Supporting Information
for
A unified approach to the important protein kinase inhibitor balanol and a proposed analogue

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Experimental details and characterization data for the prepared compounds are included. Copies of $^1$H and $^{13}$C NMR spectra of all new compounds are also provided. Data for comparison of 30 and 1 with reported data are also presented

Table of contents

1. Experimental procedures .................................................................S2

2. $^1$H- and $^{13}$C-NMR spectra of all new compounds ................................S15

3. Comparison of data ........................................................................S39

4. References .....................................................................................S40
Experimental
General
Optical rotations were recorded in spectroscopic grade chloroform on a Jasco DIP-370 polarimeter, \([\alpha]_D\) values are recorded in units of \(10^{-1}\) deg cm\(^2\) g\(^{-1}\). Infrared spectra were recorded on a Perkin-Elmer Spectrum-1 spectrophotometer purchased through a DST-FIST grant. Proton and carbon NMR spectra were recorded on a Bruker DRX-300 spectrometer. Chemical shifts are recorded relative to residual solvent or TMS as standard. Mass spectra were recorded on a JEOL-JMS 600 instrument from I. I. C. B., Kolkata or IACS, Kolkata. Petroleum ether refers to the fraction boiling in the range 60–80 °C. Silica gel (60–120 mesh) for column chromatography was purchased from Spectrochem, India.

2-(1,3-Dioxan-2-yl)-6-(methoxymethoxy)benzaldehyde (9):

\(n\)-BuLi (5.5 mL, 2 M in hexane) was added dropwise to a stirred solution of 2-(3-(methoxymethoxy)phenyl)-1,3-dioxane [1] (2.24 g, 10 mmol) in cyclohexane (15 mL) at room temperature and stirring was continued for 15 min. Then DMF (2.25 mL, 30 mmol) was slowly added to this reaction mixture and stirred for another 30 min. It was then quenched by slow addition of brine (20 mL) and extracted with ethyl acetate (2 \(\times\) 50 mL). The combined organic extract was washed successively with water (2 \(\times\) 50 mL) and brine (50 mL), and then dried (\(\text{Na}_2\text{SO}_4\)). It was filtered and the filtrate was concentrated in vacuo to leave a crude mass which on chromatographic purification over silica gel using a mixture of petroleum ether/ethyl acetate (95:5) as eluent provided compound 9 as a pale yellow solid (1.63 g, 65%). mp 58-60 °C. IR (KBr): 2930, 1694, 1598, 1590 cm\(^{-1}\).\(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 10.63 (s, 1H), 7.54–7.50 (m, 2H), 7.27–7.21 (m, 1H), 6.26 (s, 1H), 5.27 (s, 2H), 4.23 (dd, \(J = 1.6, 5.2\) Hz, 2H), 4.06 (dt, \(J = 12, 1.6\) Hz, 2H), 3.49 (s, 3H), 2.25-2.20 (m, 1H), 1.47–1.43 (m, 1H).\(^1\)C NMR (100 MHz, CDCl\(_3\)): δ 192.0, 159.8, 139.9, 134.7, 122.9, 119.9, 115.6, 97.8, 94.7, 67.6, 56.4, 25.8; HRMS (TOF MS ES+): \(m/z\) calcd for C\(_{13}\)H\(_{16}\)NaO\(_5\) (M\(^{+}\)+Na): 275.0895. Found: 275.0893.

(2-(1,3-Dioxan-2-yl)-6-(methoxymethoxy)phenyl)(2,6-bis(benzyloxy)-4-((tert-butyldiphenylsilyloxy)methyl)phenyl)methanol (10):

\(n\)-BuLi (0.7 mL, 2 M in hexane) was added dropwise to a stirred solution of 8 (0.955 g, 1.5 mmol) in THF (10 mL) at −78 °C, and stirring was continued for 5 min. A solution of the aldehyde 9 (250 mg, 1 mmol) in THF (5 mL) was then added dropwise to the reaction mixture at −78 °C. It was allowed to
come to room temperature over 2 h and then cooled to 0 °C before being quenched with saturated aqueous NH₄Cl (5 mL). It was extracted with ethyl acetate (2 × 50 mL) and the combined organic extract was washed successively with water (50 mL) and brine (50 mL). It was then dried (Na₂SO₄), filtered and the filtrate was concentrated in vacuo to leave a crude mass which was purified by chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (85:15) as eluent to provide compound 10 as a colourless viscous liquid (0.6 g, 75%). IR (KBr): 3469, 2928, cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.62 (d, J = 1.2 Hz, 4H), 7.43-7.41 (m, 3H), 7.4-7.34 (m, 4H), 7.32-7.23 (m, 6H), 7.21-7.12 (m, 4H), 6.98 (d, J = 12 Hz, 1H), 6.70 (d, J = 7.6 Hz, 1H), 6.56 (s, 2H), 6.11 (s, 1H), 5.23 (d, J = 8 Hz, 1H), 4.99 (s, 4H), 4.8 (dd, J = 10.8, 6.8 Hz, 2H), 4.63 (s, 2H), 4.13-4.08 (m, 2H), 4.63 (s, 2H), 4.13-4.08 (m, 2H), 3.98-3.82 (m, 1H), 3.69 (t, J = 12 Hz, 1H), 2.92 (s, 3H), 1.32-1.28 (m, 1H), 2.18-2.09 (m, 1H), 1.04 (s, 9H). ¹³C NMR (100 MHz, CDCl₃): δ 157.1, 154.7, 141.4, 138.2, 136.9, 135.5, 133.4, 130.5, 129.7, 128.5, 127.7, 127.2, 119.5, 118.6, 114.6, 103.7, 99.1, 93.7, 70.5, 67.3, 67.2, 66.7, 65.3, 55.4, 26.8, 25.7, 19.3. MS (TOF MS ES+): m/z (%) = 834 (M⁺+Na, 100).

(2-(1,3-Dioxan-2-yl)-6-{methoxymethoxy)phenyl][2,6-bis(benzyloxy)-4-((tert-butyldiphenylsilyloxy)methyl)phenyl)methanone (11):

