Supplementary Information

Phenylselanyl-1*H*-1,2,3-triazole-4-carbonitriles: Synthesis, Antioxidant Properties and Use as a Precursor to Highly Functionalized Tetrazoles

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Biological Assays

Animals: Male adult albino Wistar rats (150 - 250 g) were used and them were kept on a separate animal room, in a 12 h light/dark cycle, at a room temperature of 22 ± 2 °C, with free access to food and water. Animals were used according to the guidelines of the Committee on Care and Use of Experimental Animal Resources, Universidade Federal de Pelotas, Brazil.

Tissue preparation: Rats were euthanized and cortex and hippocampus were rapidly removed, placed on ice and weighed. The cortex and hippocampus were dissected, kept chilled and homogenized in 50 mM Tris–HCl at pH 7.4 (1/5, weight/volume [w/v]). The homogenate was centrifuged for 10 min at 2000 rpm to yield a pellet that was discarded and a low-speed supernatant (S_1) was obtained, which was used for lipid peroxidation, reactive species (RS) levels and δ-ALA-D activity assays.

Ferric ion reducing antioxidant power (FRAP): The ferric ion (Fe^{3+}) reducing antioxidant power (FRAP) method was used to measure the reducing capacity of compounds. The assay was performed as described by Stratil et al. with slight modifications.[1] The FRAP reagent was prepared by mixing 38 mM an hydrous sodium acetate in distilled water (pH 3.8), 20 mM $FeCl_3.6H_2O$ in distilled water and 10 mM 2,4,6-tri(2-pyridyl)-s-triazine (TPTZ) in 40 mM HCl in proportions of 10:1:1. This reagent was freshly prepared before each experiment. Different concentrations of compounds and FRAP reagent were added to each sample, and the mixture was incubated at 37 °C for 40 min in the dark. The absorbance of the resulting solution was measured at 593 nm by spectrophotometer.

Sodium nitroprusside (SNP)-induced lipid peroxidation of linoleic acid system: In this assay, we used linoleic acid as a lipid matrix to evaluate the effect of compounds on SNP-induced lipid peroxidation. This process in brain induces neurotoxicity by its ability to NO-releasing, besides generate cytotoxic OH radicals via Fenton reaction catalyzed by its iron moiety, which contribute to cause oxidative stress and injury in brain.[2(Prigol et al., 2008; Ibrahim et al., 2014)] For this purpose, emulsion linoleic acid 48.8 mM in 100 mM TrisHCl, pH 7.5 and 0.025%. SDS was prepared. Then, TrisHCl 100 mM, emulsion linoleic acid, compounds (10 - 500 μM) and sodium nitroprusside (1 mM) were added. The mixture was incubated at 37 ° C for 30 min, leads to the peroxidation of linoleic acid. After this incubation, the reaction was stopped with TCA (trichloroacetic acid) and was added thiobarbituric acid (TBA 1%). The absorbance of the organic phase was measured at 532 nm using *n*-butanol as blank. The levels of lipid peroxidation were measured at 532 nm in spectrophotometer. Results are expressed as percentage of lipid peroxidation oxidation.

Lipid peroxidation induced by SNP in rat hippocampus and cortex: Lipid peroxidation in the cortex and hippocampus was performed by the formation of thiobarbituric acid reactive substances (TBARS) during an acid-heating reaction as previously described by Ohkawa et al..[3] For this purpose, the homogenate (S_1) was added to the reaction mixture containing 100 μM SNP and compounds at different concentrations (10 - 500 μM) and subsequently pre-incubated at 37 °C for 1h. The reaction product was determined using thiobarbituric acid (TBA, 0.8%), sodium dodecyl sulfate (SDS, 8.1%) and acetic acid (pH 3.4) after incubation at 95 °C for 2 h. The levels of lipid peroxidation were measured at 532 nm in spectrophotometer. Values were calculated as % inhibition related to induction.

Reactive species (RS) levels: In order to evaluate the capacity of the compounds in prevent the formation of reactive species, the samples were diluted (1:4) in 10 mM Tris–HCl (pH 7.4) and incubated with dichlorofluorescein (DCF; 3.5 mM) in the presence or the absence of a prooxidant -1 mM sodium azide, which acts by inhibiting the electron transport in Complex IV[4] and compounds (10 - 500 μM). The reactive species levels were determined by a spectrofluorimetric method, using 2′,7′-dichlorofluorescein diacetate (DCHF-DA) assay. The DCF fluorescence intensity emission was recorded at 520 nm (with 480 nm excitation) 15 min after the addition of DCHF-DA to the medium.

δ-ALA-D activity: δ-ALA-D activity from liver, kidney and brain were assayed by the method of Sassa.[5] To this end, S_1 was pre-incubated for 10 min at 37 °C in the presence of compounds at different concentrations (10 - 500 μM) or DMSO in the control tube. The enzymatic reaction was initiated by adding the substrate (ALA) in a medium containing 45 mM phosphate

[1] P. Stratil, B. Klejdus and V. Kuban, *J. Agric. Food. Chem.*, 2006, **54**, 607.
[2] (a) M. Prigol, E. A. Wilhelm, C. C. Schneider and C. W. Nogueira, *Chem. Biol. Interact.*, 2008, **176**, 129. (b) M. Ibrahim, W. Hassan, J. Anwar, A. M. Deobald, J. P. Kamdem, D. O. Souza and J. B. T. Rocha, *Toxicol. In Vitro*, 2014, **28**, 524.
[3] H. Ohkawa, N. Ohishi and K. Yagi, *Anal. Biochem.*, 1979, **95**, 351.
[4] J. Harvey, S. C. Hardy, M. L. J. Ashford, *Br. J. Pharmacol.*, 1999, **126**, 51.
[5] S. Sassa, *Enzyme*, 1982, **28**, 133.

buffer, pH 6.8 and incubated for 3 h at 37 °C. The incubation was stopped by adding 10% trichloroacetic acid solution (TCA) with $HgCl_2$. The reaction product (porphobilinogen) was measured at 555 nm using modified Ehrlich's reagent. The values are expressed as nmol Porphobilinogen (PBG) mg/protein/h. Protein was measured by the method of Lowry et al[6] using bovine serum albumin as the standard.

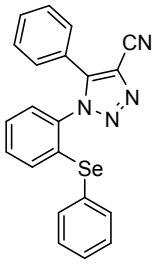
Statistical analysis: The results are presented as means ± standard error of the mean (S.E.M) for the *in vitro* tests. Statistical analysis was performed using a one-way analysis of variance (ANOVA) followed by Newman–Keuls multiple comparison tests when appropriate. All tests were performed in duplicate and repeated at least three times. Differences were considered statistically significant at a $P < 0.05$.

Chemistry

General Remarks: Proton nuclear magnetic resonance spectra (^{1}H NMR) were obtained at 400 MHz on a Bruker DPX-400 NMR spectrometer. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm, with tetramethylsilane (TMS) used as the external reference. Data are reported as follows: chemical shift (δ), multiplicity, coupling constant *(J)* in Hertz and integrated intensity. Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were obtained at 100 MHz on a Bruker DPX-400 NMR spectrometer. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm in reference to the solvent peak of $CDCl_3$. Abbreviations to denote the multiplicity of a particular signal are s (singlet), d (doublet), t (triplet), dt (doublet of triplet) and m (multiplet). Mass spectra (MS) were measured on a Shimadzu GCMS-QP2010 mass spectrometer. High resolution mass spectra (HRMS) were recorded on a Bruker Micro TOF-QII spectrometer 10416. Column chromatography was performed using a Merck Silica Gel (230-400 mesh). Thin layer chromatography (TLC) was performed using a 0.25 mm thick Merck Silica Gel GF_{254}. For visualization, TLC plates were either placed under ultraviolet light or stained with iodine vapor or acidic vanillin.

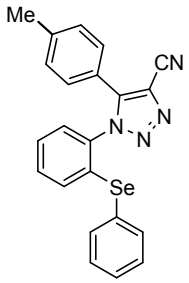
General Procedure for the Synthesis of phenylselanyl-1H-1,2,3-triazole-4-carbonitriles 3a-h: The appropriate α-keto nitrile (out of **2a-g**, 0.3 mmol) was first added to a solution of the appropriate azidophenyl phenylselenide (out of **1a-b**, 0.33 mmol) in DMSO (0.3 mL), followed by diethylamine (0.003 mmol) as catalyst. The reaction mixture was stirred in an open vial for the time indicated in Table 1 and Scheme 2. After completion of the reaction, the crude product was purified by column chromatography on silica gel with a mixture of hexane/ethyl acetate (5:1) as eluent to afford the desired product (**3a-h**). Spectral data for the products prepared are listed below.

Spectral data of products 3a-h:

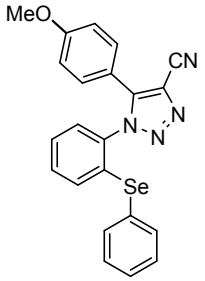


5-phenyl-1-(2-(phenylselanyl)phenyl)-1*H*-1,2,3-triazole-4-carbonitrile (3a): Yield: 0.091 g (91%); yellow solid; m.p. 94-96 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.49-7.23 (m, 14H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 144.11, 135.15, 134.79, 133.85, 132.43, 131.50, 130.97, 129.65, 129.23, 128.75, 128.70, 128.24, 128.07, 123.22, 119.69, 112.21. MS (relative intensity) m/z: 403 (6), 402 (22), 400 (12), 297 (48), 294 (100), 293 (40), 217 (53), 190 (60), 77 (41), 51 (26). HRMS: calculated to $C_{21}H_{15}N_4Se$ $[M + H]^+$: 403.0462. found 403.0470.

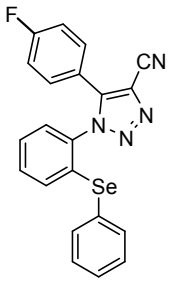
[6] O. H. Lowry, A. L. Rosebrough, A. L. Farr and R. Randall, *J. Biol. Chem.*, 1951, **193**, 265.



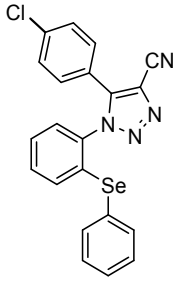
1-(2-(phenylselanyl)phenyl)-5-(*p*-tolyl)-1*H*-1,2,3-triazole-4-carbonitrile (3b): Yield: 0.112 g (80%); Orange solid; m.p. 88-90 ºC. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.36-7.16 (m, 13H), 2.34 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 144.26, 141.50, 135.34, 134.73, 133.92, 132.38, 131.42, 129.94, 129.60, 128.67, 128.55, 128.20, 128.08 (2C), 120.23, 119.41, 112.36, 21.43. MS (relative intensity) m/z: 417 (13), 416 (48), 414 (26), 387 (23), 311 (63), 309 (59), 308 (100), 298 (13), 296 (64), 294 (35), 293 (23), 232 (38), 231 (77), 216 (21), 204 (30), 179 (21), 153 (17), 152 (78), 151 (18), 77 (52), 51 (29). HRMS calcd for $C_{22}H_{17}N_4Se$ $[M + H]^+$: 417.0618. Found: 417.0596.



5-(4-methoxyphenyl)-1-(2-(phenylselanyl)phenyl)-1*H*-1,2,3-triazole-4-carbonitrile (3c): Yield: 0.102 g (79%); Yellow solid; m.p. 115-117 ºC. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.38-7.24 (m, 11H), 6.89 (dt, *J* = 8.9 and 2.9 Hz, 2H), 3.82 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 161.51, 144.05, 135.35, 134.76, 133.87, 132.40, 131.40, 130.20, 129.60, 128.68, 128.14, 128.09, 128.06, 119.01, 115.16, 114.74, 112.51, 55.37. MS (relative intensity) m/z: 433 (14), 432 (54), 430 (27), 329 (17), 327 (85), 325 (51), 324 (49), 323 (20), 312 (21), 309 (23), 296 (53), 294 (28), 248 (20), 247 (100), 232 (28), 204 (15), 152 (55), 151(14), 77 (28), 51 (17), 43 (13). HRMS calcd for $C_{22}H_{17}N_4OSe$ $[M + H]^+$: 433.0568. Found: 433.0545.

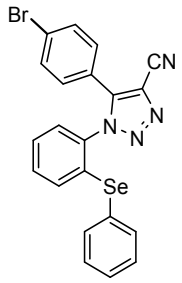


5-(4-fluorophenyl)-1-(2-(phenylselanyl)phenyl)-1*H*-1,2,3-triazole-4-carbonitrile (3d): Yield: 0.106 g (84%); Orange solid; m.p. 119-121 ºC. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7,36-7,24 (m, 11H), 7.06 (t, *J* = 8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 163.80 (d, *J* = 253 Hz), 134.97, 134.27, 133.93 (2C), 131.92, 131.53, 130.80 (d, *J* = 8.9 Hz), 129.52, 128.57, 128.21, 128.01, 127.82, 119.46, 119.24 (d, *J* = 3.5 Hz), 116.45 (d, *J* = 22.3 Hz), 111.91. MS (relative intensity) m/z: 421 (9), 420 (39), 418 (19), 391 (18), 389 (12), 315 (65), 314 (32), 313 (49), 312 (100), 311 (39), 235 (60), 232 (17), 208 (40), 183 (12), 179 (13), 153 (11), 152 (50), 77 (30), 51 (19). HRMS calcd for $C_{21}H_{14}FN_4Se$ $[M + H]^+$: 421.0368. Found: 421.0338.

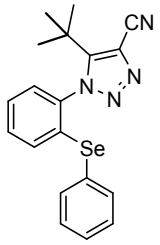


5-(4-chlorophenyl)-1-(2-(phenylselanyl)phenyl)-1*H*-1,2,3-triazole-4-carbonitrile (3e): Yield: 0.107 g (82%); Yellow solid; m.p. 99-100 ºC . ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.42-7.26 (m, 13H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 143.09, 137.49, 135.03, 134.50, 134.13, 132.18, 131.72, 129.93, 129.72, 129.66, 128.78, 128.32, 128.09, 127.89, 121.67,

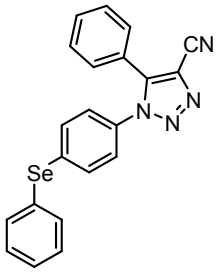
119.76, 111.97. MS (relative intensity) m/z: 438 (23), 436 (47), 434 (25), 408 (15), 407 (24), 333 (23), 331 (56), 330 (39), 329 (52), 328 (100), 327 (23), 296 (89), 294 (52), 292 (37), 251 (60), 232 (26), 224 (25), 216 (33), 190 (24), 179 (23), 157 (12), 152 (85), 77 (54), 76 (12), 51 (34). HRMS calcd for $C_{21}H_{14}ClN_4Se$ $[M + H]^+$: 437.0072. Found: 437.0071.



5-(4-bromophenyl)-1-(2-(phenylselanyl)phenyl)-1*H*-1,2,3-triazole-4-carbonitrile (3f): Yield: 0.108 g (75%); Yellow solid; m.p. 105-106 ºC. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.53 (dt, *J* = 8.8 and 2.6 Hz, 2H), 7.41-7.31 (m, 5H), 7.27-7.24 (m, 4H), 7.22 (dt, *J* = 8.8 and 2.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 143.14, 135.03, 134.47, 134.18, 132.62, 132.15, 131.73, 130.07, 129.73, 128.78, 128.34, 128.09, 127.90, 125.85, 122.14, 119.73, 111.95. MS (relative intensity) m/z: 482 (84), 481 (13), 480 (43), 478 (20), 451 (20), 377 (32), 375 (53), 374 (66), 373 (44), 372 (68), 298 (25), 297 (51), 296 (100), 295 (48), 294 (53), 293 (43), 268 (16), 232 (25), 216 (36), 190 (27), 179 (21), 152 (74), 115 (10), 114 (16), 77 (49), 51 (31). HRMS calcd for $C_{21}H_{14}BrN_4Se$ $[M + H]^+$: 480.9567. Found: 480.9583.



5-(*tert*-butyl)-1-(2-(phenylselanyl)phenyl)-1*H*-1,2,3-triazole-4-carbonitrile (3g): Yield: 0.025 g (22%); Yellow solid; m.p. 94-95 ºC. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.55-7.53 (m, 2H), 7.43-7.32 (m, 6H), 7.26-7.22 (m, 1H), 1.42 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 152.32, 136.25, 135.57, 134.75, 132.18, 131.60, 129.87, 129.15, 128.76, 128.60, 127.06, 119.10, 113.26, 32.55, 30.05. MS (relative intensity) m/z: 382 (31), 380 (16), 339 (29), 298 (24), 297 (31), 295 (19), 277 (23), 273 (10), 271 (12), 259 (16), 232 (21), 219 (15), 218 (64), 197 (21), 190 (11), 182 (26), 157 (26), 155 (26), 152 (41), 115 (11), 77 (43), 57 (100), 51 (25), 41 (50). HRMS calcd for $C_{19}H_{19}N_4Se$ $[M + H]^+$: 383.0775. Found: 383.0746.

