

**Efficient Synthesis of Promising Antidiabetic Triazinoindole Analogues via Solvent-Free
Method: Investigating the Reaction of 1,3-Diketones and 2,5-Dihydro-3H-
[1,2,4]triazino[5,6-*b*]indole-3-thione**

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SUPPLEMENTARY DATA

General Procedures for the Synthesis of 3-Methyl-2-Aroylthiazolo[3',2':2,3][1,2,4]triazino[5,6-*b*]indole Derivatives:

1,3-Diketones **19(a-j)** (1.0 mmol) and NBS (1.2 mmol) were thoroughly homogenized in a dry mortar until a thick paste was formed and then 2,5-dihydro-3*H*-[1,2,4]triazino[5,6-*b*]indole-3-thione **11** (1.0 mmol) was added. The reaction mixture was grinded for an additional 30-45 minutes under solvent-free conditions. The reaction progress was monitored by TLC with ethyl acetate-petroleum ether (30:70, v/v). After completion of the reaction, the reaction mixture was treated with distilled water and the resulting residue was filtered and recrystallized with ethanol. The solid obtained was dried to give pure compounds in high yields 77-94%. The products were characterized by IR, 1D & 2D NMR and HRMS spectrometry.

Optimization of Reaction Conditions for the Synthesis of 3-Methyl-2-Aroylthiazolo[3',2':2,3][1,2,4]triazino[5,6-*b*]indole Derivatives:

1. Table 1, Entry 1-7: Solvent-Based Reactions under Visible Light

Reactions were performed using 20 mL of various solvents (EtOH, H₂O, DMF, DCM, EtOH/H₂O mixtures) under visible-light irradiation (27 W CFL) for 12 hr. Products were isolated by filtration and recrystallized from ethanol.

2. Table 1, Entry 8-11: Reactions under Refluxing Conditions

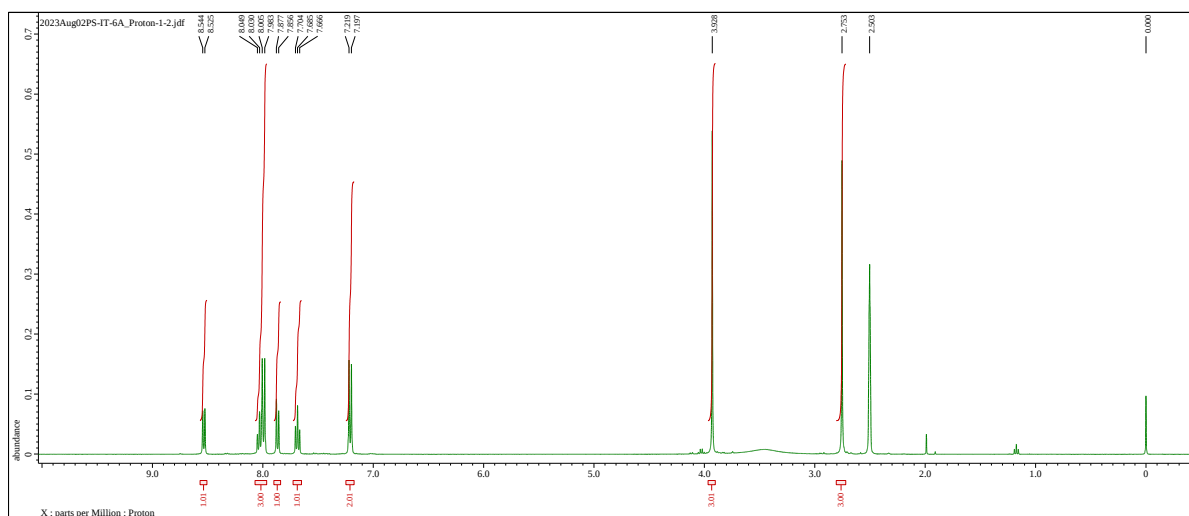
Reactions were conducted under reflux in 20 mL of different solvents (ethanol, water, DMF, and DMSO) for 4-5 hr. Products were purified by recrystallization from ethanol.

3. Table 1, Entry 12: Solvent-Free Grinding at Room Temperature

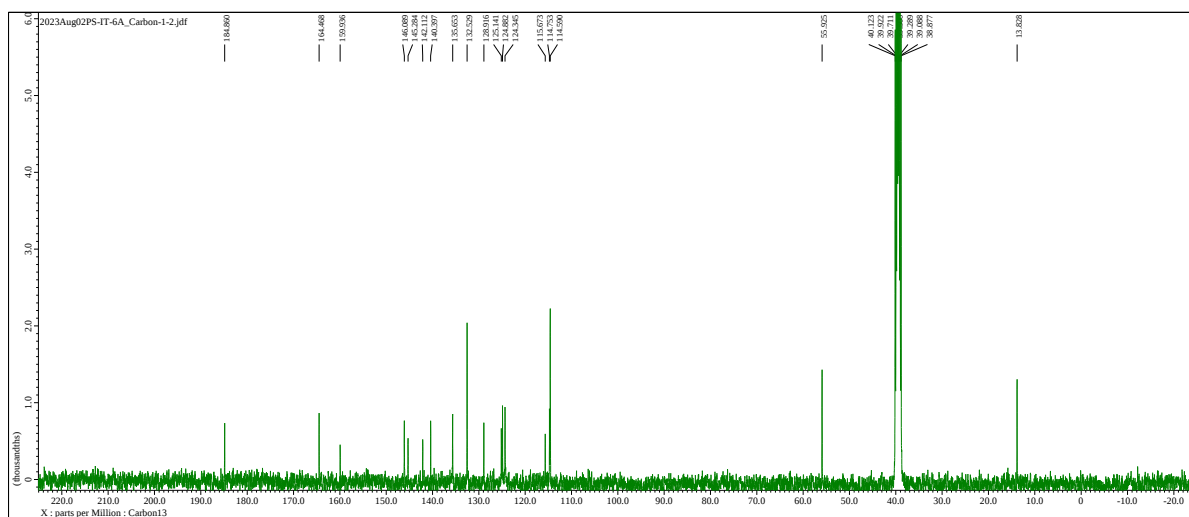
Reagents were ground together for 30 minutes at room temperature under solvent-free conditions. This method provided a 94% yield in a shorter time.

