REPUBLIC OF TURKEY
ERCIYES UNIVERSITY
GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES
DEPARTMENT OF CHEMESTRY

REACTION OF *N*-(AMINOAMIDINO)THIOUREA DERIVATIVES WITH DIMETHYLACETYLENE DICARBOXYLATE

Prepared by
IHAB ADNAN SALMAN AL-JANABI

Supervisors
Prof. Dr. Şaban PATAT
Prof. Dr. Emin SARIPINAR

MSc. Thesis

January 2018
KAYSERİ

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January 2018
KAYSERİ

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IHAB ADNAN SALMAN AL-JANABI

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The M.Sc. Thesis entitled **"Reaction of *N*-(aminoamidino)Thiourea Derivatives with Dimethylacetylene Dicarboxylate''** has been prepared in accordance with Thesis Proposal and Writing Guidelines of Graduate School of Natural and Applied Sciences of Erciyes University

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This study entitled **"Reaction of *N*-(aminoamidino)Thiourea Derivatives with Dimethylacetylene Dicarboxylate** has been prepared by **IHAB ADNAN AL-JANABI** under the supervision of Prof. Dr. Şaban PATAT & Prof. Dr. Emin SARIPINAR was accepted by the jury as a M.Sc. thesis in Department of Chemistry, Graduate School of Natural and Applied Science, Erciyes University.

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Director of the Institute

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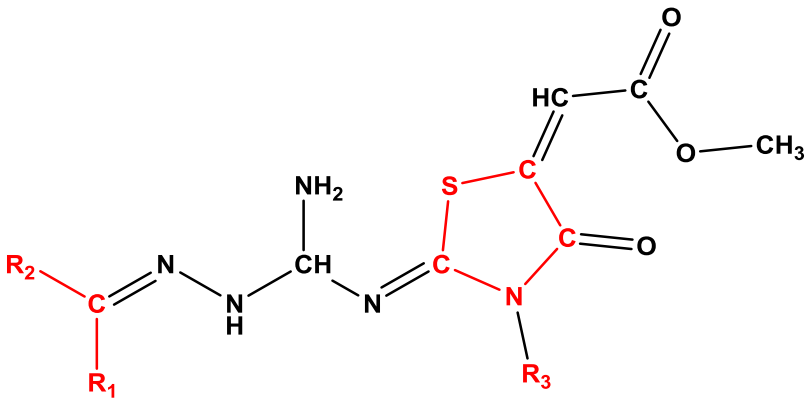
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IHAB ADNAN SALMAN AL-JANABI

Erciyes University, Graduate School of Natural and Applied Sciences
M.Sc. Thesis, January 2018
Supervisors: Prof. Dr. Şaban PATAT & Prof. Dr. Emin SARIPINAR

ABSTRACT

Dimethyl acetylenedicarboxylate (DMAD) has been used in numerous heterocyclic arrangements and considered as an essential building in a natural union. In this work, a short and productive one-pot reaction of 4-isothiazolidine-5-ylidene acetic acid derivation is described. A green and effective technique for the a mixture of more up to date 4-isothiazolidine-5-ylidene acetic acid derivation (IHB 1-16, yield 38-85%)N-(arylideneamino)-N-(arylthiocarbamyl) guanidine (AGII 1- 22) with diethylacetyylenedicarboxylate has been created in methanol by refluxing. We would like to investigate the synthesis of thiazoline compounds from thiocarbamoyl guanidines derivatives possessing N-H groups and S=C bond which react with DMAD to give highly functionalized 4- oxothiazolidin-5-ylidene acetate derivatives. In this reaction, both sulfur group and amino group are capable to react with DMAD. It was found that thiourea react with DMAD exclusively with sulfur atom. The structure of the new compounds was established by IR and NMR spectroscopy.



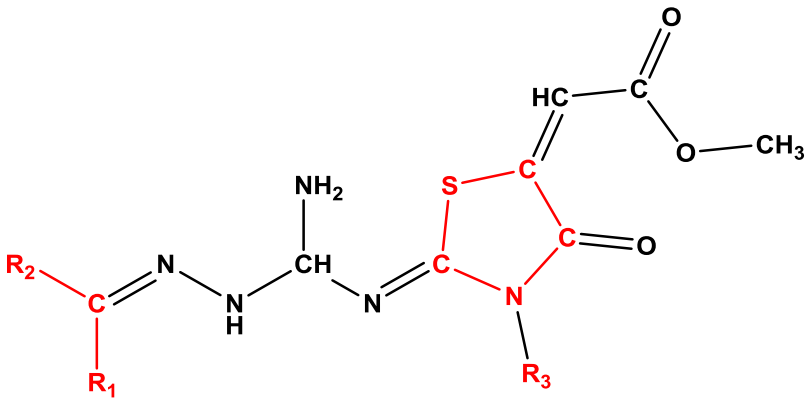
Keywords: Aminoamidino, Thiourea, Dimethylacetylene Dicarboxylate, DMAD, 3-Methoxyphenyl, Nitrobenzylidene, Naphthalen, Dimethylamino

DİMETİLASETİLEN DİKARBOKSİLATIN *N*-(AMİNOAMİDİNO)TİYOJRE TÜREVLERİ İLE REAKSİYONU

IHAB ADNAN SALMAN AL-JANABI
Erciyes Üniversitesi, Fen Bilimleri Enstitüsü
Yüksek Lisans Tezi, Ocak 2017
Danişmanlar: Prof. Dr. Şaban PATAT, Prof. Dr. Emin SARIPINAR

ÖZET

Dimetil asetilenkarboksilat (DMAD) sayısız heterosiklik düzenlemelerde kullanılmıştır ve doğal bir birleşmede önemli bir yapı olarak düşünülmüştür. Bu çalışmada, 4-isothiazolidine-5-ylidene acetic acid türevlerinin tek kademede kısa ve etkili tek-kap reaksiyonu anlatılmıştır. Yeni 4-isothiazolidine-5-ylidene acetic acid (IHB 1 - 16, yield 38 - 85%) türevlerinin çevreci ve etkili sentezi N-(arylideneamino)-N-(arylthio carbamoyl) guanidine (AGII 1- 22) ile DMAD'nin geri soğutucu altında metanolde kaynatılması ile elde edilmiştir. DMAD ile tepkimeye girerek N-H gruplarına ve S = C'ye sahip olan tiokarbamoil guanidin türevlerinden tiazolin bileşiklerinin sentezi araştırılmıştır, böylece oldukça işlevselleştirilmiş 4- oxothiazolidin-5-ylidene acetate türevleri elde edilmiştir. Bu reaksiyonda hem sülfür grubu hem de amino grubu DMAD ile reaksiyona girebilir. DMAD ile Tiyoüre'nin sadece sülfür atomunun reaksiyona girdiği anlaşılmıştır. Yeni bileşiklerin yapısı IR ve NMR spektroskopisi ile aydınlatılmıştır.



Anahtar Kelimeler: Aminoamidino, tiyoüre, dimetilasetilendikarboksilat, DMAD, 3-metoksifenil, nitrobenziliden, naftalin, dimetilamino

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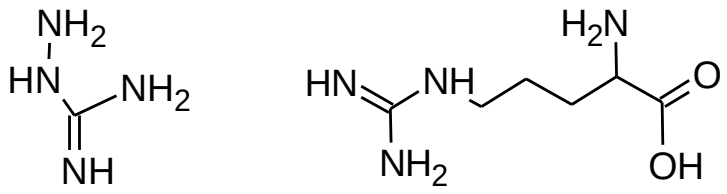
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INTRODUCTION

Aminoguanidine was discovered more than 100 years ago. Aminoguanidine is one of many derivatives of guanidine but it has many properties in common with hydrazines and is therefore often classified as hydrazine. Furthermore, AMG restrains NO synthase especially the inducible NO synthase isoform making AMG an essential pharmacological instrument. The inducible NO synthase isoform is related with generation of vast amounts of NO synthase in light of e.g. cytokines. At the point when these impacts of AMG were unveiled the first discovered effect is the inhibition of diamine oxidase which catalyzes the oxidative deamination of biologically active deamines such as histamine and putrescine. This chemical catalyzes debasement of organically dynamic diamines, for example, histamine what's more, putrescine. Information got from thinks about utilizing AMG ought to be translated with safety measure since this substance meddles with a few essential administrative frameworks [1]

Aminoguanadine (AMG) is a guanidine derivative, which has been known for about 100 years, and is included in the class of hydrazine compounds. AMG is structurally similar to L-arginine amino acid. The chemical structure of AMG and L-Arginine is shown in Figure 1, and L-Arginine contains the guanidine group. This compound is an important molecule in the formation of 1-Naphthisothiocyanate and 3-methoxy phenyl isothiocyanate (-OR) by the catalytic action of 1-Naphthisothiocyanate and 3-methoxy phenyl isothiocyanate synthase (-OR) [1]



Aminoguanidine L-Arginine

Figure 1. Chemical Structure of Aminoguanidine and L-Arginine

Recent studies have revealed that aminoguanidine and its derivatives have important biological effects. These compounds are generally found to have biological effects such as inhibition of diaminoxidase. It has been shown in different animal models that AMG, a potent antioxidant, has beneficial effects against possible complications. In addition, clinical trials are underway for the use of AMG. Studies have also been conducted on the possibility that AMG can be used against Alzheimer's and parkinson's diseases. It has been found that AMG is an anticatactic activity characteristic in cataract-formed rats. In recent times, AMG appears to be a new and hopeful compound that is retarding aging. It has been found that age-related vascular stiffness is reduced by AMG administration [2]

AMG may additionally be set up through hydration or hydrolysis of mixes identified with guanidine. AMG is one of numerous subordinates of guanidine yet it has numerous properties in a similar manner as hydrazines. It is along these lines regularly delegated a hydrazine. AMG ties chloride and sulfate particles shaping water solvent salts. The synthetic structure of AMG is appeared in Fig. 1. As can be seen AMG is fundamentally identified with the amino corrosive L-arginine from which the naturally imperative particle N=C=S is determined by means of the synergist activity of N=C=S synthase [3]

AMG and some of its subsidiaries might be utilized as explosives, a finding perceived by Thiele as of now in 1892. At the time at the point when Lieber and Smith composed their audit almost no was thought about the organic activities of AMG. Quickly, they realized that AMG directed to creatures could influence blood weight, respiratory rate and sufficiency, and caused changes in blood picture taking after vindictive iron deficiency. The first noteworthy organic impact of this compound (AMG) was revealed in the 1950 when it was demonstrated that AMG hindered diamine oxidase (histaminase), which catalyzes the oxidative deamination of the organically dynamic diamines histamine and putrescine. And discuss the treatment of hydralazine and its interaction with some compounds and clarify the negative and positive cases[3]

Aminoguanidine (AG) has been proposed as a specialist of potential advantage in the prophylaxis of the diabetic complexities of a kidney, nerve, and eye. AG

has been appeared to reduce the arrangement of collagen-connected fluorescence related to the creation of cutting edge glycosylation end products (AGE). AG has been hypothesized to piece neurotic tissue adjustments by means of hindrance of pernicious long haul changes to proteins related with hyperglycemia[4]

AG has been referred to as a "virtually non-toxic nucleophilic hydrazine. While these observations of the low toxicity of a potentially useful compound are encouraging, some caution needs to be observed when using it.

Biological effects of Aminoguanidine

Aminoguanidine (AG) is a compound that inhibits inducible nitric oxide synthase (iNOS), which is structurally related to the amino acid of L-Arginine, known for a long period of time, resulting in reduced nitric oxide (NO) formation. Important biological effects of AG have been discovered in the past years. The first biological effect to be discovered is the inhibition of diamine oxidase, which catalyses the oxidative deamination of active diamines such as histamine, putrescine. AG is an effective antioxidant and free radical scavenger. It prevents the formation of lipid peroxidation in AG cells and tissues. Many researchers have tried to explain the role of AG in the cardiovascular system through these properties. Regulation of the NO donor tone plays an important role in regulating endothelial integrity and permeability and regulating myocardial contractility.it was aimed to observe the effects of AG on the cardiovascular system.**[5]**

Firstly, AMG inhibits, invitro and in vivo, a formation of highly reactive advanced glycosylation end products (AGEs) associated with the pathogenesis of secondary complications to diabetes and with cardiovascular changes in aging. AMG ameliorates various complications to diabetes and prevents age related arterial stiffening and cardiac hypertrophy, effects probably dependent on inhibition of AGEs formation.

AMG restraints, invitro and in vivo, a development of profoundly receptive propelled glycosylation finished results (AGEs) related with the pathogenesis of optional complexities to diabetes and with cardiovascular changes in maturing. AMG enhances different inconveniences to diabetes and counteracts age related blood vessel solidifying and cardiovascular hypertrophy, impacts most likely reliant on restraint of AGEs development.

Secondly, AMG inhibits NO synthase particularly the inducible NO synthase isoform making AMG an important pharmacological tool. The inducible NO synthase isoform is associated with production of large quantities of NO synthase in response to e.g. cytokines. When these effects of AMG were disclosed it had already been known for many years that AMG, in nM concentrations, inhibits diamine oxidase

Besides, AMG restrains NO synthase especially the inducible NO synthase isoform making AMG a critical pharmacological device. The inducible NO synthase isoform is related with the creation of substantial amounts of NO synthase in light of e.g. cytokines. At the point when these impacts of AMG were unveiled it had just been known for a long time that AMG, in nM fixations, represses diamine oxidase

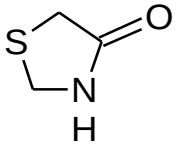
This enzyme catalyzes degradation of biologically active diamines such as histamine and putrescine. Data obtained from studies using AMG should be interpreted with precaution since this substance interferes with several important regulatory systems.

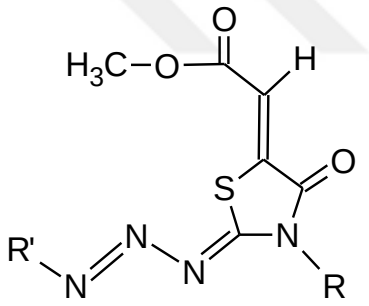
This chemical catalyzes corruption of naturally dynamic diamines, for example, histamine and putrescine. Information acquired from thinks about utilizing AMG ought to be translated with precautionary measure since this substance meddles with a few critical administrative frameworks.[1]

The thiazole ring is a notable part of numerous organically dynamic mixes with showed antimicrobial, antifungal, and calming properties[6]

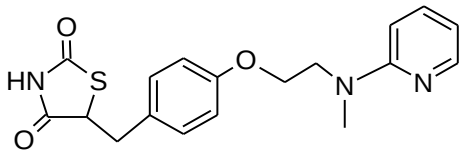
A progression of new thiazole subsidiaries were outlined and blended, and their inhibitory exercises were measured against a human. Of all the tried aggravates, various thiazole subsidiaries bearing an oxalic corrosive gathering at 4-position were observed to be powerful inhibitors esteems at low micromolar level. The nitty-gritty structure–activity connections were broke down and the coupling components of a compound. The consequences of this examination would give instructive direction to additionally improving thiazole subordinates as intense inhibitors[7]

Thiazolidines and derivatives such as guanidines are new oral antidiabetic class drugs used in Type 2 diabetes patients [3]. Thiazolidin-4-one is widely used as an intermediate in the synthesis of basic skeletal heterocyclic compounds. Activities such as anticancer, anti-inflammatory, antimicrobial antitension, antimantar, antituberculosis, antiaids are known as well as the synthesis of thiazolidinler dyes **[8].**

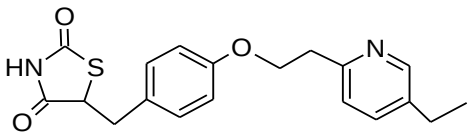




Avandia (rosiglitazone) and actos (pioglitazone) are an oral diabetes drug used to control the level of sugar in the blood [5].



Rosiglitazone



Pioglitazone

In some of the compounds developed over the last decade, it has been observed that both the Aminoguanidine structure and the new compounds containing the thiazole ring have biologically directed conservation. It is intended to synthesize novel compounds

which are promising biological activity with the above-mentioned activity, as well as new and effective Aminoguanidine structure which is promising for the treatment of the mentioned diseases

The heterocyclic compounds which form half of the organic materials are highly conservative. Heterocyclic compounds are found in the building of biologically active substances such as drugs, most vitamins, natural substances, attitude-mens, antibiotics, and antidiabetic. Part from these, they are also important compounds for paint, sensor and polymer materials. Acetylene derivatives are one of the materials used in the synthesis of important heterocyclic compounds. There are many studies on this subject.

Polyfunctionalized heterocyclic compounds are highly conservative for drug trials. In recent years, 68% of the substances in the market are heterocyclic compounds. Thus, in this work, a synthesis strategy for the synthesis of novel polyfunctionalized 4-oxo-1, 3-thiazolidin-5-ylidene acetate compounds has been developed.

CHAPTER1

GENERAL INFORMATION

1.1. Literature Studies

1.1.1. Properties of Dimethylacetylenedicarboxylate

Dimethyl acetylenedicarboxylate, commonly abbreviated as DMAD, is an electro-deficient alkyne diester. This ester, which exists as a liquid (density: 1,156 g/mL, 25 °C) at room temperature (boiling point: 95–98 °C), is highly electrophilic. As such, DMAD is used as a dienophile and a dipolarophile in cycloaddition reactions. Today, it is being used increasingly in chemical synthesis as it has proven useful in carbon–carbon bond formations. DMAD is an extremely versatile tool for organic chemists and completely new avenues have been explored for its use in combinatorial and multicomponent chemistry and heterocyclic synthesis. Following the pioneering discovery by Diels and Alder. The reactions of dimethyl acetylenedicarboxylate with heterocyclic compounds have been the subject of a great number of publications[9]

Dimethylacetylenedicarboxylate (DMAD) has been used in the synthesis of strongly reactive heterocyclic compounds for over 135 years. Over the last 10 years, the number of studies on this compound has increased. DMAD is used in the synthesis of various organic compounds. At the beginning of the most important reactions are Michael reactions to nucleophiles such as S, N and C.

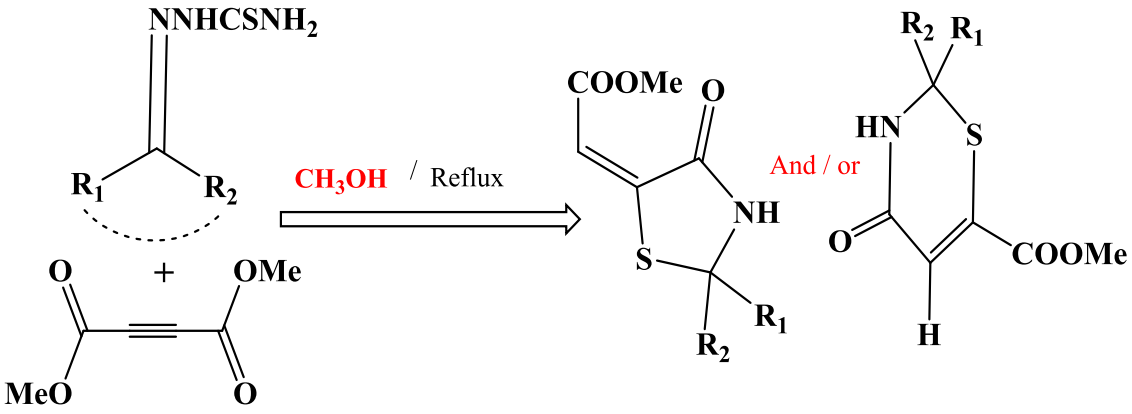
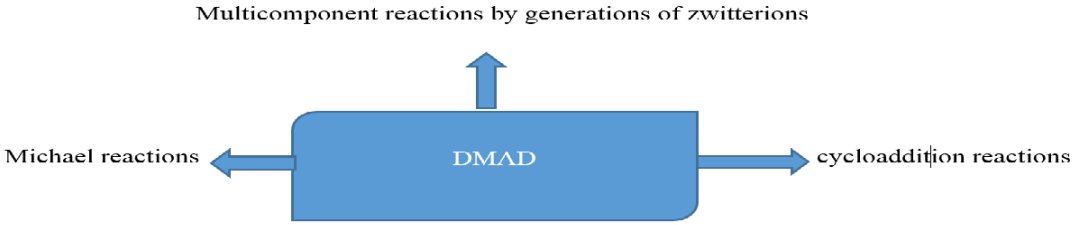


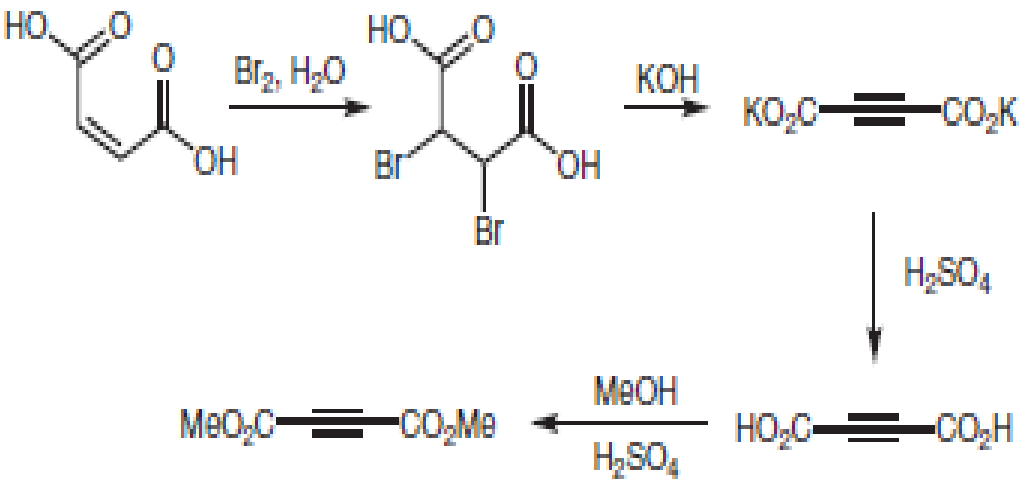
Figure 2. Graphical Abstract

Late writing cases that are both illustrative of the energy of this reagent in the development of complex heterocyclic atoms and essential for the plan of manufactured systems toward common or planned targets are talked about thus.[9]

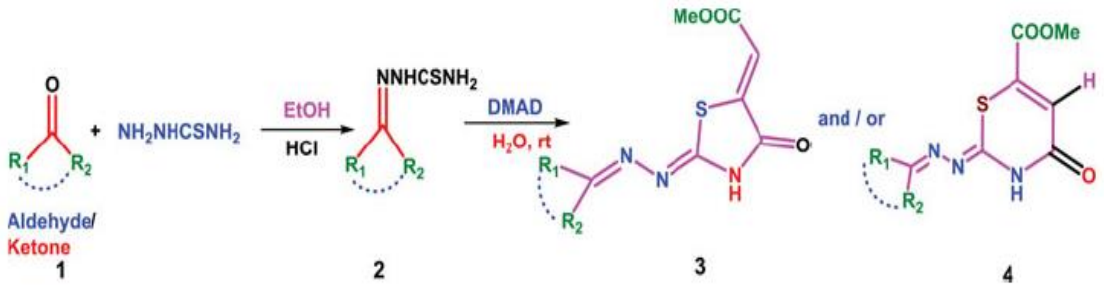


Other important reaction types are known to be multidentate reactions with amines and isocyanates.

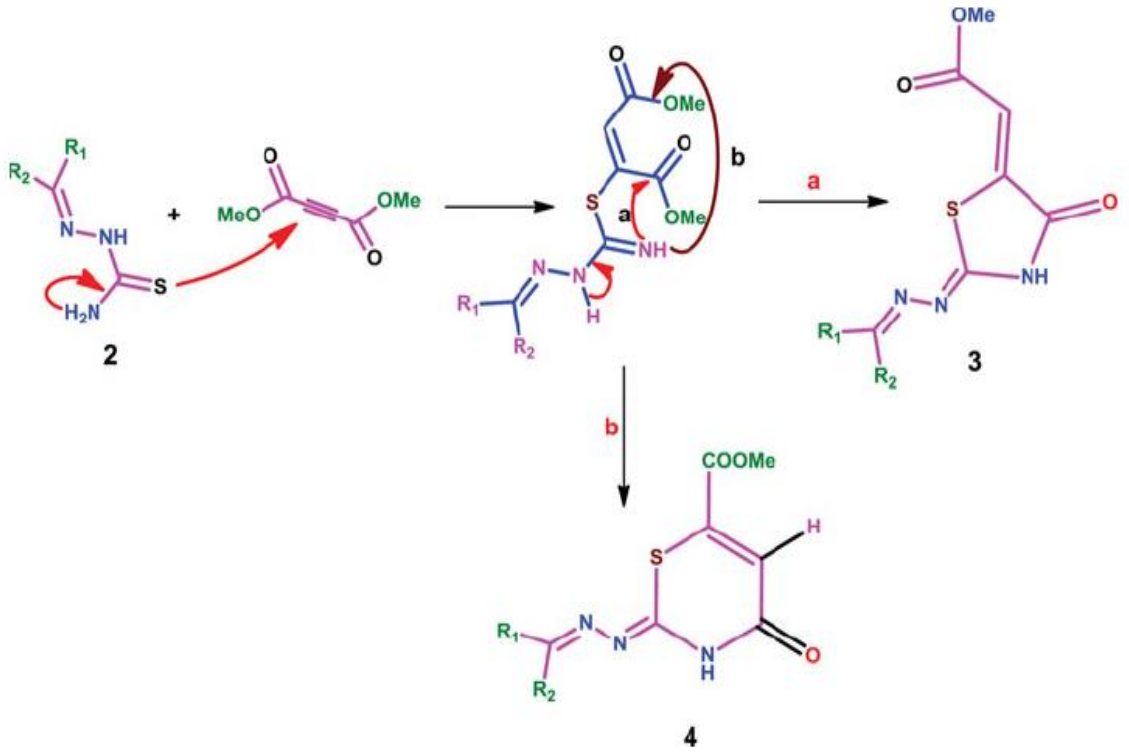
The DMAD compound can be obtained by first brominating maleic acid with dehydrohalogenation reaction. The following equation is obtained [10]



This compound can be viewed as electronically rich since it is an acetylene subordinate, yet the electron-drawing in bunches rely upon the triple cling to electronically corrupt its position. Huge responses of DMAD are given beneath.

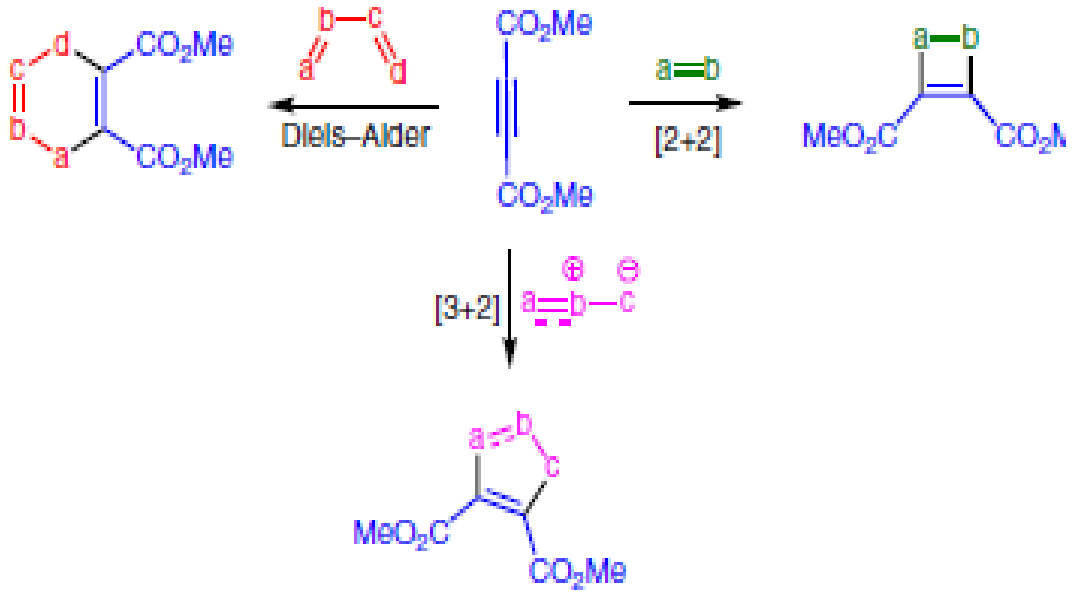


Synthetic route to synthesis of thiazolidin-4 -one derivatives 3



1.1.2. Cyclization Reactions

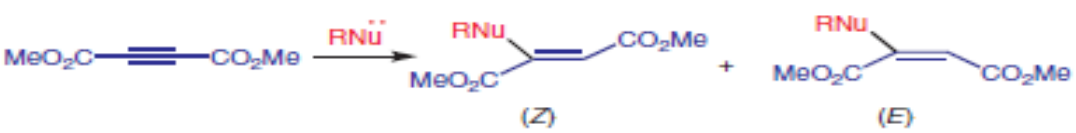
One of the other imperative responses of dimethylacetylenedicarboxylate is cyclization responses. While giving [4 + 2] cyclopropane with different dienes, it gives five rings with 1, 3-dipolar substances. It likewise gives [2 + 2] cyclization responses [10]The response condition is demonstrated as follows.



DMAD is an electron-poor alkyne diester. DMAD is used as dienophile and dipolarophile in cycling reactions. It is also widely used in the formation of C-C bonds [10]

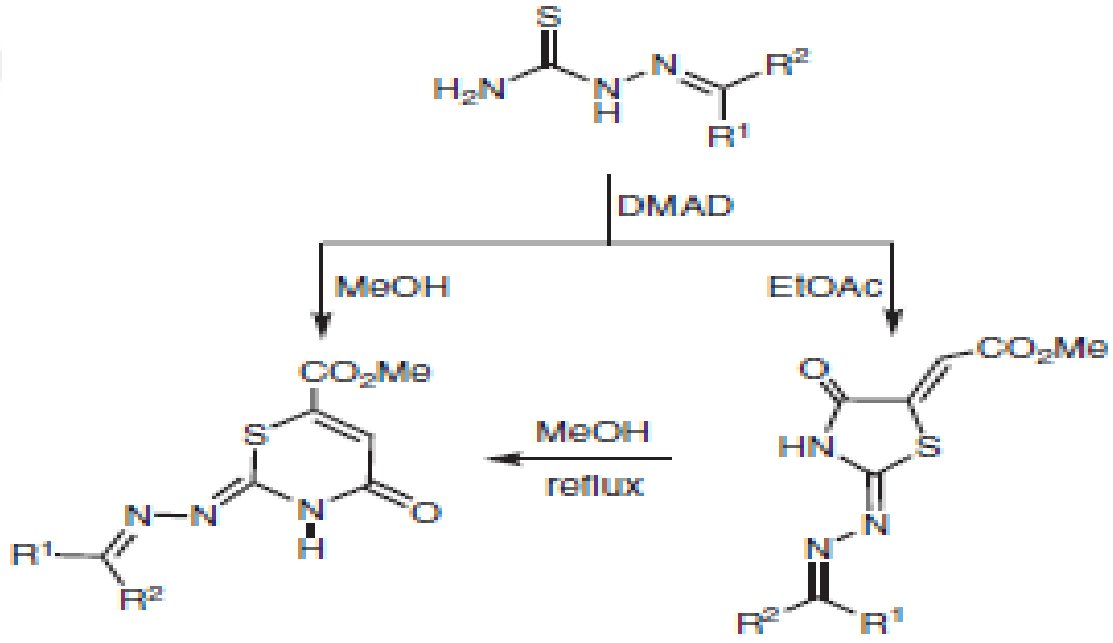
1.1.3. Michael Reactions

DMAD can be responded with different nucleophiles, for the most part S and N. DMAD is a solid Michael acceptor, for the most part since it responds with different nucleophiles containing sulfur and nitrogen. Since the triple bond frames a conjugated structure with the carbonyl gatherings, the Michael acknowledges the nucleophiles in light of the fact that they give Michael-sort responses. The condition is demonstrated as follows. After the expansion response, they may likewise give a cyclization response by losing the –OMe or - CO_2Me bunches [6]



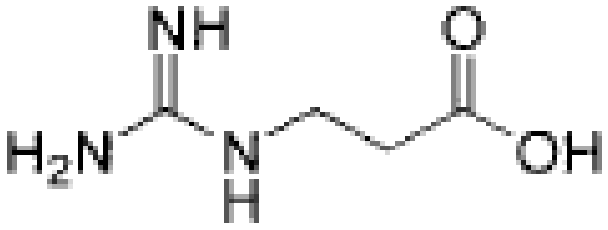
In these responses the general system is to utilize DMAD as a Michael acceptor. On the off chance that there is a moment bunch equipped for assaulting the nucleophile utilized, the DMAD responds to the ester gathering and responds by cleavage of the OR gathering. With this compound, mixes, for example, quinoline, isoquinoline, thiazole,

imidazole, quinoxaline, pyridazine, pyrimidine, and substituted subsidiaries thereof are integrated. Mixes, for example, thiazole, thiazolidine, thiazolidinone and thiazinone which are profoundly dynamic in the organic course are combined in the response of dimethylacetylenedicarboxylate with thioamidines, thiosemicarbazides and sulfur-containing nucleophiles, for example, thiourea.and afterward the ester gather aminolysis responses with 1, 3-thiazolidin-4-one mixes are orchestrated [6]. As demonstrated as follows, 1, 3-thiazol-4-one is acquired in the response of different thiosemicarbazone subsidiaries with DMAD [6]The response condition is given underneath.



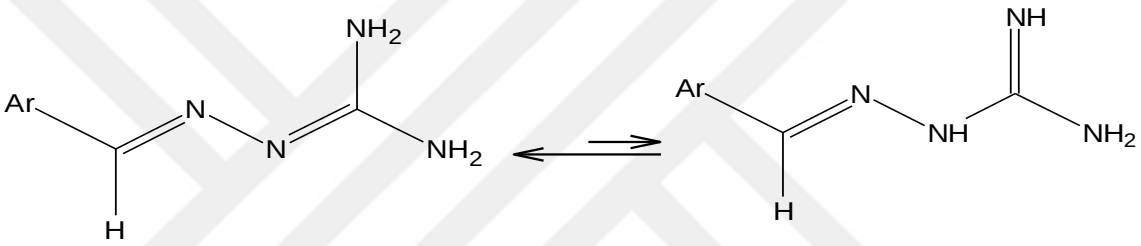
1.2. Aminoguanidine

3-guanidine propionic corrosive has been found to cause both insulin and weight reduction. It has additionally been observed to be powerful in both creatine transport and creatine kinase action [11]



3-guanidinone propionic acid

Guanylhydrazones, otherwise called aminohydrazones coming about because of buildup responses of oxino mixes of the aminoguanidine (aldehyde, ketone) are gotten. These mixes have antiprotozoal, antibacterial, antimalarial, trypanocidal, antisecretory, antidetic, anticoagulant, antihypertensive, antiviral, antileukemic, cardiotonic, anticancer exercises. Late examinations have revealed that there might be new tumor drugs. It is additionally utilized for the union of critical heterocyclic mixes other than restorative herbs. These mixes demonstrate the hydrazone tautomer of the 1, 3-H skeleton azine as demonstrated as follows.

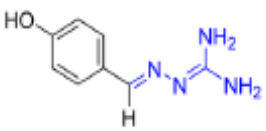


Azin Shape **Hidrazon Shape**

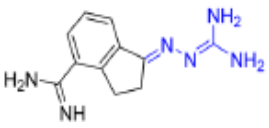
2, 3-diaza-1, 3-butadiene

Figure 3. Two possible tautomeric forms of guanyl hydrazones

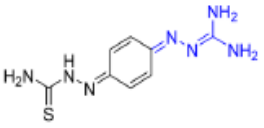
Azine tautomers were observed to be 3-8 kcal/mol more constant than hydrazone tautomers. The following are some imperative guanidine subsidiaries that are dynamic in the natural pathway [8].



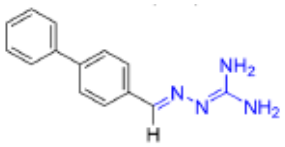
MAO Inhibitor



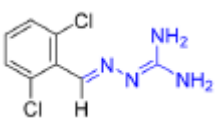
SAMDC Inhibitor



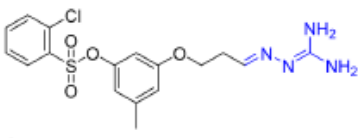
Antiseptic Agent



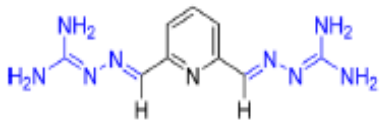
Antibacterial Agent



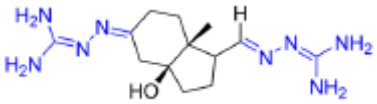
Antihypertensive Agent



Thrombin Inhibitor



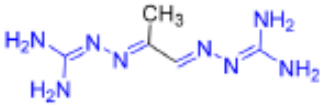
Trypanocidal agent



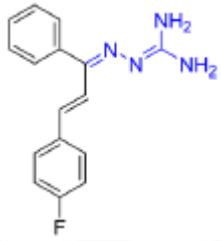
Inotropic Agent



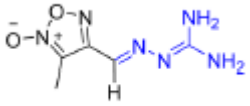
Antimalarial Agent



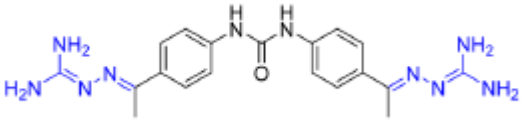
Anticancer Agent



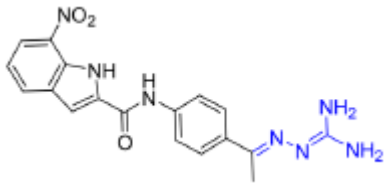
Ant tubulin Agent



High Energy material

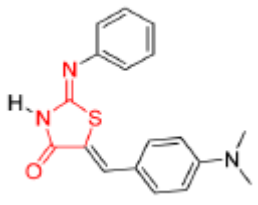


Chk Inhibitor (NSC 10956555)

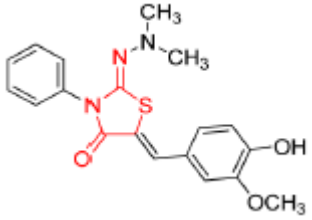


Chk Inhibitor (PV 1019)

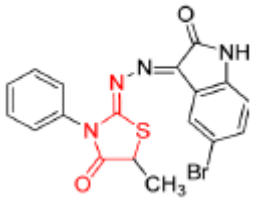
2-iminothiazolidin-4-one center is viewed as an organically dynamic gathering of pharmacophores and their blend is appeared to be a vital issue in natural science. This center has an extensive variety of organic action as demonstrated as follows. Anticancer dynamic mixes, for example, S1P1 receptor agonist, antiaids, antidiabetic, antitumor, calming cardiovascular impact, antimicrobial, tuberculosis, antihypertension, antibacterial. Some of these mixes are given beneath [9].



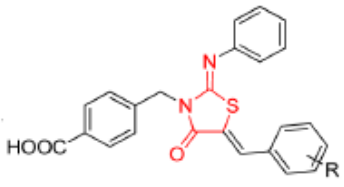
Anticancer Activity



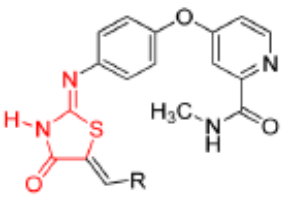
Oral S1P1 receptor agonists



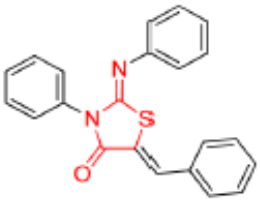
Cytotoxicity against breast and lung cancer



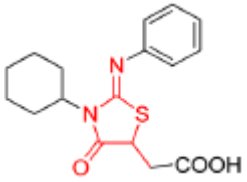
Antidiabetic Activity



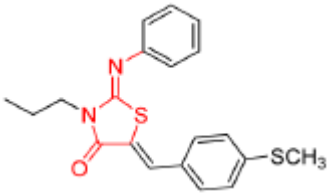
Potential Ant proliferative Agents



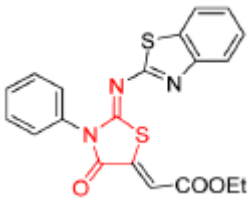
Anti-Inflammatory Activity



Cardiovascular Activity

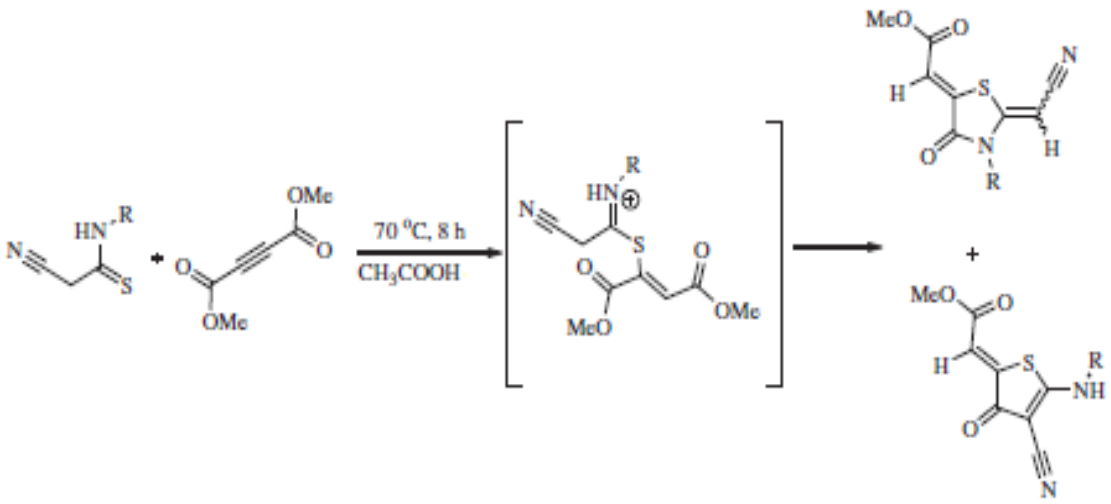


Antiamoebic activity

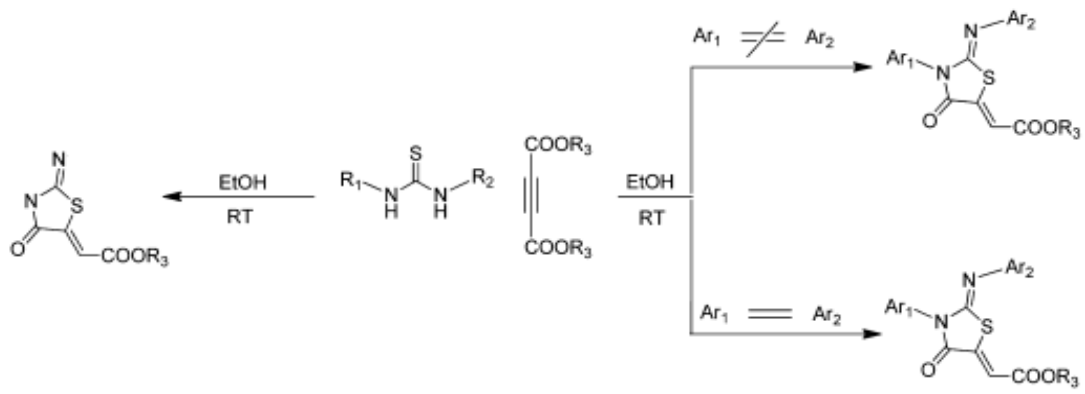


Aldose reductase inhibitor

Thiazolidine frameworks have been gotten by response of cyanothioacetamides with dimethylacetylenedicarboxylate (DMAD) [12]The response condition is beneath.

