Synthesis of "Garner" Aldehyde-Derived Cyclopropylboronic Esters

Jörg Pietruszka,*[a] Andreas Witt,[a] and Wolfgang Frey[a]

Keywords: Amino acids / Amino alcohols / Boronic esters / Cyclopropanes / Suzuki coupling

The "Garner" aldehyde has been used as a common intermediate for the preparation of the corresponding alkyne **7** and the alkenylboronic esters **12**–**16** (24–80%). Diastereoselective cyclopropanation afforded cyclopropylboronic esters **17**–**20** (60–84%, *dr* 22:78 to 92:8), the configurations of which were determined by chemical correlation (cyclopropanols **22**), X-ray structural analysis (of **21a**), and characteristic NMR spectroscopic data. The protected amino alcohols **23**–**26** and amino acids **27** have been synthesised from the cyclopropylboronic esters **19** by oxidation, Matteson homologation or Suzuki coupling.

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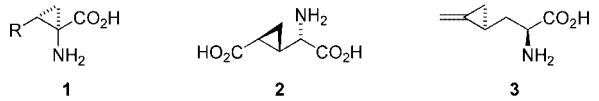
Introduction

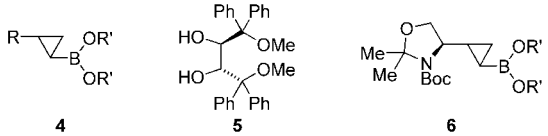
Natural and unnatural amino acids containing cyclopropyl groups exhibit various physiological properties, and the cyclopropane unit is frequently responsible for the observed biological activity.[1] Apart from fascinating complex natural products such as the peptidolactone *hormaomycin*,[2,3] which influences the secondary metabolite production of certain bacteria, or the recently isolated *belactosin A*,[4] a novel antitumor antibiotic, simpler amino acids can also show remarkable features. Among those, 1-aminocyclopropanecarboxylic acid (**1**, R = H) is structurally the simplest derivative (Figure 1), but it is nevertheless the highly important precursor of the plant hormone ethylene, which is formed by enzymatic oxidative degradation.[5,6] Moreover, substituted derivatives (**1**, R ≠ H) are generally inhibitors of the corresponding ethylene-forming enzyme.[7] Another important issue of the incorporated cyclopropane units is the inherent conformational constraint in the system, and they have consequently been used for the synthesis of several peptidomimetics.[8–13] The conformationally constrained L-glutamate analogue **2**, originally synthesised by Ohfune and co-workers in 1991,[14] was found to be an agonist for group II metabotropic glutamate receptors.[15] Of particular interest is hypoglycine A (**3**), occurring in the unripe fruits of the Jamaican ackee tree (*Blighia sapida*) and in lychee seeds (*Litchi chinensis*). Its strong hypoglycaemic effect proved to be fatal in a large number of cases.[16–19]



1 2 3

Figure 1. Natural and nonnatural analogues of amino acids containing a cyclopropyl group

Numerous syntheses of individual non-proteinogenic α-amino acids have been reported, but use of general building blocks has always been especially versatile. Many preparative approaches to enantiopure compounds have been based on radical, cationic and − more recently − anionic reagents, ultimately derived from the "chiral pool".[20–24] While organozinc derivatives have been successful (anionic) candidates for many (palladium-catalysed) couplings with electrophiles (e.g., ref.[25–29]), organoboron reagents have been used less frequently.[30–33] We thought to investigate the potential of the preparation of cyclopropane-containing amino acids from cyclopropylboronic esters **4** (Figure 2),[34–41] thus using the synthetic potential of the boron moiety for further transformations.[42–48] We recently described the synthesis of highly stable, enantiomerically pure boronic esters, the diol **5**[49,50] usually being the auxiliary and protecting group of our choice.[51–55] Consequently, one envisaged target was the "Garner" aldehyde-derived[56–60] cyclopropane **6**. Upon diastereoselective synthesis the question of matched-mismatched interaction would need to be addressed. Furthermore, it was a challenge to perform further transformations to produce either synthetically useful, orthogonally protected enantiomerically pure amino alcohols or amino acids. Preliminary results in this area have been published;[61] we now wish to report our investigations in full.



4 5 6

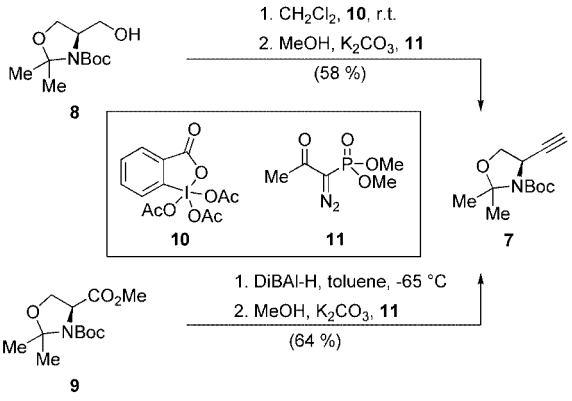
Figure 2. Cyclopropylboronic esters as general building blocks

[a] Institut für Organische Chemie der Universität Stuttgart, Pfaffenwaldring 55, 70569 Stuttgart, Germany
Fax: (internat.) + 49-(0)711/6854335
E-mail: joerg.pietruszka@po.uni-stuttgart.de

Results and Discussion

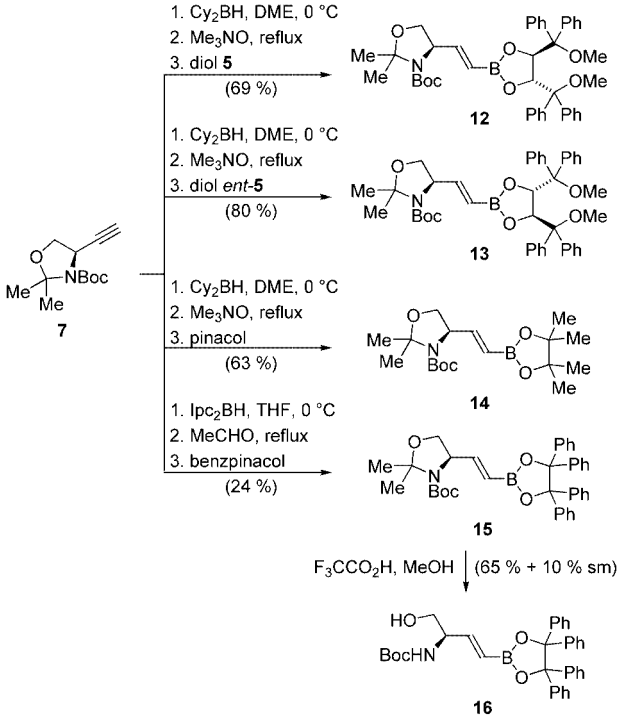
Synthesis of Cyclopropylboronic Esters

As a common starting material for the investigations, alkyne **7**[62−64] was needed. This serine derivative is usually synthesised most conveniently by a one-pot aldehyde-to-alkyne one-carbon homologation. In our hands, the best results were obtained when the intermediate "Garner" aldehyde − obtained either by oxidation of serinol **8**[59] with Dess−Martin periodinane **10**[65−67] or by reduction of ester **9**[59] with diisobutylaluminium hydride (DiBAl-H) − was not purified (Scheme 1). Instead, the crude product was directly treated with the Bestmann−Ohira reagent **11**[68−73] in basic methanol, furnishing the alkyne **7** in 58−64% yield.[74] Although the overall yield starting from ester **9** would seem superior, in our experience the alternative proved to be more reliable. For a high degree of repeatability of the reduction step it is essential to make sure that the DiBAl-H reagent is of high quality. Another requirement is for meticulous temperature control, as well as precise compliance with the workup procedure.



Scheme 1. Synthesis of alkyne **7** from alcohol **8** or ester **9** via the "Garner" aldehyde

The synthesis of alkenylboronic esters **12−16** was next investigated (Scheme 2). It is well known that direct hydroboration of sterically demanding alkynes with 1,3,2-dioxaborolanes such as pinacolborane[75,76] does not allow convenient product isolation.[55,77] The more reactive dicyclohexyl- (Cy_2BH)[78] or diisopinocampheylborane (Ipc_2BH)[79] should be used, followed by oxidation and transesterification with a suitable diol. While the isolation of the diol **5**/*ent*-**5**-derived olefins **12** and **13** (69−80%) was unproblematic, the purification of ester **14** proved troublesome: chromatographic separation from side products was possible, but slow decomposition of **14** decreased the yield (63%). The transesterification with benzpinacol was a slow process,[61] presumably due to the fact that the two hydroxy groups should preferentially exist in an antiperiplanar conformation and that the rotation around the central C−C bond is hindered. Product isolation was unproblematic, but the alkenylboronic ester **15** was obtained only in 24% yield. It is interesting to note that, despite the sluggish cleavage of the isopropylidene protecting group of **15** (MeOH/CF_3CO_2H), the primary alcohol **16** could be isolated in moderate yield (61%) with 10% recovery of starting material, but without any noticeable decomposition of the boronic ester moiety. Unfortunately, cyclopropanation of **16** could not be achieved under Simmons−Smith conditions.



Scheme 2. Synthesis of alkenylboronic esters **12−16**

Cyclopropanation of the remaining alkenylboronic esters **12−15** was preparatively unproblematic (Scheme 3). The palladium-catalysed decomposition of diazomethane (Method A) was most convenient, and the products **17−20** were isolated in 61−84% yield. The diastereoselectivity of the conversion was somewhat surprising (see below for the assignment of configuration). While the configuration of chiral auxiliary **5**/*ent*-**5** was only of minor consequence − the diastereoisomers **17a** and **18a** were preferentially formed − and no pronounced matched-mismatched interactions were observed, the change from pinacol to benzpinacol gave dramatic results. Cyclopropanation of alkene **14** gave the usually preferred diastereoisomer **19a** (*dr* 70:30), but with benzpinacol derivative **15** the ratio was almost completely reversed and cyclopropane **20b** (**20a/20b**, *dr* 24:76) dominated. The cause for the unusual observation is not clear, but since steric effects predominate in diastereoselective cyclopropanations with diazomethane/Pd^{II}, the assumption that the different diols induce a different preferred reactive conformation would seem reasonable. Unfortunately, attempts to crystallise either starting material or product failed and we could not gain further insights.