¹H NMR, ¹³C NMR, HSQC and HMBC Spectra of Final Compounds

2-(4-Methoxybenzoyl)-3-methylthiazolo[3',2':2,3][1,2,4]triazino[5,6-b]indole 12a

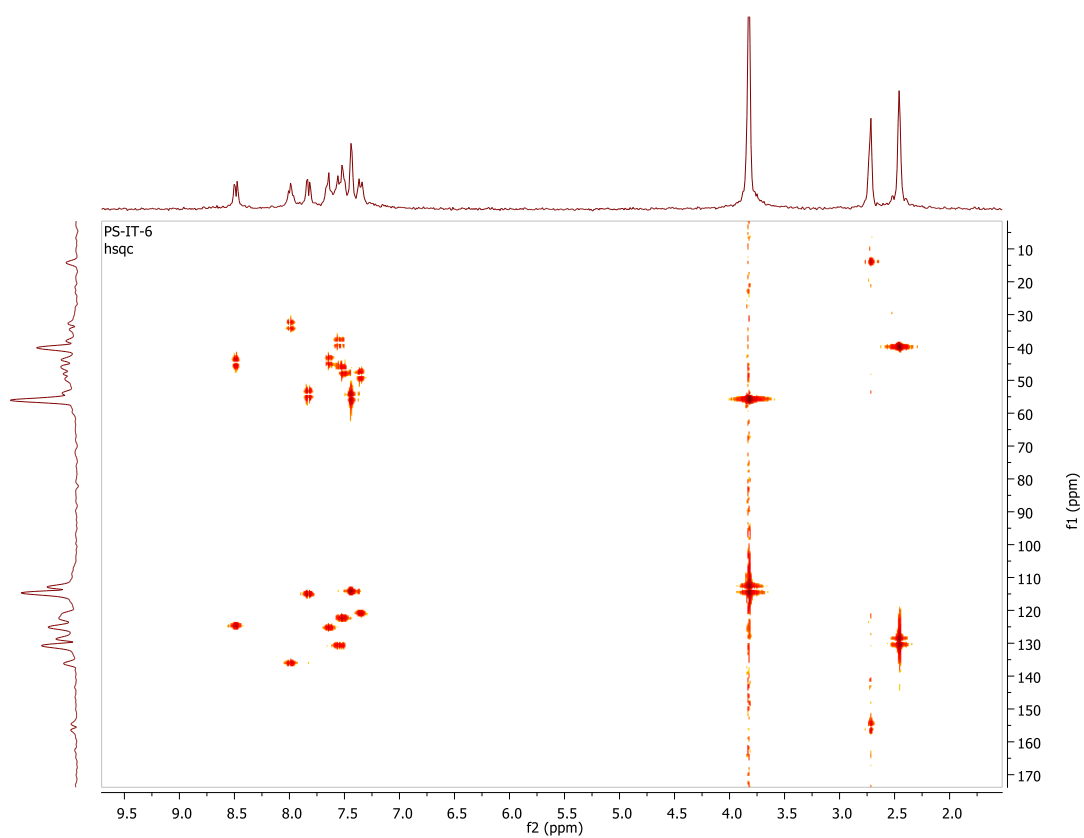


¹H NMR spectrum of 12a

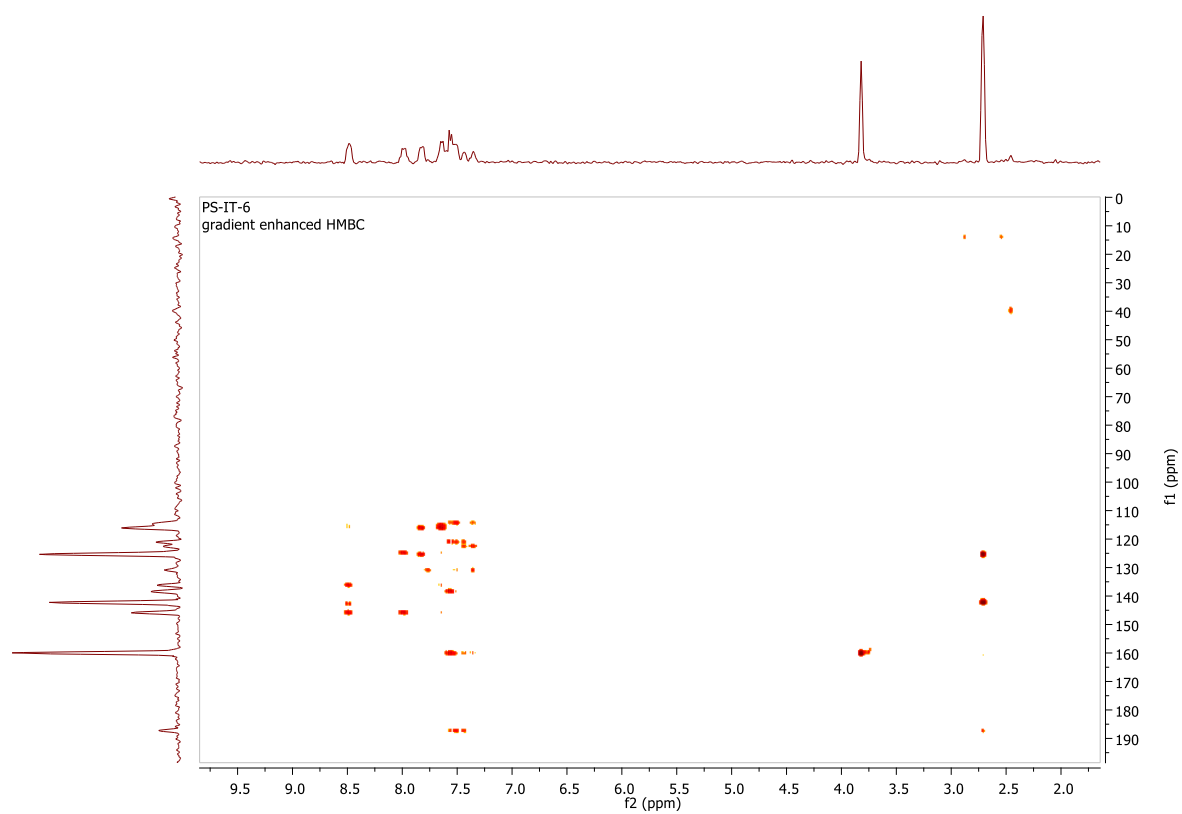


¹³C NMR spectrum of 12a

^1H - ^{13}C HSQC (12a)



^1H - ^{13}C HMBC (12a)



2023Aug01PS-IT-2a_Proton-1-2.jdf

8.52 8.52 8.03 8.03 7.97 7.97 7.90 7.90 7.84 7.70 7.70 7.30 2.51 2.51 2.50 2.50 2.49 2.49 0.00

abundance

10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0

1.01 3.06 2.90 3.00 3.00 0.00

Y : parts per Million - Proton

2023Aug01PS-IT-2a_Carbon-1-2.jdf

Intensity (a.u.)

