Luminescent *fac*-[Re(CO)$_3$(phen)] carboxylato complexes with non-steroidal anti-inflammatory drugs: Synthesis and mechanistic insights into the *in vitro* anticancer activity of *fac*-[Re(CO)$_3$(phen)(aspirin)]

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Supplementary Information

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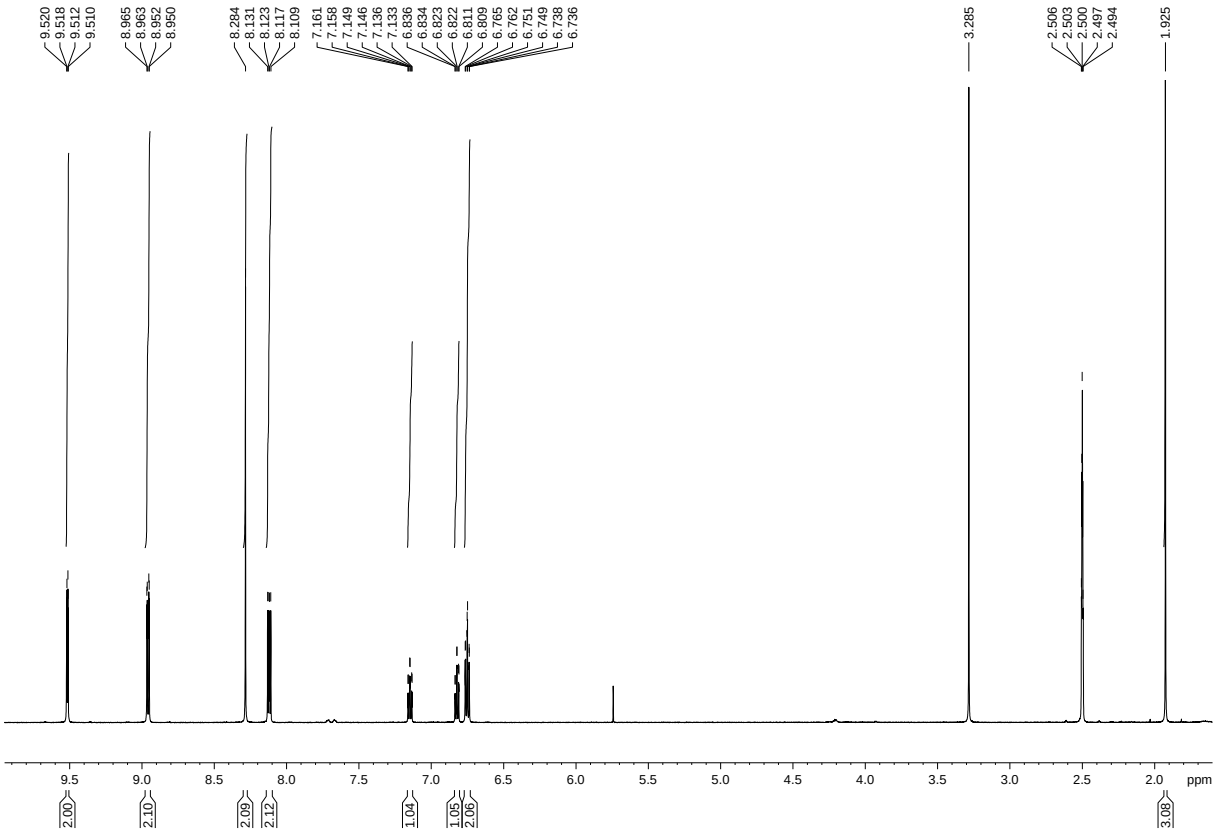

