Project Report on

"Analysis of NMR spectra of unknown compound"

Submitted By

M.Sc. SEM I Students (Roll No.1 to 6)

Guided By

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Submitted To

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Sir P.T.Science College, Modasa

SIR P.T.SCIENCE COLLEGE, MODASA

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Certificate

This is to certify that project report entitled **"Analysis of NMR spectra of Unknown Compound"** are carried out by students mentioned below. They have been satisfactorily completed their project work for academic year 2022-23. The project has been approved as it satisfies the academic requirement in respect of project work prescribed for the Master of Science. M.Sc-I

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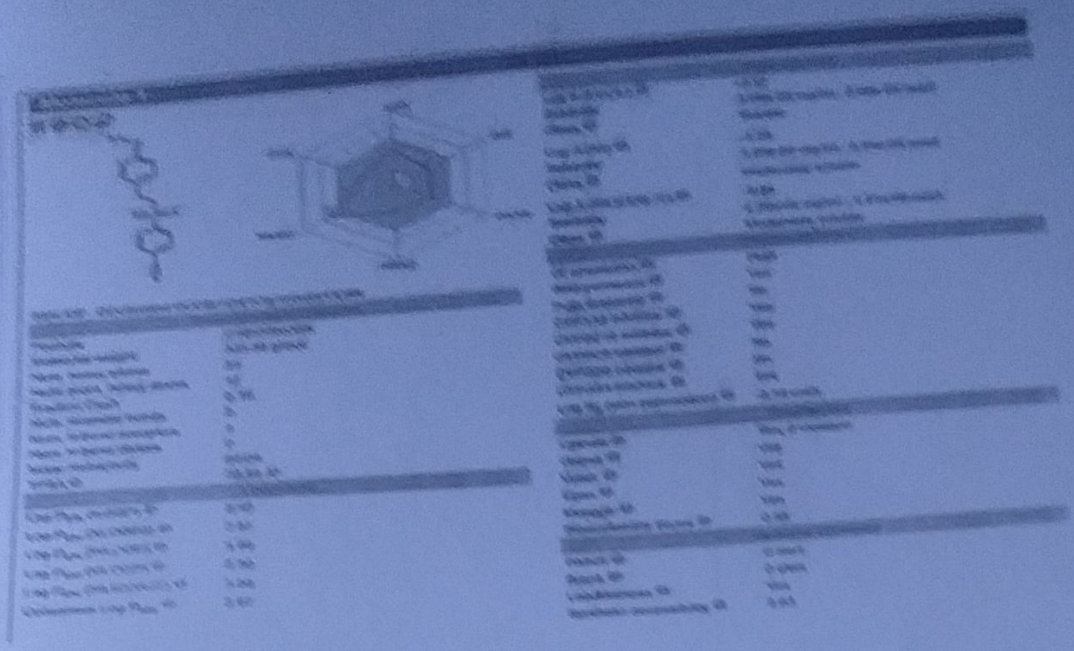
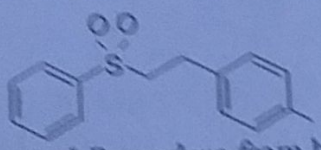
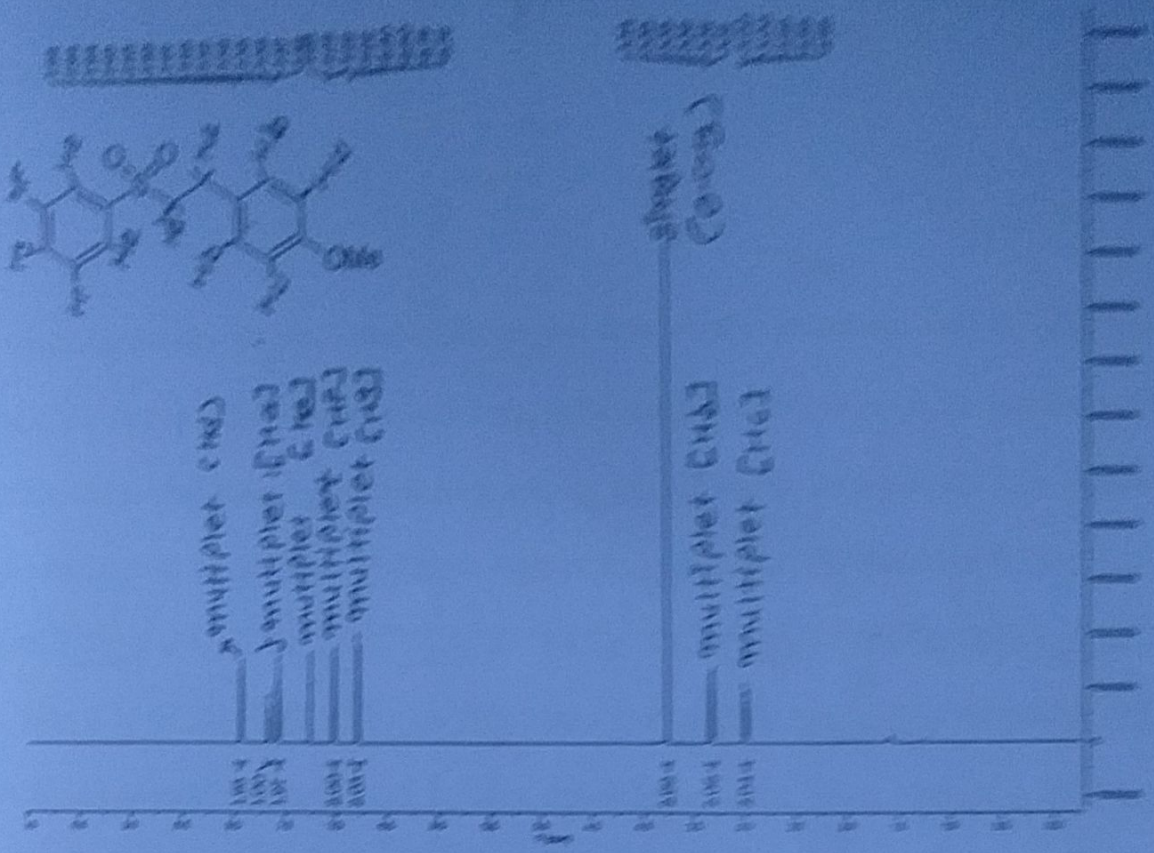
Table of Contents for Supporting Information



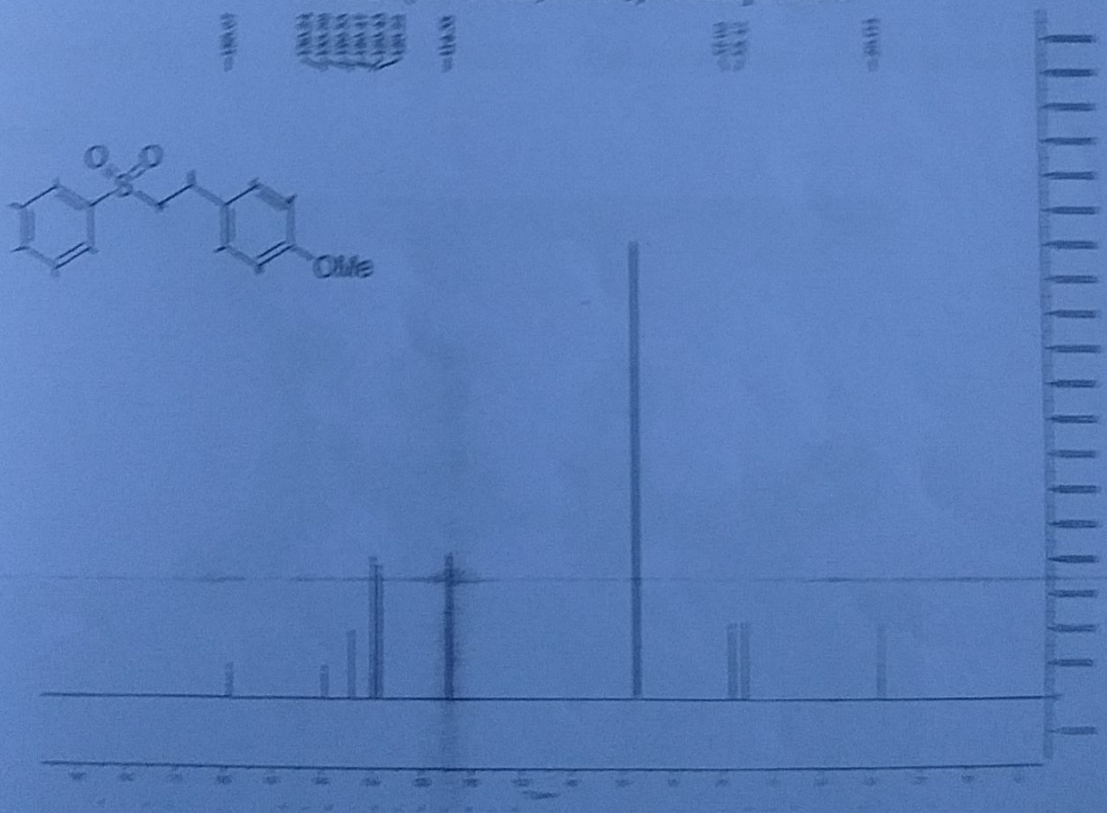
1-Methoxy-4-(2-(phenylsulfonyl)ethyl)benzene (4b)



Prepared according to the *General Procedure* from benzenesulfonyl fluoride (200 mg, 1.25 mmol, 2.5 equiv) and 4-vinylanisole (67 mg, 0.50 mmol, 1 equiv). After purification by automated flash column chromatography (from hexanes to 10% EtOAc in hexanes), the title compound **4b** was obtained as a white solid (81 mg, 0.30 mmol, 59%). **^{1}H NMR** (600 MHz, $CDCl_3$), δ (ppm) 7.96 – 7.91 (m, 2H), 7.68 – 7.64 (m, 1H), 7.61 – 7.55 (m, 2H), 7.05 – 7.00 (m, 2H), 6.82 – 6.77 (m, 2H), 3.76 (s, 3H), 3.35 – 3.30 (m, 2H), 3.02 – 2.96 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$), δ (ppm) 158.7, 139.2, 133.9, 129.53, 129.47, 129.4, 128.2, 114.4, 57.9, 55.4, 28.0. **mp** = 58 – 60 °C. **FTIR** (cm^{-1}, neat, ATR), $\tilde{\nu}$ = 1513, 1300, 1147, 1128. **HRMS (ESI)** calcd for $C_{15}H_{17}O_3S$ $[M+H]^+$: 277.0898, found 277.0895. Spectral data agreed with those reported in the literature.[3]

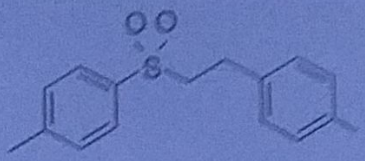


^{1}H NMR (600 MHz, $CDCl_3$) of compound 4b

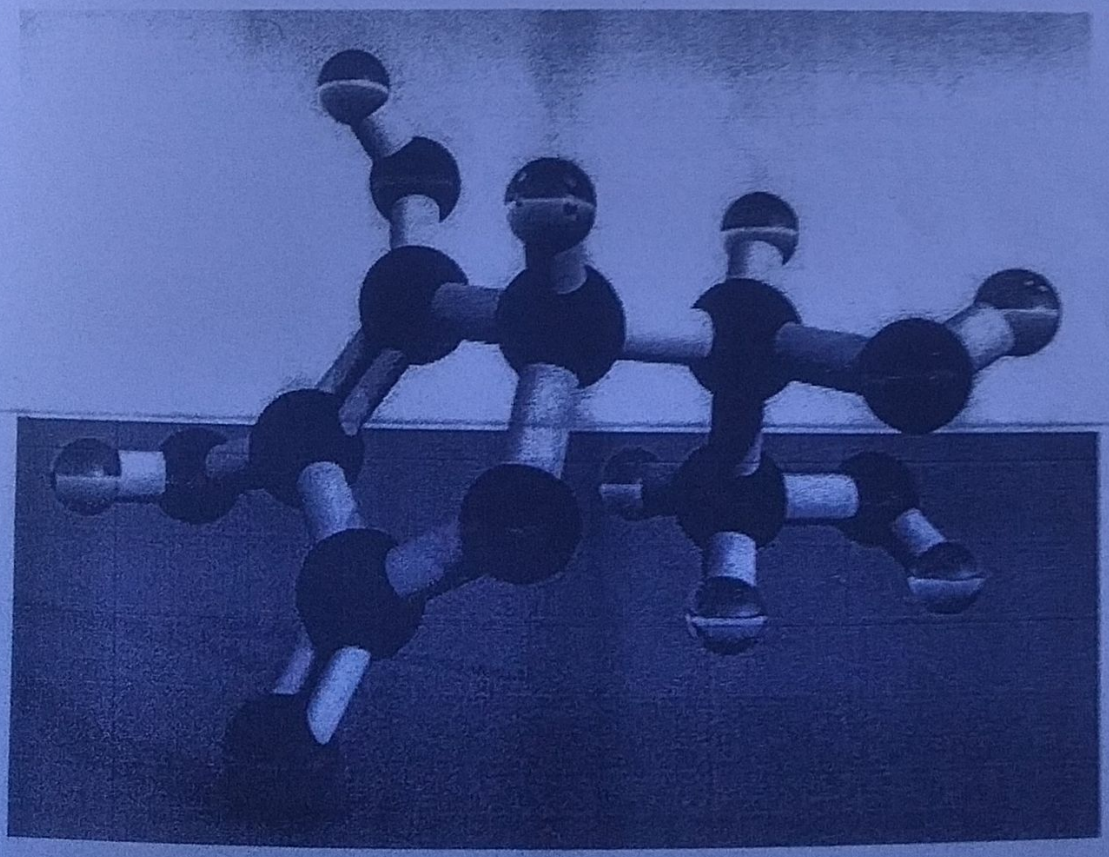


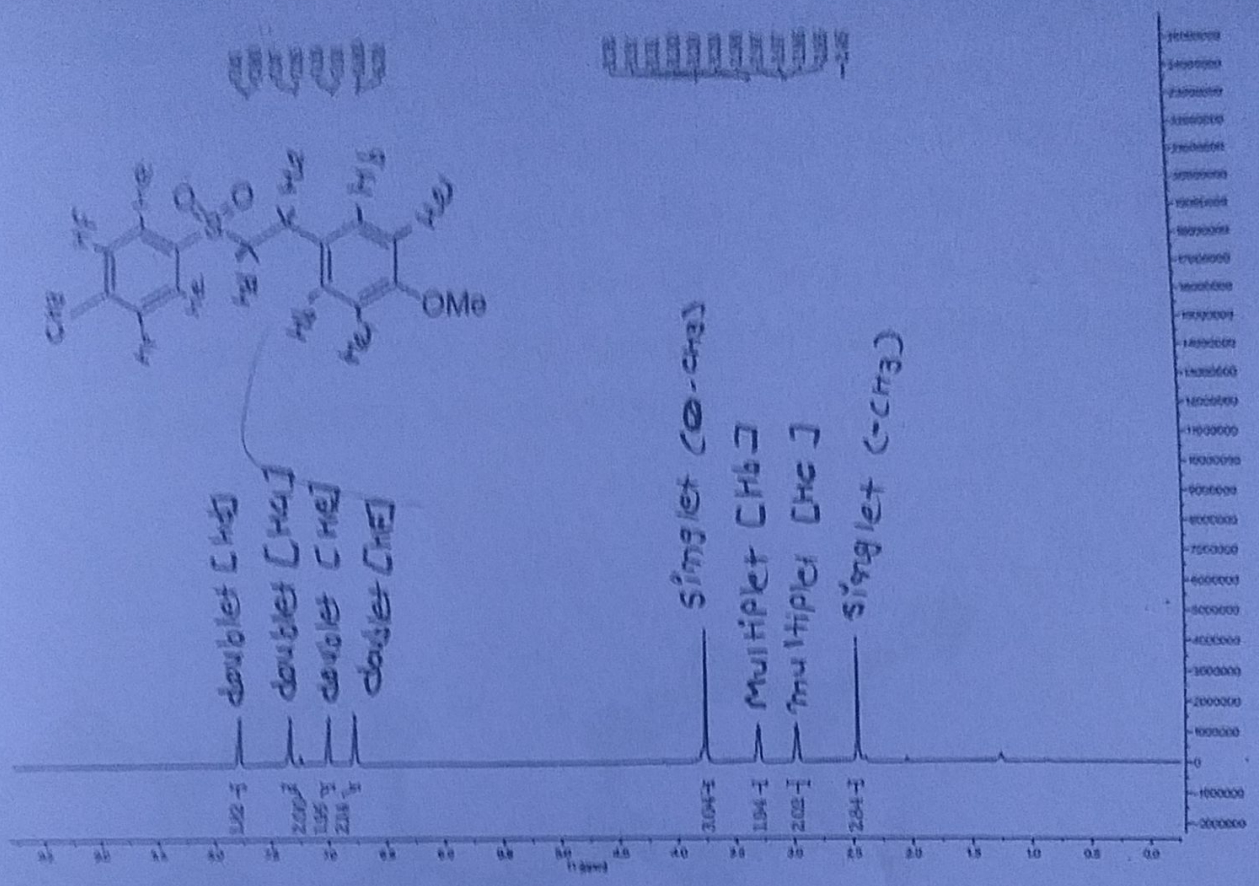
^{13}C NMR (151 MHz, $CDCl_3$) of compound 4b

