SYNTHESIS OF NOVEL CARBAZOLE DERIVATIVES BY DIELS-ALDER REACTION OF INDOLE-BASED DIENES WITH VARIOUS DIENOPHILES

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SYNTHESIS OF NOVEL CARBAZOLE DERIVATIVES BY DIELS-ALDER REACTION OF INDOLE-BASED DIENES WITH VARIOUS DIENOPHILES

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ABSTRACT

SYNTHESIS OF NOVEL CARBAZOLE DERIVATIVES BY DIELS-ALDER REACTION OF INDOLE-BASED DIENES WITH VARIOUS DIENOPHILES

Batur, Dilan
Master of Science, Chemistry
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Diels-Alder reaction is a powerful tool in organic synthesis to produce complicated molecular structures. This thesis aims to synthesize functionalized carbazole derivatives using the Diels-Alder reaction of indole-based dienes with various dienophiles. The chemistry of carbazoles has generated interest in medicinal chemistry and natural product synthesis in the labs due to its diverse biological activity. Furthermore, carbazoles are used in optoelectronic devices due to the wide band gap and charge transport properties.

Four dienes having 5-bromo, 7-bromo, *N*-H, and *N*-Me indole units were synthesized and reacted with *N*-methyl-, *N*-phenyl- and *N*-benzylmaleimides by the Diels-Alder reaction. In order to obtain the carbazole derivatives in high yields, Diels-Alder reaction conditions were optimized first. Optimization studies started with different catalysts and continued with different solvents, temperature, and catalyst loads to achieve the highest yield of the desired carbazole cycloadducts. All the optimization studies were done using *N*-methylindole substituted diene and *N*-methylmaleimide dienophile. Synthesized carbazole derivatives were characterized by spectroscopic techniques like NMR, IR and mass spetrometry.

Besides, the synthesis of novel carbazole derivatives, photophysical properties were also investigated to determine their potential use in optoelectronic devices such as OLED and solar cell applications.

Keywords: Carbazoles, Indole-substituted dienes, Diels-Alder reaction

ÖZ

DİELS-ALDER REAKSİYONU KULANILARAK İNDOLE TEMELLİ DIENLERİN ÇEŞİTLİ DİENOFİLLER İLE YENİ KARBAZOL TÜREVLERİNİN SENTEZİ

Batur, Dilan
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Eylül 2023, 52 sayfa

Diels-Alder reaksiyonu, karmaşık moleküler yapıları üretmek için organik sentezde güçlü bir araçtır. Bu tez, çeşitli dienofillerle indol temelli dienlerin Diels-Alder reaksiyonunu kullanarak fonksiyonelleştirilmiş karbazol türevlerinin sentezini amaçlamaktadır. Karbazolların kimyası, çeşitli biyolojik aktiviteye sahip olmalarından dolayı tıbbi kimya ve doğal ürün sentezi alanında ilgi çekmiştir. Ayrıca, karbazollar yüksek bant aralığı ve yük taşıma özellikleri nedeniyle optoelektronik cihazlarda kullanılmaktadır.

Yeni karbazol yapılarının sentezi için indol yapısının 5- ve 7-pozisyonlarında brom, azot üzerinde hidrojen (*N*-H) ve metil (*N*-Me) grupları içeren dört farklı indol sübstite dien bileşikleri ve *N*-metil-, *N*-fenil- ve *N*-benzilmaleimit dienofilleri ile Diels-Alder tepkimesine tabi tutulmuşlardır. Karbazol yapılarının yüksek verimle elde edilmesi için ilk olarak Diels-Alder tepkimesinin koşulları optimize edilmiştir. Optimizasyon çalışmalarına farklı katalizörler ile başlanmış, farklı çözücüler sıcaklık ve katalizör miktarları ile devam edilmiştir. Tüm optimizasyon çalışmaları *N*-metilindol sübstite dien ve *N*-metilmaleat kullanılarak gerçekleştirilmiştir. Sentezlenen karbazol türevleri NMR, IR ve kütle spektroskopik yöntemlerle karakterize edilmiştir.

Yeni karbazol türevlerini sentezlemenin yanı sıra fotofiziksel özelliklerine de bakılarak OLED ve güneş pillerri gibi optoelektronik cihazlarda kullanılma potansiyeli anlaşılmaya çalışılmıştır.

Anahtar Kelimeler: Karbazoller, İndol-sübstite dienler, Diels-alder tepkimeleri.

To the Powerpuff Girls

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ABBREVIATIONS

OLED: Organic Light-Emitting Diode

EQE: External Quantum Efficiency

CHAPTER 1

INTRODUCTION

1.1 Carbazoles and Their Importance

Due to their numerous uses in industries like drug discovery and optoelectronics, carbazole derivatives have drawn much attention in organic synthesis.[7]

A five-member pyrrole ring fused with a benzene ring makes up the tricyclic aromatic structure of the class of chemical compounds known as carbazoles. They display a variety of chemical and biological characteristics, which makes them a crucial topic for research in the field of organic chemistry. Here, we examine the importance of carbazoles and some of the domains in which they are used.

Carbazoles are helpful building blocks in the field of synthetic chemistry. They are valuable intermediates for synthesizing complex organic compounds because of their distinctive structural characteristics and reactivity. The synthesis of novel compounds with various features is made possible by the functional group transformations that carbazoles can go on.

Pharmaceuticals: Compounds based on carbazoles have demonstrated interesting biological activity, such as antioxidant, anticancer, antibacterial, anti-inflammatory, and anti-microbial characteristics. Scientists are now investigating carbazole derivatives as possible therapeutic candidates for treating various disorders. They form an essential class of medicinal chemistry molecules due to their ability to interact with biological targets such as Carprofen, Furostifoline, Atanisatin, Glycoborine, Siamenol, and the Clausine family.[8]

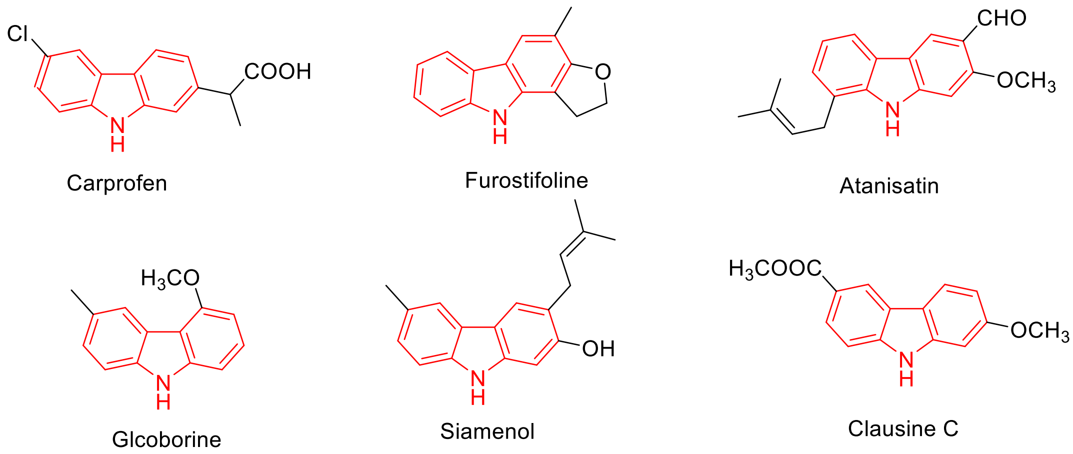


Figure 1. Carbazoles in medicinal chemistry

Novel organic compounds are created with various features in mind for optoelectronic applications. Energy levels can be chosen or adjusted appropriately with substituents for the intended application, high luminescence efficiency, high charge-carrier mobility, good stability, and appropriate morphology must be considered when designing novel OLED materials. Particularly in the solid form, the characteristics of these materials are significantly influenced by the structure of organic components.[9]

Carbazoles are excellent at transporting electrons and emitting light, which makes them a good choice for optoelectronic materials. Organic semiconductors, photovoltaic cells, and organic light-emitting diodes (OLEDs) have all been developed using carbazole-based chemicals. They help enhance next-generation electronic devices' excellent stability and effective charge-transfer properties.[9]

For instance, in Figure 5, various compounds with 1,3,5-triazine core, carbazole arms, and amino group links were synthesized and described. The estimated link between structure, charge transport characteristics, quantum efficiency, and electrochemical properties is obvious. Two well-known exciplex-forming acceptors were predicted and examined for their exciplex-forming capabilities. It was demonstrated that the compound 3CzNC's star-shaped arrangement offers the best exciplex OLED performance with EQE up to 6.84%. EQE stands for external quantum efficiency, which measures the percentage of generated light relative to electrical input. It is a crucial metric for evaluating device performance. Devices with higher EQE values efficiently convert a larger portion of injected charges into light, resulting in increased light emission efficiency.[10]

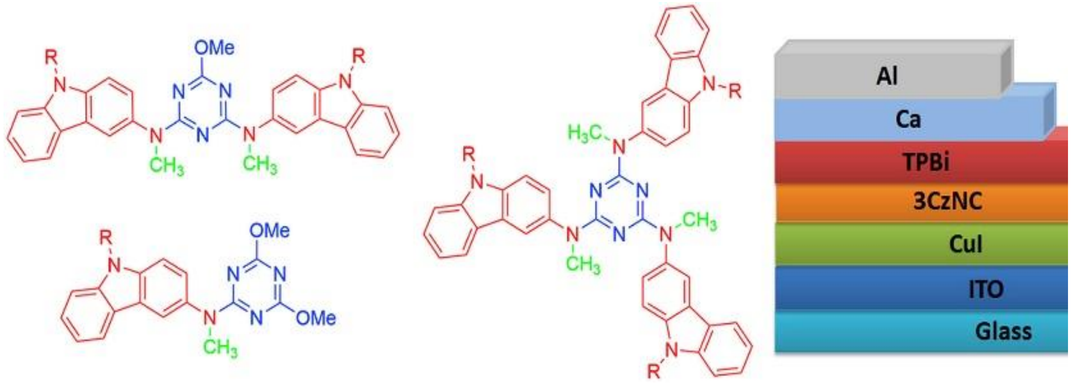


Figure 2. Carbazoles in OLEDs

The physical characteristics of carbazole derivatives, including their high thermal stability, solubility, and self-assembling nature, are exceptional, according to material science.[11] They are suitable for use in materials science because of these characteristics. Organometallic electronic devices, sensors, photovoltaics, and electrochromic devices all use polymers and copolymers based on carbazoles.[9]

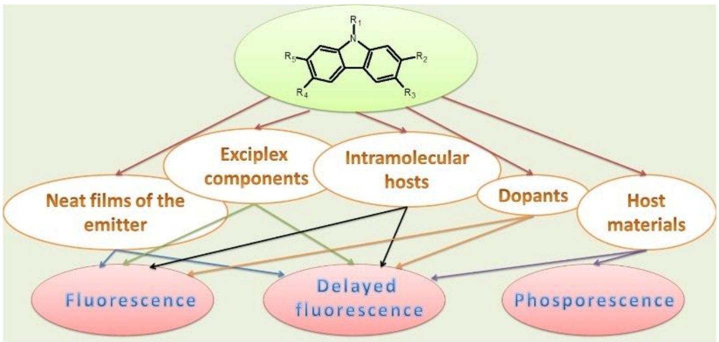


Figure 3. A diagram showing the role of the carbazole units in OLEDs related to emission phenomena[9]

In conclusion, carbazoles are adaptable substances with various uses and significance. They are helpful in chemistry, materials science, and pharmacology due to their distinct structural characteristics and wide range of chemical and biological activity. In other words, carbazole derivatives have great potential in developing novel materials, drugs, and technological advancements.

1.2 Indoles and Their Importance

The heterocyclic aromatic molecule indole has attracted much interest in organic chemistry because of its distinct structure and diverse reactivity. Its widespread use in natural products, medications, and practical materials accounts for its significance. Indole derivatives have a broad spectrum of biological functions and are used in many industries, such as materials science, agrochemicals, and drug discovery.[5]

The benzene ring is fused with a five-membered, nitrogen-containing pyrrole ring to form the structural motif of the indole. Indole gains several unique characteristics from this fused system, including aromaticity, electron richness, and propensity for electron delocalization. Due to these properties, Indole is a useful building block for synthesizing various organic compounds.[6]

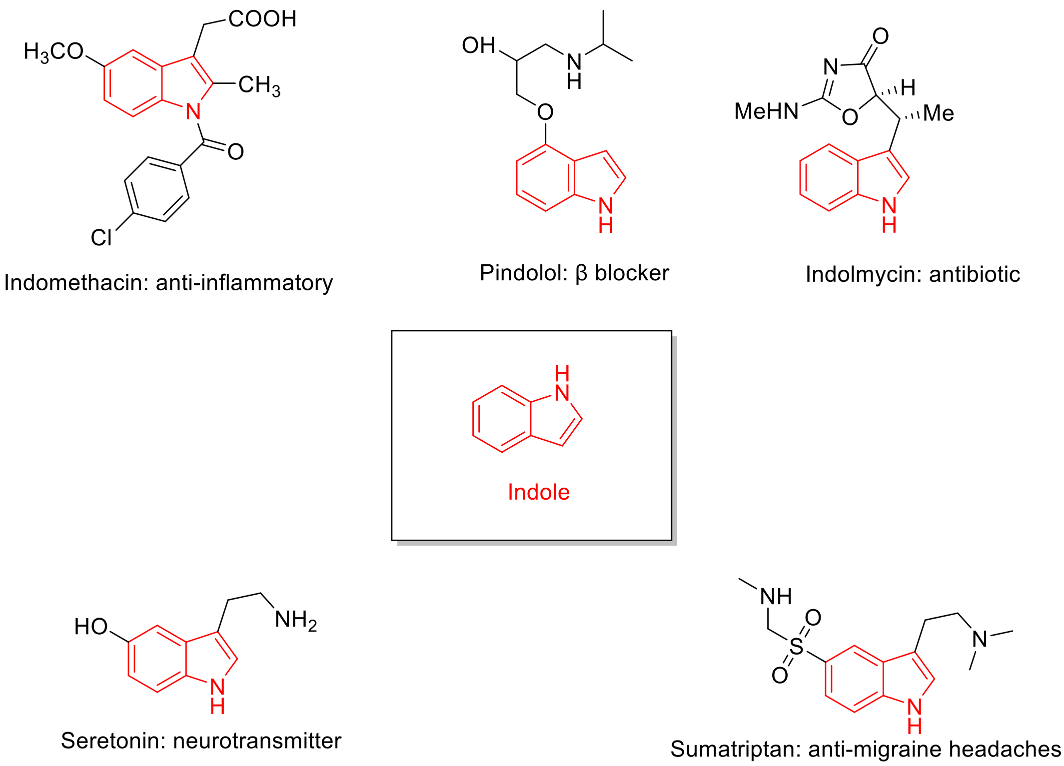


Figure 4. Examples of indole-based natural products

Indole derivatives are frequently found in natural products and contribute to the biological activities exhibited by many compounds (Figure 3). Examples include the anti-inflammatory, antiviral, and anticancer activities of indole alkaloids present in plants. Indole-containing chemicals, which act as signaling molecules and antibiotics, are frequently found in microbial metabolites.[6]

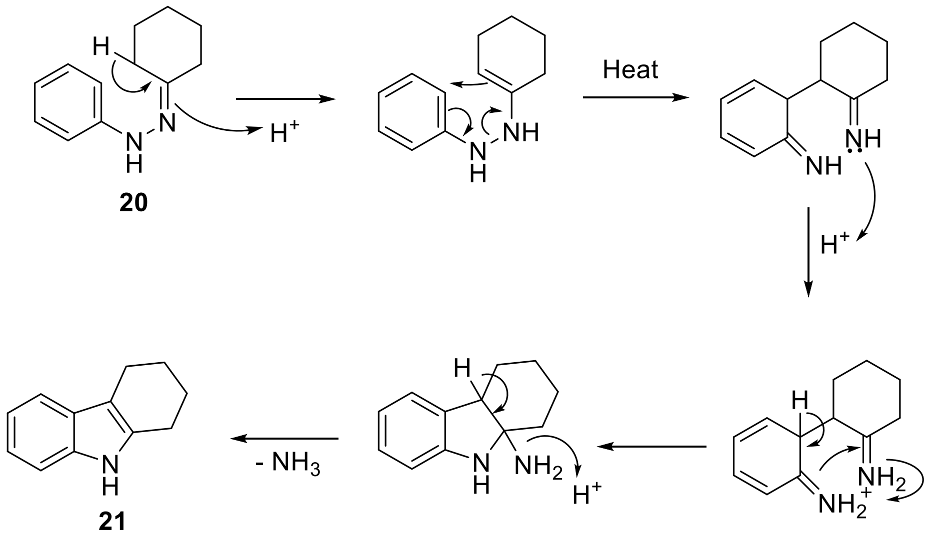
1.3 Literature carbazole synthesis

As reported in the literature, the class of aromatic heterocyclic compounds known as carbazoles can be produced in various methods. Some of these methods are listed on the following pages.