Figure S1 ^{1}H-NMR of compound **1**

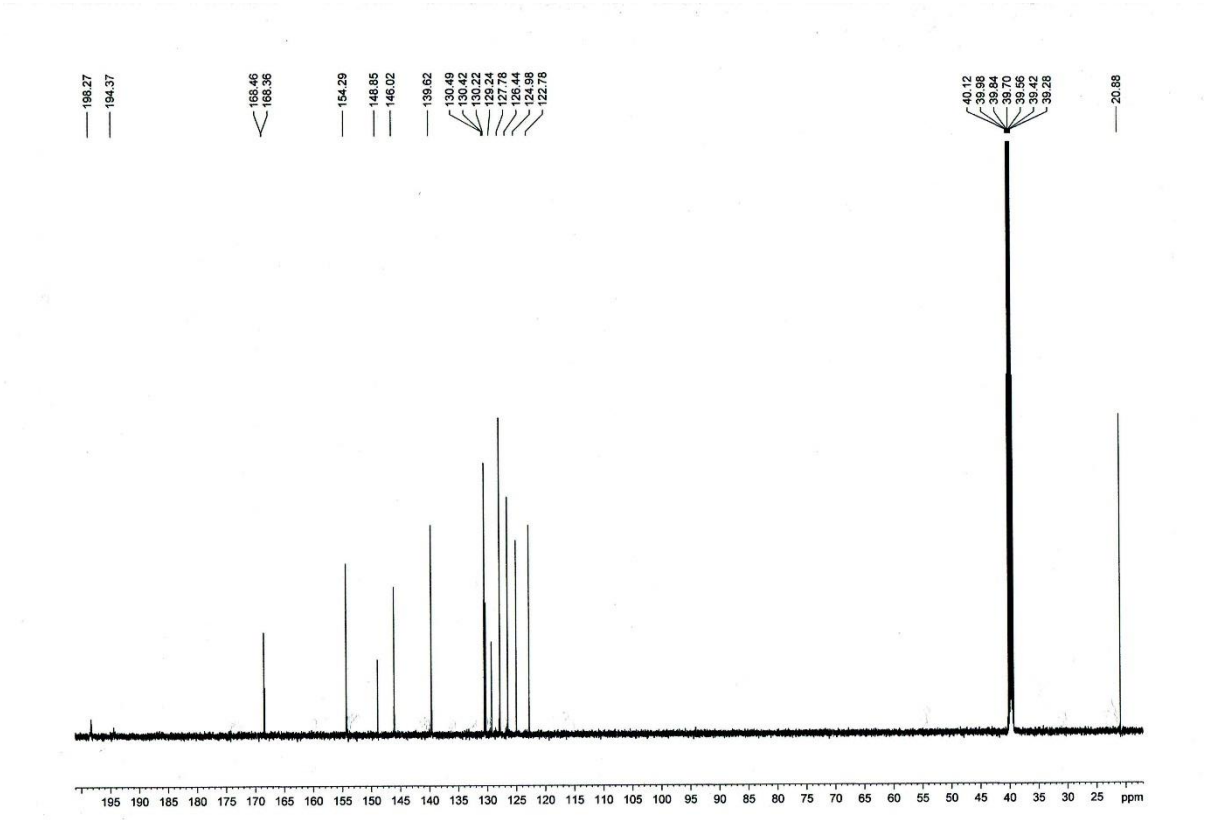

Figure S2 ^{13}C-NMR of compound **1**

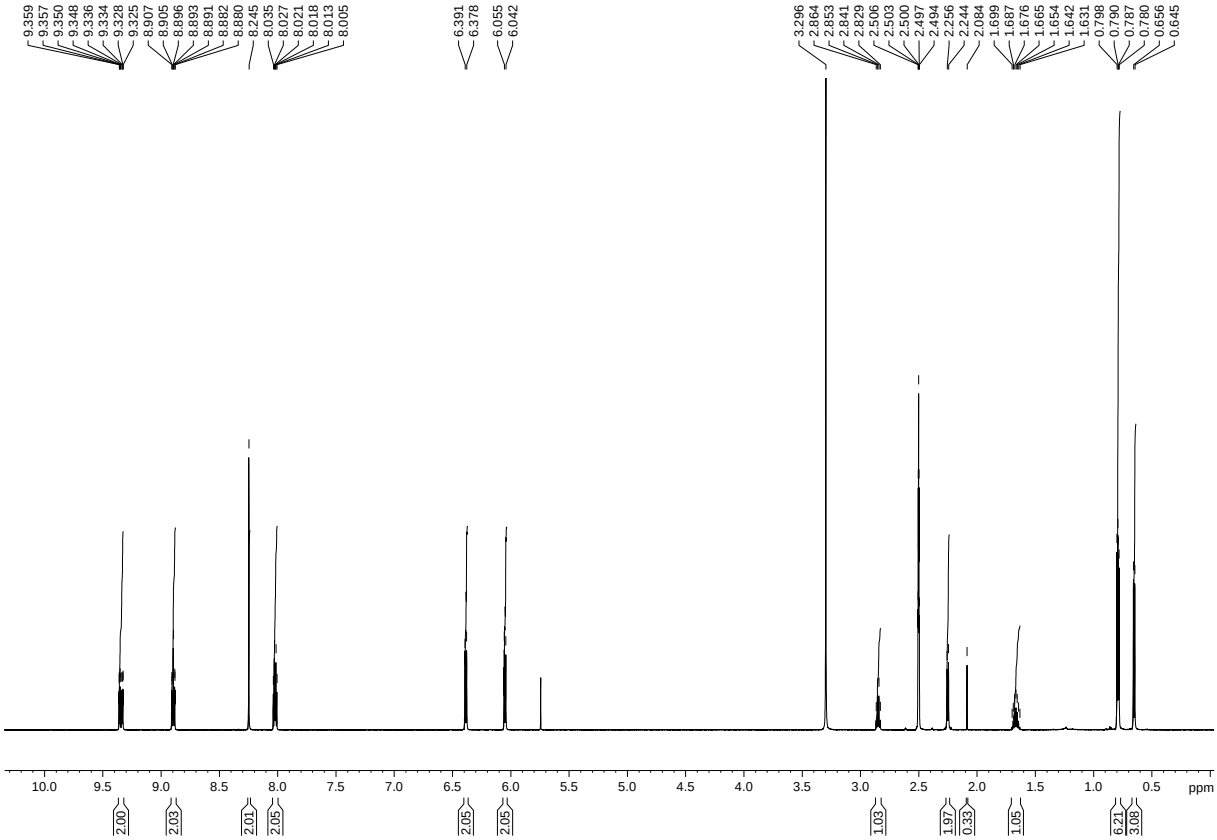

Figure S3 ^{1}H-NMR of compound **2**

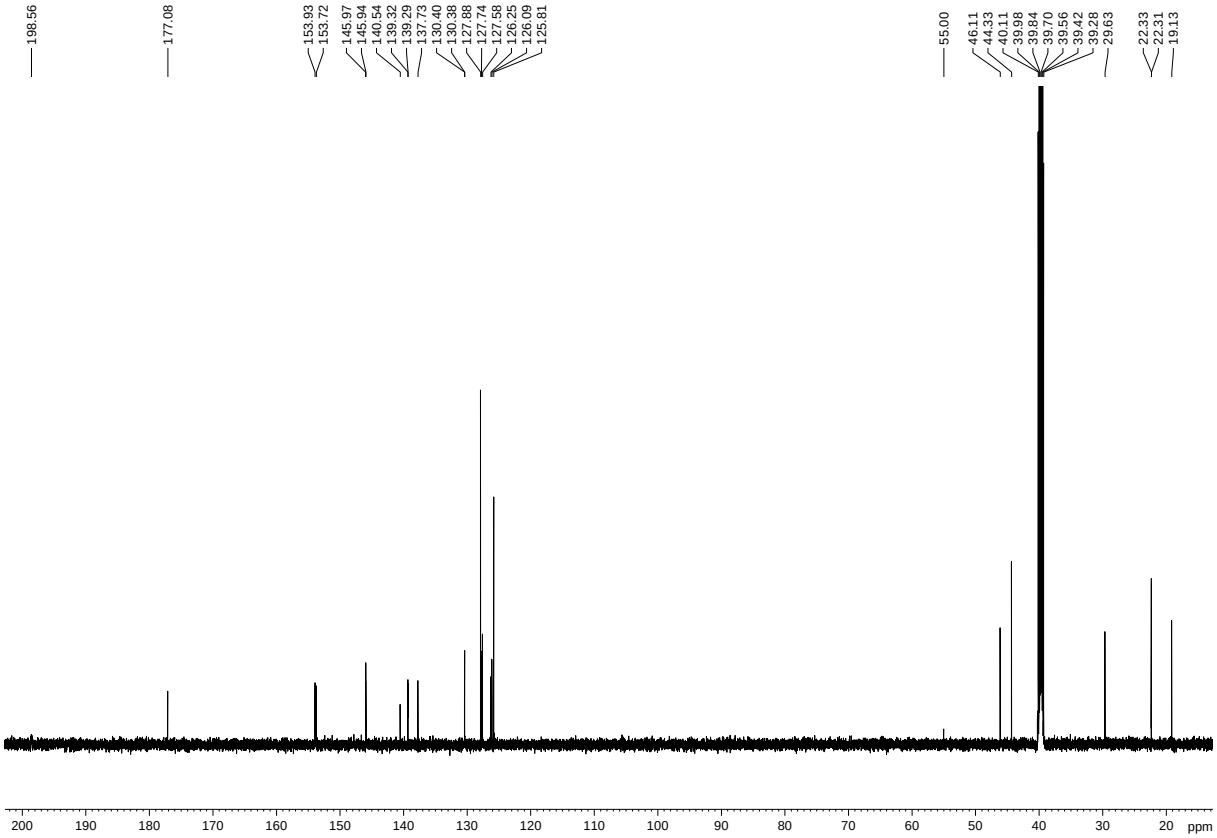

Figure S4 ^{13}C-NMR of compound **2**

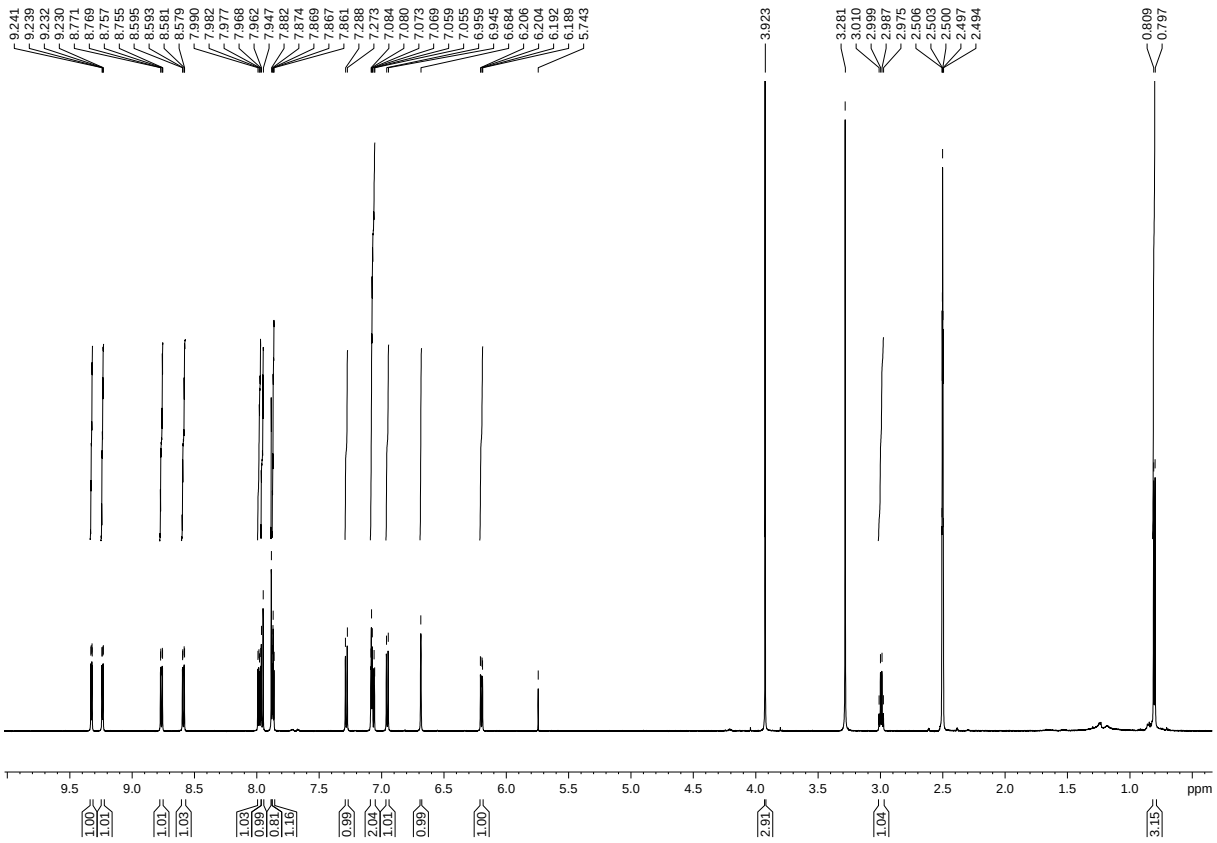

Figure S5 ^{1}H-NMR of compound **3**

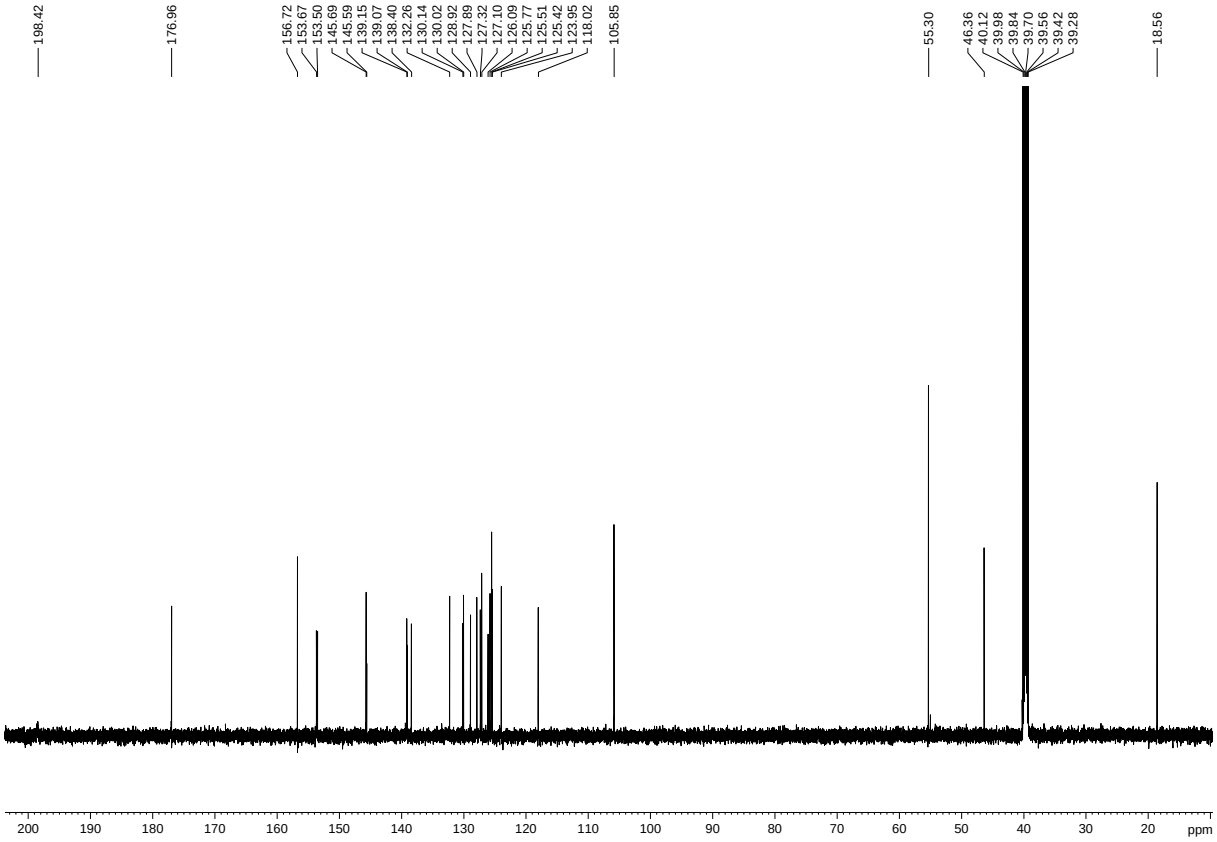

Figure S6 ^{13}C-NMR of compound **3**

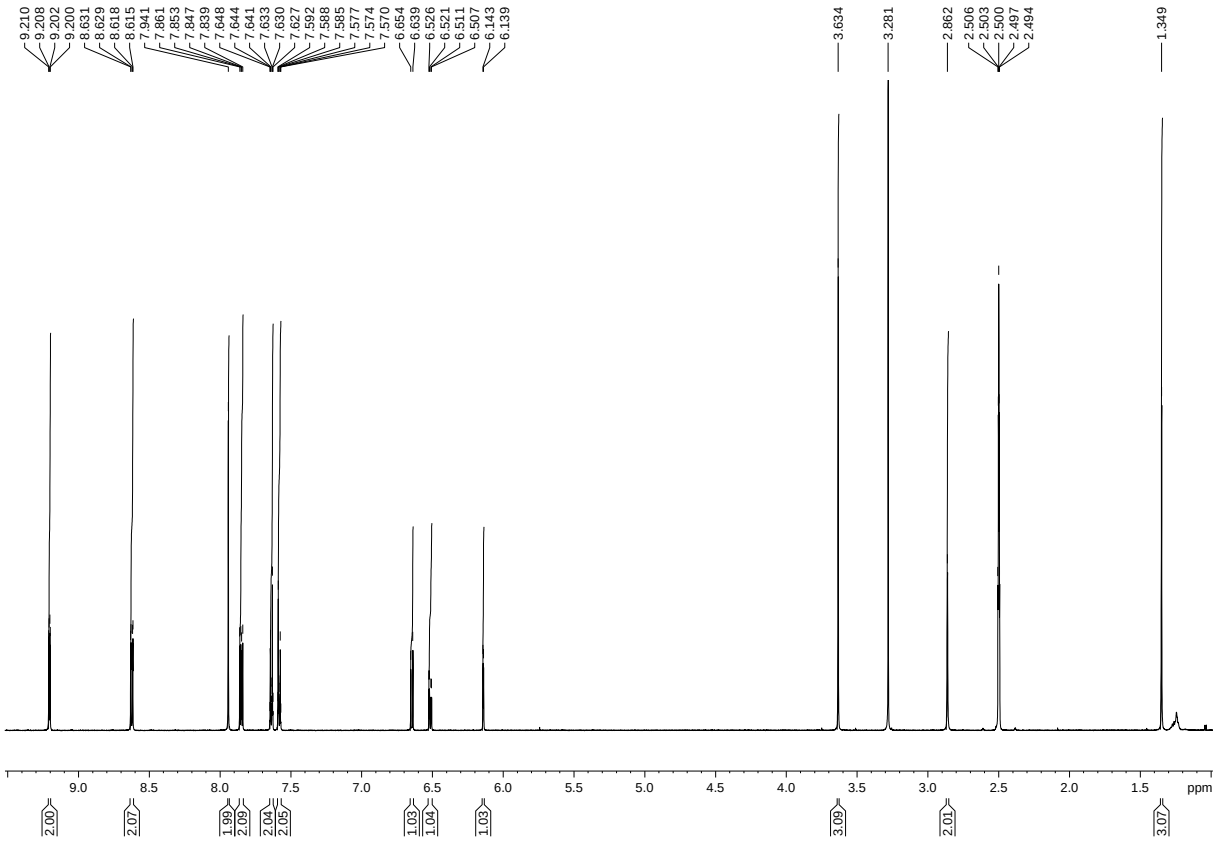

Figure S7 ^{1}H-NMR of compound **4**

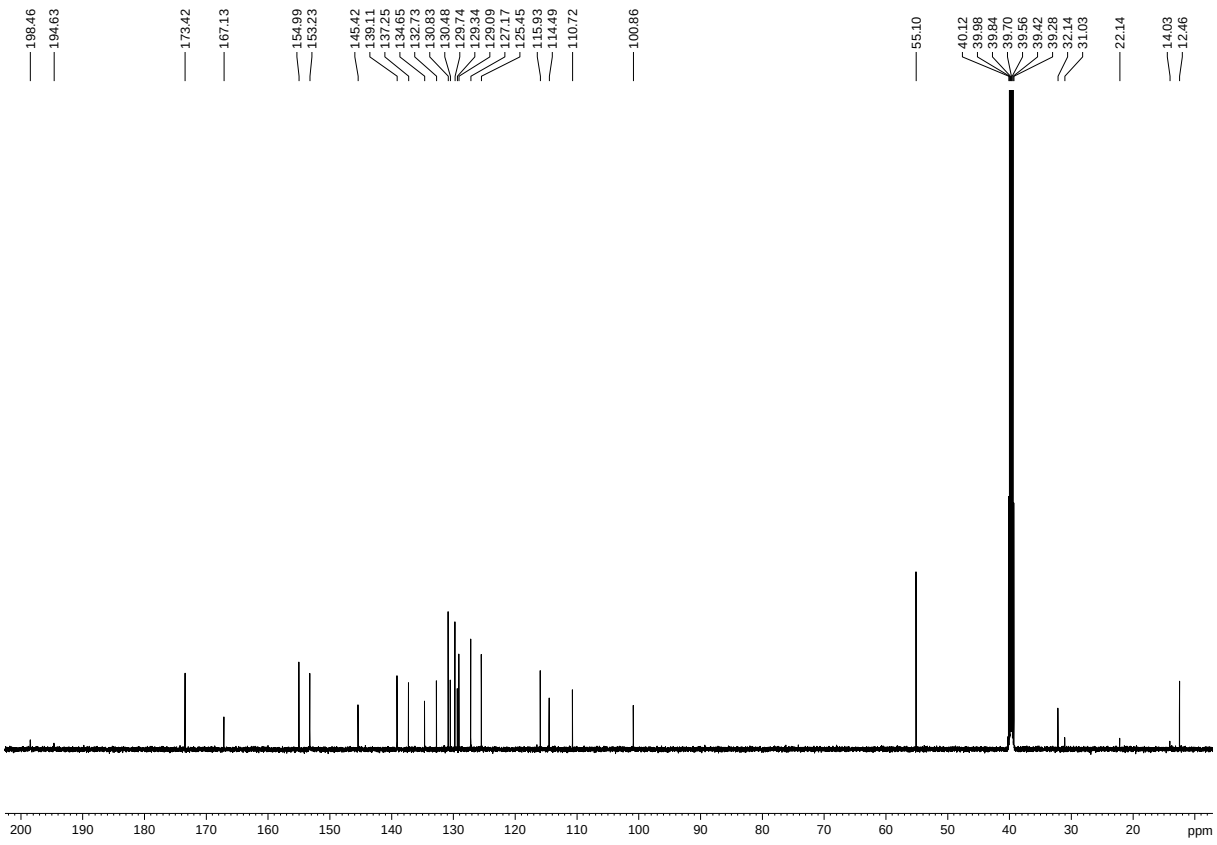

Figure S8 ^{13}C-NMR of compound **4**

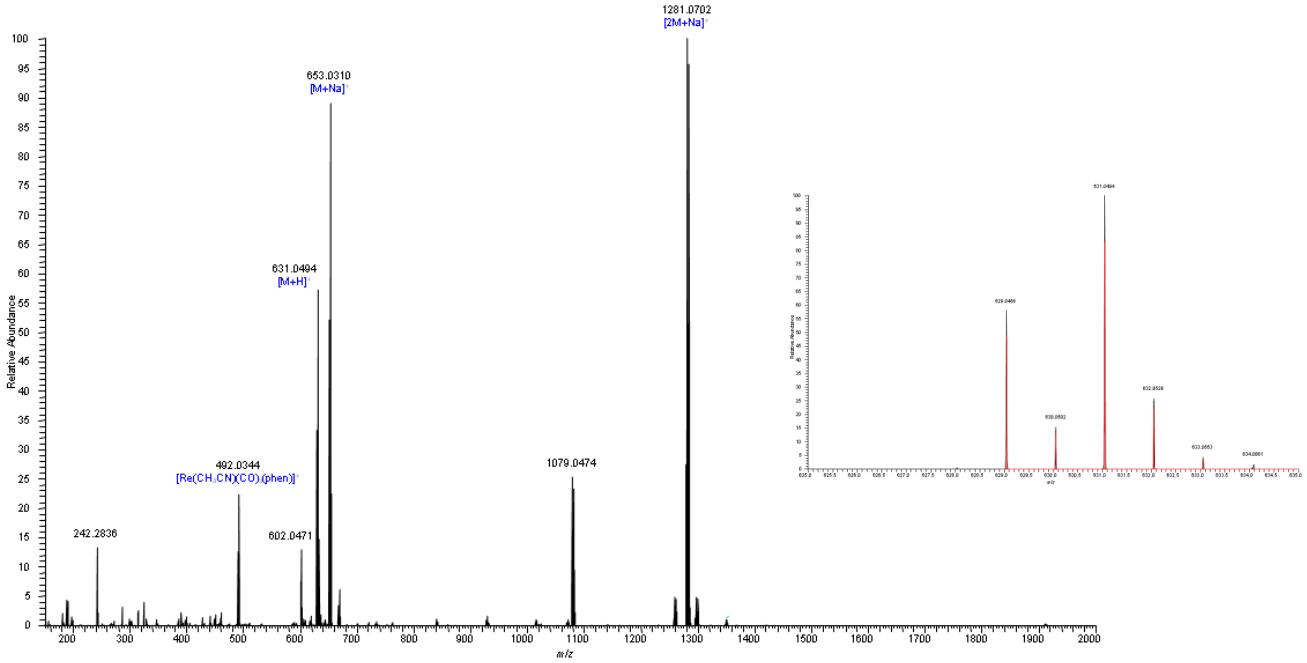

Figure S9 Positive mode ESI mass spectrum of **1** in acetonitrile recorded at a solvent flow rate of 10 µL min^{-1} together with the peak assignments. The inset shows the peak pattern of $[M+H]^+$ centered at 631.0494 Da (black) together with the simulated isotope pattern (red). The deviation between the experimental and calculated peak position is -1.6 mDa for the main signal.

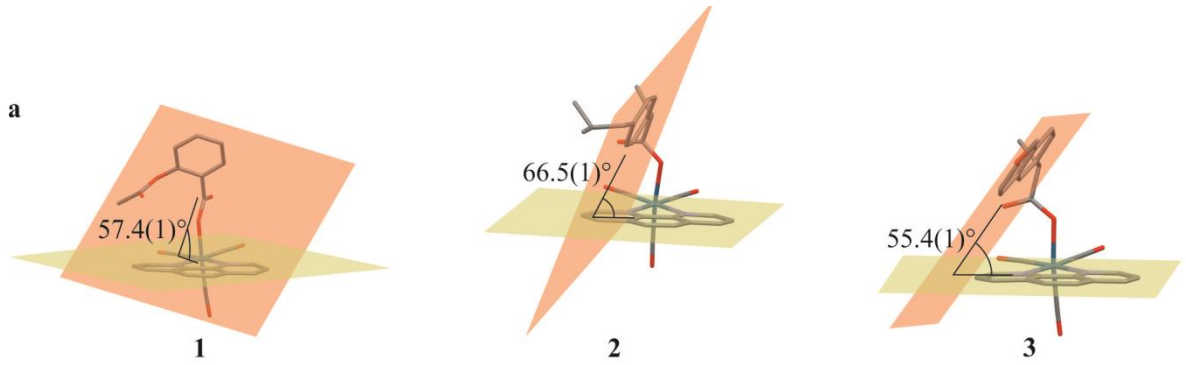

Figure S10. Mutual relations between mean-planes delineated by the non-hydrogen atoms of aromatic rings in **1**, **2** and **3**

Table S1. Crystal and structure refinement data for **1**, **2** and **3**.

Compound	**1**	**2**	**3**
Empirical formula	$C_{24}H_{15}N_2O_7Re$	$C_{28}H_{25}N_2O_5Re$	$C_{29}H_{21}N_2O_6Re$
Formula weight	629.58	655.70	679.68
Temperature/K	100(2)	100(2)	100.00(2)
Crystal system	monoclinic	orthorhombic	orthorhombic
Space group	$P2_1/n$	$P2_12_12$	$P2_12_12$
a/Å	10.7471(3)	17.8677(5)	6.16143(9)
b/Å	12.2015(3)	12.9186(4)	46.2179(6)
c/Å	16.6996(4)	10.7310(3)	9.40358(10)
