Design, Synthesis and characterization of Tricarboxyamides

M.Sc. Thesis

By
RITU

DISCIPLINE OF CHEMISTRY
INDIAN INSTITUTE OF TECHNOLOGY INDORE
JUNE, 2016

Design, Synthesis and Characterization of Tricarboxamides

A THESIS

Submitted in partial fulfillment of the requirements for the award of the degree
of
Master of Science

by
RITU

DISCIPLINE OF CHEMISTRY
INDIAN INSTITUTE OF TECHNOLOGY INDORE
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INDIAN INSTITUTE OF TECHNOLOGY INDORE

CANDIDATE'S DECLARATION

I hereby certify that the work which is being presented in the thesis entitled **Synthesis and physical characterization of Derivatives of Tricarboxamide** in the partial fulfillment of the requirements for the award of the degree of **MASTER OF SCIENCE** and submitted in the **DISCIPLINE OF CHEMISTRY, Indian Institute of Technology Indore**, is an authentic record of my own work carried out during the time period from JULY 2015 to JUNE 2016 under the supervision of Dr. Apurba K. Das, Associate Professor, discipline of Chemistry, Indian Institute of Technology Indore. The matter presented in this thesis has not been submitted by me for the award of any other degree of this or any other institute.

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This is to certify that the above statement made by the candidate is correct to the best of my knowledge.

Dr. Apurba K. Das

RITU has successfully given his M.Sc. Oral Examination held on

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Date: Date:

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Abstract

Benzene1,3,5-tricarboxamides (BTAs) have become interesting structural entities in a wide range of scientific disciplines which are showed various applications in the area of nanotechnology, polymer processing and biomedical research. We report in this project, the synthesis of BTA based two peptides named as compound **1** (2-{3,5-Bis-[carboxy-2-(4-hydroxyl-phenyl)ethylcarbamoyl] benzoylamino}-3-(4-hydroxyl-phenyl)-propionic acid) and compound **2** (2-{3,5-Bis[1-carboxyl-2-(1H-indol-3-yl)-ethylcarbamoyl]-benzoylamino}-3-(1H-indol-3-yl) propionic acid). Various spectroscopic techniques were used to characterize the reported compounds **1** and **2** such as ^{1}H NMR, ^{13}C NMR, FT-IR, TGA, UV-Vis, Fluorescence, Elemental analysis and Mass spectrometry.

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NOMENCLATURE

θ	Angle
λ	Wavelength
Å	Angstrom
nm	nm
δ	delta
cm	centimeter
°C	Celsius
%	percentage
gm	grams
mmol	millimoles
ml	milliliter

ACRONYMS

Abbreviations used for compounds, substituents, reagents, etc. are largely in accordance with the recommendations of the IUPAC. Additional abbreviations used in this thesis are listed below.

Acronyms	Full name
DMSO-d_6	Dimethyl Sulfoxide-d_6
d	Doublet
DMF	Dimethyl Formamide
ESI-MS	Electrospray Ionization Mass Spectrometry
MeOH	Methanol
NaOH	Sodium Hydroxide
NMR	Nuclear Magnetic Resonance
s	singlet
t	triplet
UV-Vis	UV-Visible Spectroscopy
HOBt	Hydroxybenzotriazole
DIPC	N,N'-Diisopropylcarbodiimide
TLC	Thin layer chromatography
HCl	Hydrochloric acid
$SOCl_2$	Thionyl chloride

Chapter 1: Introduction and Reaction Scheme:

Introduction:

The development of porous materials derived from discrete organic molecules is the key step toward the fabrication of new materials and devices.[1-4] H-bonding, metal–ion complexation, electrostatic interactions, hydrophobic interactions and combinations thereof are planned into the molecular structure of the building blocks.[5-8] Then, under mostly thermodynamically controlled conditions, spontaneous development of the porous materials is achieved if suitable conditions are applied. The benzene-1,3,5-tricarboxamide (BTA) motif comprising either three N-centred or three C=O centred amides attached to a benzene core (Figure 1). Such BTAs attracted substantial attention in the last few years in supramolecular chemistry. Three amide bonds are capable of hydrogen-bond formation, and under selected conditions the one-dimensional growth of the monomers into supramolecular polymers is achieved (Figure 2).

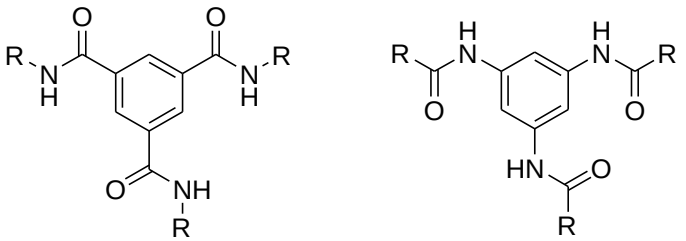


Figure 1: Structures of C=O and N-centred benzene-1,3,5-tricarboxamide (BTA) molecules.

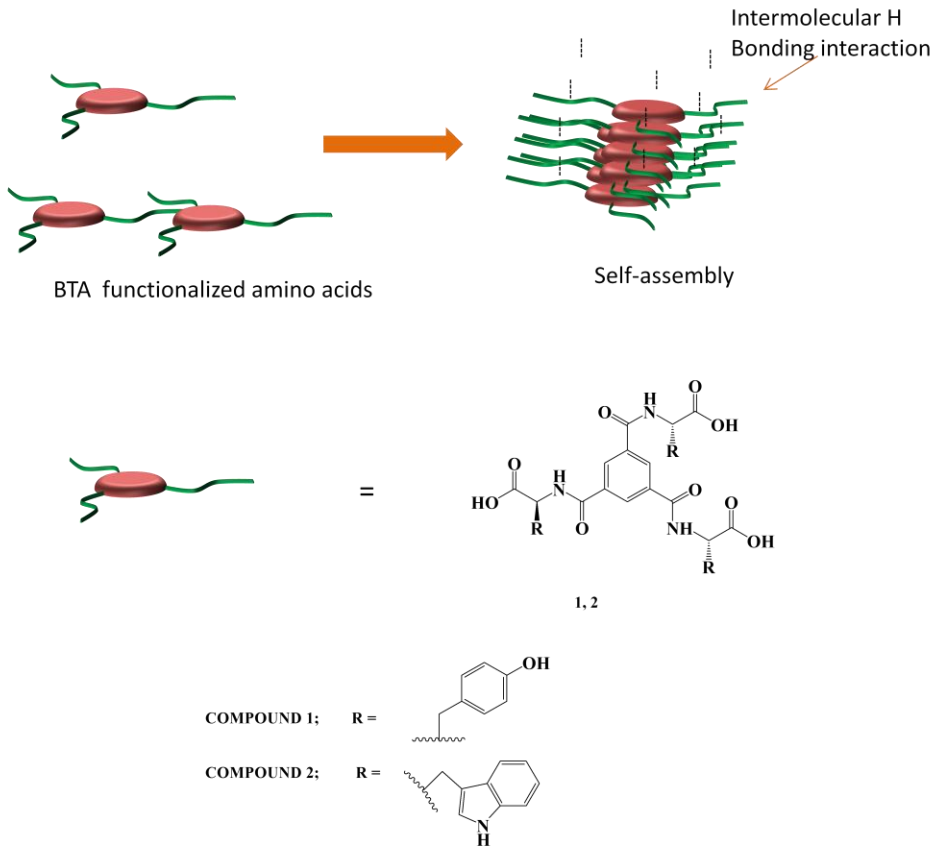
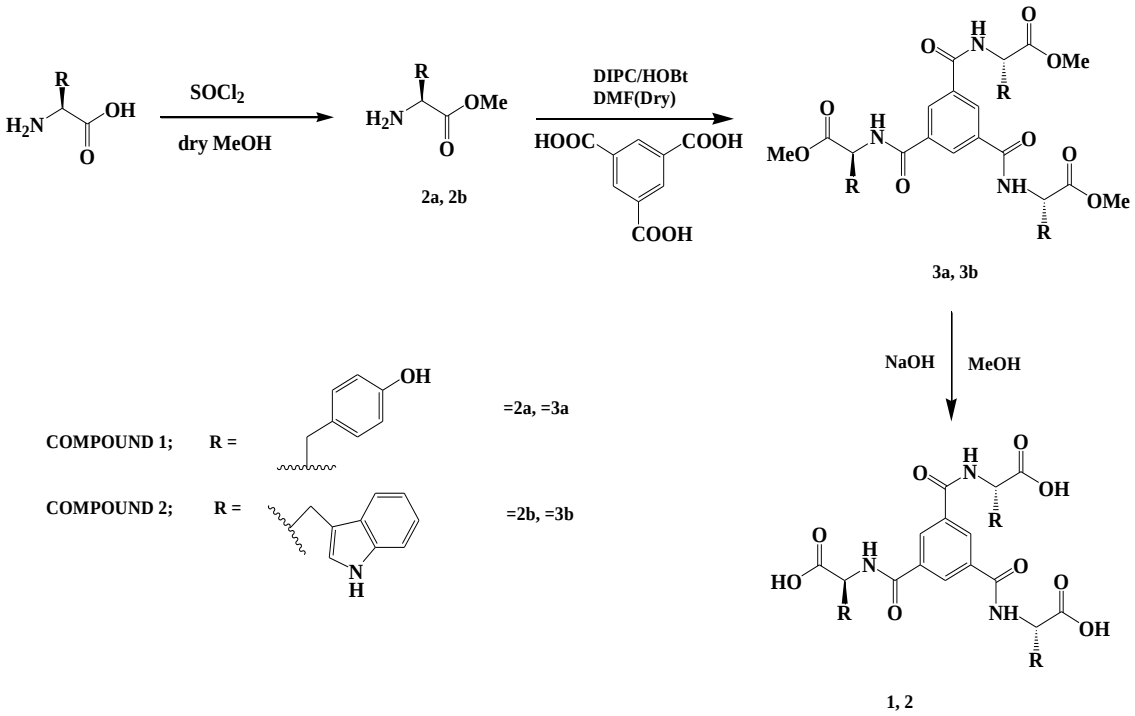


Figure 2: Pictorial representation of benzene-1,3,5-tricarboxamide self-assembly.

