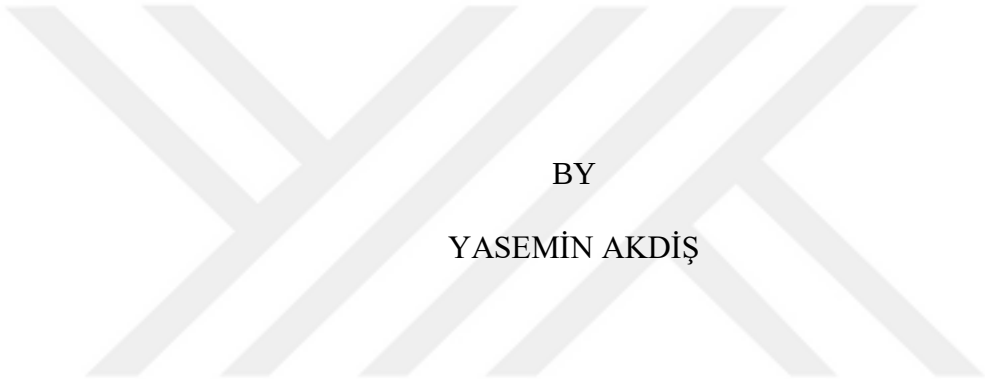


EFFECT OF PHOTOSWITCHABLE AZOBENZENE SIDE CHAIN ON
COUMARINS OPTICAL AND CHIROPTICAL BEHAVIOR

A THESIS SUBMITTED TO
THE GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES
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BY
YASEMİN AKDIŞ

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
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Approval of the thesis:

**EFFECT OF PHOTOSWITCHABLE AZOBENZENE SIDE CHAIN ON
COUMARINS OPTICAL AND CHIROPTICAL BEHAVIOR**

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ABSTRACT

EFFECT OF PHOTOSWITCHABLE AZOBENZENE SIDE CHAIN ON COUMARINS OPTICAL AND CHIROPTICAL BEHAVIOR

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Master of Science, Chemistry
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March 2025, 217 pages

The conformation/configuration of the side chain in coumarin derivatives significantly impacts their features and applications, making them versatile in various scientific and industrial fields. This versatility can be attributed to their capacity to modify chemical reactivity, binding interactions, pharmacological activity, stability, solubility, and material qualities. In this context, the objective of this study was to investigate the effect of a change in the conformation/configuration of the azobenzene-containing side chain of coumarin linked to 3rd and 7th positions. For this purpose, eight different compounds were synthesized. The fact that azobenzene derivatives can be irradiated with a specific wavelength of light to achieve photoisomerization from the *trans* to the *cis* form has allowed it to be used as a convenient and controllable side chain. To investigate the optical and chiroptical properties of the synthesized materials, we conducted a series of UV-Vis, fluorescence, and circular dichroism studies in various solvents, complemented by theoretical studies.

Keywords: Azobenzene, Coumarin, Chirality, Photoisomerization.



ÖZ

IŞIĞA DUYARLI AZOBENZEN YAN GRUBUNUN KUMARİNİN OPTİK VE KİROPTİK DAVRANIŞI ÜZERİNDEKİ ETKİSİ

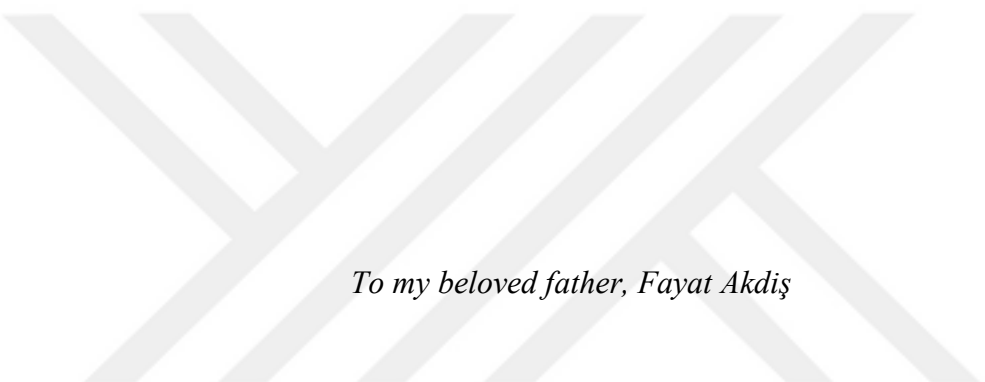
Akdiş, Yasemin
Yüksek Lisans, Kimya
Tez Yöneticisi: Prof. Dr. Akın Akdağ

