ELECTRONIC SUPPLEMENTARY INFORMATION

Viral Peptide Conjugates for Metal-Warhead Delivery to Chromatin

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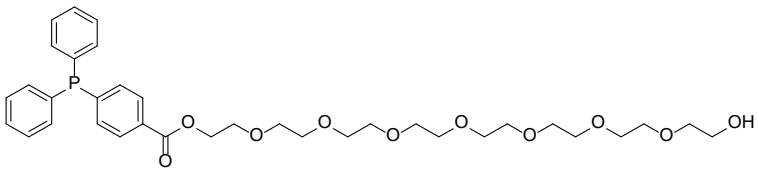
CONTENTS

SYNTHESIS & CHARACTERIZATION OF AU(I)-PEPTIDE CONJUGATES

Compound 1



4-(Diphenylphosphino)benzoic acid (1.50 g, 4.90 mmol, 1 equiv.) and *N*-ethyl-*N'*-(3-dimethlaminopropyl)carbodiimide hydrochloride (1.22 g, 6.37 mmol, 1.3 equiv.) were dissolved in dry CH_2Cl_2 (10 mL) and stirred under N_2 at room temperature for 2 h. The solution was added dropwise to a solution of octaethylene glycol (2.72 g, 7.35 mmol, 1.5 equiv.) and 4-(dimethylamino)pyridine (0.30 g, 2.44 mmol, 0.5 equiv.) in dry CH_2Cl_2 (5 mL) and the reaction stirred under N_2 at room temperature for 20 h. The reaction mixture was washed with brine (100 mL), dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure. Purification was achieved via flash column chromatography using an eluent system of CH_2Cl_2/CH_3OH. The product was washed with hexane (3 x 15 mL) and isolated as a colorless oil (1.55 g, 2.35 mmol, 48%).

Elemental Analysis (%): calcd for $C_{35}H_{47}O_{10}P.C_6H_{14}$ C 66.11 H 8.25, found C 66.31 H 8.02.

^{1}H NMR ($CDCl_3$, 400 MHz): 7.96-7.98 (2H, m, 2xO-(C=O)-(*Ar*)C-C*H*-CH-C-P), 7.30-7.36 (12H, m, 2xO-(C=O)-(*Ar*)C-CH-C*H*-C-P, 4xP-(*Ar*)C-C*H*-CH-CH, 4xP-(*Ar*)C-CH-C*H*-CH, 2xP-(*Ar*)C-CH-CH-C*H*), 4.44-4.46 (2H, m, *Ar*-(C=O)-O-C*H*$_2$-CH$_2$-O), 3.79-3.82 (2H, m, *Ar*-(C=O)-O-CH$_2$-C*H*$_2$-O), 3.58-3.72 (28H, m, *Ar*-(C=O)-O-(CH$_2$)$_2$-O-(C*H*$_2$)$_2$, *Ar*-(C=O)-O-((CH$_2$)$_2$-O)$_2$-O-(C*H*$_2$)$_2$, *Ar*-(C=O)-O-((CH$_2$)$_2$-O)$_3$-(C*H*$_2$)$_2$, *Ar*-(C=O)-O-((CH$_2$)$_2$-O)$_4$-(C*H*$_2$)$_2$, *Ar*-(C=O)-O-((CH$_2$)$_2$-O)$_5$-(C*H*$_2$)$_2$, *Ar*-(C=O)-O-((CH$_2$)$_2$-O)$_6$-(C*H*$_2$)$_2$, *Ar*-(C=O)-O-((CH$_2$)$_2$-O)$_7$-(C*H*$_2$)$_2$-OH).

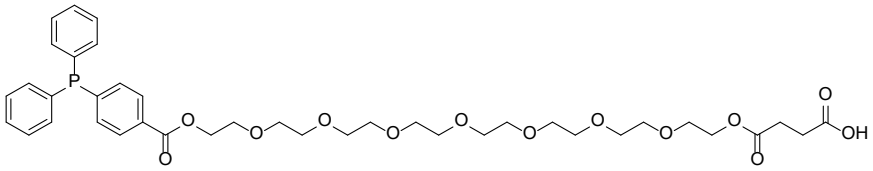
^{31}P {^{1}H} NMR ($CDCl_3$, 162 MHz): -5.08 (1P).

^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz): 165.4 (1C, O-(*C*=O)-(*Ar*)C-CH-CH-C-P), 143.2 (1C, d, O-(C=O)-(*Ar*)C-CH-CH-*C*-P, $^1J_{C,P}$ = 14 Hz), 135.2 (2C, d, 2xP-(*Ar*)*C*-CH-CH-CH, $^1J_{C,P}$ = 11 Hz), 133.0 (4C, d, 4xP-(*Ar*)C-*C*H-CH-CH, $^2J_{C,P}$ = 20 Hz), 132.2 (2C, d, 2xO-(C=O)-(*Ar*)C-CH-*C*H-C-P, $^2J_{C,P}$ = 19 Hz), 129.1 (1C, O-(C=O)-*(Ar)C*-CH-CH-C-P), 128.5 (2C, d, 2xO-(C=O)-(Ar)C-*C*H-CH-C-P, $^3J_{C,P}$ = 6 Hz), 128.2 (2C, 2xP-(*Ar*)C-CH-CH-*C*H), 127.4 (4C, d, 4xP-(*Ar*)C-CH-*C*H-CH, $^3J_{C,P}$ = 7 Hz), 71.6 (1C, O-*C*H$_2$-

CH_2-OH), 69.41-69.77 (12C, *Ar*-(C=O)-O-$(CH_2)_2$-O-($\underline{C}H_2)_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_2$-O-($\underline{C}H_2)_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_3$-($\underline{C}H_2)_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_4$-($\underline{C}H_2)_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_5$-($\underline{C}H_2)_2$, *Ar*-(C=O)-O-$((CH_2)_6$-O$)_2$-($\underline{C}H_2)_2$), 68.3 (1C, (*Ar*)-(C=O)-O-CH_2-$\underline{C}H_2$-O), 63.3 (1C, (*Ar*)-(C=O)-O-$\underline{C}H_2$-CH_2-O), 60.8 (1C, O-CH_2-$\underline{C}H_2$-OH).

HRMS (ESI(+)-QTOF): *m/z* found 681.2808 $[M+Na]^+$ $C_{35}H_{47}O_{10}PNa^+$ calculated 681.2805.

Compound 2



Compound 1 (1.200 g, 1.823 mmol, 1 equiv.) and succinic anhydride (0.274 g, 2.735 mmol, 1.5 equiv.) were dissolved in CH_2Cl_2 (5 mL). Triethylamine (0.553 g, 5.46 mmol, 0.76 mL, 3 equiv.) was added and the reaction stirred for 1 hour at r.t. under N_2. Purification was achieved via flash column chromatography using an eluent system of CH_2Cl_2/CH_3OH and the product was washed with pentane (3 x 15 mL) and isolated as a colorless oil (0.661 g, 0.871 mmol, 48 %).

Elemental Analysis (%): calcd for $C_{39}H_{51}O_{13}P.^{3/4}C_5H_{12}$ C 63.16 H 7.44 found C 62.90 H 7.73.

^{1}H NMR ($CDCl_3$, 400 MHz): 7.94-7.96 (2H, m, 2xO-(C=O)-(*Ar*)C-C$\underline{H}$-CH-C-P), 7.27-7.40 (12H, m, 2xO-(C=O)-(*Ar*)C-CH-C$\underline{H}$-C-P, 4xP-(*Ar*)C-C$\underline{H}$-CH-CH, 4xP-(*Ar*)C-CH-C$\underline{H}$-CH, 2xP-(*Ar*)C-CH-CH-C$\underline{H}$), 4.42-4.44 (2H, m, *Ar*-(C=O)-O-C$\underline{H_2}$-CH_2-O), 4.18-4.44 (2H, m, C$\underline{H_2}$-O-(C=O)-$(CH_2)_2$-(C=O)-OH), 3.79-3.81 (2H, m, *Ar*-(C=O)-O-CH_2-C$\underline{H_2}$-O), 3.59-3.67 (26H, m, *Ar*-(C=O)-O-$(CH_2)_2$-O-(C$\underline{H_2}$)$_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_2$-O-(C$\underline{H_2}$)$_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_3$-(C$\underline{H_2}$)$_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_4$-(C$\underline{H_2}$)$_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_5$-(C$\underline{H_2}$)$_2$, *Ar*-(C=O)-O-$((CH_2)_6$-O$)_2$-(C$\underline{H_2}$)$_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_7$-C$\underline{H_2}$), 2.60 (4H, s, O-(C=O)-(C$\underline{H_2}$)$_2$-(C=O)-O);

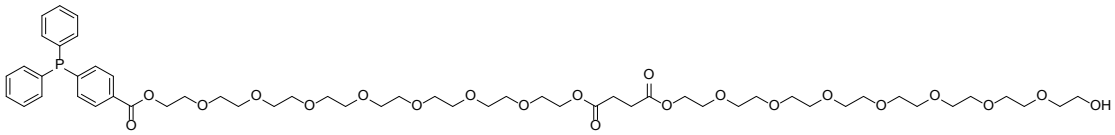
^{31}P {^{1}H} NMR ($CDCl_3$, 162 MHz): -5.08 (1P).

^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz): 173.9 (1C, O-(C=O)-$(CH_2)_2$-($\underline{C}$=O)-OH), 172.1 (1C, O-($\underline{C}$=O)-$(CH_2)_2$-(C=O)-OH), 166.0 (1C, O-($\underline{C}$=O)-(*Ar*)C-CH-CH-C-P), 143.9 (1C, d, O-(C=O)-(*Ar*)C-CH-CH-$\underline{C}$-P, $^1J_{C,P}$ = 14 Hz), 135.8 (2C, d, 2xP-(*Ar*)$\underline{C}$-CH-CH-CH, $^1J_{C,P}$ = 11 Hz), 133.6 (4C, d, 4xP-(*Ar*)C-$\underline{C}$H-CH-CH, $^2J_{C,P}$ = 20 Hz), 132.8 (2C, d,

2xO-(C=O)-(*Ar*)C-CH-<u>C</u>H-C-P, $^{2}J_{C,P}$ = 19 Hz), 129.7 (1C, O-(C=O)-*(Ar)*<u>C</u>-CH-CH-C-P), 129.1 (2C, d, 2xO-(C=O)-(Ar)C-<u>C</u>H-CH-C-P, $^{3}J_{C,P}$ = 6 Hz), 128.9 (2C, 2xP-(*Ar*)C-CH-CH-<u>C</u>H), 128.4 (4C, d, 4xP-(*Ar*)C-CH-<u>C</u>H-CH, $^{3}J_{C,P}$ = 7 Hz), 70.15-70.36 (12C, *Ar*-(C=O)-O-$(CH_2)_2$-O-(<u>C</u>$H_2)_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_2$-O-(<u>C</u>$H_2)_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_3$-(<u>C</u>$H_2)_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_4$-(<u>C</u>$H_2)_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_5$-(<u>C</u>$H_2)_2$, *Ar*-(C=O)-O-$((CH_2)_6$-O$)_2$-(<u>C</u>$H_2)_2$), 68.9 (1C, *Ar*-(C=O)-O-CH_2-<u>C</u>H_2-O), 68.7 (1C, <u>C</u>H_2-CH_2-O-(C=O)-$(CH_2)_2$-(C=O)-OH), 64.0 (1C, *Ar*-(C=O)-O-<u>C</u>H_2-CH_2-O), 63.4 (1C, <u>C</u>H_2-O-(C=O)-$(CH_2)_2$-(C=O)-OH), 29.1 (2C, O-(C=O)-(<u>C</u>$H_2)_2$-(C=O)-O);.

HRMS (ESI(+)-QTOF): *m/z* found 781.2966 $[M+Na]^+$ $C_{39}H_{51}O_{13}PNa^+$ calculated 781.2965.

<u>Compound 3</u>



Compound 2 (0.660 g, 0.870 mmol, 1 equiv.) and *N*-ethyl-*N'*-(3-dimethlaminopropyl)carbodiimide hydrochloride (0.217 g, 1.131 mmol, 1.3 equiv.) were dissolved in dry CH_2Cl_2 (10 mL) and stirred under N_2 at room temperature for 2 h. The solution was added dropwise to a solution of octaethylene glycol (0.450 g, 1.218 mmol, 1.4 equiv.) and 4-(dimethylamino)pyridine (0.053 g, 0.435 mmol, 0.5 equiv.) in dry CH_2Cl_2 (5 mL) and the reaction stirred under N_2 at r.t. for 17 h. The reaction mixture was washed with brine (50 mL), dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure. Purification was achieved via flash column chromatography using an eluent system of CH_2Cl_2/CH_3OH and the product was isolated as a colorless oil (0.695 g, 0.625 mmol, 72 %).

Elemental Analysis (%): calcd for $C_{55}H_{83}O_{21}P$ C 59.45 H 7.53; found C 59.71 H 7.71.

^{1}H NMR ($CDCl_3$, 400 MHz): 7.95-7.97 (2H, m, 2xO-(C=O)-(*Ar*)C-C<u>H</u>-CH-C-P), 7.29-7.36 (12H, m, 2xO-(C=O)-(*Ar*)C-CH-C<u>H</u>-C-P, 4xP-(*Ar*)C-C<u>H</u>-CH-CH, 4xP-(*Ar*)C-CH-C<u>H</u>-CH, 2xP-(*Ar*)C-CH-CH-C<u>H</u>), 4.43-4.46 (2H, m, *Ar*-(C=O)-O-C<u>H_2</u>-CH_2-O), 4.21-4.24 (4H, m, C<u>H_2</u>-O-(C=O)-$(CH_2)_2$-(C=O)-O-C<u>H_2</u>), 3.79-3.81 (2H, m, *Ar*-(C=O)-O-CH_2-C<u>H_2</u>-O), 3.59-3.69 (56H, m, *Ar*-(C=O)-O-$(CH_2)_2$-O-(C<u>$H_2)_2$</u>, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_2$-(C<u>$H_2)_2$</u>, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_3$-(C<u>$H_2)_2$</u>, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_4$-(C<u>$H_2)_2$</u>, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_5$-(C<u>$H_2)_2$</u>, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_6$-(C<u>$H_2)_2$</u>, *Ar*-(C=O)-O-$((CH_2)_2$-O$)_7$-C<u>H_2</u>, HO-(C<u>$H_2)_2$</u>, HO-$(CH_2)_2$-O-(C<u>$H_2)_2$</u>, HO-$((CH_2)_2$-O$)_2$-

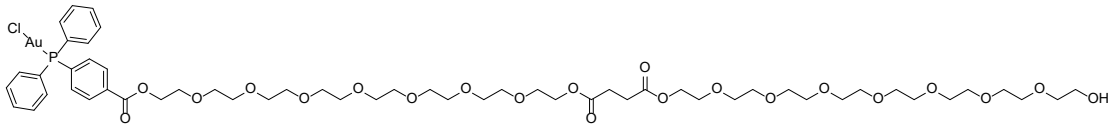
(C<u>*H*₂</u>)$_2$, HO-((CH$_2$)$_2$-O)$_3$-(C<u>*H*₂</u>)$_2$, HO-((CH$_2$)$_2$-O)$_4$-(C<u>*H*₂</u>)$_2$, HO-((CH$_2$)$_2$-O)$_5$-(C<u>*H*₂</u>)$_2$, HO-((CH$_2$)$_2$-O)$_6$-(C<u>*H*₂</u>)$_2$, HO-((CH$_2$)$_2$-O)$_7$-C<u>*H*₂</u>), 2.60 (4H, s, O-(C=O)-(C<u>*H*₂</u>)$_2$-(C=O)-O).

^{31}P {^{1}H} NMR (CDCl$_3$, 162 MHz): -5.07 (1P).

