Supporting Information for

Less Toxic Zinc(II), Diorganotin(IV), Gallium(III) and Cadmium(II) Complexes Derived from 2-benzoylpyridine N,N-dimethylthiosemicarbazone: Synthesis, Crystal Structures, Cytotoxicity and Investigations of Mechanisms of Action

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Table S1 Summary of Crystal Data and Refinement Results for Complexes 1–4.

Compound	**1**	**2**	**3**	**4**
Empirical formula	$C_{30}H_{30}N_8S_2Zn$	$C_{29}H_{28}N_4O_2SSn$	$C_{30}H_{30}GaN_9O_3S_2$	$C_{30}H_{30}CdN_8S_2$
Formula weight	632.11	615.30	698.47	679.14
Crystal size (mm)	0.50×0.41×0.23	0.38×0.25×0.17	0.68×0.23×0.09	0.49×0.34×0.26
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	*P2(1)/c*	*P2(1)/c*	*P2(1)/n*	*C2/c*
T (K)	296(2)	296(2)	293(2)	296(2)
a (Å)	16.408(3)	17.15(2)	18.441	16.9715(10)
b (Å)	8.6188(15)	10.549(13)	8.936	23.6235(15)
c (Å)	21.365(4)	16.45(2)	21.809	15.9881(10)
V (Å)^3	2995.0(9)	2914(6)	3583.8	6249.1(7)
α (°)	90.00	90.00	90.00	90.00
β (°)	97.571(3)	101.78(3)	94.29	102.8670(10)

γ (°)	90.00	90.00	90.00	90.00
D_c (g cm^{-3})	1.402	1.402	1.295	1.444
Z	4	4	4	8
μ (mm^{-1})	0.994	0.980	0.927	0.866
θ (°)	1.92–25.0	2.28–25.00	1.87–25.00	1.72–25.00
F(000)	1312	1248	1440	2768
hkl Range	$-19 \le h \le 16$, $-10 \le k \le 10$, $-24 \le l \le 25$	$-20 \le h \le 19$, $-12 \le k \le 11$, $-16 \le l \le 19$	$-21 \le h \le 15$, $-10 \le k \le 10$, $-25 \le l \le 25$	$-20 \le h \le 14$, $-27 \le k \le 27$, $-18 \le l \le 18$
Refl. collected	5264	5128	6302	5506
Refl. unique	4243	4093	2623	4679
R_{int}	0.0190	0.0377	0.1557	0.0234
Parameters	370	334	407	370
R_1,wR_2 [$I \ge 2\sigma(I)$]	0.0353, 0.1161	0.0297, 0.0745	0.1430, 0.2260	0.0281, 0.0708
R_1,wR_2 (all dates)	0.0474, 0.1243	0.0422, 0.0795	0.3635, 0.3933	0.0366, 0.0743
Goodness-of-fit on F^2	0.956	0.998	1.268	1.060
$\Delta\rho_{max,\ min}$ (e Å^{-3})	0.521, –0.251	0.360, –0.446	2.646, –0.862	0.475, –0.311

Table S2 Selected bond lengths (Å) and angles (deg) of complexes 1–4.

