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Preparation of chiral β-functionalized allylboronate reagents and their application to asymmetric synthesis of α-methylene–γ-lactams and γ-lactones

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Summary — Various chiral β-functionalized allylboronates are prepared by alkylation of α-functional vinylaluminum reagents with chiral α-chloromethylboronates with excellent yields and high regioselectivity. The ability of these new chiral allylboronates to afford the expected α-methylene–γ-lactams and γ-lactones on treatment with imines and aldehydes is also reported.

chiral chloromethylboronate / vicinal diol / chiral β-functionalized allylboronate / α-methylene–γ-lactam / α-methylene–γ-lactone

Résumé — Synthèse de divers allylboronates β-fonctionnalisés et leur application pour la synthèse asymétrique d'α-méthylène–γ-lactames et γ-lactones. La synthèse de nombreux allylboronates β-fonctionnalisés chiraux a été réalisée par condensation directe d'organovinylaluminium α-fonctionnalisés avec divers α-chlorométhylboronates chiraux. L'intérêt de ces nouveaux réactifs pour la synthèse d'α-méthylène–γ-lactames et γ-lactones via une réaction d'alcoxycarbonylallylboration avec des imines et des aldéhydes est également décrit.

chlorométhylboronate chiral / diol vicinal / allylboronate β-fonctionnalisé chiral / α-méthylène–γ-lactame / α-méthylène–γ-lactone

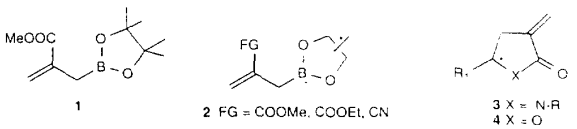
We have previously described the excellent stereocontrolled addition of organozinc reagents derived from 2-(bromoalkyl)acrylates with chiral imines of α-aminoesters or β-aminoalcohols for asymmetric synthesis of α-methylene–γ-lactams 3 [1]. The mechanism proposed to explain the high degree of stereoselectivity involves a chair-like transition state including metal chelation by the ester function or hydroxyl group of the imine which cannot be applied to the synthesis of the lactone analogues **4**.

Hence, our interest in the development of new methods and/or new organometallic reagents useful in the synthesis of both **3** and **4** has led us to explore the application of allylboronates which are known to condense with imines and aldehydes in a stereospecific manner [2].

Preparation of chiral β-functionalized allylboronate reagents

In general allylboronates are most conveniently prepared by the reaction of allylmagnesium or lithium reagents with borate or haloborate esters. Although these methods have been successfully applied for the synthesis of a variety of allylic boronates, they suffer from their inability to include functional groups sensitive to magnesium or lithium reagents [3–5].

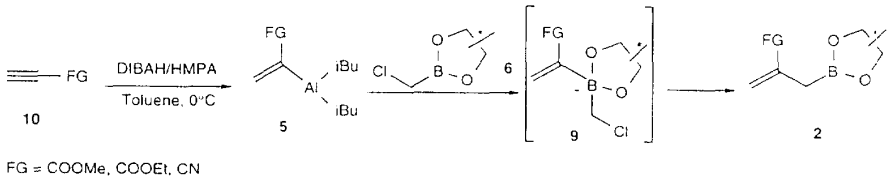
In the light of the above-mentioned limitations, we have recently studied an alternative route to the β-functionalized allylboronate **1** which overcomes these limitations and subsequent ability of this new allylic boron reagent to afford α-methylene–γ-lactams **3** and γ-lactones **4** on treatment with imines and aldehydes [6].



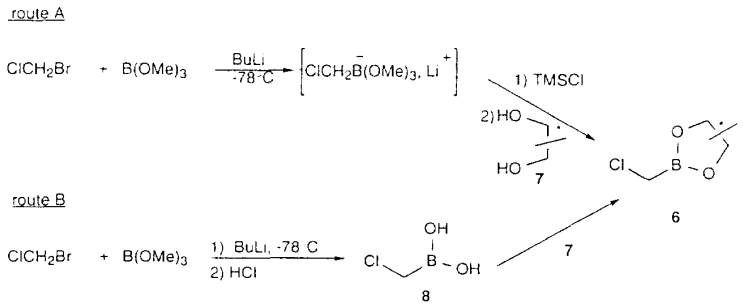
1 **2** FG = COOMe, COOEt, CN **3** X = N-R **4** X = O

In this paper, we describe the extension of this methodology to diverse chiral β-functionalized allylboronates of type **2** and our attempts to use them as chiral reagents in the asymmetric synthesis of lactams **3** and lactones **4** [7]. The most direct route to chiral β-functionalized allylboronates of type **2** consisted in

* Correspondence and reprints



Scheme 1



Scheme 2

the alkylation of α-functional vinylaluminum reagents **5** with chiral α-chloromethylboronates **6** according to scheme 1.

Using this strategy, the preparation of chiral α-chloromethylboronates **6** is the key step of the synthesis. Although several procedures for the preparation of haloalkylboronic esters have been described [3c,8–10], they cannot be easily applied when large quantities of material are required. In our approach, based on the pioneering work of Sadhu and Matteson [3f], chiral α-chloromethylboronates **6** have been prepared according to two methods (routes A and B) outlined in scheme 2.

In both routes, the intermediate chloromethyllithium was trapped with trimethyl borate. In route A, the resulting 'ate' complex was simultaneously quenched with anhydrous trimethylsilyl chloride according to Whiting's procedure [11] and transesterified with vicinal diols **7** as chiral auxiliary to afford chloromethylboronates **6** with excellent yields. In route B, acidic hydrolysis of the intermediate boronate 'ate' complex gave the chloromethylboronic acid **8** which was quite stable to storage. By reaction with the appropriate chiral vicinal diol **7** and removal of water, **8** was converted into the corresponding ester **6**. These two methods are entirely reproducible on both large and small scale (table I). All of the chiral chloromethylboronates **6** are reasonably stable and have been stored in a freezer under argon for several months without noticeable deterioration.

Chiral vicinal diols **7a** and **7b** (table I) are commercially available, while **7c** and **7d** were prepared from methyl mandelate and Grignard reagents (scheme 3). Diol **7e** (table I) was synthesized following the procedure described by Whiting [12].

The last step consisted in an 'alkylation' of the readily available vinylaluminum reagent **5** by chloromethylboronates **6**. The mechanism is known to proceed first by the intermediate of an 'ate' complex **9**, which then undergoes migration with elimination of chloride as presented in scheme 1.

Reagents **5** were generated by chemoselective conjugate reduction of **10** with diisobutylaluminum hydride (DIBAH) in the presence of hexamethylphosphoric triamide (HMPA, **3** equiv) as described by Tsuda et al [13]. The reaction proceeded smoothly (5 h) at 0 °C to give **5**, which on reaction with chloromethylboronates **6** led to the formation of β-functionalized allylboronates **2** with excellent yields (table I).

