Supporting information

A New Bifunctional Chelator p-SCN-PhPr-NE3TA for Copper-64: Synthesis, Peptidomimetic Conjugation, Radiolabeling and Evaluation for PET Imaging

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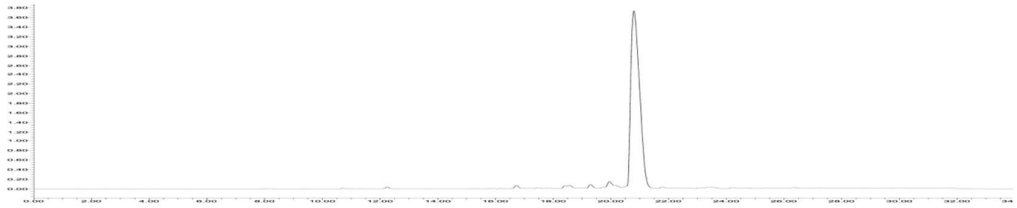


Figure S1. HPLC spectra of *p*-SCN-PhPr-NE3TA (Eluting condition: 0~2 min 0%B, 2~22 min from 0%B to 50%B, 22~23 min from 50%B to 90%B, 23~28 min 90%B, 28~29 min from 90%B to 0%B, 29~34 min 0%B)

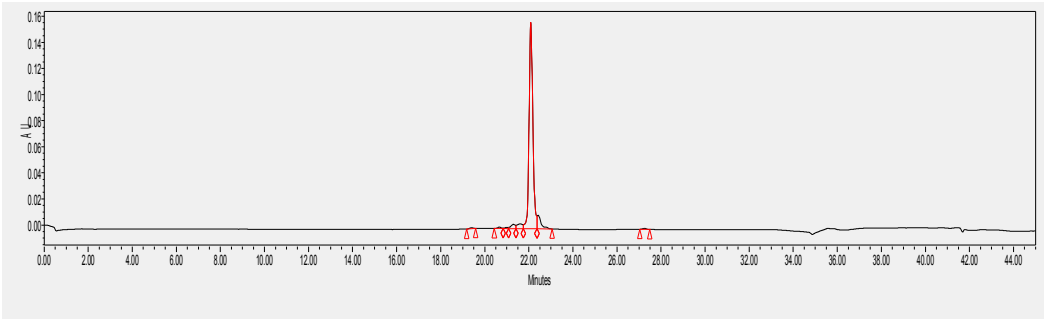


Figure S2. HPLC spectra of NE3TA-PEG$_4$-LLP2A

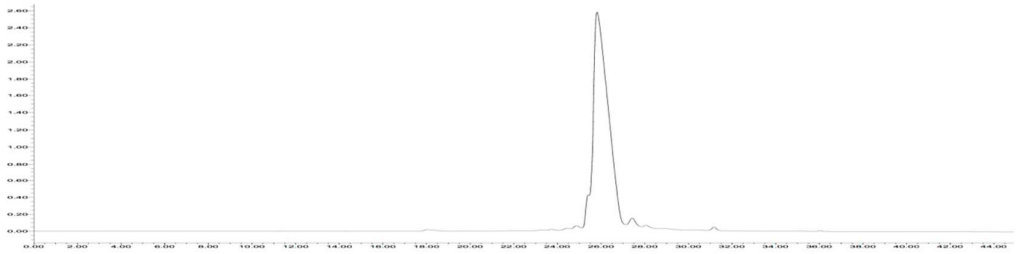


Figure S3. HPLC spectra of NOTA-PEG$_4$-LLP2A

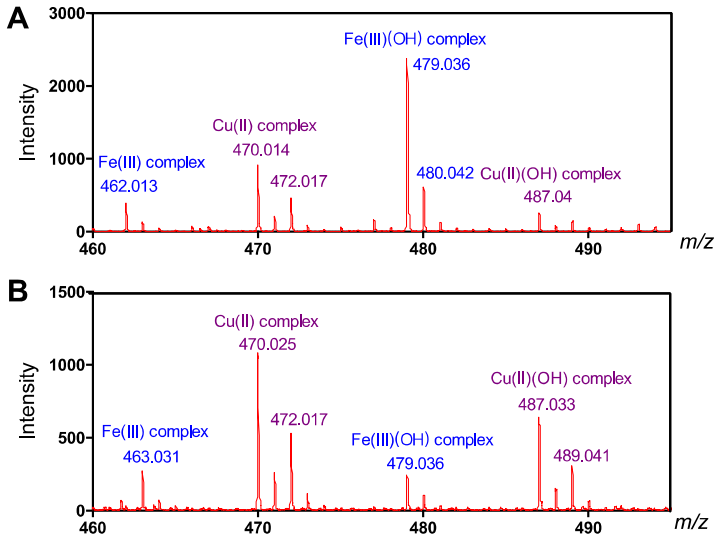


Figure S4. MS spectra of cold labeling solutions. Labeling conditions: A). *p*-NH$_2$-Bn-NOTA, Cu(II) and Fe(III) were mixed at molar ratios 6:1:1 in 0.1 M pH 4 NH$_4$OAc buffer and incubated at 70 ^{o}C for 30 min. B).

p-NH_2-Bn-NOTA, Cu(II) and Fe(III) were mixed at molar ratios 1:1:10 in 0.1 M pH 4 NH_4OAc buffer and incubated at room temperature for 30 min

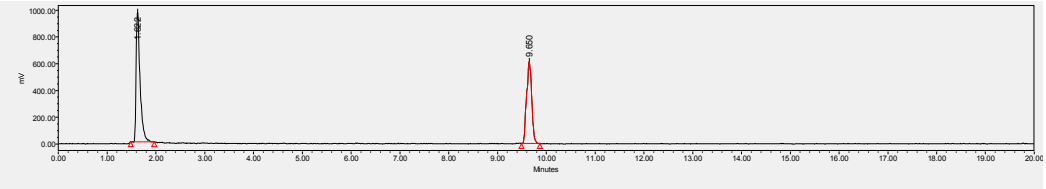


Figure S5. Labeling result of 100 pmol NOTA-PEG_4-LLP2A with 400 µCi ^{64}Cu in 0.1 M NH_4OAc buffer (pH 4.0) after incubation at 37 ^oC for 30 min

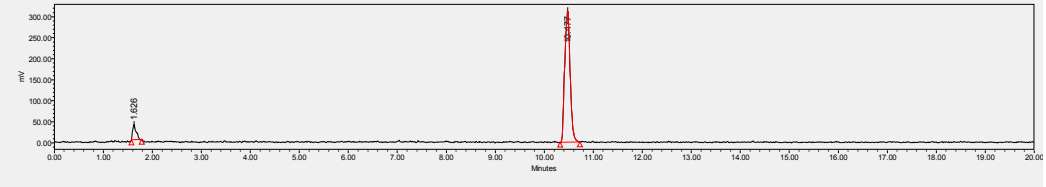


Figure S6. Labeling result of 100 pmol NE3TA-PEG_4-LLP2A with 400 µCi ^{64}Cu in 0.1 M NH_4OAc buffer (pH 4.0) after incubation at 37 ^oC for 30 min

