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Release of Reactive Selenium Species from phthalic selenoanhydride in the presence of hydrogen sulfide and glutathione with implications for cancer research

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General procedure for the synthesis of chalcogen anhydrides

The phthalic selenoanhydride (R-Se) and the phthalic thioanhydride (R-S) have been synthetized following a modification of a procedure previously described[1,2]. Briefly, a suspension of grey selenium (7.0 mmol) for R-Se or elemental sulfur for R-S (7.0 mmol) in water-free tetrahydrofuran is reduced by a dropwise addition of lithium aluminium hydride (7 mL of a 1M solution in tetrahydrofuran). After the completion of the reaction (easily monitored thanks to the ceasing of the generation of molecular hydrogen), 1.41 g (6.9 mmol) of phthaloyl chloride solved in 20 mL of dichlorometane is added to the reaction. The mixture is left reacting 1 h at 50ºC with magnetic stirring). Then, the solution is filtered to eliminate the metallic salts generated during the process, and over the filtrate, 10 mL of concentrated sulfuric acid are added dropwise during 5 min. The solid is filtered and washed with chloroform (4×15 mL). The evaporation of the organic layer allowed the isolation of the impure desired product.

Synthesis of R-Se

Elemental grey selenium (1.10 g, 7.0 mmol), 1 M solution of lithium aluminium hydride (7 mL, 7.0 mmol), phthaloyl chloride (1.41 g, 6.9 mmol) and concentrated sulphuric acid (10 mL) were employed. 1-benzo[*c*]selenophene-1,3-dione (R-Se) was obtained as a brown solid that was recrystallized from hexane to isolate a light orange/yellow solid. Yield: 80% (1160 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (dd, 2H, H_3+H_6, J_1 = 5.7 Hz, J_2 = 3.2 Hz,); 7.76 (dd, 2H, H_4+H_5). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 123.8 (C_3+C_6); 135.1 (C_1+C_2), 141.9 (C_4+C_5), 194.2 (COSeCO). LC/MS±: purity: 100.0%, tR = 6.49 min.

Synthesis of R-S

Elemental sulfur (0.45 g, 7.0 mmol), 1 M solution of lithium aluminium hydride (7 mL, 7.0 mmol), phthaloyl chloride (1.41 g, 6.9 mmol) and concentrated sulphuric acid (10 mL) were employed. 1-benzo[*c*]thiophene-1,3-dione (R-S) was obtained as a yellow solid that was recrystallized from hexane to isolate a light yellow solid. Yield: 84% (951 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.97 (dd, 2H, H_3+H_6, J_1 = 5.7 Hz, J_2 = 3.0 Hz,); 7.81 (dd, 2H, H_4+H_5). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 123.9 (C_3+C_6); 135.2 (C_1+C_2), 138.9 (C_4+C_5), 190.0 (COSCO). LC/MS±: purity: 100.0%, tR = 5.84 min.

NMR and LC-MS data

In next pages are provided as images the ^{1}H NMR, the ^{13}C NMR and LC-MS spectra of R-Se and R-S. The spectroscopic results are in accordance with previously published data. The molecular ion is no visible, but it is also in accordance with previous results, its abundance is low in this structures.

Notes and references

1 E. Domínguez-Álvarez, D. Plano, M. Font, A. Calvo, C. Prior, C. Jacob, J.A. Palop and C. Sanmartín, *Eur J Med Chem*, 2014, **73**, 153-166.
2 Domínguez-Álvarez E. PhD Dissertation. University of Navarra (Spain), 2012.

