Supporting Information

Stereocomplementary Synthesis of a Natural Product Derived
Compound Collection on the Solid Phase

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Supporting Table 1: Results of the enantioselective allylation of aldehyde 3.

Experimental procedures and characterization of compounds
Supplementary Material (ESI) for Chemical Communications

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**Supporting Table 1:** Results of the enantioselective allylation of aldehyde 3.

<table>
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<tr>
<th>Entry</th>
<th>Equiv of 2</th>
<th>T[°C], time</th>
<th>Purity [%][a]</th>
<th>Yield [%][b]</th>
<th>e.r. [c]</th>
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<td>79</td>
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<td>83</td>
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<td>71</td>
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</table>

[a] Based on GC/MS analysis. [b] Isolated yield after allylation and cleavage from the resin. [c] Enantiomer ratio (e.r.) determined by 1H NMR analysis of the Mosher esters.

**General:** unless otherwise noted, chemicals were obtained from Aldrich, Acros or Fluka and were used without further purification. Regular hydroxymethylpolystyrene (0.98 mmolg⁻¹, 1% DVB, 100-200 mesh) and Wang resin (1.10 mmolg⁻¹, 1% DVB, 100-200 mesh) were purchased from Novabiochem. All solvents were distilled by standard procedures. All reactions were performed under argon with freshly distilled and dried solvents. Analytical chromatography was performed by using Merck silica gel 60 F₅0₄ aluminium sheets. Flash chromatography was performed by using Acros silica gel 0.035-0.07 mm. ¹H and ¹³C NMR data were recorded on a Bruker DRX 500, a Bruker DRX 400 or a Varian Mercury 400 spectrometer at room temperature. NMR spectra were calibrated to the solvent signals of CDCl₃ (7.26 ppm and 77.00 ppm) and the next abbreviations are used to indicate signal multiplicities: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), sept (septet), br (broad). GC-MS (EI) analysis was performed on a Hewlett-Packard 6890 series gas chromatograph connected to a
Hewlett-Packard 5973 series mass spectrometer; column: J&W 128-5522 DB-5MS, capillary: 25.0x201\(\mu\)mx0.33\(\mu\)mm nominal. Chiral GC analysis was performed on an Agilent Technologies 6890N; column Lipodex-E (25m, 0.025mm). LC-MS was performed on a Hewlett-Packard 1100 series connected to a Finnigan LCQ ESI-spectrometer. High resolution mass spectra (HRMS) were measured on a Finnigan MAT 8200 spectrometer. IR spectra were measured on a Bruker Vector 22 spectrometer with an A527 diffuse reflectance head from Spectra Tech. UV spectra were measured on a Perkin Elmer Cary 50 spectrometer. Optical rotations were measured on a Schmidt & Haensch Polartronic HH8 polarimeter.

**Immobilized aldehyde, 3:** Hydroxypolystyrene resin (PSOH, 0.98 mmolg\(^{-1}\), 4.9 mmol, 5g) was swollen for 30 min in CH\(_2\)Cl\(_2\). The commercially available carboxylic acid 1 (2 equiv, 9.8 mmol) dissolved in CH\(_2\)Cl\(_2\), DCC (2 equiv, 1M in CH\(_2\)Cl\(_2\)) and DMAP (10 mol\%, 0.98 mmol) were successively added and the mixture was stirred overnight at room temperature. The resin was filtered off, washed successively with CH\(_2\)Cl\(_2\), DMF, CH\(_2\)Cl\(_2\) and MeOH and dried in vacuum for 12h.

