

## Supplementary Materials

### Copper(II) complexes with 1-(isoquinolin-3-yl)heteroalkyl-2-ones: Synthesis, Structure and Evaluation of Anticancer, Antimicrobial and Antioxidant Potential

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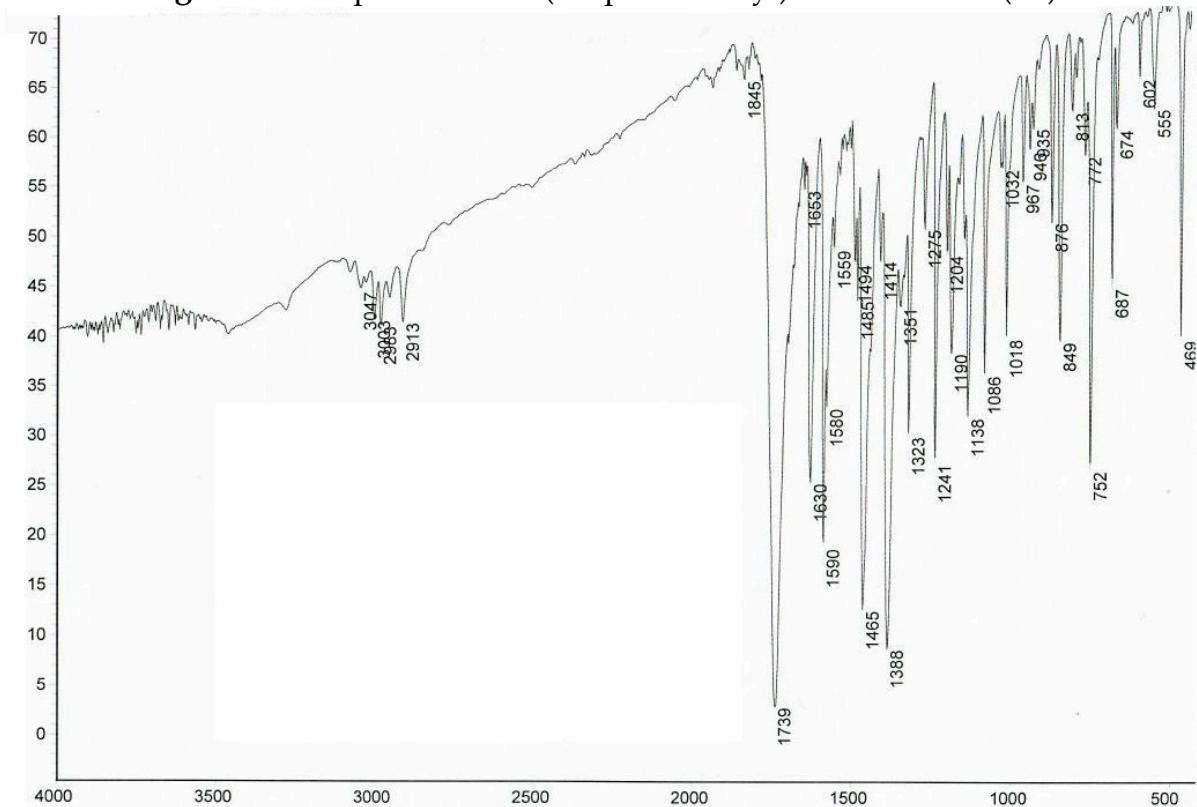
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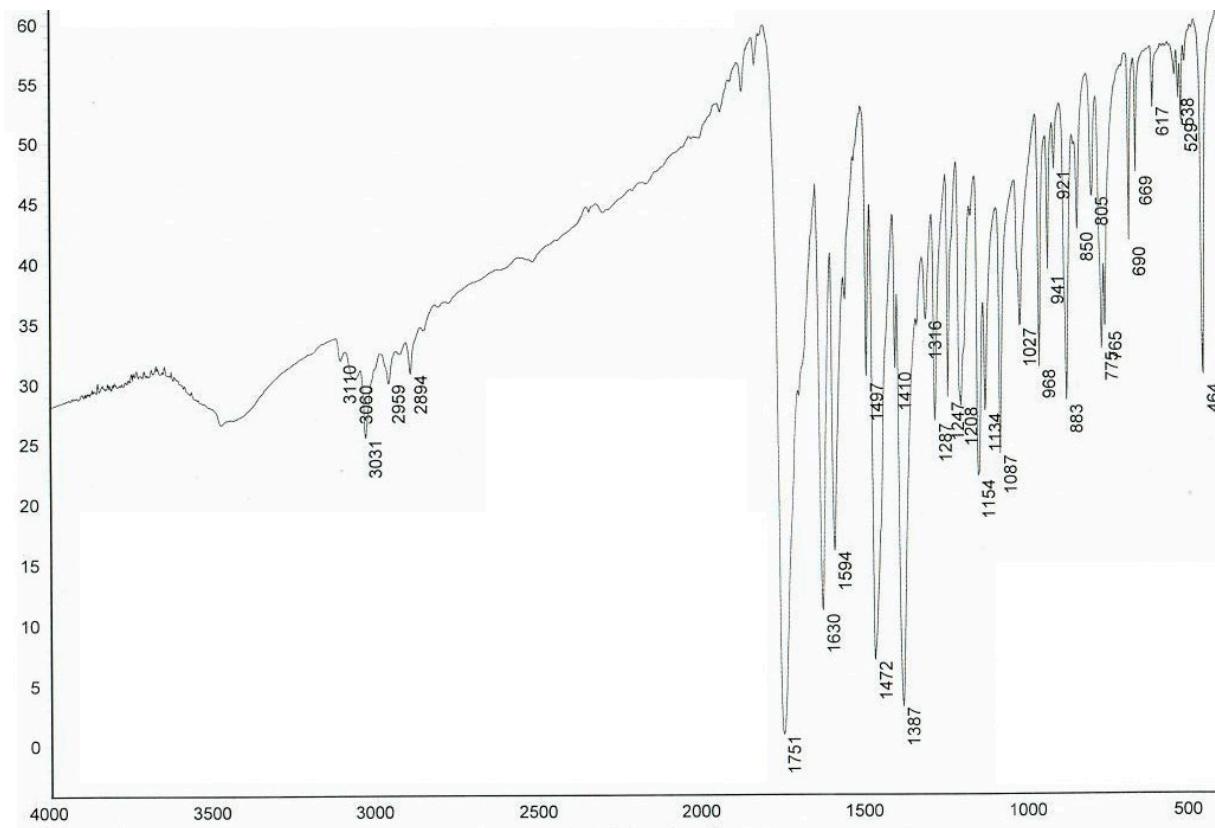
