Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary Information

Emergent Antibacterial Activity of N-(thiazol-2-yl)benzenesulfonamides in Conjunction with Cell-Penetrating Octaarginine

Poonam Ratrey[1], Amarjyoti Das Mahapatra[2], Shiny Pandit[3], Murtuza Hadianawala[2], Sasmita Majhi[1], Abhijit Mishra[1], Bhaskar Datta[*, 2,3]

[1]Department of Materials Science and Engineering,[2]Department of Chemistry, [3]Department of Biological Engineering, Indian Institute of Technology, Gandhinagar, Gujarat, India

* Corresponding author

* Bhaskar Datta, Department of Chemistry & Biological Engineering, Indian Institute of Technology Gandhinagar, Palaj, Gandhinagar 382355 India.

Telephone: 079-2395-2073; Fax: 079-2397-2622; E-mail: bdatta@iitgn.ac.in

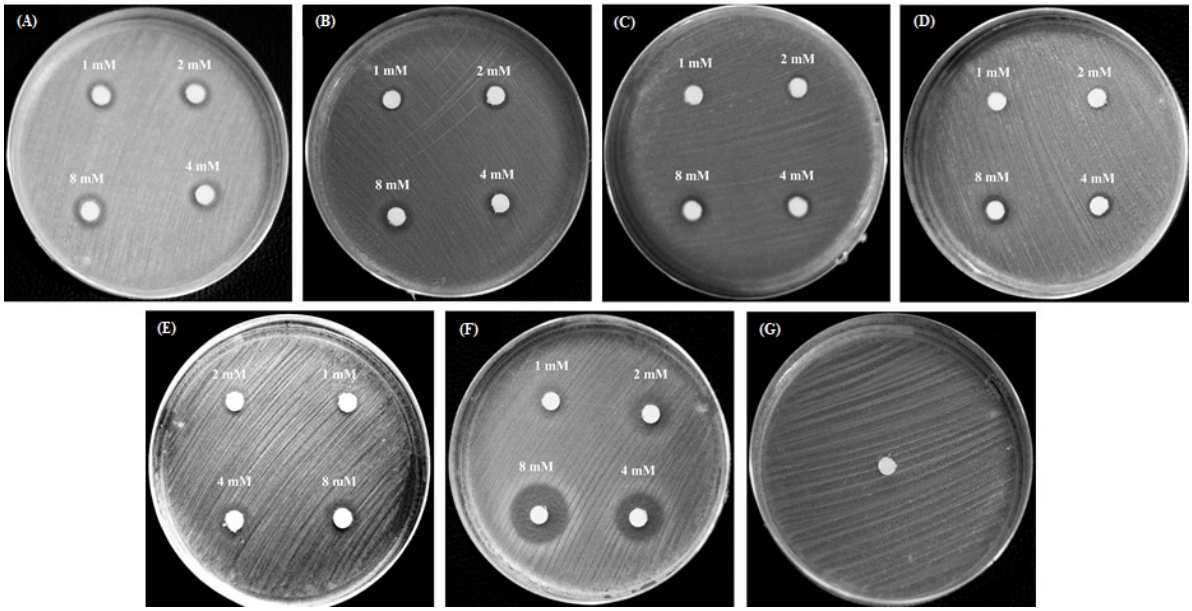


Figure S1. Zone of inhibition of active compounds (A) tert-butyl (B) isopropyl (C) chlorine (D) methyl (E) H (F) positive control (*Chloramphenicol*) and (G) negative control (DMSO) against *Escherichia coli* at different diluted concentrations (1 mM, 2 mM, 4 mM, 8 mM).

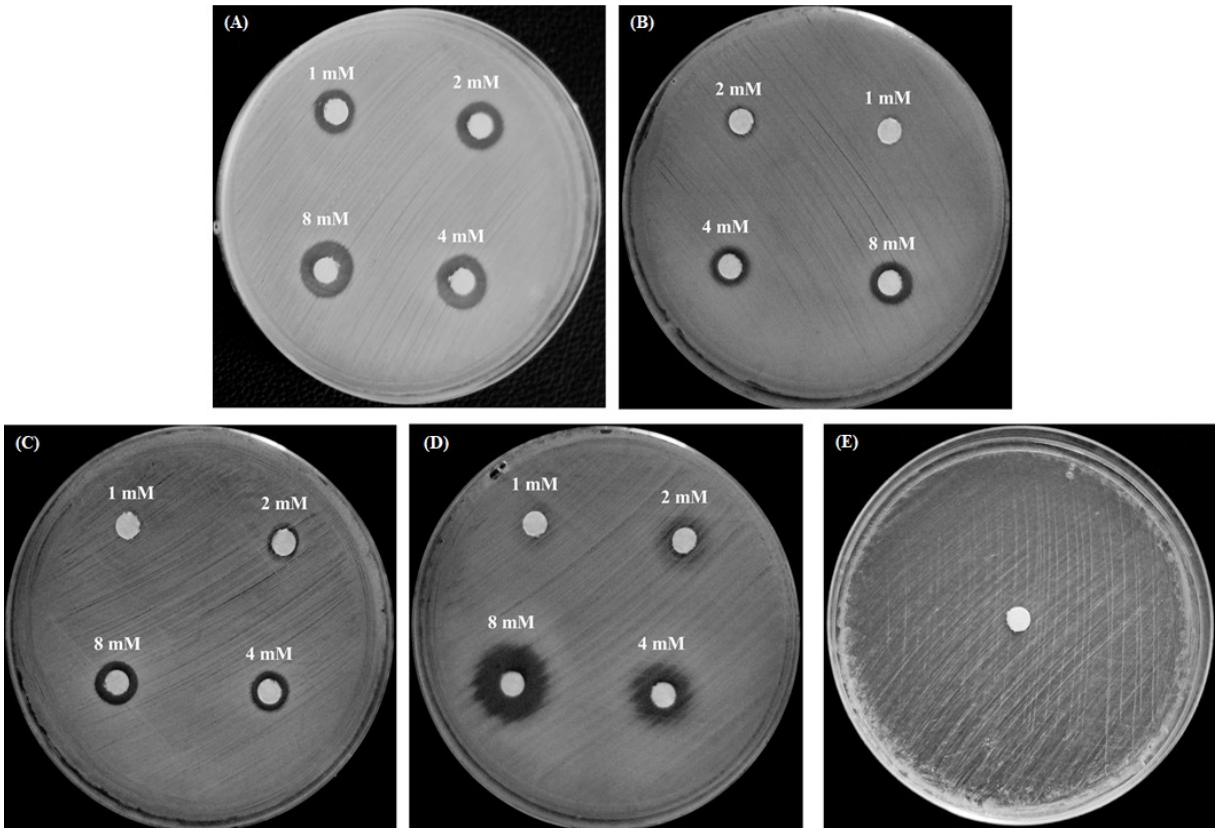


Figure S2. Zone of inhibition of active compounds (A) tert-butyl (B) isopropyl (C) chlorine (D) positive control (*Chloramphenicol*) and (E) negative control (DMSO) against *Staphylococcus aureus* at different diluted concentrations (1 mM, 2 mM, 4 mM, 8 mM).

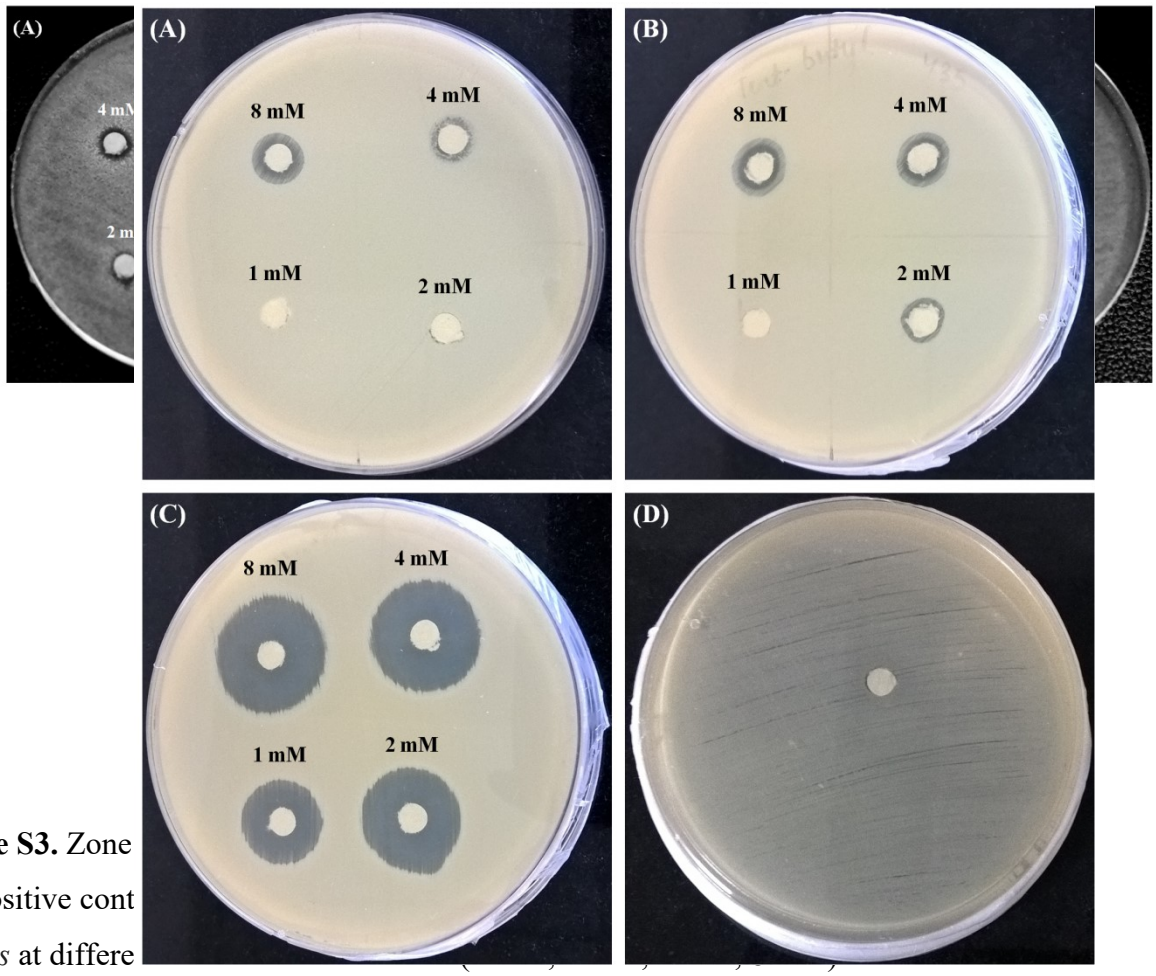


Figure S3. Zone
(D) positive cont
subtilis at differe

Figure S4. Zone of inhibition of active compounds (A) isopropyl (B) tert-butyl (C) positive control (*Chloramphenicol*) (D) negative control (DMSO) against *Staphylococcus epidermidis* at different diluted concentrations (1 mM, 2 mM, 4 mM, 8 mM).

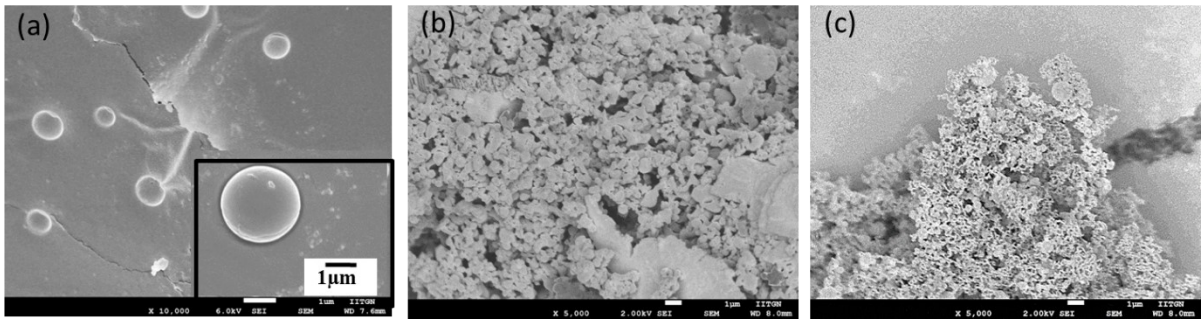


Figure S5. Powder scanning electron micrographs (a) Bare peptide with inset showing a zoomed particle, (b) bare 5a drug and (c) 5a-peptide complex

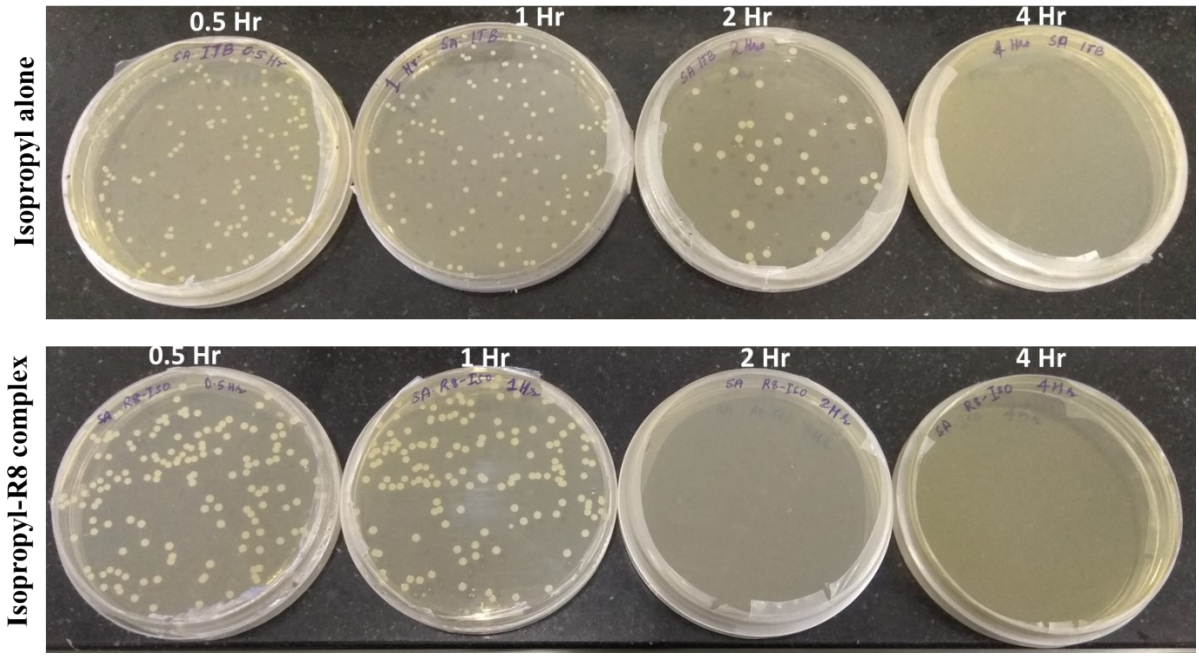


Figure S6. Time-kill assay – Agar plates showing *S. aureus* colonies and killing of all the cells within 2h hours for isopropyl-R8 complex while 4 hours for isopropyl alone.

