Supporting Information

trans-Hydrogenation: Application to a Concise and Scalable Synthesis of Brefeldin A**

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| Autor (*), Year | Ref. | shown substrate | "real" substrate | macrocyclization method | Steps ($\sum$) | Amount | Comments |
|----------------|------|-----------------|------------------|------------------------|----------------|--------|----------|
| Corey, 1976    | 1    | cyclopentadiene | lactonization    | nr                     | $\geq 22$      | nr      | racemic  |
| Bartlett, 1978 | 2    | lactonization   | 37               | $\geq 17$              | 1 mg           | racemic |
| Kitahara, Mori, 1979 | 3 | lactonization | 42               | $\geq 31$              | 2.9 mg         |        |
| Greene, 1980   | 4,5  | lactonization   | $\geq 18$        | 16.1 mg                |                |        |
| Winterfeldt, 1980 | 6 | lactonization   | nr               | $> 15$                 | nr             | racemic |
| Yamaguchi, 1981 | 7 | lactonization   | $\geq 21$        | nr                     |                | racemic |
| Gais, 1984     | 8    | lactonization   | $\geq 24$        | nr                     |                |        |
| Corey, 1990    | 9    | lactonization   | nr               | $\geq 17$              | nr             |        |
| Takano, 1990   | 10   | lactonization   | $\geq 25$        | nr                     | Birch-reduction ($\Delta^{10,11}$) |
| Taber, 1991    | 11   | lactonization   | $\geq 23$        | 1.1 mg                 |                |        |
| Nokami, 1991   | 12   | lactonization   | $\geq 16$        | nr                     |                |        |
| Solladié, 1993 | 13  | lactonization   | 50               | $\geq 38$              | 4.2 mg         |        |
| Kajiwara, 1994 | 14  | lactonization   | $\geq 22$        | nr                     | Birch-reduction ($\Delta^{10,11}$) |
| Name    | Year | Step | Substrate                  | Process     | Yield | Amount |
|---------|------|------|----------------------------|-------------|-------|--------|
| Roberts | 1994 | 15   | cyclopentadiene            | lactonization | 80    | 14     |
|         |      |      |                            |             |       | 5.2 mg |
| Haynes  | 1997 | 16   | cyclopentadiene (?)        | lactonization | 78    | > 16   |
|         |      |      |                            |             |       | 5.9 mg |
| Suh     | 1998 | 17   | malic acid                 | lactonization | 51    | ≈ 18   |
|         |      |      |                            |             |       | 2.2 mg |
| Romo    | 2002 | 18   | HWE @ Δ²,₃                 |              | 41    | ≈ 15   |
|         |      |      |                            |             |       | nr     |
| Kim     | 2002 | 19   | ethyl lactate              | nitrile-oxide cycloadd. | 78ʰ | ≈ 23   |
|         |      |      |                            |             |       | 14.8 mg|
| Trost   | 2002 | 20   | furan                     | lactonization | 61    | ≈ 18   |
|         |      |      |                            |             |       | 8.1 mg |
| Wu      | 2004 | 21   |                            | lactonization | 81    | ≈ 16   |
|         |      |      |                            |             |       | 14 mg  |
| Suh     | 2006 | 22   | HWE @ Δ²,₃                |              | 59    | ≈ 15   |
|         |      |      |                            |             |       | nr     |
| Tae     | 2009 | 23   | RCM @ Δ¹₀,₁₁              |              | 81    | ≈ 14   |
|         |      |      |                            |             |       | 4.8 mg |

[a] first appearance; “variants” are considered under one entry if the overall strategy is unchanged
[b] substrate with which the sequence described in the cited reference starts
[c] compound from which the substrate shown in the publication has been made according to the cited literature; not in all cases this may be the actual point of departure; (?) indicates cases, where the real starting material is not clear (best guess by the present authors)
[d] the step count is not necessarily unambiguous
[e] amount of brefeldin A shown in the Experimental Part of the publication
[f] strategic elements related to the present synthesis are indicated in blue
[g] also reports an attempted but unsuccessful macrocyclization via intramolecular 1,4-addition
[h] yield of a mixture of diastereomers
[i] yield over more than one step; the yield of the macrocyclization itself is not specified

nr = not reported; HWE = Horner-Wadsworth-Emmons olefination; RCM = ring closing alkene metathesis
| Autor (*) | Year\(^{[a]}\) | Ref. | shown Substrate\(^{[b]}\) | “real” substrate\(^{[c]}\) | Steps (\(\sum\) \(^{[d]}\)) | Comments |
|-----------|----------------|------|-------------------------|-----------------|-----------------|--------|
| Ohrui     | 1980           | 24   |                         | glucose         | >> 20           | intercepts ref. 7 |
| Winterfeldt | 1981       | 25   | cyclopentadiene (?)     | racemic, HWE @ \(\Delta^{2,3}\) (yield not reported) | intercepts ref. 6 |
| Greene    | 1982           | 5    |                         | >> 13           |                 | racemic; intercepts ref. 1 |
| Isoe      | 1985           | 26   |                         | \(\approx 18\) |                 | intercepts ref. 2 |
| Sakai     | 1985           | 27   |                         | >> 20           |                 | intercepts ref. 3 |
| Trost     | 1986           | 28   | mannitol                | \(\approx 20\) |                 | intercepts ref. 1 |
| Nakai     | 1995           | 29   |                         | \(\approx 20\) |                 | no route established at the time is intercepted |
| Greene    | 1995           | 30   |                         | \(\approx 18\) |                 | intercepts ref. 5 |
| Kobayashi | 1996           | 31   | cyclopentadiene (?)     | \(\approx 15\) |                 | intercepts ref. 2 |
| Author     | Year | Entry | Reaction | Interception |
|------------|------|-------|----------|--------------|
| Mioskowski | 1999 | 32    | propargyl alcohol (?) | > 20 | intercepts ref. 8a |
| Kim       | 2002 | 33    | tri-O-acetyl-D-glucal | ≈ 27 | intramol. nitrile-oxide cycloadd. (84%) |
|            |      |       |          |              | Birch-reduction ($\Delta^{10,11}$) |
| Kim       | 2002 | 33    | tri-O-acetyl-D-glucal | ≈ 22 | RCM @ $\Delta^{10,11}$ (42%, E:Z = 2.2:1); intercepts ref. 19 |
| Helmchen   | 2006 | 34    | 2-buten-1,4-diol     | ≈ 19 | intercepts ref. 11 |
| Zercher    | 2007 | 35    | malic acid           | ≈ 17 | RCM @ $\Delta^{10,11}$ (64%, E:Z = 3.5:1) & ring expansion |

**Notes:**

[a] first appearance; “variants” are considered under one entry if the overall strategy is unchanged
[b] substrate with which the sequence described in the cited reference starts
[c] compound from which the substrate shown in the publication has been made according to the cited literature; not in all cases this may be the actual point of departure; (?) indicates cases, where the real starting material is not clear (best guess by the present authors)
[d] projected number of steps towards the final product if the synthesis were completed according to the intercepted route; the step count is not necessarily unambiguous
### TOTAL AND FORMAL SYNTHESSES OF BREFELDIN C

| Autor (*) | Year<sup>a</sup> | Ref. | shown Substrate<sup>b</sup> | “real” substrate<sup>c</sup> | Macrocyclization (yield %) | Steps (Σ)<sup>d</sup> | Amount<sup>e</sup> | Comments<sup>f</sup> |
|-----------|------------------|------|-----------------------------|-----------------------------|---------------------------|-----------------|----------------|-----------------|
| Schreiber | 1988             | 37   | ![Schreiber Substrate](image) | NHK (60%)                   | ≈ 16                       | ≈ 5 mg          |                |                 |
| Takano    | 1989             | 38   | ![Takano Substrate](image)  | lactonization (85%)         | ≈ 22                       | nr              |                | Birch-reduction ($\Delta^{10,11}$) |
| Guingant  | 2005             | 39   | ![Guingant Substrate](image) | lactonization (79%)         | ≈ 18                       | 50 mg           |                |                 |
| Tsunoda   | 2011             | 40   | ![Tsunoda Substrate](image) | lactonization (89%)         | ≈ 23                       | nr              |                |                 |

<sup>a</sup> first appearance; “variants” are considered under one entry if the overall strategy is unchanged

<sup>b</sup> substrate with which the sequence described in the cited reference starts

<sup>c</sup> compound from which the substrate shown in the publication has been made according to the cited literature; not in all cases this may be the actual point of departure; (?) indicates cases, where the real starting material is not clear (best guess by the present authors)

