Supporting Information (SI-1) for

Contribution of Phosphates and Adenine to the Potency of Adenophostins at the IP$_3$ Receptor: Synthesis of all Possible Bisphosphates of Adenophostin A

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(2'R,3'R)-Ethyl-4,6-di-*O*-benzyl-2,3-di-*O*-(2', 3'-dimethoxy butane-2',3'-diyl)-1-thio-*β*-D-glucopyranoside (10). To a solution of 2,3-BDA derivative **9** (5g, 14.77 mmol) in DMF (50 mL) was added NaH (2g, 60% in oil, 50 mmol) at 0ºC and the mixture was stirred for 10 min. BnBr (6 mL, 50 mmol) was then added dropwise at 0 ºC, stirring continued at 0 ºC for 30 min and then the temperature was raised to rt and stirring was continued for another 2h, when TLC showed the presence of no more starting material. The DMF was evaporated off and the residue was taken up in ethyl acetate. The usual aqueous work up was followed by column chromatography with 10% ethyl acetate–hexane to yield dibenzyl ether **10** as a white crystalline solid (7.66 g, 100%). M.p- 101 ºC; $[\alpha]_D$ -110.9 (c 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): 1.31 (t, 3H, 7.40 Hz, -S-CH_2-C*H*$_3$), 1.34 (s, 3H, C-C*H*$_3$), 1.37 (s, 3H, C-C*H*$_3$), 2.68-2.82 (m, 2H, S-C*H*$_2$), 3.30 (s, 3H, O-C*H*$_3$), 3.32 (s, 3H, O-C*H*$_3$), 3.51 (ddd, 1H, 9.57 Hz, 4.78 Hz, 1.30 Hz, H-5), 3.61 (t, 1H, 9.57 Hz, H-2), 3.68 (t, 1H, 9.57 Hz, H-4), 3.69 (dd, 1H, 10.87 Hz, 4.78 Hz, H-6$_A$), 3.75 (dd, 1H, 10.87 Hz, 1.30 Hz, H-6$_B$), 3.92 (t, 1H, 9.57 Hz, H-3), 4.56 (AB q, 2H, 27.83 Hz, 12.17 Hz, PhC*H*$_2$), 4.57 (d, 1H, 9.57 Hz, H-1), 4.74 (AB q, 2H, 146.95 Hz, 10.89 Hz, PhC*H*$_2$), 7.20-7.40 (m, 10 H, 2x*Ph*). ^{13}C NMR (100 MHz, $CDCl_3$): 14.94 (S-CH_2-*C*H$_3$), 17.50 (C-*C*H$_3$, BDA), 17.66 (C-*C*H$_3$, BDA), 24.43 (S-*C*H$_2$-Me), 47.74 (O-CH_3), 47.96 (O-CH_3), 68.89 (C-2), 69.00 (C-6), 73.18 (Ph*C*H$_2$), 74.65 (C-4), 74.83 (Ph*C*H$_2$), 75.32 (C-3), 79.23 (C-5), 82.45 (C-1), 99.31 (*C*Me$_2$), 99.81 (*C*Me$_2$), 127.36, 127.50, 127.58, 127.86, 128.14, 128.18 (aromatic carbons), 138.11 (2 x ipso carbons). Elemental analysis calcd for $C_{28}H_{38}O_7S$ C, 64.84; H, 7.38 Found C, 64.8; H, 7.38. m/z (ES+) = 541.2 [(M+Na)$^+$, 100%]; HRMS: Mass calcd for $C_{28}H_{42}O_7NS$ [M+NH4]$^+$, 536.2676; Found, 536.2680.

Ethyl-4,6-di-*O*-benzyl-1-thio-*β*-D-glucopyranoside (11). A solution of dibenzyl ether **10** (5.5 g, 10.6 mmol) in 80% AcOH (50 mL) was refluxed for 1h. After 1 h, the solvent and butanedione were evaporated off. The residue was chromatographed with 40% ethyl acetate–hexane to give pure diol **11** as a colorless solid (4.28 g, 99%). M.p. 67 ºC; [α]$_D$ -14.8 (c 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): 1.32 (t, 3H, 7.37 Hz, -S-CH_2-C*H*$_3$), 2.66-2.86 (m, 3H, S-C*H*$_2$ & OH), 2.86-3.14 (br, 1H, -OH), 3.40 (ddd, 1H, 9.69 Hz, 8.85 Hz, 2.11 Hz, H-2), 3.48 (ddd, 1H, 9.69 Hz, 4.21 Hz, 1.69 Hz, H-5), 3.54 (dd, 1H, 9.69 Hz, 8.85 Hz, H-4), 3.68 (dt, 1H, 8.85 Hz, 2.11 Hz, H-3), 3.69-3.73 (m, 1H, H-6$_A$), 3.77 (dd, 1H, 10.95 Hz, 1.69 Hz, H-6$_B$), 4.31 (d, 1H, 9.69 Hz, H-1), 4.59 (AB q, 2H, 29.91 Hz, 12.22 Hz, PhC*H*$_2$), 4.71 (AB q, 2H, 80.68 Hz, 11.17 Hz, PhC*H*$_2$), 7.22-7.38 (m, 10 H, 2x*Ph*). ^{13}C NMR (100 MHz, $CDCl_3$): 15.34 (S-CH_2-*C*H_3), 24.39 (S-*C*H_2-Me), 68.94 (C-6), 72.62 (C-2), 73.38 (Ph*C*H_2), 74.64 (Ph*C*H_2), 77.18 (C-4), 78.20 (C-3), 79.01 (C-5), 85.64 (C-1), 127.59, 127.76, 127.84, 127.97, 128.30, 128.44 (aromatic carbons), 138.01, 138.09 (ipso carbons). Elemental analysis calcd for $C_{22}H_{28}O_5S$ C, 65.32; H, 6.98 Found C, 65.25; H, 7.06. m/z (ES+) = 427.1 [$(M+Na)^+$, 100%]; HRMS: Mass calcd for $C_{22}H_{32}O_5NS$ $[M+NH4]^+$, 422.1996; Found, 422.1999.

Ethyl-2,4,6-tri-*O*-benzyl-1-thio-*β*-D-glucopyranoside (12). Method 1: A suspension of diol **11** (225 mg, 0.556 mmol), Bu_2SnO (177 mg, 0.71 mmol), TBAB (210 mg, 0.65 mmol) and BnBr (110 µL, 0.92 mmol) in acetonitrile (20 mL) was refluxed in a RB flask attached with soxhlet thimble containing 3 Å molecular sieves for 24 h. Triethylamine (2 mL) was then added and the mixture refluxed for a further 1h, cooled to rt and ether (10 mL) and satd. $NaHCO_3$ solution (10 mL) were then added. After filtration through a small pad of celite, the concentrated filtrate was worked up in ethyl acetate. The crude mixture was then chromatographed with 25% ethyl acetate –hexane to afford tribenzyl ether **12** (74 mg, 27%), tribenzyl ether **13** (63 mg, 23%) and the diol **11** (81 mg, 36%).

Method 2: To a solution of diol **11** (135 mg, 0.33 mmol) in DMF (3 mL) was added NaH (27 mg, 60% in oil, 0.67 mmol) and the mixture was stirred for 10 min at rt. BnBr (40 µL, 0.33 mmol) was then added and stirring continued for 2h at rt. The usual work-up was followed by chromatography providing **12** (30 mg, 18%), **13** (26 mg, 16%), tetrabenzyl ether **14** (62.5 mg, 32%) and the diol **11** (32 mg, 24%).

