evropský sociální fond v ČR
EVROPSKÁ UNIE
MINISTERSTVO ŠKOLSTVÍ, MLÁDEŽE A TĚLOVÝCHOVY
OP Vzdělávání pro konkurenceschopnost
INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

Název: Monitoring of nucleic acids interaction with coordination compounds of copper and nickel, their characterization including mass spectrometry

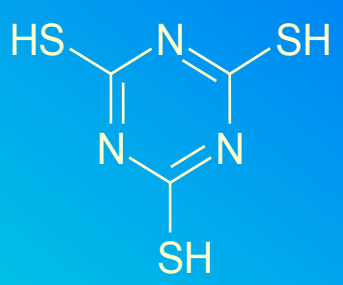
Školitel: Pavel Kopel

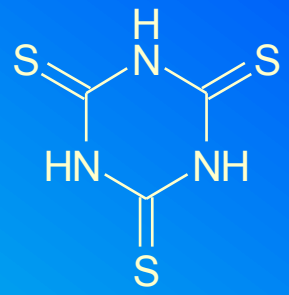
Datum: 19.4.2013

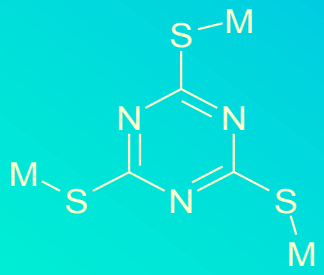
Reg.č.projektu: CZ.1.07/2.3.00/20.0148

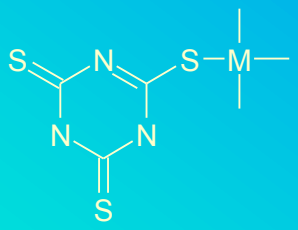
Název projektu: Mezinárodní spolupráce v oblasti "in vivo" zobrazovacích technik

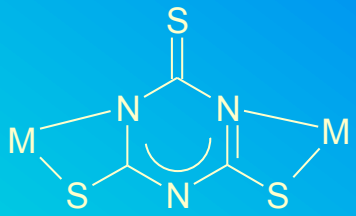
Trithiocyanuric acid (2,4,6-Trimerkapto-s-triazine)