^{13}C {^{1}H} NMR (CDCl$_3$, 101 MHz): 172.3 (2C, O-(<u>*C*</u>=O)-(CH$_2$)$_2$-(<u>*C*</u>=O)-O), 166.4 (1C, *Ar*-(<u>*C*</u>=O)-O), 144.2 (1C, d, O-(C=O)-(*Ar*)C-CH-CH-<u>*C*</u>-P, $^1J_{C,P}$ = 14 Hz), 136.2 (2C, d, 2xP-(*Ar*)<u>*C*</u>-CH-CH-CH, $^1J_{C,P}$ = 11 Hz), 134.0 (4C, d, 4xP-(*Ar*)C-<u>*C*</u>H-CH-CH, $^2J_{C,P}$ = 20 Hz), 133.2 (2C, d, 2xO-(C=O)-(*Ar*)C-CH-<u>*C*</u>H-C-P, $^2J_{C,P}$ = 19 Hz), 130.1 (1C, O-(C=O)-*(Ar)*<u>*C*</u>-CH-CH-C-P), 129.5 (2C, d, 2xO-(C=O)-(Ar)C-<u>*C*</u>H-CH-C-P, $^3J_{C,P}$ = 6 Hz), 129.2 (2C, 2xP-(*Ar*)C-CH-CH-<u>*C*</u>H), 128.8 (4C, d, 4xP-(*Ar*)C-CH-<u>*C*</u>H-CH, $^3J_{C,P}$ = 7 Hz), 72.7 (1C, O-<u>*C*</u>H$_2$-CH$_2$-OH), 70.39-70.70 (24H, *Ar*-(C=O)-O-(CH$_2$)$_2$-O-(<u>*C*</u>H$_2$)$_2$, *Ar*-(C=O)-O-((CH$_2$)$_2$-O)$_2$-(<u>*C*</u>H$_2$)$_2$, *Ar*-(C=O)-O-((CH$_2$)$_2$-O)$_3$-(<u>*C*</u>H$_2$)$_2$, *Ar*-(C=O)-O-((CH$_2$)$_2$-O)$_4$-(<u>*C*</u>H$_2$)$_2$, *Ar*-(C=O)-O-((CH$_2$)$_2$-O)$_5$-(<u>*C*</u>H$_2$)$_2$, *Ar*-(C=O)-O-((CH$_2$)$_2$-O)$_6$-(<u>*C*</u>H$_2$)$_2$, HO-(CH$_2$)$_2$-O-(<u>*C*</u>H$_2$)$_2$, HO-((CH$_2$)$_2$-O)$_2$-(<u>*C*</u>H$_2$)$_2$, HO-((CH$_2$)$_2$-O)$_3$-(<u>*C*</u>H$_2$)$_2$, HO-((CH$_2$)$_2$-O)$_4$-(<u>*C*</u>H$_2$)$_2$, HO-((CH$_2$)$_2$-O)$_5$-(<u>*C*</u>H$_2$)$_2$, HO-((CH$_2$)$_2$-O)$_6$-(<u>*C*</u>H$_2$)$_2$), 69.3 (1C, *Ar*-(C=O)-O-CH$_2$-<u>*C*</u>H$_2$-O), 69.1 (2C, 2x<u>*C*</u>H$_2$-CH$_2$-O-(C=O)-(CH$_2$)$_2$-(C=O)-O), 64.3 (1C, *Ar*-(C=O)-O-<u>*C*</u>H$_2$-CH$_2$-O), 64.0 (2C, <u>*C*</u>H$_2$-O-(C=O)-(CH$_2$)$_2$-(C=O)-O-<u>*C*</u>H$_2$), 61.8 (1C, -O-CH$_2$-<u>*C*</u>H$_2$-OH), 29.1 (2C, O-(C=O)-(<u>*C*</u>H$_2$)$_2$-(C=O)-O).

HRMS (ESI(+)-QTOF): *m/z* found 1133.5081 $[M+Na]^+$ $C_{55}H_{83}O_{21}PNa^+$ calculated 1133.5062.

<u>Compound 4</u>



Compound 3 (0.700 g, 0.630 mmol, 1 equiv.) and freshly prepared Au(I)Cl(tht) (0.202 g, 0.630 mmol, 1 equiv.) were stirred in dry CH_2Cl_2 (10 mL) for 20 h under N_2, darkness and at r.t.. Purification was achieved via flash column chromatography using an eluent system of CH_2Cl_2/CH_3OH and the product was isolated as a clear oil (0.831 g, 0.619 mmol, 98 %).

Elemental Analysis (%): calcd for $C_{55}H_{83}AuClO_{21}P$ C 49.17 H 6.23; found C 49.17 H 6.14.

^{1}H NMR (CDCl$_3$, 400 MHz): 8.06-8.08 (2H, m, 2xO-(C=O)-(*Ar*)C-C<u>*H*</u>-CH-C-P), 7.44-7.56 (12H, m, 2xO-(C=O)-(*Ar*)C-CH-C<u>*H*</u>-C-P, 4xP-(*Ar*)C-C<u>*H*</u>-CH-CH, 4xP-

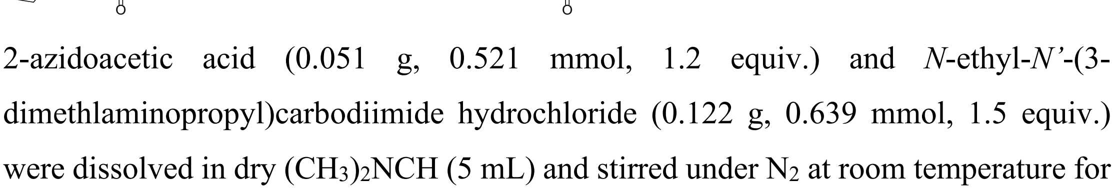
(*Ar*)C-CH-C*H*-CH, 2xP-(*Ar*)C-CH-CH-C*H*), 4.43-4.45 (2H, m, *Ar*-(C=O)-O-CH_2-CH_2-O), 4.17-4.20 (4H, m, CH_2-O-(C=O)-(CH_2)$_2$-(C=O)-O-CH_2), 3.77-3.79 (2H, m, *Ar*-(C=O)-O-CH_2-CH_2-O), 3.54-3.67 (56H, m, *Ar*-(C=O)-O-(CH_2)$_2$-O-(CH_2)$_2$, *Ar*-(C=O)-O-((CH_2)$_2$-O)$_2$-(CH_2)$_2$, *Ar*-(C=O)-O-((CH_2)$_2$-O)$_3$-(CH_2)$_2$, *Ar*-(C=O)-O-((CH_2)$_2$-O)$_4$-(CH_2)$_2$, *Ar*-(C=O)-O-((CH_2)$_2$-O)$_5$-(CH_2)$_2$, *Ar*-(C=O)-O-((CH_2)$_2$-O)$_6$-(CH_2)$_2$, *Ar*-(C=O)-O-((CH_2)$_2$-O)$_7$-CH_2, HO-(CH_2)$_2$, HO-(CH_2)$_2$-O-(CH_2)$_2$, HO-((CH_2)$_2$-O)$_2$-(CH_2)$_2$, HO-((CH_2)$_2$-O)$_3$-(CH_2)$_2$, HO-((CH_2)$_2$-O)$_4$-(CH_2)$_2$, HO-((CH_2)$_2$-O)$_5$-(CH_2)$_2$, HO-((CH_2)$_2$-O)$_6$-(CH_2)$_2$, HO-((CH_2)$_2$-O)$_7$-CH_2), 2.60 (4H, s, O-(C=O)-(CH_2)$_2$-(C=O)-O).

^{31}P {^{1}H} NMR ($CDCl_3$, 162 MHz): 32.97 (Au-P).

^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz): 172.2 (2C, O-(*C*=O)-(CH_2)$_2$-(*C*=O)-O), 165.3 (1C, *Ar*-(*C*=O)-O), 134.2 (1C, d, O-(C=O)-(*Ar*)C-CH-CH-*C*-P, $^1J_{C,P}$ = 60 Hz), 134.1 (4C, d, 4xP-(*Ar*)C-*C*H-CH-CH, $^2J_{C,P}$ = 14 Hz), 133.9 (2C, d, 2xO-(C=O)-(*Ar*)C-CH-*C*H-C-P, $^2J_{C,P}$ = 14 Hz), 133.2 (1C, d, O-(C=O)-(*Ar*)*C*-CH-CH-C-P, $^4J_{C,P}$ = 2 Hz), 132.3 (2C, d, 2xO-(C=O)-(Ar)C-*C*H-CH-C-P, $^3J_{C,P}$ = 3 Hz), 130.1 (2C, d, 2xP-(*Ar*)C-CH-CH-*C*H, $^4J_{C,P}$ = 12 Hz), 129.4 (4C, d, 4xP-(*Ar*)C-CH-*C*H-CH, $^3J_{C,P}$ = 12 Hz), 127.8 (2C, d, 2xP-(*Ar*)*C*-CH-CH-CH, $^1J_{C,P}$ = 63 Hz), 72.5 (1C, O-*C*H_2-CH_2-OH), 70.28-70.62 (24H, *Ar*-(C=O)-O-(CH_2)$_2$-O-(*C*H_2)$_2$, *Ar*-(C=O)-O-((CH_2)$_2$-O)$_2$-(*C*H_2)$_2$, *Ar*-(C=O)-O-((CH_2)$_2$-O)$_3$-(*C*H_2)$_2$, *Ar*-(C=O)-O-((CH_2)$_2$-O)$_4$-(*C*H_2)$_2$, *Ar*-(C=O)-O-((CH_2)$_2$-O)$_5$-(*C*H_2)$_2$, *Ar*-(C=O)-O-((CH_2)$_2$-O)$_6$-(*C*H_2)$_2$, HO-(CH_2)$_2$-O-(*C*H_2)$_2$, HO-((CH_2)$_2$-O)$_2$-(*C*H_2)$_2$, HO-((CH_2)$_2$-O)$_3$-(*C*H_2)$_2$, HO-((CH_2)$_2$-O)$_4$-(*C*H_2)$_2$, HO-((CH_2)$_2$-O)$_5$-(*C*H_2)$_2$, HO-((CH_2)$_2$-O)$_6$-(*C*H_2)$_2$), 69.0 (3C, *Ar*-(C=O)-O-CH_2-*C*H_2-O, 2x*C*H_2-CH_2-O-(C=O)-(CH_2)$_2$-(C=O)-O), 64.7(1C, *Ar*-(C=O)-O-*C*H_2-CH_2-O), 63.8 (2C, *C*H_2-O-(C=O)-(CH_2)$_2$-(C=O)-O-*C*H_2), 61.7 (1C, -O-CH_2-*C*H_2-OH), 29.0 (2C, O-(C=O)-(*C*H_2)$_2$-(C=O)-O).

HRMS (ESI(+)-QTOF): *m/z* found 694.2166 $[M+2Na]^{2+}$ $C_{55}H_{81}AuClO_{21}PNa_2^+$ calculated 694.2157.

Compound 5



2-azidoacetic acid (0.051 g, 0.521 mmol, 1.2 equiv.) and *N*-ethyl-*N'*-(3-dimethlaminopropyl)carbodiimide hydrochloride (0.122 g, 0.639 mmol, 1.5 equiv.) were dissolved in dry $(CH_3)_2NCH$ (5 mL) and stirred under N_2 at room temperature for

1 h. The solution was to a solution of **Compound 4** (0.572 g, 0.426 mmol, 1 equiv.) and 4-(dimethylamino)pyridine (0.026 g, 0.213 mmol, 0.5 equiv.) in dry $(CH_3)_2NCH$ (5 mL) and the reaction stirred under N_2 at room temperature for 48 h. The $(CH_3)_2NCH$ was removed with N_2 and the crude was dissolved in CH_2Cl_2 (30 mL), washed with brine (100 mL), dried over anhydrous sodium sulphate, filtered and concentrated under reduced pressure. Purification was achieved via flash column chromatography using an eluent system of CH_2Cl_2/CH_3OH. The product was washed with pentane (3 x 50 mL) and isolated as a yellow-brown oil (0.326 g, 0.229 mmol, 54 %).

(%): calcd for $C_{57}H_{84}AuClN_3O_{22}P.^{3/2}C_5H_{12}$ C 50.63 H 6.78 N 2.73; found C 50.59 H 6.80 N 2.49.

^{1}H NMR ($CDCl_3$, 400 MHz): 8.08-8.11 (2H, m, 2xO-(C=O)-(*Ar*)C-C*H*-CH-C-P),7.46-7.58 (12H, m, 2xO-(C=O)-(*Ar*)C-CH-C*H*-C-P, 4xP-(*Ar*)C-C*H*-CH-CH, 4xP-(*Ar*)C-CH-C*H*-CH, 2xP-(*Ar*)C-CH-CH-C*H*), 4.45-4.47 (2H, m, *Ar*-(C=O)-O-C*H*$_2$-CH_2-O), 4.31-4.33 (2H, m, C*H*$_2$-O-(C=O)-CH_2-N_3), 4.19-4.22 (4H, m, C*H*$_2$-O-(C=O)-$(CH_2)_2$-(C=O)-O-C*H*$_2$), 3.89 (2H, s, O-(C=O)-C*H*$_2$-N_3), 3.78-3.81 (2H, m, *Ar*-(C=O)-O-CH_2-C*H*$_2$-O), 3.59-3.74 (54H, m, *Ar*-(C=O)-O-$(CH_2)_2$-O-(C*H*$_2$)$_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O)$_2$-(C*H*$_2$)$_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O)$_3$-(C*H*$_2$)$_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O)$_4$-(C*H*$_2$)$_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O)$_5$-(C*H*$_2$)$_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O)$_6$-(C*H*$_2$)$_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O)$_7$-C*H*$_2$, N_3-CH_2-(C=O)-O-CH_2-C*H*$_2$, N_3-CH_2-(C=O)-O-$(CH_2)_2$-O-(C*H*$_2$)$_2$, N_3-CH_2-(C=O)-O-$((CH_2)_2$-O)$_2$-(C*H*$_2$)$_2$, N_3-CH_2-(C=O)-O-$((CH_2)_2$-O)$_3$-(C*H*$_2$)$_2$, N_3-CH_2-(C=O)-O-$((CH_2)_2$-O)$_4$-(C*H*$_2$)$_2$, N_3-CH_2-(C=O)-O-$((CH_2)_2$-O)$_5$-(C*H*$_2$)$_2$, N_3-CH_2-(C=O)-O-$((CH_2)_2$-O)$_6$-(C*H*$_2$)$_2$, N_3-CH_2-(C=O)-O-$((CH_2)_2$-O)$_7$-C*H*$_2$), 2.62 (4H, s, O-(C=O)-(C*H*$_2$)$_2$-(C=O)-O).

^{31}P {^{1}H} NMR ($CDCl_3$, 162 MHz): 33.00 (Au-P).

