Supplementary Information

Tandem oxidative radical fragmentation-rearrangement of 2-amino-1,3-benzylidene acetals: A short entry to densely functionalised fully differentiated oxazolidinones

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1. General

All fine chemicals were obtained from Sigma-Aldrich and used as obtained. Solvents were either used as-obtained (DMF, DMSO, Aldrich Sure-seal®) or dried using standard protocols. Dichloromethane and triethylamine were distilled over calcium hydride. THF and toluene were distilled over sodium metal in the presence of benzophenone indicator. $^1$H and $^{13}$C NMR spectra were obtained on a 600 MHz Bruker NMR spectrometer and $^{31}$P NMR spectra were obtained on a 200 MHz Bruker NMR spectrometer, unless otherwise stated. Chemical shifts are reported in units of δ (ppm) and coupling constants ($J$) are expressed in Hz. Mass spectra were run on a Micromass Quattro Ultima spectrometer fitted with a direct injection probe (DIP) with ionization energy set at 70 eV and HRMS (EI) were performed with a Micromass Q-TOF Ultima spectrometer. IR spectra were obtained on a Nicolet 510 FT-IR spectrometer on NaCl plates with absorptions given in cm$^{-1}$. Thin layer chromatography (TLC) was run using Macherey-Nagel aluminum-backed plates. Melting points were obtained on an Electronic Research Associates Inc. melting point apparatus corrected against an external calibrant. Atom numbering in the compound structures shown below is provided for unambiguous assignment with spectral details and may not correspond to systematic atom numbering. Standard abbreviations for reagents and solvents are used in the experimental descriptions (Boc = tert-butyloxycarbonyl, BPO = benzoyl peroxide, NBS = N-bromosuccinimide, PTSA = paratoluene sulfonic acid, DCM = dichloromethane, DMF = dimethylformamide, THF = tetrahydrofuran).

5-Hydroxymethyl-5-(N-tert-butoxycarbonyl)amino-2-phenyl-1,3-dioxana-benzylidene 7a.$^{1,2}$

![Chemical structure image]
Tris(hydroxymethyl)aminomethane (THAM, 3.210 g, 26.50 mmol, 1.0 eq) and Boc₂O (6.6523 g, 30.48 mmol, 1.15 eq) were dissolved in dry DMF (24 mL) and stirred 24 h at rt. Benzaldehyde dimethyl acetal (5.1 g, 5.0 mL, 33 mmol, 1.2 eq) was added with catalytic para-toluenesulfonic acid monohydrate (PTSA, 0.192 g, 1.01 mmol, 0.06 eq) and stirred an additional 24 h. The mixture was diluted with Et₂O (60 mL) and extracted with sat’d NaHCO₃ (60 mL) mixed with additional water (20 mL). The aqueous layer was further diluted with water (30 mL) and washed with Et₂O (60 mL × 3), followed by a final dilution with water (20 mL) and final wash with Et₂O (100 mL). The organic layers were combined, dried over MgSO₄ and the solvent removed under reduced pressure. The product was recrystallised from Et₂O/hexane to give 7a as a mixture of two separable (on silica-gel) isomers in a 60:40 ratio (6.666 g, 21.55 mmol, 81.3%). Isomer #1 (less polar): IR (4000-625ν cm⁻¹, NaCl): 3424, 3322, 3036, 2977, 2927, 2867, 1686, 1541, 1500, 1454, 1391, 1368, 1316, 1286, 1250, 1172, 1104, 1084, 1057, 989, 747, 699. ¹H NMR (600 MHz, CDCl₃): δ1.46 (9H, s, H-10/11/12), 3.71 (2H, s, H-13), 3.84 (2H, d, J = 11.6 Hz, H-4/6), 4.21 (2H, d, J = 11.6 Hz, H-4/6), 5.48 (1H, s, H-2), 5.8 (broad, 1H, s, NH-7), 7.40 (3H, m, H-17/18/19), 7.51 (2H, dd J = 1.5Hz, 8.1 Hz, H-16/20). ¹³C NMR (CDCl₃, 150 MHz): δ 28.4 (C-10/11/12), 53.7 (C-5), 65.0 (C-13), 72.0 (C-4/6), 80.8 (C-9), 102.1 (C-2), 126.1 (C-17/19), 128.5 (C-16/20), 129.4 (C-18), 137.6 (C-15), 156.9 (C-8). Isomer #2 (more polar): IR (4000-625ν cm⁻¹, NaCl): 3258, 3070, 2986, 2950, 2929, 2871, 2856, 1682, 1557, 1499, 1456, 1393, 1368, 1319, 1284, 1249, 1214, 1175, 1115, 1050, 1025, 984, 964, 941, 907, 871, 759, 697. ¹H NMR (600 MHz, CDCl₃): δ1.45 (9H, s, H-10/11/12), 4.08 (2H, s, H-13), 4.10 (2H, s, J = 11.1 Hz, H-4/6), 4.20 (2H, d, J = 11.1 Hz, H-4/6), 4.74 (1H, s, NH-7), 5.52 (1H, s, H-2), 7.36 (3H, m, H-17/18/19), 7.46 (2H, dd, J = 2.4Hz, 8.4 Hz, H-16/20). ¹³C NMR (CDCl₃, 150 MHz): δ28.4 (C-10/11/12), 52.0 (C-5), 63.3 (C-13), 69.4 (C-4/6), 72.0 (C-9), 101.7 (C-2), 126.3 (C-17/19), 128.5
(C-18/20), 129.2 (C-18), 137.6 (C-15), 155.4 (C-8). MS (ESI⁺, TOF): Calc’d. for [C₁₆H₂₄NO₅⁺]: 310.1654; found 310.1658.

4-Hydroxymethyl-4-benzoyloxymethyl-2-oxazolidinone 8a.

To a flame-dried flask fitted with a condenser under argon was added sequentially compound 7a (0.0502 g, 0.162 mmol, 1.0 eq), NBS (0.0309 g, 0.174 mmol, 1.05 eq), BPO (75% BPO in H₂O, 0.0020 g, 0.0062 mmol, 0.04 eq), and chlorobenzene (2.0 mL) and the mixture heated at 70 ºC for 110 mins. A second portion of NBS (0.008 g, 0.05 mmol, 0.3 eq) and BPO (75% BPO in H₂O, 0.001 g, 0.003 mmol, 0.02 eq) were added and the solution was heated at 70 ºC for an additional 25 mins. The mixture was then cooled to room temperature and sat’d aqueous NaHCO₃ (2 mL) was added, with subsequent removal of the organic layer. The aqueous layer was washed with DCM (5 mL × 3), the organic layers combined, dried over MgSO₄, filtered, and the solvent removed under reduced pressure. Purification was obtained through silica column chromatography (75:25 hexanes:ethyl acetate) yielding 7a as colourless crystals (0.0313 g, 0.124 mmol, 77%). IR (4000-625ν cm⁻¹, NaCl): 3248 (OH), 2923 (C-H), 2853 (C-H), 1712 (C=O), 1466, 1446, 1430, 1314, 1270 (C-O), 1178, 1114 (C-O), 1054 (C-O), 990, 961, 935, 926, 767, 708. ¹H NMR (CDCl₃, 600 MHz): δ2.58 (1H, s, OH-15), 3.69 (1H, dd, J = 5.2, 11.4 Hz, H-14), 3.73 (1H, dd, J = 5.2, 11.4 Hz, H-14) 4.33 (2H, dd, J = 9.0 Hz, 16.8 Hz, H-6), 4.42 (1H, d, J = 11.6 Hz, H-5), 4.54 (1H, d, J = 11.6 Hz, H-5), 7.48 (2H, t, J = 7.8 Hz, H-10/12), 7.61 (1H, t, J = 7.7 Hz, H-11), 8.02 (2H, d, J = 7.7 Hz, H-9/13). ¹³C NMR (CDCl₃, 150 MHz): 60.5 (C-4), 63.5
(C-14), 64.6 (C-5), 68.9 (C-6), 128.2 (C-10/12), 129.4 (C-9/13), 133.4 (C-11), 138.2 (C-8), 157.9 (C-2), 166.2 (C-8). MS (EI, TOF): Calc’d for [C_{12}H_{14}NO_5]^+ 252.0872; found 252.0936. M.p.: 129.8 – 131.1 °C.