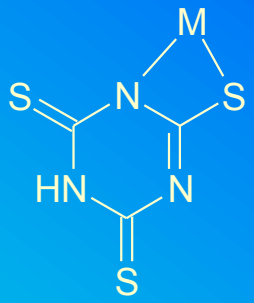


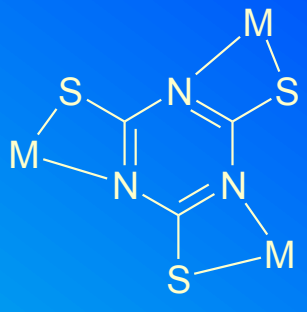


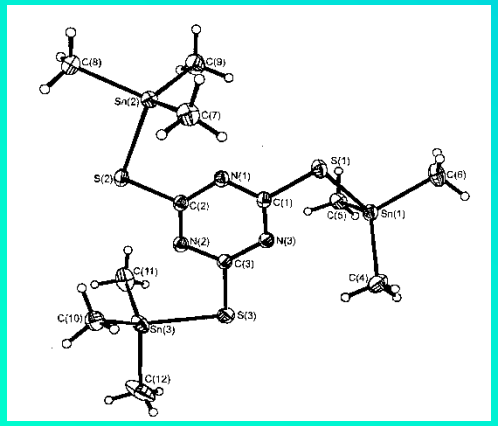


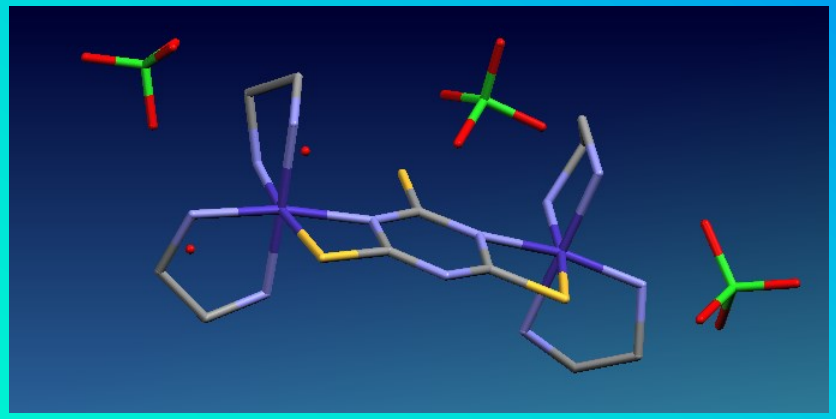


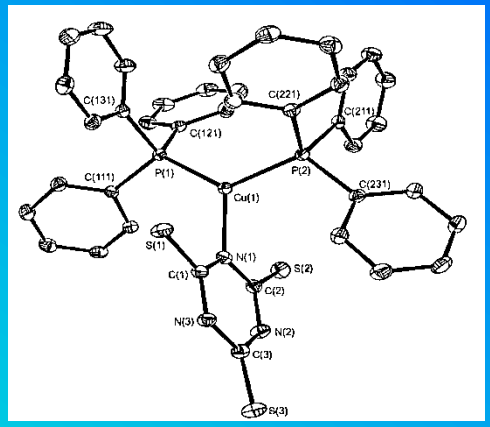








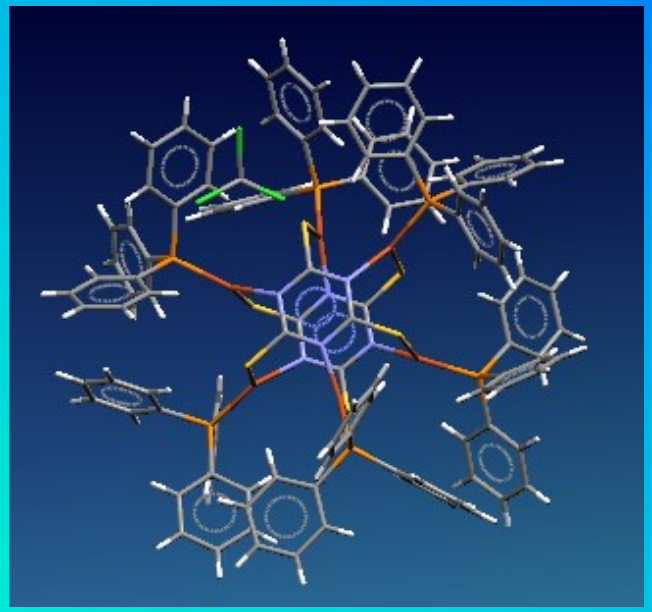


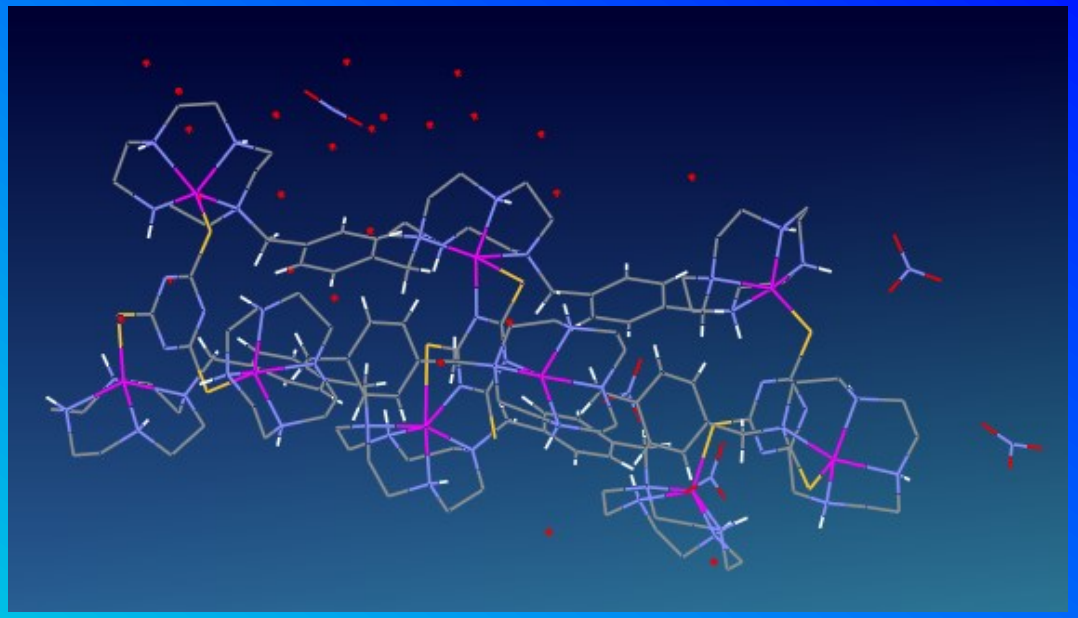


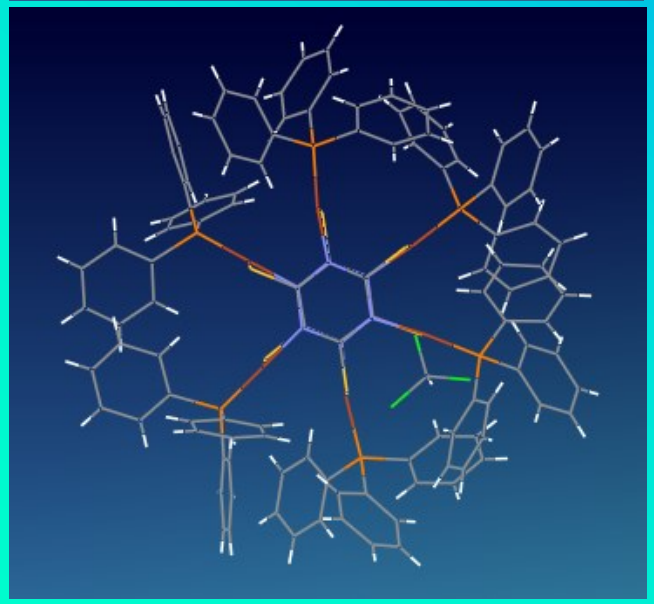
$(SnMe_3)_3(ttc)$

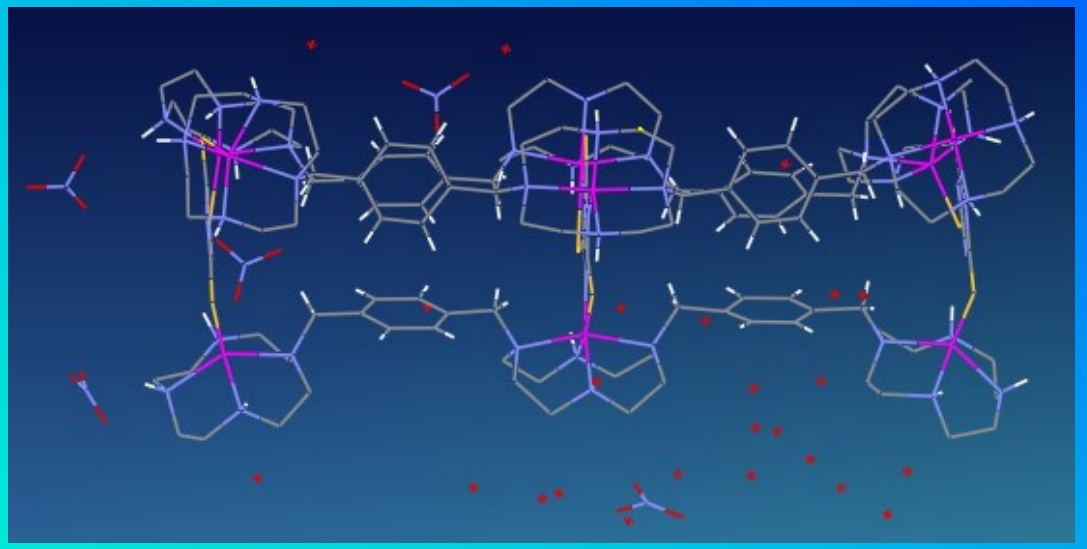
$[(Co(en)_2)_2(ttc)](ClO_4)_3.2H_2O$
(en = ethylenediamine)

$Cu(PPh_3)_2(ttcH_2)$



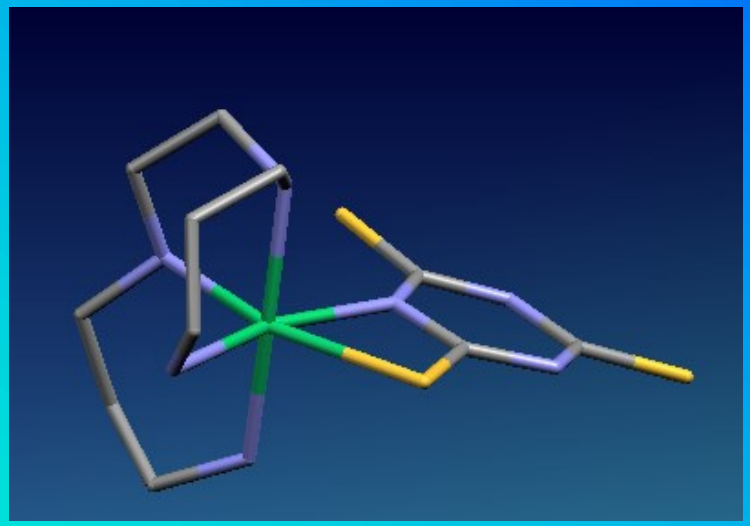




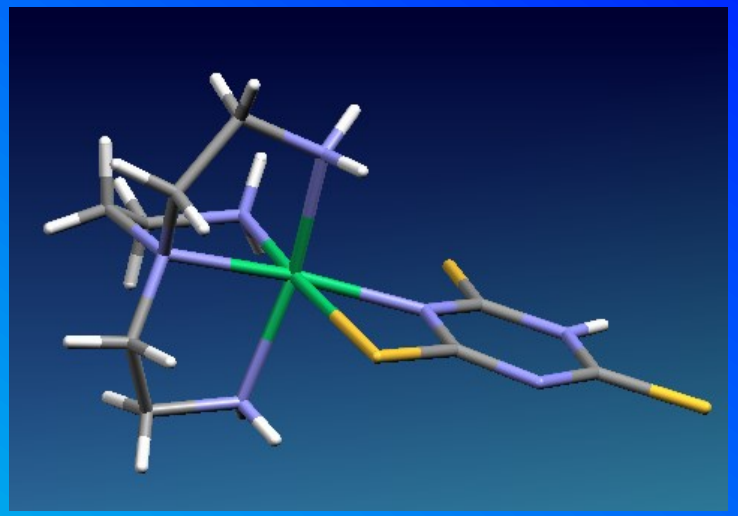


$[\{Cu(PPh_3)\}_6(ttc)_2]$

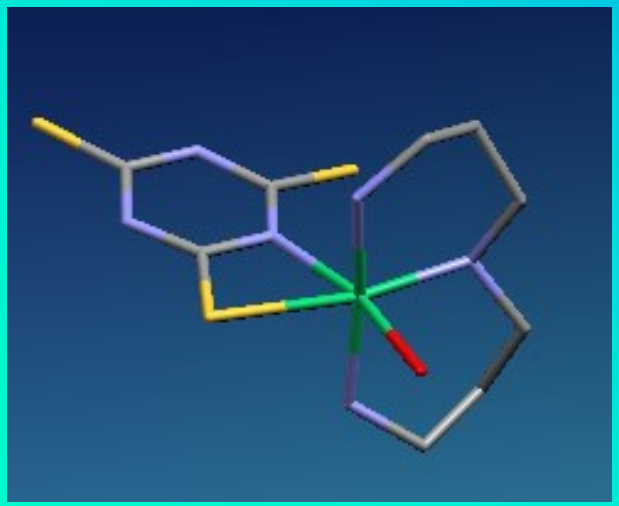
cyclen = 1,4,7,10-tetraazacyclododecane



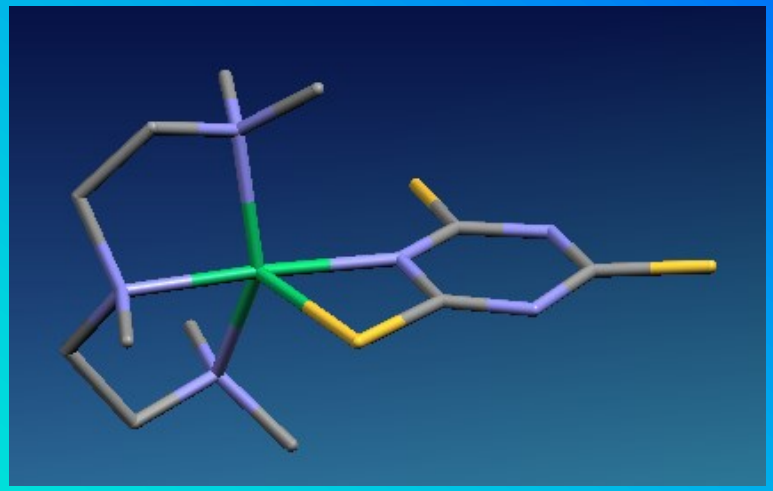
[Ni(bapen)(ttcH)]·2H2O
(bapen = N,N´-bis(3-aminopropyl) ethylenediamine)



