Synthetic Studies on Calyculin A: A Convenient Asymmetric Synthesis of *anti*-Vicinal Diols

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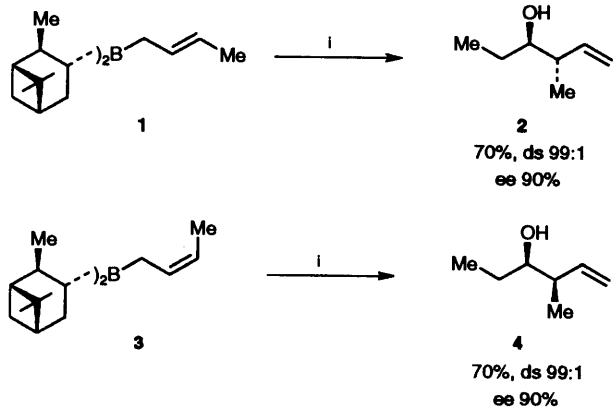
anti-Vicinal diols have been prepared with excellent relative and absolute stereocontrol *via* the reaction of aldehydes with *B*-{3-[(diisopropylamino)dimethylsilyl]allyl}diisopinocampheylborane in THF and diethyl ether and work-up using potassium fluoride, potassium hydrogen carbonate and hydrogen peroxide in aqueous methanol. Absolute stereoselectivities of reactions were determined by conversion of four product diols into bis[(*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate] esters. The reactions are relevant to the synthesis of the marine phosphatase inhibitor calyculin A.

The condensation of allylmetallic reagents with aldehydes represents a most powerful method for the stereocontrolled preparation of homoallylic alcohols.[1] For example, Brown and coworkers have introduced several monoterpene derived allyl- and crotyl-boranes that are especially useful in asymmetric synthesis.[2] These methods, which are exemplified by the conversion of boranes **1** and **3**, respectively, into alcohols **2** and **4** (Scheme 1), are particularly useful for the preparation of 4-hydroxy- and 4-hydroxy-3-methylalk-1-enes. In most cases, the products were formed with both excellent relative and absolute stereochemical control. In an adaptation of this chemistry, we have introduced *B*-[(*E*)-3-(diphenylamino)-allyl]diisopinocampheylborane **5**[3] and *B*-[(*E*)-3-(diphenyl methyleneamino)allyl]diisopinocampheylborane **6**[4] and their respective antipodes for the highly stereoselective synthesis of *anti*-β-amino alcohols. In addition, we have repeatedly applied the Brown methods in the total synthesis of nikkomycin B[5] and in approaches to the total synthesis of avermectin[6] and calyculin A **7**.[7] Herein, we report experimental details of a convenient method[8] to prepare *anti*-vicinal diols using allylborane methodology. The method, which is an adaptation of Tamao chemistry,[9] has proven to be particularly useful for the stereospecific synthesis of the terminal amino acid unit of calyculin A **7**. Elsewhere, Roush has reported an equivalent allylboronate methodology for the synthesis of related diol arrays.[10]



Scheme 1 *Reagents and conditions:* i, EtCHO, −78 °C; ii, H_2O_2, NaOH

Table 1 Reactions of aldehydes with boranes **10** and **14**

Entry	Aldehyde	Borane	Products (%)[a]	Mosher ester (%)[a]
1	PhCHO	**10**	**12a** (50)	**16a** (83)
2		**14**	**15a** (47)	**17a** (79)
3	2-C_4H_3SCHO[b]	**10**	**12b** (44)	**16b** (95)
4		**14**	**15b** (47)	**17b** (82)
5	$CH_3(CH_2)_5CHO$	**10**	**12c** (46)	*c*
6	c-$C_6H_{11}CHO$	**10**	**12d** (45)	*c*
7	**18**	**10**	**19** (57)	*c*
8		**14**	**19** (30), **20** (15)	*c*

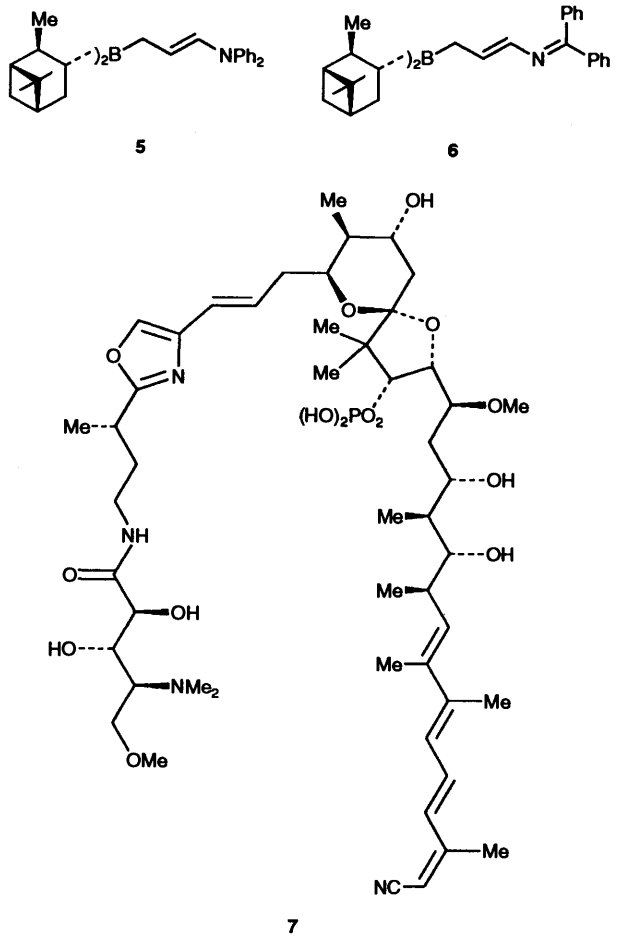
[a] All products were formed with diastereomeric excesses of ≥95:5. [b] Thiophene-2-carbaldehyde. [c] Mosher ester not prepared.