Mart 2025, 217 sayfa

Kumarin türevlerindeki yan zincirin konformasyonu/konfigürasyonu; özellikleri ve uygulamaları üzerinde kapsamlı ve önemli bir etkiye sahiptir. Çeşitli bilimsel ve endüstriyel alanlardaki çok yönlülükleri; kimyasal reaktiviteyi, bağlanma etkileşimlerini, farmakolojik aktiviteyi, kararlılığı, çözünürlüğü ve malzeme niteliklerini değiştirme kapasitelerine dayandırılabilir. Bu kapsamda, kumarinin 3 veya 7 numaralı pozisyonlarına bağlı azobenzen içeren yan zincirinin konformasyon/konfigürasyon değişikliğinin etkisinin araştırılması amaçlanmıştır. Bu doğrultuda sekiz adet yeni bileşik sentezlenmiştir. Azobenzen türevlerinin belirli bir dalga boyundaki ışığa maruziyeti sonucu *trans* formundan *cis* formuna fotoisomerizasyonun sağlanabilir oluşu, onu kullanışlı ve kontrol edilebilir bir yan zincir olarak kullanmaya olanak sağlamıştır. Bu bağlamda sentezlenmiş olan maddelerin UV-Vis, floresans ve dairesel dikroizm spektroskopisi çalışmaları yapılarak optik ve kiroptik özellikleri incelenmiş ve bu incelemeler teorik çalışmalarla da desteklenmiştir.

Anahtar Kelimeler: Azobenzen, Kumarin, Kiralite, Fotoizomerizasyon.





To my beloved father, Fayat Akdiş

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Festina lente... Science requires patience and care. However, it is not always easy to show this patience and care consistently. Luckily, I have always been surrounded by people who have helped me maintain this throughout this process because my master's journey coincided with one of the most challenging periods of my life, pushing me to grow both intellectually and emotionally. This instructive experience will leave a valuable and lasting impression.

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TABLE OF CONTENTS

ABSTRACT	v
ÖZ	vii
ACKNOWLEDGMENTS.....	x
TABLE OF CONTENTS.....	xii
LIST OF TABLES.....	xvi
LIST OF SCHEMES	xvii
LIST OF FIGURES	xix
LIST OF ABBREVIATIONS	xxi
CHAPTERS	
1 INTRODUCTION.....	1
1.1 Azobenzene	1
1.1.1 Historical Perspective	1
1.1.2 Structural Features and Chemical Properties	2
1.1.3 Photochemistry and Isomerization of Azobenzenes.....	4
1.1.4 Spectroscopic Signatures For Characterization.....	8
1.1.5 Synthesis of Azobenzene	9
1.1.6 Applications	14
1.2 Coumarin.....	22
1.2.1 Introduction to Coumarin and its Derivatives	22
1.2.2 Synthesis of Coumarin Derivatives	23
1.2.3 Fluorescence and UV-Vis Properties of Coumarin	25
1.2.4 Applications of Coumarin Derivatives	27
1.3 Polarized Light and Circular Dichroism	28

1.3.1	Polarized Light	28
1.3.2	Circularly Polarized Light and Circular Dichroism Spectroscopy...	30
1.4	Chirality	32
1.4.1	Discovery of Concept of Chirality and Chirality Types	32
1.4.2	Chirality Transfer and Chirality Induction	36
2	AIM OF THE STUDY	41
3	RESULTS AND DISCUSSION	43
3.1	Synthesis	43
3.1.1	Synthesis of Azobenzene Cores	43
3.1.2	Synthesis of Coumarin Units and Coupling with Azobenzene Cores	46
3.2	Photophysical Studies	54
3.2.1	UV-Vis and Fluorescence Studies	55
3.3	Computational Studies	67
3.4	Circular Dichroism Studies	76
3.5	Calculated CD Spectrum.....	79
4	CONCLUSIONS.....	81
5	EXPERIMENTAL	83
5.1	General Information.....	83
5.2	Synthesis of Compounds.....	85
5.2.1	Synthesis of (<i>E</i>)-4-(phenyldiazenyl)phenol	85
5.2.2	Synthesis of <i>E</i> -3-(4-(phenyldiazenyl)phenoxy)propan-1-ol.....	86
5.2.3	Synthesis of <i>E</i> -3-(4-(phenyldiazenyl)phenoxy)octan-1-ol	86

5.2.4	Synthesis of (<i>E</i>)-3-(4-(phenyldiazenyl)phenoxy)propyl 4-methylbenzenesulfonate.....	87
5.2.5	Synthesis of (<i>E</i>)-8-(4-(phenyldiazenyl)phenoxy)octyl 4-methylbenzenesulfonate.....	88
5.2.6	Synthesis of ethyl 7-hydroxy-2-oxo-2 <i>H</i> -chromene-3-carboxylate ...	89
5.2.7	Synthesis of AzoCoum-1a	90
5.2.8	Synthesis of AzoCoum-1b	91
5.2.9	Synthesis of 7-butoxy-2-oxo-2 <i>H</i> -chromene-3-carboxylic acid	92
5.2.10	Synthesis of AzoCoum-2a	93
5.2.11	Synthesis of AzoCoum-2b	94
5.2.12	Synthesis of 7-(diethylamino)-2-oxo-2 <i>H</i> -chromene-3-carboxylic acid	95
5.2.13	Synthesis of AzoCoum-3a	96
5.2.14	Synthesis of AzoCoum-3b	97
5.2.15	Synthesis of AzoCoum-1a'	98
5.2.16	Synthesis of ((3 <i>aR</i> ,4 <i>R</i> ,6 <i>R</i> ,6 <i>aR</i>)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4- <i>d</i>][1,3]dioxol-4-yl)methanol	99
5.2.17	Synthesis of AzoCoumR-1	99
5.2.18	Synthesis of ((3 <i>aS</i> ,4 <i>S</i> ,6 <i>S</i> ,6 <i>aS</i>)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4- <i>d</i>][1,3]dioxol-4-yl)methyl 4-methylbenzenesulfonate	101
5.2.19	Synthesis of Ethyl 7-(((3 <i>aR</i> ,4 <i>R</i> ,6 <i>R</i> ,6 <i>aR</i>)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4- <i>d</i>][1,3]dioxol-4-yl)methoxy)-2-oxo-2 <i>H</i> -chromene-3-carboxylate	102
5.2.20	Synthesis of AzoCoumR-2	103

