Intramolecular allylboration of γ-(ω-formylalkoxy)allylboronates for syntheses of trans- or cis-2-(ethenyl)tetrahydropyran-3-ol and 2-(ethenyl)oxepan-3-ol

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Abstract: 3-Alkoxy-1-alkynes 4 were hydroborated with pinacolborane (HBpin) to give 3-alkoxy-1-alkenylboronates 5. The latter gave (E)-3-alkoxyallylboronates (8: (E)-(MeO)₂CHCH₂(CH₂)nCH₂OCH=CHCH₂Bpin, n=1-3) when they were subjected to iridium-catalyzed isomerization of the double bond. The corresponding (Z)-isomers 10 were synthesized by nickel-catalyzed isomerization of 5. Both allylboronates underwent intramolecular allylboration leading to the formation of trans-2-(ethenyl)tetrahydropyran-3-ol or 2-(ethenyl)oxepan-3-ol from 8 and the corresponding cis-isomers from 10 in the presence of Yb(OTf)₃ (20 mol %) in aqueous acetonitrile at 90 °C.
1. Introduction

Reactions of allylboron compounds with aldehydes or ketones\(^1\) have proved to be very efficient for diastereoselective building of several adjacent chiral centers, intramolecular versions of which have recently developed to achieve five-, six-, seven-, or eight-membered cyclization with diastereoselectivity analogous to that of intermolecular reactions.\(^2,3,4\) Although the protocol had been hampered by the lack of effective method for the synthesis of desired \(\omega\)-acylallylboron compounds, several methods are now available. One-carbon homologation of isomerically pure 1-halo-1-alkenes to allylboronates \(\textit{via}\) alkenyllithium intermediates stereoselectively provides both \((E)\)- and \((Z)\)-allylboronates (Eq. 1).\(^5\) Palladium-catalyzed coupling reaction of pinBCH\(_2\)ZnI (pin=pinacolato) with 1-halo-1-alkenes is an alternative for direct homologation of 1-halo-1-alkenes (Eq. 2).\(^2b,4a,6\) One-carbon homologation of 1-alkenylboronates is convenient for the synthesis of \((E)\)-allylboronates since \((E)\)-1-alkenylboronates are easily accessible \(\textit{via}\) hydroboration of terminal alkynes. The
reaction of 1-alkenylboronates with LiCH₂Cl, *in situ* generated from ICH₂Cl and BuLi at -100 °C, afforded the corresponding allylboronates with retention of *E*-configuration (Eq. 3). Two-methods are available for borylation of allyl nucleophiles or electrophiles. Palladium-catalyzed coupling reaction of diboron (pinBBpin) with allyl acetates or allyl chlorides stereospecifically yields (*E*)-allylboronates (Eq. 4). Metalation of allyl ethers is used for the synthesis of (*Z*)-allyllithiums and their transmetalation to *i*-PrOBpin (Eq. 5). We recently demonstrated the synthesis of (*E*)-allylboronates from (*E*)-1-alkenylboronates via isomerization of the double bond. Various cationic iridium complexes converted 3-alkoxyl-1-alkenylboronates to the corresponding allylboronates at room temperature with high *E*-selectivities (Eq. 6). For the synthesis of ω-acylallylboron compounds from organolithiums, aldehyde and ketone carboxyls are protected as acetals and deprotected during allylboration. On the other hand, the catalytic coupling reactions shown in Eqs 2 and 4 tolerate to carbonyl functionalities, thus allowing direct preparation from ω-acyl-1-halo-1-alkenes and their *in situ* cyclization. High stability of pinacol ester derivatives (Bpin) in the presence of water or air is advantageous for the synthesis and isolation of boron compounds.
Herein, we report an alternative method for the synthesis of \((E)\)- or \((Z)\)-3-alkoxyallylboron compounds \((8, 10)\) via catalyzed isomerization of 1-alkenylboronates \((5)\) and their cyclization to \textit{cis}- or \textit{trans}-2-(ethenyl)tetrahydropyran-3-ol \((9a, 11a)\) or 2-(ethenyl)oxepan-3-ol \((9b, 11b)\) (Schemes 1-4). For simplicity of the synthetic route, we used \((E)\)-3-alkoxyalkenylboronates \((5a-c)\) as common intermediates of both \((E)\)- and \((Z)\)-allylboronates. Iridium-catalyzed isomerization of the double bond of 5 stereoselectively gave \((E)\)-allylboronates \((8a-c, >99\%)\), as was previously demonstrated in the intermolecular reaction.\(^{10}\) Isomerization by a nickel catalyst gave \((Z)\)-isomers \((10a-c)\) with selectivities in a ranging from 84 to 93%.