*Representative procedure for ozonolysis on bead:* the resulting resin was swollen for 15 min in CH\(_2\)Cl\(_2\) and cooled to -78°C. Ozone was bubbled until the color turned deep green or blue and then 8-10 min more. Argon was then bubbled to remove excess of ozone and PPh\(_3\) (5 equiv) was added and the mixture was shaken from -78°C to room temperature overnight. The resin was filtered off, washed with CH\(_2\)Cl\(_2\) and MeOH and dried in vacuum. IR (SiC): \(\nu_{\text{max}}\) \(=\) 3059 (CH alkene), 3024 (CH alkane), 2924 (CH alkane), 2715 (CH aldehyde), 1720 cm\(^{-1}\) (C=O ester and aldehyde). Loading = 0.9 mmolg\(^{-1}\).\(^1\)
Methyl (R)-10-hydroxytridec-12-enoate, 4. *Representative procedure for allylation on solid support and release from the resin with NaOMe:* To the resin-bound aldehyde 3 (800 mg) in THF (8 mL) at -78°C was added a 1 M solution of 2 in Et₂O (1.5 mmol, 1.5 mL) and the mixture was stirred overnight while the temperature rising slowly to 0°C. After quenching by adding MeOH (1 mL), the resin was washed consecutively with pH 7 buffer, H₂O, THF, Et₂O, CH₂Cl₂ and MeOH. Afterwards, the resin was suspended in a mixture of DMF/MeOH 1/1 (5 mL each) and at 0 °C were added H₂O₂ (30%, 2 mL) and pH 7 buffer (2 mL). The mixture was then shaken from 0 °C to rt for 2h and filtered. The resin was washed with H₂O, THF, Et₂O, CH₂Cl₂ and MeOH and dried overnight under vacuum. Water was added, the mixture was filtered and the product was extracted with Et₂O. After filtration through silica gel, product 4 was obtained as colorless syrup (86 mg, 71%). \([\alpha]_{20}^D = +4.3 \text{ (c} = 1, \text{ CHCl}_3)\), \(1^H\) NMR (400 MHz, CDCl₃) \(\delta = 1.29\) (m, 10H), 1.42 (broad s, 1H), 1.59 (m, 2H), 2.12 (m, 1H), 2.29 (m, 3H), 3.63 (m, 1H), 3.66 (s, 3H), 5.11 (ddd, \(J = 4.5, 2.0, 1.0\) Hz, 1H), 5.14 (ddd, \(J = 7.3, 2.0, 1.0\) Hz, 1H), 5.82 ppm (m, 1H); \(1^C\) NMR (100.6 MHz, CDCl₃): \(\delta = 25.0, 25.7, 29.2, 29.3, 29.5, 29.6, 34.2, 36.9, 51.6, 70.7, 118.2, 135.0, 174.5\) ppm (CO); MS (70eV, EI): \(m/z\) (%): 201 (11) [M⁺-C₃H₅], 169 (100), 81 (50), 67(32), 55 (38); HRMS (FAB, m-NBA): calc. for C₁₄H₂₇O₃ [M+H]⁺ 243.1960, found 243.1946.
Enantioselective synthesis of Cryptocarya diacetate

**Resin 8:** The immobilized aldehyde 7 on Wang resin was submitted to allylation employing l-Ipc2Ball (ent-2) and following the representative procedure given before. The resulting homoallylic alcohol was protected as tert-butyldimethylsilyloxy group.

**General procedure for the protection of secondary alcohols with a TBS group on solid support:** The resin-bound secondary alcohol (1 g) was swollen in a mixture of CH$_2$Cl$_2$ (10 mL) and DMF (10 mL) at room temperature. After addition of TBSCl (1.13 g, 7.5 mmol) and DMAP (5 mg, 0.075 mmol) and imidazole (0.51 g, 7.5 mmol) the resin was shaken for 12 h. The resin was filtered and washed with DMF, THF/H$_2$O, THF and CH$_2$Cl$_2$ and dried under vacuum for 5 h (monitored by FT-IR until the bands at 3504 cm$^{-1}$ and 3062 cm$^{-1}$ completely disappeared).

**Resin 9:** The resin 8 was subjected to ozonolysis and allylation with l-Ipc2Ball (ent-2) following the representative procedures given before. The resulting homoallylic alcohol was then submitted to acrylation.