One of the oldest methods was cyclizing cyclohexanone with arylhydrazones under acid catalysis, known as the **Borsche-Drechsel cyclization**, a chemical process used to produce tetrahydrocarbazoles. Edmund Drechsel and Walter Borsche were the first to describe the reaction in 1888 and 1908, respectively.[12]

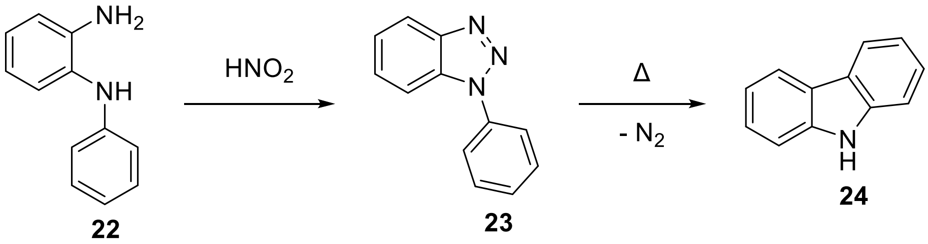
In the Borsche-Drechsel method, phenylhydrazine and cyclohexanone are combined to create the equivalent imine in the first step. The second stage involves a ring-closing reaction to tetrahydrocarbazole that is catalyzed by hydrochloric acid. This substance is oxidized to produce carbazole in the third stage.

A different approach involves conducting the reaction in acetic acid, which combines both stages into one.



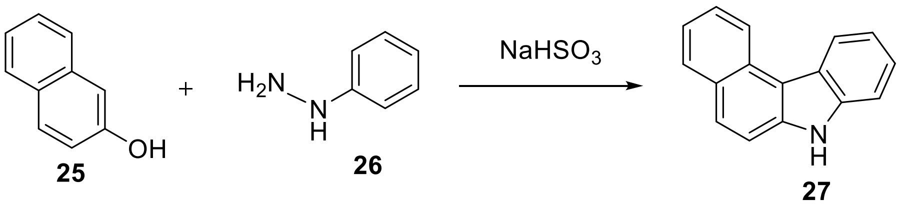
Scheme 1. Mechanism of Borsche-Drechsel cyclization

The **Graebe-Ullmann reaction** is another way of synthesizing carbazoles. In the first step, N-phenyl-1,2-diaminobenzene is transformed into a diazonium salt with HNO_2, instantly creating a 1,2,3-triazole. Because the triazole is unstable, it releases nitrogen at high temperatures to make carbazole (Scheme 6).[13]



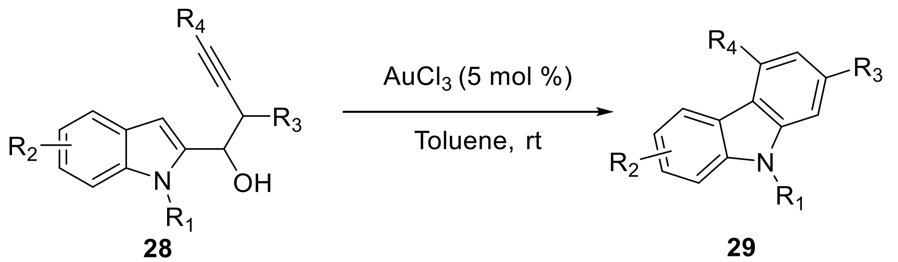
Scheme 2. Graebe-Ullmann reaction

Another method is the **Bucherer carbazole synthesis,** which uses sodium bisulfite to create carbazoles from naphthols and aryl hydrazines. Hans Theodor Bucherer is honored with the reaction's name.[14]



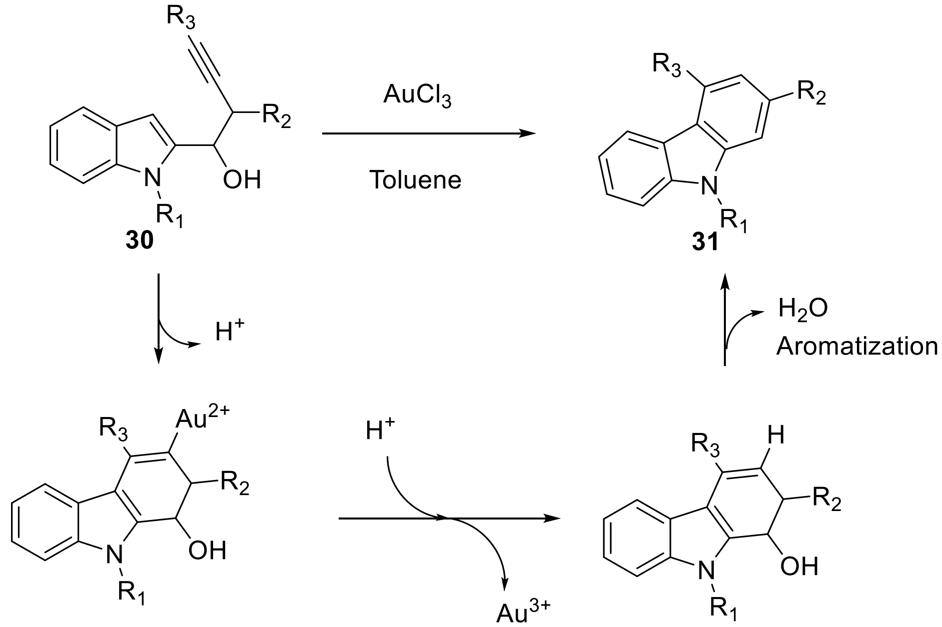
Scheme 3. Bucherer carbazole synthesis

Other methods include transition metals as catalysts. For example, **$AuCl_3$-catalyzed cyclizations** of 1-(indol-2-yl)-3-alkyne-1-ols occurred smoothly in toluene at room temperature, leading to a series of carbazole derivatives efficiently. They use Au(III) as a catalyst which coordinates to the triple bond then cyclication takes place. (Scheme 8).[15]



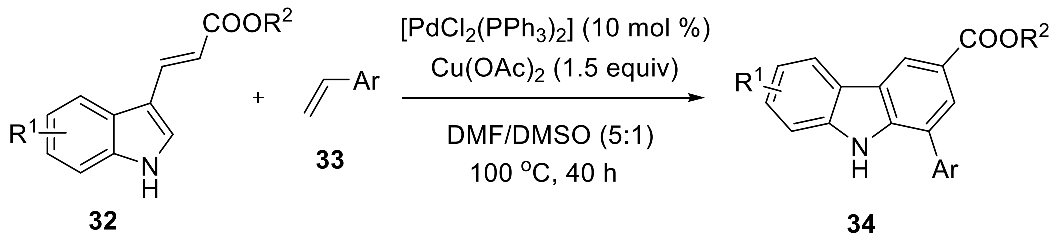
Scheme 4. $AuCl_3$-catalyzed cyclizations

A possible mechanism has been proposed as shown in Scheme **9**.[15]



Scheme 5. Possible mechanism of $AuCl_3$-catalyzed cyclization reaction

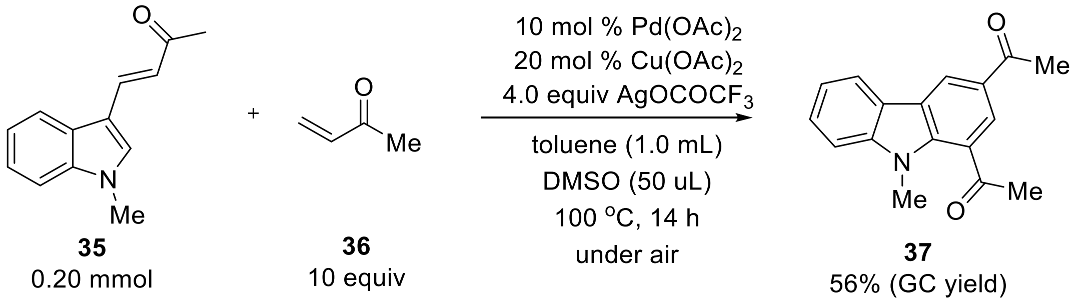
Another example of transition metal catalysts is the **Pd(II)-Catalyzed C-H Activation of Styrylindoles**. The direct synthesis of highly functionalized carbazoles from unprotected styrylindoles has been achieved using a unique Pd(II)-catalyzed method. Numerous olefin substrates are present in the reaction, and they are easily switchable by delicately adjusting the reaction conditions. Studies on the mechanism imply that enamine formation is the first step in the C-H activation (Scheme 10).[16]



Scheme 6. C-H activation of styryl indoles with styrenes

.

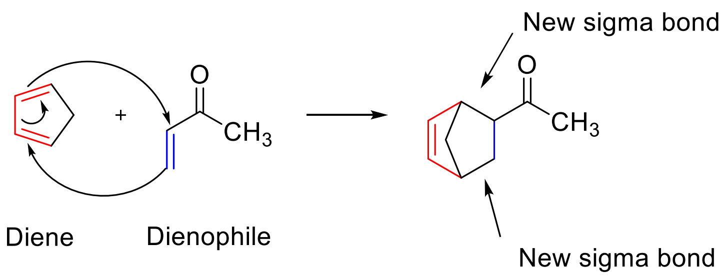
Finally, the **Diels-Alder reaction** has been used in several methods for synthesizing carbazole derivatives because it is an effective tool for creating intricate cyclic structures. In the literature, a trimetallic Pd, Cu, and Ag system can transform indoles to carbazoles using electron-deficient alkenes as two-carbon units (Scheme 11). Upon investigation of the reaction mechanism, it appears that this one-step extension of indole-to-carbazole extension is likely to occur through the sequence of Pd/Cu-catalyzed indole C–H alkenylation therefore without this step product will not occurs, then Ag-promoted Diels–Alder reaction and dehydrogenative aromatization occurs. Therefore, without even one catalyst yields are dropping signifiicantly.[17] The methods for synthesizing carbazoles discussed above have benefits, limitations, and potential drawbacks.



Scheme 7. One-shot indole-to-carbazole by a Pd-Cu-Ag trimetallic system

1.4 Diels-Alder Reaction

The Diels-Alder reaction makes the efficient creation of complicated cyclic structures possible, a crucial transformation in organic chemistry. A cyclic product known as a cycloadduct is produced by the interaction between a conjugated diene and a dienophile. Numerous uses for this reaction have been discovered in the manufacture of drugs, natural products, and materials.[1]



Scheme 8. Diel-Alder reaction scheme

Scheme **1** shows the mechanism of the Diels-Alder reaction, in which the diene's electrons engage with the dienophile's electron-deficient site to produce two new bonds concurrently. Due to the regioselectivity and stereospecificity of this reaction, the locations and stereochemistry of the newly generated bonds can be controlled.[2]

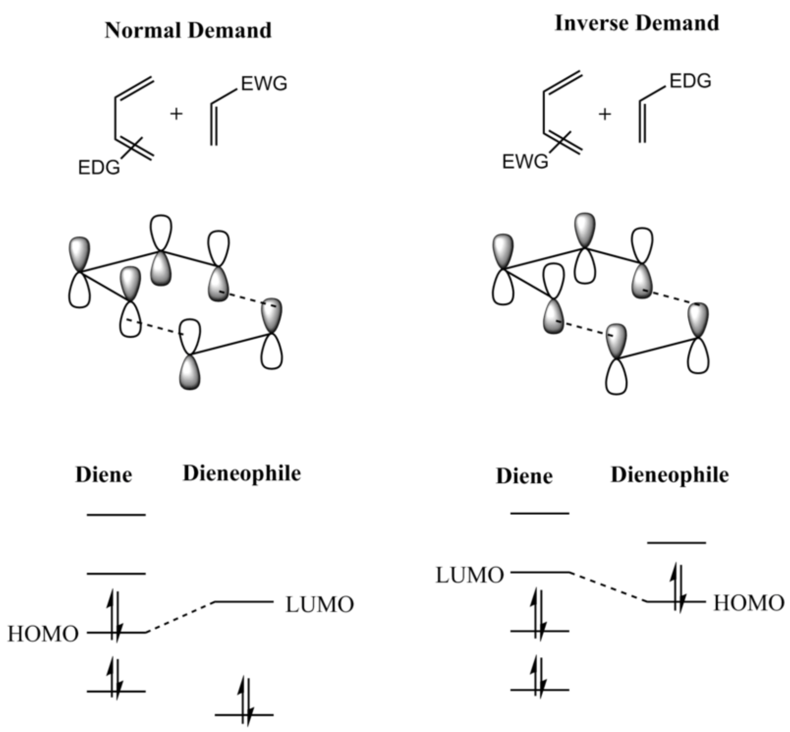


Figure 5. Normal vs. inverse demand Diels-Alder reaction

The diene is electron-rich for the normal demand Diels-Alder Reaction, and the dienophile is electron-deficient. The electron-donating groups on the diene, like the alkyl or alkoxy substituents, increase the diene's electron density and nucleophilicity. In contrast, the dienophile has electron-withdrawing units like carbonyl or nitro groups that reduce electron density and increase electrophilicity. A new six-member ring is formed due to the two-sigma bond formation.[1]

In inverse demand Diels-Alder Reaction, the diene is electron-deficient while the dienophile is electron-rich. The diene in this example has electron-withdrawing groups, like cyano or carbonyl groups, which reduce its electron density and increase its electrophilicity. The presence of electron-donating groups in the dienophile, such as alkyl or alkoxy substituents, raises its electron density and improves its nucleophilicity. Again, a new six-member ring is formed by creating two new sigma bonds.

The reverse demand Diels-Alder reaction has drawn attention for its synthetic value in specific situations, although less frequent than the normal demand Diels-Alder reaction. Access to strained cyclic systems or the production of reactive intermediates for additional transformations is possible.

The words "normal demand" and "reverse demand" should be understood to be relative and dependent on the specific electron-donating and electron-withdrawing characteristics of the diene and dienophile involved in the reaction. Based on the relative electron densities of the diene and dienophile, a Diels-Alder reaction is classified as either normal or reverse demand. This categorization can change depending on the particular reaction circumstances and substituents present. In this thesis, our dienophile has two electron-withdrawing carbonyl groups. Therefore, the Diels-Alder reaction in our studies is expected to follow the normal demand.

The use of the Diels-Alder reaction has been increased by advancements in catalysts, reaction conditions, and the choice of dienes and dienophiles, enabling the synthesis of various cyclic compounds. As a result of recent advancements, the Diels-Alder reaction is now a valuable tool for accessing sophisticated molecular structures.

This thesis focuses on creating new novel carbazole compounds by the Diels-Alder reaction. We seek to effectively access carbazoles with potential uses in diverse sectors by utilizing the efficiency of this reaction and carefully selecting reaction conditions.

1.4.1 Regioselectivity in Diels-Alder Reaction

The regioselectivity patterns seen in the Diels-Alder reactions of substituted systems have been explained using the frontier molecular orbital theory.[3] The ortho product is major, and the meta product is minor.