α/°	90	90	90
β/°	92.127(2)	90	90
γ/°	90	90	90
Volume/Å^3	2188.32(9)	2477.00(12)	2677.84(6)
Z	4	4	4
ρ_{calc}g/cm^3	1.911	1.758	1.686
μ/mm^{-1}	5.603	4.948	9.260
Radiation	Mo$K\alpha$ (λ = 0.71073 Å)	Mo$K\alpha$ (λ = 0.71073 Å)	Cu$K\alpha$ (λ = 1.54184 Å)
Final R indexes [I>=2σ (I)]	R_1 = 0.0254, wR_2 = 0.0511	R_1 = 0.0443, wR_2 = 0.0761	R_1 = 0.0347, wR_2 = 0.0770
Final R indexes [all data]	R_1 = 0.0342, wR_2 = 0.0555	R_1 = 0.0506, wR_2 = 0.0795	R_1 = 0.0349, wR_2 = 0.0771
Flack parameter	–	-0.025(8)	0.007(9)

Table S2. Bond lengths for **1**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C(1)	O(1)	1.147(4)	C(15)	N(1)	1.365(3)
C(1)	Re(1)	1.914(3)	C(16)	C(17)	1.513(4)
C(2)	O(2)	1.153(3)	C(16)	O(4)	1.292(3)
C(2)	Re(1)	1.918(3)	C(16)	O(5)	1.219(3)
C(3)	O(3)	1.157(4)	C(17)	C(18)	1.374(4)
C(3)	Re(1)	1.903(3)	C(17)	C(22)	1.386(4)
C(4)	C(5)	1.393(4)	C(18)	C(19)	1.388(4)
C(4)	N(1)	1.332(4)	C(18)	O(6A)	1.407(4)
C(5)	C(6)	1.370(4)	C(18)	O(6B)	1.416(14)
C(6)	C(7)	1.405(4)	C(19)	C(20)	1.383(4)
C(7)	C(8)	1.442(4)	C(20)	C(21)	1.384(4)
C(7)	C(15)	1.404(4)	C(21)	C(22)	1.390(4)
C(8)	C(9)	1.349(5)	C(23A)	C(24)	1.503(5)
C(9)	C(10)	1.432(4)	C(23A)	O(6A)	1.350(4)
C(10)	C(11)	1.406(5)	C(23A)	O(7A)	1.192(4)
C(10)	C(14)	1.405(4)	C(23B)	C(24)	1.551(14)
C(11)	C(12)	1.362(5)	C(23B)	O(6B)	1.426(14)
C(12)	C(13)	1.392(4)	C(23B)	O(7B)	1.225(14)
C(13)	N(2)	1.329(4)	N(1)	Re(1)	2.173(2)
C(14)	C(15)	1.425(4)	N(2)	Re(1)	2.175(2)
C(14)	N(2)	1.360(3)	O(4)	Re(1)	2.127(2)

Table S3. Valence angles for **1**.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
O(1)	C(1)	Re(1)	176.9(3)	C(20)	C(19)	C(18)	119.5(3)
O(2)	C(2)	Re(1)	178.0(3)	C(19)	C(20)	C(21)	119.8(3)