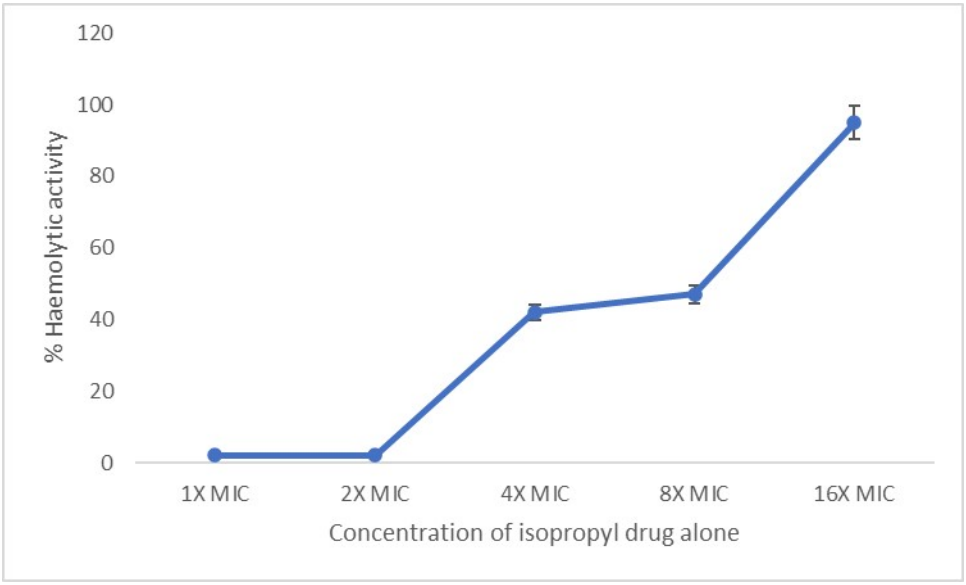


Figure S7. Haemolytic activity of isopropyl alone (without complexation) against human RBCs

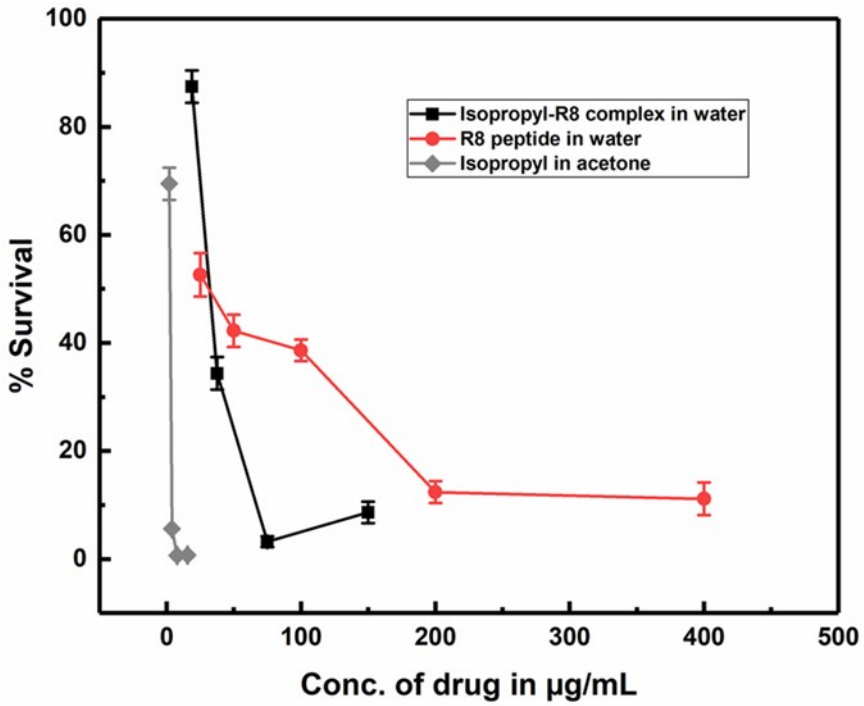
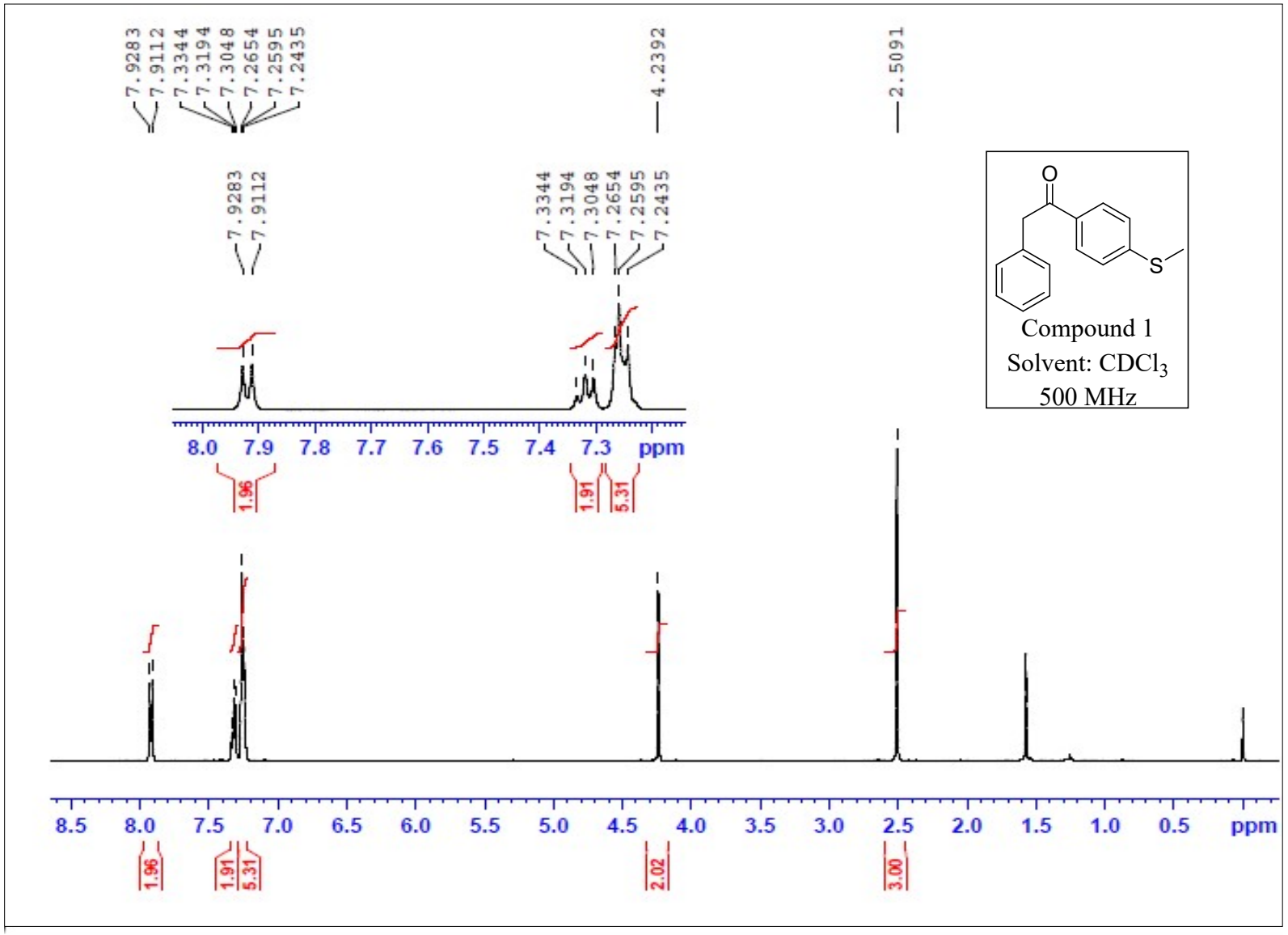
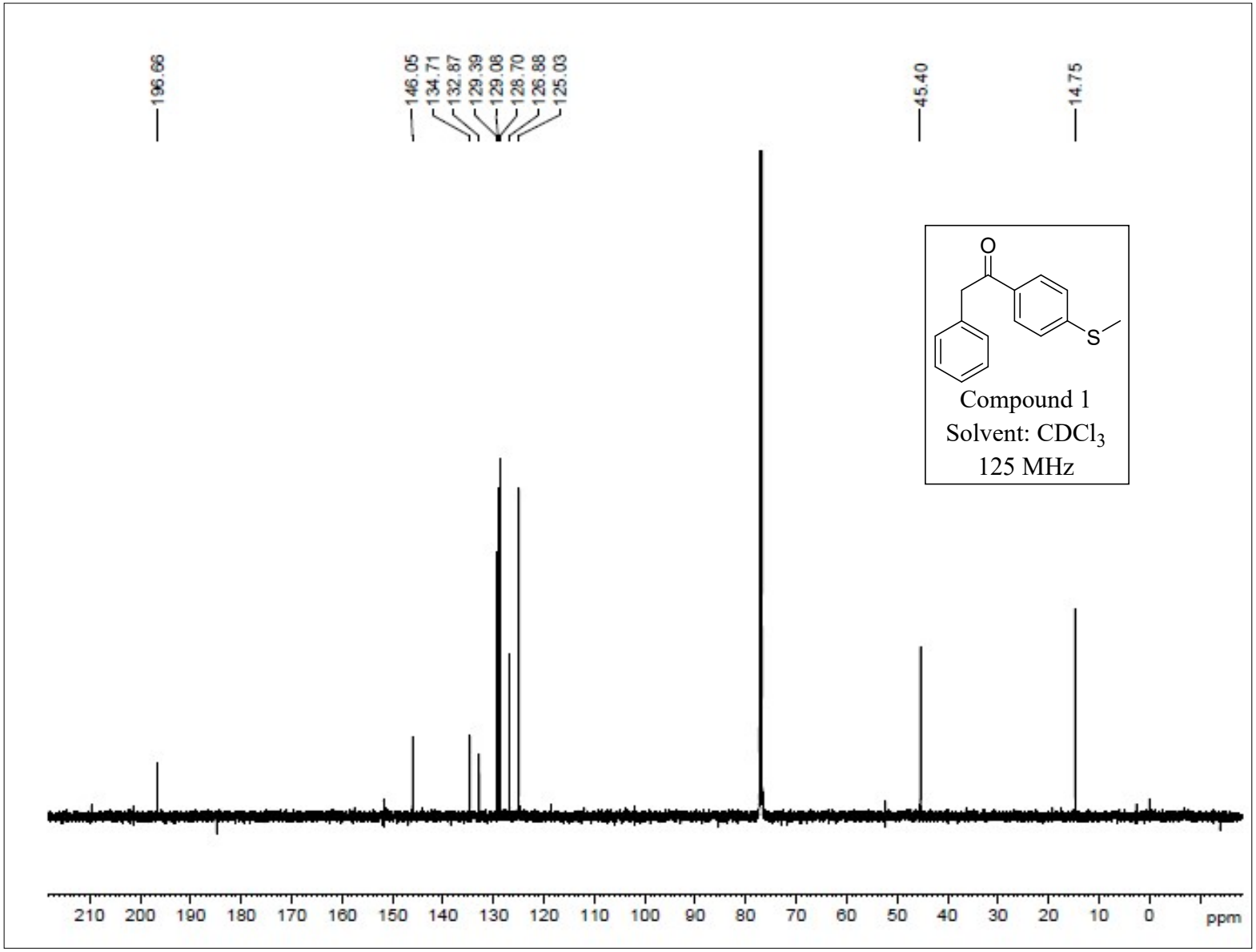


