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SYNTHESES, CHARACTERIZATION AND DETERMINATION OF ANTI-MICROBIAL ACTIVITIES OF SCHIFF BASE DERIVED FROM ETHYLENEDIAMMINE AND 2-HYDROXY-1-NAPHTHALDEHYDE AND ITS COMPLEXES WITH COBALT (II) AND NIKEL (II) METAL IONS.

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ABSTRACT

The Schiff base 1- {(E) - [2- {(2-hydroxynaphthalene-1-yl) methylidene] amino} ethyl} naphthalene-2-ol was derived from ethylenediamine and 2-hydroxy-1-naphthaldehyde and its complexes with nickel(II) and cobalt(II). The UV-Visible result showed molar absorptivity above 1000 $Lmol^{-1}cm^{-1}$ ($\pi\sim\pi^*$) in the complexes, the FT-IR result showed absorption about 1600 nm (N=C) in all. The ligand and the complexes were screen for anti-microbial activity and the cobalt (II) complex was found to inhibit growth in *B. subtilis*, *S. aureus*, *E. coli*, *S. sp* and *P. auruginosa* in that order, with minimum inhibition concentration in *B. subtilis at* 20 µg/ml which is comparable to standard drugs

Introduction:

A Schiff base (named after Hugo Schiff, a German Chemist) is a compound with the general structure $R_2C=NR^1$ ($R^1\neq H$). They can be considered as sub-class of imines, being either secondary ketimines or secondary aldimines depending on their structure. The term is often synonymous with azomethine which refers specially to secondary aldimines.

The term Schiff bases is normally applies to these compounds when they are

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while 500 µg/ml in the others which is too high. The nickel (II) and the Schiff base ligand only have growth inhibition against *B. subtilis, E. coli,* and *S. sp* with minimum inhibition concentration at 500 µg/ml which is too high compared to standard drug values.

being used as ligands to form coordination complexes with metal ions. Such complexes do occur naturally, for instance in corrin, but the majority of Schiff bases are synthesized for a wide range of application (IUPAC, 1997). For instance, metals neodymium(III) and thallium(III) complexes of the Schiff base derived 4-chlorobenzenesulphonyl chloride and aminobenzothiazole were screened *in vitro* for their anti-bacterial activities against *E.coli, S.aureus* and *P.aeruginosa* and were found to be more active against the microorganisms screened relative to ciprofloxacin, gentamicin and co-trimoxazole (Obasi *et al*., 2017). Metal complexes of Cu^{2+}, Co^{2+}, Ni^{2+} and Mn^{2+} with Schiff bases derived from O-phthalaldehyde and amino acids such as glycine, L-alanine, and phenyl-alanine were tested against three fungi. It was found that Cu^{2+} and Ni^{2+} complexes exhibited growth inhibition towards the entire studied fungi. However Co^{2+} and Mn^{2+} complexes exhibited less growth inhibition (Neelakantan *et al*., 2008). Glutamic acid-salicylaldehyde Schiff base metal complexes were bound into bovine serum albumin (BSA), which afforded BSA binding Schiff base metal complexes (BSA-sal, GluM, M=Cu, Co, Ni, Zn). It showed the antioxidant capacity of BSA increased more than 10 times after binding Schiff base metal complexes (Wang *et al*., 2007). Schiff base derived from 4-aminoantipyrine and benzaldehyde derivatives were tested for anti-inflammatory activity and the result was promising which could be beneficial for use in the treatment of inflammatory diseases (Alam, *et al*., 2012).

PROCEDURES

Reagents, Synthesis and Characterization of the ligand 1-{(E)-[2-{(2-hydroxynaphthalene-1-yl)methylidene]amino}ethyl}naphthalene-2-ol and its nickel (II) and cobalt (II) complexes