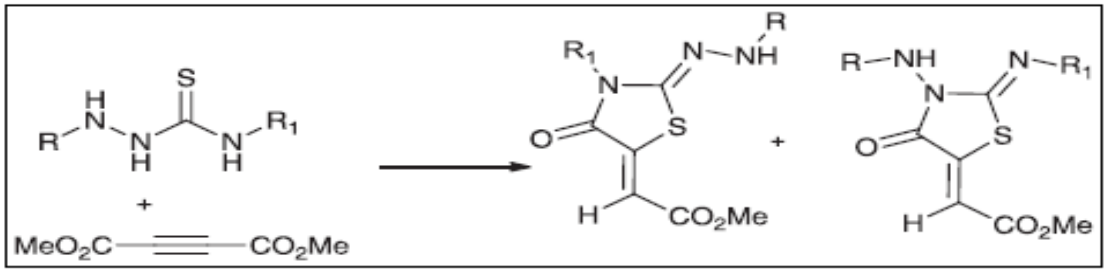


The 4-oxothiazolidine derivatives were synthesized in an environmentally and efficacious manner without catalysing the symmetric and asymmetric 1, 3-diarylthiourea and dimethylacetylenedicarboxylate (DMAD) in ethanol solution at room temperature. The reaction equation is shown below.



In the literature, thiourethane is reacted with dimethylacetylenedicarboxylate (DMAD) to yield 5 and 6 urea heterocyclic compounds. It is generally used as a solvent reaction medium such as methyl alcohol, acetone, anhydrous dichloromethane, THF, ethyl lactate [9].

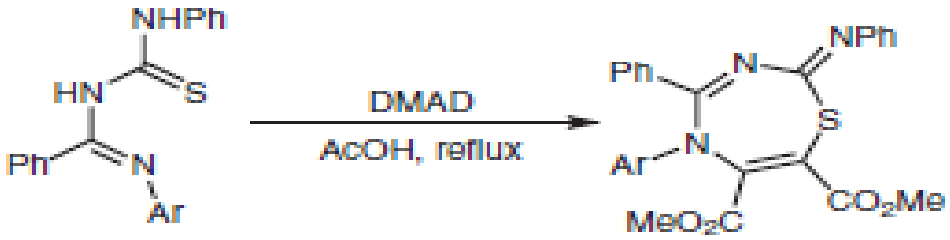
Thiazoles are synthesized by reacting hydrazine carbothioamides (thiosemararbazides) with electronically incompatible compounds. Reaction of thiosemicarbazides with DMAD yielded thiazolidin-4-ones. Hydrazinecarbontioamides are reacted with dimethyl acetylenedicarboxylate in high yield to give 4-oxo-Z- (thiazolidin-5-ylidene) acetate derivatives. Some possible reaction mechanisms exist in the literature [13]



These compounds are various biologically active compounds. These compounds are antimicrobial, antimicrobacterial, antiaids, antiinflammatory and anticancer properties [14]Thiazolidin-4-ones have been synthesized in the reaction of thiosemicarbazides with DMAD [13]

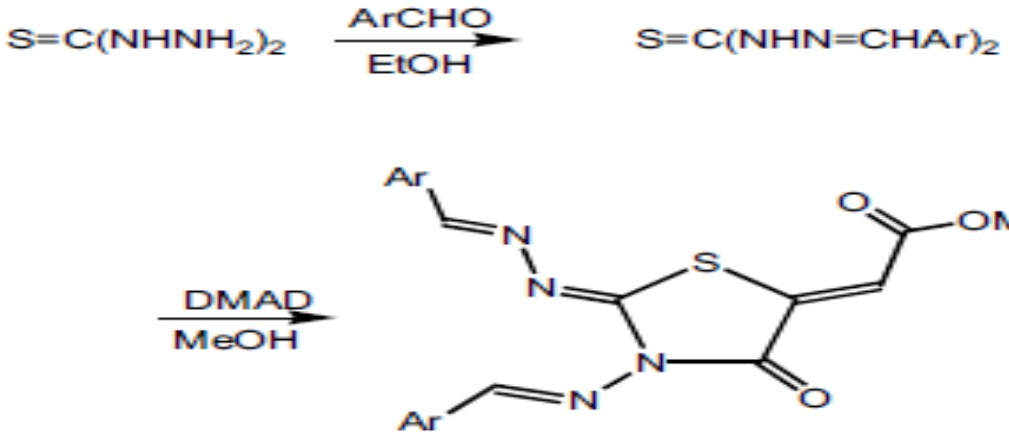
4-thiazolidinone derivatives are prepared in the reaction of DMAD with thiourea. Also these derivatives are prepared with various thiosemicarbazone derivatives.

Thiothiazepines with seven rings are obtained by re-boiling thiosemicarbazones in acetic acid under reflux [10]. The reaction equation is shown below.

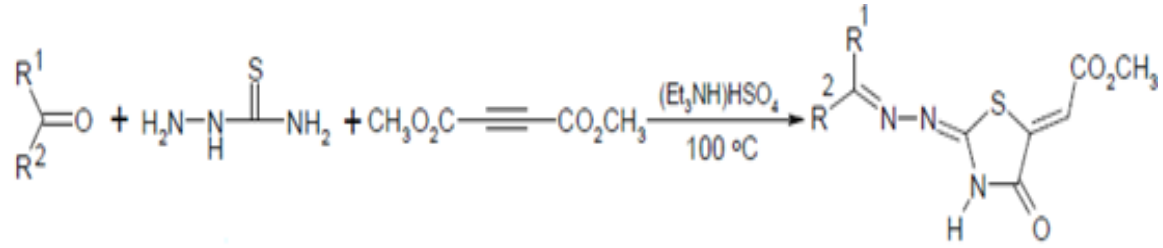


Ar = 4-$MeOC_6H_4$, 4-MeC_6H_4, 4-ClC_6H_4, 4-$O_2NC_6H_4$, Ph

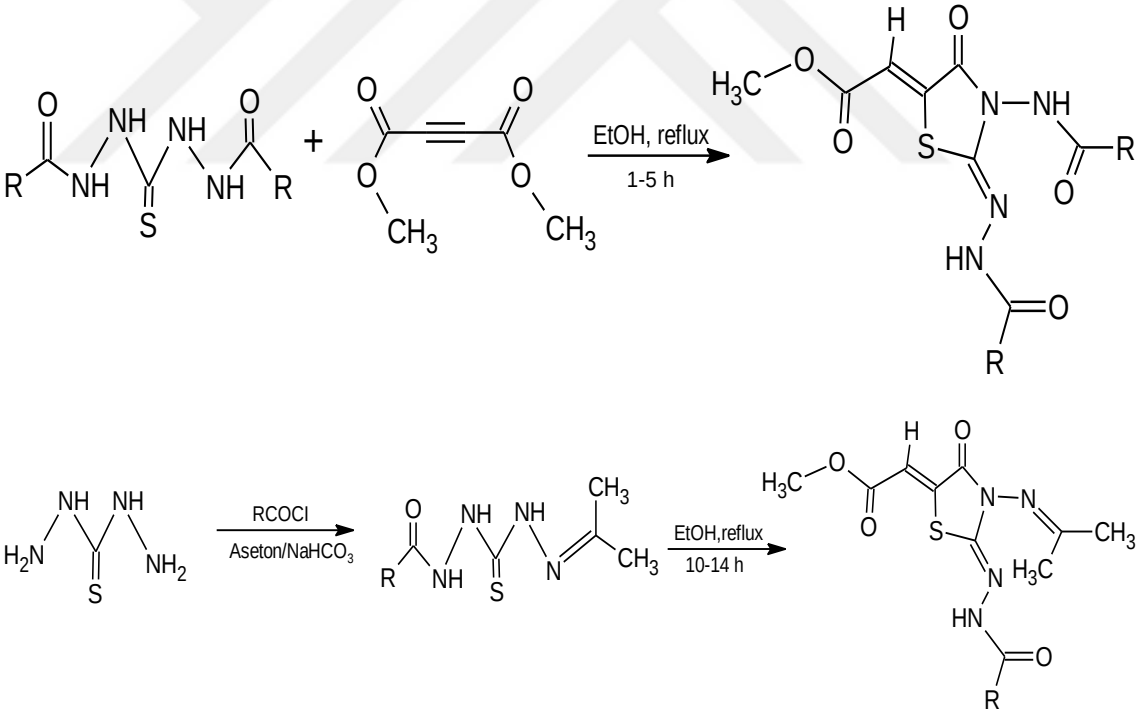
Trisubstituted thiazolidin-4-one compounds were synthesized by methanolysis of thiocarbonodihydrazones with DMAD [14]. Trisubstituted thiazolidin-4-one compounds were synthesized by methanolysis of thiocarbonodihydrazones with DMAD [14]



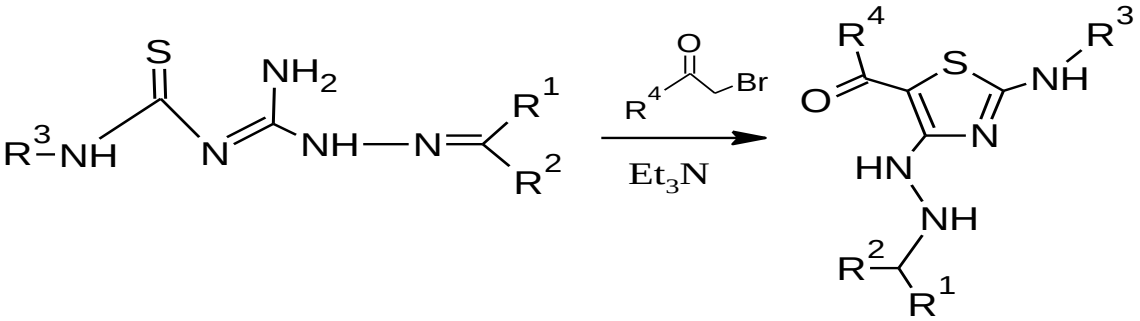
In the reaction of thiosemicarbazones with DMAD, 4-oxo-thiazolidin-5-ylidene is obtained. The one-step, multi-component reaction of thiazolidines, carbonyl compounds and DMAD from thiosemicarbazides is given below [14].



4-Oxo-thiazolidin-5-ylidine acetates are obtained with high yield in the reaction of diacyl thiocarbohydrazides with DMAD. When diacylthiocarbohydrazides are reacted with dimethyl but-2-ynnethioates in ethanol at reflux, they produce high yield of 4-oxa-thiazolidine-5-ylidene-acetate. Reaction of the firstly synthesized N- (2- (propan-2-ylidene) hydrazine-carbonothioyl) arylhydrazides with methyl but-2-ynethioates gave (Z) -methyl-2-arylhydrazide-4-oxo-3- (propan-2-ylideneamino) thiazolidine -5-ylidene) -acetates. Mechanism and antitumor and antioxidant activities are given in the study.



4-hydrazinothiazoles have been synthesized in a mildly-labile reaction of N-(aminoamidino) thiourea with α-haloketones [15]



In this study, it was planned to synthesize new compounds containing aminoguanidine structure and thiazole ring in the structural skeleton which we thought could have biological orientation. We intend to synthesize guanyl-thiazolidine derivatives by using N- (aminoamidino) thiourea as the starting material with DMAD and their reactions to synthesize new and active compounds which promise promise for the treatment of the mentioned diseases with the abovementioned activity.

In this examination, it was wanted to incorporate new mixes containing aminoguanidine structure and thiazole ring in the auxiliary skeleton which we thought could have organic introduction. We expect to integrate guanyl-thiazolidine subsidiaries by utilizing N-(aminoamidino) thiourea as the beginning material with DMAD and their responses to orchestrate new and dynamic mixes which guarantee for the treatment of the said maladies with the previously mentioned action.

Previous studies have yielded results as shown in the table below[16]

COMPOUND	**Ar_1**	**R_1**	**Ar_2**	**Melting point**	**Yield %**
NUR0	P-methyl-phenol	-methyl	-phenol	237-239	70
NUR1	P-methyl-phenol	-H	-phenol	209-210	66
NUR2	-phenol	-H	-phenol	231-232	81
NUR3	-phenol	-H	-phenol	214-215	52
NUR4	p-nitro -phenol	-H	-phenol	229-230	69
NUR5	o-chloro-phenol	-H	-phenol	211-212	62
NUR6	p-ethoxy-phenol	-H	-phenol	192-193	53
NUR7	2,4-diethoxy-phenol	-H	-phenol	199-200	67
NUR8	p-ethoxy-phenol	-methyl	-phenol	238-239	56
NUR9	P-methyl-phenol	-H	p-nitro -phenol	217-218	50
NUR10	-phenol	-methyl	p-nitro -phenol	248-250	84
NUR11	-phenol	-H	p-nitro -phenol	222-223	37
NUR12	o-chloro-phenol	-H	p-nitro -phenol	229-230	32
NUR13	p-ethoxy-phenol	-H	p-nitro -phenol	219-220	29
NUR14	P-methyl-phenol	-H	1-Naphthol	207-209	47
NUR15	p-chloro-phenol	-H	1-Naphthol	198-199	8,5

CHAPTER 2

MATERIALS AND METHODS

2.1. Chemical Substances Used in Experiment

Main chemical substances used in experiments; Merck, Sigma-Aldrich. Organic solvents such as methyl alcohol, toluene, ethyl alcohol, diethyl ether were used without further purification in the reaction medium and in purification processes.

2.2. Tools and Devices Benefiting from the Experiment

The IR spectra of all the compounds obtained in this study were obtained from Erciyes University Technology Research and Application Center (ERÜ TAUM), with ^{1}H-NMR and ^{13}C-NMR spectra. During the study, the following devices were used where necessary.

- Bruker- 400 MHz Ultra Shield NMR Spectrophotometer.
- Shimadzu 8400 FT-IR Spectrophotometer.
- Electrothermal Brand 9200 Model Melting point Device.
- Vacuum Pump.
- Heated Magnetic Mixer.
- Heidolph Brand Laborota 4001 HB digital Rotary Evaporator.
- Camag Brand Thin Layer Chromatogram Device (254/366 nm)
- DC Alufolien Kieselgel 60/254 Merck TLC plates
- Core Brand FN-500 Model Ovens (0-300^{o}C)
- Vacucell-MMM vacuum oven.

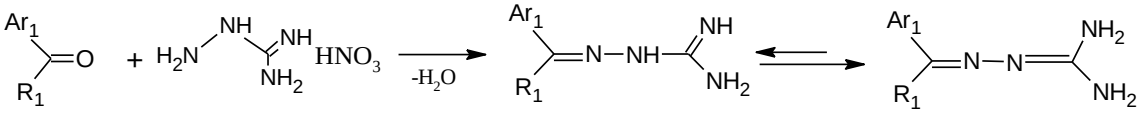
2.3. Methods Used in Experiment

In this study, the most optimal reaction conditions were determined by repeated experiments, taking into account the most important parameters that determine the course of chemical reactions, such as temperature, time, and catalyst, and concentration, type of solvent, structure and activity of reactants. The progress of the reactions and the purity of the products obtained were monitored and checked by thin layer chromatography (TLC). The synthesized compounds were purified by washing with appropriate solvents and crystallization, and the melting point was determined and then the IR and NMR spectrometers were used to elucidate the structure.

Interpretation of NMR spectra in solvents such as $CHCl_3$ and DMSO was made using literature information, some helpful books and computer programs. NMR analyzes were carried out at Erciyes University Technology Research and Application Center (ERÜ TAUM).

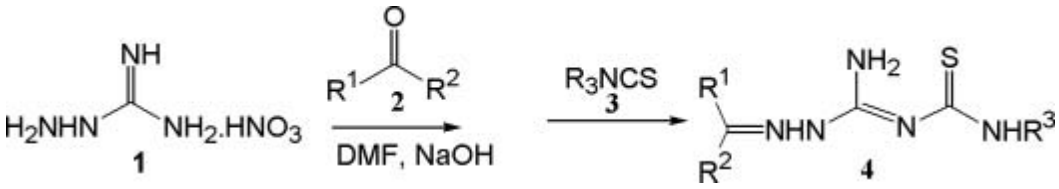
2.4. Synthesis Studies of Aminoguanadine

Aminoguanidine is found in the salt form. It is a strong base used in organic chemistry. In this work, Aminoguanidine was synthesized by reacting with various aldehydes and ketones. Since Aminoguanidine show tautomerism, they can be found in two possible ways. It has been found that the amine structure is more stable in X-ray, NMR, and quantum chemical calculations. According to the calculations, 3-12 kcal/mol amine structure was found to be more stable than hydrazine structure [8].

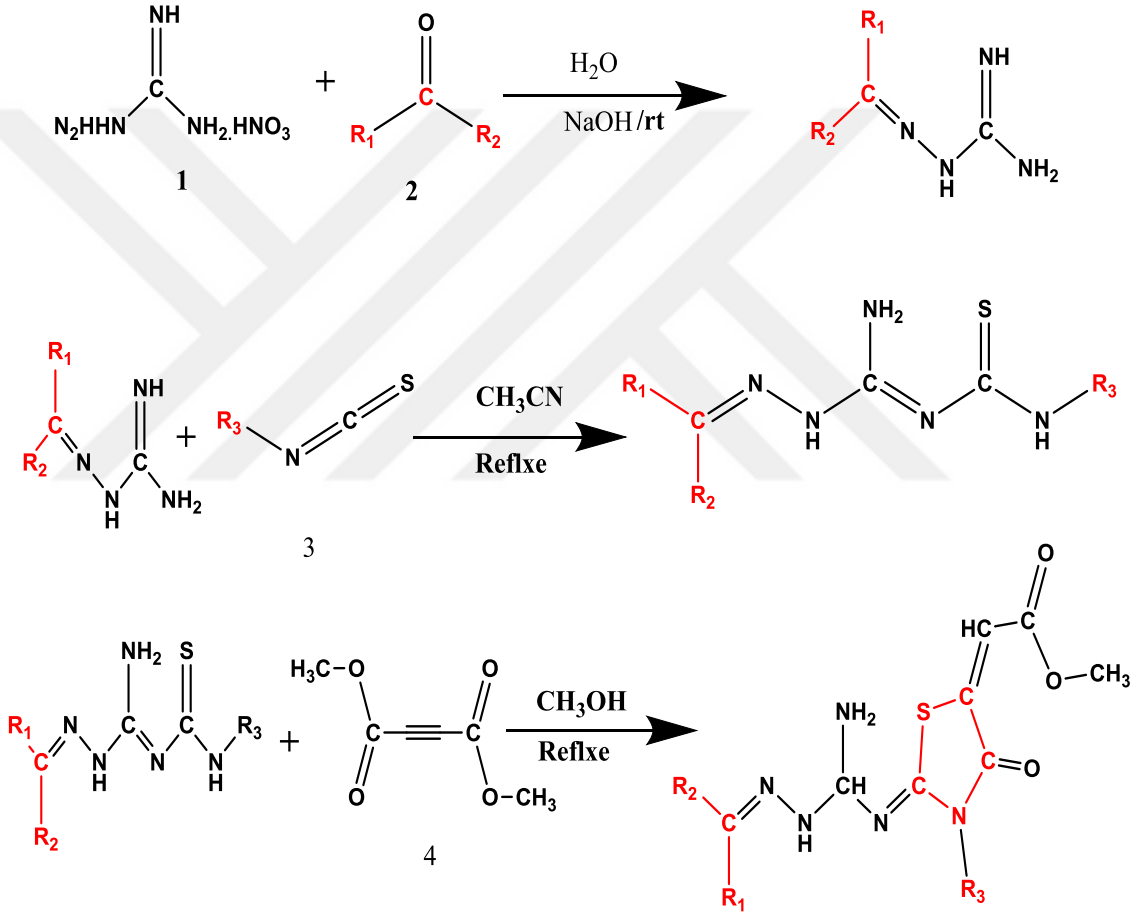


5 grams (36.46 mmol) of Aminoguanadine nitrate salt are weighed. Equivalent mole is neutralized with NaOH. It is dissolved in water and stirred for 1 hours under room conditions.

Aminoguanidine 1 was responded with a specific carbonyl compound 2 in H_2O containing NaOH. The relating hydrazone subordinates framed were responded hence with isothiocyanates 3 to bear the cost of the title mixes 4 in great yield as the sole significant item.



The disengaged items were sanitized by straightforward crystallization from fluid water. The structures of all the new mixes were affirmed on the premise of expository information and ghastly investigations of the mixes.



R_1= H,CH_3

R_2=Cl,H,CH_3,CH_3CH_2,OCH_3,OCH_3CH_2,$N(CH_3)_2$,NO_2

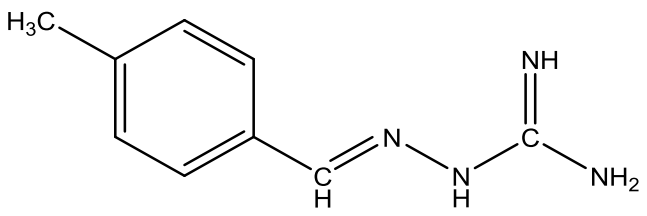
R_3=1-Naphthyl, 3-methoxyphenyl

Table 2.1. Melting point and percent yield values of some aminoguanidine derivatives

COMPOUND	Ar_1	R_1	Melting point	Yield %
AGI1	4-methylbenzaldehyde	-H	215 - 217	70%
AGI2	benzaldehyde	-H	179 - 182	67%
AGI3	Acetophenone	-Methyl	181 - 183	73%
AGI4	4-methylacetophenone	-Methyl	186 - 188	44%
AGI5	2-chlorobenzaldehyde	-H	129 - 130	39%
AGI6	2-chloro-6-fluorobenzaldehyde	-H	172 - 174	78%
AGI7	4-methoxyBenzaldehyde	-H	152 - 155	67%
AGI8	4-methoxyaceto phenone	-Methyl	221 - 223	58%
AGI9	4-chloroaceto phenone	-Methyl	181 - 183	71%
AGI10	4-ethoxy benzaldehyde	-H	145 - 147	43%
AGI11	4-(Dimethyl amino) Benzaldehyde	-H	158 - 160	37%
AGI12	4-Nitrobenzaldehyde	-H	205 - 207	53%
AGI13	4-Chlorobenzaldehyde	-H	184 - 186	65%
AGI14	4-(Trifluoromethyl)-benzaldehyde	-H	133 - 135	43%
AGI15	3,4,5-Trimethoxybenzaldehyde	-H	199 - 201	54%
AGI16	3,4-Dimethoxybenzaldehyde	-H	219 - 220	61%

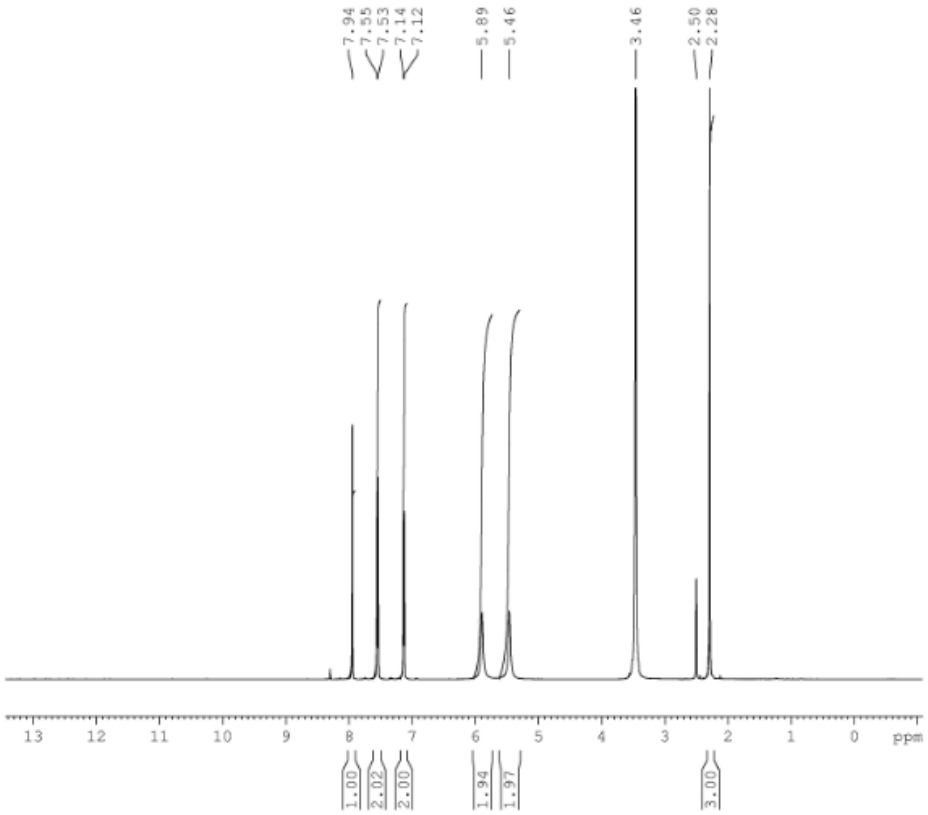
2.4.1. (E) -2- (4-methylbenzylid ANA) hydrazine-1-carboximidami in ((Synthesis of 4-methylbenzaldehyde)) AGI1

5 g (36.46 mmol) of the Aminoguanadine nitrate salt is dissolved in distilled water. After that, 1.46 g NaOH is added to neutralize the medium. The magnetic fish is discarded and allowed to mix in room conditions. After 1 hours, Add 4.29 ml of 4-methylbenzaldehyde. It is mixed for 1 day in room conditions. The material is filtered. Crystallize in ethanol + water. The crystallized material is left in the refrigerator for 1 day and cold filtration is carried out the next day. Dry in a vacuum oven. (3.5g, yield 70 %): Melting point (215 - 217) ˚C

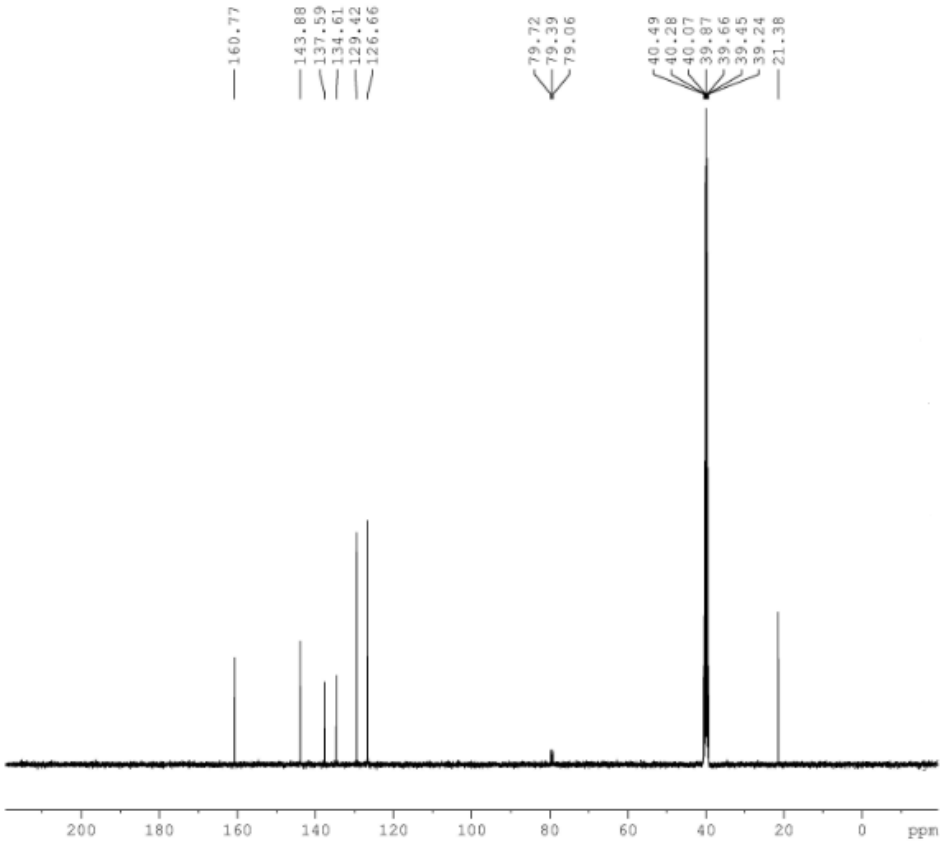


(*E*)-2-(4-methylbenzylidene)hydrazine-1-carboximidamide

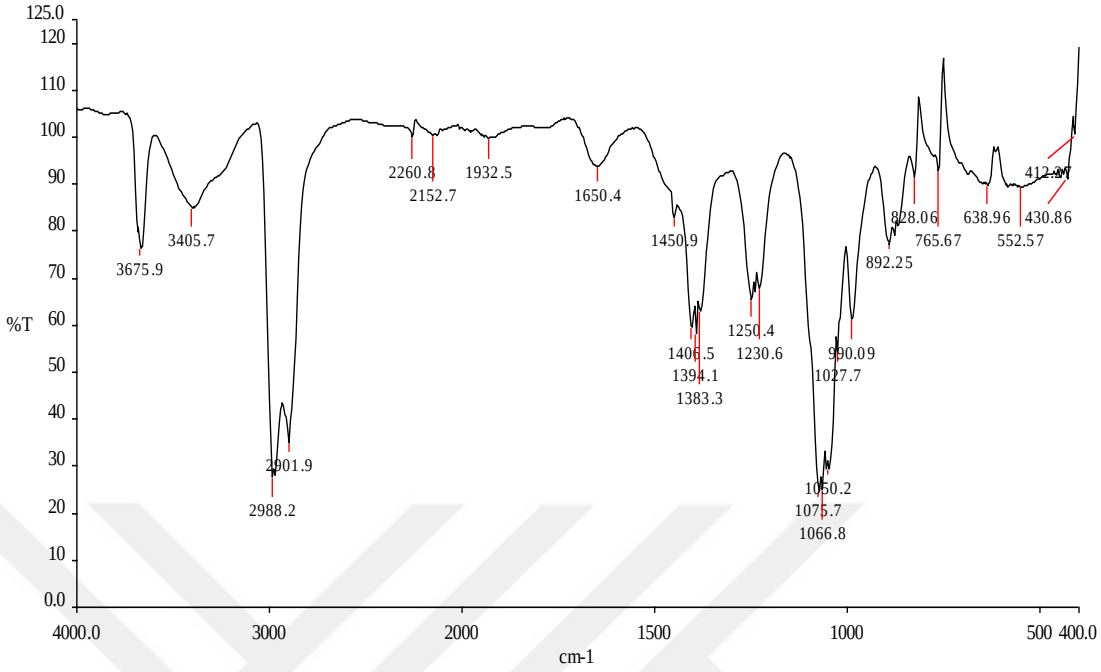
AGI1



^{1}H –NMR Spectrum AGI1



^{13} C-NMR Spectrum AGI1

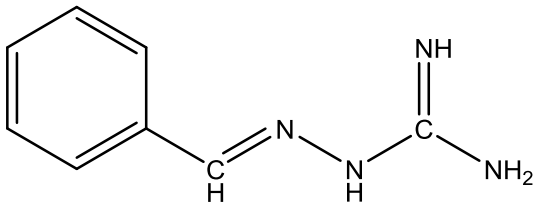


IR Spectrum AGI1

^{1}H-NMR (400 MH$_Z$, DMSO- δ_6) 7.94 (m, 1H), 7.55-7.53 (m, 2H), 7.14-7.12 (m, 2H), 6.83 (s, 1H), 5.89 (s, 2H), 5.46 (s, 2H), 2.5-2.28(m, 3H). ^{13}C-NMR (100 MHz, DMSO-δ_6) 160.77, 143.88, 137.59, 134.61, 129.42, 126.66, 79.72, 79.39, 79.06, 21.38. IR (cm^{-1}) 3403-3675 N-H stretching, 2901-2988 -C-H stretching, 1650 C = O stretching, 1450 C = C stretching, 1406 C = N stretching, 1383 C - N stretching, 1230-1250 C - O stretching, 1050-1066 C - C stretching.

2.4.2. (E)-2-benzylidene hydrazine-1-carboximidamide ((Synthesis of Benzaldehyde)) AGI2

5 g (36.46 mmol) of the Aminoguanadine nitrate salt is dissolved in distilled water. After that, 1.46 g NaOH is added to neutralize the medium. The magnetic fish is discarded and allowed to mix in room conditions. After 1 hours, Add 3.68 ml of Benzaldehyde. It is mixed for 1 day in room conditions. The material is filtered. Crystallize in ethanol + water. The crystallized material is left in the refrigerator for 1 day and cold filtration is carried out the next day. Dry in a vacuum oven. (3.38 g, yield 67%): Melting point (179 - 182) ˚C

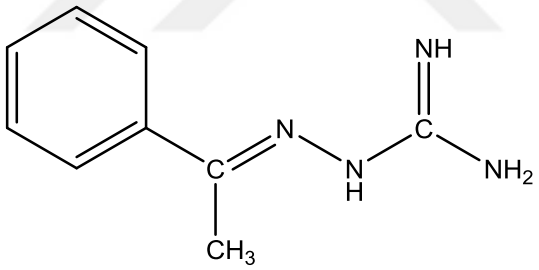


(*E*)-2-benzylidenehydrazine-1-carboximidamide

AGI2

2.4.3. (E)-2-(1-phenylethylidene) hydrazine-1-carboximidamide ((Synthesis of Acetophenone)) AGI3

3 g (21.88 mmol) of the Aminoguanadine nitrate salt is dissolved in distilled water. After that, 0.876 g NaOH is added to neutralize the medium. The magnetic fish is discarded and allowed to mix in room conditions. After 1 hours, Add 2.55 ml of Acetophenone. It is mixed for 1 day in room conditions. The material is filtered. Crystallize in ethanol + water. The crystallized material is left in the refrigerator for 1 day and cold filtration is carried out the next day. Dry in a vacuum oven. (2.2 g, yield73 %): Melting point (181-183) ˚C



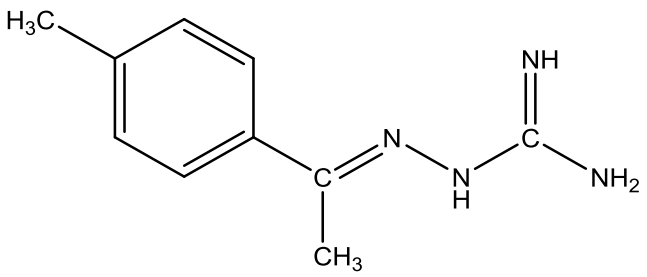
(*E*)-2-(1-phenylethylidene)hydrazine-1-carboximidamide

AGI3

2.4.4. (E)-2-(1-(p-tolyl) ethylidene) hydrazine-1-carboximidamide ((Synthesis of 4-methylacetophenone)) AGI4

5 g (36.46 mmol) of the Aminoguanadine nitrate salt is dissolved in distilled water. After that, 1.46 g NaOH is added to neutralize the medium. The magnetic fish is discarded and allowed to mix in room conditions. After 1 hours, Add 3.285 ml of 4-methylacetophenone. It is mixed for 1 day in room conditions. The material is filtered. Crystallize in ethanol + water. The crystallized material is left in the refrigerator for 1

day and cold filtration is carried out the next day. Dry in a vacuum oven. (2.23 g, yield 44 %): Melting point (186 - 188) ˚C

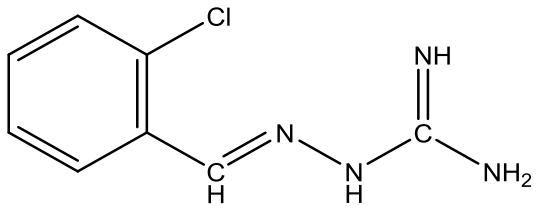


(*E*)-2-(1-(*p*-tolyl)ethylidene)hydrazine-1-carboximidamide

AGI4

2.4.5. (E)-2-(2-chlorobenzylidene) hydrazine-1-carboximidamide ((Synthesis of 2-chlorobenzaldehyde)) AGI5

5 g (36.46 mmol) of the Aminoguanadine nitrate salt is dissolved in distilled water. After that, 1.46 g NaOH is added to neutralize the medium. The magnetic fish is discarded and allowed to mix in room conditions. After 1 hours, Add 0.42 ml of 2-chlorobenzaldehyde. It is mixed for 1 day in room conditions. The material is filtered. Crystallize in ethanol + water. The crystallized material is left in the refrigerator for 1 day and cold filtration is carried out the next day. Dry in a vacuum oven. (1.97g, yield 39 %): Melting point (129 - 130) ˚C



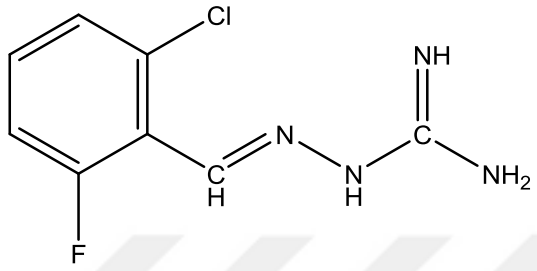
(*E*)-2-(2-chlorobenzylidene)hydrazine-1-carboximidamide

AGI5

2.4.6. (E)-2-(2-chloro-6-fluorobenzylidene) hydrazine-1-carboximidamide ((Synthesis of 2-chloro-6-fluoroBenzaldehyde)) AGI6

5 g (36.46 mmol) of the Aminoguanadine nitrate salt is dissolved in distilled water. After that, 1.46 g NaOH is added to neutralize the medium. The magnetic fish is

discarded and allowed to mix in room conditions. After 1 hours, Add 0.746 ml of 2-chloro-6-fluoroBenzaldehyde. It is mixed for 1 day in room conditions. The material is filtered. Crystallize in ethanol + water. The crystallized material is left in the refrigerator for 1 day and cold filtration is carried out the next day. Dry in a vacuum oven. (3.9 g, yield 78 %): Melting point (172 - 174) ˚C

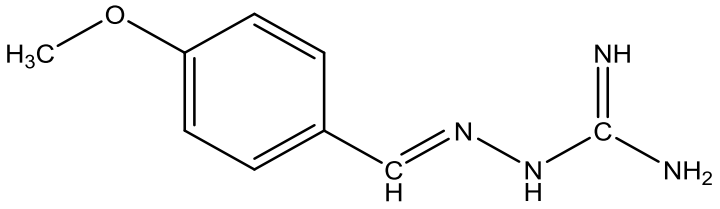


(*E*)-2-(2-chloro-6-fluorobenzylidene)hydrazine-1-carboximidamide

AGI6

2.4.7. (E)-2-(4-methoxybenzylidene) hydrazine-1-carboximidamide ((Synthesis of 4-methoxyBenzaldehyde)) AGI7

5 g (36.46 mmol) of the Aminoguanadine nitrate salt is dissolved in distilled water. After that, 1.46 g NaOH is added to neutralize the medium. The magnetic fish is discarded and allowed to mix in room conditions. After 1 hours, Add 2.66 ml of 4-methoxyBenzaldehyde. It is mixed for 1 day in room conditions. The material is filtered. Crystallize in ethanol + water. The crystallized material is left in the refrigerator for 1 day and cold filtration is carried out the next day. Dry in a vacuum oven. (3.35 g, yield 67 %): Melting point (152 - 155) ˚C

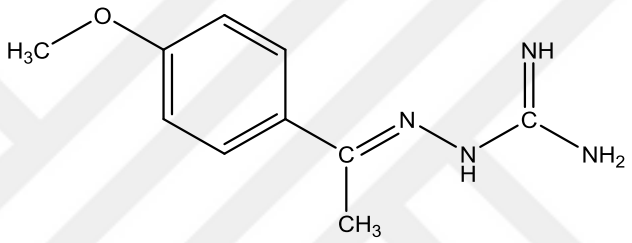


(*E*)-2-(4-methoxybenzylidene)hydrazine-1-carboximidamide

AGI7

2.4.8. (E)-2-(1-(4-methoxyphenyl) Eethylidene) hydrazine-1-carboximidamide ((Synthesis of 4-methoxyacetophenone)) AGI8

5 g (36.46 mmol) of the Aminoguanadine nitrate salt is dissolved in distilled water. After that, 1.46 g NaOH is added to neutralize the medium. The magnetic fish is discarded and allowed to mix in room conditions. After 1 hours, Add 3.25 ml of 4-methoxyacetophenone. It is mixed for 1 day in room conditions. The material is filtered. Crystallize in ethanol + water. The crystallized material is left in the refrigerator for 1 day and cold filtration is carried out the next day. Dry in a vacuum oven. (2.9 g, yield 58%): Melting point (221 - 223) ˚C

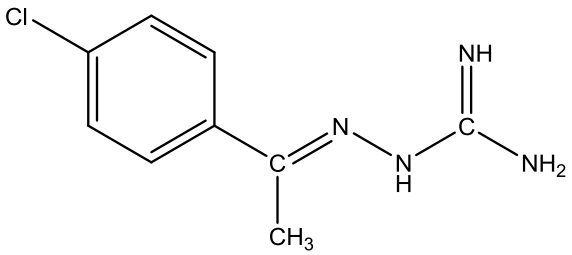


(*E*)-2-(1-(4-methoxyphenyl)ethylidene)hydrazine-1-carboximidamide

AGI8

2.4.9. (E)-2-(1-(4-chlorophenyl) ethylidene) hydrazine-1-carboximidamide ((Synthesis of 4-chloroacetophenone)) AGI9