A solution of the benzylic alcohol 10 (0.81 g, 1 mmol) in CH₃CN (15 mL) was stirred for 15 min in the presence of molecular sieves (4 Å, 2 g). 4-Methylmorpholine N-oxide (0.175 g, 1.5 mmol) and tetrapropylammonium perruthenate (17.5 mg, 0.05 mmol) were then sequentially added and the resulting mixture was stirred for 18 h at room temperature. It was then diluted with ethyl acetate, filtered through Celite, concentrated in vacuo and the residual mass was purified by chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (85:15) to provide compound 11 as a colourless viscous liquid (0.645 g, 80%). IR (KBr): 2930, 2865, 1674, 1606, 1589 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.61 (d, J = 6.8 Hz, 4H), 7.43 (dt, J = 6.4, 0.8 Hz, 3H), 7.35 (m, 5H), 7.25-7.21 (m, 6H), 7.11-7.10 (m, 4H), 6.98 (d, J = 8 Hz, 1H), 6.55 (s, 2H), 5.61 (s, 1H), 4.96 (s, 4H), 4.73 (s, 2H), 4.66 (s, 2H), 4.08 (dd, J = 11.2, 4.4 Hz, 2H), 3.74 (t, J = 12 Hz, 2H), 2.95 (s, 3H), 2.1-2.14 (m, 1H), 1.31-1.24 (m, 1H), 1.06 (s, 9H). ¹³C NMR (100 MHz, CDCl₃): δ 194.7, 157.8, 154.2, 145.5, 138.2, 136.7, 135.5, 133.2, 132.1, 130.2, 129.8, 128.4, 127.8, 127.5, 126.9, 119.9, 119.8, 115.2, 102.8, 99.5, 94.1, 70.0, 67.3, 65.3, 55.5, 26.8, 25.7, 19.3. HRMS (TOF MS ES+): m/z calcd for C₅₀H₃₃O₈Si(M⁺+H): 809.3501. Found: 809.3505 (M⁺+H).
2-(2,6-Bis(benzyloxy)-4-((tert-butyldiphenylsilyloxy)methyl)benzoyl)-3-(methoxymethoxy)benzaldehyde (12):

p-Toluenesulfonic acid (25 mg) was added to a solution of the benzophenone 11 (0.81 g, 1 mmol) in acetone/water (20 mL, 9:1) and the resulting solution was refluxed gently for 4 h. It was allowed to come to room temperature, concentrated in vacuo and then diluted with ethyl acetate (200 mL). The ethyl acetate extract was washed successively with water (100 mL) and brine (100 mL), and then dried (Na₂SO₄). It was filtered and the filtrate was concentrated in vacuo to leave a crude mass which was purified by chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (85:15) as eluent to provide compound 12 as a colourless viscous liquid (0.67 g, 89%).

IR (KBr): 2932, 2859, 1693, 1672, 1584 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 9.95 (s, 1H), 7.63 (d, J = 6.8 Hz, 4H), 7.46-7.43 (m, 3H), 7.38-7.35 (m, 5H), 7.25-7.19 (m, 7H), 7.11-7.08 (m, 4H), 6.61 (s, 2H), 4.93 (s, 4H), 4.81 (s, 2H), 4.70 (s, 2H), 3.00 (s, 3H), 1.08 (s, 9H).

¹³C NMR (100 MHz, CDCl₃): δ 194.0, 191.3, 157.7, 154.6, 146.2, 136.5, 136.2, 136.1, 135.5, 133.2, 130.5, 129.9, 128.5, 127.9, 127.8, 127.2, 120.9, 119.5, 119.2, 102.7, 94.2, 70.4, 65.3, 55.8, 26.9, 19.3. MS (TOF MS ES⁺): m/z (%) = 774 (M⁺+Na, 100).

General procedure of the NaClO₂-oxidation of an aldehyde to a carboxylic acid:

Aq. NaH₂PO₄ (1.5 mL, 1 M), 1-methylcyclohexene (120 µL, 1 mmol) and NaClO₂ (181 mg, 2 mmol) were sequentially added to a solution of the aldehyde (0.5 mmol) in THF-t-BuOH-water (5 mL, 4:4:1), and the resulting mixture was stirred for 6-8 h at room temperature before being treated with aqueous KHSO₄ (5 mL, 0.5 M). The resulting reaction mixture was concentrated in vacuo and then extracted with ethyl acetate (2 × 50 mL). The combined organic extract was washed successively with water (50 mL), saturated aqueous sodium sulfite (10 mL) and brine (50 mL). It was then dried (Na₂SO₄), filtered and the filtrate was concentrated in vacuo to leave a crude mass which was purified by chromatography over silica gel to produce the corresponding pure carboxylic acid.

2-(2,6-Bis(benzyloxy)-4-((tert-butyldiphenylsilyloxy)methyl)benzoyl)-3-(methoxymethoxy)benzoic acid (13):

Yield: 82%. IR (KBr): 3403, 1767, 1696 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 8.43 (s), 7.63 (dd, J = 7.6, 1.2 Hz), 7.46-7.35 (m), 7.22-7.21 (m), 7.08-7.06 (m), 6.80-6.78 (m), 6.55 (brs), 5.23 (brs), 5.16 (d, J = 6.4 Hz), 5.50 (d, J = 6.4 Hz), 4.92 (br s), 4.71-4.69 (overlapping singlets), 3.17(s), 1.07 (s). ¹³C NMR (100 MHz, CDCl₃): δ 191.8, 170.7, 169.1, 159.1, 156.9, 154.1, 151.1, 146.6, 144.2, 139.7, 136.4, 135.5,
135.2, 133.2, 130.7, 129.9, 129.1, 129.0, 128.7, 128.5, 128.3, 127.8, 127.6, 127.3, 123.7, 119.4, 118.9, 117.8, 112.0, 105.6, 104.5, 104.1, 102.9, 94.5, 93.8, 72.7, 70.7, 70.5, 65.3, 65.0, 55.9, 55.8, 29.7, 26.8, 19.3. HRMS (TOF MS ES+): m/z calcd for C47H46NaO8Si (M+ + Na): 789.2860. Found: 789.2858. [spectral data revealed the presence of an equilibrium between ketocarboxilic acid and its hemiketal form and hence counting of protons is not included. This has also been observed [2] by Nicolaou et al.].

3,5-Bis(benzyloxy)-4-(2-benzylxoy)-6-benzylxycarbonylbenzoic acid (7):

Yield: 87%. IR (KBr): 3441, 1718, 1698, 1652, 1583 cm⁻¹. mp 158-160 °C [Lit. [2] mp 158-160 °C]; ¹H NMR (400 MHz, CDCl₃): δ 7.33-7.0 (m, 16H), 7.14 (t, J = 7.2 Hz, 2H), 7.08-7.07 (m, 4H), 6.97 (d, J = 8.4 Hz, 1H), 6.85 (d, J = 7.6 Hz, 2H), 5.14 (s, 2H), 4.80 (s, 4H), 4.72 (s, 2H). ¹³C NMR (100 MHz, CDCl₃): δ 191.7, 171.0, 167.6, 157.9, 156.5, 136.1, 135.8, 135.6, 133.1, 131.7, 131.6, 130.9, 128.4, 128.3, 128.0, 127.7, 127.2, 124.7, 122.1, 115.2, 107.2, 70.6, 70.4, 67.2.