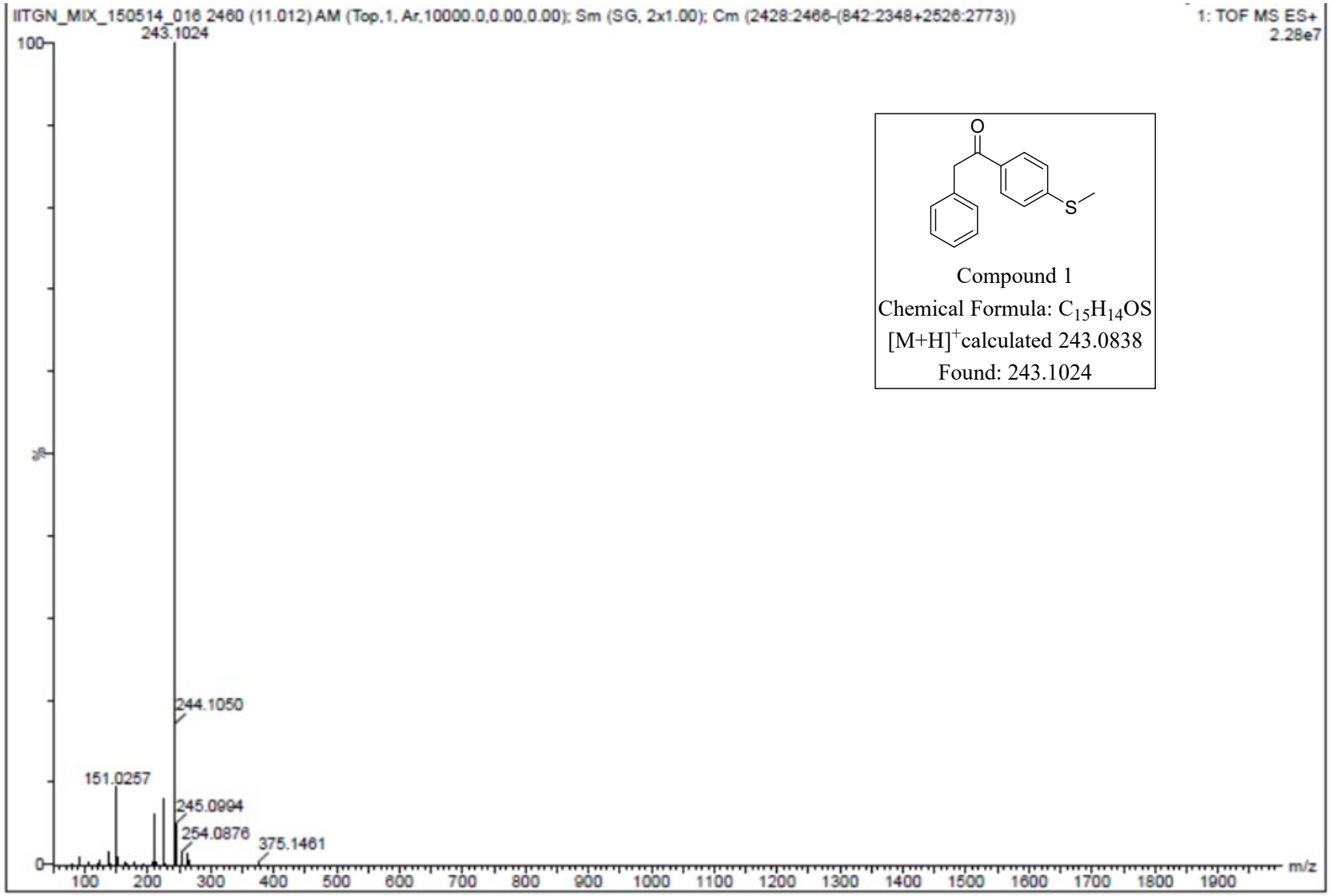
Figure S8: Antibacterial activity of isopropyl/5a alone, R8 alone and complex of isopropyl and R8 against *S. aureus*



