COPPER(II) COORDINATION COMPOUNDS BASED ON *BIS*-HYDRAZONES OF 2,6-DIACETYLPYRIDINE: SYNTHESIS, STRUCTURE AND CYTOTOXIC ACTIVITY

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Table S1. Experimental and calculated (for isomer **a**) IR spectral data of *bis*(4,6-dimethylpyrimidine--2-hydrazone)-2,6-diacetylpyridine **(H_2L^1)**

Assignment	Calculated		Experimental
	Frequency, cm^{-1}	Intensity, kM mol^{-1}	Frequency, cm^{-1} (intensity*)
ν(NH)	3426	15	3413(m)
ν(CH)	3088 3064	19 4	3078(w)
ν(CH_3)	3017 2995 2951	49 18 44	2953(m)
ν(C=N)$_{azom}$	1597	146	1592(s)
Py + Pyrimid. rings	1573 1556 1546	347 81 1469	1567(s) 1556(s) 1538(m)
ν(NH–C) + δ(NH)	1526 1521	114 670	1519 (m)
δ(CH_3) + δ(CH)	1460 1453 1447 1436	154 180 184 306	1462(s) 1454(s)
ν(NH-C=N)$_{pyrimid}$	1331	455	1344(m)
Pyrimid. rings	1323	404	1302(m)
Py ring	1281	394	1261(w)
ν(N-NH-)$_{hydrazon}$	1175	711	1179(s)

*Intensities are denoted as follows: vs-very strong, s-strong, m-medium, w-weak.

Table S2. Experimental and calculated (for isomer **a**) IR spectral data of *bis*(benzimidazoline-2-hydrazone)-2,6-diacetylpyridine ($\mathbf{H_2L^2}$)

Assignment	Calculated		Experimental
	Frequency, cm^{-1}	Intensity, kM mol^{-1}	Frequency, cm^{-1} (intensity*)
$\nu(NH)_{benzim}$	3556	70	3332(m)
$\nu(NH)_{hydrazon}$	3445	37	3268(m)
$\nu(CH)$	3087 3078	67 65	3057(w)
$\nu(CH_3)$	2951 2912	38 32	2969(w) 2937(w)
$\nu(C=N)_{benzim}$	1630	966	1697(s)
$\nu(C=N)_{azom}$	1592	499	1627(s)
Py + Benzimid. rings	1579 1563 1553	39 396 935	1608(s) 1577(m) 1542(s)
$\nu(C\text{-}NH)_{benzim}$	1485	80	1481 (m)
$\delta(CH_3) + \delta(CH)$	1455 1437 1423	166 196 530	1462(s)
$\nu(NH\text{-}C=N)_{benzim}$	1394	50	1413(w)
Py ring	1315 1283	36 185	1312(s)
Benzymid. rings	1245	51	1255(w)
$\nu(N\text{-}NH\text{-})_{hydrazon}$	1186 1158	468 727	1205(s) 1185(m)

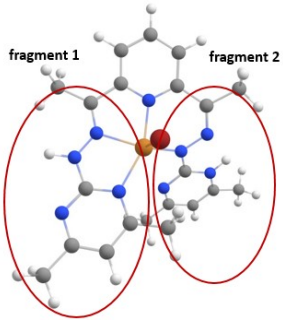
*Intensities are denoted as follows: vs-very strong, s-strong, m-medium, w-weak.

Table S3. Experimental and calculated (for isomer **a**) IR spectral data of *bis*(phthalazine-1-hydrazone)-2,6-diacetylpyridine ($\mathbf{H_2L^3}$)

Assignment	Calculated		Experimental
	Frequency, cm^{-1}	Intensity, kM mol^{-1}	Frequency, cm^{-1} (intensity*)
$\nu(NH)_{phtal}$	3498	53	3324(m)
$\nu(CH)$	3084 3071	67 32	3052(w)
$\nu(CH_3)$	3065 2990 2945	17 27 17	2924(w)
$\nu(C=N)_{azom}$	1603	1155	1604(s)
$\nu(C=N)_{phtal}$	1589	87	1589(s)
Py + Phtal. rings	1566 1552 1523	41 458 680	1560(m) 1531(s)
$\delta(CH_3) + \delta(CH)$	1454 1448 1439 1419	44 29 253 315	1477(m) 1443(s)
$\nu(N=NH)_{phtal}$	1331	121	1370(m)
Phtal. rings	1329	222	1346(s)
Py ring	1280	162	1293(m)
$\nu(\text{-}N=N\text{-})$	1089 1033	164 189	1075(s) 1033(s)

*Intensities are denoted as follows: vs-very strong, s-strong, m-medium, w-weak.

