Supporting Information

Amphphilic \( \alpha \)-helix mimetics based on a benzoylurea scaffold

Sam Thompson, Andrew D. Hamilton*

Department of Chemistry, Chemistry Research Laboratory,
University of Oxford, Mansfield Road, Oxford, OX1 3TA, U.K.

andrew.hamilton@chem.ox.ac.uk

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1. General Information

Reactions were carried out under a nitrogen or argon atmosphere in oven-dried glassware unless otherwise stated. Standard inert atmosphere techniques were used in handling all air and moisture sensitive reagents.

1.1. Solvent & reagents
Anhydrous tetrahydrofuran and dichloromethane (from commercial sources) were obtained by filtration through activated alumina (powder ~150 mesh, pore size 58 Å, basic, Sigma-Aldrich) columns, or were dried on an MB-SPS-800 dry solvent system. Other solvents and reagents were used directly as received from commercial suppliers. Petrol refers to distilled light petroleum of fraction (30 °C - 40 °C).

1.2. Chromatography
Flash column chromatography was carried out using VWR Kieselgel 60 silica gel (60-63 μm). Thin-layer chromatography was carried out using Merck Kieselgel 60 F254 (230-400 mesh) fluorescent treated silica, visualized under UV light (250 nm) and by staining with aqueous potassium permanganate solution.

1.3. Spectroscopy
$^1$H and $^{13}$C NMR spectra were recorded using a Bruker 500, 400, 300 or 250 MHz spectrometer running Topspin™ software and are quoted in ppm for measurement against a tetramethylsilane (TMS) or residual solvent peaks as internal standards. Chemical shifts (δ) are given in parts per million (ppm), and coupling constants (J) are given in Hertz (Hz). The $^1$H NMR spectra are reported as follows: δ / ppm (number of protons, multiplicity, coupling constant J / Hz (where appropriate), assignment). Multiplicity is abbreviated as follows: s = singlet, br = broad, d = doublet, dd = doublet of doublets, t = triplet, dt = doublet of triplet, q = quartet, dq = doublet of quartet, quint. = quintet, sept. = septet, m = multiplet, v = very. Compound names are those generated by ChemBioDraw™ (CambridgeSoft) following IUPAC nomenclature. However, the NMR assignment numbering used is arbitrary and does not follow any particular convention. Numbering of compounds is illustrated on the spectra themselves; vide infra. The $^{13}$C NMR spectra are reported in δ / ppm. Two-dimensional (COSY, HSQC, HMBC) NMR spectroscopy was used to assist the
assignment of signals in the $^1$H and $^{13}$C NMR spectra. IR spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer from a thin film deposited onto a sodium chloride plate or a diamond ATR module. Only selected maximum absorbances ($\nu_{\text{max}}$) of the most intense peaks are reported (cm$^{-1}$). Low-resolution mass spectra were recorded on a Waters LCT premier XE Micromass spectrometer (ESI). High-resolution mass spectra were recorded on a Bruker MicroTof mass spectrometer (ESI) by the internal service at the Department of Organic Chemistry, University of Oxford. Melting points were recorded using a Leica Galen III hot-stage microscope apparatus and are reported uncorrected in degrees Celsius (˚C).

2. Practical experimental

_Benzyl 3,5-dihydroxybenzoate: 1_

\[
\begin{align*}
\text{HO} & \quad \text{KHCO}_3, \text{BnBr} \quad \text{DMF, 40 °C, 1h} \\
\text{HO} & \quad \text{O} \quad \\
\text{HO} & \quad \text{O} \quad \\
\text{Bn} & \quad \text{Bn} \\
\text{O} & \quad \text{O} \\
\end{align*}
\]

According to a literature preparation\(^1\) benzyl bromide (11.7 mL, 98.4 mmol) was added to a stirred solution of 3,5-dihydroxybenzoic acid (10.1 g, 65.6 mmol) and potassium hydrogen carbonate (7.87 g, 78.7 mmol) in N,N-dimethylformamide (110 mL). After overnight stirring at 40 °C the reaction was diluted with dichloromethane (700 mL), partitioned with ammonium chloride (700 mL) and extracted with dichloromethane (3 x 500 mL). The organic layers were combined, dried (magnesium sulfate), filtered and concentrated _in vacuo_. The residue was purified by flash column chromatography (2 : 1, petrol : diethyl ether) affording the title compound 1 (15.8 g, 64.8 mmol, 99 % yield) as a clear oil.

$\nu_{\text{max}}$ (neat) 3353, 1694, 1608, 1387, 1227, 1104, 1001, 969; $\delta_H$ (500 MHz, (CD$_3$)$_2$SO) 9.66 (2H, s, OH), 7.47 - 7.29 (5H, m, Ar-H), 6.88 (2H, d, $J$ 2.2, H-1, H-5), 6.47 (1H, t, $J$ 2.2, H-3), 5.30 (2H, s, CH$_2$); $\delta_C$ (125 MHz, (CD$_3$)$_2$SO) 166.5, 159.5, 137.1, 132.1, 129.4, 129.0, 128.9, 127.3, 108.4, 108.2, 108.0, 66.9; HRMS (ESI) found 267.0631; C$_{14}$H$_{12}$NaO$_4$ [M+Na]$^+$ requires 267.0628.
**Benzyl 3-hydroxy-5-isopropoxybenzoate: 2**

Isopropyl iodide (2.48 mL, 24.8 mmol) was added to a stirred solution of benzyl 3,5-dihydroxybenzoate 1 (5.05 g, 20.7 mmol) and potassium carbonate (4.57 g, 31.1 mmol) in N,N-dimethylformamide (25 mL). After overnight stirring at 60 °C the reaction was diluted with dichloromethane (500 mL), partitioned with ammonium chloride (500 mL) and extracted with dichloromethane (3 x 300 mL). The organic layers were combined, dried (magnesium sulfate), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (20 : 1 → 1 : 2 petrol : diethyl ether) affording, in order of elution, 3,5-diisopropoxybenzoic acid 3 (1.64 g, 5.00 mmol, 24 % yield), the title compound 2 (2.69 g, 9.41 mmol, 45 % yield) and starting material 1 (1.54 g, 6.31 mmol, 30 % yield) as clear oils.

ν<sub>max</sub> (neat) 3390, 2978, 1693, 1594, 1449, 1318, 1226, 1154, 1105, 1025, 766, 696; δ<sub>H</sub> (500 MHz, CDCl<sub>3</sub>) 7.50 - 7.35 (5H, m, Ar-H), 7.29 - 7.21 (2H, m, H-1, H-5), 6.70 (1H, t, J 2.2, H-3), 6.47 (1H, s, OH), 5.49 (2H, s, CH₂), 4.59 (1H, sept, J 6.1, CH(CH₃)₂), 1.37 (6H, d, J 6.1, CH(CH₃)₂); δ<sub>C</sub> (125 MHz, CDCl<sub>3</sub>) 167.2, 159.6, 157.5, 136.1, 132.3, 129.1, 128.9, 128.8, 128.6, 128.0, 110.1, 109.8, 109.7, 109.6, 108.8, 70.9, 70.7, 67.6, 22.4; HRMS (ESI) found 309.1084; C₁₇H₁₈NaO₄ [M+Na]<sup>+</sup> requires 309.1097.

