Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Efficient and regioselective one-step synthesis of 7-aryl-5-methyl- and 5-aryl-7-methyl-2-amino-[1,2,4]triazolo[1,5-*a*]pyrimidine derivatives.

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Supporting Information

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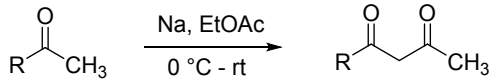
General procedure for the synthesis of 1-aryl-1,3-butanediones (5b-k) by Claisen–Schmidt condensation.[1]

To a solution of the suitable acetophenone (10 mmol) in dry EtOAc (30 mL) maintained at 0 °C, sodium (20 mmol) was added portion-wise. The reaction mixture was maintained at room temperature for 3 h and, then, it was poured into ice/water and extracted with EtOAc. The organic layers were dried over sodium sulphate and evaporated to dryness obtaining the compound with sufficient purity to be used in the next step without further purification, otherwise indicated.

Table S1. Preparation of 1-aryl-1,3-butanediones.



5b-k

Entry	R	Time (h)	Product	Crude Yield (%)
1	*p*-$CH_3C_6H_5$	3	**5b**	97
2	*p*-$CH_3SC_6H_5$	4	**5c**	70
3	*p*-BrC_6H_5	3	**5d**	65
4	*o*-ClC_6H_5	3	**5e**	79
5	*m*-$CF_3C_6H_5$	3	**5f**	67
6	*m,p-Di*-$CH_3OC_6H_5$	4	**5g**	93
7	*m,p-Di*-ClC_6H_5	1	**5h**	58
8	1-Naphthyl	3	**5i**	100
9	4-Pyridinyl	8	**5k**	34

4-Hydroxy-4-*p*-tolylbut-3-en-2-one (5b).[2] Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.16 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 6.13 (s, 1H, H-3), 7.22 and 7.75 (d, J = 8.2 Hz, each 2H, aromatic CH), 16.18 (s, 1H, OH).

4-Hydroxy-4-(4-(methylthio)phenyl)but-3-en-2-one (5c). Light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.16 (s, 3H, CH_3), 2.49 (s, 3H, CH_3), 6.11 (s, 1H, H-3), 7.24 and 7.77 (d, J = 6.3 Hz, each 2H, aromatic CH), 16.18 (s, 1H, OH).

4-(4-Bromophenyl)-4-hydroxybut-3-en-2-one (5d).[3] Light yellow solid after treatment with Et_2O. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.17 (s, 3H, CH_3), 6.11 (s, 1H, H-3), 7.55 and 7.71 (dd, J = 2.1 and 8.5 Hz, each 2H, aromatic CH), 16.04 (s, 1H, OH).

4-(2-Chlorophenyl)-4-hydroxybut-3-en-2-one (5e).[2] Yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.16 (s, 3H, CH_3), 6.01 (s, 1H, H-3), 7.28-7.36 (m, 2H, aromatic CH), 7.40 (dd, J = 1.2 and 7.7 Hz, 1H, aromatic CH), 7.55 (dd, J = 1.8 and 7.3 Hz, 1H, aromatic CH), 15.67 (s, 1H, OH).

4-Hydroxy-4-(3-(trifluoromethyl)phenyl)but-3-en-2-one (5f).[2] Yellow oil after purification by flash chromatography eluting with petroleum ether/EtOAc (9:1). ^1H NMR (400 MHz, $CDCl_3$) δ: 2.20 (s, 3H, CH_3), 6.18 (s, 1H, H-3), 7.56 (t, J = 7.8 Hz, 1H, aromatic CH), 7.74 (d, J = 7.8 Hz, 1H aromatic CH), 8.03 (d, J = 7.8 Hz, 1H, aromatic CH), 8.09 (s, 1H, aromatic CH), 16.00 (s, 1H, OH).

4-(3,4-Dimethoxyphenyl)-4-hydroxybut-3-en-2-one (5g).[2] White solid. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.15 (s, 3H, CH_3), 3.91 (s, 3H, CH_3), 3.92 (s, 3H, CH_3), 6.10 (s, 1H, H-3), 6.87 (d, J = 8.3 Hz, 1H, aromatic CH), 7.43 (d, J = 2.0 Hz, 1H, aromatic CH), 7.47 (dd, J = 2.0 and 8.3 Hz, 1H, aromatic CH), 16.18 (s, 1H, OH).

4-(3,4-Dichlorophenyl)-4-hydroxybut-3-en-2-one (5h). White solid after treatment with cyclohexane. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.16 (s, 3H, CH_3), 6.65 (s, 1H, H-3), 7.77 (d, J = 8.3 Hz, 1H, aromatic CH), 7.89 (dd, J = 1.7 and 8.3 Hz, 1H, aromatic CH), 8.14 (d, J = 1.7 Hz, 1H, aromatic CH), 16.03 (bs, 1H, OH).

4-Hydroxy-4-(naphthalen-1-yl)but-3-en-2-one (5i).[2] Yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.19 (s, 3H, CH_3), 6.01 (s, 1H, H-3), 7.45-7.56 (m, 4H, aromatic CH), 7.69 (dd, J = 0.8 and 7.0 Hz, 1H aromatic CH), 7.86 (d, J = 7.6 Hz, 1H, aromatic CH), 7.93 (d, J = 8.2 Hz, 1H, aromatic CH), 8.43 (d, J = 8.2 Hz, 1H, aromatic CH), 16.20 (s, 1H, OH).

4-Hydroxy-4-(pyridin-4-yl)but-3-en-2-one (5k).[2] The title compound was obtained as an orange solid in 34% yield following the general procedure for the synthesis of 1-aryl-1,3-butanediones, with the exception that, during the work-up, the reaction mixture was poured into ice/water, neutralized with 2N HCl, and then extracted with EtOAc, giving a solid that was treated with cyclohexane. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.22 (s, 3H, CH_3), 6.19 (s, 1H, H-3), 7.64 and 8.72 (d, J = 5.6 Hz, each 2H, aromatic CH), 15.73 (s, 1H, OH).

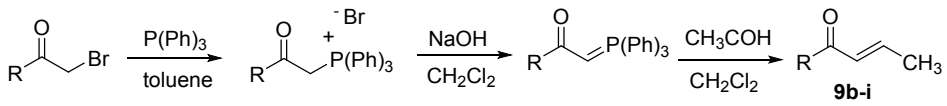
General procedure for the synthesis of 1-aryl-2-buten-1-ones (9b-i).

Synthesis of triphenylphosphonium bromide.[4] A solution of the suitable 2-bromoacetophenone (10 mmol) in toluene (10 mL) was added dropwise over 10 min to a solution of triphenylphosphine (10 mmol) in toluene (10 mL). The reaction mixture was maintained at room temperature overnight. Then, the precipitate obtained was filtered and washed with Et_2O, to give the triphenylphosphonium salt as white solid.

(2-Oxo-2-(pyridin-4-yl)ethyl)triphenylphosphonium bromide.[5] A solution of triphenylphosphine (0.93 g, 0.0035 mmol) in dry deoxygenated THF (20 mL) was added dropwise to suspension of 2-bromo-1-(pyridin-4-yl)ethan-1-one hydrobromide (1.0 g, 0.0035 mmol) in dry THF (10 mL). Then, the reaction mixture was added of Et_3N (0.5 mL, 0.0035 mmol), maintained at rt for 1h, and refluxed overnight. After cooling, it was filtered obtaining the triphenylphosphonium salt as orange solid.

Wittig reaction.[6] A solution of the triphenylphosphonium bromide (7 mmol) in CH_2Cl_2 (15 mL) was stirred overnight with 2N NaOH (10 mL). Then, the phases was separated and water was extracted with CH_2Cl_2. The combined organic layers were dried over sodium sulfate and to these, acetaldehyde (42 mmol) was added dropwise over 1 h. The reaction mixture was maintained at room temperature overnight. Then, it was evaporated to dryness to give a residue that was treated with cyclohexane to give a solid (triphenylphosphine oxide) that was filtered. The filtrate was evaporated to dryness to give 1-aryl-2-buten-1-ones with sufficient purity to be used in the next step without further purification, otherwise indicated.

Table S2. Preparation of unsymmetrically 1-aryl-2-buten-1-ones.



Entry	R	phosphonium salt Crude Yield (%)	Product	1-aryl-2-buten-1-one Crude Yield (%)
1	*p*-$CH_3C_6H_5$	87%	**9b**	87%
2	*p*-$CH_3OC_6H_5$	75%	**9c**	90%
3	*p*-$NO_2C_6H_5$	94%	**9d**	56%

4	*p*-ClC_6H_5	86%	**9e**	86%
5	*m*-BrC_6H_5	94%	**9f**	85%
6	*o*-FC_6H_5	81%	**9g**	70%
7	*o,p-Di*-FC_6H_5	85%	**9h**	74%
8	4-Pyridinyl	97%	**9i**	55%

1-*p*-Tolylbut-2-en-1-one (9b).[7] Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.96 (dd, *J* = 1.4 and 6.7 Hz, 3H, CH*CH$_3$*), 2.38 (s, 3H, CH_3), 6.86-6.91 and 6.99-7.08 (m, each 1H, CH=CH), 7.23 and 7.82 (d, *J* = 8.1 Hz, each 2H, aromatic CH).

1-(4-Methoxyphenyl)but-2-en-1-one (9c).[7] Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.96 (dd, *J* = 1.2 and 6.7 Hz, 3H, CH*CH$_3$*), 3.84 (s, 3H, CH_3), 6.88-6.94 (m, 3H, *CH*=CH and aromatic CH), 6.99-7.08 (m, 1H, CH=*CH*), 7.92 (d, *J* = 8.8 Hz, 2H, aromatic CH).

1-(4-Nitrophenyl)but-2-en-1-one (9d).[7] White solid after purification by flash chromatography eluting with cyclohexane/EtOAc (7:3). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.01 (dd, *J* = 1.5 and 6.8 Hz, 3H, CH*CH$_3$*), 3.84 (s, 3H, CH_3), 6.82-6.87 and 7.06-7.15 (m, each 1H, CH=CH), 8.01 and 8.29 (dd, *J* = 2.1 and 8.7 Hz, each 2H, aromatic CH).

1-(4-Chlorophenyl)but-2-en-1-one (9e).[7] Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.98 (dd, *J* = 1.5 and 6.9 Hz, 3H, CH*CH$_3$*), 6.82-6.87 and 7.02-7.11 (m, each 1H, CH=CH), 8.01 and 8.29 (dd, *J* = 2.0 and 8.5 Hz, each 2H, aromatic CH).

1-(3-Bromophenyl)but-2-en-1-one (9f). Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.98 (dd, *J* = 1.0 and 6.9 Hz, 3H, CH*CH$_3$*), 6.80-6.84 and 7.02-7.11 (m, each 1H, CH=CH), 7.32 (t, *J* = 7.8 Hz, 1H, aromatic CH), 7.65 (d, J = 8.1 Hz, 1H, aromatic CH), 7.81 (d, *J* = 7.7 Hz, 1H, aromatic CH), 8.01 (s, 1H, aromatic CH).

1-(2-Fluorophenyl)but-2-en-1-one (9g).[8] Brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.95 (dd, *J* = 1.3 and 6.8 Hz, 3H, CH*CH$_3$*), 6.69-6.74 and 6.92-7.02 (m, each 1H, CH=CH), 7.09 (dd, *J* = 8.3 and 10.6 Hz, 1H, aromatic CH), 7.19 (t, *J* = 7.5 Hz, 1H, aromatic CH), 7.43-7.47 (m, 1H, aromatic CH), 7.67 (dt, *J* = 1.6 and 7.5 Hz, 1H, aromatic CH).

1-(2,4-Difluorophenyl)but-2-en-1-one (9h). Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.95 (dd, J = 1.5 and 6.9 Hz, 3H, CHCH_3), 6.72 (dq, J = 1.5 and 15.3 Hz, 1H, CH=CH), 6.80-6.86 (m, 1H, aromatic CH), 6.92 (dt, J = 2.3 and 8.3 Hz, 1H, aromatic CH), 6.96-7.05 (m, 1H, CH=CH), 7.72-7.78 (m, 1H, aromatic CH).

1-(Pyridin-4-yl)but-2-en-1-one (9i).[9] Red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.00 (dd, J = 1.3 and 6.5 Hz, 3H, CHCH_3), 6.76-6.80 and 7.04-7.13 (m, each 1H, CH=CH), 7.64 and 8.76 (d, J = 5.8 Hz, each 2H, pyridine CH).

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^{1}H NMR and ^{13}C NMR spectra

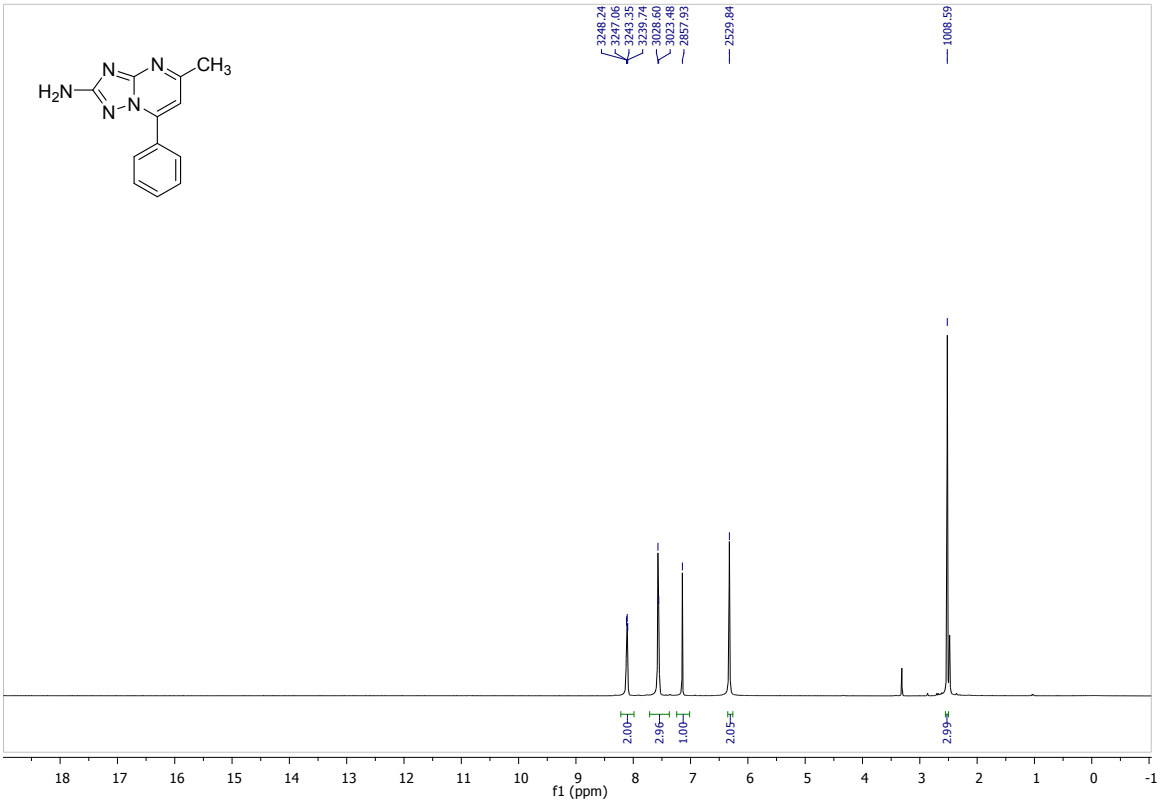

Figure S1. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **1a**.

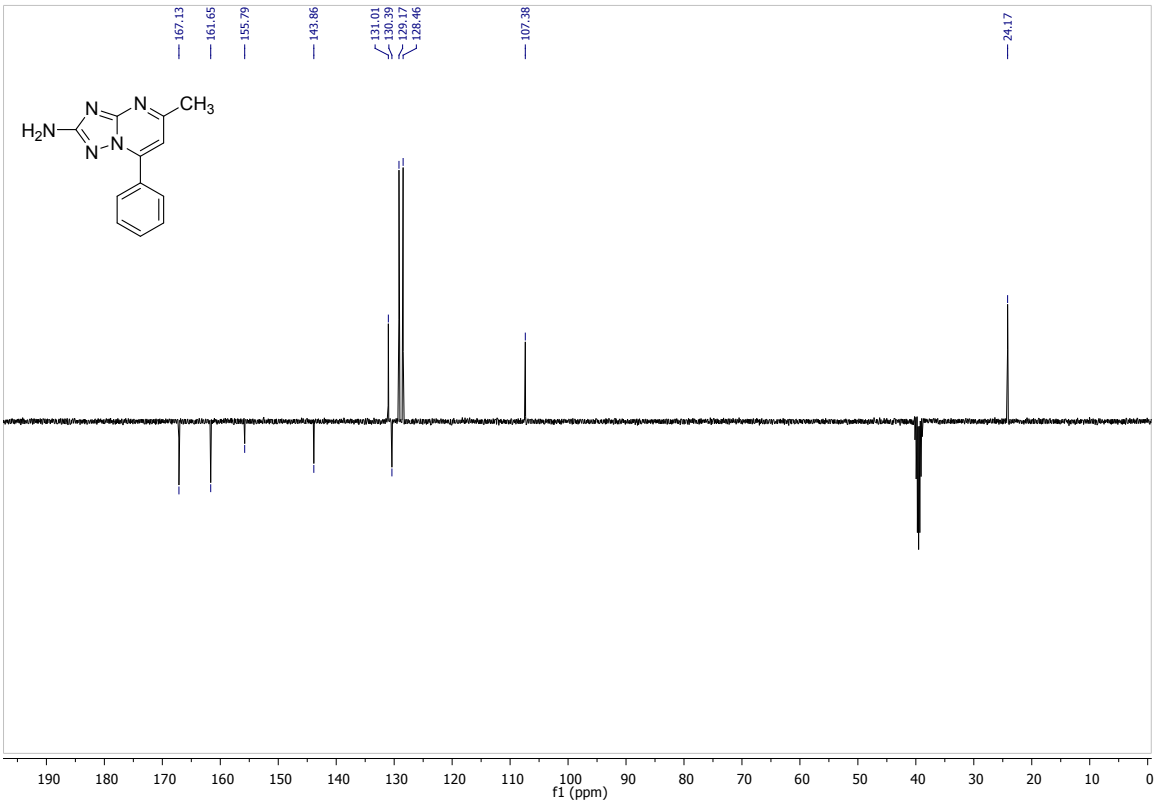

Figure S2. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **1a**.

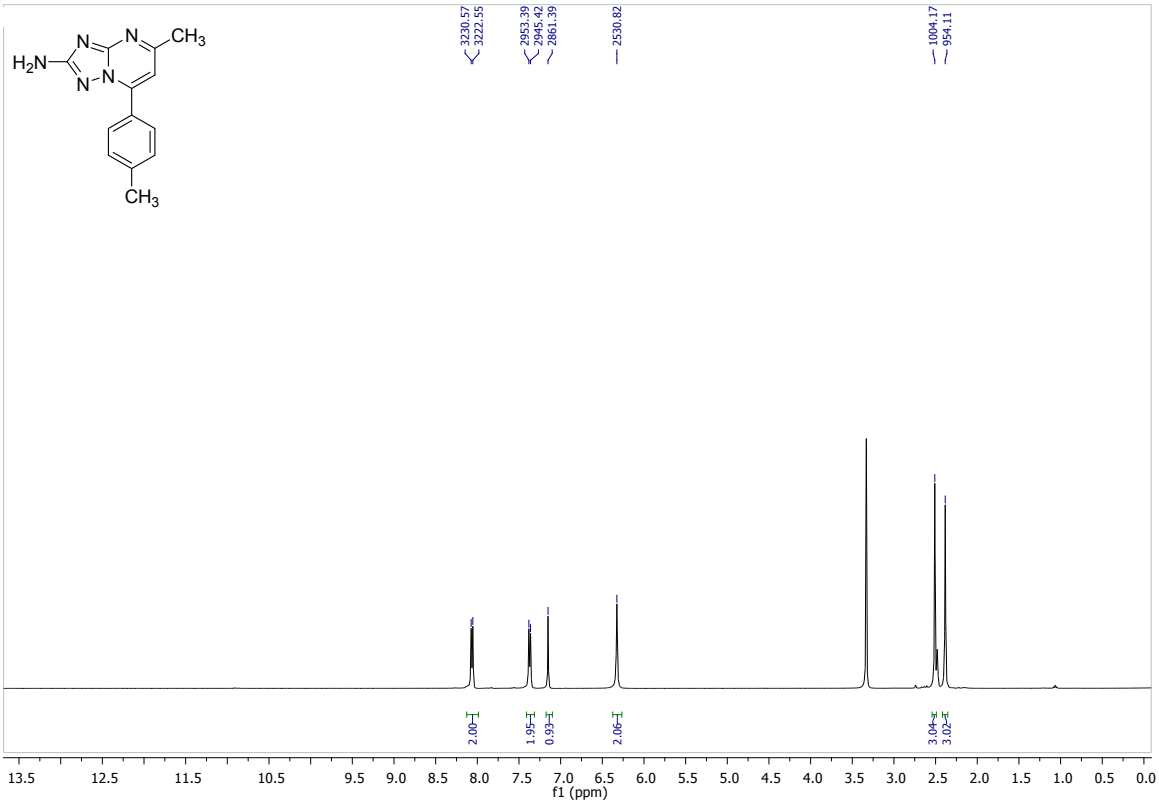

Figure S3. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **1b**.

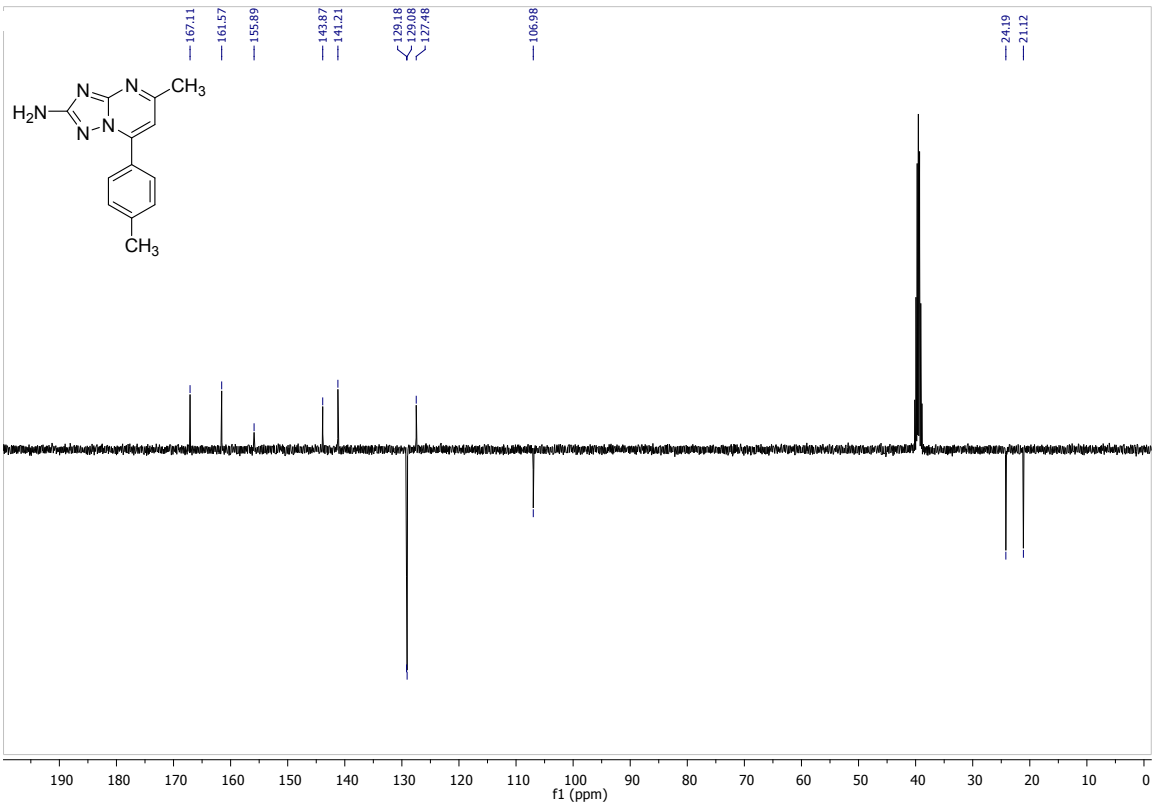

Figure S4. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **1b**.

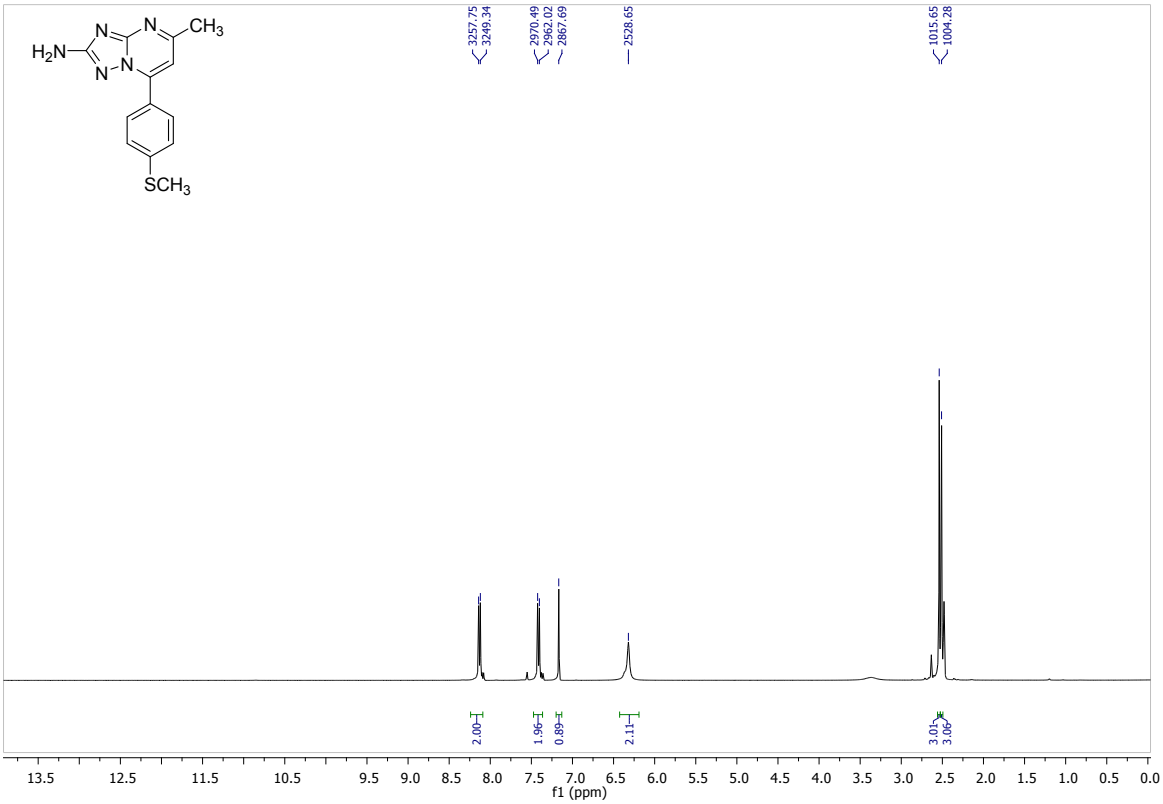

Figure S5. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **1c**.

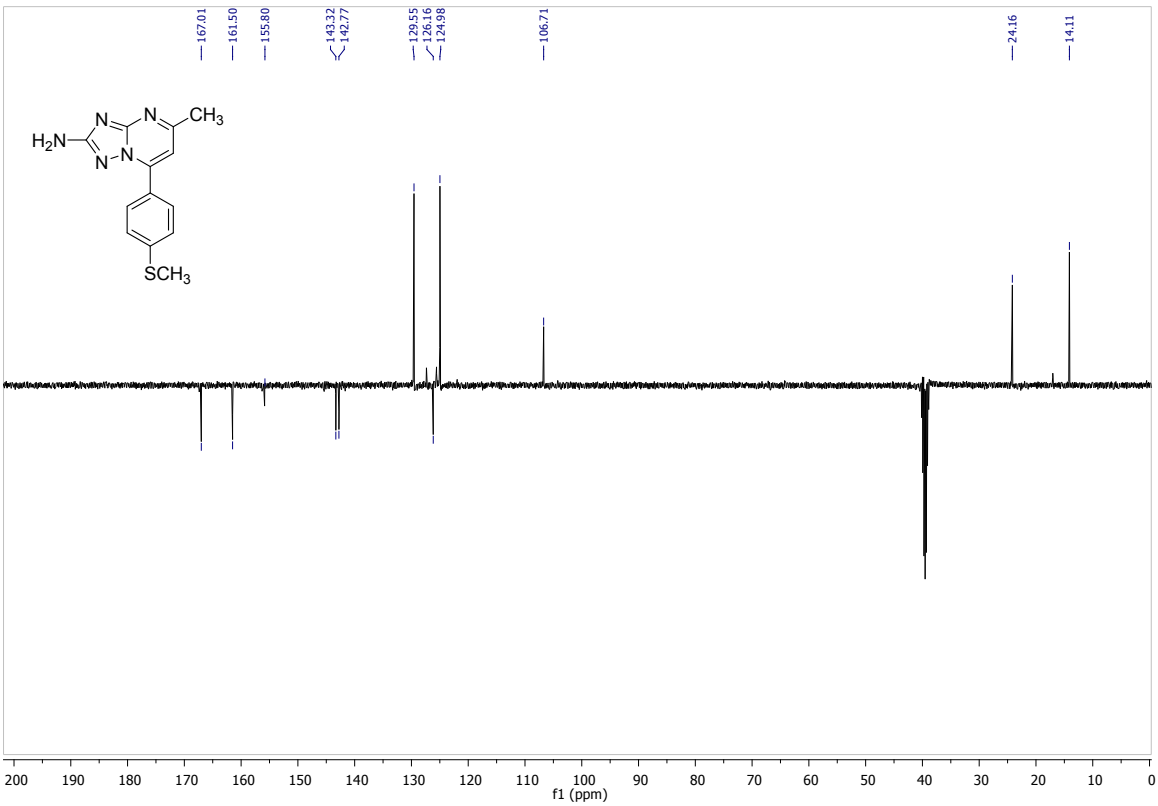

Figure S6. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **1c**.

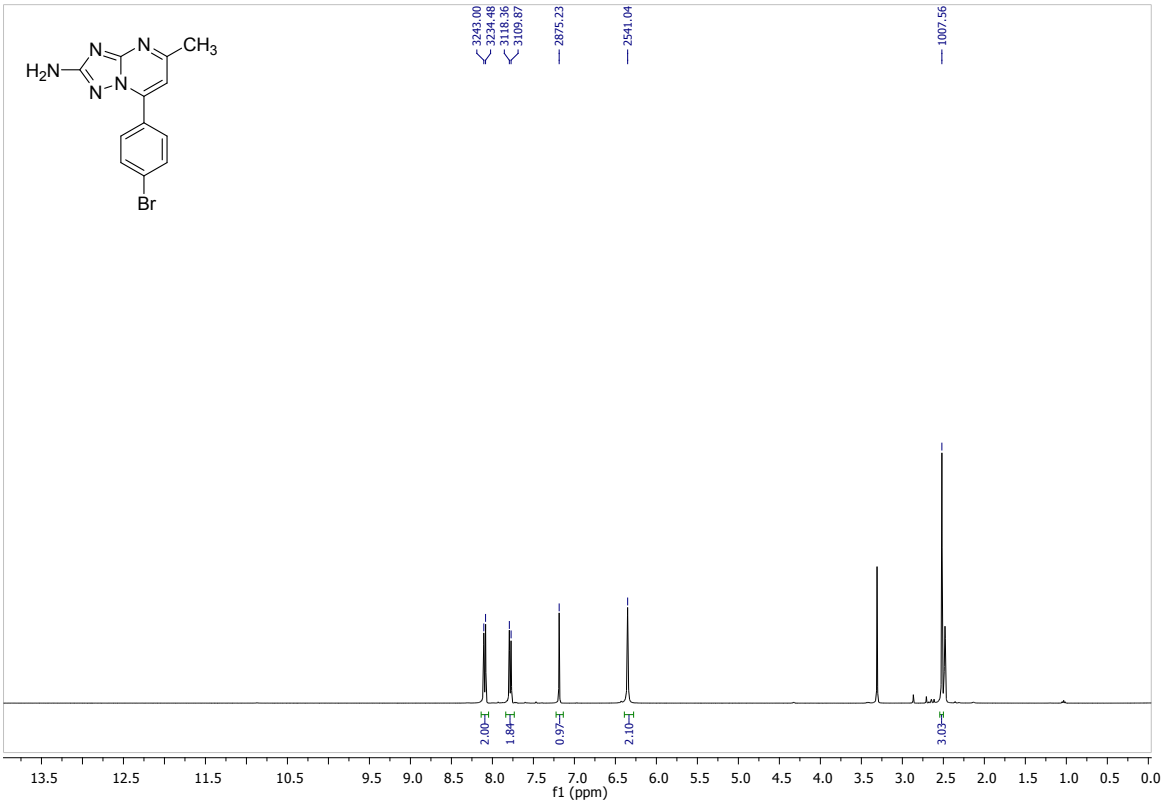

Figure S7. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **1d**.

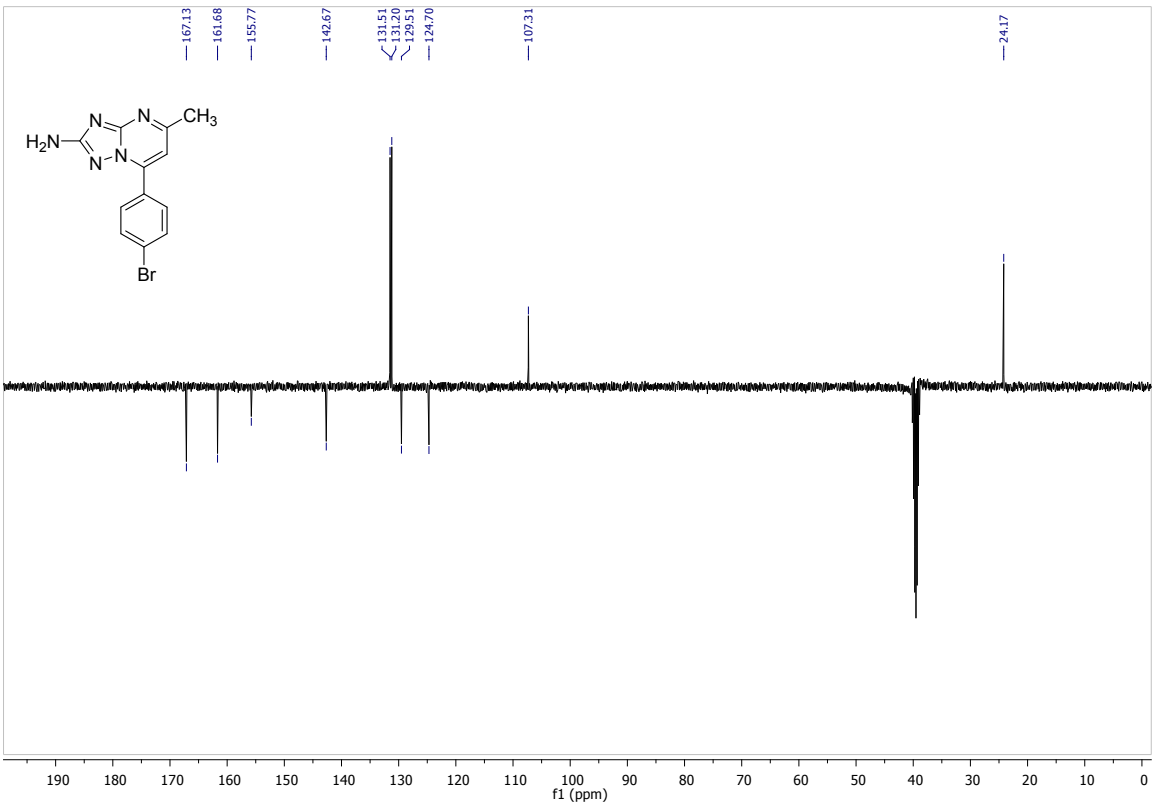

Figure S8. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **1d**.

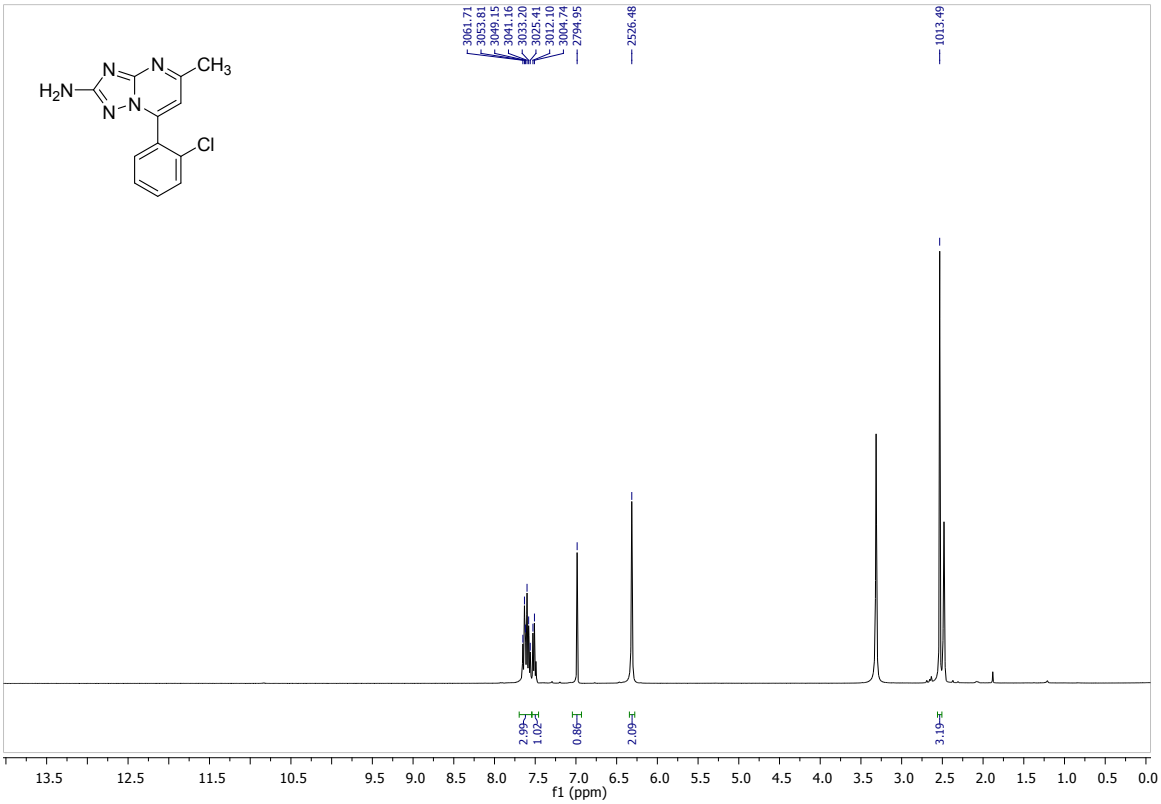

Figure S9. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **1e**.

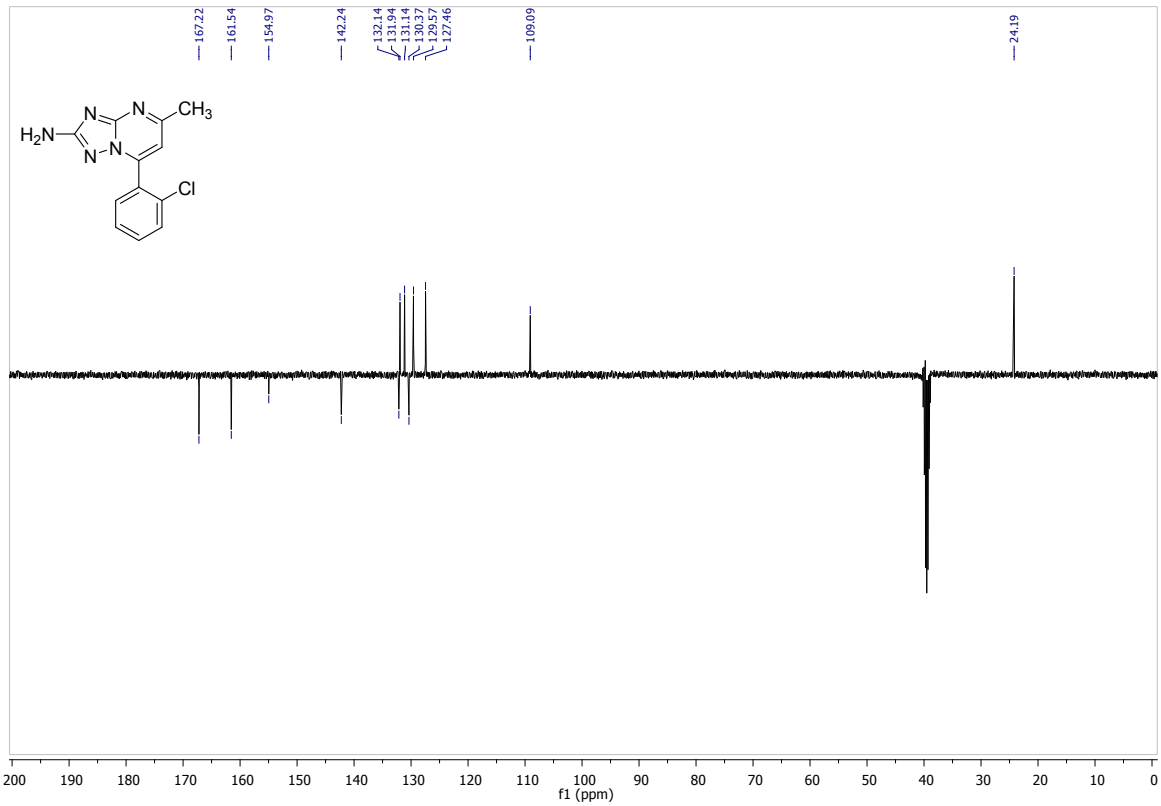

Figure S10. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **1e**.

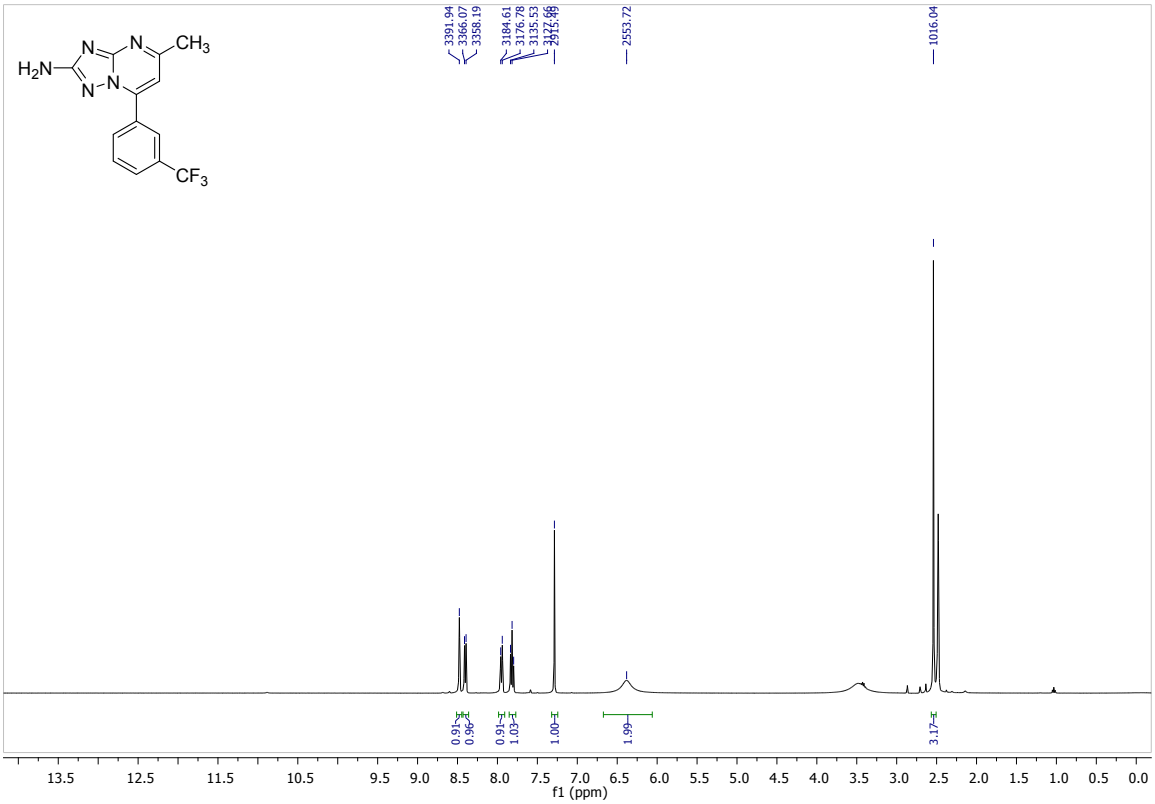

Figure S11. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **1f**.

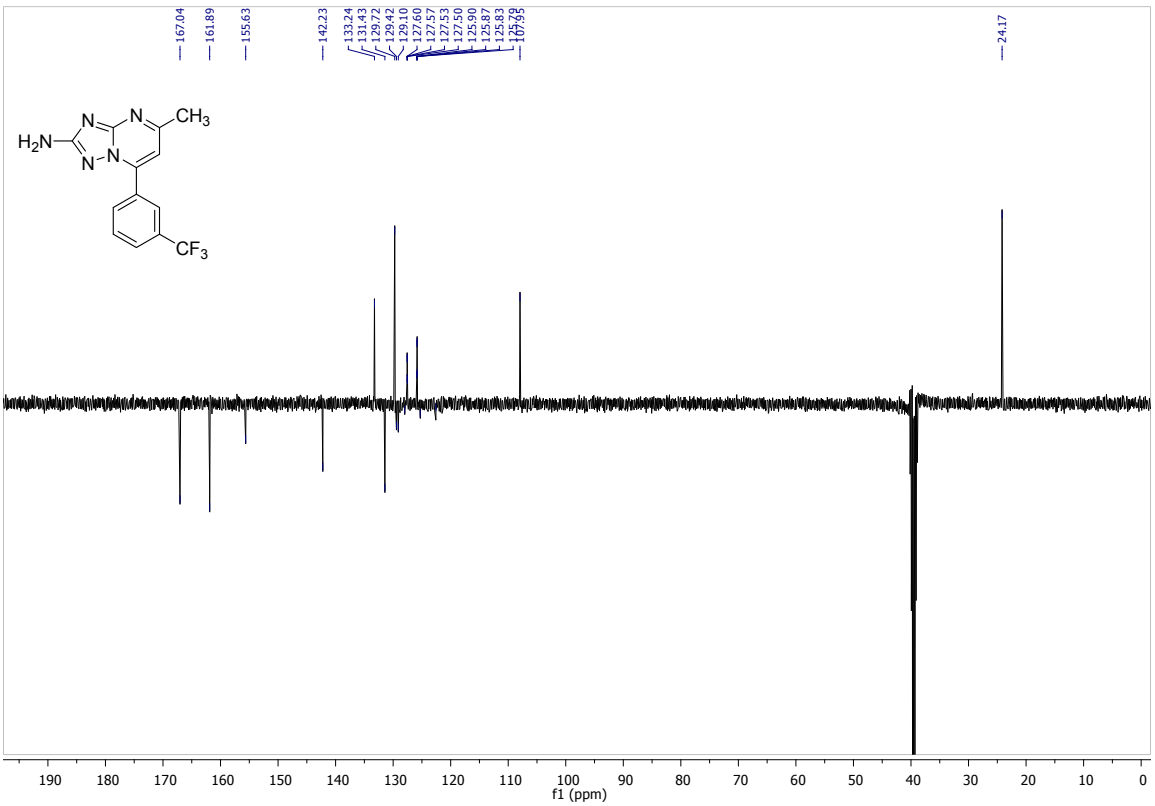

Figure S12. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **1f**.

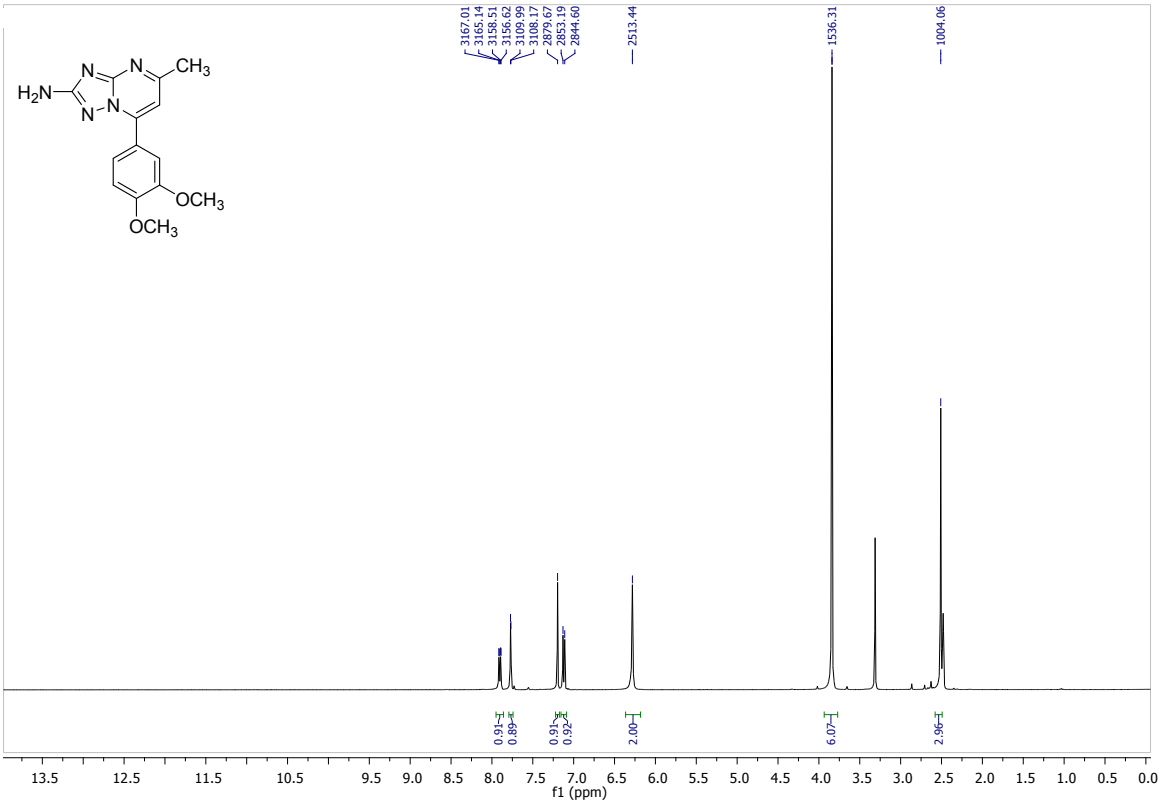

Figure S13. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **1g**.

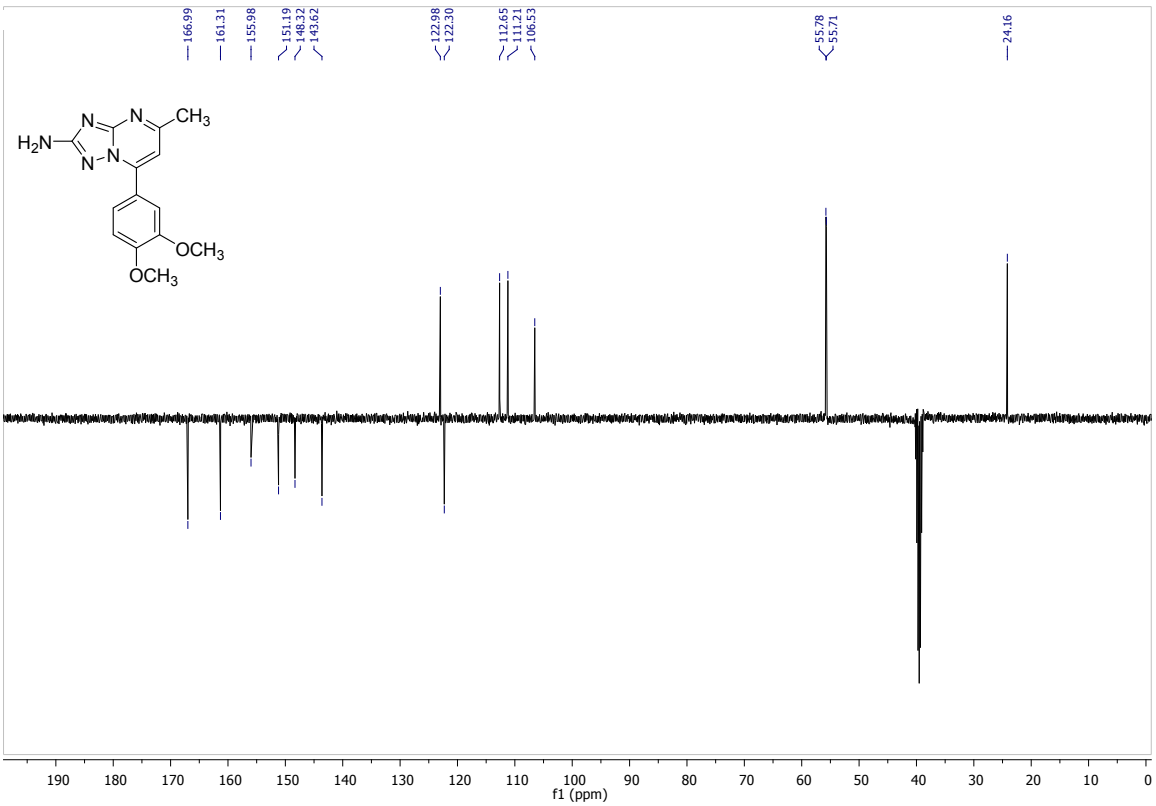

Figure S14. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **1g**.

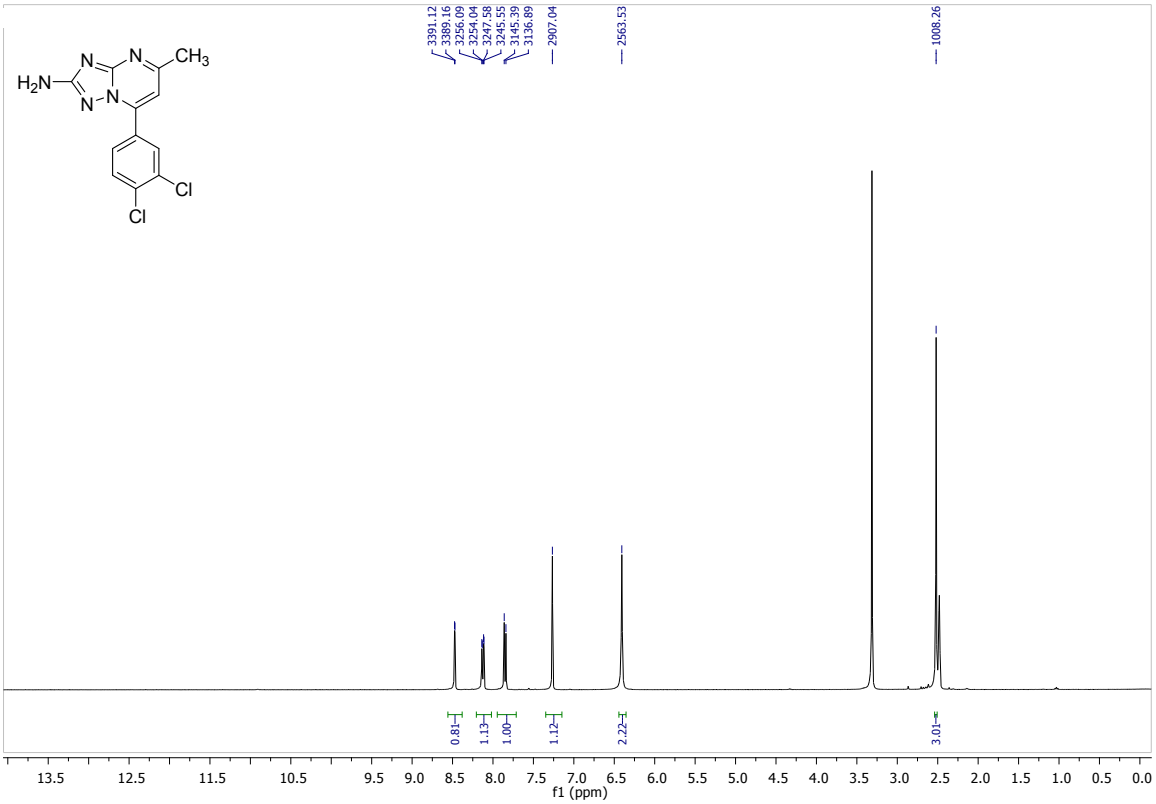

Figure S15. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **1h**.

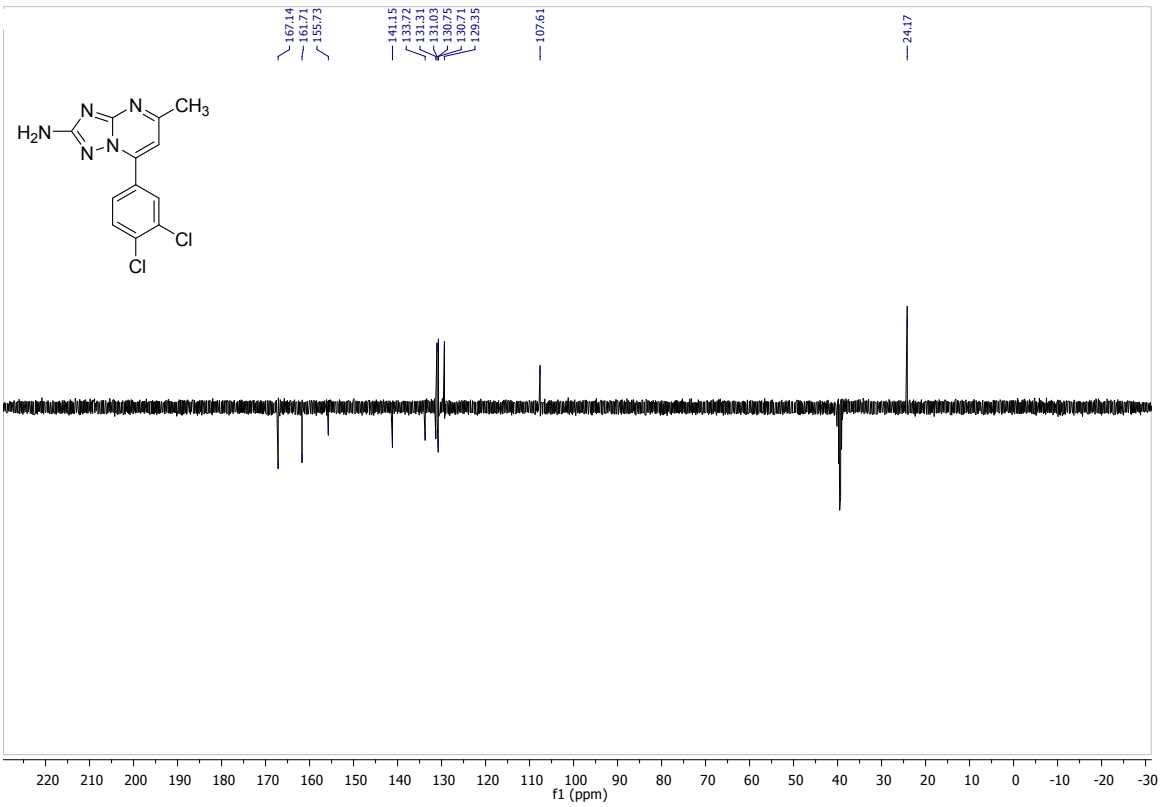

Figure S16. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **1h**.

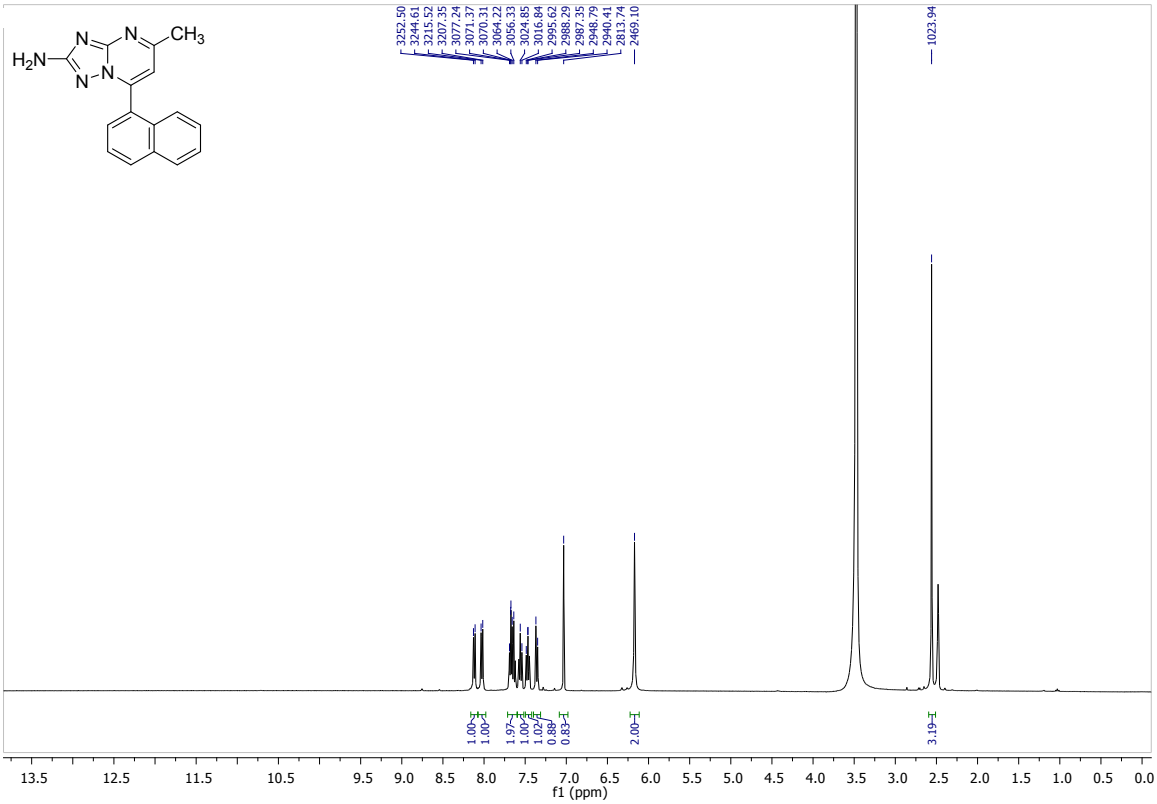

Figure S17. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **1i**.

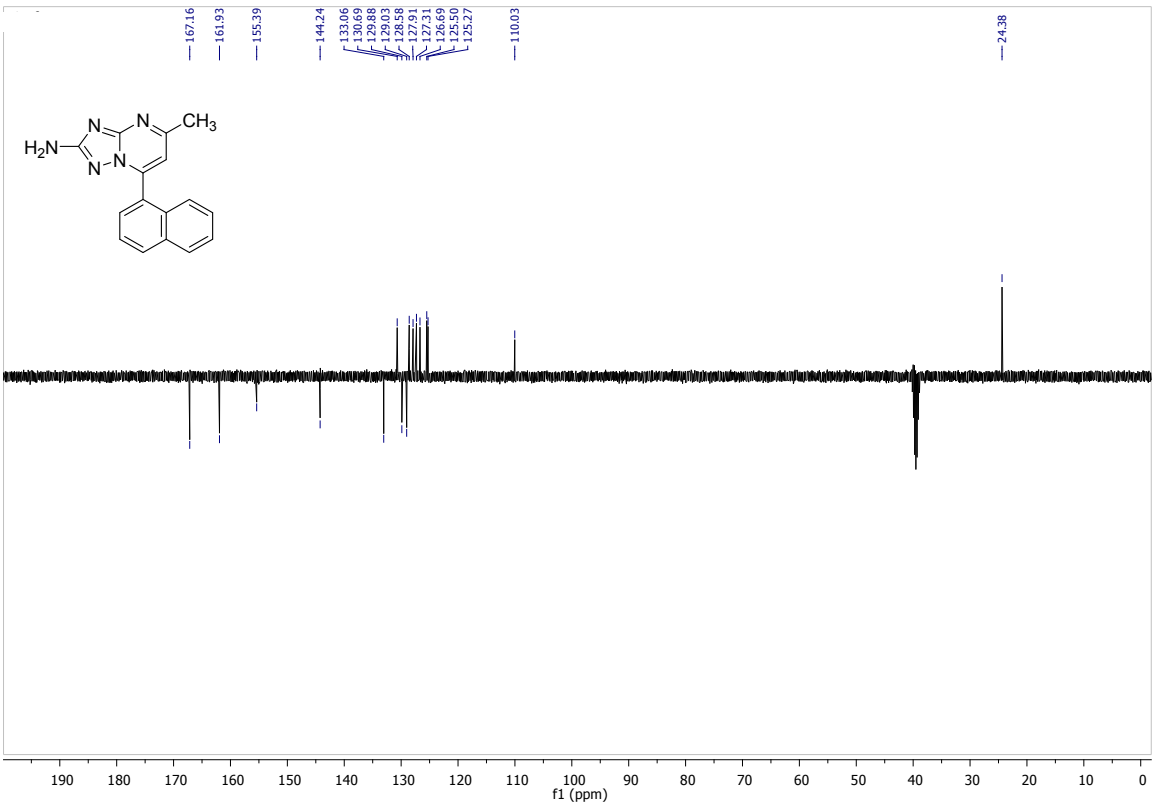

Figure S18. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **1i**.

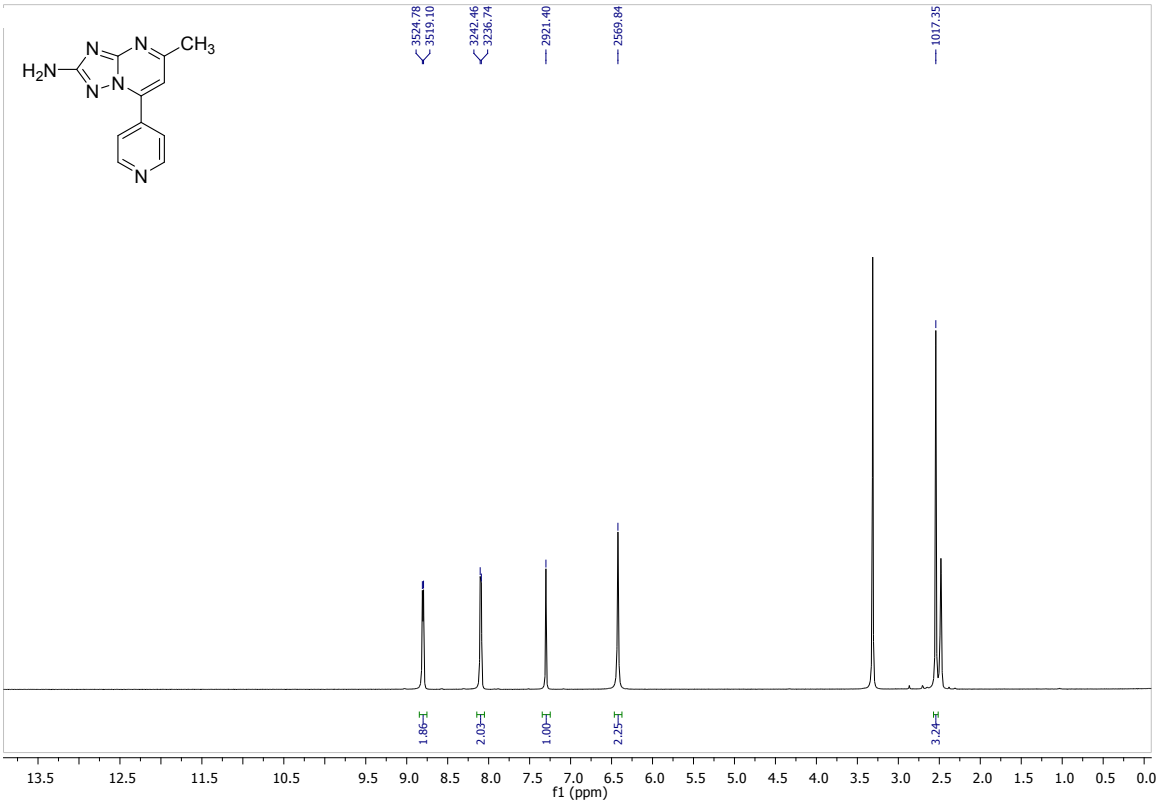

Figure S19. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **1k**.

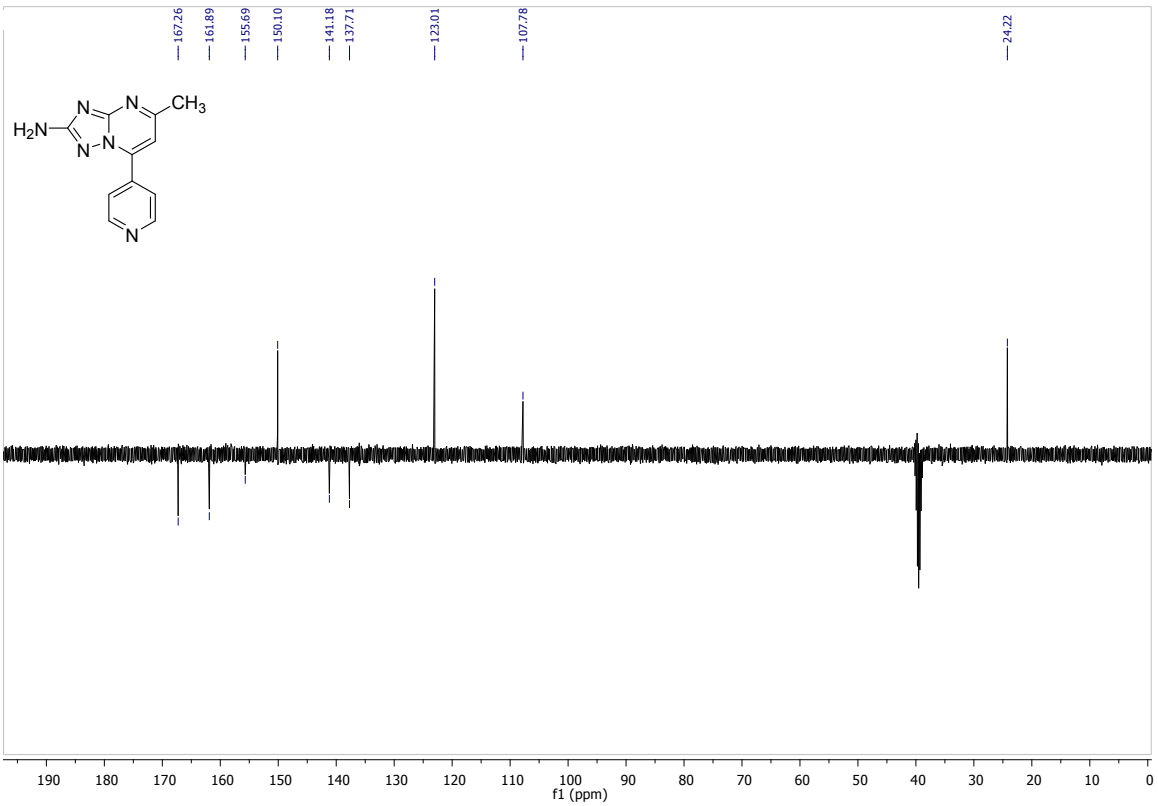

Figure S20. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **1k**.

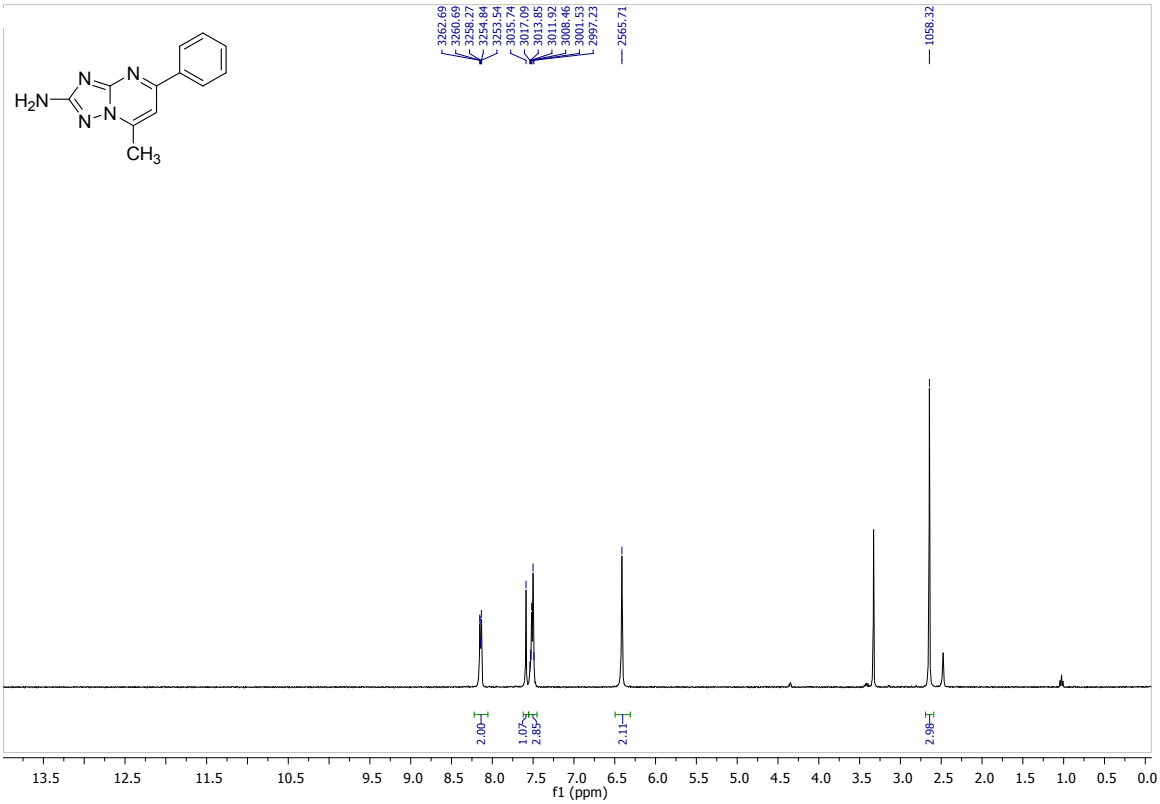

Figure S21. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **2a**.

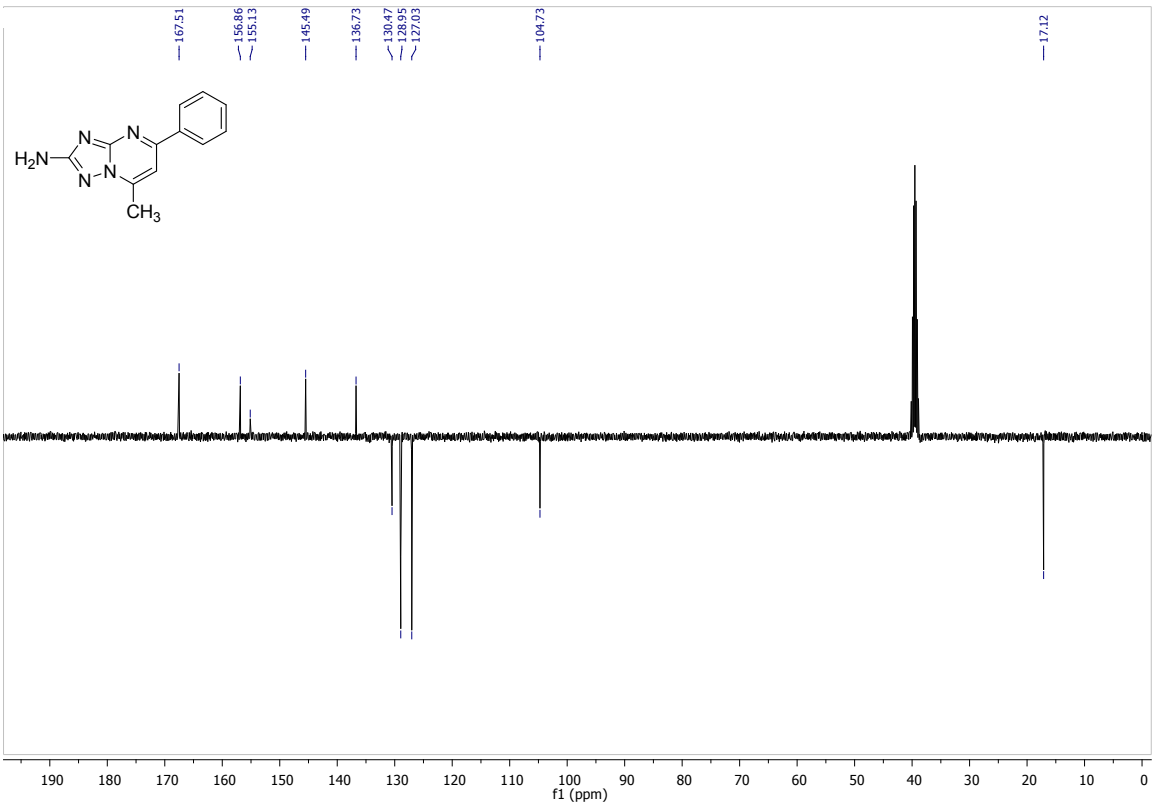

Figure S22. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **2a**.

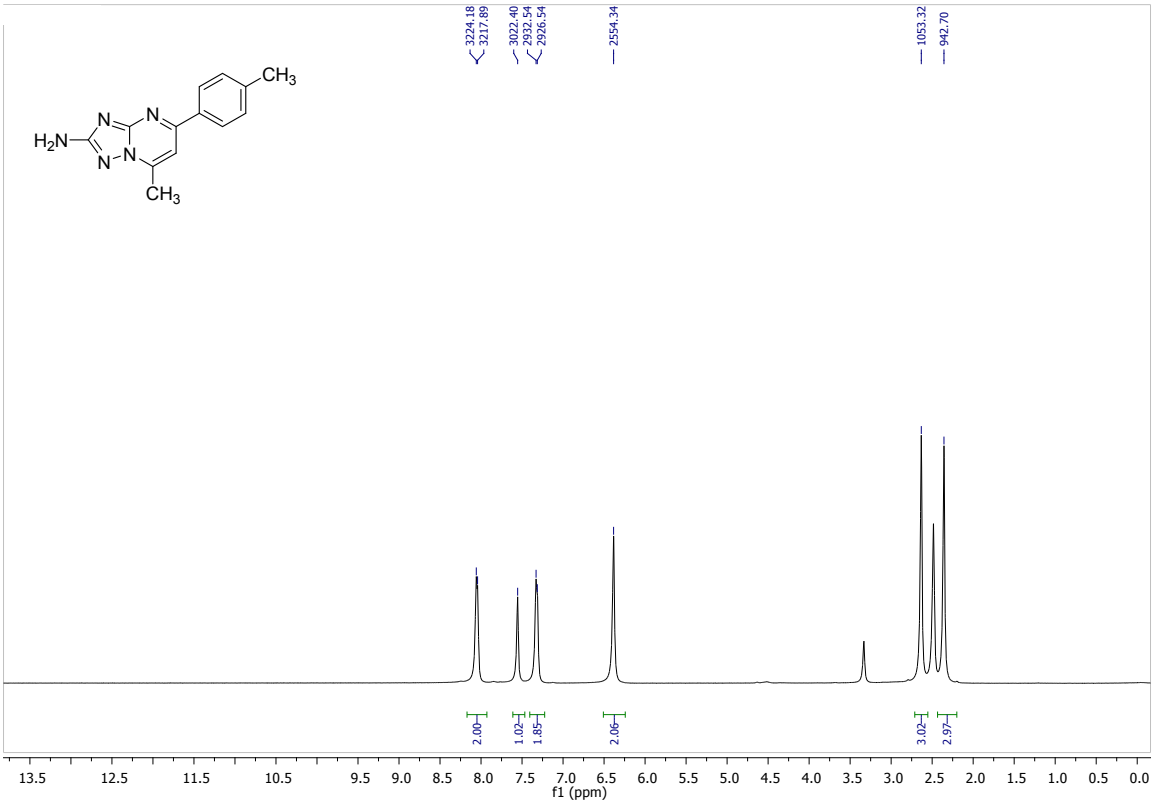

Figure S23. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **2b**.

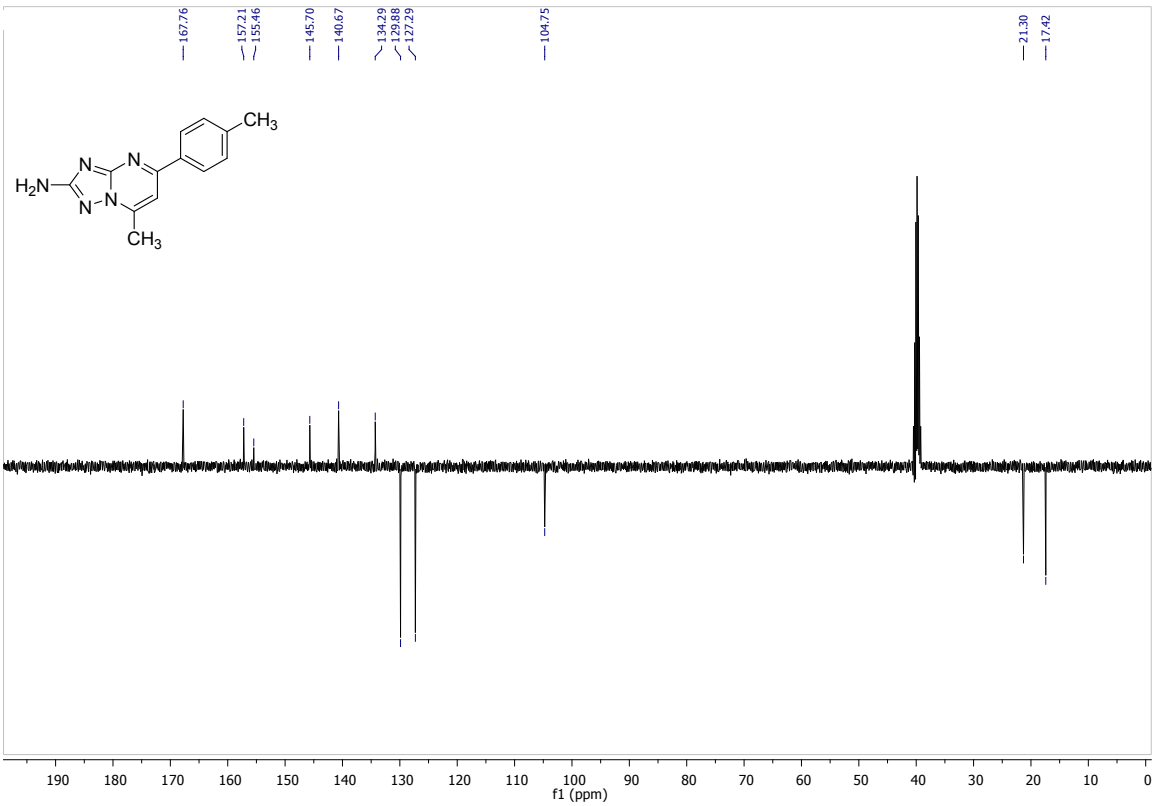

Figure S24. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **2b**.

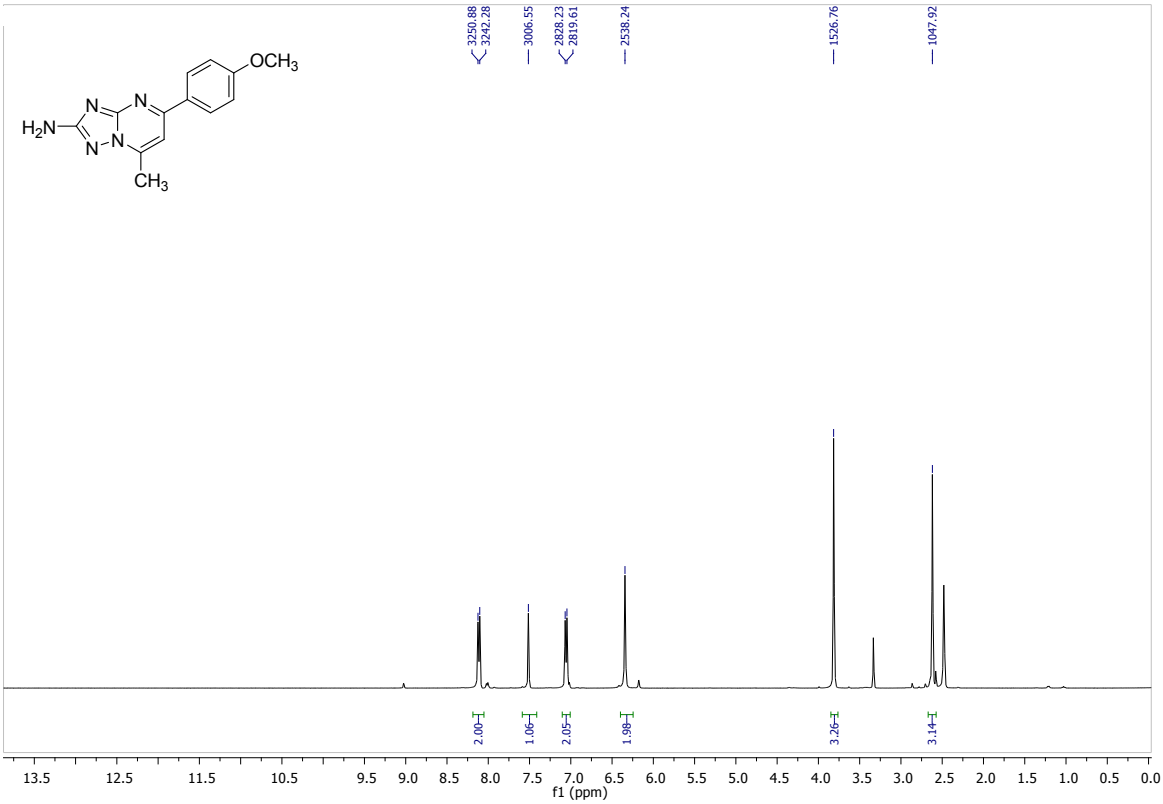

Figure S25. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **2c**.

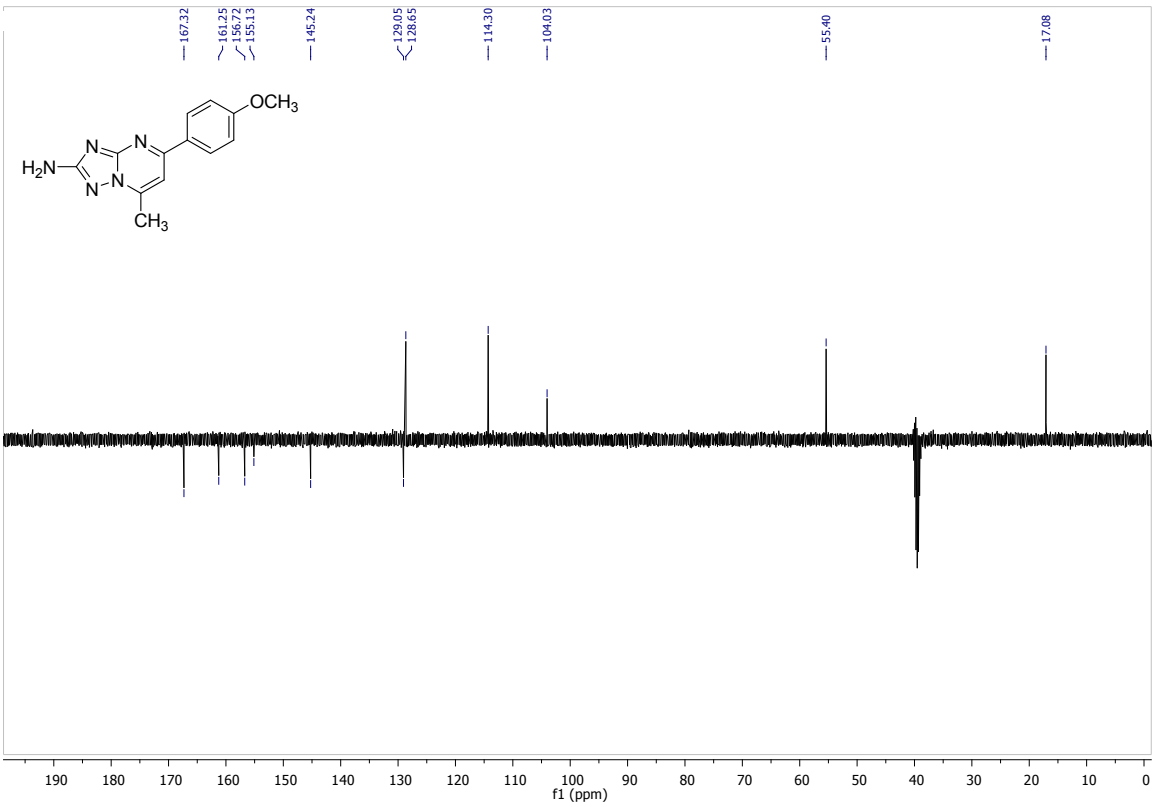

Figure S26. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **2c**.