2-(2,6-Bis(benzyloxy)-4-(hydroxymethyl)benzoyl)-3-hydroxybenzoic acid (14):

Hydrochloric acid (12 N, 0.2 mL) was added to a solution of the carboxylic acid 13 (380 mg, 0.5 mmol) in methanol (6 mL) and the resulting mixture was stirred at 50 °C for 2 h. It was then concentrated in vacuo, diluted with water (25 mL) and extracted with ethyl acetate (2 × 25 mL). The combined organic extract was successively washed with saturated sodium bicarbonate (2 × 25 mL), water (25 mL) and brine (25 mL). It was then dried (Na₂SO₄), filtered and the filtrate was concentrated in vacuo to leave a crude solid which was purified over silica gel using a mixture of petroleum ether/ethyl acetate/methanol (50:48:2) to provide compound 14 as a colourless solid (200 mg, 83%). mp 210-212 °C. IR (KBr): 3488, 2865, 1692, 1625, 1610, 1576 cm⁻¹. ¹H NMR (400 MHz, DMSO-d₆): δ 10.04 (s, 1H), 7.28-7.24 (m, 7H), 7.20-7.18 (m, 4H), 7.02 (d, J = 7.6 Hz, 1H), 6.89 (dd, J = 8, 0.4 Hz, 1H), 6.72 (s, 2H), 5.36 (brs, 1H), 4.98 (s, 4H), 4.48 (s, 2H). ¹³C NMR (100 MHz, DMSO-d₆): δ 193.1, 169.4, 158.3, 156.7, 147.8, 137.4, 134.8, 131.3, 128.6, 128.5, 127.8, 127.3, 120.0, 119.4, 118.5, 103.8, 70.1, 63.2. Anal. Calcd for C₂₉H₂₄O₇: C, 71.89; H, 4.99. Found: C, 71.62; H, 5.27.
Benzyl 3-(benzyloxy)-2-(2,6-bis(benzyloxy)-4 (hydroxymethyl)benzoyl) benzoate (15):

Potassium carbonate (175 mg, 1.25 mmol) was added to a stirred solution of 14 (0.242 g, 0.5 mmol) and benzyl bromide (125 µL, 1.05 mmol) in N,N-dimethylformamide (10 mL) and the resulting solution was stirred for 24 h at room temperature. The reaction mixture was then poured into water (50 mL) and extracted with ethyl acetate (2 × 25 mL). The combined organic extract was successively washed with water (2 × 25 mL) and brine (25 mL). It was then dried (Na₂SO₄), filtered and concentrated in vacuo to leave a crude solid which was purified over silica gel using a mixture of petroleum ether/ethyl acetate (6:4) to provide the O-benzylated compound 15 as a colourless solid (0.26 g, 78%). mp 138-140 °C [Lit. [2] mp 138.5-139.5 °C]; IR (KBr): 3293, 1697, 1656, 1614, 1535 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.22-7.21 (m, 5H), 7.20-7.15 (m, 9H), 7.13-7.12 (m, 2H), 7.09-7.06 (m, 4H), 6.97 (d, J = 7.2 Hz, 2H), 6.89 (d, J = 8 Hz, 1H), 6.50 (s, 2H), 5.12 (s, 2H), 4.77 (s, 6H), 4.60 (d, J = 3.2 Hz, 2H) 1.89 (brs, 1H). ¹³C NMR (100 MHz, CDCl₃): δ 192.4, 167.0, 159.0, 155.8, 147.0, 136.6, 136.3, 136.0, 134.4, 131.5, 129.6, 128.3, 128.2, 128.1, 127.9, 127.6, 127.5, 127.2, 127.1, 122.2, 118.3, 115.6, 103.4, 70.5, 70.4, 66.8, 64.6. HRMS (TOF MS ES+): m/z calcd for C₄₃H₃₆NaO₇: 687.2359 (M⁺+Na): Found : 687.2357.

Benzyl 3-(benzyloxy)-2-(2,6-bis(benzyloxy)-4-formylbenzoyl) benzoate (16):

A solution of the alcohol 15 (332 mg, 0.5 mmol) in dichloromethane (10 mL) was stirred with MnO₂ (435 mg, 5 mmol) for 12 h. It was then filtered through Celite and the filtrate was concentrated in vacuo to leave a crude mass which was purified over silica gel using a mixture of petroleum ether/ethyl acetate (3:1) as eluent to provide the aldehyde 16 as a colourless solid (300 mg, 91%). mp 110-112 °C [Lit. [2] mp 110-112 °C]; IR (KBr): 1721, 1695, 1670, 1579 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 9.81 (s, 1H), 7.3 (t, J = 8 Hz, 1H), 7.26-7.21 (m, 13H), 7.11-7.06 (m, 6H), 6.97 (d, J = 8.4 Hz, 1H), 6.90 (s, 2H), 6.83 (d, J = 7.6 Hz, 2H), 5.14 (s, 2H), 5.81 (s, 4H), 4.70 (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 191.5, 191.4, 167.6, 158.3, 156.7, 138.2, 136.0, 135.8, 135.5, 133.4, 131.3, 131.1, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.1, 125.3, 122.0, 115.1, 106.5, 70.6, 70.4, 67.2. MS (TOF MS ES+): m/z (%) = 685 (M⁺+Na, 100).

(R)-tert-Butyl 4-((allylamino)methyl)-2,2-dimethylloxazolidine-3-carboxylate (18):

A solution of Garner’s aldehyde 17 (1.15 g, 5 mmol) in tetrahydrofuran (15 mL) was stirred at room temperature with allyl amine (410 µL, 5.5 mmol) and MgSO₄ (2.65 g, 22 mmol) under nitrogen for
12 h. Then it was cooled to 0 °C and NaBH₄ (0.208 g, 5.5 mmol) was added in portions under nitrogen atmosphere. The reaction mixture was allowed to come to room temperature and stirred for 12 h. It was then quenched by adding of 5% NH₄Cl solution at 0 °C. It was diluted with water (50 mL) and extracted with ethyl acetate (2 × 50 mL). The combined organic layer was washed successively with water (2 × 50 mL) and brine (50 mL). It was then dried (Na₂SO₄), filtered and the filtrate was concentrated in vacuo to leave a pale yellow liquid which was purified by chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (93:7) as eluent to give the product 18 as a colourless liquid (1.28 g, 94%). 

**IR (KBr):** 3438, 1700 cm⁻¹. **¹H NMR (400MHz, CDCl₃):** δ 5.77-5.69 (m, 1H), 5.02 (d, J=17.2 Hz, 1H), 4.94 (br m, 1H), 3.79 (s, 2H), 3.68 (br s, 1H), 3.12-3.11 (m, 2H), 2.76-2.65 (m, 1H), 2.50-2.48 (m, 1H), 1.48-1.33 (overlapping singlets, 15H). **¹³C NMR (100MHz, CDCl₃):** δ 152.4 (151.7), 136.8, 115.8, 93.3 (93.7), 80.1 (79.6), 66.3, 57.4 (57.1), 52.3 (52.2), 51.0 (50.9), 28.4, 27.5 (26.7), 24.3 (23.0).