<sup>d</sup> the step count is not necessarily unambiguous

<sup>e</sup> amount of brefeldin A shown in the Experimental Part

<sup>f</sup> strategic elements related to the present synthesis are indicated in blue

nr = not reported; NHK = Nozaki-Hiyama-Kishi reaction
A SELECTION OF SIGNIFICANT ANALOGUES

| Autor (*) | Year         | Ref. | Structure$^a$ | Amount                                      |
|-----------|--------------|------|---------------|---------------------------------------------|
| Hori      | 1997/2000    | 41   | various derivatives | prepared by derivatization of BFA |
| Cushman   | 1998         | 42   | various prodrugs  | prepared by derivatization of BFA           |
| Helmchen  | 2006         | 34   |               | nr                                          |
| Helmchen  | 2006         | 34   |               | nr                                          |
| Wu        | 2008         | 43   |               | 14 mg                                       |
| Helmchen  | 2008/2011    | 44,45|               | 14.3 mg (for total synthesis) 125 mg (via partial synthesis) |
| Guingant  | 2010         | 39a  |               | 58 mg                                       |
| Helmchen  | 2011         | 45   |               | 10.8 mg                                     |
| Helmchen   | Year | Molecule | Yield | Notes                                      |
|------------|------|----------|-------|--------------------------------------------|
|            | 2011 | ![Molecule](image1.png) | 23 mg (via partial synthesis) | Helmchen 2011, R = Et, 43 mg, R = CF<sub>3</sub>, 18.8 mg, R = vinyl, 78.6 mg, Ar = Ph, 42 mg, Ar = 1-naphthyl, 25.8 mg, Ar = 6-quinolinyl, 21.4 mg, Ar = 4-dimethylaminophenyl, 18.7 mg, Ar = 4-trifluoromethylphenyl, 37.4 mg, Ar = 4-fluoromethyl, 33.4 mg (all via partial synthesis) |
|            | 2013 | ![Molecule](image2.png) |       | [a] modified site and/or modification relative to the natural product shown in red |

[a] modified site and/or modification relative to the natural product shown in red
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Figure S-1. Structure of compound 8 in the solid state; anisotropic displacement parameters are drawn at the 50% probability level, hydrogen atoms are omitted for clarity; brefeldin numbering scheme (CCDC-1036054)

X-ray Crystal Structure Analysis of Compound 8: C7 H10 O3, Mr = 142.15 g · mol⁻¹, colorless plate, crystal size 0.32 x 0.19 x 0.12 mm, monoclinic, space group P21, a = 5.3098(4) Å, b = 10.2790(7) Å, c = 12.3060(9) Å, β = 97.493(4)°, V = 665.92(8) Å³, T = 100 K, Z = 4, Dcalc = 1.418 g · cm⁻³, λ = 1.54178 Å, μ(Cu-Kα) = 0.930 mm⁻¹, Empirical absorption correction (Tmin = 0.77, Tmax = 0.90), Bruker AXS X8 Proteum diffractometer, 3.623 < θ < 66.290°, 14753 measured reflections, 2300 independent reflections, 2182 reflections with I > 2σ(I), Structure solved by direct methods and refined by full-matrix least-squares against F² to R₁ = 0.030 [I > 2σ(I)], wR₂ = 0.078, 183 parameters, H atoms riding, absolute structure parameter = 0.0(2), S = 1.040, residual electron density 0.2 / -0.2 e Å⁻³.

Figure S-2. Structure of adduct 12 in the solid state; anisotropic displacement parameters are drawn at the 50% probability level, hydrogen atoms are omitted for clarity (CCDC-1036055)

X-ray Crystal Structure Analysis of Compound 12: C8 H10 Cl2 O2, Mr = 209.06 g · mol⁻¹, colorless plate, crystal size 0.21 x 0.20 x 0.17 mm, orthorhombic, space group P212121, a = 8.0685(5) Å, b = 9.3727(5) Å, c = 11.7206(7) Å, V = 886.35(9) Å³, T = 100 K, Z = 4, Dcalc = 1.567 g · cm⁻³, λ = 1.54178 Å, μ(Cu-Kα) = 6.234 mm⁻¹, Empirical absorption correction (Tmin = 0.34, Tmax = 0.49), Bruker AXS X8 Proteum
diffractometer, 6.045 < θ < 67.622°, 40841 measured reflections, 1594 independent reflections, 1587 reflections with I > 2σ(I), Structure solved by direct methods and refined by full-matrix least-squares against F² to R₁ = 0.025 [I > 2σ(I)], wR₂ = 0.061, 109 parameters, absolute structure parameter = 0.012(5), H atoms riding, S = 1.098, residual electron density 0.1 / -0.3 e Å⁻³.

**Figure S-3.** Structure of cycloalkyne 20 in the solid state in two different orientations; anisotropic displacement parameters are drawn at the 50% probability level; except for H3 shown in the top projection, all hydrogen atoms are omitted for clarity (CCDC-1036056)

**X-ray Crystal Structure Analysis of Compound 20:** C₁₆H₂₂O₄, Mᵣ = 278.33 g · mol⁻¹, colorless plate, crystal size 0.21 x 0.11 x 0.07 mm, orthorhombic, space group P2₁2₁2₁, a = 7.4004(2) Å, b = 10.6316(3) Å, c = 18.5415(5) Å, V = 1458.81(7) Å³, T = 100 K, Z = 4, D_cal = 1.267 g · cm⁻³, λ = 1.54178 Å, μ(Cu-Kα) = 0.732 mm⁻¹, Semi-empirical absorption correction (T_min = 0.87, T_max = 0.95), Bruker AXS X8 Proteum diffractometer, 4.770 < θ < 67.815°, 65420 measured reflections, 2618 independent reflections, 2541 reflections with I > 2σ(I), Structure solved by direct methods and refined by full-matrix least-squares against F² to R₁ = 0.032 [I > 2σ(I)], wR₂ = 0.078, 190 parameters, absolute structure parameter = 0.07(6), H atoms riding, S = 1.108, residual electron density 0.1 / -0.2 e Å⁻³.

S2
**Figure S-4.** Structure of brefeldin A (1) in the solid state; anisotropic displacement parameters are drawn at the 50% probability level, hydrogen atoms are omitted for clarity (CCDC-1036057)

**X-ray Crystal Structure Analysis of 9022:** C_{16}H_{24}O_{4}, M_r = 280.35 g · mol^{-1}, colorless plate, crystal size 0.187 x 0.172 x 0.040 mm, orthorhombic, space group P2_12_2_1, a = 7.3601(3) Å, b = 10.8657(5) Å, c = 18.7697(9) Å, V = 1501.06(12) Å³, T = 100 K, Z = 4, D_{calc} = 1.241 g · cm⁻³, λ = 1.54178 Å, μ(Cu-Kα) = 0.712 mm⁻¹, Empirical absorption correction (T_{min} = 0.90, T_{max} = 0.97), Bruker AXS X8 Proteum diffractometer, 4.702 < θ < 67.536°, 62428 measured reflections, 2704 independent reflections, 2644 reflections with I > 2σ(I), Structure solved by direct methods and refined by full-matrix least-squares against F² to R₁ = 0.030 [I > 2σ(I)], wR₂ = 0.072, 198 parameters, absolute structure parameter = 0.00(6), H atoms riding, S = 1.096, residual electron density 0.1 / -0.2 e Å⁻³.

CCDC-1036054 (8), CCDC-1036055 (12), CCDC-1036056 (20) and CCDC-1036057 (1) contain the supporting crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).

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1 For a previous report on the X-ray structure of brefeldin A, see: H. P. Weber, D. Hauser, H. P. Sigg, *Helv. Chim. Acta* **1971**, *54*, 2763-2766.
**General.** Unless stated otherwise, all reactions were carried out under Ar in flame-dried glassware. The solvents were purified by distillation over the indicated drying agents and were transferred under Ar: THF, Et₂O (Mg/anthracene), CH₂Cl₂, hexane, toluene (Na/K), dioxane, DMF, MeCN, NEt₃, and pyridine were dried by an adsorption solvent purification system based on molecular sieves. Thin layer chromatography (TLC): Macherey-Nagel precoated plates (POLYGRAM® SIL/UV254); Flash chromatography: Merck silica gel 60 (40–63 μm) with predistilled or HPLC grade solvents. NMR: Spectra were recorded on Bruker DPX 300, AV400, AV500 or AVIII 600 spectrometer in the solvents indicated; chemical shifts (δ) are given in ppm relative to TMS, coupling constants (J) in Hz. The solvent signals were used as references and the chemical shifts converted to the TMS scale (CDCl₃). Isotropization (Δν) and dipolar coupling constants (J) were measured with a Perkin-Elmer Model 343 polarimeter. Unless stated otherwise, all commercially available compounds (Alfa Aesar, Aldrich, Fluka, Lancaster) were used as received. Complexes 26[¹] and [Cp*Ru(MeCN)₃]PF₆[²] were prepared according to literature procedures.

(1R,2S)-Diethyl cyclohex-4-ene-1,2-dicarboxylate (3).[³] H₂SO₄ (conc., 25 mL, 469 mmol) was added to a solution of cis-1,2,3,6-tetrahydrophthalic anhydride (60.0 g, 394 mmol) in MeOH (600 mL) and the resulting mixture was stirred overnight at reflux temperature. The mixture was then concentrated under reduced pressure and the remaining oil diluted with water (100 mL). Solid NaHCO₃ was carefully added until the pH was neutral. The aqueous phase was extracted with tert-butyl methyl ether (4 x 100 mL), and the combined organic phases were dried over Na₂SO₄, filtered and concentrated to give product 3 as a clear oil (75.0 g, 96%). ¹H NMR (400 MHz, CDCl₃): δ = 5.65 (s, 2H), 3.67 (s, 6H), 3.02 (t, J = 5.3, 2H), 2.53 (dd, J = 5.3, 16.2 Hz, 2H), 2.32 (dd, J = 5.3, 16.2 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 173.8, 125.2, 51.9, 39.8, 25.8; IR (film) ʋ = 3029, 2952, 2848, 1729, 1435, 1200, 1163, 1025, 660; MS (EI): m/z: 198 (0.25), 167 (14), 138 (35), 107 (9), 91 (1), 79 (100), 59 (9); HRMS (ESI): m/z: calc. for C₁₉H₁₄O₄Na: 221.0784 [M+Na⁺], found: 221.0785.

