Supporting Information

Identification of Dihydropyrazolo[1,5-*a*]pyrazin-4(5*H*)-ones as Cyclic Products of β-Amidomethyl Vinyl Sulfone Alphavirus Cysteine Protease Inhibitors

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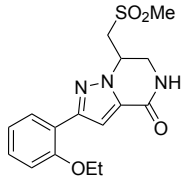
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Table S1: nsP2 Protease Inhibition Data



2

Compound	nsP2 Protease (pIC_{50}) [a]
2	i.a.

[a]Data from a 10-point dose response curve in triplicate. i.a. = inactive at 200 µM. Assay performed as described in [1].

1. Merten, E.M.; Sears, J.D.; Leisner, T.M.; Hardy, P.B.; Ghoshal, A.; Hossain, M.A.; Asressu, K.H.; Brown, P.J.; Stashko, M.A.; Herring, L.E.; et al. Discovery of a cell-active chikungunya virus nsP2 protease inhibitor using a covalent fragment-based screening approach. *bioRxiv* **2024**, doi:10.1101/2024.03.22.586341.

Figure S1: GSH capture

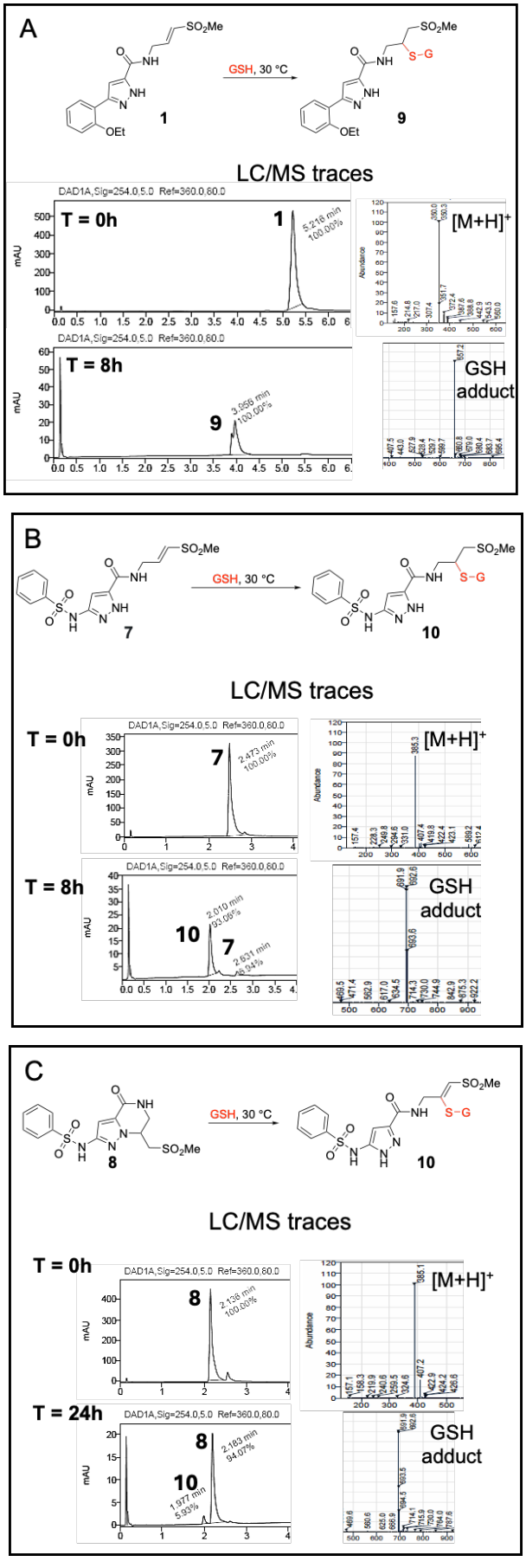


Figure S2: ^{1}H NMR (500 MHz, DMSO-d_6) for **1•TFA**

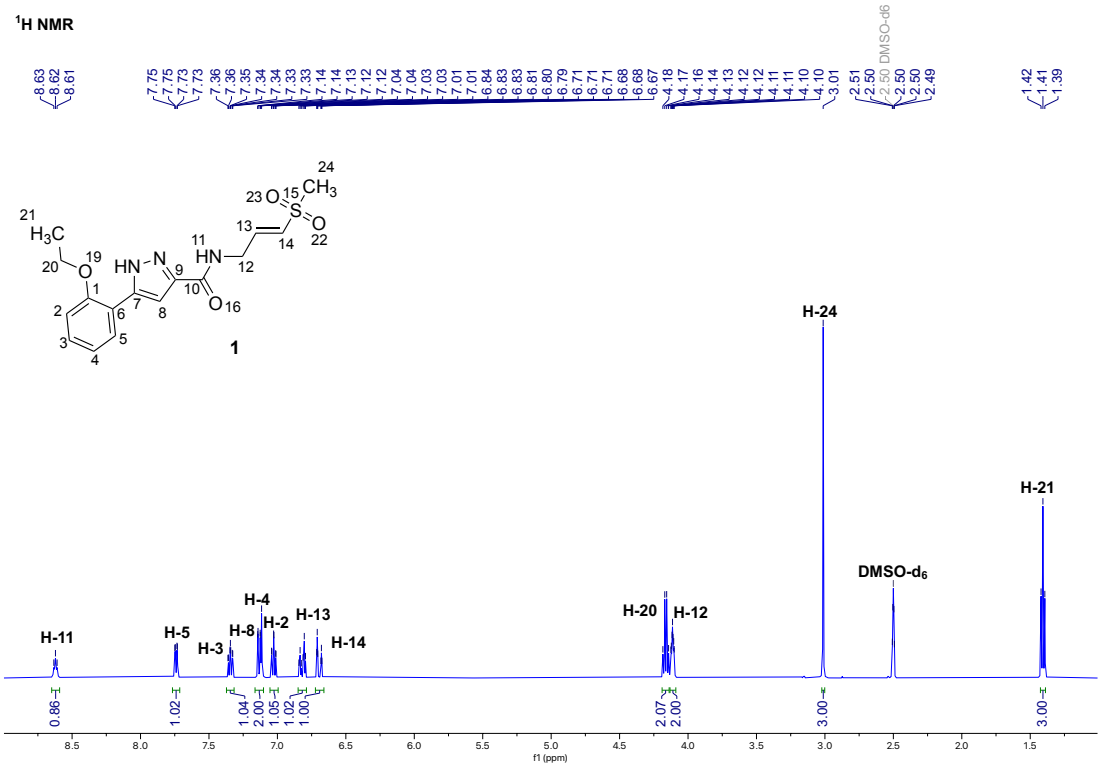


Figure S3: ^{13}C NMR (126 MHz, DMSO-d_6) for **1•TFA**

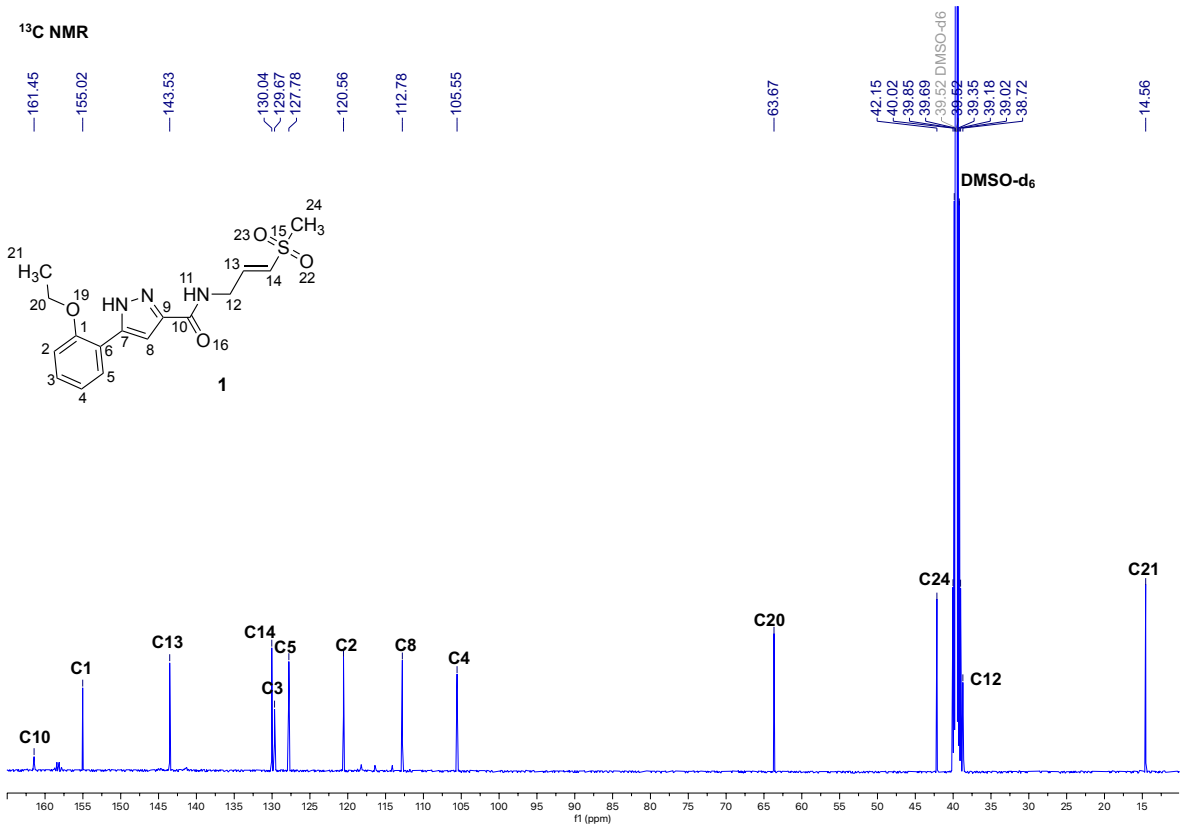


Figure S4: ^{13}C NMR DEPT-135 (126 MHz, DMSO-d_6) for **1•TFA**

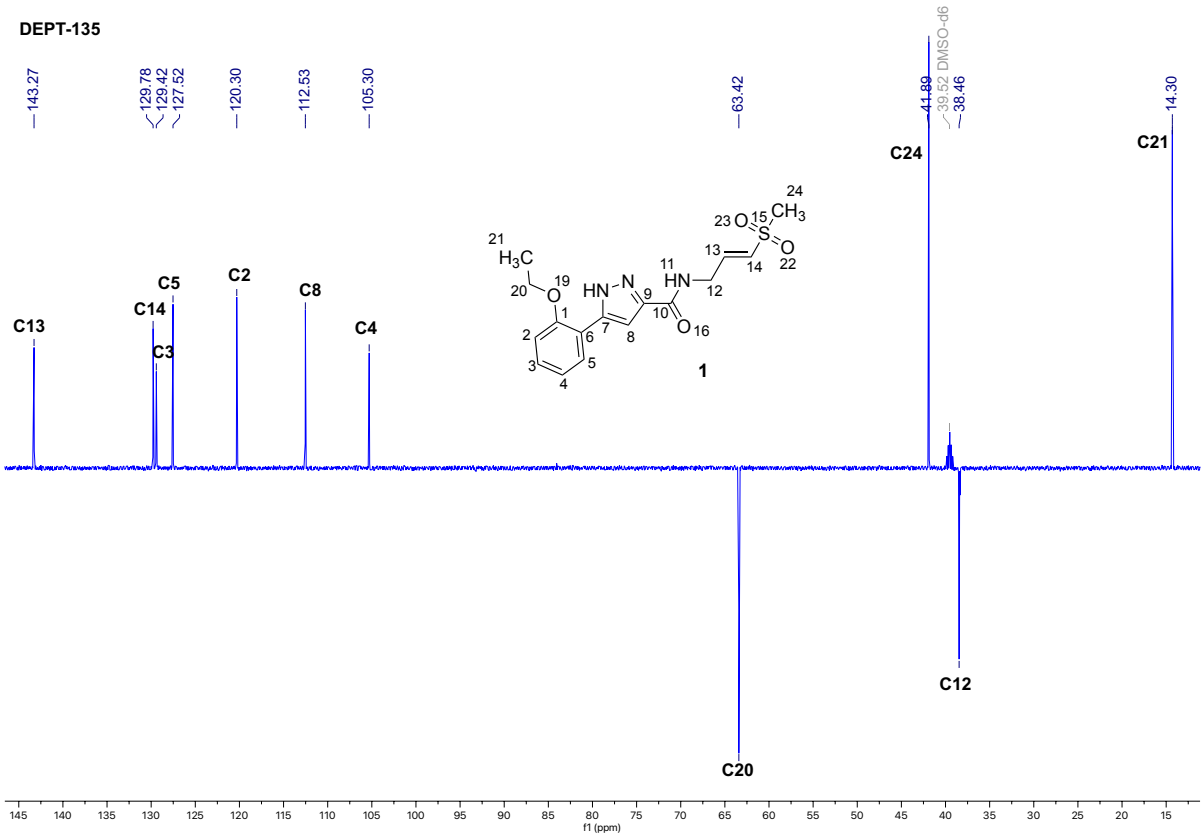


Figure S5: ^{19}F NMR (500 MHz, DMSO-d_6) for **1•TFA**

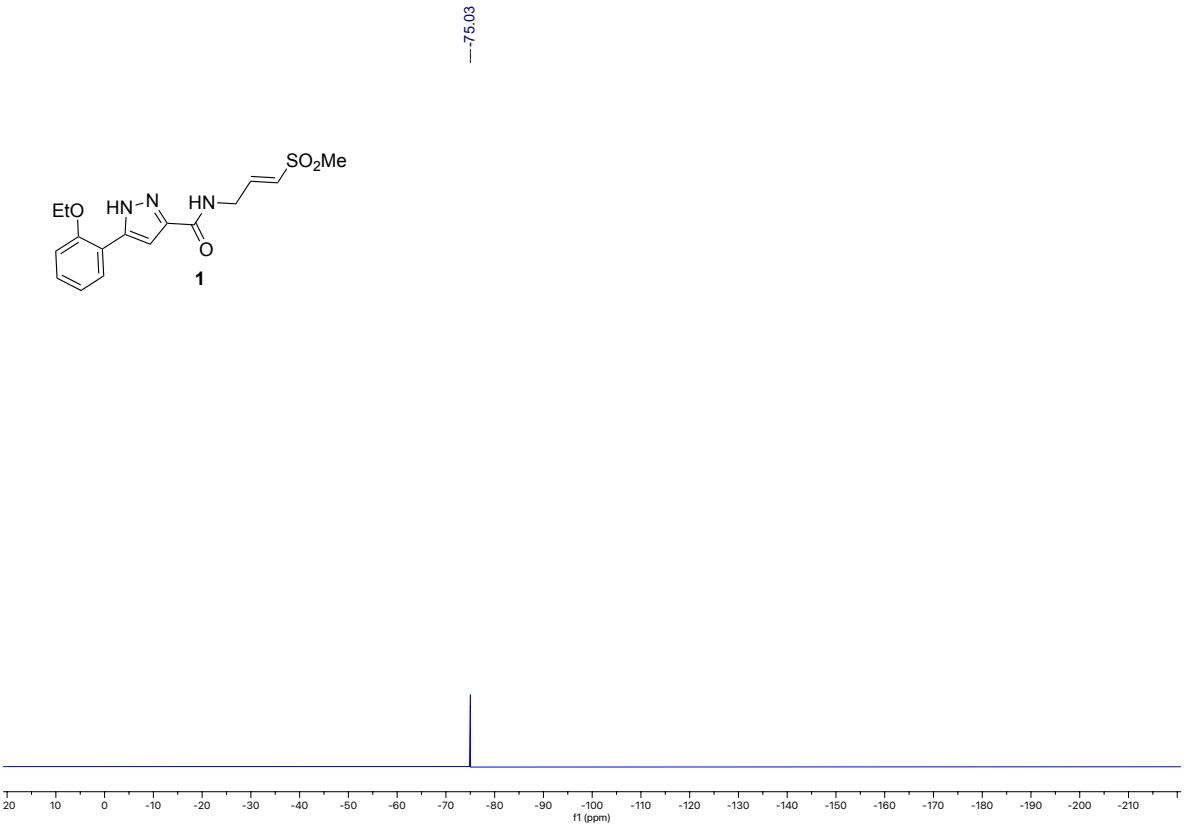


Figure S6: ^{1}H-^{1}H COSY NMR (DMSO-d_6) for **1•TFA**

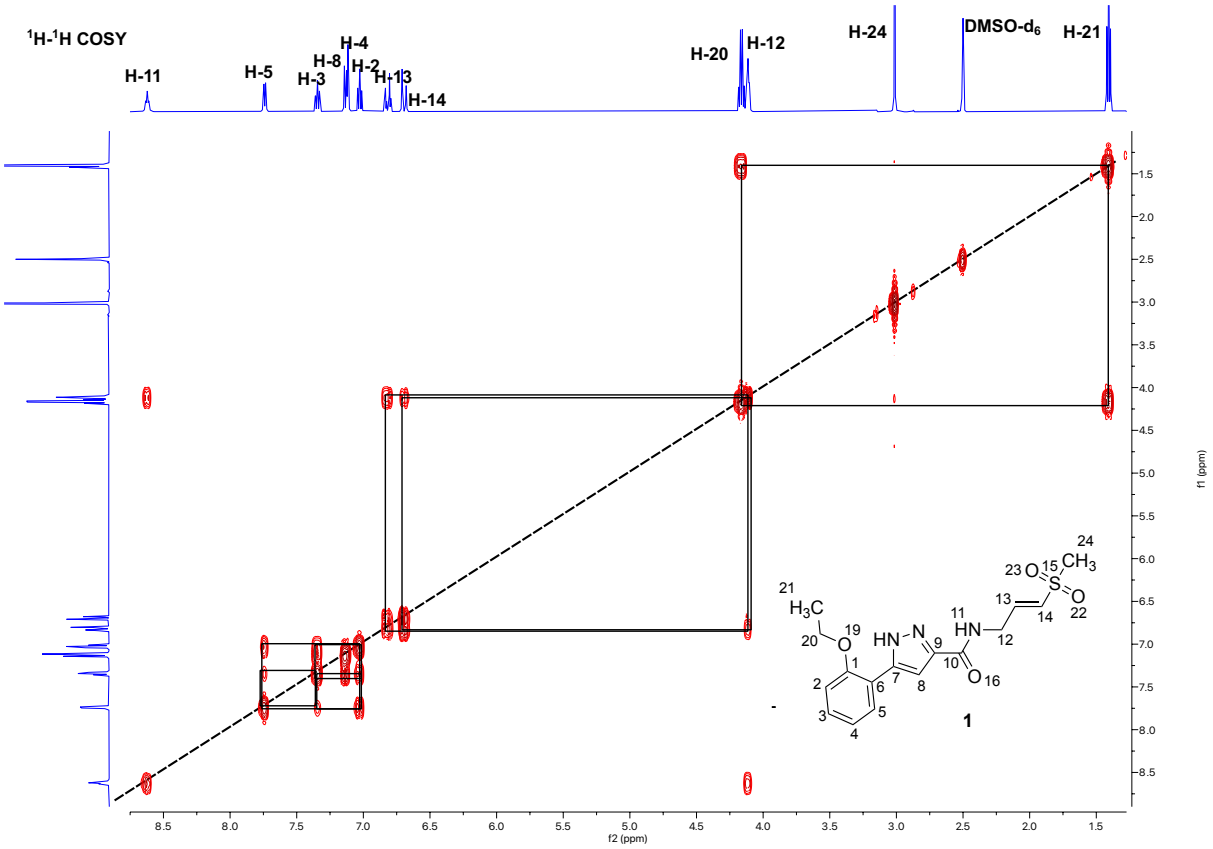


Figure S7: ^{1}H-^{13}C HSQC NMR (DMSO-d_6) for **1•TFA**

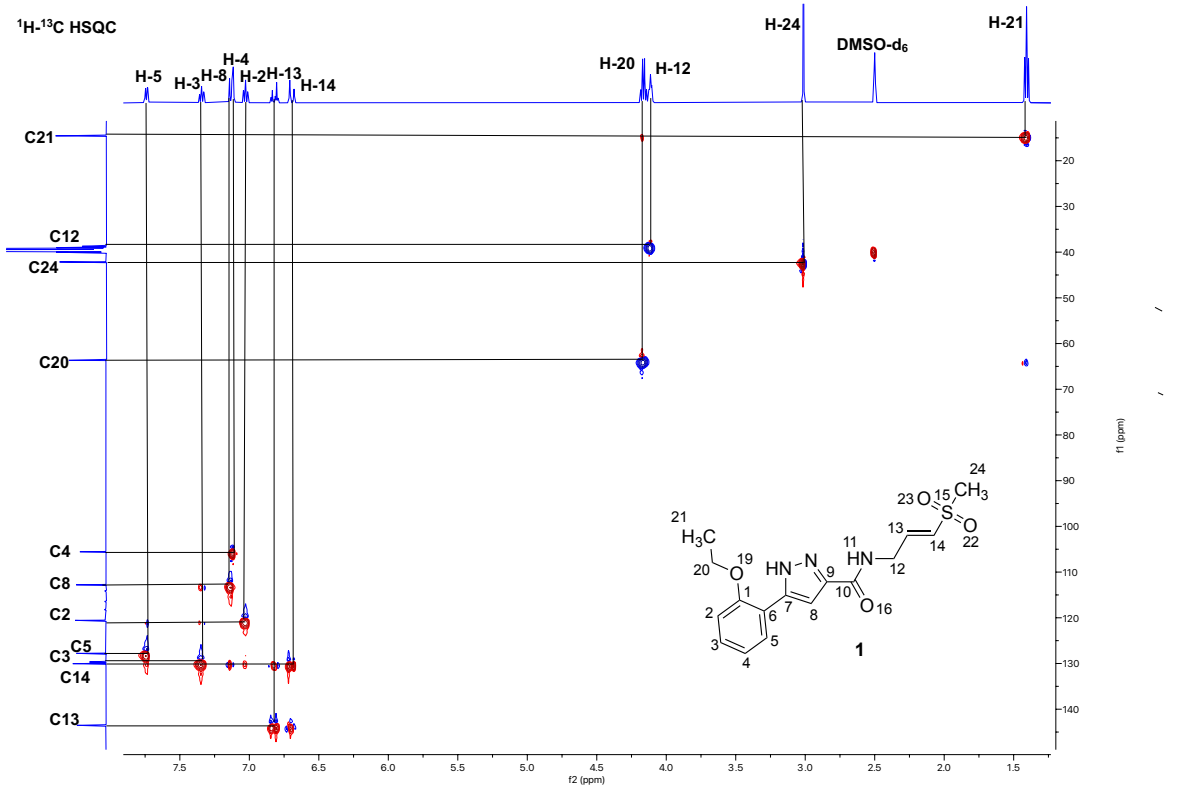


