Design, synthesis, and toward a side-ring optimization of tricyclic thieno[2,3-*d*]pyrimidin-4(3*H*)-ones and their effect on melanin synthesis in murine B16 cells

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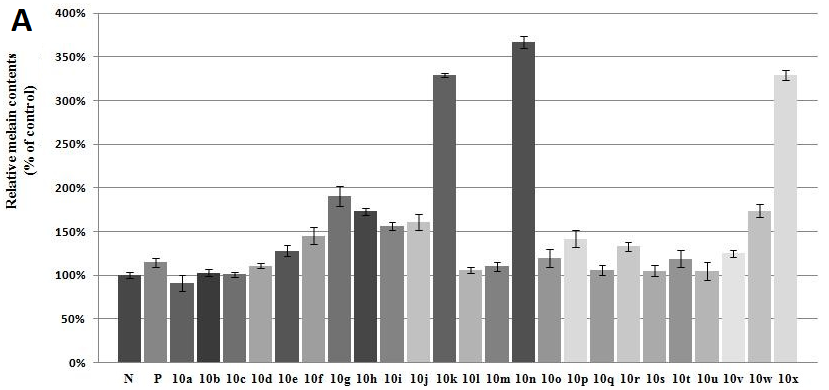
**Supplemental Materials**

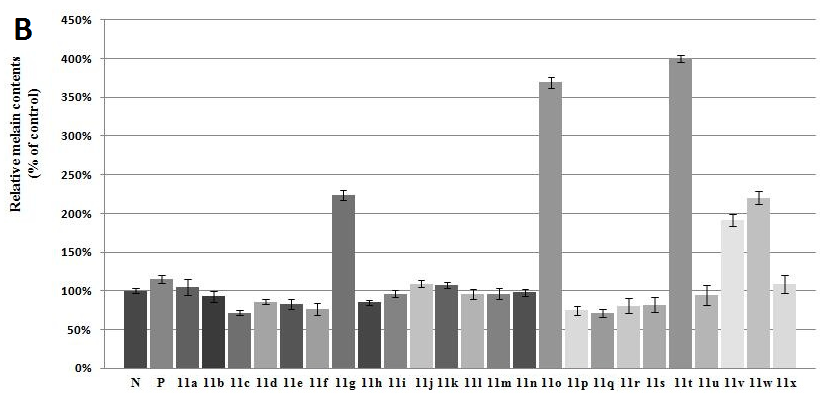
***2-Methyl-3-nitrothieno[2,3-d]dihydropyrrolo[1,2-a]pyrimidin-4-one (6)*.** Yield: 85%, white solid, mp 175-177 °С. 1Н NMR (400 MHz, CDCl3) δ: 4.21 (t, J=7.5 Hz, 2H), 3.28 (td, J=8.4 Hz, J=4.0 Hz, 2H), 2.31 – 2.37 (m, 2H), 2.14 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 187.41, 186.03, 171.84, 154.47, 107.91, 96.5, 47.50, 33.70, 21.61, 18.83.

***2-Methyl-3-nitrothieno[2,3-d]tetrahydroazepino[1,2-a]pyrimidin-4-one (7)*.** Yield: 86%, white solid, mp 117-119 °С. 1Н NMR (400 MHz, CDCl3) δ: 4.36 (t, J=4.8 Hz, 2H), 3.10 (t, J=5.6 Hz, 2H), 2.15 (s, 3H), 1.89 – 1.93 (m, 6H). 13C NMR (100 MHz, CDCl3) δ 186.5, 184.8, 172.0, 155.3, 106.9, 96.2, 42.8, 38.2, 29.4, 26.5, 23.9, 21.6.

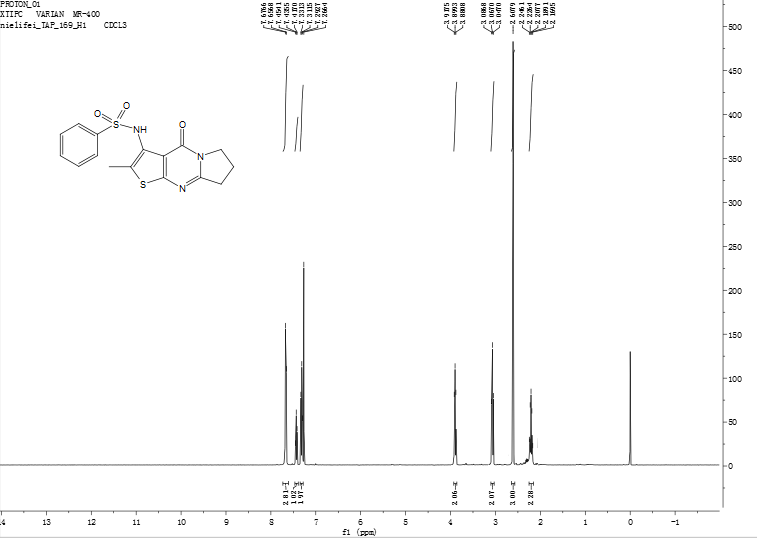


**Figure S 1**. Biologically relevant thieno[2,3-*d*]pyrimidine scaffolds.

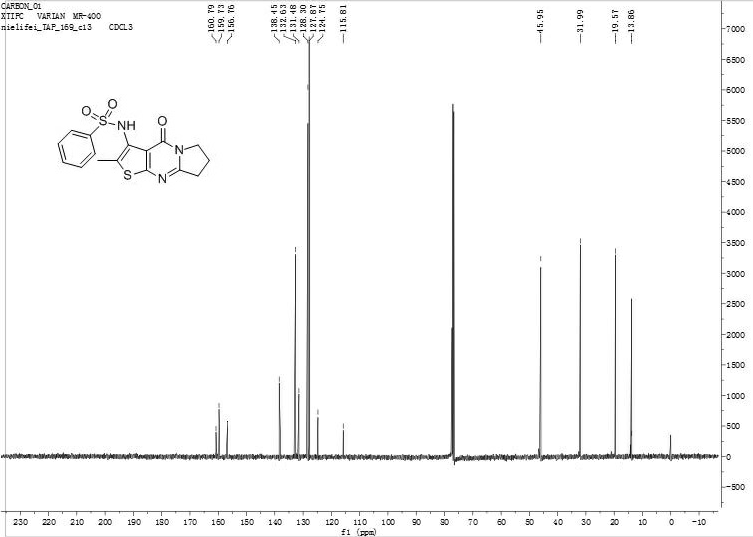




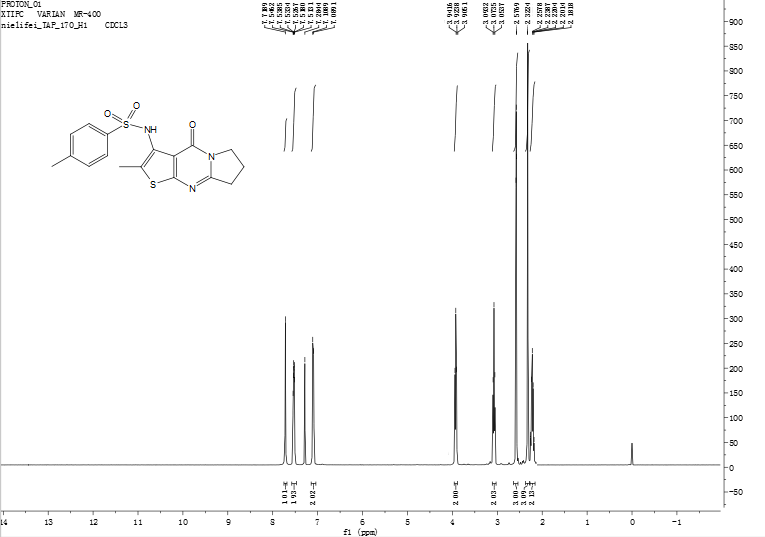
**Figure S 2**. Stimulation of melanin content of B16 cells by compounds **10a-x** (A) and **11a-x** (B). N means negative control; P means positive control (8-MOP); The B16 cells were treated with 50 µM of selected samples for 48 h. After that, melanin content was measured directly. The data are the mean ± SD (bars) of three experiments in duplicate.



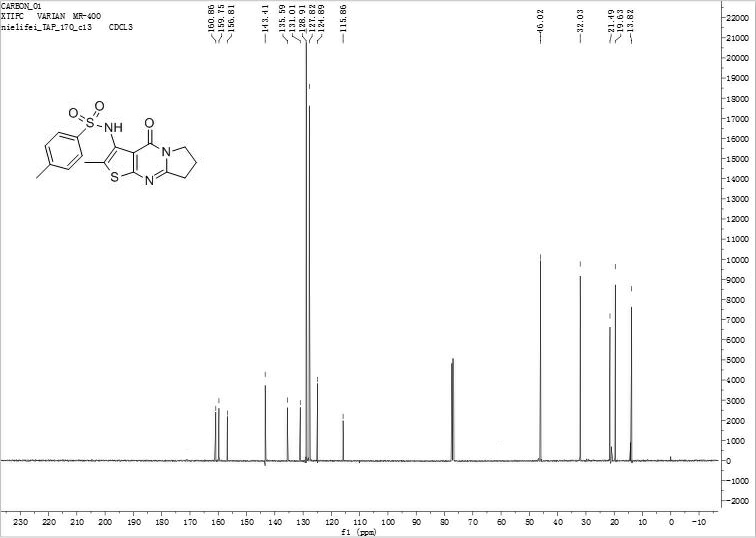
**Figure S 3:** 1H NMR spectrum of compound **10a**



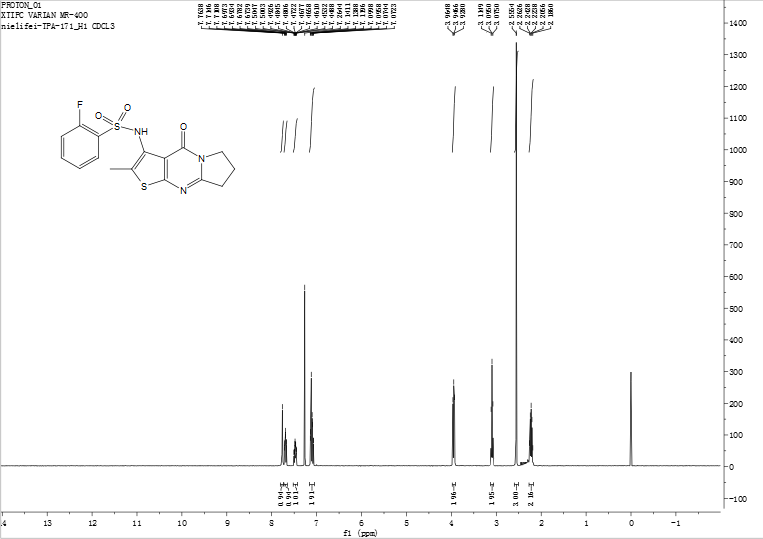
**Figure S 4:** 13C NMR spectrum of compound **10a**



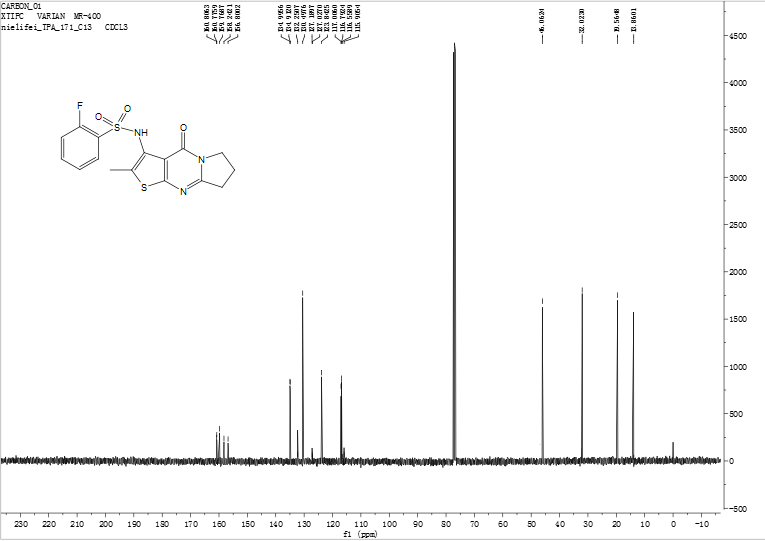
**Figure S 5:** 1H NMR spectrum of compound **10b**



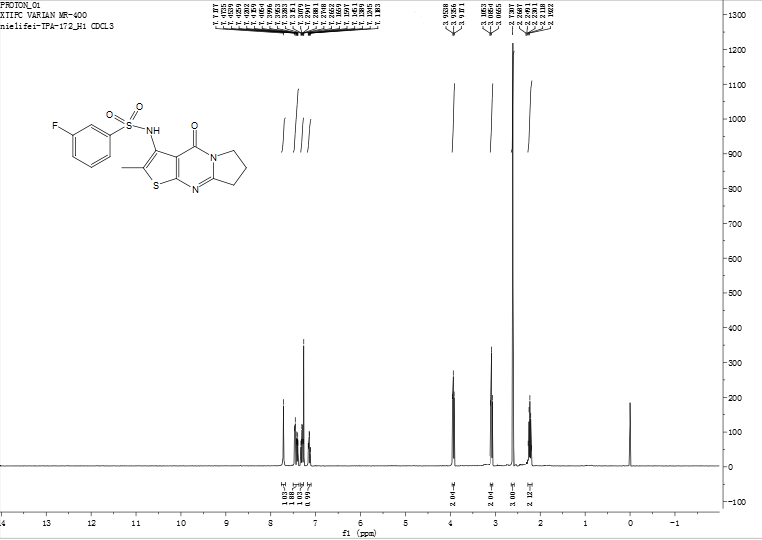
**Figure S 6:** 13C NMR spectrum of compound **10b**



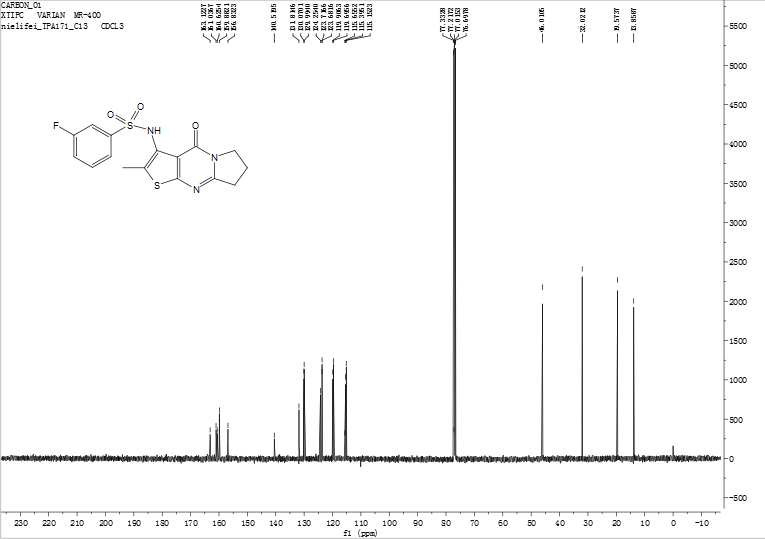
**Figure S 7:** 1H NMR spectrum of compound **10c**



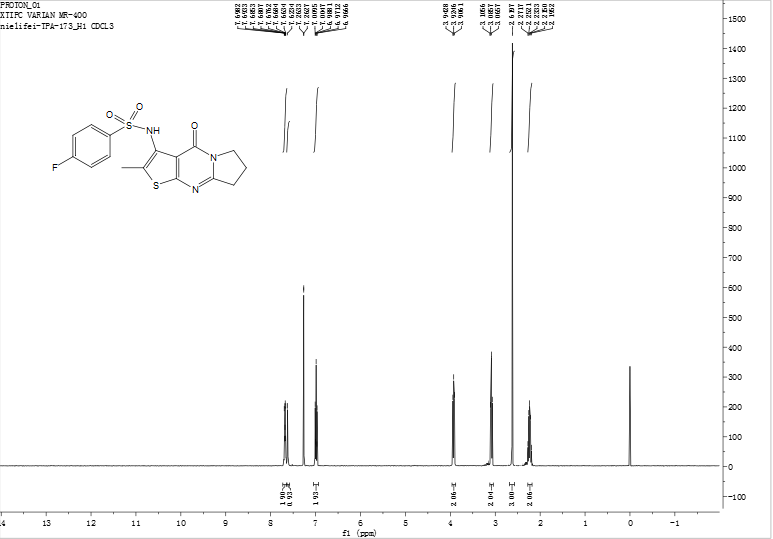
**Figure S 8:** 13C NMR spectrum of compound **10c**

