SYNTHESIS, CHARACTERISATION AND ANTIMICROBIAL STUDY OF NOVEL HETEROCYCLIC DERIVATIVE COMPOUNDS

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Abstract: **Synthesis and biological analysis of novel heterocyclic derivatives from Indoline-2-3-dionemolecules.The novel heterocyclic derivatives was characterised by the FT-IR, ^{1}H proton magnetic resonance and ^{13}C proton magnetic resonance. The novel heterocyclic derivatives at differing kinds of compounds 3a, 3b, 3c, 3d, and 3e were ready indoline-2-3-dione molecule. Spectral analysis and antimicrobial study were accustomed characterize these 3a-3e samples and mentioned.**

***Keywords*-Heterocyclic compounds, Dione molecules, Indole derivatives, Antimicrobial Activity.**

1.INTRODUCTION

Heterocyclic blends have a monster variety of utility. they're dominatingly used as specialist recommended meds, as agrochemicals and as veterinary things. they moreover discover groups as sanitizers, makers, cell fortifications, as disintegration inhibitors, as copolymers.
Portrayed as cyclic combinations containing ring part bits of carbon and in any occasion an extra segment (a longside nitrogen, oxygen and sulfur), heterocycles are not peculiar in science, giving in an expansive grouping of developments from impetus co-factors through to amino acids and proteins. They play a fundamental limit inside the processing of all home things, and are utilized at essentially every level of the diverse biochemical cycles imperative to help presence. [1].

Heterocyclic combinations incorporate among the biochemical material important to lifestyles. for example, nucleic acids, the compound materials that pass on the inherited information controlling heritage, consolidate long chains of heterocyclic devices held with everything taken into account by using different sorts of substances. Various unmistakably happening shades, enhancements, and against microbial are heterocyclic blends, as are most limit hallucinogenic medications. Current culture is depending upon made hetero cycles to be used as compartments, creepy crawly showers, shadings, and plastics [2].
In this substance were referred to mix and characterisation of novel heterocyclic subordinates from Indoline-2-three-dionemolecules yield with stand-apart mixtures.

2. EXPERIMENTAL

2.1 *Synthesis of novel 5'-benzoyl-1'-methyl-1'',2''-dihydro-2H-dispiro[acenaphthylene-1,2'-pyrrolidine-4',3''-indole]-2,2''-dione derivatives* (3a-e)(Sheme 1)

The equimolar concentration of compounds (3a-e), Acenaphthenequinone and Sarcosine mixed with 100 ml of ethanol and 1ml of diethyl amine. The whole content was refluxed in 1200 RPM for 12 hrs at ice cold temperature. It was refluxed with stirring for 14 hours followed by the addition of (10 ml) acetic acid. The final precipitate was subjected to repeat washing with ethanol (cold) and finally recrystallized from glacial acetic acid to give the required 3a-e compound [3].

2.2 CHARECTERISATION

For the confirmation of the structure, the FT-IR spectra monomers were gathered or collected by the spectrometer of Perkin-Elmer 781 infrared in presence of NaCl. ^{13}C and ^{1}H NMR spectra were also gathered or collected on the NMR spectrometer of Bruker 500MHz in addition to CDCl3 and DMSO being solvents.

2.3 ANIMICROBIAL STUDY

Developing cells in Mueller Hinton Broth (Himedia) at 37 °C for 24 hours, was used to prepare Bacteria inoculums. The above cell suspensions were disposed with sterile MHB to give initial cell counts of about 10^{-4} CFU/millilitre. Sabouraud dextrose (SDB) yeast grown for 48 hours at 28°C [4].

3. RESULTS AND DISCUSSION

5'-(4-methoxybenzoyl)-1'-methyl-1'',2''-dihydro-2H-dispiro[acenaphthylene-1,2'-pyrrolidine-4',3''-indole]-2,2''-dione (3a) (Figure 1-1.4)

Yield: 1.302 g (80%). M.p.: 131^{0}C. IR data (KBr, v/cm-1): 1632, 1758, 3434. 1H NMR (DMSO/400 MHz, δ/ppm): 2.51 (s, 3H), 3.36 (s, 2H), 4.26 (d, 1H), 6.29-7.75 (m, aromatic), 12.05 (br, NH). 13C NMR (DMSO/400 MHz, δ/ppm): δ 21.15, 22.74, 39.98, 129.72-193.71. Mass: 476.2100.UV-Vis Spectra (Ethanol): 248, 343 nm.

5'-(4-hydroxybenzoyl)-1'-methyl-1'',2''-dihydro-2H-dispiro[acenaphthylene-1,2'-pyrrolidine-4',3''-indole]-2,2''-dione (3b): (Figure 2-2.4)

Ylide: 1.318 g (75%). M.P.: 133-134 °C. IR data (KBr, *v*/cm^{-1}): 1648, 1692, 3465. ^{1}H NMR (DMSO/400 MHz, δ/ppm): 2.04 (s, 3H), 2.63 (s, OH), 3.35 (s, 2H), 4.28 (d, 1H), 7.44-7.56 (m, aromatic), 10.03 (br, NH). ^{13}C NMR (DMSO/400 MHz, δ/ppm): δ 21.52, 39.98, 40.58, 129.03-193.71. Mass: 462.5600. UV-Vis Spectra (Ethanol): 243, 336 nm.

5'-benzoyl-1'-methyl-1'',2''-dihydro-2H-dispiro[acenaphthylene-1,2'-pyrrolidine-4',3''-indole]-2,2''-dione (3c): (Figure 3-3.4)

Yield: 1.256 g (79%) M.P.: 115-117 °C. IR data (KBr, *v*/cm^{-1}): 1601, 1719, 3405. ^{1}H NMR (DMSO/400 MHz, δ/ppm): 2.62 (s, 3H), 3.17 (s, 2H), 4.26 (d, 1H), 6.31-7.76 (m, aromatic), 11.54 (br, NH). ^{13}C NMR (DMSO/400 MHz, δ/ppm): δ 22.73, 40.45, 123.79-169.31.
Mass: 458.8350. UV-Vis Spectra (Ethanol): 245, 329 nm.

5'-(4-chlorobenzoyl)-1'-methyl-1'',2''-dihydro-2H-dispiro[acenaphthylene-1,2'-pyrrolidine-4',3''-indole]-2,2''-dione (3d): (Figure 4-4.4)

Yield: 1.326 g (81%). M.P.: 134-135 °C.IR data (KBr, *v*/cm^{-1}): 1618, 1708, 3410.^{1}H NMR (DMSO/400 MHz, δ/ppm): 2.51 (s, 3H), 3.37 (s, 2H), 4.26 (d, 1H), 6.29-7.75 (m, aromatic), 12.84 (br, NH).^{13}C NMR (DMSO/400 MHz, δ/ppm): δ 22.89, 39.97, 126.56-173.14.Mass: 480.5400.UV-Vis Spectra (Ethanol): 247, 341 nm.

1'-methyl-5'-(4-nitrobenzoyl)-1'',2''-dihydro-2H-dispiro[acenaphthylene-1,2'-pyrrolidine-4',3''-indole]-2,2''-dione (3e): (Figure 5-5.4)

Yield: 1.253 g (72%). M.P.: 139-141 °C. IR data (KBr, *v*/cm^{-1}): 1656, 1750, 3392. ^{1}H NMR (DMSO/400 MHz, δ/ppm): 2.66 (s, 3H), 3.39 (s, 2H), 4.26 (d, 1H), 6.82-8.64 (m, aromatic), 10.06 (br, NH). ^{13}C NMR (DMSO/400 MHz, δ/ppm): δ 34.48, 39.49, 114.08-169.88.
Mass: 491.1200. UV-Vis Spectra (Ethanol): 244, 338 nm.

The novel heterocyclic compounds was synthesized from the reaction of Indoline-2,3-dione and acetophenone derivatives, and followed by acenaphthenequinone and sarcosine [5]. The yield percentage of synthesized compounds obtained nearly 72-82%. The melting point of the compounds are between 60-80^{0}C

The IR spectrum of the hetero compounds were confirmed from the peaks corresponding to carbonyl (1719 cm^{-1}) and NH (3405 cm^{-1})groups and other frequencies. The ^{1}H NMR spectrum shows further confirmation of the formation of hetero compounds [6].

The proton signals obtained for aliphatic (2.62, 3.17 and 4.26 ppm), aromatic (6.31-7.76 ppm) and amine (11.54 ppm) protons. The obtained ^{13}C NMR spectrum of the hetero compounds shows the corresponding carbon signals of the hetero compounds. The mass spectrum shows the molecular weight of synthesized compounds.