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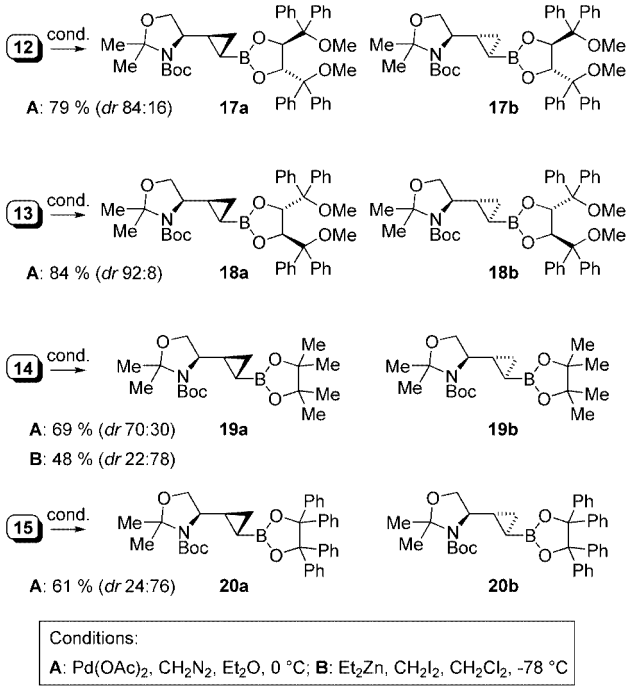
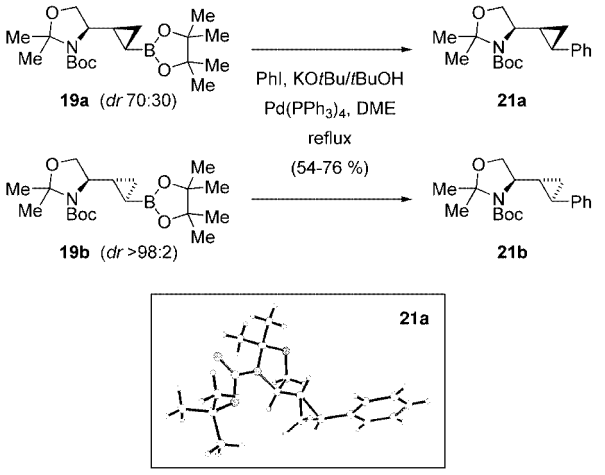
It is interesting to note that Simmons-Smith-type cyclopropanations[80] of pinacol-derived alkenylboronic ester **14** failed at ambient temperature and even at −20 °C. Product **19** was only isolated (48%) when the conversion was performed at −78 °C (Method B); in relation to the cyclopropanation with diazomethane, the selectivity is − as would be expected − reversed (**19a/19b**, *dr* 22:78). Attempts to separate the diastereoisomers fully failed and only small amounts of pure fractions could be obtained at this stage.



Scheme 3. Synthesis of cyclopropylboronic esters **17**−**20**



Scheme 4. Establishing the absolute configuration of cyclopropylboronic esters **19** by an X-ray structural analysis of the Suzuki cross-coupling product **21a**

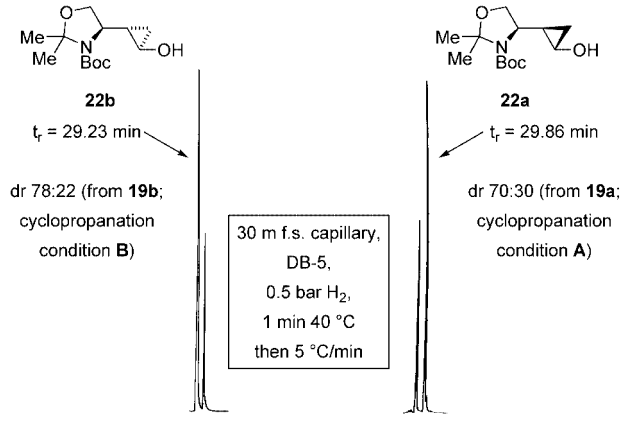


Figure 3. Gas chromatographic correlation of cyclopropylboronic esters through the diastereoisomeric cyclopropanols **22**

Determination of Configuration

First of all we needed to establish a reliable method to determine the configurations of all cyclopropylboronic esters **17**−**20**. We thought we might correlate the esters with the known[81] phenyl derivatives **21**. Suzuki coupling of **19** with phenyl iodide gave the product in 54−76% yield (Scheme 4). While comparison of the NMR spectroscopic data allowed the assignment of diastereoisomer **21b** (synthesised by an alternative approach by Bernabé et al.[81]), compound **21a** was found to crystallise conveniently out of the crude product mixture, with highly enriched **21b** remaining as an oil. X-ray structural analysis indirectly established the configuration of **19a** and so was the foundation for all following efforts.

A more convenient analytical tool is the correlation *and* determination of diastereomeric ratios by GLC. We found that it was most reliable to transform analytical samples of all cyclopropylboronic esters into cyclopropanols **22** under standard conditions (Figure 3).[51] Since we had unambiguously assigned pinacol-derived esters **19**, we could now correlate the remaining esters **17**, **18** and **20** either with **22a** or with **22b**.

Finally, we were also able to make use of characteristic NMR spectroscopic data for the correlation of the different cyclopropylboronic esters **17**−**20**. Although the chemical shifts are usually less pronounced than in other esters derived from diol **5**, and signals of 2′-H or 3′-H are not diagnostic at all, a certain trend is followed for the two diastereoisomeric series (Figure 4). Independently of the diol used, the 1′-H and the C-3′ signals could be used to assign the configuration. In the ′**a**′ diastereoisomer, the 1′-H signal always has a relative (to the ′**b**′ isomer) high-field shift, while the C-3′ signal is shifted to lower fields.

Transformations of Cyclopropylboronic Esters 19

Cyclopropylboronic esters **19** should be ideal intermediates for the syntheses of amino alcohols and amino acids. For analytical samples we had already established that oxidation to cyclopropanols **22** was possible. On preparative scales it was more convenient to isolate not the alcohol, but the *tert*-butyldiphenylsilyl-protected (TPS) derivative **23** (74%; Scheme 5). Separation of the diastereoisomers was not possible, but the primary alcohols **24a** and **24b** were

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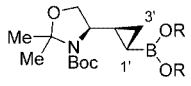
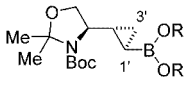
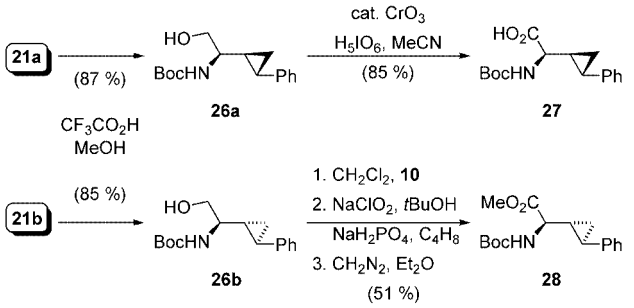



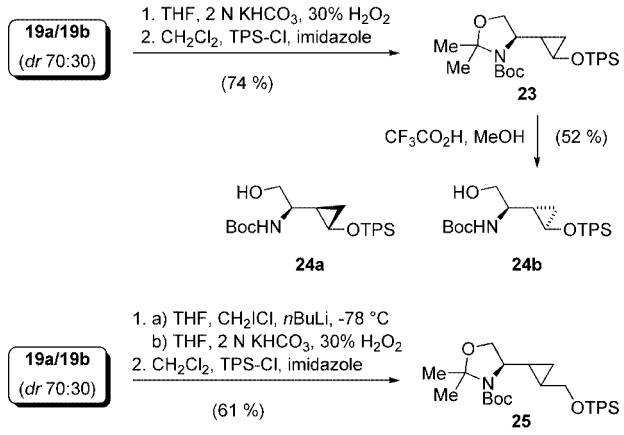
Compound	1'-H [ppm]	C-3' [ppm]	Compound	1'-H [ppm]	C-3' [ppm]
17a	-0.69	11.8	**17b**	-0.23	8.0
18a	-0.86	11.9	**18b**	-0.38	8.0
19a	-0.28	11.3	**19b**	0.02	7.9
20a	0.24	11.4	**20b**	0.71	8.3

Figure 4. Characteristic NMR spectroscopic data ($CDCl_3$, 300 MHz/75 MHz, 330 K) of cyclopropylboronic esters



Scheme 6. Synthesis of cyclopropane-containing amino acid derivatives **27** and **28**

conveniently separated after cleavage of the isopropylidene acetal (52%). Matteson homologation[47] was also possible, but the process was rather slow and complete conversion was not observed. Consequently, oxidation not only gave the desired product, but also yielded minor amounts of cyclopropanols **22**. Purification was achieved after derivatisation: TPS-protected alcohols **25** were obtained in 61% yield. Separation of diastereoisomers was not possible either at this stage or after deprotection of the N,O-acetal. We did not pursue the approach further.



Scheme 5. Synthesis of cyclopropane-containing amino alcohols **23**–**25**

Finally, we used the Suzuki coupling products **21a** and **21b** (vide supra) for further transformations (Scheme 6). While separation of the diastereoisomers by crystallisation was possible, it was even more convenient to separate the primary alcohols **26a** (87%) and **26b** (86%) after deprotection. The amino acids were obtained either by direct oxidation (by the procedure of Zhao et al.[82]) or by a more conventional two-step approach. In our hands the direct conversion into **27** (85%) proved superior; in order to purify the diastereoisomeric acid, the crude product was treated with diazomethane to yield the ester **28** (51%).

Conclusion

In conclusion, we have developed a synthetic route to new cyclopropylboronic esters from the "Garner" aldehyde. The configurations of all derivatives could be assigned by chemical correlation by use of glc, NMR and X-ray analysis. With these building blocks to hand, we should now have a fairly general access to cyclopropane-containing amino alcohols or amino acids. To test this hypothesis, a number of transformations were evaluated. Since the separation of diastereoisomers was most convenient for the phenyl derivatives **21** or **26**, respectively, we utilised the intermediates for their conversion into the unusual amino acids **27** and **28**.