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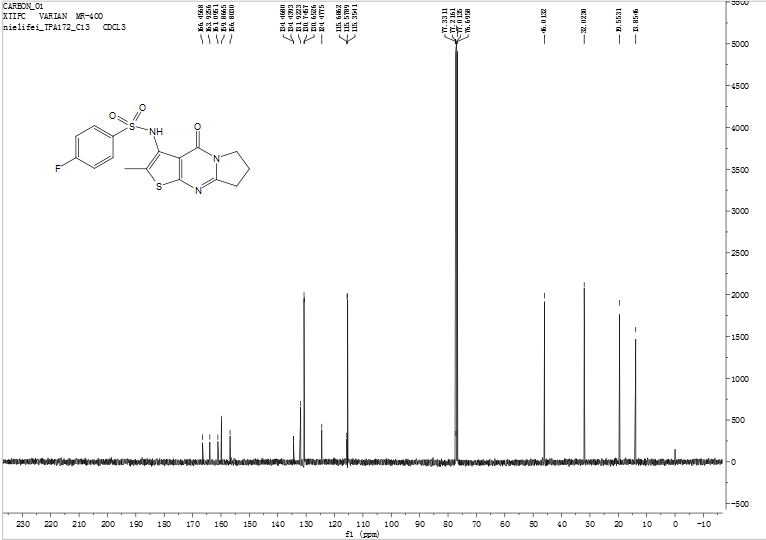
**Figure S 9:** 1H NMR spectrum of compound **10d**



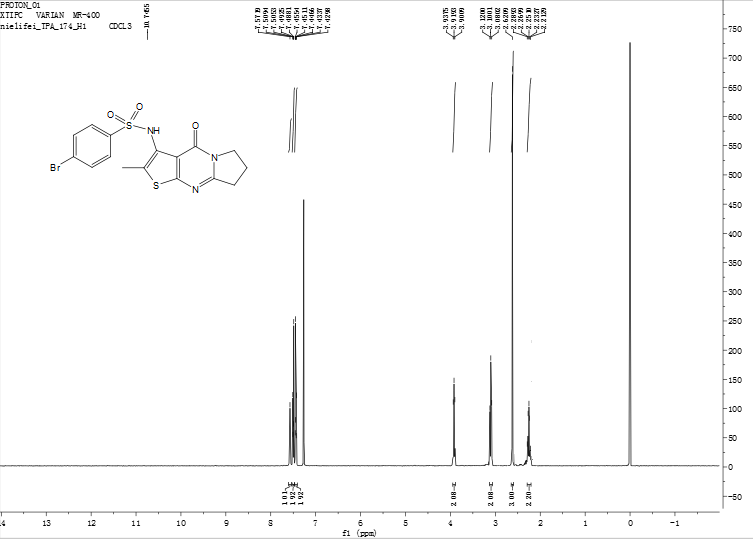
**Figure S 10:** 13C NMR spectrum of compound **10d**



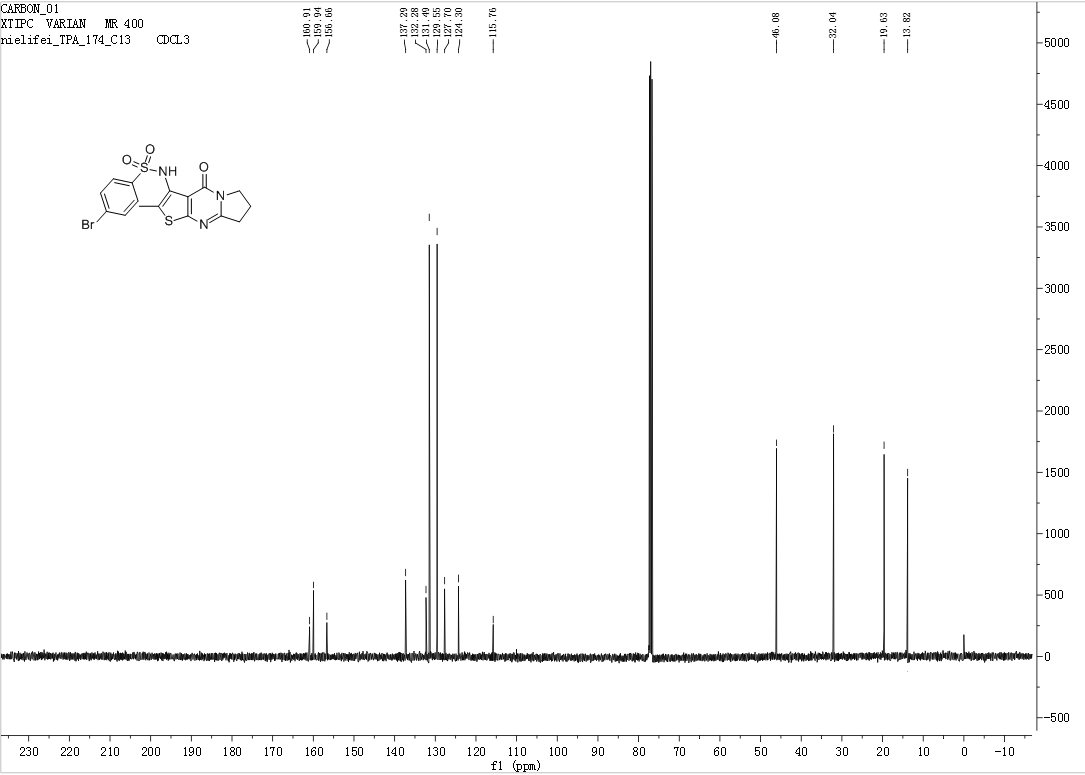
**Figure S 11:** 1H NMR spectrum of compound **10e**



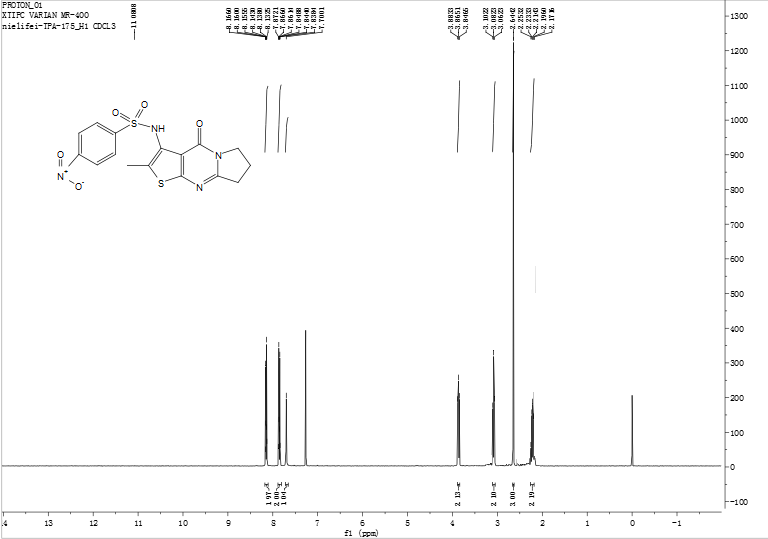
**Figure S 12:** 13C NMR spectrum of compound **10e**



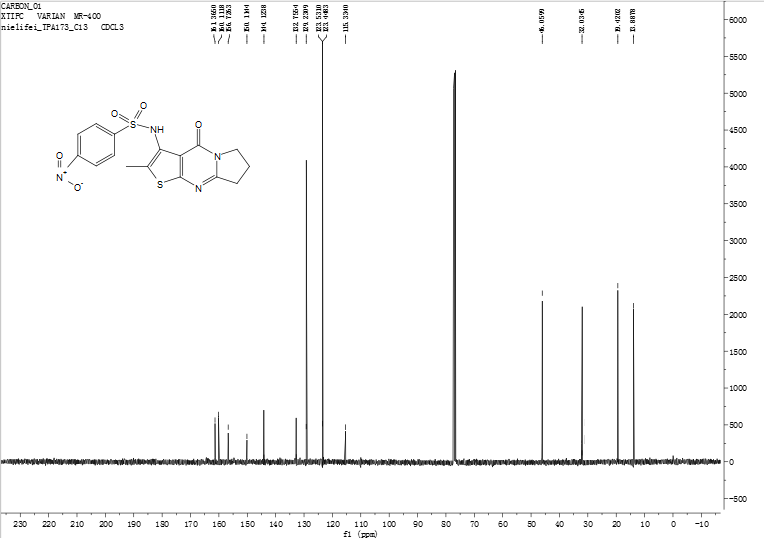
**Figure S 13:** 1H NMR spectrum of compound **10f**



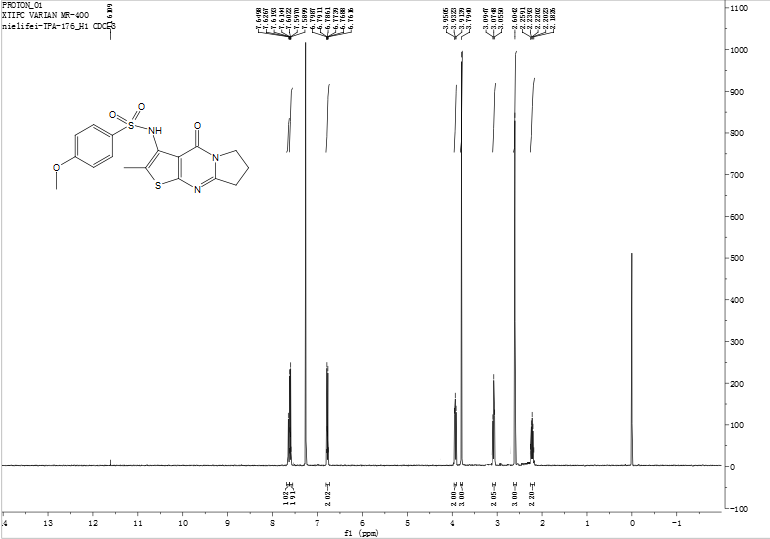
**Figure S 14:** 13C NMR spectrum of compound **10f**

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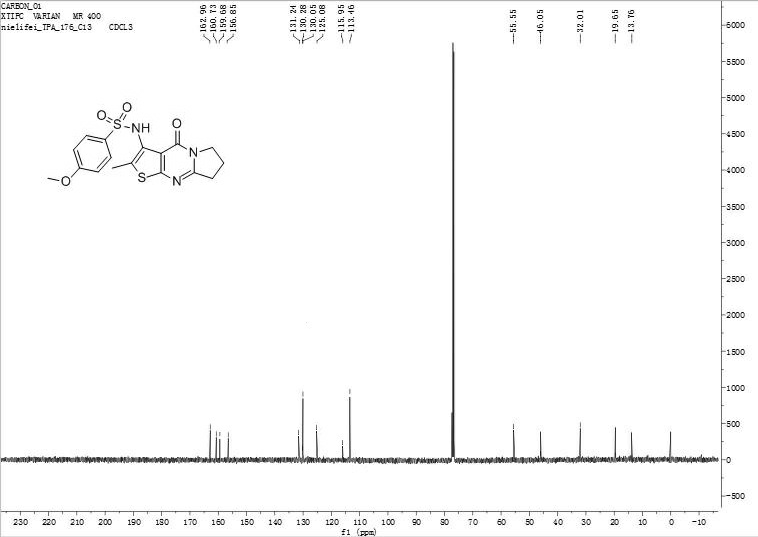
**Figure S 15:** 1H NMR spectrum of compound **10g**



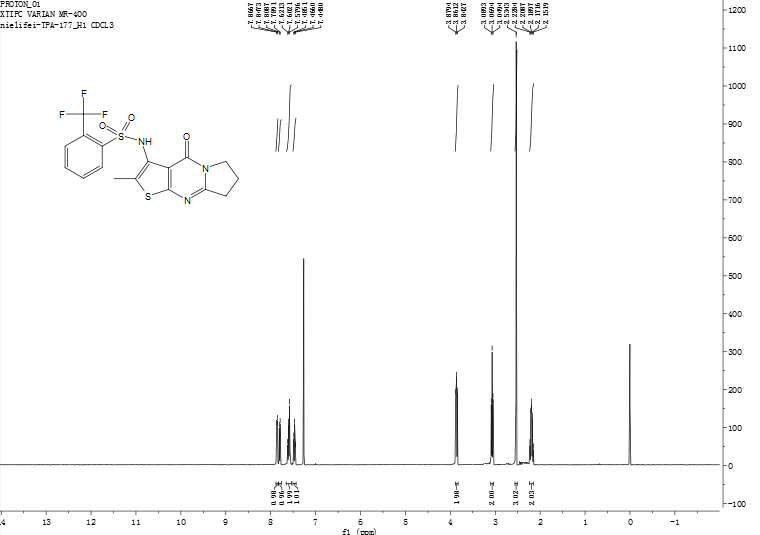
**Figure S 16:** 13C NMR spectrum of compound **10g**

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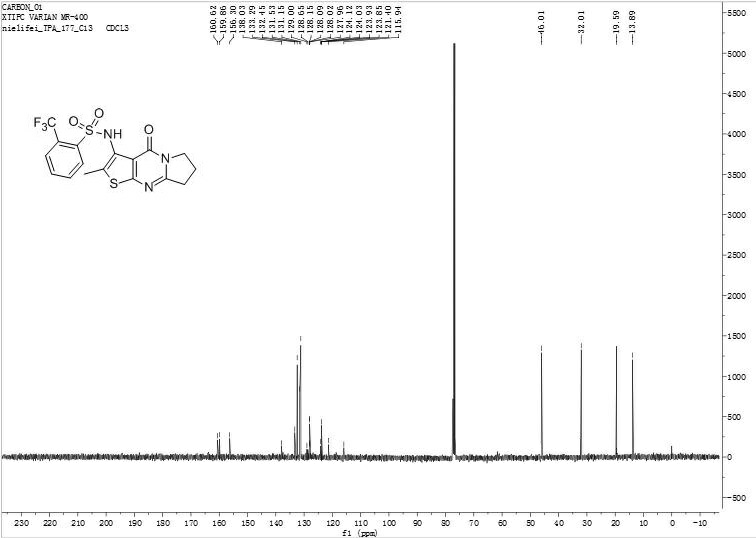
**Figure S 17:** 1H NMR spectrum of compound **10h**

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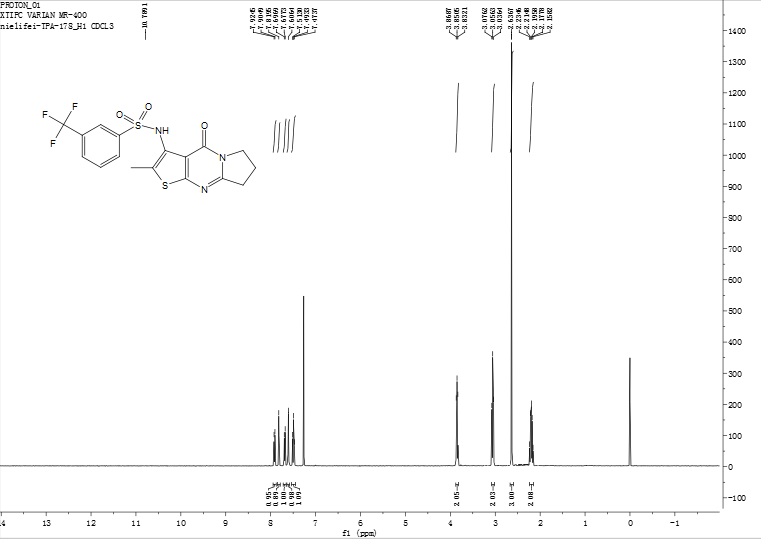
**Figure S 18:** 13C NMR spectrum of compound **10h**

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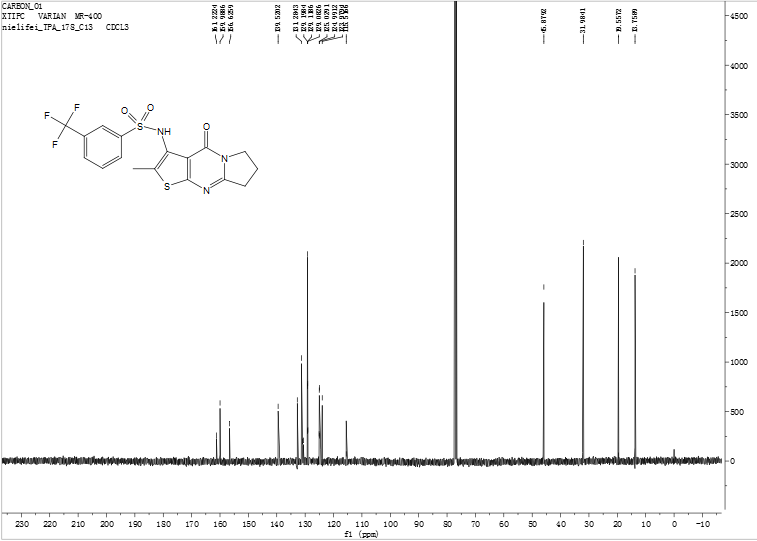
**Figure S 19:** 1H NMR spectrum of compound **10i**

