Synthesis and Biological Evaluation of Hybrid G-Quadruplex-HSP90 Ligand Conjugates As Telomerase Inhibitors

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Experimental:

General: 1H and 13C-NMR spectra were recorded on a Bruker AV(III) 500 (Cryoprobe) (500 MHz (1H) and 125 MHz (13C)), Bruker AV(III) 400 Bruker AV 400 Bruker DPX 400 (400MHz (1H) and 100 MHz (13C)) spectrometers. Chemical shifts are expressed in parts per million (ppm) and the spectra are calibrated to residual solvent signals of CDCl3 (7.26 (1H) and 77.0 (13C)). Coupling constant are given in hertz (Hz) and the following notations indicate the multiplicity of the signals: s (singlet), d (doublet), brd (broad doublet), t (triplet), q (quartet), p (pentet), m (multiplet). High Resolution Mass Spectra were recorded on VG micron Autospec or Bruker microTOF. Fourier Transform Infrared Spectroscopy (FT-IR) spectra were obtained on Perkin Elmer 1600 series or Bruker Tensor 27 spectrometer. UV absorption was measured on Philips PU8720 series UV/VIS spectrometer. Thin layer chromatography were carried on Merck precoated silica gel plates (60F-254) or Merck aluminium backed aluminium oxide 60 F254 coated plates and visualised using ultra violet light or KMnO4 solution or p-anisaldehyde solution. Column chromatography was performed at ambient temperature using Merck silica gel 60 (0.063-0.200 mm) or BDH neutral aluminium oxide, and eluents containing c.NH3(aq) refer to the mixed eluent with the water removed prior to use. THF was freshly distilled from sodium-benzophenone; dichloromethane was dried over calcium hydride. Acetone and
solid CO$_2$ was used to obtain -78 °C. Where necessary, reaction requiring anhydrous conditions were performed in dry solvents in flame dried or oven-dried apparatus under nitrogen or argon atmosphere.

3,6-Bis(3-pyrrolidin-1-ylpropionamido)-9-chloroacridine (2)

\[
\text{H}_\text{N} \quad \text{Cl} \\
\text{O} \quad \text{N} \quad \text{O} \\
\text{N} \quad \text{O}
\]

Compound 3,6-Bis[3-(pyrrolidino)propionamido]-9(10H)-acridone (5.78 g, 12.2 mmol) was slowly added at reflux POCl$_3$ (87 mL) over 10 minutes (care: HCl evolution), then heated at reflux for a further 3 h. The reaction mixture was cooled to 0° C and anhydrous diethyl ether was added to precipitate the product, which was then isolated by filtration. Solids were washed with diethyl ether, then redissolved in chloroform (100 mL) and water (100 mL) and made basic with dilute ammonia. The organic phase was collected, washed with brine (50 mL) and evaporated to dryness to give the title compound (4.85 g, 81%) as a dark yellow powder; $R_f$ 0.73 (85:10:5 dichloromethane / methanol / triethylamine); $\delta$$_{\text{H}}$ (400 MHz, CDCl$_3$) 11.72 (2H, s), 8.35 (2H, d, $J$ 9.4 Hz), 8.12 (2H, $J$ 1.8 Hz), 7.98 (2H, dd, $J$ 9.4 and 1.8 Hz), 2.94 (4H, t, $J$ 6.2 Hz), 2.77 (8H, m), 2.65 (4H, t, $J$ 6.2 Hz), 1.99 (8H, m); $\delta$$_C$ (101 MHz, CDCl$_3$) 171.46, 150.27, 141.20, 140.62, 125.61, 121.74, 120.79, 115.06, 53.19, 51.36, 34.77, 23.78; $m/z$ (ESI) 516.2 (M+Na$^+$, 7%), 494.2 (M+H$^+$, 100), 411.2 (88), 328.1 (51), 286.1 (21); HRMS: Found 494.2304. C$_{27}$H$_{33}$Cl$_1$N$_5$O$_2$ (M+H$^+$) Requires 494.2317.

General Procedure for the Preparation of Diazidoalkanes

The dibromoalkane (1 mmol) and sodium azide (2.5 mmol) in water (2 mL) were placed in a 10 mL crimp-sealed thick-walled glass microwave tube along with a magnetic stirrer. The reaction tube was placed inside the cavity of a Biotage Initiator™ microwave
synthesiser and heated to 120-140º C for 1-4 hours. After completion of the reaction as monitored by $^1$H NMR, the diazide was extracted with diethyl ether and the combined organic layers dried over anhydrous sodium sulfate. Removal of the solvent in vacuo afforded the product as colourless-pale yellow oil.