Experimental Section

General Remarks: All reagents were used as purchased from commercial suppliers without further purification. Alcohol **8**,[59] ester **9**,[57][59] Dess–Martin periodinane **10**[65,66] and the Bestmann–Ohira reagent **11**[68–73] were prepared according to the references given. The reactions were carried out by use of standard Schlenk techniques under dry nitrogen. Glassware was oven-dried at 150 °C overnight. Solvents were dried and purified by conventional methods prior to use; diethyl ether (Et_2O), 1,2-dimethoxyethane (DME) and tetrahydrofuran (THF) were freshly distilled from sodium/benzophenone. "Petroleum ether" refers to the fraction with a boiling point between 40–60 °C. **Caution:** The generation and handling of diazomethane[83–86] requires special precautions. Flash column chromatography: Merck silica gel 60, 0.040–0.063 mm (230–400 mesh). TLC: pre-coated sheets, Alugram SIL G/UV_{254} Macherey–Nagel; detection by UV extinction or by use of cerium molybdenum solution [phosphomolybdic acid (25 g), $Ce(SO_4)_2{\cdot}H_2O$ (10 g), concd. H_2SO_4 (60 mL), H_2O (940 mL)]. Preparative MPLC: Gilson (Spectrochrom), with a packed column (49 × 500 mm), LiChroprep, Si60 (15–25 μm), and UV detector (254 nm). ^1H and ^{13}C NMR spectra were recorded – at room temperature in $CDCl_3$ unless otherwise indicated – with a Bruker ARX 500/300. Chemical shifts (δ) are given in ppm relative to resonances of the solvent (^1H: $CDCl_3$, δ = 7.25 ppm; ^{13}C: $CDCl_3$, δ = 77.0 ppm), coupling constants (*J*) are given in Hertz; in spectra of higher order δs and *J*s were not corrected. ^{13}C signals were assigned by means of C-H and H-H-COSY spectra. Microanalysis: performed at the Institut für Organische Chemie, Stuttgart. Melting points (Büchi 510) were not corrected. Specific

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rotations were measured at 20 °C unless otherwise stated. $[\alpha]_D$ values are given in 10^{-1} deg·cm^2·g^{-1}.

X-ray Crystallographic Study:[87] The crystal data for compound **21a** were determined by use of a Siemens P4 diffractometer with graphite monochromator in Omega scan modus with Cu-K_α (λ = 1.54178 A) radiation: $C_{19}H_{27}NO_3$, M_r = 317.4, colourless, T = 293 K, crystal size 0.5 × 0.5 × 0.5 mm, orthorhombic, $P2_12_12_1$, a = 10.9590(5) Å, b = 11.9785(7) Å, c = 14.1744(14) Å, $\alpha = \beta = \gamma = 90°$, V = 1860.7(2) Å^3, Z = 4, $d_{calcd.}$ = 1.133 g cm^{-3}, μ = 0.604 mm^{-1}, $F(000)$ = 688, Θ range 4.83−66.00°, 1739 measured/independent reflections, 1579 reflections with $[I > 2\sigma(I)]$. Solved by direct methods and refined by full-matrix, least-squares on F^2 for all data weights to R = 0.051, R_w = 0.133, S = 1.063, H atoms riding, max. shift/error < 0.001, residual ρ_{max} = 0.172 Å^{-3}.

(*R*)-3-*tert*-Butoxycarbonyl-4-ethynyl-2,2-dimethyl-1,3-oxazolidine (7). Method A: (From alcohol **8**[59]). Dess−Martin periodinane (**10**[65,66], 34.0 g, 80.0 mmol) was added in small portions at ambient temperature to a stirred solution of serinol **8** (12.3 g, 53.0 mmol) in CH_2Cl_2 (150 mL). Stirring was continued for 3−4 h until TLC indicated full consumption of the starting material. The reaction mixture was poured into an aqueous solution (700 mL) of sodium bicarbonate (50 g) and sodium thiosulfate (50 g) and stirred vigorously. The two phases were separated and the aqueous layer was extracted twice with CH_2Cl_2 (2 × 300 mL). The combined organic layers were dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The residue was dissolved in MeOH (150 mL) and the Bestmann−Ohira reagent (**11**,[68−73] 12.5 g, 65.0 mmol) was added. After the mixture had been cooled to 0 °C, K_2CO_3 (13.5 g, 100 mmol) was added in small portions. The reaction mixture was kept at ambient temperature for 4 h until TLC indicated full consumption of the starting material. Petroleum ether (400 mL) was added, and the reaction mixture was quenched with saturated aqueous NH_4Cl solution (300 mL). The aqueous layer was extracted twice with petroleum ether (2 × 300 mL), the combined organic layers were dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. Distillation of the residue yielded product **7** as a colourless oil; yield: 6.95 g (31.0 mmol, 58% over 2 steps).

Method B: (From ester **9**[57,59]). Ester **9** (13.0 g, 50.0 mmol) in dried toluene (120 mL) was placed in a three-necked round-bottom flask, fitted with an addition funnel and a thermometer. The solution was cooled to −78 °C and DiBAl-H (88 mL of 1 M solution in heptane, 88 mmol) was slowly added, the temperature never exceeding −65 °C. After 2 h at −70 °C no starting material could be detected by TLC. Hydrolyses of the complex was achieved by careful addition of pre-cooled MeOH (20 mL). Again, the temperature should not exceed −65 °C. The mixture was poured into a cooled (0 °C) 1 N solution of hydrochloric acid and extracted three times with ethyl acetate (3 × 300 mL). The combined organic layers were dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The residue was further converted into alkyne **7** as described above. Yield: 7.22 g (32.0 mmol, 64% over 2 steps).

Compound 7: B.p. 75 °C (1−2 Torr). $[\alpha]_D^{23}$ = −90.2 (c = 2.63, $CHCl_3$). IR (film, NaCl): $\tilde{\nu}$ = 3265 cm^{-1}, 2968, 2919, 2860, 2089, 1700, 1370, 1065. ^{1}H NMR (500 MHz, [D$_6$]DMSO, 373 K): δ = 0.99 (s, 3 H, CH_3), 1.00 [s, 9 H, C(CH_3)$_3$], 1.08 (s, 3 H, CH_3), 2.50 (br. s, 1 H, 2′-H), 3.43 (dd, J = 8.7, J = 2.4 Hz, 1 H, 5-H$_a$), 3.59 (dd, J = 8.7, J = 6.1 Hz, 1 H, 5-H$_b$), 4.08 (ddd, J = 6.1, J = 2.4, J = 2.3 Hz, 1 H, 4-H) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO, 373 K): δ = 24.0, 25.6 (CH$_3$), 27.5 [C(*C*H$_3$)$_3$], 47.5 (C-2′), 67.9 (C-5), 71.5 (C-4), 79.2 [*C*(CH$_3$)$_3$], 82.8 (C-1′), 93.0 (C-2), 150.3 (C=O) ppm. $C_{12}H_{19}NO_3$ (225.28): calcd. C 63.98, H 8.50, N 6.22; found C 63.70, H 8.73, N 6.10.

Alkenylboronic Esters 12−16. Method A: (With Cy_2BH). BH_3·SMe_2 complex (1.0 equiv. of a 12 M solution in dimethyl sulfide) in 1,2-dimethoxyethane (1 mL/mmol borane) was cooled to 0 °C under dry nitrogen. After addition of cyclohexene (2.0 equiv.) and removal of the cooling bath, a colourless precipitate formed. After 2 h the reaction mixture was cooled to 0 °C, followed by the addition of alkyne **7** (1.0 equiv.). The mixture was stirred at this temperature for 15 min, and then warmed to room temperature. While stirring was continued for 2−4 h, a clear solution formed. Trimethylamine *N*-oxide[88−90](2 equiv.) was carefully added at a rate suitable to keep the reaction under gentle reflux. After 2 h at room temperature the appropriate diol (1 equiv.) was added. The reaction mixture was stirred until complete consumption of diol (as judged by TLC) was indicated. The solvent was removed under reduced pressure and the crude product was subjected to flash column chromatography on silica gel.

Method B: (With Ipc_2BH). BH_3·SMe_2 complex (1 mL of a 10 M solution in dimethyl sulfide, 10 mmol) in THF (10 mL) was cooled to 0 °C under dry nitrogen. After addition of α-pinene (3.2 mL, 20 mmol) and removal of the cooling bath, a colourless precipitate formed. After 2 h the reaction mixture was cooled to −35 °C, followed by the slow addition of alkyne **7** (2.2 g, 10 mmol). The mixture was stirred at this temperature for 15 min, and then warmed to room temperature. Acetaldehyde (11.0 mL, 200 mmol) was carefully added (strongly exothermic reaction!), and the formed solution was heated at reflux for 12 h. After removal of all volatile components under reduced pressure, the residue was dissolved in THF (10 mL) and benzpinacol (3.7 g, 50 mmol) was added. After 5−6 h at room temperature, the solvent was removed under reduced pressure and the crude product was subjected to MPLC.

Method C: (Deprotection). Alkenylboronic ester **15** (1.25 g, 2.00 mmol) in MeOH (20 mL) was treated with trifluoroacetic acid (1 mL) at ambient temperature. CH_2Cl_2 was added to the suspension until a clear solution formed. After 1 day, H_2O was added and the aqueous layer was thoroughly extracted with CH_2Cl_2. The combined organic layers were dried with $MgSO_4$ and filtered, and the solvents were removed under reduced pressure. After flash column chromatography, pure product **16** was isolated.

Compound 12. Method A: Alkenylboronic ester **12** (950 mg, 1.38 mmol, 69%) was obtained from alkyne **7** (450 mg, 2.00 mmol) and diol **5** (910 mg, 2.00 mmol) after flash column chromatography on silica gel (pentane/Et_2O, 9:1 to 4:1); m.p. 106 °C. $[\alpha]_D^{20}$ = −72.1 (c = 1.32, $CHCl_3$). IR (film, NaCl): $\tilde{\nu}$ = 2950 cm^{-1}, 2910, 1690, 1635, 1375, 1165, 1060, 740, 680. MS (FAB, NBA + NaI): *m*/*z* (%) = 712 (1) [M + Na]$^+$, 197 (100) [Ph$_2$COCH$_3^+$]. ^{1}H NMR (500 MHz, [D$_6$]DMSO, 373 K): δ = 1.35 [s, 9 H, C(CH_3)$_3$], 1.46 (s, 3 H, CH_3), 1.50 (s, 3 H, CH_3), 2.96 (s, 6 H, OCH_3), 3.60 (dd, J = 8.7, J = 2.5 Hz, 1 H, 5"-H$_a$), 3.92 (dd, J = 8.7, J = 6.5 Hz, 1 H, 5"-H$_b$), 4.19 (m, 1 H, 4"-H), 5.16 (d, J = 17.9 Hz, 1 H, 1′-H), 5.33 (s, 2 H, 4-H/5-H), 6.12 (dd, J = 17.9, J = 6.2 Hz, 1 H, 2′-H), 7.21−7.32 (m, 20 H, arom. C*H*) ppm. ^{13}C NMR (125 MHz, [D$_6$]DMSO, 373 K): δ = 26.5 (*C*H$_3$), 28.5 [C(*C*H$_3$)$_3$], 51.9 (O*C*H$_3$), 60.4 (C-4"), 67.9 (C-5"), 77.6 [*C*(CH$_3$)$_3$], 77.9 (C-4/C-5), 83.4, 83.5 (*C*Ph$_2$OMe), 94.1 (C-2′′), ≈ 119 (br., C-1′), 127.3, 127.8 (2 C), 127.9, 128.7, 129.6 (arom. *C*H), 141.3, 141.5 (arom. C$_{ipso}$), 151.0 (C-2′), 151.9 (*C*=O) ppm. $C_{42}H_{48}BNO_7$ (689.64): calcd. C 73.15, H 7.02, N 2.03; found C 73.22, H 7.17, N 1.82.