REFERENCES	105
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APPENDICES

A.	NMR Spectra.....	115
B.	Infrared (IR) Spectra.....	147
C.	High Resolution Mass Spectra (HRMS).....	155
D.	UV-Vis Spectra	161
E.	Fluorescence Spectra	173
F.	Circular Dichroism (CD) Spectra.....	185
G.	XYZ Coordinates of Optimized Structures.....	187

LIST OF TABLES

TABLES

Table 3.1 Transitions with their oscillator strengths for calculated wavelengths ...72

Table 3.2 Rotatory strengths of **AzoCoumR-1** and **AzoCoumR-2** at calculated wavelengths 80



LIST OF SCHEMES

SCHEMES

Scheme 1.1. <i>E</i> and <i>Z</i> form of azobenzene molecule.....	4
Scheme 1.2. Proposed mechanisms for isomerization of azobenzene	7
Scheme 1.3. Proposed mechanism for diazotization and coupling	10
Scheme 1.4. Proposed mechanism for Wallach Rearrangement.....	11
Scheme 1.5. A general representative example of Mills Reaction.....	12
Scheme 1.6. A general representation of reduction of aromatic nitro derivatives for azobenzene synthesis	13
Scheme 1.7. A general representation of oxidation of amino compounds for azobenzene synthesis	14
Scheme 1.8. Proposed binding mode of azobenzene containing chemosensor with Al ⁺³	15
Scheme 1.9. Representation of FraC derivatized azobenzene containing peptides	19
Scheme 1.10. Various methods of coumarin synthesis	25
Scheme 3.1. Synthesis of 4-hydroxyazobenzene	43
Scheme 3.2. Synthesis of compounds 2 and 3	44
Scheme 3.3. Synthesis of compounds 4 and 5	45
Scheme 3.4. Synthesis of compound 6	46
Scheme 3.5. Synthesis of AzoCoum-1a and AzoCoum-1b	47
Scheme 3.6. Synthesis of compound 7	48
Scheme 3.7. Synthesis of AzoCoum-2a and AzoCoum-2b	49
Scheme 3.8. Synthesis of compound 8	50
Scheme 3.9. Synthesis of AzoCoum-3a and AzoCoum-3b	51
Scheme 3.10. Synthesis of AzoCoum-1a'	51
Scheme 3.11. Synthesis of compound 9	52
Scheme 3.12. Synthesis of AzoCoumR-1	53

Scheme 3.13. Synthesis of compound 10 and 11	53
Scheme 3.14. Synthesis of AzoCounR-2	54



LIST OF FIGURES

FIGURES

Figure 1.1. Azobenzene	1
Figure 1.2 Aniline Yellow and Bismarck Brown	2
Figure 1.3. Excitation transitions of azobenzene	6
Figure 1.4. Azopolymer unit that used for CO ₂ seperation.....	16
Figure 1.5. Structures of some azobenzene derivatives restoring vision loss	18
Figure 1.6. Chemical structure of azopolymer that gained chiral memory (R)-(+)- Limonene and (S)-(-)-Limonene	21
Figure 1.7. Coumarin	22
Figure 1.8. Examples of some coumarin derivatives.....	23
Figure 1.9. Examples of some coumarin-based medicines.....	28
Figure 1.10. The three main forms of polarized light.....	29
Figure 1.11. Illustration of CD spectroscopy instrumentation	32
Figure 1.12. Chemical structure of enantiomers of tartaric acid and hemihedral crystals of double sodium-ammonium tartrates	33
Figure 1.13 Structural examples of types of chiralies	35
Figure 1.14. Representation of chirality induction	38
Figure 3.1. UV-Vis spectra of compound 2 and 7 in DCM.....	56
Figure 3.2. UV-Vis spectra of aliphatic azo-alcohol (compound 2) upon irradiation in DCM	57
Figure 3.3. UV-Vis and fluorescence spectra of AzoCoun-1a in DCM.....	58
Figure 3.4. UV-Vis and fluorescence spectra of AzoCoun-1b in DCM.....	60
Figure 3.5. UV-Vis and fluorescence spectra of AzoCoun-2a in DCM.....	60
Figure 3.6. UV-Vis and fluorescence spectra of AzoCoun-2b in DCM.....	61
Figure 3.7. UV-Vis spectra of AzoCoun-3a and AzoCoun-3b in DCM.....	63
Figure 3.8. Fluorescence spectra of AzoCoun-3a and AzoCoun-3b in DCM.....	63
Figure 3.9. UV-Vis and fluorescence spectra of AzoCounR-1 in DCM	65
Figure 3.10. UV-Vis and fluorescence spectra of AzoCounR-2 in DCM	66