1-Methoxy-4-(2-tosylethyl)benzene (4c)



Prepared according to the *General Procedure* from 4-toluenesulfonyl fluoride (218 mg, 1.25 mmol, 2.5 equiv) and 4-vinylanisole (67 mg, 0.50 mmol, 1 equiv). After purification by automated flash column chromatography (from hexanes to 20% EtOAc in hexanes), the title compound **4c** was obtained as an off-white solid (51 mg, 0.18 mmol, 35%). **^{1}H NMR** (600 MHz, $CDCl_3$), δ (ppm) 7.81 (d, J = 7.9 Hz, 2H), 7.36 (d, J = 7.8 Hz, 2H), 7.02 (d, J = 8.1 Hz, 2H), 6.79 (d, J = 8.2 Hz, 2H), 3.76 (s, 3H), 3.33 – 3.27 (m, 2H), 3.00 – 2.94 (m, 2H), 2.45 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$), δ (ppm) 158.6, 144.9, 136.2, 130.1, 129.6, 129.4, 128.2, 114.3, 58.0, 55.4, 28.1, 21.8. **mp** = 92 – 94 °C. **FT-IR** (cm^{-1}, neat, ATR), $\tilde{\nu}$ = 1511, 1494, 1247, 1145. **HRMS (ESI)** calcd for $C_{16}H_{19}O_3S$ $[M+H]^+$: 291.1055, found 291.1057. Spectral data agreed with those reported in the literature.[2]

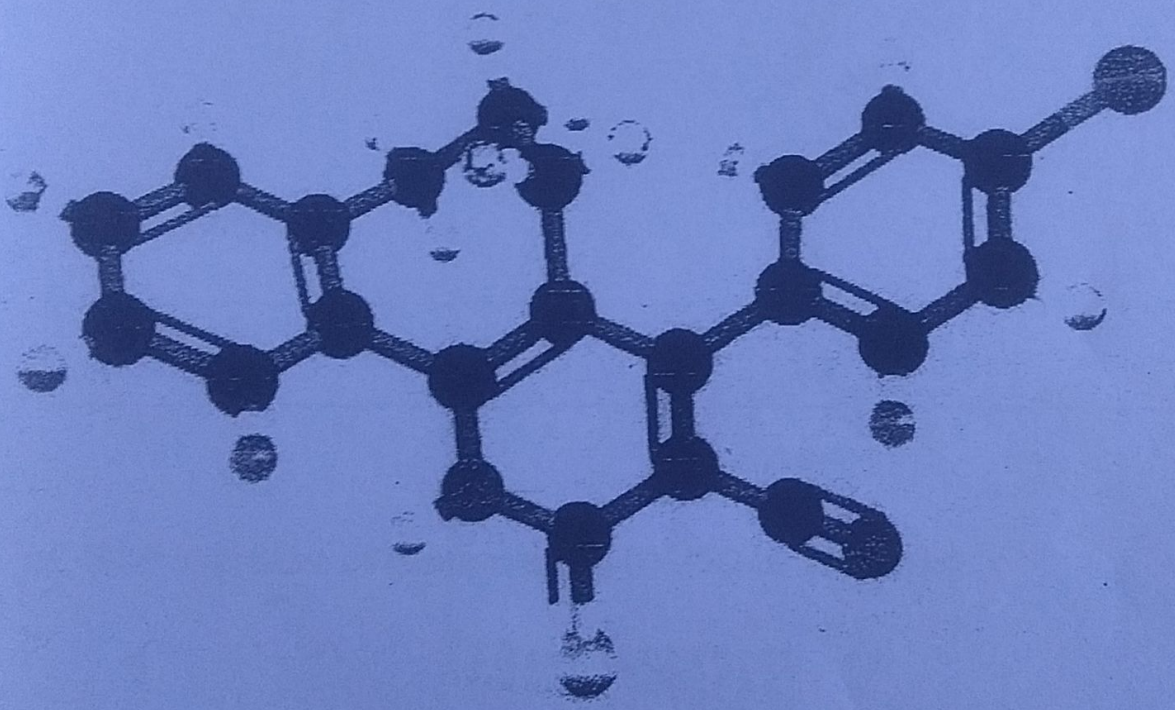




^{1}H NMR (600 MHz, $CDCl_3$) of compound 4c

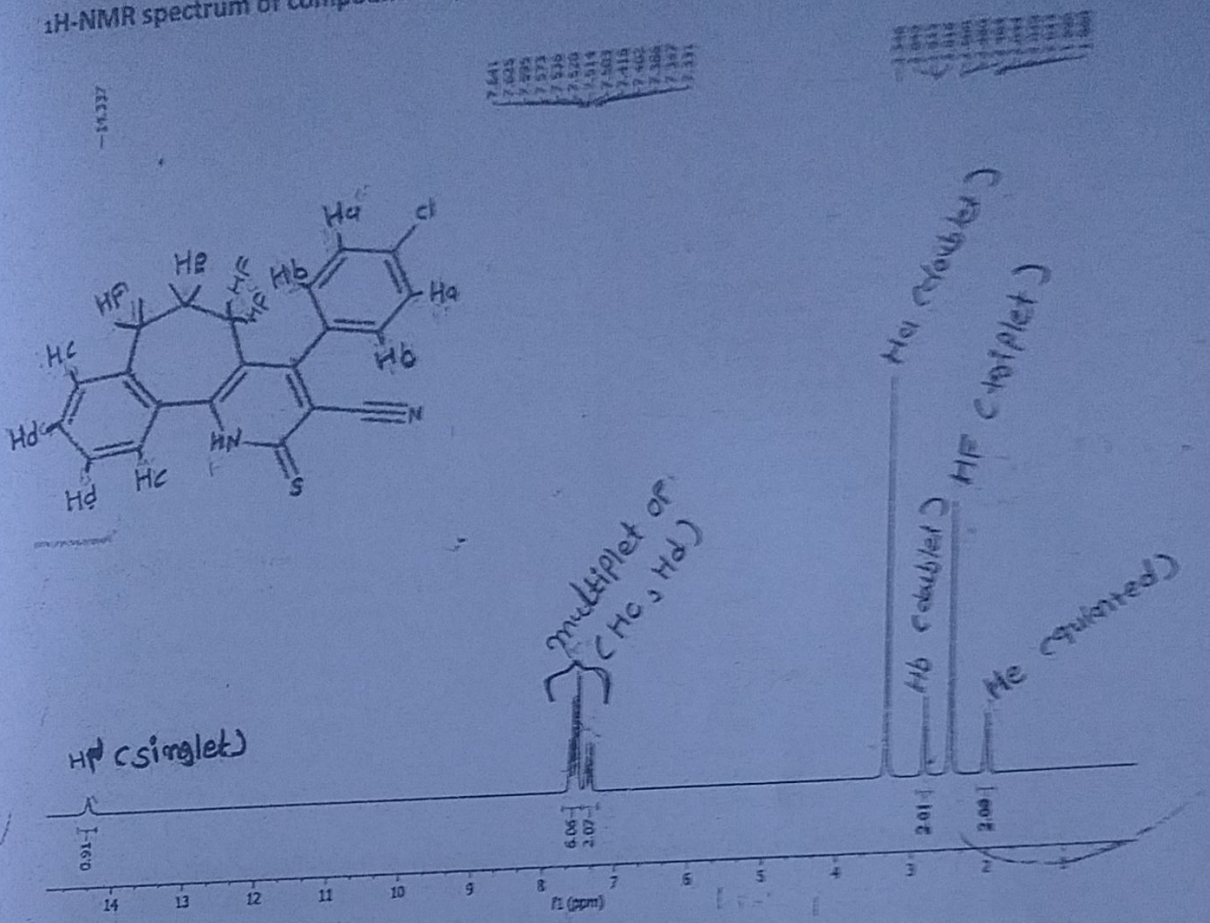
2.1.1. 4-(4-Chlorophenyl)-2-thioxo-2,5,6,7-tetrahydro-1*H*-benzo[6,7]cyclohepta[1,2-*b*]pyridine-3-carbonitrile (3a).

Yellow solid (dioxane, 74%); m.p. 198-200 °C; IR (υ cm^{-1}): 3335 (NH), 2210 (CN); ^{1}H-NMR (DMSO-d_6): δ 2.01 (quint, J = 6.4 Hz, 2H, CH_2), 2.48 (t, J = 6.4 Hz, 2H, CH_2), 2.83 (t, J = 6.4 Hz, 2H, CH_2), 7.32 (d, J = 6.4 Hz, 1H, ArH), 7.40 (t, J = 6.4 Hz, 1H, ArH), 7.50-7.53 (m, 3H, ArH), 7.58 (d, J = 8.8 Hz, 2H, ArH), 7.63 (d, J = 6.4 Hz, 1H, ArH), 14.33 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6): δ 24.5, 25.7, 30.8, 127.0, 128.6, 128.8, 129.1, 129.4, 129.5, 131.2, 132.6, 133.5, 133.9, 135.6, 138.0, 138.1, 139.3, 196.5; Anal. calcd for $C_{21}H_{15}ClN_2S$ (362.8): C, 69.51; H, 4.17; N, 7.72; found: C, 69.35; H, 4.01; N, 7.90%.

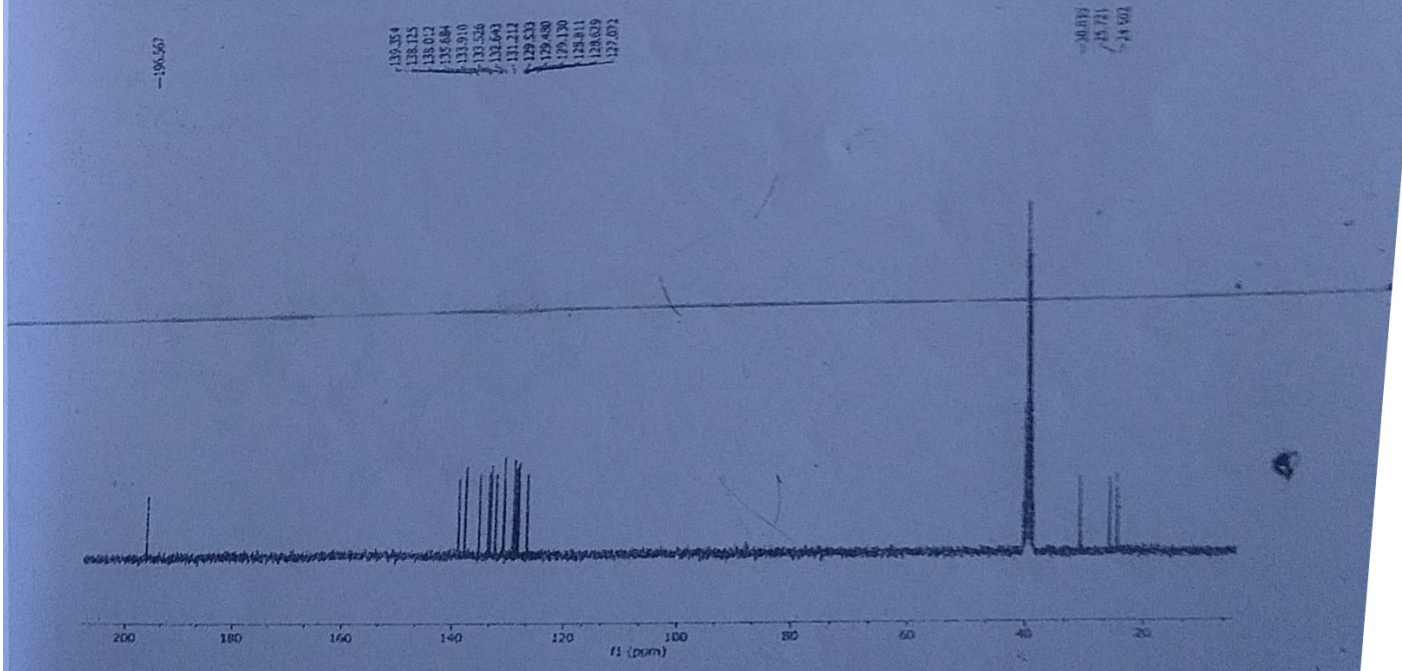


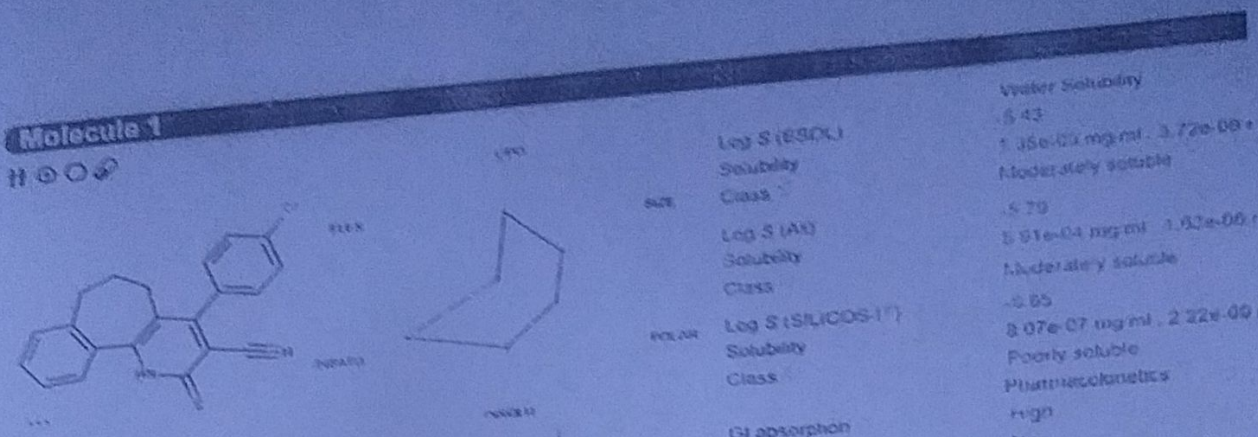
3. NMR spectral data

1H-NMR spectrum of compound 3a (DMSO-d_6 400 MHz).



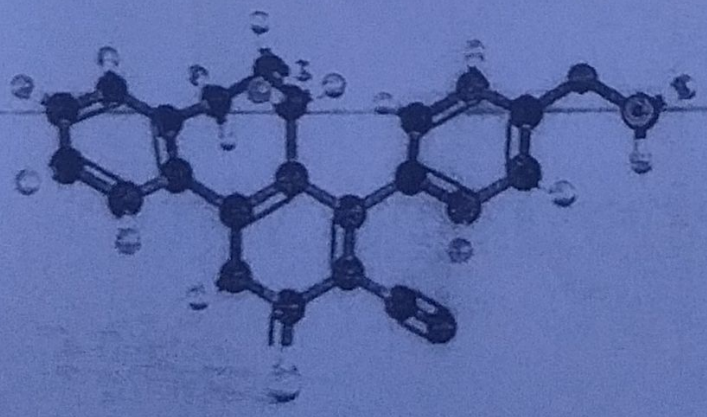
13C-NMR spectrum of compound 3a (DMSO-d_6 100 MHz).



