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# Supporting Information

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for

# Use of Click Chemistry to Define the Substrate Specificity of *Leishmania* β-1,2-Mannosyltransferases

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*2,3,4,6-Tetra*-O-*acetyl-α-D-mannosyl trichloroacetimidate* (**5**)

*i) 2,3,4,6-Tetra-O-acetyl-α-D-mannose* (**4**)

A mixture of mannose pentaacetate (**3**) (1.09 g, 2.79 mmol) and ammonium carbonate (2.49 g, 15.8 mmol) in DMF (9 mL) was stirred at room temperature overnight. The mixture was diluted with EtOAc, washed with water (3 × 50 mL) and brine (50 mL). The organic phase was dried ($MgSO_4$) and the solvent evaporated under reduced pressure to afford the hemiacetal (**4**) as a pale yellow oil (0.58 g).

*ii) 2,3,4,6-Tetra*-O-*acetyl-α-D-mannosyl trichloroacetimidate* (**5**)

DBU (51 μL, 0.34 mmol) was added to a stirred mixture of the crude hemiacetal (**4**) (0.58 g, 1.7 mmol) and trichloroacetonitrile (76 μL, 7.6 mmol) in $CH_2Cl_2$ (10 mL) at 0 °C. After 2 h, the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography (1:2 EtOAc/pet. spirits) to afford the imidate (**5**) as a pale orange oil (0.59 g, 43% over 2 steps), $[\alpha]_D$ = + 52° (c = 1.15 in $CHCl_3$), lit.[1] + 53°; $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 1.95, 2.00, 2.03, 2.14 (4s, 12H, $CH_3$), 4.06, dd ($J_{5,6}$ 7.2 Hz, H6), 4.11- 4.16 (m, H5), 4.22 (dd,

$J_{5,6}$ 4.8, $J_{6,6}$ 12.0 Hz, H6), 5.33- 5.37 (m, H2,4), 5.41 (dd, $J_{2,3}$ 2.0, $J_{3,4}$ 2.8 Hz, H3), 6.22 (d, $J_{1,2}$ 1.6 Hz, H1), 8.76 (bs, NH); $^{13}$C NMR (100 MHz, $CDCl_3$): *d* = 20.51, 20.58, 20.67, 20.94 (4C, $CH_3$), 61.90, 65.21, 67.71, 68.67, 71.07 (C2,3,4,5), 94.36 (C1), 159.57 (C=NH), 169.51, 169.61, 169.69, 170.46 (4C, C=O).

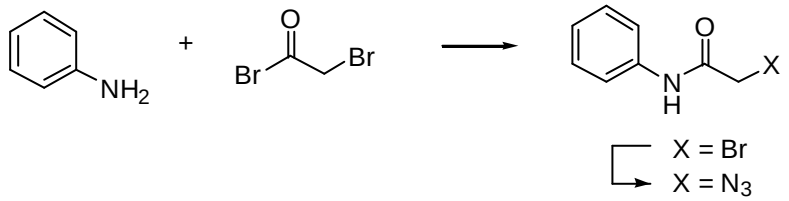
**General procedure for the synthesis of ω-bromoacylamides**

ω-Bromoacyl chloride or bromide (1.2 equiv) was added to a stirred solution of the amine (1 equiv) in dichloromethane (15- 20 mL) in the presence of pyridine (2 equiv) at 0 ºC over 15- 30 min. The reaction was stirred for a further 60 min at room temp. Water (1 mL) was added and the mixture stirred vigorously for 5 min, then was sequentially washed with water, 1 M HCl, and sat. aq. $NaHCO_3$. The organic phase was dried ($MgSO_4$) and the solvent evaporated under reduced pressure.

**General procedure for the synthesis of ω-azidoacylamides**

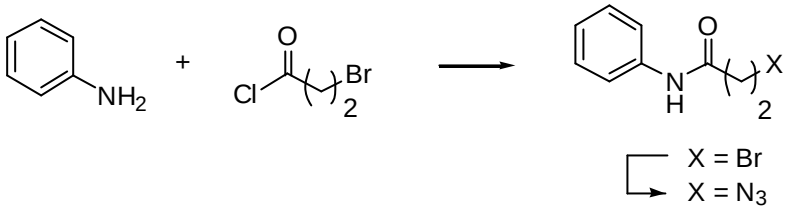
A mixture of ω-bromoacylamides (1 equiv) and $NaN_3$ (1.5 equiv) in DMSO (10 mL) was stirred for 2- 4 h or until the reaction was complete as indicated by tlc. The reaction mixture was diluted with ice/water (20 mL). The mixture was extracted with dichloromethane (3 × 10 mL) and the combined organic extract washed with water (2 × 20 mL), and brine (20 mL). The organic phase was dried ($MgSO_4$), filtered and the solvent removed under reduced pressure.

*Preparation of* N-*phenyl-2-azidoacetamide* (**9**)



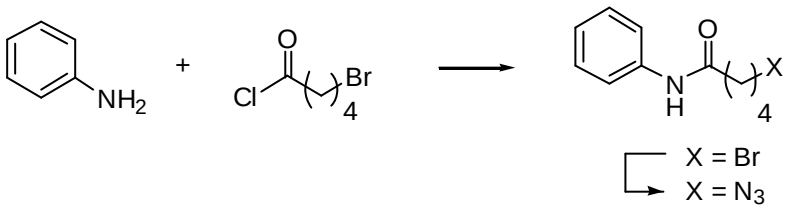

According to the general procedure for the synthesis of ω-bromoacylamides, bromoacetyl bromide and aniline gave the crude bromide (4.44 g), which was used directly in the next step. According to the general procedure for the synthesis of ω-bromoacylamides, the crude bromide afforded the azide (**9**) as brown needles (2.58 g, 68% over two steps); m.p. 83- 84 °C (EtOAc/pet. spirits; lit.[2] 83 °C); $^1$H NMR (300 MHz, $CDCl_3$) *d* 4.12 (s, 2H, $CH_2$), 7.13- 7.54 (5H, Ph), 8.07 (bs, NH); $^{13}$C NMR (100 MHz, $CDCl_3$) *d* 54.04 ($CH_2$), 121.79, 126.13, 130.19, 137.83 (Ph), 165.66 (C=O); IR ν ($cm^{-1}$) 1672 sharp (C=O), 2102 sharp ($N_3$).