^{13}C {^{1}H} NMR ($CDCl_3$, 101 MHz): 172.3 (2C, O-(*C*=O)-$(CH_2)_2$-(*C*=O)-O), 168.4 (1C, O-(*C*=O)-CH_2-N_3), 165.4 (1C, *Ar*-(*C*=O)-O), 134.3 (1C, d, O-(C=O)-(*Ar*)C-CH-CH-*C*-P, $^1J_{C,P}$ = 60 Hz), 134.2 (4C, d, 4xP-(*Ar*)C-*C*H-CH-CH, $^2J_{C,P}$ = 14 Hz), 133.9 (2C, d, 2xO-(C=O)-(*Ar*)C-CH-*C*H-C-P, $^2J_{C,P}$ = 14 Hz 133.3 (1C, d, O-(C=O)-*(Ar)C*-CH-CH-C-P, $^4J_{C,P}$ = 2 Hz), 132.4 (2C, d, 2xO-(C=O)-(Ar)C-*C*H-CH-C-P, $^3J_{C,P}$ = 3 Hz), 130.2 (2C, d, 2xP-(*Ar*)C-CH-CH-*C*H, $^4J_{C,P}$ = 12 Hz), 129.5 (4C, d, 4xP-(*Ar*)C-CH-*C*H-CH, $^3J_{C,P}$ = 12 Hz), 127.9 (2C, d, 2xP-(*Ar*)*C*-CH-CH-CH, $^1J_{C,P}$ = 63 Hz), 70.58-70.69 (25C, *Ar*-(C=O)-O-$(CH_2)_2$-O-(*C*H_2)$_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O)$_2$-(*C*H_2)$_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O)$_3$-(*C*H_2)$_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O)$_4$-(*C*H_2)$_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O)$_5$-(*C*H_2)$_2$, *Ar*-(C=O)-O-$((CH_2)_2$-O)$_6$-(*C*H_2)$_2$, N_3-CH_2-(C=O)-O-CH_2-*C*H_2, N_3-CH_2-

(C=O)-O-$(CH_2)_2$-O-($\underline{C}H_2)_2$, N_3-CH_2-(C=O)-O-(($CH_2)_2$-O)$_2$-($\underline{C}H_2)_2$, N_3-CH_2-(C=O)-O-(($CH_2)_2$-O)$_3$-($\underline{C}H_2)_2$, N_3-CH_2-(C=O)-O-(($CH_2)_2$-O)$_4$-($\underline{C}H_2)_2$, N_3-CH_2-(C=O)-O-(($CH_2)_2$-O)$_5$-($\underline{C}H_2)_2$, N_3-CH_2-(C=O)-O-(($CH_2)_2$-O)$_6$-($\underline{C}H_2)_2$), 69.1 (3C, (*Ar*-(C=O)-O-CH_2-$\underline{C}H_2$-O,2x$\underline{C}H_2$-CH_2-O-(C=O)-($CH_2)_2$-(C=O)-O), 68.8 (1C, $\underline{C}H_2$-O-(C=O)-CH_2-N_3), 64.7 (1C, (*Ar*)-(C=O)-O-$\underline{C}H_2$-CH_2-O), 63.9 (2C, $\underline{C}H_2$-O-(C=O)-($CH_2)_2$-(C=O)-O-$\underline{C}H_2$), 50.28 (1C, N_3-$\underline{C}H_2$-(C=O)-O), 29.0 (2C, O-(C=O)-($\underline{C}H_2)_2$-(C=O)-O).

HRMS (ESI(+)-QTOF): *m/z* found 1448.4567 $[M+Na]^+$ $C_{57}H_{84}AuClN_3O_{22}PNa^+$ calculated 1448.4536.

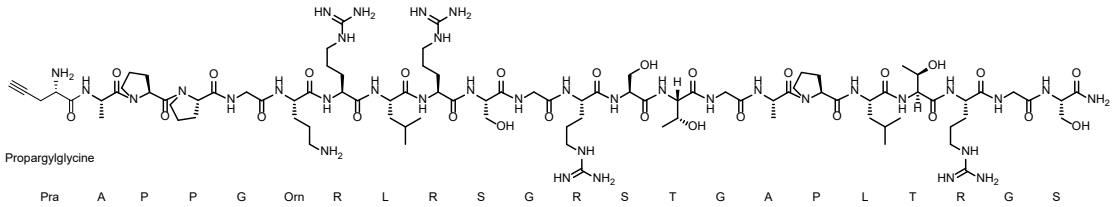
Peptides

The peptides were synthesised on an automated peptide synthesiser (Advanced ChemTech 348Ω parallel peptide synthesiser (AAPPTec)) using standard Fmoc solid phase chemistry on Rink Amide MBHA resin (25 μmol scale, 0.3 mmol/g loading). The amide coupling was performed twice for each for each amino acid (10 equiv.) using base NMM (10 equiv.), HATU (4 equiv.) and HOBt (4 equiv.) with an incubation of 30 minutes. The Fmoc groups were removed by incubating the resin twice with piperidine (6 equiv., 20 % (v/v)) in DMF. The resin was washed 4 times before and 5 times after Fmoc removal with DMF (3 mL). The peptides were capped using a capping mixture of acetic anhydride (5 % (v/v)) and lutidine (6 % (v/v)) in DMF.

The final peptides were deprotected and cleaved from the resin via incubation 90 % TFA, 2.5 % H_2O, 2.5 % thioanisole, 2.5 % phenol and 2.5 % EDT under agitation for 4 hours at room temperature. The resin was removed by vacuum filtration and the peptides were precipitated with cold diethyl ether (50 mL) at -20 °C. The precipitated peptides were collected via centrifugation, washed with cold diethyl ether (2 x 30 ml) and lyophilised.

Peptides were purified with a HPLC system (Prep LC 2535 HPLC, Waters) using a preparative C18 reverse-phase column (SunfireTM prep C18 OBD 10 μm, 100 Å, 19x250 mm, Waters) with a flow rate of 20 ml min-1 and a linear gradient of 10-50% v/v solvent B in 40 min (A: 99.9% v/v H2O and 0.1% v/v TFA; B: 99.9% v/v ACN and 0.1% v/v TFA). Fractions containing the desired peptide were lyophilised.

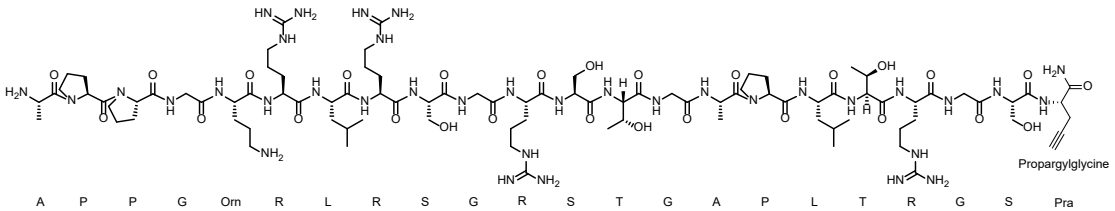
Peptide L1



Analytical RP-HPLC: 63.8%.

HRMS (ESI(+)-QTOF): *m/z* found 1101.6240 $[M+2H]^{2+}$ $C_{92}H_{162}N_{36}O_{27}^{2+}$ calculated 1101.6205.

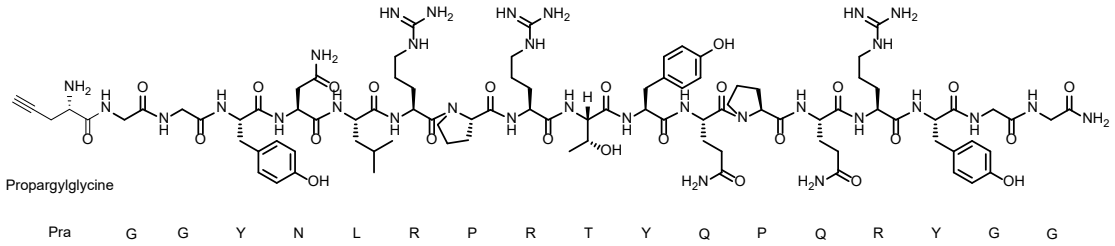
Peptide L2



Analytical RP-HPLC: 66.1%.

HRMS (ESI(+)-QTOF): *m/z* found 1101.6228 $[M+2H]^{2+}$ $C_{92}H_{162}N_{36}O_{27}^{2+}$ calculated 1101.6205.

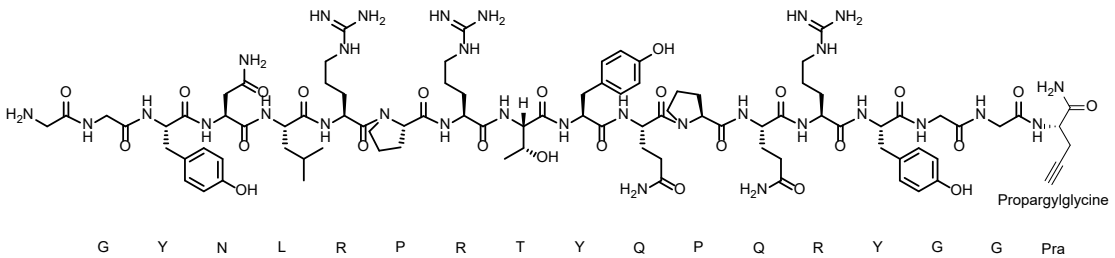
Peptide L3



Analytical RP-HPLC: 93.7%.

HRMS (ESI(+)-QTOF): *m/z* found 1039.0308 $[M+2H]^{2+}$ $C_{92}H_{139}N_{31}O_{25}^{2+}$ calculated 1039.0280.

Peptide L4



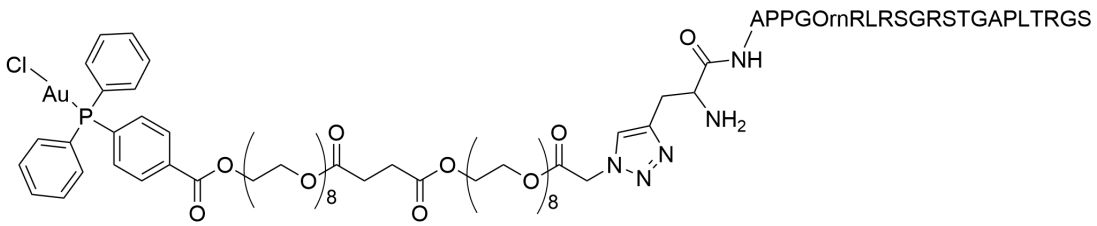
Analytical RP-HPLC: 81.4%.

HRMS (ESI(+)-QTOF): *m/z* found 1039.0299 $[M+2H]^{2+}$ $C_{92}H_{139}N_{31}O_{25}^{2+}$ calculated 1039.0280.

Gold-peptide conjugates

Compound 5 (1.1 equiv.) and the appropriate **peptide** (1 equiv.) were dissolved in *tert*-butyl alcohol (2 mL) and milliQ water (2 mL) in the presence of 1 mol % of copper(II) sulphate and 10 mol % of sodium ascorbate. The reaction was stirred vigorously at r.t. under N_2 for 24 h. The solvent was removed with a flow of N_2. Purification was achieved via preparative HPLC using acetonitrile/water (10 %-45 %) as eluent over 30 minutes. The product was lyophilised and isolated as a white solid.

Gold(I)-LANA conjugate: (Au-LANA)



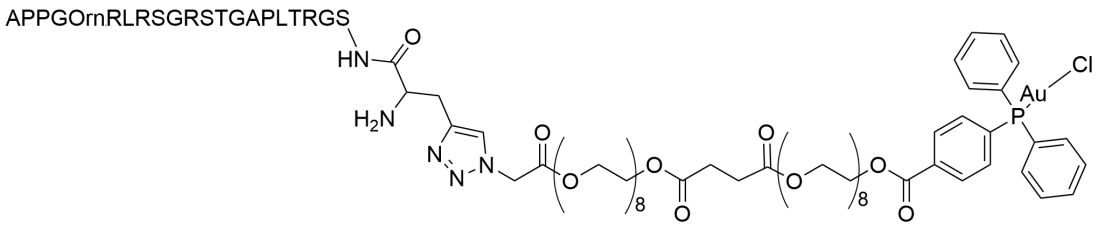
According to the general procedure, **Compound 5** (0.039 g, 0.0275, 1.1 equiv.), **peptide L1** (0.050 g, 0.0227 mmol, 1 equiv.). Yield 16.06 mg, 0.00464 mmol, 20 %.

Analytical RP-HPLC: 89.2 %.

^{31}P {^{1}H} NMR (100mM NaCl in D_2O, 162 MHz): 42.34 (1P).

HRMS (ESI(+)-QTOF): *m/z* found 898.9393 $[M-Cl+3H]^{4+}$ $C_{149}H_{247}AuN_{39}O_{49}P^{4+}$ calculated 898.9367.

Gold(I)-LANA conjugate: (LANA-Au)



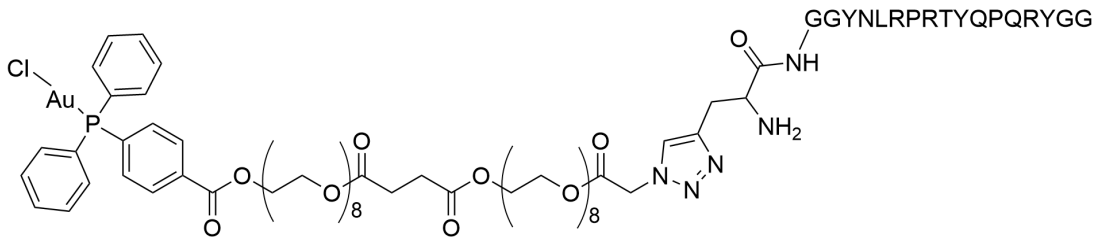
According to the general procedure, **Compound 5** (0.039 g, 0.0275, 1.1 equiv.), **peptide L2** (0.050 g, 0.0227 mmol, 1 equiv.). Yield 21.88 mg, 0.00632 mmol, 28 %.

Analytical RP-HPLC: 91.0%.

^{31}P {^{1}H} NMR (100mM NaCl in D_2O, 162 MHz): 42.67 (1P).

HRMS (ESI(+)-QTOF): *m/z* found 898.9382 $[M\text{-}Cl+3H]^{4+}$ $C_{149}H_{247}AuN_{39}O_{49}P^{4+}$ calculated 898.9367.

Gold(I)-GAG conjugate: (Au-GAG)



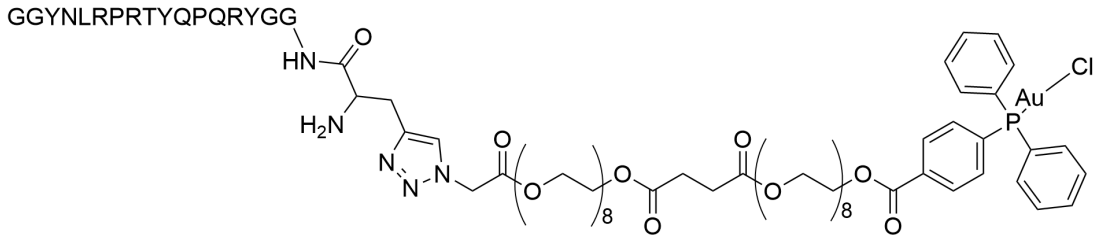
According to the general procedure, **Compound 5** (0.038 g, 0.0265, 1.1 equiv.), **peptide L3** (0.050 g, 0.0241 mmol, 1 equiv.). Yield 25.03 mg, 0.00783 mmol, 33 %.

Analytical RP-HPLC: 90.1 %.

^{31}P {^{1}H} NMR (100mM NaCl in D_2O, 162 MHz): 42.51 (1P).

HRMS (ESI(+)-QTOF): *m/z* found 867.6437 $[M\text{-}Cl+3H]^{4+}$ $C_{149}H_{224}AuN_{34}O_{47}P^{4+}$ calculated 867.6404.