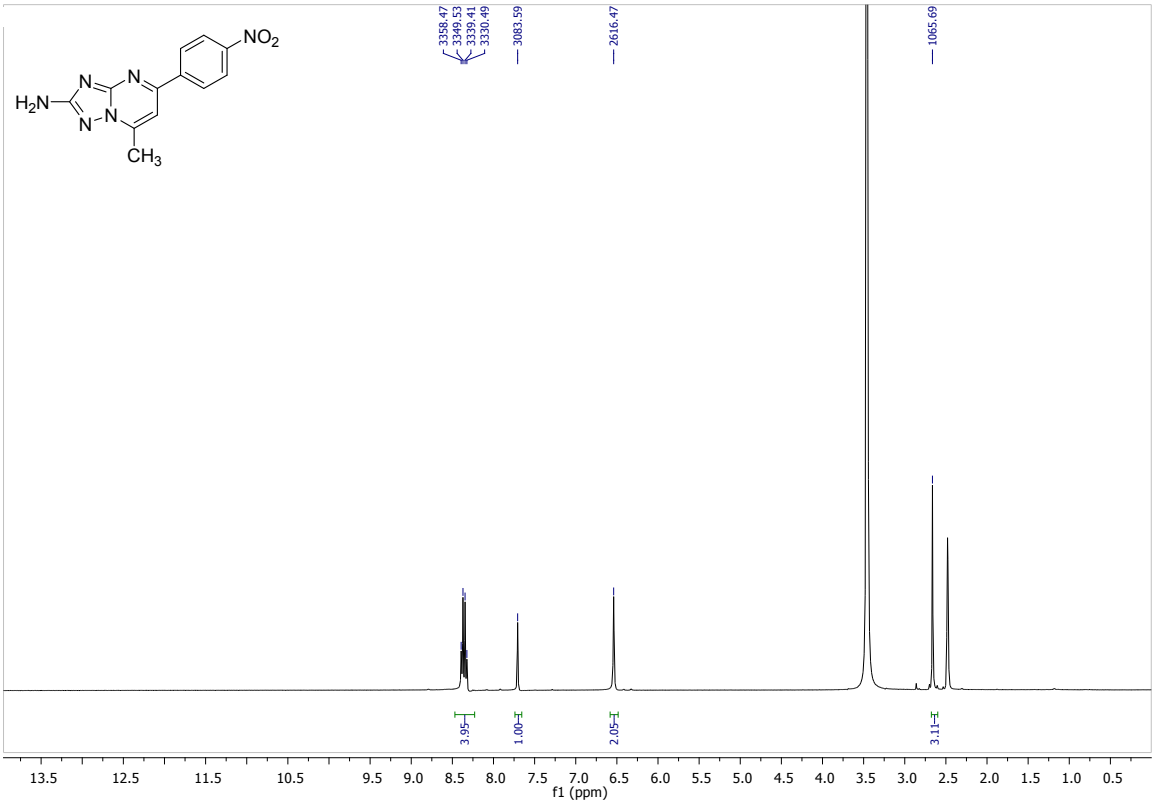

Figure S27. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **2d**.

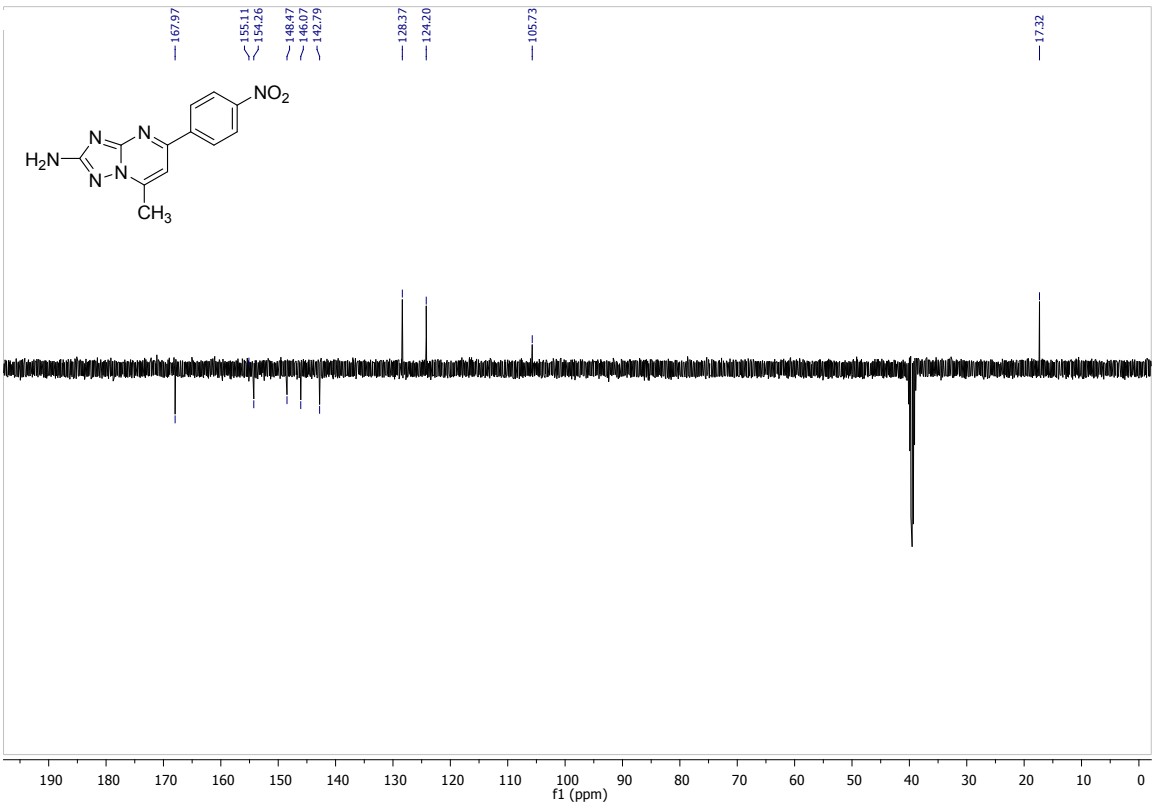

Figure S28. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **2d**.

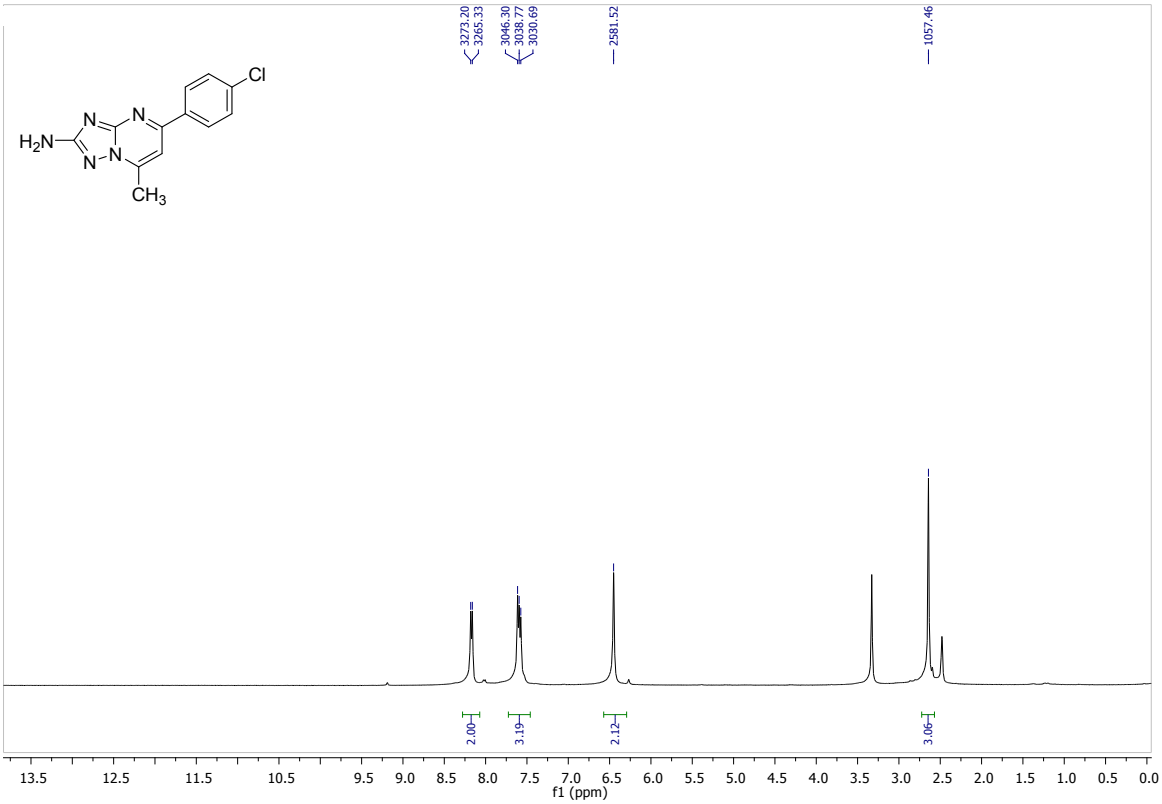

Figure S29. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **2e**.

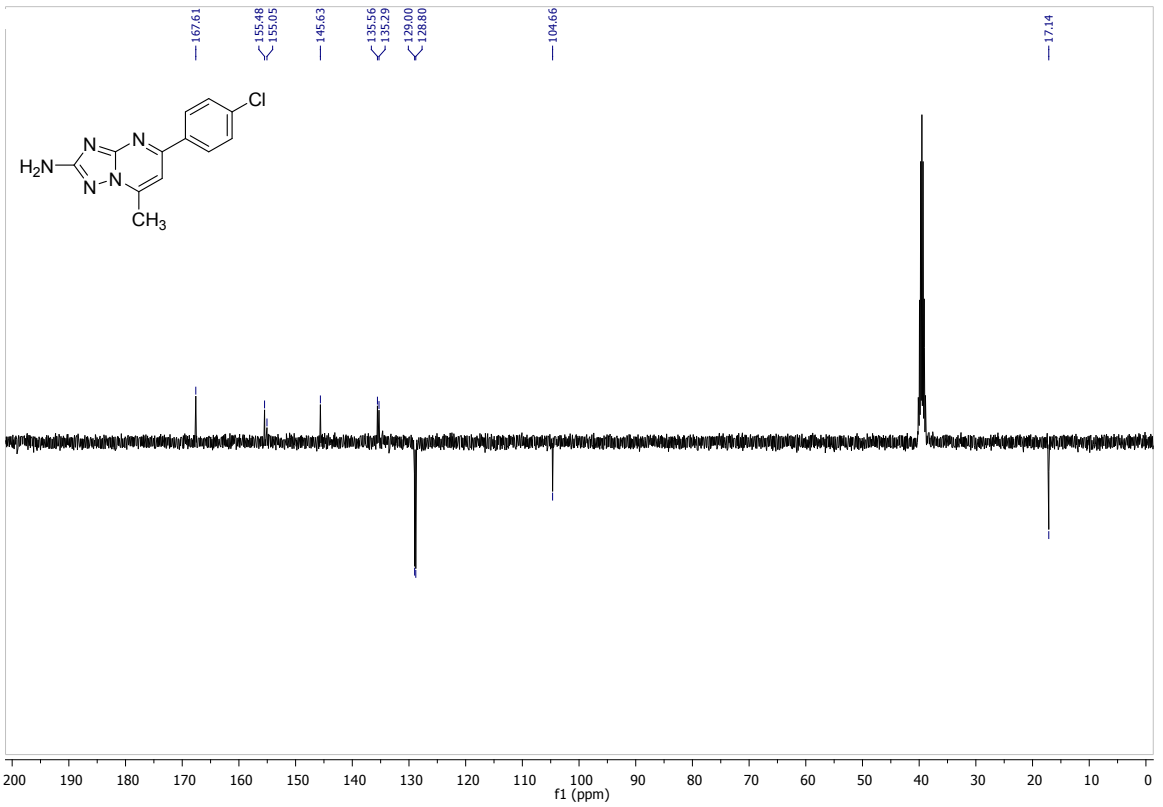

Figure S30. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **2e**.

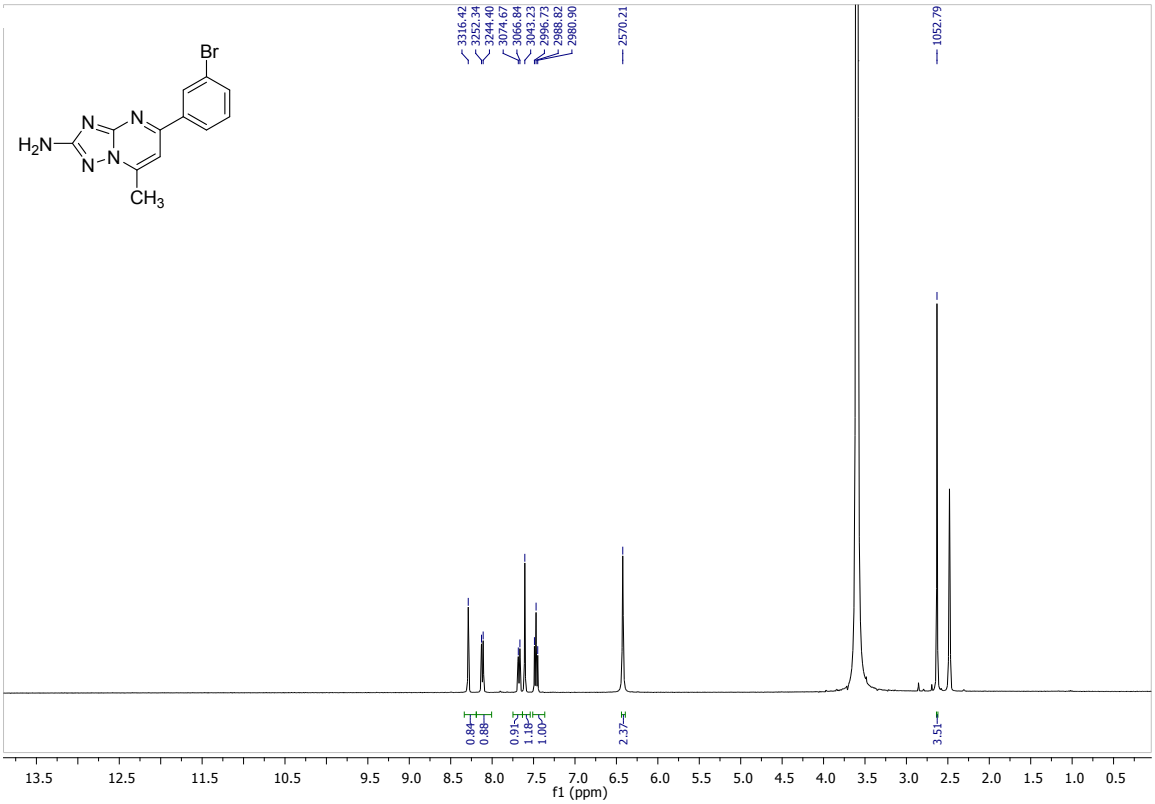

Figure S31. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **2f**.

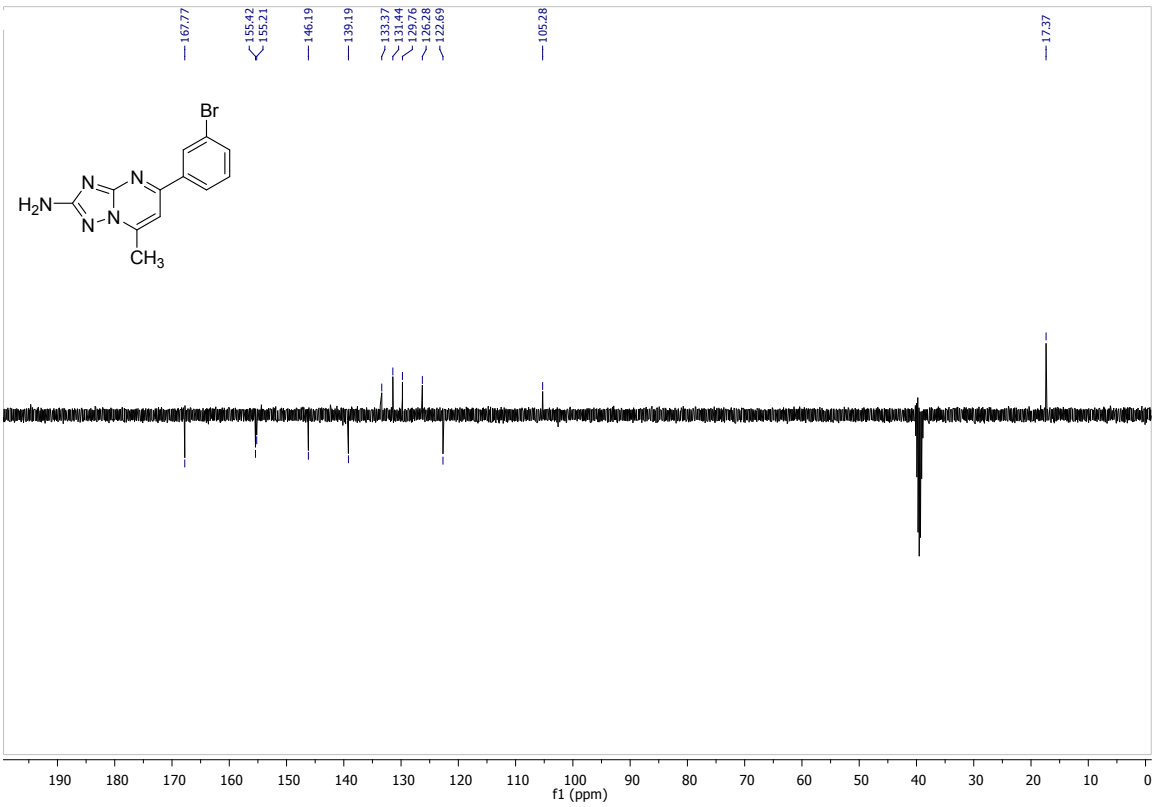

Figure S32. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **2f**.

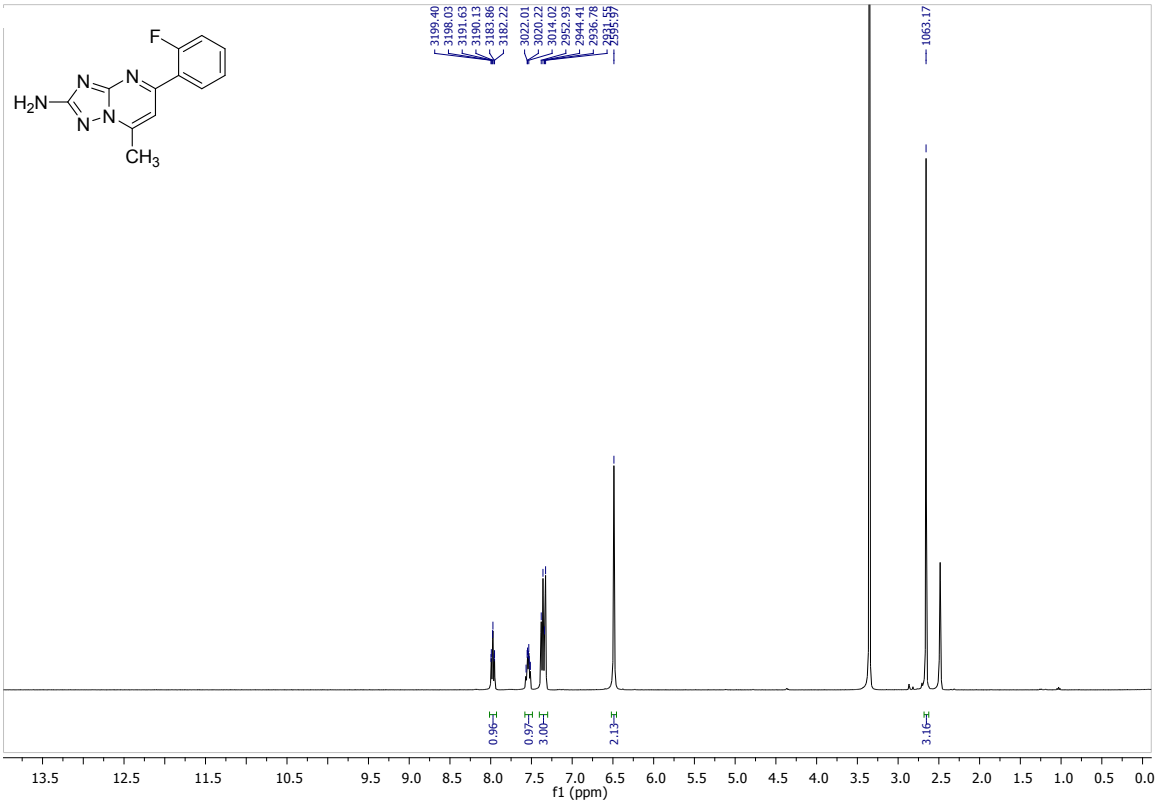

Figure S33. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **2g**.

