

Electronic Supplementary Information (ESI) for

Synthesis and Characterization of the Copper(II) Complexes of New N₂S₂-donor Macrocyclic Ligands: Synthesis and In Vivo Evaluation of the ⁶⁴Cu Complexes

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Biodistribution in male, Lewis rats were injected with either complex **5** or **6** (~40 μ Ci in 150 μ L)
Rats were examined at 3 time points

Tissue	$[^{64}\text{Cu}(\text{NEC-SE})]$ (7), %ID/g		
	1 hour	4 hour	24 hour
blood	0.8504 \pm 0.0510	0.8968 \pm 0.0795	0.7682 \pm 0.0402
lung	0.8379 \pm 0.0652	0.7684 \pm 0.0445	0.7232 \pm 0.0355
liver	3.9192 \pm 0.3631	3.9045 \pm 0.5402	3.3138 \pm 0.4755
spleen	0.5595 \pm 0.0251	0.7305 \pm 0.1742	1.0456 \pm 0.1056
kidney	8.6624 \pm 0.5512	7.8487 \pm 1.0991	4.9062 \pm 0.2107
muscle	0.3804 \pm 0.0318	0.3436 \pm 0.0122	0.3091 \pm 0.0262
fat	0.3341 \pm 0.0541	0.2662 \pm 0.0676	0.1630 \pm 0.0256
heart	0.6723 \pm 0.0860	0.7739 \pm 0.0964	1.0412 \pm 0.0704
brain	0.0657 \pm 0.0057	0.0867 \pm 0.0077	0.1184 \pm 0.0092
pituitary	1.9725 \pm 0.4205	2.5130 \pm 0.5310	1.8935 \pm 0.2981
bone	1.1308 \pm 0.0720	1.2740 \pm 0.0818	0.9840 \pm 0.0756
marrow	1.1998 \pm 0.0866	1.7506 \pm 0.1976	1.8567 \pm 0.1073
adrenals	0.8236 \pm 0.1082	0.7201 \pm 0.0038	0.8125 \pm 0.0413
pancreas	0.9588 \pm 0.1101	0.8789 \pm 0.0557	0.5753 \pm 0.0298
stomach	1.7355 \pm 0.3881	1.0373 \pm 0.3447	0.6244 \pm 0.1113
sm int	2.3124 \pm 0.1486	2.2358 \pm 0.2385	1.8489 \pm 0.2293
u lg int	1.7819 \pm 0.3146	1.6331 \pm 0.2672	1.2160 \pm 0.1536
l lg int	0.6423 \pm 0.0679	1.1553 \pm 0.1475	1.2616 \pm 0.1638

Tissue	$[^{64}\text{Cu}(\text{NEC-SE})]$ (7), %ID/organ		
	1 hour	4 hour	24 hour
blood	5.1534 \pm 0.3561	5.4724 \pm 0.5594	4.7033 \pm 0.2089
lung	0.4694 \pm 0.0442	0.4378 \pm 0.0397	0.4208 \pm 0.0148
liver	15.3573 \pm 1.0388	13.1702 \pm 1.7796	14.9870 \pm 1.2475
spleen	0.1485 \pm 0.0086	0.1841 \pm 0.0538	0.2951 \pm 0.0230
kidney	4.3418 \pm 0.1435	3.8251 \pm 0.3763	2.5616 \pm 0.1046
muscle	13.4720 \pm 0.6191	12.2713 \pm 0.4962	11.0724 \pm 0.6845
fat	4.0217 \pm 0.7255	3.2042 \pm 0.8501	1.9697 \pm 0.3209
heart	0.2803 \pm 0.0401	0.2943 \pm 0.0559	0.4430 \pm 0.0386
brain	0.1012 \pm 0.0131	0.1311 \pm 0.0136	0.1820 \pm 0.0133
pituitary	0.0073 \pm 0.0012	0.0079 \pm 0.0012	0.0060 \pm 0.0006
bone	10.6703 \pm 0.7474	12.1058 \pm 1.0076	9.3739 \pm 0.5135
marrow	0.0544 \pm 0.0062	0.0851 \pm 0.0200	0.0879 \pm 0.0139
adrenals	0.0296 \pm 0.0028	0.0256 \pm 0.0034	0.0318 \pm 0.0031
pancreas	0.8063 \pm 0.0981	0.7154 \pm 0.0357	0.5036 \pm 0.0262
stomach	3.1488 \pm 2.7473	1.5791 \pm 0.1204	1.1546 \pm 0.1309
sm int	4.4501 \pm 0.2827	4.2208 \pm 0.4785	3.8251 \pm 0.3618
u lg int	3.8146 \pm 0.5804	3.7430 \pm 0.5009	3.6785 \pm 0.1930
l lg int	2.7884 \pm 0.2751	5.0148 \pm 0.2899	5.8678 \pm 1.7170