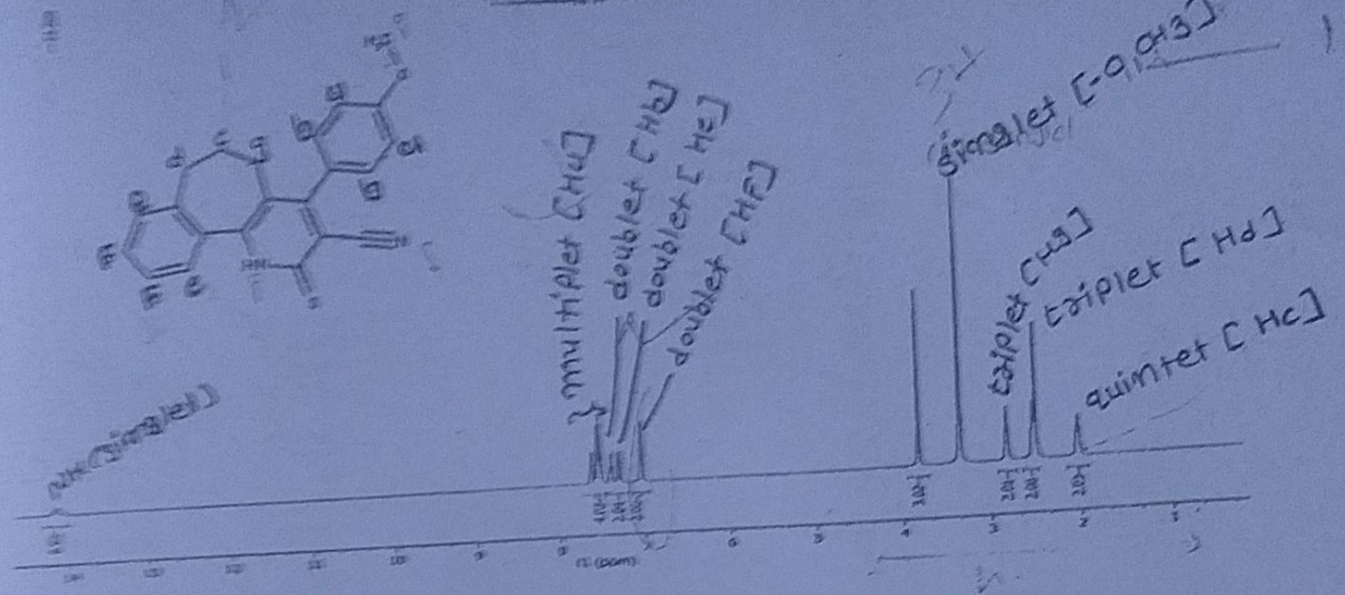


2.1.2. 4-(4-Methoxyphenyl)-2-thioxo-2,5,6,7-tetrahydro-*1H*-benzo[6,7]cyclohepta[1,2-*b*]pyridine-3-carbonitrile (3b).

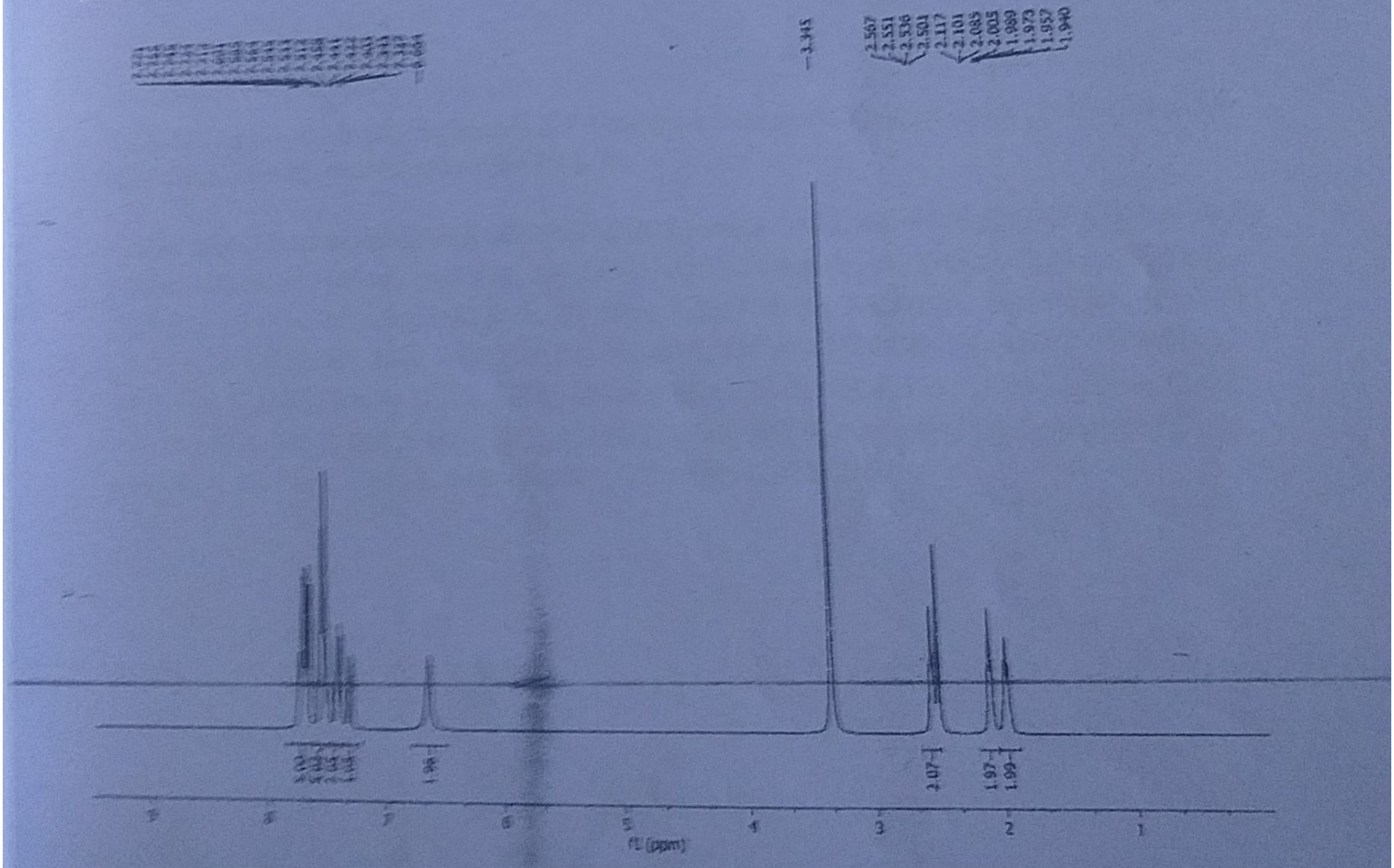
Yellow solid (dioxane / ethanol mixture, 77%); m.p. 230-231 ₀C; IR (υ cm-1): 3327 (NH), 2211 (CN); 1H-NMR (DMSO-d6): δ 2.02 (quint, *J* = 6.4 Hz, 2H, CH_2), 2.52 (t, *J* = 6.4 Hz, 2H, CH_2), 2.82 (t, *J* = 6.4 Hz, 2H, CH_2), 3.81 (s, 3H, *p*-OCH_3), 7.04 (d, *J* = 8.4 Hz, 2H, ArH), 7.30 (d, *J* = 6.4 Hz, 1H, ArH), 7.39 (t, *J* = 6.4 Hz, 1H, ArH), 7.50-7.56 (m, 3H, ArH), 7.62 (d, *J* = 6.4 Hz, 1H, ArH), 14.20 (s, 1H, NH); Anal. calcd for $C_{22}H_{18}N_2OS$ (358.4): C, 73.72; H, 5.06; N, 7.82; found: C, 73.57; H, 5.13; N, 7.69%.

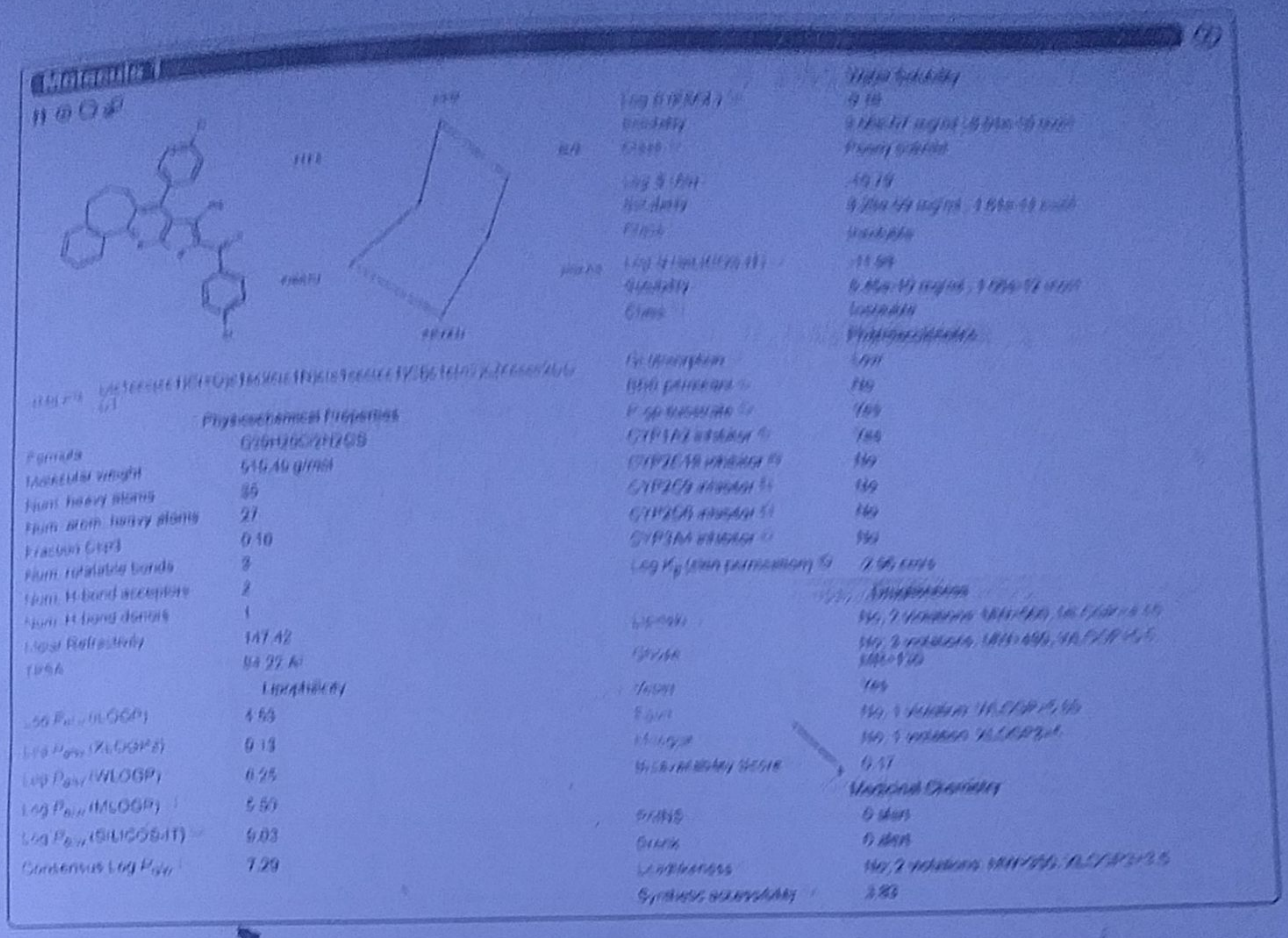


^{1}H-NMR spectrum of compound 3b (DMSO-*d*$_6$ 400 MHz).



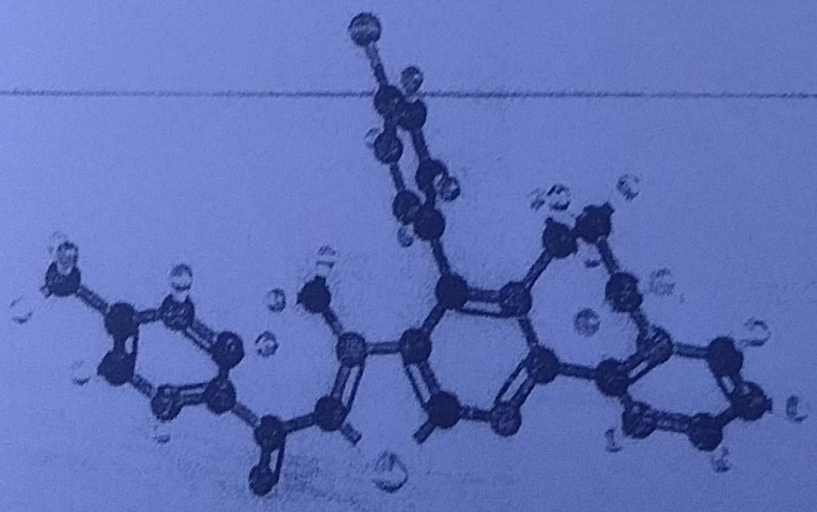
^{1}H-NMR spectrum of compound 5a (DMSO-*d*$_6$ 400 MHz).



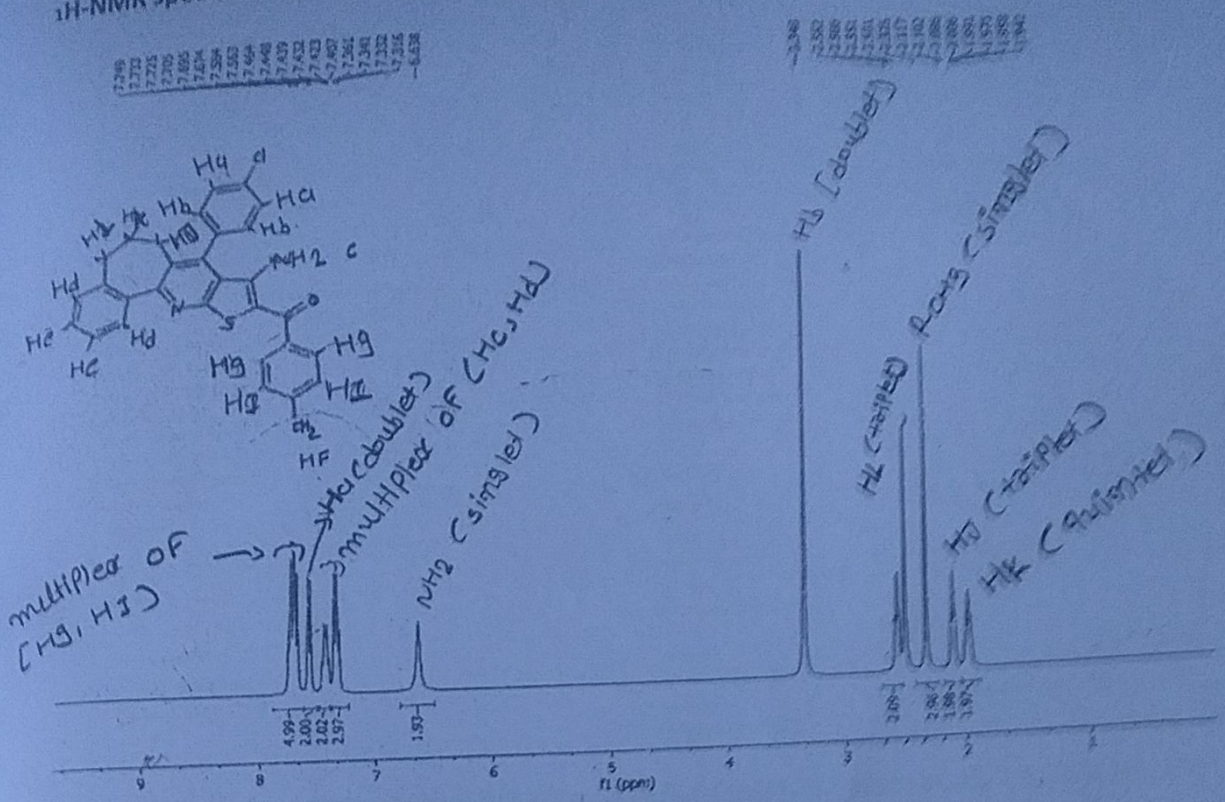


2.2.5. (9-Amino-8-(4-chlorophenyl)-6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*b*]thieno[3,2-*e*]pyridin-10-yl)(*p*-tolyl)methanone (5c). 10

