

Supporting Information for

Telescoped continuous flow generation of a library of highly substituted 3-thio-1,2,4-triazoles

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1. GENERAL PROCEDURE FOR THE BATCH SYNTHESIS OF HYDRAZIDES 1b-d

The respective ester (3 mmol), and hydrazine monohydrate (882 μ L, 18 mmol) were refluxed in ethanol/methanol overnight. The reaction was diluted in 20 mL of water, and extracted with EtOAc (6 x 20 mL). The organic phase was evaporated under reduced pressure to give the desired products.

4-nitrobenzohydrazide (1b). Quantitative. Compound description: light yellow solid. ^1H NMR (400 MHz, DMSO- d_6): δ 10.17 (s, 1 H), 8.30 (d, J = 8.7 Hz, 2 H), 8.06 (d, J = 8.7 Hz, 2 H); ^{13}C NMR (101 MHz, DMSO- d_6): δ 164.3 (C_0), 149.4 (C_0), 139.5 (C_0), 128.9 (CH), 124.0 (CH). This data was consistent with published data [C. V. Yelamaggad, A. S. Achalkumar, D. S. S. Rao and S. K. Prasad, *J. Org. Chem.*, 2009, **74**, 3168–3171].

Picolinohydrazide (1c). Quantitative. Compound description: white solid. ^1H NMR (250 MHz, CDCl_3): δ 8.54 – 8.37 (m, 1 H), 8.08 (d, J = 7.8 Hz, 1 H), 7.75 (td, J = 7.7, 1.7 Hz, 1 H), 7.34 (ddd, J = 7.6, 4.8, 1.1 Hz, 1 H); ^{13}C NMR (63 MHz, CDCl_3): δ 164.6 (C_0), 149.1 (C_0), 148.3 (CH), 137.2 (CH), 126.3 (CH), 122.2 (CH). This data was consistent with published data [J. Xie, X. Zhu, M. Huang, F. Meng, W. Chen and Y. Wan, *European J. Org. Chem.*, 2010, 3219–3223].

3,5-dimethoxybenzohydrazide (1d). Quantitative. Compound description: white solid. ^1H NMR (400 MHz, CDCl_3): δ 7.44 (s, 1 H), 6.86 (d, J = 2.2 Hz, 2 H), 6.59 (t, J = 2.2 Hz, 1 H), 3.82 (s, 6 H). ^{13}C NMR (101 MHz, CDCl_3): δ 168.6 (C_0), 161.0 (C_0), 134.8 (C_0), 104.8 (CH), 103.9 (CH), 55.6 (CH_3).

7. ^1H and ^{13}C NMR spectra of compounds

nov09mfsH1_MF530
Mariana "MF-430" dmsol/ Av400MHz nov09mfsH1

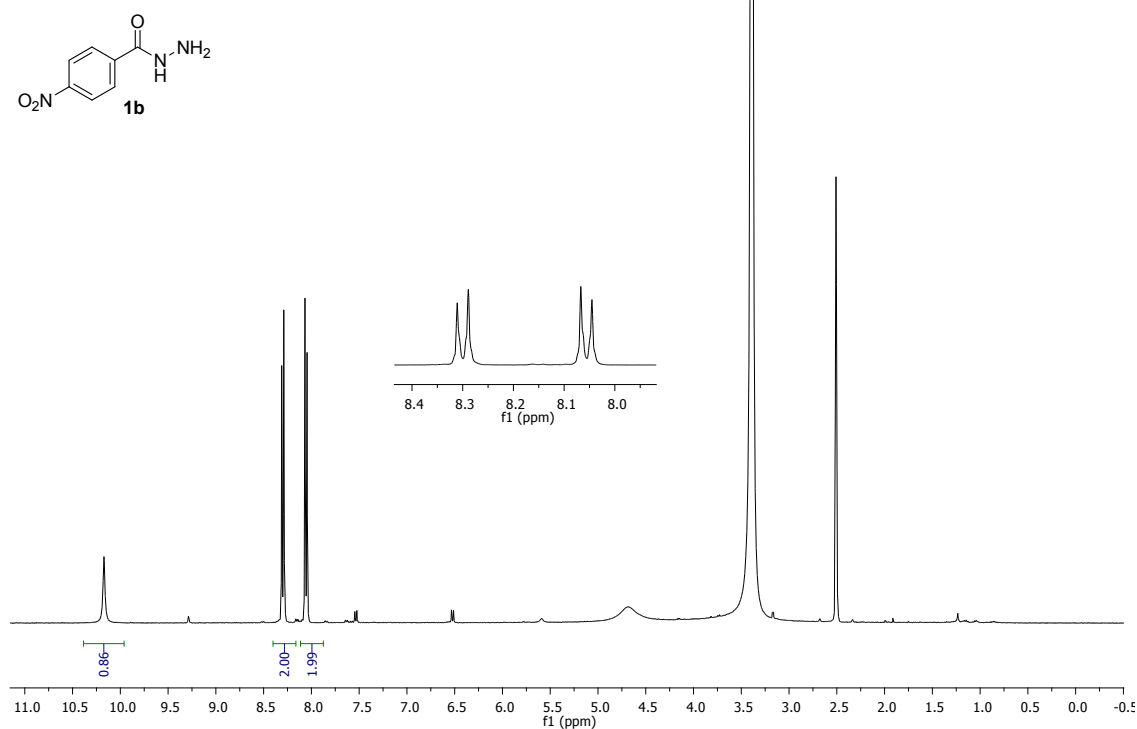


Figure S1. ^1H NMR spectrum (DMSO- d_6 , 400 MHz) of compound **1b**.

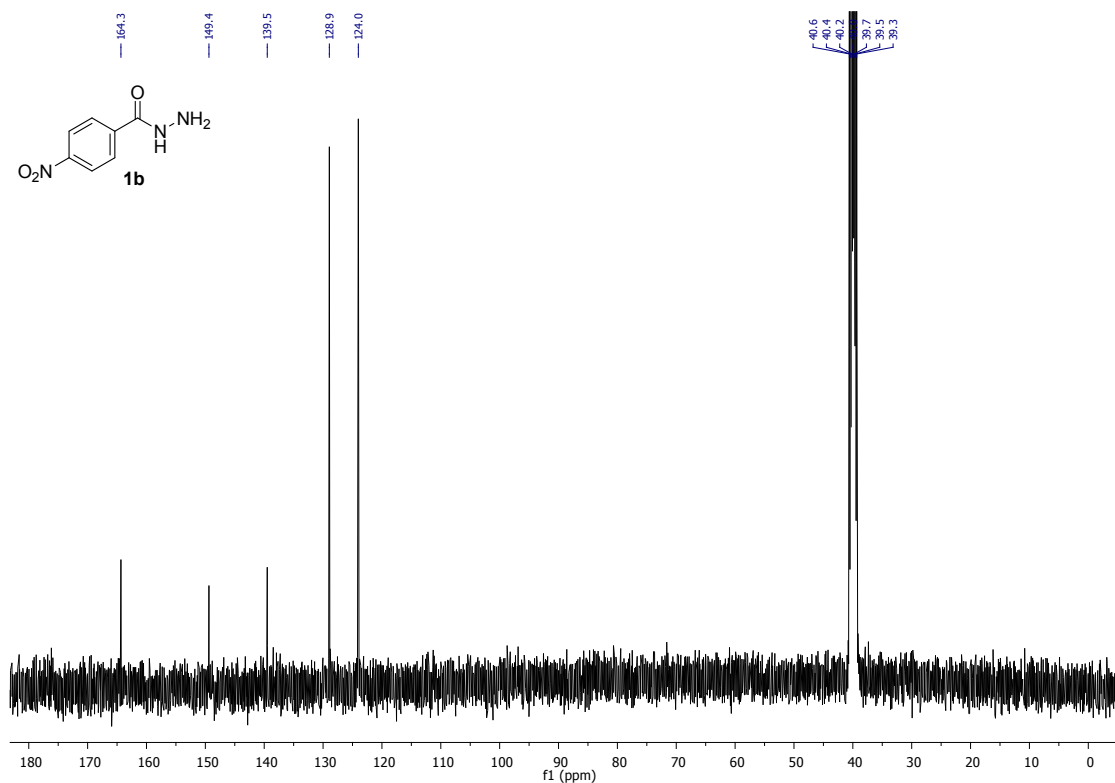


Figure S2. ^{13}C NMR spectrum (DMSO- d_6 , 101 MHz) of compound **1b**.

fev24mfsh2_MF-427
fev24mfsh2/Py-hydrazide/CDCl₃/250

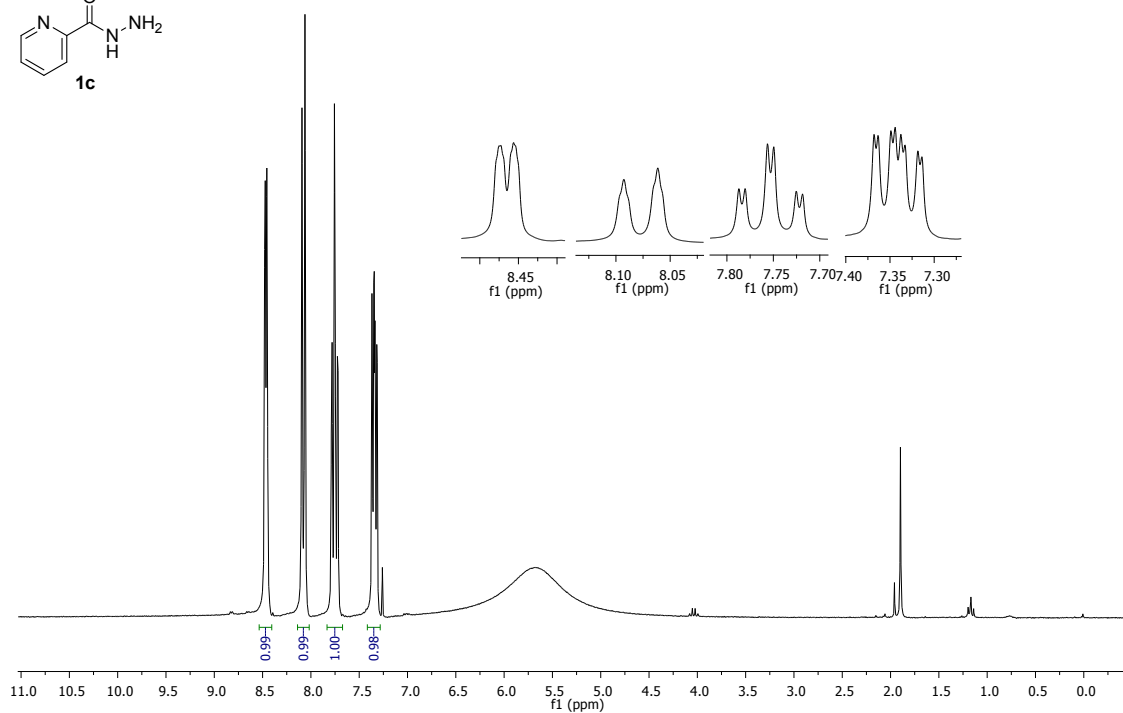
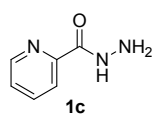


Figure S3. ¹H NMR spectrum (CDCl₃, 250 MHz) of compound **1c**.

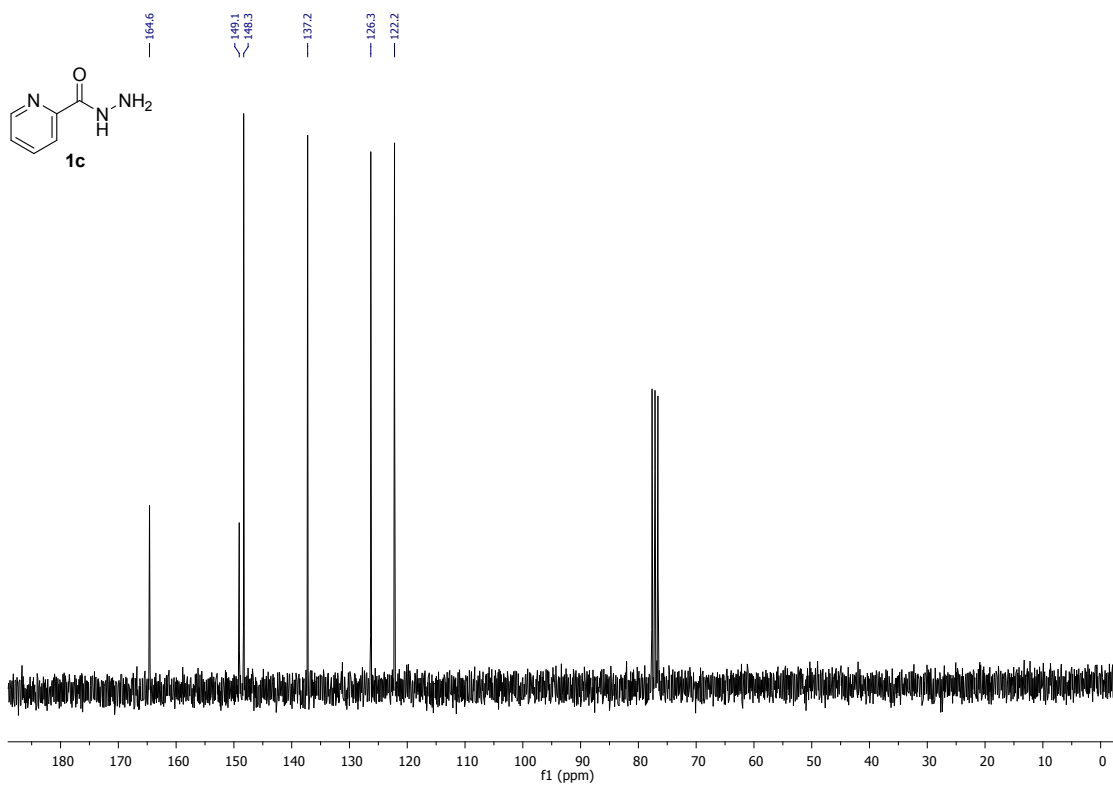


Figure S4. ¹³C NMR spectrum (DMSO-d₆, 63 MHz) of compound **1c**.

nov09mfsH2_MF531
Mariana "MF-431" cdcl3/ Av400MHz nov09mfsH2

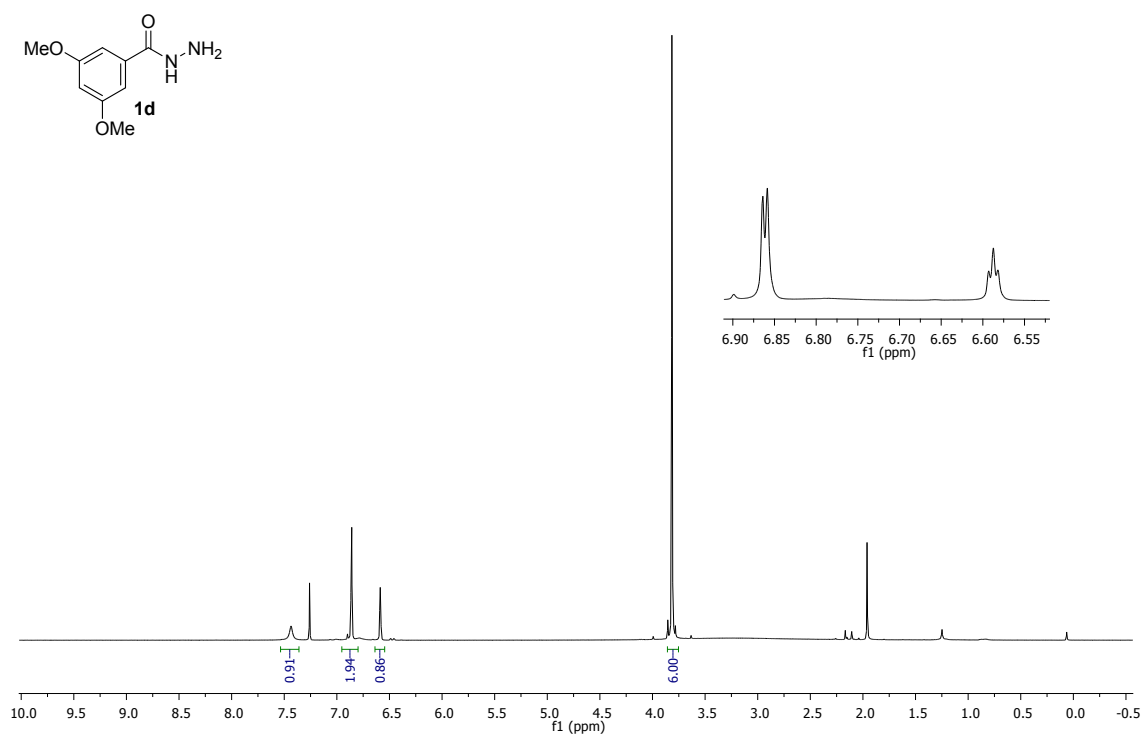


Figure S5. ¹H NMR spectrum (CDCl₃, 400 MHz) of compound **1d**.