Chemical Shift (ppm)

13.587

40.123

38.927

38.926

38.925

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38.920

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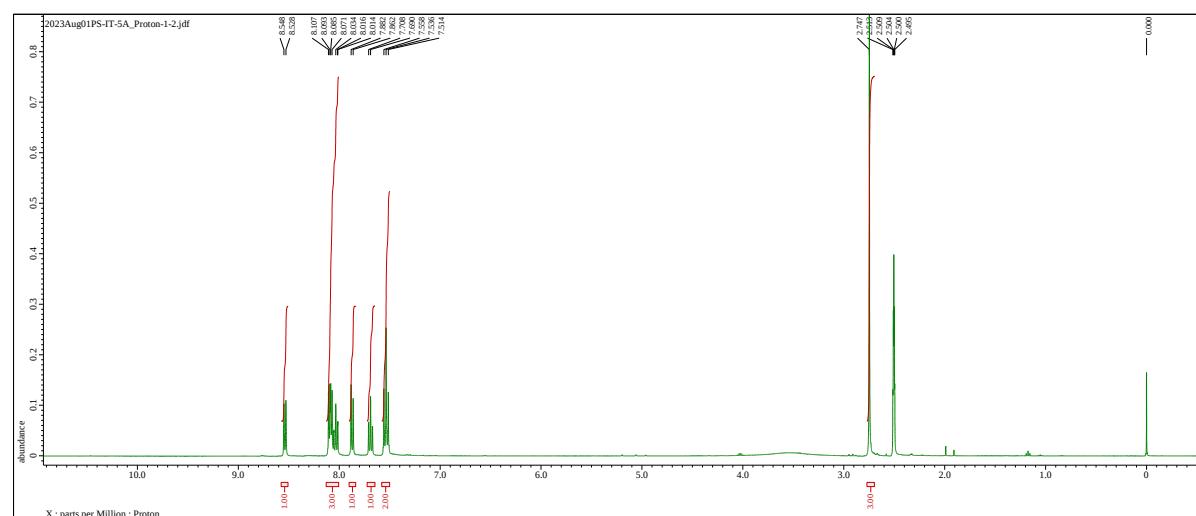
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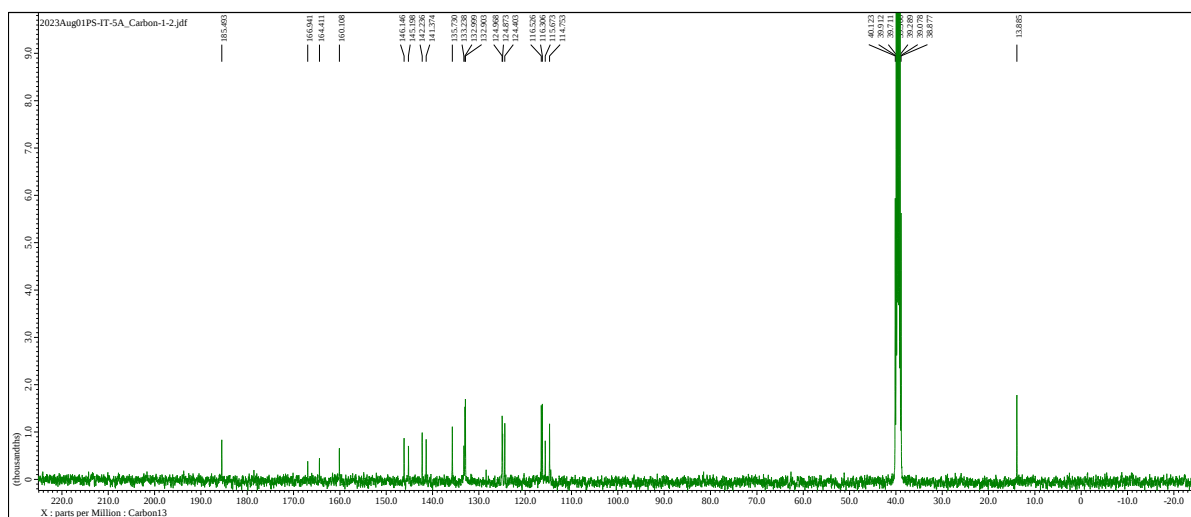
146.543

146.54

2-(4-Fluorobenzoyl)-3-methylthiazolo[3',2':2,3][1,2,4]triazino[5,6-b]indole (12c)

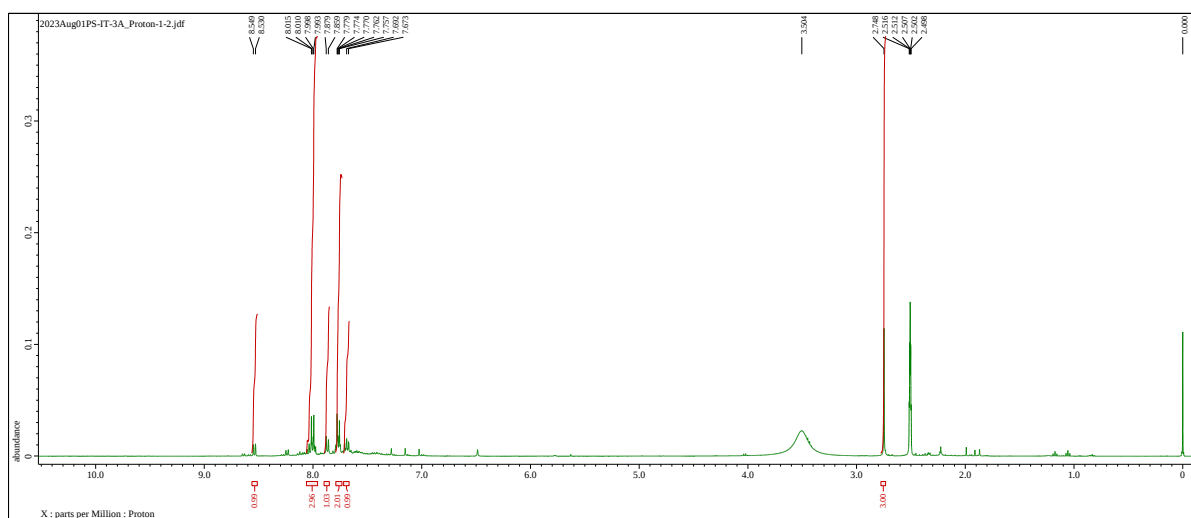
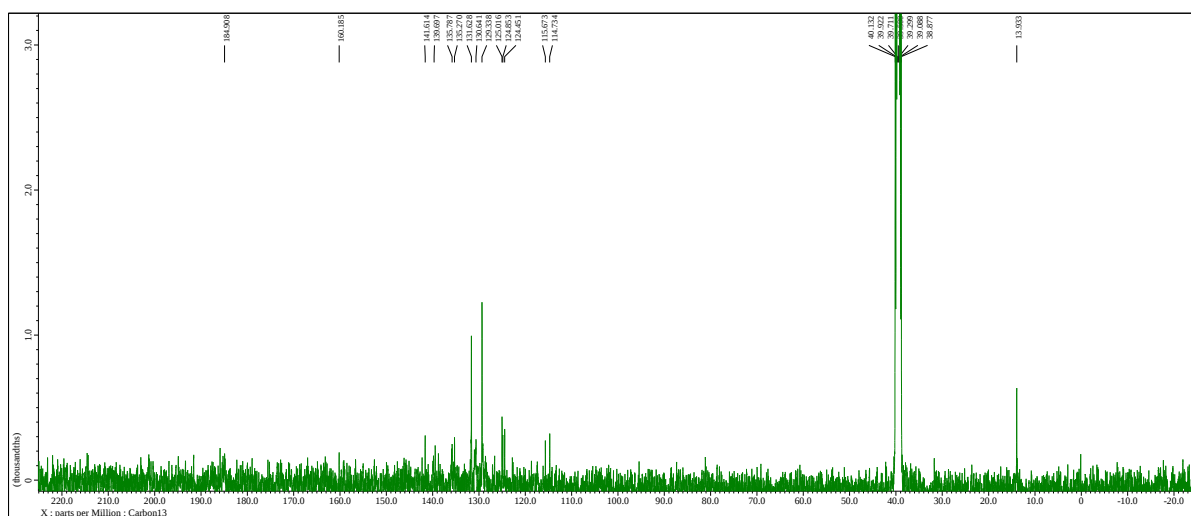