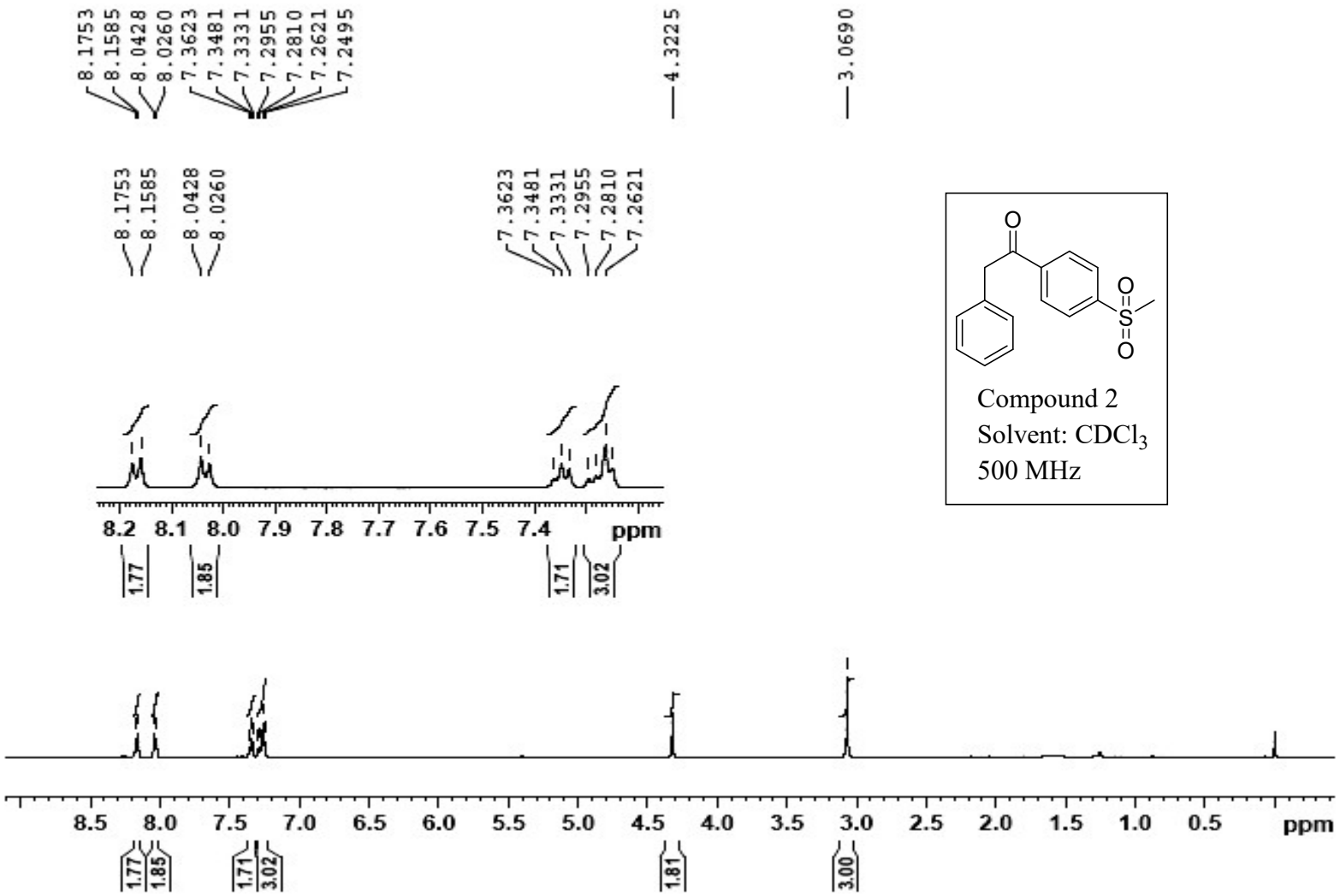
^{1}H NMR of Compound **1**



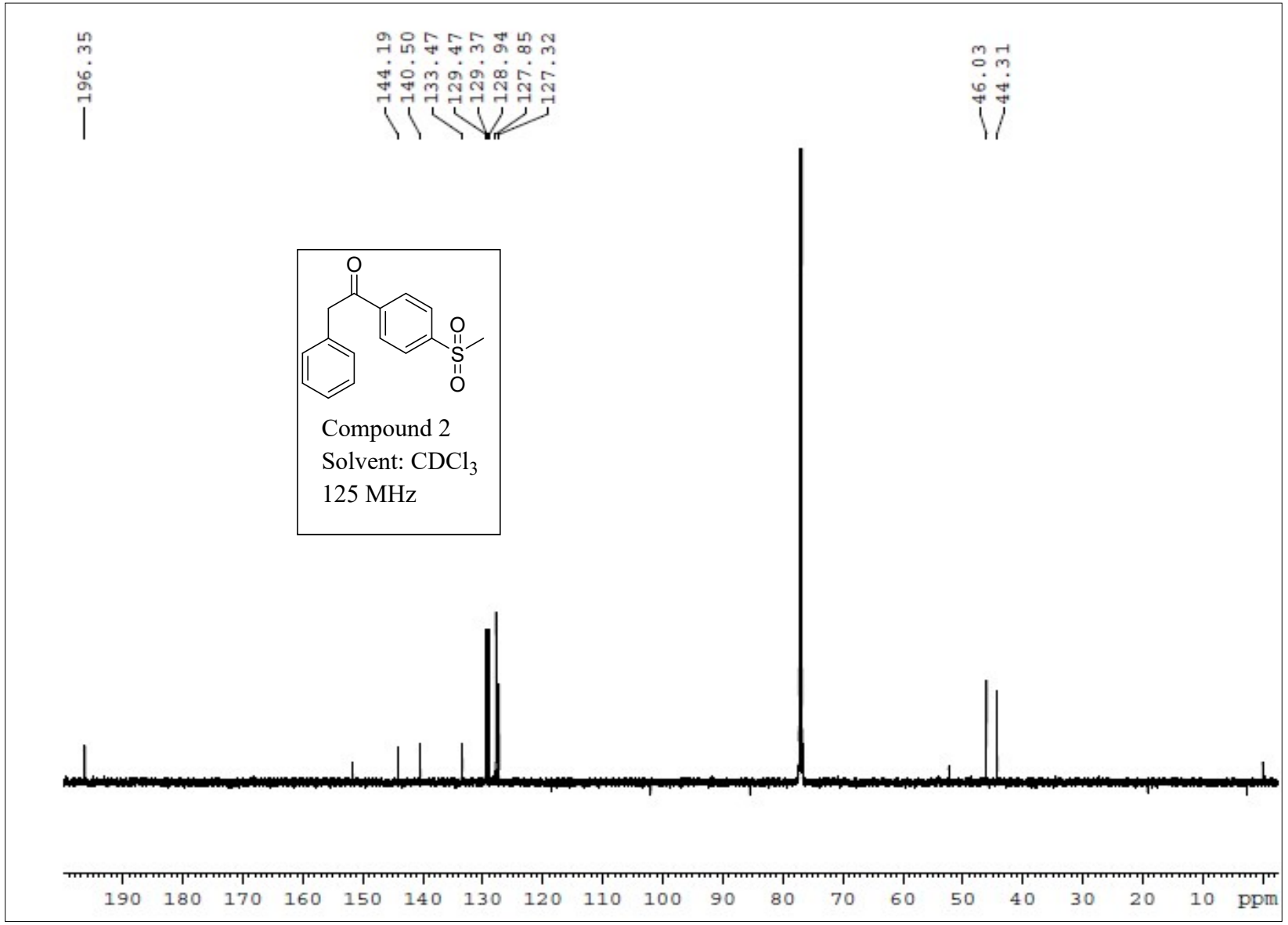
^{13}C NMR of Compound **1**



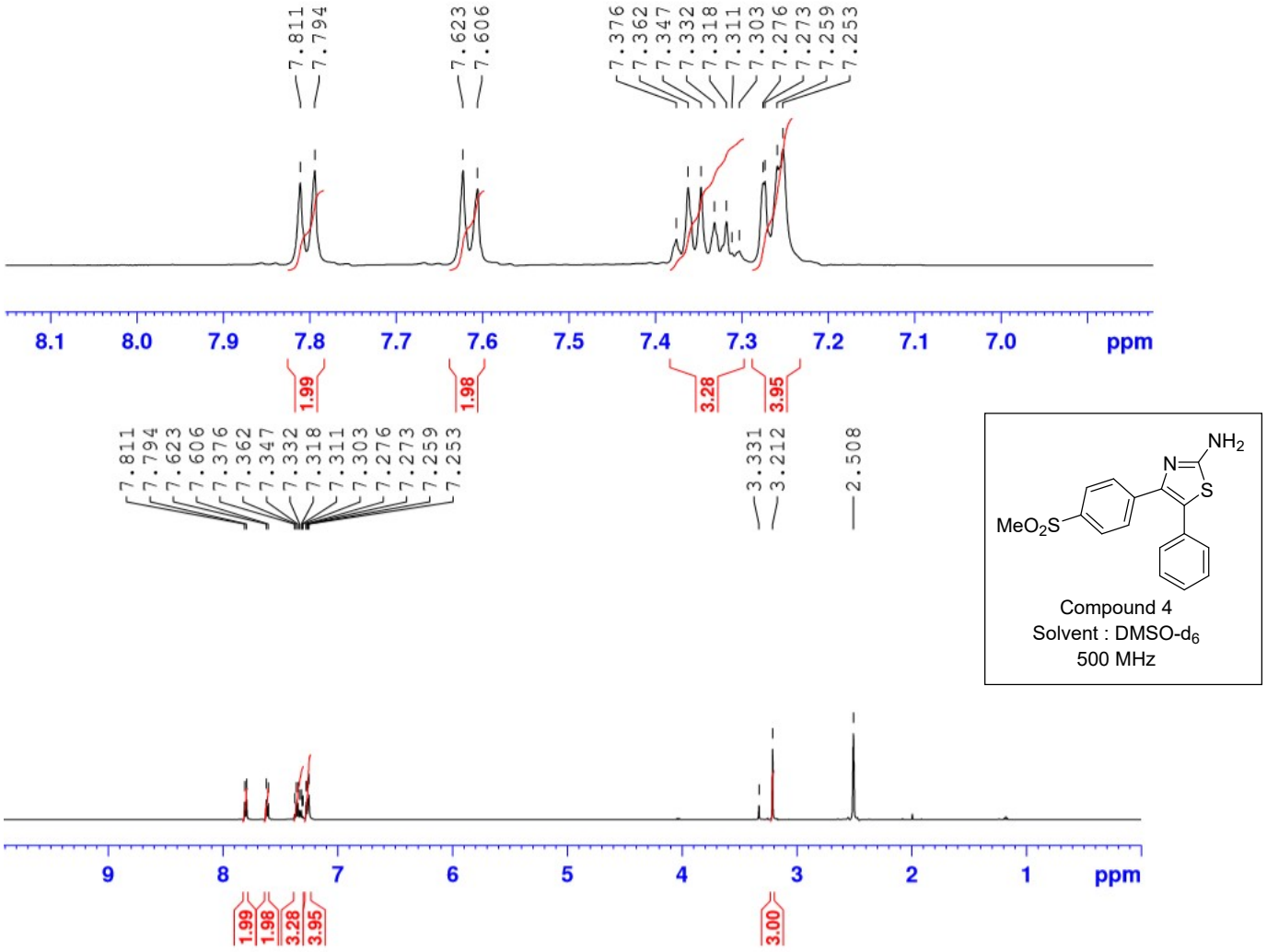
LC-ESIMS of Compound **1**



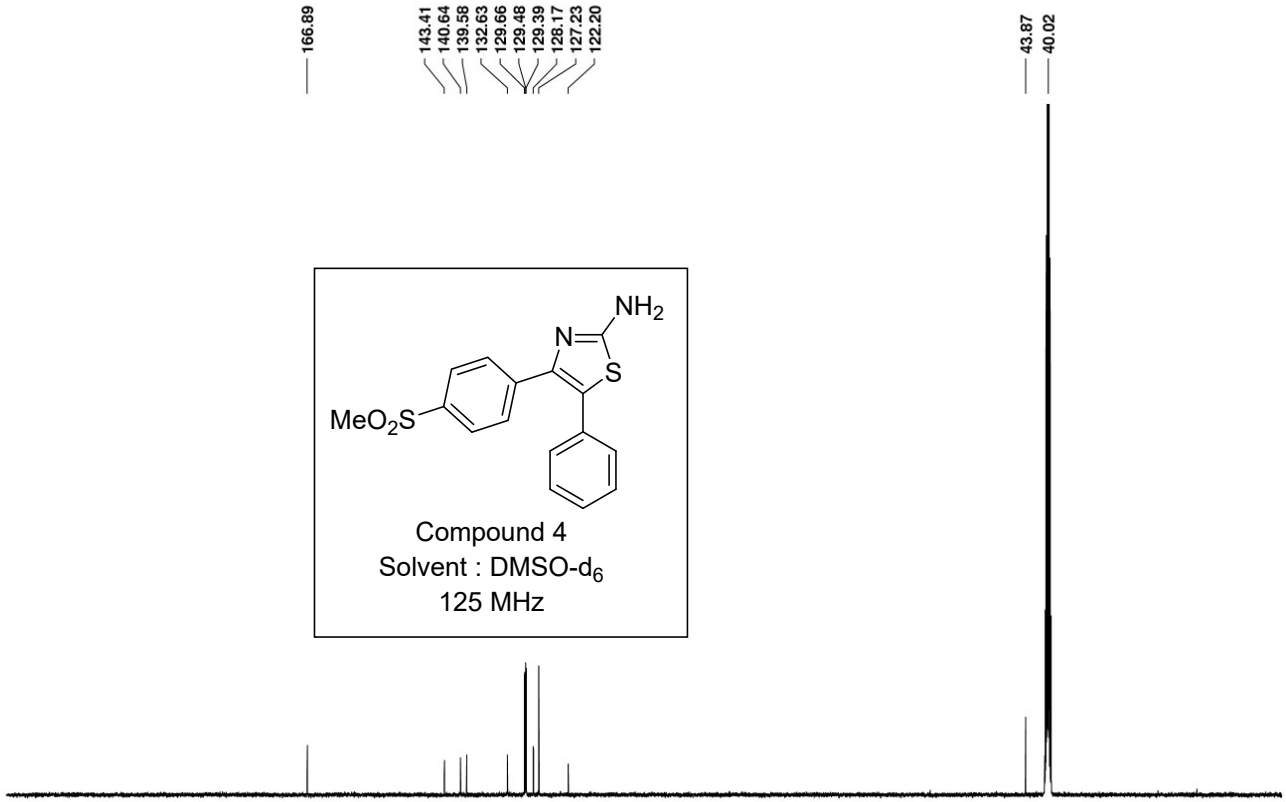
^{1}H NMR of Compound **2**



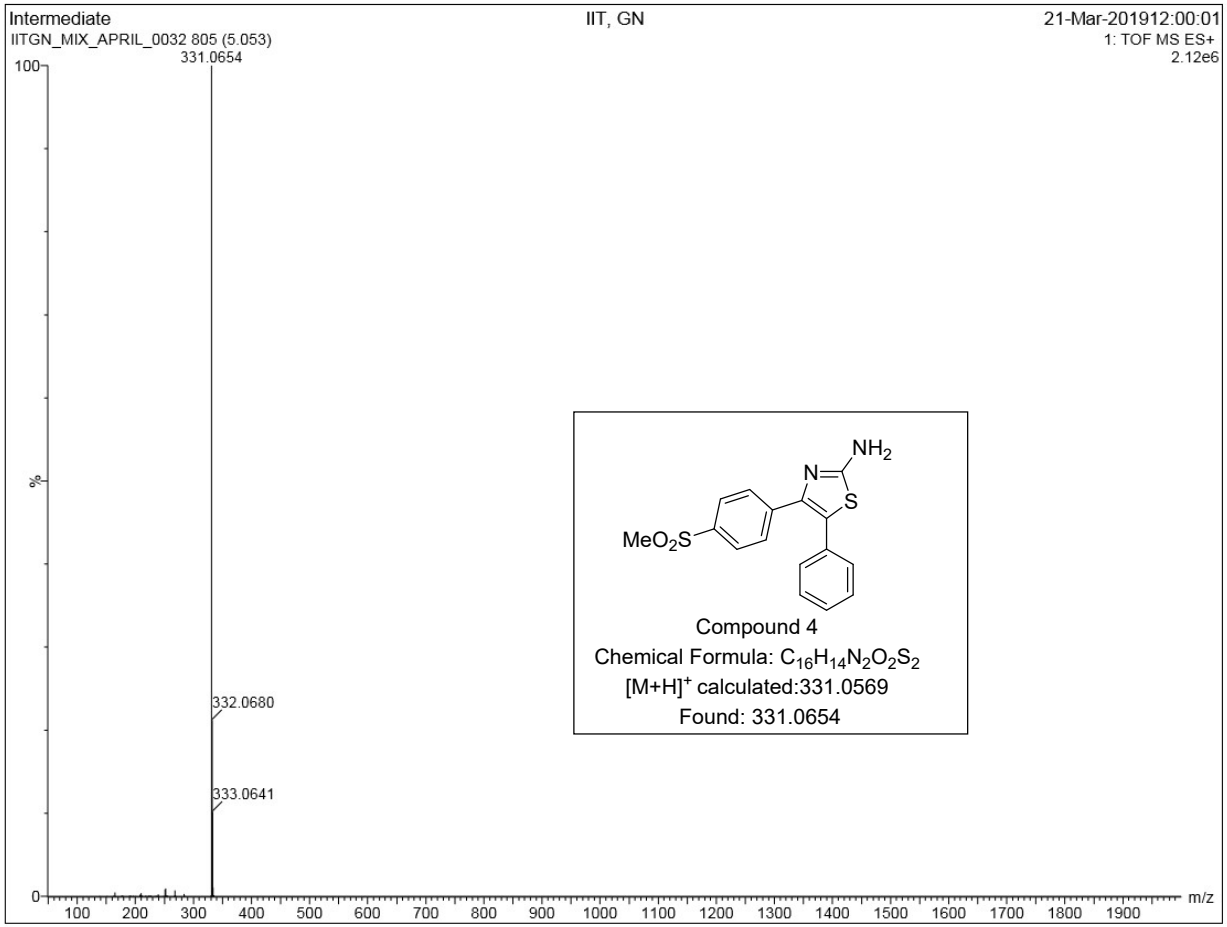
^{13}C NMR of Compound **2**



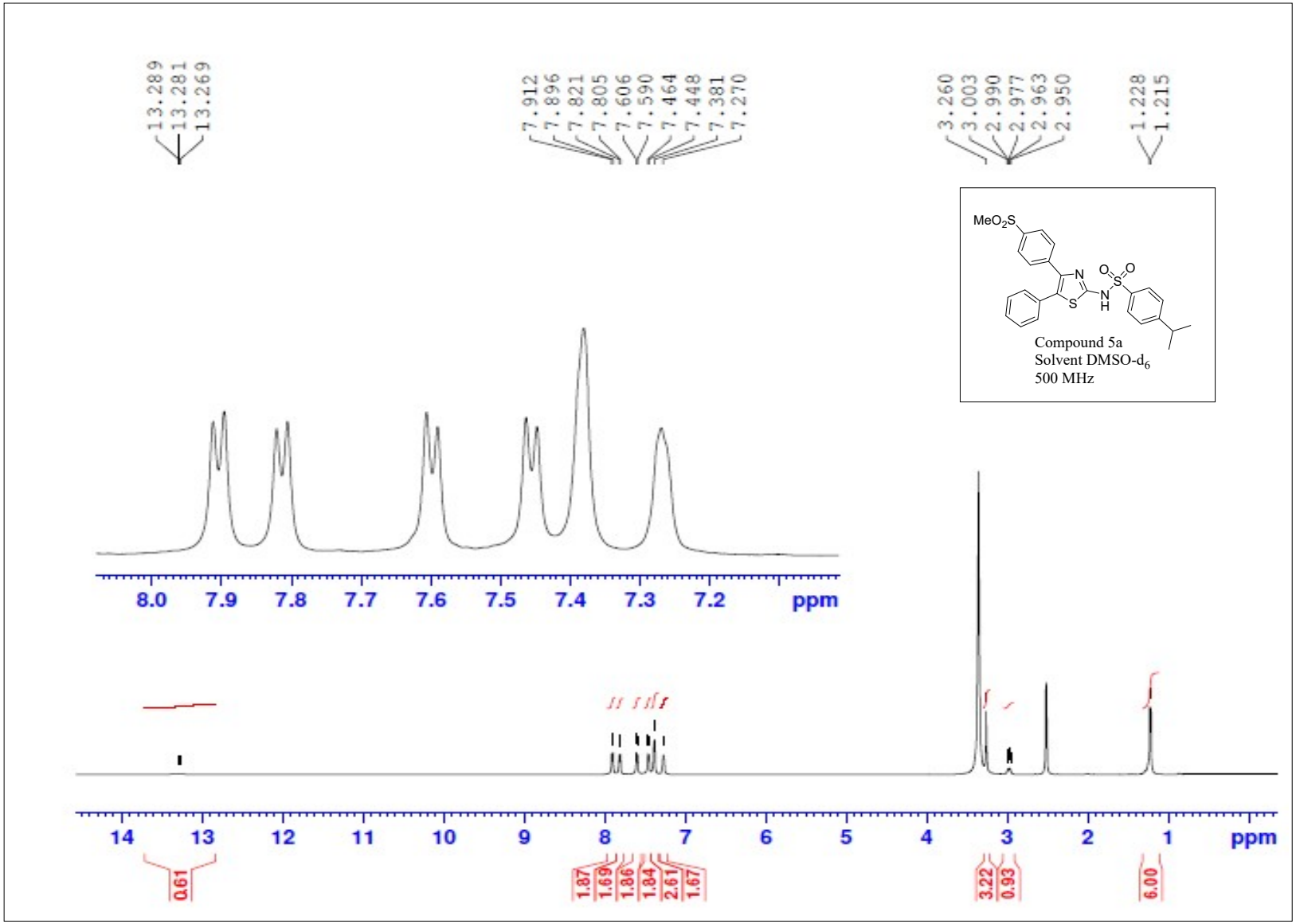
^{1}H NMR of compound **4**



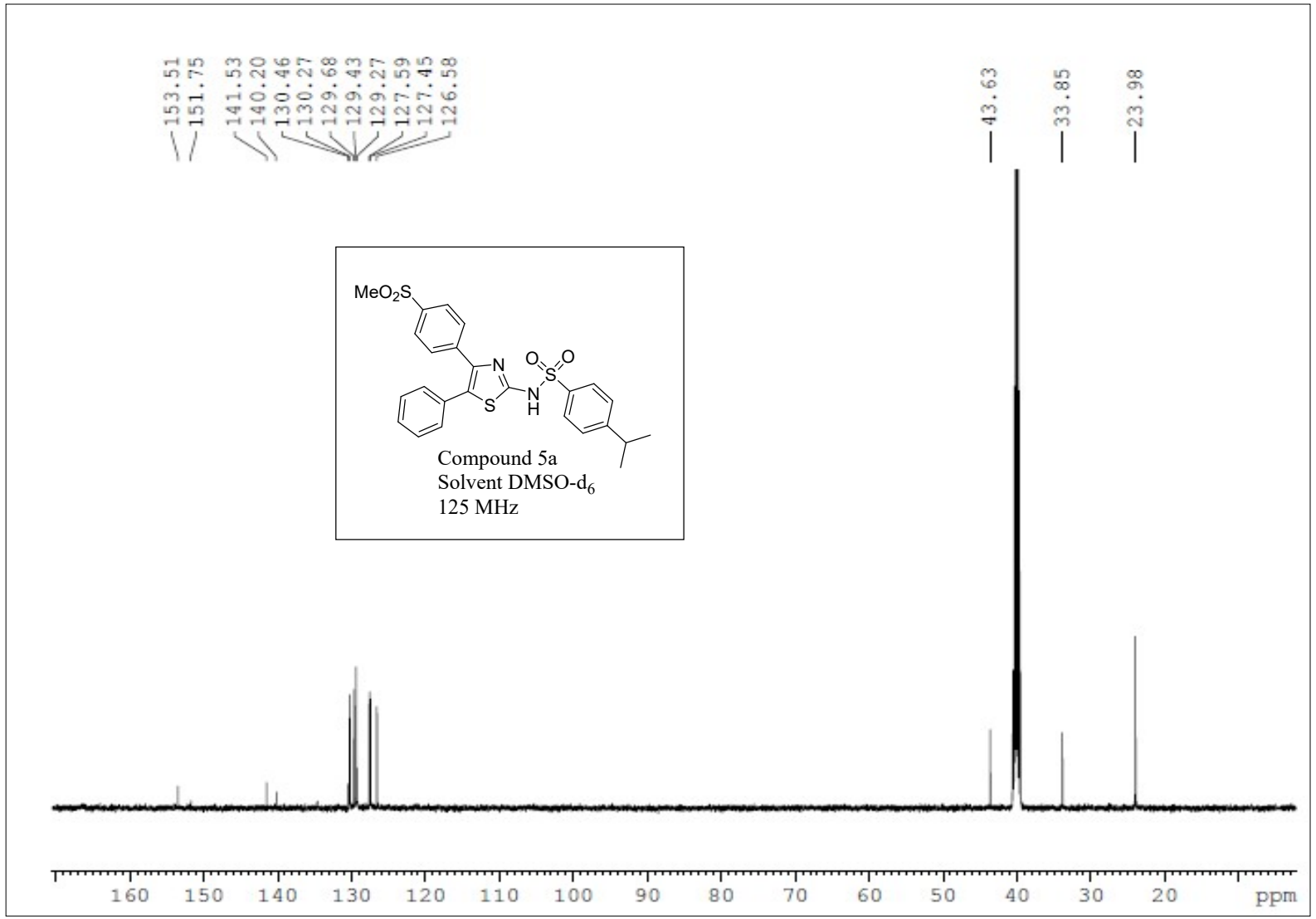
^{13}C NMR of Compound 4



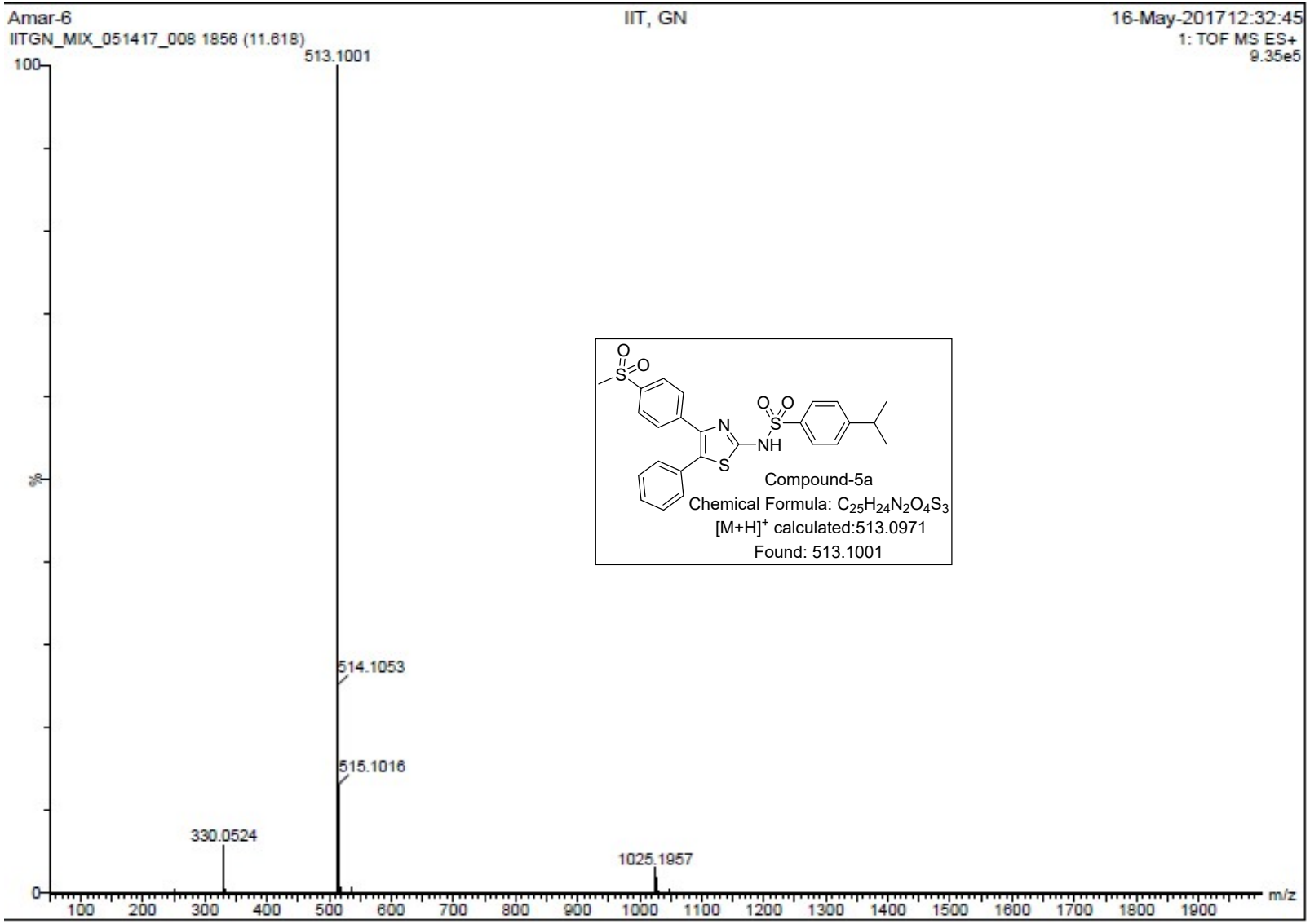
LC-ESIMS of Compound **4**



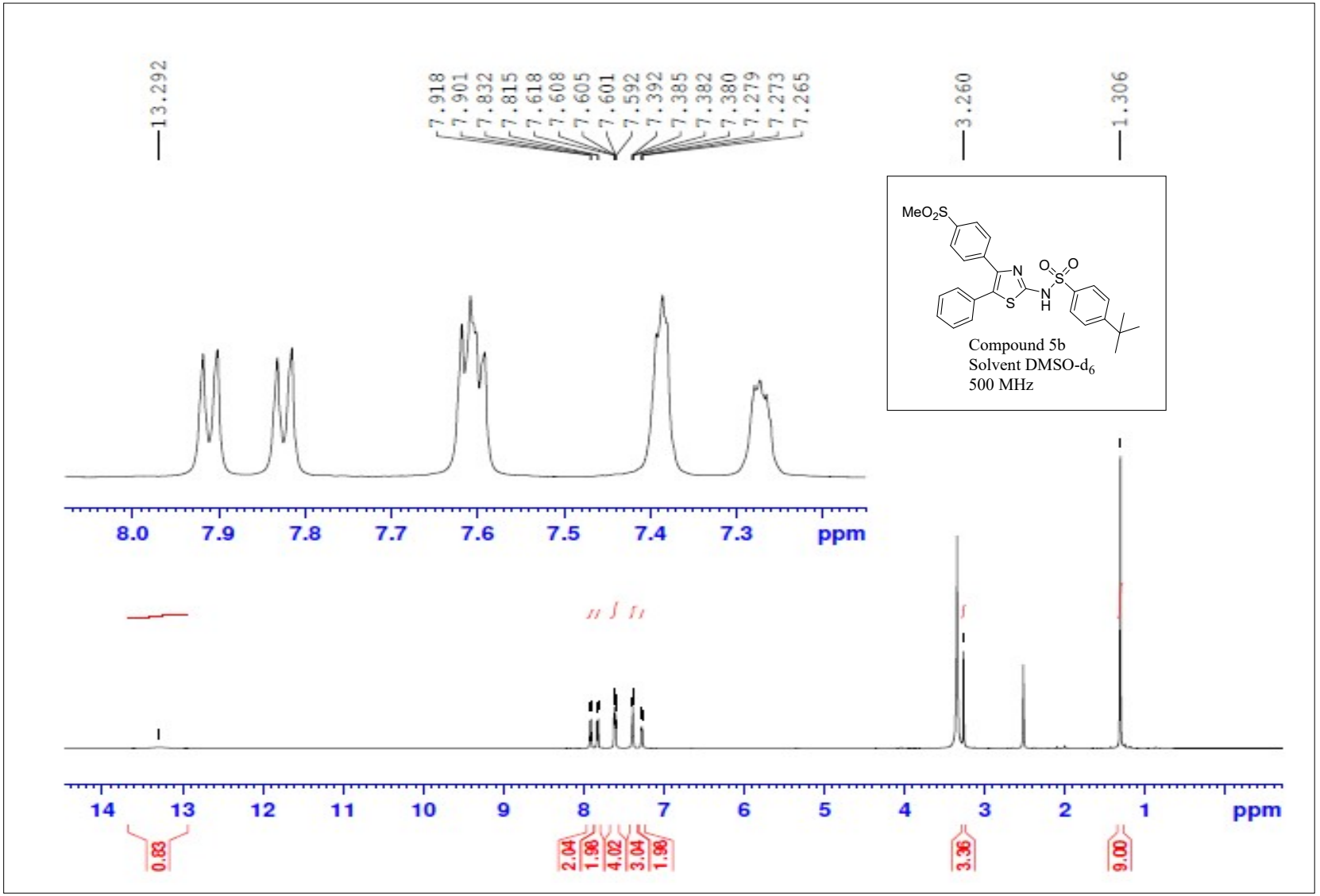
^{1}H NMR of Compound **5a**



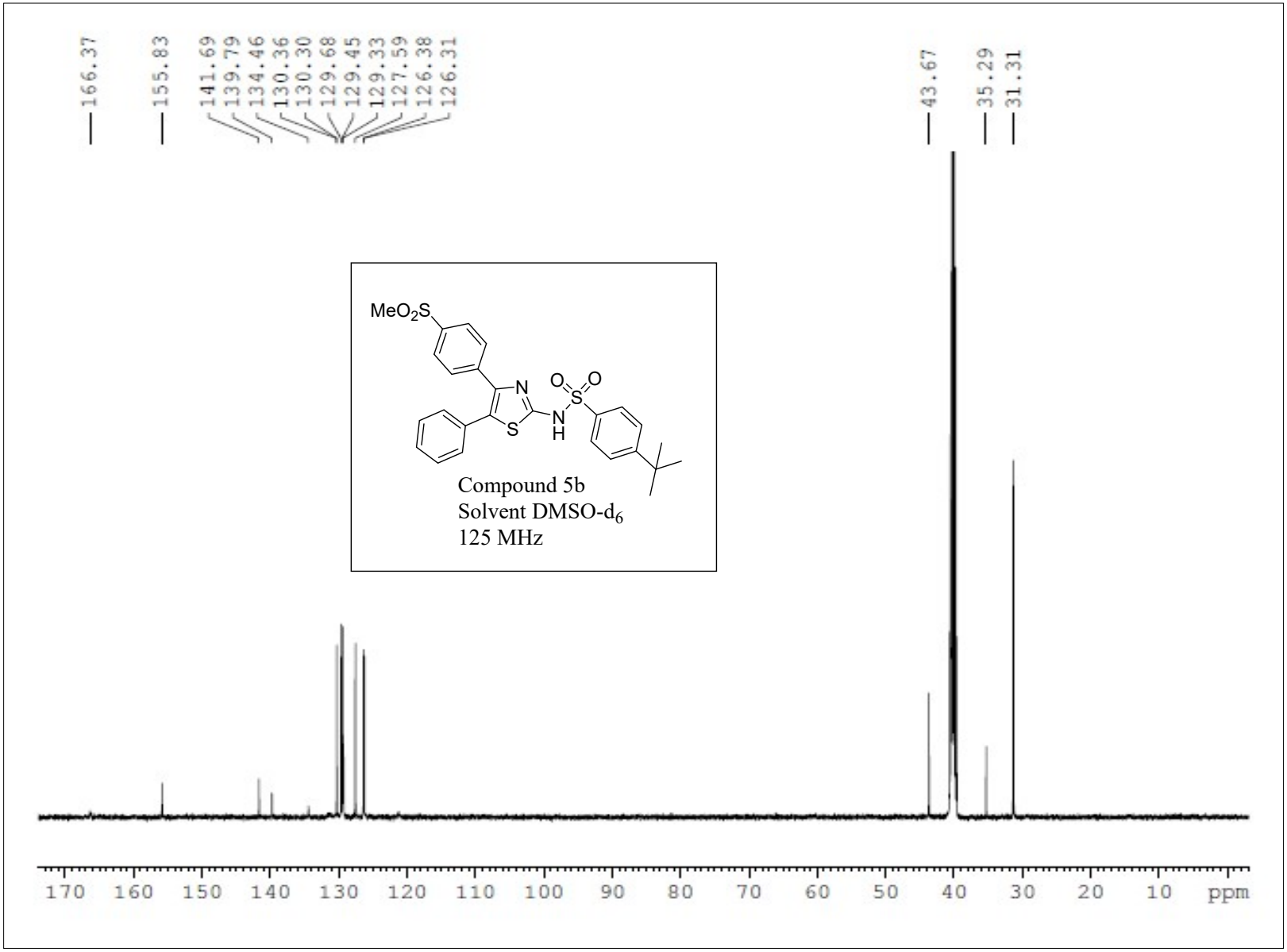
^{13}C NMR of Compound **5a**



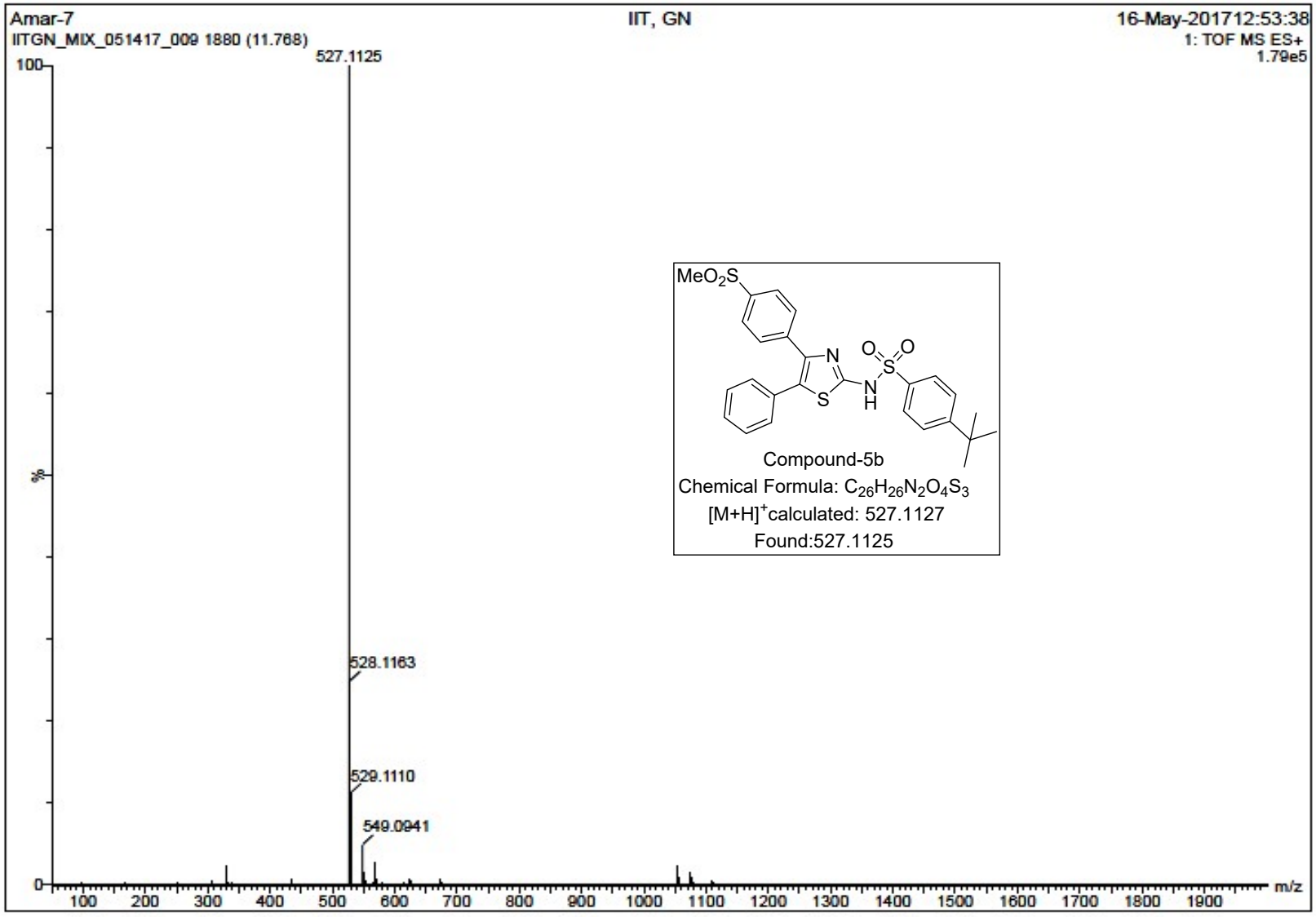
LC-ESIMS of Compound 5a



