J. Braz. Chem. Soc., Vol. 00, No. 00, S1-S26, 2010.
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0103 - 5053 $6.00+0.00

Chemoenzymatic Synthesis of Organoselenium(IV) Compounds and their Evaluation as Cysteine Protease Inhibitors

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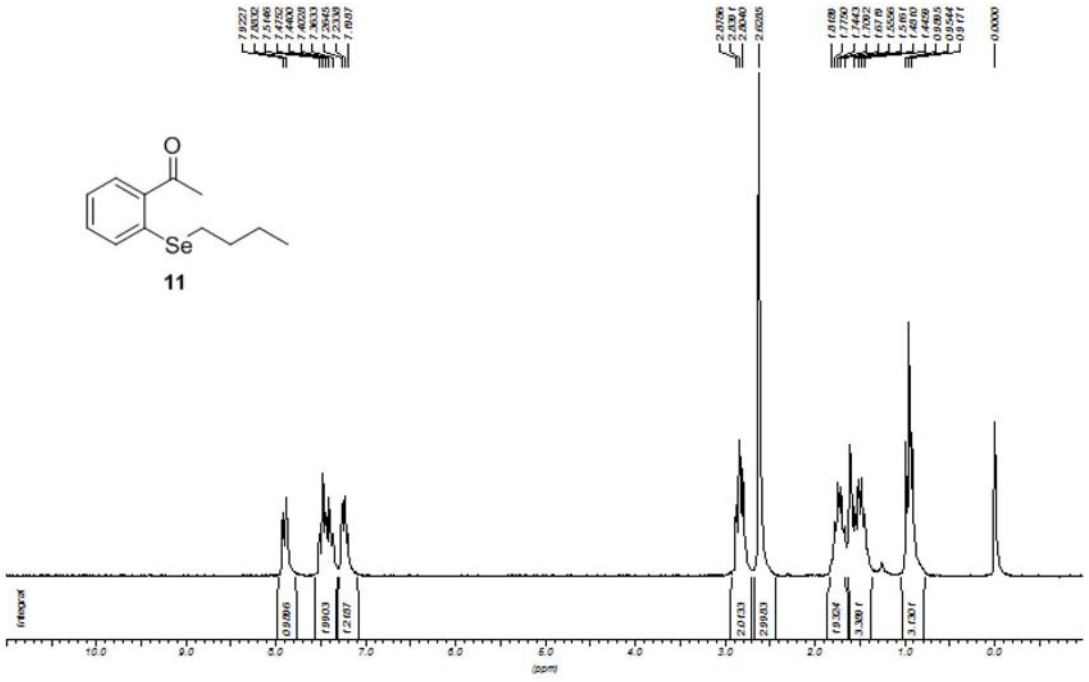

Figure S1. ^{1}H NMR (200 MHz, $CDCl_3$) spectrum of 1-(2-(butylselanyl)phenyl)ethanone (**11**).

*e-mail: rodrigo.cunha@ufabc.edu.br; leandroh@iq.usp.br

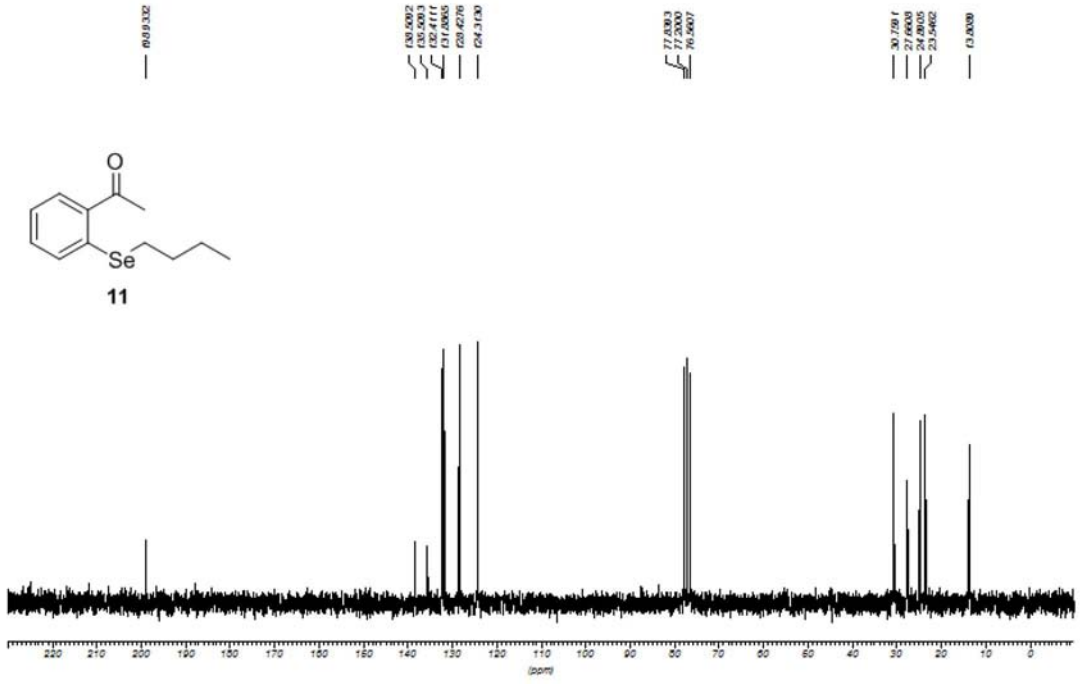

Figure S2. ^{13}C NMR (50 MHz, $CDCl_3$) spectrum of 1-(2-(butylselanyl)phenyl)ethanone (**11**).

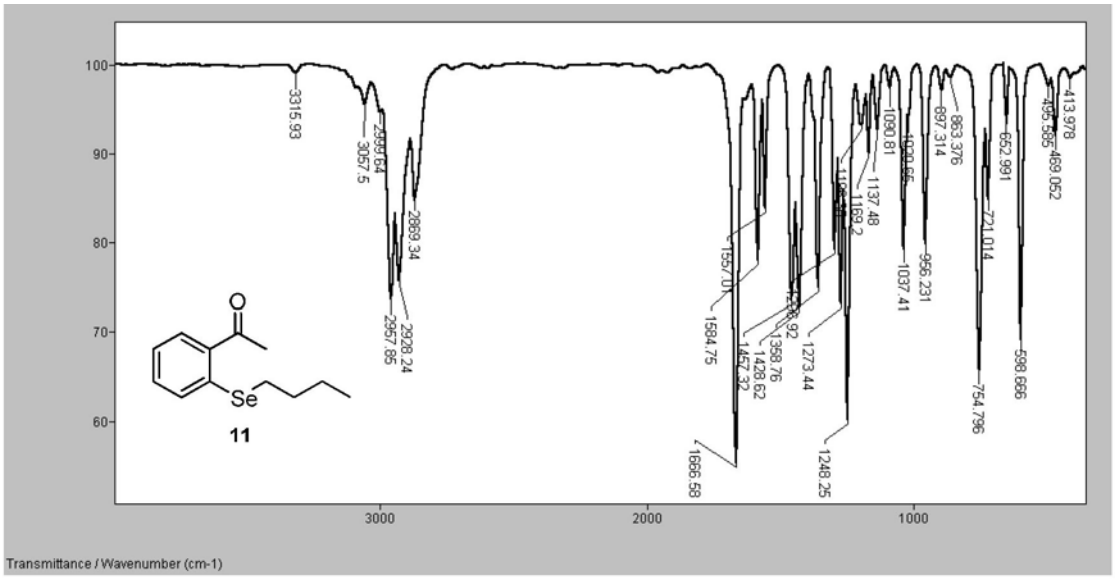

Figure S3. Infrared spectrum of 1-(2-(butylselanyl)phenyl)ethanone (**11**).

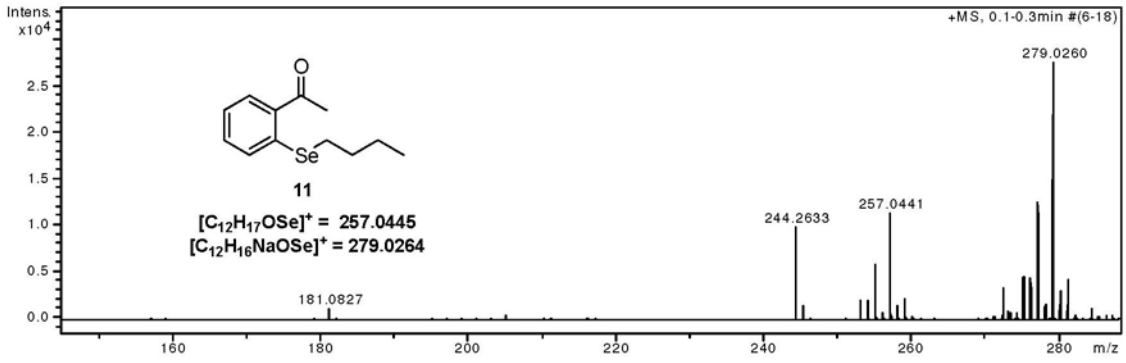

Figure S4. High resolution mass spectrum (ESI) of 1-(2-(butylselanyl)phenyl)ethanone (**11**).

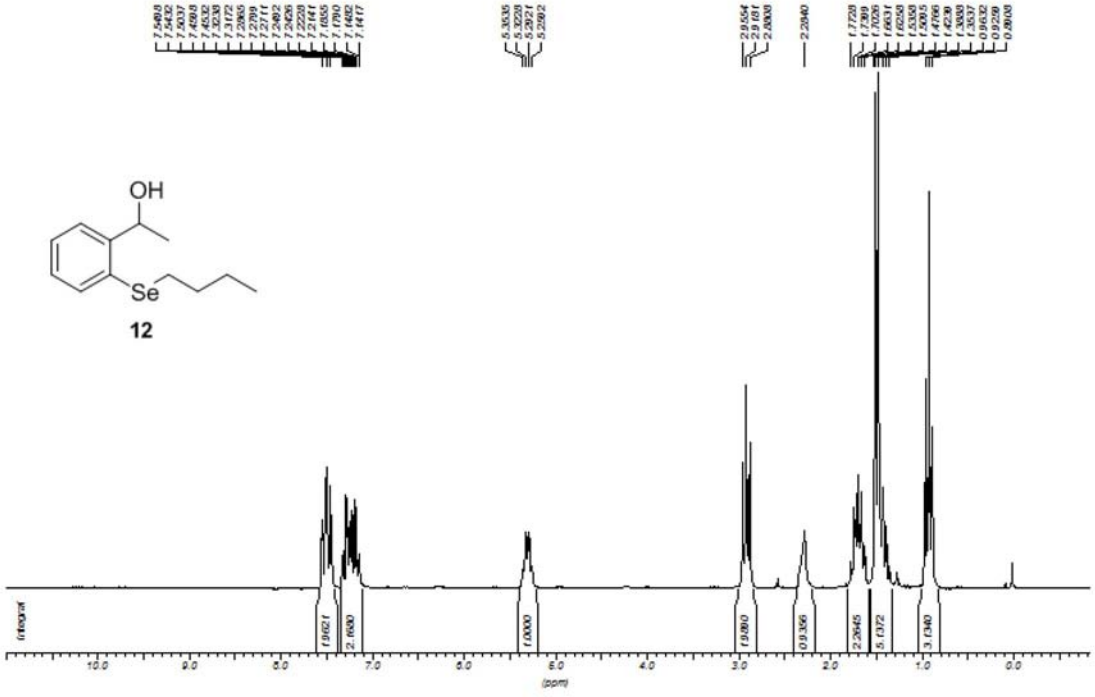

Figure S5. ^{1}H NMR (200 MHz, $CDCl_3$) spectrum of 1-(2-(butylselanyl)phenyl)ethanol (**12**).

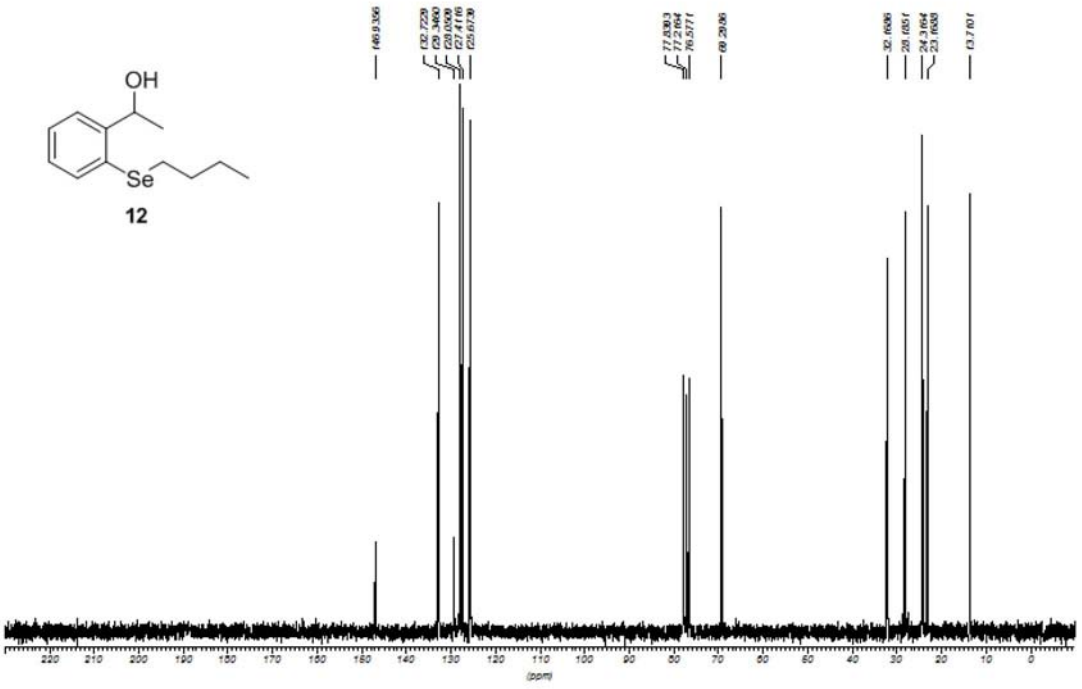

Figure S6. ^{13}C NMR (50 MHz, CDCl3) spectrum of 1-(2-(butylselanyl)phenyl)ethanol (**12**).

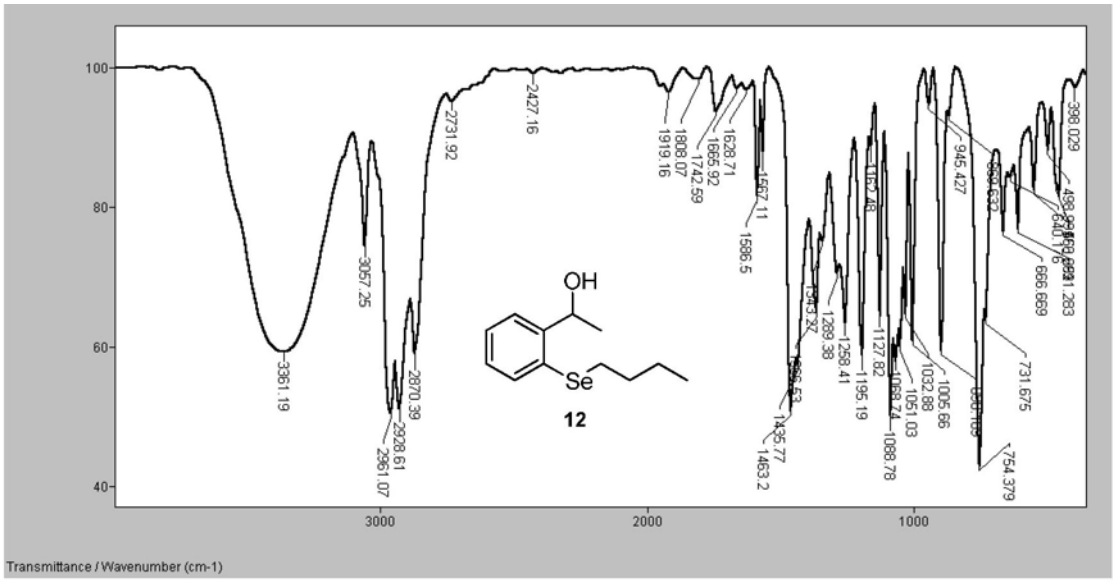

Figure S7. Infrared spectrum of 1-(2-(butylselanyl)phenyl)ethanol (**12**).