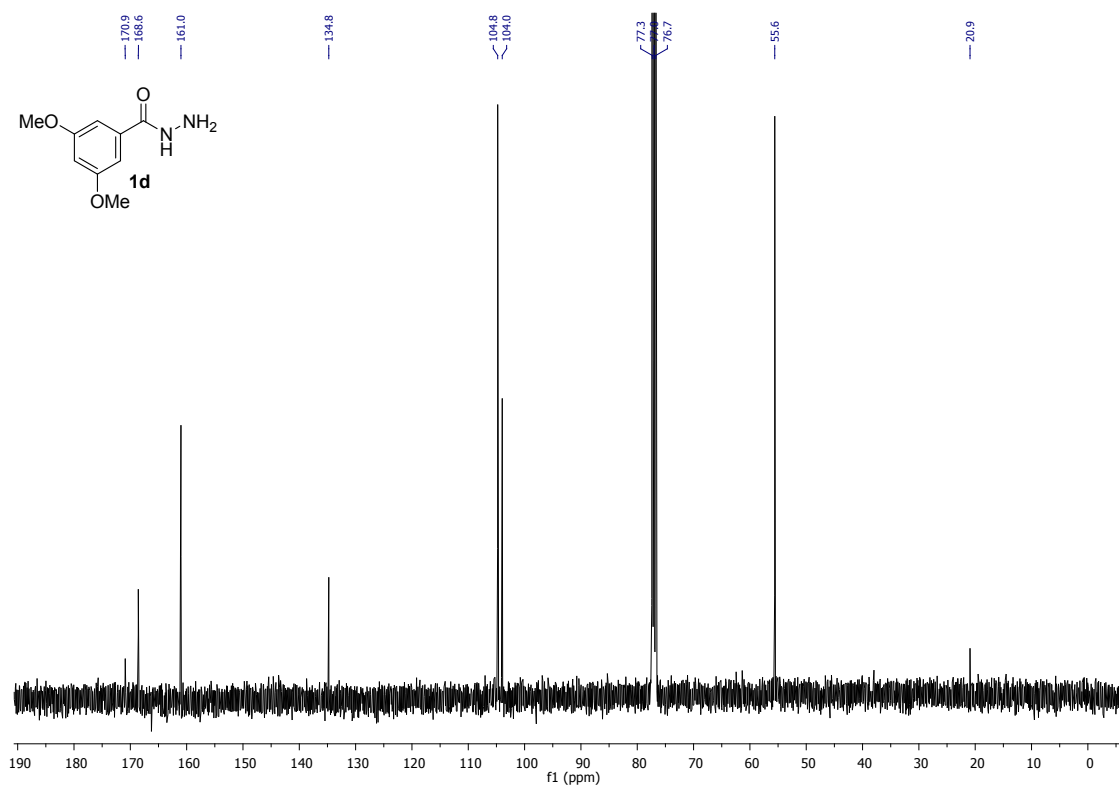


Figure S6. ¹³C NMR spectrum (CDCl₃, 101 MHz) of compound **1d**.

abr03mfsH1_tiourea
Mariana - MFTIOU - DMSO - Avance 500 MHz - abr03mfsH1 - 1H

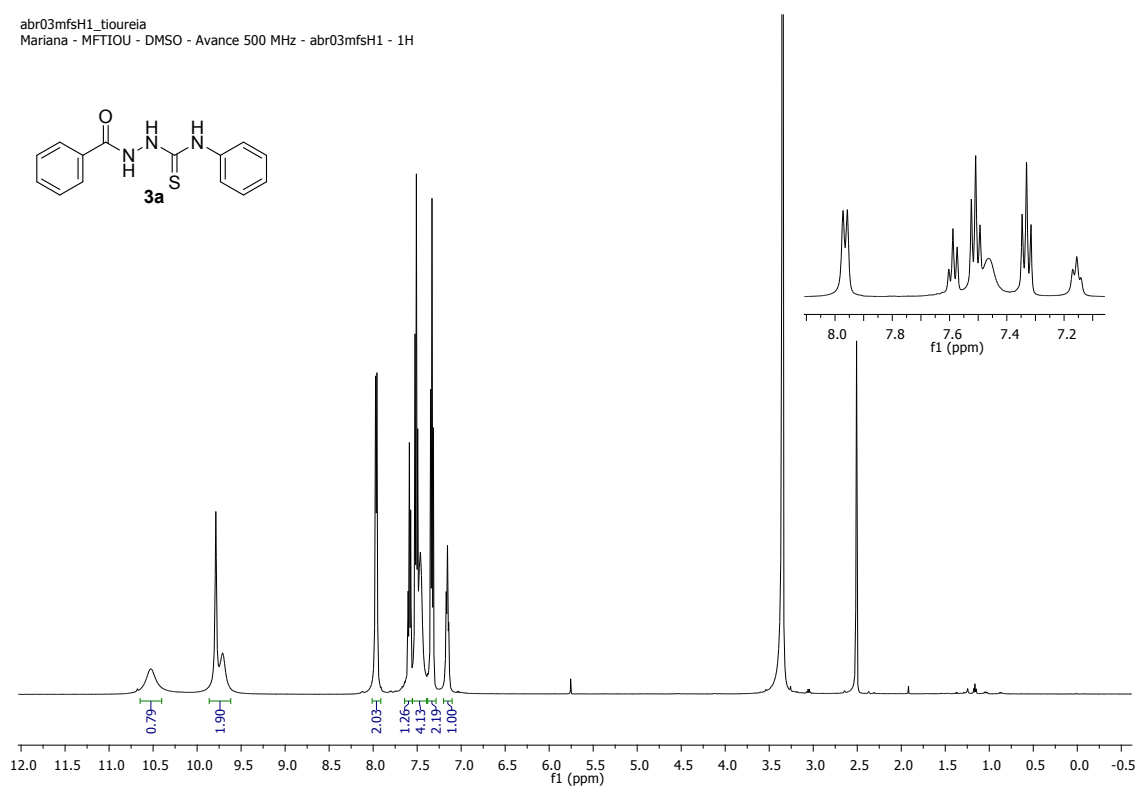


Figure S7. ^1H NMR spectrum (DMSO- d_6 , 500 MHz) of compound **3a**.

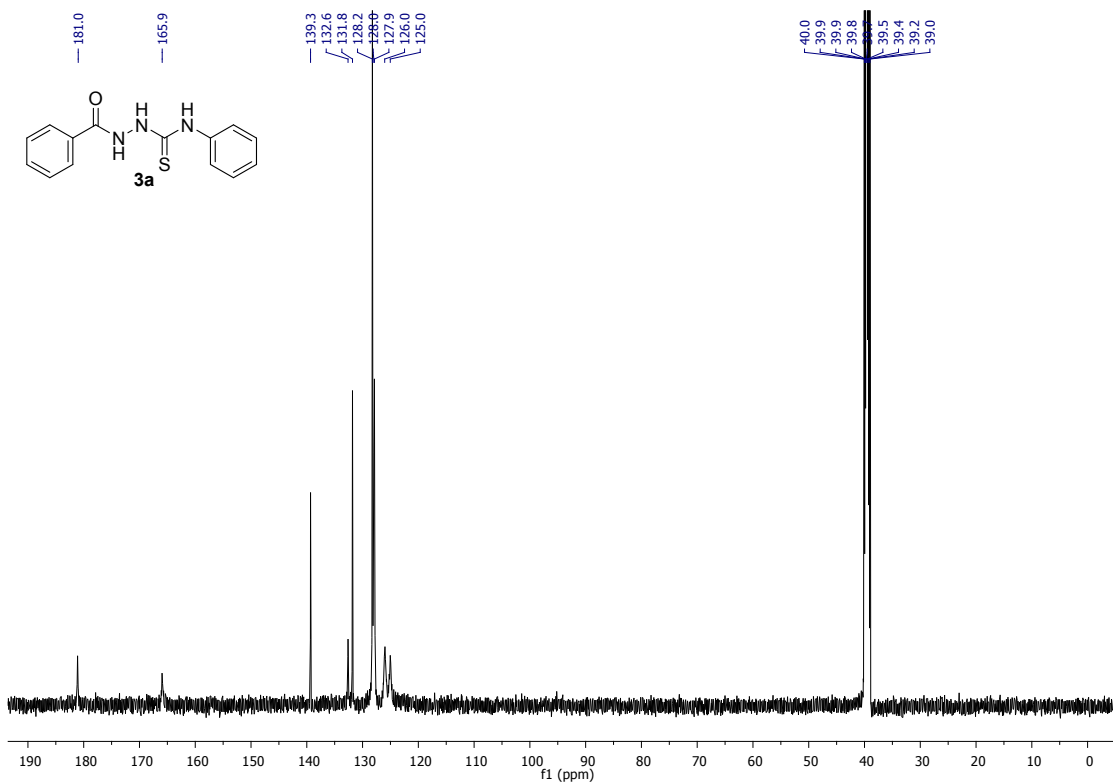


Figure S8. ^{13}C NMR spectrum (DMSO- d_6 , 126 MHz) of compound **3a**.

dez14mfsH1_mf-3-65_500
Mariana - MF-3-65 - DMSO - Av 500MHz - dez14mfsH1

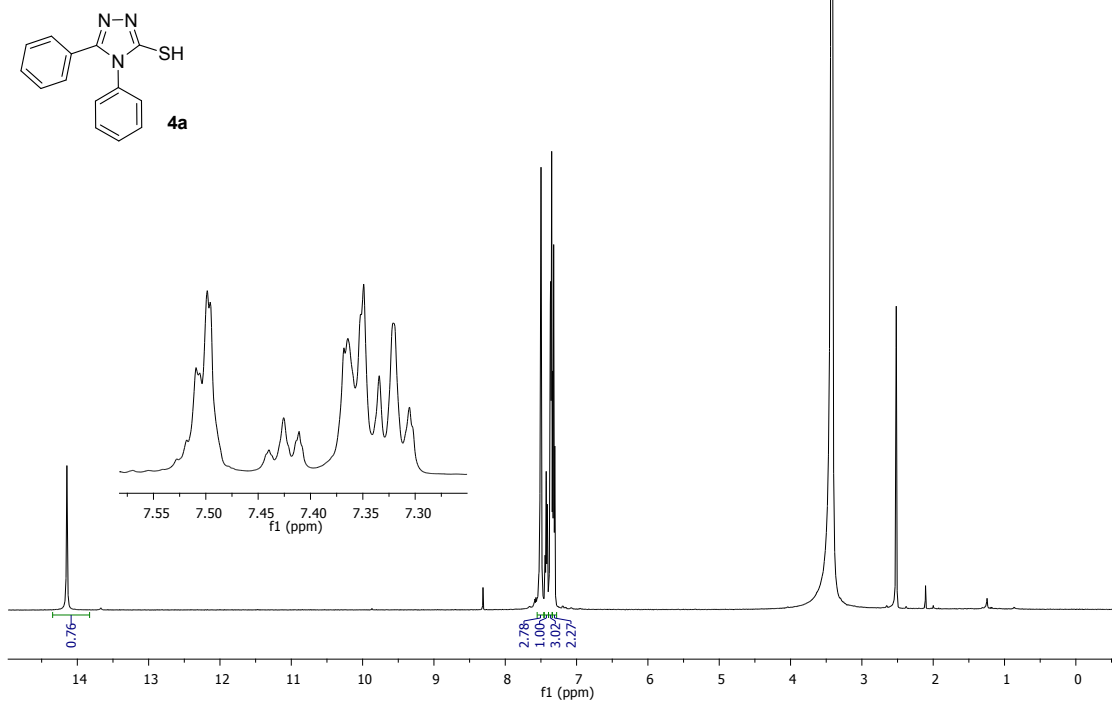


Figure S9. ^1H NMR spectrum (DMSO- d_6 , 500 MHz) of compound **4a**.

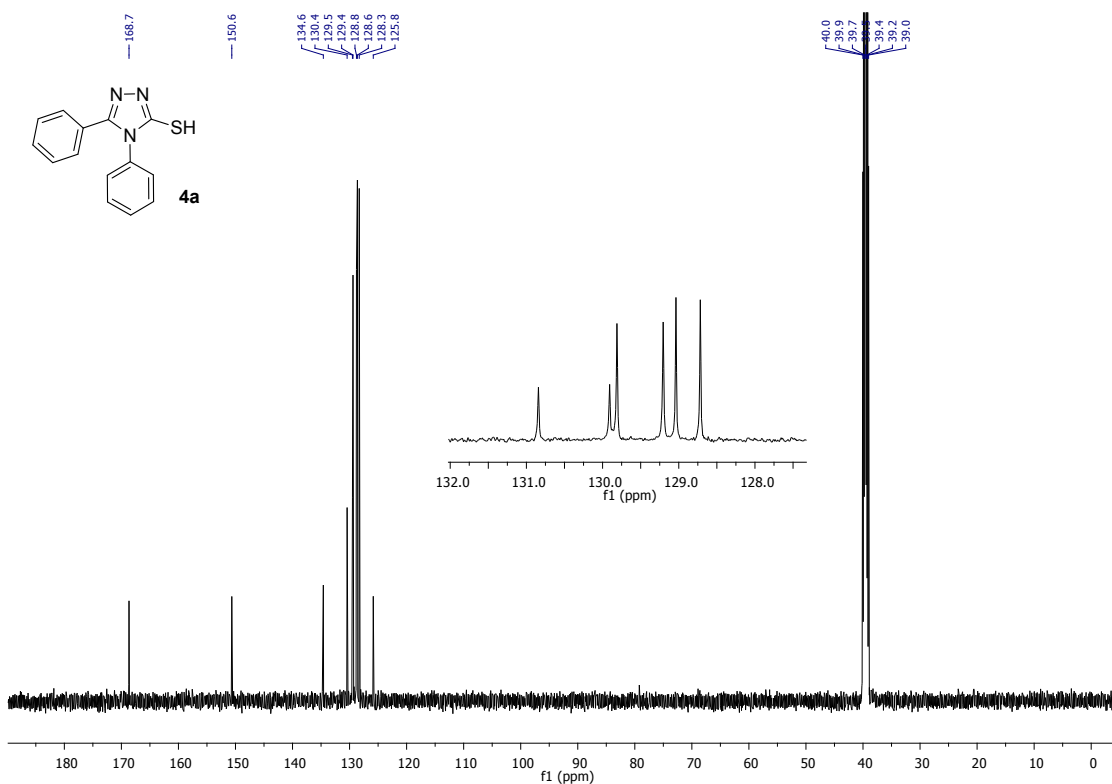


Figure S10. ^{13}C NMR spectrum (DMSO- d_6 , 126 MHz) of compound **4a**.

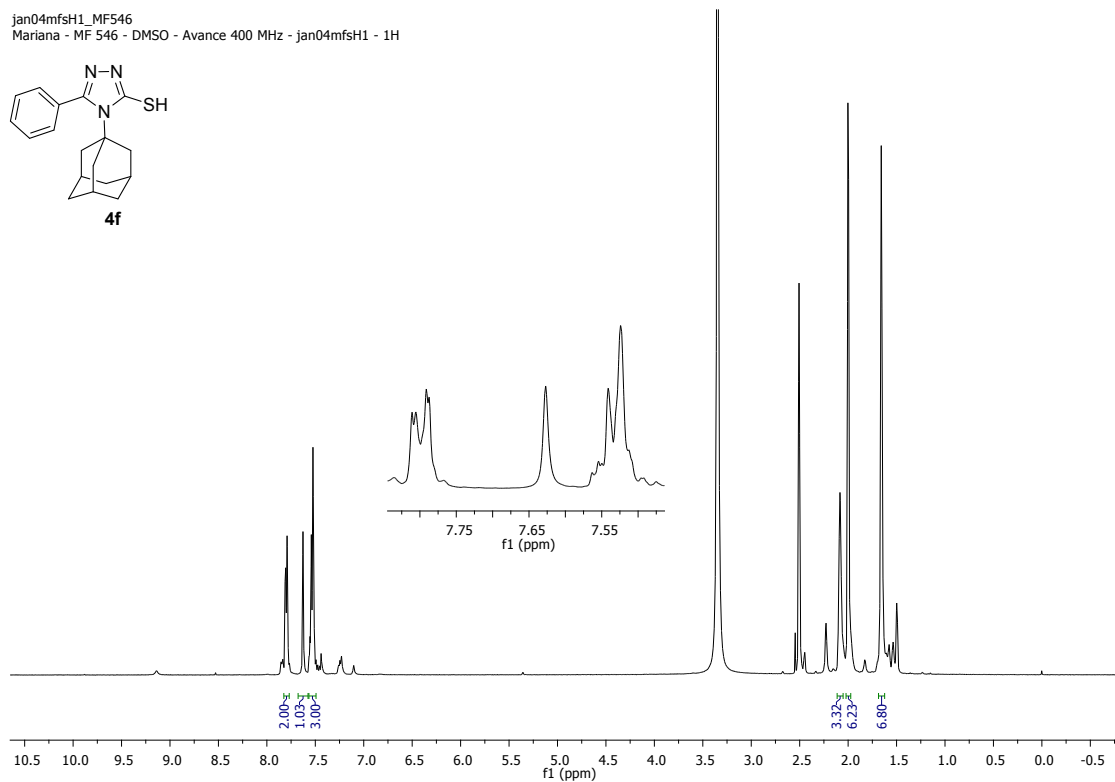


Figure S11. ¹H NMR spectrum (DMSO-d₆, 400 MHz) of compound **4f**.