[Ni(taa)(ttcH)]
(taa = tris-(2-aminoethyl)amine)



[Ni(dpta)(ttcH)(H2O)]·H2O
(dpta = dipropylenetriamine)



[Ni(pmdien)(ttcH)]
(pmdien = N,N,N´,N´´,N´´- pentamethyldiethylenetriamine)

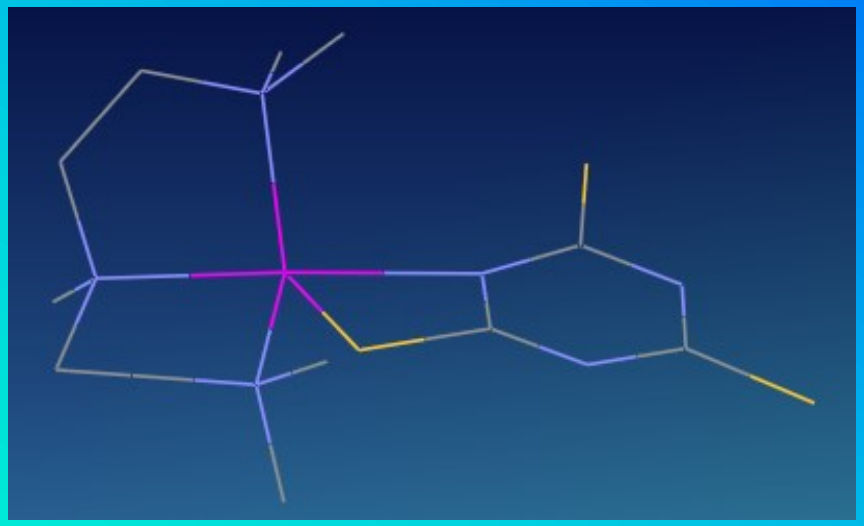
	K-562	MCF7	G361	HOS
(1) [Zn(pmdien)(ttcH)]	>25	>25		
(2) [Zn(taa)(ttcH)]·H_2O	>100	>100		
(3) [Fe(nphen)$_2$(ttcH)]·H_2O	5.1	3.9	3.4	3.0
(4) [Fe(dmbpy)$_3$](ttcH_2)$_2$·4H_2O	9.8	22.7		
(5) [Mn(phen)$_2$(ttcH)]·H_2O	2.7	6.0	3.8	1.6
(6) Mn(bpy)(ttcH)·H_2O	65.6	45.3		
(7) [Ni(taa)(ttcH)]·H_2O	>25	>25		
(8) [Ni(phen)$_3$](ttcH)·5H_2O	>25	>25		
ttcNa_3·9H_2O	>100	>100	>100	>100
oxaliplatin	8.8	18.2	7.1	6.8
cisplatin	4.7	10.9	4.7	3.0

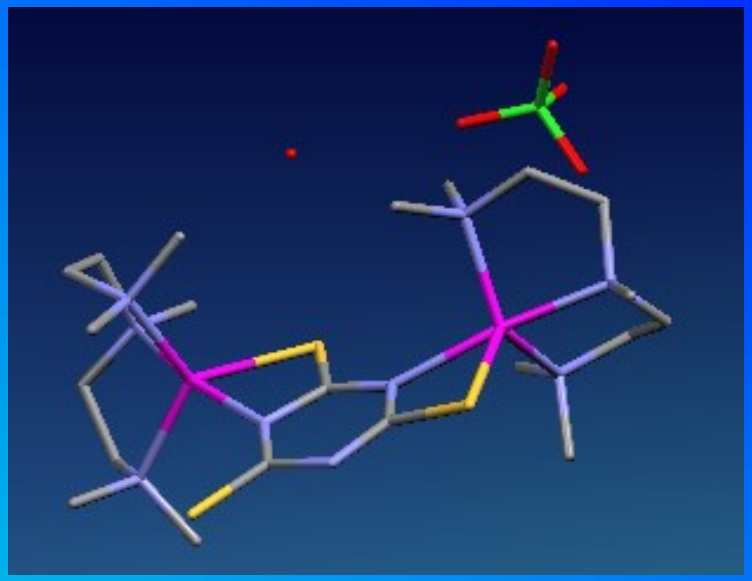
Cytotoxicity of complexes was studied on tumor lines:

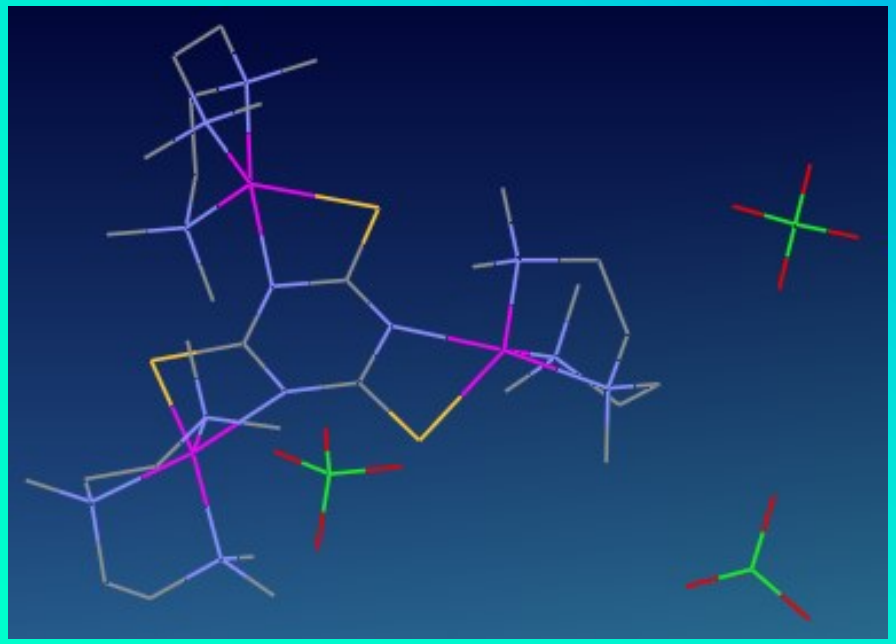
K-562-human chronic myelogenous leukaemia, MCF7-human breast adenocarcinoma, G361-Human malignant melanoma, HOS-human osteogenic sarcoma.

Values of IC50 (μM) are listed in table.