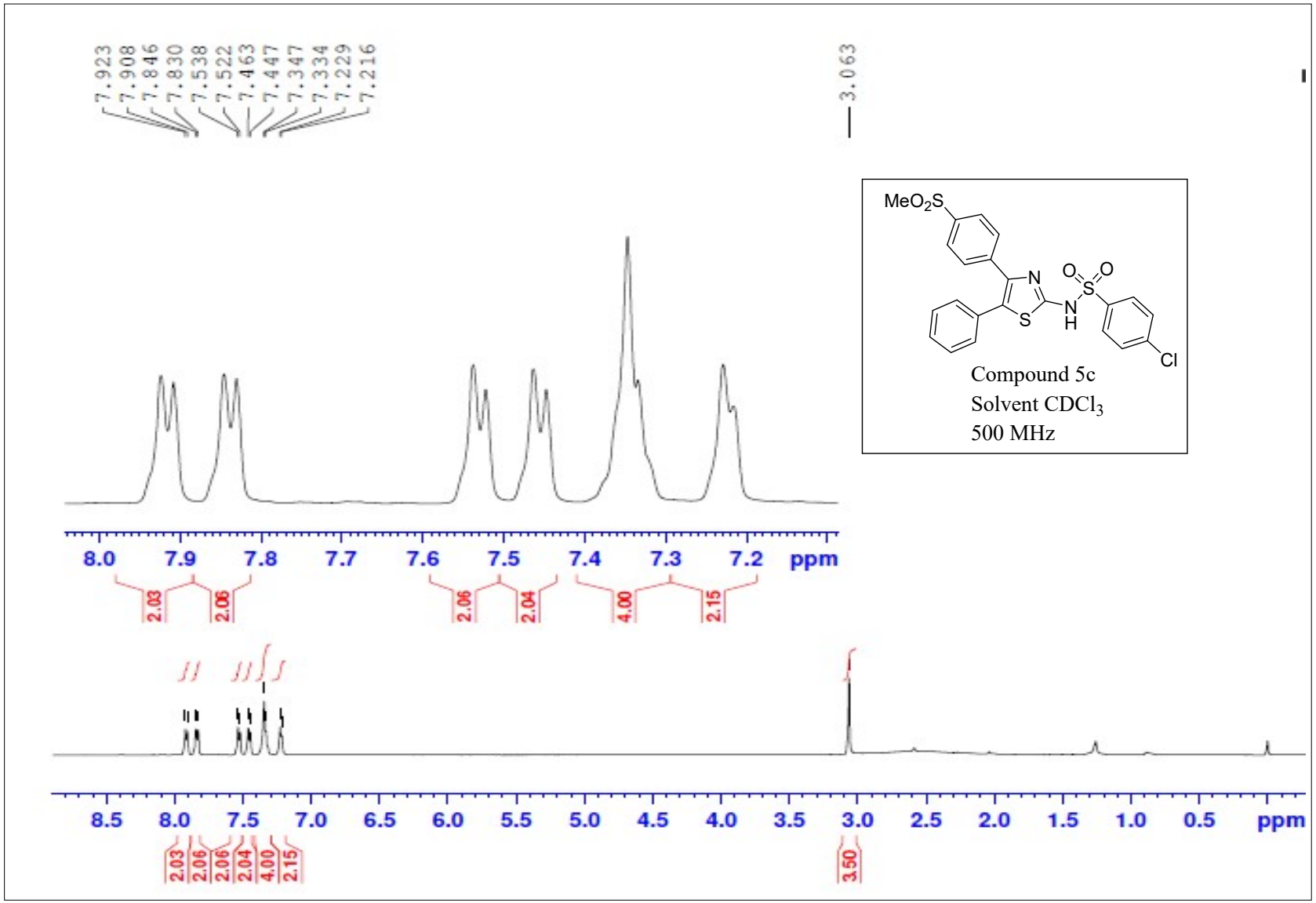
^{1}H NMR of Compound **5b**



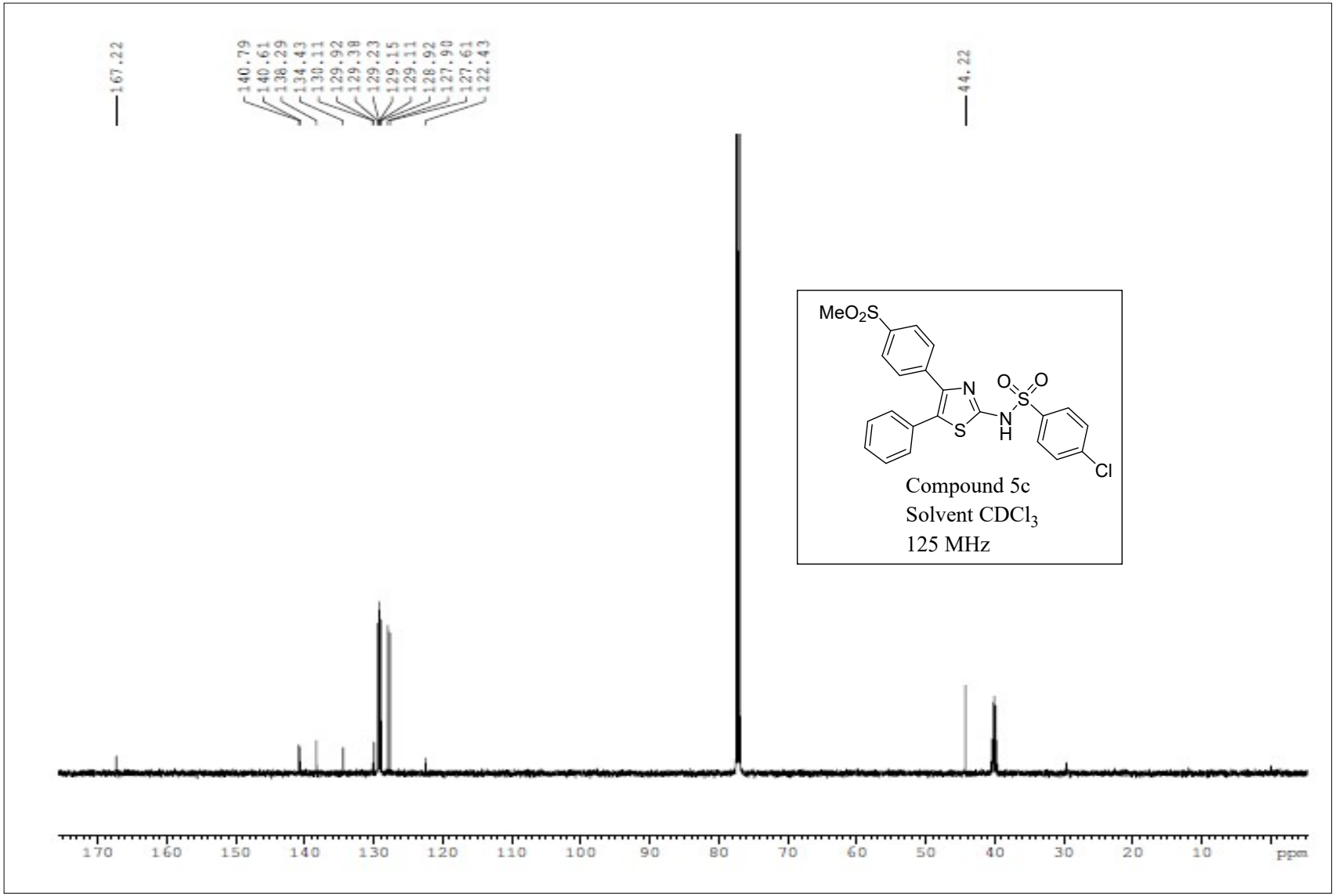
^{13}C NMR of Compound **5b**



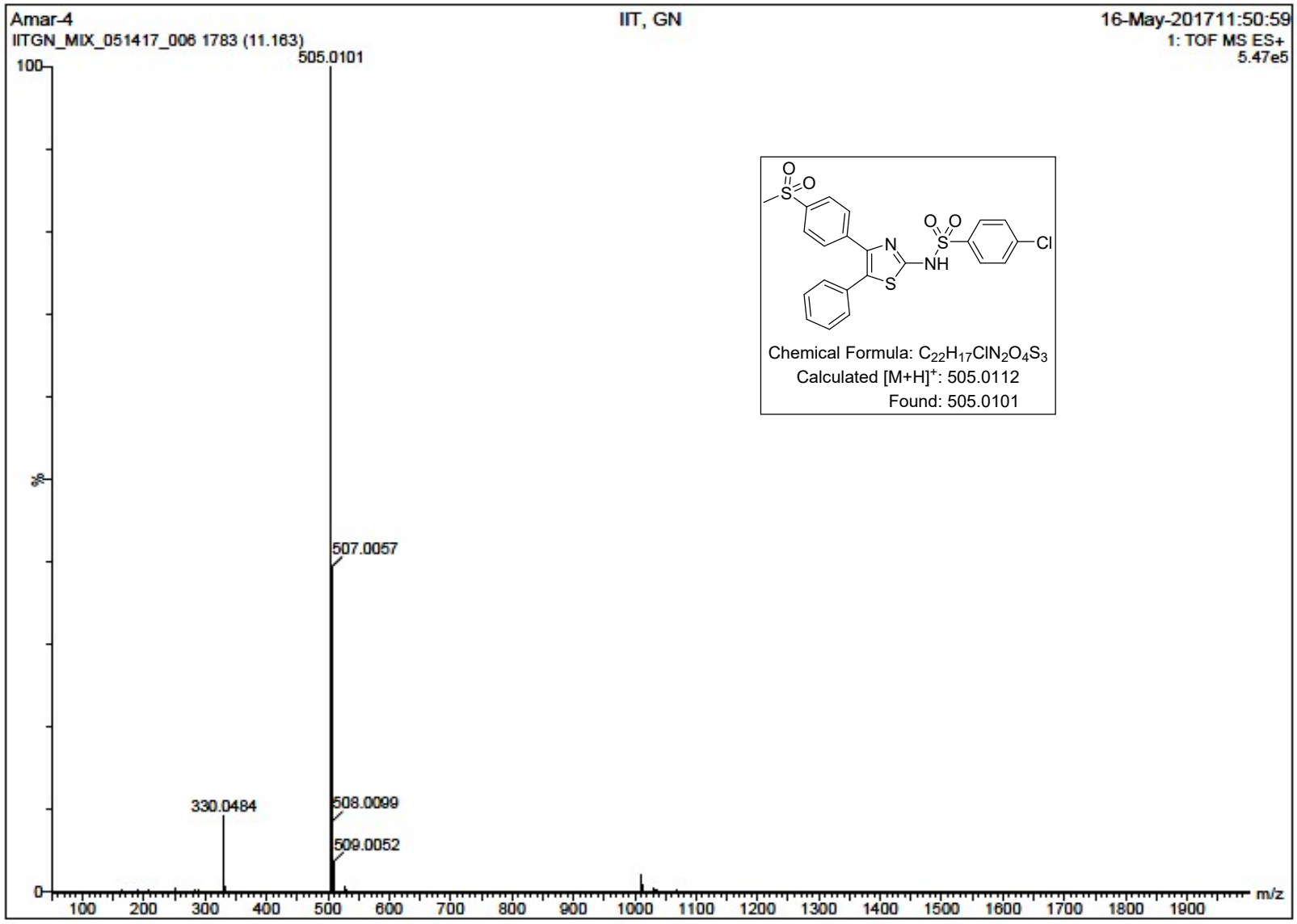
LC-ESIMS of Compound 5b



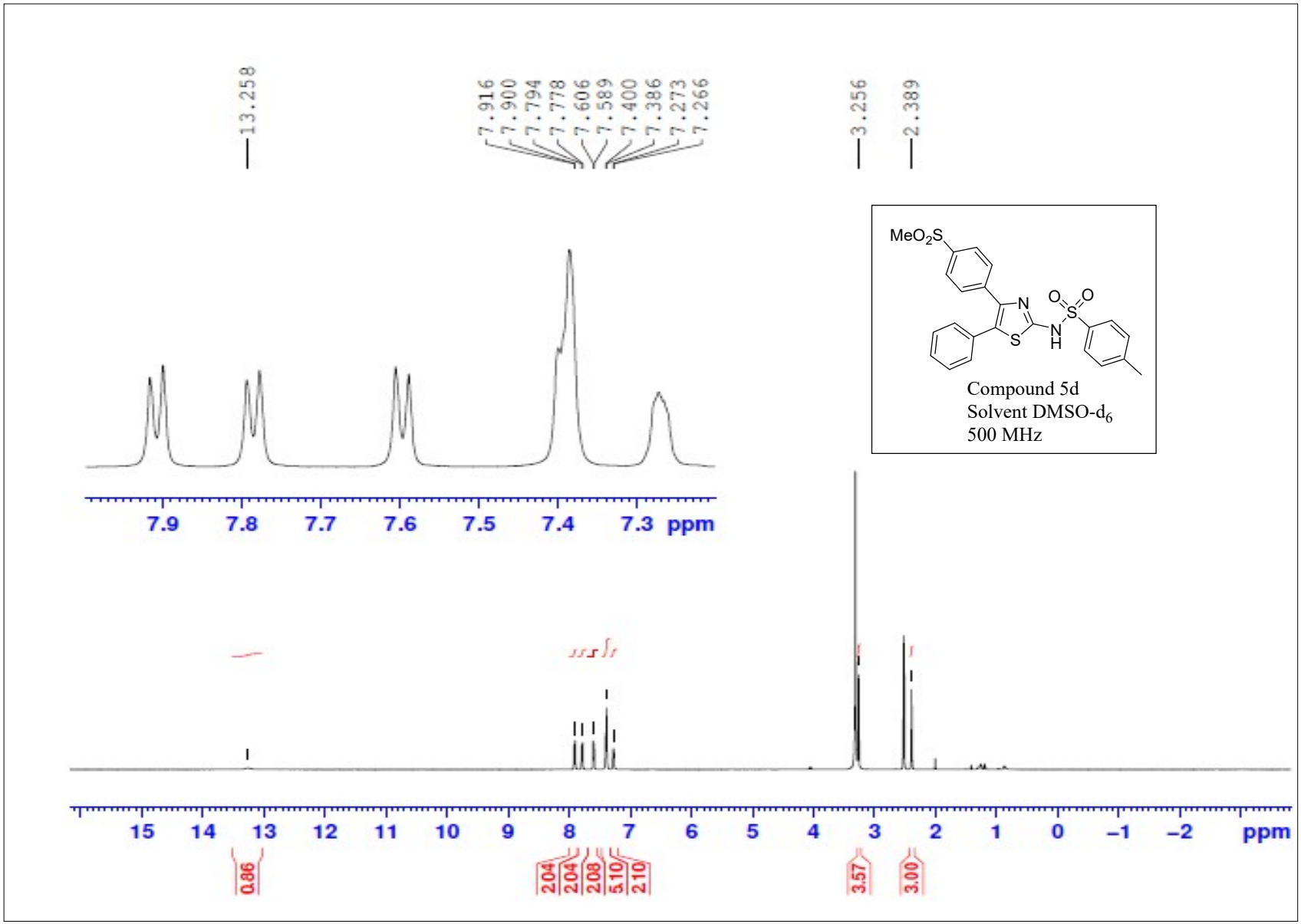
^{1}H NMR of Compound **5c**



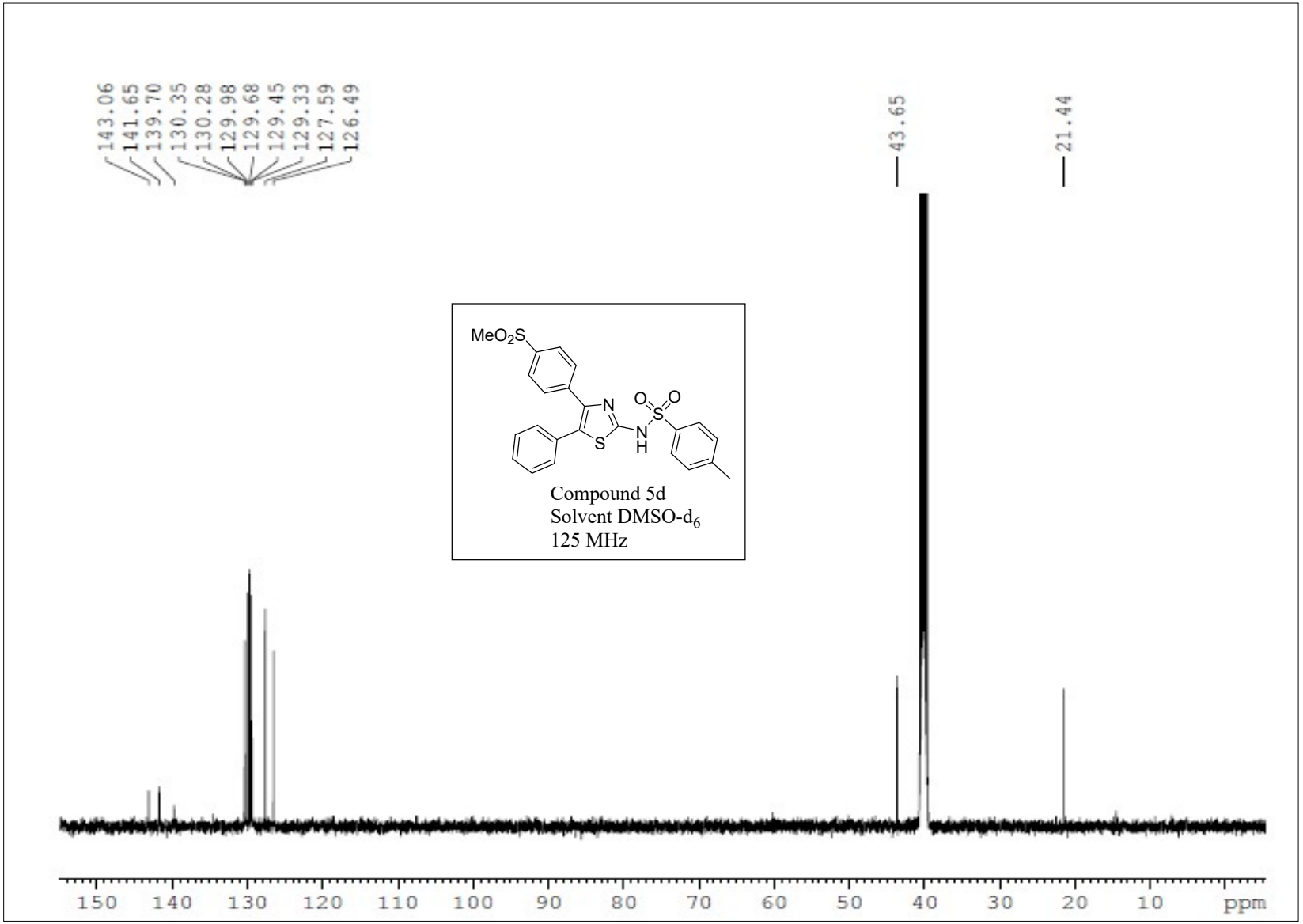
^{13}C NMR of Compound **5c**



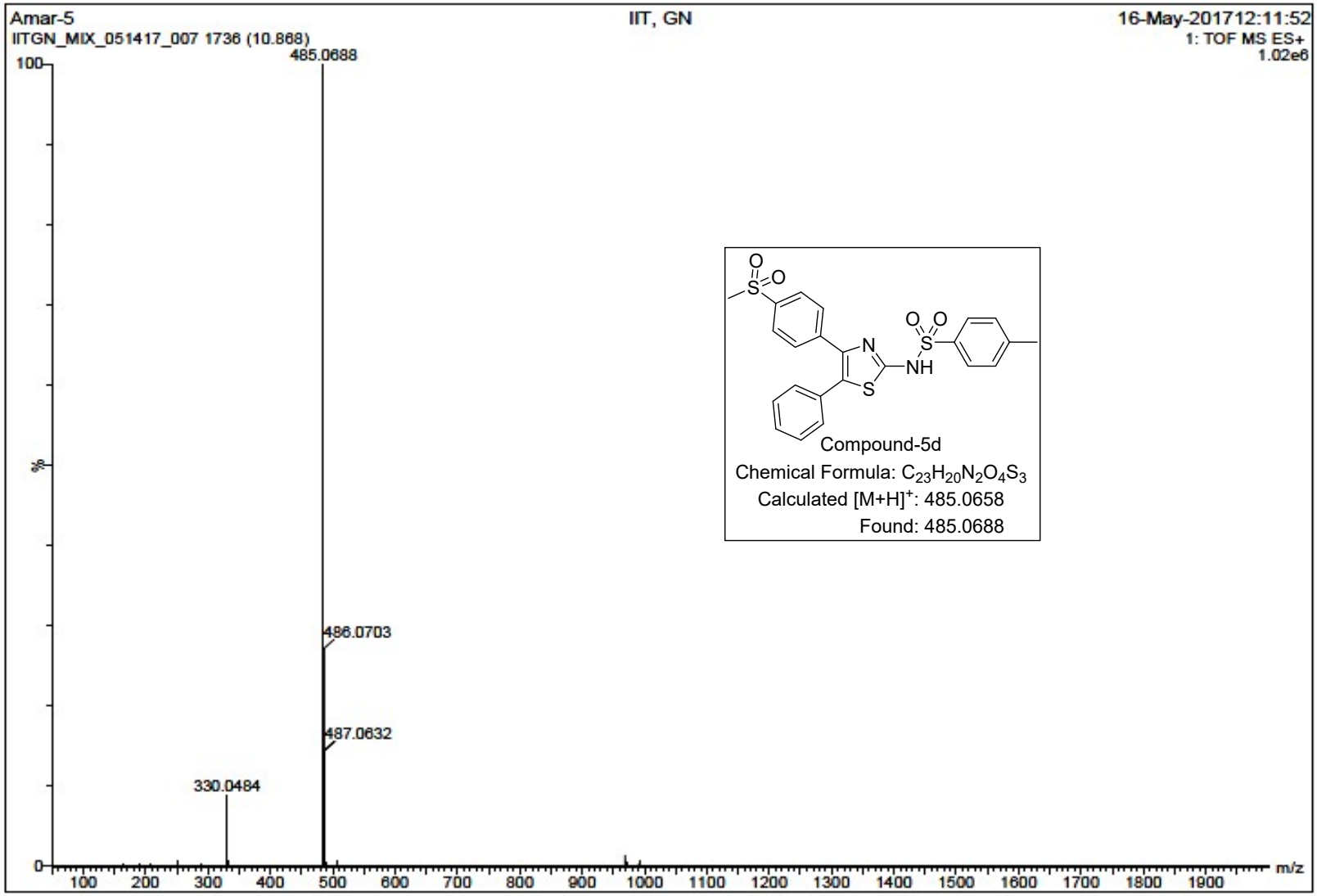
LC-ESIMS of Compound **5c**



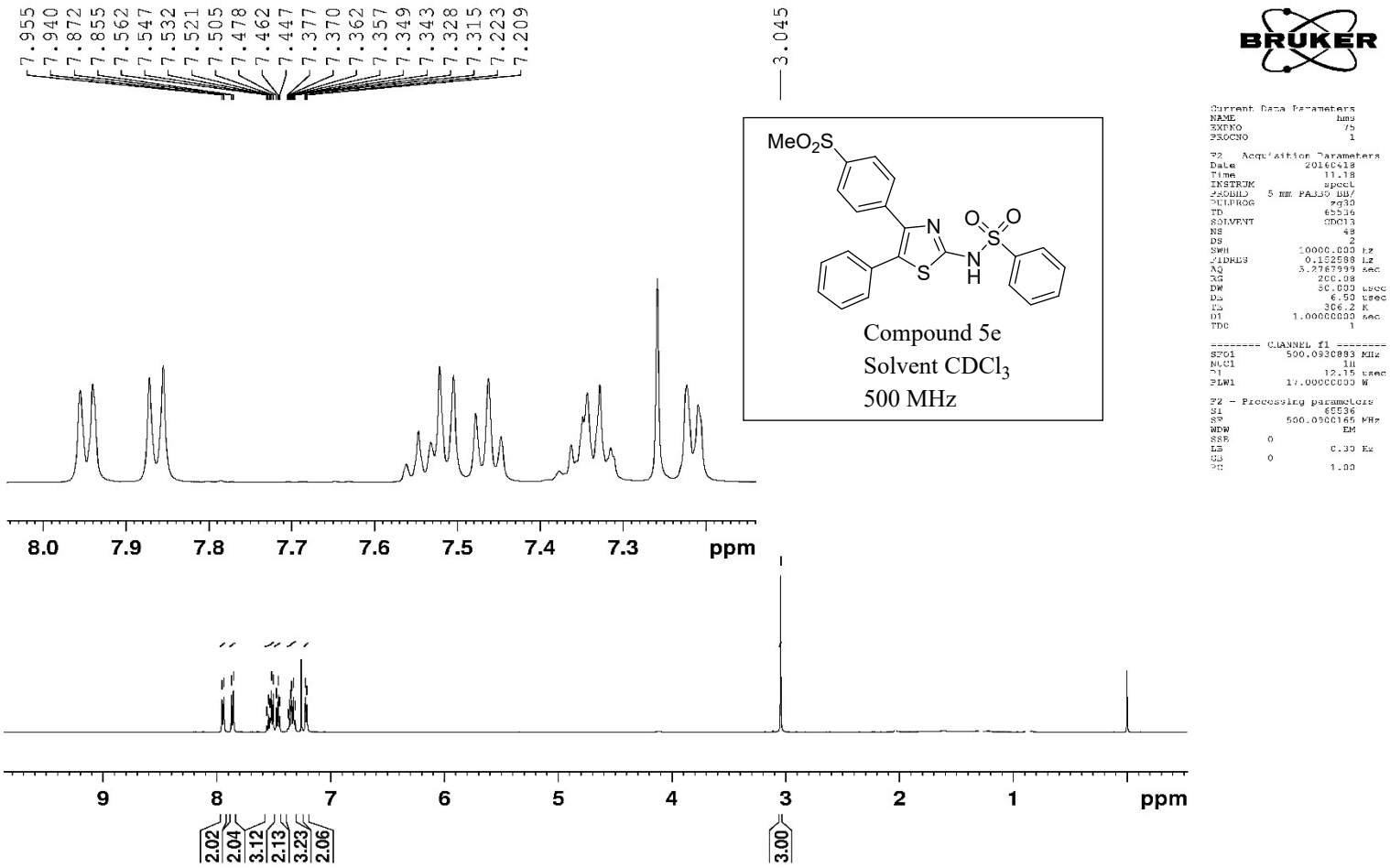
^{1}H NMR of Compound **5d**



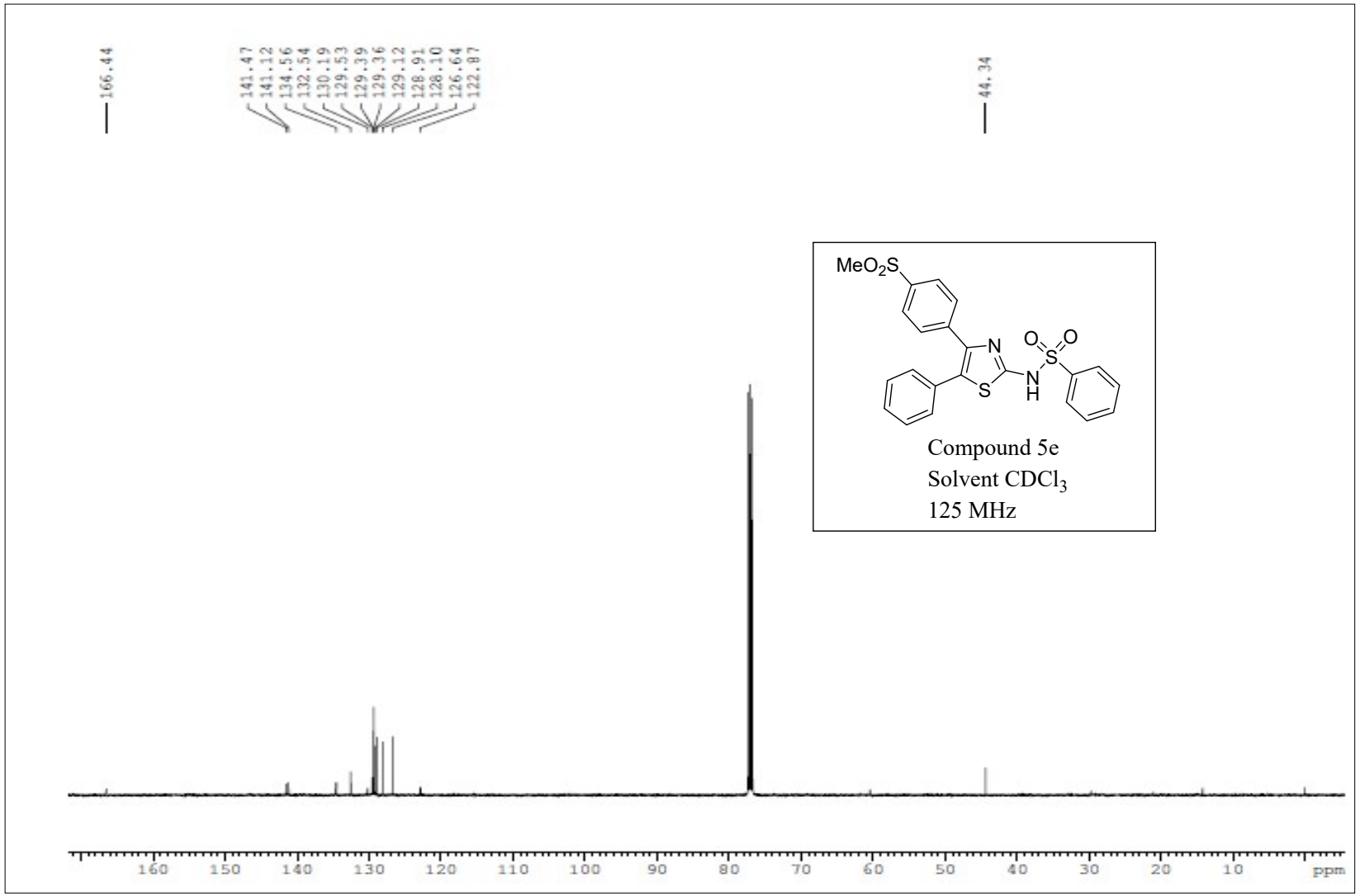
^{13}C NMR of Compound **5d**



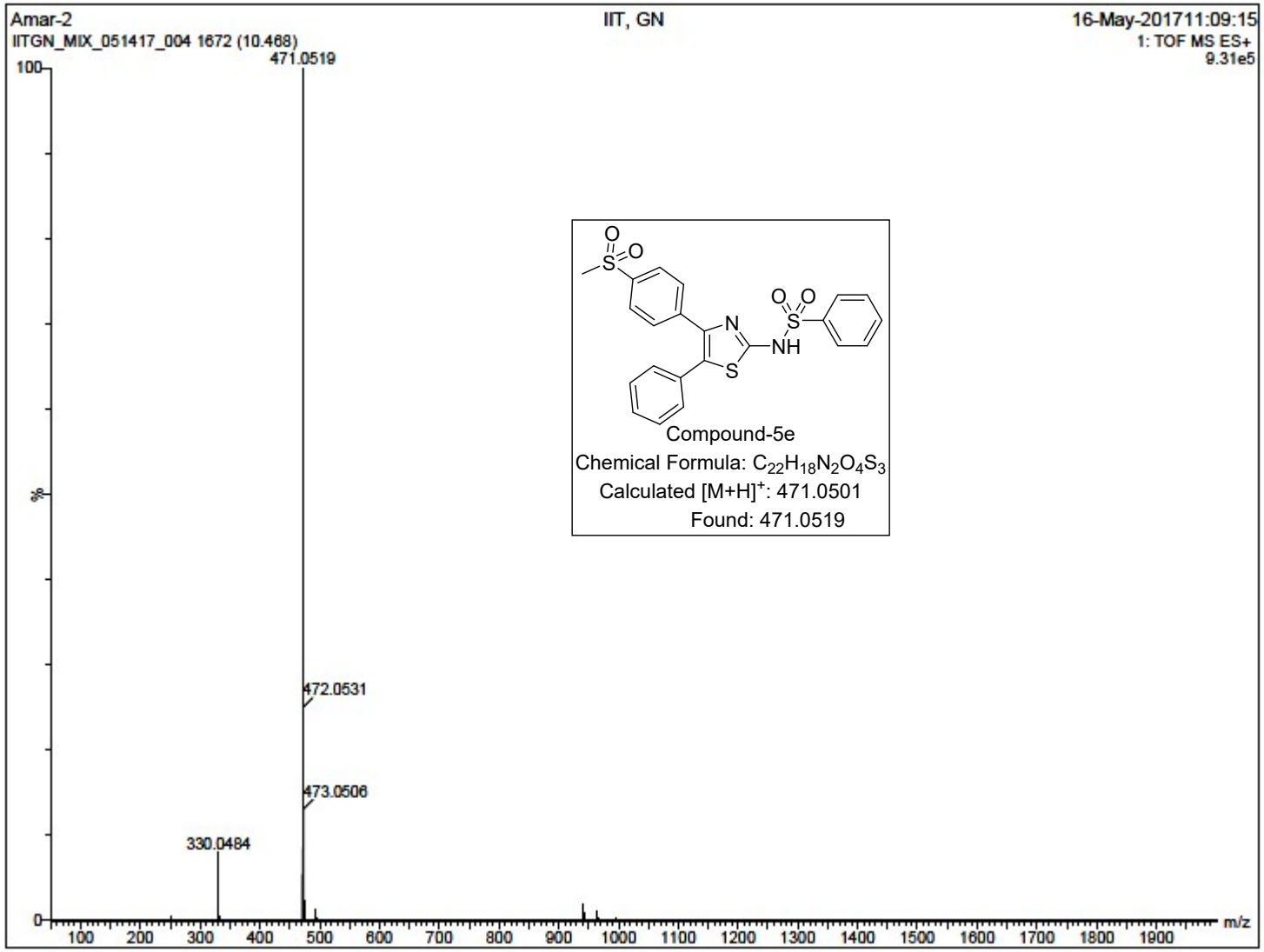
LC-ESIMS of Compound **5d**



^{1}H NMR of Compound **5e**



^{13}C NMR of Compound **5e**



LC-ESIMS of Compound **5e**

Table S1 Experimental details (SCXRD data of **compound 4**)