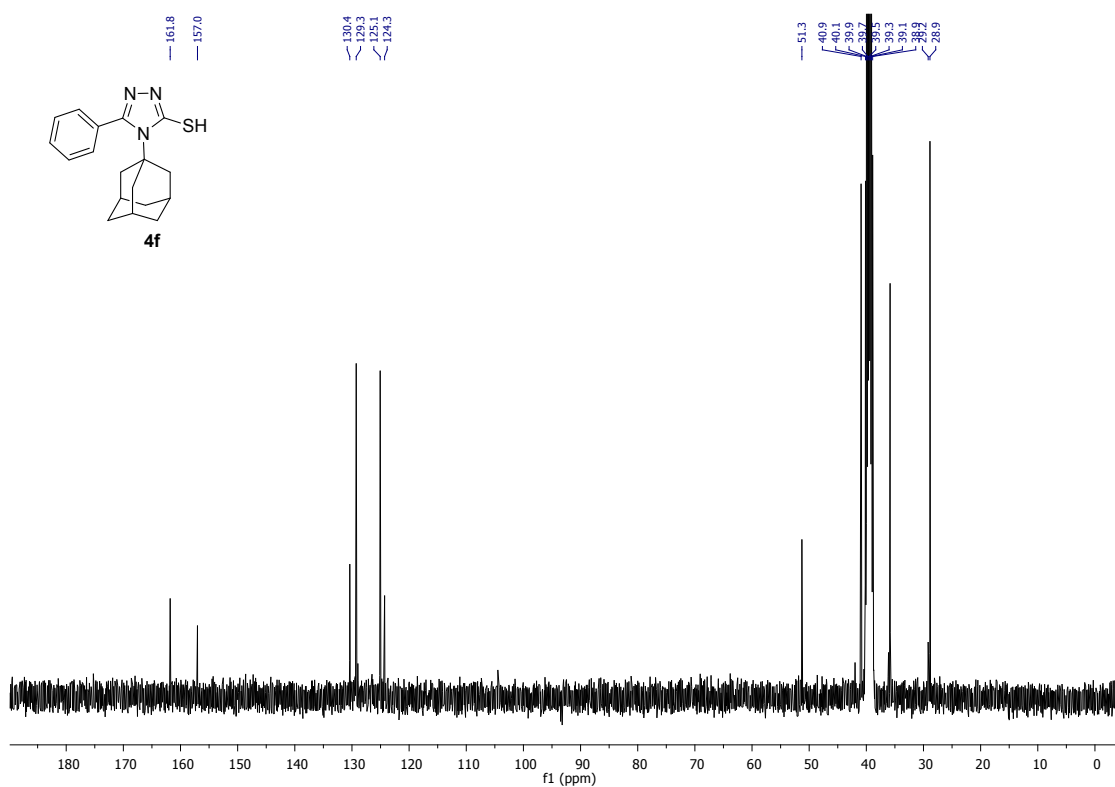


Figure S12. ¹³C NMR spectrum (DMSO-d₆, 101 MHz) of compound **4f**.

out10mfsH3_MF506
Mariana - MF 506 - CDCl₃ - Avance 600 MHz - out10mfsH3 - 1H

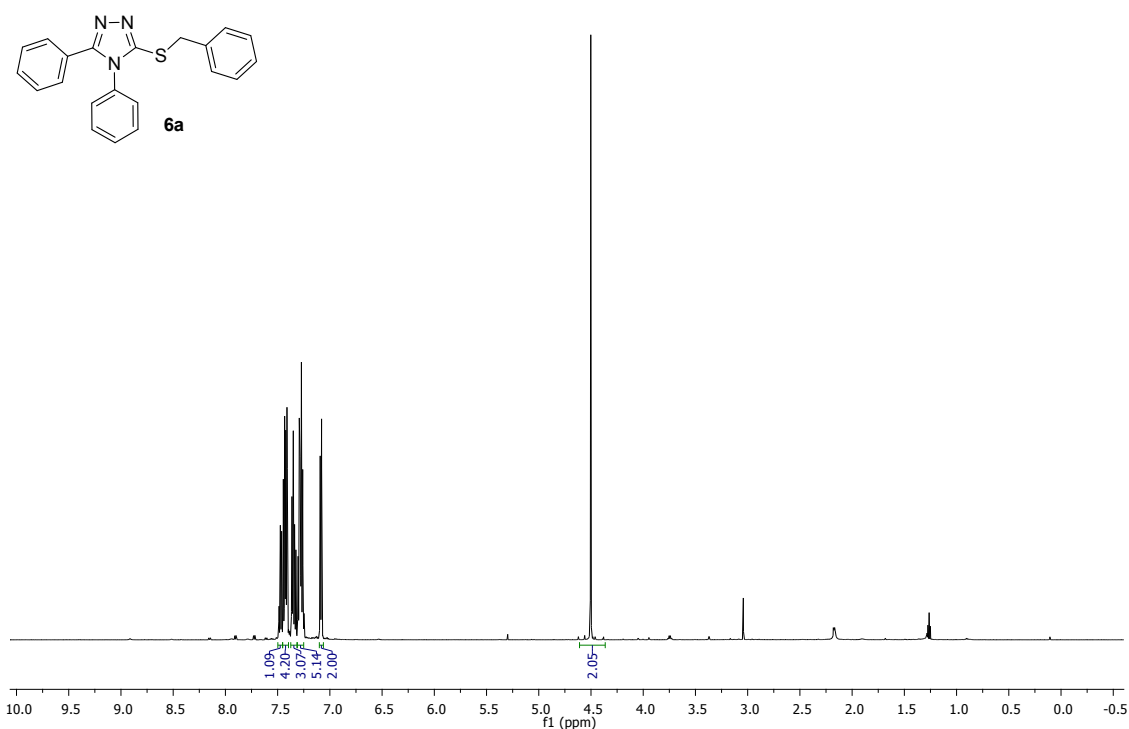


Figure S13. ¹H NMR spectrum (CDCl₃, 600 MHz) of compound **6a**.

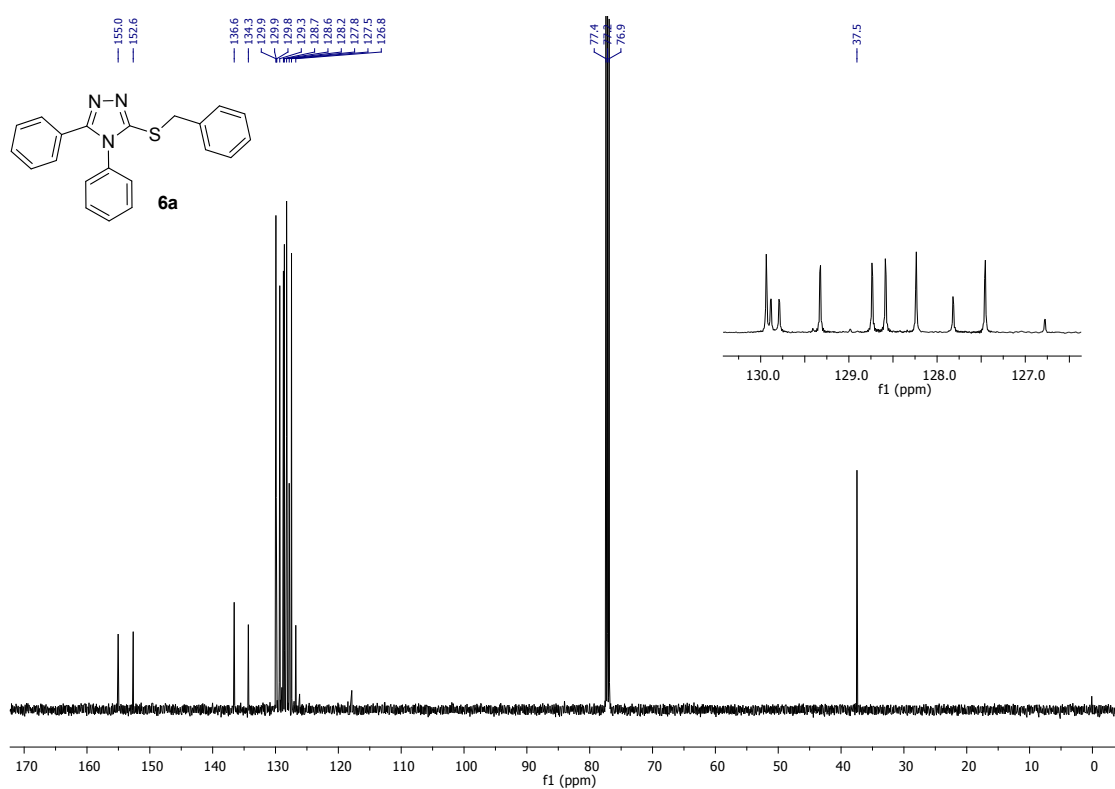


Figure S14. ¹³C NMR spectrum (CDCl₃, 151 MHz) of compound **6a**.

out10mfsH1_MF503

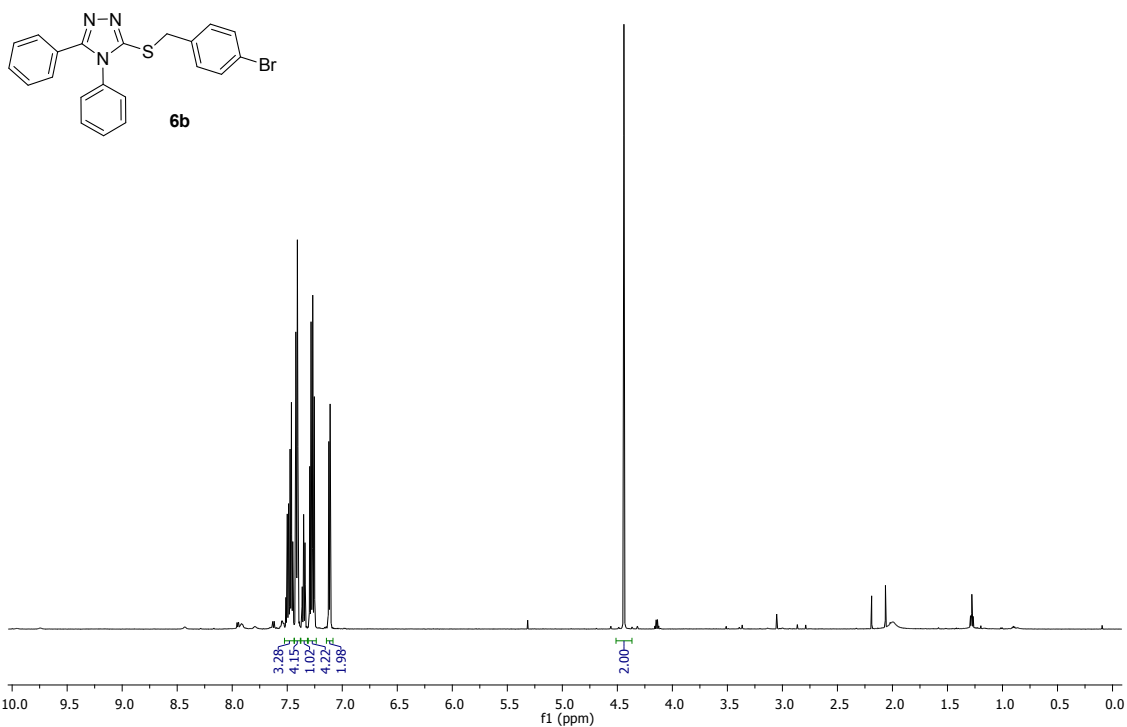
Mariana - MF 503 - CDCl₃ - Avance 600 MHz - out10mfsH1 - 1H

Figure S15. ¹H NMR spectrum (CDCl₃, 500 MHz) of compound **6b**.

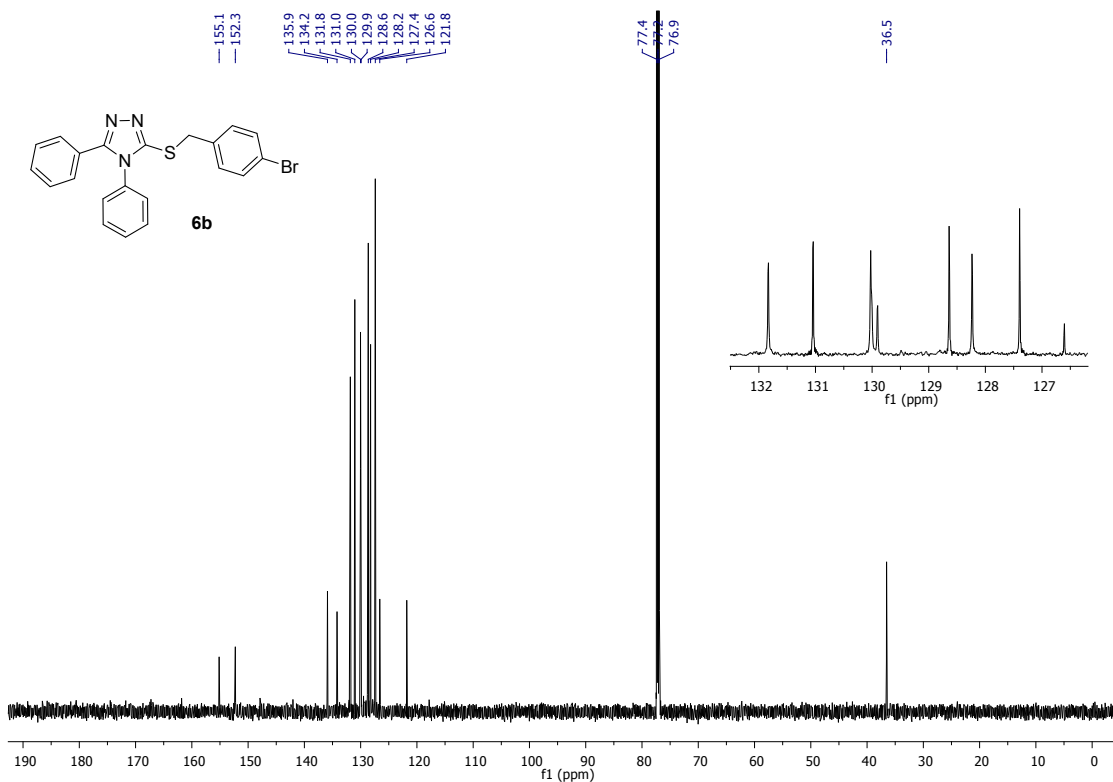


Figure S16. ¹³C NMR spectrum (CDCl₃, 126 MHz) of compound **6b**.

out10mfsH2_MF504
Mariana - MF 504 - CDCl₃ - Avance 600 MHz - out10mfsH2 - 1H

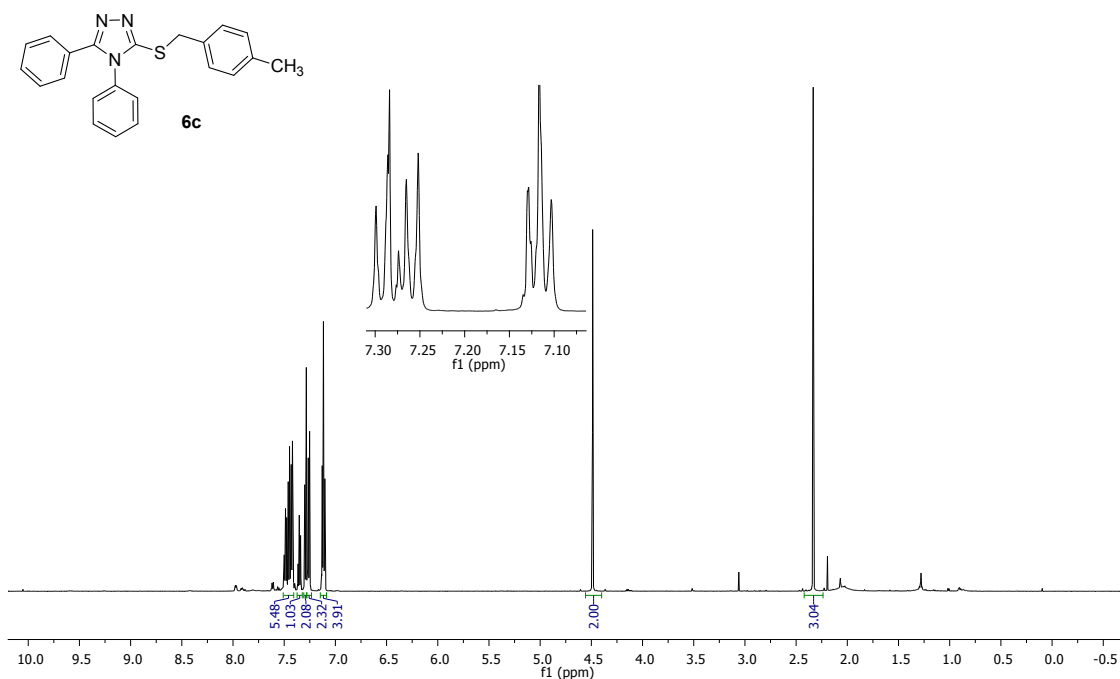


Figure S17 ¹H NMR spectrum (CDCl₃, 600 MHz) of compound **6c**.