Zinc complexes with pentamethyldiethylenetriamine





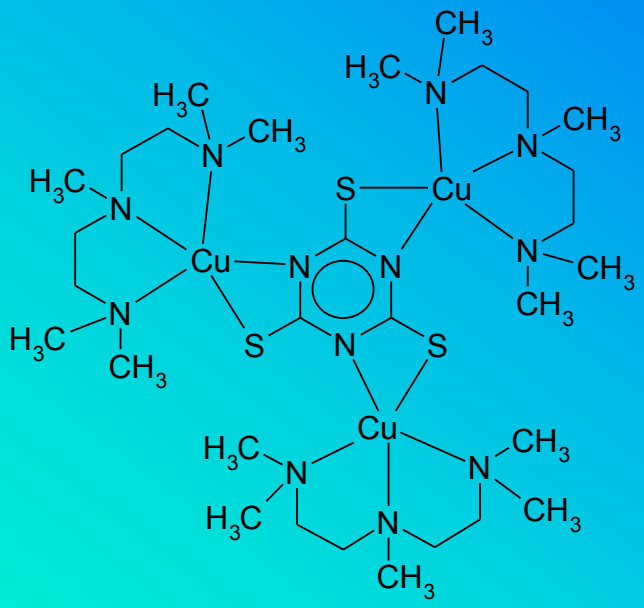


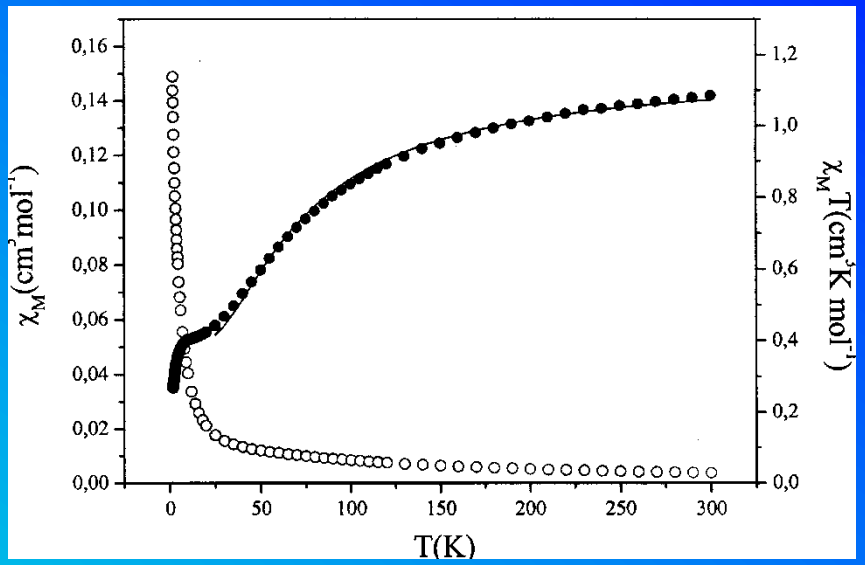
$[Zn(pmdien)(ttcH)]$

$[Zn_2(pmdien)_2(ttc)](ClO_4).H_2O$

$[Zn_3(pmdien)_3(ttc)](ClO_4)_3$

$[Cu_3(pmdien)_3(ttc)](ClO_4)_3$





Temperature dependence χ_M (◦) a $\chi_M T$ (•)

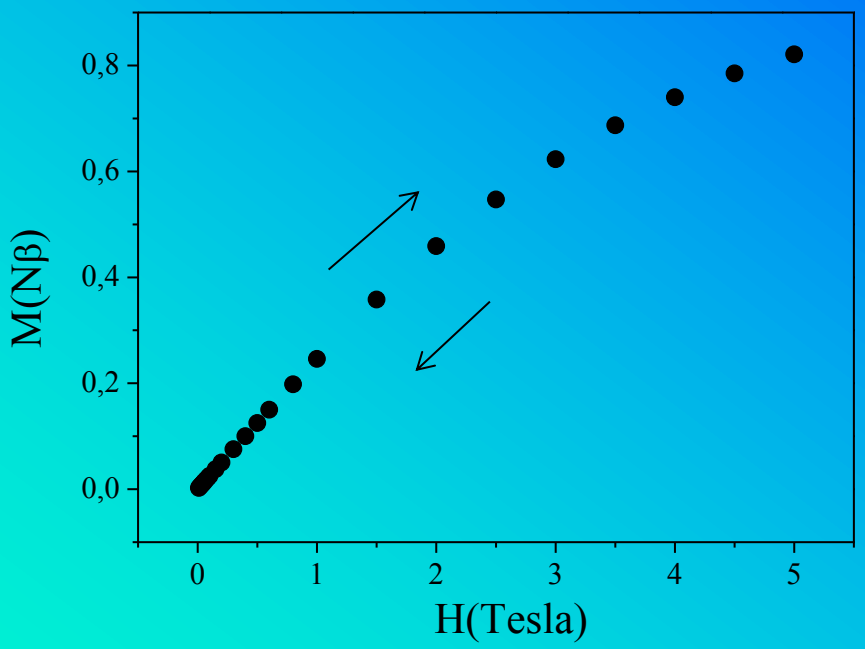
$\chi_M T \approx 0.41 \pm 0.01$ $cm^3mol^{-1}K$

μ_{eff} 1.81 B.M., J = -23 cm^{-1}, g = 2.08

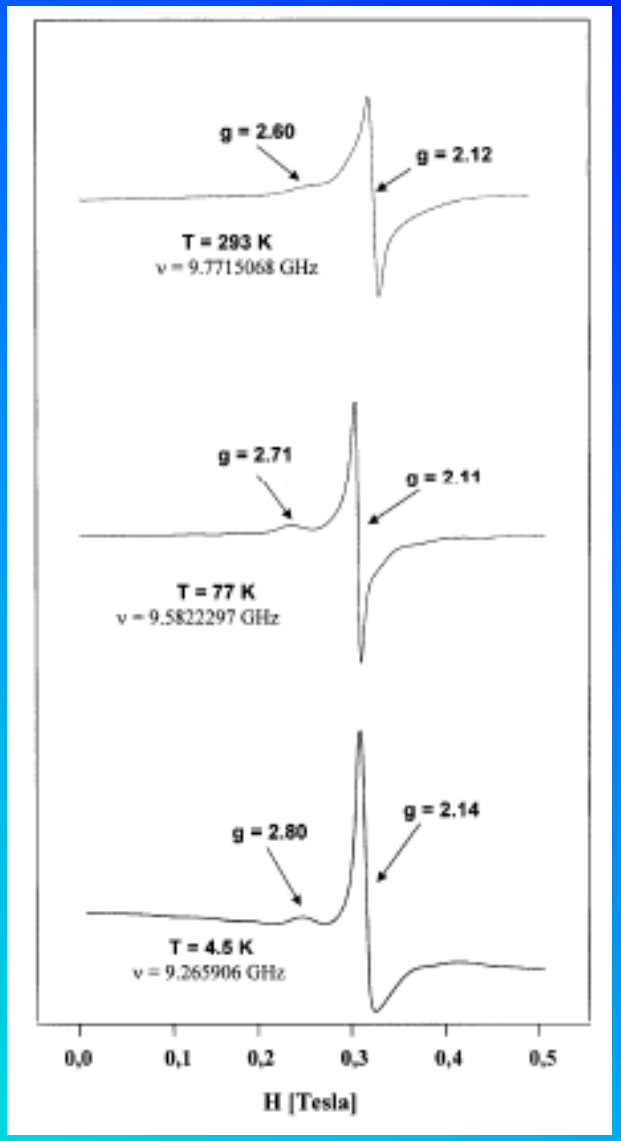
ESI$^+$ MS (m/z): 1182, 1083, 984,
885 $[Cu_3(pmdien)_3(ttc)H]^+$,
711 $[Cu_3(pmdien)_3H]^+$,
648 $[Cu_2(pmdien)_3H]^+$,
237 $[Cu(pmdien)H]^+$,
178 $[ttcH]^+$, 175 $[pmdienH]^+$

Curie –Weiss 200 – 300 K
C = 1.26 $cm^3mol^{-1}K$
Θ = -4.8 K
$\chi_M T$ = 1.08 $cm^3mol^{-1}K$ (300 K)
0.268 $cm^3mol^{-1}K$ (1.8 K)
μ_{eff} = 2.95 B.M. (300 K)
1.47 B.M. (1.8 K)

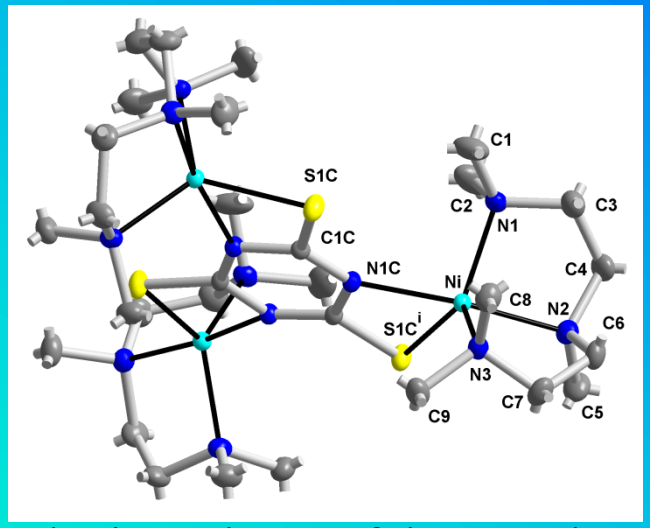
$[Cu_3(pmdien)_3(ttc)](ClO_4)_3$



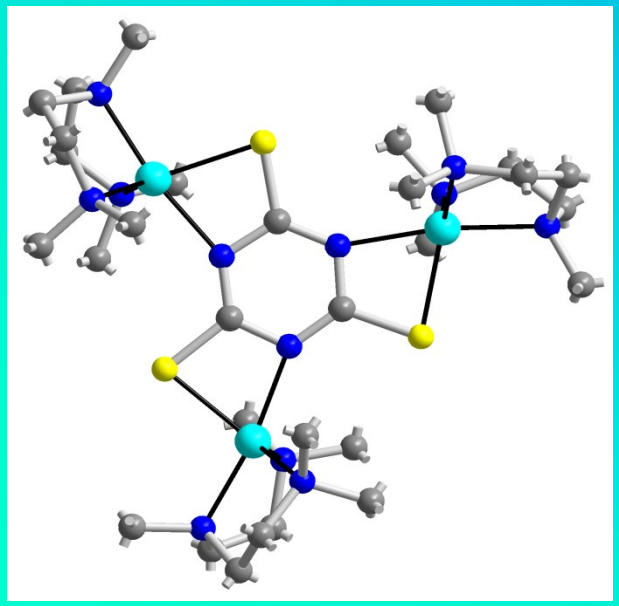
The plot of the magnetization per trimer molecule versus applied field at T = 2K.