2. Results and Discussion

2.1. Synthesis of 1-alkenylboronates \((5)\)

A difficulty in intramolecular allylmetalations is the necessity to synthesize an allylmetal moiety in the presence of a carbonyl group or to synthesize a carbonyl
function in the presence of a labile allylmethyl moiety. The former synthesis can be achieved by protection of the carbonyl group with a dimethyl acetal during the preparation of the allylboron moiety, as was amply demonstrated by Hoffman.\textsuperscript{1} We adopted their protection-deprotection strategy for the synthesis of 3-alkoxyallylboronates (8, 10) and their subsequent intramolecular allylboration. Mono-propargylation of diols (1a-c) was followed by Swern oxidation and acetalization with CH(OMe)\textsubscript{3}/H\textsuperscript{+} to give protected propargyl ethers (4a-c) (Scheme 1). Although RhCl(CO)(PPh\textsubscript{3})\textsubscript{2}\textsuperscript{11a} failed the catalyzed hydroboration of 4 with pinacolborane (HBpin), a platinum(0) catalyst generated \textit{in situ} from Pt(dba)\textsubscript{2} and TTMPP (2 eqs, TTMPP=tris(2,4,6-trimethoxyphenyl)phosphine)\textsuperscript{11b} furnished three alkenylboronates (5a-c) required for six-, seven- and eight-membered cyclization.

\textbf{2.2 Isomerization of 1-alkenylboronates to allylboronates}

Since 1-alkenylboronates are much less sensitive to acidic water than allylboronates during deprotection of the carbonyl group, we first examined the isomerization of 6 to 7, which would \textit{in situ} undergo intramolecular allylboration. However, all attempts at

\<<Scheme 1>>
catalyzed isomerization of 6 failed completely. Alkenylboronate (6) remained intact, presumably due to a chelation to a carbonyl group.

<<Scheme 2>>

The effect of catalysts on positional isomerization of 5 is shown in Table 1. Felkin's cationic iridium(I) complex isomerizes the double bond via a π-allyl mechanism in predominating (E)-alkenes.\textsuperscript{10,12} Thus, E-selective isomerization of the double bond in 5 to the γ-position giving 8 was carried out in ethyl acetate at room temperature in the presence of 3 mol\% of [IrH\textsubscript{2}(solv)\textsubscript{2}(PPh\textsubscript{2}Me)\textsubscript{2}]PF\textsubscript{6}, which was generated \textit{in situ} by passing a stream of H\textsubscript{2} into a solution of [Ir(cod)(PPh\textsubscript{2}Me)\textsubscript{2}]PF\textsubscript{6}.\textsuperscript{10} High E-selectivities exceeding 99\% and high conversions in a range of 97-99\% were easily achieved for 5a-c (entries 1-3). On the other hand, we followed the nickel-catalyzed procedure\textsuperscript{13} in preparing (Z)-isomers since t-BuOK in DMSO\textsuperscript{14} was hampered by the sensitivity of the allylboron moiety to the base. The conversions and selectivities of the nickel-catalyzed isomerization\textsuperscript{13} were found to be very sensitive to the phosphine ligands (entries 4-7). Among the complexes used, PPh\textsubscript{2}Me was recognized to be the best ligand to achieve both high conversions and Z-selectivities for 5a-c (entries 7-9).
2.3. Cyclization via intramolecular allylboration

A sequence of $E$-selective isomerization of 5 and their six- or seven-membered cyclization is shown in Scheme 3. Because of the high sensitivity of allylboronates (8) to chromatography on silica gel, the synthesis of 8 was directly followed by cyclization to 9. Yields of 9 were highly depended on the catalysts and solvents used for hydrolysis of acetal.\textsuperscript{2,15,16} The use of protic acids such as HCl and TfOH resulted in significantly low yields, presumably due to a competitive, hydrolytic B-C bond cleavage of the allylboron intermediate. Among the metal salts that facilitate the hydrolysis of acetal in aqueous acetonitrile at 90 °C, ytterbium(III) triflate (20 mol%) afforded the best yield for the six-membered cyclization (9a); e.g., LiBF$_4$ (56%), CuOTf (44%), AgOTf (42%), Sm(OTf)$_3$ (55%), Er(OTf)$_3$ (58%), Yb(OTf)$_3$ (77%). Allylboration is faster in less-polar solvents than that of donating to the boron atom, but acetonitrile was recognized to be the best solvent; e.g., acetonitrile (77%), 1,2-dichloroethane (58%), THF (28%), and DMF (18%). Analogously, the cyclization of 5b gave 9b in 56% yield, but the protocol completely failed the eight-membered cyclization of 8c, presumably due to an
intermolecular reaction giving polymeric materials. Such eight-membered cyclization
has been limitedly reported in the corresponding allylboronates possessing a Z-double
bond in a main chain because it fixes a conformation favorable for cyclization.$^2f$

Analogously, $Z$-selective isomerization of 5 to 10 was directly followed by
intramolecular allylboration to give 11a or 11b (Scheme 4). Since the cyclization
proceeds through a chair-like, six-membered transition state as was demonstrated in the
intramolecular allylboration of carbonyl compounds,$^1$ cis-isomers (11a,b) were
selectively given from (Z)-allylboronates (10a,b). The reactions resulted in slightly
lower cis-selectivities than that of Z-selectivities of 10, thus suggesting E-Z
isomerization of 10 before allylboration. Again, the protocol failed the eight-membered
cyclization of 10c.