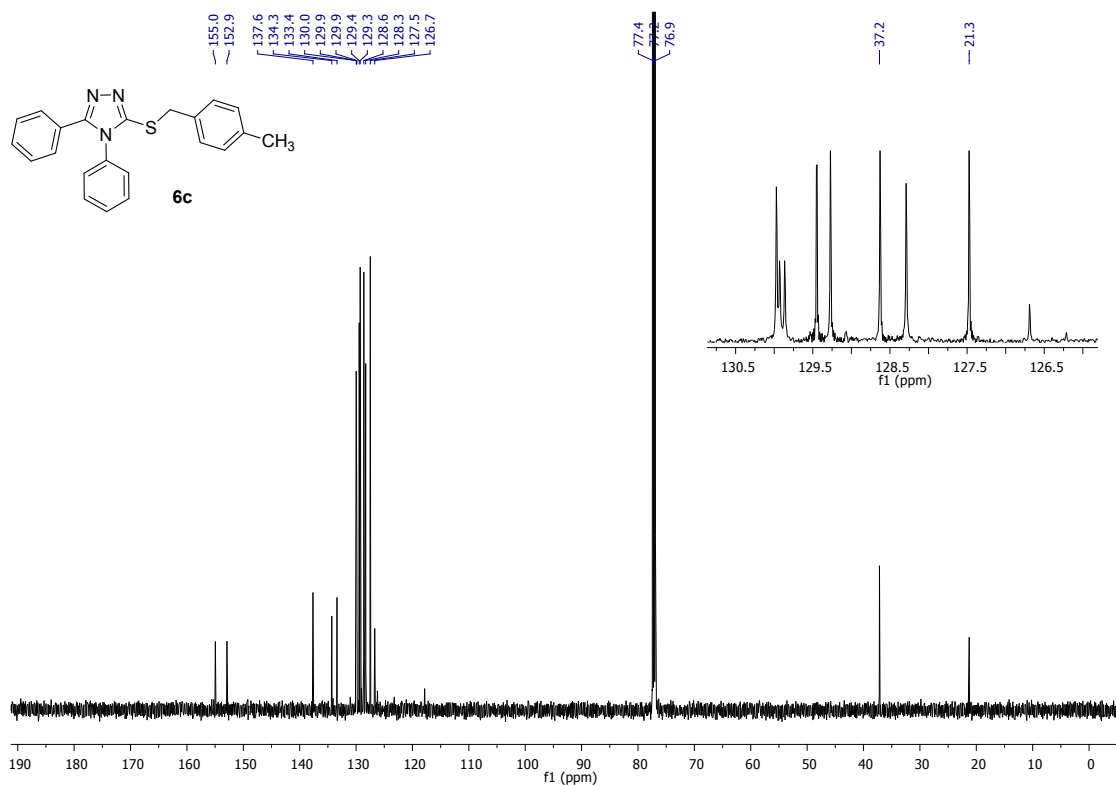


Figure S18 ¹³C NMR spectrum (CDCl₃, 151 MHz) of compound **6c**.

jan17mfsH1_MF505
Mariana - MF 505 - CDCl₃ - Avance 400 MHz - jan17mfsH1 - 1H

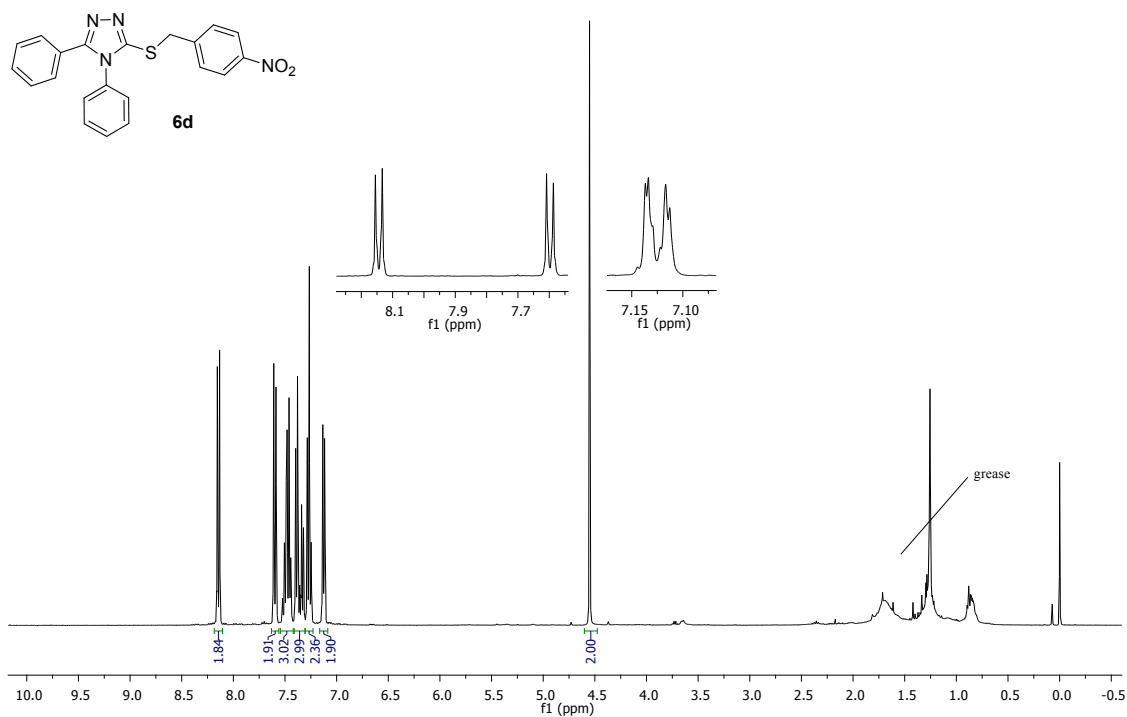


Figure S19. ¹H NMR spectrum (CDCl₃, 400 MHz) of compound **6d**.

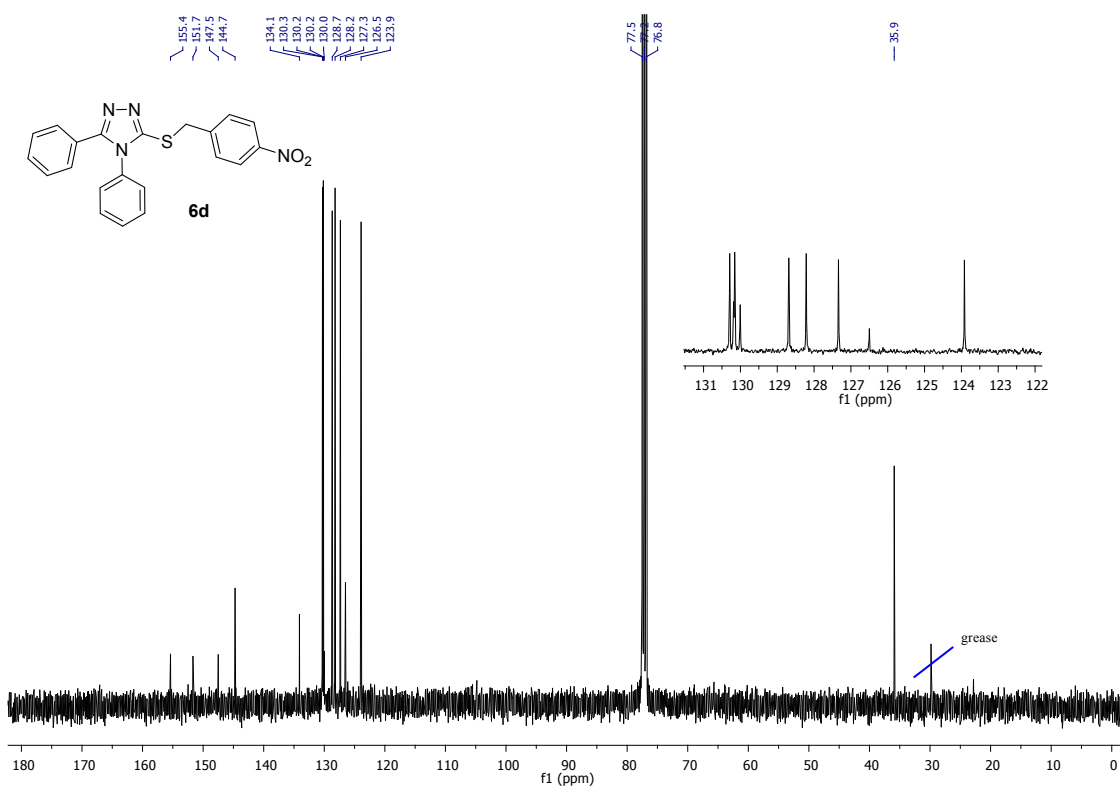


Figure S20. ¹³C NMR spectrum (CDCl₃, 101 MHz) of compound **6d**.

out13mfsH1_MF508
Mariana - MF 508 - CDCl₃ - Avance 600 MHz - out11mfsH1 - 1H

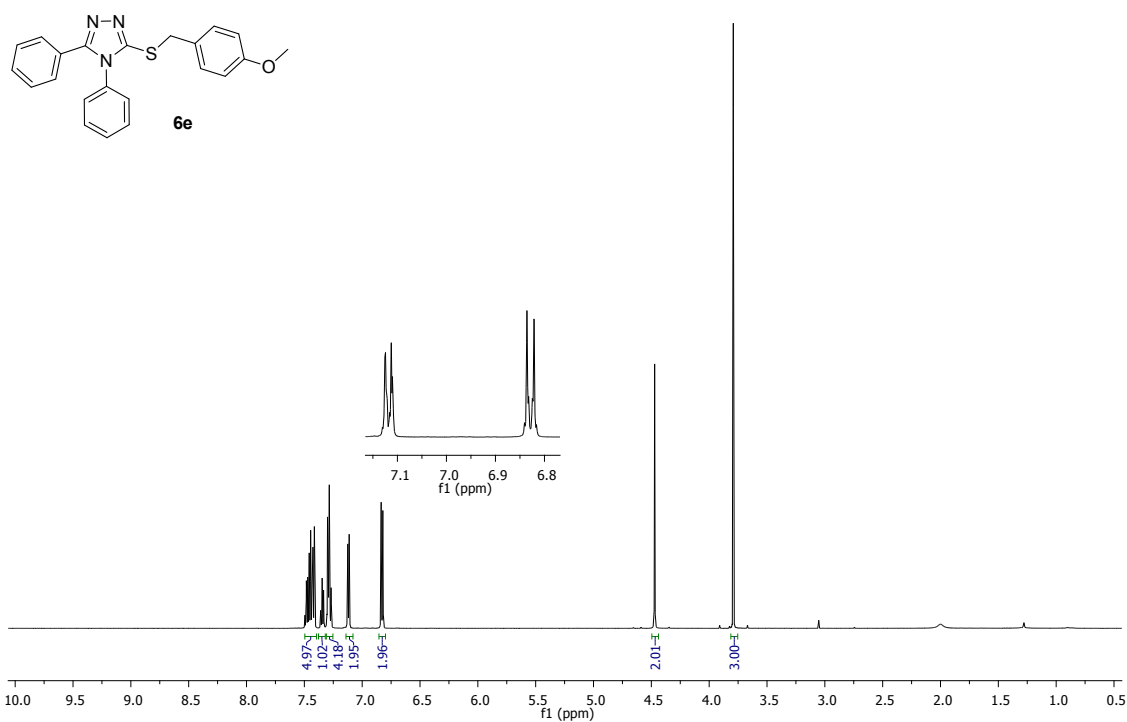


Figure S21. ¹H NMR spectrum (CDCl₃, 600 MHz) of compound **6e**.

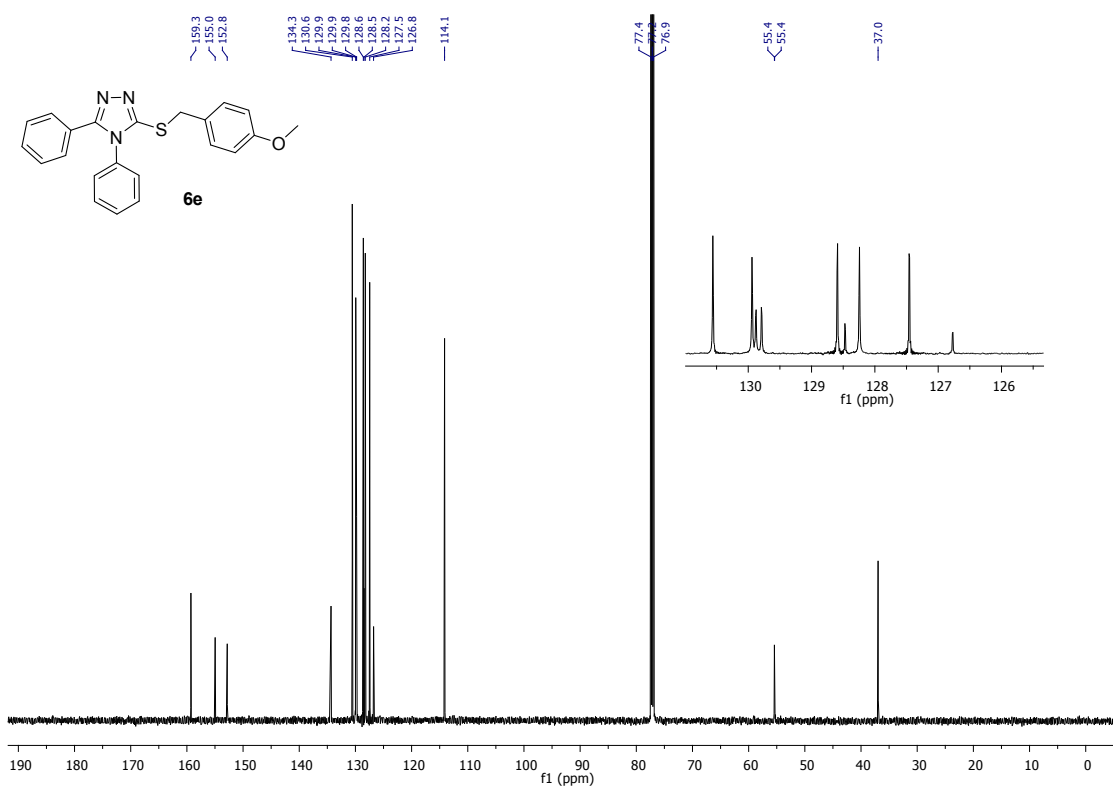


Figure S22. ¹³C NMR spectrum (CDCl₃, 151 MHz) of compound **6e**.

out03mfsH1_MF500
Mariana "MF-500" cdcl3/ Av500MHz out03mfsH1

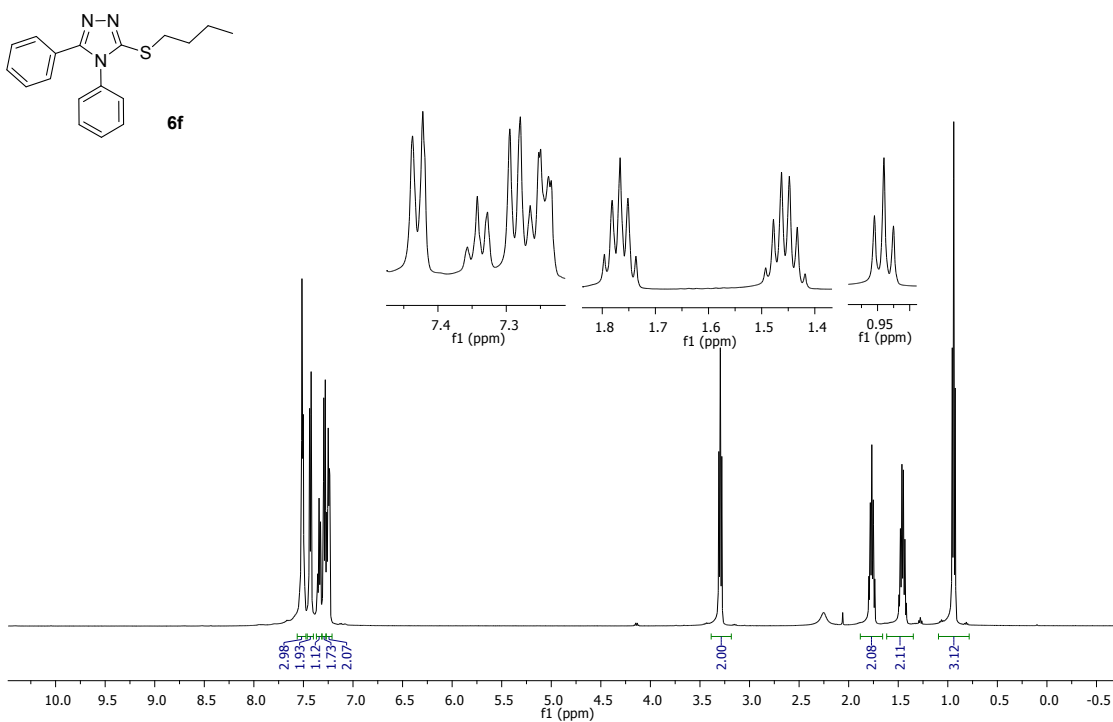


Figure S23. ^1H NMR spectrum (CDCl_3 , 500 MHz) of compound **6f**.