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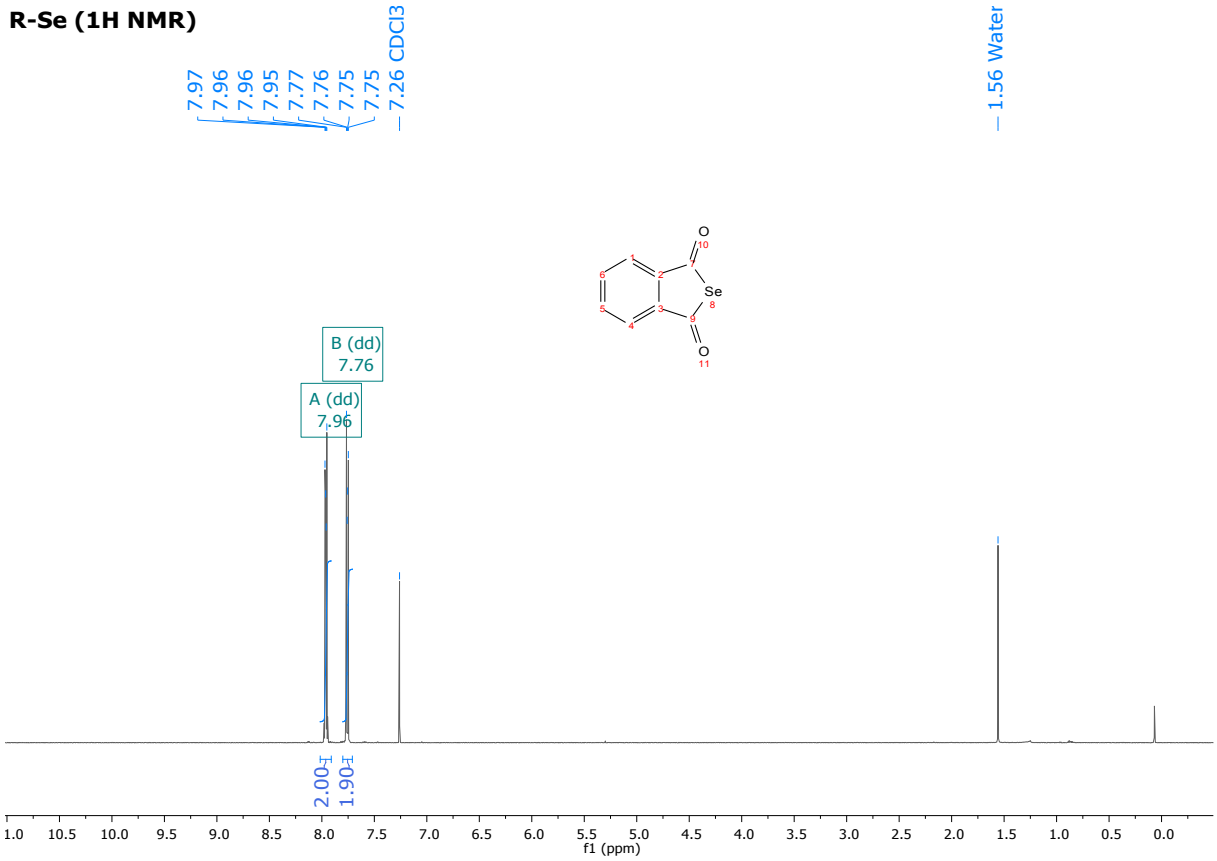
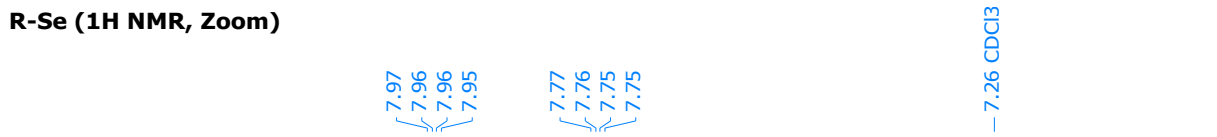
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