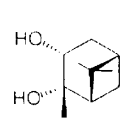
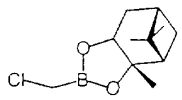
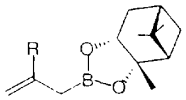
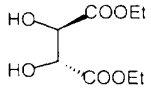
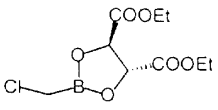
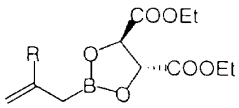
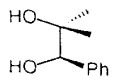
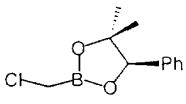
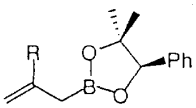
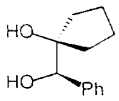
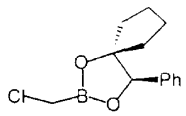
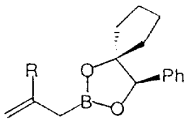
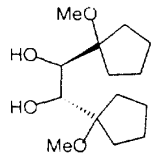
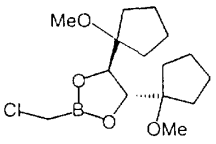
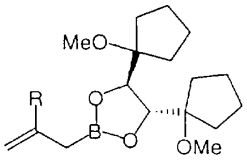
The whole process from vinylaluminum **5** to allylboronates **2a–e** may be carried out either in a two-step preparation (method B), in which pinacol allylboronates **2f–g** are first isolated and then converted into **2a–e** after an oxidative cleavage of the pinacol derivative followed by esterification with chiral diols **7**, or as one-pot procedure (method A) where **5** was treated directly with chiral chloromethylboronates **6** (scheme 4).

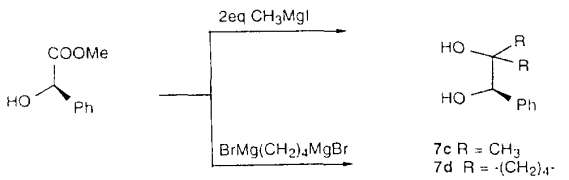
Addition to imines and aldehydes

Results of reaction of **2** with several representative imines and aldehydes are summarized in table II. The best results have been consequently obtained using pure reagents either without any solvent at room temperature (method C) or in refluxing toluene (method D) (scheme 5). Homoallylic alcohols **11** could be isolated when the reaction was carried out without any solvent at room temperature. Further treatment of these alcohols with sodium hydride in tetrahydrofuran at 0 °C provided the expected lactones **4** (scheme 5).

β-functionalized allylboronates **2** add to imines and aldehydes much more slowly than their unsubstituted derivatives. Hence, 7 to 14 days in reflux of toluene were required to obtain lactams **3** and lactones **4** with fair to good yields (70–95%). This result undoubtedly reflects the fact that allylboronates of type **2** are somewhat less reactive than their unsubstituted and non-functionalized derivatives.

Table I. Preparation of chiral chloromethylboronates **6** and chiral allylboronates **2**.

Diols **7**	*Chloromethyl-boronates* **6**	*Routes*	*Yield (%)*	*Allylboronates* **2**	*Method*	*Yield (%)*
 **7 a**	 **6 a**	A	76			
		B	56	R = COOMe **2a1**	A	90
				R = COOEt **2a2**	A	85
				R = CN **2a3**	A	90
 **7 b**	 **6 b**	A	75	 R = COOMe **2b**	A	Non-isolated
 **7 c**	 **6 c**	A	90			
		B	57		A	80
				R = COOMe **2c1**	B	85
				R = COOEt **2c2**	A	87
 **7 d**	 **6 d**	A	85			
		B	95			
				R = COOMe **2d1**	A/B	80/90
				R = COOEt **2d2**	A/B	80/85
				R = CN **2d3**	A	90
 **7 e**	 **6 e**	B	85	 R = COOMe **2e**	A	60
					B	82

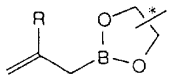
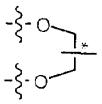
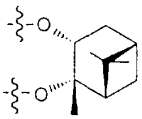
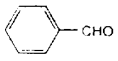
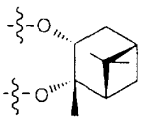
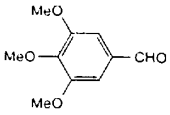
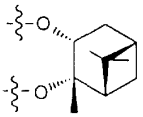
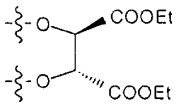
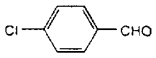
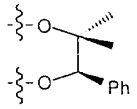
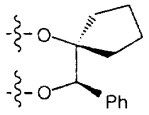
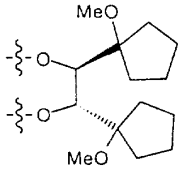
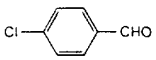


Scheme 3

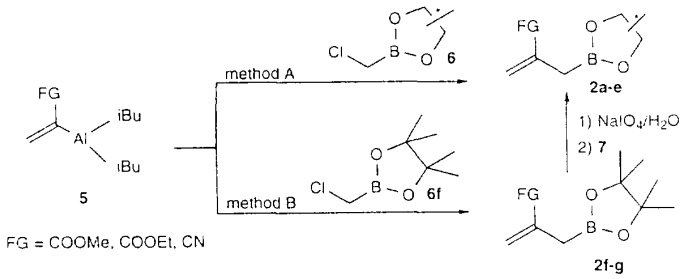
Interestingly, it is clear that in contrast to the results with unsubstituted and non-functionalized allylboronates, the ester function of **2** has a significantly negative influence on the outcome of these single asymmetric induction experiments. The mediocre performance of **2** for the asymmetric alkoxycarbonylallylboration reaction might be a consequence of an interaction between the ester function and boron atom that lowers their reactivity with imines and aldehydes.

It is also apparent that chiral auxiliaries are ineffective. In fact, molecular modelling of such reactive intermediates (**2** and aldehydes or imines) indicates that steric interactions are low, especially between the alkoxycarbonyl substituent and the chiral boronate moiety. These data indicate that increasing the size of the chiral boronate auxiliary or using an *N*-substituted oxazaborolidine would lead to higher enantioselectivity. From this point of view, new organoboronate reagents are in progress and results will be reported in due course [7].

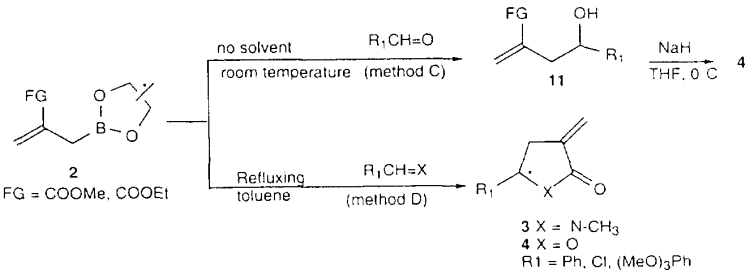
Table II. Reaction of chiral allylboronates of type **2** with imines and aldehydes.