Tissue	⁶⁴ Cu(NEC-SP) (8), %ID/g		
	1 hour	4 hour	24 hour
blood	0.8204 ± 0.0461	0.8348 ± 0.0206	0.7740 ± 0.0307
lung	0.7762 ± 0.0891	0.7365 ± 0.0086	0.7707 ± 0.0613
liver	3.1507 ± 0.2856	3.4176 ± 0.3705	3.1821 ± 0.1876
spleen	0.4826 ± 0.0538	0.7043 ± 0.0141	1.0777 ± 0.0990
kidney	9.4382 ± 1.0190	7.8182 ± 0.6632	5.0696 ± 0.5182
muscle	0.3931 ± 0.0546	0.3524 ± 0.0165	0.3187 ± 0.0305
fat	0.3182 ± 0.0738	0.2137 ± 0.0235	0.1530 ± 0.0189
heart	0.6570 ± 0.0253	0.7359 ± 0.0482	1.0130 ± 0.0775
brain	0.0708 ± 0.0073	0.0865 ± 0.0108	0.1206 ± 0.0074
pituitary	2.3166 ± 0.5941	2.1296 ± 0.1239	1.5167 ± 0.2158
bone	1.0986 ± 0.0977	1.2549 ± 0.0402	0.9986 ± 0.0647
marrow	1.1274 ± 0.0404	1.6730 ± 0.0385	1.8999 ± 0.0503
adrenals	0.7995 ± 0.2038	0.7159 ± 0.0142	0.7352 ± 0.0868
pancreas	0.8859 ± 0.0708	0.8686 ± 0.0189	0.5714 ± 0.0434
stomach	1.1381 ± 0.1548	1.1291 ± 0.2482	0.5979 ± 0.1881
sm int	2.1204 ± 0.2397	2.2102 ± 0.1866	1.8591 ± 0.1783
u lg int	1.5406 ± 0.2163	1.5746 ± 0.1370	1.2246 ± 0.1285
l lg int	0.6184 ± 0.0745	1.1438 ± 0.0344	1.2009 ± 0.0909

Tissue	[⁶⁴Cu(NEC-SP)] (8), %ID/organ		
	1 hour	4 hour	24 hour
blood	5.0815 ± 0.2045	5.4621 ± 0.1852	4.6416 ± 0.1062
lung	0.4004 ± 0.0591	0.4249 ± 0.0229	0.4466 ± 0.0469
liver	12.1934 ± 0.9247	13.3691 ± 0.5757	14.5346 ± 0.3398
spleen	0.1201 ± 0.0256	0.1950 ± 0.0180	0.2886 ± 0.0271
kidney	4.9000 ± 0.6496	4.1334 ± 0.2921	2.5881 ± 0.1932
muscle	14.2360 ± 1.6459	13.4920 ± 0.1519	11.1814 ± 0.7838
fat	3.8721 ± 0.8096	2.7506 ± 0.2269	1.8088 ± 0.2138
heart	0.2838 ± 0.0140	0.3171 ± 0.0354	0.4086 ± 0.0334
brain	0.1115 ± 0.0101	0.1331 ± 0.0171	0.1844 ± 0.0140
pituitary	0.0083 ± 0.0014	0.0075 ± 0.0010	0.0053 ± 0.0007
bone	10.5819 ± 0.6005	12.7803 ± 0.2140	9.3194 ± 0.3564
marrow	0.0458 ± 0.0083	0.0758 ± 0.0101	0.0813 ± 0.0160
adrenals	0.0272 ± 0.0101	0.0294 ± 0.0043	0.0266 ± 0.0048
pancreas	0.7401 ± 0.0402	0.7799 ± 0.0648	0.4986 ± 0.0382
stomach	1.7949 ± 0.0561	1.7978 ± 0.0947	1.3370 ± 0.2653
sm int	4.4502 ± 0.2188	4.5194 ± 0.4399	3.8927 ± 0.4469
u lg int	3.7927 ± 0.3612	4.0661 ± 0.2241	3.5477 ± 0.1964
l lg int	2.9545 ± 0.1889	5.4550 ± 0.1347	6.5743 ± 0.3327