cis/trans-5-(Methoxymethyl)methyloxy-5-(N-tert-butoxycarbonyl)amino-2-phenyl-1,3-dioxane 7b.

To a flame-dried 2-neck flask was weighed the alcohol 7a (0.20 g, 0.65 mmol, 1 eq) to which was added dry DCM (2.0 mL), MOM-Cl (0.15 mL, 0.16 g, 2.0 mmol, 3.1 eq) and diisopropylethylamine (0.68 mL, 0.50g, 3.9 mmol, 6.0 eq). The mixture was stirred for 70 min at which time a second portion of DCM (1.5 mL) was added. The mixture was stirred for an additional 130 min, and the solvent subsequent removed under reduced pressure. Purification was performed through silica gel column chromatography (15:85 v/v, ethyl acetate:hexanes) to give 7b as a colourless solid (1:1.4 isomer ratio, 0.1643 g, 0.4649 mmol, 72%). IR (4000-625ν cm⁻¹, NaCl): 3427, 3353, 2977, 2933, 2886, 1718, 1500, 1456, 1392, 1367, 1313, 1287, 1248, 1218, 1167, 1109, 1077, 1046, 977, 918, 870, 825, 747, 699. ¹H NMR (CDCl₃, 600 MHz): δ 1.48 (9H, s, H-10/11/12), 3.36 (major, 3H, s, H-15), 3.40 (minor, 3H, s, H-15), 3.81 (major, 2H, s, H-13), 3.96 (major, 2H, d, J = 11.2 Hz, H-4/6), 4.01 (minor, 2H, s, H-13), 4.16 (minor, 2H, d, J = 11.3 Hz, H-4/6), 4.34 (major, 2H, d, J = 11.2 Hz, H-4/6), 4.42 (minor, 2H, s-broad, H-4/6), 4.61 (major, 2H, s, H-14), 4.70 (minor, 2H, s, H-14), 4.83 (minor, 1H, s-broad, NH-7), 5.13 (major, 1H, s, NH-7), 5.48 (major, 1H, s, H-2), 5.54 (minor, 1H, s, H-2), 7.38 (3H, m, H-18/19/20), 7.46 (minor, 2H, dd, J = 1.8, 7.9 Hz, H-17/21), 7.51 (2H, d, J = 6.6 Hz, H-17/21). ¹³C NMR (major,
CDCl₃, 150 MHz): δ28.5 (C-10/11/12), 52.3 (C-15), 55.5 (C-5), 69.1 (C-13), 70.9 (C-4/6), 96.9 (C-14), 101.8 (C-2), 126.2 (C-17/21), 128.5 (C-18/20), 129.3 (C-19), 137.9 (C-16), 155.2 (C-8).

13C NMR (minor, CDCl₃, 150 MHz): δ28.5 (C-10/11/12), 51.1 (C-15), 55.6 (C-5), 66.9 (C-4/6), 68.0 (C-13), 97.0 (C-14), 126.3 (C-17/21), 128.5 (C-18/20), 129.2 (C-19), 137.9 (C-16), 154.7 (C-8).

MS (EI, TOF): Cal’d for [C₁₆H₂₃NO₅ + H⁺]: 354.1917; found: 354.1906.

4-(Methoxymethyl)methyloxy-4-benzoyloxymethyl-2-oxazolidinone 8b.³

Compound 7b (0.045 g, 0.13 mmol, 1.0 eq), NBS (0.0238 g, 0.133 mmol, 1.0 5eq), and BPO (75% in H₂O, 0.005 g, 0.03 mmol, 0.2 eq) were dissolved in chlorobenzene (2.5 mL) and the mixture heated at 70 °C for 75 min. The mixture was then cooled to room temperature and the solvent removed under reduced pressure. Purification was performed through column chromatography (85:15 v/v, hexanes:ethyl acetate) to give 8b as a colorless solid (0.018 g, 47%).

¹H NMR (CDCl₃, 200 MHz): δ3.36 (3H, s, H-17), 3.70 (2H, s, H-15), 4.26 (1H, d, J = 9.0 Hz, H-6), 4.35 (1H, d, J = 11.5 Hz, H-5), 4.38 (1H, d, J = 9.0 Hz, H-6), 4.54 (1H, d, J = 11.5 Hz, H-5), 4.66 (2H, s, H-16), 7.46 (2H, t, J = 7.5, 7.6 Hz, H-11/13), 7.60 (1H, t, J = 7.5 Hz, H-12), 8.02 (2H, d, J = 7.6 Hz, H-10/14). ¹³C NMR (CDCl₃, 150 MHz): δ55.9 (C-17), 60.0 (C-4), 65.6 (C-15), 69.8 (C-5), 69.9 (C-6), 97.1 (C-16), 128.8 (C-11/13), 129.2 (C-12), 129.9 (C-10/14), 133.8 (C-9), 158.4 (C-2), 166.2 (C-8). MS (EI, TOF): Cal’d for [C₁₆H₁₇NO₅ + H⁺]: 296.1134; found: 296.1140.
cis/trans-2-Phenyl-5-(N-tert-butyloxycarbonyl)amino-1,3-dioxane 16.