3,5-Diisopropoxybenzoic acid 3; ν<sub>max</sub> (neat) 2977, 1719, 1592, 1448, 1376, 1296, 1156, 1113, 1003, 766; δ<sub>H</sub> (500 MHz, CDCl<sub>3</sub>) 7.48 - 7.31 (5H, m, Ar-H), 7.19 (2H, d, J 2.3, Ar-H), 6.62 (1H, t, J 2.3, Ar-H), 5.35 (2H, s, CH₂), 4.57 (2H, sept, J 6.1, CH(CH₃)₂), 1.34 (12H, d, J 6.1, CH(CH₃)₂); δ<sub>C</sub> (125 MHz, CDCl<sub>3</sub>) 166.8, 159.4, 136.5, 132.4, 129.0, 128.6, 128.6, 109.5, 109.3, 70.7, 67.2, 22.4; HRMS (ESI) found 351.1555; C₂₀H₂₄NaO₄ [M+Na]<sup>+</sup> requires 351.1567.

**Benzyl 3-(2-(tert-butoxy)-2-oxoethoxy)-5-isopropoxybenzoate: 4**
tert-Butyl bromoacetate (330 µL, 2.19 mmol) was added to a stirred solution of benzyl 3-hydroxy-5-isopropoxybenzoate 2 (521 mg, 1.82 mmol) and potassium carbonate (502 mg, 3.64 mmol) in N,N-dimethylformamide (3.0 mL). After 15 mins at 90 °C, t.l.c. (2 : 1, petrol : diethyl ether) indicated complete consumption of starting material (Rf 0.5) and the formation of a major product (Rf 0.8). The reaction was diluted with dichloromethane (50 mL), partitioned with ammonium chloride (50 mL) and extracted with dichloromethane (3 x 40 mL). The organic layers were combined, dried (magnesium sulfate), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (8 : 1, petrol : diethyl ether) affording the title compound 4 (720 mg, 1.80 mmol, 99 % yield) as a clear oil.

\[ \nu_{\text{max}} \text{(neat)} = 2978, 1752, 1719, 1594, 1452, 1370, 1299, 1223, 1144, 1107, 1012, 844, 765, 697; \delta_H \text{ (500 MHz, CDCl}_3\text{)} = 7.50 - 7.36 (5H, m, Ar-H), 7.32 (1H, br, Ar-H), 7.20 (1H, br, Ar-H), 6.73 (1H, t, J 2.3, H-3), 5.39 (2H, s, CH\text{2}), 4.61 (1H, sept, J 6.1, CH(CH\text{3})\text{2}), 4.57 (2H, s, CH\text{2}), 1.53 (9H, s, C(CH\text{3})\text{3}), 1.38 (6H, d, J 6.1, CH(CH\text{3})\text{2}); \delta_C \text{ (125 MHz, CDCl}_3\text{)} = 168.1, 166.5, 159.4, 159.4, 136.4, 132.4, 129.0, 128.7, 128.6, 111.0, 108.4, 107.5, 82.9, 70.8, 67.3, 66.2, 28.5, 23.1, 22.4; HRMS (ESI) found 423.1765; C\text{23}H\text{28}NaO\text{6} \ [\text{M+Na}]^+ \text{ requires 423.1778.}

3-(2-(tert-Butoxy)-2-oxoethoxy)-5-isopropoxybenzoic acid: 5

Palladium on carbon (28 mg, wet degussa type, 5 % palladium by weight) was added to a stirred solution of benzyl 3-(2-(tert-butoxy)-2-oxoethoxy)-5-isopropoxybenzoate 4 (137 mg, 0.34 mmol) in ethanol (2.0 mL). The solution was degassed three times with argon using a pump-flood procedure, and placed under hydrogen. After 3 h, t.l.c. (2 : 1, petrol : diethyl ether) indicated complete consumption of starting material (Rf 0.8) and the formation of a major product (Rf 0.1). The reaction was filtered (CeliteTM), washed with dichloromethane (80 mL) and concentrated in vacuo. Recrystallization (ethanol) afforded the title compound 5 (878 mg, 2.83 mmol, 91 % yield) as clear crystals.

\[ \nu_{\text{max}} \text{(neat)} = 2982, 1745, 1685, 1595, 1144, 766, 729; \delta_H \text{ (500 MHz, CDCl}_3\text{)} = 11.10 \]
(1H, v br, CO2H), 7.33 (1H, br, Ar-H), 7.22 (1H, br, Ar-H), 6.77 (1H, t, J 2.2, H-3), 4.62 (1H, sept, J 6.0, CH(CH3)2), 4.59 (2H, s, CH2), 1.55 (9H, s, C(CH3)3), 1.38 (6H, d, J 6.0, CH(CH3)2); δC (125 MHz, CDCl3) 172.2, 168.2, 159.5, 159.4, 131.7, 111.2, 109.4, 107.8, 83.1, 70.9, 66.2, 28.5, 22.3; HRMS (ESI) found 333.1307; C16H22NaO6 [M+Na]+ requires 333.1309.

3-Isopropoxy-2-nitrophenol: 8

Isopropyl iodide (775 µL, 7.74 mmol) was added to a stirred solution of 2-nitroresorcinol (1.00 g, 6.45 mmol) and potassium carbonate (1.42 g, 10.32 mmol) in N,N-dimethylformamide (5.0 mL). After 18 h stirring at 60 °C the reaction was diluted with dichloromethane (70 mL), partitioned with ammonium chloride (70 mL) and extracted with dichloromethane (3 x 50 mL). The organic layers were combined, dried (magnesium sulfate), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (4 : 1 → 2 : 1 petrol : diethyl ether) affording, in order of elution, 1,3-diisopropoxy-2-nitrobenzene 9 (501 mg, 2.10 mmol, 32 % yield) and the title compound 8 (684 mg, 3.47 mmol, 54 % yield) as clear oils.

νmax (neat) 3390, 2982, 1588, 1531, 1462, 1353, 1182, 1104, 1053, 913, 857, 789; δH (400 MHz, CDCl3) 9.93 (1H, br, OH), 7.35 (1H, t, J 8.4, Ar-H), 6.64 (1H, dd, J 8.4, 1.1, Ar-H), 6.53 (1H, d, J 8.4, Ar-H), 4.66 (1H, sept, J 6.1, CH(CH3)2), 1.40 (6H, d, J 6.1, CH(CH3)2); δC (63 MHz, CDCl3) 155.8, 154.7, 135.7, 128.7, 110.4, 106.4, 72.8, 22.3; HRMS (ESI) found 196.0611; C9H10NO4 [M-H]− requires 196.0615.