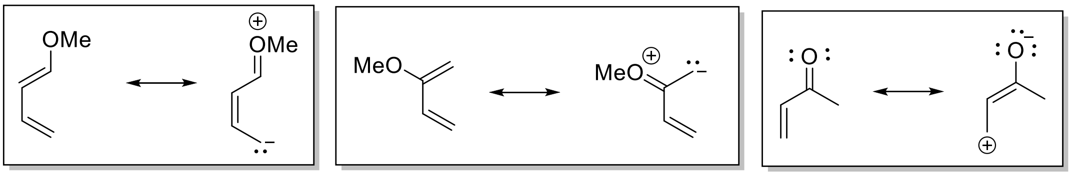
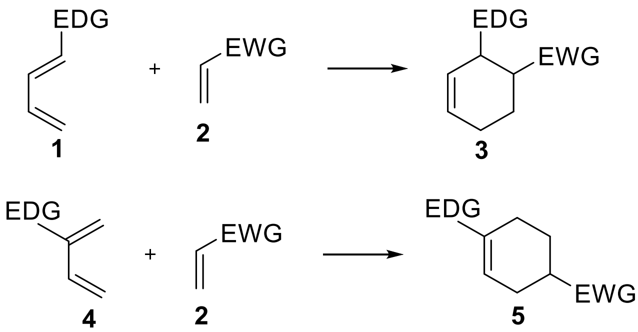
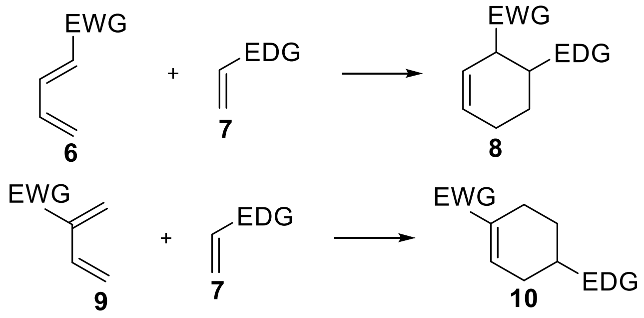


Figure 6. Resonance structures of normal-demand dienes and dienophiles

Regioselectivity applies to both normal electron demand reactions and inverse electron demand reactions. The ortho-para rule, so named because the cyclohexene product contains substituents in locations comparable to the ortho and para positions of disubstituted arenes, governs Diels-Alder reactions (Scheme 2).



Scheme 9. Regioselectivity in normal demand Diels-Alder reactions

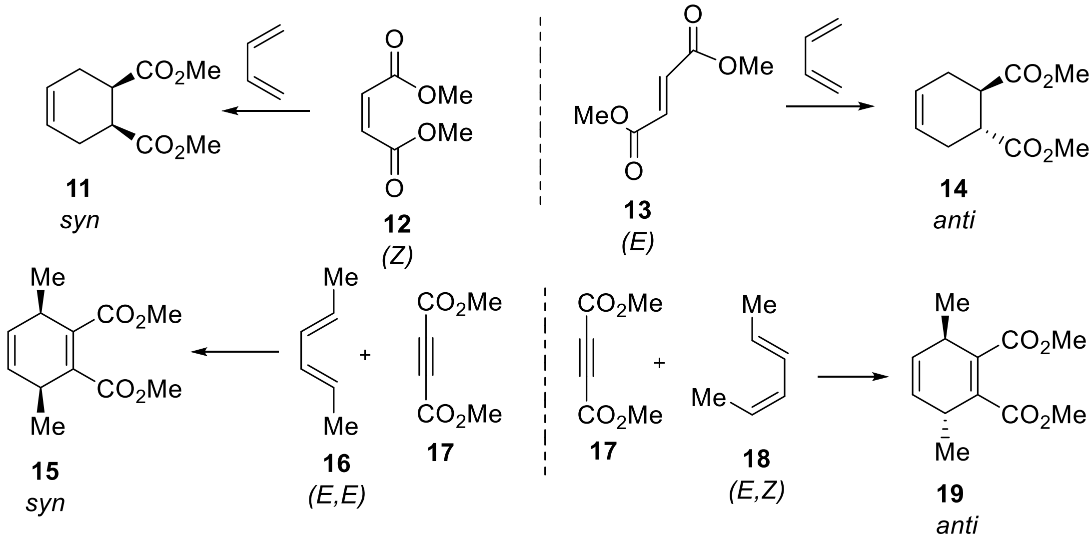


Scheme 10. Regioselectivity in inverse demand Diels-Alder reactions

Scheme 2 and 3 shows that the final product results in the ortho and para product, not the meta-product, favoring the results from the experiments.

1.4.2 Stereospecificity and Stereoselectivity

Diels-Alder's reactions are stereospecific. In *syn* addition, for each component, the results retain the stereochemical information of the diene and the dienophile. As shown in Scheme 4, *E, E*-disubstituted diene leads to the *syn-cycloadducts*, and *E, Z-disubstituted* diene leads to the *anti*-cycloadduct. Similarly, *cis*-dienophiles form *cis*-disubstituted cycloadducts, and the *trans*-dienophiles form the *trans*-disubstituted cycloadducts. This means the substituents attached to the diene and dienophile retain their stereochemistry.[4]



Scheme 11. Diels-Alder stereochemistry

Furthermore, in Diels-Alder reactions, the *endo* product is favored over the *exo* product. The *endo* derivative appears to exhibit a significantly greater degree of steric hindrance. However, a secondary orbital interaction is believed to be the effective factor for forming the *endo* product.

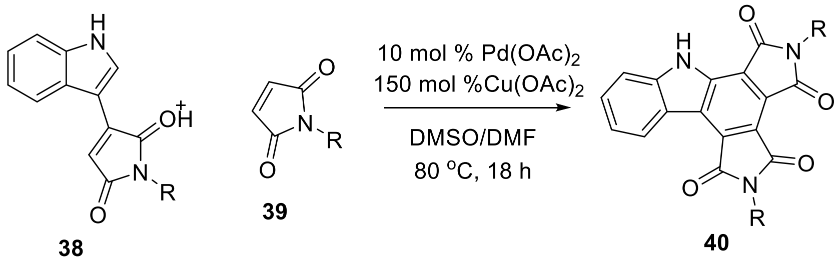
1.4.3 Disadvantages of the Method in Carbazole Synthesis

The processes for synthesizing carbazoles discussed above have benefits but also have some restrictions and potential drawbacks. Here are a few things to be considered:

Reaction complexity: Some processes involve multiple steps, like the Borsche-Drechsel cyclization. The method requires further aromatization of tetrahydro carbazole **21** to get carbazole.

Finally, the cost and availability of reagents are among the most significant problems. Some procedures may require specific reagents, catalysts, or ligands, but they may not always be inexpensive or accessible. For researchers who may need to consider the materials' pricing and accessibility, this could provide practical challenges. For instance, the amount of catalyst required for an $AuCl_3$-catalyzed cyclization is high, and it is a very expansive catalyst. The catalysts employed in a trimetallic system are high. Even if only one catalyst is not utilized, the yield falls to 23% (Scheme 11). The study aims to synthesize carbazole derivatives using the Diels-Alder reaction under milder conditions.

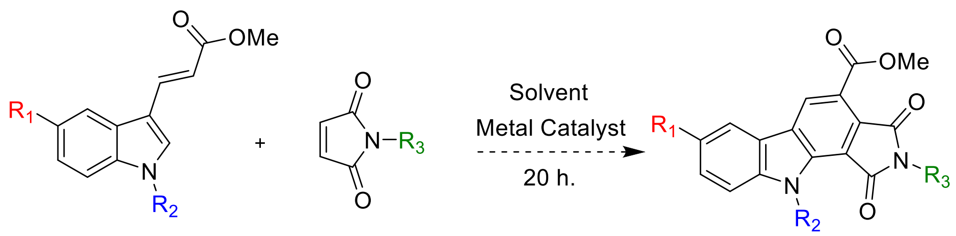
Another example to the use of the Diels-Alder reaction for carbazole synthesis was reported by Zhao et al. (Scheme 12) with 1.5 equivalent $Cu(OAc)_2$.[18]



Scheme 12. Synthesis of carbazoles by using Diels-Alder reaction.

1.4.4 Aim of the Study

The purpose of this study is to focus on the development of a milder methodology for carbazole synthesis. Literature methods often require harsh conditions or complex and expensive catalysts/reagents, etc. To achieve our aim, we planned to start with indole-based dienes that can be synthesized easily by literature methods. Then react them with maleimides by Diels-Alder reaction using different catalysts. We planned to synthesize 12 new carbazole derivatives and fully characterize them using spectroscopic techniques. In addition, we also wanted to find out the potential use of the synthesized carbazoles in optoelectronic devices.



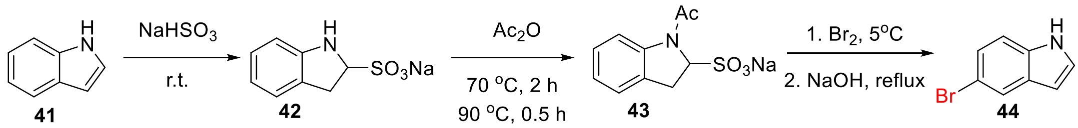
Scheme 13. Aim of the study

CHAPTER 2

RESULTS AND DISCUSSIONS

2.1 Synthesis of Indole Substituted Dienes

We started our experimental work by synthesizing dines necessary for the Diels-Alder reaction. For this purpose, we began with indole and introduced bromide to the fifth position to have different derivatives of indole-based dienes. Bromide was introduced to indole, as reported in the literature with a yield of 98 %, 83% and 98% respectively. (Scheme 13).[19]

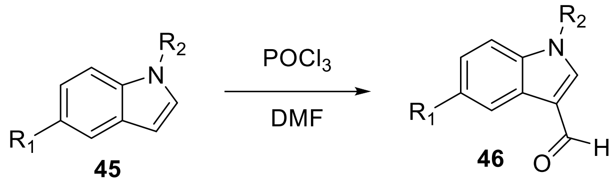


Scheme 14. 5-Bromo substituted indole synthesis

As shown in Scheme 13, the reaction of indole (**41**) with $NaHSO_3$ yielded the corresponding sodium indoline-2-sulfonate monohydrate **42**. The next step was the nitrogen protection with the acetyl group, which was achieved easily by using acetic anhydride. In the final step, compound **43** was reacted with bromine, which introduced bromide to the desired position of **43,** and then NaOH treatment reconstructed the indole unit and cleaved the acetyl group by forming compound **44**.

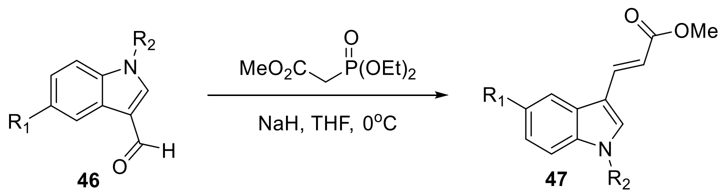
A versatile process in organic chemistry for introducing an aldehyde group to electron-rich aromatic units is called the Vilsmeier-Haack reaction. There are two essential reagents, *N*,*N*-dimethylformamide (DMF) and phosphoryl oxy chloride ($POCl_3$), with a suitable solvent, such as dichloromethane (DCM).[19]

The reaction between DMF and $POCl_3$ produces an iminium ion intermediate at the very beginning. Then, the electrophilic iminium ion reacts easily with the electron-rich aromatic compound, and hydrolysis completes the process. We have used this reaction to introduce an aldehyde group to our indole derivative with a yield of 90%. (Scheme 14).[20]



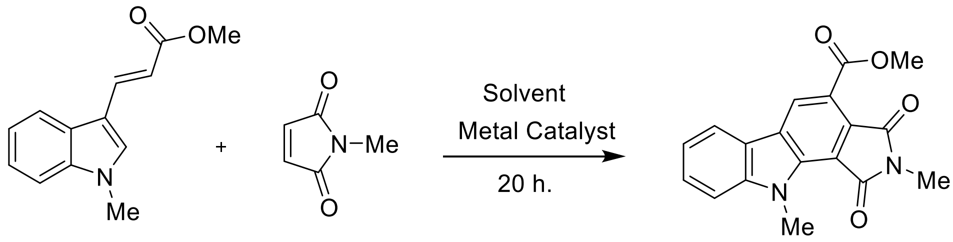
Scheme 15. Vilsmeier-Haack reaction

Another useful reaction of organic chemistry is the Horner-Wadsworth-Emmons (HWE) reaction.[18] It is the most powerful and common synthetic route for the carbon-carbon double bond formation in organic chemistry. This methodology has been utilized to synthesize our indole substituted dienes (Scheme 15).[21] The reaction of indole carboxyaldehyde **46** with diethylphosphonoacetate synthesized by the literature procedure[22] provided the desired indole-substituted diene **47** in the presence of NaH in THF.



Scheme 16. Synthesis of indole substituted dienes by Horner–Wadsworth–Emmons reaction.

2.2 Optimization of the Diels-Alder Reaction Conditions



Scheme 17. General Reaction Scheme

2.2.1 Catalyst Screening

Different transition metal salts, including $Cu(CH_3CN)_4BF_4$, $Zn(OTf)_2$, AgOAc, AgOTf, CuOAc, and $AgSbF_6$, have been tried as the Lewis acid catalyst for the Diels-Alder reaction. The results of these studies were summarized in Table **1**. While $Cu(CH_3CN)_4BF_4$ and $Zn(OTf)_2$ gave almost no product (entries 1 and 2), AgOTf, CuOAc, and $AgSbF_6$ provided cycloadducts in 43%, 19%, and 21% yields respectively (entries 4-6). Overall, the highest reaction yield (80%) was obtained using AgOAc as the Lewis acid catalyst (entry 3). Good catalytic effect of the AgOAc may result both from the metal and the more basic character of the acetate ion which helps aromatization. Similar results were also observed in the literature.[17] After deciding on the metal catalyst, further optimizations were continued with this transition metal salt.

Table 1. Results of the catalyst screening

Entry	Metal	Yield
1	$Cu(CH_3CN)_4BF_4$	Trace amount
2	$Zn(OTf)_2$	No reaction
3	AgOAc	80
4	AgOTf	43
5	CuOAc	19
6	$AgSbF_6$	21

2.2.2 Solvent Screening

The impact of different solvents on reaction yield was evaluated by using toluene, DMSO, THF, DCE, and DMF. The findings from the solvent screening experiment are summarized in Table **2.**

Except THF all the other solvents provided the Diels-Alder cycloadduct in various amounts (entries 1-5). In polar solvents, DMSO, and DMF, the product was isolated in 19% and 35% yields, respectively (entries 2 and 5). The low yield of the product in these solvents is more likely due to coordination of solvent molecules to Lewis acids, which lowers the catalytic effect of the transition metals. Although DCE gave the product in acceptable yield (53%, entry 4), toluene demonstrated the highest reaction yield by forming the product at 80% (entry 1).

Table 2. Results of the solvent screening studies

Entry	Solvent	Yield
1	Toluene	80
2	DMSO	19
3	THF	trace
4	DCE	53
5	DMF	35

2.2.3 Temperature Screening

The next parameter for the optimization of the Diels-Alder reaction was the temperature. For this purpose, we run the reaction at different temperatures, starting with room temperature (rt). The results of these studies were summarized in Table **3**. After seeing that the product formation was only a trace amount at rt (entry 1), we increased the temperature to 70 °C. At this temperature, the reaction yield was 80% (entry 2). Increasing the temperature to 100 °C and 130 °C didn't provide better yields (entries 3 and 4). Therefore, we decided to do Diels-Alder reactions at 70 ºC.