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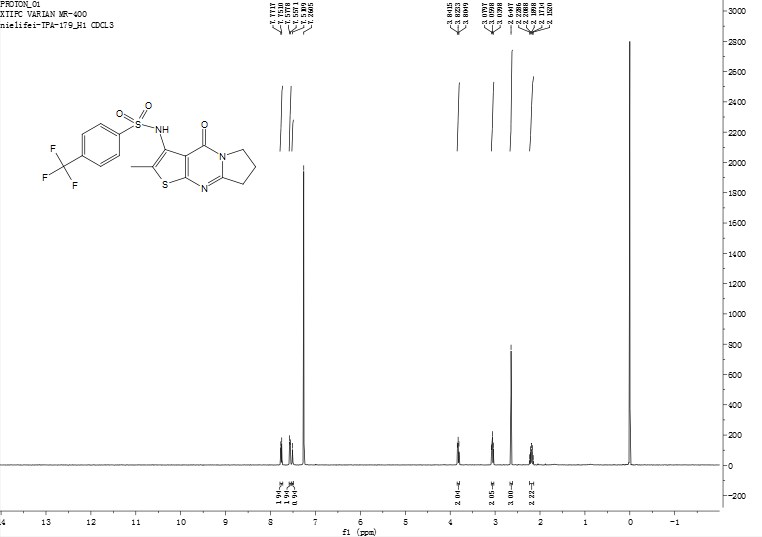
**Figure S 20:** 13C NMR spectrum of compound **10i**

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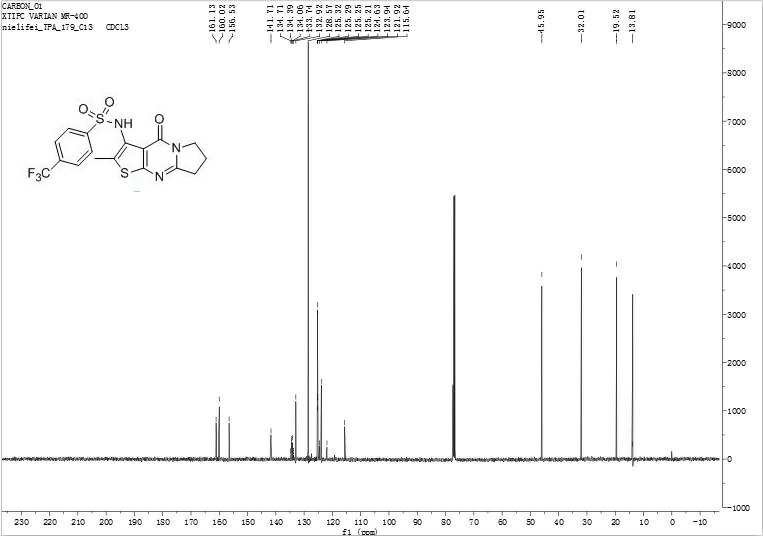
**Figure S 21:** 1H NMR spectrum of compound **10j**



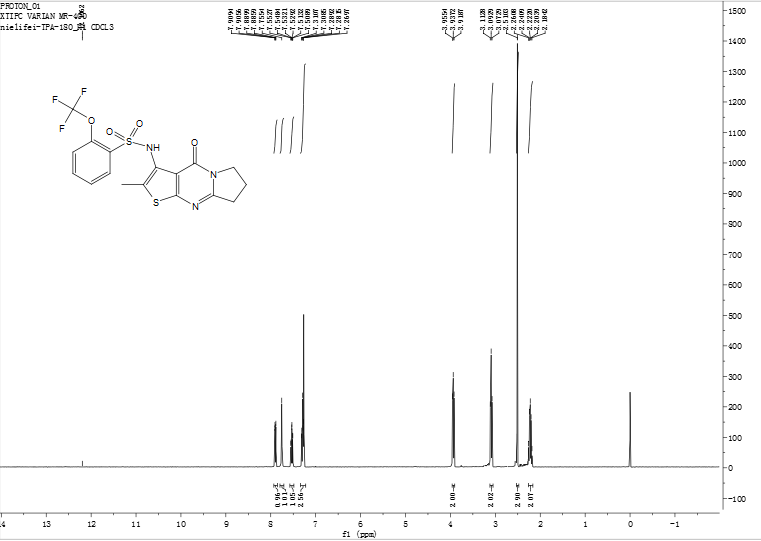
**Figure S 22:** 13C NMR spectrum of compound **10j**



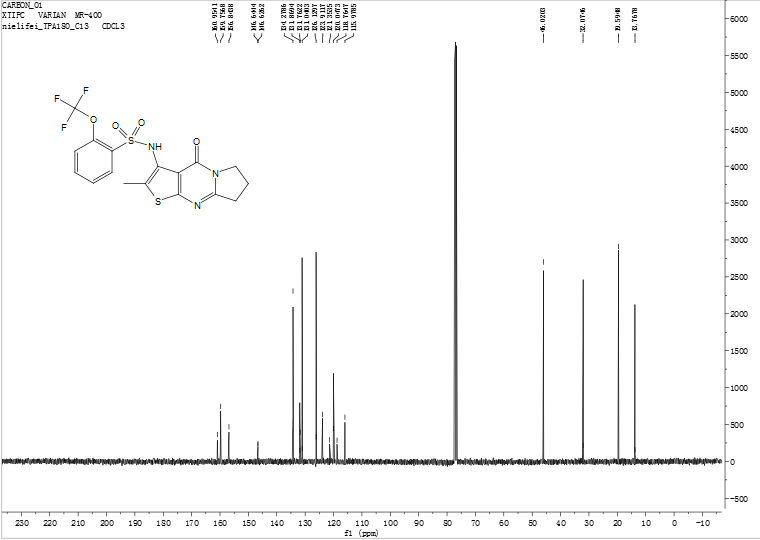
**Figure S 23:** 1H NMR spectrum of compound **10k**



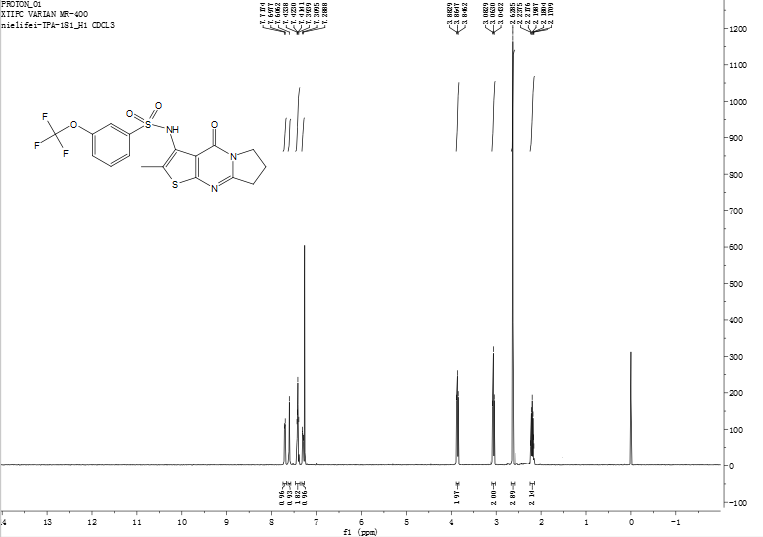
**Figure S 24:** 13C NMR spectrum of compound **10k**



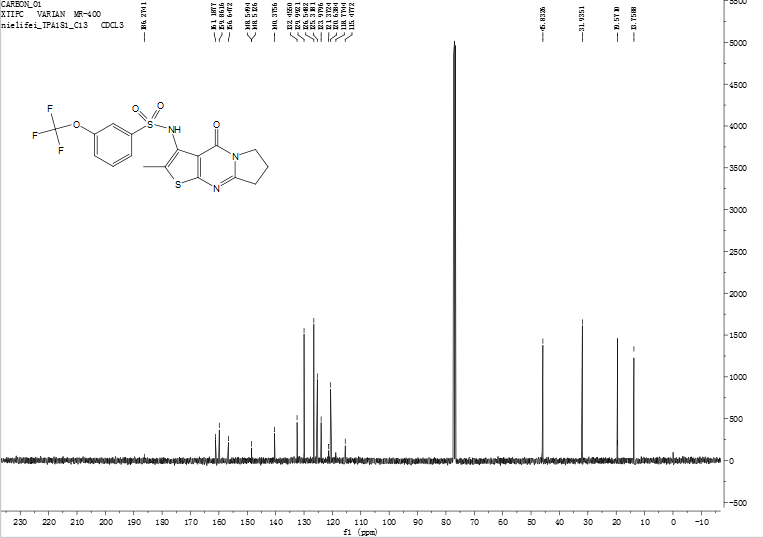
**Figure S 25:** 1H NMR spectrum of compound **10l**



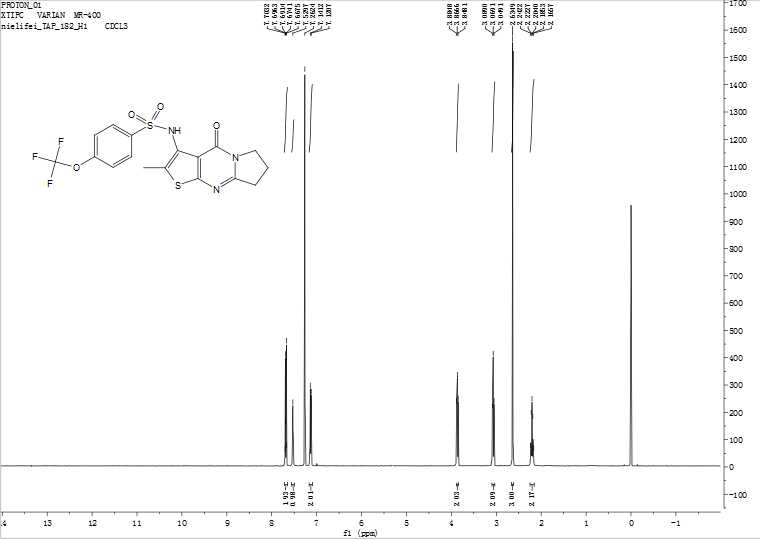
**Figure S 26:** 13C NMR spectrum of compound **10l**

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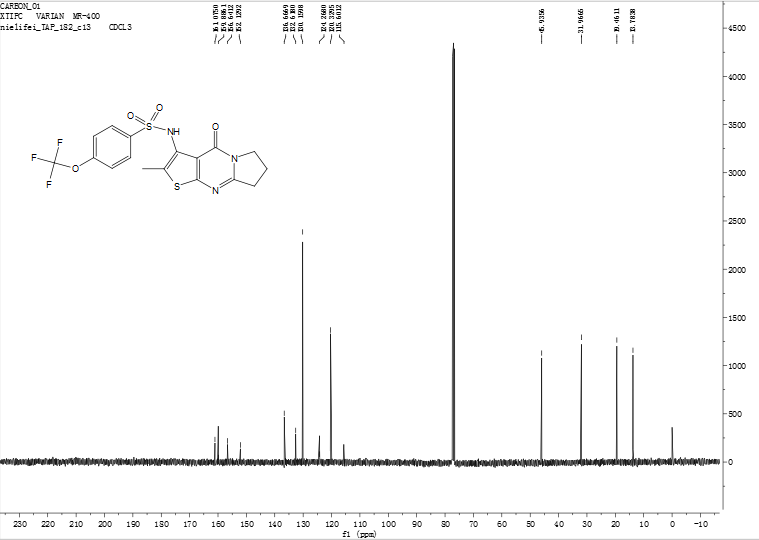
**Figure S 27:** 1H NMR spectrum of compound **10m**



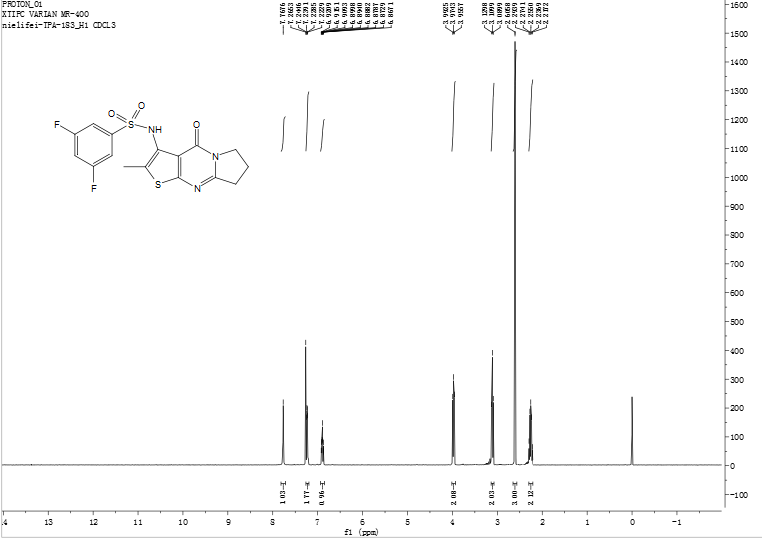
**Figure S 28:** 13C NMR spectrum of compound **10m**



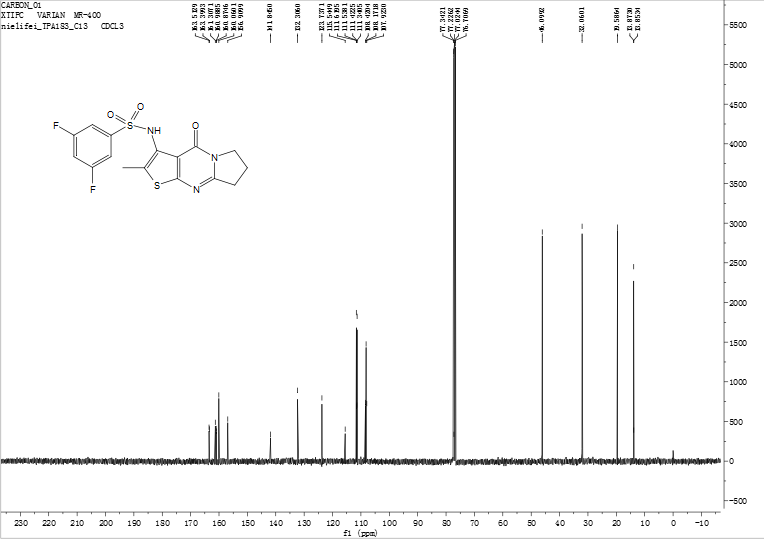
**Figure S 29:** 1H NMR spectrum of compound **10n**



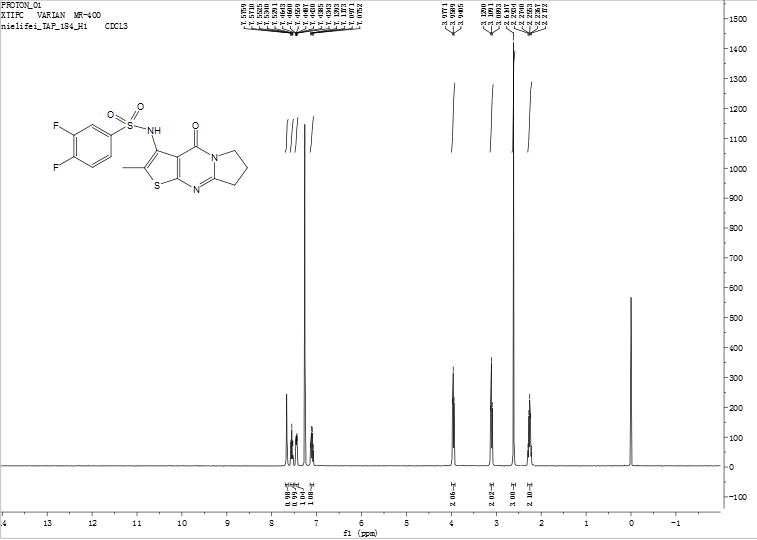
**Figure S 30:** 13C NMR spectrum of compound **10n**



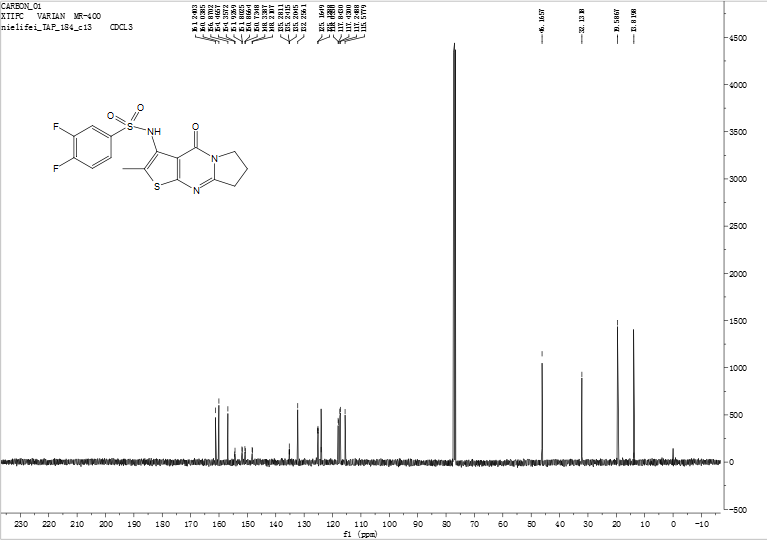
**Figure S 31:** 1H NMR spectrum of compound **10o**