REAGENTS

Methanol, Ethylenediamine, 2– hydroxyl – 1 – naphthaldehyde, Distilled water,

$NiSO_4.6H_2O$,$CoCl_2.6H_2O$,

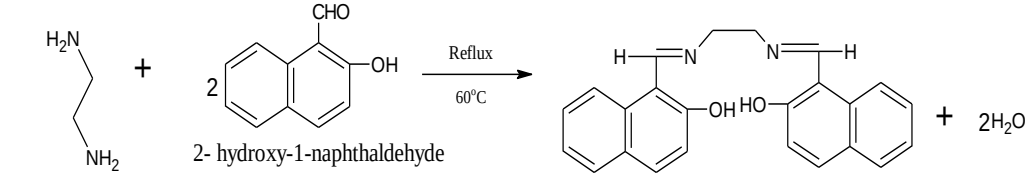
Apparatus and Equipments

Beakers, Measuring cylinders , Reflux condenser, Weighing balance, Magnetic stirrer with heater

WTW Conductimeter, model LFT 90 made in Germany, Fischer-Johns melting apparatus 220VAC, made in USA, UV-1800 series machine made in Japan, IR-infinity model made in Japan.

Synthesis of 1-{(E)-[2-{(2-hydroxynaphthalene-1-yl) methylidene] amino} ethyl} naphthalene-2-ol

The synthesis as carried out by Cleiton *et al.*, (2009). About 1ml (1.0g, 16.67 mol) of ethylenediammine was measured and dissolved in little amount of water, then 5.73g (33.31mol) of 2 – hydroxyl – 1 – naphthaldehyde was weighed and dissolved in methanol. The two solutions were mixed and refluxed while stirring with a magnetic stirrer at a temperature of 60 ^oC for about 30 min. A yellow coloured precipitate was formed which was filtered and dried in a desiccators. The dried solid product was recrystallized from DMSO by dissolving it in DMSO at high temperature and the resulting clear solution filtered while hot and allowed to cool. After cooling the yellow precipitate was reformed which was filtered then washed with a little quantity of methanol and dried in a desiccators, then weighed and labeled EDNA.



Ethylenediamine

1-{(*E*)-[(2-{[(2-hydroxynaphthalen-1-yl) methylidene]amino}ethyl)imino]methyl} naphthalen-2-ol

Equation:5 Synthesis of Schiff base derived from ethylenediamine and 2-Hydroxy-1-naphthaldehyde

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Complexations

The bidentate ligand 1-{(E)-[2-{(2-hydroxynaphthalene-1-yl) methylidene] amino} ethyl} naphthalene-2-ol was used to form chelate complexes with Ni (II) and Co (II) ions (Shetye*, et al*., 1999).

Nickel-ligand complexation

As use by Selma Bal and Sedat Salih Bal, (2014). Exactly 2.56g (20 mmol) of the $CoCl_2.6H_2O$ salt was weighed and dissolved with a minimum amount of water in a beaker and 3.68 g (10 mmol) of the ligand 1-{(E)-[2-{(2-hydroxynaphthalene-1-yl)methylidene]amino}ethyl}naphthalene-2-ol was weighed and dissolved in DMSO on heating. The two solutions were mixed and heated with continuous stirring using magnetic stirrer for 30 min. A greenish-brown precipitate was formed which was filtered and dried in a desiccators. The dried precipitate was recrystallized from DMF by dissolving it at high temperature, filtered and allowed to cool. On cooling the precipitate crystallized out of solution and was filtered and dried in a desiccators then weighed and labeled NiEDNA and stored.

Cobalt-Ligand Complexation

As used by Arumugam et al (2017). Exactly 2.56g (20 mmol) of $CoCl_2.6H2O$ salt was weighed and dissolved with a minimum amount of methanol in a beaker and 68 g (10 mmol) of the ligand 1-{(E)-[2-{(2-hydroxynaphthalene-1-yl)methylidene]amino}ethyl}naphthalene-2-ol was weighed and dissolved in DMSO on heating. The two solutions were mixed and heated with continuous stirring using magnetic stirrer for 30 min. A reddish-pink precipitate was formed which was filtered and dried in a desiccators. The dried precipitate was recrystallized from DMF by dissolving it at high temperature, filtered and allowed to cool. On cooling the precipitate crystallized out of solution and was filtered and dried in a desiccators then weighed and labeled CoEDNA and stored.

Determination of minimum inhibitory concentration (MIC) of the complexes using the broth micro dilution method.

This was conducted at the laboratory of the department of pharmacy of the University of Nigeria, Nsukka.

