

(*R*)-[(2*R*,6*S*)-6-Ethoxy-5,6-dihydro-2*H*-pyran-2-yl](phenyl)methanol (4a): Compound **1** (9.60 mg, 0.020 mmol) and powdered BaO (400 mg) were added to a mixture of 3-boronoacrolein pinacolate **2** (364 mg, 2.00 mmol) and ethyl vinyl ether (1.90 mL, 20.0 mmol) in an oven-dried round-bottomed flask (10 mL) containing a stirbar. After stirring for 1.5 h at ambient temperature (23 °C), benzaldehyde (424 mg, 4.00 mmol) was added to the reaction mixture. The reaction mixture was stirred at 40 °C for 24 h, then diluted with EtOAc and filtered through celite. The EtOAc solution was stirred for 30 min with an aqueous saturated solution of $NaHCO_3$. After this time, the organic layer was separated and the aqueous layer was extracted with EtOAc (2 × 20 mL). The combined organic layers were washed with an aqueous saturated solution of NaCl (20 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated to afford **4a** as a crude product. Purification by flash-column chromatography (deactivated silica-gel, hexanes/ether 9:1) led to the pure product **4a** (384 mg, 82 %) as a clear oil. $[\alpha]_D^{23}$ +24.9 (c = 1.0 in $CHCl_3$); IR (CH_2Cl_2, cast): $\tilde{\nu}$ = 3451, 3035, 2877, 1640, 1257 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.26–7.40 (m, 5H), 5.75–5.79 (m, 1H), 5.36–5.40 (m, 1H), 4.78 (dd, J = 5.9, 5.9 Hz, 1H), 4.56 (dd, J = 7.4, 1.5 Hz, 1H), 4.28–4.32 (m, 1H), 3.96 (dq, J = 9.7, 7.1 Hz, 1H), 3.58 (dq, J = 9.7, 7.1 Hz, 1H), 3.11 (br s, 1H), 2.10–2.12 (m, 2H), 1.25 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 139.8, 128.3, 128.0, 127.2, 125.4, 124.8, 98.5, 78.7, 76.8, 64.5, 31.1, 15.3 ppm; HRMS (ESI) m/z: calcd for $C_{14}H_{18}O_3Na$: 257.1154; found: 257.1152 $[M+Na]^+$; assay of enantiomeric excess: chiral HPLC analysis (chiralpak AD-RH, 50 % isopropanol/water, 0.300 mL min^{-1}, 210.8 nm), t_R(major) = 8.60 min; t_R(minor) = 10.64 min): 96 % *ee*.

(*R*)-[(2*R*,6*S*)-6-Ethoxy-5,6-dihydro-2*H*-pyran-2-yl](4-nitrophenyl)methanol (4b): Same procedure as for **4a**, except that the allylboration with 4-nitrobenzaldehyde (604 mg, 4.00 mmol) took place at ambient temperature for 24 h. Purification by flash-column chromatography (deactivated silica-gel, hexanes/ether 9:1) led to the pure product **4b** (512 mg, 92 %) as a brown solid. M.p. 102–103 °C; $[\alpha]_D^{23}$ = +23.0 (c = 1.0 in $CHCl_3$); IR (CH_2Cl_2, cast) $\tilde{\nu}$ = 3442, 2977, 1604, 1519, 1431 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.21 (d, J = 8.7 Hz, 2H), 7.58 (d, J = 8.7 Hz, 2H), 5.82–5.88 (m, 1H), 5.46–5.50 (m, 1H), 4.79 (dd, J = 6.3, 3.9 Hz, 1H), 4.75 (dd, J = 4.9, 4.9 Hz, 1H), 4.35–4.39 (m, 1H), 3.83 (dq, J = 9.6, 7.1 Hz, 1H), 3.52 (dq, J = 9.6, 7.1 Hz, 1H), 3.39 (d, J = 3.9 Hz, 1H), 2.18–2.25 (m, 2H), 1.25 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 147.8, 147.5, 127.8, 125.6, 124.7, 123.4, 98.1, 77.8, 75.6, 64.7, 30.8, 15.3 ppm; HRMS (EI): m/z: calcd for $C_{14}H_{16}O_5N$: 278.1028 $[M-H]^+$; found: 278.1027.

(*R*)-[(2*R*,6*S*)-6-Ethoxy-5,6-dihydro-2*H*-pyran-2-yl](4-methoxyphenyl)methanol (4c): Same procedure as for **4a**, except that the allylboration with *p*-anisaldehyde (544 mg, 4.00 mmol) took place at 45 °C for 24 h. Purification by flash-column chromatography (deactivated silica-gel, hexane/ether 9:1) led to the pure product **4c** (428 mg, 81 %) as a clear oil. $[\alpha]_D^{23}$ = +24.3 (c = 1.0 in $CHCl_3$); IR (CH_2Cl_2, cast): $\tilde{\nu}$ = 3442, 2977, 1604, 1519,

1431 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32 (d, J = 8.1 Hz, 2H), 6.85 (d, J = 8.1 Hz, 2H), 5.72–5.78 (m, 1H), 5.32–5.36 (m, 1H), 4.79 (dd, J = 7.7, 5.3 Hz, 1H), 4.50 (d, J = 7.7 Hz, 1H), 4.26–4.30 (m, 1H), 4.01 (dq, J = 9.6, 7.1 Hz, 1H), 3.80 (s, 3H), 3.59 (dq, J = 9.6, 7.1 Hz, 1H), 3.18 (br s, 1H), 2.19–2.23 (m, 2H), 1.23 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.4, 131.9, 128.5, 125.4, 124.7, 113.7, 98.5, 78.8, 76.4, 64.5, 55.2, 31.1, 15.2 ppm; HRMS (EI) m/z: calcd for $C_{15}H_{20}O_4$: 264.1362; found: 264.1367.