*5-Azido*-N-*phenylpropionamide* (**10**)




According to the general procedure for the synthesis of ω-bromoacylamides, 3-bromopropionyl chloride and aniline gave the crude bromide, which was used directly in the next step. According to the general procedure for the synthesis of ω-bromoacylamides, the crude bromide afforded the azide (**10**) as yellow plates (97%); m.p. 50- 53 ºC; $^{1}$H NMR (300 MHz, $CDCl_3$) *d* 2.56, 3.64 (2 × t, 2 × 2H, *J* 6.3 Hz, $CH_2$), 7.07- 7.51 (5H, Ph), 8.14 (bs, NH); $^{13}$C NMR (75.5 MHz, $CDCl_3$) *d* 36.17, 47.04 ($CH_2$), 120.45, 124.49, 128.72, 137.36 (Ph), 168.94 (C=O); IR ν ($cm^{-1}$) 1660 sharp (C=O), 2102 sharp ($N_3$).

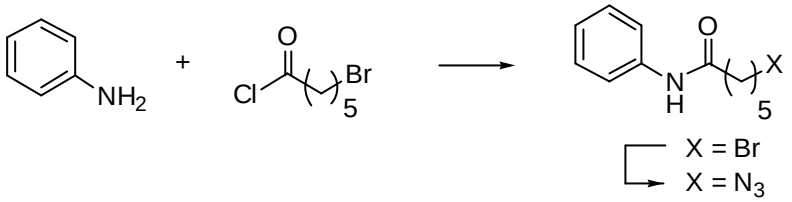
*5-Azido*-N-*phenylvaleramide* (**12**)




According to the general procedure for the synthesis of ω-bromoacylamides, 5-bromovaleryl chloride and aniline gave the crude bromide as a beige plates, which was used without purification in the next step; m.p. 76- 78 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) 1.87- 2.03 (m, 4H, H3,4), 2.41, 3.46 (2 × t, *J* 6.4 Hz, 2 × 2H, H2,5), 7.12 (t, *J* 7.6 Hz, 1H, H4'), 7.17 (s, 1H, NH), 7.33 (t, *J* 7.6 Hz, 2H, H3',5'), 7.52 (d, *J* 7.6 Hz, 2H, H2',6').

According to the general procedure for the synthesis of ω-azidoacylamides, the crude bromide gave 5-azido-*N*-phenylvaleramide (**12**) as beige plates (51% over 2 steps); m.p. 62- 63 °C (EtOAc/pet. spirits); $^{1}$H NMR (500 MHz, $CDCl_3$) *d* 1.56- 1.76 (m, 4H, H3,4), 2.34, 3.24 (2 × t, 2 × 2H, H2,5), 7.01 (t, 1H, *J* 7.8 Hz, H4'), 7.23 (t, 2H, *J* 7.8 Hz, H3',5'), 7.51 (d, 2H, *J* 7.8 Hz, H2',6'), 8.67 (s, 1H, NH); $^{13}$C NMR (125 MHz, $CDCl_3$) *d* 22.76, 28.38, 36.56, 51.17 (4C, C2,3,4,5), 120.00, 123.93, 128.84, 138.50 (6C, Ar), 171.37 (1C, C=O); IR ν ($cm^{-1}$) ? 2095 ($N_3$), 1638 (C=O).

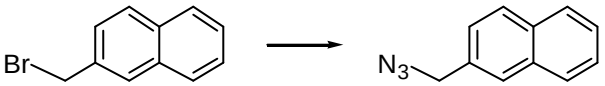
*5-Azido*-N-*phenylhexanamide* (**13**)




According to the general procedure for the synthesis of ω-bromoacylamides, 6-bromohexanoyl chloride and aniline gave the crude bromide as a white powder, which was used without purification in the next step; m.p. 128- 130 ºC; $^{1}$H NMR (400 MHz, $CDCl_3$) *d* 1.48- 1.96 (m, 6H, $CH_2$), 2.37 (t, *J* 6.9 Hz, $CH_2$), 3.41 (2H, t, *J* 6.6 Hz, $CH_2$), 7.05- 7.56 (m, 6H, Ph,NH).

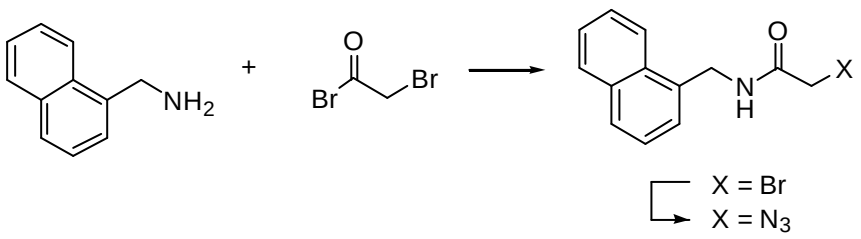
According to the general procedure for the synthesis of ω-azidoacylamides, the crude bromide gave the azide (**13**) as colourless plates (91% over two steps); m.p. 128- 130 ºC; $^{1}$H NMR (300 MHz, $CDCl_3$) *d* 1.40- 1.95 (m, 6H, 3 × $CH_2$), 2.37, 3.40 (2 × t, 2 × 2H, *J* 7.8 Hz, $CH_2N_3$, $CH_2CO$), 7.05- 7.60 (m, 5H, Ph), 7.60 (br d, NH); $^{13}$C NMR (100 MHz, $CDCl_3$) *d* 24.95, 26.18, 28.45, 37.14, 51.04 ($CH_2$), 119.96, 124.14, 128.78, 137.84 (Ph), 171.44 (C=O); IR ν ($cm^{-1}$) 1668 sharp (C=O), 2097 sharp ($N_3$).