^{1}H NMR of R-Se and R-S

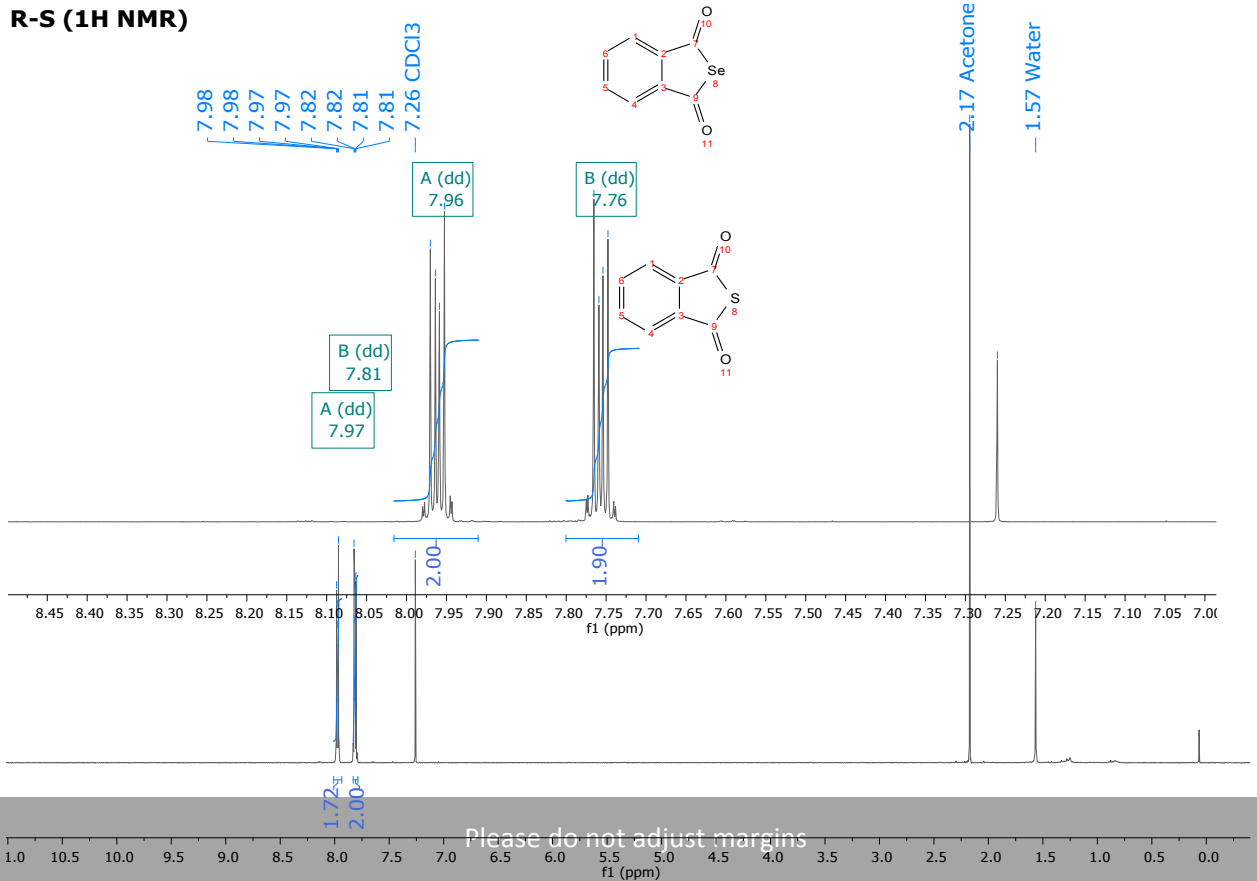
R-Se (1H NMR)



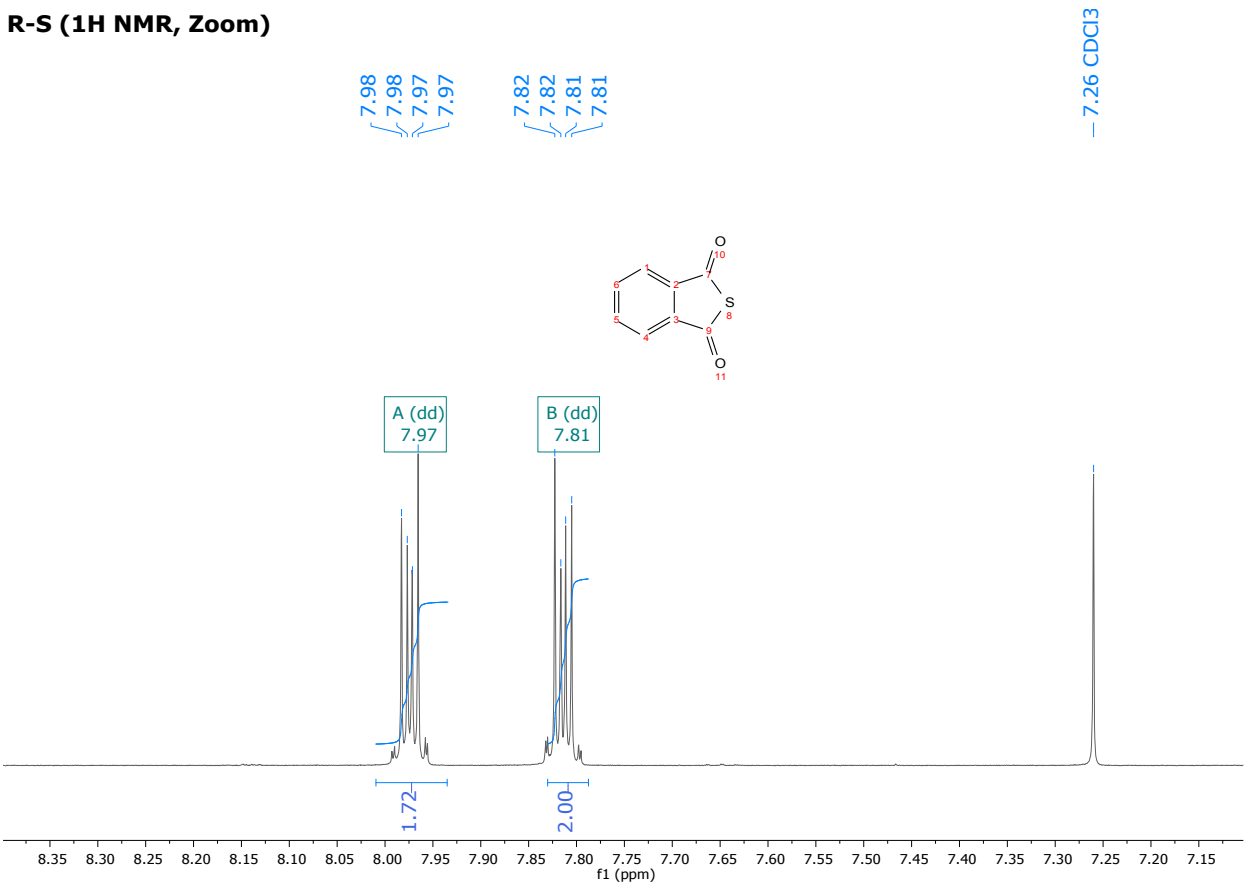
R-Se (1H NMR, Zoom)