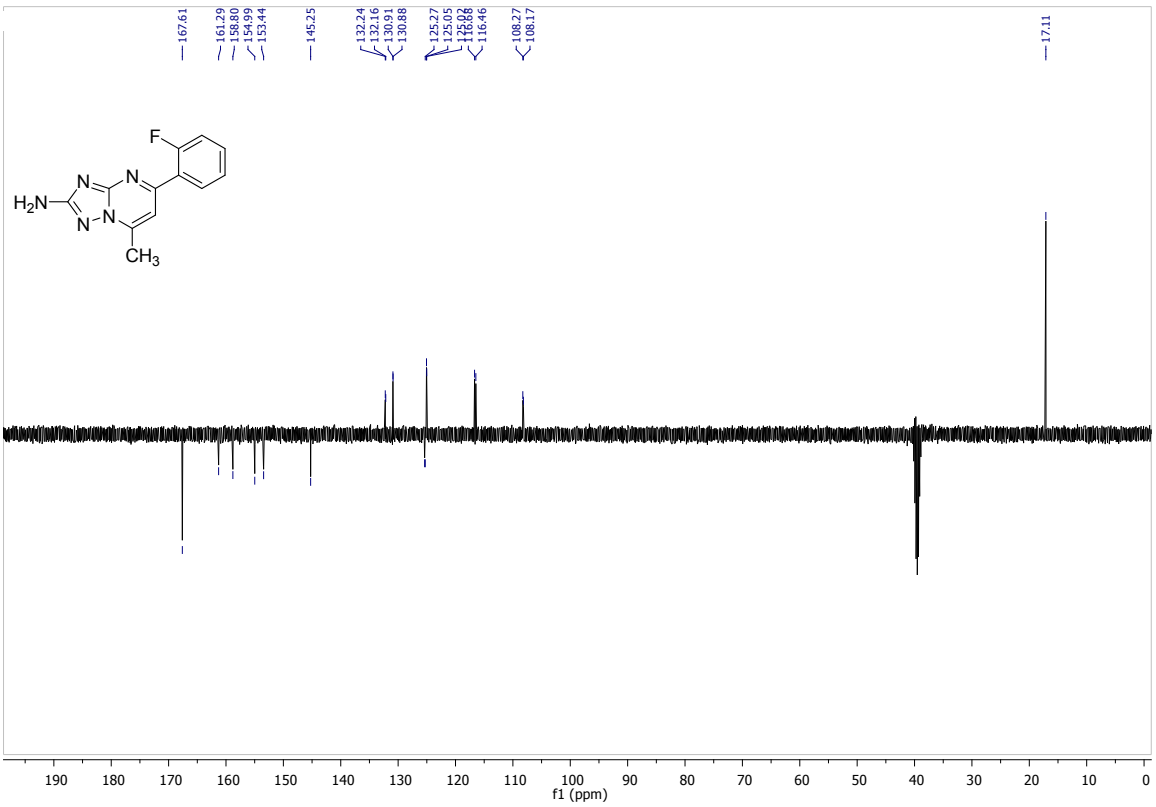

Figure S34. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **2g**.

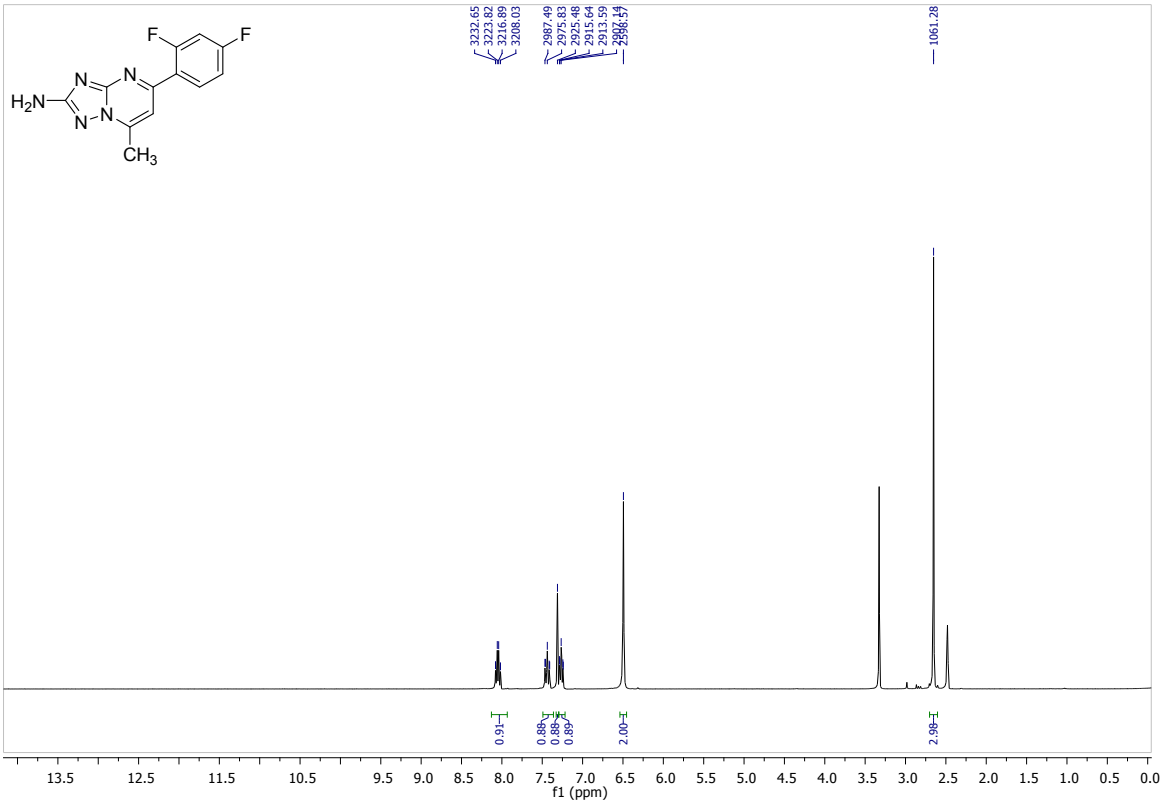

Figure S35. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **2h**.

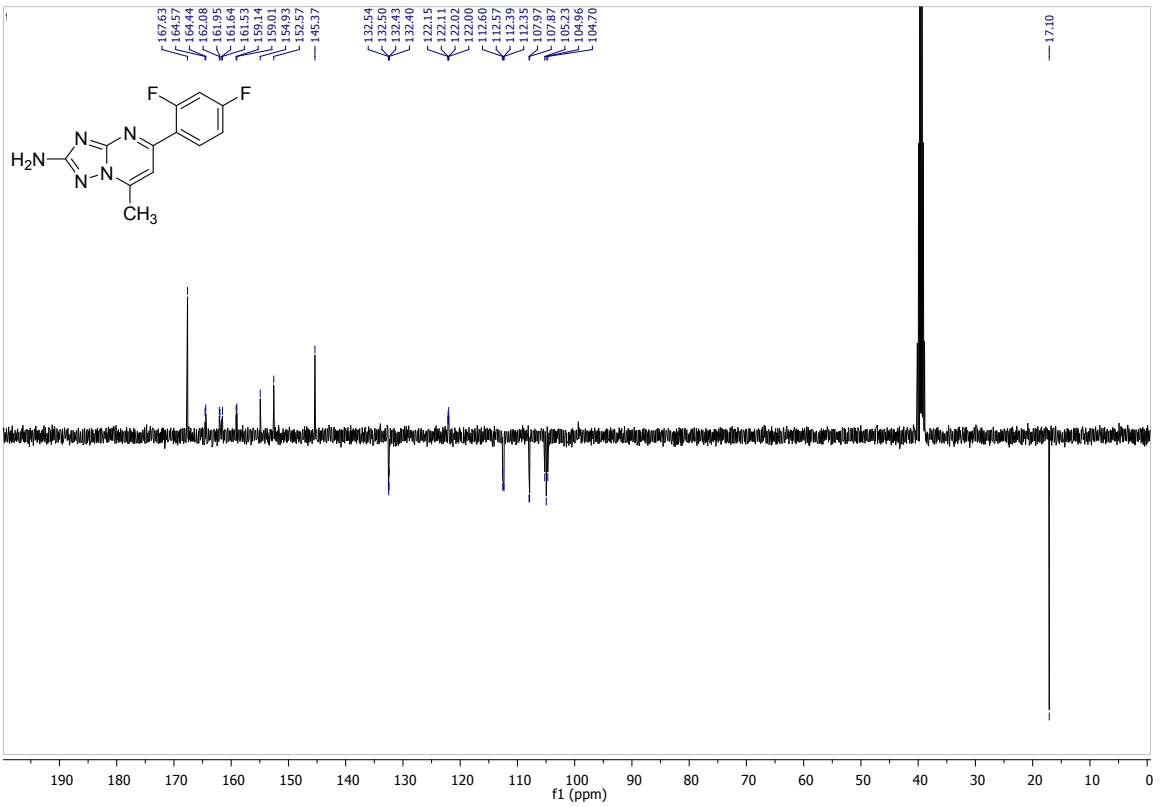

Figure S36. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **2h**.

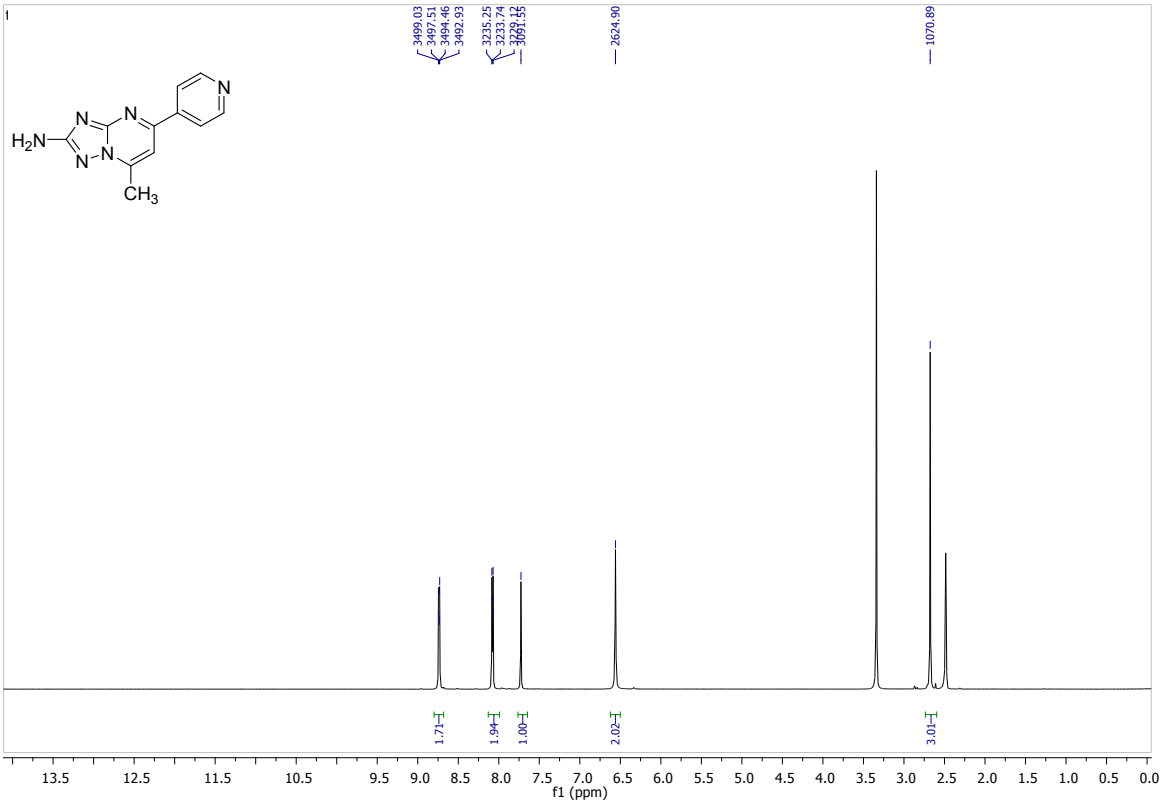

Figure S37. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **2i**.

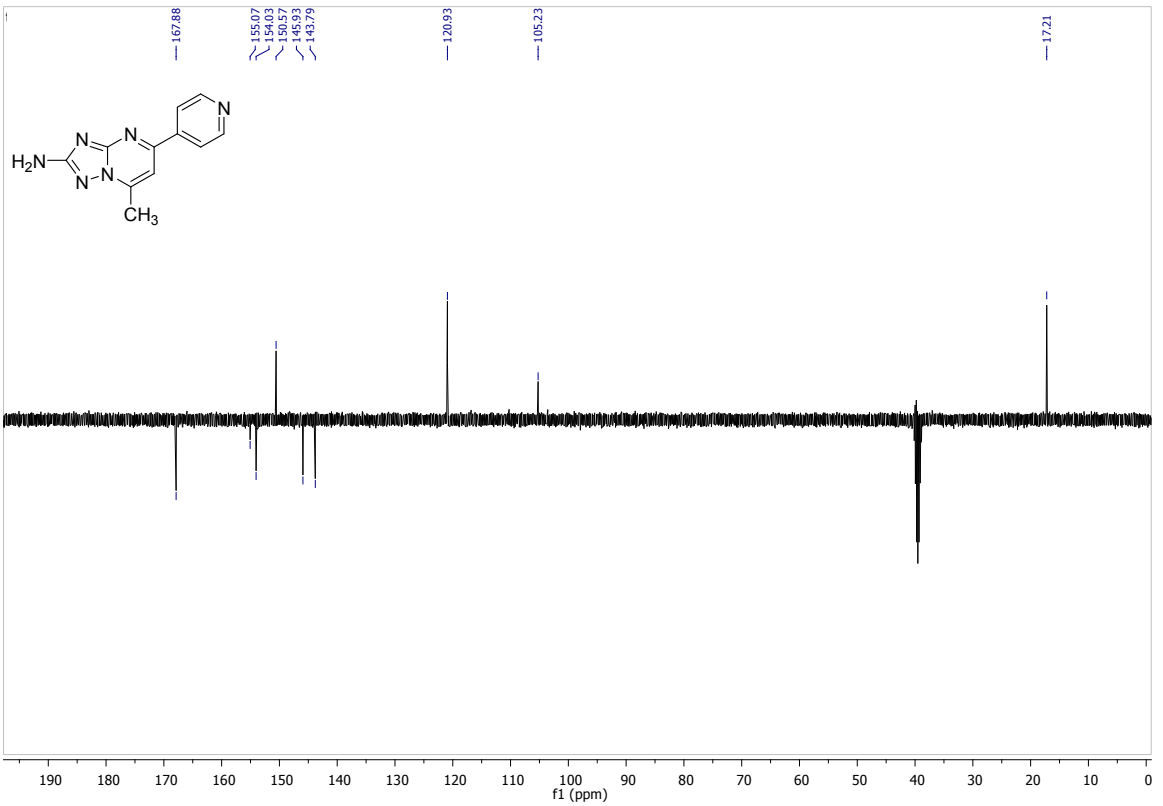

Figure S38. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **2i**.

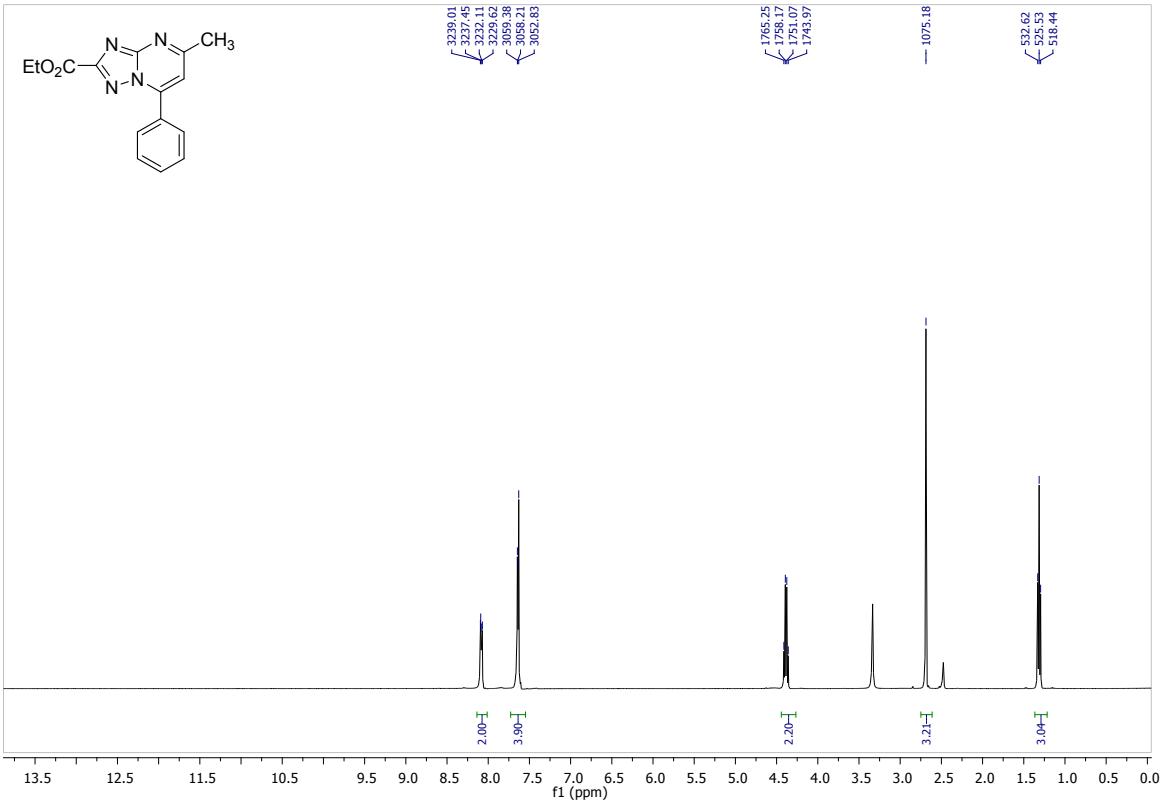

Figure S39. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **7a**.

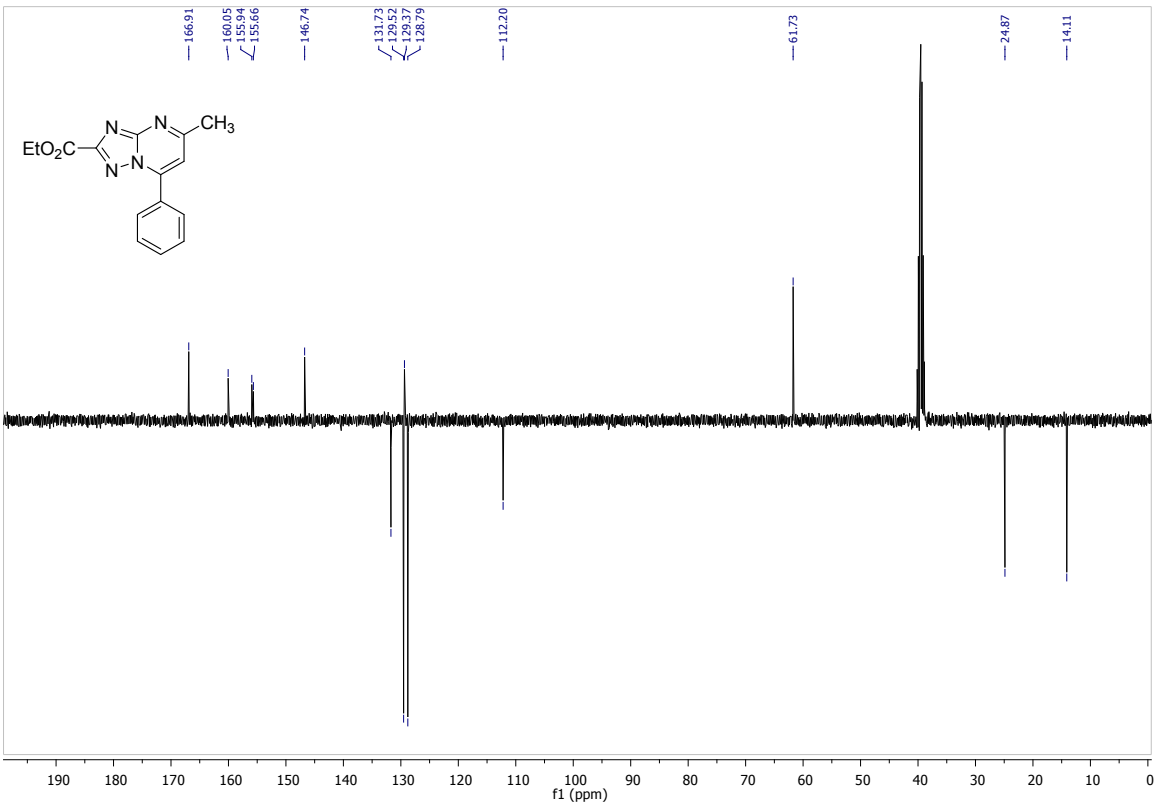

Figure S40. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **7a**.

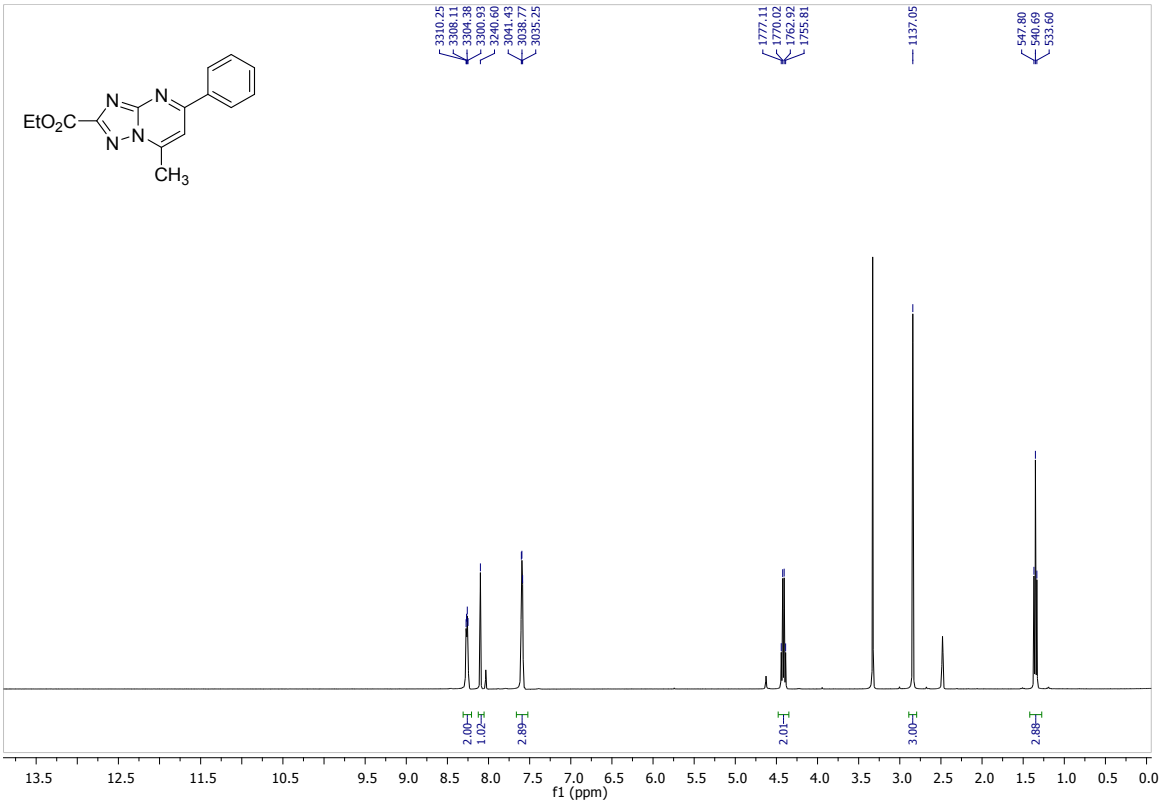

Figure S41. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **8a**.

