

Supplementary Material

Transition-metal-free visible light-promoted photoredox oxidative dehydrogenative cyclization: expeditious approach to 1,2,4-thiadiazoles

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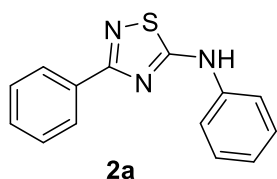
1. General information

Unless otherwise specified, all reagents and solvents were obtained from commercial suppliers and used without further purification. All products were isolated by short chromatography on a silica gel (200-300 mesh) column using petroleum ether (60-90°C) and ethyl acetate. ^1H NMR spectra were recorded on Bruker Advance DRX-400 spectrometers at ambient temperature with CDCl_3 or $\text{DMSO}-d_6$ as solvent and tetramethylsilane (TMS) as the internal standard. All chemical shift values are quoted in ppm and coupling constants quoted in Hz. Compounds for HRMS were analyzed by positive mode electrospray ionization (ESI) using Agilent 6530 QTOF mass spectrometer. All the prepared compounds **2a-x** are known compounds, their spectral data are in agreement with those reported in the literature¹⁻⁷.

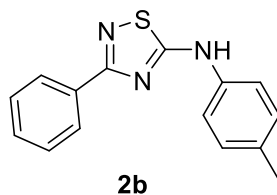
2. General procedure for 3,5-disubstituted 1,2,4-thiadiazoles **2**

In an oven-dried single-necked bottle (10 mL) equipped with a stir bar, amidine hydrochloride (0.2 mmol), isothiocyanate **2** (0.2 mmol), NEt_3 (0.4 mmol), and CH_3OH (2 mL) were added and stirred at room temperature until the conversion was completed as indicated by TLC. The resulted imidoyl thiourea **1** was obtained without the isolation. Then, rhodamine 6G (0.5 mol %) was added, the reaction mixture was open to the air and stirred at room temperature under the irradiation of a 18 W LED lamp for 8 h. After completion of the reaction, the resulting mixture was extracted with EtOAc and the organic phase was then removed under vacuum. The residue was purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give the desired products **2**.

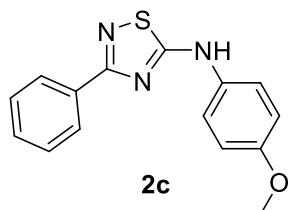
3. Characterization Data for products **2**



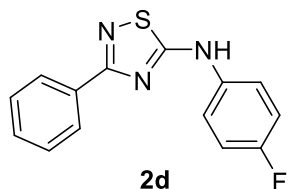
N,3-diphenyl-1,2,4-thiadiazol-5-amine¹ (2a). ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 11.08 (s, 1H), 8.20 (d, J = 7.8 Hz, 2H), 7.67 (d, J = 7.8 Hz, 2H), 7.52 (s, 3H), 7.45 (t, J = 8.0 Hz, 2H), 7.11 (t, J = 7.2 Hz, 1H).



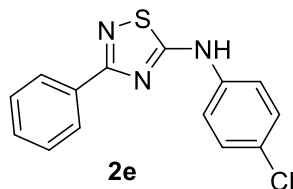
3-phenyl-N-(p-tolyl)-1,2,4-thiadiazol-5-amine¹ (2b). ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 10.96 (s, 1H), 8.18 (d, J = 7.6 Hz, 2H), 7.51 (d, J = 6.4 Hz, 5H), 7.23 (d, J = 8.0 Hz, 2H), 2.29 (s, 3H).



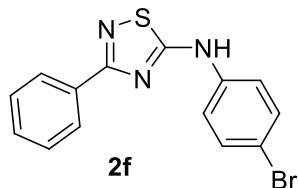
N-(4-methoxyphenyl)-3-phenyl-1,2,4-thiadiazol-5-amine¹ (2c). ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.87 (s, 1H), 8.21 (d, *J* = 7.8 Hz, 2H), 7.59 (d, *J* = 8.8 Hz, 2H), 7.52 (d, *J* = 7.2 Hz, 3H), 7.03 (d, *J* = 8.8 Hz, 2H), 3.78 (s, 3H).



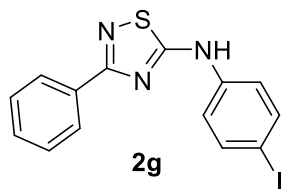
N-(4-fluorophenyl)-3-phenyl-1,2,4-thiadiazol-5-amine¹ (2d). ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.08 (s, 1H), 8.20 (d, *J* = 7.8 Hz, 2H), 7.67 (d, *J* = 7.8 Hz, 2H), 7.52 (s, 3H), 7.45 (t, *J* = 8.0 Hz, 2H), 7.11 (t, *J* = 7.2 Hz, 1H).



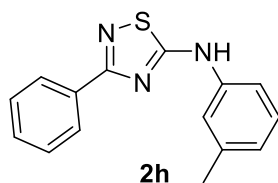
N-(4-chlorophenyl)-3-phenyl-1,2,4-thiadiazol-5-amine¹ (2e). ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.15 (s, 1H), 8.26 – 8.18 (m, 2H), 7.74 (d, *J* = 8.8 Hz, 2H), 7.53 (d, *J* = 6.0 Hz, 3H), 7.51 – 7.47 (m, 2H).



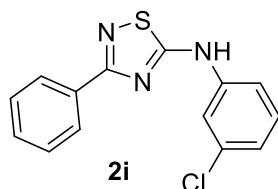
N-(4-bromophenyl)-3-phenyl-1,2,4-thiadiazol-5-amine² (2f). ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.14 (s, 1H), 8.26 – 8.15 (m, 2H), 7.71 – 7.65 (m, 2H), 7.61 (d, *J* = 8.8 Hz, 2H), 7.57 – 7.50 (m, 3H).



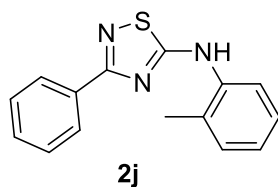
N-(4-iodophenyl)-3-phenyl-1,2,4-thiadiazol-5-amine¹ (2g). ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.12 (s, 1H), 8.19 (dd, *J* = 7.4, 2.4 Hz, 2H), 7.85 – 7.69 (m, 2H), 7.66 – 7.42 (m, 5H).



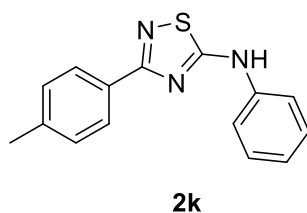
3-phenyl-N-(o-tolyl)-1,2,4-thiadiazol-5-amine¹ (2h). ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.02 (s, 1H), 8.20 (d, *J* = 6.0 Hz, 2H), 7.53 (d, *J* = 7.0 Hz, 4H), 7.40 (s, 1H), 7.33 (t, *J* = 7.8 Hz, 1H), 6.93 (d, *J* = 7.4 Hz, 1H), 2.36 (s, 3H).



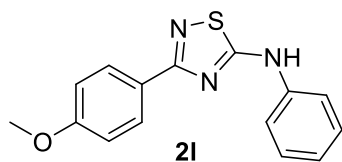
3-(4-chlorophenyl)-N-phenyl-1,2,4-thiadiazol-5-amine³ (2i). ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.22 (s, 1H), 8.20 (d, *J* = 6.0 Hz, 2H), 7.88 (s, 1H), 7.59 (d, *J* = 8.2 Hz, 1H), 7.54 (d, *J* = 7.0 Hz, 3H), 7.46 (t, *J* = 8.2 Hz, 1H), 7.16 (d, *J* = 8.6 Hz, 1H).



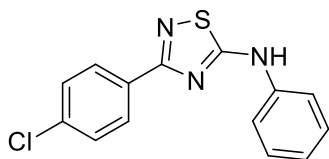
3-phenyl-N-(m-tolyl)-1,2,4-thiadiazol-5-amine¹ (2j). ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.26 (s, 1H), 8.17 (d, *J* = 7.6 Hz, 2H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 6.8 Hz, 3H), 7.32 (t, *J* = 8.2 Hz, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 2.34 (s, 3H).



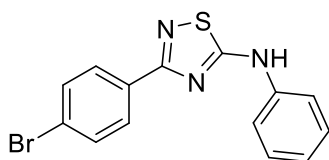
N-phenyl-3-(p-tolyl)-1,2,4-thiadiazol-5-amine⁴ (2k). ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.03 (s, 1H), 8.08 (d, *J* = 8.0 Hz, 2H), 7.65 (d, *J* = 7.8 Hz, 2H), 7.43 (t, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.09 (t, *J* = 7.2 Hz, 1H), 2.36 (s, 3H).



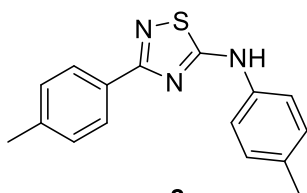
3-(4-methoxyphenyl)-N-phenyl-1,2,4-thiadiazol-5-amine⁵ (2l). ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.03 (s, 1H), 8.14 (d, *J* = 8.6 Hz, 2H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.11 (d, *J* = 7.4 Hz, 1H), 7.07 (d, *J* = 8.6 Hz, 2H), 3.84 (s, 3H).

**2m**

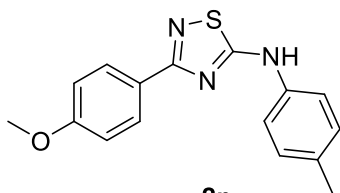
3-(4-chlorophenyl)-N-phenyl-1,2,4-thiadiazol-5-amine⁵ (2m). ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.07 (s, 1H), 8.18 (d, *J* = 8.4 Hz, 2H), 7.65 (d, *J* = 7.8 Hz, 2H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.44 (t, *J* = 8.0 Hz, 2H), 7.11 (t, *J* = 7.2 Hz, 1H).

**2n**

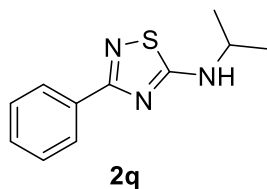
3-(4-bromophenyl)-N-phenyl-1,2,4-thiadiazol-5-amine⁵ (2n). ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.08 (s, 1H), 8.11 (d, *J* = 8.4 Hz, 2H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.65 (d, *J* = 8.0 Hz, 2H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.11 (t, *J* = 7.2 Hz, 1H).