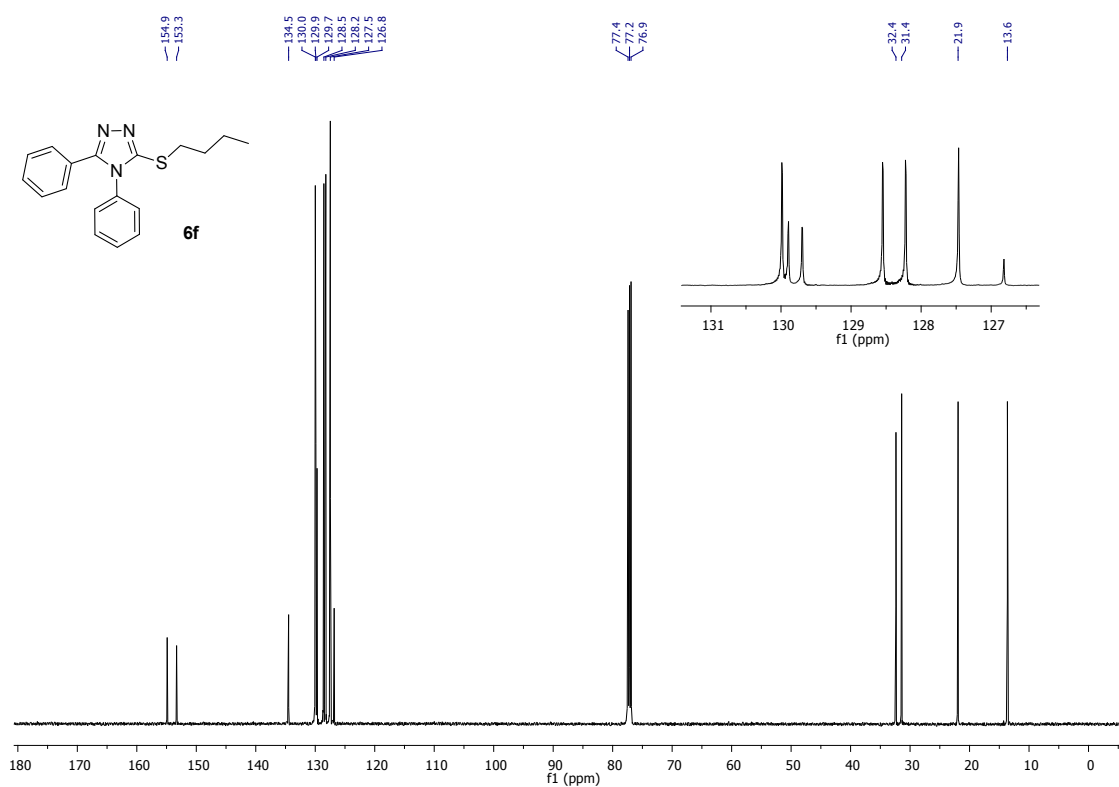


Figure S24. ^{13}C NMR spectrum (CDCl_3 , 126 MHz) of compound **6f**.

out10mfsH4_MF507
Mariana - MF 507 - CDCl₃ - Avance 600 MHz - out10mfsH4 - 1H

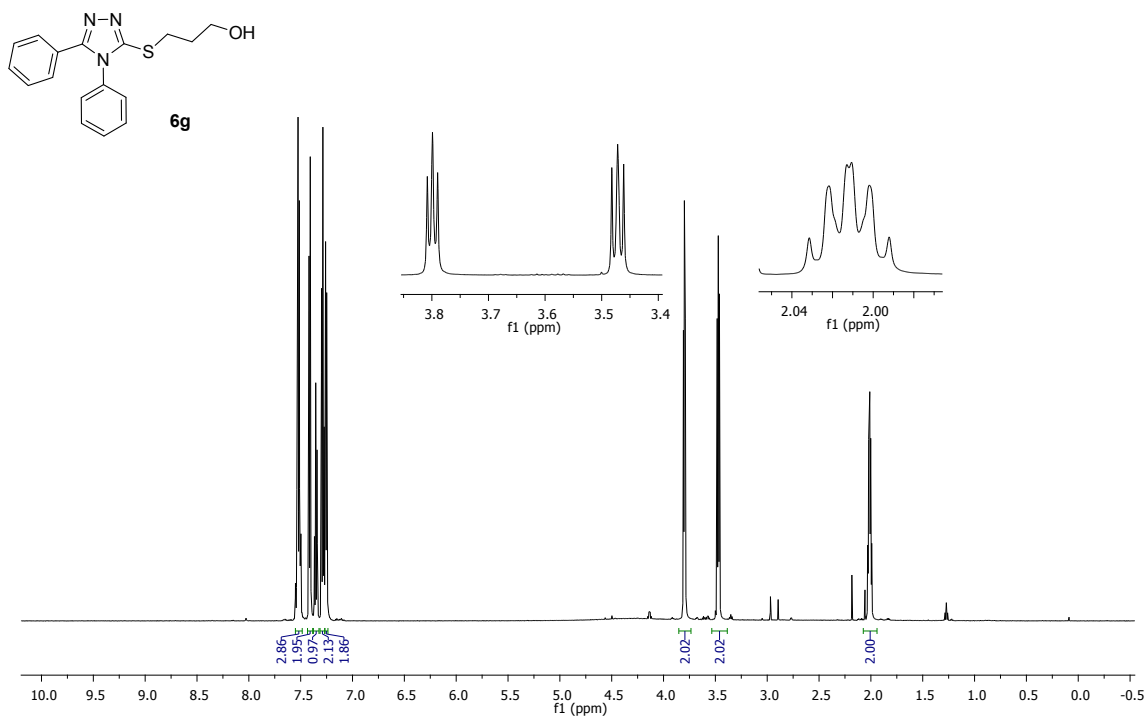


Figure S25. ¹H NMR spectrum (CDCl₃, 600 MHz) of compound **6g**.

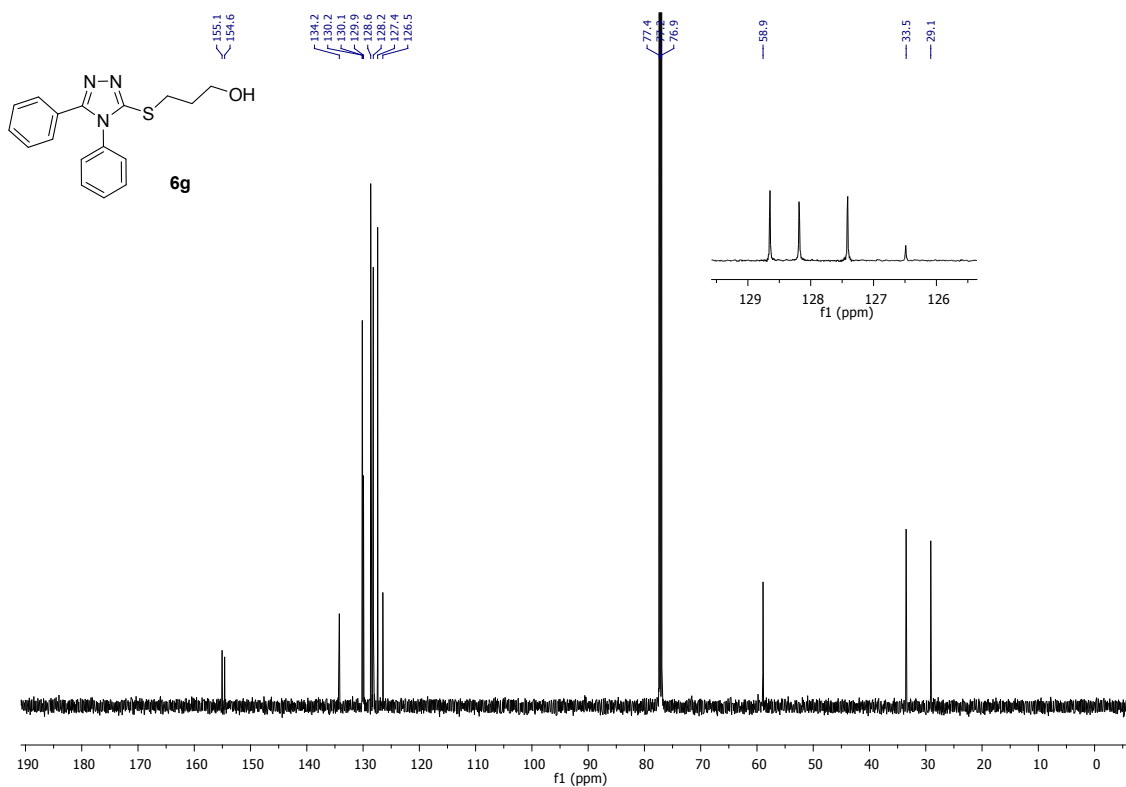


Figure S26. ¹³C NMR spectrum (CDCl₃, 151 MHz) of compound **6g**.

out26mfsH1_MF510
Mariana - MF 510 - CDCl₃ - Avance 400 MHz - out26mfsH1 - 1H

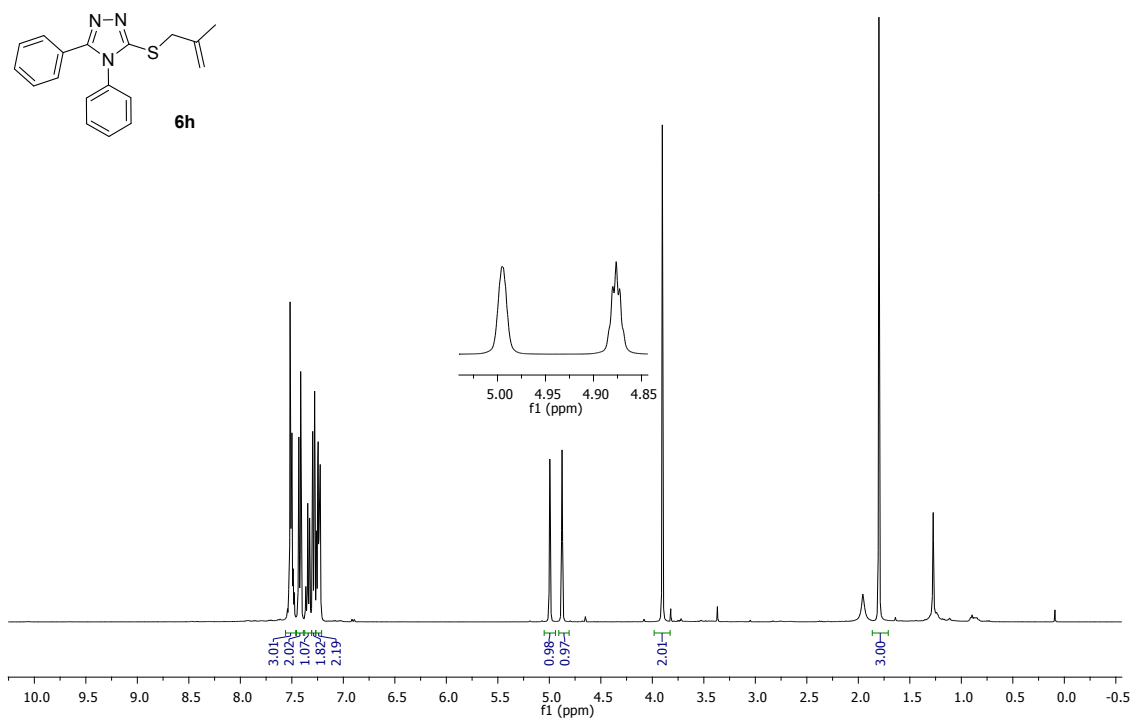


Figure S27. ¹H NMR spectrum (CDCl₃, 400 MHz) of compound **6h**.

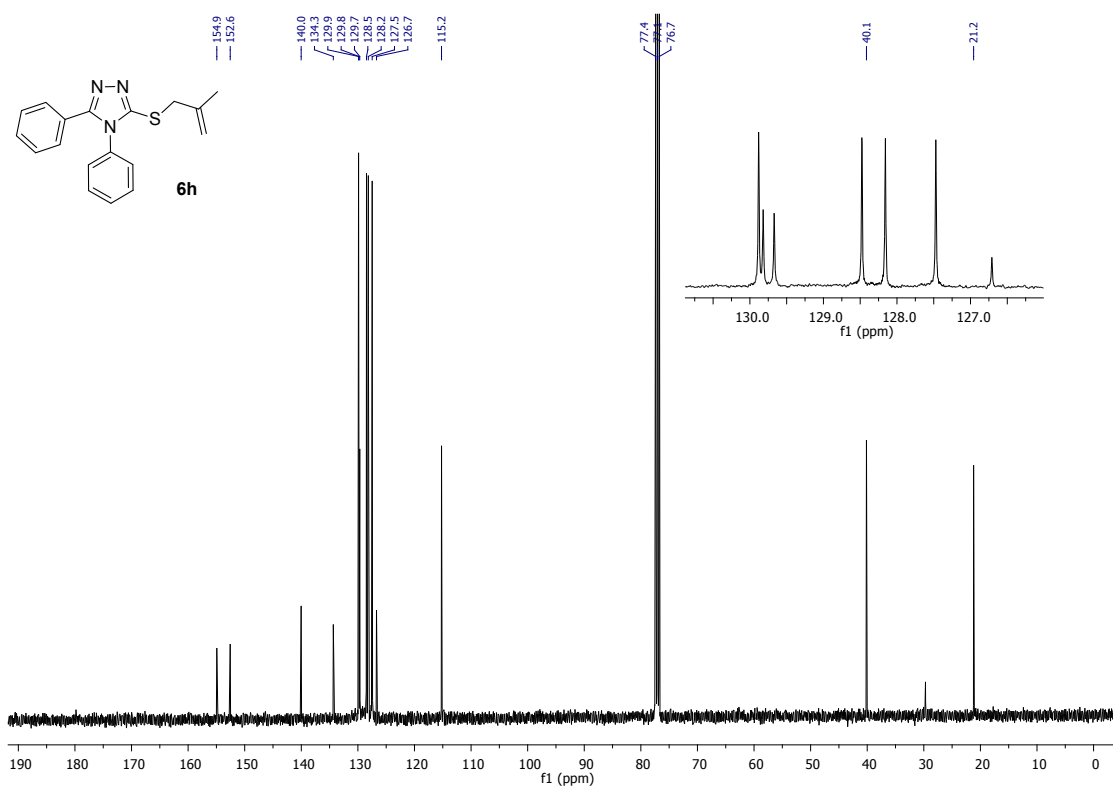


Figure S28. ¹³C NMR spectrum (CDCl₃, 101 MHz) of compound **6h**.

out13mfsH2_MF509
Mariana - MF 509 - CDCl₃ - Avance 600 MHz - out11mfsH2 - 1H

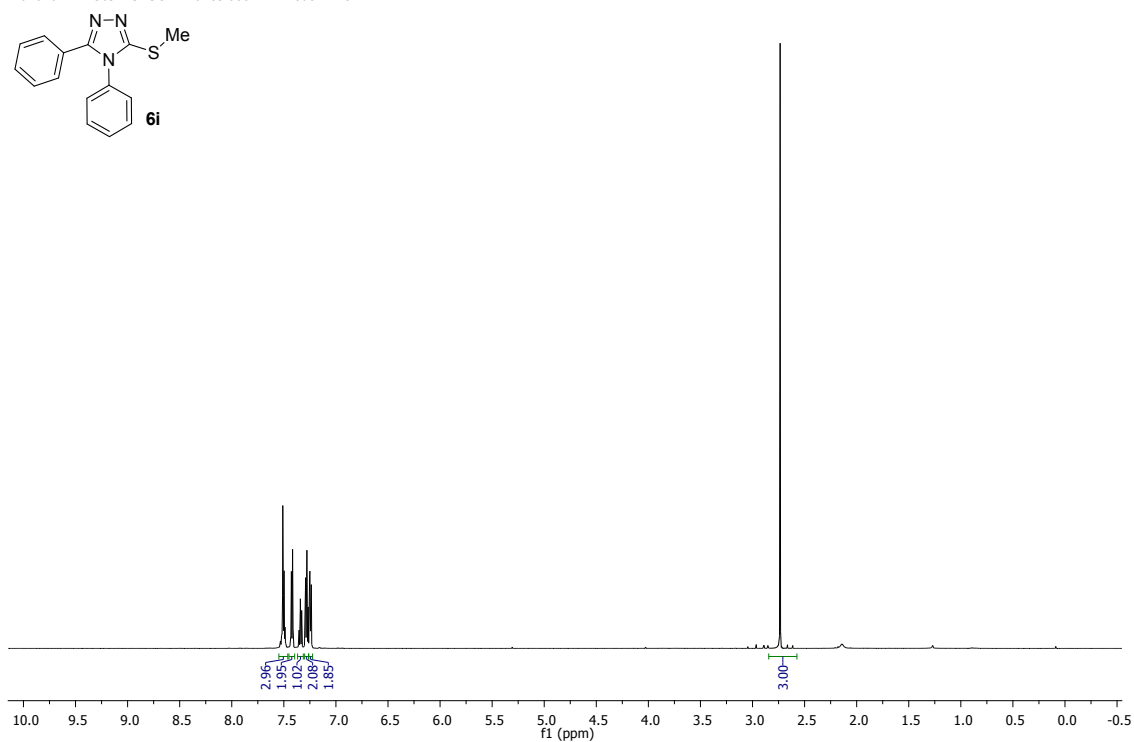


Figure S29. ¹H NMR spectrum (CDCl₃, 600 MHz) of compound **6i**.