*2-(Azidomethyl)naphthalene* (**14**)




Sodium azide (0.44 g, 6.83 mmol) was added to a heated solution of 2-(bromomethyl)naphthalene (1.01 g, 4.57 mmol) in DMSO (10 mL). The mixture was stirred at 75 °C for 1.5 h. The reaction mixture was diluted with dichloromethane (50 mL) and the combined mixture was washed with distilled water (3 × 50 mL) and brine (10 mL). The organic extract was dried ($MgSO_4$), filtered and the filtrate concentrated under reduced pressure to yield a pale yellow solid. The crude solid was crystallized to yield the azide (**14**) as a white solid (0.61 g, 73%); m.p. 39- 41 °C (EtOH/water); $^{1}$H NMR (299.9 MHz, $CDCl_3$) *d* 4.51 (s, 2H, $CH_2$), 7.41- 7.53, 7.78- 7.89 (2m, 7H, Ar); IR ν ($cm^{-1}$) 2127, sharp ($N_3$).

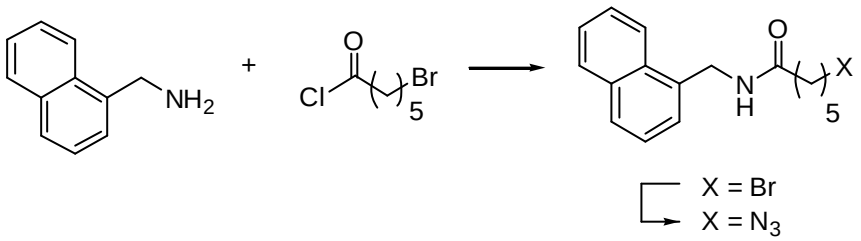
*2-Azido*-N-*(naphth-1-ylmethyl)acetamide* (**15**)



According to the general procedure for the synthesis of ω-bromoacylamides, 1-naphthylmethylamine and bromoacetyl bromide gave 2-bromo-*N*-(naphth-1-ylmethyl)acetamide as white needles (13%); m.p. 129- 131 °C (75% EtOH); $^{1}$H NMR (400 MHz, $CDCl_3$) *d* 3.92 (s, 2H, $CH_2Br$), 4.92 (d, *J* 1.2 Hz, 2H, $CH_2$), 6.73 (bs, 1H, NH), 7.44- 7.57, 7.83- 7.99 (m, 7H, Ar).

According to the general procedure for the synthesis of ω-azidoacylamides, 2-bromo-*N*-(naphth-1-ylmethyl)propionamide gave 2-azido-*N*-(naphth-1-ylmethyl)acetamide as yellow crystals (69%); m.p. 106- 109°C; $^{1}$H NMR (400 MHz, $CDCl_3$) *d* 3.99 (s, 2H, $CH_2N_3$), 4.90 (d, *J* 5.2 Hz, 2H, $CH_2NH$), 6.65 (bs, 1H, NH), 7.43- 7.58, 7.82- 7.99 (m, 7H, Ar); $^{13}$C NMR (100.1 MHz, $CDCl_3$) *d* 41.54 ($CH_2NH$), 52.50 ($CH_2N_3$), 123.20, 125.33, 126.06, 126.75, 126.82, 128.81, 128.84, 131.25, 132.64, 133.80 (Ar), 166.23 (C=O); IR ν ($cm^{-1}$) 2101 $cm^{-1}$, ($N_3$).

*6-Azido*-N-*(naphthalen-1-ylmethyl)hexanamide* (**16**)

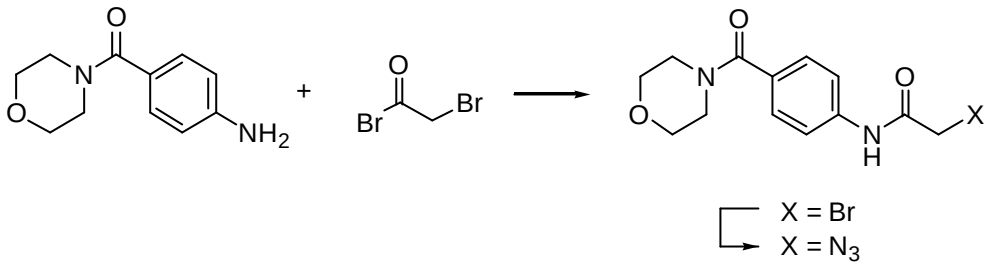



According to the general procedure for the synthesis of ω-bromoacylamides, 6-bromohexanoyl chloride and 1-napthylenemethylamine afforded the bromide as a yellow brown oil, which was used directly in the next step. $^{1}$H NMR (400 MHz, $CDCl_3$) *d* 1.47, 1.97, 1.87 (3 × m, 6H, H3,4,5), 2.21, 3.39 (2 × t, *J* 7.2 Hz, 4H, H2,6), 4.91 (d, 2H, $CH_2N$), 5.64 (s, 1H, NH), 7.45, 7.55, 7.84, 7.88- 7.91, 8.01- 8.04 (5 × m, 7H, Ar); $^{13}$C NMR (100 MHz, $CDCl_3$) *d* 24.72, 27.68, 32.34, 33.58, 36.30, 41.74 ($CH_2$), 123.48, 125.33, 126.00, 126.60, 126.78, 128.63, 128.74, 131.30, 133.47, 133.80 (Ar), 172.27 (C=O).

According to the general procedure for the synthesis of ω-azidoacylamides, 6-bromo-*N*-(naphthalen-1-ylmethyl)hexanamide gave 6-azido-*N*-(naphthalen-1-ylmethyl)hexanamide (**16**) as yellow crystals (25% over 2 steps); m.p. 60- 62 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) *d* 1.35, 1.51- 1.70 (2 × m, 6H, H3,4,5), 2.17, 3.21 (2 × t, *J* 7.2 Hz, 2 × 2H, H2,6), 4.86 (d, *J* 5.2 Hz, 2H, $CH_2N$), 5.90 (s, 1H, NH), 7.42, 7.53, 7.78- 7.90, 8.02 (4 × m, 7H, Ar); $^{13}$C NMR (100 MHz, $CDCl_3$) *d* 25.30, 26.48, 28.71, 36.49, 41.88 (5C, C2,3,4,5,6), 51.34 (1C, $CH_2N$),

123.69, 125.53, 126.19, 126.76, 126.92, 128.80, 128.93, 131.51, 133.73, 134.00 (10C, Ar), 172.47 (1C, C=O); IR ν ($cm^{-1}$) 2097 ($N_3$), 1644 (C=O).