3.1 ANTIMICROBIAL ACTIVITY

The antibacterial activity of the 3a-e compounds listed out in Table 1. A number of bacteria and fungi were able to counter antimicrobial activity of the synthesizedhetero compounds 3a-e in vitro. The experiments were performed with the tool agar location. For this study, test cultures of the bacterial strains *Staphylococcus aureus, E.coli, Vibrio spp., Pseudomonas aeroginosa, Aeromonas spp., Klebsiella spp., Salmonella spp., Proteus spp, Vibrio parahaemolytics and Bacillus spp.* were each inoculated into Mueller Hinton broth. Normal antibiotics on the respective plates were also found as positive controls for each culture and for a comparative extract analysis using an antibiotic. Antimicrobial compounds were isolated at DMSO at 500µg/mL, and each normal antibiotic at DMSO at 10µg/mL. The plates were held at 37 C during the night in an incubator and the inhibition zones are measured at mm [7].

All the hetero compounds showed a good antibacterial activity against.Staphylococcus aureus, E.coli, Vibrio spp., Pseudomonas aeroginosa, Aeromonas spp., Klebsiella spp., Salmonella spp., Proteus spp, Vibrio parahaemolytics and Bacillus sppcompared to standard ciprofloxacin drug.

4. CONCLUSION

Synthesis and biological evaluation of novel heterocyclic derivatives from Indoline-2-3-dionemolecules.The novel heterocyclic derivatives was characterized by the FT-IR, ^{1}H NMR and ^{13}C NMR. The novel heterocyclic derivatives at different types of compounds 3a, 3b, 3c, 3d, and 3e were prepared indoline-2-3-dione molecule. All the hetero compounds showed a good antibacterial activity against.Staphylococcus aureus, E .coli, Vibrio spp., Pseudomonas aeroginosa, Aeromonas spp., Klebsiella spp., Salmonella spp., Proteus spp, Vibrio parahaemolytics and Bacillus sppcompared to standard ciprofloxacin drug.

5. ACKNOWLEDGEMENT

The authors gratefully acknowledge the P.B. College of Engineering and Centre for research, Bharathiar University for their constant support.

6. REFERENCES

1. Malebari, A.M.; Darren, F.; Nathwani, S.M.; O'Connell, F.; Noorani, S.; Twamley, B.; O'Boyle, N.M.; O'Sullivan, J.; Zisterer, D.M.; Meegan, M.J. β-Lactams with antiproliferative and antiapoptotic activity in breast and chemo resistant colon cancer cells. *Eur. J. Med. Chem.* **2020**, *189*, 112050.
2. Ashore, H.F.; Abou-Zeid, L.A.; El-Sayed, M.A.A.; Selim, K.B. 1,2,3-Triazole-Chalcone hybrids: Synthesis, in vitro cytotoxic activity and mechanistic investigation of apoptosis induction in multiple myeloma RPMI-8226. *Eur. J. Med. Chem.* **2020**, *189*, 112062.

3. El-Azab, A.; Abdel-Aziz, A.A.M.; Bua, S.; Nocentini, A.; El-Gendy, M.A.; Mohamed, M.A.; Shawer, T.Z.; AlSaif, N.A.; Supuran, C.T. Synthesis of benzensulfonamides linked to quinazoline scaffolds as novel carbonic anhydrase inhibitors. *Bioorg. Chem.* **2019**, *87*, 78–90.
4. Jain, S.; Chandra, V.; Jain, P.K.; Pathak, K.; Pathak, D.; Vaidya, A. Comprehensive review on current developments of quinoline-based anticancer agents. *Arabian J. Chem.* **2019**, *12*, 4920–4946.
5. Kuskovsky, R.; Lloyd, D.; Arora, K.; Plotkin, B.J.; Green, J.M.; Boshoff, H.I.; Barry, C.; Deschamps, J.; Konaklieva, M.I. C4-Phenylthio β-lactams: Effect of the chirality of the β-lactam ring on antimicrobial activity. *Bioorg. Med. Chem.* **2019**, *27*, 115050.
6. Jain, S.; Chandra, V.; Jain, P.K.; Pathak, K.; Pathak, D.; Vaidya, A. Comprehensive review on current developments of quinoline-based anticancer agents. *Arabian J. Chem.* **2019**, *12*, 4920–4946.
7. Sun, L.; Huang, T.; Dick, A.; Meuser, M.E.; Zalloum, W.A.; Chen, C.H.; Ding, X.; Gao, P.; Cocklin, S.; Lee, K.H.; et al. Design, synthesis and structure-activity relationships of 4-phenyl-1H-1,2,3-triazole phenylalanine derivatives as novel HIV-1 capsid inhibitors with promising antiviral activities. *Eur. J. Med. Chem.* **2020**, *190*, 112085.

Figure captions

Scheme1. Synthesis of novel 5'-benzoyl-1'-methyl-1",2"-dihydro-2H dispiro [Acenaphthylene-1,2'-pyrrolidine-4',3"-indole]-2,2"-dione derivatives (3a-3e).

Figure 1. 5'-(4-methoxybenzoyl)-1'-methyl-1",2"-dihydro-2H-dispiro[acenaphthylene 1,2'-pyrrolidine-4',3"-indole]-2,2"-dione (3a)

Figure 1.1. IR spectrum of compound 3a

Figure 1.2. ^{1}H NMR Spectrum of the compound 3a

Figure 1.3. ^{13}C NMR spectrum of the compound

Figure 1.4. Mass spectrum of the compound 3a

Figure2. 5'-(4-hydroxybenzoyl)-1'-methyl-1",2"-dihydro-2H-dispiro[acenaphthylene-1,2'-pyrrolidine-4',3"-indole]-2,2"-dione (3b

Figure 2.1 IR spectrum of compound 3b

Figure 2.2 1H NMR Spectrum of the

Figure 2.3 ^{13}C NMR spectrum of the compound 3b

Figure 2.4 Mass spectrum of the compound 3b

Figure 3: 5'-benzoyl-1'-methyl-1",2"-dihydro-2H-dispiro[acenaphthylene-1,2'-pyrrolidine-4',3"-indole]-2,2"-dione (3c)

Figure 3.1 IR spectrum of compound 3c

Figure 3.2 ^{1}H NMR Spectrum of the compoun

Figure 3.3. ^{13}C NMR Spectrum of the compound 3c

Figure 3.4. Mass spectrum of the compound 3c

Figure 4 5'-(4-chlorobenzoyl)-1'-methyl-1",2"-dihydro-2H-dispiro[acenaphthylene-1,2'-pyrrolidine-4',3"-indole]-2,2"-dione (3d)

Figure4.1 IR spectrum of the compound 3d

Figure4.2 ^{1}H NMR spectrum of the compound 3d

Figure4.3 ^{13}C NMR spectrum of the compound 3d

Figure4.4 Mass spectrum of the compound 3d

Figure5 1'-methyl-5'-(4-nitrobenzoyl)-1",2"-dihydro-2H-dispiro[acenaphthylene-1,2'-pyrrolidine-4',3"-indole]-2,2"-dione (3e)

Figure5.1 IR spectrum of the compound 3e

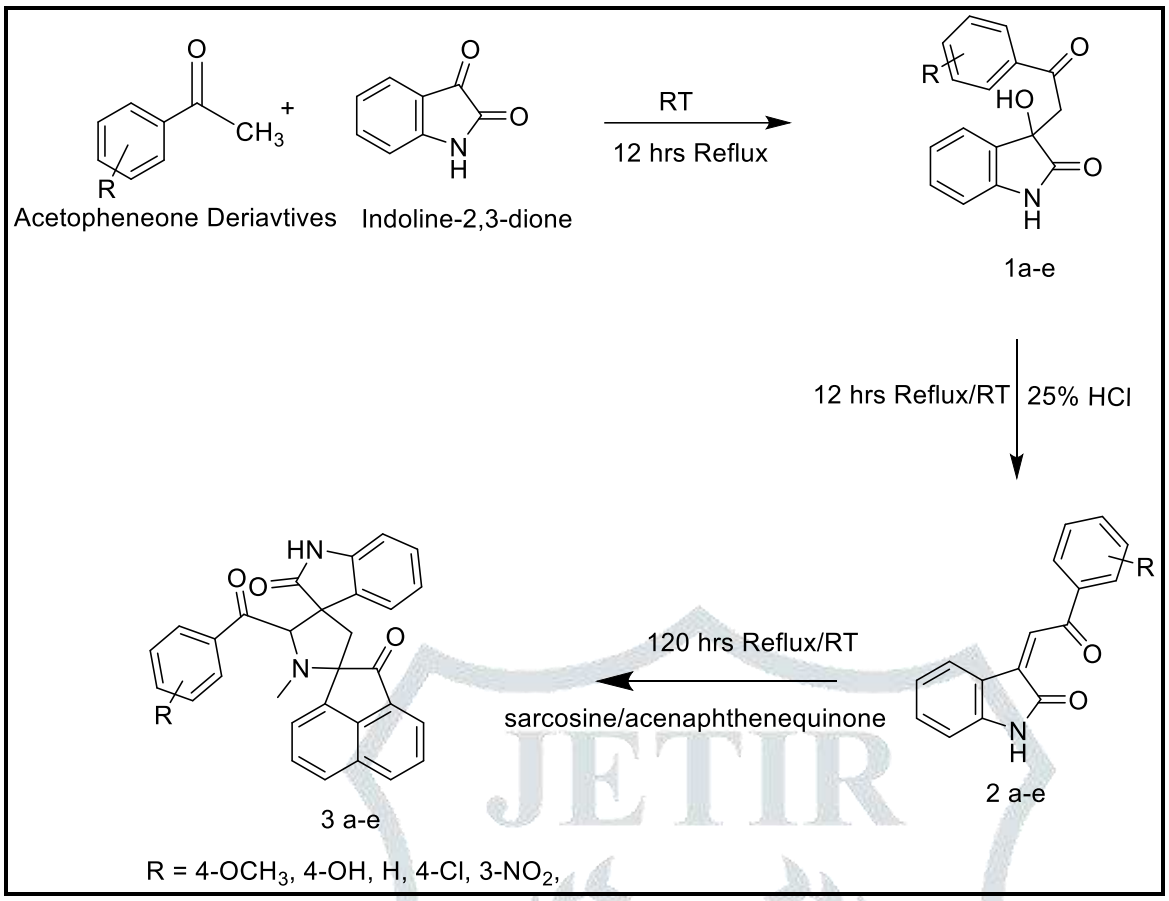
Figure5.2 ^{1}H NMR Spectrum of the compound 3e