Method 3: To a solution of diol **11** (100 mg, 0.25 mmol) in DCM (4 mL) was added Bu_4NHSO_4 (85 mg, 0.25 mmol), 5% aq NaOH (4 mL) and BnBr (35μL, 0.29 mmol) and the mixture was then stirred at 55 ºC overnight. After work up in ethyl acetate, chromatography gave **12** (90 mg, 74%), **13** (10 mg, 8.2%) and **14** (14 mg, 10%).

For scale-up **method 3** was adopted using diol **11** (3.47 g, 8.58mmol), DCM (135 mL), Bu_4NHSO_4 (3g, 8.84 mmol), 5% NaOH (135 mL) and BnBr (1.03 mL, 8.58 mmol) to yield **12** (2.83g, 67%), **13** (280 mg, 6.6%), **14** (150 mg, 3%) and **11** (347 mg, 10%).

Data for **12**: $[\alpha]_D$ +4.3 (c 1.4, $CHCl_3$);^{1}H NMR (400 MHz, $CDCl_3$): 1.33 (t, 3H, 7.59 Hz, CH_3), 2.48 (d, 1H, 2.23 Hz, OH), 2.70-2.84 (m, 2H, S-CH_2), 3.30 (dd, 1H, 9.82 Hz, 8.92 Hz, H-2), 3.44 (ddd, 1H, 9.82 Hz, 4.91 Hz, 1.79 Hz, H-5), 3.51 (dd, 1H, 9.82 Hz, 8.92 Hz, H-4), 3.68 (dd, 1H, 10.71 Hz, 4.91 Hz, H-6_A), 3.73 (dt, 1H, 8.92 Hz, 2.2 Hz, H-3), 3.76 (dd, 1H, 10.71 Hz, 1.79 Hz, H-6_B), 4.44 (d, 1H, 9.82 Hz, H-1), 4.58 (AB q, 2H, 26.77 Hz, 12.05 Hz, $PhCH_2$), 4.69 (AB q, 2H, 87.01 Hz, 11.16 Hz, $PhCH_2$), 4.82 (AB q, 2H, 117.36 Hz, 10.71 Hz, $PhCH_2$), 7.22-7.42 (m, 15 H, 3x*Ph*). ^{13}C NMR (100 MHz, $CDCl_3$): 15.06 (CH_3), 25.00 (S-*C*H_2-Me), 69.03 (C-6), 73.33 (Ph*C*H_2), 74.54 (Ph*C*H_2), 75.06 (Ph*C*H_2), 77.42 (C-4), 78.46 (C-3), 78.68 (C-5), 81.31 (C-2), 84.57 (C-1), 127.54, 127.70, 127.75, 127.91, 127.99, 128.23, 128.36, 128.39, 128.52 (aromatic carbons), 137.94, 138.06, 138.14 (ipso carbons). Elemental analysis calcd for $C_{29}H_{34}O_5S$ C, 70.42; H, 6.93 Found C, 70.12; H, 6.96. m/z (ES+) = 517.2 [$(M+Na)^+$, 100%]; HRMS: Mass calcd for $C_{29}H_{38}O_5NS$ $[M+NH4]^+$, 512.2465; Found, 512.2470.

Ethyl-3-*O*-acetyl-2,4,6-tri-*O*-benzyl-1-thio-*β*-D-glucopyranoside (15). To a solution of tribenzyl ether **12** (2 g, 4.04 mmol) in pyridine (10 mL) was added Ac_2O (3 mL, 31.7 mmol) at rt and the mixture was stirred overnight. Pyridine was evaporated off and the residue was worked up in ethyl acetate and chromatographed with 10% ethyl acetate–hexane to afford the known[1] acetate **15** (2.052 g, 95%) as white crystalline solid. Although **15** is known, full characterization data have never been reported. Also, notably, our [α]$_D$ value is different and of opposite sign to the reported value. Thus, full characterization data are provided. M.p. 85 ºC; [α]$_D$ -2.7 (c 1.1, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): 1.34 (t, 3H, 7.37 Hz, CH$_3$), 1.85 (s, 3H, COCH_3), 2.71-2.86 (m, 2H, S-CH$_2$), 3.42 (dd, 1H, 9.69 Hz, 9.27 Hz, H-2), 3.52 (ddd, 1H, 9.69 Hz, 3.79 Hz, 2.11 Hz, H-5), 3.67 (t, 1H, 9.69 Hz, H-4), 3.72 (dd, 1H, 10.95 Hz, 3.79 Hz, H-6$_A$), 3.76 (dd, 1H, 10.95 Hz, 2.11 Hz, H-6$_B$), 4.52 (d, 1H, 9.69 Hz, H-1), 4.53 (s, 2H, PhCH_2), 4.60 (AB q, 2H, 36.23 Hz, 12.22 Hz, PhCH_2), 4.72 (AB q, 2H, 123.01 Hz, 11.38 Hz, PhCH_2), 5.28 (t, 1H, 9.27 Hz, H-3), 7.16-7.40 (m, 15 H, 3x*Ph*). ^{13}C NMR (100 MHz, CDCl$_3$): 15.02 (CH$_3$), 20.87 (CO*C*H$_3$), 25.14 (S-*C*H$_2$-Me), 68.54 (C-6), 73.35 (Ph*C*H$_2$), 74.23 (Ph*C*H$_2$), 74.68 (Ph*C*H$_2$), 75.94 (C-4), 77.00 (C-3), 78.69 (C-5), 79.46 (C-2), 84.94 (C-1), 127.57, 127.68, 127.71, 127.73, 127.82, 128.01, 128.26, 128.27, 128.30 (aromatic carbons), 137.63, 137.66, 137.90 (ipso carbons), 169.85 (O-*C*O-CH$_3$). Elemental analysis calcd for $C_{31}H_{36}O_6S$ C, 69.38; H, 6.76 Found C, 69.6; H, 6.83. m/z (ES+) = 559.4 [(M+Na)$^+$, 100%]; HRMS: Mass calcd for $C_{31}H_{40}O_6NS$ [M+NH$_4$]$^+$, 554.2571; Found, 554.2575.

3'-*O*-acetyl-5,2',4',6'-tetra-*O*-benzyl-3-*O*-(*α*-D-glucopyranosyl)-1,2-*O*-isopropylidene -*α*-D-ribofuranoside (17). ^{13}C NMR (100 MHz, CDCl$_3$): 21.02 (CO*C*H$_3$), 26.61 (*C*H$_3$, isopropylidene), 26.69 (*C*H$_3$, isopropylidene), 67.65 (C-6'), 67.71 (C-5), 70.14 (C-4' or C-5'), 70.90 (Ph*C*H$_2$), 72.38 (C-3), 73.36 (C-3'), 73.47 (Ph*C*H$_2$), 73.52 (Ph*C*H$_2$), 74.31 (Ph*C*H$_2$), 75.74 (C-5' or C-4'), 76.12 (C-2'), 76.18 (C-2), 77.55 (C-4), 94.21 (C-1'), 104.29 (C-1), 112.91 (*C*Me$_2$), 127.49, 127.53, 127.56, 127.61, 127.72, 127.76, 127.81, 127.87, 127.91, 128.05, 128.15, 128.23, 128.26, 128.32, 128.36 (aromatic carbons), 137.56, 137.85, 137.95, 138.00 (ipso carbons), 169.85 (O*C*OCH$_3$).

Ethyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-1-thio-*β*-D-glucopyranoside (24). Tetraacetate **22** (8.625g, 22 mmol) was stirred with NaOMe (35 mg, 0.65 mmol) in methanol (50 mL) for 30 min at rt. When TLC showed complete disappearance of starting material (DCM: acetone, 10:1 v/v), a few granules of Dowex-H^+ were added and the mixture was stirred for 5 min and then filtered. The filtrate was evaporated and co-evaporated several times with toluene and dried under vacuum. The residue was then dissolved in DMF (80 mL) and the solution heated with benzaldehyde dimethyl acetal (3.75 mL, 25 mmol) in the presence of camphorsulfonic acid (0.79 g, 3.4 mmol) at 50 °C for 2h. When the reaction was complete (TLC), Et_3N (5 mL) was added and the solution evaporated partially to remove the methanol and excess Et_3N. To the remaining DMF solution was added NaH (3.6 g, 60% in oil, 90 mmol) and then BnBr (10.6 mL, 88.3 mmol) and the mixture stirred at rt overnight. DMF was evaporated off under vacuo, work-up was in ethyl acetate and the crude product was chromatographed with 10% ethyl acetate-hexane to afford the known[1] dibenzyl ether **24** (9.312g, 86%).

Ethyl 2,3,6-tri-*O*-benzyl-1-thio-*β*-D-glucopyranoside (25). To a solution of **24** (3.5 g, 7.1 mmol) and triethylsilane (5.7 mL, 35.7 mmol) in DCM was added TFA (2.737 mL, 36.85 mmol) dropwise at 0 °C over 10 min. Gradually, the temperature was raised to 20 °C over 2h. When the reaction was complete (TLC), the reaction mixture was diluted with ethyl acetate and the solution was washed with satd $NaHCO_3$ solution. The organic layer was dried ($MgSO_4$) and evaporated. The residue was chromatographed with 20% ethyl acetate–hexane to give the known[2] tribenzyl ether **25** (3.128g, 89%).

Ethyl 4-*O*-acetyl-2,3,6-tri-*O*-benzyl-*β*-thio-glucopyranoside (26). To a solution of tribenzyl ether **25** (1.35 g, 2.73 mmol) in pyridine (9 mL) was added Ac_2O (3 mL, 31.7 mmol) dropwise at room temperature. The reaction mixture was stirred at rt overnight and worked up in ethyl acetate as usual and the residue thus obtained was chromatographed to obtain the known acetate **26**[2] (1.362 g, 93%).

3-*O*-(4'-*O*-acetyl-2',3',6'-tri-*O*-benzyl-*α*-D-glucopyranosyl)-5-*O*-benzyl-1,2-*O*-isopropylidene-*α*-D-ribofuranoside (27). ^{13}C NMR (100 MHz, CDCl$_3$): 20.81 (CO*C*H$_3$), 26.57 (*C*H$_3$, isopropylidene), 26.72 (*C*H$_3$, isopropylidene), 67.88 (C-5), 68.11 (C-6'), 68.96 (C-5'), 69.90 (C-4'), 72.11 (Ph*C*H$_2$), 72.66 (C-3), 73.42 (Ph*C*H$_2$), 73.52 (Ph*C*H$_2$), 75.12 (Ph*C*H$_2$), 76.15 (C-2), 77.47 (C-4), 78.94 (C-2'), 79.03 (C-3'), 94.34 (C-1'), 104.18 (C-1), 112.93 (*C*Me$_2$), 127.46, 127.55, 127.59, 127.77, 127.83, 127.99, 128.23, 128.27, 128.42 (aromatic carbons), 137.61, 137.90, 137.95, 138.65 (ipso carbons), 169.50 (O*C*OCH$_3$).

3-*O*-(4'-*O*-acetyl-2',3',6'-tri-*O*-benzyl-*α*-D-glucopyranosyl)-5-*O*-benzyl-1,2-di-*O*-acetyl-*α*/*β*-D-ribofuranoside (28). ^{13}C NMR (100 MHz, CDCl$_3$): 20.44 (CO*C*H$_3$), 20.72 (CO*C*H$_3$), 20.88 (CO*C*H$_3$), 68.52 (C-6'), 69.38 (C-5'), 69.58 (C-5), 70.32 (C-4'), 73.11 (Ph*C*H$_2$), 73.32 (C-2), 73.43 (Ph*C*H$_2$), 73.46 (Ph*C*H$_2$), 73.70 (C-3), 75.11 (Ph*C*H$_2$), 78.87 (C-3'), 78.94 (C-2'), 81.45 (C-4), 96.68 (C-1'), 98.37 (C-1), 127.21, 127.46, 127.50, 127.56, 127.59, 127.72, 127.80, 128.18, 128.22, 128.28 (aromatic carbons), 137.61, 137.83, 138.01, 138.37 (ipso carbons), 169.28 (O*C*OCH$_3$), 169.49 (O*C*OCH$_3$), 169.88 (O*C*OCH$_3$).

2',3"-di-*O*-acetyl-5',2",4",6"-tetra-*O*-benzyl-6-chloro-3'-*O*-(*α*-D-glucopyranosyl)-9-*β*-D-ribo-furanosylpurine (19). ^{13}C NMR (100 MHz, CDCl$_3$): 20.31 (CO*C*H$_3$), 21.02 (CO*C*H$_3$), 67.81 (C-6"), 68.64 (C-5'), 70.88 (C-5"), 72.88 (Ph*C*H$_2$), 73.15 (C-3"), 73.52 (Ph*C*H$_2$), 73.59 (Ph*C*H$_2$), 74.12 (C-2'), 74.53 (Ph*C*H$_2$), 75.06 (C-3'), 75.85 (C-4"), 77.11 (C-2"), 82.60 (C-4'), 86.88 (C-1'), 97.55 (C-1"), 127.63, 127.68, 127.79, 127.81, 127.88, 128.04, 128.35, 128.37, 128.57 (aromatic carbons), 131.98 (C-5), 136.95, 137.40, 137.59, 137.68 (ipso carbons), 143.74 (C-8), 151.00 (C-6 or C-4), 151.23 (C-4 or C-6), 152.06 (C-2), 169.90 (O-*C*OCH$_3$), 170.12 (O-*C*OCH$_3$).

6-amino-5',2",4",6"-tetra-*O*-benzyl-3'-*O*-(*α*-D-glucopyranosyl)-9-*β*-D-ribofuranosylpurine (20). ^{13}C NMR (100 MHz, CDCl$_3$): 68.19 (C-6"), 69.59 (C-5'), 71.04 (C-5"), 73.22 (C-3"), 73.38 (Ph*C*H$_2$), 73.47 (Ph*C*H$_2$), 74.27 (Ph*C*H$_2$), 74.87 (Ph*C*H$_2$), 75.07

(C-2'), 77.44 (C-4"), 78.48 (C-3'), 78.88 (C-2"), 82.28 (C-4'), 88.29 (C-1'), 98.80 (C-1"), 119.41 (C-5), 127.62, 127.66, 127.70, 127.75, 127.81, 127.88, 128.24, 128.28, 128.30, 128.42, 128.52, 128.53 (aromatic carbons), 136.79, 137.30, 137.60, 138.08 (ipso carbons), 138.72 (C-8), 149.60 (C-4), 153.08 (C-2), 155.52 (C-6).