Entry	*Allylboronates* **2**	*Chiral auxiliary* **7**	*Substrate*	*Yield (%)*	*ee*[a] *(%)*
					
1	R = COOMe			70	10
2	R = COOEt			95	6
3	R = COOMe		Ph–CH=N–Me	85	44
	R = COOEt			90	30
4	R = COOMe			30	20
			Ph–CH=N–Me	45	13
5	R = COOMe		Ph–CH=N–Me	90	13
6	R = COOMe		Ph–CH=N–Me	85	6
7	R = COOMe			90	20
			Ph–CH=N–Me	90	27

[a] ee are determined from ^{1}H NMR spectra by using chiral reagent Eu(hfc)$_3$ or by HPLC analysis on a CHIRACEL OD-H column from established conditions on racemic compounds.



Scheme 4



Scheme 5

Experimental section

^{1}H NMR spectra were recorded in $CDCl_3$ on a Bruker AC 200; chemical shifts are expressed in parts per million (ppm) referenced to residual chloroform (7.27 ppm). Coupling constants (J) are given in hertz (Hz). Multiplicities are recorded as s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). ^{13}C NMR spectra were recorded on a Bruker AMX 400 spectrometer. Mass spectra (m/z (% base peak)) were recorded on a HP 5889A spectrometer EI (70 eV). For high-performance liquid chromatography (HPLC) analysis a Hewlett Packard model (HP 1050) equipped with a UV detector (254) and a CHIRACEL OD-H column was employed. Optical rotations were measured on a AA.10 Optical activity polarimeter. Melting points were determined on a C Reichert microscope apparatus and are uncorrected. Elemental analyses were carried out on a Perkin-Elmer 2400 C, H, N elemental analyser. Tetrahydrofuran (THF) was prepared by pre-drying with KOH followed by distillation from Na/benzophenone, diethyl ether was distilled from Na/benzophenone, dichloromethane, ethyl acetate, dried by distillation over P_2O_5. Hexane was dried by distillation over $CaCl_2$ and toluene was distilled from sodium. Aldehydes are distilled prior to use. Imines are prepared according to classical procedures [14]. Flash chromatography was performed on silica-gel Merck 60, 230–400 mesh. Thin-layer chromatography was performed on precoated plates of silica gel 60F 254 (Merck, Art 7735).

α-Chloromethylboronates **6**

- *Route A*

A solution of freshly distilled trimethyl borate (5.7 mL, 50 mmol) and bromochloromethane (3.6 mL, 55 mmol, 1.1 equiv) in 50 mL of dry THF was cooled to −78 °C under argon and stirred magnetically during dropwise addition of n-BuLi (1.6 M in hexane, 35 mL) from a dropping funnel. 1 h after the addition of BuLi, freshly distilled Me_3SiCl (7.6 mL, 60 mmol, 1.2 equiv) was added at once. The mixture was warmed to room temperature and stirring was continued overnight. Then, a solution of the appropriate diol **7** (50 mmol) in 20 mL of dry diethyl ether was added resulting in dissolution of the precipitate of lithium chloride. After stirring for 5 h at room temperature, the solution was worked up with water (50 mL) and extracted with diethyl ether (3 × 20 mL). The organic layers were dried over anhydrous $MgSO_4$, then filtered and concentrated. The residue was purified by vacuum distillation.

- *Route B*

Preparation of α-chloromethylboronic acid **8**: A 250 mL, 3-neck round bottom flask equipped with mechanical stirring, dropping funnel and septum was charged under argon with freshly distilled trimethyl borate (5.7 mL, 50 mmol) and bromochloromethane (3.4 mL, 52 mmol) in THF (50 mL) and cooled at −78 °C. n-BuLi (1.6 M in hexane, 31.9 mL, 51 mmol) was added dropwise. After 1 h, the reaction mixture was allowed to reach room temperature and stirred overnight. The mixture was then hydrolyzed with 1 N aqueous HCl solution until pH = 1, diluted with saturated aqueous NaCl (50 mL) and H_2O (50 mL). The product was extracted with diethyl ether (3 × 15 mL), washed with water and dried over $MgSO_4$. After vacuum distillation of the solvent, the residue was washed with pentane to give 2.8 g of **8** (60%) as a pure white solid. Mp = 71 °C.

IR: 3 390 (OH) 1 360 (B–O).

^{1}H NMR (200 MHz, CD_3COCD_3) δ: 2.94 (s, 2H, CH_2B), 5.94 (s, 2H, OH).

^{13}C NMR (50.3 MHz, CD_3COCD_3, T = −20 °C) δ: 15.7 (CH_2B broad signal).

MS: m/z = 95 (M + H) CI (CH_4).

General procedure for esterification of α-chloromethyl boronic acid ***8*** *with chiral diols* ***7***: The chloromethylboronic acid **8** (3 g, 32 mmol) was added to a solution of the appropriate diol **7** (20 mmol) in diethyl ether (20 mL) and methanol (1 mL). The resulting solution was stirred overnight at room temperature, then washed with H_2O (3 × 10 mL) and dried over $MgSO_4$. After vacuum distillation of the solvent, the residue was purified by chromatography or vacuum distillation.

• *(3aS)-2-(Chloromethyl)-3a,5,5-trimethyl-hexahydro-4,6-methano-1,3,2-benzodioxaborole* **6a**

Compound **6a** was obtained according to route A or B using (*S*)(+) pinanediol **7a** as chiral diol auxilliary. The crude residue was purified by vacuum distillation.

Bp_{13} = 128–130 °C; $[\alpha]_D^{25}$ = +48 (*c* = 1.65, toluene).

IR (film): 1 460 (C–B) 1 350 (B–O) 850 (C–Cl).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.85 (s, 3H, CH_3), 1.16 (d, 1H, ^3J = 11, CH), 1.3 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.8–2.4 (m, 5H, $2CH_2$ + 1CH pinyl), 3.01 (s, 2H, CH_2B), 4.37 (dd, 1H, ^3J = 1.8, ^3J = 8.7, CHOB pinyl).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 23.0 (s, CH_2B), 23.8 (CH_3), 26.2 (CH_2), 26.9, 28.3 ($2CH_3$), 35.1 (CH_2), 38.1 (Cq pinyl), 39.1, 51.1, 78.6 (3CH), 86.9 (Cq pinyl).

MS: *m/z* = 228 ($M^{+}\cdot$, 5), 213 ($-CH_3\cdot$, 35), 187 (27), 159 (59), 134 (34), 96 (59), 83 (100), 81 (70), 67 (51), 55 (48), 43 (70), 27 (19).

• *Diethyl (4R,5R)-2-(chloromethyl)-1,3,2-dioxaborolane-4,5-dicarboxylate* **6b**

The general route A applied to (*R,R*)(−) diethyl tartrate **7b** gave after purification by vacuum distillation the title compound.

$Bp_{0.05}$ = 112 °C; $[\alpha]_D^{25}$ = −57 (*c* = 1.8, toluene).

IR (film): 1 740 (C=O ester) 1 370 (B–O).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.34 (t, 6H, ^3J = 7.2, $2CH_3$), 3.14 (s, 2H, CH_2B), 4.31 (q, 4H, ^3J = 7.2, $2CH_2$), 4.97 (s, 2H, 2CH).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 13.7 (CH_3), 22.7 (s, CH_2B), 62.0, (CH_2), 77.8 (CH), 168.5 (C=O).