In conclusion, we have found a reliable route to the syntheses of (E)- and
(Z)-3-alkoxyallylboronates starting from the corresponding 1-alkenylboronates, which
are easily accessible by hydroboration of terminal alkynes. Six- and seven-membered
trans- or cis-2-ethenyl-3-oxacycloalkanols were diastereoselectively obtained by cyclization via the intramolecular allylboration of 3-alkoxyallylboronates.

3. Experimental

3.1. Reagents

All phosphine ligands were commercially available and purified by distillation if necessary. Yb(OTf)$_3$, Cu(OTf), Ag(OTf), Nb(OTf)$_3$, Sm(OTf)$_3$, Er(OTf)$_3$ and LiBHEt$_3$ in THF were purchased from Sigma-Aldrich. Pt(dba)$_2$, $^{17}$ [Ir(cod)(PPh$_2$Me)$_2$]PF$_6$, $^{18}$ NiCl$_2$(PPh)$_3$, $^{19}$ NiCl$_2$(PPh$_2$Me)$_2$, $^{20}$ NiCl$_2$(dppb), $^{21}$ and NiCl$_2$(dpf) $^{22}$ were synthesized by the reported procedures. Pinacolborane was prepared from borane-methylsulfide complex and pinacol. $^{23}$

3.2. Syntheses of 2a-2c (Scheme 1)

3.2.1. 4-(Prop-2-ynyloxy)butan-1-ol (2a). A solution of 1,4-butanediol (54.1 g, 0.6 mol) in DMF (50 ml) was dropwise added into a suspension of sodium hydride (13.2 g, 0.55 mol) in DMF (100 ml) at 0°C. After being stirred for 0.5 h at 0°C, a solution of propargyl bromide (17.8 g, 0.15 mol) in DMF (50 ml) was added. The mixture was then
stirred for 24 h at room temperature. The product was extracted with ether, washed with water, dried over MgSO$_4$, and finally concentrated in vacuo. Distillation afforded 2a (16.3 g, 85%); Bp 65-70 °C/0.05 mmHg; IR (neat): 3375, 3291, 2111 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.63-1.75 (m, 4H), 1.91 (s, 1H), 2.44 (t, $J$ = 2.4 Hz, 1H), 3.57 (t, $J$ = 5.9 Hz, 2H), 3.67 (t, $J$ = 6.0 Hz, 2H), 4.16 (d, $J$ = 2.4 Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 26.2, 29.8, 58.1, 62.6, 70.0, 74.4, 79.6; MS (EI): $m/z$ 39 (66), 69 (56), 71 (100), 81 (15), 89 (14), 127 (2); exact mass calcd for C$_7$H$_{12}$O$_2$: 127.0759 (M$^+$-1), found: 127.0763.

3.2.2. 5-(Prop-2-ynyloxy)pentan-1-ol (2b). Yield: 64%; Bp 61°C/0.15 mmHg; IR (neat): 3386, 3291, 2125 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.43-1.50 (m, 3H), 1.57-1.68 (m, 4H), 2.42 (t, $J$ = 2.3 Hz, 1H), 3.53 (t, $J$ = 6.5 Hz, 2H), 3.66 (t, $J$ = 6.5 Hz, 2H), 4.14 (t, $J$ = 2.3 Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 22.3, 29.2, 32.4, 58.0, 62.8, 70.0, 74.2, 79.9; MS (EI): $m/z$ 39 (100), 55 (59), 69 (76), 84 (61), 101 (21), 141 (2); exact mass calcd for C$_8$H$_{14}$O$_2$: 141.0916 (M$^+$-1), found: 141.0923.

3.2.3. 6-(Prop-2-ynyloxy)hexan-1-ol (2c). Yield: 66%; Bp 71-76°C/0.03 mmHg; IR (neat): 3362, 3292, 2114 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.34-1.44 (m, 4H),
1.55-1.65 (m, 4H), 1.92 (s, 1H), 3.43 (t, $J = 2.4$ Hz, 1H), 3.52 (t, $J = 6.6$ Hz, 2H), 3.64 (t, $J = 6.6$ Hz, 2H), 4.14 (d, $J = 2.4$ Hz, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 25.5, 25.8, 29.4, 32.6, 58.0, 62.8, 70.1, 74.1, 79.9; MS (FAB): m/z 55 (35), 83 (41), 107 (21), 137 (80), 157 (78); exact mass calcd for C$_9$H$_{16}$O$_2$: 157.1229 (M$^+$+1), found: 157.1224.

