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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*)-$(MeO)_2CHCH_2(CH_2)_nCH_2OCH{=}CHCH_2Bpin$, 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 ω-acylallylboron compounds, several methods are now available. One-carbon homologation of isomerically pure 1-halo-1-alkenes to allylboronates *via* alkenyllithium intermediates stereoselectively provides both (*E*)- and (*Z*)-allylboronates (Eq. 1).[5] Palladium-catalyzed coupling reaction of $\mathrm{pinBCH_2ZnI}$ (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 *via* hydroboration of terminal alkynes. The reaction of 1-alkenylboronates with $LiCH_2Cl$, *in situ* generated from ICH_2Cl and BuLi at -100 °C, afforded the corresponding allylboronates with retention of *E*-configuration (Eq. 3).[7] 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).[4b,8] Metalation of allyl ethers is used for the synthesis of (*Z*)-allyllithiums and their transmetalation to *i*-PrOBpin (Eq. 5).[9] 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).[10] For the synthesis of ω-acylallylboron compounds from organolithiums, aldehyde and ketone carbonyls 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.

<<Eqs. 1-6>>

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 *cis*- or *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 allylmetal 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.[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 $CH(OMe)_3/H^+$ to give protected propargyl ethers (**4a**-**c**) (Scheme 1). Although $RhCl(CO)(PPh_3)_2$[11a] failed the catalyzed hydroboration of **4** with pinacolborane (HBpin), a platinum(0) catalyst generated *in situ* from $Pt(dba)_2$ and TTMPP (2 eqs, TTMPP=tris(2,4,6-trimethoxyphenyl)phosphine)[11b] furnished three alkenylboronates (**5a**-**c**) required for six-, seven- and eight-membered cyclization.

<<Scheme 1>>

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 *in situ* undergo intramolecular allylboration. However, all attempts at 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.[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 $[IrH_2(solv)_2(PPh_2Me)_2]PF_6$, which was generated *in situ* by passing a stream of H_2 into a solution of $[Ir(cod)(PPh_2Me)_2]PF_6$.[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[13] in preparing (*Z*)-isomers since *t*-BuOK in DMSO[14] was hampered by the sensitivity of the allylboron moiety to the base. The conversions and selectivities of the nickel-catalyzed isomerization[13] were found to be very sensitive to the phosphine ligands (entries 4-7). Among the complexes used, PPh_2Me was recognized to be the best ligand to achieve both high conversions and *Z*-selectivities for **5a-c** (entries 7-9).

<<Table 1>>

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.[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]

<<Scheme 3>>

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**.

<<Scheme 4>>

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] $[Ir(cod)(PPh_2Me)_2]PF_6$,[18] $NiCl_2(PPh_3)_2$,[19] $NiCl_2(PPh_2Me)_2$,[20] $NiCl_2(dppb)$,[21] and $NiCl_2(dppf)$ [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}; ^1H NMR (400 MHz, $CDCl_3$): δ 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, $CDCl_3$): δ 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 $C_7H_{12}O_2$: 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}; ^1H NMR (400 MHz, $CDCl_3$) δ 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, $CDCl_3$): δ 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 $C_8H_{14}O_2$: 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}; ^1H NMR (400 MHz, $CDCl_3$): δ 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$_3$): δ 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 $C_9H_{16}O_2$: 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 dropwise 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$_3$): δ 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$_3$):δ 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), 127 (32); exact mass calcd for $C_7H_{10}O_2$: 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, $CDCl_3$): 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); ^{13}C NMR (100 MHz, $CDCl_3$): 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 $C_8H_{12}O_2$: 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, $CDCl_3$): 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); ^{13}C NMR (100 MHz, $CDCl_3$): 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 $C_9H_{14}O_2$: 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_2SO_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}; ^1H NMR (400 MHz, $CDCl_3$): δ 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, $CDCl_3$): δ 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 $C_9H_{16}O_3$: 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}; ^1H NMR (400 MHz, $CDCl_3$): δ 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, $CDCl_3$): δ 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

(M^+-1), found: 185.1190.

