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PREPARING AND CHARACTERIZING SOME NEW DERIVATIVES OF ORGANIC CYCLIC COMPOUNDS DERIVED FROM SOME DRUGS AND STUDYING THEIR BIOLOGICAL ACTIVITY

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Abstract

This study involved synthesis some of derivatives via that a Suzuki-Miyaura cross-coupling procedure was used in order to produce a wide variety of Baclofen derivatives. After beginning with the reaction of 4-methoxy carbonyl phenyl boronic acid by the use of the reflex method, the treatment of Baclofen with a number of other boronic acids was carried out. The subsequent stage was the incorporation of Pd(0)(PPh3)4, and lastly, once the reaction had reached a state of equilibrium,Ethyl Acetoacetate (EtOAc) was incorporated into the mixture. Taking this action was necessary in order to finish the procedure. Using the thin layer chromatography (TLC)technique, the observation of the reaction was carried out in order to carry out the observation. In order to accomplish the job of characterizing all of the unique Baclofen derivatives that were discussed in the preceding paragraphs [1-6], the analytical procedures of Fourier Transform Infrared (FT-IR) , Proton nuclear magnetic resonance (1H-NMR) ,Carbon-13 nuclear magnetic resonance (13C-NMR) , and C.H.N were used. Furthermore, a wide range of other physical characteristics, such as color, Rf, and mechanical capabilities, were investigated and appraised. The objective of the experiment was to determine whether or not the treatment was effective against two different types of bacteria according to the biological standards. One of the objectives of the experiment was to do this. There was one species of fungus, which was Candida albicans, and one of the bacteria was positive (Staphylococcus aureus). The other bacterium was negative (Escherichia coli), and there was one type of bacteria. Of the bacteria, two were found to be positive. Following the assessment of the compounds' bacterial inhibitory biological activity [1-6], it was shown that the derivatives had an exceptionally high degree of effectiveness at a certain concentration. An additional accomplishment was the successful completion of a molecular docking investigation of novel Baclofen derivatives. [1-6]**.**

Keywords: *Heterocycli compounds, Baclofen, Suzuki reaction.*

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Introduction

Heterocyclic compounds are among the most significant forms of organic molecules [1, 2], and the field of medicinal chemistry spans a wide variety of diverse subject areas [3]. Heterocyclic compounds are very important. This is the present situation that has arisen as a consequence of the enormous number of heterocyclic compounds that are used in the area of medicine as remedies for a wide range of illnesses. A number of qualities, including antifungal, anti-inflammatory, antibacterial, herbicide, and antifungal effect, are possessed by these substances. Cancer[4]. May be broken down into four distinct categories. The partnership that exists between the disciplines of chemistry and medical chemistry has resulted in the development of a significant area of research that has evolved as a consequence of this relationship. The heterocyclic compounds that are present in the field of medicinal chemistry make up the great majority of the molecules that are there. And problems that arise in the field of medicine as a consequence of the endeavor to investigate prevalent diseases and the many therapies that may be used for treating them [5]. The area of medical chemistry has emerged as the primary focus of attention for researchers from all over the globe. This is due to the fact that medical chemistry is sometimes considered to be the foundation upon which the many subfields of chemistry, particularly organic chemistry [6], are constructed. A major proportion of the reactions that take place in organic chemistry are reactions that entail the production of a new carbon atom family between two distinct types of hydrocarbons that pair in a medium that is catalyzed by a base [7]. These reactions are responsible for the development of a new carbon atom family. The development of a new family of carbon atoms is a characteristic that is associated with these events. In comparison to the many other sorts of answers, these are the ones that are most often used. When it comes to the field of organic chemistry, the Suzuki reaction is often regarded as one of the most important types of coupling reactions[8]. As a result of the importance it carries, it is regarded as one of the most significant types of coupling reactions. The production of a novel family of carbon-carbon compounds is the distinguishing characteristic that sets this one-of-a-kind reaction apart from other reactions. This is the reason why it is considered to be unique. The coupling reaction, regardless of the kind of coupling reaction that is regarded as being among the most important types of chemical reactions that occur the most often in the field of medicinal chemistry [9], is considered to be among the most common types of chemical reactions. In the early aftermath of the creation of amide bonds, the transformation is the transformation that is used an average of two times more often than any other transformation. Additionally referred to as the metamorphosis. Numerous drugs that have been approved for use are related with heteroaryl or biphenyl groups. These groups are associated with the pharmaceuticals. Both of these types of classifications are able to be discovered in the medications that are now being analyzed. The fact that this is the case demonstrates the importance of this response in regard to the situation that has arisen. Palladium is assumed to be responsible for one of the coupling processes that it catalyzes [10], and it plays a vital role in the development of organic chemistry. Palladium is also essential to the survival of organic

chemistry. It carries out this essential role, which is quite important. This answer, which was referred to by its name at the time of its first publication in 2010, came into being for the very first time in the year 2010. It was in 1979 when the renowned scientist Suzuki was presented with the coveted Nobel Prize in Chemistry [11].

According to the consensus of the scientific community, baclofen[12] and its derivatives are examples of compounds that are not only effective in therapeutic applications but also have biological activity. One of the most effective anti-spasm drugs, baclofen is often used in therapeutic settings because of its effectiveness. Moreover, it is one of the drugs that is used the most often. This illness may have its origins in multiple sclerosis or in abnormalities in the spinal cord. Both of these possibilities are equally plausible. An additional advantage is that it helps reduce muscular tension and promotes the mobility of the muscles, which is a significant benefit. This particular advantage is a significant advantage. There are twelve of them. Baclofen has the potential to reduce the efficacy of the pharmaceutical components that are acting on the device [13], which is in addition to the fact that it has the capability of doing so. Other medications that are covered include barbiturates and benzodiazepines. This drug is also considered to be one of the most significant medications for the management and treatment of nerve pain because it functions in a way that is comparable to that of the central nervous system[14].

Experimental

General information

Using the SMP equipment (Gallenkamp), we were able to do analysis and determine the melting points of the materials. The Fourier transform infrared spectrophotometer that was created by Perkin Elmer was used for the purpose of acquiring infrared spectra. These findings were obtained by the employment of both [13C-NMR] and [1HNMR] in order to record the outcomes of the Fourier transformation, which ultimately led to the acquisition of these findings. The administration of the exams was the responsibility of the Department of Chemistry of Tehran University, which is located in Iran. In addition to using DMSO-d6, they used a Bruker spectrometer that was operating at a frequency of 500 meters per second. The burden for these actions fell on the shoulders of this specific department. For the aim of carrying out the research of the microelements (C.H.N.), it was discovered that the Shimadzu Vario Elemental Analyzer 3000 was the instrument that was the best suitable for the task at hand. As part of the process of carrying out the study, an analytical silica gel thin layer chromatography (TLC) analysis was carried out with the assistance of Merck plates.Sixty-four F254 is the number. [0.2 mm thick].

Methods

General Procedure for the Preparation of compounds [1-6] [15]

The following components are present in a mixture that is composed of aromatic boric acid [0.50 mmol], 4-Amino-3-(4-chlorophenyl) butanoic acid [0.50 mmol], and Pd(PPh3)4 [0.04 mg] present in [25 mL] of 1-propanol and [7 mL] of potassium carbonate: The solution was maintained at a temperature that ranged from 80 to 90 degrees Celsius for a period of sixteen hours while being agitated. We had the ability to track the progression of the solution that was being delivered thanks to the use of thin layer chromatography (TLC) . After the addition of [5 ml] of distilled water, the reaction should be allowed to cool to room temperature before ethyl acetate is used to extract the chemical. When the reaction has reached room temperature, the material may be extracted. It is important to finish this step before commencing the extraction procedure. After washing the organic layers that have been combined with a solution of sodium carbonate, the subsequent step is to filter and concentrate them in a vacuum environment. This is done after the organic layers have been mixed together. The procedure of recrystallization, which was carried out with the assistance of ethanol, was used in order to purify the solid residue that was produced.