**1,3-Diazidopropane**

![1,3-Diazidopropane](image)

The reaction of 1,3-dibromo-propane (2.15 g, 7.3 mmol) and sodium azide (1.18 g, 18.2 mmol) was carried out as described in the general procedure and afforded the title compound (0.72 g, 78%) as a colourless oil; R$_f$ 0.50 (6:1 hexane / ethyl acetate); $\delta_H$ (400 MHz, CDCl$_3$) 3.42 (4H, t, $J$ 6.5 Hz), 1.83 (2H, p, $J$ 6.5 Hz).

**1,5-Diazidopentane**

![1,5-Diazidopentane](image)

The reaction of 1,5-dibromopentane (1.61 g, 7.0 mmol) and sodium azide (1.14 g, 17.5 mmol) was carried out as described in the general procedure and afforded the title compound (1.01 g, 94%) as a colourless oil; $\delta_H$ (400 MHz, CDCl$_3$) 3.29 (4H, t, $J$ 6.8 Hz), 1.59-1.68 (4H, m), 1.42-1.51 (2H, m).

**1,7-Diazidoheptane**

![1,7-Diazidoheptane](image)

The reaction of 1,7-dibromoheptane (1.61 g, 6.3 mmol) and sodium azide (1.02 g, 15.6 mmol) was carried out as described in the general procedure and afforded the title compound as a solution in diethyl ether which was used directly in the next reaction; $\delta_H$ (400 MHz, CDCl$_3$) 3.27 (4H, t, $J$ 6.91 Hz), 1.60 (4H, m), 1.33-1.43 (6H, m).

**1,9-Diazidononane**

![1,9-Diazidononane](image)

The reaction of 1,9-dibromononane (1.61 g, 5.6 mmol) and sodium azide (0.91 g, 14.1 mmol) was carried out as described in the general procedure and afforded the title
compound as a solution in diethyl ether which was used directly in the next reaction; \( \delta_H \) (400 MHz, CDCl\(_3\)) 3.27 (4H, t, \( J 7.0 \) Hz), 1.61 (4H, m), 1.29-1.43 (10H, m).

1,9-Diaimidodecane

\[
\begin{array}{c}
\text{N}_3 \\
\hline
\text{N}_3
\end{array}
\]

The reaction of 1,10-dibromodecane (1.61 g, 5.4 mmol) and sodium azide (0.87 g, 13.4 mmol) was carried out as described in the general procedure and afforded the title compound as a solution in diethyl ether which was used directly in the next reaction; \( \delta_H \) (400 MHz, CDCl\(_3\)) 3.26 (4H, t, \( J 7.0 \) Hz), 1.60 (4H, m), 1.27-1.41 (12H, m).

General Procedure for the Preparation of Azido-aminoalkanes:

To a solution of the di-azide (1 mmol) in diethyl ether (1 mL), ethyl acetate (1 mL) and 5% aqueous hydrochloric acid (3 mL) was added triphenylphosphine (0.98 mmol) portionwise over 1 hour at 0\(^\circ\) C and stirred for 16 hours at room temperature. The organic layer was discarded and the aqueous layer was washed with (3 × 6 mL) CH\(_2\)Cl\(_2\). The resultant aqueous phase was basified with sodium hydroxide (pH>12), and then extracted with (3 × 6 mL) CH\(_2\)Cl\(_2\). The combined extracts were dried over anhydrous sodium sulfate, filtered and concentrated \textit{in vacuo} to give pure amino azide.

1-Azido-3-aminopropane (9)

\[
\begin{array}{c}
\text{N}_3 \\
\hline
\text{NH}_2
\end{array}
\]

The reaction of 1,3-diazidopropane (2.42 g, 19.2 mmol) according to the general procedure afforded the title compound (0.90 g, 55%) as a pale yellow oil; \( \delta_H \) (400 MHz, CDCl\(_3\)) 3.40 (2H, t, \( J 6.8 \) Hz), 2.83 (2H, t, \( J 6.8 \) Hz), 1.75 (2H, p, \( J 6.8 \) Hz), 1.31 (2H, br s).
1-Azido-5-aminopentane (10)

\[
\begin{align*}
\text{N}_3 & \quad \text{NH}_2 \\
\end{align*}
\]

The reaction of 1,5-diazidopentane (1.30 g, 8.5 mmol) according to the general procedure afforded the title compound (0.85 g, 81%) as a pale yellow oil; \( \delta_H \) (400 MHz, CDCl\(_3\)) 3.27 (2H, t, \( J = 6.9 \) Hz), 2.70 (2H, t, \( J = 6.8 \) Hz), 1.62 (2H, m), 1.36-1.51 (4H, m), 1.19 (2H, br s).