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}; ^1H NMR (400 MHz, $CDCl_3$): δ 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, $CDCl_3$): δ 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, $CDCl_3$): δ 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); ^{13}C NMR (100 MHz, $CDCl_3$): δ 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-dioxaborolane (**5b**). Yield: 71%; IR (neat): 1643 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 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); ^{13}C NMR (100 MHz, $CDCl_3$): δ 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, $CDCl_3$): δ 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, $CDCl_3$): δ 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 $C_{17}H_{33}O_5B_1$: 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 $[Ir(cod)(PPh_2Me)_2]PF_6$ (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. ^1H NMR analysis of the residue gave the conversions and the *trans*/*cis*-selectivities shown in Table 1 and Scheme 3. **8a**: ^1H NMR (400 MHz, $CDCl_3$) δ 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**: ^1H NMR (400 MHz, $CDCl_3$): δ 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**: ^1H NMR (400 MHz, $CDCl_3$): δ 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)

$NiCl_2(PPh_2Me)_2$ (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, $CDCl_3$): δ 1.24 (s, 12H), 1.66-1.71 (m, 6H), 3.31 (s, 6H), 3.71-3.74 (broad t, 2H), 4.38 (brs, 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, $CDCl_3$): δ 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, $CDCl_3$): δ 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}; ^1H NMR (400 MHz, $CDCl_3$): δ 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, $CDCl_3$): δ 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 $C_7H_{12}O_2$: 129.0916 (M^++1), found: 129.0903.

3.9.2. *trans*-2-(Ethenyl)oxepan-3-ol (**9b**). Yield: 56%; IR (neat): 3425 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 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, $CDCl_3$): δ 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 $C_8H_{14}O_2$:

165.0891 (M^++23), found: 165.0880.

3.9.3. *cis*-2-(Ethenyl)tetrahydropyran-3-ol (**11a**). Yield: 61%; IR (neat): 3427 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 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, $CDCl_3$）: δ 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 $C_7H_{12}O_2$: 129.0916 (M^++1), found: 129.0916.

3.9.4. cis-2-(Ethenyl)oxepan-3-ol (11b). Yield: 66%; IR (neat): 3434 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 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, $CDCl_3$): δ 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 $C_8H_{14}O_2$: 165.0891 (M^++23), found: 165.0878.

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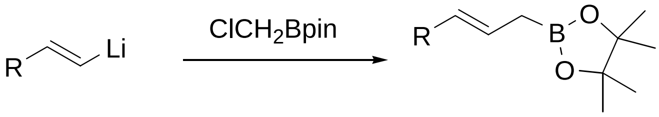
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R
B
O
O

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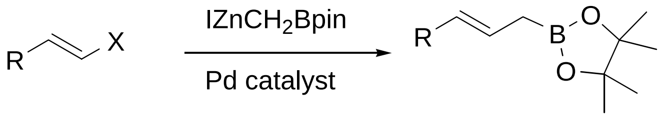
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Pd catalyst
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O
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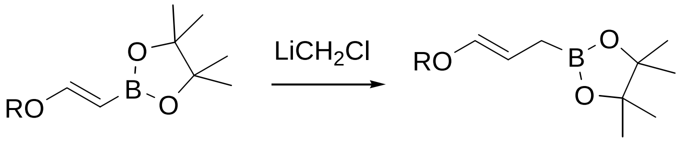
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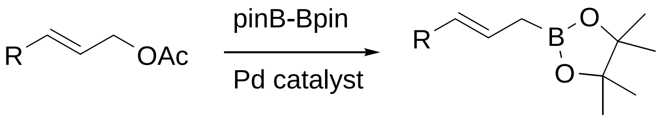
(3)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B
O
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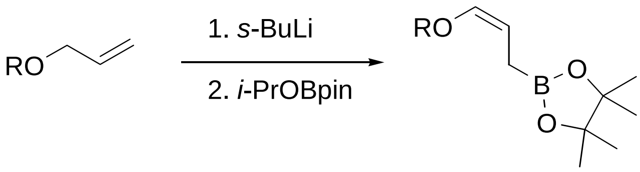
(4)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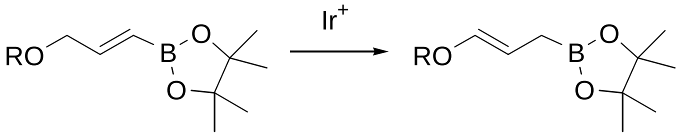
2. *i*-PrOBpin
RO
B
O
O