Table S4 Experimental and calculated IR spectral data of complex **1**

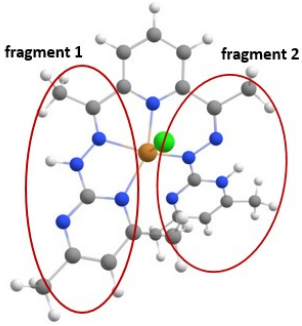


Optimized structure of complex **1**

Assignment	Calculated		Experimental
	Frequency, cm^{-1}	Intensity, kM, mol^{-1}	Frequency, cm^{-1} (intensity*)
$\nu(NH_{hydraz})$	3449	36	3436(m)
$\nu(NH_{pyrim})$	3398	43	3327(m)
ν(-C=N_{azom}-NH-)fragment 1	1642	82	1653(m)
Pyrimid. ring, fragment 2	1614	213	1617(s)
Py + Pyrimid. rings + $\nu(C=N_{azom}\text{-}N=C)_{fragment\ 2}$	1597 1594 1579	544 490 972	1593 (s), 1544 (s)
Pyrimid. ring, fragment 1	1529	152	1525(s)
Pyrimid. ring, fragment 1 + $\nu(C\text{-}NH_{hydraz})$	1498	72	1481(m)
δ(CH,arom), δ(CH3)	1445, 1446	161, 46	1474(m), 1455 (s)

*Intensities are denoted as follows: s-strong, m-medium, w-weak

Table S5 Experimental and calculated IR spectral data of complex **2**

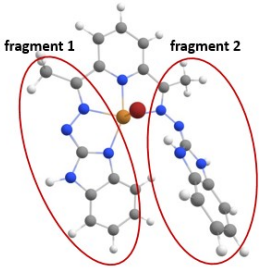


Optimized structure of complex **2**

Assignment	Calculated		Experimental
	Frequency, cm^{-1}	Intensity, kM,mol^{-1}	Frequency, cm^{-1} (intensity*)
$\nu(NH_{hydraz})$	3453	38	3416(m)
$\nu(NH_{pyrimid})$	3398	62	3262(m)
ν(-C=N_{azom}-NH-)fragment 1	1641	81	1655(m)
Pyrimid. ring, fragment 2	1613	218	1638(m)
Py + Pyrimid. rings + $\nu(C=N_{azom}\text{-}N=C)_{fragment\ 2}$	1598 1595 1579	526 506 895	1597 (s), 1547 (vs)
Pyrimid. ring, fragment 1	1529	156	1524(s)
δ(CH,arom), δ(CH3)	1446, 1404	59, 141	1437(s), 1408(m)
Pyrimid. ring, fragment 1 + $\nu(C\text{-}NH_{hydraz})$	1338	126	1345(s)

*Intensities are denoted as follows: vs – very strong, s-strong, m-medium, w-weak

Table S6. Experimental and calculated IR spectral data of complex **3**

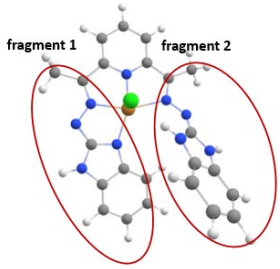


Optimized cation structure of complex **3**

Assignment	Calculated		Experimental
	Frequency, cm^{-1}	Intensity, kM mol^{-1}	Frequency, cm^{-1} (intensity*)
$\nu(NH)_{benzimid,\ fragment\ 2}$	3555	75	3437(w)
$\nu(NH)_{benzimid,\ fragment\ 1}$	3549	88	3136(w)
$\nu(NH_{hydrazon}\ldots Br)$	2973	855	2906 (m)
$\nu(N{=}C_{benzimid})_{fragment\ 2}$ + Benzim ring	1623	928	1658(m)
Benzim ring, fragment 2	1612	13	1622(m)
Benzim ring, fragment 1	1609	30	1604(m)
Py ring	1581	74	1575(s)
$\nu(C{=}N)_{azom,\ fragment\ 1}$ + Py ring	1566	111	1535(m)
$\nu(C{=}N)_{azom,\ fragment\ 2}$ + Py ring	1548	129	
$\nu(N{=}C_{benzimid})_{fragment\ 1}$ + Benzim ring	1512	823	1517(m)
Py + Benzim rings	1478	109	1473(m)
$\delta(CH_{arom})$, $\delta(CH_3)$	1462, 1459,1427	108, 113,121	1458 (s)
$\nu(C{=}N)_{benzim,\ fragment\ 1}$ + Py ring	1401	314	1359(m)
$\nu(C{=}N)_{benzim,\ fragment\ 2}$ + Py ring	1377	118	
$\nu(N{=}N)$	1233	379	1278(m)

*Intensities are denoted as follows: vs-very strong, s-strong, m-medium, w-weak.

