Sulfonamide-containing copper(II) complexes: New insights on biophysical interactions and antibacterial activities

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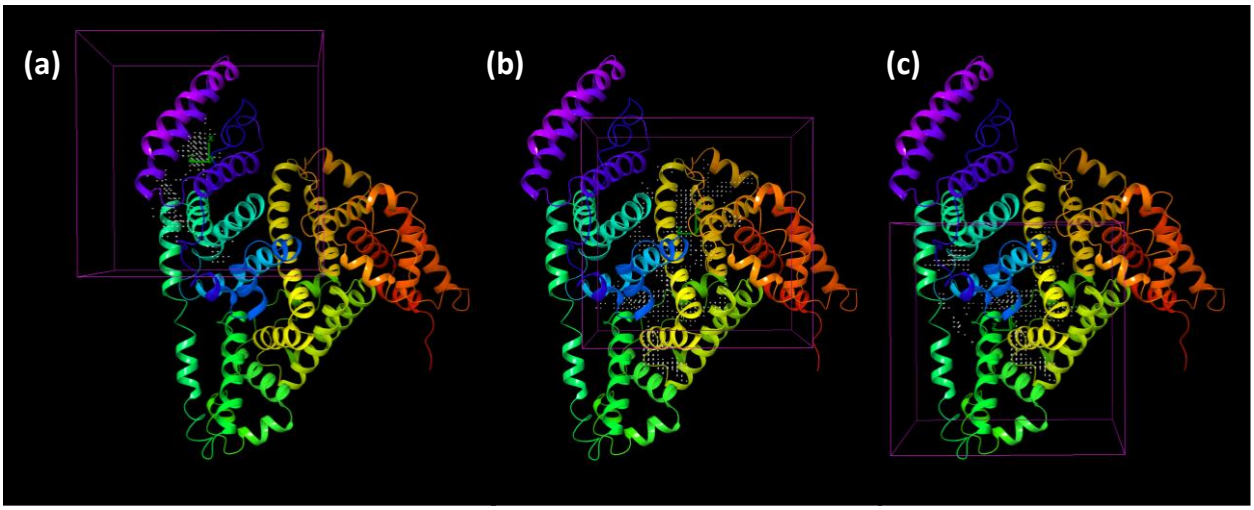

Figure S1. The three receptor grids considered for docking calculations on BSA (PDB ID 4F5S) are represented (pink cubes), along with the possible binding sites found using SiteMap (white dots).

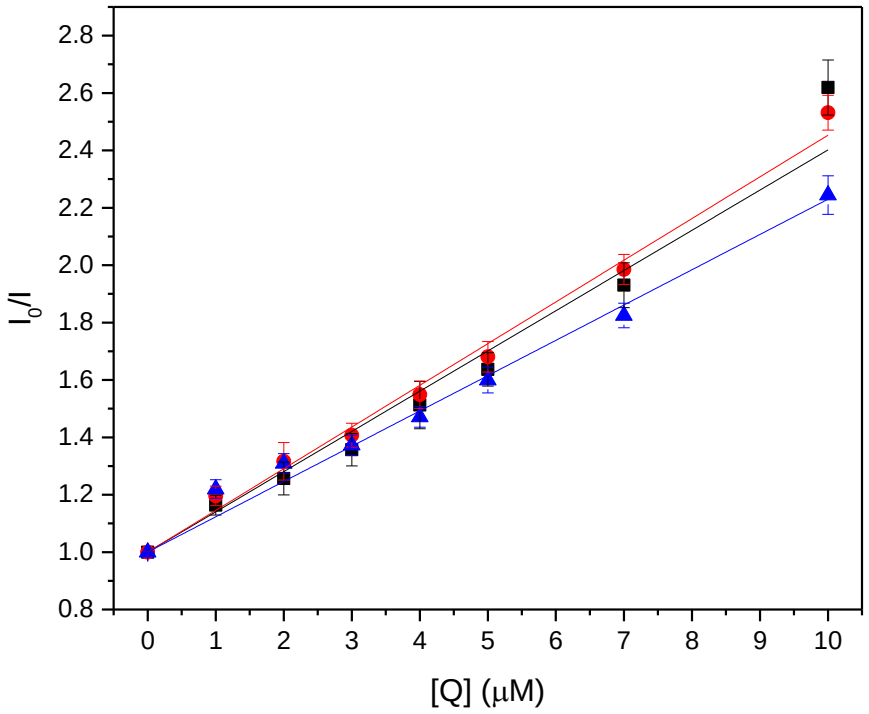

Figure S2. Stern-Volmer plots for the fluorescence quenching of BSA samples (2.5 μM) by compounds **1** (black), **2** (red) and **3** (blue).