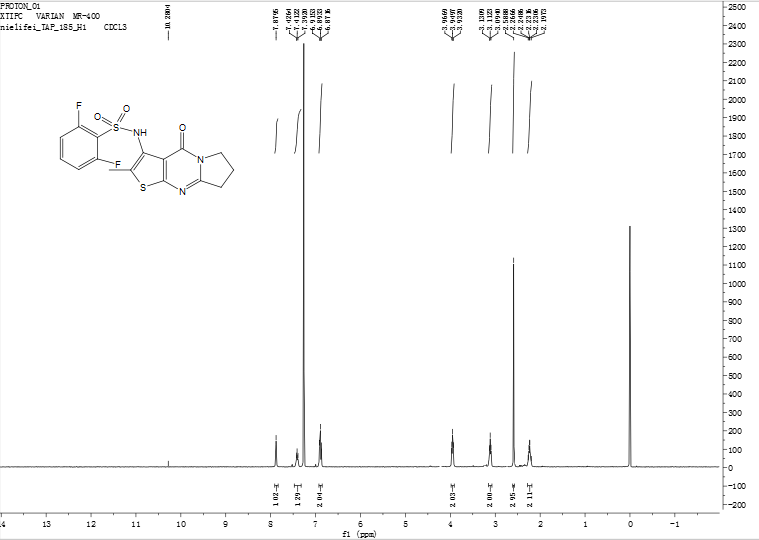
**Figure S 32:** 13C NMR spectrum of compound **10o**

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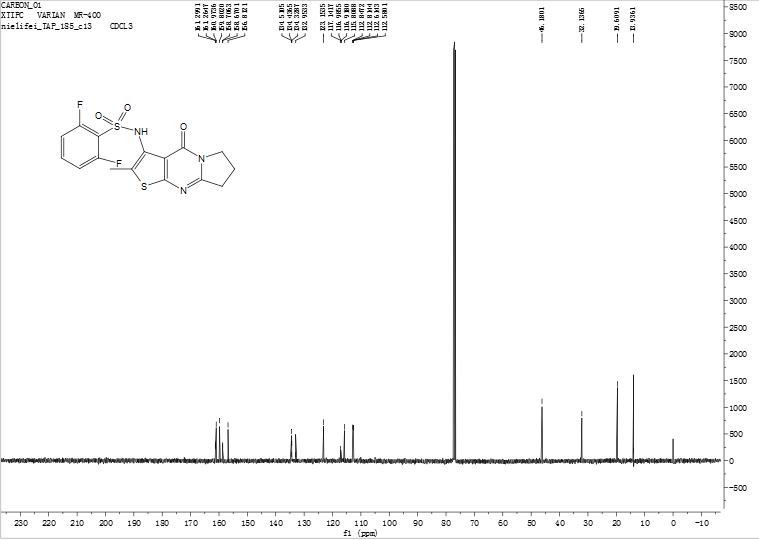
**Figure S 33:** 1H NMR spectrum of compound **10p**



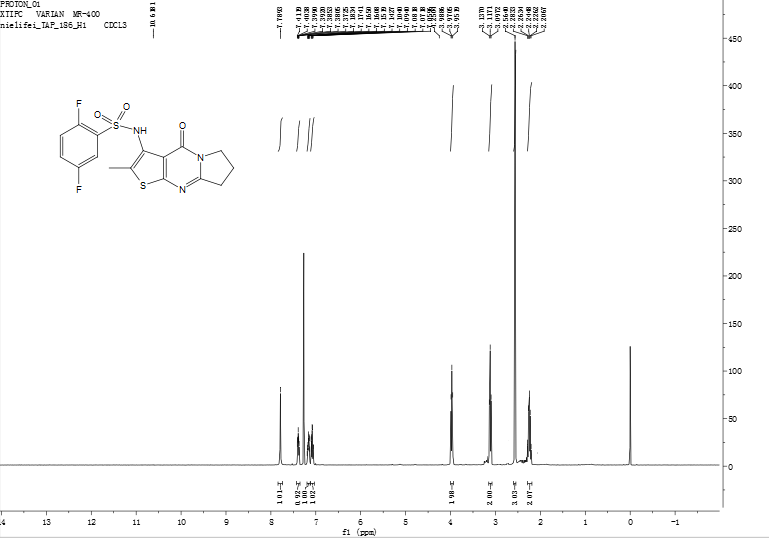
**Figure S 34:** 13C NMR spectrum of compound **10p**



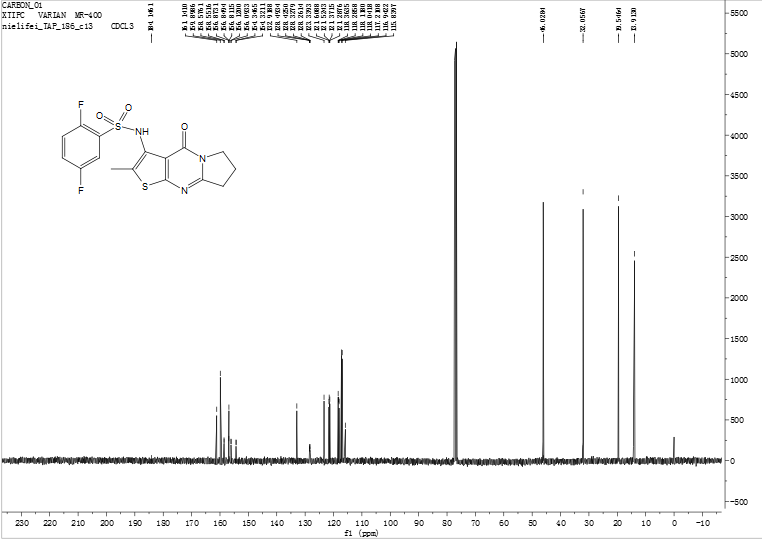
**Figure S 35:** 1H NMR spectrum of compound **10q**



**Figure S 36:** 13C NMR spectrum of compound **10q**



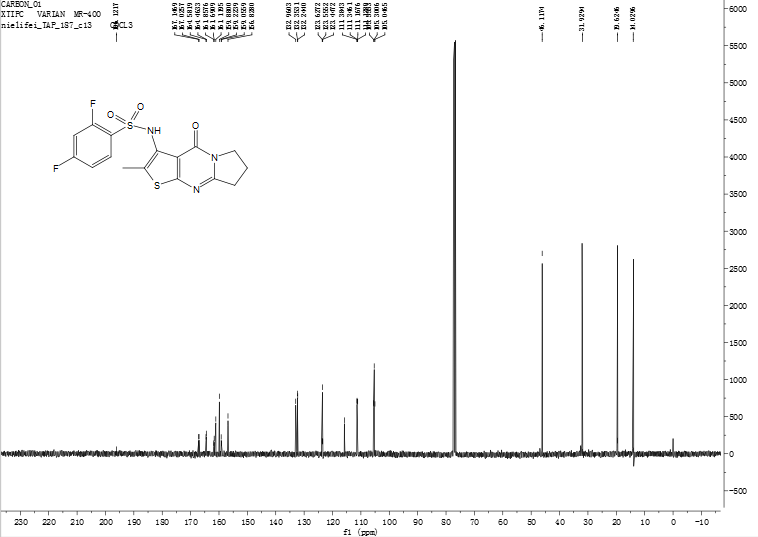
**Figure S 37:** 1H NMR spectrum of compound **10r**



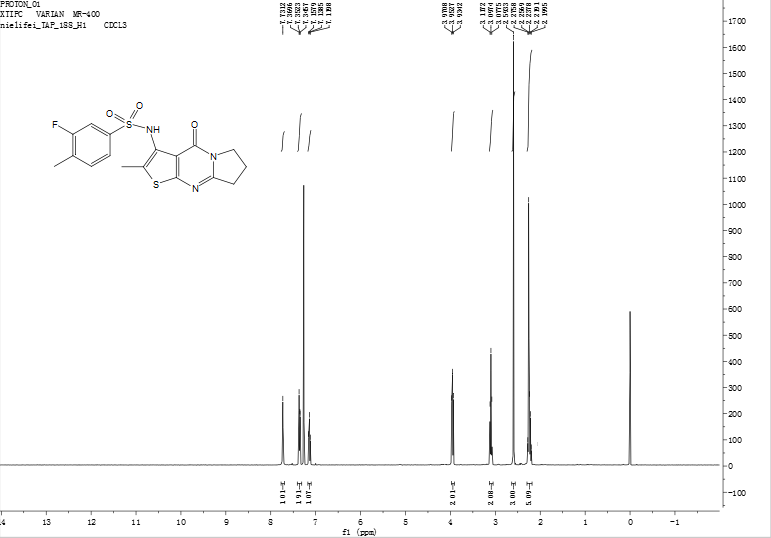
**Figure S 38:** 13C NMR spectrum of compound **10r**



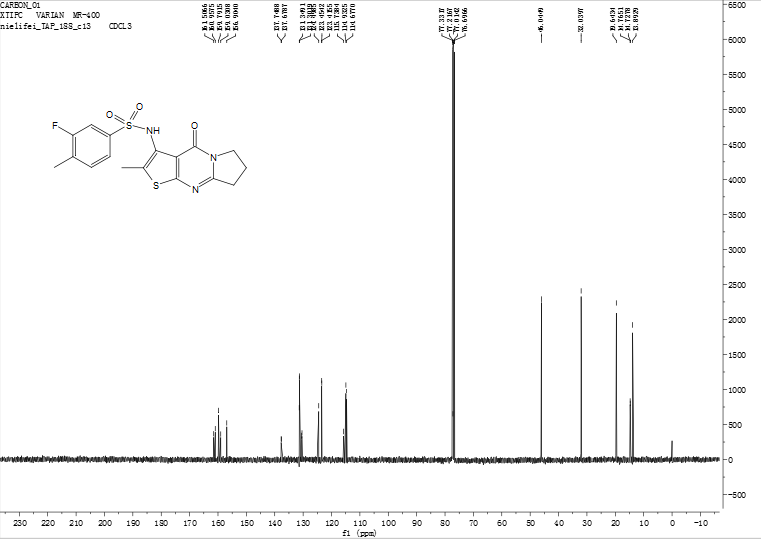
**Figure S 39:** 1H NMR spectrum of compound **10s**



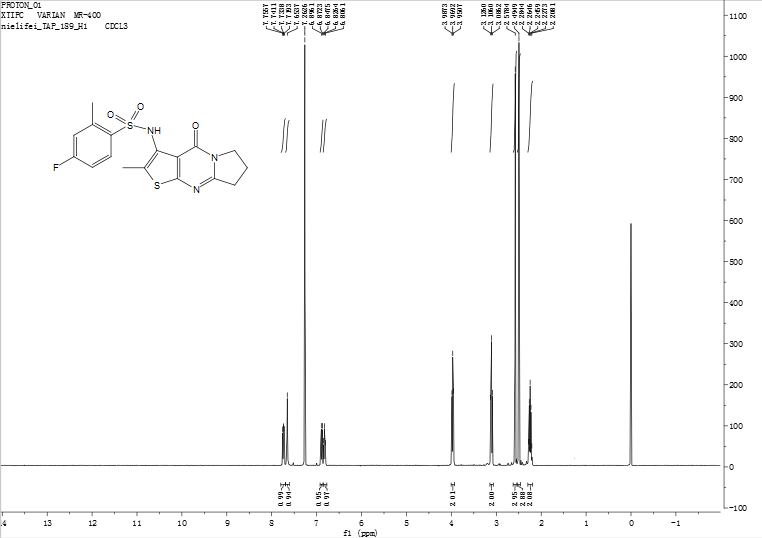
**Figure S 40:** 13C NMR spectrum of compound **10s**



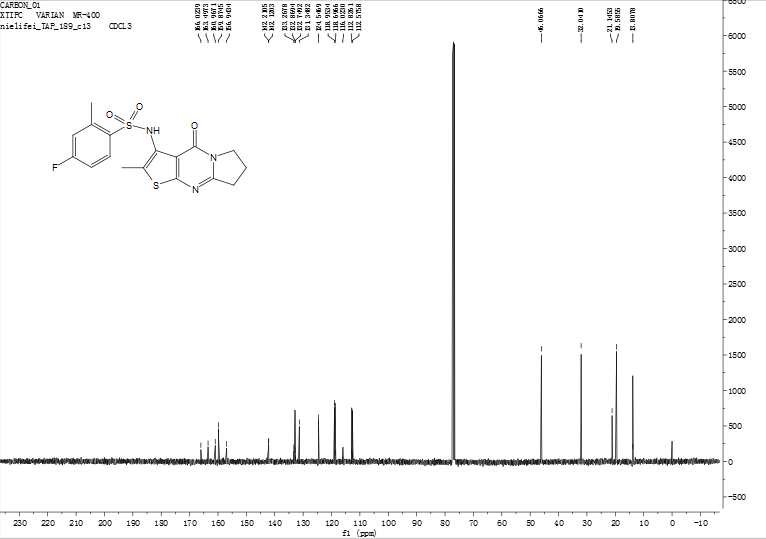
**Figure S 41:** 1H NMR spectrum of compound **10t**



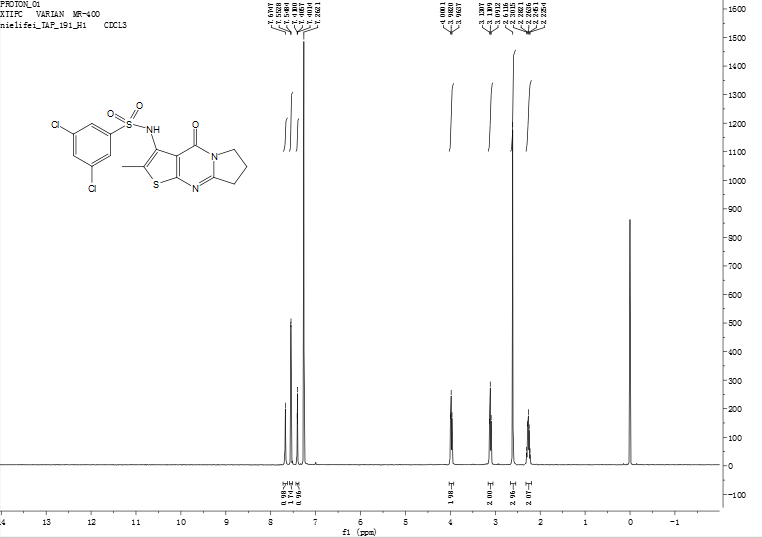
**Figure S 42:** 13C NMR spectrum of compound **10t**



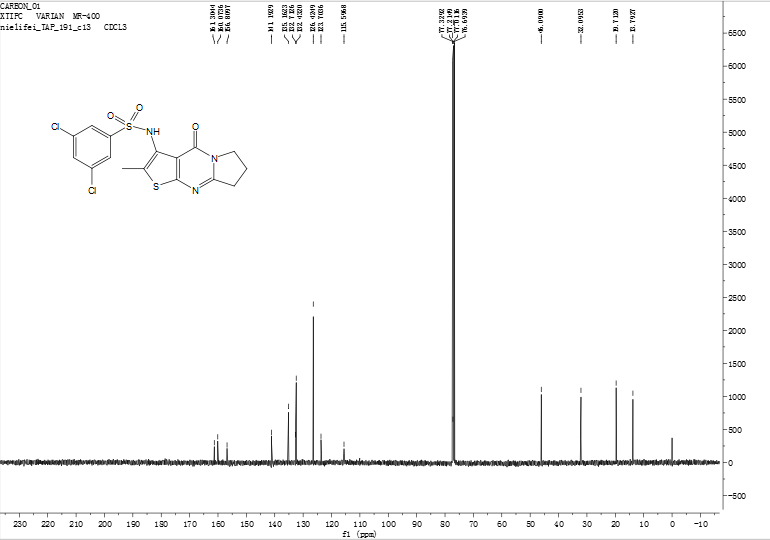
**Figure S 43:** 1H NMR spectrum of compound **10u**