(1R,6S)-6-(Methoxycarbonyl)cyclohex-3-enecarboxylic acid (4).[⁴] Diester 3 (74.5 g, 376 mmol) was suspended in phosphate buffer (1340 mL, 100 mM, pH = 7.0). Pig liver esterase (10.9 kU, 728 mg lyophilized powder) and ammonium sulfate (3 M in water, 3.16 mL) were added and the pH was kept constant by addition of NaOH (1 M) via a pH-stat for 2 d. For work up, the pH was adjusted to ≈ 10 by the addition of NaOH (1 M) and the obtained slurry was extracted with tert-butyl methyl ether (2 x 500 mL). The aqueous phase was acidified with conc. HCl until a pH 1 was reached, which led to significant precipitation of the enzyme. To facilitate the extraction, tert-butyl methyl ether (500 mL) was added and the mixture was filtered through a pad of Celite, which was carefully washed with water (100 mL) and tert-butyl methyl ether (100 mL). The
phases were separated and the aqueous phase was extracted with tert-butyl methyl ether (2 x 500 mL). The combined organic layers of the second extraction step (under acidic conditions) were dried over Na₂SO₄, filtered and concentrated to give compound 4 as a pale yellow oil (65.2 g, 94%). 

\[ \alpha_{D}^{10} = +17.7 \text{ [c = 1.0, EtOH, lit.]}.^{[5]} +17.7 \text{ [c = 1.0, EtOH]} \]; H NMR (400 MHz, CDCl₃): δ = 5.67 (s, 2H), 3.69 (s, 3H), 3.10-3.03 (m, 2H), 2.61-2.54 (m, 2H), 2.40-2.33 (m, 2H); C H NMR (100 MHz, CDCl₃): δ = 179.8, 173.8, 125.3, 125.2, 52.1, 39.7, 39.6, 25.9, 25.7; IR (film) ν = 3100br, 3031, 2952, 2851, 1731, 1704, 1655, 1436, 1297, 1269, 1033, 736, 663; MS (EI): m/z: 184 (1), 166 (8), 153 (11), 138 (24), 124 (27), 107 (7), 97 (4), 79 (100); HRMS (ESI): m/z: calc. for C₉H₁₄O₄Na₂: 229.0448 [M+2Na]⁺, found: 229.0448.

(3aS,7aR)-3a,4,7,7a-Tetrahydroisobenzofuran-1(3H)-one (5). A flame-dried round bottom flask equipped with a dropping funnel was charged with LiEt₂BH (1 m in THF, 608 mL, 608 mmol) under argon. The solution was cooled to 0 °C before a solution of compound 4 (28.0 g, 152 mmol) in THF (20 mL) was added over a period of 30 min. Once the addition was complete, the mixture was stirred for 1 h at 0 °C and for 3 h at room temperature. For work up, the mixture was cooled to 0 °C and the reaction was carefully quenched by addition of aq. HCl (6 M, 500 mL). The resulting mixture was stirred overnight before it was extracted with tert-butyl methyl ether (4 x 200 mL). The combined organic layers were dried over Na₂SO₄, filtered and concentrated. The residue was purified by flash chromatography (SiO₂, pentane/tert-butyl methyl ether, 3/1) to give the title compound as colorless oil, which was dried under high vacuum for 1 h (20.5 g, 98%). 

\[ \alpha_{D}^{10} = +49.7 \text{ [c = 1.8, EtOAc, lit.]},^{[6]} +82.5 \text{ [c = 2.0, EtOAc]} \]; H NMR (400 MHz, CDCl₃): δ = 5.73 (s, 2H), 4.30 (dd, J = 5.2, 8.8 Hz, 1H), 4.01 (dd, J = 1.9, 8.8 Hz, 1H), 2.83-2.69 (m, 1H), 2.66-2.57 (m, 1H), 2.52-2.48 (m, 1H), 2.44-2.32 (m, 1H), 2.29-2.23 (m, 1H), 1.93-1.87 (m, 1H); C H NMR (100 MHz, CDCl₃): δ = 179.2, 125.3, 124.9, 72.8, 37.4, 32.1, 24.8, 22.1; IR (film) ν = 3031, 2969, 2905, 2851, 1731, 1704, 1655, 1436, 1297, 1269, 1033, 736, 663; MS (EI): m/z: 138 (41), 123 (9), 110 (5), 93 (100), 79 (89); HRMS (ESI): m/z: calc. for C₉H₈O₂: 138.0681 [M]⁺, found: 138.0681.

2,2’-[(3R,4S)-2-Oxotetrahydrofuran-3,4-diyl]diacetic acid (6). A solution of lactone 5 (200 mg, 1.45 mmol) in acetone (1 mL) and added dropwise over a period of 1 h to a solution of KMnO₄ (699 mg, 4.42 mmol) in water (5 mL) at 0 °C. The brown slurry was stirred for 1 h at 0 °C, warmed to room temperature and stirred overnight. NaHSO₄ was added in order to destroy any remaining KMnO₄. The resulting slurry was filtered through a pad of Celite and the filter cake carefully rinsed with water/THF (1/1, 25 mL). The combined filtrate was acidified to pH 2, saturated with NaCl and extracted with tert-butyl methyl ether/THF (2/3, 6 x 40 mL). The combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure (the bath temperature must not exceed 30 °C). The remaining while solid material was dried under high vacuum and found pure enough for immediate further use (283 mg, 97%). The reaction was also performed on much larger scale, using KMnO₄ (119.4 g, 0.76 mol) in water (650 mL) and lactone 5 (26.1 g, 189 mmol) in acetone (139 mL) to give analytically pure 6 (27.3 g, 71%) which analyzed as follows: m.p. = 162-164 °C (EtOAc, lit.⁶ 144-157 °C); \[ \alpha_{D}^{10} = -75.3 \text{ [c = 1.0, } \]
The reaction was also performed on larger scale, using Ac₂O (124 mL, 134 g, 1.31 mol), diacid 6 (10.0 g, 49.5 mmol), K₂CO₃ (6.84 g, 49.5 mmol) and THF (370 mL) to give analytically pure 7 (3.86 g, 56%) which analyzed as follows: m.p. = 81-82 °C (EtOAc, lit.:[49] 84 °C for ent-6); \([\alpha]_D^{20} = +80.6 \) [c = 1.1, CH₂Cl₂, lit.:[49] –67.8 (c = 2.59, CH₂Cl₂, for ent-6)]; ¹H NMR (400 MHz, CDCl₃): δ = 4.53 (dd, J = 5.9, 9.6 Hz, 1H), 4.25 (d, J = 11.5, 1H), 3.40-3.11 (m, 2H), 2.79-2.51 (m, 3H), 2.21 (dd, J = 8.3, 19.1 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 214.0, 178.1, 71.8, 42.2, 40.8, 39.3, 36.3; IR (film) \(\tilde{\nu} = 2975, 2920, 1765, 1732, 1403, 1371, 1308, 1185, 1173, 1097, 1033, 975\); MS (El): \(m/z\): calc. for C₉H₆O₃Na: 225.0370 [M+Na]⁺, found: 225.0370.

**Diacid 6** (998 mg, 4.94 mmol) was suspended in Ac₂O (10 mL, 10.8 g, 106 mmol) and the mixture stirred at 130 °C (bath temperature) for 1 h. After cooling to room temperature, the mixture was diluted with MeOH (10 mL) and the mixture stirred for 30 min at 0 °C. Sat. aq. NH₄Cl (20 mL) and CH₂Cl₂ (20 mL) were added and stirring continued for 20 min at 0 °C. Phase separation followed by extraction of the aqueous layer with CH₂Cl₂ (3 x 25 mL) gave a combined organic phase, which was dried over Na₂SO₄, filtered and concentrated. The crude product was purified by flash chromatography (SiO₂, hexane/EtOAc, 1/1) to give the title compound as a pale yellow solid (504 mg, 73%).

The reaction was also performed on larger scale, using Ac₂O (124 mL, 134 g, 1.31 mol), diacid 6 (10.0 g, 49.5 mmol), K₂CO₃ (6.84 g, 49.5 mmol) and THF (370 mL) to give analytically pure 7 (3.86 g, 56%) which analyzed as follows: m.p. = 81-82 °C (EtOAc, lit.:[49] 84 °C for ent-6); \([\alpha]_D^{20} = +80.6 \) [c = 1.1, CH₂Cl₂, lit.:[49] –67.8 (c = 2.59, CH₂Cl₂, for ent-6)]; ¹H NMR (400 MHz, CDCl₃): δ = 4.53 (dd, J = 5.9, 9.6 Hz, 1H), 4.25 (d, J = 11.5, 1H), 3.40-3.11 (m, 2H), 2.79-2.51 (m, 3H), 2.21 (dd, J = 8.3, 19.1 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 214.0, 178.1, 71.8, 42.2, 40.8, 39.3, 36.3; IR (film) \(\tilde{\nu} = 2975, 2920, 1765, 1732, 1403, 1371, 1308, 1185, 1173, 1097, 1033, 975\); MS (El): \(m/z\): calc. for C₉H₆O₃Na: 225.0370 [M+Na]⁺, found: 225.0370.
C\textsubscript{13}H\textsubscript{16}O\textsubscript{3}: 142.0630 [M]\textsuperscript{+}, found: 142.0628. Single crystals suitable for X-ray diffraction were obtained from a solution in EtOAc upon slow evaporation of the solvent.