3.3. Syntheses of 3a-3c (Scheme 1)

3.3.1. 4-(Prop-2-ynyloxy)butanal (3a). Dimethyl sulfoxide (11 ml, 156 mmol) was droppedwise added into a solution of oxalyl chloride (7.6 ml, 87 mmol) in dichloromethane (100 ml) at -78°C. After being stirred for 15 min, a solution of 2a (9.3 g, 72 mmol) in dichloromethane (10 ml) was added. The resulting mixture was stirred for 15 min at -78°C. Triethylamine (49 ml, 351 mmol) was then added. The mixture was allowed to reach 0°C slowly before addition of water (200 ml). The product was extracted with dichloromethane. Distillation gave 3a (10.1 g, 99%). Bp 56°C/0.4 mmHg; IR (neat): 3280, 2128, 1719 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.91 (tt, $J = 6.1$, 7.1 Hz, 2H), 2.40 (t, $J = 2.5$ Hz, 1H), 2.53 (dt, $J = 1.4$, 7.1 Hz, 2H), 3.53 (t, $J = 6.0$ Hz, 2H), 4.10 (d, $J = 2.5$ Hz, 2H), 9.76 (t, $J = 1.4$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 22.2, 40.7, 58.1, 68.8, 74.3, 76.6, 202.1; MS (EI): m/z 71 (42), 77 (20), 89 (24), 107 (27), 125 (40), 137 (80), 157 (78); exact mass calcd for C$_9$H$_{16}$O$_2$: 157.1229 (M$^+$+1), found: 157.1224.
127 (32); exact mass calcd for C₇H₁₀O₂: 127.0759 (M⁺+1), found: 127.0767.

3.3.2. 5-(Prop-2-ynyloxy)pentanal (3b). Yield: 93 %; Bp 49 °C/0.23 mmHg; IR (neat): 3282, 2121, 1720 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.61-1.78 (m, 4H), 2.43 (t, J = 2.4 Hz, 1H), 2.48 (dt, J = 1.7, 7.3 Hz, 2H), 3.54 (t, J = 6.6 Hz, 2H), 4.14 (d, J = 2.4 Hz, 2H), 9.78 (t, J = 1.7 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 18.8, 22.8, 43.5, 58.0, 69.5, 74.2, 79.8, 202.4; MS (FAB): m/z 39 (67), 41 (71), 68 (44), 69 (73), 85 (100), 95 (10), 141 (5); exact mass calcd for C₈H₁₂O₂: 141.0916 (M⁺+1), found: 141.0920.

3.3.3. 6-(Prop-2-ynyloxy)hexanal (3c). Yield: 81%; Bp 60 °C/0.25 mmHg; IR (neat): 3278, 2127, 1720 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 1.38-1.46 (m, 2H), 1.59-1.70 (m, 4H), 2.42 (t, J = 2.4 Hz, 1H), 2.45 (dt, J = 1.7, 7.3 Hz, 2H), 3.52 (t, J = 6.5 Hz, 2H), 4.13 (d, J = 2.4 Hz, 2H), 9.77 (t, J = 1.7 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 21.8, 25.7, 29.2, 43.7, 58.0, 69.8, 74.1, 79.9, 202.6; MS (FAB): m/z 55 (42), 69 (57), 93 (100), 97 (49), 115 (45), 153 (40), 155 (20); exact mass calcd for C₉H₁₄O₂: 155.1072 (M⁺+1), found: 155.1072.

3.4. Syntheses of 4a-4c (Scheme 1)

3.4.1. 3-[4,4-(dimethoxy)butoxy]propyne (4a). To a solution of 3a (3.78 g, 30 mmol)
in anhydrous methanol (37 ml) were added $p$-toluenesulfonic acid (2 g) and (trimethoxy)methane (40 ml, 366 mmol). After being stirred for 1 day at room temperature, the product was extracted with diethyl ether, washed in saturated aqueous Na$_2$SO$_4$ and brine, and then dried over MgSO$_4$. Distillation gave 4a (5.1 g, 99%). Bp 46 °C/0.06 mmHg; IR (neat): 3260, 2135 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.62-1.72 (m, 4H), 2.42 (t, $J = 2.4$ Hz, 1H), 3.32 (s, 6H), 3.54 (t, $J = 6.1$ Hz, 2H), 4.14 (d, $J = 2.4$ Hz, 2H), 4.39 (t, $J = 5.4$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 24.6, 29.1, 52.7, 58.0, 69.7, 74.2, 79.9, 104.3; MS (EI): $m/z$ 39 (58), 47 (74), 55 (74), 75 (100), 85 (89), 101 (30), 109 (25), 141 (82), 171 (4); exact mass calcd for C$_9$H$_{16}$O$_3$: 171.1021 (M$^+$-1), found: 171.1011.