5 g (36.46 mmol) of the Aminoguanadine nitrate salt is dissolved in distilled water. After that, 1.46 g NaOH is added to neutralize the medium. The magnetic fish is discarded and allowed to mix in room conditions. After 1 hours, Add 1.9 ml of 4-chloroacetophenone. It is mixed for 1 day in room conditions. The material is filtered. Crystallize in ethanol + water. The crystallized material is left in the refrigerator for 1 day and cold filtration is carried out the next day. Dry in a vacuum oven. (3.35 g, yield 71 %): Melting point (181 - 183) ˚C

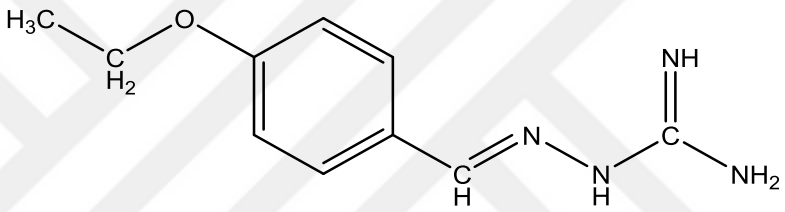


(*E*)-2-(1-(4-chlorophenyl)ethylidene)hydrazine-1-carboximidamide

AGI9

2.4.10. (E)-2-(4-ethoxybenzylidene) hydrazine-1-carboximidamide ((Synthesis of 4-ethoxybenzaldehyde)) AGI10

5 g (36.46 mmol) of the Aminoguanadine nitrate salt is dissolved in distilled water. After that, 1.46 g NaOH is added to neutralize the medium. The magnetic fish is discarded and allowed to mix in room conditions. After 1 hours, Add 2.32 ml of 4-ethoxybenzaldehyde. It is mixed for 1 day in room conditions. The material is filtered. Crystallize in ethanol + water. The crystallized material is left in the refrigerator for 1 day and cold filtration is carried out the next day. Dry in a vacuum oven. (2.15 g, yield 43 %): Melting point (145 - 147) ˚C

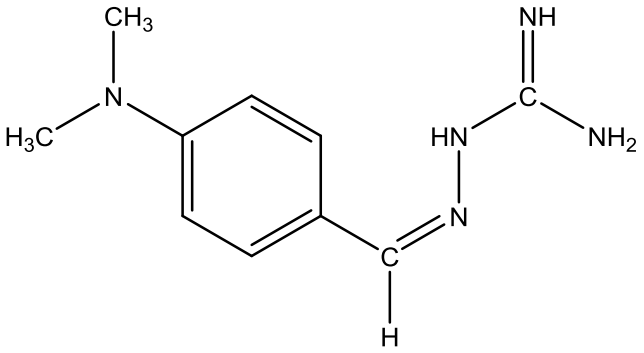


(*E*)-2-(4-ethoxybenzylidene)hydrazine-1-carboximidamide

AGI10

2.4.11. (Z)-2-(4-(dimethylamino) benzylidene) hydrazine-1-carboximidamide ((Synthesis of 4-(Dimethyl amino) Benzaldehyde)) AGI11

5 g (36.46 mmol) of the Aminoguanadine nitrate salt is dissolved in distilled water. After that, 1.46 g NaOH is added to neutralize the medium. The magnetic fish is discarded and allowed to mix in room conditions. After 1 hours, Add 5.44 g of 4-(Dimethyl amino) Benzaldehyde. It is mixed for 1 day in room conditions. The material is filtered. Crystallize in ethanol + water. The crystallized material is left in the refrigerator for 1 day and cold filtration is carried out the next day. Dry in a vacuum oven. (1.85 g, yield 37 %): Melting point (158 - 160) ˚C

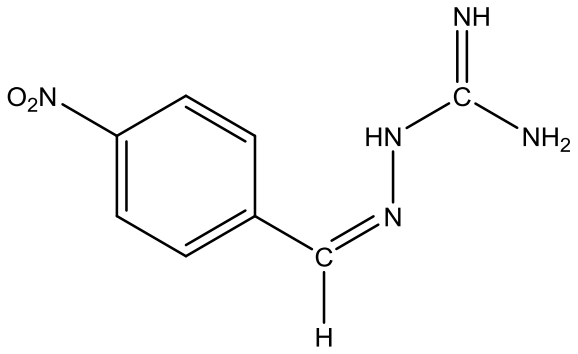


(*Z*)-2-(4-(dimethylamino)benzylidene)hydrazine-1-carboximidamide

AGI11

2.4.12. (Z)-2-(4-nitrobenzylidene) hydrazine-1-carboximidamide ((Synthesis of 4-Nitrobenzaldehyde)) AGI12

5 g (36.46 mmol) of the Aminoguanadine nitrate salt is dissolved in distilled water. After that, 1.46 g NaOH is added to neutralize the medium. The magnetic fish is discarded and allowed to mix in room conditions. After 1 hours, Add 5.51 g of 4-Nitrobenzaldehyde. It is mixed for 1 day in room conditions. The material is filtered. Crystallize in ethanol + water. The crystallized material is left in the refrigerator for 1 day and cold filtration is carried out the next day. Dry in a vacuum oven. (2.65 g, yield 53 %): Melting point (205 - 207) ˚C



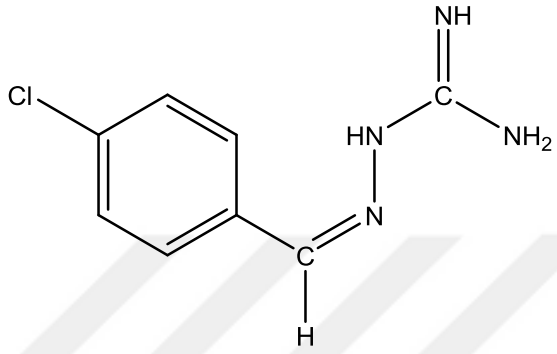
(*Z*)-2-(4-nitrobenzylidene)hydrazine-1-carboximidamide

AGI12

2.4.13. (Z)-2-(4-chlorobenzylidene) hydrazine-1-carboximidamide ((Synthesis of 4-Chlorobenzaldehyde)) AGI13

5 g (36.46 mmol) of the Aminoguanadine nitrate salt is dissolved in distilled water. After that, 1.46 g NaOH is added to neutralize the medium. The magnetic fish is

discarded and allowed to mix in room conditions. After 1 hours, Add 5.12 g of 4-Chlorobenzaldehyde. It is mixed for 1 day in room conditions. The material is filtered. Crystallize in ethanol + water. The crystallized material is left in the refrigerator for 1 day and cold filtration is carried out the next day. Dry in a vacuum oven. (3.25 g, yield 65 %): Melting point (184 - 186) ˚C

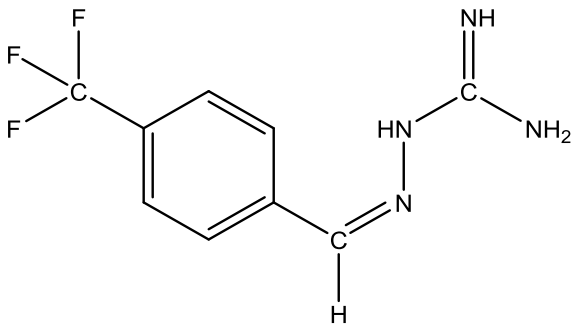


(*Z*)-2-(4-chlorobenzylidene)hydrazine-1-carboximidamide

AGI13

2.4.14. (Z)-2-(4-(trifluoromethyl) benzylidene) hydrazine-1-carboximidamide ((Synthesis of 4-(Trifluoromethyl)-benzaldehyde)) AGI14

5 g (36.46 mmol) of the Aminoguanadine nitrate salt is dissolved in distilled water. After that, 1.46 g NaOH is added to neutralize the medium. The magnetic fish is discarded and allowed to mix in room conditions. After 1 hours, Add 5.24 ml of 4-(Trifluoromethyl)-benzaldehyde. It is mixed for 1 day in room conditions. The material is filtered. Crystallize in ethanol + water. The crystallized material is left in the refrigerator for 1 day and cold filtration is carried out the next day. Dry in a vacuum oven. (2.15 g, yield 43 %): Melting point (133 - 135) ˚C

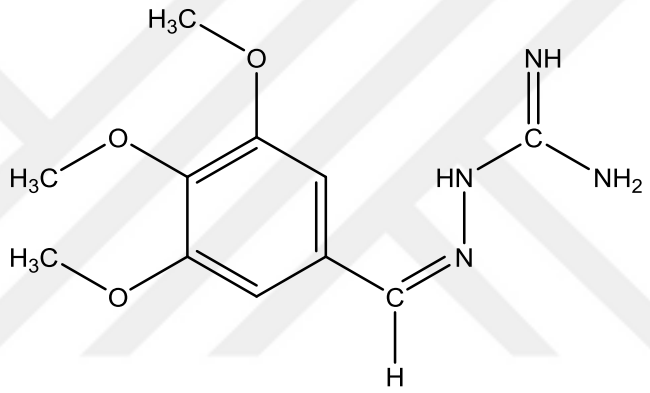


(*Z*)-2-(4-(trifluoromethyl)benzylidene)hydrazine-1-carboximidamide

AGI14

2.4.15. (Z)-2-(3, 4, 5-trimethoxybenzylidene) hydrazine-1-carboximidamide ((Synthesis of 3, 4, 5-Trimethoxybenzaldehyde)) AGI15

5 g (36.46 mmol) of the Aminoguanadine nitrate salt is dissolved in distilled water. After that, 1.46 g NaOH is added to neutralize the medium. The magnetic fish is discarded and allowed to mix in room conditions. After 1 hours, Add 7.15 g of 3, 4, 5-Trimethoxybenzaldehyde. It is mixed for 1 day in room conditions. The material is filtered. Crystallize in ethanol + water. The crystallized material is left in the refrigerator for 1 day and cold filtration is carried out the next day. Dry in a vacuum oven. (2.7g, yield 54 %): Melting point (199 - 201) ˚C

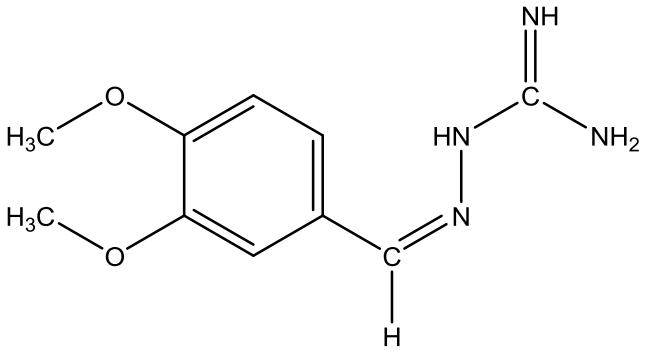


(*Z*)-2-(3,4,5-trimethoxybenzylidene)hydrazine-1-carboximidamide

AGI15

2.4.16. (Z)-2-(3, 4-dimethoxybenzylidene) hydrazine-1-carboximidamide ((Synthesis of 3, 4-Dimethoxybenzaldehyde)) AGI16

5 g (36.46 mmol) of the Aminoguanadine nitrate salt is dissolved in distilled water. After that, 1.46 g NaOH is added to neutralize the medium. The magnetic fish is discarded and allowed to mix in room conditions. After 1 hours, Add 6.05 g of 3, 4-Dimethoxybenzaldehyde. It is mixed for 1 day in room conditions. The material is filtered. Crystallize in ethanol + water. The crystallized material is left in the refrigerator for 1 day and cold filtration is carried out the next day. Dry in a vacuum oven. (3.05 g, yield 61 %): Melting point (219 - 220) ˚C



(*Z*)-2-(3,4-dimethoxybenzylidene)hydrazine-1-carboximidamide

AGI16

2.5. Reactions of Aminoguanadine with Various Isothiocyanate; Synthesis of N-(amino-amidino) thiourea:

Aminoguanidine is highly potent nucleophiles which, when reacted with isothiocyanate, give an addition reaction yielding straight chain hydrazine-1-carboximidamide derivatives [17]. The Aminoguanidine is heated in 5-10 ml of acetonitrile, then isothiocyanate is added in an equivalent amount, and the mixture is refluxed for 1 hour. The reaction mixture is filtered and the filtrate is washed with hot ethanol.

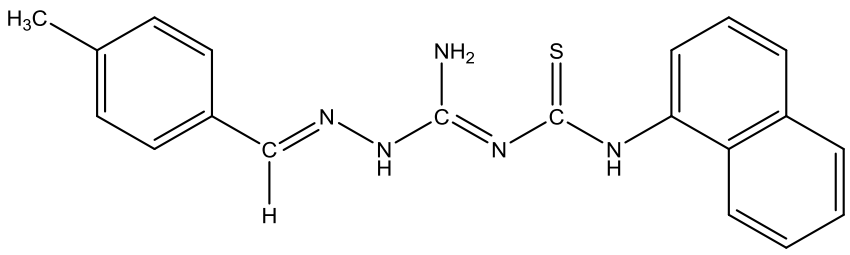
The aim of making these compounds is to synthesize new compounds by reacting them with DMAD. Since some of these compounds are not in the literature and the synthesis is different, their construction is described in detail below.

Table 2.2. Melting point and percent yield values of some aminoguanidine derivatives with isothiocyanate

#	Step1		Step2	Melting point	Yield %	Name of Reaction
1	4-methylbenzaldehyde AG	+	1-Naphthisothiocyanate	178-180	66%	AGII1
2	4-methylbenzaldehyde AG	+	3-methoxyphenyl isothiocyanate	165-167	72%	AGII2
3	benzaldehyde AG	+	1-Naphthisothiocyanate	179-180	47%	AGII3
4	benzaldehyde AG	+	3-methoxyphenyl isothiocyanate	134-138	38%	AGII4
5	Acetophenone AG	+	1-Naphthisothiocyanate	166-168	61%	AGII5
6	4-methylacetophenone AG	+	1-Naphthisothiocyanate	164-166	57%	AGII6
7	4-methylacetophenone AG	+	3-methoxyphenyl isothiocyanate	149-150	44%	AGII7
8	2-chlorobenzaldehyde AG	+	1-Naphthisothiocyanate	195-197	51%	AGII8
9	2-chlorobenzaldehyde AG	+	3-methoxyphenyl isothiocyanate	149-150	48%	AGII9
10	2-chloro-6-fluoro benzaldehyde AG	+	1-Naphthisothiocyanate	197-198	37%	AGII10
11	2-chloro-6-fluoro benzaldehyde AG	+	3-methoxyphenylisothiocyanate	173 - 175	53%	AGII11
12	4-methoxy Benzaldehyde AG	+	1-Naphthisothiocyanate	175-177	62%	AGII12
13	4-methoxyaceto phenone AG	+	1-Naphthisothiocyanate	148-150	67%	AGII13
14	4-methoxyaceto phenone AG	+	3-methoxyphenylisothiocyanate	144-146	63%	AGII14
15	4-chloroaceto phenone AG	+	1-Naphthisothiocyanate	166-168	62%	AGII15
16	4-chloroaceto phenone AG		3-methoxyphenylisothiocyanate	140-143	41%	AGII16
17	4-ethoxy benzaldehyde AG	+	1-Naphthisothiocyanate	159-161	53%	AGII17
18	4-Nitrobenzaldehyde AG	+	1-Naphthisothiocyanate	198-199	72%	AGII18
19	4-Chlorobenzaldehyde AG	+	1-Naphthisothiocyanate	188-190	69%	AGII19
20	4-Chlorobenzaldehyde AG	+	3-methoxyphenyl isothiocyanate	178-179	56%	AGII20
21	4-(Dimethyl amino) Benzaldehyde AG	+	1-Naphthisothiocyanate	176-177	48%	AGII21
22	4-(Dimethyl amino) Benzaldehyde AG	+	3-methoxyphenyl isothiocyanate	175-177	41%	AGII22

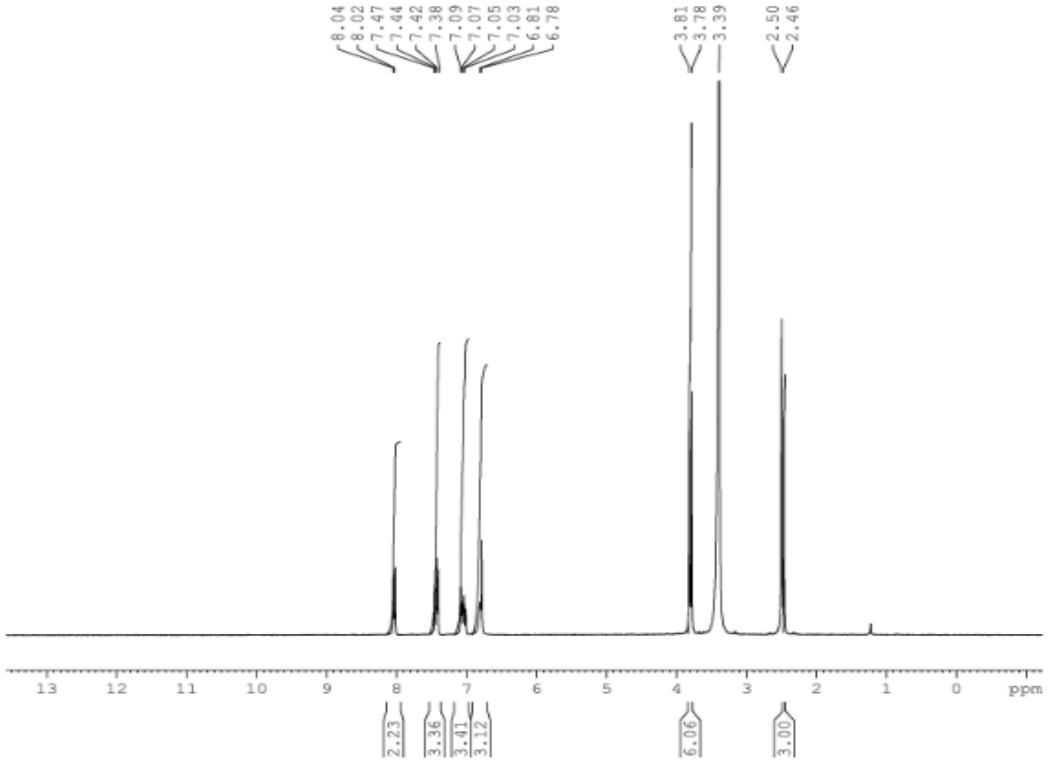
2.5.1. (E)-2-((E)-4-methylbenzylidene)-N'-(naphthalen-1-ylcarbamothioyl) hydrazine-1-carboximidamide AGII1

Add 0.5 g (2.84 mmol) of AG1 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. 0.526 g (2.84 mmol) of 1-Naphthisothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.33 g, yield 66%) of $C_{20}H_{19}N_5S$, 361.47 g / mol, Melting point (178 - 180) ˚C

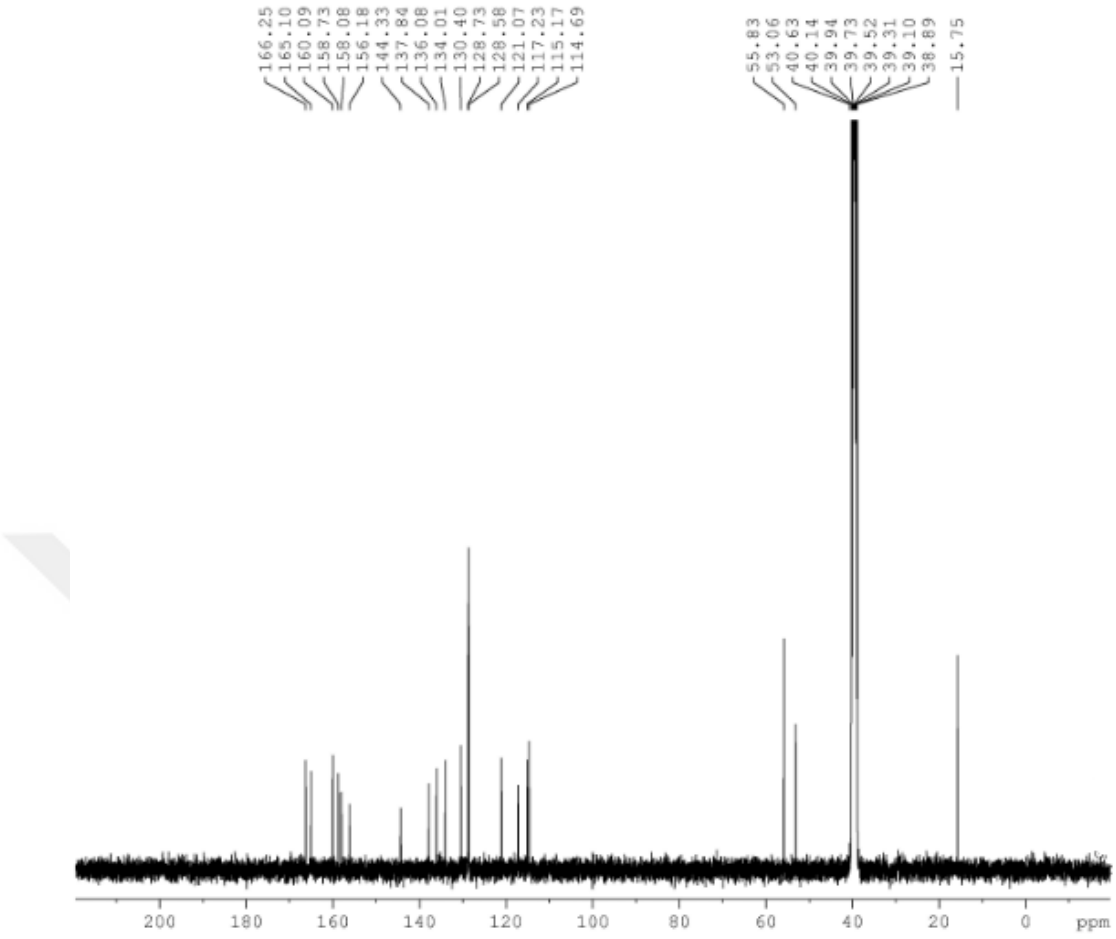


(*E*)-2-((*E*)-4-methylbenzylidene)-*N*'-(naphthalen-1-ylcarbamothioyl)hydrazine-1-carboximidamide

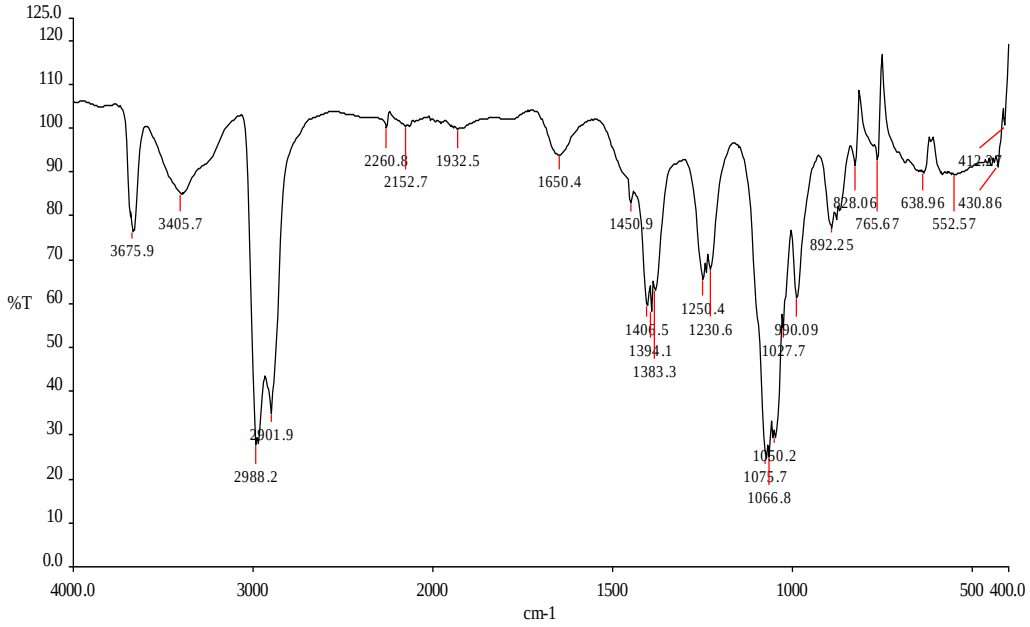
AGII1



^{1}H –NMR Spectrum AGII1



^{13}C-NMR Spectrum AGII1

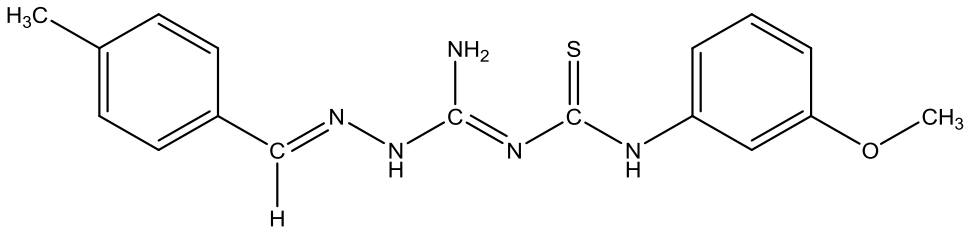


IR Spectrum AGII1

^{1}H -NMR (400 MHz, DMSO- δ_6) 8.40 (d, J = 8.4 Hz, 2H), 8.26 (s, 1H), 7.86-7.78 (m, 4H) 2H), 6.83 (s, 1H), 6.76 (s, 2H), 4.07 (q, J = 6.9 Hz, 2H), 3.82 (s, 2H), 1.34 (t, J = 6.9 Hz, 3H). ^{13}C-NMR (100 MHz, DMSO- δ_6) 166.25, 165.10, 160.09, 158.73, 158.08, 156.18, 144.33, 137.84, 136.08, 134.01, 130.40, 128.73, 128.58, 121.07, 117.23, 115.17, 114.69, 53.83, 53.06, 15.75. IR (cm^{-1}) 3403-3675 N-H stretching, 2901-2988 - C-H stretching, 1650 C = O stretching, 1450 C = C stretching, 1406 C = N stretching, 1383 C - N stretching, 1230-1250 C - O stretching, 1050-1066 C - C stretching.

2.5.2. (E)-N'-((3-methoxyphenyl) carbamothioyl)-2-((E)-4-methylbenzylidene) hydrazine-1-carboximidamide AGII2

Add 0.5 g (2.84 mmol) of AG1 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. 0.398 g (401 mmol) of 3-methoxyphenylIsothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.36 g, yield 72%) of $C_{17}H_{19}N_5OS$, 341.43 g / mol, Melting point (165 -167) ˚C



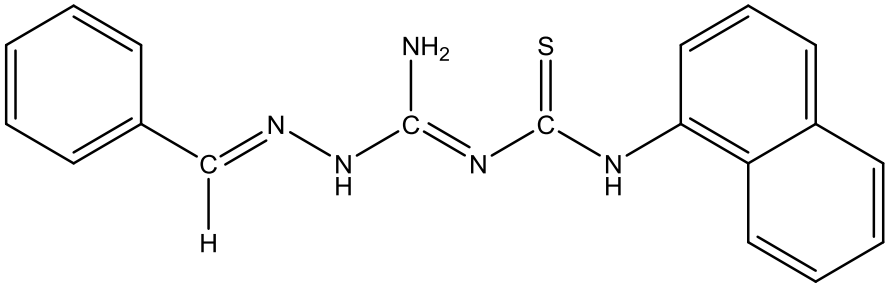
(*E*)-*N*'-((3-methoxyphenyl)carbamothioyl)-2-((*E*)-4-methylbenzylidene)hydrazine-1-carboximidamide

AGII2

2.5.3. (E)-2-((E)-benzylidene)-N'-(naphthalen-1-ylcarbamothioyl) hydrazine-1-carboximidamide AGII3

Add 0.8g (4.932 mmol) of AG 2over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. 0.913 g (4.928 mmol) of 1-Naphthisothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC

(thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.376g, yield 47%) of $C_{19}H_{17}N_5S$, 347.44 g / mol, Melting point (179 - 180) ˚C

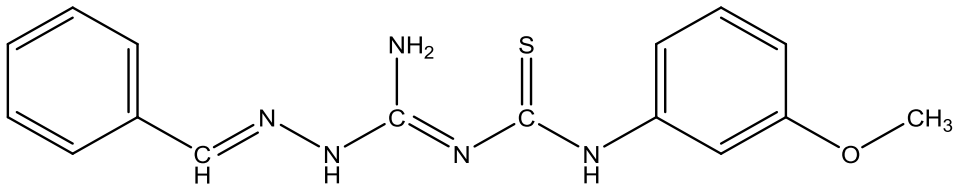


(*E*)-2-((*E*)-benzylidene)-*N*'-(naphthalen-1-ylcarbamothioyl)hydrazine-1-carboximidamide

AGII3

2.5.4. (E)-2-((E)-benzylidene)-N'-((3-methoxyphenyl) carbamothioyl) hydrazine-1-carboximidamide AGII4

Add 0.8 g (4.932 mmol) of AG2 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. (0.691 mmol) of 3-methoxyphenylIsothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P2O5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.304 g, yield 38%) of $C_{16}H_{17}N_5OS$, 327.41 g / mol, Melting point (134 - 138) ˚C

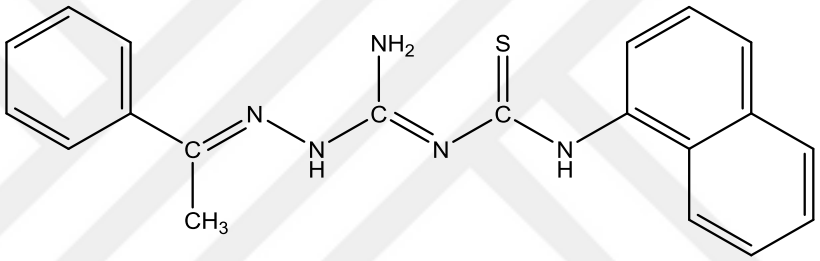


(*E*)-2-((*E*)-benzylidene)-*N*'-((3-methoxyphenyl)carbamothioyl)hydrazine-1-carboximidamide

AGII4

2.5.5. (1E, 2E)-N'-(naphthalen-1-ylcarbamothioyl)-2-(1-phenylethylidene) hydrazine-1-carboximidamide AGII5

Add 0.8 g (1.135 mmol) of AG3 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. 0.21 g of 1-Naphthisothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P2O5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.48g, yield 61%) of $C_{20}H_{19}N_5S$, 361.47 g / mol, Melting point (166 -168) ˚C

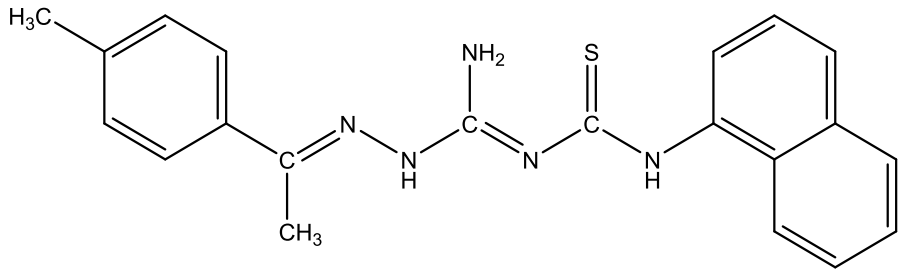


(1*E*,2*E*)-*N*'-(naphthalen-1-ylcarbamothioyl)-2-(1-phenylethylidene)hydrazine-1-carboximidamide

AGII5

2.5.6. (1E, 2E)-N'-(naphthalen-1-ylcarbamothioyl)-2-(1-(p-tolyl) ethylidene) hydrazine-1-carboximidamide AGII6

Add 0.2 g (1.051 mmol) of AG4 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. 0.159 g of 1-Naphthisothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.114 g, yield 57%) of $C_{21}H_{21}N_5S$, 375.49 g / mol, Melting point (164 - 166) ˚C

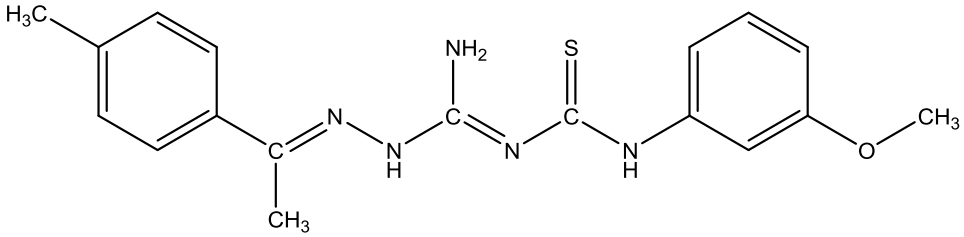


(1*E*,2*E*)-*N*'-(naphthalen-1-ylcarbamothioyl)-2-(1-(*p*-tolyl)ethylidene)hydrazine-1-carboximidamide

AGII6

2.5.7. (1E, 2E)-N'-((3-methoxyphenyl) carbamothioyl)-2-(1-(p-tolyl) ethylidene) hydrazine-1-carboximidamide AGII7

Add 0.2 g (1.051 mmol) of AG4 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. (0.147mmol) of 3-methoxyphenylIsothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.088 g, yield 44%) of $C_{18}H_{21}N_5OS$, 355.46 g / mol, Melting point (149 - 150) ˚C



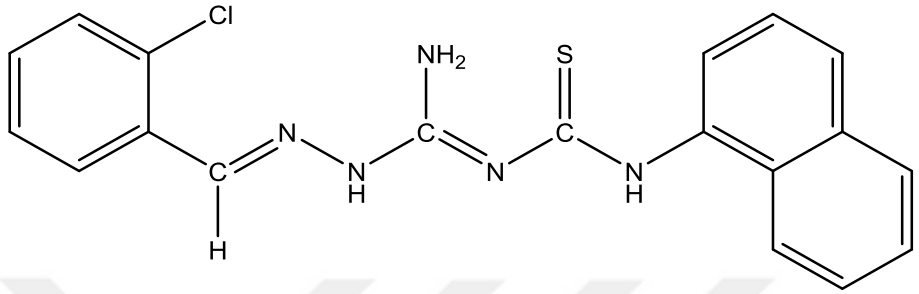
(1*E*,2*E*)-*N*'-((3-methoxyphenyl)carbamothioyl)-2-(1-(*p*-tolyl)ethylidene)hydrazine-1-carboximidamide

AGII7

2.5.8. (E)-2-((E)-2-chlorobenzylidene)-N'-(naphthalen-1-ylcarbamothioyl) hydrazine-1-carboximidamide AGII8

Add 0.2 g (1.017 mmol) of AG5 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. 0.188 g of 1-Naphthisothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow

colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.102 g, yield 51%) of $C_{19}H_{16}ClN_5S$, 381.88 g / mol, Melting point (195 - 197) ˚C

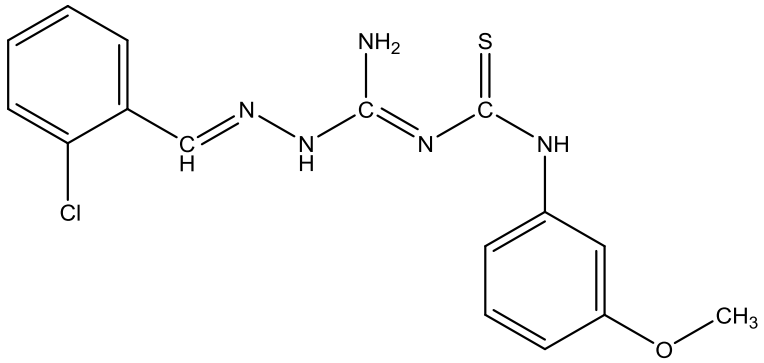


(*E*)-2-((*E*)-2-chlorobenzylidene)-*N*'-(naphthalen-1-ylcarbamothioyl)hydrazine-1-carboximidamide

AGII8

2.5.9. (E)-2-((E)-2-chlorobenzylidene)-N'-((3-methoxyphenyl) carbamothioyl) hydrazine-1-carboximidamide

Add 0.2 g (1.017 mmol) of AG5 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. (0.134mmol) of 3-methoxyphenylIsothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.096 g, yield 48%) of $C_{16}H_{16}ClN_5S$, 361.88 g / mol, Melting point (149 - 150) ˚C

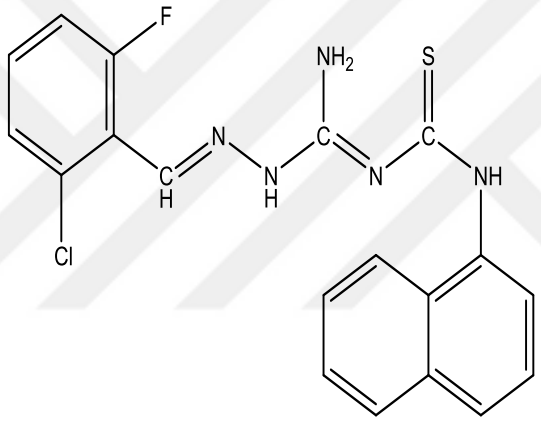


(*E*)-2-((*E*)-2-chlorobenzylidene)-*N*'-((3-methoxyphenyl)carbamothioyl)hydrazine-1-carboximidamide

AGII9

2.5.10. (E)-2-((E)-2-chloro-6-fluorobenzylidene)-N'-(naphthalen-1-ylcarbamothioyl) hydrazine-1-carboximidamide AGII10

Add 0.2 g (0.931 mmol) of AG6 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. 0.181 g of 1-Naphthisothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.074 g, yield 37%) of $C_{19}H_{15}ClFN_5S$, 399.87 g / mol, Melting point (197 - 198) ˚C



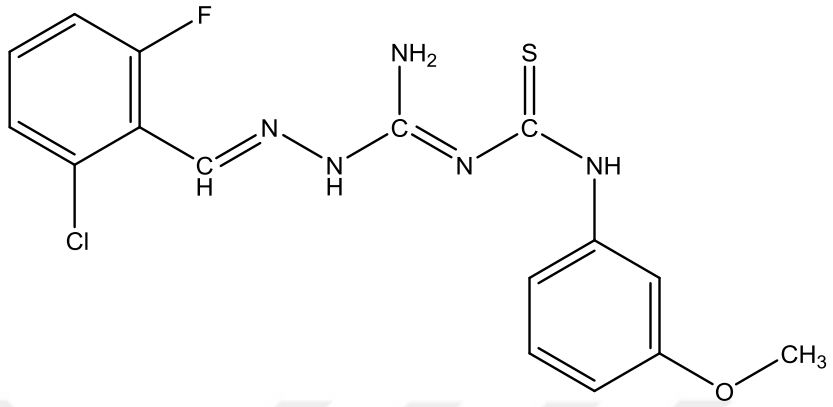
(*E*)-2-((*E*)-2-chloro-6-fluorobenzylidene)-*N*'-(naphthalen-1-ylcarbamothioyl)hydrazine-1-carboximidamide

AGII10

2.5.11. (E)-2-((E)-2-chloro-6-fluorobenzylidene)-N'-((3-methoxyphenyl) carbamothioyl) hydrazine-1-carboximidamide AGII11

Add 0.2 g (0.977 mmol) of AG6 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. (0.137mmol) of 3-methoxyphenylIsothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5

in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.106 g, yield 53%) of $C_{16}H_{15}ClFN_5OS$, 379.84 g / mol, Melting point (173 - 175) ˚C

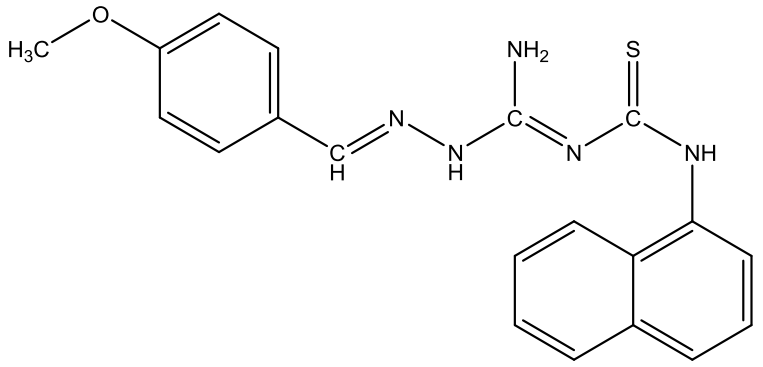


(*E*)-2-((*E*)-2-chloro-6-fluorobenzylidene)-*N*'-((3-methoxyphenyl)carbamothioyl)hydrazine-1-carboximidamide

AGII11

2.5.12. (E)-2-((E)-4-methoxybenzylidene)-N'-(naphthalen-1-ylcarbamothioyl) hydrazine-1-carboximidamide AGII12

Add 0.2g (1.04 mmol) of AG7 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. 0.192 g of 1-Naphthisothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.124 g, yield 62%) of $C_{20}H_{19}N_5OS$, 377.47 g / mol, Melting point (175 - 177) ˚C

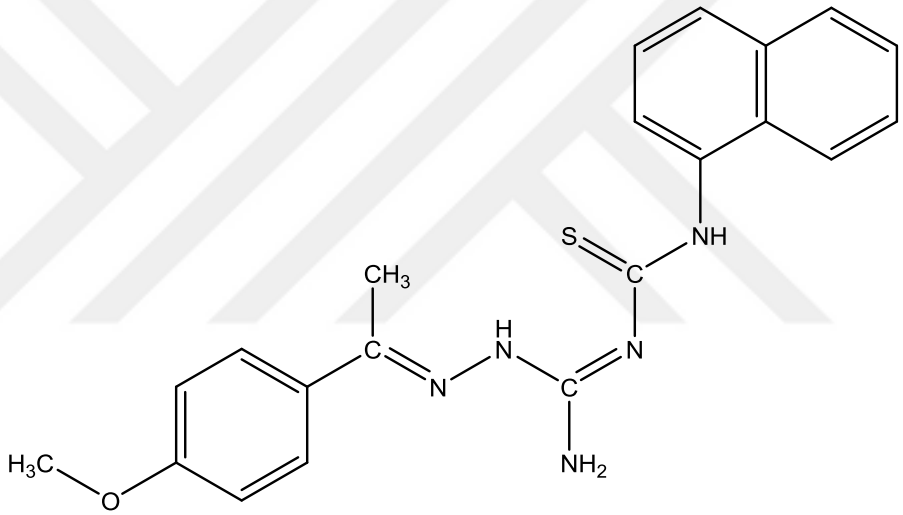


(*E*)-2-((*E*)-4-methoxybenzylidene)-*N*'-(naphthalen-1-ylcarbamothioyl)hydrazine-1-carboximidamide