O(3)	C(3)	Re(1)	176.5(3)	C(20)	C(21)	C(22)	119.8(3)
N(1)	C(4)	C(5)	122.8(3)	C(17)	C(22)	C(21)	120.7(3)
C(6)	C(5)	C(4)	119.9(3)	O(6A)	C(23A)	C(24)	110.1(3)
C(5)	C(6)	C(7)	119.0(3)	O(7A)	C(23A)	C(24)	125.9(4)
C(6)	C(7)	C(8)	123.9(3)	O(7A)	C(23A)	O(6A)	123.9(3)
C(15)	C(7)	C(6)	117.7(3)	O(6B)	C(23B)	C(24)	112.6(10)
C(15)	C(7)	C(8)	118.4(3)	O(7B)	C(23B)	C(24)	123.3(12)
C(9)	C(8)	C(7)	121.2(3)	O(7B)	C(23B)	O(6B)	124.0(14)
C(8)	C(9)	C(10)	121.0(3)	C(4)	N(1)	C(15)	117.8(2)
C(11)	C(10)	C(9)	123.6(3)	C(4)	N(1)	Re(1)	127.12(19)
C(14)	C(10)	C(9)	119.1(3)	C(15)	N(1)	Re(1)	114.84(19)
C(14)	C(10)	C(11)	117.3(3)	C(13)	N(2)	C(14)	118.4(2)
C(12)	C(11)	C(10)	119.4(3)	C(13)	N(2)	Re(1)	127.03(19)
C(11)	C(12)	C(13)	120.0(3)	C(14)	N(2)	Re(1)	114.54(18)
N(2)	C(13)	C(12)	122.3(3)	C(16)	O(4)	Re(1)	126.06(17)
C(10)	C(14)	C(15)	119.8(3)	C(23A)	O(6A)	C(18)	115.5(3)
N(2)	C(14)	C(10)	122.5(3)	C(18)	O(6B)	C(23B)	102.6(10)
N(2)	C(14)	C(15)	117.7(2)	C(1)	Re(1)	C(2)	88.98(13)
C(7)	C(15)	C(14)	120.4(3)	C(1)	Re(1)	N(1)	96.37(11)
N(1)	C(15)	C(7)	122.8(3)	C(1)	Re(1)	N(2)	172.29(11)
N(1)	C(15)	C(14)	116.8(2)	C(1)	Re(1)	O(4)	96.89(11)
O(4)	C(16)	C(17)	112.5(2)	C(2)	Re(1)	N(1)	172.54(10)
O(5)	C(16)	C(17)	121.1(3)	C(2)	Re(1)	N(2)	98.69(10)
O(5)	C(16)	O(4)	126.3(3)	C(2)	Re(1)	O(4)	96.00(10)
C(18)	C(17)	C(16)	119.9(3)	C(3)	Re(1)	C(1)	90.44(13)
C(18)	C(17)	C(22)	118.7(3)	C(3)	Re(1)	C(2)	88.27(13)
C(22)	C(17)	C(16)	121.4(2)	C(3)	Re(1)	N(1)	96.86(11)
C(17)	C(18)	C(19)	121.4(3)	C(3)	Re(1)	N(2)	90.53(11)
C(17)	C(18)	O(6A)	115.6(3)	C(3)	Re(1)	O(4)	171.56(10)
C(17)	C(18)	O(6B)	123.9(6)	N(1)	Re(1)	N(2)	75.93(9)
C(19)	C(18)	O(6A)	122.3(3)	O(4)	Re(1)	N(1)	78.24(8)
C(19)	C(18)	O(6B)	103.9(6)	O(4)	Re(1)	N(2)	81.65(9)