S5



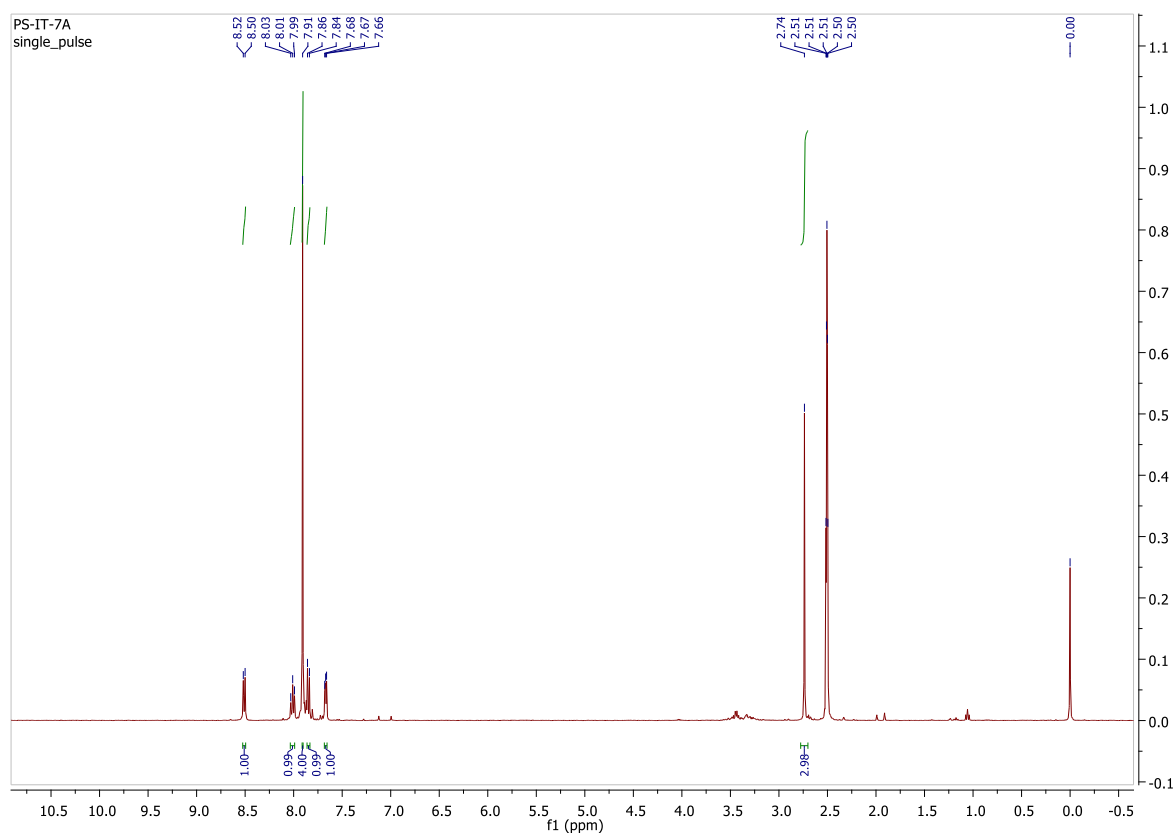
¹³C NMR spectrum of **12c**

2-(4-Chlorobenzoyl)-3-methylthiazolo[3',2':2,3][1,2,4]triazino[5,6-b]indole (12d)