AGII12

2.5.13. (1Z, 2E)-2-(1-(4-methoxyphenyl) ethylidene)-N'-(naphthalen-1-ylcarbamothioyl) hydrazine-1-carboximidamide AGII13

Add 0.2 g (0.969 mmol) of AG8 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. 0.18 g of 1-Naphthisothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.134 g, yield 67%) of $C_{21}H_{21}N_5OS$, 391.49 g / mol, Melting point (148 - 150) ˚C

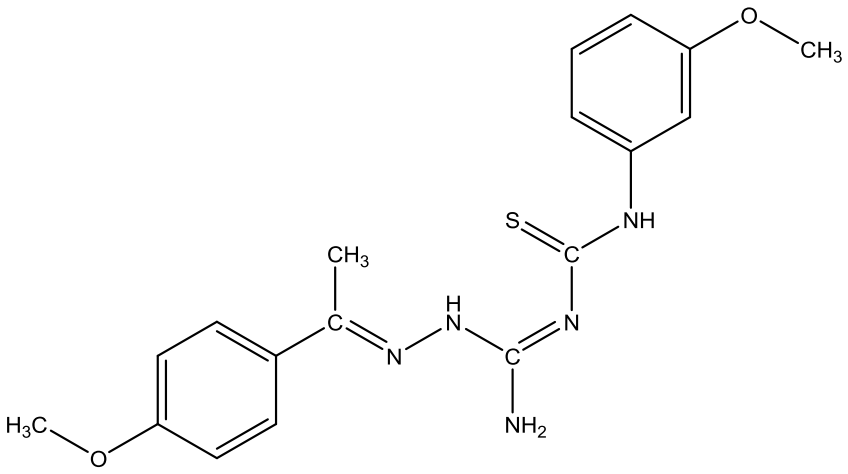


(1*Z*,2*E*)-2-(1-(4-methoxyphenyl)ethylidene)-*N*'-(naphthalen-1-ylcarbamothioyl)hydrazine-1-carboximidamide

AGII13

2.5.14. (1Z, 2E)-N'-((3-methoxyphenyl) carbamothioyl)-2-(1-(4-methoxyphenyl) ethylidene) hydrazine-1-carboximidamide AGII14

Add 0.2 g (0.969 mmol) of AG8 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. (0.135mmol) of 3-methoxyphenylIsothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.126g, yield 63%) of $C_{18}H_{21}N_5O_2S$, 371.46 g / mol, Melting point (144 - 146) ˚C

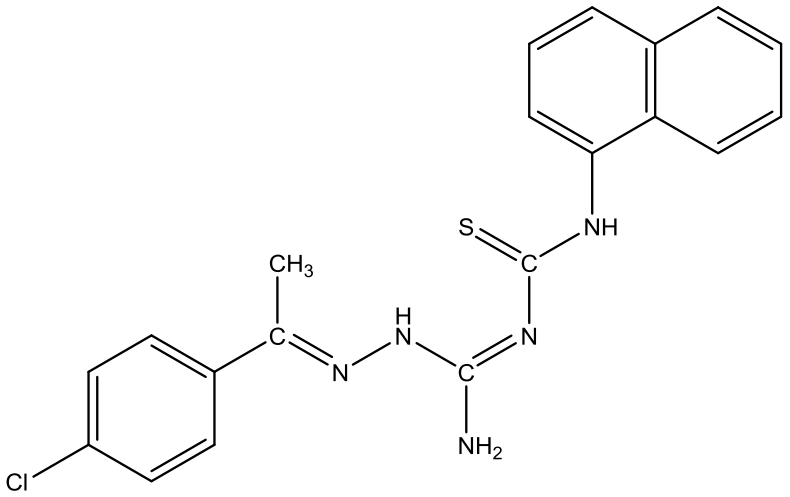


(1*Z*,2*E*)-*N*'-((3-methoxyphenyl)carbamothioyl)-2-(1-(4-methoxyphenyl)ethylidene)hydrazine-1-carboximidamide

AGII14

2.5.15. (1Z, 2E)-2-(1-(4-chlorophenyl) ethylidene)-N'-(naphthalen-1-ylcarbamothioyl) hydrazine-1-carboximidamide AGII15

Add 0.1 g (0.474 mmol) of AG9 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. 0.088 g of 1-Naphthisothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.062 g, yield 62%) of $C_{20}H_{18}ClN_5S$, 395.91g / mol, Melting point (166 - 168) ˚C

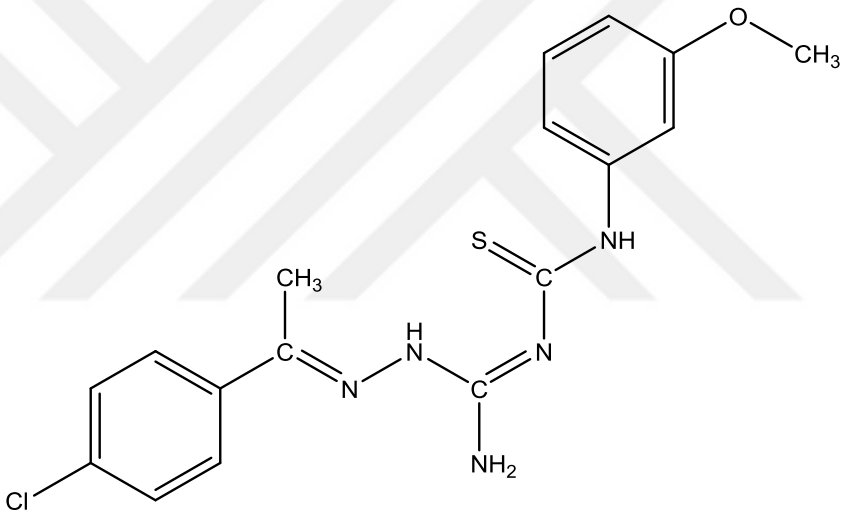


(1*Z*,2*E*)-2-(1-(4-chlorophenyl)ethylidene)-*N*'-(naphthalen-1-ylcarbamothioyl)hydrazine-1-carboximidamide

AGII15

2.5.16. (1Z, 2E)-2-(1-(4-chlorophenyl) ethylidene)-N'-((3-methoxyphenyl) carbamot hioyl) hydrazine-1-carboximidamide AGII16

Add 0.1 g (0.474 mmol) of AG9 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. (0.067mmol) of 3-methoxyphenylIsothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.041 g, yield 41%) of $C_{17}H_{18}ClN_5OS$, 375.88 g / mol, Melting point (140 - 143) ˚C



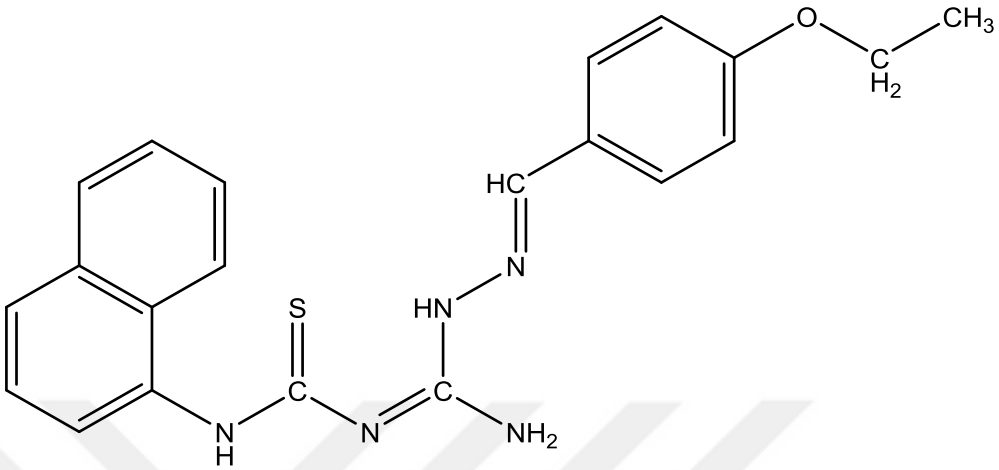
(1*Z*,2*E*)-2-(1-(4-chlorophenyl)ethylidene)-*N*'-((3-methoxyphenyl)carbamothioyl)hydrazine-1-carboximidamide

AGII16

2.5.17. (Z)-2-((E)-4-ethoxybenzylidene)-N'-(naphthalen-1-ylcarbamothioyl) hydrazine-1-carboximidamide AGII17

Add 0.2 g (0.969 mmol) of AG10 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. 0.179 g of 1-Naphthisothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a

vacuum oven set at 60 ° C or in a vacuum desiccator. (0.106 g, yield 53%) of $C_{21}H_{21}N_5OS$, 391.49 g / mol, Melting point (159 - 161) ˚C

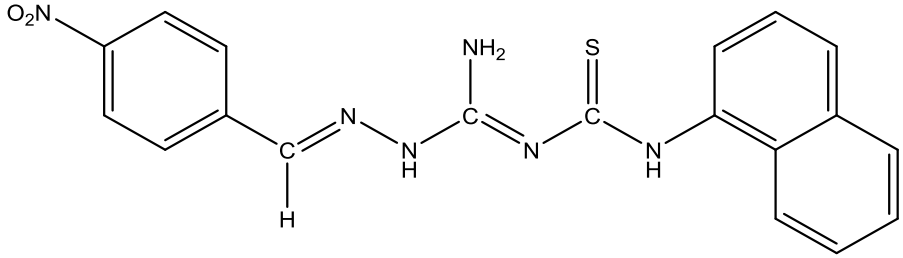


(*Z*)-2-((*E*)-4-ethoxybenzylidene)-*N*'-(naphthalen-1-ylcarbamothioyl)hydrazine-1-carboximidamide

AGII17

2.5.18. (E)-N'-(naphthalen-1-ylcarbamothioyl)-2-((E)-4-nitrobenzylidene) hydrazine-1-carboximidamide AGII18

Add 0.3 g (1.447 mmol) of AG12 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. 0.268 g of 1-Naphthisothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.216 g, yield 72%) of $C_{19}H_{16}N_6O_2S$, 392.44g / mol, Melting point (198 - 199) ˚C

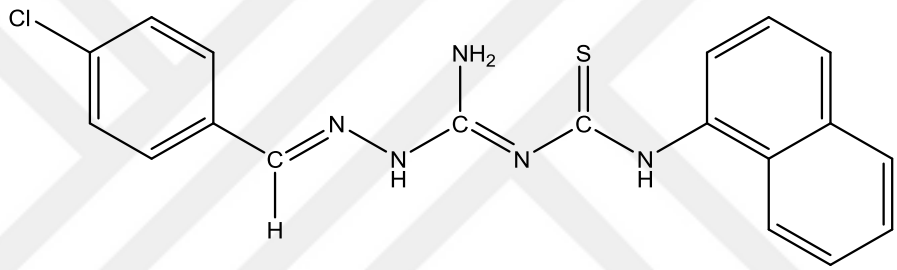


(*E*)-*N*'-(naphthalen-1-ylcarbamothioyl)-2-((*E*)-4-nitrobenzylidene)hydrazine-1-carboximidamide

AGII18

2.5.19. (E)-2-((E)-4-chlorobenzylidene)-N'-(naphthalen-1-ylcarbamothioyl) hydrazine-1-carboximidamide AGII19

Add 0.3 g (1.525 mmol) of AG13 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. 0.282 g of 1-Naphthisothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.207 g, yield 69%) of $C_{19}H_{16}CLN_5S$, 381.88 g / mol, Melting point (188 - 190) ˚C

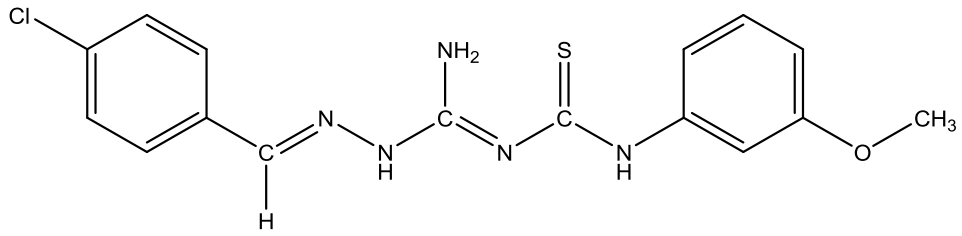


(*E*)-2-((*E*)-4-chlorobenzylidene)-*N*'-(naphthalen-1-ylcarbamothioyl)hydrazine-1-carboximidamide

AGII19

2.5.20. (E)-2-((E)-4-chlorobenzylidene)-N'-((3-methoxyphenyl) carbamothioyl) hydrazine-1-carboximidamide AGII20

Add 0.3 g (1.525 mmol) of AG13 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. (0.213mmol) of 3-methoxyphenylIsothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.168 g, yield 56%) of $C_{16}H_{16}CLN_5OS$, 361.85 g / mol, Melting point (178 - 179) ˚C

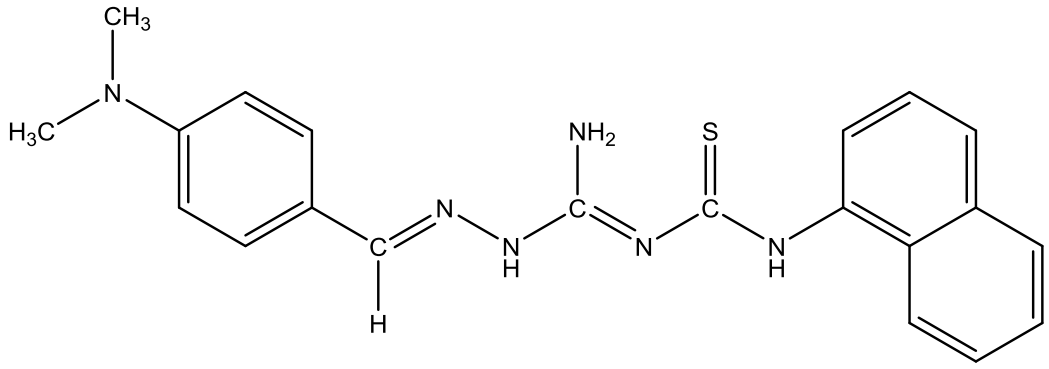


(*E*)-2-((*E*)-4-chlorobenzylidene)-*N*'-((3-methoxyphenyl)carbamothioyl)hydrazine-1-carboximidamide

AGII20

2.5.21. (E)-2-((E)-4-(dimethylamino) benzylidene)-N'-(naphthalen-1-ylcarbamot hioyl) hydrazine-1-carboximidamide AGII21

Add 0.3 g (1.461 mmol) of AG11 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. 0.27 g of 1-Naphthisothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.144g, yield 48%) of $C_{21}H_{22}N_6S$, 390.51 g / mol, Melting point (176 - 177) ˚C



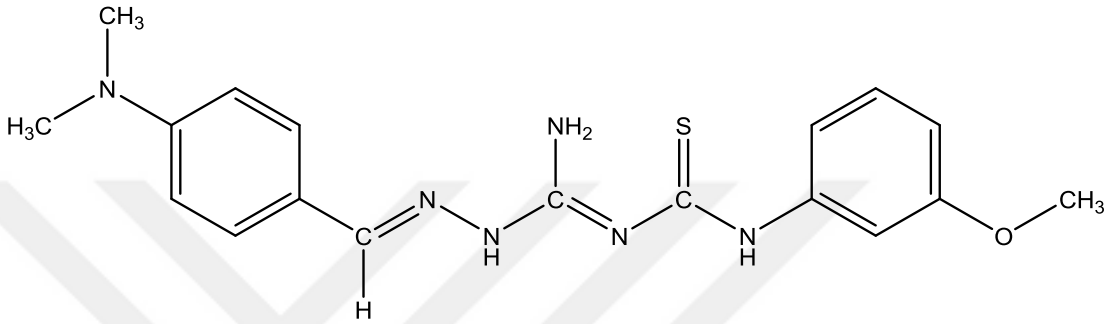
(*E*)-2-((*E*)-4-(dimethylamino)benzylidene)-*N*'-(naphthalen-1-ylcarbamothioyl)hydrazine-1-carboximidamide

AGII21

2.5.22. (E)-2-((E)-4-(dimethylamino) benzylidene)-N'-((3-methoxyphenyl) carba mothioyl) hydrazine-1-carboximidamide AGII22

Add 0.3 g (1.461 mmol) of AG11 over 15 ml of acetonitrile and reflux for 5-10 min. It is observed that there is no clear solution in this heating. (0.204mmol)

of 3-methoxyphenylIsothiocyanate is added to the hot suspension under reflux and refluxed for 1 hour. The reaction is followed by TLC. It is left to 24 hours. The yellow colored substance is filtered off and washed with hot ethanol. TLC (thin layer chromatography) detects the impurity of the substance. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (0.123 g, yield 41%) of $C_{18}H_{22}N_5OS$, 370.48 g / mol, Melting point (175 - 177) ˚C



(*E*)-2-((*E*)-4-(dimethylamino)benzylidene)-*N*'-((3-methoxyphenyl)carbamothioyl)hydrazine-1-carboximidamide

AGII22

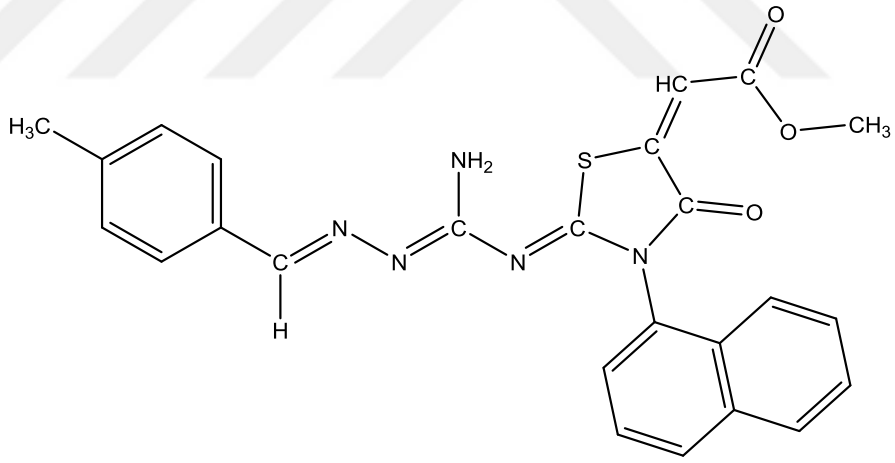
2.6. Reactions of Dimethyl acetylene Dicarboxylate (DMAD) with N-(aminoamidino) thioureas: Synthesis of 4-oxo-1, 3-thiazolidin-5-ylidene acetate derivatives

Dimethylacetylenedicarboxylate is an electronically poor compound. The DMAD compound can be obtained by first brominating maleic acid with dehydrohalogenation reaction [6].

The following are the various optimum conditions for the compounds we synthesize. Experiments were carried out on benzene, ethanol, and methanol. Optimum conditions were met in methanol. Temperature scans were done. As a result of different experiments, optimum conditions were optimized and reactions were carried out according to these conditions. Interactions of the compounds will be discussed in the mechanism part.

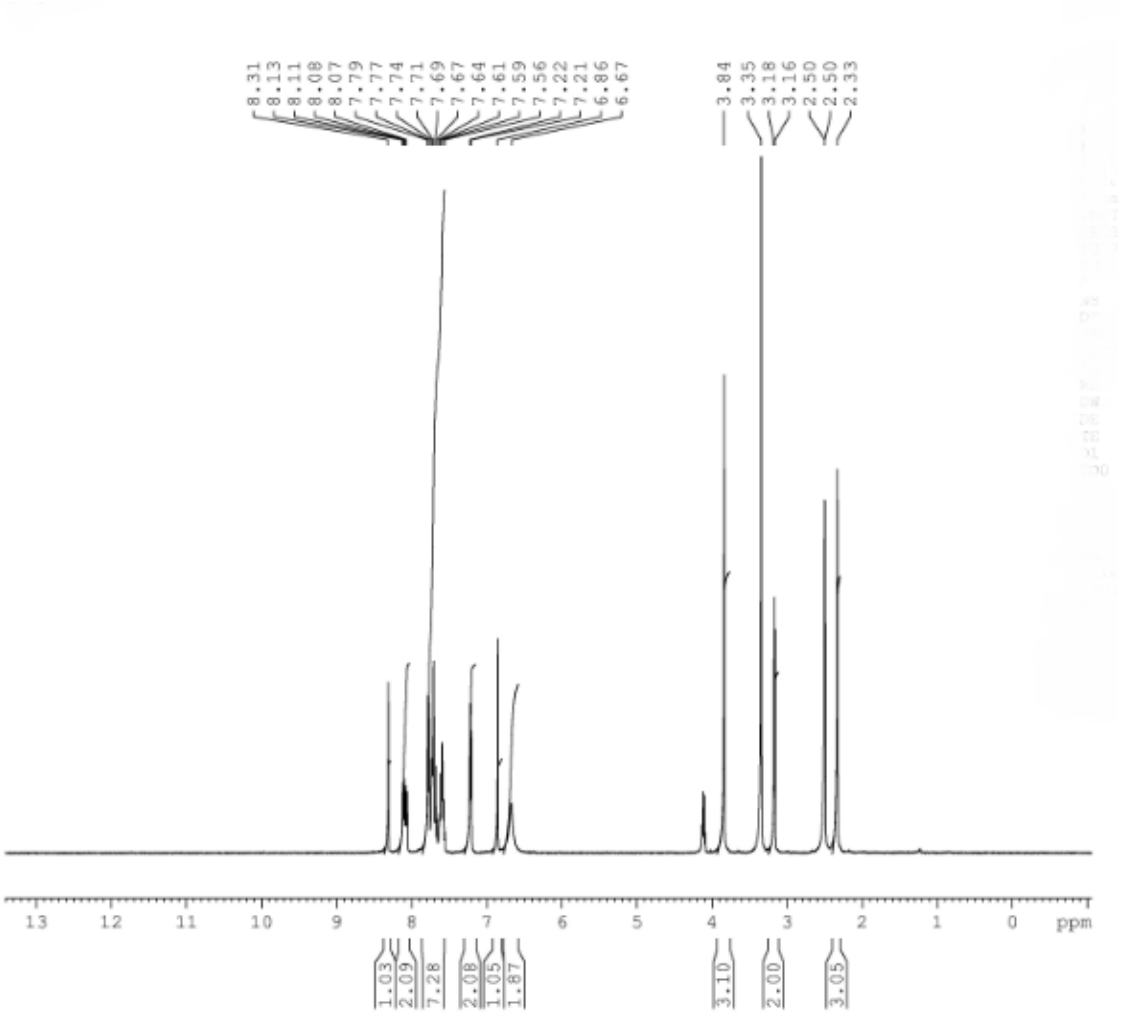
2.6.1.Methyl (E)-2-((Z)-2-(((E)-N'-((E)-4-methylbenzylidene) carbamohydrazonoyl) imino)-3-(naphthalen-1-yl)-4-oxothiazolidin-5-ylidene) acetate IHB1

To 0.1 g (0.276mmol) of (AGII1) is added 15 ml of methanol and the mixture is heated under reflux for 8-14 min. When 0.034 ml of Dimethylacetylenedicarboxylate (DMAD) is added to the hot suspension in suspension, orange colored precipitates form in the solution medium. Continue heating for 2-5 minutes under the cooler. The reaction is followed by TLC. It was observed that the solution color became darker by the heating process. It is observed that precipitation with the effect of temperature increases. It is left to cool overnight and the solution is filtered and washed in hot 5 ml of methanol. The impurity of the material is checked by TLC, and in the case of impurities, the washing process is repeated. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (Hand)(0.044g, yield 44%) of $C_{25}H_{21}N_5O_3S$, 471.54 g / mol, Melting point (146-148) ˚C

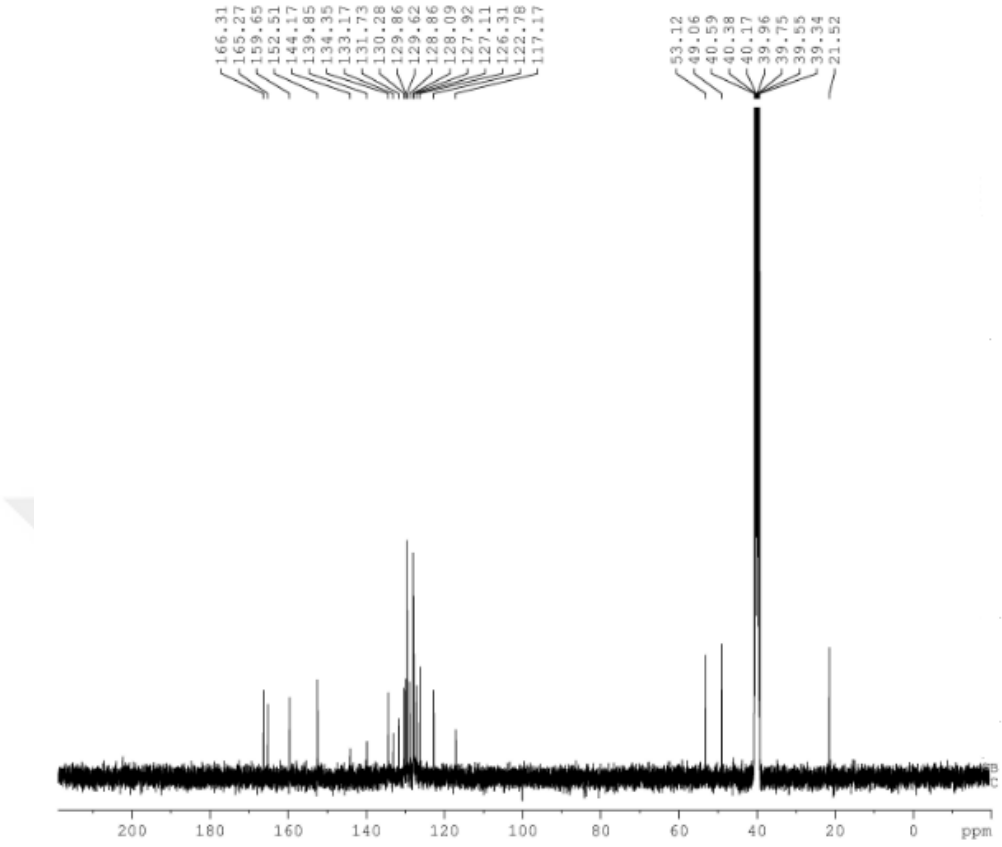


methyl (*E*)-2-((*Z*)-2-(((*E*)-*N*'-((*E*)-4-methylbenzylidene)carbamohydrazonoyl)imino)-3-(naphthalen-1-yl)-4-oxothiazolidin-5-ylidene)acetate

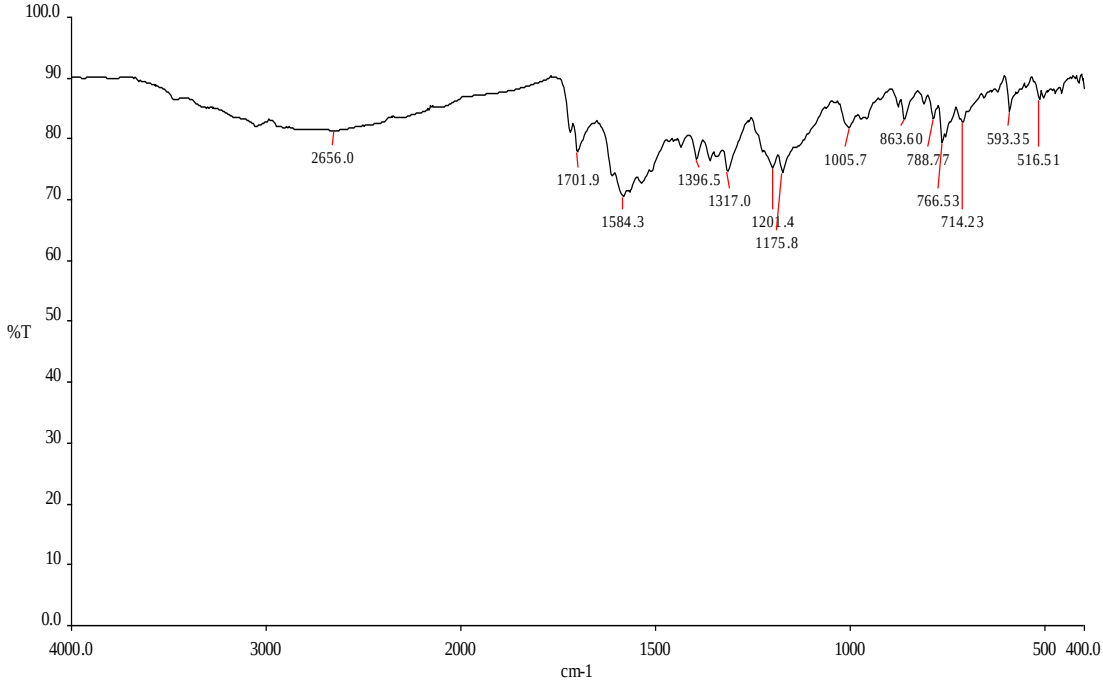
IHB1



^{1}H –NMR Spectrum IHB1



^{13}C-NMR Spectrum IHB1

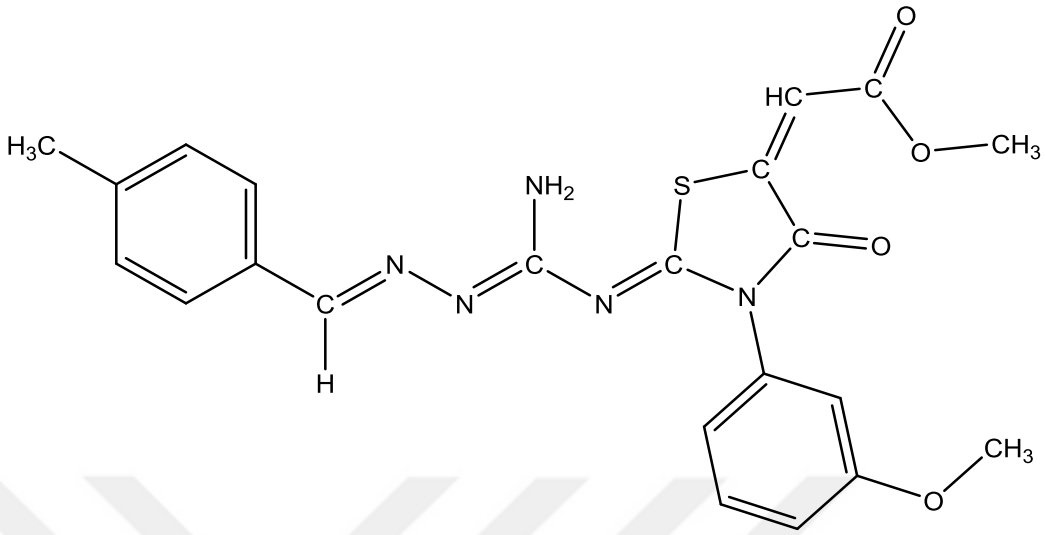


IR Spectrum IHB1

^{1}H-NMR (400 MH_Z, DMSO- δ_6) 8.31(m,1H), 8.13-8.07 (d, J = 8.4 Hz, 2H), 7.77-7.56 (q, J = 7.7 Hz, 7H), 7.22-7.21 (m, 2H), 6.86 (m, 1H), 6.67 (m, 2H), 3.84 (m, 3H), 3.82 (s, 2H), 2.32 (m, 3H). ^{13}C-NMR (100 MHz, DMSO- δ_6) 166.31, 165.27, 159.65, 152.51, 144.17, 139.85, 134.35, 133.17, 131.73, 130.28, 129.86, 129.62, 128.86, 128.09, 127.92, 127.11, 126.31, 122.78, 117.17, 53.12, 49.06, 21.52, IR (cm^{-1}) 3392-3517 N-H stretching, 3126 = C-H stretching, 1709 C = O stretching, 1604-1634C = N stretching, 1589 C = C stretching

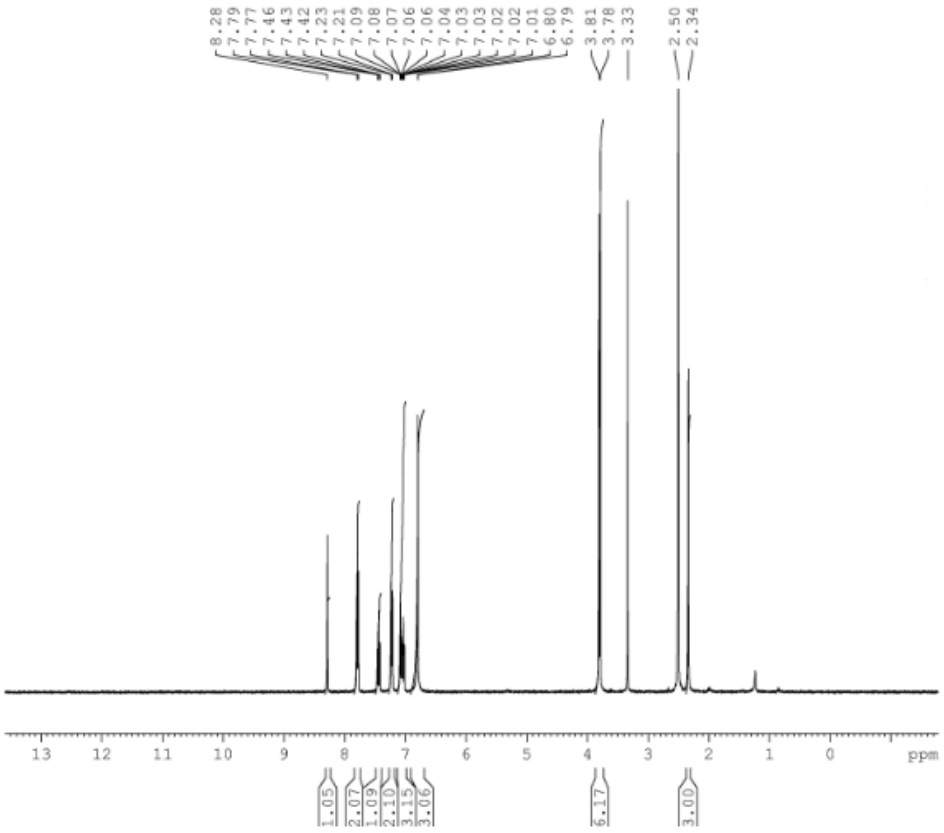
2.6.2. Methyl (E)-2-((Z)-3-(3-methoxyphenyl)-2-(((E)-N'-((E)-4-methylbenzylidene) carbamohydrazonoyl) imino)-4-oxothiazolidin-5-ylidene) acetate IHB2

To 0.1 g (0.293 mmol) of (AGII2) is added 15 ml of methanol and the mixture is heated under reflux for 8-12 min. When 0.036 ml of Dimethylacetylenedicarboxylate (DMAD) is added to the hot suspension in suspension, orange colored precipitates form in the solution medium. Continue heating for 2-5 minutes under the cooler. The reaction is followed by TLC. It was observed that the solution color became darker by the heating process. It is observed that precipitation with the effect of temperature increases. It is left to cool overnight and the solution is filtered and washed in hot 5 ml of methanol. The impurity of the material is checked by TLC, and in the case of impurities, the washing process is repeated. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (Hand)(0.070 g, yield 70%) of $C_{22}H_{21}N_5O_4S$, 451.5 g / mol, Melting point (209- 210) ˚C

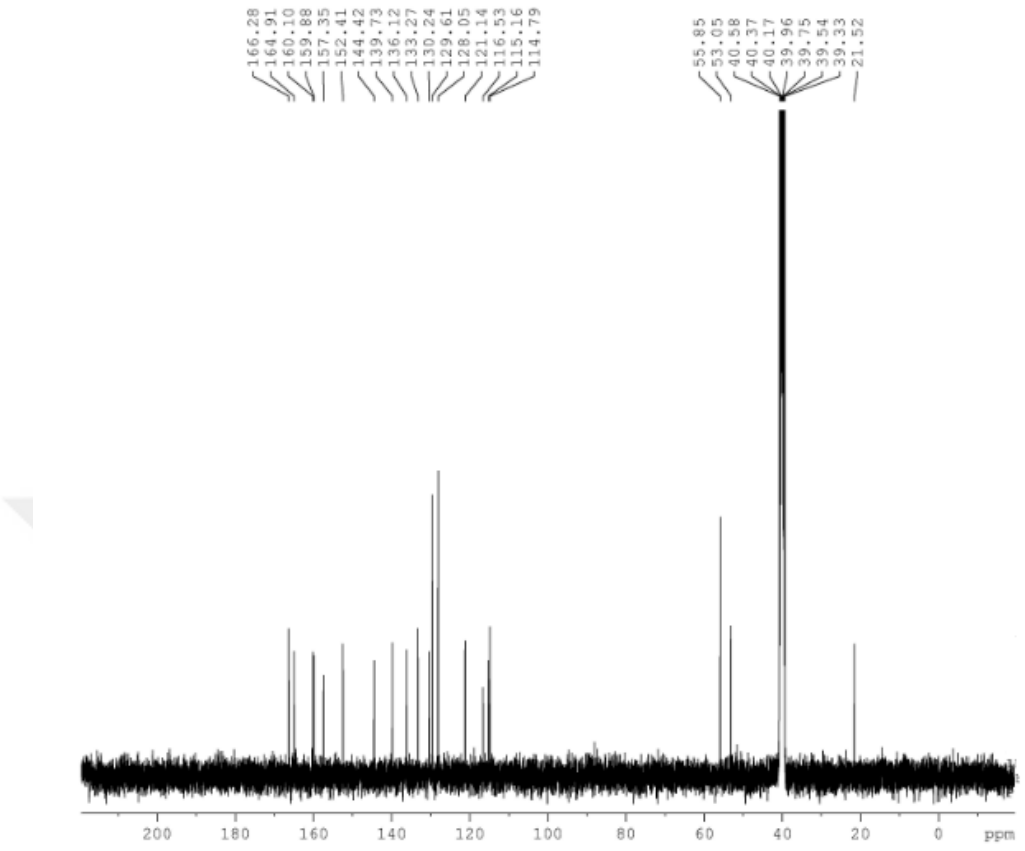


methyl (*E*)-2-((*Z*)-3-(3-methoxyphenyl)-2-(((*E*)-*N*'-((*E*)-4-methylbenzylidene)carbamohydrazonoyl)imino)-4-oxothiazolidin-5-ylidene)acetate

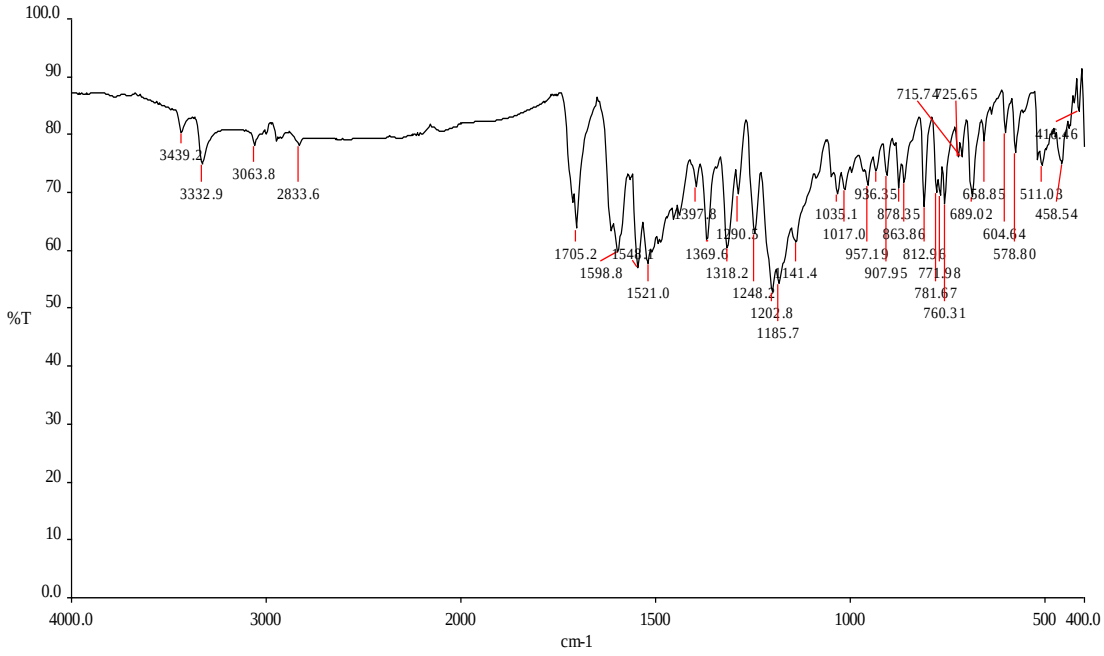
IHB2



^{1}H –NMR Spectrum IHB2



^{13}C-NMR Spectrum IHB2

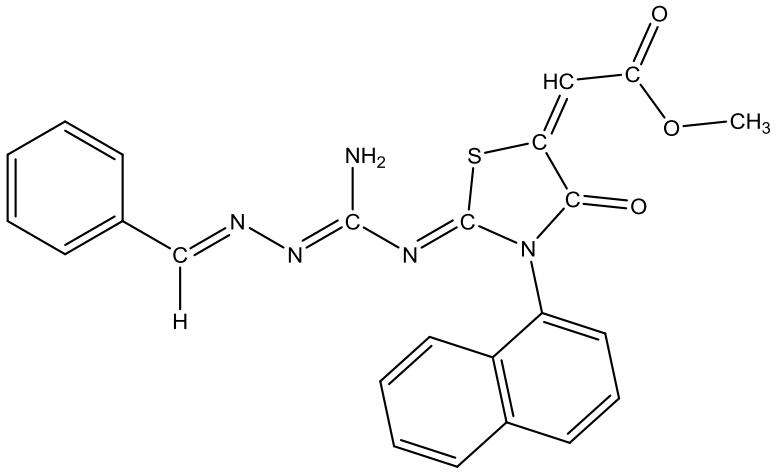


IR Spectrum IHB2

^{1}H-NMR (400 MH_Z, DMSO- δ_6) 8.28 (m, 1H), 7.79-7.77 (d, J=7.4 Hz, 2H), 7.47-7.42 (s, 1H), 7.23-7.21 (s, 2H), 6.83 (s, 1H), 7.09-7.02(q, J = 6.9 Hz, 3H), 6.79 (d, J=6.7Hz, 3H), 3.81 (m, 6H), 2.50 (m, 3H), 2.34 (s, 0H). ^{13}C-NMR (100 MHz, DMSO- δ_6) 166.28, 164.91, 160.10, 159.88, 157.735, 152.41, 144.42, 139.73, 136.12, 133.27,130.24, 129.61, 128.05, 121.14, 116.53, 115.16, 114.79, 55.85, 53.05 ,21.52, IR (cm^{-1}) 3332-3439 N-H stretching, 2833-3063 = C-H stretching, 1705 C = O stretching, 1548-11598C = N stretching, 1521 C = C stretching