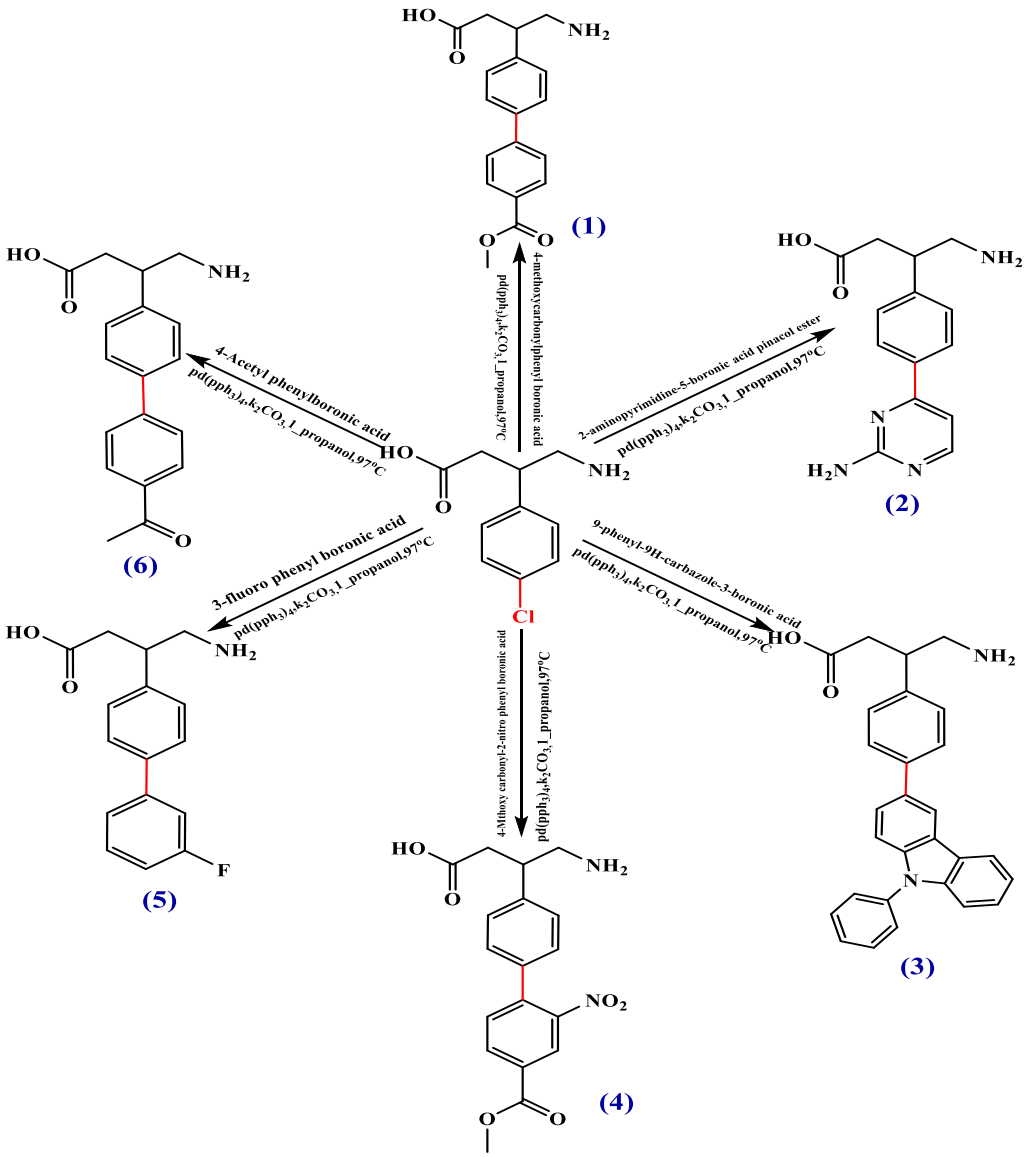


Figure [1]: Synthesis of some Baclofen derivatives by Suzuki reaction

Compound [1]: 4-Amino-3-(4'-(methoxycarbonyl)-[1,1'-biPhenyl]-4-yl)butanoic acid

RF 0.49, m.p261-263 Co. IR [KBr,cm¯1]: 3390 [OH], 1279 [C-O], 1493 [C=C], and 1712 [C=O] are the parameters that constitute the physical state of the substance. There were 12.52 [s,OH], 7.34 -8.03 [d,H-aromatic], and 1.6 [t,NH] in the 1H NMR spectrum of DMSO-d6 ppm. There were 166.2 [C=O], 127.5-143 [C-aromatic], and 176.3 [COOH] in the 13C NMR spectrum of DMSO-d6 ppm. The following values were computed for C18H19NO4: C=69.00, H=5.52, and N=4.47. The values that were found were C=68.4, H=4.92, and N=3.87..

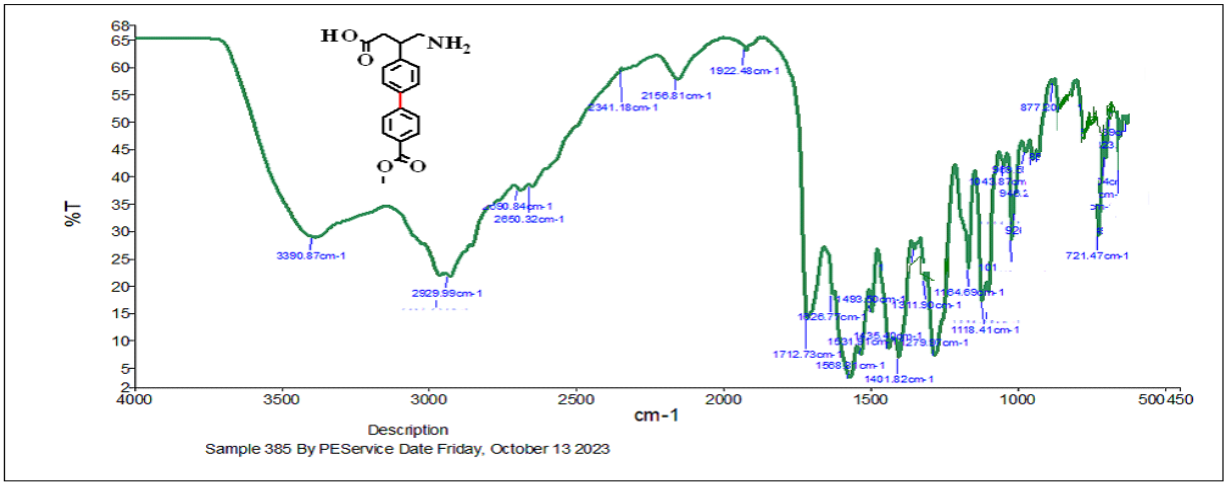


Fig 2: FT-IR spectra of compound [1]

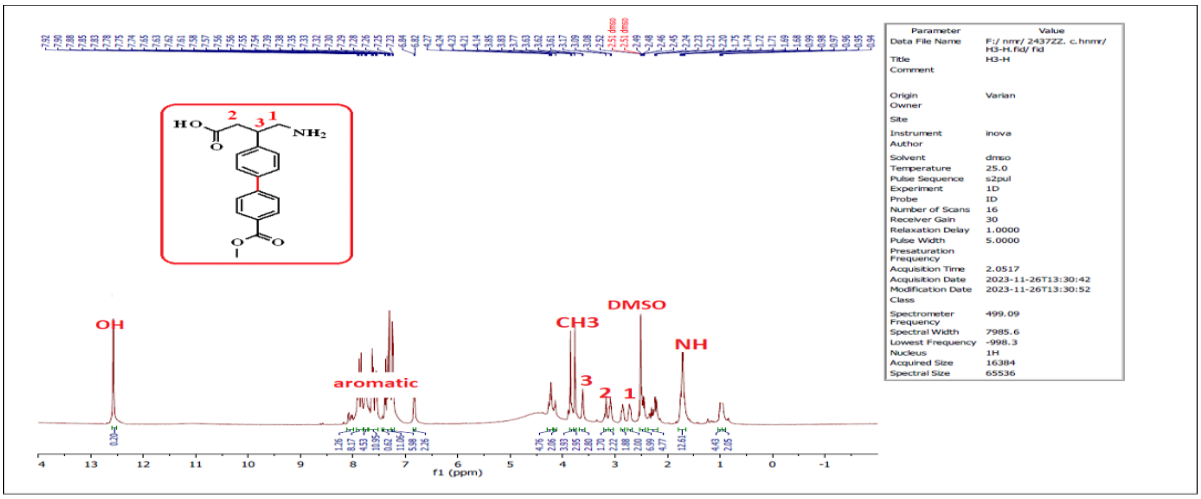


Fig 3 :^{1}H-NMR spectrum of compound [1]