Figure5.3 ^{13}C NMR Spectrum of the compound 3e

Figure 5.4 Mass spectrum of compound 3

Table caption

Table.1 Antibacterial activity of the synthesized heterocyclic compounds 3a-e



Scheme1. Synthesis of novel 5'-benzoyl-1'-methyl-1'',2''-dihydro-2H dispiro [acenaphthylene-1,2'-pyrrolidine-4',3''-indole]-2,2''-dione derivatives (3a-3e).

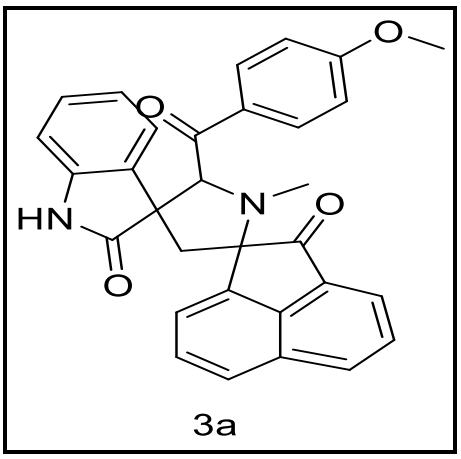


Figure 2. 5'-(4-methoxybenzoyl)-1'-methyl-1'',2''-dihydro-2H-dispiro[acenaphthylene-1,2'-pyrrolidine-4',3''-indole]-2,2''-dione (3a)