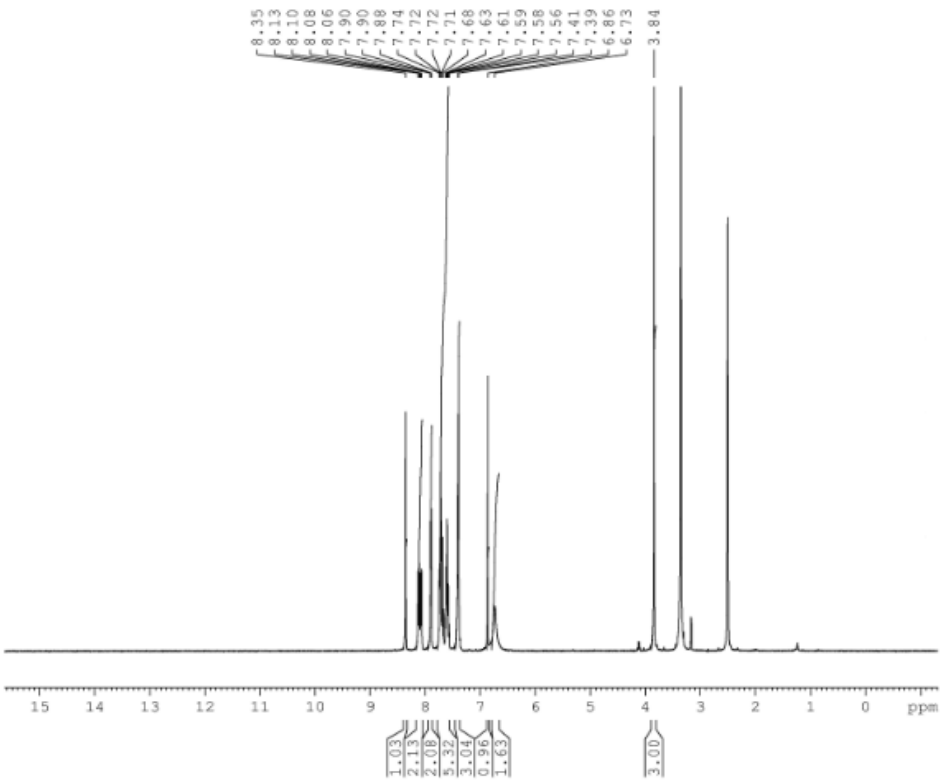
2.6.3. Methyl (E)-2-((Z)-2-(((E)-N'-((E)-benzylidene) carbamohydrazonoyl) imino)-3-(naphthalen-1-yl)-4-oxothiazolidin-5-ylidene) acetate IHB3

To 0.1 g (0.288 mmol) of (AGII3) is added 15 ml of methanol and the mixture is heated under reflux for 8-12 min. When 0.036 ml of Dimethylacetylenedicarboxylate (DMAD) is added to the hot suspension in suspension, orange colored precipitates form in the solution medium. Continue heating for 2-5 minutes under the cooler. The reaction is followed by TLC. It was observed that the solution color became darker by the heating process. It is observed that precipitation with the effect of temperature increases. It is left to cool overnight and the solution is filtered and washed in hot 5 ml of methanol. The impurity of the material is checked by TLC, and in the case of impurities, the washing process is repeated. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (Hand) (0.052 g, yield52%) of $C_{24}H_{19}N_5O_3S$, 457.51 g / mol, Melting point (183 - 185) ˚C

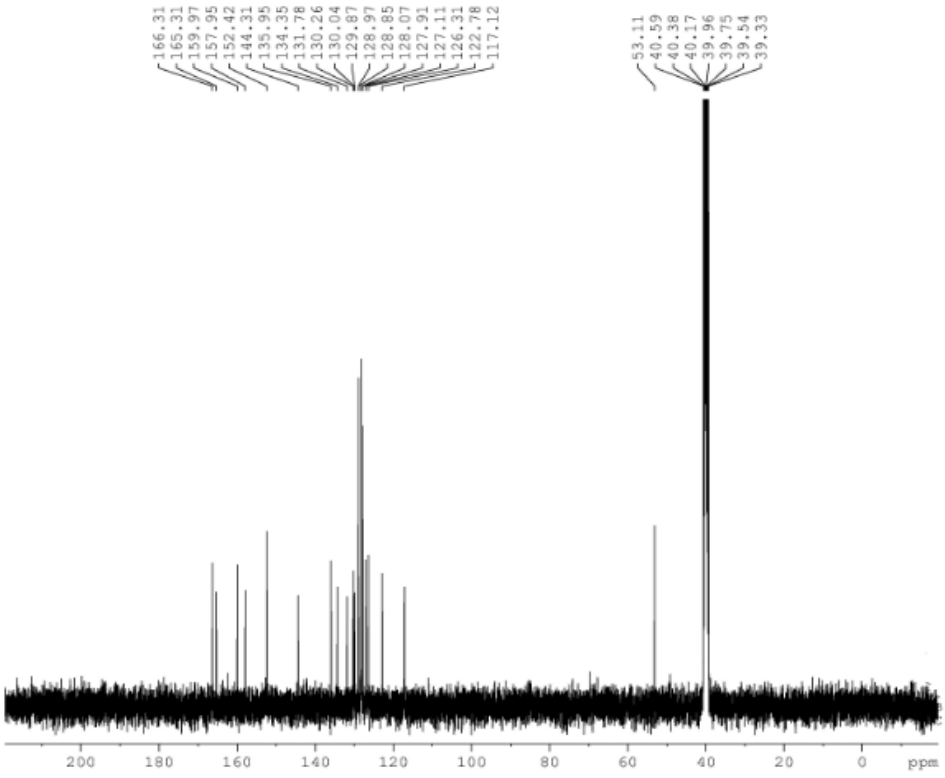


methyl (*E*)-2-((*Z*)-2-(((*E*)-*N*'-((*E*)-benzylidene)carbamohydrazonoyl)imino)-3-(naphthalen-1-yl)-4-oxothiazolidin-5-ylidene)acetate

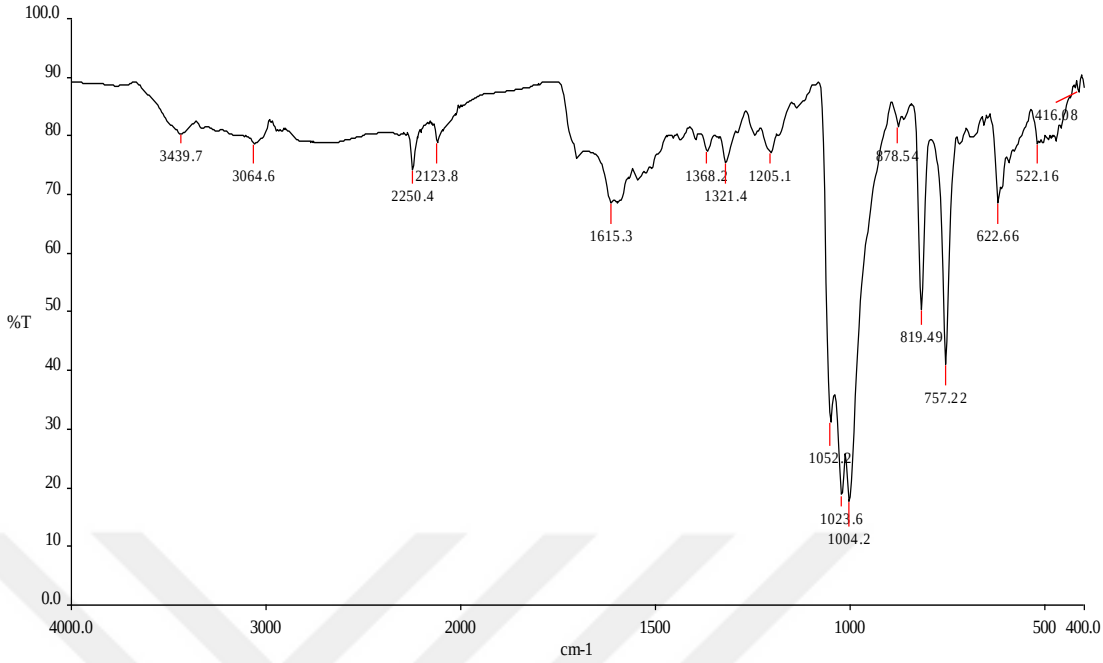
IHB3



^{1}H –NMR Spectrum IHB3



^{13} C-NMR Spectrum IHB3



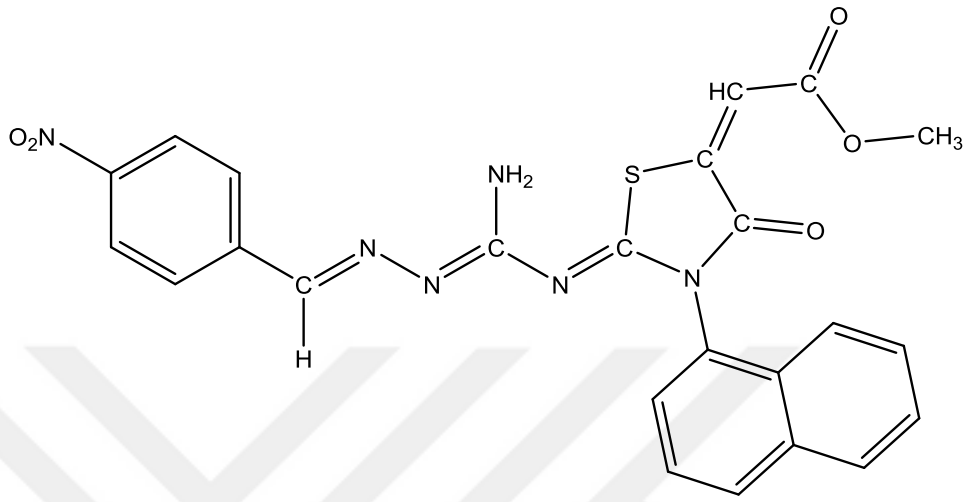
IR Spectrum IHB3

^{1}H-NMR (400 MH$_Z$, DMSO- δ_6) 8.35 (m, 1H), 8.13-7.90 (d, J=7.4 Hz, 2H), 7.88 (m, 2H), 7.74-7.59 (d, J=7.6 Hz, 5H), 7.39 (m, 3H), 6.86(m, 1H), 6.73 (d, J=6.7Hz, 2H), 3.84 (m, 3H). ^{13}C-NMR (100 MH$_Z$, DMSO- δ_6) 166.31, 165.31, 159.97, 157.95, 152.42, 144.31, 135.95, 134.35, 131.78, 130.26, 130.04, 129.78, 128.97, 128.85, 128.07, 126.31, 122.78, 117.12, 53.11, IR (cm^{-1}) 3439 N-H stretching, 3064 = C-H stretching, 1615 C = O stretching, 1321-1368 C - N stretching, 1205 C - O stretching

2.6.4. Methyl (E)-2-((Z)-3-(naphthalen-1-yl)-2-(((E)-N'-((E)-4-nitrobenzylidene) carbamohydrazonoyl) imino)-4-oxothiazolidin-5-ylidene) acetateIHB4

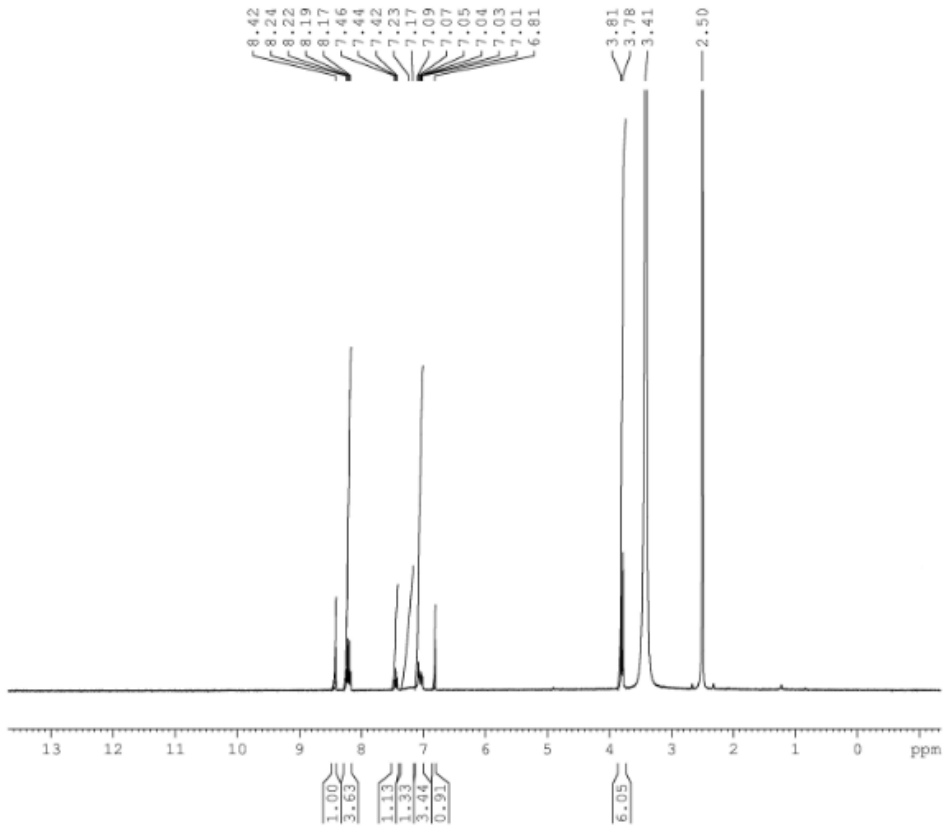
To 0.082 g (0.220 mmol) of (AGII17) is added 15 ml of methanol and the mixture is heated under reflux for 8-12 min. When 0.027 ml of Dimethylacetylenedicarboxylate (DMAD) is added to the hot suspension in suspension, orange colored precipitates form in the solution medium. Continue heating for 2-5 minutes under the cooler. The reaction is followed by TLC. It was observed that the solution color became darker by the heating process. It is observed that precipitation with the effect of temperature increases. It is left to cool overnight and the solution is filtered and washed in hot 5 ml of methanol. The impurity of the material is checked by TLC, and in the case of impurities,

the washing process is repeated. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (Hand) (1.47 g, yield 73%) of $C_{21}H_{18}N_6O_6S$, 482.47 g / mol, Melting point (211 - 212) ˚C

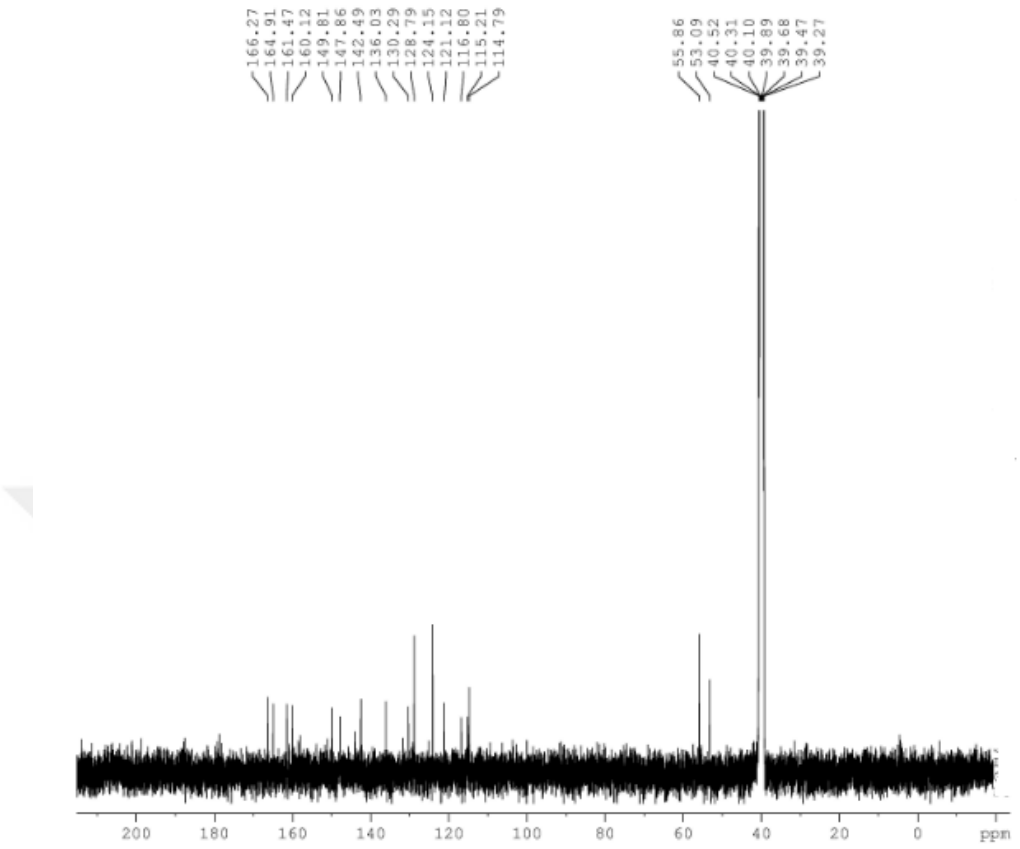


methyl (*E*)-2-((*Z*)-3-(naphthalen-1-yl)-2-(((*E*)-*N*'-((*E*)-4-nitrobenzylidene)carbamohydrazonoyl)imino)-4-oxothiazolidin-5-ylidene)acetate

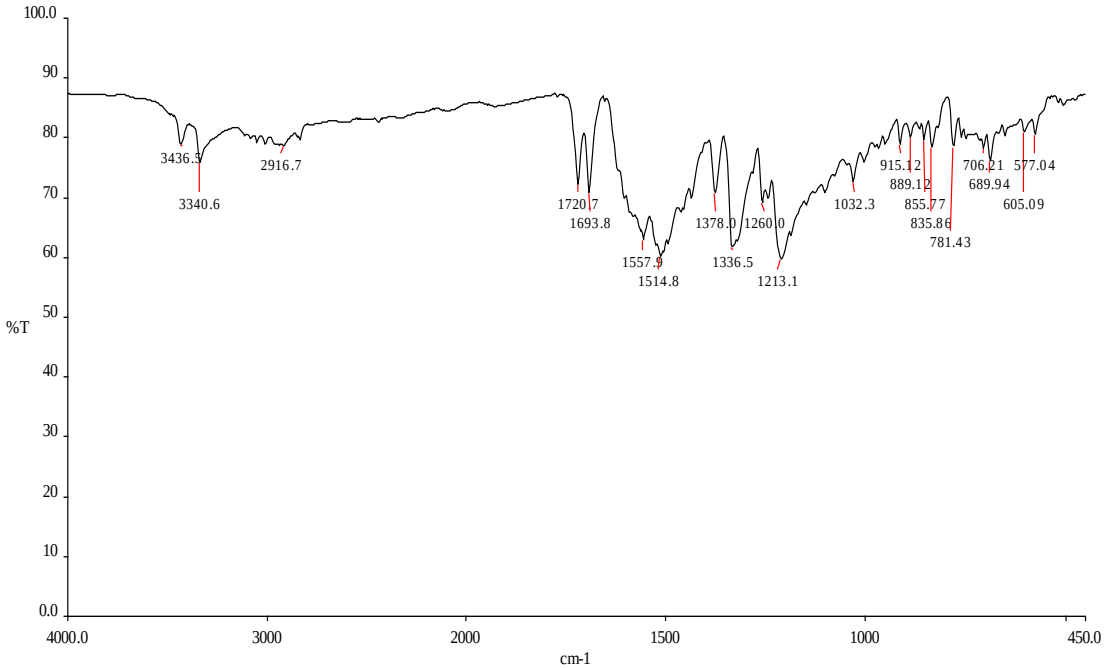
IHB4



^{1}H –NMR Spectrum IHB4



^{13}C-NMR Spectrum IHB4

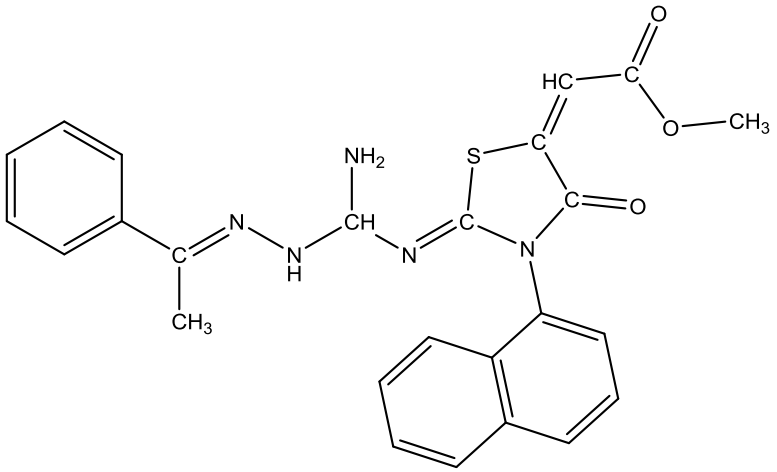


IR Spectrum IHB4

^{1}H-NMR (400 MH_Z, DMSO- δ_6) 8.42 (m, 1H), 8.24-8.17 (t, J=8.4 Hz, 4H), 7.46-7.42 (m, 1H), 7.23-7.17 (m 1H), 7.09-7.01 (m, 3H), 6.81(m, 1H), 3.81 (m, 6H). ^{13}C-NMR (100 MH_Z, DMSO- δ_6) 166.27, 164.91, 161.47, 160.12, 149.81, 147.86, 142.49, 136.03, 130.29, 128.79, 124.15, 121.12, 116.80, 115.21, 114.79, 55.86, 53.09, IR (cm^{-1}) 3340-3436 N-H stretching, 2916 = C-H stretching, 1720 C = O stretching, 1514-1557 C = N stretching, 1693 C = C stretching , 1336-1378 C - N stretching, 1213 -1260 C - O stretching, 1023 C - C stretching.

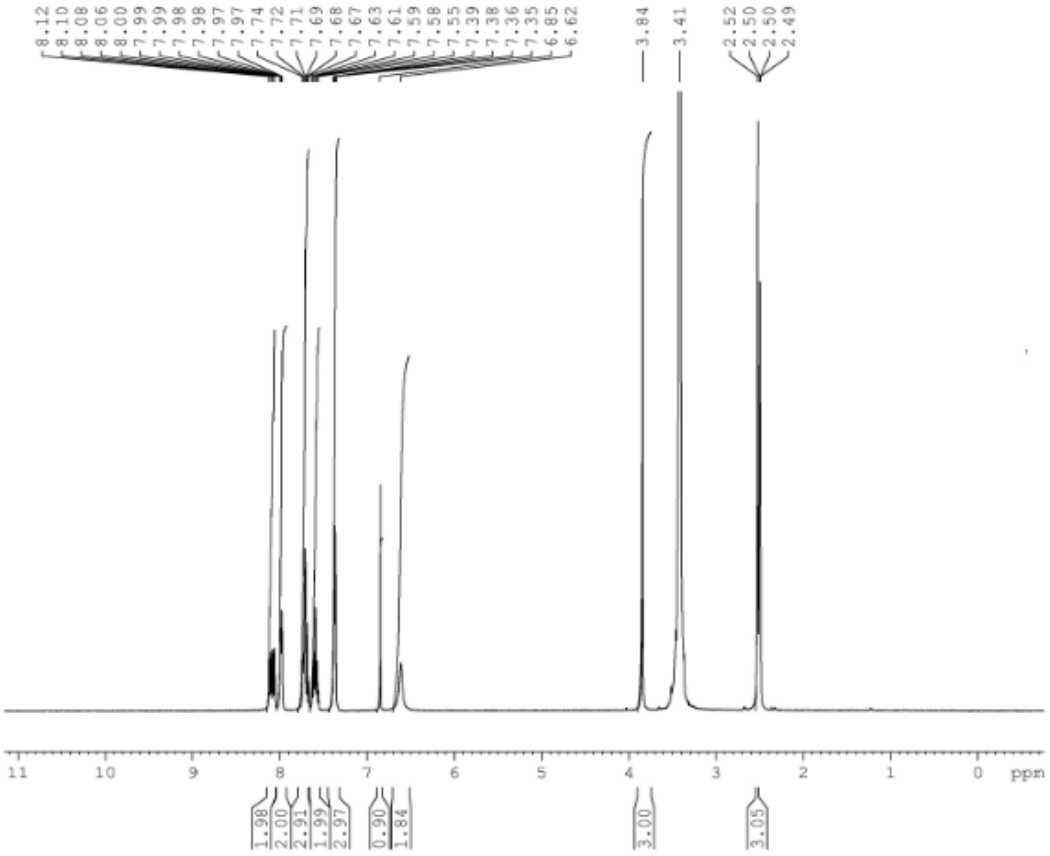
2.6.5: Methyl (E)-2-((Z)-2-((amino (2-((E)-1-phenylethylidene) hydrazinyl) methyl) imino)-3-(naphthalen-1-yl)-4-oxothiazolidin-5-ylidene) acetate IHB5

To 0.1 g (0.276 mmol) of (AGII5) is added 15 ml of methanol and the mixture is heated under reflux for 8-12 min. When 0.034 ml of Dimethylacetylenedicarboxylate (DMAD) is added to the hot suspension in suspension, orange colored precipitates form in the solution medium. Continue heating for 2-5 minutes under the cooler. The reaction is followed by TLC. It was observed that the solution color became darker by the heating process. It is observed that precipitation with the effect of temperature increases. It is left to cool overnight and the solution is filtered and washed in hot 5 ml of methanol. The impurity of the material is checked by TLC, and in the case of impurities, the washing process is repeated. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (Hand) (0.068 g, yield 68%) of $C_{25}H_{23}N_5O_3S$, 473.55 g / mol, Melting point (237 -238) ˚C

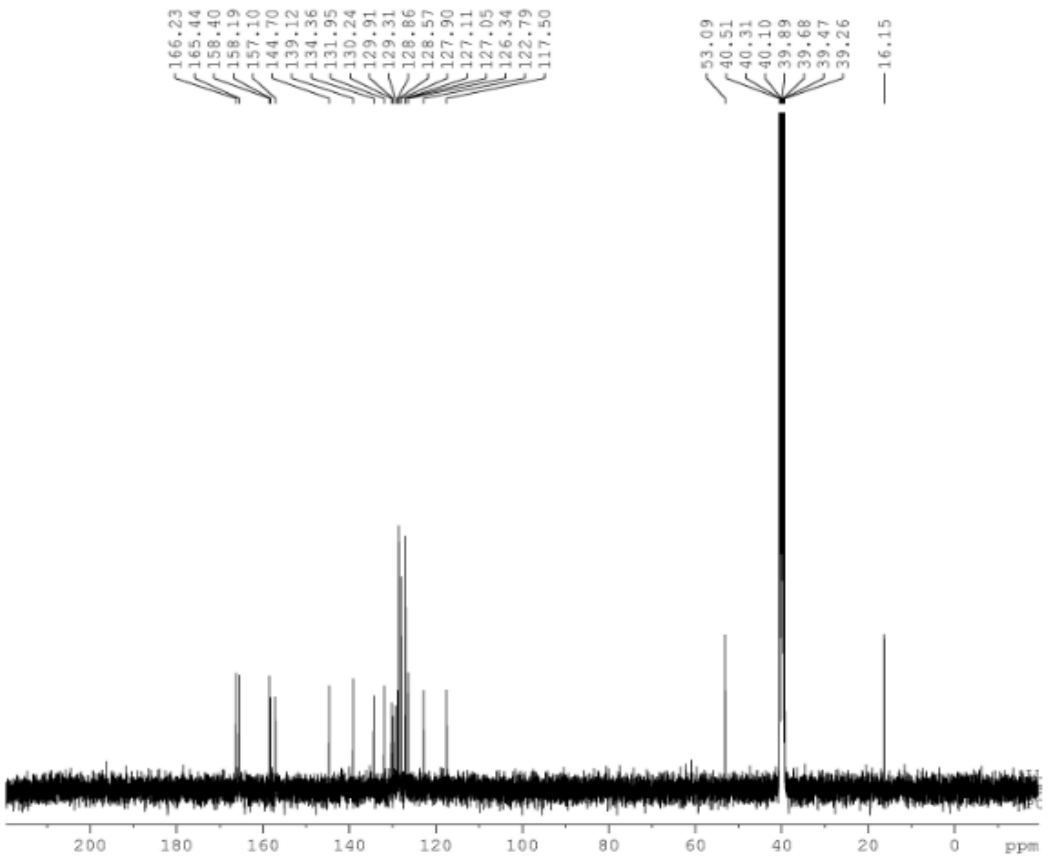


methyl (*E*)-2-((*Z*)-2-((amino(2-((*E*)-1-phenylethylidene)hydrazinyl)methyl)imino)-3-(naphthalen-1-yl)-4-oxothiazolidin-5-ylidene)acetate

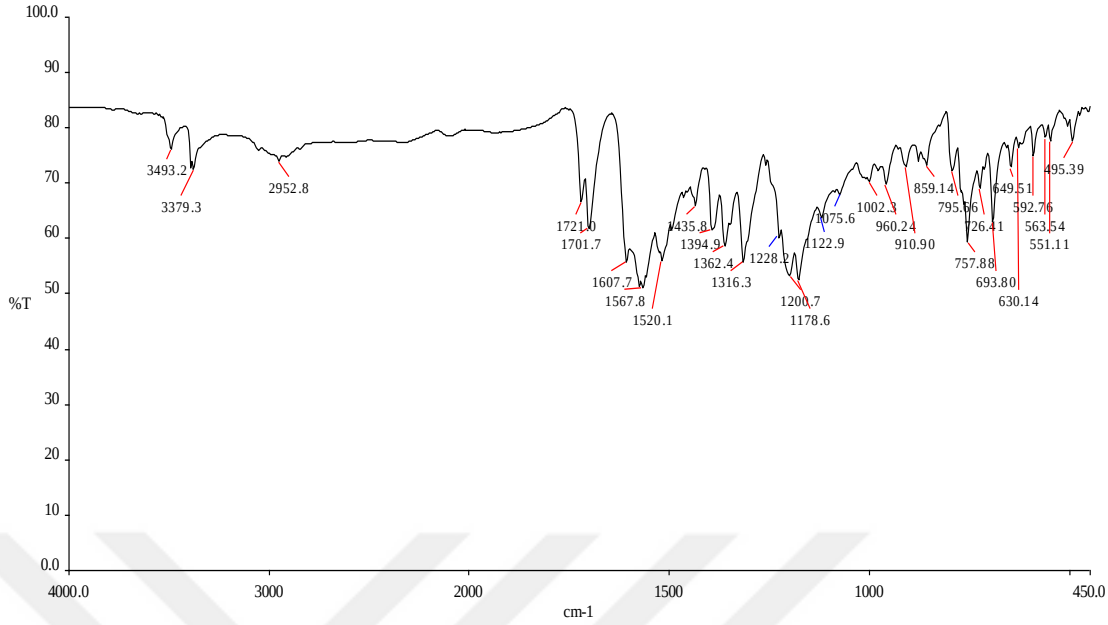
IHB5



[1]H –NMR Spectrum IHB5



[13] C-NMR Spectrum IHB5



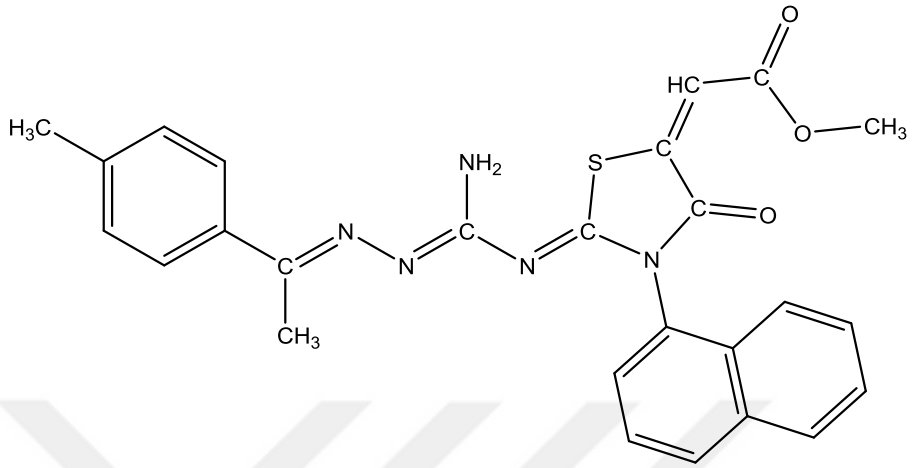
IR Spectrum IHB5

^{1}H-NMR (400 MH$_Z$, DMSO- δ_6) 8.12-7.98 (d, J=8.2 Hz, 2H), 7.97 (d, J=7.6 Hz, 2H), 7.74-7.67 (d, J=7.4 Hz, 3H), 7.63-7.55 (d, J=7.6 Hz, 2H), 7.39 (m, 3H), 6.85(m, 1H), 6.62 (s, 2H), 3.84 (m, 3H), 2.52-2.49 (m, 3H). ^{13}C-NMR (100 MH$_Z$, DMSO- δ_6) 166.23, 165.44, 158.40, 158.19, 157.10, 144.70, 139.12, 134.36, 131.95,130.24, 129.91, 129.31, 128.86, 128.57, 127.90, 127.11, 127.05, 126.34, 122.79, 117.05, 53.09 ,16.15, IR (cm^{-1}) 3379-3493 N-H stretching, 2952 = C-H stretching, 1701-1720 C = O stretching, 1520-1567 C = N stretching, 1607 C = C stretching , 1316-1336 C - N stretching, 1200 - 1228 C - O stretching, 1075-1122 C - C stretching.

2.6.6. Methyl (E)-2-((Z)-3-(naphthalen-1-yl)-4-oxo-2-(((E)-N'-((E)-1-(p-tolyl) ethy lidene) carbamohydrazonoyl) imino) thiazolidin-5-ylidene) acetate IHB6

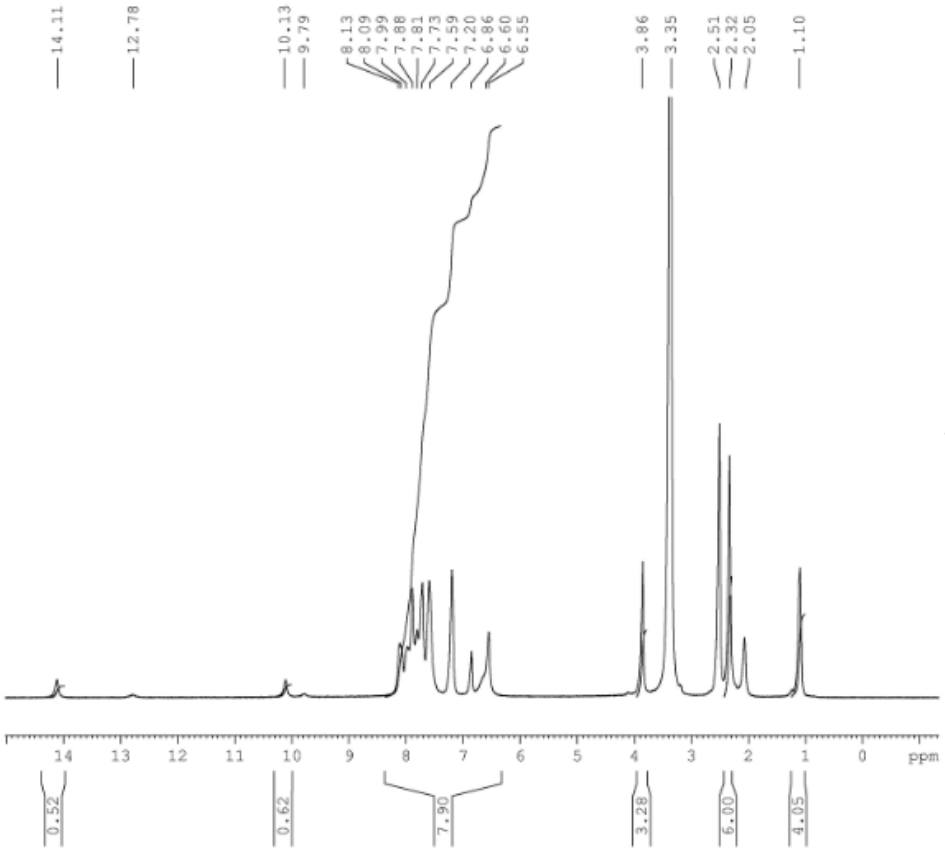
To 0.1 g (0.266 mmol) of (AGII6) is added 15 ml of methanol and the mixture is heated under reflux for 8-12 min. When 0.033ml of Dimethylacetylenedicarboxylate (DMAD) is added to the hot suspension in suspension, orange colored precipitates form in the solution medium. Continue heating for 2-5 minutes under the cooler. The reaction is followed by TLC. It was observed that the solution color became darker by the heating process. It is observed that precipitation with the effect of temperature increases. It is left to cool overnight and the solution is filtered and washed in hot 5 ml of methanol. The impurity of the material is checked by TLC, and in the case of impurities, the washing process is repeated. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum

desiccator. (Hand) (0.073 g, yield 73%) of $C_{26}H_{23}N_5O_3S$, 485.56g / mol, Melting point (187 - 191) ˚C

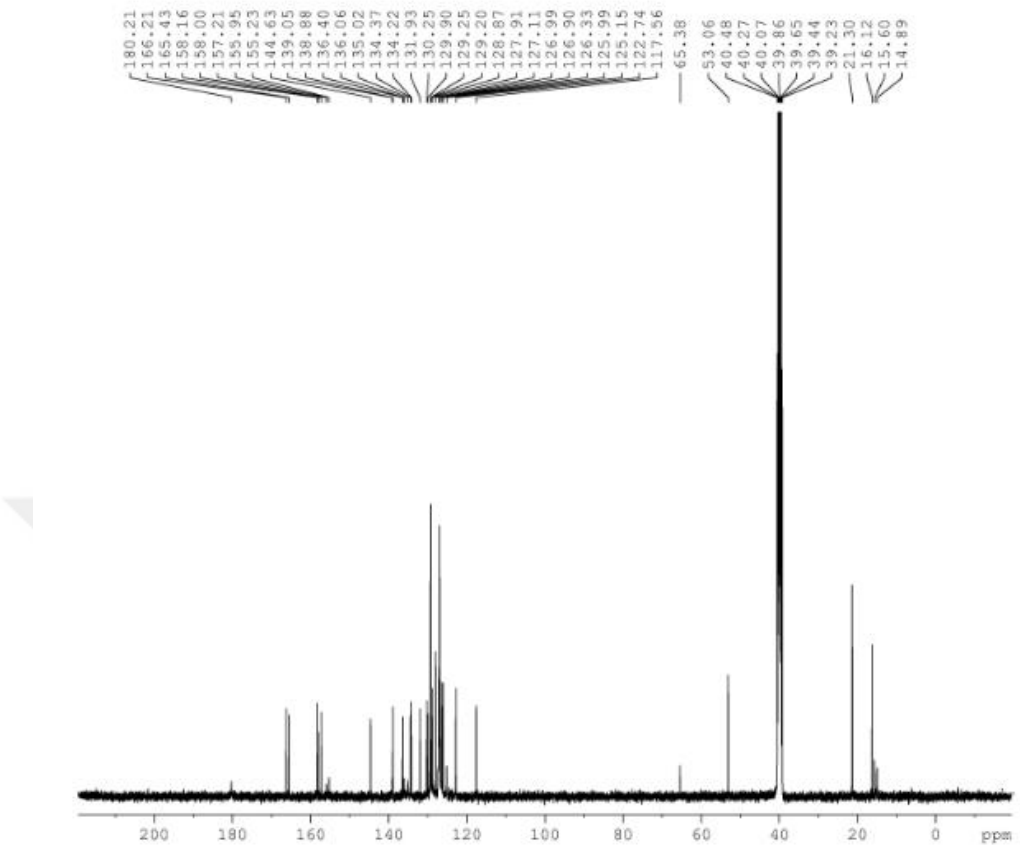


methyl (*E*)-2-((*Z*)-3-(naphthalen-1-yl)-4-oxo-2-(((*E*)-*N*'-((*E*)-1-(*p*-tolyl)ethylidene)carbamohydrazonoyl)imino)thiazolidin-5-ylidene)acetate

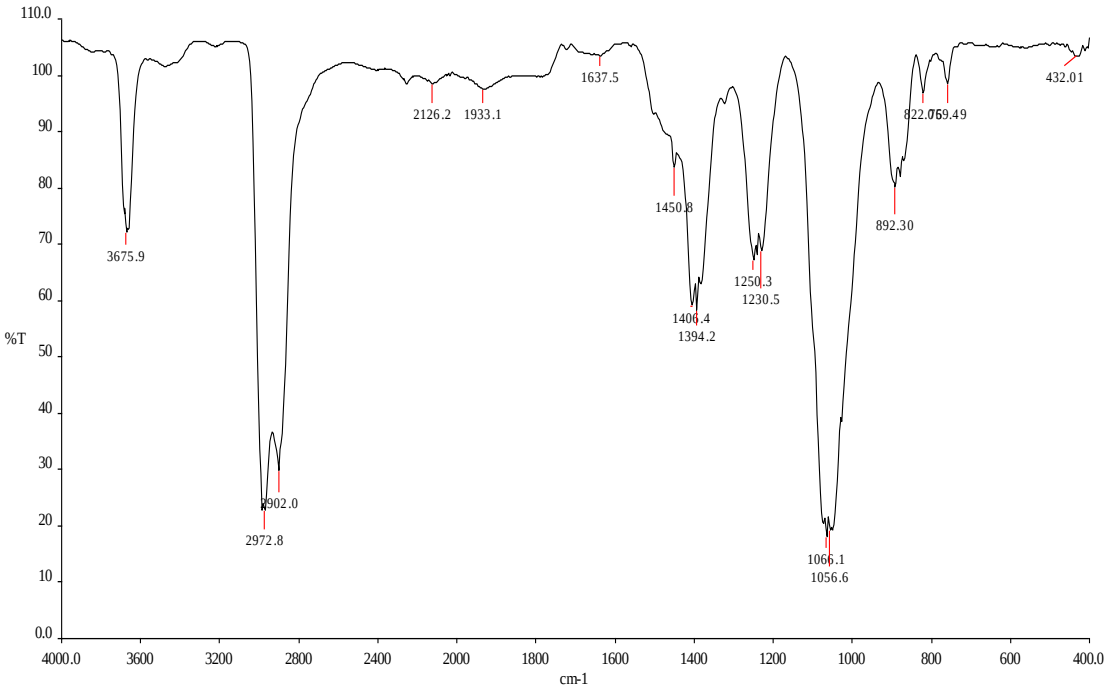
IHB6



^{1}H –NMR Spectrum IHB6



^{13}C-NMR Spectrum IHB6

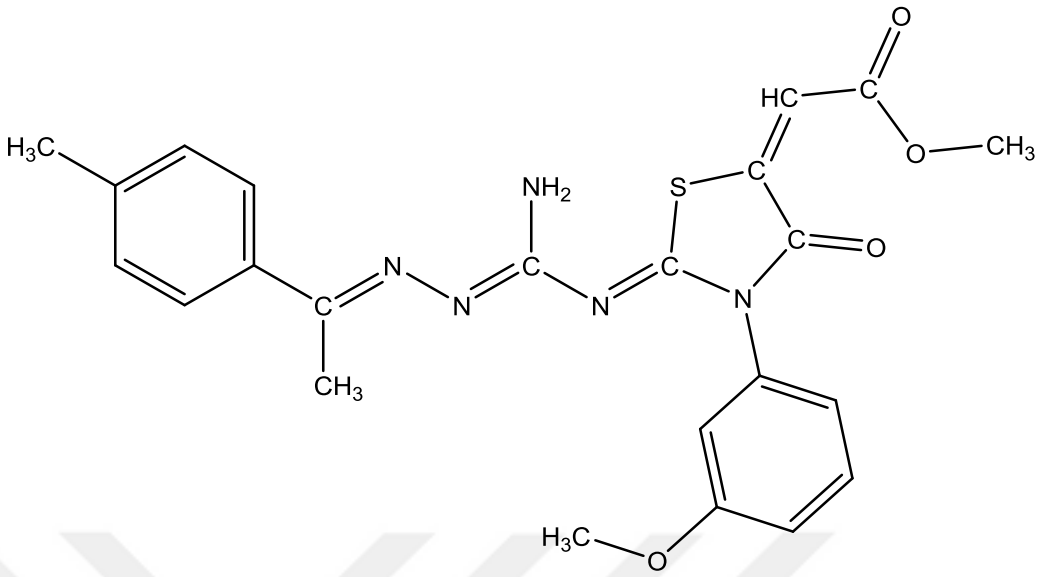


IR Spectrum IHB6

^{1}H-NMR (400 MH_Z, DMSO- δ_6) 14.11 (s, 0H), 10.13(s, 0H), 8.13-7.59 (d, J = 8.4 Hz, 4H), 7.20-7.78 (m, 2H), 6.6-6.55 (s, 2H), 3.86 (m, 3H), 2.51-205 (m, 6H), 1.1 (m, 4H). ^{13}C-NMR (100 MH_Z, DMSO- δ_6) 180.21, 166.21, 165.43, 158.16, 158.00, 157.21, 155.95, 155.23, 144.63, 139.05, 138.88, 136.40, 13606, 135.02, 134.37, 134.22, 131.93,130.25, 129.90, 129.25, 128.87, 127.91, 127.11, 126.99, 126.90, 126.33, 125.99, 125.15, 122.74, 117.56, 65.38, 53.06, 21.30, 16.12, 15.60, 14.89 . IR (cm^{-1}) 3675 N-H stretching, 2902-2972 = C-H stretching, 1933 C = O stretching, 1637 C = C stretching, 1394 C - N stretching, 1230-1250 C - O stretching, 1056-1066 C - C stretching.