Into a 10 mL flask was weighed serinol (0.1318 g, 1.447 mmol, 1.0 eq) and dry DMF (1.1 mL) under nitrogen. Boc₂O (0.3452 g, 1.582 mmol, 1.09 eq) was added and the mixture was stirred at rt for 4.5 h. Benzaldehyde dimethyl acetal (0.28 mL, 0.28 g, 1.9 mmol, 1.3 eq) and PTSA monohydrate (0.0176 g, 0.0925 mmol, 0.064 eq) were sequentially added, and the mixture was subsequently stirred at room temperature for an additional 19 h. A spatula of solid NaHCO₃ was added and the mixture was diluted with Et₂O (12 mL). The ether phase was washed with sat’d LiCl (5 mL × 3) and the combined organic layer dried over Na₂SO₄, filtered, and the solvent removed under reduced pressure. Purification was performed via recrystallization from Et₂O and hexanes to afford compound 16 as colourless crystals (0.2071 g, 0.7414 mmol, 51%) in a 1:1 ratio as determined by ¹H NMR. IR (4000-625 ν cm⁻¹, NaCl): 3450, 3345, 2977, 2931, 2861, 1712, 1501, 1455, 1392, 1367, 1305, 1237, 1171, 1108, 1014, 978, 748, 699. ¹H NMR (600 MHz, DMSO-d₆): δ 1.39 (9H, s, H-16/17/18), 1.41 (9H, s, H-16/17/18), 3.43 (1H, d, J = 6.6 Hz, H-5), 3.56 (2H, t, J = 10.8 Hz, H-4/6), 3.64-3.74 (1H, m, H-5), 3.99 (2H, dd, J = 1.1, 11.8 Hz, H-4/6), 4.08 (2H, d, J = 11.8 Hz, H-4/6), 4.10 (2H, dd, J = 4.8, 10.8 Hz, H-4/6), 5.39 (1H, s, H-2), 5.55 (1H, s, H-2), 6.97 (1H, dd, J = 6.6, 15.0 Hz, NH-13), 7.33-7.38 (6H, m, H-9/10/11), 7.39-7.43 (2H, m, H-8/12), 7.47-7.50 (2H, s, H-8/12). ¹³C NMR (150 MHz, DMSO-d₆): δ 28.2 (C-17/18/19), 28.2 (C-17/18/19), 43.1 (C-5), 44.9 (C-5), 69.3 (C-4/6), 78.0 (C-16), 78.2 (C-16), 100.3 (C-2), 100.6 (C-2), 126.4 (C-9/11), 126.4 (C-9/11), 127.9 (C-8/12), 128.0 (C-8./12), 128.7 (C-10), 128.7 (C-10), 138.0 (C-7), 138.5 (C-7), 155.0 (C-14), 155.3 (C-14). MS (ESI+): Calc’d for [C₁₅H₂₂NO₄⁺]: 280.1549, found: 280.1546.
4-Benzoyloxymethyl-2-oxazolidinone 17.\(^4\)

Into a tapered microwave vial was added sequentially the protected serinol 16 (0.0415 g, 0.149 mmol, 1.0 eq), NBS (0.0305 g, 0.171, 1.15 eq), and BPO (75% in H\(_2\)O, 0.0057 g, 0.12 eq). The atmosphere was replaced with nitrogen followed by addition of chlorobenzene (0.5 mL). The mixture was heated at 65 °C for 4.5 h, at which time further portions of NBS (0.0157 g, 0.0882 mmol, 0.59 eq) and BPO (75% in H\(_2\)O, 0.0032 g, 0.0099 mmol, 0.066 eq) were added. The mixture was heated for a further 60 min, and then cooled to rt. The mixture was diluted with DCM (2 mL), and washed with sat’d NaHCO\(_3\) (2 mL). The aqueous layer was extracted with DCM (2 mL × 3), the organic layers combined, dried over Na\(_2\)SO\(_4\), filtered, and the solvent removed under reduced pressure. Purification was conducted via silica gel column chromatography (100% hexanes, slowly increasing to 70:30 v/v, hexanes:ethyl acetate) to afford compound 17 as an off-white solid (0.0238 g, 0.1076 mmol, 72%). IR (4000-625ν cm\(^{-1}\), NaCl): 3285, 3070, 2952, 1758, 1718, 1601, 1452, 1409, 1316, 1276, 1180, 1071, 1028, 934, 713. \(^1\)H NMR (600 MHz, CDCl\(_3\)): δ4.23-4.27 (1H, m, H-4), 4.31 (1H, dd, \(J = 5.5, 11.5\) Hz, H-5), 4.31 (1H, dd, \(J = 5.0, 8.7\) Hz, H-6), 4.47 (1H, dd, \(J = 4.1, 11.5\) Hz, H-5), 4.59 (1H, t, \(J = 8.7\) Hz, H-6), 5.4 (1H, broad s, NH-3), 7.47 (2H, dt, \(J = 1.7, 7.5\) Hz, H-11/13), 7.60 (1H, tt, \(J = 1.3, 7.4\) Hz, H-12), 8.03 (2H, dd, \(J = 1.3, 8.3\) Hz, H-10/14). \(^{13}\)C NMR (150 MHz, CDCl\(_3\)): δ51.4 (C-4), 65.6 (C-5), 67.1 (C-6), 128.8 (C-11/13), 129.1 (C-9), 129.9 (C-10/14), 133.8 (C-12), 158.9 (C-2), 166.3 (C-8).
**cis/trans-2-Phenyl-5-(N- tert-butyloxycarbonyl)aminomethyl-1,3-dioxolane 19.**

3-Amino-1,2-propanediol (0.1033 g, 1.134 mmol, 1.0 eq) was dissolved in DMF (1.0 mL) in a 10 mL flame-dried flask. Boc$_2$O (0.265 g, 1.22 mmol, 1.08 eq) was added and the solution stirred for 7 h at room temperature. Benzaldehyde dimethyl acetal (0.20 g, 1.3 mmol, 0.22 mL, 1.2 eq) and PTSA monohydrate (0.0125 g, 0.0657 mmol, 0.060 eq) were then sequentially added and stirred at room temperature for an additional 16 h. The mixture was washed with 1:1 sat’d NaHCO$_3$:H$_2$O (4 mL) and separated, the aqueous layer was partitioned further with Et$_2$O (3 x 3 mL). The combined organic phase was dried over MgSO$_4$, filtered, and the solvent removed under reduced pressure. The residue was purified over silica gel column chromatography (100% hexanes, with gradient elution to 70:30 v/v, hexanes:ethyl acetate) yielding compound 19 as an inseparable, 1:1.3 mixture of cis/trans-isomers (colourless solid, 0.1441 g, 0.5159 mmol, 46%).

IR (4000-625 v cm$^{-1}$, NaCl): 3316, 3001, 2947, 1873, 1667, 1520, 1479, 1406, 1088, 1071, 981, 914, 758. $^1$H NMR (major isomer, 600 MHz, CDCl$_3$): δ1.48 (9H, s, H-15/16/17), 3.25-3.35 (2H, m, H-6), 3.88 (1H, dd, J = 5.6, 8.2 Hz, H-4), 4.09 (1H, dd, J = 7.4, 8.1 Hz, H-4), 4.29-4.37 (1H, m, H-5), 4.8 (1H, broad, NH-12), 5.79 (1H, s, H-2), 7.39 (3H, m, H-8/9/10), 7.49 (2H, dd, J = 2.0, 7.5 Hz, H-7/11). $^1$H NMR (minor isomer, 600 MHz, CDCl$_3$): δ1.49 (9H, s, H-15/16/17), 3.41-3.54 (2H, m, H-6), 3.72 (1H, dd, J = 7.0, 8.2 Hz, H-4), 4.23 (1H, dd, J = 6.5, 8.3 Hz, H-4), 4.29-4.37 (1H, m, H-5), 4.9 (1H, broad, NH-12), 5.94 (1H, s, H-2), 7.39 (3H, m, H-8/9/10), 7.46 (2H, dd, J = 1.8, 7.6 Hz, H-7/11). $^{13}$C NMR (mixture of isomers, CDCl$_3$, 150 MHz): δ28.0 (C-15/16/17), 28.4 (C-15/16/17), 42.4 (C-6), 43.0 (C-6), 67.8 (C-4), 67.9 (C-4), 75.6 (C-5), 75.9 (C-
5), 79.6 (C-14), 79.6 (C-14), 103.5 (C-2), 104.3 (C-2), 126.4 (C-7/11), 126.6 (C-7/11), 128.4 (C-8/10), 128.5 (C-8/10), 129.3 (C-9), 129.5 (C-9), 137.2 (C-6), 137.9 (C-6), 156.2 (C-13). MS (ESI+): Calc’d for [C_{15}H_{21}NO_{4}Na^+] : 302.1368; found 302.1362.