Table S4. Torsion angles for **1**.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
C(4)	C(5)	C(6)	C(7)	-0.3(5)	C(15)	C(14)	N(2)	Re(1)	-1.2(3)
C(5)	C(4)	N(1)	C(15)	2.0(5)	C(16)	C(17)	C(18)	C(19)	175.9(3)
C(5)	C(4)	N(1)	Re(1)	-172.2(2)	C(16)	C(17)	C(18)	O(6A)	-13.6(4)
C(5)	C(6)	C(7)	C(8)	-177.7(3)	C(16)	C(17)	C(18)	O(6B)	37.5(7)
C(5)	C(6)	C(7)	C(15)	2.5(5)	C(16)	C(17)	C(22)	C(21)	-175.3(3)
C(6)	C(7)	C(8)	C(9)	180.0(3)	C(17)	C(16)	O(4)	Re(1)	-175.04(17)
C(6)	C(7)	C(15)	C(14)	177.5(3)	C(17)	C(18)	C(19)	C(20)	-0.8(5)
C(6)	C(7)	C(15)	N(1)	-2.7(5)	C(17)	C(18)	O(6A)	C(23A)	118.8(3)
C(7)	C(8)	C(9)	C(10)	1.6(5)	C(17)	C(18)	O(6B)	C(23B)	-87.4(11)
C(7)	C(15)	N(1)	C(4)	0.4(4)	C(18)	C(17)	C(22)	C(21)	2.0(5)
C(7)	C(15)	N(1)	Re(1)	175.3(2)	C(18)	C(19)	C(20)	C(21)	2.4(5)
C(8)	C(7)	C(15)	C(14)	-2.4(4)	C(19)	C(18)	O(6A)	C(23A)	-70.8(4)
C(8)	C(7)	C(15)	N(1)	177.5(3)	C(19)	C(18)	O(6B)	C(23B)	128.3(10)
C(8)	C(9)	C(10)	C(11)	178.3(3)	C(19)	C(20)	C(21)	C(22)	-1.8(5)
C(8)	C(9)	C(10)	C(14)	-0.5(5)	C(20)	C(21)	C(22)	C(17)	-0.4(5)
C(9)	C(10)	C(11)	C(12)	-177.4(3)	C(22)	C(17)	C(18)	C(19)	-1.4(5)
C(9)	C(10)	C(14)	C(15)	-2.0(5)	C(22)	C(17)	C(18)	O(6A)	169.2(3)
C(9)	C(10)	C(14)	N(2)	177.5(3)	C(22)	C(17)	C(18)	O(6B)	-139.8(6)
C(10)	C(11)	C(12)	C(13)	-0.1(5)	C(24)	C(23A)	O(6A)	C(18)	-177.6(3)
C(10)	C(14)	C(15)	C(7)	3.5(4)	C(24)	C(23B)	O(6B)	C(18)	-171.0(10)
C(10)	C(14)	C(15)	N(1)	-176.4(3)	N(1)	C(4)	C(5)	C(6)	-2.1(5)
C(10)	C(14)	N(2)	C(13)	-0.1(4)	N(2)	C(14)	C(15)	C(7)	-176.1(3)
C(10)	C(14)	N(2)	Re(1)	179.2(2)	N(2)	C(14)	C(15)	N(1)	4.1(4)
C(11)	C(10)	C(14)	C(15)	179.0(3)	O(4)	C(16)	C(17)	C(18)	-69.9(3)
C(11)	C(10)	C(14)	N(2)	-1.4(5)	O(4)	C(16)	C(17)	C(22)	107.3(3)
C(11)	C(12)	C(13)	N(2)	-1.5(5)	O(5)	C(16)	C(17)	C(18)	110.8(3)
C(12)	C(13)	N(2)	C(14)	1.6(5)	O(5)	C(16)	C(17)	C(22)	-72.0(4)
C(12)	C(13)	N(2)	Re(1)	-177.6(2)	O(5)	C(16)	O(4)	Re(1)	4.2(4)
C(14)	C(10)	C(11)	C(12)	1.5(5)	O(6A)	C(18)	C(19)	C(20)	-170.7(3)
C(14)	C(15)	N(1)	C(4)	-179.7(3)	O(6B)	C(18)	C(19)	C(20)	144.6(6)
C(14)	C(15)	N(1)	Re(1)	-4.8(3)	O(7A)	C(23A)	O(6A)	C(18)	1.5(5)
C(15)	C(7)	C(8)	C(9)	-0.2(5)	O(7B)	C(23B)	O(6B)	C(18)	5(2)
C(15)	C(14)	N(2)	C(13)	179.4(3)					

Table S5. Bond lengths for **2**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C(1)	O(1)	1.148(10)	C(16)	C(17)	1.520(10)
C(1)	Re(1)	1.926(9)	C(16)	O(4)	1.292(9)
C(2)	O(2)	1.158(11)	C(16)	O(5)	1.226(10)
C(2)	Re(1)	1.907(9)	C(17)	C(18)	1.535(10)
C(3)	O(3)	1.151(9)	C(17)	C(28)	1.536(11)
C(3)	Re(1)	1.923(7)	C(18)	C(19)	1.395(11)
C(4)	C(5)	1.390(12)	C(18)	C(23)	1.384(11)
C(4)	N(1)	1.330(10)	C(19)	C(20)	1.385(12)
C(5)	C(6)	1.361(12)	C(20)	C(21)	1.389(11)
C(6)	C(7)	1.413(12)	C(21)	C(22)	1.383(10)
C(7)	C(8)	1.429(12)	C(21)	C(24)	1.505(11)
C(7)	C(15)	1.411(10)	C(22)	C(23)	1.391(11)
C(8)	C(9)	1.340(12)	C(24)	C(25A)	1.487(13)
C(9)	C(10)	1.447(11)	C(24)	C(25B)	1.62(3)
C(10)	C(11)	1.397(12)	C(25A)	C(26A)	1.538(16)
C(10)	C(14)	1.397(11)	C(25A)	C(27)	1.478(14)
C(11)	C(12)	1.369(11)	C(25B)	C(26B)	1.53(4)
C(12)	C(13)	1.409(11)	C(25B)	C(27)	1.45(3)
C(13)	N(2)	1.338(10)	N(1)	Re(1)	2.194(6)
C(14)	C(15)	1.436(10)	N(2)	Re(1)	2.170(6)
C(14)	N(2)	1.364(9)	O(4)	Re(1)	2.152(5)
C(15)	N(1)	1.360(9)			