1		**2**		**3**		**4**	
Zn1–N7	2.1332(19)	Sn1–C22	2.178(4)	Ga1–N7	1.994(8)	Cd1–N3	2.3751(19)
Zn1–N3	2.1441(19)	Sn1–C16	2.183(4)	Ga1–N3	2.053(8)	Cd1–N7	2.384(2)
Zn1–N4	2.213(2)	Sn1–O2	2.355(3)	Ga1–N4	2.111(8)	Cd1–N8	2.396(2)
Zn1–N8	2.2455(19)	Sn1–N3	2.395(3)	Ga1–N8	2.130(8)	Cd1–N4	2.420(2)
Zn1–S1	2.4331(8)	Sn1–O1	2.432(3)	Ga1–S1	2.368(3)	Cd1–S1	2.5609(7)
Zn1–S2	2.4371(8)	Sn1–N4	2.459(3)	Ga1–S2	2.372(3)	Cd1–S2	2.5616(7)
S1–C3	1.719(3)	Sn1–S1	2.612(3)	S1–C3	1.712(11)	S1–C3	1.729(3)
S2–C18	1.725(3)	S1–C3	1.762(3)	S2–C18	1.667(11)	S2–C18	1.740(3)
N2–C3	1.344(3)	N2–C3	1.347(4)	N2–C3	1.269(12)	N2–C3	1.336(3)
N2–N3	1.367(3)	N2–N3	1.376(3)	N2–N3	1.344(11)	N2–N3	1.362(2)
N3–C4	1.289(3)	N3–C4	1.324(4)	N3–C4	1.294(11)	N3–C4	1.301(3)
N6–C18	1.333(3)	C22–Sn1–C16	167.67(12)	N6–C18	1.359(13)	N6–C18	1.331(3)
N6–N7	1.348(3)	C22–Sn1–O2	89.80(10)	N6–N7	1.388(11)	N6–N7	1.367(2)
N7–C19	1.299(3)	C16–Sn1–O2	91.06(9)	N7–C19	1.310(13)	N7–C19	1.298(3)
N7–Zn1–N3	161.11(8)	C22–Sn1–N3	87.51(12)	N7–Ga1–N3	174.9(3)	N3–Cd1–N7	151.03(6)
N7–Zn1–N4	93.77(7)	C16–Sn1–N3	97.19(11)	N7–Ga1–N4	98.9(3)	N3–Cd1–N8	95.00(7)
N3–Zn1–N4	73.99(7)	O2–Sn1–N3	152.98(8)	N3–Ga1–N4	78.0(3)	N7–Cd1–N8	67.99(6)
N7–Zn1–N8	73.91(7)	C22–Sn1–O1	86.71(13)	N7–Ga1–N8	78.5(3)	N3–Cd1–N4	68.38(6)
N3–Zn1–N8	91.62(7)	C16–Sn1–O1	83.69(12)	N3–Ga1–N8	97.1(3)	N7–Cd1–N4	86.63(6)
N4–Zn1–N8	90.90(7)	O2–Sn1–O1	55.21(8)	N4–Ga1–N8	85.6(3)	N8–Cd1–N4	86.23(7)
N7–Zn1–S1	111.35(6)	N3–Sn1–O1	151.17(7)	N7–Ga1–S1	100.1(2)	N3–Cd1–S1	74.74(5)
N3–Zn1–S1	79.53(6)	C22–Sn1–N4	82.06(11)	N3– Ga1 –S1	82.6(2)	N7–Cd1–S1	126.85(5)

N4–Zn1–S1	153.47(5)	C16–Sn1–N4	89.04(11)	N4–Ga1–S1	159.7(3)	N8–Cd1–S1	91.77(5)
N8–Zn1–S1	88.16(6)	O2–Sn1–N4	137.58(9)	N8–Ga1–S1	91.0(2)	N4–Cd1–S1	142.71(5)
N7–Zn1–S2	79.71(5)	N3–Sn1–N4	68.53(11)	N7–Ga1–S2	81.9(2)	N3–Cd1–S2	121.22(5)
N3–Zn1–S2	113.81(6)	O1–Sn1–N4	82.70(11)	N3–Ga1–S2	102.0(2)	N7–Cd1–S2	74.43(5)
N4–Zn1–S2	89.54(6)	C22–Sn1–S1	97.14(13)	N4–Ga1–S2	90.5(3)	N8–Cd1–S2	142.10(5)
N8–Zn1–S2	153.59(5)	C16–Sn1–S1	95.11(12)	N8–Ga1–S2	159.2(2)	N4–Cd1–S2	96.49(5)
S1–Zn1–S2	102.82(3)	O2–Sn1–S1	79.78(6)	S1–Ga1–S2	99.41(12)	S1–Cd1–S2	107.28(3)
		N3–Sn1–S1	73.90(8)				
		O1–Sn1–S1	134.87(8)				
		N4–Sn1–S1	142.42(6)				

Table S3 The cytotoxicity of the tested compounds against HepG2 cells and QSG7701 cells. $n = 4$. Mean ± SD.

	Tested compounds				
Hepatocellular cells	Bp44mT	1	2	3	4
HepG2	1.45 ± 0.1	6.68 ± 1.0	3.61 ± 0.15	1.7 ± 0.25	2.47 ± 0.18
QSG7701	7.3 ± 0.18	77.64 ± 10.05	9.42 ± 0.31	0.67 ± 0.069	17.05 ± 1.67

Table S4 Effects of **1** on intracellular ROS in HepG2 cells. $n = 4$. Mean ± SD.

	Concentrations (μM)			
intracellular ROS	0	1	5	10
Measured data	2307	3245	5015	6670
	2614	2628	4891	6715
	2689	3482	5113	6779
	2623	3190	5518	5656
Mean value	2558.25	3136.25	5134.25	6455
Relative value (% of control)	100.0 ± 0.058	122.60 ± 0.12	200.70 ± 0.091	252.32 ± 0.18

Table S5 Effect of 1 on MMP in HepG2 cells, the cells were loaded with membrane-sensitive probe Rh123. $n = 4$. Mean ± SD.

	Concentrations (μM)			
Rh123	0	1	5	10
Measured data	27022	11559	14274	7491
	24109	12280	15062	7702
	25379	17927	8320	6129
	28022	13454	8645	9348
Mean value	26133	13805	11575.25	7667.5
Relative value (% of control)	100.0 ± 0.057	52.83 ± 0.095	44.29 ± 0.12	29.34 ± 0.044

Table S6 Effects of **1**-induced activations of caspase-3. *n* = 4. Mean ± SD.