CCDC NO: 2022439	BD_AMAR_INTER_0m_a
Crystal data	
Chemical formula	$C_{16}H_{14}N_2O_2S_2$
M_r	330.40
Crystal system, space group	Monoclinic, *C*2/*c*
Temperature (K)	293
a, *b*, *c* (Å)	24.050 (2), 12.3593 (12), 11.5347 (11)
β (°)	115.134 (3)
V (Å^3)	3103.9 (5)
Z	8
Radiation type	Mo *K*α
μ (mm^{-1})	0.35
Crystal size (mm)	0.55 × 0.13 × 0.06
Data collection	
Diffractometer	Bruker *APEX*-II CCD
Absorption correction	–
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	10077, 3774, 3103
R_{int}	0.032
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.666

Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.041, 0.147, 1.07
No. of reflections	3774
No. of parameters	208
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.29, −0.31

Computer programs: Bruker *APEX2*, Bruker *SAINT*, *SHELXS97* (Sheldrick 2008), *SHELXL2014* (Sheldrick 2014), Bruker *SHELXTL*.

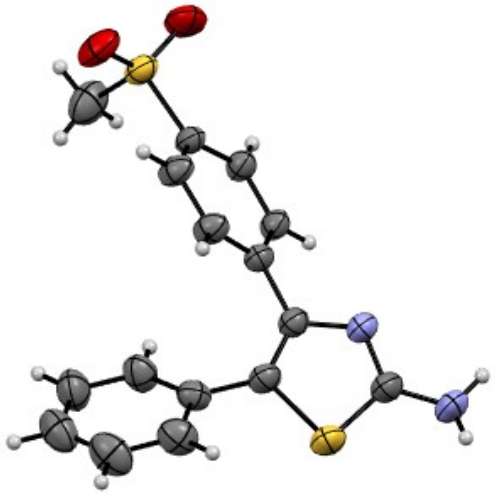


Figure S5. ORTEP diagram with 50% ellipsoid probability of compound 4.

Table S2 Experimental details (SCXRD data of **compound 5c)**

CCDC NO: 2021297	BD_AMAR_CL_TAS_0m_a
Crystal data	
Chemical formula	$C_{22}H_{17}ClN_2O_4S_3$
M_r	505.01
Crystal system, space group	Triclinic, *P*
Temperature (K)	273
a, *b*, *c* (Å)	10.4187 (3), 10.7457 (3), 11.0763 (3)
α, β, γ (°)	109.621 (1), 93.081 (1), 102.004 (1)
V (Å^3)	1132.19 (6)
Z	2
Radiation type	Mo *K*α
μ (mm^{-1})	0.48
Crystal size (mm)	0.25 × 0.08 × 0.05
Data collection	
Diffractometer	Bruker *APEX*-II CCD
Absorption correction	–
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	14259, 5555, 4680