The R groups in BTAs can be aliphatic or aromatic, polar or apolar, charged or neutral, chiral non-racemic, racemic or achiral. When three R groups connected to the amides are identical, the formed BTA molecules are C_3 symmetric. During the last few years, a broad range of N- and C=O-centred BTA molecules have been synthesized and studied in detail.[9] BTA structures coupled with R-groups such as alky, aryl, pyridyl, bipyridyl, porphyrinyl, triphenylyl, amino acid, dipeptide, oligopeptide, oligo(ethyleneoxy), and benzocrown ethers have been obtained.[10-20] These BTA derivatives have a large variety of applications such as hydrogels, organogels, liquid crystals, nanostructured materials, MRI contrast reagents, nucleating agents for polymers, metal complexation reagents, and microcapsules for drug delivery.[21-25] The adsorption of

important gases, like carbon dioxide, methane and hydrogen, in porous materials is a demanding research field for energetic and environmental reasons for the future benefits.[26-31] A large variety of strategies exploiting materials of widely differing nature and structure have been used. Among the most conventional examples we can specify zeolites and clays, as well as carbonaceous derivatives.[32-40] Metal- organic frameworks (MOFs), mesoporous metal oxides, porous organosilicas, organic polymers and crystals [43-46] have emerged as suitable alternatives for better storage capacity and selectivity. Each class presents important prototypes with appropriate advantages towards specific achievements. On the other hand, new strategies are required for future breakthroughs. In porous materials, a variety of unrealized structures is constructed with the help of biological building blocks. In principle, they suggest the possibility of exploiting targeted interactions and are readily available, biocompatible and biodegradable.[47-49] Biological systems containing permanent pores in the form of nanochannels can offer a multiplicity of particular functions but their development as materials is still rare.[50-52] Recently, covalent organic frameworks (COFs) have been synthesized and structurally characterized. The retention of geometry, reversibility of dynamic covalent reactions and multiplicity of building blocks is the key factor of reticular design and synthesis of COFs. Here the organic building units are held together by strong covalent bonds (C-C, C-O, B-O, and Si-C) rather than metal ions to produce materials with high porosity and low crystal density. The ability of crystals is done by several techniques in which a balance is struck between the thermodynamic reversibility of the involving reactions and their kinetics. These characteristics make COFs excellent candidates for gas storage, adsorption, optoelectricity, photonic, and catalytic applications.[53-58]

Reaction Scheme:



Chapter 2: Results and discussion:

2.1. Synthesis of compounds:

In this project, our desire compounds, 2–{3,5-Bis-[1–carboxy-2-(4–hydroxyl–phenyl)–ethylcarbamoyl]–benzoylamino}–3–(4–hydroxyl–phenyl)–propionic acid **(1)** and 2–{3,5-Bis[1-carboxyl-2-(1H-indol-3-yl)-ethylcarbamoyl]–benzoylamino}-3-(1H-indol-3-yl)-propionic acid **(2)** were synthesized according to described reaction scheme. Starting from commercially available L-Tyrosine and L-Tryptophan, which were treated with thionyl chloride ($SOCl_2$) in dry MeOH medium followed by esterification to synthesize 2-amino-3-(4-hydroxy-phenyl)-propionic acid methyl ester (**2a**) and 2-amino-3-(1H-indol-3-yl)-propionic acid methyl ester **(2b)** according to reported method. Then, coupling of 2-amino-3-(4-hydroxy-phenyl)-propionic acid methyl ester (**2a**) and 2-amino-3-(1H-indol-3-yl)-propionic acid methyl ester **(2b)** with benzene-1,3,5-tricarboxylic acid in presence of coupling reagents N,N'-diisopropylcarbodiimide (DIPC), hydroxybenzotriazole (HOBt) in dry N,N-dimethyl formamide (DMF) medium 2-{3,5-bis-[2-(4-hydroxy-phenyl)-1-methoxycarbonyl-ethylcarbamoyl]-benzoylamino}-3-(4-hydroxy-phenyl)-propionic acid methyl ester **(3a)** and 2-{3,5-bis-[2-(1H-indol-3-yl)-1-methoxycarbonyl-ethylcarbamoyl]-benzoylamino}-3-(1H-indol-3-yl)-propionic acid methyl ester **(3b)** were synthesized.[37] Compounds **(1)** and **(2)** were synthesized by base catalyzed hydrolysis of compounds **(3a)** and **(3b)**.[38]

2.2. UV-Vis spectroscopy:

UV-Vis absorption spectra of compounds **3a** and **1** were recorded using a Varian Cary100 Bio UV-Vis spectrophotometer. The characteristic absorption peaks for aromatic moiety observed at 249 nm for both **3a** and

1 in solution (Figure 3). These intense absorption peaks correspond to the π - π* transition of the aromatic moiety of tyrosine amino acid.

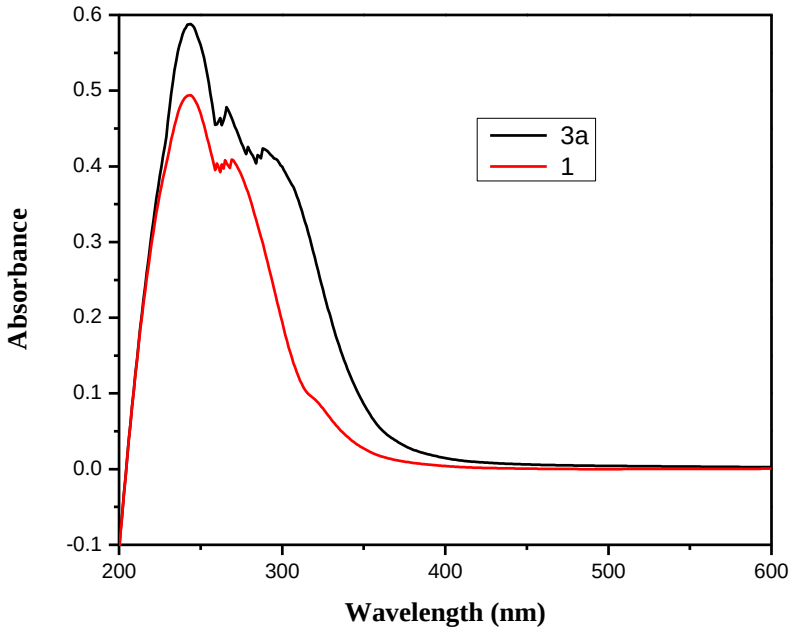


Figure 3: UV-Vis spectra of compounds **3a** and **1**.

Similarly, UV-Vis absorption spectra of compounds **3b** and **2** were also recorded using a Varian Cary100 Bio UV-Vis spectrophotometer. The characteristic absorption peaks for aromatic moiety observed at 276 nm for **3b** and 260 nm for **2** in solution (figure 4). These intense absorption peaks correspond to the π - π* transition of the aromatic moiety of tryptophan amino acid.

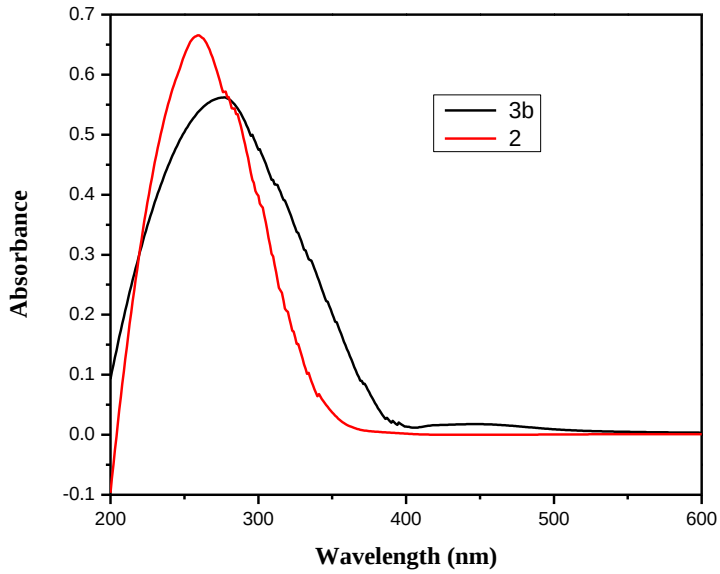


Figure 4: UV-Vis spectra of compounds **3b** and **2**.

2.3. Fluorescence spectroscopy:

Fluorescence emission spectra of compounds (2 mmol L^{-1}) were recorded on a Horiba Scientific Fluoromax-4 spectrophotometer with a 1 cm path length quartz cell at room temperature. The slit width for the excitation and emission was set at 5 nm and 1 nm data pitch. Excitation of compounds **3a** and **1** were performed at 280 nm and the data range was in between 290 to 330 nm. The characteristic emission peaks for compounds **3a** and **1** appears at 306 nm in the solution (Figure 5). The fluorescence emission spectra reveal that the emission maxima at 306 nm is due to the tyrosine moiety in compounds **3a** and **1**.