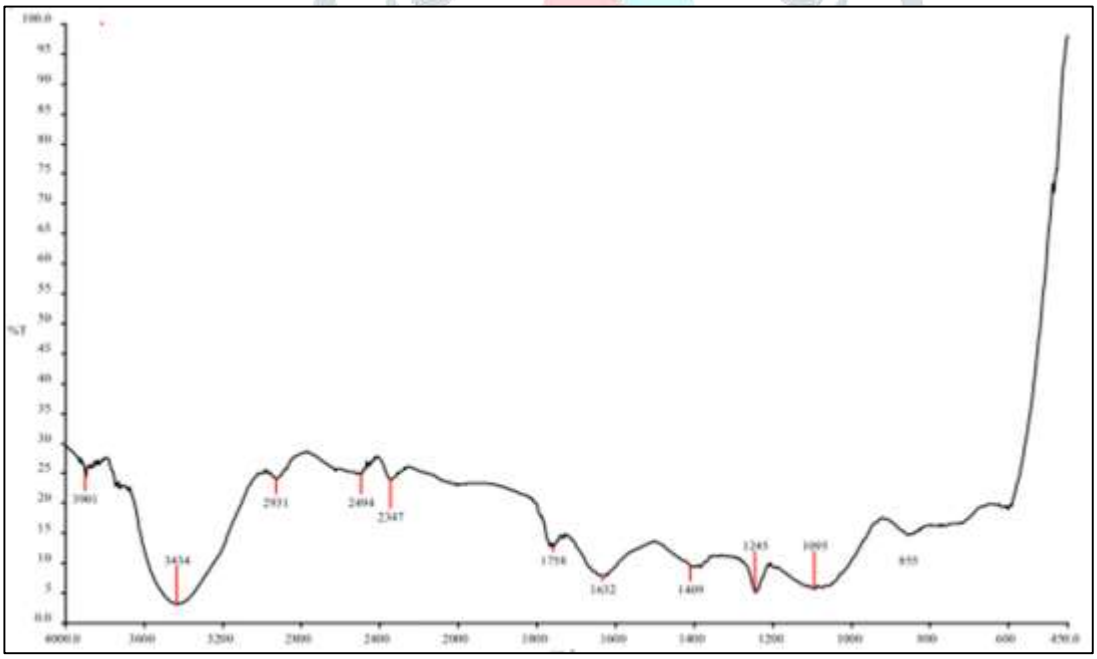


Figure 1.1 IR spectrum of compound 3a

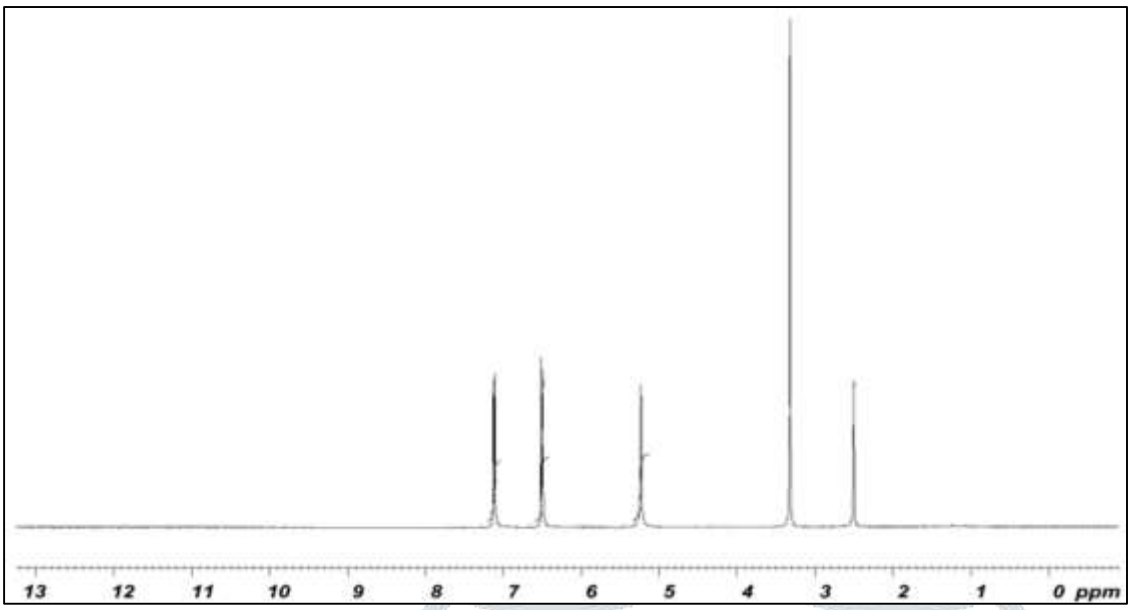


Figure 1.2, ^{1}H NMR Spectrum of the compound 3a

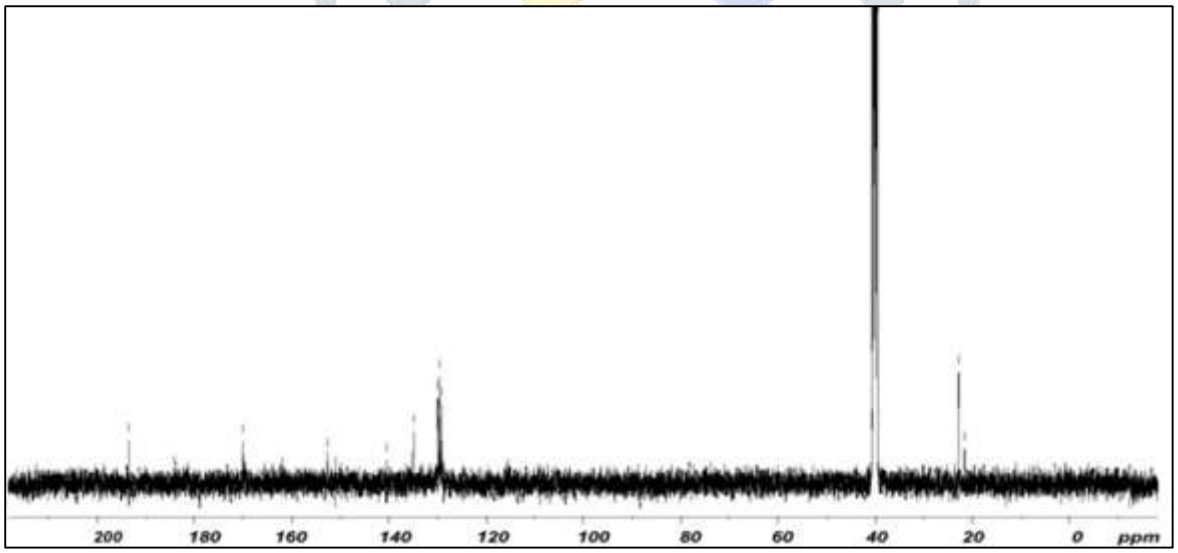


Figure 1.3, ^{13}C NMR spectrum of the compound 3a

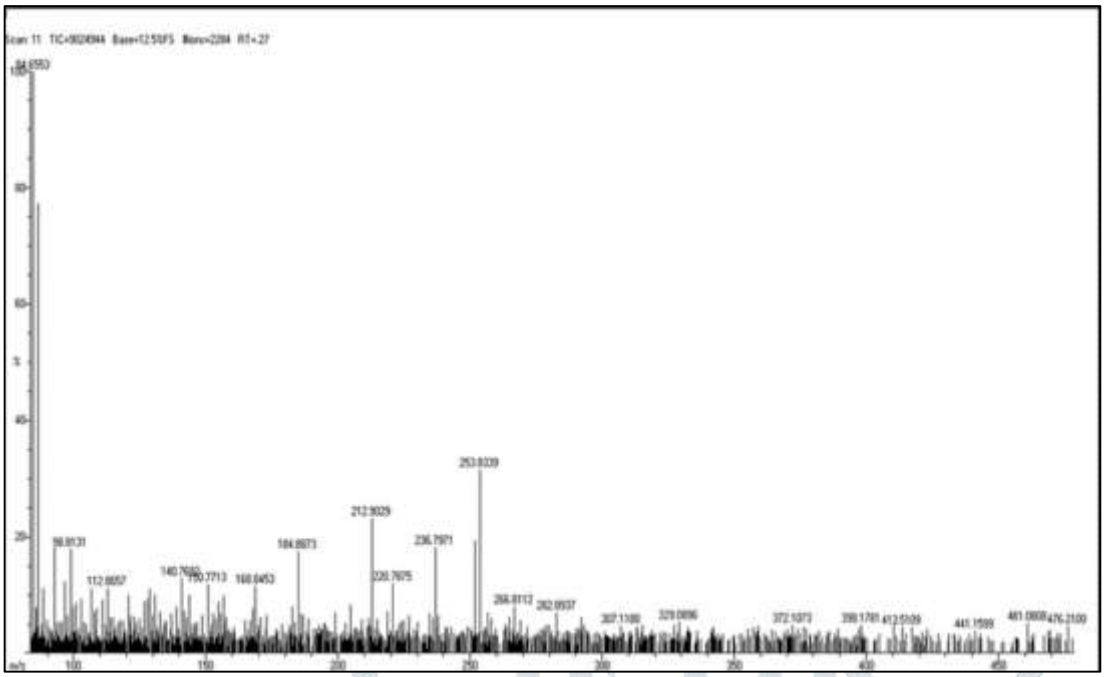


Figure 1.4 Mass spectrum of the compound 3a

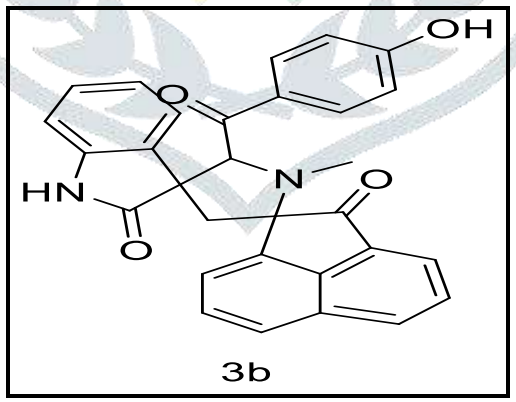


Figure 2. 5'-(4-hydroxybenzoyl)-1'-methyl-1'',2''-dihydro-2H-dispiro[acenaphthylene-1,2'-pyrrolidine-4',3''-indole]-2,2''-dione (3b)