(3aS,5R,6aR)-5-[[tert-Butyldimethylsilyloxy]hexahydro-1H-cyclopenta[c]furan-1-one \(9\). TBSOTf (9.78 mL, 11.3 g, 42.6 mmol) was added dropwise at 0 °C to a solution of 2,6-lutidine (6.6 mL, 6.09 g, 56.8 mmol) and hydroxylactone \(6\) (4.04 g, 28.4 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (38 mL). After stirring for 1 h at 0 °C, the reaction was quenched by the addition of sat. aq. NaHCO\textsubscript{3} (ca. 10 mL) and the aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organic phases were washed with aq. CuSO\textsubscript{4} (1 M, 5 x 15 mL) and brine (10 mL), before they were dried over Na\textsubscript{2}SO\textsubscript{4}, filtered and concentrated. The residue was dried under high vacuum to give pure \(9\) as pale yellow solid (7.12 g, 98%). m.p. = 48-49 °C (EtOAc); [\(\alpha\)]\textsubscript{D}\textsubscript{20} = −20.3 (c = 1.6, CH\textsubscript{2}Cl\textsubscript{2}); \(^1\)H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta = 4.51\ (t, J = 8.7, 1H), 4.34-4.32\ (m, 1H), 4.17-4.14\ (m, 1H), 3.04-2.99\ (m, 2H), 2.20\ (d, J = 13.5 Hz, 1H), 1.94-1.85\ (m, 2H), 1.75\ (d, J = 13.6 Hz, 1H), 0.85\ (s, 9H), 0.04\ (s, 6H); \(^{13}\)C NMR (100 MHz, CDCl\textsubscript{3}): \(\delta = 181.1, 74.9, 74.2, 43.7, 43.5, 40.7, 37.2, 26.0, 18.2, −4.62, −4.65\); IR (film) \(\tilde{\nu} = 2958, 2928, 2856, 1751, 1377, 1255, 1195, 1045, 1023, 908, 833, 773\); MS (EI): m/z: 241 (3), 199 (93), 169 (12), 141 (14), 125 (4), 105 (7), 89 (6), 75 (100), 59 (7); HRMS (ESI): m/z: calc. for C\textsubscript{13}H\textsubscript{16}O\textsubscript{3}SiNa: 279.1387 [M+Na]\textsuperscript{+}, found: 279.1383.

\{(1S,2R,4S)-4-[[tert-Butyldimethylsilyloxy]-2-(prop-1-yn-1-yl)cyclopentyl]methanol \(11\). A flame-dried 2-neck round bottom flask, equipped with a reflux condenser and a dropping funnel, was charged with PPh\textsubscript{3} (43.4 g, 165 mmol). THF (450 mL) and the lactone \(9\) (5.31 g, 20.7 mmol) were added and the mixture was stirred at reflux temperature (oil-bath temperature \(\approx 80 \) °C). A solution of CCl\textsubscript{4} (50 mL, 79.5 g, 516 mmol) in THF (50 mL) was added dropwise over a period of 3.5 h. Once the addition was complete, stirring was continued at this temperature for 3 h, before the mixture was cooled and the reaction quenched with water (10 mL). The mixture was extracted with tert-butyl methyl ether (3 x 200 mL), the combined organic phases were washed with sat. aq. NaHCO\textsubscript{3} (100 mL) and brine (50 mL), before they were dried over Na\textsubscript{2}SO\textsubscript{4}, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (SiO\textsubscript{2}, hexane/EtOAc, 50/1) to give the dichloro-olefin \(10\) (containing minor PPh\textsubscript{3} impurities) which was immediately used for the subsequent reaction. Characteristic data of \(10\): \(^1\)H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta = 4.45\ (t, J = 8.6, 1H), 4.32-4.26\ (m, 2H), 3.39\ (dt, J = 4.6, 9.3 Hz, 1H), 3.21\ (s, 1H), 3.02-2.92\ (m, 1H), 2.06-2.02\ (m, 2H), 1.94-1.88\ (m, 1H), 1.72-1.66\ (m, 1H), 0.87\ (s, 9H), 0.04\ (s, 6H); \(^{13}\)C NMR (100 MHz, CDCl\textsubscript{3}): \(\delta = 159.5, 79.5, 77.4, 74.5, 46.0, 41.4, 41.4, 40.6, 25.8, 18.0, −4.7, −4.9\).

A flame-dried Schlenk tube was charged with Fe(acac)\textsubscript{3} (896 mg, 2.54 mmol), ortho-phenylene-diamine (548 mg, 5.07 mmol), Et\textsubscript{2}O (120 mL) and the crude dichloro-olefin \(10\) from the previous reaction. The solution was cooled to 0 °C before MeLi (1.6 M in Et\textsubscript{2}O, 39.6 mL, 63.4 mmol) was slowly added. The mixture was stirred for 10 min at 0 °C and for 2 h at room temperature. For work up, the mixture was cooled to 0 °C before the reaction was carefully quenched with water (20 mL). The aqueous phase was extracted with tert-butyl methyl ether (3 x 100 mL) and the combined organic
layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (SiO₂, hexane/EtOAc, 15/1) to give alkyne 11 as an oil (3.02 g, 55%). [α]_D^20 = −2.6 (c = 2.0, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ = 4.14 (quint, J = 6.5, 1H), 3.82 (dd, J = 7.6, 11.4 Hz, 1H), 3.69-3.64 (m, 1H), 2.80-2.73 (m, 1H), 2.62 (bs, 1H), 2.25-2.16 (m, 2H), 1.98-1.91 (m, 1H), 1.81 (d, J = 2.5 Hz, 3H), 1.73-1.66 (m, 1H), 1.42 (dt, J = 13.1, 6.5 Hz, 1H), 0.87 (s, 9H), 0.04 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ = 80.2, 78.5, 72.7, 65.1, 42.8, 42.7, 38.4, 30.2, 26.0, 18.2, 3.7, −4.6, −4.7; IR (film) ¯ν = 3414br, 2954, 2929, 2885, 2857, 1472, 1463, 1361, 1256, 1099, 1034, 896, 835, 775, 738; MS (EI): m/z: 268 (0.2), 253 (1), 211 (50), 193 (6), 181 (14), 169 (17), 155 (10), 141 (18), 119 (37), 105 (8), 91 (28), 75 (100); HRMS (ESI): m/z: calc. for C₁₅H₂₈O₂SiNa: 291.1751 [M+Na]⁺, found: 291.1749.

**Compound 12.** Lactone 9 (8.85 g, 20.7 mmol) was added to a solution of PPh₃ (71.5 g, 273 mmol) in THF (800 mL) and the resulting mixture was stirred at reflux temperature (oil bath temperature ca. 80 °C) when a solution of CCl₄ (83 mL, 132 g, 860 mmol) in THF (50 mL) was added dropwise over a period of 3.5 h. Once the addition was complete, stirring was continued at this temperature for an additional 3 h, before the mixture was allowed to cool and the reaction was quenched with water (10 mL). The mixture was extracted with tert-butyl methyl ether (3 x 200 mL), the combined organic phases were washed with sat. aq. NaHCO₃ (100 mL) and brine (50 mL), before they were dried over Na₂SO₄, filtered and concentrated under reduced pressure (Note: GC-MS shows that the desired dichloro-olefin 10 was the major component at this point). The crude product was suspended in CH₂Cl₂ (ca. 40 mL) and the solution was ultrasonicated in a laboratory cleaning bath for 1 min. The obtained slurry was purified by flash chromatography (SiO₂, hexane/EtOAc, 20/1 to 4/1) to give product 12 as a white solid (4.59 g, 64%). m.p. = 51-54 °C (hexane/EtOAc 4/1); [α]_D^20 = +38.2 (c = 0.8, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 5.67 (s, 1H), 4.46 (d, J = 0.5, 1H), 4.01 (dd, J = 8.2, 3.7 Hz, 1H), 3.91 (d, J = 8.2, 1H), 2.97-2.96 (m, 1H), 2.70-2.65 (m, 1H), 2.09-2.00 (m, 2H), 1.72-1.68 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ = 112.5, 76.6, 74.0, 71.8, 48.5, 39.5, 38.4, 37.8; IR (film) ¯ν = 2999, 2973, 2957, 2883, 1437, 1310, 1214, 1140, 1056, 998, 920, 760, 730; MS (El): m/z: 208 (4), 172 (16), 164 (16), 137 (100), 125 (22), 107 (25), 97 (24), 80 (100), 67 (94); HRMS (ESI): m/z: calc. for C₅H₉OCl₂Na: 230.9950 [M+Na]⁺, found: 230.9951. Crystals suitable for X-ray diffraction were obtained by sublimation of a sample at 40°C in vacuum (10⁻³ mbar).