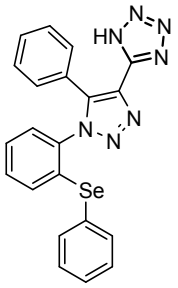


5-phenyl-1-(4-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carbonitrile (3h): Yield: 0.108 g (90%); Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.59-7.56 (m, 2H), 7.50-7.33 (m, 10H), 7.18 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 142.85, 136.13, 134.87, 133.49, 131.64, 131.09, 129.74, 129.41, 128.84, 128.67, 128.32, 125.50, 123.15, 120.56, 111.92. MS (relative intensity) m/z: 402 (14), 400 (7), 374 (28), 371 (6), 295 (25), 294 (100), 293 (14), 232 (21), 230 (11), 218 (12), 217 (62), 216 (12), 190 (34), 179 (10), 165 (8), 157 (15), 153 (10), 152 (27), 115 (23), 114 (12), 77 (27), 51 (16). HRMS calcd for $C_{21}H_{15}N_4Se$ $[M + H]^+$: 403.0462. Found: 403.0447.

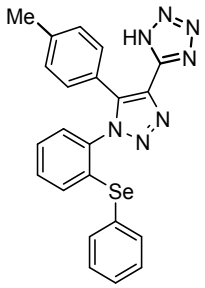
General Procedure for the Synthesis of 5-aryl-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazol-4-yl)-1H-tetrazoles 4a-f: A mixture of the appropriate phenylselanyl-1*H*-1,2,3-triazole-4-carbonitrile (out of **3a-f**, 0.3 mmol), sodium azide (0.5 mmol), $Al_2O_3/FeCl_3$ (0.018 g) and DMF (1.5 mL) was taken in a round-bottomed flask and stirred at 120 °C temperature for 48 h under air atmosphere. After this time, HCl (3 M, 2 mL) and ethyl acetate (10 mL) were added, and vigorous stirring was continued until no solid was present and the aqueous layer had a pH of 2. The resultant organic layer was separated and the aqueous layer was extracted with ethyl acetate (2x 10 mL). The combined organic layers were dried with $MgSO_4$ and

evaporated under reduced pressure. The resultant products were isolated in chromatography column with hexane/ethyl acetate as eluent and recrystallized if necessary to afford the desired product (**4a-f**). Spectral data for the products prepared are listed below.

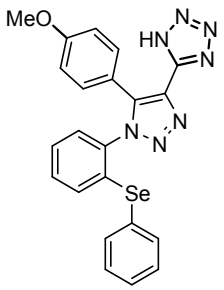
Spectral data of products 4a-f.



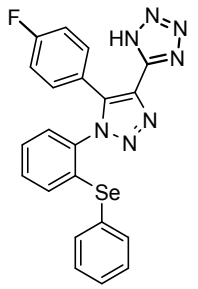
5-(5-phenyl-1-(2-(phenylselanyl)phenyl)-1*H*-1,2,3-triazol-4-yl)-1*H*-tetrazole (4a): Yield: 0.084 g (63%); white solid; m.p. 241-242 ºC; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.48-7.26 (m, 15H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 138.13, 135.19, 134.30, 132.92, 132.16, 131.16, 130.66, 129.96, 129.62, 129.23, 128.20, 128.07, 127.95, 127.84, 127.32, 124.22. MS (relative intensity) m/z: 446 (9), 445 (36), 443 (20), 402 (16), 360 (15), 340 (21), 297 (36), 294 (61), 293 (26), 281 (32), 280 (28), 271 (66), 269 (38), 232 (49), 217 (29), 205 (34), 190 (35), 179 (17), 152 (78), 151 (27), 139 (16), 129 (32), 111 (21), 103 (25), 97 (38), 77 (81), 69 (60), 63 (15), 60 (20), 57 (76), 51 (42), 44 (52), 43 (95), 41 (54), 40 (100). HRMS calcd for $C_{21}H_{16}N_7Se$ $[M + H]^+$: 446.0632. Found: 446.0621.



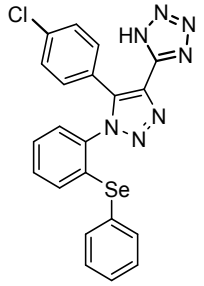
5-(1-(2-(phenylselanyl)phenyl)-5-(*p*-tolyl)-1*H*-1,2,3-triazol-4-yl)-1*H*-tetrazole (4b): Yield: 0.095 g (75%); Yellow solid; m.p. 149-151 ºC; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.38-7.23 (m, 12H), 7.15 (d, *J* = 8 Hz, 2H), 2.34 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 148.26, 140.72, 139.37, 135.74, 134.75, 133.74, 132.68, 131.15, 130.73, 130.31, 129.61, 129.30, 128.69, 128.58, 128.32, 127.80, 121.08, 21.44. MS (relative intensity) m/z: 461 (15), 460 (19), 459 (72), 457 (38), 416 (20), 374 (20), 354 (26), 326 (22), 308 (52), 285 (100), 283 (59), 246 (29), 232 (45), 231 (74), 217 (31), 204 (26), 152 (72), 143 (29), 117 (27), 91 (28), 78 (23), 77 (66), 57 (21), 55 (20), 51 (35), 44 (18), 43 (28), 40 (35). HRMS calcd for $C_{22}H_{18}N_7Se$ $[M + H]^+$: 460.0789. Found: 460.0747.



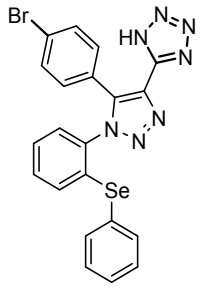
5-(5-(4-methoxyphenyl)-1-(2-(phenylselanyl)phenyl)-1*H*-1,2,3-triazol-4-yl)-1*H*-tetrazole (4c): Yield: 0.081 g (57%); white solid; m.p. 193-195 ºC; ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 7.68-7.66 (m, 1H), 7.46-7.44 (m, 2H), 7.39-7.35 (m, 7H), 7.28-7.26 (m, 1H), 6.96 (d, *J* = 8.5 Hz, 2H), 3.77 (s, 3H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ = 160.34, 148.22, 138.32, 135.47, 134.12, 133.06, 131.67, 131.56, 131.40, 130.61, 129.78, 128.95, 128.58, 128.28, 128.22, 116.10, 113.78, 55.16. MS (relative intensity) m/z: 475 (2), 368 (11), 298 (8), 232 (8), 152 (17), 133 (14), 129 (14), 121 (13), 111 (21), 98 (27), 97 (37), 83 (50), 77 (17), 71 (44), 69 (54), 57 (100), 56 (24), 55 (92), 44 (33), 43 (86), 42 (15), 41 (51), 40 (31). HRMS calcd for $C_{22}H_{18}N_7OSe$ $[M + H]^+$: 476.0738. Found: 476.0700.



5-(5-(4-fluorophenyl)-1-(2-(phenylselanyl)phenyl)-1*H*-1,2,3-triazol-4-yl)-1*H*-tetrazole (4d): Yield: 0.078 g (56%); brown solid m.p. 92-94 ºC; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.52-7.48 (m, 2H), 7.34-7.27 (m, 9H), 7.05 (t, *J* = 8.7 Hz, 2H).. ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 163.72 (d, *J* = 252 Hz), 148.07, 138.30, 134.64, 133.61, 132.64, (d, *J* = 8.7 Hz), 132.02, 131.42, 130.93, 129.70, 128.72, 128.30, 128.15, 127.92, 120.03 (d, *J* = 2.6 Hz), 119.16, 115.88 (d, *J* = 22.0 Hz). MS (relative intensity) m/z: 383 (2), 355 (3), 155 (14), 137 (8), 127 (15), 125 (10), 111 (20), 98 (22), 97 (38), 85 (32), 84 (25), 77 (7), 73 (18), 71 (51), 67 (23), 57 (100), 56 (26), 55 (83), 44 (44), 43 (98), 41 (45), 40 (14). HRMS calcd for $C_{21}H_{15}FN_7Se$ $[M + H]^+$: 464.0538. Found: 464.0529.

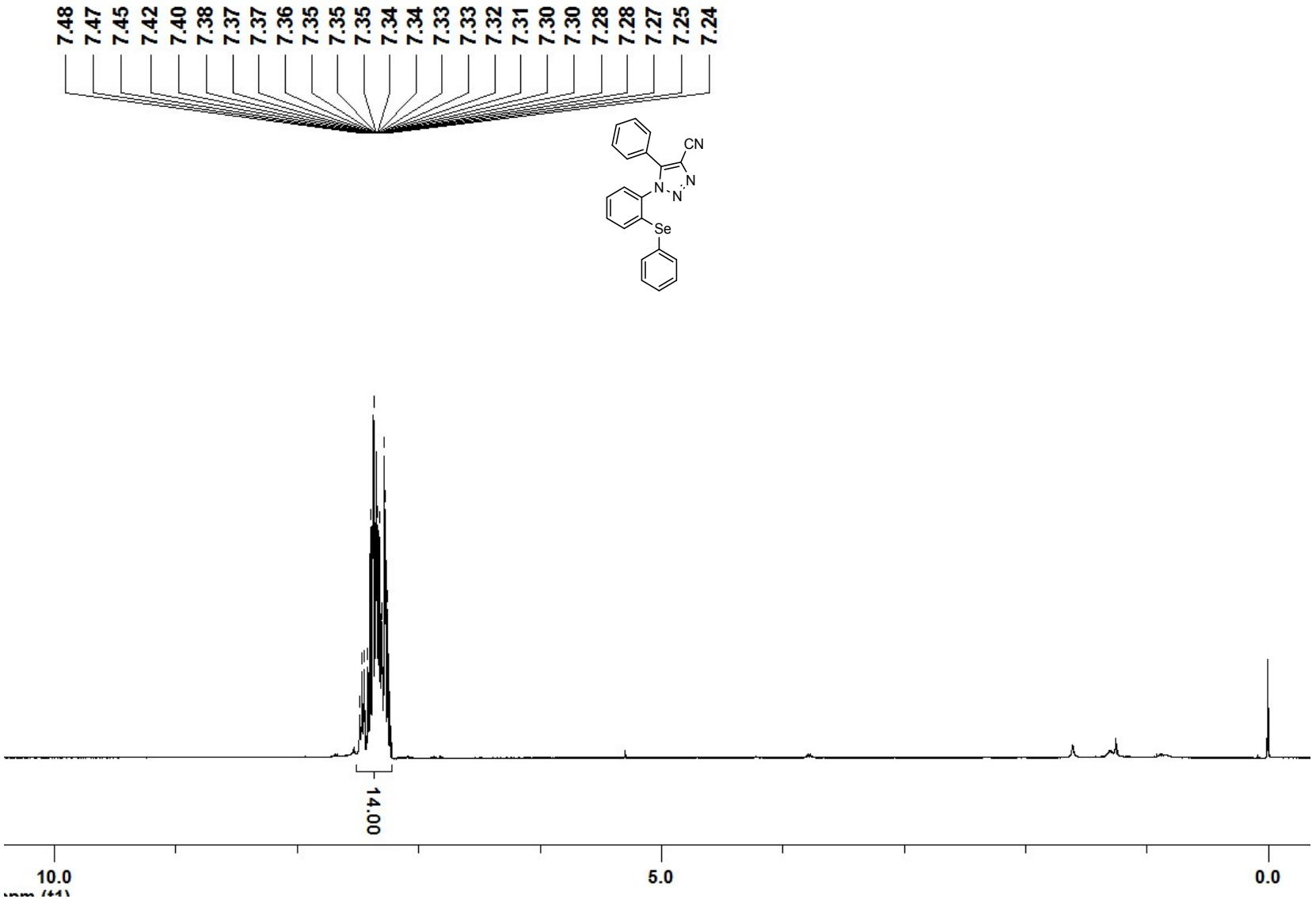


5-(5-(4-chlorophenyl)-1-(2-(phenylselanyl)phenyl)-1*H*-1,2,3-triazol-4-yl)-1*H*-tetrazole (4e): Yield: 0.139 g (96%); white solid; m.p. 238-240 ºC; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.46 (d, *J* = 8.5 Hz, 2H), 7.36-7.27 (m, 12H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 147.88, 138.17, 136.91, 135.22, 134.55, 133.83, 132.47, 131.78, 131.52, 130.80, 129.74, 128.96, 128.73, 128.27, 128.20, 128.03, 122.41. MS (relative intensity) m/z: 479 (2), 367 (11), 339 (6), 313 (9), 239 (9), 171 (8), 152 (6), 137 (9), 135 (9), 129 (13), 123 (14), 121 (10), 111 (21), 110 (10), 109 (19), 98 (30), 97 (41), 95 (36), 85 (32), 71 (43), 70 (15), 69 (56), 57 (98), 55 (100), 44 (11), 43 (73), 42 (10), 41 (46). HRMS calcd for $C_{21}H_{15}ClN_7Se$ $[M + H]^+$: 480.0243. Found: 480.0353.

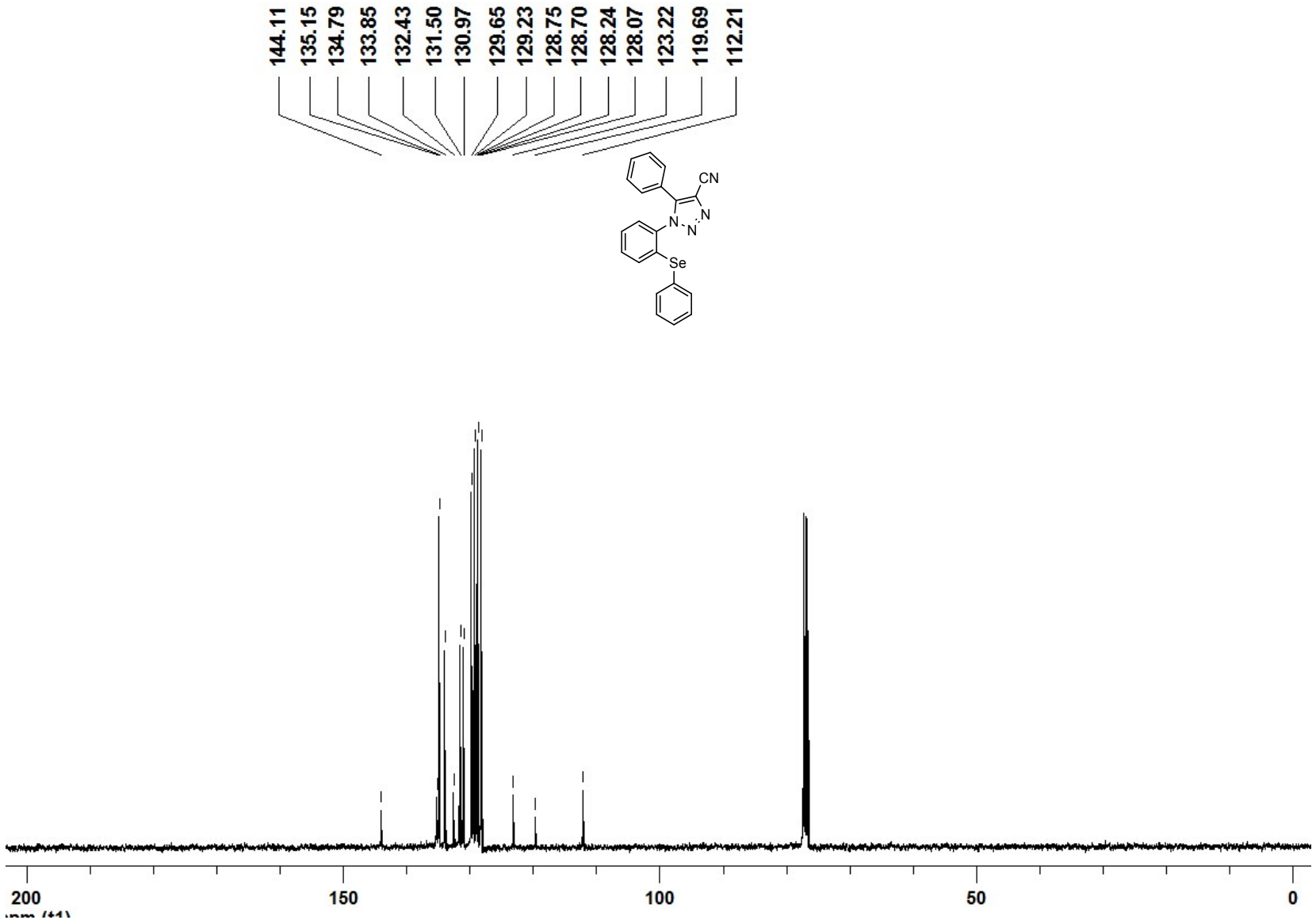


5-(5-(4-bromophenyl)-1-(2-(phenylselanyl)phenyl)-1*H*-1,2,3-triazol-4-yl)-1*H*-tetrazole (4f): Yield: 0.094 g (59%); white solid; m.p. 216-217 ºC; ^{1}H NMR (DMSO-d_6, 400 MHz) δ = 7.18-7.16 (m, 1H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.94-6.89 (m, 2H), 6.88-6.72 (m, 9H). ^{13}C NMR (DMSO-d_6, 100 MHz) δ = 148.38, 137.32, 135.11, 133.99, 133.17, 132.21, 131.79, 131.37, 131.20 (2C), 129.80, 129.04, 128.60, 128.40, 128.06, 123.88, 123.72. MS (relative intensity) m/z: 525 (19), 523 (24), 480 (17), 374 (32), 372 (34), 349 (22), 311 (23), 296 (50), 295 (23), 231 (53), 190 (27), 157 (22), 152 (87), 97 (35), 89 (21), 71 (39), 69 (55), 57 (88), 55 (99), 50 (32), 43 (100), 42 (21), 41 (64), 40 (73). HRMS calcd for $C_{21}H_{15}BrN_7Se$ $[M + H]^+$: 523.9738. Found: 523.9727.