6-amino-5',2",4",6"-tetra-*O*-benzyl-2',3"-bis-*O*-(dibenzyloxyphosphoryl)-3'-*O*-(*α*-D-glucopyran-osyl)-9-*β*-D-ribofuranosylpurine (21). ^{13}C NMR (100 MHz, $CDCl_3$): 67.93 (C-6"), 68.97 (C-5'), 69.03, 69.10, 69.15, 69.53, 69.59, 69.76, 69.81(*C*H$_2$Ph, ^{31}P coupled), 70.63 (C-5"), 71. 46 (*C*H$_2$Ph), 72.69 (d, 4.6 Hz, C-3', ^{31}P coupled), 73.46 (*C*H$_2$Ph), 73.49 (*C*H$_2$Ph), 74.36 (*C*H$_2$Ph), 76.43 (d, 3.07 Hz, C-4", ^{31}P coupled), 76.87 (d, 5.37 Hz, C-2', ^{31}P coupled), 77.02 (C-2", ^{31}P coupled), 79.82 (d, 6.90 Hz, C-3", ^{31}P coupled), 82.01 (C-4'), 85.93 (d, 4.60 Hz, C-1', ^{31}P coupled), 95.46 (C-1"), 119.82 (C-5), 127.49, 127.57, 127.62, 127.72, 127.73, 127.78, 127.84, 127.91, 128.01, 128.07, 128.14, 128.20, 128.25, 128.32, 128.36, 128.39, 128.41, 128.44, 128.46, 128.50 (aromatic carbons), 134.94, 135.01, 135.09, 135.94, 136.01, 136.08, 136.15 (ipso carbons of P-O-CH$_2$-Ph, ^{31}P coupled), 137.34, 137.55, 137.60, 137.81 (ipso carbons of C-O-CH$_2$-Ph), 139.47 (C-8), 149.88 (C-4), 152.86 (C-2), 155.30 (C-6).

3'-O-(*α*-D-glucopyranosyl)-adenosine-2',3"-bisphosphate (4). ^{13}C NMR (100 MHz, D_2O): 60.30 (C-6"), 61.00 (C-5'), 68.79 (C-4", ^{31}P coupled), 70.40 (C-5"), 70.43 (C-2", ^{31}P coupled), 73.58 (d, 3.83 Hz, C-3', ^{31}P coupled), 75.64 (d, 4.6 Hz, C-2', ^{31}P coupled), 78.61 (d, 6.13 Hz, C-3", ^{31}P coupled), 84.44 (C-4'), 87.20 (d, 4.6 Hz, C-1', ^{31}P coupled), 98.12 (C-1"), 118.96 (C-5), 143.35 (C-8), 144. 39 (C-2), 148.25 (C-4), 149.91 (C-6).

2',4"-di-*O*-acetyl-5',2",3",6"-tetra-*O*-benzyl-6-chloro-3'-*O*-(*α*-D-glucopyranosyl)-9-*β*-D-ribofuranosylpurine (29). ^{13}C NMR (100 MHz, $CDCl_3$): 20.27 (CO*C*H$_3$), 20.78 (CO*C*H$_3$), 68.98 (C-6"), 69.4 (C-5'), 69.82 (C-5"), 70.41 (C-4"), 73.34 (Ph*C*H$_2$), 73.55 (Ph*C*H$_2$), 73.68 (Ph*C*H$_2$), 75.27 (Ph*C*H$_2$), 75.51 (C-2'), 77.48 (C-3'), 78.78 (C-3"), 79.07 (C-2"), 83.70 (C-4'), 85.99 (C-1'), 98.73 (C-1"), 127.64, 127.65, 127.72, 127.78, 127.83, 127.90, 127.97, 128.14, 128.27, 128.36, 128.39, 128.64 (aromatic carbons), 131.83 (C-5), 136.86, 137.50, 137.68, 138.29 (ipso carbons), 143.59 (C-8), 151.13 (C-6), 151.68 (C-4), 152.09 (C-2), 169.68 (O-*C*OCH$_3$), 169.95 (O-*C*OCH$_3$).

6-amino-5',2",3",6"-tetra-*O*-benzyl-3'-*O*-(*α*-D-glucopyranosyl)-9-*β*-D-ribofuranosylpurine (30). ^{13}C NMR (100 MHz, CDCl$_3$): 69.14 (C-6"), 69.60 (C-5'), 70.18 (C-4"), 71.59 (C-5"), 73.49 (Ph*C*H$_2$), 73.51 (Ph*C*H$_2$), 73.97 (Ph*C*H$_2$), 74.54 (C-2'), 75.54 (Ph*C*H$_2$), 78.46 (C-3'), 78.74 (C-2"), 81.66 (C-3"), 82.41 (C-4'), 88.63 (C-1'), 99.10 (C-1"), 119.54 (C-5), 127.56, 127.63, 127.85, 127.88, 128.18, 128.27, 128.32, 128.45, 128.49, 128.53 (aromatic carbons), 137.01, 137.34, 137.72, 138.30 (ipso carbons), 138.94 (C-8), 149.74 (C-4), 152.86 (C-2), 155.36 (C-6).

3'-*O*-(*α*-D-glucopyranosyl)-adenosine-2', 4"-bisphosphate (5). ^{13}C NMR (100 MHz, D$_2$O): 60.05 (C-6"), 60.82 (C-5'), 70.94 (C-2"), 71.21 (d, 5.37 Hz, C-5", ^{31}P coupled), 71.53 (d, 1.53 Hz, C-3", ^{31}P coupled), 73.73 (d, 3.83 Hz, C-3'), 74.35 (d, 6.13 Hz, C-4", ^{31}P coupled), 75.86 (d, 4.60 Hz, C-2', ^{31}P coupled), 84.28 (C-4'), 87.07 (d, 4.60 Hz, C-1', ^{31}P coupled), 98.05 (C-1"), 118.82 (C-5), 143.20 (C-8), 144.37 (C-2), 148.11 (C-4), 149.77 (C-6).

6-amino-5',2",6"-tri-*O*-benzyl-3",4"-bis-*O*-(dibenzyloxyphosphoryl)-3'-*O*-(*α*-D-glucopyranosyl)-9-*β*-D-ribofuranosylpurine (34). ^{13}C NMR (100 MHz, CDCl$_3$): 68.04 (C-6"), 69.42, 69.47, 69.52, 69.55, 69.84, 69.90 (multiple peaks, *C*H$_2$Ph, ^{31}P coupled & C-5'), 70.33 (d, ^{31}P coupled, C-5"), 73.23 (*C*H$_2$Ph), 73.48 (*C*H$_2$Ph), 73.97 (t, ^{31}P coupled, C-4"), 74.08 (*C*H$_2$Ph), 74.31 (C-2'), 77.12 (C-2", ^{31}P coupled), 78.04 (C-3", ^{31}P coupled), 78.77 (C-3' or C-4'), 82.09 (C-4' or C-3'), 88.69 (C-1'), 98.28 (C-1"), 119.78 (C-5), 127.56, 127.62, 127.65, 127.85,, 127.88, 127.93, 128.05, 128.23, 128.27, 128.32, 128.37, 128.42, 128.49, 128.55, 128.58 (aromatic carbons), 135.51, 135.58, 135.70, 135.77, 135.80, 135.87, 135.90, 135.98 (ipso carbons of P-O-CH_2-Ph, ^{31}P coupled), 136.76, 137.37, 137.83 (ipso carbons of C-O-CH_2-Ph), 139.13 (C-8), 149.72 (C-4), 152.89 (C-2), 155.33 (C-6).

3'-*O*-(*α*-D-glucopyranosyl)-adenosine-3", 4"-bisphosphate (6). ^{13}C NMR (100 MHz, D_2O): 60.08 (C-6"), 60.79 (C-5'), 70.48 (C-2", ^{31}P coupled), 71.60 (d, 3.83 Hz, C-5", ^{31}P coupled), 72.83 (C-4", ^{31}P coupled), 73.48 (C-2'), 76.37 (C-3'), 77.71 (C-3", ^{31}P coupled), 83.95 (C-4'), 88.23 (C-1'), 99.02 (C-1"), 118.91 (C-5), 142.81 (C-8), 144.43 (C-2), 148.16 (C-4), 149.91 (C-6).