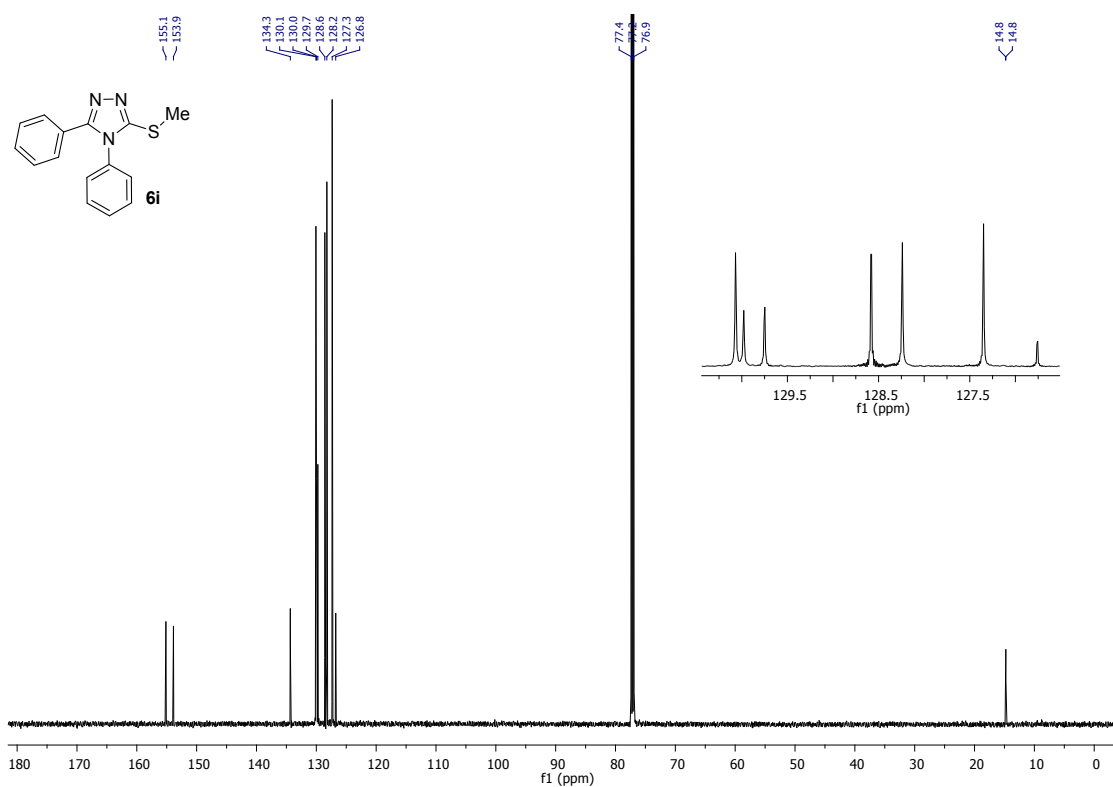


Figure S30. ¹³C NMR spectrum (CDCl₃, 151 MHz) of compound **6i**.

out27mfsH1_MF515
Mariana - MF 515 - CDCl₃ - Avance 600 MHz - out27mfsH1 - 1H

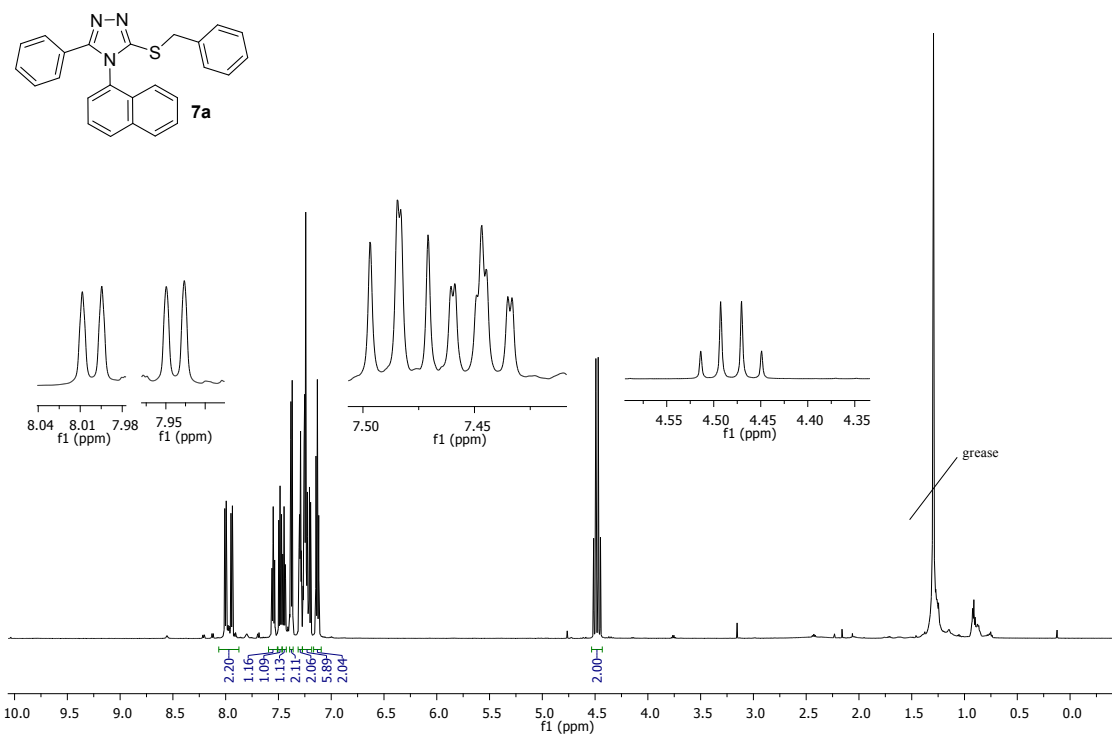


Figure S31. ¹H NMR spectrum (CDCl₃, 600 MHz) of compound **7a**.

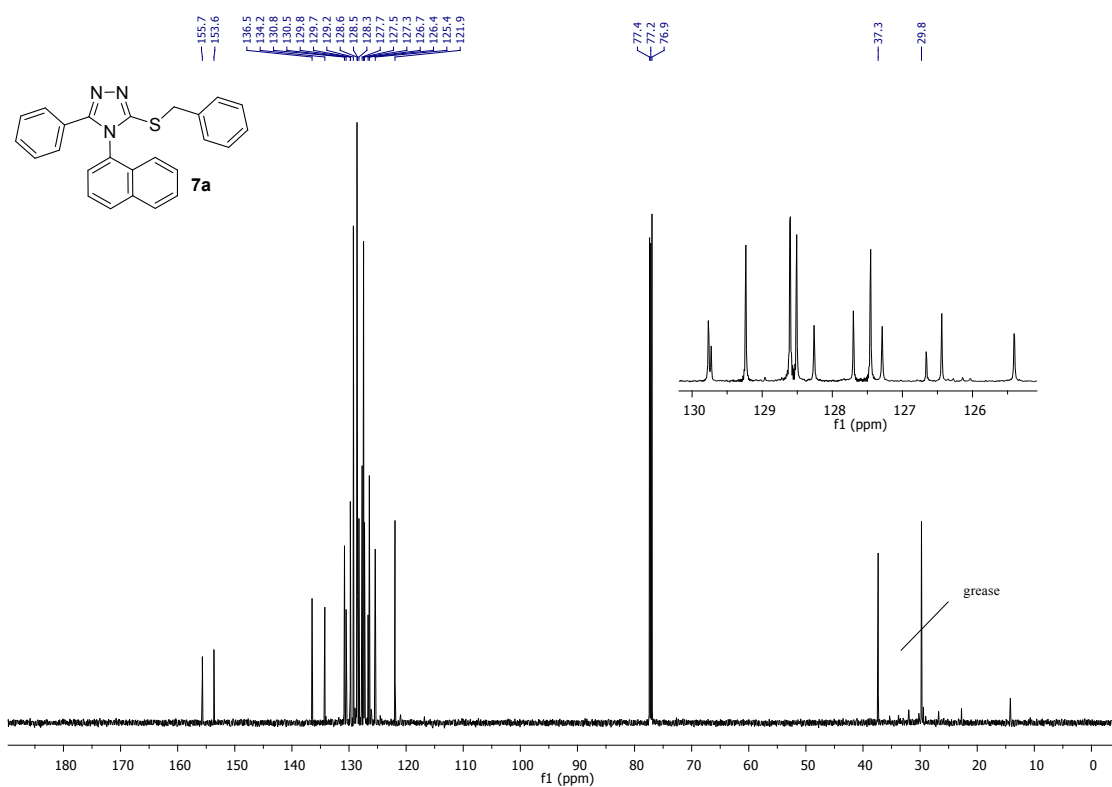


Figure S32. ¹³C NMR spectrum (CDCl₃, 151 MHz) of compound **7a**.

out31mfsH1_MF513b
Mariana - MF 513b - CDCl₃ - Avance 600 MHz - out31mfsH1 - 1H

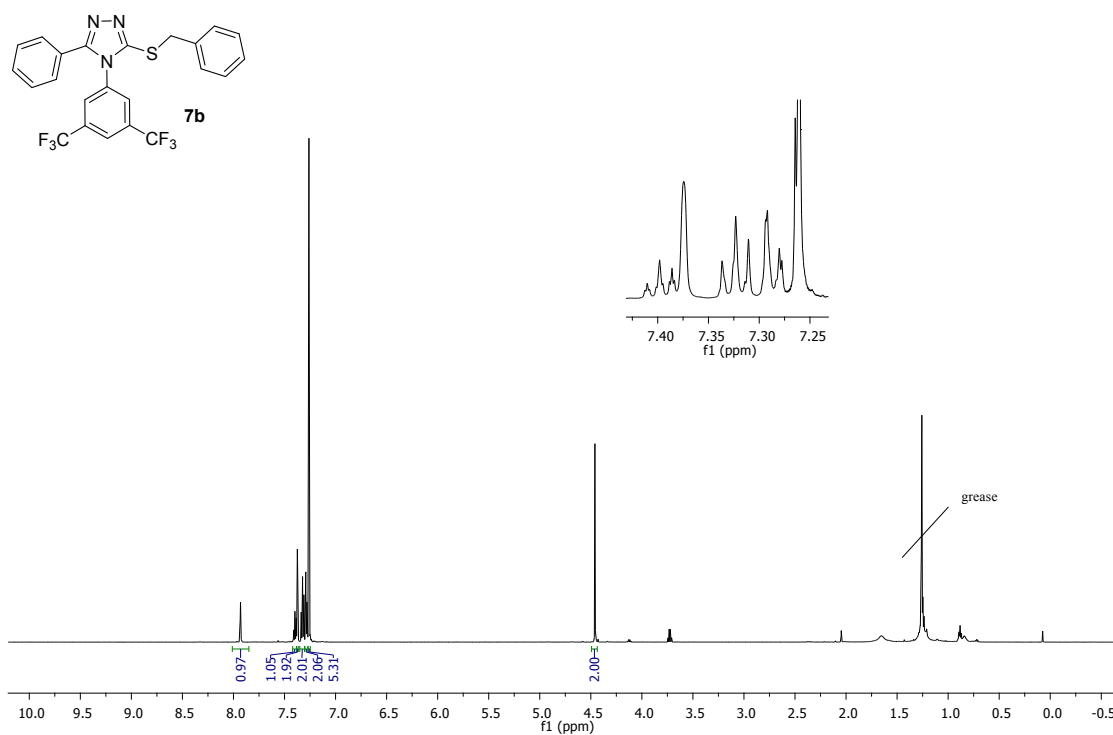


Figure S33. ¹H NMR spectrum (CDCl₃, 600 MHz) of compound **7b**.

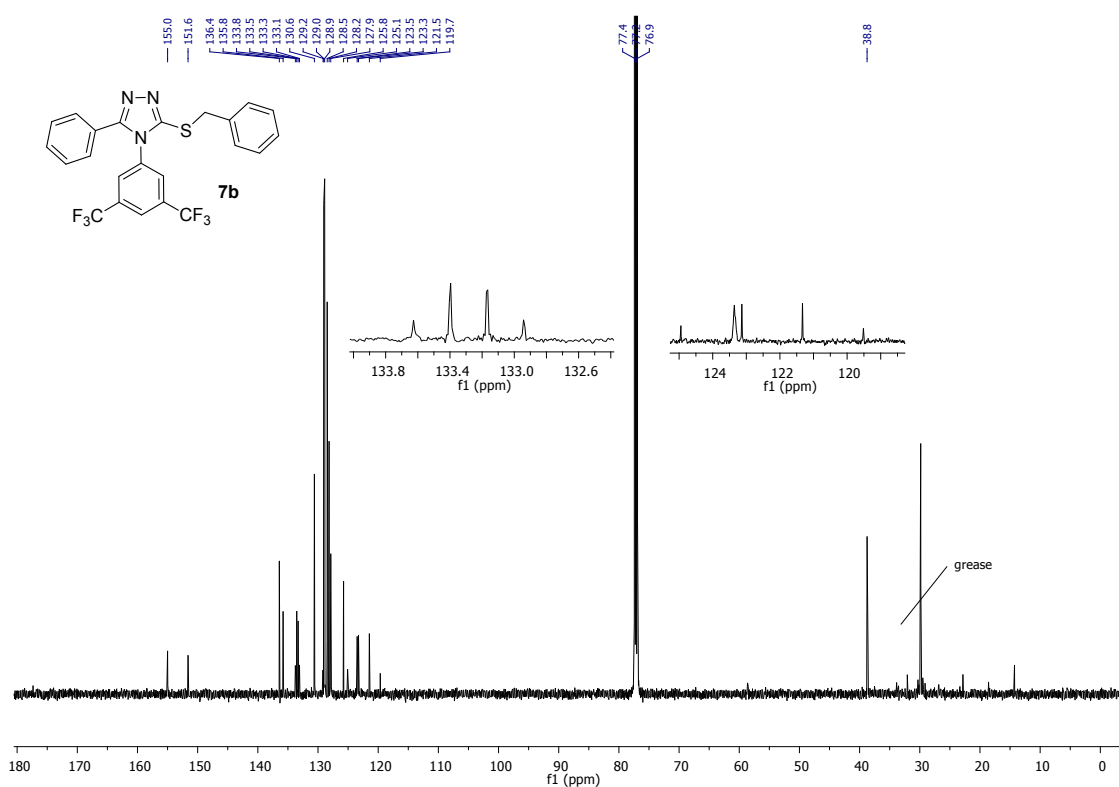


Figure S34. ¹³C NMR spectrum (CDCl₃, 151 MHz) of compound **7b**.

