

FeCl₃/HCl-photocatalyzed synthesis of benzylidenearbituric acids from methylarenes

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General experimental

All reagents were obtained from local commercial suppliers and used without further purification. The progress of the reaction was monitored by TLC using analytical-grade silica gel plates (GF₂₅₄) under UV light. ¹H NMR spectra were recorded in DMSO-*d*₆ on 400 MHz instrument using TMS as internal standard. Chemical shifts are given in parts per million (δ , ppm) and the coupling constants *J* values are given in Hz. Mass spectrometry was performed on an LCMS-2010 EV (Shimadzu) instrument with an ESI source. GC analyses are performed on an Agilent 7890A instrument (Column: Agilent 19091J-413: 30 m $\times$ 320 μ m $\times$ 0.25 μ m, carrier gas: H₂, FID detection).

General procedure for the synthesis of 3a~m

Methylarene **1** (1 mmol), barbituric acid **2** (0.2 mmol), FeCl₃ (0.5 mol%), HCl (12 mol/L, 10 mol %) and MeCN (2.0 mL) was added to a 6 mL tube equipped with magnetic stirring bar. The tube was placed 2 cm away from two purple LEDs (2 $\times$ 3W, 395 nm). The reaction mixture was irradiated for 12 h under encapsulated air atmosphere at 25 °C. After reaction completion, the mixture was transferred to a 10 mL round-bottom flask and the solvent was removed *in vacuo*. The pure product was obtained by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1).

Note: the size of the reaction tube is very important. This reaction is conducted in a 6-mL reaction tube, with a solvent volume of 2 mL and a headspace volume of 4 mL. Excessively large reaction tubes lead to a decrease in reaction yield, whereas excessively small tubes result in incomplete conversion.

Reaction tube and photoreactor



Control experiments

(a) Radical trapping experiment

Toluene **1a** (1 mmol), 1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione **2a** (0.2 mmol), FeCl₃ (0.5 mol%), HCl (12 mol/L, 10 mol %), TEMPO (0.6 mmol) and MeCN (2.0 mL) was added to a 6 mL tube equipped with magnetic stirring bar. The tube was placed 2 cm away from two purple LEDs (2 × 3W, 395 nm). The reaction mixture was irradiated for 12 h under encapsulated air atmosphere at 25 °C. After the reaction was complete, TLC analysis was performed, followed by sampling for GC-MS analysis. No desired product **3a** was observed. The adducts **4** between benzyl radical and TEMPO were detected by GC-MS (EI, *m/z* 247.2).

(b) Air-control experiment

Toluene **1a** (0.2 mmol), FeCl₃ (0.5 mol%), HCl (12 mol/L, 10 mol %) and MeCN (2.0 mL) was added to a 6 mL tube equipped with magnetic stirring bar. The tube was placed 2 cm away from two purple LEDs (2 × 3W, 395 nm) and open to air. The reaction mixture was irradiated for 12 h at 25 °C. After the reaction was complete, a sample was taken for GC-MS analysis. Toluene was converted to benzoic acid **5** in 99% yield.

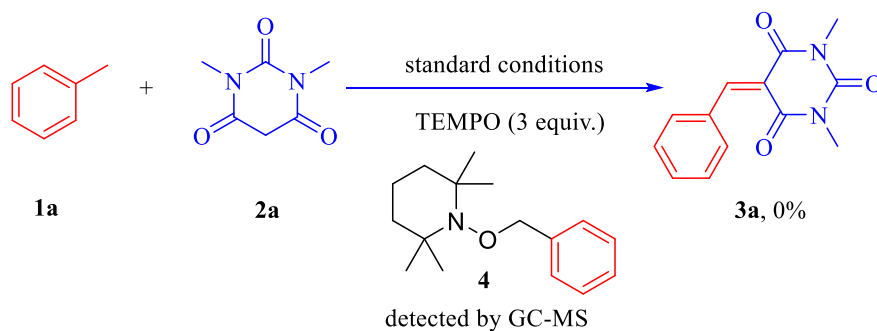
Moreover, the reaction between **1a** (1 mmol) and **2a** (0.2 mmol) was carried out using the above standard reaction conditions. The tube was placed 2 cm away from two purple LEDs (2 × 3W, 395 nm) and open to air. The reaction mixture was irradiated for 12 h at 25 °C. After reaction, the mixture was transferred to a 10 mL round-bottom flask and the solvent was concentrated *in vacuo*. The pure product **3a** was obtained by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) in 46% yield.

(c) Comparative experiment on catalytic activity

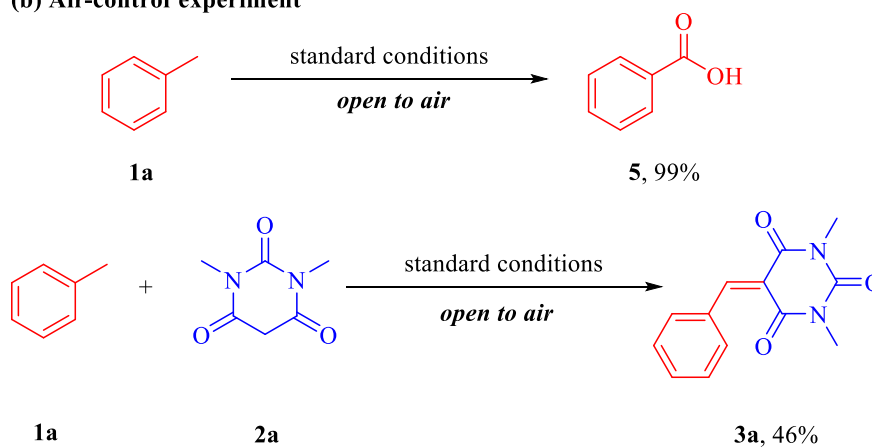
To three reaction tubes, the following reagents were added respectively: (1) benzaldehyde (0.2 mmol), **2a** (0.2 mmol), and FeCl₃ (0.5 mol%) and acetonitrile (2 mL); (2) benzaldehyde (0.2 mmol), **2a** (0.2 mmol), HCl (10 mol%) and acetonitrile (2 mL); and (3) benzaldehyde (0.2 mmol), **2a** (0.2 mmol), FeCl₃ (0.5 mol%), HCl (10 mol%) and acetonitrile (2 mL). The reactions were stirred at 25 °C for 12 h. After reaction, the mixture was transferred to a 10 mL round-bottom flask and the solvent was concentrated *in vacuo*. The

pure product **3a** was obtained by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) in 48%, 82% and 99%, respectively.

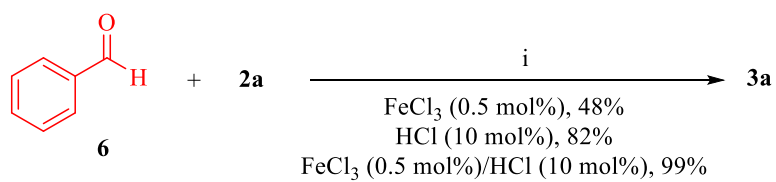
(a) Radical trapping experiment



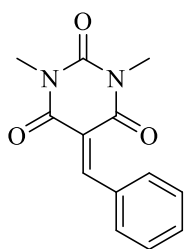
(b) Air-control experiment



(c) Comparative experiment on catalytic activity

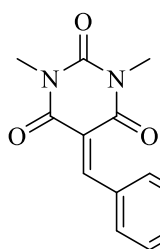


Characterization data



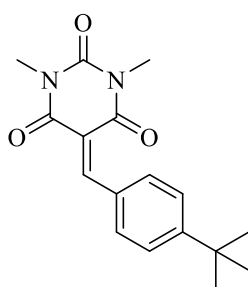
5-Benzylidene-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**3a**).^{S1} Yield: 45 mg (93%);

¹H NMR (400 MHz, DMSO-*d*₆) δ 8.35 (s, 1H), 8.03 (d, *J* = 7.5 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 3.23 (s, 3H), 3.18 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 162.1, 160.3, 155.5, 151.1, 134.6, 132.8, 132.1, 128.0, 119.0, 28.6, 28.0; MS (ESI) *m/z* 245.1 [M + H]⁺.



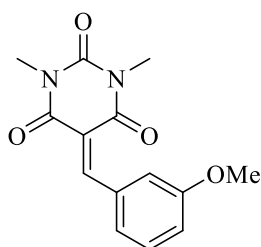
5-(4-Methoxybenzylidene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**3b**).^{S1}

Yield: 47 mg (86%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.33 (d, *J* = 8.6 Hz, 2H), 8.31 (s, 1H), 7.06 (d, *J* = 8.5 Hz, 2H), 3.88 (s, 3H), 3.22 (s, 3H), 3.20 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 163.9, 163.1, 161.2, 156.2, 151.5, 137.8, 125.6, 115.8, 114.4, 56.2, 29.1, 28.5; MS (ESI) *m/z* 275.1 [M + H]⁺.



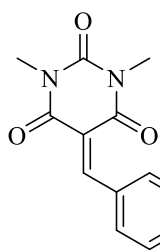
5-(4-(*tert*-Butyl)benzylidene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**3c**).^{S2}

Yield: 49 mg (82%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.33 (s, 1H), 8.06 (d, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 8.5 Hz, 2H), 3.23 (s, 3H), 3.19 (s, 3H), 1.31 (s, 9H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 162.3, 160.4, 155.9, 155.6, 151.1, 133.5, 130.0, 125.0, 117.9, 34.9, 30.7, 28.6, 28.0; MS (ESI) *m/z* 301.2 [M + H]⁺.



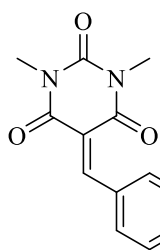
5-(3-Methoxybenzylidene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**3d**).^{S3}

Yield: 44 mg (80%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.32 (s, 1H), 7.73 (s, 1H), 7.57 (d, *J* = 7.7 Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.12 (dd, *J* = 8.2, 2.1 Hz, 1H), 3.80 (s, 3H), 3.23 (s, 3H), 3.18 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 166.2, 160.3, 158.6, 155.3, 151.1, 134.0, 129.1, 125.6, 119.1, 118.0, 117.6, 55.2, 28.6, 28.1; MS (ESI) *m/z* 275.1 [M + H]⁺.



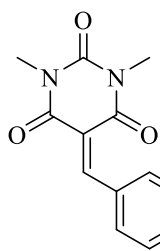
5-(4-Chlorobenzylidene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**3e**).^{S1}

Yield: 46 mg (83%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.32 (s, 1H), 8.04 (d, *J* = 8.2 Hz, 2H), 7.54 (d, *J* = 8.3 Hz, 2H), 3.23 (s, 3H), 3.18 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 162.4, 160.8, 154.3, 151.5, 137.1, 134.9, 132.1, 128.5, 119.9, 29.1, 28.5; MS (ESI) *m/z* 279.1 [M + H]⁺.