(*R*)-[(2*R*,6*S*)-6-Ethoxy-5,6-dihydro-2*H*-pyran-2-yl](4-chlorophenyl)methanol (4d): Same procedure as for **4a**, except that the allylboration with 4-chlorobenzaldehyde (280 mg, 2.00 mmol) took place at 40 °C for 24 h. Purification by flash-column chromatography (deactivated silica-gel, hexane/ether 9:1) led to the pure product **4d** (206 mg, 77 %) as a clear oil. $[\alpha]_D^{23}$ = +48.4 (c = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34 (s, 4H), 5.78–5.82 (m, 1H), 5.40 (dd, J = 10.3, 1.8 Hz, 1H), 4.79 (t, J = 5.5 Hz, 1H), 4.61 (d, J = 7.0 Hz, 1H), 4.24–4.33 (m, 1H), 3.98 (dq, J = 9.6, 7.1 Hz, 1H), 3.58 (dq, J = 9.6, 7.1 Hz, 1H), 3.30 (br s, 1H), 2.20–2.27 (m, 2H), 1.26 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.6, 133.7, 128.6, 128.5, 125.2, 125.1, 98.4, 78.4, 76.0, 64.5, 30.9; 15.2 ppm; elemental analysis calcd for $C_{14}H_{17}ClO_3$: C 62.57, H 6.38; found: C 62.76, H 6.81.

(*R*)-[(2*R*,6*S*)-6-Ethoxy-5,6-dihydro-2*H*-pyran-2-yl](4-fluorophenyl)methanol (4e): Same procedure as for **4a**, except that the allylboration with 4-fluorobenzaldehyde (248 mg, 2.00 mmol) took place at 40 °C for 24 h. Purification by flash-column chromatography (deactivated silica-gel, hexane/ether 9:1) led to the pure product **4e** (189 mg, 75 %) as a solid. M.p. 69 °C; $[\alpha]_D^{23}$ = +13.7 (c = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.49 (m, 2H), 7.01–7.22 (m, 2H), 5.72–5.87 (m, 1H), 5.33–5.47 (m, 1H), 4.83 (t, J = 5.4 Hz, 1H), 4.65 (dd, J = 7.3, 2.2 Hz, 1H), 4.27–4.39 (m, 1H), 4.06 (dq, J = 9.5, 7.1 Hz, 1H), 3.67 (dq, J = 9.5, 7.1 Hz, 1H), 3.43 (br s, 1H), 2.22–2.32 (m, 2H), 1.30 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 162.4 (J(C,F) = 4.8 Hz), 135.8 (J(C,F) = 0.1 Hz), 135.7, 129.0, 128.9, 125.2, 125.1, 115.4, 115.0, 98.5, 78.7, 76.2, 64.6, 31.0; 15.2; elemental analysis calcd for $C_{14}H_{17}FO_3$: C 68.16, H 7.63; found: C 68.16, H 7.81.

(1*R*)-1-[(2*R*,6*S*)-6-Ethoxy-5,6-dihydro-2*H*-pyran-2-yl]-2-phenylethanol (4f): Same procedure as for **4a**, except that the allylboration with phenylacetaldehyde (240 mg, 2.00 mmol) took place at 45 °C for 24 h. Purification by flash-column chromatography (deactivated silica-gel, hexane/ether 9:1) led to the pure product **4f** (204 mg, 82 %) as a clear oil. $[\alpha]_D^{23}$ = +23.7 (c = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.25–7.50 (m, 5H), 5.82–5.94 (m, 1H), 5.62–5.70 (m, 1H), 4.80 (t, J = 5.4 Hz, 1H), 4.13–4.21 (m, 1H), 4.09 (dq, J = 9.5, 7.1 Hz, 1H), 3.72–3.89 (m, 1H), 3.66 (dq, J = 9.5, 7.1 Hz, 1H), 3.02 (d, J = 13.5, 6.9 Hz, 1H), 2.92 (d, J = 12.5, 7.1 Hz, 1H,), 2.60 (br s, 1H), 2.22–2.29 (m, 2H), 1.25 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.9, 129.8, 128.9, 127.3, 126.8, 125.4, 98.9, 75.7, 74.7, 64.9, 40.0, 31.4, 15.7 ppm; HRMS (EI): m/z: calcd for $C_{13}H_{14}O_2$: 202.0994 [$M-HOC_2H_5$]$^+$; found: 202.0990.

(1*R*)-1-[(2*R*,6*S*)-6-Ethoxy-5,6-dihydro-2*H*-pyran-2-yl]-3-phenylpropan-1-ol (4g): Same procedure as for **4a**, except that the allylboration with hydrocinnamaldehyde (264 mg, 2.00 mmol) took place at 45 °C for 24 h. Purification by flash-column chromatography (deactivated silica-gel, hexane/ether 9:1) led to the pure product **4g** (193 mg, 74 %) as a clear oil. $[\alpha]_D^{23}$ = +70.7 (c = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.16–7.34 (m, 5H), 5.80–5.89 (m, 1H), 5.64 (dq, J = 10.3, 1.7 Hz, 1H), 4.76 (dd, J = 5.4, 6.0 Hz, 1H), 4.15–4.22 (m, 1H), 3.98 (dq, J = 9.5, 7.1 Hz, 1H), 3.53–3.65 (m, 2H), 2.84–2.96 (m, 1H), 2.68–2.81 (m, 1H), 2.58 (br d, J = 5.8 Hz, 1H), 2.20–2.28 (m, 2H), 1.82–2.02 (m, 2H), 1.30 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 142.2, 128.5, 128.4, 126.5, 125.8, 124.9, 98.5, 77.3, 72.6, 64.4, 35.0, 32.0, 31.0, 15.2 ppm; HRMS (EI): m/z: calcd for $C_{14}H_{16}O_2$: 216.1150 [$M-HOC_2H_5$]$^+$; found: 216.1150.