3.4.2. 3-[5,5-(Dimethoxy)pentyloxy]propyne (4b). Yield: 83%; Bp 60-67 °C/0.37 mmHg; IR (neat): 3260, 2112 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.36-1.43 (m, 2H), 1.57-1.63 (m, 4H), 2.39 (t, $J = 2.5$ Hz, 1H), 3.28 (s, 6H), 3.49 (t, $J = 6.5$ Hz, 2H), 4.10 (d, $J = 2.5$ Hz, 2H), 4.33 (t, $J = 5.8$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 22.1, 29.2, 32.2, 52.6, 58.0, 69.9, 74.1, 79.9, 104.4; MS (EI): $m/z$ 39 (10), 41 (10), 47 (11), 67 (12), 71 (22), 75 (100), 101 (7), 155 (23), 185 (1); exact mass calcd for C$_{10}$H$_{18}$O$_3$: 185.1178
3.4.3. 3-[6,6-(Dimethoxy)hexyloxy]propyne (4c). Yield: 92%; Bp 68-74 °C/0.25 mmHg; IR (neat): 3260, 2135 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.29-1.41 (m, 4H), 1.55-1.65 (m, 4H), 2.39 (t, \(J = 2.2\) Hz, 1H), 3.28 (s, 6H), 3.48 (t, \(J = 6.5\) Hz, 2H), 4.10 (d, \(J = 2.2\) Hz, 2H), 4.33 (t, \(J = 5.7\) Hz, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 24.4, 25.9, 29.4, 32.4, 52.6, 58.0, 70.1, 74.1, 80.0, 104.4; MS (EI): \(m/z\) 39 (24), 41 (30), 47 (35), 71 (70), 75 (100), 81 (57), 97 (11), 113 (15), 143 (6), 169 (75), 199 (2); exact mass calcd for C\(_{11}\)H\(_{20}\)O\(_3\): 199.1334 (M\(^+\)-1), found: 199.1335.

3.5. Syntheses of 5a-5c (Scheme 1)

3.5.1.

2-{(E)-3-[4,4-(Dimethoxy)butoxy]propen-1-yl}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5a). Pinacolborane (8.5 g, 67 mmol), Pt(dba)\(_2\) (1.0 g, 1.64 mmol), and tris(2,4,6-trimethoxyphenyl)phosphine (3.5 g, 6.6 mmol) were added into a solution of 4a (9.0 g, 52.2 mmol) in toluene (150 ml) at 0°C. After being stirred for 1 day, the mixture was treated with methanol (20 ml) and poured into a buffer solution (pH 7). The product was extracted with ether, dried over MgSO\(_4\). Chromatography on silica gel with
hexane/ethyl acetate (10/1) afforded 5a (12.6 g, 80%). IR (neat): 1644 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.24 (s, 12H), 1.57-1.69 (m, 4H), 3.29 (s, 6H), 3.42 (t, \(J = 6.1\) Hz, 2H), 3.54 (t, \(J = 5.4\) Hz, 1H), 4.01 (dd, \(J = 1.7, 4.6\) Hz, 2H), 5.67 (dt, \(J = 1.7, 18.3\) Hz, 1H), 6.61 (dt, \(J = 4.6, 18.3\) Hz, 1H); \(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 24.7, 24.8, 29.2, 52.7, 70.2, 77.3, 83.2, 104.3, 149.5; MS (EI): \(m/z\) 71 (100), 75 (31), 85 (93), 101 (20), 117 (13), 197 (15), 269 (62), 299 (10); exact mass calcd for C\(_{15}\)H\(_{29}\)BO\(_5\): 299.2030 (M\(^+\)-1), found: 299.2029.

3.5.2.

2-\{(\(E\))-3-[5,5-(Dimethoxy)pentyloxy]propen-1-yl\}-4,4,5,5-tetramethyl-1,3,2-dioxabrolane (5b). Yield: 71%; IR (neat): 1643 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.24 (s, 12H), 1.35-1.43 (m, 2H), 1.54-1.61 (m, 4H), 3.29 (s, 6H), 3.41 (t, \(J = 6.6\) Hz, 2H), 4.01 (dd, \(J = 1.8, 4.6\) Hz, 2H), 4.33 (t, \(J = 5.8\) Hz, 1H), 5.67 (dt, \(J = 1.8, 18.1\) Hz, 1H), 6.61 (dt, \(J = 4.6, 18.1\) Hz, 1H); \(^1\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 21.3, 24.7, 29.5, 32.3, 52.6, 70.5, 72.4, 76.7, 83.2, 104.4, 149.5; MS (EI): \(m/z\) 57 (25), 75 (41), 85 (100), 99 (33), 115 (31), 167 (30), 197 (20), 283 (66), 313 (5); exact mass calcd for C\(_{16}\)H\(_{31}\)BO\(_5\): 313.2186 (M\(^+\)-1), found: 313.2171
3.4.3

2-\{(E)-3-[6,6-(Dimethoxy)hexyloxy]propen-1-yl\}-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5c). Yield: 69%; IR (neat): 1644 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.27 (s, 12H), 1.33-1.43 (m, 4H), 1.56-1.63 (m, 4H), 3.31 (s, 6H), 3.43 (t, \(J = 6.6\) Hz, 2H), 4.04 (dd, \(J = 1.7, 4.6\) Hz, 2H), 4.36 (t, \(J = 5.7\) Hz, 1H), 5.69 (dt, \(J = 1.7, 18.1\) Hz, 1H), 6.64 (dt, \(J = 4.6, 18.1\) Hz, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 24.5, 24.8, 26.1, 29.7, 32.4, 52.6, 70.6, 72.4, 83.2, 104.5, 149.6; MS (EI): \(m/z\) 71 (83), 81 (88), 99 (73), 113 (75), 129 (51), 167 (42), 197 (47), 297 (100), 327 (10); exact mass calcd for C\(_{17}\)H\(_{33}\)O\(_5\)B\(_2\): 327.2343 (M\(^+\)-1), found: 327.2340.