Gold(I)-GAG conjugate: (GAG-Au)

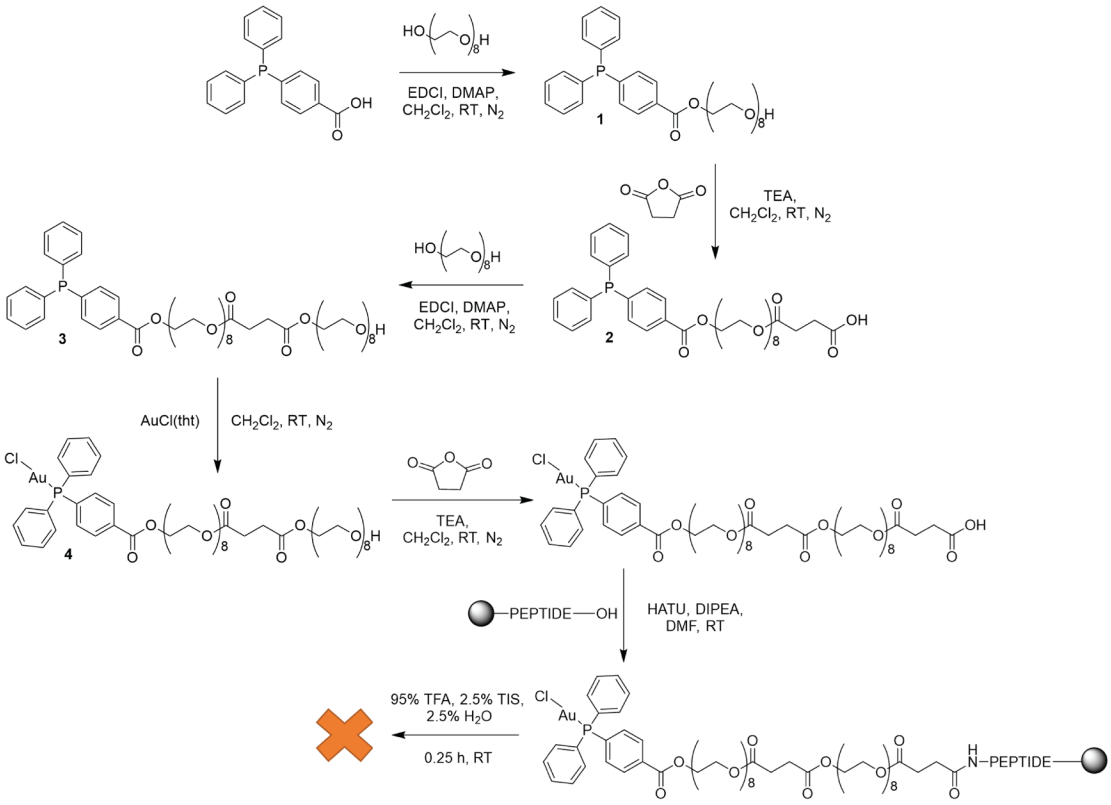


According to the general procedure, **Compound 5** (0.019 g, 0.0132, 1.1 equiv.), **Peptide L4** (0.025 g, 0.0120 mmol, 1 equiv.). Yield 24.46 mg, 0.00765 mmol, 64 %.

Analytical RP-HPLC: 85.6 %.

^{31}P {^{1}H} NMR (100mM NaCl in D_2O, 162 MHz): 42.61 (1P).

HRMS (ESI(+)-QTOF): *m/z* found 867.6442 $[M\text{-}Cl+3H]^{4+}$ $C_{149}H_{224}AuN_{34}O_{47}P^{4+}$ calculated 867.6404.



Scheme S1. Initial strategy used for the synthesis of the Au-peptide conjugates. As the peptide synthesis was performed using standard Fmoc solid state chemistry, the Au(I) complex could be considered as another amino acid and potentially introduced using typical amide coupling conditions employing 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b] pyridinium-3-oxide hexafluorophosphate (HATU) and *N,N*-diisopropylethylamine (DIPEA). However, as the peptide side groups are still present and the N-terminus of the peptide remains attached to the resin, a deprotection step is required. This process is problematic due to the harsh conditions required to detach the peptide from the resin. Typically, 90% trifluoroacetic acid (TFA), 2.5% water, 2.5% phenol, 2.5% ethanedithiol (EDT) and 2.5% thioanisol are used. However, the use of thiol-containing EDT and thioanisol was not advisable as they can react with the gold centre, therefore alternative conditions were used: 95% TFA, 2.5% triisopropylsilane (TIS), and 2.5% water. The resulting Au(I)-peptide conjugates were purified using RP-HPLC and the relevant fractions were lyophilised. However, although the desired products were observed via high resolution mass spectrometry, the peaks were of very low intensity and multiple unidentifiable peaks of greater intensity indicated degradation of the products.

Table S1. Data collection and refinement statistics for NCP treated with LANA agents.

	LANA	**Au-LANA**	**LANA-Au**
Data collection			
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
Cell dimensions			
a (Å)	109.71	108.11	109.52
b (Å)	109.88	109.61	109.45
c (Å)	184.88	183.77	184.79
Resolution (Å)	2.50─49.1 (2.50─2.64)	2.30─48.9 (2.30─2.43)	2.80─49.0 (2.80─2.95)
R_{merge} (%)	5.8 (283)	4.7 (159)	8.5 (316)
R_{pim} (%)	1.7 (84.4)	1.4 (64.2)	2.5 (102)
$I/\sigma I$	23.0 (1.1)	27.3 (1.1)	19.5 (0.8)
Completeness (%)	99.8 (98.9)	99.9 (99.4)	99.8 (99.3)
CC½ (%)	100 (66.7)	100 (65.1)	100 (60.2)
Redundancy	13.3 (12.7)	12.2 (7.7)	13.0 (11.2)
Refinement			
Resolution (Å)	2.50─49.1	2.30─48.9	2.80─49.0
No. reflections	76,005	95,237	54,231
R_{work} / R_{free} (%)	21.8 / 26.8	22.4 / 26.2	20.6 / 24.9
No. atoms	12,155	12,178	12,155
B-factors (Å^2)	108	94	121
R.m.s. deviations			
Bond lengths (Å)	0.007	0.007	0.007
Bond angles (°)	1.50	1.48	1.48
Validation			
R_{free}	0.268	0.262	0.249
Clash	8	6	8
Outliers (%)			
Ramachandran	0.7	0.5	0.8
Sidechain	6.8	6.3	6.2
RSRZ	2.5	4.3	1.7

Single crystal data sets; Values in parentheses are for the highest resolution shell. **LANA**: 15-hour incubation of NCP crystal with a 2 mM concentration of the 21-residue LANA peptide used for the Au(I)-LANA conjugates. **Au-LANA**: 73-hour incubation of NCP crystal with a 1 mM concentration of Au-LANA. **LANA-Au**: 72-hour incubation of NCP crystal with a 1 mM concentration of LANA-Au.

Table S2. Data collection and refinement statistics for NCP treated with GAG agents.

	GAG	Au-GAG	GAG-Au
Data collection			
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
Cell dimensions			
a (Å)	107.17	107.19	107.66
b (Å)	109.64	109.56	109.66
c (Å)	183.56	183.68	184.18
Resolution (Å)	2.17─48.8 (2.17─2.29)	2.60─48.8 (2.60─2.74)	2.49─48.9 (2.49─2.63)
R_{merge} (%)	6.4 (186)	8.6 (198)	6.4 (211)
R_{pim} (%)	2.0 (64.2)	2.6 (66.4)	1.9 (70.6)
$I/\sigma I$	20.3 (1.2)	19.6 (1.2)	25.2 (1.1)
Completeness (%)	98.2 (88.1)	93.6 (58.9)	99.2 (95.0)
CC½ (%)	100 (57.3)	99.9 (56.7)	100 (46.8)
Redundancy	12.2 (9.7)	12.5 (9.7)	12.8 (10.3)
Refinement			
Resolution (Å)	2.17─48.8	2.60─48.8	2.49─48.9
No. reflections	109,713	61,370	74,713
R_{work} / R_{free} (%)	23.6 / 26.9	21.3 / 26.2	22.1 / 25.2
No. atoms	12,197	12,197	12,197
B-factors (Å^2)	80	95	92
R.m.s. deviations			
Bond lengths (Å)	0.008	0.008	0.007
Bond angles (°)	1.50	1.61	1.48
Validation			
R_{free}	0.269	0.262	0.252
Clashscore	6	9	7
Outliers (%)			
Ramachandran	0.7	1.0	0.7
Side Chain	7.0	8.4	7.2
RSRZ	4.8	1.1	1.9

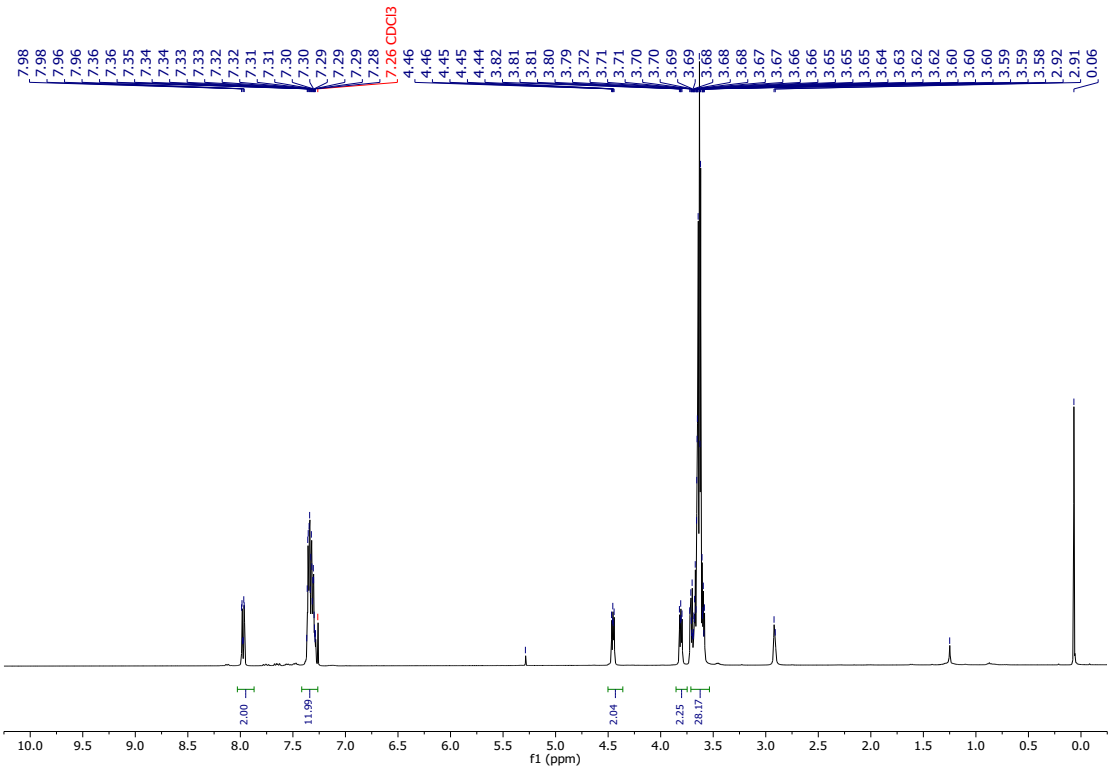
Single crystal data sets; Values in parentheses are for the highest resolution shell. **GAG**: 29-hour incubation of NCP crystal with a 2 mM concentration of Au-GAG (short incubation to maximize quality of bound viral peptide model). **Au-GAG**: 91-hour incubation of NCP crystal with a 1 mM concentration of Au-GAG. **GAG-Au**: 72-hour incubation of NCP crystal with a 1 mM concentration of GAG-Au.

Table S3. Gold(I) binding sites in NCP treated with the conjugates.

	Anomalous Difference Peak Height (σ)			
Conjugate	AU1	AU1'	H2B H46	Depot
Au-LANA	7.0	4.8	--	5.0
LANA-Au	--	--	--	4.2
Au-GAG	--	4.5	4.3	7.1
GAG-Au	4.0	--	--	9.0

Values correspond to anomalous difference electron density map peak magnitudes >3.5σ.

"Depot" refers to what is apparently residual, unreacted AuDPPBX (gold group), which is likely akin to depot binding.


7.98
7.98
7.96
7.96
7.36
7.36
7.35
7.34
7.34
7.33
7.33
7.32
7.32
7.31
7.31
7.30
7.30
7.29
7.29
7.29
7.28
7.26 CDCl3
4.46
4.46
4.45
4.45
4.44
3.82
3.81
3.81
3.80
3.79
3.72
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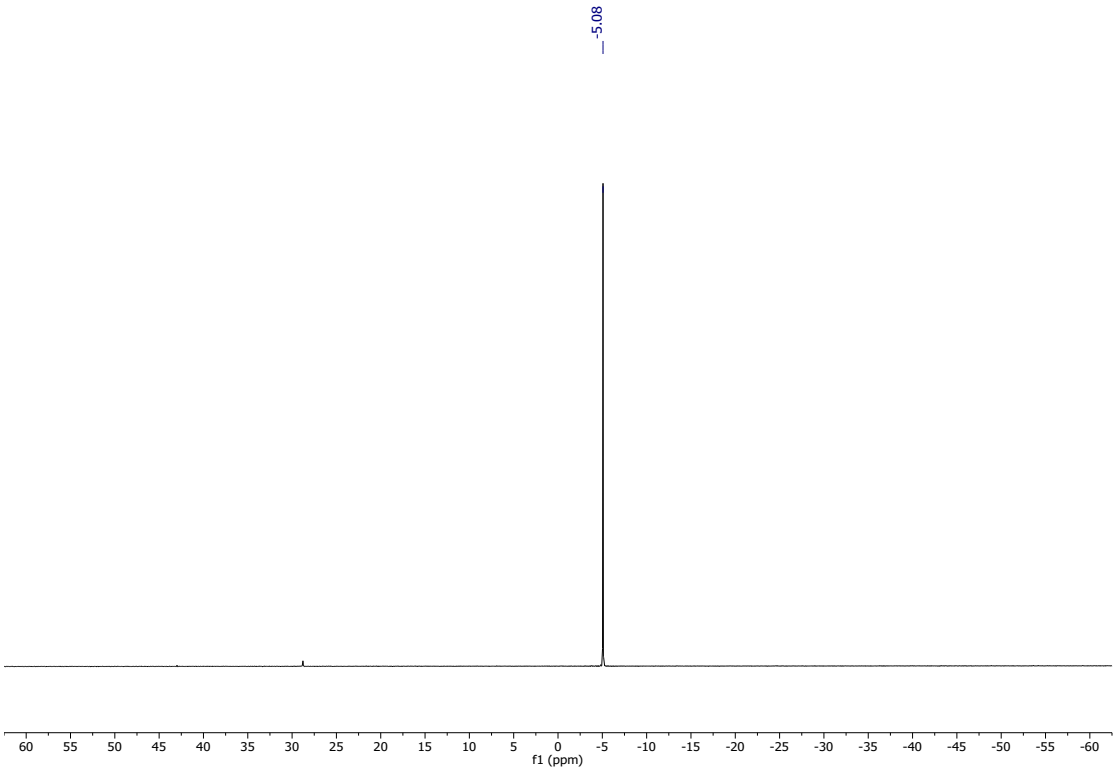
3.59
3.58
2.92
2.91
0.06
2.00
11.99
2.04
2.25
28.17
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


-5.08
60 55 50 45 40 35 30 25 20 15 10 5 0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60
f1 (ppm)