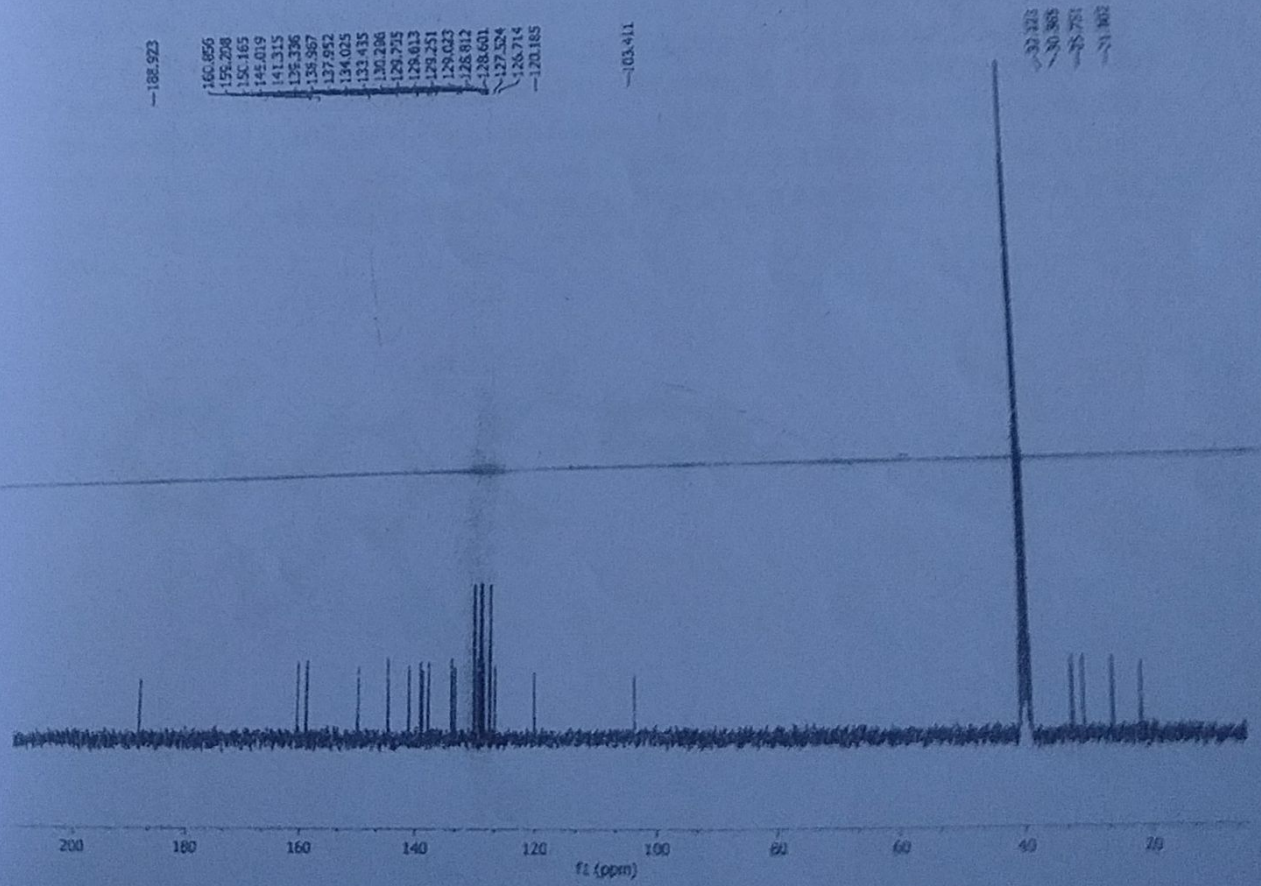
Yellow solid (dioxane, 86%); m.p. 256-257 ₀C; IR (υ cm-1): 3452, 3214 (NH_2), 1632 (CO); ₁H-NMR (DMSO-d6): δ 1.97 (quint, *J* = 6.4 Hz, 2H, CH_2), 2.10 (t, *J* = 6.4 Hz, 2H, CH_2), 2.32 (s, 3H, *p*-CH_3), 2.56 (t, *J* = 6.4 Hz, 2H, CH_2), 6.63 (br s, 2H, NH_2), 7.31-7.36 (m, 3H, ArH), 7.40-7.46 (m, 2H, ArH), 7.57 (d, *J* = 8.4 Hz, 2H, ArH), 7.67-7.74 (m, 5H, ArH); 13C-NMR (DMSO-d6): δ 21.1, 25.7, 30.3, 32.1, 103.4, 120.1, 126.7, 127.5, 128.6, 128.8, 129.0, 129.2, 129.6, 129.7, 130.2, 133.4, 134.0, 137.9, 138.9, 139.3, 141.3, 145.0, 150.1, 159.2, 160.8, 188.9; Anal. calcd for $C_{30}H_{23}ClN_2OS$ (495.0): C, 72.79; H, 4.68; N, 5.66; found: C, 72.93; H, 4.54; N, 5.72%.

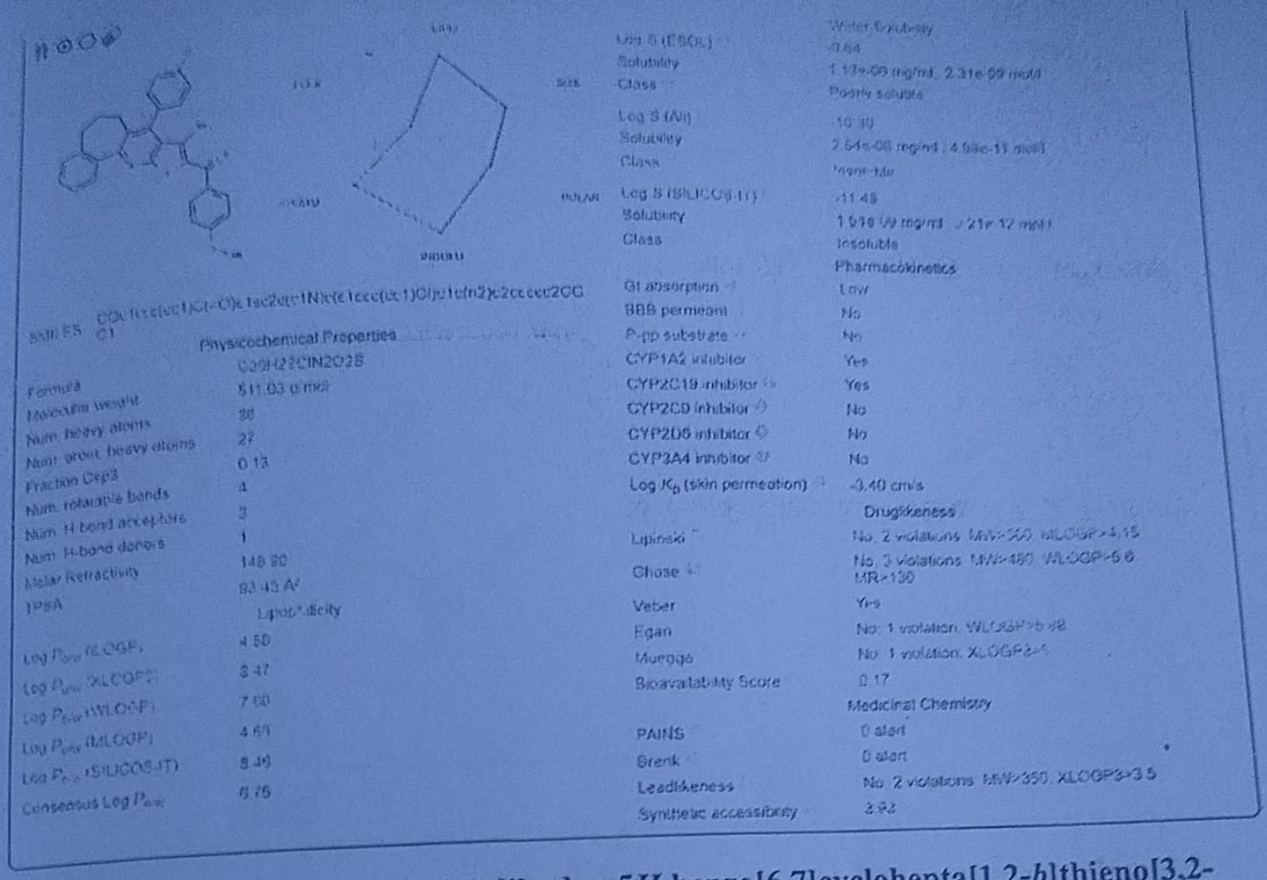


^{1}H-NMR spectrum of compound 5c (DMSO-d_6 400 MHz).



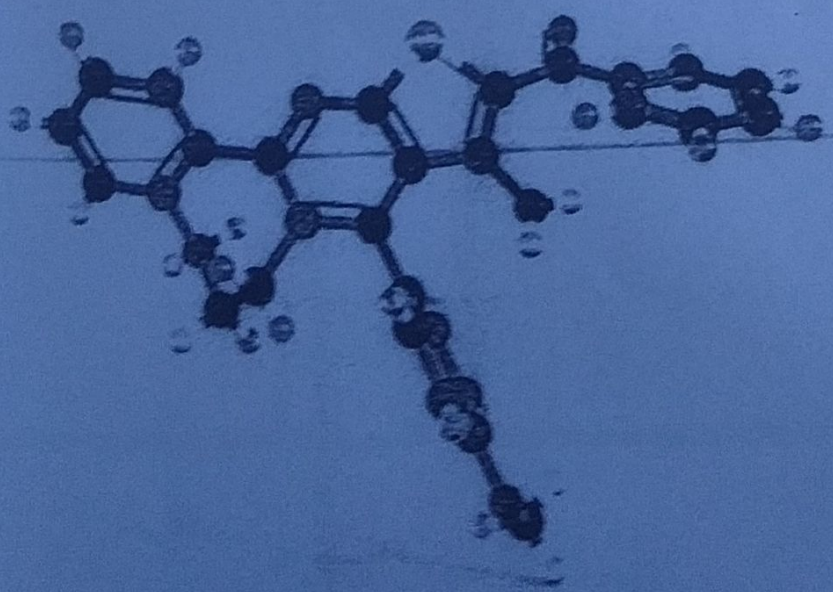
^{13}C-NMR spectrum of compound 5c (DMSO-d_6 100 MHz).



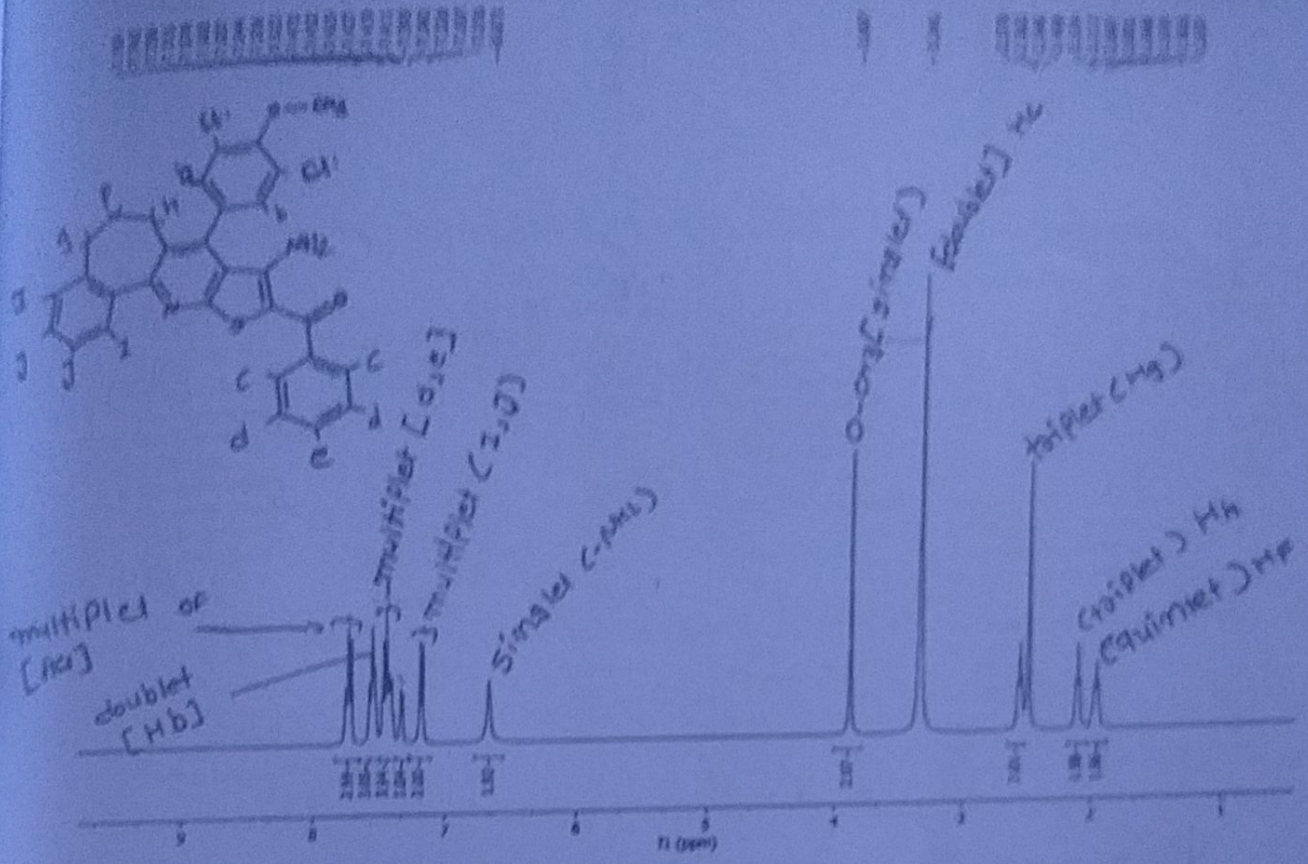


(9-Amino-8-(4-methoxyphenyl)-6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*b*]thieno[3,2-*e*]pyridin-10-yl)(phenyl)methanone (5e).

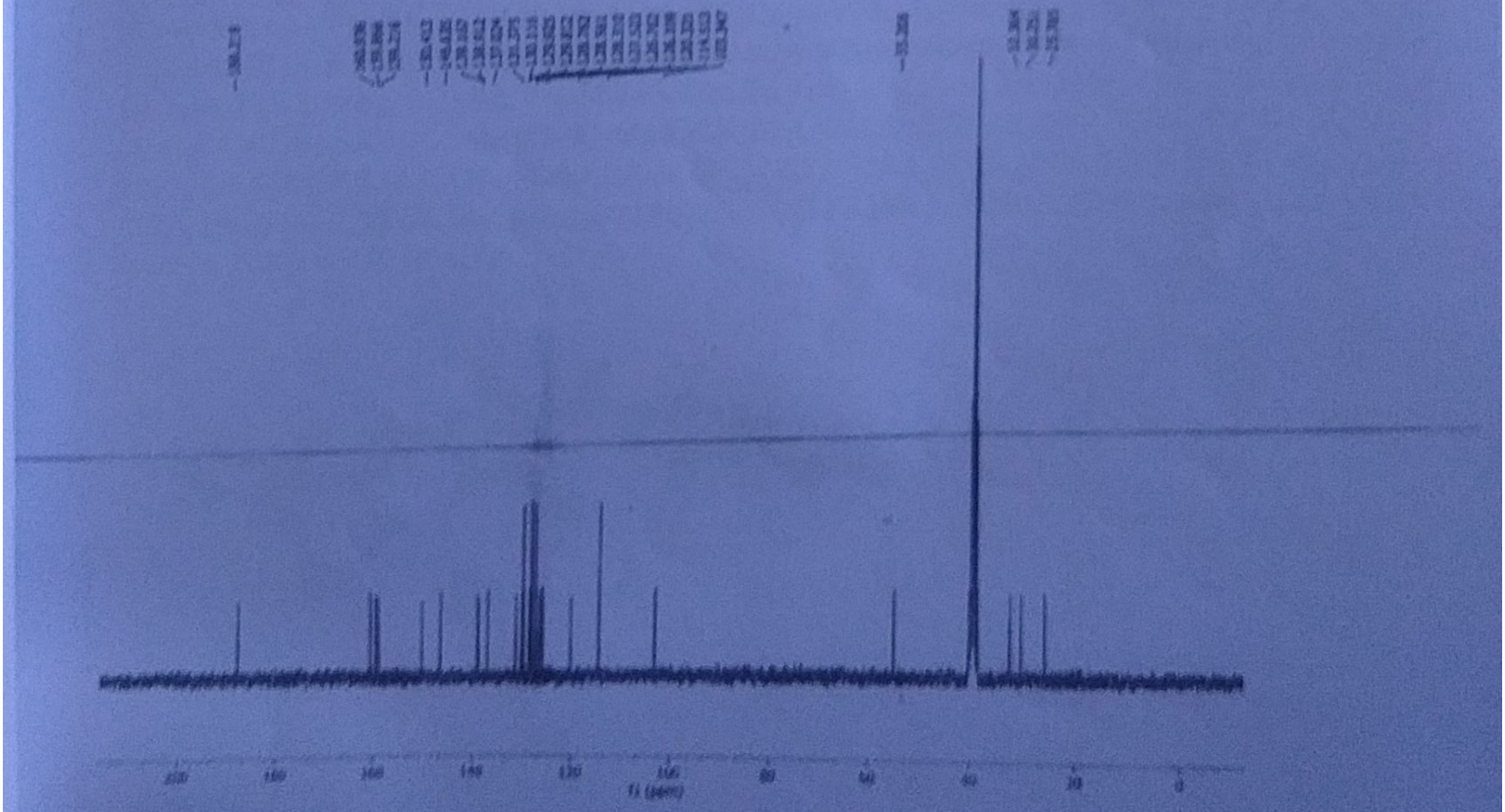
Yellow solid (dioxane, 90%); m.p. 280-281 ₀C; IR (υ cm-1): 3415, 3242 (NH_2), 1633 (CO); ^{1}H-NMR (DMSO-d6): δ 1.97 (quint, *J* = 6.4 Hz, 2H, CH_2), 2.11 (t, *J* = 6.4 Hz, 2H, CH_2), 2.56 (t, *J* = 6.4 Hz, 2H, CH_2), 3.88 (s, 3H, *p*-OCH_3), 6.67 (br s, 2H, NH_2), 7.18 (d, *J* = 8.4 Hz, 2H, ArH), 7.33 (d, *J* = 6.4 Hz, 1H, ArH), 7.41-7.47 (m, 4H, ArH), 7.52-7.57 (m, 3H, ArH), 7.71-7.75 (m, 3H, ArH); ^{13}C-NMR (DMSO-d6): δ 25.7, 30.2, 32.3, 55.2, 103.3, 114.5, 120.3, 126.1, 126.7, 127.5, 128.3, 128.5, 128.7, 129.8, 129.9, 130.1, 131.3, 137.0, 138.9, 139.1, 146.6, 150.4, 159.2, 159.8, 160.9, 188.2; Anal. calcd for $C_{30}H_{24}N_2O_2S$ (476.5): C, 75.61; H, 5.08; N, 5.88; found: C, 75.49; H, 4.92; N, 6.04%.