**2o**

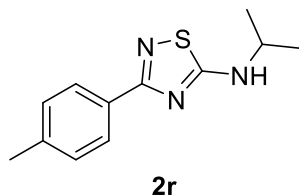
N,3-di-p-tolyl-1,2,4-thiadiazol-5-amine³ (2o). ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.33 (s, 1H), 7.95 (d, *J* = 8.0 Hz, 2H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 8.2 Hz, 2H), 2.37 (s, 3H), 2.24 (s, 3H).

**2p**

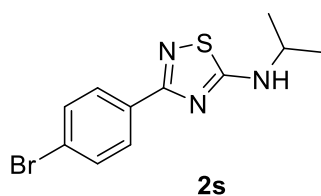
3-(4-methoxyphenyl)-N-(p-tolyl)-1,2,4-thiadiazol-5-amine⁴ (2p). ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.29 (s, 1H), 8.09 – 7.97 (m, 2H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.10 – 6.97 (m, 4H), 3.83 (s, 3H), 2.23 (s, 3H).



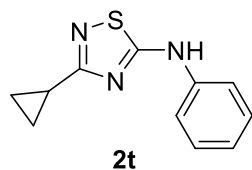
N-isopropyl-3-phenyl-1,2,4-thiadiazol-5-amine⁶ (2q). ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.47 (s, 1H), 8.09 (dd, *J* = 6.8, 2.4 Hz, 2H), 7.54 – 7.40 (m, 3H), 3.82 (br, 1H), 1.25 (d, *J* = 6.4 Hz, 6H).



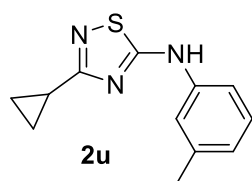
N-isopropyl-3-(p-tolyl)-1,2,4-thiadiazol-5-amine⁴ (2r). ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.46 (s, 1H), 7.98 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 3.82 (br, 1H), 2.35 (s, 3H), 1.24 (d, *J* = 6.4 Hz, 6H).



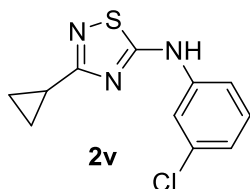
3-(4-bromophenyl)-N-isopropyl-1,2,4-thiadiazol-5-amine⁶ (2s). ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.53 (s, 1H), 8.03 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 2H), 3.84 (br, 1H), 1.26 (d, *J* = 6.4 Hz, 6H).



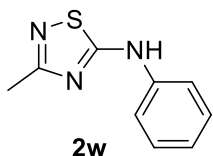
3-cyclopropyl-N-phenyl-1,2,4-thiadiazol-5-amine⁷ (2t). ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.87 (s, 1H), 7.49 (d, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 8.0 Hz, 2H), 7.06 (t, *J* = 7.2 Hz, 1H), 2.19 – 2.05 (m, 1H), 0.98 (d, *J* = 5.6 Hz, 4H).



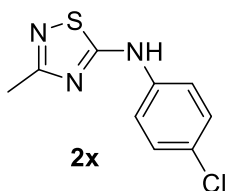
3-cyclopropyl-N-(m-tolyl)-1,2,4-thiadiazol-5-amine^[7] (2u). ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.82 (s, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.25 (d, *J* = 7.6 Hz, 2H), 6.86 (d, *J* = 7.0 Hz, 1H), 2.29 (s, 3H), 2.15 – 2.02 (m, 1H), 0.96 (d, *J* = 5.6 Hz, 4H).



N-(3-chlorophenyl)-3-cyclopropyl-1,2,4-thiadiazol-5-amine⁷ (2v). ¹H NMR (400 MHz, DMSO-*d*₆) δ 11.02 (s, 1H), 7.74 (d, *J* = 2.4 Hz, 1H), 7.40 (dd, *J* = 4.7, 1.8 Hz, 2H), 7.09 (dt, *J* = 5.0, 2.4 Hz, 1H), 2.14 (p, *J* = 6.6 Hz, 1H), 1.00 (d, *J* = 7.0 Hz, 4H).



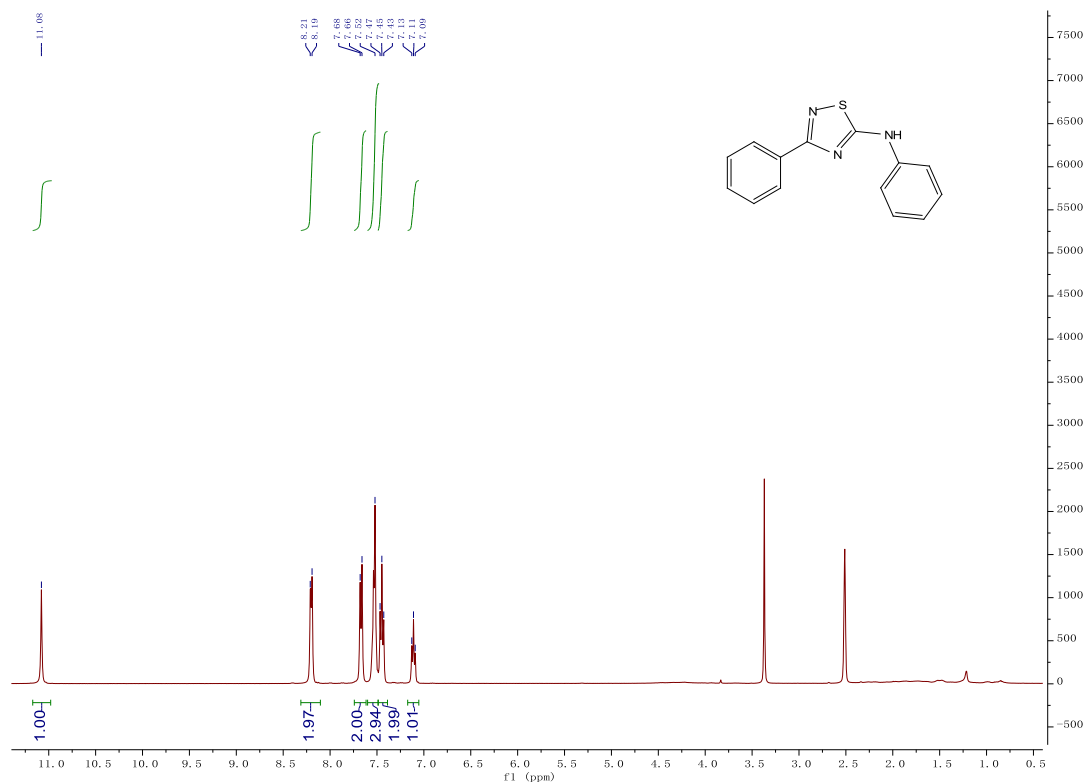
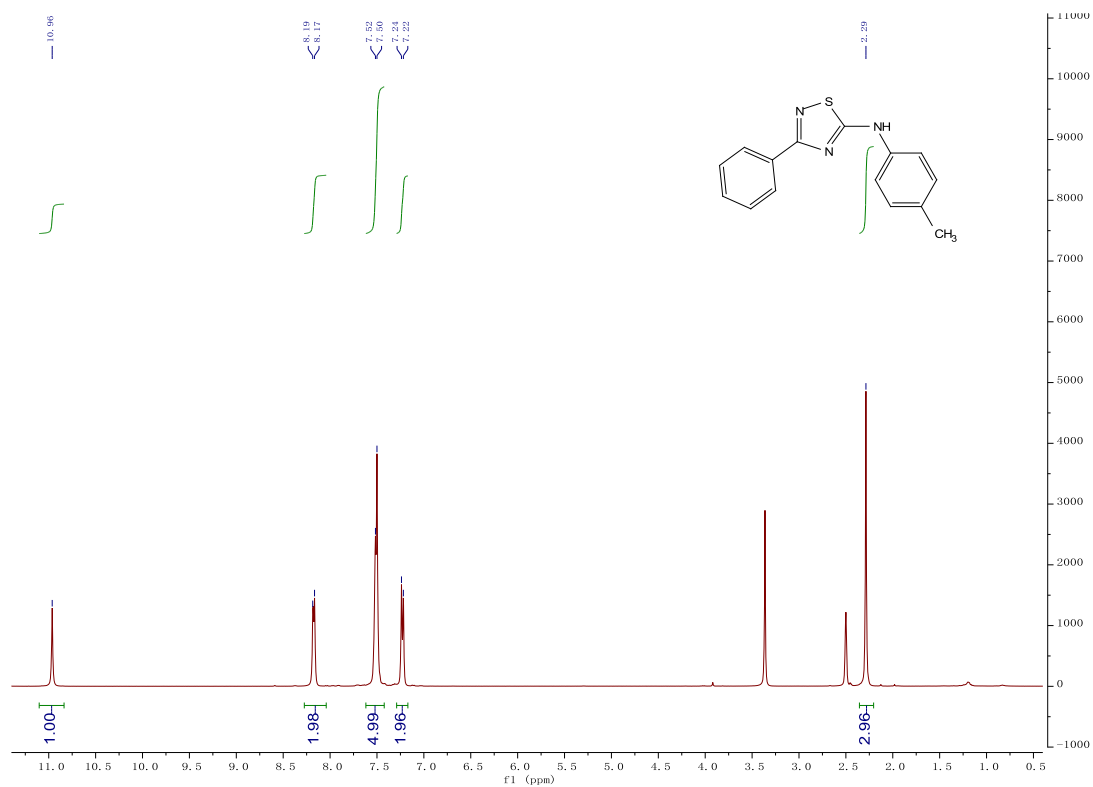
3-methyl-N-phenyl-1,2,4-thiadiazol-5-amine(2w)⁸. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.87 (s, 1H), 7.55 (d, *J* = 7.6 Hz, 2H), 7.39 (t, *J* = 8.0 Hz, 2H), 7.06 (t, *J* = 7.4 Hz, 1H), 2.40 (s, 3H).

