SUPLEMENTARY MATERIAL

Structural, antioxidant, antiproliferative and *in–silico* study of pyridine-based hydrazonyl–selenazoles and their sulphur isosteres

Jovana B. Araškov[a], Milan Nikolić[a], Stevan Armaković[b], Sanja Armaković[b], Marko Rodić[b], Aleksandar Višnjevac[c], José M. Padrón[d], Tamara R. Todorović[a,*], Nenad R. Filipović[e,*]

[a]University of Belgrade - Faculty of Chemistry, Studentski trg 12-16, 11000 Belgrade, Serbia

[b]University of Novi Sad, Faculty of Sciences, Trg Dositeja Obradovića 4, 21000, Novi Sad, Serbia

[c] Zavod za fizičku kemiju, Institut Ruđer Bošković, Zagreb, Croatia

[d]Instituto Universitario de Bio-Orgánica "Antonio González", Universidad de La Laguna, 38206 La Laguna, Spain,

[e] University of Belgrade - Faculty of Agriculture, Nemanjina 6, 11000 Belgrade, Serbia

*Corresponding authors:

Tamara R. Todorović, PhD, Associate Professor, University of Belgrade – Faculty of Chemistry, Studentski Trg 12, 11000 Belgrade, Serbia
E-mail: tamarat@chem.bg.ac.rs

Nenad R. Filipović, PhD, Associate Professor, University of Belgrade – Faculty of Agriculture, Nemanjina 6, 11000 Belgrade, Serbia
E-mail: nenadf@agrif.bg.ac.rs

HPLC analysis

The purity of tested compounds was evaluated using a HPLC method. The HPLC analysis was performed on Agilent 1200 system (Agilent Technologies, Palo Alto, CA, USA), equipped with binary pump, manual injector (20 µl sample loop) and DAD detector. The column chosen was Zorbax Extend C18 (150 mm × 4.6 mm, 5 µm particle size). The mobile phase consisted of acetonitrile and water (50:50, V/V). The column temperature was adjusted to 30ºC and the flow rate was 1 ml/min. The UV detection was performed at 220, 240, 254, 260 and 300 nm. Sample chromatograms are presented below.

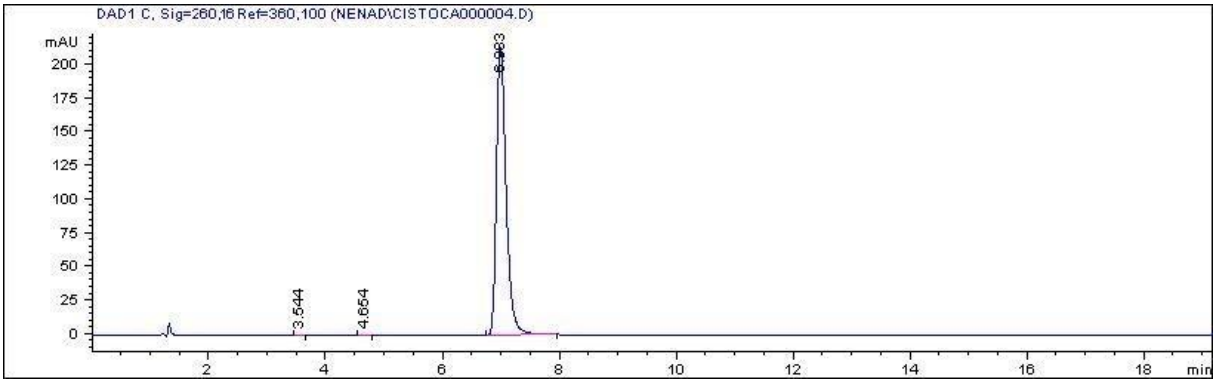

Figure SM1. Chromatogram of HLS[1]