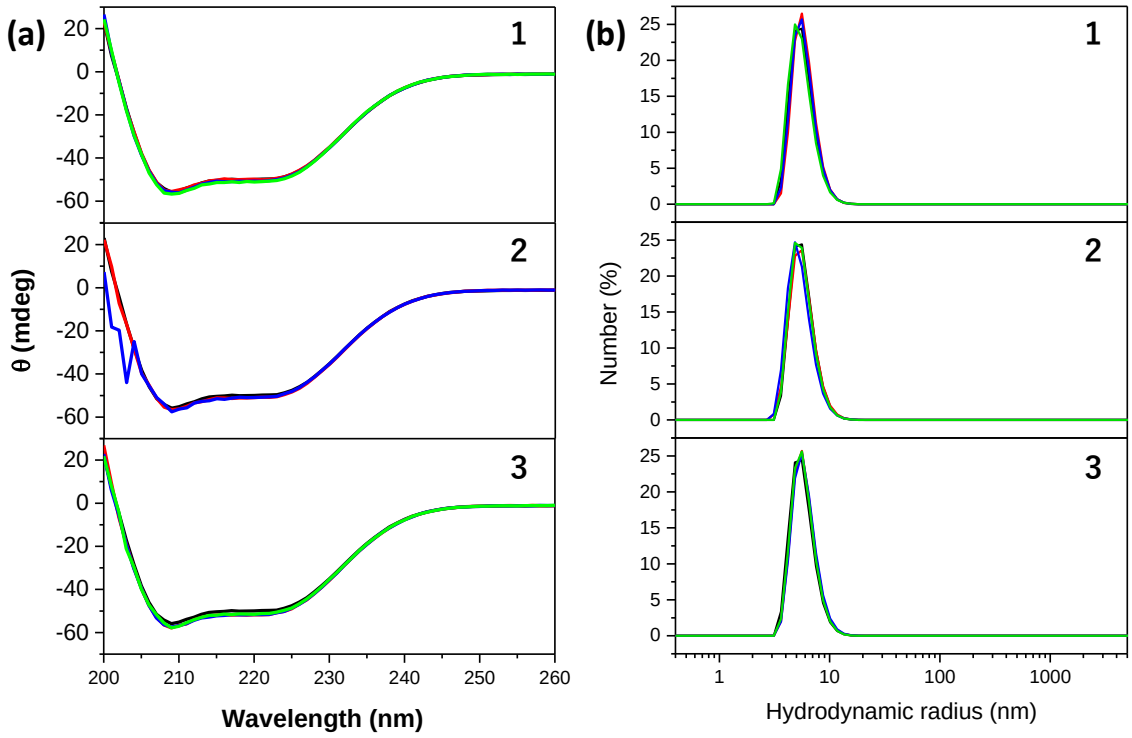

Figure S3. (a) Circular dichroism spectra of bovine serum albumin (0.5 μM) in the presence of compounds **1 - 3**. Black line: free BSA; Red line: r_i ([compound]/ [BSA]) = 1.0; Blue line: r_i = 5.0; Green line: r_i = 10.0. The interaction of BSA with compound **2** at the highest molar ratio (10.0) resulted in high noise, so the data is not shown. **(b)** Hydrodynamic radius of BSA (100 μM) in PB (pH = 7.4, 10 mM) in the presence of increasing amounts of compounds **1 - 3**. Black line: free BSA; Red line: r_i ([compound]/ [BSA]) = 0.1; Blue line: r_i = 0.5; Green line: r_i = 1.0.