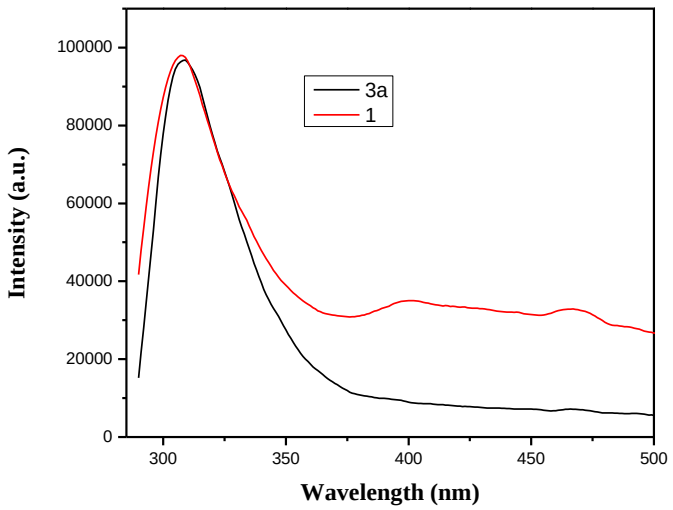


Figure 5: Fluorescence emission spectra of compounds **3a** and **1** (λex= 280 nm).

Similarly, Excitation of compounds **3b** and **2** were performed at 280 nm and the data range was in between 300 to 350 nm. The characteristic emission peaks for compounds **3b** and 2 appears at 315 nm in the solution (Figure 6). The fluorescence emission spectra reveal that the emission maxima at 315 nm is due to the tryptophan moiety in compounds **3b** and **2**.

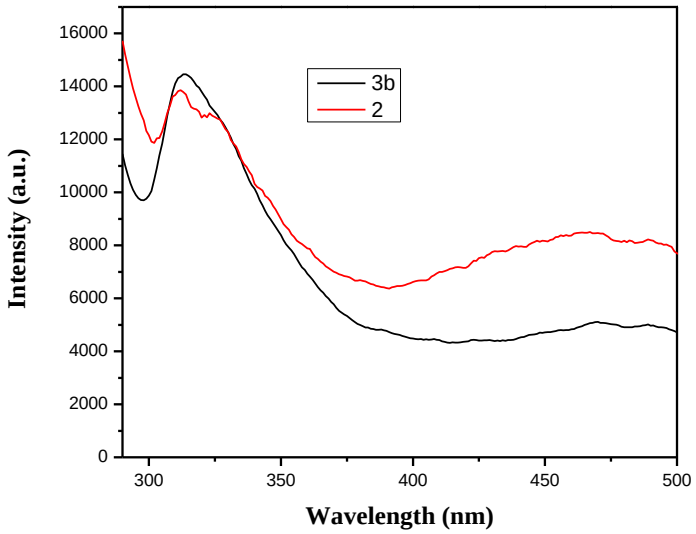


Figure 6: Fluorescence emission spectra of compounds **3b** and **2** (λex= 280 nm).

2.4. Thermogravimetric Analysis:

To examine the thermal stability, compounds **3a** and **1** were heated at 10 °C min^{-1} under the nitrogen atmosphere (Figure 7). The decomposition temperatures at 15% weight loss of compounds **3a** and **1** were calculated as 155 and 150 °C respectively. So the thermal stability of compound **3a** is higher upto 15% weight loss of the compound. Again the decomposition temperature at 65% weight loss of compounds **3a** and **1** was 295 and 321 °C respectively. So, the thermal stability of compound **1** is higher as the decomposition temperature is higher for compound **1**.

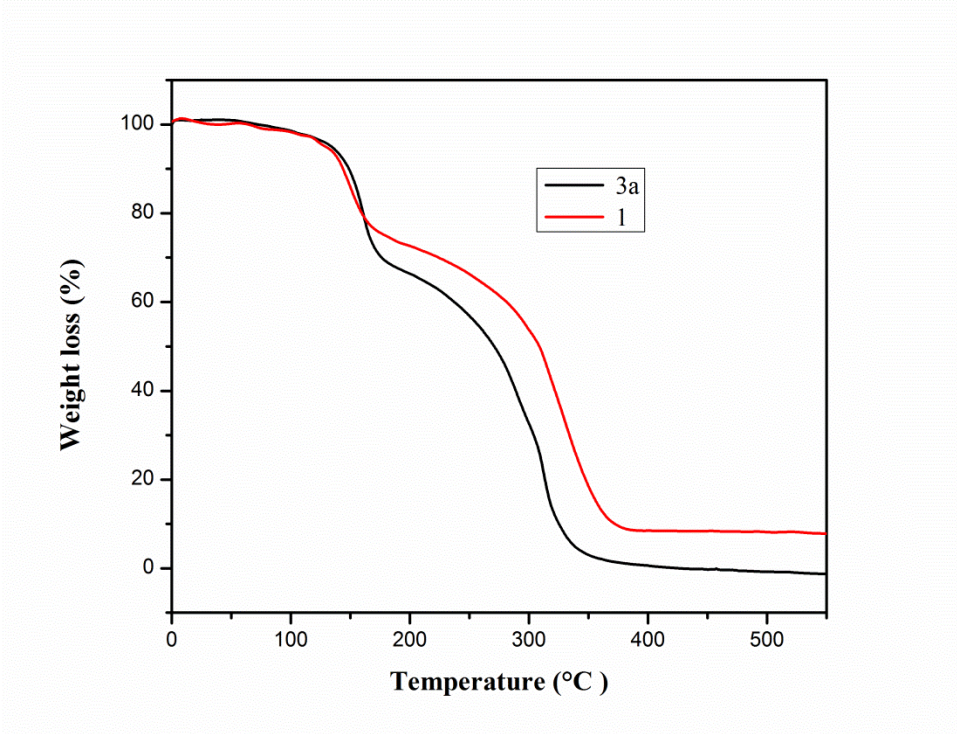


Figure 7: TGA thermograms of compounds **3a** and **1**at a heating rate of 10 °C/min under nitrogen gas.

Similarly, To examine the thermal stability, compounds **3b** and **2** were heated at 10 °C min^{-1} under the nitrogen atmosphere (Figure 8). The decomposition temperatures at 15% weight loss of compounds **3b** and **2** were calculated as 172 and 144 °C respectively. So the thermal stability of compound **3b** is higher upto 15% weight loss of the compound. Again the

decomposition temperature at 65% weight loss of compounds **3b** and **2** was 312 and 331 °C respectively. So, the thermal stability of compound **2** is higher as the decomposition temperature is higher for compound **2**.

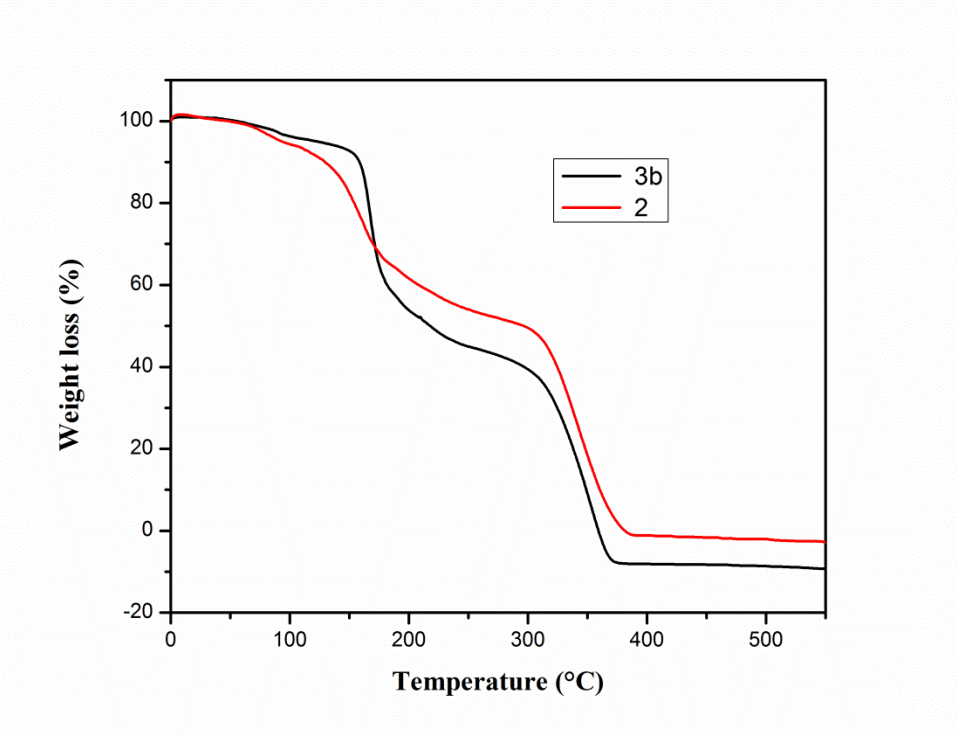


Figure 8: TGA thermograms of compounds **3b** and **2** at a heating rate of 10 °C/min under nitrogen gas.

Table 2.4.A. Thermogravimetric analysis of compounds at a heating rate of 10 ^{o}C/ minute under nitrogen atmosphere:

Sr. No	Compound	Weight loss (%)	Decomposition Temperature (° C)
1	3a	15	155
2	1	15	150
3	3b	15	172
4	2	15	144
5	3a	65	295
6	1	65	321
7	3b	65	312
8	2	65	331

2.5. FT-IR Study:

FT-IR spectroscopy of all reported compounds was performed using a Bruker (Tensor-27) FT-IR spectrophotometer. The KBr pellet technique was used and scanned between 700 cm^{-1} to 3600 cm^{-1} over 16 scans at a resolution of 4 cm^{-1} and at an interval of 1 cm^{-1}.[41-42] The FT-IR study of the solid compounds was performed to investigate the structural arrangement of the compounds. N-H band were observed at 3246 and 3305 cm^{-1} for compounds **3a** and **1** respectively, which indicates the hydrogen bonding interaction in both cases. In solid compound **3a**, a peak appeared at 1612 cm^{-1} corresponding to the C=O stretching vibration of amide, along with an absorption band at 1535 cm^{-1} corresponding to the N–H bending. In solid compound **1**, a peak appeared at 1644 cm^{-1} corresponding to the C=O stretching vibration of amide, along with an absorption band at 1528 cm^{-1} corresponding to the N–H bending, which indicates hydrogen bonding interaction in compounds **3a and 1**.