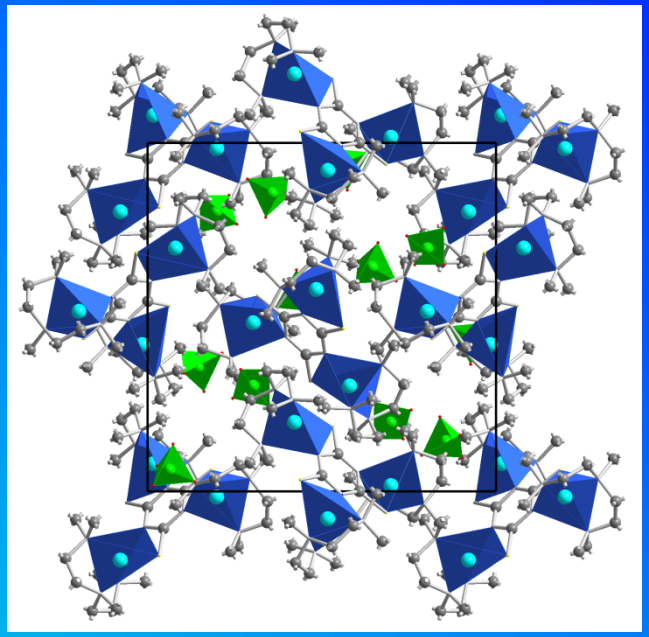
X – ray study of $[Ni_3(pmdien)_3(ttc)](ClO_4)_3$



Numbering scheme of the complex



Projection along crystallographic three fold axis

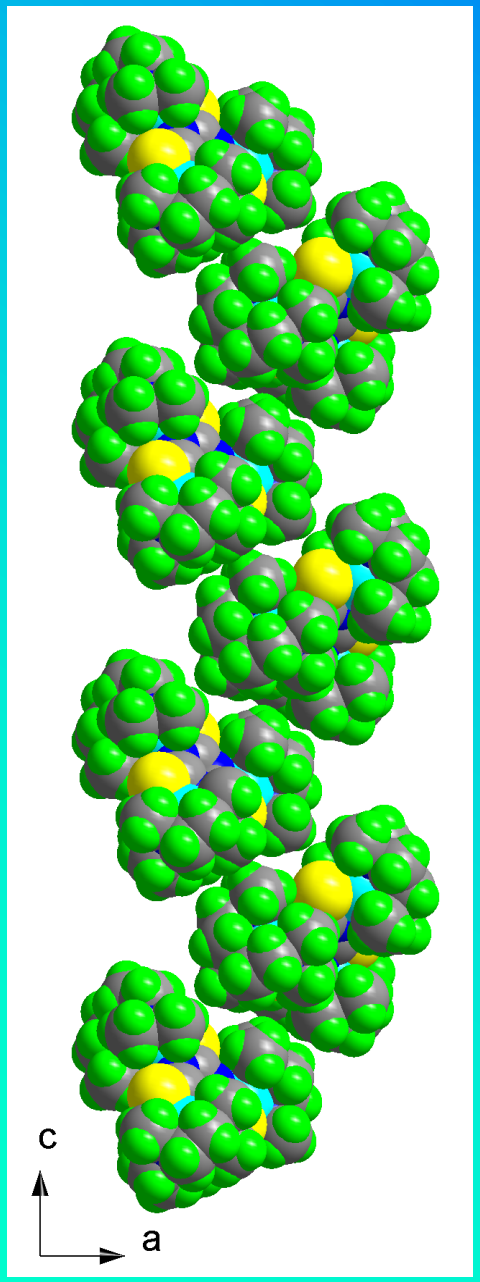


Unit cell in a view along a axis.

Ni polyhedra in blue.

Perchlorate tetrahedra in green.

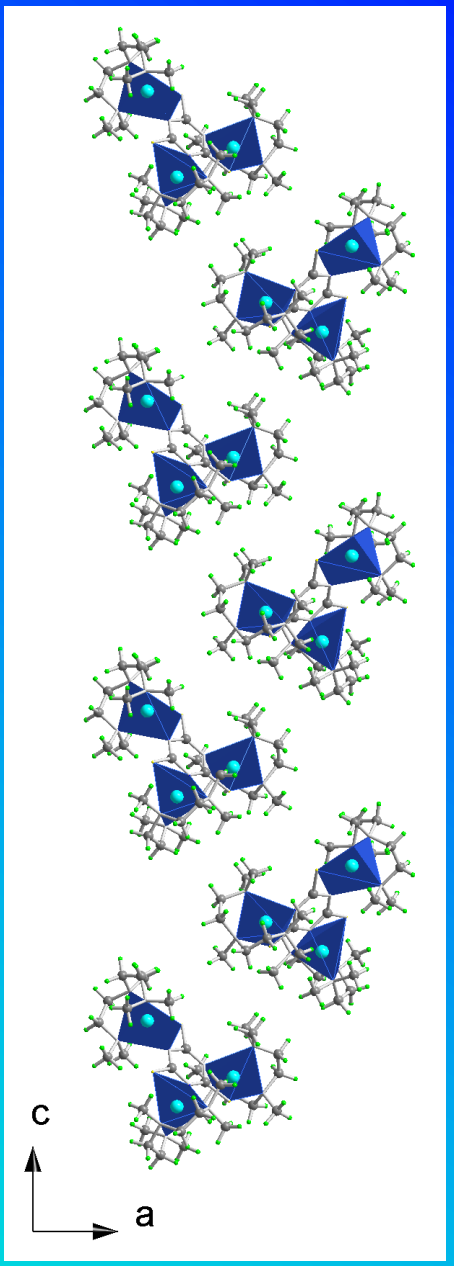
$[Ni_3(pmdien)_3(ttc)](ClO_4)_3$



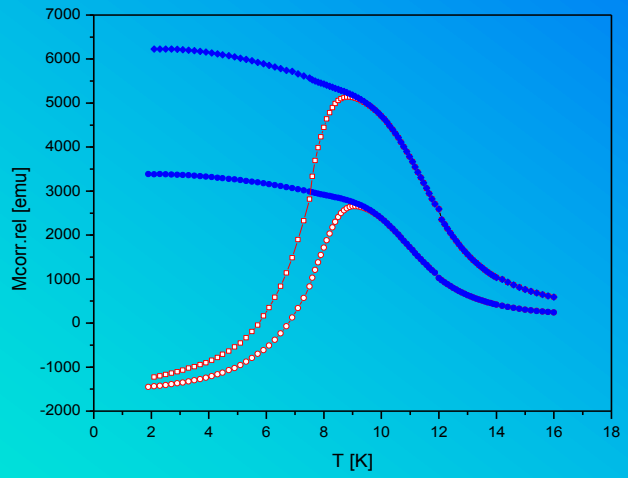
Right-handed helical arrangements of nickel complexes.