Table 3. Results of the temperature Screening

Entry	Temperatures	Yield
1	Room Temperature	Trace
2	50 ºC	22
3	70 ºC	80
4	100 ºC	68
5	130 ºC	23

2.2.4 Catalyst Load Screening

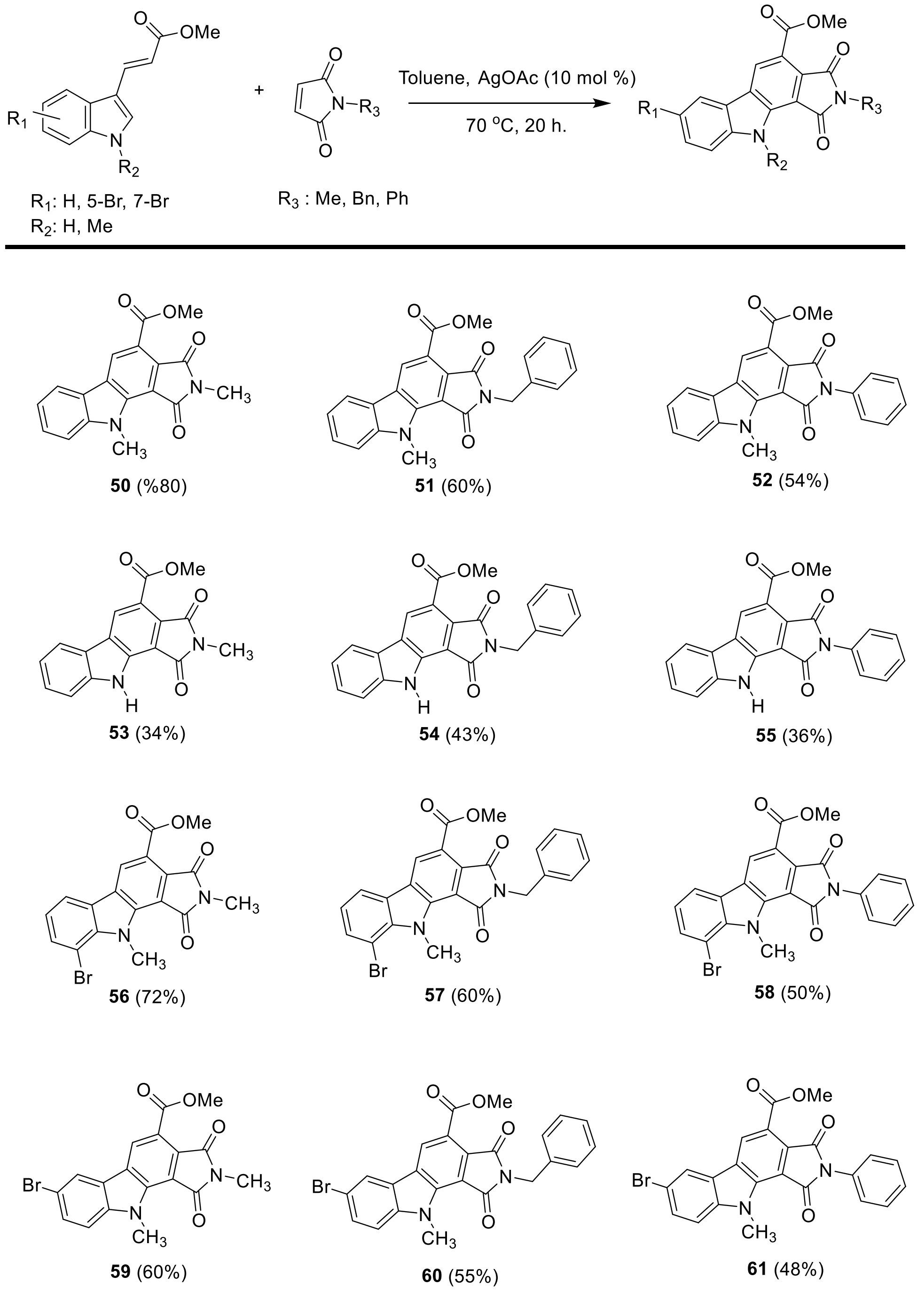
As the last parameter for optimization, we studied the effect of catalyst load on the reaction yield, summarized in Table 4. When the reaction was carried out with a 5 mol % catalyst, the yield for the cycloadduct was 56% (entry 1). Increasing the catalyst load to 10 mol % increased the reaction yield to 80% (entry 2). When the reaction was tried with 20 mol % or 30 mol % catalyst, the amount of isolated product dropped to 61% and 33%, respectively (entries 3 and 4). With this observation, it was decided to stay at 10 mol % catalyst loads for the Diels-Alder reaction.

Table 4. Results of the catalyst load screening

Entry	**Catalyst load (mol %)**	**Yield**
1	5	56
2	10	80
3	20	61
4	30	33

2.3 Synthesis of the Novel Carbazole Derivatives by the Diels-Alder Reaction

After optimizing the reaction parameters for the Diels-Alder reaction, synthesized indole substituted dienes were reacted with three different dienophiles: *N*-methylmaleimide, *N*-phenylmaleimide, and *N*-benzylmaleimide. Synthesized carbazole derivatives were listed in Scheme 16.



Scheme 18. Synthesized carbazole derivatives

As shown in Scheme 16, Diels-Alder reaction of *N*-methylindole substituted diene with *N*-methylmaleimide, *N*-benzylmaleimide *N*-phenylmaleimide provided the carbazole derivatives **50**, **51,** and **52** in 80%, 60%, and 54% yields respectively. As an example to the use of NMR for the characterization, we have given ^{1}H and ^{13}C NMR spectra of carbazole **50** in Figure 7.

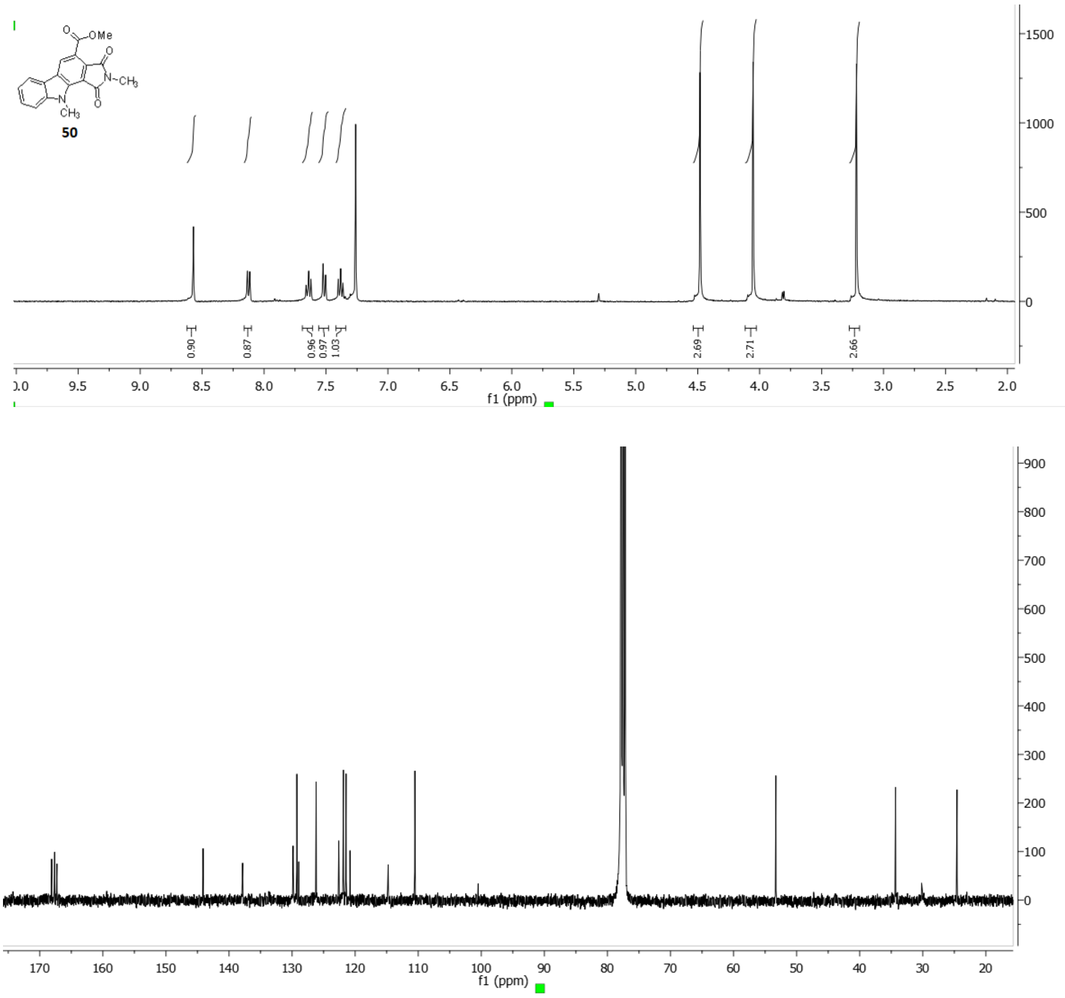


Figure 7. ^{1}H and ^{13}C NMR spectra of compound **50**

In the ^{1}H NMR spectrum of carbazole **50**, there are three methyl peaks at 4.48, 4.05, and 3.22ppm which belong to indole-methyl, methoxy methyl and maleimide methyl groups respectively. Four aromatic protons of the indole group appeared between 8.3-7.3 ppm. The singlet at about 8.6 ppm is for the remainin aromatic proton of the carbazole **50**. In the ^{13}C NMR three carconyl carbons appeared at around 168 ppm and three methyl carbons corresponding to ester, indole and maleimide methyl groups appeared at 53.30, 34.32, and 24.58 respectively. Signals corresponding to twelve aromatic carbons are seen between 110-145 ppm.

In the second series of carbazole synthesis, indole substituted dienes were reacted with the same maleimides. With *N*-methylmaleimide cycloadductct **53** was obtained in 34% yield. For the *N*-benzylmaleimide and *N*-phenylmaleimide cycloaddition products **54**, and **55** were obtained in 43% and 36% yields. Lower yields compared to first series can be attıributed to strong coordination of unsabstituted indole nitrogen to the lewis acid. As a result of this catalytic effect of the Lewis acid is lowered.

For the 7-bromosubstituted indole dienes the Diels–Alder reaction with the same dienophiles provided expected cycloadducts **56**, **57** and **58** in 72%, 60% and 50% yields respectively. Finally, when the carbazole synthesis was carried out with 5-bromosubstituted indole diene with the same dienophiles formed the products **59**, **60** and **61** in 60%, 55% and 48% yields respectively.

After synthesizing and characterizing the novel carbazoles, we looked for the photoluminescence spectrum of the carbazole **55**.

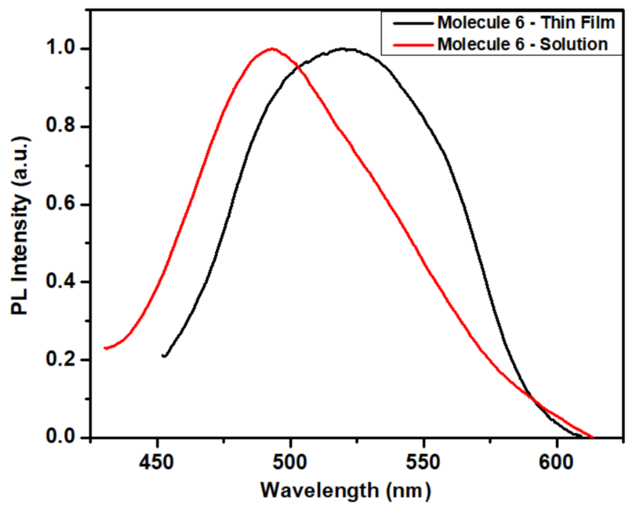


Figure 8. Photoluminescence spectrum of carbazole **55** as a thin film and in solution

The photoluminescence spectra of carbazole **55** in solution and as a thin film shown in Figure **8** provided significant intensity and a 32 nm red-shifted fluorescent emission via intermolecular π–π stacking. This is important in solar cell applications by capturing a broader range of wavelengths.[23] These findings suggest that the synthesized carbazoles may have potential applications in OLED technology. Further research may lead to more significant response efficiency and increase in yields of the carbazoles.

CHAPTER 3

CONCLUSION

In conclusion, we used the Diels-Alder reaction between various dienophiles and an indole-based dienes for the synthesis of 12 novel carbazole derivatives under optimized reaction conditions. All the new compounds were fully characterized by using NMR, IR, and mass spectroscopic techniques. Different than the literature we have shown that 10 mol% AgOAc can serve as a Lewis acid catalyst to provide various carbazole derivatives with the yields ranging between 34%-80%. The yields varied depending on the diene. The lowest yields were obtained with indole substituted diene which may be due to strong complexation of Lewis acid with lone pair electrons of nitrogen of the indole unit.

Additionally, the thesis emphasizes on the potential use of the synthesized carbazole derivatives in optoelectronics. Owing to their changeable emission wavelengths, effective charge transmission, and beneficial film-forming traits, these constituents showcase encouraging attributes for use in organic light-emitting diodes (OLEDs) and organic solar cells. According to photoluminescence studies, these carbazole-based materials have the potential to be used in advance optoelectronic technology.

CHAPTER 4

EXPERIMENTAL

4.1 General Experimental Procedure

Reagints are obtain from Merck, Across, and Sigma-Aldrich. The catalysts, reagents, and solvents were dried and purified before use. TLC (thin-layer chromatography) was used to track the reactions' progress using UV light. Ninhydrin and phosphomolybdic acid coloring were employed to highlight UV-inactive areas. Column chromatography on silica gel (230–400 mesh) was used to purify the crude products.

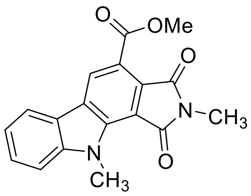
With reference to TMS (tetramethylsilane), the produced compounds were examined using Bruker Spectrospin Avance III DPX-400 equipment at 400 MHz and 100 MHz Bruker Platinum ATR-IR equipment collected infrared (IR) spectra, which were then reported in cm^{-1}. For the melting points Stuart SMP50 automatig melting point instrument used.

Overall, existing techniques reported in the literature were used to create starting material for the novel carbazoles.[19,21]

4.2 General Procedure for the Carbazole Synthesis

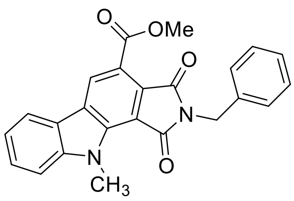
Caped tubes were used for the reactions. Initially, distilled toluene was used to dissolve one equivalent of methyl indole 3-acrylate. The mixture was then supplemented with maleimide (1.50 equivalent) and silver acetate (0.10 equivalent). The mixture was then agitated for 20 hours at 70°C. A silica gel column was used for purification using an ethyl acetate and hexane as mobile phase.

4.2.1 Characterization of methyl 2,10-dimethyl-1,3-dioxo-1,2,3,10-tetrahydropyrrolo[3,4-a]carbazole-4-carboxylate



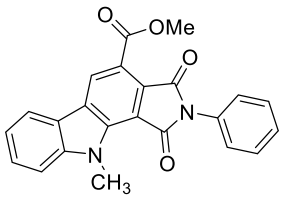
Using the general procedure, compound **50** was obtained as a yellow solid in 80% yield, mp: 239–245 ºC, *Rf* = 0.42 ($CHCl_3$). **^{1}H NMR** (400 MHz, Chloroform-d) δ 8.57 (s, 1H), 8.12 (d, *J* = 7.8, 1.0 Hz, 1H), 7.64 (t, *J* = 8.3, 7.1, 1.1 Hz, 1H), 7.51 (d, 1H), 7.38 (t, *J* = 8.0, 7.1, 1.1 Hz, 1H), 4.48 (s, 3H), 4.05 (s, 3H), 3.22 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.12, 167.65, 167.28, 144.12, 137.84, 129.85, 129.24, 128.95, 126.19, 122.60, 121.86, 121.43, 120.81, 114.76, 110.53, 53.30, 34.32, 24.58. **IR** (cm^{-1}): 2955, 2161, 1753, 1715, 1698. **HRMS** (*m/z*): calculated for $C_{18}H_{14}N_2O_4$ $[M+H]^+$: 323.1062 and found: 323.1024.