3.6. Iridium-catalyzed isomerization (Table 1 and Scheme 3)

A dry 25 ml two-neck flask, equipped with a magnetic bar and a rubber septum, was charged with [Ir(cod)(PPh\(_2\)Me)\(_2\)]PF\(_6\) (0.023 g, 0.03 mmol) and flushed with argon. AcOEt (5 ml) was then added. Hydrogen gas was bubbled for 3 min into the solution through a needle to give a light yellow solution. The excess hydrogen was thoroughly replaced with argon by passing into the solution for 3 min. To the catalyst solution thus obtained was added 5a (1.0 mmol) and the mixture was then stirred at room temperature
for 3 h. The reaction was quenched with a pH 7 buffer solution. The product was extracted with ether, dried (MgSO$_4$), and concentrated. $^1$H NMR analysis of the residue gave the conversions and the trans/cis-selectivities shown in Table 1 and Scheme 3. 8a:

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.24 (s, 12H), 1.50 (d, $J = 7.6$ Hz, 2H), 1.66-1.70 (m, 4H), 3.31 (s, 6H), 3.63 (brs, 2H), 4.38 (brs, 1H), 4.78 (dt, $J = 7.6$, 12.5 Hz, 1H), 6.22 (d, $J = 12.5$ Hz, 1H). 8b: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.22 (s, 12H), 1.36-1.43 (m, 2H), 1.51-1.62 (m, 6H), 3.29 (s, 6H), 3.60 (t, $J = 6.6$ Hz, 2H), 4.33 (t, $J = 5.8$ Hz, 1H), 4.75 (dt, $J = 7.6$, 12.5 Hz, 1H), 6.18 (dt, $J = 1.5$, 12.5 Hz, 1H). 8c: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.25 (s, 12H), 1.30-1.45 (m, 4H), 1.50-1.68 (m, 6H), 3.33 (s, 6H), 3.51 (t, $J = 6.6$ Hz, 2H), 4.35 (t, $J = 5.0$ Hz, 1H), 4.78 (dt, $J = 6.6$, 12.5 Hz), 6.23 (d, $J = 12.5$ Hz, 1H).

3.7. Nickel-catalyzed isomerization (Table 1 and Scheme 4)

NiCl$_2$(PPh$_2$Me)$_2$ (0.021 g, 0.04 mmol) was added to a solution of 5a (1.0 mmol) in anhydrous THF (3 ml) at 0°C. LiBHET$_3$ in THF (1 M, 0.04 ml, 0.04 mmol) was then added and the mixture was stirred for 1 day at 30°C. The reaction was quenched with a pH 7 buffer solution. The product was extracted with ether, dried over MgSO$_4$, and
concentrated. The residue was then analyzed by $^1$H NMR to estimate the conversions and the selectivities shown in Table 1 and Scheme 4.  

**10a**: $^1$H NMR (400 MHz, CDCl$_3$):
$\delta$ 1.24 (s, 12H), 1.66-1.71 (m, 6H), 3.31 (s, 6H), 3.71-3.74 (broad t, 2H), 4.38 (bres, 1H), 4.44 (dt, $J = 6.1$, 7.4 Hz, 1H), 5.95 (d, $J = 6.1$ Hz, 1H).

**10b**: $^1$H NMR (400 MHz, CDCl$_3$):
$\delta$ 1.25 (s, 12H), 1.35-1.45 (m, 2H), 1.59-1.66 (m, 6H), 3.32 (s, 6H), 4.42 (dt, $J = 6.2$, 7.6 Hz, 1H), 5.95 (d, $J = 6.2$ Hz, 1H).

**10c**: $^1$H NMR (400 MHz, CDCl$_3$):
$\delta$ 1.25 (s, 12H), 1.32-1.43 (m, 4H), 1.52-1.70 (m, 6H), 3.31 (s, 6H), 3.70 (t, $J = 6.6$ Hz, 2H), 4.36 (t, $J = 5.8$ Hz, 1H), 4.44 (dt, $J = 6.1$, 7.7 Hz), 5.95 (dt, $J = 1.7$, 6.1 Hz, 1H).

### 3.8. Procedures for cyclization via intramolecular allylboration (Scheme 3 and 4)

The residue obtained by the procedure 3.6. (8a) was dissolved in acetonitrile (10 ml). Water (1.1 ml) and ytterbium triflate (0.124 g, 0.2 mmol) were then added. After being stirred for 2 h at 90°C, ether and 1 M hydrochloric acid were added. The product was extracted with ether and dried over MgSO$_4$. Chromatography on silica gel with pentane/diethyl ether (1/1) gave 9a (98 mg, 77%).