Table S7. Experimental and calculated IR spectral data of complex **4**

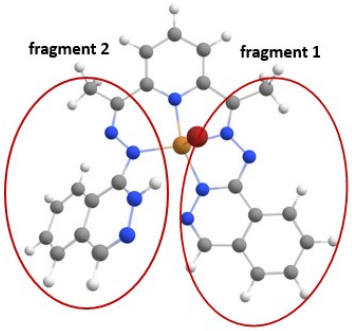


Optimized cation structure of complex **4**

Assignment	Calculated		Experimental
	Frequency, cm^{-1}	Intensity, kM mol^{-1}	Frequency, cm^{-1} (intensity*)
$\nu(NH)_{benzimid,\ fragment\ 2}$	3555	74	3314(w)
$\nu(NH)_{benzimid,\ fragment\ 1}$	3549	88	3144 (w)
$\nu(NH_{hydrazon}\ldots Cl)$	2909	887	2915 (m)
$\nu(N{=}C_{benzimid})_{fragment\ 2}$ + Benzim ring	1623	904	1659(m)
Benzim ring, fragment 2	1612	10	1632(m)
Benzim ring, fragment 1	1609	27	1609(m)
Py ring	1581	74	1592(m)
$\nu(C{=}N)_{azom,\ fragment\ 1}$ + Py ring	1566	126	1562(m)
$\nu(C{=}N)_{azom,\ fragment\ 2}$ + Py ring	1549	132	
$\nu(N{=}C_{benzimid})_{fragment\ 1}$ + Benzim ring	1513	833	1526(m)
Py + Benzim rings	1478	118	1474(m)
$\delta(CH_{arom})$, $\delta(CH_3)$	1462, 1459,1427	108, 129,121	1456 (s)
$\nu(C{=}N)_{benzim,\ fragment\ 1}$ + Py ring	1402	327	1361(m)
$\nu(C{=}N)_{benzim,\ fragment\ 2}$ + Py ring	1380	115	
$\nu(N{=}N)$	1234	389	1260(m)

*Intensities are denoted as follows: vs-very strong, s-strong, m-medium, w-weak.

Table S8. Experimental and calculated IR spectral data of complex **5**

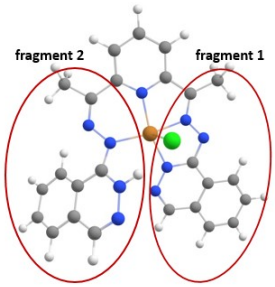


Optimized cation structure of complex **5**

Assignment	Calculated		Experimental
	Frequency, cm^{-1}	Intensity, kM mol^{-1}	Frequency, cm^{-1} (intensity*)
ν(CH)	3087 3082 3074	32 47 24	3194(w), 3142(w),
ν(CH_3)	3069 3036 2968	22 10 18	3050(w)
ν(NH…Br)	2794	1297	2707(w)
Phtal. ring, fragment 2	1616 1598	175 28	1585(s)
ν($C=N_{azom}$)+ Py +Phtal. rings	1575 1572 1567	30 97 66	1545 (m), 1510(s)
Phtal. ring, fragment 1	1472	104	1478(m)
ν($C=N_{Pyridine}$) + δ(CH_3)	1447	38	1464(m)
Phtal. ring, fragment 2	1426	60	1408(m)
ν$(N=C)_{fragment\ 1}$+ ν$(C=N)_{Phtal\ 1}$	1419	67	1375(s)
ν$(N=C)_{fragment\ 2}$ + δ(CH_3)	1390	381	1360(m)
δ(CH_{arom}), δ(CH_3)	1373, 1360	208, 207	1326(m)
ν$(C\text{-}NH)_{Phtal\ 2}$	1330	213	1308(m)
ν(N=N)	1273	228	1255(m)

*Intensities are denoted as follows: vs-very strong, s-strong, m-medium, w-weak.

Table S9. Experimental and calculated IR spectral data of complex **6**



Optimized cation structure of complex **6**

Assignment	Calculated		Experimental
	Frequency, cm^{-1}	Intensity, kM mol^{-1}	Frequency, cm^{-1} (intensity*)
ν(CH)	3087 3082 3074	32 47 24	3150(w), 3060 (w)
ν(CH_3)	3069 3036 2968	22 10 18	3044 (w), 2982 (w)
ν(NH…Cl)	2794	1297	2890(w)
Phtal. ring, fragment 2	1616 1598	175 28	1590(s)

$\nu(C=N_{azom})$+ Py +Phtal. rings	1575 1572 1567	30 97 66	1532 (m), 1517 (m)
Phtal. ring, fragment 1	1472	104	1466(s)
$\nu(C=N_{Pyridine}) + \delta(CH_3)$	1447	38	1454(m)
Phtal. ring, fragment 1	1426	60	1416(m)
$\nu(N=C)_{fragment\ 1} + \nu(C=N)_{Phtal\ 1}$	1419	67	1370(m)
$\nu(N=C)_{fragment\ 2} + \delta(CH_3)$	1390	381	1349(m)
$\delta(CH_{arom}), \delta(CH_3)$	1373, 1360	208, 207	1338(m)
$\nu(C\text{-}NH)_{Phtal\ 2}$	1330	213	1315(m)
$\nu(N=N)$	1273	228	1252(m)

*Intensities are denoted as follows: vs-very strong, s-strong, m-medium, w-weak.