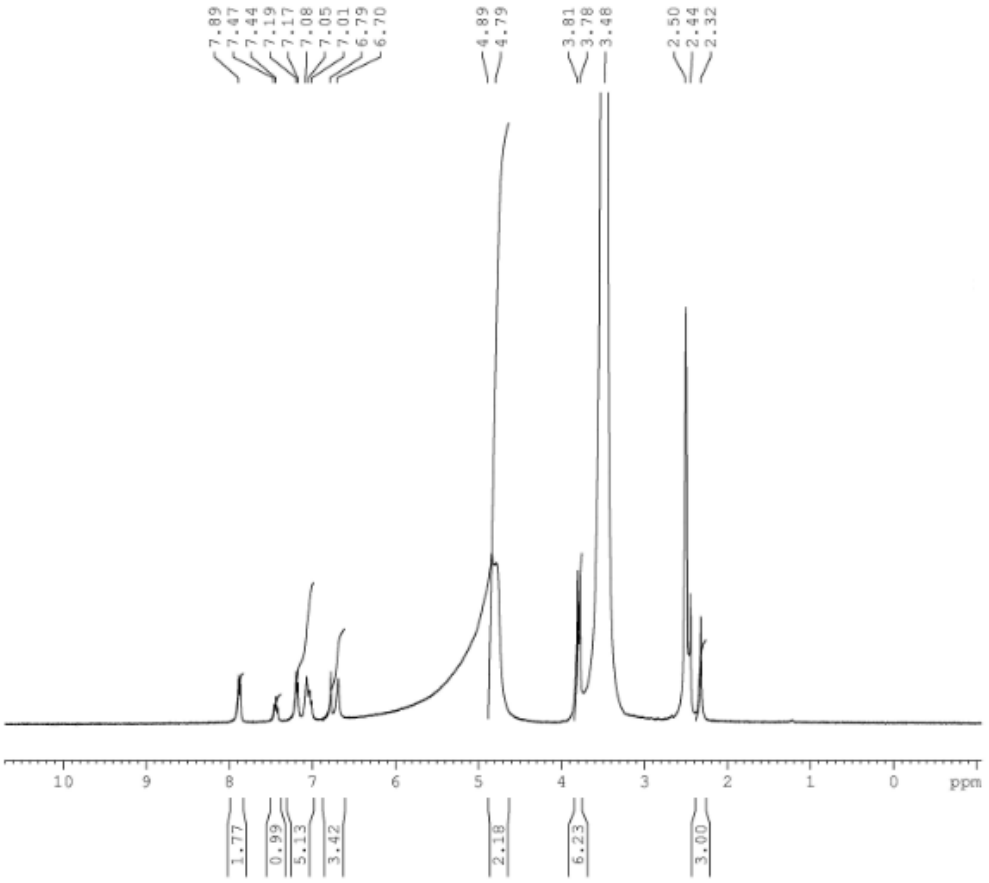
2.6.7. Methyl (E)-2-((Z)-3-(3-methoxyphenyl)-4-oxo-2-(((E)-N'-((E)-1-(p-tolyl) ethylidene) carbamohydrazonoyl) imino) thiazolidin-5-ylidene) acetate IHB7

To 0.07 g (0.197 mmol) of (AGII7) is added 15 ml of methanol and the mixture is heated under reflux for 8-12 min. When 0.024ml of Dimethylacetylenedicarboxylate (DMAD) is added to the hot suspension in suspension, orange colored precipitates form in the solution medium. Continue heating for 2-5 minutes under the cooler. The reaction is followed by TLC. It was observed that the solution color became darker by the heating process. It is observed that precipitation with the effect of temperature increases. It is left to cool overnight and the solution is filtered and washed in hot 5 ml of methanol. The impurity of the material is checked by TLC, and in the case of impurities, the washing process is repeated. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (Hand) (0.051 g, yield 72.85%) of $C_{23}H_{23}N_5O_4S$, 465.53g / mol, Melting point (219 - 221) ˚C

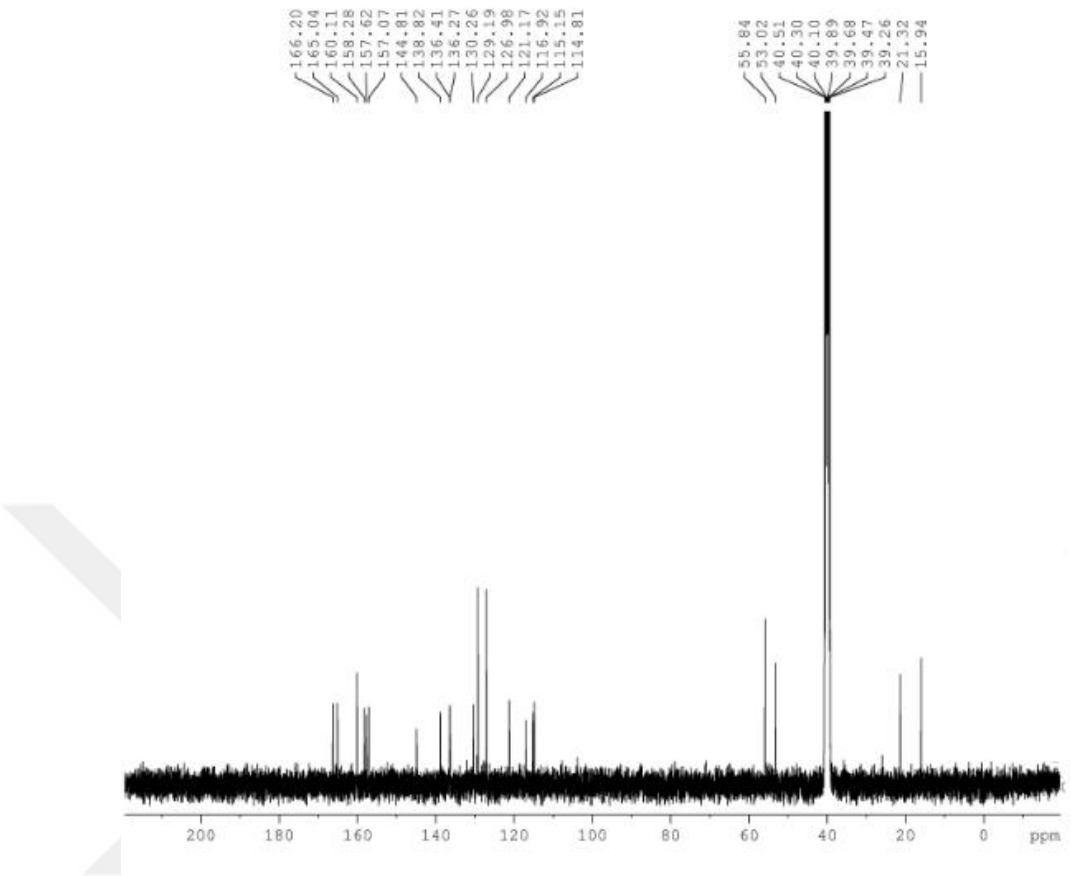


methyl (*E*)-2-((*Z*)-3-(3-methoxyphenyl)-4-oxo-2-(((*E*)-*N*'-((*E*)-1-(*p*-tolyl)ethylidene)carbamohydrazonoyl)imino)thiazolidin-5-ylidene)acetate

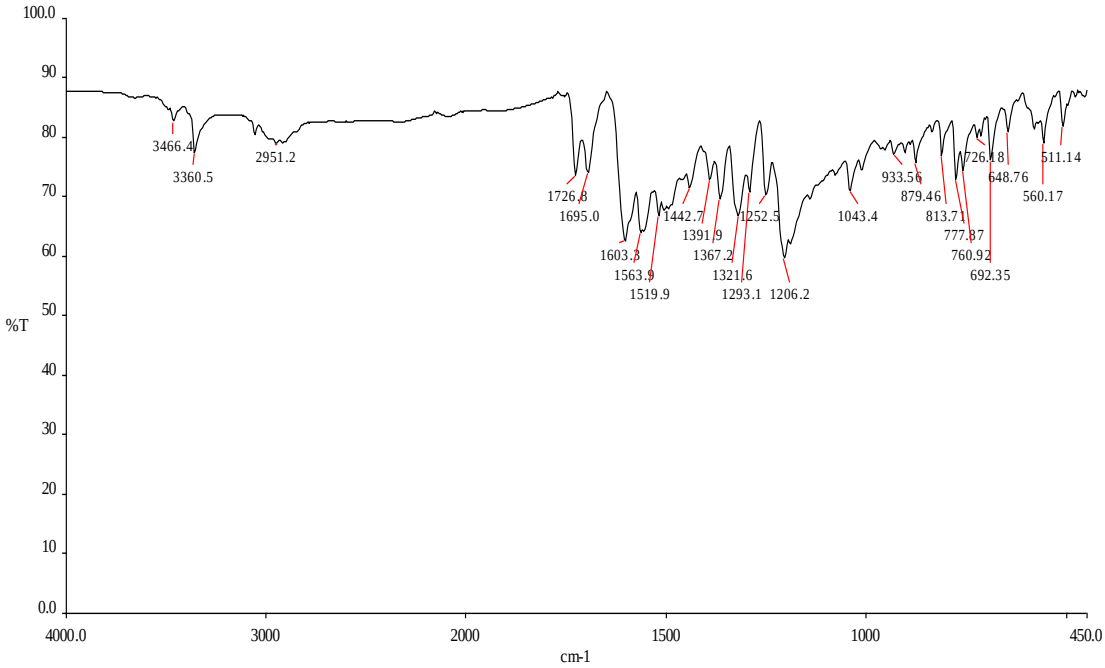
IHB7



^{1}H –NMR Spectrum IHB7



^{13}C-NMR Spectrum IHB7

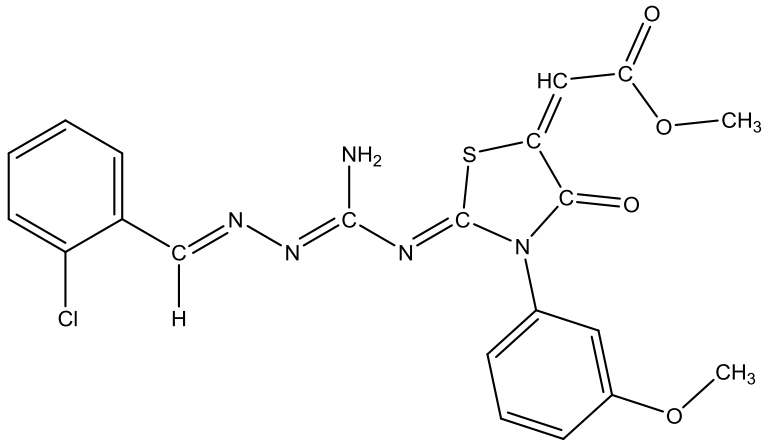


IR Spectrum IHB7

^{1}H-NMR (400 MH_Z, DMSO- δ_6) 7.89 (s, 2H), 7.47-7.44 (s, 1H), 7.19-7.01 (m, 5H), 6.79 (s, 3H), 4.89 (d, J = 4.9 Hz, 2H), 3.81 (m, 6H), 2.44 (m, 3H). ^{13}C-NMR (100 MH_Z, DMSO- δ_6) 166.20, 165.04, 160.11, 158.28, 157.62, 157.07, 144.81, 138.82, 136.41, 136.27, 130.26, 129.19, 126.98, 121.17, 116.92, 115.15, 114.81, 55.84, 53.02, 21.32, 15.94. IR (cm^{-1}) 3360-3466 N-H stretching, 2951 = C-H stretching, 1726 C = O stretching, 1563-1603 C = N stretching, 1695 C = C stretching, 1367-1391 C - N stretching, 1206 C - O stretching, 1043 C - C stretching.

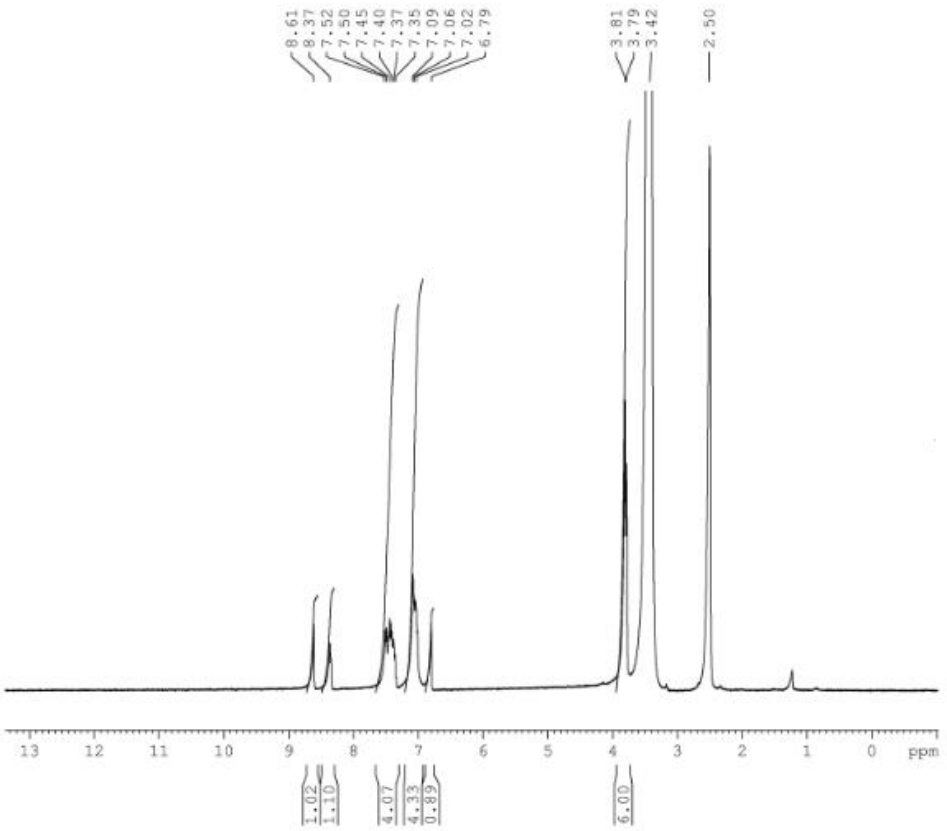
2.6.8. Methyl (E)-2-((Z)-2-(((E)-N'-((E)-2-chlorobenzylidene) carbamohydrazonoyl) imino)-3-(3-methoxyphenyl)-4-oxothiazolidin-5-ylidene) acetate IHB8

To 0.096 g (0.265 mmol) of (AGII9) is added 15 ml of methanol and the mixture is heated under reflux for 8-12 min. When 0.033 ml of Dimethylacetylenedicarboxylate (DMAD) is added to the hot suspension in suspension, orange colored precipitates form in the solution medium. Continue heating for 2-5 minutes under the cooler. The reaction is followed by TLC. It was observed that the solution color became darker by the heating process. It is observed that precipitation with the effect of temperature increases. It is left to cool overnight and the solution is filtered and washed in hot 5 ml of methanol. The impurity of the material is checked by TLC, and in the case of impurities, the washing process is repeated. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (Hand)(0.071 g, yield 74%) of $C_{21}H_{18}ClN_5O_4S$, 491.95g / mol, Melting point (237 - 238) ˚C

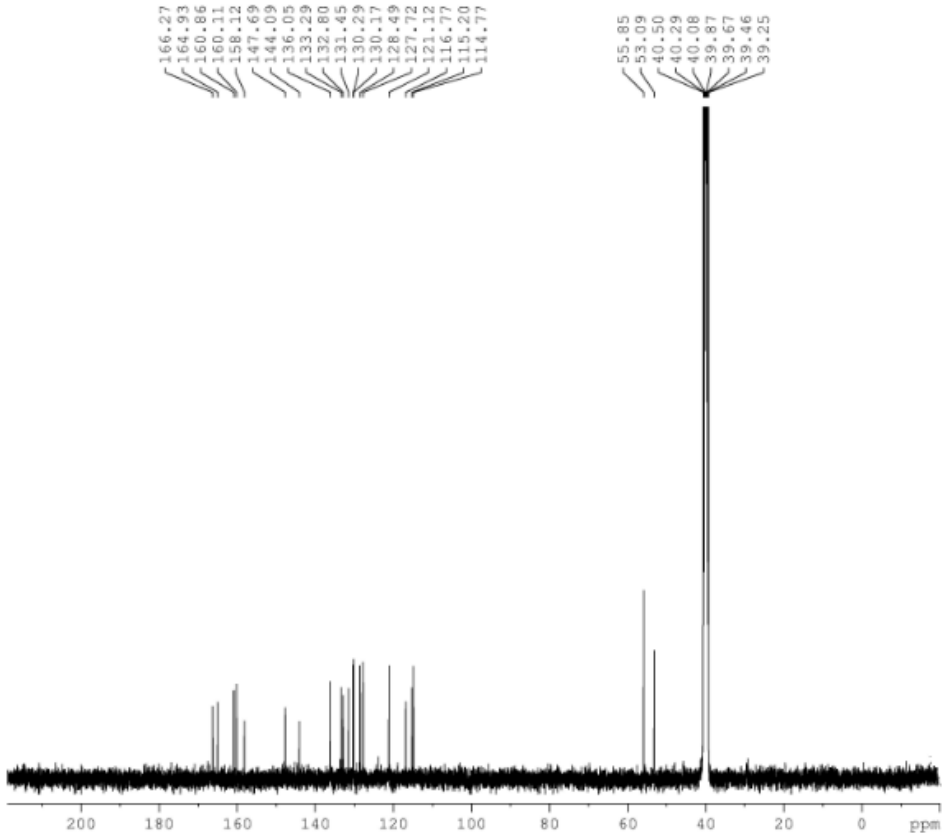


methyl (*E*)-2-((*Z*)-2-(((*E*)-*N*'-((*E*)-2-chlorobenzylidene)carbamohydrazonoyl)imino)-3-(3-methoxyphenyl)-4-oxothiazolidin-5-ylidene)acetate

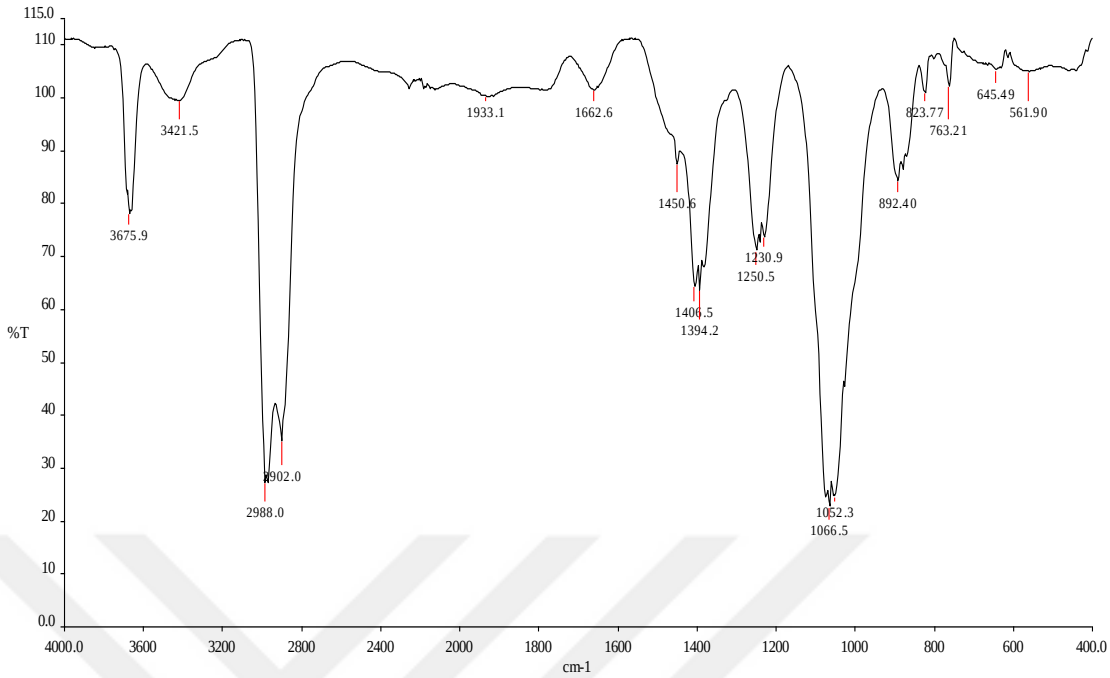
IHB8



[1]H –NMR Spectrum IHB8



[13] C-NMR Spectrum IHB8



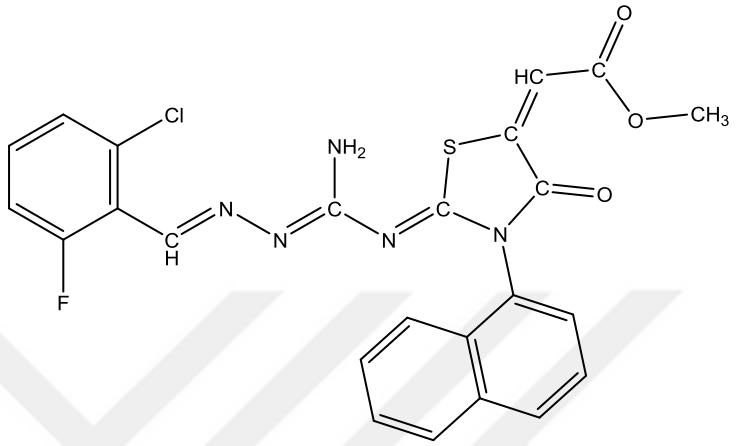
IR Spectrum IHB8

^{1}H-NMR (400 MH_Z, DMSO- δ_6) 8.61(s, 1H), 8.37 (s, 1H), 7.52-7.35 (m, 4H), 7.09-7.02 (m, 4H), 6.79 (s, 1H), 3.81 (d, J = 3.9 Hz, 6H). ^{13}C-NMR (100 MH_Z, DMSO- δ_6) 166.27, 164.93, 160.86, 160.11, 158.12, 147.69, 144.09, 136.05, 133.29, 132.80, 131.45, 130.29, 130.17, 128.49, 127.72, 121.12, 116.77, 115.20, 114.77, 55.85, 53.09. IR (cm^{-1}) 3421 N-H stretching, 2902-2988 - C-H stretching, 1662 C = O stretching, 1406 C = N stretching, 1450 C = C stretching, 1394 C - N stretching, 1230-1250 C - O stretching, 1052-1066 C - C stretching.

2.6.9. Methyl (E)-2-((Z)-2-(((E)-N'-((E)-2-chloro-6-fluorobenzylidene) carbamo hydrazonoyl) imino)-3-(naphthalen-1-yl)-4-oxothiazolidin-5-ylidene) acetate IHB9

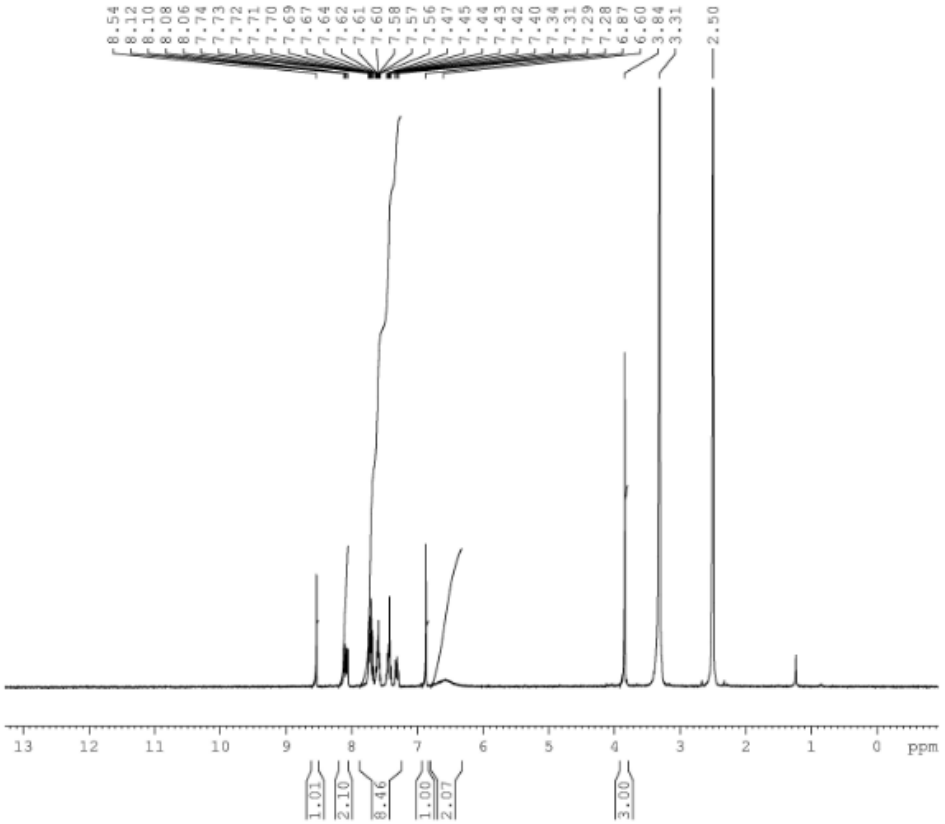
To 0.1 g (0.250 mmol) of (AGII10) is added 15 ml of methanol and the mixture is heated under reflux for 8-12 min. When 0.031 ml of Dimethylacetylenedicarboxylate (DMAD) is added to the hot suspension in suspension, orange colored precipitates form in the solution medium. Continue heating for 2-5 minutes under the cooler. The reaction is followed by TLC. It was observed that the solution color became darker by the heating process. It is observed that precipitation with the effect of temperature increases. It is left to cool overnight and the solution is filtered and washed in hot 5 ml of

methanol. The impurity of the material is checked by TLC, and in the case of impurities, the washing process is repeated. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (Hand) (0.059 g, yield 59%) of $C_{24}H_{17}ClFN_5O_3S$, 509.94g / mol, Melting point (206 - 208) ˚C

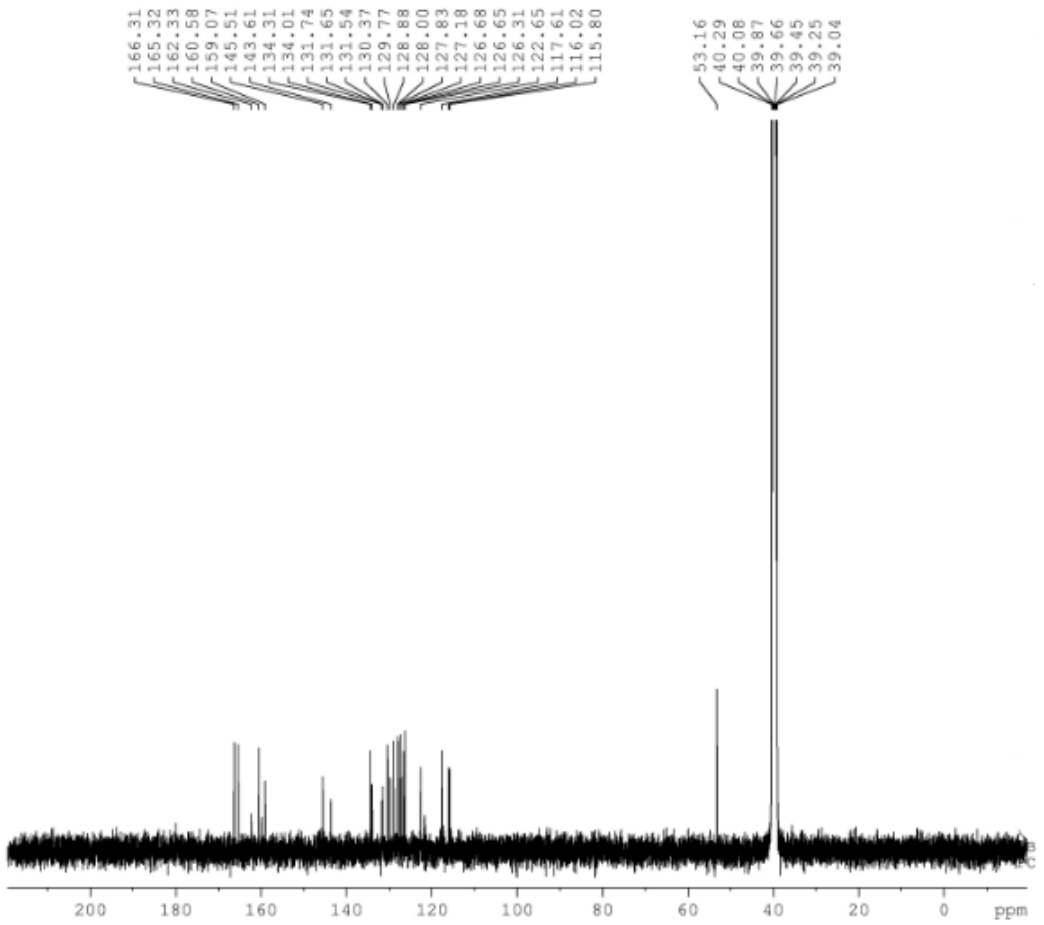


methyl (*E*)-2-((*Z*)-2-(((*E*)-*N*'-((*E*)-2-chloro-6-fluorobenzylidene)carbamohydrazonoyl)imino)-3-(naphthalen-1-yl)-4-oxothiazolidin-5-ylidene)acetate

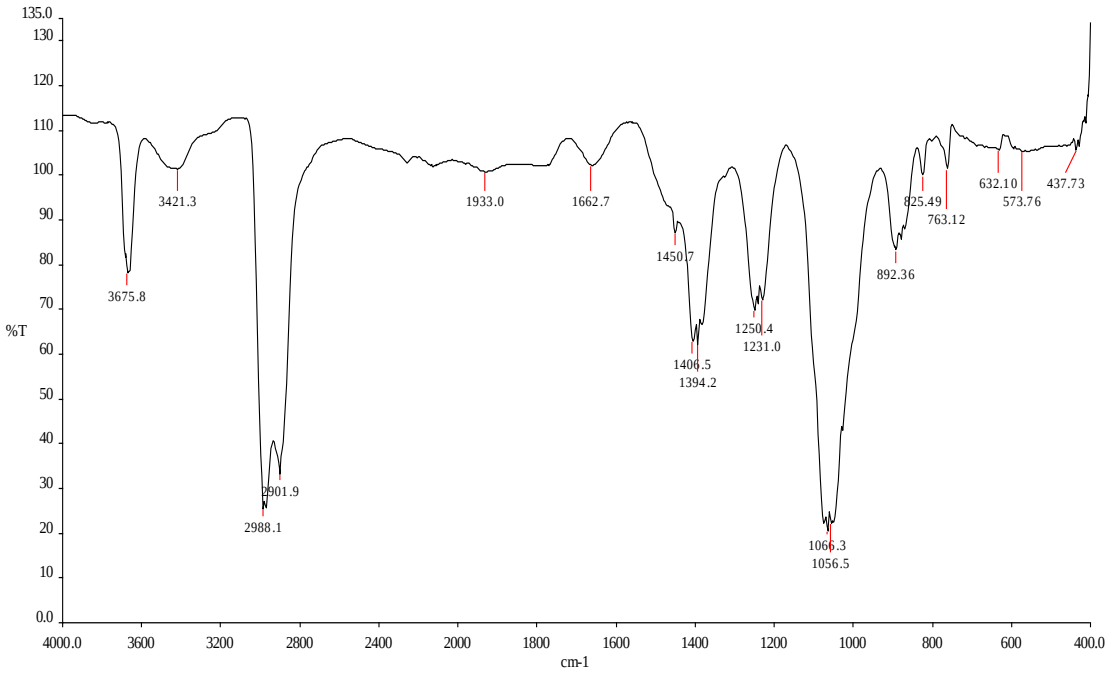
IHB9



^{1}H –NMR Spectrum IHB9



^{13}C-NMR Spectrum IHB9

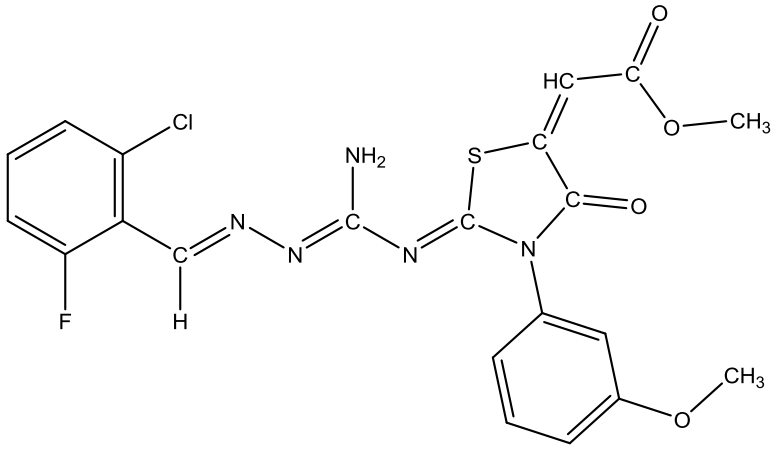


IR Spectrum IHB9

^{1}H-NMR (400 MH_Z, DMSO- δ_6) 8.54(s, 1H), 8.08 (s, 2H), 7.69-7.45 (d, J = 7.7 Hz, 8H), 7.29 (m, 1H), 6.60 (s, 2H), 3.84(d, J = 3.9 Hz, 3H). ^{13}C-NMR (100 MH_Z, DMSO- δ_6) 166.31, 165.32, 162.33, 160.58, 159.07, 145.51, 143.61, 134.31, 131.74, 131.65, 131.54, 130.37, 129.77, 128.88, 127.83, 127.18, 126.68, 126.65, 126.31, 117.61, 116.02, 115.80, 53.16. IR (cm^{-1}) 3421-3675 N-H stretching, 2902-2988 - C-H stretching, 1662 C = O stretching, 1406 C = N stretching, 1450 C = C stretching, 1394 C - N stretching, 1231-1250 C - O stretching, 1056-1066 C - C stretching.