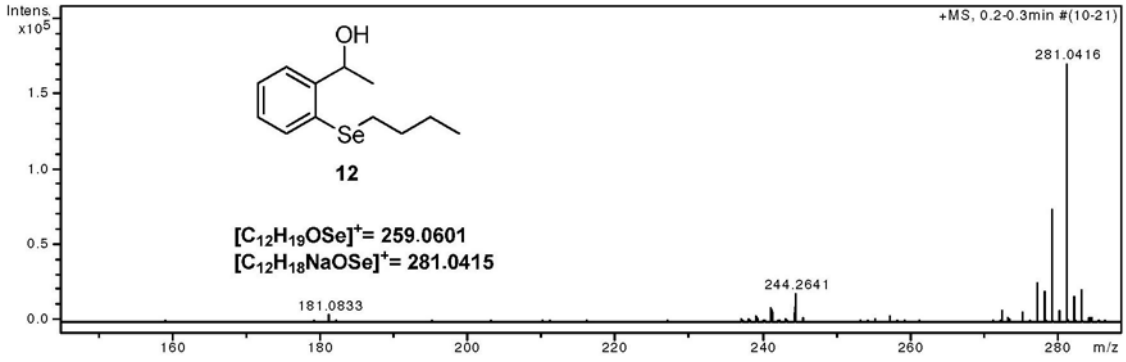

Figure S8. High resolution mass spectrum (ESI) of 1-(2-(butylselanyl)phenyl)ethanol (**12**).

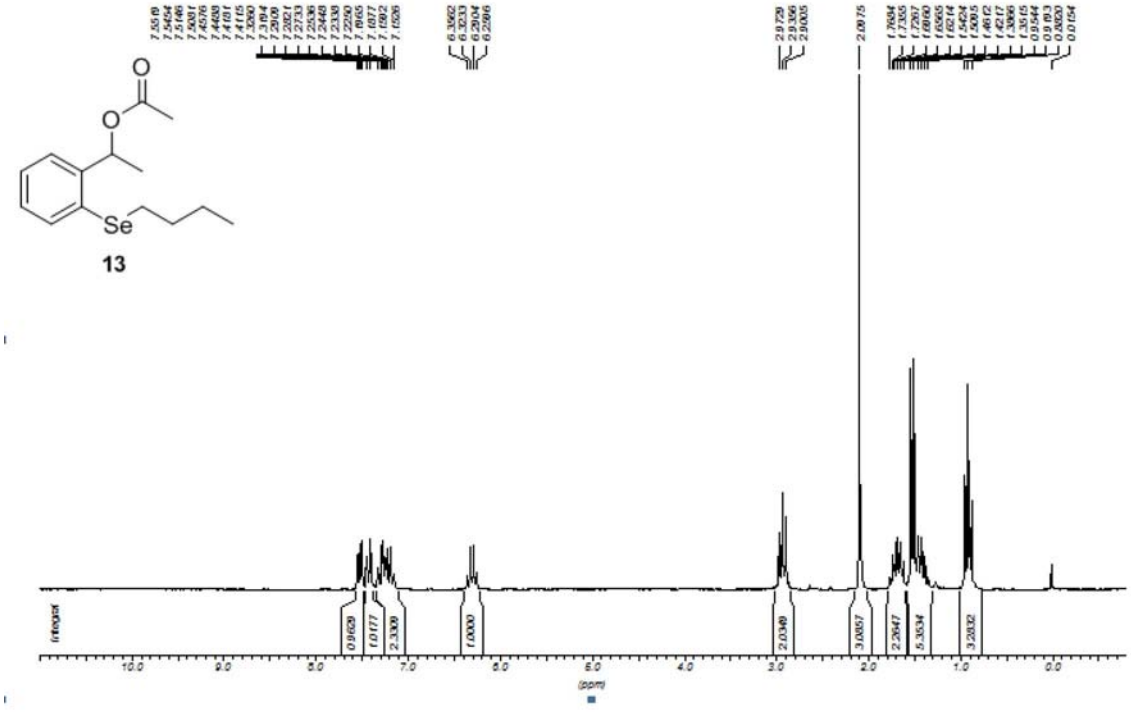

Figure S9. ^{1}H NMR (200 MHz, $CDCl_3$) spectrum of 1-(2-(butylselanyl)phenyl)ethyl acetate (**13**).

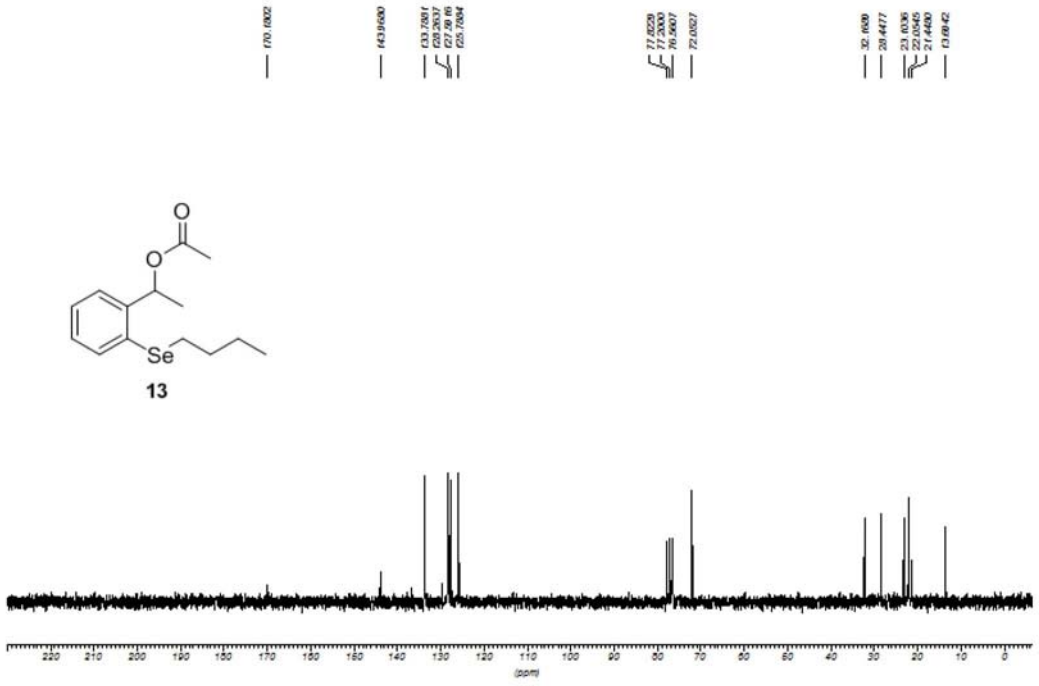

Figure S10. ^{13}C NMR (50 MHz, $CDCl_3$) spectrum of 1-(2-(butylselanyl)phenyl)ethyl acetate (**13**).

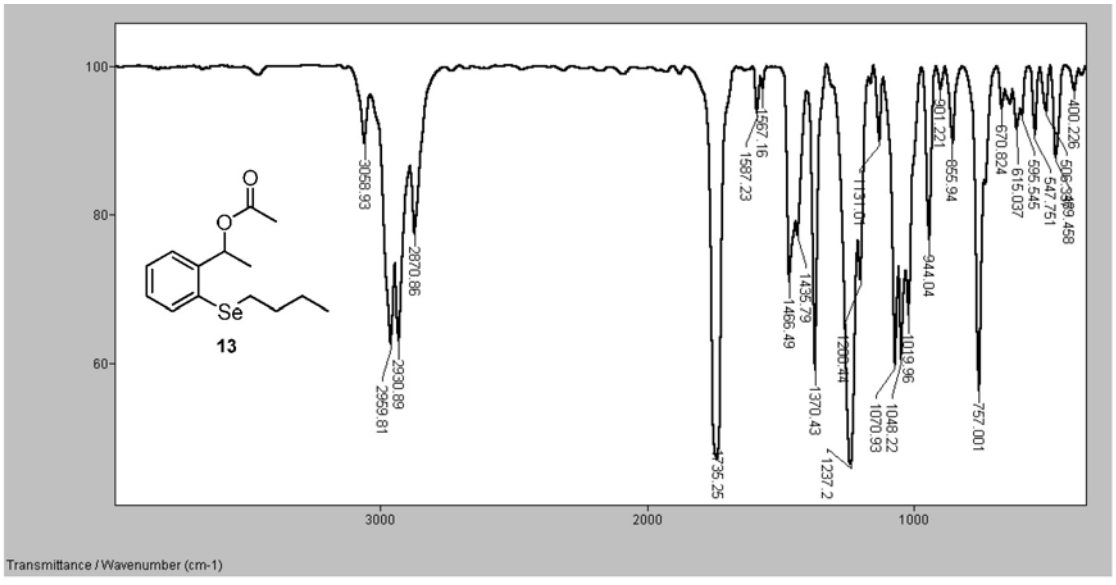

Figure S11. Infrared spectrum of 1-(2-(butylselanyl)phenyl)ethyl acetate (**13**).

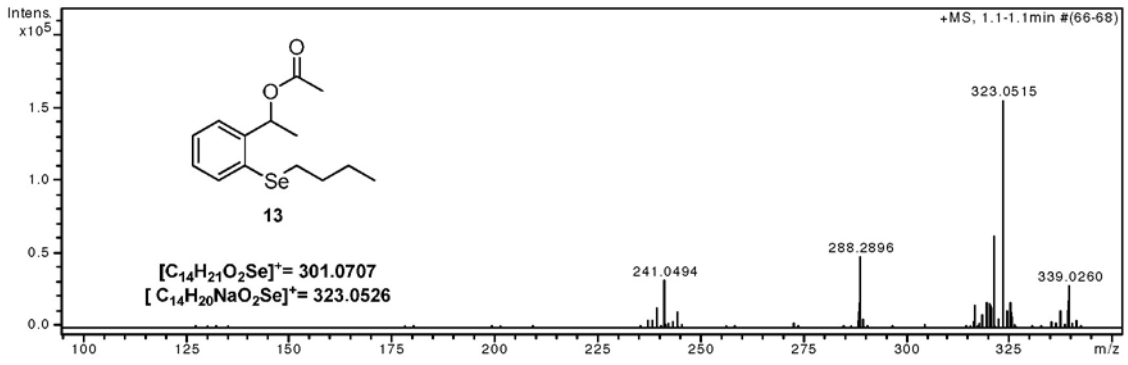

Figure S12. High resolution mass spectrum (ESI) of 1-(2-(butylselanyl)phenyl)ethyl acetate (**13**).

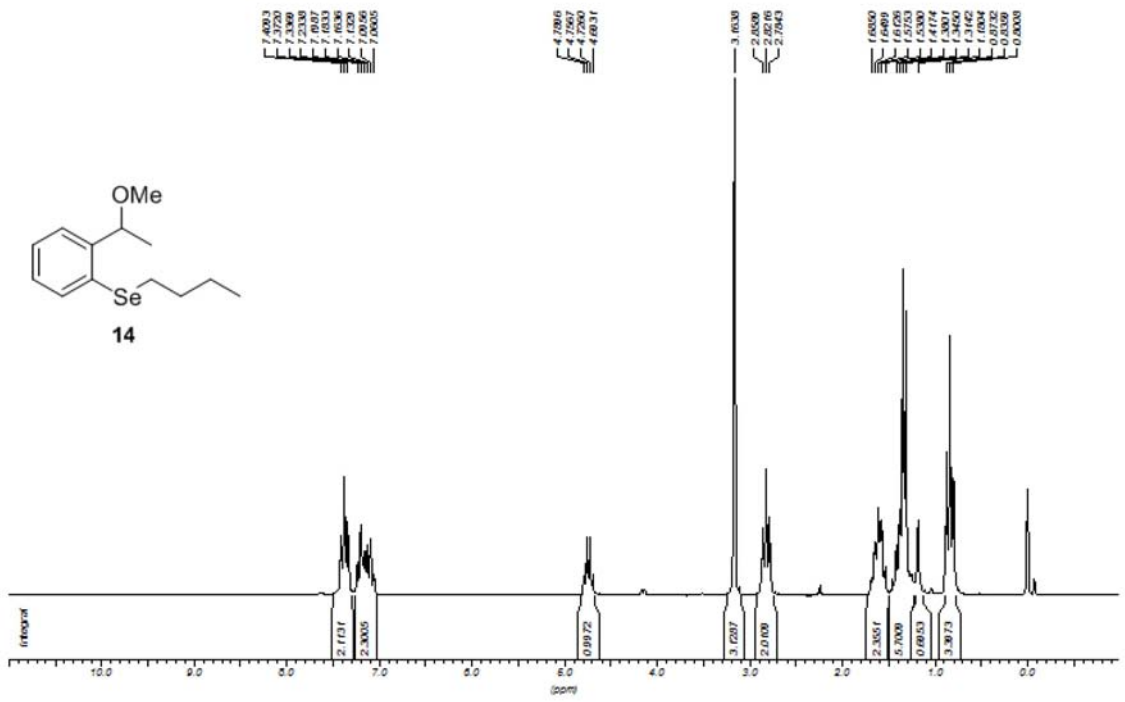

Figure S13. ^{1}H NMR (200 MHz, $CDCl_3$) spectrum of butyl(2-(1-methoxyethyl)phenyl)selane (**14**).

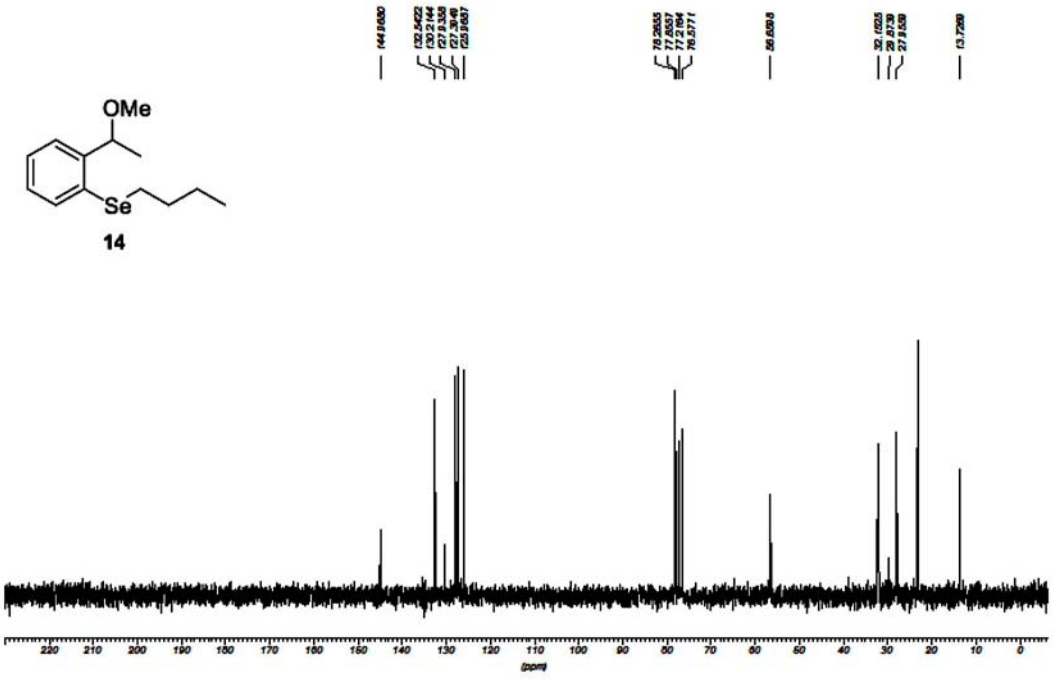

Figure S14. ^{13}C NMR (50 MHz, $CDCl_3$) spectrum of butyl(2-(1-methoxyethyl)phenyl)selane (**14**).