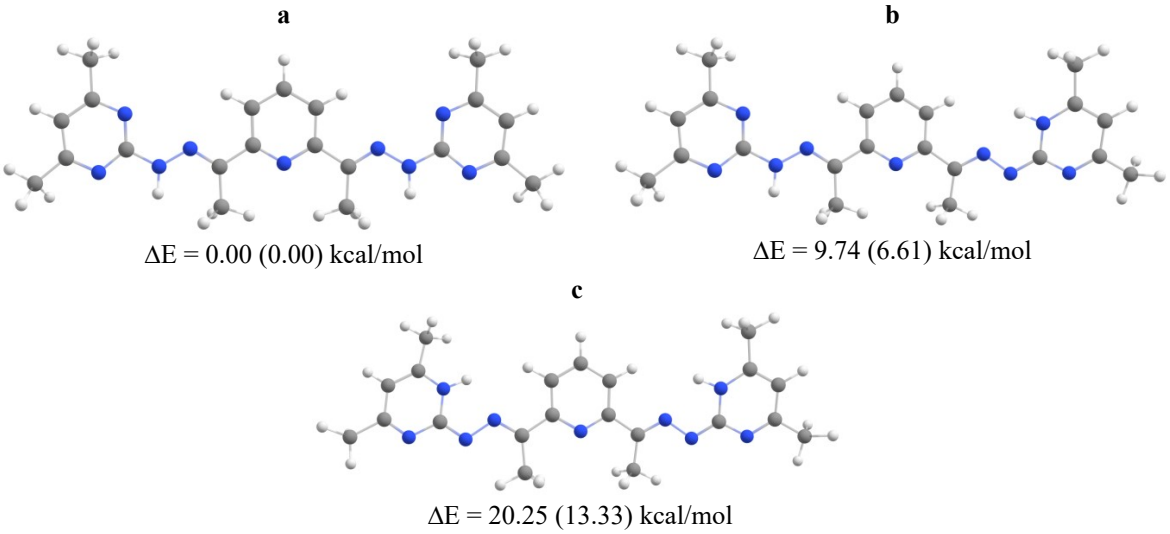


Figure S1 Optimized structures and relative energies of the selected most stable tautomeric forms of $\mathbf{H_2L^1}$ in the gas phase and DMSO solution (value in parenthesis – for DMSO solution)

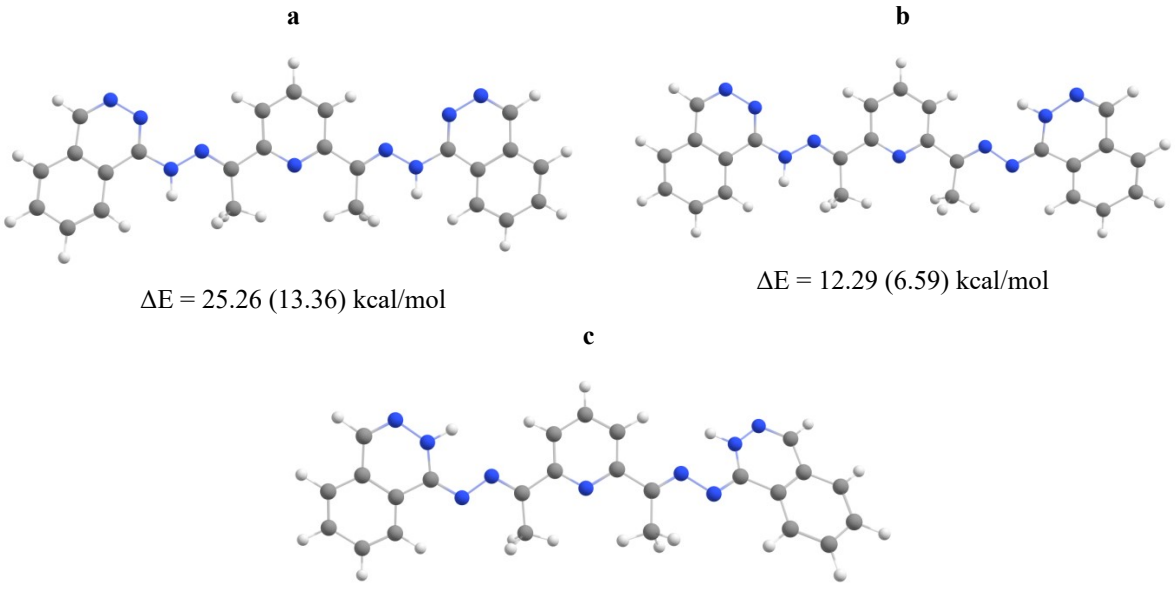


Figure S2 Optimized structures and relative energies of the selected most stable tautomeric forms of $\mathbf{H_2L^3}$ in the gas phase and DMSO solution (value in parenthesis – for DMSO solution)