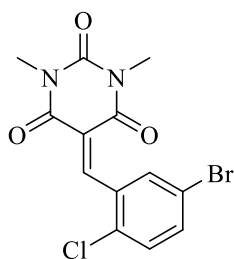
5-(4-Bromobenzylidene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**3f**).^{S1} Yield:

51 mg (80%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.30 (s, 1H), 7.94 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J* = 8.5 Hz, 2H), 3.23 (s, 3H), 3.17 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 161.9, 160.2, 154.0, 151.0, 134.3, 131.9, 130.9, 125.7, 119.5, 28.6, 28.0; MS (ESI) *m/z* 323.0 [M + H]⁺.



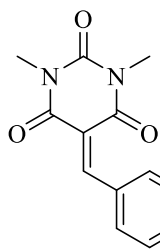
5-(4-Fluorobenzylidene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione (**3g**).^{S4} Yield:

40 mg (77%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.34 (s, 1H), 8.22 – 8.14 (m, 2H), 7.37 – 7.28 (m, 2H), 3.23 (s, 3H), 3.18 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 164.6 (d, *J* = 247.5 Hz), 162.1, 160.4, 154.2, 151.1, 136.1 (d, *J* = 9.3 Hz), 129.3 (d, *J* = 3.0 Hz), 118.5, 115.2 (d, *J* = 21.7 Hz), 28.6, 28.0; MS (ESI) *m/z* 263.1 [M + H]⁺.

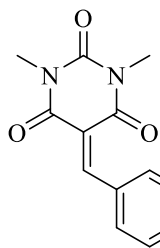


5-(5-Bromo-2-chlorobenzylidene)-1,3-dimethylpyrimidine-2,4,6(1H,3H,5H)-trione

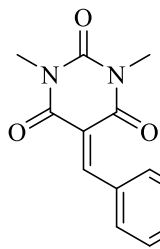
(**3h**). Yield: 56 mg (79%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.26 (s, 1H), 7.84 (d, *J* = 2.0 Hz, 1H), 7.68 – 7.64 (m, 1H), 7.52 (d, *J* = 8.6 Hz, 1H), 3.24 (s, 3H), 3.13 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 161.1, 159.6, 151.0, 148.9, 134.9, 133.9, 133.3, 131.8, 130.8, 122.5, 119.1, 28.5, 28.0; MS (ESI) *m/z* 357.0 [M + H]⁺.



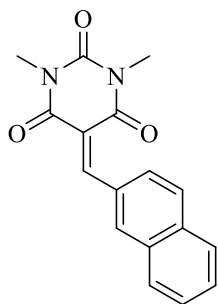
(3i).^{S5} Yield: 47 mg (87%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.37 (s, 1H), 7.95 – 7.89 (m, 4H), 3.23 (s, 3H), 3.15 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 162.0, 160.4, 153.1, 151.5, 138.6, 132.1, 132.0, 122.0, 119.0, 113.1, 29.1, 28.5; MS (ESI) *m/z* 270.1 [M + H]⁺.



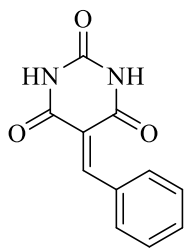
1,3-Dimethyl-5-(4-nitrobenzylidene)pyrimidine-2,4,6(1H,3H,5H)-trione (3j).^{S6} Yield: 49 mg (85%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.42 (s, 1H), 8.27 (d, *J* = 8.5 Hz, 2H), 7.98 (d, *J* = 8.4 Hz, 2H), 3.25 (s, 3H), 3.15 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 162.0, 160.4, 152.5, 151.8, 151.5, 148.4, 140.8, 132.4, 128.4, 123.3, 123.2, 122.5, 29.1, 28.5; MS (ESI) *m/z* 290.1 [M + H]⁺.



1,3-Dimethyl-5-(4-(trifluoromethyl)benzylidene)pyrimidine-2,4,6(1H,3H,5H)-trione (3k).^{S7} Yield: 47 mg (76%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.40 (s, 1H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.80 (d, *J* = 8.3 Hz, 2H), 3.24 (s, 3H), 3.15 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 161.7, 160.0, 153.1, 151.1, 137.5, 131.7, 130.1 (q, *J* = 28.0 Hz), 124.60 (q, *J* = 3.7 Hz), 123.9 (q, *J* = 275.0 Hz), 121.3, 28.6, 28.0; MS (ESI) *m/z* 313.1 [M + H]⁺.



1,3-Dimethyl-5-(naphthalen-2-ylmethylene)pyrimidine-2,4,6(1H,3H,5H)-trione (3l).^{S7} Yield: 48 mg (82%); ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.63 (s, 1H), 8.52 (s, 1H), 8.15 (d, *J* = 8.6 Hz, 1H), 8.02 (d, *J* = 8.1 Hz, 1H), 7.97 (t, *J* = 8.8 Hz, 2H), 7.67 (t, *J* = 7.4 Hz, 1H), 7.60 (t, *J* = 7.4 Hz, 1H), 3.26 (s, 3H), 3.21 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 162.7, 160.8, 155.9, 151.6, 135.4, 134.8, 132.6, 131.1, 129.7, 129.1, 128.8, 128.0, 127.6, 127.2, 119.3, 29.1, 28.6; MS (ESI) *m/z* 295.1 [M + H]⁺.



5-Benzylidenepyrimidine-2,4,6(1H,3H,5H)-trione (**3m**).^{S6} Yield: 32 mg (75%); ¹H NMR

(400 MHz, DMSO-*d*₆) δ 11.40 (s, 1H), 11.24 (s, 1H), 8.28 (s, 1H), 8.08 (d, *J* = 7.4 Hz, 2H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.47 (t, *J* = 7.4 Hz, 2H). ¹³C NMR (100 MHz, DMSO-*d*₆) δ 163.4, 161.6, 154.7, 150.2, 133.1, 132.7, 132.2, 128.1, 119.1; MS (ESI) *m/z* 217.1 [M + Na]⁺.

References

- [S1] P. G. Patil, Y. Satkar and D. H. More, *Synth. Commun.*, 2020, **50**, 3804; <https://doi.org/10.1080/00397911.2020.1811987>.
- [S2] M. Piringer, M. Hofer, L. S. Vogl, P. Mayer and M. Waser, *Adv. Synth. Catal.*, 2024, **366**, 2115; <https://doi.org/10.1002/adsc.202400038>.
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- [S5] T. K. Das, A. M. R. Treviño, S. Pandiri, S. Irvankoski, J. H. Siitonen, S. M. Rodriguez, M. Yousufuddin and L. Kürti, *Green Chem.*, 2023, **25**, 746; <https://doi.org/10.1039/D2GC04315G>.
- [S6] P. J. Patel, H. R. Chaudhary, V. K. Gupta and D. M. Patel, *Res. Chem. Intermed.*, 2024, **50**, 1231; <https://doi.org/10.1007/s11164-023-05168-3>.
- [S7] C.-C. Wang, J. Zhou, Z.-W. Ma, X.-P. Chen and Y.-J. Chen, *Org. Biomol. Chem.*, 2019, **17**, 9200; <https://doi.org/10.1039/C9OB01992H>.