(1*R*)-1-[(2*R*,6*S*)-6-Ethoxy-5,6-dihydro-2*H*-pyran-2-yl]-3-methylbutan-1-ol (4h): Same procedure as for **4a** except that the allylboration was carried out with isovaleraldehyde (344 mg, 4.00 mmol). Purification by flash-column chromatography (deactivated silica-gel, hexane/ether 9:1) led to the pure product **4h** (347 mg, 81 %) as a clear oil. $[\alpha]_D^{23}$ = +98.0 (c = 1.0 in $CHCl_3$); IR (CH_2Cl_2, cast): $\tilde{\nu}$ = 3446, 3041, 1467, 1293 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.79–6.05 (m, 1H), 5.62–5.68 (m, 1H), 4.73 (dd, J = 5.5, 5.5 Hz, 1H), 4.07–4.11 (m, 1H), 3.96 (dq, J = 9.6, 7.1 Hz, 1H), 3.50–3.66 (m, 2H), 2.42 (d, J = 5.7 Hz, 1H), 2.18–2.23 (m, 2H), 1.80–1.90 (m, 1H), 1.50–1.60 (m, 1H), 1.22–1.38 (m, 4H), 0.96 (d, J = 7.8 Hz, 3H), 0.93 ppm (d, J = 7.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 126.6, 124.7, 98.4, 77.7, 71.4, 64.2, 41.9, 31.1, 24.4, 23.6, 21.8, 15.1 ppm; HRMS (ESI): m/z: calcd for $C_{12}H_{22}O_3Na$: 237.1461; found: 237.1461.

(1*R*)-2-{[*tert*-Butyl(dimethyl)silyl]oxy}-1-[(2*R*,6*S*)-6-ethoxy-5,6-dihydro-2*H*-pyran-2-yl]ethanol (4i): Same procedure as for **4a** except that the allylboration was carried out with *tert*-butyl(dimethylsilyloxy)acetaldehyde (697 mg, 4.00 mmol). Purification by flash-column chromatography (deactivated silica-gel, hexane/ether 9:1) led to the pure product **4i** (496 mg, 82 %) as clear oil. $[\alpha]_D^{23}$ = +34.5 (c = 1.0 in $CHCl_3$); IR (CH_2Cl_2, cast): $\tilde{\nu}$ = 3324, 3038, 2857, 1317 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.78–5.86 (m, 1H), 5.66–5.70 (m, 1H), 4.76 (dd, J = 6.2, 4.7 Hz, 1H), 4.41–4.45 (m, 1H), 3.93 (dq, J = 9.6, 7.1 Hz, 1H), 3.60–3.76 (m, 3H), 3.50 (dq, J = 9.6, 7.1 Hz, 1H), 2.62 (d, J = 5.9 Hz, 1H), 2.18–2.22 (m, 2H), 1.25 (t, J = 7.1 Hz, 3H), 0.86 (s, 9H), 0.02 ppm (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 126.8, 124.5, 98.4, 73.9, 73.2, 64.4, 63.2, 31.0, 25.9, 18.2, 15.1, −5.4, −5.5 ppm; HRMS (ESI): m/z: calcd for $C_{15}H_{30}O_4NaSi$: 325.1806; found: 325.1804.

(1*R*)-1-[(2*R*,6*S*)-6-Ethoxy-5,6-dihydro-2*H*-pyran-2-yl]undecan-1-ol (4j): Same procedure as for **4a** except that the allylboration was carried out with undecanal (680 mg, 4.00 mmol). Purification by flash-column chromatography (deactivated silica-gel, hexane/ether 9:1) led to the pure product **4j** (530 mg, 89 %) as a clear oil. $[\alpha]_D^{23}$ = +54.7 (c = 1.0 in $CHCl_3$); IR (CH_2Cl_2, cast): $\tilde{\nu}$ = 3454, 3040, 2854, 1209 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.80–5.86 (m, 1H), 5.62–5.68 (m, 1H), 4.76 (dd, J = 5.5, 5.5 Hz, 1H), 4.12–4.16 (m, 1H), 3.96 (dq, J = 9.5, 7.1 Hz, 1H), 3.46–3.62 (m, 2H), 2.42 (d, J = 5.7 Hz, 1H), 2.19–2.23 (m, 2H), 1.20–1.60 (m, 21H), 0.88 ppm (t, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 126.7, 124.7, 98.5, 77.2, 73.3, 64.3, 33.0, 31.9, 31.1 29.7, 29.6, 29.6, 29.5, 29.3, 25.6, 22.6, 15.1, 14.0 ppm; HRMS (EI): m/z: calcd for $C_{18}H_{34}O_3$: 298.2508; found: 298.2504.