Compound 13. Method A: Alkenylboronic ester **13** (1.10 g, 1.60 mmol, 80%) was obtained from alkyne **7** (450 mg, 2.00 mmol) and diol *ent*-**5** (910 mg, 2.00 mmol) after flash column chromatog-

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raphy on silica gel (pentane/Et_2O, 9:1 to 4:1); m.p. 109 °C. $[\alpha]_D^{23}$ = −59.1 (*c* = 1.43, $CHCl_3$). IR (film, NaCl): $\tilde{\nu}$ = 2977 cm^{-1}, 1698, 1640, 1387, 1178, 1077, 758, 701. MS (EI, 70 eV): *m/z* (%) = 689 (< 1) [M^+], 657 (2) [$M - CH_3OH]^+$, 197 (100) [$Ph_2COCH_3^+$]. ^1H NMR (500 MHz, [D_6]DMSO, 373 K): δ = 1.37 [s, 9 H, C(CH_3)$_3$], 1.44 (s, 3 H, CH_3), 1.47 (s, 3 H, CH_3), 2.97 (s, 3 H, OCH_3), 2.98 (s, 3 H, OCH_3), 3.62 (dd, *J* = 8.9, *J* = 2.5 Hz, 1 H, 5"-H_a), 3.97 (dd, *J* = 8.9, *J* = 6.4 Hz, 1 H, 5"-H_b), 4.29 (m, 1 H, 4"-H), 5.14 (dd, *J* = 18.0, *J* = 1.1 Hz, 1 H, 1′-H), 5.33 (s, 2 H, C*H*CPh$_2$), 6.07 (dd, *J* = 18.0, *J* = 5.8 Hz, 1 H, 2′-H), 7.29−7.38 (m, 20 H, arom. C*H*) ppm. ^{13}C NMR (125 MHz, [D_6]DMSO, 373 K): δ = 23.4, 25.9 (*C*H_3), 27.5 [C(*C*H_3)$_3$], 50.93, 50.96 (O*C*H_3), 59.9 (C-4"), 66.5 (C-5′′), 77.6 [*C*(CH_3)$_3$], 78.5 (*C*HCPh$_2$), 82.8 (*C*Ph$_2$OMe), 92.7 (C-2′′), 126.6, 126.9, 127.2, 127.7, 128.5, 129.7 (arom. *C*H), 140.1, 140.5 (arom. C_{ipso}), 150.3 (C-2′), 150.6 (*C*=O) ppm. $C_{42}H_{48}BNO_7$ (689.64): calcd. C 73.15, H 7.02, N 2.03; found C 72.96, H 6.96, N 1.96.

Compound 14. Method A: Alkenylboronic ester **14** (5.58 g, 16.0 mmol, 63%) was obtained from alkyne **7** (5.60 g, 25.0 mmol) and pinacol (3.00 g, 25.0 mmol) after flash column chromatography on silica gel (petroleum ether/Et_2O, 9:1); m.p. 52−54 °C. $[\alpha]_D^{23}$ = −31.2 (*c* = 0.98, $CHCl_3$). IR (film, NaCl): $\tilde{\nu}$ = 2978 cm^{-1}, 2935, 1691, 1643, 1329, 1293, 1098, 1057, 851, 770. MS (FAB): *m/z* (%) = 354 (22) [[M + 1]$^+$], 298 (100), 238 (40), 57 (35). ^1H NMR (500 MHz, [D_6]DMSO, 373 K): δ = 1.23 [s, 12 H, C(CH_3)$_2$], 1.44 [s, 9 H, C(CH_3)$_3$], 1.50 (s, 3 H, CH_3), 1.56 (s, 3 H, CH_3), 3.75 (dd, *J* = 9.02, *J* = 3.1 Hz, 1 H, 5′′-H_a), 4.08 (dd, *J* = 9.0, *J* = 6.6 Hz, 1 H, 5′′-H_b), 4.37 (dddd, *J* = 6.6, *J* = 3.1, *J* = 6.2, *J* = 1.3 Hz, 1 H, 4′′-H), 5.48 (dd, *J* = 17.9, *J* = 1.3 Hz, 1 H, 1′-H), 6.46 (dd, *J* = 17.9, *J* = 6.2 Hz, 1 H, 2′-H) ppm. ^{13}C NMR (125 MHz, [D_6]DMSO, 373 K): δ = 23.6 (*C*H_3), 24.0 [C(*C*H_3)$_2$], 25.9 (*C*H_3), 27.5 [C(*C*H_3)$_3$], 59.5 (C-4′′), 66.7 (C-5′′), 78.6 [*C*(CH_3)$_3$], 82.4 (C-4/C-5), 92.8 (C-2′′), ≈119 (br., C-1′), 150.8 (C-2′), 150.8 (C=O) ppm. $C_{18}H_{32}BNO_5$ (353.26): calcd. C 61.20, H 9.13, N 3.96; found C 61.35, H 9.09, N 4.24.

Compound 15. Method B: Alkenylboronic ester **15** (1.46 g, 2.40 mmol, 24%) was obtained from alkyne **7** (2.20 g, 10.0 mmol) and benzpinacol (3.70 g, 50.0 mmol) after MPLC (petroleum ether/MTBE, 19:1); m.p. 45−50 °C. $[\alpha]_D^{23}$ = −36.2 (*c* = 1.09, $CHCl_3$). IR (film, NaCl): $\tilde{\nu}$ = 2960 cm^{-1}, 2900, 1695, 1643, 1480, 1435, 1360, 1240, 1080, 851, 740, 680. MS (FAB): *m/z* (%) = 601 (61) [M^+], 363 (32), 261 (29), 183 (28), 165 (100), 84 (46), 57 (64). ^1H NMR (500 MHz, [D_6]DMSO, 373 K): δ = 1.39 [s, 9 H, C(CH_3)$_3$], 1.47 (s, 3 H, CH_3), 1.57 (s, 3 H, CH_3), 3.86 (m, 1 H, 5′′-H_a), 4.12 (m, 1 H, 5′′-H_b), 4.51 (m, 1 H, 4′′-H), 5.85 (d, *J* = 17.9 Hz, 1 H, 1′-H), 6.87 (dd, *J* = 17.9, *J* = 6.1 Hz, 1 H, 2′-H), 7.11−7.20 (m, 20 H, arom. C*H*) ppm. ^{13}C NMR (125 MHz, [D_6]DMSO, 373 K): δ = 26.4 (*C*H_3), 26.7 (*C*H_3), 28.3 [C(*C*H_3)$_3$], 60.7 (C-4′′), 67.4 (C-5′′), 79.4 [*C*(CH_3)$_3$], 93.4 (C-2′′), 95.7 [*C*(Ph_3)$_2$], ≈118 (br., C-1′), 127.6, 127.7, 128.2, 128.4 (br., arom. *C*H), 151.6 (C-2′), 154.7 (C=O) ppm. $C_{38}H_{40}BNO_5$ (601.54): calcd. C 75.87, H 6.70, N 2.33; found C 75.98, H 7.04, N 2.27.

Compound 16. Method C: Product **16** (720 mg, 1.30 mmol, 65%) was obtained from alkenylboronic ester **15** (1.25 g, 2.00 mmol) after flash column chromatography (petroleum ether/ethyl acetate, 9:1 to 1:1); m.p. 109 °C. $[\alpha]_D^{23}$ = −3.4 (*c* = 1.0, $CHCl_3$). IR (film, NaCl): $\tilde{\nu}$ = 3400 cm^{-1}, 2950, 1700, 1635, 1485, 1435, 1360, 1160, 760, 680. MS (FAB, NBA + NaI): *m/z* (%) = 584 (7) [M + Na]$^+$, 561 [M^+] (14), 506 (100), 165 (40), 105 (40), 57 (23). ^1H NMR (500 MHz, [D_6]DMSO, 373 K): δ = 1.47 [s, 9 H, C(CH_3)$_3$], 2.03 (s, 1 H, O*H*), 3.76 (m, 1 H, 4′-H_a), 3.83 (m, 1 H, 4′-H_b), 4.49 (m, 1 H, 3′-H), 4.99 (s, 1 H, N*H*), 6.05 (dd, *J* = 18.2, *J* = 1.9 Hz, 1 H, 1′-H), 6.94 (d, *J* = 18.2, *J* = 4.3 Hz, 1 H, 2′-H), 7.03−7.26 (m, 20 H, arom. C*H*) ppm. ^{13}C NMR (125 MHz, [D_6]DMSO, 373 K): δ = 28.4 [C(*C*H_3)$_3$], 60.4 (C-3′), 65.1 (C-4′), 80.0 [*C*(CH_3)$_3$], 96.1 [*C*(Ph_3)$_2$], ≈ 119 (br., C-1′), 127.0, 127.2, 128.5 (arom. *C*H), 142.4 (2 C, arom. C_{ipso}), 151.5 (C-2′), 155.0 (C=O) ppm. $C_{35}H_{36}BNO_5$ (561.48): calcd. C 74.87, H 6.46, N 2.49; found C 74.59, H 6.48, N 2.43.

Cyclopropylboronic Esters 17−20. Method A: (With CH_2N_2). The alkenylboronic ester (1 equiv.) was dissolved in Et_2O (≈ 1 mL/mmol boronic ester), and 5−10 mol % palladium(II) acetate was added. The suspension was treated for 2 min in an ultrasonic bath. After the mixture had been cooled to 0 °C, CH_2N_2 [83−86] (25 mL/mmol boronic ester of an approx. 0.5 M solution in Et_2O) was slowly (1.5 mL/min) added with the aid of a syringe-pump.[86] Unchanged CH_2N_2 was destroyed by stirring the reaction mixture vigorously. Filtration through Celite and evaporation of the solvent under reduced pressure, followed by chromatographic purification, gave the cyclopropylboronic esters.