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

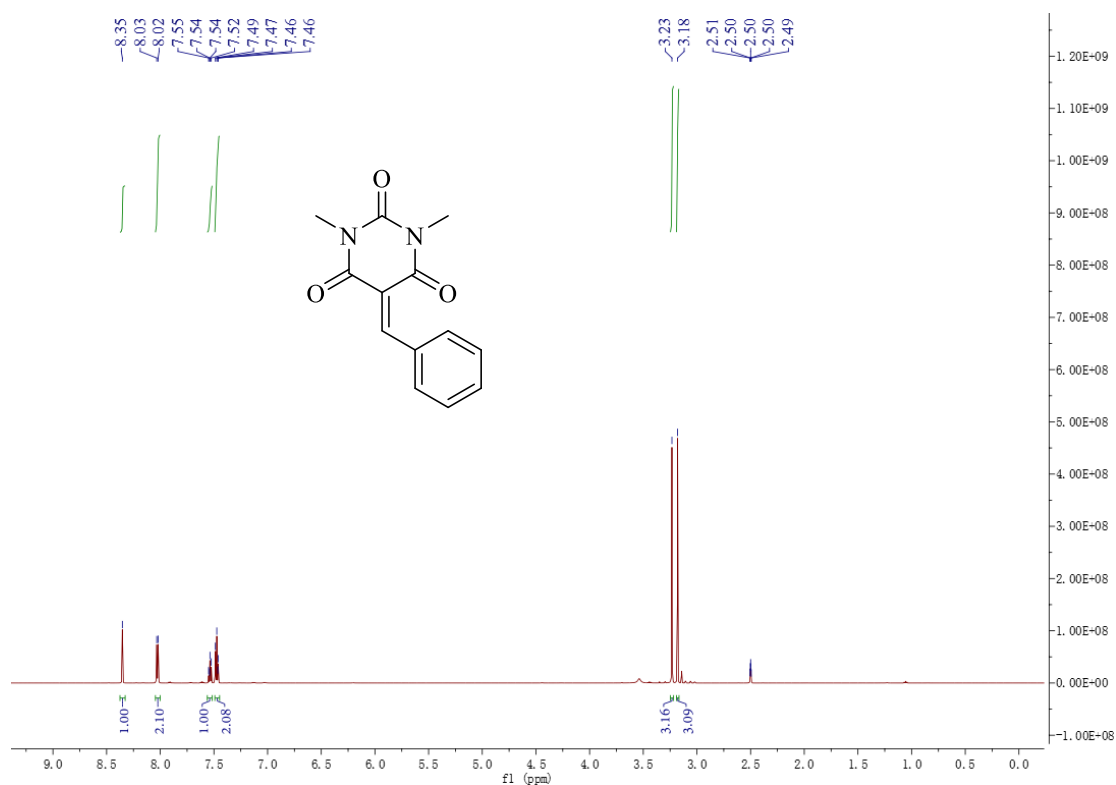


Figure S1. ^1H NMR of 3a

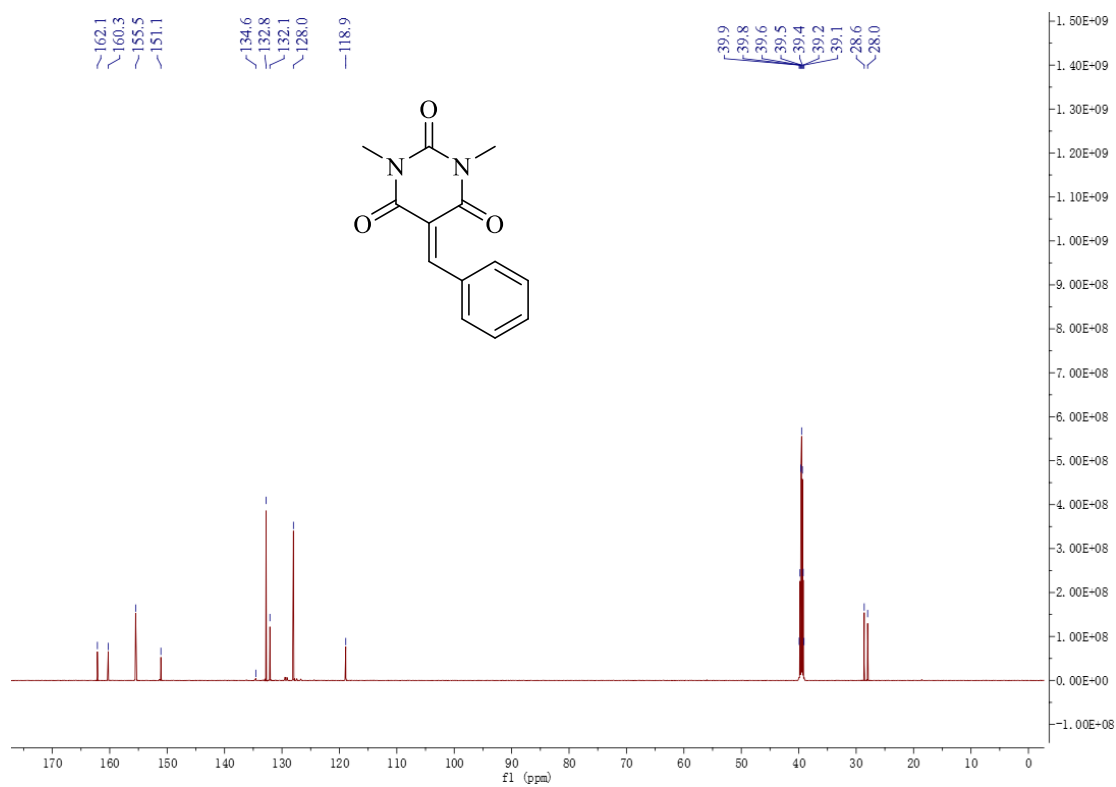


Figure S2. ^{13}C NMR of 3a

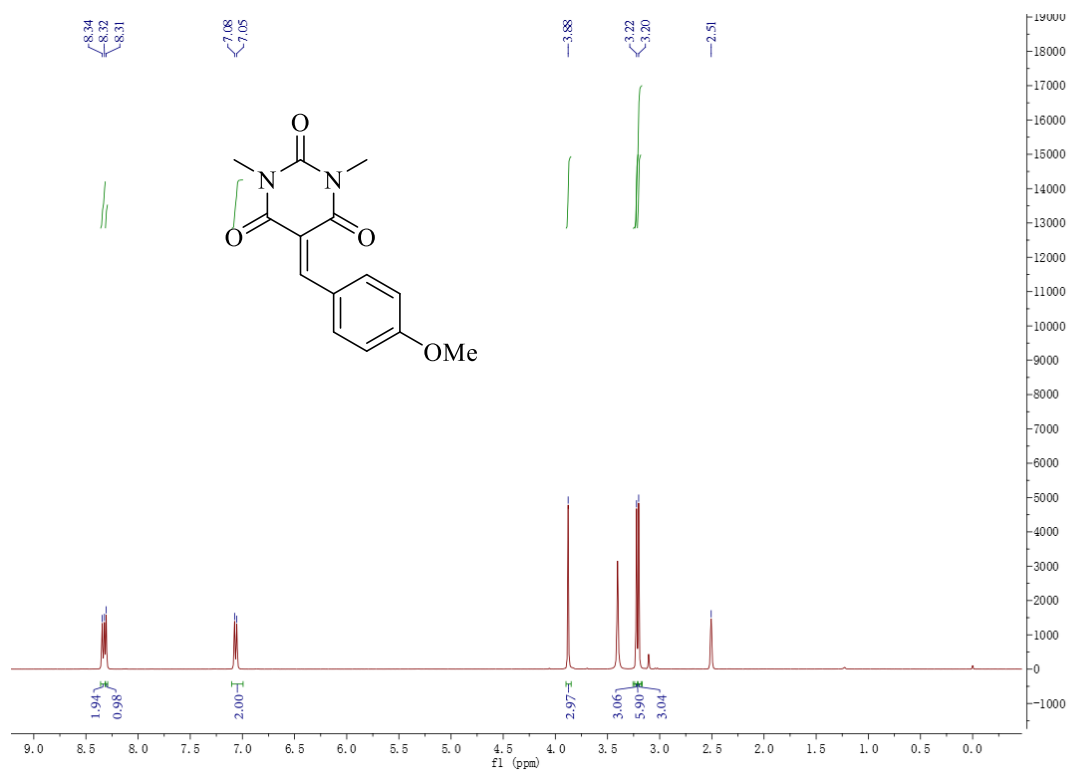


Figure S3. ¹H NMR of **3b**

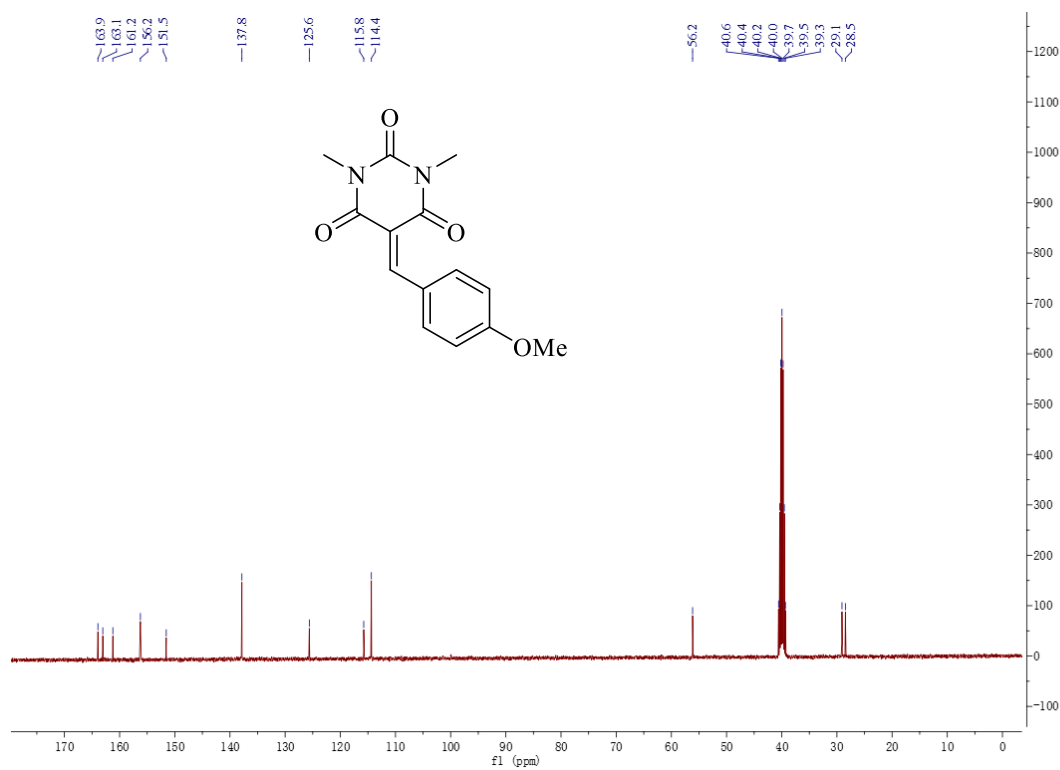