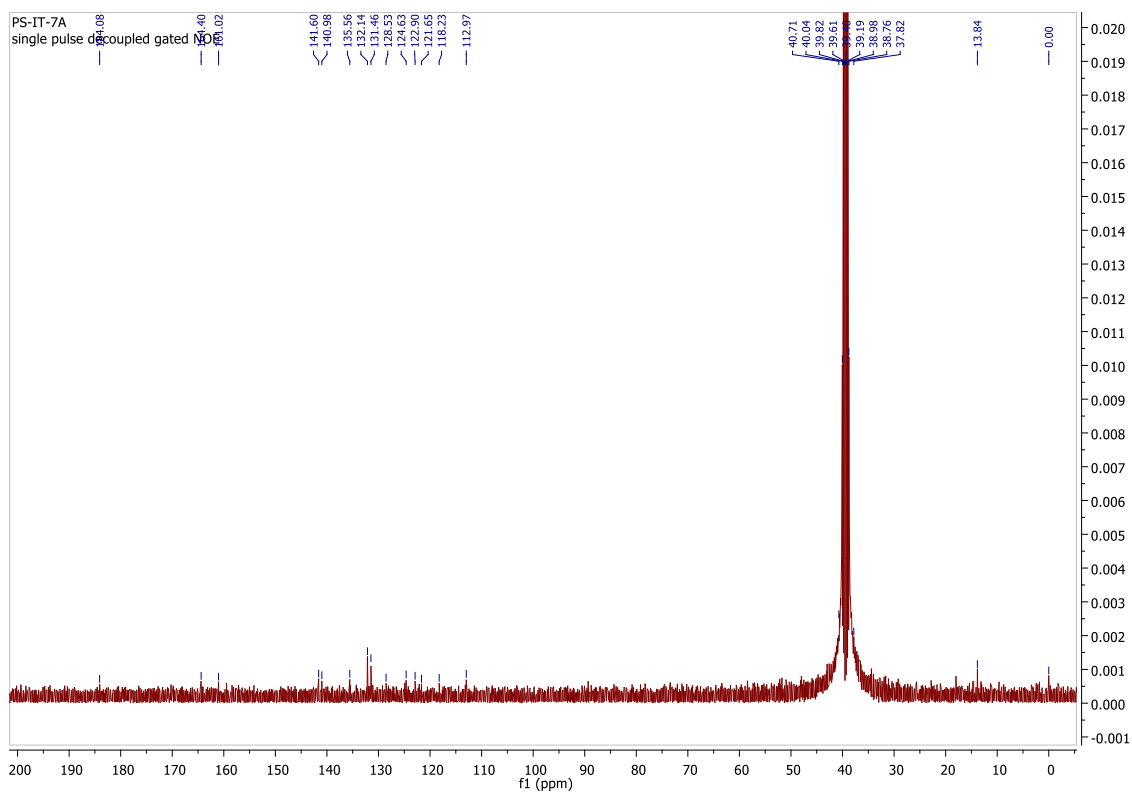
¹H NMR spectrum of **12d**

¹³C NMR spectrum of **12d**

2-(4-Bromobenzoyl)-3-methylthiazolo[3',2':2,3][1,2,4]triazino[5,6-b]indole (12e)