4.2.2 Characterization of methyl 2-benzyl-10-methyl-1,3-dioxo-1,2,3,10-tetrahydropyrrolo[3,4-a]carbazole-4-carboxylate



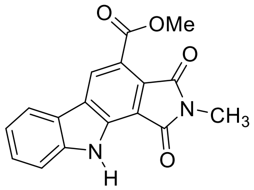
Using the general procedure, compound **51** was obtained as a yellow solid in 60% yield, mp: 254–259 ºC, *Rf* = 0.48 ($CHCl_3$)..**^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.67 (s, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.57 – 7.48 (m, 5H), 7.45 (q, *J* = 7.3, 6.8 Hz, 2H), 4.54 (s, 3H), 4.07 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.15, 166.93, 166.25, 143.42, 137.25, 136.34, 134.07, 129.23, 128.65, 128.56, 128.27, 128.10, 127.68, 125.73, 121.88, 121.25, 120.80, 120.20, 113.98, 109.92, 52.77, 41.68, 33.78. **IR** (cm^{-1}): 2950, 2293, 1750, 1727, 1697. **HRMS** (*m*/*z*): calculated for $C_{24}H_{18}N_2O_4$ $[M+H]^+$: 399.1266 and found: 399.1353.

4.2.3 Characterization of methyl 10-methyl-1,3-dioxo-2-phenyl-1,2,3,10-tetrahydropyrrolo[3,4-a]carbazole-4-carboxylate



Using the general procedure, compound **52** was obtained as a yellow solid in 54% yield, mp: 200–204 °C, *Rf* = 0.45 ($CHCl_3$). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.56 (s, 1H), 8.12 (d, *J* = 7.9, 2.8 Hz, 1H), 7.63 (t, 1H), 7.53 – 7.49 (m, 4H), 7.38 – 7.34 (m, 3H), 7.33 – 7.28 (m, 2H), 4.90 (s, 3H), 4.47 (s, 4H), 4.08 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.13, 166.92, 166.23, 143.48, 137.30, 136.36, 129.27, 128.89, 128.64, 128.54, 128.52, 127.64, 125.71, 121.93, 121.24, 120.80, 120.28, 114.04, 109.90, 52.78, 41.68. **IR** (cm^{-1}): 2949, 2055, 1760, 1697, 1602 **HRMS** (*m*/*z*): calculated for $C_{23}H_{16}N_2O_4$ $[M+H]^+$: 385.1110 and found: 385.1184.

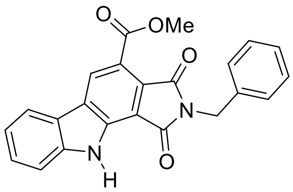
4.2.4 Characterization of methyl 2-methyl-1,3-dioxo-1,2,3,10-tetrahydropyrrolo[3,4-a]carbazole-4-carboxylate



Using the general procedure, compound **53** was obtained as a yellow solid in 34% yield, mp: 186–190 °C, *Rf* = 0.26 ($CHCl_3$). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.43 (s, 1H), 8.72 (s, 1H), 8.15 (d, 1H), 7.62 – 7.57 (m, 2H), 7.41 – 7.35 (m, 1H), 4.07 (s, 3H), 3.23 (s, 3H). **^{13}C NMR** (101 MHz, DMSO) δ 161.70, 161.53, 160.84, 134.85, 133.91, 131.06, 129.10, 128.94, 123.45, 123.14, 122.60, 120.46, 120.05, 117.33, 116.02, 109.44, 99.13, 47.72, 36.67. **IR** (cm^{-1}): 3347, 2151, 1759, 1688,

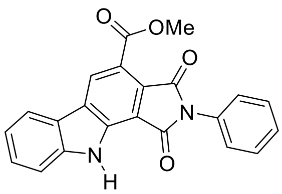
1642. **HRMS** (*m/z*): calculated for $C_{17}H_{12}N_2O_4$ $[M+H]^+$: 309.0797 and found: 309.0879.

4.2.5 Characterization of methyl 2-benzyl-1,3-dioxo-1,2,3,10-tetrahydropyrrolo[3,4-a]carbazole-4-carboxylate



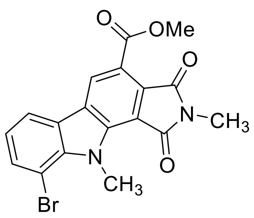
Using the general procedure, compound **54** was obtained as a yellow solid in 43% yield, mp: 235–237 °C, *Rf* = 0.42 ($CHCl_3$). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.41 (s, 1H), 8.71 (s, 1H), 8.15 (d, *J* = 9.8 Hz, 1H), 7.60 – 7.55 (m, 2H), 7.52 – 7.47 (m, 2H), 7.43 – 7.29 (m, 4H), 4.90 (s, 2H), 4.07 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.86, 166.20, 166.17, 141.72, 136.25, 134.84, 128.96, 128.86, 128.56, 128.53, 127.70, 127.06, 126.85, 121.70, 121.61, 121.33, 120.46, 114.13, 111.76, 52.66, 41.60. **IR** (cm^{-1}): 3350, 2151, 1762, 1687, 1616. **HRMS** (*m/z*): calculated for $C_{23}H_{16}N_2O_4$ $[M+H]^+$: 385.1110 and found: 385.1194.

4.2.6 Characterization of methyl 1,3-dioxo-2-phenyl-1,2,3,10-tetrahydropyrrolo[3,4-a]carbazole-4-carboxylate



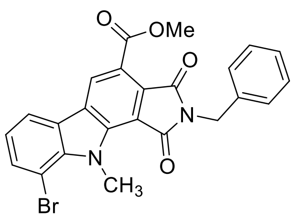
Using the general procedure, compound **55** was obtained as a yellow solid in 36% yield, mp: 235–237 °C, *Rf* = 0.32 ($CHCl_3$). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 9.58 (s, 1H), 8.80 (s, 1H), 8.21 (d, *J* = 8.0 Hz, 1H), 7.66 – 7.51 (m, 6H), 7.51 – 7.40 (m, 2H), 4.08 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.82, 166.77, 165.99, 143.06, 136.77, 136.40, 128.80, 128.69, 128.54, 128.47, 127.68, 125.35, 121.57, 121.07, 120.56, 119.98, 113.65, 109.70, 33.52. **IR** (cm^{-1}): 3343, 2983, 2160, 1759, 1667, 1602. **HRMS** (*m/z*): calculated for $C_{22}H_{14}N_2O_4$ $[M+H]^+$: 371.0953 and found: 371.1038.

4.2.7 Characterization of methyl 9-bromo-2,10-dimethyl-1,3-dioxo-1,2,3,10-tetrahydropyrrolo[3,4-a]carbazole-4-carboxylate



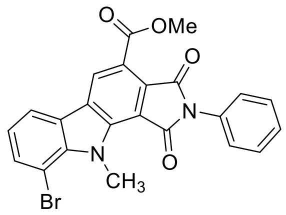
Using the general procedure, compound **56** was obtained as a yellow solid in 72% yield, mp: 189–195 ^oC, *Rf* = 0.50 ($CHCl_3$). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.43 (s, 1H), 7.97 (d, *J* = 7.7 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.11 (t, *J* = 7.7 Hz, 1H), 4.73 (s, 3H), 3.98 (s, 3H), 3.15 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.01, 166.88, 166.38, 139.94, 138.93, 134.19, 129.22, 128.48, 125.44, 125.20, 122.44, 121.02, 119.92, 114.64, 104.23, 52.80, 37.65, 24.10. **IR** (cm^{-1}): 2902, 1778, 1705, 1699, 626. **HRMS** (*m*/*z*): calculated for $C_{18}H_{13}BrN_2O_4$ $[M+H]^+$: 401.0058 and found: 401.0144 and 403.0126.

4.2.8 Characterization of methyl 2-benzyl-9-bromo-10-methyl-1,3-dioxo-1,2,3,10-tetrahydropyrrolo[3,4-a]carbazole-4-carboxylate



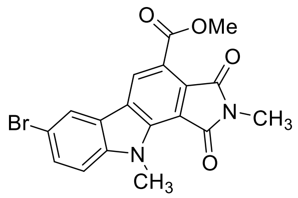
Using the general procedure, compound **57** was obtained as a yellow solid in 60% yield, mp: 210–212 ^oC, *Rf* = 0.74 ($CHCl_3$). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.45 (s, 1H), 7.98 (d, 1H), 7.68 (d, 1H), 7.41 (d, *J* = 7.4 Hz, 2H), 7.29 – 7.22 (m, 3H), 7.10 (t, *J* = 7.8 Hz, 1H), 4.82 (s, 2H), 4.73 (s, 3H), 3.97 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.80, 166.66, 165.97, 139.98, 139.04, 136.19, 134.23, 134.07, 128.58, 128.27, 127.73, 125.60, 125.18, 122.47, 121.15, 119.94, 114.57, 104.26, 52.85, 41.80, 37.76**. IR** (cm^{-1}): 2922, 1717, 1702, 1697, 627. **HRMS** (*m*/*z*): calculated for $C_{23}H_{15}BrN_2O_4$ $[M+H]^+$: 463.0215 and found: 463.0305 and 465.0297.

4.2.9 Characterization of methyl 9-bromo-10-methyl-1,3-dioxo-2-phenyl-1,2,3,10-tetrahydropyrrolo[3,4-a]carbazole-4-carboxylate



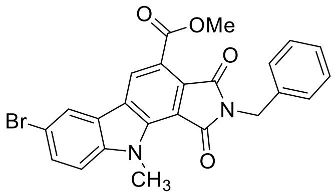
Using the general procedure, compound **58** was obtained as a yellow solid in 50% yield, mp: 233–237 °C, *Rf* = 0.65 ($CHCl_3$). **^{1}H NMR** (400 MHz,) δ 8.56 (s, 1H), 8.07 (d, *J* = 7.9, 1.6 Hz, 1H), 7.78 (d, *J* = 7.9, 1.5 Hz, 1H), 7.55 – 7.52 (m, 1H), 7.49 – 7.41 (m, 3H), 7.37 – 7.31 (m, 1H), 7.21 (t, 1H), 4.81 (s, 3H), 4.03 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.09, 166.05, 165.33, 140.09, 139.09, 134.36, 134.07, 131.49, 129.00, 128.17, 127.83, 126.93, 125.93, 125.76, 125.18, 122.57, 121.55, 119.99, 104.33, 77.20, 52.91, 37.78. **IR** (cm^{-1}): 2922, 1758, 1705, 1699, 630. **HRMS** (*m*/*z*): calculated for $C_{23}H_{15}BrN_2O_4$ $[M+H]^+$: 463.0215 and found: 463.0305 and 465.0297.

4.2.10 Characterization of methyl 7-bromo-2,10-dimethyl-1,3-dioxo-1,2,3,10-tetrahydropyrrolo[3,4-a]carbazole-4-carboxylate



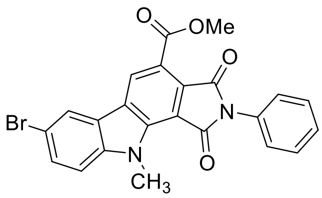
Using the general procedure, compound **59** was obtained as a yellow solid in 60% yield, mp: 237–244 °C, *Rf* = 0.49 ($CHCl_3$). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.50 (s, 1H), 8.21 (s, 1H), 7.70 (d, *J* = 8.7 Hz, 1H), 7.37 (d, *J* = 8.8 Hz, 1H), 4.44 (s, 3H), 4.05 (s, 3H), 3.21 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.25, 166.67, 166.44, 142.04, 137.31, 131.38, 128.95, 127.86, 125.97, 123.52, 123.50, 120.49, 114.52, 114.27, 111.48, 77.22, 77.21, 52.81, 33.93, 24.07. **IR** (cm^{-1}): 2950, 1757, 1720, 1695, 607. **HRMS** (*m*/*z*): calculated for $C_{18}H_{13}BrN_2O_4$ $[M+H]^+$: 401.0058 and found: 401.0121 and 403.0085.

4.2.11 Characterization of methyl 2-benzyl-7-bromo-10-methyl-1,3-dioxo-1,2,3,10-tetrahydropyrrolo[3,4-a]carbazole-4-carboxylate



Using the general procedure, compound **60** was obtained as a yellow solid in 55% yield, mp: 237–244 °C, *Rf* = 0.71 ($CHCl_3$). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.51 (s, 1H), 8.21 (d, *J* = 1.9 Hz, 1H), 7.69 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.49 – 7.46 (m, 2H), 7.38 – 7.31 (m, 3H), 7.31 – 7.27 (m, 1H), 4.88 (s, 2H), 4.44 (s, 3H), 4.05 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.89, 166.54, 165.99, 142.04, 137.41, 136.21, 131.40, 128.78, 128.63, 128.58, 128.56, 127.92, 127.73, 126.12, 123.52, 120.62, 114.47, 114.28, 111.46, 52.83, 41.76, 34.00. **IR** (cm^{-1}): 2946, 1759, 1734, 1698, 617. **HRMS** (*m*/*z*): calculated for $C_{24}H_{17}BrN_2O_4$ $[M+H]^+$: 477.0371 and found: 477.0463 and 479.0450.

4.2.12 Characterization of methyl 7-bromo-10-methyl-1,3-dioxo-2-phenyl-1,2,3,10-tetrahydropyrrolo[3,4-a]carbazole-4-carboxylate



Using the general procedure, compound **61** was obtained as a yellow solid in 48% yield, mp: 270–272 °C, *Rf* = 0.65 ($CHCl_3$). **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 8.59 (s, 1H), 8.28 (s, 1H), 7.74 (d, *J* = 8.8, 1.9 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.48 – 7.39 (m, 4H), 4.50 (s, 3H), 4.04 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.87, 166.33, 165.35, 142.22, 137.55, 131.55, 131.49, 128.98, 128.32, 128.28, 128.14, 126.89, 126.33, 123.62, 123.58, 121.09, 114.42, 114.10, 111.56, 52.86, 34.06. **IR** (cm^{-1}): 2959, 1773, 1700, 1708, 628. **HRMS** (*m*/*z*): calculated for $C_{23}H_{15}BrN_2O_4$ $[M+H]^+$: 463.0215 and found: 463.0305 and 465.0297.

REFERENCES

(1) Houk, K. N.; Lin, Y. T.; Brown, F. K. Evidence for the Concerted Mechanism of the Diels-Alder Reaction of Butadiene with Ethylene. *J Am Chem Soc* **1986**, *108*, 554–556.

(2) Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. The Diels-Alder Reaction in Total Synthesis. *Angewandte Chemie - International Edition*. 2002, pp 1668–1698.

(3) Sultan, M. A.; Karama, U.; Almansour, A. I.; Soliman, S. M. Theoretical Study on Regioselectivity of the Diels-Alder Reaction between 1,8-Dichloroanthracene and Acrolein. *Molecules* **2016**, *21*.

(4) Kloetzel, M. C. The Diels-Alder Reaction with Maleic Anhydride Address, University of Southern California, Los Angeles, California. *Organic Reactions* **2011**, 1–59.

(5) Sravanthi, T. V; Manju, S. L. Indoles — A Promising Scaffold for Drug Development. *European Journal of Pharmaceutical Sciences* **2016**, *91*, 1–10.

(6) Patil, S. A.; Patil, R.; Miller, D. D. Indole Molecules as Inhibitors of Tubulin Polymerization: Potential New Anticancer Agents. *Future Med Chem* **2012**, *4* (16), 2085–2115.

(7) Vlaar, C.; Castillo-Pichardo, L.; Medina, J.; Marrero, C.; Velez, E.; Ramos, Z.; Hernandez, E. Design, Synthesis and Biological Evaluation of New Carbazole Derivatives as Anti-Cancer and Anti-Migratory Agents. *Bioorg Med Chem* **2018**, *26*.

(8) Tian, X.; Song, L.; Hashmi, A. S. K. Synthesis of Carbazoles and Related Heterocycles from Sulfilimines by Intramolecular C−H Aminations. *Angewandte Chemie - International Edition* **2020**, *59*, 12342–12346.