1,3-Diisopropoxy-2-nitrobenzene 9; νmax (neat) 2981, 1609, 1583, 1535, 1475, 1374, 1259, 1107, 1074; δH (500 MHz, CDCl3) 7.25 (1H, t, J 8.6, Ar-H), 6.58 (2H, d, J 8.6, Ar-H), 4.59 (2H, sept, J 6.1, CH(CH3)2), 1.33 (12H, d, J 6.1, CH(CH3)2); δC (125 MHz, CDCl3) 150.9, 135.1, 130.9, 107.0, 72.8, 22.3; HRMS (ESI) found 262.1046; C12H17NNaO4 [M+Na]+ requires 262.1050.
tert-Butyl 2-(3-isopropoxy-2-nitrophenoxy)acetate: 10

tert-Butyl bromoacetate (270 µL, 1.81 mmol) was added to a stirred solution of 3-isopropoxy-2-nitrophenol 8 (297 mg, 1.51 mmol) and potassium carbonate (417 mg, 3.02 mmol) in N,N-dimethylformamide (2.0 mL). After 30 mins at 90 °C, t.l.c. (2 : 1, petrol : diethyl ether) indicated complete consumption of starting material (R_f 0.3) and the formation of a major product (R_f 0.4). The reaction was diluted with dichloromethane (30 mL), partitioned with ammonium chloride (30 mL) and extracted with dichloromethane (3 x 30 mL). The organic layers were combined, dried (magnesium sulfate), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (4 : 1, petrol : diethyl ether) affording the title compound 10 (459 mg, 1.48 mmol, 98 % yield) as a clear oil.

\[ \nu_{\text{max}} = 2981, 1750, 1611, 1587, 1536, 1478, 1371, 1228, 1113, 734; \delta_{\text{H}} (400 MHz, CDCl_3) \]

ν_{\text{max}} (neat) 2981, 1750, 1611, 1587, 1536, 1478, 1371, 1228, 1113, 734; \delta_{\text{H}} (400 MHz, CDCl_3) 7.26 (1H, t, J 8.5, Ar-H), 6.66 (1H, d, J 8.5, Ar-H), 6.44 (1H, d, J 8.5, Ar-H), 4.60 (1H, sept, J 6.1, CH(CH_3)_2), 4.57 (2H, s, CH_2), 1.46 (9H, s, C(CH_3)_3), 1.33 (6H, d, J 6.1, CH(CH_3)_2); \delta_{\text{C}} (63 MHz, CDCl_3) 167.2, 151.0, 150.8, 134.2, 131.0, 108.2, 105.3, 83.3, 73.0, 66.8, 28.4, 22.3; HRMS (ESI) found 334.1257; C_{15}H_{21}NNaO_6 [M+Na]^+ requires 334.1261.

tert-Butyl 2-(2-amino-3-isopropoxyphenoxy)acetate: 11

Palladium on carbon (25 mg, wet degussa type, 5 % palladium by weight) was added to a stirred solution of tert-Butyl 2-(3-isopropoxy-2-nitrophenoxy)acetate 10 (126 mg, 0.405 mmol) in ethanol (3.0 mL). The solution was degassed three times with argon using a pump-flood procedure, and placed under hydrogen. After 12 h, t.l.c. (2 : 1, petrol : diethyl ether) indicated complete consumption of starting material (R_f 0.4) and the formation of a major product (R_f 0.3). The reaction was filtered (Celite™), washed with dichloromethane (80 mL) and concentrated in vacuo, affording the title compound 11 (112 mg, 0.40 mmol, 99 % yield) as a clear oil.
ν<sub>max</sub> (neat) 3160, 2975, 1687, 1611, 1509, 1432, 1389, 1275, 1260, 1114, 1091, 1019, 770; δ<sub>H</sub> (250 MHz, CDCl<sub>3</sub>) 6.70 - 6.56 (2H, m, Ar-H), 6.45 (1H, dd, J 7.6, 1.6, Ar-H), 4.58 (2H, s, CH<sub>2</sub>), 4.56 (1H, sept, J 6.1, CH(CH<sub>3</sub>)<sub>2</sub>), 3.96 (2H, v br, NH<sub>2</sub>), 1.54 (9H, s, C(CH<sub>3</sub>)<sub>3</sub>), 1.39 (6H, d, J 6.1, CH(CH<sub>3</sub>)<sub>2</sub>); δ<sub>C</sub> (63 MHz, CDCl<sub>3</sub>) 168.9, 146.8, 146.3, 128.3, 116.9, 108.5, 106.4, 82.6, 71.4, 67.5, 28.5, 22.8; HRMS (ESI) found 282.1698; C<sub>15</sub>H<sub>24</sub>N<sub>4</sub>O<sub>4</sub> [M+H]<sup>+</sup> requires 282.1700.

**tert-Butyl 2-(2-isocyanato-3-isopropoxyphenoxy)acetate: 12**

[Diagram of 12]

Triphosgene (58 mg, 0.19 mmol) was added to a vigorously stirred emulsion of tert-butyl 2-(2-amino-3-isopropoxyphenoxy)acetate 11 (109 mg, 0.39 mmol) and sodium hydrogen carbonate (65 mg, 0.776 mmol) in water (1.5 mL) and dichloromethane (1.5 mL). After 40 mins, t.l.c. (2 : 1, petrol : diethyl ether) indicated complete consumption of starting material (R<sub>f</sub> 0.3) and the formation of a major product (R<sub>f</sub> 0.9). The reaction was diluted with dichloromethane (30 mL), partitioned with water (30 mL) and extracted with dichloromethane (3 x 30 mL). The organic layers were combined, dried (sodium sulfate), filtered and concentrated <i>in vacuo</i>. The residue was carried forward without further purification.

δ<sub>H</sub> (250 MHz, CDCl<sub>3</sub>) 7.04 (1H, t, J 8.4, Ar-H), 6.62 (1H, d, J 8.4, Ar-H), 6.44 (1H, dd, J 8.4, 1.0, Ar-H), 4.63 (1H, sept, J 6.1, CH(CH<sub>3</sub>)<sub>2</sub>), 4.62 (2H, s, CH<sub>2</sub>), 1.51 (9H, s, C(CH<sub>3</sub>)<sub>3</sub>), 1.42 (6H, d, J 6.1, CH(CH<sub>3</sub>)<sub>2</sub>); δ<sub>C</sub> (63 MHz, CDCl<sub>3</sub>) 167.9, 153.1, 152.3, 132.4, 125.5, 114.7, 107.8, 105.7, 82.9, 72.4, 66.9, 28.4, 22.5

**tert-Butyl 2-(3-(allylcarbamoyl)-5-isopropoxyphenoxy)acetate: 6**

[Diagram of 6]

N,N-dimethylformamide (2 drops) was added to a stirred solution of 3-(2-(tert-butoxy)-2-oxoethoxy)-5-isopropoxybenzoic acid 5 (331 mg, 1.07 mmol) and oxalyl chloride (0.90 mL) in dichloromethane (10 mL). After 1 h, the reaction was concentrated, re-dissolved in dichloromethane (5.0 mL) and cooled to 0 °C. Hünig’s Base (300 µL, 1.71 mmol) and allylamine (112 µL, 1.50 mmol) were added
successively. After overnight stirring, the reaction was diluted with dichloromethane (30 mL), partitioned with ammonium chloride (30 mL) and extracted with dichloromethane (3 x 25 mL). The organic layers were combined, dried (magnesium sulfate), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (1 : 1, petrol : diethyl ether) affording the title compound 6 (373 mg, 1.07 mmol, 100 % yield) as a clear oil.