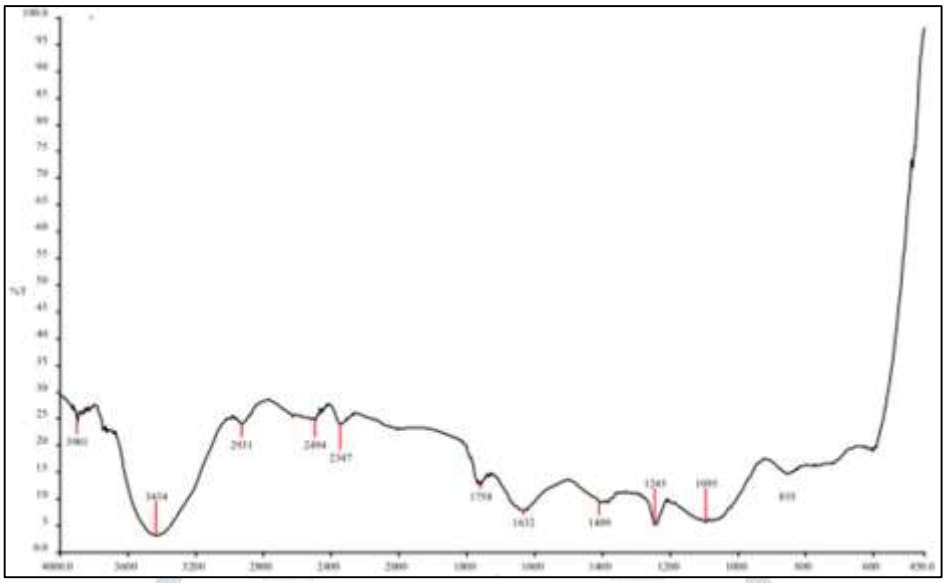


Figure 2.1 IR spectrum of compound 3b

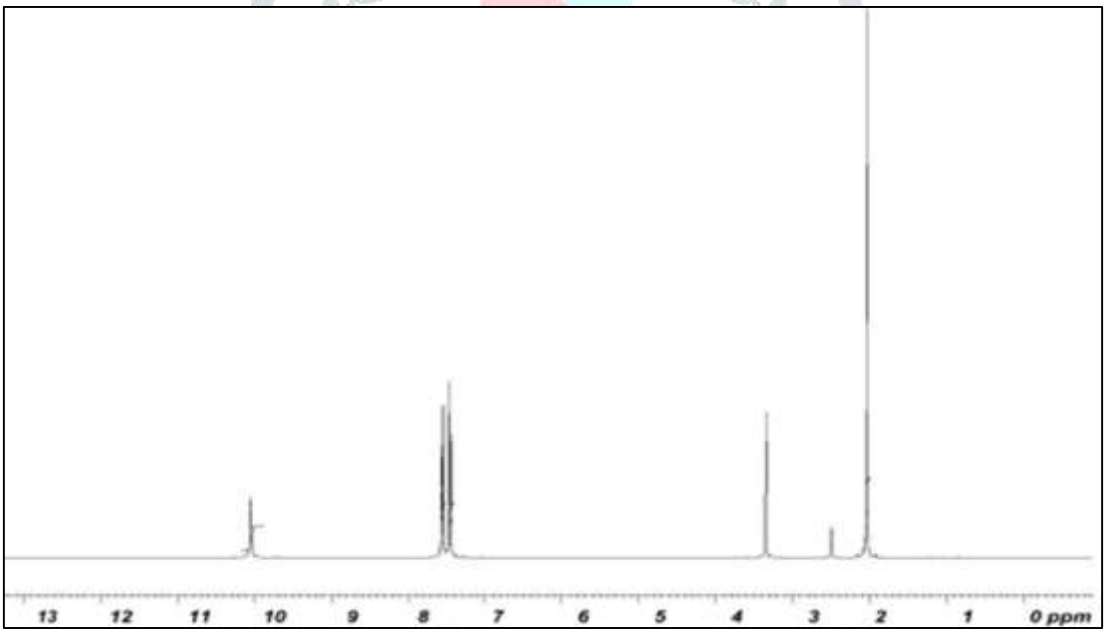


Figure 2.2 ^{1}H NMR Spectrum of the compound 3b

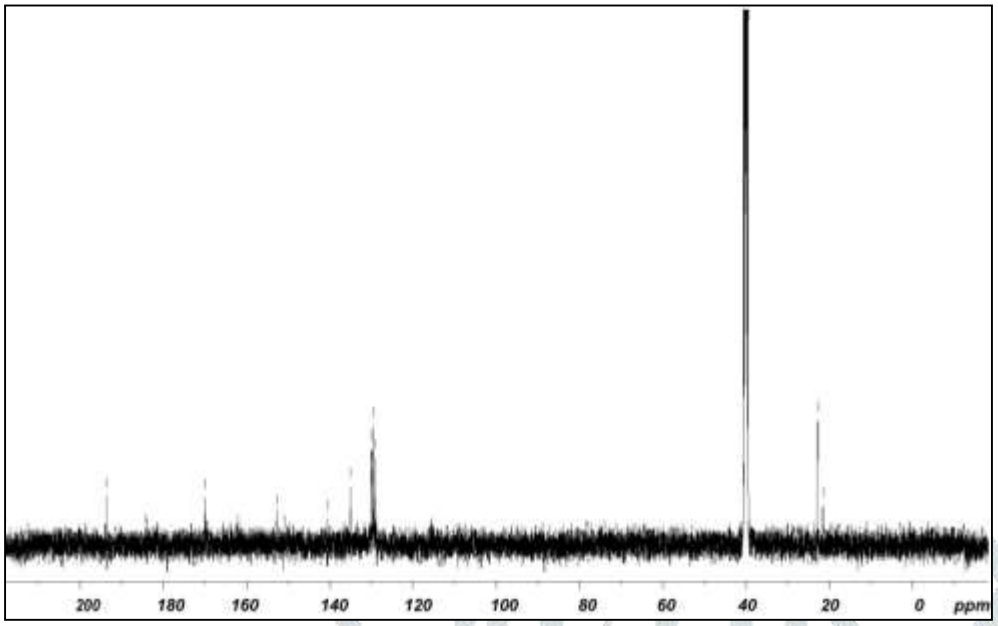


Figure 2.3 ^{13}C NMR spectrum of the compound 3b

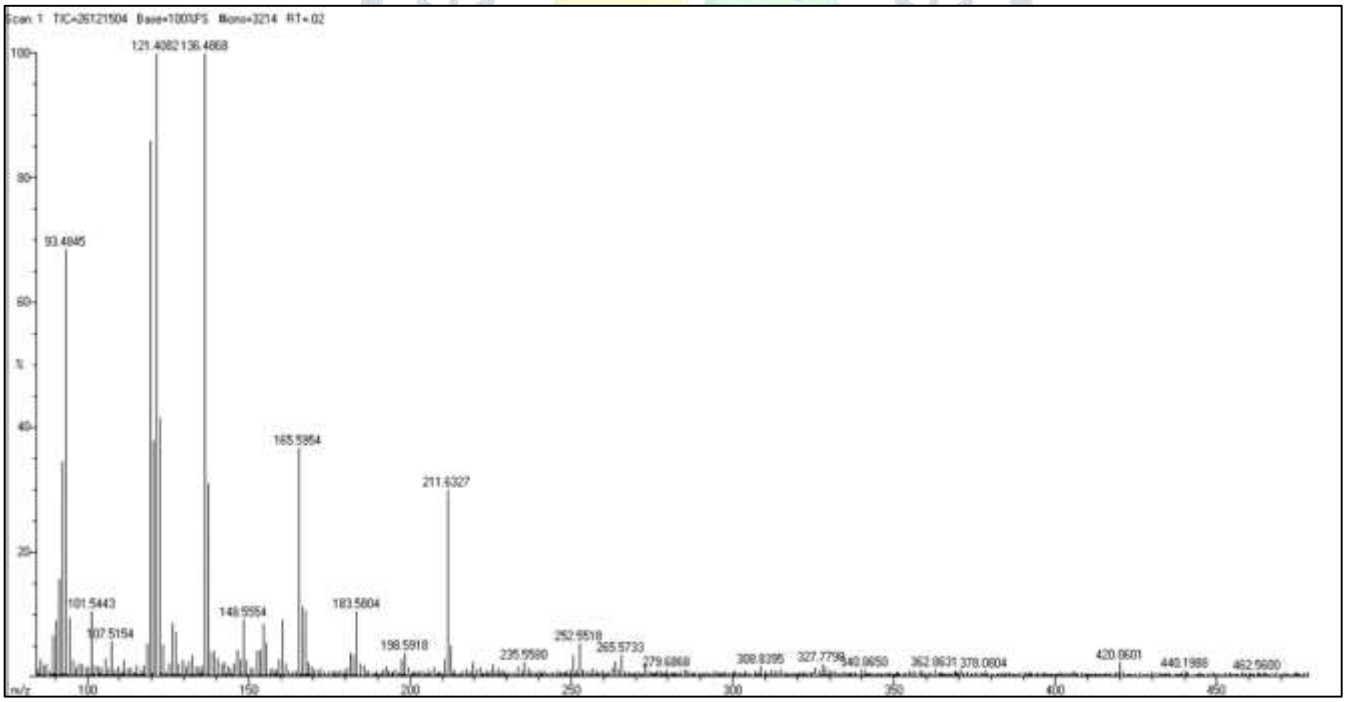


Figure 2.4, Mass spectrum of the compound 3b

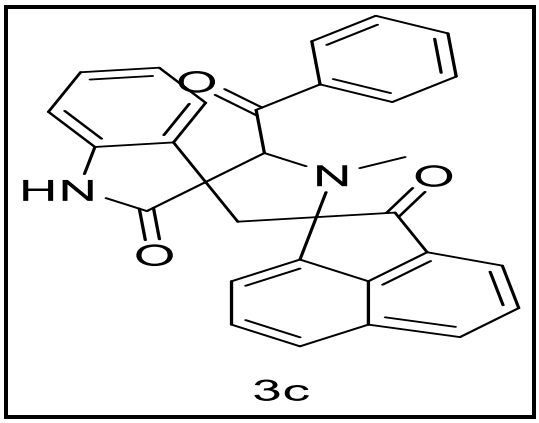


Figure 3: 5'-benzoyl-1'-methyl-1'',2''-dihydro-2H-dispiro[acenaphthylene-1,2'-pyrrolidine-4',3''-indole]-2,2''-dione (3c)