R-S (1H NMR)

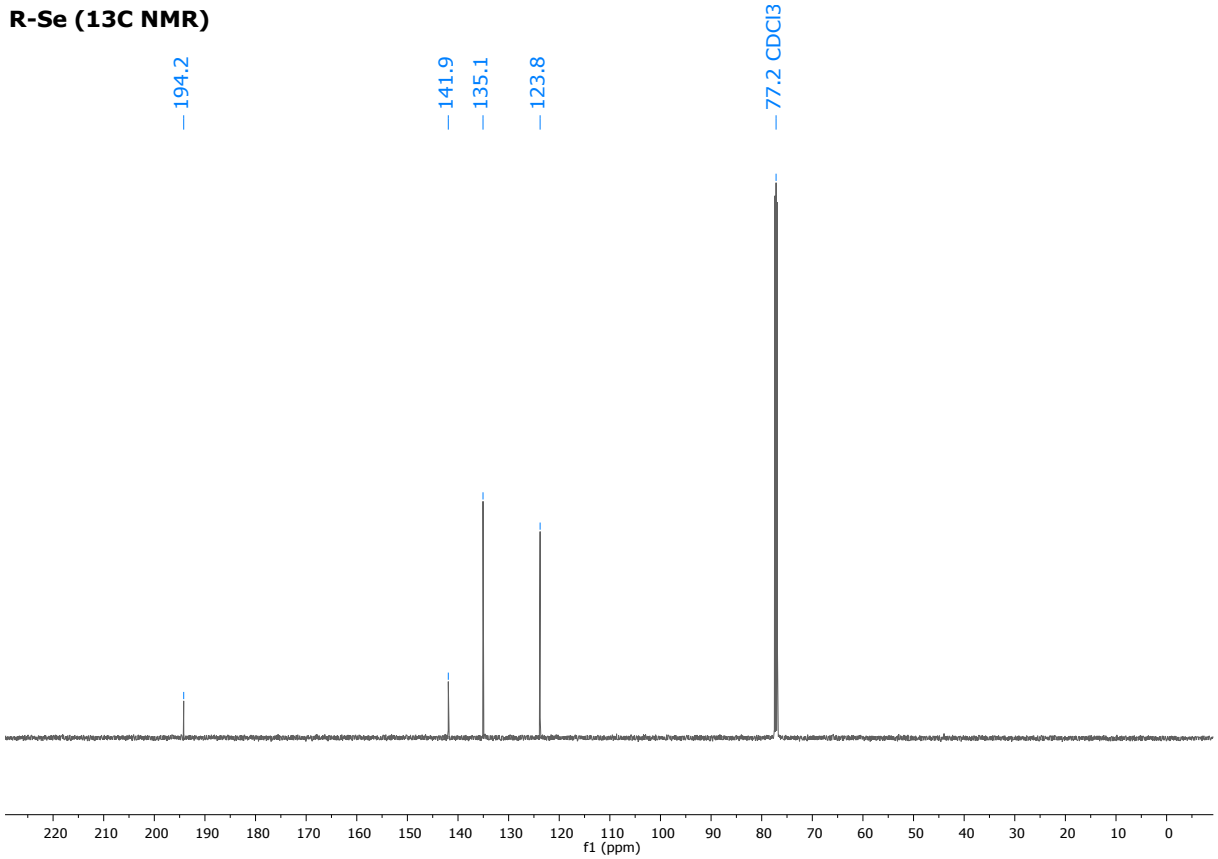


R-S (1H NMR, Zoom)