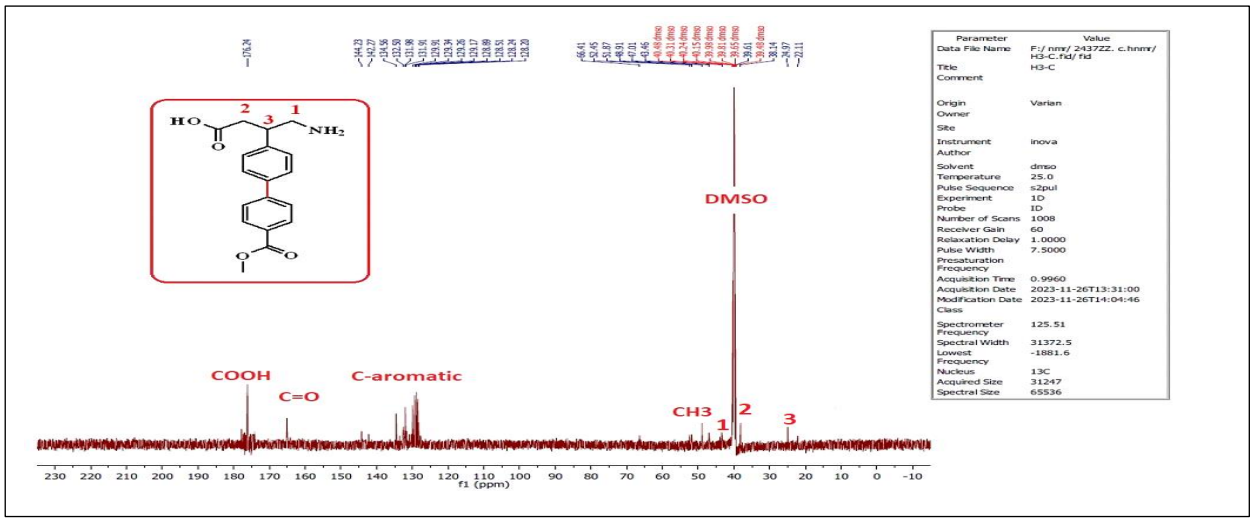


Fig 4 :13C-NMR spectrum of compound [1]

Compound [2]: 4-Amino-3-(4-(2- aminopyrimidine-4-yl)Phenyl)butanoic acid

Co.IR [KBr, cm¯1] of 3500 [OH], 2950 [C-H], 1684 [C=O], and 1492 [C=C] are seen in brown crystals with an RF, which is 0.28, and a m.p., which ranges from 156 to 158. An occurrence of brown crystals in their physical state. The values that were obtained from 1H NMR [DMSO-d6 ppm] are 1.49 [s,OH] and 7.15 -8.16 [d,H-aromatic]. Within the 13C NMR spectra of DMSO-d6 ppm, there were 157.2 [C=N], 125.5-133 [C-aromatic], and 177.2 [COOH] atoms. C equals 61.75, H equals 5.92, and N equals 20.58. This is the formula for the chemical formula C14H16N4O2. It is the case that C equals 61.05, H equals 5.22, and N equals 19.88.

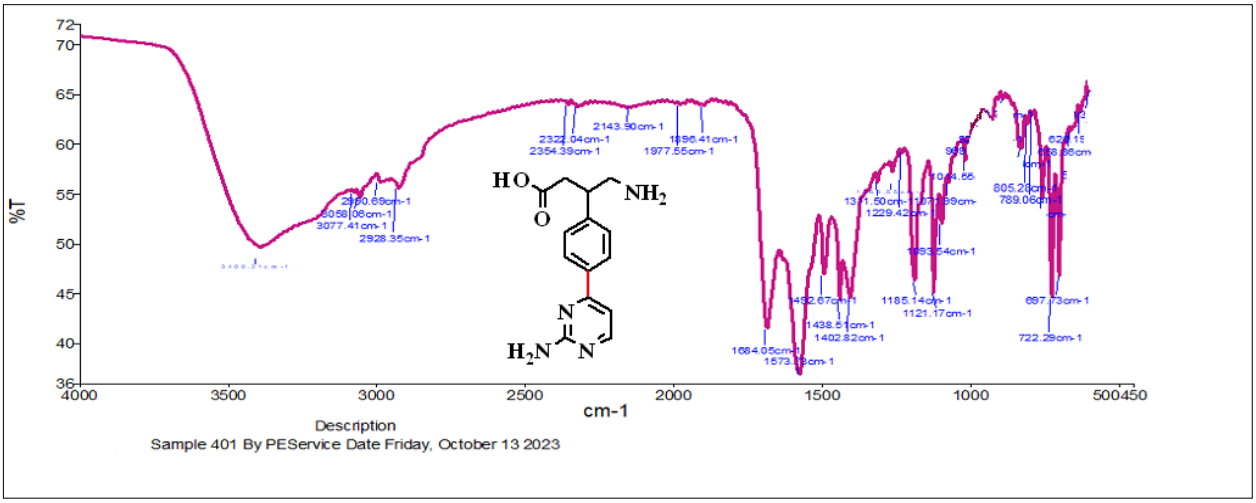


Fig 5: FT-IR spectra of compound [2]

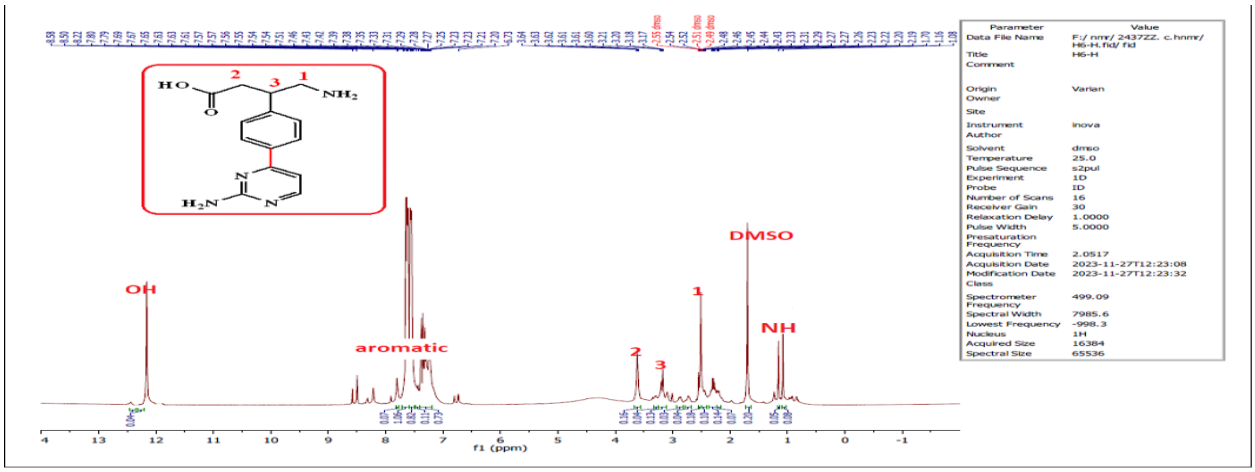


Fig 6 :[1]H-NMR spectrum of compound [2]