Figure 3.11. Frontier molecular orbitals of <i>trans</i>-AzoCoum-1a	68
Figure 3.12. Frontier molecular orbitals of <i>trans</i>-AzoCoum-2a	68
Figure 3.13. Frontier molecular orbitals of <i>cis</i>-AzoCoum-1a	69
Figure 3.14. Frontier molecular orbitals of <i>cis</i>-AzoCoum-2a	70
Figure 3.15. Frontier molecular orbitals of <i>trans</i>-AzoCoum-3a	71
Figure 3.16. Frontier molecular orbitals of <i>cis</i>-AzoCoum-3a	71
Figure 3.17. Frontier molecular orbitals of <i>trans</i>-AzoCoumR-1	74
Figure 3.18 Frontier molecular orbitals of <i>cis</i>-AzoCoumR-1	74
Figure 3.19. Frontier molecular orbitals of <i>trans</i>-AzoCoumR-2	75
Figure 3.20. Frontier molecular orbitals of <i>cis</i>-AzoCoumR-2	75
Figure 3.21. CD spectra of AzoCoumR-1 and AzoCoumR-2 in different solvents	76
Figure 3.22. CD spectra of AzoCoumR-1 in DCM and THF upon irradiation.....	77
Figure 3.23. CD spectra of AzoCoumR-2 in DCM and THF upon irradiation.....	78

LIST OF ABBREVIATIONS

ABBREVIATIONS

CD	Circular Dichroism
CPL	Circularly Polarized Light
EPL	Elliptically Polarized Light
FTIR	Fourier Transform Infrared
NMR	Nuclear Magnetic Resonance
HRMS	High Resolution Mass Spectrometry
EDC.HCl	1-ethyl 3-(3-dimethylaminopropyl)carbodiimide hydrochloride

CHAPTER 1

INTRODUCTION

1.1 Azobenzene

1.1.1 Historical Perspective

Azobenzene, which made a breakthrough with its discovery at the beginning of the nineteenth century and paved the way for many new studies, is still an interesting subject of research (Figure 1.1). This substance, which was named after the double bonded nitrogen atoms ($-N=N-$) that provide its characteristic properties, entered the world of chemical science with Mysterlich's reduction of nitrobenzene in 1834.¹ It immediately took its place as the first azo-dyes of its time, and with its vivid and bright colours that make it interesting, it maintained its popularity as a synthetic dye in the industry from the end of the 19th century to the beginning of the 20th century. Some examples of azo- dyes used at the time are shown in Figure 1.2.²

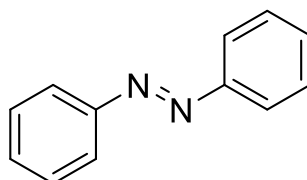


Figure 1.1. Azobenzene

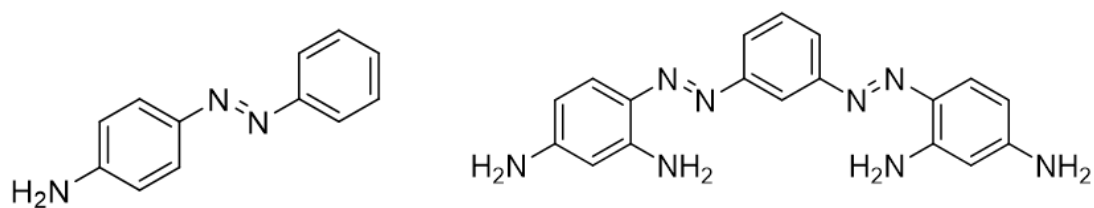


Figure 1.2 Aniline Yellow and Bismarck Brown

1.1.2 Structural Features and Chemical Properties

Azobenzene itself is essentially a molecule consisting of two nitrogen atoms ($N=N$) linked by a double bond bridging two phenyl rings. The term “azo” or “azobenzene”, on the other hand, covers the naming of a wide range of compounds. In the literature, they are referred to as “diazenes”. According to Rau's categorization, azobenzene-containing compounds fall into three classes: azobenzene-type molecules, aminoazobenzene-type molecules and pseudostilbenes.³ Despite having many properties in common with stilbenes, azobenzene also has other properties that make it superior in many ways when it comes to photoswitching. To explain, the *cis* and *trans* absorption spectra of the molecules of the two categories of substances, azobenzene and aminoazobenzene, do not overlap, requiring the use of different wavelengths for the transition between the *trans*-*cis* states. This is not the case for the pseudo-stilbene class, which is revealed by the overlap of the absorption spectra for the *cis* and *trans* configurations of the molecules of this substance.⁴ This difference leads azobenzenes to be known better as a photo-switch.