**Representative procedure for acrylation of alcohols on solid support:** The resin-bound secondary alcohol (0.5 g) was swollen in CH$_2$Cl$_2$ (5 mL) and the suspension was cooled to 0 °C. To the cold suspension was added diisopropylethyl amine (0.75 mL, 4.3 mmol), DMAP (10 mg, 0.08 mmol) and acryloyl chloride (0.3 mL, 4 mmol) and the suspension was shaken for 24 h at RT. The resin was filtered and washed successively with THF, THF/H$_2$O, THF and CH$_2$Cl$_2$ and dried under vacuum for 5 h. (The reaction was monitored by FT-IR which showed the disappearance of bands around 3500 cm$^{-1}$ and the appearance of a broad peak at 1725 to 1730 cm$^{-1}$).

**Resin 10:** **General procedure for ring closing metathesis on the solid support:** The resin-bound diene 9 (0.25 g, ~0.5 mmol/g loading) was swollen in CH$_2$Cl$_2$ (10 mL) and the suspension was degassed with argon. To the degassed suspension, Grubbs second
generation catalyst (0.02 mmol) was added and the mixture was heated to reflux and stirred over night. After 14 h, another portion of Grubbs second generation catalyst (0.02 mmol) was added and the reaction mixture was refluxed further for a total of ca. 20 h. The suspension was allowed to attain room temperature and was then filtered and washed successively with CH$_2$Cl$_2$, THF, CH$_2$Cl$_2$ and dried under vacuum.

**Cryptocarya diacetate 11:** Resin 10 (430 mg, 0.13 mmol) was swollen in TFA/CH$_2$Cl$_2$ 1:2 (20 mL/g resin, 8.6 mL) and shaken for 20 min at rt. Afterwards, the resin was filtered and rinsed with CH$_2$Cl$_2$. The filtrate was co-evaporated with toluene. The residue was filtered through silica gel (CH$_2$Cl$_2$:MeOH 9:1) to yield a mixture of the free diol and the monoprotected compound as byproduct. The diol was acetylated with Ac$_2$O (0.05 mL), Et$_3$N (0.07 mL) and a catalytic amount of DMAP in CH$_2$Cl$_2$ (1 mL). The mixture was stirred for 3 h from 0°C to RT, after which 1 mL of a saturated solution of NaHCO$_3$ was added. The aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 1 mL). The combined organic extracts were dried over Na$_2$SO$_4$. The solvent was removed under reduced pressure and the crude product was purified by silica gel chromatography (CH$_2$Cl$_2$ to CH$_2$Cl$_2$/EtOAc 2:1) to yield cryptocarya diacetate 11 with other minor isomers. After a second careful chromatography (petroleum ether/EtOAc 1:1) 4 mg (11%) of pure cryptocarya diacetate were obtained. \(\alpha\)$_{20}^D$ = +47.20 (c 0.50, CHCl$_3$), Lit.: \(\alpha\)$_{20}^D$ = +45.40 (c 0.33, CHCl$_3$),$^3$ \(\alpha\)$_{20}^D$ = +55.8 (c 1.06, CHCl$_3$);$^4$ $^1$H NMR (400 MHz, CDCl$_3$): \(\delta\) = 6.86 (ddd, \(J\) = 9.8, 5.9, 2.5 Hz, 1H), 6.02 (ddd, \(J\) = 9.8, 2.7, 1.0 Hz, 1H), 5.10 (dddd, \(J\) = 8.4, 7.0, 6.0, 3.7 Hz, 1H), 4.98 (ap sext, \(J\) = 6.0 Hz, 1H), 4.49 (ddt, \(J\) = 10.4, 6.6, 3.9 Hz, 1H), 2.45 (dddd, \(J\) = 18.2, 5.9, 3.9, 1.0 Hz, 1H), 2.26-2.35 (ddt, \(J\) = 18.4, 11.5, 2.6 Hz, 1H), 2.16 (ddd, \(J\) = 14.8, 8.6, 6.6 Hz, 1H), 2.07 (s, 3H), 2.04 (s, 3H), 2.01 (ddd, \(J\) = 14.4, 7.4, 7.4 Hz, 1H), 1.91-1.97 (ddd, \(J\) = 14.7, 6.5, 3.7 Hz, 1H), 1.79 (dt, \(J\) = 14.3, 5.8 Hz, 1H), 1.26 (d, \(J\) = 6.2 Hz, 3H); $^{13}$C NMR
Compounds 12a-d: These compounds were synthesized starting from the resin-bound aldehyde 7 and following the same synthetic sequence described for cryptocarya diacetate but releasing the compounds from the resin with DDQ. The allylation step was carried out in turns with 2 and ent-2 (see Scheme 3) following the procedure described before as well as for the other steps.