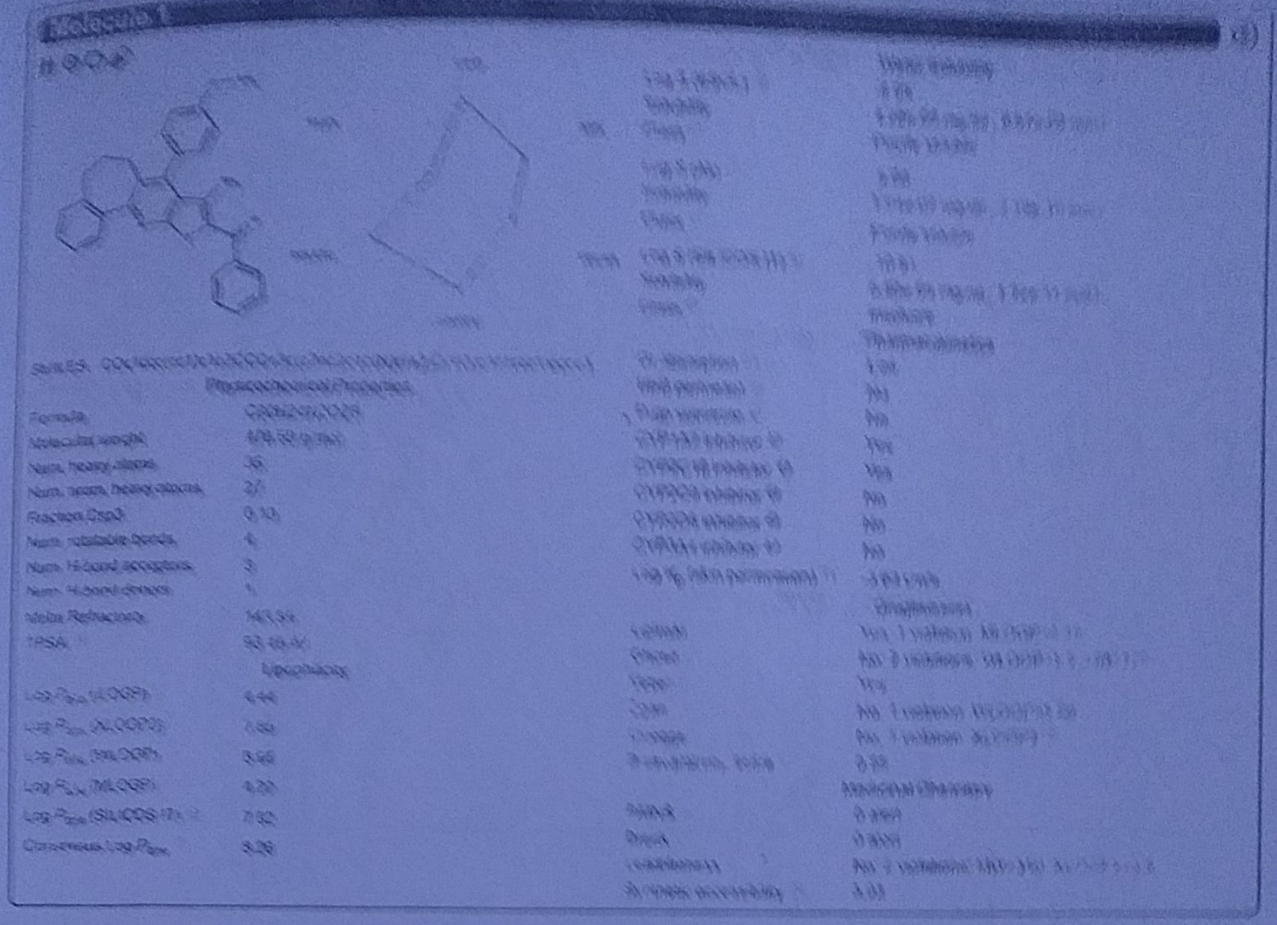


¹H-NMR spectrum of compound 5e (DMSO-*d*₆ 400 MHz).



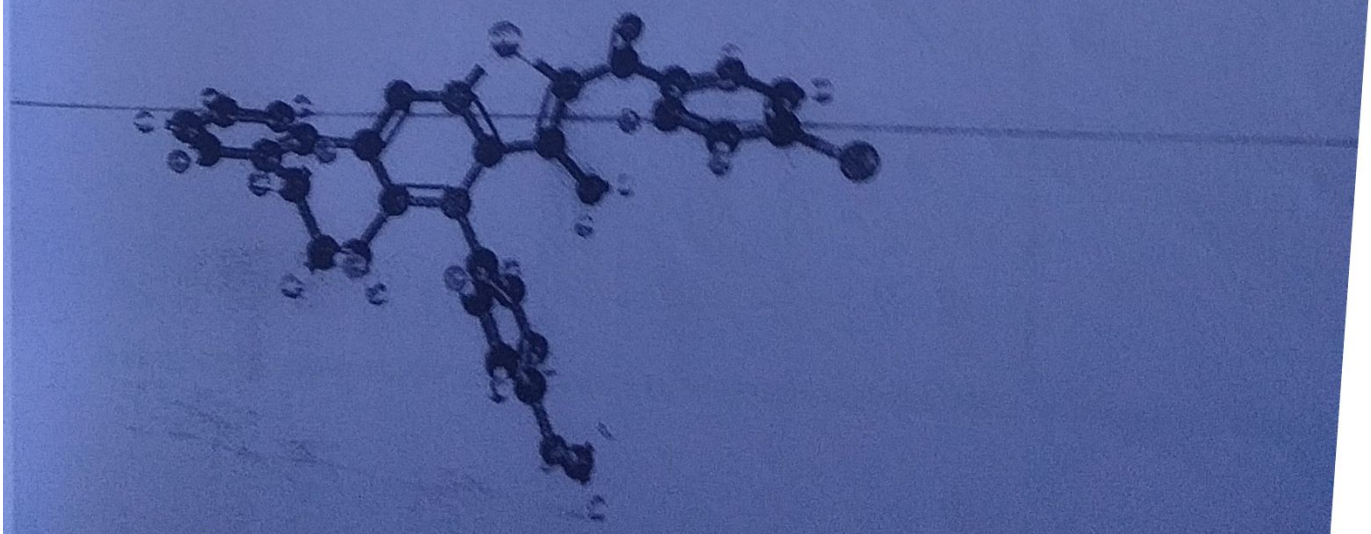
¹³C-NMR spectrum of compound 5e (DMSO-*d*₆ 100 MHz).



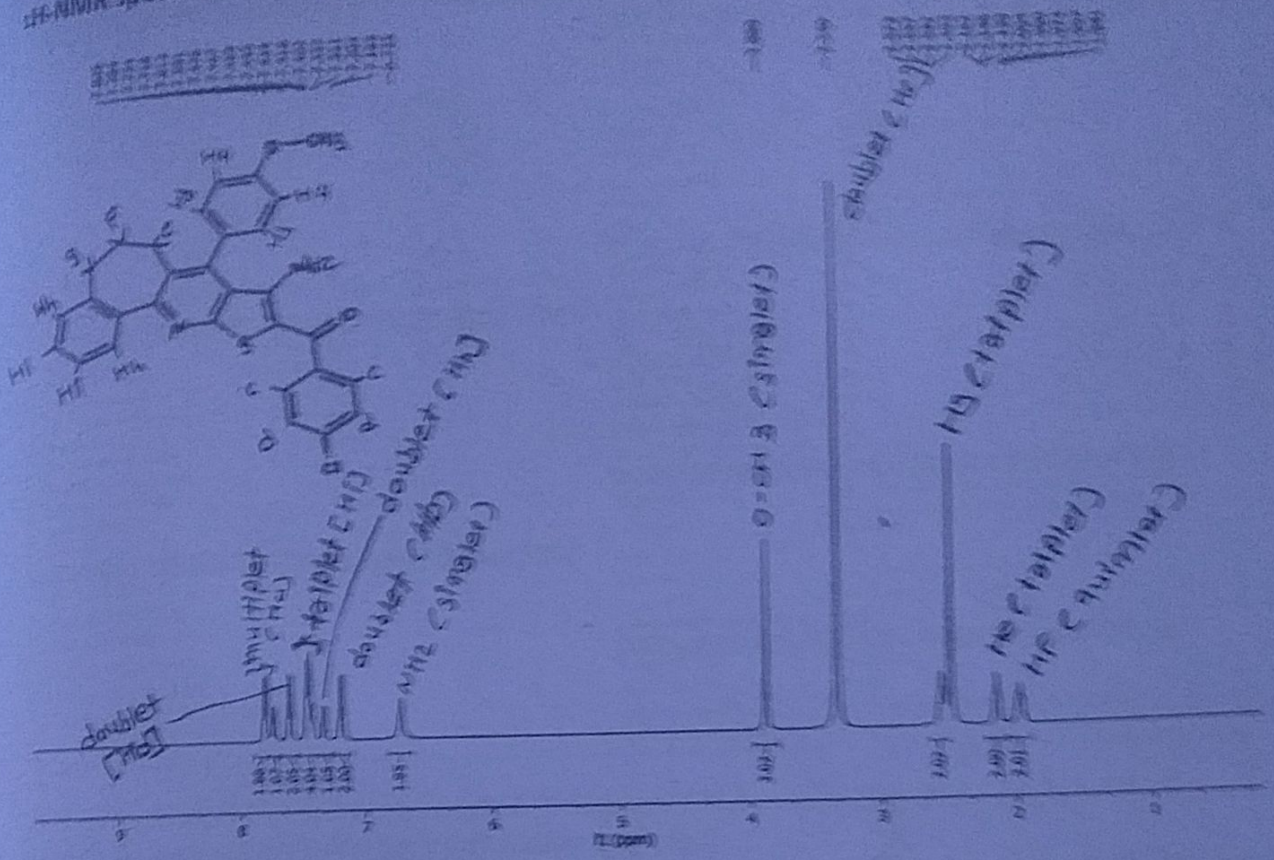


2.2.8. (9-Amino-8-(4-methoxyphenyl)-6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*b*]thieno[3,2-*e*]pyridin-10-yl)(4-chlorophenyl)methanone (5l),

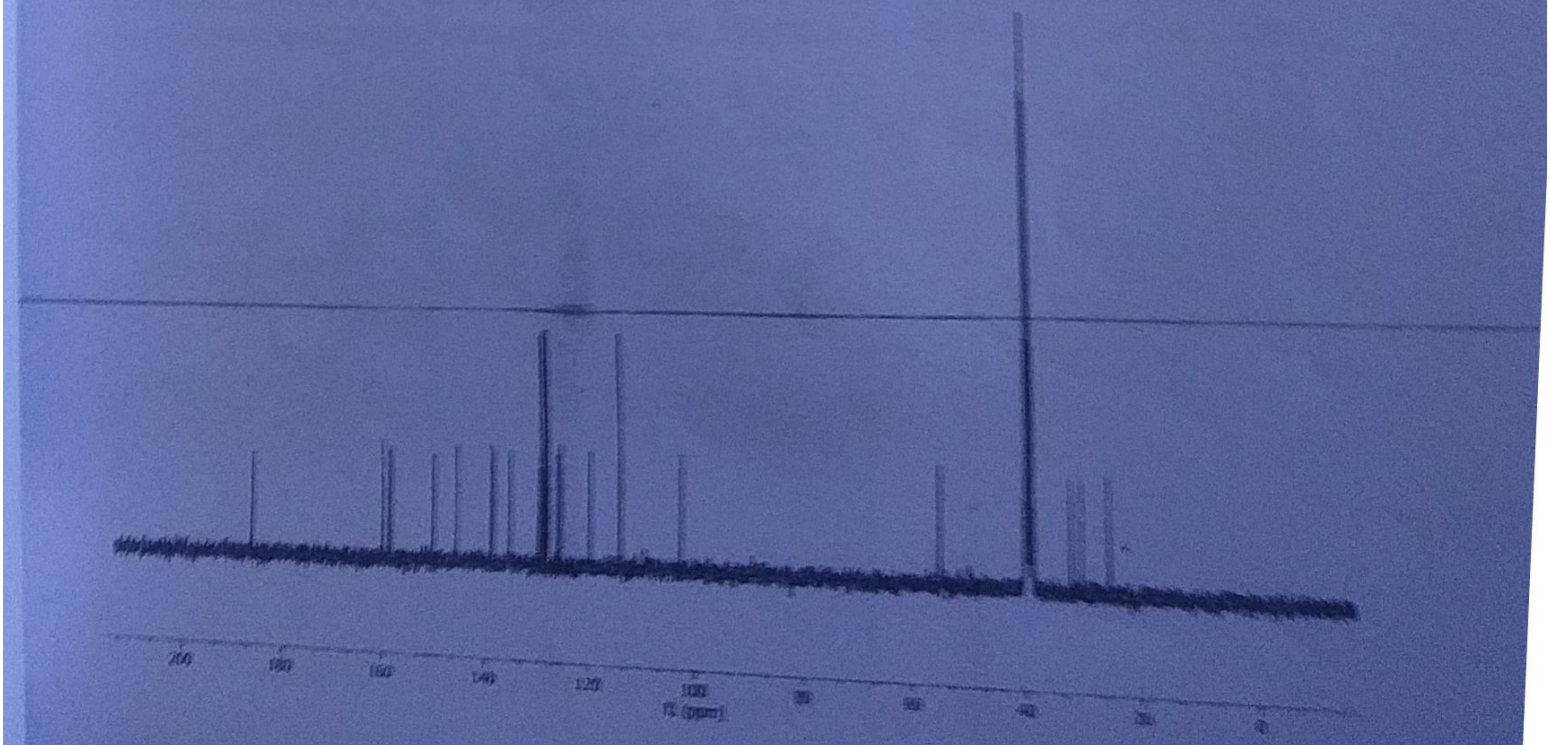
Yellow solid (dioxane, 91%); m.p. 180-182 ₀C; IR (υ cm-1): 3423, 3247 (NH_2), 1627 (CO); ^{1}H-NMR (DMSO-d6): δ 1.97 (quint, *J* = 6.4 Hz, 2H, CH_2), 2.14 (t, *J* = 6.4 Hz, 2H, CH_2), 2.55 (t, *J* = 6.4 Hz, 2H, CH_2), 3.88 (s, 3H, *p*-OCH_3), 6.72 (br`s, 2H, NH_2), 7.19 (d, *J* = 8.4 Hz, 2H, ArH), 7.32 (d, *J* = 6.4 Hz, 1H, ArH), 7.40-7.45 (m, 4H, ArH), 7.60 (d, *J* = 8.4 Hz, 2H, ArH), 7.72 (d, *J* = 6.4 Hz, 1H, ArH), 7.79 (d, *J* = 8.4 Hz, 2H, ArH); ^{13}C-NMR (DMSO-d6): δ 25.6, 30.4, 32.2, 55.3, 103.0, 114.7, 120.5, 126.2 126.7, 128.6, 128.7, 128.8, 129.3, 129.7, 130.0, 130.1, 135.9, 139.1, 139.3, 139.4, 146.4, 150.9, 159.4, 159.7, 161.0, 187.4; Anal. calcd for $C_{30}H_{23}ClN_2O_2S$ (511.0): C, 70.51; H, 4.54; N, 5.48; found: C, 70.63; H, 4.62; N, 5.33%.