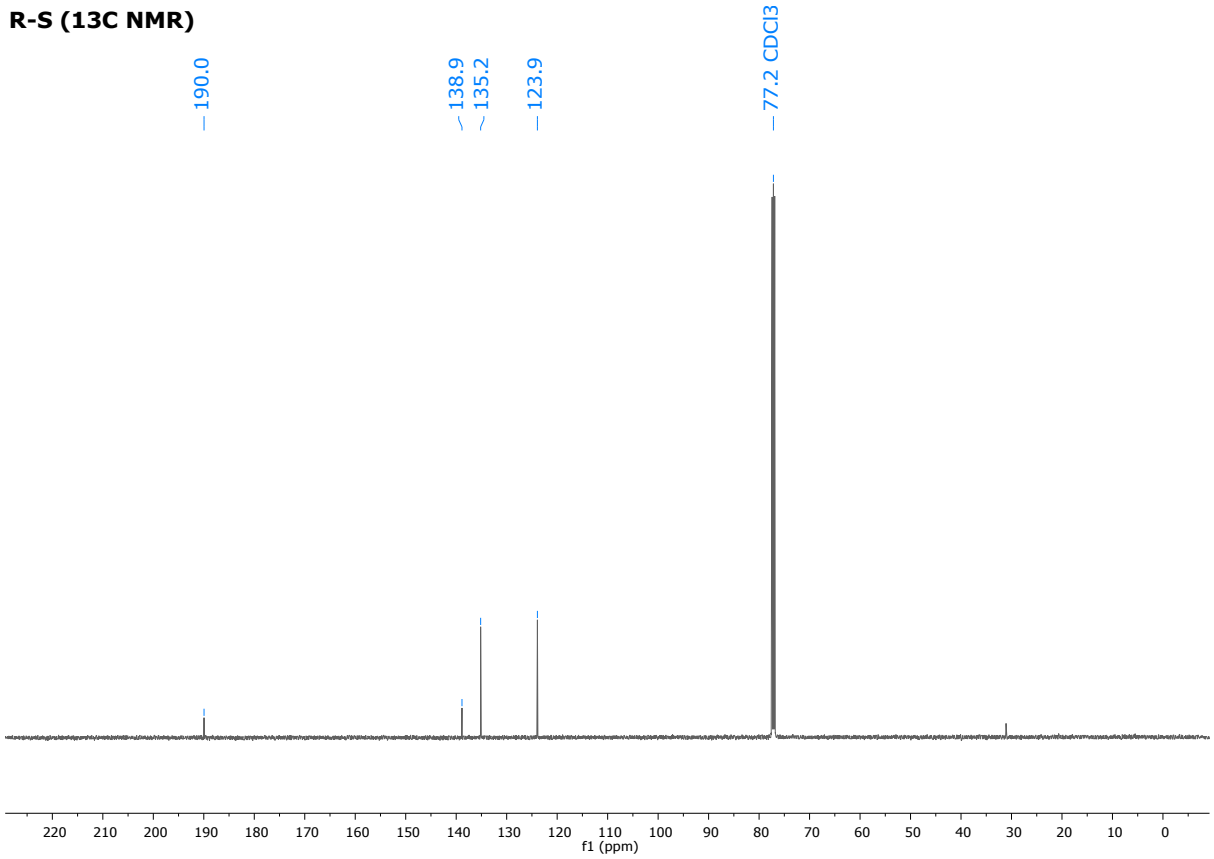


^{13}C NMR of R-Se and R-S

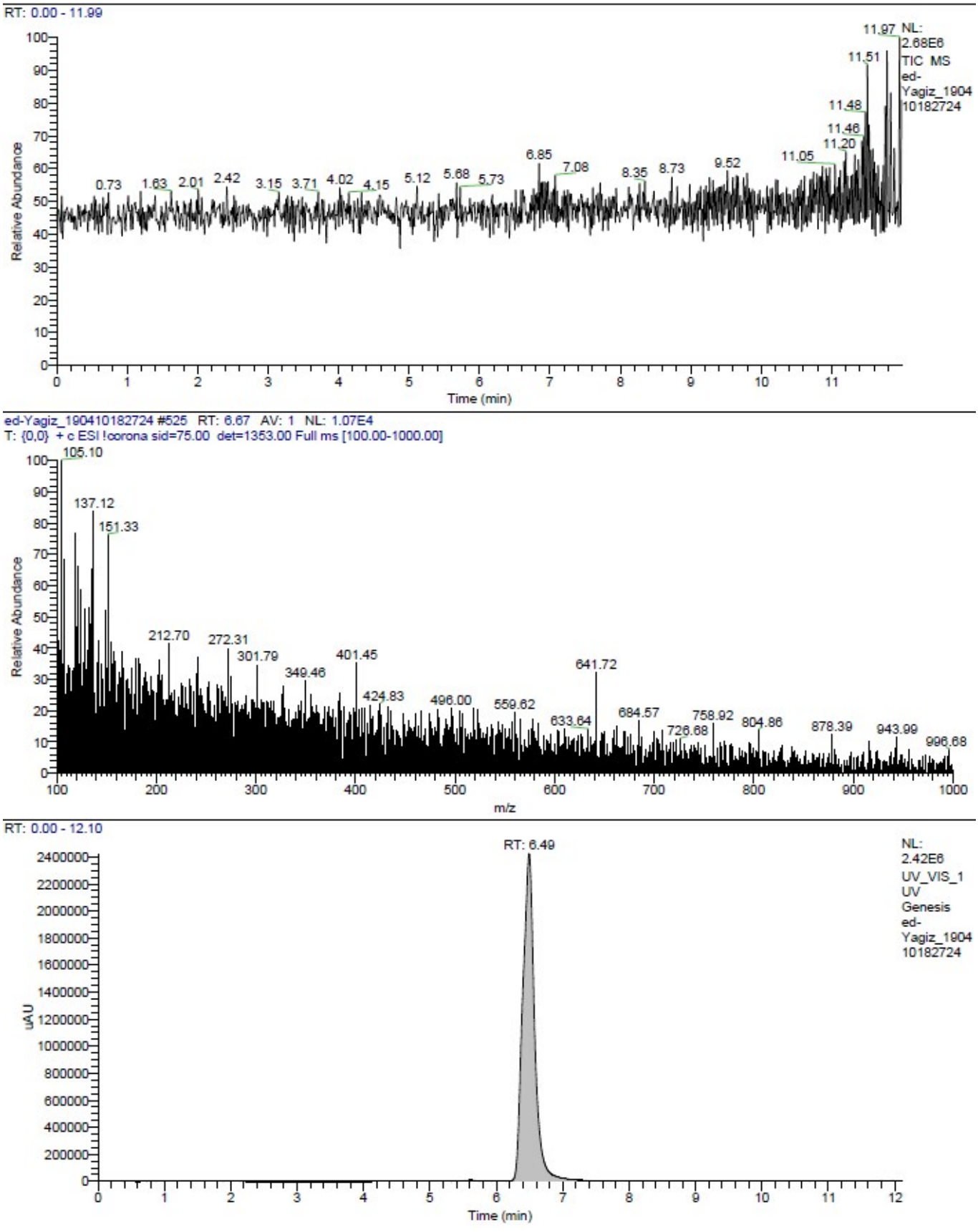
R-Se (13C NMR)



R-S (13C NMR)



LC-MS of R-Se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Relative Abundance
Time (min)
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11.51
11.48
11.46
11.20
11.05
9.52
8.73
8.35
7.08
6.85
5.73
5.68
5.12
4.15
4.02
3.71
3.15
2.42
2.01
1.63
0.73
ed-Yagiz_190410182724 #525 RT: 6.67 AV: 1 NL: 1.07E4
T: {0,0} + c ESI !corona sid=75.00 det=1353.00 Full ms [100.00-1000.00]
Relative Abundance
m/z
105.10
137.12
151.33
212.70
272.31
301.79
349.46
401.45
424.83
496.00
559.62
633.64
641.72
684.57
726.68
758.92
804.86
878.39
943.99
996.68
RT: 0.00 - 12.10
RT: 6.49
NL: 2.42E6 UV_VIS_1 UV Genesis ed-Yagiz_190410182724
uAU
Time (min)

LC-MS of R-S