Groups linked by a diazo bond also have an effect on the properties of the azobenzene derivative. Those containing aryl groups are classified as aromatic, while those containing alkyl groups belong to the aliphatic group. Naturally, these structural differences cause the substances to have completely different properties.⁵

Aromatic azo derivatives contain two or more aromatic rings linked together by one or more azo linkages. A considerable number of these compounds exhibit bright colors because they have the capacity to absorb visible light (400-700 nm). A wide range of spectral colors can be obtained by adjusting the overall composition of the molecular structures by design variations such as the identification of different aromatic rings, the presence of electron-donating or electron-accepting groups, and the modification of the conjugation.⁶

The formation of a typical aromatic azo core is the result of the conjunction of two or more aromatic rings, which are linked by two nitrogen atoms that are sp^2 hybridized and linked by double bond (N=N). The light-absorbing properties of these stiff structures have led them to be called azo-chromophores. The ability of azo groups to form covalent bonds with rings has been exploited in various studies, ranging from benzene and naphthalene derivatives to heterocyclics and other aromatic rings. The convenience of azo linkage formation has additionally permitted the formation of multiple azo bonds within a single molecule, thereby influencing the nomenclature of compounds with multiple azo linkages. Depending on the number of azo bonds they contain, these compounds can be called mono-, di-, tri-, or tetra-azo.⁶ The azo bonded rings can have a variety of substituents, which can also be incorporated later and used to impart certain properties to the substance.

When at least one side of the azo group is attached to an alkyl group, these substances are classified as “aliphatic azo compounds”. This group of compounds, which have considerable differences from their aromatic counterparts, are often unstable because the stabilizing effect of conjugation is absent here.⁷ It is notable, however, that these compounds possess a diverse range of applications, particularly in the field of polymer research and industrial production.⁸

Azobenzene and its derivatives are compounds with such high thermal resilience and resistance to high temperatures that these properties enable them to be used in materials resistant to high temperatures.⁷ This stability is attributed to the hybridization of the carbon atom attached to the azo group in aromatic azo

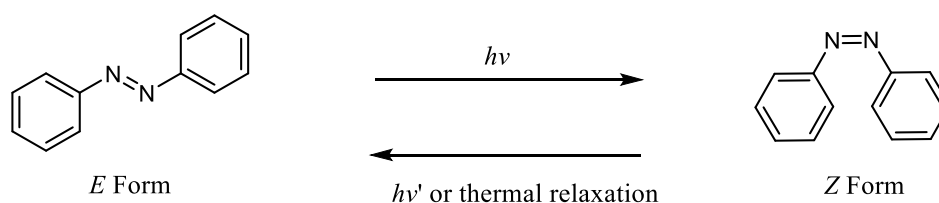
compounds. The fact that both nitrogen atoms have sp^2 hybridization leads to a conjugation that reduces the total energy of the molecule and provides stability. However, these azo compounds can also be degraded by several different mechanisms. These heterolytic or homolytic processes can be triggered photochemically, enzymatically or thermally.⁹

1.1.3 Photochemistry and Isomerization of Azobenzenes

Isomerization entails a chemical transformation of a compound into one of its isomeric forms. Although isomeric forms have the same molecular composition, they have different structural or configurational properties, which consequently result in the acquisition of disparate physical and chemical properties. Photoisomerization is an isomerization process initiated by exposure to light.

Hartley's pioneering observations of the *trans-cis* photoisomerization of azobenzene have been the subject of extensive research by numerous scientific investigators. Hartley's findings revealed that both the forward and reverse isomerization reactions of azobenzene are stimulated by light, while the thermal reaction occurs at a remarkably slow rate.⁵

Azobenzenes undergo a geometric isomerization, a photochromic reaction that is regarded as reversible *E-Z* isomerization.



Scheme 1.1. *E* and *Z* form of azobenzene molecule

In general, the *E* isomer is thermodynamically more stable than the *Z* isomer, although the opposite is true for diazocines. In addition, this photoisomerization is so fast that it occurs on a timescale of only hundreds of femtoseconds to picoseconds.¹¹

Exposure of *trans*-azobenzene to light between 320 and 380 nm is known to yield *trans-cis* isomerization, whereas exposure of the *cis* isomer between 400 and 450 nm has been observed to promote *cis-trans* isomerization. By irradiation with light of a specific wavelength, it is possible to control the configuration of each of the *trans-cis* photostable states.¹²

Trans-azobenzene displays an n- π^* transition band at 440 nm and a π - π^* transition band at 314 nm, while *cis*-azobenzene displays an n- π^* transition band at 430 nm and a π - π^* transition band at 280 nm.⁵ These bands appear with different intensities for each isomer.⁷ This is attributed to selection rules¹³ since most theoretical studies and ab initio calculations show that the planar structure with C_{2h} symmetry is the most stable structure of *trans*-azobenzene whereas *cis*-azobenzene exhibits a non-planar conformation with C₂ symmetry, consistent with the fact that the n- π^* transition is symmetry forbidden for the *trans* isomer, while this is not the case for the *cis* isomer.^{14,15} It should also be pointed out that groups on the phenyl rings also have an effect on the absorption intensity of azobenzene compounds.