MS: *m/z* = 265 (M + H, 16), 191 ($M^{+}\cdot$ − COOEt, 34), 163 ($-CO^+$, 5), 119 (21), 83 (24), 29 (100).

Anal calc for $C_9H_{14}O_6BCl$: C, 40.87; H, 5.33. Found: C, 40.73; H, 5.77.

• *(5R)-2-(Chloromethyl)-4,4-dimethyl-5-phenyl-1,3,2-dioxaborolane* **6c**

Compound **6c** was obtained according to route A or B using (*R*)(−) 1,1-dimethyl-2-phenylethane-1,2-diol **7c** as chiral diol auxiliary. The crude residue was purified by vacuum distillation.

Bp_{10} = 131 °C; $[\alpha]_D^{25}$ = −35 (*c* = 1.8, toluene).

IR (film): 1355 (B–O) 845 (C–Cl).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.85 (s, 3H, CH_3), 1.57 (s, 3H, CH_3), 3.12 (s, 2H, CH_2B), 5.19 (s, 1H, CH), 7.3 (m, 5H, H arom).

^{13}C NMR (50.3 MHz, $CDCl_3$, *T* = −30 °C) δ: 24.5 (s, CH_2B), 25.1 (CH_3), 28.6 (CH_3), 84.6 (Cq), 87.3 (CH), 125.1, 127.9, 128.2 (CH arom), 136.9 (Cq arom).

MS: *m/z* = 226/224 ($M^{+}\cdot$, 4/11), 209 ($M^{+}\cdot$ $-CH_3\cdot$, 3), 166 ($-CO^+$, 7), 165 (7), 130 ($-Cl\cdot$, 18), 104 (42), 91 (33), 77 (19), 59 (100), 43 (11), 41 (12).

Anal calc for $C_{11}H_{14}O_2BCl$: C, 58.85; H, 6.28. Found: C, 58.63; H, 6.42.

• *(4R)-2-(Chloromethyl)-4-phenyl-1,3-dioxa-2-boraspiro[4.4]nonane* **6d**

Compound **6d** was synthesized according to route A or B using (*R*)(−) 1-cyclopentyl-2-phenylethane-1,2-diol **7d** as chiral diol auxiliary. The crude residue was purified by chromatography on florisil (hexane/diethyl ether 1:1).

$[\alpha]_D^{24}$ = −28 (*c* = 2.5, $CHCl_3$).

IR (film): 1 350 (B–O) 845 (C–Cl).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.8–2.2 (m, 8H, H cyclopentyl), 3.11 (s, 2H, CH_2B), 5.32 (s, 1H, CH), 7.3 (m, 5H, H arom).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 22.7, 23.4, 35.6, 39.9 ($4CH_2$ cyclopentyl), 24.1 (CH_2B broad), 85.0 (CH), 94.3 (Cq cyclopentyl), 125.7, 127.9, 128.2 (CH arom), 137.5 (Cq arom).

MS: *m/z* = 252/250 ($M^{+}\cdot$, 29/10), 207 (19), 159 (37), 105 (20), 91 (100), 85 (42), 77 (25), 41 (18).

• *(4R,5R)-4,5-Bis(1-methoxycyclopentyl)-2-(chloromethyl)-1,3,2-dioxaborolane* **6e**

The general route B applied to (*R,R*)(−) 1,2-bis(1-methoxycyclopentyl)ethane-1,2-diol **7e** gave after purification by vacuum distillation the title compound.

$Bp_{0.05}$ = 150 °C; $[\alpha]_D^{35}$ = −56 (*c* = 1.3, $CHCl_3$).

IR (film): 1 350 (B–O) 845 (C–Cl).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.55–1.85 (m, 16H, H cyclopentyl), 3.00 (s, 2H, CH_2B), 3.25 (s, 6H, $2OCH_3$), 4.40 (s, 2H, 2CH).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 24.1 (CH_2B broad), 24.2, 24.3, 30.2, 30.6 (8 CH_2, cyclopentyl), 50.3 (2 OCH_3), 81.0 (2CH), 87.4 (Cq cyclopentyl).

MS: *m/z* = 334 (M + 18) (CI, NH_3); (IE) 99 (100), 67 (24), 41 (8).

• *1-(Chloromethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane* **6f**

It was prepared according to route A using pinacol as non chiral diol.

Yield: 90%; Bp_9 = 69–70 °C.

IR (film): 2 980 (CH) 1 460 (C–B) 850 (C–Cl).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.29 (s, 12H, CH_3), 2.96 (s, 2H, CH_2Cl).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 24.7(CH_3), 84.5 (Cq pinacol).

MS: *m/z* = 176 ($M^{+}\cdot$, 5), 163/161 ($-CH_3$, 33), 118 ($-CH_3CO^+$, 9), 85 (62), 83 (49), 59 (57), 43 (54), 41 (63), 27 (9).

Anal calc for $C_7H_{14}O_2BCl$: C, 47.65; H, 8.00. Found: C, 47.42; H, 8.02.

• *(1R)(−)-2-Methyl-1-phenylpropane-1,2-diol* **7c**

The Grignard reagent prepared from magnesium (1.5 g, 62 mmol) and methyl iodide (8.52 g, 60 mmol) and dry diethyl ether (20 mL) was cooled in ice-cold water, and (*R*)(−) methyl (2-hydroxy-2-phenyl)acetate (3.3 g, 20 mmol) in dry diethyl ether (10 mL) was added dropwise. After the mixture had been stirred overnight at room temperature, it was decomposed in the usual manner by ice and a saturated aqueous NH_4Cl solution, and the liberated glycol extracted with ethyl acetate. After drying the organic layers over $MgSO_4$ and removing the solvent, the resulting oil was purified by chromatography on a silica gel column by using hexane/ethyl acetate (80:20) as eluents.

Yield = 82%; Mp = 62 °C; $[\alpha]_D^{16}$ = −16.5 (*c* = 2, MeOH).

IR: 3 350 (OH) 1 490 (C=C arom).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.07 (s, 3H, CH_3), 1.19 (s, 3H, CH_3), 2.7 (s, 1H, OH), 3.35 (s, 1H, OH), 4.48 (s, 1H, CH), 7.32 (m, 5H, H arom).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 23.7 (CH_3), 26.5 (CH_3), 73.4 (C1), 80.8 (C2), 127.4, 127.7, 127.9 (CH arom), 140.6 (C arom).

MS: m/z = 166 ($M^+\cdot$) (CI); (IE) 149 (−OH·, 1), 133 (6), 108 (100), 79 (59), 77 (26), 59 (95), 31(16), 18(16).

Anal calc for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.41; H, 8.92.