Solvent-free procedure for the preparation of 4k and 4m–4p: The cycloaddition reaction was carried out by using the same procedure as that for **4a**. After the completion of the cycloaddition reaction, the ethyl vinyl ether was evaporated in vacuo and the aldehyde (4.00 mmol) was added to the residue. The reaction was stirred at ambient or an elevated temperature for 18–48 h, then diluted with EtOAc and filtered through celite. The EtOAc solution was stirred for 30 min with an aqueous saturated solution of $NaHCO_3$. The organic layer was separated and the aqueous layer was extracted with EtOAc (2×20 mL). The combined organic layers were washed with an aqueous saturated solution of NaCl then dried over anhydrous $MgSO_4$, filtered, and concentrated to afford **4k** or **4m–4p** as a crude product. Purification by flash-column chromatography (deactivated silica-gel, hexanes/ether) led to the pure product **4k** or products **4m–4p**.

(1*R*)-1-[(2*R*,6*S*)-6-Ethoxy-5,6-dihydro-2*H*-pyran-2-yl]-2-methylpropan-1-ol (4k): Colorless oil; Yield: 270 mg, 78 %; $[\alpha]_D^{23}$ = −71.0 (c = 1.6 in $CHCl_3$); IR (CH_2Cl_2, cast): $\tilde{\nu}$ = 3454, 3039, 1471, 1237 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.79–5.86 (m, 1H), 5.61–5.66 (m, 1H), 4.75 (dd, J = 6.0, 5.0 Hz, 1H), 4.32–4.37 (m, 1H), 3.96 (dq, J = 9.6, 7.1 Hz, 1H), 3.58 (dq, J = 9.6, 7.1 Hz, 1H), 3.21 (ddd, J = 7.0, 7.0, 3.9 Hz, 1H), 2.32 (d, J = 7.2 Hz, 1H), 2.19–2.25 (m, 2H), 1.91 (octet, J = 6.8 Hz, 1H), 1.62–1.66 (m, 6H), 1.25 (t, J = 7.1 Hz, 3H), 1.02 (d, J = 6.8 Hz, 3H), 0.98 ppm (d, J = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 127.4, 124.6, 98.4, 78.1, 75.0, 64.3, 30.9, 30.6, 19.5, 18.1, 15.1 ppm; HRMS (ESI): m/z: calcd for $C_{11}H_{20}O_3Na$: 223.1305; found: 223.1303.

(1*R*,2*E*)-1-[(2*R*,6*S*)-6-Ethoxy-5,6-dihydro-2*H*-pyran-2-yl]-2-methylbut-2-en-1-ol (4m): Colorless oil; Yield: 323 mg, 76 %; $[\alpha]_D^{23}$ = +57.1 (c = 1.0 in $CHCl_3$); IR (CH_2Cl_2, cast): $\tilde{\nu}$ = 3462, 3041, 1650, 1256 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.76–5.82 (m, 1H), 5.46–5.62 (m, 2H), 4.78 (dd, J = 6.2, 5.0 Hz, 1H), 4.22–4.28 (m, 1H), 3.86–4.02 (m, 2H), 3.58 (dq, J = 9.6, 7.1 Hz, 1H), 2.80 (br s, 1H), 2.19–2.23 (m, 2H), 1.62–1.66 (m, 6H), 1.23 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 133.8, 126.0, 124.4, 124.2, 98.6, 79.9, 76.0, 63.4, 31.1, 15.2, 13.1, 11.6 ppm; HRMS (ESI): m/z: calcd for $C_{12}H_{20}O_3Na$: 235.1305; found: 235.1299.

Ethyl-(2*E*,4*R*)-4-[(2*R*,6*S*)-6-ethoxy-5,6-dihydro-2*H*-pyran-2-yl]-4-hydroxy-3-methylbut-2-enoate (4n): Colorless oil; Yield: 476 mg, 88%; $[\alpha]_D^{23}=-53.3$ ($c=1.0$ in $CHCl_3$); IR (CH_2Cl_2, cast): $\tilde{\nu}=3464$, 2977, 1714, 1652 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta=6.02$ (s, 1H), 5.82–5.88 (m, 1H), 5.58–5.62 (m, 1H), 4.73–4.77 (m, 1H), 4.41–4.45 (m, 1H), 4.15 (q, $J=7.1$ Hz, 2H), 3.97–4.01 (m, 1H), 3.86 (dq, $J=9.6$, 7.1 Hz, 1H), 3.52 (dq, $J=9.6$, 7.1 Hz, 1H), 3.12 (d, $J=6.3$ Hz, 1H), 2.19–2.26 (m, 2H), 2.18 (s, 3H), 1.26 (t, $J=7.1$ Hz, 3H), 1.23 ppm (t, $J=7.1$ Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=166.5$, 156.7, 125.8, 124.8, 117.1, 97.7, 77.8, 74.9, 64.4, 59.5, 30.4, 15.2, 15.0, 14.2 ppm; HRMS (ESI): *m/z*: calcd for $C_{14}H_{22}O_5Na$: 293.1359; found: 293.1136.