(R)-**tert-Butyl 4-((allyl(benzyloxy carbonyl)amino)methyl)-2,2-dimethyloxazolidine-3-carboxylate** (19):

Water (0.5 mL) and benzyl chloroformate (0.78 mL, 5.5 mmol) were added sequentially at room temperature to a stirred solution of the amine 18 (1.35 g, 5 mmol) and sodium bicarbonate (1.26 g, 15 mmol) in ethyl acetate (20 mL), and the resulting reaction mixture was stirred overnight. It was quenched by dropwise addition of pyridine (350 µL, 4.3 mmol) and then stirred for 10 min before being diluted with ethyl acetate (50 mL). The combined organic layer was washed successively with 1 N HCl (50 mL), water (50 mL), brine (50 mL) and then dried over Na₂SO₄. It was filtered and the filtrate was concentrated under reduced pressure to leave a pale yellow liquid which was purified by chromatography over silica gel with petroleum ether/ethyl acetate (93:7) as eluent to give the product 19 as a colourless liquid (1.8 g, 95 %). [α]D²⁵ = +5 (c 1.75, CHCl₃). **IR (neat):** 1697, 1645, 1398, 1233, 1075,769 cm⁻¹. **¹H NMR (400MHz, CDCl₃):** δ 7.38-7.35 (m, 5H), 5.79 (br s, 1H), 5.16 (m, 4H), 4.11-4.01 (m, 5H), 3.95-3.87 (m, 1H), 3.65-3.26 (m, 1H), 1.6-1.48 (overlapping singlets,15H). **¹³C NMR (75 MHz, CDCl₃):** δ 155.9 (156.5), 151.5 (152.1), 136.4, 133.0, 127.7 (128.3), 127.2, 126.7, 116.5 (117.0), 93.3 (94.0), 79.8 (80.0), 67.1, 65.1 (65.7), 55.7 (55.9), 49.8 (50.0), 47.4 (48.0), 28.2, 26.8 (27.4), 22.9 (24.2). **HRMS (TOF MS ES+):** m/z calcd for C₂₂H₃₂N₂NaO₅ 427.2209 (M⁺+Na): Found: 427.2208.
**(R)-benzyl allyl(2-[[tert-butoxycarbonyl]amino]-3-hydroxypropyl)carbamate (20)**

Hydrochloric acid (1.25 mL, 5%) was added dropwise while stirring to an ice-cooled solution of compound 19 (0.5 g, 1.24 mmol) in methanol (10 mL) and stirring was continued for 1 h at 0 °C, and then at room temperature for 5 h. The reaction mixture was quenched with saturated sodium bicarbonate solution and then extracted with ethyl acetate (2 x 25 mL). The combined organic extract was washed successively with water (10 mL), brine (10 mL) and then dried (Na₂SO₄). It was filtered and the filtrate was concentrated under reduced pressure to leave a crude product which on chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (4:1) afforded the product 20 as a colourless viscous liquid (405 mg, 90%). \[\alpha\]D²⁵² = -8 (c 3.00, CHCl₃). IR (neat): 3435, 1702, 1693, 1391, 1248, 1169, 1063 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.37-7.25 (m, 5H), 5.79-5.72 (m, 1H), 5.17-5.14 (m, 4H), 3.97 (dd, J = 14, 5 Hz, 1H), 3.80 (dd, J = 16, 5.5 Hz, 1H), 3.68-3.62 (m, 1H), 3.59-3.56 (m, 3H), 3.50-3.47 (m, 1H), 3.13(dd, J = 14, 5 Hz, 1H), 1.68 (br s, 1H), 1.42 (s, 9H). ¹³C NMR (75 MHz, CDCl₃): δ 157.6, 155.6, 136.1, 132.8, 128.4, 128.0, 127.6, 117.2, 79.3, 67.6, 64.8, 61.4, 50.1, 46.6, 28.2; MS (TOF MS ES+): m/z (%) = 387 (M⁺ + Na, 100).

**tert-Butyl (2R,3R)-1-(N-benzyloxycarbonyl(allyl)amino)-3-hydroxypent-4-en-2-ylcarbamate (22) and tert-butyl (2R,3S)-1-(N-benzyloxycarbonyl(allyl)amino)-3-hydroxypent-4-en-2-ylcarbamate (23):**

A solution of DMSO (310 μL, 4.2 mmol) in CH₂Cl₂ (2 mL) was added dropwise to a stirred solution of oxalyl chloride (155 μL, 1.8 mmol) in CH₂Cl₂ (3 mL) at −78 °C. It was then stirred for 20 min at the same temperature. A solution of the alcohol 20 (0.55 g, 1.5 mmol) in CH₂Cl₂ (5 mL) was then added dropwise to the reaction mixture. It was then warmed to −25 °C and stirred at this temperature for 35 min followed by dropwise addition of diisopropylethylamine (1.8 mL, 10.5 mmol). Stirring was continued at the same temperature for another 10 min. The reaction mixture was cooled back to −78 °C and diluted with THF (20 mL). Then vinylmagnesium bromide (6 mL, 1 M solution in THF) was added dropwise to the reaction mixture. The reaction mixture was allowed to warm to −40 °C and stirred at this temperature for 2 h. Then the reaction mixture was allowed to come to room temperature and stirred for 8 h before being quenched by slow addition of saturated aq NH₄Cl (10 mL) at 0 °C. It was extracted with ethyl acetate (2 x 25 mL) and the combined organic extract was washed successively with HCl (1 N, 2 x 20 mL), H₂O (2 x 20ml) and brine (20 mL). After drying (Na₂SO₄), it was filtered and the filtrate was concentrated in vacuo to leave a pale yellow crude product which on chromatographic purification over silica gel using a mixture of petroleum...
ether/ethyl acetate (85:15) as eluent provided sequentially the diastereomeric alcohols 22 and 23 as colorless liquids in a combined yield of 64%.

**Compound 22:** Yield: 0.255 mg (43.5%). \([\alpha]_D^{25} = -8 (c 1.5, \text{CHCl}_3)\). IR (neat): 3416, 1687 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.36-7.34 (m, 5H), 5.85-5.74 (m, 2H), 5.37 (d, \(J = 16\) Hz, 1H), 5.21-5.15 (m, 5H), 4.94 (d, \(J = 8\) Hz, 1H), 4.16-3.98 (br m, 3H), 3.89-3.62 (br m, 3H), 3.14(dd, \(J = 13.6, 4.8\) Hz, 1H), 1.45-1.41 (s, 9H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 157.9, 156.0, 136.7, 136.2, 132.8, 128.6, 128.2, 127.8, 117.6, 116.0, 79.4, 69.4, 67.9, 52.5, 50.3, 47.7, 28.3 (27.9). HRMS (TOF MS ES+) \(m/z\) calcd for C\(_{21}\)H\(_{30}\)N\(_2\)NaO\(_5\) (M\(^+\)+Na): 413.2052. Found. 413.2051.