**{(1S,2R,4S)-4-[[tert-Butyldimethylsilyloxy]-2-(prop-1-yn-1-yl)cyclopentane-1-carbaldehyde} (S1).**

Pyridine (5.80 mL, 71.7 mmol) and Dess-Martin-periodinane (5.63 g, 13.3 mmol) were successively added to a solution of alcohol 11 (2.38 g, 8.8 mmol) in CH₂Cl₂ (46 mL). The mixture was stirred for 3 h at room temperature before the reaction was quenched with sat. aq. NaHCO₃ (ca. 10 mL). The mixture was extracted with tert-butyl methyl ether (3 x 30 mL), the combined organic layers were washed with aq. CuSO₄ (1 M, 4 x 10 mL) and brine (2 x 5 mL) before they were dried over Na₂SO₄. Evaporation of the solvent followed by purification of the crude product by flash chromatography (SiO₂, hexane/EtOAc, 40/1) yielded the title compound in the form of a colorless oil (2.09 g, 89%). [α]_D^20 = +31.4 (c = 1.0, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ =
9.92 (d, J = 3.2 Hz, 1H), 4.24 (quint, J = 5.9 Hz, 1H), 3.00 (tdd, J = 11.0, 5.5, 2.5 Hz, 1H), 2.72-2.65 (m, 1H), 2.4 (ddd, J = 13.8, 8.3, 6.0 Hz, 1H), 1.99-1.96 (m, 2H), 1.79-1.72 (m, 1H), 1.78 (d, J = 2.5 Hz, 3H), 0.87 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H); $^1$H NMR (100 MHz, CDCl$_3$): δ = 204.1, 79.9, 78.3, 72.9, 51.5, 43.2, 36.8, 29.5, 25.9, 18.1, 3.7, −4.65, −4.68; IR (film) $	ilde{v}$ = 2930, 2857,1723, 1472, 1361, 1255, 1115, 896, 775; MS (EI): m/z: 266 (0.12), 251 (0.89), 209 (72), 179 (3), 165 (4), 143 (100), 129 (7), 117 (4), 91 (4), 75 (77); HRMS (ESI): m/z: calc. for C$_{14}$H$_{20}$O$_2$SiNa: 289.1594 [M+Na]$^+$, found: 289.1596.

(1R,2R,4S)-4-[(tert-Butyldimethylsilyl)oxy]-2-(prop-1-yn-1-yl)cyclopentane-1-carboxaldehyde (13). K$_2$CO$_3$ (2.17 g, 15.7 mmol) was added in one portion to a solution of aldehyde S1 (2.09 g, 7.84 mmol) in MeOH (200 mL) and the resulting mixture was stirred for 3 h at room temperature. EtOAc (ca. 70 mL) was added, followed by aq. sat. NH$_4$Cl. The aqueous phase was extracted with EtOAc (x 2 70 mL) and the combined organic layers were washed with brine (5 mL), dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The remaining crude material was purified by flash chromatography (SiO$_2$ hexane/toluene, 2/1) to give the title compound as colorless oil (1.84 g, 88%). [α]$_D^{20}$ = −22.4 (c = 1.0, CH$_2$Cl$_2$); $^1$H NMR (400 MHz, CDCl$_3$): δ = 9.73 (d, J = 1.8, 1H), 4.19 (quint., J = 5.7 Hz, 1H), 3.07 (qd, J = 9.0, 1.8 Hz, 1H), 2.79 (dddd, J = 11.3, 9.0, 6.7, 2.4 Hz, 1H), 2.28 (ddd, J = 13.6, 8.3, 5.8 Hz, 1H), 1.93 (ddd, J = 13.5, 8.6, 6.4 Hz, 1H), 1.83 (ddd, J = 13.3, 9.2, 4.2 Hz, 1H), 1.78 (d, J = 2.4 Hz, 3H), 1.76-1.69 (m, 1H), 0.88 (s, 9H), 0.04 (s, 3H), 0.04 (s, 3H); $^1$C NMR (100 MHz, CDCl$_3$): δ = 202.3, 80.6, 77.4, 72.2, 57.1, 43.5, 35.9, 29.1, 25.9, 18.2, 3.7, −4.64, −4.66; IR (film) $	ilde{v}$ = 3097, 2929, 2857, 1725, 1331, 1302, 1253, 1112, 835, 773; MS (EI): m/z: 209 (100), 195 (3), 179 (3), 169 (8), 151 (3), 143 (14), 117 (10), 105 (20), 97 (8), 91 (4), 75 (77); HRMS (ESI): m/z: calc. for C$_{15}$H$_{20}$O$_2$SiNa: 289.1594 [M+Na]$^+$, found: 289.1594.

1-Bromo-3-pentyn-1-ol (14).$^{[13]}$ Br$_2$ (6.65 g, 41.6 mmol) was added dropwise at 0 °C to a solution of PPh$_3$(11.7 g, 44.6 mmol) in MeCN (62 mL) and Et$_3$O (114 mL) and the resulting mixture was stirred for 20 min at this temperature. Imidazole (3.0 g, 44.66 mmol) was then added in portions before 3-pentyn-1-ol (2.5 g, 29.7 mmol) was slowly introduced. The slurry was stirred for 30 min at 0 °C and for 2 h at ambient temperature. The reaction was quenched with sat. aq. NaHCO$_3$ and the aqueous phase extracted with pentane (2 x 100 mL). The combined extracts were dried over Na$_2$SO$_4$, filtered and concentrated (450-350 mbar, 30 °C bath temperature). The obtained solution was filtered twice through a large pad of silica, eluting with pentane. Concentration of the pentane fractions (350 mbar, 30 °C bath temperature) gave the title compound as clear oil (4.35 g, quant.). $^1$H NMR (400 MHz, CDCl$_3$): δ = 3.41 (t, J = 7.4, 2H), 2.69 (tq, J = 2.5, 7.3 Hz, 2H), 1.79 (t, J = 2.5 Hz, 3H); $^1$C NMR (100 MHz, CDCl$_3$): δ = 78.1, 76.2, 30.5, 23.5, 3.6; IR (film) $	ilde{v}$ = 2969, 2919, 2855, 1436, 1336, 1271, 1212, 919, 871, 745, 698, 637, 566, 503; MS (EI): m/z: 148 (42), 146 (43), 93 (2), 67 (100), 53, (16), 41 (41); HRMS (EI): m/z: calc. for C$_7$H$_{12}$BrO: 145.9732 [M], found: 145.9731.

(R)-6-Octyn-2-ol (S2).$^{[14]}$ Bromide 14 (3.59, 24.4 mmol) was added dropwise to a suspension of activated magnesium$^{[15]}$ (832 mg, 34.2 mmol) at 0 °C. The mixture was stirred for 30 min at 0 °C and for 40 min at room temperature. After cooling to −78 °C (15 min cooling time), CuCN (219 mg, 2.44 mmol) followed by (R)-propylene oxide (1.14 mL, 947 mg, 16.3
mmol) was introduced. The resulting mixture was stirred for 30 min at −78 °C before the cooling bath was removed and stirring was continued for 16 h. For work up, the reaction was quenched at 0 °C by the careful addition of sat. aq. NH₄Cl (ca. 30 mL), the obtained slurry was filtered through a pad of Celite to remove the remaining magnesium powder and the filtrate was extracted with tert-butyl methyl ether (4 x 50 mL). The combined organic phases were dried over Na₂SO₄, filtered and concentrated, and the residue was subjected to flash chromatography (SiO₂, hexane/tert-butyl methyl ether, 4/1) to yield the title compound as a pale yellow oil (1.8 g, 88%). \[ \alpha \]D = −10.6 (c = 1.2, CHCl₃); \(^1\)H NMR (400 MHz, CDCl₃): δ = 3.83-3.80 (m, 1H), 2.19-2.13 (m, 2H), 1.78 (t, J = 2.5 Hz, 3H), 1.63-1.48 (m, 4H), 1.36 [s(br), 1H], 1.20 (d, J = 6.2 Hz, 3H); \(^1\)C NMR (100 MHz, CDCl₃): δ = 79.1, 76.0, 67.9, 38.6, 25.4, 23.7, 18.9, 3.6; IR (film) \( \tilde{\nu} = 3351 \text{br}, 2965, 2920, 2863, 1455, 1435, 1373, 1331, 1182, 1127, 1084, 1045, 1004, 990, 943, 862, 733\); MS (EI): m/z: 111 (23), 93 (84), 91 (20), 84 (71), 79 (24), 77 (26), 71 (41), 66 (100), 54 (41), 45 (78); HRMS (EI): m/z: calc. for C₁₇H₂₀O: 236.1415; found: 236.1414.