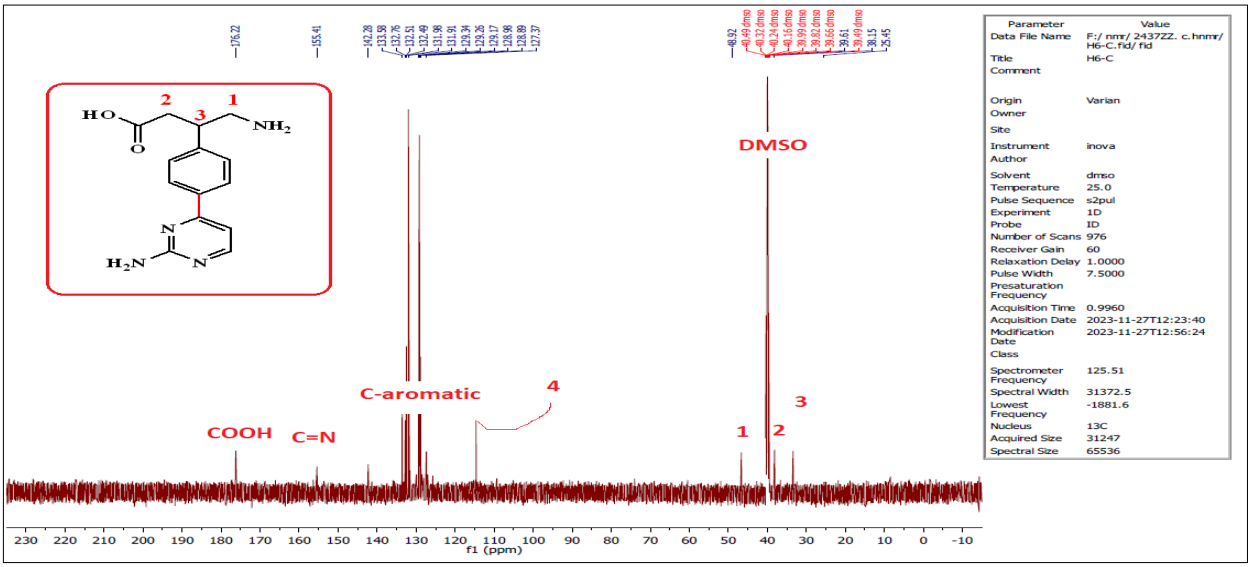


Fig 7 :^{13}C-NMR spectrum of compound [2]

Compound [3]: 4-Amino-3-(4(9-phenyl-9H-carbazol-3-yl)phenyl)butanoic acid

[KBr, cm¯1] in the infrared spectrum: 3368 [OH], 2924 [C-H], 1574 [C=C], and 1681 [C=O]. Brown crystals with a refractive index of 0.62 and a molecular weight of 272-274Co are the condition of the substance in its physical state. The values that were acquired via the use of 1H NMR are as follows: 7.3 - 8.71 [d,H-aromatic], 1.58 [t,NH], and 12.5 [s,OH] are the values. The values that were acquired via the use of 13C NMR are as follows: 177.3 [COOH], 115.0-146.2 [C-aromatic] for that matter. Listed below are the values that have been calculated for C28H24N2O2: N equals 6.66, C equals 79.98, and H equals 5.75. The values C = 79.28, H = 5.05, and N = 5.96 have been found..

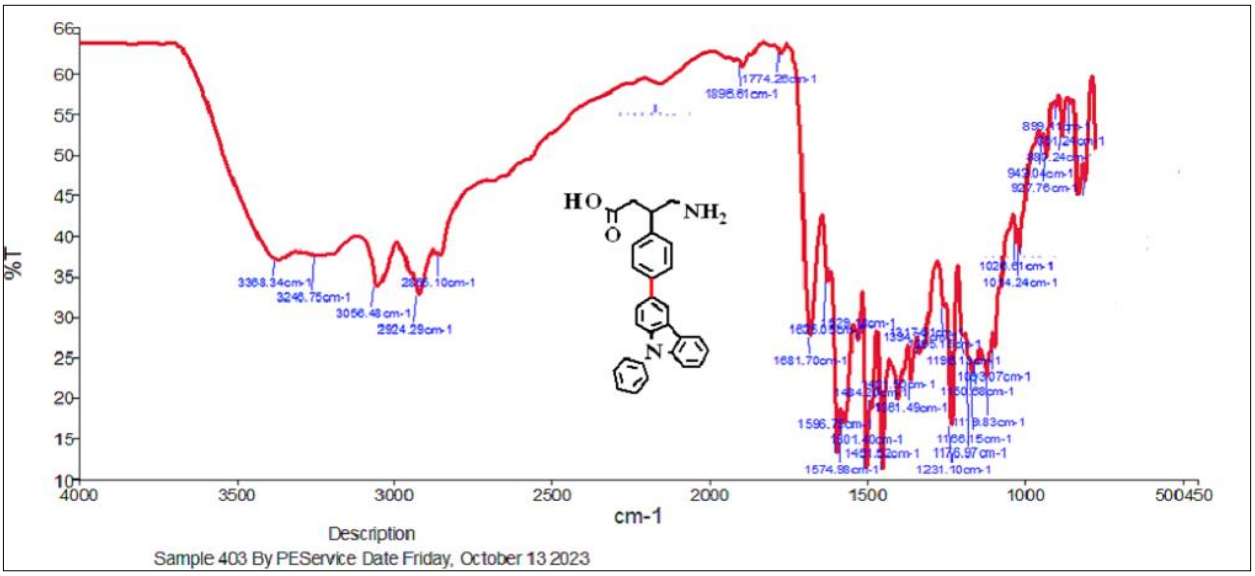


Fig 8: FT-IR spectra of compound [3]

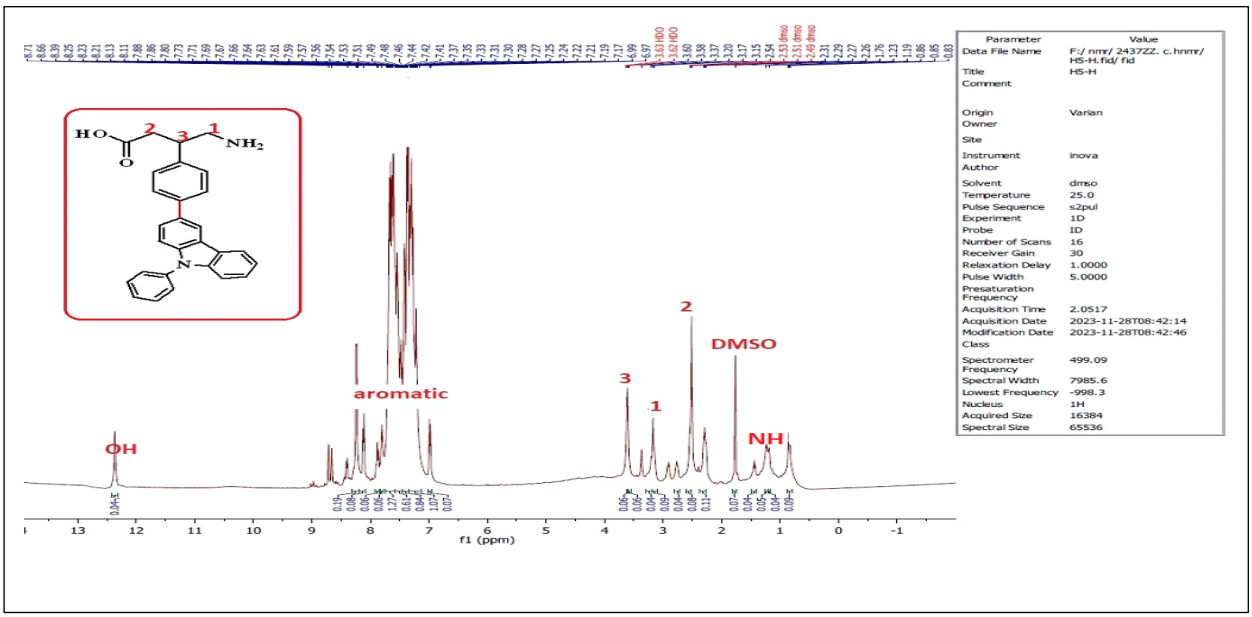


Fig 9 :1H-NMR spectrum of compound [3]