(1*R*)-1-[(2*R*,6*S*)-6-Ethoxy-5,6-dihydro-2*H*-pyran-2-yl]prop-2-en-1-ol (4o): Colorless oil; Yield: 73%; $[\alpha]_D^{23}=+101.95$ ($c=5.2$ in $CHCl_3$); IR (CH_2Cl_2, cast): $\tilde{\nu}=3448$, 3042, 1648, 1210 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta=5.80$–5.98 (m, 2H), 5.63–5.69 (m, 1H), 5.40 (ddd, $J=16.3$, 1.7, 1.7 Hz, 1H), 5.27 (ddd, $J=10.4$, 1.7, 1.7 Hz, 1H), 4.78 (dd, $J=6.3$, 4.3 Hz, 1H), 4.15–4.21 (m, 1H), 4.05 (dd, $J=6.2$, 6.2 Hz, 1H), 4.02 (dq, $J=9.6$, 7.1 Hz, 1H), 3.58 (dq, $J=9.6$, 7.1 Hz, 1H), 2.82 (brs, 1H), 2.30–2.20 (m, 2H), 1.25 ppm (t, $J=7.1$ Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=$ 136.8, 125.7, 124.7, 117.3, 98.2, 77.1, 74.9, 64.4, 30.9, 15.1 ppm; HRMS (ESI): *m/z*: calcd for $C_{10}H_{16}O_3Na$: 207.0992; found: 207.0990.

(1*R*)-1-[(2*R*,6*S*)-6-Ethoxy-5,6-dihydro-2*H*-pyran-2-yl]oct-2-yn-1-ol (4p): Colorless oil; Yield: 86%; $[\alpha]_D^{23}=+87.16$ ($c=1.0$ in $CHCl_3$); IR (CH_2Cl_2, cast): $\tilde{\nu}=3441$, 3043, 1652, 1210 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta=$ 5.78–5.95 (m, 2H), 4.82 (dd, $J=6.4$, 4.0 Hz, 1H), 4.22–4.32 (m, 1H), 4.02 (dq, $J=9.6$, 7.1 Hz, 1H), 3.58 (dq, $J=9.6$, 7.1 Hz, 1H), 2.92 (d, $J=4.0$ Hz, 1H), 2.19–2.26 (m, 4H), 1.50–1.58 (m, 2H), 1.30–1.40 (m, 4H), 1.26 (t, $J=7.1$ Hz, 3H), 0.88 ppm (t, $J=7.0$ Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=125.5$, 124.8, 98.1, 87.0, 77.6, 77.4, 65.4, 64.5, 31.0, 30.8, 28.2, 22.1, 18.7, 15.1, 13.9 ppm; HRMS (ESI): *m/z*: calcd for $C_{15}H_{24}O_3Na$: 275.1618; found: 275.1619.

(1*R*,2*E*)-1-[(2*R*,6*S*)-6-Ethoxy-5,6-dihydro-2*H*-pyran-2-yl]-3-(4-nitrophenyl)prop-2-en-1-ol (4l): The cycloaddition reaction was carried out by using the same procedure as that for **4a**. After the completion of cycloaddtion, the ethyl vinyl ether was evaporated in vacuo. The residue was dissolved in CH_2Cl_2 (1 mL) and 4-nitrocinnamaldehyde (708 mg, 4.00 mmol) was added to the solution. The reaction was stirred at 40°C for 24 h, then diluted with EtOAc and filtered through celite. The EtOAc solution was stirred for 30 min with an aqueous saturated solution of $NaHCO_3$. The organic layer was then separated and the aqueous layer extracted with EtOAc (2×20 mL). The combined organic layers were washed with an aqueous saturated solution of NaCl, dried over anhydrous $MgSO_4$, filtered, and concentrated to afford the title compound as a crude product. Purification by flash-column chromatography (deactivated silica-gel, hexanes/ether 9:1) led to the pure **4l** (495 mg, 81%) as a brown solid. M.p. 99–100°C; $[\alpha]_D^{23}=+55.0$ ($c=1.0$ in $CHCl_3$); IR (CH_2Cl_2, cast): $\tilde{\nu}=3426$, 1650, 1596, 1432, 1210 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta=8.18$ (d, $J=8.7$ Hz, 2H), 7.50 (d, $J=8.7$ Hz, 2H), 6.80 (d, $J=$ 16.0 Hz, 1H), 6.45 (dd, $J=16.0$, 5.2 Hz, 1H), 5.83–5.88 (m, 1H), 5.66–5.71 (m, 1H), 4.80 (dd, $J=6.4$, 3.8 Hz, 1H), 4.25–4.32 (m, 2H), 3.95 (dq, $J=9.6$, 7.1 Hz, 1H), 3.57 (dq, $J=9.6$, 7.1 Hz, 1H), 3.02 (brs, 1H), 2.15–2.35 (m, 2H), 1.25 ppm (t, $J=7.1$ Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=146.9$, 143.1, 133.2, 129.9, 127.0, 125.2, 125.2, 123.9, 98.1, 77.1, 74.3, 64.7, 30.9, 15.2 ppm; HRMS (ESI): *m/z*: calcd for $C_{16}H_{19}O_5NNa$: 328.1161; found: 328.1165.