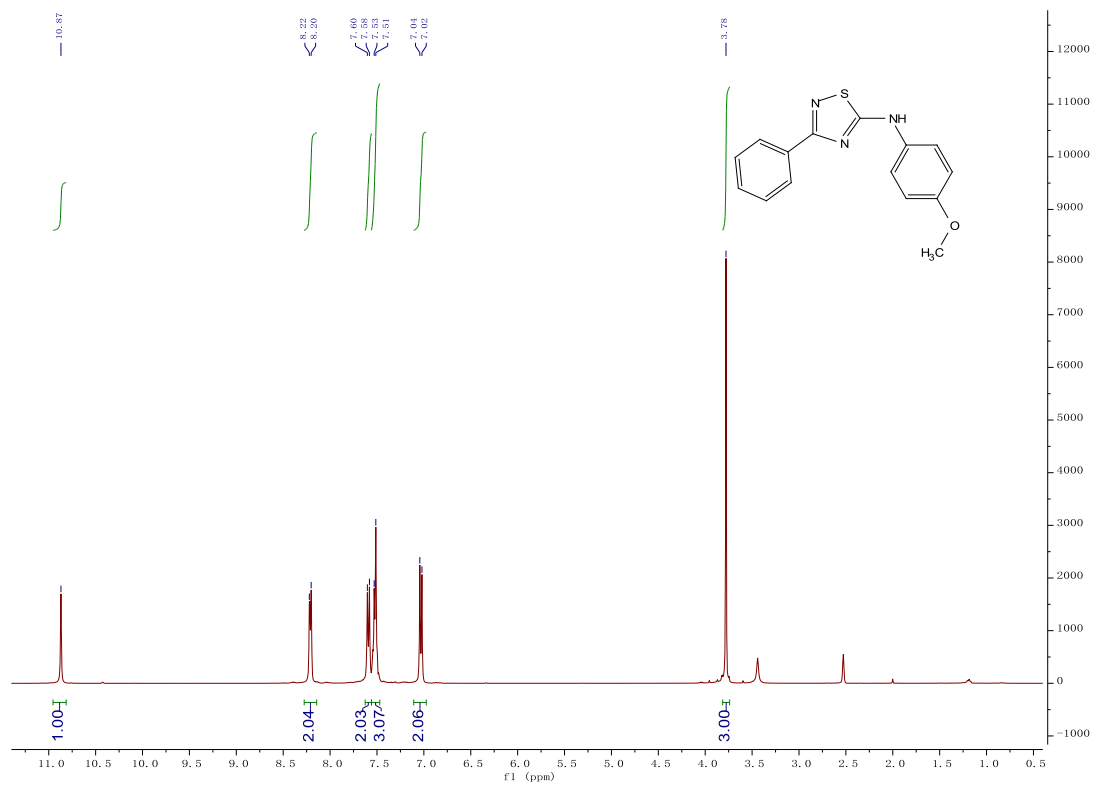
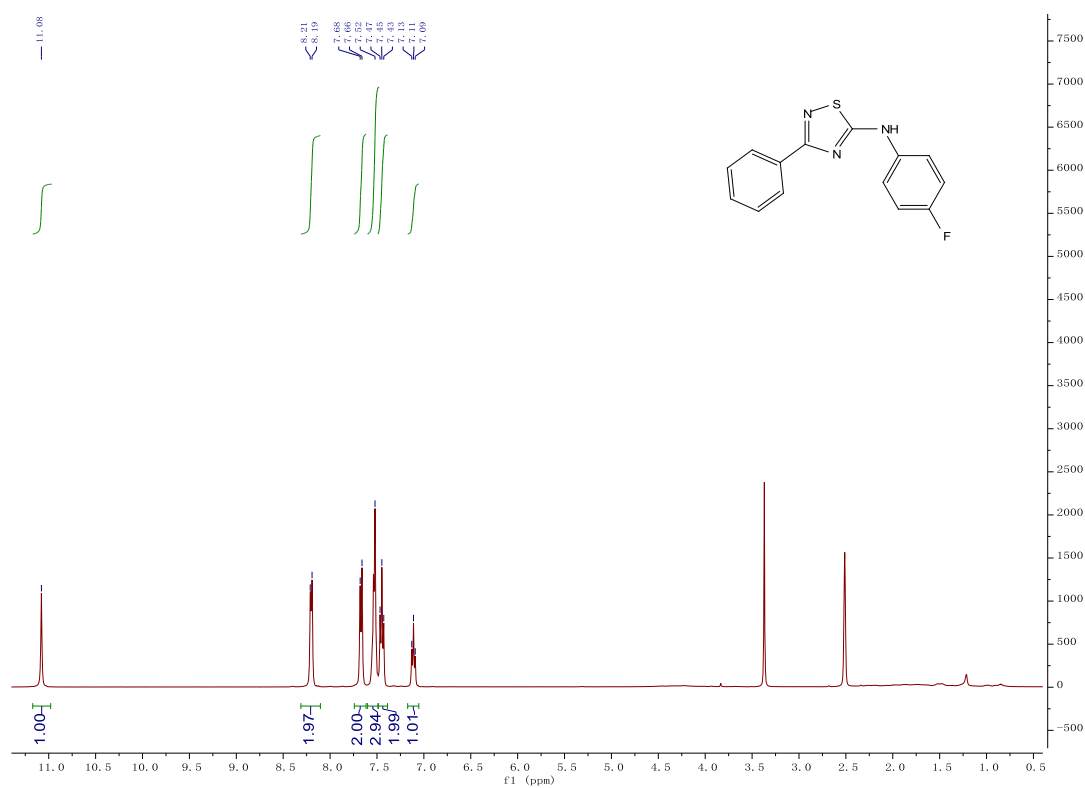


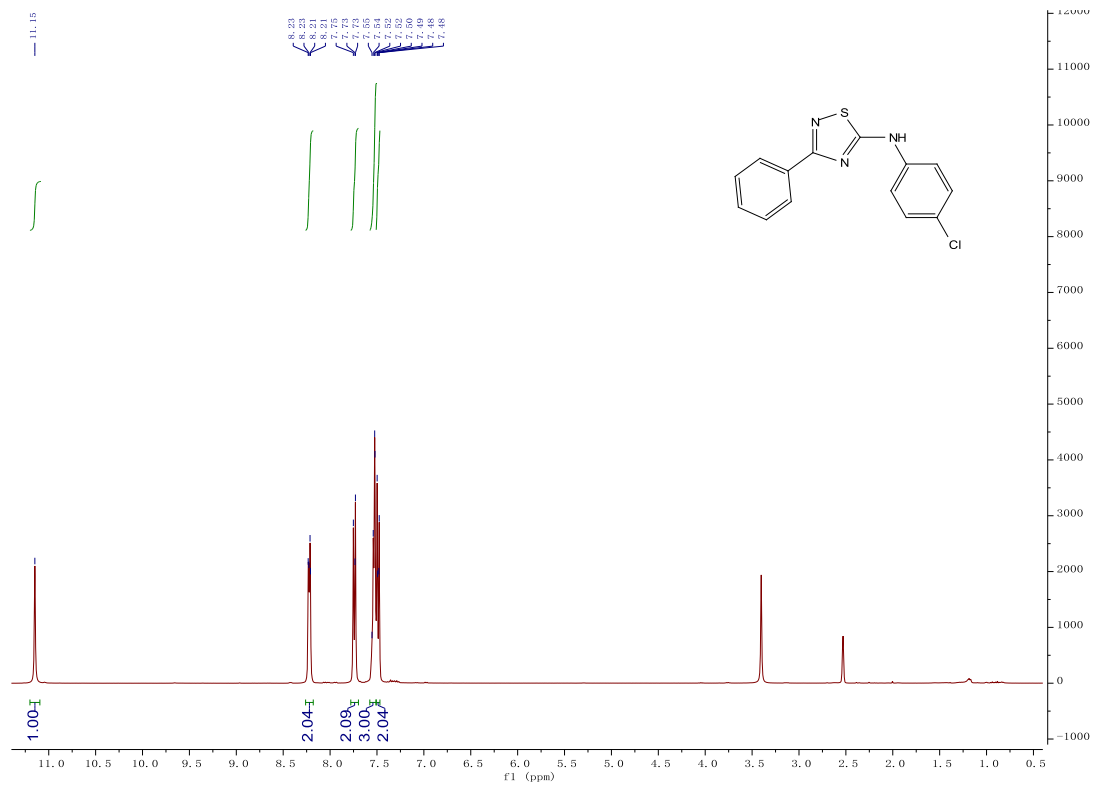
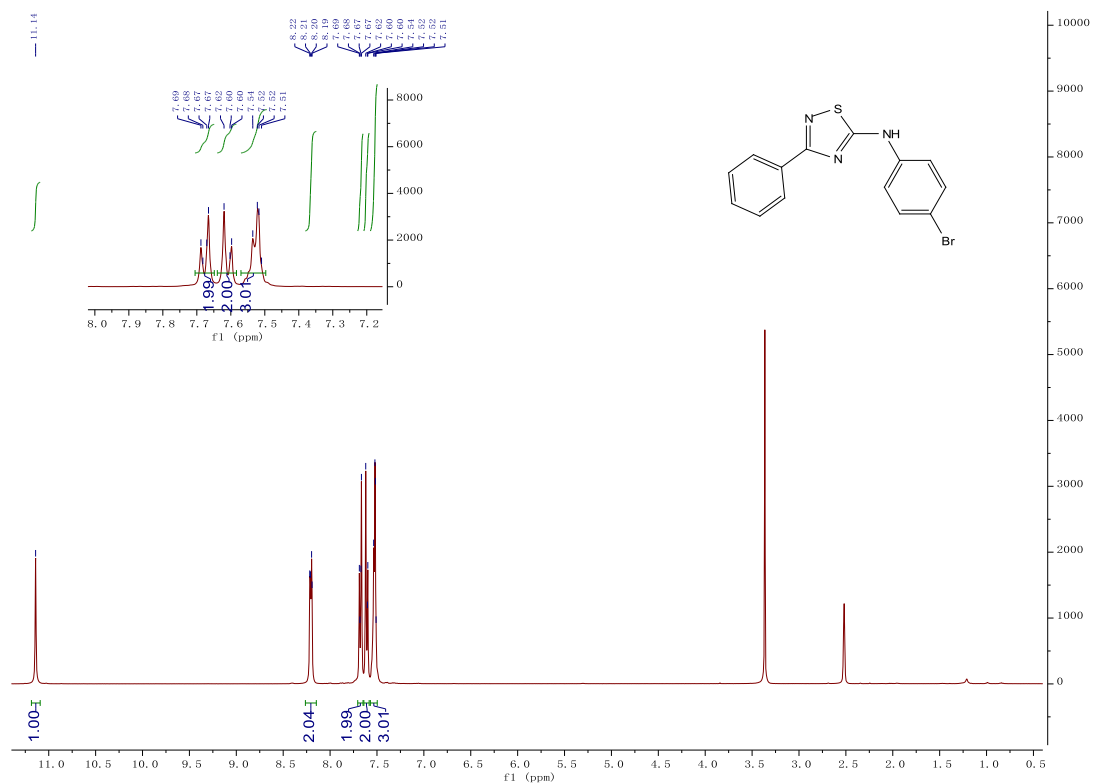
N-(4-chlorophenyl)-3-methyl-1,2,4-thiadiazol-5-amine(2x)⁹. ¹H NMR (400 MHz, DMSO-*d*₆) δ 10.96 (s, 1H), 7.60 (d, *J* = 8.9 Hz, 2H), 7.42 (d, *J* = 8.9 Hz, 2H), 2.40 (s, 3H).