In solid compound **3a**, a peak appeared at 1760 cm^{-1} which supports the formation of a methyl ester (Figure 21). However, in compound **1,** the peak is shifted to 1725 cm^{-1} that clearly indicates that ester is converted into carboxylic acid in compound **1** (Figure 22).

Similarly, N-H band were observed at 3395 and 3397 cm^{-1} for compounds **3b** and **2** respectively. In solid compound **3b**, a peak appeared at 1645 cm^{-1} corresponding to the C=O stretching vibration of amide, along with an absorption band at 1534 cm^{-1} corresponding to the N–H bending. In solid compound **2**, a peak appeared at 1645 cm^{-1} corresponding to the C=O stretching vibration of amide, along with an absorption band at 1527 cm^{-1} corresponding to the N–H bending. In solid compound **3b**, a peak appeared at 1739 cm^{-1} which supports the formation of a methyl ester (Figure 23). However, in compound **2,** the peak is shifted to 1725 cm^{-1} that clearly indicates that ester is converted into carboxylic acid in compound **2** (Figure 24).

Table 2.5.A. FTIR analysis of compounds:

S. No.	Compound	Amide N-H vibration	Amide II	Amide I	C=O vibration of COOH/COOMe
1	3a	3246	1535	1612	1760
2	1	3305	1528	1644	1725
3	3b	3395	1534	1645	1739
4	2	3397	1527	1645	1725

Chapter 3

Experimental sections:

3.1. Synthesis and characterizations of compounds:

3.1.1. General method:

All the chemicals and reagents were obtained commercially. All NMR spectra were recorded at 400 MHz Bruker Advance III 400 NMR. Compounds concentrations were in the range of 1-10 mmol in $(CD_3)_2SO$. Mass spectra were recorded on Bruker micrOTOF-Q II by positive mode electrospray ionizations. All the solvents, which were used in the reactions and for column chromatography were properly dried and distilled. All the synthesized products were dried under high vacuum pump before sample characterizations (^{1}H NMR, ^{13}C NMR, ESI-MS, TGA, FTIR, UV-Vis, Fluorescence, Elemental analysis). Milli-Q water was used for reaction purposes.

3.1.2. Synthesis of 2-amino-3-(4-hydroxy-phenyl)-propionic acid methyl ester (2a):

60 mL dry methanol was taken in 250 mL round bottom flask stirring with a magnetic bar. Methanol was cooled in ice bath for 10 min. Thionyl chloride ($SOCl_2$) 3.65 mL was added dropwise in cooled methanol. Then, amino acid (3gm, 16.56 mmol) was added to the reaction mixture. The reaction mixture was stirred for overnight. The reaction mixture was evaporated on rotavapor. Then, the reaction mixture was washed with diethyl ether. The compound was dried on a vacuum pump.

3.1.3. Synthesis of 2-{3,5-Bis-[2-(4-hydroxy-phenyl)-1-methoxycarbonyl- ethylcarbamoyl]-benzoylamino}-3-(4-hydroxy-phenyl)-propionic acid methyl ester (3a):

0.5 g (2.37 mmol) of benzene-1,3,5- tricarboxylic acid was dissolved in a mixture of 1.5 mL of dry N,N-dimethyl formamide (DMF) and cooled in an ice-water bath. H-Tyr-OMe **(2a)** was isolated from 2.46g (10.67 mmol) of the corresponding methyl ester hydrochloride by neutralization with saturated sodium carbonate, subsequent extraction with ethyl acetate and this was added to the reaction mixture, followed immediately by 0.986 g (3.3 mmol) of N,N'-diisopropylcarbodiimide(DIPC) and 0.966 g (3 mmol) of hydroxybenzotriazole(HOBt).The reaction mixture was allowed to come to room temperature and stirred for 24h . DMF was evaporated, and the residue was taken in ethyl acetate. N,N'-diisopropylurea was filtered off. The organic layer was washed with 1N HCl (3 × 20 mL), brine water (3 × 20mL), 1N sodium carbonate (3 × 20mL). Then the organic layer was dried over anhydrous sodium sulphate and evaporated under vaccum. to yield 0.91g (51.00%) trisamide **(3a)**. **^{1}H NMR (400 MHz, DMSO-d_6, TMS, r.t)** δ8.37 (s, 3H, ArH), 7.08(d, 6H, Tyr ring H), 6.66 (d, 6H, Tyr ring H), 9.10 (s, 3H, Tyr ring –OH), 9.01(d, 3H, -NH), 3.0 (m, 6H, -CH_2), 4.59 (q, 3H, -CH), 3.62ppm (s, 9H, -OCH_3); **^{13}C NMR (100 MHz, DMSO-d_6)**; δ 172.62, 166.10, 156.50, 134.59, 130.43, 127.98, 115.60, 55.41, 52.39, 36.98; **Elemental analysis**; Anal. Calcd For $C_{39}H_{39}N_3O_{12}$

(%): C, 63.15; H, 5.30; N, 5.67; Found (%): C, 54.91; H, 4.47; N, 4.73; **MS (ESI) m/z** for $C_{39}H_{39}N_3O_{12}$ calcd.:741.25, found:742.2 $(M+H)^+$.

3.1.4. Synthesis of 2–{3,5-Bis-[1–carboxy-2-(4–hydroxyl–phenyl)–ethyl carbamoyl]–benzoylamino}–3–(4–hydroxyl–phenyl)–propionic acid (1):

A solution of **3a** (200 mg, 0.285 mmol) in 60 mL of dry MeOH was allowed to react with 2M NaOH solution. The progress of the reaction was monitored by thin layer chromatography (TLC). The reaction mixture was stirred for 6 h. Then, methanol was removed under vacuum. The residue was taken in water and washed with diethyl ether (2 x 20 mL). The pH of aqueous layer was adjusted to 2 using 2 M HCl and it was extracted with ethyl acetate (3 x 30 mL). The ethyl acetate layer was dried over anhydrous sodium sulfate and evaporated under vacuum to yield desire product **(1)**. Yield=100mg (50%);**^{1}H NMR (400 MHz, DMSO-d6)**: δ 12.56 (s, 3H, -COOH), 9.10 (s, 3H, Tyr ring - OH), 9.01 (d, 3H, -NH), 7.08 (d, 6H, Tyr ring H), 6.66 (d, 6H, Tyr ring H),), 4.54 (q, 3H, -CH), 3.01(m, 6H, $-CH_2$),) 8.36 ppm (s, 3H, ArH), **; ^{13}C NMR (100 MHz, DMSO-d_6)**: δ1173.5, 166.1, 156.31, 134.89, 130.4, 129.60, 29.20, 115.53, 55.53, 36.97; **Elemental analysis**; Anal. Calcd For $C_{36}H_{33}N_3O_{12}$ (%): C, 61.80; H, 4.75; N, 6.01; Found (%): C, 59.47; H, 4.99; N, 4.75; **MS (ESI) m/z** for $C_{36}H_{33}N_3O_{12}$ calcd.: 699.20., found: 722.0 $(M+Na)^+$.

3.1.4. Synthesis of 2-amino-3-(1H-indol-3-yl)-propionic acid methyl ester (2b):

60 mL dry methanol was taken in 250 mL round bottom flask stirring with a magnetic bar. Methanol was cooled in ice bath for 10 min. Thionyl chloride ($SOCl_2$) 2.13 mL was added dropwise in cooled methanol. Then, amino acid (3gm, 14.699 mmol) was added to the reaction mixture. The reaction mixture was stirred for overnight. The reaction mixture was

evaporated on rotavapor. Then,the reaction mixture was washed with diethyl ether.The compound was dried on a vacuum pump.

3.1.5. Synthesis of 2-{3,5-Bis-[2-(1H-indol-3-yl)-1-methoxycarbonyl-ethylcarbamoyl]-benzoylamino}-3-(1H-indol-3-yl)-propionic acid methyl ester (3b):

0.5 g (2.37 mmol) of benzene-1,3,5- tricarboxylic acid was dissolved in a mixture of 1.5mL of dry N,N-dimethyl formamide (DMF) and cooled in an ice-water bath. H-Trp-OMe **(2b)** was isolated from 2.72 g (10.67 mmol) of the corresponding methyl ester hydrochloride by neutralization with saturated sodium carbonate, subsequent extraction with ethyl acetate and this was added to the reaction mixture, followed immediately by 0.96g (3.3 mmol) of N,N'-diisopropylcarbodiimide (DIPC) and 0.966g (3 mmol) of hydroxybenzotriazole (HOBt). The reaction mixture was allowed to come to room temperature and stirred for 24h . DMF was evaporated, and the residue was taken in ethyl acetate. N,N'-diisopropylurea was filtered off. The organic layer was washed with 1N HCl (3 × 20 mL), brine water (3 × 20mL), 1N sodium carbonate (3 × 20mL). Then the organic layer was dried over anhydrous sodium sulphate and evaporated under vaccum. to yield 0.95g (49.00%) trisamide **(3b)**. **^{1}H NMR (400 MHz, DMSO-d_6, TMS, r.t)** δ 8.43 (s, 3H, ArH), 7.56 (d, 3H, Trp ring H), 7.30 (d, 3H, Trp ring H), 10.82 (s, 3H, Trp ring –NH), 9.15 (d, 3H, -NH), 3.21 (m, 6H, -CH_2), 4.73 (q, 3H, -CH), 7.05 (s, 3H, Trp ring H), 7.03 (t, 3H Trp ring H), 6.97 (t, 3H, Trp ring H), 3.62 ppm (s, 9H, -OCH_3); **^{13}C NMR (100 MHz, DMSO-d_6)**; δ172.82, 166.06, 136.58, 134.63, 129.83, 127.48, 124.69, 121.47, 118.44, 111.95, 110.30, 79.64, 54.46, 52.42: **Elemental analysis**: Anal. Calcd For $C_{45}H_{42}N_6O_9$ (%): C, 66.66; H, 5.22; N, 10.36; Found (%): C, 67.82; H, 5.10; N, 9.58; **MS (ESI) m/z** for $C_{45}H_{42}N_6O_9$ calcd.:810.2, found:811.3 $(M+H)^+$.