Allyl 2,6-di-*O*-benzyl-3,4-bis-*O*-(dibenzyloxyphosphoryl)-*α*-D-glucopyranoside (38). ^{13}C NMR (100 MHz, $CDCl_3$): 68.25 (C-6), 68.60 (O*C*H_2CH=CH_2), 69.16 (^{31}P-coupled, *C*H_2Ph), 69.30 (C-5), 69.38, 69.43 and 69.74 (^{31}P-coupled, *C*H_2Ph), 73.11 and 73.23 (*C*H_2Ph), 74.69 (^{31}P-coupled, C-4), 78.04 (C-2), 78.62 (^{31}P-coupled, C-3), 95.43 (C-1), 118.00 (OCH_2CH=*C*H_2), 127.43, 127.61, 127.76, 127.85, 127.89, 128.01, 128.02, 128.08, 128.22, 128.26, 128.31, 128.33, 128.36, 128.39 and 128.46 (Ph *C*H), 133.50 (OCH_2*C*H=CH_2), 135.80, 135.97, 136.28 and 136.29 (*ipso* carbons of P-O-CH_2-Ph, ^{31}P coupled), 138.02 and 138.19 (*ipso* carbons of C-O-CH_2-Ph).

2,6-Di-*O*-benzyl-3,4-bis-*O*-(dibenzyloxyphosphoryl)-D-glucopyranose (39). ^{13}C NMR (100 MHz, $CDCl_3$): 68.25 (C-6 in *α*-anomer), 68.81 (C-6 in *β*-anomer), 69.16 (^{31}P-coupled, C-5 in *α*-anomer), 69.17–69.83 (^{31}P-coupled, *C*H_2Ph), 72.98 and 73.23 (O*C*H_2Ph in *α*-anomer), 73.34 (O*C*H_2Ph in *β*-anomer), 73.58 (^{31}P-coupled, C-5 in *β*-anomer), 73.70 (O*C*H_2Ph in *β*-anomer), 74.49 (C-4 in *α*-anomer), 74.71 (C-4 in *β*-anomer), 78.05 (C-2 in *α*-anomer), 78.32 (C-3 in *α*-anomer), 80.53 (C-3 in *β*-anomer), 80.62 (C-2 in *β*-anomer), 90.53 (C-1 in *α*-anomer), 97.25 (C-1 in *β*-anomer), 135.72–136.20 (*ipso* carbons of POCH_2*Ph*, ^{31}P coupled), 137.53, 137.91, 138.05 and 138.29 (*ipso* carbons of OCH_2*Ph*).

D-Glucopyranose 3,4-bisphosphate (7). ^{13}C NMR (100 MHz, D_2O, Na^+salt, Chelex-100-treated, approx. 1:3 mixture of *α*- and *β*-anomers): 60.62 (C-6 in *α*-anomer), 60.70 (C-6 in *β*-

anomer), 71.21 and 71.27 (^{31}P-coupled, C-4 in α- and β-anomers), 71.89 (C-5 in α-anomer), 72.81 (C-2 in α-anomer), 75.37 (C-2 or C-5 in β-anomer), 75.42 (^{31}P-coupled, C-3 in α-anomer), 76.15 (C-2 or C-5 in β-anomer), 78.11 (^{31}P-coupled, C-3 in β-anomer), 91.89 (C-1 in α-anomer), 96.24 (C-1 in β-anomer).

D-*myo*-inositol 4,5-bisphosphate (2). ^{13}C NMR (100 MHz, Na$^+$ salt, Chelex-100-treated): 71.28 (C-1), 71.74 (C-2), 72.14 (broad,^{31}P-coupled, C-3), 72.97 (broad,^{31}P-coupled, C-6), 74.85 (^{31}P-coupled, C-4,), 76.96 (^{31}P-coupled C-5).

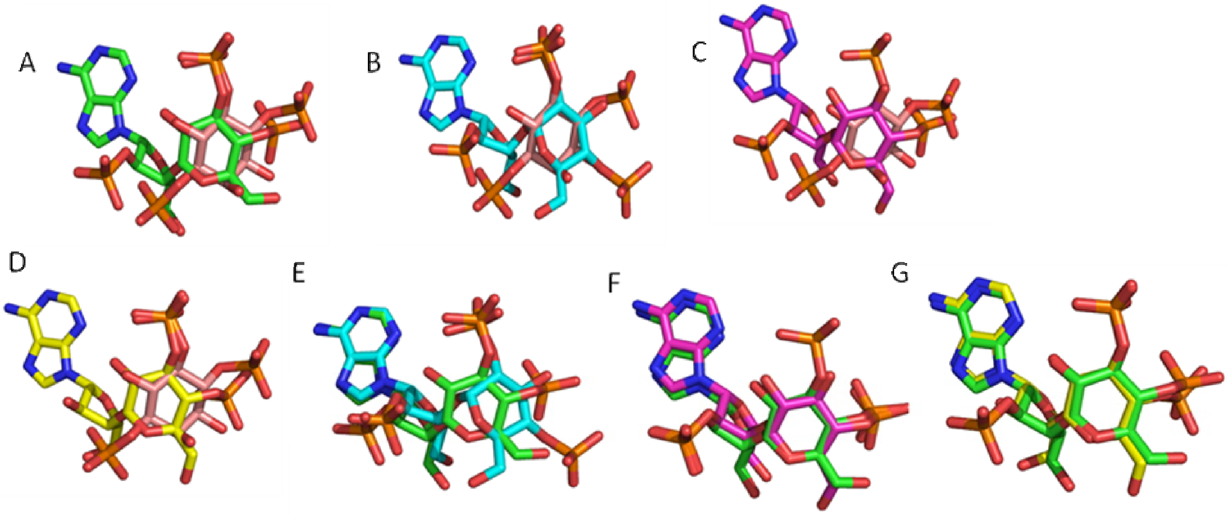

Figure S1. Overlays of IP$_3$ (buff carbons), adenophostin (green carbons), compound **40** (cyan carbons), compound **5** (purple carbons), and compound **6** (yellow carbons). A. IP$_3$ and Adenophostin. B. IP$_3$ and **40**. C. IP$_3$ and **5**. D. IP$_3$ and **6**. E. Adenophostin and **40.** F. Adenophostin and **5**. G. Adenophostin and **6**.