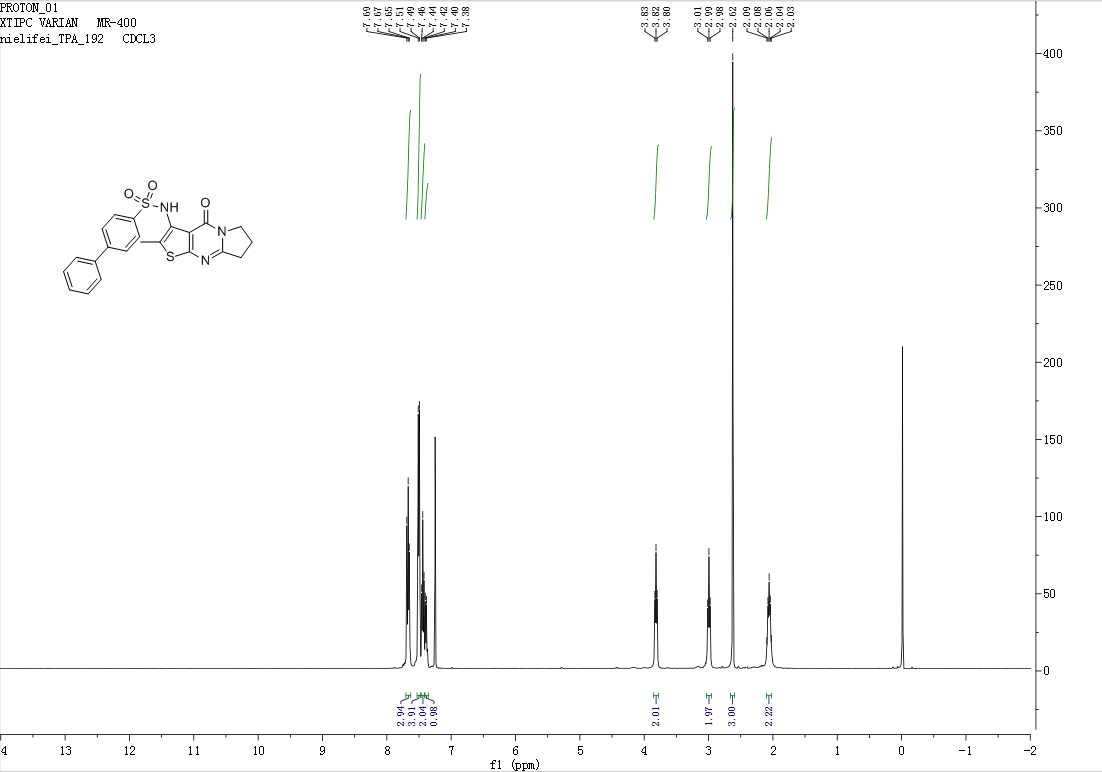
**Figure S 44:** 13C NMR spectrum of compound **10u**



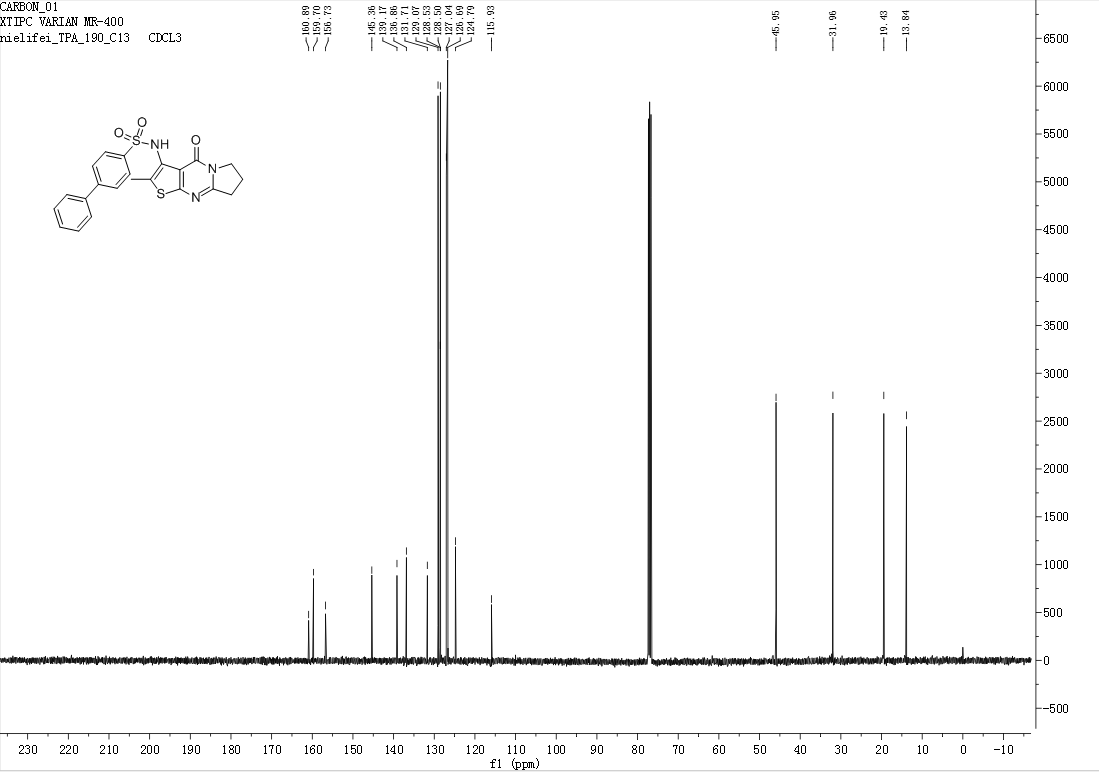
**Figure S 45:** 1H NMR spectrum of compound **10w**



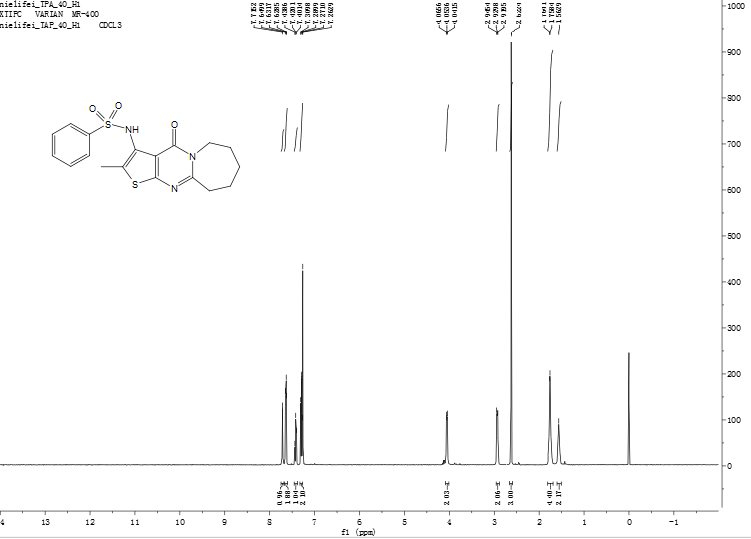
**Figure S 46:** 13C NMR spectrum of compound **10w**



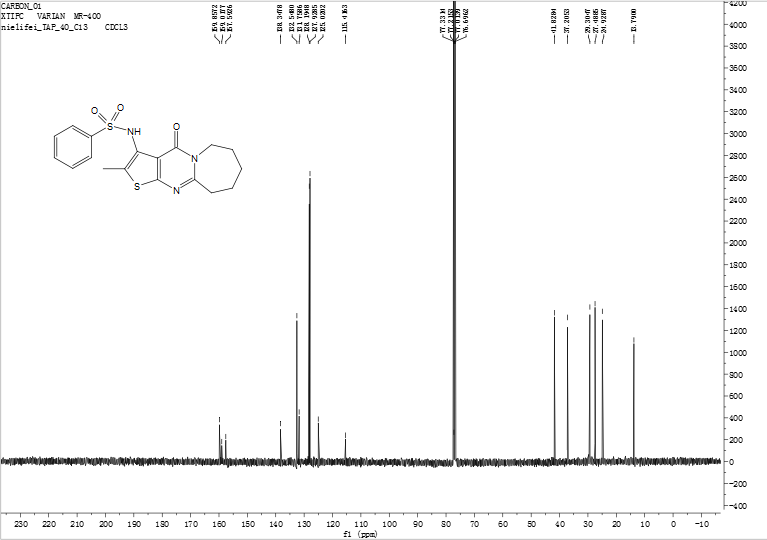
**Figure S 47:** 1H NMR spectrum of compound **10x**



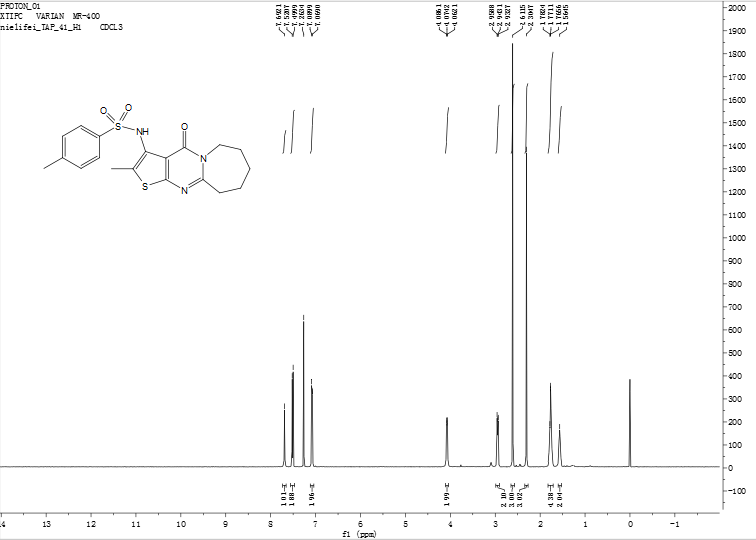
**Figure S 48:** 13C NMR spectrum of compound **10x**



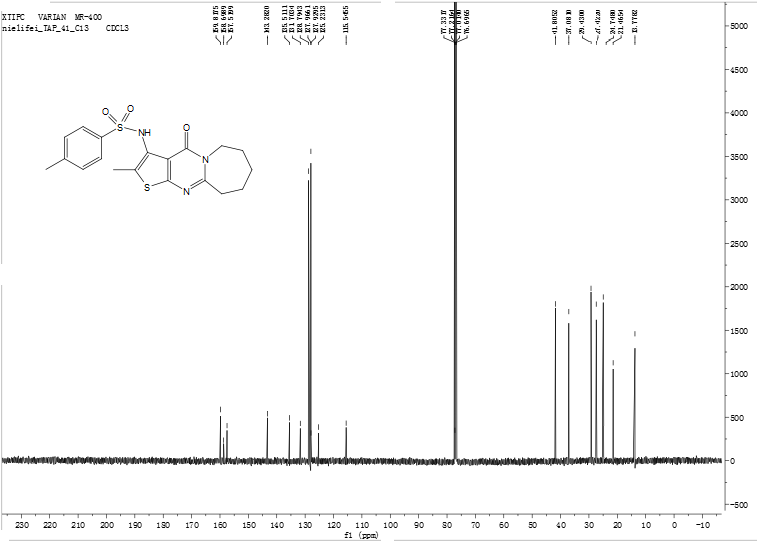
**Figure S 49:** 1H NMR spectrum of compound **11a**

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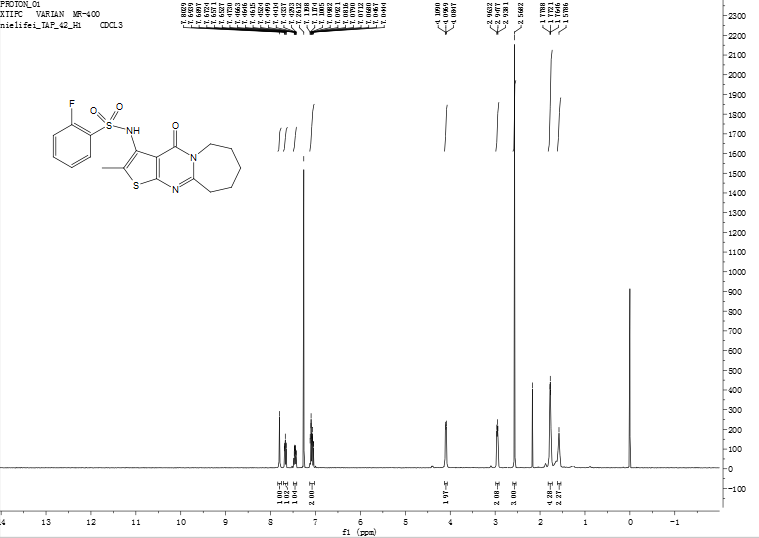
**Figure S 50:** 13C NMR spectrum of compound **11a**

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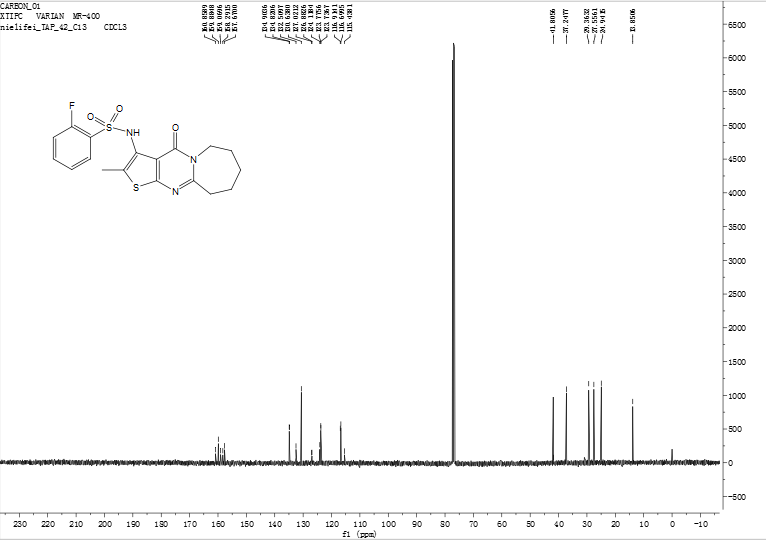
**Figure S 51:** 1H NMR spectrum of compound **11b**

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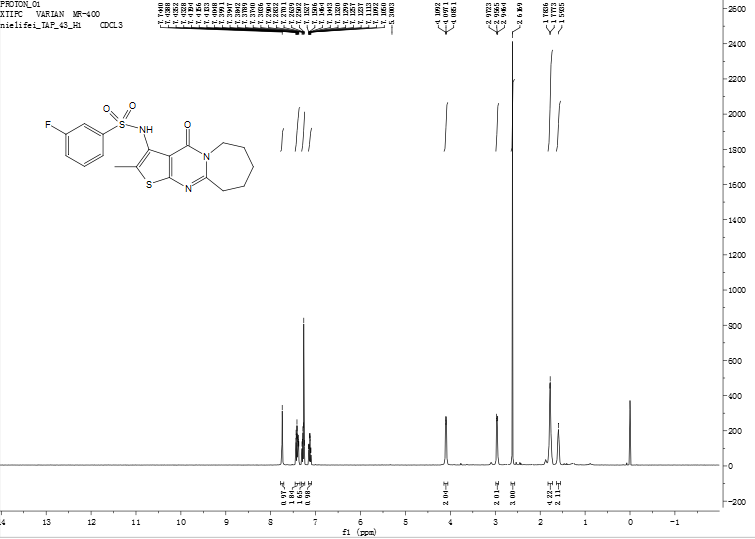
**Figure S 52:** 13C NMR spectrum of compound **11b**



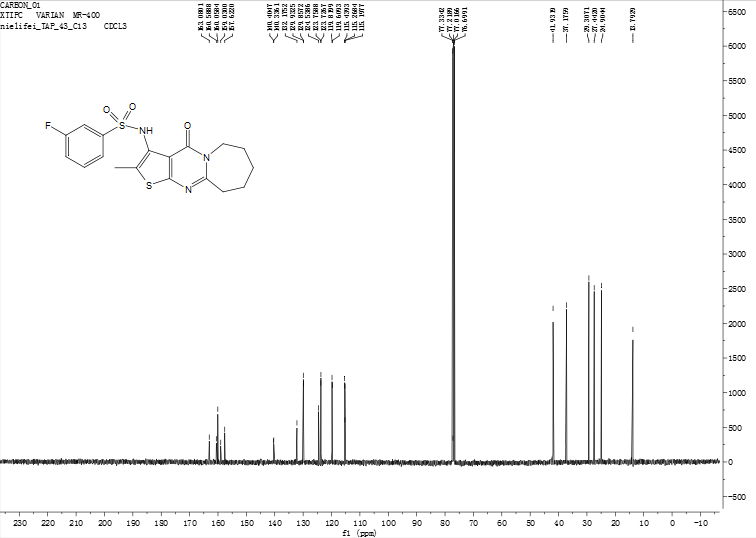
**Figure S 53:** 1H NMR spectrum of compound **11c**