Compounds ent-12a-d were synthesized starting from ent-7.

Compound 12a: 420 mg (0.13 mmol) of resin were suspended in CH₂Cl₂ (30 mL/g resin, 13 mL) and pH=7 buffer (1.7 mL/g resin, 0.7 mL). Then, DDQ (10 equiv, 1.3 mmol, 295 mg) was added at 0°C and the suspension was shaken overnight at rt. The resin was filtrated off and rinsed with CH₂Cl₂. The filtrates were washed with a saturated solution of NaHCO₃ (3 x 15 mL), then with brine and finally dried over Na₂SO₄. After removal of solvent under reduced pressure, the residue was filtrated through silica gel (CH₂Cl₂/EtOAc 20-50%) to get 15 mg (38%) of 12a. A second careful chromatography (CH₂Cl₂/CH₃CN 20-40%) allowed obtaining 11.4 mg of an enriched mixture of 12a (90:10). Data taken from the mixture: Rₐ = 0.25 (silica gel, ethyl acetate/petroleum ether 40/60); [α]²⁰_D = +29.65 (c 1.43, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 6.88 (ddd, J = 9.6, 6.6, 3.3 Hz, 1H), 6.02 (ap d, J = 9.8 Hz, 1H), 4.51-4.58 (ap sept, J = 4.6 Hz, 1H), 4.20-4.26 (ap sept, J = 4.2
Compounds 14a-c: These compounds were synthesized following the same iterative sequence described for cryptocarya diacetate and the same representative procedures shown above for alkylation, ozonolysis, RCM, protection of secondary alcohols and release from the resin with DDQ.

Yield: 3.2 mg (from 270 mg resin), 9.3 %; Rf = 0.2 (silica gel, ethyl acetate), [α]D20° = +55.6° (c 0.27, CHCl3); Lit. [5] [α]D25° = +62.1° (c 1, CHCl3); 1H NMR (400 MHz, CDCl3): δ 7.29-7.21 (m, 2H), 7.19-7.15 (m, 3H), 6.89 (td, J = 9.9, 4.1 Hz, 1H), 6.02 (d, J = 9.9 Hz, 1H), 4.70-4.62 (m, 1H), 4.14-4.09 (m, 1H), 3.90-3.82 (m, 1H), 2.62 (t, J = 7.4 Hz, 2H), 2.42-2.38 (m, 2H), 2.08-1.95 (m, 1H), 1.80-1.74 (m, 1H), 1.70-1.45 (m, 8H); 13C NMR (125.77 MHz, CDCl3): δ = 164.0, 145.3, 142.4, 128.4, 128.3, 125.7, 121.2, 76.3, 72.9, 69.8, 42.8, 42.3, 38.1, 35.8, 31.3, 29.4, 24.9; MS (ESI): m/z: 318 [M+] ; HRMS (FAB, m-NBA): calc. for C19H27O4 [M+H]+ 319.1909, found: 319.1935.