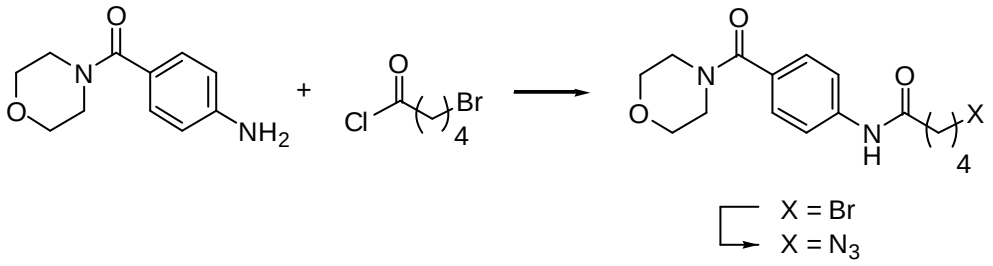
*4-(4-Azidoacetamidobenzoyl)morpholine* (**17**)




According to the general procedure for the synthesis of ω-bromoacylamides, bromoacetyl bromide and 4-(4-aminobenzoyl)morpholine[3] afforded the bromide as brown plates (43%); $^1$H NMR (299.9 MHz, $CDCl_3$) *d* 3.70 (bs, 8H, 2 × NC*H*$_2$C*H*$_2$O), 4.01 (s, 2H, $CH_2Br$), 7.37-7.56 (AB q, 4H, Ar), 8.52 (s, 1H, NH).

According to the general procedure for the synthesis of ω-azidoacylamides, 4-(4-bromoacetylamidobenzoyl)morpholine gave the azide (**17**) as a yellow solid (0.090 g, 45%); m.p. 132-134 ºC (EtOAc/petroleum spirits); $^1$H NMR (299.9 MHz, $CDCl_3$) *d* 3.70 (br s, 8H, 2 × NC*H*$_2$C*H*$_2$O), 4.15 (s, 2H, C*H*$_2$N$_3$), 7.30- 7.63 (AB q, 4H, Ar), 8.25 (s, 1H, NH); IR ν ($cm^{-1}$) 1702 sharp (C=O), 2109 sharp ($N_3$).

*4-[4-(5-Azidovaleryl)amidobenzoyl]morpholine* (**19**)

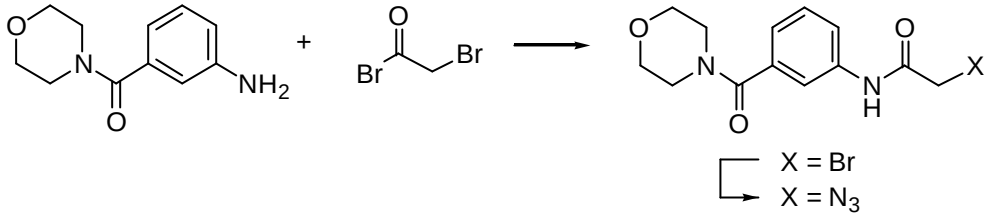



According to the general procedure for the synthesis of ω-bromoacylamides, 5-bromovaleryl chloride (1.00 mL, 7.47 mmol) and 4-(4-aminobenzoyl)morpholine[3] (0.49 g, 2.39 mmol) gave the bromide as a crude brown gum; $^1$H NMR (299.9 MHz, $CDCl_3$) *d* 1.79- 2.10 (m, 4H, $COCH_2C$*H*$_2$), 2.34- 2.46 (m, 2H, CO*CH*$_2$), 3.36- 3.82 (m, 8H, alkyl), 7.32- 7.56 (AB system, 4H, Ar), 7.77 (bs, 1H, NH).

According to the general procedure for the synthesis of ω-azidoacylamides, 4-[4-(5-bromovaleryl)amidobenzoyl]morpholine (0.88 g, 2.39 mmol) gave the azide (**19**) as pale orange crystals (0.116 g, 15%); m.p. 85- 86 ºC (EtOAc/petroleum spirits); $^1$H NMR (299.9 MHz,

$CDCl_3$) *d* 1.48- 2.10 (m, 4H, $COCH_2CH_2$), 2.31- 2.52 (m, 2H, $COCH_2$), 3.21- 3.84 (m, 12H, alkyl), 7.30- 7.58 (AB q, 4H, Ar), 7.70 (s, 1H, NH); IR ν ($cm^{-1}$) 2096 sharp ($N_3$).

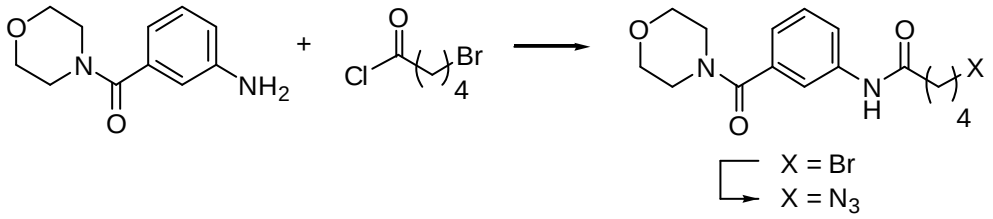
*4-(3-Azidoacetamidobenzoyl)morpholine* (**20**)




According to the general procedure for the synthesis of ω-bromoacylamides, bromoacetyl bromide (1.15 mL, 13.3 mmol) and 4-(3-aminobenzoyl)morpholine[4] (1.10 g, 5.31 mmol) gave the bromide as a beige powder (0.32 g, 19%); m.p. 159- 162 ºC (EtOAc/petroleum spirits); $^1$H NMR (299.9 MHz, $CDCl_3$) *d* 3.46- 3.80 (m, 8H, 2 × $NCH_2CH_2O$), 3.99 (s, 2H, $CH_2Br$), 7.16 (d, 1H, $J_{4,5}$ 7.5 Hz, H4), 7.37 (t, 1H, $J_{5,6}$ 8.1 Hz, H5), 7.60 (m, 2H, H2, 6), 8.65 (s, 1H, NH).