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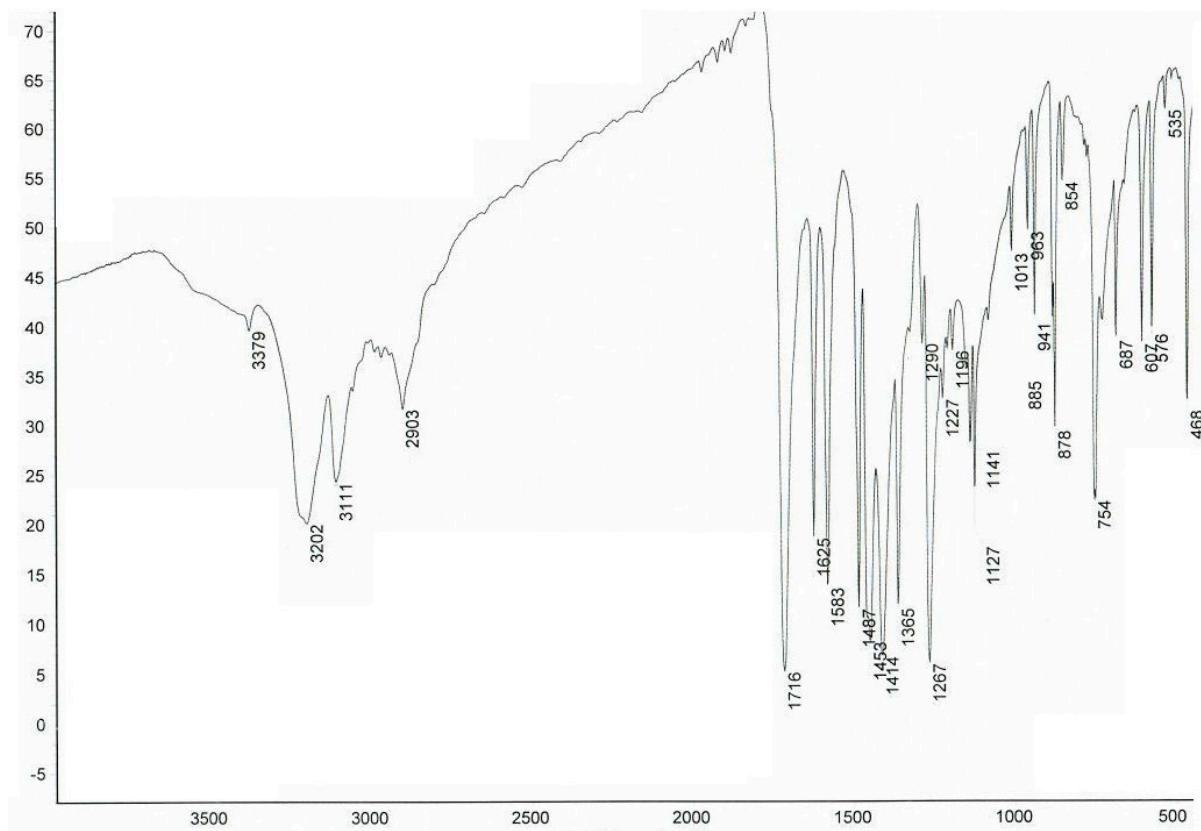
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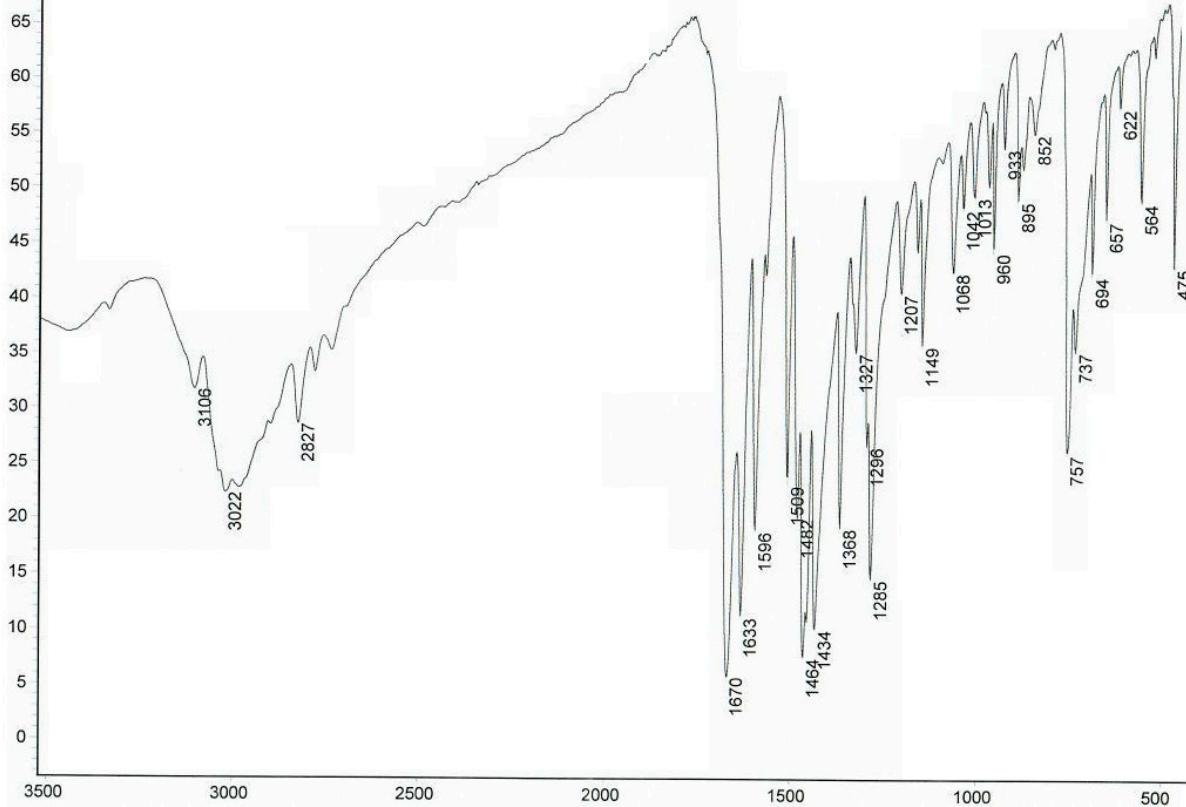
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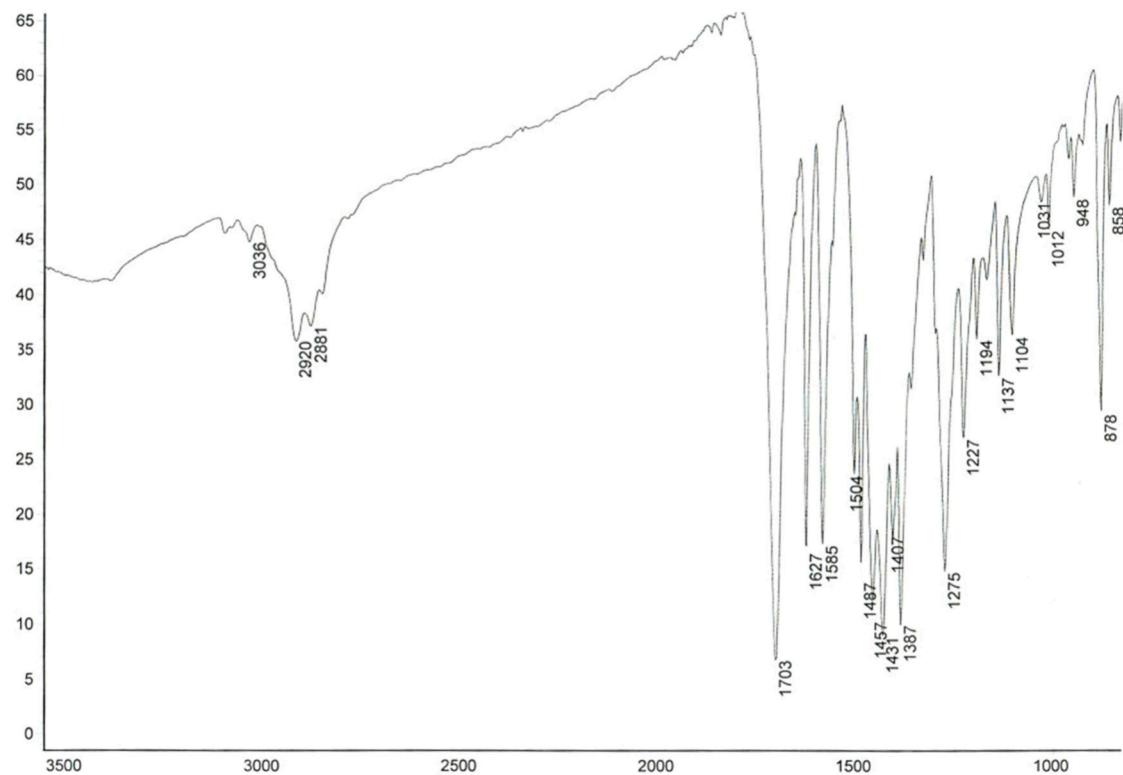
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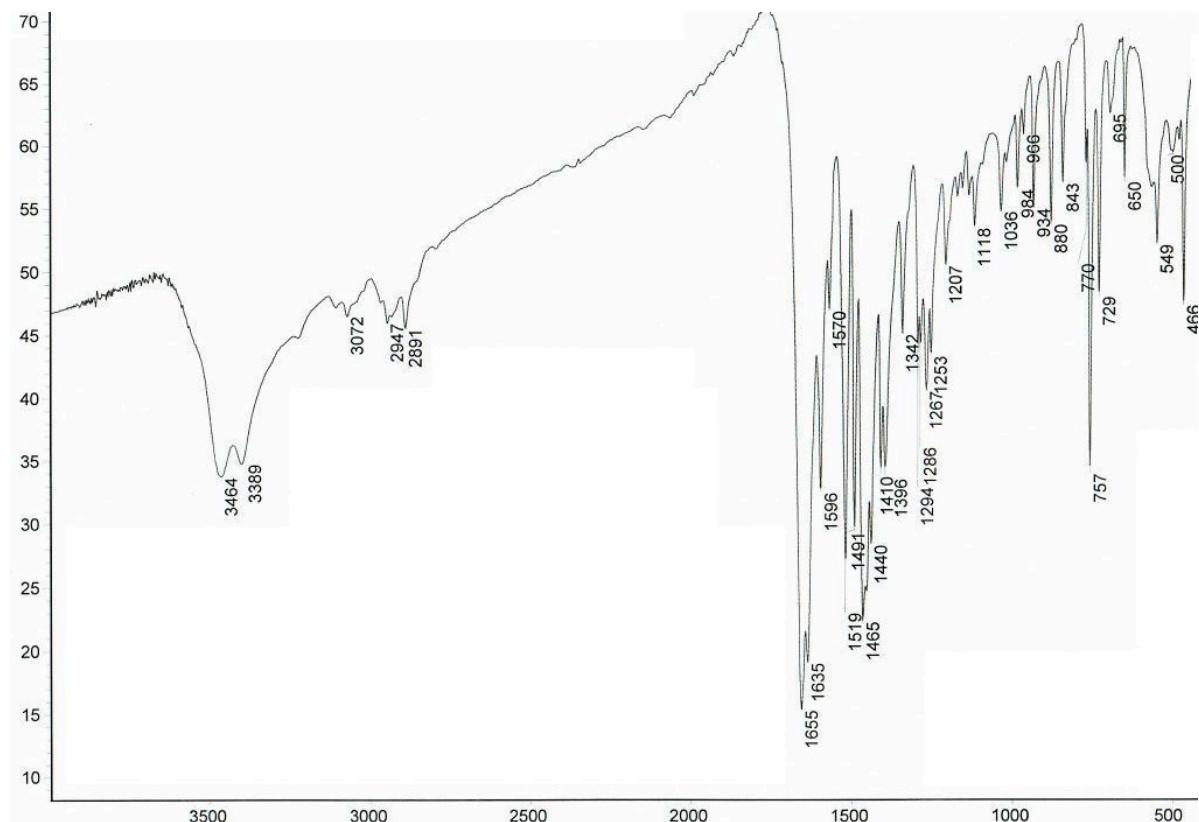