In azobenzene, *trans-cis* isomerization occurs with S₀-S₁ and S₀-S₂ excitation, whereas the *cis-trans* isomerization process can be observed with excitation to the S₁ or S₂ state (Figure 1.3).^{16,17}

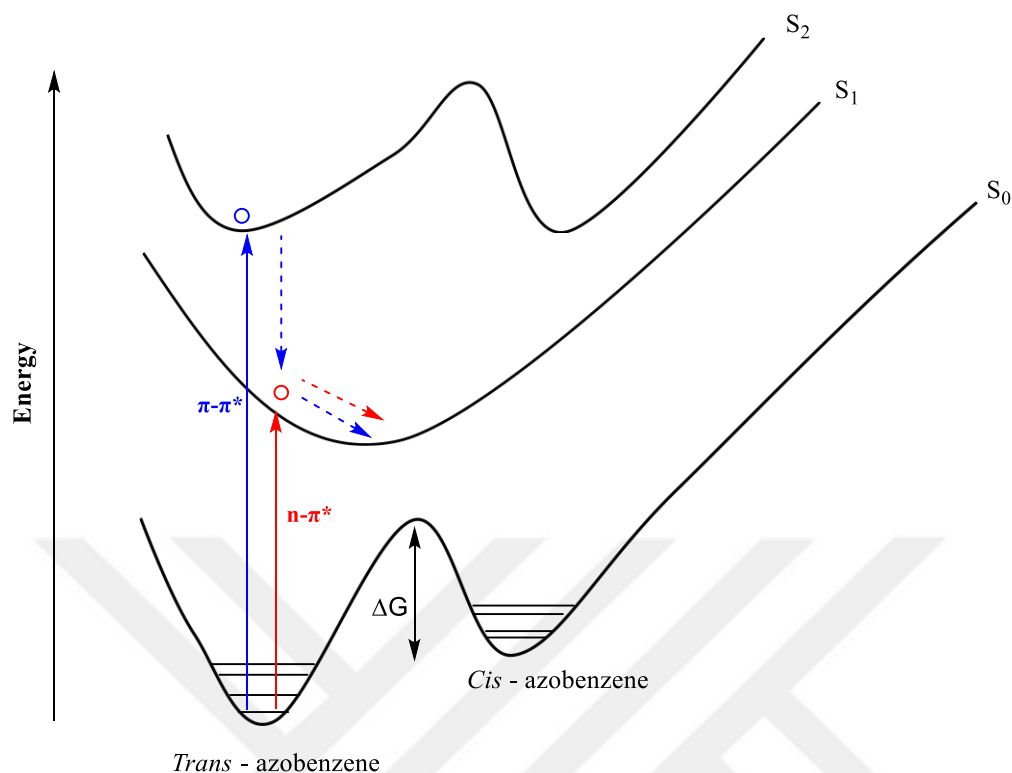
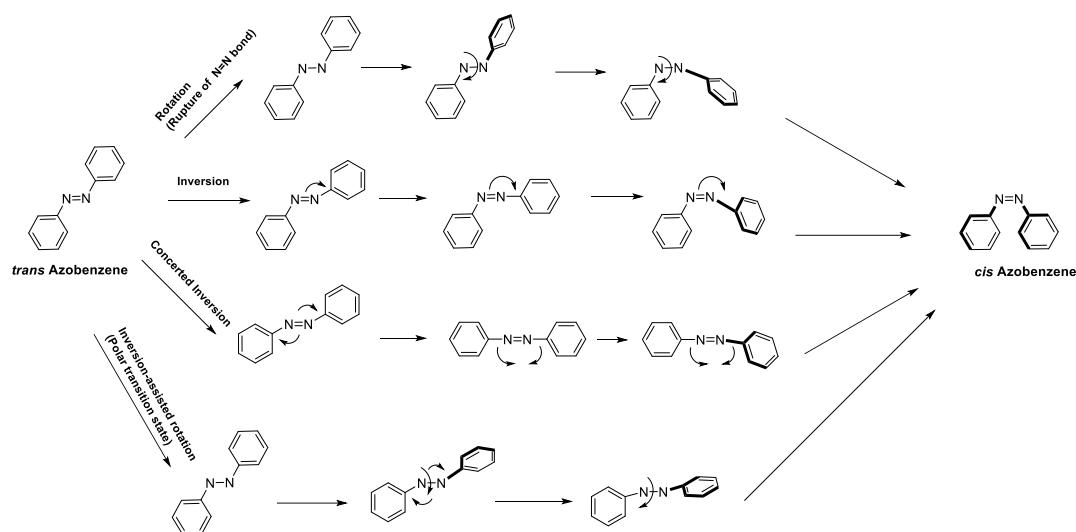


Figure 1.3 Excitation transitions of azobenzene

However, the combined quantum yield of these processes is found to deviate from unity, which is a proof for existence of more than one pathway for isomerization. In contrast, stilbene, the carbon analogue of azobenzene, exhibits isomerization solely through rotation, with a quantum yield of 1 for both transformations.¹⁸ Despite extensive research on azobenzene isomerization, the underlying mechanism remains a topic of ongoing investigation. The lack of scientific consensus on the mechanism of this photoisomerization is attributed to the thermal instability of the *cis* form and the difficulty of isolating it. Currently proposed mechanisms include rotation, inversion, concerted inversion, and inversion-assisted rotation (Scheme 1.2).¹¹ In conclusion, the mechanism of isomerization of azobenzene remains a subject of debate, with no consensus having been reached.