**Compound 23:** Yield: 0.12 g (20.5%). \([\alpha]_D^{25} = +9 (c 2.0, \text{CHCl}_3)\). IR (KBr): 3437, 2977, 2930, 1698 cm\(^{-1}\). \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.37-7.33 (m, 5H), 5.88-5.73 (m, 2H), 5.30 (d, \(J = 17\) Hz, 1H), 5.16-5.10 (m, 7H), 4.14 (br s, 1H), 3.94-3.78 (m, 3H), 3.56-3.52 (m, 1H), 3.33-3.30 (m, 1H), 1.43 (s, 9H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 157.5, 156.3, 137.0, 136.3, 133.0, 128.5, 128.1, 127.8, 117.2, 115.7, 79.7, 73.8, 67.6, 54.0, 50.0, 46.0, 28.3. HRMS (TOF MS ES+) \(m/z\) calcd for C\(_{21}\)H\(_{30}\)N\(_2\)NaO\(_5\) (M\(^+\)+Na): 413.2052. Found. 413.2054.

**Mitsunobu inversion of 23 to 22:**

4-Nitrobenzoic acid (167 mg, 1 mol), PPh\(_3\) (262 mg, 1 mmol) and diethylazodicarboxylate (157.5 µL, 1 mmol) were sequentially added to a solution of 23 (195 mg, 0.5 mmol) in anhydrous THF (10 mL) at 0 °C. Then the reaction mixture was allowed to come to room temperature and stirred for 24 h. Then it was diluted with ethyl acetate (25 mL) and washed successively with saturated aqueous NaHCO\(_3\) and then with water (20 mL) and brine (20 mL). It was then dried (Na\(_2\)SO\(_4\)), filtered and the filtrate was concentrated in vacuo to leave a crude product which was used without further purification for the next step. A solution of this crude product in methanol/water (10 mL, 9:1) was stirred with K\(_2\)CO\(_3\) (350 mg, excess) for 4 h. Then the reaction mixture was filtered and concentrated in vacuo, diluted with ethyl acetate (25 mL), washed with water (20 mL) and brine (20 mL), and then dried (Na\(_2\)SO\(_4\)), filtered and concentrated in vacuo to provide a crude liquid which was purified by column chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (85:15) to produce compound 22 as colourless liquid (140 mg, 72%).
(3R,4R)-5-\{(N-Benzyloxycarbonyl(allyl)amino)-4-(\textit{\textit{tert}}-butoxycarbonylamino)\}pent-1-en-3-yl acetate (24):

Acetic anhydride (71 μL, 0.75 mmol) and DMAP (0.01 g) were added to a stirred solution of the alcohol 22 (195 mg, 0.5 mmol) in CH₂Cl₂ (5 mL) at room temperature under nitrogen and the reaction mixture was stirred for 12 h before being poured into ice-cooled water (20 mL). The resulting mixture was stirred for 30 min and then extracted with CH₂Cl₂ (2 × 25 mL). The combined organic extract was washed with H₂O (2 × 25 mL) followed by brine (25 mL). It was dried over Na₂SO₄, filtered and the filtrate was concentrated in vacuo to leave a crude product which was purified by column chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (9:1) to produce compound 24 as a colourless liquid (182 mg, 84%). [\(\alpha\rceil_{D}^{25} = -15\) (c 2.0, CHCl₃). IR (neat): 3352, 1745, 1712, 1644, 1502, 1367, 1235, 1166, 1025, 770, 699 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.39-7.36 (m, 5H), 5.84-5.73 (m, 2H), 5.31-5.14 (m, 7H), 4.91 (d, \(J = 9.6\) Hz, 1H), 4.17-4.06 (m, 2H), 3.82-3.78 (m, 1H), 3.38-3.24 (m, 1H), 2.13 (1.89) (s, 3H), 1.46 (1.42) (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 170.5 (170.3), 157.3, 155.8 (155.5), 136.5 (136.2), 133.2, 133.1 (132.7), 128.6, 128.5, 128.3 (128.0), 127.7, 118.3 (118.1), 117.1 (117.6), 79.5 (79.9), 73.6 (73.5), 67.4 (67.7), 51.0 (50.5), 49.3 (49.7), 45.4 (44.7), 35.4, 28.3, 21.0 (20.8). MS (TOF MS ES⁺): m/z (%) = 455 (M⁺ + Na, 100). Anal. Calcd for C₂₃H₃₂N₂O₆: C, 63.87; H, 7.46; N, 6.48. Found: C, 64.09; H, 7.65; N, 6.61.

(3R,4R,2)-Benzyl 4-acetoxy-3-\{(\textit{\textit{tert}}-butoxycarbonylamino)\}2,3,4,7-tetrahydro-1H-azepine-1-carboxylate (26):

Catalyst 25 (0.011 g, 0.0125 mmol) was added to a stirred solution of the diene 24 (110 mg, 0.24 mmol) in dry and degassed CH₂Cl₂ (25 mL) under argon and the homogeneous mixture was gently refluxed for 12 h. It was then concentrated in vacuo to leave a crude product which was purified by chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (85:15) to produce compound 26 as colourless viscous liquid (95 mg, 89 %); [\(\alpha\rceil_{D}^{25} = -12\) (c 2.0, CHCl₃). IR(KBr): 3350, 1738, 1713, 1699, 1504,1367, 1240, 1167, 1037, 771 cm⁻¹. ¹H NMR (400MHz, CDCl₃): δ 7.39-7.33 (m,5H), 5.74-5.48 (m,3H), 5.24-5.12 (m, 2H), 4.79 (d, \(J = 9.2\), 1H), 4.59-4.46 (m, 1H), 4.25-4.11 (m, 1H), 3.89-3.65 (m, 2H), 3.51 (dd, \(J = 15, 7.2\), 1H), 2.06-2.02 (m,3H), 1.43-1.38 (singlets, 9H). ¹³C NMR (75 MHz, CDCl₃): δ 170.4 (170.3), 156.5 (155.5), 155.3 (154.9), 136.1, 129.4, 129.0, 128.5 (128.4), 128.1, 127.7 (127.2), 79.2 (79.4), 72.9 (72.0), 67.6, 53.6 (52.8), 49.9 (49.0), 48.3 (47.9), 28.2, 20.7 (20.8). HRMS (TOF MS ES⁺): calcld for C₂₁H₂₉N₂O₆ (M⁺ + Na): 427.1845. Found: 427.1848.
(3R,4R,Z)-Benzyl 3-(tert-butoxycarbonylamino)-4-hydroxy-2,3,4,7-tetrahydro-1H-azepine-1-carboxylate (27):