Table S6. Valence angles for **2**.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
O(1)	C(1)	Re(1)	178.1(7)	C(22)	C(21)	C(20)	117.2(7)
O(2)	C(2)	Re(1)	177.3(8)	C(22)	C(21)	C(24)	120.5(7)
O(3)	C(3)	Re(1)	177.2(7)	C(21)	C(22)	C(23)	121.8(8)
N(1)	C(4)	C(5)	122.5(8)	C(18)	C(23)	C(22)	120.8(8)
C(6)	C(5)	C(4)	119.7(8)	C(21)	C(24)	C(25B)	118.3(11)
C(5)	C(6)	C(7)	120.1(8)	C(25A)	C(24)	C(21)	110.7(7)
C(6)	C(7)	C(8)	124.5(7)	C(24)	C(25A)	C(26A)	108.7(10)
C(15)	C(7)	C(6)	116.5(8)	C(27)	C(25A)	C(24)	117.0(10)
C(15)	C(7)	C(8)	119.0(8)	C(27)	C(25A)	C(26A)	108.4(9)
C(9)	C(8)	C(7)	122.2(8)	C(26B)	C(25B)	C(24)	112(2)
C(8)	C(9)	C(10)	120.0(8)	C(27)	C(25B)	C(24)	111.2(17)
C(11)	C(10)	C(9)	122.8(8)	C(27)	C(25B)	C(26B)	118(3)
C(14)	C(10)	C(9)	119.5(8)	C(4)	N(1)	C(15)	118.5(7)
C(14)	C(10)	C(11)	117.7(8)	C(4)	N(1)	Re(1)	127.5(6)
C(12)	C(11)	C(10)	119.4(8)	C(15)	N(1)	Re(1)	113.8(5)
C(11)	C(12)	C(13)	119.8(8)	C(13)	N(2)	C(14)	117.8(6)
N(2)	C(13)	C(12)	122.0(7)	C(13)	N(2)	Re(1)	126.9(5)
C(10)	C(14)	C(15)	120.0(7)	C(14)	N(2)	Re(1)	115.2(5)
N(2)	C(14)	C(10)	123.3(7)	C(16)	O(4)	Re(1)	124.6(5)
N(2)	C(14)	C(15)	116.6(7)	C(1)	Re(1)	N(1)	96.2(3)
C(7)	C(15)	C(14)	119.3(7)	C(1)	Re(1)	N(2)	171.3(3)
N(1)	C(15)	C(7)	122.7(7)	C(1)	Re(1)	O(4)	97.9(3)
N(1)	C(15)	C(14)	118.0(7)	C(2)	Re(1)	C(1)	87.6(4)
O(4)	C(16)	C(17)	114.0(7)	C(2)	Re(1)	C(3)	87.0(4)
O(5)	C(16)	C(17)	120.6(7)	C(2)	Re(1)	N(1)	175.5(3)
O(5)	C(16)	O(4)	125.3(8)	C(2)	Re(1)	N(2)	100.1(3)
C(16)	C(17)	C(18)	111.5(6)	C(2)	Re(1)	O(4)	93.9(3)
C(16)	C(17)	C(28)	111.6(7)	C(3)	Re(1)	C(1)	89.0(3)
C(18)	C(17)	C(28)	111.1(6)	C(3)	Re(1)	N(1)	95.3(3)
C(19)	C(18)	C(17)	120.4(7)	C(3)	Re(1)	N(2)	95.6(3)
C(23)	C(18)	C(17)	121.9(7)	C(3)	Re(1)	O(4)	173.1(3)
C(23)	C(18)	C(19)	117.6(7)	N(2)	Re(1)	N(1)	76.0(2)
C(20)	C(19)	C(18)	121.2(8)	O(4)	Re(1)	N(1)	83.3(2)
C(19)	C(20)	C(21)	121.3(7)	O(4)	Re(1)	N(2)	77.4(2)
C(20)	C(21)	C(24)	122.2(7)				

Table S7. Torsion angles for **2**.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
C(4)	C(5)	C(6)	C(7)	-0.5(11)	C(15)	C(14)	N(2)	Re(1)	6.0(8)
C(5)	C(4)	N(1)	C(15)	-0.6(11)	C(16)	C(17)	C(18)	C(19)	176.9(7)
C(5)	C(4)	N(1)	Re(1)	-175.3(6)	C(16)	C(17)	C(18)	C(23)	-6.5(11)
C(5)	C(6)	C(7)	C(8)	179.0(7)	C(17)	C(16)	O(4)	Re(1)	178.2(5)
C(5)	C(6)	C(7)	C(15)	1.2(10)	C(17)	C(18)	C(19)	C(20)	175.0(8)
C(6)	C(7)	C(8)	C(9)	-179.3(8)	C(17)	C(18)	C(23)	C(22)	-175.7(8)
C(6)	C(7)	C(15)	C(14)	-179.8(6)	C(18)	C(19)	C(20)	C(21)	0.4(13)
C(6)	C(7)	C(15)	N(1)	-1.7(10)	C(19)	C(18)	C(23)	C(22)	0.9(12)
C(7)	C(8)	C(9)	C(10)	-1.0(13)	C(19)	C(20)	C(21)	C(22)	1.8(12)
C(7)	C(15)	N(1)	C(4)	1.4(10)	C(19)	C(20)	C(21)	C(24)	-175.3(8)
C(7)	C(15)	N(1)	Re(1)	176.8(5)	C(20)	C(21)	C(22)	C(23)	-2.7(12)
C(8)	C(7)	C(15)	C(14)	2.3(10)	C(20)	C(21)	C(24)	C(25A)	118.9(9)
C(8)	C(7)	C(15)	N(1)	-179.6(7)	C(20)	C(21)	C(24)	C(25B)	69.7(15)
C(8)	C(9)	C(10)	C(11)	-177.5(9)	C(21)	C(22)	C(23)	C(18)	1.3(13)
C(8)	C(9)	C(10)	C(14)	2.8(12)	C(21)	C(24)	C(25A)	C(26A)	175.7(8)
C(9)	C(10)	C(11)	C(12)	179.7(8)	C(21)	C(24)	C(25A)	C(27)	-61.1(11)
C(9)	C(10)	C(14)	C(15)	-2.1(11)	C(21)	C(24)	C(25B)	C(26B)	180(2)
C(9)	C(10)	C(14)	N(2)	180.0(7)	C(21)	C(24)	C(25B)	C(27)	44(2)
C(10)	C(11)	C(12)	C(13)	0.5(12)	C(22)	C(21)	C(24)	C(25A)	-58.2(10)
C(10)	C(14)	C(15)	C(7)	-0.4(10)	C(22)	C(21)	C(24)	C(25B)	-107.4(14)
C(10)	C(14)	C(15)	N(1)	-178.6(7)	C(23)	C(18)	C(19)	C(20)	-1.8(12)
C(10)	C(14)	N(2)	C(13)	0.2(11)	C(24)	C(21)	C(22)	C(23)	174.6(8)
C(10)	C(14)	N(2)	Re(1)	-176.0(6)	C(28)	C(17)	C(18)	C(19)	-57.9(10)
C(11)	C(10)	C(14)	C(15)	178.2(7)	C(28)	C(17)	C(18)	C(23)	118.7(8)
C(11)	C(10)	C(14)	N(2)	0.3(12)	N(1)	C(4)	C(5)	C(6)	0.1(12)
C(11)	C(12)	C(13)	N(2)	0.0(12)	N(2)	C(14)	C(15)	C(7)	177.7(6)
C(12)	C(13)	N(2)	C(14)	-0.4(11)	N(2)	C(14)	C(15)	N(1)	-0.5(10)
C(12)	C(13)	N(2)	Re(1)	175.4(6)	O(4)	C(16)	C(17)	C(18)	-78.9(8)
C(14)	C(10)	C(11)	C(12)	-0.6(12)	O(4)	C(16)	C(17)	C(28)	156.1(7)
C(14)	C(15)	N(1)	C(4)	179.6(7)	O(5)	C(16)	C(17)	C(18)	100.3(9)
C(14)	C(15)	N(1)	Re(1)	-5.1(8)	O(5)	C(16)	C(17)	C(28)	-24.7(11)
C(15)	C(7)	C(8)	C(9)	-1.6(12)	O(5)	C(16)	O(4)	Re(1)	-0.9(11)
C(15)	C(14)	N(2)	C(13)	-177.8(6)					

Table S8. Bond lengths for **3**.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
C(1)	O(1)	1.125(11)	C(16)	C(17)	1.530(14)
C(1)	Re(1)	1.947(10)	C(16)	O(4)	1.289(11)
C(2)	O(2)	1.165(13)	C(16)	O(5)	1.232(12)
C(2)	Re(1)	1.923(11)	C(17)	C(18)	1.516(13)
C(3)	O(3)	1.163(11)	C(17)	C(29)	1.510(15)
C(3)	Re(1)	1.903(9)	C(18)	C(19)	1.426(14)
C(4)	C(5)	1.393(13)	C(18)	C(27)	1.357(14)
C(4)	N(1)	1.333(12)	C(19)	C(20)	1.375(12)
C(5)	C(6)	1.361(14)	C(20)	C(21)	1.409(14)
C(6)	C(7)	1.423(13)	C(21)	C(22)	1.423(12)
C(7)	C(8)	1.444(12)	C(21)	C(26)	1.423(14)
C(7)	C(15)	1.398(12)	C(22)	C(23)	1.348(14)
C(8)	C(9)	1.348(14)	C(23)	C(24)	1.407(14)
C(9)	C(10)	1.439(13)	C(23)	O(6)	1.386(11)
C(10)	C(11)	1.397(13)	C(24)	C(25)	1.374(13)
C(10)	C(14)	1.398(13)	C(25)	C(26)	1.412(14)
C(11)	C(12)	1.371(13)	C(26)	C(27)	1.431(13)
C(12)	C(13)	1.394(13)	C(28)	O(6)	1.426(14)
C(13)	N(2)	1.328(12)	N(1)	Re(1)	2.194(8)
C(14)	C(15)	1.432(12)	N(2)	Re(1)	2.173(7)
C(14)	N(2)	1.370(11)	O(4)	Re(1)	2.149(6)
C(15)	N(1)	1.363(12)			