(1*S*,2*R*)-2-{[*tert*-Butyl(diphenyl)silyl]oxy}-1-[(2*R*,6*S*)-6-ethoxy-5,6-dihydro-2*H*-pyran-2-yl]-2-phenylethanol (11): Same procedure as for **4k**, except that, after the hetero Diels–Alder, the cycloadduct was distilled by using a Kugelrohr apparatus (b.p. 90–95°C/0.01 mm Hg). The allylboration with (*R*)-[*tert*-butyldiphenylsilyl)oxy](phenyl)acetaldehyde was carried out at 70°C for 10 h. Purification by flash-column chromatography (deactivated silica-gel, hexane:ether 95:5) led to the pure product **11** (652 mg, 65%) as a white solid. $[\alpha]_D^{23}=+39.3$ ($c=1.0$ in $CHCl_3$); m.p.= 139°C; ^1H NMR (300 MHz,$CDCl_3$): $\delta=7.68$ (dd, $J=7.8$, 1.4 Hz, 2H). 7.12–7.50 (m, 13H), 5.73–5.89 (m, 1H), 5.58–5.70 (m, 1H), 4.82 (d, $J=$ 7.6 Hz, 1H), 4.70–4.77 (m, 1H), 4.63 (dd, $J=6.1$, 4.6 Hz, 1H), 3.78 (td, $J=7.8$, 2.6 Hz, 1H), 3.72 (dq, $J=9.5$, 7.1 Hz, 1H), 3,30 (dq, $J=9.5$, 7.1 Hz, 1H), 2.47 (d, $J=7.9$ Hz, 1H), 2.13–2.24 (m, 2H), 1.18 (t, $J=$ 7.1 Hz, 3H), 1.02 ppm (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta=141.7$, 136.5, 136.4, 134.4, 133.7, 129.8, 128.4, 128.2, 127.8, 127.6, 127.9, 124.9, 98.4, 77.3, 76.3, 73.5, 64.6, 31.2, 27.4, 19.8, 15.5 ppm; HRMS (EI): *m/z*: calcd for $C_{25}H_{23}O_3Si$: 399.1417 $[M-HOC_2H_5-tBu]^+$; found: 399.1410.

(1*S*,2*S*)-2-{[*tert*-Butyl(diphenyl)silyl]oxy}-1-[(2*R*,6*S*)-6-ethoxy-5,6-dihydro-2*H*-pyran-2-yl]-2-phenylethanol (12): Same procedure as for **11**, except that the allylboration took place at 70°C for 36 h, producing the product (550 mg, 65%) as a clear oil and a mixture of two diastereoisomers (10:1). $[\alpha]_D^{23}=+24.2$ ($c=0.75$ in $CHCl_3$); major diastereoisomer **12**: ^1H NMR (500 MHz, $CDCl_3$): $\delta=7.70$–7.77 (m, 2H), 7.20–7.48 (m, 13H), 5.72–5.78 (m, 1H), 5.57 (dq, $J=10.2$, 1.6 Hz, 1H), 4.82 (d, $J=7.6$ Hz, 1H), 4.47 (dd, $J=6.1$, 7.2 Hz, 1H), 3.84–3.90 (m, 1H), 3.75 (ddd, $J=1.9$, 7.0, 7.6 Hz, 1H), 3.62 (dq, $J=7.0$, 9.5 Hz, 1H), 3.35 (dq, $J=7.0$, 9.5 Hz, 1H), 2.70 (d, 1H, $J=7.0$ Hz), 2.02–2.21 (m, 2H), 1.17 (t, $J=7.0$ Hz, 3H), 1.06 ppm (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta=141.0$, 133.8, 133.3, 136.0, 135.8, 129.6, 129.4, 128.0, 127.9, 127.6 127.5, 127.4, 124.4, 98.0, 77.7, 77.3, 72.9, 64.0, 30.7, 27.0, 19.2, 15,2 ppm; HRMS (EI): *m/z*: calcd for $C_{25}H_{23}O_3Si$: 399.1416 $[M-tBu-C_2H_5OH]^+$; found: 399.141 $[M-CHOH(C_5H_6O)OC_2H_5]^+$; calcd for $C_{23}H_{25}OSi$: 345.1675; found: 345.1670; minor isomer (characteristic signals): ^1H NMR (500 MHz, $CDCl_3$): $\delta=7.65$–7.68 (m, 2H), 5.63–5.70 (m, 1H), 4.92 (d, $J=4.5$ Hz, 1H,), 4.3 (t, $J=5.5$ Hz, 1H), 3.4.5 (dq, $J=7.0$, 9.5 Hz, 1H), 3.08–317 ppm (m, 1H).

(*R*)-phenyl[(3α*R*,6*R*,7α*S*)-2,3,3α,7α-tetrahydro-6*H*-furo [2,3−β]pyran-6-yl]methanol (19): Catalyst **1** (48.0 mg, 0.100 mmol) and BaO (400 mg) were added to a mixture of 3-boronoacrolein pinacolate **2** (182 mg, 1.00 mmol) and 2,3-dihydrofuran **16** (700 mg, 10.0 mmol) in an oven-dried round-bottomed flask(10 mL) containing a stirbar. After 1.5 h of stirring at ambient temperature (23°C), **16** was evaporated in vacuo and benzaldehyde (212 mg, 2.00 mmol) was added to the residue. The reaction was allowed to stir at room temperature for 24 h, and was then diluted with EtOAc and filtered through celite. The EtOAc solution was stirred for 30 min with an aqueous saturated solution of $NaHCO_3$. The organic layer was then separated and the aqueous layer extracted with EtOAc (2×20 mL). The combined organic layers were washed with an aqueous saturated solution of NaCl, dried over anhydrous $MgSO_4$, filtered, and concentrated to afford **19** as a crude product. Purification by flash-column chromatography (deactivated silica-gel, hexanes/EtOAc 4:1) led to the pure product **19** (141 mg, 61%) as an oil, which crystallized when stored at −5°C. $[\alpha]_D^{23}=-10.2$ ($c=1.23$ in $CHCl_3$); IR (CH_2Cl_2, cast): $\tilde{\nu}=3435$, 3046, 2877, 1257 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta=$ 5.85 (ddd, $J=10.2$, 4.4, 2.3 Hz, 1H), 5.56 (ddd, $J=10.2$, 1.7, 1.7 Hz, 1H), 5.18 (d, $J=4.1$ Hz, 1H), 4.61 (d, $J=7.5$ Hz, 1H), 4.28–4.31 (m, 1H), 4.22 (ddd, $J=8.2$, 8.2, 4.8 Hz, 1H), 3.96 (ddd, $J=7.7$, 7.7, 7.5 Hz, 1H), 3.42 (brs, 1H), 2.52–2.60 (m, 1H), 2.15–2.22 (m, 1H), 1.73–1.82 ppm (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=139.9$, 128.3, 128.1, 127.3, 127.1, 125.8, 100.6, 77.2, 76.6, 68.2, 38.4, 30.4 ppm; HRMS (ESI) : *m/z*: calcd for $C_{14}H_{16}O_3Na$: 255.0992; found: 255.0993.