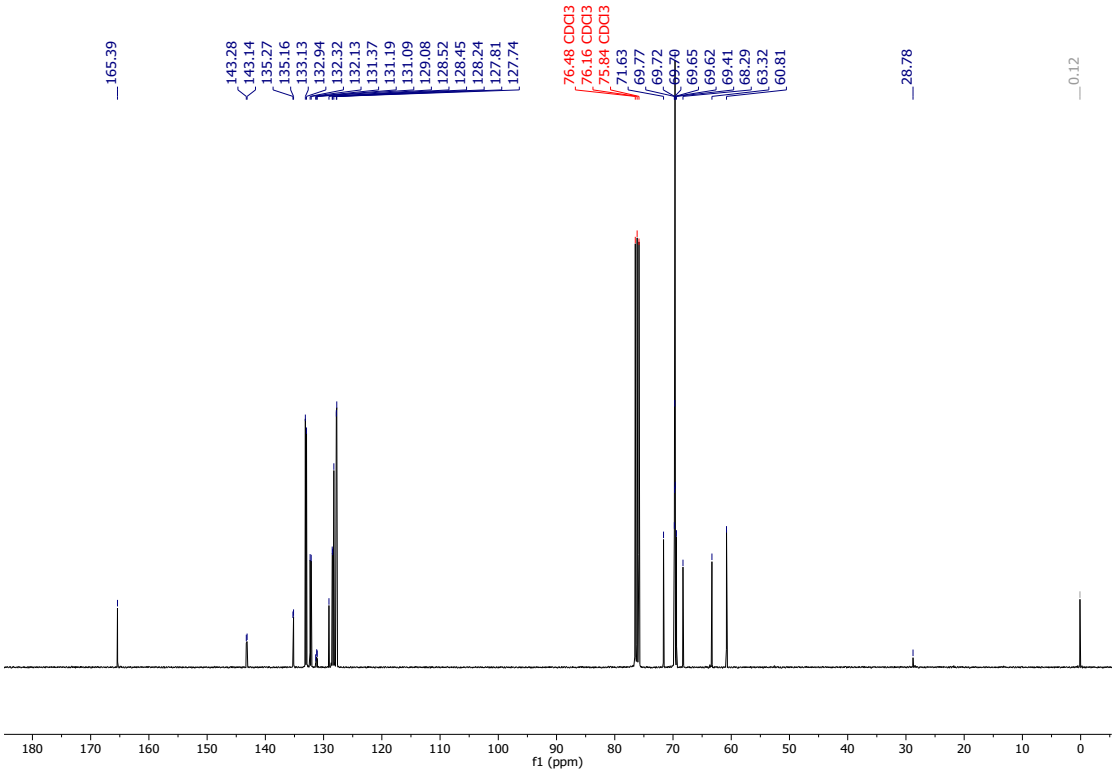
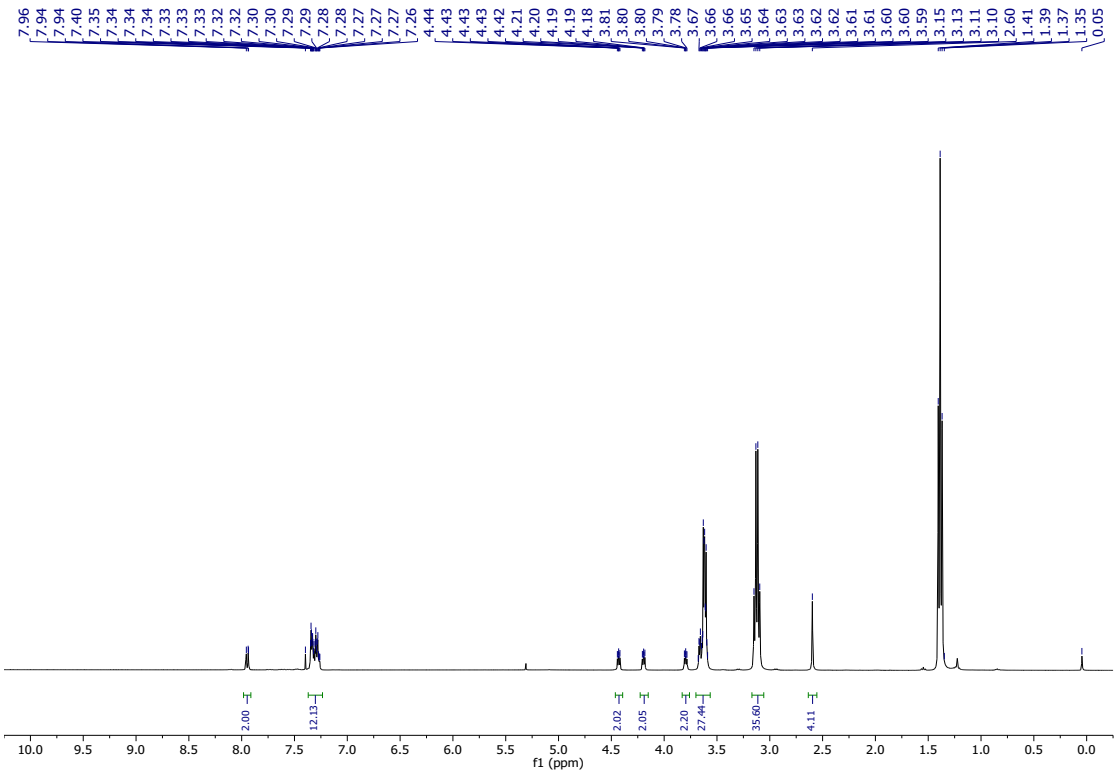
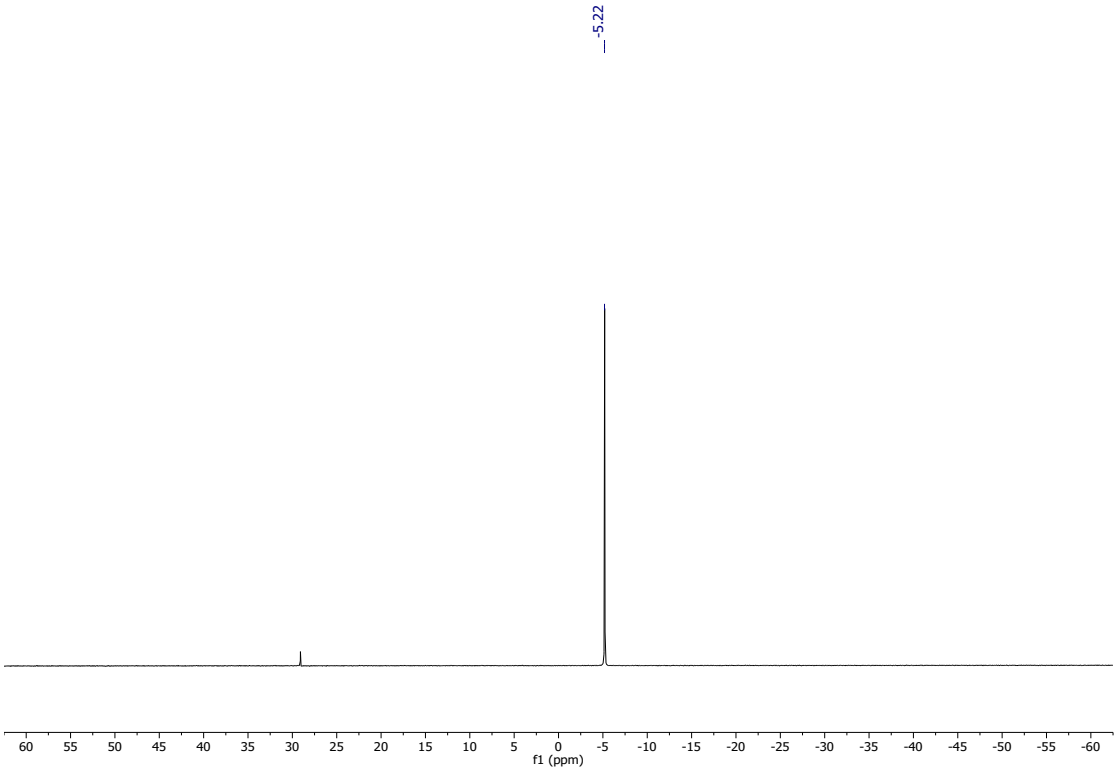


Figure S1. ^{1}H (top), ^{31}P (middle), ^{13}C (bottom) NMR spectra of **1** in $CDCl_3$ at RT.


7.96 7.94 7.94 7.40 7.35 7.34 7.34 7.33 7.33 7.33 7.32 7.30 7.29 7.29 7.28 7.28 7.27 7.27 7.27 7.26 4.44 4.43 4.43 4.42 4.21 4.20 4.19 4.19 4.18 3.81 3.80 3.80 3.79 3.78 3.67 3.66 3.66 3.65 3.64 3.63 3.63 3.62 3.62 3.61 3.61 3.60 3.60 3.59 3.15 3.13 3.11 3.10 2.60 1.41 1.39 1.37 1.35 0.05
2.00
12.13
2.02
2.05
2.20
27.44
35.60
4.11
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


-5.22
60 55 50 45 40 35 30 25 20 15 10 5 0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60
f1 (ppm)

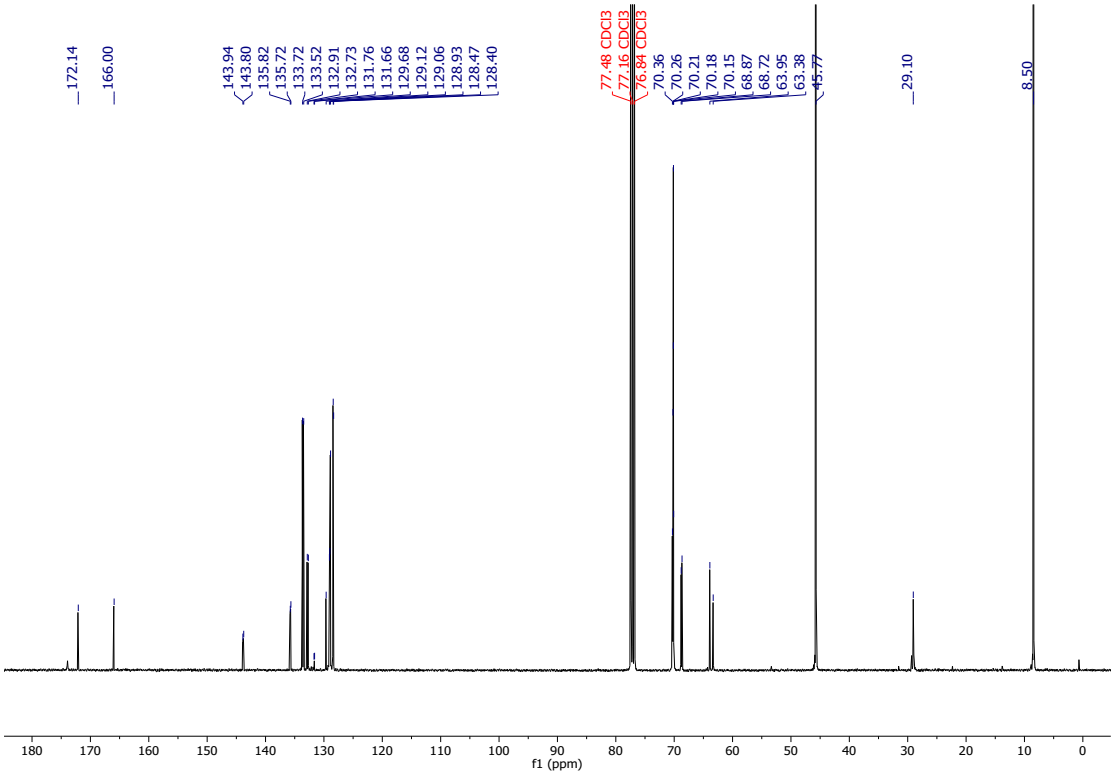
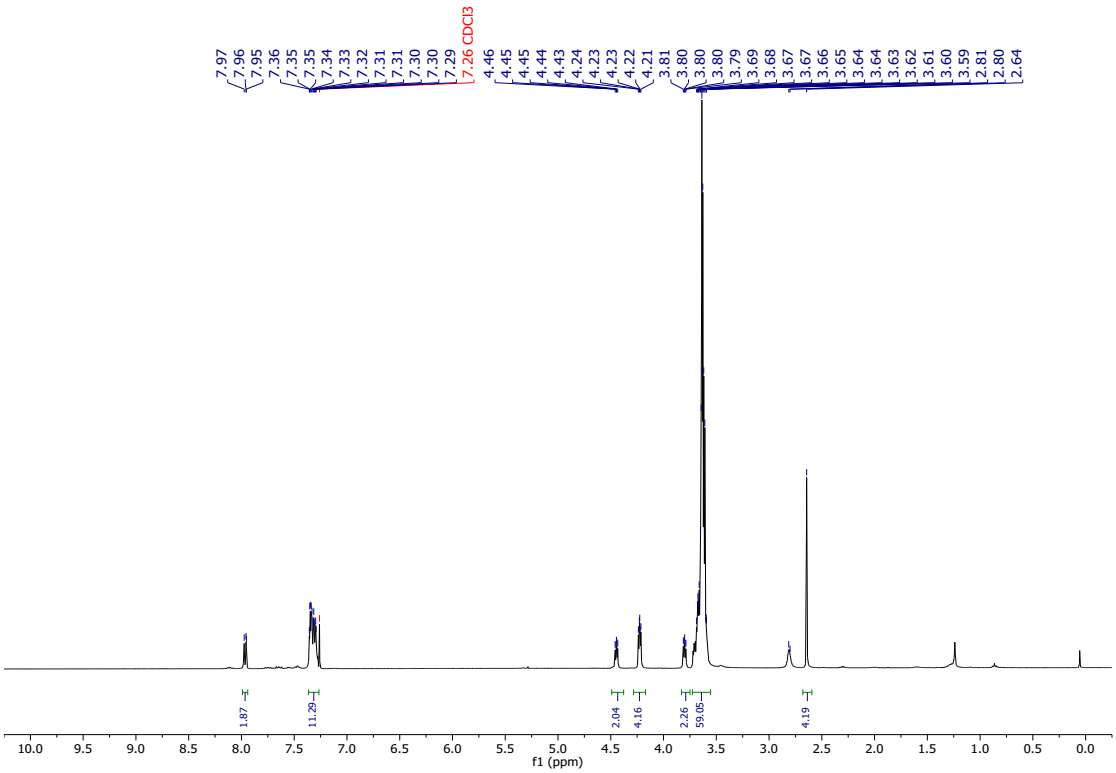
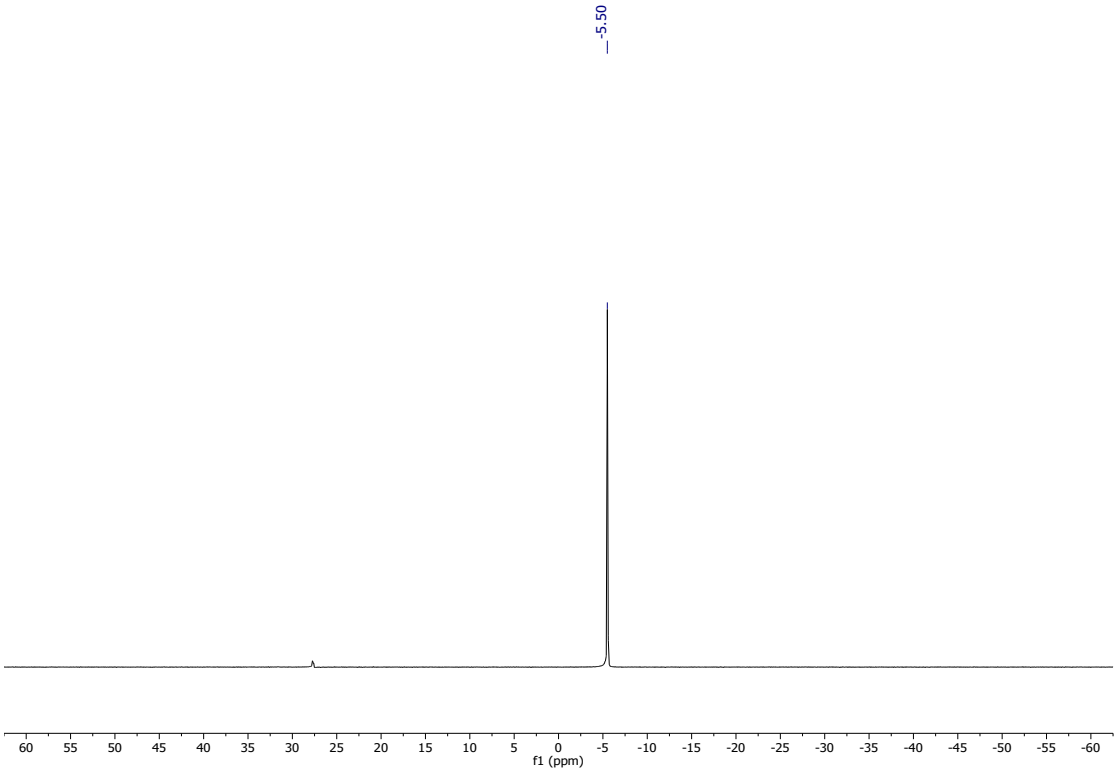


Figure S2. ^{1}H (top), ^{31}P (middle), ^{13}C (bottom) NMR spectra of **2** in $CDCl_3$ at RT.