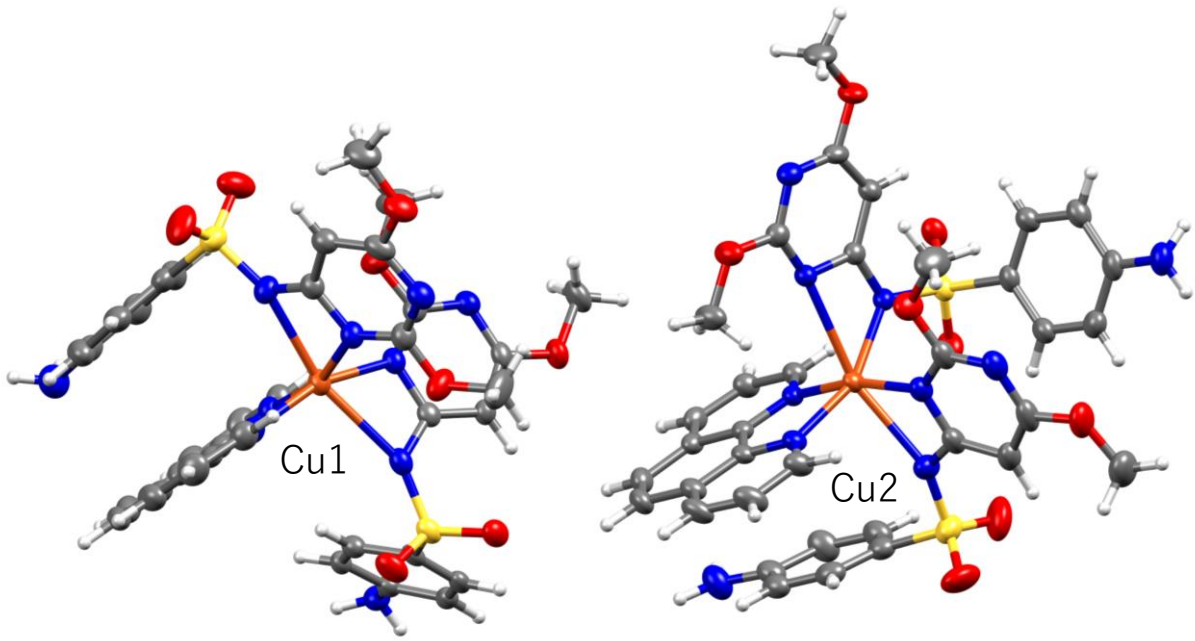

Figure S4. The asymmetric unit of compound **2**, showing two coordination isomers that were used as input for the docking calculations. The disordered water molecules are not shown, for the clarity of the figure. Thermal displacement ellipsoids were drawn at the 50 % probability level. Figure generated using CCDC entry #1812151 (JIMRIJ).