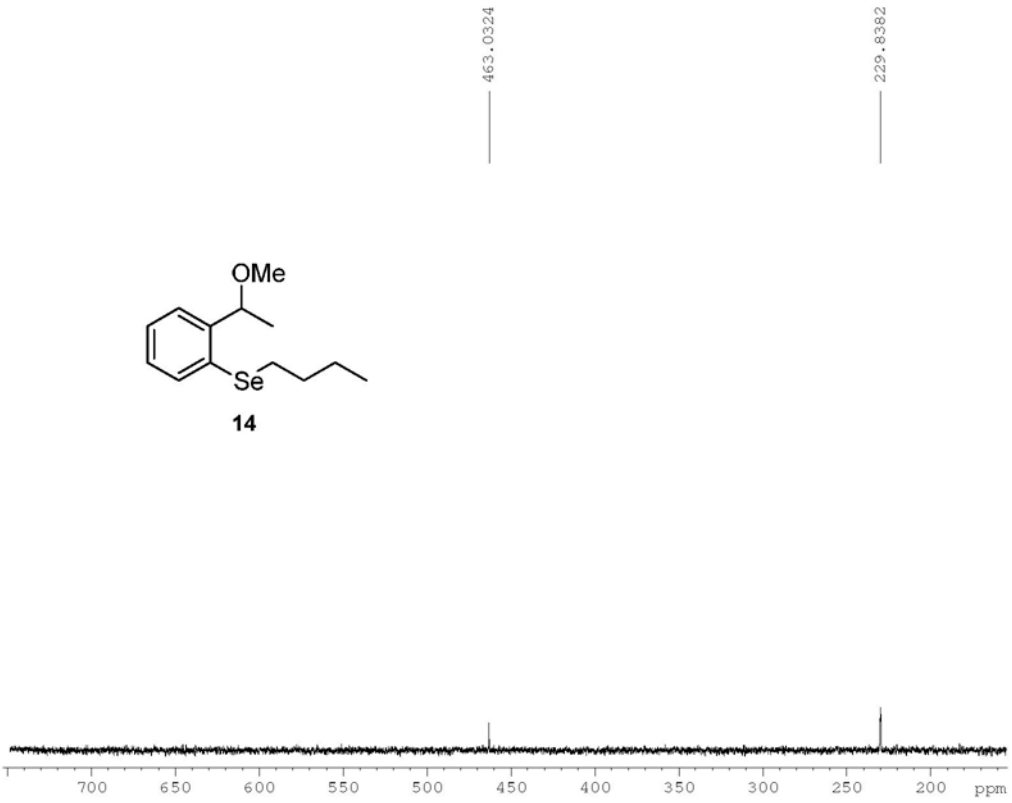

Figure S15. ^{77}Se NMR (57.24 MHz, $CDCl_3$) spectrum of butyl(2-(1-methoxyethyl)phenyl)selane (**14**).

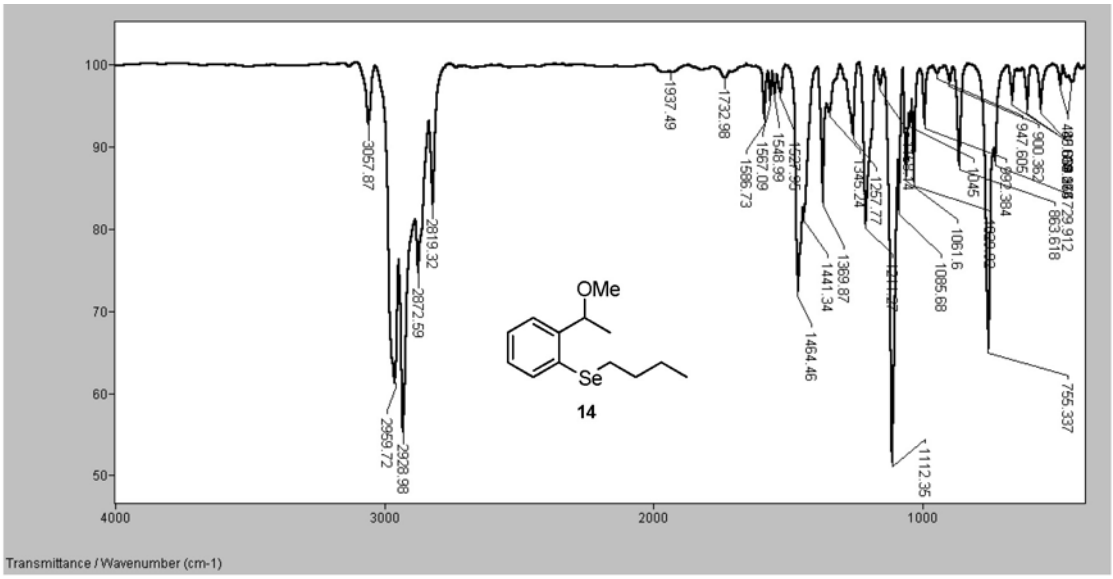

Figure S16. Infrared spectrum of butyl(2-(1-methoxyethyl)phenyl)selane (**14**).

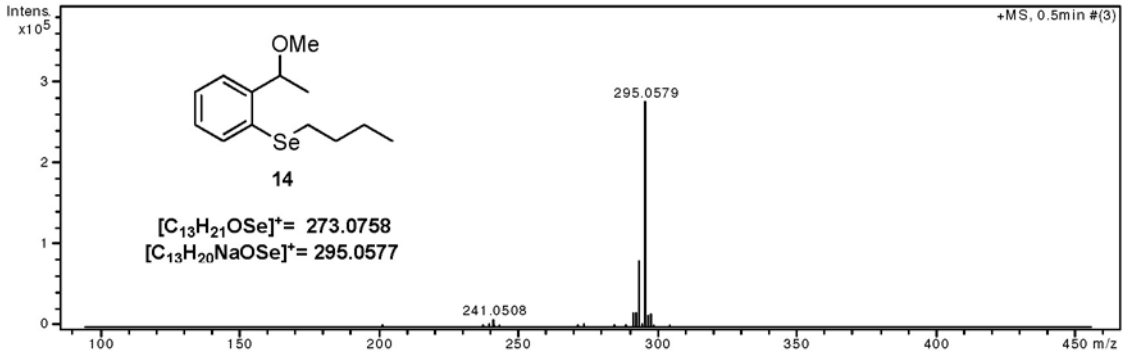

Figure S17. High resolution mass spectrum (ESI) of butyl(2-(1-methoxyethyl)phenyl)selane (**14**).

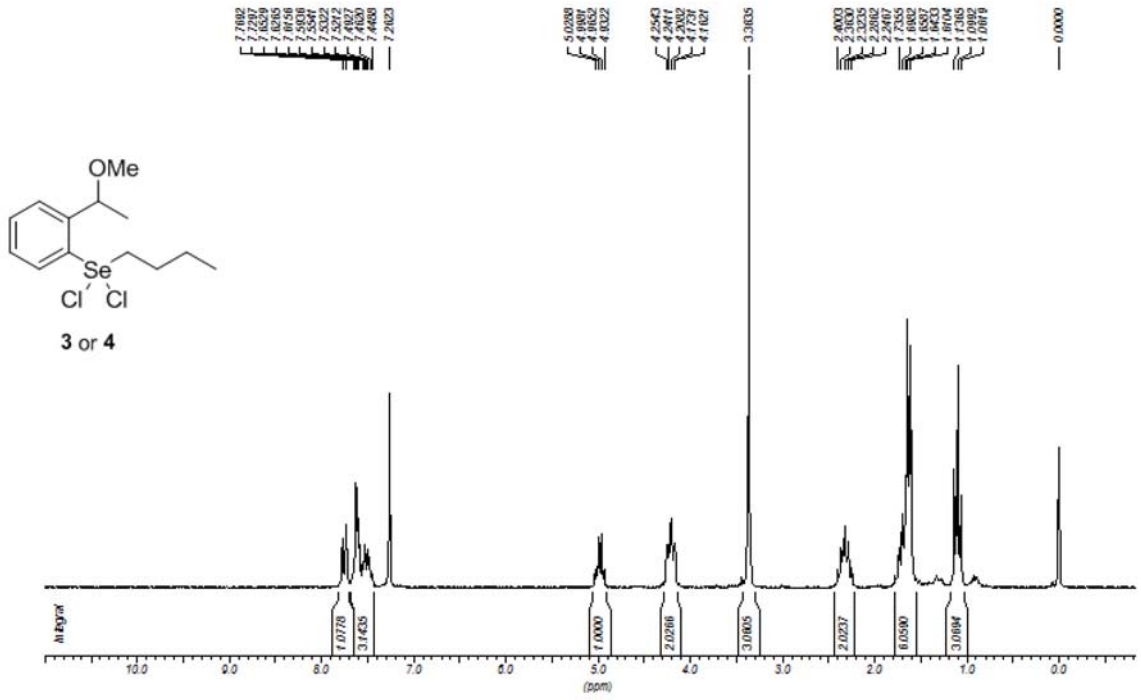

Figure S18. ^{1}H NMR (200 MHz, $CDCl_3$) spectrum of selenane (**3** or **4**).

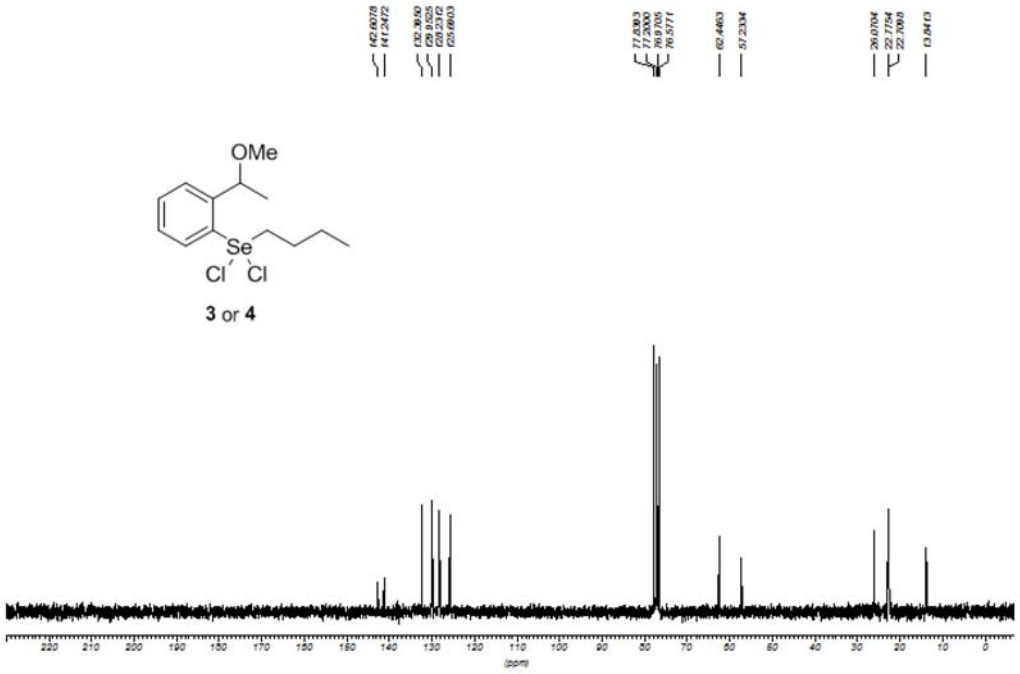

Figure S19. ^{13}C NMR (50 MHz, $CDCl_3$) spectrum of selenane (**3** or **4**).

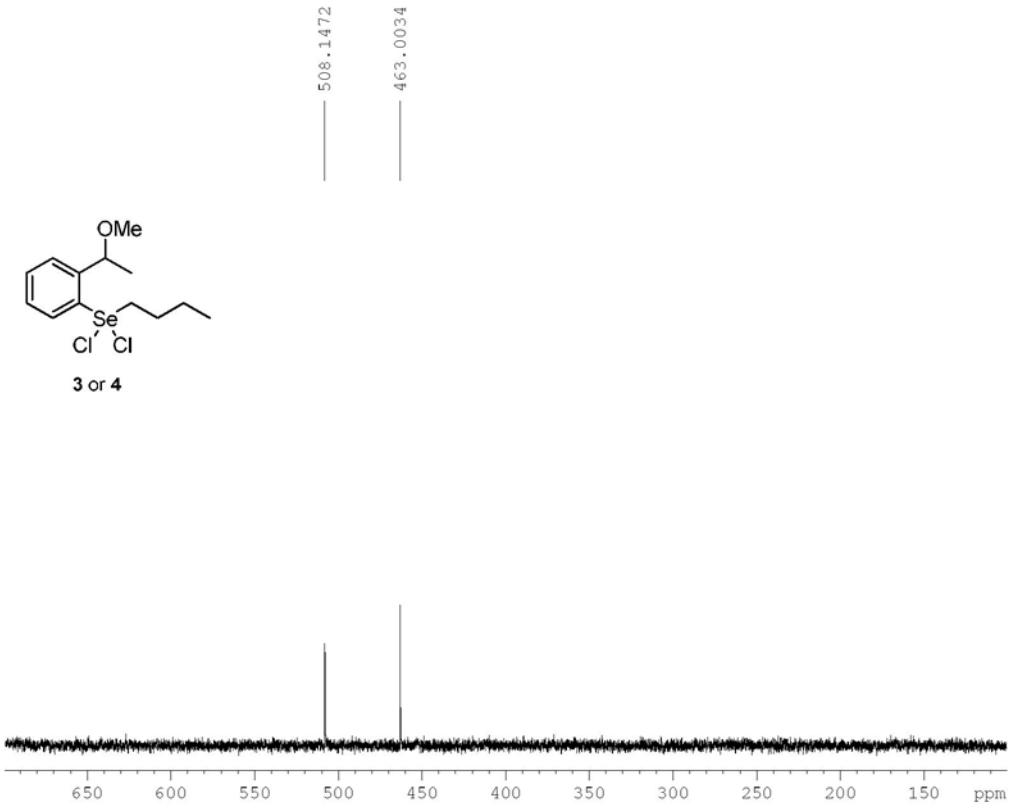

Figure S20. ^{77}Se NMR (57.24 MHz, $CDCl_3$) spectrum of selenane (**3** or **4**).

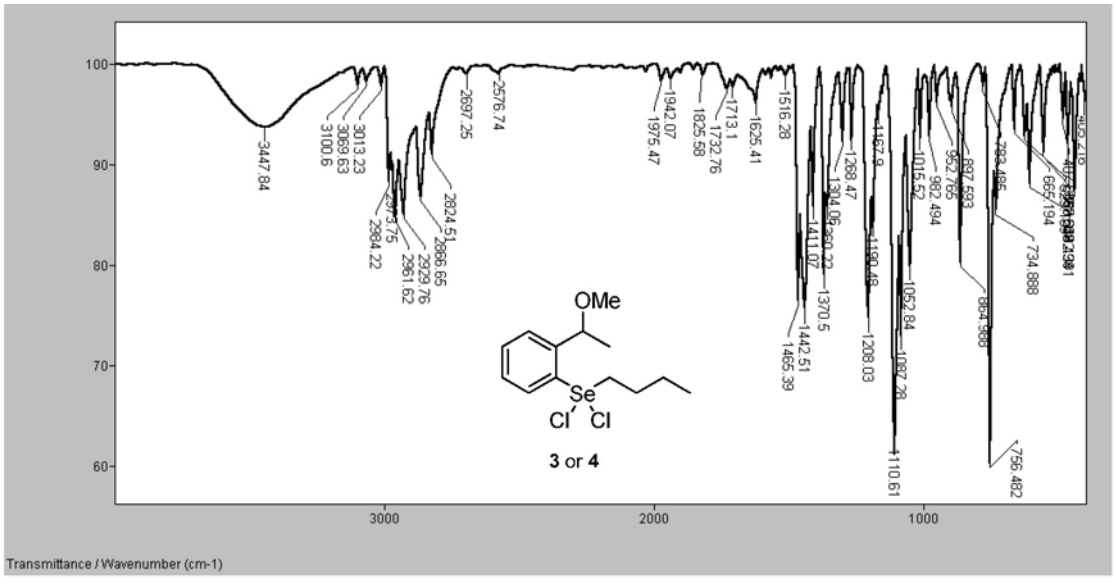

Figure S21. Infrared spectrum of selenane (**3** or **4**).