1-Bromo-2-benzyloxy-3-(N-tert-butyloxycarbonyl)aminopropane 20.

![Chemical structure of compound 20](image)

Compound 19 (0.0491 g, 0.176 mmol, 1.0 eq), NBS (0.0528 g, 0.297 mmol, 1.76 eq), and BPO (75% in H₂O, 0.0094 g, 0.029 mmol, 0.17 eq) were dissolved in chlorobenzene (2.3 mL) and the solution heated at 70 ºC for 5 h. The mixture was the cooled to room temperature and the solvent removed under reduced pressure. The crude product was purified over silica gel column chromatography (100% hexanes, gradient elution to 90:10 v/v, hexanes:ethyl acetate) to afford compound 20 as a colourless solid (0.0300 g, 0.0837 mmol, 48%). IR (4000-625ν cm⁻¹, NaCl): 3372, 2977, 1721, 1518, 1367, 1271, 1111, 1910, 711. ¹H NMR (600 MHz, CDCl₃): δ1.35 (9H, s, H-1/2/3), 3.46-3.54 (2H, m, H-7/9), 3.56 (1H, d, J = 5.2 Hz, H-9), 3.59 (1H, dd, J = 5.0, 11.1 Hz, H-7), 4.72 (1H, broad, NH-6), 5.23 (1H, q, J = 5.4 Hz, H-8), 7.39 (2H, t, J = 7.6 Hz, H-13/15), 7.52 (1H, t, J = 7.5, 7.6 Hz, H-14), 8.00 (2H, d, J = 7.5 Hz, H-12/16). ¹³C NMR (150 MHz, CDCl₃): δ28.4 (C-1/2/3), 31.5 (C-9), 42.6 (C-7), 72.4 (C-8), 80.1 (C-4), 128.6 (C-13/15), 129.7 (C-11), 130.0 (C-12/16), 133.6 (C-14), 156.0 (C-5), 165.9 (C-10). MS (ESI⁺, TOF): Calc’d for [C_{15}H_{20}BrNO_{4}Na^+] : 380.0468, 382.0453; found 380.0480, 382.0511.
cis/trans-5-Formyl-5-(N-tert-butyloxycarbonyl)amino-2-phenyl-1,3-dioxane 23.³

Oxalyl chloride (0.30 mL, 0.44g, 3.5mmol, 2.1eq) was dissolved in DCM (9 mL) and cooled to -78 °C. DMSO (040 mL, 0.44g, 5.6mmol, 3.4eq) was added slowly and the reaction was stirred for 40 mins. A solution of alcohol 7a (0.5045g, 1.631 mmol, 1.0 eq) in DCM (2.5 mL) was added dropwise to the mixture over 3 mins and stirring continued at -78 °C for 55 min. TEA (1.5 mL, 1.1g, 11mmol, 6.6eq) was added to the reaction dropwise and the solution was slowly allowed to warm to room temperature with stirring over 2h. The reaction was carefully quenched with 1M HCl (1 mL) and the organic (DCM) phase partitioned with sat’d aqueous NaHCO₃, followed by brine. The organic phase was dried over Na₂SO₄ and the solvent was removed under reduced pressure. Purification was performed over silica gel silica column chromatography (100% hexanes with slow gradient elution to 80:20 v/v, hexanes:ethyl acetate) to give 23 as the inseparable cis/trans-isomers (colorless solid, 0.3963g, 1.289mmol, 79%). IR (4000-625ν cm⁻¹, NaCl): 3341 (N-H), 2978, 2932, 2871, 1728 (C=O), 1700 (C=O), 1499, 1455, 1393, 1369, 1278, 1250, 1165, 1137, 1103, 1080, 1052, 989, 747, 699. ¹H NMR (Major isomer, 600MHz, CDCl₃): δ1.48 (9H, s, H₁₀/₁₁/₁₂), 4.14 (2H, d, J = 11.4Hz, H₄/₆), 4.28 (2H, d, J = 11.4Hz, H₄/₆), 5.5 (1H, s, H₂), 5.7 (1H, s, NH-7), 7.34-7.42 (3H, m, H₁₆/₁₇/₁₈), 7.50 (2H, dd, J = 1.5, 7.9Hz, H₁₅/₁₉), 9.59 (1H, s, H₁₃). ¹H NMR (Minor isomer, 600MHz, CDCl₃): δ1.44 (9H, s, H₁₀/₁₁/₁₂), 4.34 (2H, d, J = 9.4Hz, H₄/₆), 4.52 (2H, d, J = 9.4Hz, H₄/₆), 5.25 (1H, s, NH-7), 5.70 (1H, s, H₂), 7.34-7.42 (3H, m, H₁₆/₁₇/₁₈), 7.48 (2H, dd, J = 1.5, 7.2Hz, H₁₅/₁₉), 10.20 (0.5H, s, H₁₃). ¹³C NMR (Major isomer, 150MHz, CDCl₃): δ28.4 (C₁₀/₁₁/₁₂), 60.6 (C₄), 69.7 (C₃/₅), 81.4 (C₉), 101.8 (C₁), 126.3 (C₁₅/₁₉), 128.5 (C₁₆/₁₈), 129.5 (C₁₇), 137.2 (C-
14), 155.9 (C-8), 198.5 (C-13). $^{13}$C NMR (Minor isomer, 150MHz, CDCl$_3$): δ28.4 (C-10/11/12), 56.3 (C-4), 69.0 (C-3/5), 80.9 (C-9), 101.7 (C-1), 126.0 (C-15/19), 128.6 (C-16/18), 129.5 (C-17), 137.0 (C-14), 154.4 (C-8), 200.5 (C-13). MS (ESI$^+$): Calc’d. for [C$_{16}$H$_{21}$NO$_3$Li$^+$] 314.1580; found 314.1579.

cis/trans-5-Phenylhydroxymethyl-5-(N-tert-butlyoxycarbonyl)amino-2-phenyl-1,3-dioxane 24a.