(9) Ledwon, P. Recent Advances of Donor-Acceptor Type Carbazole-Based Molecules for Light Emitting Applications. *Org Electron* **2019**, *75*, 105422.

(10) Zassowski, P.; Ledwon, P.; Kurowska, A.; Herman, A. P.; Lapkowski, M.; Cherpak, V.; Hotra, Z.; Turyk, P.; Ivaniuk, K.; Stakhira, P.; Sych, G.; Volyniuk, D.; Grazulevicius, J. V. 1,3,5-Triazine and Carbazole Derivatives for OLED Applications. *Dyes and Pigments* **2018**, *149*, 804–811.

(11) Niu, P.; Huang, H.; Zhao, L.; Zhang, C.; Shen, Z.; Li, M. Preparation of Poly(Carbazole-TEMPO) Electrode and Its Electrochemical Performance. *Journal of Electroanalytical Chemistry* **2021**, *894*, 115352.

(12) Li, J. Borsche-Drechsel Cyclization. **2003**

(13) Alekseyev, R.; Kurkin, A.; Yurovskaya, M. Use of the Graebe-Ullmann Reaction in the Synthesis of 8-Methyl-γ-carboline and Isomeric Aromatic Aza-γ-carbolines. *Chem Heterocycl Compd (N Y)* **2012**, *48*, 1235.

(14) Li, J. Bucherer Carbazole Synthesis; 2006.

(15) Qiu, Y.; Kong, W.; Fu, C.; Ma, S. Carbazoles via AuCl3-Catalyzed Cyclization of 1-(Indol-2-Yl)-3-Alkyn-1-Ols. *Org Lett* **2012**, *14*, 6198–6201.

(16) Saunthwal, R. K.; Patel, M.; Kumar, S.; Danodia, A. K.; Verma, A. K. Pd(II)-Catalyzed C□H Activation of Styrylindoles: Short, Efficient, and Regioselective Synthesis of Functionalized Carbazoles. *Chemistry – A European Journal* **2015**, *21*, 18601–18605.

(17) Ozaki, K.; Zhang, H.; Ito, H.; Lei, A.; Itami, K. One-Shot Indole-to-Carbazole π-Extension by a Pd–Cu–Ag Trimetallic System. *Chem Sci* **2013**, *4*, 3416–3420. https://doi.org/10.1039/C3SC51447A.

(18) An, Y.-L.; Yang, Z.-H.; Zhang, H.-H.; Zhao, S.-Y. Palladium-Catalyzed Tandem Regioselective Oxidative Coupling from Indoles and Maleimides: One-Pot Synthesis of Indolopyrrolocarbazoles and Related Indolylmaleimides. *Org Lett* **2016**, *18* , 152–155.

(19) Russell, H. F.; Harris, B. J.; Hood, D. B.; Thompson, E. G.; Watkins, A. D.; Williams, R. D. 5-Substituted Indoles via Sodium-Indoline-2-Sulfonate. A Reexamination.; 1986.

(20) Bollyn, M. Thermal Hazards of the Vilsmeier−Haack Reaction on N,N-Dimethylaniline. *Org Process Res Dev* **2005**, *9*, 982–996.

(21) Kuday, H. *İndol Halkasi İçeren Şalkonlara Katilma Reaksiyonlarinin İncelenmesi Doktora Tezi*.

(22) Davies, S. G.; Fletcher, A. M.; Roberts, P. M.; Smith, A. D. Asymmetric Synthesis of Sedum Alkaloids via Lithium Amide Conjugate Addition. *Tetrahedron* **2009**, *65* (49), 10192–10213.

(23) Cao, X.; Meng, L.; Li, Z.-H.; Mao, Y.; Lan, H.; Chen, L.; Fan, Y.; Yi, T. Large Red-Shifted Fluorescent Emission via Intermolecular π–π Stacking in 4-Ethynyl-1,8-Naphthalimide-Based Supramolecular Assemblies. *Langmuir* **2014**, *30*.