3.1.6. Synthesis of 2–{3,5-Bis[1-carboxyl-2-(1H-indol-3-yl)-ethylcarbamoyl]–benzoylamino}-3-(1H-indol-3-yl)-propionic acid (2) :

A solution of (**3b**) (200 mg, 0.246 mmol) in 60 mL of dry MeOH was allowed to react with 2M NaOH solution. The progress of the reaction was monitored by thin layer chromatography (TLC). The reaction mixture was stirred for 6 h. Then, methanol was removed under vacuum. The residue was taken in water and washed with diethyl ether (2 x 20 mL). The pH of aqueous layer was adjusted to 2 using 2 M HCl and it was extracted with ethyl acetate (3 x 30 mL). The ethyl acetate layer was dried over anhydrous sodium sulfate and evaporated under vacuum to yield desire product (**2**). Yield=120mg (63%); **^{1}H NMR (400 MHz, DMSO-d6, TMS, r.t)**: δ 8.41 (s, 3H, ArH), 7.61 (d, 3H, Trp ring H), 7.32 (d, 3H, Trp ring H), 10.80 (s, 3H, Trp ring –NH), 8.98 (d, 3H, -NH), 3.21 (m, 6H, -CH2), 4.72 (q, 3H, -CH), 7.19 (s, 3H, Trp ring H), 7.05 (t, 3H Trp ring H), 6.99 (t, 3H,Trp ring H), 12.66 ppm (s, 3H, -COOH); **^{13}C NMR (100 MHz, DMSO-d6)**; δ173.83, 166.08, 136.56, 134.87, 129.60, 127.57, 124.01, 121.42, 118.89, 110.57, 111.89, 110.76, 60.23, 54.28; **MS (ESI) m/z** for $C_{42}H_{36}N_6O_9$ calcd.:768.25, found:769.2 $(M+H)^+$.

Chapter 4: Conclusion and Scope of future work:

2–{3,5-Bis-[1–carboxy-2-(4–hydroxyl–phenyl)–ethylcarbamoyl]–benzoylamino}–3–(4– hydroxyl–phenyl)–propionic acid **(1)** and 2–{3,5-Bis[1-carboxyl-2-(1H-indol-3-yl)-ethylcarbamoyl]–benzoylamino}-3-(1H-indol-3-yl)-propionic acid **(2)** were synthesized in liquid phase by protecting carboxylic acid group of C-terminal amino acids by esterification using $SOCl_2$/MeOH and the amine group of N-terminal amino acids was coupled with benzene- 1,3,5-tricarboxylic acid. The formation of compounds **1** and **2** was confirmed by ^{1}H NMR, ^{13}C NMR, TGA, UV-Vis, Fluorescence, FT-IR, Elemental analysis and Mass spectrometry. The yield of compounds **1** and **2** was obtained to be 50% and 63% respectively.

In future, we want to develop various self-assembled morphological structures of synthesized compounds **1** and **2** and their utilization in gas adsorption, gas senescing, gel formation.

Appendix A:

^{1}H NMR , ^{13}C NMR , FTIR and Mass spectra of compounds:

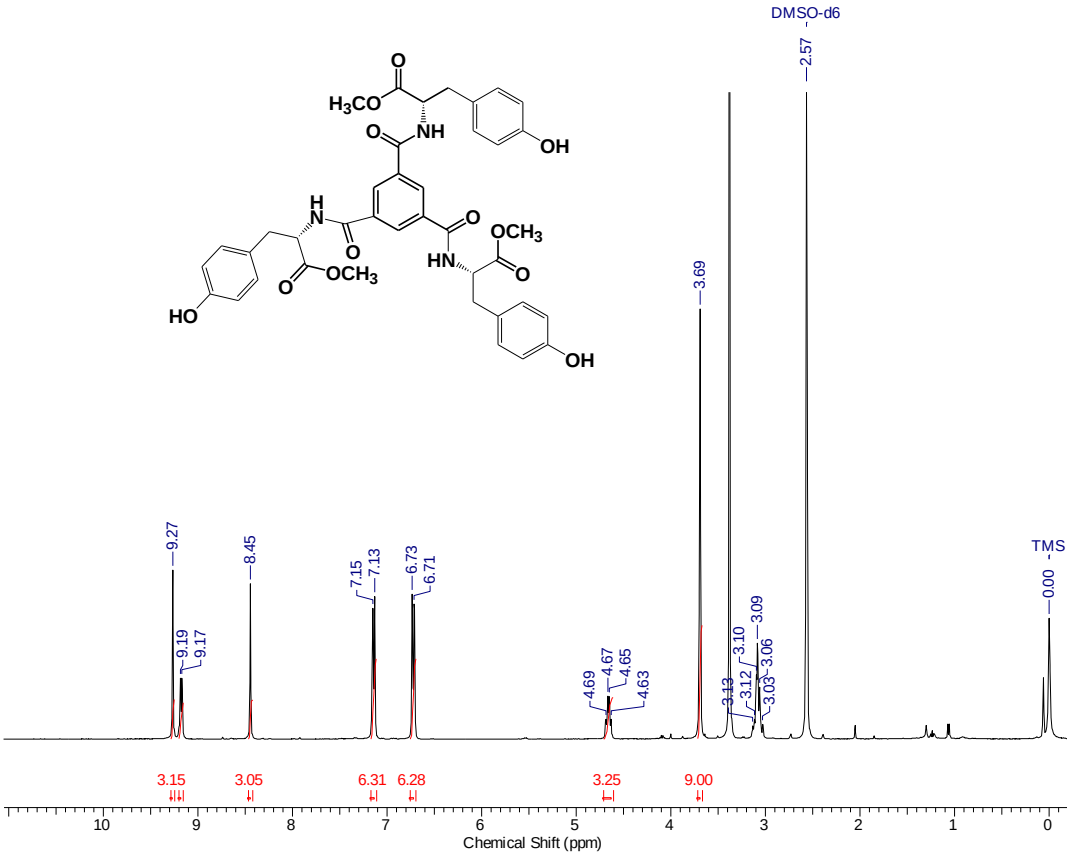


Figure 9: ^{1}H NMR spectrum of compound **3a** in DMSO-d_6.

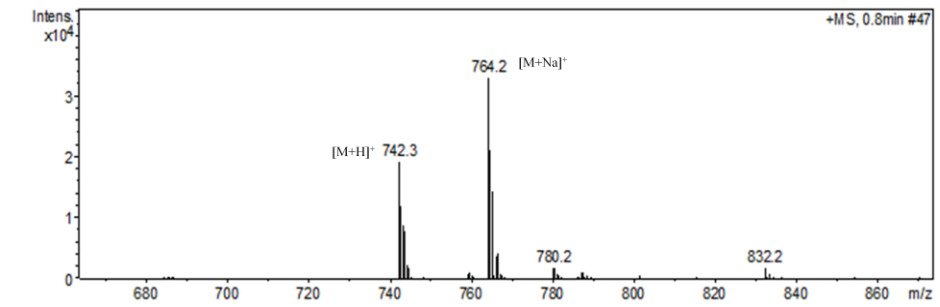


Figure 10: ESI-MS spectrum of compound **3a**.

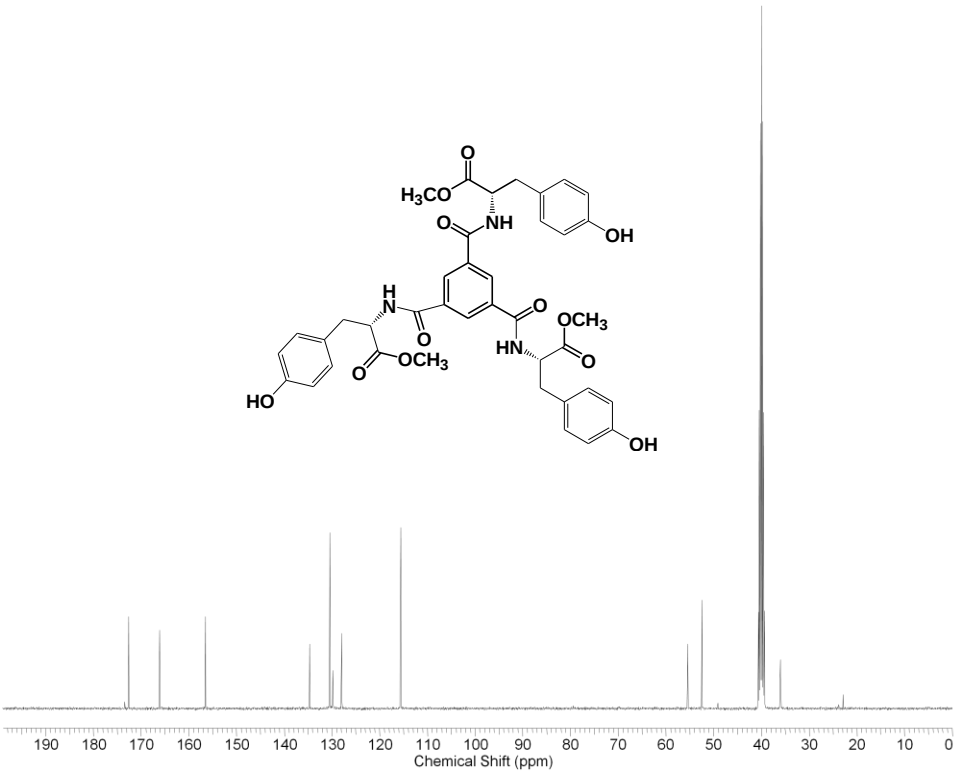


Figure 11: ^{13}C NMR spectrum of compound **3a** in DMSO-d_6.