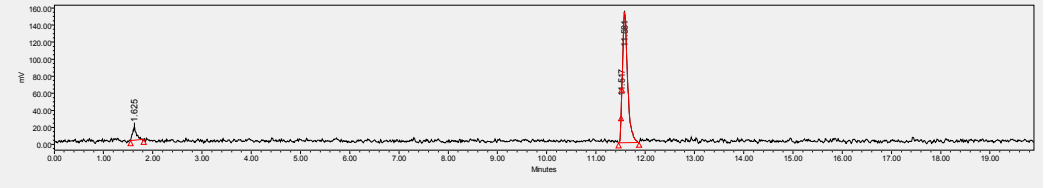


Figure S7. Radio-HPLC spectra of ^{64}Cu-NOTA-LLP2A after incubation in human serum at 37^oC for 24 hrs

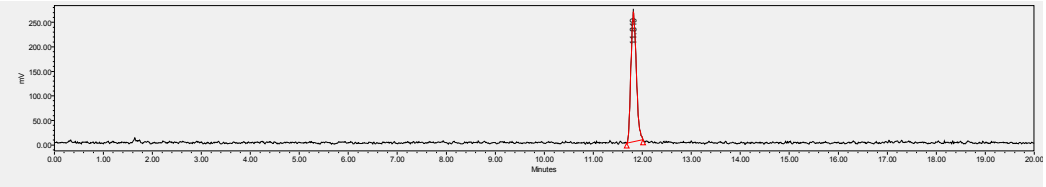
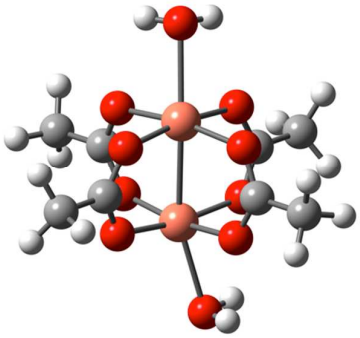


Figure S8. Radio-HPLC spectra of ^{64}Cu-NOTA-LLP2A after incubation in human serum at 37^oC for 24 hrs

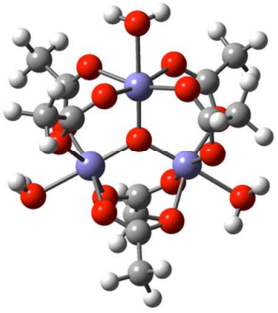
DFT Computational method.

All calculations were performed using Gaussian09 suite of program.[1] Density functional theory method was used, employing uB3LYP hybrid functional.[2] Geometry optimization was done using a combined basis set 6-31+G(d,p). Frequency calculation was done at the same level of theory as geometry optimization, to confirm the stationary

points to be minima. Single point energy calculations were done using B3LYP method at a larger basis set 6-311++G(d,p). Solvent effect was accounted for using self-consistent reaction field (SCRF) method, using SMD model and UAKS radii.[3] Water was used as the solvent.



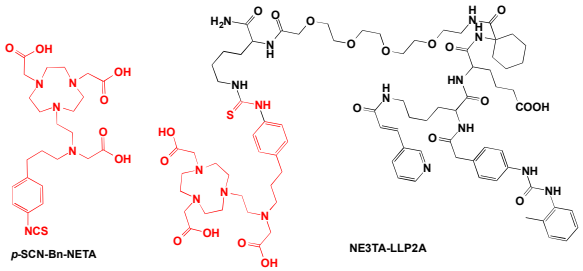
$Cu_2(OAc)_4(H_2O)_2$



$Fe_3(\mu\text{-}O)(OAc)_6(H_2O)_3$

DFT computation data:

a): Our developed p-SCN-PhPr-NETA and the targeting probe conjugated tracer



Fe NE3TA-LLP2A_1.log

Zero-point correction=	0.634229 (A. U.)
Thermal correction to Energy=	0.670301
Thermal correction to Enthalpy=	0.671245
Thermal correction to Gibbs Free Energy=	0.567699
Sum of electronic and zero-point Energies=	-3416.183938
Sum of electronic and thermal Energies=	-3416.147867
Sum of electronic and thermal Enthalpies=	-3416.146922
Sum of electronic and thermal Free Energies=	-3416.250468

SCF Done: E(UB3LYP) = -3417.43827010 A.U.

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	26	0	1.796126	0.482227	0.285898
2	7	0	3.444227	0.944231	-0.804507
3	7	0	1.158409	2.364957	-0.127103
4	6	0	2.392784	3.177493	-0.323683
5	6	0	3.353920	2.389961	-1.220357
6	7	0	0.913371	-0.077344	-1.519462
7	6	0	1.986306	0.014638	-2.574182
8	6	0	3.406184	0.026975	-1.974642
9	6	0	0.324809	2.359211	-1.378552
10	6	0	-0.156814	0.955835	-1.714993
11	6	0	2.300611	-3.673784	0.142953
12	6	0	2.944910	-2.306349	0.431716
13	8	0	4.177385	-2.209686	0.424278
14	8	0	2.082635	-1.357357	0.617533
15	6	0	4.573731	0.752680	0.155404
16	6	0	4.110905	1.218300	1.544467
17	8	0	4.907695	1.587830	2.388799
18	8	0	2.799456	1.189265	1.710539
19	6	0	-0.383097	1.516096	1.607189
20	6	0	0.362013	2.750938	1.077017
21	8	0	0.158618	0.380043	1.298281
22	8	0	-1.410976	1.664926	2.271437
23	6	0	-0.181954	-3.766053	0.361238
24	6	0	-1.369372	-4.434854	-0.352941
25	6	0	-3.197671	-2.913443	0.548178
26	6	0	-3.681263	-2.228369	-0.575921
27	6	0	0.167296	-1.403531	-1.545571

28	6	0	0.893170	-2.780209	-1.669975
29	7	0	0.997703	-3.647969	-0.498528
30	6	0	-2.701116	-4.340127	0.431308
31	6	0	-3.084764	-2.192631	1.745185
32	6	0	-3.960104	-0.860816	-0.536973
33	7	0	-3.838846	1.277358	0.720827
34	6	0	-4.341811	2.121611	-0.233391
35	6	0	-3.374179	-0.831666	1.808105
36	6	0	-3.775134	-0.143368	0.654663
37	16	0	-3.505237	3.508851	-0.737313
38	7	0	-5.557287	1.819800	-0.758682
39	6	0	-6.583940	0.988268	-0.134694
40	1	0	2.833363	3.356686	0.655644
41	1	0	2.156194	4.148916	-0.777779
42	1	0	3.019374	2.429438	-2.258547
43	1	0	4.350296	2.843359	-1.192702
44	1	0	1.815523	0.925001	-3.154943
45	1	0	1.898431	-0.816493	-3.280710
46	1	0	3.695781	-0.960036	-1.614270
47	1	0	4.128879	0.329768	-2.746338
48	1	0	0.925175	2.768804	-2.193956
49	1	0	-0.547234	3.010680	-1.254959
50	1	0	-0.975779	0.680417	-1.050715
51	1	0	-0.540073	0.926808	-2.744315
52	1	0	3.020152	-4.219589	-0.481023
53	1	0	2.229518	-4.224319	1.086576
54	1	0	5.468731	1.300191	-0.156977
55	1	0	4.788207	-0.318186	0.232114
56	1	0	1.055949	3.069797	1.857820
57	1	0	-0.342204	3.557650	0.855913
58	1	0	0.104707	-4.392482	1.212827
59	1	0	-0.484590	-2.800023	0.791800
60	1	0	-1.525693	-3.975913	-1.337214