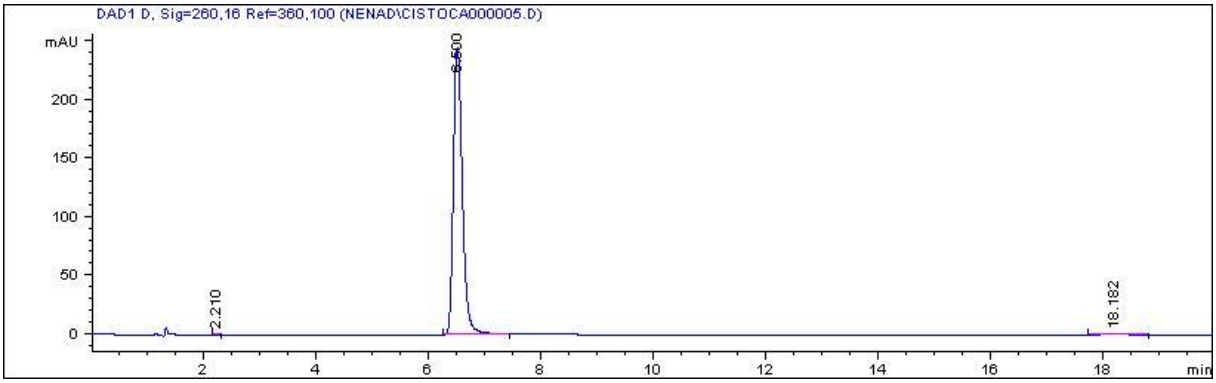

Figure SM2. Chromatogram of HLS[2]

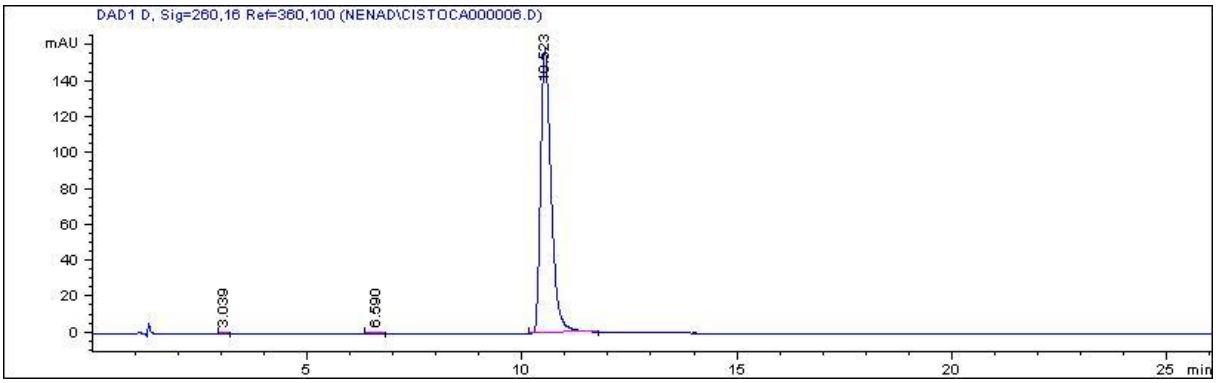

Figure SM3. Chromatogram of HLS[3]

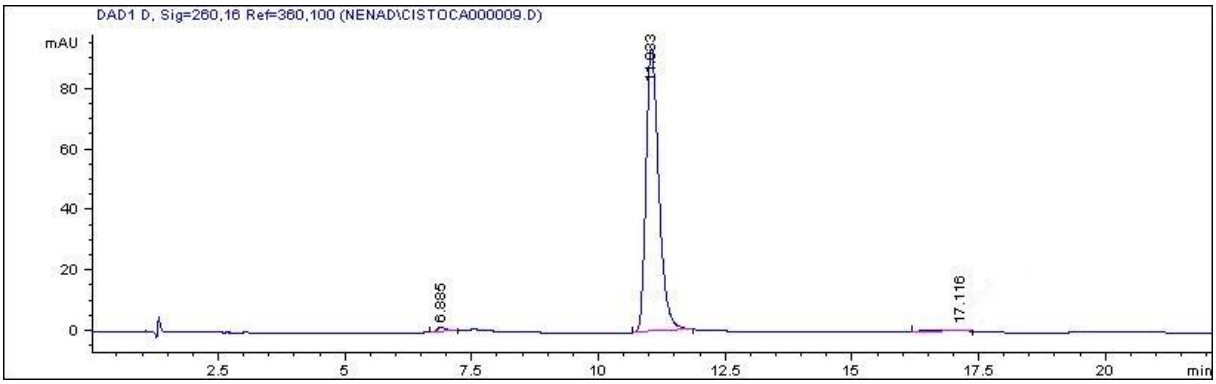

Figure SM4. Chromatogram of HLSe[1]