Table S9. Valence angles for **3**.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
O(1)	C(1)	Re(1)	177.3(9)	C(20)	C(21)	C(26)	118.5(8)
O(2)	C(2)	Re(1)	177.3(9)	C(26)	C(21)	C(22)	119.5(9)
O(3)	C(3)	Re(1)	177.8(8)	C(23)	C(22)	C(21)	120.0(9)
N(1)	C(4)	C(5)	121.6(9)	C(22)	C(23)	C(24)	121.3(9)
C(6)	C(5)	C(4)	121.2(9)	C(22)	C(23)	O(6)	125.7(9)
C(5)	C(6)	C(7)	118.1(9)	O(6)	C(23)	C(24)	113.0(9)
C(6)	C(7)	C(8)	122.8(9)	C(25)	C(24)	C(23)	120.2(9)
C(15)	C(7)	C(6)	117.9(9)	C(24)	C(25)	C(26)	120.5(9)
C(15)	C(7)	C(8)	119.3(8)	C(21)	C(26)	C(27)	118.8(9)
C(9)	C(8)	C(7)	120.8(8)	C(25)	C(26)	C(21)	118.5(9)
C(8)	C(9)	C(10)	121.0(8)	C(25)	C(26)	C(27)	122.7(9)
C(11)	C(10)	C(9)	123.7(8)	C(18)	C(27)	C(26)	122.0(9)
C(11)	C(10)	C(14)	117.3(9)	C(4)	N(1)	C(15)	118.8(8)
C(14)	C(10)	C(9)	119.0(8)	C(4)	N(1)	Re(1)	126.8(7)
C(12)	C(11)	C(10)	119.3(9)	C(15)	N(1)	Re(1)	114.3(6)
C(11)	C(12)	C(13)	120.1(9)	C(13)	N(2)	C(14)	117.5(8)
N(2)	C(13)	C(12)	122.5(9)	C(13)	N(2)	Re(1)	126.9(6)
C(10)	C(14)	C(15)	120.4(8)	C(14)	N(2)	Re(1)	115.6(6)
N(2)	C(14)	C(10)	123.3(8)	C(16)	O(4)	Re(1)	122.9(6)
N(2)	C(14)	C(15)	116.3(8)	C(23)	O(6)	C(28)	116.3(8)
C(7)	C(15)	C(14)	119.6(8)	C(1)	Re(1)	N(1)	97.1(3)
N(1)	C(15)	C(7)	122.4(8)	C(1)	Re(1)	N(2)	172.7(3)
N(1)	C(15)	C(14)	117.9(8)	C(1)	Re(1)	O(4)	97.3(3)
O(4)	C(16)	C(17)	113.5(8)	C(2)	Re(1)	C(1)	90.5(4)
O(5)	C(16)	C(17)	121.1(9)	C(2)	Re(1)	N(1)	170.3(3)
O(5)	C(16)	O(4)	125.4(9)	C(2)	Re(1)	N(2)	96.7(4)
C(18)	C(17)	C(16)	110.9(8)	C(2)	Re(1)	O(4)	90.8(3)
C(29)	C(17)	C(16)	112.6(9)	C(3)	Re(1)	C(1)	88.4(4)
C(29)	C(17)	C(18)	110.9(8)	C(3)	Re(1)	C(2)	87.2(4)
C(19)	C(18)	C(17)	117.5(9)	C(3)	Re(1)	N(1)	99.0(3)
C(27)	C(18)	C(17)	123.9(9)	C(3)	Re(1)	N(2)	93.3(3)
C(27)	C(18)	C(19)	118.5(8)	C(3)	Re(1)	O(4)	174.1(3)
C(20)	C(19)	C(18)	121.1(9)	N(2)	Re(1)	N(1)	75.6(3)
C(19)	C(20)	C(21)	121.1(9)	O(4)	Re(1)	N(1)	82.2(3)
C(20)	C(21)	C(22)	122.0(9)	O(4)	Re(1)	N(2)	81.4(3)

Table S10. Torsion angles for **3**.

A	B	C	D	Angle/°	A	B	C	D	Angle/°
C(4)	C(5)	C(6)	C(7)	-0.2(14)	C(17)	C(16)	O(4)	Re(1)	-168.9(6)
C(5)	C(4)	N(1)	C(15)	-0.6(13)	C(17)	C(18)	C(19)	C(20)	-179.9(8)
C(5)	C(4)	N(1)	Re(1)	-175.9(6)	C(17)	C(18)	C(27)	C(26)	178.7(8)
C(5)	C(6)	C(7)	C(8)	-177.9(8)	C(18)	C(19)	C(20)	C(21)	0.8(13)
C(5)	C(6)	C(7)	C(15)	-0.3(13)	C(19)	C(18)	C(27)	C(26)	-2.5(13)
C(6)	C(7)	C(8)	C(9)	177.1(9)	C(19)	C(20)	C(21)	C(22)	176.9(8)
C(6)	C(7)	C(15)	C(14)	-178.3(8)	C(19)	C(20)	C(21)	C(26)	-1.4(13)
C(6)	C(7)	C(15)	N(1)	0.4(13)	C(20)	C(21)	C(22)	C(23)	-178.2(8)
C(7)	C(8)	C(9)	C(10)	0.4(14)	C(20)	C(21)	C(26)	C(25)	180.0(8)
C(7)	C(15)	N(1)	C(4)	0.1(13)	C(20)	C(21)	C(26)	C(27)	0.1(12)
C(7)	C(15)	N(1)	Re(1)	175.9(6)	C(21)	C(22)	C(23)	C(24)	-1.4(13)
C(8)	C(7)	C(15)	C(14)	-0.7(12)	C(21)	C(22)	C(23)	O(6)	178.1(8)
C(8)	C(7)	C(15)	N(1)	178.1(8)	C(21)	C(26)	C(27)	C(18)	1.9(13)
C(8)	C(9)	C(10)	C(11)	-179.4(9)	C(22)	C(21)	C(26)	C(25)	1.7(12)
C(8)	C(9)	C(10)	C(14)	0.8(13)	C(22)	C(21)	C(26)	C(27)	-178.2(8)
C(9)	C(10)	C(11)	C(12)	-179.1(8)	C(22)	C(23)	C(24)	C(25)	1.1(14)
C(9)	C(10)	C(14)	C(15)	-2.0(12)	C(22)	C(23)	O(6)	C(28)	-9.0(13)
C(9)	C(10)	C(14)	N(2)	178.1(8)	C(23)	C(24)	C(25)	C(26)	0.6(13)
C(10)	C(11)	C(12)	C(13)	0.4(14)	C(24)	C(23)	O(6)	C(28)	170.5(8)
C(10)	C(14)	C(15)	C(7)	1.9(12)	C(24)	C(25)	C(26)	C(21)	-2.0(13)
C(10)	C(14)	C(15)	N(1)	-176.9(8)	C(24)	C(25)	C(26)	C(27)	177.9(8)
C(10)	C(14)	N(2)	C(13)	1.4(12)	C(25)	C(26)	C(27)	C(18)	-178.0(8)
C(10)	C(14)	N(2)	Re(1)	-179.2(7)	C(26)	C(21)	C(22)	C(23)	0.0(13)
C(11)	C(10)	C(14)	C(15)	178.3(8)	C(27)	C(18)	C(19)	C(20)	1.2(13)
C(11)	C(10)	C(14)	N(2)	-1.6(13)	C(29)	C(17)	C(18)	C(19)	-75.0(12)
C(11)	C(12)	C(13)	N(2)	-0.7(14)	C(29)	C(17)	C(18)	C(27)	103.9(11)
C(12)	C(13)	N(2)	C(14)	-0.3(13)	N(1)	C(4)	C(5)	C(6)	0.6(14)
C(12)	C(13)	N(2)	Re(1)	-179.6(7)	N(2)	C(14)	C(15)	C(7)	-178.2(8)
C(14)	C(10)	C(11)	C(12)	0.6(13)	N(2)	C(14)	C(15)	N(1)	3.0(11)
C(14)	C(15)	N(1)	C(4)	178.8(8)	O(4)	C(16)	C(17)	C(18)	-80.7(11)
C(14)	C(15)	N(1)	Re(1)	-5.3(9)	O(4)	C(16)	C(17)	C(29)	154.2(9)
C(15)	C(7)	C(8)	C(9)	-0.5(13)	O(5)	C(16)	C(17)	C(18)	96.2(12)
C(15)	C(14)	N(2)	C(13)	-178.5(7)	O(5)	C(16)	C(17)	C(29)	-28.8(14)
C(15)	C(14)	N(2)	Re(1)	0.9(9)	O(5)	C(16)	O(4)	Re(1)	14.3(15)
C(16)	C(17)	C(18)	C(19)	159.0(8)	O(6)	C(23)	C(24)	C(25)	-178.4(8)
C(16)	C(17)	C(18)	C(27)	-22.1(13)					

Table S11. Concentration depended lysis of L929 and HeLa cell lines upon exposure to **1** expressed as percentages of lysed cells detected by LDH leakage compared to totally lysed control (C 100%). Incubation time was 24 h.