Into a 25 mL 2-neck flask, fitted with a condensor and under nitrogen, was added magnesium turnings (0.1205 g, 4.959 mmol, 6.5 eq), iodine (0.0075g, 0.0030 mmol, 0.04 eq) and dry Et$_2$O (2.5mL). Iodobenzene (0.15 mL, 0.27 g, 1.3 mmol, 1.7 eq) was added and the solution warmed to reflux for 20 mins to initiate the reaction. The remaining iodobenzene (0.41 mL, 0.75 g, 3.7 mmol, 4.9 eq) was added slowly over 20 minutes and the solution was refluxed for an additional 60 min. This process provided 3.0 mL of a stock Grignard solution (~1.65M). In a separate flask, the aldehyde 23 (0.232 g, 0.755 mmol, 1 eq) was dissolved in Et$_2$O (3mL) under nitrogen and the solution cooled to 0 ºC whereupon a 2.0 mL portion (3.3 mmol, 4.3 eq) of the stock Grignard solution was added. The mixture was warmed to rt and allowed to stir for 105 min. Sat’d aqueous ammonium chloride (3.0 mL) was added and allowed to stir for 1h. The solution was separated and the aqueous layer was washed with Et$_2$O (4 mL × 3), the combined organic layers were dried over Na$_2$SO$_4$, filtered and the solvent removed under reduced pressure. Purification was conducted over silica gel silica column chromatography (100 hexanes, increasing to 80:20 v/v, hexanes:ethyl acetate) to give 24a as a 50:50 mixture of the cis/trans-isomers (0.2389 g,
0.6189 mmol, 82%). IR (4000-625 cm\(^{-1}\), NaCl): 3414 (O-H), 3331 (O-H), 3064, 3034, 2978, 2931, 2869, 1713 (C=O), 1683 (C=O), 1508, 1454, 1392, 1368, 1292, 1250, 1163, 1126, 1088, 1049, 1029, 982, 937, 874, 787, 744, 699, 636. \(^1\)H NMR (CDCl\(_3\), 600 MHz): \(\delta\) 1.44 (9H, s, H-10/11/12), 1.50 (9H, s, H-10/11/12), 3.85 (1H, dd, \(J = 2.25\), 11.4Hz, H-4/6), 3.90 (1H, d, \(J = 11.4\)Hz, H-4/6), 3.95 (1H, d, \(J = 12.2\)Hz, H-4/6), 4.03 (1H, d, \(J = 11.7\)Hz, H-4/6), 4.04 (1H, d, \(J = 11.5\)Hz, H-4/6), 4.11-4.16 (1H, m, H-4/6), 4.57 (1H, s, OH-13), 4.12-4.75 (2H, m, H-4/6), 4.83 (1H, d, \(J = 10.3\)Hz, OH-14), 5.12 (1H, s, NH-7), 5.44 (1H, s, H-2), 5.53 (1H, d, \(J = 5.7\)Hz, H-13), 5.63 (1H, s, H-2), 6.31 (1H, d, \(J = 8.3\)Hz, H-13), 7.22-7.52 (18H, m, H-16/17/18/19/20/23/24/25), 7.55 (2H, dd, \(J = 1.5\), 8.2Hz, H-22/26). \(^1\)C NMR (both isomers, CDCl\(_3\), 150 MHz): \(\delta\) 28.4 (C-10/11/12), 28.5 (C-10/11/12), 54.6 (C-5), 56.0 (C-5), 70.3 (C-13), 70.4 (C-13), 72.1 (C-4/6), 73.4 (C-4/6), 81.2 (C-9), 101.8 (C-2), 102.2 (C-2), 126.2 (C-18), 126.5 (C-23/25), 127.0 (C-23/25), 127.7 (C-17/19), 128.1 (C-17/19), 128.3 (C-16/20), 128.3 (C-16/20), 128.5 (C-22/26), 128.6 (C-22/26), 129.3 (C-24), 129.3 (C-24), 137.7 (C-21), 137.7 (C-21), 139.9 (C-15), 139.9 (C-15). MS (ESI\(^+\)): Calc’d for [C\(_{22}\)H\(_{28}\)NO\(_5\)]\(^+\): 386.1967; found 386.1960.

cis/trans-5-(4'-Chloro)phenylhydroxymethyl-5-(N-tert-butyloxycarbonyl)amino-2-phenyl-
1,3-dioxane 24b.

![Chemical Structure](image)

Into a 10 mL 2-neck flask, fitted with a condenser and under nitrogen, was added magnesium turnings (0.0354 g, 1.46 mmol, 2.4 eq), iodine (0.0028g, 0.011 mmol, 0.018eq) and dry THF (0.6
mL). 4-Chlorobromobenzene (0.276 g, 1.44 mmol, 2.3 eq) was dissolved in THF (0.5 mL) and an aliquot (0.15 mL) of this mixture was added to the magnesium suspension solution and the solution heated to 70 °C to initiate the reaction. Once the reaction began, the remaining 4-chlorobromobenzene mixture was added slowly over 30 mins. The mixture was heated for a further 60 mins before being cooled to 0 °C. Aldehyde 23 (0.1895 g, 0.6166 mmol, 1.0 eq) dissolved in THF (1 mL) was added over 2 mins and the reaction allowed to warm to rt while and stirred for an additional 2h. Sat’d aqueous NH₄Cl (3.0 mL) was then added and the solution stirred for 60 min. The reaction mixture was partitioned with Et₂O, the aqueous layer was washed with Et₂O (2 mL × 3) and the combined organic phase dried over Na₂SO₄, filtered, and the solvent removed under reduced pressure. Purification was performed over silica gel silica column chromatography to yield 24b as a 50:50 mixture of the cis/trans-isomers mixture of isomers, a pale orange solid (0.1275 g, 0.3036 mmol, 49%). IR (4000-625ν cm⁻¹, NaCl): 3409 (OH), 3326 (OH), 3067, 2979, 2931, 2868, 1714 (C=O), 1683 (C=O), 1597, 1507, 1491, 1456, 1393, 1368, 1291, 1250, 1200, 1162, 1126, 1091, 1048, 1015, 988, 941, 914, 876, 841, 743, 698.

¹H NMR (mixture of cis/trans isomers in a 1:1 ratio, 600MHz, CDCl₃): δ1.44 (9H, s, H-10/11/12), 1.49 (9H, s, H-10/11/12), 3.80 (1H, dd, J = 2.8, 11.7Hz, H-4/6), 3.87 (1H, d, J = 11.6Hz, H-4/6), 3.95 (1H, d, J = 12.1Hz, H-4/6), 3.98 (1H, d, J = 11.9Hz, H-4/6), 4.00 (1H, d, J = 11.7Hz), 4.06 (1H, d, J = 11.1Hz, H-4/6), 4.36 (1H, s, OH-14), 4.48 (1H, s, NH-7), 4.66-4.72 (2H, m, H-4/6), 4.85 (1H, d, J = 9.3 Hz, OH-14), 5.12 (1H, s, NH-7), 5.44 (1H, s, H-2), 5.49 (1H, d, J = 5.6Hz, H-13), 5.62 (1H, s, H-2), 6.38 (1H, d, J = 8.6 Hz, H-13), 7.19 (2H, d, J = 8.4Hz), 7.30-7.44 (12H over 2 isomers, m), 7.46 (2H, dd, J = 1.9, 8.0Hz, H-22/26), 7.54 (2H, dd, J = 1.5, 8.1Hz, H-22/26).

¹³C NMR (cis/trans isomers, 150MHz, CDCl₃): δ28.4 (C-10/11/12), 28.4 (C-10/11/12), 54.6 (C-5), 55.9 (C-5), 70.1 (C-9), 70.2 (C-4/6), 70.4 (C-9), 72.1 (C-4/6),
76.3 (C-13), 81.5 (C-13), 101.9 (C-2), 102.3 (C-2), 126.1, 126.4, 128.3, 128.5, 128.5, 128.6, 129.0, 129.4, 129.4, 133.9, 133.9, 137.5, 138.5, 138.5. MS (ESI+): Calc’d for [C_{22}H_{27}ClNO_5]^+: 420.1578; found 420.1559.

4-Benzoyloxymethyl-4-benzoyl-2-oxazolidinone 25a.