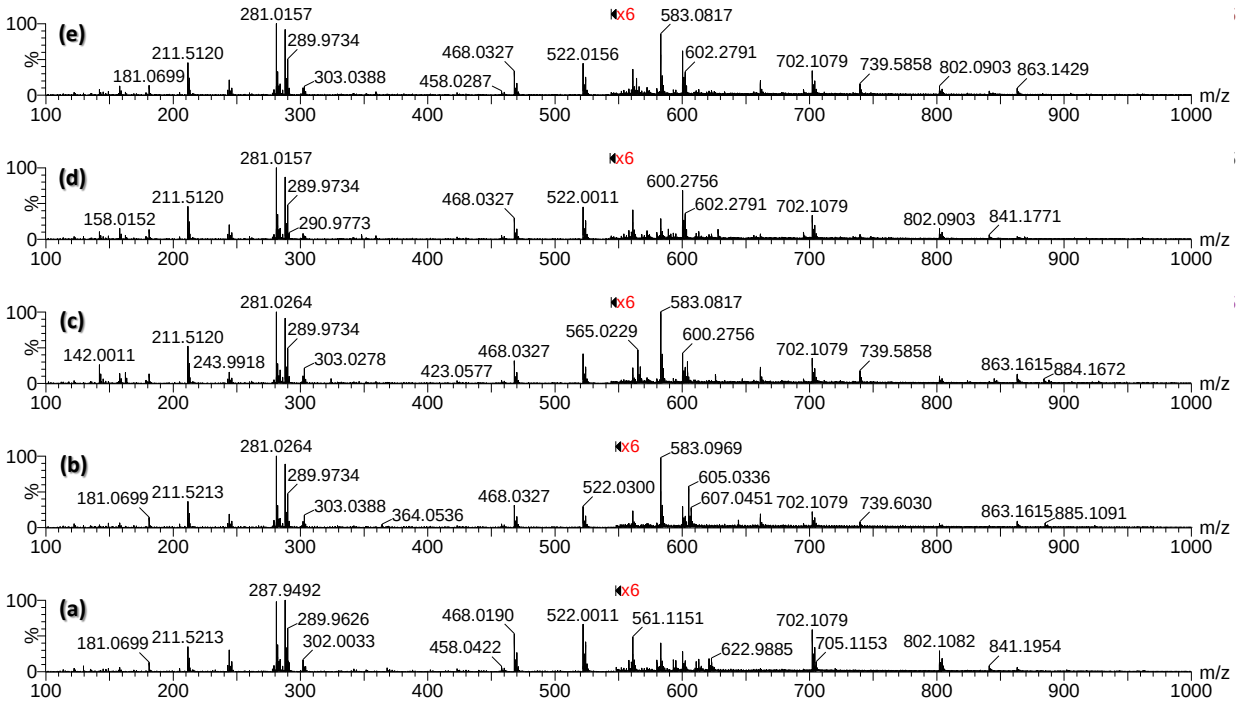

Figure S5. Mass spectra of **(a)** compound **1** and its interaction with **(b)** gmp, **(c)** cmp, **(d)** amp and **(e)** tmp. The region from 550 to 1000 *m/z* was zoomed in six-fold in order to improve visualization of low abundance species. Only spectra acquired immediately after mixing are represented, since the spectra after 24 hours of reaction did not show significant alterations.

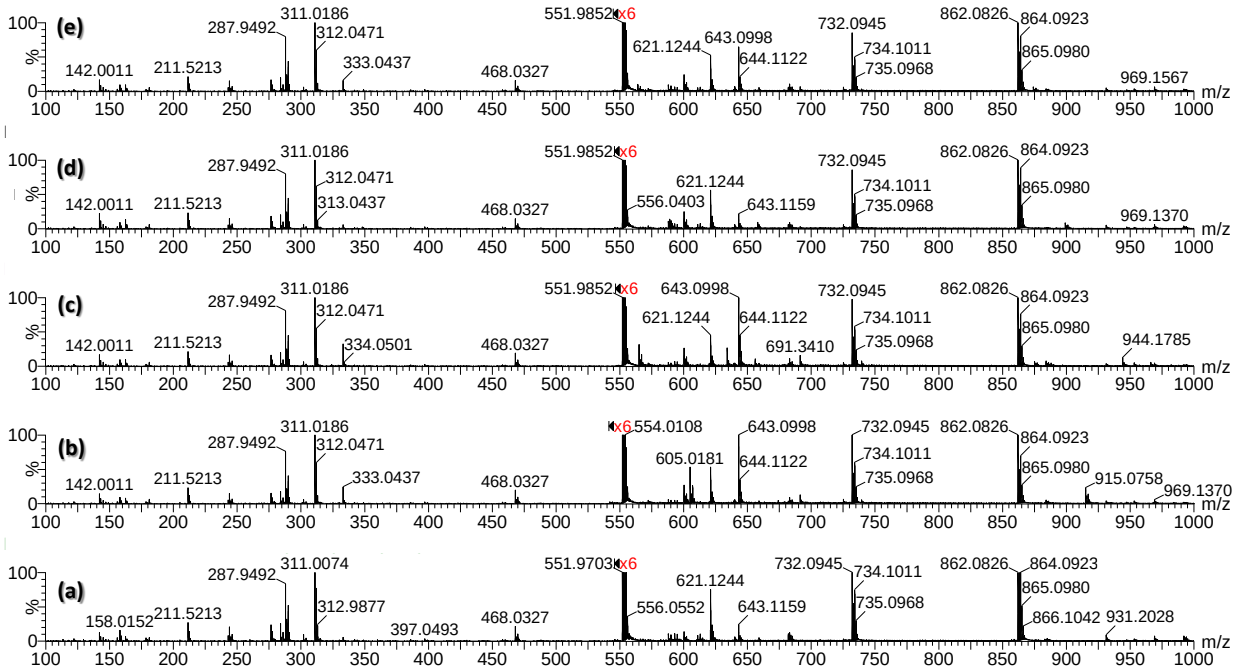

Figure S6. Mass spectra of **(a)** compound **2** and its interaction with **(b)** gmp, **(c)** cmp, **(d)** amp and **(e)** tmp. The region from 550 to 1000 *m/z* was zoomed in six-fold in order to improve visualization of low abundance species. Only spectra acquired immediately after mixing are represented, since the spectra after 24 hours of reaction did not show significant alterations.