• *1-((αR)-α-Hydroxybenzyl)cyclopentanol* **7d**

The Grignard reagent prepared from magnesium (4 g, 166 mmol) in dry diethyl ether and 1,4-dibromobutane (6.50 g, 60 mmol) and dry diethyl ether (50 mL) was refluxed for 1 h and then (*R*)(−) methyl (2-hydroxy-2-phenyl)acetate (5.0 g, 30 mmol) in dry diethyl ether (20 mL) was added dropwise. The reaction was vigorous. After the mixture had been stirred overnight at room temperature, hydrolysis was performed with a saturated aqueous NH_4Cl solution, extracted with diethyl ether and washed with a saturated aqueous NaCl solution. After drying the organic layers over $MgSO_4$ and removing the solvent, the resulting oil was purified by chromatography on a silica gel column by using dichloromethane/ethyl acetate (80:20) as eluents.

Yield = 86%; Mp = 57 °C; $[\alpha]_D^{35}$ = −36.5 (c = 1.2, toluene).

IR: 3 300 (OH) 1 490 (C=C).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.2–1.9 (m, 8H, CH_2), 1.95 (s, 1H, 0H), 2.7 (s, 1H, OH), 4.59 (s, 1H, CH), 7.25–7.39 (m, 5H, H arom).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 23.6, 23.7, 36.0, 37.5 (CH_2), 79.6 (C2), 84.8 (C1), 127.3, 127.8, 128.1 (CH arom), 141.9 (C arom).

MS: m/z = 192 ($M^+\cdot$) (CI); (IE) 175 (−OH), 108 (100), 85 ($C_5H_9O^+$, 49), 67 (−OH ,42), 41 (20), 27 (7).

Anal calc for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.43; H, 8.93.

β-Functionalized allylboronates **2**

Method A: To a stirred solution of toluene (25 mL) and HMPA (3.13 mL, 18 mmol) at 0 °C under argon, was added a 1 M solution of DIBAH in toluene (9 mL, 9 mmol). After 1 h, methyl propiolate **10** (0.53 mL, 6.0 mmol) was added. The reaction mixture was stirred for 5 h at 0 °C and then chloromethylboronate **6** (7.2 mmol) was added. The mixture was allowed to warm to room temperature, stirred for 5 h and then hydrolysed with a 1 N aqueous HCl solution (30 mL) and extracted with diethyl ether (60 mL). The combined organic layers were washed three times with 1 N aqueous HCl solution (25 mL), saturated aqueous $NaHCO_3$ (25 mL) and H_2O (50 mL). The ether solution was dried over anhydrous $MgSO_4$, filtered and concentrated. The residue was purified either by distillation under vacuum or by chromatography on florisil column.

Method B: A solution of pinacol allylboronate **2f** (1.35g, 6 mmol) and sodium periodate (3 g, 15 mmol) in acetone (30 mL) and water (3 mL) was stirred until TLC indicated complete reaction. The resulting mixture was concentrated and the crude residue diluted with diethyl ether (20 mL) was washed with water (3 × 10 mL). Then, chiral diol **7** (5 mmol) was added to the organic layer and the mixture stirred until the reaction was judged complete by TLC analysis. After vacuum distillation of the solvent, the residue was chromatographed on florisil column.

• *Methyl 2-[((3aS)-3a,5,5-trimethyl-hexahydro-4,6-methano-1,3,2-benzodioxaborol-2-yl)methyl]prop-2-enoate* **2a$_1$**

S(+): $[\alpha]_D^{25}$ = +23.5 (c = 1.5, toluene); R(−): $[\alpha]_D^{25}$ = −22 (c = 1.7, toluene).

IR (film): 1 720 (C=O) 1 630 (C=C) 1 430 (B–C) 1 350 (B–O).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.85 (s, 3H, CH_3), 1.16 (d, 1H, ^3J = 11, CH), 1.3 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.8–2.4 (m, 5H, $2CH_2$ + 1CH pinyl), 2.0 (s, 2H, CH_2B), 3.73 (s, 3H, OCH_3), 4.28 (dd, 1H, ^3J = 1.8, ^3J = 8.7, CHOB pinyl), 5.56 (m, 1H, ^2J = 1.5, ^4J = 1.5, H), 6.10 (m, 1H, ^2J = 1.5, ^4J = 0.7, H).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 16.8 (CH_2B broad), 23.8 (CH_3), 26.2 (CH_2), 26.9, 28.3 ($2CH_3$), 35.1 (CH_2), 38.1 (Cq pinyl), 39.1, 51.1 (2CH), 51.8 (OCH_3), 78.6 (CH), 86.9 (Cq pinyl), 124.5 (C=CH_2), 137.4 (C=CH_2), 167.0 (C=O).

MS: m/z = 278 ($M^+\cdot$, 21), 263 (−$CH_3\cdot$, 3), 208 (77), 193 (81), 180 (28), 165 (17), 127 (100), 83 (51), 67 (35), 55 (32), 43 (39), 41 (40).

• *Ethyl 2-[((3aS)(+)-3a,5,5-trimethyl-hexahydro-4,6-methano-1,3,2-benzodioxaborol-2-yl)methyl]prop-2-enoate* **2a$_2$**

$[\alpha]_D^{30}$ = +16,5 (c = 1.2, $CHCl_3$).

IR (film): 1 720 (C=O ester) 1 630 (C=C).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.84 (s, 3H, CH_3), 1.2 (d, 1H, ^3J = 14, CH), 1.29 (t, 3H, ^3J = 7.2, CH_3CH_2), 1.31 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.78–2.4 (m, 5H, $2CH_2$ + 1 CH pinyl), 2.01 (s, 2H, CH_2B), 4.19 (q, 2H, ^3J = 7.2, CH_3CH_2), 4.28 (dd, 1H, ^3J = 2, ^3J = 8.8, CHOB pinyl), 5.55 (m, 1H, ^2J = 1.4, ^4J = 1.4, H), 6.10 (m, 1H, ^2J = 1.4, ^4J = 0.7, H).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 14.1 (CH_3CH_2), 17.1 (CH_2B broad), 23.8 (CH_3), 26.1 (CH_2), 26.9, 28.4 ($2CH_3$), 35.3 (CH_2), 38.0 (Cq pinyl), 39.4, 51.1 (2CH), 60.4 (CH_2CH_3), 77.6 (CH), 85.6 (Cq pinyl), 123.8 (C=CH_2), 137.7 (C=CH_2), 167.2 (C=O).

MS: m/z = 292 ($M^+\cdot$, 3), 277 (−$CH_3\cdot$, 7), 222 (43), 207 (68), 127 (100), 83 (55), 67 (25), 55 (22), 43 (39), 41 (40).

• *2-[((3aS)(+)-3a,5,5-Trimethyl-hexahydro-4,6-methano-1,3,2-benzodioxaborol-2-yl)methyl]prop-2-enenitrile* **2a$_3$**

$[\alpha]_D^{25}$ = +19 (c = 1.2, $CHCl_3$).