1-Azido-7-aminoheptane (11)

\[
\begin{align*}
\text{N}_3 & \quad \text{NH}_2 \\
\end{align*}
\]

The reaction of 1,7-diazidoheptane (2.28 g, 12.5 mmol) according to the general procedure afforded the title compound (0.86 g, 52%) as a pale yellow oil; \( \delta_H \) (400 MHz, CDCl\(_3\)) 3.24 (2H, t, \( J = 6.9 \) Hz), 2.66 (2H, t, \( J = 7.0 \) Hz), 1.58 (2H, m), 1.26-1.48 (10H).

1-Azido-9-aminononane (12)

\[
\begin{align*}
\text{N}_3 & \quad \text{NH}_2 \\
\end{align*}
\]

The reaction of 1,9-diazidononane (2.37 g, 11.3 mmol) according to the general procedure afforded the title compound (0.41 g, 23%) as a pale yellow oil; \( \delta_H \) (400 MHz, CDCl\(_3\)) 3.23 (2H, t, \( J = 6.9 \) Hz), 2.65 (2H, t, \( J = 7.0 \) Hz), 1.55 (2H, m), 1.23-1.47 (14H).

1-Azido-10-aminodecane (13)

\[
\begin{align*}
\text{N}_3 & \quad \text{NH}_2 \\
\end{align*}
\]

The reaction of 1,10-diazidodecane (2.41 g, 10.7 mmol) according to the general procedure afforded the title compound (0.27 g, 15%) as a colourless oil; \( \delta_H \) (400 MHz, CDCl\(_3\)) 3.25 (2H, t, \( J = 6.9 \) Hz), 2.67 (2H, t, \( J = 7.0 \) Hz), 1.55 (2H, m), 1.24-1.49 (16H, m).
Tethering of the amino-azide linkers to bis-amidochloroacridine (2):

\[
\begin{array}{c}
\text{NH}_2 \\
\text{N} \\
\text{N} \\
\text{H} \\
\text{O} \\
\text{N} \\
\text{O} \\
\text{N} \\
\text{H} \\
\text{N} \\
\text{H} \\
\text{O} \\
\text{N} \\
\text{O} \\
\text{N} \\
\text{Cl} \\
\end{array}
\begin{array}{c}
\text{N}_3 \\
\text{H}_2 \\
\text{N} \\
\text{N} \\
\text{H} \\
\text{N} \\
\text{H} \\
\text{O} \\
\text{N} \\
\text{O} \\
\text{N} \\
\text{H} \\
\text{N} \\
\text{O} \\
\text{N} \\
\text{Cl} \\
\end{array}
\]

Coupling of the amino azides with the bis-amidochloroacridine (2) went in good yields in CHCl₃. (Purification was achieved by column chromatography on silica with 85:10:5, DCM:MeOH:NH₃(aq)).

**N-[9-(3-Azido-propylamino)-6-(3-pyrrolidin-1-yl-propionylamino)-acridin-3-yl]-3-pyrrolidin-1-yl-propionamide (14)**

To a solution of the 3,6-bisamido-9-chloroacridine (2, 0.45 g, 0.9 mmol) in CHCl₃ (4.5 mL) was added 1-azido-3-aminopropane (9, 100 mg, 1.0 mmol), and the resultant mixture was stirred at reflux for 40 hours. The reaction mixture was made basic with saturated aqueous K₂CO₃ solution (3 mL), then extracted with CHCl₃ (3 × 5 mL). The combined extracts were dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. Purification by column chromatography over silica gel (eluting with 85:10:5 CH₂Cl₂:MeOH:c.NH₃(aq)) gave the title compound (300 mg, 59%) as an amorphous yellow glass; R_f 0.17 (90:6:4 CH₂Cl₂:CH₃OH:c.NH₃(aq)); ν_max (CHCl₃)/cm⁻¹ 2968, 2102 (azide), 1675 (amide), 1613; δ H (400 MHz, CDCl₃) 11.60 (2H, br s), 7.82-8.06 (4H, m), 7.77 (2H, s), 5.28 (1H, br s), 3.88 (2H, t, J 6.2 Hz), 3.52 (2H, t, J 6.2 Hz), 2.88 (4H, t, J 5.6 Hz), 2.70 (8H, m), 2.59 (4H, t, J 5.6 Hz), 2.01 (2H, p, J 6.2 Hz), 1.92 (8H, m); δ C (75 MHz, CDCl₃) 171.3, 150.6, 150.3, 140.6, 123.7, 117.8, 115.2, 113.5, 53.1, 51.3, 49.5, 48.3, 34.7, 30.3, 23.6; m/z (ESI) 558.3 (M+H⁺, 100%), 476.3 (6), 279.7 (27); HRMS: Found 580.3109. C₃₀H₃₉N₅NaO₂ (M+Na⁺) Requires 580.3119.
N-[9-(5-Azido-pentylamino)-6-(3-pyrrolidin-1-yl-propionylamino)-acridin-3-yl]-3-pyrrolidin-1-yl-propionamide (15)