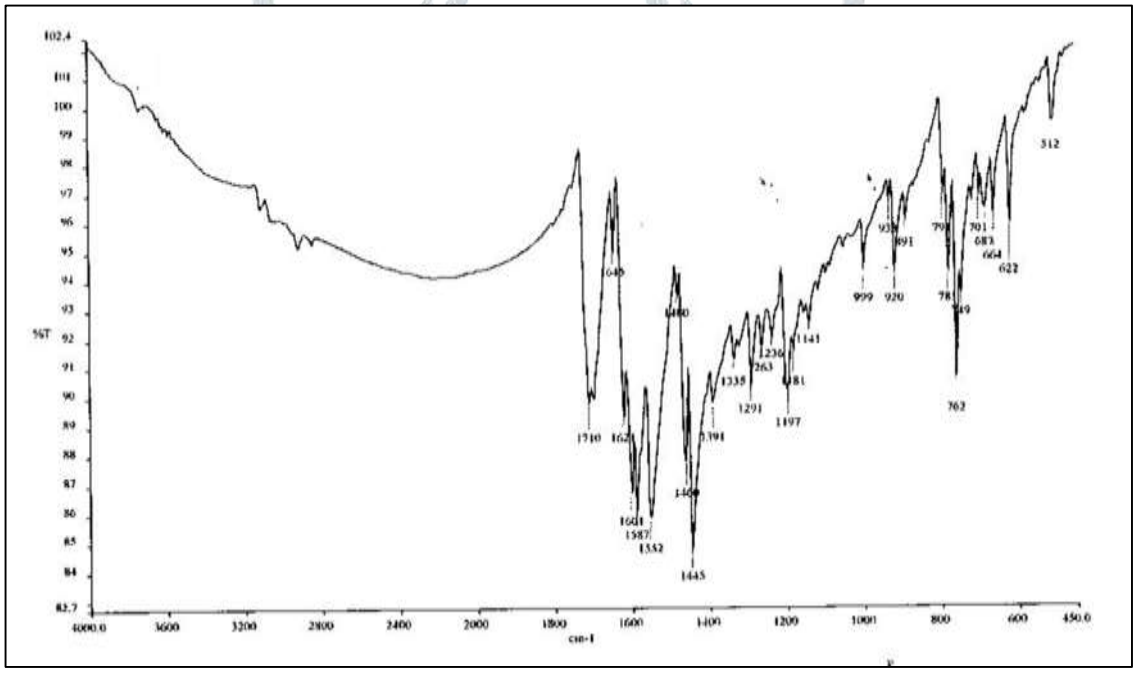


Figure 3.1.IR spectrum of compound 3c

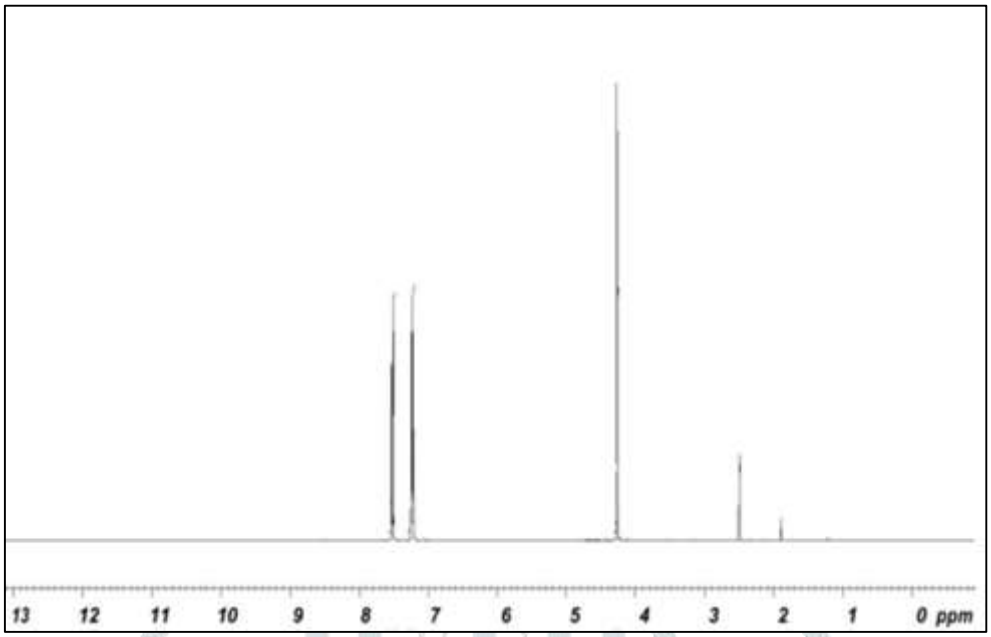


Figure 3.2 ^{1}H NMR Spectrum of the compound 3c

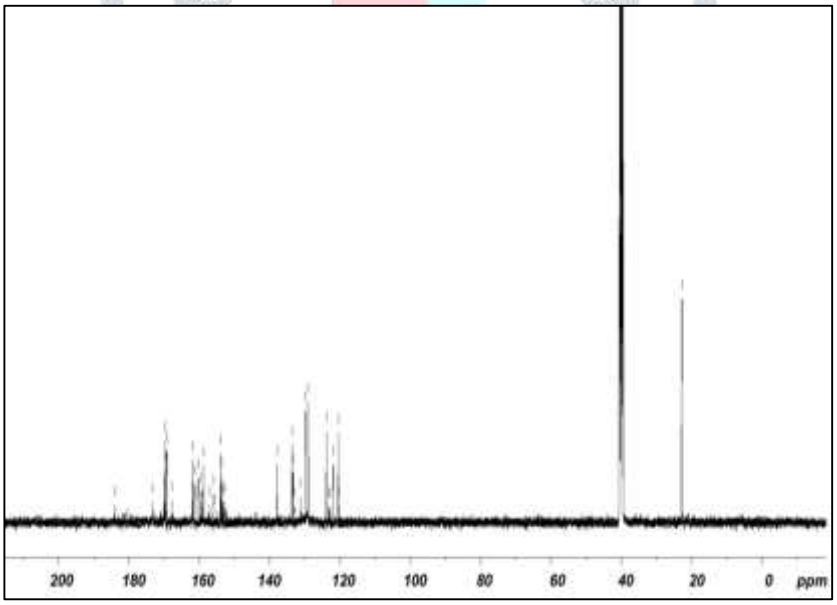


Figure 3.3. ^{13}C NMR Spectrum of the compound 3c

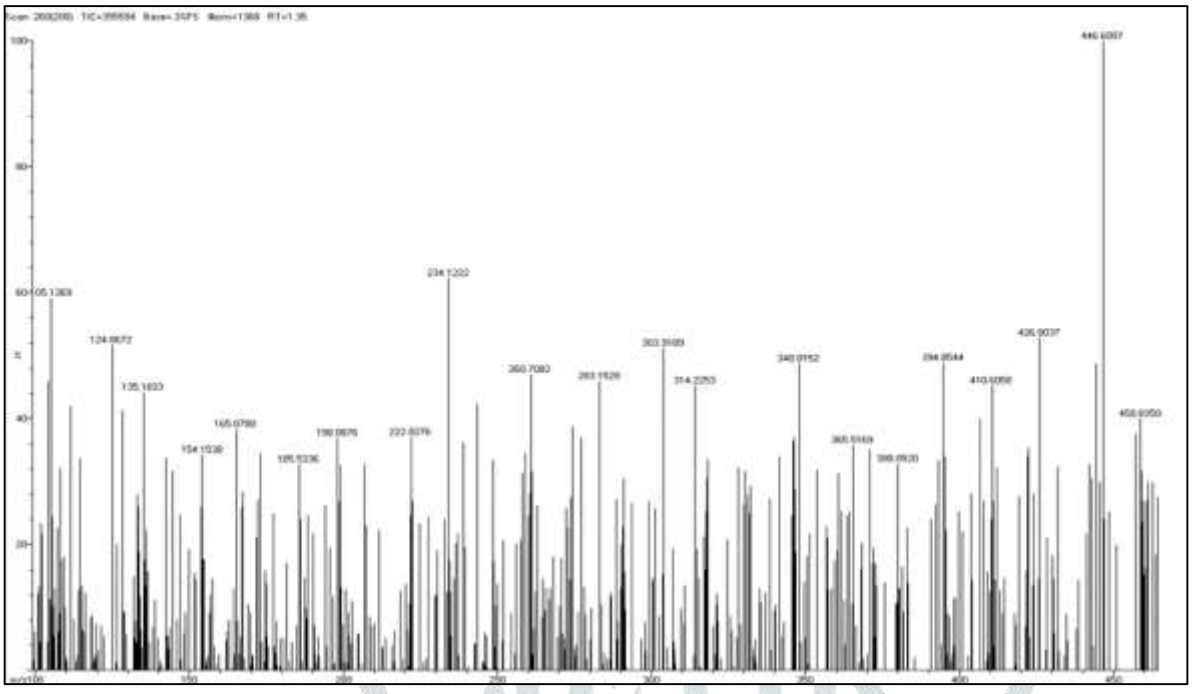
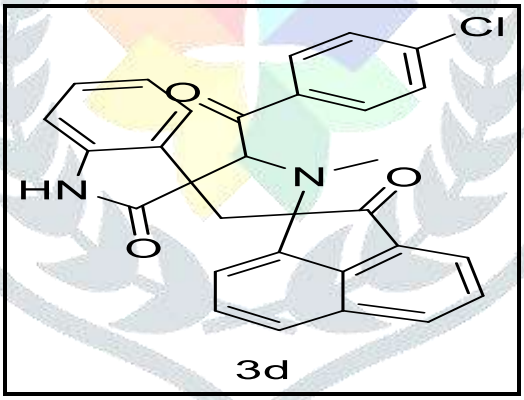


Figure 3.4. Mass spectrum of the compound 3c



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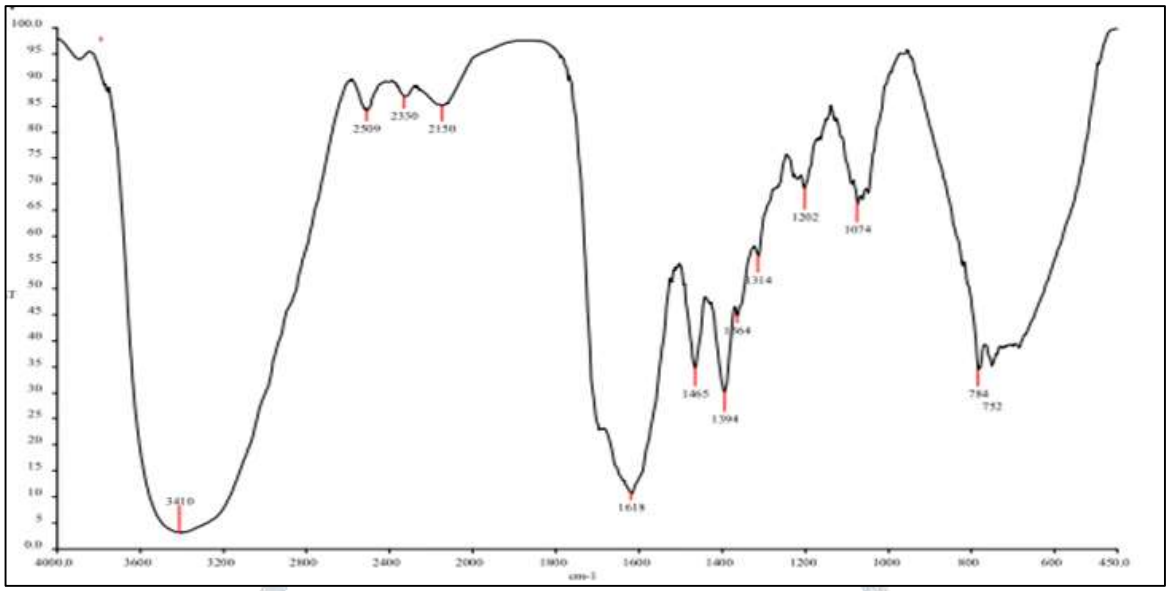