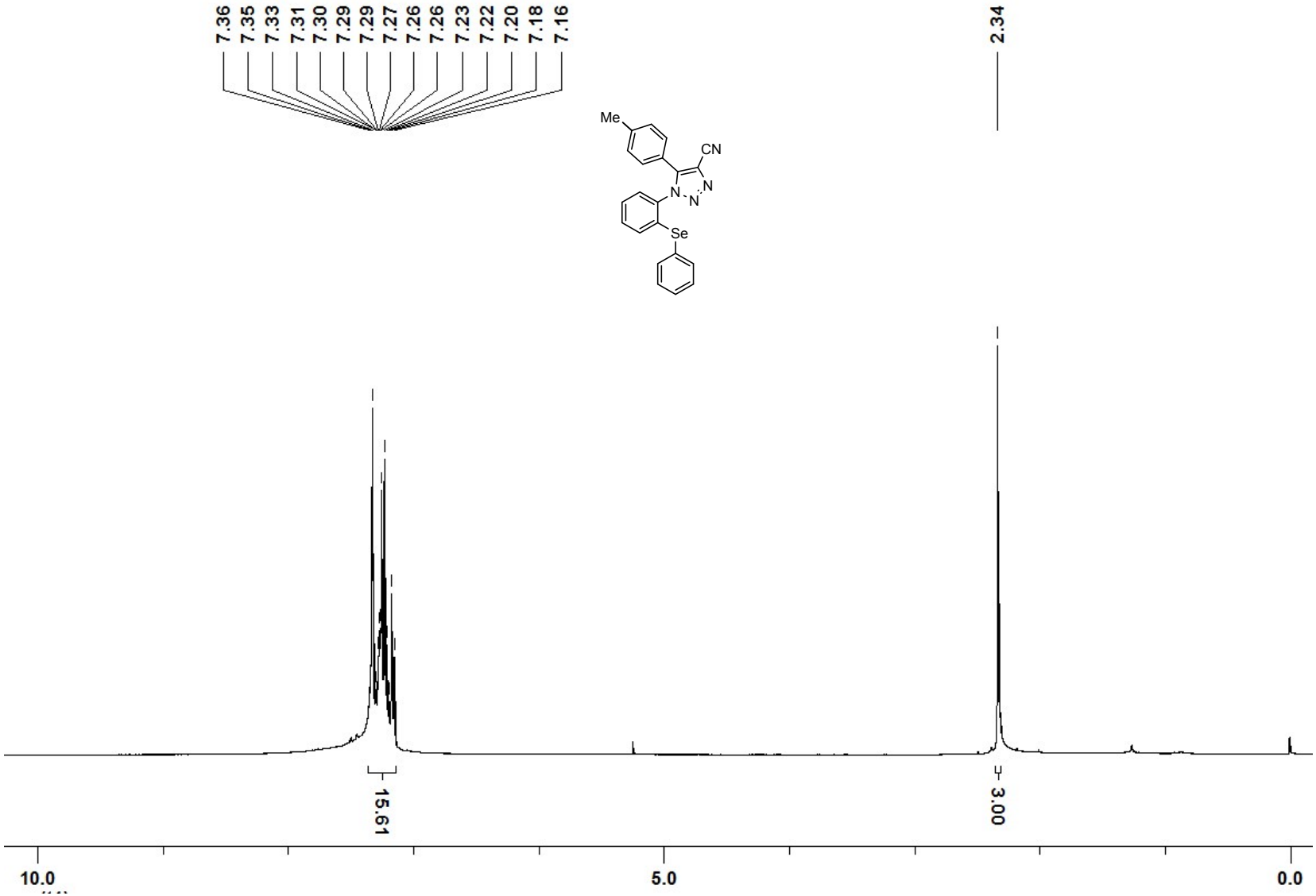
SELECTED SPECTRA



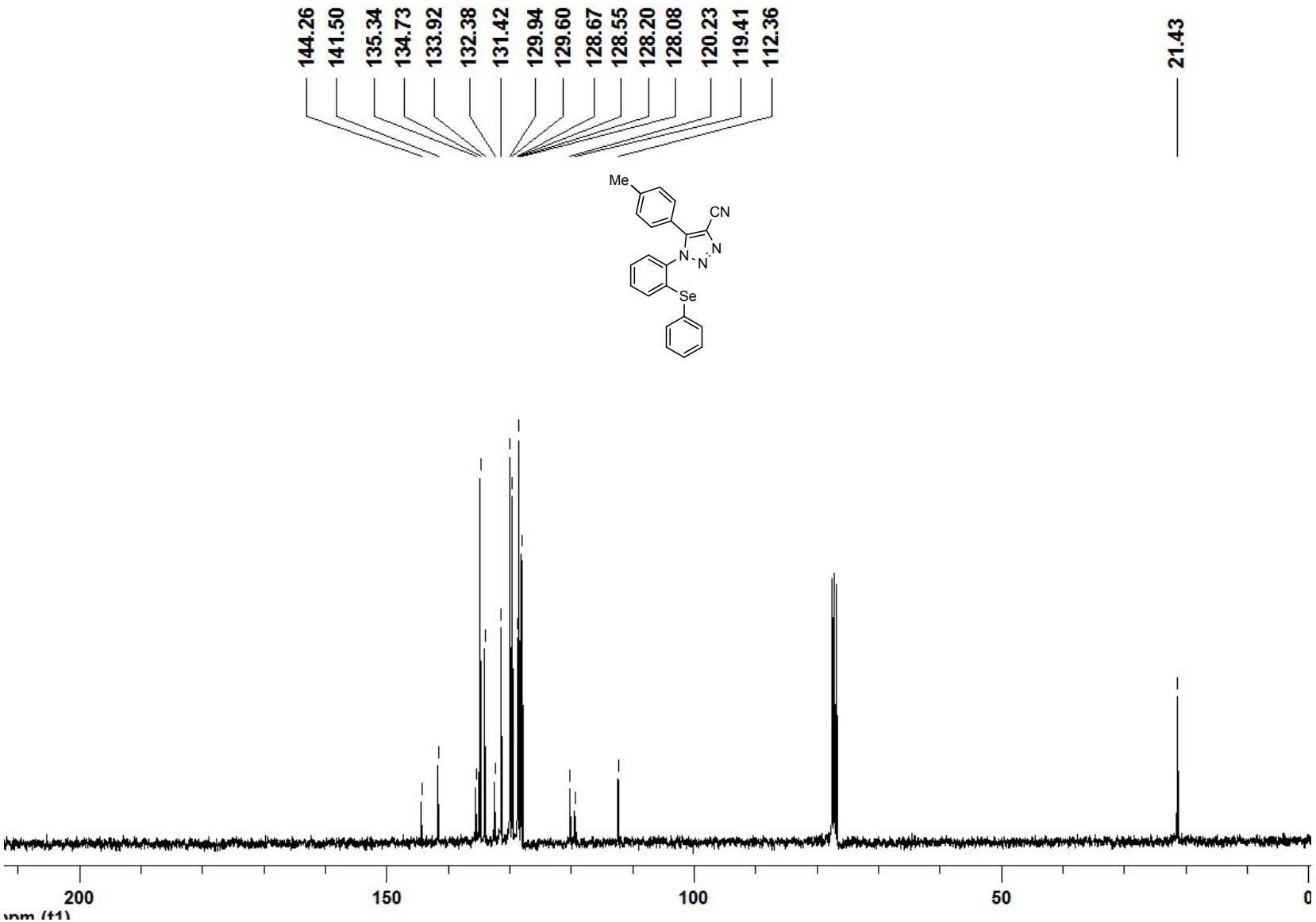
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of ***5-phenyl-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carbonitrile (3a)***



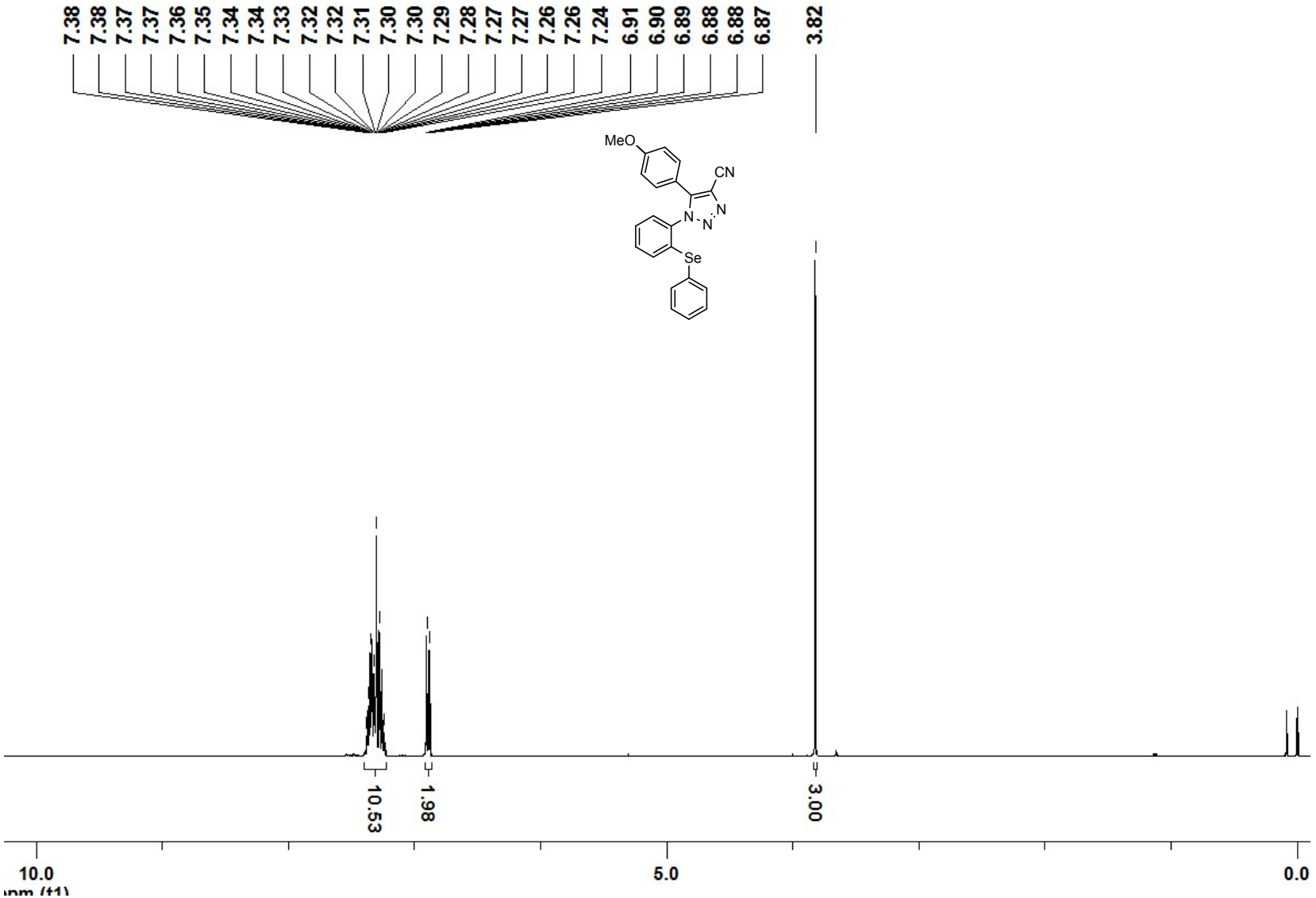
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of ***5-phenyl-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carbonitrile (3a)***



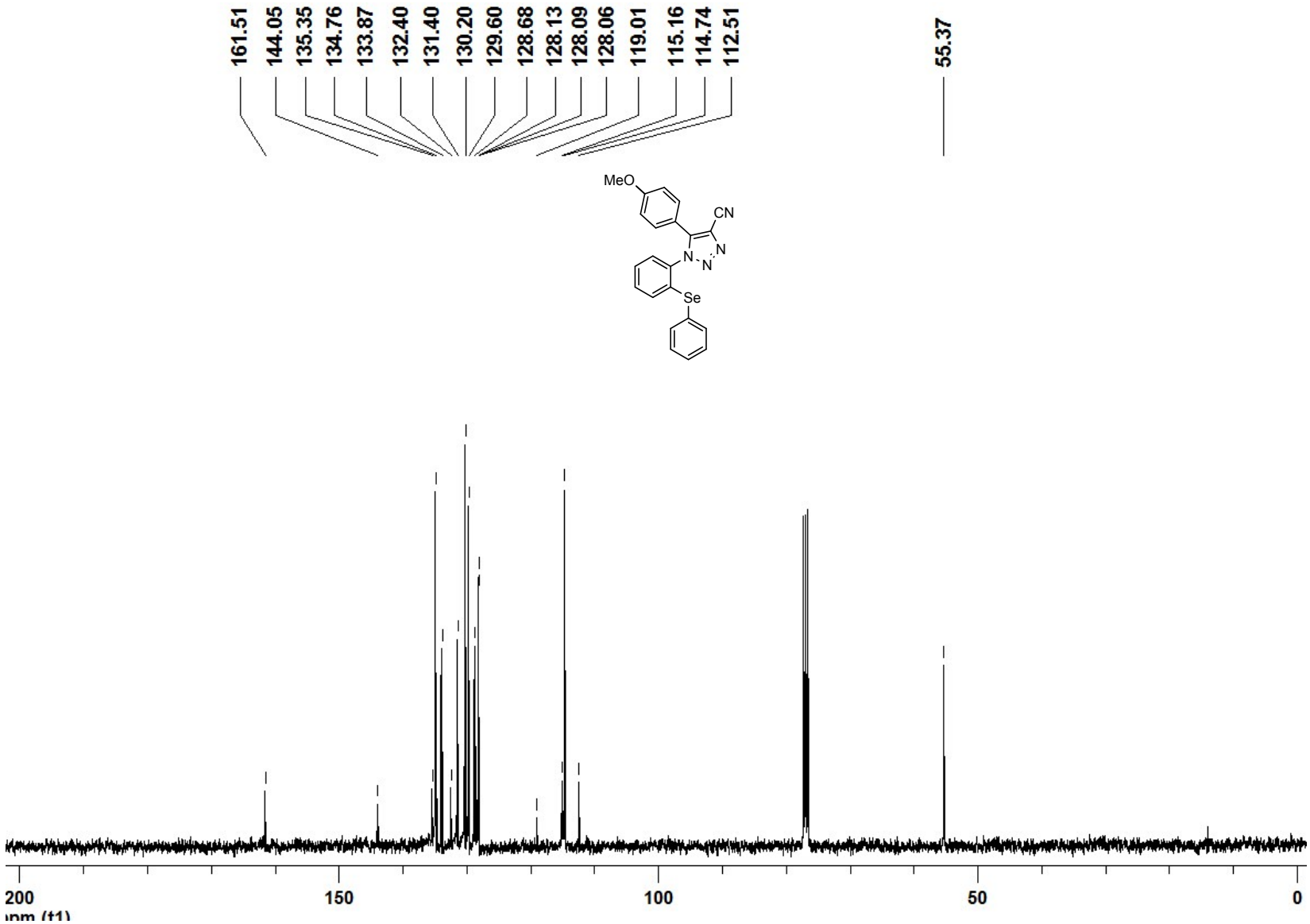
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of ***1-(2-(phenylselanyl)phenyl)-5-(p-tolyl)-1H-1,2,3-triazole-4-carbonitrile (3b)***