61	1	0	-1.122449	-5.486583	-0.542151
62	1	0	-3.805868	-2.760474	-1.516824
63	1	0	-0.501283	-1.328178	-2.413959
64	1	0	-0.458770	-1.395910	-0.654654
65	1	0	1.898850	-2.666190	-2.086778
66	1	0	0.326610	-3.319539	-2.441001
67	1	0	-2.572472	-4.769541	1.432639
68	1	0	-3.448078	-4.959933	-0.080418
69	1	0	-2.723445	-2.692950	2.639854
70	1	0	-4.275897	-0.348897	-1.440311
71	1	0	-3.070389	1.675882	1.267268
72	1	0	-3.212965	-0.279763	2.727228
73	1	0	-5.852206	2.474375	-1.469915
74	1	0	-7.561155	1.430192	-0.343496
75	1	0	-6.433700	0.958749	0.947089
76	1	0	-6.571035	-0.039449	-0.513199

Cu NE3TA-LLP2A.log

Zero-point correction= 0.628669 (A. U.)

Thermal correction to Energy= 0.666748

Thermal correction to Enthalpy= 0.667692

Thermal correction to Gibbs Free Energy= 0.557194

Sum of electronic and zero-point Energies= -3792.968606

Sum of electronic and thermal Energies= -3792.930527

Sum of electronic and thermal Enthalpies= -3792.929583

Sum of electronic and thermal Free Energies= -3793.040081

SCF Done: E(UB3LYP) = -3794.33561533 A.U.

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	29	0	1.864671	-0.525582	-0.649212
2	7	0	3.736981	-1.037863	0.880439
3	7	0	1.264090	-2.311425	0.330628
4	6	0	2.458043	-3.157093	0.564197
5	6	0	3.519458	-2.398988	1.382617
6	7	0	1.230480	0.444240	1.735201
7	6	0	2.393535	0.213073	2.619137
8	6	0	3.748846	0.008578	1.902378
9	6	0	0.558424	-2.025973	1.619038
10	6	0	0.164271	-0.568788	1.876009
11	6	0	2.470997	3.579508	-0.499888
12	6	0	2.971084	2.161252	-0.859214
13	8	0	4.194268	1.954450	-0.835730
14	8	0	2.028930	1.325486	-1.127891
15	6	0	4.832652	-0.984040	-0.099159
16	6	0	4.442509	-1.628763	-1.452222
17	8	0	5.322888	-2.217859	-2.093214
18	8	0	3.211326	-1.488657	-1.810461
19	6	0	-0.642296	-1.826066	-1.179783
20	6	0	0.341463	-2.901536	-0.669947
21	8	0	-0.181600	-0.638206	-1.196173
22	8	0	-1.779839	-2.200900	-1.535664
23	6	0	-0.006529	3.563461	-0.404650
24	6	0	-1.142749	4.342563	0.276336
25	6	0	-3.074754	2.865516	-0.529746
26	6	0	-3.791543	2.348262	0.559764
27	6	0	0.591114	1.760368	1.962541
28	6	0	1.342773	3.082408	1.647357
29	7	0	1.264815	3.678102	0.309162
30	6	0	-2.488172	4.261614	-0.485649

31	6	0	-2.844527	2.012698	-1.618503
32	6	0	-4.223540	1.020687	0.586663
33	7	0	-4.237340	-1.219392	-0.473450
34	6	0	-5.209702	-1.858176	0.229728
35	6	0	-3.273173	0.687788	-1.611232
36	6	0	-3.954446	0.174875	-0.499805
37	16	0	-5.010375	-3.420983	0.851742
38	7	0	-6.399225	-1.198478	0.417104
39	6	0	-6.981846	-0.232494	-0.513818
40	1	0	2.858318	-3.424449	-0.413494
41	1	0	2.180022	-4.085884	1.089555
42	1	0	3.218779	-2.353436	2.434012
43	1	0	4.453992	-2.981385	1.357250
44	1	0	2.188391	-0.641630	3.277615
45	1	0	2.523867	1.069802	3.295221
46	1	0	4.033521	0.934254	1.397284
47	1	0	4.505862	-0.181862	2.690444
48	1	0	1.183279	-2.388250	2.437638
49	1	0	-0.365534	-2.616917	1.659829
50	1	0	-0.625178	-0.291748	1.176726
51	1	0	-0.271410	-0.543472	2.896043
52	1	0	3.297261	4.080025	0.018668
53	1	0	2.304201	4.129045	-1.434506
54	1	0	5.740058	-1.482194	0.275829
55	1	0	5.050048	0.064675	-0.317375
56	1	0	0.940847	-3.237244	-1.522549
57	1	0	-0.208818	-3.758226	-0.260320
58	1	0	0.151161	3.992557	-1.401440
59	1	0	-0.296044	2.517963	-0.576799
60	1	0	-1.301607	3.974562	1.298752
61	1	0	-0.840820	5.394405	0.367774
62	1	0	-3.991293	2.984285	1.420235
63	1	0	0.303980	1.824414	3.032057

64	1	0	-0.344368	1.756014	1.399938
65	1	0	2.402098	2.992133	1.910903
66	1	0	0.921290	3.805155	2.364144
67	1	0	-2.342265	4.629850	-1.509805
68	1	0	-3.200309	4.945807	-0.005848
69	1	0	-2.281633	2.375854	-2.474180
70	1	0	-4.741925	0.633312	1.458230
71	1	0	-3.444446	-1.795513	-0.792341
72	1	0	-3.024464	0.023307	-2.430486
73	1	0	-7.048918	-1.767276	0.941021
74	1	0	-8.069328	-0.339865	-0.479583
75	1	0	-6.643810	-0.425176	-1.537094
76	1	0	-6.722022	0.799538	-0.257494

Cu NE3TA-LLP2A_1.log

Zero-point correction= 0.628357 (A. U.)

Thermal correction to Energy= 0.666729

Thermal correction to Enthalpy= 0.667673

Thermal correction to Gibbs Free Energy= 0.555371

Sum of electronic and zero-point Energies= -3792.961220

Sum of electronic and thermal Energies= -3792.922848

Sum of electronic and thermal Enthalpies= -3792.921904

Sum of electronic and thermal Free Energies= -3793.034206

SCF Done: E(UB3LYP) = -3794.34056876 A.U.