Figure4.1.IR spectrum of the compound 3d

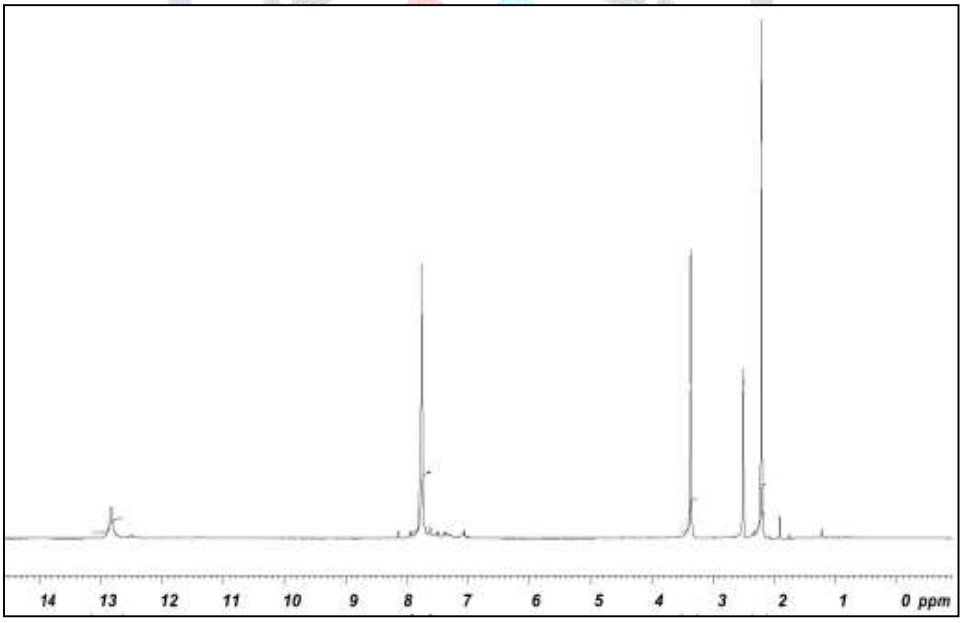

Figure4.2.^{1}H NMR spectrum of the compound 3d

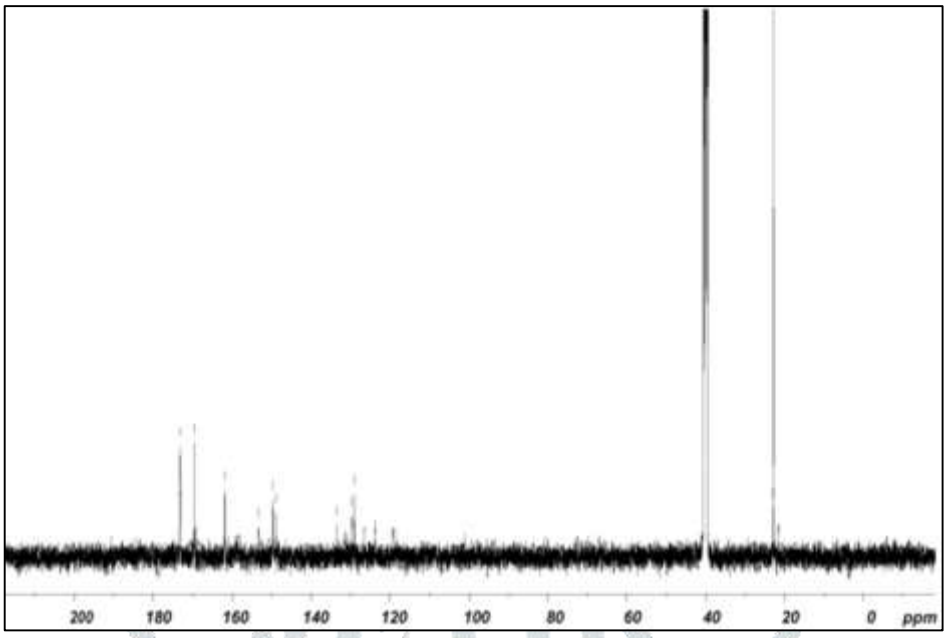

Figure4.3, ^{13}C NMR spectrum of the compound 3d

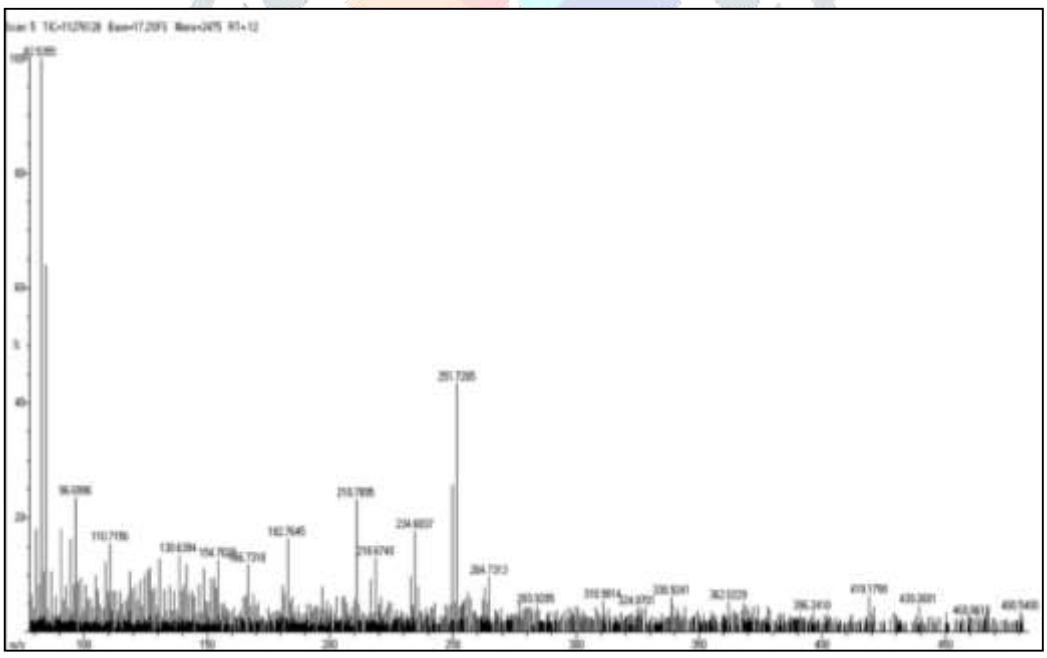

Figure4.4, Mass spectrum of the compound 3d

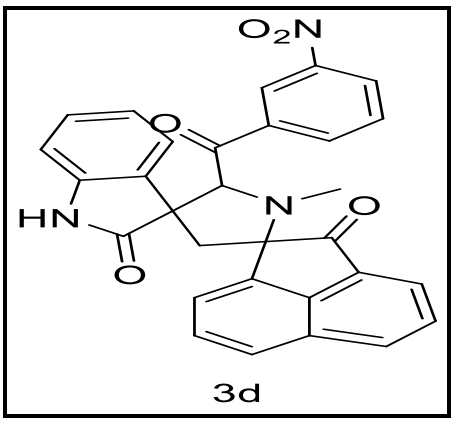

Figure5: 1'-methyl-5'-(4-nitrobenzoyl)-1'',2''-dihydro-2H-dispiro[acenaphthylene-1,2'-pyrrolidine-4',3''-indole]-2,2''-dione (3e)