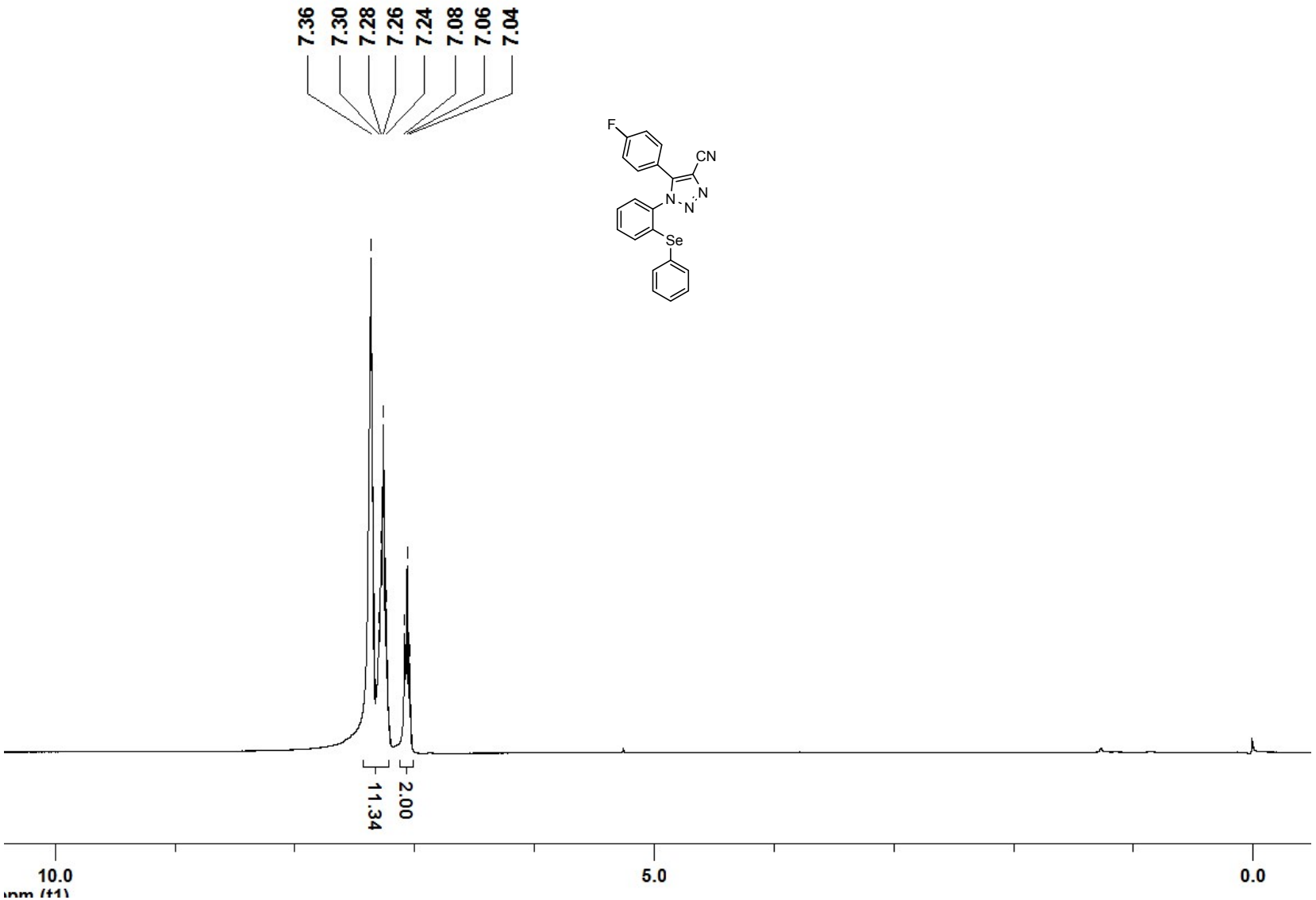
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of ***1-(2-(phenylselanyl)phenyl)-5-(p-tolyl)-1H-1,2,3-triazole-4-carbonitrile (3b)***



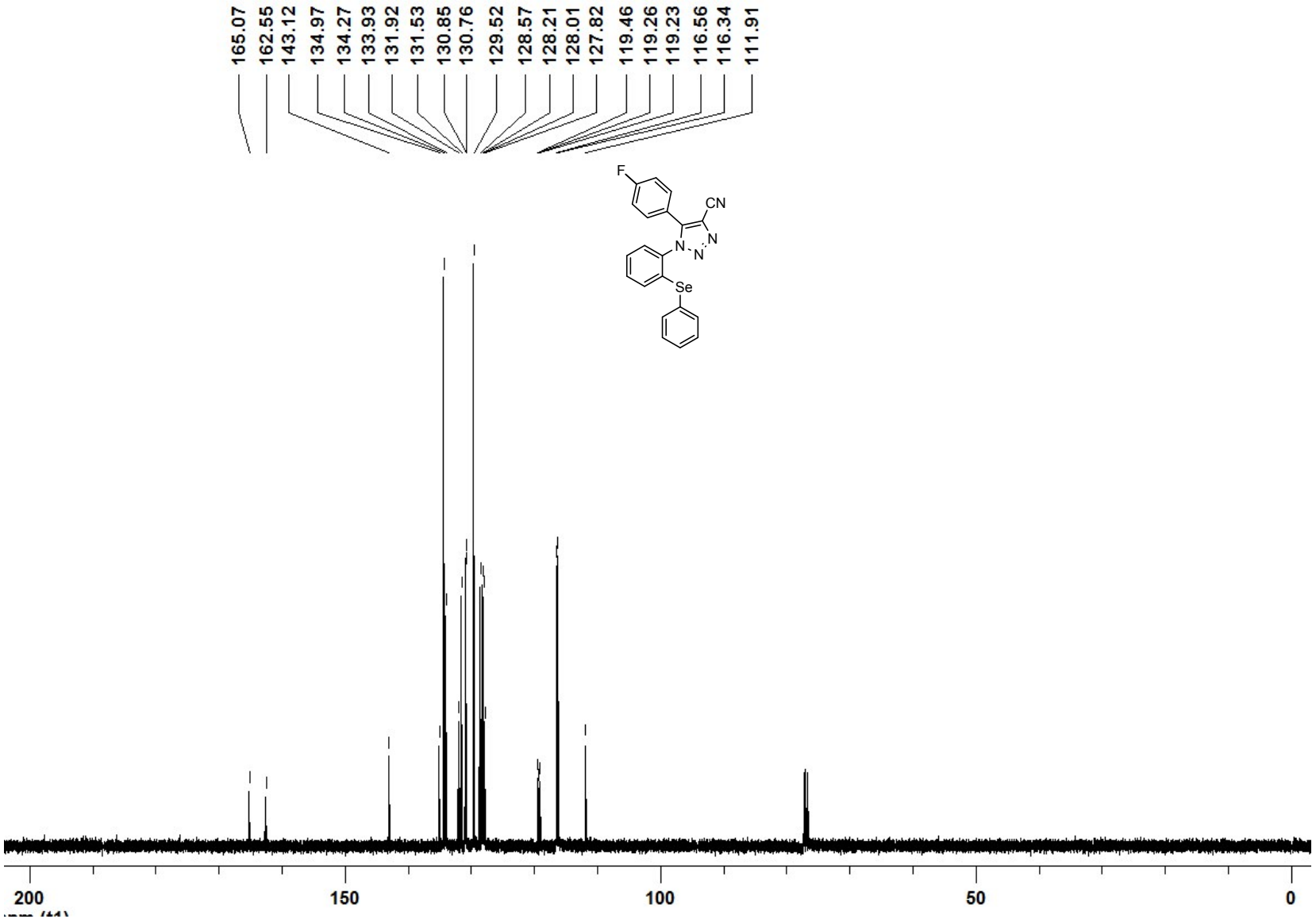
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of ***5-(4-methoxyphenyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carbonitrile (3c)***



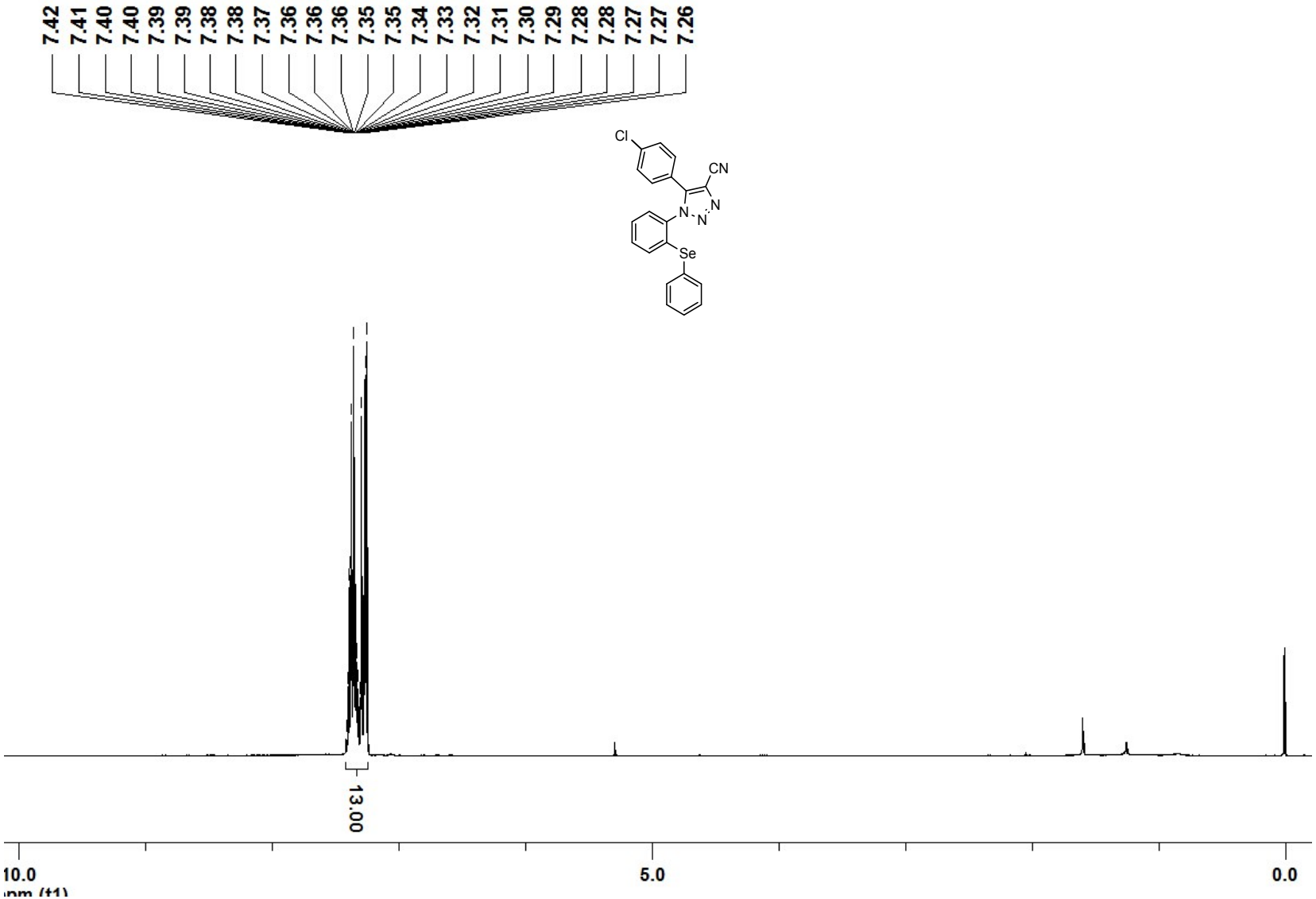
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of ***5-(4-methoxyphenyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carbonitrile (3c)***



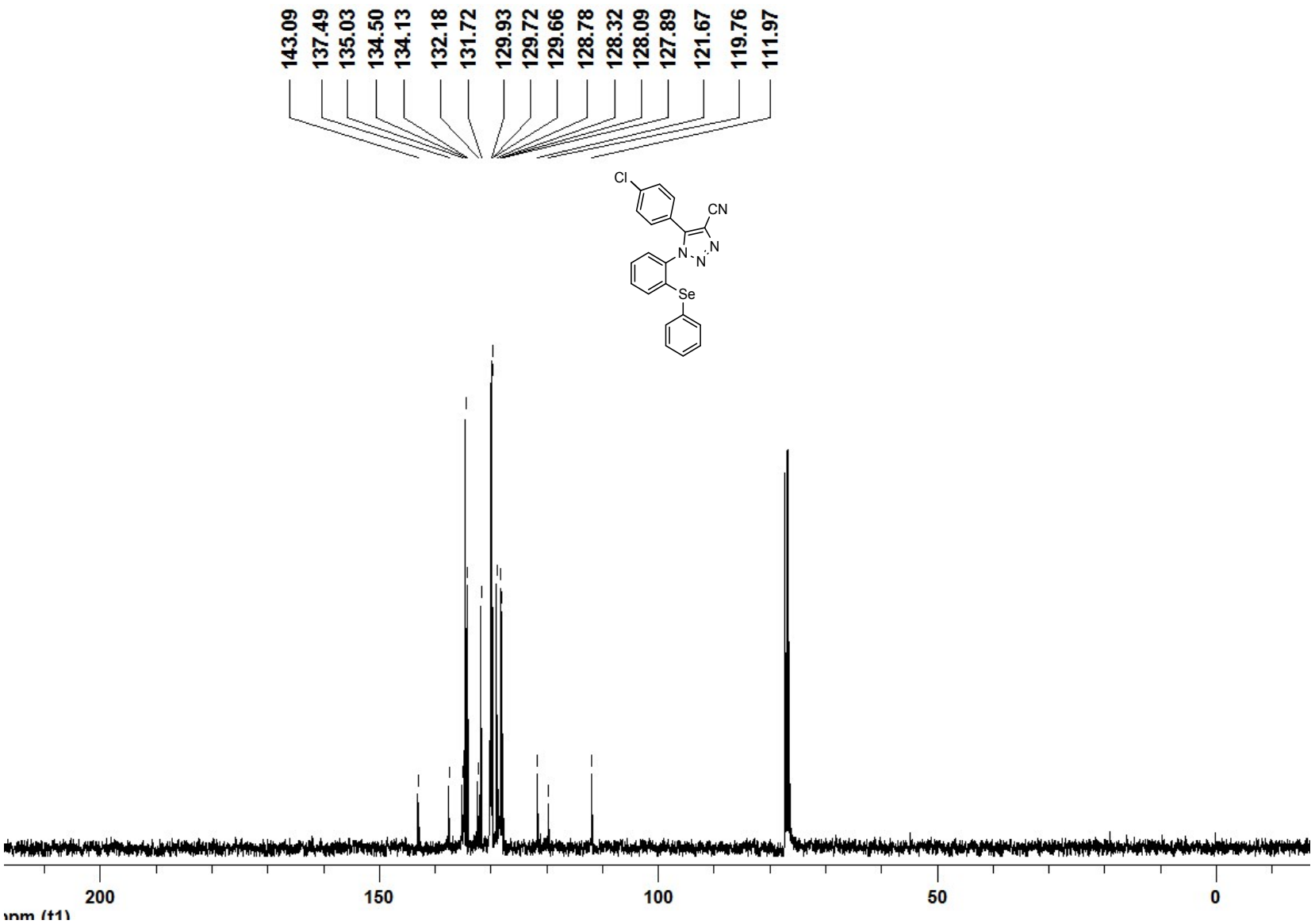
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of ***5-(4-fluorophenyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carbonitrile (3d)***



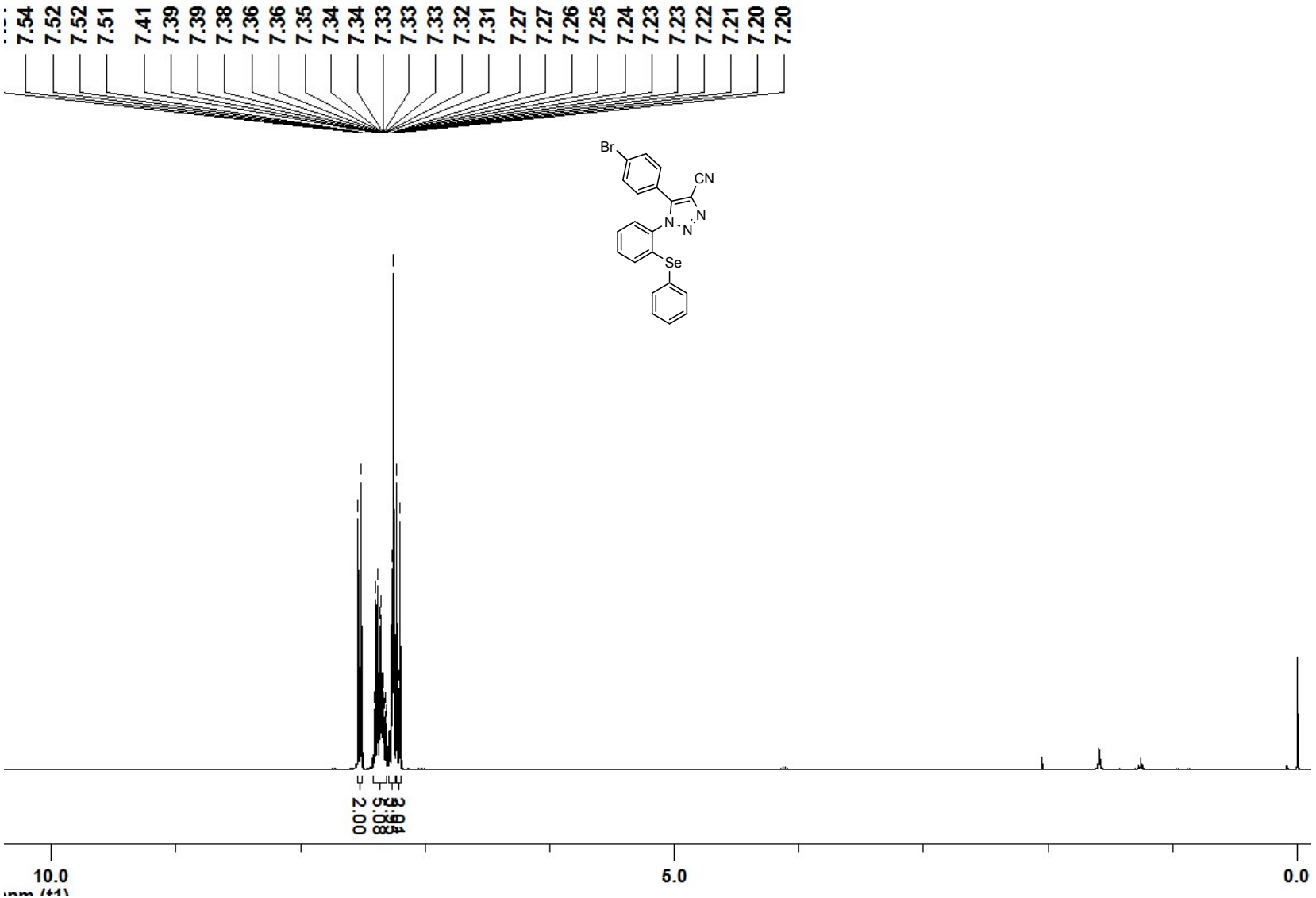
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of ***5-(4-fluorophenyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carbonitrile (3d)***