**Preparation of (S)-Oct-6-yn-2-yl propiolate (16).** Propiolic acid (1.19 g, 16.6 mmol) was dissolved in THF (15 mL) and the solution cooled to 0 °C before diisopropyl azodicarboxylate (2.42 mL, 2.46 g, 12.2 mmol) was added. Next, a solution of alcohol 52 (1.40 g, 11.1 mmol) and PPh₃ (3.79 g, 14.4 mmol) in THF (15 mL) was introduced over the course of 1 h. tert-Butyl methyl ether (100 mL) was added and the obtained red solution was washed with H₂O₂ (10 wt-% in water, 3 x 30 mL) and sat. aq. NaHCO₃ (50 mL). The organic phase was dried over Na₂SO₄, filtered and concentrated to ca. 10 mL (250 mbar). This residue was subjected to flash chromatography (SiO₂, hexane/tert-butyl methyl ether, 30/1) to give the title compound as pale yellow oil (1.30 g, 66%). \[ \alpha \]D = +28.8 (c = 1.2, CHCl₃); \(^1\)H NMR (400 MHz, CDCl₃): δ = 5.04 (dqd, J = 7.5, 6.2, 5.1 Hz, 1H), 2.85 (s, 1H), 2.15 (tt, J = 7.0, 2.6 Hz, 2H), 1.77 (t, J = 2.6 Hz, 3H), 1.75-1.47 (m, 4H), 1.29 (d, J = 6.2 Hz, 3H); \(^1\)C NMR (100 MHz, CDCl₃): δ = 152.5, 78.6, 76.3, 75.2, 74.3, 73.6, 35.0, 24.9, 19.9, 18.7, 3.6; IR (film) \( \tilde{\nu} = 3264, 2981, 2939, 2865, 2115, 1453, 1381, 1231, 1130, 1080, 755;\) MS (EI): m/z: 163 (0.4), 135 (3), 121 (5), 108 (12), 93 (95), 79 (25), 66 (100), 53 (86); HRMS (ESI): m/z: calc. for C₁₁H₁₄O: 201.0887 [M+Na]⁺, found: 201.0886.

**Preparation of (R)-bis(3,5-di-tert-Butylphenyl)(1-methylpyrrolidin-2-yl)methanol (25).** This ligand was prepared in analogy to a literature protocol.\[^{[9][16]}\] Magnesium turnings (682 mg, 28.1 mmol) were combined with iodine (ca. 4 mg) in a 2-neck round bottom flask, equipped with a reflux condenser. The iodine was sublimed via a heatgun and THF (6 mL) was introduced after the iodine vapor had settled, followed by the dropwise addition of a solution of the 3,5-bis-tert-butylphenylbromide in THF (10 mL). The reaction was initiated via gentle heating after addition of ca. 1/3 of the bromide. Once the addition was complete, the mixture was stirred at 80 °C for 2 h. The resulting solution was slowly added to a solution of benzyl 2-methyl (R-pyrrolidine)-1,2-dicarboxylate (N-Cbz d-proline methyl ester, 1.79 g, 6.80 mmol) in THF (7.4 mL) at 0 °C. The mixture was warmed to room temperature and after 8 h, the mixture was filtered through a pad of Celite to remove the remaining magnesium powder and the filtrate was extracted with tert-butyl methyl ether (4 x 50 mL). The combined organic phases were dried over Na₂SO₄, filtered and concentrated to ca. 10 mL (250 mbar). This residue was subjected to flash chromatography (SiO₂, hexane/tert-butyl methyl ether, 4/1) to yield the title compound as a pale yellow oil (1.8 g, 88%). \[ \alpha \]D = −10.6 (c = 1.2, CHCl₃); \(^1\)H NMR (400 MHz, CDCl₃): δ = 3.83-3.80 (m, 1H), 2.19-2.13 (m, 2H), 1.78 (t, J = 2.5 Hz, 3H), 1.63-1.48 (m, 4H), 1.36 [s(br), 1H], 1.20 (d, J = 6.2 Hz, 3H); \(^1\)C NMR (100 MHz, CDCl₃): δ = 79.1, 76.0, 67.9, 38.6, 25.4, 23.7, 18.9, 3.6; IR (film) \( \tilde{\nu} = 3351 \text{br}, 2965, 2920, 2863, 1455, 1435, 1373, 1331, 1182, 1127, 1084, 1045, 1004, 990, 943, 862, 733\); MS (EI): m/z: 111 (23), 93 (84), 91 (20), 84 (71), 79 (24), 77 (26), 71 (41), 66 (100), 54 (41), 45 (78); HRMS (EI): m/z: calc. for C₁₇H₂₀O: 236.1415; found: 236.1414.
temperature and stirred for 2 h. The reaction was carefully quenched with sat. aq. NH₄Cl (10 mL) and extracted with tert-butyl methyl ether (3 x 100 mL). The combined organic phases were washed with sat. aq. NaHCO₃ (30 mL) and brine (30 mL) before they were dried over Na₂SO₄, filtered and concentrated. The residue was purified by flash chromatography (SiO₂, hexane/EtOAc, 9/1) to give a mixture of the target compound 25 and di-tert-butylbenzene.

This mixture was dissolved in THF (90 mL) and cooled to 0 °C before LiAlH₄ (684 mg, 18.0 mmol) was added portionwise over a period of 5 min. The cooling bath was removed and the mixture stirred at 90 °C for 30 min. The reaction was carefully quenched at 0°C with sat. aq. NH₄Cl (ca. 10 mL). A saturated aqueous solution of Rochelle’s salt (5 mL) was added and the mixture was stirred for 45 min. Insoluble material was filtered off through a pad of Celite, the filtrate was checked for a pH > 8 and extracted with tert-butyl methyl ether (3 x 100 mL). The combined organic phases were dried over Na₂SO₄, filtered and concentrated to give a colorless oil containing small amounts of a white solid. This material was dissolved in hexane and kept at 4 °C to allow for crystallization (scratching of the flask with a glass rod was necessary). After 16 h, compound 25 was collected as a white amorphous solid (2.58 g, 77%); after concentration of the mother liquor and repeated crystallization, a second crop of product was obtained (380 mg, 11%). m.p. = 138-142 °C (hexane); [α]D₂₀ = −13.7 (c = 1.0, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 7.55 (d, J = 1.8 Hz, 2H), 7.41 (d, J = 1.8 Hz, 2H), 7.16 (d, J = 2.8, 1.8 Hz, 2H), 4.65 (s, 1H), 3.58 (dd, J = 9.5, 4.9 Hz, 1H), 3.08 (dd, J = 9.5, 7.4 Hz, 1H), 2.45-2.39 (m, 1H), 1.82-1.77 (m, 1H), 1.73 (s, 3H), 1.71-1.57 (m, 3H), 1.30 (s, 18H), 1.29 (s, 18H); ¹³C NMR (100 MHz, CDCl₃): δ = 149.9, 149.8, 147.7, 146.2, 120.1, 119.8, 119.7, 119.5, 77.9, 73.2, 59.5, 43.0, 35.1, 35.0, 31.74, 31.72, 30.0, 24.0; IR (film) υ = 2962, 2904, 2868, 2787, 1598, 1362, 1214, 742, 668; MS (EI): m/z: 476 (0.3), 407 (0.7), 392 (2), 302 (0.6), 217 (4), 161 (2), 133 (1), 84 (100), 57 (5); HRMS (ESI): m/z: calc. for C₃₄H₄₄NO: 492.4200 [M+H]⁺, found: 492.4200.

(5)-Oct-6-yn-2-yl (S)-4-{{(1R,2R,4S)-4-{{(tert-butyldimethylsilyl)oxy}-2-{prop-1-yn-1-yl)cyclopentyl}}-4-hydroxybut-2-ynoate (17). Compound 25 (101 mg, 0.21 mmol, 27.5 mol-%) was dissolved in dry toluene (600 µL). Ester 16 (207 mg, 1.16 mmol) was added, followed by careful addition of Me₂Zn (1.2 M in toluene, 940 µL, 1.13 mmol) and a solution of aldehyde 13 (200 mg, 0.75 mmol) in toluene (840 µL). The mixture was stirred for 16 h at ambient temperature before the reaction was carefully quenched with sat. aq. NH₄Cl. The mixture was extracted with EtOAc (3 x 25 mL), the combined organic phases were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The remaining yellow oil was purified by flash chromatography (SiO₂, hexane/EtOAc, 50/1) to give the title compound as colorless oil (247 mg, 74%).

The reaction was also performed on larger scale, using aldehyde 13 (1.67 g, 6.28 mmol), ester 16 (1.73 g, 9.73 mmol), dimethylzinc (1.2 M in toluene, 7.85 mL, 9.42 mmol), 25 (772 mg, 1.57 mmol, 25 mol-%) and toluene (12 mL) to give the title compound (1.84 g, 66%), which analyzed as follows: [α]D₂₀ = −12.3 (c = 1.0, CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): δ = 5.02 (dd, J = 7.6, 6.2, 5.1 Hz, 1H), 4.68 (dd, J = 7.0, 3.3 Hz, 1H), 4.23 (p, J = 5.8 Hz, 1H), 2.63-2.46 (m, 2H), 2.39 (d, J = 7.0 Hz, 1H), 2.31 (ddd, J
= 13.4, 7.5, 6.1 Hz, 1H), 2.17-2.12 (m, 2H), 1.78-1.77 (m, 6H), 1.75-1.40 (m, 7H), 1.28 (d, J = 6.2 Hz, 3H), 0.88 (s, 9H), 0.04 (s, 6H); 13C NMR (100 MHz, CDCl3): δ = 153.1, 86.3, 81.1, 78.6, 77.7, 77.4, 76.2, 73.3, 71.8, 63.6, 49.8, 43.8, 36.6, 35.0, 30.0, 26.0, 24.9, 20.0, 18.7, 18.2, 3.7, 3.6, −4.61, −4.63; IR (film) υ = 3461br, 2929, 2856, 2233, 1709, 1462, 1378, 1360, 1252, 1112, 1051, 836, 775; MS (EI): m/z: 401 (5), 387 (30), 279 (39), 209 (12), 187 (14), 169 (11), 161 (11), 159 (13), 141 (12), 131 (17), 115 (11), 109 (93), 105 (19), 91 (20), 75 (100), 67 (42); HRMS (ESI): m/z: calc. for C26H40O5SiNa: 467.2597 [M+Na]+, found: 467.2588.