IR(film): 2 210 (C≡N) 1 620 (C=C) 1 340 (B–O).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.85 (s, 3H, CH_3), 1.16 (d, 1H, ^3J = 11, CH), 1.3 (s, 3H, CH_3), 1.43 (s, 3H, CH_3), 1.8–2.4 (m, $2CH_2$ + 1 CH pinyl), 1.98 (s, 2H, CH_2B), 4.33 (dd, 1H, ^3J = 1.8, ^3J = 8.7, CHOB pinyl), 5.73 (m, 1H, ^2J = 0.7, ^4J = 1, H), 5.81 (m, 1H, ^2J = 0.7, ^4J = 0.5, H).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 19.0 (CH_2B broad), 23.9 (CH_3), 26.3 (CH_2), 26.4, 28.1 ($2CH_3$), 35.2 (CH_2), 38.1 (Cq pinyl), 39.3, 51.1 (2CH), 78.3 (CH), 86.5 (Cq pinyl), 119.2, 120.4 (CN et C=CH_2), 130.3 (C=CH_2).

MS: m/z = 263 (M + 18) (CI + NH_3); (IE) 245 ($M^+\cdot$, 1), 230 (−$CH_3\cdot$, 4), 181 (4), 135 (15), 112 (9), 71 (100), 43 (13), 29 (24).

• *Methyl 2-[((5R)(−)-4,4-dimethyl-5-phenyl-1,3,2-dioxaborolan-2-yl)methyl]prop-2-enoate* **2c$_1$**

$[\alpha]_D^{30}$ = 17 (c = 2.1, $CHCl_3$).

IR (film): 1 710 (C=O ester) 1 620 (C=C) 1 450 (B–C) 1 340 (B–O).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.80 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 2.08 (s, 2H, CH_2B), 3.77 (s, 3H, OCH_3), 5.09 (s, 1H, CH), 5.62 (s, 1H, H), 6.14 (s, 1H, H), 7.29 (m, 5H, H arom).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 16.7 (CH_2B broad), 24.9 (CH_3), 28.9 (CH_3), 51.6 (OCH_3), 83.0 (Cq), 86.9 (CH), 124.3 (C=CH_2), 125.3 127.5, 127.9, (CH arom) 137.1 (C arom), 138.2 (C=CH_2) 167.7 (C=O).

MS: m/z = 274 (M^+·, 3), 259 ($-CH_3$·, 2), 216 ($-CH_3CO$·, 89), 201 (23), 105 (69), 91 (100), 77 (56), 59 (37).

• *Ethyl 2-[((5R)(−)-4,4-dimethyl-5-phenyl-1,3,2-dioxaborolan-2-yl)methyl]prop-2-enoate* **2c$_2$**

$[\alpha]_D^{26}$ = −15 (c = 1.2, $CHCl_3$).

IR (film): 1 720 (C=O ester) 1 625 (C=C) 1 350 (B–O).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.81 (s, 3H, CH_3), 1.29 (t, 3H, ^3J = 7.2, CH_3CH_2), 1.52 (s, 3H, CH_3), 2.0 (s, 2H, CH_2B), 4.19 (q, 2H, ^3J = 7.2, CH_3CH_2), 5.09 (s, 1H, CH), 5.6 (s, 1H, H), 6.10 (s, 1H, H), 7.29 (m, 5H, Harom).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 14.0 (CH_3CH_2), 16.9 (CH_2B broad), 24.9 (CH_3), 28.9 (CH_3), 60.4 (CH_3CH_2), 83.0 (Cq), 86.9 (CH), 124.3 (C=CH_2), 125.3, 127.6, 127.9, (CH arom), 137.1 (C arom), 138.1 (C=CH_2), 167.7 (C=O).

MS: m/z = 288 (M^+·, 10), 273 (M^+· $-CH_3$·, 6), 230 ($-CH_3CO$·, 37), 201 (−Et·, 63), 141 (42), 83 (100), 68 (34).

• *Methyl 2-[((4R)(−)-4-phenyl-1,3-dioxa-2-boraspiro[4.4]nonan-2-yl)methyl]prop-2-enoate* **2d$_1$**

$[\alpha]_D^{32}$ = −13,5 (c = 2.21, $CHCl_3$).

IR (film): 1 720 (C=O ester) 1 625 (C=C) 1 430 (B–C) 1 350 (B–O).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.8–1.9 (m, 8H, CH_2 cyclopentyl), 2.08 (s, 2H, CH_2B), 3.77 (s, 3H, OCH_3), 5.22 (s, 1H, CH), 5.62 (m, 1H, ^2J = 1.5, ^4J = 1.5, H), 6.15 (m, 1H, ^2J = 1.5, ^4J = 0.7, H), 7.30 (m, 5H, H arom).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 17.9 (CH_2B broad), 22.7, 23.4, 35.6, 39.9 (4CH_2 cyclopentyl), 51.9 (OCH_3), 85.0 (CH), 94.3 (Cq cyclopentyl), 124.6 (C=CH_2), 126.0, 127.9, 128.2 (CH arom), 137.1 (C arom), 139.0 (C=CH_2), 167.7 (C=O).

MS: m/z = 300 (M^+·, 10), 285 ($-CH_3$·, 2), 223 (37), 194 (22), 83 (100), 77 (85), 68 (34).

• *Ethyl 2-[((4R)(−)-4-phenyl-1,3-dioxa-2-boraspiro[4.4]nonan-2-yl)methyl]prop-2-enoate* **2d$_2$**

$[\alpha]_D^{32}$ = −21.5 (c = 1.2, $CHCl_3$).

IR (film): 1 720 (C=O ester) 1 625 (C=C) 1 350 (B–O).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.8–1.9 (m, 8H, CH_2 cyclopentyl), 1.31 (t, 3H, ^3J = 7.2, CH_3CH_2), 2.07 (s, 2H, CH_2B), 4.23 (q, 2H, ^3J = 7.2, CH_3CH_2), 5.22 (s, 1H, CH), 5.59 (m, 1H, ^2J = 1.4, ^4J = 1.4, H), 6.12 (m, 1H, ^2J = 1.4, ^4J = 0.8, H), 7.29 (m, 5H, H arom).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 14.0 (CH_3CH_2), 16.9 (CH_2 broad), 22.7, 23.4, 35.6, 39.9 (4CH_2 cyclopentyl), 60.4 (CH_2CH_3), 85.0 (CH), 94.2 (Cq cyclopentyl), 124.5 (C=CH_2), 125.9, 127.9, 128.2 (CH arom), 137.2 (C arom), 138.9 (C=CH_2), 167.5 (C=O).

MS: m/z = 314 (M^+·, 3), 237 (28), 208 (37), 179 (−Et·, 61), 83 (100), 77 (83), 68 (43).

• *2-[((4R)(−)-4-Phenyl-1,3-dioxa-2-boraspiro[4.4]nonan-2-yl)methyl]prop-2-enenitrile* **2d$_3$**

$[\alpha]_D^{25}$ = −23 (c = 1.2, $CHCl_3$).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 0.8–1.9 (m, 8H, CH_2 cyclopentyl), 2.10 (s, 2H, CH_2B), 5.29 (s, 1H, CH), 5.79 (m, 1H, ^2J = 0.7, ^4J = 1, H), 5.84 (m, 1H, ^2J =0.7, ^4J = 0.5, H), 7.3 (m, 5H, H arom).