APPENDICES

A. NMR Spectra

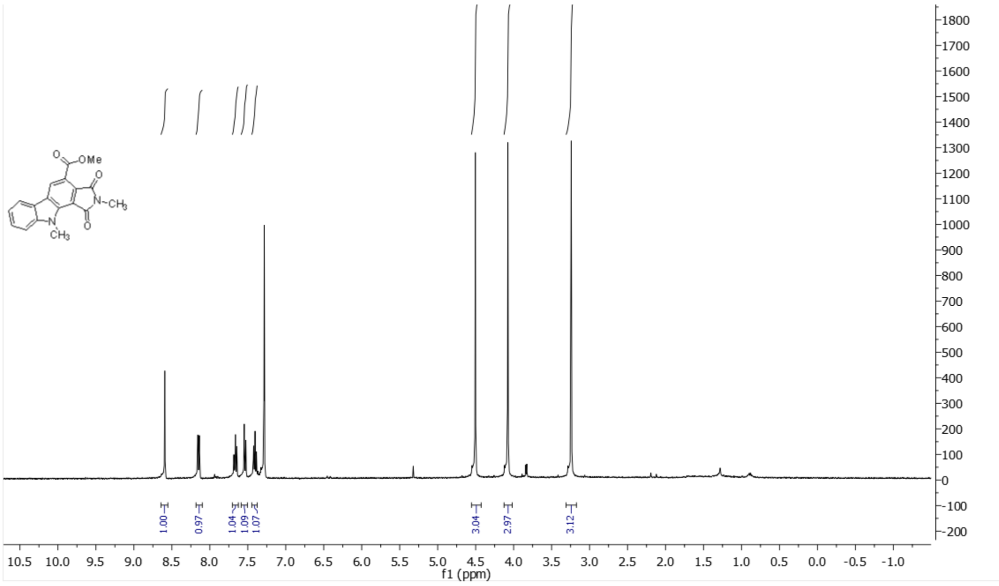


Figure 9. ^{1}H NMR Spectrum of compound **50**

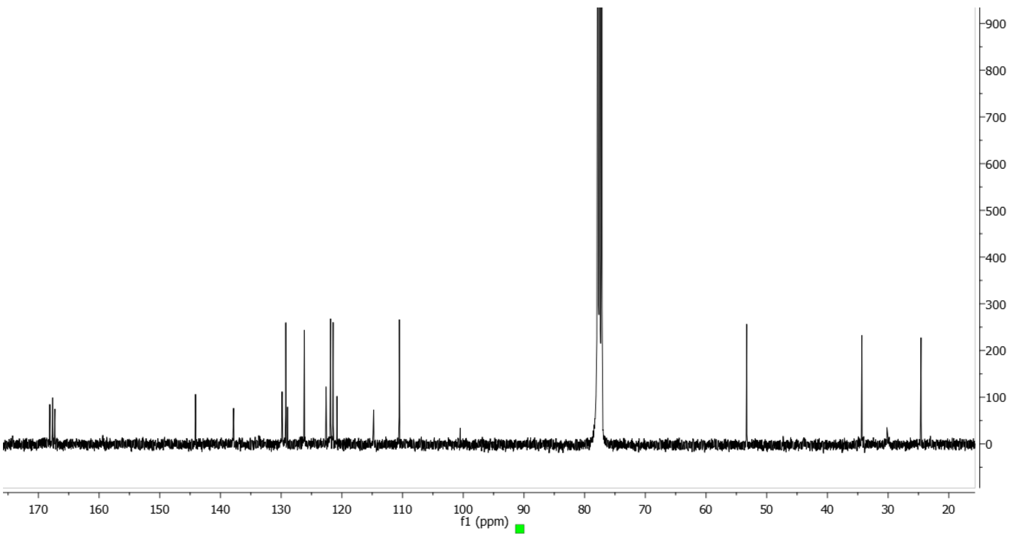


Figure 10. ^{13}C NMR Spectrum of compound **50**

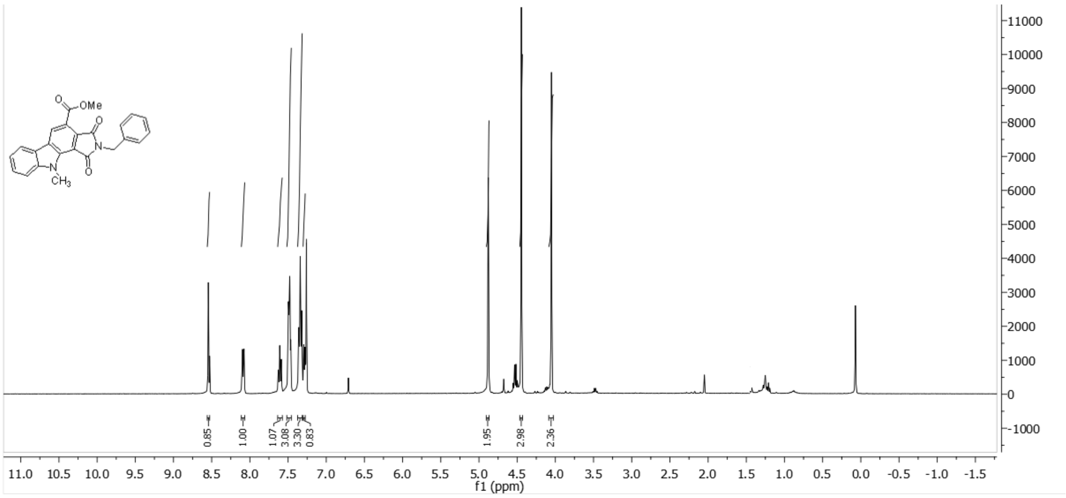


Figure 11. ^{1}H NMR Spectrum of compound **51**

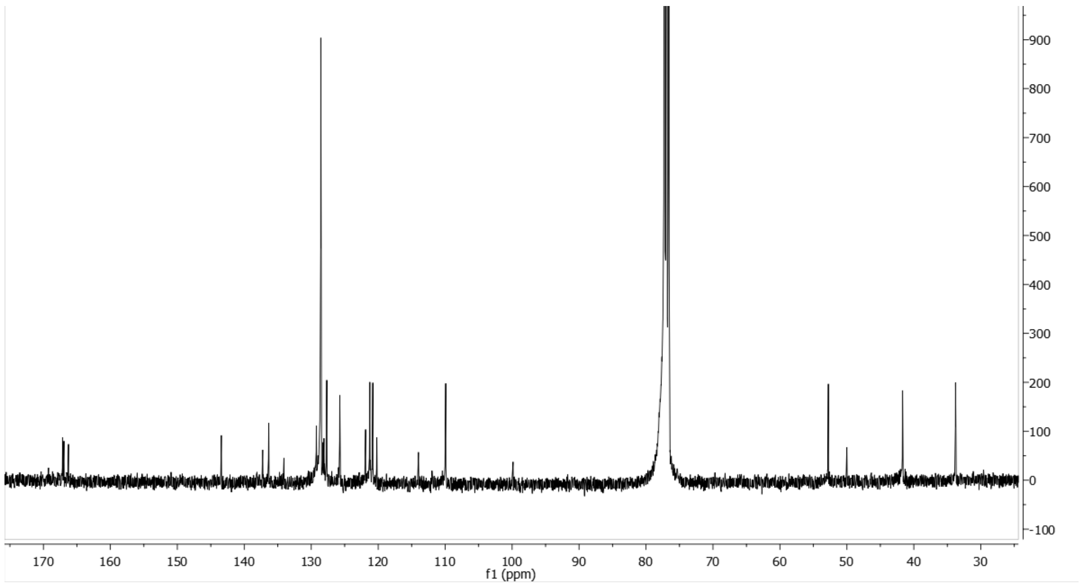


Figure 12. ^{13}C NMR Spectrum of compound **51**

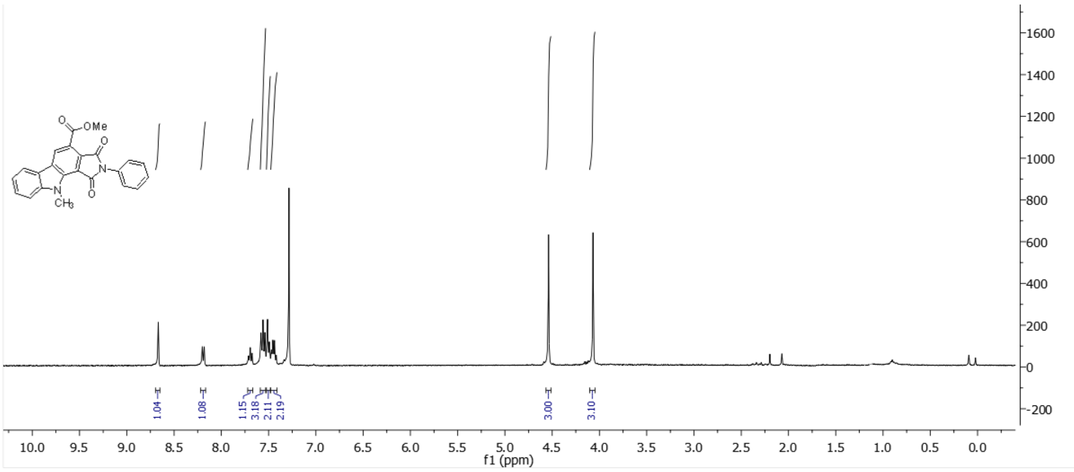


Figure 13. ^{1}H NMR Spectrum of compound 5**2**

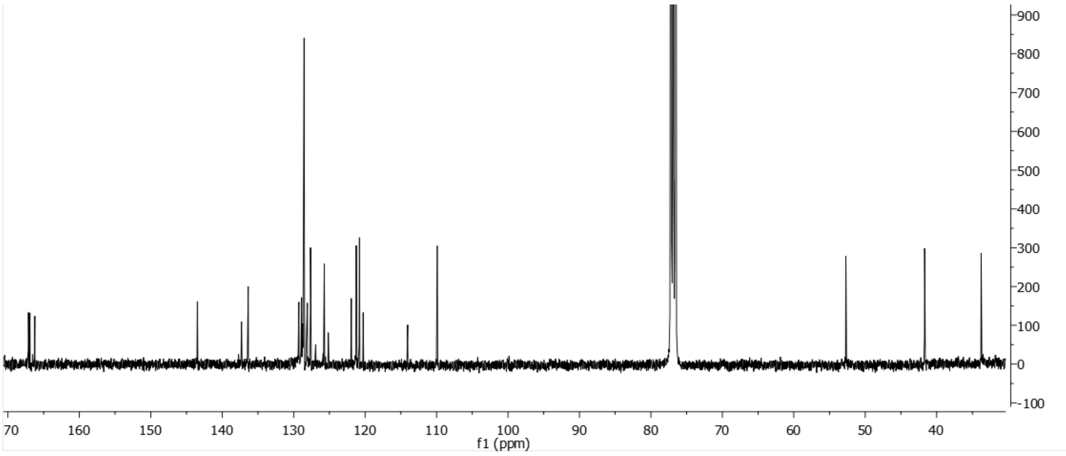


Figure 14. ^{13}C NMR Spectrum of compound **52**

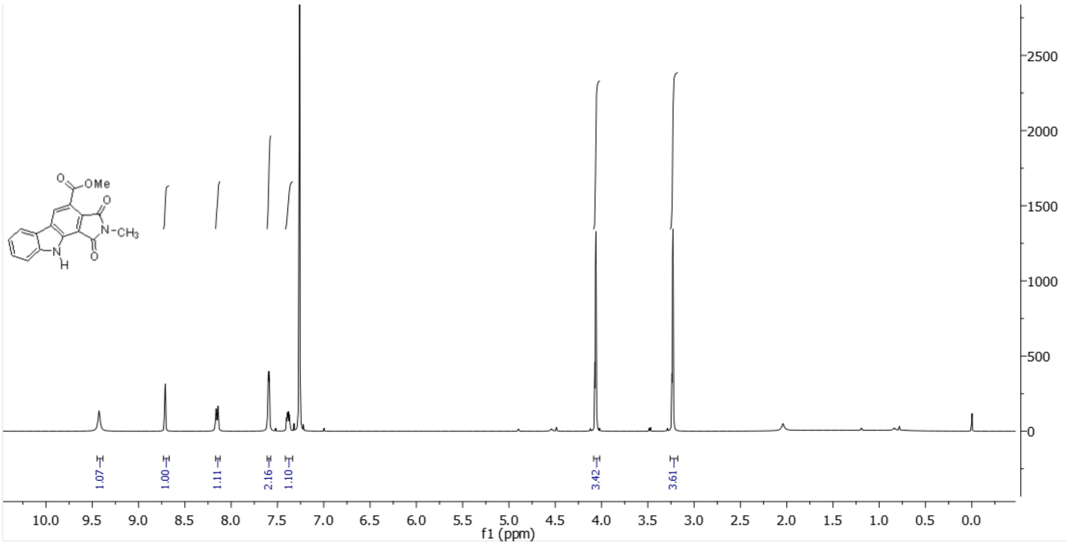


Figure 15. ^{1}H NMR Spectrum of compound **53**

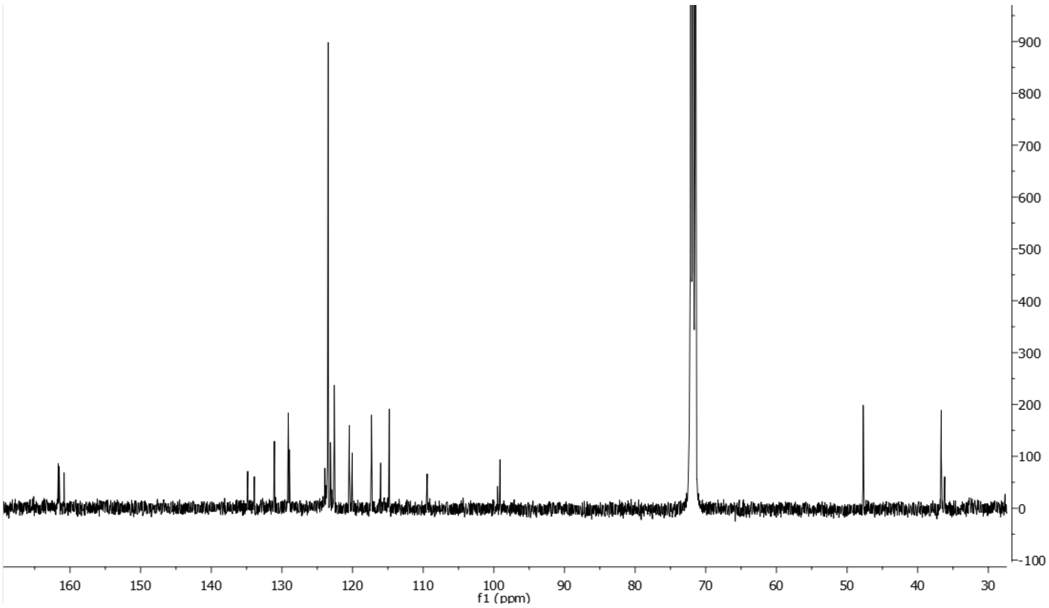


Figure 16. ^{13}C NMR Spectrum of compound **53**

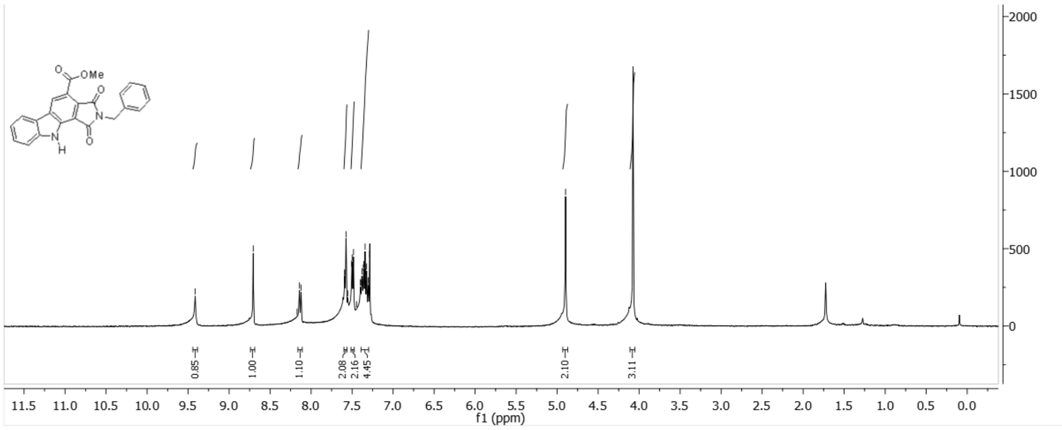


Figure 17. ^{1}H NMR Spectrum of compound **54**

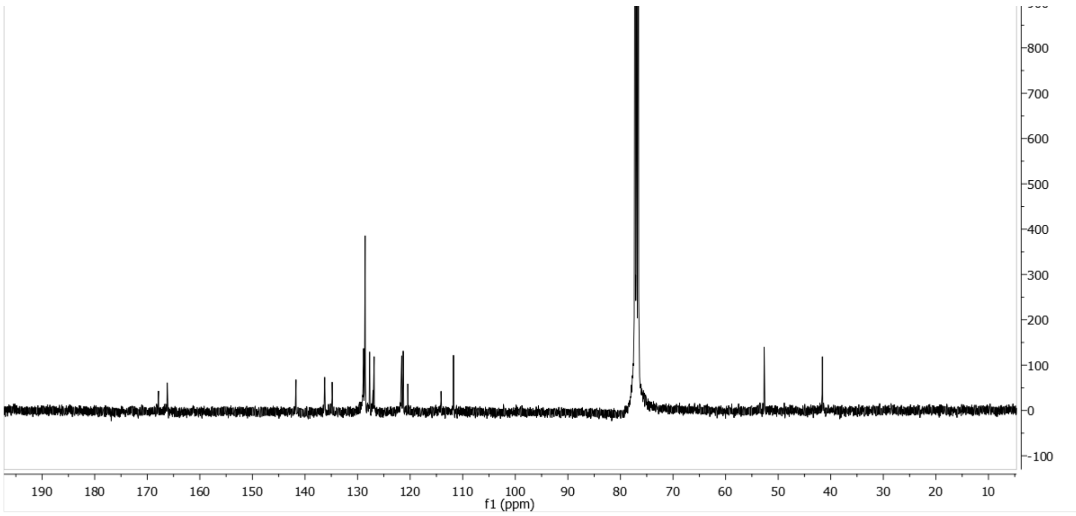


Figure 18. ^{13}C NMR Spectrum of compound **54**

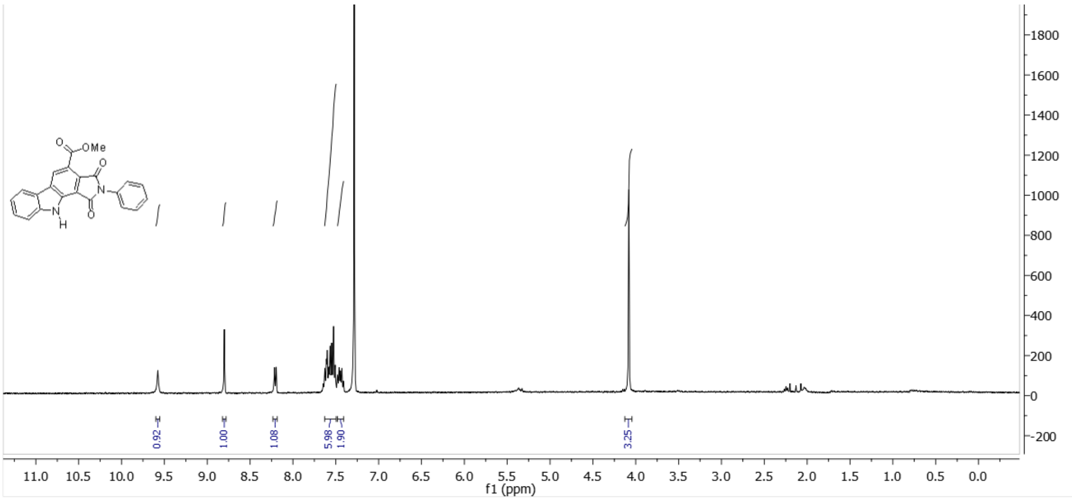


Figure 19. ^{1}H NMR Spectrum of compound **55**

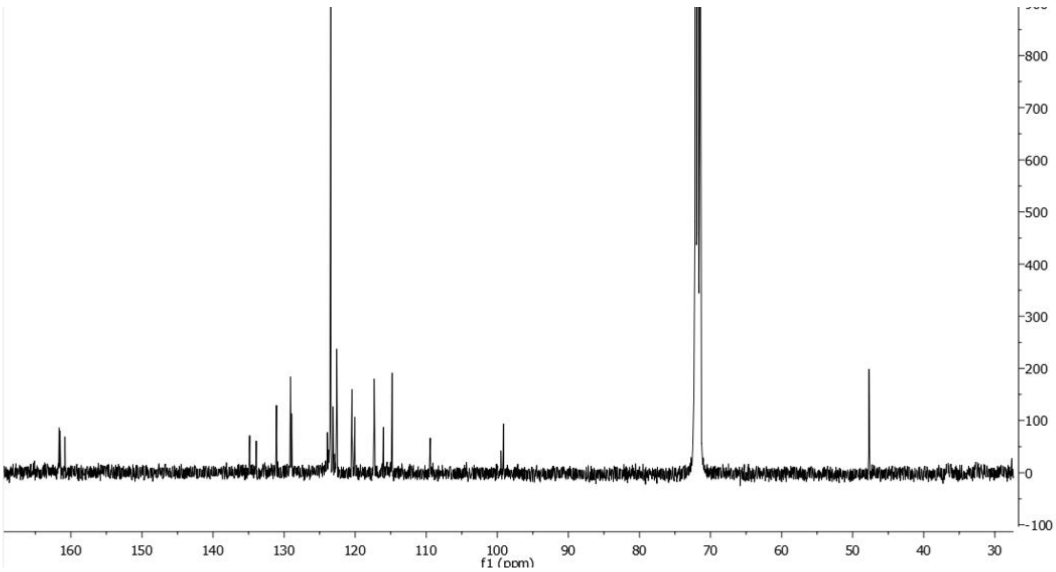


Figure 20. 13C NMR Spectrum of compound **55**