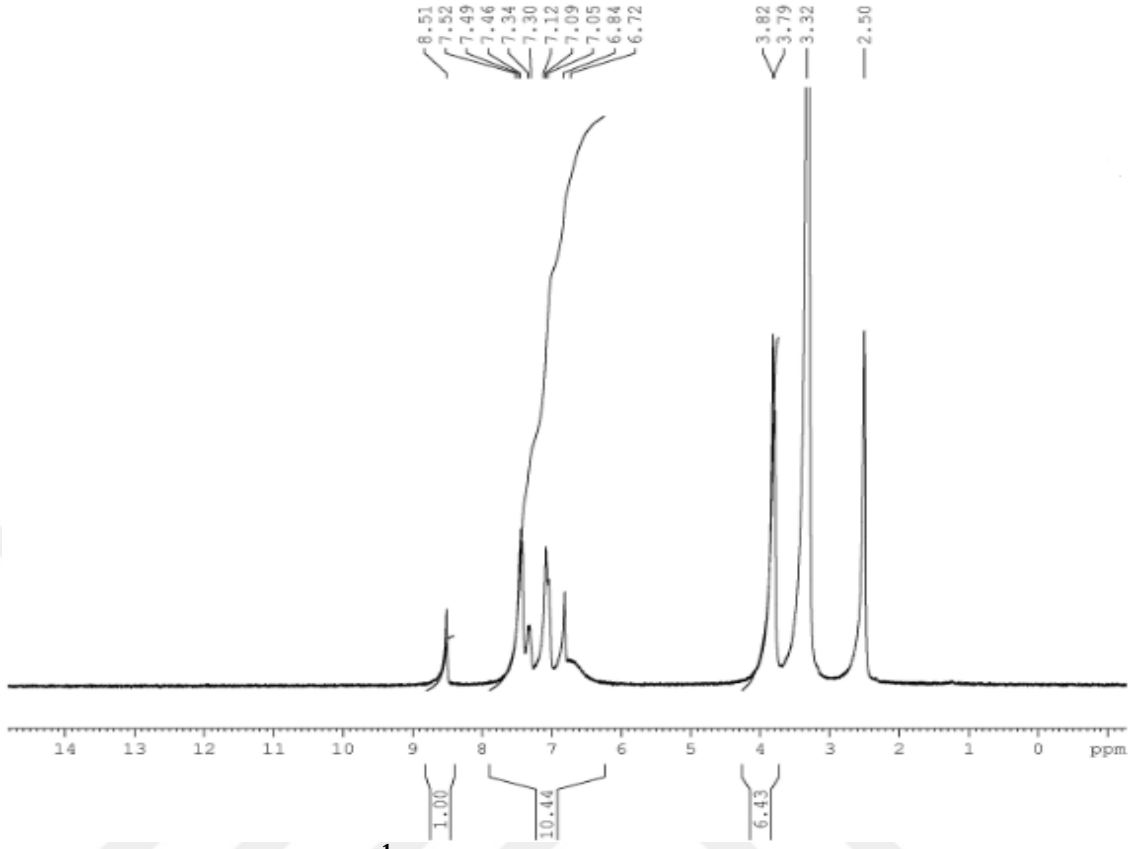
2.6.10. Methyl (E)-2-((Z)-2-(((E)-N'-((E)-2-chloro-6-fluorobenzylidene) carbamo hydrazonoyl) imino)-3-(3-methoxyphenyl)-4-oxothiazolidin-5-ylidene) acetate IHB10

To 0.1g (0.250 mmol) of (AGII11) is added 15 ml of methanol and the mixture is heated under reflux for 8-12 min. When 0.031 ml of Dimethylacetylenedicarboxylate (DMAD) is added to the hot suspension in suspension, orange colored precipitates form in the solution medium. Continue heating for 2-5 minutes under the cooler. The reaction is followed by TLC. It was observed that the solution color became darker by the heating process. It is observed that precipitation with the effect of temperature increases. It is left to cool overnight and the solution is filtered and washed in hot 5 ml of methanol. The impurity of the material is checked by TLC, and in the case of impurities, the washing process is repeated. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (Hand) (0.054 g, yield 54%) of $C_{21}H_{17}ClFN_5O_4S$, 489.91g / mol, Melting point (217 - 219) ˚C

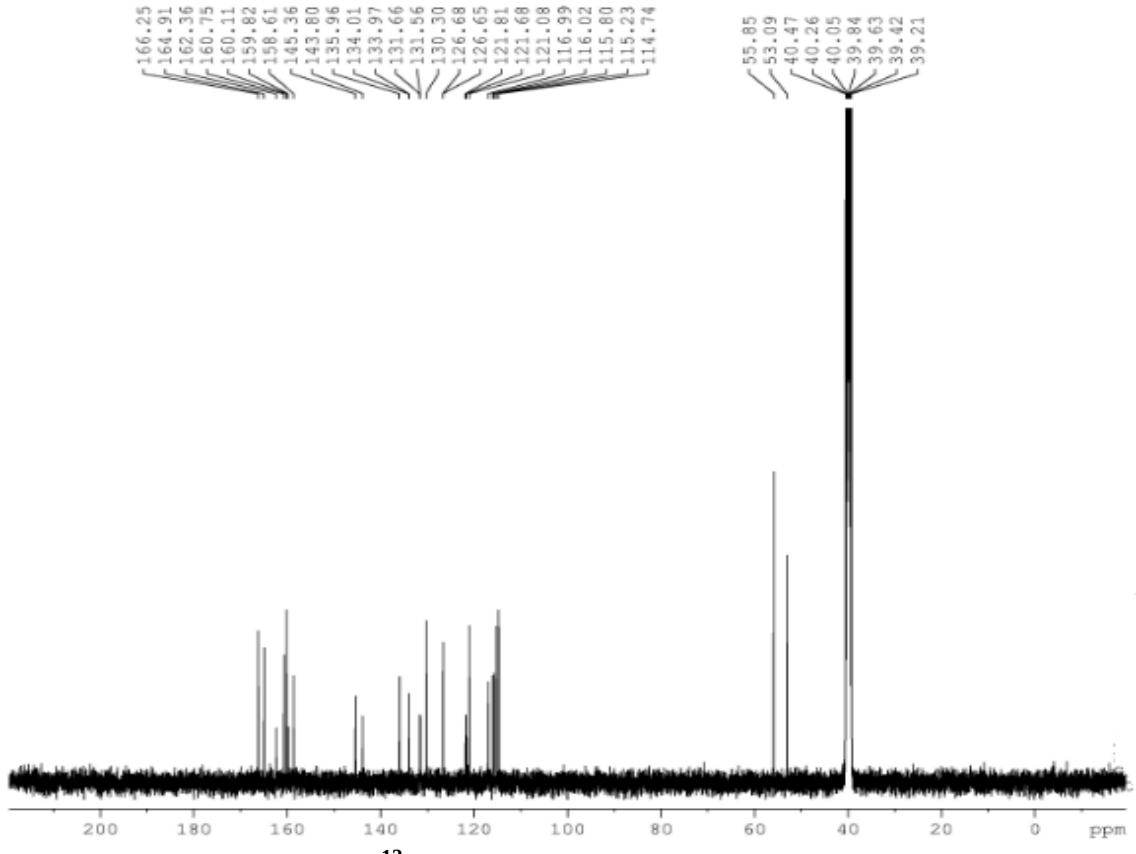


methyl (*E*)-2-((*Z*)-2-(((*E*)-*N*'-((*E*)-2-chloro-6-fluorobenzylidene)carbamohydrazonoyl)imino)-3-(3-methoxyphenyl)-4-oxothiazolidin-5-ylidene)acetate

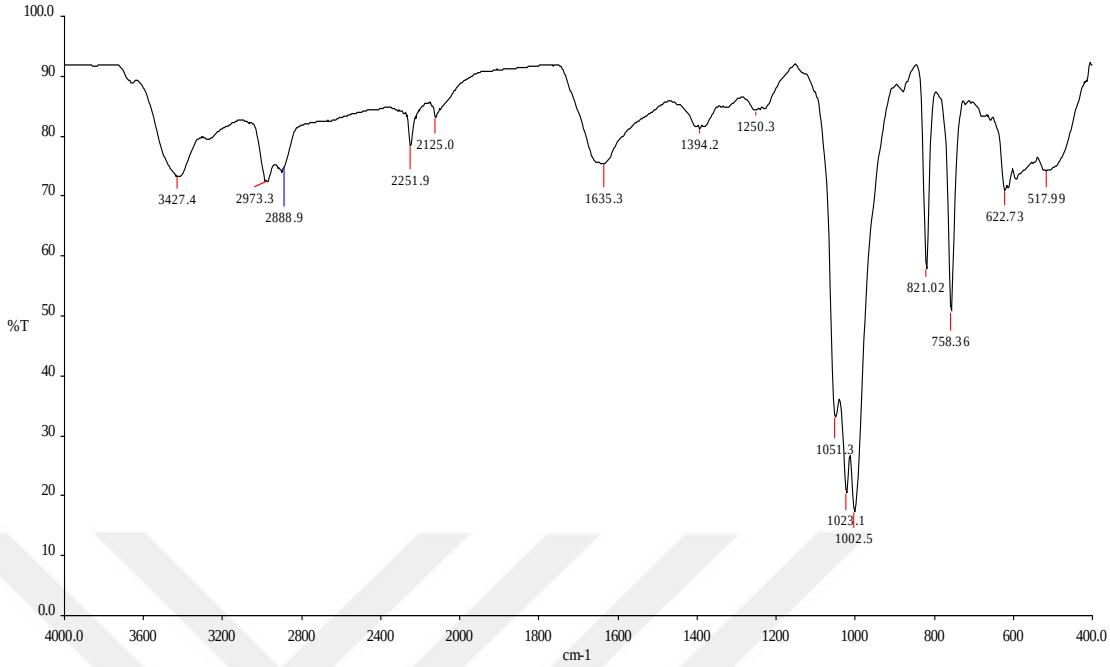
IHB10



^{1}H –NMR Spectrum IHB10



^{13}C-NMR Spectrum IHB10



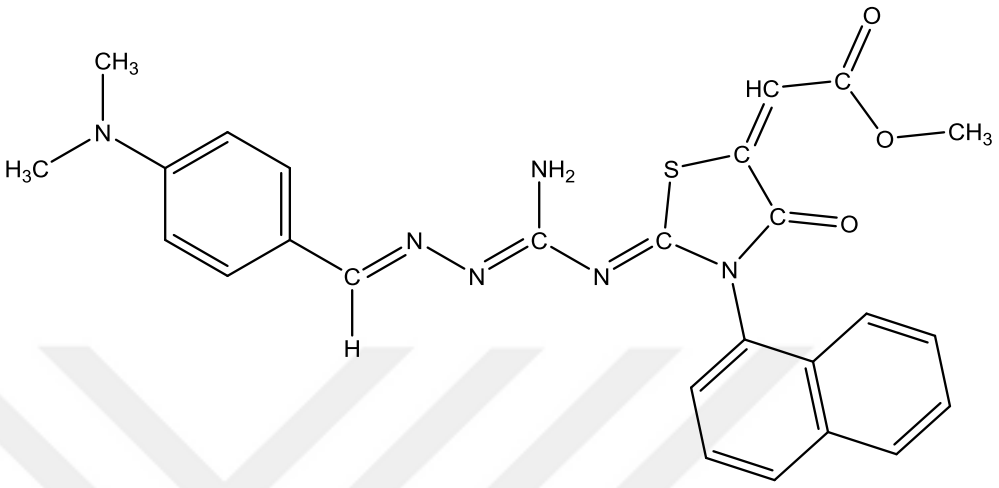
IR Spectrum IHB10

^{1}H-NMR (400 MH_Z, DMSO- δ_6) 8.51 (s, 1H), 7.52-6.72 (m, 10H), 3.82 (d, J = 3.9 Hz, 6H). ^{13}C-NMR (100 MH_Z, DMSO- δ_6) 166.25, 164.91, 162.36, 160.75, 160.11, 159.82, 158.61, 145.36, 143.80, 134.01, 133.97, 131.66, 131.56, 130.30, 130.17, 126.68, 126.65, 121.81, 121.68, 121.08, 116.99, 116.02, 115.80, 115.23, 114.74, 55.85, 53.09. IR (cm^{-1}) 3427 N-H stretching, 2888-2973 -C-H stretching, 1635 C = O stretching, 1394 C = N stretching, 1051 C - N stretching, 1250 C - O stretching, 1002-1023 C - C stretching.

2.6.11. Methyl (E)-2-((Z)-2-(((E)-N'-((E)-4-(dimethylamino) benzylidene) carbamo hydrazonoyl) imino)-3-(naphthalen-1-yl)-4-oxothiazolidin-5-ylidene) acetate IHB11

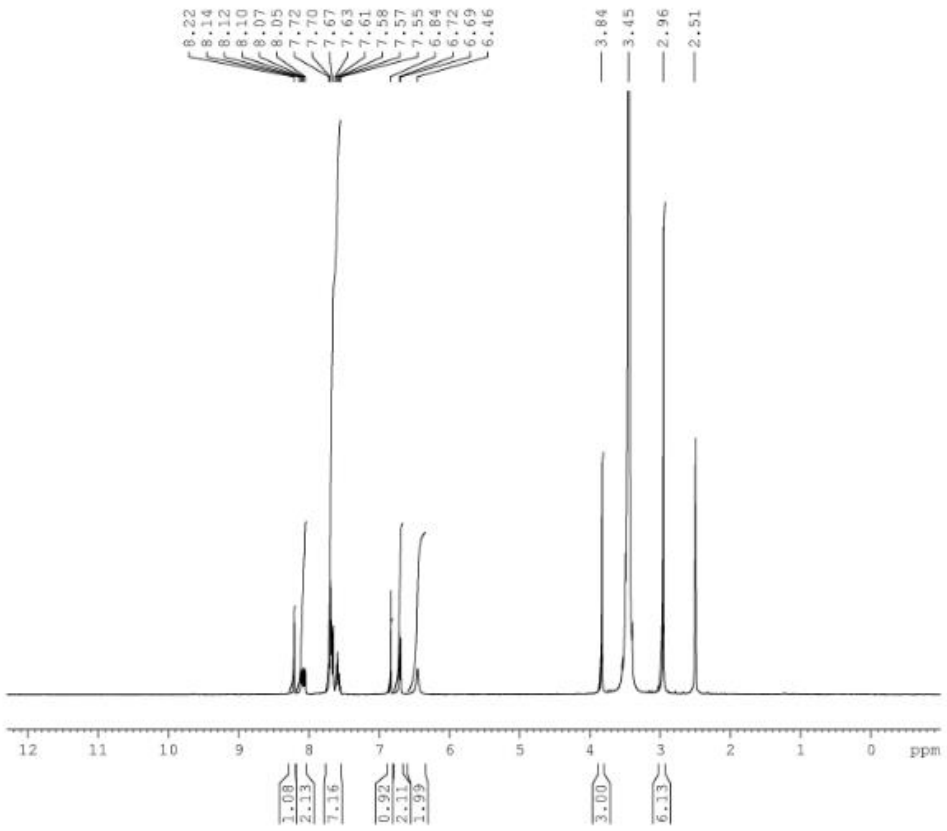
To 0.2 g (0.512 mmol) of (AGII21) is added 15 ml of methanol and the mixture is heated under reflux for 8-12 min. When 0.064 ml of Dimethylacetylenedicarboxylate (DMAD) is added to the hot suspension in suspension, orange colored precipitates form in the solution medium. Continue heating for 2-5 minutes under the cooler. The reaction is followed by TLC. It was observed that the solution color became darker by the heating process. It is observed that precipitation with the effect of temperature increases. It is left to cool overnight and the solution is filtered and washed in hot 5 ml of methanol. The impurity of the material is checked by TLC, and in the case of impurities,

the washing process is repeated. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (Hand) (0.094 g, yield 47%) of $C_{26}H_{24}N_6O_3S$, 500.58g / mol, Melting point (159 - 161) ˚C

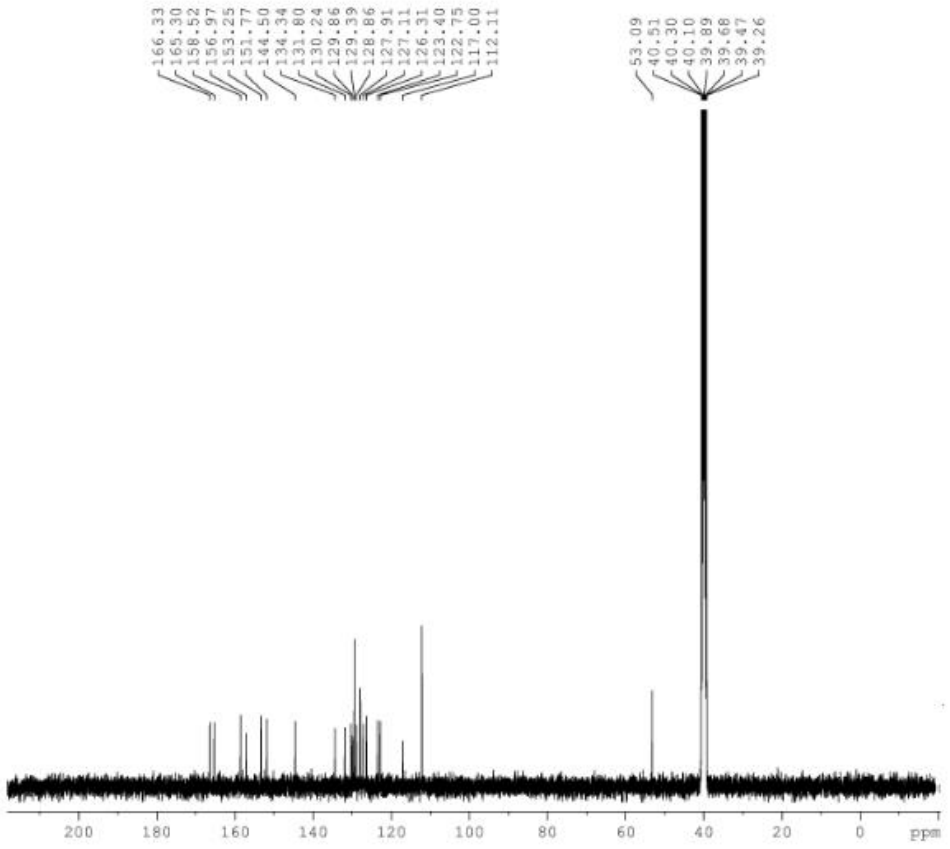


methyl (*E*)-2-((*Z*)-2-(((*E*)-*N*'-((*E*)-4-(dimethylamino)benzylidene)carbamohydrazonoyl)imino)-3-(naphthalen-1-yl)-4-oxothiazolidin-5-ylidene)acetate

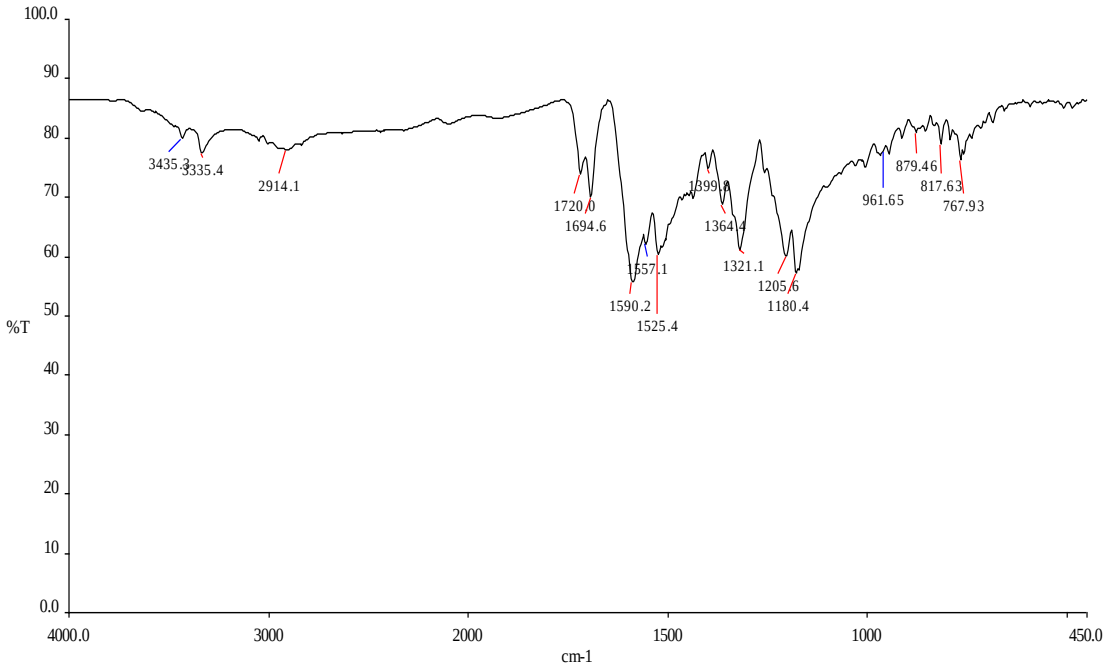
IHB11



^{1}H –NMR Spectrum IHB11



^{13}C-NMR Spectrum IHB11

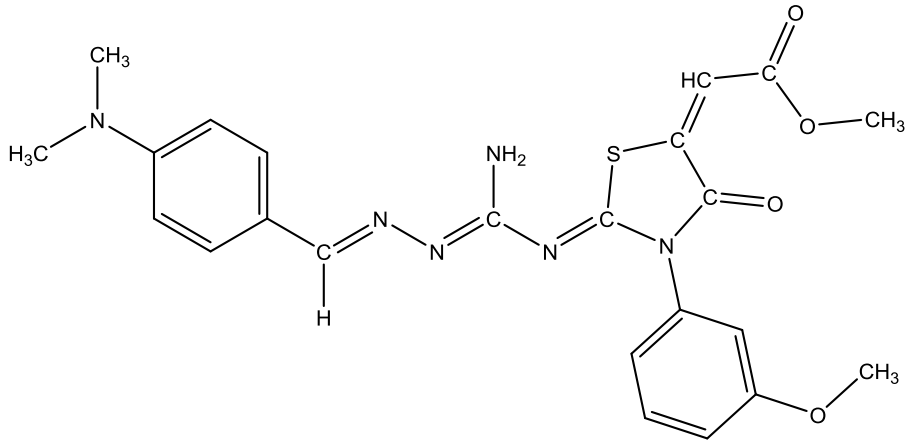


IR Spectrum IHB11

^{1}H-NMR (400 MH_Z, DMSO- δ_6) 8.22 (s, 1H), 8.12 (s, 2H), 7.72-7.55 (d, J = 7.9 Hz, 7H), 6.84 (s, 1H), 6.69 (s, 2H), 6.46 (s, 2H), 3.84 (m, 3H), 2.96 (m, 6H). ^{13}C-NMR (100 MH_Z, DMSO- δ_6) 166.33, 165.30, 158.52, 156.97, 153.25, 151.77, 144.50, 134.34, 131.80, 130.24, 129.86, 129.39, 128.86, 127.91, 127.11, 126.31, 123.40, 122.75, 117.00, 112.11, 53.09. IR (cm^{-1}) 3335-3435 N-H stretching, 2914 -C-H stretching, 1720 C = O stretching, 1694 C = C stretching, 1557-1590 C = N stretching, 1321-1364 C - N stretching, 1205 C - O stretching, 1180 C - C stretching.

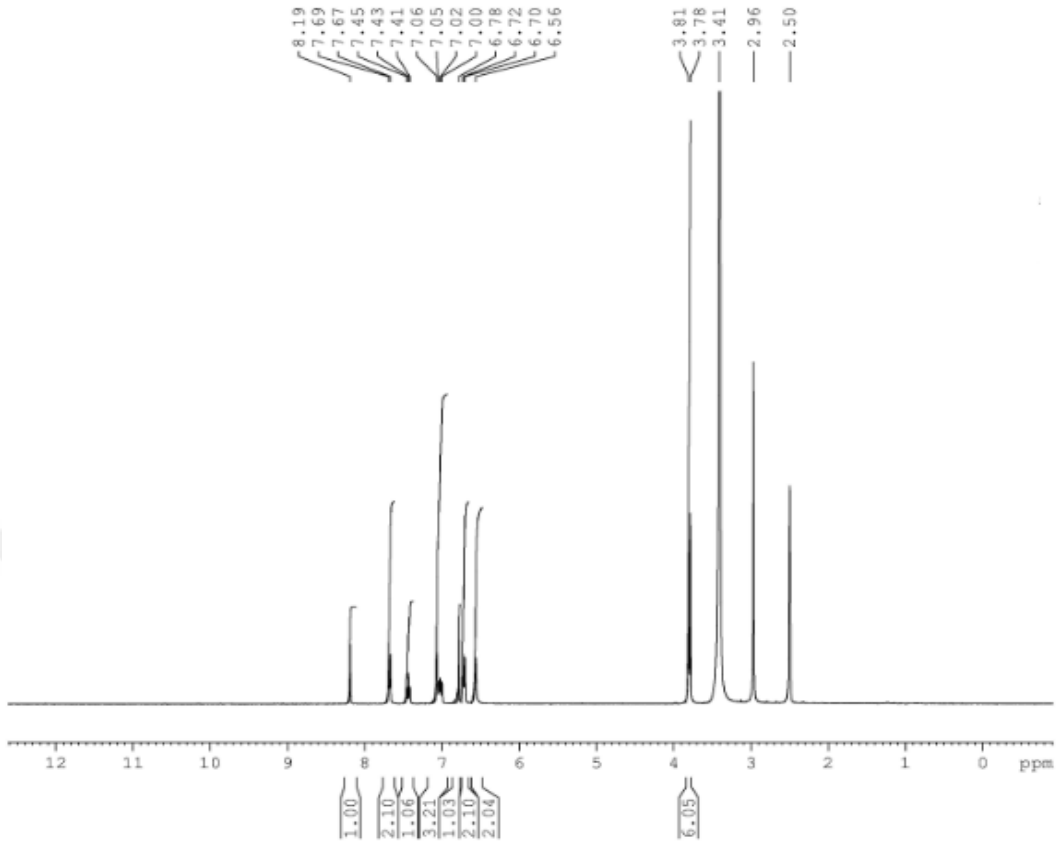
2.6.12. Methyl (E)-2-((Z)-2-(((E)-N'-((E)-4-(dimethylamino) benzylidene) carbamo hydrazonoyl) imino)-3-(3-methoxyphenyl)-4-oxothiazolidin-5-ylidene) aceta te IHB12

To 0.2 g (0.61 mmol) of (AGII22) is added 15 ml of methanol and the mixture is heated under reflux for 8-12 min. When 0.066 ml of Dimethylacetylenedicarboxylate (DMAD) is added to the hot suspension in suspension, orange colored precipitates form in the solution medium. Continue heating for 2-5 minutes under the cooler. The reaction is followed by TLC. It was observed that the solution color became darker by the heating process. It is observed that precipitation with the effect of temperature increases. It is left to cool overnight and the solution is filtered and washed in hot 5 ml of methanol. The impurity of the material is checked by TLC, and in the case of impurities, the washing process is repeated. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (Hand) (0.076 g, yield38%) of $C_{23}H_{24}N_6O_4S$, 480.54g / mol, Melting point (198 - 199) ˚C

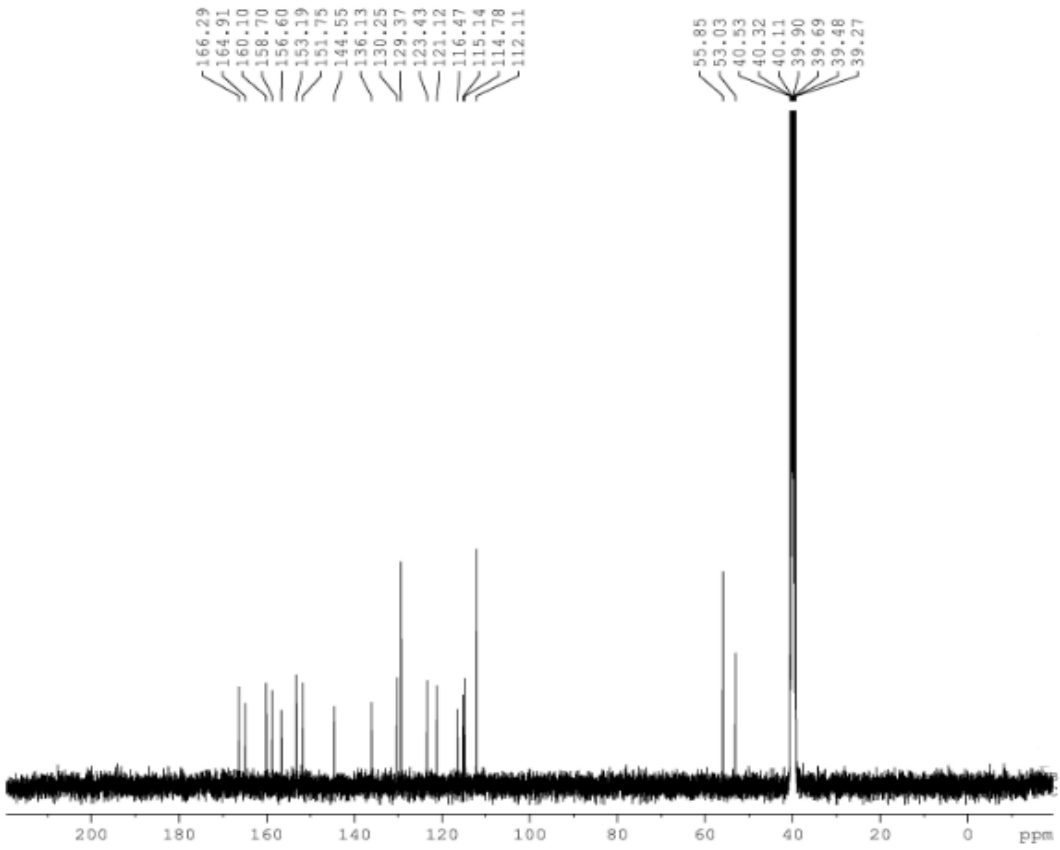


methyl (*E*)-2-((*Z*)-2-(((*E*)-*N*'-((*E*)-4-(dimethylamino)benzylidene)carbamohydrazonoyl)imino)-3-(3-methoxyphenyl)-4-oxothiazolidin-5-ylidene)acetate

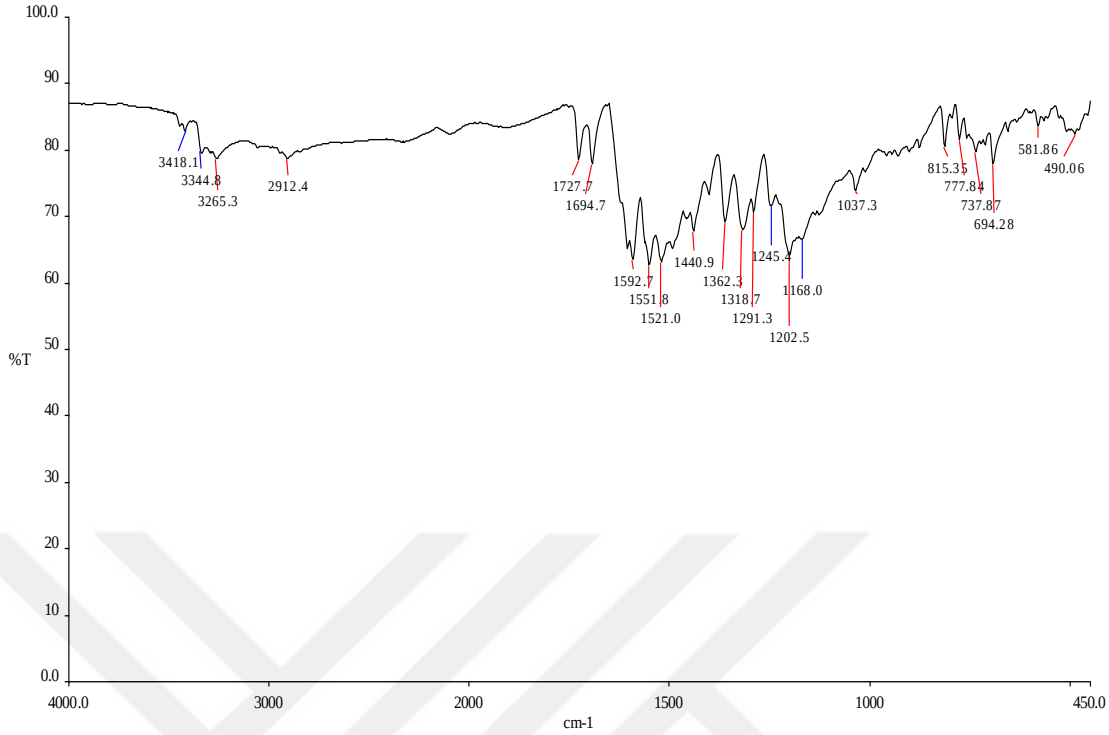
IHB12



^{1}H –NMR Spectrum IHB12



^{13}C-NMR Spectrum IHB12



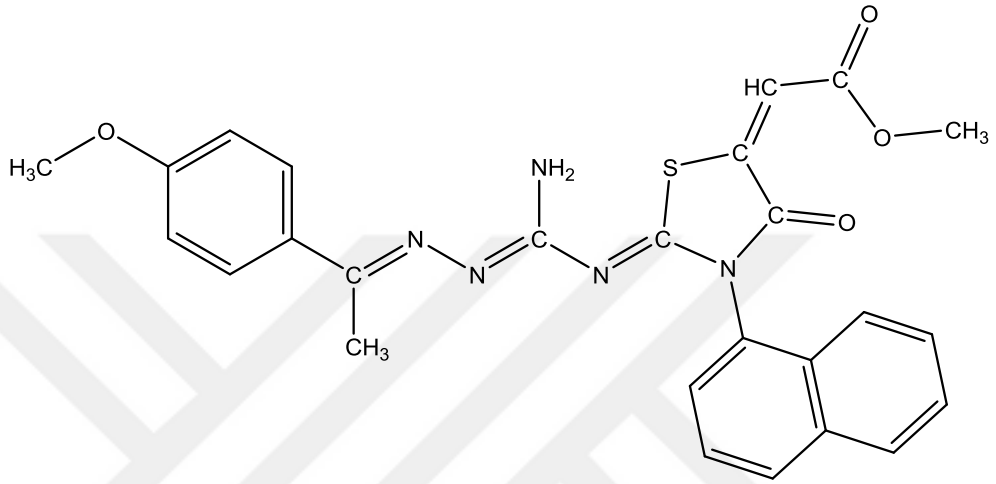
IR Spectrum IHB12

^{1}H-NMR (400 MH$_Z$, DMSO- δ_6) 8.19 (s, 1H), 7.69 (m, 2H), 7.34 (m, 1H), 7.06 (s, 3H), 6.78 (s, 1H), 6.70 (d, J = 6.9 Hz, 2H), 6.56 (s, 2H), 3.81 (m, 6H). ^{113}C-NMR (100 MH$_Z$, DMSO- δ_6) 166.29, 164.91, 160.10, 158.70, 156.60, 153.19, 151.75, 144.55, 136.13, 130.25, 129.37, 123.43, 121.12, 116.47, 115.14, 114.78, 112.11, 55.85, 53.03. IR (cm^{-1}) 3344-3418 N-H stretching, 2912 -C-H stretching, 1727 C = O stretching, 1694 C = C stretching, 1521-1592 C = N stretching, 1318-1362 C - N stretching, 1168-1245 C - O stretching, 1037 C - C stretching.

2.6.13. Methyl (E)-2-((Z)-2-(((E)-N'-((E)-1-(4-methoxyphenyl) ethylidene) carbamo hydrazonoyl) imino)-3-(naphthalen-1-yl)-4-oxothiazolidin-5-ylidene) acetate IHB13

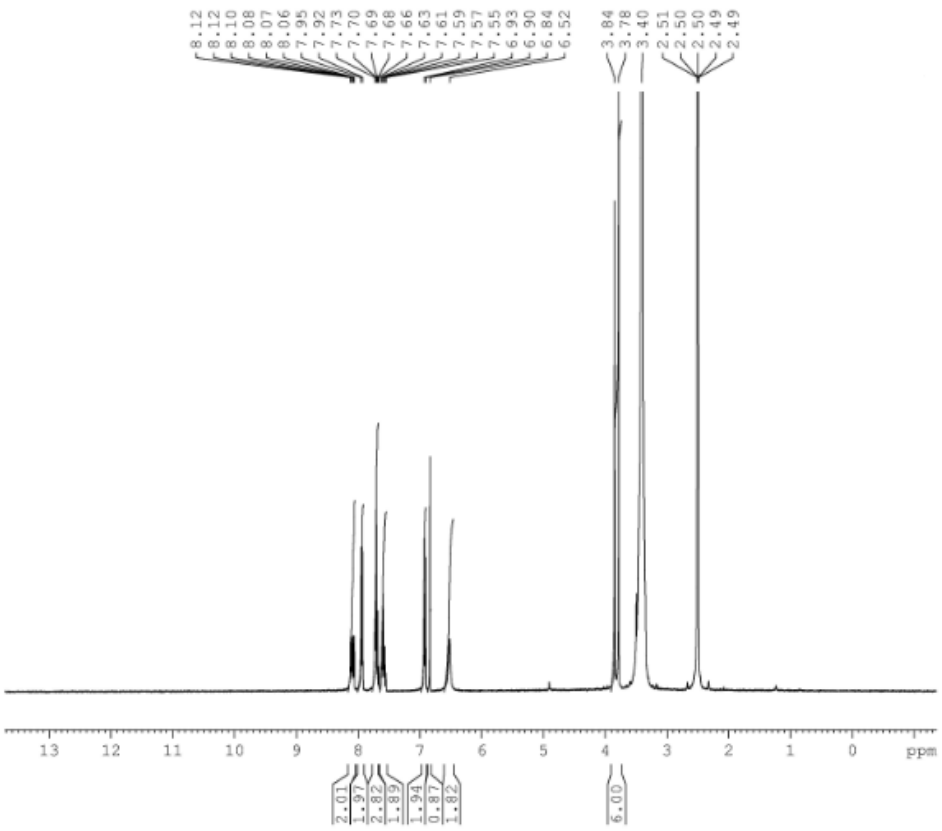
To 0.082 g (0.209 mmol) of (AGII13) is added 15 ml of methanol and the mixture is heated under reflux for 8-12 min. When 0.026 ml of Dimethylacetylenedicarboxylate (DMAD) is added to the hot suspension in suspension, orange colored precipitates form in the solution medium. Continue heating for 2-5 minutes under the cooler. The reaction is followed by TLC. It was observed that the solution color became darker by the heating process. It is observed that precipitation with the effect of temperature increases.

It is left to cool overnight and the solution is filtered and washed in hot 5 ml of methanol. The impurity of the material is checked by TLC, and in the case of impurities, the washing process is repeated. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (Hand) (0.053 g, yield 65%) of $C_{26}H_{23}N_5O_4S$, 501.56g / mol, Melting point (194 -195) ˚C

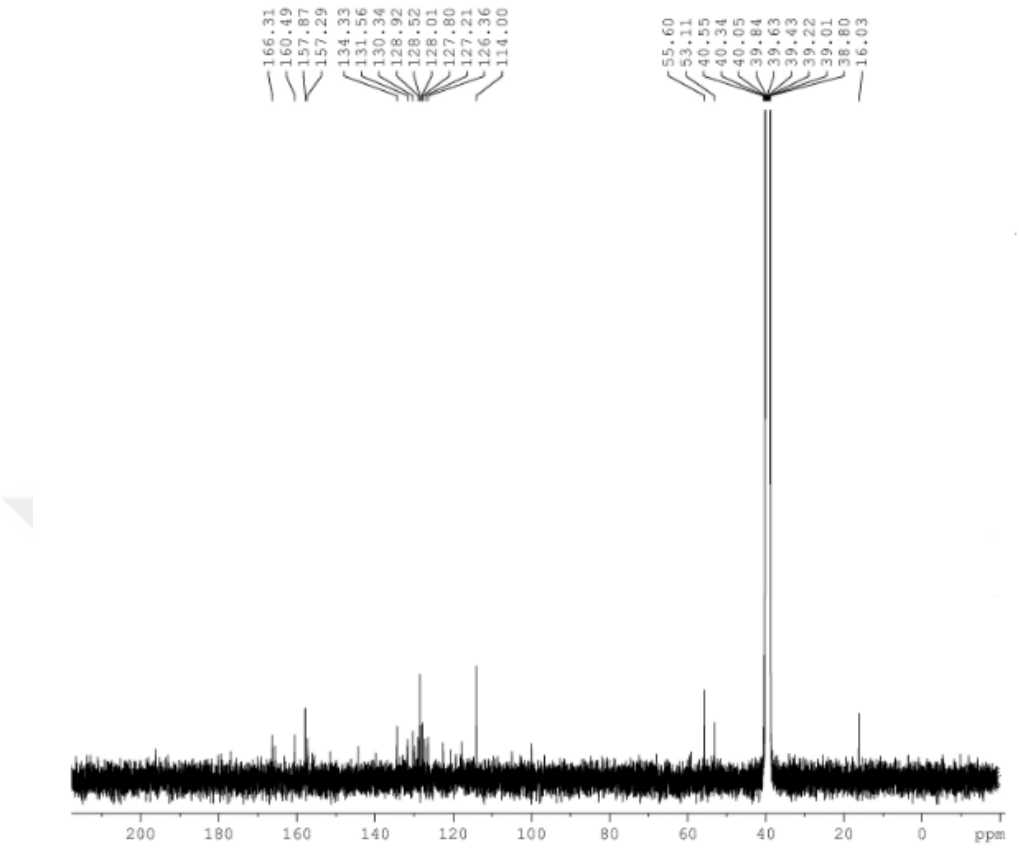


methyl (*E*)-2-((*Z*)-2-(((*E*)-*N*'-((*E*)-1-(4-methoxyphenyl)ethylidene)carbamohydrazonoyl)imino)-3-(naphthalen-1-yl)-4-oxothiazolidin-5-ylidene)acetate

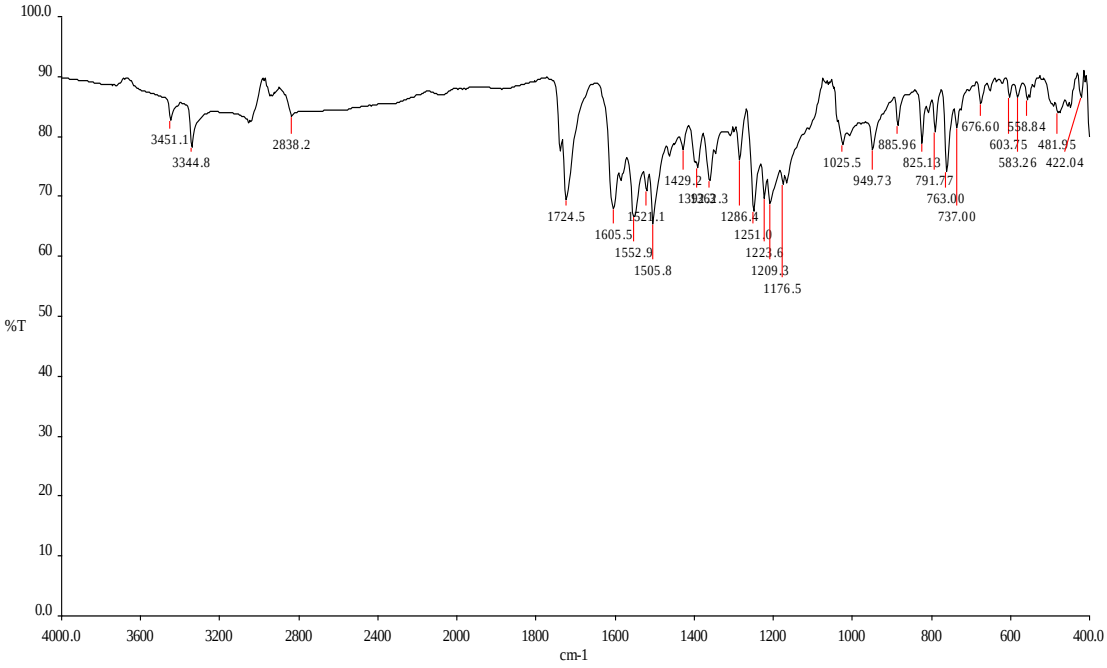
IHB13



^{1}H –NMR Spectrum IHB13



^{13}C-NMR Spectrum IHB13

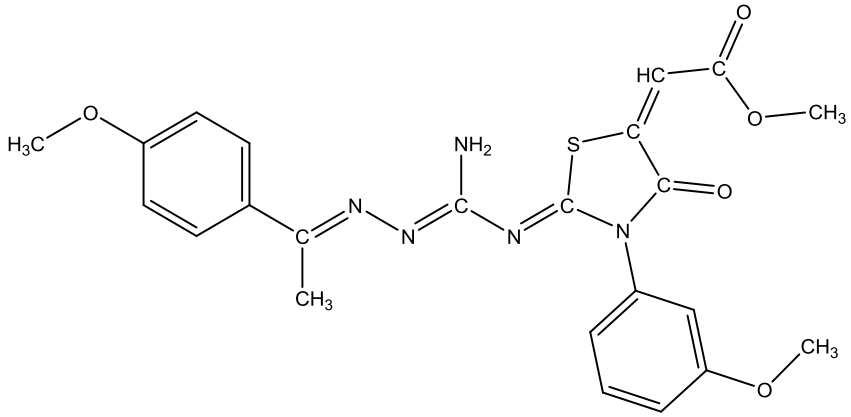


IR Spectrum IHB13

^{1}H-NMR (400 MH_Z, DMSO- δ_6) 8.12 (d, J = 8.4 Hz, 2H), 8.10 (m, 1H), 7.92 (m, 2H), 7.70 (m, 2H), 6.93 (m, 2H), 6.84 (m, 0H), 6.52 (m, 1H), 3.84 (d, J = 3.9 Hz, 6H). ^{13}C-NMR (100 MH_Z, DMSO- δ_6) 166.31, 160.49, 157.87, 157.29, 134.33, 131.56, 130.34, 128.92, 128.52, 128.01, 127.80, 127.21, 126.36, 114.00, 55.60, 53.11, 16.03. IR (cm^{-1}) 3344-3451 N-H stretching, 2838 -C-H stretching, 1724 C = O stretching, 1605 C = C stretching, 1505-1555 C = N stretching, 1262-1392 C - N stretching, 1176-1223 C - O stretching, 1025 C - C stretching.