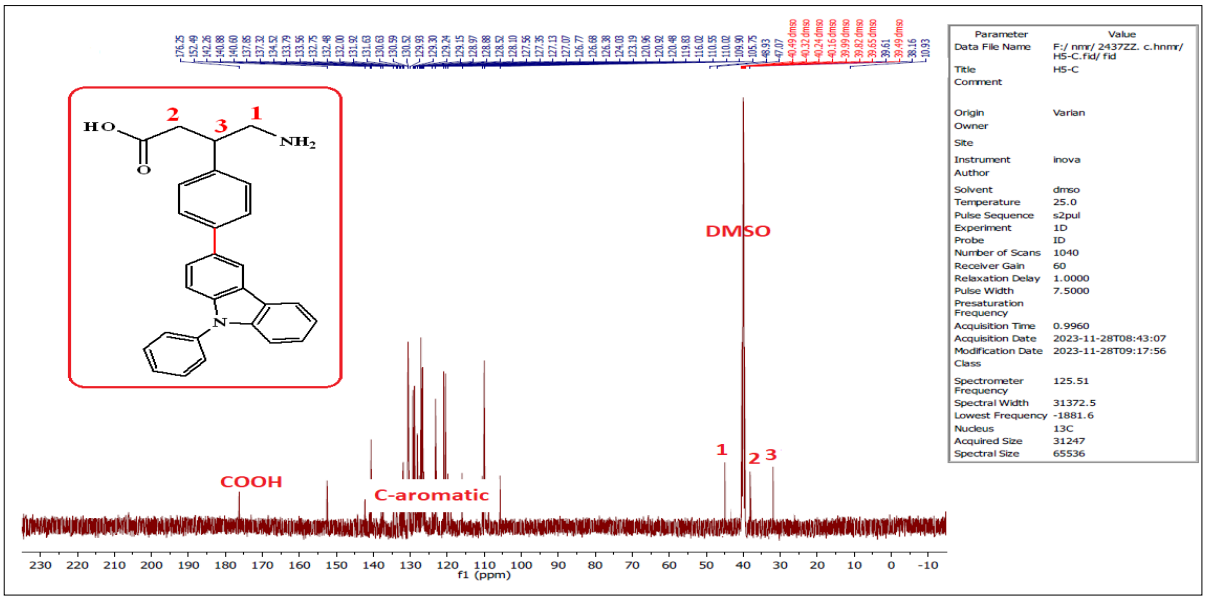


Fig 10 :^{13}C-NMR spectrum of compound [3]

Compound [4]: 4-Amino-3-(4'-(methoxycarbonyl)-2'-nitro-[1,1'-biphenyl]-4-yl) Fig butanoic acid

A total of 3354 [OH], 2925 [C-H], 1487 [C=C], and 1671 [C=O] are the IR [KBr, cm¯1] values. Yellow crystals with a molecular weight of 108-110 Co and an RF intensity of 0.58 are the physical condition of the substance. The values that were acquired via the use of 1H NMR are as follows: 12.40 [s,OH], 1.6 [t,NH], and 7.57–7.71 [d,H-aromatic] are the other values. The computed values for 13C NMR in DMSO-d6 ppm are as follows: 166.9 [C=O], 120-140 [C-

aromatic], and 177.3 [COOH]. Listed below are the values that have been calculated for C18H18N2O6: N equals 7.82, C equals 60.33, and H equals 5.06. It was found that C=59.83, H=4.56, and N=6.32 were all correct.

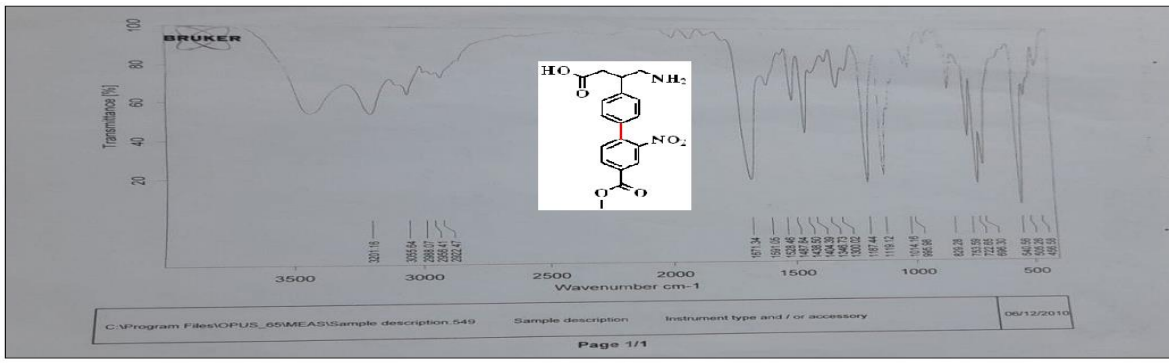


Fig11: FT-IR spectra of compound [4]

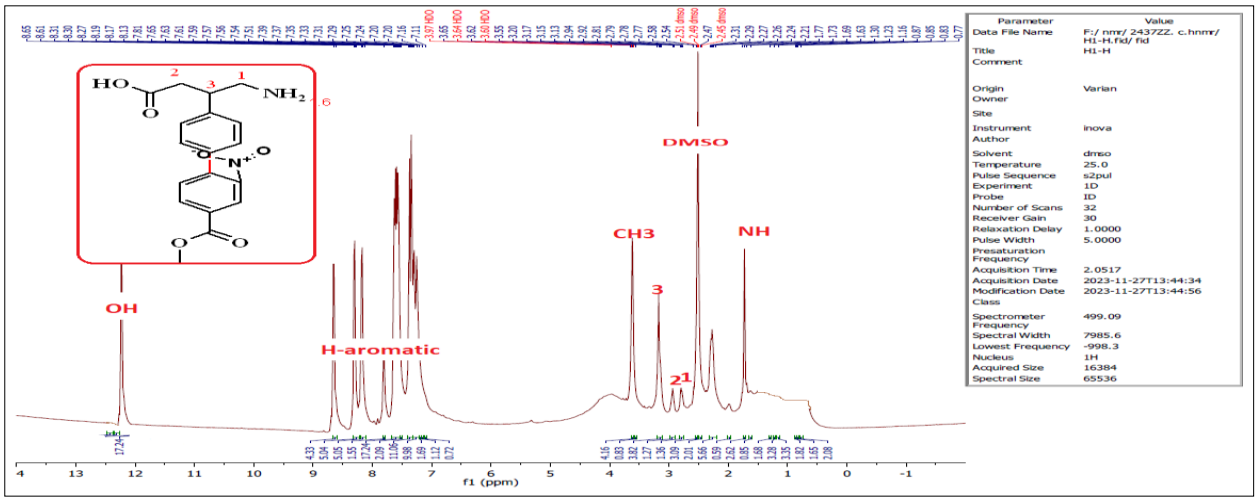


Fig12 :^{1}H-NMR spectrum of compound [4]

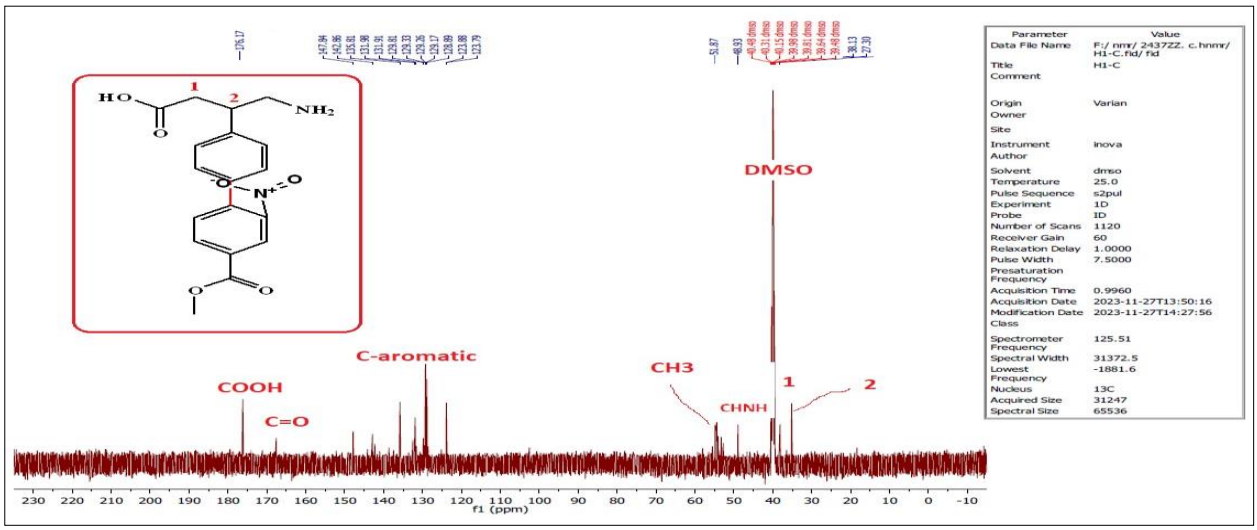


Fig13 :^{13}C-NMR spectrum of compound [4]