Figure S8: ^{1}H-^{13}C HMBC NMR (DMSO-d_6) for **1•TFA**

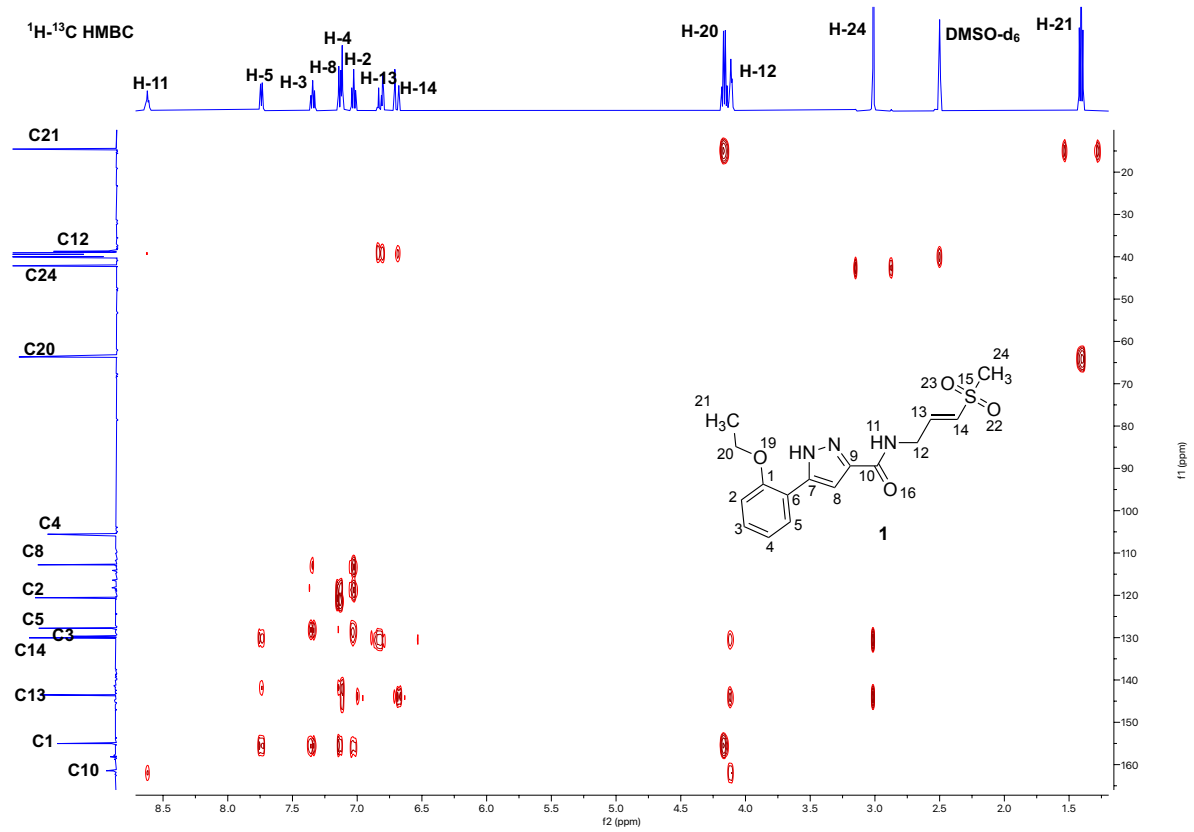


Figure S9: ^{1}H NMR (500 MHz, DMSO-d_6) for **2**

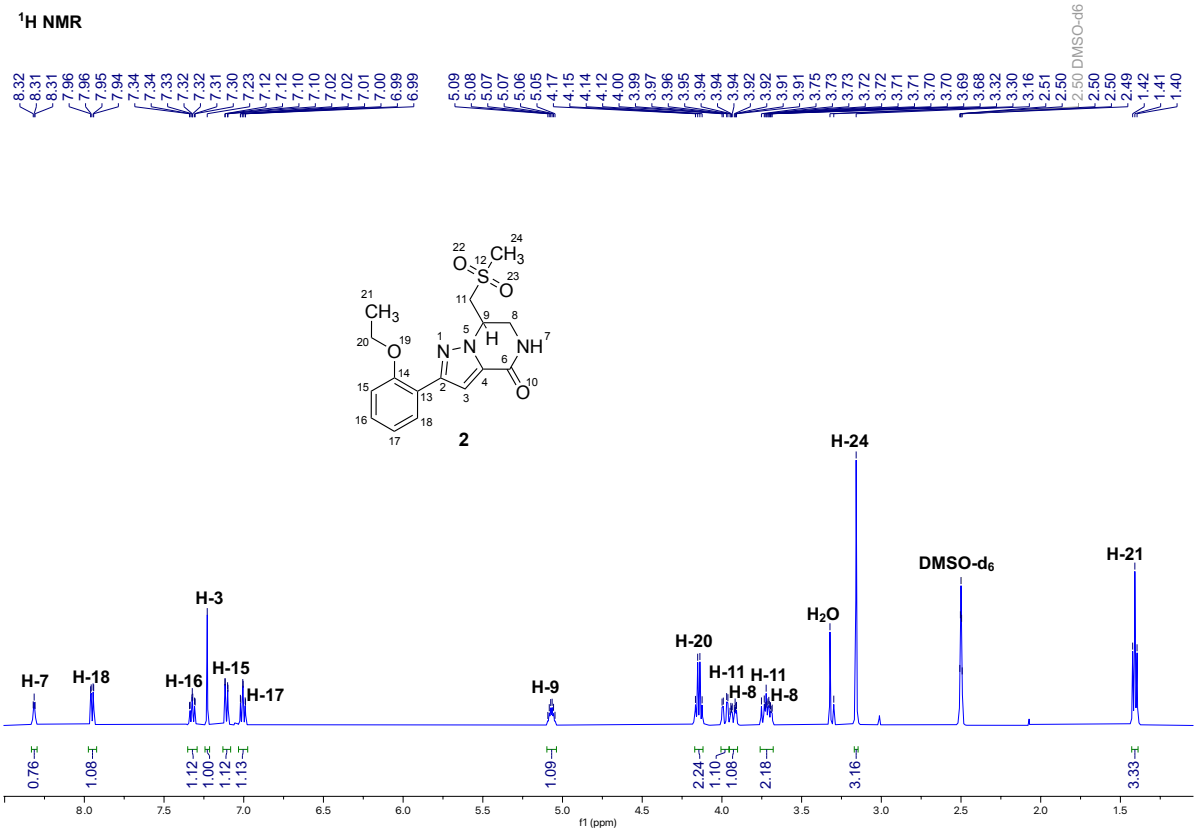


Figure S10: ^{13}C NMR (126 MHz, DMSO-d_6) for **2**

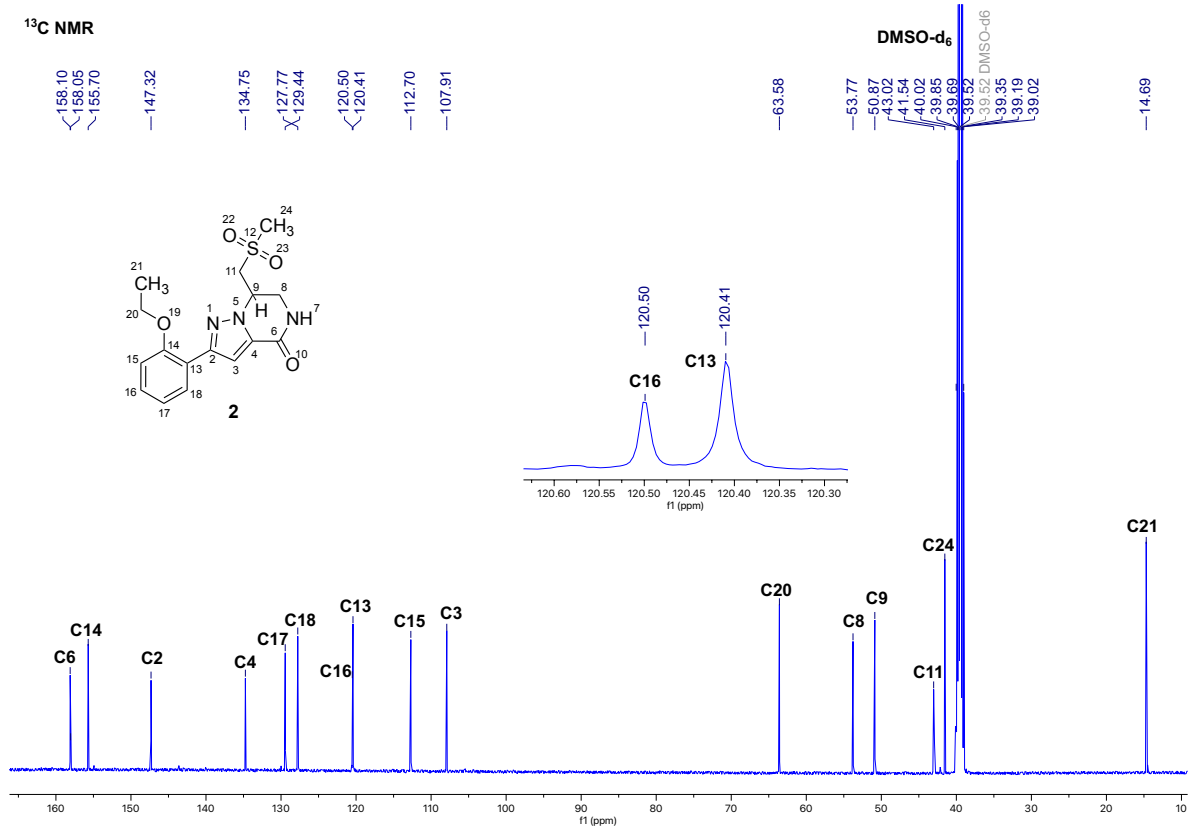


Figure S11: ^{13}C NMR DEPT-135 (126 MHz, DMSO-d_6) for **2**

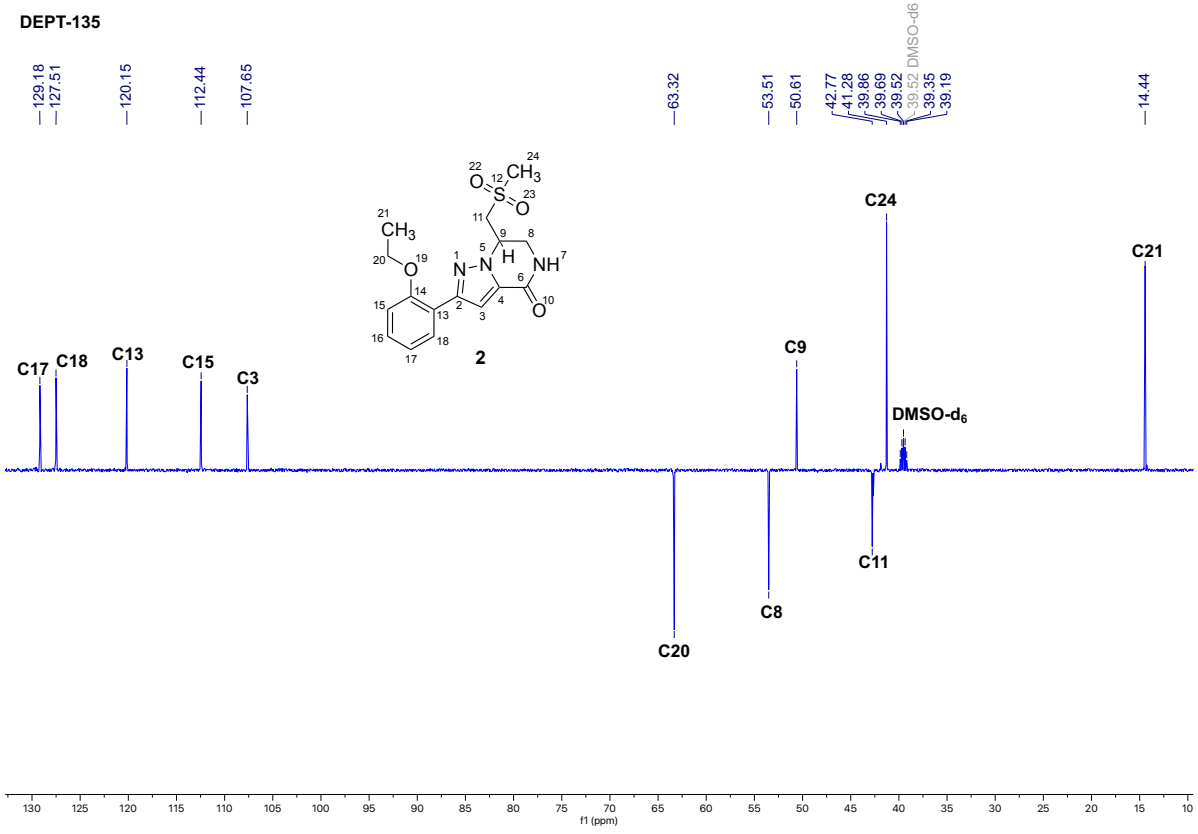


Figure S12: ^{1}H-^{1}H COSY NMR (DMSO-d_6) for **2**

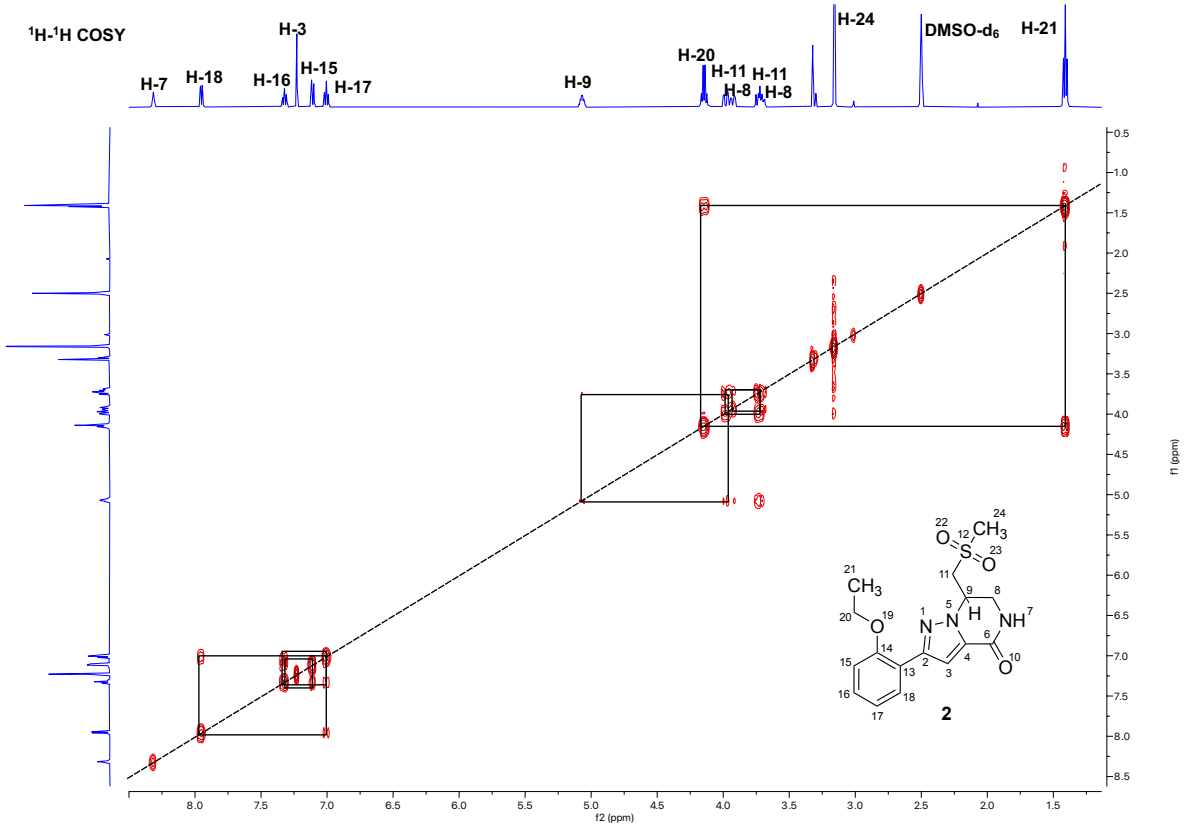


Figure S13: ^{1}H-^{13}C HSQC NMR (DMSO-d_6) for **2**

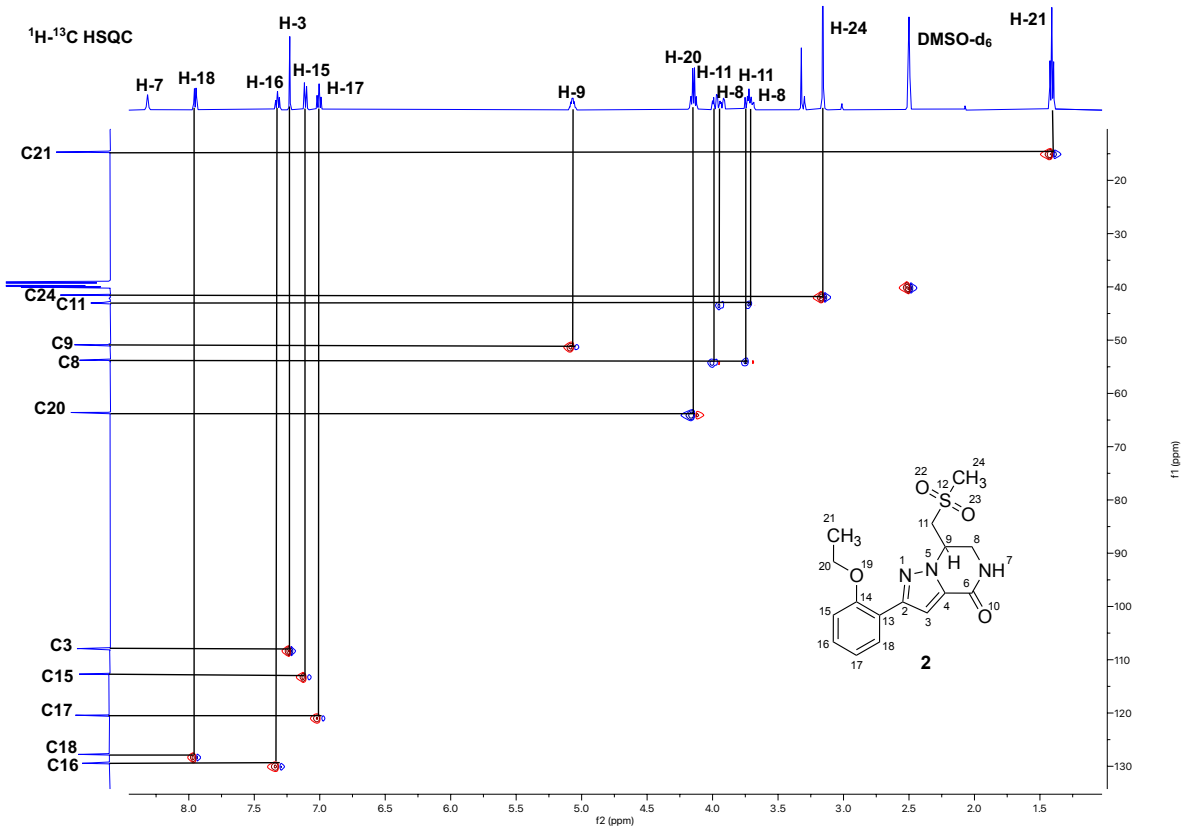


Figure S14: ^{1}H-^{13}C HMBC NMR (DMSO-d_6) for **2**

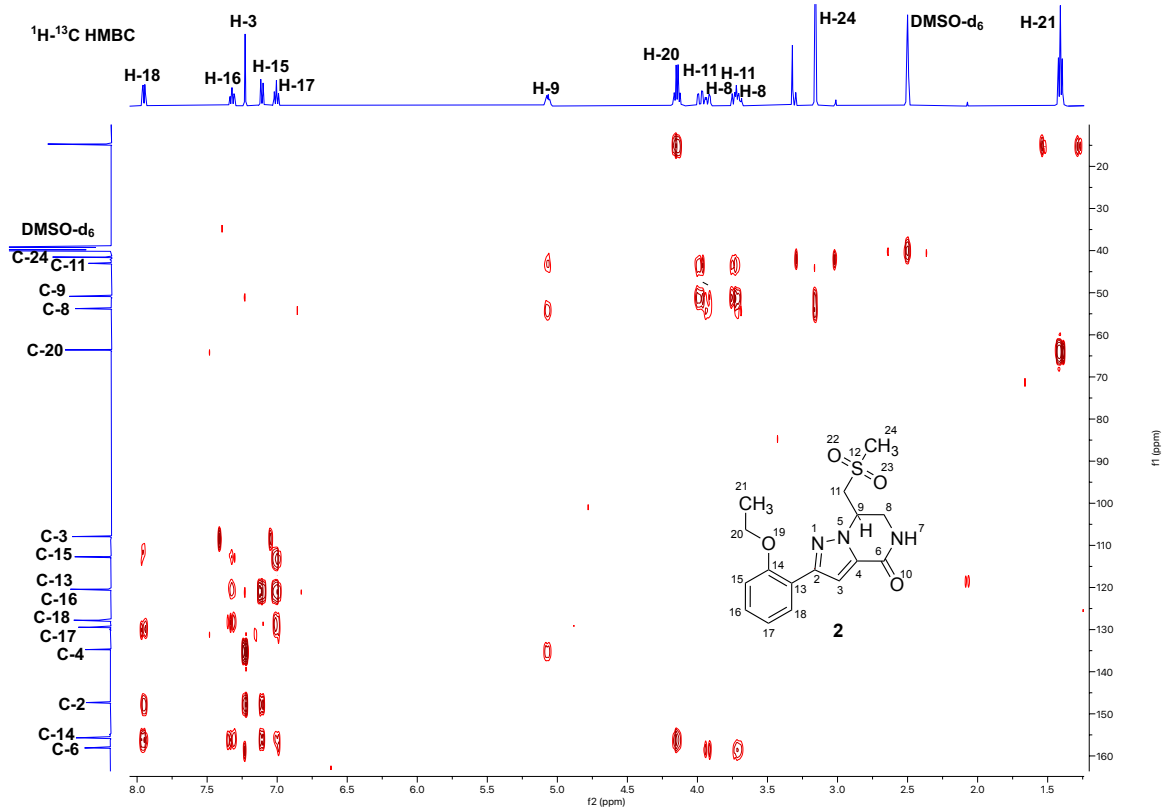


Figure S15: ^{1}H-^{13}C HMBC NMR (DMSO-d_6) of expanded aromatic region for **2**