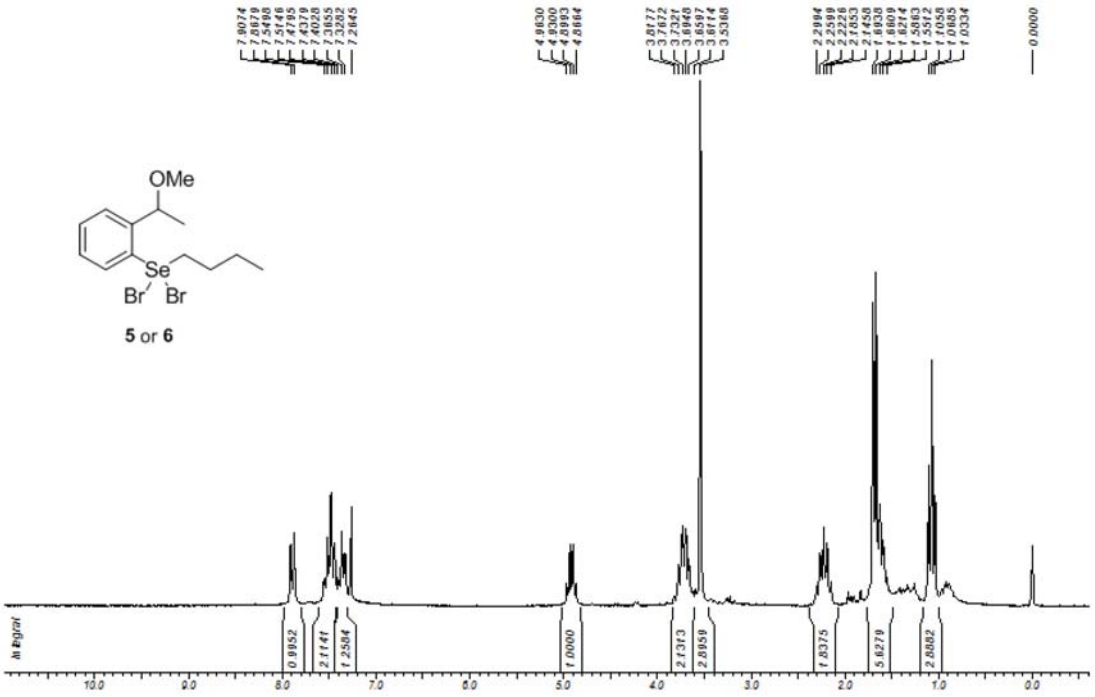

Figure S22. ^{1}H NMR (200 MHz, $CDCl_3$) spectrum of selenane (**5** or **6**).

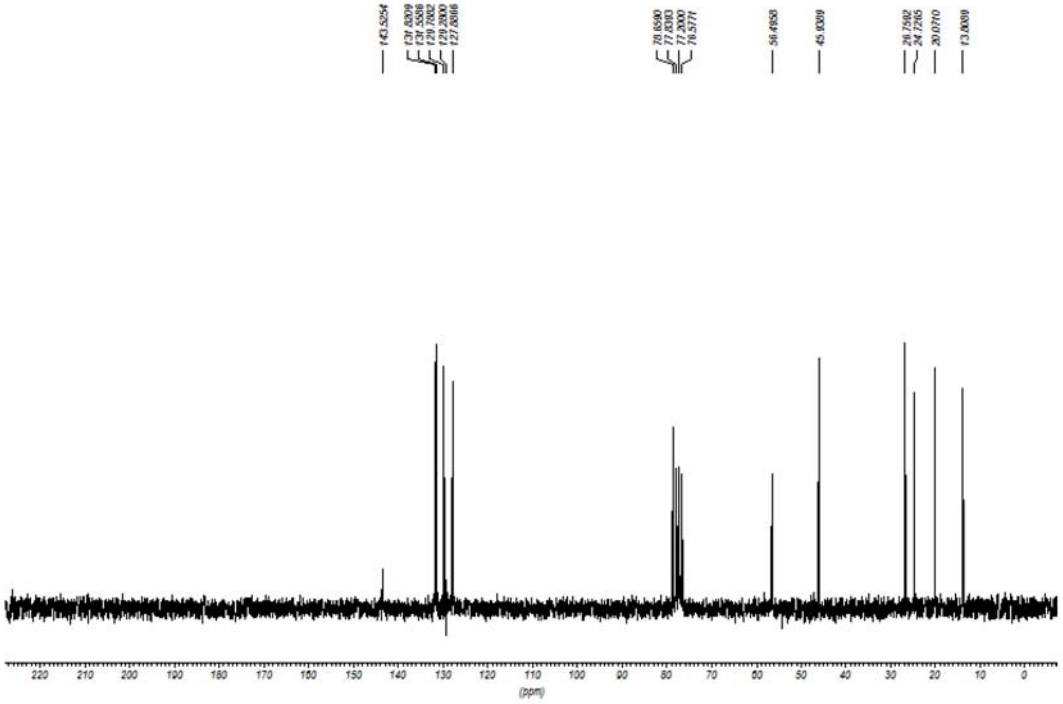

Figure S23. ^{13}C NMR (50 MHz, $CDCl_3$) spectrum of selenane (**5** or **6**).

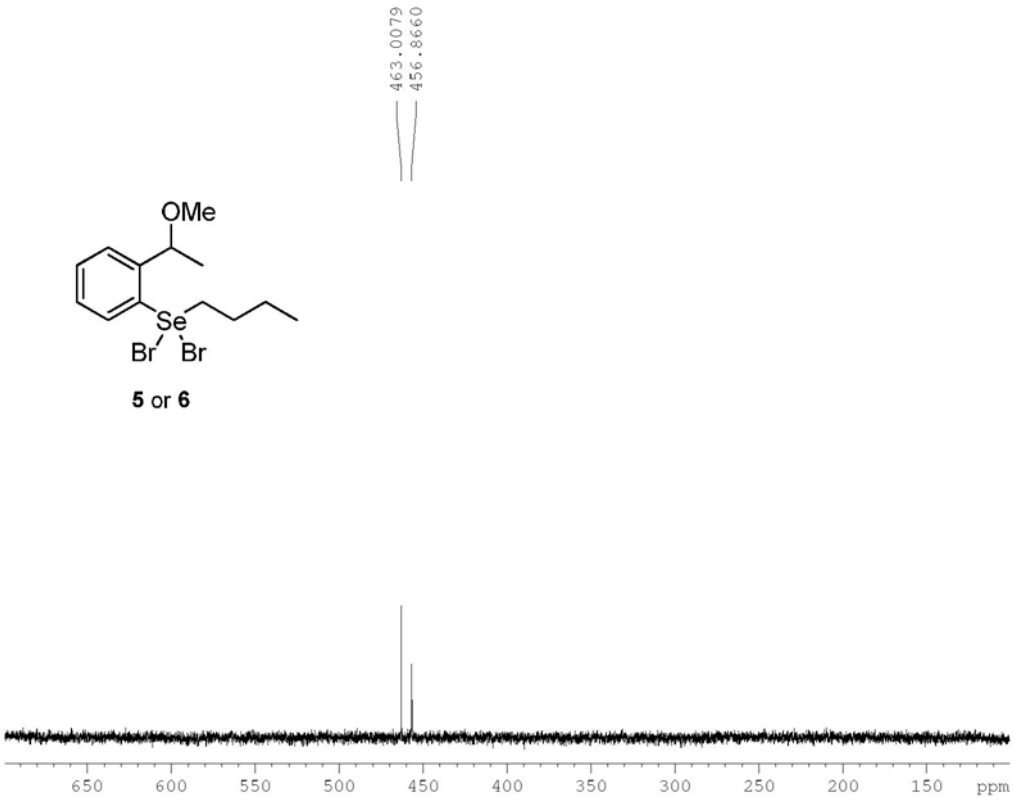

Figure S24. ^{77}Se NMR (57.24 MHz, $CDCl_3$) spectrum of selenane (**5** or **6**).

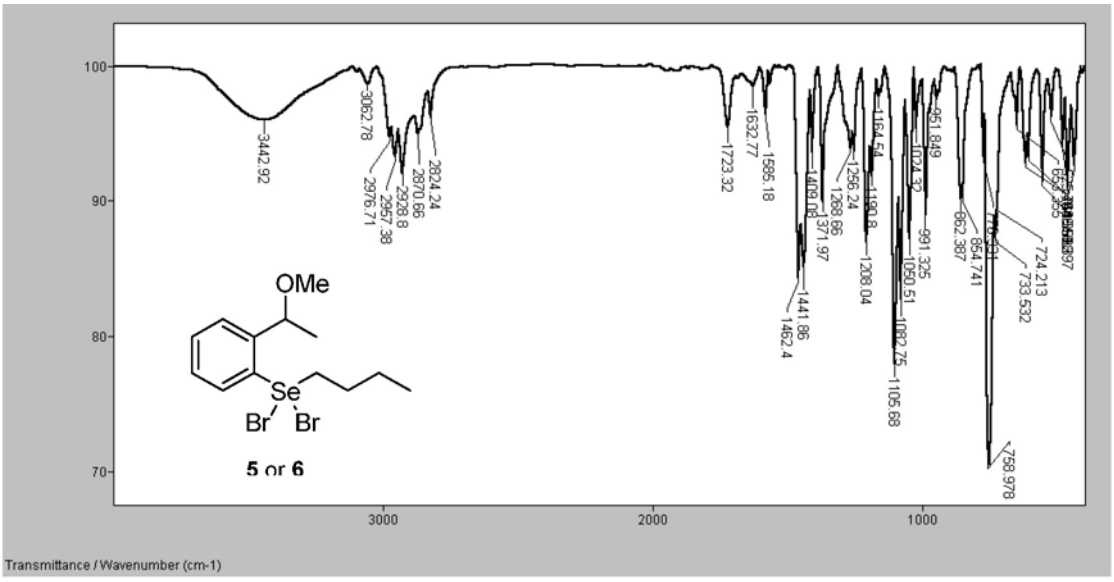

Figure S25. Infrared spectrum of selenane (**5** or **6**).

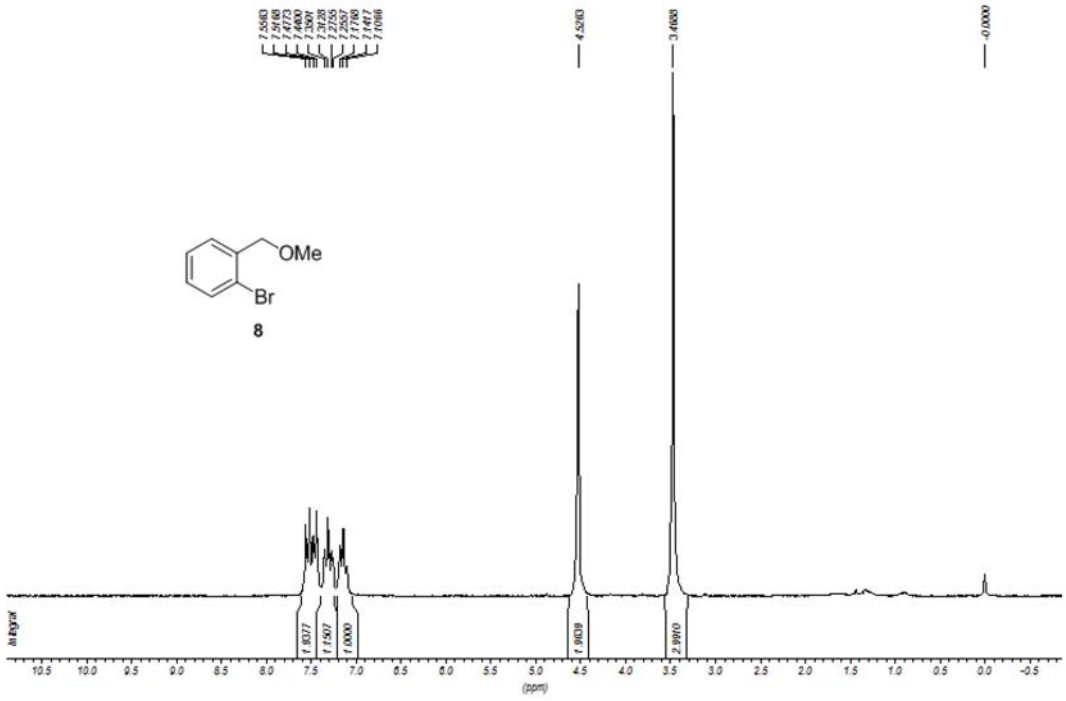

Figure S26. ^{1}H NMR (200 MHz, $CDCl_3$) spectrum of 1-bromo-2-(methoxymethyl)benzene (**8**).

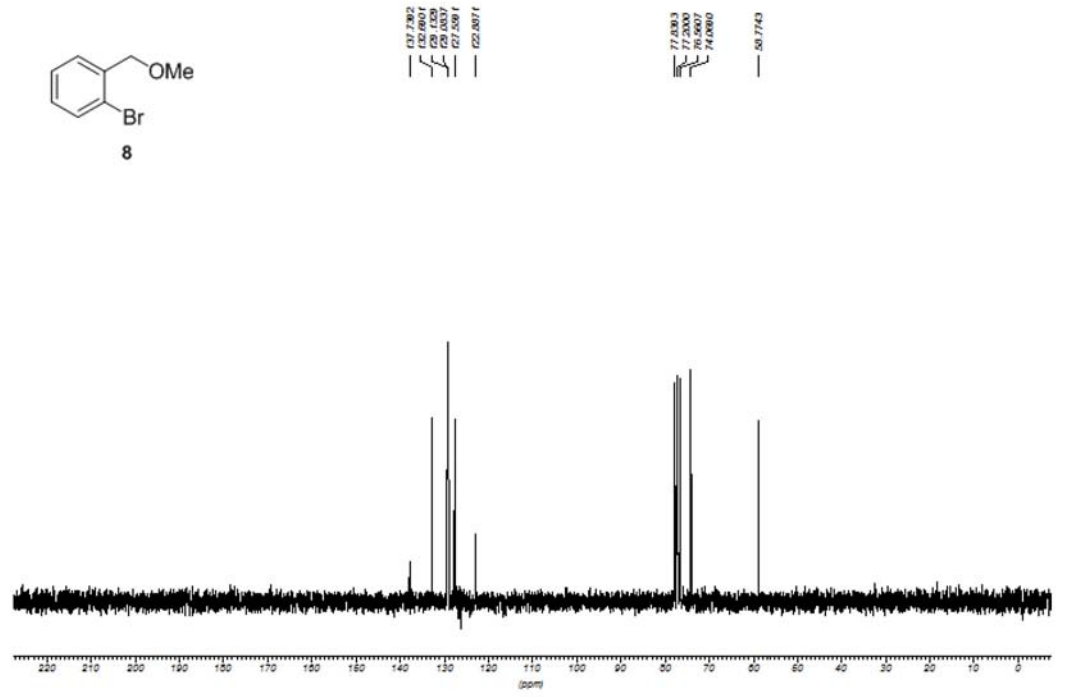

Figure S27. ^{13}C NMR (50 MHz, $CDCl_3$) spectrum of 1-bromo-2-(methoxymethyl)benzene (**8**).

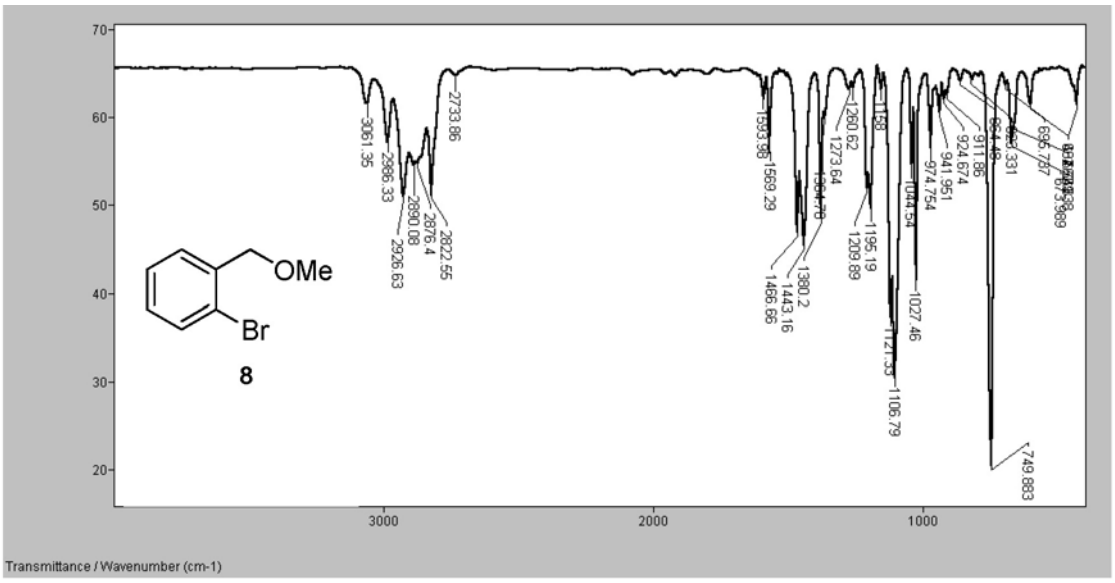

Figure S28. Infrared spectrum of 1-bromo-2-(methoxymethyl)benzene (**8**).

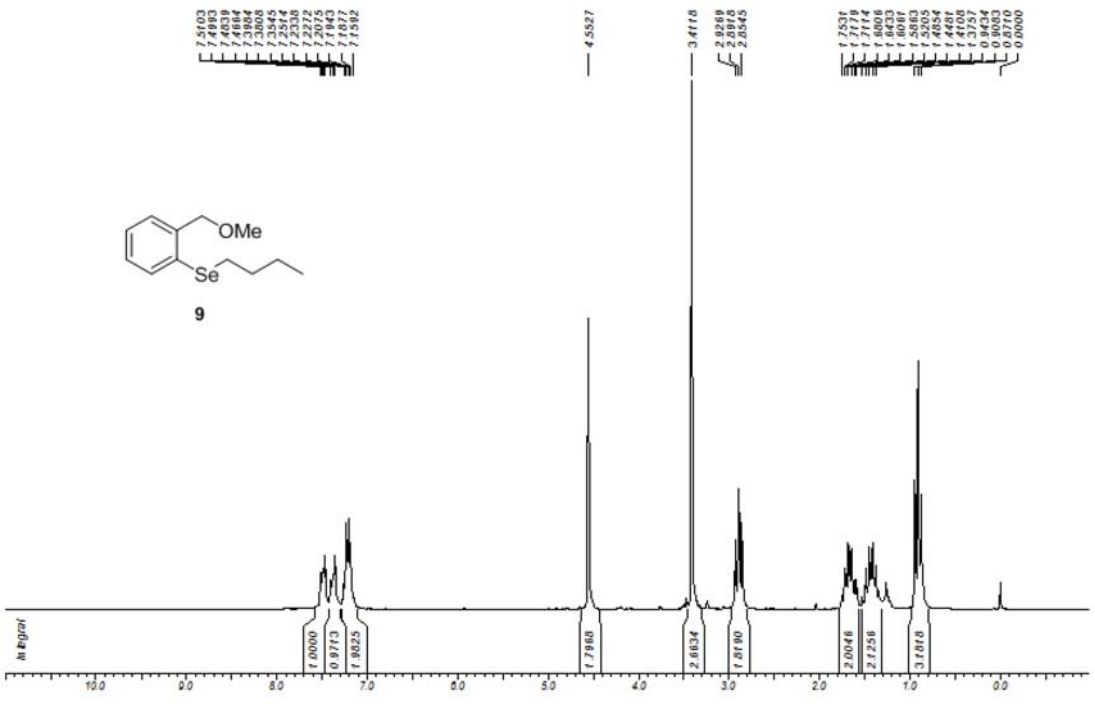

Figure S29. ^{1}H NMR (200 MHz, $CDCl_3$) spectrum of butyl(2-(methoxymethyl)phenyl)selane (**9**).

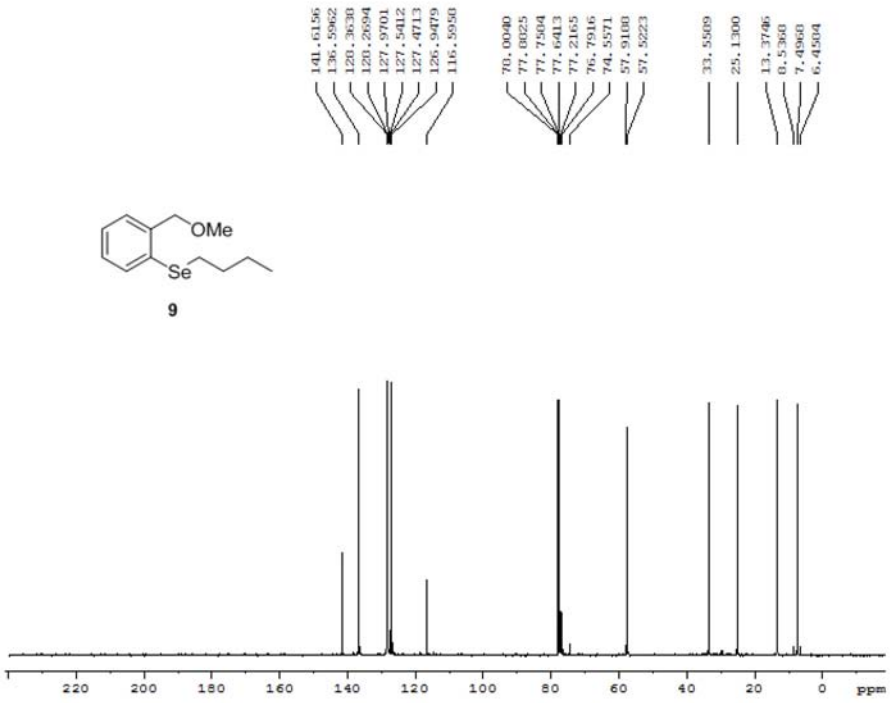

Figure S30. ^{13}C NMR (75 MHz, $CDCl_3$) spectrum of butyl(2-(methoxymethyl)phenyl)selane (**9**).

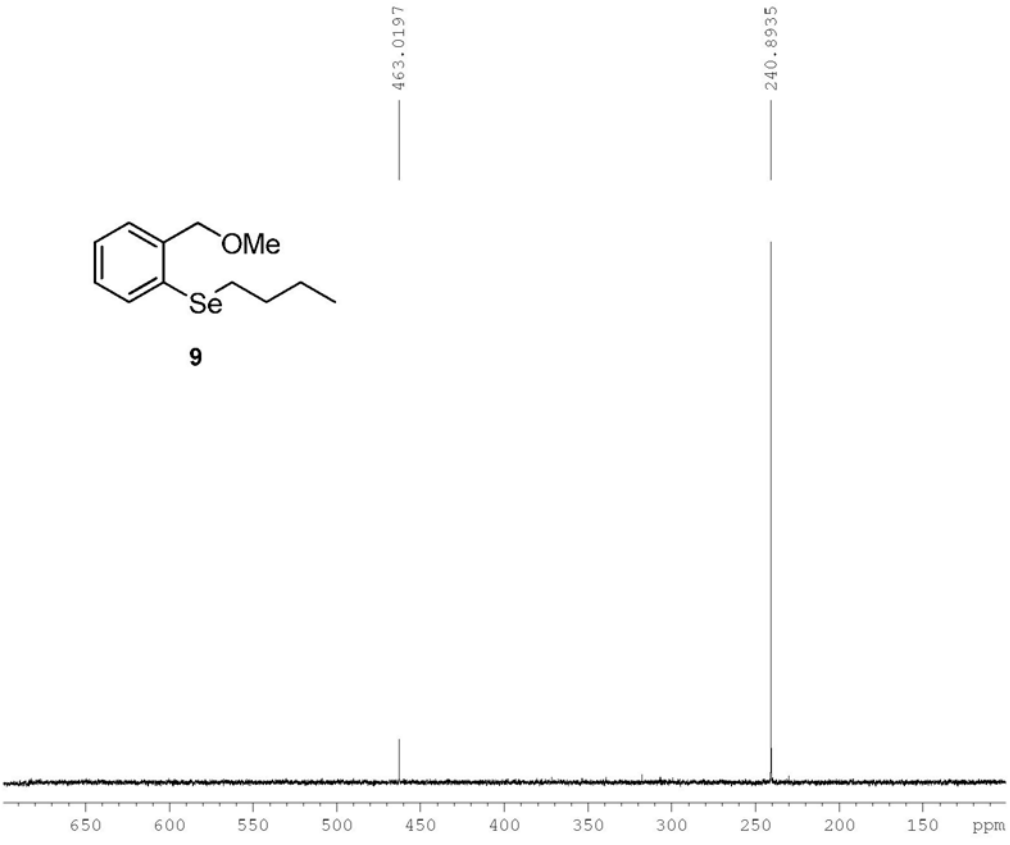

Figure S31. ^{77}Se NMR (57.24 MHz, $CDCl_3$) spectrum of butyl(2-(methoxymethyl)phenyl)selane (**9**).

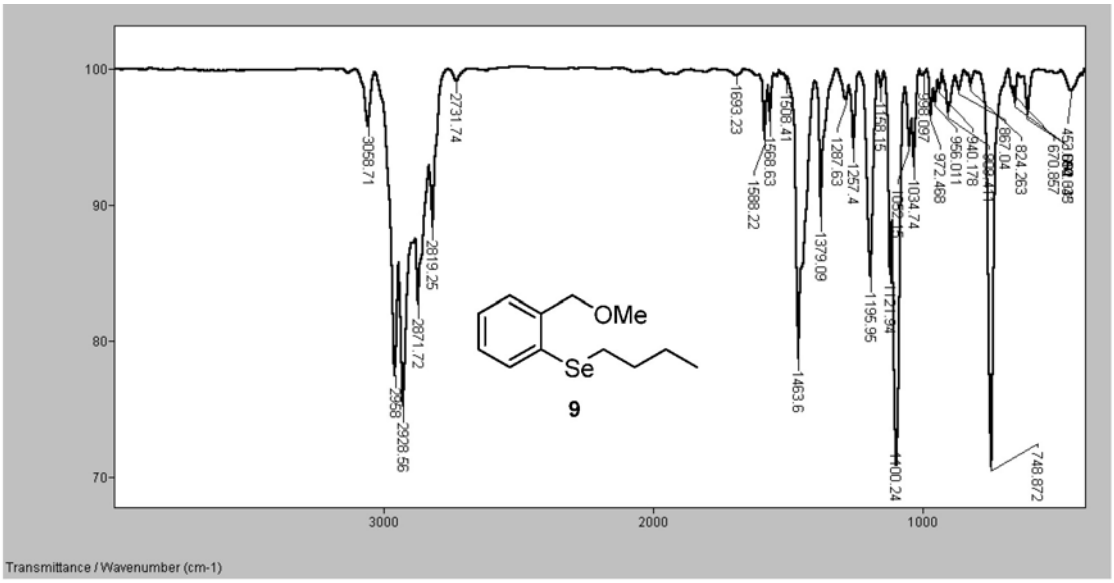

Figure S32. Infrared spectrum of butyl(2-(methoxymethyl)phenyl)selane (**9**).

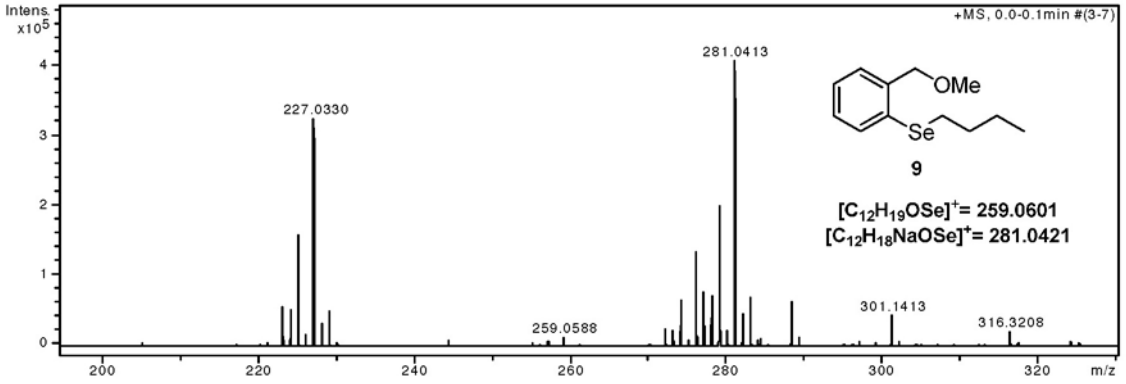

Figure S33. High resolution mass spectrum (ESI) of butyl(2-(methoxymethyl)phenyl)selane (**9**).

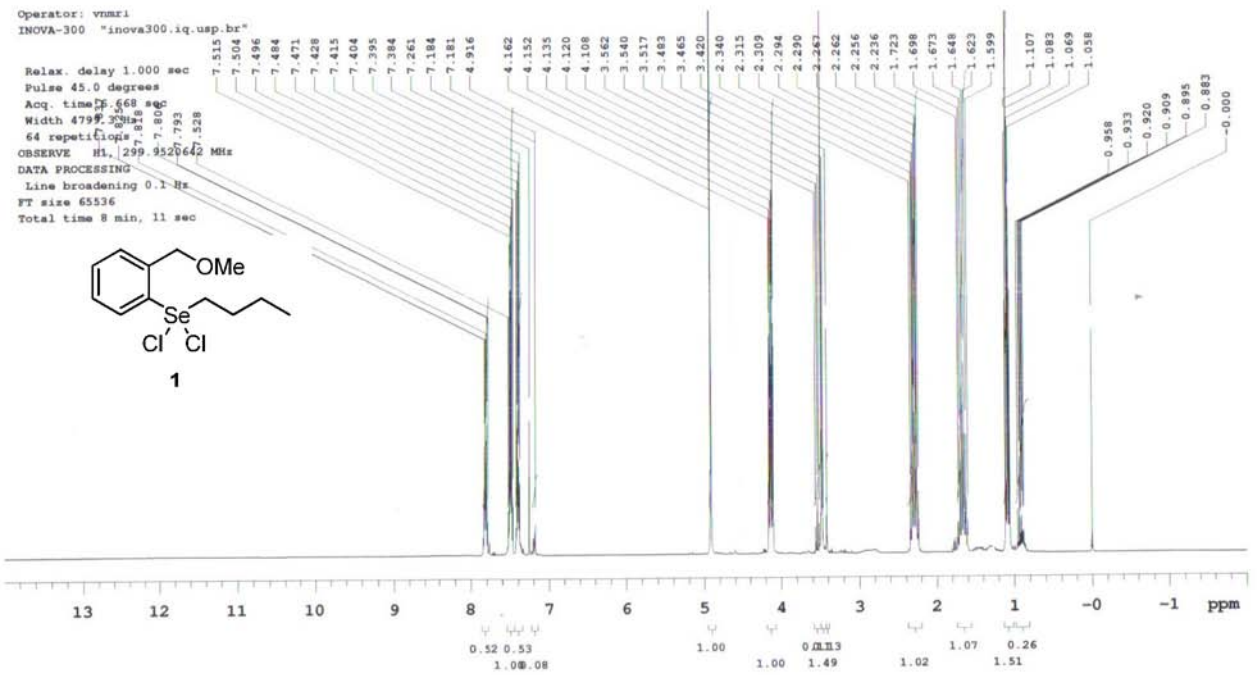

Figure S34. ^{1}H NMR (200 MHz, $CDCl_3$) spectrum of selenane **1**.