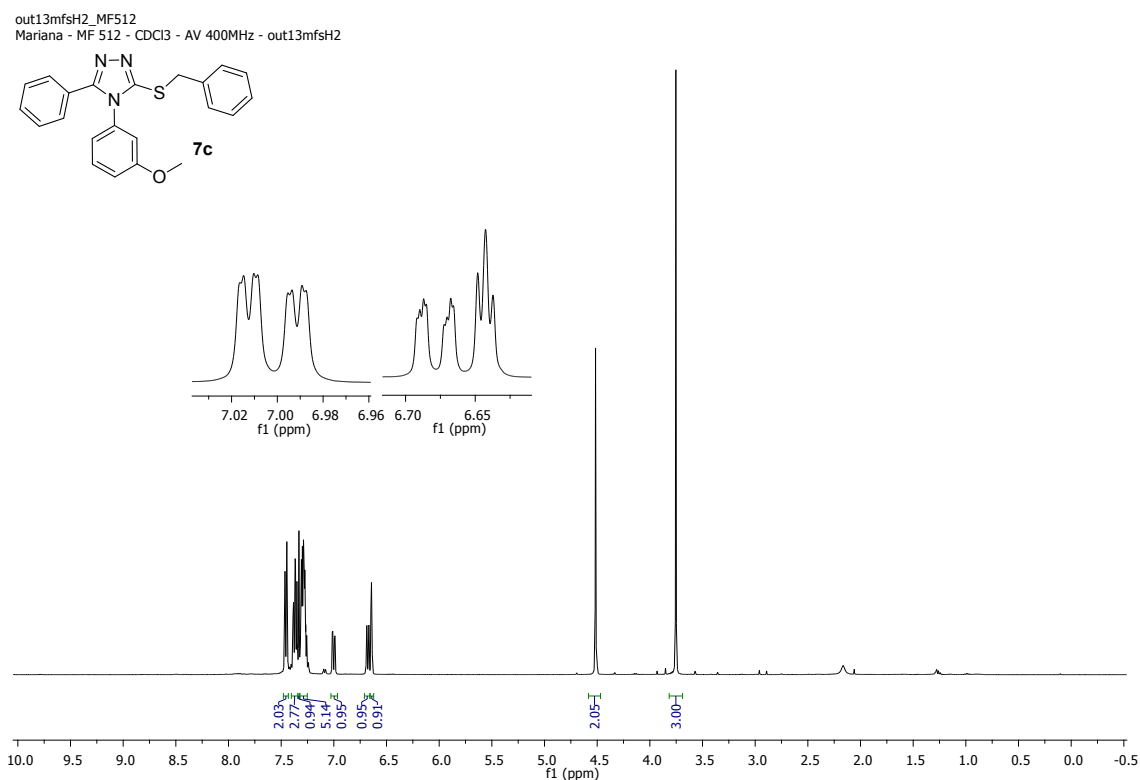


Figure S35. ¹H NMR spectrum (CDCl₃, 400 MHz) of compound **7c**.

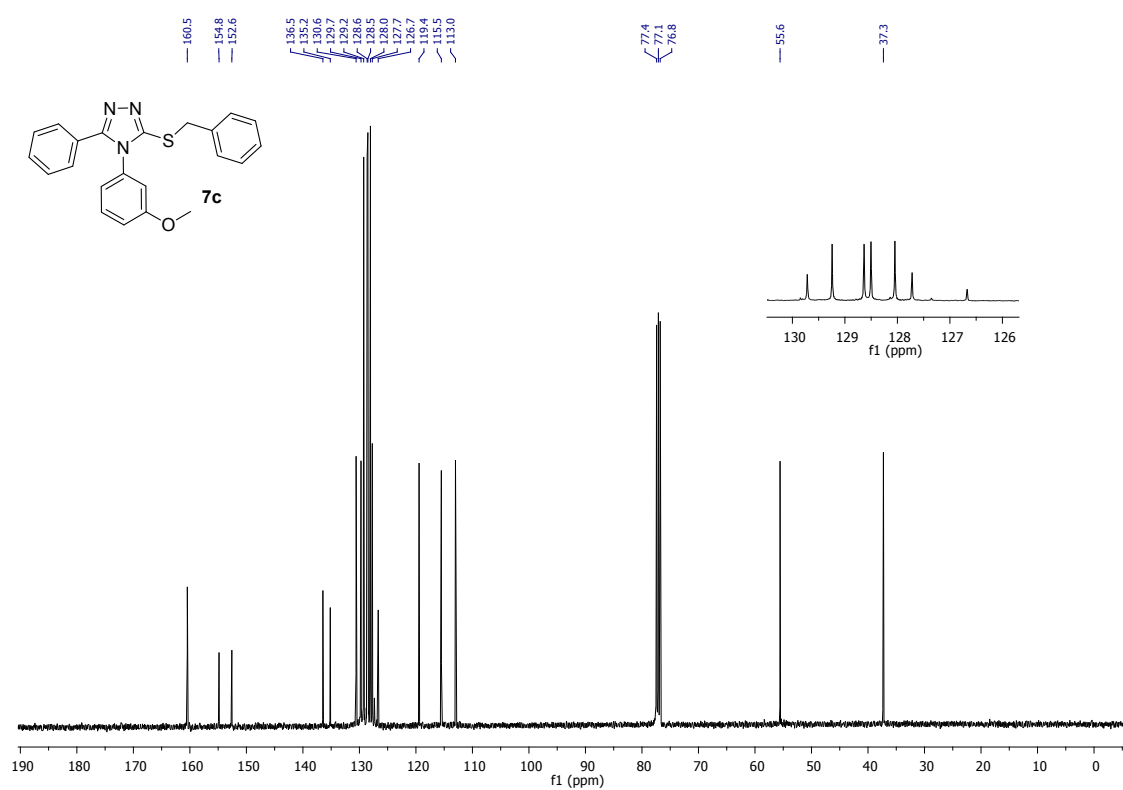


Figure S36. ¹³C NMR spectrum (CDCl₃, 101 MHz) of compound **7c**.

out21mfsH1_MF520
Mariana "MF-520" cdcl3/ Av500MHz out21mfsH1

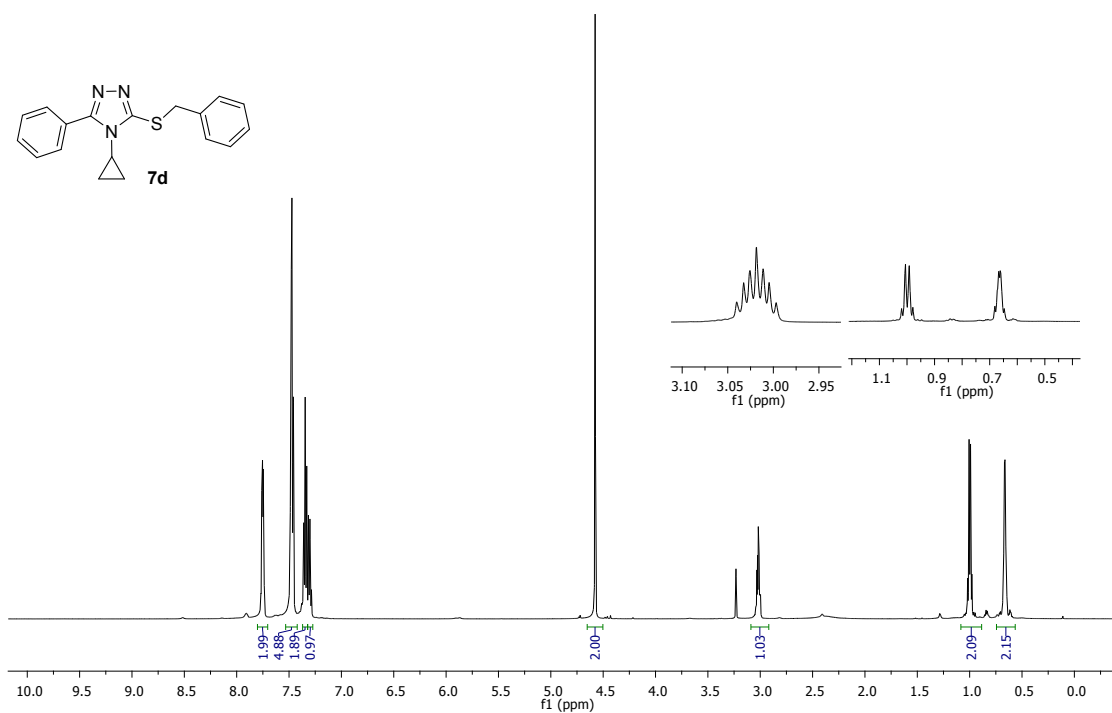


Figure S37. ¹H NMR spectrum (CDCl₃, 500 MHz) of compound **7d**.

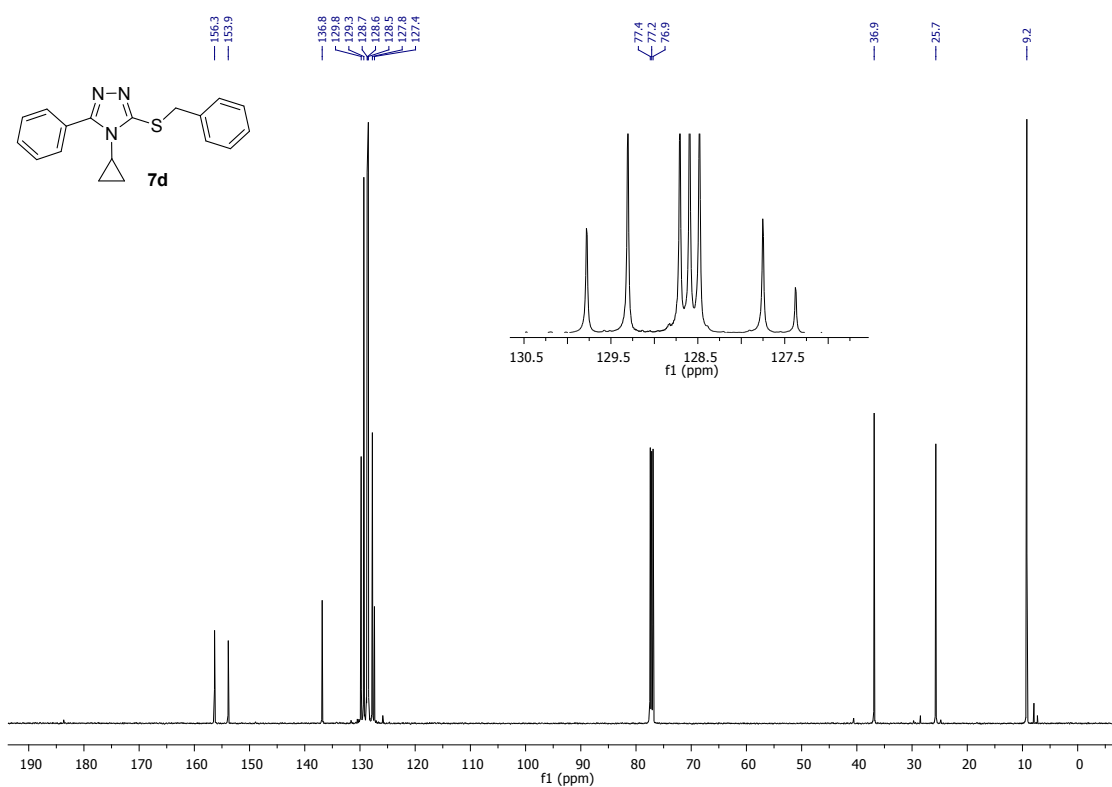


Figure S38. ¹³C NMR spectrum (CDCl₃, 126 MHz) of compound **7d**.

jan10mfsH1_MF551
Mariana - MF 551 - CDCl₃ - Avance 500 MHz - jan10mfsH1 - 1H

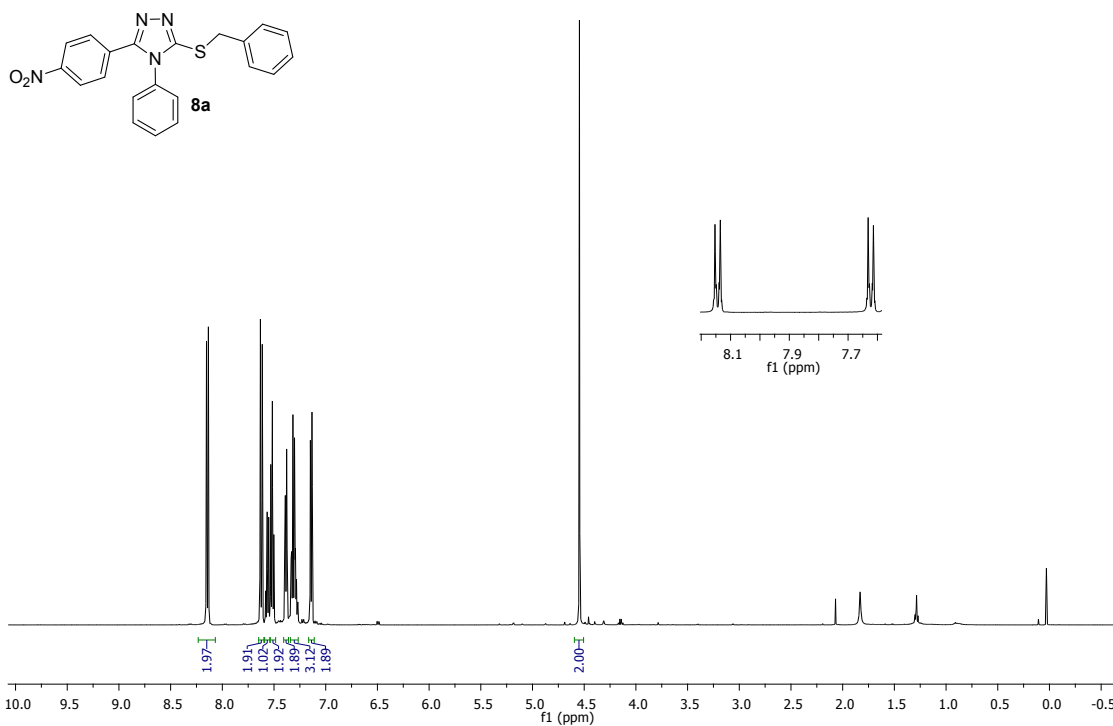


Figure S39. ¹H NMR spectrum (CDCl₃, 500 MHz) of compound **8a**.

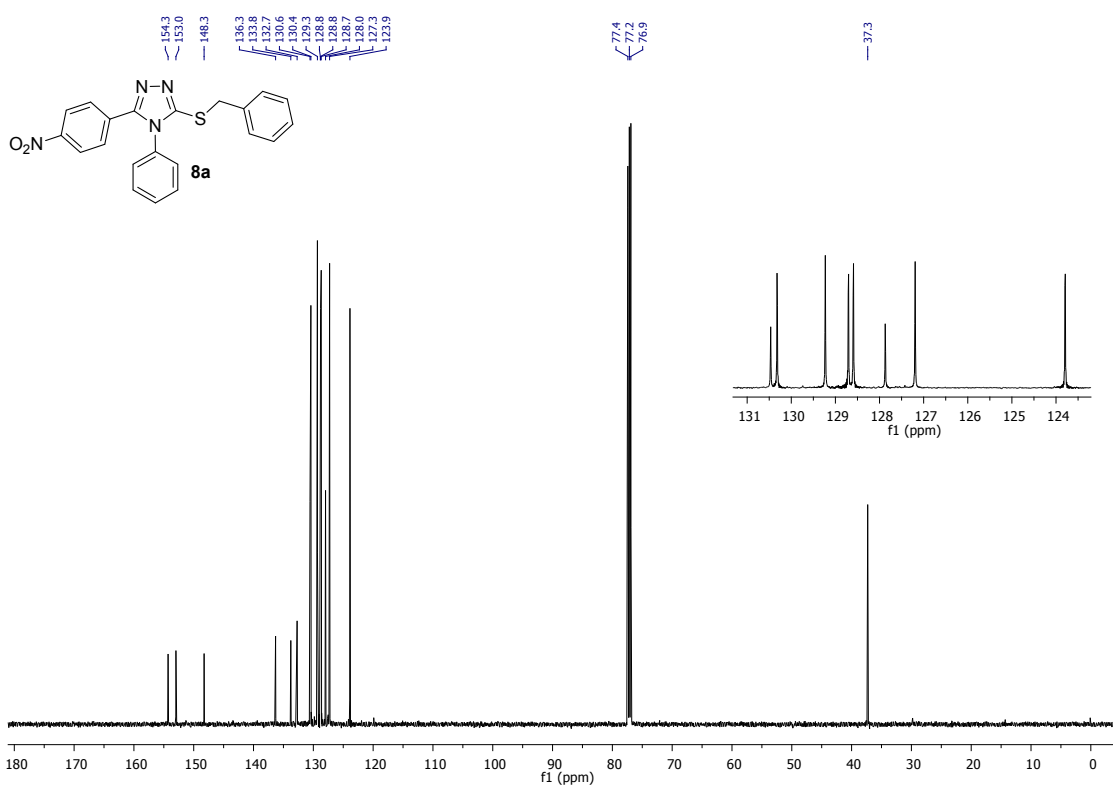


Figure S40. ¹³C NMR spectrum (CDCl₃, 126 MHz) of compound **8a**.

dez15mfsH2_MF534
Mariana - MF 534 - CDCl₃ - Av 400MHz - dez15mfsH2

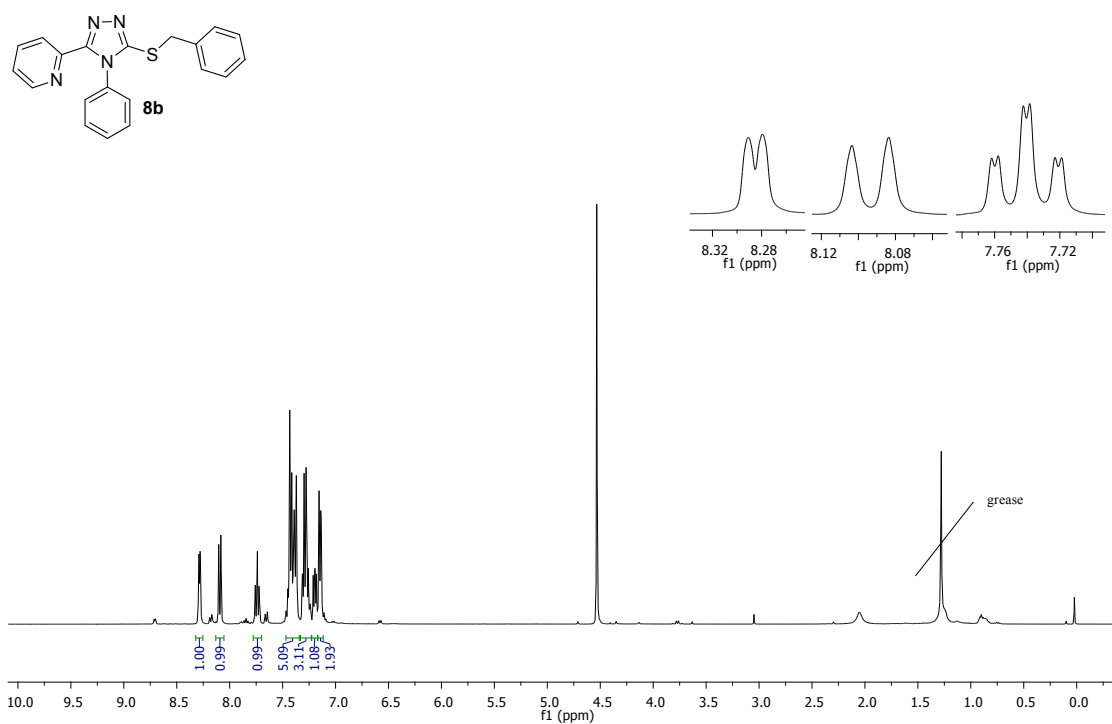


Figure S41. ¹H NMR spectrum (CDCl₃, 400 MHz) of compound **8b**.