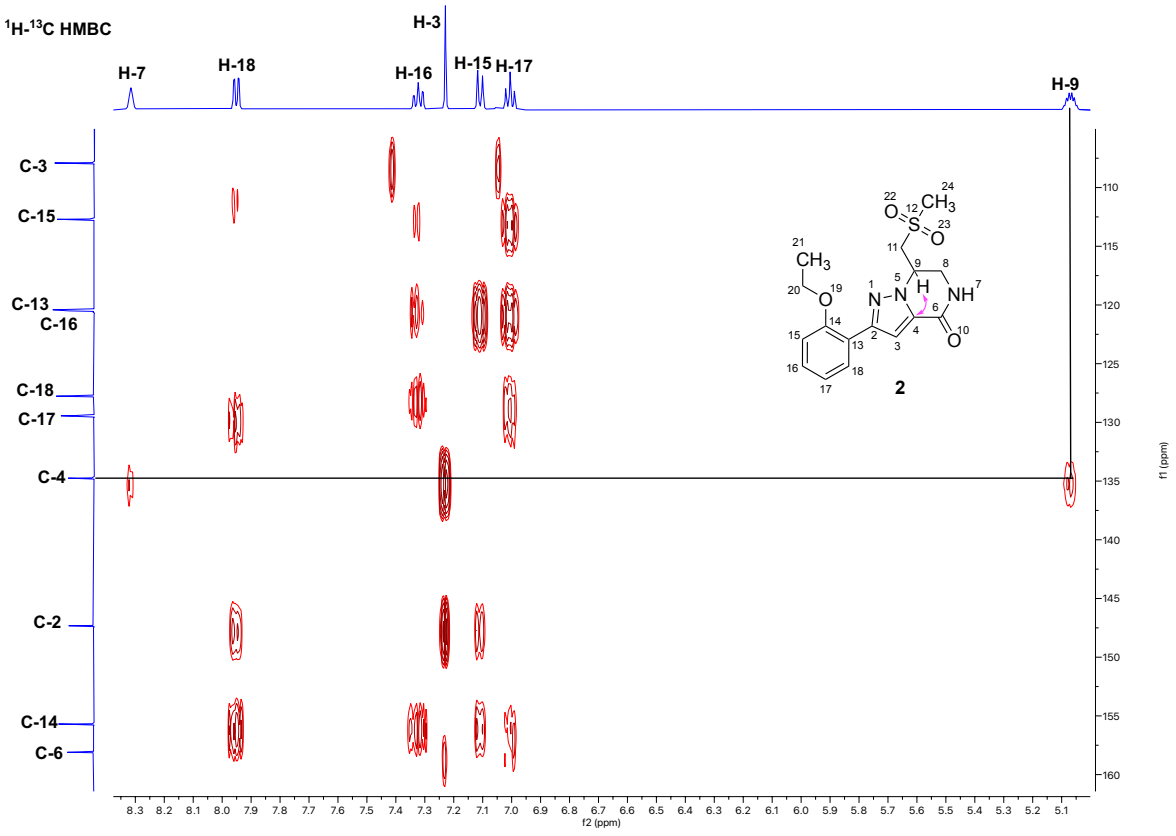


Figure S16: ^{1}H NMR (500 MHz, DMSO-d_6) for **7•TFA**

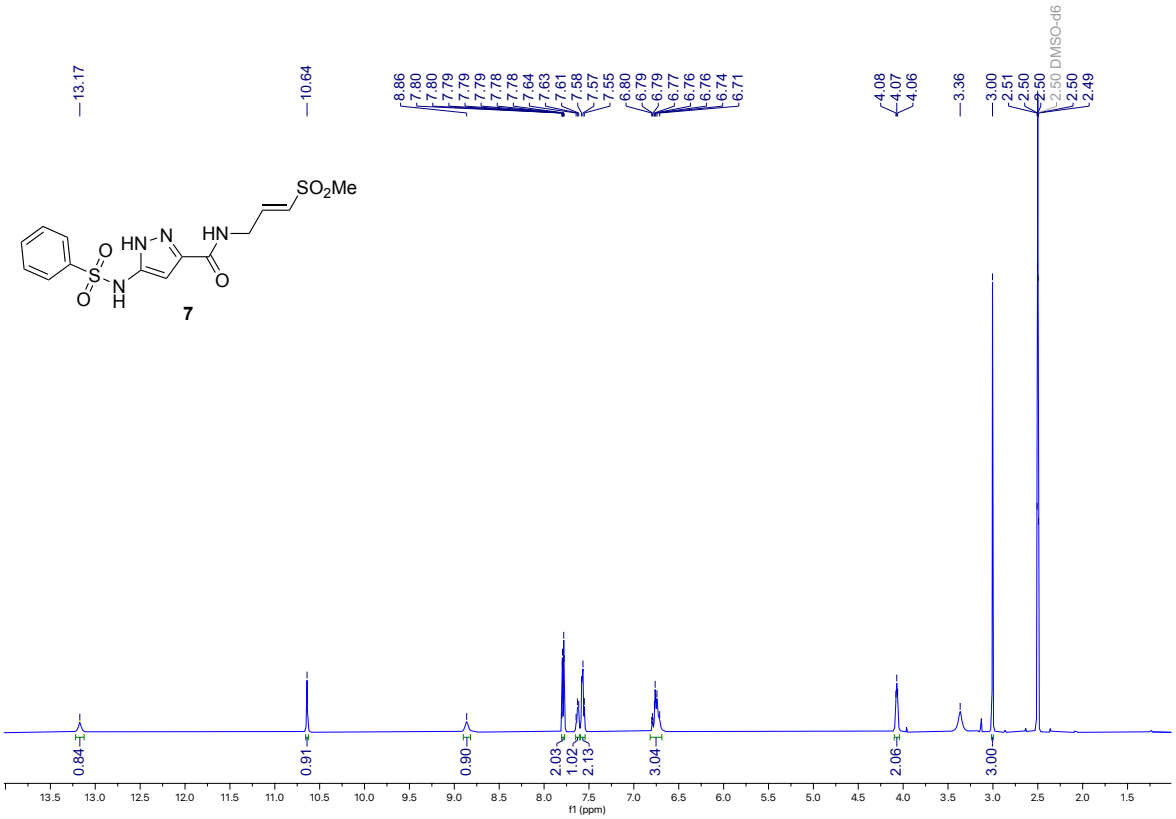


Figure S17: ^{1}H NMR (500 MHz, DMSO-d_6) for **5**

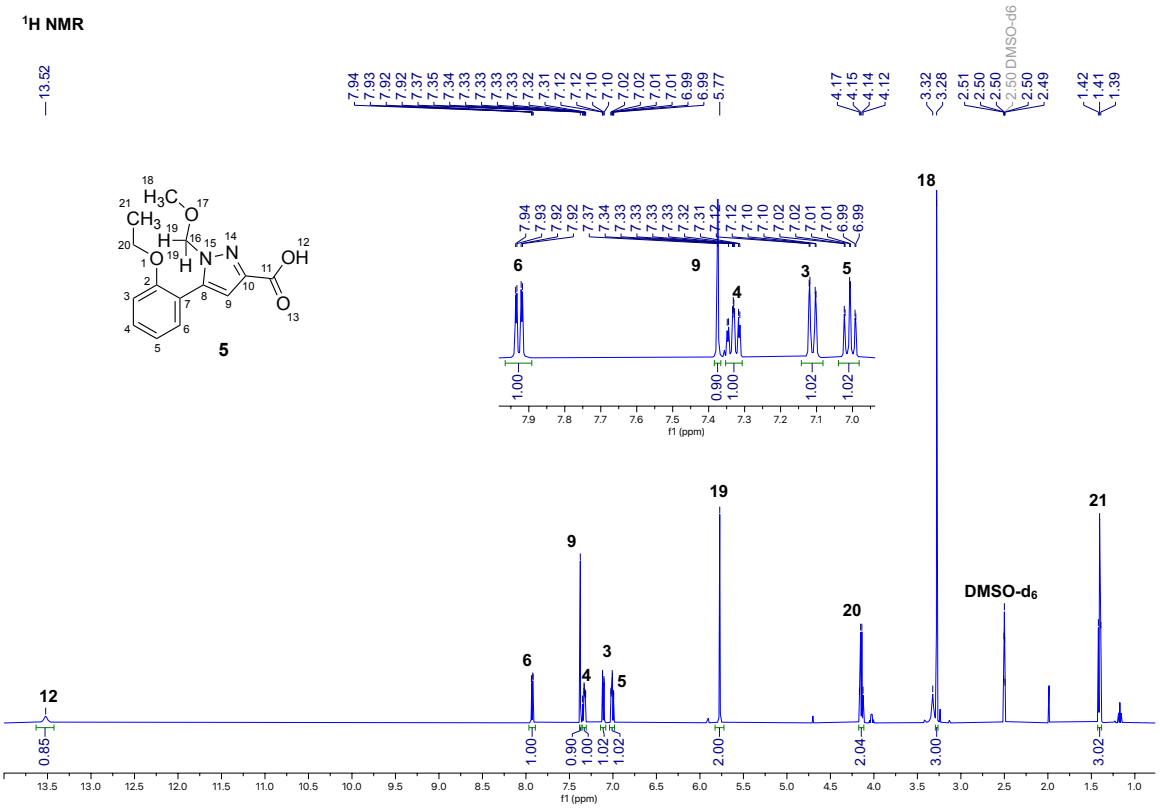


Figure S18: ^{13}C NMR (126 MHz, DMSO-d_6) for **5**

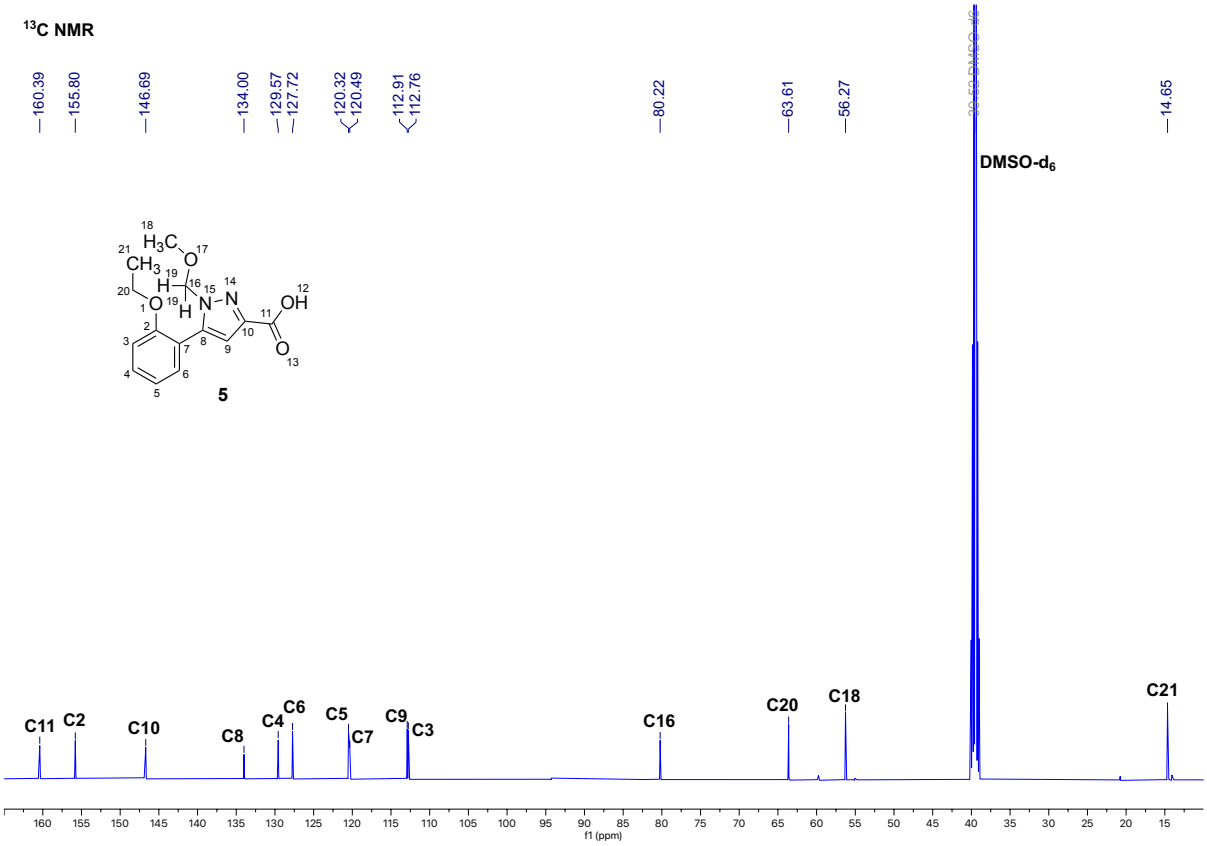


Figure S19: ^{13}C NMR DEPT-135 (126 MHz, DMSO-d_6) for **5**