Compound [5]: 4-Amino-3-(3'-fluoro-[1,1'-biphenyl]-4-yl)butanoic acid

R.F. [KBr,cm ¯1]: 3377 [OH], 2921 [C-H], 1341 [C-F], 1681 [C=O] is the chemical formula that describes the material's physical state, which is that of brown crystals. Both the molecular weight of the drug, which is 0.64, and the molecular weight of 170-172 Co are both present. The following elements were discovered during the process of studying the 1H NMR spectra of DMSO-d6 ppm: 12.38 [s,OH], 7.43-7.9 [d,H- aromatic], and 1.6 [t,NH]. When DMSO-d6 was present at a concentration of d6 parts per million, the 13C NMR spectra produced 178.3 [COOH] and 120.0-147.2 [C-aromatic]. Although the values that were estimated for C16H16FNO2 were C=70.30, H=5.90, and N=5.12, the actual values that were found to be C=69.7, H=5.2, and N=4.52 were found to be more accurate.

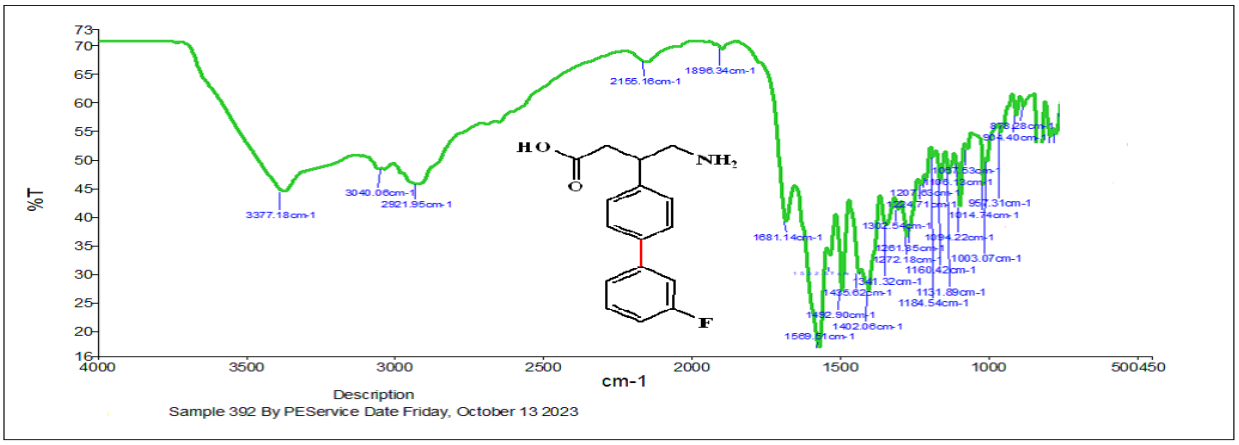


Fig14: FT-IR spectra of compound [5]

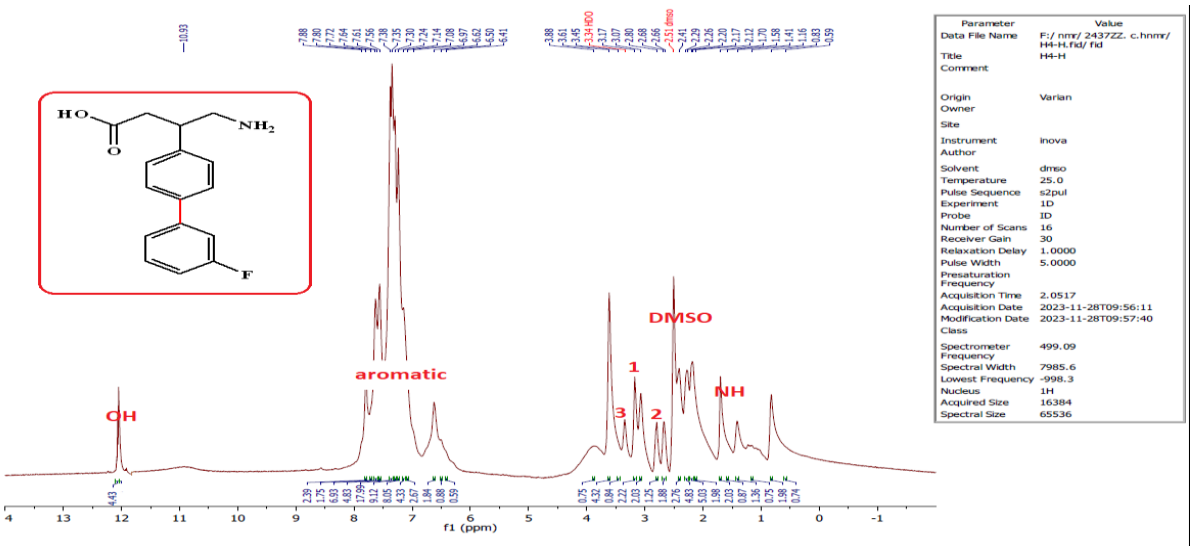


Fig15 :^{1}H-NMR spectrum of compound [5]

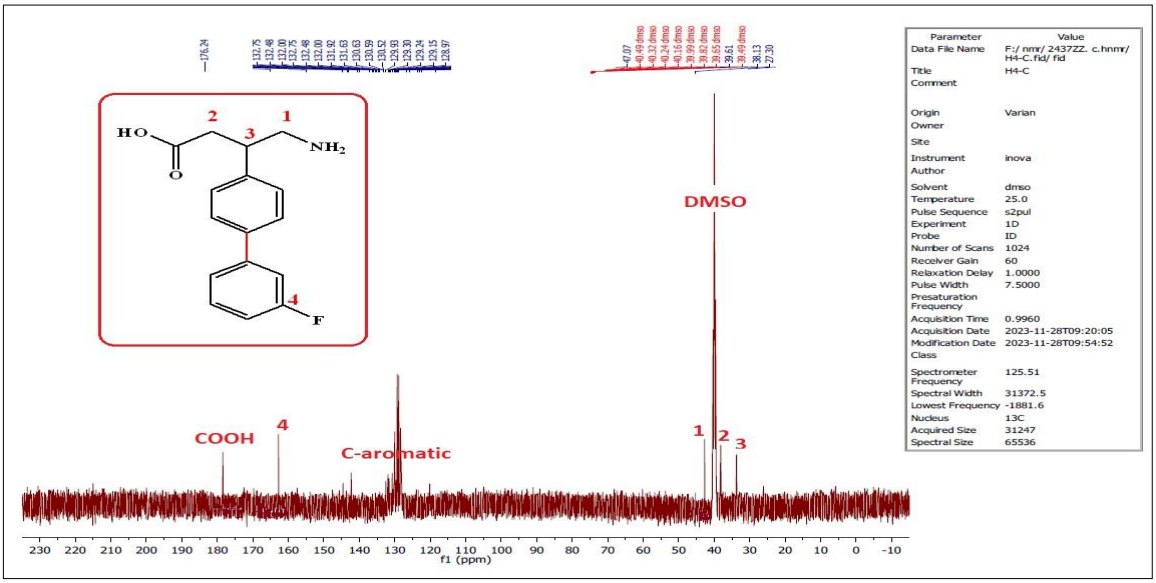


Fig16 :^{13}C-NMR spectrum of compound [5]

Compound [6]: 3-(4'-acetyl-[1,1'-biphenyl]-4-yl)-4-aminobutanoic acid

The chemical formulae for orange crystals are as follows: 3400 [OH], 2922 [C-H], 1572 [C=C], and 1680 [C=O]. The RF of these crystals is 0.46, and their m.p178-180 Co. IR spectrum is composed of the following elements. The 1H NMR spectrum of DMSO-d6 ppm contains 12.4 [s,OH], 7.35 - 8.3 [d,H-aromatic], and 1.4 [t,NH]. These are the elements that are present. The 13C NMR spectra of DMSO-d6 ppm had 197.3 [C=O], 123.0-147.2 [C-aromatic], and 177.3 [COOH]. These were the elements that were present. Listed below are the values that have been calculated for C18H19NO3: N equals 4.71, C equals 72.71, and H equals 6.44. It was found that C=72.11, H=5.74, and N=4.01 were all correct.