Figure S4. ¹³C NMR of **3b**

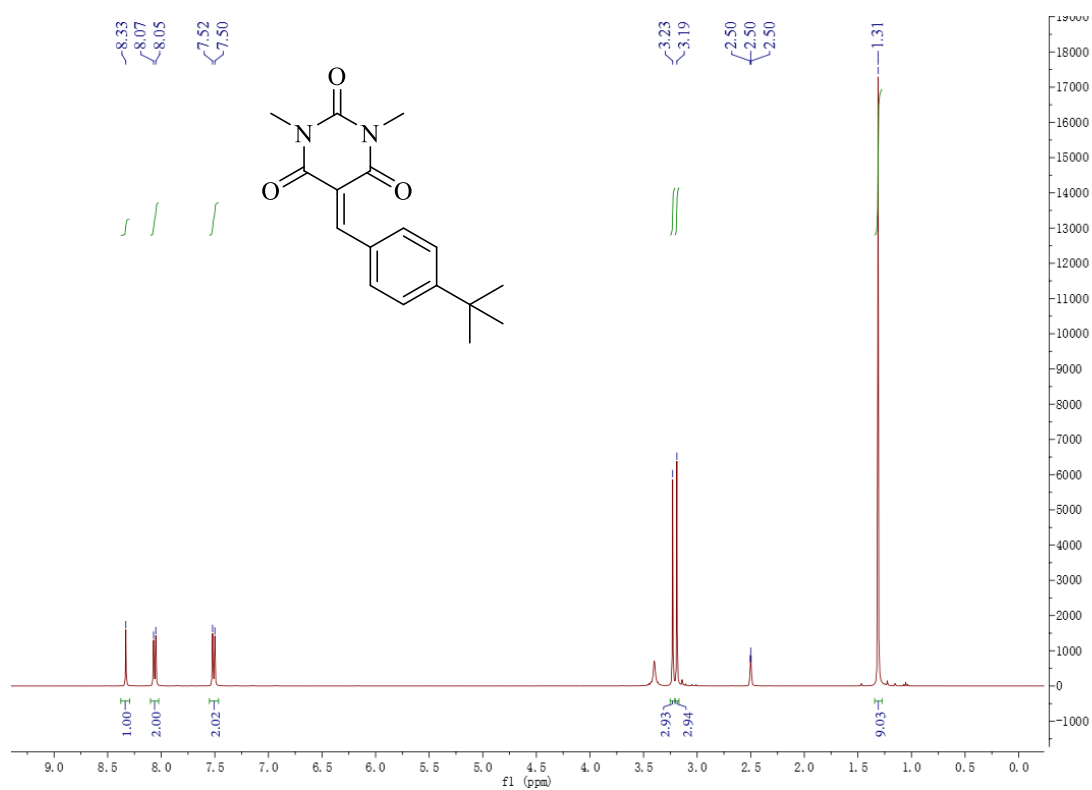


Figure S5. ¹H NMR of **3c**

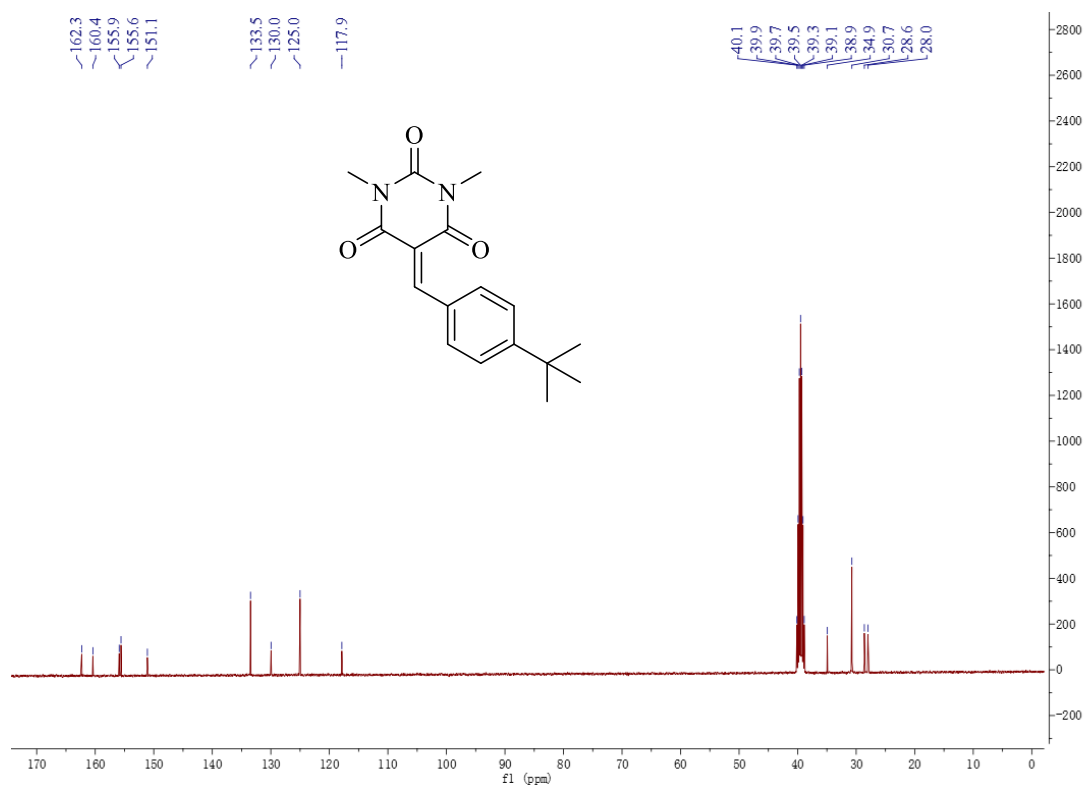


Figure S6. ¹³C NMR of **3c**

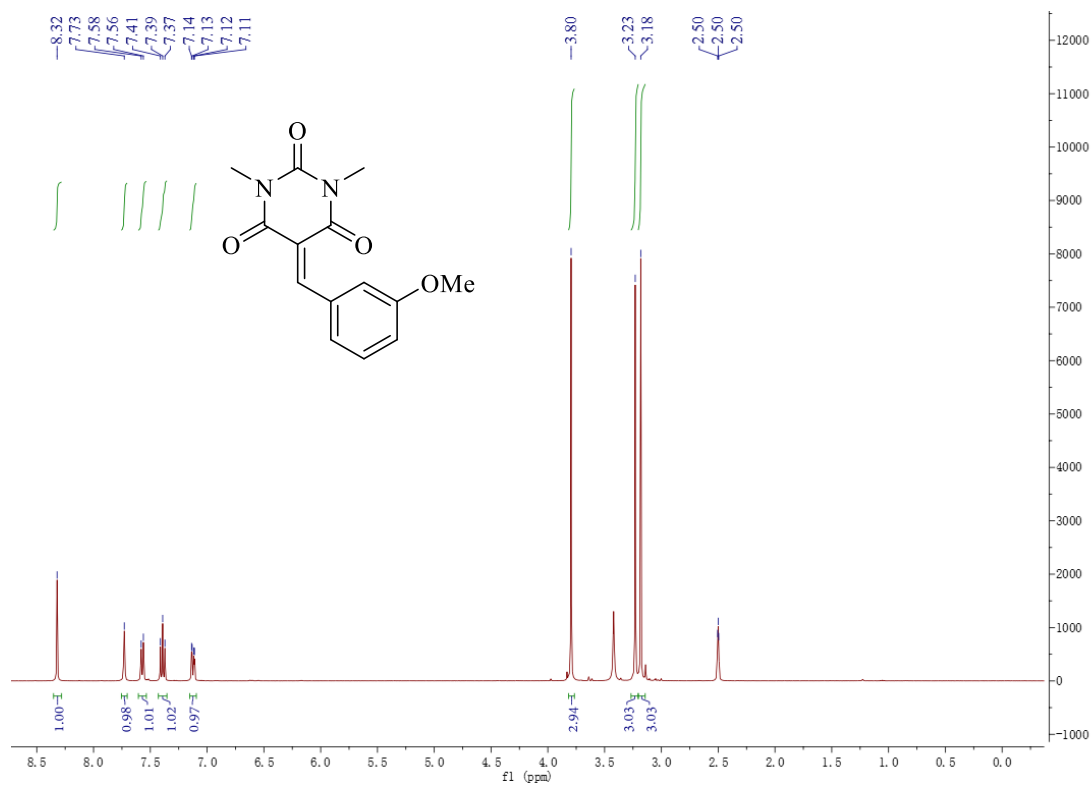


Figure S7. ¹H NMR of **3d**

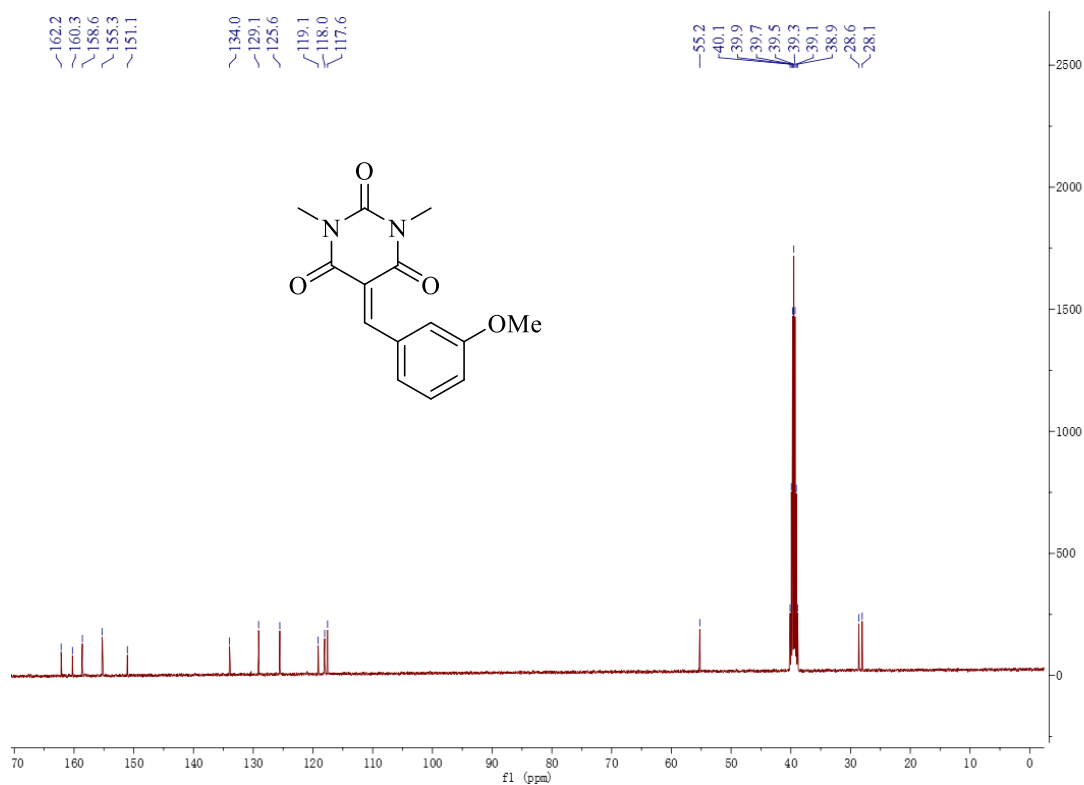


Figure S8. ¹³C NMR of **3d**