(5)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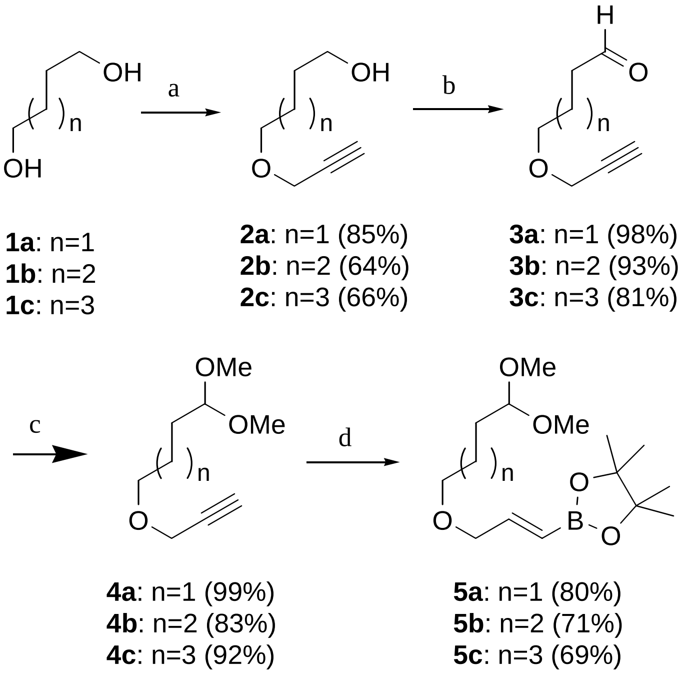
B
O
O
Ir$^+$
RO
B
O
O

(6)



1a: n=1
1b: n=2
1c: n=3

2a: n=1 (85%)
2b: n=2 (64%)
2c: n=3 (66%)

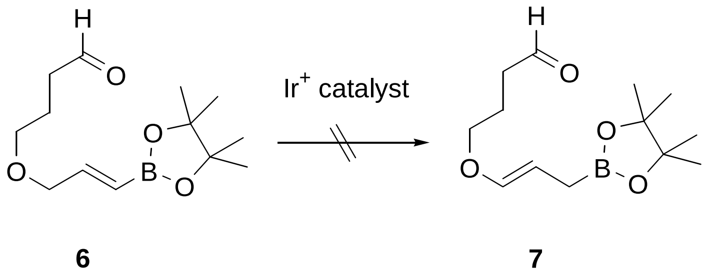
3a: n=1 (98%)
3b: n=2 (93%)
3c: n=3 (81%)

4a: n=1 (99%)
4b: n=2 (83%)
4c: n=3 (92%)

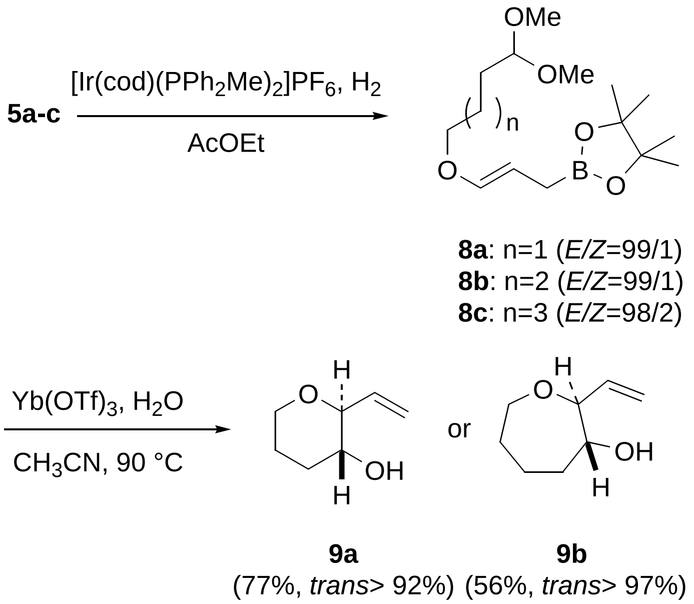
5a: n=1 (80%)
5b: n=2 (71%)
5c: n=3 (69%)

a) propargyl bromide, NaH
b) Swern oxidation
c) $CH(OMe)_3$, TsOH
d) pinacolborane, $Pt(dba)_2$, $P(2,4,6\text{-}(MeO)_3C_6H_2)_3$