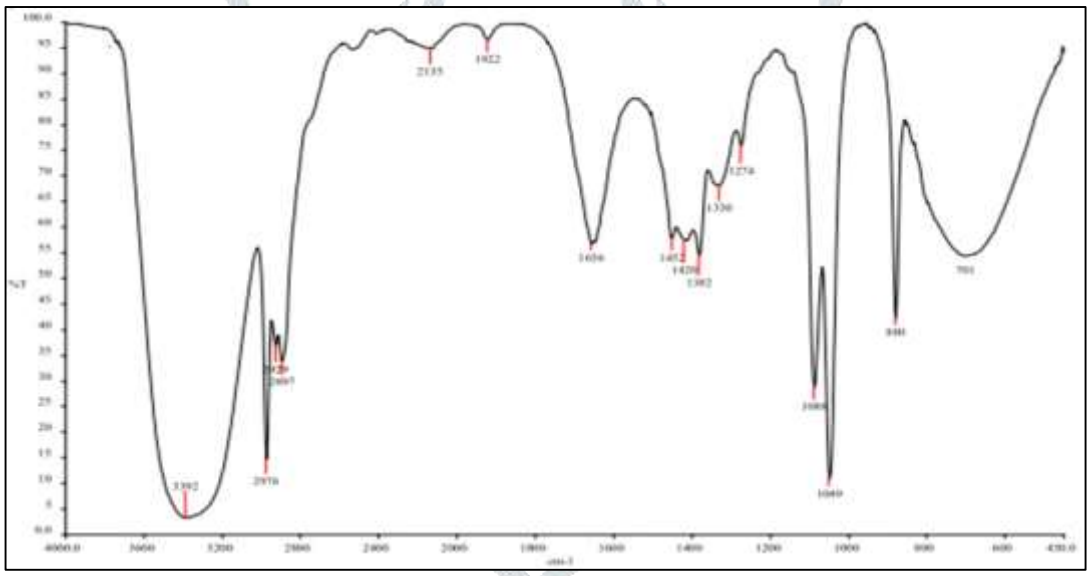

Figure5.1. IR spectrum of the compound 3e

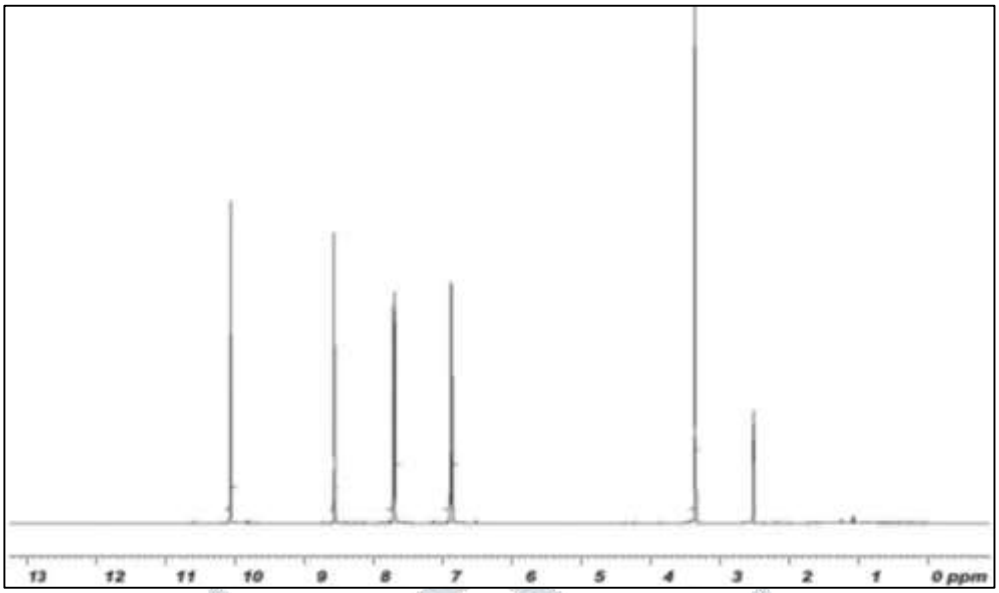

Figure5.2. ^{1}H NMR Spectrum of the compound 3e

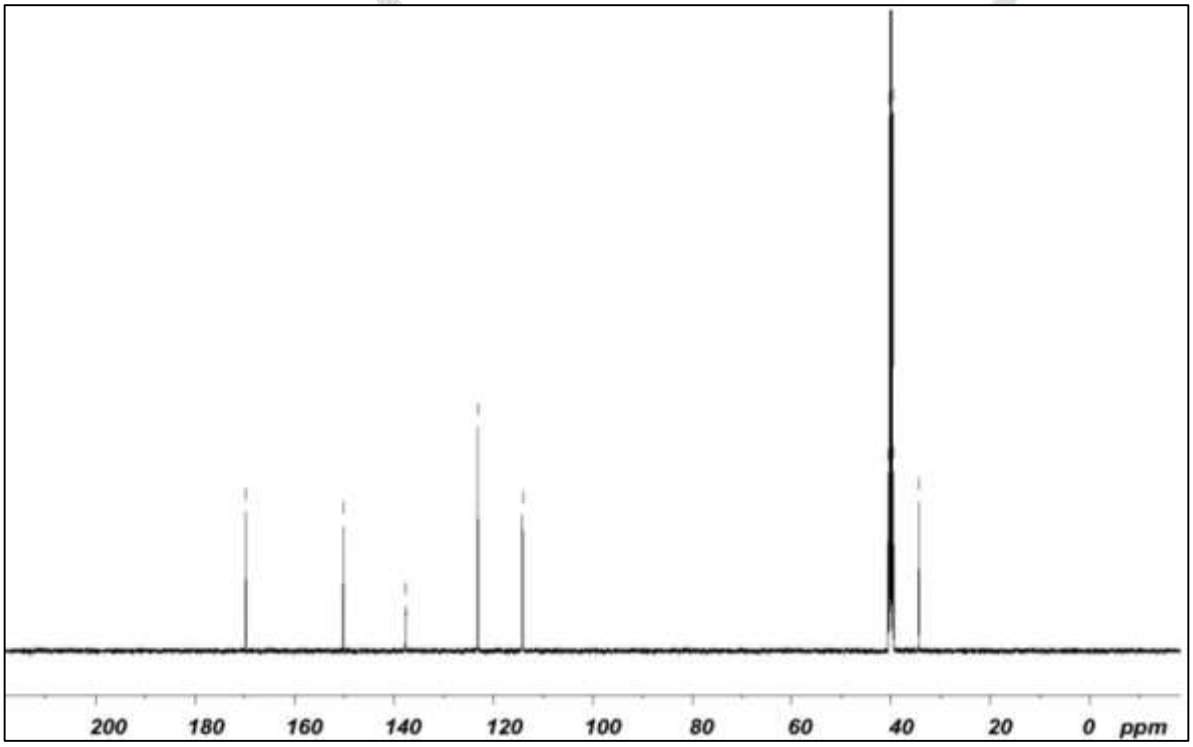

Figure5.3. ^{13}C NMR Spectrum of the compound 3e

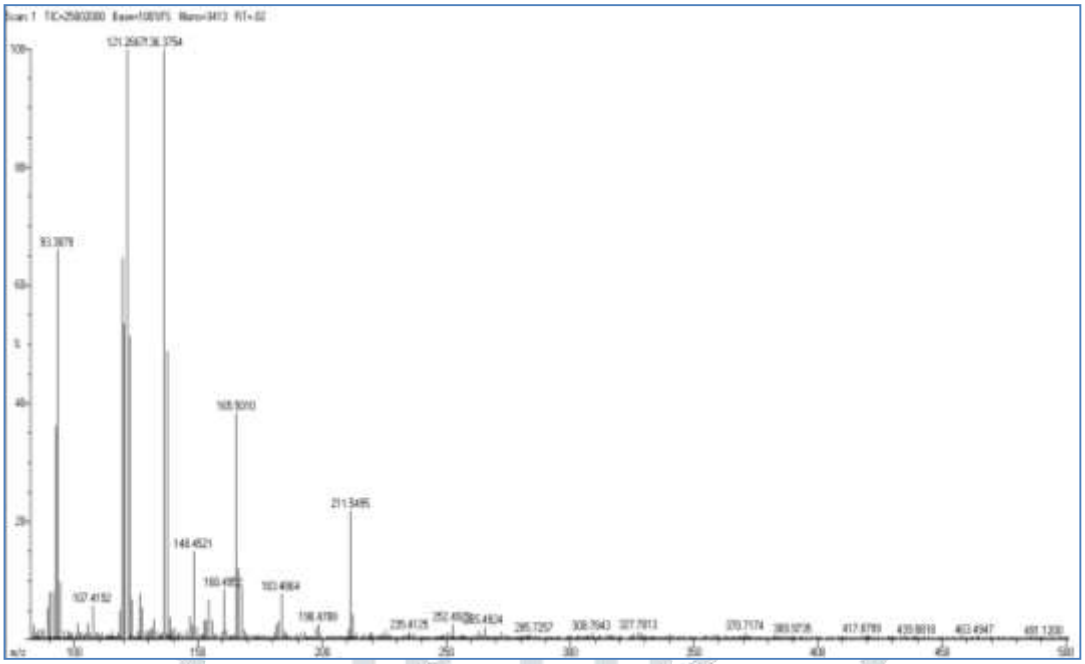

Figure 5.4 Mass spectrum of compound 3e

Organisms	Zone of Inhibition (mm) Concentration (µg/mL)					Cipro (1 mg/mL)	DMSO
	1000		750		500		
	3a	3b	3c	3d	3e		
Aeromonas spp.	10	8	7	5	5	25 mm	-
Bacillus spp.	9	8	6	5	4	14 mm	-
E. coli	10	9	8	6	5	20 mm	-
Klebsiella spp.	14	11	12	9	8	20 mm	-
Proteus spp.	12	10	10	8	9	20 mm	-
Pseudomonas aeroginosa	16	13	13	11	9	29 mm	-
Salmonella spp.	20	17	10	8	8	21 mm	-
Staphylococcus aureu	15	12	10	7	4	23 mm	-
Vibrio parahaemolytic	10	9	8	7	5	26 mm	-
Vibrio spp.	8	7	5	3	3	10 mm	-

Table.1 Antibacterial activity of the synthesized heterocyclic compounds 3a-e