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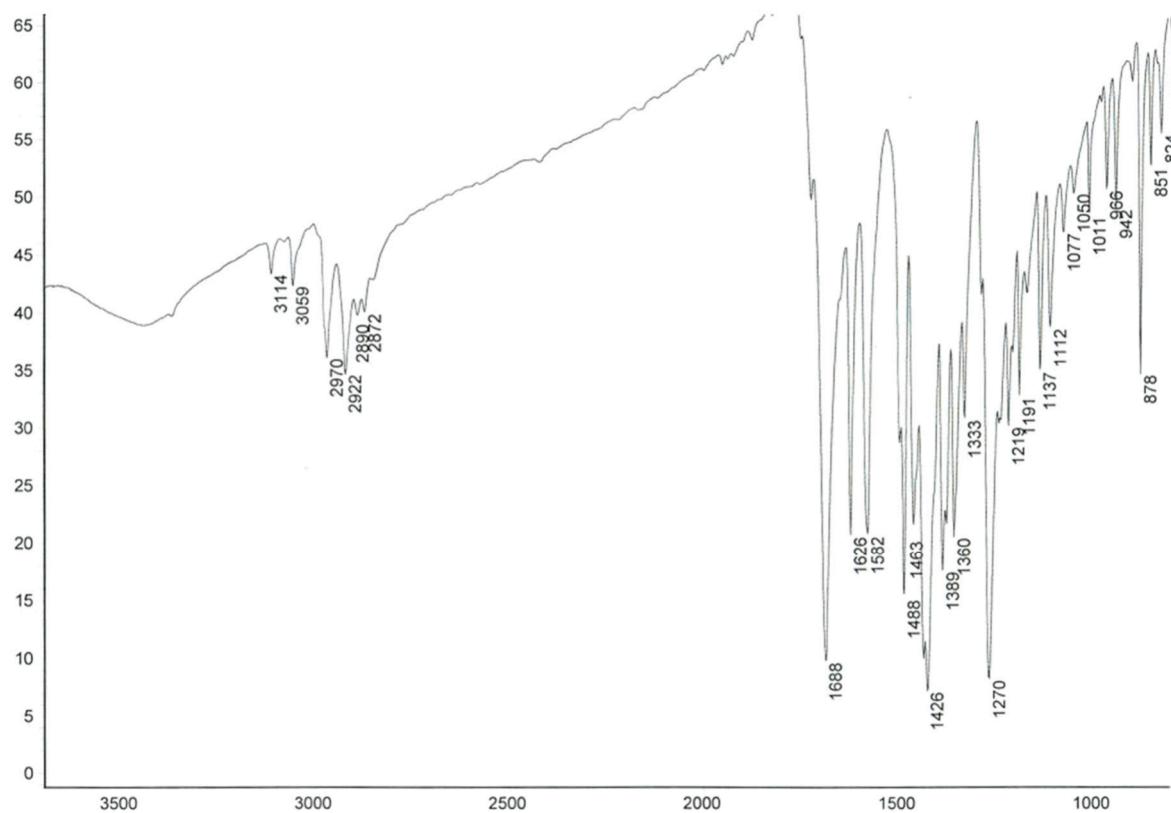
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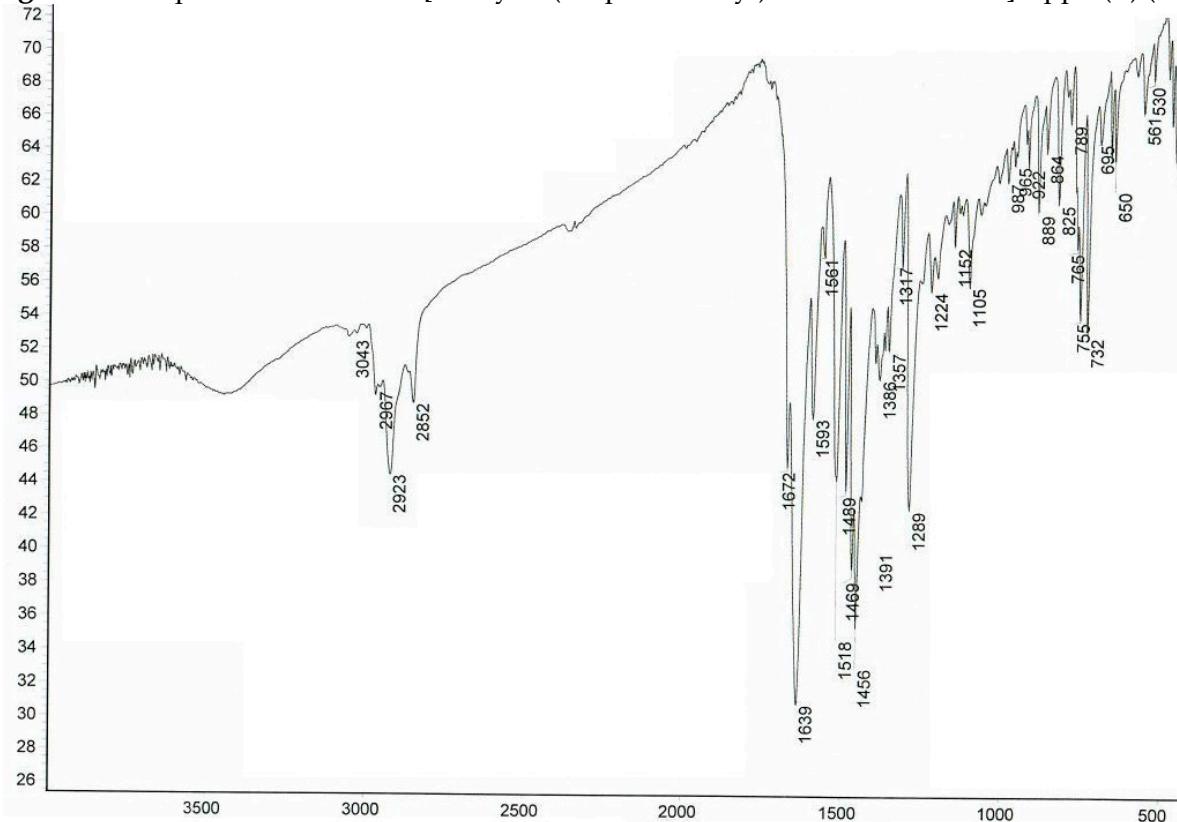
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**Figure S8.** IR spectrum of dichloro[1-ethyl-3-(isoquinolin-3-yl)imidazolidin-2-one]copper(II) (**C4**)



**Table S1.** Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ( $\text{\AA}^2$ ) for dichloro{bis[1-isoquinolin-3-yl]azetidin-2-one]}copper(II) (**C1**).

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
Cu1	0.500000	0.000000	0.500000	0.00995 (8)
Cl1	0.23838 (5)	-0.12393 (5)	0.52949 (4)	0.01433 (9)
O1	0.28721 (17)	0.02252 (15)	0.25132 (13)	0.0165 (2)
N1	0.50018 (18)	0.24980 (16)	0.62494 (14)	0.0108 (2)
N2	0.24107 (18)	0.27378 (17)	0.41036 (14)	0.0121 (2)
C8	0.5275 (2)	0.58846 (19)	0.82372 (17)	0.0115 (3)
C9	0.3912 (2)	0.51364 (19)	0.66173 (17)	0.0122 (3)
H9	0.307577	0.577491	0.616620	0.015*
C10	0.3803 (2)	0.34690 (19)	0.56935 (16)	0.0105 (3)
C11	0.2070 (2)	0.1368 (2)	0.27445 (17)	0.0123 (3)
C12	0.0401 (2)	0.1894 (2)	0.17116 (17)	0.0141 (3)
H12A	-0.084783	0.103418	0.127707	0.017*
H12B	0.059295	0.225729	0.085859	0.017*
C13	0.0852 (2)	0.3444 (2)	0.32834 (17)	0.0145 (3)
H13A	0.128603	0.461918	0.325388	0.017*
H13B	-0.016877	0.340283	0.366351	0.017*
C2	0.6334 (2)	0.32299 (19)	0.77590 (17)	0.0128 (3)
H2	0.720149	0.258492	0.814485	0.015*
C3	0.6539 (2)	0.49048 (19)	0.88244 (17)	0.0118 (3)
C4	0.7934 (2)	0.5599 (2)	1.04538 (17)	0.0149 (3)
H4	0.880324	0.495567	1.084149	0.018*
C5	0.8021 (2)	0.7199 (2)	1.14637 (18)	0.0170 (3)
H5	0.894685	0.766227	1.255298	0.020*
C6	0.6728 (2)	0.8162 (2)	1.08812 (18)	0.0166 (3)
H6	0.677603	0.925287	1.159760	0.020*
C7	0.5407 (2)	0.7547 (2)	0.93019 (18)	0.0152 (3)
H7	0.458501	0.823030	0.892227	0.018*

**Table S2.** Atomic displacement parameters ( $\text{\AA}^2$ ) for dichloro{bis[1-isoquinolin-3-yl]azetidin-2-one}copper(II) (**C1**).

	$U^{11}$	$U^{22}$	$U^{33}$	$U^{12}$	$U^{13}$	$U^{23}$
Cu1	0.01242 (13)	0.00748 (12)	0.00888 (12)	0.00298 (9)	0.00399 (9)	0.00188 (9)
Cl1	0.01544 (18)	0.01271 (17)	0.01375 (16)	0.00215 (13)	0.00709 (13)	0.00263 (13)
O1	0.0224 (6)	0.0134 (5)	0.0116 (5)	0.0075 (4)	0.0047 (4)	0.0034 (4)
N1	0.0133 (6)	0.0092 (5)	0.0099 (5)	0.0032 (5)	0.0051 (4)	0.0030 (4)
N2	0.0118 (6)	0.0140 (6)	0.0116 (5)	0.0050 (5)	0.0041 (5)	0.0066 (5)
C8	0.0139 (7)	0.0097 (6)	0.0123 (6)	0.0020 (5)	0.0075 (5)	0.0038 (5)
C9	0.0141 (7)	0.0115 (6)	0.0123 (6)	0.0048 (5)	0.0063 (5)	0.0044 (5)
C10	0.0124 (7)	0.0112 (6)	0.0089 (6)	0.0026 (5)	0.0054 (5)	0.0040 (5)
C11	0.0122 (7)	0.0117 (6)	0.0123 (6)	0.0007 (5)	0.0036 (5)	0.0066 (5)
C12	0.0132 (7)	0.0133 (7)	0.0125 (6)	0.0024 (5)	0.0022 (5)	0.0043 (5)
C13	0.0134 (7)	0.0157 (7)	0.0133 (6)	0.0063 (6)	0.0038 (5)	0.0049 (5)
C2	0.0142 (7)	0.0110 (6)	0.0116 (6)	0.0035 (5)	0.0037 (5)	0.0042 (5)
C3	0.0141 (7)	0.0099 (6)	0.0104 (6)	0.0009 (5)	0.0055 (5)	0.0028 (5)
C4	0.0170 (7)	0.0138 (7)	0.0118 (6)	0.0013 (6)	0.0046 (5)	0.0048 (5)
C5	0.0209 (8)	0.0151 (7)	0.0106 (6)	-0.0027 (6)	0.0066 (6)	0.0018 (5)
C6	0.0225 (8)	0.0111 (7)	0.0149 (7)	-0.0003 (6)	0.0113 (6)	0.0005 (5)
C7	0.0194 (8)	0.0105 (7)	0.0171 (7)	0.0038 (6)	0.0105 (6)	0.0030 (5)

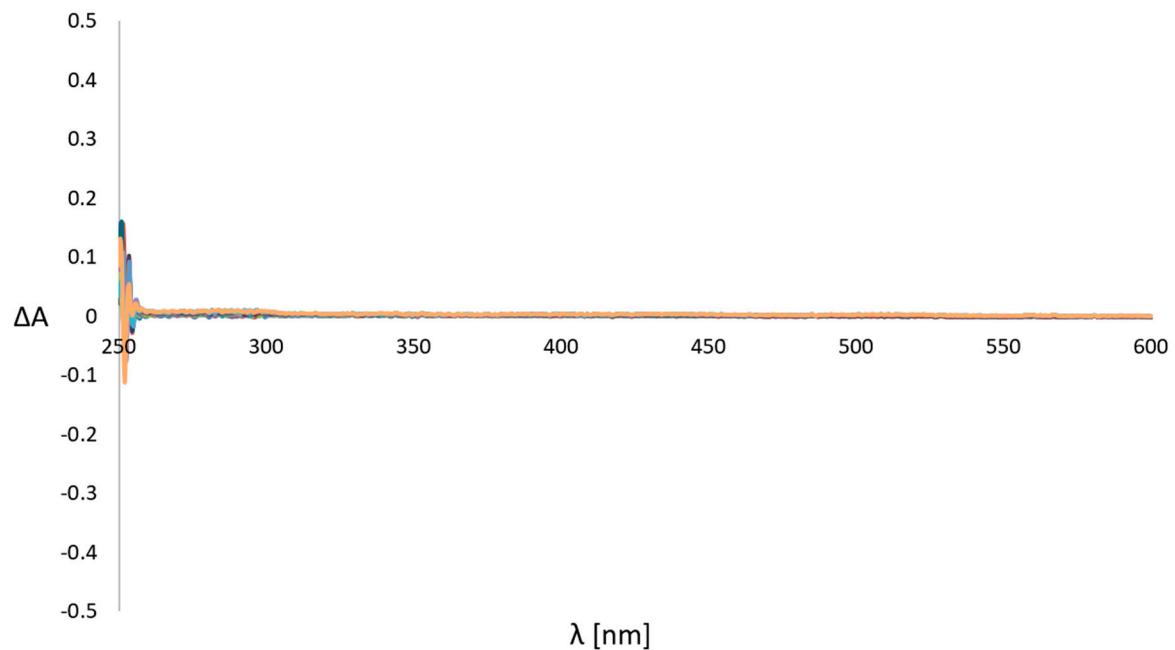
**Table S3.** Geometric parameters ( $\text{\AA}$ ,  $^\circ$ ) for dichloro{bis[1-isoquinolin-3-yl]azetidin-2-one]}copper(II) (**C1**).

$\text{Cu1—Cl1}^i$	2.3051 (4)	$\text{C11—C12}$	1.521 (2)
$\text{Cu1—Cl1}$	2.3051 (4)	$\text{C12—H12A}$	0.9900
$\text{Cu1—O1}$	2.4210 (11)	$\text{C12—H12B}$	0.9900
$\text{Cu1—O1}^i$	2.4210 (11)	$\text{C12—C13}$	1.555 (2)
$\text{Cu1—N1}$	2.0666 (12)	$\text{C13—H13A}$	0.9900
$\text{Cu1—N1}^i$	2.0666 (12)	$\text{C13—H13B}$	0.9900
$\text{O1—C11}$	1.2139 (19)	$\text{C2—H2}$	0.9500
$\text{N1—C10}$	1.3695 (19)	$\text{C2—C3}$	1.412 (2)
$\text{N1—C2}$	1.3301 (18)	$\text{C3—C4}$	1.423 (2)
$\text{N2—C10}$	1.3971 (18)	$\text{C4—H4}$	0.9500
$\text{N2—C11}$	1.3667 (19)	$\text{C4—C5}$	1.373 (2)
$\text{N2—C13}$	1.4789 (19)	$\text{C5—H5}$	0.9500
$\text{C8—C9}$	1.410 (2)	$\text{C5—C6}$	1.419 (2)
$\text{C8—C3}$	1.416 (2)	$\text{C6—H6}$	0.9500
$\text{C8—C7}$	1.4211 (19)	$\text{C6—C7}$	1.373 (2)
$\text{C9—H9}$	0.9500	$\text{C7—H7}$	0.9500
$\text{C9—C10}$	1.379 (2)		
$\text{Cl1}^i—\text{Cu1—Cl1}$	180.0	$\text{O1—C11—C12}$	135.88 (14)
$\text{Cl1—Cu1—O1}$	88.91 (3)	$\text{N2—C11—C12}$	92.33 (12)
$\text{Cl1}^i—\text{Cu1—O1}$	91.09 (3)	$\text{C11—C12—H12A}$	114.3
$\text{Cl1—Cu1—O1}^i$	91.09 (3)	$\text{C11—C12—H12B}$	114.3
$\text{Cl1}^i—\text{Cu1—O1}^i$	88.91 (3)	$\text{C11—C12—C13}$	85.96 (11)
$\text{O1}^i—\text{Cu1—O1}$	180.0	$\text{H12A—C12—H12B}$	111.5
$\text{N1—Cu1—Cl1}^i$	88.54 (4)	$\text{C13—C12—H12A}$	114.3
$\text{N1}^i—\text{Cu1—Cl1}^i$	91.46 (4)	$\text{C13—C12—H12B}$	114.3
$\text{N1}^i—\text{Cu1—Cl1}$	88.54 (4)	$\text{N2—C13—C12}$	86.83 (11)
$\text{N1—Cu1—Cl1}$	91.46 (4)	$\text{N2—C13—H13A}$	114.2
$\text{N1—Cu1—O1}$	89.50 (4)	$\text{N2—C13—H13B}$	114.2
$\text{N1}^i—\text{Cu1—O1}$	90.50 (4)	$\text{C12—C13—H13A}$	114.2
$\text{N1—Cu1—O1}^i$	90.50 (4)	$\text{C12—C13—H13B}$	114.2
$\text{N1}^i—\text{Cu1—O1}^i$	89.50 (4)	$\text{H13A—C13—H13B}$	111.3
$\text{N1}^i—\text{Cu1—N1}$	180.0	$\text{N1—C2—H2}$	117.9
$\text{C11—O1—Cu1}$	112.59 (9)	$\text{N1—C2—C3}$	124.15 (14)
$\text{C10—N1—Cu1}$	127.35 (10)	$\text{C3—C2—H2}$	117.9
$\text{C2—N1—Cu1}$	115.44 (10)	$\text{C8—C3—C4}$	119.99 (13)
$\text{C2—N1—C10}$	117.21 (12)	$\text{C2—C3—C8}$	117.94 (13)
$\text{C10—N2—C13}$	128.25 (12)	$\text{C2—C3—C4}$	122.05 (14)

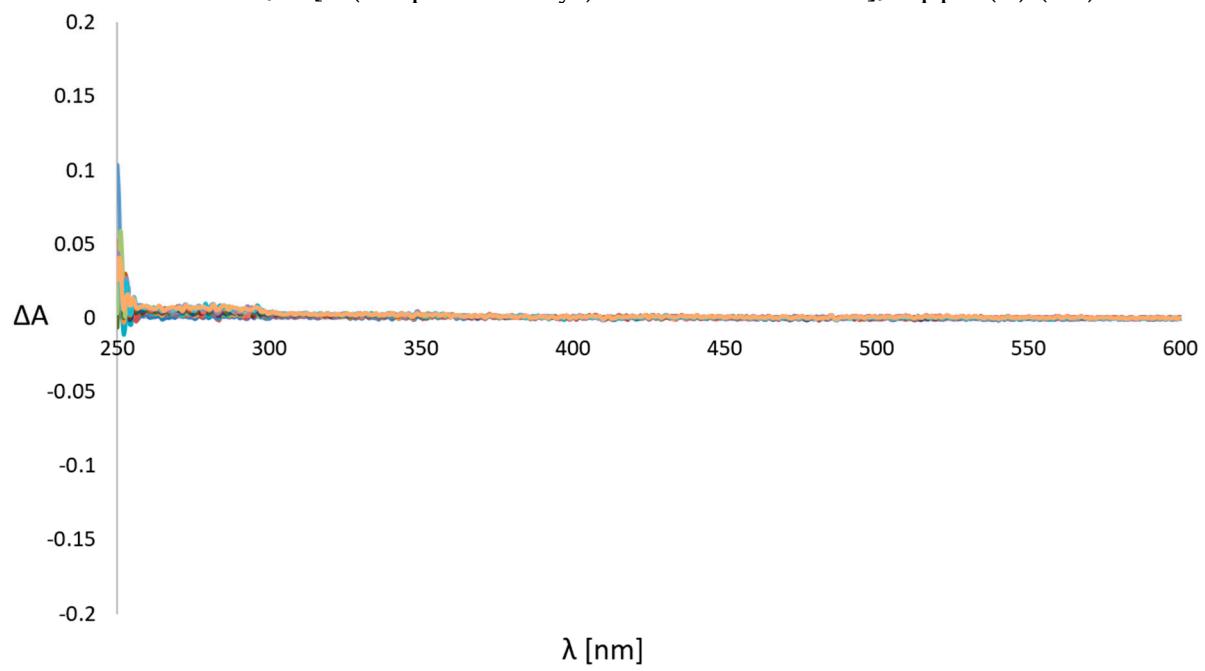
C11—N2—C10	136.46 (13)	C3—C4—H4	120.1
C11—N2—C13	94.88 (11)	C5—C4—C3	119.86 (15)
C9—C8—C3	117.84 (13)	C5—C4—H4	120.1
C9—C8—C7	123.09 (14)	C4—C5—H5	120.0
C3—C8—C7	119.05 (13)	C4—C5—C6	120.01 (14)
C8—C9—H9	120.3	C6—C5—H5	120.0
C10—C9—C8	119.41 (14)	C5—C6—H6	119.4
C10—C9—H9	120.3	C7—C6—C5	121.27 (14)
N1—C10—N2	118.23 (12)	C7—C6—H6	119.4
N1—C10—C9	123.37 (13)	C8—C7—H7	120.1
C9—C10—N2	118.39 (13)	C6—C7—C8	119.76 (15)
O1—C11—N2	131.77 (14)	C6—C7—H7	120.1
Cu1—O1—C11—N2	14.7 (2)	C11—N2—C10—N1	-15.7 (2)
Cu1—O1—C11—C12	-167.31 (15)	C11—N2—C10—C9	163.70 (16)
Cu1—N1—C10—N2	-0.52 (19)	C11—N2—C13—C12	0.55 (12)
Cu1—N1—C10—C9	-179.87 (11)	C11—C12—C13—N2	-0.49 (11)
Cu1—N1—C2—C3	-178.19 (11)	C13—N2—C10—N1	173.63 (13)
O1—C11—C12—C13	-177.94 (19)	C13—N2—C10—C9	-7.0 (2)
N1—C2—C3—C8	-1.5 (2)	C13—N2—C11—O1	178.01 (17)
N1—C2—C3—C4	177.08 (15)	C13—N2—C11—C12	-0.56 (12)
N2—C11—C12—C13	0.53 (12)	C2—N1—C10—N2	179.06 (13)
C8—C9—C10—N1	-2.2 (2)	C2—N1—C10—C9	-0.3 (2)
C8—C9—C10—N2	178.47 (13)	C2—C3—C4—C5	-177.01 (14)
C8—C3—C4—C5	1.6 (2)	C3—C8—C9—C10	2.8 (2)
C9—C8—C3—C2	-1.0 (2)	C3—C8—C7—C6	-1.1 (2)
C9—C8—C3—C4	-179.66 (14)	C3—C4—C5—C6	-0.3 (2)
C9—C8—C7—C6	177.61 (15)	C4—C5—C6—C7	-1.7 (2)
C10—N1—C2—C3	2.2 (2)	C5—C6—C7—C8	2.4 (2)
C10—N2—C11—O1	5.3 (3)	C7—C8—C9—C10	-175.99 (14)
C10—N2—C11—C12	-173.24 (17)	C7—C8—C3—C2	177.77 (13)
C10—N2—C13—C12	174.13 (14)	C7—C8—C3—C4	-0.9 (2)

Symmetry code: (i)  $-x+1, -y, -z+1$ .

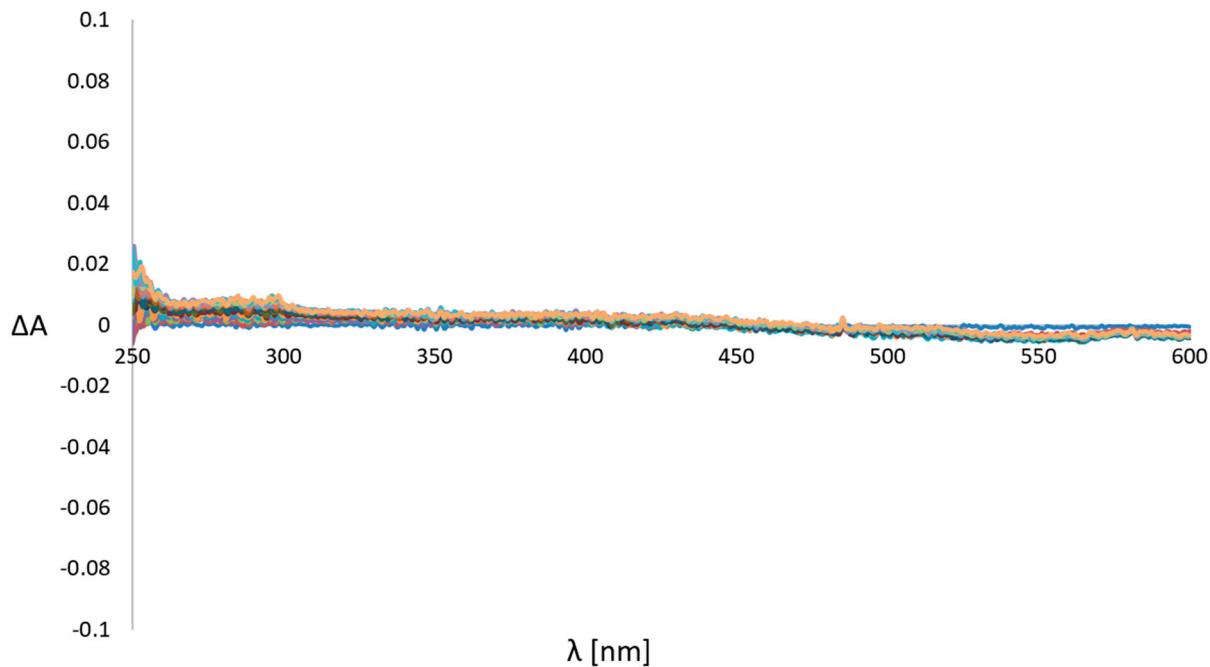
**Figure S9.** Time-dependent UV-vis spectra of dichloro{bis[1-(isoquinolin-3-yl)azetidin-2-one]}copper(II) (**C1**)



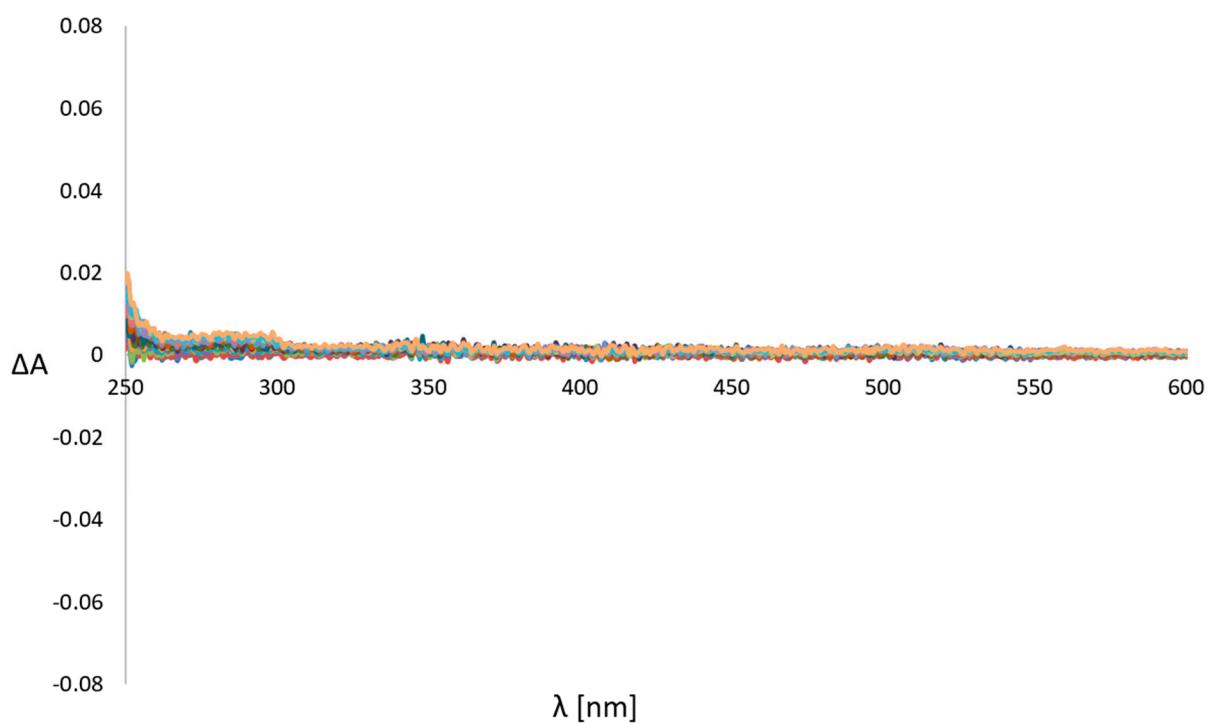
**Figure S10.** Time-dependent UV-vis spectra of dichloro{bis[1-(isoquinolin-3-yl)imidazolidin-2-one]}copper(II) (**C2**)



**Figure S11.** Time-dependent UV-vis spectra of dichloro[1-(isoquinolin-3-yl)-3-methylimidazolidin-2-one]copper(II) (**C3**)



**Figure S12.** Time-dependent UV-vis spectra of dichloro[1-ethyl-3-(isoquinolin-3-yl)imidazolidin-2-one]copper(II) (**C4**)



**Table S4.** Predicted physicochemical, pharmacokinetic and drug-likeness properties of copper(II) complexes C1-4

	Molecule	C1	C2	C3	C4
Physicochemical Properties	Formula	C <sub>24</sub> H <sub>20</sub> Cl <sub>2</sub> CuN <sub>4</sub> O <sub>2</sub>	C <sub>24</sub> H <sub>22</sub> Cl <sub>2</sub> CuN <sub>6</sub> O <sub>2</sub>	C <sub>13</sub> H <sub>13</sub> Cl <sub>2</sub> CuN <sub>3</sub> O	C <sub>14</sub> H <sub>15</sub> Cl <sub>2</sub> CuN <sub>3</sub> O
	MW	530.89	560.92	361.71	375.74
	Heavy atoms	33	35	20	21
	Aromatic heavy atoms	20	20	10	10
	Fraction Csp <sup>3</sup>	0.17	0.17	0.23	0.29
	Rotatable bonds	2	2	1	2
	H-bond acceptors	4	4	2	2
	H-bond donors	0	2	0	0
	MR	135.26	149.47	85.49	90.30
	TPSA	66.40	90.46	36.44	36.44
Lipophilicity	iLOGP	0.00	0.00	0.00	0.00
	XLOGP3	4.61	4.40	3.18	3.55
	WLOGP	4.56	3.38	4.56	3.36
	MLOGP	3.79	3.05	1.99	2.24
	Silicos-IT LogP	2.26	1.55	1.44	1.78
	Consensus LogP	3.04	2.48	1.87	2.14
Water Solubility	ESOL Log S <sub>ESOL</sub>	-6.35	-6.38	-4.39	-4.63
	Solubility (mg/ml) <sub>ESOL</sub>	2.36e-04	2.34e-04	1.47e-02	8.88e-03
	Solubility (mol/l)	4.44e-07	4.16e-07	4.07e-05	2.36e-05
	ESOL Class	Poorly soluble	Poorly soluble	Moderately soluble	Moderately soluble
	Ali Log S	-5.73	-6.02	-3.62	-4.00
	Ali Solubility (mg/ml)	9.90e-04	5.40e-04	8.75e-02	3.76e-02
	Ali Solubility (mol/l)	1.86e-06	9.62e-07	2.42e-04	9.99e-05
	Ali Class	Moderately soluble	Poorly soluble	Soluble	Moderately soluble
	Silicos-IT LogSw	-3.76	-3.81	-3.49	-3.89
	Silicos-IT Solubility (mg/ml)	9.23e-02	8.61e-02	1.18e-01	4.83e-02

	Silicos-IT				
	Solubility (mol/l)	1.74e-04	1.53e-04	3.26e-04	1.29e-04
	Silicos-IT class	Soluble	Soluble	Soluble	Soluble
Pharmacokinetics	GI absorption	High	High	High	High
	BBB permeant	Yes	No	Yes	Yes
	Pgp substrate	Yes	Yes	Yes	Yes
	CYP1A2 inhibitor	No	No	No	No
	CYP2C19 inhibitor	No	Yes	Yes	Yes
	CYP2C9 inhibitor	No	No	No	No
	CYP2D6 inhibitor	No	No	No	No
	CYP3A4 inhibitor	No	No	No	No
	log K <sub>p</sub> (cm/s)	-6.27	-6.60	-6.25	-6.07
	Lipinski violations	1	1	0	0
Drug-likeness	Ghose violations	2	2	0	0
	Veber violations	0	0	0	0
	Egan violations	0	0	0	0
	Muegge violations	0	0	0	0
	Bioavailability Score	0.55	0.55	0.55	0.55
Medicinal Chemistry	PAINS alerts	0	0	0	0
	Brenk alerts	0	0	0	0
	Leadlikeness violations	2	2	1	2
	Synthetic Accessibility	2.73	3.33	2.46	2.56