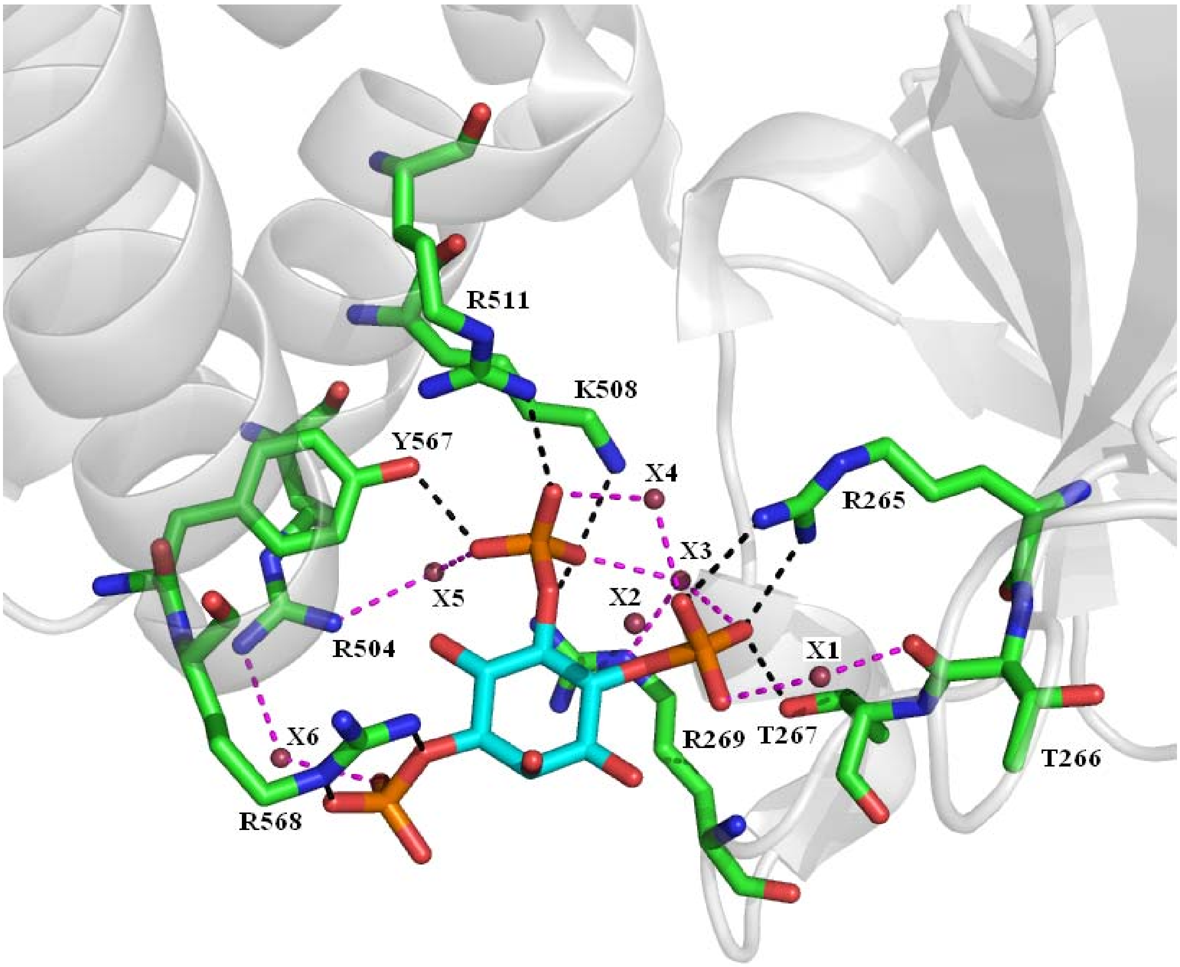

Figure S2a. IP$_3$. Hydrogen bonds between the ligand and the protein are shown as dashed lines. Purple dashed lines indicate hydrogen bonds involving a water molecule. The six water molecules are numbered X1- X6.

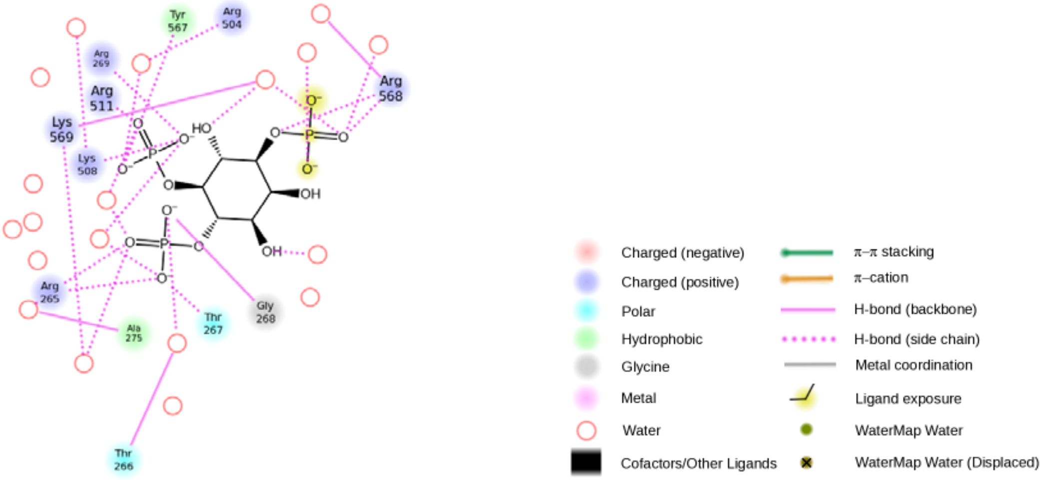

Figure S2b. Ligand Interaction Diagram and key for IP$_3$ and IP$_3$R, based on a minimised 1N4K crystal structure.

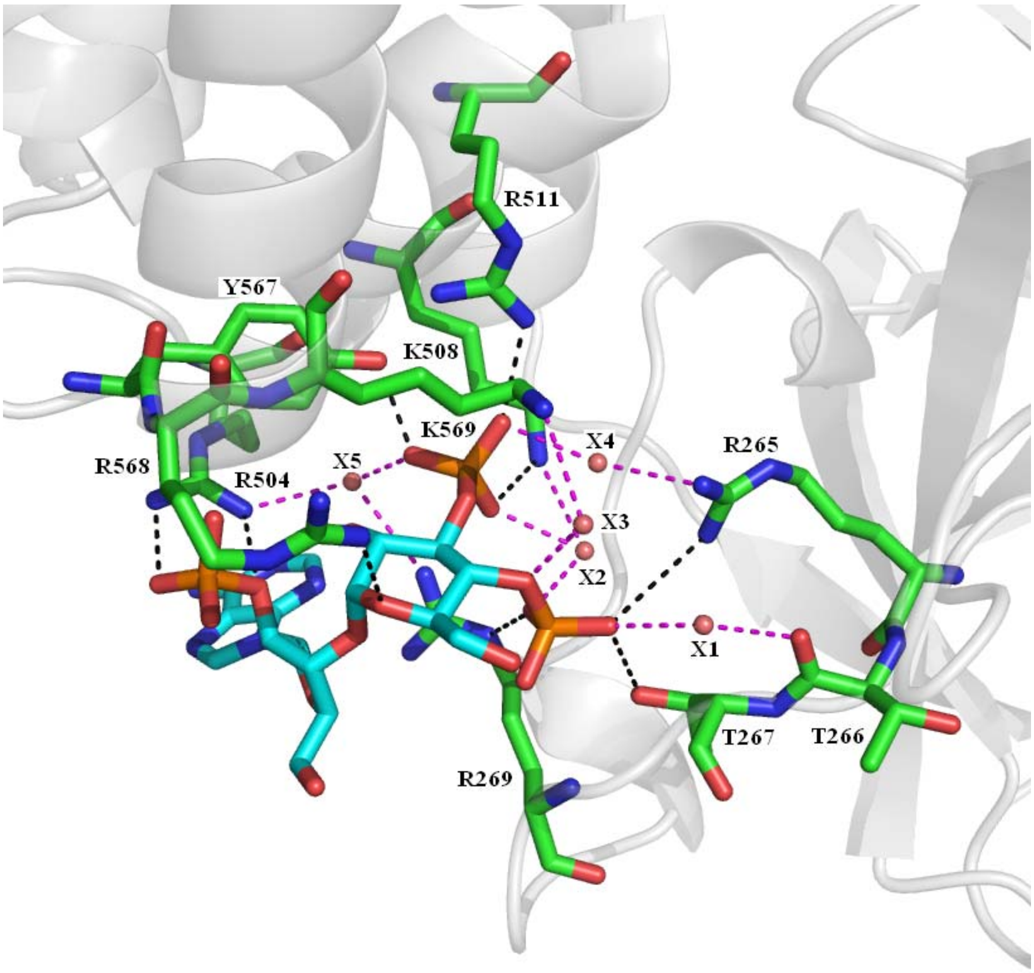

Figure S3a. Adenophostin A. Hydrogen bonds between the ligand and the protein are shown as dashed lines. Purple dashed lines indicate hydrogen bonds involving a water molecule. The five water molecules are numbered X1- X5.