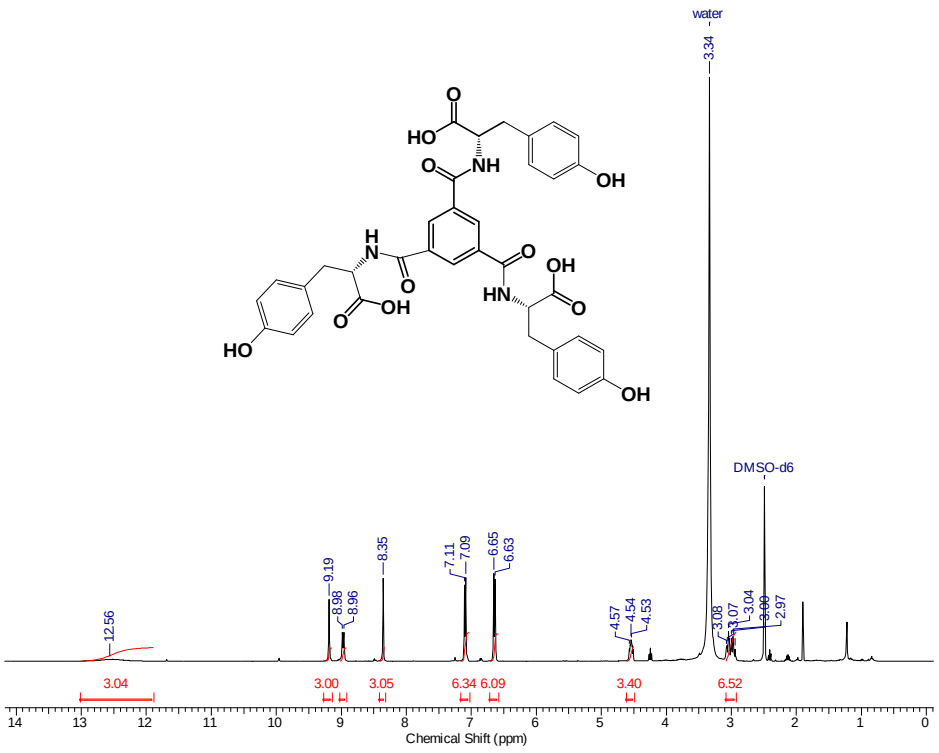


Figure 12: ^{1}H NMR spectrum of compound **1** in DMSO-d_6.

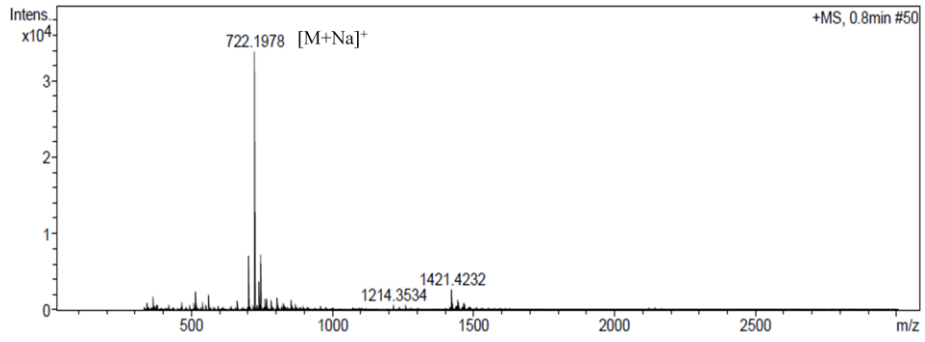


Figure 13: ESI-MS spectrum of compound **1**.

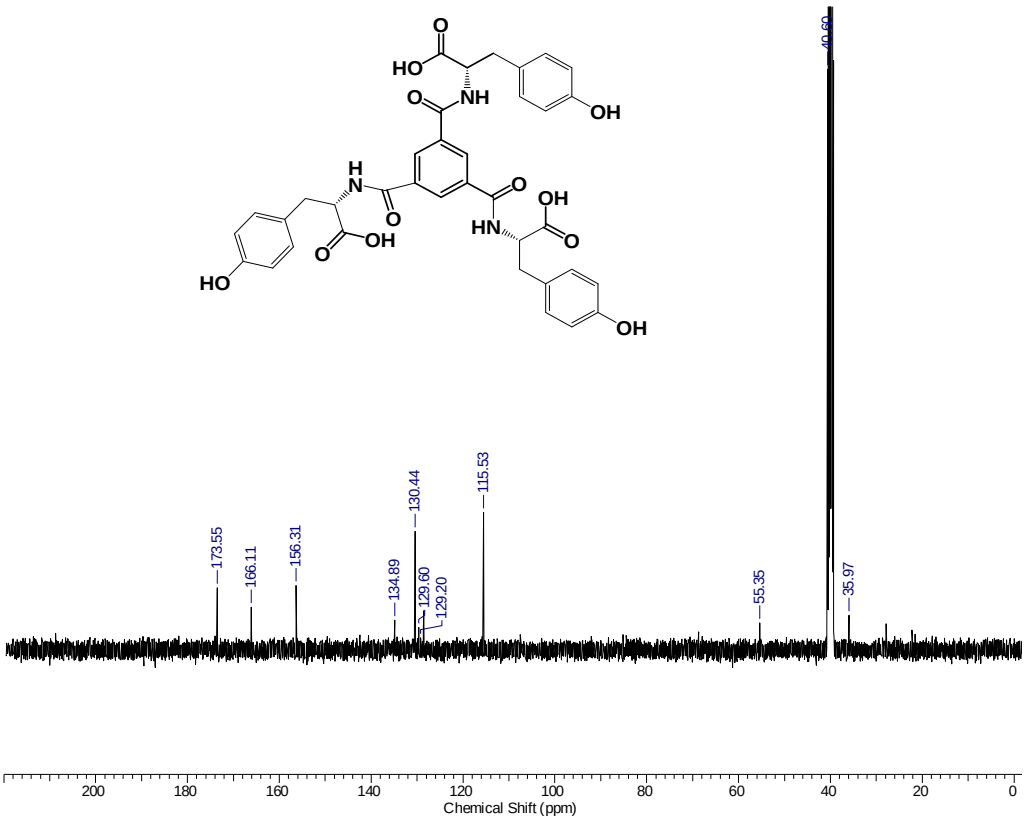


Figure 14: ^{13}C NMR spectrum of compound **1** in DMSO-d_6.

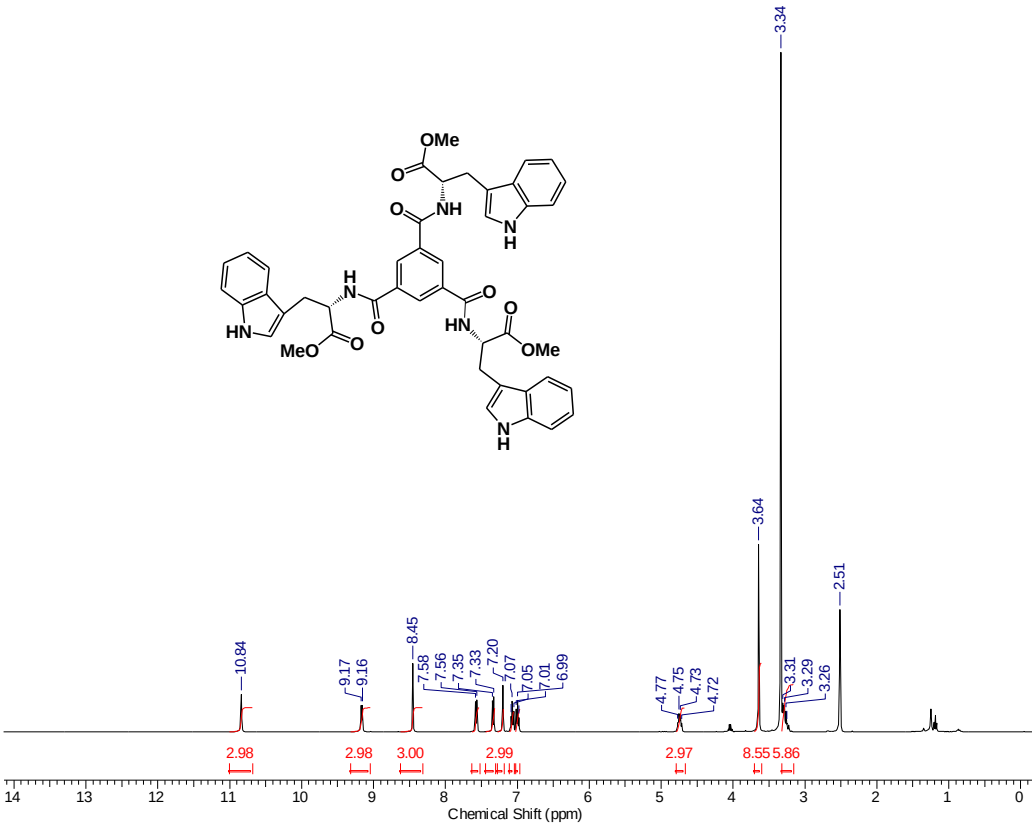


Figure 15: ^{1}H NMR spectrum of compound **3b** in DMSO-d_6.