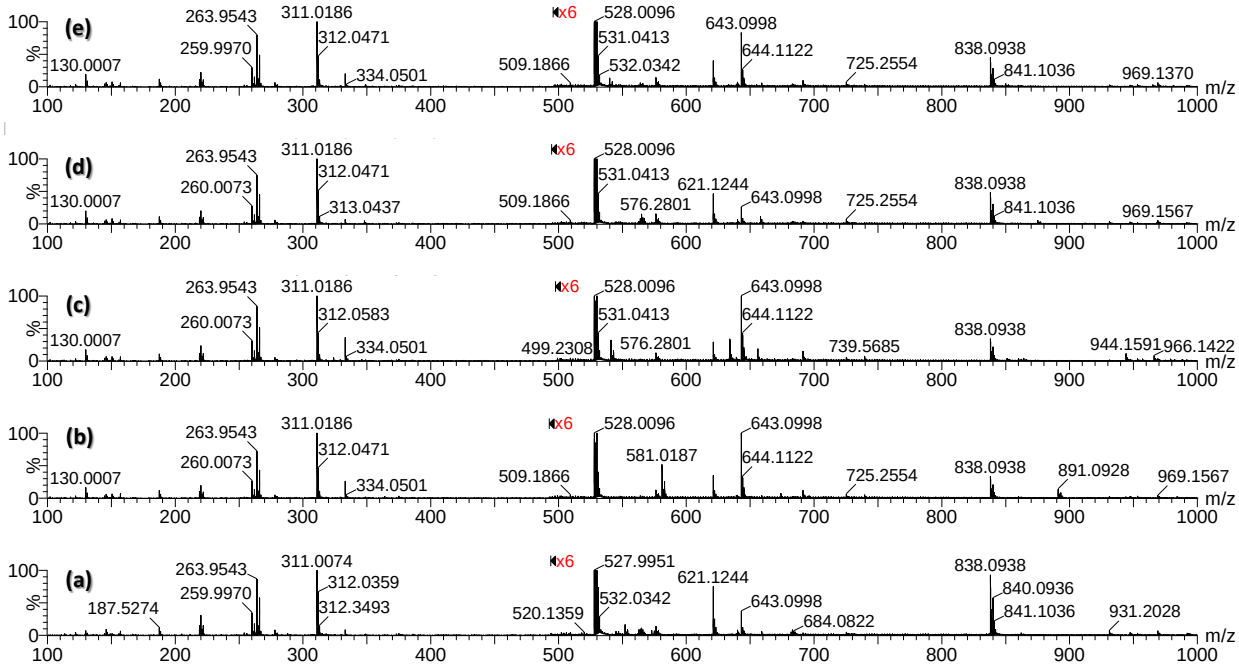

Figure S7. Mass spectra of **(a)** compound **3** and its interaction with **(b)** gmp, **(c)** cmp, **(d)** amp and **(e)** tmp. The region from 500 to 1000 *m/z* was zoomed in six-fold in order to improve visualization of low abundance species. Only spectra acquired immediately after mixing are represented, since the spectra after 24 hours of reaction did not show significant alterations.

Table S1. Observed ions and calculated *m/z* in the mass spectra of compounds **1** and its interaction with nucleotides gmp, cmp, amp and tmp. The list of ions of the interactions only list species that were not observed on the corresponding spectra of the complexes. The table lists species observed both instantly after mixing and after 24 hours, since no new signals appeared after this time. Most of the species that appeared after interaction are of low abundance (< 5%, marked with * in this table) and cannot be seen in **Figure S5**.