Method B: (With Et_2Zn/CH_2I_2). The alkenylboronic ester (1.0 equiv.) in CH_2Cl_2 (1 mL/mmol boronic ester) was added to preformed cyclopropanation reagent [6.0 equiv. CH_2I_2 dissolved in CH_2Cl_2 (10 mL/mmol boronic ester), treated at −78 °C with Et_2Zn solution (3 equiv. of a 1 M solution in hexane)]. Stirring was continued at room temperature for 12 h. After the reaction had been quenched with saturated aqueous NH_4Cl, the aqueous layer was thoroughly extracted with CH_2Cl_2. The combined organic layers were dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography.

Determination of *dr*: For the determination of the *dr* of the cyclopropylboronic esters **17−20**, a sample (0.1−0.3 mmol) was dissolved in THF (5 mL). MeLi (3 equiv., 1 M solution in hexane) was added at −78 °C, and the mixture was warmed to room temperature. Stirring was continued while 2−3 mL of 30% aqueous H_2O_2 was carefully added. Hydrolysis after 2−3 h (TLC monitoring) with saturated aqueous NH_4Cl solution, separation of the organic layer, extraction with CH_2Cl_2, drying over $MgSO_4$, filtration and removal of the solvents under reduced pressure furnished the crude cyclopropanols **22a** and **22b**. The GLC traces were used to determine the *dr* of the corresponding cyclopropanation (conditions and retention times: see Figure 3).

Compounds 17a and 17b. Method A: Products **17a** and **17b** (720 mg, 1.02 mmol, 79%) were isolated from alkenylboronic ester **12** (900 mg, 1.30 mmol) after flash column chromatography (pentane/Et_2O, 9:1); separation of diastereoisomers (*dr* 84:16) could not be achieved by MPLC (all data from mixture): IR (film, NaCl): $\tilde{\nu}$ = 2978 cm^{-1}, 2935, 1691, 1643, 1329, 1293, 1098, 1057, 851, 770. MS (FAB, NBA + NaI): *m/z* (%) = 726 (25) [M + Na$^+$], 197 (100). HRMS: $C_{43}H_{50}{}^{10}BNO_7Na$: calcd. 725.3624; found 725.3614. $C_{43}H_{50}BNO_7$ (703.67): calcd. C 73.40, H 7.16, N 1.99; found C 72.82, H 7.26, N 1.85.

Major Diastereoisomer 17a: ^1H NMR (300 MHz, $CDCl_3$, 330 K): δ = −0.69 (ddd, *J* = 9.9, *J* = 6.2, *J* = 5.8 Hz, 1′-H), 0.56 (ddd, *J* = 7.7, *J* = 6.3, *J* = 3.7 Hz, 3′-H_{trans}), 0.75 (br., 3′-H_{cis}), 0.80−0.87 (m, 2′-H), 1.45 [s, C(CH_3)$_3$], 1.42 (s, CH_3), 1.61 (s, CH_3), 2.98 (s, OCH_3), 3.03−3.14 (m, 4′′-H), 3.68 (dd, *J* = 8.5, *J* = 1.4 Hz, 5′′-H_a), 3.82 (dd, *J* = 8.5, *J* = 5.8 Hz, 5′′-H_b), 5.26 (s, 4-H/5-H), 7.19−7.45 (m, arom. C*H*) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 330 K): δ = −3.1 (br., C-1′), 11.8 (C-3′), 22.1 (C-2′), 23.9 (*C*H_3), 26.9 [C(*C*H_3)$_3$], 27.3 (*C*H_3), 51.7 (O*C*H_3), 62.3 [*C*(CH_3)$_3$], 68.3 (C-5′′), 78.0 (C-4′′), 78.2 (C-4/C-5), 83.6 (*C*Ph$_2$OMe), 93.9 (C-2′′), 127.2, 127.3, 127.4, 127.7, 128.5, 129.7 (arom. *C*H), 141.3, 141.5 (arom. C_{ipso}), 152.3 (C=O).

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Minor Diastereoisomer 17b: ^{1}H NMR (300 MHz, $CDCl_3$, 330 K): δ = −0.23 (m, 1′-H), 0.06 (ddd, *J* = 8.0, *J* = 6.3, *J* = 3.8 Hz, 3′-H_{trans}), 0.28 (m, 3′-H_{cis}), 0.8−0.87 (m, 2′-H), 1.38 (s, CH_3), 1.43 [s, C(CH_3)$_3$], 1.52 (s, CH_3), 2.99 (s, OCH_3), 3.03−3.14 (m, 4′′-H), 3.50 (dd, *J* = 8.9, *J* = 1.3 Hz, 5′′-H_a), 3.76 (dd, *J* = 8.9, *J* = 6.0 Hz, 5′′-H_b), 5.26 (s, 4-H/5-H), 7.19−7.45 (m, arom. C*H*) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 330 K): δ = −3.1 (br., C-1′), 8.0 (C-3′), 21.2 (C-2′), 22.8 (*C*H_3), 27.3 (*C*H_3), 28.4 [C(*C*H_3)$_3$], 51.7 (O*C*H_3), 60.1 [*C*(CH$_3$)$_3$], 67.6 (C-5′′), 78.5 (C-4′′), 79.5 (C-4/C-5), 83.5 (*C*Ph$_2$OMe), 93.9 (C-2′′), 125.8, 127.3, 127.4, 128.6, 129.3, 129.7 (arom. *C*H), 141.1, 141.6 (arom. C_{ipso}), 151.8 (C=O) ppm.

Compounds 18a and 18b. Method A: Products **18a** and **18**b (500 mg, 0.71 mmol, 84%) were isolated from alkenylboronic ester **13** (590 mg, 0.85 mmol) after flash column chromatography (pentane/Et_2O, 9:1); separation of diastereoisomers (*dr* 92:8) could not be achieved by MPLC (all data from mixture): IR (film, NaCl): $\tilde{\nu}$ = 2978 cm^{-1}, 2935, 1691, 1643, 1329, 1293, 1098, 1057, 851, 770. MS (FAB, NBA + NaI): *m*/*z* (%) = 726 (10) [M + Na$^+$], 197 (100). $C_{43}H_{50}BNO_7$ (703.67): calcd. C 73.40, H 7.16, N 1.99; found C 73.50, H 7.35, N 1.89.

Major Diastereoisomer 18a: ^{1}H NMR (300 MHz, $CDCl_3$, 330 K): δ = −0.86 (ddd, *J* = 9.9, *J* = 6.2, *J* = 5.8 Hz, 1′-H), 0.01 (ddd, *J* = 7.7, *J* = 6.3, *J* = 3.7 Hz, 3′-H_{trans}), 0.45 (br., 3′-H_{cis}), 0.76−0.93 (m, 2′-H), 1.20 [s, C(CH_3)$_3$], 1.22 (s, CH_3), 1.31 (s, CH_3), 2.78 (s, OCH_3), 2.90 (ddd, *J* = 8.6, *J* = 5.8, *J* = 1.3 Hz, 4′′-H), 3.38 (dd, *J* = 8.6, *J* = 1.3 Hz, 5′′-H_a), 3.55 (dd, *J* = 8.6, *J* = 5.8 Hz, 5′′-H_b), 5.06 (s, 4-H/5-H), 6.99−7.39 (m, arom. C*H*) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 330 K): δ = −3.1 (br., C-1′), 11.9 (C-3′), 22.2 (C-2′), 23.9 (*C*H_3), 26.9 [C(*C*H_3)$_3$], 27.4 (*C*H_3), 51.7 (O*C*H_3), 61.8 (C-4′′), 67.7 (C-5′′), 78.0 (C-4/5), 79.5 [*C*(CH$_3$)$_3$], 83.6 (*C*Ph$_2$OMe), 93.9 (C-2′′), 127.2, 127.3, 127.4, 127.7, 128.5, 129.7 (arom. *C*H), 141.3, 141.5 (arom. C_{ipso}), 152.3 (C=O) ppm.

Minor Diastereoisomer 18b: ^{1}H NMR (300 MHz, $CDCl_3$, 330 K): δ = −0.38 (m, 1′-H), 0.20 (ddd, *J* = 8.0, *J* = 6.3, *J* = 3.7 Hz, 3′-H_{trans}), 0.64 (m, 3′-H_{cis}), 0.76−0.93 (m, 2′-H), 1.20 [s, C(CH_3)$_3$], 1.22 (s, CH_3), 1.31 (s, CH_3), 2.74 (s, OCH_3), 2.75 (m, 4′′-H), 3.47 (dd, *J* = 8.6, *J* = 1.3 Hz, 5′′-H_a), 3.63 (dd, *J* = 8.6, *J* = 6.0 Hz, 5′′-H_b), 5.02 (s, 4-H/5-H), 6.99−7.39 (m, 20 H, arom. C*H*) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 330 K): δ = −3.1 (br., C-1′), 8.0 (C-3′), 21.2 (C-2′), 23.9 (*C*H_3), 27.3 (*C*H_3), 28.4 [C(*C*H_3)$_3$], 51.7 (O*C*H_3), 62.3 (C-4′′), 67.6 (C-5′′), 78.3 (C-4/5), 79.7 [*C*(CH$_3$)$_3$], 83.6 (*C*Ph$_2$OMe), 93.9 (C-2′′), 125.8, 127.3, 127.4, 128.6, 129.3, 129.6 (arom. *C*H), 141.4, 141.7 (arom. C_{ipso}), 152.4 (C=O) ppm.

Compounds 19a and 19b. Method A: Products **19a** and **19b** (640 mg, 1.74 mmol, 69%) were isolated from alkenylboronic ester **14** (900 mg, 2.54 mmol) after kugelrohr distillation; separation of diastereoisomers (*dr* 70:30) could not be achieved.

Method B: Products **19a** and **19b** (80 mg, 0.22 mmol, 48%) were isolated from alkenylboronic ester **14** (160 mg, 0.45 mmol) after flash column chromatography (petroleum ether/ethyl acetate, 95:5). Separation of diastereoisomers (*dr* 22:78) could not be fully achieved, but isolation of some pure fractions allowed the assignment of data: IR (film, NaCl): $\tilde{\nu}$ = 2979 cm^{-1}, 2935, 2872, 1692, 1368, 1255, 1169, 1145, 1089, 1060, 860, 770. MS (FAB): *m*/*z* (%) = 368 (51) [M + 1]$^+$, 312 (96), 252 (100), 212 (31), 57 (60). $C_{19}H_{34}BNO_5$ (367.29): calcd. C 62.13, H 9.33, N 3.81; found C 61.79, H 9.22, N 3.88.