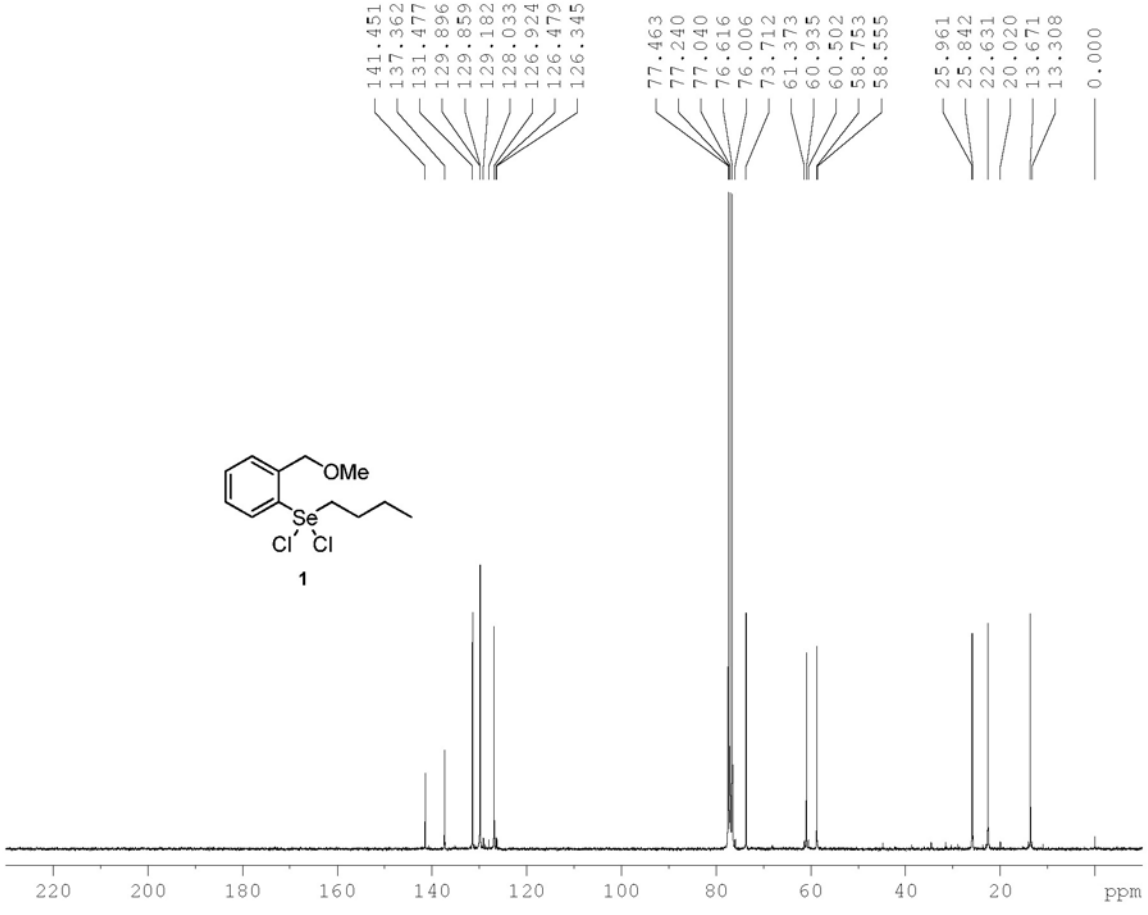

Figure S35. ^{13}C NMR (75 MHz, $CDCl_3$) spectrum of selenane **1**.

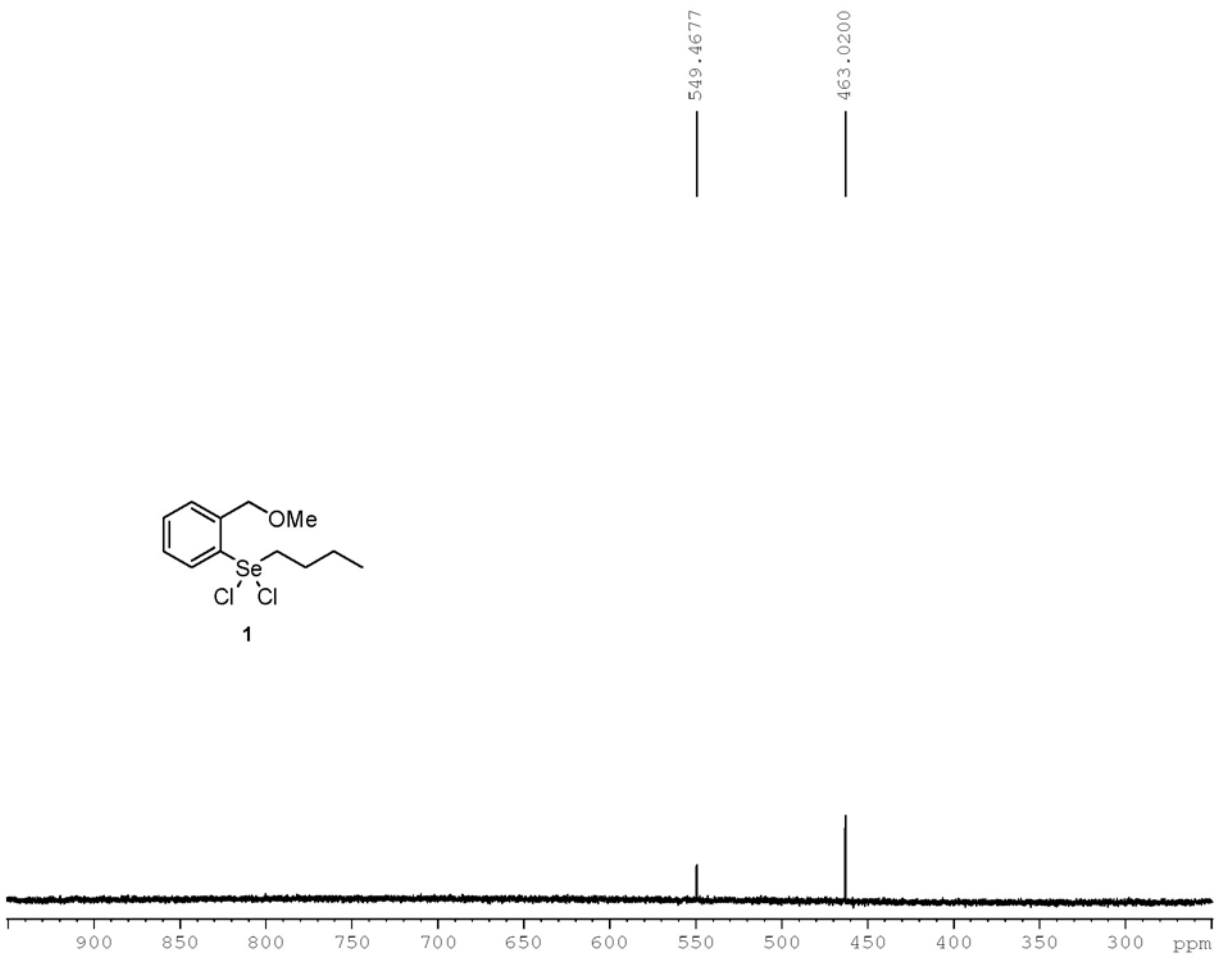

Figure S36. ^{77}Se NMR (57.24 MHz, $CDCl_3$) spectrum of selenane **1**.

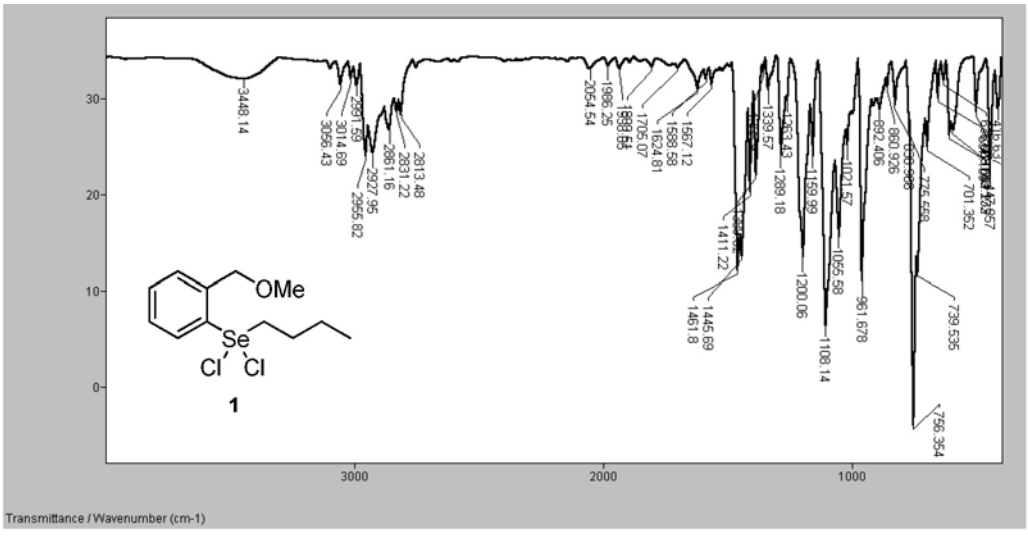

Figure S37. Infrared spectrum of selenane **1**.

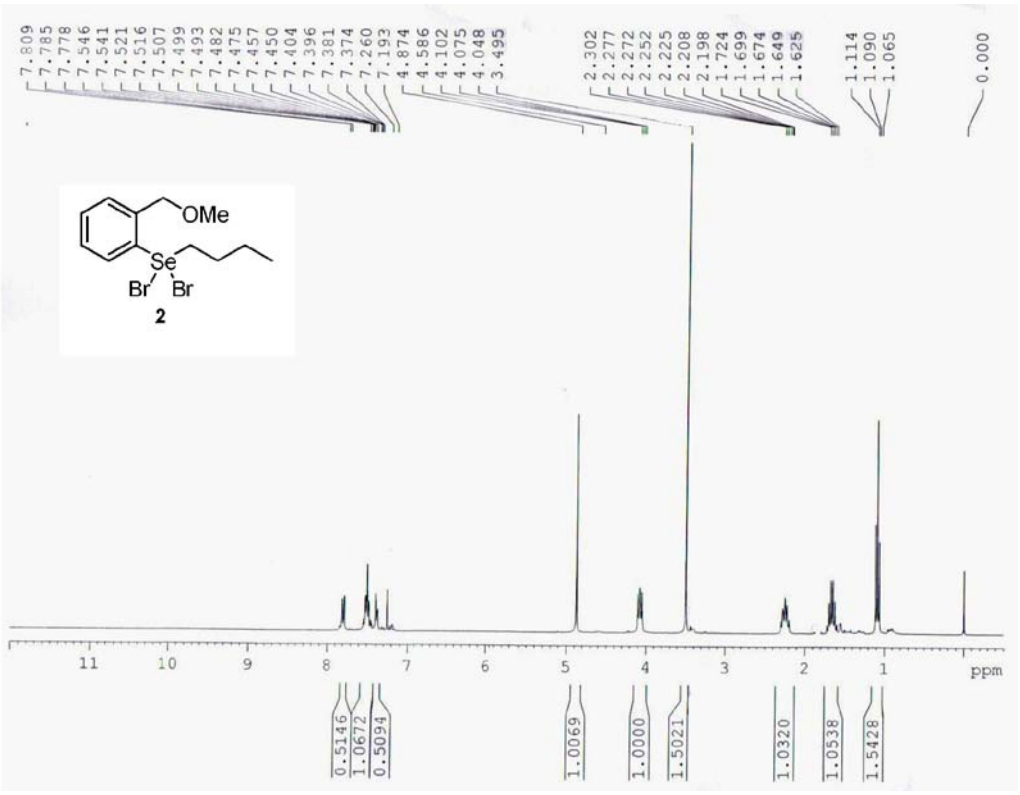

Figure S38. ^{1}H NMR (300 MHz, $CDCl_3$) spectrum of selenane **2**.

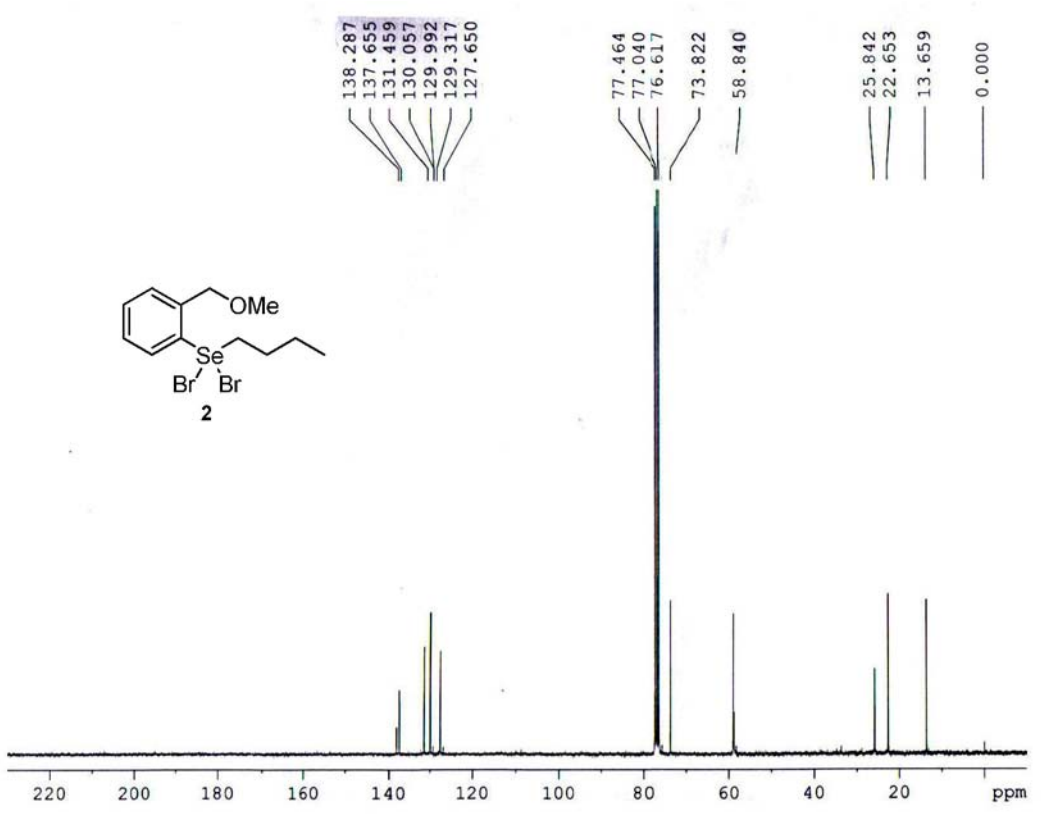

Figure S39. ^{13}C NMR (75 MHz, $CDCl_3$) spectrum of selenane **2**.

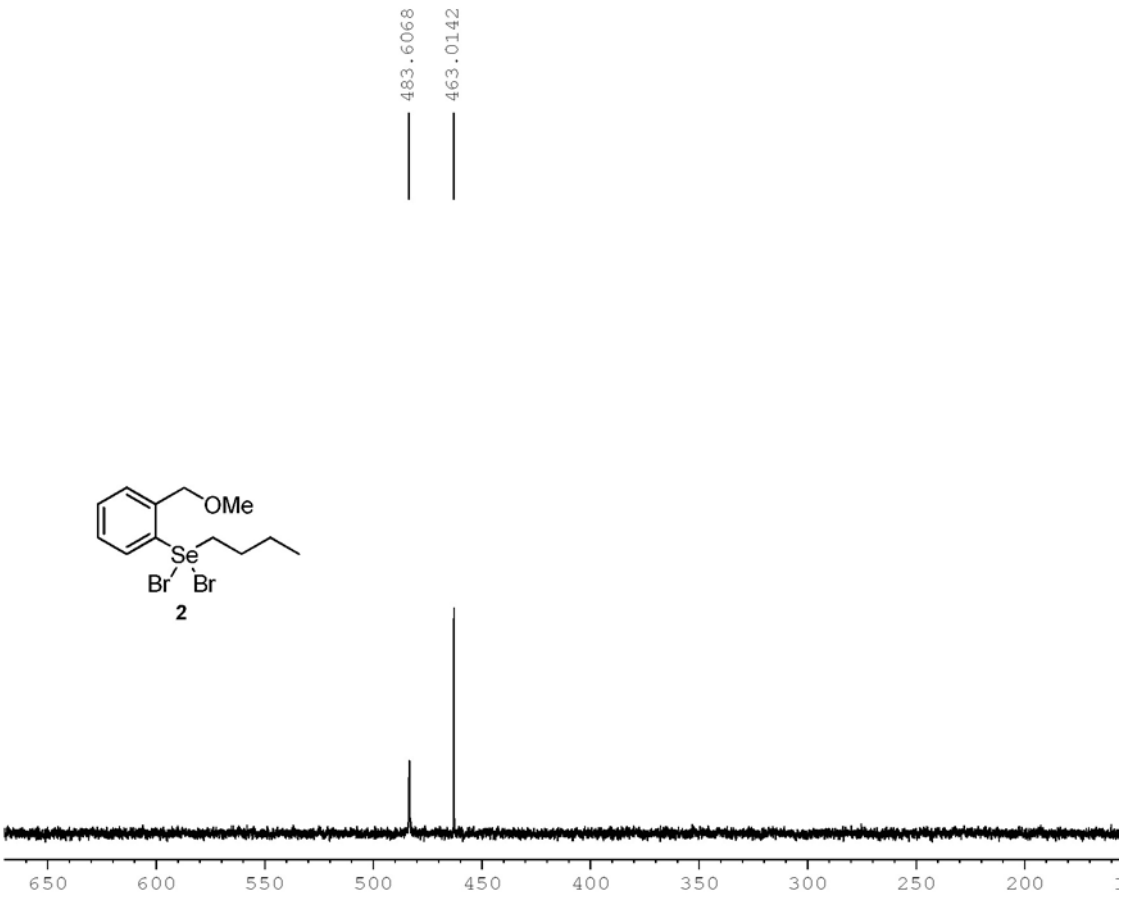

Figure S40. ^{77}Se NMR (57.24 MHz, $CDCl_3$) spectrum of selenane **2**.