Species	Composition	Observed m/z	Calculated m/z
Compound **1**			
$[smtrH + H]^+$	$[C_{11}H_{12}N_4O_3S + H]^+$	281.0157	281.0708
$[(smtrH)_2 + H]^+$	$[(C_{11}H_{12}N_4O_3S)_2 + H]^+$	561.1151	561.1339
$[(smtrH)_2 + Na]^+$	$[C_{11}H_{12}N_4O_3S + Na]^+$	583.0969	583.1158
$[Cu(I)(phen)_2]^{2+}$	$[Cu(C_{12}H_8N_2)_2]^+$	211.5213	211.5336
$[Cu(II)(formate^-)(phen)]^+$	$[Cu(CHO_2)(C_{12}H_8N_2)]^+$	287.9492	287.9960
$[Cu(II)(formate^-)(phen)_2]^+$	$[Cu(CHO_2)(C_{12}H_8N_2)_2]^+$	468.0190	468.0648
$[Cu(II)(smtr^-)(phen)]^+$	$[Cu(C_{11}H_{11}N_4O_3S)(C_{12}H_8N_2)]^+$	522.0011	522.0535
$[Cu(II)(smtr^-)(phen)_2]^+$	$[Cu(C_{11}H_{11}N_4O_3S)(C_{12}H_8N_2)_2]^+$	702.1079	702.1223
$[Cu(II)(smtr^-)_2(phen) + H]^+$	$[Cu(C_{11}H_{11}N_4O_3S)_2(C_{12}H_8N_2) + H]^+$	802.1082	802.1165
Compound **1** + **gmp**			
$*[gmp + H]^+$	$[C_{10}H_{14}N_5O_8P + H]^+$	364.0536	364.0658
$*[(gmp)(SMTRH) + H]^+$	$[(C_{10}H_{14}N_5O_8P)(C_{11}H_{12}N_4O_3S) + H]^+$	644.1283	644.1288
$[Cu(II)(gmp^-)(phen)]^+$	$[Cu(C_{10}H_{13}N_5O_8P)(C_{12}H_8N_2)]^+$	605.0336	605.0485
$*[Cu(II)(smtr^-)(gmp)(phen)]^+$	$[Cu(C_{11}H_{11}N_4O_3S)(C_{10}H_{14}N_5O_8P)(C_{12}H_8N_2)]$	885.1091	885.1115
Compound **1** + **cmp**			
$[cmp + H]^+$	$[C_9H_{14}N_3O_8P + H]^+$	324.0429	324.0597
$[(cmp)(smtrH) + H]^+$	$[(C_9H_{14}N_3O_8P)(C_{11}H_{12}N_4O_3S) + H]^+$	604.0992	604.1227
$*[(cmp)(smtrH) + Na]^+$	$[(C_9H_{14}N_3O_8P)(C_{11}H_{12}N_4O_3S) + Na]^+$	626.0910	626.1046
$[Cu(II)(cmp^-)(phen)]^+$	$[Cu(C_9H_{13}N_3O_8P)(C_{12}H_8N_2)]^+$	565.0229	565.0424
$*[Cu(II)(smtr^-)(cmp)(phen)]^+$	$[Cu(C_{11}H_{11}N_4O_3S)(C_9H_{14}N_3O_8P)(C_{12}H_8N_2)]$	845.0762	845.1054
Compound **1** + **amp**			
$[amp + H]^+$	$[C_{10}H_{14}N_5O_7P + H]^+$	348.0630	348.0709
$*[(amp)_2 + H]^+$	$[(C_{10}H_{14}N_5O_7P)_2 + H]^+$	695.2603	695.1340
$*[Cu(II)(amp^-)(phen)]^+$	$[Cu(C_{10}H_{13}N_5O_7P)(C_{12}H_8N_2)]^+$	589.0311	589.0536
$*[Cu(II)(smtr^-)(amp)(phen)]^+$	$[Cu(C_{11}H_{11}N_4O_3S)(C_{10}H_{14}N_5O_7P)(C_{12}H_8N_2)]$	869.0864	869.1166
Compound **1** + **tmp**			
$*[Cu(II)(tmp^-)(phen)]^+$	$[Cu(C_{10}H_{14}N_2O_8P)(C_{12}H_8N_2)]^+$	564.0296	564.0471
$*[Cu(II)(smtr^-)(tmp)(phen)]^+$	$[Cu(C_{11}H_{11}N_4O_3S)(C_{10}H_{15}N_2O_8P)(C_{12}H_8N_2)]^+$	844.1006	844.1101

Table S2. Observed ions and calculated *m/z* in the mass spectra of compounds **2** and its interaction with nucleotides gmp, cmp, amp and tmp. The list of ions of the interactions only list species that were not observed on the corresponding spectra of the complexes. The table lists species observed both instantly after mixing and after 24 hours, since no new signals appeared after this time. Most of the species that appeared after interaction are of low abundance (< 5%, marked with * in this table) and cannot be seen in **Figure S6**.