Percentages of lysed cells [%]							
concentration [μM]	12.5	25	50	100	200	400	C100%
L929	23	22	22	21	88	100	100
HeLa	26	28	36	72	99	102	100

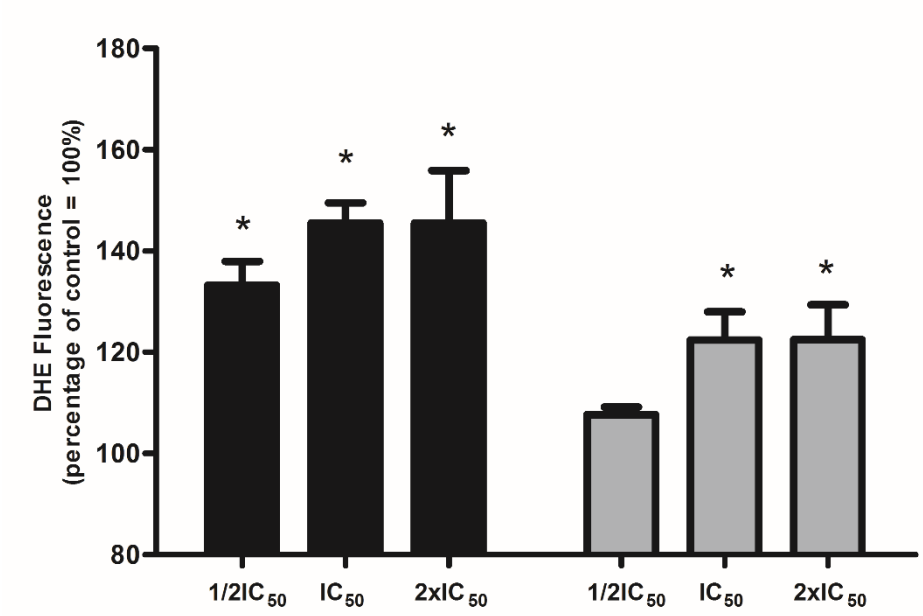

Fig S11. The relative ROS levels generated by **1** (grey) and **A** (white) in HeLa cells. The cells were incubated with concentrations of $0.5\times IC_{50}$, IC_{50}, $2\times IC_{50}$ for 3 h and then the level of ROS was determined with the cell-permeable fluorogenic probe dihydroethidium (DHE). The results represent mean ± S.E.M. of data from 3 experiments. *$P < 0.05$ versus control

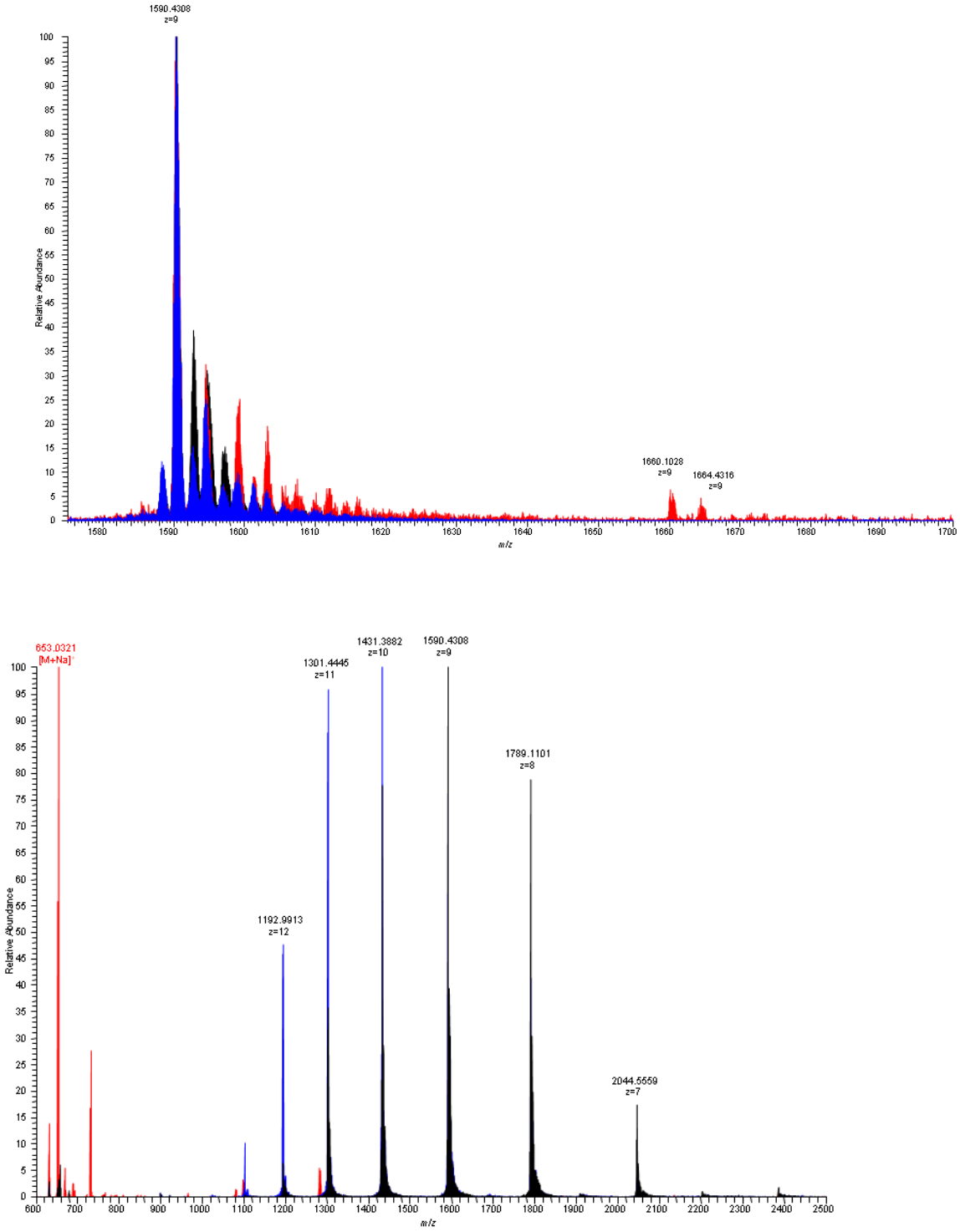

Fig. S12 Positive mode ESI mass spectrum of hen egg white lysozyme (HEWL) in pure water recorded at a solvent flow rate of 100 µL min^{-1} (black) as well as samples incubated with **1** for (red) 0 and (blue) 20 h, respectively. The upper spectrum shows a close-up view of the +9H protonation state.

Biological section

Methods

Antibacterial assay

The *in vitro* antimicrobial activity of **1**-**4** was evaluated against the reference strains of Gram-negative (*Escherichia coli* NCTC 8196, *Proteus vulgaris* ATCC 49990, *Proteus mirabilis* ATCC 29906, *Pseudomonas aeruginosa* NCTC 6749), and Gram-positive (*Staphylococcus aureus* ATCC 6538, *Staphylococcus aureus* ATCC 29213, *Staphylococcus epidermidis* ATCC 12228) bacterial species. The minimal inhibitory concentration (MIC) was determined as the lowest concentration of the compound preventing growth of the tested microorganism using microdilution method according to EUCAST guidelines ISO 20776-1 (2006). The 96-well microplates were used; 50 µl of recommended Mueller–Hinton broth with a series of twofold dilutions of the tested compound in the range of the final concentrations from 4 to 400 µM was inoculated with 50 µl of microbial suspension with a final bacterial cell number concentration approximately 5 x 10^5 CFU/mL. All of the tested compounds were dissolved in dimethyl sulfoxide (DMSO) and its final concentration on plate (2%) had no influence on growth of microorganisms. The incubation was carried out at 37°C for 18 h and optical density (OD_{600}) was measured. Ampicillin and streptomycin were used as control antimicrobials. All evaluations were performed in triplicates.

Cytotoxicity assay

The cytotoxic effect on L929 and HeLa cells of compound **1** was measured by lactate dehydrogenase (LDH) release in colorimetric reaction (Promega, CytoTox 96® Non-Radioactive Cytotoxicity Assay). LDH is a stable cytosolic enzyme that is released upon cell lysis, and can be used to measure membrane integrity. L929 or HeLa cells were plated in 96-well microplates at density of 1×10^4 cells per well. After overnight incubation compound **1** was added in twofold dilutions from 12.5 to 400 µM. All of the tested compounds were

dissolved in DMSO and its final concentration on plate (1%) had no influence on cells viability. After 18 h incubation with compound, 50 μL aliquots from each wells were transferred to a fresh 96-well plate, 50μL of the CytoTox 96R reagent was added and incubated for 30 min at room temperature in the dark. The Stop solution was then added and the absorbance at 490 nm was measured. The results of the experiments were shown as mean arithmetic values from three repeats in each of two independent experiments and the percentage of tested compound cytotoxicity in comparison to maximum LDH release control, treated with lysis solution for 45 minutes before experiment, was calculated for each concentration.

Oxidative stress

The intracellular level of reactive oxygen species (ROS) was determined on the basis of oxidative conversion of non-fluorescent dihydroethidium (hydroethidine or DHE) by superoxide to form fluorescent 2-hydroxyethidium or by non-specific oxidation by other sources of reactive oxygen species (ROS) to form ethidium. The HeLa cells were seeded in complete IMDM medium with 10% FBS at the density of 2 x 10^4 cells/well onto black 96-well microculture plate. After overnight incubation the cells were incubated for 3 hours with compound **1** or **A** at concentration 1/2 $IC_{50,}$ IC_{50} and 2xIC_{50}. Then the plate was centrifuged 5 minutes, 1600 rpm, medium above cell was carefully aspirated and 200 μL of 5 mM DHE was added. The plate was incubated for 20 minutes at 37˚C protected from light. After incubation the cells monolayer was washed twice with phosphate buffered saline (PBS) and the florescence was measured using an excitation wavelength 535 nm and emission 635 nm. All evaluations were performed in triplicates. One way ANOVA analysis of variance with a Tukey post hoc was used for multiple comparisons. All statistics were calculated with Prism GraphPad 7 software. A P value of <0.05 was considered significant.