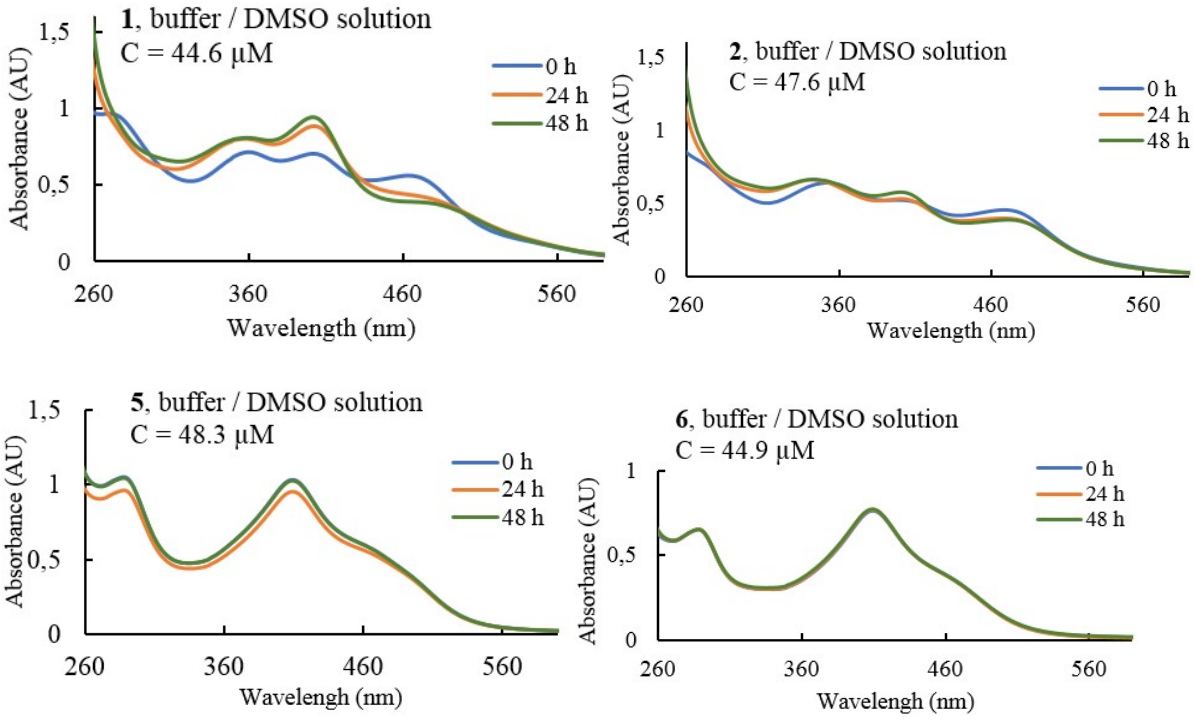
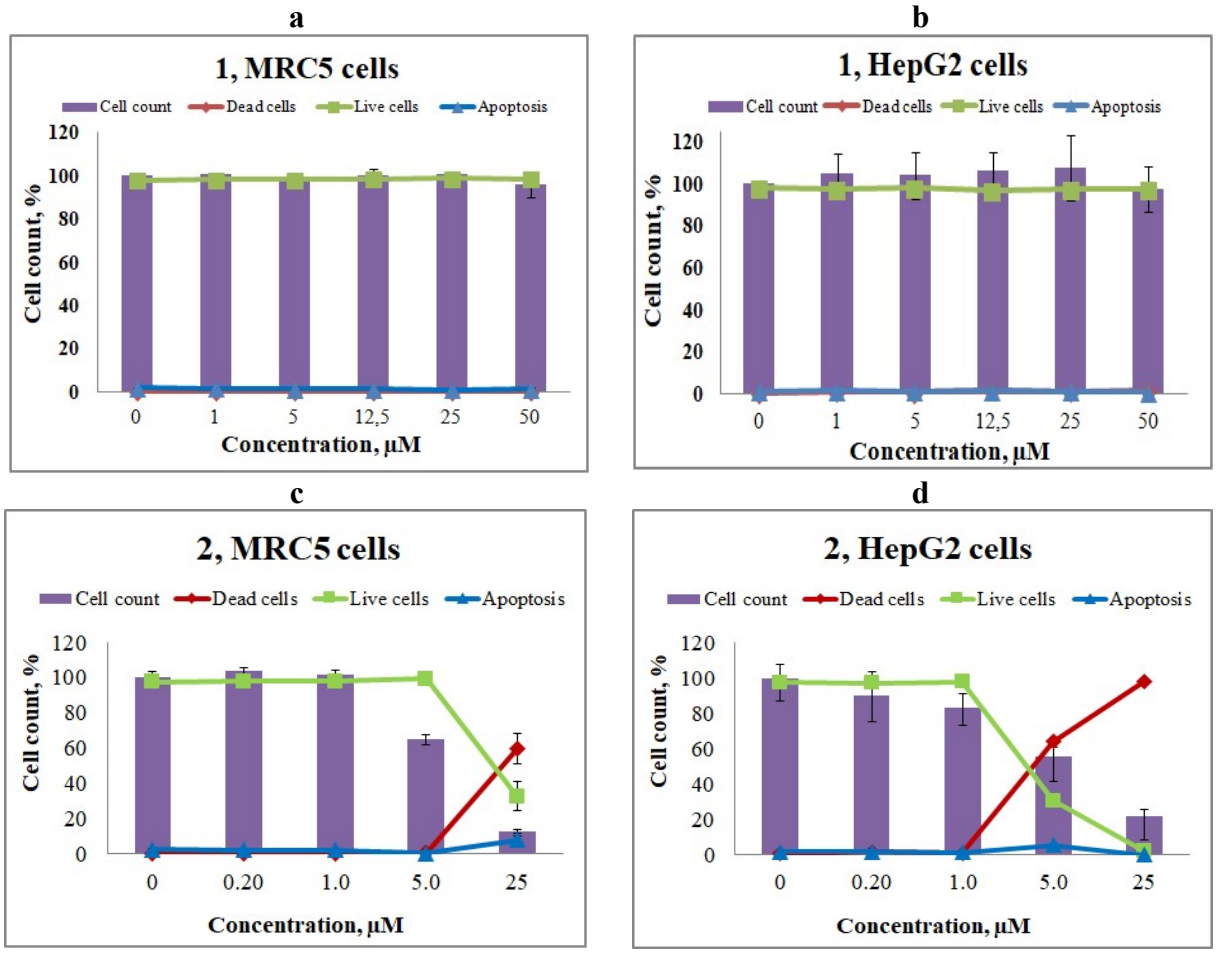