According to the general procedure for the synthesis of ω-azidoacylamides, 4-(3-bromoacetamidobenzoyl)morpholine afforded 4-(3-azidoacetamidobenzoyl)morpholine (**20**) as a white solid (87%); m.p. 130- 132 °C (EtOAc/pet. spirits); $^1$H NMR (400 MHz, $CDCl_3$) *d* 3.50- 3.90 (m, 8H, morpholino), 4.12 (s, 2H, $CH_2N_3$), 7.16, 7.59 (2 × d, $J_{4',5'} \sim J_{5',6'}$ 7.8 Hz, 2 × H, H4',6'), 7.38 (t, $J_{4',5'} \sim J_{5',6'}$ 7.8 Hz, 1H, H5'), 8.42 (s, 1H, NH); $^{13}$C NMR (125 MHz, $CDCl_3$) *d* 41.88, 44.46 (2C, C3",5"), 53.03 (1C, $CH_2N_3$), 67.02 (2C, C2",6"), 119.03, 121.69, 123.49, 129.64, 136.09, 137.44 (6C, Ar), 165.20, 170.01 (2C, C=O); IR ν ($cm^{-1}$) 2108 ($N_3$), 1620 (C=O).

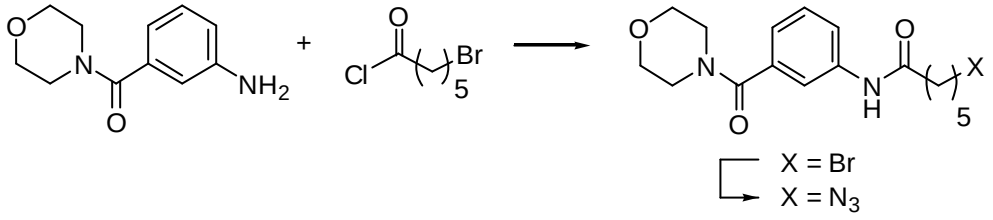
*4-(3-(5-Azidovaleramido)benzoyl)morpholine* (**21**)




According to the general procedure for the synthesis of ω-bromoacylamides, 5-bromovaleryl chloride and 4-(3-aminobenzoyl)morpholine[4] afforded 4-(3-(5-bromovaleramido)benzoyl)-morpholine as a yellow powder (93%); m.p. 235 ºC (EtOAc/pet. spirits; dec.); $^1$H NMR (400 MHz, $CDCl_3$) *d* 1.84- 2.04 (m, 4H, H3,4), 2.43, 3.46 (2 × t, 4H, $J_{2,3} \sim J_{4,5}$ 6.2 Hz, H2,5), 3.42- 3.86 (m, 8H, morpholino), 7.15, 7.37, 7.40, 7.56 (4H, H2',4',5',6'), 7.64 (s, 1H, NH).

According to the general procedure for the synthesis of ω-azidoacylamides, 4-(3-(5-bromovaleramido)benzoyl)morpholine gave 4-(3-(5-azidovaleramido)benzoyl)morpholine (**21**) as a pale yellow oil (91%); $^{1}$H NMR (400 MHz, $CDCl_3$) *d* 1.63- 1.84 (m, 4H, H3,4), 2.39, 3.34 (2 × t, $J_{2,3} \sim J_{4,5}$ 6.8 Hz, 2 × 2H, H2,5), 3.38- 3.87 (m, 8H, morpholino), 7.11, 7.34, 7.57 (3m, 4H, Ar), 7.86 (s, 1H, NH); $^{13}$C NMR (125 MHz, $CDCl_3$) *d* 22.77, 28.51, 36.49, 51.35 (4C, C2,3,4,5), 42.83, 48.45 (2C, C3",5"), 67.03 (2C, C2",6"), 118.87, 121.62, 122.39, 129.43, 135.75, 138.68 (6C, Ar), 170.41, 171.32 (2C, C=O); IR ν ($cm^{-1}$) 2100 ($N_3$), 1630 (C=O).

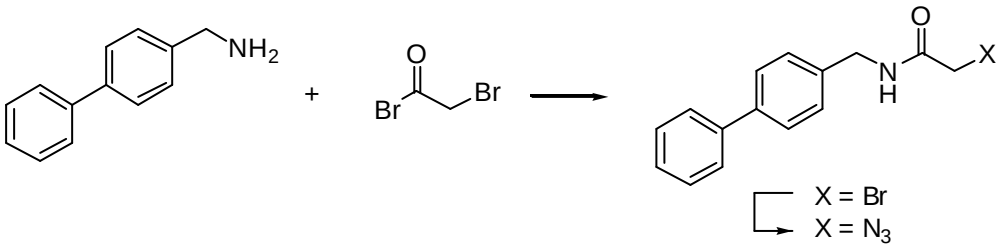
*4-(3-(6-Azidohexanamido)benzoyl)morpholine* (**22**)




According to the general procedure for the synthesis of ω-bromoacylamides, 6-bromohexanoyl chloride and 4-(3-aminobenzoyl)morpholine[4] afforded 4-(3-(5-bromohexanamido)benzoyl)morpholine as a pale yellow powder (82%); m.p. 80- 82 °C; $^{1}$H NMR (400 MHz, $CDCl_3$) *d* 1.50 (m, 4H, H4), 1.72, 1.89 (2 × m, 2 × 2H, H3,5), 2.35, 3.42 (2 × t, $J_{2,3} \sim J_{5,6}$ 6.9 Hz, 4H, H2,6), 3.47- 3.79 (m, 8H, morpholino), 7.07, 7.32, 7.60 (3H, H4',5',6'), 7.54 (s, 1H, H2'), 8.21 (s, 1H, NH).