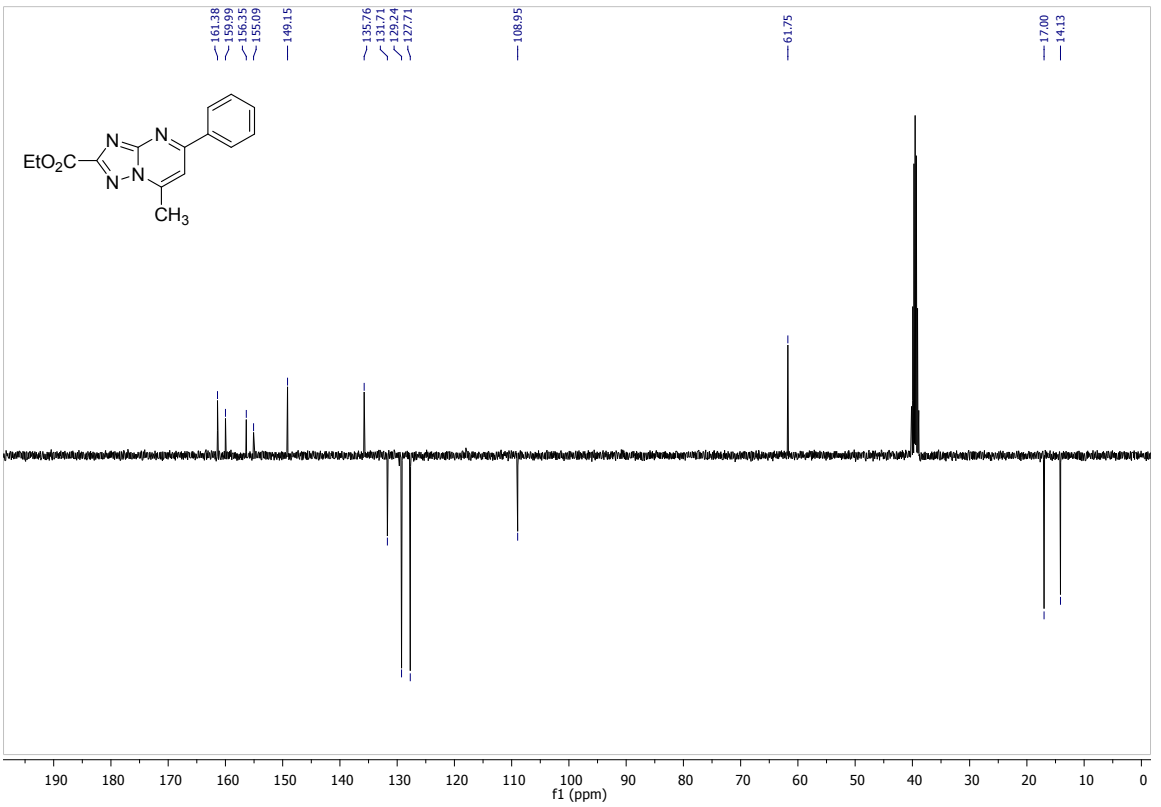

Figure S42. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **8a**.

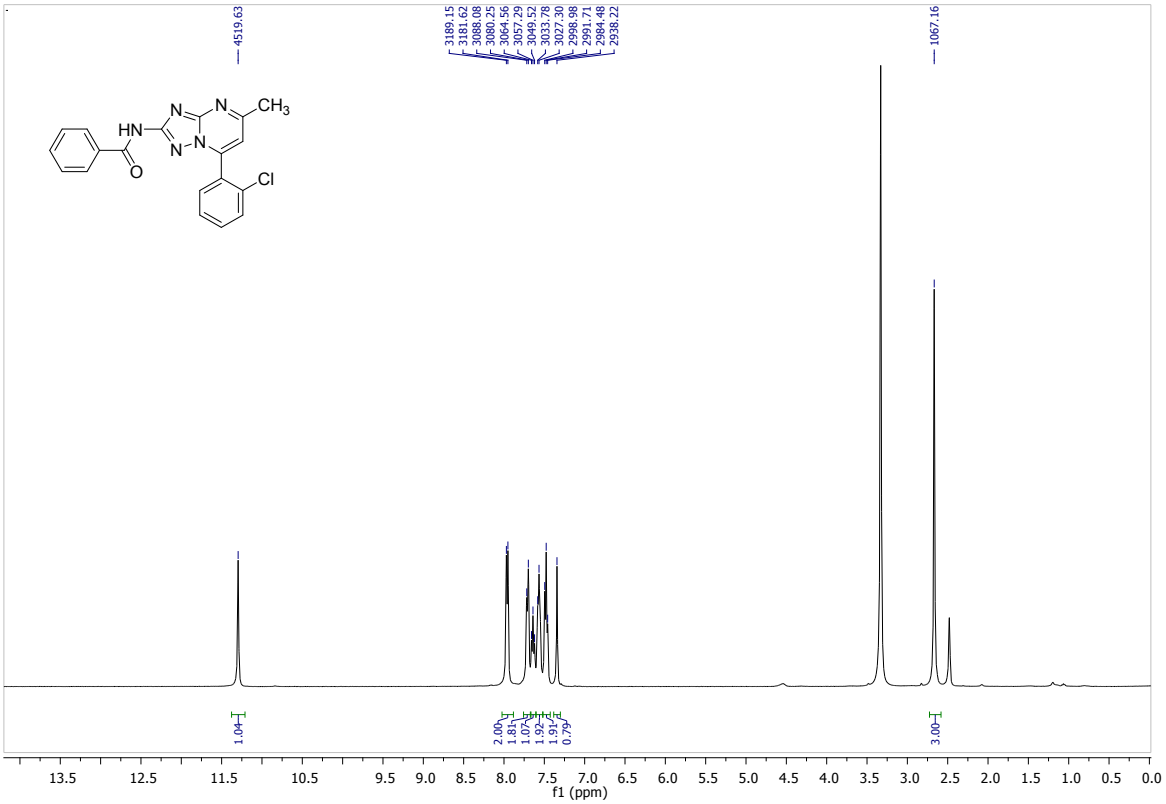

Figure S43. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **12**.

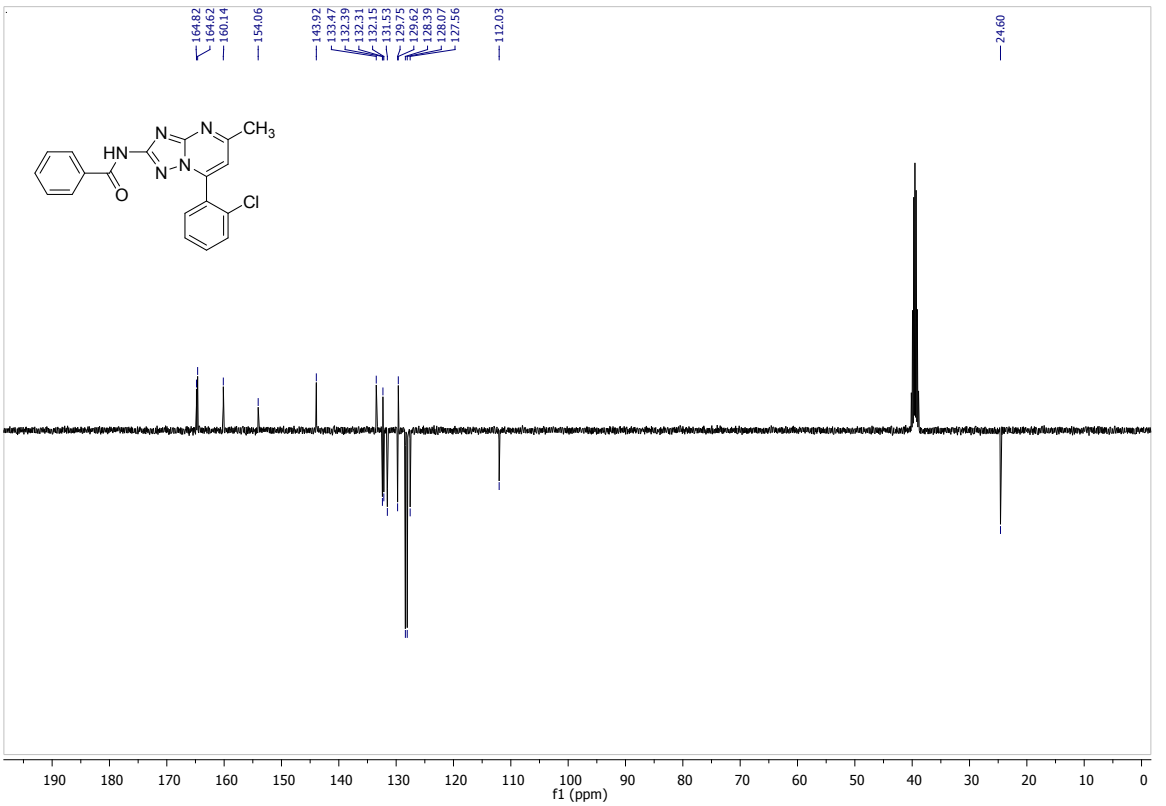

Figure S44. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **12**.

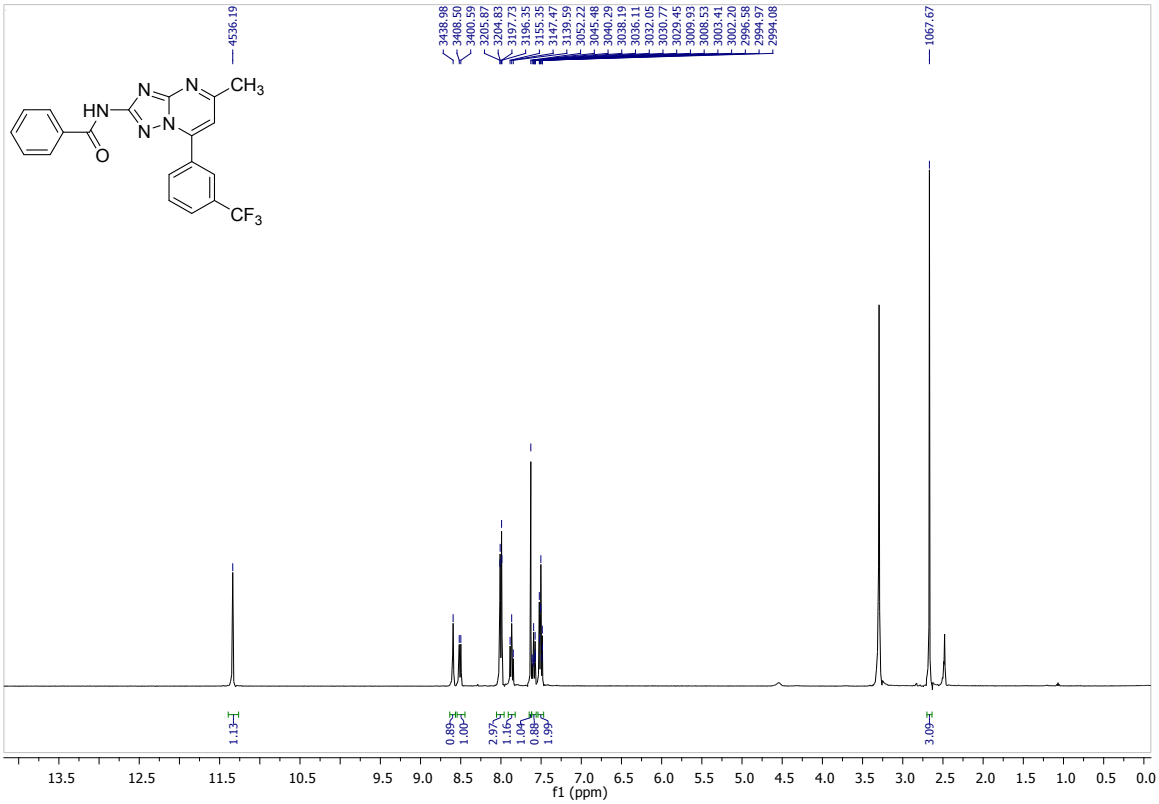

Figure S45. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **13**.

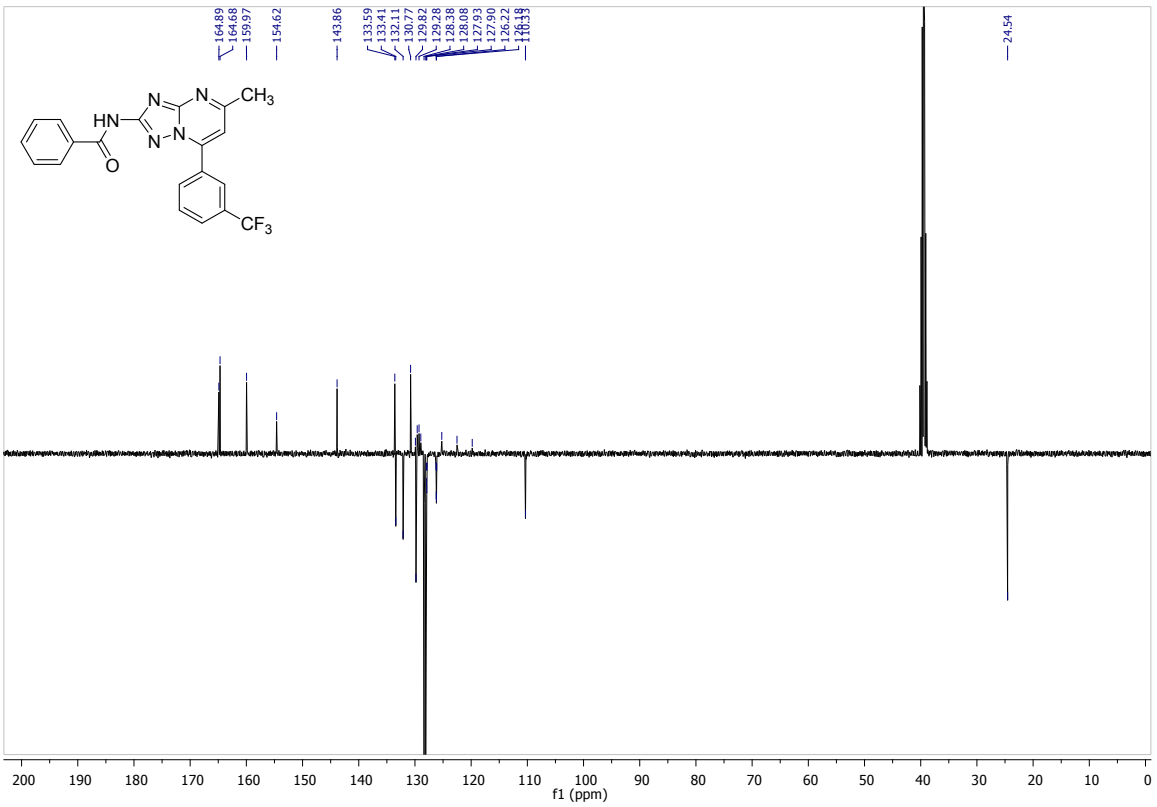

Figure S46. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **13**.

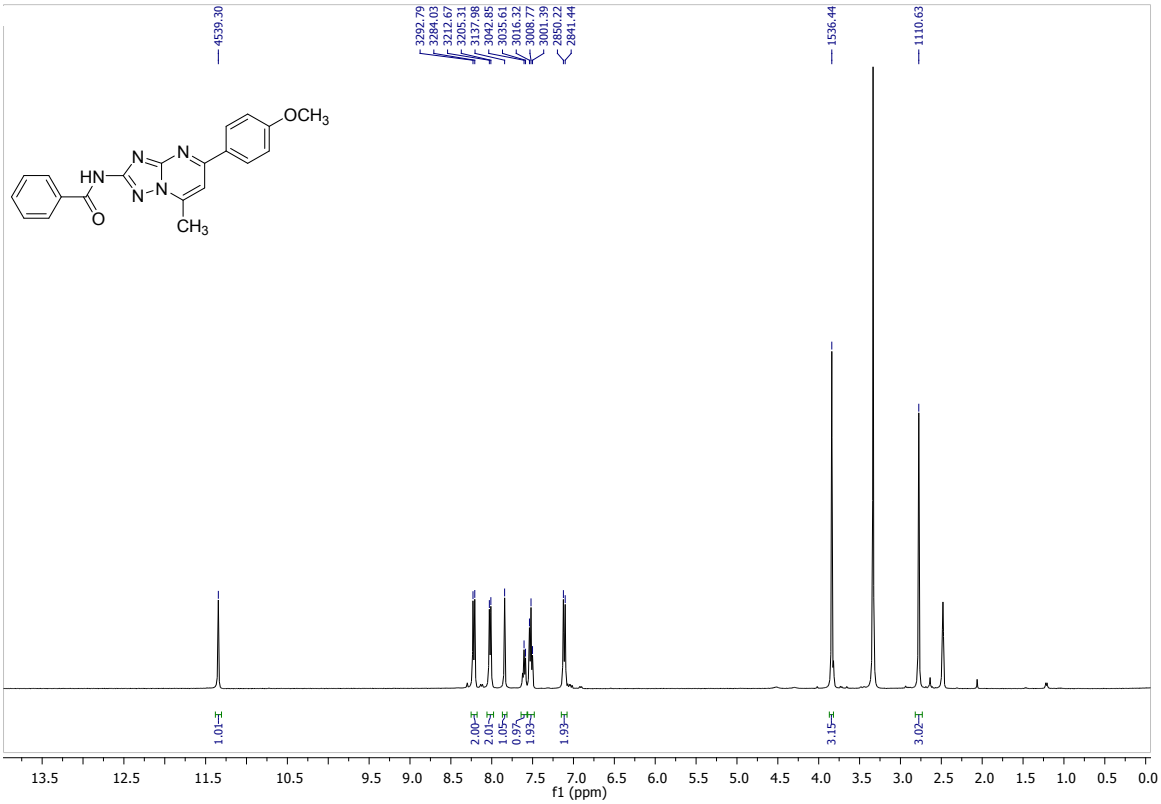

Figure S47. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **14**.

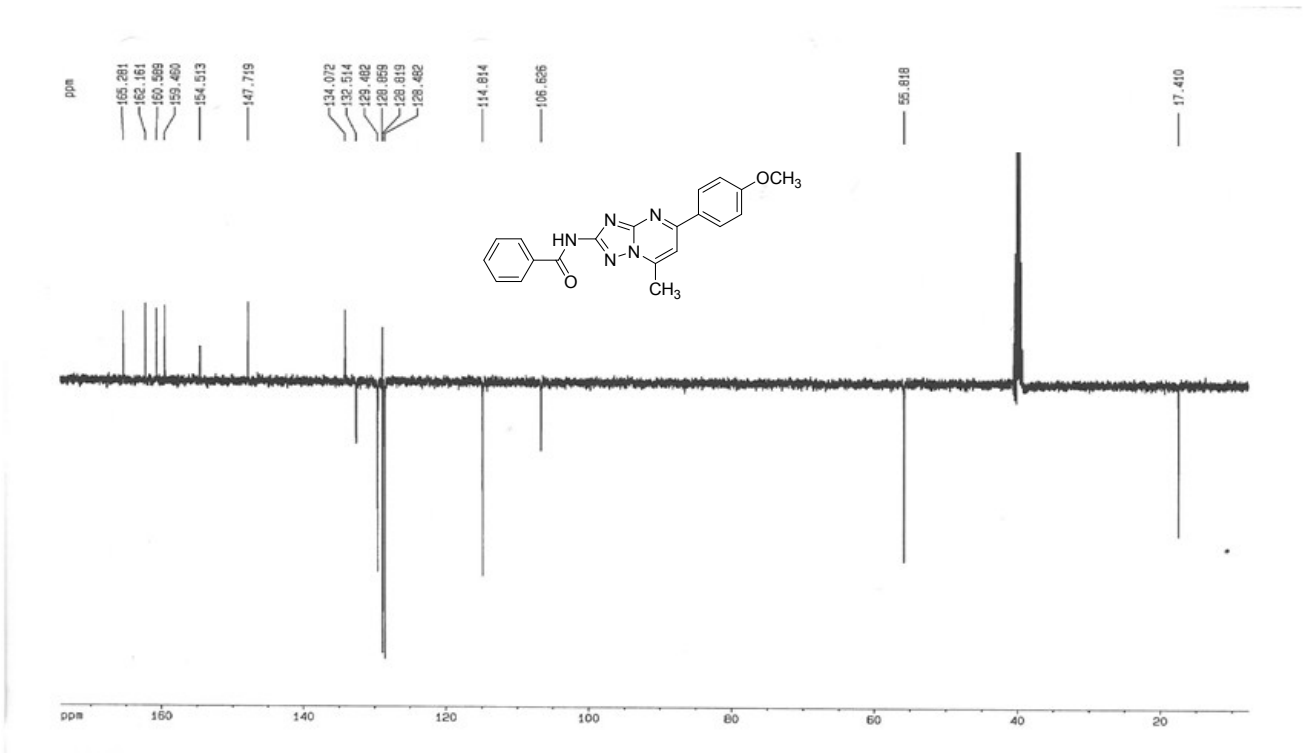

Figure S48. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **14**.

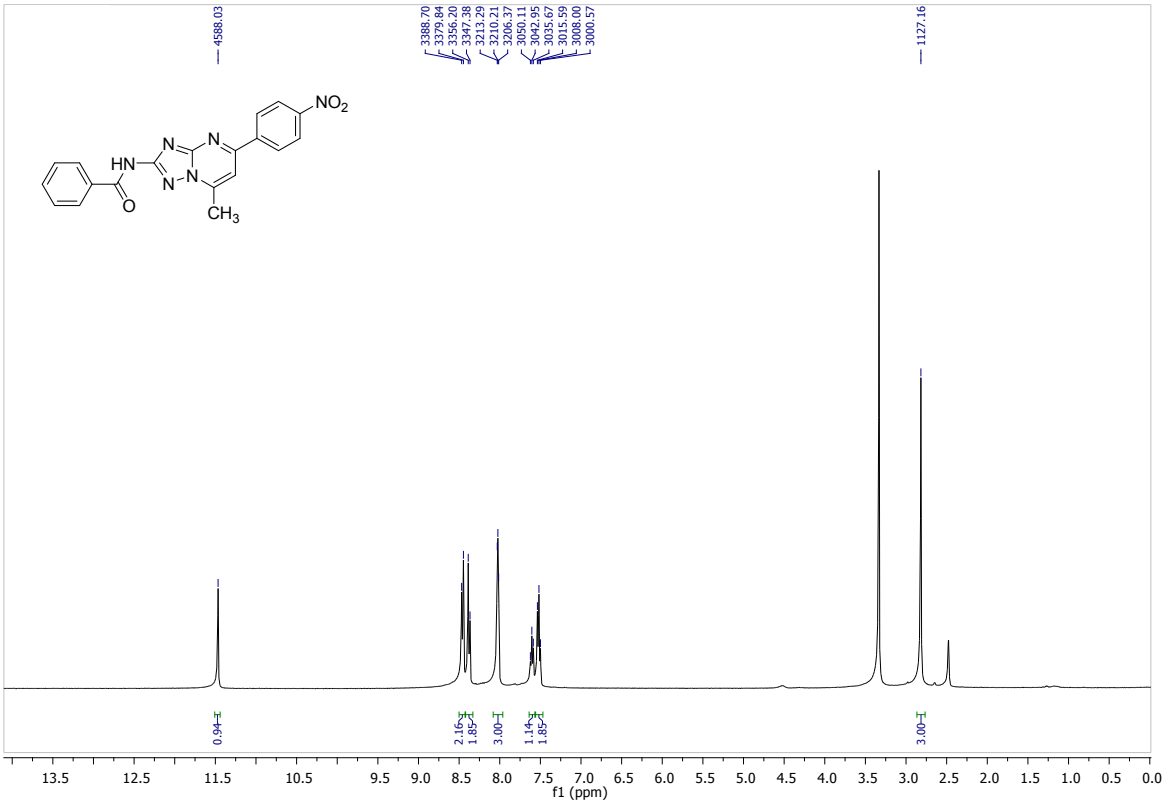

Figure S49. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **15**.