Figure S3 Evolution of the UV–vis absorption spectra of the complexes **1, 2, 5** and **6** in phosphate buffer saline – DMSO solution (1:40 by volume) at t = 0, 24, 48 h.



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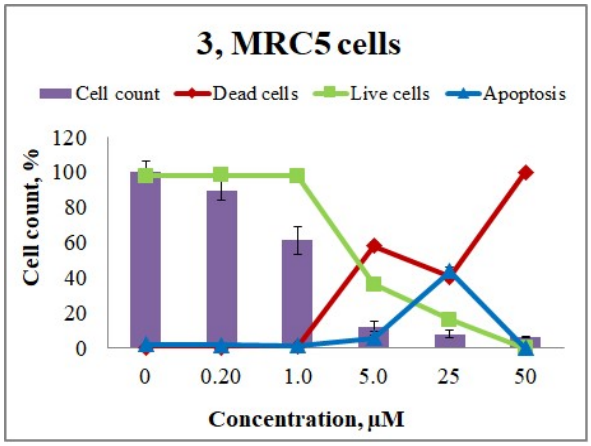
3, MRC5 cells
Cell count
Dead cells
Live cells
Apoptosis
Cell count, %
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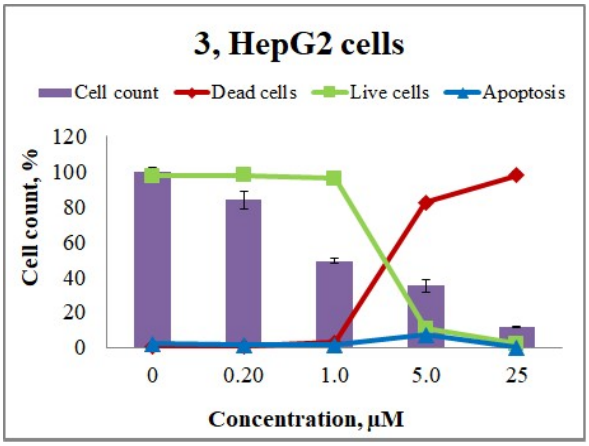
100
80
60
40
20
0
0
0.20
1.0
5.0
25
50
Concentration, µM

f


3, HepG2 cells
Cell count
Dead cells
Live cells
Apoptosis
Cell count, %
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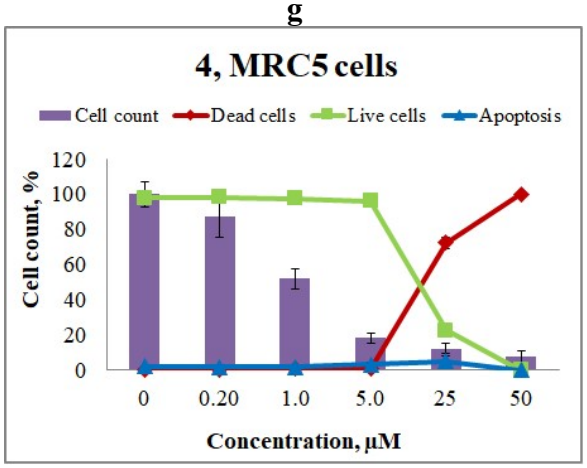
0
0.20
1.0
5.0
25
Concentration, µM