ν\textsubscript{max} (neat) 3322, 1978, 1752, 1640, 1590, 1534, 1442, 1304, 1229, 1147, 844; δ\textsubscript{H} (500 MHz, CDCl\textsubscript{3}) 6.96 (1H, br, Ar-H), 6.91 (1H, br, Ar-H), 6.63 (1H, t, J 2.2, H-3), 6.18 (1H, br, N-H), 5.97 (1H, ddt, J 17.2, 10.2, 5.7, H-10), 5.30 (1H, ddt, J 17.2, 1.6, 1.3, H-11), 5.23 (1H, ddt, J 10.2, 1.6, 1.3, H-11'), 5.23 (1H, ddt, J 10.2, 1.6, 1.3, H-11'), 4.61 (1H, sept, J 6.0, CH(CH\textsubscript{3})\textsubscript{2}), 4.57 (2H, s, CH\textsubscript{2}), 4.11 (2H, tt, J 5.7, 1.6, H-9), 1.54 (9H, s, C(CH\textsubscript{3})\textsubscript{3}), 1.38 (6H, d, J 6.0, CH(CH\textsubscript{3})\textsubscript{2}); δ\textsubscript{C} (125 MHz, CDCl\textsubscript{3}) 168.1, 167.4, 159.6, 159.6, 137.2, 134.4, 117.2, 108.2, 106.1, 105.4, 83.0, 70.8, 66.2, 42.9, 28.5, 22.4; HRMS (ESI) found 350.1956; C\textsubscript{19}H\textsubscript{28}N\textsubscript{5}O\textsubscript{5}[M+H]\textsuperscript{+} requires 350.1962.

tert-Butyl 2-(3-(but-3-en-1-ylcarbamoyl)-5-isopropoxyphenoxy)acetate: 7

\[ \text{\textit{N,N}-dimethylformamide (2 drops) was added to a stirred solution of 3-} \]
\[ \text{(2-(tert-butoxy)-2-oxoethoxy)-5-isopropoxybenzoic acid 5 (360 mg, 1.16 mmol) and oxalyl chloride (1.00 mL) in dichloromethane (15 mL). After 1 h, the reaction was} \]
\[ \text{concentrated, re-dissolved in dichloromethane (5.0 mL) and cooled to 0 °C. Hünig’s Base (570 \textmu L, 3.25 mmol) and 3-butynylamine hydrochloride (175 mg, 1.62 mmol) were added successively. After overnight stirring, the reaction was diluted with dichloromethane (30 mL), partitioned with ammonium chloride (30 mL) and extracted with dichloromethane (3 x 25 mL). The organic layers were combined, dried (magnesium sulfate), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (1 : 1, petrol : diethyl ether) affording the title compound 7 (421 mg, 1.16 mmol, 100 % yield) as a clear oil.} \]

ν\textsubscript{max} (neat) 2991, 2978, 1753, 1640, 1590, 1538, 1441, 1147, 844; δ\textsubscript{H} (500 MHz,
Potassium hexamethyldisilazane (440 μL as a 0.5 molar solution in toluene, 0.22 mmol) was added dropwise to a stirred solution of tert-butyl 2-(3-(allylcarbamoyl)-5-isoproxyphenoxy)acetate 6 (70 mg, 0.20 mmol) in tetrahydrofuran at –78 °C. After 15 mins stirring, a solution of tert-butyl 2-(2-isocyanato-3-isoproxyphenoxy)acetate 12 (68 mg, 0.22 mmol) was added dropwise over 15 mins. After a further 45 mins at –78 °C acetic acid (5 drops) was added. The reaction mixture was diluted with dichloromethane (10 mL), partitioned with ammonium chloride (10 mL) and extracted with dichloromethane (3 x 10 mL). The organic layers were combined, dried (magnesium sulfate), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (2 : 1 → 1 : 1, petrol : diethyl ether) affording the title compound 13 (34 mg, 51.8 μmol, 25 % yield) and recovered tert-butyl 2-(3-(allylcarbamoyl)-5-isoproxyphenoxy)acetate 6 (11 mg, 31.5 μmol, 16 % yield) as clear oils.

ν<sub>max</sub> (neat) 3252, 2979, 1553, 1722, 1657, 1539, 1518, 1371, 1152; δ<sub>H</sub> (400 MHz, CDCl<sub>3</sub>) 10.23 (1H, s, N-H), 7.11 (1H, t, J 8.4, Ar-H), 6.66 (1H, t, J 1.8, Ar-H), 6.63 (1H, d, J 8.2, Ar-H), 6.57 (1H, t, J 2.0, Ar-H), 6.55 (1H, t, J 2.2, Ar-H), 6.46 (1H, d, J 8.4, Ar-H), 5.88 (1H, ddt, J 17.4, 10.6, 5.5, H-20), 5.16 (1H, dd, J 10.6, 1.1, H-22), 5.12 (1H, dd, J 17.4, 1.1, H-22'), 4.57 - 4.46 (2H, m, CH(CH<sub>3</sub>)<sub>2</sub>), 4.57 (2H, s, CH<sub>2</sub>).
4.50 (2H, s, CH₂), 4.37 (2H, d, J 4.8, H-20), 1.50 (9H, s, C(CH₃)₃), 1.47 (9H, s, C(CH₃)₃), 1.34 (6H, d, J 6.0, CH(CH₃)₂), 1.33 (6H, d, J 6.0, CH(CH₃)₂); δC (63 MHz, CDCl₃) 174.6, 168.6, 168.0, 159.5, 159.4, 154.7, 154.3, 152.9, 138.4, 134.6, 127.5, 117.1, 116.7, 108.5, 107.4, 106.2, 105.4, 104.7, 83.0, 82.5, 67.4, 66.2, 49.5, 28.5, 22.6, 22.4; HRMS (ESI) found 679.3199; C₃₅H₄₈N₂NaO₈ [M+Na]⁺ requires 679.3201.