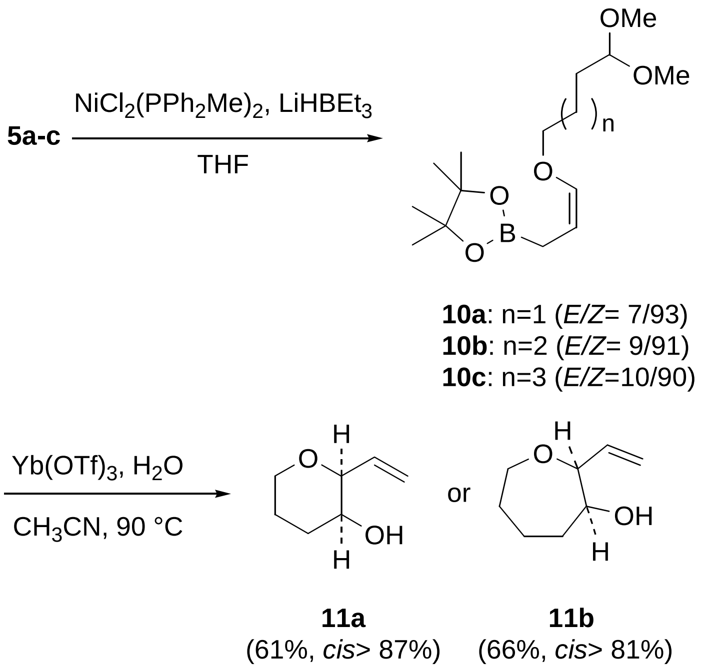
Scheme 1. Synthesis of pinacol 1-alkenylboronate (**5**)



Scheme 2


5a-c
[Ir(cod)(PPh2Me)2]PF6, H2
AcOEt
OMe
OMe
n
O
O
B
O
8a: n=1 (E/Z=99/1)
8b: n=2 (E/Z=99/1)
8c: n=3 (E/Z=98/2)
Yb(OTf)3, H2O
CH3CN, 90 °C
H
O
OH
H
or
H
O
OH
H
9a
(77%, trans> 92%)
9b
(56%, trans> 97%)

Scheme 3



10a: n=1 (*E/Z*= 7/93)
10b: n=2 (*E/Z*= 9/91)
10c: n=3 (*E/Z*=10/90)

11a (61%, *cis*> 87%)

11b (66%, *cis*> 81%)

Scheme 4

Table 1. Isomerization of **5** to (*E*)- or (*Z*)-γ-alkoxyallylboronates (**8** or **10**)[a]

entry	**5**	catalyst	temp (°C)/time (h)	solvent	convn/%[b]	selectivity/%[b]
1	**5a**	$[Ir(cod)(PPh_2Me)_2]PF_6/H_2$	20/0.5	AcOEt	99	*E*>99
2	**5b**	$[Ir(cod)(PPh_2Me)_2]PF_6/H_2$	20/0.5	AcOEt	97	*E*>99
3	**5c**	$[Ir(cod)(PPh_2Me)_2]PF_6/H_2$	20/0.5	AcOEt	98	*E*>98
4	**5a**	$NiCl_2(dppb)/LiBHEt_3$	20/18	THF	92	*Z*>86
5	**5a**	$NiCl_2(dppf)/LiBHEt_3$	20/18	THF	87	*Z*>93
6	**5a**	$NiCl_2(PPh_3)_2/LiBHEt_3$	20/18	THF	33	*Z*>94
7	**5a**	$NiCl_2(PPh_2Me)_2/LiBHEt_3$	20/18	THF	89	*Z*>93
8	**5b**	$NiCl_2(PPh_2Me)_2/LiBHEt_3$	20/18	THF	92	*Z*>91
9	**5c**	$NiCl_2(PPh_2Me)_2/LiBHEt_3$	20/18	THF	93	*Z*>90

[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.