K$_2$CO$_3$ (345 mg, 2.5 mmol) was added to a stirred solution of 26 (100 mg, 0.25 mmol) in MeOH (2 mL) and the resulting mixture was stirred for 4 h at room temperature. Then the reaction mixture was filtered, concentrated in vacuo and extracted with ethyl acetate (2 × 25 mL). The ethyl acetate extract was washed with water (2 × 25 mL) and brine (25 mL), and dried (Na$_2$SO$_4$). It was filtered and the filtrate was concentrated in vacuo to leave a crude product which on chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (5:1) provided the product 27 as a colourless viscous liquid (80 mg, 89%); [α]$_D^{25}$ = - 20.0 (c 2.0, CHCl$_3$). IR (neat): 3410, 1694 cm$^{-1}$. $^1$H NMR (400MHz, CDCl$_3$) : δ 7.37-7.35 (m, 5H), 6.35 (br s, 1H), 5.69 (d, J = 8 Hz, 1H), 5.41 (d, J = 11 Hz, 1H), 5.21-5.12 (m, 2H), 4.58-4.54 (m, 2H), 4.17-4.11 (m, 1H), 3.92-3.91 (m, 1H), 3.82 (d, J = 15 Hz, 1H), 3.67-3.62 (m, 1H), 3.50 (dd, J = 15, 6 Hz, 1H), 1.45-1.40 (s, 9H); $^{13}$C NMR (400MHz, CDCl$_3$) : δ 157.9, 157.0, 136.1, 134.2 (133.5), 128.8, 128.6, 128.4, 128.3, 127.8, 124.4, 80.3, 73.8, (68.0) 67.8, 58.1 (56.7), 49.2, 48.7 (48.4), 28.4; HRMS (TOF MS ES+): m/z calcd for C$_{19}$H$_{26}$N$_2$NaO$_5$ (M$^+$+Na): 385.1740. Found: 385.1755.

(3R,4R,Z)-Benzyl 3-amino-4-hydroxy-2,3,4,7-tetrahydro-1H-azepine-1-carboxylate (28):

An ice-cooled solution of TFA (1 mL, excess) in CH$_2$Cl$_2$ (1 mL) was added to the alcohol 27 (70 mg, 0.2 mmol) at 0 °C. The reaction mixture was allowed to come to room temperature and stirred for another 1 h. Then the reaction mixture was concentrated in vacuo, basified by slow addition of saturated aqueous sodium bicarbonate (10 mL), and extracted with CH$_2$Cl$_2$ (2 × 25 mL). The combined organic extract was washed successively with water (2 × 25 mL) and brine (25 mL), dried (Na$_2$SO$_4$), filtered and the filtrate was concentrated in vacuo to provide a crude mass. It was then purified by chromatography over silica gel using a mixture of chloroform/methanol (95:5) to provide the product 28 as colourless liquid (39 mg, 76 %). [α]$_D^{25}$ = - 12.8 (c 1.3, CHCl$_3$). IR(KBr): 3357, 3290,1683 cm$^{-1}$. $^1$H NMR (400MHz, CDCl$_3$) : δ 7.37-7.35 (m, 5H), 5.77-5.71 (m, 2H), 5.20-5.11 (m, 2H), 4.16-4.10 (m, 1H), 3.99 (t, J = 13 Hz, 1H), 3.85-3.80 (m, 2H), 3.47-3.37 (m, 1H), 2.89-2.85 (m, 1H), 2.55 (br s, 3H). $^{13}$C NMR (400MHz, CDCl$_3$): δ 156.1 (155.6), 136.5, 135.2 (134.7), (128.6) 128.5, 128.2, 128.1, 127.7, (126.7) 126.3, 73.1 (72.6), (67.5) 67.4, 55.6 (55.3), 53.3 (52.9), (46.7) 46.5. HRMS (TOF MS ES+): m/z calcd for C$_{14}$H$_{19}$N$_2$O$_3$ (M$^+$+H): 263.1396. Found: 263.1395.
(3R,4R,Z)-Benzyl 3-(4-(benzyloxy)benzamido)-4-hydroxy-2,3,4,7-tetrahydro-1H-azepine-1-carboxylate (29):

A suspension of the amino alcohol 28 (33 mg, 0.125 mmol), p-benzyloxybenzoic acid (28 mg, 0.125 mmol) and EDC·HCl (29 mg, 0.125 mmol) in CH₂Cl₂ (2.5 mL) was treated with DMAP (8 mg, 0.06 mmol) at room temperature under nitrogen and the resulting solution was stirred for 24 h. It was then quenched with water (5 mL) and extracted with CH₂Cl₂ (2 × 20 mL). The combined organic extract was washed successively with water (2 × 20 mL) and brine (20 mL), and dried (Na₂SO₄). It was filtered and the filtrate was concentrated in vacuo to provide a crude mass which was purified by chromatography over silica gel using a mixture of petroleum ether/ethyl acetate/methanol (60:40:1) as eluent to provide compound 29 as a gummy liquid (51 mg, 84%).

IR (KBr): 3391, 1720, 1661 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 8.67 (d, J = 5.6 Hz, 1H), 7.84 (d, J = 8.8 Hz, 2H), 7.45-7.35 (m, 11H), 7.03 (d, J = 8.8 Hz, 2H), 5.74 (d, J = 12 Hz, 1H), 5.43-5.41 (m, 1H), 5.21 (s, 2H), 5.13 (s, 2H), 4.66-4.61 (m, 2H), 4.30 (dd, J = 12.0, 5.8 Hz, 1H), 4.0-3.92 (m, 1H), 3.71 (d, J = 18 Hz, 1H), 3.62 (dd, J = 15.2, 5.6 Hz, 1H). ¹³C NMR (400 MHz, CDCl₃): δ 168.8, 161.7, 157.7, 136.4, 136.0, 134.6, 129.2, 128.7, 128.6, 128.4, 128.2, 127.9, 127.5, 125.6, 123.9, 114.7, 74.6, 70.1, 68.1, 59.4, 48.8 48.5. MS (TOF MS ES⁺): m/z (%) = 495 (M⁺+Na, 100).

(3R,4R)-Benzyl 3-(4-(benzyloxy)benzamido)-4-hydroxyazepane-1-carboxylate (30):

A solution of the olefin 29 (25 mg, 0.022 mmol) in ethyl acetate (2 mL) was stirred vigorously in the presence of Pd/C (5%, 5 mg) at room temperature under hydrogen for 30 min. It was then filtered through Celite, washed with ethyl acetate (5 mL) and the combined filtrate was concentrated in vacuo to provide a crude product which on column chromatography over silica gel using a mixture of petroleum ether/ethyl acetate/methanol (60:40) as eluent produced compound 30 as a colourless solid (16 mg, 66%). mp 120-122 °C [Lit. [2] mp: 123 °C]. [α]D: -72.0 (c 2.0, CHCl₃). [Lit. [2] [α]D: -73.0 (c 1.0, CHCl₃)]. IR (KBr): 3442, 1502, 1367, 1235, 1166, 1025, 770,699 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.72 (d, J = 5.4 Hz, 1H), 7.81 (d, J = 8.8 Hz, 2H), 7.44-7.29 (m, 10H), 7.02 (d, J = 8.8 Hz, 2H), 5.43 (br s, 1H), 5.20 (ABq, J = 12.3 Hz, 2H), 5.13 (s, 2H), 4.20 (dd, J = 14.2, 3.75 Hz, 2H), 4.16 (d, J = 15.8 Hz, 1H), 4.10-4.06 (m, 1H), 3.76 (dd, J = 8.9, 6.5 Hz, 1H), 3.34 (s, 2H), 3.29 (d, J = 5.1, 15.3 Hz, 1H), 2.79 (dt, J = 13.6, 3.4 Hz, 1H), 1.97-1.93 (m, 1H), 1.90-1.81 (m, 2H), 1.70-1.67 (m, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 168.5, 161.6, 157.7, 136.2, 129.1, 128.6, 128.4, 128.2, 128.1, 127.7, 127.4, 125.7, 114.7, 79.5, 70.0, 67.8, 60.7, 50.4, 50.2, 32.7, 27.2. MS (TOF MS ES⁺): m/z (%) = 513 (M⁺+K, 100).
(35,45,Z)-Benzy 3-(4-(benzylxoy)benzamido)-4-(3,5-bis(benzyloxy)-4-(2-benzylxoyl-6-(benzyloxy-carbonyl)benzoyl)benzoyloxy)-2,3,4,7-tetrahydro-1H-azepine-1-carboxylate (31):