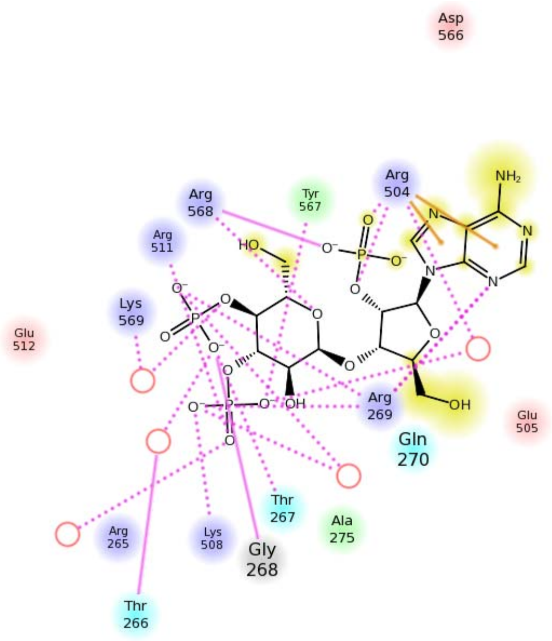

Figure S3b. Ligand Interaction Diagram for adenophostin and IP$_3$R. Based on a minimised structure of adenophostin docked into IP$_3$R

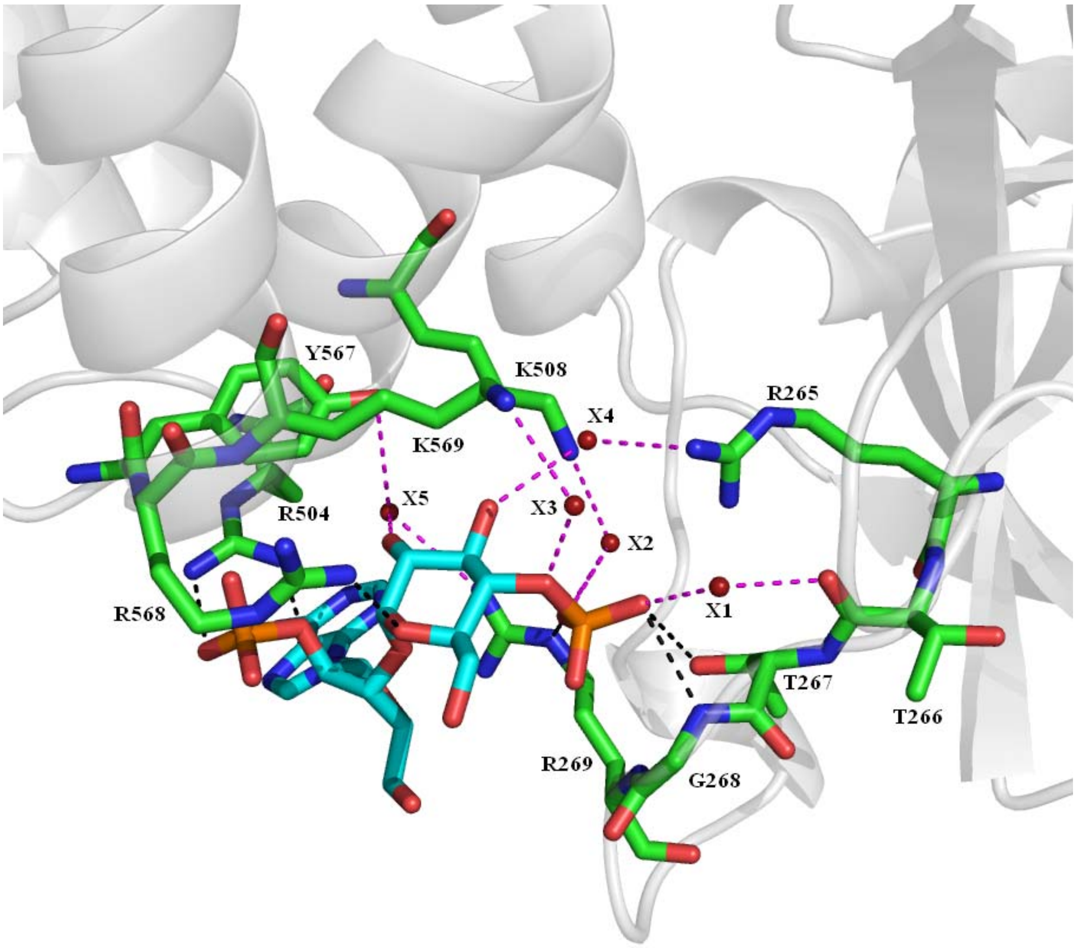

Figure S4a. Compound **5**. Hydrogen bonds between the ligand and the protein are shown as dashed lines. Purple dashed lines indicate hydrogen bonds involving a water molecule. The five water molecules are numbered X1- X5

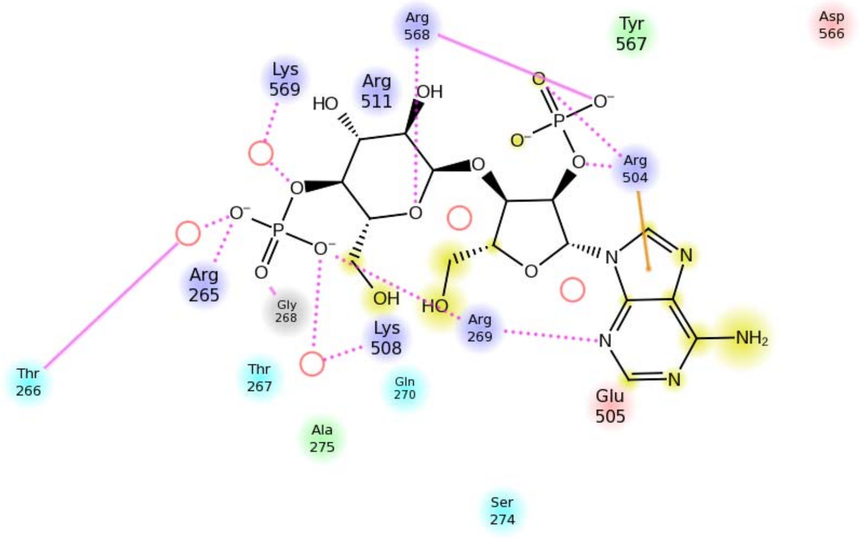

Figure S4b. Ligand Interaction Diagram for compound **5** and IP$_3$R. Based on a minimised structure of compound **5** docked into IP$_3$R.