(S)-Oct-6-yn-2-yl (R,E)-4-[(1R,2R,4S)-4-[(tert-butylidimethylsilyl)oxy]-2-{prop-1-yn-1-yl)cyclopentyl]-4-hydroxybut-2-enoate (S3).[10] Red-Al (65 wt-% in toluene, 3.03 mL, 10.1 mmol) was added dropwise at −78 °C to a solution of compound 17 (2.25 g, 5.05 mmol) in THF (76 mL) and the resulting mixture was stirred at this temperature for 20 min. Sat. aq. NH4Cl was then used to quench the reaction. The resulting mixture was allowed to warm to room temperature before it was extracted with EtOAc [4 x 50 mL, in order to facilitate extraction, saturated aq. Rochelle’s salt solution (15 mL) was added]. The combined organic phases were dried over Na2SO4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (SiO2, hexane/EtOAc , 12/1) to give the title compound as pale yellow oil (2.10 g, 93%). [α]D20 = −9.5 (c = 1.0, CH2Cl2); 1H NMR (400 MHz, CDCl3): δ = 6.98 (dd, J = 4.5, 15.6 Hz, 1H), 6.06 (dd, J = 1.8, 15.6 Hz, 1H), 4.99 (sext., J = 6.3 Hz, 1H), 4.52-4.48 (m, 1H), 4.21-4.15 (m, 1H), 2.51-2.43 (m, 1H), 2.38-2.24 (m, 2H), 2.14 (tq, J = 7.0, 2.5 Hz, 2H), 1.79-1.77 (m, 6H), 1.73-1.46 (m, 7H), 1.26 (d, J = 6.2 Hz, 3H), 0.87 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H); 13C NMR (100 MHz, CDCl3): δ = 166.2, 149.1, 121.2, 81.3, 78.8, 76.9, 76.1, 72.0, 71.1, 70.9, 49.8, 43.7, 35.3, 35.2, 30.6, 26.0, 25.1, 20.2, 18.8, 18.2, 3.7, 3.6, −4.60, −4.61; IR (film) υ = 3472br, 2952, 2929, 2857, 2857, 1716, 1699, 1462, 1360, 1254, 1172, 1114, 1084, 1051, 903, 835, 774; MS (EI): m/z: 403 (8), 389 (50), 347 (15), 281 (18), 189 (18), 169 (15), 129 (17), 109 (75), 75 (100), 67 (46); HRMS (ESI): m/z: calc. for C26H40O5SiNa: 469.2745 [M+Na]+, found: 469.2745.

(S)-Oct-6-yn-2-yl (R,E)-4-[(tert-butylidimethylsilyl)oxy]-4-[(1R,2R,4S)-4-[(tert-butylidimethylsilyl)oxy]-2-{prop-1-yn-1-yl)cyclopentyl]but-2-enoate (18). Pyridine (614 µL, 60 mg, 7.59 mmol) and TBSOTf (871 µL, 1.00 g, 3.79 mmol) were added at 0 °C to a solution of compound S3 (1.13 g, 2.53 mmol) in CH2Cl2, and the resulting mixture was stirred at this temperature for 30 min. The reaction was quenched with sat. aq. NaHCO3 and the mixture extracted with EtOAc (3 x 20 mL). The combined organic phases were washed with aq. CuSO4 (1 M, 5 x 10 mL) and brine (10 mL), dried over Na2SO4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (neutral Al2O3, hexane/EtOAc, 20/1) to give the title compound as colorless oil (1.32 g, 93%). [α]D20 = −16.4 (c = 1.0, CHCl3); 1H NMR (400 MHz, CDCl3): δ = 6.89 (dd, J = 4.8, 15.6 Hz, 1H), 5.93 (dd, J = 1.7, 15.6 Hz, 1H), 4.98 (dq, J = 12.4, 6.2 Hz, 1H), 4.48-4.46 (m, 1H), 4.16-4.10 (m, 1H), 2.43-2.34 (m, 1H), 2.27-2.11 (m, 4H), 1.79-1.77 (m, 6H), 1.75-1.58 (m, 4H), 1.54-1.39 (m, 3H), 1.26 (d, J = 6.2 Hz, 3H), 0.92 (s, 9H), 0.86 (s, 9H), 0.08 (s, 3H), 0.02 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H); 13C
NMR (100 MHz, CDCl₃): δ = 166.3, 150.6, 120.6, 81.4, 78.8, 76.4, 76.0, 72.2, 70.74, 70.72, 50.5, 43.7, 35.3, 34.3, 30.7, 26.04, 26.02, 25.1, 20.2, 18.8, 18.31, 18.27, 3.7, 3.6, –4.1, –4.6, –5.0; IR (film) û = 2954, 2930, 2898, 2857, 1719, 1658, 1472, 1463, 1361, 1256, 1170, 1129, 712, 776; MS (EI): m/z: 503 (83), 395 (18), 371 (23), 295 (9), 263 (33), 245 (13), 197 (10), 171 (19), 109 (64), 75 (75), 73 (100), 67 (33); HRMS (ESI): m/z: calc. for C₉₇H₅₅O₃Si₂Na: 583.3611 [M+Na]⁺; found: 583.3609.

**Cycloalkyne 19.** A flame-dried round bottom flask, equipped with a reflux condenser, was charged with molecular sieves (5Å, 3.75 g, powder (dried prior to use at 150 °C under high vacuum)). A solution of diyne 18 (1.25 g, 2.23 mmol) in dry toluene (560 mL) was added and the slurry was stirred for 30 min before it was heated to 80 °C (oil bath temperature). The reaction was initiated by the addition of a solution of complex 26 (123 mg, 118 µmol, 5 mol-%) in toluene (5 mL). After stirring for 45 min the mixture was diluted with EtOAc (60 mL) and filtered through a pad of neutral Al₂O₃ which was rinsed with EtOAc (70 mL). The combined filtrates were concentrated under reduced pressure and the residue purified by flash chromatography (neutral Al₂O₃, hexane/EtOAc, 80/1) to give the title compound as colorless oil (752 mg, 67%). [α]D²⁰ = −28.6 (c = 1.1, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 7.59 (dd, J = 2.9, 15.4 Hz, 1H), 5.95 (dd, J = 1.9, 15.4 Hz, 1H), 5.02-4.93 (m, 1H), 4.21-4.14 (m, 1H), 3.96 (dddd, J = 1.9, 3.0, 9.4 Hz, 1H), 2.35-2.14 (m, 4H), 2.01-1.88 (m, 2H), 1.79-1.60 (m, 4H), 1.56-1.38 (m, 2H), 1.28 (dd, J = 6.4 Hz, 3H), 0.93 (s, 9H), 0.87 (s, 9H), 0.05 (s, 3H), 0.03 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ = 166.6, 152.4, 118.5, 82.9, 81.9, 76.1, 71.8, 71.0, 53.9, 41.9, 36.0, 31.5, 29.9, 26.0, 24.8, 21.1, 19.4, 18.3, 18.2, −4.0, −4.6, −4.7; IR (film) û = 2954, 2929, 2856, 1717, 1463, 1362, 1255, 837, 775; MS (EI): m/z: 449 (84), 373 (6), 317 (16), 289 (7), 251 (100), 197 (8), 73 (64); HRMS (ESI): m/z: calc. for C₂₆H₂₅O₃Si₂Na: 529.3142 [M+Na]⁺; found: 529.3140.