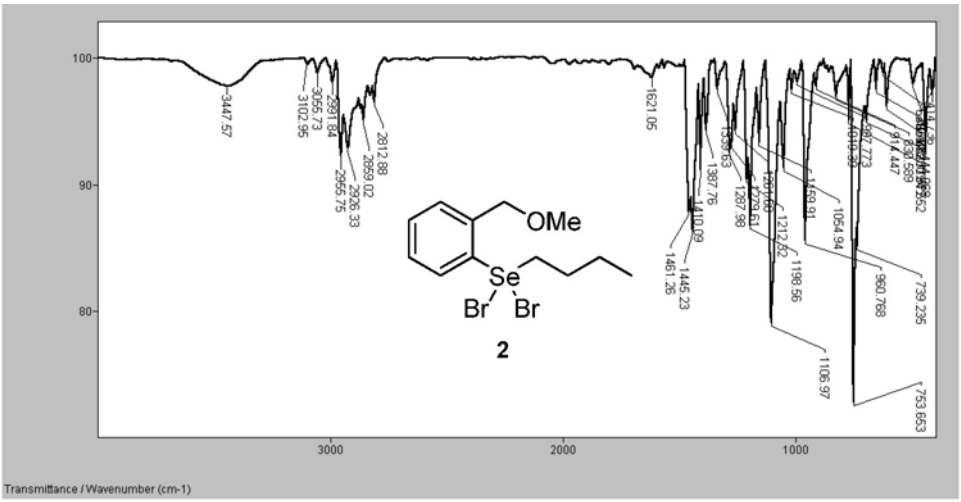

Figure S41. Infrared spectrum of selenane **2**.

Inhibition of cysteine cathepsins V and S by organoselenides ***9***, ***11***, ***12*** *and* ***14***

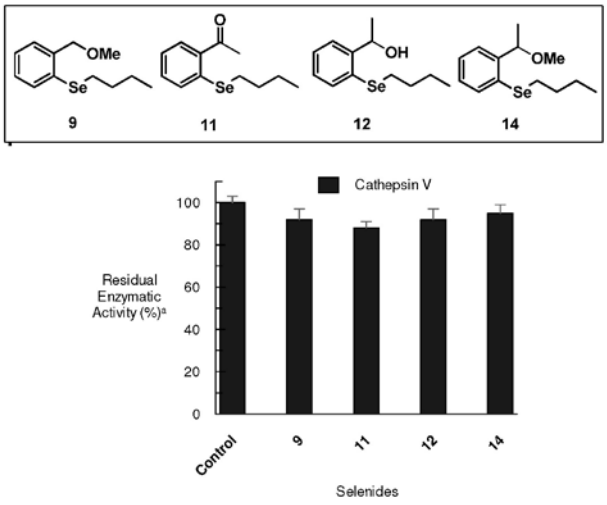

Figure S42. Inhibition profile for cathepsin V using selenides **9**, **11**, **12** and **14** (1 μmol L^{-1}). Conditions: Cathepsin V in sodium acetate buffer (50 mmol.L^{-1}; pH 5.5) containing EDTA (2.5 mmol L^{-1}).[a] Average of three determinations.

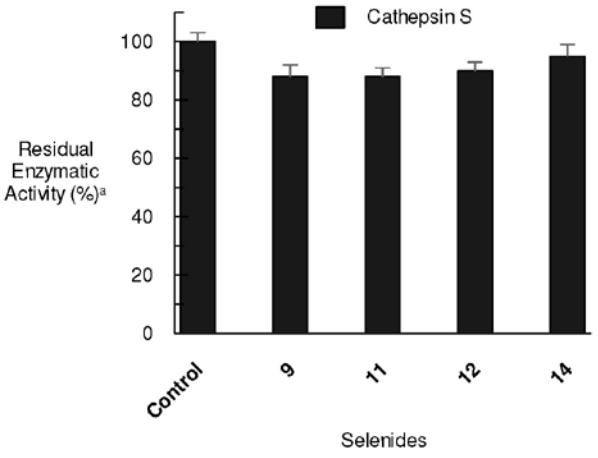

Figure S43. Inhibition profile for cathepsin S using selenides **9**, **11**, **12** and **14** (1 μmol.L^{-1}). Conditions: Cathepsin V in sodium phosphate buffer (50 mmol L^{-1}; pH 6.5) containing EDTA (2.5 mmol L^{-1}). [a]Average of three determinations.

Enzyme kinetics for cathepsins

Time course of the hydrolysis of fluorogenic substrate (Cbz-FR-AMC) in the presence and absence of organoselenanes in the indicated concentrations; relation of the observed first-order inactivation constants (k_{obs}) and the used organoselanes concentrations

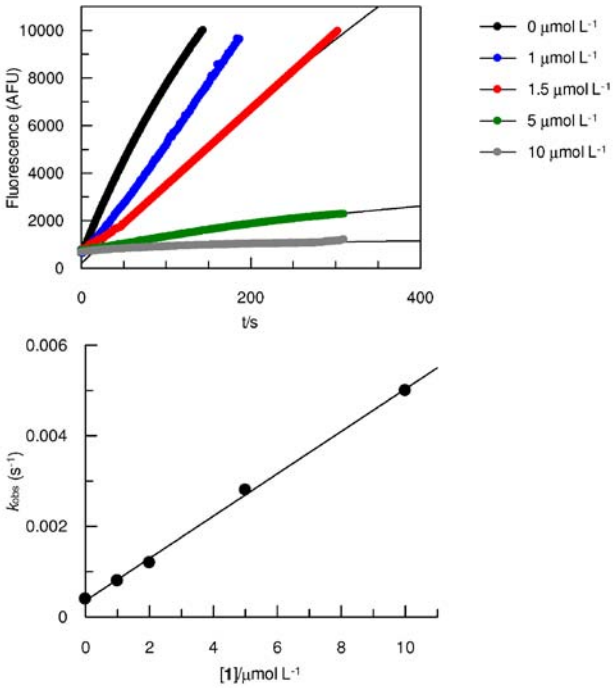

Figure S44. Enzyme kinetic for cathepsin V using selenane **1** as inhibitor**.**

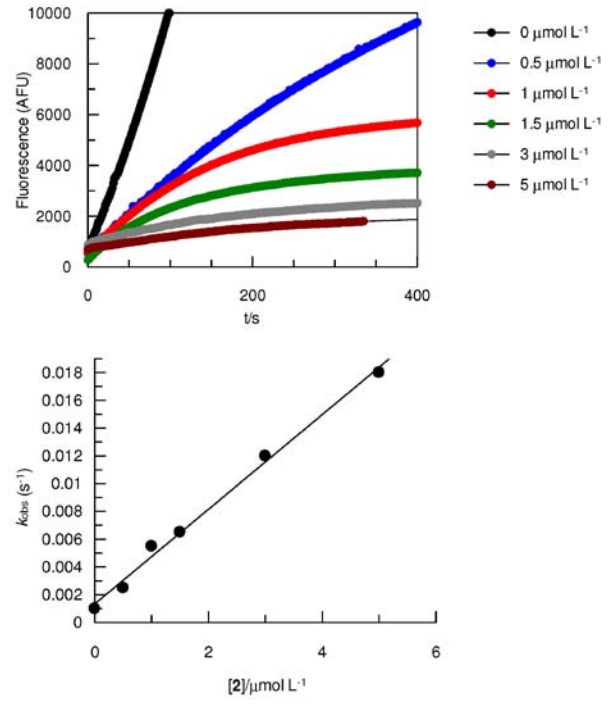

Figure S45. Enzyme kinetic for cathepsin V using selenane **2** as inhibitor**.**

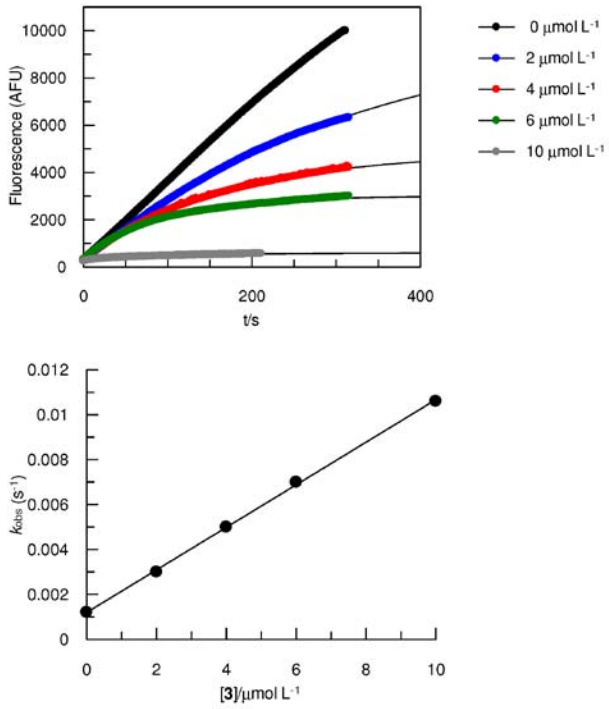

Figure S46. Enzyme kinetic for cathepsin V using selenane **3** as inhibitor**.**

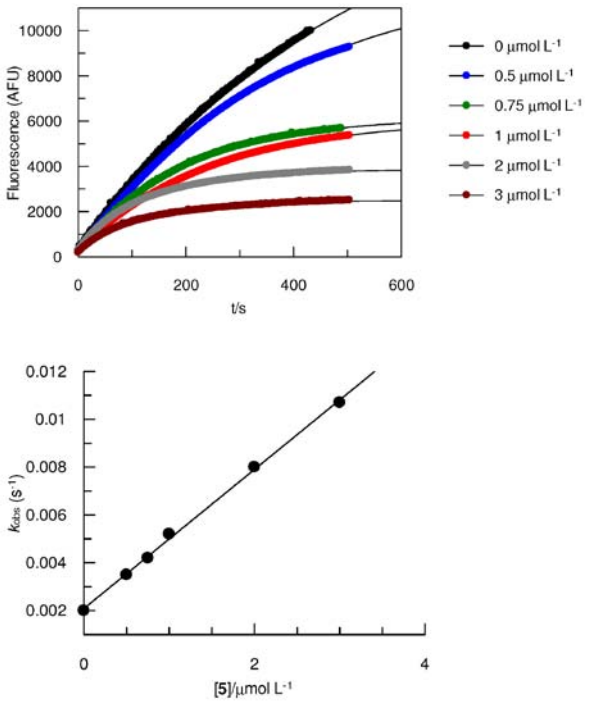

Figure S48. Enzyme kinetic for cathepsin V using selenane **5** as inhibitor**.**

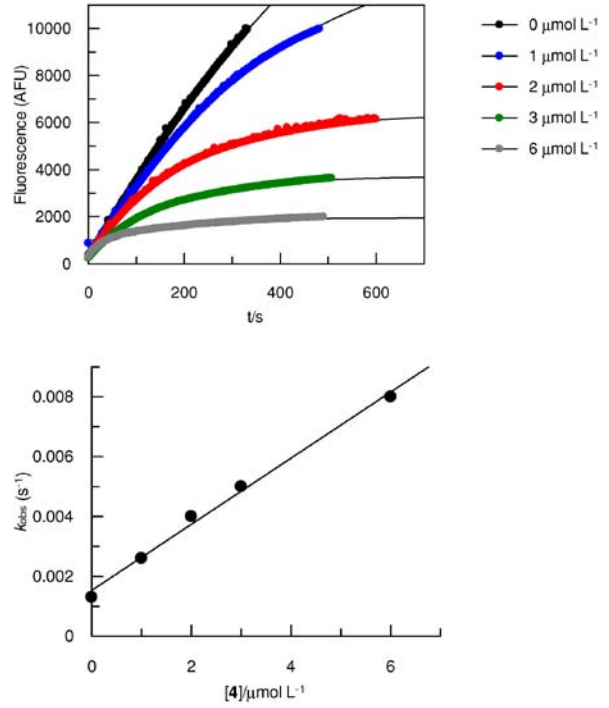

Figure S47. Enzyme kinetic for cathepsin V using selenane **4** as inhibitor**.**

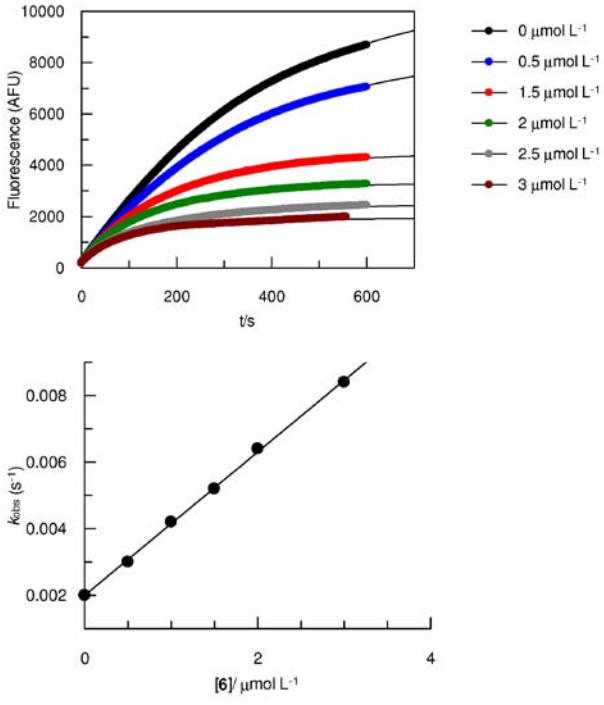

Figure S49. Enzyme kinetic for cathepsin V using selenane **6** as inhibitor**.**

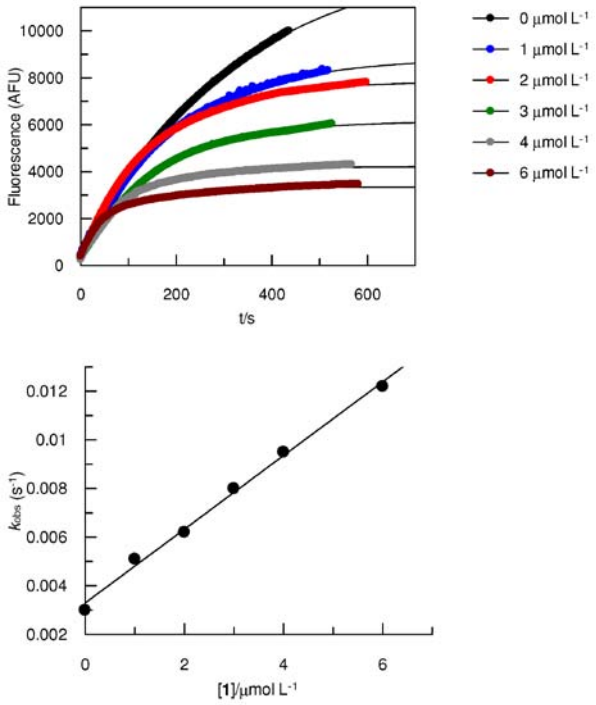

Figure S50. Enzyme kinetic for cathepsin S using selenane **1** as inhibitor**.**