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	29	0	2.591326	0.420761	0.428636
2	7	0	4.686250	0.617885	-0.150737

3	7	0	2.404787	2.080626	-0.864585
4	6	0	3.651316	2.855635	-0.652867
5	6	0	4.883316	1.947234	-0.793503
6	7	0	2.812641	-0.809948	-2.114761
7	6	0	4.246990	-0.619590	-2.328237
8	6	0	5.072599	-0.505572	-1.027712
9	6	0	2.250548	1.687694	-2.296096
10	6	0	1.893361	0.226659	-2.596034
11	6	0	0.903545	-2.436774	1.045530
12	6	0	2.329144	-2.306096	1.618795
13	8	0	2.762706	-3.219110	2.332025
14	8	0	3.009861	-1.251011	1.307083
15	6	0	5.374488	0.567682	1.167567
16	6	0	4.736057	1.566814	2.179157
17	8	0	5.499393	2.071015	3.020672
18	8	0	3.483346	1.757295	2.025352
19	6	0	0.145385	1.756265	0.181212
20	6	0	1.203685	2.762458	-0.319786
21	8	0	0.616315	0.626486	0.579817
22	8	0	-1.042477	2.104467	0.200854
23	6	0	-0.503707	-2.102019	-0.952200
24	6	0	-1.521921	-3.230004	-0.623739
25	6	0	-3.444823	-1.872045	0.418520
26	6	0	-4.748569	-2.173592	-0.007104
27	6	0	2.298938	-2.158286	-2.411630
28	6	0	1.800989	-2.961420	-1.192373
29	7	0	0.842453	-2.221835	-0.396533
30	6	0	-2.422125	-2.973979	0.615069
31	6	0	-3.120887	-0.520211	0.621173
32	6	0	-5.696083	-1.173077	-0.231582
33	7	0	-6.281014	1.226872	-0.286781
34	6	0	-7.634126	1.233258	-0.102436
35	6	0	-4.058347	0.489626	0.402492

36	6	0	-5.352340	0.167577	-0.017401
37	16	0	-8.652869	2.129443	-1.118149
38	7	0	-8.142433	0.521029	0.941563
39	6	0	-7.443705	0.173879	2.179948
40	1	0	3.612138	3.251631	0.360177
41	1	0	3.721748	3.692475	-1.367644
42	1	0	5.128878	1.801249	-1.848976
43	1	0	5.744447	2.456503	-0.343329
44	1	0	4.427487	0.252514	-2.969247
45	1	0	4.664339	-1.472834	-2.882353
46	1	0	4.933211	-1.415423	-0.438064
47	1	0	6.140976	-0.434937	-1.302267
48	1	0	3.171822	1.954617	-2.820388
49	1	0	1.459190	2.299825	-2.749551
50	1	0	0.918710	0.009131	-2.153173
51	1	0	1.768385	0.177016	-3.699431
52	1	0	0.536549	-3.428306	1.356435
53	1	0	0.283381	-1.665722	1.516951
54	1	0	6.444775	0.788903	1.052985
55	1	0	5.249068	-0.440114	1.570807
56	1	0	1.515810	3.334381	0.558998
57	1	0	0.758629	3.452297	-1.047631
58	1	0	-0.908900	-1.136196	-0.634827
59	1	0	-0.402736	-2.043556	-2.041638
60	1	0	-2.178863	-3.381413	-1.490981
61	1	0	-0.982238	-4.175017	-0.478013
62	1	0	-5.028258	-3.211451	-0.176346
63	1	0	3.082230	-2.753620	-2.902660
64	1	0	1.486474	-2.073888	-3.149129
65	1	0	2.661117	-3.200055	-0.562181
66	1	0	1.415865	-3.933489	-1.569025
67	1	0	-1.795286	-2.738838	1.480064
68	1	0	-2.949200	-3.906154	0.855622

69	1	0	-2.127599	-0.222604	0.942556
70	1	0	-6.693610	-1.428077	-0.576823
71	1	0	-5.985803	1.900293	-0.982705
72	1	0	-3.761441	1.523282	0.553135
73	1	0	-9.148466	0.591730	0.987391
74	1	0	-8.178271	0.162241	2.988930
75	1	0	-6.678715	0.919130	2.414545
76	1	0	-6.962717	-0.806902	2.123570

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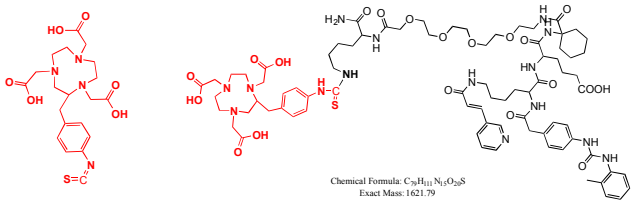
b) commercialized *p*-SCN-Bn-NOTA and the targeting probe conjugated tracer



Fe NOTA-LLP2A.log

Zero-point correction= 0.499759 A.U.

Thermal correction to Energy= 0.531055

Thermal correction to Enthalpy= 0.531999

Thermal correction to Gibbs Free Energy= 0.435549

Sum of electronic and zero-point Energies= -3203.706484

Sum of electronic and thermal Energies= -3203.675188

Sum of electronic and thermal Enthalpies= -3203.674244

Sum of electronic and thermal Free Energies= -3203.770694

SCF Done: E(UB3LYP) = -3204.80914077 A.U.

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	26	0	-2.792179	0.181909	0.353724

2	7	0	-1.311218	1.364421	-0.317640
3	7	0	-3.650108	0.440273	-1.452422
4	6	0	-2.899902	1.459903	-2.246922
5	6	0	-1.958684	2.256766	-1.337246
6	7	0	-1.740165	-1.338996	-0.475006
7	6	0	-0.291314	-0.894889	-0.405601
8	6	0	-0.191993	0.556972	-0.887870
9	6	0	-3.595417	-0.920745	-2.086093
10	6	0	-2.224440	-1.570598	-1.871147
11	6	0	-1.998419	-2.442261	0.496809
12	6	0	-1.828025	-1.845469	1.915268
13	8	0	-1.478139	-2.554606	2.845941
14	8	0	-2.046940	-0.556614	1.960310
15	6	0	-0.976352	2.158950	0.904749
16	6	0	-2.313840	2.572564	1.566175
17	8	0	-2.375557	3.572315	2.260902
18	8	0	-3.310921	1.769830	1.273221
19	6	0	-5.464759	-0.187850	0.068786
20	6	0	-5.052698	0.778273	-1.074459
21	8	0	-4.443124	-0.725645	0.694702
22	8	0	-6.643010	-0.414768	0.280136
23	1	0	-3.594446	2.137536	-2.754805
24	1	0	-2.336502	0.941864	-3.027899
25	1	0	-1.194964	2.780792	-1.926342
26	1	0	-2.530994	3.007598	-0.792587
27	1	0	-0.058669	-0.896322	0.659992
28	1	0	0.775833	0.980821	-0.603637
29	1	0	-0.247910	0.605569	-1.980443
30	1	0	-3.824739	-0.849334	-3.157632
31	1	0	-4.368386	-1.529634	-1.619255
32	1	0	-2.282054	-2.641809	-2.092117
33	1	0	-1.494779	-1.146745	-2.564435
34	1	0	-3.033138	-2.772749	0.378735