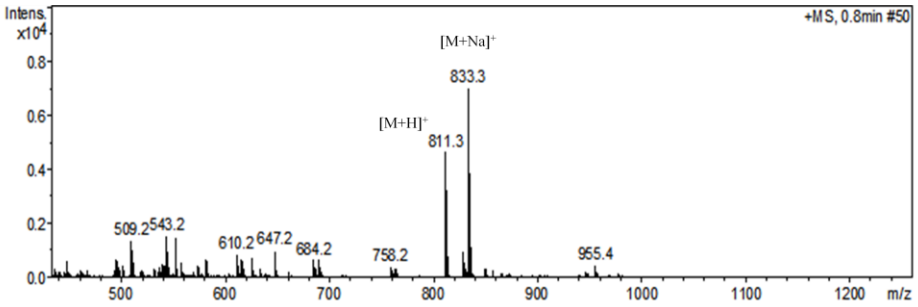


Figure 16: ESI-MS spectrum of compound **3b**.

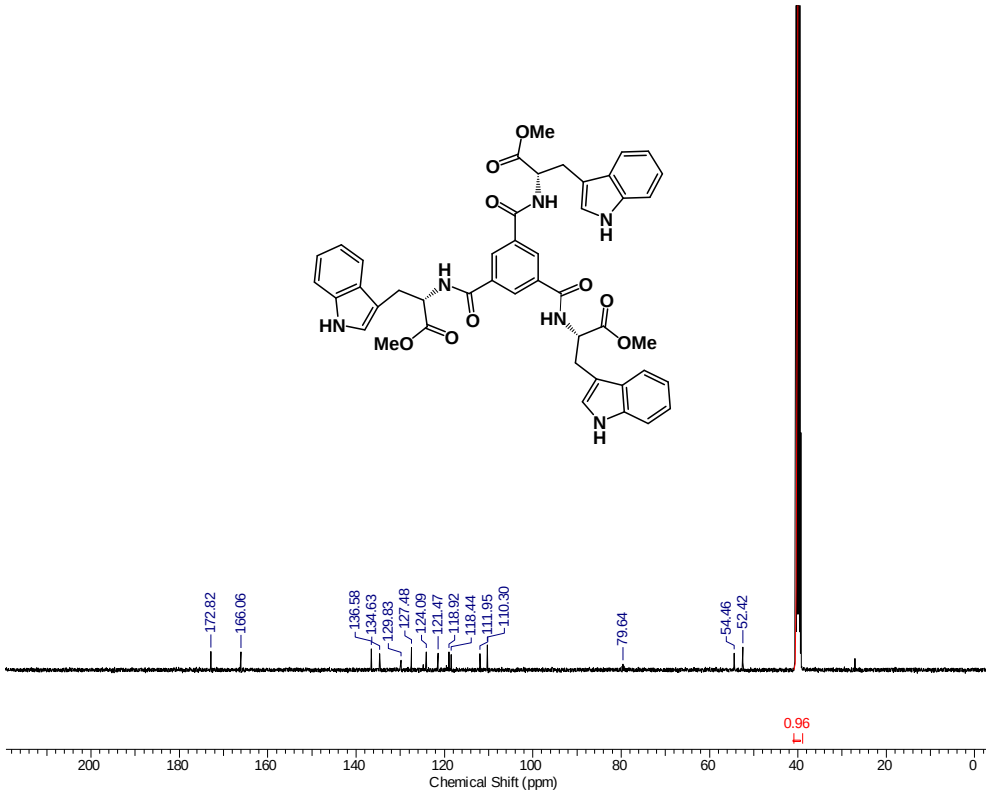


Figure 17: ^{13}C NMR spectrum of compound **3b** in DMSO-d_6.

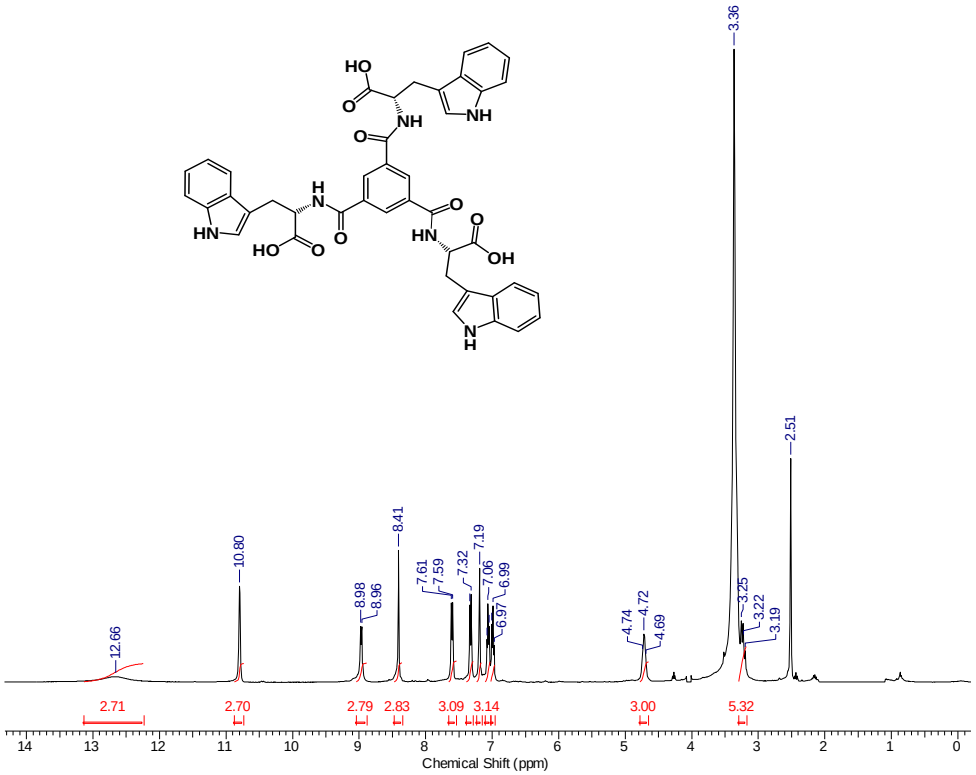


Figure 18: ^{1}H NMR spectrum of compound **3b** in DMSO-d_6.

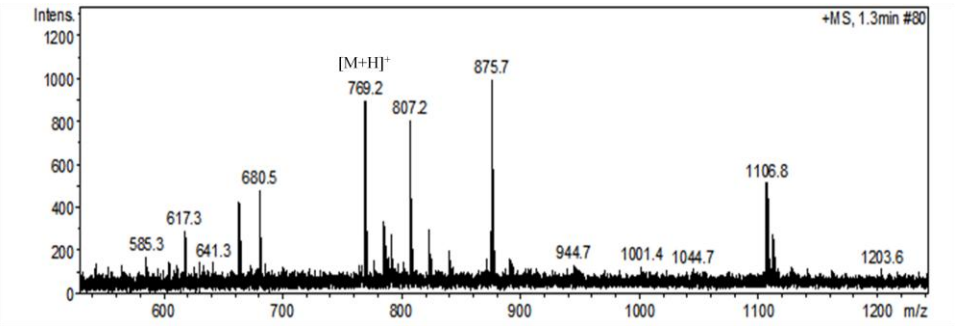


Figure 19: ESI-MS spectrum of compound **3b**.

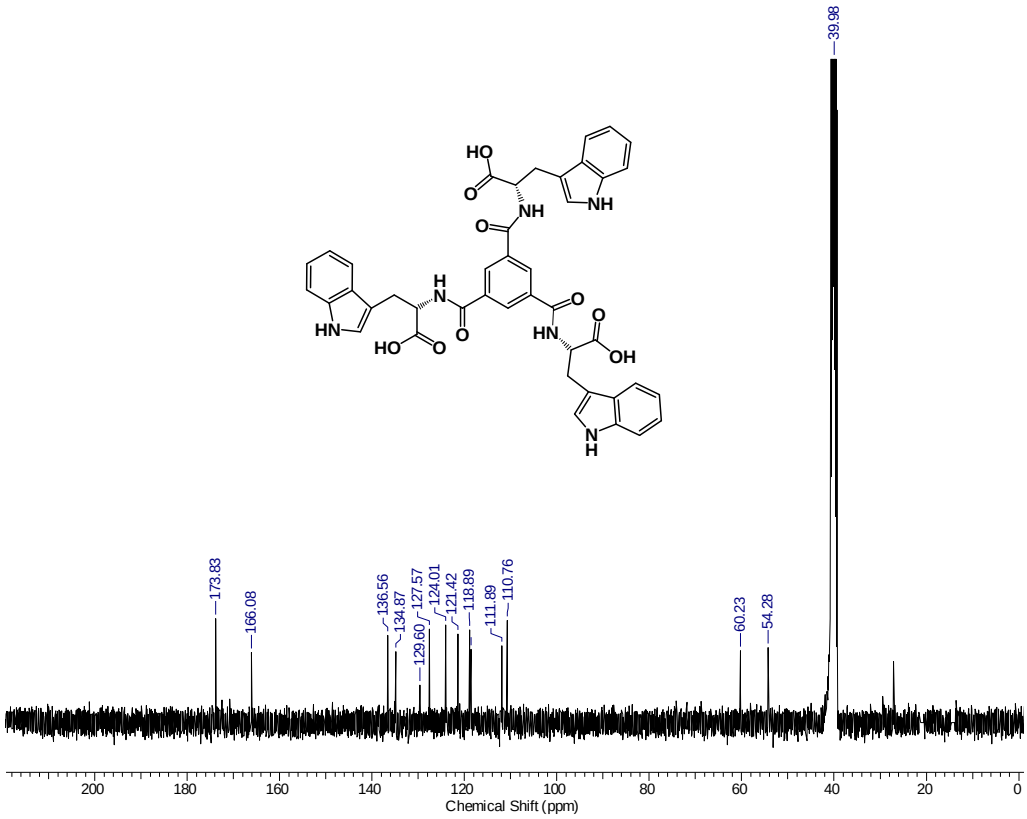


Figure 20: ^{13}C NMR spectrum of compound **2** in DMSO-d_6.