R_{int}	0.027
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.666
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.038, 0.147, 1.11

No. of reflections	5555
No. of parameters	290
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.47, −0.50

Computer programs: Bruker *APEX2*, Bruker *SAINT*, *SHELXS97* (Sheldrick 2008), *SHELXL2014* (Sheldrick 2014), Bruker *SHELXTL*

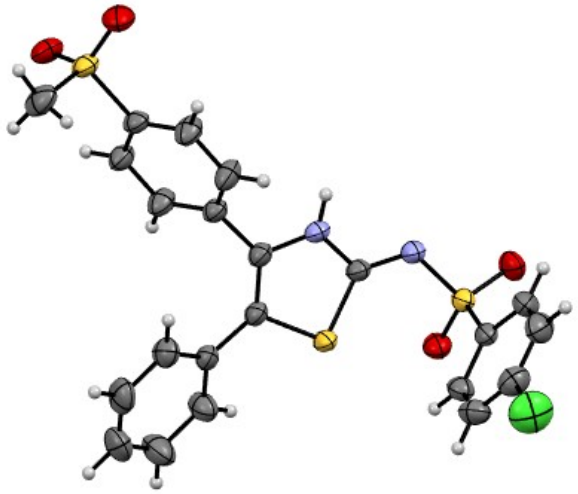


Figure S6. ORTEP diagram with 50% ellipsoid probability of compound 5c.

Crystallization conditions

The compounds were dissolved in minimum amount of acetone followed by addition of suitable amount of hexane. The resulting solution was subjected to slow solvent evaporation at room temperature to obtain good quality crystals.