7.97
7.96
7.95
7.36
7.35
7.35
7.34
7.33
7.32
7.31
7.31
7.30
7.30
7.29
7.26 CDCl3
4.46
4.45
4.45
4.44
4.43
4.24
4.23
4.23
4.22
4.21
3.81
3.80
3.80
3.80
3.79
3.69
3.68
3.67
3.67
3.66
3.65
3.64
3.64
3.63
3.62
3.61
3.60
3.59
2.81
2.80
2.64
1.87
11.29
2.04
4.16
2.26
59.05
4.19
f1 (ppm)


-5.50
f1 (ppm)

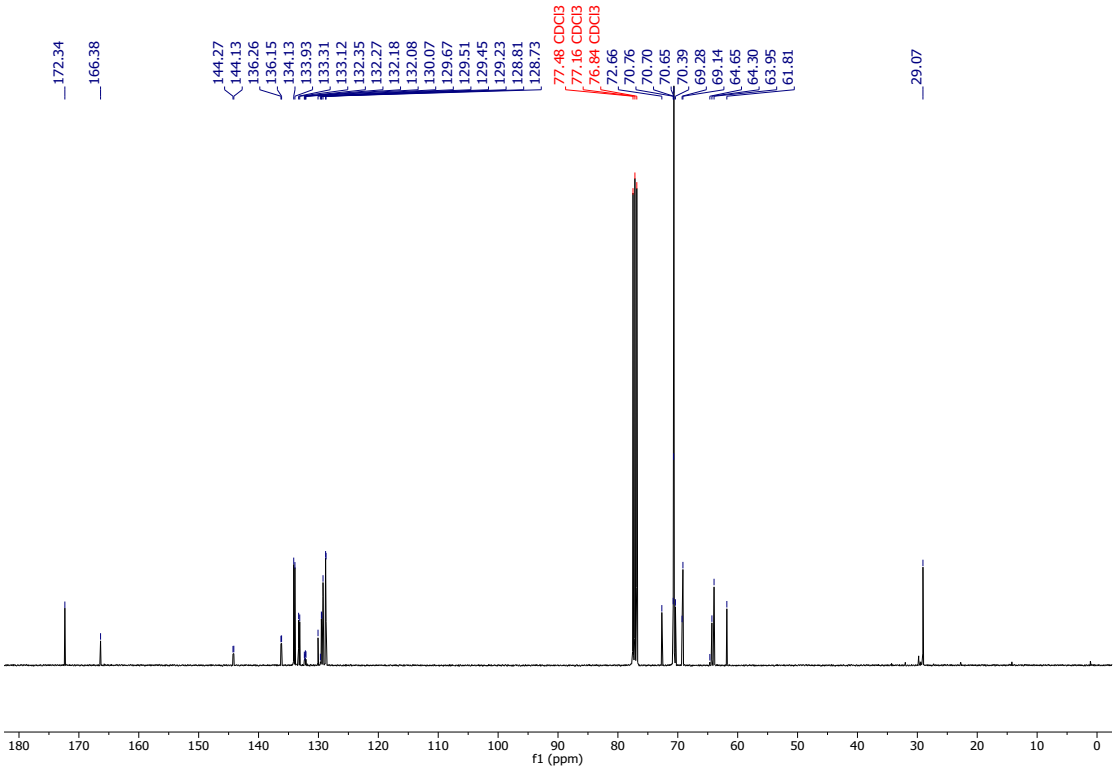
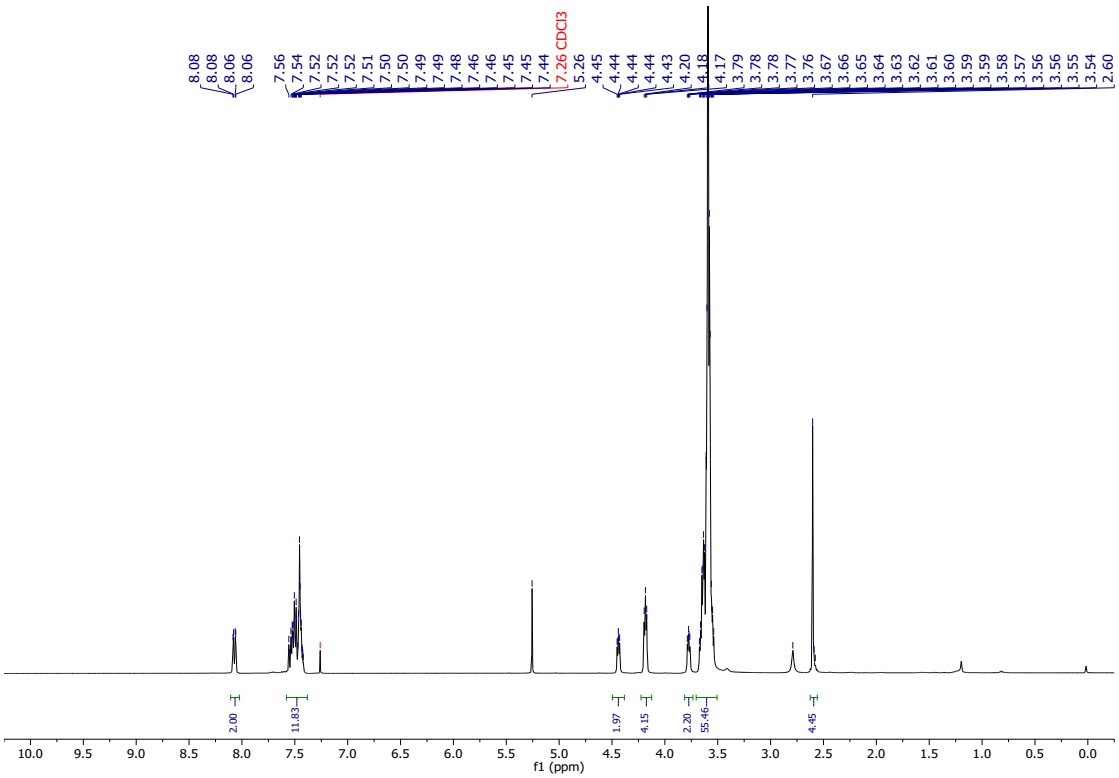
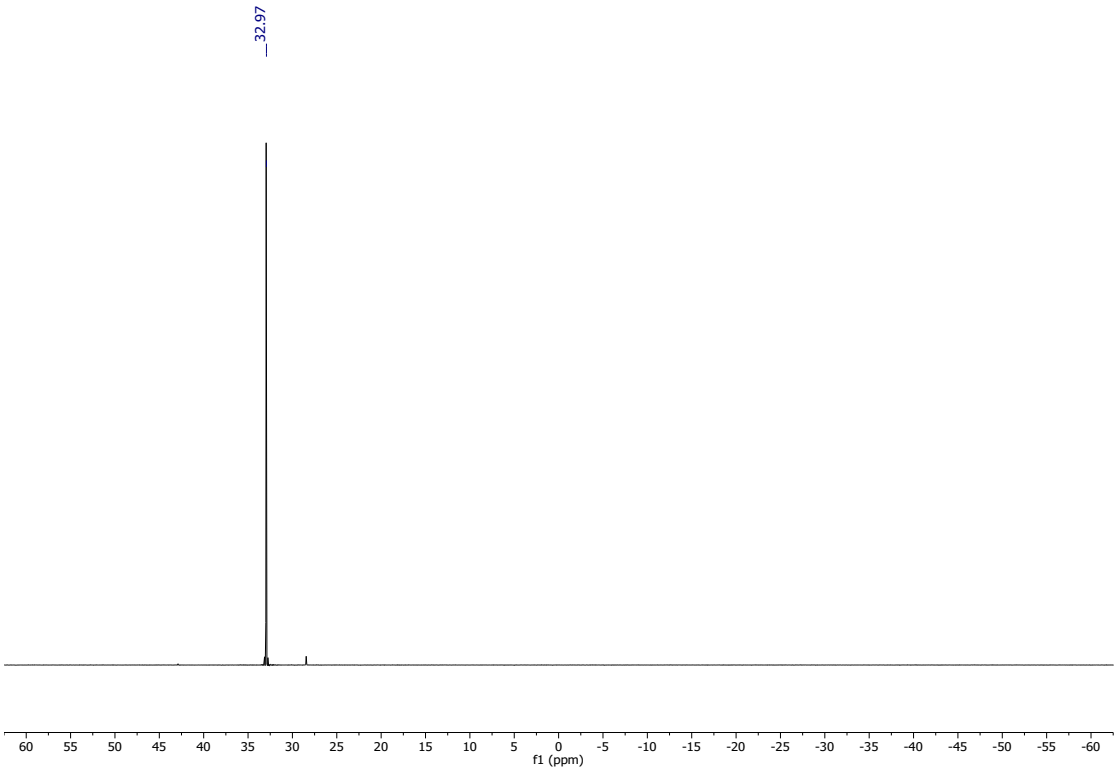


Figure S3. ^{1}H (top), ^{31}P (middle), ^{13}C (bottom) NMR spectra of **3** in $CDCl_3$ at RT.


8.08
8.08
8.06
8.06
7.56
7.54
7.52
7.52
7.52
7.51
7.50
7.50
7.49
7.49
7.48
7.46
7.46
7.45
7.45
7.44
7.26 CDCl3
5.26
4.45
4.44
4.44
4.44
4.43
4.20
4.18
4.17
3.79
3.78
3.78
3.77
3.76
3.67
3.66
3.65
3.64
3.63
3.62
3.61
3.60
3.59
3.59
3.58
3.57
3.56
3.56
3.55
3.54
2.60
2.00
11.83
1.97
4.15
2.20
55.46
4.45
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


32.97
60 55 50 45 40 35 30 25 20 15 10 5 0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60
f1 (ppm)

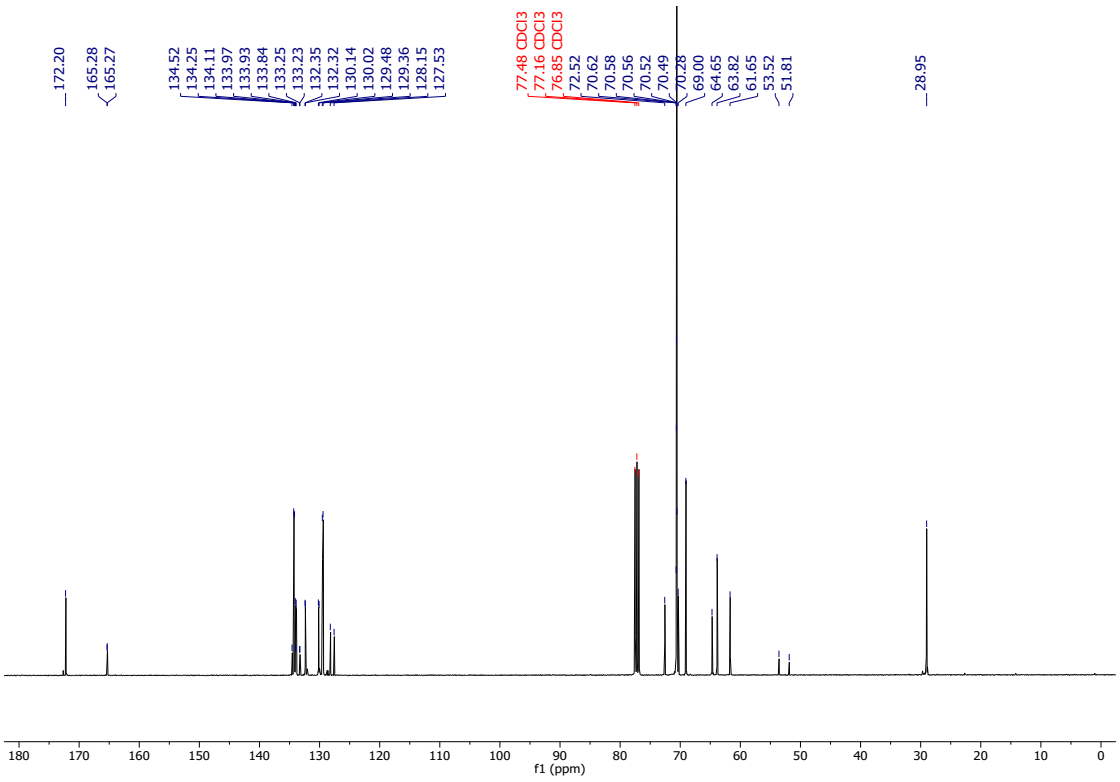
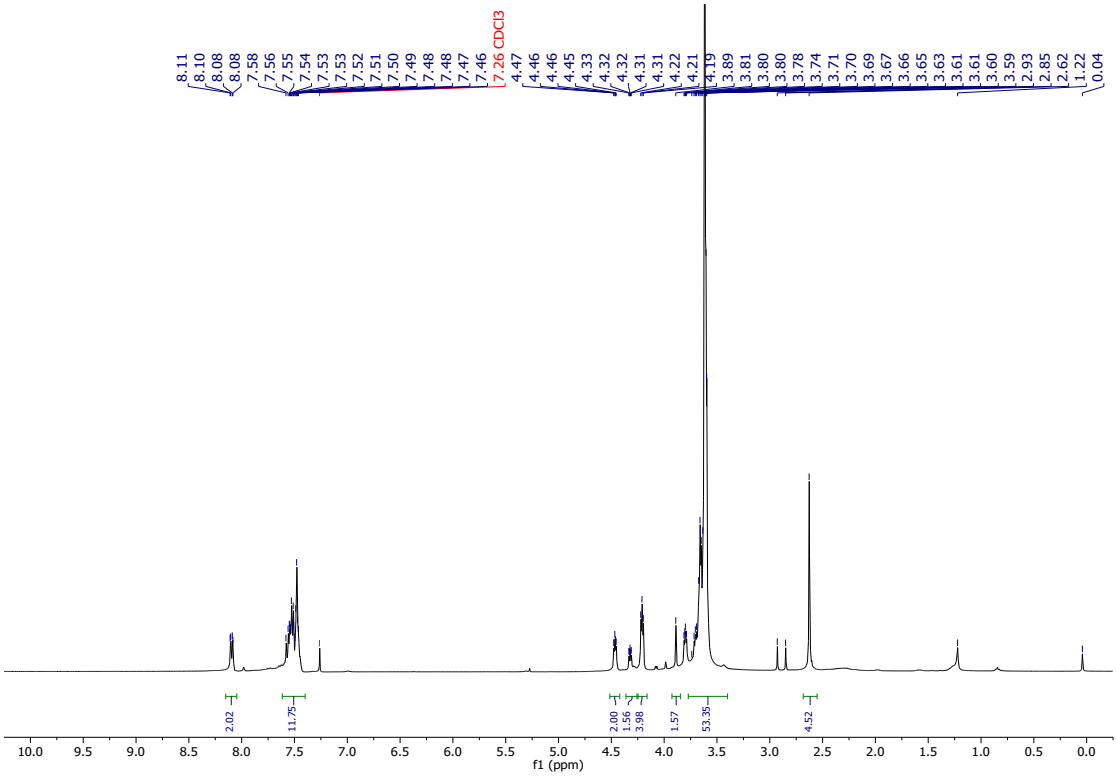
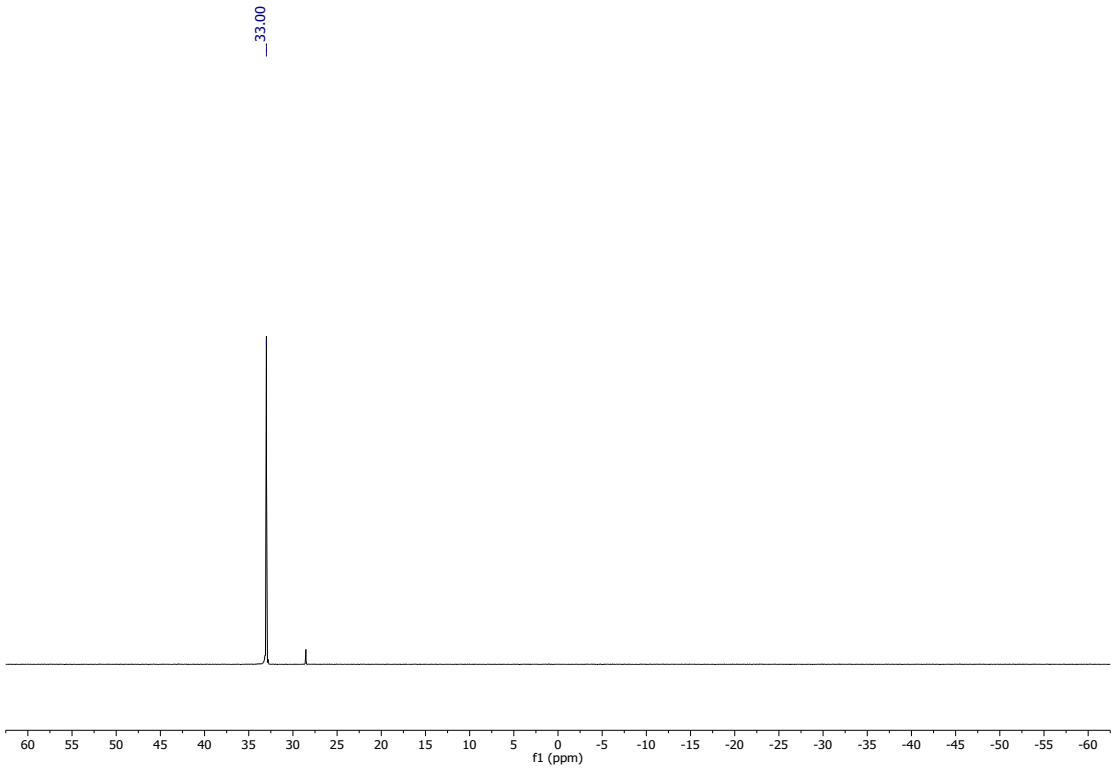


Figure S4. ^{1}H (top), ^{31}P (middle), ^{13}C (bottom) NMR spectra of **4** in $CDCl_3$ at RT.