Results and Discussion

An ethereal solution of the allylsilane **8**[9] was cooled to 0 °C and allowed to react with butyllithium and TMEDA. After 4 h, the yellow solution was cooled to −78 °C and (−)-*B*-methoxydiisopinocampheylborane **13** in diethyl ether was added to it. After 1 h the solution, presumably containing the 'ate' complex **9**, was treated with BF_3·OEt_2 to generate the corresponding trialkylborane **10**. This intermediate was not isolated but was allowed to react directly with benzaldehyde, followed by work-up with hydrogen peroxide under basic conditions. This resulted in the oxidative cleavage of the carbon–silicon bond in the intermediate **11a**, and hydrolysis of the boronate ester to reveal the *anti*-diol **12a** in 50% overall yield (Scheme 2). Additionally, under identical reaction conditions, the antipodal borane reagent **14** gave the enantiomeric diol **15a**.

The relative stereochemical assignments of the products **12a** and **15a** were determined by comparison of ^{1}H NMR data with literature values for the corresponding racemic *anti*-diols.[11] Both diols **12a** and **15a** showed δ 4.66 (d, 1 H, *J* 4.3 Hz) and 4.21 (m, 1 H) for the [C*H*(OH)C*H*(OH)] unit. This value is in good agreement with the reported values for the racemic compound.[11] In contrast, the corresponding racemic *syn*-vicinal diol showed a larger coupling constant (7 Hz) for the [C*H*(OH)C*H*(OH)] unit.

The determination of the enantiomeric purity of the diols **12a** and **15a** was carried out by conversion of both into the corresponding diesters **16a** and **17a** with (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (Mosher esters).[12] Careful comparison of the ^{1}H NMR spectra for the diesters **16a** and **17a** showed that the enantioselectivities of reactions leading to the diols **12a** and **15a** were both >95: <5. The assignment of absolute stereochemistry for both diols **12a** and **15a** rests upon analogy with the known absolute stereochemical biases of

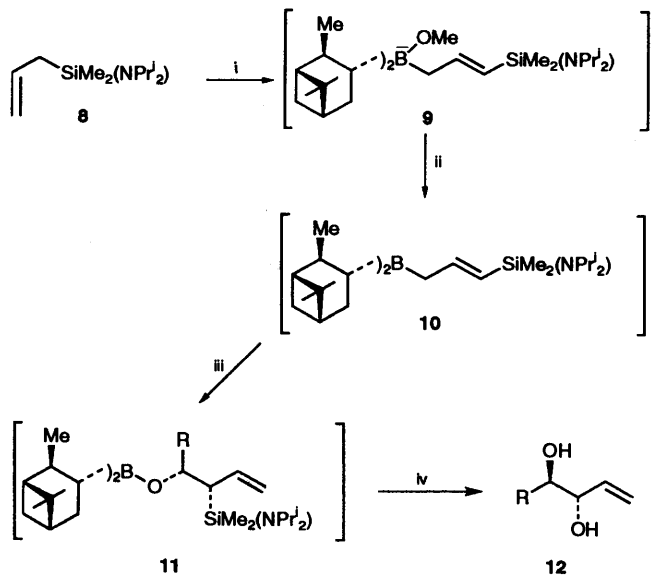


reagents such as the boranes **1** and **3** and their respective antipodes.[1,2] In one case, *vide infra*, the absolute stereochemical bias of the reagent **10** was rigorously established.

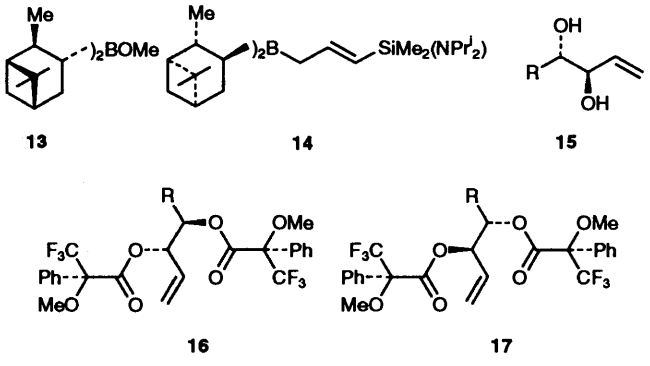
The diol methodology was applied to additional aldehydes in order to investigate the scope of the reaction. Thus, a range of aldehydes were converted into the corresponding *anti*-vicinal diols **12a–d** and **15a**, **b** in good overall yield and essentially as single stereoisomers. In each case, the relative stereoselectivity of reaction was determined from the ^{1}H NMR spectrum. Additionally, in one further case, enantioselectivities were determined by Mosher esterification and comparisons of the ^{1}H NMR spectra for pairs of the diesters **16b** and **17b**. All these results are listed in Table 1.