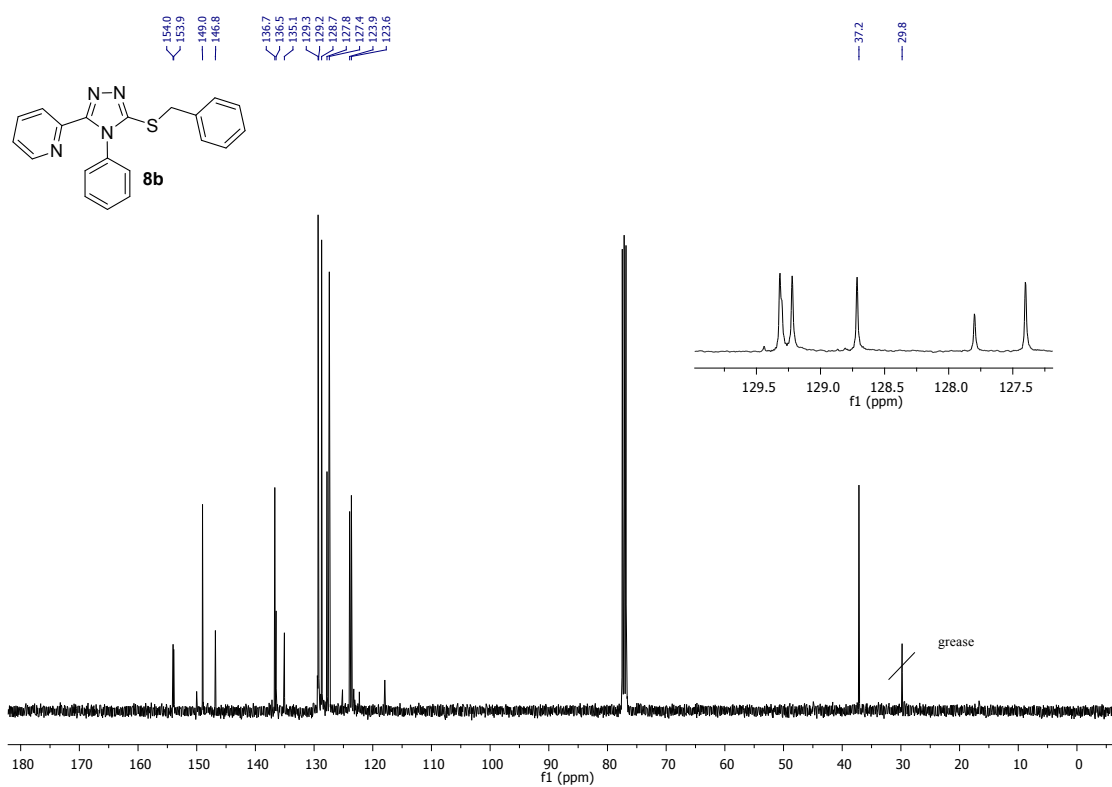


Figure S42. ¹³C NMR spectrum (CDCl₃, 101 MHz) of compound **8b**.

dez15mfsH1_MF533
Mariana - MF 533 - CDCl₃ - Av 400MHz - dez15mfsH1

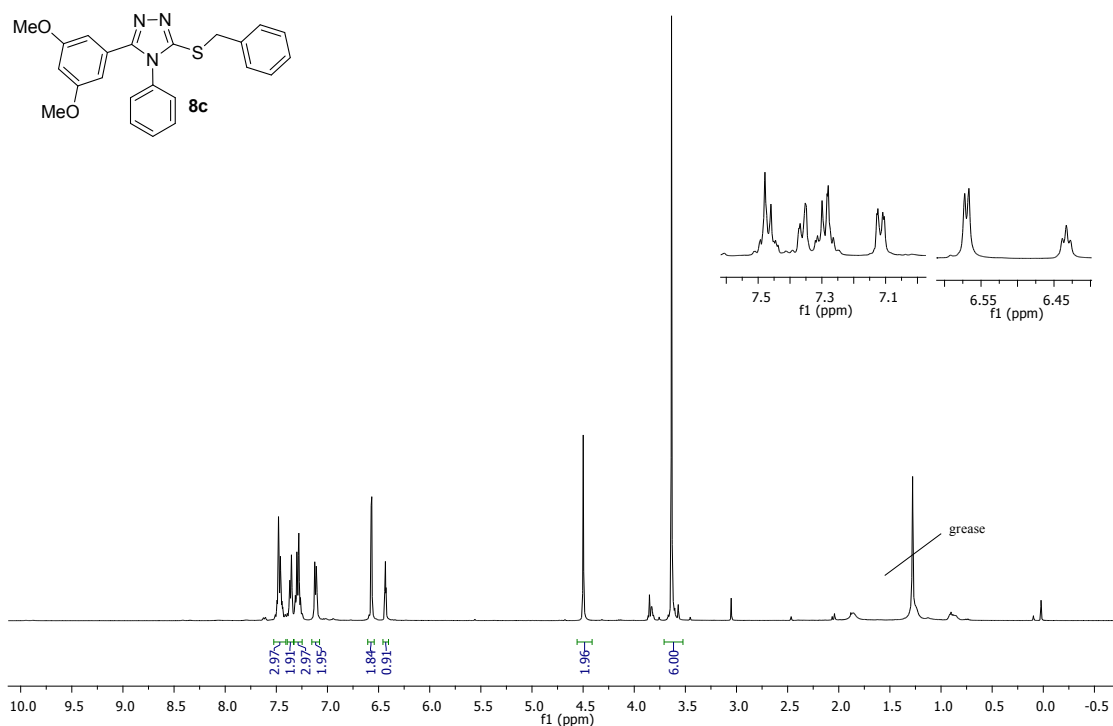


Figure S43. ¹H NMR spectrum (CDCl₃, 400 MHz) of compound **8c**.

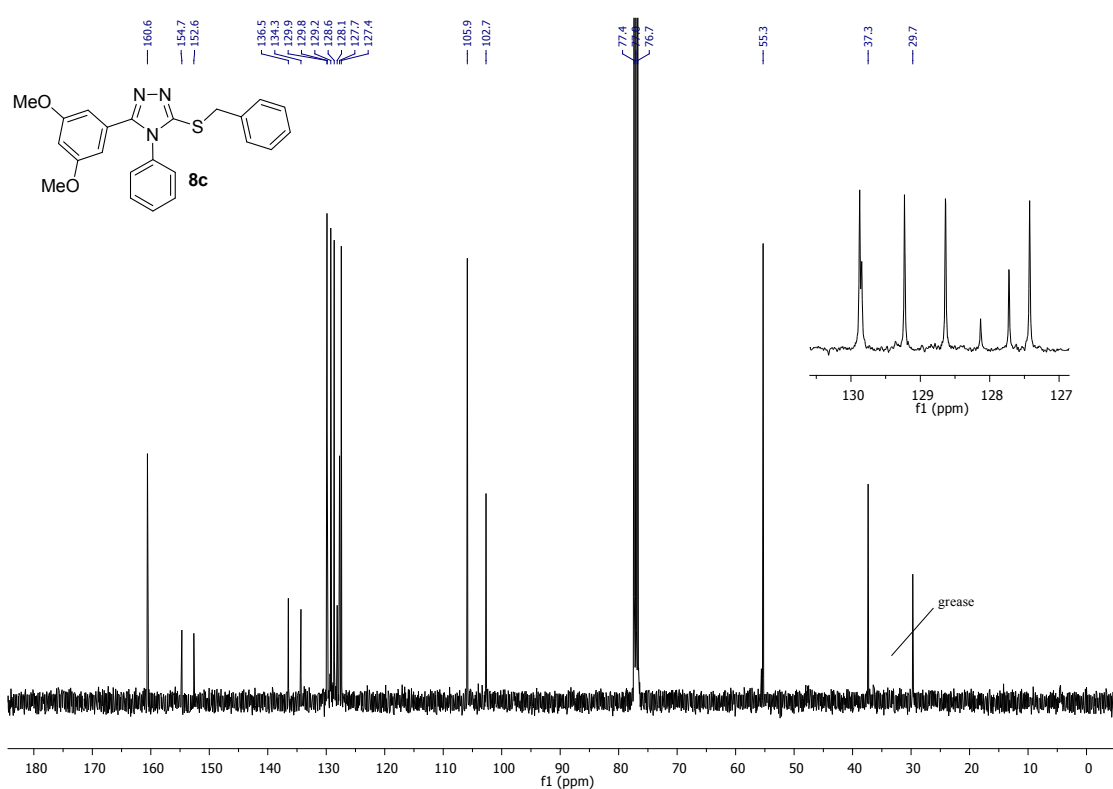


Figure S44. ¹³C NMR spectrum (CDCl₃, 101 MHz) of compound **8c**.

jan27mfsH1_MF553
Mariana - MF 553 - CDCl₃ - Avance 400 MHz - jan27mfsH1 - 1H

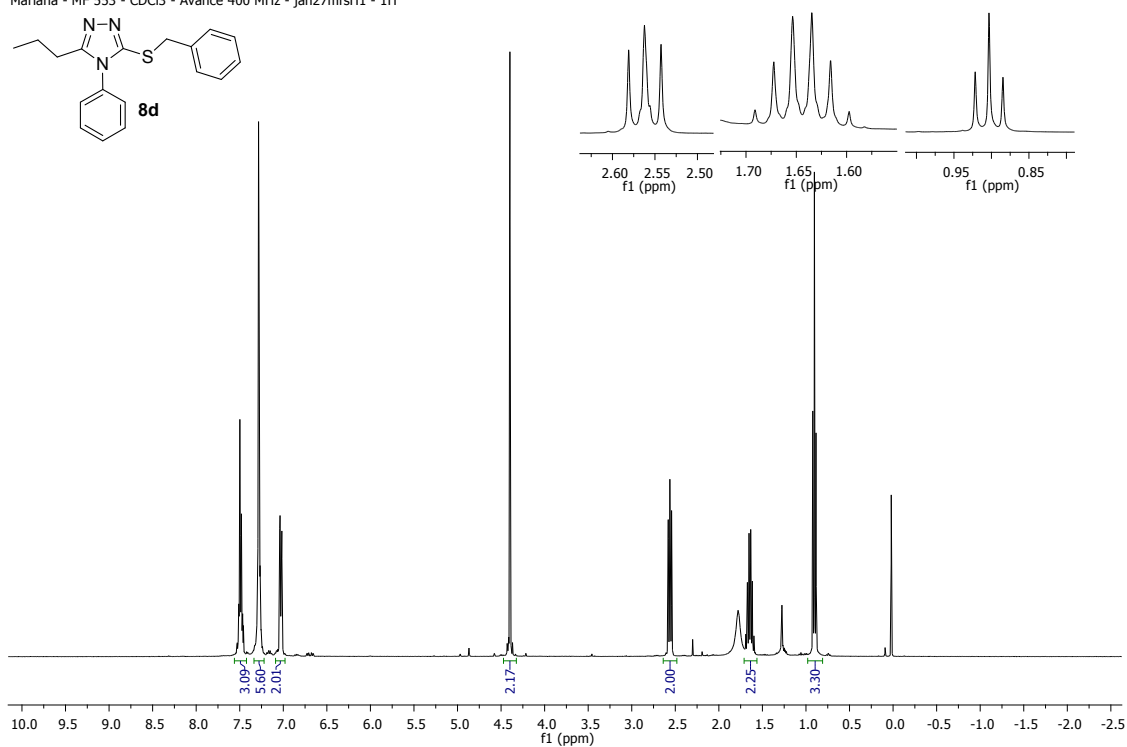


Figure S45. ¹H NMR spectrum (CDCl₃, 400 MHz) of compound **8d**.

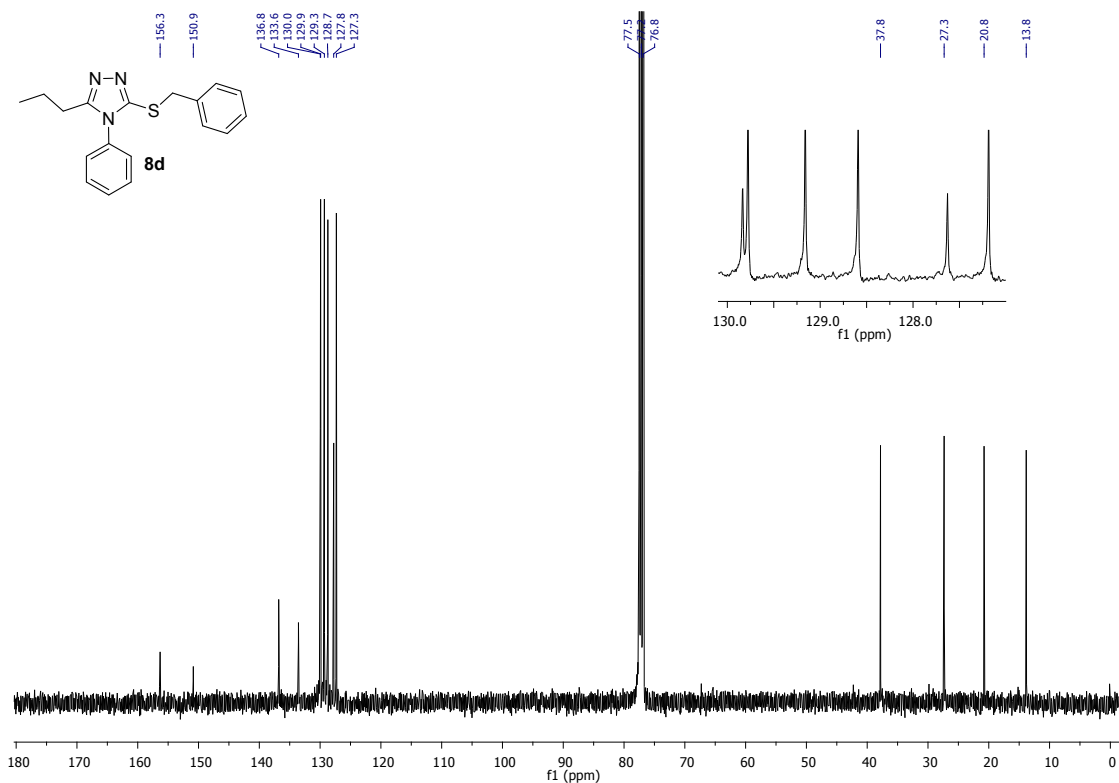


Figure S46. ¹³C NMR spectrum (CDCl₃, 101 MHz) of compound **8d**.