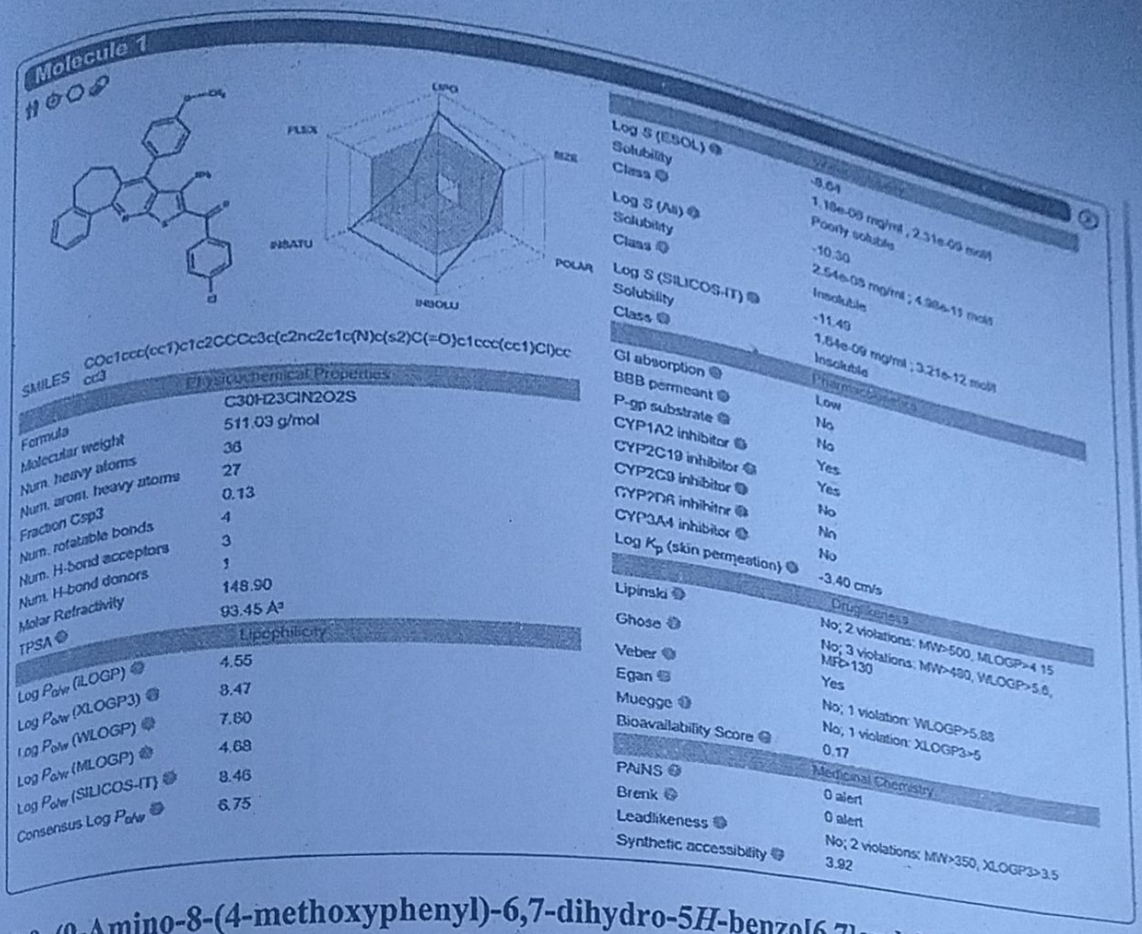


^{1}H-NMR spectrum of compound 5f (DMSO-d_6 400 MHz).



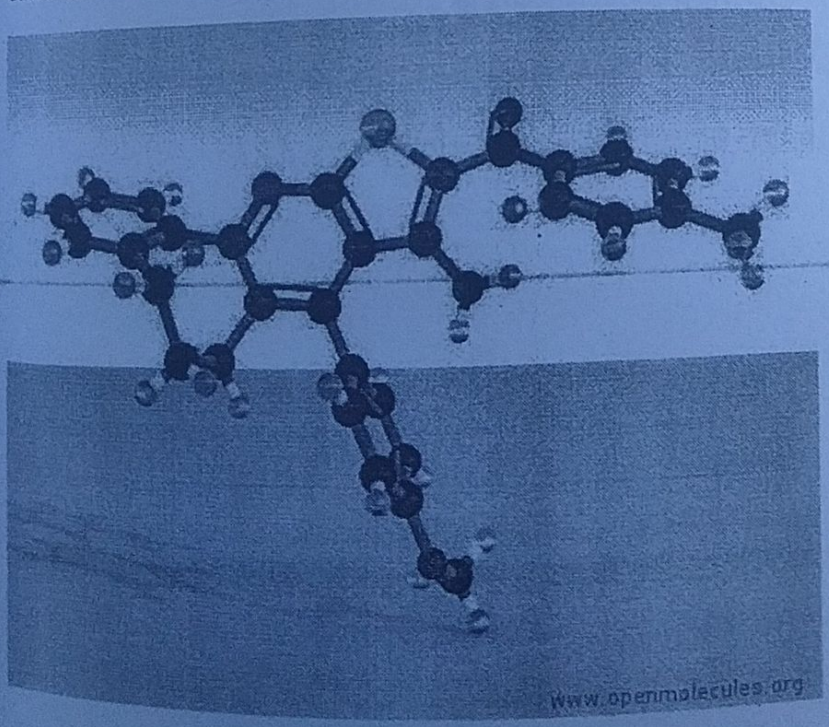
^{13}C-NMR spectrum of compound 5f (DMSO-d_6 100 MHz).



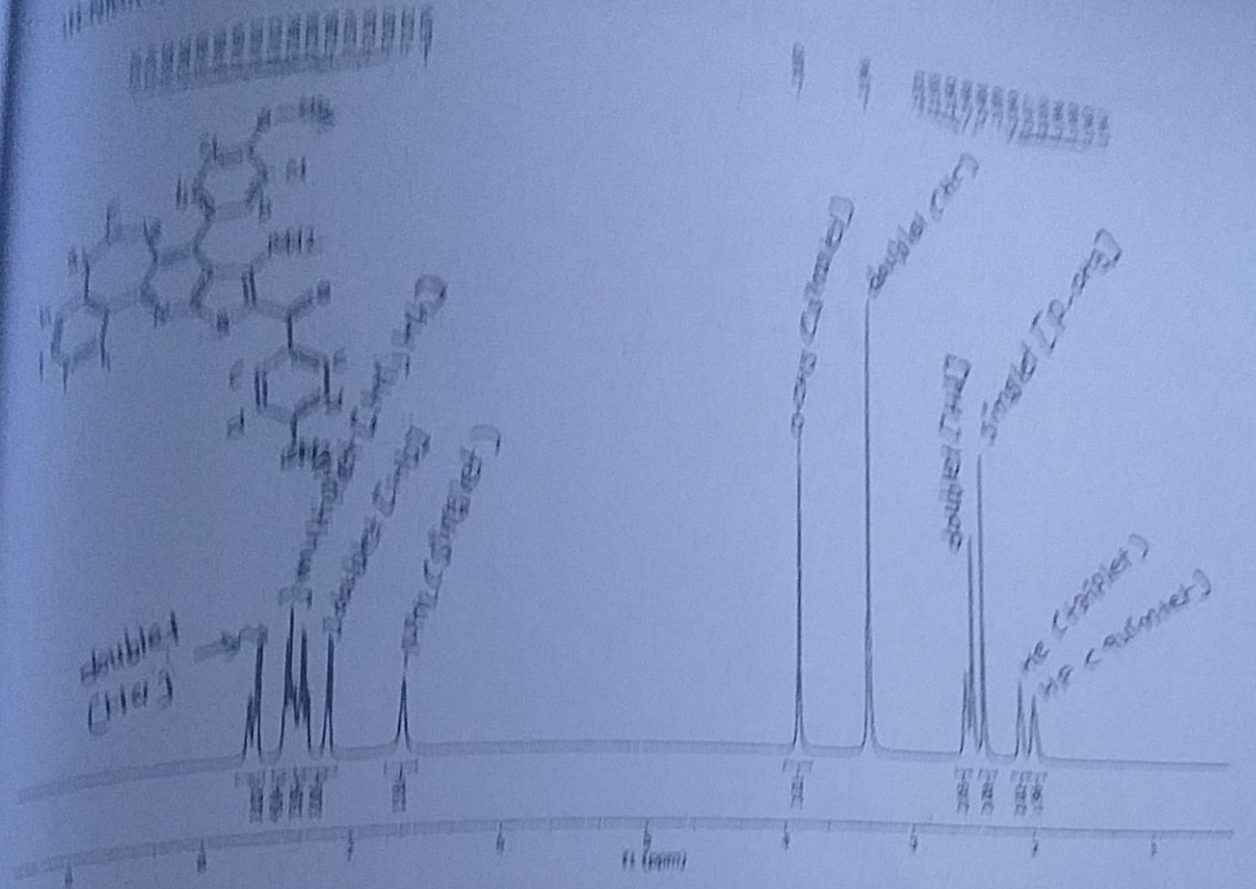


2.2.9. (9-Amino-8-(4-methoxyphenyl)-6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*b*]thieno[3,2-*e*]pyridin-10-yl)(*p*-tolyl)methanone (5g).

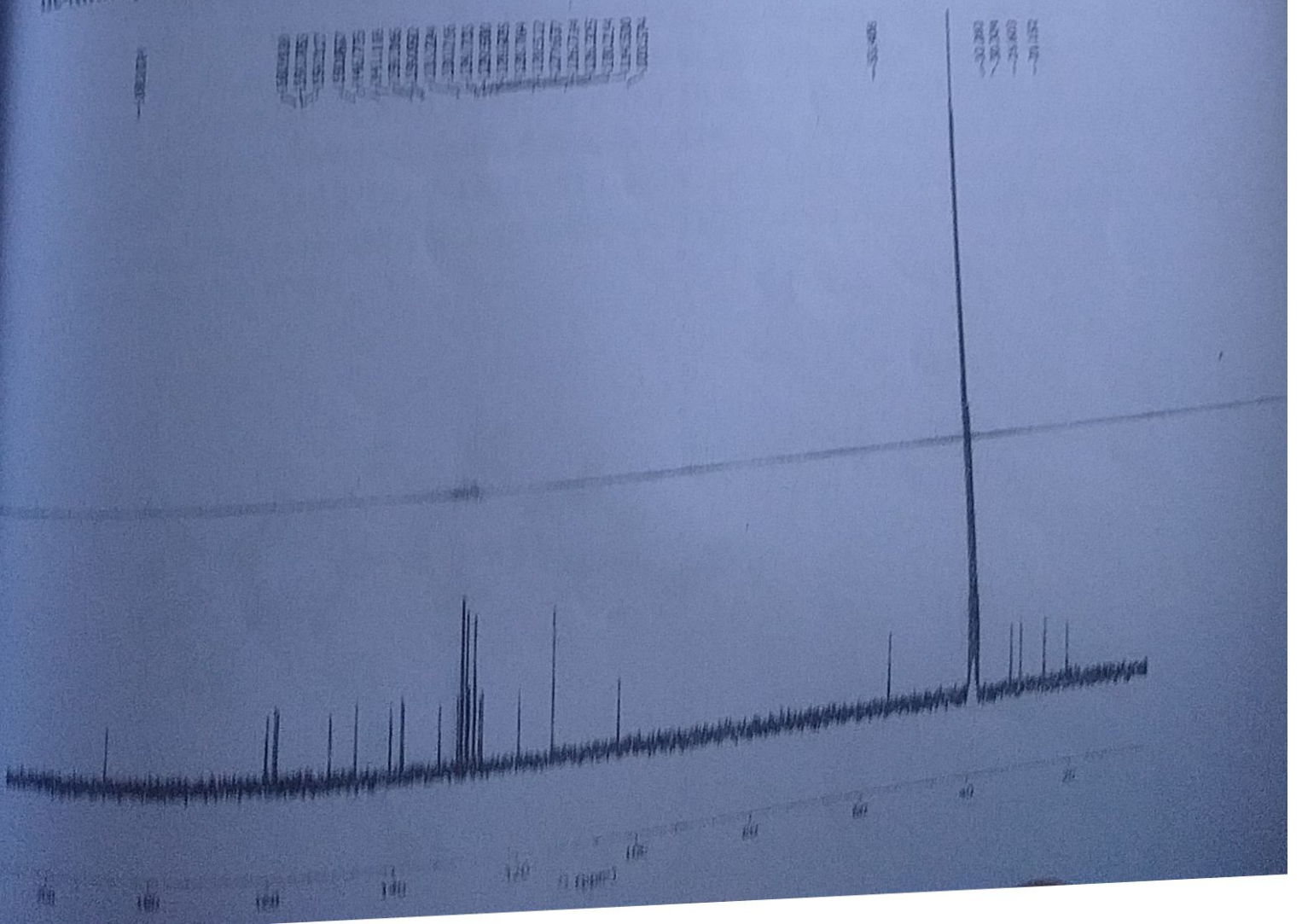
Yellow solid (dioxane, 89%); m.p. 250-253 ₀C; IR (υ cm-1): 3444, 3227 (NH_2), 1631 (CO); ₁H-NMR (DMSO-d6): δ 1.98 (quint, *J* = 6.4 Hz, 2H, CH_2), 2.09 (t, *J* = 6.4 Hz, 2H, CH_2), 2.40 (s, 3H, *p*-CH_3), 2.55 (t, *J* = 6.4 Hz, 2H, CH_2), 3.89 (s, 3H, *p*-OCH_3), 6.67 (br s, 2H, NH_2), 7.18 (d, *J* = 8.4 Hz, 2H, ArH), 7.32 (d, *J* = 6.4 Hz, 1H, ArH), 7.36 (d, *J* = 8.0 Hz, 2H, ArH), 7.41-7.43 (m, 2H, ArH), 7.46 (d, *J* = 8.4 Hz, 2H, ArH), 7.67 (d, *J* = 8.4 Hz, 2H, ArH), 7.72 (d, *J* = 6.4 Hz, 1H, ArH); ₁₃C-NMR (DMSO-d6): δ 21.1, 25.6, 30.3, 32.2, 55.4, 103.5, 114.5, 120.2, 126.3, 126.7, 127.6, 128.5, 128.7, 128.9, 129.5, 129.7, 130.2, 133.2, 139.0, 139.3, 141.1, 146.7, 150.8, 159.3, 159.7, 160.9, 188.8; Anal. calcd for $C_{31}H_{26}N_2O_2S$ (490.6): C, 75.89; H, 5.34; N, 5.71; found: C, 75.80; H, 5.47; N, 5.92%.

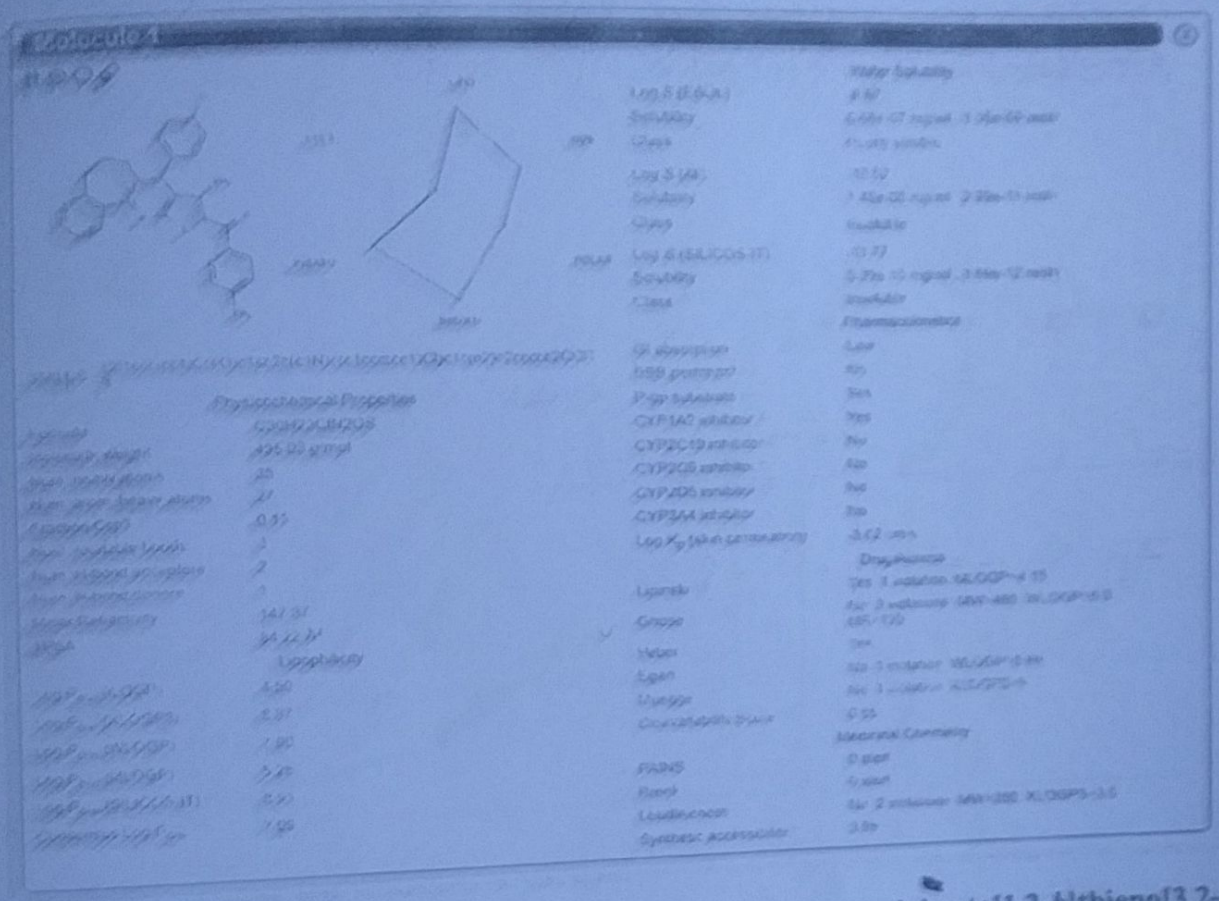


¹H-NMR spectrum of compound 5g (DMSO-d_6 400 MHz).