The serinal derivative **18**[13] was also allowed to react with the allyldiisopinocampheylborane reagent **10** (entry 7). In this case, oxidative work-up in the usual way gave the desired *anti* diol **19** as a single diastereoisomer. Interestingly, and in contrast to the reaction with borane **10**, the chiral aldehyde **18** was found to react with the antipodal reagent **14** to provide both diols **19** (30%) and **20** (15%). Clearly in this case, the reagent and substrate (Felkin–Ahn control) stereochemical biases are mismatched.

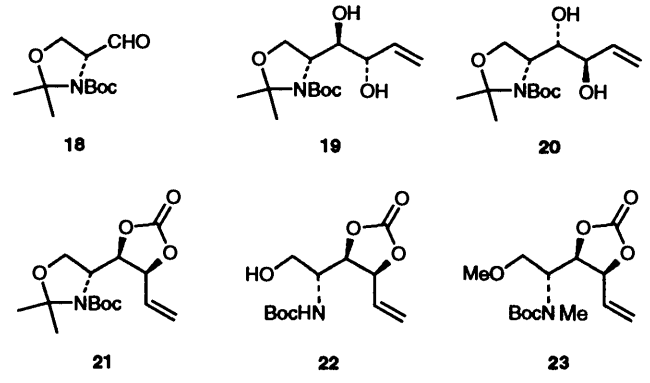
The stereochemistry of the diol **19** was unambiguously established through an X-ray crystal structure of the derived carbonate **21**. Thus, reaction of the diol **19** with 4-nitrophenyl chloroformate in pyridine solution gave the crystalline cyclic carbonate **21** (82%). Details of the single crystal X-ray structure of the carbonate **21** are reported elsewhere.[14] Finally, careful reaction of the carbonate **21** with toluene-4-sulfonic acid in methanol resulted in selective deprotection to reveal the amino alcohol **22** (82%). Prolonged reaction also resulted in cleavage of the carbamate functionality. Subsequent reaction of the



Scheme 2 *Reagents and conditions:* i, BuLi, TMEDA, Et_2O, 0 °C; **13**, −78 °C; ii, BF_3·OEt_2, −78 °C; iii, RCHO, −78 °C; iv, H_2O_2, KF, $KHCO_3$, MeOH, THF



Structures **11**, **12**, **15**, **16**, **17** refer to **a** R = Ph, **b** R = 2-thienyl, **c** n-C_6H_{13}, **d** c-C_6H_{11}



amino alcohol **22** with iodomethane afforded the dimethyl derivative **23** in 75% yield.

This study further demonstrates the utility of pinene-derived compounds in asymmetric synthesis. The direct conversion of aldehydes into enantiomerically pure *anti*-vicinal diols *via* an experimentally simple one-pot process should find considerable use in synthesis. Further applications of this chemistry in the synthesis of natural products including calyculin A **7** will be reported in due course.

Experimental

All reactions were carried out under an atmosphere dry

nitrogen or argon. M.p.s were determined on a Reichert hot-stage apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 283 or Perkin-Elmer 1600 Series FTIR spectrophotometer. Optical rotations, recorded on a Perkin-Elmer 24 polarimeter, are expressed in units of 10^{-1} deg cm^2 g^{-1}. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian XL-400 or a Bruker ACE-300 spectrometer. Mass spectra were recorded on a VG70-250SE mass spectrometer by the Analytical Services Laboratory, Northwestern University. Elemental analyses were determined at G.D. Searle and Company, Skokie, IL. Chromatography on silica refers to Merck silica gel 60 (Art. 9385), eluents are given in parenthesis. Thin layer chromatography was performed on Merck pre-coated silica gel 60F_{254} plates.

Solvents for chromatography were purified by distillation. Anhydrous THF and Et_2O were distilled from sodium benzophenone ketyl. DMF was distilled at reduced pressure from BaO and stored over 4 Å molecular sieves. CH_2Cl_2 was distilled from CaH_2. TMEDA was distilled from CaH_2 and stored over KOH. All other chemicals were used without further purification unless otherwise noted.