A mixture of the amido alcohol 29 (25 mg, 0.05 mmol), acid 7 (35 mg, 0.05 mmol) and 2-chloro-1-methylpyridinium iodide (16.5 mg, 0.065 mmol) in CH$_2$Cl$_2$ (2.5 mL) was treated with Et$_3$N (15 μL, 0.1 mmol) at room temperature under nitrogen and stirred for 30 min. Then DMAP (3 mg, 0.025 mmol) was added and the resulting mixture was stirred for another 1 h at room temperature. It was then filtered through a pad of silica, concentrated in vacuo to produce a crude mass which on chromatographic purification over silica gel using a mixture of petroleum ether/ethyl acetate (7:3) as eluent provided the compound 31 (41 mg, 73%). $\left[\alpha\right]^{25}_D^\circ = -66.1$ (c 1.1, CHCl$_3$). IR (KBr): 3351, 2924, 1728, 1660 cm$^{-1}$. $^1$H NMR (400MHz, CDCl$_3$): δ 7.86 (d, $J = 8.8$ Hz, 1H), 7.76 (d, $J = 8.4$ Hz, 2H), 7.45-7.35 (m, 12H), 7.30-7.28 (m, 4H), 7.25-7.24 (m, 3H), 7.21-7.71 (m, 14H), 7.11-7.10 (m, 6H), 7.06-7.02 (m, 2H), 6.92-6.89 (m, 2H), 6.83-6.82 (m, 2H), 5.80-5.73 (m, 2H), 5.67-5.64 (m, 1H), 5.36-5.33 (m, 1H), 5.26-5.23 (m, 1H), 5.10-5.07 (m, 3H), 5.04-5.03 (m, 3H), 4.9-4.79 (m, 6H), 4.68 (s, 2H), 4.07-4.03 (m, 1H), 3.77 (d, $J = 16.4$ Hz, 1H), 3.68 (dd, $J = 15$, 6.8 Hz, 1H). $^{13}$C NMR (400MHz, CDCl$_3$): δ 191.7, 167.33, (166.1) 165.9, 161.4, 158.1 (158.0), 157.4 (156.2), 156.4 (156.0), 135.8, 132.6 (132.4), 130.5 (130.4), 129.6, 128.9, 128.7 (128.6), 128.5, 128.9, 127.7 (128.6), 128.5, 128.4, 128.3, 128.2, 128.18, 128.0, 127.9, 127.7, 127.5, 127.4, 127.3, 127.0, 126.6, 126.1, 123.7, 122.0, 115.4, 114.7, 107.1, 75.1, 70.5, 70.0, 68.2, 67.0, 52.8, 50.0, 49.1. HRMS (TOF MS ES+): m/z calcd for C$_{71}$H$_{60}$N$_2$O$_{12}$Na (M$^+$+Na): 1155.4044. Found: 1155.4070. [The compound exhibited extensive rotamerism and hence the number of proton and carbon signals exceeds. This has also been observed [3] by Nicolaou et al.]

Balanol (1):

To a solution of protected balanol 31 (20 mg, 0.018 mmol) in formic acid (5 mL) was added palladium black (50 mg) and the reaction mixture was allowed to stir vigorously for 18 h. The reaction mixture was then filtered through a pad of silica gel and the filtrate was concentrate under vacuo to provide a crude mass which on repeated purification by preparative TLC following Nicolaou’s protocol provided (−)-balanol (1) as yellowish amorphous powder (4 mg, 41%). $\left[\alpha\right]^{25}_D^\circ = -106.0$ (c 0.10 MeOH) [ Lit. [3] $\left[\alpha\right]^{25}_D^\circ = -111.0$ (c 0.10 MeOH)] [ Lit. [4] $\left[\alpha\right]^{25}_D^\circ = -107.0$ (c 0.252 MeOH)]. $^1$H NMR (500MHz, CD$_3$OD+ D$_2$O): 7.58 (d, $J = 8.4$ Hz, 2H), 7.39 (d, $J = 7.2$ Hz, 1H), 7.18 (t, $J = 9.0$ Hz, 1H), 6.82 (s, 2H), 6.71 (d, $J = 7.6$ Hz, 2H), 5.39 (m, 1H), 4.47 (m, 1H), 3.52-2.92 (m, 4H), 2.19-2.02 (m, 4H). MS (TOF MS ES+): m/z = 573.4 (M$^+$+Na).
(3R,4S)-Benzyl 3-(4-(benzyloxy)benzamido)-4-(3,5-bis(benzyloxy)-4-(2-(benzyloxy)-6-(benzylolcarbonyl)benzoyl)benzyloxy)-5,6-dihydroxyazepane-1-carboxylate (32):