Scheme 1.2. Proposed mechanisms for isomerization of azobenzene

*(Curved arrows represent rotational motions.)

In a study conducted by Crecca and Roitberg,¹⁹ the impact of substituents on the isomerization of azobenzene was examined. In this study, the authors analyzed three-dimensional potential energy surfaces for both the ground state (S_0) and the excited state (S_1) using ab initio methods, thereby determining the relevant energy barriers. In azobenzene molecules following the inversion pathway, it was observed that the introduction of electron-donating groups resulted in an increase in the isomerization barrier, while the incorporation of electron-withdrawing groups led to a reduction in this barrier. This study revealed that the transition of azobenzene molecules from the *trans* configuration to *cis* is feasible; however, it is accompanied by energy barriers and the absence of intersection points between the ground state and the excited state. Moreover, they proposed that following the $\pi \rightarrow \pi^*$ (S_0 - S_2) excitation, sufficient energy may be accessible to allow for concerted inversion, the additional pathway proposed by Diau.²⁰ The potential energy surfaces elucidate the variations in *trans-cis* quantum yields observed experimentally. This study demonstrates that the

rotation method is the sole viable option for both $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ excitations, as the concerted inversion pathway is inaccessible for azobenzenes.

1.1.4 Spectroscopic Signatures For Characterization

The azo group, which exhibits *E* and *Z* forms, is planar, as well as displaying antisymmetric wave functions of the ethenic electron system and a distinctive *n*-electron structure. From the perspective of the molecular plane, there are symmetric *n*-orbital interactions between the nitrogen atoms. These orbitals can be subdivided into molecular orbitals with a significant energy differential and a high degree of interaction. Aromatic azo compounds exhibit an extended π system. The N=N distance for *E*-azobenzene, as determined by X-ray analysis, is 124.7 pm, while the C-N distance is 142.8 pm.³ Since the properties of the azo group were understood using azomethane, it can be said that azobenzene is not substantially different from azomethane. The photostability of azo compounds can be enhanced by extending the conjugation, although this may result in a reduction in their excitation energy. The $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ energy difference is highly dependent on substitution, which affects the spectroscopic and photochemical properties of azoaromatics.³ Additionally, *trans-cis* isomerisation in azo functional groups acts as the most significant mechanism for dispersion of energy. The environmental conditions, such as stiffness or low temperature, lead to a reduction in the probability of the emitting state being deactivated non-radiatively.^{21,22}

In general, the radiative transitions (phosphorescence and fluorescence) of azo substances are not observable by standard spectroscopic techniques. However, in some cases, they do emit light at low temperatures in strong acids.⁵ Azo-containing macrocycles have also been studied and reported to show unexpected fluorescence due to their rigidity.²³

The mechanism and dynamics of the photoisomerization of aromatic compounds have been investigated with picosecond and femtosecond lasers. The study of excited state properties has been facilitated by the short pulse durations and high photon intensities of these lasers. The lowest and highest excited states of azobenzene are detected.⁵ However, the focus of research in this area has generally been on the dynamics of isomerisation.

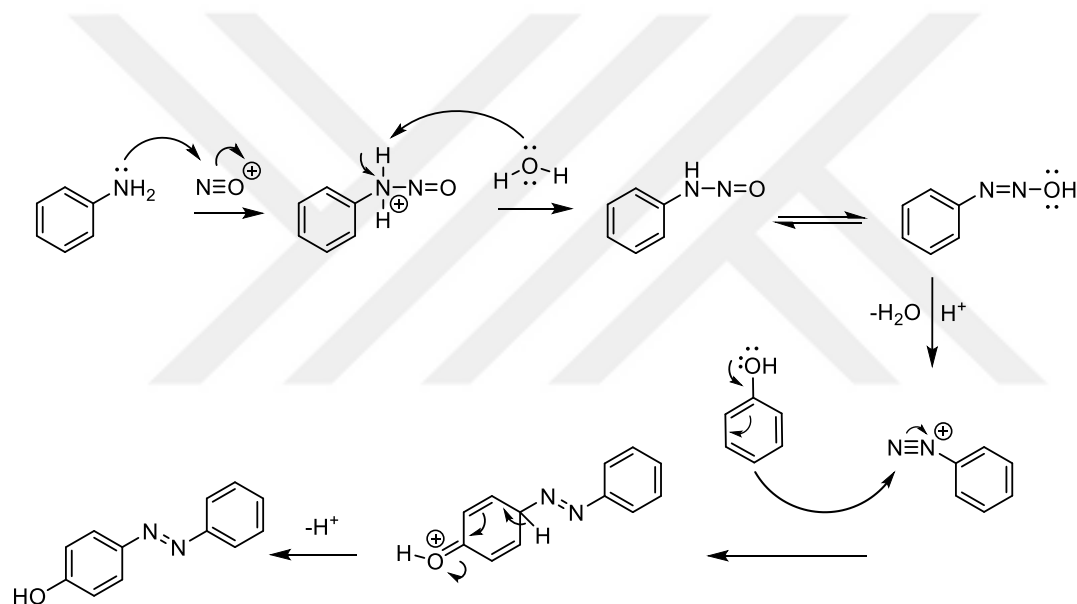
N=N and C-N (Ph-N) stretching vibrations and torsional vibrations around the C-N bond are among the vibrations used to characterize azobenzene.²⁴ Since the *E*-azobenzene molecule has an inversion center, the N=N vibration is infrared inactive but Raman active and is positioned at 1442 cm⁻¹, while in *Z*-azobenzene the N=N vibration is placed at 1511 cm⁻¹.²⁵ IR spectroscopy detects the symmetric C-N stretching vibration at 1223 cm⁻¹ in *E*-azobenzene and 866 cm⁻¹ in *Z*-azobenzene.²⁶