![Chemical Structure](image)

Compound 24a (0.1563 g, 0.4055 mmol, 1.0 eq), NBS (0.2197 g, 1.234 mmol, 3.0 eq), BPO (75% in H_2O, 0.0416 g, 0.1288 mmol, 0.32 eq), and chlorobenzene (4.0 mL) were added to a 2-neck 50 mL rbf fitted with a condenser under nitrogen. The mixture was heated at 70 ºC for 2 h, then cooled to rt. Sat’d aqueous NaHCO_3 (4 mL) and DCM (2 mL) were added and the organic layer removed. The aqueous layer was washed with DCM (4 mL × 3) and the combined organic phase dried over Na_2SO_4, filtered, and the solvent removed under reduced pressure. Purification was conducted over silica gel column chromatography (100 hexanes, gradually increasing to 50:50 v/v, hexanes:ethyl acetate) to give 25a as colourless crystals (0.0854 g, 0.263 mmol, 65%). IR (4000-625ν cm\(^{-1}\), NaCl): 3351 (N-H), 3065, 2923, 1764 (C=O), 1725 (C=O), 1686, 1598, 1582, 1450, 1395, 1270, 1179, 1110, 1050, 1027, 710, 689. \(^1\)H NMR (600 MHz, CDCl_3): \(\delta\) 4.75 (1H, d, \(J = 11.7\) Hz, H-5), 4.78 (1H, d, \(J = 11.7\) Hz, H-5), 4.78 (1H, d, \(J = 11.9\) Hz, H-13), 4.81 (1H, d, \(J = 11.9\) Hz, H-13), 5.96 (1H, s – broad, NH-3), 7.45 (2H, t, \(J = 7.7\) Hz, H-17/19), 7.54 (2H, t, \(J = 7.8\) Hz, H-9.11), 7.59 (1H, tt, \(J = 1.2, 7.4\) Hz, H-16), 7.66 (1H, tt, \(J = 1.1, 7.4\) Hz, H-10), 7.85 (2H, dd, \(J = 1.3, 8.3\) Hz, H-8/12), 7.96 (2H, dd, \(J = 1.3, 8.4\) Hz, H-16/20). \(^{13}\)C NMR (150 MHz, CDCl_3): \(\delta\) 68.0 (C-5), 68.3 (C-4), 69.2 (C-13), 128.7 (C-15), 128.8 (C-9/11), 129.0
(C-17/19), 129.5 (C-8/12), 129.9 (16/20), 132.9 (C-7), 134.0 (C-18), 134.6 (C-10), 157.2 (C-2), 166.1 (C-14), 195.9 (C-6). MS (ESI\(^+\), TOF): Calc’d for [C\(_{18}\)H\(_{15}\)NO\(_5\) + H\(^+\)]: 326.1028; found 326.1016. M.p.: 137.1 - 138.7 °C (from EtOAc).

4-Benzoyloxymethyl-4-(4’-chloro)benzoyl-2-oxazolidinone 25b.

Into a tapered microwave vial was weighed compound 24b (0.0325 g, 0.0722 mmol, 1.0 eq), NBS (0.0560 g, 0.315 mmol, 4.4 eq), and a catalytic amount of BPO (75% in H\(_2\)O, 0.0118 g, 0.0365 mmol, 0.47 eq) added. The flask was gently flushed with nitrogen, chlorobenzene (0.6 mL) was added and the mixture heated at 70 °C for 6 h. The reaction was then cooled sat’d aqueous NaHCO\(_3\) (1 mL) and DCM (0.5 mL) were added. The layers were separated and the aqueous phase was washed with DCM (3 x 1.0 mL). The organic layers were combined, dried over Na\(_2\)SO\(_4\), filtered and the solvent removed under reduced pressure. Purification was conducted over silica gel column chromatography (Hexane:EtOAc) to yield compound 25b as a clear, colourless, amorphous solid (0.0216 g, 0.0600 mmol, 78%). IR (4000-625 ν cm\(^{-1}\), NaCl): 3345 (NH), 3070, 2977, 2929, 1763 (C=O), 1725 (C=O), 1690 (C=O), 1588, 1488, 1451, 1397, 1369, 1271, 1178, 1110, 1095, 1071, 1051, 1027, 961, 843, 712. \(^1\)H NMR (600 MHz, CDCl\(_3\)): δ4.67-4.80 (4H, m, H-5/13), 6.48 (1H, s-broad, NH-3), 7.43 (2H, t, J = 7.8 Hz, H-17/19), 7.49 (2H, d, J = 8.6Hz, H-9/11), 7.58 (1H, dt, J = 0.7, 7.2 Hz, H-18), 7.81 (2H, d, J = 8.6 Hz, H-8/12), 7.94 (2H, dd, J = 0.7, 7.8 Hz, H-16/20). \(^13\)C NMR (150 MHz, CDCl\(_3\)): δ67.8 (C-4), 68.2 (C-5), 69.2 (C-13), 128.7, 128.8 (C-9/11), 129.8 (C-17/19), 130.0 (C-16/20), 130.4 (C-8/12), 131.4 (C-
7), 134.0 (C-18), 141.2 (C-10), 157.5 (C-2), 166.1 (C-14), 195.11 (C-6). MS (ESI+): Calc’d for [C_{18}H_{14}ClNO_{5} + H^+] 360.0639; found 360.0628.

4-(4’-Octylphenyl)ethyl-4-benzoyloxymethyl-2-oxazolidinone 28.

N-Boc-benzylidene protected-FTY720 27 was prepared from aldehyde 23 following to the literature protocol.\(^3\) Into a 5 mL reaction vial was weighed compound 27 (0.0197 g, 0.0397 mmol, 1.0 eq) and NBS (0.0082 g, 0.070 mmol, 1.8 eq). The flask was gently flushed with nitrogen and BPO (75% in H_2O, 0.0016 g, 0.0050 mmol, 0.12 eq) and chlorobenzene (0.4 mL) sequentially added. The solution was heated at 70 °C for 120 min at which time second portions of NBS (0.0046 g, 0.039 mmol, 0.98 eq) and BPO (75% in H_2O, 0.0012 g, 0.037 mmol, 0.093 eq) were added and heating continued for an additional 60 min (at 70 °C). The mixture was cooled, diluted with sat’d aqueous NaHCO_3 (0.8 mL) and DCM (0.8 mL) and the organic phase separated. The aqueous layer was extracted with DCM (3 x 1 mL), the organic layers combined, dried over Na_2SO_4, filtered, and the solvent removed under reduced pressure. Purification over silica gel column chromatography (100% hexanes, slow gradient elution to 90:10 v/v, hexanes:ethyl acetate) yielded compound 28 as a colorless amorphous solid (0.0093 g, 0.021 mmol, 54%). \(^1\)H NMR (600 MHz, CDCl_3): \(\delta\)0.81 (3H, t, \(J = 7.0\) Hz, H-29), 1.15-1.28 (12H, m, H-23/24/25/26/27/28), 1.93-2.02 (2H, m, H-14), 2.50 (2H, t, \(J = 7.7\) Hz, H-22), 2.60-2.70 (2H, m, H-15), 4.17 (1H, d, \(J = 9.0\) Hz, H-6), 4.23 (1H, d, \(J = 11.6\) Hz, H-5), 4.30 (2H, d, \(J = 9.0\) Hz, H-6), 4.38 (2H, d, \(J = 11.6\) Hz, H-5), 5.0 (1H, broad s, NH-3), 7.02 (2H, d, \(J = 8.1\) Hz, H-18/20),
7.05 (2H, d, J = 8.1 Hz, H-17/21), 7.40 (2H, t, J = 7.8 Hz, H-10/12), 7.53 (1H, tt, J = 1.1, 7.4 Hz, H-11), 7.95 (2H, dd, J = 1.2, 8.0 Hz, H-9/13). $^{13}$C NMR (CDCl$_3$, 150 MHz): δ14.3 (C-29), 22.8 (C-28), 29.4, 29.5, 29.6, 31.7, 32.0, 35.7, 37.8 (C-14), 60.0 (C-4), 67.7 (C-5), 71.8 (C-6), 128.2, 128.8 (C10/12), 129.0, 129.2 (C-8), 129.9 (C-9/13), 133.8 (C-11), 137.2, 141.5, 158.4 (C-2), 166.3 (C-7). MS (ESI$^+$, TOF): Calc’d for [C$_{27}$H$_{36}$NO$_4$]+: 438.2644; found 438.2636.