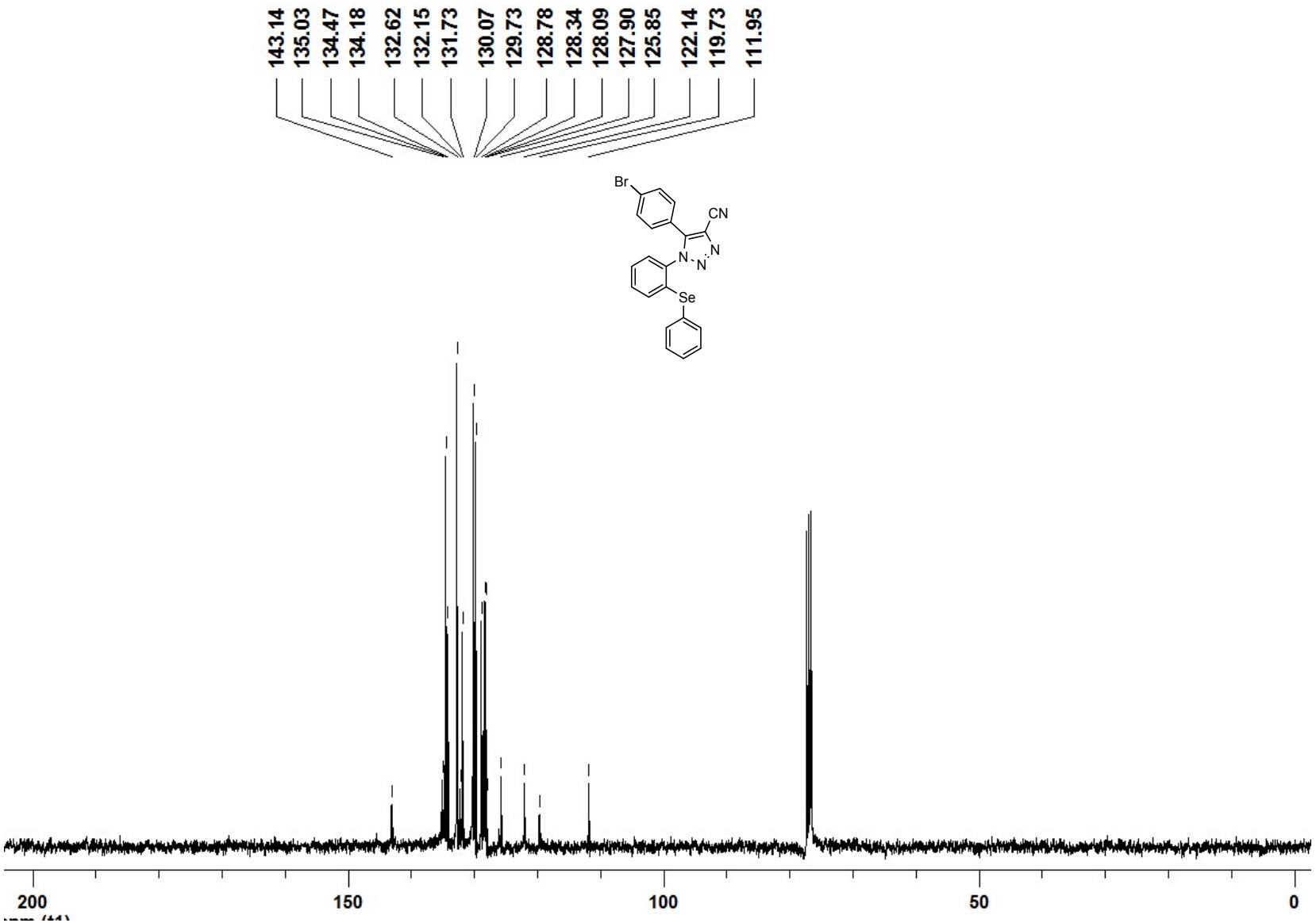
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of ***5-(4-chlorophenyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carbonitrile (3e)***



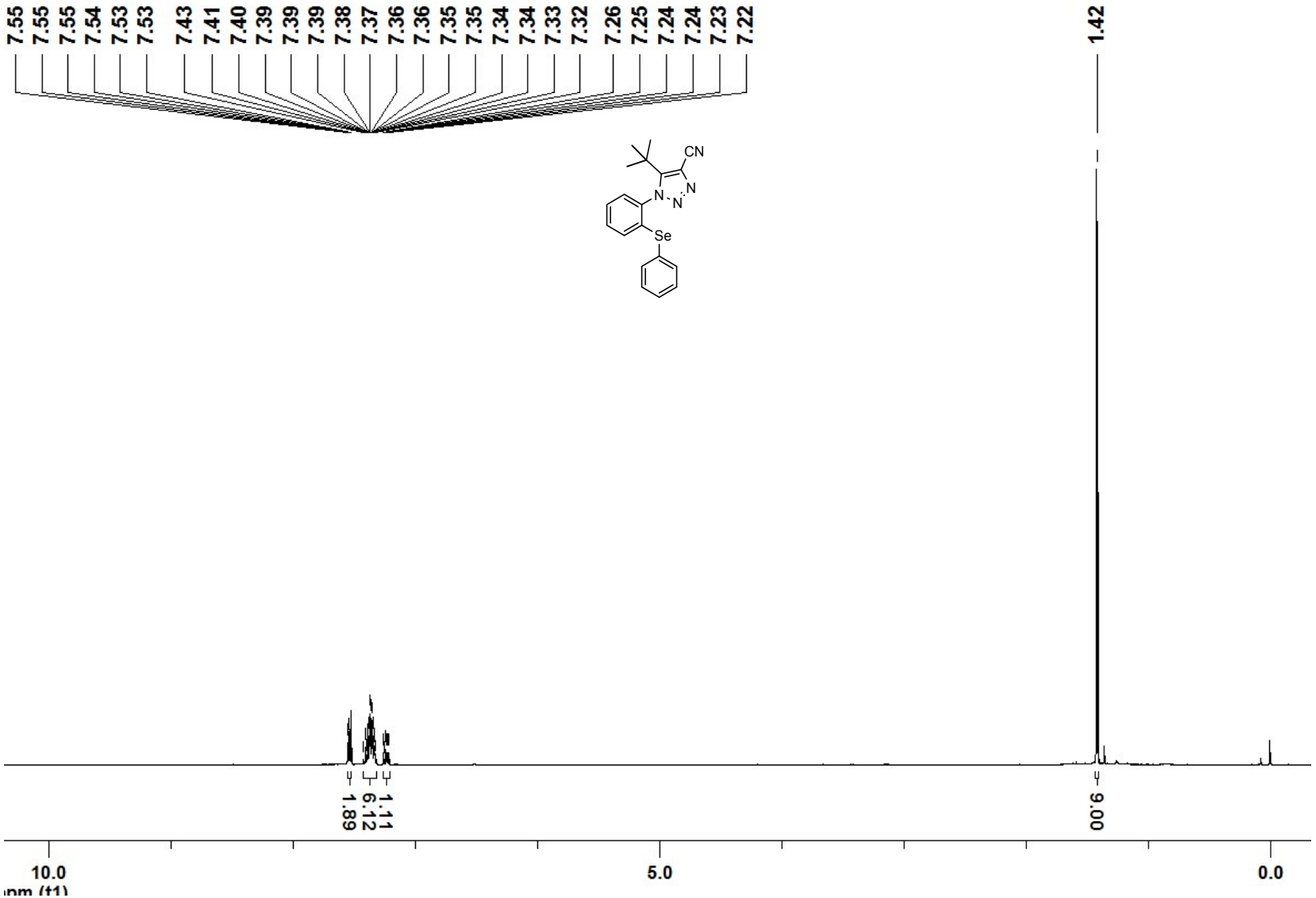
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of ***5-(4-chlorophenyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carbonitrile (3e)***



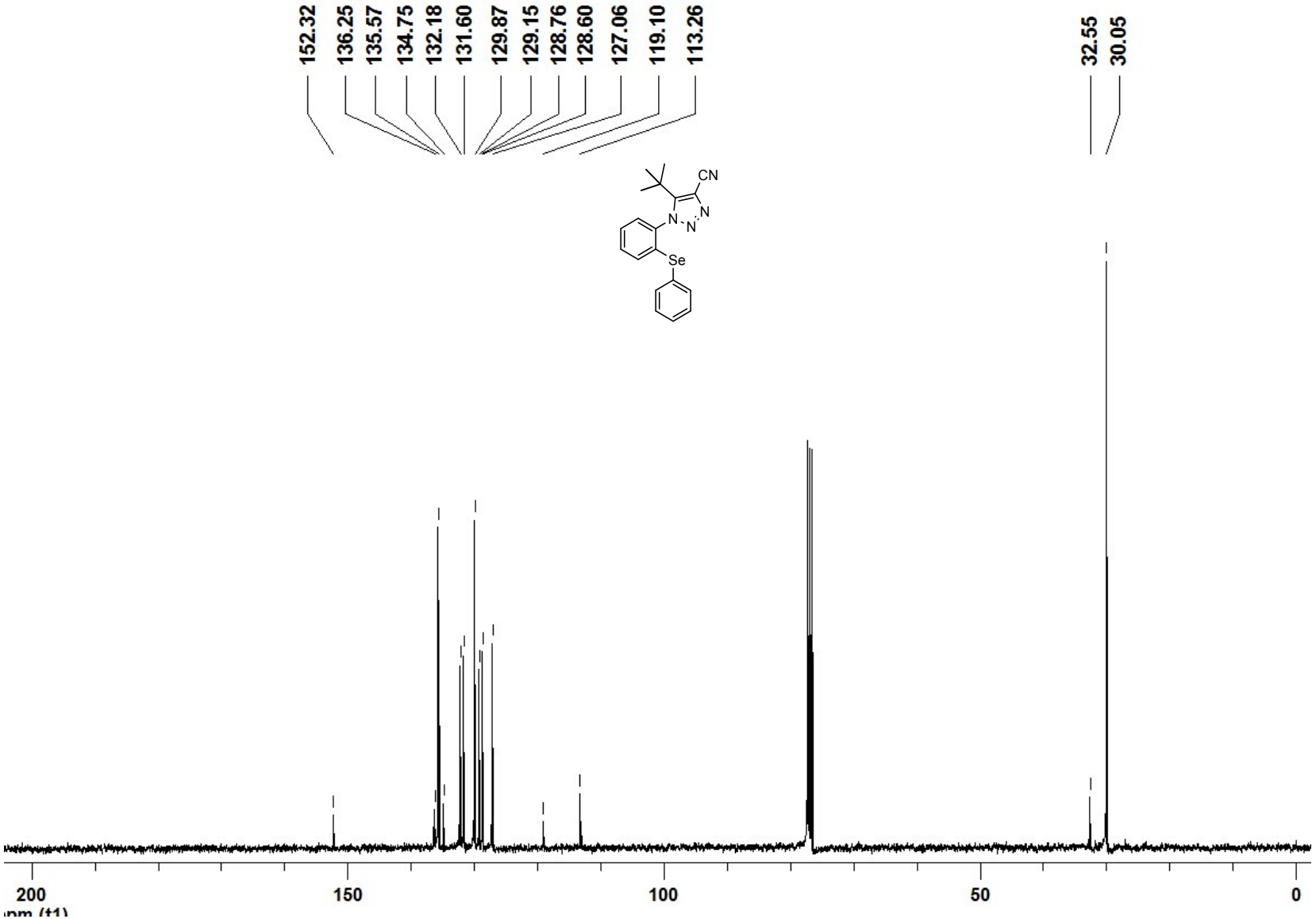
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of ***5-(4-bromophenyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carbonitrile (3f)***



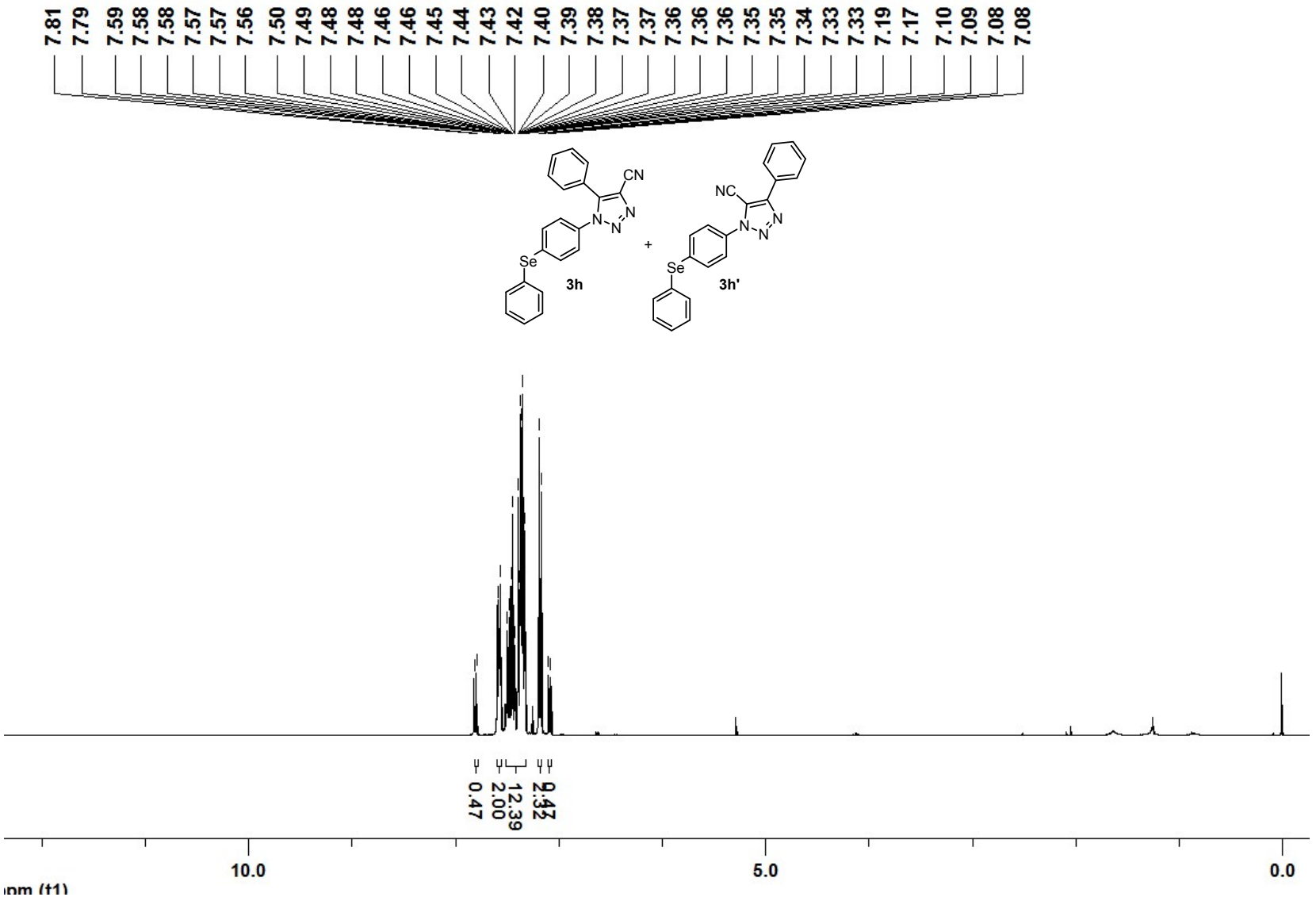
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of ***5-(4-bromophenyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carbonitrile (3f)***