• *Methyl 2-{[(4R,5R)(−)-4,5-bis(1-methoxycyclopentyl)-1,3,2-dioxaborolan-2-yl]methyl}prop-2-enoate* **2e**

$[\alpha]_D^{24}$ = −39 (c = 1.2, $CHCl_3$).

IR (film): 1 720 (C=O ester) 1 625 (C=C) 1 350 (B–O).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.45–1.85 (m, 16H, CH_2 cyclopentyl), 2.0 (s, 2H, CH_2B), 3.23 (s, 6H, 2OCH_3), 3.73 (s, 3H, $COOCH_3$), 4.33 (s, 2H, 2CH), 5.55 (m, 1H, ^2J = 1.5, ^4J = 1.5, H), 6.09 (m, 1H, ^2J = 1.5, ^4J = 0.7, H).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 16.9 (CH_2B broad), 24.49, 24.53, 30.7, 31.1 (8CH_2 cyclopentyl), 50.3 (2OCH_3), 51.7 ($COOCH_3$), 80.9 (CH), 87.8 (Cq cyclopentyl), 124.3 (C=CH_2), 137.1 (C=CH_2), 167.8 (C=O).

MS: m/z = 284 (M + 18)(CI, NH_3); (IE) 366 (M^+·). 335 ($-OCH_3$·), 303, 235 ($-C_5H_8$·), 207 ($-CO^+$), 141, 99 ($C_5H_8OCH_3^+$, 100), 67 (19), 45 (4), 41 (4).

• *Methyl 2-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]prop-2-enoate* **2f$_1$**

It was prepared according to the method A.

Yield = 90%; Bp_{13} = 114–115 °C.

IR: 1 720 (C=O ester) 1 625 (C=C) 1 350 (B–O).

^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.24 (s, 12H, 4 CH_3), 1.91 (s, 2H, CH_2B), 3.74 (s, 3 H, OCH_3), 5.54 (m, 1H, ^2J = 1.5, ^4J = 1.5, H), 6.09 (m, 1H, ^2J = 1.5, ^4J = 0.7, H).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 18 (CH_2B, broad), 24.7 (CH_3), 51.8 (OCH_3), 83.4 (Cq pinacolic), 124.5 (C=CH_2), 137.4 (C=CH_2), 169.9 (C=O).

^{11}B NMR (96.3 MHz, $CDCl_3$) δ: 32.5.

Anal calc for $C_{11}H_{19}O_4B$: C, 58.44; H, 8.47. Found: C, 58.09; H, 8.33.

• *Ethyl 2-[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]prop-2-enoate* **2f$_2$**

It was prepared according to method A.

Yield = 88%; Bp_1 = 90 °C.

IR (film): 1 720 (C=O ester) 1 625 (C=C) 1 350 (B–O).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.25 (s, 12H, 4CH_3), 1.29 (t, 3H, ^3J = 7.2, CH_3CH_2),1.91 (s, 2H, CH_2B), 4.19 (q, 2H, ^3J = 7.2, CH_3CH_2), 5.54 (m, 1H, ^2J = 1.6, ^4J = 1.3. H), 6.09 (m, 1H, ^2J = 1.6, ^4J = 0.8, H).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 14.0 (CH_3CH_2), 17.1 (CH_2B, broad), 24.6 (CH_3 pinacolic), 60.4 (CH_3CH_2), 83.1 (Cq pinacolic), 123.8 (C=CH_2), 137.6 (C=CH_2), 167.2 (C=O).

MS: m/z = 240 (M^+·, 10), 225 ($-CH_3$·, 6),182 ($-CH_3CO^+$·, 37), 153 (−Et·, 66), 141 (42), 83 (100), 68 (34), 50 (37).

• *2-[(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]prop-2-enenitrile* **2f$_3$**

It was prepared according to the method A.

Yield = 52%.

IR: 2 210 (C≡N) 1 620 (C=C) 1 340 (B–O).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.28 (s, 12H, 4CH_3 pinacolic), 1.94 (s, 2H, CH_2B), 5.72 (m, 1H, ^2J = 0.7, ^4J = 1, =CH_2), 5.80 (m, 1H, ^2J = 0.7, ^4J = 0.5, =CH_2).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 19.3 (CH_2B, broad), 24.6 (4CH_3 pinacolic), 84.1 (2Cq pinacolic), 125.7, 128.3 (C=CH_2 and CN) 130.4 (C=CH_2).

MS: m/z = 193 ($M^{+}\cdot$, 17), 178 ($M^{+}\cdot - CH_3\cdot$, 32), 135 (−CO, 31), 134 (47), 120 (16), 94 (38), 85 (70), 67 (44), 59 (100), 43 (72), 41 (96).

General procedure for allylboration of imines and aldehydes

• *Lactams* **3**

Method C: A mixture of allylboronate **2** (1.2 equiv) *N*-benzylidenemethylamine (1 equiv) was stirred under argon for two weeks. After chromatography on a silica gel column with a mixture of hexane/dichloromethane (1:1) **3** was obtained.

Method D: A mixture of allylboronate **2** (1 equiv) and *N*-benzylidenemethylamine (1 equiv) in toluene was refluxed under argon for two weeks. After vacuum distillation of the solvent, the product was chromatographed on a silica gel column with a mixture of hexane/dichloromethane (1:1) to afford **3**.

• *1-Methyl-3-methylidene-5-phenylpyrrolidin-2-one* **3**

^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.62 (m, 1H, ^2J = 17.26, ^3J = 4.04, ^4J = 2.5 and 2.7 CH_2), 2.75 (s, 3H, N-CH_3), 3.20 (m, 1H, ^2J = 17.26, ^3J = 8.56, ^4J = 2.5 and 2.7 CH_2), 4.50 (dd, 1H, ^3J = 4.04 and 8.56 CHPh), 5.34 (m, 1H, ^2J = 0.4, ^4J = 2.7 =CH_2), 6.06 (m, 1H, ^2J = 0.4, ^4J = 2.7, =CH_2), 7.17 (m, 5H, H arom).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 28.5 (CH_3N), 34.8, 61.4, 115.4 (C=CH_2), 126.3 (C arom), 128.3, 129 (CH arom), 138.7 (C arom), 140.8 (C=CH_2), 168.8 (C=O).

MS: m/z = 249 (28), 182(28), 172 (100), 77(37).

• *Lactones 4*

Method C; homoallylic alcohols **11**: A mixture of allylboronate **2** (1.2 equiv) and aldehyde (1 equiv) was stirred under argon for two weeks. After chromatography on a silica gel column with a mixture of hexane/dichloromethane (1:1) **11** was obtained.

• *Methyl 4-hydroxy-2-methyl-4-phenylidenebutanoate* **11a**

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.90 (s, 1H, OH), 2.65 (m, 1H, ^2J = 14, ^3J = 8, ^4J = 1, CH_2), 2.77 (m, 1H, ^2J = 14, ^3J = 4.6, ^4J = 1, CH_2) 3.74 (s, 3H, CH_3), 4.86 (dd, 1H, ^3J = 4.6, ^3J = 8, C*H*OH), 5.58 (m, 1H, ^2J = 1.2 ^4J = 1, =CH_2), 6.21 (d, 1H, ^2J = 1.2, =CH_2), 7.29 (m, 5H, H arom).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 42.1 (CH_2), 51.7 (CH_3), 72.7 (CHOH), 125.6, 127.2, 128.3, 128.1 (C=CH_2), 136.7 (C=CH_2), 167.9 (C=O).