General Procedure for the Preparation of the anti *Diols* **12** *and* **15**.—To a solution of the silyl compound **8** (5.0 mmol) in Et_2O (5.5 cm^3) at 0 °C was added TMEDA (1.0 equiv.) and BuLi (1.0 equiv.). The solution was kept at 0 °C for 4 h and then cooled to −78 °C. The reaction mixture was treated with either (+)- or (−)-β-methoxydiisopinocampheylborane **13** (1.2 equiv.) in Et_2O (2.5 cm^3). The solution was maintained at −78 °C for 1 h and then BF_3·OEt_2 (1.3 equiv.) was added to it followed by the aldehyde (0.7 equiv.). The mixture was stirred at −78 °C for 3.5 h and then treated with THF (5 cm^3), MeOH (5 cm^3), KF (2 equiv.), $KHCO_3$ (2 equiv.) and 30% H_2O_2 (20 equiv.). The mixture was stirred at room temperature for 16 h, cooled to 0 °C, and quenched with the addition of $Na_2S_2O_3$. The mixture was filtered through Celite and the Celite pad washed with EtOAc (150 cm^3). The organic solution was dried ($MgSO_4$), concentrated under reduced pressure, and the residue chromatographed on silica to yield the *anti* diols.

(1R,2S)-1-*Phenylbut*-3-*ene*-1,2-*diol* **12a**.—This compound was prepared from (−)-β-methoxydiisopinocampheylborane **13** to yield the diol **12a** (290 mg, 50%) as a colourless oil: R_f 0.50 (1:1, hexanes–EtOAc); $[\alpha]_D$ −75.7 (*c* 1.1, $CHCl_3$); ν_{max}(film)/cm^{-1} 3396, 3030, 1494, 1452, 1028 and 723; δ_H(300 MHz, $CDCl_3$) 7.32–7.19 (m, 5 H), 5.71 (ddd, 1 H, *J* 17.1, 10.7, 6.1), 5.19–5.09 (m, 2 H), 4.66 (d, 1 H, *J* 4.3), 4.21 (m, 1 H) and 3.23 (s br, 2 H); δ_C(76 MHz, $CDCl_3$) 139.8, 135.5, 128.0, 127.6, 126.6, 117.4, 76.4 and 76.3; *m*/*z* (EI) 164 (M$^{+\cdot}$), 147, 107, 79 and 58 [Found: *m*/*z* 147.0771. Calc. for $C_{10}H_{11}O$ (M − OH$^+$): 147.0810].

(1S,2R)-1-*Phenylbut*-3-*ene*-1,2-*diol* **15a**. This compound was prepared from (+)-β-methoxydiisopinocampheylborane to give the diol **15a** (272 mg, 47%) as a colourless oil: $[\alpha]_D$ +74.1 (*c* 1.2, $CHCl_3$); spectra were identical with those of (1*R*,2*S*)-1-phenylbut-3-ene-1,2-diol **12a**.

(1S,2S)-1-(2-*Thienyl*)*but*-3-*ene*-1,2-*diol* **12b**. This compound was prepared from (−)-β-methoxydiisopinocampheylborane **13** to afford the diol **12b** (260 mg, 44%) as a clear oil: R_f 0.40 (1:1, hexanes–EtOAc); $[\alpha]_D$ −34.6 (*c* 1.1, $CHCl_3$); ν_{max}(film)/cm^{-1} 3388, 2885, 1436, 1036, 931 and 703; δ_H(300 MHz, $CDCl_3$) 7.24 (dd, 1 H, *J* 4.4, 1.8), 6.96 (m, 2 H), 5.78 (m, 1 H), 5.32–5.17 (m, 2 H), 4.89 (d, 1 H, *J* 4.4), 4.30 (m, 1 H), 3.48 (s br, 1 H) and 3.03 (s br, 1 H); δ_C(76 MHz, $CDCl_3$) 142.9, 135.5, 126.4, 125.2, 118.0, 76.2 and 73.0.

(1R,2R)-1-(2-*Thienyl*)*but*-3-*ene*-1,2-*diol* **15b**. This compound was prepared from (+)-β-methoxydiisopinocampheylborane to yield the diol **15b** (280 mg, 47%) as a clear oil: $[\alpha]_D$ +29.6 (*c* 1.4, $CHCl_3$); spectra were identical with those of (1*S*,2*S*)-1-(2-thienyl)but-3-ene-1,2-diol **12b**.

(3S,4R)-*Dec*-1-*ene*-3,4-*diol* **12c**. This compound was prepared from (−)-β-methoxydiisopinocampheylborane **13** to afford the diol **12c** (315 mg, 52%) as a white solid: m.p. 53–54 °C; R_f 0.38 (1:1, hexanes–EtOAc); $[\alpha]_D$ −2.0 (*c* 1.0, $CHCl_3$); ν_{max}(CHCl$_3$)/cm^{-1} 3343, 3229, 2916, 1479 and 1064; δ_H(300 MHz, $CDCl_3$) 5.93 (ddd, 1 H, *J* 17.2, 10.6, 6.4), 5.37–5.26 (m, 2 H), 4.11 (m, 1 H), 3.70 (m, 1 H), 2.00 (s br, 2 H), 1.52–1.28 (m, 10 H) and 0.86 (t, 3 H, *J* 6.6); δ_C(76 MHz, $CDCl_3$) 136.1, 117.6, 76.0, 74.1, 32.1, 31.7, 29.3, 25.8, 22.6 and 14.0; *m*/*z* (EI) 174 (M + 2), 171, 155, 113, 97 and 58 [Found: *m*/*z* 155.1424. Calc. for $C_{10}H_{19}O$ (M − OH$^+$): 155.1436] (Found: C, 69.4; H, 11.7. Calc. for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70%).