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1. From the stock (2500 µg/ml) of the complexes, five different concentrations (500, 100, 20, 4, 2 µg/ml) were prepared in Muellarhinton broth.
2. Fresh cultures of the test pathogens (*Bacillus subtilis, Staphylococcus aureus, Streptococcus sp., Escherichia coli* and *Pseudomonas aeruginosa*) were obtained and adjusted to a clear or less turbid suspension.
3. Exactly 100 µL of the adjusted cell suspension is introduced into the Muellarhinton broth containing different concentrations of the complexes.
4. This is followed by a 24 h-incubation at room temperature.
5. The minimum inhibitory concentration is defined as the lowest concentrations of the complexes which prevented visible growth of the test pathogen.

Spectroscopic Analyses

FT – IR (Fourier Transformed Infrared)

The FT – IR Spectroscopic analysis was carried out at Agilent Technologies in Zaria Kaduna State, Nigeria with IR-1900 series and the result reported in Chapter Four of this work.

UV-Visible Spectroscopic analysis of the samples

A UV-1800 series spectrophotometer was used to determine the absorbance and wavelength of absorptions in the range of 200 nm-700 nm of the samples dissolved in DMSO in a 1 cm cell with sample concentration of 0.0005 M and the result reported in chapter four.

Result, Discussion and Conclusion

Results

Percentage yield of:

(i) The 1-{(E)-[2-{(2-hydroxynaphthalene-1-yl) methylidene] amino} ethyl} naphthalene-2-ol ligand

$$\% \text{ yield} = \frac{\text{Actual yield}}{\text{Theoretical yield}} \times 100\%$$

Actual yield = 5.41g

Theoretical yield = 6.13g

% yield = 88.25%

(ii) Ni-1-{(E)-[2-{(2-hydroxynaphthalene-1-yl)methylidene]amino}ethyl}naphthalene-2-ol
Actual yield = 4.68
Theoretical yield = 6.79
% yield = 68.92%

(iii) Co-1-{(E)-[2-{(2-hydroxynaphthalene-1-yl)methylidene]amino}ethyl}naphthalene-2-ol
Actual yield = 4.80g
Theoretical yield = 6.19g
% yield = 78.12%

FT – IR Result

Table 1: IR Results

EDNA (cm^{-1})	NiEDNA (cm^{-1})	CoEDNA (cm^{-1})	Band Assignment
1614	1603	1618	V(C = N)
3679	3347	3753	V(O – H)
1204	1252	1252	V(C – O)
3049	–	3056	V(Ar – H)

Conductivity Result

Table 2: Conductivity of 1% solutions of the Complexes

Complex	Conductivity μscm^{-1}
NiEDNA	51.6
CoEDNA	71.6

Table 3: Elemental Analysis result for EDNA

Element	Calculated	Found
C	78.26	64.40
H	5.43	6.10
N	7.61	5.60

Inhibitory activities of the Schiff base and its complexes of nickel (II) and cobalt (II) ions.

Table 4: Inhibitory activities of complexes on selected pathogens

Complexes	Inhibitory zone diameters, IZD (in cm)				
	B. subtilis	*S. aureus*	*S. sp*	*E. coli*	*P.aeruginosa*
CoEDNA	2.5	2.0	1.6	1.8	1.0
NiEDNA	1.2	Nil	Nil	1.1	Nil
EDNA	1.2	Nil	Nil	1.2	Nil

Inhibitory activities of the Schiff base and its complexes of nickel (II) and cobalt (II) ions.

Table 5: Inhibitory activities of complexes on selected pathogens

Complexes	Inhibitory zone diameters, IZD (in cm)				
	B. subtilis	*S. aureus*	*S. sp*	*E. coli*	*P.aeruginosa*
CoEDNA	2.5	2.0	1.6	1.8	1.0
NiEDNA	1.2	Nil	Nil	1.1	Nil
EDNA	1.2	Nil	Nil	1.2	Nil

MIC (µg/ml) result

Table 6: MIC (µg/ml) of the complexes against Gram-positive and Gram-negative bacteria.