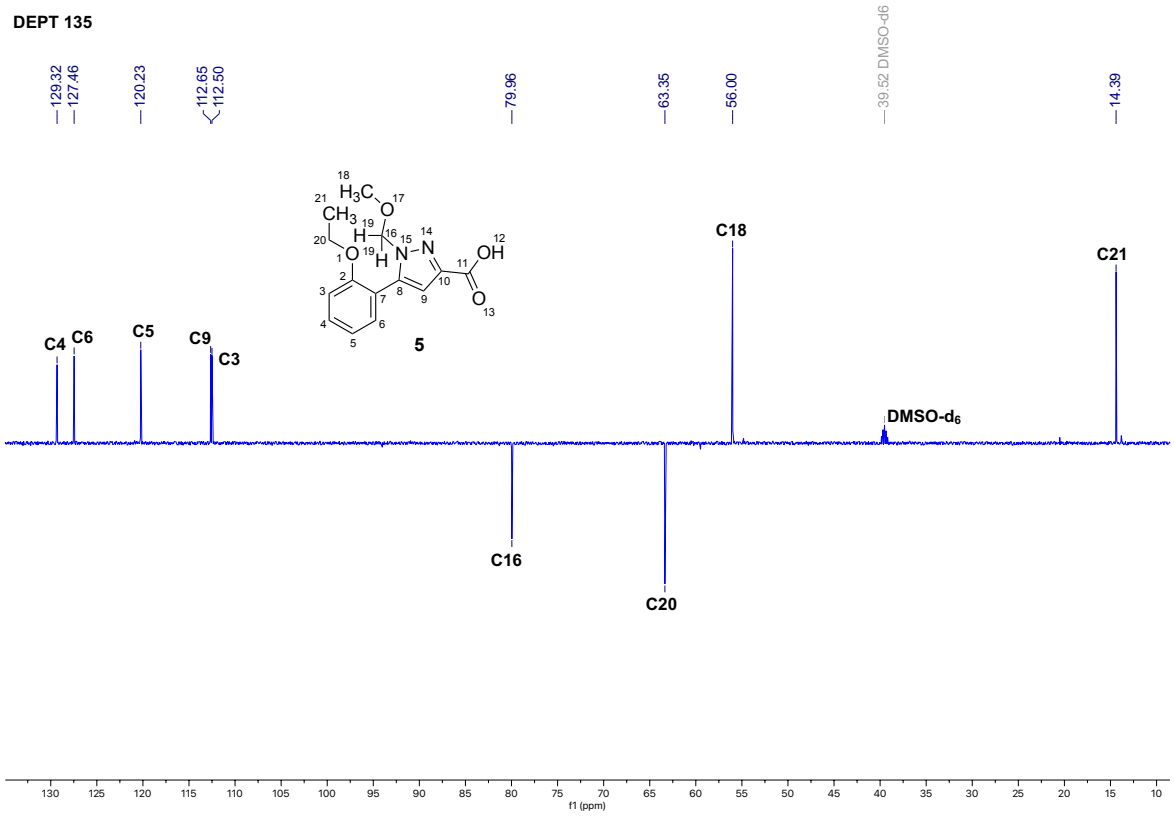


Figure S20: ^{1}H-^{1}H COSY NMR (DMSO-d_6) for **5**

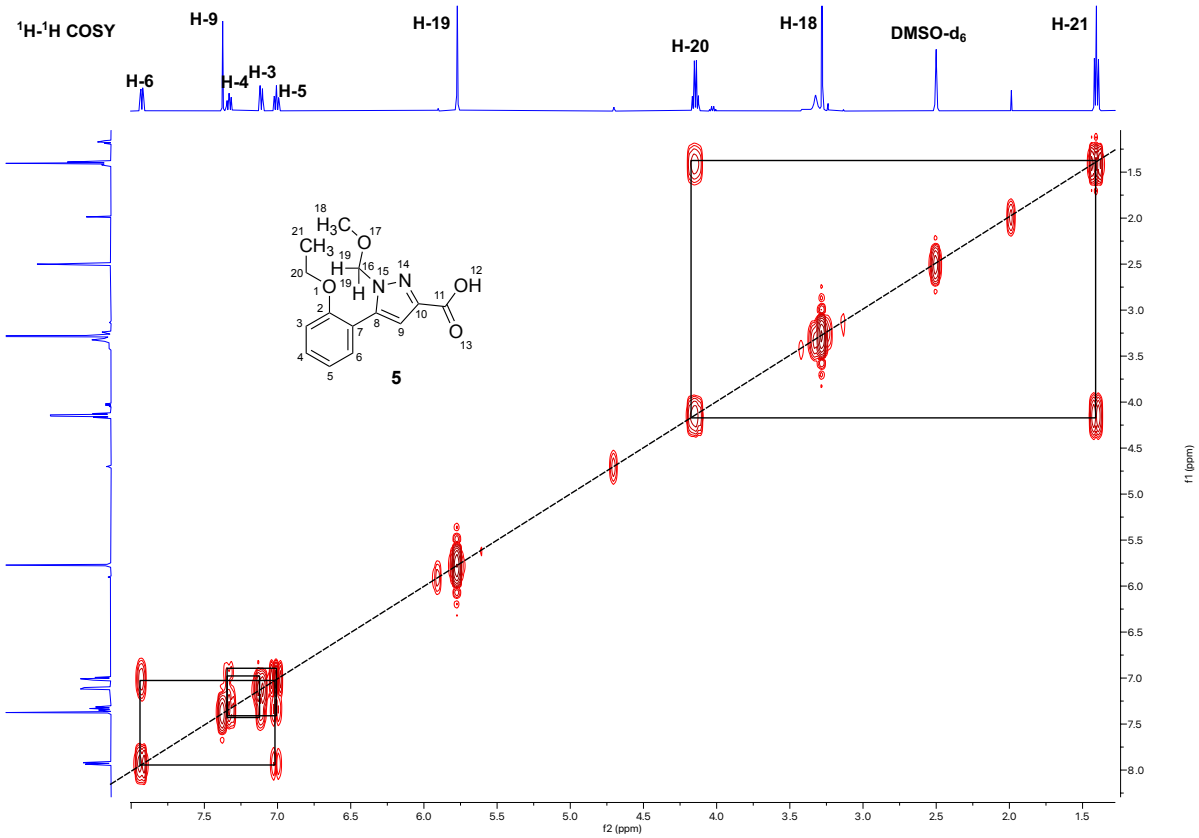


Figure S21: ^{1}H-^{13}C HSQC NMR (DMSO-d_6) for **5**

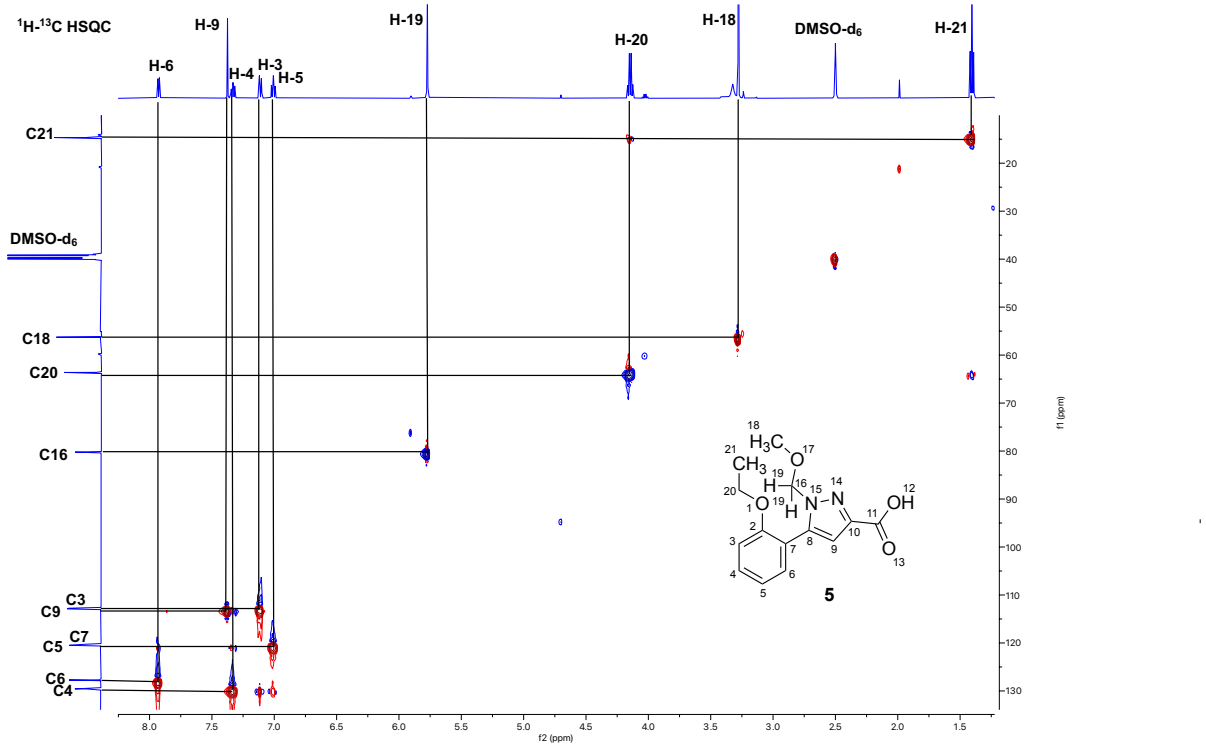


Figure S22: ^{1}H-^{13}C HMBC NMR (DMSO-d_6) of expanded region for **5**

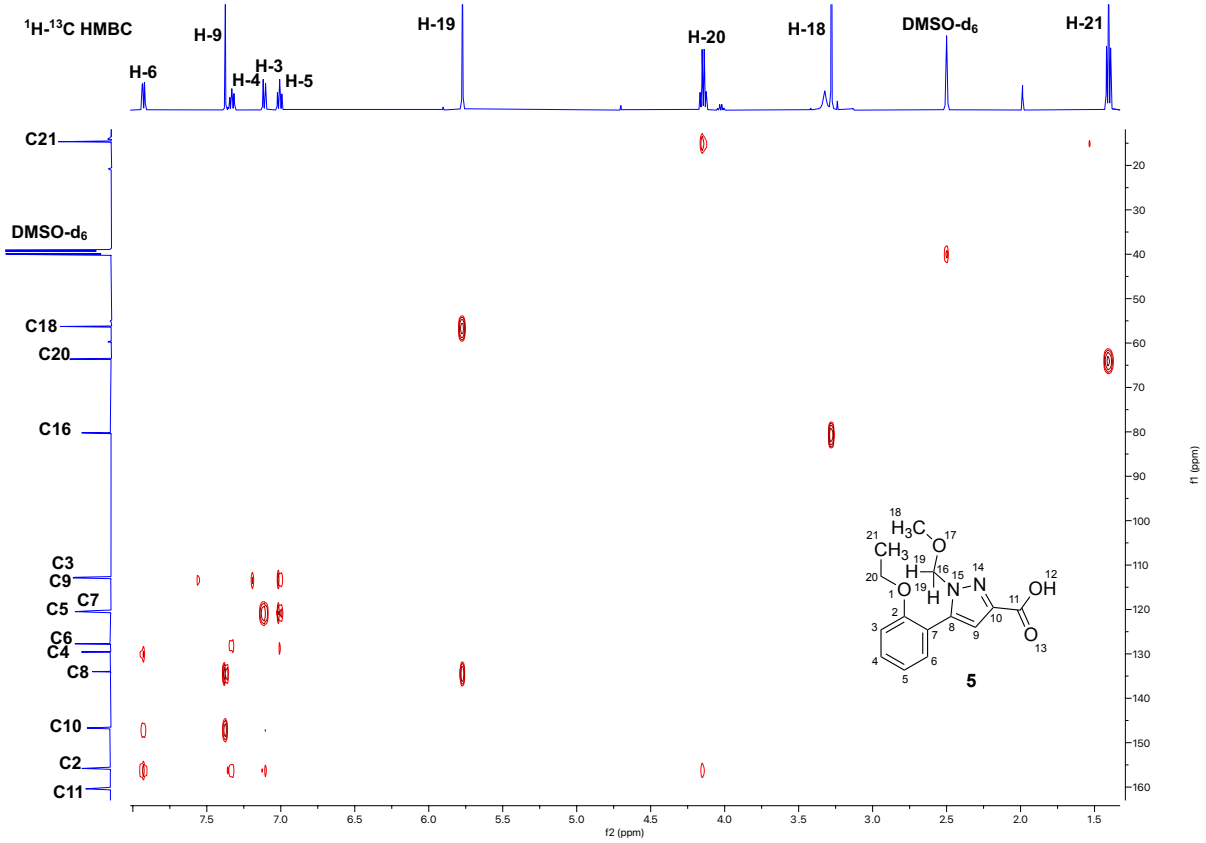


Figure S23: ^{1}H-^{13}C HMBC NMR (DMSO-d_6) of expanded region for **5**

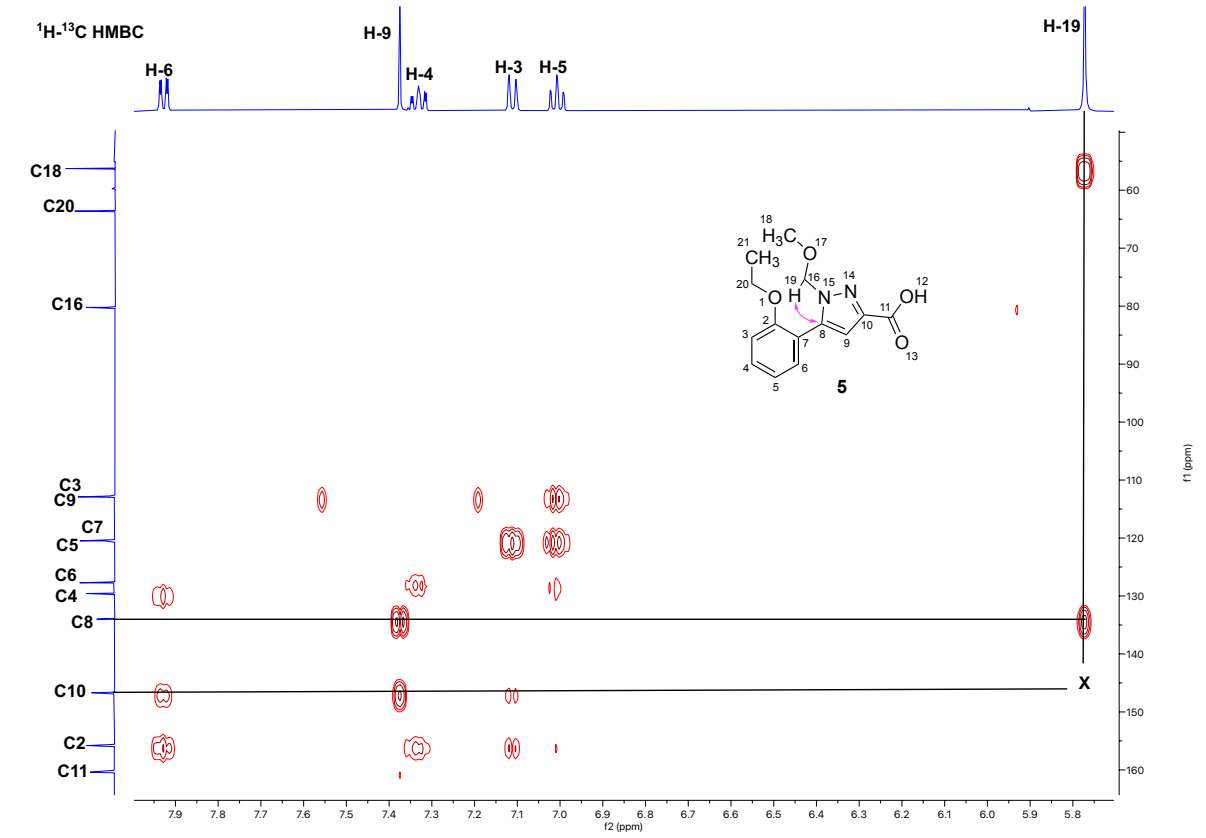


Figure S24: ^{1}H NMR (500 MHz, DMSO-d_6) for **6**

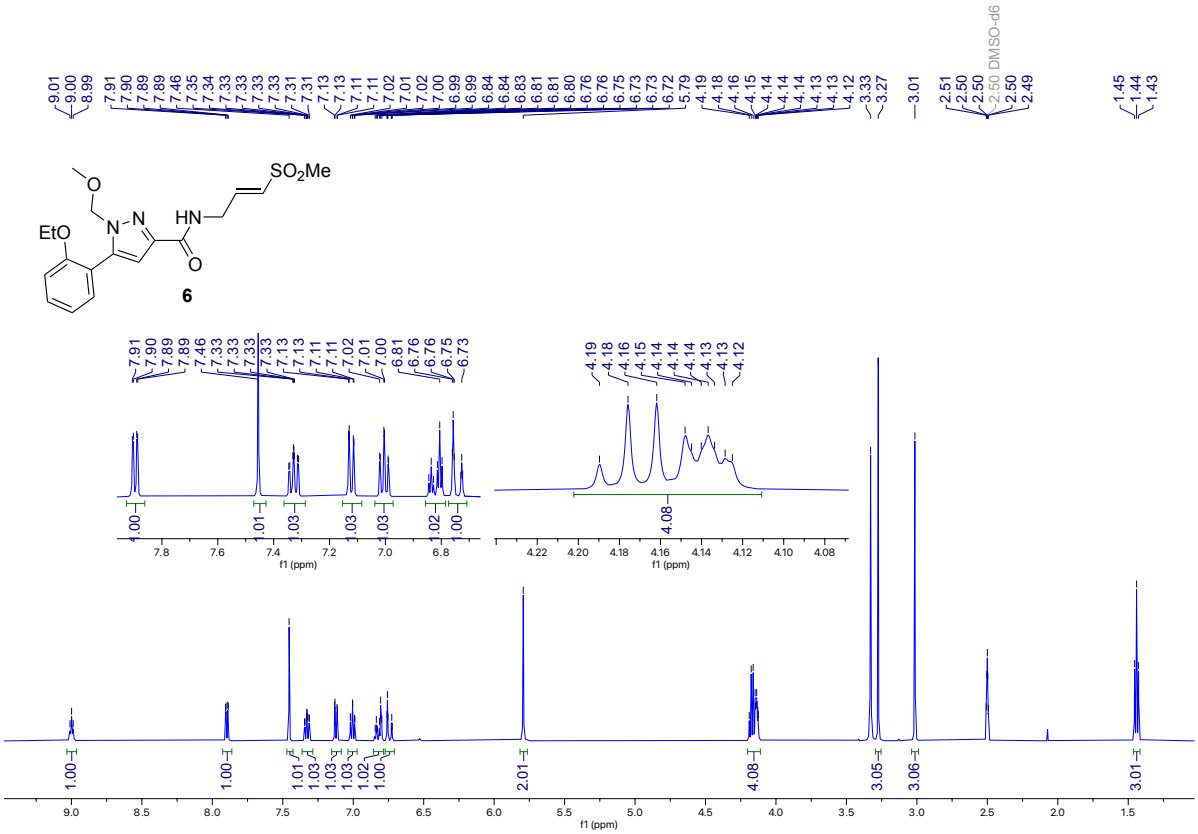


Figure S25: ^{13}C NMR (126 MHz, DMSO-d_6) for **6**

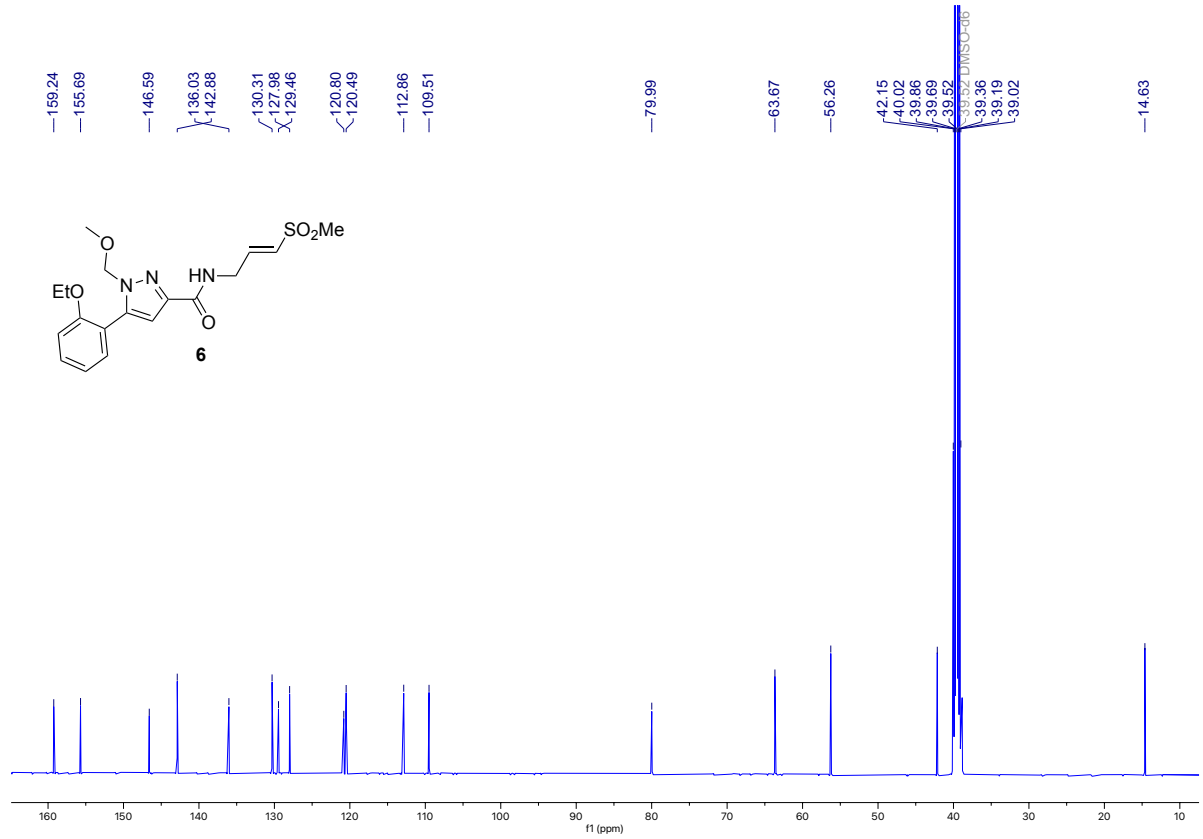


Figure S26: ^{13}C NMR (126 MHz, DMSO-d_6) for **7•TFA**

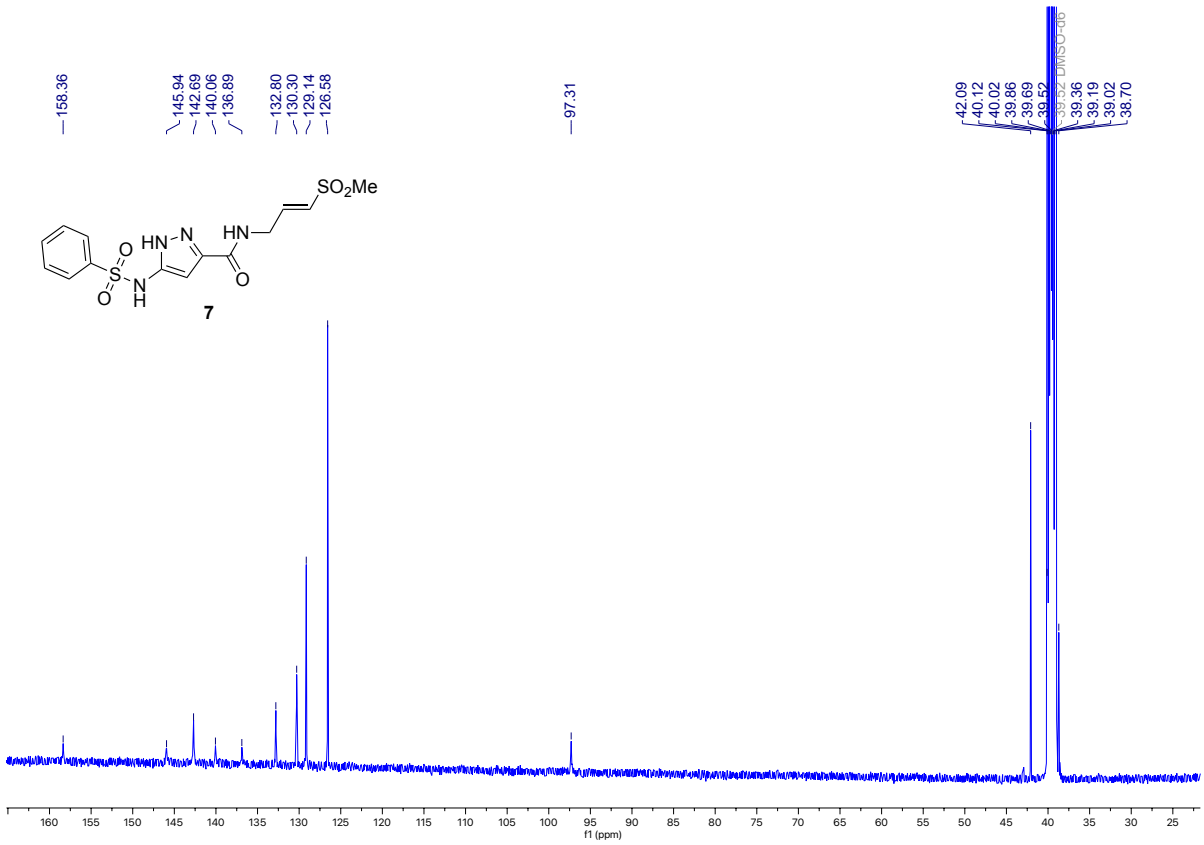


Figure S27: ^{1}H NMR (500 MHz, DMSO-d_6) for **8•TFA**

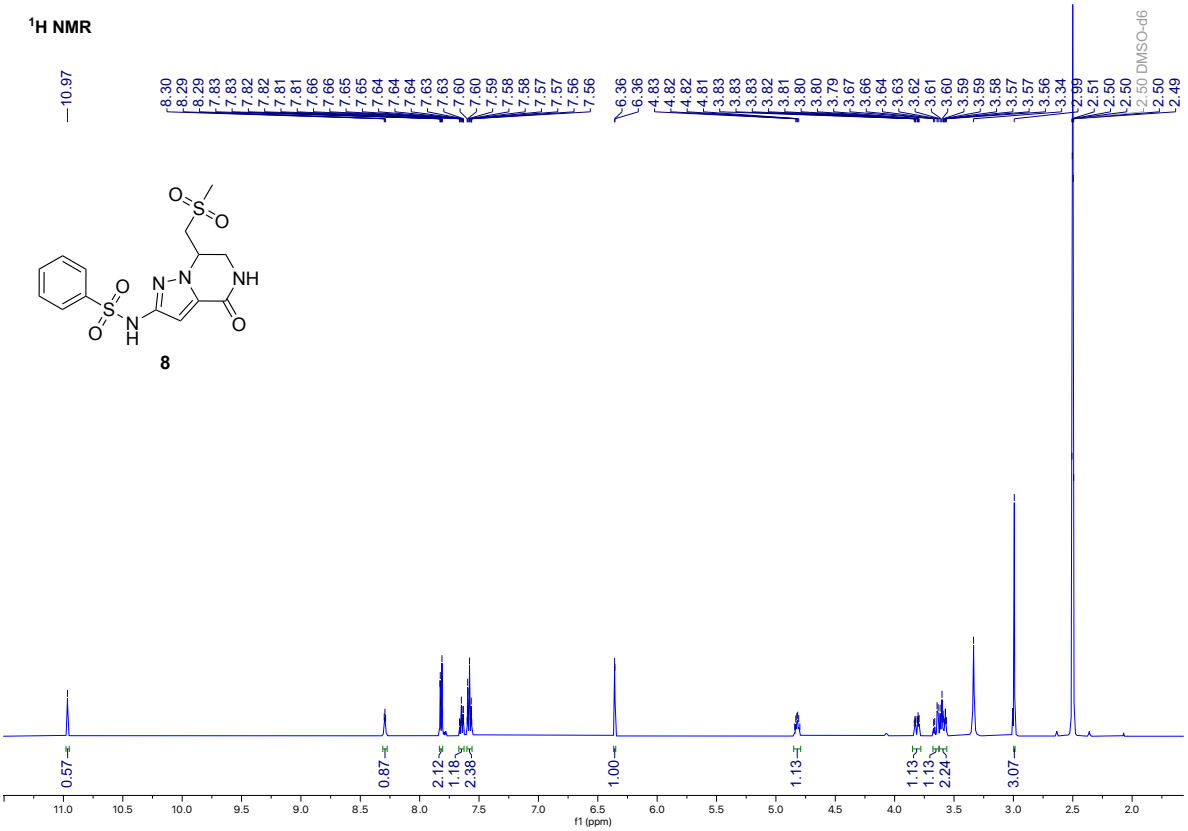


Figure S28: ^{13}C NMR (176 MHz, DMSO-d_6) for **8•TFA**

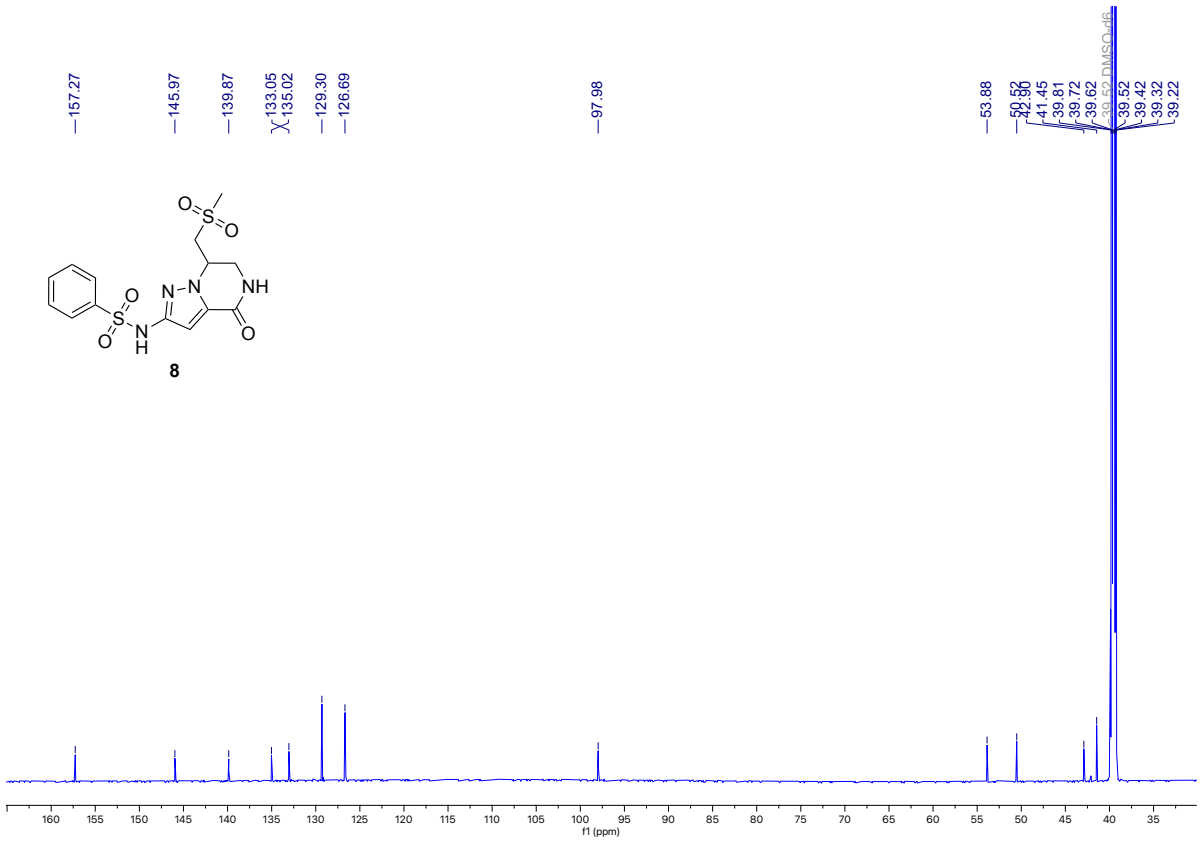


Figure S29: LC/MS purity for **1•TFA**

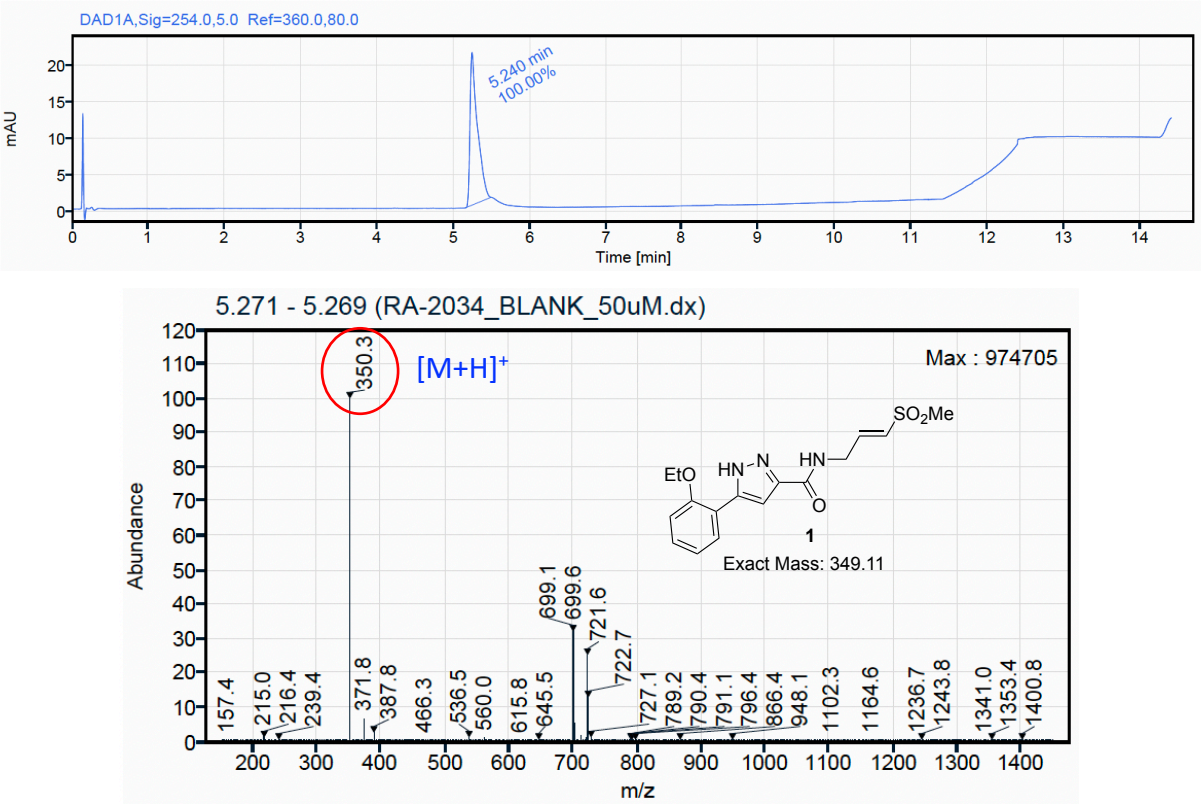


Figure S30: LC/MS purity for **2**

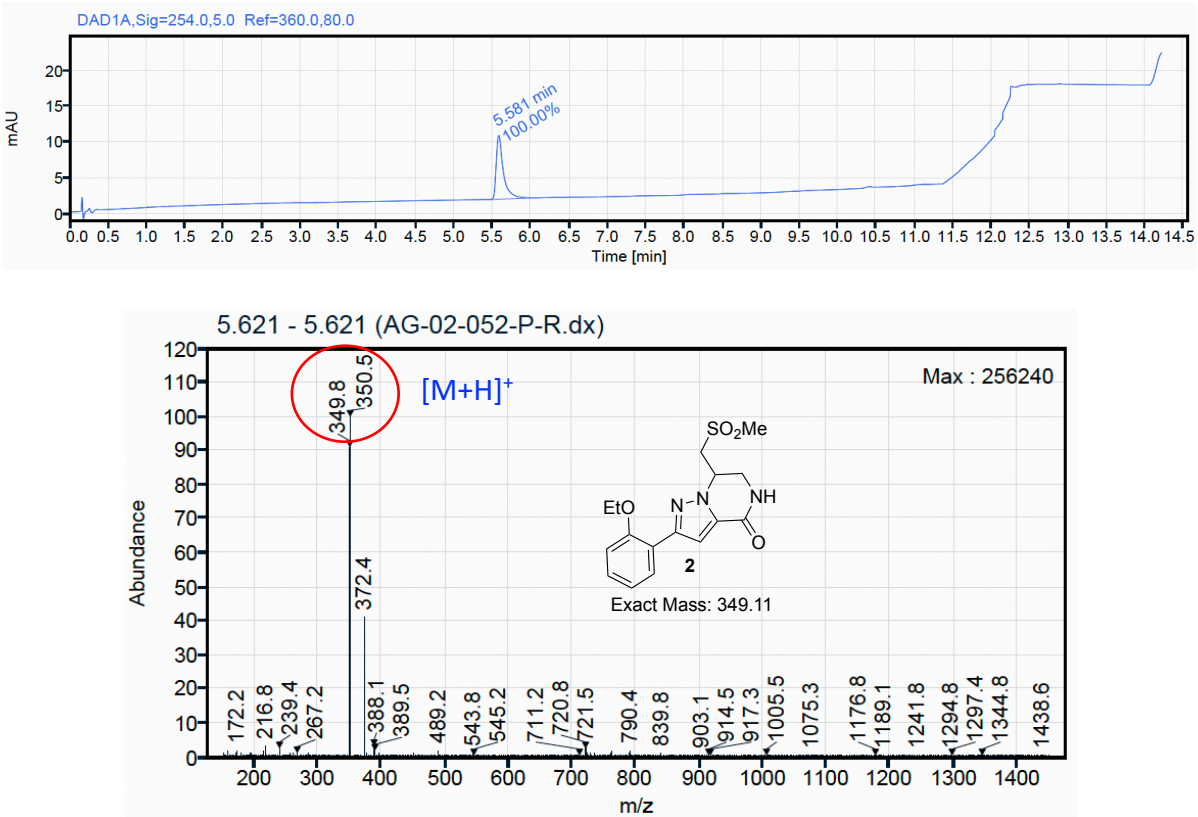


Figure S31: LC/MS purity for **7•TFA**