(1R,2S)-1-*Cyclohexylbut*-3-*ene*-1,2-*diol* **12d**. This compound was prepared from (−)-β-methoxydiisopinocampheylborane **13** to give the diol **12d** (375 mg, 63%) as a white solid, m.p. 72–73 °C; R_f 0.40 (1:1, hexanes–EtOAc); $[\alpha]_D$ −16.9 (*c* 1.9, $CHCl_3$); ν_{max}(CHCl$_3$)/cm^{-1} 3357, 2925, 2852, 1446, 1059 and 988; δ_H(300 MHz, $CDCl_3$) 5.98 (ddd, 1 H, *J* 17.2, 10.5, 6.6), 5.32 (m, 2 H), 4.23 (m, 1 H), 3.42 (dd, 1 H, *J* 8.2, 3.9), 2.11 (s, 2 H), 2.02 (m, 1 H), 1.81–1.61 (m, 4 H) and 1.48–0.97 (m, 6 H); δ_C(76 MHz, $CDCl_3$) 135.7, 117.8, 78.1, 73.4, 39.8, 29.0, 28.8, 26.3, 25.9 and 25.7; *m*/*z* (EI) 169 (M − H$^+$) [Found: *m*/*z* 153.1266. Calc. for $C_{10}H_{17}O$ (M − OH$^+$) 153.1279] (Found: C, 70.4; H, 10.7. Calc. for $C_{10}H_{18}O_2$: C, 70.54; H, 10.65%).

General Procedure for the Preparation of (R)-α-*Methoxy*-α-(*trifluoromethyl*)*phenylacetates* **16** *and* **17**.—To the diol **12** or **15** (0.21 mmol) was added (*R*)-α-methoxy-α-(trifluoromethyl)-phenylacetic acid (2.1 equiv.) in CH_2Cl_2 (0.21 cm^3). The solution was treated with 1,3-dicyclohexylcarbodiimide (2.1 equiv.) and a catalytic amount of (4-dimethylamino)pyridine after which the mixture was stirred at room temperature for 3 h. It was then diluted with CH_2Cl_2 (5 cm^3) and the resulting solid filtered off. The organic solution was evaporated and the residue chromatographed on silica (5:1, light petroleum–EtOAc) to afford the title compounds.

(1R,2S)-1,2-*Bis*[(R)-α-*Methoxy*-α-(*trifluoromethyl*)*phenylacetoxy*]-1-*phenylbut*-3-*ene* **16a**.—This compound was prepared from the diol **12a** to give the diester **16a** (83%) as a colourless oil: R_f 0.57 (3:1, light petroleum–EtOAc); $[\alpha]_D$ +14.4 (*c* 2.5, $CHCl_3$); ν_{max}(film)/cm^{-1} 2952, 1753, 1452, 1271, 1171 and 1018; δ_H(300 MHz, $CDCl_3$) 7.40–7.07 (m, 15 H), 6.11 (d, 1 H, *J* 4.1), 5.85–5.77 (m, 2 H), 5.37–5.32 (m, 2 H) and 3.41 (s, 6 H); δ_C(76 MHz, $CDCl_3$) 165.6, 165.1, 134.1, 132.0, 129.7, 129.5, 128.9, 128.4, 128.31, 128.26, 127.4, 127.3, 127.1, 125.1, 122.7, 77.9, 77.5, 55.6 and 55.4; *m*/*z* (EI) 596 (M$^{+\cdot}$), 527, 421, 362, 323, 189, 129 and 83 [Found: *m*/*z* 596.1599. Calc. for $C_{30}H_{26}F_6O_6$ (M$^{+\cdot}$): 596.1633].

(1S,2R)-1,2-*Bis*[(R)-α-*Methoxy*-α-(*trifluoromethyl*)*phenylacetoxy*]-1-*phenylbut*-3-*ene* **17a**. This compound was prepared from the diol **15a** to give the diester **17a** (79%) as a white solid: m.p. 104–106 °C; R_f 0.56 (3:1, light petoleum–EtOAc); $[\alpha]_D$ +77.9 (*c* 1.4, $CHCl_3$); ν_{max}(CHCl$_3$)/cm^{-1} 1747, 1268, 1229, 1186 and 1027; δ_H(300 MHz, $CDCl_3$) 7.36–7.24 (m, 15 H), 6.15 (d, 1 H, *J* 6.1), 5.74 (dd, 1 H, *J* 7.1, 6.3), 5.62–5.50 (m, 1 H), 5.19 (m, 2 H), 3.37 (d, 3 H, *J* 1.1) and 3.28 (d, 3 H, *J* 1.1); δ_C(76 MHz, $CDCl_3$) 165.4, 165.3, 134.5, 132.0, 130.0, 129.6, 129.5, 129.3, 128.6, 128.3, 128.1, 127.4, 127.2, 125.0, 122.1, 121.2, 77.3, 55.4 and 55.3; *m*/*z* (EI) 596 (M$^{+\cdot}$), 527, 421, 362, 323, 295, 189 and 105 [Found: *m*/*z* 596.1634. Calc. for $C_{30}H_{26}F_6O_6$ (M$^{+\cdot}$): 596.1633].