2-(3-(Allyl((2-(carboxymethoxy)-6-isopropoxyphenyl)carbamoyl)carbamoyl)-5-isopropoxyphenoxy)acetic acid: 14

Trifluoroacetic acid (0.5 mL) was added to a stirred solution of tert-butyl 2-(3-(allyl((2-(2-(tert-butoxy)-2-oxoethoxy)-6-isopropoxyphenyl)carbamoyl)carbamoyl)-5-isopropoxyphenoxy)acetate 13 (25 mg, 38.1 µmol) in dichloromethane (0.5 mL) at 0 °C. After 10 mins, t.l.c. (1 : 1, petrol : diethyl ether) indicated complete consumption of starting material (Rf 0.4) and the formation of a major product (Rf 0.0). Chloroform (2.0 mL) was added, the mixture concentrated in vacuo and this process repeated several times; affording the title compound 14 as a white amorphous solid.

νmax (neat) 2980, 1762, 1737, 1692, 1594, 1376, 1116; δH (500 MHz, CDCl₃) 10.91 (1H, s, N-H), 7.38 (2H, v br, CO₂H), 7.23 (1H, t, J 8.5, Ar-H), 6.75 - 6.70 (2H, m, Ar-H), 6.66 - 6.63 (2H, m, Ar-H), 6.61 (1H, d, J 8.5, Ar-H), 5.91 (1H, ddt, J 17.3, 10.3, 4.8, H-21), 5.26 (1H, d, J 10.3, H-22), 5.17 (1H, d, J 17.3, H-22'), 4.84 (2H, s, CH₂), 4.72 (2H, s, CH₂), 4.62 (1H, sept, J 6.1, CH(CH₃)₂), 4.59 (1H, sept, J 6.1, CH(CH₃)₂), 4.45 (2H, d, J 4.6, H-20), 1.43 (6H, d, J 6.1, CH(CH₃)₂), 1.39 (6H, d, J 6.1 CH(CH₃)₂); δC (125 MHz, CDCl₃) 175.1, 172.8, 171.1, 159.8, 159.1, 153.8, 153.3, 151.9, 137.7, 134.0, 128.1, 117.0, 115.7, 108.4, 107.7, 105.8, 104.6, 104.2, 72.3, 71.0, 65.8, 65.3, 49.9, 22.6; HRMS (ESI) found 567.1949; C₂₇H₃₂N₂NaO₁₀ [M+Na]⁺ requires 567.1949.
**4-Isopropoxy-3-nitrobenzoic acid: 15**

Isopropanol (81 µL, 1.06 mmol) was added dropwise to a stirred slurry of sodium hydride (74 mg, 1.84 mmol as a 60 % dispersion oil) in tetrahydrofuran (4.0 mL) at °C. After 15 mins, 4-fluoro-3-nitrobenzoic acid (131 mg, 0.71 mmol) was added and the cooling bath removed after a further 30 mins of stirring. After a further 3 h, t.l.c. (90 : 10 : 1, dichloromethane : methanol : acetic acid) indicated complete consumption of starting material (R<sub>f</sub> 0.7) and the formation of a major product (R<sub>f</sub> 0.65). The reaction was diluted with dichloromethane (15 mL), partitioned with 1.0 N hydrochloric acid (aqueous, 15 mL) and extracted with dichloromethane (15 mL). The organic layers were combined, dried (magnesium sulfate), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (200 : 10 : 1, dichloromethane : methanol : acetic acid) affording the title compound 15 (157 mg, 0.70 mmol, 98 % yield) as an amorphous brown solid.

ν<sub>max</sub> (neat) 2923, 1701, 1613, 1534, 1288, 1104, 759; δ<sub>H</sub> (500 MHz, CD<sub>3</sub>OD) 8.31 (1H, d, J 2.2, H-1), 8.15 (1H, dd, J 8.8, 2.2, H-5), 7.30 (1H, d, J 8.9, H-4), 4.9 (1H, sept, J 6.1, CH(CH<sub>3</sub>)₂), 1.38 (6H, d, J 6.1, CH(CH<sub>3</sub>)₂); δ<sub>C</sub> (125 MHz, CD<sub>3</sub>OD) 166.7, 154.6, 140.7, 135.0, 126.7, 123.0, 115.5, 73.2, 21.1; HRMS (ESI) found 248.0532; C<sub>10</sub>H<sub>11</sub>NaO<sub>5</sub>[M+Na]<sup>+</sup> requires 248.0529.

**(4-Isopropoxy-3-nitrophenyl)methanol: 16**

Borane tetrahydrofuran complex (570 µL as a 1.0 molar solution) was added dropwise to a stirred solution of 4-isopropoxy-3-nitrobenzoic acid 15 (81 mg, 0.36 mmol) in tetrahydrofuran (1.0 mL) at −10 °C. The reaction mixture was allowed to attain room temperature over 1 h, with t.l.c. (90 : 10 : 1, dichloromethane, methanol, acetic acid) indicating complete consumption of starting material (R<sub>f</sub> 0.4) and the formation of a major product (R<sub>f</sub> 0.6). The reaction mixture was diluted with dichloromethane (10 mL), cooled to 0 °C and quenched cautiously with acetic acid : water (50 : 50) until evolution of gas ceased. The resultant mixture was partitioned with sodium hydrogen carbonate (15 mL) and extracted with dichloromethane (15 mL). The organic layers
were combined, dried (magnesium sulfate), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (2 : 1, diethyl ether : petrol) affording the title compound 16 (70 mg, 0.33 mmol, 92 %) as a clear oil.

\[ \nu_{\text{max}} \text{ (neat)} 3353, 2981, 1621, 1526, 1351, 1277, 1259, 1105, 948, 810; \delta_H \text{ (500 MHz, CDCl}_3) 7.80 \text{ (1H, br, Ar-H)}, 7.52 \text{ (1H, dd, J 8.5, 2.0, Ar-H)}, 7.10 \text{ (1H, d, J 8.5, Ar-H)}, 4.70 \text{ (1H, sept, J 6.1, CH(CH}_3}_2), 4.69 \text{ (2H, br, CH}_2), 2.36 \text{ (1H, br, OH)}, 1.42 \text{ (6H, d, J 6.1, CH(CH}_3}_2); \delta_C \text{ (125 MHz, CDCl}_3) 151.0, 141.3, 133.6, 132.7, 124.8, 73.3, 64.1, 22.3; HRMS (ESI) found 234.0733; C\text{\textsubscript{10}}H\text{\textsubscript{13}}NNaO\text{\textsubscript{4}}[M+Na]^+ requires 234.0737.