According to the general procedure for the synthesis of ω-azidoacylamides, 4-(3-(5-bromohexanamido)benzoyl)morpholine gave 4-(3-(6-azidohexanamido)benzoyl)morpholine (**22**) as a yellow oil (72%); $^{1}$H NMR (500 MHz, $CDCl_3$) *d* 1.44 (m, 2H, H4), 1.63, 1.73 (2 × m, 4H, H3,5), 2.34, 3.29 (2 × t, $J_{2,3} \sim J_{5,6}$ 5.6 Hz, 2 × 2H, H2,6), 3.47- 3.58 (m, 8H, morpholino), 7.08, 8.32, 7.57 (3H, H4',5',6'), 7.55 (1H, H2'), 8.09 (s, 1H, NH); $^{13}$C NMR (125 MHz, $CDCl_3$) *d* 25.13, 26.56, 28.85, 37.38, 51.45 (5C, C2,3,4,5,6), 42.34, 48.52 (2C, C3",5"), 67.06 (2C, C2",6"), 118.89, 121.57, 122.45, 129.45, 135.86, 138.70 (6C, Ar), 170.38, 171.66 (2C, C=O); IR ν ($cm^{-1}$) 2097 ($N_3$), 1637 (C=O).

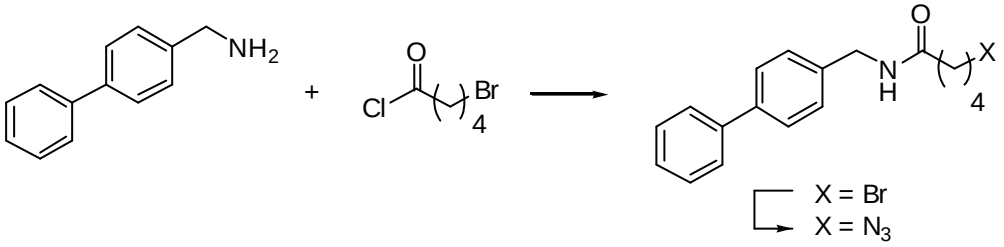
*4-Azido*-N-*(4-phenylbenzyl)acetamide* (**23**)



According to the general procedure for the synthesis of ω-bromoacylamides, bromoacetyl bromide and 4-phenylbenzylamine afforded the bromide. $^1$H NMR (300 MHz, $CDCl_3$) *d* 3.96 (3H, s, $CH_2N_3$), 4.52 (2H, d, *J* 4.5 Hz, $CH_2Ar$), 6.82 (bs, 1H, NH), 7.36- 7.60 (m, 9H, Ar); $^{13}$C NMR (100 MHz, $CDCl_3$) *d* 29.18, 43.89 (2 × $CH_2$), 127.06, 127.42, 127.55, 128.20, 128.80, 136.22, 140.53, 140.79 (Ar), 165.32 (C=O).

According to the general procedure for the synthesis of ω-azidoacylamides, the crude bromide afforded the azide (**23**) as colourless plates (84%); m.p. 134- 136 ºC; $^1$H NMR (300 MHz, $CDCl_3$) *d* 4.07 (s, 3H, $CH_2N_3$), 4.52 (d, 2H, *J* 4.5 Hz, $CH_2Ar$), 6.66 (br s, 1H, NH), 7.34- 7.60 (m, 9H, Ar); IR ν ($cm^{-1}$) 2118 ($N_3$), 1655 (C=O).

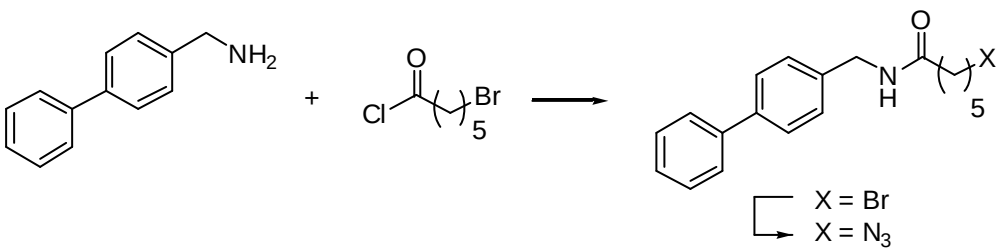
*4-Azido*-N-*(4-phenylbenzyl)valeramide* (**25**)




According to the general procedure for the synthesis of ω-bromoacylamides, 5-bromovaleryl chloride and 4-phenylbenzylamine afforded the bromide as white plates; m.p. 143- 145 ºC; $^1$H NMR (300 MHz, $CDCl_3$) *d* 1.78- 1.99 (4H, m, $CH_2$), 2.27 (2H, t, *J* 6.9 Hz, $CH_2$), 3.43 (2H, t, *J* 6.6 Hz, $CH_2$), 4.47 (2H, d, *J* Hz, $CH_2Ar$), 6.34 (bs, 1H, NH), 7.33- 7.59 (m, 9H, Ar).

According to the general procedure for the synthesis of ω-azidoacylamides, the crude bromide afforded the azide (**25**) as off-white plates (94%); m.p. 140- 142 ºC; $^1$H NMR (300 MHz, $CDCl_3$) *d* 1.61- 1.78 (m, 4H, $CH_2CH_2$), 2.26 (t, *J* 7.2 Hz, 2H, $CH_2$), 3.29 (2H, t, *J* 6.9 Hz, $CH_2$), 4.47 (2H, d, *J* 5.7 Hz, $CH_2Ar$), 5.88 (bs, 1H, NH), 7.32- 7.58 (m, 9H, Ar); IR ν ($cm^{-1}$) 1634 sharp (C=O), 2123 sharp ($N_3$).