To a solution of the 3,6-bisamido-9-chloroacridine (2, 0.70 g, 1.4 mmol) in CHCl₃ (7 mL) was added 1-azido-5-aminopentane (10, 200 mg, 1.3 mmol), and the resultant mixture was stirred at reflux for 40 hours. The reaction mixture was made basic with saturated aqueous K₂CO₃ solution (8 mL), then extracted with CHCl₃ (3 × 10 mL). The combined extracts were dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. Purification by column chromatography over silica gel (eluting with 85:10:5 CH₂Cl₂:MeOH:c.NH₃(aq)) gave the title compound (531 mg, 64%) as an amorphous yellow glass; R_f 0.43 (85:10:5 CH₂Cl₂:CH₃OH:c.NH₃(aq)); ν_max (CHCl₃)/cm⁻¹ 2938, 2819, 2100 (azide), 1674 (amide), 1613; δ_H (400 MHz, CDCl₃) 11.56 (2H, br s), 8.00 (2H, d, J 9.3 Hz), 7.91 (2H, m), 7.72 (2H, s), 5.03 (1H, br s), 3.78 (2H, t, J 7.2 Hz), 3.26 (2H, t, J 6.7 Hz), 2.87 (4H, t, J 5.8 Hz), 2.69 (8H, m), 2.58 (4H, t, J 5.8 Hz), 1.92 (8H, m), 1.78 (2H, p, J 7.4 Hz), 1.62 (2H, m), 1.50 (2H, m); δ_C (101 MHz, CDCl₃) 171.3, 150.8, 150.2, 140.5, 123.8, 117.2, 114.7, 113.0, 53.0, 51.2, 51.0, 50.1, 34.7, 31.0, 28.4, 23.9, 23.5; m/z (ESI) 586.4 (M+H⁺, 100%), 392.2 (12), 293.7 (18); HRMS: Found 586.3601. C₃₂H₄₄N₉O₂ (M+H⁺) Requires 586.3612.

N-[9-(7-Azido-heptylamino)-6-(3-pyrrolidin-1-yl-propionylamino)-acridin-3-yl]-3-pyrrolidin-1-yl-propionamide (16)

To a solution of the 3,6-bisamido-9-chloroacridine (2, 0.63 g, 1.3 mmol) in CHCl₃ (9.5 mL) was added 1-azido-5-aminoheptane (11, 300 mg, 1.9 mmol), and the resultant
mixture was stirred at reflux for 40 hours. The reaction mixture was made basic with saturated aqueous K$_2$CO$_3$ solution (10 mL), then extracted with CHCl$_3$ (3 × 15 mL). The combined extracts were dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. Purification by column chromatography over silica gel (eluting with 90:6:4 CH$_2$Cl$_2$:CH$_3$OH:c.NH$_3$(aq)) gave the title compound (500 mg, 64%) as an amorphous yellow glass; R$_f$ 0.33 (90:6:4 CH$_2$Cl$_2$:CH$_3$OH:c.NH$_3$(aq)); $\nu_{max}$ (CHCl$_3$)/cm$^{-1}$ 3011, 2750, 2100 (azide), 1674 (amide), 1613; $\delta$H (400 MHz, CDCl$_3$) 11.57 (2H, br s), 7.95 (2H, d, $J$ 8.7 Hz), 7.84 (2H, d, $J$ 8.7 Hz), 7.66 (2H, s), 5.29 (1H, br s), 3.68 (2H, m), 3.13 (2H, t, $J$ 6.8 Hz), 2.77 (4H, m), 2.57 (8H, m), 2.49 (4H, m), 1.78 (8H, m), 1.66 (2H, m), 1.45 (2H, m), 1.16-1.35 (6H, m); $\delta$C (101 MHz, CDCl$_3$) 171.1, 150.7, 150.5, 140.4, 123.7, 117.2, 114.9, 112.8, 52.9, 51.1, 51.0, 50.3, 34.6, 31.2, 28.6, 28.4, 26.5, 26.3, 23.4; m/z (ESI) 614.4 (M+H$^+$, 100%), 420.2 (17), 308.2 (28), 307.7 (72); HRMS: Found 614.3914. C$_{34}$H$_{48}$N$_9$O$_2$ (M+H$^+$) Requires 614.3925.