4-Isopropoxy-3-nitrobenzaldehyde: 17

Manganese dioxide (278 mg, 3.20 mmol) was added to a stirred solution of (4-isopropoxy-3-nitrophenyl)methanol 16 (45 mg, 0.21 mmol) in dichloromethane (3.0 mL). After overnight stirring t.l.c. (2 : 1, diethyl ether : petrol) indicated complete consumption of starting material (R\text{f} 0.3) and the formation of a major product (R\text{f} 0.6). The reaction mixture was filtered (Celite\textsuperscript{TM}), washed with dichloromethane (40 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (1 : 1, petrol : diethyl ether) affording the title compound 17 (40 mg, 0.19 mmol, 89 % yield) as a clear oil.

\[ \delta_H \text{ (500 MHz, CDCl}_3) 9.96 \text{ (1H, s, CHO)}, 8.33 \text{ (1H, d, J 2.0, H-1)}, 8.08 \text{ (1H, dd, J 8.6, 2.2, Ar-H)}, 7.26 \text{ (1H, d, J 8.7, Ar-H)}, 4.88 \text{ (1H, sept, J 6.1, CH(CH}_3}_2), 1.50 \text{ (6H, d, J 6.1, CH(CH}_3}_2); \delta_C \text{ (125 MHz, CDCl}_3) 189.2, 156.2, 141.3, 134.6, 128.9, 127.9, 115.8, 73.9, 22.2; HRMS (ESI) found 264.0843; C\text{\textsubscript{11}}H\text{\textsubscript{15}}NNaO\text{\textsubscript{5}}[M+Na]^+ requires 264.0737.

tert-Butyl 3-(4-isopropoxy-3-nitrophenyl)acrylate: 18

(tert-Butoxycarbonyl-methylene)triphenyl-phosphorane (66 mg, 0.17 mmol) was added to a stirred solution of 4-isopropoxy-3-nitrobenzaldehyde 17 (28 mg, 0.13 mmol) in acetonitrile (3.0 mL). After overnight stirring at 40 °C, t.l.c. (1 : 1, petrol :
diethyl ether) indicated complete consumption of starting material (Rf 0.3) and formation of a major product (Rf 0.8). The reaction mixture was concentrated in vacuo and the residue purified by flash column chromatography (10 : 1, petrol : diethyl ether), affording the title compound 18 as an inseparable 15 : 1 mixture of (E) and (Z) isomers (39 mg, 0.13 mmol, 95 % yield) as a clear oil.

\[ \nu_{\text{max}} \text{ (neat)} \] 3045, 2360, 1706, 1279, \[ \delta \text{H} \] (250 MHz, CDCl\(_3\)) major isomer: 7.94 (1H, d, \( J \) 2.2, H-1), 7.63 (1H, dd, \( J \) 8.7, 2.2, Ar-H), 7.51 (1H, d, \( J \) 16.0, H-7), 7.10 (1H, d, \( J \) 8.8, Ar-H), 6.32 (1H, d, \( J \) 16.0, H-8), 4.74 (1H, sept, \( J \) 6.1, CH(CH\(_3\))\(_2\)), 1.55 (9H, s, C(CH\(_3\))\(_3\)), 1.43 (6H, d, \( J \) 6.1, CH(CH\(_3\))\(_2\)); \[ \delta \text{C} \] (63 MHz, CDCl\(_3\)) 168.2, 152.7, 141.4, 141.0, 133.2, 127.4, 125.1, 121.0, 116.3, 81.2, 73.3, 28.6, 22.2; HRMS (ESI) found 330.1300; C\(_{16}\)H\(_{21}\)NNaO\(_5\) \([\text{M+Na}]^+\) requires 330.1312.

\textit{tert-Butyl 3-(3-amino-4-isopropoxyphenyl)propanoate: 19}

Palladium on carbon (110 mg, wet degussa type, 5 % palladium by weight) was added to a stirred solution of \textit{tert}-butyl 3-(4-isopropoxy-3-nitrophenyl)acrylate 18 (1.11 g, 3.61 mmol) in ethanol (10 mL). The solution was degassed three times with argon using a pump-flood procedure, and placed under hydrogen. After 14 h, t.l.c. (6 : 1, petrol : diethyl ether) indicated complete consumption of starting material (Rf 0.3) and the formation of a major product (Rf 0.2). The reaction was filtered (CeliteTM), washed with dichloromethane (220 mL) and concentrated in vacuo. The residue was purified by flash column chromatography (6 : 1, petrol : diethyl ether) affording the title compound 19 (944 mg, 3.38 mmol, 94 % yield) as a clear oil.

\[ \nu_{\text{max}} \text{ (neat)} \] 3377, 2975, 1727, 1617, 1514, 1368, 1223, 1144; \[ \delta \text{H} \] (500 MHz, CDCl\(_3\)) 6.76 (1H, d, \( J \) 8.1, Ar-H), 6.62 (1H, d, \( J \) 2.2, Ar-H), 6.57 (1H, dd, \( J \) 8.1, 2.2, Ar-H), 4.52 (1H, sept, \( J \) 6.1, CH(CH\(_3\))\(_2\)), 2.82 (2H, t, \( J \) 7.6, H-7), 2.53 (2H, t, \( J \) 7.6, H-8), 1.48 (9H, s, C(CH\(_3\))\(_3\)), 1.38 (6H, d, \( J \) 6.1, CH(CH\(_3\))\(_2\)); \[ \delta \text{C} \] (125 MHz, CDCl\(_3\)) 173.0, 144.2, 137.6, 134.1, 118.4, 115.9, 114.3, 80.6, 71.3, 37.8, 31.0, 28.5, 22.7; HRMS (ESI) found 280.1896; C\(_{16}\)H\(_{26}\)NO\(_3\) \([\text{M+H}]^+\) requires 280.1907.
**tert-Butyl 3-(3-isocyanato-4-isopropoxyphenyl)propanoate: 20**

Triphosgene (428 mg, 1.44 mmol) was added to a vigorously stirred emulsion of tert-butyl 3-(3-amino-4-isopropoxyphenyl)propanoate 19 (944 mg, 3.38 mmol) and sodium hydrogen carbonate (606 mg, 7.22 mmol) in water (30 mL) and dichloromethane (30 mL). After 50 mins, t.l.c. (6 : 1, petrol : diethyl ether) indicated complete consumption of starting material (Rf 0.2) and the formation of a major product (Rf 0.5). The reaction was diluted with dichloromethane (70 mL), partitioned with water (70 mL) and extracted with dichloromethane (3 x 70 mL). The organic layers were combined, dried (sodium sulfate), filtered and concentrated in vacuo. The residue was carried forward without further purification.

\[ \delta_H (500 \text{ MHz, CDCl}_3) \quad 6.99 (1H, dd, J 6.4, 2.0, Ar-H), 6.88 (1H, d, J 2.0, Ar-H), 6.85 (1H, d, J 6.4, Ar-H), 4.64 (1H, sept, J 6.1, CH(CH}_3)_2), 2.85 (2H, d, J 7.6, H-7), 2.53 (2H, d, J 7.6, H-8), 1.47 (9H, s, C(CH}_3)_3), 1.43 (6H, d, J 6.1, CH(CH}_3)_2); \delta_C (125 \text{ MHz, CDCl}_3) \quad 172.6, 150.6, 133.7, 131.6, 126.1, 125.2, 124.1, 113.4, 80.9, 72.2, 37.5, 30.6, 28.5, 22.3 \]

**tert-Butyl 3-(3-(3-allyl-3-(3-(2-(tert-butoxy)-2-oxoethoxy)-5-isopropoxybenzoyl)ureido)-4-isopropoxyphenyl)propanoate: 21**