Compound	*B. subtilis*	*S. aureus*	*Str. sp*	*E. coli*	*P.aeruginosa*
CoEDNA	20	500	500	500	500
NiEDNA	500	-	-	500	-
EDNA	500	-	-	500	-

Discussion

A Schiff base 1-{(E)-[2-{(2-hydroxynaphthalene-1-yl) methylidene] amino} ethyl} naphthalene-2-ol was derived from ethylenediamine and 2-hydoxy-1-naphthaldehyde and its complexes with Ni (II) and Co (II) ions were synthesized. The ligand is yellow in colour with a melting point of 310 ^{o}C, its nickel (II) complex is greenish-brown while its cobalt (II)

complex is reddish-pink in colour. There is appearance of absorption at around 1600 cm^{-1} in the IR spectra indicating the presence of the azomethine group (N=C), the complexes are characterized by molar absorptivity above 1000 $Lmol^{-1}cm^{-1}$ which is not seen in the ligand from which they were derived indicating modification in the electronic transition that led to stronger absorption in the UV-Visible region of the electromagnetic radiation.

The anti-microbial assay carried out on some selected microorganisms showed the cobalt complex inhibits growth in *B. subtilis, S. aureus, S.sp, E. coli,* and *P. aeruginosa* while both the nickel complex and the ligand show growth inhibition only on *B. subtilis,* and *E. coli.* The ligand and its nickel and cobalt (II) complexes are only soluble in dimethylsolphoxide (DMSO) and dimethylformamide (DMF) at high temperature which led to unsuccessful attempt at ^{1}H and ^{13}C NMR.

Conclusion

The spectroscopic data obtained shows the successful synthesis of the Schiff base 1-{(E)-[2-{(2-hydroxynaphthalene-1-yl) methylidene] amino} ethyl} naphthalene-2-ol. The differences in the molar absorptivity and the anti-microbial activities between the complexes and the ligand from which they were derive proved the successful modification of the Schiff base through formation of complexes.

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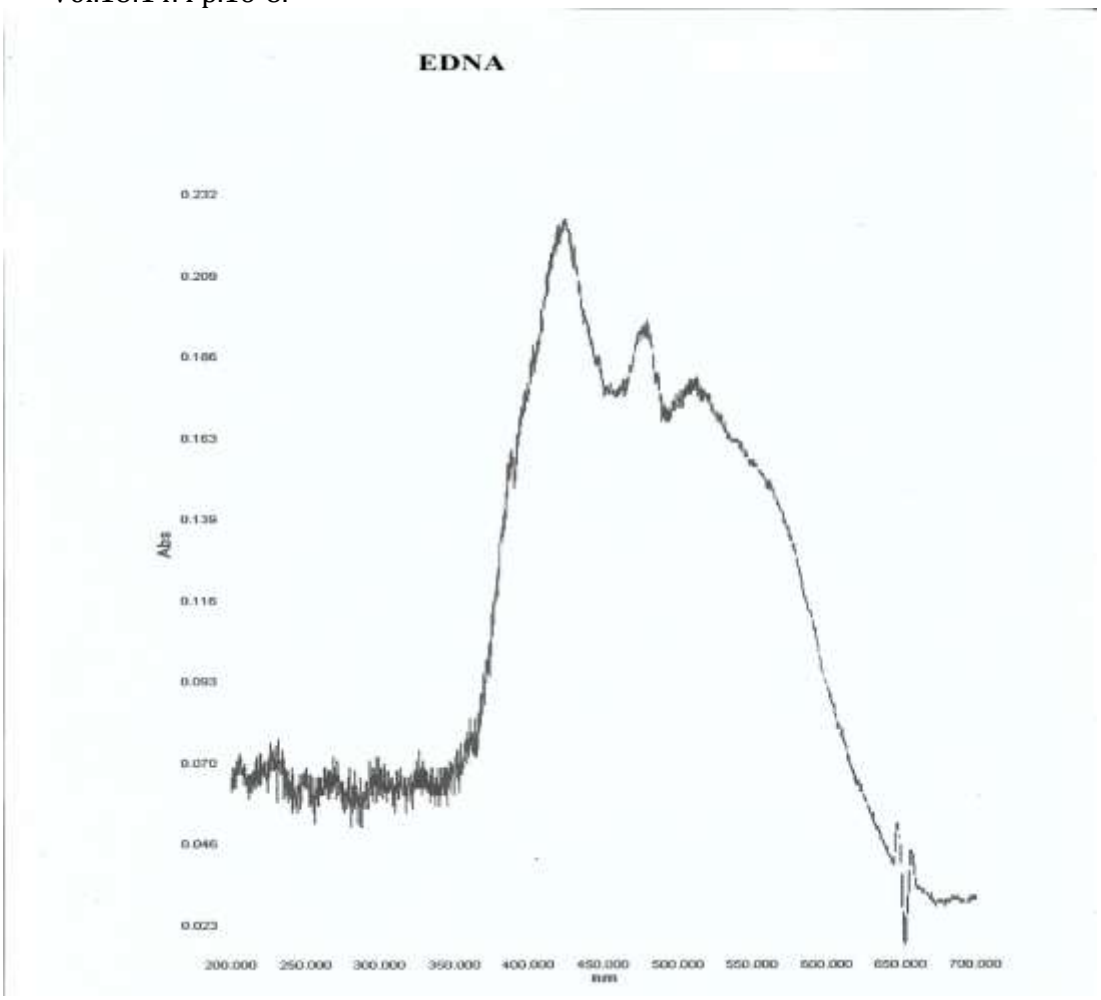