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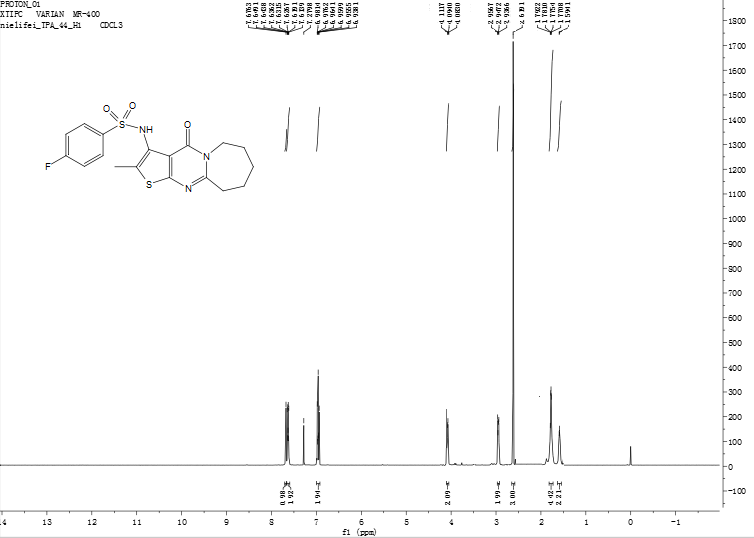
**Figure S 54:** 13C NMR spectrum of compound **11c**



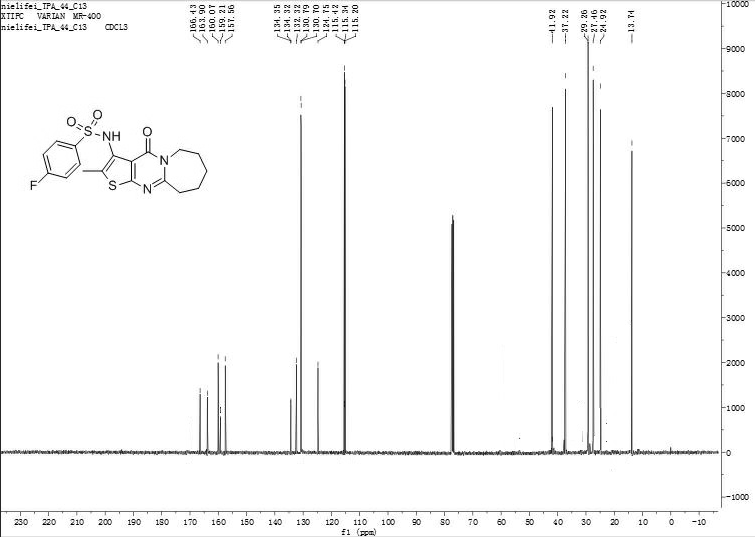
**Figure S 55:** 1H NMR spectrum of compound **11d**

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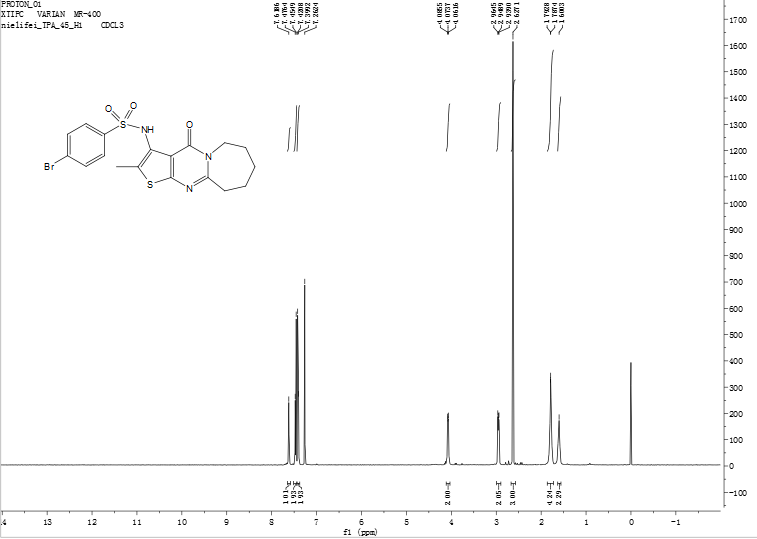
**Figure S 56:** 13C NMR spectrum of compound **11d**

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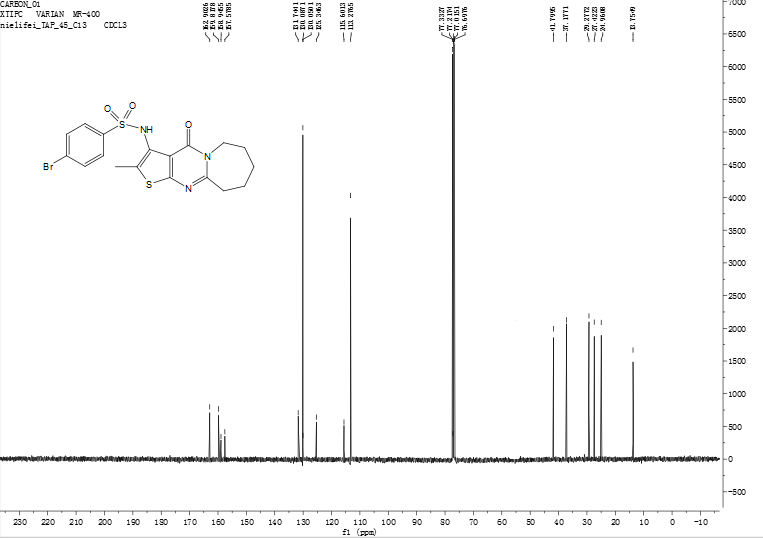
**Figure S 57:** 1H NMR spectrum of compound **11e**

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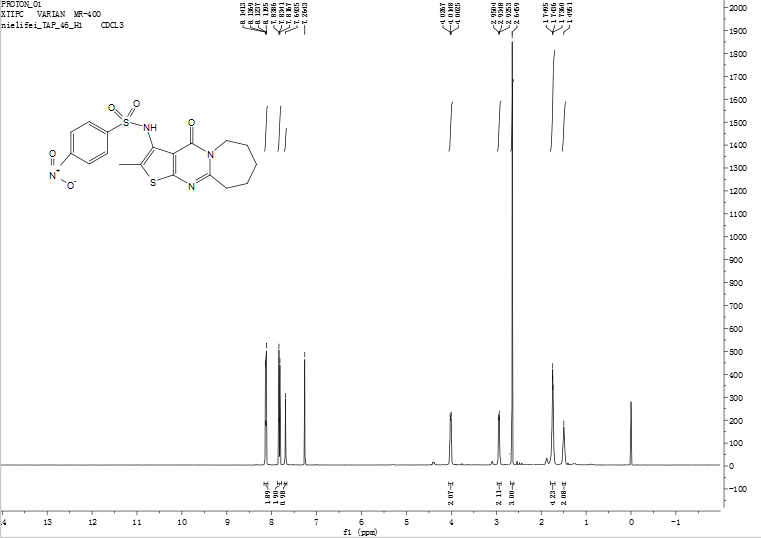
**Figure S 58:** 13C NMR spectrum of compound **11e**

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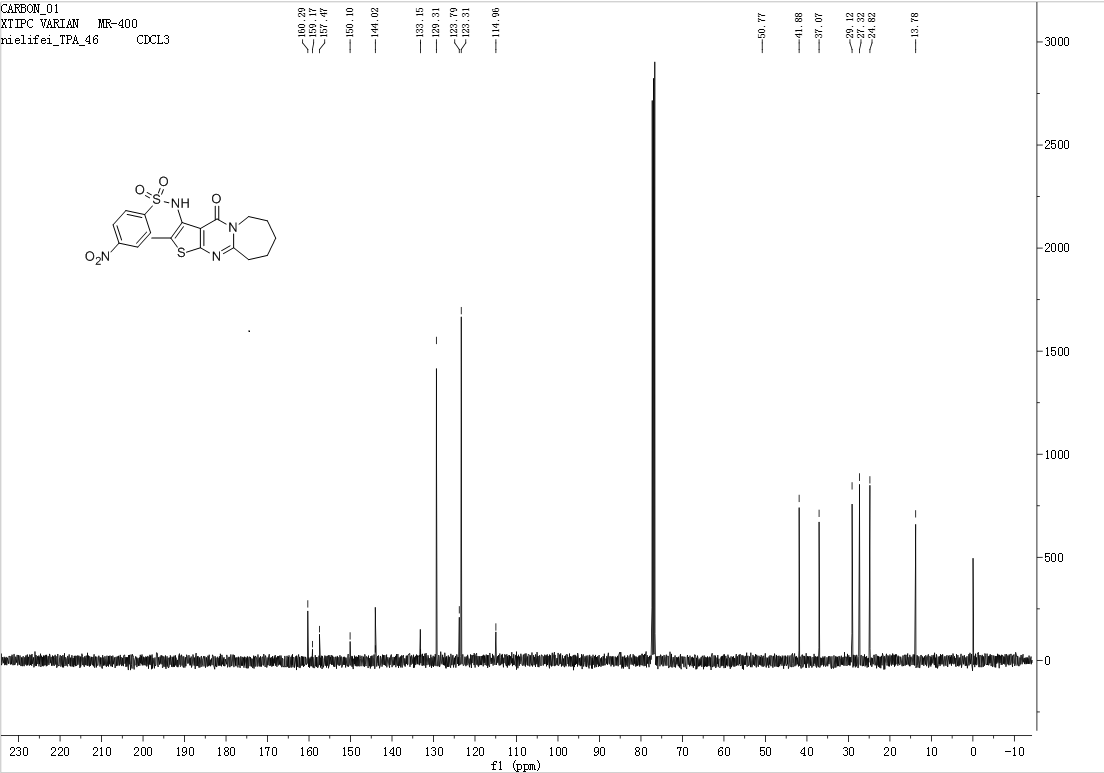
**Figure S 59:** 1H NMR spectrum of compound **11f**

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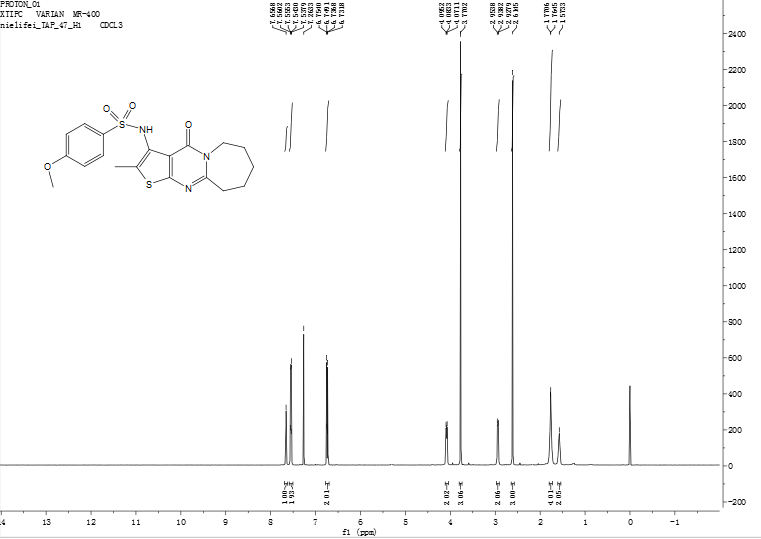
**Figure S 60:** 13C NMR spectrum of compound **11f**

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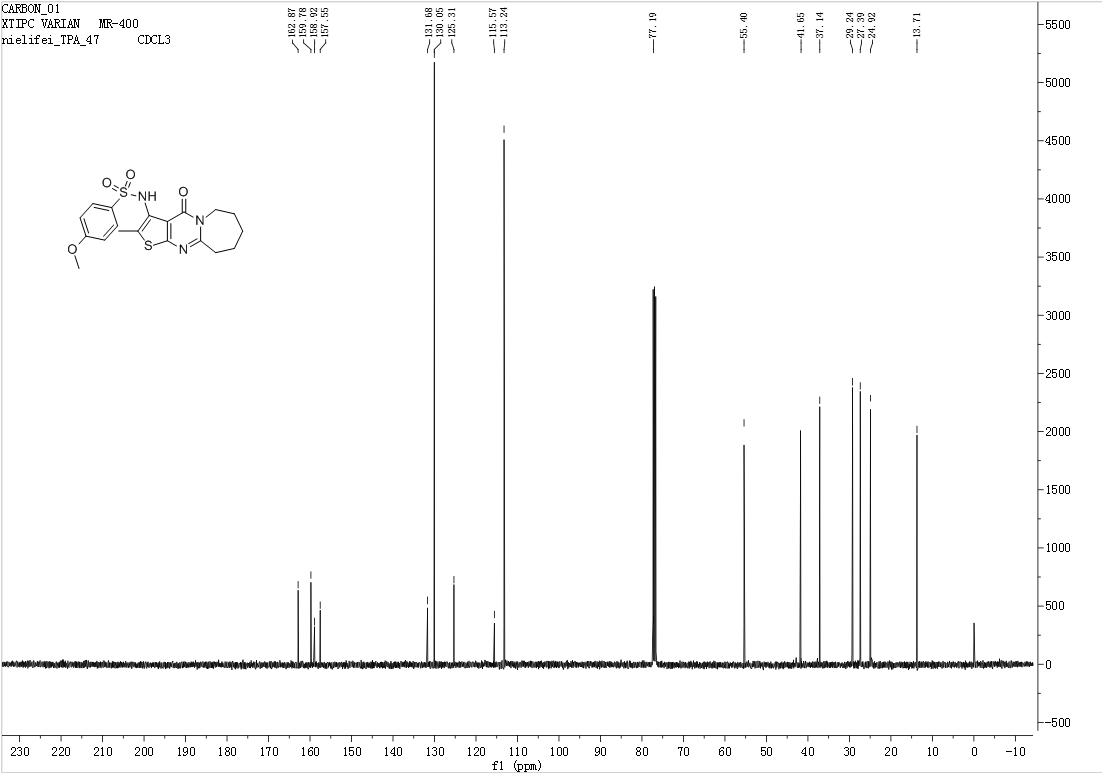
**Figure S 61:** 1H NMR spectrum of compound **11g**

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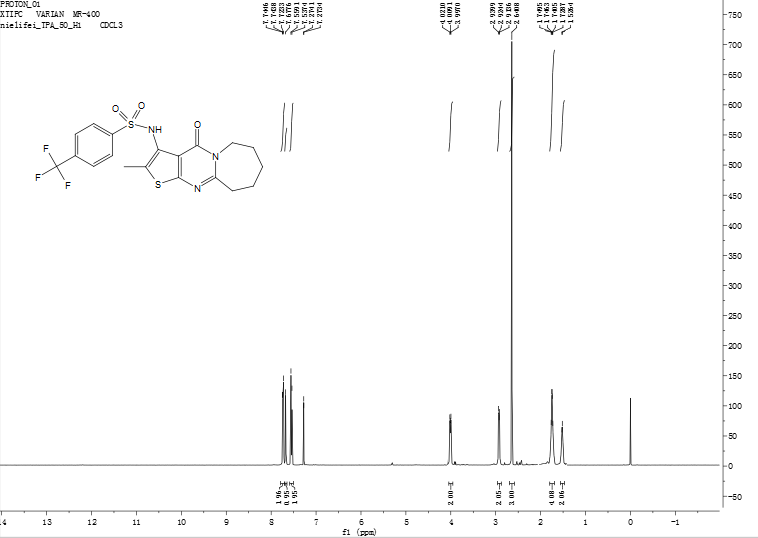
**Figure S 62:** 13C NMR spectrum of compound **11g**



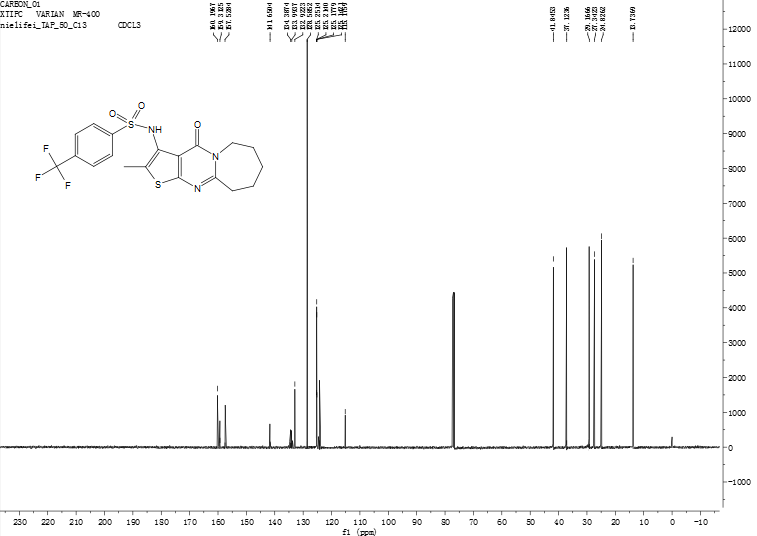
**Figure S 63:** 1H NMR spectrum of compound **11h**