Potassium hexamethyldisilazane (940 µL as a 0.5 molar solution in toluene, 0.47 mmol) was added dropwise to a stirred solution of tert-butyl 2-(3-(allylcarbamoyl)-5-isopropoxyphenoxy)acetate 6 (119 mg, 0.39 mmol) in tetrahydrofuran at –78 °C. After 15 mins stirring, a solution of tert-butyl 3-(3-isocyanato-4-isopropoxyphenyl)propanoate 20 (136 mg, 0.39 mmol) was added dropwise over 15 mins. After a further 45 mins at –78 °C acetic acid (10 drops) was added. The reaction mixture was diluted with dichloromethane (25 mL), partitioned with ammonium chloride (25 mL) and extracted with dichloromethane (3 x 25 mL). The
organic layers were combined, dried (magnesium sulfate), filtered and concentrated \textit{in vacuo}. The residue was purified by flash column chromatography (4 : 1, petrol : diethyl ether) affording the title compound \textit{21} (157 mg, 0.24 mmol, 61 \% yield) as a clear oil.

\begin{align*}
\nu_{\text{max}} \text{ (neat)} & \quad 2978, 1753, 1712, 1659, 1592, 1537, 1440, 1147, 877; \quad \delta_{\text{H}} \text{ (}500 \text{ MHz, } \text{CDCl}_3\text{)} \quad 11.67 \text{ (}1\text{H, s, } N-\text{H}), 8.28 \text{ (}1\text{H, d, } J 1.9, \text{ Ar-H}), 6.91 \text{ (}1\text{H, dd, } J 8.3, 1.9, \text{ Ar-H}), 6.88 \text{ (}1\text{H, d, } J 8.3, \text{ Ar-H}), 6.65 \text{ (}1\text{H, br, Ar-H}), 6.60 \text{ (}1\text{H, t, } J 2.2, \text{ Ar-H}), 6.57 \text{ (}1\text{H, br, Ar-H}), 5.92 \text{ (}1\text{H, dtt, } J 17.3, 10.5, 4.9, \text{ H-21}), 5.22 \text{ (}1\text{H, dd, } J 10.5, 0.9, \text{ H-22}), 5.13 \text{ (}1\text{H, dd, } J 17.3, 0.9, \text{ H-22'}), 4.62 \text{ (}1\text{H, sept, } J 6.1, \text{ CH(CH}_3)_2\text{)), 4.56 \text{ (}1\text{H, sept, } J 6.1, \text{ CH(CH}_3)_2\text{)), 4.55 \text{ (}2\text{H, s, CH}_2\text{)), 4.43 \text{ (}2\text{H, d, } J 4.9, \text{ H-20}), 2.92 \text{ (}2\text{H, t, } J 7.6, \text{ H-17}), 2.59 \text{ (}2\text{H, t, } J 7.6, \text{ H-18}), 1.55 \text{ (}9\text{H, s, C(CH}_3)_3\text{)), 1.48 \text{ (}9\text{H, s, C(CH}_3)_3\text{)), 1.44 \text{ (}6\text{H, d, } J 6.1, \text{ CH(CH}_3)_2\text{)), 1.38 \text{ (}6\text{H, d, } J 6.1, \text{ CH(CH}_3)_2\text{)); } \delta_{\text{C}} \text{ (}125 \text{ MHz, } \text{CDCl}_3\text{)} \quad 174.7, 172.9, 167.9, 159.6, 159.6, 151.9, 145.7, 138.3, 134.4, 133.9, 129.5, 123.7, 120.4, 116.9, 113.7, 107.2, 105.3, 104.5, 83.1, 80.6, 72.3, 70.9, 66.2, 49.4, 37.9, 31.3, 28.5, 28.5, 22.7, 22.5; \text{ HRMS (ESI) found 677.3409; } C_{36}H_{50}N_2NaO_9 [M+Na]^+ \text{ requires 677.3409.}
\end{align*}

3-(3-(3-Allyl-3-(carboxymethoxy)-5-isopropoxybenzoyl)ureido)-4-isopropoxyphenyl)propanoic acid: 23

Trifluoroacetic acid (0.5 mL) was added to a stirred solution of \textit{tert}-butyl 3-(3-(3-allyl-3-(3-(2-(\textit{tert}-butoxy)-2-oxoethoxy)-5-isopropoxybenzoyl)ureido)-4-isopropoxyphenyl)propanoate \textit{21} (13 mg, 19.9 µmol) in dichloromethane (0.5 mL) at 0 °C. After 10 mins, t.l.c. (4 : 1, petrol : diethyl ether) indicated complete consumption of starting material (R\textit{f} 0.3) and the formation of a major product (R\textit{f} 0.0). Chloroform (2.0 mL) was added, the mixture concentrated \textit{in vacuo} and this process repeated several times; affording the title compound \textit{23} as a white amorphous solid.

\begin{align*}
\nu_{\text{max}} \text{ (neat)} & \quad 2979, 1711, 1593, 1540, 1441, 1378; \quad \delta_{\text{H}} \text{ (}500 \text{ MHz, } \text{CDCl}_3\text{)} \quad 11.42 \text{ (}1\text{H, s,}
\end{align*}
N-H), 8.54 (2H, br, CO₂H), 8.25 (1H, s, Ar-H), 6.92 (1H, dd, J 8.3, 1.6, Ar-H), 6.88 (1H, d, J 8.3, Ar-H), 6.71 (1H, br, Ar-H), 6.63 (1H, t, J 2.2, Ar-H), 6.57 (1H, br, Ar-H), 5.89 (1H, ddt, J 17.4, 10.4, 3.7, H-21), 5.20 (1H, d, J 10.4, H-22), 5.14 (1H, d, J 17.4, H-22'), 4.71 (2H, s, CH₂), 4.62 (1H, sept, J 6.1, CH(CH₃)₂), 4.58 (1H, sept, J 6.1, CH(CH₃)₂), 4.41 (2H, d, J 8.3, Ar-H), 2.96 (2H, t, J 7.5, H-17), 2.73 (2H, t, J 7.5, H-18), 1.44 (6H, d, J 6.1, CH(CH₃)₂), 1.38 (6H, d, J 6.1, CH(CH₃)₂); δC (125 MHz, CDCl₃) 179.0, 174.4, 173.8, 159.8, 159.1, 152.1, 146.0, 138.2, 134.3, 133.1, 129.2, 123.9, 120.5, 116.9, 113.6, 107.8, 105.7, 103.8, 72.2, 70.9, 65.2, 49.4, 36.3, 30.8, 22.5, 22.4; HRMS (ESI) found 565.2159; C₂₈H₃₄N₂NaO₉ [M+Na]⁺ requires 565.2157.