**Compound 20.** HCl (2 mL, 1 mL) was added to a solution of compound 19 (75 mg, 0.15 mmol) in THF (5.5 mL) and water (5.5 mL). The mixture was stirred for 39 h before the reaction was quenched with sat. aq. NaHCO₃ (ca. 4 mL) and extracted with tert-butyl methyl ether (3 x 25 mL). The combined organic phases were dried over Na₂SO₄, filtered and concentrated and the residue was purified by flash chromatography (SiO₂, hexane/EtOAc, 1/2) to give the title compound as a white solid (38 mg, 92%). m.p. = 189-191 °C (CDCl₃); [α]D²⁰ = −13.7 (c = 0.66, acetone); ¹H NMR (400 MHz, CD₃OD): δ = 7.76 (dd, J = 15.5, 2.8 Hz, 1H), 5.90 (dd, J = 15.5, 2.0 Hz, 1H), 4.94-4.83 (m, 1H), 4.23-4.18 (m, 1H), 4.01 (dt, J = 9.4, 2.3 Hz, 1H), 2.47 (dddt, J = 11.2, 9.0, 5.0, 3.1 Hz, 1H), 2.38 (dd, J = 13.1, 8.6 Hz, 1H), 2.30-2.23 (m, 1H), 2.10-2.00 (m, 2H), 1.97-1.89 (m, 1H), 1.83-1.70 (m, 3H), 1.69-1.59 (m, 2H), 1.26 (d, J = 6.3 Hz, 3H), 1.18-1.10 (m, 1H); ¹³C NMR (100 MHz, CD₃OD): δ = 168.4, 155.0, 118.0, 83.8, 82.8, 76.1, 72.7, 72.0, 54.5, 44.4, 41.6, 36.9, 32.7, 25.9, 21.1, 19.9; IR (film) û = 3364 (br), 3278 (br), 2970, 2948, 2926, 2865, 1711, 1438, 1258, 1111, 1064, 987; MS (ESI): m/z: 301 [M+Na]⁺; HRMS (ESI): m/z: calc. for C₂₈H₂₆O₃Na: 301.1410 [M+Na]⁺; found: 301.1411. Crystals suitable for X-ray diffraction were obtained by slow evaporation of the solvent from a solution of the compound in MeOH/acetone.
Compound 21. In a flame dried Schlenk tube [Cp*Ru(MeCN)_3]PF_6 (57 mg, 0.11 mmol, 5 mol-%) was dissolved in CH_2Cl_2 (15 mL). A solution of cycloalkyne 19 (1.15 g, 2.27 mmol) in CH_2Cl_2 (5 mL) was added with stirring before this mixture was transferred under Ar via cannula into a pre-dried autoclave. The Schlenk tube was rinsed with additional CH_2Cl_2 (8 mL), which was also added. The autoclave was pressurized with H_2 (30 bar). After stirring for 4 h, the autoclave was vented and the remaining yellow solution filtered through a pad of neutral Al_2O_3 which was carefully rinsed with EtOAc (50 mL). The combined filtrates were concentrated and the remaining pale brown oil was subjected to flash chromatography (neutral Al_2O_3, hexane/EtOAc, 90/1) to give a mixture of 21 and isomers (981 mg, 85%) (as well as a small amount of overreduced product). This material was purified by preparative HPLC (Nucleodur C18 H Tec, 10 μm, 250 x 40, eluent MeOH/H_2O 95/5, 75 mL/min) to give pure 21 as a colorless oil (642 mg, 56%). \[^{10}\alpha_2^D = +20.1 \text{ [c} = 0.9, \text{ CHCl}_3, \text{ lit.}^{[11]} \] \[^{10}\alpha_2^D = +22 \text{ [c} = 0.72, \text{ CHCl}_3] \]. \(^1\)H NMR (300 MHz, CDCl_3): \( \delta = 7.28 \) (dd, \( J = 3.2, 15.5 \) Hz, 1H), 5.87 (dd, \( J = 1.8, 15.5 \) Hz, 1H), 5.62 (ddd, \( J = 4.5, 10.1, 14.9 \) Hz, 1H), 5.26 (dd, \( J = 9.5, 15.2 \) Hz, 1H), 4.89 (ddq, \( J = 1.8, 6.3, 10.9 \) Hz, 1H), 4.22-4.16 (m, 1H), 4.01 (dd, \( J = 1.7, 3.0, 9.2 \) Hz, 1H), 2.30-2.17 (m, 1H), 2.09-1.93 (m, 4H), 1.87-1.64 (m, 3H), 1.59-1.42 (m, 3H), 1.25 (d, \( J = 6.2 \) Hz, 3H), 1.00-0.93 (m, 1H), 0.93 (s, 9H), 0.88 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H); \(^{13}\)C NMR (75 MHz, CDCl_3): \( \delta = 166.6, 152.6, 137.5, 129.5, 118.3, 76.6, 73.0, 71.5, 53.0, 44.0, 43.9, 42.3, 34.3, 32.0, 26.9, 26.0, 21.1, 18.3, 18.2, –3.9, –4.57, –4.60, –4.7; IR (film) \( \tilde{\nu} = 2954, 2930, 2857, 1716, 1472, 1462, 1361, 1254, 1122, 1078, 837, 775; MS (EI): m/z: 508 (3), 493 (2), 451 (100), 433 (18), 361 (24), 343 (13), 319 (33), 301 (18), 291 (12), 227 (13), 199 (26), 185 (11), 147 (12), 129 (11), 73 (62); HRMS (ESI): m/z: calc. for C_{20}H_{23}O_{5}Si_{2}Na: 531.3297 [M+Na]^+; found: 531.3296.

(+) - Brefeldin A (1). \(^{[11]}\) HCl (2 M in water, 8.2 mL) was added to a solution of compound 21 (632 mg, 1.24 mmol) in THF (46 mL) and water (46 mL) and the resulting mixture was stirred for 39 h at ambient temperature. The reaction was quenched by the addition of aq. sat. NaHCO_3 and the aqueous layer extracted with tert-butyl methyl ether (3 x 50 mL). The combined extracts were dried over Na_2SO_4, filtered and concentrated and the residue was purified by flash chromatography (SiO_2, hexane/EtOAc, 1/2) to give (+)-brefeldin A as a white solid (327 mg, 94%). m.p. = 202-204 °C (MeOH, lit.\(^{[12]}\) 202-203 °C); \(^1\)H NMR (400 MHz, CD_3OD): \( \delta = 7.46 \) (dd, \( J = 15.6, 3.0 \) Hz, 1H), 5.82 (dd, \( J = 15.7, 2.0 \) Hz, 1H), 5.75 (ddd, \( J = 4.6, 10.5, 15.0 \) Hz, 1H), 5.28 (dd, \( J = 9.6, 15.1 \) Hz, 1H), 4.80 (ddq, \( J = 1.8, 6.3, 11.0 \) Hz, 1H), 4.24-4.19 (m, 1H), 4.04 (ddd, \( J = 2.0, 3.1, 9.5 \) Hz, 1H), 2.39 (quint, \( J = 8.5 \) Hz, 1H), 2.13 (ddd, \( J = 5.3, 8.8, 13.2 \) Hz, 1H), 2.05-1.98 (m, 2H), 1.89-1.73 (m, 5H), 1.62-1.54 (m, 1H), 1.45 (dd, \( J = 1.3, 5.4, 8.0, 13.3 \) Hz, 1H), 1.24 (d, \( J = 6.2 \) Hz, 3H), 0.94 – 0.85 (m, 1H); \(^{13}\)C NMR (100 MHz, CD_3OD): \( \delta = 168.3, 155.1, 138.1, 131.4, 117.7, 76.6, 73.2, 73.0, 53.2, 45.4, 44.1, 41.8, 35.0, 33.0, 28.0, 21.1; IR (film) \( \tilde{\nu} = 3352 \) (br), 3307 (br), 2923, 2893, 2854, 2495, 2455, 1709, 1448, 1255, 1109, 1070, 975; MS (ESI): m/z: 303 [M+Na]^+; HRMS (ESI): m/z: calc. for C_{19}H_{22}O_{5}Na: 303.1567 [M+Na]^+; found: 303.1567. Crystals suitable for X-ray diffraction were obtained by slow evaporation of the solvent from a solution of the compound in MeOH/acetone.
### Table S-1. Comparison of $^1$H NMR data ([D$_4$]-MeOH) of (+)-Brefeldin A

| $\delta$, ppm | $J$ (Hz) | literature$^{[12]}$ | $\Delta\delta$ (ppm) |
|---------------|----------|---------------------|---------------------|
| $\delta$, ppm | $J$ (Hz) | $\delta$, ppm | $J$ (Hz) | $\delta$, ppm |
| 7.46 | 15.6, 3.0 | 7.45 | 15.6, 3.0 | 0.01 |
| 5.82 | 15.7, 2.0 | 5.82 | 15.7, 2.0 | 0.00 |
| 5.75 | 4.6, 10.5, 15.0 | 5.75 | 4.6, 10.2, 15.0 | 0.00 |
| 5.28 | 9.6, 15.1 | 5.27 | 9.6, 15.1 | 0.01 |
| 4.80 | 1.8, 6.3, 11.0 | 4.78 | - | 0.02 |
| 4.24-4.19 | - | 4.21 | - | 0.00 |
| 4.04 | 2.0, 3.1, 9.5 | 4.03 | - | 0.01 |
| 2.39 | 8.5 | 2.38 | 8.7 | 0.01 |
| 2.13 | 5.3, 8.8, 13.2 | 2.12 | 5.4, 8.7, 13.6 | 0.01 |
| 2.05-1.98 | - | 2.05-1.97 | - | 0.00 |
| 1.89-1.73 | - | 1.90-1.70 | - | 0.01 |
| 1.62-1.54 | - | 1.55 | - | 0.03 |
| 1.45 | 1.3, 5.4, 8.0, 13.3 | 1.42 | - | 0.03 |
| 1.24 | 6.2 | 1.23 | 6.2 | 0.01 |
| 0.94-0.85 | - | 0.90 | - | 0.00 |

### Table S-2. Comparison of $^{13}$C NMR data ([D$_4$]-MeOH) of (+)-Brefeldin A

| $\delta$, ppm | literature$^{[12]}$ | $\Delta\delta$ (ppm) |
|---------------|---------------------|---------------------|
| $\delta$, ppm | $\delta$, ppm | $\Delta\delta$ (ppm) |
| 168.3 | 168.7 | -0.4 |
| 155.1 | 155.4 | -0.3 |
| 138.1 | 138.4 | -0.3 |
| 131.4 | 131.7 | -0.3 |
| 117.7 | 118.1 | -0.4 |
| 76.6 | 76.9 | -0.3 |
| 73.2 | 73.5 | -0.3 |
| 73.0 | 73.3 | -0.3 |
| 53.2 | 53.5 | -0.3 |
| 45.4 | 45.8 | -0.4 |
| 44.1 | 44.4 | -0.3 |
| 41.8 | 42.1 | -0.3 |
| 35.0 | 35.3 | -0.3 |
| 33.0 | 33.3 | -0.3 |
| 28.0 | 28.3 | -0.3 |
| 21.1 | 21.3 | -0.2 |
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