N-[9-(9-Azido-nonylamino)-6-(3-pyrrolidin-1-yl-propionylamino)-acridin-3-yl]-3-pyrrolidin-1-yl-propionamide (17)

To a solution of the 3,6-bisamido-9-chloroacridine (2, 0.54 g, 1.1 mmol) in CHCl$_3$ (5.4 mL) was added 1-azido-9-aminononane (12, 300 mg, 1.6 mmol), and the resultant mixture was stirred at reflux for 40 hours. The reaction mixture was made basic with saturated aqueous K$_2$CO$_3$ solution (10 mL), then extracted with CHCl$_3$ (3 × 15 mL). The combined extracts were dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. Purification by column chromatography over silica gel (eluting with 90:6:4 CH$_2$Cl$_2$:CH$_3$OH:c.NH$_3$(aq)) gave the title compound (252 mg, 36%) as an amorphous yellow glass; R$_f$ 0.26 (90:6:4 CH$_2$Cl$_2$:CH$_3$OH:c.NH$_3$(aq)); $\nu_{max}$ (CHCl$_3$)/cm$^{-1}$ 3011, 2965, 2099 (azide), 1674 (amide), 1613; $\delta$H (400 MHz, CDCl$_3$) 11.57 (2H, br s), 8.03 (2H, d, $J$ 9.2 Hz), 7.99 (2H, m), 7.71 (2H, s), 5.29 (1H, br s), 3.81 (2H, t, $J$ 6.8 Hz), 3.26 (2H, t, $J$ 6.8 Hz), 2.90 (4H, t, $J$ 6.4 Hz), 2.73 (8H, m), 2.61 (4H, t, $J$ 6.4 Hz), 1.82 (8H, m), 1.78
N-[[9-(10-Azido-decylamino)-6-(3-pyrrolidin-1-yl-propionylamino)-acridin-3-yl]-3-pyrrolidin-1-yl-propionamide (18)