**4-Benzoyloxymethyl-4-(4’-toluenesulfonyl)methyloxy-2-oxazolidinone 29.**

[Chemical structure image]

Oxazolidinone 8a (0.3197 g, 1.272 mmol, 1.0 eq) and tosyl chloride (0.7410 g, 3.886 mmol, 3.05 eq) were added to a flame-dried 25 mL flask under N$_2$. Lutidine (3.0 mL) was added and the mixture stirred for 20.5h at rt. The thick, dark-red mixture was partitioned between DCM and water and the organic phase concentrated under reduced pressure. Purification was performed through column chromatography (hexane-packed, eluted using 80:20 v/v, hexanes:ethyl acetate) to give 8a as a colourless crystalline solid (0.4493 g, 1.108 mmol, 87%). IR (4000-625ν cm$^{-1}$, NaCl): 3343, 3066 (aromatic C-H), 3032, 2957, 2918, 1765 (C=O), 1725 (C=O carbamate), 1599 (C=C aromatic), 1585 (C=C aromatic), 1532, 1451 (C=C aromatic), 1401 (C=C aromatic), 1366, 1315, 1269 (C-O), 1212, 1191, 1177, 1113, 1097, 1071, 1050, 1027, 1019, 992, 937, 830 (p-sub’d aromatic C-H), 814, 793, 764, 712, 686, 667. $^1$H NMR (600 MHz, CDCl$_3$): δ2.37 (3H, s, H-13), 4.15 (2H, dd, J = 10.2, 16.3 Hz, H-6), 4.24 (1H, d, J = 9.4 Hz, H-14), 4.30 (1H, d, J = 11.6 Hz, H-5), 4.31 (1H, d, J = 9.4 Hz, H-14), 4.44 (1H, d, J = 9.4 Hz, H-5), 5.59 (1H, s, NH-3), 7.30 (2H, d, J = 8.1 Hz, H-9/11), 7.45 (2H, dd, J = 1.7, 7.4, 8.2 Hz, H-18/20), 7.61 (1H, dddd, J
= 1.3, 1.3, 7.4, 7.4 Hz, H-19), 7.77 (2H, dd, J = 1.6, 8.2 Hz, H-8/12), 7.91 (2H, dd, J = 1.3, 8.2 Hz, H-17/21). 13C NMR (CDCl3, 150 MHz): δ21.8 (C-13), 59.2 (C-4), 64.9 (C-5), 69.1 (C-6), 69.3 (C-14), 128.1 (C-9/11), 128.8 (C-18/20), 129.9 (C-17/21), 130.3 (C-8/12), 131.8 (C-10), 134.0 (C-19), 146.0 (C-7), 157.7 (C-2), 165.8 (C-15). MS (Cl): Calc’d for [C19H19NO7S + H+]: 406.0960, found (minor): 406.1000. Calc’d for [C19H19NO7S – OTos-]: 234.0766; found: 234.0752. M.p.: 118.9 - 122.0 ºC.

4-Azidomethyl-4-benzoyloxymethyl-2-oxazolidinone 30.

A flame-dried 2-neck flask was charged with the oxazolidinone 29 (0.2010 g, 0.04958 mmol, 1.0 eq), DMF (1.4 mL) and sodium azide (0.1796 g, 0.2763 mmol, 5.5 eq). The solution was heated at 80 ºC for 5 h. The solvent was removed under reduced pressure, and the resulting solid taken into DCM (4 x 3 mL). The combined DCM phase was concentrated under reduced pressure to afford a white solid (0.1505 g, 0.4724 mmol, 95.3%). IR (4000-625ν cm−1, NaCl): 3312, 3071, 2957, 2918, 2867, 2112, 1759 (C=O), 1725 (C=O), 1602, 1584, 1535, 1491, 1475, 1451, 1401, 1350, 1316, 1272, 1179, 1161, 1114, 1072, 1048, 1028, 1000, 961, 937, 806, 767, 712, 687, 668. 1H NMR (600 MHz, CDCl3): δ3.61 (1H, d, J = 12.4 Hz, H-14), 3.67 (1H, d, J = 12.4 Hz, H-14), 4.29 (1H, d, J = 9.2 Hz, H-6), 4.33 (1H, d, J = 11.4 Hz, H-5), 4.33 (1H, d, J = 9.2 Hz, H-6), 4.48 (1H, d, J = 11.4 Hz, H-5), 5.78 (1H, s, NH-3), 7.48 (2H, dd, J = 7.6, 7.8 Hz, H-10/12), 7.61 (1H, dd, J = 7.6 Hz, H-11), 8.02 (2H, d, J = 7.8 Hz, H-9/13). 13C NMR (CDCl3, 150 MHz): δ54.9 (C-14), 60.1 (C-4), 65.7 (C-5), 69.9 (C-6), 128.8 (C-10/12), 128.9 (C-8), 129.9 (C-9/13), 134.0 (C-
11), 158.3 (C-2), 166.1 (C-7). MS. (ESI+, TOF): Calc’d for [C_{12}H_{12}N_{4}O_{4} + H^+] = 277.0937; found: 277.0928. Colorless crystals suitable for X-ray analysis were deposited from slow evaporation of a solution in dichloromethane in the refrigerator. M.p. 120 ºC (decomp).

Synthesis of chloropropyl-triazole 31a.