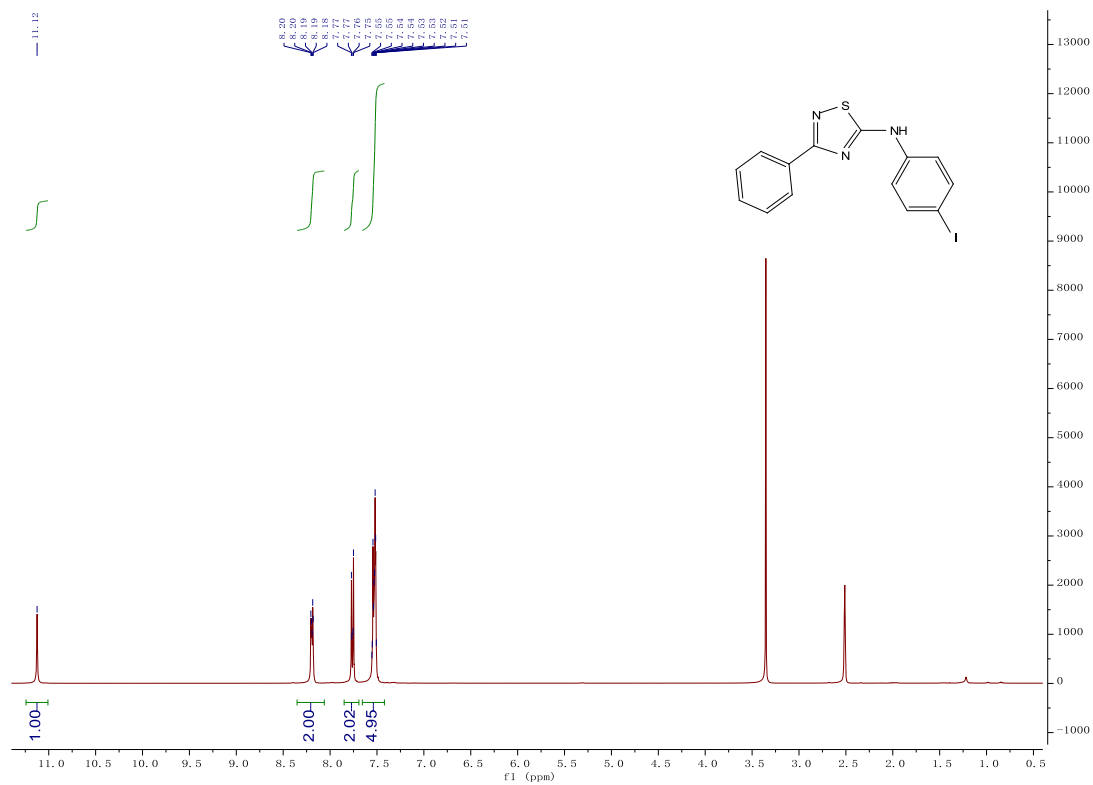
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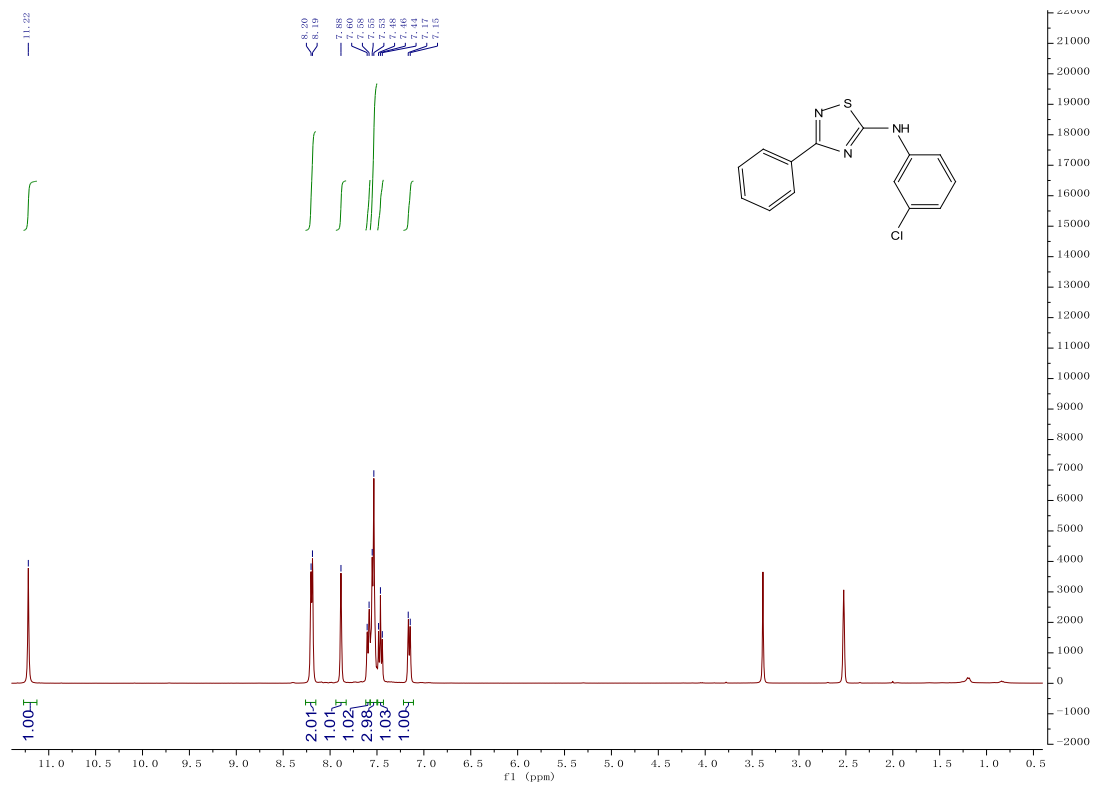
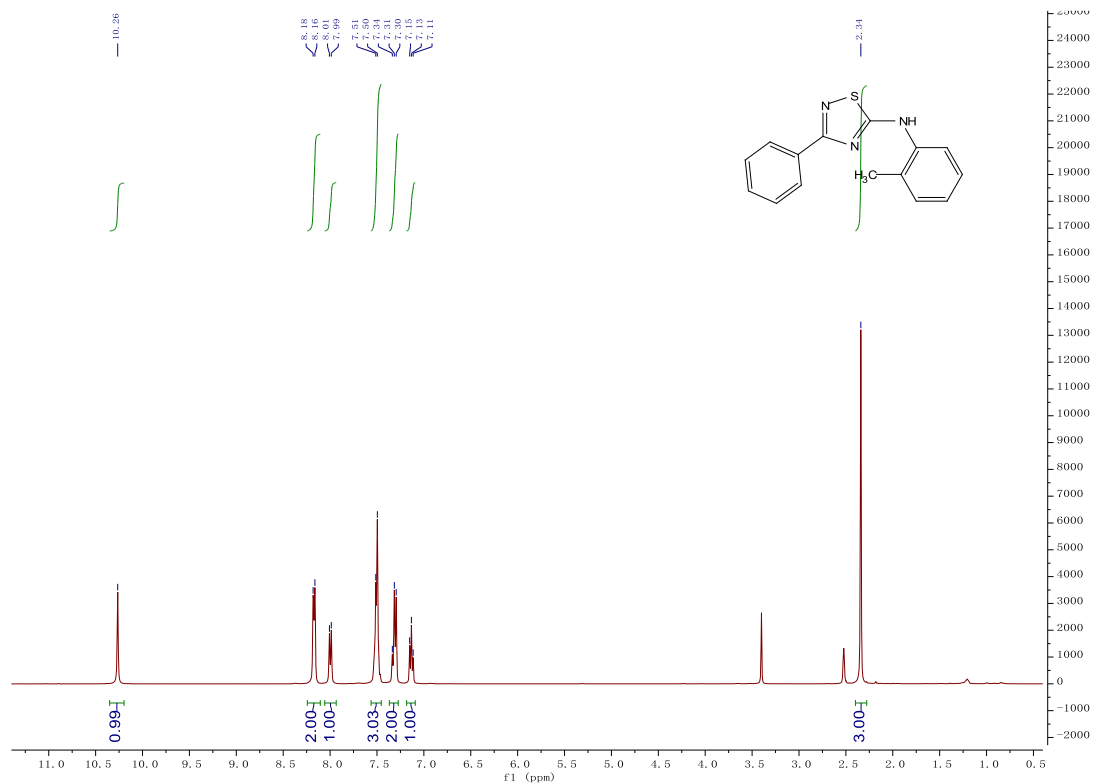
1. A. Mariappan, K. Rajaguru, N. M. Chola, Muthusubramanian, S. N. Bhuvanesh, *J. Org. Chem.* **2016**, *81*, 6573.
2. N. Jatangi, N. Tumula, K. P. Radha, M. Nakka, *J. Org. Chem.* **2018**, *83*, 5715.
3. Z. Yang, T. Cao, S. Liu, A. Li, K. Liu, T. Yang, C. Zhou, *New J. Chem.* **2019**, *43*, 6465.
4. B. Wang, Y. Meng, Y. Zhou, L. Ren, J. Wu, W. Yu, J. Chang, *J. Org. Chem.* **2017**, *82*, 5898.
5. L. Chai, Z. Lai, Q. Xia, J. Yuan, Q. Bian, M. Yu, W. Zhang, Y. Xu, H. Xu, *J. Org. Chem.* **2018**, 4338.
6. W. Yu, Y. Huang, J. Li, X. Tang, W. Wu, H. Jiang, *J. Org. Chem.* 2018, **83**, 9334.
7. Q. Zhong, S. Shou, J. Chen, *Phosphorus, Sulfur, and Silicon and the Related Elements*, **2020**, *195*, 988.
8. L. Yang, L. Song, S. Tang, L. Li, H. Li, B. Yuan, G. Yang, *Eur. J. Org. Chem.* **2019**, 1281.
9. H. Ngoy, S. K. Shresthay, K. D. Greeny, S. Garneau-Tsodikova, *Bioorg. Med.Chem.* **2016**, *24*, 6298.