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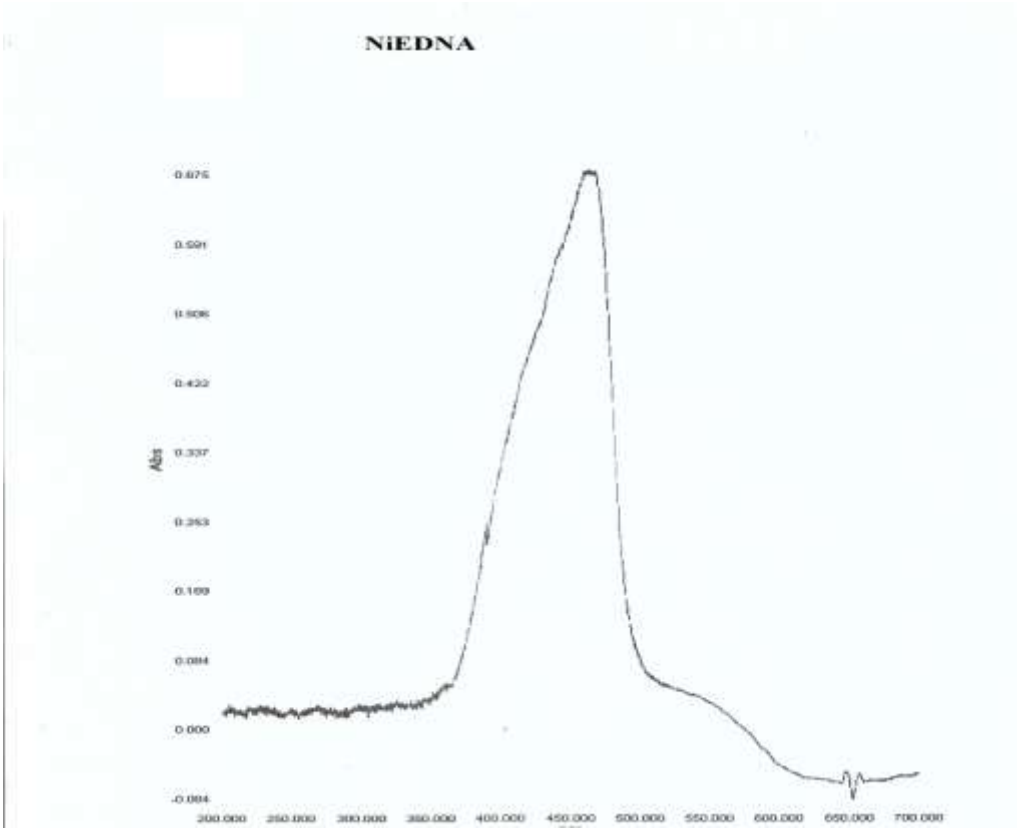