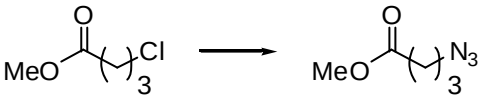
*4-Azido*-N-*(4-phenylbenzyl)hexanamide* (**26**)



According to the general procedure for the synthesis of ω-bromoacylamides, 6-bromohexanoyl chloride and 4-phenylbenzylamine afforded the bromide as colourless plates; m.p. 128- 130 ºC; $^1$H NMR (300 MHz, $CDCl_3$) *d* 1.44- 1.96 (m, 6H, $CH_2$), 2.25 (2H, t, *J* 6.9 Hz, $CH_2$), 3.42 (2H, t, *J* 6.9 Hz, $CH_2$), 4.89 (2H, d, *J* 5.7 Hz, $CH_2Ar$), 5.74 (bs, 1H, NH), 7.34- 7.60 (9H, m, Ar).

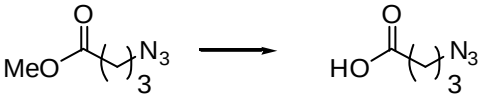
According to the general procedure for the synthesis of ω-azidoacylamides, the crude bromide afforded the azide (**26**) as colourless plates (97%); m.p. 128- 130 ºC; $^1$H NMR (400 MHz, $CDCl_3$) *d* 1.38- 1.75 (m, 6H, $CH_2CH_2CH_2$), 2.24 (2H, t, *J* 7.2 Hz, $CH_2$), 3.27 (2H, t, *J* 6.9 Hz, $CH_2$), 4.47 (d, *J* 5.7 Hz, $CH_2Ph$), 5.83 (bs, 1H, NH), 7.33- 7.59 (m, 9H, Ar); IR ν ($cm^{-1}$) 1638 sharp (C=O), 2122 sharp ($N_3$).

*Methyl 4-azidobutyrate*




A mixture of sodium azide (0.81 g, 12.4 mmol) and methyl 4-chlorobutyrate (1.00 mL, 8.20 mmol) in DMSO (5 mL) was stirred at 50 °C for 24 h. The reaction mixture was allowed to cool to room temperature and stirring was continued for a further 67 h. Water (20 mL) was added to the reaction mixture and the combined mixture was extracted with diethyl ether (3 × 15 mL). The organic extract was washed with brine (3 × 20 mL), dried ($MgSO_4$), filtered and the filtrate concentrated under reduced pressure to give a colourless oil (0.593 g, 50%); $^1$H NMR (299.9 MHz, $CDCl_3$) *d* 1.77- 1.93 (m, 2H, $CH_2CH_2CO_2$), 2.38 (t, 2H, *J* 7.2 Hz, $CH_2CO_2$), 3.32 (t, 2H, *J* 6.6 Hz, $N_3CH_2$), 3.65 (s, 3H, $OCH_3$); IR ν ($cm^{-1}$) 2097 ($N_3$).

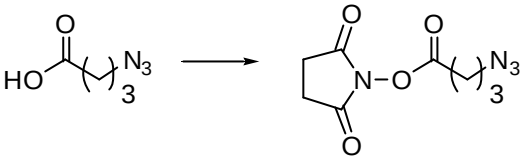
*4-Azidobutyric acid*




NaOH (1 M, 16.6 mL, 16.7 mmol) was added to the crude methyl 4-azidobutylrate (0.59 g, 4.14 mmol), then sufficient methanol was introduced to form a homogenous mixture (approx 10 mL). The reaction mixture was stirred at room temperature overnight then the methanol was removed under reduced pressure. The aqueous residue was acidified by addition of 1 M HCl (5 mL) then extracted with diethyl ether (3 × 20 mL). The organic extract was dried ($MgSO_4$), filtered and the filtrate concentrated under reduced pressure to yield a crude colourless oil (0.32 g, 54%); $^1$H NMR (400 MHz, $CDCl_3$) *d* 1.87 (m, 2H, H3), 2.42 (t, $J_{3,4}$ 7.0 Hz,

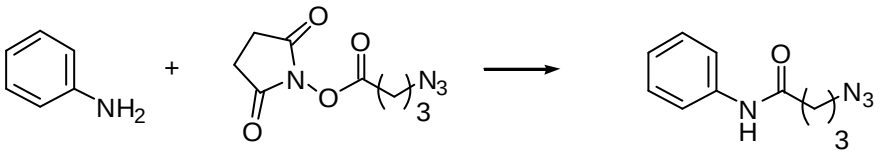
2H, H4), 3.33 (t, $J_{2,3}$ 7.0 Hz, 2H, H2), 8.56 (s, 1H, $CO_2H$); IR ν ($cm^{-1}$) 1713 sharp (C=O), 2099 sharp ($N_3$).

*4-Azidobutyric acid* N-*hydroxysuccinimide ester*



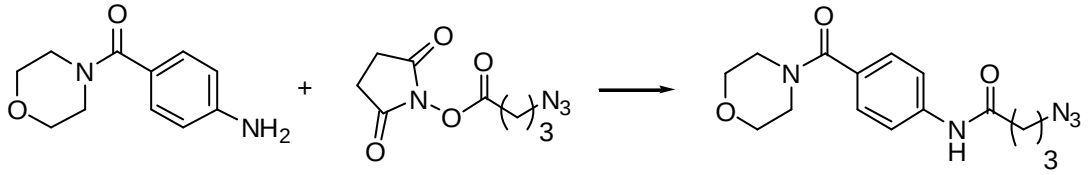
*N*-Hydroxysuccinimide (1.89 g, 16.4 mmol) and dicyclohexylcarbodiimide (5.42 g, 26.2 mmol) were added to a stirring solution of 4-azidobutyric acid in $CH_2Cl_2$ (50 mL). The solution was allowed to stir for 6 h. The solution was washed with $H_2O$, aq. 1 M NaOH, dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure to yield a pale yellow oil containing a white precipitate. The precipitate was removed by filtration and the remaining oil purified by flash chromatography (EtOAc) to yield 4-azidobutyric acid *N*-hydroxysuccinimide ester as a pale yellow oil (2.55 g, 69%); $^1$H NMR (400 MHz, $CDCl_3$) *d* 1.98 (m, 2H, H3), 2.70 (t, $J_{3,4}$ 7.0 Hz, 2H, H4), 2.81 (s, 4H, 2 × succinimide, $CH_2$), 4.42 (t, $J_{2,3}$ 7.0 Hz, 2H, H2); $^{13}$C NMR (125 MHz, $CDCl_3$) *d* 24.33, 25.81, 28.31 (3C, C2,3,4), 50.19, 50.68 (2C, 2 × succinimide $CH_2$), 168.20 (3C, 3 × C=O); IR ν ($cm^{-1}$) 2098 ($N_3$).