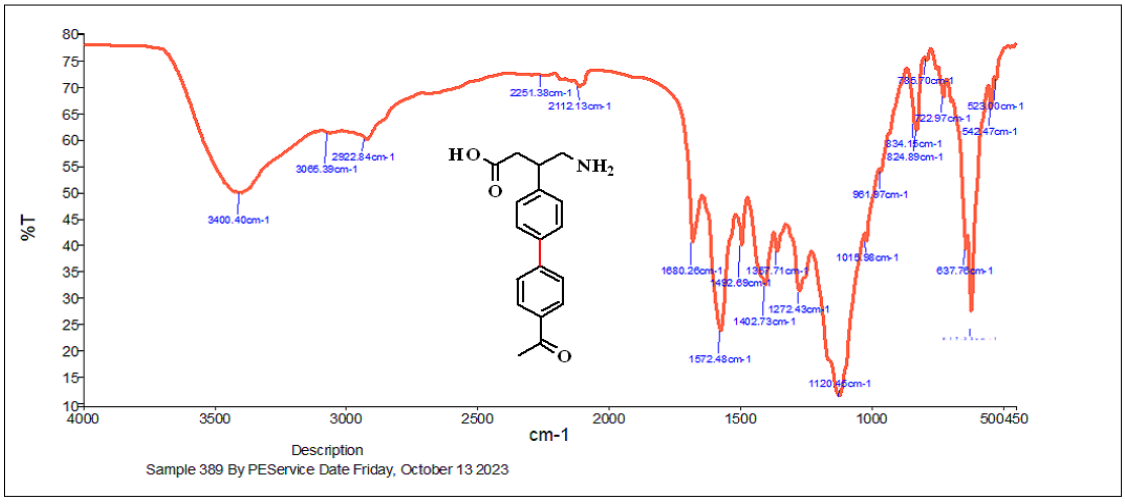


Fig17: FT-IR spectra of compound [6]

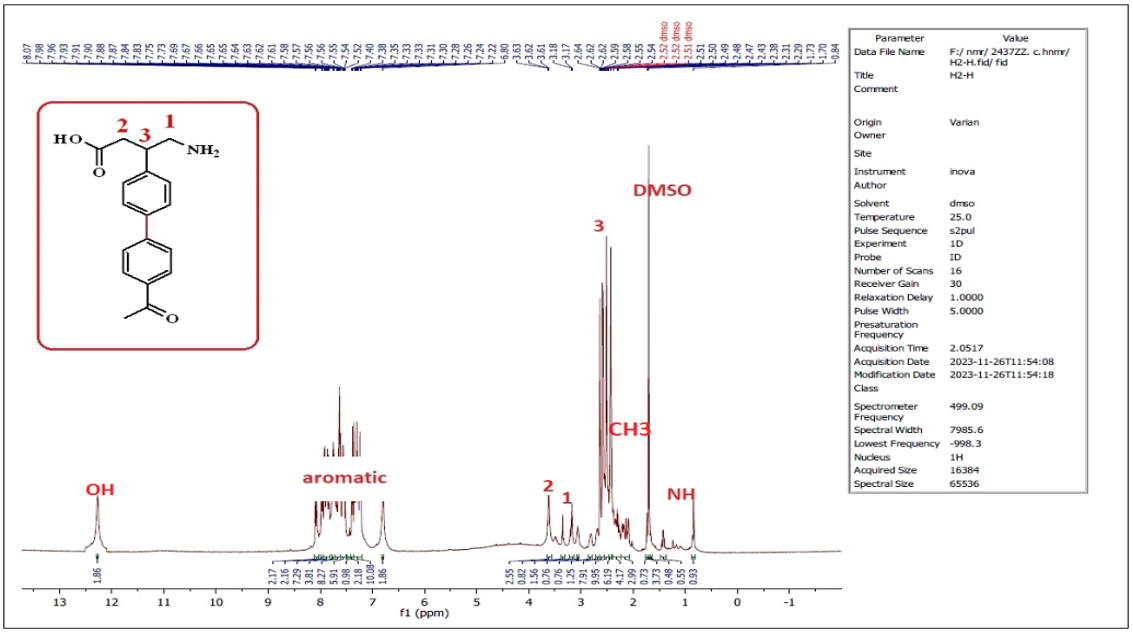


Fig18 :^{1}H-NMR spectrum of compound [6]

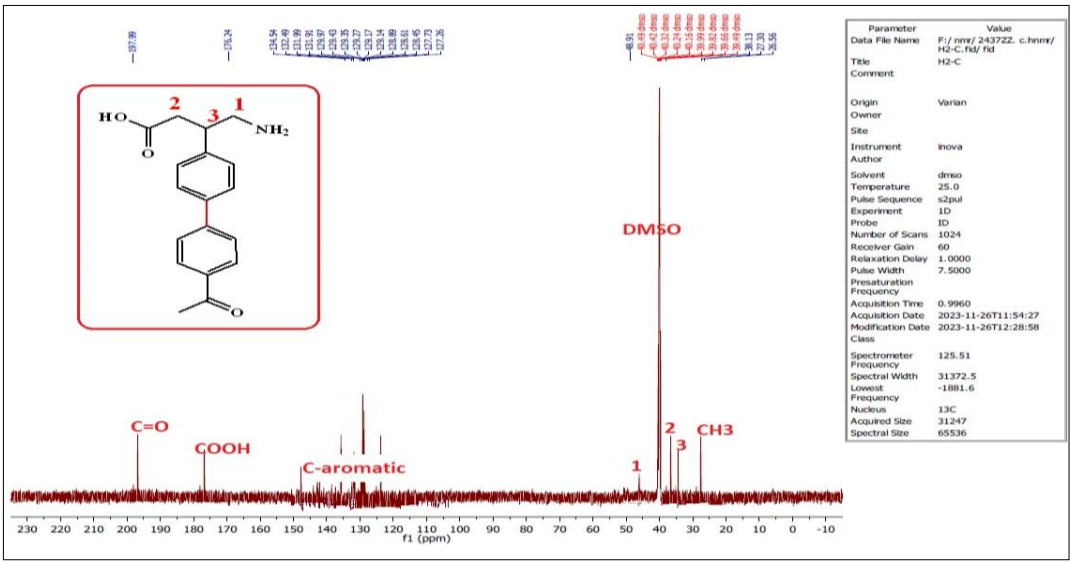


Fig19 :^{13}C-NMR spectrum of compound [6]

Biological activity

In recent years, there has been an increase in the number of bacteria that are resistant to antibiotics. This presents a threat not only to the health of people all over the globe but also to the advancement of civilization. Additional factors that should be taken into account include the fact that there has been a steady increase in the number of antibiotics that are being used. Because of the widespread use of antibiotics, the rapid evolution of bacteria that are resistant to a wide variety of medications, and the lack of new antibiotics that are effective, there is a significant threat that is posed to the health systems of the entire

world as well as to the overall development of the world as a whole. This threat is a significant one. The hazard is exacerbated by each and every one of these elements. Staphylococcus aureus, which was found to be positive, and Escherichia coli, which was found to be negative, were the two types of bacteria that were researched in order to assess the biological effectiveness of these bacteria in comparison to the chemicals that were developed. The results of this investigation were in contrast to the chemicals that were created. In addition, Candida albicans, which is a kind of fungus, was examined to see whether or not it was efficient against the bacteria that were involved in the case. In the aftermath of the conclusion of the examination, the findings were scrutinized, and the analysis was carried out after that. An investigation of the biological activity of substances that prevent the generation of bacteria was carried out via the use of an experiment. Chemicals in question are responsible for preventing the development of bacteria. [1-6].