[⁶⁴Cu(NEC-SB)] (9), %ID/g

	1 hr.			4 hr.			24 hr.		
<i>blood</i>	0.8738	+/-	0.1398	0.8793	+/-	0.1117	0.6925	+/-	0.1509
<i>lung</i>	1.6730	+/-	0.2253	0.9489	+/-	0.1087	0.7464	+/-	0.1430
<i>liver</i>	4.1054	+/-	0.4646	3.8664	+/-	0.6354	3.2960	+/-	0.7279
<i>spleen</i>	0.6976	+/-	0.1679	0.8151	+/-	0.1366	0.9235	+/-	0.2070
<i>kidney</i>	8.8945	+/-	0.6124	7.0956	+/-	1.0588	4.7376	+/-	0.6171
<i>muscle</i>	0.4111	+/-	0.0557	0.3299	+/-	0.0500	0.3016	+/-	0.0330
<i>fat</i>	0.3709	+/-	0.0731	0.2183	+/-	0.0371	0.1360	+/-	0.0350
<i>heart</i>	0.8394	+/-	0.2282	0.7522	+/-	0.0594	0.9232	+/-	0.1891
<i>brain</i>	0.0792	+/-	0.0113	0.0903	+/-	0.0068	0.1086	+/-	0.0195
<i>pituitary</i>	3.1498	+/-	0.8057	2.1487	+/-	0.9642	1.9032	+/-	1.6195
<i>bone</i>	1.1426	+/-	0.1954	1.1546	+/-	0.1606	0.8548	+/-	0.1879
<i>marrow</i>	1.1164	+/-	0.1591	1.5088	+/-	0.2664	1.7238	+/-	0.3234
<i>adrenals</i>	0.8655	+/-	0.1851	0.7541	+/-	0.1404	0.9363	+/-	0.1988
<i>pancreas</i>	0.8952	+/-	0.1283	0.8456	+/-	0.1745	0.5935	+/-	0.1429
<i>stomach</i>	1.5054	+/-	0.5496	1.2625	+/-	0.4010	0.6760	+/-	0.2047
<i>sm int</i>	2.3465	+/-	0.3124	2.1002	+/-	0.2551	1.7107	+/-	0.1795
<i>u lg int</i>	1.7314	+/-	0.1940	1.5708	+/-	0.2721	1.1087	+/-	0.1641
<i>l lg int</i>	0.6986	+/-	0.1439	1.1160	+/-	0.2475	1.2342	+/-	0.1904
<i>tail</i>	2.2282	+/-	1.6246	3.0701	+/-	2.0105	1.4050	+/-	0.2416

	$[^{64}\text{Cu}(\text{NEC-SB})]$ (9), %ID/organ			1 hr.			4 hr.			24 hr.		
<i>blood</i>	4.6204	+/-	0.3514	5.1034	+/-	0.6410	3.8784	+/-	0.6381			
<i>lung</i>	0.9193	+/-	0.1413	0.5729	+/-	0.0535	0.4637	+/-	0.0867			
<i>liver</i>	12.6959	+/-	0.9281	12.3851	+/-	1.0954	13.5960	+/-	2.2414			
<i>spleen</i>	0.1430	+/-	0.0183	0.1878	+/-	0.0439	0.2208	+/-	0.0410			
<i>kidney</i>	3.9939	+/-	0.3514	3.5244	+/-	0.6605	2.3495	+/-	0.1922			
<i>muscle</i>	12.7603	+/-	0.5338	11.1404	+/-	0.5636	9.9542	+/-	0.7406			
<i>fat</i>	3.8850	+/-	0.6169	2.4763	+/-	0.1207	1.5077	+/-	0.3369			
<i>heart</i>	0.2992	+/-	0.0895	0.2778	+/-	0.0335	0.3422	+/-	0.0457			
<i>brain</i>	0.1185	+/-	0.0147	0.1361	+/-	0.0069	0.1694	+/-	0.0309			
<i>pituitary</i>	0.0069	+/-	0.0010	0.0058	+/-	0.0011	0.0070	+/-	0.0057			
<i>bone</i>	9.3966	+/-	0.7776	10.3772	+/-	0.4961	7.4533	+/-	1.2477			
<i>marrow</i>	0.0483	+/-	0.0072	0.0696	+/-	0.0183	0.0732	+/-	0.0114			
<i>adrenals</i>	0.0250	+/-	0.0047	0.0249	+/-	0.0022	0.0330	+/-	0.0062			
<i>pancreas</i>	0.6493	+/-	0.0427	0.6852	+/-	0.1136	0.4539	+/-	0.0819			
<i>stomach</i>	1.6760	+/-	0.2189	1.5921	+/-	0.1399	1.0439	+/-	0.2958			
<i>sm int</i>	3.7978	+/-	0.2140	3.6529	+/-	0.2885	3.3009	+/-	0.3217			
<i>u lg int</i>	3.3693	+/-	0.1347	3.8394	+/-	0.5064	3.0604	+/-	0.4085			
<i>l lg int</i>	2.7473	+/-	0.2807	5.0136	+/-	1.7315	6.3314	+/-	0.6913			
<i>tail</i>	4.8471	+/-	4.3162	6.6370	+/-	4.3945	3.0631	+/-	0.4170			