Species	**Composition**	**Observed m/z**	**Calculated m/z**
Compound **2**			
$[sdmxH + H]^+$	$[C_{12}H_{14}N_4O_4S + H]^+$	311.0074	311.0814
$[(sdmxH)_2 + H]^+$	$[(C_{12}H_{14}N_4O_4S)_2 + H]^+$	621.1244	621.1550
$[(sdmxH)_2 + Na]^+$	$[(C_{12}H_{14}N_4O_4S)_2 + Na]^+$	643.1159	643.1369
$[Cu(I)(phen)_2]^{2+}$	$[Cu(C_{12}H_8N_2)_2]^+$	211.5213	211.5336
$[Cu(II)(formate^-)(phen)]^+$	$[Cu(CHO_2)(C_{12}H_8N_2)]^+$	287.9492	287.9960
$[Cu(II)(formate^-)(phen)_2]^+$	$[Cu(CHO_2)(C_{12}H_8N_2)_2]^+$	468.0327	468.0648
$[Cu(II)(sdmx^-)(phen)]^+$	$[Cu(C_{12}H_{13}N_4O_4S)(C_{12}H_8N_2)]^+$	551.9703	552.0641
$[Cu(II)(sdmx^-)(phen)_2]^+$	$[Cu(C_{12}H_{13}N_4O_4S)(C_{12}H_8N_2)_2]^+$	732.0945	732.1329
$[Cu(II)(sdmx^-)_2(phen) + H]^+$	$[Cu(C_{12}H_{13}N_4O_4S)_2(C_{12}H_8N_2) + H]^+$	862.0826	862.1377
Compound **2** + **gmp**			
$*[gmp + H]^+$	$[C_{10}H_{14}N_5O_8P + H]^+$	364.0536	364.0658
$*[(gmp)(sdmxH) + H]^+$	$[(C_{10}H_{14}N_5O_8P)(C_{12}H_{14}N_4O_4S) + H]^+$	674.1290	674.1394
$[Cu(II)(gmp^-)(phen)]^+$	$[Cu(C_{10}H_{13}N_5O_8P)(C_{12}H_8N_2)]^+$	605.0181	605.0485
$*[Cu(II)(sdmx^-)(gmp)(phen)]^+$	$[Cu(C_{12}H_{13}N_4O_4S)(C_{10}H_{14}N_5O_8P)(C_{12}H_8N_2)]$	915.0758	915.1221
Compound **2** + **cmp**			
$*[cmp + H]^+$	$[C_9H_{14}N_3O_8P + H]^+$	324.0429	324.0597
$*[(cmp)(sdmxH) + H]^+$	$[(C_9H_{14}N_3O_8P)(C_{12}H_{14}N_4O_4S) + H]^+$	634.1043	634.1332
$*[(cmp)(sdmxH) + Na]^+$	$[(C_9H_{14}N_3O_8P)(C_{12}H_{14}N_4O_4S) + Na]^+$	656.0953	656.1152
$[Cu(II)(cmp^-)(phen)]^+$	$[Cu(C_9H_{13}N_3O_8P)(C_{12}H_8N_2)]^+$	565.0229	565.0424
$*[Cu(II)(sdmx^-)(cmp)(phen)]^+$	$[Cu(C_{12}H_{13}N_4O_4S)(C_9H_{14}N_3O_8P)(C_{12}H_8N_2)]$	875.0750	875.1160
Compound **2** + **amp**			
$*[amp + H]^+$	$[C_{10}H_{14}N_5O_7P + H]^+$	348.0511	348.0709
$*[(amp)(sdmxH) + H]^+$	$[(C_{10}H_{14}N_5O_7P)(C_{12}H_{14}N_4O_4S) + H]^+$	658.1249	658.1445
$*[Cu(II)(amp^-)(phen)]^+$	$[Cu(C_{10}H_{13}N_5O_7P)(C_{12}H_8N_2)]^+$	589.0311	589.0536
$*[Cu(II)(sdmx^-)(amp)(phen)]^+$	$[Cu(C_{12}H_{13}N_4O_4S)(C_{10}H_{14}N_5O_7P)(C_{12}H_8N_2)]$	899.0897	899.1272
Compound **2** + **tmp**			
$*[Cu(II)(tmp^-)(phen)]^+$	$[Cu(C_{10}H_{14}N_2O_8P)(C_{12}H_8N_2)]^+$	564.0296	564.0471
$*[Cu(II)(sdmx^-)(tmp)(phen)]^+$	$[Cu(C_{12}H_{13}N_4O_4S)(C_{10}H_{15}N_2O_8P)(C_{12}H_8N_2)]^+$	874.0822	874.1207

Table S3. Observed ions and calculated *m/z* in the mass spectra of compounds **3** and its interaction with nucleotides gmp, cmp, amp and tmp. The list of ions of the interactions only list species that were not observed on the corresponding spectra of the complexes. The table lists species observed both instantly after mixing and after 24 hours, since no new signals appeared after this time. Most of the species that appeared after interaction are of low abundance (< 5%, marked with * in this table) and cannot be seen in **Figure S7**.