35	1	0	-0.371264	3.039649	0.662922
36	1	0	-0.425887	1.516879	1.597391
37	1	0	-5.074476	1.802965	-0.694920
38	1	0	-5.741729	0.684285	-1.921451
39	6	0	2.590113	-1.792996	0.596534
40	6	0	2.145668	-1.546265	-0.710782
41	6	0	3.064686	-1.019620	-1.627775
42	6	0	4.380598	-0.729625	-1.266696
43	6	0	4.802823	-0.949390	0.050886
44	6	0	3.896485	-1.491849	0.974723
45	1	0	1.914099	-2.216853	1.335338
46	1	0	2.756390	-0.840899	-2.655410
47	1	0	5.069679	-0.327059	-1.996390
48	1	0	4.211902	-1.672563	1.999449
49	6	0	0.710449	-1.837425	-1.108398
50	1	0	0.615148	-1.759929	-2.197746
51	1	0	0.461575	-2.870800	-0.841047
52	6	0	6.985989	0.321017	0.155041
53	7	0	6.127332	-0.715164	0.482884
54	1	0	6.382450	-1.240827	1.310088
55	7	0	8.217758	0.162337	0.716365
56	1	0	8.460867	-0.749937	1.079011
57	16	0	6.589883	1.652974	-0.780342
58	6	0	9.307292	1.115575	0.555668
59	1	0	8.998188	2.105496	0.898407
60	1	0	10.147932	0.769373	1.161051
61	1	0	9.617187	1.198599	-0.491539
62	1	0	-1.326008	-3.293598	0.353017

Cu NOTA-LLP2A_1.log

Zero-point correction= 0.496847 (A. U.)

Thermal correction to Energy= 0.529312

Thermal correction to Enthalpy= 0.530256

Thermal correction to Gibbs Free Energy= 0.431157

Sum of electronic and zero-point Energies= -3580.326950

Sum of electronic and thermal Energies= -3580.294485

Sum of electronic and thermal Enthalpies= -3580.293540

Sum of electronic and thermal Free Energies= -3580.392639

SCF Done: E(UB3LYP) = -3581.49414691 A.U.

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	29	0	2.863782	0.337470	-0.383645
2	7	0	1.250529	1.199021	0.350050
3	7	0	3.569994	0.244622	1.572382
4	6	0	2.692139	1.120854	2.399862
5	6	0	1.806938	1.993117	1.507542
6	7	0	1.675734	-1.637714	0.404061
7	6	0	0.286109	-1.162576	0.277200
8	6	0	0.163866	0.267241	0.821476
9	6	0	3.555880	-1.182544	1.989544
10	6	0	2.201286	-1.889666	1.739352
11	6	0	2.109225	-2.505172	-0.690809
12	6	0	2.001941	-1.768606	-2.050716
13	8	0	1.775912	-2.417908	-3.066438
14	8	0	2.109762	-0.470121	-2.023437
15	6	0	0.819236	2.120965	-0.747056
16	6	0	2.060991	2.847364	-1.336795

17	8	0	1.880440	3.846880	-2.021912
18	8	0	3.193977	2.313021	-1.012553
19	6	0	5.481629	0.091210	0.050608
20	6	0	4.949277	0.741925	1.340755
21	8	0	4.543066	-0.295120	-0.798895
22	8	0	6.667140	-0.077929	-0.152156
23	1	0	3.295802	1.759134	3.055393
24	1	0	2.090275	0.483349	3.051251
25	1	0	0.974295	2.423318	2.079358
26	1	0	2.393790	2.806936	1.086394
27	1	0	0.089507	-1.111629	-0.795309
28	1	0	-0.803716	0.691928	0.540208
29	1	0	0.192769	0.248899	1.914762
30	1	0	3.817821	-1.261418	3.055155
31	1	0	4.339552	-1.687804	1.421651
32	1	0	2.353636	-2.961092	1.936539
33	1	0	1.470047	-1.554717	2.480827
34	1	0	3.158740	-2.778707	-0.540606
35	1	0	0.088465	2.843786	-0.367429
36	1	0	0.355008	1.518929	-1.532384
37	1	0	4.911022	1.823650	1.179763
38	1	0	5.615316	0.524575	2.183401
39	6	0	-2.661164	-1.818139	-0.789866
40	6	0	-2.204342	-1.722699	0.533272
41	6	0	-3.103480	-1.255355	1.501420
42	6	0	-4.408070	-0.881115	1.178345
43	6	0	-4.840362	-0.951444	-0.152228
44	6	0	-3.955216	-1.430898	-1.130221
45	1	0	-2.002795	-2.192577	-1.570028
46	1	0	-2.788360	-1.193807	2.540668
47	1	0	-5.080938	-0.529288	1.948182
48	1	0	-4.278712	-1.496419	-2.166350
49	6	0	-0.782251	-2.104458	0.891921

50	1	0	-0.678411	-2.133169	1.983626
51	1	0	-0.566479	-3.116362	0.528169
52	6	0	-6.995746	0.374061	-0.108223
53	7	0	-6.156477	-0.631789	-0.554955
54	1	0	-6.425029	-1.059311	-1.432794
55	7	0	-8.228178	0.308346	-0.687311
56	1	0	-8.486575	-0.546943	-1.161058
57	16	0	-6.580737	1.577928	0.980512
58	6	0	-9.300339	1.255933	-0.414884
59	1	0	-8.975595	2.273366	-0.644085
60	1	0	-10.148283	0.995036	-1.052068
61	1	0	-9.606228	1.224390	0.636257
62	1	0	1.528289	-3.435518	-0.771419

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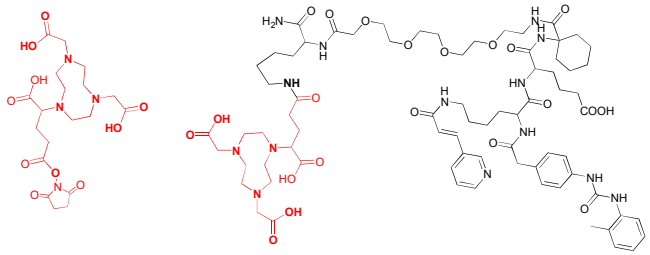
c) commercialized NODAGA and the targeting probe conjugated tracer



Fe NODAGA-LLP2A_2.log 0 2

opt freq ub3lyp/6-31+g(d,p)

Zero-point correction= 0.433927 (A. U.)

Thermal correction to Energy= 0.459870

Thermal correction to Enthalpy= 0.460814

Thermal correction to Gibbs Free Energy= 0.378385

Sum of electronic and zero-point Energies= -2633.711125

Sum of electronic and thermal Energies= -2633.685182

Sum of electronic and thermal Enthalpies= -2633.684238

Sum of electronic and thermal Free Energies= -2633.766667

SCF Done: E(UB3LYP) = -2634.66989594 A.U.