Into a flame-dried tapered microwave vial under N_2 was added the azide 30 (0.030g, 0.11mmol, 1.0 eq). Copper (I) iodide (0.0013g, 0.0068mmol, 0.06eq), and copper (II) acetate monohydrate (0.0015 g, 0.0075mmol, 0.079 eq) were dissolved in dry THF (0.2mL) and added to the azide. 5-chloro-1-pentyne (0.018mL, 0.017g, 0.17mmol, 1.5eq) was added, the vial was septa-sealed and the mixture was heated at 50 ºC for 18h. Small portions of THF added occasionally to retain the original volume. The mixture was cooled to room temperature, the solvent removed under pressure and the crude material purified over silica gel column chromatography (silica gel, 80:20 v/v, hexanes:ethyl acetate, slowly increasing the ratio to 50:50 hexanes:ethyl acetate). Compound 31a was isolated as an unstable solid (0.0292 g, 0.0771 mmol, 70%). IR (4000-625v cm^{-1}, NaCl): 3341 (N-H), 3126, 3013, 2920, 1765, 1747 (C=O), 1715 (C=O), 1471, 1451, 1439, 1426, 1395, 1350, 1335, 1313, 1299, 1277 (C-O), 1264 (C-O), 1225, 1177, 1163, 1123, 1110, 1097, 1071, 1041 (C-N), 999, 951, 929, 910, 863, 826, 82, 766, 706 (C-Cl), 696, 651. $^1$H NMR (CDCl$_3$, 600MHz): δ2.13 (2H, tt, J = 6.3, 7.3Hz, H-18), 2.87 (2H, t, J = 7.3Hz, H-17), 3.54 (2H, t, J = 6.3Hz, H-19), 4.29 (1H, d, J = 11.7Hz, H-4), 4.41 (1H, d, J = 9.2Hz, H-6), 4.41 (1H, d, J =
11.7Hz, H-14), 4.51 (1H, d, 9.2Hz, H-6), 4.60 (1H, d, J = 14.4Hz, H-5), 4.66 (1H, d, J = 14.4Hz, H-5), 6.76 (1H, s, NH-3), 7.46 (2H, dd, 7.2, 8.1Hz, H-10/12), 7.47 (1H, s, H-15), 7.61 (1H, t, J = 7.2Hz, H-11), 8.01 (2H, d, J = 8.1Hz, H-9/13). $^{13}$C NMR (CDCl$_3$, 150MHz): 22.6 (C-18), 31.7 (C-17), 44.2 (C-19), 53.4 (C-14), 60.3 (C-4), 65.9 (C-5), 69.8 (C-6), 123.2 (C-15), 128.7 (C-8), 128.9 (C-10/12), 129.9 (C-9/13), 134.1 (C-11), 147.1 (C-16), 158.2 (C-2), 165.9 (C-7).

Synthesis of phenyl triazole 31b.

Into a flame-dried tapered microwave vial under N$_2$ was added azide 30 (0.0091g, 0.33mmol, 1.0 eq). Copper (I) iodide (0.0008g, 0.0042mmol, 0.13 eq) and copper acetate monohydrate (0.006 g, 0.003mmol, 0.09eq) were dissolved in dry THF (0.07mL) and added to the azide. Phenylacetylene (0.004mL, 0.0037g, 0.036mmol, 1.1 eq) was added, the vial was septa-sealed and the mixture heated at 50 °C for 5.5h, then temperature was lowered and the mixture was heated at 40 °C for a further 18h. Small portions of THF were added occasionally to retain the original volume. The mixture was cooled to room temperature and diluted with water (0.2mL), then extracted into DCM. The combined organic phase was rinsed with saturated NaHCO$_3$, separated and the solvent removed under reduced pressure. Purification was conducted over silica gel silica column chromatography (80:20 v/v, hexanes:ethyl acetate, slowly increasing the ratio to 50:50 hexanes:ethyl acetate) to give 31b as a white solid (0.0089g,0.024 mmol, 71.3%). IR (4000-625ν cm$^{-1}$, NaCl): 2920 (C-H), 2850, 2110, 1760 (C=O), 1722 (C=O), 1700 (C=O), 1700, 1406, 1318, 1266 (C-O), 1181, 1111, 1073,
1042, 1028, 909, 765, 713. $^1$H NMR (CDCl$_3$, 600MHz): δ4.32 (1H, d, $J$ = 11.7Hz, H-14), 4.44 (1H, d, $J$ = 9.3Hz, H-6), 4.45 (1H, d, $J$ = 11.7Hz, H-14), 4.53 (1H, d, $J$ = 9.3Hz, H-6), 4.65 (1H, d, $J$ = 14.4Hz, H-5), 4.69 (1H, d, $J$ = 14.4Hz, H-5), 6.5 (1H, s – broad, NH-3), 7.34 (1H, tt, $J$ = 1.1, 7.5Hz, H-20), 7.41 (2H, t, $J$ = 7.5Hz, H-19/21), 7.45 (2H, t, $J$ = 7.5, 8.1Hz, H-10/12), 7.60 (1H, tt, $J$ = 1.2, 8.1Hz, H-11), 7.78 (2H, dd, $J$ = 1.1, 7.3Hz, H-18/22), 7.87 (1H, s, H-15), 8.00 (2H, dd, $J$ = 1.2, 8.1Hz, H-9/13). $^{13}$C NMR (150MHz, DMSO-d$_6$): δ54.1 (C-4), 60.7 (C-14), 60.8 (C-14), 67.3 (C-5), 69.9 (C-6), 123.2 (C-20), 126.3 (C-18/22), 128.8 (C-11), 129.5 (C-19/21), 129.7 (C-10/12), 130.5 (C-17), 130.5 (C-9/13), 132.0 (C-8), 134.4 (C-15), 148.1 (C-16), 158.3 (C-2), 158.3 (C-2), 166.4 (C-7). MS (CI): Calc’d for [C$_{20}$H$_{18}$N$_4$O$_4$ + H$^+$]: 379.1406; found: 379.1405.

4-Benzoyloxymethyl-4-(methoxymethyl)methyloxy-3-phenyl-2-oxazolidinone 32.

![Diagram](image)

Into a flame-dried tapered microwave vial under N$_2$ was added CuI (0.0322g, 0.169mmol, 2.70eq), dioxane (0.20 mL), then trans-1,2-diaminocyclohexane (0.020 mL, 0.019g, 0.0169mmol, 2.70eq). The mixture was heated at 40 ºC for 5 mins, then cooled to rt. Bromobenzene (0.020 mL, 0.19mmol, 0.030g, 3.0eq) was then added and the mixture was stirred for 20 mins at rt, followed by addition of the MOM-protected oxazolidinone 8b (0.0162g, 0.0625mmol, 1.0eq) and K$_2$CO$_3$ (0.0221g, 0.160mmol, 2.56eq). The vial was subsequently capped and the mixture heated at 110 ºC for 24h. The solution was diluted with dioxane (0.30 mL) and heated at 110 ºC for a further 3 days. After cooling, the solvent was removed under reduced pressure and purification was performed via silica column chromatography (100%
hexanes, gradient elution to 70:30 v/v, hexanes:ethyl acetate) to afford 32 as a white solid (0.0144g, 0.0388mmol, 62%). $^1$H NMR (600MHz, CDCl$_3$): δ3.38 (3H, s, H-22), 3.60 (1H, d, J = 10.0 Hz, H-20), 3.70 (1H, d, J = 10.0 Hz, H-20), 4.22 (1H, d, J = 11.9 Hz, H-5), 4.48 (1H, d, J = 12.0 Hz, H-5), 4.49 (1H, d, J = 8.9 Hz, H-12), 4.57 (1H, d, J = 8.9 Hz, H-12), 4.66 (2H, dd, J = 6.7, 9.1 Hz, H-21), 7.26-7.28 (2H, m, H-8/10), 7.37 (1H, tt, J = 1.3, 6.2 Hz, H-9), 7.41 (2H, tt, J = 1.4, 7.0 Hz, H-7/11), 7.47 (2H, dt, J = 8.2 Hz, H-16/18), 7.61 (1H, tt, J = 1.3, 7.5 Hz, H-17), 7.99 (2H, dd, J = 1.2, 8.3 Hz, H-15-19). $^{13}$C NMR (150MHz, CDCl$_3$): δ56.1 (C-22), 64.5 (C-4), 64.5 (C-20), 68.3 (C-12), 68.4 (C-5), 97.1 (C-21), 128.9 (C-16/18), 128.9 (C-7/11), 129.1 (C-9), 129.3 (C-17), 129.9 (C-8/10), 129.9 (C-15/19), 133.9 (C-14), 134.4 (C-6), 157.6 (C-2), 166.0 (C-13).

References: