Synthesis, characterization and cytotoxicity of Zn(II) complex with *N*-substituted glycine hydrazone

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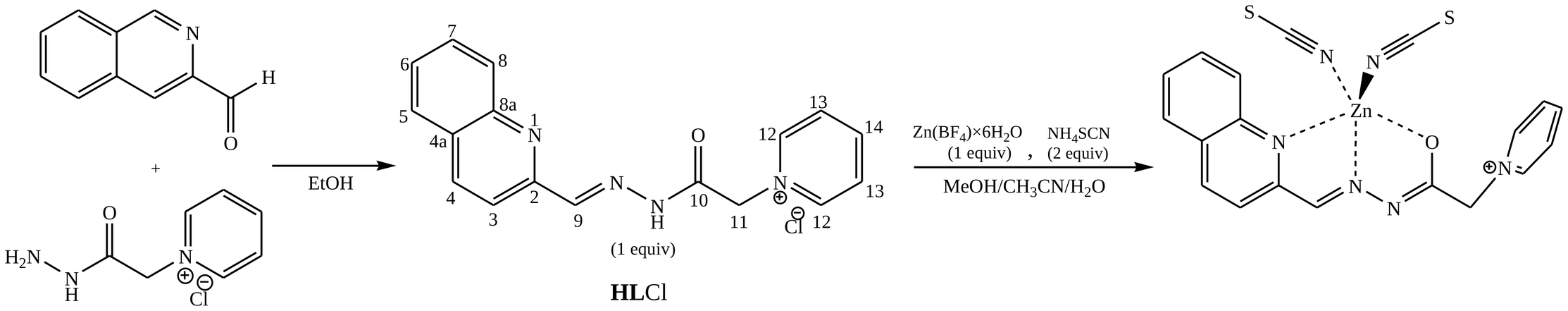
• The (*E*)-1-(2-oxo-2-(2-(quinolin-2-ylmethylene)hydrazinyl)ethyl)pyridin-1-ium chloride ligand, **HL**Cl, was obtained from the condensation reaction of 2-quinolinecarboxaldehyde and Girard's P reagent in ethanol. Reaction of the ligand **HL**Cl with $Zn(BF_4)_2 \cdot 6H_2O$ and NH_4SCN in molar ratio 1 : 1 : 2 in methanol/acetonitrile/water mixture resulted in formation of the mononuclear thiocyanato Zn(II) complex with composition [Zn**L**$(NCS)_2$]. The composition of the complex was determined by elemental analysis, complex was characterized by spectroscopic techniques and structure was determined by X-ray analysis.



HLCl

• **Scheme 1**. Synthesis of the **HL**Cl and [Zn**L**$(NCS)_2$] complex

• *X-ray*

• Complex [Zn**L**$(NCS)_2$] crystallizes with two independent molecules in the asymmetric unit of the triclinic P-1 space group. The two molecules, displayed in Figure 1, differ for the ligand conformation, but present the same coordination geometry (Table 1). In both molecules the zinc coordination is fivefold and can be described as a distorted trigonal bipyramid, with two NCS and one N of the ONN chelating system in the equatorial plane, and the trans N- and O atom at the apical positions. In both cases the coordinated zwitterionic **L** ligand forms two five-membered chelation rings which result practically co-planar with the quinoline moiety, apart for a slight deviation of the oxygen atom out of the plane (deviating 0.15 and 0.27 Å for O1 and O2 respectively).

Table 1. Crystal data and structure refinement for [Zn**L**$(NCS)_2$]

Identification code	**ZnL(SCN)$_2$**
Empirical formula	$C_{19}H_{14}N_6OS_2Zn$
Formula weight	471.85
Temperature/K	300.5
Crystal system	Triclinic
Space group	P-1
a/Å	8.421(1)
b/Å	14.288(2)
c/Å	17.258(3)
α/°	91.238(4)
β/°	97.966(4)
γ/°	91.943(4)
Volume/Å^3	2054.4(6)
Z	4
ρ_{calc}g/cm^3	1.526
μ/mm^{-1}	1.422
F(000)	960.0
Crystal size/mm^3	0.10 × 0.10 × 0.09
Radiation /Å	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.768 to 51.532
Index ranges	-10 ≤ h ≤ 10, -17 ≤ k ≤ 17, -21 ≤ l ≤ 21
Reflections collected	34725
Independent reflections	7813 [R_{int} = 0.0392, R_{sigma} = 0.0389]
Data/restraints/parameters	7813/0/523
Goodness-of-fit on F^2	1.044
Final R indexes [I>=2σ (I)]	R_1 = 0.0407, wR_2 = 0.1060
Final R indexes [all data]	R_1 = 0.0614, wR_2 = 0.1226
Largest DF max/min / e Å^{-3}	0.59/-0.42

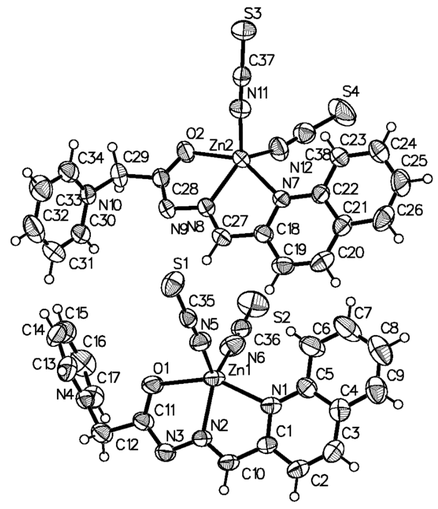


Figure 1. Molecular structures of the two independent molecules observed in the crystal structure of [Zn**L**$(NCS)_2$], with atom labelling and thermal displacement ellipsoids displayed at the 50% probability level.

• *Cytotoxic activity*

• The [Zn**L**$(SCN)_2$] complex showed moderate cytotoxic activity against HeLa, A375 and A549 malignant cells (IC_{50} values of 59.13 μM, 57.35 and 54.79 μM). This complex showed lower cytotoxicity against normal keratinocytes HaCaT when comparing its activity against these three malignant cell lines (IC_{50} value of 69.29 μM). The complex exerted lower cytotoxic effects on PC-3 cells with IC_{50} value of 87.23 μM, while the lowest cytotoxicity was observed against MCF7 cells (IC_{50} value of 106.17 μM). The complex exhibited higher cytotoxic effects on examined cell lines in comparison with its ligand **HL**Cl, with the exception of the effect on MCF7 cells. The obtained IC_{50} values for **HL**Cl were in the range of 74.05-183.95 μM. Treatment of HeLa cells with $2IC_{50}$ concentration of the complex induced increase in the percentage of cells within G2/M cell cycle phase when compared with control cells.

Table 2. Cytotoxic activity of the complex and its precursor compounds

	HeLa	A375	MCF7	PC-3	A549	HaCaT
	IC_{50} [μM] average ± SD					
HLCl	78.17±6.35	86.01±3.43	74.05±5.21	183.95±2.56	156.93±1.98	83.82±7.65
[ZnL(SCN)$_2$]	59.13±4.31	57.35±1.45	106.17±8.84	87.23±5.83	54.79±0.65	69.29±5.35
NH_4SCN	>200	175.88±14.53	>200	199.97±0.05	>200	182.87±14.65
$Zn(BF_4)_2$ x $6H_20$	171.06±2.85	131.85±11.88	198.78±1.72	192.77±2.63	199.22±1.10	114.15±8.75