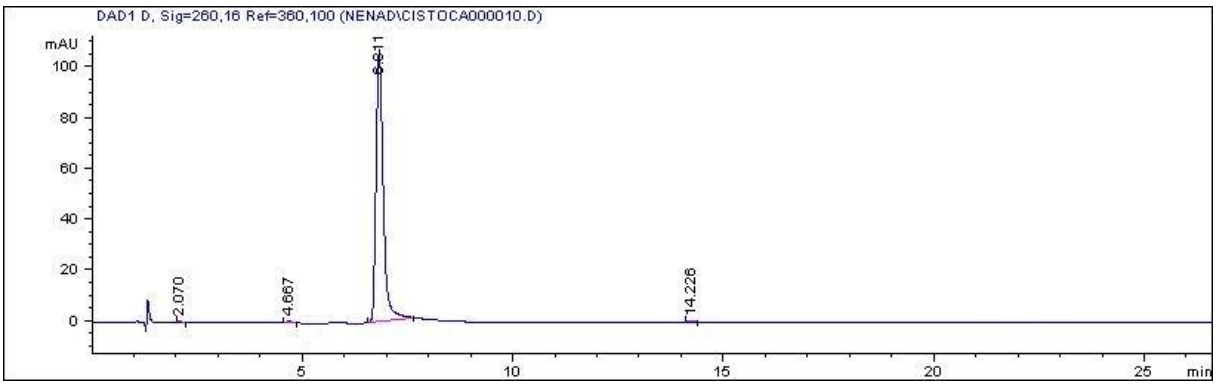

Figure SM5. Chromatogram of HLSe[2]

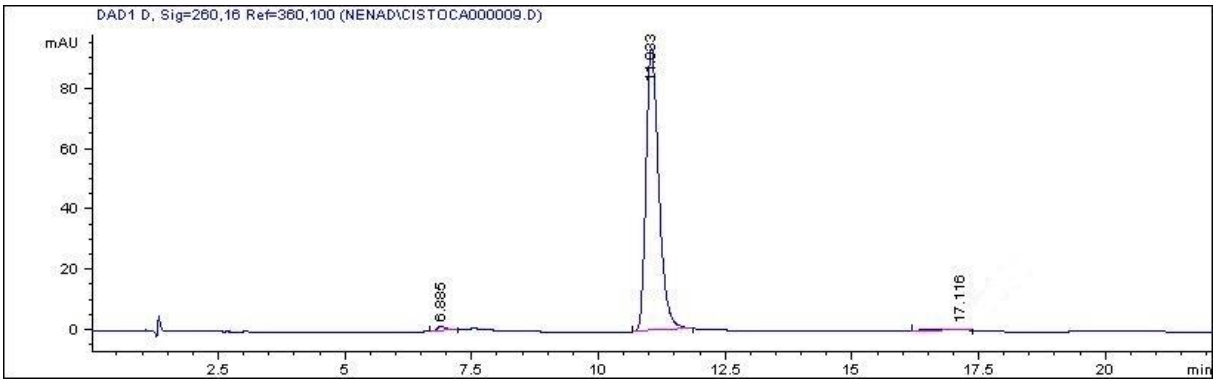

Figure SM6. Chromatogram of $HLSe^3$

Table SM1. Selected bond lengths and angles

	E-HLS^3	HLS^3×HBr	*Z*-HLS^3
Bond lengths [Å]			
N4–C11	1.342(2)	1.348(4)	1.343(6)
C11–C10	1.465(2)	1.446(4)	1.414(6)
C10–N3	1.277(2)	1.281(4)	1.260(6)
N3–N2	1.360(19)	1.343(4)	1.337(6)
N2–C1	1.362(2)	1.360(4)	1.363(6)
C1–S1	1.738(17)	1.734(3)	1.700(4)
S1–C2	1.723(19)	1.721(3)	1.690(5)
C2–C3	1.357(2)	1.354(4)	1.349(6)
C3–N1	1.388(2)	1.384(4)	1.373(5)
N1–C1	1.300(2)	1.290(4)	1.265(6)
C12–C11	1.394(2)	1.386(4)	1.369(7)
C14-C13	1.380(3)	1.389(5)	1.345(8)
C15–C14	1.374(3)	1.364(5)	1.363(7)
Angles **[°]**			
N4–C11–C10	115.54(14)	116.8(3)	119.0(4)
C11–C10–N3	119.78(15)	118.3(3)	131.4(4)
C10–N3–N2	117.63(14)	116.4(3)	117.7(4)
N3–N2–C1	116.98(14)	119.2(3)	118.0(4)
N2–C1–S1	120.15(12)	120.8(2)	119.7(3)
C1–S1–C2	87.88(8)	88.13(14)	87.8(2)
S1–C2–C3	111.26(13)	110.7(2)	111.3(3)
C2–C3–N1	114.82(15)	115.1(3)	113.9(4)
C3–N1–C1	109.99(13)	110.2(3)	109.8(4)
C11–N4–C15	117.51(14)	123.4 (3)	118.0 (4)

Root-mean-square deviation (RMSD) analysis

To confirm the stability of performed MD simulations, we have analyzed the RMSD both numerically and visually. Numerical values of RMSD for molecules studied in this work, calculated with respect to the frame at the middle of MD simulation (frame number 500 out of 1000), have been summarized in Table SM2. Visual inspection of RMSD values has also been performed, through polar plots of RMSD for each molecule (Figure SM7).