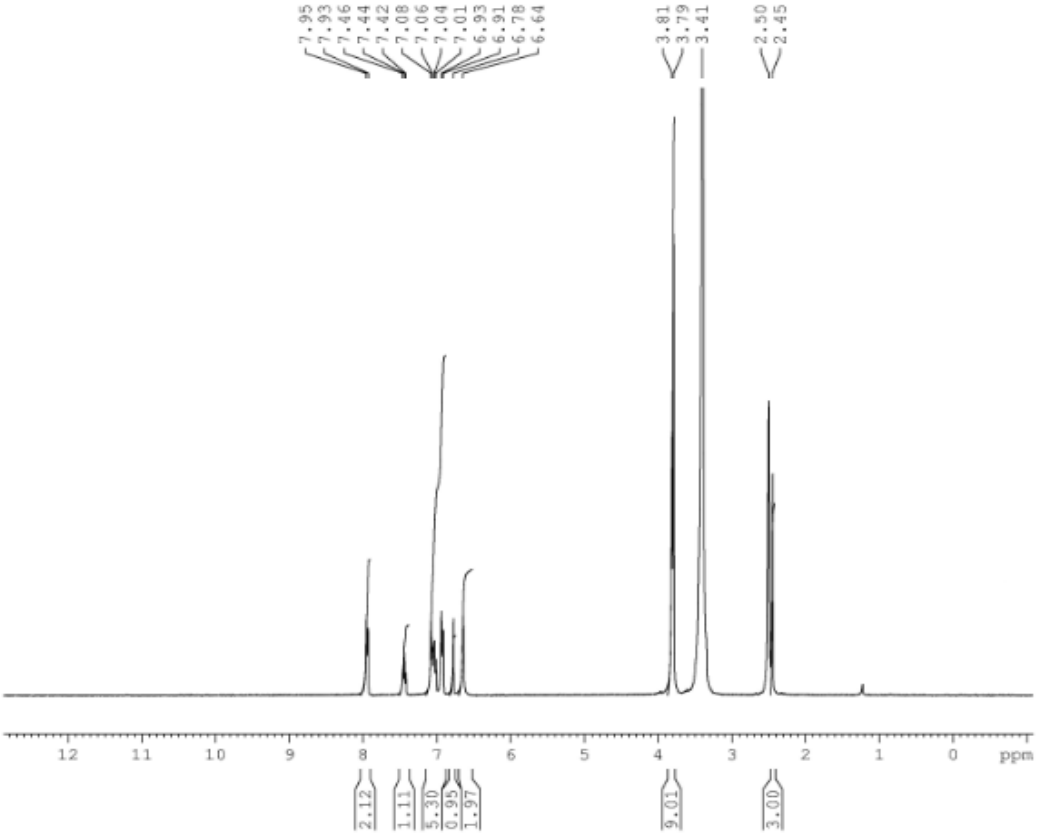
2.6.14.Methyl (E)-2-((Z)-3-(3-methoxyphenyl)-2-(((E)-N'-((E)-1-(4-methoxyphenyl) ethylidene) carbamohydrazonoyl) imino)-4-oxothiazolidin-5-ylidene) aceta te IHB14

To 0.1 g (0.269mmol) of (AGII14) is added 15 ml of methanol and the mixture is heated under reflux for 8-12 min. When 0.033ml of Dimethylacetylenedicarboxylate (DMAD) is added to the hot suspension in suspension, orange colored precipitates form in the solution medium. Continue heating for 2-5 minutes under the cooler. The reaction is followed by TLC. It was observed that the solution color became darker by the heating process. It is observed that precipitation with the effect of temperature increases. It is left to cool overnight and the solution is filtered and washed in hot 5 ml of methanol. The impurity of the material is checked by TLC, and in the case of impurities, the washing process is repeated. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (Hand) (0.085 g, yield 85%) of $C_{23}H_{23}N_5O_5S$, 481.53 g / mol, Melting point (203 - 206) ˚C

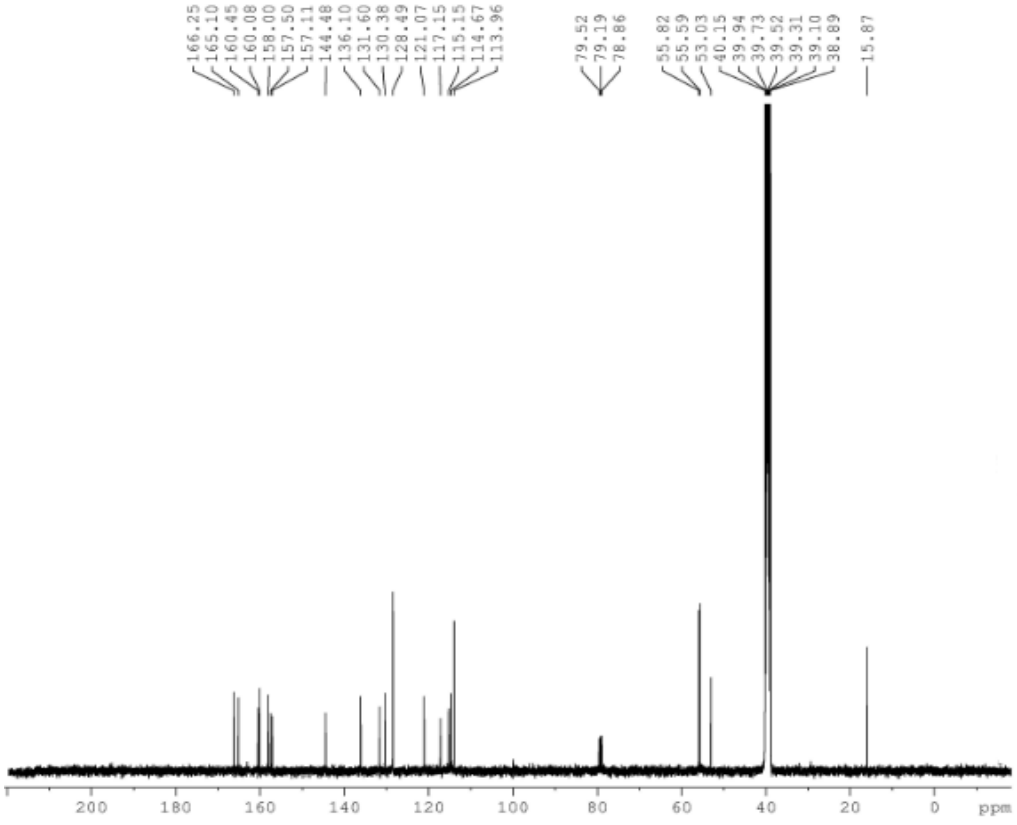


methyl (*E*)-2-((*Z*)-3-(3-methoxyphenyl)-2-(((*E*)-*N*'-((*E*)-1-(4-methoxyphenyl)ethylidene)carbamohydrazonoyl)imino)-4-oxothiazolidin-5-ylidene)acetate

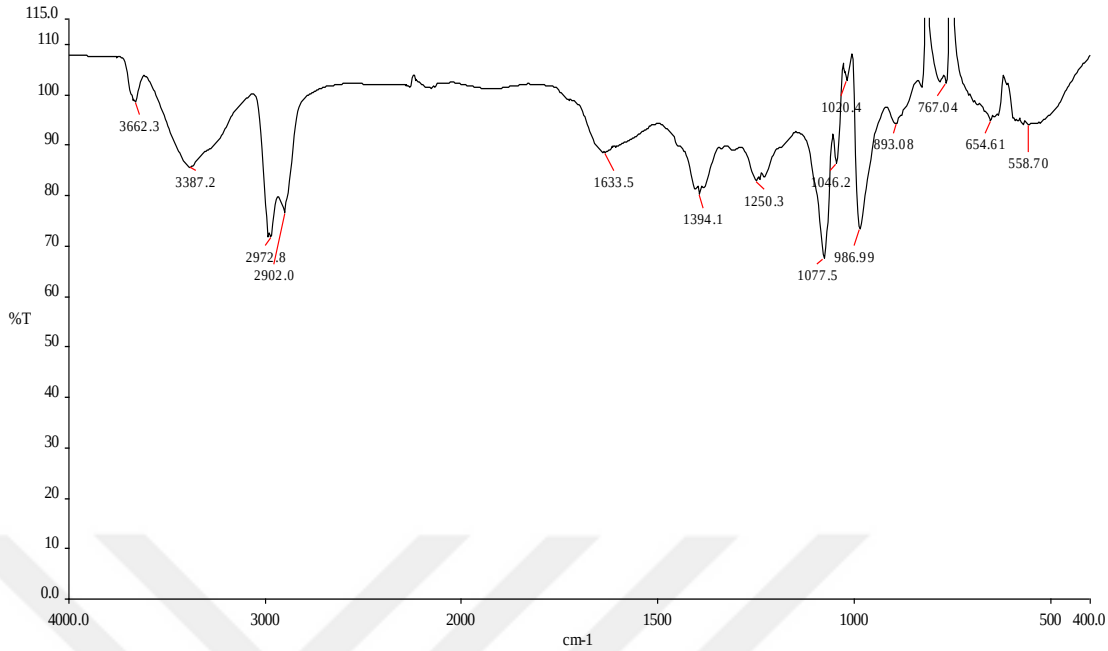
IHB14



^{1}H –NMR Spectrum IHB14



^{13}C-NMR Spectrum IHB14



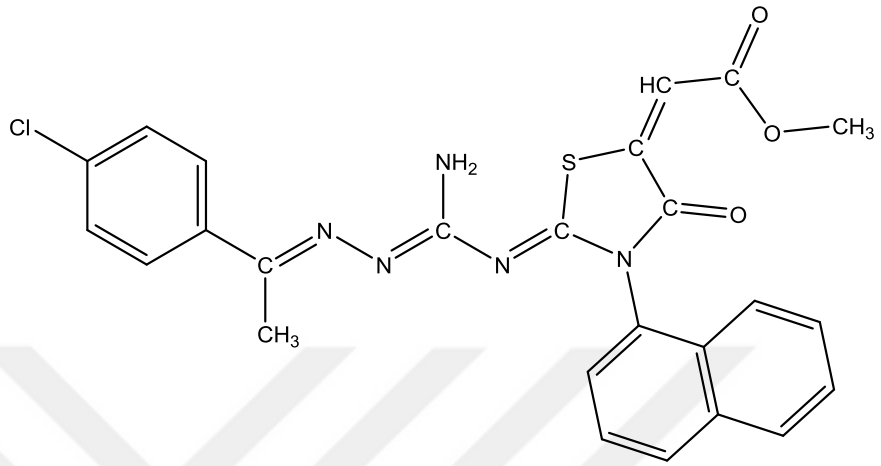
IR Spectrum IHB14

^{1}H -NMR (400 MHz, DMSO- δ_6) 7.95 (m, 2H), 7.46 (s, 1H), 7.08-7.01 (q, J = 7.2 Hz, 5H), 6.91 (s, 1H), 6.64 (m, 2H), 3.81 (d, J = 3.9 Hz, 9H), 2.50 (d, J = 2.9 Hz, 3H). ^{13}C-NMR (100 MH_Z, DMSO- δ_6) 166.25, 165.10, 160.45, 160.08, 158.00, 157.50, 157.11, 144.48, 136.10, 131.60, 130.38, 128.49, 121.07, 117.5, 115.15, 114.67, 113.96, 79.52, 79.19, 78.86, 55.82, 55.59, 53.11, 15.87. IR (cm^{-1}) 3387 N-H stretching, 2902-2972 -C-H stretching, 1633 C = O stretching, 1394 C - N stretching, 1250 C - O stretching, 1046-1077 C - C stretching.

2.6.15. Methyl (E)-2-((Z)-2-(((E)-N'-((E)-1-(4-chlorophenyl) ethylidene) carbamo hydrazonoyl) imino)-3-(naphthalen-1-yl)-4-oxothiazolidin-5-ylidene) acetate IHB15

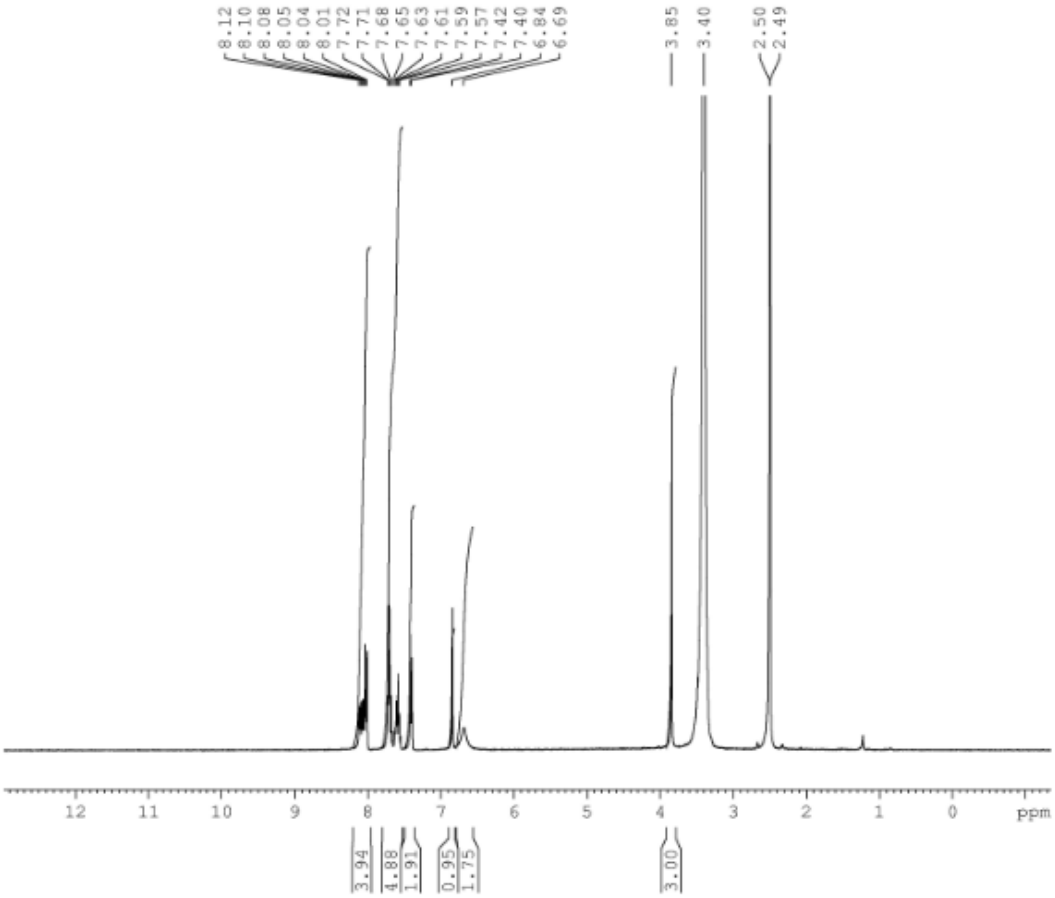
To 0.062 g (0.156 mmol) of (AGII19) is added 15 ml of methanol and the mixture is heated under reflux for 10-16 min. When 0.020 ml of Dimethylacetylenedicarboxylate (DMAD) is added to the hot suspension in suspension, orange colored precipitates form in the solution medium. Continue heating for 2-5 minutes under the cooler. The reaction is followed by TLC. It was observed that the solution color became darker by the heating process. It is observed that precipitation with the effect of temperature increases. It is left to cool overnight and the solution is filtered and washed in hot 5 ml of methanol. The impurity of the material is checked by TLC, and in the case of impurities,

the washing process is repeated. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (Hand) (0.026 g, yield 41.93%) of $C_{25}H_{20}ClN_5O_3S$, 489.91g / mol, Melting point (226 - 228) ˚C

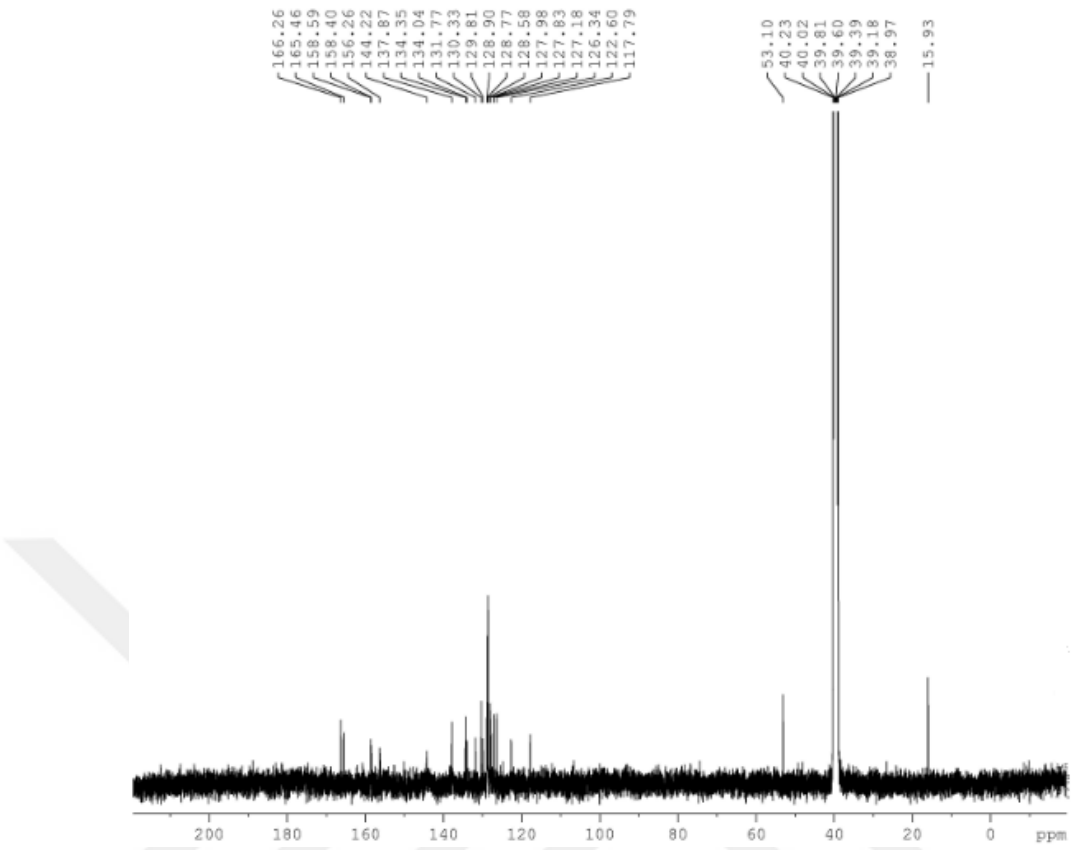


methyl (*E*)-2-((*Z*)-2-(((*E*)-*N*'-((*E*)-1-(4-chlorophenyl)ethylidene)carbamohydrazonoyl)imino)-3-(naphthalen-1-yl)-4-oxothiazolidin-5-ylidene)acetate

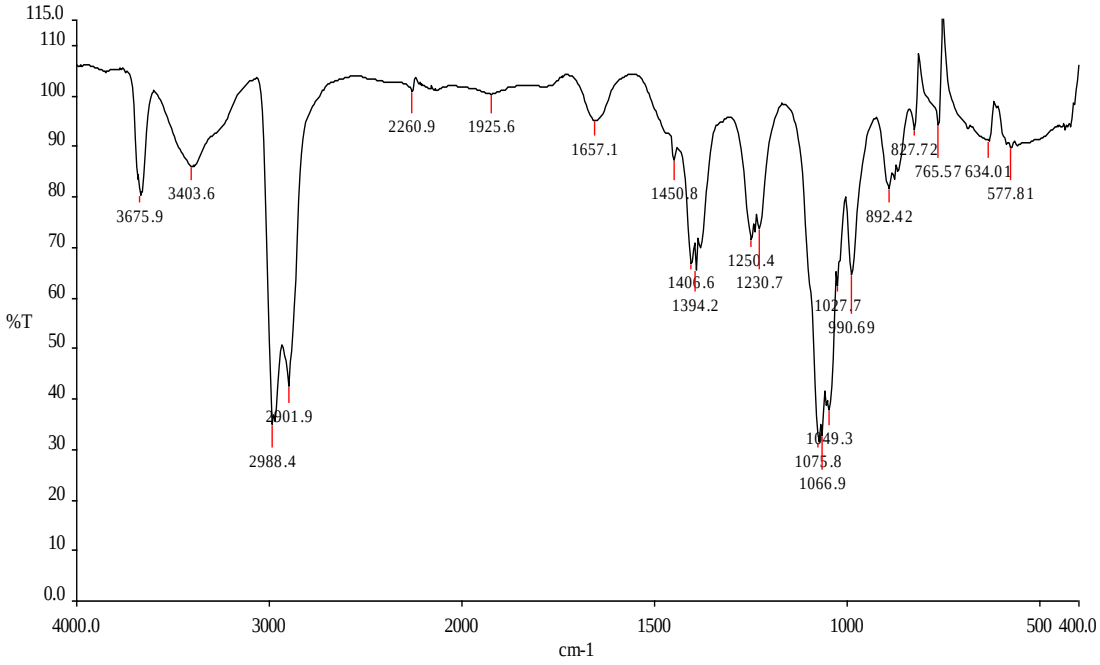
IHB15



^{1}H –NMR Spectrum IHB15



^{13}C-NMR Spectrum IHB15

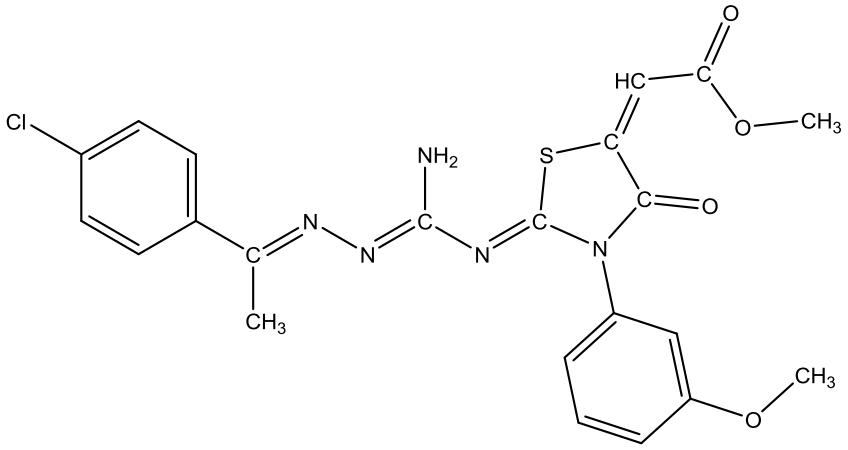


IR Spectrum IHB15

^{1}H-NMR (400 MH_Z, DMSO- δ_6) 8.12 (d, J = 8.4 Hz, 4H), 7.72-7.59 (t, J = 6.9 Hz, 5H), 7.40 (m, 2H), 6.84 (s, 1H), 6.69 (m, 2H), 3.85 (d, J = 3.9 Hz, 3H). ^{13}C-NMR (100 MH_Z, DMSO- δ_6) 166.26, 165.46, 158.59, 156.26, 144.22, 137.87, 134.35, 134.04, 131.77, 130.33, 129.81, 128.90, 128.77, 128.58, 127.98, 127.83, 127.18, 126.34, 122.60, 117.79, 112.11, 53.10, 15.93. IR (cm^{-1}) 3403-3675 N-H stretching, 2901-2988 -C-H stretching, 1657 C = O stretching, 1450 C = C stretching, 1406 C = N stretching, 1394 C - N stretching, 1230-1250 C - O stretching, 1049-1075 C - C stretching.

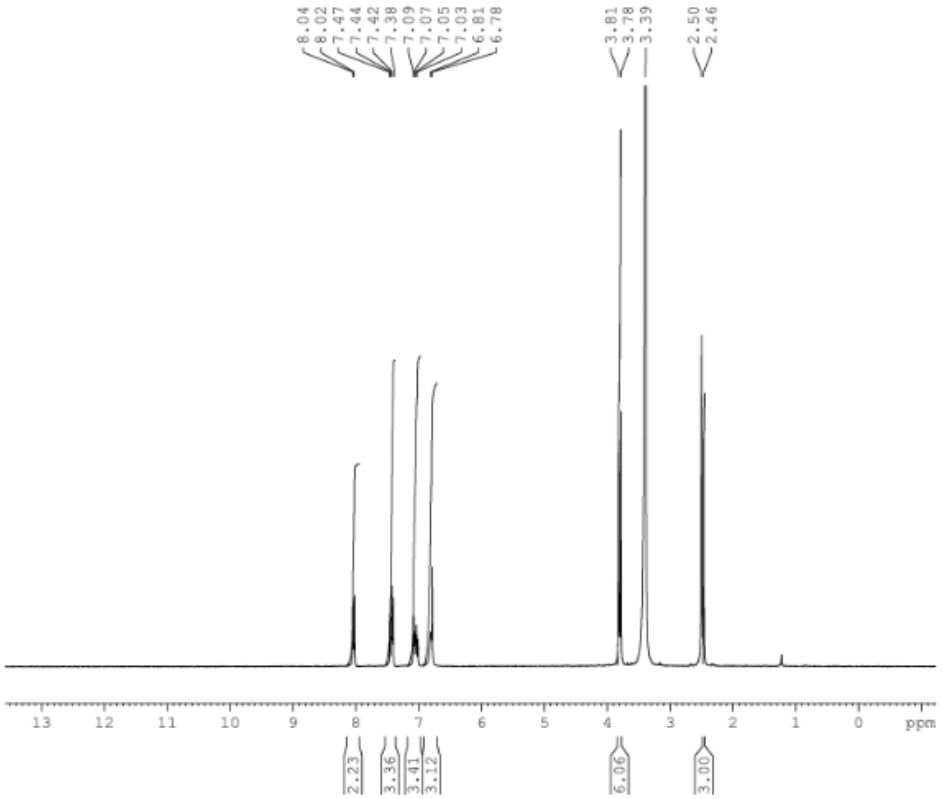
2.6.16. Methyl (E)-2-((Z)-2-(((E)-N'-((E)-1-(4-chlorophenyl) ethylidene) carbamo hydrazonoyl) imino)-3-(3-methoxyphenyl)-4-oxothiazolidin-5-ylidene) aceta te IHB16

To 0.1g (0.266 mmol) of (AGII20) is added 15 ml of methanol and the mixture is heated under reflux for 8-12 min. When 0.033 ml of Dimethylacetylenedicarboxylate (DMAD) is added to the hot suspension in suspension, orange colored precipitates form in the solution medium. Continue heating for 2-5 minutes under the cooler. The reaction is followed by TLC. It was observed that the solution color became darker by the heating process. It is observed that precipitation with the effect of temperature increases. It is left to cool overnight and the solution is filtered and washed in hot 5 ml of methanol. The impurity of the material is checked by TLC, and in the case of impurities, the washing process is repeated. Dry on P_2O_5 in a vacuum oven set at 60 ° C or in a vacuum desiccator. (Hand) (0.067 g, yield 67%) of $C_{22}H_{20}ClN_5O_4S$, 485.94g / mol, Melting point (219 - 221) ˚C

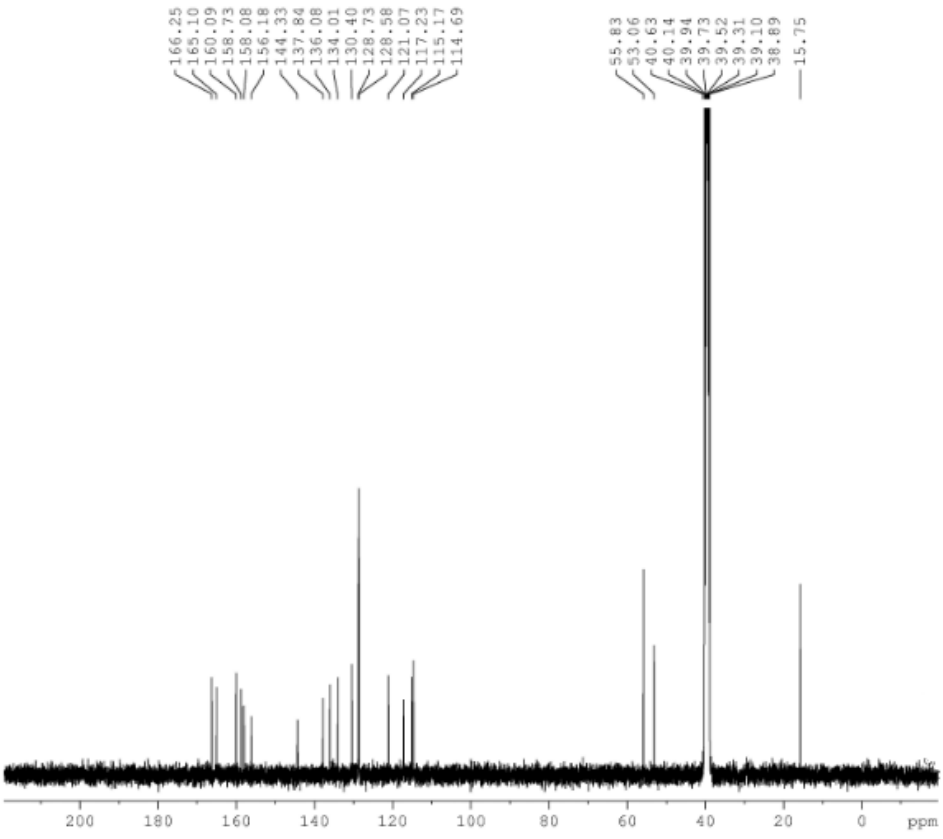


methyl (*E*)-2-((*Z*)-2-(((*E*)-*N*'-((*E*)-1-(4-chlorophenyl)ethylidene)carbamohydrazonoyl)imino)-3-(3-methoxyphenyl)-4-oxothiazolidin-5-ylidene)acetate

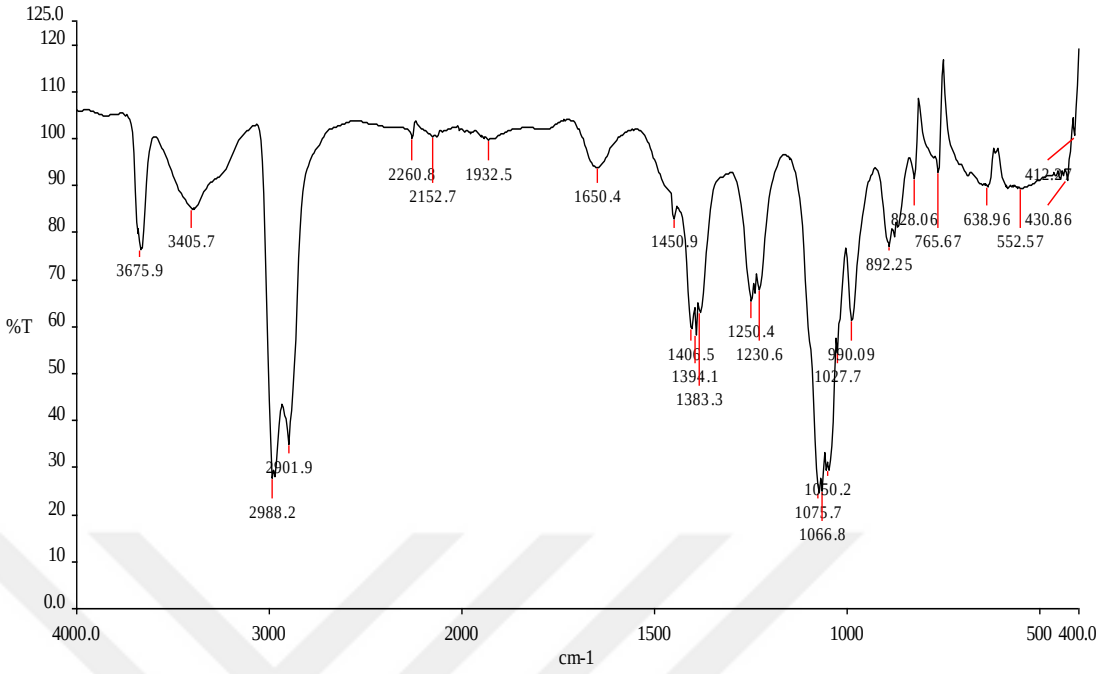
IHB16



^{1}H –NMR Spectrum IHB16



^{13} C-NMR Spectrum IHB16



IR Spectrum IHB16

^{1}H-NMR (400 MH$_Z$, DMSO- δ_6) 8.04 (d, J = 8.2 Hz, 2H), 7. 47 (d, J = 7.4 Hz, 3H) 7.09 (d, J = 7.2 Hz, 3H), 6.81 (d, J = 6.9 Hz, 3H), 3.81 (d, J = 3.9 Hz, 6H), 2.50 (d, J = 2.9 Hz, 3H). ^{13}C-NMR (100 MH$_Z$, DMSO- δ_6) 166.25, 165.10, 160.09, 158.73, 158.08, 156.18, 144.33, 137.84, 136.08, 134.01, 130.40, 128.73, 128.58, 121.07, 117.23, 115.17, 114.69, 53.83, 53.06, 15.75. IR (cm^{-1}) 3403-3675 N-H stretching, 2901-2988 - C-H stretching, 1650 C = O stretching, 1450 C = C stretching, 1406 C = N stretching, 1383 C - N stretching, 1230-1250 C - O stretching, 1050-1066 C - C stretching.

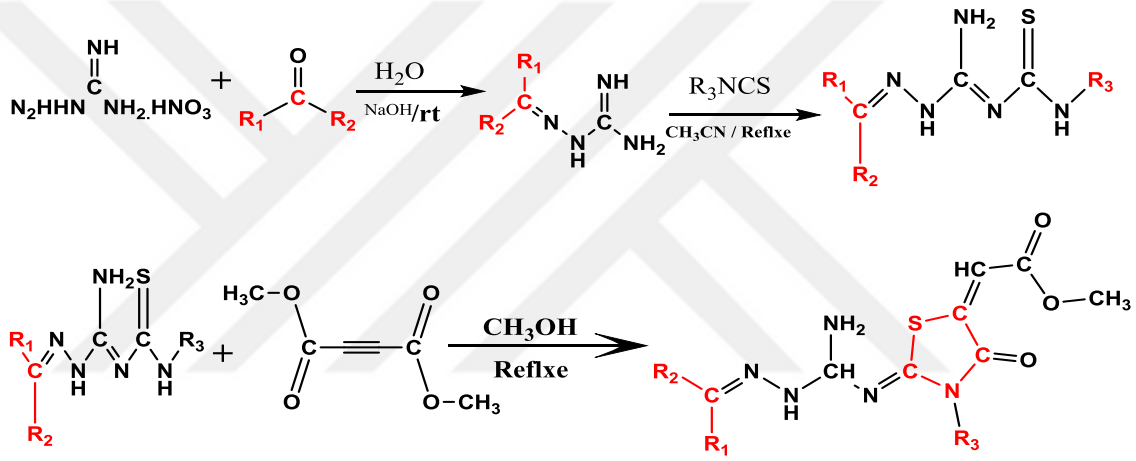
CHAPTER 3

DISCUSSION AND CONCLUSION

Guanidine, aminoguanidine and its subordinates; Antidiabetic specialists, for example, anticancerogenic, antifungal, antiprotozoal, antibacterial, antimalarial, tripanocidal, antisecretory, antidiarrheal, anticoagulant, antihypertensive, antiviral, antileukemic, cardiotonic, anticancerantantiogulant have comparable pharmacological exercises. Thiazolidines having comparative exercises and hostile to tumor action have the pharmacological action which can be utilized as a part of the treatment of a few sorts of growth with the reason. There is no such union work on thiazolidin-5-ylidene acetic acid derivation subsidiaries. Inside the extent of the investigation, the focused on aminoguanidine-thiazolidine subsidiaries; they are imperative as a result of their pharmacological properties. They have an including aminoguanidine group and aminoguanidine group as derivatives, they are utilized on account of their hostile to tumor movement, they have potential pharmacological action and it is certain to impact new to blends. In spite of the fact that there are vital examinations in the writing with respect to aminoguanidine-determined medications and thiazolidine subordinates, there are no subsidiaries of the focused on two gatherings in this investigation. The mixes said in the objective piece of the work were integrated and new mixes were gotten in the writing. It is expected that these blended mixes may likewise have organic safeguarding.

In the literature aminoguanidine-derived drugs and thiazolidine important about their derivatives although studies are available, this study both targeted groups No derivatives containing one are present. Goal of study specified in were synthesized and novel compounds it gained. This synthesized it is estimated that the compounds may also have biological preservation. For the synthesis of these compounds, the aminoguanidine nitrate salt is reacted with various aldehydes, ketones reaction occurs as carboxyamides.

With the isothiocyanate derivatives of the carboxyamides. The resulting N-(aminoamidino) thiourea comes to the fore. This compound dimethylacetylenedicarboxylate to give 4-oxo-1, 3-thiazolidin-5-ylidene acetate obtained. The resulting 4-oxo-1, 3-thiazolidin-5-ylidene acetate compounds Due to the presence of α, β-unsaturated ester structures in the position, Michael type reactions it is possible to do. Also, because of the carbonyl group in the 4 position position we think that reactions of carbonyl groups can be done. With calculations it was found that the X-ray structure was harmonious. Also includes NH2 group can be activated by various electrophilic character constellations. Reaction equation is as follow



R_1= H,CH_3
R_2=Cl,H,CH_3,CH_3CH_2,OCH_3,OCH_3CH_2,$N(CH_3)_2$,NO_2
R_3=1-Naphthyl, 3-methoxyphenyl

Table 3.1. Reactions of Dimethyl acetylene Dicarboxylate (DMAD) with N-(aminoamidino) thioureas, Synthesis of 4-oxo-1, 3-thiazolidin-5-ylidene acetate derivatives

COMPOUND	R_1	R_2	R_3	Melting point	Yield %
IHB1	-H	4-CH_3(C_6H_5)	1-Naphthyl	146-148	44%
IHB2	-H	4-CH_3(C_6H_5)	3-methoxyphenyl	209-210	70%
IHB3	-H	-(C_6H_5)	1-Naphthyl	183-185	52%
IHB4	-H	4-NO_2(C_6H_5)	3-methoxyphenyl	211-212	73%
IHB5	-CH_3	-(C_6H_5)	1-Naphthyl	237-238	68%
IHB6	-CH_3	4-CH_3(C_6H_5)	1-Naphthyl	187-191	73%
IHB7	-CH_3	4-CH_3(C_6H_5)	3-methoxyphenyl	219-221	73%
IHB8	-H	2-CL(C_6H_5)	3-methoxyphenyl	237-238	74%
IHB9	-H	2-Cl-6-F(C_6H_5)	1-Naphthyl	206-208	59%
IHB10	-H	2-Cl-6-F(C_6H_5)	3-methoxyphenyl	217-219	54%
IHB11	-H	4-di$CH_3)_2$N(C_6H_5)	1-Naphthyl	159-161	47%
IHB12	-H	4-di$CH_3)_2$N(C_6H_5)	3-methoxyphenyl	198-199	38%
IHB13	-CH_3	4-OCH_3(C_6H_5)	1-Naphthyl	194-195	65%
IHB14	-CH_3	4-OCH_3(C_6H_5)	3-methoxyphenyl	203-206	85%
IHB15	-CH_3	4-CL(C_6H_5)	1-Naphthyl	226-228	42%
IHB16	-CH_3	4-CL(C_6H_5)	3-methoxyphenyl	219-221	67%

REFERENCES

1. Nilsson, B. O. (1999). Biological effects of aminoguanidine: an update. **Inflammation Research**, **48**(10), 509-515.
2. Vojinović-Ješić, L. S., Radanović, M. M., Rodić, M. V., Živković-Radovanović, V., Jovanović, L. S., & Leovac, V. M. (2016). Syntheses and characterization of 2-acetylpyridine-aminoguanidine and its copper (II) complexes: Crystallographic and antimicrobial study. **Polyhedron**, **117**, 526-534.
3. Joglekar, M. M., Bavkar, L. N., Sistla, S., & Arvindekar, A. U. (2017). Effective inhibition of protein glycation by combinatorial usage of limonene and aminoguanidine through differential and synergistic mechanisms. **International Journal of Biological Macromolecules**, **99**, 563-569.
4. Ou, P., & Wolff, S. P. (1993). Aminoguanidine: a drug proposed for prophylaxis in diabetes inhibits catalase and generates hydrogen peroxide in vitro. **Biochemical pharmacology**, **46**(7), 1139-1144.
5. Özgüneş, H., Atasayar, S. (2009). Aminoguanidin ve Hastalıklardaki Önemi. **Turkiye Klinikleri Journal of Medical Sciences**, **29**(4), 976-986.
6. Bueno, J. M., Carda, M., Crespo, B., Cuñat, A. C., de Cozar, C., León, M. L., ... & Sanz-Cervera, J. F. (2016). Design, synthesis and antimalarial evaluation of novel thiazole derivatives. **Bioorganic & medicinal chemistry letters**, **26**(16), 3938-3944.
7. Zhao, H., Cui, G., Jin, J., Chen, X., & Xu, B. (2016). Synthesis and Pin1 inhibitory activity of thiazole derivatives. **Bioorganic & medicinal chemistry**, **24**(22), 5911-5920.
8. Singla, R., Gautam, D., Gautam, P., & Chaudhary, R. P. (2016). Efficient "on water" green route heterocyclization of thiosemicarbazones with DMAD. **Phosphorus, sulfur, and silicon and the related elements**, **191**(5), 740-745.
9. Lieber, E., & Smith, G. B. L. (1939). The Chemistry of Aminoguanidine and Related Substances. **Chemical Reviews**, **25**(2), 213-271.

10. Neochoritis, C. G., Zarganes-Tzitzikas, T., & Stephanidou-Stephanatou, J. (2014). Dimethyl Acetylenedicarboxylate: A versatile tool in organic synthesis. **Synthesis**, **46**(05), 537-585.

11. Vaillancourt, V. A., Larsen, S. D., Tanis, S. P., (2001). Synthesis and biological activity of aminoguanidine and diaminoguanidine analogues of the antidiabetic/antiobesity agent 3-guanidinopropionic acid. **Journal of medicinal chemistry**, **44**(8), 1231-1248.

12. Lukas, T. J., Schiltz, G. E., Arrat, H., Scheidt, K., & Siddique, T. (2014). Discovery of 1, 3, 4-oxidiazole scaffold compounds as inhibitors of superoxide dismutase expression. **Bioorganic & medicinal chemistry letters**, **24**(6), 1532-1537.

13. Benmohammed, A., Khoumeri, O., Djafri, A., Terme, T., & Vanelle, P. (2014). Synthesis of novel highly functionalized 4-thiazolidinone derivatives from 4-phenyl-3-thiosemicarbazones. **Molecules**, **19**(3), 3068-3083.

14. Dar, B. A., Ahmad, S. N., Wagay, M. A., Hussain, A., Ahmad, N., Bhat, K. A., ... & Singh, B. (2013). Ultrasound promoted expeditious, catalyst-free and solvent-free approach for the synthesis of N, N′-diarylsubstituted formamidines at room temperature. **Tetrahedron Letters**, **54**(36), 4880-4884.

15. Moghaddam, F. M., Khodabakhshi, M. R., & Latifkar, A. (2014). A one-pot multicomponent synthesis of polysubstituted thiophenes via the reactions of an isocyanide, α-haloketones, and β-ketodithioesters in water. **Tetrahedron Letters**, **55**(6), 1251-1254.

16. Doğan N., (2017). Çok Fonksiyonlu 4-Oksotiyoazolidin sentezi ve kuantum hesaplamaları, Erciyes Üniversitesi Fen Bilimleri Enstitüsü, (Yüksek Lisans Tezi).

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