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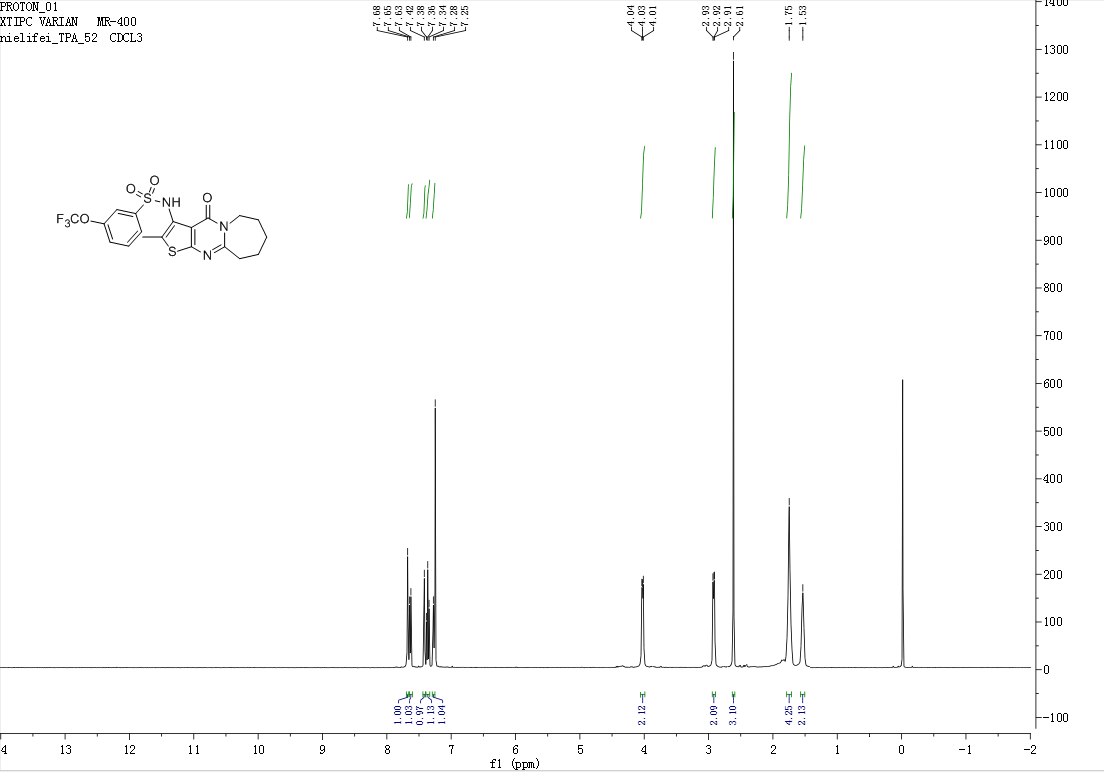
**Figure S 64:** 13C NMR spectrum of compound **11h**

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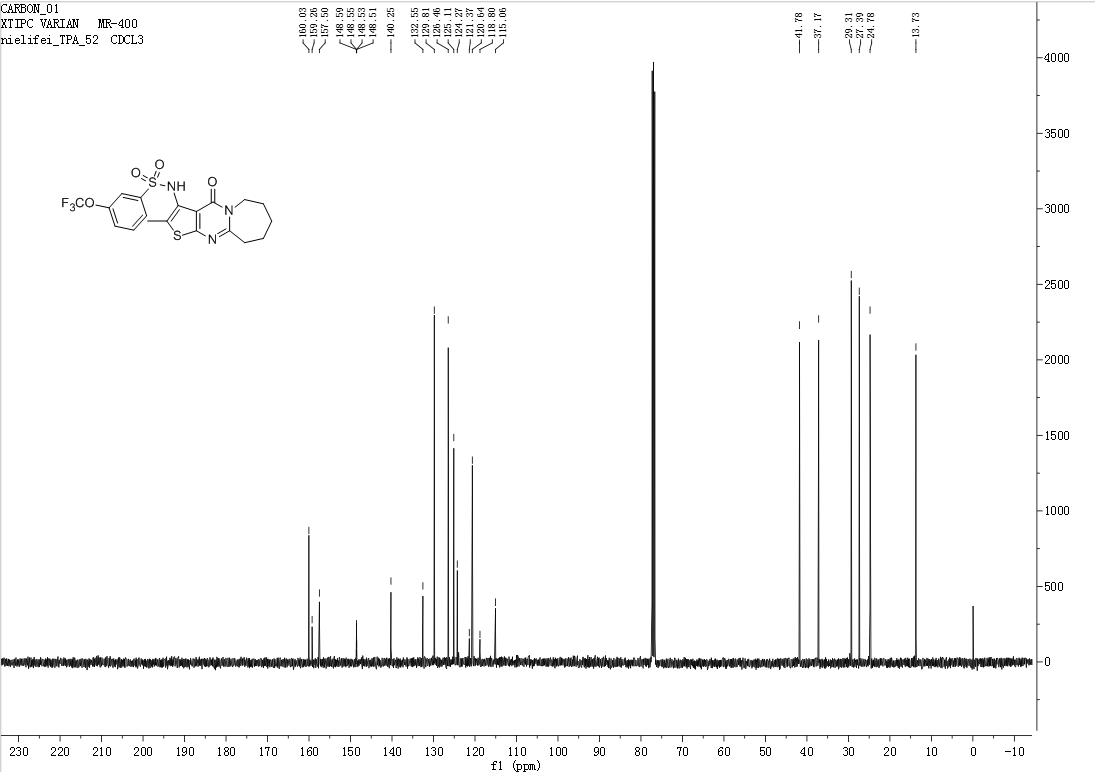
**Figure S 65:** 1H NMR spectrum of compound **11k**

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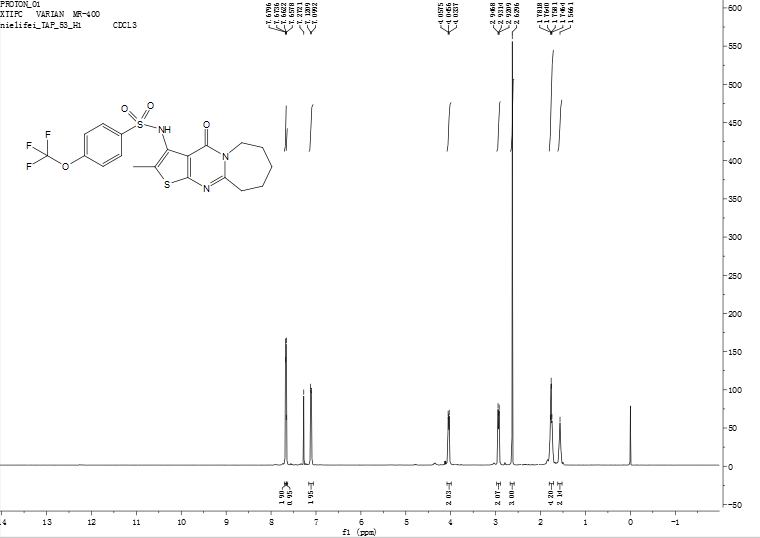
**Figure S 66:** 13C NMR spectrum of compound **11k**

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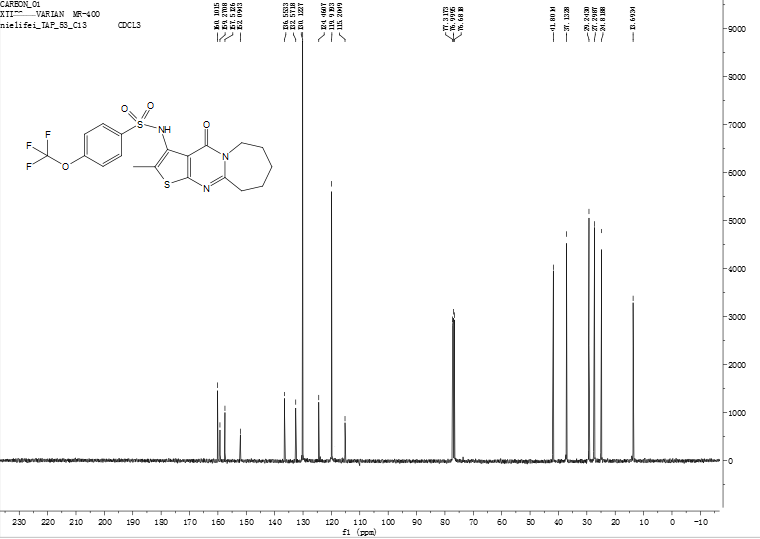
**Figure S 67:** 1H NMR spectrum of compound **11m**

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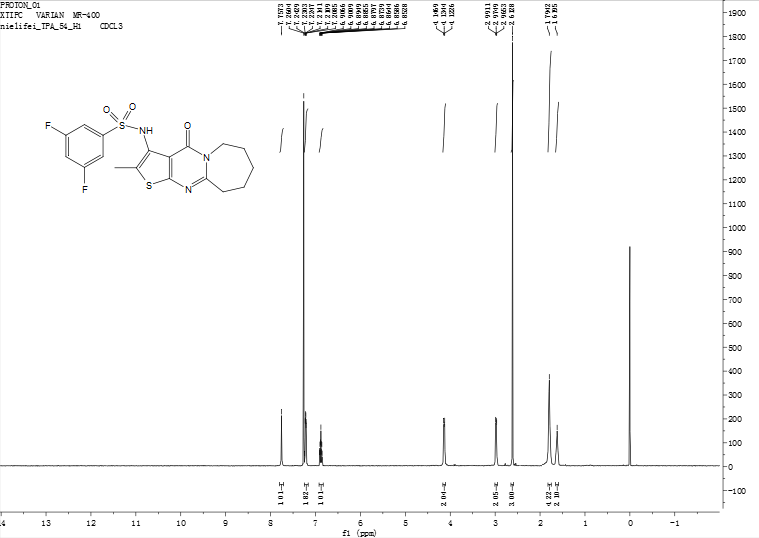
**Figure S 68:** 13C NMR spectrum of compound **11m**



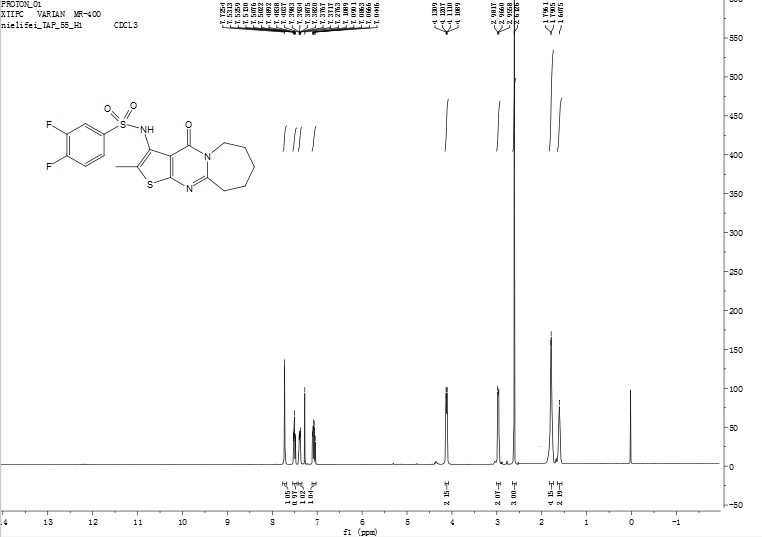
**Figure S 69:** 1H NMR spectrum of compound **11n**

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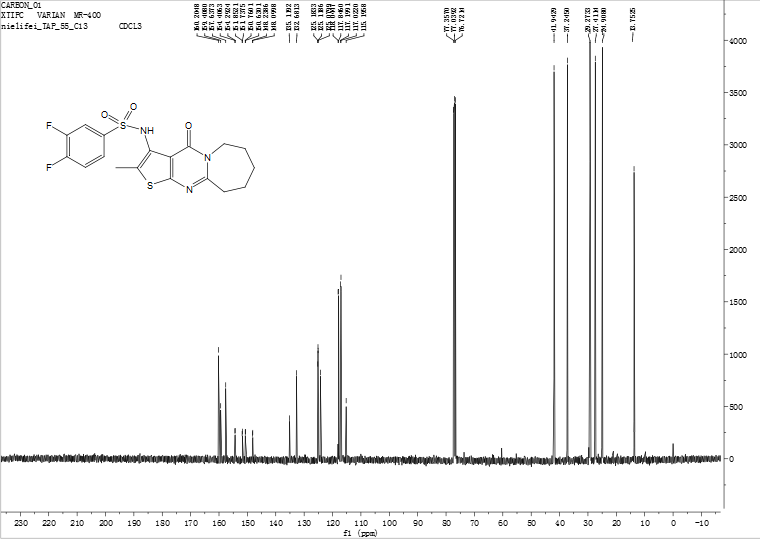
**Figure S 70:** 13C NMR spectrum of compound **11n**

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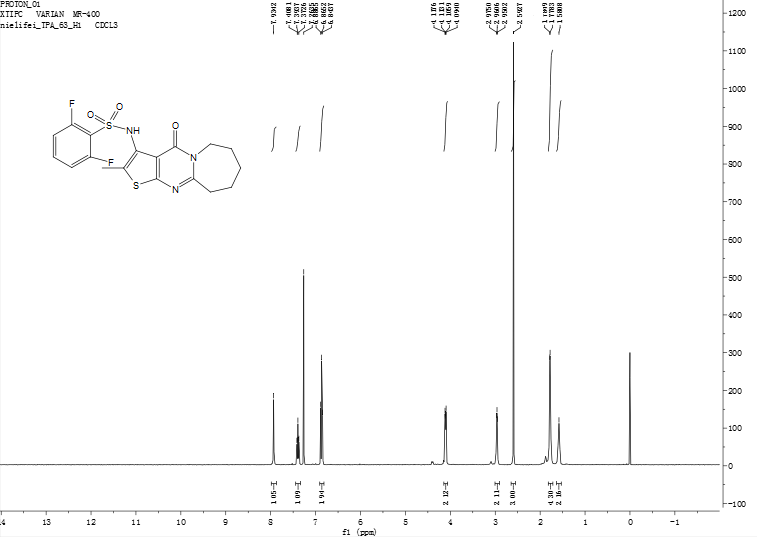
**Figure S 71:** 1H NMR spectrum of compound **11o**



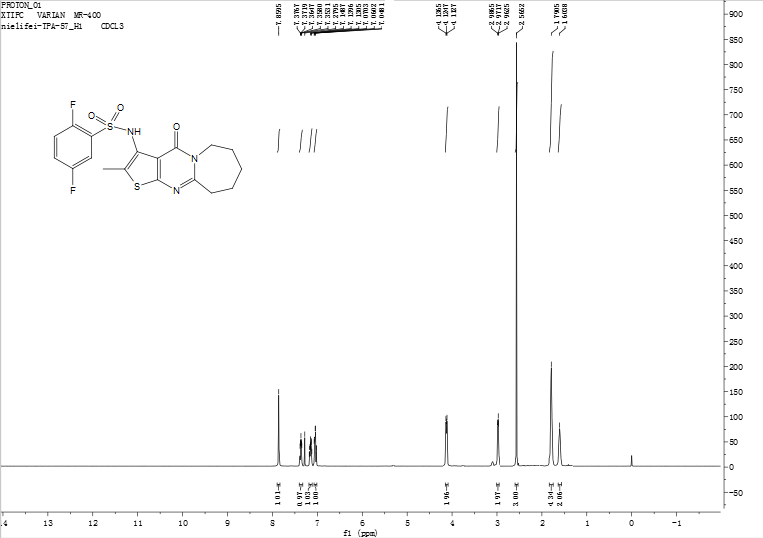
**Figure S 72:** 1H NMR spectrum of compound **11p**

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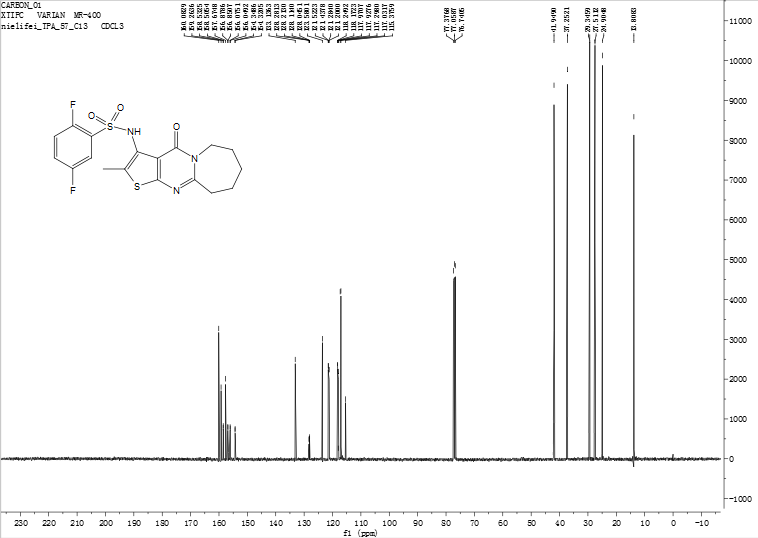
**Figure S 73:** 13C NMR spectrum of compound **11p**