Second Eluted Diastereoisomer 19a: Colourless oil. $[\alpha]_D^{20}$ = −2.6 (*c* = 0.9, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 330 K): δ = −0.28 (ddd, *J* = 9.7, *J* = 6.4, *J* = 5.6 Hz, 1 H, 1′-H), 0.78 (ddd, *J* = 9.7, *J* = 5.3, *J* = 3.6 Hz, 1 H, 3′-H_{cis}), 0.90 (ddd, *J* = 7.6, *J* = 6.4, *J* = 3.6 Hz, 1 H, 3′-H_{trans}), 1.19 [s, 12 H, C(CH_3)$_2$], 1.31 (m, 1 H, 2′-H), 1.47 [s, 9 H, C(CH_3)$_3$], 1.49 (s, 3 H, CH_3), 1.61 (s, 3 H, CH_3), 3.41 (br., 1 H, 4′′-H), 3.72 (dd, *J* = 8.7, *J* = 1.7 Hz, 1 H, 5′′-H_a), 3.90 (dd, *J* = 8.7, *J* = 5.8 Hz, 1 H, 5′′-H_b) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 330 K): δ = 11.0 (C-3′), 21.7 (C-2′), 23.9 (*C*H_3), 24.7 [C(*C*H_3)$_2$], 27.0 (*C*H_3), 28.5 [C(*C*H_3)$_3$], 60.8 (C-4′′), 67.4 (C-5′′), 79.6 [*C*(CH$_3$)$_3$], 83.0 (C-4, C-5), 94.0 (C-2′′), 152.3 (C=O) ppm.

First Eluted Diastereoisomer 19b: M.p. 58 °C. $[\alpha]_D^{20}$ = −46.1 (*c* = 0.92, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 330 K): δ = 0.02 (ddd, *J* = 9.4, *J* = 6.4, *J* = 5.1 Hz, 1 H, 1′-H), 0.39 (ddd, 1 H, *J* = 9.4, *J* = 5.5, *J* = 3.6 Hz, 1 H, 3′-H_{cis}), 0.53 (ddd, *J* = 7.9, *J* = 6.4, *J* = 3.6 Hz, 1 H, 3′-H_{trans}), 1.09 [s, 12 H, C(CH_3)$_2$], 1.17 (m, 1 H, 2′-H), 1.38 (s, 3 H, CH_3), 1.39 [s, 9 H, C(CH_3)$_3$], 1.50 (s, 3 H, CH_3), 3.44 (br., 1 H, 4′′-H), 3.61 (dd, *J* = 8.7, *J* = 1.6 Hz, 1 H, 5′′-H_a), 3.75 (dd, *J* = 8.7, *J* = 5.8 Hz, 1 H, 5′′-H_b) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 330 K): δ = 7.6 (C-3′), 22.2 (C-2′), 24.6 [C(*C*H_3)$_2$], 24.7 (*C*H_3), 27.0 (*C*H_3), 28.5 [C(*C*H_3)$_3$], 61.5 (C-4′′), 68.2 (C-5′′), 79.7 [*C*(CH$_3$)$_3$], 82.9 (C-4, C-5), 94.1 (C-2′′), 152.3 (C=O) ppm.

Compounds 20a and 20b. Method A: Products **20a** and **20b** (75 mg, 0.12 mmol, 61%) were isolated from alkenylboronic ester **15** (120 mg, 0.20 mmol) after flash column chromatography (petroleum ether/ethyl acetate, 92.5:7.5); separation of diastereoisomers (*dr* 24:76) could not be achieved by MPLC (all data from mixture): IR (film, NaCl): $\tilde{\nu}$ = 2960 cm^{-1}, 2900, 1695, 1643, 1480, 1435, 1360, 1240, 1080, 851, 740, 680. MS (FAB): *m*/*z* (%) = 616 (18) [M + 1]$^+$, 560 (27), 377 (35), 212 (100), 165 (81), 105 (38), 57 (45). $C_{39}H_{42}BNO_5$ (615.57): calcd. C 76.10, H 6.88, N 2.28; found C 76.20, H 7.11, N 2.17.

Minor Diastereoisomer 20a: ^{1}H NMR (300 MHz, $CDCl_3$, 330 K): δ = 0.24 (m_c, 1′-H), 1.13−1.18 (m, 3′-H_a and 3′-H_b), 1.51 (s, CH_3), 1.56 [s, C(CH_3)$_3$], 1.65 (s, CH_3), 3.68 (m_c, 4′′-H), 3.83 (dd, *J* = 8.8, *J* = 1.6 Hz, 5′′-H_a), 4.00 (dd, *J* = 8.8, *J* = 5.8 Hz, 5′′-H_b) ppm, 2′-H signal (covered). ^{13}C NMR (75 MHz, $CDCl_3$, 330 K): δ = 11.4 (C-3′), 23.4 (C-2′), 25.0 (*C*H_3), 27.1 (*C*H_3), 28.5 [C(*C*H_3)$_3$], 53.5 (C-4′′), 68.6 (C-5′′), 79.9 [*C*(CH$_3$)$_3$], 94.1 (C-2′′), 95.8 (C-4, C-5), 126.9, 2 × 127.2, 2 × 128.4, 128.5 (arom. *C*H), 142.2, 142.9 (arom. C_{ipso}), 152.1 (*C*=O) ppm.

Major Diastereoisomer 20b: ^{1}H NMR (300 MHz, $CDCl_3$, 330 K): δ = 0.67−0.78 (m, 1′-H and 3′-H_a), 0.98−1.02 (m, 3′-H_b), 1.48 (s, CH_3), 1.54 [s, C(CH_3)$_3$], 1.67 (s, CH_3), 3.59 (br., 4′′-H), 3.90 (dd, *J* = 8.6, *J* = 1.3 Hz, 5′′-H_a), 4.01 (dd, *J* = 8.6, *J* = 5.6 Hz, 5′′-H_b), 2′-H signal (covered) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 330 K): δ = 8.3 (C-3′), 22.7 (C-2′), 23.3 (*C*H_3), 26.9 [C(*C*H_3)$_3$], 27.1 (*C*H_3), 53.4 (C-4′′), 67.8 (C-5′′), 79.9 [*C*(CH$_3$)$_3$], 95.7 (C-2′′), 95.8 (C-4, C-5), 126.9, 2 × 127.2, 2 × 128.4, 128.5 (arom. *C*H), 142.8, 142.9 (arom. C_{ipso}), 152.1 (*C*=O) ppm.

Phenylcyclopropanes 21 by Suzuki Coupling of Boronic Esters 19: Dioxaborolane **19** (400 mg, 1.08 mmol; *dr* 70:30) was dissolved in DME (12 mL). After addition of [Pd(PPh$_3$)$_4$] (140 mg, 122 μmol) and KO*t*Bu (2.8 mL of a 1 M solution in *t*BuOH) the mixture was carefully deoxygenated by freeze techniques. Phenyl iodide (180 μL, 1.62 mmol) was added. After 48 h at 90 °C the mixture was diluted with toluene (15 mL) and filtered through a pad of Celite, and the solvents were removed under reduced pressure. The residue was purified by flash column chromatography (petroleum ether/Et_2O, 19:1 to 4:1). The product **21** (252 mg, 0.82 mmol, 76%) was obtained as colourless oil.

21: IR (KBr): $\tilde{\nu}$ = 3060 cm^{-1}, 3040, 2994, 2970, 2860, 1682, 1670, 1380, 1242, 1065, 840, 750, 730, 680. MS (FAB): *m*/*z* (%) = 318 (41) [M + 1]$^+$, 261 (91), 144 (100), 57 (41). $C_{19}H_{27}NO_3$ (317.42): calcd. C 71.89, H 8.57, N 4.41; found C 71.68, H 8.55, N 4.41. The

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diastereoisomers could not be separated by chromatography, but the major product **21a** crystallised upon standing and could be isolated. An X-ray structure analysis was obtained (see Scheme 4). The experiment was repeated with essentially diastereoisomerically pure **19b** (63 mg, 0.17 mmol; *dr* > 98:2); yield **21b**: 29 mg (0.09 mmol, 54%).

Compound 21a: M.p. 109−111 °C. $[\alpha]_D^{20}$ = −20.0 (*c* = 0.95, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 330 K): δ = 1.00 (ddd, *J* = 8.7, *J* = 5.3, *J* = 5.3 Hz, 1 H, 3′-H_a), 1.25 (m, 1 H, 3′-H_b), 1.36−1.46 (m, 1 H, 1′-H), 1.49 [s, 9 H, C(CH_3)$_3$], 1.50 (s, 3 H, CH_3), 1.62 (s, 3 H, CH_3), 1.80 (m, 1 H, 2′-H), 3.68 (m, 1 H, 4-H), 3.85 (dd, *J* = 8.6, *J* = 1.2 Hz, 1 H, 5-H_a), 3.97 (dd, *J* = 8.6, *J* = 5.7 Hz, 1 H, 5-H_b), 7.04−7.36 (m, 5 H, arom. C*H*) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.4 (C-5), 20.4 (C-4), 23.3 (C-3), 24.6 (CH_3), 27.0 (*C*H$_3$), 28.5 [C(*C*H$_3$)$_3$], 60.3 (C-4), 67.9 (C-5), 79.8 [*C*(CH$_3$)$_3$], 125.6, 125.9, 128.3 (arom. *C*H), 94.1 (C-2), 142.4 (arom. C_{ipso}), 152.2 (C=O) ppm.

Compound 21b: M.p. 64 °C. $[\alpha]_D^{20}$ = −86.8 (*c* = 1.16, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 330 K): δ = 0.79−0.90 (m, 2 H, 3′-H_a/3′-H_b), 1.36−1.46 (m, 1 H, 1′-H), 1.49 [s, 9 H, C(CH_3)$_3$], 1.50 (s, 3 H, CH_3), 1.60 (s, 3 H, CH_3), 2.27 (br., 1 H, 2′-H), 3.68 (m, 1 H, 4-H), 3.81 (dd, *J* = 8.8, *J* = 1.4 Hz, 1 H, 5-H_a), 3.97 (dd, *J* = 8.6, *J* = 5.7 Hz, 1 H, 5-H_b), 7.04−7.36 (m, 5 H, arom. C*H*) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.4 (C-5), 20.4 (C-4), 23.3 (C-3), 24.6 (CH_3), 27.0 (*C*H$_3$), 28.5 [C(*C*H$_3$)$_3$], 60.3 (C-4), 67.9 (C-5), 79.8 [*C*(CH$_3$)$_3$], 125.6, 125.9, 128.3 (arom. *C*H), 94.1 (C-2), 142.4 (arom. C_{ipso}), 152.2 (C=O) ppm.