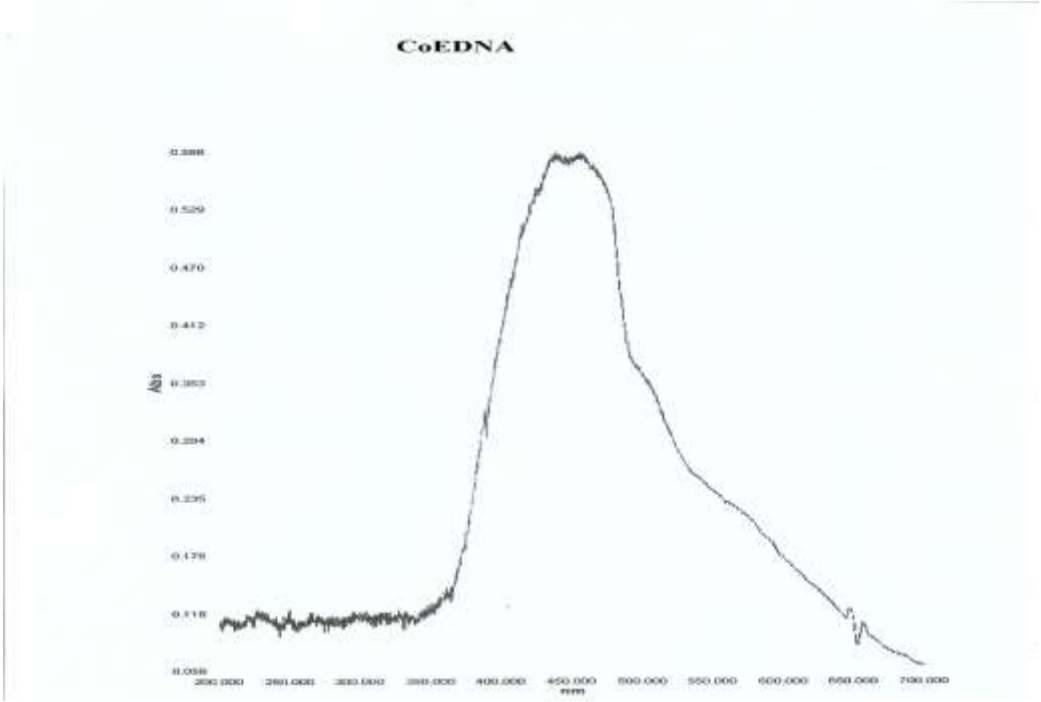

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Agilent Technologies

Sample ID:EDNA
Sample Scans:30
Background Scans:16
Resolution:8
System Status:Good
Method Name:Transmittance Method
User:Admin
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Apodization:Happ-Genzel
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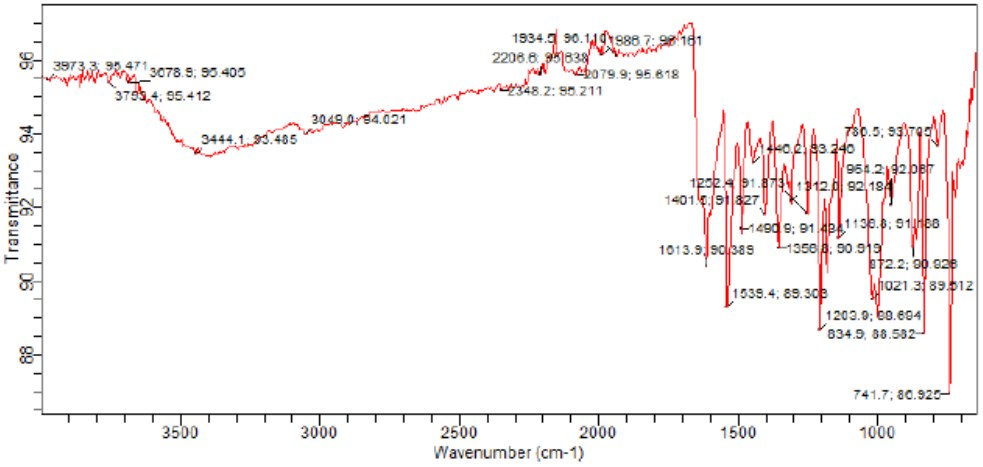