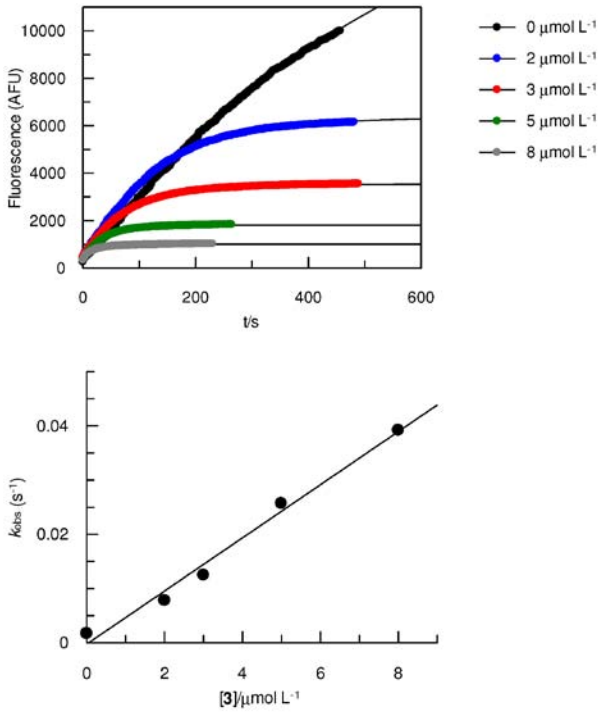

Figure S52. Enzyme kinetic for cathepsin S using selenane **3** as inhibitor**.**

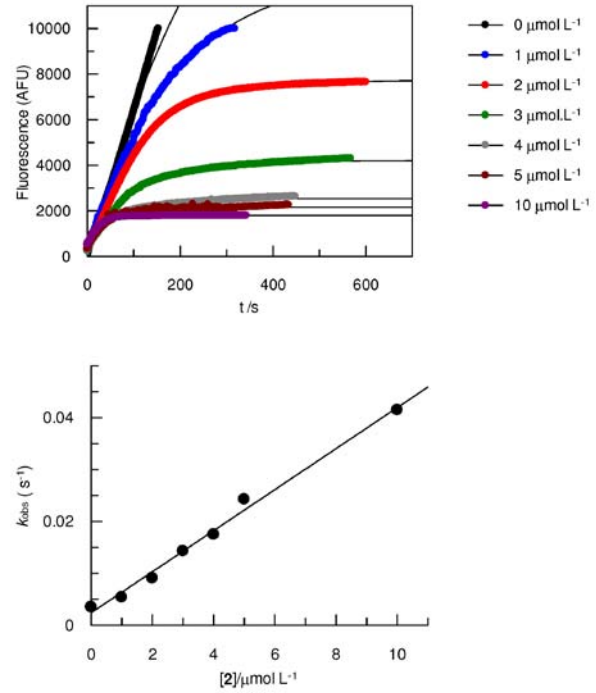

Figure S51. Enzyme kinetic for cathepsin S using selenane **2** as inhibitor**.**

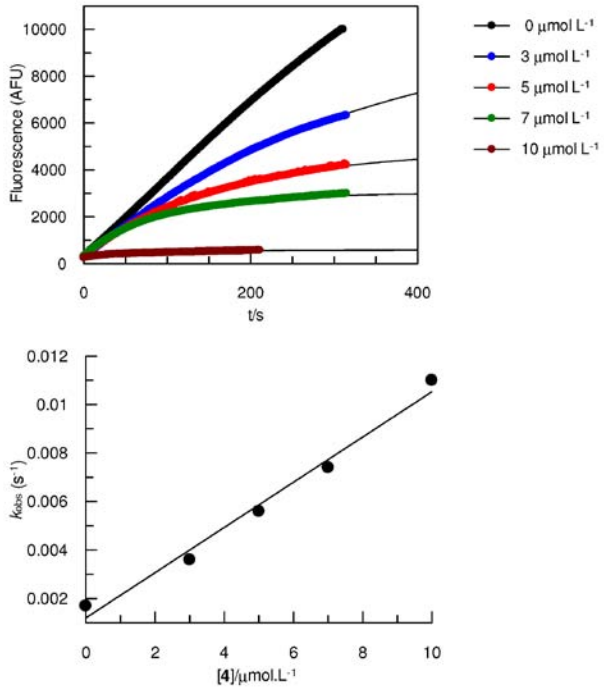

Figure S53. Enzyme kinetic for cathepsin S using selenane **4** as inhibitor**.**

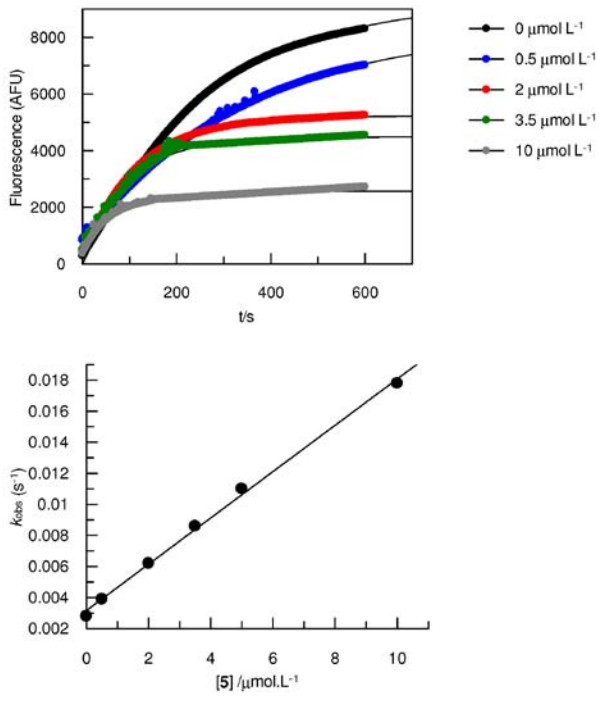

Figure S54. Enzyme kinetic for cathepsin S using selenane **5** as inhibitor**.**

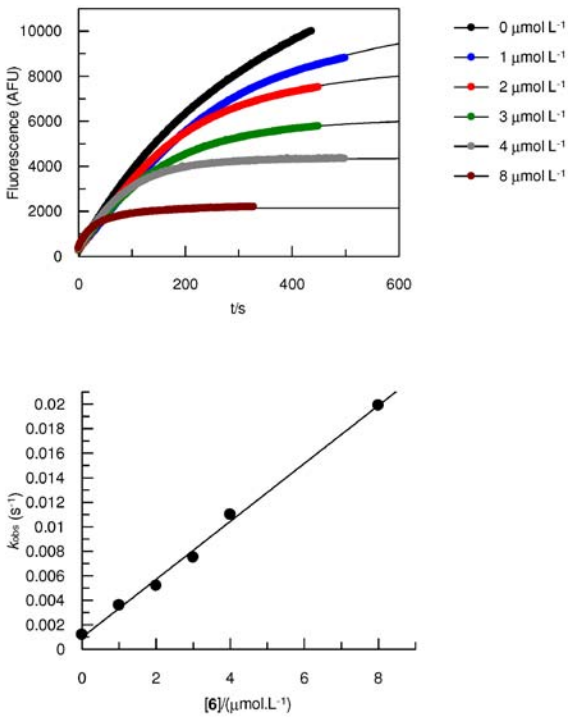

Figure S55. Enzyme kinetic for cathepsin S using selenane **6** as inhibitor**.**

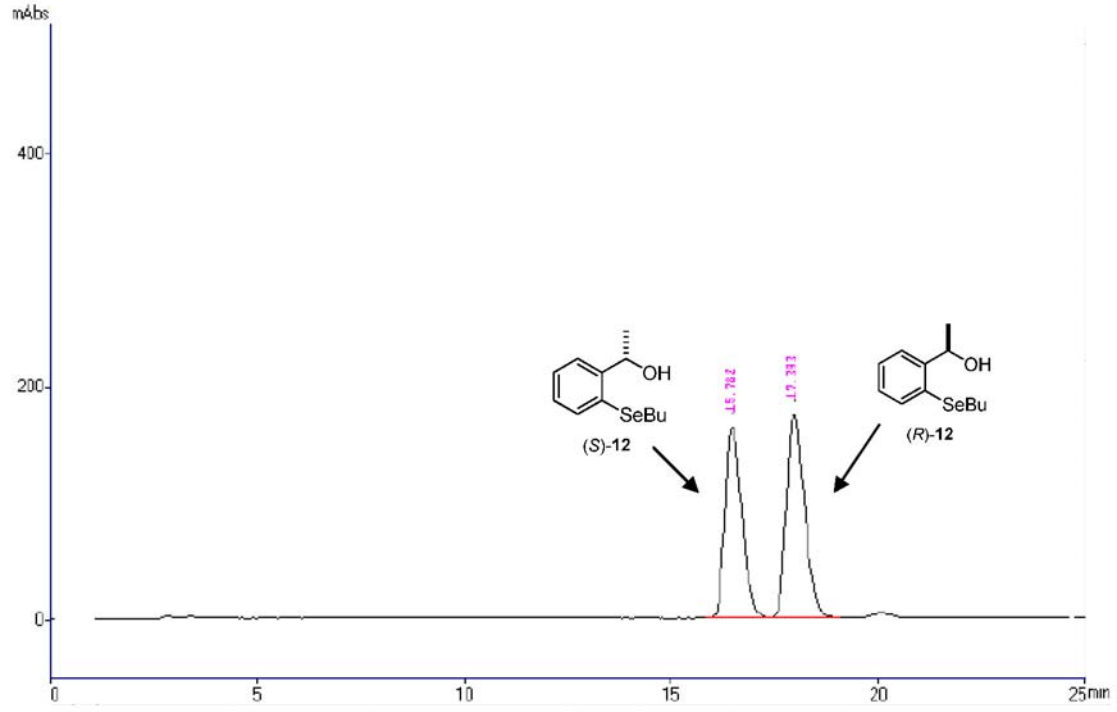

Figure S56. Enzymatic kinetic resolution of (*RS*)-**12**. The enantioenriched compounds (*S*)-**12** and (*R*)-**12** were prepared according to the method described in the text.

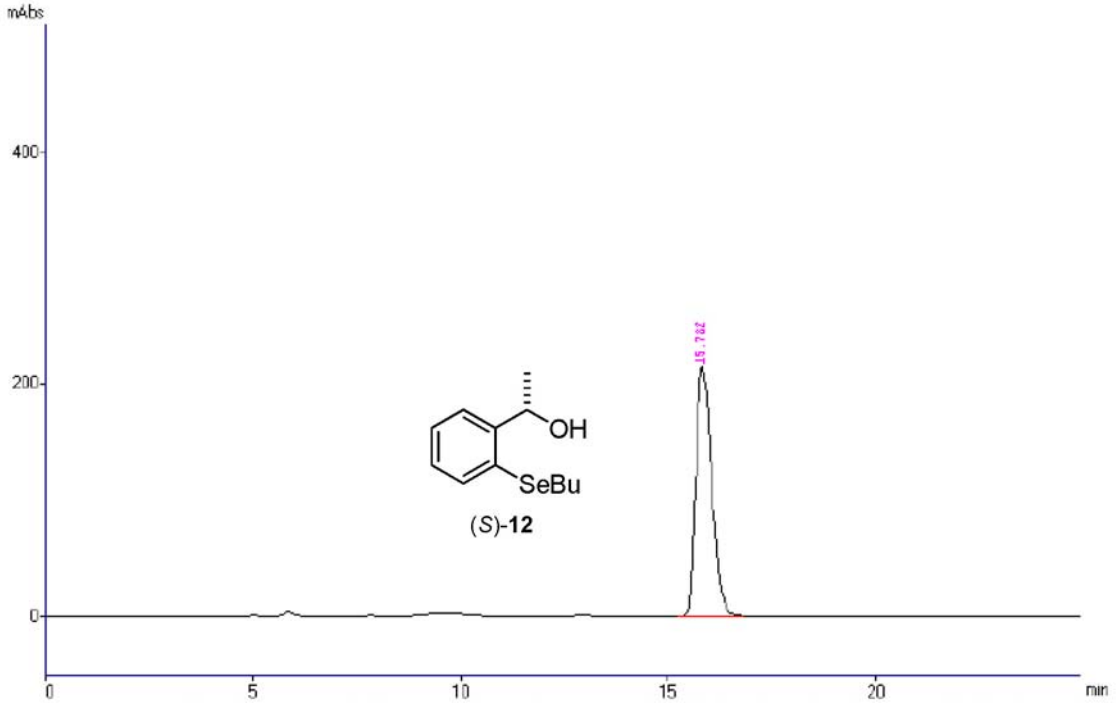

Figure S57. (*S*)-1-(2-(butylselanyl)phenyl)ethanol (**12**): Isolated yield = 45%; Enantiomeric excess > 99%; $[\alpha]_D^{22}$ = −23.9 (*c* = 0.78; $CHCl_3$). HPLC condition: Chiralcel® OJ-H column, *n*-hexane/*i*-PrOH (99:1), 1.0 mL min^{-1}, 254 nm UV detector, t_R = 15.8 min.

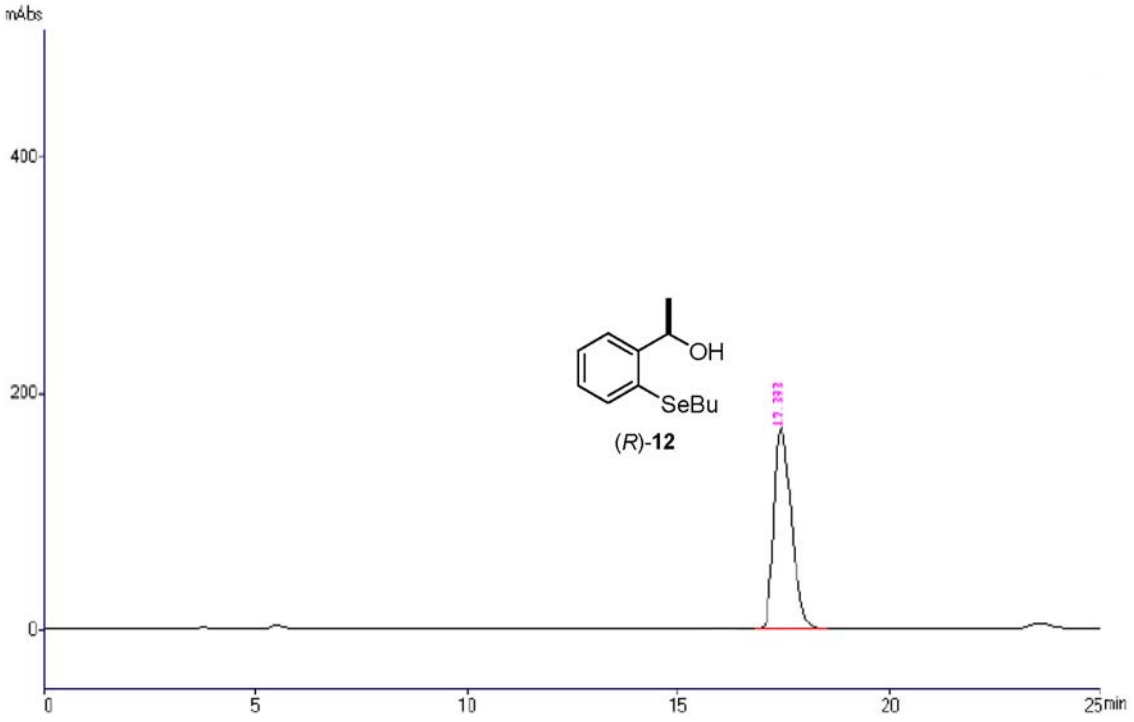

Figure S58. (*R*)-1-(2-(butylselanyl)phenyl)ethanol (**12**): Isolated yield = 45%; Enantiomeric excess > 99%; $[\alpha]_D^{22}$ = + 24.1 (*c* = 0.80; $CHCl_3$). HPLC condition: Chiralcel® OJ-H column, *n*-hexane/*i*-PrOH (99:1), 1.0 mL min^{-1}, 254 nm UV detector, t_R = 17.3 min.