Silyl-Protected Cyclopropanol 23: Cyclopropylboronic ester **19** (330 mg, 0.90 mmol; *dr* 70:30) was dissolved in THF (2 mL) and a mixture of aqueous $KHCO_3$ (2 N, 1 mL) and aqueous H_2O_2 (30%, 1 mL) was added. After 3 h, saturated aqueous NH_4Cl solution (2 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried with $MgSO_4$ and filtered, and the solvents were removed under reduced pressure. The crude product **22** was dissolved in CH_2Cl_2 (5 mL), and imidazole (68 mg, 1.0 mmol) was added. After addition of *tert*-butyldiphenylsilyl chloride (275 mg, 1.00 mmol; TPS-Cl), the mixture was stirred until complete consumption of the alcohol (as judged by TLC) was indicated. Hydrolysis with saturated aqueous NH_4Cl solution (5 mL) was followed by extraction with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried with $MgSO_4$ and filtered, and the solvents were removed under reduced pressure. The crude product was purified by flash column chromatography (petroleum ether/Et_2O, 4:1) and MPLC (petroleum ether/MTBE, 19:1); separation of diastereoisomers **23a** and **23b** could not be achieved, and complete assignment of data was not possible. Yield: 330 mg (0.67 mmol, 74%), colourless oil.

Compound 23: IR (film, NaCl): $\tilde{\nu}$ = 3064 cm^{-1}, 3003, 2982, 2930, 2856, 1686, 1361, 1184, 1055, 859, 741, 702. MS (FAB, NBA + NaI): *m*/*z* (%) = 518 (100) [M + Na]$^+$, 382 (34), 252 (100), 135 (68), 100 (48), 57 (56). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.35−0.94 (m, 2 × 3-H), 1.03 [s, TPS-C(CH_3)$_3$], 1.30−1.35 (m, 2-H), 1.23 (s, CH_3), 1.43, 1.44 [s, Boc-C(CH_3)$_3$], 1.57 (s, CH_3), 2.82 (m, 1-H), 3.20−3.75 (m, 1′-H, 4′-H, 5′-H_a, 5′-H_b), 7.37−7.45 (arom. C*H*), 7.36−7.73 (arom. C*H*) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 12.3 (C-3), 19.0 [TPS-*C*(CH$_3$)$_3$], 24.5 (C-2), 25.3 (*C*H$_3$), 26.7 [TPS-C(*C*H$_3$)$_3$], 26.9 (*C*H$_3$), 28.3 [Boc-C(*C*H$_3$)$_3$], 53.3 (C-1), 58.7 (C-5′), 66.8 (C-4′), 79.6 [Boc-*C*(CH$_3$)$_3$], 93.8 (C-2′), 127.7, 129.8, 133.5 (arom. *C*H), 135.5 (arom. C_{ipso}), 156.5 (C=O) ppm. $C_{29}H_{41}NO_4Si$ (495.73): calcd. C 70.26, H 8.34, N 2.83; found C 70.26, H 7.15, N 2.80.

Alcohol 24: Oxazolidine **23** (650 mg, 1.30 mmol; *dr* 70:30) was dissolved in MeOH (5 mL), and trifluoroacetic acid (0.5 mL) was added at 0 °C. After 3 h the mixture was diluted with CH_2Cl_2 (15 mL) and washed with saturated aqueous Na_2CO_3 solution, and the aqueous layer was extracted twice with CH_2Cl_2. The combined organic layers were dried with $MgSO_4$ and filtered, and the solvents were removed under reduced pressure. The crude product was purified by flash column chromatography (petroleum ether/ethyl acetate, 3:1). The product **24** (310 mg, 0.68 mmol, 52%) was obtained as a colourless oil. IR (KBr): $\tilde{\nu}$ = 3413 cm^{-1}, 3071, 3050, 2932, 2856, 1712, 1392, 1112, 1055, 889, 742, 701. The diastereoisomers could be separated by MPLC (petroleum ether/ethyl acetate, 3:1):

Compound 24a: $[\alpha]_D^{20}$ = −20.0 (*c* = 0.95, $CHCl_3$). MS (FAB): *m*/*z* (%) = 478 (12) [M + Na]$^+$, 456 (15) [M + 1]$^+$, 199 (73), 144 (100), 135 (93). HRMS: $C_{26}H_{38}NO_4Si$ [M + 1]: calcd. 456.2570; found 456.2561. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.55 (m_c, 1 H, 3-H_{trans}), 0.82 (ddd, *J* = 9.9, *J* = 5.8, *J* = 3.1 Hz, 1 H, 3-H_{cis}), 1.02 [s, 9 H, TPS-C(CH_3)$_3$], 1.11 (m_c, 1 H, 2-H), 1.38 [s, 9 H, Boc-C(CH_3)$_3$], 2.46 (br., 1 H, O*H*), 2.82 (m, 1 H, 1′-H), 3.28 (dd, *J* = 11.1, *J* = 5.9 Hz, 1 H, 2′-H_a), 3.37 (ddd, *J* = 9.9, *J* = 5.9, *J* = 5.8 Hz, 1 H, 1-H), 3.43 (dd, *J* = 11.1, *J* = 3.4 Hz, 1 H, 2′-H_b), 4.69 (d, *J* = 6.4 Hz, 1 H, N*H*), 7.37−7.45 (m, 6 H, arom. C*H*), 7.68−7.71 (m, 4 H, arom. C*H*) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 12.7 (C-3), 19.0 [TPS-*C*(CH$_3$)$_3$], 22.4 (C-2), 26.7 [TPS-C(*C*H$_3$)$_3$], 28.3 [Boc-C(*C*H$_3$)$_3$], 53.3 (C-1), 55.1 (C-1′), 65.6 (C-2′), 79.6 [Boc-*C*(CH$_3$)$_3$], 127.7, 129.8, 133.5 (arom. *C*H), 135.5 (arom. C_{ipso}), 156.5 (C=O) ppm.

Compound 24b: $[\alpha]_D^{20}$ = +21.8 (*c* = 1.40, $CHCl_3$). MS (FAB): *m*/*z* (%) = 478 (7) [M + Na]$^+$, 456 (17) [M + 1]$^+$, 199 (77), 144 (100), 135 (80). HRMS: $C_{26}H_{38}NO_4Si$ [M + 1]: calcd. 456.2570; found 456.2563. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.55 (m_c, 1 H, 3-H_{trans}), 0.87 (ddd, *J* = 10.0, *J* = 5.9, *J* = 3.1 Hz, 1 H, 3-H_{cis}), 1.02 [s, 9 H, TPS-C(CH_3)$_3$], 1.03−1.08 (m, 1 H, 2-H), 1.38 [s, 9 H, Boc-C(CH_3)$_3$], 2.76 (m, 2 H, 1′-H and O*H*), 3.43 (dd, *J* = 11.1, *J* = 6.0 Hz, 1 H, 2′-H_a), 3.46 (m_c, 1 H, 1-H), 3.43 (dd, *J* = 11.1, *J* = 3.0 Hz, 1 H, 2′-H_b), 4.40 (d, *J* = 7.1 Hz, 1 H, N*H*), 7.37−7.45 (m, 6 H, arom. C*H*), 7.68−7.71 (m, 4 H, arom. C*H*) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.6 (C-3), 19.0 [TPS-*C*(CH$_3$)$_3$], 22.0 (C-2), 26.7 [TPS-C(*C*H$_3$)$_3$], 28.3 [Boc-C(*C*H$_3$)$_3$], 52.6 (C-1), 55.6 (C-1′), 65.7 (C-2′), 79.7 [Boc-*C*(CH$_3$)$_3$], 127.8, 129.9, 133.8 (arom. *C*H), 135.5 (arom. C_{ipso}), 156.5 (C=O).

Silyl-Protected Cyclopropylmethanol 25: Cyclopropylboronic ester **19** (570 mg, 1.50 mmol; *dr* 70:30) and chloroiodomethane (220 μL, 3.00 mmol) were dissolved in THF (9 mL), and the solution was cooled to −78 °C. Butyllithium (1.9 mL of a 1.6 M solution in hexane, 3.00 mmol) was slowly added, and the reaction mixture was warmed to room temperature and stirred for 7 d. A 1:1 mixture of H_2O_2 (30%, 5 mL) and aqueous NaOH solution (3 N, 5 mL) was carefully added and stirring was continued until TLC indicated complete consumption of the intermediate. Dilution with CH_2Cl_2 (20 mL) was followed by the addition of a saturated aqueous NH_4Cl solution (20 mL). After extraction of the aqueous layer, drying with $MgSO_4$ and evaporation of the organic solvents under reduced pressure, the crude product was dissolved in CH_2Cl_2 (5 mL), and imidazole (102 mg, 1.50 mmol) was added. After addition of *tert*-butyldiphenylsilyl chloride (412 mg, 1.50 mg; TPS-Cl), the mixture was stirred until complete consumption of the alcohol (as judged by TLC) was indicated. Hydrolysis with saturated aqueous NH_4Cl solution (5 mL) was followed by extraction with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried with $MgSO_4$ and filtered, and the solvents were removed under reduced pressure. The crude product was purified by flash column chroma-

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tography (petroleum ether/Et_2O, 4:1) and MPLC (petroleum ether/MTBE, 19:1); separation of diastereoisomers **25a** and **25b** could not be achieved, and complete assignment of data was not possible. Yield: 465 mg (0.91 mmol, 61%), colourless oil. IR (film, NaCl): $\tilde{\nu}$ = 3064 cm^{-1}, 3003, 2977, 2932, 2859, 1694, 1385, 1255, 1172, 1087, 703. MS (FAB, NBA + NaI): *m/z* (%) = 532 (18) [M + Na]$^+$, 382 (21), 199 (62), 135 (82), 100 (39), 57 (100). HRMS: $C_{30}H_{44}NO_4Si$ [M + 1]: calcd. 510.3040; found 510.3052. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.34−0.47, 0.75−0.97 (m, 1′-H, 3′-H_a, 3′-H_b), 1.02 [s, TPS-C(CH_3)$_3$], 1.26−1.39 (m, 2′-H), 1.41 (s, CH_3), 1.42 [s, C(CH_3)$_3$], 1.55 (s, CH_3), 3.20−3.75 (m, 1-H_a, 1-H_b, 4′′-H, 5′′-H_a, 5′′-H_b), 7.37−7.45 (arom. C*H*), 7.36−7.73 (arom. C*H*) ppm. $C_{30}H_{43}NO_4Si$ (509.75): calcd. C 70.69, H 8.50, N 2.75; found C 70.14, H 8.48, N 2.72.