Ethyl-(2*E*,4*R*)-4-[(2*R*,5*R*,6*S*)-6-ethoxy-5-heptyl-5,6-dihydro-2*H*-pyran-2-yl]-4-hydroxy-3-methylbut-2-enoate (23): Compound **1** (29.0 mg, 0.060 mmol) and powdered BaO (600 mg) were added to a mixture of 3-boronoacrolein pinacolate **2** (0.360 g, 2.00 mmol) and (*Z*)-ethoxy-non-1-ene **17** (0.510 g, 3.00 mmol) in an oven-dried round-bottomed flask (10 mL) containing a stirbar. After being stirred for 5 h at 20°C, the reaction mixture was diluted with ether (10 mL), filtered through Celite, and concentrated in vacuo. The catalyst was removed by using a short column (deactivated silica-gel, hexanes/ether 9:1), and the excess of **17** was partly recovered by bulb-to-bulb distillation. A mixture of the resulting hetero-Diels–Alder cycloadduct **20** and ethyl 3-methyl-4-oxocrotonate **21** (0.570 g, 4.00 mmol) was stirred at 110°C for 36 h under argon. After being cooled to ambient temperature, a saturated aqueous solution of $NaHCO_3$ (2 mL) was added to the reaction mixture, which was stirred for 30 min. The resulting mixture was then extracted with diethyl ether (2×10 mL). The ethereal layers were combined, washed with brine (10 mL), and dried over anhydrous $MgSO_4$. After filtration and concentration in vacuo to evaporate ether, ethyl 3-methyl-4-oxocrotonate was partly recovered by bulb-to-bulb distillation. The residue was purified by flash-column chromatography (deactivated silica-gel, hexanes/ether 6:1) to afford **23** (0.545 g, 74%). $[\alpha]_D^{23}=+3.34$ ($c=1.0$ in $CHCl_3$); IR ($CHCl_3$,

cast): $\tilde{\nu}$ = 3413, 2926, 1717, 1655 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 6.05 (s, 1H), 5.83 (ddd, J = 2.9, 2.9, 10.4 Hz, 1H), 5.62 (ddd, J = 2.0, 2,0, 10.4 Hz, 1H), 4.72 (d, J = 3.7 Hz, 1H), 4.48–4.53 (m, 1H), 4.16 (q, J = 7.2 Hz, 2H), 3.97 (dd, J = 4.5, 4.5 Hz, 1H), 3.90 (dq, J = 11.6, 7.1 Hz, 1H), 3.45–3.53 (m, 2H), 2.22–2.28 (m, 1H), 2.18 (s, 3H), 1.54–1.62 (m, 1H), 1.20–1.42 (m, 17H), 0.89 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.6, 157.0, 129.5, 124.8, 116.8, 98.9, 77.8, 74.3, 65.1, 59.6, 38.1, 31.8, 29.8, 29.7, 29.2, 26.8, 22.6, 15.3, 14.8, 14.3, 14.0 ppm; HRMS (ESI): m/z: calcd for $C_{21}H_{36}O_5Na$: 391.2455; found: 391.2454; assay of enantiomeric excess: chiral HPLC analysis (Chiralpak AS, 98% hexane/isopropanol, 1.00 mL min^{-1}, 210.8 nm, t_R (major) = 5.384 min; t_R (minor) = 4.932 min): 96% *ee*.

Ethyl-(2*E*,4*R*)-4-[(2*R*,5*R*,6*S*)-6-ethoxy-5-methyl-5,6-dihydro-2*H*-pyran-2-yl]-4-hydroxy-3-methylbut-2-enoate (26) (allylboration product of 24): Compound **1** (15.0 mg, 0.030 mmol) and powdered BaO (0.300 g) were added to a mixture of 3-boronoacrolein pinacolate **2** (0.182 g, 1.00 mmol) and ethyl 1-propenyl ether **18** (*Z*/*E* 3:1, 0.170 g, 2.00 mmol) in an oven-dried round-bottomed flask (10 mL) containing a stirbar. After being stirred for 14 h at 20 °C (^1H NMR spectroscopy showed that the ratio of ethyl (*Z*)-1-propenyl ether and ethyl (*E*)-1-propenyl ether in the flask was about 1:1 after completion of the cycloaddition). The reaction mixture was then diluted with ether (5 mL), filtered through Celite, and concentrated in vacuo. The catalyst was removed by using a short column (deactivated silica-gel, hexanes/ether 9:1) to afford the cycloadducts **24** and **25** (^1H NMR spectroscopy showed that the ratio of the two cycloadducts was about 95:5).