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	26	0	1.095655	0.076921	-0.301686
2	7	0	1.014254	1.507687	1.113360
3	7	0	2.241662	-0.939156	0.984939
4	6	0	2.576970	-0.109137	2.181912
5	6	0	2.290086	1.365688	1.888479
6	7	0	-0.508056	-0.774070	0.609604
7	6	0	-1.203740	0.381613	1.282935
8	6	0	-0.193122	1.301058	1.972074
9	6	0	1.435227	-2.156149	1.342339
10	6	0	-0.032428	-1.792847	1.597072
11	6	0	-1.254874	-1.303448	-0.590423
12	6	0	-1.288290	-0.121742	-1.608164
13	8	0	-2.191951	-0.039221	-2.436256
14	8	0	-0.298763	0.710079	-1.479217
15	6	0	1.035866	2.769894	0.319576
16	6	0	2.091012	2.581082	-0.794687
17	8	0	2.651456	3.540119	-1.295226
18	8	0	2.311292	1.318881	-1.080885
19	6	0	2.809152	-1.807852	-1.240377
20	6	0	3.392990	-1.333841	0.115457
21	8	0	1.623903	-1.306513	-1.507285
22	8	0	3.430665	-2.592986	-1.934332
23	1	0	3.626418	-0.244834	2.464867
24	1	0	1.974022	-0.461988	3.023111
25	1	0	2.242520	1.948635	2.817712

26	1	0	3.090553	1.780069	1.275238
27	1	0	-1.943580	0.035427	2.009432
28	1	0	-1.736491	0.935925	0.512945
29	1	0	-0.667990	2.258878	2.210606
30	1	0	0.133531	0.869281	2.922180
31	1	0	1.869760	-2.655352	2.218096
32	1	0	1.500812	-2.848376	0.503024
33	1	0	-0.649544	-2.695249	1.550362
34	1	0	-0.160114	-1.379734	2.600941
35	1	0	-0.563778	-2.016842	-1.054009
36	1	0	1.274985	3.639552	0.941567
37	1	0	0.055731	2.908265	-0.143063
38	1	0	4.016028	-0.452568	-0.058695
39	1	0	3.995540	-2.125009	0.575078
40	6	0	-2.585136	-2.059759	-0.388343
41	6	0	-3.642559	-1.587250	0.627886
42	6	0	-4.301410	-0.205594	0.533269
43	1	0	-3.020335	-2.120112	-1.391838
44	1	0	-2.346419	-3.095689	-0.117514
45	1	0	-4.471537	-2.305624	0.575791
46	1	0	-3.268076	-1.664157	1.652641
47	8	0	-4.702083	0.344145	1.565879
48	7	0	-4.485171	0.323934	-0.698151
49	6	0	-5.134639	1.618183	-0.865663
50	1	0	-3.929859	-0.023396	-1.477149
51	1	0	-5.254486	1.808330	-1.933228
52	1	0	-6.114496	1.610888	-0.382539
53	1	0	-4.545836	2.429560	-0.421441

%chk=NODAGA_LLP2A.chk 1 2

Zero-point correction= 0.429392 (A. U.)

Thermal correction to Energy= 0.456733

Thermal correction to Enthalpy= 0.457677

Thermal correction to Gibbs Free Energy= 0.371758

Sum of electronic and zero-point Energies= -3010.505613

Sum of electronic and thermal Energies= -3010.478273

Sum of electronic and thermal Enthalpies= -3010.477328

Sum of electronic and thermal Free Energies= -3010.563247

SCF Done: E(UB3LYP) = -3011.57535573 A.U.

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	29	0	1.337416	0.143897	-0.529070
2	7	0	1.138031	1.433707	1.141217
3	7	0	2.097263	-1.229132	1.014324
4	6	0	2.412865	-0.435078	2.220528
5	6	0	2.349446	1.072847	1.928167
6	7	0	-0.791326	-0.739374	0.685531
7	6	0	-1.238175	0.518812	1.277014
8	6	0	-0.099192	1.299361	1.957390
9	6	0	1.099337	-2.293132	1.241301
10	6	0	-0.312101	-1.769021	1.592780
11	6	0	-1.423952	-1.183344	-0.564368
12	6	0	-1.388647	-0.016837	-1.612483
13	8	0	-2.372891	0.130254	-2.369459
14	8	0	-0.329832	0.685945	-1.623590
15	6	0	1.293243	2.777560	0.525744
16	6	0	2.446138	2.790182	-0.520438
17	8	0	2.947434	3.890092	-0.784844
18	8	0	2.755702	1.639902	-0.994231

19	6	0	2.892015	-2.034233	-1.203852
20	6	0	3.270914	-1.734452	0.271716
21	8	0	1.930310	-1.309877	-1.679413
22	8	0	3.512574	-2.914749	-1.801122
23	1	0	3.411701	-0.683899	2.605015
24	1	0	1.706915	-0.701236	3.012659
25	1	0	2.383049	1.640423	2.872525
26	1	0	3.214831	1.360395	1.329860
27	1	0	-2.033753	0.392021	2.031496
28	1	0	-1.656888	1.132698	0.479010
29	1	0	-0.474107	2.294097	2.231860
30	1	0	0.162401	0.806903	2.899102
31	1	0	1.432809	-2.982221	2.037804
32	1	0	1.043277	-2.873697	0.317158
33	1	0	-0.980391	-2.645275	1.622533
34	1	0	-0.317076	-1.368138	2.612370
35	1	0	-0.732108	-1.912181	-1.010580
36	1	0	1.475193	3.545928	1.290036
37	1	0	0.361573	3.015302	0.003004
38	1	0	4.036618	-0.951311	0.260341
39	1	0	3.699590	-2.635492	0.733555
40	6	0	-2.784081	-1.926610	-0.436965
41	6	0	-3.805708	-1.472573	0.622709
42	6	0	-4.619292	-0.181861	0.477426
43	1	0	-3.237426	-1.941038	-1.433135
44	1	0	-2.561251	-2.975764	-0.200069
45	1	0	-4.567108	-2.258999	0.713555
46	1	0	-3.338595	-1.419626	1.611540
47	8	0	-5.321441	0.197996	1.427429
48	7	0	-4.583162	0.463262	-0.707150
49	6	0	-5.325710	1.697223	-0.900759
50	1	0	-3.861794	0.225607	-1.402859
51	1	0	-5.121675	2.064507	-1.908438

52	1	0	-6.401465	1.526967	-0.784862
53	1	0	-5.032470	2.462214	-0.171527

Fe^{3+}

Zero-point correction= 0.000000 (A. U.)

Thermal correction to Energy= 0.001416

Thermal correction to Enthalpy= 0.002360

Thermal correction to Gibbs Free Energy= -0.016342

Sum of electronic and zero-point Energies= -1261.266099

Sum of electronic and thermal Energies= -1261.264683

Sum of electronic and thermal Enthalpies= -1261.263739

Sum of electronic and thermal Free Energies= -1261.282442

SCF Done: E(UB3LYP) = -1262.82741592 A.U.

Cu^{2+}

Zero-point correction= 0.000000 (A. U.)

Thermal correction to Energy= 0.001416

Thermal correction to Enthalpy= 0.002360

Thermal correction to Gibbs Free Energy= -0.016509

Sum of electronic and zero-point Energies= -1639.251805

Sum of electronic and thermal Energies= -1639.250389

Sum of electronic and thermal Enthalpies= -1639.249445

Sum of electronic and thermal Free Energies= -1639.268315

SCF Done: E(UB3LYP) = -1639.95476965 A.U.

A:

Center	Atomic	Atomic	Coordinates (Angstroms)

Number	Number	Type	X	Y	Z
1	29	0	2.895259	0.043222	-0.272100
2	6	0	0.334837	1.067921	-1.160704
3	8	0	1.561894	1.292634	-1.437482
4	8	0	-0.646962	1.750125	-1.487337
5	7	0	-3.742445	-0.689942	-0.469943
6	8	0	2.973777	-1.659055	-1.273986
7	8	0	4.256722	-2.737528	-2.782654
8	7	0	1.123570	-0.460687	0.727711
9	7	0	4.239765	-0.983801	1.411961
10	7	0	4.715726	0.464561	-1.178038
11	7	0	3.061639	1.706779	1.110004
12	6	0	1.667899	1.823569	1.626049
13	6	0	0.998945	0.470634	1.883373
14	6	0	1.142430	-1.900506	1.147324
15	6	0	2.205640	-2.332543	2.172024
16	6	0	3.679332	-2.313932	1.741468
17	6	0	5.501513	-1.108501	0.663747
18	6	0	5.821656	0.082904	-0.256311
19	6	0	4.784891	1.899209	-1.587735
20	6	0	4.697921	2.928424	-0.453039
21	6	0	3.392152	2.953567	0.350836
22	6	0	4.061407	1.435809	2.175925
23	6	0	4.274355	-0.055600	2.545594
24	6	0	3.933884	-1.740277	-2.143329
25	6	0	4.684449	-0.413123	-2.386441
26	6	0	0.063974	-0.244514	-0.331440
27	6	0	-1.382795	-0.310452	0.189936
28	6	0	-2.354961	-0.734093	-0.920820
29	6	0	-4.643368	0.320238	-0.589369
30	6	0	-7.090091	0.540627	0.300642
31	6	0	-5.765713	-0.128180	0.080769

32	7	0	-5.488159	-1.375764	0.567139
33	7	0	-4.266246	-1.710355	0.237131
34	8	0	-9.787083	1.058081	1.124953
35	6	0	-12.017715	0.368129	-0.444414
36	6	0	-8.270895	-0.328947	-0.158230
37	6	0	-9.620289	0.303367	0.168509
38	7	0	-10.640783	-0.041451	-0.675024
39	1	0	1.093520	2.375158	0.882068
40	1	0	1.651704	2.413232	2.556022
41	1	0	1.448905	-0.003704	2.753409
42	1	0	-0.052164	0.646332	2.141282
43	1	0	1.286595	-2.474248	0.229139
44	1	0	0.162359	-2.167826	1.565329
45	1	0	1.977770	-3.383787	2.390411
46	1	0	2.064797	-1.823901	3.132452
47	1	0	4.276929	-2.803297	2.532119
48	1	0	3.768893	-2.918909	0.836815
49	1	0	5.434563	-2.014830	0.058885
50	1	0	6.362865	-1.242058	1.342913
51	1	0	6.078744	0.950872	0.347879
52	1	0	6.720732	-0.168277	-0.837719
53	1	0	3.943957	2.058864	-2.267135
54	1	0	5.716707	2.069677	-2.149673
55	1	0	4.767684	3.911395	-0.935486
56	1	0	5.576682	2.880688	0.199808
57	1	0	3.421986	3.806307	1.048515
58	1	0	2.566782	3.104479	-0.347527
59	1	0	3.791630	1.980541	3.093913
60	1	0	5.011137	1.855553	1.848060
61	1	0	5.229213	-0.123122	3.097537
62	1	0	3.501133	-0.359506	3.251461
63	1	0	5.696552	-0.609625	-2.758825
64	1	0	4.128691	0.113789	-3.167959

65	1	0	0.234142	-1.063928	-1.040823
66	1	0	-1.692396	0.674734	0.550008
67	1	0	-1.481216	-1.024344	1.014742
68	1	0	-2.257686	-0.058466	-1.771628
69	1	0	-2.155947	-1.759090	-1.246539
70	1	0	-4.417386	1.234826	-1.116309
71	1	0	-7.227431	0.772013	1.361907
72	1	0	-7.103933	1.499365	-0.228941
73	1	0	-12.532176	0.483927	-1.402064
74	1	0	-12.565068	-0.357170	0.170866
75	1	0	-12.009745	1.324725	0.080048
76	1	0	-8.219172	-1.295985	0.357615
77	1	0	-8.194955	-0.542297	-1.231670
78	1	0	-10.452905	-0.717359	-1.400710

B.

In solvent: SCF Done: E(UB3LYP) = -3393.91003662 A.U.

Thermal correction to Gibbs Free Energy= 0.595373

Total Gibbs Free Energy in solvent: -3393.31466362

A. U.

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	29	0	1.593784	-0.387657	0.059438
2	6	0	0.713635	3.953846	-0.674084
3	8	0	1.674486	4.347630	-1.376253

4	8	0	-0.339527	4.542329	-0.333722
5	7	0	-1.572282	1.604428	1.693464
6	8	0	2.392755	-0.126053	1.835493
7	8	0	2.836011	-1.181830	3.774789
8	7	0	1.853752	1.569775	-0.628659
9	7	0	3.602876	-1.150501	-0.712254
10	7	0	1.281140	-2.371232	0.740781
11	7	0	0.901771	-0.863046	-1.884257
12	6	0	0.634214	0.476904	-2.489043
13	6	0	1.702962	1.489885	-2.115377
14	6	0	3.222704	2.047259	-0.219802
15	6	0	4.428760	1.279600	-0.789187
16	6	0	4.663689	-0.174116	-0.347339
17	6	0	3.735354	-2.398477	0.063238
18	6	0	2.421445	-3.181793	0.221896
19	6	0	-0.037898	-2.954143	0.352186
20	6	0	-0.334868	-2.997871	-1.149963
21	6	0	-0.375000	-1.645834	-1.868939
22	6	0	1.976959	-1.602661	-2.617853
23	6	0	3.437866	-1.342793	-2.158627
24	6	0	2.289409	-1.110056	2.678728
25	6	0	1.347950	-2.238486	2.224944
26	6	0	0.762850	2.476118	-0.086959
27	6	0	0.751115	2.516418	1.456375
28	6	0	-0.647324	2.705949	2.038370
29	6	0	-2.925561	1.636982	1.733600
30	6	0	-4.710563	-0.194007	1.169811
31	6	0	-3.334581	0.372225	1.347211
32	7	0	-2.211051	-0.355243	1.086496
33	7	0	-1.148071	0.391147	1.302525
34	8	0	-6.727451	-1.881974	-0.164801
35	6	0	-8.924349	-0.556302	-1.260097
36	6	0	-5.284716	0.051486	-0.242043