(1S,2S)-1,2-*Bis*[(R)-α-*Methoxy*-α-(*trifluoromethyl*)*phenylacetoxy*]-1-(2-*thienyl*)*but*-3-*ene* **16b**. This compound was prepared from the diol **12b** to afford the diester **16b** (79%) as a clear oil: R_f 0.40 (5:1, hexanes–EtOAc); $[\alpha]_D$ +73.5 (*c* 1.3, $CHCl_3$);

ν_{max}(film)/cm^{-1} 2951, 1754, 1715, 1497, 1452, 1237, 1122, 1016 and 716; δ_H(300 MHz, $CDCl_3$) 7.42–7.23 (m, 11H), 6.97 (dd, 1 H, *J* 3.5, 1.1), 6.89 (dd, 1 H, *J* 5.1, 3.6), 6.39 (d, 1 H, *J* 4.3), 5.88–5.81 (m, 2 H), 5.56–5.40 (m, 2 H), 3.42 (d, 3 H, *J* 1.2) and 3.41 (d, 3 H, *J* 1.2); δ_C(76 MHz, $CDCl_3$) 165.4, 165.1, 135.5, 131.9, 131.8, 129.9, 129.5, 128.7, 128.4, 128.2, 127.2, 127.1, 126.4, 125.1, 123.5, 121.4, 77.3, 73.1, 55.6 and 55.4.

(1R,2R)-1,2-*Bis*[(R)-α-*methoxy*-α-(*trifluoromethyl*)*phenylacetoxy*]-1-(2-*thienyl*)*but*-3-*ene* **17b**. This compound was prepared from the diol **15b** to yield the diester **17b** (82%) as a colourless oil; R_f 0.42 (5:1, hexanes–EtOAc); $[\alpha]_D$ −6.3 (*c* 1.0, $CHCl_3$); ν_{max}(film)/cm^{-1} 2951, 1754, 1452, 1271, 1240, 1171, 1017 and 716; δ_H(300 MHz, $CDCl_3$) 7.39–7.25 (m, 11 H), 7.18 (dd, 1 H, *J* 3.6, 1.1), 6.97 (dd, 1 H, *J* 5.1, 3.6), 6.42 (d, 1 H, *J* 5.7), 5.80 (dd, 1 H, *J* 6.9, 5.8), 5.64–5.47 (m, 1 H), 5.22 (m, 2 H), 3.37 (d, 3H, *J* 1.2) and 3.29 (d, 3H, *J* 1.2); δ_C(76 MHz, $CDCl_3$) 165.2, 165.0, 135.9, 132.1, 132.0, 129.8, 129.6, 129.5, 129.4, 128.3, 127.6, 127.2, 126.7, 125.2, 122.5, 121.2, 76.8, 72.6 and 55.4.

(4R)-tert-*Butyl* 4-[(1R,2S)-1,2-*Dihydroxybut*-3-*enyl*]-2,2-*dimethyloxazolidine*-3-*carboxylate* **19**.—To a solution of the allylsilane **8** (1.28 g, 6.4 mmol) in dry Et_2O (7 cm^3) at 0 °C was added TMEDA (0.97 cm^3, 6.4 mmol) and BuLi (1.79 mol dm^{-3} solution in hexanes; 3.6 cm^3, 6.4 mmol). The yellow solution was kept at 0 °C for 4 h after which it was cooled to −78 °C and treated with (−)-β-methoxydiisopinocampheylborane **13** (2.4 g, 7.6 mmol) in Et_2O (1.5 cm^3) added *via* a cannula. The solution was maintained at −78 °C for 2 h after which it was treated with BF_3·OEt_2 (1.0 cm^3, 8.3 mmol) and the aldehyde **18** (1.05 g, 4.5 mmol) in Et_2O (1.0 cm^3). The reaction mixture was stirred at −78 °C for 3 h after which THF (6 cm^3), MeOH (6 cm^3), potassium fluoride (720 mg, 12.8 mmol), potassium hydrogen carbonate (1.24 g, 12.8 mmol), and 30% H_2O_2 (14 cm^3) were added to it. The mixture was stirred at ambient temperature for 20 h, cooled to 0 °C and quenched by the addition of $Na_2S_2O_3$. The mixture was then diluted with EtOAc (50 cm^3) and filtered through a Celite pad. The Celite pad was washed thoroughly with EtOAc (100 cm^3). The combined filtrate and washings were dried ($MgSO_4$) and concentrated under reduced pressure, and the residue was chromatographed on silica (3:1, hexanes–EtOAc) to give the diol **19** (740 mg, 57%) as a white solid: m.p. 56–57 °C; R_f 0.36 (1:1, hexanes–EtOAc); $[\alpha]_D$ −3.3 (*c* 1.1, $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 3448, 2979, 1700, 1670, 1397, 1367 and 1172; δ_H(300 MHz, $CDCl_3$) 5.96 (ddd, 1 H, *J* 17.3, 10.7, 4.5), 5.35 (d br, 1 H, *J* 17.3), 5.16 (d br, 1 H, *J* 10.7), 4.28–3.96 (m, 4 H), 3.70 (s br, 1 H), 1.57 (s, 3 H), 1.51 (s, 3 H) and 1.49 (s, 9 H); δ_C(76 MHz, $CDCl_3$) 153.7, 136.8, 114.8, 93.9, 81.1, 74.5, 65.1, 58.5, 28.3, 26.9 and 24.2; *m*/*z* (EI) 272 (M − Me$^+$), 231, 200, 172, 144, 100 and 57 [Found: *m*/*z* 272.1507. Calc. for $C_{13}H_{22}NO_5$(M − Me$^+$): 272.1498] (Found: C, 58.3; H, 8.7; N, 4.7. Calc. for $C_{14}H_{25}NO_5$: C, 58.51; H, 8.77; N, 4.87%).