Cytotoxic activity
G-361 (IC50 = 31.6 μM)
HOS (IC50 = 15.5 μM),
K-562 (IC50 = 45.9 μM)
MCF7 (IC50 = 25.1 μM).
Cisplatin (2.9, 3.0, 4.7 and 10.9 μM)
Oxaliplatin (7.1, 6.8, 8.8 and 18.2 μM)

ESI^+ MS (m/z): 1069, 969,
869 $[Ni_3(pmdien)_3(ttc)H]^+$,
699 $[Ni_3(pmdien)_3H]^+$,
636 $[Ni_2(pmdien)_3H]^+$,
232 $[Ni(pmdien)H]^+$,
178 $[ttcH]^+$,
174 $[pmdienH]^+$

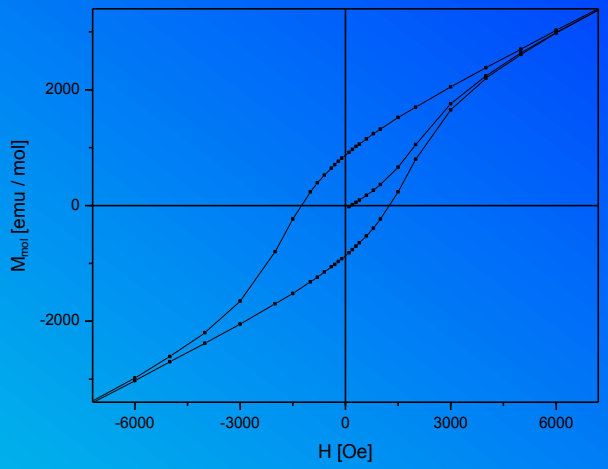


Magnetization measurements of $[Ni_3(pmdien)_3(ttc)](ClO_4)_3$

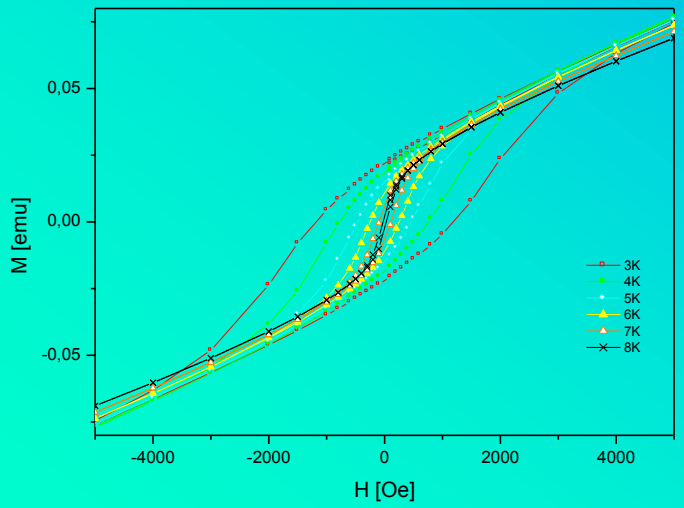


Temperature dependence of magnetization in 16 – 2 K range and a field of 50 and 25 Oe, respectively:

■,● – FCM (field cooled magnetization), □,○ – ZFCM



Hysteresis loop including the virgin curve for **1** at 2 K.



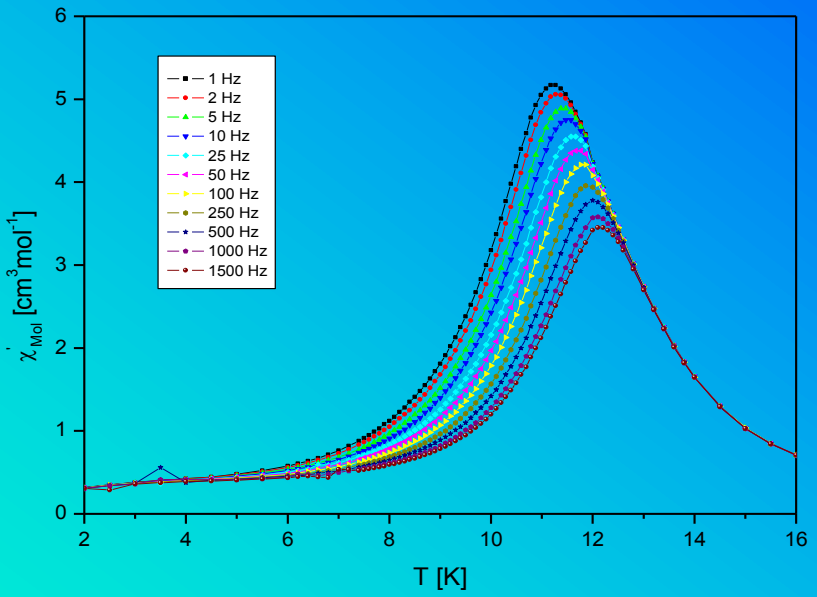
Hysteresis loops at variable temperature.

Ferromagnetic transition

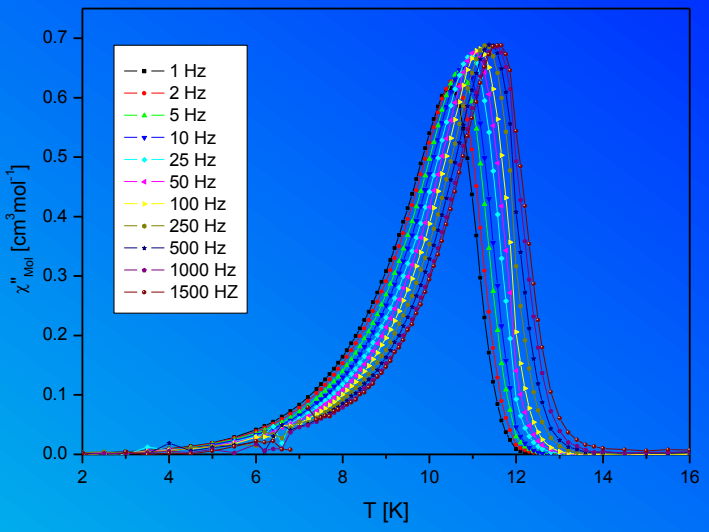
increasing M when T decreases below

$T_c = 10$ K.

AC magnetic susceptibility data of $[Ni_3(pmdien)_3(ttc)](ClO_4)_3$



In-phase molar magnetic susceptibility



Out-of-phase molar magnetic susceptibility

Conclusion

The AC data shows a behaviour that is not compatible with a SMM, while it may be appropriate for a spin glass system.
The magnetic data reveal a ferromagnetic exchange coupling that is further tuned by asymmetric and/or antisymmetric exchange. The occurence of a magnetic phase transition was confirmed by FCM and ZFCM measurements. The magnetization measurements show on ferromagnetic coupling.

Molecular structure of $[Mn_2(phen)_4(\mu\text{-ttc})](ClO_4)$

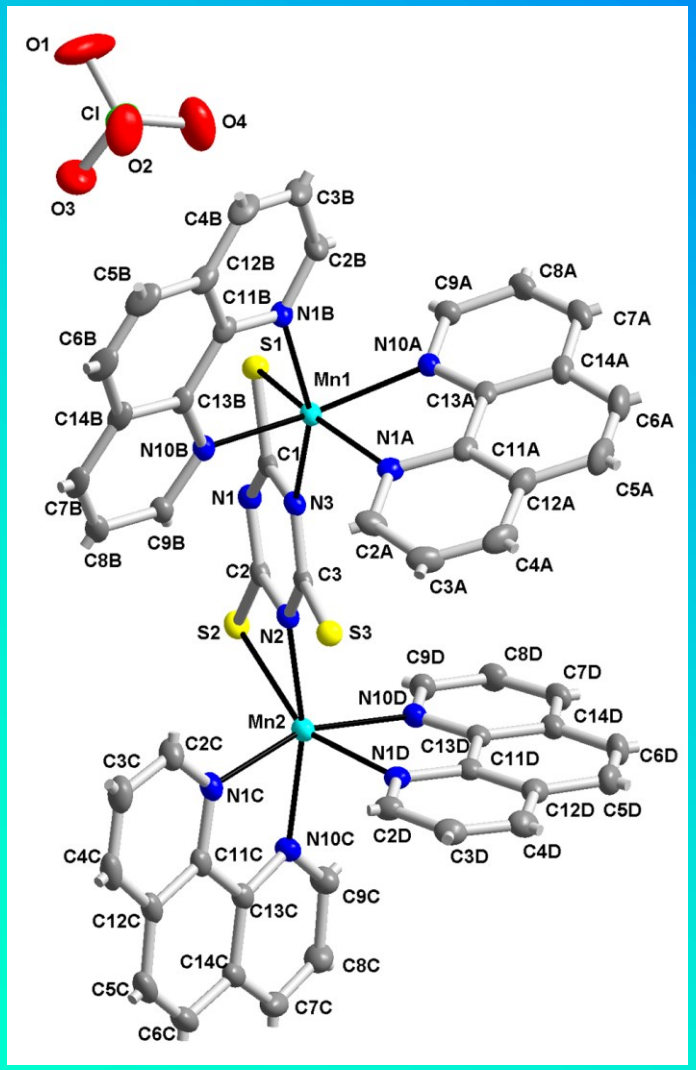
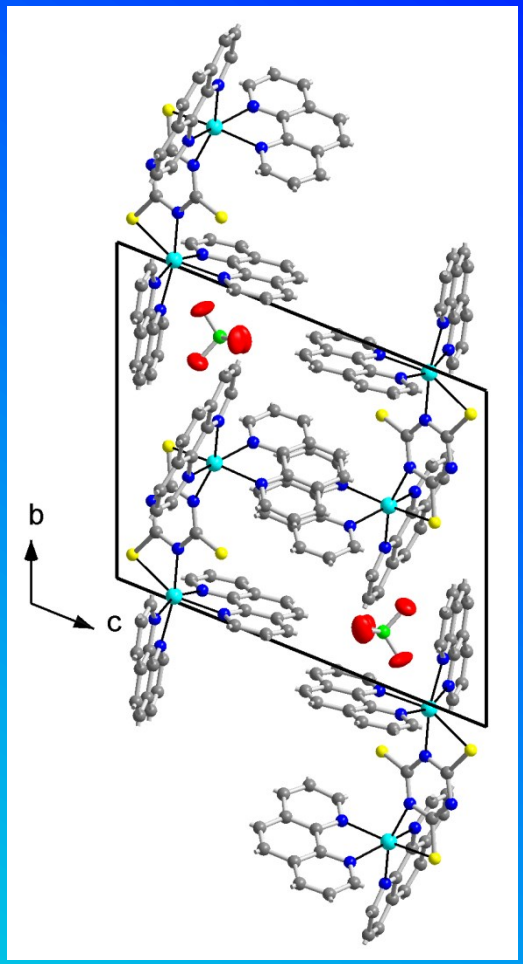