### 3.9. Syntheses of 9a,b and 11a,b (Scheme 3 and Scheme 4)

The iridium-catalyzed isomerization of 5 (procedure 3.6) was directly followed by
cyclization without isolation of 8 (procedure 3.8.) to synthesize 9. A sequence of nickel-catalyzed isomerization (procedure 3.7.) and cyclization (procedure 3.8.) gave 11.

3.9.1. *trans*-2-(Ethenyl)tetrahydropyran-3-ol (9a). Yield: 77%; IR (neat): 3409 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.40-1.51 (m, 1H), 1.69-1.79 (m, 3H), 2.14-2.18 (m, 1H), 3.30-3.51 (m, 3H), 3.90-3.96 (m, 1H), 5.33 (dd, \(J = 0.8, 10.5\) Hz, 1H), 5.44 (dd, \(J = 0.9, 17.5\) Hz, 1H), 5.88 (ddd, \(J = 7.1, 10.5, 17.5\) Hz, 1H); \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 25.3, 31.5, 67.4, 69.5, 84.0, 118.9, 136.1; MS (FAB): \(m/z\) 41 (97), 55 (100), 71 (61), 77 (53), 83 (62), 91 (61), 95 (40), 101 (37), 129 (39); exact mass calcd for C\(_7\)H\(_{12}\)O\(_2\): 129.0916 (M\(^+\)+1), found: 129.0903.

3.9.2. *trans*-2-(Ethenyl)oxepan-3-ol (9b). Yield: 56%; IR (neat): 3425 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.56-1.81 (m, 6H), 2.04 (m, 1H), 3.57 (ddd, \(J = 4.1, 8.0, 12.0\) Hz, 1H), 3.63-3.69 (m, 2H), 3.96 (ddd, \(J = 5.6, 6.0, 11.7\) Hz, 1H), 5.26 (d, \(J = 10.5\) Hz, 1H), 5.35 (d, \(J = 17.3\) Hz, 1H), 5.93 (ddd, \(J = 6.3, 10.5, 17.3\) Hz, 1H); \(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 20.6, 30.2, 35.1, 70.0, 74.4, 85.6, 117.0, 137.6; MS (ESI): \(m/z\) 41 (38), 55 (38), 85 (63), 101 (45), 136 (100), 154 (86), 165 (20); exact mass calcd for C\(_8\)H\(_{14}\)O\(_2\):
165.0891 (M$^+$+23), found: 165.0880.

3.9.3. *cis*-2-(Ethenyl)tetrahydropyran-3-ol (11a). Yield: 61%; IR (neat): 3427 cm$^{-1}$; 

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.39-1.48 (m, 1H), 1.66-1.75 (m, 1H), 1.85 (s, 1H), 1.92-2.00 (m, 2H), 3.47-3.60 (m, 1H), 3.74 (s, 1H), 3.94-3.95 (m, 1H), 4.06 (dd, J = 4.4, 10.6 Hz, 1H), 5.29 (ddd, J = 1.4, 1.5, 10.7 Hz, 1H), 5.38 (ddd, J = 1.5, 1.7, 17.5 Hz, 1H), 5.88 (ddd, J = 4.4, 10.7, 17.5 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 19.1, 31.5, 66.6, 68.2, 79.9, 116.7, 135.8; MS (FAB): m/z 41(50), 55 (41), 71 (100), 83 (54), 101 (51), 111 (60), 129 (42); exact mass calcd for C$_7$H$_{12}$O$_2$: 129.0916 (M$^+$+1), found: 129.0916.

3.9.4. *cis*-2-(Ethenyl)oxepan-3-ol (11b). Yield: 66%; IR (neat): 3434 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 1.56-1.81 (m, 4H), 1.87-2.18 (m, 3H), 3.73-3.78 (m, 1H), 3.83-3.87 (m, 2H), 3.93-3.99 (m, 1H), 5.21 (dd, J = 0.8, 10.7 Hz, 1H), 5.36 (dd, J = 0.8, 17.3 Hz, 1H), 5.94 (ddd, J = 5.1, 10.7, 17.3 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 19.5, 30.0, 36.4, 69.0, 71.9, 78.8, 115.8, 137.1; MS (ESI): m/z 135 (3), 139 (1), 143 (4), 157 (34), 165 (100); exact mass calcd for C$_8$H$_{14}$O$_2$: 165.0891 (M$^+$+23), found: 165.0878.
References