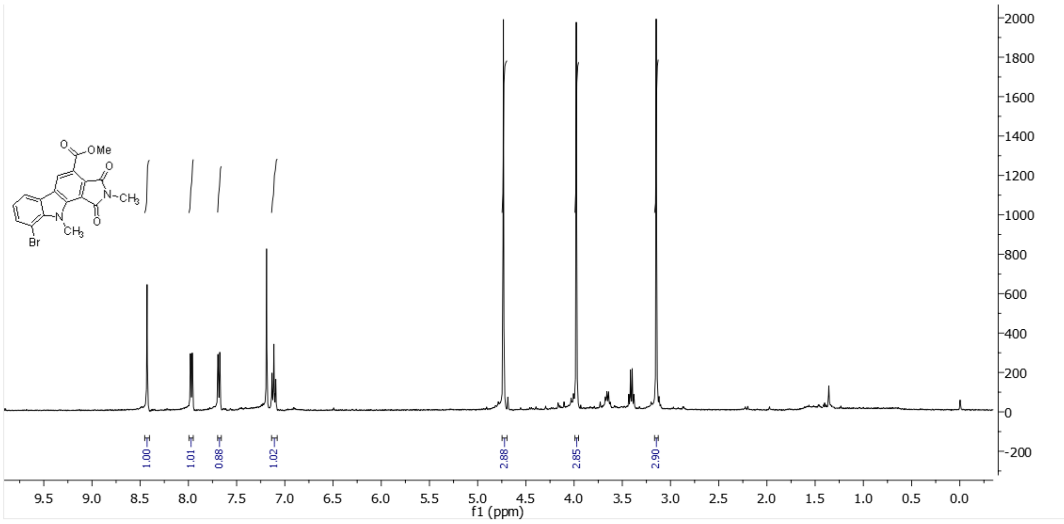


Figure 21. ^{1}H NMR Spectrum of compound **56**

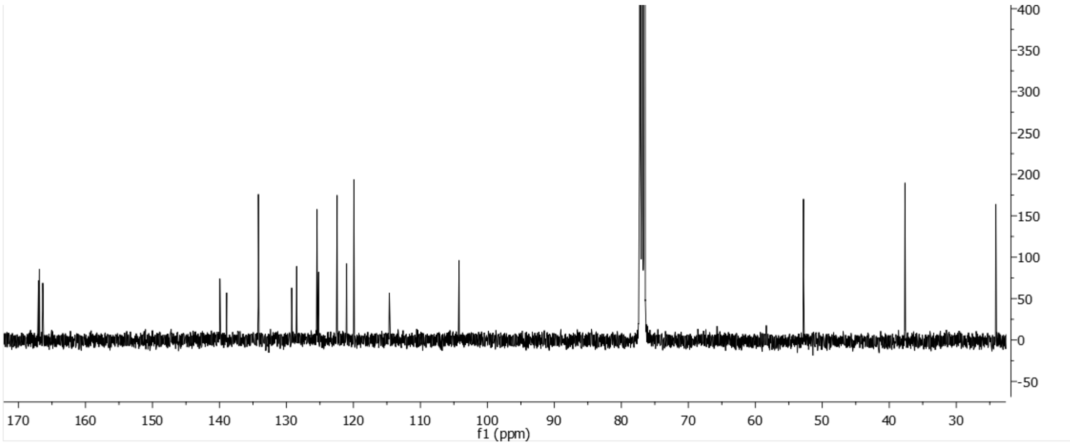


Figure 22. ^{13}C NMR Spectrum of compound **56**

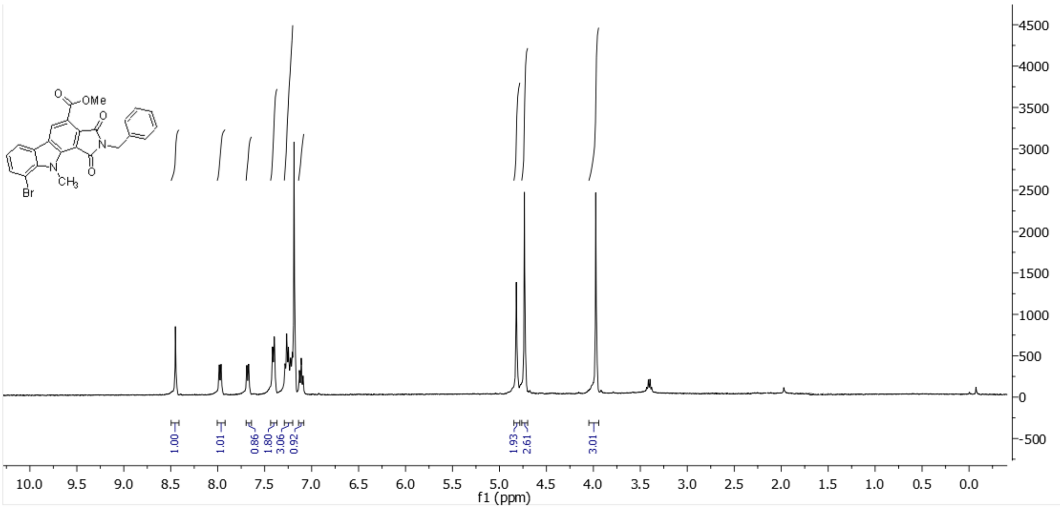


Figure 23. ^{1}H NMR Spectrum of compound **57**

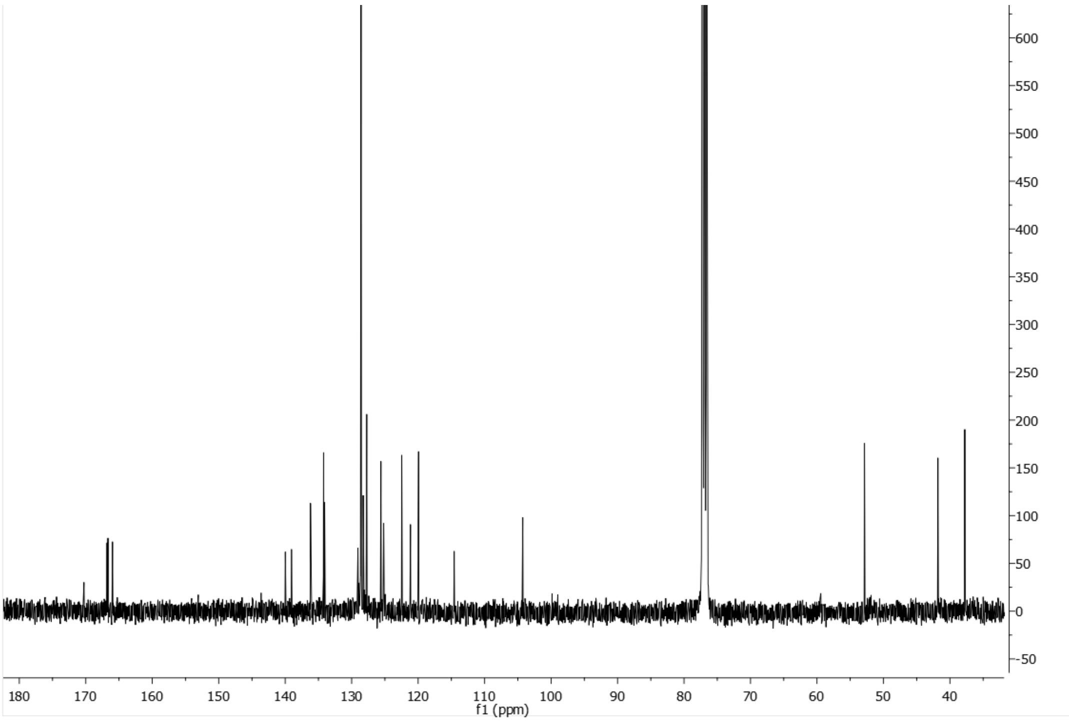


Figure 24. ^{13}C NMR Spectrum of compound **57**

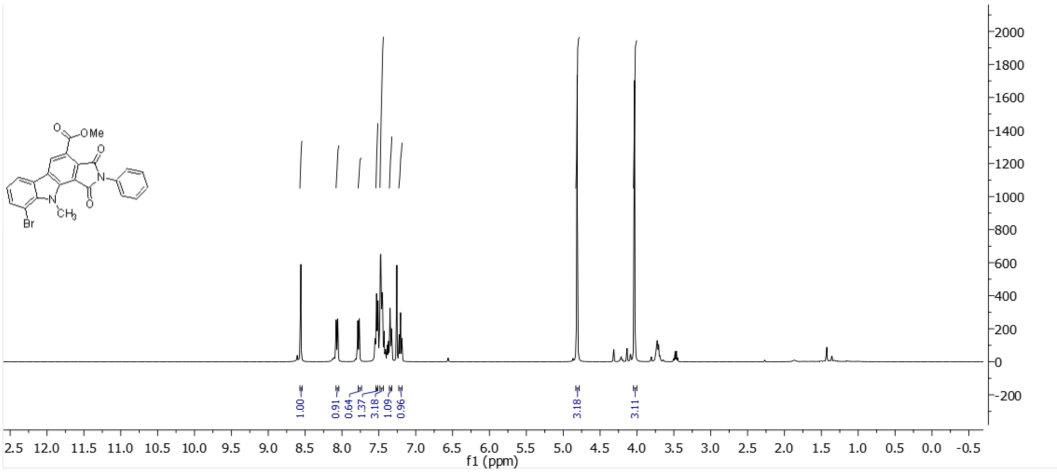


Figure 25. ^{1}H NMR Spectrum of compound **58**

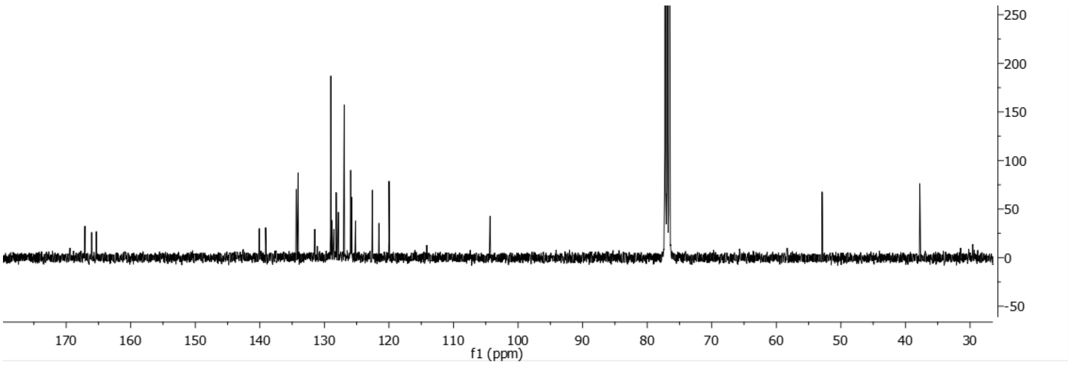


Figure 26. ^{13}C NMR Spectrum of compound **58**

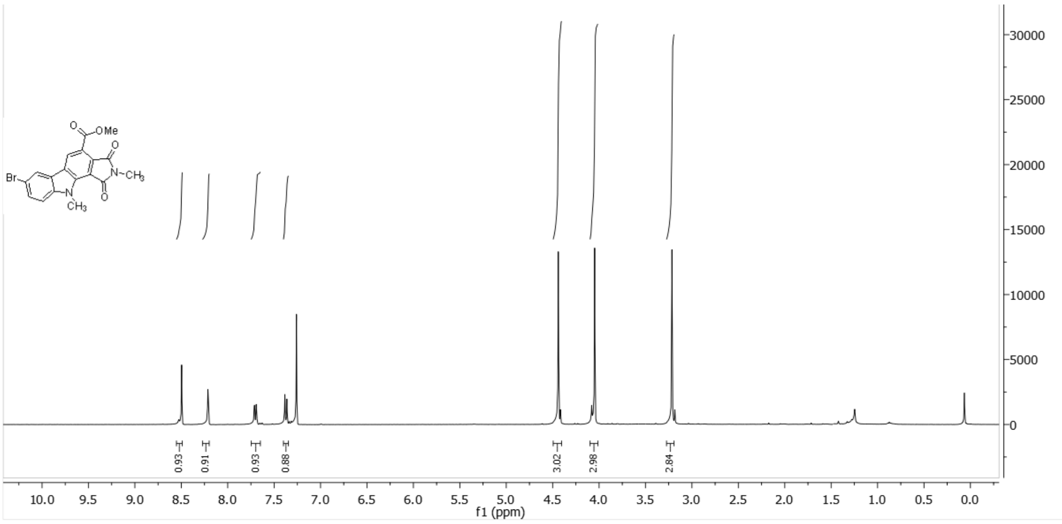


Figure 27. ^{1}H NMR Spectrum of compound **59**

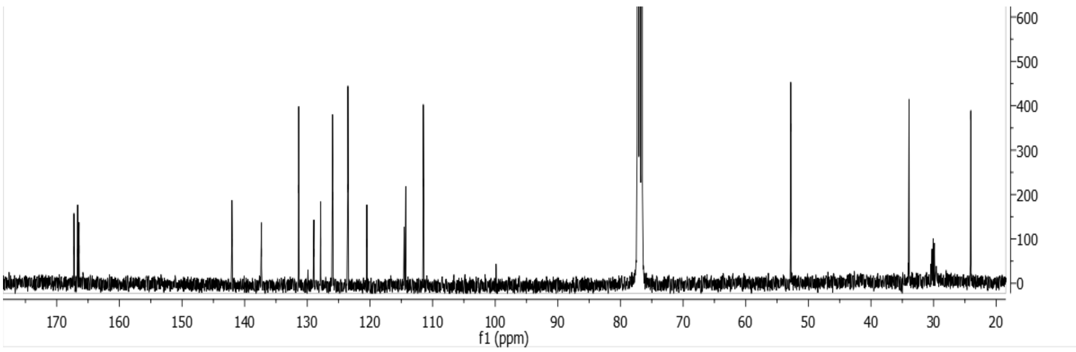


Figure 28. ^{13}C NMR Spectrum of compound **59**

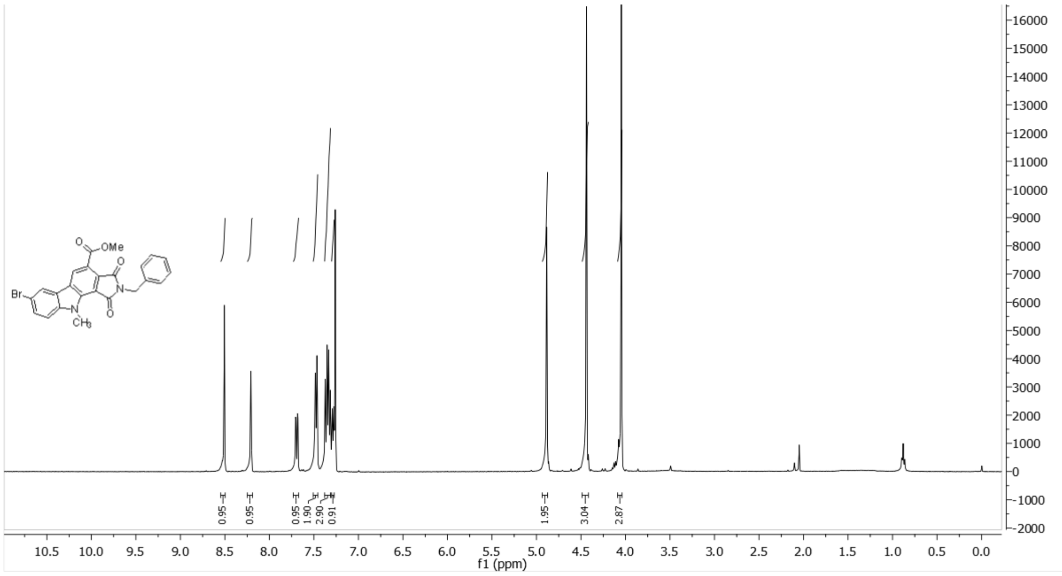


Figure 29. ^{1}H NMR Spectrum of compound **60**

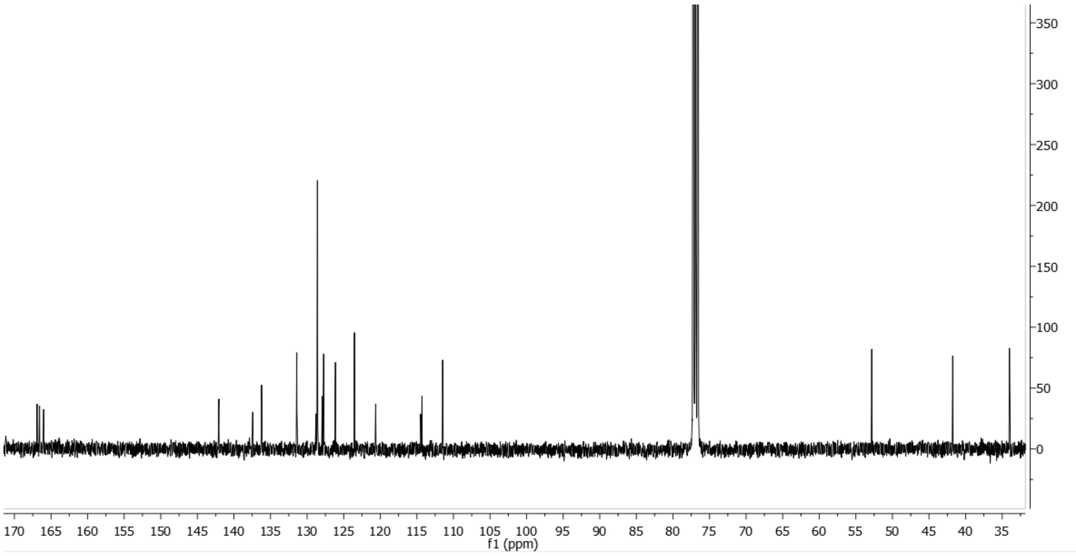


Figure 30. ^{13}C NMR Spectrum of compound **60**

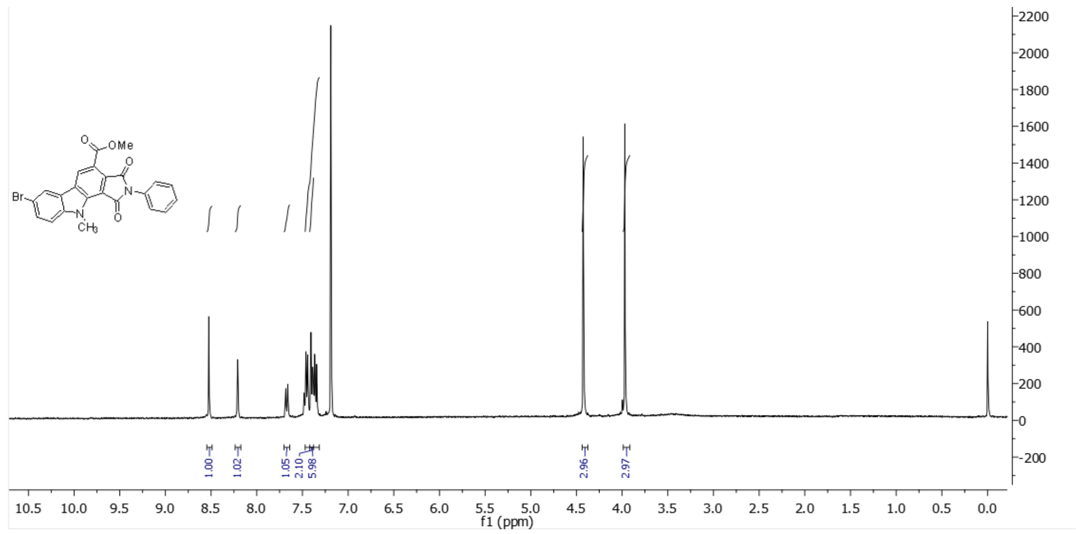


Figure 31. ^{1}H NMR Spectrum of compound **61**

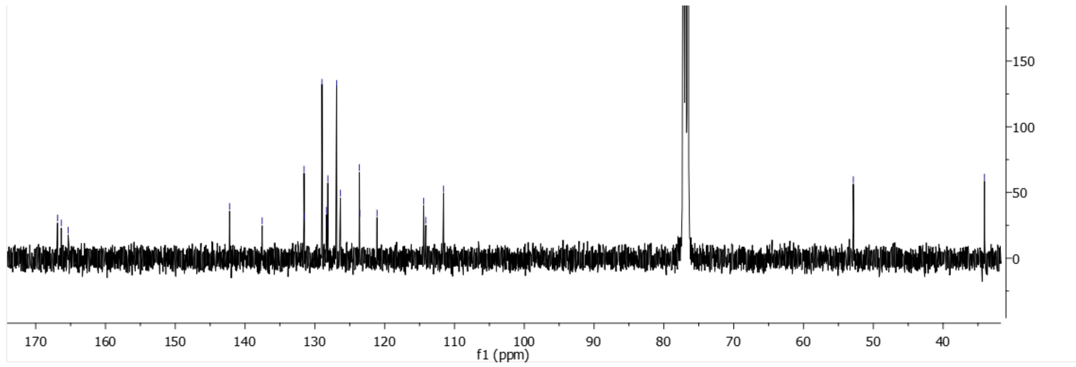


Figure 32. ^{13}C NMR Spectrum of compound **61**