37	6	0	-6.601981	-0.691099	-0.447221
38	7	0	-7.628733	0.041199	-0.964975
39	1	0	-0.339880	0.808616	-2.123055
40	1	0	0.557628	0.391723	-3.583245
41	1	0	2.654290	1.200757	-2.554620
42	1	0	1.464773	2.481291	-2.512187
43	1	0	3.253653	1.988739	0.869512
44	1	0	3.295918	3.095452	-0.527762
45	1	0	5.307224	1.832032	-0.431463
46	1	0	4.482183	1.377708	-1.879102
47	1	0	5.639999	-0.507825	-0.740905
48	1	0	4.723388	-0.186848	0.742873
49	1	0	4.115462	-2.130911	1.050751
50	1	0	4.476677	-3.078274	-0.392324
51	1	0	2.129853	-3.606743	-0.737545
52	1	0	2.607138	-4.032294	0.893689
53	1	0	-0.806237	-2.345168	0.834657
54	1	0	-0.113476	-3.975585	0.757704
55	1	0	-1.344396	-3.416421	-1.244034
56	1	0	0.310737	-3.713030	-1.671021
57	1	0	-0.708421	-1.803699	-2.907058
58	1	0	-1.118633	-1.017298	-1.372915
59	1	0	1.907379	-1.373605	-3.691014
60	1	0	1.764762	-2.665406	-2.523075
61	1	0	4.048118	-2.186608	-2.524839
62	1	0	3.821989	-0.456142	-2.661527
63	1	0	1.635068	-3.186089	2.695391
64	1	0	0.350062	-1.968647	2.582626
65	1	0	-0.166573	2.010286	-0.418471
66	1	0	1.343383	3.366025	1.813382
67	1	0	1.200491	1.616036	1.875549
68	1	0	-0.591472	2.759711	3.131016
69	1	0	-1.086133	3.622224	1.636526

70	1	0	-3.467913	2.525535	2.018423
71	1	0	-4.681003	-1.272404	1.346622
72	1	0	-5.387263	0.236693	1.916596
73	1	0	-9.638625	0.239884	-1.478560
74	1	0	-8.867081	-1.234783	-2.118616
75	1	0	-9.273964	-1.129776	-0.398253
76	1	0	-4.577685	-0.334092	-0.986486
77	1	0	-5.394276	1.126348	-0.428445
78	1	0	-7.465310	1.003939	-1.217359

Cu(II)

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	29	0	0.392272	0.060332	1.232971
2	29	0	-0.391596	0.061514	-1.229075
3	8	0	2.250513	0.164811	0.443572
4	8	0	0.456340	-1.953091	1.034930
5	8	0	0.250563	2.036623	1.108569
6	8	0	-1.539214	-0.059476	1.693360
7	8	0	-2.247811	0.179409	-0.443578
8	8	0	-0.469133	-1.951603	-1.027329
9	8	0	1.536375	-0.072423	-1.691708
10	8	0	-0.235114	2.036796	-1.106114
11	6	0	-0.005376	-2.526794	0.003069
12	6	0	-2.434261	0.054877	0.806313
13	6	0	0.007186	2.603046	0.001565
14	6	0	2.433845	0.043574	-0.806588
15	6	0	3.874414	0.070306	-1.295517

16	1	0	3.960755	-0.434765	-2.257951
17	1	0	4.168935	1.117469	-1.423990
18	1	0	4.536739	-0.382322	-0.555789
19	6	0	0.028845	-4.047321	-0.014227
20	1	0	0.977801	-4.361899	-0.462218
21	1	0	-0.022710	-4.443260	1.000836
22	1	0	-0.784336	-4.441212	-0.625634
23	6	0	-3.879313	0.009255	1.280765
24	1	0	-4.248482	-1.014458	1.155888
25	1	0	-3.943909	0.279012	2.335055
26	1	0	-4.497770	0.670227	0.670978
27	6	0	-0.028153	4.124831	0.007549
28	1	0	-1.061164	4.438543	0.192382
29	1	0	0.602226	4.517038	0.806192
30	1	0	0.279605	4.513962	-0.963898
31	8	0	1.564322	-0.377381	3.216292
32	1	0	2.439280	-0.171163	2.855827
33	1	0	1.485172	-1.341149	3.164010
34	8	0	-1.563775	-0.373711	-3.213767
35	1	0	-2.438426	-0.172456	-2.849683
36	1	0	-1.480954	-1.337401	-3.166384

Fe(III)

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z

1	26	0	1.498038	-0.987987	-0.095310
2	26	0	0.102420	1.774504	0.078606
3	8	0	0.010070	-0.010085	-0.004283

4	26	0	-1.588943	-0.817356	0.011742
5	8	0	1.246109	2.000368	-1.507537
6	8	0	-0.990852	1.972816	1.679417
7	8	0	1.670622	1.929463	1.229632
8	8	0	-1.453150	2.181067	-1.082545
9	8	0	-2.535997	0.391372	1.253696
10	8	0	-2.349044	0.162634	-1.516850
11	8	0	-1.190894	-2.256219	-1.249657
12	8	0	-1.215353	-1.955114	1.545338
13	8	0	0.910979	-2.495240	1.043389
14	8	0	1.004493	-1.976463	-1.689685
15	8	0	2.560075	0.187879	-1.236793
16	8	0	2.355733	-0.203472	1.494677
17	6	0	2.256607	1.280488	-1.789982
18	6	0	-0.159132	-2.623608	1.718581
19	6	0	-2.072448	1.367884	1.922774
20	6	0	-2.226845	1.405948	-1.721713
21	6	0	-0.137988	-2.472405	-1.920414
22	6	0	2.360637	1.032737	1.791308
23	6	0	3.253511	1.471207	2.933976
24	1	0	4.053901	0.749762	3.106647
25	1	0	3.664077	2.462657	2.731130
26	1	0	2.644717	1.543438	3.842096
27	6	0	3.194689	1.796718	-2.862283
28	1	0	3.668537	0.963442	-3.383954
29	1	0	2.658151	2.436878	-3.565211
30	1	0	3.981478	2.393130	-2.385764
31	6	0	-2.884014	1.830753	3.114566
32	1	0	-3.931684	1.954203	2.825826
33	1	0	-2.846131	1.059798	3.891420
34	1	0	-2.489110	2.766505	3.511400
35	6	0	-3.061653	2.026401	-2.823117
36	1	0	-3.777742	1.307895	-3.223433

37	1	0	-3.586595	2.905723	-2.438750
38	1	0	-2.399121	2.364192	-3.626721
39	6	0	-0.264454	-3.395507	-3.115197
40	1	0	-0.752663	-2.851639	-3.931460
41	1	0	0.717684	-3.732112	-3.449581
42	1	0	-0.898063	-4.248884	-2.860949
43	6	0	-0.153556	-3.660675	2.821810
44	1	0	-1.147284	-3.764589	3.258214
45	1	0	0.180515	-4.621782	2.420009
46	1	0	0.559878	-3.360684	3.596315
47	8	0	0.172691	3.854136	0.032942
48	1	0	-0.600176	4.020118	-0.533016
49	8	0	3.211369	-2.166756	-0.058925
50	1	0	2.875840	-2.888443	0.500494
51	8	0	-3.472451	-1.707321	0.033933
52	1	0	-3.788367	-1.584855	-0.874371
53	1	0	0.948292	4.013180	-0.527691
54	1	0	3.809008	-1.650415	0.503782
55	1	0	-3.951823	-1.067873	0.586737

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