g


4, MRC5 cells
Cell count
Dead cells
Live cells
Apoptosis
Cell count, %
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80
60
40
20
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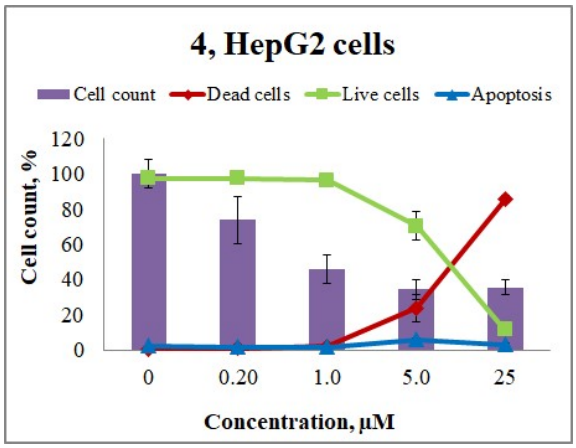
1.0
5.0
25
50
Concentration, µM

h


4, HepG2 cells
Cell count
Dead cells
Live cells
Apoptosis
Cell count, %
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100
80
60
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20
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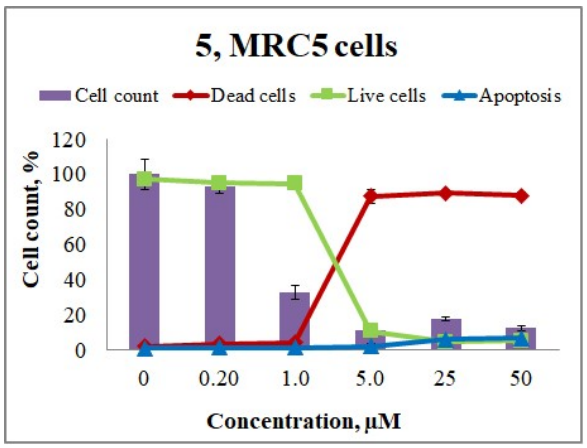
0.20
1.0
5.0
25
Concentration, µM

i


5, MRC5 cells
Cell count
Dead cells
Live cells
Apoptosis
Cell count, %
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80
60
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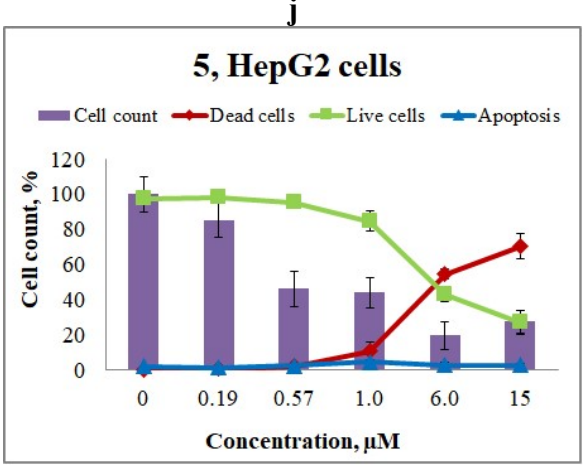
5.0
25
50
Concentration, µM

j


5, HepG2 cells
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Dead cells
Live cells
Apoptosis
Cell count, %
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0.19
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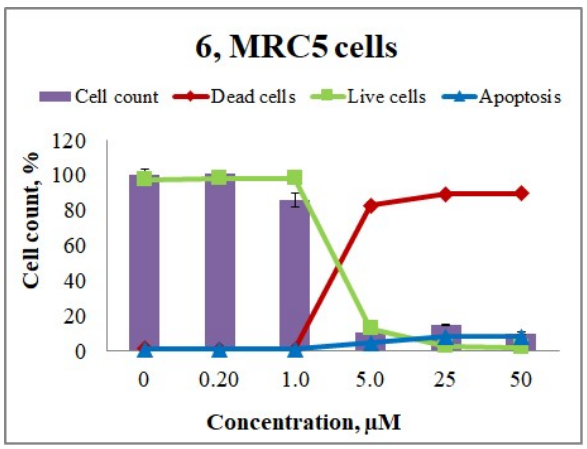
1.0
6.0
15
Concentration, µM