Table. Bond lengths [Å]

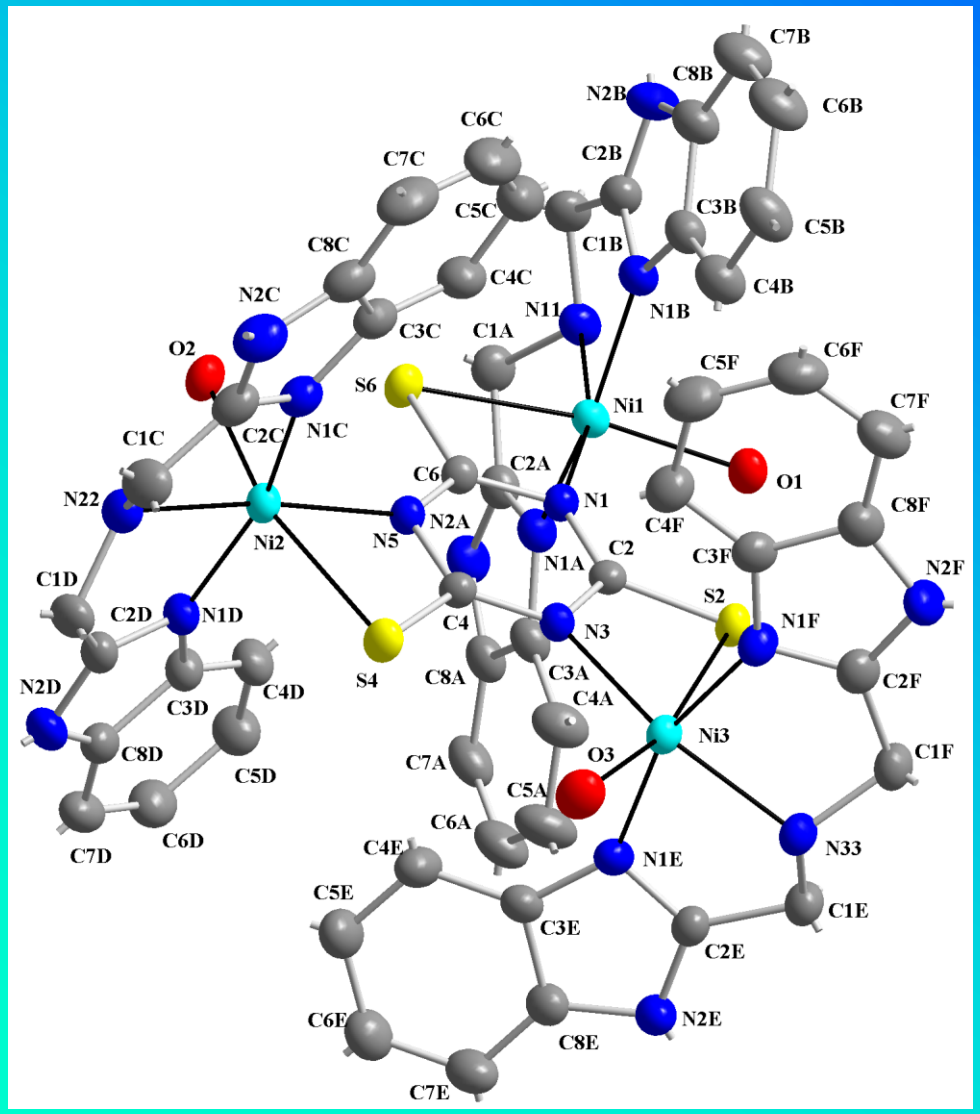
Mn(1)-N(3)	2.180(2)
Mn(1)-N(10B)	2.255(2)
Mn(1)-N(10A)	2.257(3)
Mn(1)-N(1B)	2.294(2)
Mn(1)-N(1A)	2.308(3)
Mn(1)-S(1)	2.6118(9)
Mn(2)-N(2)	2.220(2)
Mn(2)-N(1C)	2.229(3)
Mn(2)-N(10D)	2.254(3)
Mn(2)-N(10C)	2.290(3)
Mn(2)-N(1D)	2.295(3)
Mn(2)-S(2)	2.6143(10)
S(1)-C(1)	1.729(3)
S(2)-C(2)	1.732(3)
S(3)-C(3)	1.695(3)



Trinuclear complexes $[Mn_3(nphen)_6(\mu\text{-ttc})](ClO_4)_3$, $[Mn_3(baphen)_6(\mu\text{-ttc})](ClO_4)_3$

Molecular structure of $[Ni_3(abb)_3(H_2O)_3(\mu\text{-ttc})](ClO_4)_3 \cdot 3H_2O \cdot EtOH$

abb = 2,2′-azadimethylenebis(benzimidazole)