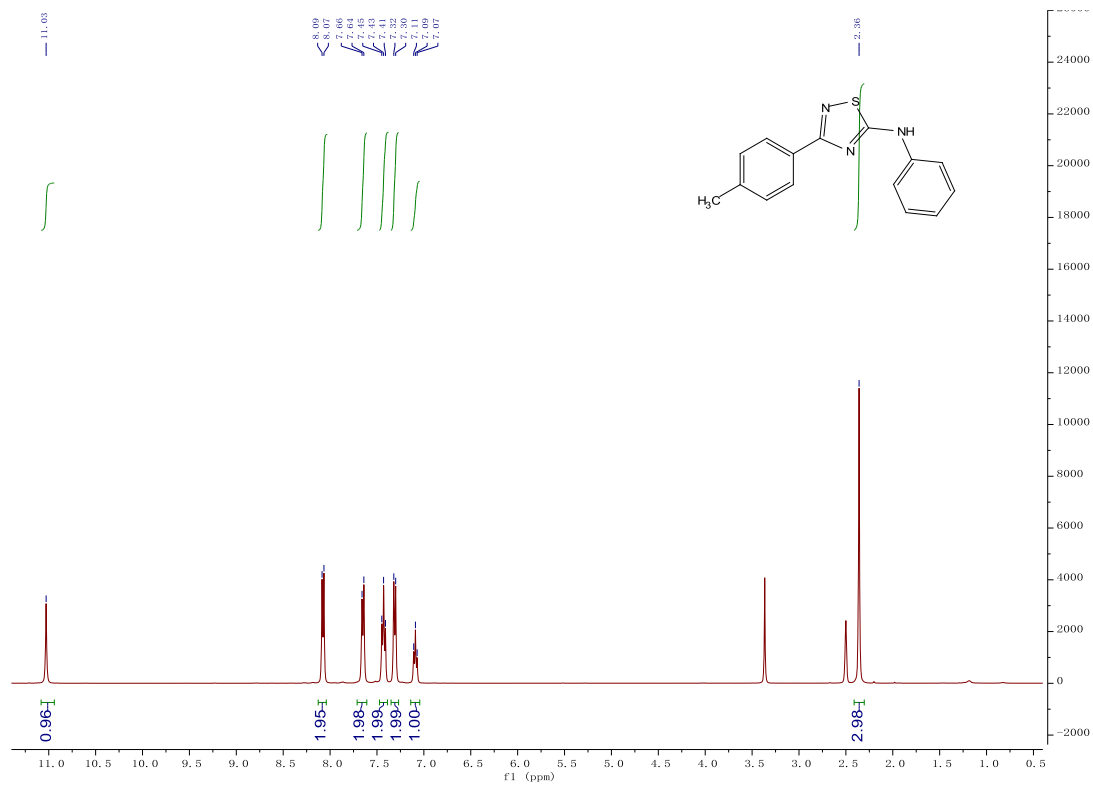
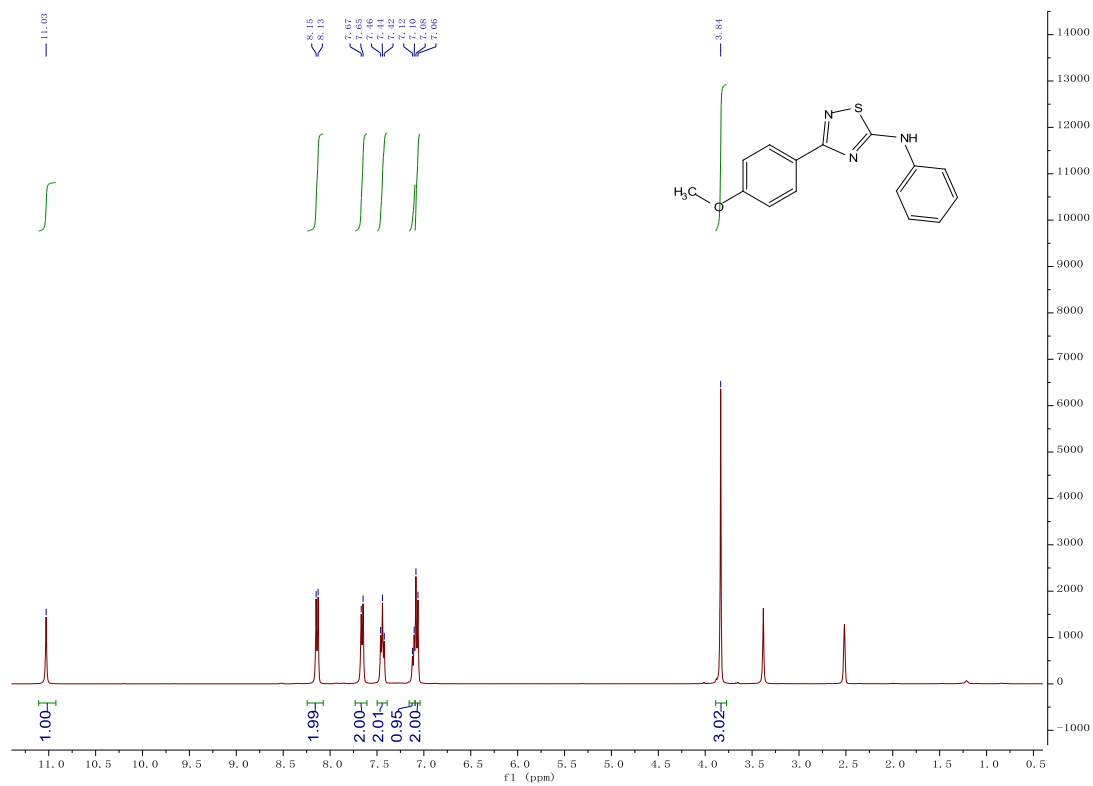
5. Scanned ^1H NMR Spectra of 2 CompoundsFigure S 1: ^1H NMR of 2a.Figure S 2: ^1H NMR of 2b.

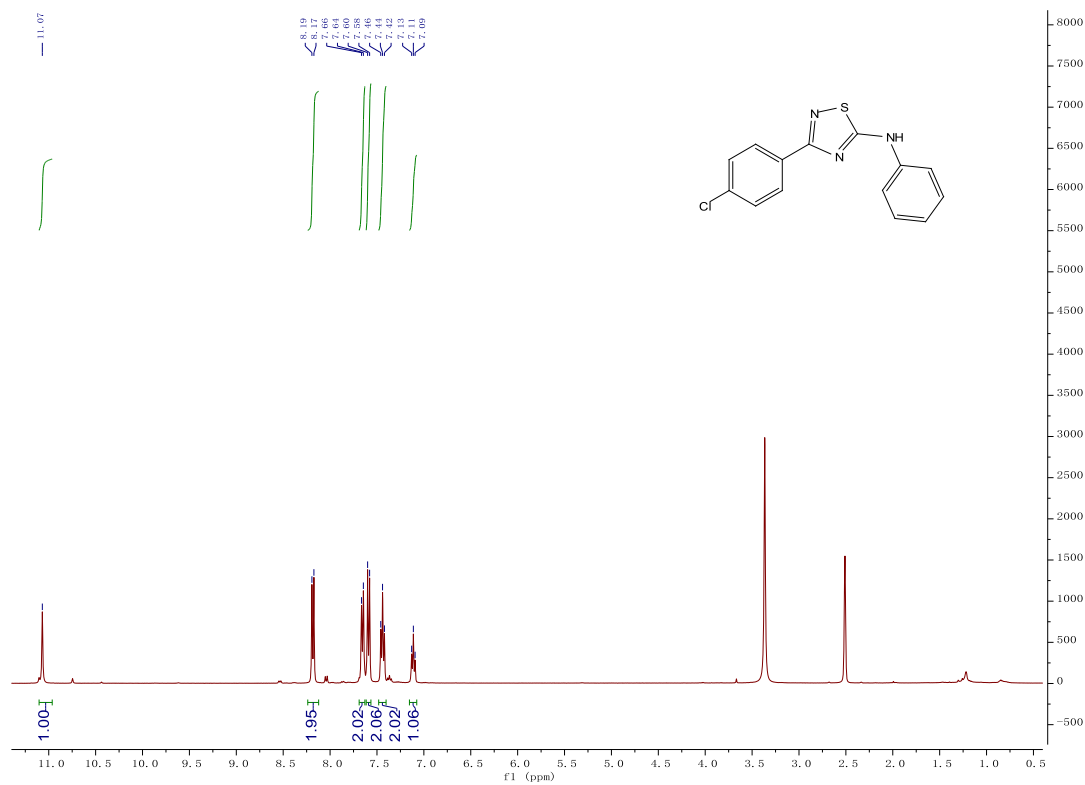
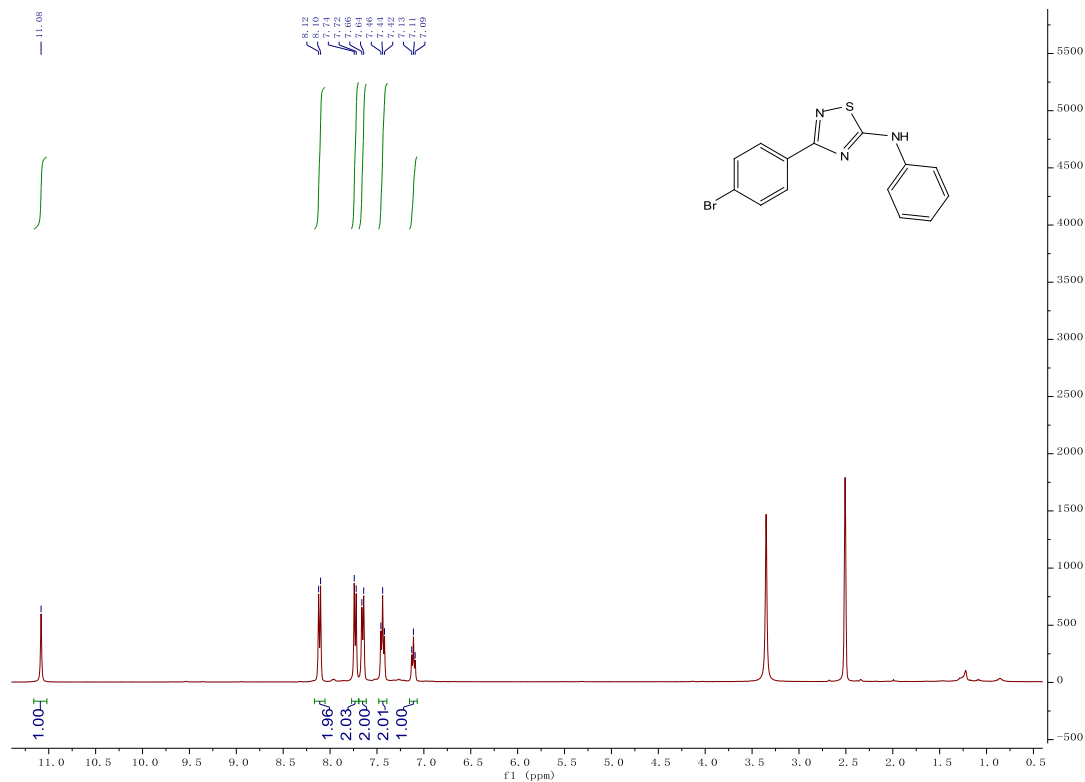
Figure S 3: ^1H NMR of 2c.Figure S 4: ^1H NMR of 2d.