(4R)-tert-*Butyl* 4-[(1S,2R)-1,2-*Dihydroxybut*-3-*enyl*]-2,2-*dimethyloxazolidine*-3-*carboxylate* **20**.—To a solution of the allylsilane **8** (1.61 g, 8.1 mmol) in dry Et_2O (10 cm^3) at 0 °C was added TMEDA (1.2 cm^3, 8.1 mmol) and BuLi (1.79 mol dm^{-3} solution in hexanes; 5.0 cm^3, 8.1 mmol). The yellow solution was maintained at 0 °C for 4 h after which it was cooled to −78 °C and (+)-β-methoxydiisopinocampheylborane (3.1 g, 9.7 mmol) in Et_2O (4 cm^3) was added to it *via* a cannula. The solution was kept at −78 °C for 2 h after which it was treated with BF_3·OEt_2 (1.3 cm^3, 10.8 mmol) and the aldehyde **18** (1.3 g, 5.7 mmol) in Et_2O (3 cm^3). The mixture was stirred at −78 °C for 3 h after which THF (8 cm^3), MeOH (8 cm^3), potassium fluoride (941 mg, 16.2 mmol), $KHCO_3$ (1.62 g, 16.2 mmol) and 30% H_2O_2 (16 cm^3) were added to it. The mixture was stirred at room temperature for 20 h, cooled to 0 °C and quenched by the addition of solid $Na_2S_2O_3$. The mixture was diluted with EtOAc (70 cm^3) and filtered through a Celite pad. The Celite pad was washed with EtOAc (150 cm^3) and the combined filtrate and washings were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed on silica (3:1, hexanes–EtOAc) to give the diol **19** (486 mg, 30%) and the diol **20** (245 mg, 15%) as a colourless oil: R_f 0.52 (1:1, hexanes–EtOAc); $[\alpha]_D$ +79.0 (*c* 2.5, $CHCl_3$); ν_{max}(film)/cm^{-1} 3436, 2979, 1698, 1667, 1397, 1368 and 1172; δ_H(300 MHz, $CDCl_3$) 5.98 (ddd, 1 H, *J* 17.1, 10.8, 5.9), 5.37 (dd, 1 H, *J* 17.2, 1.5), 5.25 (dd, 1 H, *J* 10.7, 1.5), 4.28 (m, 1 H), 4.10–3.87 (m, 5 H), 3.57 (m, 1 H) and 1.62–1.43 (m, 15 H); δ_C(76 MHz, $CDCl_3$) 155.0, 136.9, 116.4, 94.3, 81.5, 73.1, 66.0, 57.6, 28.1, 26.4 and 24.0; *m*/*z* (EI) 288 (M + H$^+$), 272, 231, 200, 174, 144, 100 and 57. [Found: *m*/*z* 272.1490. Calc. for $C_{13}H_{22}NO_5$ (M − Me$^+$): 272.1498].

(4R)-tert-*Butyl* 2,2-*Dimethyl*-4-[(4R,5S)-2-*oxo*-5-*vinyl*-1,3-*dioxolan*-4-*yl*]*oxazolidine*-3-*carboxylate* **21**.—To a solution of the diol **19** (790 mg, 2.75 mmol) in pyridine (10 cm^3) was added 4-nitrophenyl chloroformate (610 mg, 3.0 mmol). The mixture was stirred at room temperature for 4 days and then concentrated under reduced pressure. The residue was chromatographed on silica (3:1, hexanes–EtOAc) to give recovery of the starting material **19** (280 mg) and the carbonate **21** (450 mg, 82% based on recovered starting material) as a white solid: m.p. 82–83 °C; R_f 0.31 (3:1, hexanes–EtOAc); $[\alpha]_D$ +73.0 (*c* 1.2, $CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 2981, 1813, 1697, 1394 and 1177 cm^{-1}; δ_H(300 MHz, $CDCl_3$) 5.81 (ddd, 1 H, *J* 17.0, 10.9, 5.6), 5.50 (d, 1 H, *J* 17.1), 5.42 (d, 1 H, *J* 10.7), 5.26–5.15 (m, 2 H), 4.08 (m, 1 H), 3.93 (d, 2 H, *J* 4.6), 1.53 (s, 3 H), 1.46 (s, 9 H) and 1.42 (s, 3 H); δ_C(76 MHz, $CDCl_3$) 153.9, 152.4, 129.5, 121.0, 94.1, 81.2, 78.6, 62.7, 56.5, 28.3, 26.4 and 24.6; *m*/*z* (EI) 298 (M − Me$^+$), 242, 198, 144, 100, 84 and 57 [Found: *m*/*z* 298.1277. Calc. for $C_{14}H_{20}NO_6$ (M − Me$^+$): 298.1291] (Found: C, 57.2; H, 7.5; N, 4.4. Calc. for $C_{15}H_{23}NO_6$: C, 57.49; H, 7.39; N, 4.46%).