8.11
8.10
8.08
8.08
7.58
7.56
7.55
7.54
7.53
7.53
7.52
7.51
7.50
7.49
7.48
7.48
7.47
7.46
7.26 CDCl3
4.47
4.46
4.46
4.45
4.33
4.32
4.32
4.31
4.31
4.22
4.21
4.19
3.89
3.81
3.80
3.80
3.78
3.74
3.71
3.70
3.69
3.67
3.66
3.65
3.63
3.61
3.61
3.60
3.59
2.93
2.85
2.62
1.22
0.04
2.02
11.75
2.00
1.56
3.98
1.57
53.35
4.52
f1 (ppm)


33.00
f1 (ppm)

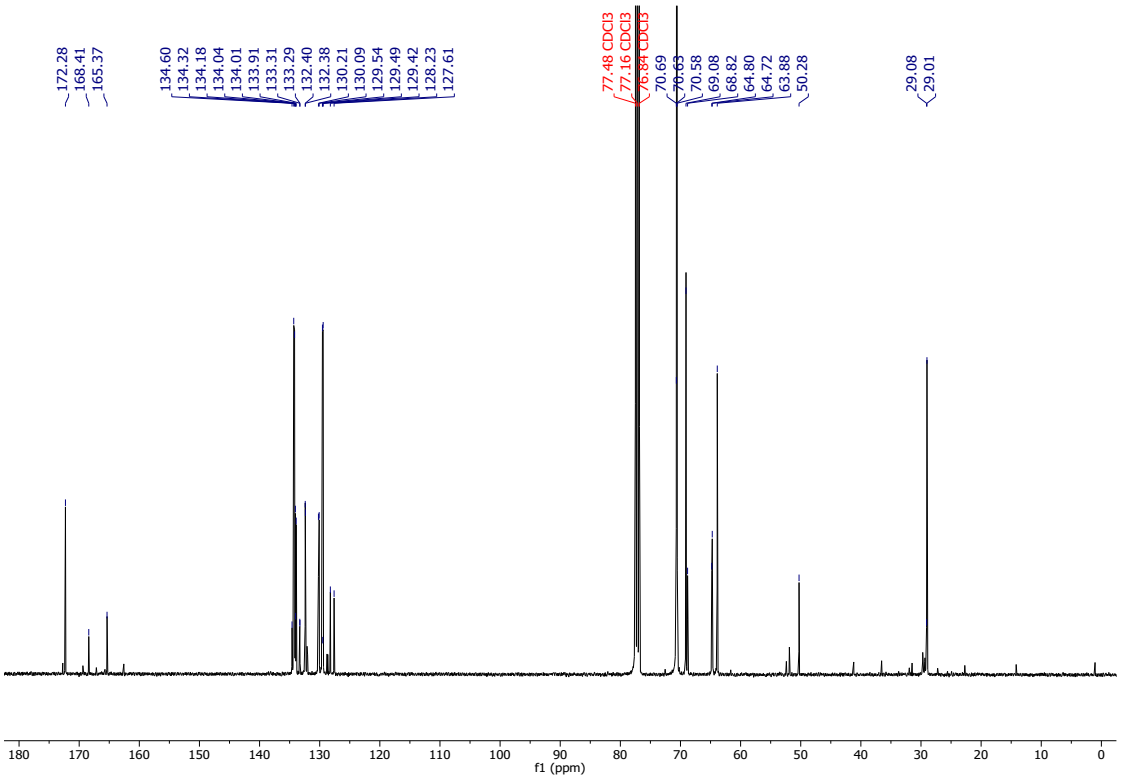


Figure S5. ^{1}H (top), ^{31}P (middle), ^{13}C (bottom) NMR spectra of **5** in $CDCl_3$ at RT.

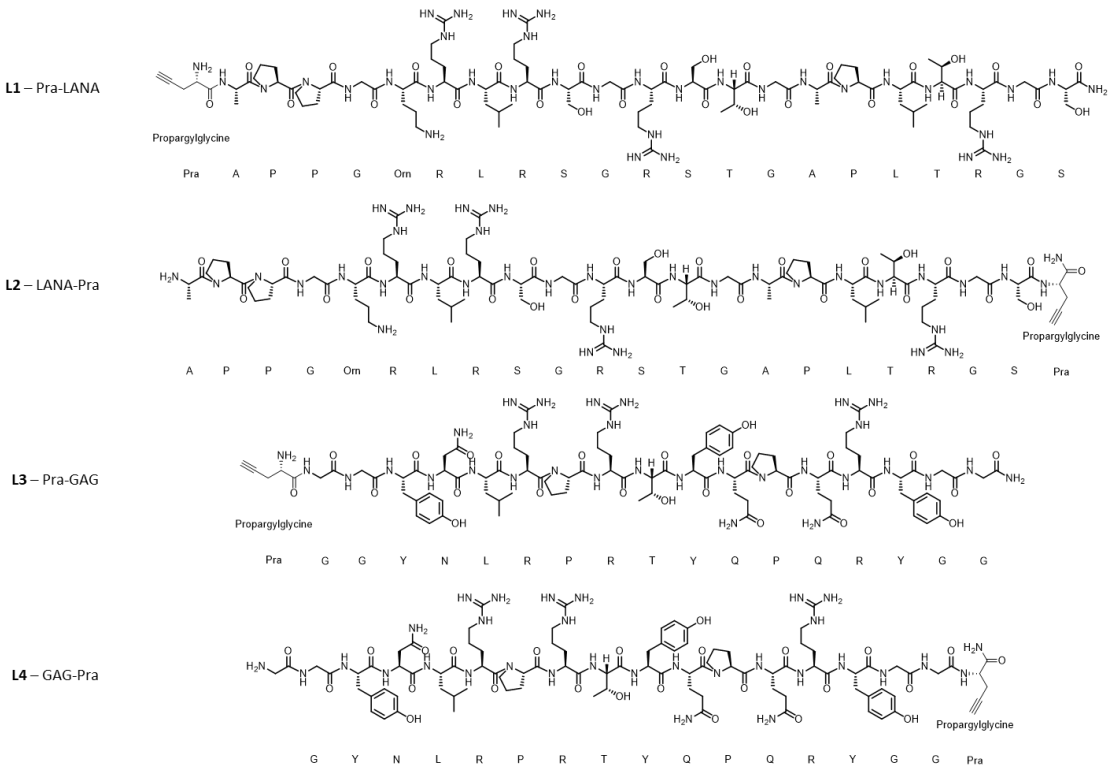


Figure S6. Structures of the viral peptides modified with a propargylglycine group (L1–L4).

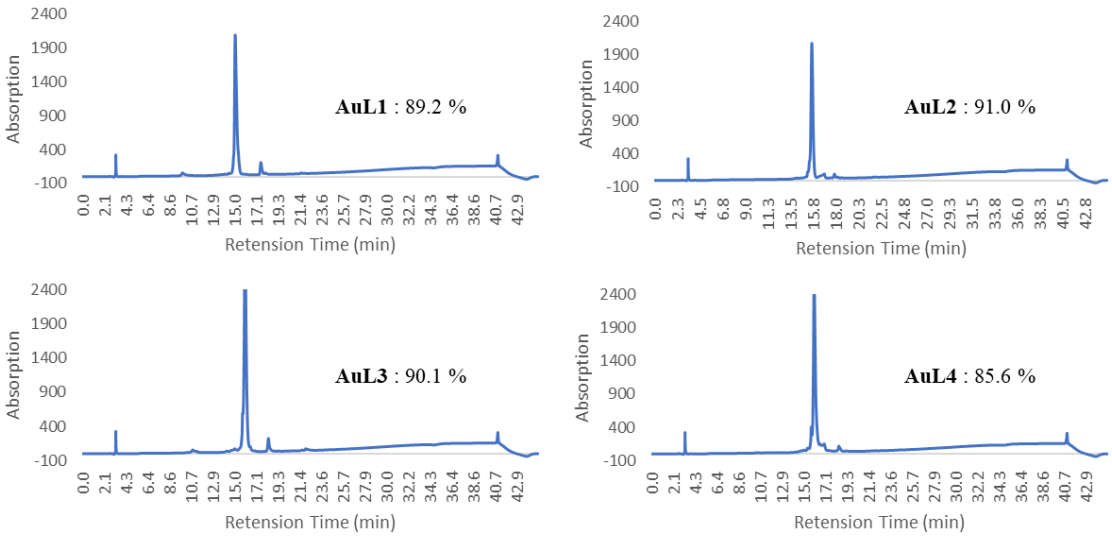


Figure S7. HPLC traces for the Au(I)-peptide conjugates: Au-LANA, LANA-Au, Au-GAG and GAG-Au.

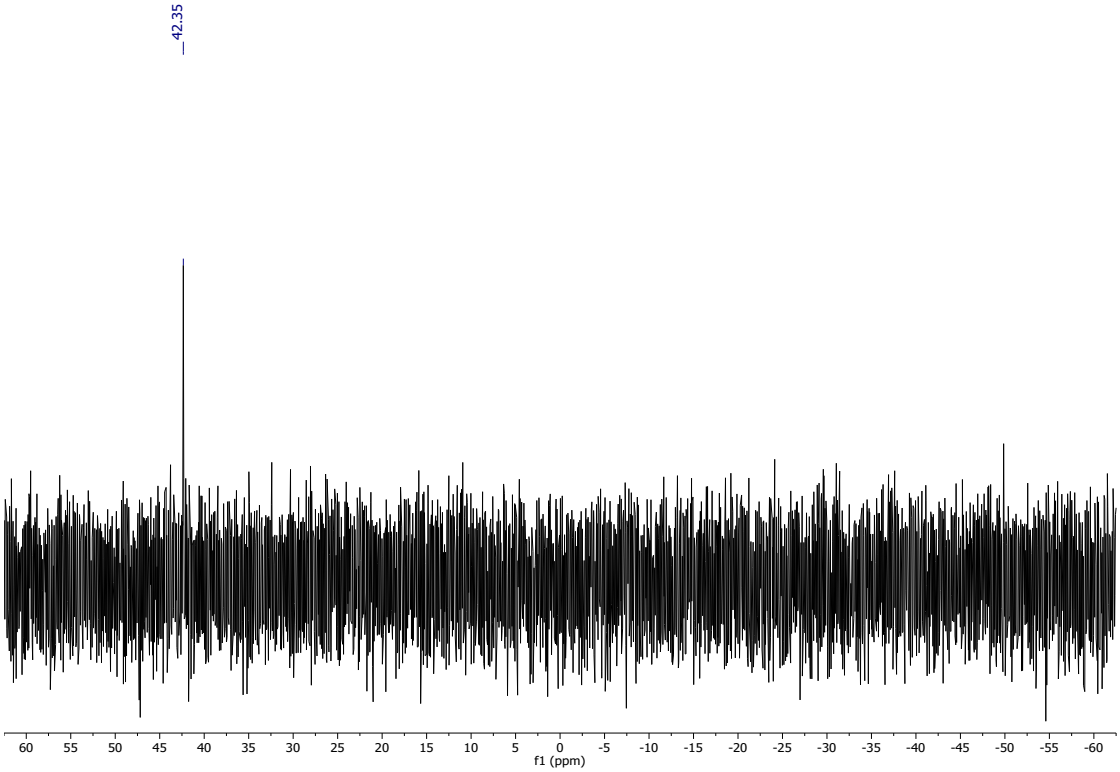


Figure S8. ^{31}P NMR spectrum of Au-LANA in D_2O at RT.

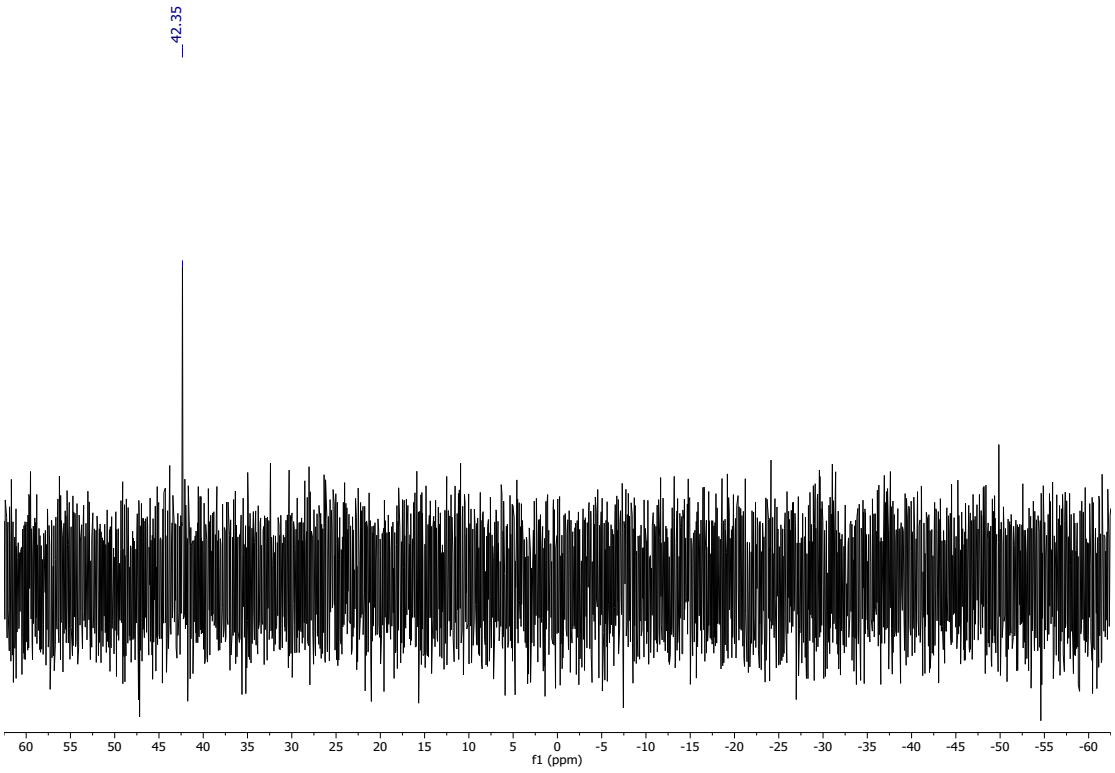


Figure S9. ^{31}P NMR spectrum of LANA-Au in D_2O at RT.