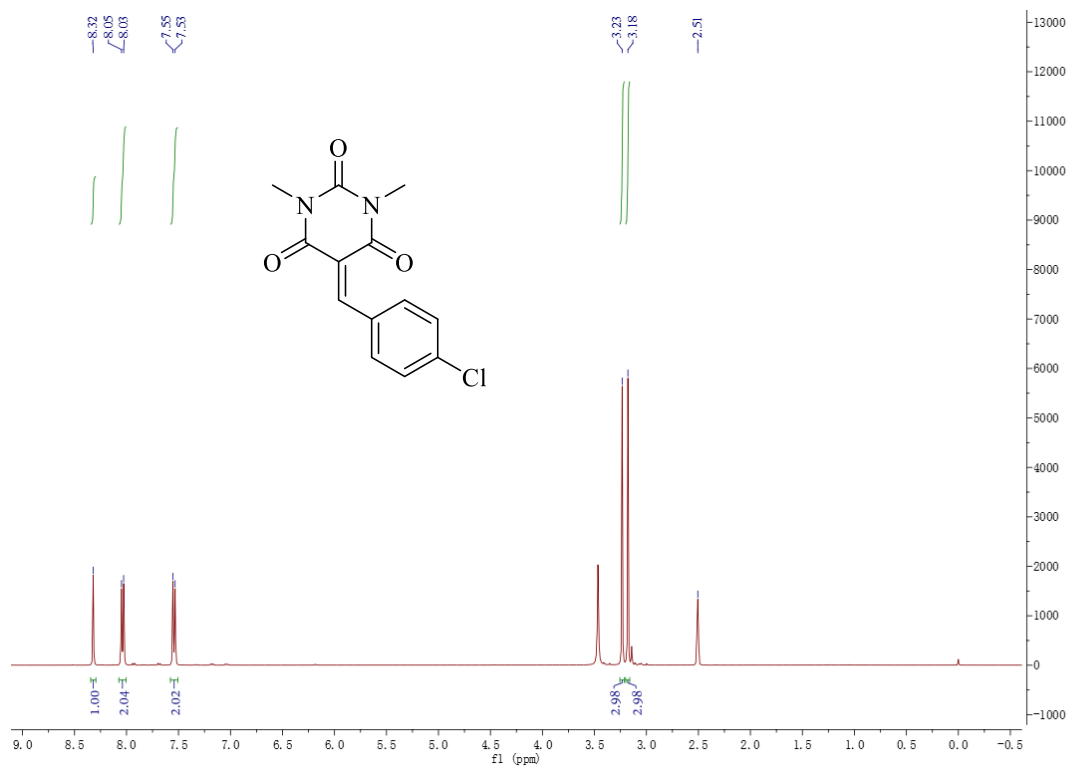


Figure S9. ¹H NMR of **3e**

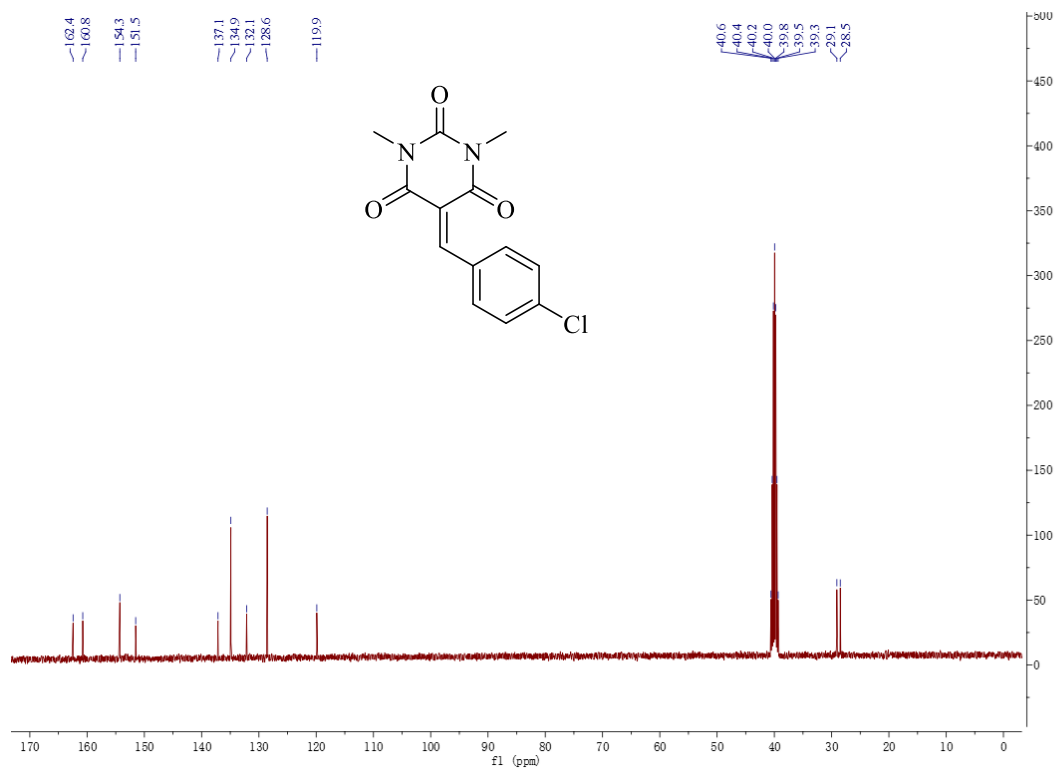


Figure S10. ¹³C NMR of **3e**

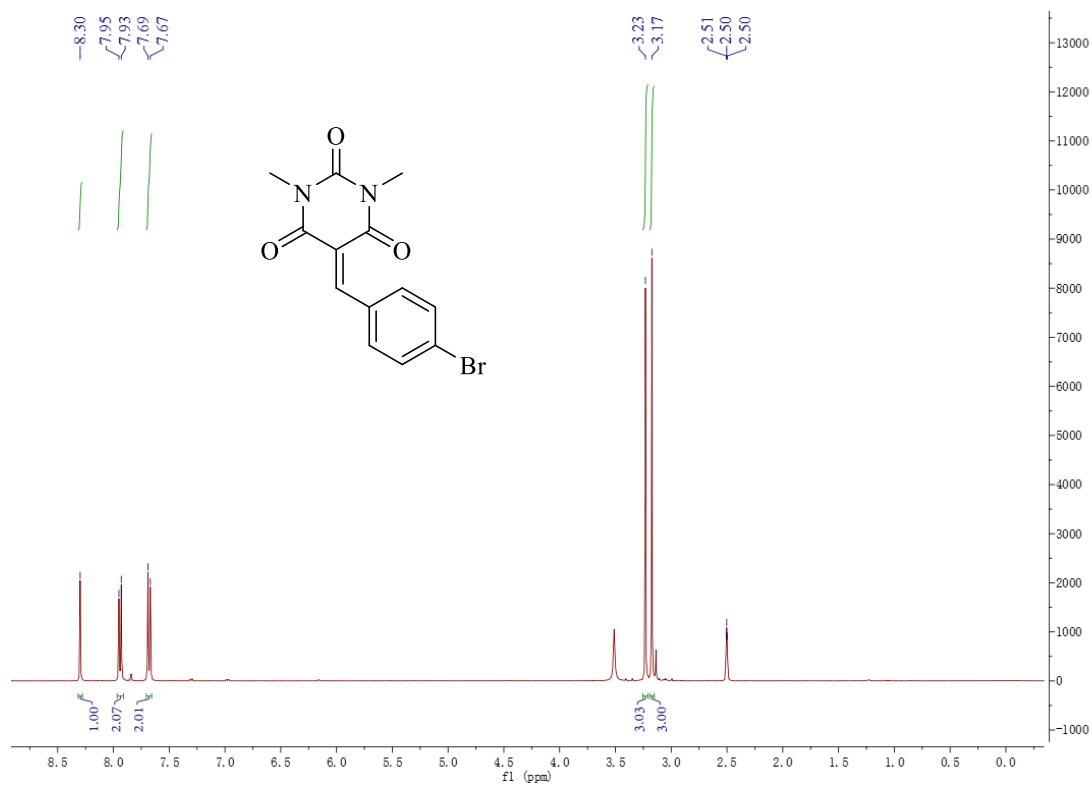


Figure S11. ¹H NMR of **3f**

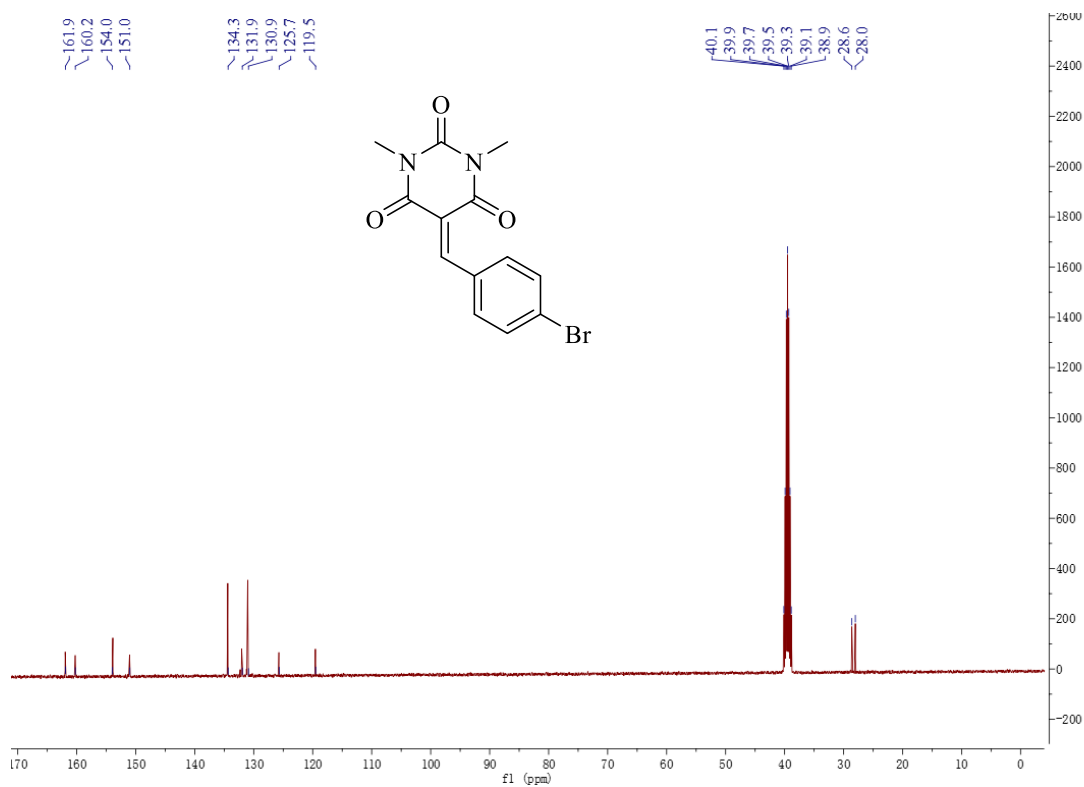


Figure S12. ¹³C NMR of **3f**

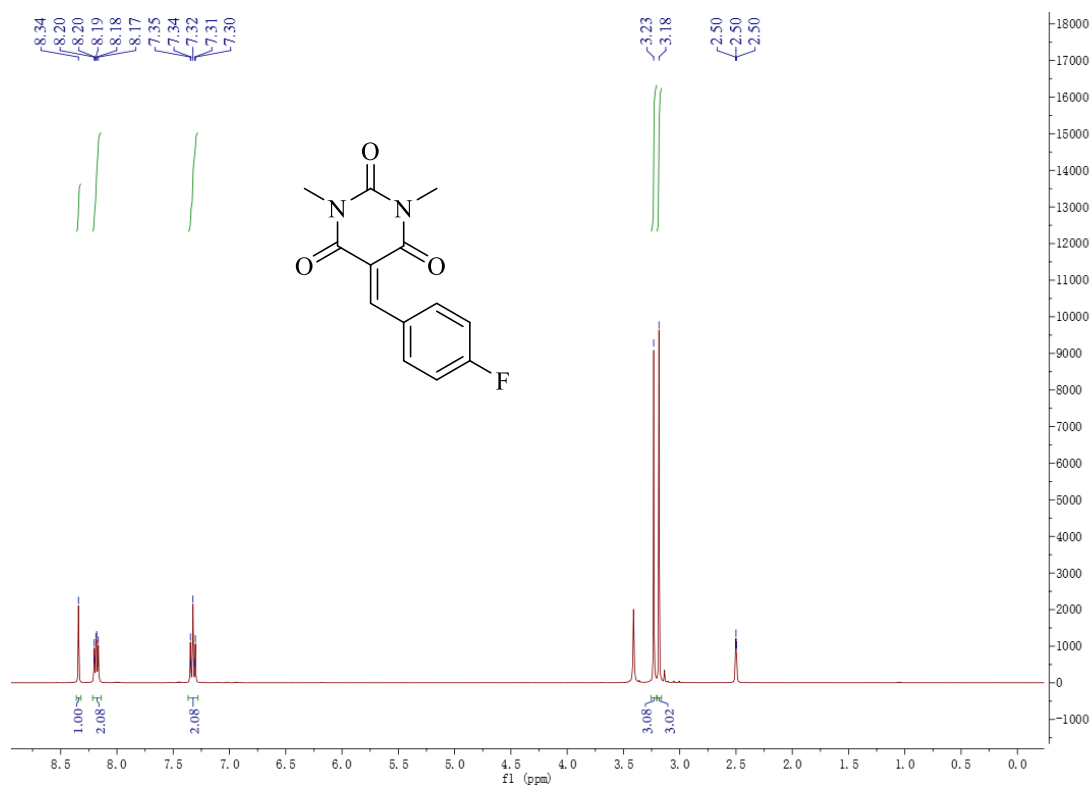