Species	**Composition**	**Observed m/z**	**Calculated m/z**
Compound **3**			
$[sdmxH + H]^+$	$[C_{12}H_{14}N_4O_4S + H]^+$	311.0074	311.0814
$[(sdmxH)_2 + H]^+$	$[(C_{12}H_{14}N_4O_4S)_2 + H]^+$	621.1244	621.1550
$[(sdmxH)_2 + Na]^+$	$[(C_{12}H_{14}N_4O_4S)_2 + Na]^+$	643.0998	643.1369
$[Cu(I)(bipy)_2]^{2+}$	$[Cu(C_{10}H_8N_2)_2]^+$	187.5274	187.5336
$[Cu(II)(formate^-)(bpy)]^+$	$[Cu(CHO_2)(C_{10}H_8N_2)]^+$	263.9543	263.9960
$[Cu(II)(sdmx^-)(bpy)]^+$	$[Cu(C_{12}H_{13}N_4O_4S)(C_{10}H_8N_2)]^+$	527.9951	528.0641
$[Cu(II)(sdmx^-)_2(bpy) + H]^+$	$[Cu(C_{12}H_{13}N_4O_4S)_2(C_{10}H_8N_2) + H]^+$	838.0938	838.1377
Compound **3** + **gmp**			
$*[gmp + H]^+$	$[C_{10}H_{14}N_5O_8P + H]^+$	364.0416	364.0658
$*[(gmp)(sdmxH) + H]^+$	$[(C_{10}H_{14}N_5O_8P)(C_{12}H_{14}N_4O_4S) + H]^+$	674.1126	674.1394
$[Cu(II)(gmp^-)(bpy)]^+$	$[Cu(C_{10}H_{13}N_5O_8P)(C_{10}H_8N_2)]^+$	581.0187	581.0485
$*[Cu(II)(sdmx^-)(gmp)(bpy)]^+$	$[Cu(C_{12}H_{13}N_4O_4S)(C_{10}H_{14}N_5O_8P)(C_{10}H_8N_2)]$	891.0928	891.1221
Compound **3** + **cmp**			
$[cmp + H]^+$	$[C_9H_{14}N_3O_8P + H]^+$	324.0429	324.0597
$[(cmp)(sdmxH) + H]^+$	$[(C_9H_{14}N_3O_8P)(C_{12}H_{14}N_4O_4S) + H]^+$	634.1043	634.1332
$*[(cmp)(sdmxH) + Na]^+$	$[(C_9H_{14}N_3O_8P)(C_{12}H_{14}N_4O_4S) + Na]^+$	656.0953	656.1152
$[Cu(II)(cmp^-)(bpy)]^+$	$[Cu(C_9H_{13}N_3O_8P)(C_{10}H_8N_2)]^+$	541.0131	541.0424
$*[Cu(II)(sdmx^-)(cmp)(bpy)]^+$	$[Cu(C_{12}H_{13}N_4O_4S)(C_9H_{14}N_3O_8P)(C_{10}H_8N_2)]$	851.0711	851.1160
Compound **3** + **amp**			
$*[amp + H]^+$	$[C_{10}H_{14}N_5O_7P + H]^+$	348.0511	348.0709
$*[(amp)(sdmxH) + H]^+$	$[(C_{10}H_{14}N_5O_7P)(C_{12}H_{14}N_4O_4S) + H]^+$	658.1249	658.1445
$*[Cu(II)(amp^-)(bpy)]^+$	$[Cu(C_{10}H_{13}N_5O_7P)(C_{10}H_8N_2)]^+$	565.0229	565.0536
$*[Cu(II)(sdmx^-)(amp)(bpy)]^+$	$[Cu(C_{12}H_{13}N_4O_4S)(C_{10}H_{14}N_5O_7P)(C_{10}H_8N_2)]$	875.0937	875.1272
Compound **3** + **tmp**			
$*[Cu(II)(tmp^-)(bpy)]^+$	$[Cu(C_{10}H_{14}N_2O_8P)(C_{10}H_8N_2)]^+$	540.0264	540.0471
$*[Cu(II)(sdmx^-)(tmp)(bpy)]^+$	$[Cu(C_{12}H_{13}N_4O_4S)(C_{10}H_{15}N_2O_8P)(C_{10}H_8N_2)]^+$	850.0920	850.1207