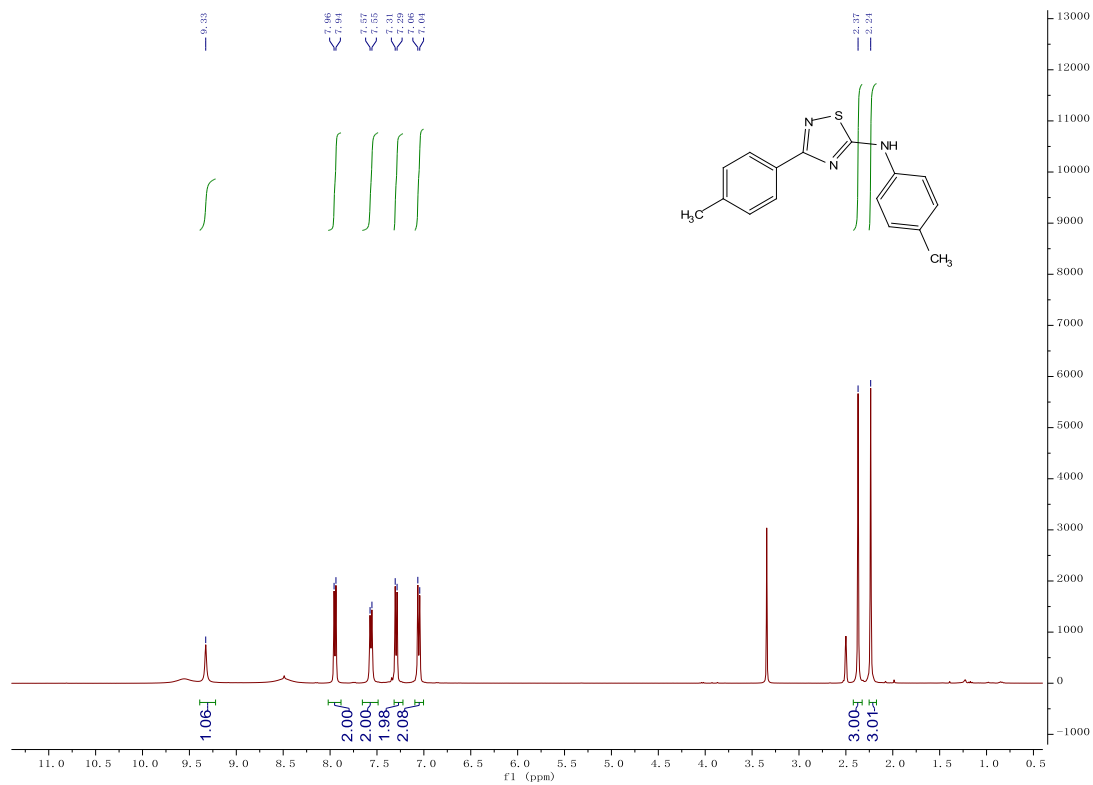
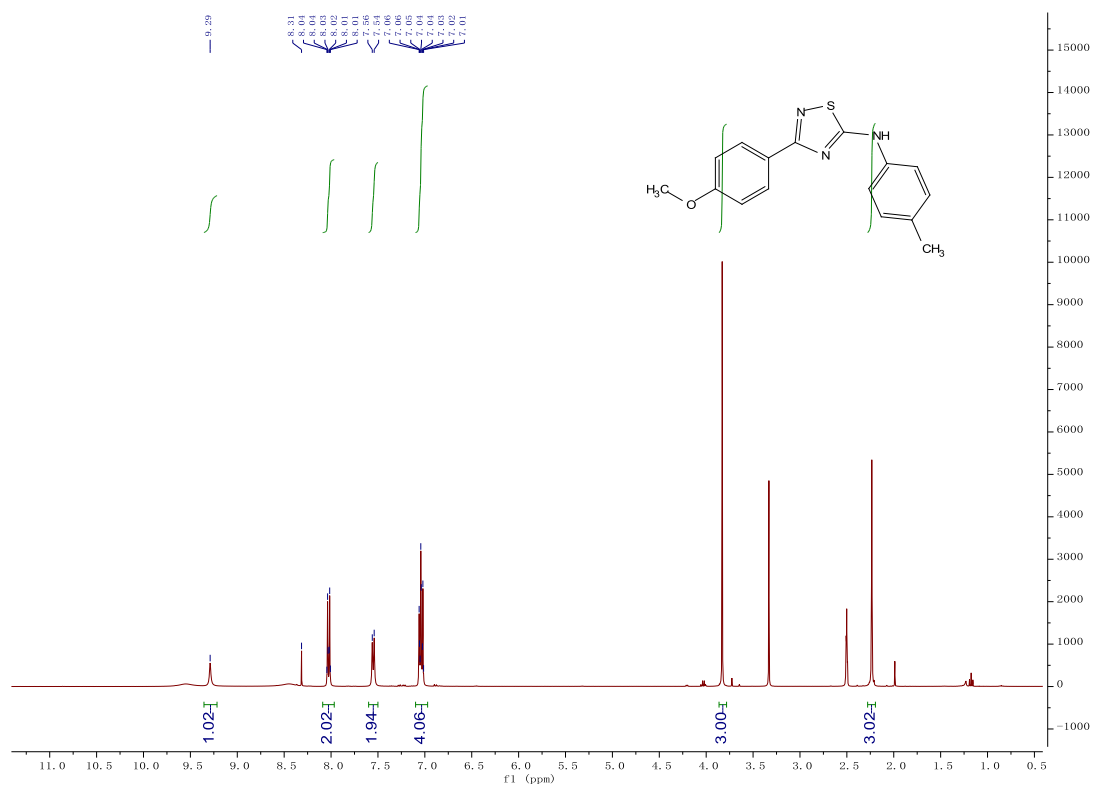
Figure S5: ¹H NMR of 2e.Figure S 6: ¹H NMR of 2f.

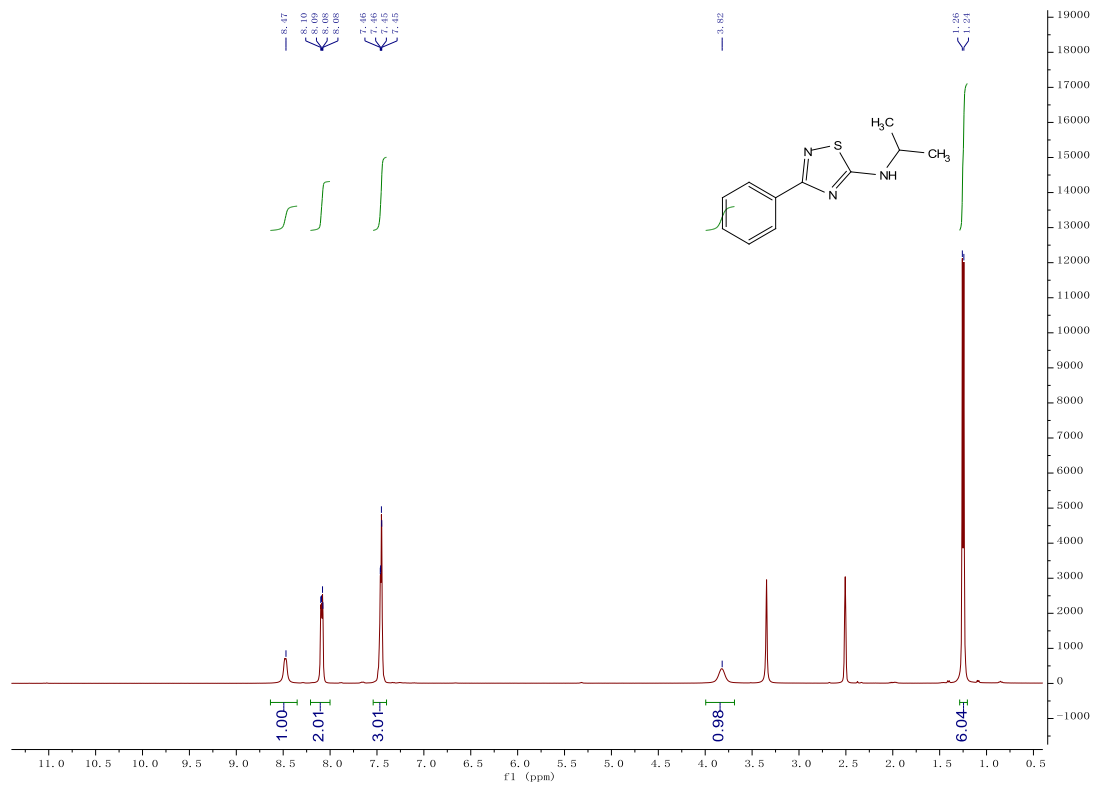
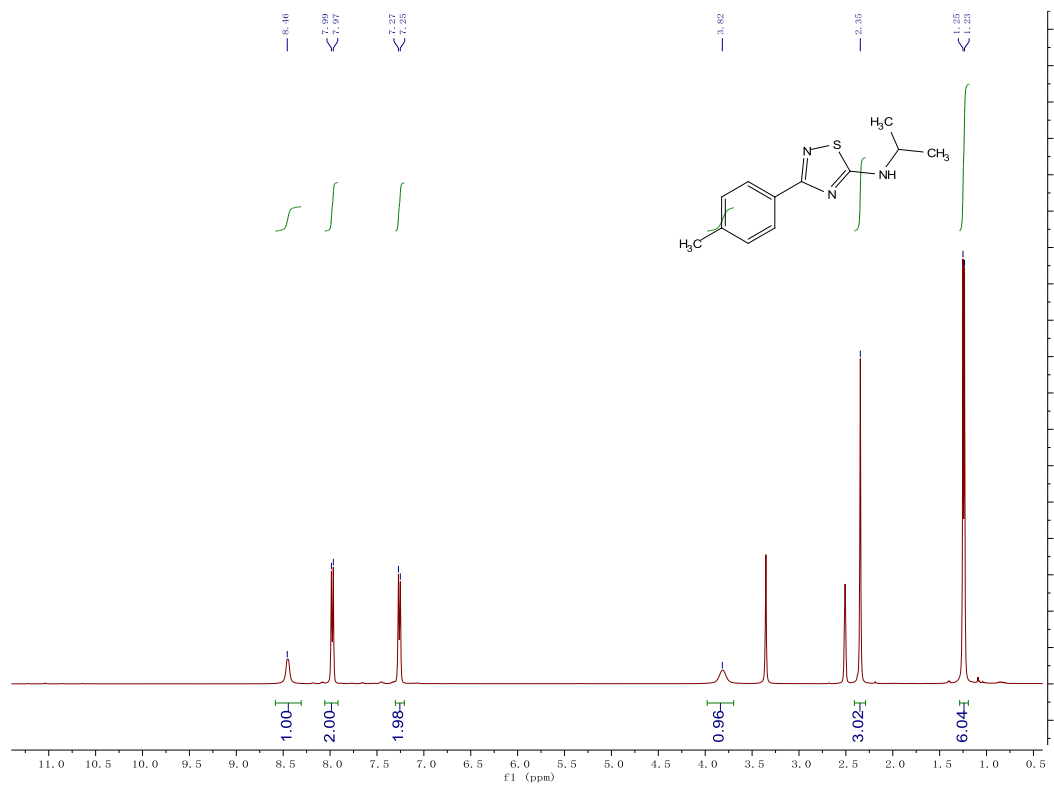