	Concentrations (μM)			
caspase-3	0	1	5	10
Measured data	2330	2998	3668	6280
	2416	3088	3910	9693
	2097	3211	3856	8345
	2100	2875	3722	7628
Mean value	2235.75	3043	3789	7986.5
Relative activity	1.0 ± 0.063	1.36 ± 0.055	1.70 ± 0.044	3.57 ± 0.55

Table S7 Effects of **1** on the activation of the p21 gene in HepG2 cells by using in vitro kinase test. n = 4. Mean ± SD.

	Concentrations (μM)			
p21 gene	0	1	5	10
Measured data	3106	3322	3217	5899
	2761	3854	4581	6590
	3116	3789	4356	6675
	2767	3387	3442	5814
Mean value	2937.5	3588	3899	6244.5
Relative activity	1.0 ± 0.059	1.21 ± 0.080	1.33 ± 0.19	2.13 ± 0.13

Table S8 Effects of **1** on the activation of the p53 gene in HepG2 cells by using in vitro kinase test. n = 4. Mean ± SD.

	Concentrations (μM)			
p53 gene	0	1	5	10
Measured data	3451	3561	4321	6891
	2897	2672	2156	4781
	3621	3156	3476	6671
	2455	3899	2915	5253
Mean value	3106	3322	3217	5899
Relative activity	1.0 ± 0.15	1.07 ± 0.15	1.04 ± 0.25	1.90 ± 0.29

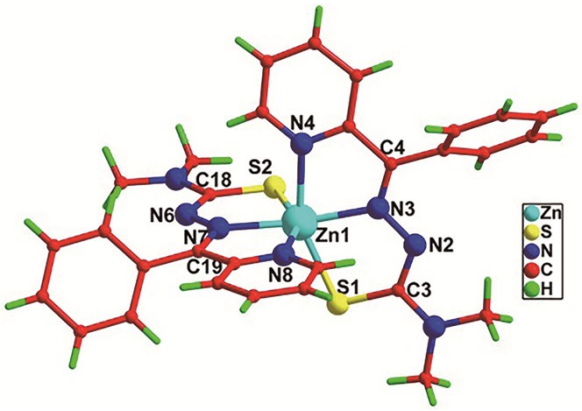

Figure S1. Structure of complex **1** with atomic numbering scheme.

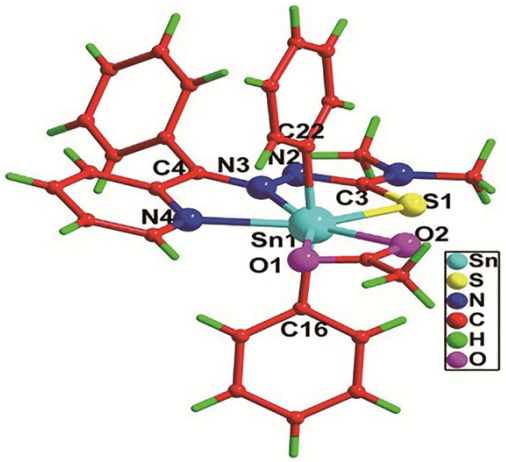

Figure S2. Structure of complex **2** with atomic numbering scheme.

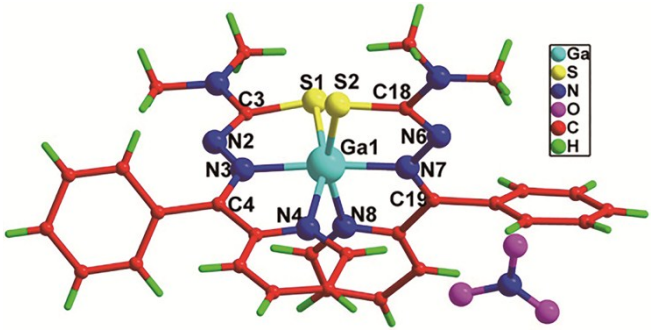

Figure S3. Structure of complex **3** with atomic numbering scheme.

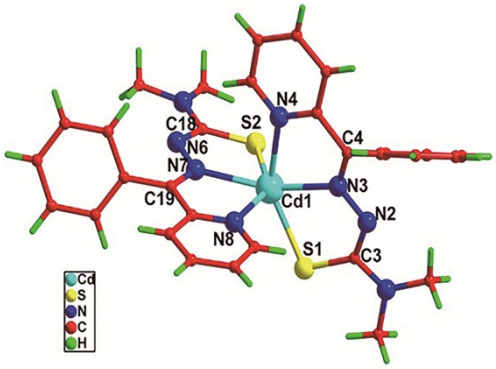

Figure S4. Structure of complex **4** with atomic numbering scheme.