To a solution of the 3,6-bisamido-9-chloroacridine (2, 0.17 g, 0.3 mmol) in CHCl₃ (1.7 mL) was added 1-azido-10-aminodecane (13, 100 mg, 0.5 mmol), and the resultant mixture was stirred at reflux for 40 hours. The reaction mixture was made basic with saturated aqueous K₂CO₃ solution (4 mL), then extracted with CHCl₃ (3 × 5 mL). The combined extracts were dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. Purification by column chromatography over silica gel (eluting with 90:6:4 CH₂Cl₂:CH₃OH:c.NH₃(aq)) gave the title compound (114 mg, 52%) as an amorphous yellow glass; Rf 0.29 (90:6:4 CH₂Cl₂:CH₃OH:c.NH₃(aq)); ʋ_max (CHCl₃)/cm⁻¹ 3011, 2931, 2100 (azide), 1672 (amide), 1613; δ_H (400 MHz, CDCl₃) 11.57 (2H, br s), 7.99 (2H, d, J 9.1 Hz), 7.73 (2H, dd, J 9.1 and 1.6 Hz), 7.71 (2H, s), 3.82 (2H, t, J 6.8 Hz), 3.59 (2H, m), 2.85 (4H, t, J 6.4 Hz), 2.66 (8H, m), 2.58 (4H, t, J 6.4 Hz), 1.87 (8H, m), 1.75 (2H, m), 1.53 (2H, m), 1.20-1.45 (12H, m); m/z (ESI) 656.4 (M+H⁺, 1%), 631.4 (100), 316.7 (28), 316.2 (70); HRMS: Found 656.4385. C₃₇H₅₄N₉O₂ (M+H⁺) Requires 656.4395.
To a solution of Geldanamycin (4, 506 mg, 0.9 mmol) in dimethylformamide (11.7 mL) in a flame dried flask under nitrogen was added a solution of propargylamine (104 μL, 1.6 mmol) in DMF (1 mL) slowly via syringe pump over a period of 1 hour at room temperature. The mixture was then stirred at room temperature for an additional 16 hours. Concentration of the reaction mixture in vacuo at 50 ºC followed by repeated dissolution and re-concentration from chloroform gave the title compound (516.8 mg, 98%) as a purple solid; Rf 0.35 (95:5 CH2Cl2/ CH3OH); vmax (CHCl3)/cm–1 3620.7, 1727.9, 1688.6, 1579.7; δH (400 MHz, CDCl3) 9.08 (1H, s), 7.29 (1H, s), 6.94 (1H, d, J 11.4 Hz), 6.57 (1H, t, J 11.4 Hz), 6.31 (1H, t, J 5.5 Hz), 5.82-5.90 (2H, m), 5.18 (1H, s), 4.90 (2H, br s), 4.27-4.33 (3H, m), 3.95 (1H, br m), 3.54-3.60 (1H, br m), 3.41-3.46 (1H, br m), 3.35 (3H, s), 3.26 (3H, s), 2.68-2.78 (2H, br m), 2.40 (1H, s), 2.31-2.38 (1H, br m), 2.02 (3H, s), 1.79 (3H, s), 1.63-1.77 (2H, m), 0.95-1.02 (7H, m); δC (101 MHz, CDCl3) 183.59, 181.55, 168.31, 156.09, 143.90, 140.71, 135.89, 134.88, 133.56, 132.85, 126.95, 126.47, 110.26, 109.08, 81.56, 81.27, 81.11, 78.18, 73.93, 72.58, 72.58, 57.08, 56.69, 35.39, 34.92, 34.35, 32.25, 28.55, 22.85, 12.77, 12.57, 12.35; m/z (ESI) 1189.6 (2M+Na+, 90.5%), 606.3 (M+Na+, 100), 491.3 (14.8); HRMS: Found 606.2773. C31H41N3NaO8 (M+Na+) Requires 606.2786.
General Procedure for the Preparation of Geldanamycin-bis-amido-acridine analogues:

To a solution of the acridine-azide (14-18, 1 equiv) and the propargyl-Geldanamycin (6, 1 equiv), in a mixture of (1:1 butanol : water) (20 vols) was added anhydrous CuSO$_4$ (5 mol%) followed by sodium ascorbate (0.2 equiv). The reaction mixture was stirred at room temperature for 16 hours after which time the azide had been consumed according to TLC in either (90:6:4 CH$_2$Cl$_2$:CH$_3$OH:c.NH$_3$(aq) or 85:10:5 CH$_2$Cl$_2$:CH$_3$OH:c.NH$_3$(aq)) and a fine brown solid had formed. The reaction mixture was concentrated in vacuo diluted with water (50 vols), then stirred for 30 minutes. The mixture was filtered and the collected solid washed with 3 × CHCl$_3$ (30 vols) to remove any residual starting materials. Mass spectrometry data were collected in MeOH.

<table>
<thead>
<tr>
<th>Triazole product</th>
<th>linker length, n</th>
<th>Yield (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>SR372</td>
<td>3</td>
<td>0$^a$</td>
</tr>
<tr>
<td>SR361</td>
<td>5</td>
<td>45</td>
</tr>
<tr>
<td>SR362</td>
<td>7</td>
<td>62</td>
</tr>
<tr>
<td>SR374</td>
<td>9</td>
<td>31</td>
</tr>
<tr>
<td>SR375</td>
<td>10</td>
<td>16</td>
</tr>
</tbody>
</table>

$^a$ reaction failed; $^b$ yields are based on isolated solids that have not been purified.
SR361: HRMS (ESI) (m/z): [M-H]^+ calcd for C_{63}H_{83}N_{12}O_{10}, 1167.6350; found 1167.6231.

SR362: HRMS (ESI) (m/z): [M]^+ calcd for C_{62}H_{88}N_{12}O_{10}, 1196.6736; found 1196.6718.

SR374: HRMS (ESI) (m/z): [M+H]^+ calcd for C_{67}H_{93}N_{12}O_{10}, 1225.7132; found 1225.7126.

SR375: HRMS (ESI) (m/z): [M]^+ calcd for C_{68}H_{94}N_{12}O_{10}, 1238.7204; found 1238.7124.

References:

(2) In PCT Int. Appl., 9501342, 12 Jan 1995.
Isolated as a solution in diethyl ether.