*4-Azido*-N-*phenylbutyramide* (**11**)



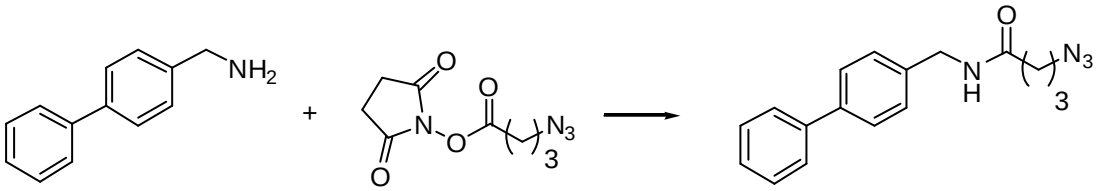
A mixture of aniline (0.583 g, 6.26 mmol), pyridine (1.01 mL, 12.5 mmol) and 4-azidobutyric acid *N*-hydroxysuccinimide ester (**39**) (1.70 g, 7.51 mmol) in $CH_2Cl_2$ (34 mL) was stirred for 67 h. $H_2O$ (5 drops) was added and the organic solution was washed with $H_2O$, 1 M aq. HCl and sat. aq. $NaHCO_3$ (3 ×). The organic phase was dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure to yield a pale yellow oil, which was recrystallised from EtOAc/pet. spirits to afford 4-azido-*N*-phenylbutyramide (**11**) as a colourless powder (134 mg, 11%); m.p. 69- 71 °C (EtOAc/pet. spirits); $^1$H NMR (400 MHz, $CDCl_3$) *d* 2.04 (m, 2H, H3), 2.48 (t, $J_{3,4}$ 6.8 Hz, 2H, H4), 3.44 (t, $J_{2,3}$ 6.8 Hz, 2H, H2), 7.13 (t, *J* 7.6 Hz, 1H, H4'), 7.20 (s, 1H, NH), 7.34 (t, 2H, *J* 7.6 Hz, H3',5'), 7.51 (d, 2H, *J* 7.6 Hz, H2',6'); $^{13}$C NMR (500 MHz, $CDCl_3$) *d* 24.81, 34.35, 50.90 (3C, C2,3,4), 120.00, 124.65, 129.27, 137.85 (6C, Ar), 170.11 (1C, C=O); IR ν ($cm^{-1}$) 2097 ($N_3$), 1662 (C=O).

*4-[4-(4-Azidobutryl)amidobenzoyl]morpholine* (**18**)



4-(4-Aminobenzoyl)morpholine[3] (0.61 g, 2.98 mmol) and pyridine (0.50 mL, 6.19 mmol) were added to a solution of 4-azidobutyric acid *N*-hydroxysuccinimide ester (0.81 g, 3.56 mmol) in dichloromethane (20.0 mL) and the reaction mixture stirred at room temperature for 26 h. Pyridine (0.24 mL, 2.97 mmol) and 4-dimethylamino pyridine (0.04 g, 0.30 mmol) were introduced to the reaction after 4 and 23 h, respectively. The reaction mixture was diluted with dichloromethane (50 mL) then washed with water (3 × 20 mL), 1 M HCl (3 × 20 mL) and saturated $NaHCO_3$ (2 ×20 mL). The organic extract was dried ($MgSO_4$), filtered and the filtrate concentrated to yield a crude brown gum, which crystallized upon standing overnight. The crude material was purified by recrystallization to yield (**18**) as a brown crystalline solid (0.24 g, 26%); m.p. 83- 85 ºC (EtOAc/petroleum spirits); $^1$H NMR (399.7 MHz, $CDCl_3$) *d* 1.84- 2.05 (m, 2H, C*H*$_2$CH$_2$CO), 2.46 (t, 2H, *J* 5.4 Hz, COC*H*$_2$), 3.36- 3.89 (m, 10H, alkyl), 7.30- 7.53 (AB q, 4H, Ar), 7.96 (s, 1H, NH); IR ν (cm$^{-1}$) 2097, sharp ($N_3$).

*4-Azido*-N-*(4-phenylbenzyl)butyramide* (**24**)



4-Phenylbenzylamine (0.14 g, 0.74 mmol) and pyridine (0.12 mL, 1.49 mmol) was added to a solution of 4-azidobutyric acid *N*-hydroxysuccinimide ester (0.21 g, 0.91 mmol) in dichloro-methane (5 mL) and the reaction mixture stirred at room temperature for 2.5 h. The mixture was then diluted with dichloromethane (25 mL) and washed with water (3 × 10 mL), 1 M HCl (3 × 10 mL) and saturated $NaHCO_3$ (3 × 10 mL). The organic extract was dried ($MgSO_4$), filtered and the filtrate concentrated under reduced pressure to yield a crude yellow solid. The crude material was purified by crystallization to yield (**24**) as a colourless solid (0.06 g, 25%); m.p. 141- 142 ºC (EtOAc/petroleum spirits); $^1$H NMR (299.9 MHz, $CDCl_3$) *d* 1.97 (m, 2H, *J* 3.5 Hz, CH$_2$C*H*$_2$CH$_2$), 2.33 (t, 2H, *J* 3.6 Hz, COC*H*$_2$), 3.38 (t, 2H, *J* 3.2 Hz, N$_3$C*H*$_2$), 4.49 (d, 2H, *J* 2.9 Hz, C*H*$_2$NH), 7.34- 7.58 (m, 9H, Ar); IR ν (cm$^{-1}$) 2121, sharp ($N_3$).

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