1. $R^\equiv Li$ + ClCH$_2$Bpin
   $\xrightarrow{}$ R$^\equiv B$O

2. R$^\equiv X$ + i-ZnCH$_2$Bpin
   $\xrightarrow{\text{Pd catalyst}}$ R$^\equiv B$O

3. RO$^\equiv$B-O + LiCH$_2$Cl
   $\xrightarrow{}$ RO$^\equiv$B-O

4. R$^\equiv$OAc + pinB-Bpin
   $\xrightarrow{\text{Pd catalyst}}$ R$^\equiv B$O

5. RO$^\equiv$ + 1. s-BuLi
   $\xrightarrow{}$ RO$^\equiv$B-O
   $\xrightarrow{2. \text{i-PrOBpin}}$ RO$^\equiv$B-O

6. RO$^\equiv$B-O $\xrightarrow{\text{Ir}^+}$ RO$^\equiv$B-O
**Scheme 1.** Synthesis of pinacol 1-alkenylboronate (5)

a) propargyl bromide, NaH  
b) Swern oxidation  
c) CH(OMe)_3, TsOH  
d) pinacolborane, Pt(dba)_2, P(2,4,6-(MeO)_3C_6H_2)_3
Scheme 2
Scheme 3

5a-c $\xrightarrow{[\text{Ir}((\text{cod})(\text{PPh}_2\text{Me})_2)]\text{PF}_6, \text{H}_2, \text{AcOEt}}$ 8a: $n=1$ ($E/Z=99/1$)

8b: $n=2$ ($E/Z=99/1$)

8c: $n=3$ ($E/Z=98/2$)

$\xrightarrow{\text{Yb(OTf)}_3, \text{H}_2\text{O, CH}_3\text{CN, 90 °C}}$ 9a (77%, trans $>$ 92%)

9b (56%, trans $>$ 97%)

(77%, trans $>$ 92%) (56%, trans $>$ 97%)
Scheme 4

Yb(OTf)$_3$, H$_2$O
CH$_3$CN, 90 °C

11a (61%, $cis > 87%$) 11b (66%, $cis > 81%$)

$\text{NiCl}_2$(PPh$_2$Me)$_2$, LiHBEt$_3$
THF

$5a\text{--}c$

10a: $n=1$ ($E/Z = 7/93$)
10b: $n=2$ ($E/Z = 9/91$)
10c: $n=3$ ($E/Z = 10/90$)
### Table 1. Isomerization of 5 to (E)- or (Z)-γ-alkoxyallylboronates (8 or 10)\(^a\)

<table>
<thead>
<tr>
<th>entry</th>
<th>5</th>
<th>catalyst</th>
<th>temp (°C)/time (h)</th>
<th>solvent</th>
<th>convn/% (^b)</th>
<th>selectivity/% (^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5a</td>
<td>[Ir(cod)(PPh$_2$Me)$_2$]PF$_6$/H$_2$</td>
<td>20/0.5</td>
<td>AcOEt</td>
<td>99</td>
<td>(E)&gt;99</td>
</tr>
<tr>
<td>2</td>
<td>5b</td>
<td>[Ir(cod)(PPh$_2$Me)$_2$]PF$_6$/H$_2$</td>
<td>20/0.5</td>
<td>AcOEt</td>
<td>97</td>
<td>(E)&gt;99</td>
</tr>
<tr>
<td>3</td>
<td>5c</td>
<td>[Ir(cod)(PPh$_2$Me)$_2$]PF$_6$/H$_2$</td>
<td>20/0.5</td>
<td>AcOEt</td>
<td>98</td>
<td>(E)&gt;98</td>
</tr>
<tr>
<td>4</td>
<td>5a</td>
<td>NiCl$_2$(dpbb)/LiBHEt$_3$</td>
<td>20/18</td>
<td>THF</td>
<td>92</td>
<td>Z&gt;86</td>
</tr>
<tr>
<td>5</td>
<td>5a</td>
<td>NiCl$_2$(dpff)/LiBHEt$_3$</td>
<td>20/18</td>
<td>THF</td>
<td>87</td>
<td>Z&gt;93</td>
</tr>
<tr>
<td>6</td>
<td>5a</td>
<td>NiCl$_2$(PPh$_3$)$_2$/LiBHEt$_3$</td>
<td>20/18</td>
<td>THF</td>
<td>33</td>
<td>Z&gt;94</td>
</tr>
<tr>
<td>7</td>
<td>5a</td>
<td>NiCl$_2$(PPh$_3$)$_2$/LiBHEt$_3$</td>
<td>20/18</td>
<td>THF</td>
<td>89</td>
<td>Z&gt;93</td>
</tr>
<tr>
<td>8</td>
<td>5b</td>
<td>NiCl$_2$(PPh$_2$Me)$_2$/LiBHEt$_3$</td>
<td>20/18</td>
<td>THF</td>
<td>92</td>
<td>Z&gt;91</td>
</tr>
<tr>
<td>9</td>
<td>5c</td>
<td>NiCl$_2$(PPh$_2$Me)$_2$/LiBHEt$_3$</td>
<td>20/18</td>
<td>THF</td>
<td>93</td>
<td>Z&gt;90</td>
</tr>
</tbody>
</table>

\(^a\) All reactions were carried out at 20 °C for in the presence of 5 (1 mmol) and catalyst (Ir cat: 3 mol%, Ni cat: 4 mol%). \(^b\) Determined by $^1$H-NMR of crude products.