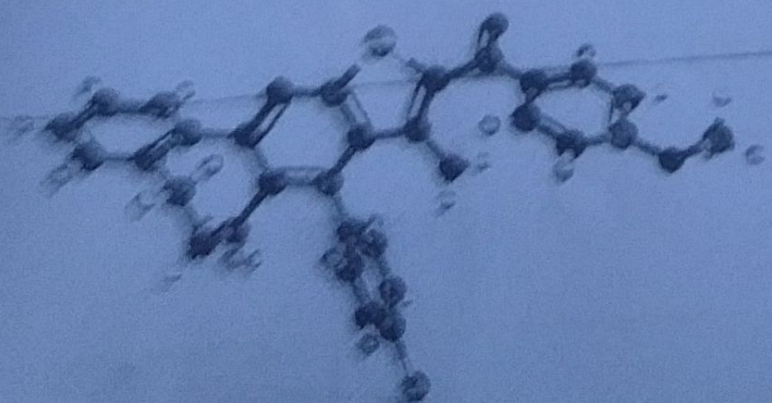
¹³C-NMR spectrum of compound 5g (DMSO-d_6 100 MHz).



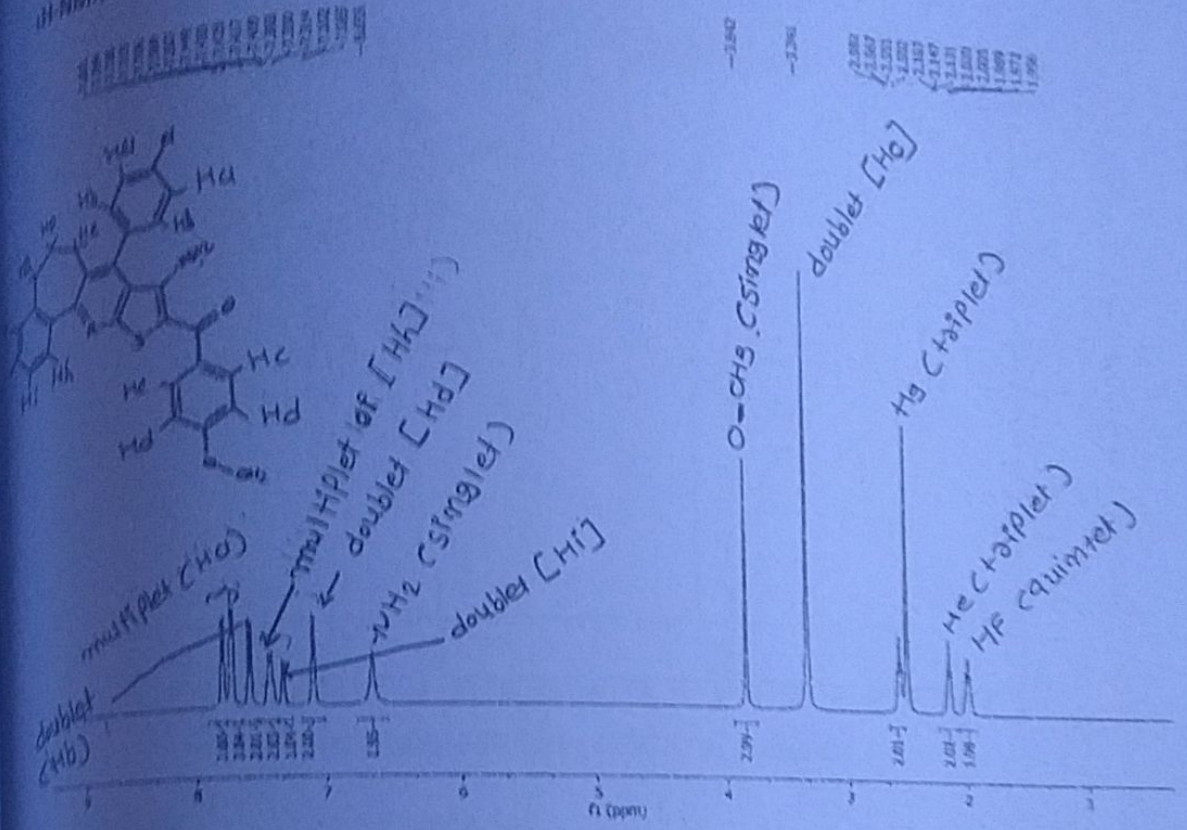


2,2,6-(9-Amino-8-(4-chlorophenyl)-6,7-dihydro-5*H*-benzo[6,7]cyclohepta[1,2-*b*]thieno[3,2-*e*]pyridin-10-yl)(4-methoxyphenyl)methanone (5d).

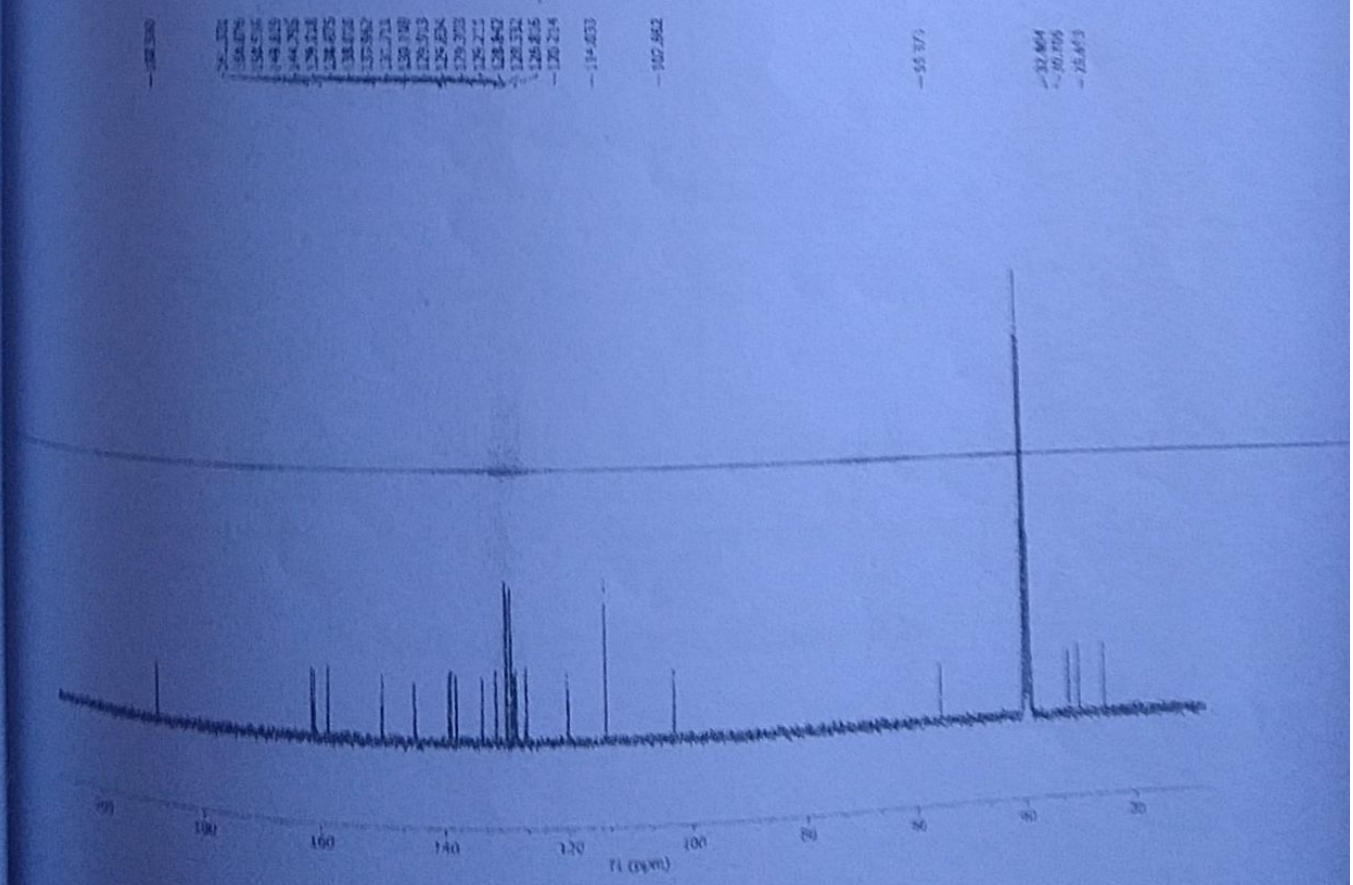
Yellow solid (dioxane, 90%); m.p. 212-213 ºC; IR (υ cm-1): 3423, 3237 (NH_2), 1629 (CO); ¹H-NMR (DMSO-d6): δ 1.98 (quint, *J* = 6.4 Hz, 2H, CH_2), 2.14 (t, *J* = 6.4 Hz, 2H, CH_2), 2.56 (t, *J* = 6.4 Hz, 2H, CH_2), 3.84 (s, 3H, *p*-OCH_3), 6.65 (br s, 2H, NH_2), 7.09 (d, *J* = 6.8 Hz, 2H, ArH), 7.32 (d, *J* = 6.4 Hz, 1H, ArH), 7.39-7.44 (m, 2H, ArH), 7.57 (d, *J* = 8.4 Hz, 2H, ArH), 7.70-7.72 (m, 3H, ArH), 7.79 (d, *J* = 6.8 Hz, 2H, ArH); ¹³C-NMR (DMSO-d6): δ 25.6, 30.2, 32.0, 55.3, 102.8, 114.0, 120.2, 126.8, 128.5, 128.8, 129.2, 129.3, 129.8, 129.9, 130.1, 131.7, 133.9, 138.0, 138.8, 139.1, 144.7, 149.8, 158.5, 160.8, 161.3, 188.5; Anal. calcd for $C_{30}H_{23}ClN_2O_2S$ (511.0): C, 70.51; H, 4.54; N, 5.48; found: C, 70.35; H, 4.42; N, 5.40%

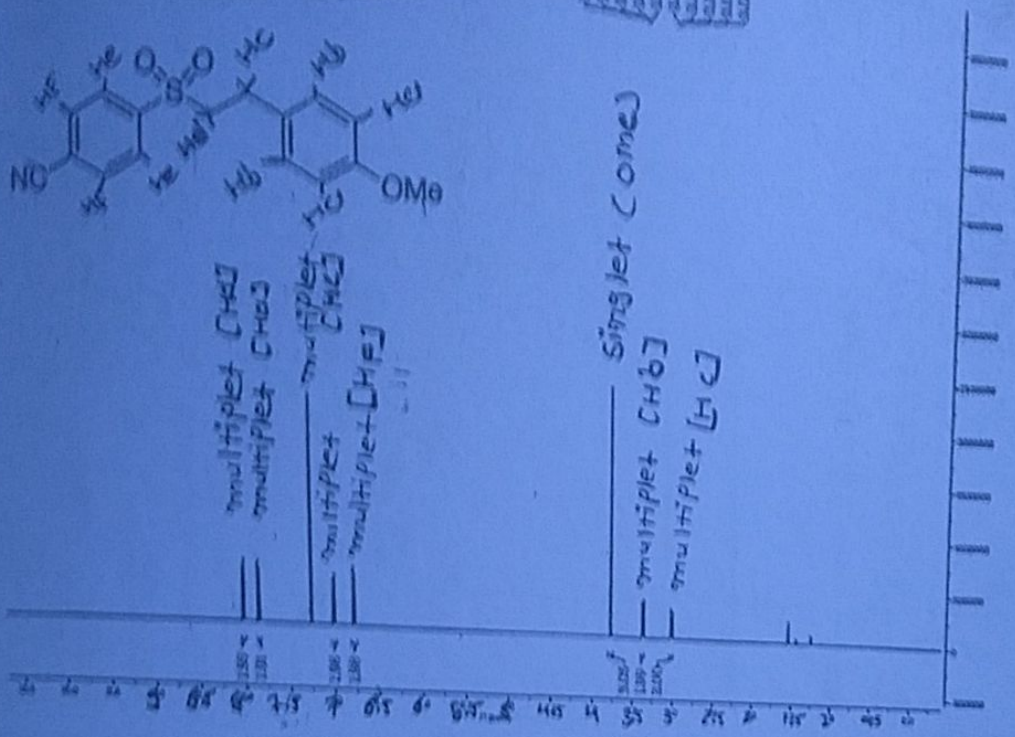


¹H-NMR spectrum of compound 5d (DMSO-d_6 400 MHz).

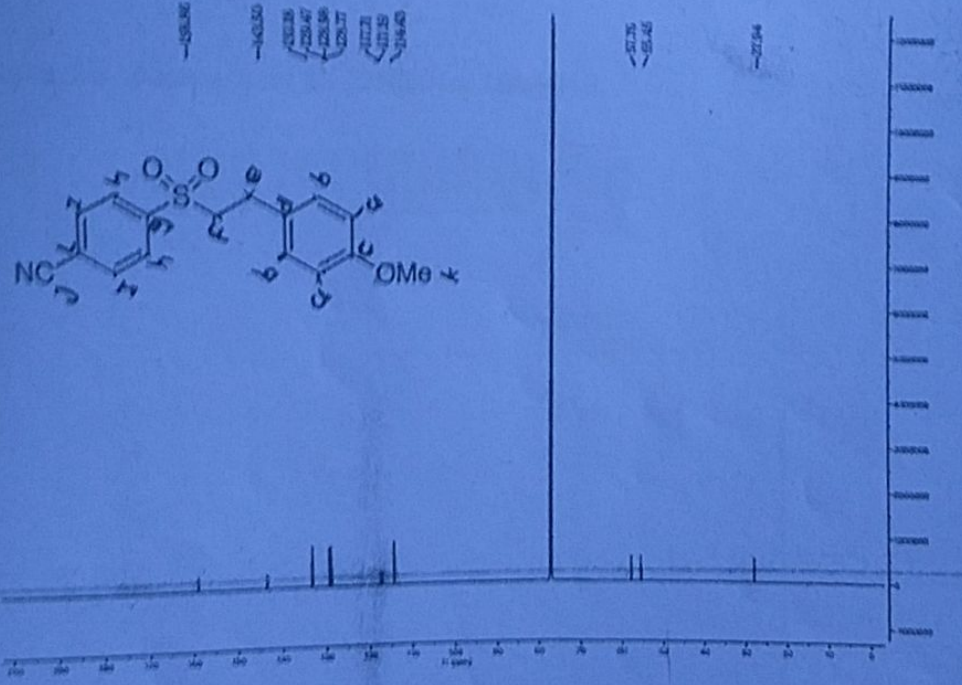


¹³C-NMR spectrum of compound 5d (DMSO-d_6 100 MHz).