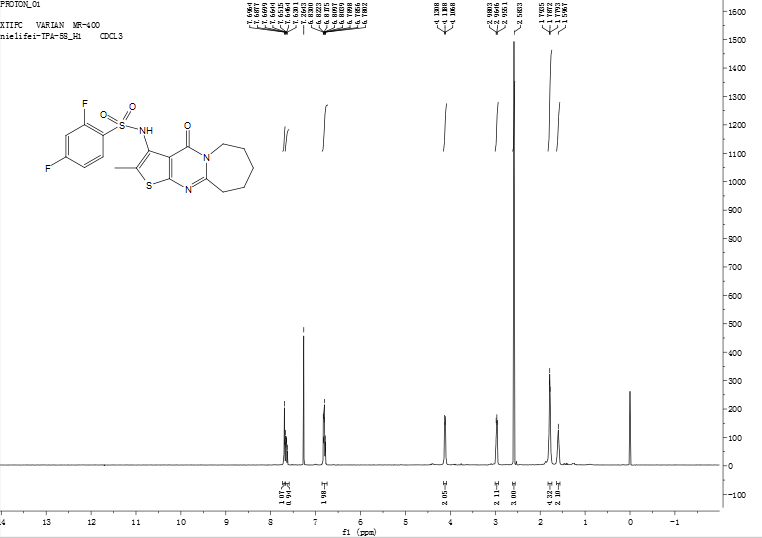
**Figure S 74:** 1H NMR spectrum of compound **11q**

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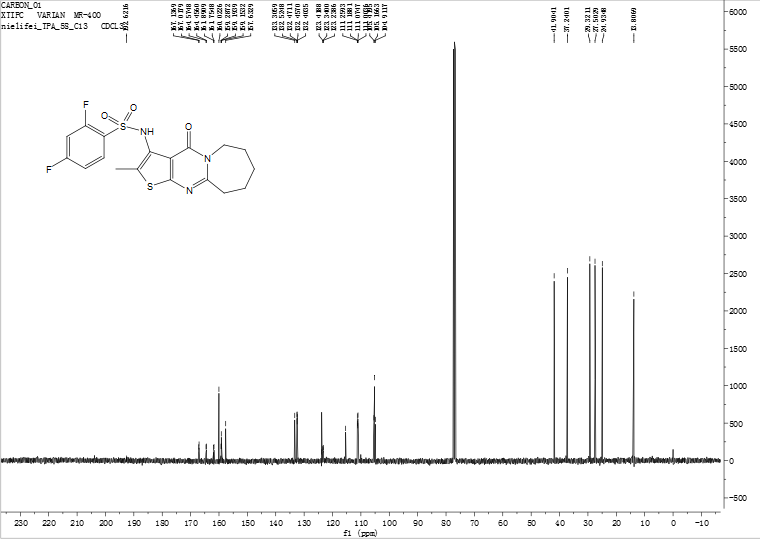
**Figure S 75:** 1H NMR spectrum of compound **11r**

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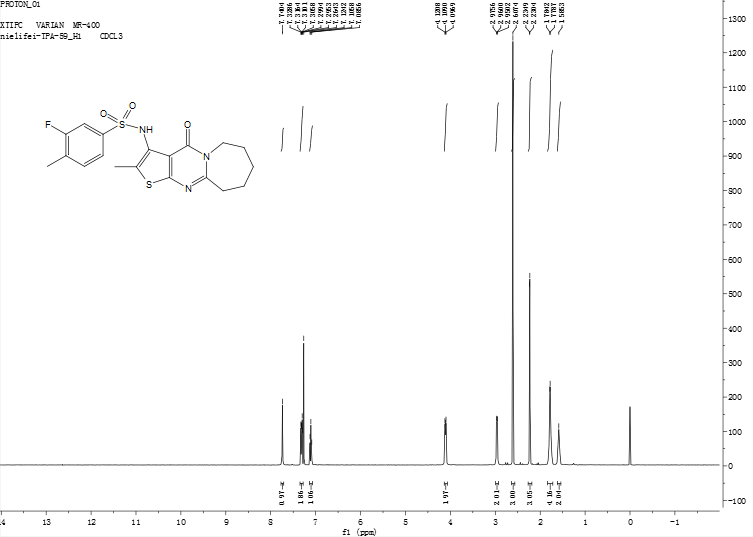
**Figure S 76:** 13C NMR spectrum of compound **11r**



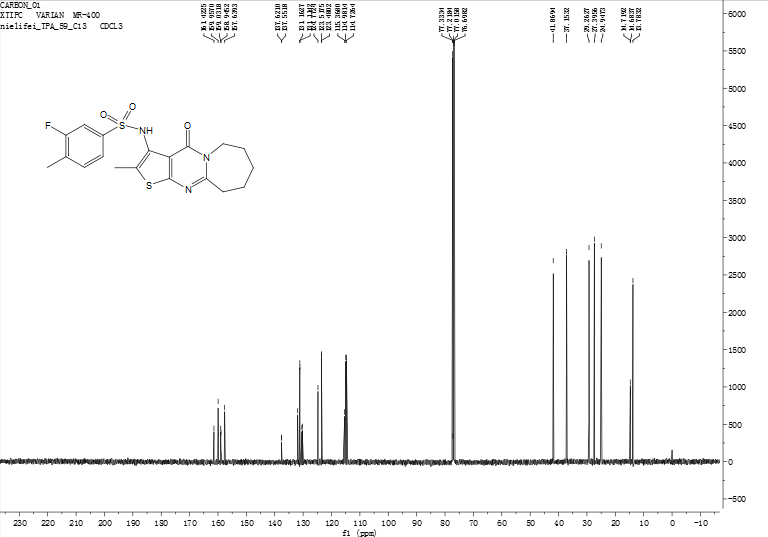
**Figure S 77:** 1H NMR spectrum of compound **11s**

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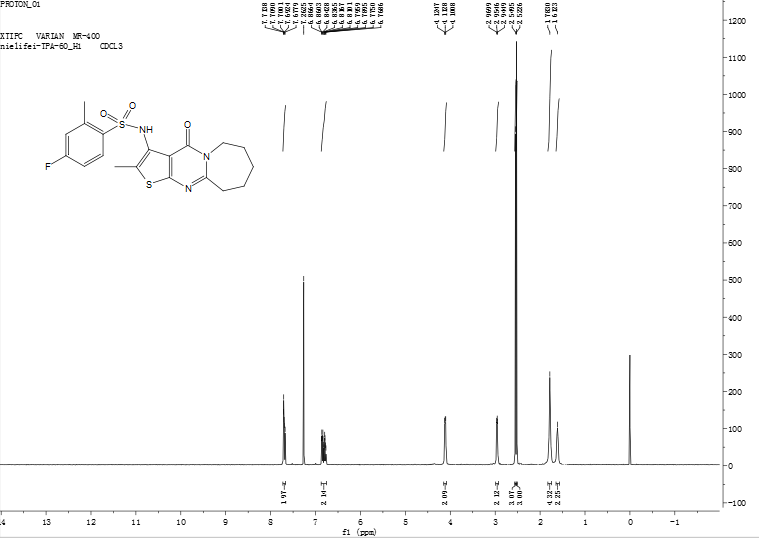
**Figure S 78:** 13C NMR spectrum of compound **11s**

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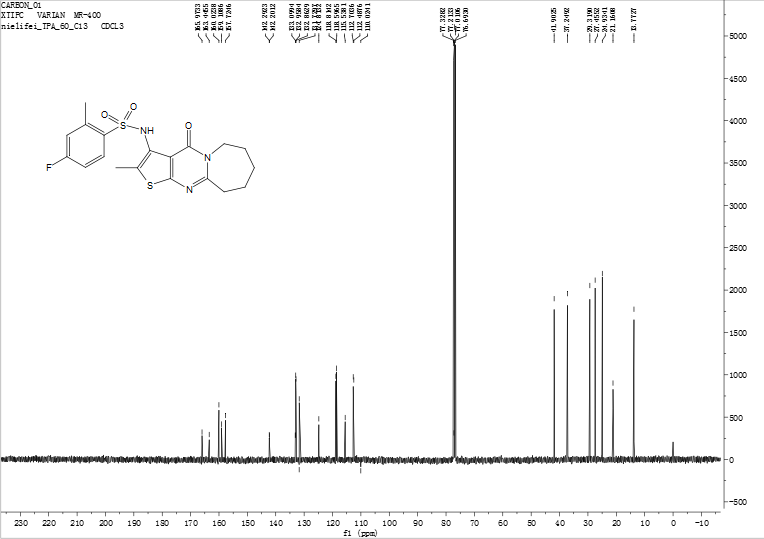
**Figure S 79:** 1H NMR spectrum of compound **11t**

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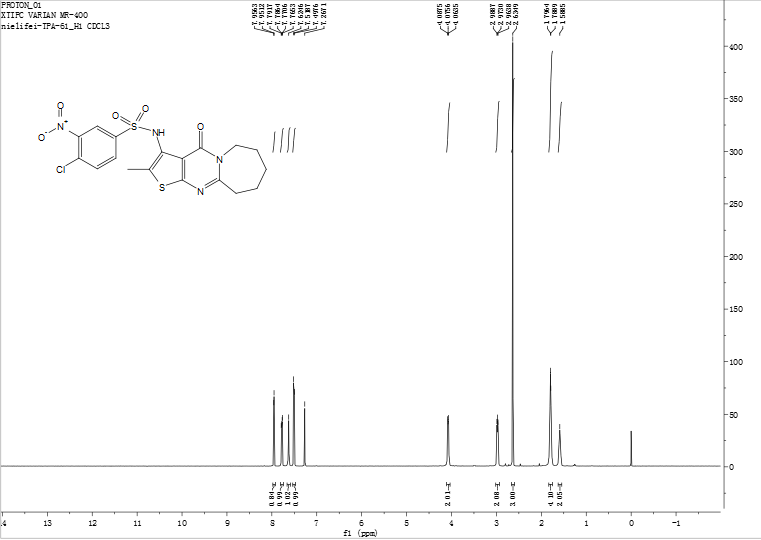
**Figure S 80:** 13C NMR spectrum of compound **11t**



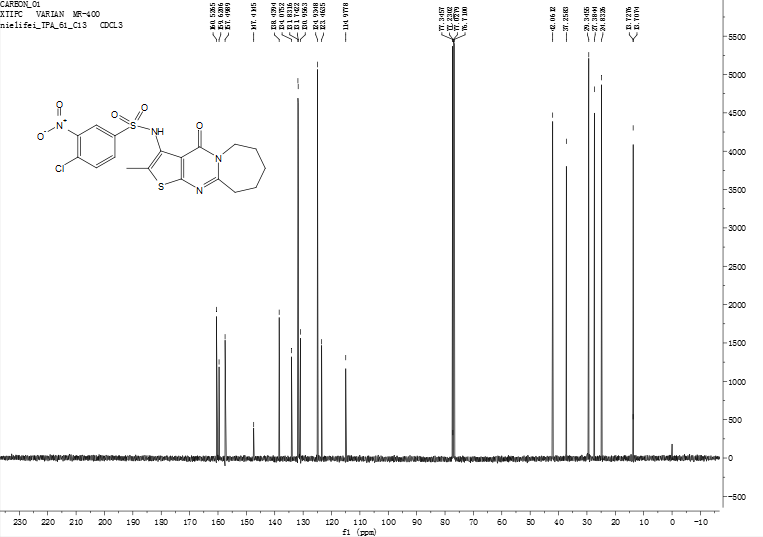
**Figure S 81:** 1H NMR spectrum of compound **11u**

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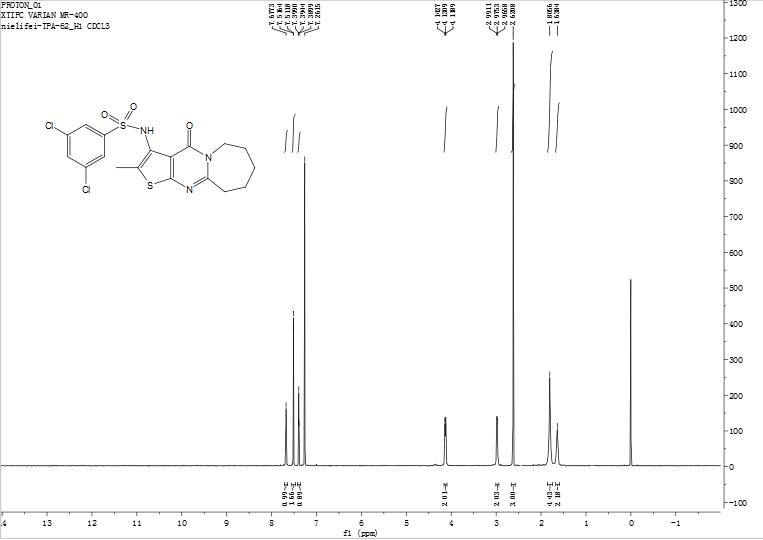
**Figure S 82:** 13C NMR spectrum of compound **11u**

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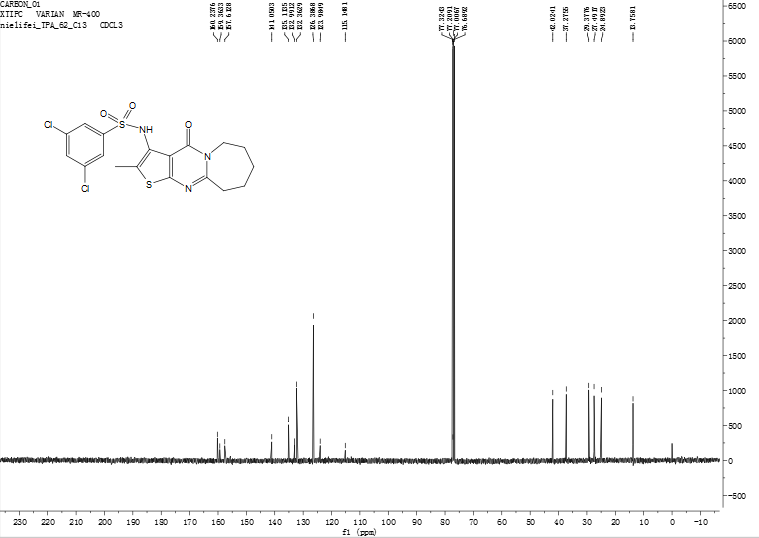
**Figure S 83:** 1H NMR spectrum of compound **11v**

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**Figure S 84:** 13C NMR spectrum of compound **11v**

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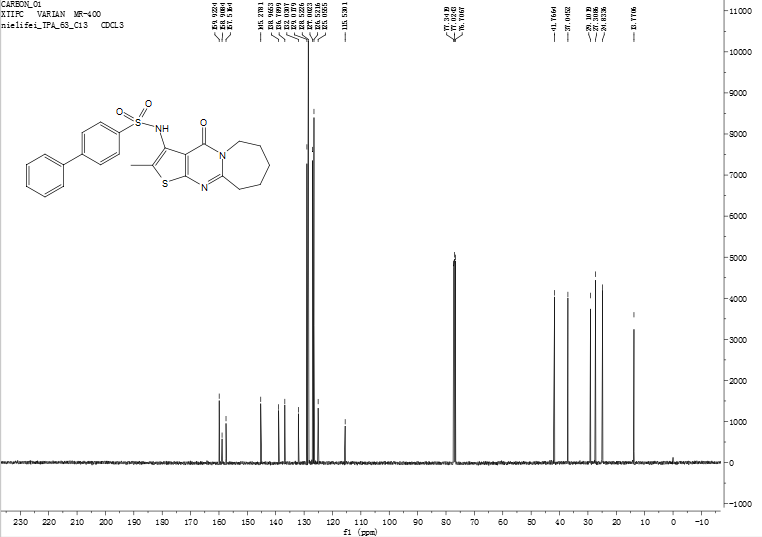
**Figure S 85:** 1H NMR spectrum of compound **11w**

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**Figure S 86:** 13C NMR spectrum of compound **11w**

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**Figure S 87:** 1H NMR spectrum of compound **11x**

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**Figure S 88:** 13C NMR spectrum of compound **11x**