(4R,5S)-4-{(1R)-2-*Hydroxy*-1-[(tert-*butoxycarbonylamino*)*ethyl*]}-5-*vinyl*-1,3-*dioxan*-2-*one* **22**.—To a solution of the carbonate **21** (1.1 g, 3.5 mmol) in MeOH (35 cm^3) was added toluene-*p*-sulfonic acid monohydrate (50 mg, 0.2 mmol). The solution was kept at room temperature for 15 h and then diluted with pH 7 buffer and concentrated under reduced pressure. The aqueous residue was extracted with CH_2Cl_2 (3 × 50 cm^3) and the combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed on silica (3:1, hexanes–EtOAc ⟶ 1:1, hexanes–EtOAc) to give recovery of the carbonate **21** (808 mg) and the carbamate **22** (240 mg). The recovered starting material **21** was recycled twice to yield additional carbamate **22** (708 mg, 82% based on recovered **21**) as a colourless oil: R_f 0.26 (1:1, hexanes–EtOAc); $[\alpha]_D$ −18.2 (*c* 1.95, $CHCl_3$); ν_{max}(film)/cm^{-1} 3378, 2979, 1809, 1694, 1526, 1167 and 1051; δ_H(300 MHz, $CDCl_3$) 5.97 (ddd, 1 H, *J* 17.0, 10.4, 6.7), 5.52 (d, 1 H, *J* 17.0), 5.47 (d, 1 H, *J* 10.4), 5.33 (d, 1 H, *J* 8.8), 5.24 (apparent triplet, 1 H, *J* 7.0), 4.87 (apparent triplet, 1 H, *J* 8.4), 3.92–2.71 (m, 3 H), 3.21 (s br, 1 H) and 1.43 (s, 9 H); δ_C(76 MHz, $CDCl_3$) 155.0, 154.2, 128.9, 121.4, 80.3, 79.5, 61.6, 50.3 and 28.2; *m*/*z* (EI) 258 (M − Me$^+$), 234, 218, 200, 160, 142 and 57 [Found: *m*/*z* 258.0964. Calc. for $C_{11}H_{16}NO_6$ (M − Me$^+$): 258.0978].

(4R,5S)-4-{(1R)-2-*Methoxy*-1-[(tert-*butoxycarbonyl*)(*methyl*)*amino*]*ethyl*}-5-*vinyl*-1,3-*dioxan*-2-*one* **23**.—To a solution of the alcohol **22** (605 mg, 2.2 mmol) in DMF (6.6 cm^3) was added methyl iodide (2.2 cm^3, 35.4 mmol) and silver oxide (4.1 g, 17.7 mmol). The mixture was stirred at ambient temperature for 14 h

and then filtered through Celite. The Celite pad was washed with CH_2Cl_2 (150 cm^3) and the combined filtrate and washings were dried (Na_2SO_4) and concentrated under reduced pressure. The residue was chromatographed on silica (3:1, hexanes–EtOAc) to afford the ether **23** (504 mg, 75%) as a colourless oil: R_f 0.29 (3:1, hexanes–EtOAc); $[\alpha]_D$ +15.4 (*c* 1.0, $CHCl_3$); ν_{max}(film)/cm^{-1} 2978, 2932, 1810, 1694, 1454, 1367, 1156 and 1053; δ_H(300 MHz, $CDCl_3$) 5.83 (ddd, 1 H, *J* 17.0, 10.3, 6.7), 5.37 (m, 2 H), 5.03 (m, 2 H), 4.07 (m, 1 H), 3.60 (m, 1 H), 3.46 (dd, 1 H, *J* 9.9, 3.3), 3.25 (s, 2 H), 2.73 (s, 3 H) and 1.36 (s, 9 H); δ_C(76 MHz, $CDCl_3$) 155.3, 153.6, 129.2, 121.1, 80.1, 79.5, 77.6, 70.7, 58.8, 54.4, 32.8 and 28.1; *m/z* (CI) 302 ($M + H^+$), 263, 246, 202, 184, 156 and 88 (Found: C, 55.6; H, 7.7; N, 4.5. Calc. for $C_{14}H_{23}NO_6$: C, 55.80; H, 7.69; N, 4.64%).

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