Figure S13. ¹H NMR of **3g**

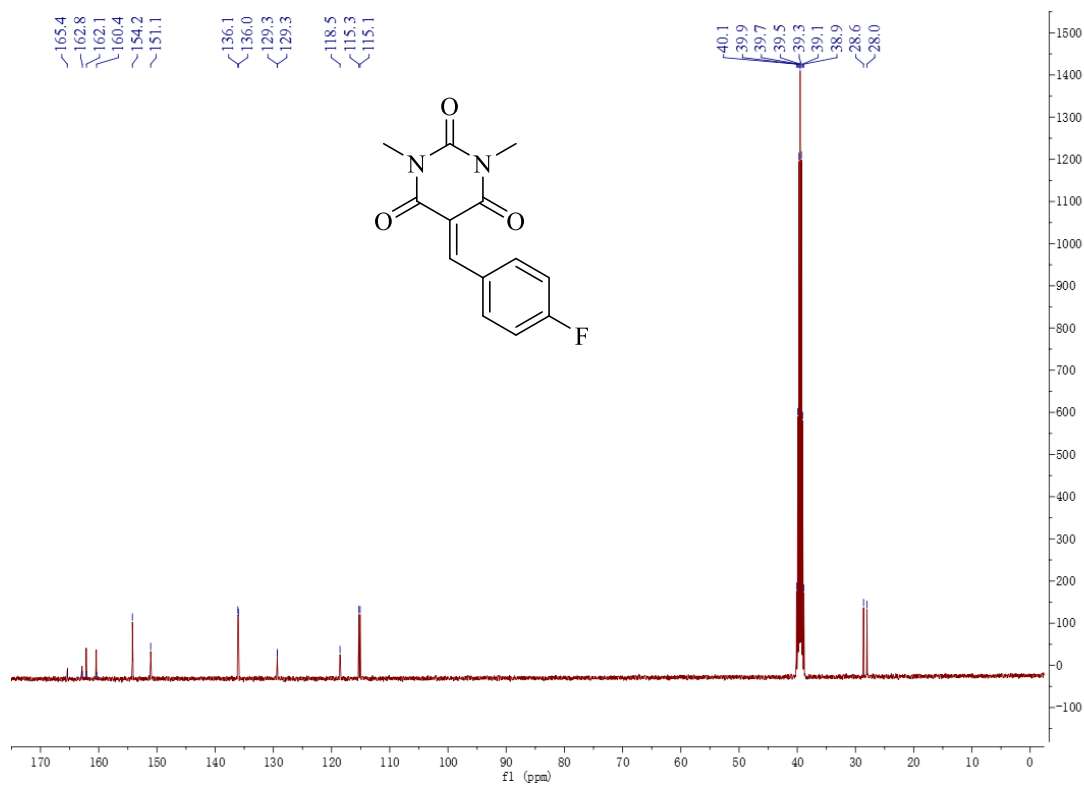


Figure S14. ¹³C NMR of **3g**

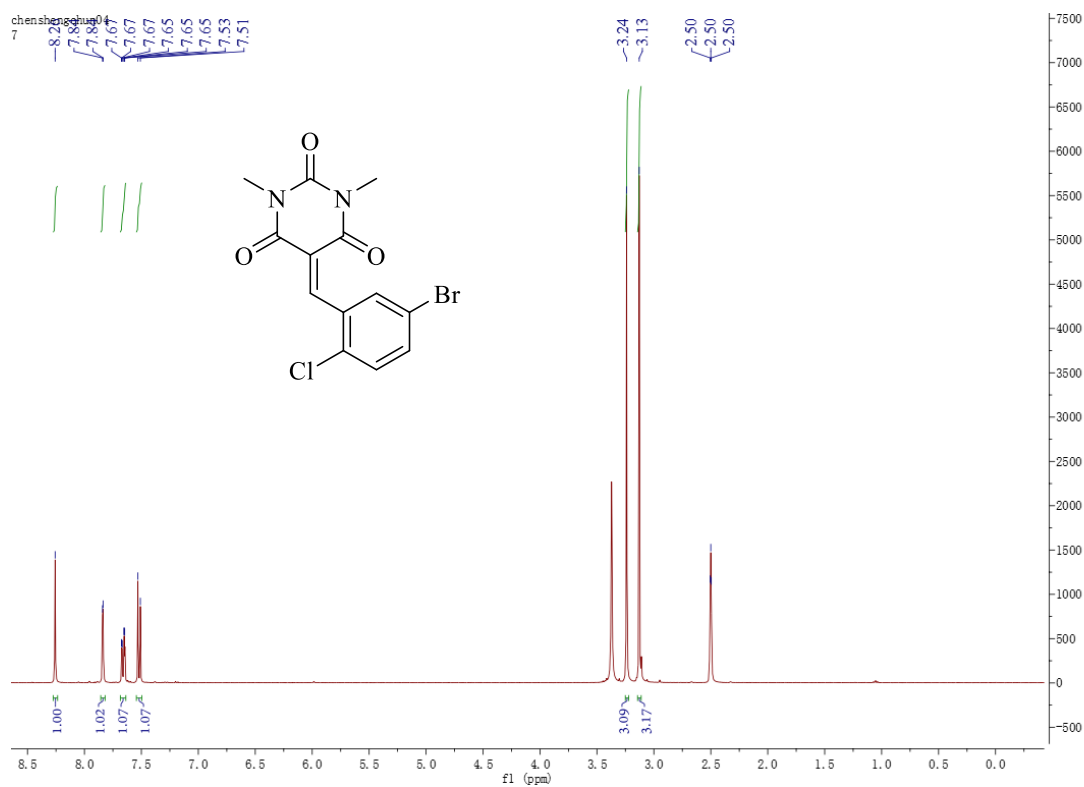


Figure S15. ^1H NMR of **3h**

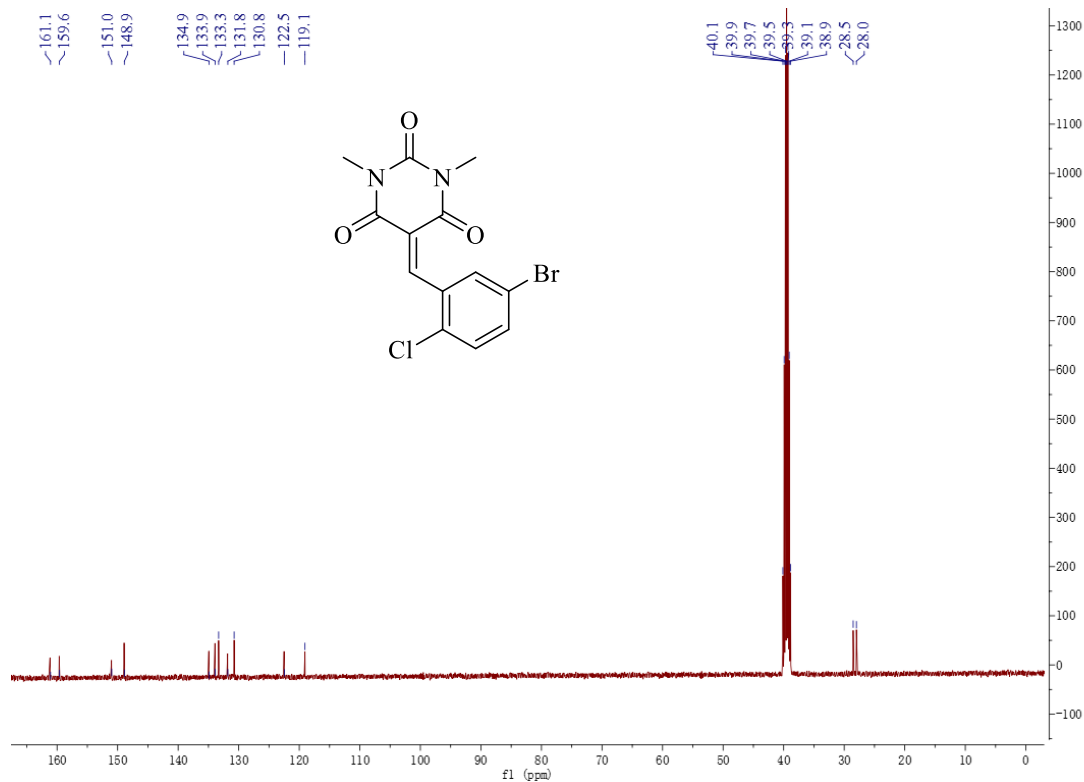


Figure S16. ^{13}C NMR of **3h**

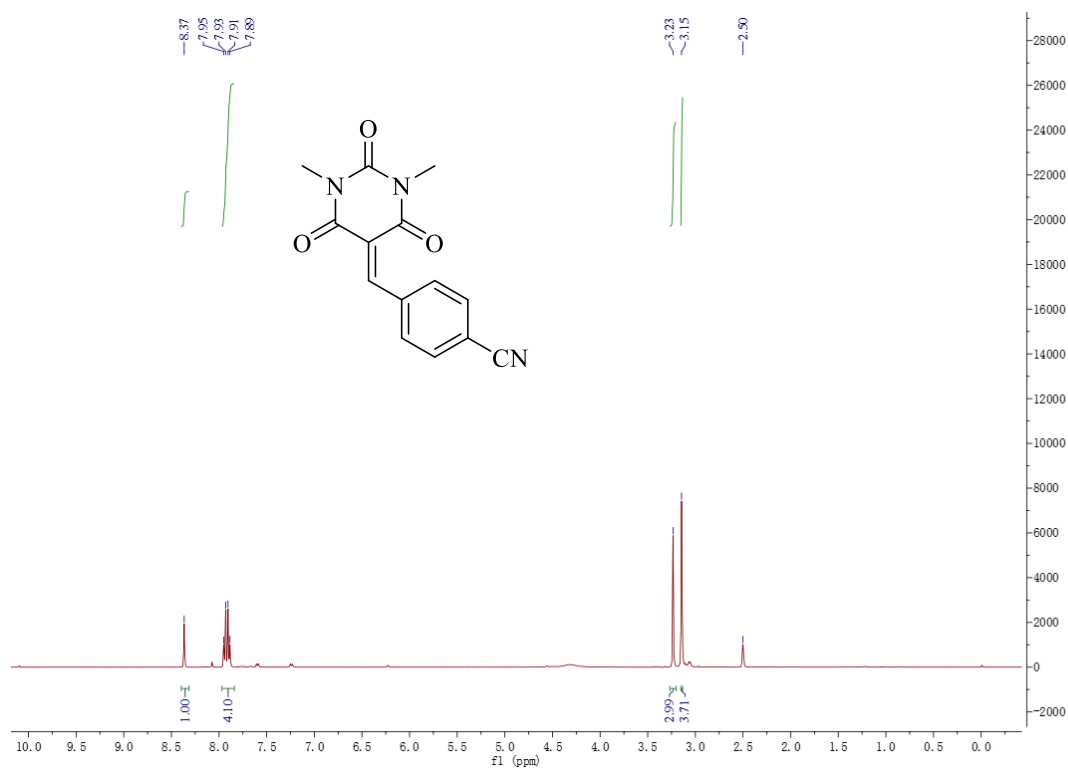