A mixture of hetero-Diels–Alder cycloadducts **24** and **25** and ethyl 3-methyl-4-oxocrotonate **21** (0.280 g, 2.00 mmol) was stirred at 110 °C for 36 h under argon. After being cooled to ambient temperature, an aqueous saturated $NaHCO_3$ solution (2 mL) was added to the reaction mixture, which was stirred for a further 30 min. After this time, the resulting mixture was extracted with ether (2 × 10 mL). The ethereal layers were combined, washed with brine (10 mL), then dried over anhydrous $MgSO_4$. After filtration and concentration in vacuo to evaporate ether, ethyl 3-methyl-4-oxocrotonate was partly recovered by bulb-to-bulb distillation. The residue was purified by flash-column chromatography (deactivated silica-gel, hexanes/ether 6:1) to afford allylboration product **26** (0.213 g, 75%). $[\alpha]_D^{23}$ = +19.2 (c = 2.8 in $CHCl_3$); IR ($CHCl_3$, cast): $\tilde{\nu}$ = 3410, 2978, 1716, 1653 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 6.04 (s, 1H), 5.79 (ddd, J = 2.5, 3.8, 10.3 Hz, 1H), 5.58 (ddd, J = 1.9, 1.9, 10.3 Hz, 1H), 4.69 (d, J = 3.6 Hz, 1H), 4.44–4.49 (m, 1H), 4.16 (q, J = 7.1 Hz, 2H), 3.94–4.02 (m, 1H), 3.90 (dq, J = 9.7, 7.1 Hz, 1H), 3.52 (dq, J = 9.7, 7.1 Hz, 1H), 3.35–3.42 (m, 1H), 2.30–2.43 (m, 1H), 2.20 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3H), 1.08 ppm (d, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.6, 156.8, 131.2, 124.7, 117.0, 99.4, 77.9, 74.6, 65.0, 59.6, 33.2, 15.3, 14.9, 14.3, 14.3 ppm; HRMS (ESI): m/z: calcd for $C_{15}H_{24}O_5Na$: 307.1516; found: 307.1513; Assay of enantiomeric excess: chiral HPLC analysis (Chiralpak AS, 100% hexanes, 1.00 mL min^{-1}, 210.8 nm, t_R(major) = 10.113 min; t_R(minor) = 9.546 min) 96% *ee*.

***rac*-Ethyl-(2*E*,4*R*)-4-[(2*R*,5*S*,6*S*)-6-ethoxy-5-methyl-5,6-dihydro-2*H*-pyran-2-yl]-4-hydroxy-3-methylbut-2-enoate (27) (allylboration product of 25)**: [Yb(fod)$_3$] (106 mg, 0.100 mmol) was added to a mixture of 3-boronoacrolein pinacolate **2** (0.182 g, 1.00 mmol) and ethyl 1-propenyl ether **18** (*Z*/*E* 3:1) (0.170 g, 2.00 mmol) in an oven-dried round-bottomed flask (10 mL) containing a stirbar. After being stirred for 14 h at 20 °C (^1H NMR spectroscopy showed that the ratio of ethyl (*Z*)-1-propenyl ether and ethyl (*E*)-1-propenyl ether in the flask was about 3:1 after the completion of the reaction), the reaction mixture was diluted with ether (5 mL), filtered through Celite, and concentrated in vacuo. The catalyst was removed by using a short column (deactivated silica-gel, hexanes/ether 9:1) to afford the cycloadducts **24** and **25** (^1H NMR spectroscopy showed that the ratio of two cycloadducts was about 3:1).

A mixture of hetero-Diels–Alder cycloadducts **24** and **25** and ethyl 3-methyl-4-oxocrotonate **21** (0.280 g, 2.00 mmol) was stirred at 110 °C for 36 h under argon. After being cooled to ambient temperature, an aqueous saturated $NaHCO_3$ solution (2 mL) was added to the reaction mixture, which was stirred for 30 min. The resulting mixture was then extracted with ether (2 × 10 mL). The ethereal layers were combined, washed with brine (10 mL), then dried over anhydrous $MgSO_4$. After filtration and concentration in vacuo to evaporate ether, ethyl 3-methyl-4-oxocrotonate was partly recovered by bulb-to-bulb distillation. The residue was purified by flash-column chromatography (deactivated silica-gel, hexanes/ether 6:1) to afford the racemic allylboration product **26** (0.159 g, 56%), for which the spectroscopic data were in full agreement with the enantioenriched compound, and allylboration product **27** (0.0540 mg, 19%). The relative stereochemistries of **26** and **27** were partly confirmed by TROESY experiments. IR ($CHCl_3$, cast): $\tilde{\nu}$ = 3472, 3034, 1716, 1653 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 6.02 (s, 1H), 5.72 (ddd, J = 2.4, 2.8, 10.3 Hz, 1H), 5.56 (ddd, J = 1.9, 1.9, 10.3 Hz, 1H), 4.37–4.42 (m, 1H), 4.33 (d, J = 6.0 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 3.99 (d, J = 4.5 Hz, 1H), 3.90 (dq, J = 9.6, 7.1 Hz, 1H), 3.52 (dq, J = 9.6, 7.1 Hz, 1H), 3.10 (br s, 1H), 2.22–2.36 (m, 1H), 2.20 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3H), 1.02 ppm (d, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.5, 156.4, 131.7, 124.6, 117.5, 103.5, 78.1, 75.0, 64.9, 59.8, 34.8, 16.8, 15.4, 15.2, 14.4 ppm. HRMS (ESI): m/z: calcd for $C_{15}H_{24}O_5Na$: 307.1516; found: 307.1514.

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