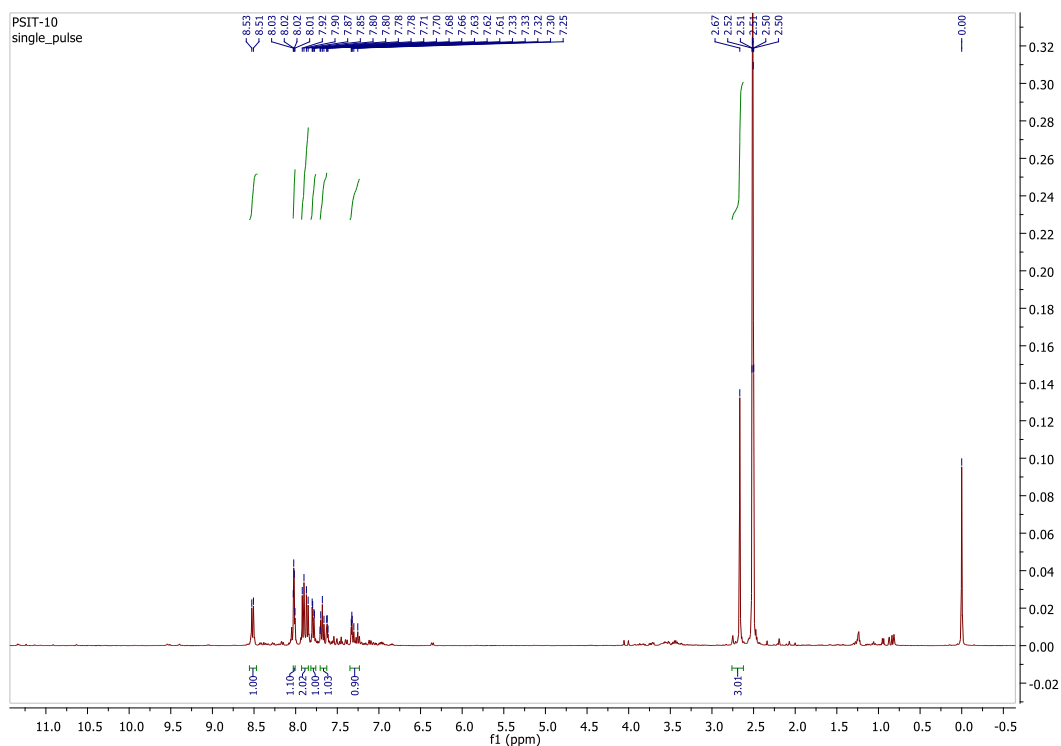


¹H NMR spectrum of **12e**

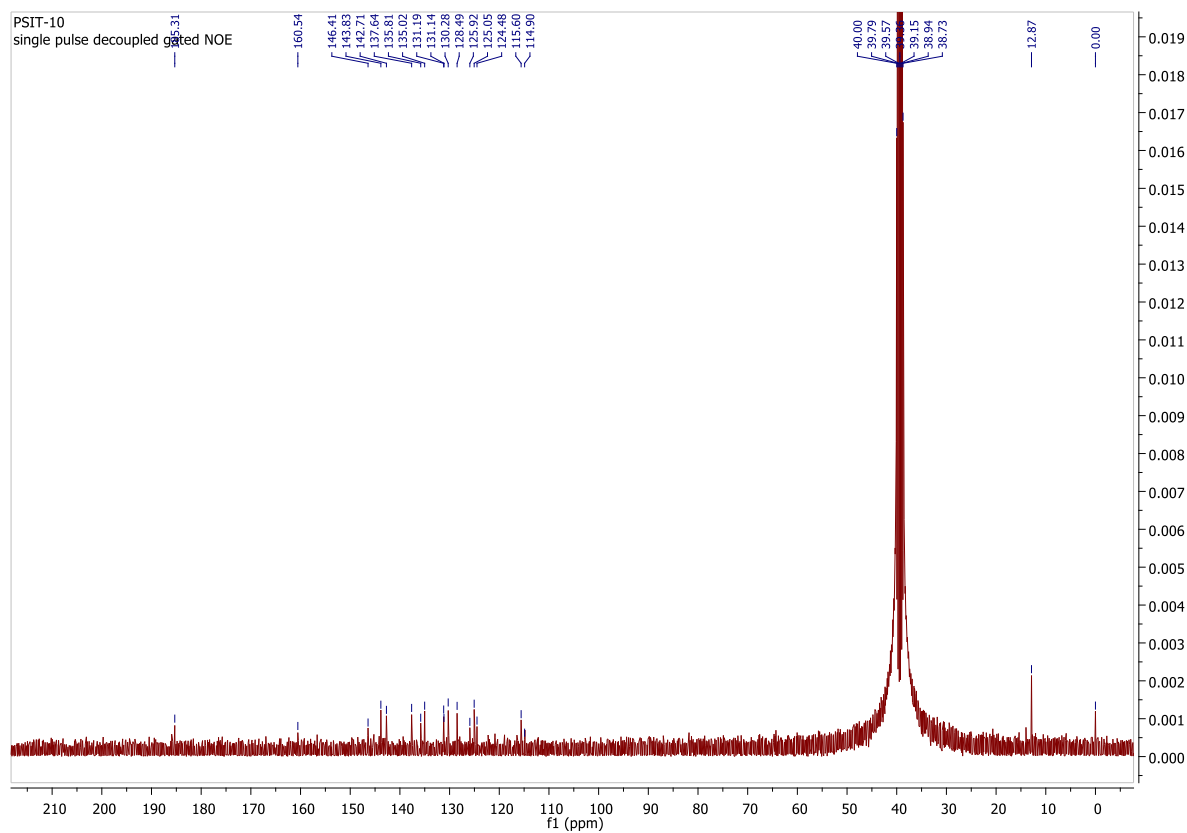


¹³C NMR spectrum of **12e**

2-(2,4-Dichlorobenzoyl)-3-methylthiazolo[3',2':2,3][1,2,4]triazino[5,6-b]indole 12f

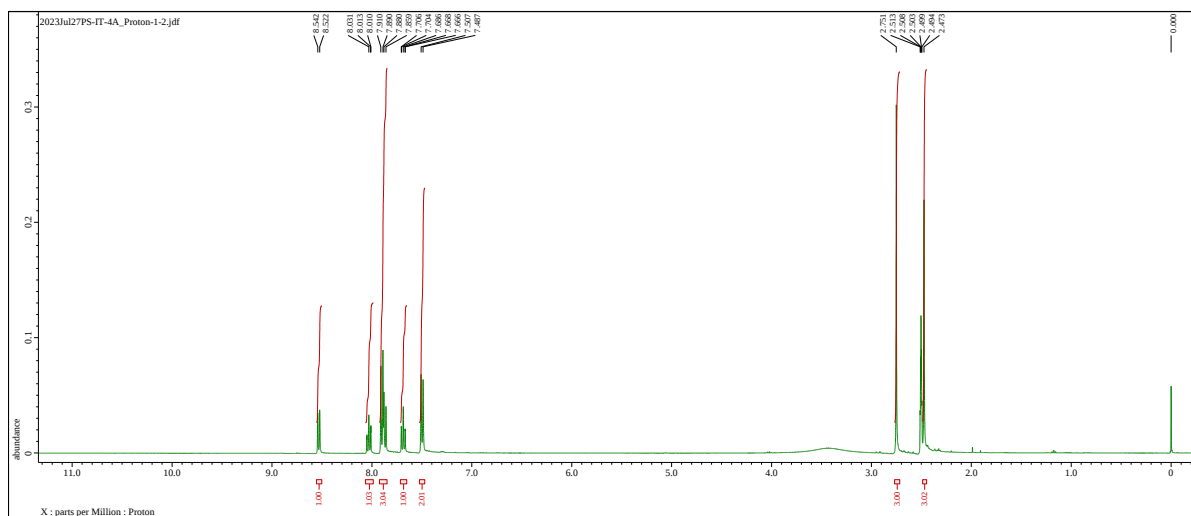


¹H NMR spectrum of **12f**

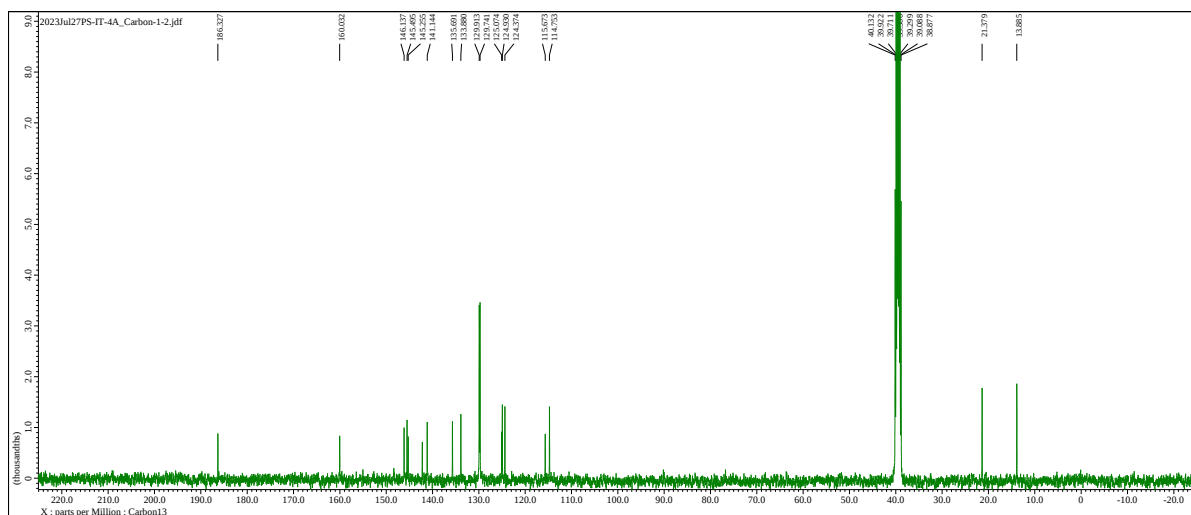


¹³C NMR spectrum of **12f**

3-Methyl-2-(4-methylbenzoyl)thiazolo[3',2':2,3][1,2,4]triazino[5,6-b]indole (12g)



¹H NMR spectrum of **12g**



¹³C NMR spectrum of **12g**

PSIT-8
single_pulse

Chemical shift (ppm): 8.54, 8.52, 8.05, 8.03, 8.01, 7.88, 7.86, 7.70, 7.68, 7.67, 7.66, 7.62, 7.61, 7.59, 7.56, 7.55, 7.54, 7.48, 7.41, 7.41, 7.40, 7.39, 7.38, 3.87, 2.76, 2.51, 2.51, 2.51, 2.50, 0.00.

Integration values: 1.00, 1.00, 1.00, 2.01, 1.00, 1.00, 3.00, 3.00, 0.00.