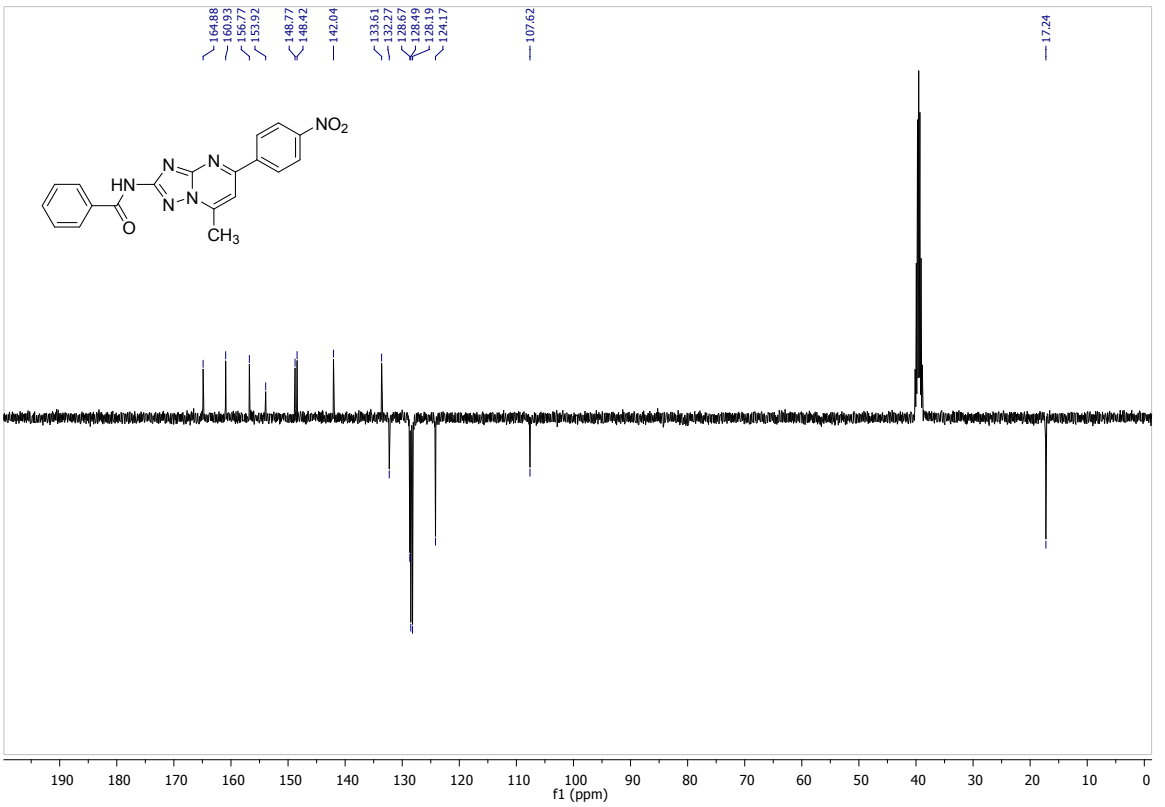

Figure S50. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **15**.

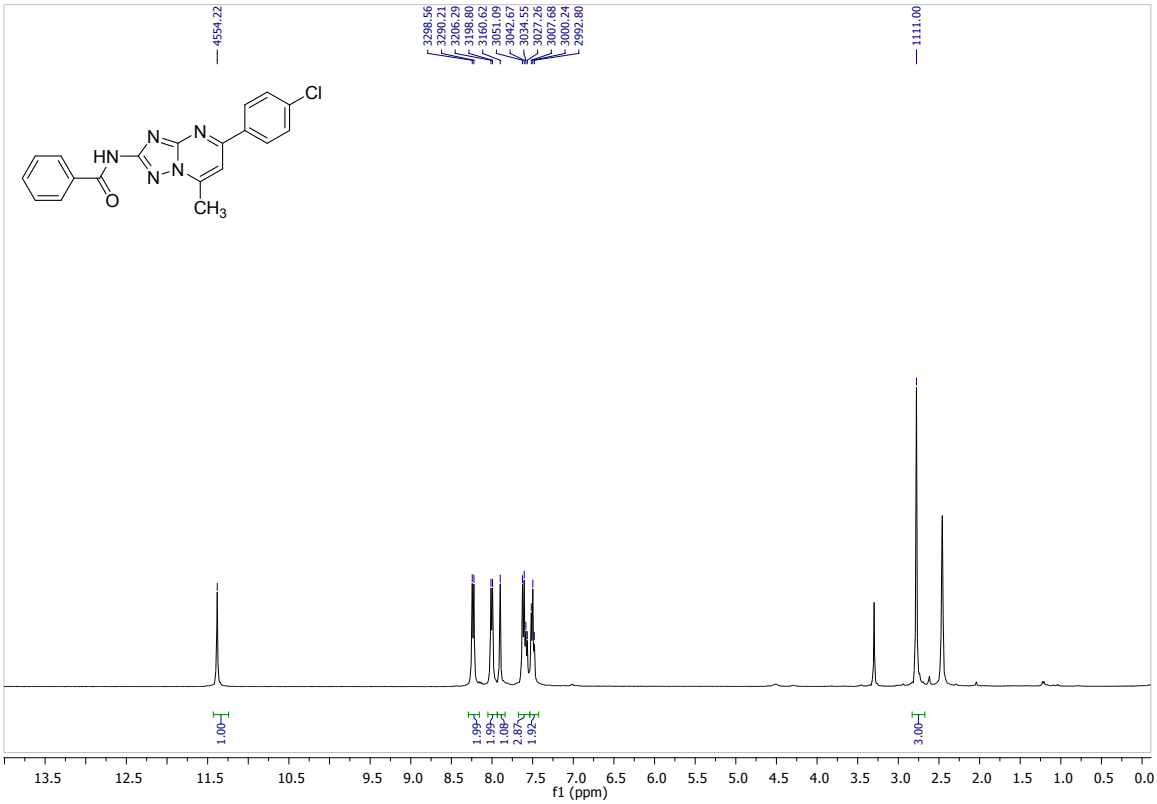

Figure S51. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **16**.

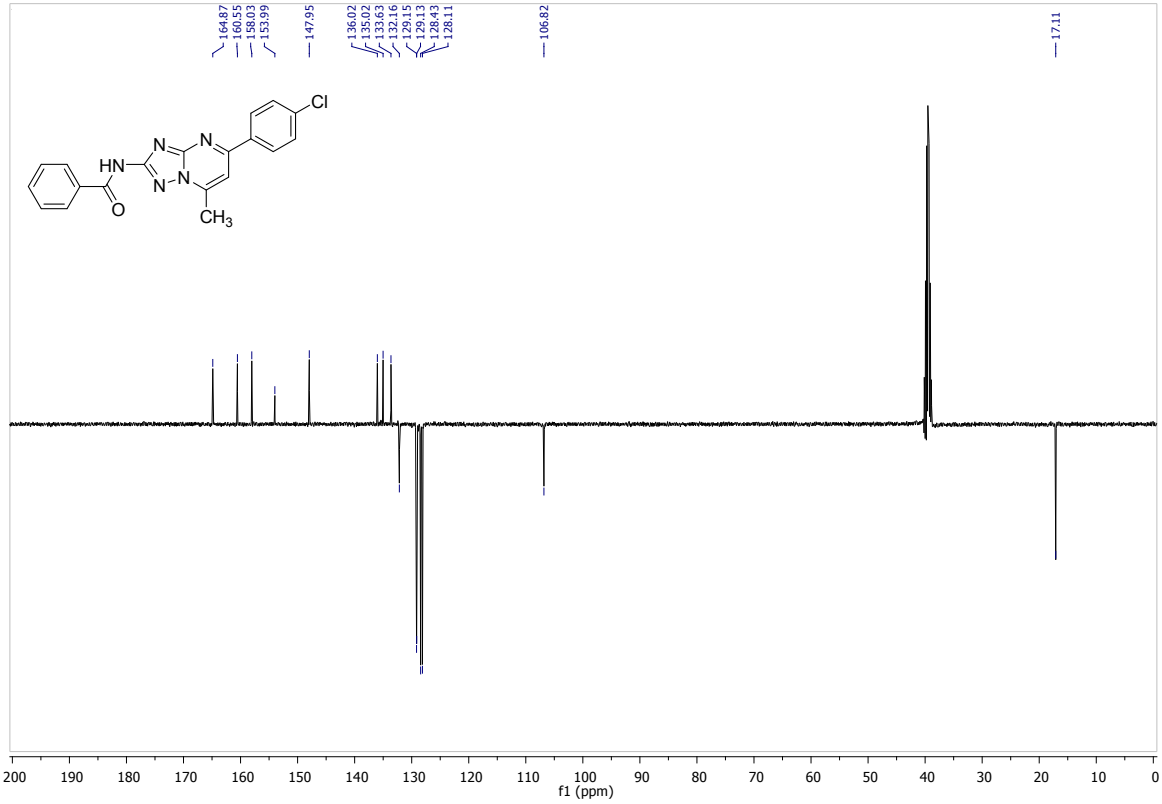

Figure S52. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **16**.

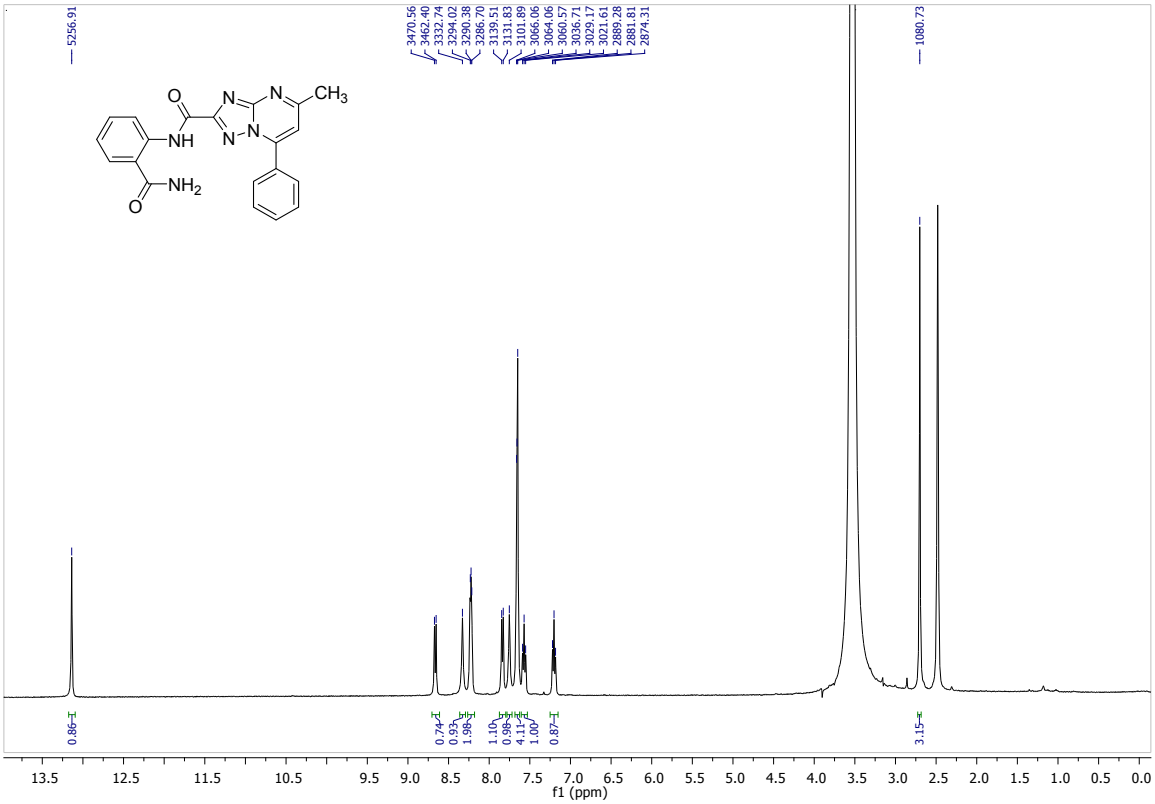

Figure S53. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **19**.

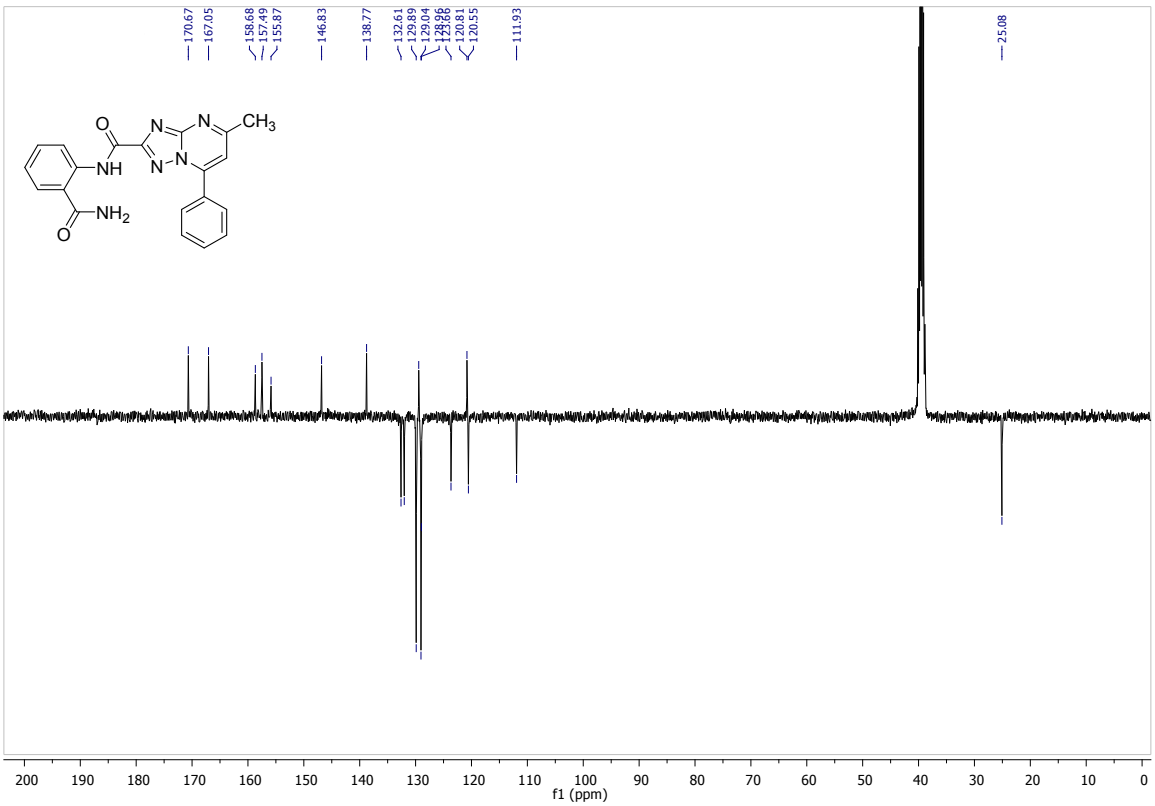

Figure S54. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **19**.

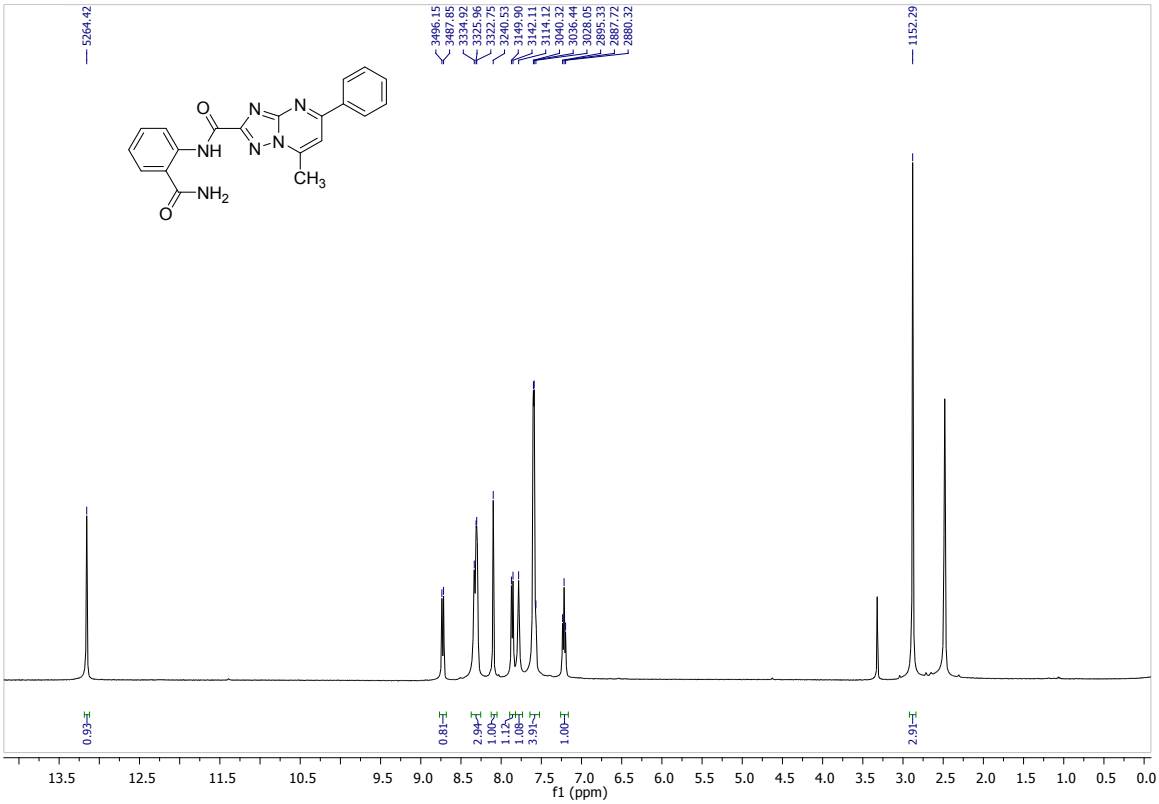

Figure S55. ^{1}H NMR (400 MHz, DMSO-d_6) spectrum of **20**.

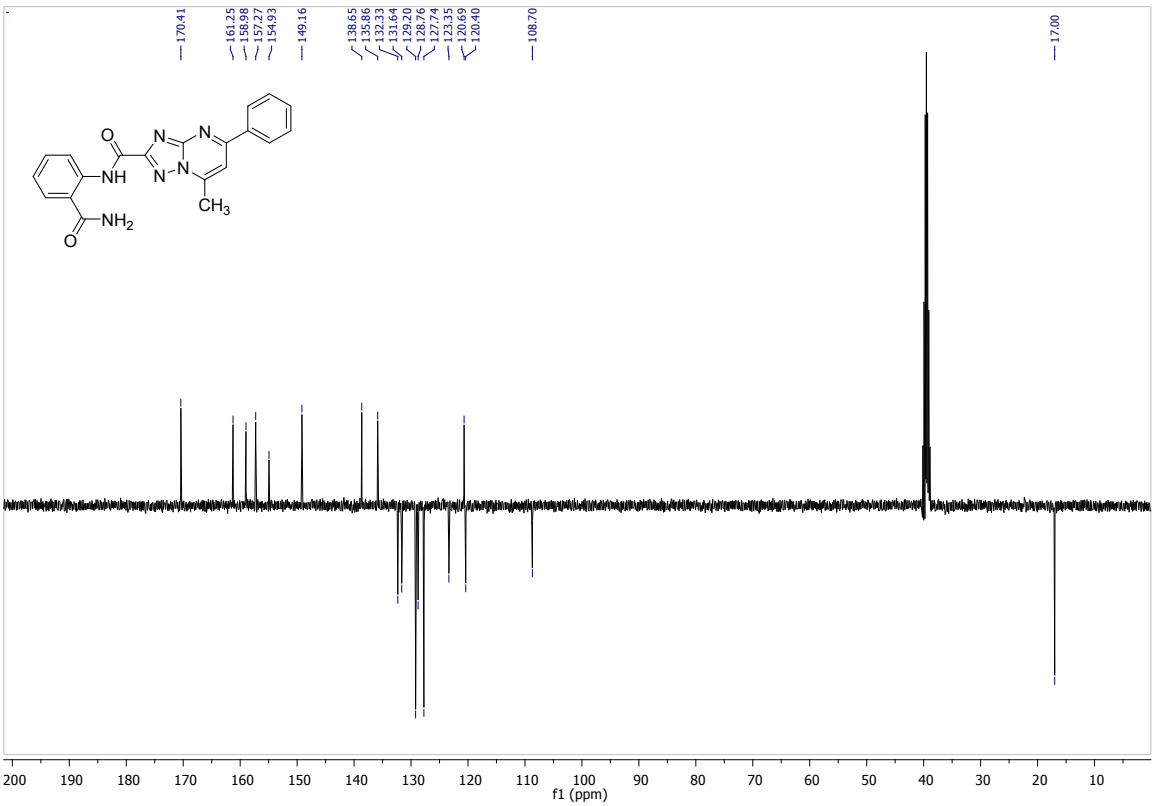

Figure S56. ^{13}C NMR (101 MHz, DMSO-d_6) spectrum of **20**.