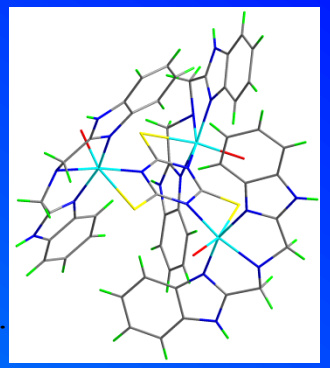
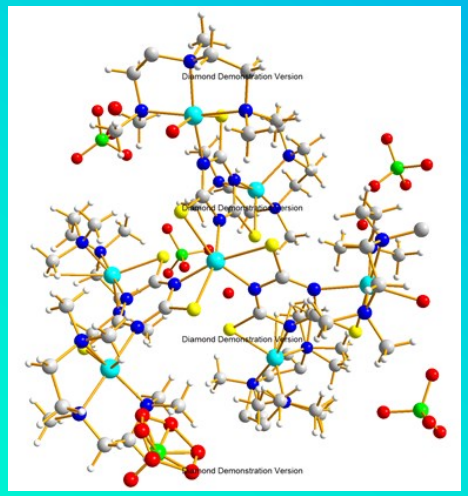
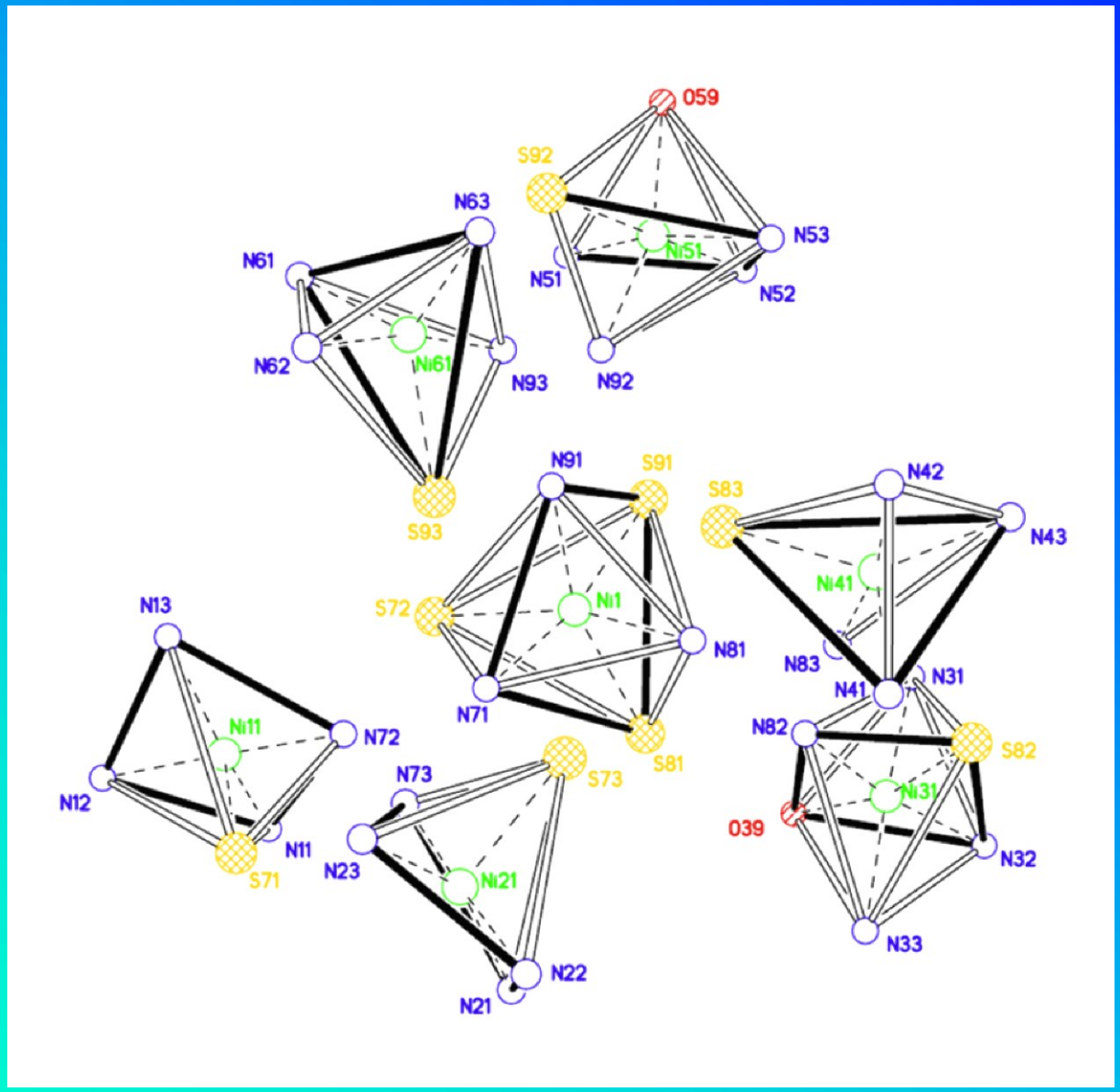


Table. Bond lengths [Å].

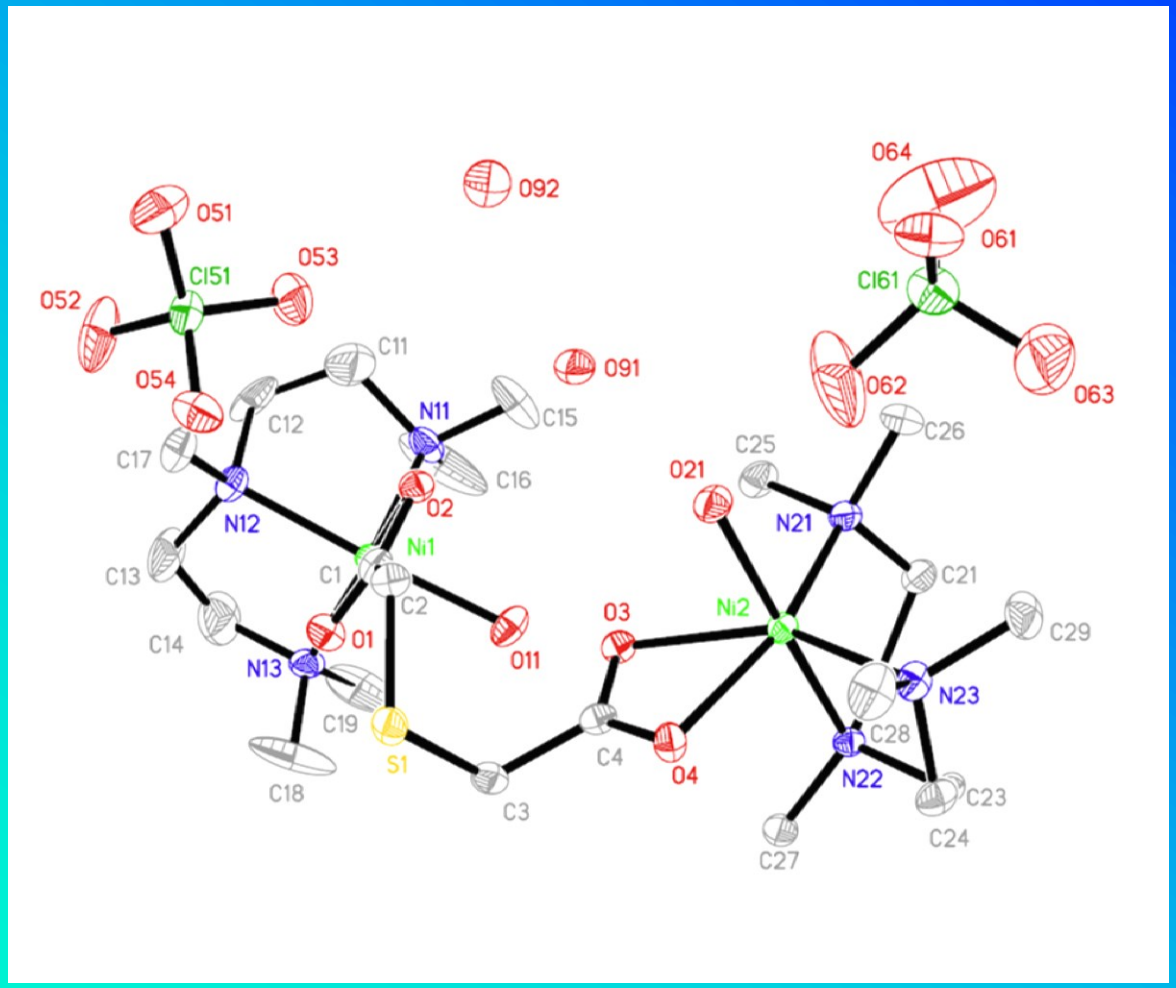
Ni1-N1B	2.041(3)
Ni1-N1	2.047(3)
Ni1-N1A	2.057(3)
Ni1-O1	2.102(3)
Ni1-N11	2.121(3)
Ni1-S6	2.5566(11)
Ni2-N5	2.030(3)
Ni2-N1C	2.056(4)
Ni2-N1D	2.062(4)
Ni2-N22	2.101(4)
Ni2-O2	2.109(3)
Ni2-S4	2.5549(12)
Ni3-N1F	2.044(3)
Ni3-N3	2.043(3)
Ni3-N1E	2.057(3)
Ni3-O3	2.100(3)
Ni3-N33	2.107(3)
Ni3-S2	2.5622(11)

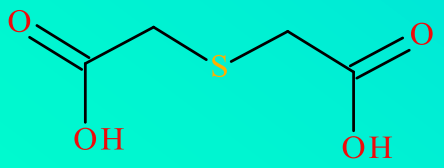
Molecular structure of $[Ni_7(pmdien)_6(H_2O)_2(\mu\text{-}ttc)_3](ClO_4)_5 \cdot 3H_2O$





Molecular structure of $[Ni_2(pmdien)_2(H_2O)(\mu\text{-tdga})](ClO_4)_2 \cdot 2H_2O$





Thiodiglycolic acid = thiodiacetic acid

Acknowledgements

Jerzy Mrozinski

Vratislav Langer

Alina Bieńko

Božena Kalińska

Andrzej Pochaba

Roman Boča

Karel Doležal

Financial support from CYTORES GA CR P301/10/0356, NANIMEL GA CR 102/08/1546, NANOLABSYS CZ.1.07/2.3/.00/20.148 and CEITEC CZ.1.05/1.1.00/02.0068 is highly acknowledged.