MS: m/z = 206 (1), 189(16), 174 (9), 107(100).

Anal calc for $C_{12}H_{14}O_3$ C, 69.88; H, 6.84. Found: C, 69.53; H, 6.95.

• *Ethyl 4-hydroxy-2-methylidene-4-(3,4,5-trimethoxyphenyl)butanoate* **11b**

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.32 (t, 3H, ^3J = 7.1, CH_3), 2.64 (m, 1H, ^2J = 14, ^3J = 8.5, ^4J = 0.7, CH_2), 2.78 (m, 1H, ^2J = 14, ^3J = 4.2, ^4J = 0.9, CH_2), 2.85 (d, 1H, ^3J = 2.9, OH), 3.82 (s, 6H, OCH_3), 3.87 (s, 3H, OCH_3), 4.25 (q, 2H, ^3J = 7.1, CH_2CH_3), 4.82 (m, 1H, ^3J = 2.9, ^3J = 4.2 and 8.5, C*H*OH), 5.65 (m, 1H, ^2J = 1.5, ^4J = 0.7 and 0.9, =CH_2), 6.26 (d, 1H, ^2J = 1.5, =CH_2), 6.60 (s, 2H, H arom).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 14.2 (CH_3), 42.5 (CH_2), 56.2 (OCH_3), 60.8 (OCH_3), 61.3 (OCH_3), 73.1 (CHOH), 102.5, 128.1 (C=CH_2), 136.7 (C=CH_2), 139.9 (C arom), 152.9 (O–C arom), 168.2(C=O).

MS: m/z = 310 (5), 264(68), 197(100).

Anal calc for $C_{16}H_{22}O_6$: C, 61.92; H, 7.14. Found: C, 61.57; H, 7.38.

• *Methyl 4-(4-chlorophenyl)-4-hydroxy-2-methylidenebutanoate* **11c**

^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.61 (m, 1H, ^2J = 14, ^3J = 8, ^4J = 0.7, CH_2), 2.75 (m, 1H, ^2J = 14, ^3J = 4.5, ^4J = 1, CH_2), 2.95 (d, 1H, ^3J = 3.5, OH), 3.75 (s, 3H, CH_3), 4.84 (m, 1H, ^3J = 3.5, ^3J = 4.5 and 8, CHOH), 5.57 (m, 1H, ^2J = 1.2, ^4J = 0.7 and 1, =CH_2), 6.22 (d, 1H, ^2J = 1.2, =CH_2), 7.28 (s, 5H, H arom).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 42.5 (CH_2), 52.2 (OCH_3), 72.4 (CHOH), 127.2, 128.5 (CH arom), 128.7 (C=CH_2), 133.1 (C arom), 136.6 (C=CH_2), 142.4 (C arom), 168.2 (C=O).

MS: m/z = 240 (3), 208 (11), 68 (100).

Anal calc for $C_{12}H_{13}O_3Cl$: C, 59.88; H, 5.44. Found: C, 59.42; H, 5.60.

Lactonisation of homoallylic alcohols **11**: To a cooled suspension of sodium hydride (33.6 mg, 1.4 mmol) in THF (2 mL) was added **11** (1.36 mmol) in THF (1 mL). The resulting mixture was stirred for 2 min, then treated with buffer phosphate (5 mL, pH = 7). The aqueous phase was separated and extracted with diethyl ether (3 × 5 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under vacuo. The crude product was chromatographed on a silica gel column using hexane/CH_2Cl_2 (1:1) as eluents. Yield = 85%.

Method D: A mixture of allylboronate **2** (1.2 equiv) and aldehyde (1 equiv) in toluene was refluxed under argon for two weeks. After vacuum distillation of the solvent, the product was chromatographed on a silica gel column with a mixture of hexane/dichloromethane (1:1) to afford **4**.

• *3-Methylidene-2-oxo-5-phenyl-tetrahydrofuran* **4a** *[15, 16]*

^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.70–3.1 (m, 1H, ^2J = 17, ^3J = 8, ^4J = 2.5, CH_2), 3.2–3.7 (m, 1H, ^2J = 17, ^3J = 8, ^4J = 2.5, CH_2), 5.5 (dd, 1H, ^3J = 8, CHPh), 5.7 (t, 1H, ^4J = 2.5, =CH_2), 6.3 (t, 1H, ^4J = 2.5, =CH_2), 7.4 (m, 5H, H arom).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 36.3 (CH_2), 77.2 (CH), 122.6 (C=CH_2), 126.7, 128.8, 128.9 (CH arom), 133.9 (C arom), 136.7 (C=CH_2), 167.9 (C=O).

MS: m/z = 174 (8), 97 (100), 77 (18), 68 (38).

• *Methylidene-2-oxo-5-phenyl-tetrahydrofuran* **4b** *[17]*

^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.88 (m, 1H, ^2J = 17, ^3J = 6.8, ^4J = 2.6 and 2.9, CH_2), 3.40 (m, 1H, ^2J = 17, ^3J = 8, ^4J = 2.6 and 2, CH_2), 3.84 (s, 6H, OCH_3), 3.86 (s, 3H, OCH_3), 5.45 (dd, 1H, ^3J = 6.9 and 8, CHPh), 5.7 (dd, 1H, ^4J = 2 and 2.6, =CH_2), 6.3 (dd, 1H, ^4J = 2.9 and 2.6, =CH_2), 6.52 (s, 2H, H arom).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 36.4 (CH_2), 56.3 (OCH_3), 60.9 (OCH_3), 78(CH), 102.6 (CH arom), 122.5 (C=CH_2), 134.5, 135.5 (C arom), 138.2 (C=CH_2), 153.7 (C arom) 168.2 (C=O).

MS: m/z = 264 (11), 97 (100), 197 (73).

• *5-(4-Chlorophenyl)-3-methylidene-2-oxo-tetrahydrofuran* **4c** *[16]*

^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.86 (m, 1H, ^2J = 17, ^3J = 6.5, ^4J = 2.6 and 2.9, CH_2), 3.40 (m, 1H, ^2J = 17, ^3J = 8, ^4J = 2.5 and 2, CH_2), 5.49 (dd, 1H, ^3J = 6.5 and 8, CHPh), 5.7 (dd, 1H, ^4J = 2 and 2.6, $=CH_2$), 6.3 (dd, 1H, ^4J = 2.5 and 2.9, $=CH_2$), 7.30 (dd, 4H, ^3J = 8.4, H arom).

^{13}C NMR (50.3 MHz, $CDCl_3$) δ: 36.1 (CH_2), 77.1 (CH), 122.7 (C=CH_2), 126.7, 129.0 (CH arom), 133.7, 134.4 (C arom), 138.3 (C=CH_2), 169.8 (C=O).

MS: m/z = 208 (13), 173(7), 128 (5), 68 (100).

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