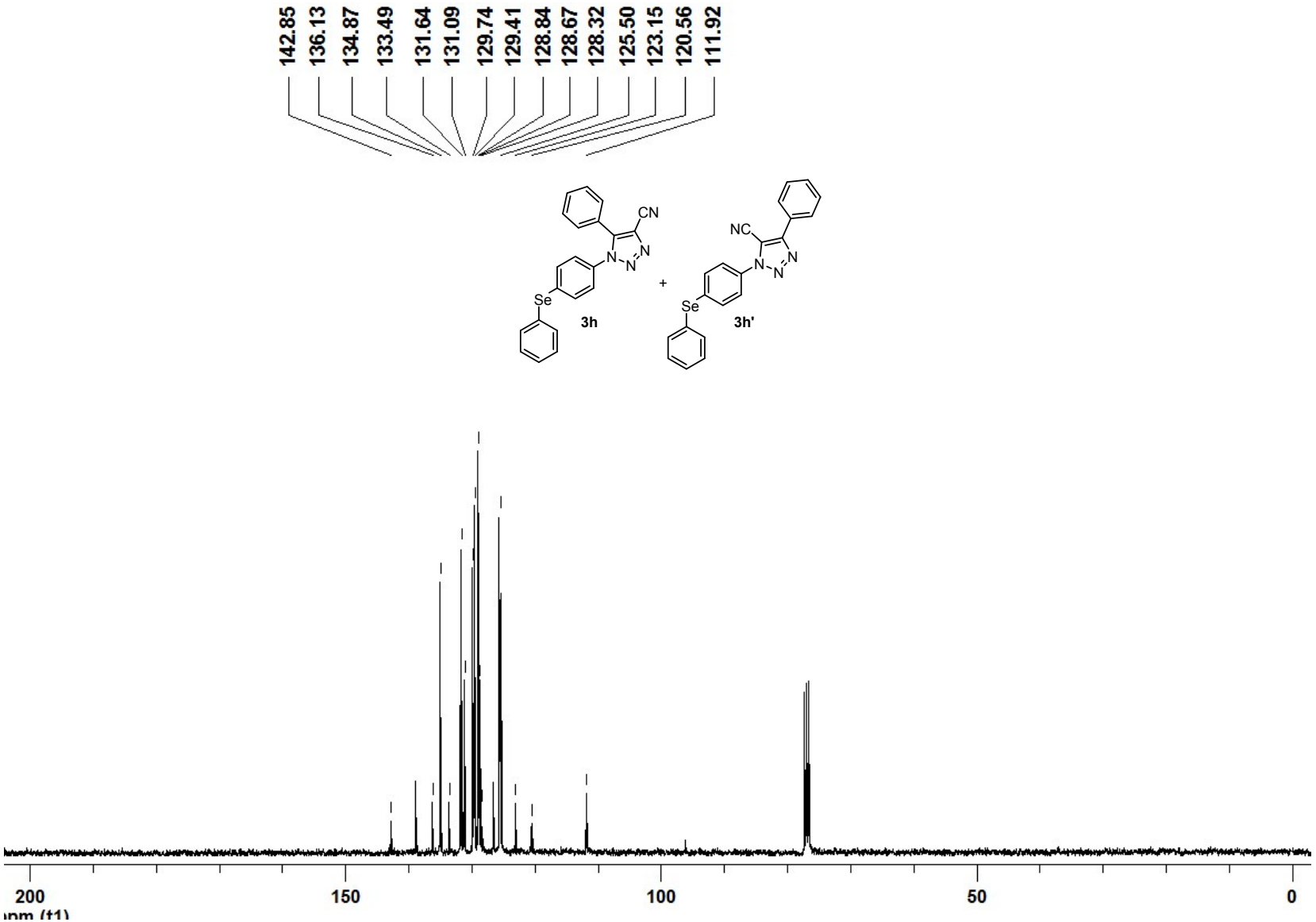
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of ***5-(tert-butyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carbonitrile (3g)***



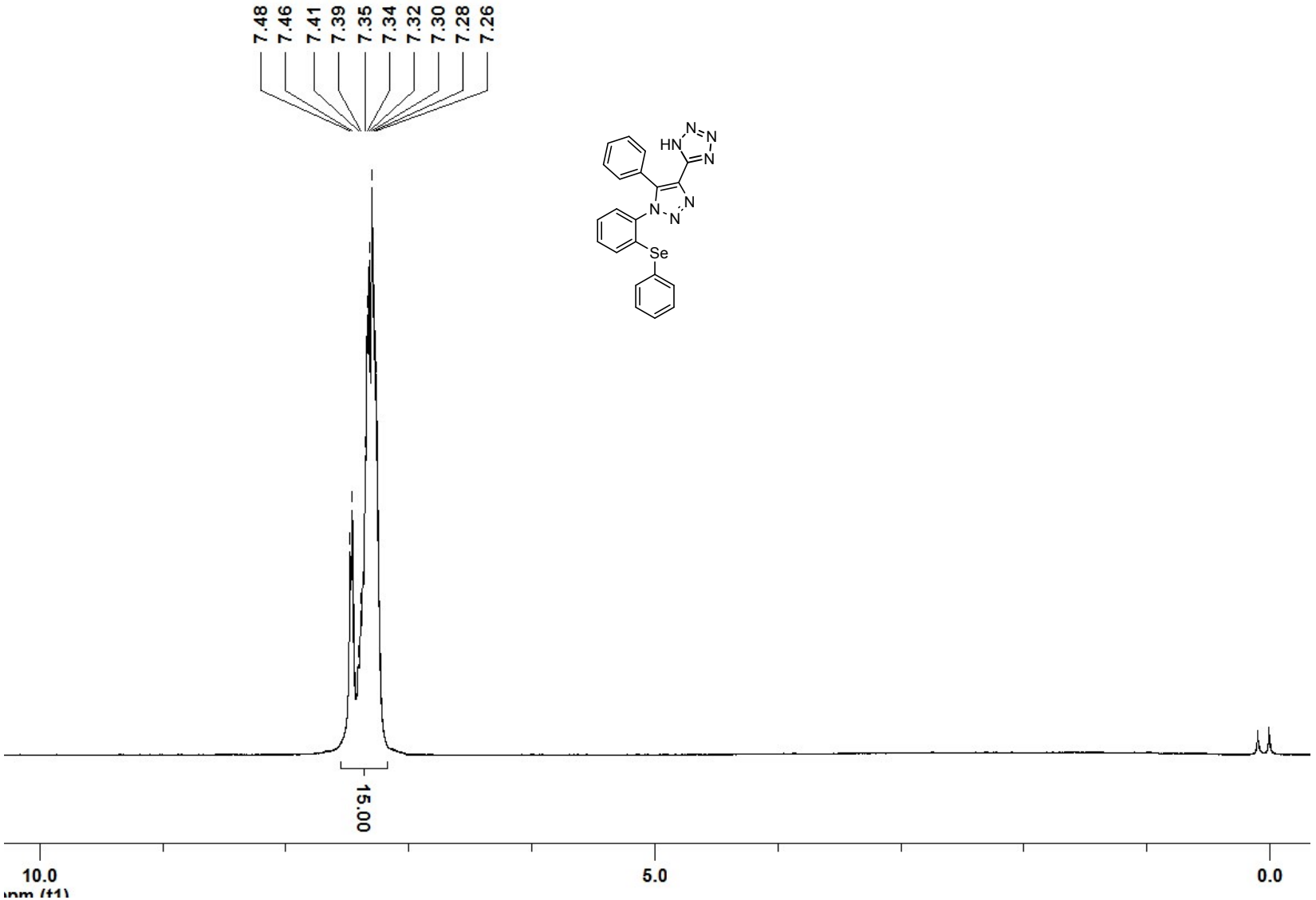
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of ***5-(tert-butyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carbonitrile (3g)***



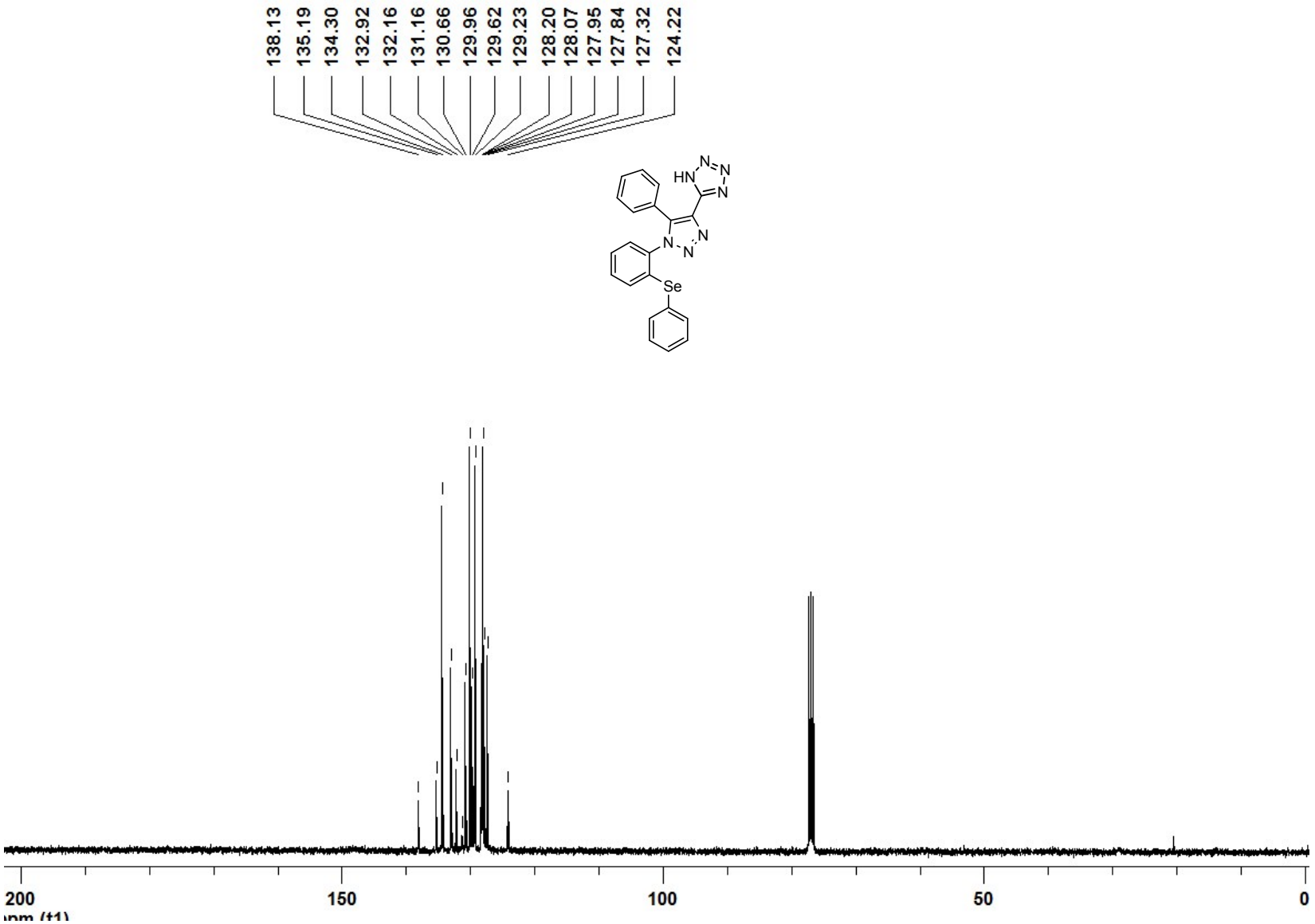
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of ***5-phenyl-1-(4-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carbonitrile (3h)***



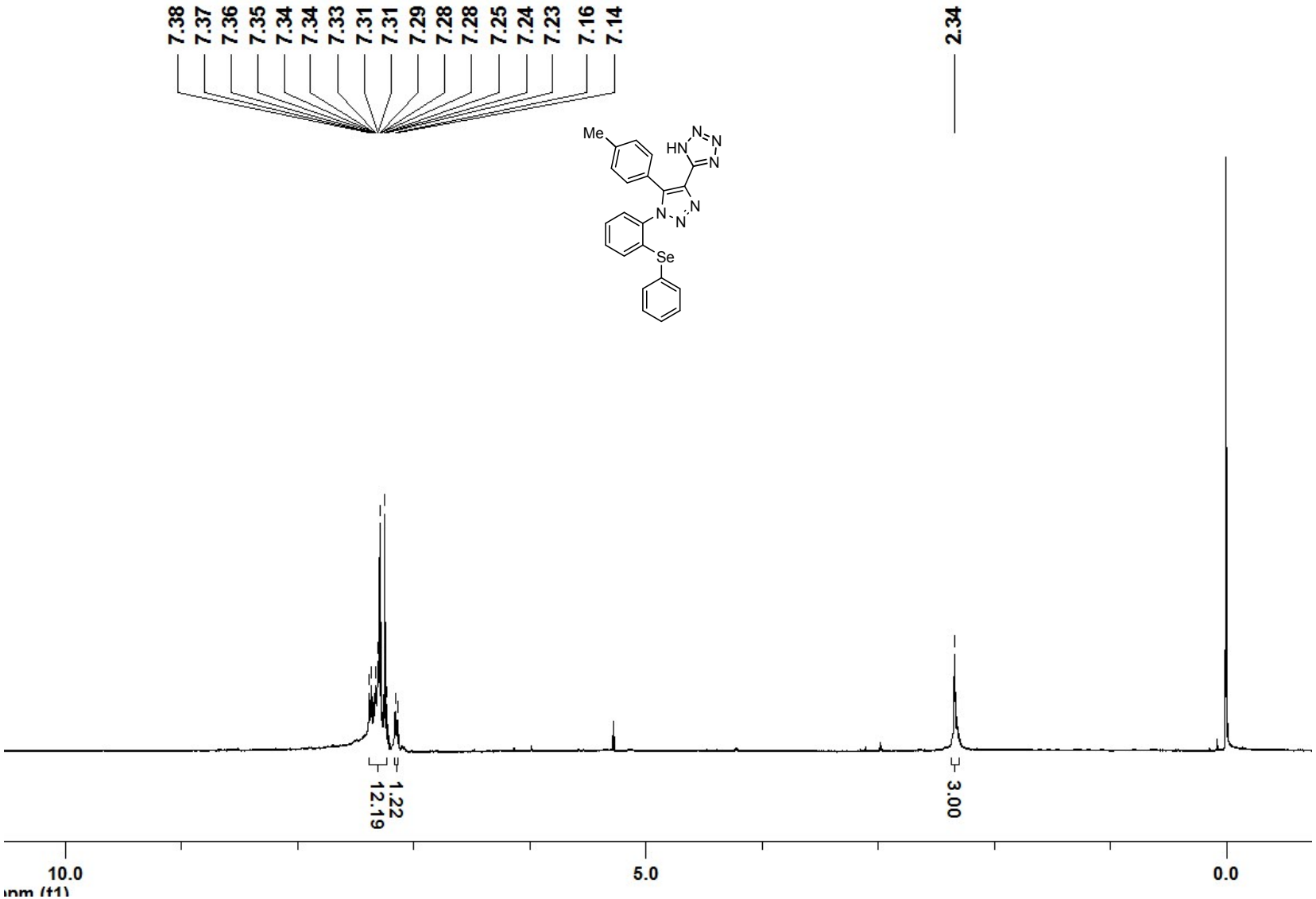
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of ***5-phenyl-1-(4-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carbonitrile (3h)***