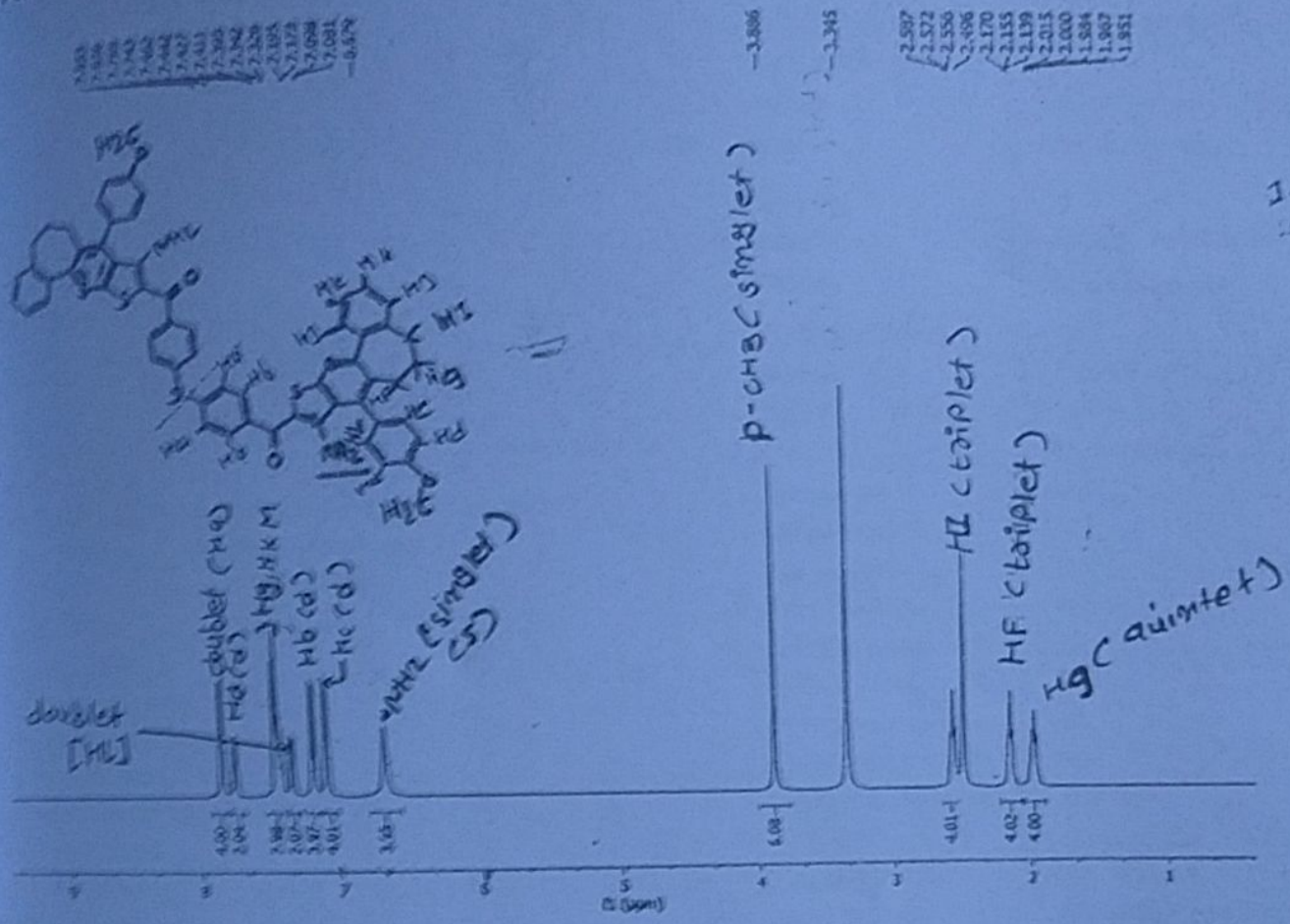


^{1}H NMR (600 MHz, $CDCl_3$) of compound **4a**

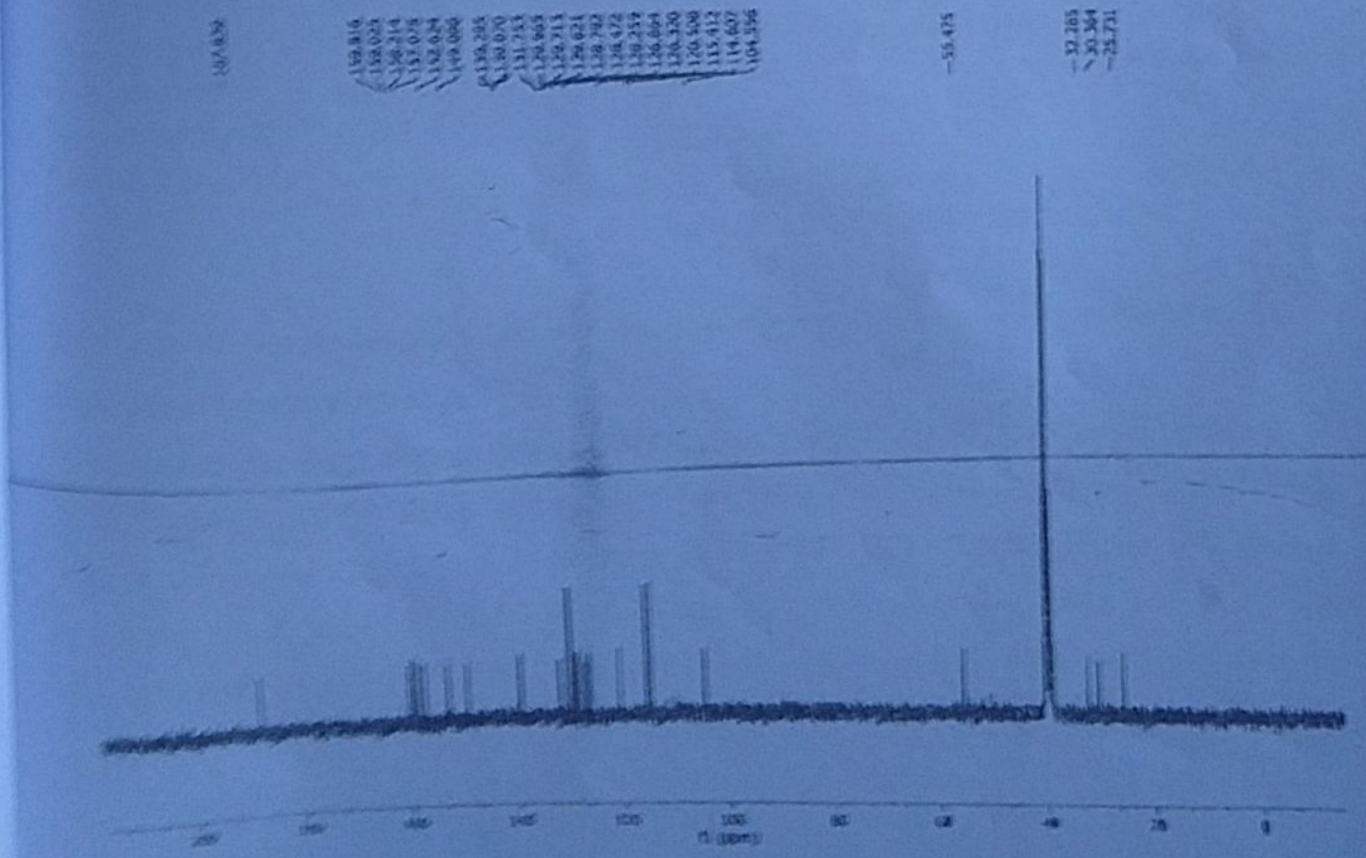


^{13}C NMR (151 MHz, $CDCl_3$) of compound **4a**

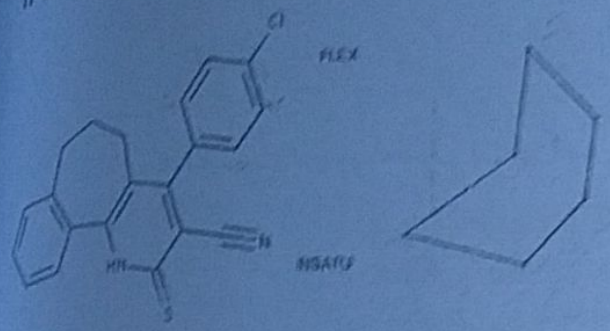
¹H-NMR spectrum of compound 8b (DMSO-*d*₆ 400 MHz).



¹³C-NMR spectrum of compound 8b (DMSO-*d*₆ 100 MHz).



Molecule 1



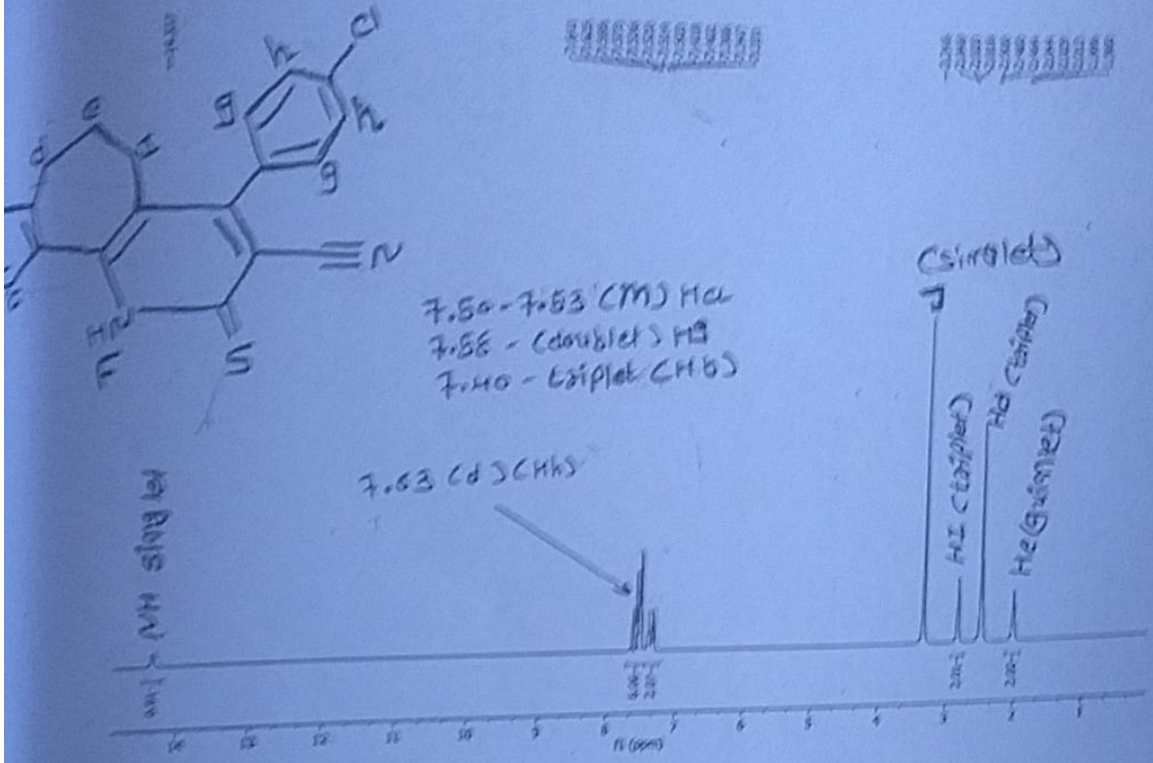
SMILES N#Cc1c(=S)[nH]c2c(c1c1ccccc1)CCCCc1ccccc21

Physicochemical Properties	
Formula	C21H15ClN2S
Molecular weight	362.88 g/mol
Num. heavy atoms	25
Num. arom. heavy atoms	18
Fraction Csp3	0.14
Num. rotatable bonds	1
Num. H-bond acceptors	1
Num. H-bond donors	1
Molar Refractivity	104.85
TPSA	71.87 Å²
Lipophilicity	
Log $P_{o/w}$ (iLOGP)	3.23
Log $P_{o/w}$ (XLOGP3)	4.56
Log $P_{o/w}$ (WLOGP)	6.09
Log $P_{o/w}$ (MLOGP)	3.80
Log $P_{o/w}$ (SILICOS-IT)	7.64
Consensus Log $P_{o/w}$	5.06

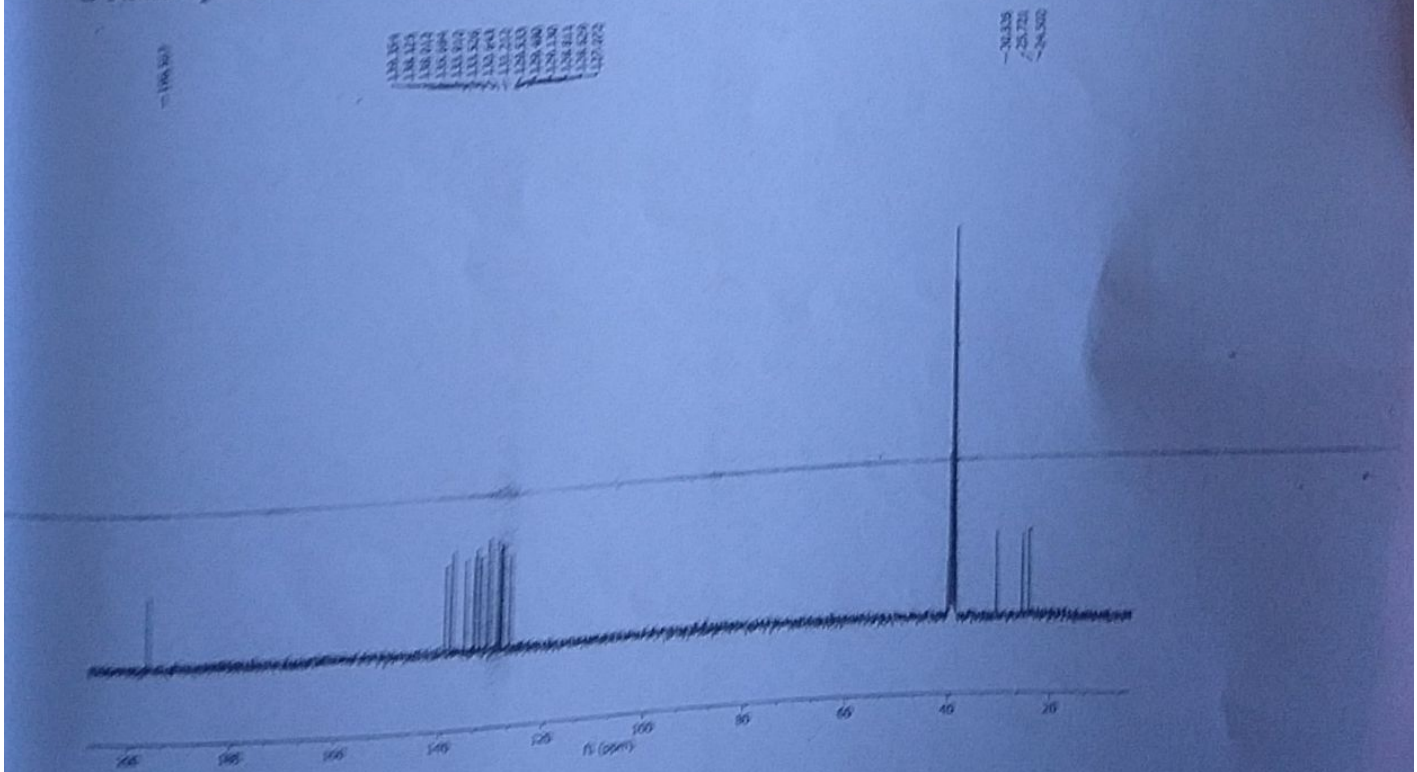
		Water Solubility
	Log S (ESOL)	-5.40
	Solubility	1.35e-03 mg/ml ; 3.72e-06
SIZE	Class	Moderately soluble
	Log S (Ali)	-5.73
	Solubility	5.31e-04 mg/ml ; 1.85e-06
	Class	Moderately soluble
POLAR	Log S (SILICOS-IT)	-8.85
	Solubility	3.67e-07 mg/ml ; 2.22e-09
	Class	Poorly soluble
		Pharmacokinetics
	GI absorption	High
	BBB permeant	No
	P-gp substrate	Yes
	CYP1A2 inhibitor	Yes
	CYP2C19 inhibitor	Yes
	CYP2C9 inhibitor	Yes
	CYP2D6 inhibitor	No
	CYP3A4 inhibitor	Yes
	Log K_p (skin permeation)	-5.28 cm/s
		Druglikeness
	Lipinski	Yes; 0 violation
	Ghose	No; 1 violation: WLOGP<-5
	Veber	Yes
	Egan	No; 1 violation: WLOGP<-5
	Muegge	Yes
	Bioavailability Score	0.55
		Medicinal Chemistry
	PAINS	0 alert
	Brenk	1 alert: thiocarbonyl_group
	Leadlikeness	No; 2 violations: MW>350, XLOGP3>3.5
	Synthetic accessibility	3.93

2.1.2. 4-(4-Methoxyphenyl)-2-thioxo-2,5,6,7-tetrahydro-*1H*-benzo[6,7]cyclohepta[1,2-*b*]pyridine-3-carbonitrile (3b).

Yellow solid (dioxane / ethanol mixture, 77%); m.p. 230-231 °C; IR (ν cm⁻¹): 3327 (NH), 2211 (CN); ^{1}H-NMR (DMSO-d_6): δ 2.02 (quint, J = 6.4 Hz, 2H, CH_2), 2.52 (t, J = 6.4 Hz, 2H, CH_2), 2.82 (t, J = 6.4 Hz, 2H, CH_2), 3.81 (s, 3H, *p*-OCH_3), 7.04 (d, J = 8.4 Hz, 2H, ArH), 7.30 (d, J = 6.4 Hz, 1H, ArH), 7.39 (t, J = 6.4 Hz, 1H, ArH), 7.50-7.56 (m, 3H, ArH), 7.62 (d, J = 6.4 Hz, 1H, ArH), 14.20 (s, 1H, NH); Anal. calcd for $C_{22}H_{18}N_2OS$ (358.4): C, 73.72; H, 5.06; N, 7.82; found: C, 73.57; H, 5.13; N, 7.69%.



^{13}C-NMR spectrum of compound 3a (DMSO-d_6 100 MHz).



^{1}H-NMR spectrum of compound 3b (DMSO-d_6 400 MHz).