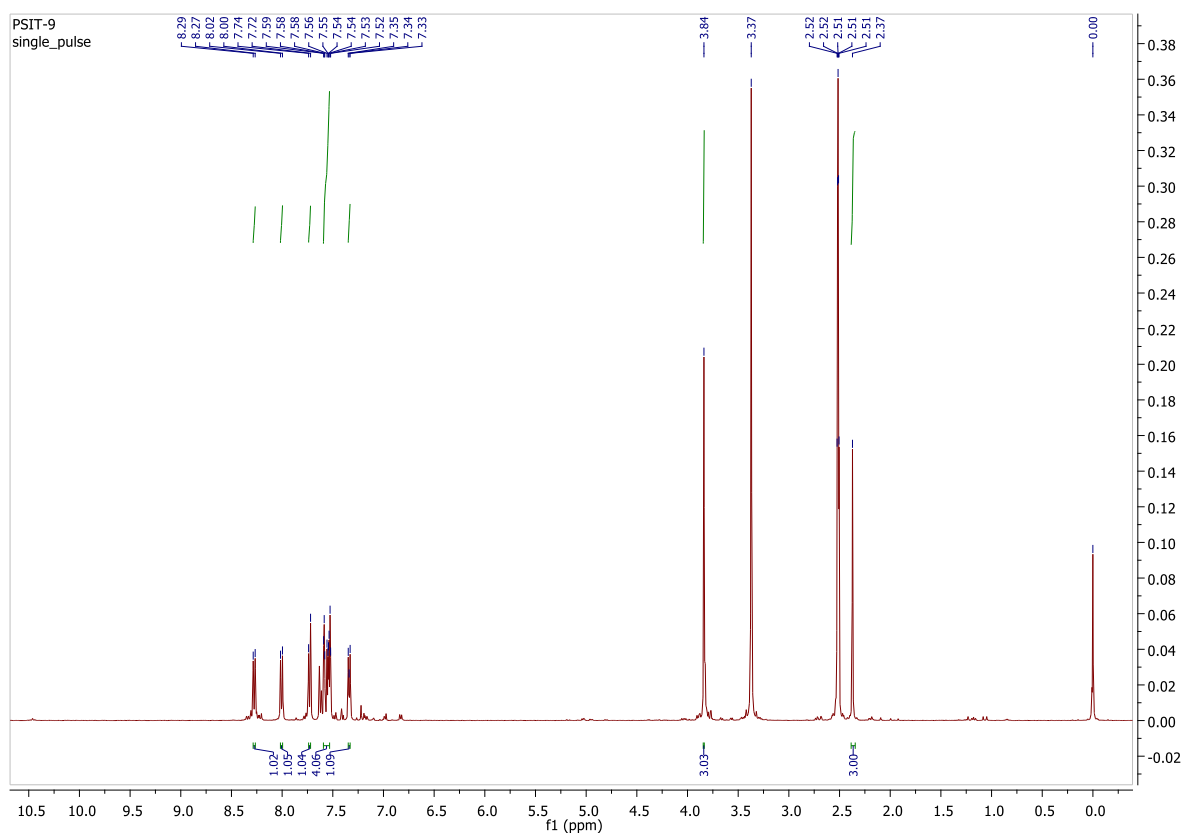
13C NMR spectrum (CDCl₃) of compound 14a.

Chemical Shifts (ppm): 189.23, 160.59, 160.06, 146.75, 145.96, 142.82, 142.28, 138.43, 136.26, 130.98, 125.48, 125.40, 124.94, 122.61, 121.16, 118.55, 116.37, 114.48, 56.18, 40.65, 40.44, 40.22, 39.80, 39.59, 39.38, 14.41.

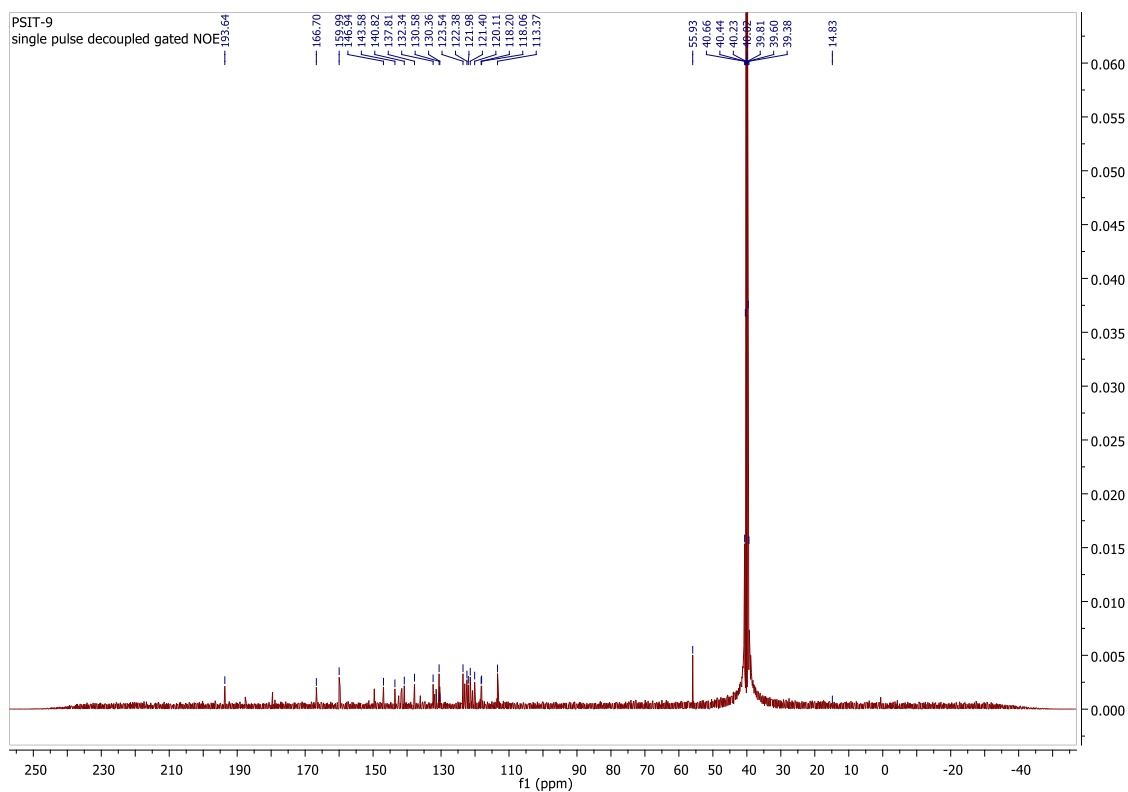
Peak Assignments:

- Aromatic carbons: 189.23, 160.59, 160.06, 146.75, 145.96, 142.82, 142.28, 138.43, 136.26, 130.98, 125.48, 125.40, 124.94, 122.61, 121.16, 118.55, 116.37, 114.48 ppm.
- Solvent (DMSO-d₆): 40.00, 56.18 ppm.
- CDCl₃ solvent triplet: 14.41 ppm.