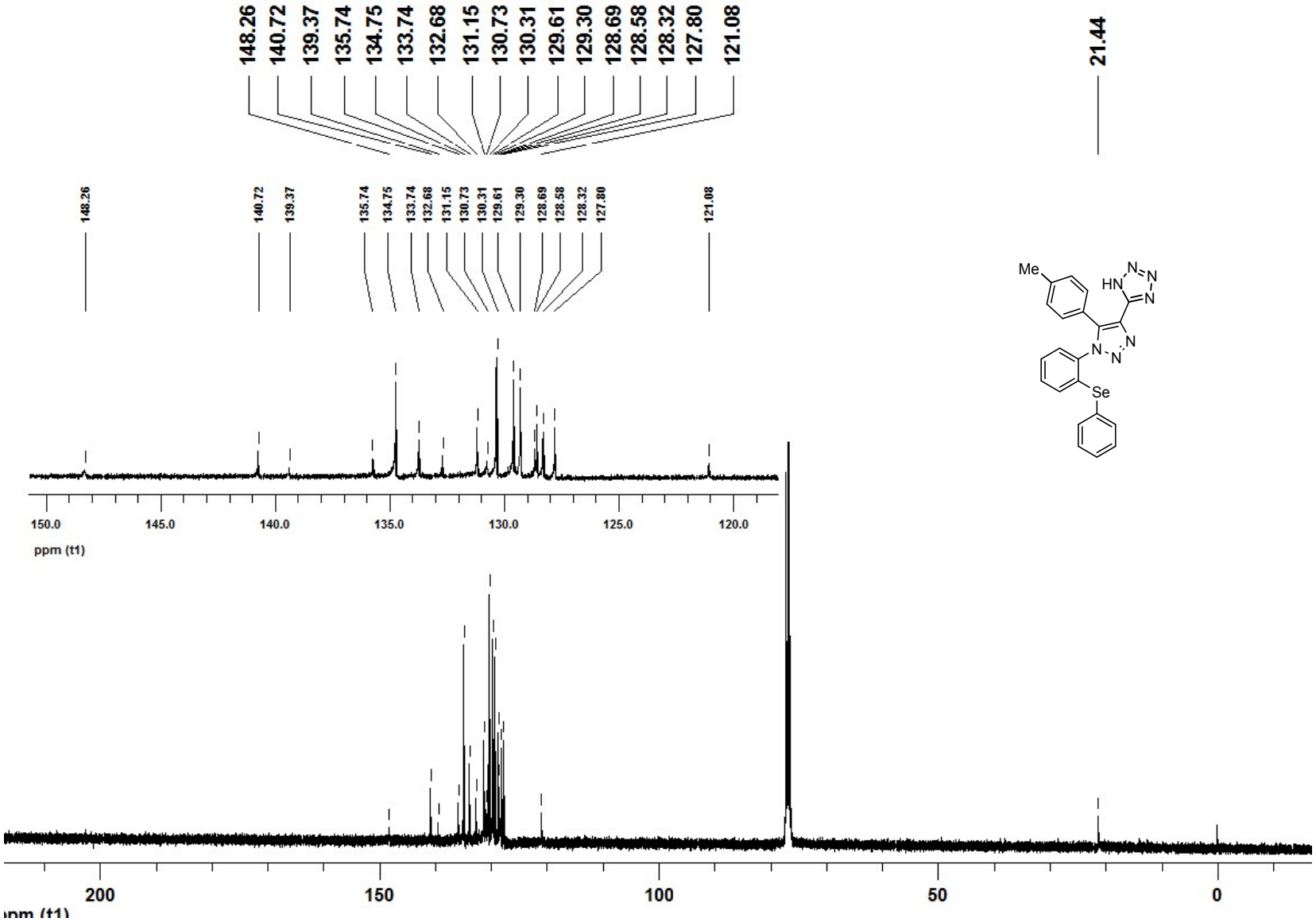
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of ***5-(5-phenyl-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazol-4-yl)-1H-tetrazole (4a)***



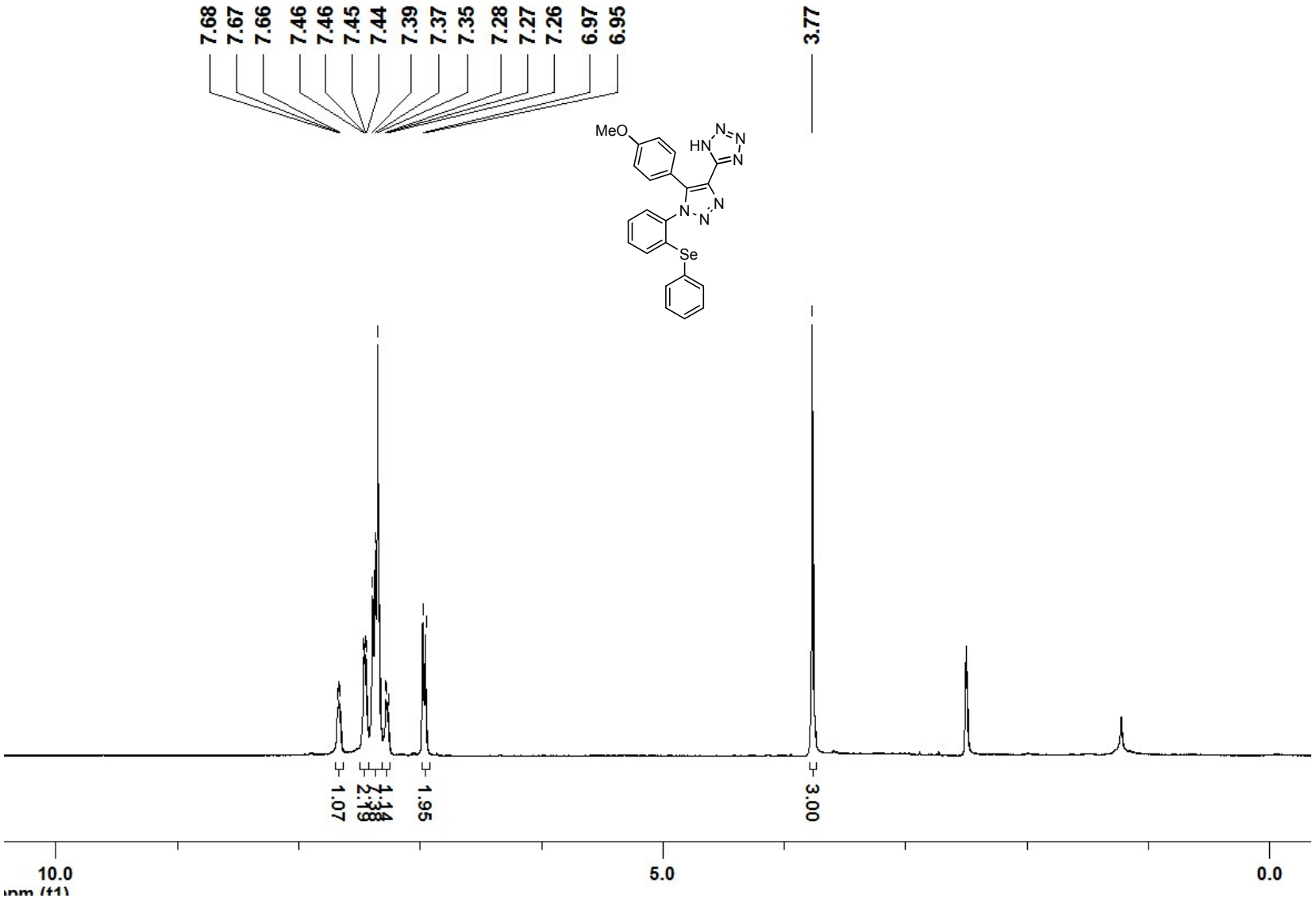
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of ***5-(5-phenyl-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazol-4-yl)-1H-tetrazole (4a)***



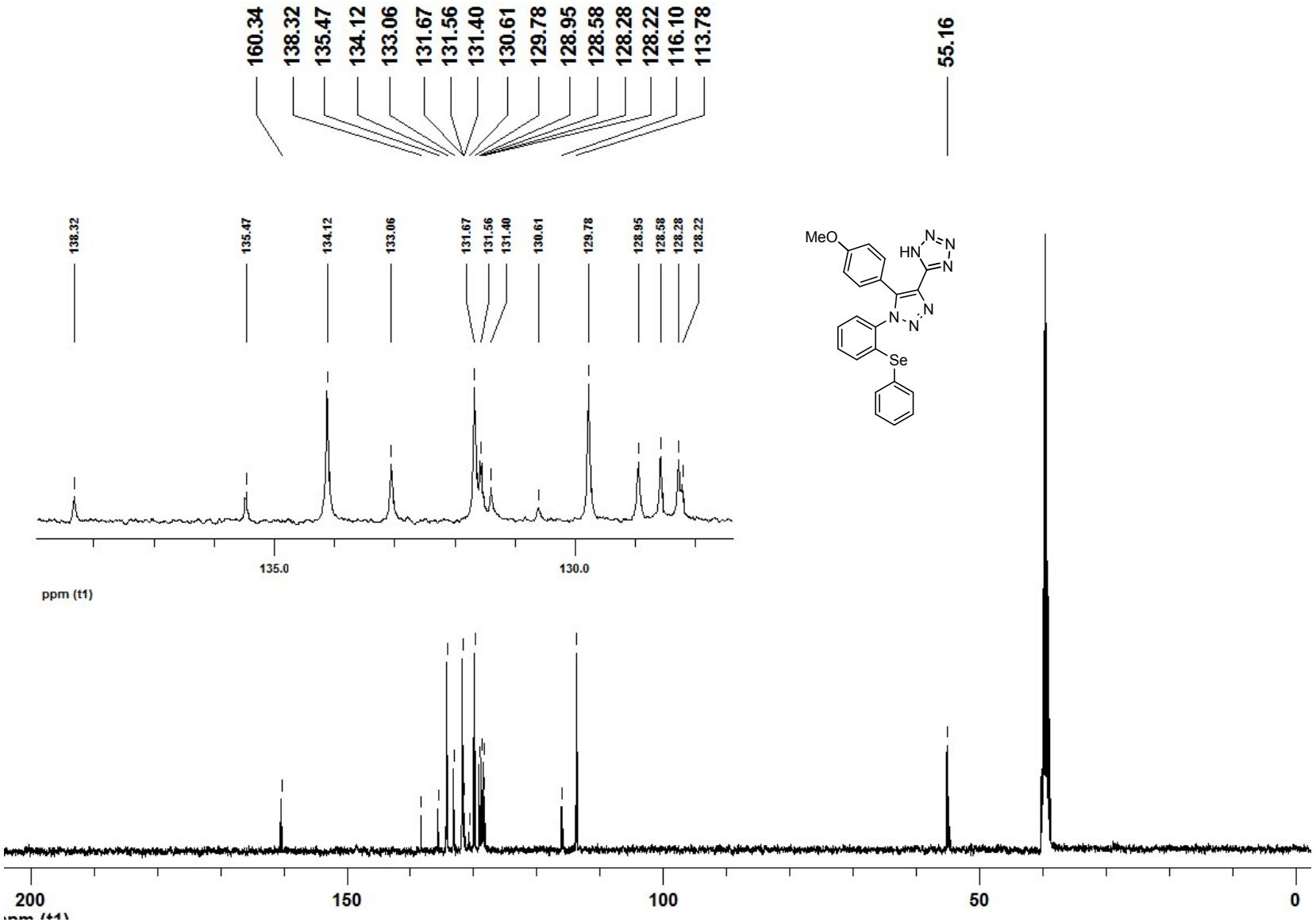
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of ***5-(1-(2-(phenylselanyl)phenyl)-5-(p-tolyl)-1H-1,2,3-triazol-4-yl)-1H-tetrazole (4b)***



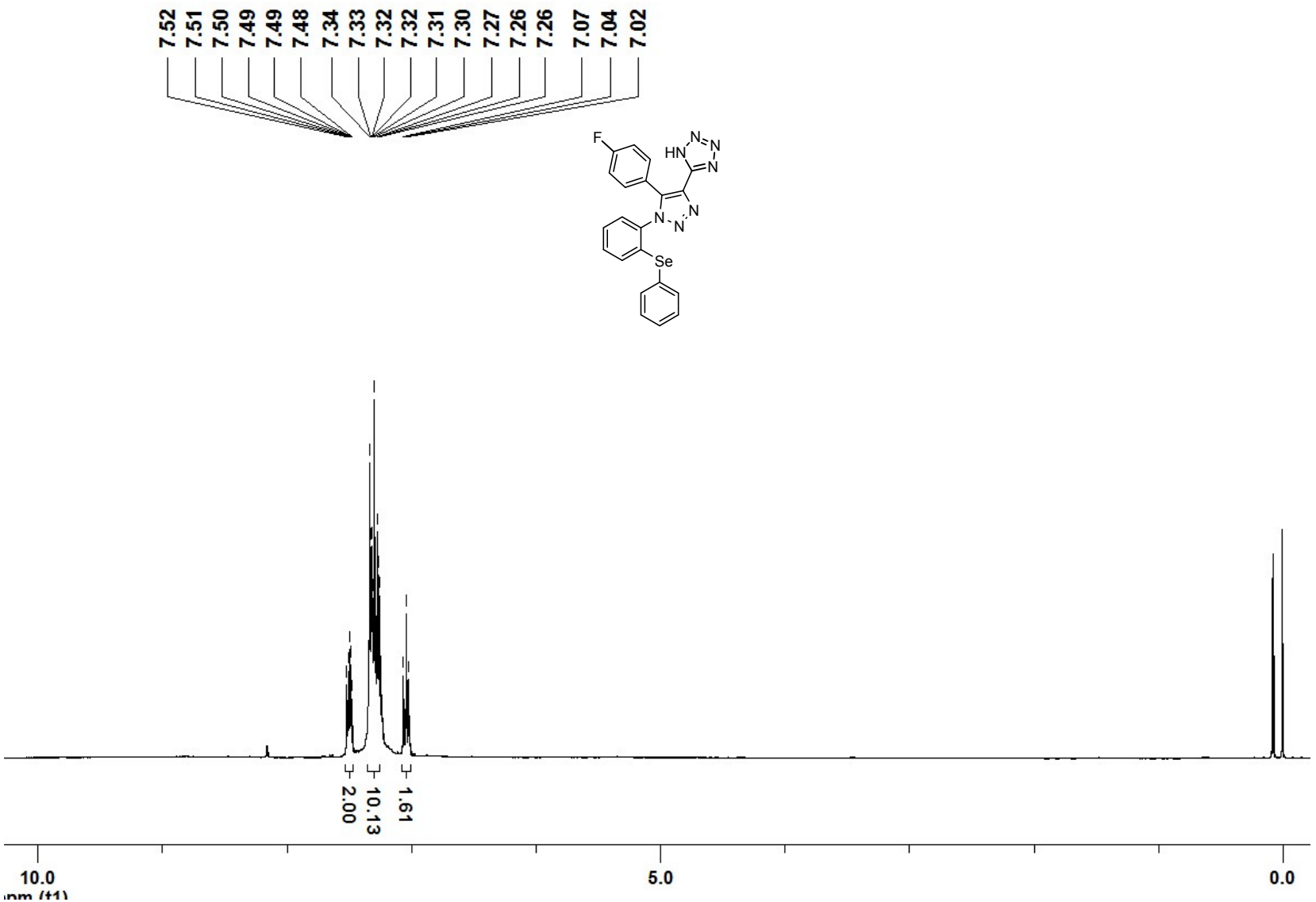
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of ***5-(1-(2-(phenylselanyl)phenyl)-5-(p-tolyl)-1H-1,2,3-triazol-4-yl)-1H-tetrazole (4b)***



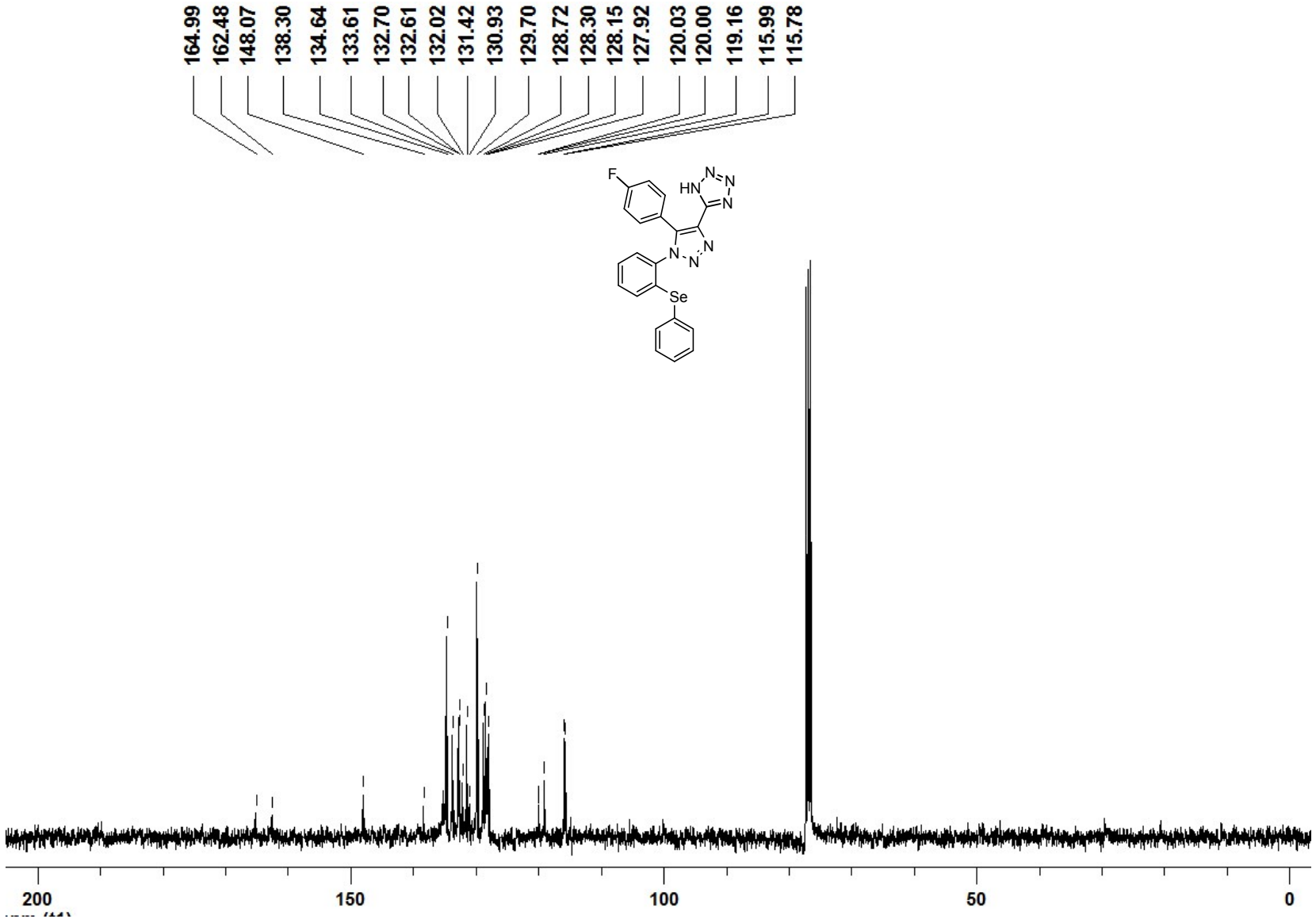
^{1}H NMR (400 MHz, DMSO-d_6) spectrum of ***5-(5-(4-methoxyphenyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazol-4-yl)-1H-tetrazole (4c)***