k


6, MRC5 cells
Cell count
Dead cells
Live cells
Apoptosis
Cell count, %
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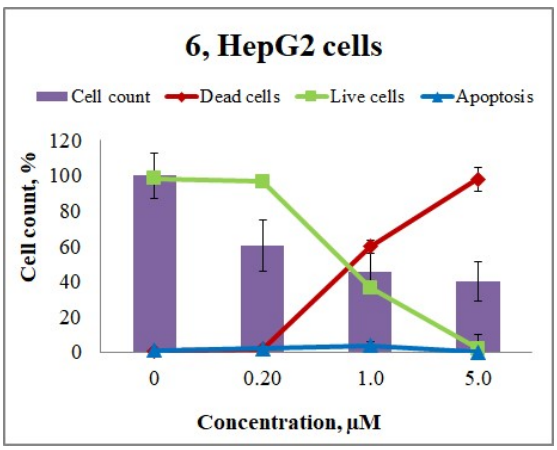
100
80
60
40
20
0
0
0.20
1.0
5.0
25
50
Concentration, µM

l


6, HepG2 cells
Cell count
Dead cells
Live cells
Apoptosis
Cell count, %
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80
60
40
20
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0
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1.0
5.0
Concentration, µM

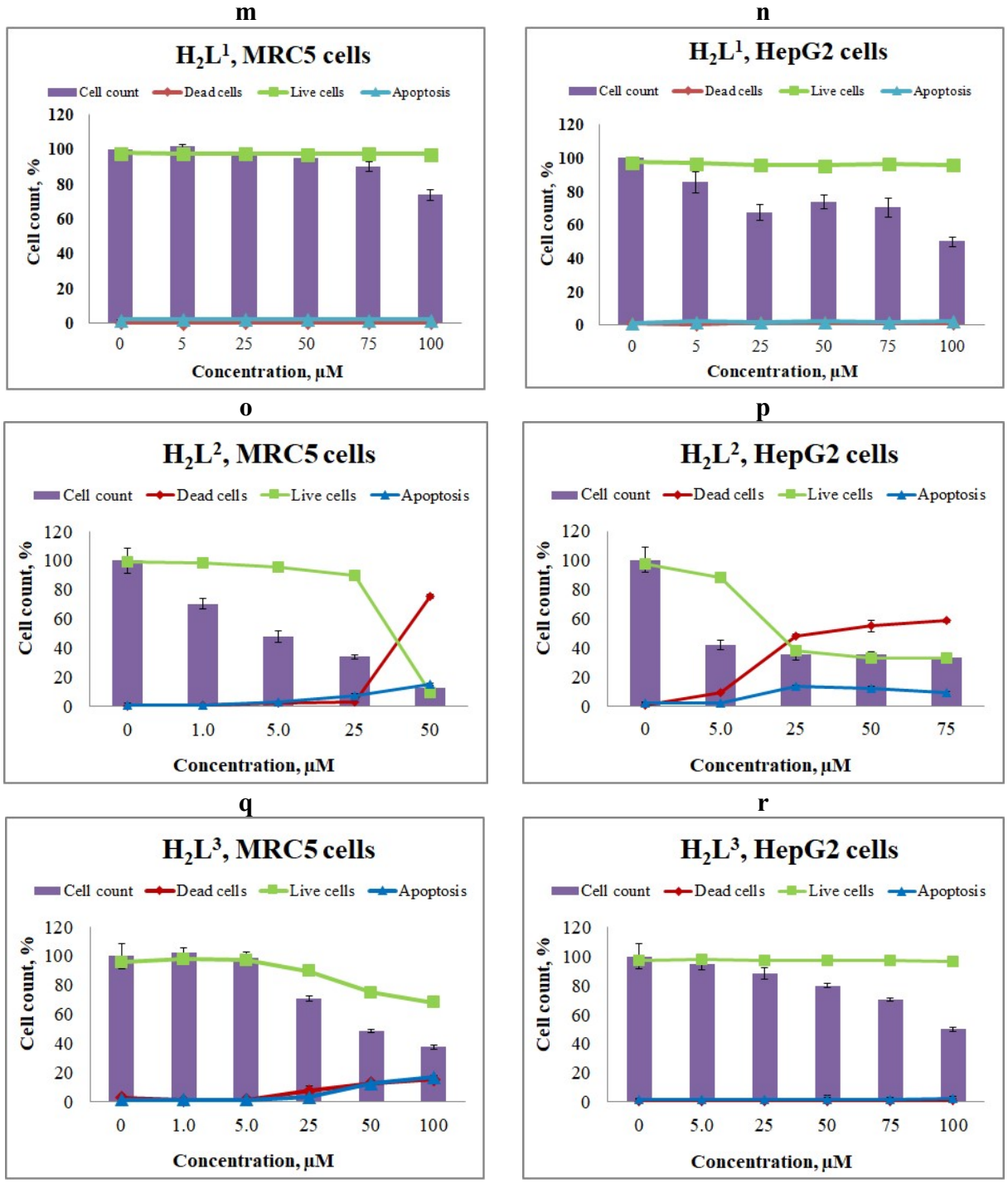

Fig. S4. Effect of **1**-**6** and ligands on the viability of HepG2 and MRC-5 cells determined by dual staining with Hoechst 33342/propidium iodide.