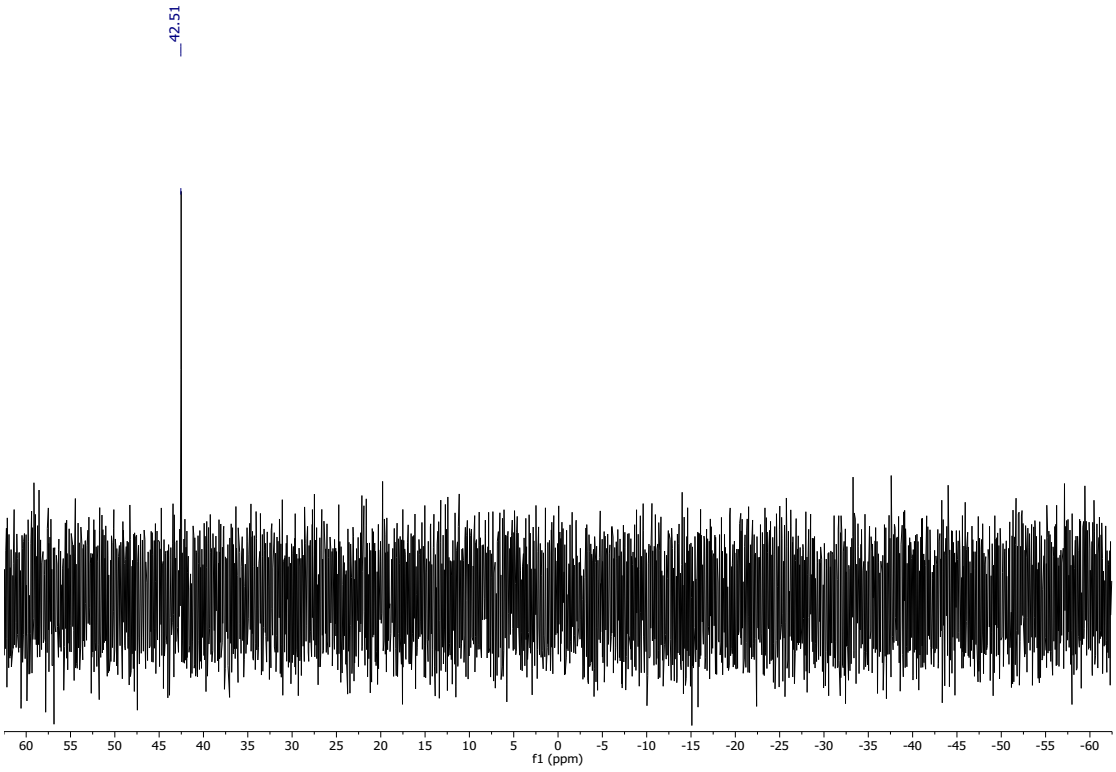


Figure S10. ^{31}P NMR spectrum of Au-GAG in D_2O at RT.

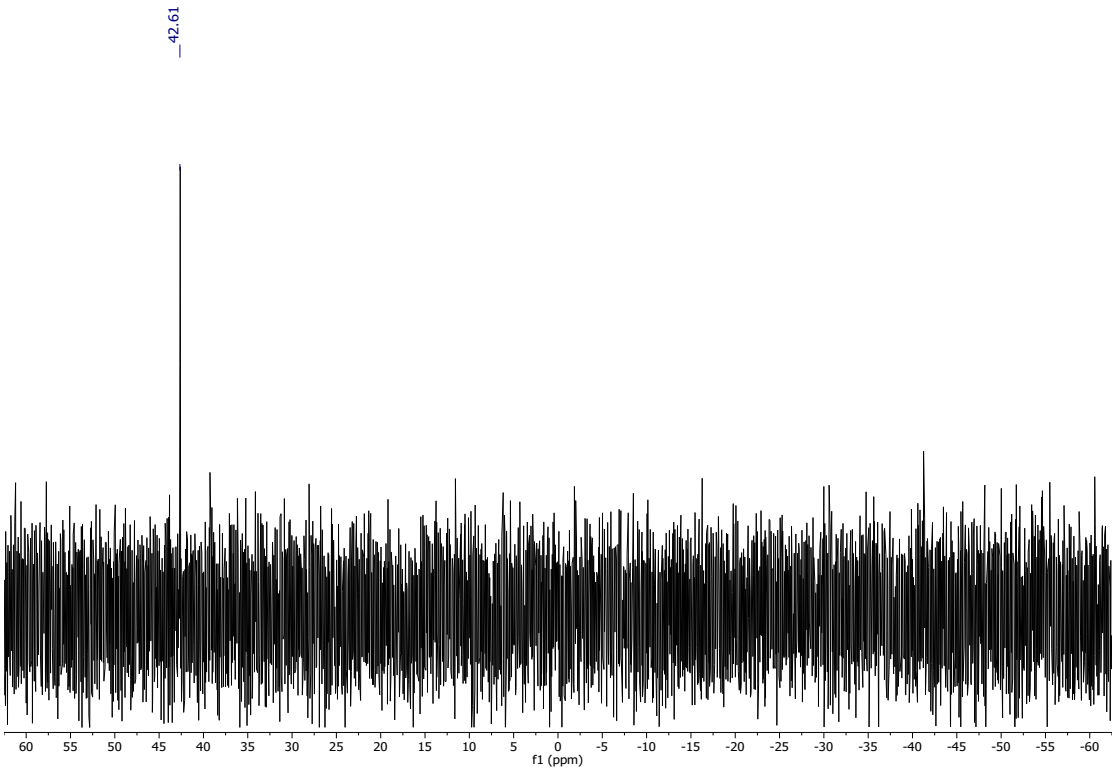


Figure S11. ^{31}P NMR spectrum of GAG-Au in D_2O at RT.

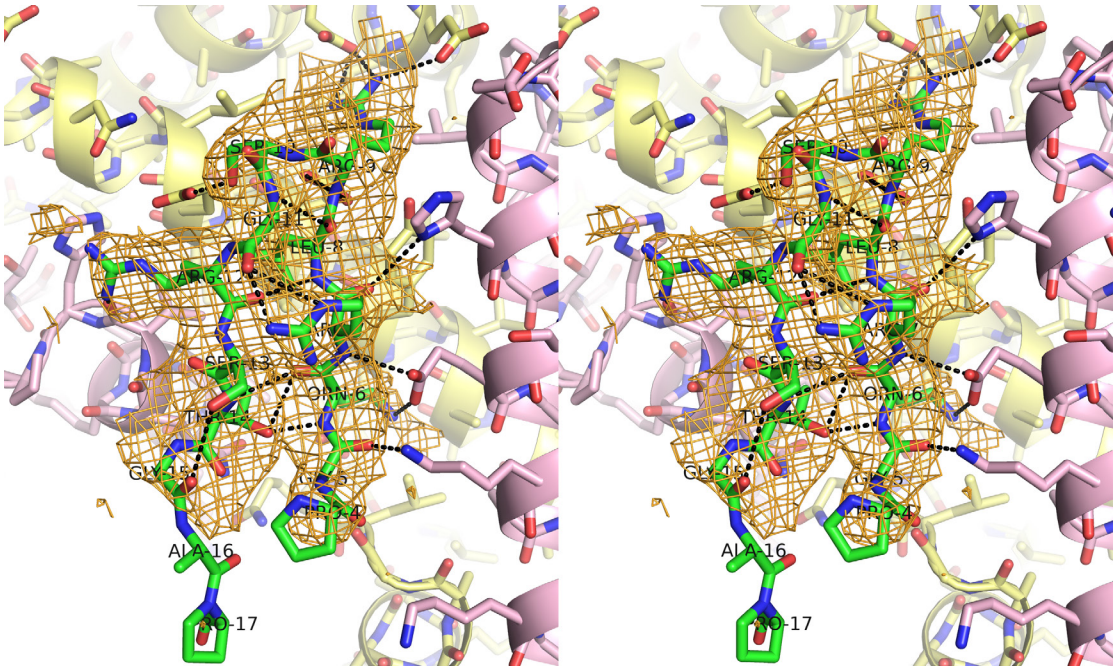


Figure S12. Experimental electron density corresponding to the NCP-bound LANA peptide used in the Au(I)-viral peptide conjugates (in stereo view). An F_O-F_C omit electron density map (orange; contoured at 2σ; prior to inclusion of LANA peptide in the model) in the vicinity of the omitted atoms is superimposed onto the refined model. Histone proteins are shown with a yellow (H2A) and pink (H2B) carbon backbone and the LANA peptide with a bright green carbon backbone. Hydrogen bonds are represented by black dashed lines. The X-ray crystallographic data set stems from a 15-hour incubation of NCP crystals with a 2 mM concentration of a 21-residue LANA peptide engineered with a Met to Orn substitution (at residue postion 6): 2-APPGOrnRLRSGRSTGAPLTRGS-22. Note that the first two N-terminal and last five C-terminal residues are not visible in the electron density maps and thus only residues 4-PGOrnRLRSGRSTGAP-17 are included in the model.

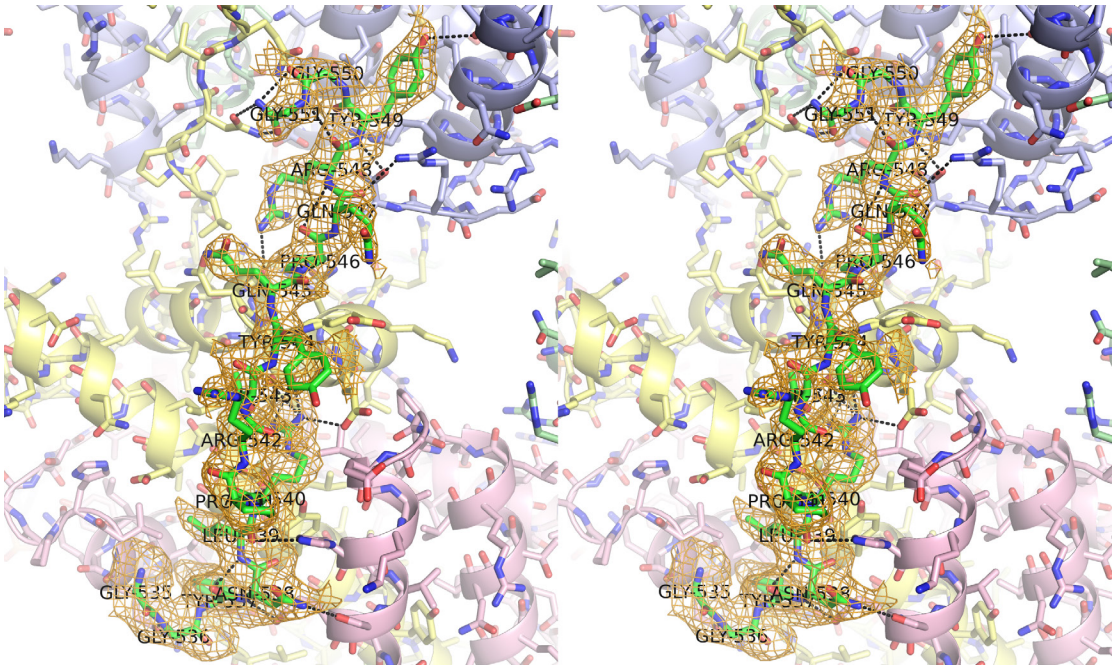


Figure S13. Experimental electron density corresponding to the NCP-bound GAG peptide used in the Au(I)-viral peptide conjugates (in stereo view). An F_O-F_C omit electron density map (orange; contoured at 2σ; prior to inclusion of GAG peptide in the model) in the vicinity of the omitted atoms is superimposed onto the refined model. Histone proteins are shown with a purple (H3), pale green (H4), yellow (H2A), and pink (H2B) carbon backbone and the GAG peptide with a bright green carbon backbone. Hydrogen bonds are represented by black dashed lines. The X-ray crystallographic data set stems from a 29-hour incubation of NCP crystals with a 2 mM concentration of Au-GAG, which comprises the 17-residue GAG peptide: 535-GGYNLRPRTYQPQRYGG-551.

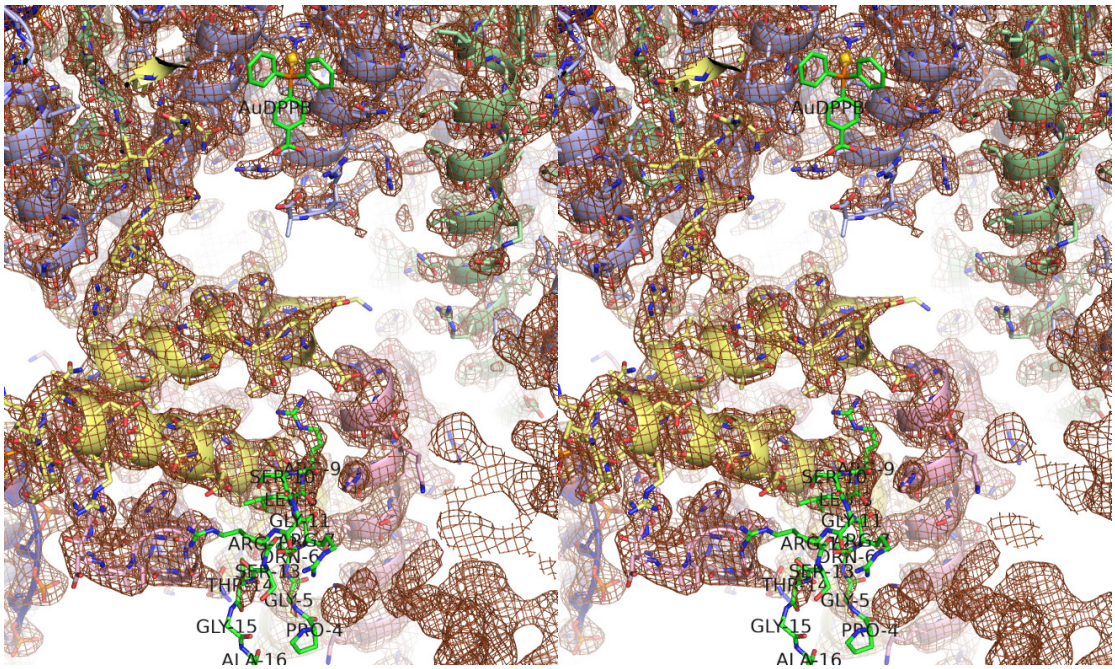


Figure S14. Electron density corresponding to the NCP treated with the Au-LANA Au(I)-viral peptide conjugate (in stereo view). A $2F_O-F_C$ electron density map (brown; contoured at 1.5σ) is superimposed onto the refined model. The Au-LANA adduct (LANA peptide and AuDPPB group) is displayed with a bright green carbon backbone. Histone proteins are shown in purple (H3), pale green (H4), yellow (H2A) and pink (H2B), and DNA strands are orange and dark blue. The X-ray crystallographic data set stems from a 73-hour incubation of NCP crystals with a 1 mM concentration of the Au-LANA conjugate, wherein the 21-residue LANA peptide is engineered with a Met to Orn substitution (at residue postion 6): 2-APPGOrnRLRSGRSTGAP-LTRGS-22. See Figure 2a for further details, including the experimental electron density associated with the Au-LANA adduct.