N-Methylmorpholine N-oxide (3.5 mg, 0.03 mmol) and OsO₄ (32.5 μL, 1% aq solution) were sequentially added to a solution of 31 (28 mg, 0.025 mmol) in acetone/water (1:1) and the resulting mixture was stirred at room temperature for 12 h before being quenched by addition of saturated aqueous sodium bisulfite (0.1 mL). The resulting mixture was concentrated in vacuo and then diluted with water (10 mL). It was extracted with ethyl acetate (2 × 15 mL) and the combined organic extract was washed successively with water (2 × 20 mL) and brine (20 mL) and dried (Na₂SO₄). After filtration, the filtrate was concentrated in vacuo to provide a crude mass which was roughly purified by chromatography over flash silica using a mixture of petroleum ether/ethyl acetate (1:1) as eluent to provide a mixture (81:19) of isomers 31 as a viscous liquid (20 mg, 68%). IR (KBr): 3436, 1719, 1667, 1605, 1580, 1498 cm⁻¹.¹H NMR (400MHz, CDCl₃) : δ 7.81 (d, J=8.4 Hz, 1H), 7.70 (d, J = 8.4 Hz, 2H), 7.41-7.32 (m, 11H), 7.23-7.19 (m, 16H), 7.12-7.02 (m, 9H), 6.90-6.87 (m, 3H), 6.82 (d, J=7.2 Hz, 2H), 5.30-5.22 (m, 2H), 5.16-5.08 (m, 4H), 5.00-5.08 (m, 2H), 5.00 (s, 1H), 4.97-4.88 (m, 1H), 4.86-4.79 (m, 3H), 4.75 (d, J=2.8 Hz, 1H), 4.71-4.64 (m, 2H), 4.35 (br s, 1H), 4.19 (dd, J=14.4, 6 Hz, 1H), 4.04 (d, J=15 Hz, 2H), 3.67 (dd, J = 15, 6.4 Hz, 1H). ¹³C NMR (100MHz,CDCl₃) : δ 191.7, 171.2, 167.2, 166.6, 166.0, 161.4, 158.1, 157.6, 156.2, 137.6, 136.4, 136.3, 135.9, 135.8, 135.3, 132.5, 130.4, 130.1, 128.9, 128.8, 128.7, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.5, 127.4, 127.3, 127.2, 126.9, 126.3, 123.6, 122.0, 115.5, 114.9, 114.7, 107.1, 78.7, 75.1, 70.5, 70.4, 70.0, 68.4, 68.2, 67.0, 60.4, 52.0, 50.0, 49.9. HRMS (TOF MS ES+): m/z calcd for C₇₁H₆₂N₂NaO₁₄ (M⁺+Na): 1189.4099. Found: 1189.4105.
| **1H NMR data of compound 30 (500 MHz, CDCl3)** | **1H NMR data of compound 30 (500 MHz, CDCl3) reported by Nicolaou et. al.** | **13C NMR data of compound 30** | **13C NMR data of compound 30 reported** |
|---------------------------------------------|---------------------------------------------------------------|---------------------------------|---------------------------------|
| 8.72 (d, J = 5.4 Hz, 1H),                 | 8.75 (d, J = 5.5 Hz, 1H),                                     | 168.5                          | 168.5                          |
| 7.81 (d, J = 8.8 Hz, 2H),                 | 7.82 (ddd, J = 8.8, 2.8, 1.9 Hz, 2H)                          | 161.6                          | 161.5                          |
| 7.44-7.29 (m, 10H),                       | 7.45-7.29 (m, 10H),                                           | 157.7                          | 157.7                          |
| 7.02 (d, J = 8.8 Hz, 2H),                 | 7.02 (ddd, J =8.8, 2.8, 1.9 Hz, 2H)                           | 136.4                          | 136.3                          |
| 5.43 ( br s, 1H), 5.20 (AB q, J = 12.3 Hz, 2H), | 5.21, 5.18 ( AB , J = 12.3 Hz, 2H)                       | 136.2                          | 136.1                          |
| 5.13 (s, 2H),                             | 5.13 (s, 2H),                                                 | 129.1                          | 129.1                          |
| 4.20 (dd, J=14.2, 3.75Hz, 1H)             | 4.19 (dd, J = 14.3, 3.8 Hz, 1H),                             | 128.6                          | 128.62                         |
| 4.16 (d, J = 15.8 Hz, 1H)                 | 4.15 (d, J = 15.4 Hz, 1H),                                    | 128.4                          | 128.56                         |
| 4.10- 4.06 (m, 1H),                       | 4.10 (m, 1H),                                                 | 128.2                          | 128.2                          |
| 3.76 (dd, J =8.9, 6.5Hz, 1H),             | 3.77 (ddd, J =10.2, 6.1, 1.6 Hz, 1H)                          | 128.1                          | 128.1                          |
| 3.34 (dd, J =15.3, 5.1 Hz,1H)             | 3.35 (dd, J = 15.4, 5.1 Hz, 1H),                             | 127.7                          | 127.7                          |
| 2.79 (dt, J = 3.4, 13.6Hz, 1H)            | 2.79 (ddd,J =14.3, 13.2, 3.5 Hz,1H)                           | 127.4                          | 127.4                          |
| 1.97-1.93 (m, 1H), 1.90-1.81 (m, 2H),     | 1.95-1.81 (m, 3H),                                           | 125.7                          | 125.6                          |
| 1.70-1.67 (m, 1H).                        | 1.66 (m, 1H).                                                 | 79.5                           | 79.7                           |
|                                           |                                                                | 70.0                           | 70.0                           |
|                                           |                                                                | 67.8                           | 67.8                           |
|                                           |                                                                | 60.7                           | 60.7                           |
|                                           |                                                                | 50.4                           | 50.4                           |
|                                           |                                                                | 50.2                           | 50.2                           |
|                                           |                                                                | 32.7                           | 32.7                           |
|                                           |                                                                | 27.2                           | 27.3                           |
\[ ^1H \text{NMR}(500 \text{ MHz, CDCl}_3) \text{ data of } (-)\text{-balanol reported by Nicolaou et. al} \ [2] \]

| \text{δ (ppm)} | \text{J (Hz)} | \text{Multiplicity} |
|----------------|-------------|--------------------|
| 7.60           | 8.7         | d (2H)             |
| 7.26           | 7.3         | d (1H)             |
| 7.17           | 7.9         | dd (1H)            |
| 6.91           |             | s (2H)             |
| 6.79           | 7.7         | d (1H)             |
| 6.76           | 8.7         | d (2H)             |
| 5.29           |             | m (1H)             |
| 4.33           |             | br m (1H)          |
| 3.44-2.98      |             | br m (4H)          |
| 2.11-1.85      |             | br m (4H)          |

\[ ^1H \text{NMR}(500 \text{ MHz, CDCl}_3) \text{ data of compound 1} \]

| \text{δ (ppm)} | \text{J (Hz)} | \text{Multiplicity} |
|----------------|-------------|--------------------|
| 7.58           | 8.4         | d (2H)             |
| 7.18           | 9.0         | t (1H)             |
| 6.94           | 8.4         | d (1H)             |
| 6.82           |             | s (2H)             |
| 6.71           | 7.6         | d (2H)             |
| 5.39           |             | m (1H)             |
| 4.47           |             | m (1H)             |
| 3.52-2.92      |             | m (4H)             |
| 2.19-2.02      |             | m (4H)             |

References

1. Hollinshead, S. P.; Nichols, J. B.; Wilson, J. W. J. \textit{Org. Chem.} 1994, 59, 6703–6709. doi:10.1021/jo00101a032

2. Nicolaou, K. C.; Koide, K.; Bunnage, M. E. \textit{Chem.–Eur. J.} 1995, 1, 454–466. doi:10.1002/chem.19950010711

3. Nicolaou, K. C.; Bunnage, M. E.; Koide, K. \textit{J. Am. Chem. Soc.} 1994, 116, 8402–8403. doi:10.1021/ja00097a072

4. Lampe, J. W.; Hughes, P. F.; Biggers, C. K.; Smith, S. H.; Hu, H. \textit{J. Org. Chem.} 1994, 59, 5147–5148. doi:10.1021/jo00097a014