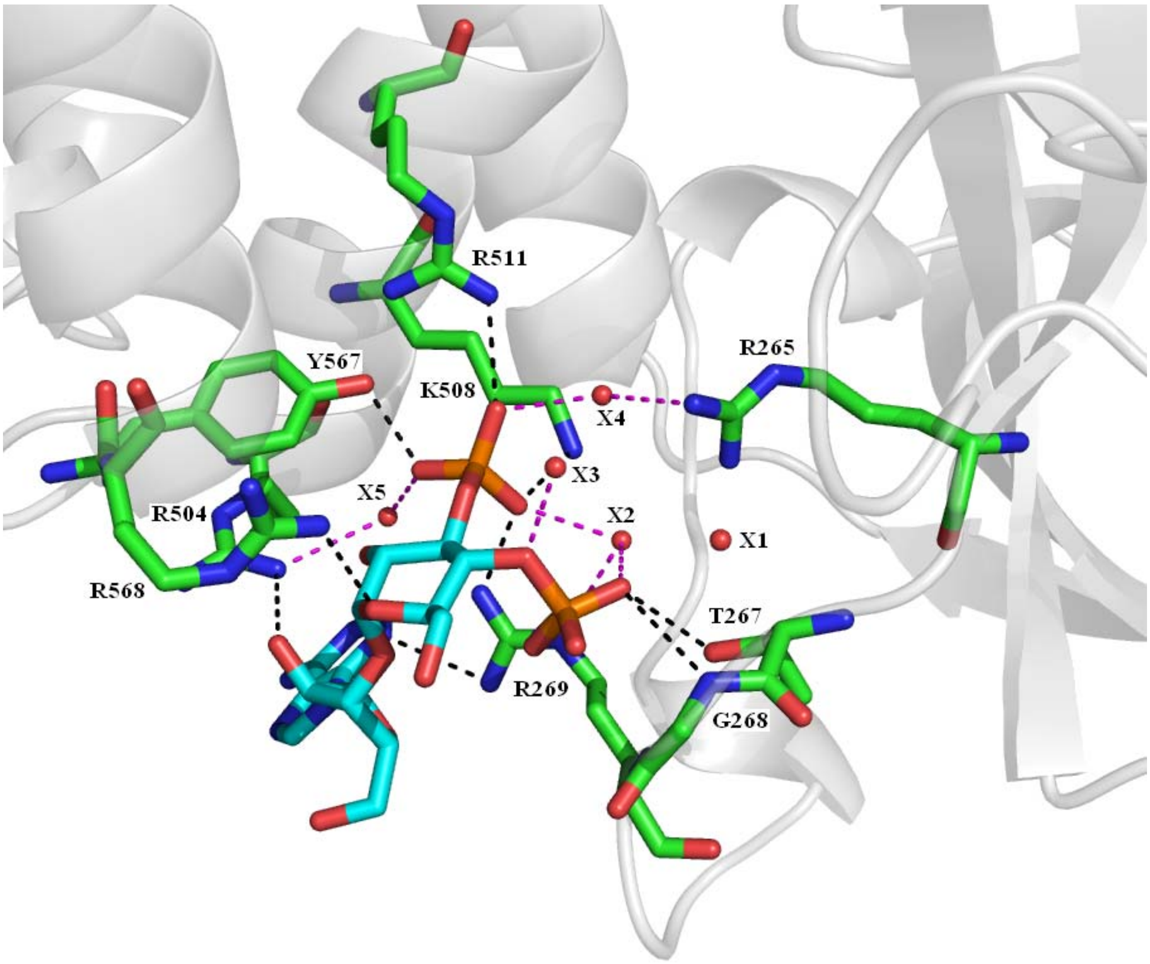

Figure S5a. Compound **6.** Hydrogen bonds between the ligand and the protein are shown as dashed lines. Purple dashed lines indicate hydrogen bonds involving a water molecule. The five water molecules are numbered X1- X5.

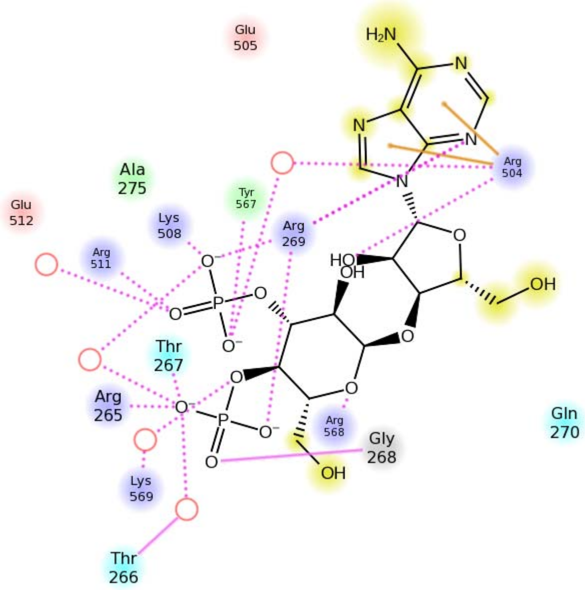

Figure S5b. Ligand Interaction Diagram for compound **6** and IP$_3$R. Based on a minimised structure of compound **6** docked into IP$_3$R.

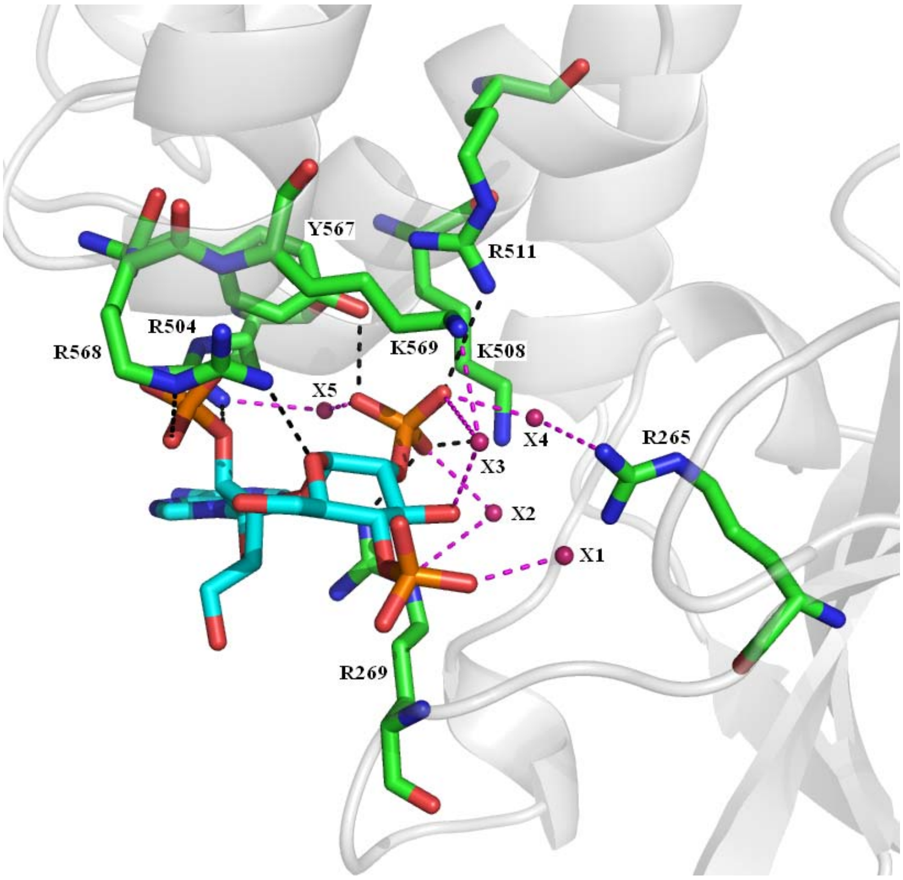

Figure S6a. Compound **40**. Hydrogen bonds between the ligand and the protein are shown as dashed lines. Purple dashed lines indicate hydrogen bonds involving a water molecule. The five water molecules are numbered X1- X5.

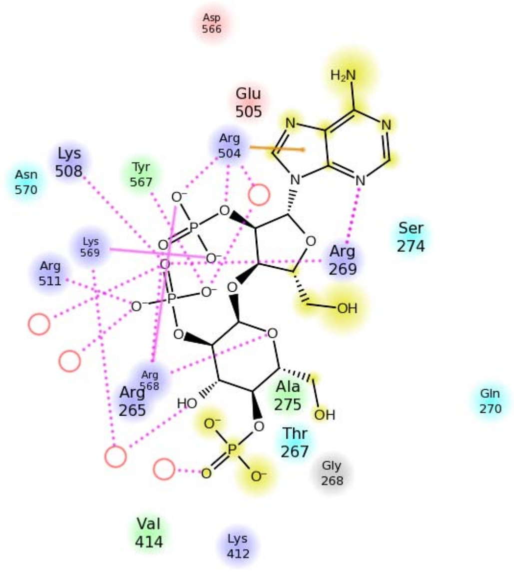

Figure S6b. Ligand Interaction Diagram for compound **40** and IP$_3$R. Based on a minimised structure of compound **40** docked into IP$_3$R.

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