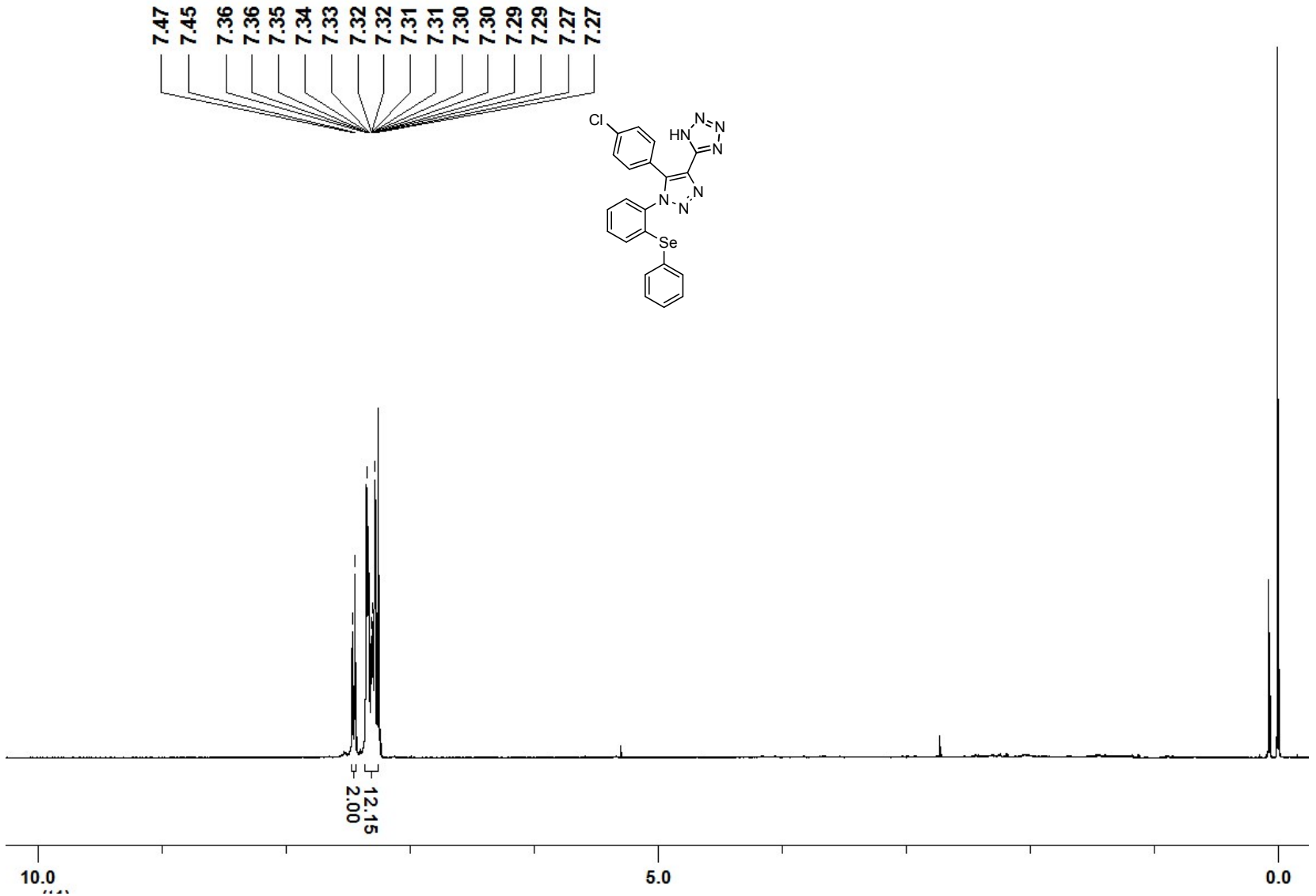
^{13}C NMR (100 MHz, DMSO-d_6) spectrum of ***5-(5-(4-methoxyphenyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazol-4-yl)-1H-tetrazole (4c)***



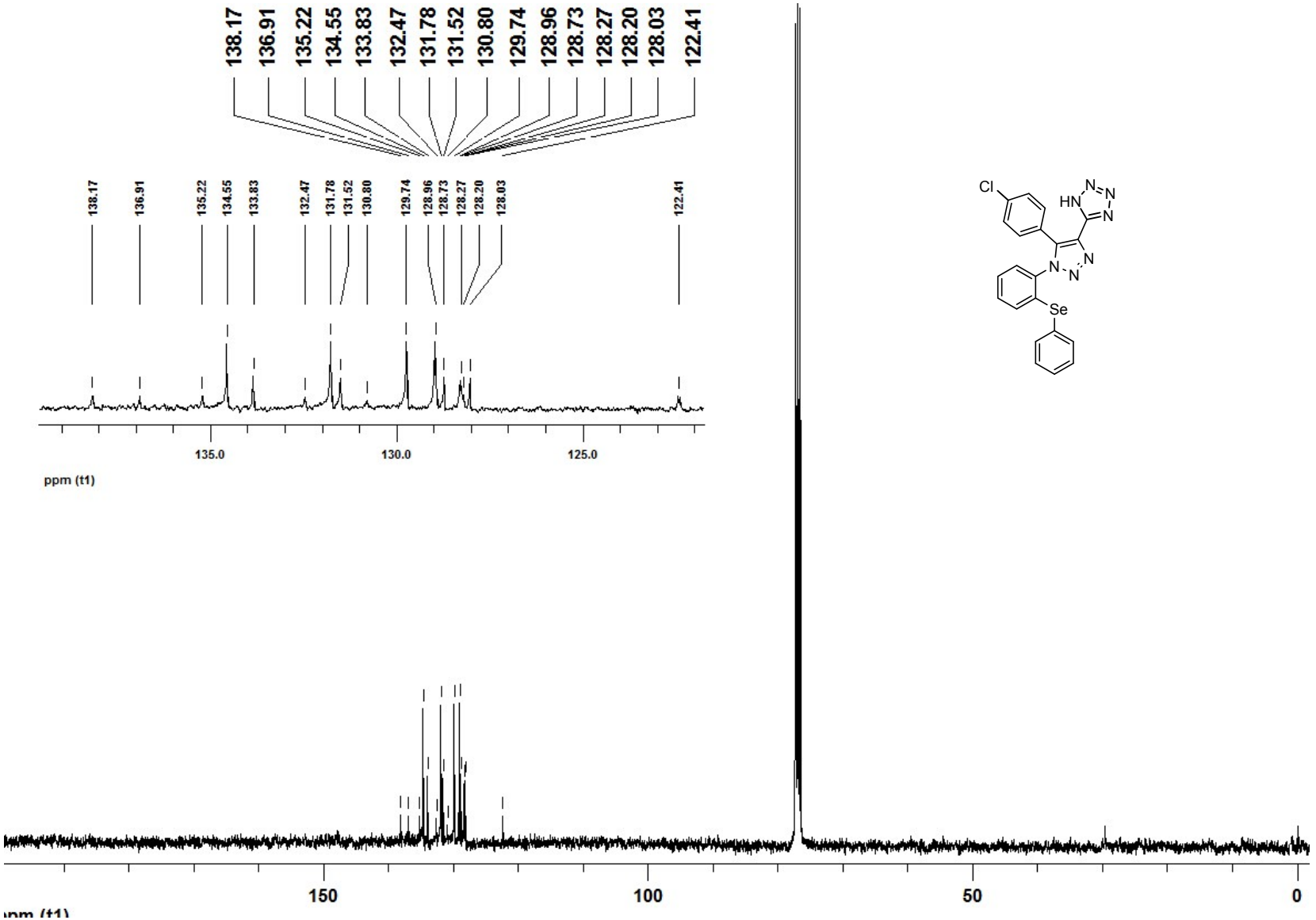
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of ***5-(5-(4-fluorophenyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazol-4-yl)-1H-tetrazole (4d)***



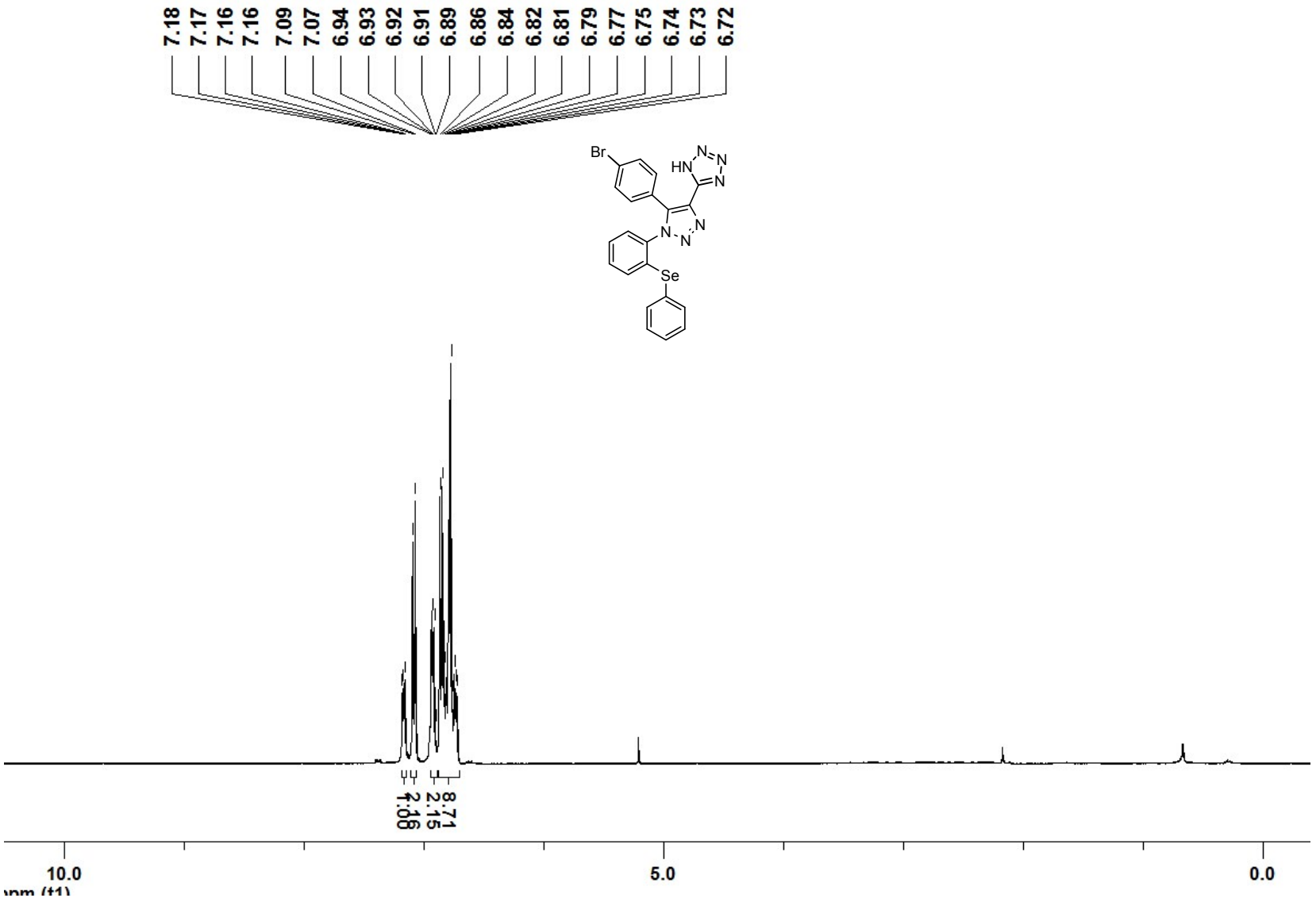
^{13}C NMR (100 MHz, $CDCl_3$) spectrum of ***5-(5-(4-fluorophenyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazol-4-yl)-1H-tetrazole (4d)***



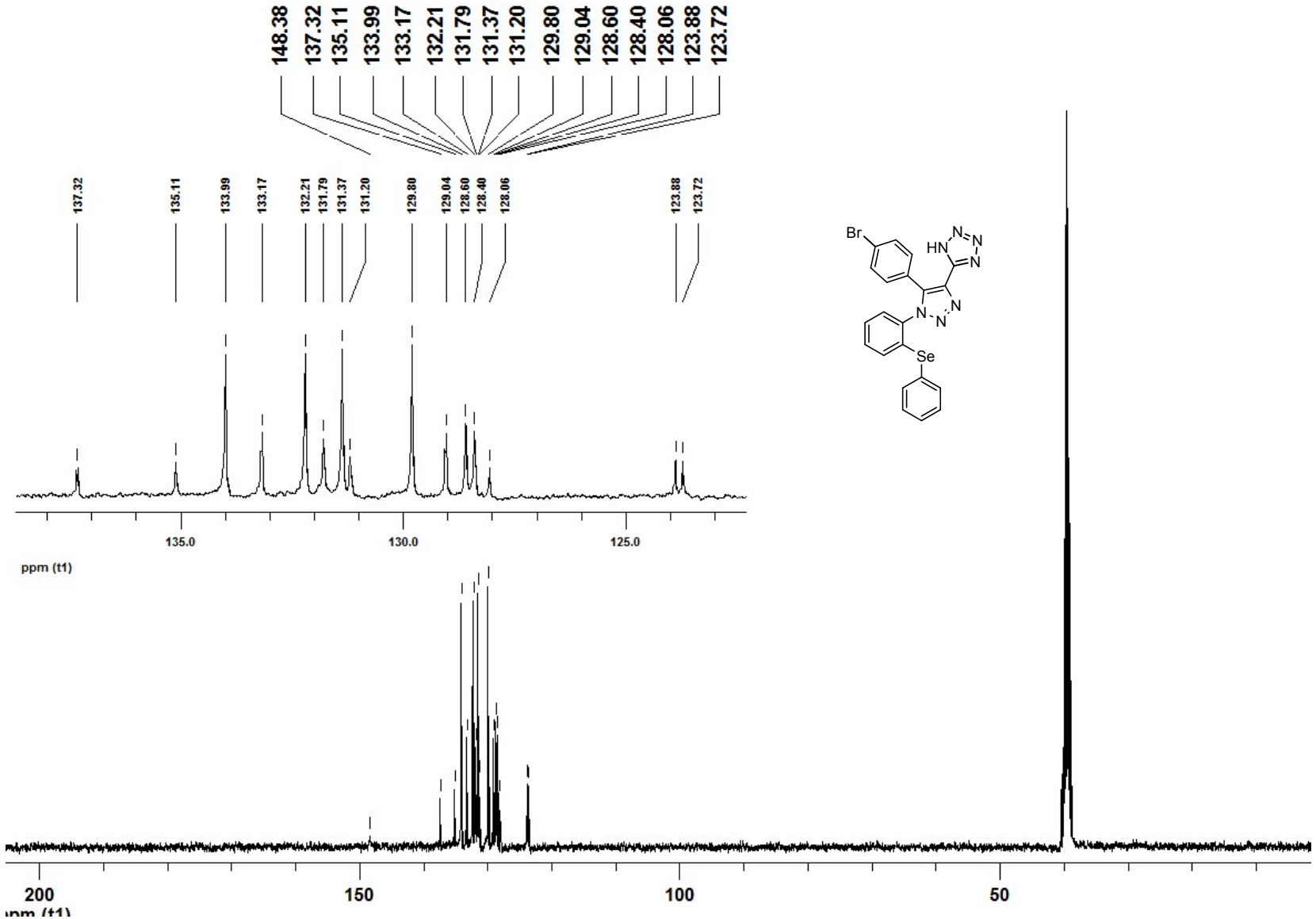
^{1}H NMR (400 MHz, $CDCl_3$) spectrum of ***5-(5-(4-chlorophenyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazol-4-yl)-1H-tetrazole (4e)***



^{13}C NMR (100 MHz, $CDCl_3$) spectrum of ***5-(5-(4-chlorophenyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazol-4-yl)-1H-tetrazole (4e)***



^{1}H NMR (400 MHz, DMSO-d_6) spectrum of ***5-(5-(4-bromophenyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazol-4-yl)-1H-tetrazole (4f)***



^{13}C NMR (100 MHz, DMSO-d_6) spectrum of ***5-(5-(4-bromophenyl)-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazol-4-yl)-1H-tetrazole (4f)***