Table SM2. RMSD values obtained for studied molecules, with respect to the frame at the half of MD simulation

Molecule in MD simulations	RMSD [Å]
E-HLS[1]	0.847
E-HLS[2]	1.039
E-HLS[3]	0.938
E-HLSe[1]	1.059
E-HLSe[2]	1.187
E-HLSe[3]	0.823

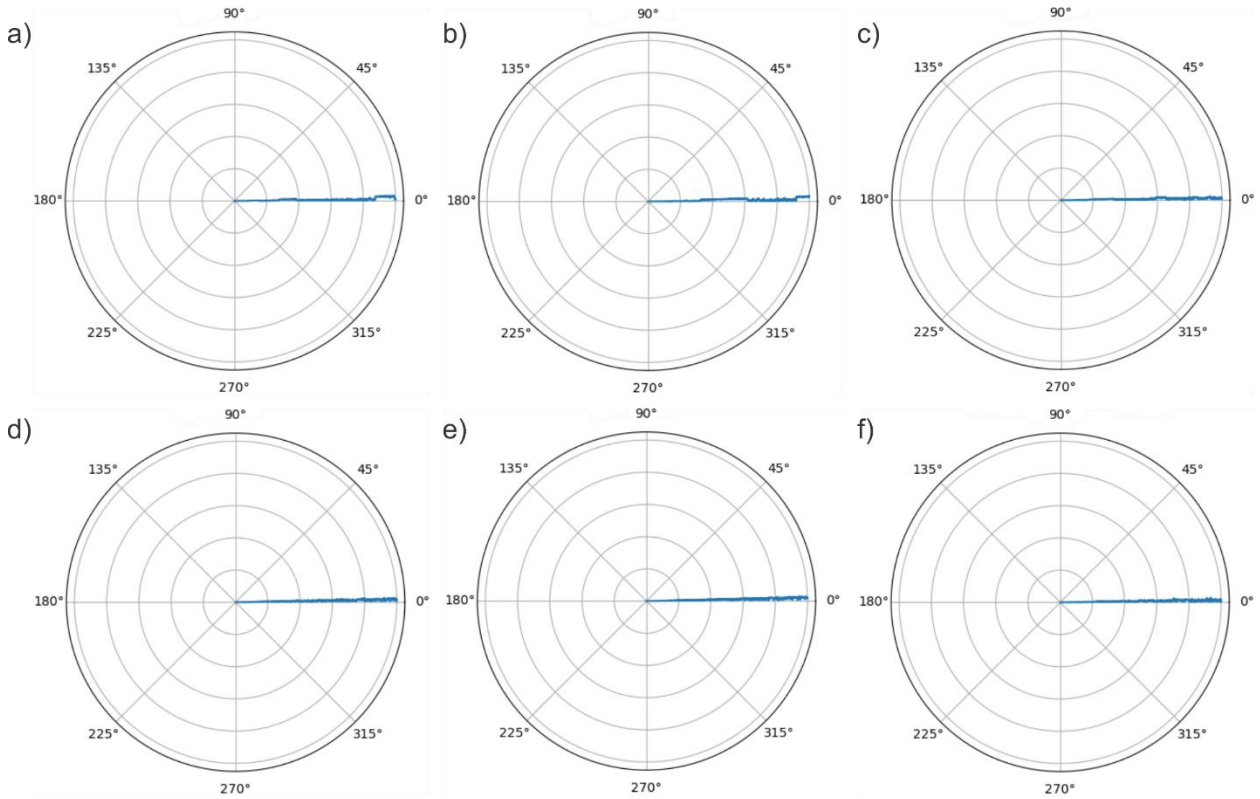

Figure SM7. Polar plots of RMSD values for a) *E*-HLS[1], b) *E*-HLS[2], c) *E*-HLS[3], d) *E*-HLSe[1], e) *E*-HLSe[2] and f) *E*-HLSe[3]