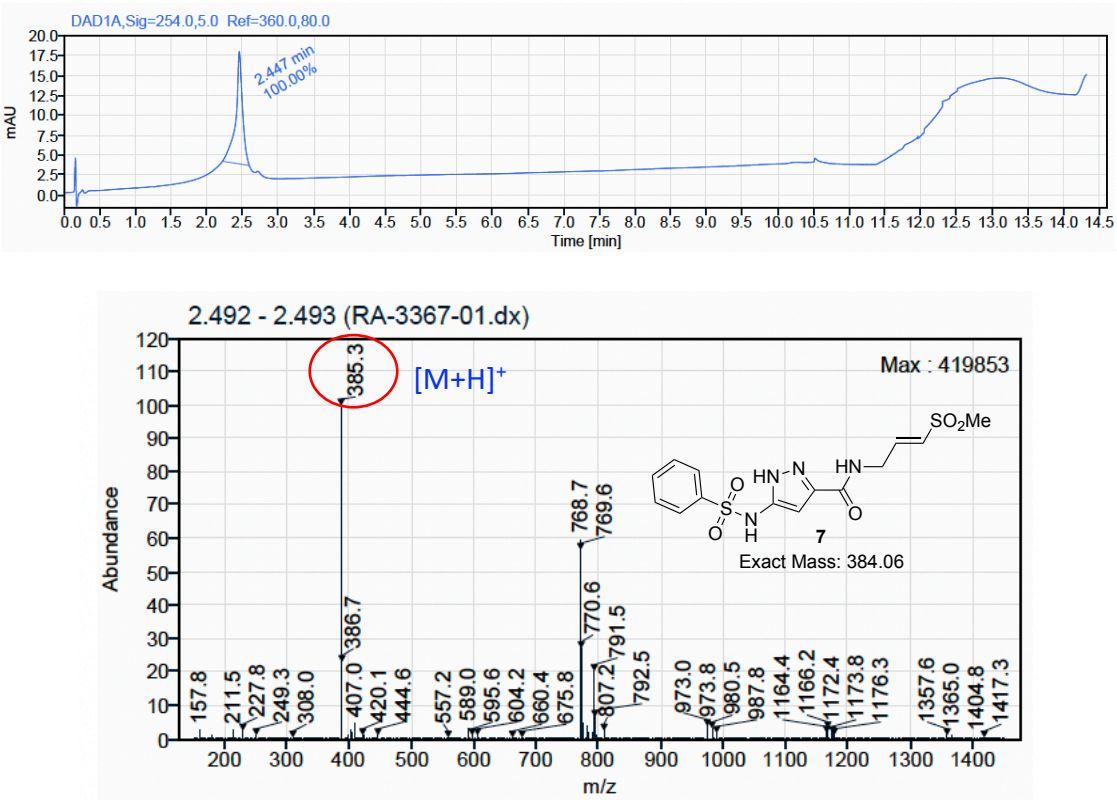


Figure S32: LC/MS purity for **8•TFA**

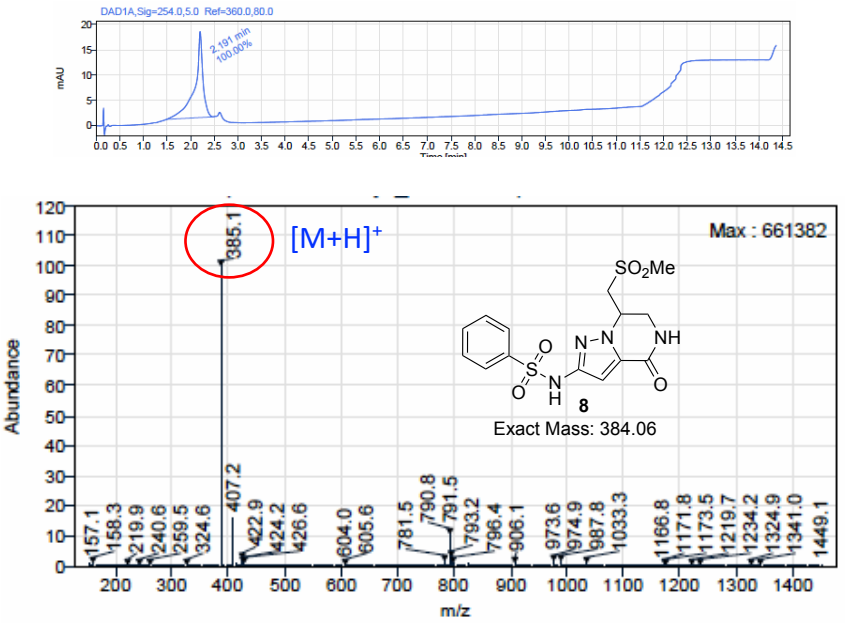


Figure S33: HRMS spectrum for **1•TFA**

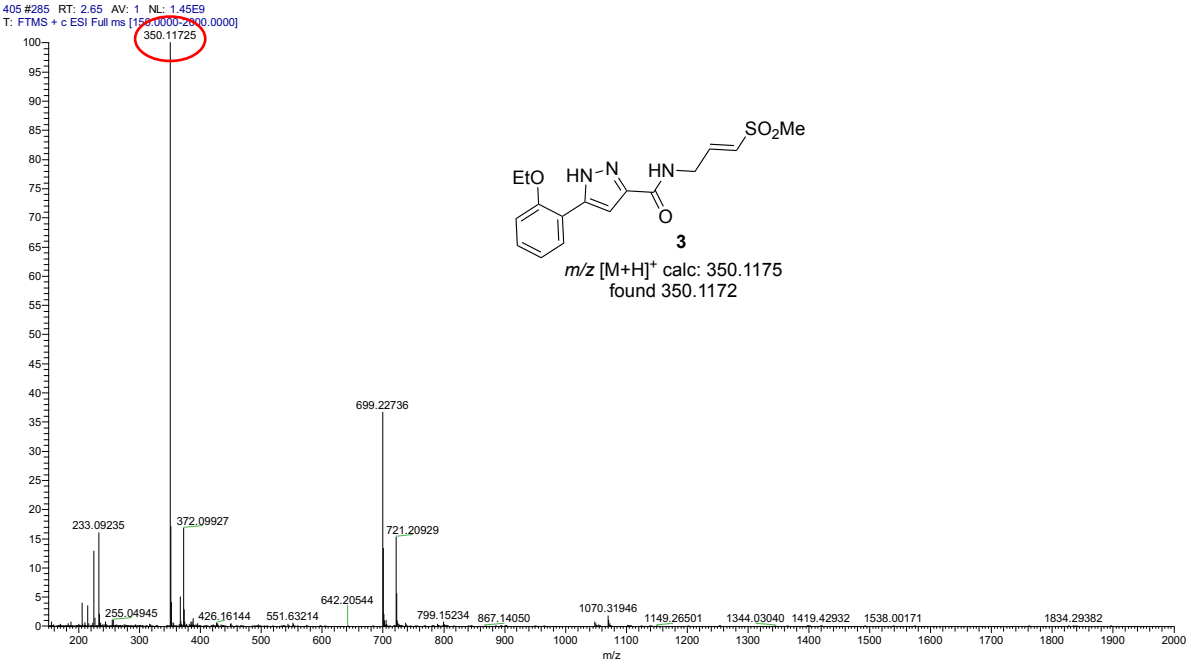


Figure S34: HRMS spectrum for **2**

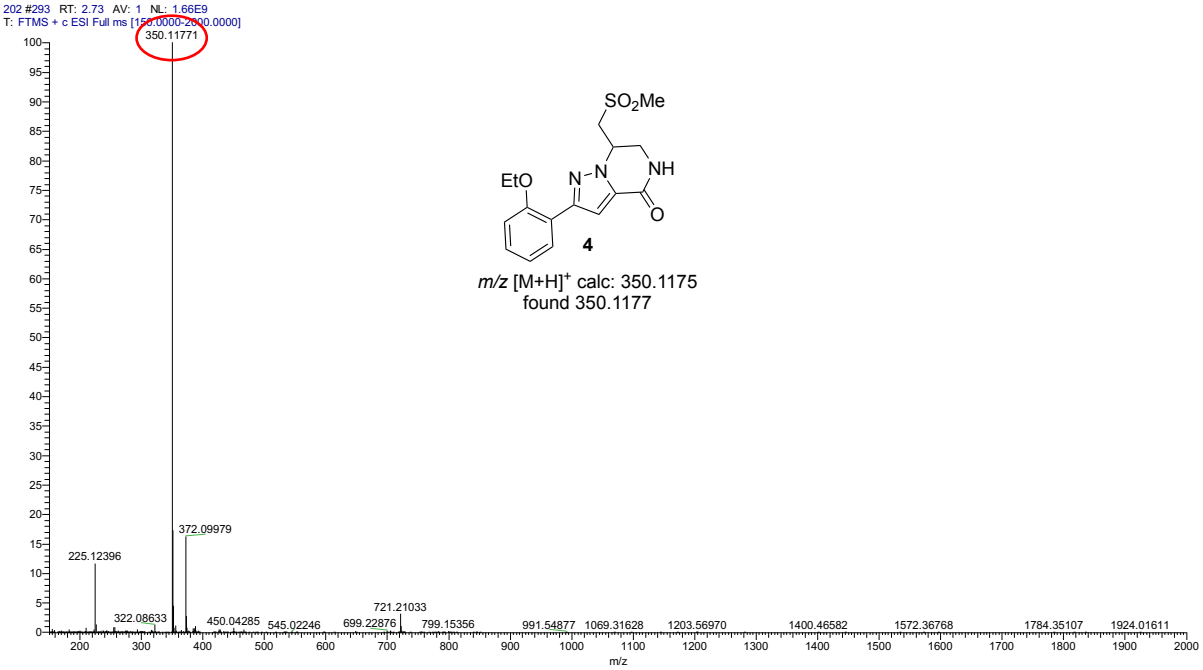


Figure S35: HRMS spectrum for **7•TFA**

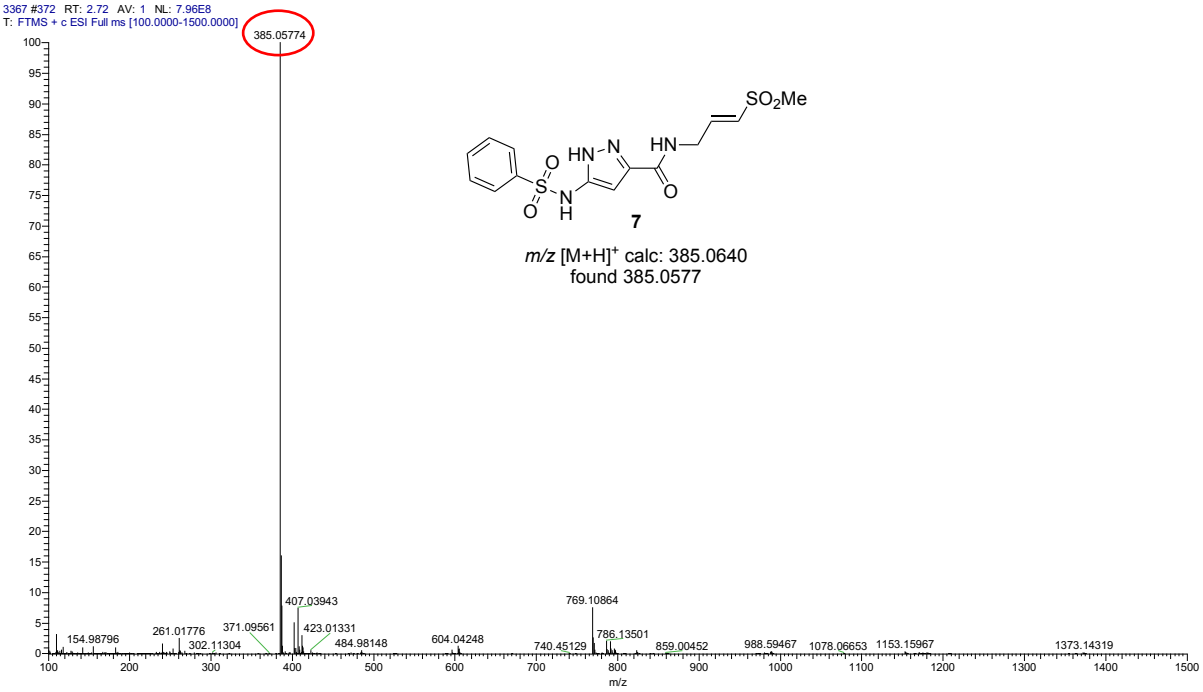


Figure S36: HRMS spectrum for **8•TFA**