**tert-Butyl 3-(3-(3-(but-3-en-1-yl)-3-(3-(2-tert-butoxy)-2-oxoethoxy)-5-isoproxybenzoyl)ureido)-4-isoproxyphenyl)propanoate: 22**

Potassium hexamethyldisilazane (1.70 mL as a 0.5 molar solution in toluene, 0.71 mmol) was added dropwise to a stirred solution of tert-butyl 2-(3-(but-3-en-1-ylcarbamoyl)-5-isoproxyphenoxy)acetate 7 (218 mg, 0.71 mmol) in tetrahydrofuran at –78 °C. After 15 mins stirring, a solution of tert-butyl 3-(3-isocyanato-4-isoproxyphenyl)propanoate 20 (259 mg, 0.71 mmol) was added dropwise over 15 mins. After a further 45 mins at –78 °C acetic acid (10 drops) was added. The reaction mixture was diluted with dichloromethane (40 mL), partitioned with ammonium chloride (40 mL) and extracted with dichloromethane (3 x 40 mL). The organic layers were combined, dried (magnesium sulfate), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (4 : 1, petrol : diethyl ether) affording the title compound 22 (305 mg, 0.46 mmol, 64 % yield) as a clear oil.

νₘₐₓ (neat) 2978, 1753, 1708, 1591, 1367, 1146, 1113, 845, 732; δH (250 MHz, CDCl₃) 11.55 (1H, br, N-H), 8.27 (1H, d, J 1.5, Ar-H), 6.95 - 6.83 (2H, m, Ar-H), 6.64 (1H, br, Ar-H), 6.60 (1H, t, J 2.2, Ar-H), 6.55 (1H, br, Ar-H), 5.76 - 5.54 (1H, m, H-22), 5.11 - 4.98 (2H, m, H-23, H-23'), 4.60 (1H, sept, J 6.1, CH(CH₃)₂), 4.58 (1H,
sept, J 6.1, CH(CH$_3$)$_2$), 4.56 (2H, s, CH$_2$), 3.88 (2H, t, J 7.3, H-20), 2.92 (2H, t, J 7.9, H-17), 2.59 (2H, t, J 7.9, H-18), 2.39 (2H, dt, J 7.2, 7.1, H-21), 1.54 (9H, s, C(CH$_3$)$_3$), 1.48 (9H, s, C(CH$_3$)$_3$), 1.42 (6H, d, J 6.1, CH(CH$_3$)$_2$), 1.38 (6H, d, J 6.1, CH(CH$_3$)$_2$);

δ$_C$ (125 MHz, CDCl$_3$) 174.1, 172.4, 167.4, 159.3, 159.3, 151.6, 145.3, 138.1, 134.2, 133.5, 129.0, 123.2, 119.8, 117.6, 113.3, 107.0, 104.7, 104.2, 82.6, 80.1, 71.8, 70.4, 65.7, 46.3, 37.5, 34.0, 30.9, 28.1, 28.1, 22.1, 21.9; HRMS (ESI) found 691.3539; C$_{37}$H$_{52}$N$_2$NaO$_9$ [M+Na]$^+$ requires 691.3565.

3. References


4. NMR Spectra
Benzyl 3,5-dihydroxybenzoate: 1

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Benzyl 3-hydroxy-5-isopropoxybenzoate: 2
3,5-Diisopropoxybenzoic acid: 3

\[
\text{\ding{127}O}_2\text{Obn}
\]

3

CDCl$_3$

$^1$H 500 MHz

$^{13}$C 125 MHz
Benzyl 3-((2-(tert-butoxy)-2-oxoethoxy)-5-isopropoxybenzoate: 4

4 CDCl3
1H 500 MHz
13C 125 MHz
3-(2-(tert-Butoxy)-2-oxoethoxy)-5-isopropoxybenzoic acid: 5
3-Isopropoxy-2-nitrophenol: 8
1,3-Diisopropoxy-2-nitrobenzene: 9
tert-Butyl 2-(3-isopropoxy-2-nitrophenoxy)acetate: 10

![NMR Spectrum](image)

**1H** 400 MHz

**13C** 83 MHz

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tert-Butyl 2-(2-amino-3-isopropoxyphenoxy)acetate: 11
** tert-Butyl 2-(2-isocyanato-3-isopropoxyphenoxy)acetate: 12 **

![Chemical Structure](Image)

1. 

1H 250 MHz

13C 63 MHz
tert-Butyl 2-(3-(allylcarbamoyl)-5-isopropoxyphenoxy)acetate: 6

\[
\begin{align*}
\text{CDCl}_3 \\
{^1}H\text{ 500 MHz} \\
{^{13}}C\text{ 125 MHz}
\end{align*}
\]
tert-Butyl 2-(3-(but-3-en-1-ylcarbamoyl)-5-isoproxyphenoxy)acetate: 7

[Chemical structure image]

Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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tert-Butyl 2-(3-(allyl((2-(2-(tert-butoxy)-2-oxoethoxy)-6-isopropoxyphenyl)carbamoyl)carbamoyl)-5-isopropoxyphenoxo)acetate: 13
2-(3-(Allyl((2-(carboxymethoxy)-6-isopropoxyphenyl)carbamoyl)carbamoyl)-5-isopropoxyphenoxy)acetic acid: 14
4-Isopropoxy-3-nitrobenzoic acid: 15

CD<sub>3</sub>OD

$^1$H 500 MHz

$^{13}$C 125 MHz
(4-Isopropoxy-3-nitrophenyl)methanol: 16

![NMR spectrum of 16 in CDCl₃, ¹H 500 MHz, ¹³C 125 MHz]
4-Isopropoxy-3-nitrobenzaldehyde: 17

![Chemical structure](image)

**Chemical Information:)**
- Compound: 4-Isopropoxy-3-nitrobenzaldehyde (17)
- Solvent: CDCl₃
- NMR Spectra Details:
  - ¹H NMR: 600 MHz
  - ¹³C NMR: 125 MHz

**Chemical Structure:***
- OH: 2.00 ppm
- H: 5.00 ppm
- Cl: 77.90 ppm
- C: 128.85 ppm
- NO₂: 10.00 ppm
tert-Butyl 3-(4-isoproxy-3-nitrophenyl)acrylate: 18
tert-Butyl 3-(3-amino-4-isopropoxyphenyl)propanoate: 19

1H 500 MHz
13C 125 MHz
**tert-Butyl 3-(3-isocyanato-4-isopropoxyphenyl)propanoate: 20**

![NMR Spectrum](image)

20 in CDCl$_3$

$^1$H 600 MHz

$^{13}$C 125 MHz
tert-Butyl 3-(3-allyl-3-(3-(2-(tert-butoxy)-2-oxoethoxy)-5-isopropoxybenzoyl)ureido)-4-isopropoxyphenyl)propanoate: 21
3-(3-Allyl-3-(carboxymethoxy)-5-isopropoxybenzoyl)ureido)-4-isopropoxyphenyl)propanoic acid: 23
tert-Butyl 3-((3但-3-en-1-yl)-3-(2( tert-butoxy)-2-oxoethoxy)5-isopropoxybenzoyl)ureido)-4-isopropoxyphenyl)propanoate: 22