Figure S17. ^1H NMR of **3i**

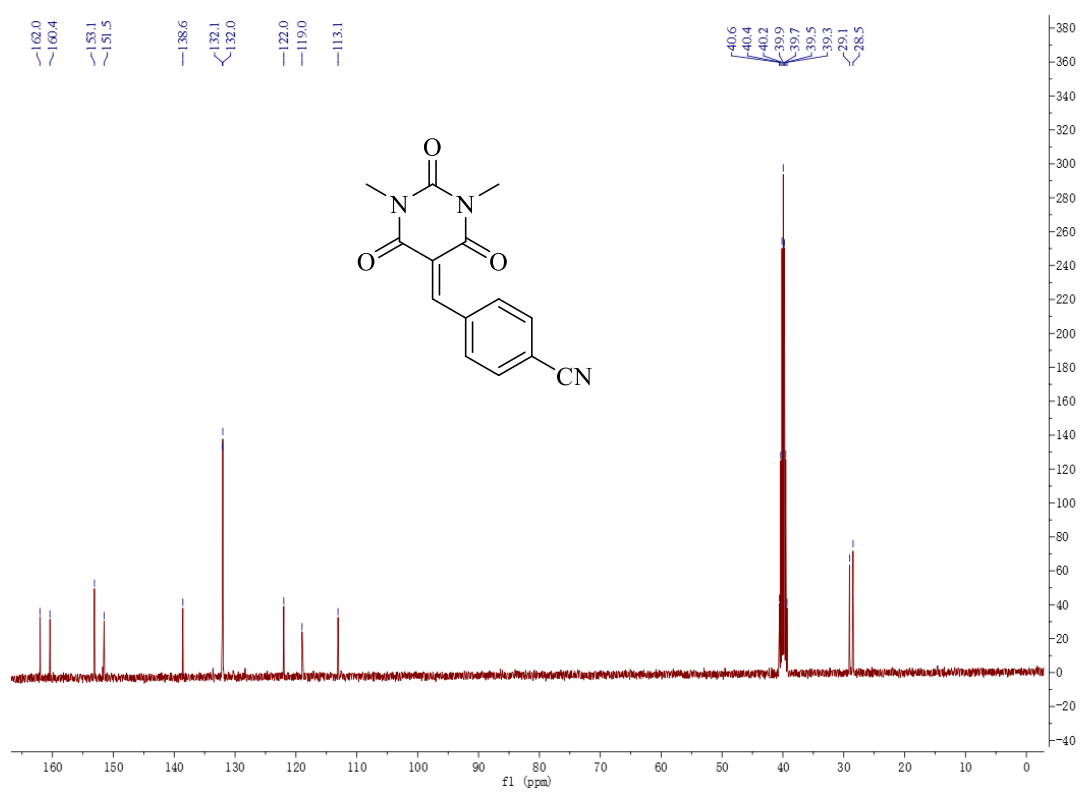


Figure S18. ^{13}C NMR of **3i**

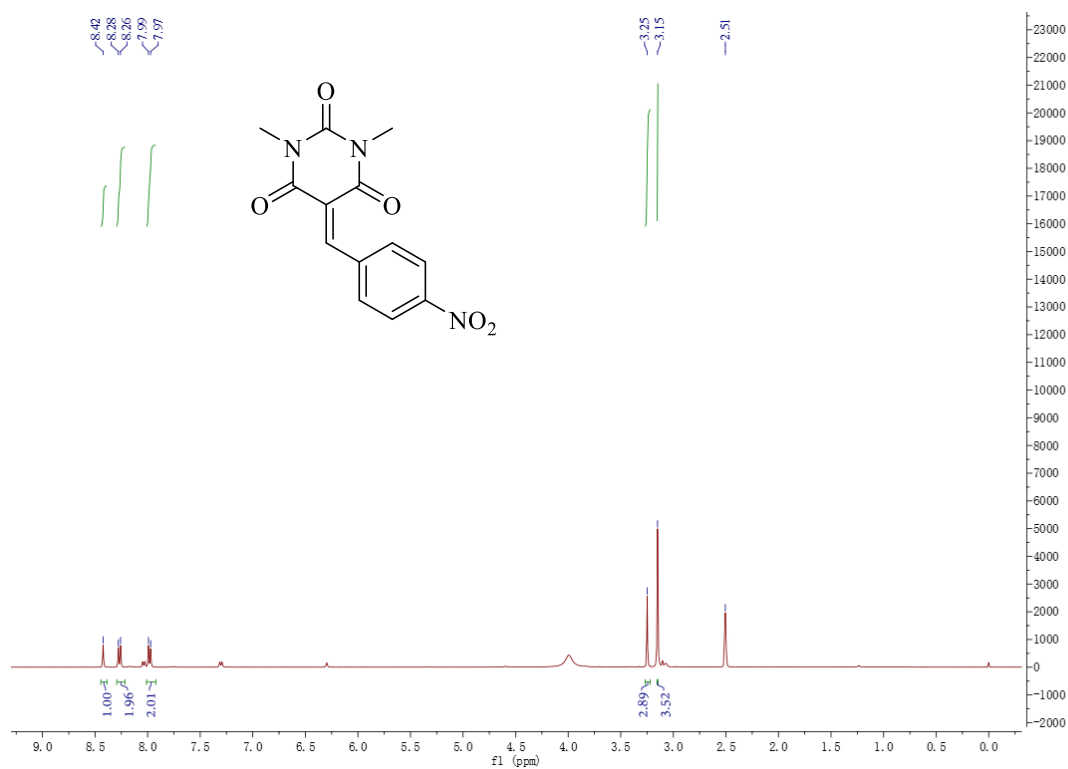


Figure S19. ¹H NMR of **3j**

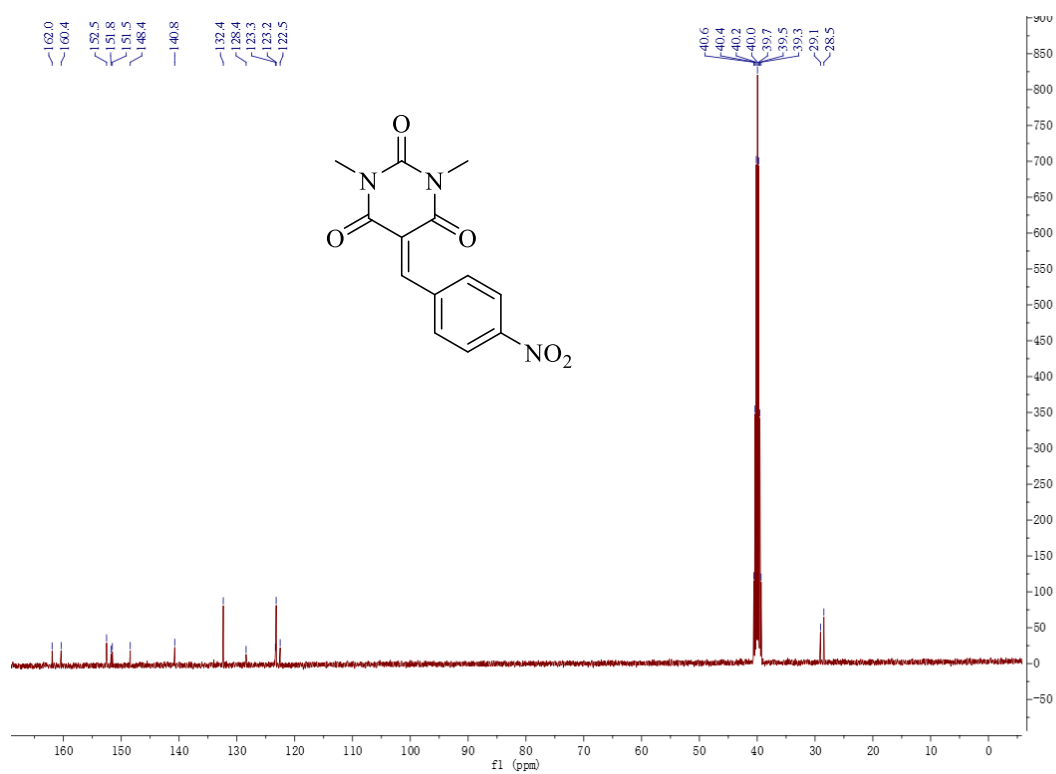


Figure S20. ¹³C NMR of **3j**



Figure S21. ¹H NMR of **3k**

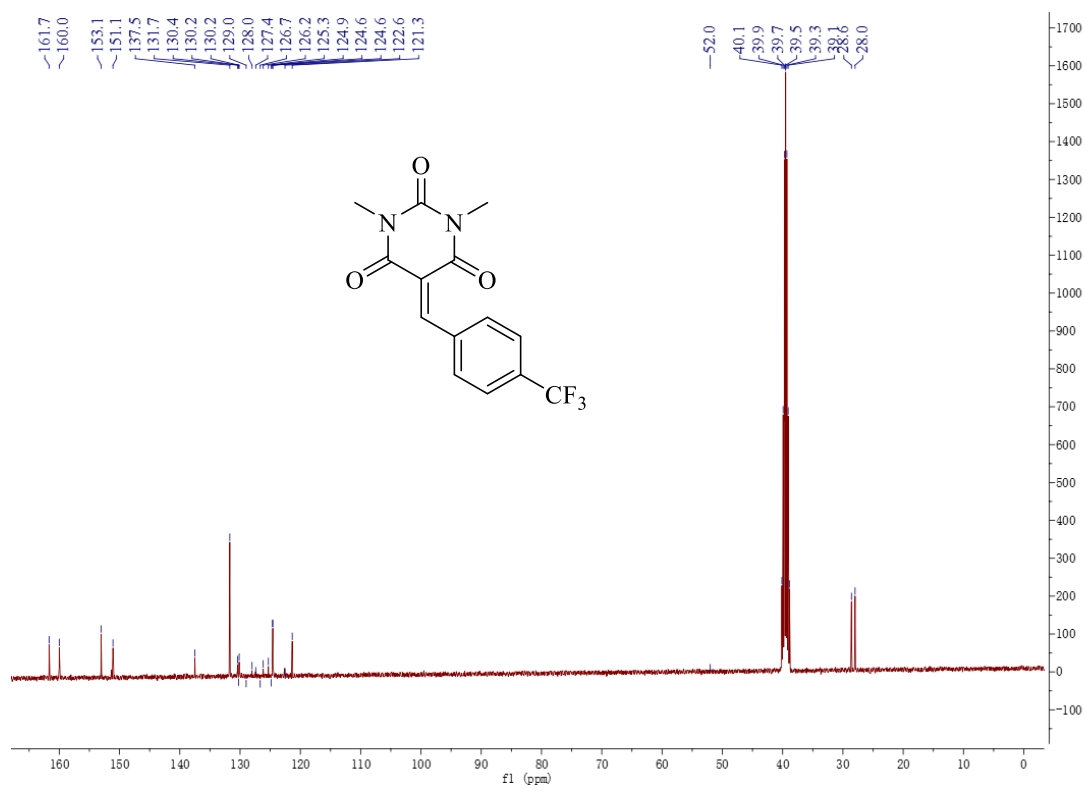