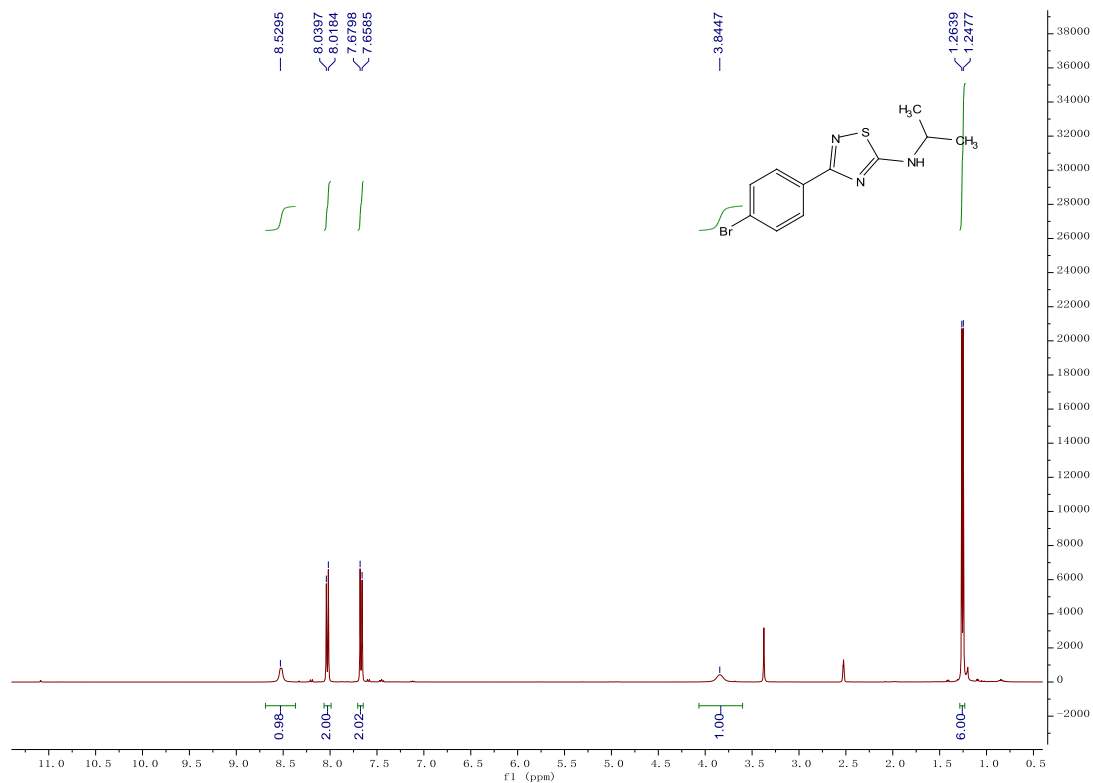
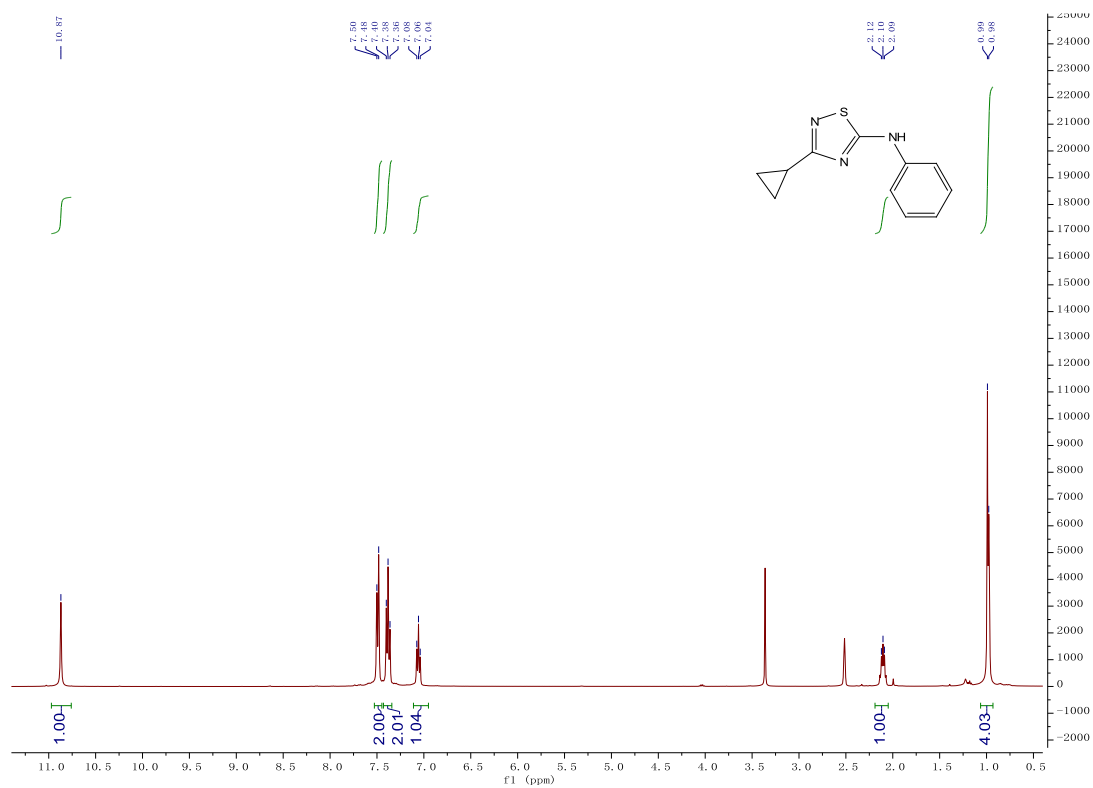
Figure S 9: ¹H NMR of **2i**.Figure S10: ¹H NMR of **2j**.