Amino Alcohol 26a: Oxazolidine **21a** (330 mg, 1.04 mmol) in MeOH (5 mL) was treated at 0 °C with trifluoroacetic acid (1 mL). After 3 h at ambient temperature, CH_2Cl_2 (15 mL) was added, the reaction was quenched with saturated aqueous Na_2CO_3 solution, and the aqueous layer was thoroughly extracted with CH_2Cl_2. The combined organic layers were dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. After flash column chromatography (petroleum ether/ethyl acetate, 9:1 to 2:1), pure product **26a** was isolated. Yield: 250 mg (0.90 mmol, 87%). M.p. 88−89 °C. $[\alpha]_D^{20}$ = +42.4 (*c* = 1.14, $CHCl_3$). IR (film, NaCl): $\tilde{\nu}$ = 3401 cm^{-1}, 3064, 3003, 2977, 2932, 2876, 1684, 1499, 1366, 1248, 1167, 1055, 859, 753, 739, 698. MS (FAB): *m/z* (%) = 278 (43) [M + 1]$^+$, 222 (100), 252 (100), 178 (23), 143 (23), 104 (43), 57 (31). ^{1}H NMR (300 MHz, $CDCl_3$, 330 K): δ = 0.91 (ddd, *J* = 8.5, *J* = 5.2, *J* = 5.2 Hz, 1 H, 3′-H_a), 1.01 (ddd, 1 H, *J* = 8.9, *J* = 5.2, ^2J = 5.2 Hz, 1 H, 3′-H_b), 1.12 (m, 1 H, 1′-H), 1.40 [s, 9 H, C(CH_3)$_3$], 1.83 (m, 1 H, 2′-H), 2.69 (br., 1 H, O*H*), 3.15 (m, 1 H, 2-H), 3.63 (dd, *J* = 11.0, *J* = 6.1 Hz, 1 H, 1-H_a), 3.75 (m, 1 H, 1-H_b), 5.22 (br., 1 H, N*H*), 6.97−7.20 (m, 5 H, arom. C*H*). ^{13}C NMR (125 MHz, $CDCl_3$, 330 K): δ = 13.6 (C-3′), 21.9 (C-2′), 24.6 (C-1′), 28.3 [C(*C*H$_3$)$_3$], 57.2 (C-2), 66.3 (C-1), 79.9 [*C*(CH$_3$)$_3$], 125.8, 125.9, 128.4 (arom. *C*H), 141.9 (arom. C_{ipso}), 156.6 (C=O) ppm. $C_{16}H_{23}NO_3$ (277.36): calcd. C 69.29, H 8.36, N 5.05; found C 69.00, H 8.39, N 5.07.

Amino Alcohol 26b: Oxazolidine **21b** (490 mg, 1.50 mmol) in MeOH (5 mL) was treated at 0 °C with trifluoroacetic acid (1 mL). After the mixture had been kept for 3 h at ambient temperature, CH_2Cl_2 (15 mL) was added, the reaction was quenched with saturated aqueous Na_2CO_3 solution, and the aqueous layer was thoroughly extracted with CH_2Cl_2. The combined organic layers were dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. After flash column chromatography (petroleum ether/ethyl acetate, 9:1 to 2:1) and MPLC (petroleum ether/ethyl acetate, 3:1) product **26b** was isolated, its spectroscopic data in agreement with those given in the literature.[81] Yield: 353 mg (1.30 mmol, 85%). $[\alpha]_D^{20}$ = −38.2 (*c* = 1.20, $CHCl_3$). MS (CI, CH_4): *m/z* (%) = 193 (80), 165 (100), 133 (61), 109 (69), 93 (88). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.92 (m, 2 H, 3′-H_a and 3′-H_b), 1.12 (m, 1 H, 1′-H), 1.37 [s, 9 H, C(CH_3)$_3$], 1.99 (m, 1 H, 2′-H), 3.12 (br., 1 H, O*H*), 3.48 (m, 1 H, 2-H), 3.63 (dd, *J* = 11.0, *J* = 5.8 Hz, 1 H, 1-H_a), 3.75 (dd, *J* = 11.0, *J* = 3.1 Hz, 1 H, 1-H_b), 4.83 (br., 1 H, N*H*), 6.97−7.20 (m, 5 H, arom. C*H*) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.6 (C-3′), 21.4 (C-2′), 24.9 (C-1′), 28.3 [C(*C*H$_3$)$_3$], 58.0 (C-2), 65.8 (C-1), 79.8 [*C*(CH$_3$)$_3$], 125.8, 126.0, 128.4 (arom. *C*H), 142.3 (arom. C_{ipso}), 156.6 (C=O) ppm.

α-Amino Acid 27: Amino alcohol **26a** (120 mg, 0.40 mmol) in MeCN/0.75% H_2O (5 mL) was treated dropwise at 0 °C with 2.3 mL of a stock solution containing H_5IO_6 (20 g, 88 mmol), CrO_3 (40 mg, 0.4 mmol), MeCN (198.5 mL) and H_2O (1.5 mL). After 30 min no starting material could be detected by TLC. The reaction mixture was diluted with toluene and quenched with phosphate buffer (pH = 5.8). The organic layer was washed with brine and $NaHSO_3$ solution (0.66 g in 15 mL H_2O), dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. Yield: 100 mg (0.34 mmol, 85%). $[\alpha]_D^{20}$ = +25.9 (*c* = 1.15, $CHCl_3$). MS (EI, 70 eV): *m/z* (%) = 291 (4) [M$^+$], 236 (55), 192 (3), 146 (8), 57 (100). HRMS: $C_{16}H_{21}NO_4$: calcd. 291.1471; found 291.1471. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.99 (m, 1 H, 3′-H_a), 1.09 (m, 1 H, 3′-H_b), 1.37 (br., 1 H, 1′-H), 1.45 [s, 9 H, C(CH_3)$_3$], 2.09 (br., 1 H, 2′-H), 3.92−4.10 [m, 1 H, 2-H; two rotamers ≈ 2:1], 5.22 and 6.71 (br., 1 H, N*H*; two rotamers ≈ 2:1), 7.06−7. 07 (m, 2 H, arom. C*H*), 7.13−7.16 (m, 1 H, arom. C*H*), 7.22−7.25 (m, 2 H, arom. C*H*), ≈ 10.5 (br., 1 H, CO_2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$; two rotamers ≈ 2:1, minor rotamer in *italics*): δ = 12.5/*12.9* (C-3′), *21.0*/21.3 (C-2′), *24.5*/24.7 (C-1′), 28.3 [C(*C*H$_3$)$_3$], 55.9/*57.0* (C-2), 80.3/*81.8* [*C*(CH$_3$)$_3$], 125.9, 126.2, 128.3 (arom. *C*H), 141.3 (arom. C_{ipso}), 155.6/*156.7* (C=O), *175.8*/176.4 (C=O) ppm.

α-Amino Ester 28: Dess−Martin periodinane (**10**,[65,66] 190 mg, 0.45 mmol) was added in small portions at ambient temperature to a stirred solution of amino alcohol **26b** (85 mg, 0.3 mmol) in CH_2Cl_2 (0.5 mL). Stirring was continued for 3−4 h until TLC indicated full consumption of the starting material. The reaction mixture was poured into an aqueous solution of $NaHCO_3/Na_2S_2O_3$ (1 mL) and stirred vigorously. The two phases were separated and the aqueous layer was extracted twice with CH_2Cl_2 (2 × 5 mL). The combined organic layers were dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The residue was dissolved in *t*BuOH (5 mL), and 2-methyl-2-butene (3 mL) was added. After slow addition of NaH_2PO_4 (100 mg) and $NaClO_2$ (70 mg) in H_2O (2 mL), the mixture was stirred at ambient temperature until TLC indicated completion of reaction. The mixture was treated with NaOH (1 mL of a 20% aqueous solution), followed by removal of the solvents under reduced pressure. The residue was taken up in H_2O, washed twice with Et_2O, acidified (pH = 2.5) with diluted H_2SO_4, and extracted thoroughly with Et_2O. The combined organic layers were washed with saturated $Na_2S_2O_3$ solution and water, dried with $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. The crude product was dissolved in Et_2O (2.5 mL) and CH_2N_2 [83−86] (0.5 M solution in Et_2O) was carefully added until the solution remained yellow. The excess of the reagent was destroyed by stirring the solution vigorously. Removal of the solvent under reduced pressure and chromatographic purification [flash column chromatography (petroleum ether/ethyl acetate, 9:1) and MPLC (diethyl ether/ethyl acetate, 95:5)] gave product **28** that still contained some minor unidentified impurities. Yield: ≈48 mg (0.16 mmol, 51%). $[\alpha]_D^{20}$ = −80.4 (*c* = 1.20, $CHCl_3$). IR (film, NaCl): $\tilde{\nu}$ = 3369 cm^{-1}, 3064, 3004, 2978, 2954, 1745, 1714, 1499, 1165, 1052, 859, 759, 699. MS (CI, CH_4): *m/z* (%) = 306 (25) [M + 1]$^+$, 249 (89), 206 (100), 188 (44), 129 (43). HRMS: $C_{17}H_{24}NO_4$: calcd. 306.1705; found 306.1697. ^{1}H NMR (500 MHz, $CDCl_3$; two rotamers ≈ 1:1, 2nd rotamer in *italics*): δ = 1.05 (ddd, *J* = 8.6, *J* = 5.6, *J* = 5.6 Hz, 1 H, 3′-H_a), 1.16 (ddd, 1 H, *J* = 9.0, *J* = 5.5, *J* = 5.5 Hz, 1 H, 3′-H_b), 1.34 (m, 1 H, 1′-H), 1.45/*1.46* [s, 9 H, C(CH_3)$_3$], 2.02−2.09 (m, 1 H, 2′-H), 3.76/*3.78* (s, 3 H, OCH_3), 3.98/*4.04* (m_c, 1 H, 2-H), 5.15−5.19 (m, 1 H, N*H*), 7.03−7. 06 (m, 2 H, arom. C*H*), 7.14−7.17 (m, 1 H, arom. C*H*), 7.23−7.26 (m, 2 H, arom. C*H*) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.3 (C-3′), 21.1 (C-2′), 24.9 (C-1′), 28.3 [C(*C*H$_3$)$_3$], 52.4 (O*C*H$_3$), 56.4 (C-2), 80.0 [*C*(CH$_3$)$_3$], 125.9, 126.1, 128.3 (arom. *C*H), 141.6 (arom. C_{ipso}), 155.2 (C=O), 172.4 (C=O) ppm. $C_{17}H_{23}NO_4$ (305.37): calcd. C 66.86, H 7.59, N 4.59; found C 66.44, H 7.72, N 4.59.

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