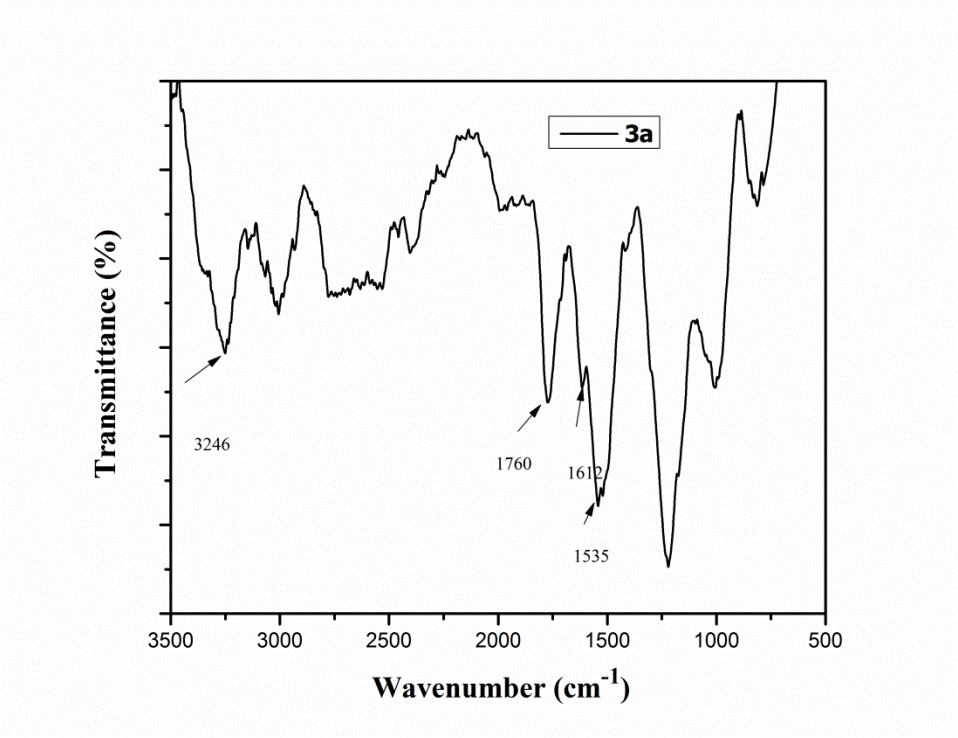


Figure 21: FTIR spectrum of compound **3a**.

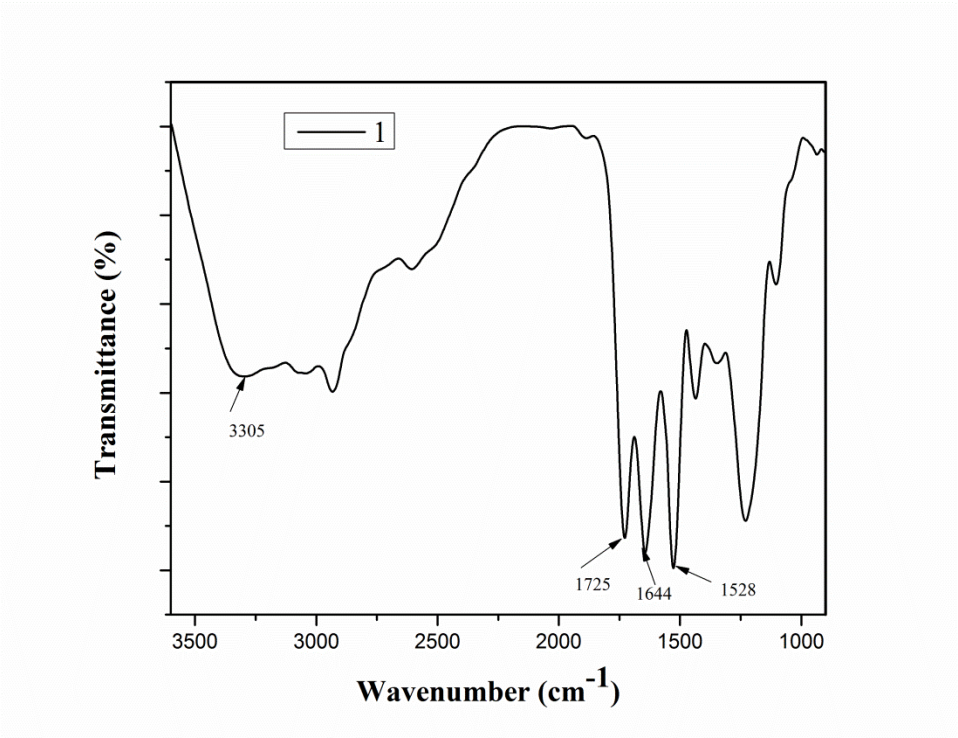


Figure 22: FTIR spectrum of compound **1**.

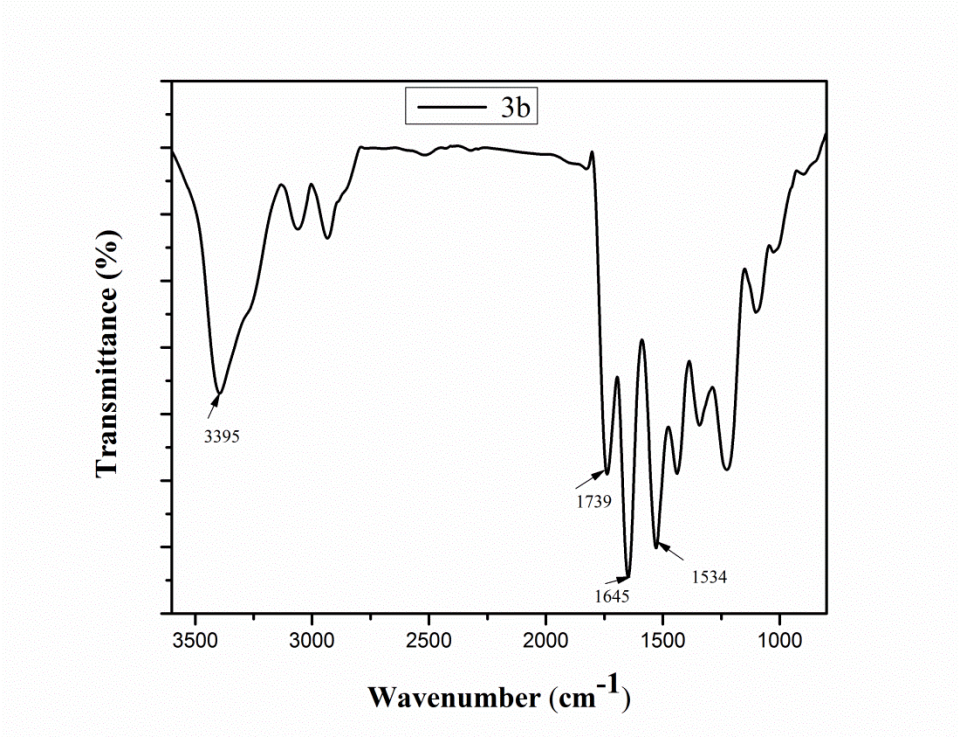


Figure 23: FTIR spectrum of compound **3b**.

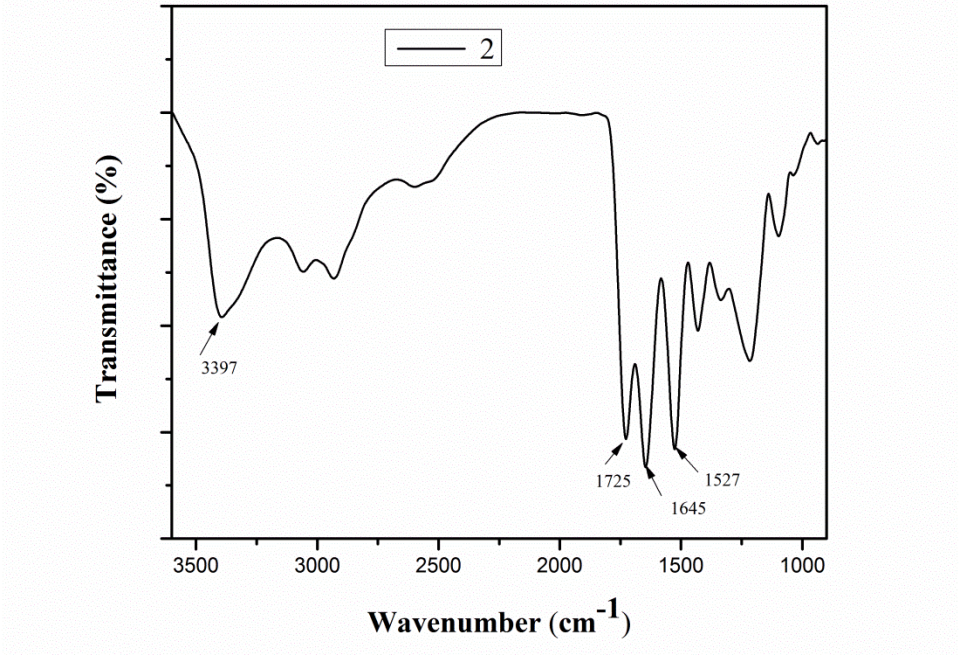


Figure 24: FTIR spectrum of compound **2**.

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