Table [1]: shows the values of the radii of the inhibition zone (mm) against *Staphylococcus Aureus*.

	Staphylococcus. Aureu	
Derivative symbol	concentration	test results
1	100	28
	50	23
2	100	27
	50	23
3	100	25
	50	18
4	100	28
	50	23
5	100	30
	50	28
6	100	30
	50	29

Table [2]: shows the values of the radii of the inhibition zone (mm) against *Pseudomonas aeruginosa*

Derivative symbol	concentration	test results
1	100	-
	50	-
2	100	9
	50	-
3	100	-
	50	-
4	100	-
	50	-
5	100	-
	50	-
6	100	9
	50	-

Table [3]: Shows the values of the radii of the inhibition zone (mm) against *Candida albicans*

Derivative symbol	concentration	test results
1	100	12
	50	10
2	100	11
	50	0
3	100	12
	50	10
4	100	10
	50	0
5	100	17
	50	14
6	100	14
	50	10

Molecular Docking Study

Throughout the procedure, the application known as Autodock was used in order to examine the molecular docking of [1-6] of the compounds that were created with the protein that is responsible for breast cancer. This would allow for the investigation of the molecular docking of the compounds. In the interest of your convenience, the results of our inquiry are presented to you in Table [4], which you may browse through.

Table [4] shows the results of molecular docking between some compounds and the protein responsible for breast cancer, 2J6M

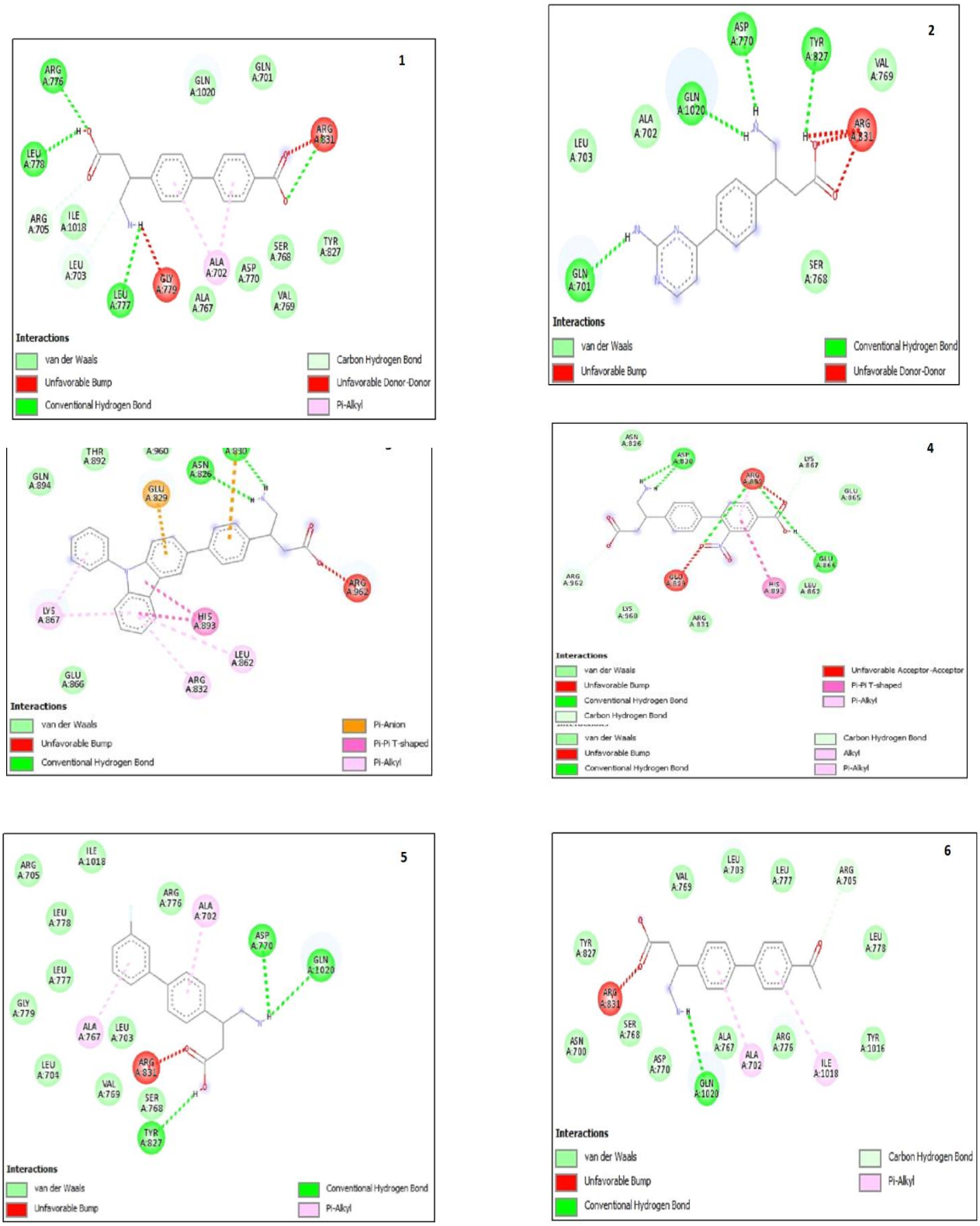
Compound NO.	Lowest Binding Energy	Run
1	-10.20	3
2	7.50	44
3	-9.04	42
4	-10.57	13
5	-8.33	17
6	-8.40	42

Table [5] shows the hydrogen bonds of compounds [1-6] with the protein responsible for breast cancer:

Comp .No	Lowest binding energy	Distance H- A	AA	H- bond NO.
1	-10.20	3.57 1.98 2.71 2.18	ASP770A LEU778A LEU778A TYR827A	4
2	-7.50	1.92 1.78 2.03 2.63	GLN701A ASP770A TYR827A GLN1020A	4
3	-9.04	2.75 2.03	ASN826A ASN826A	2
4	-10.57	3.15 2.03	ASP830A GLU866A	2
5	-8.33	2.65 2.47 3.18	ASP770A TYR827A GLN1020A	3
6	-8.40	2.93 2.61 3.04 2.79	ARG705A TYR827A GLN1020A GLN1020A	4

Table [6] shows the hydrophobic interactions, the salt bridge, and the π-bond of compounds [1-6] with the protein responsible for breast cancer

Comp .No	Lowest binding energy	Salt Bridges	π-Stacking	Hydrophobic Interaction AA
1	-10.20	ARG705A ARG776A ARG831A	_	3.37 ALA702A 3.85 LEU703A 3.32 ASP770A 3.94 ARG776A 3.92 ILE1018A
2	-7.50	ARG962A	_	3.99 ASP770A 3.67 GLN1020A
3	-9.04	ARG831A	HIS893A ARG831A	3.86 GLU829A 3.77 ARG832A 3.12 LEU862A 3.53 LYS867A 3.19 LYS867A
4	-10.57	ARG 962A LYS 867A ARG 832A	HIS 893A	3.78 GLU 829A 3.29 ARG 832A
5	-8.33	ARG831A	_	3.82 ALA702A 3.98 ALA767A
6	-8.40	ARG831A	_	3.52 ALA702A 3.85 ASP770A 3.71 ILE1018A



Fig[19]:The docking interactions of compounds [1-6] with the catalytic site of PKL1 enzyme by molecular docking technology

Conclusions

Following are the findings that we have uncovered as a consequence of our investigation: The results of the investigation demonstrate that a Suzuki-Miyaura cross-coupling process was used in order to generate a diverse assortment of Baclofen derivatives. By using the reflex approach, baclofen was exposed to a variety of boronic acids during the course of the experiment. This was then followed by the addition of Pd(0)(PPh3)4, and finally, once the reaction had cooled down, EtOAc was added as the last step.This was accomplished by the use of IR, 1H NMR, and 13C NMR spectra, in addition to elemental analysis, in order to provide a spectrally based explanation of the process and the components of the molecule. This is something that can be discussed from a biological point of view. Although the results of the biological activity study were confirmed by the molecular docking simulation, which also offered an explanation of the nature of the interactions that take place between the molecule and the active area of the protein, the findings of the research on biological activity were supported by the simulation. As an additional point of interest, the simulation served to confirm the findings of the research.to v.

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