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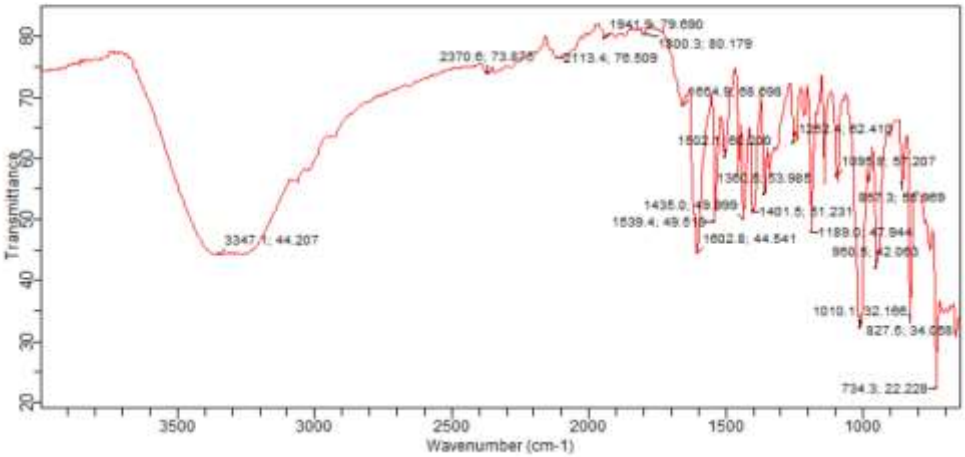

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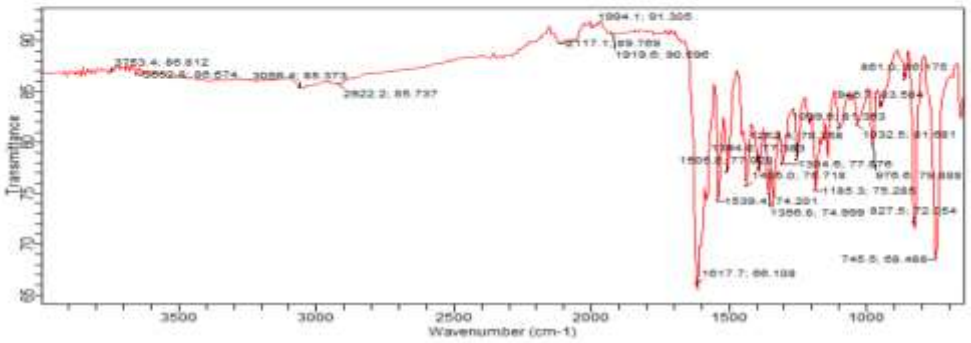


EDNA: for this sample we couldn't have 1H and 13C Spectra, for reasons of solubility. Even with hot DMSO, it dissolve and instantly return to build a precipitate.

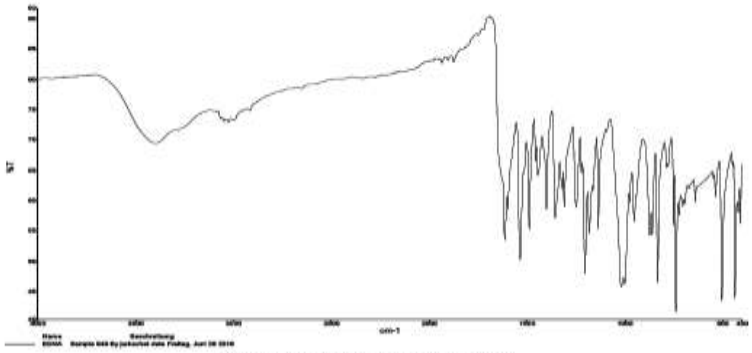
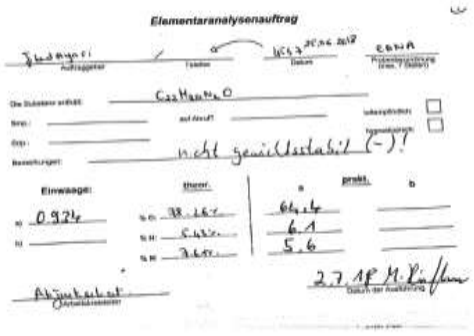


Figure 13. IR Spectra of compound **EDNA**.

- Elemental analysis relating to compound **EDNA**

Anal. Calcd (%) for $C_{22}H_{26}ON_2$: C 78.26, H 5.43, N 7.61. Found: C 64.4, H 6.1, N 5.6.

The sample does not have a stable weigh.



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