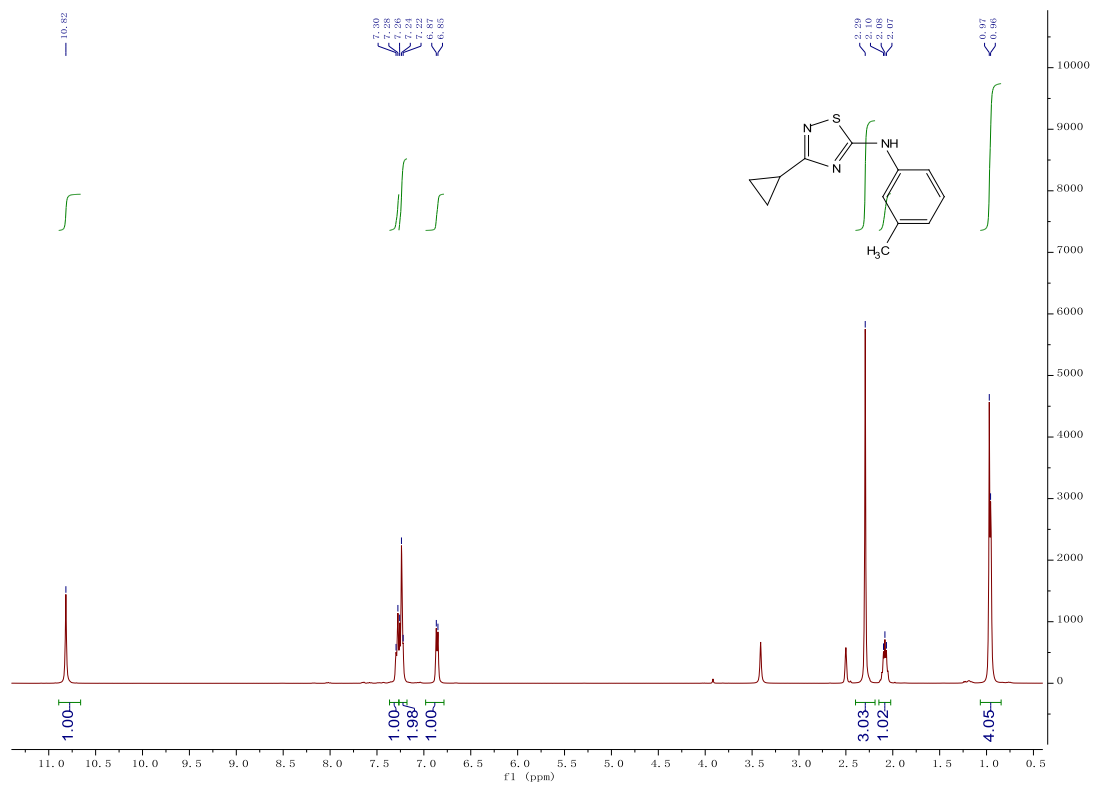
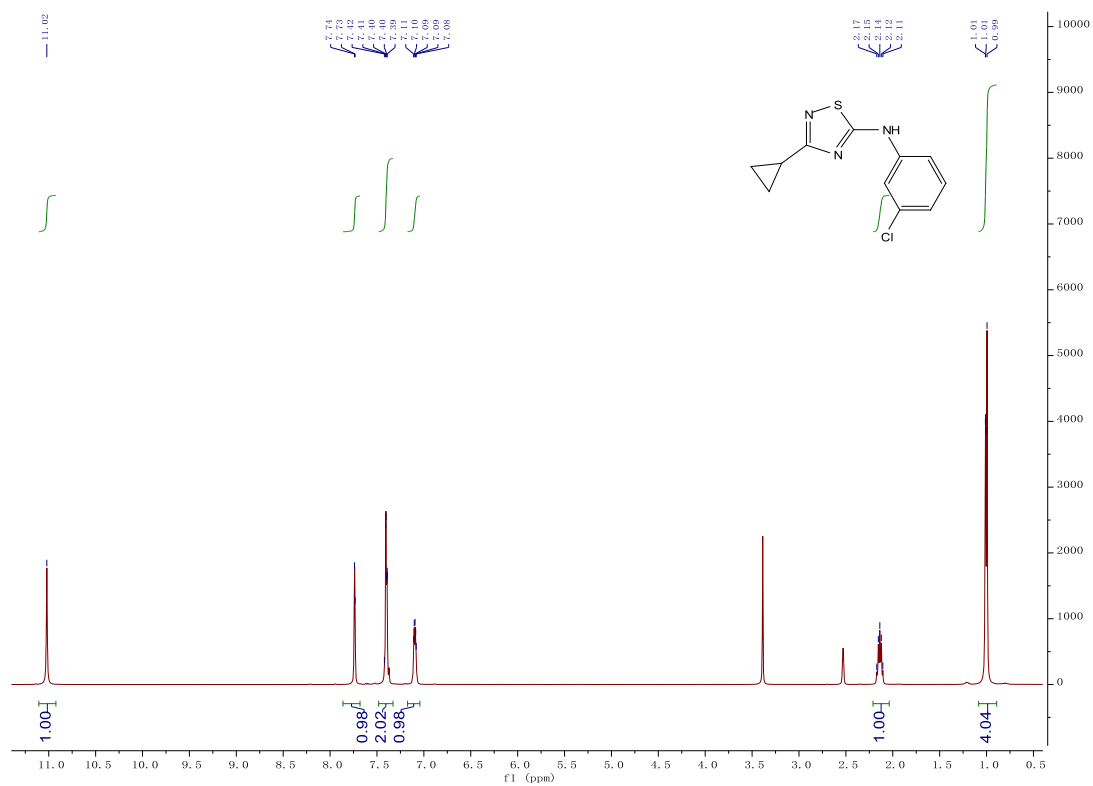
Figure S 11: ¹H NMR of 2k.Figure S 12: ¹H NMR of 2l.

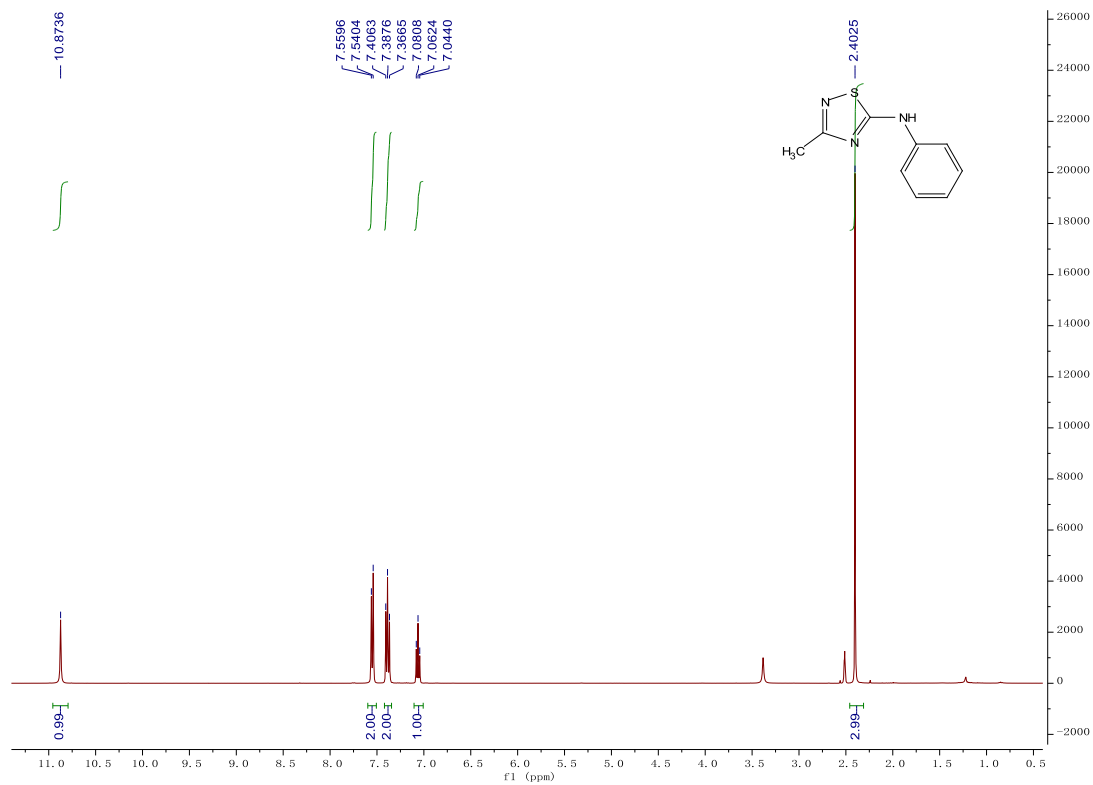
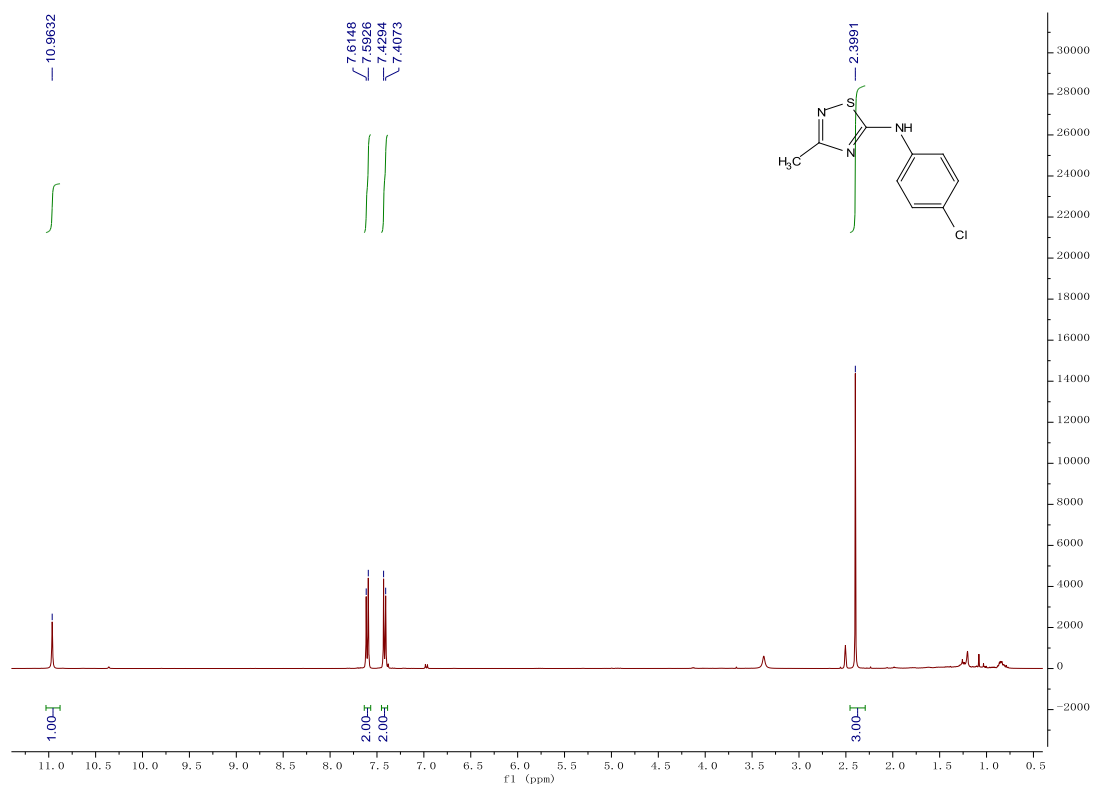
Figure S 13: ¹H NMR of 2m.Figure S 14: ¹H NMR of 2n.

Figure S 15: ¹H NMR of 2o.Figure S 16: ¹H NMR of 2p.

Figure S 17: ¹H NMR of 2q.Figure S 18: ¹H NMR of 2r.

Figure S 19: ¹H NMR of 2s.Figure S 20: ¹H NMR of 2t.

Figure S 21: ¹H NMR of **2u**.Figure S 22: ¹H NMR of **2v**.

Figure S 23: ¹H NMR of 2w.Figure S 24: ¹H NMR of 2x.