2-(2-Methoxybenzoyl)-3-methylthiazolo[3',2':2,3][1,2,4]triazino[5,6-b]indole (12i)

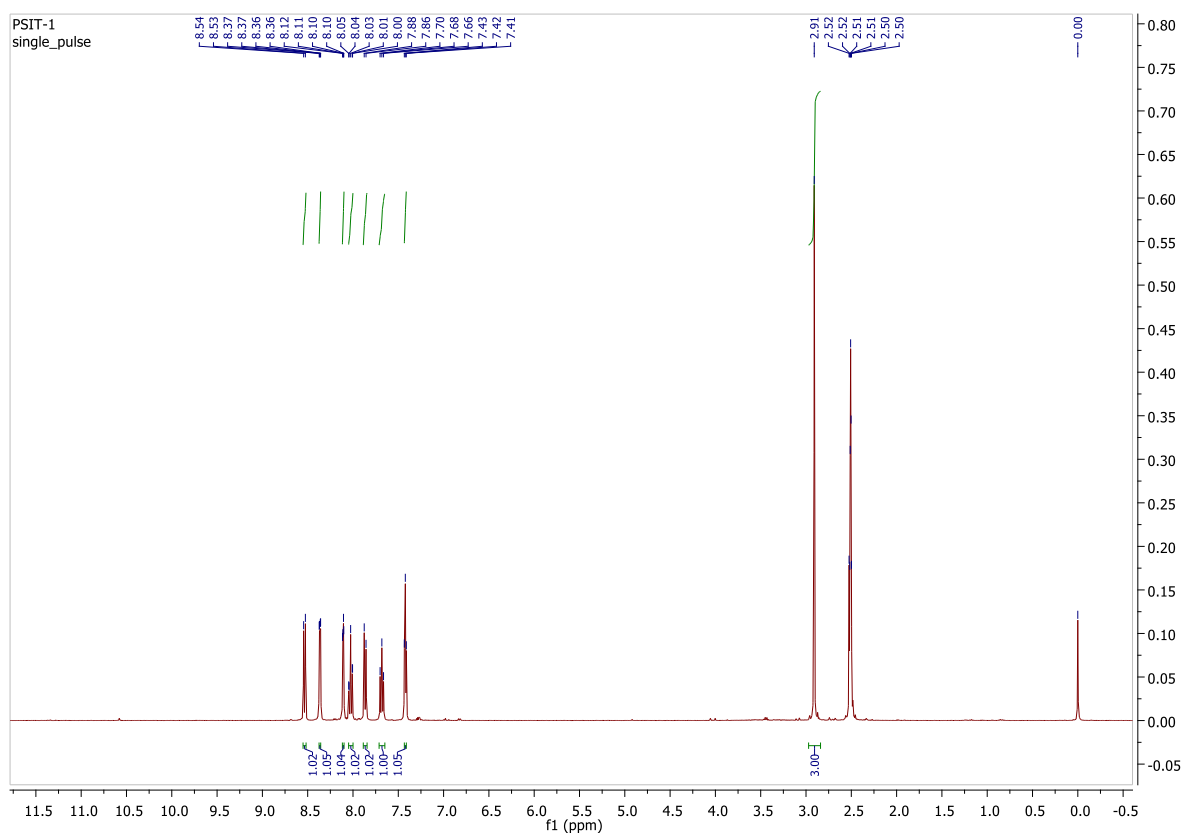


¹H NMR spectrum of 12i

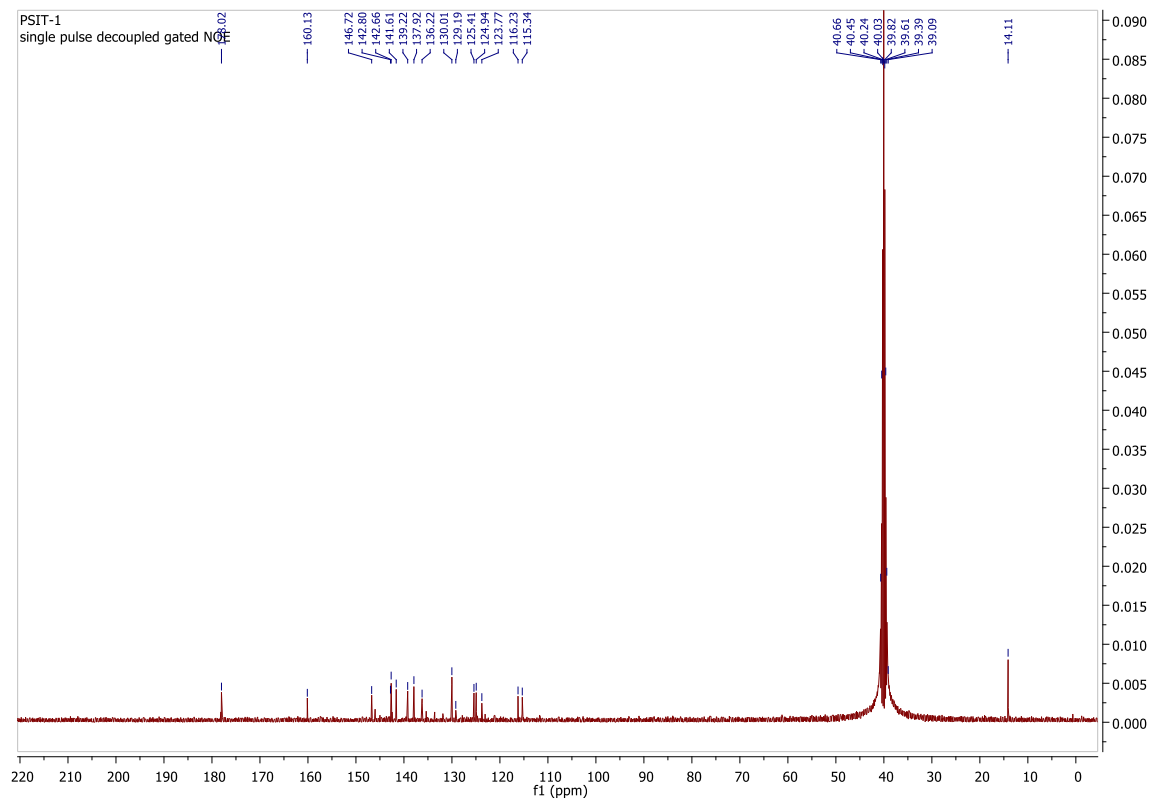


¹³C NMR spectrum of 12i

3-Methyl-2-((2-thiophen)oyl)thiazolo[3',2':2,3][1,2,4]triazino[5,6-b]indole (12j)



¹H NMR spectrum of 12j



¹³C NMR spectrum of 12j