Figure S22. ¹³C NMR of **3k**

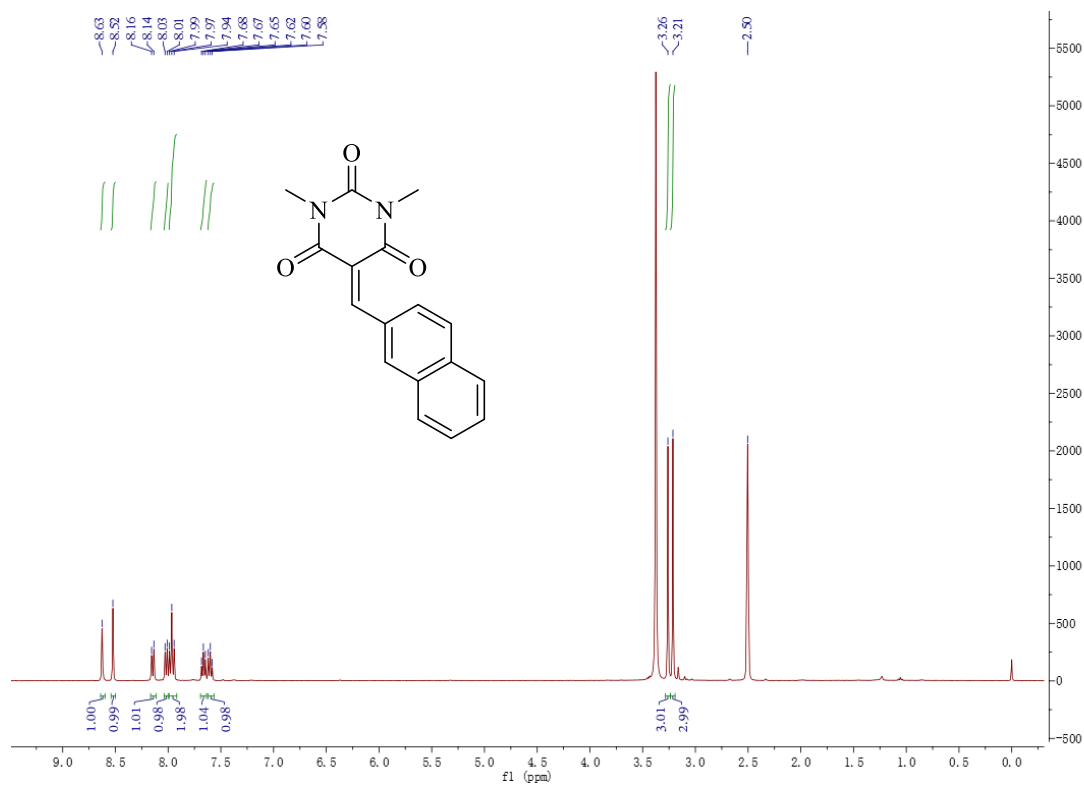


Figure S23. ¹H NMR of **3l**

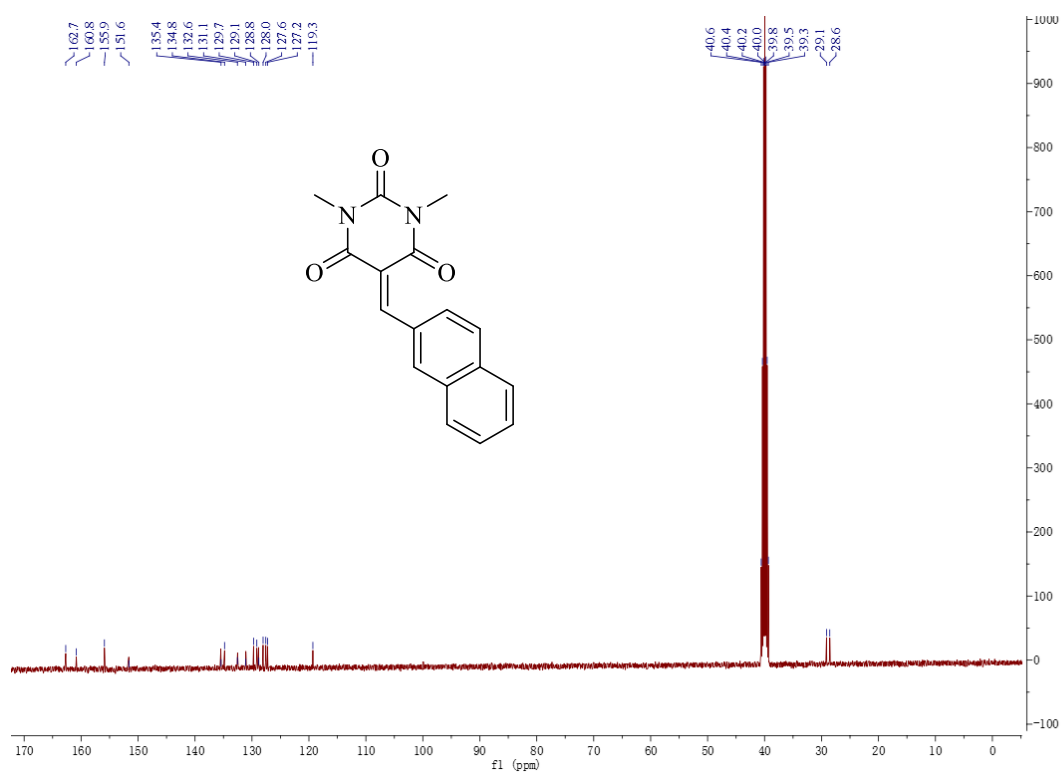


Figure S24. ¹³C NMR of **3l**

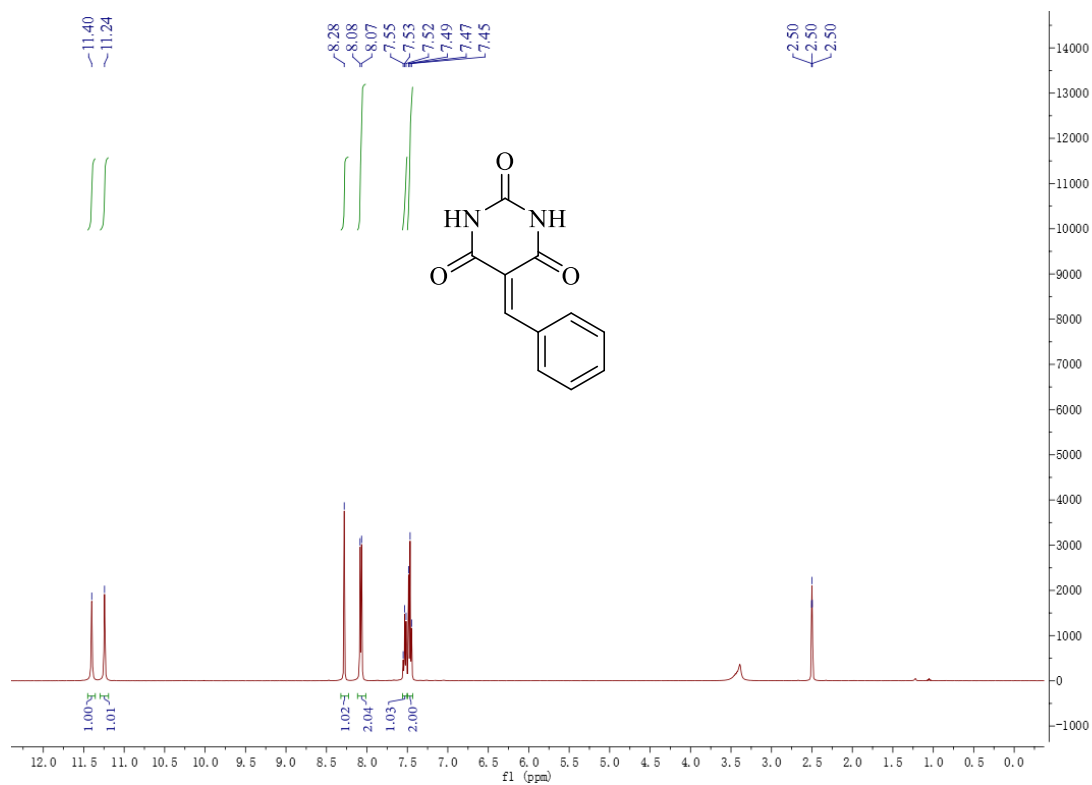


Figure S25. ¹H NMR of **3m**

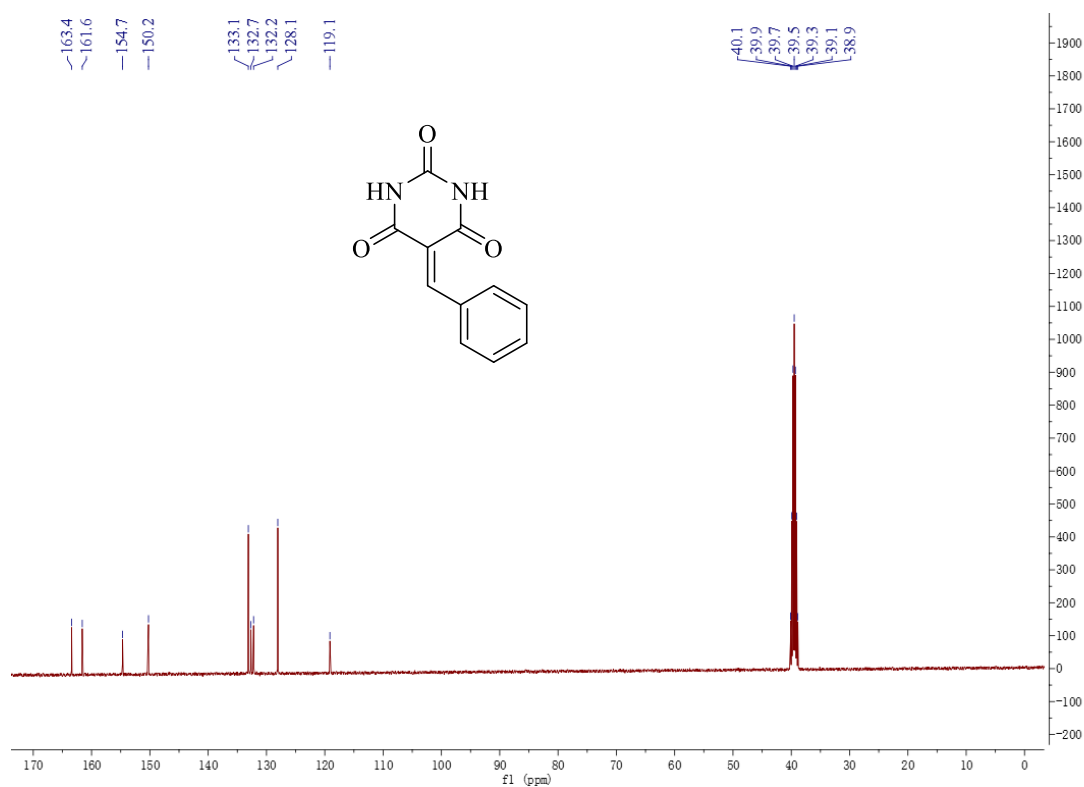


Figure S26. ¹³C NMR of **3m**