1.1.5 Synthesis

1.1.5.1 Diazotization and Coupling Reaction

This reaction represents the most popular method for the synthesis of azobenzene, primarily due to its simplicity and responsible for the majority of azobenzene production. The process begins with the transformation of an aromatic primary amine into a diazonium salt via nitrites, mainly sodium nitrite, at 0°C. This is followed by a reaction with an aromatic nucleophile that is electron rich. This method typically yields high quantities of the desired product and allows for the completion of the reaction in a shorter period of time.²⁷ Diazonium salts produce azobenzenes when they react with electron-rich species.²⁸ This class of substitution reaction typically occurs at the para position of the activated aromatic ring, which serves as a nucleophile. If this position is already occupied by another functional group, the

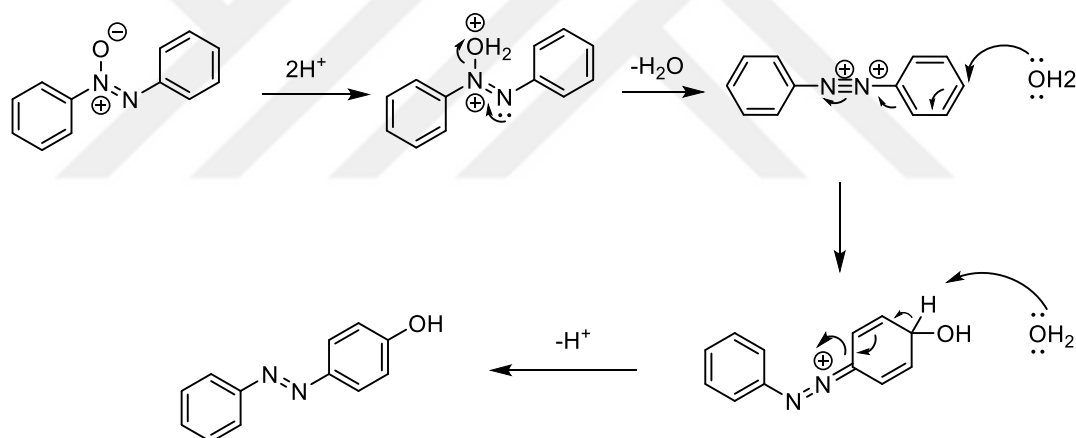
reaction occurs in the ortho position. The pH of the process is important. With regard to the reactivity of the initial reactants, it is essential that phenols undergo coupling in their ionised form, as the neutral species lack the required nucleophilicity. In this instance, the diazonium salt is converted to a diazohydroxide in the presence of a base, which inhibits coupling. Therefore, slightly alkaline solutions are necessary. To protect the nitrogen from protonation in acidic conditions, phenol coupling must be done in mildly basic media at a controlled pH. The opposite is true for aromatic amines, which should be reacted in weakly acidic media.²⁷ Proposed mechanism is represented in Scheme 1.3.²⁷



Scheme 1.3 Proposed mechanisms for diazotization and coupling

1.1.5.2 Wallach Rearrangement

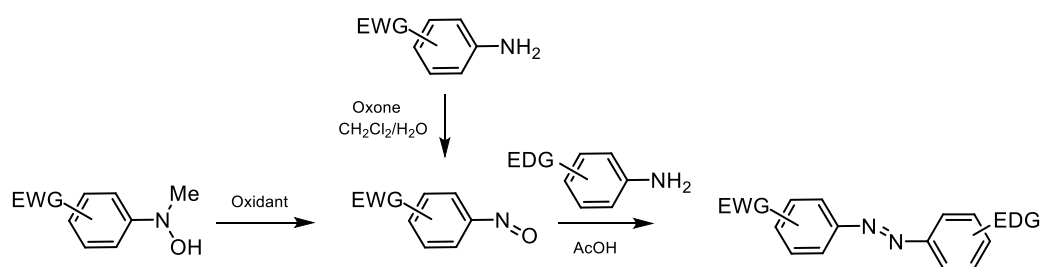
Another method for obtaining azobenzene is the Wallach rearrangement, which was developed over a century ago. This involves the treatment of azoxybenzenes with concentrated sulfuric acid, which yields 4-hydroxy- or 2-hydroxy-azobenzene. Azoxybenzenes can be readily prepared from nitrosobenzenes, with the rearrangement being directed by substituents attached to the initial azoxybenzenes.²⁹ Mechanism is depicted in Scheme 1.4.²⁷



Scheme 1.4 Proposed mechanism for Wallach Rearrangement

1.1.5.3 Mills Reaction

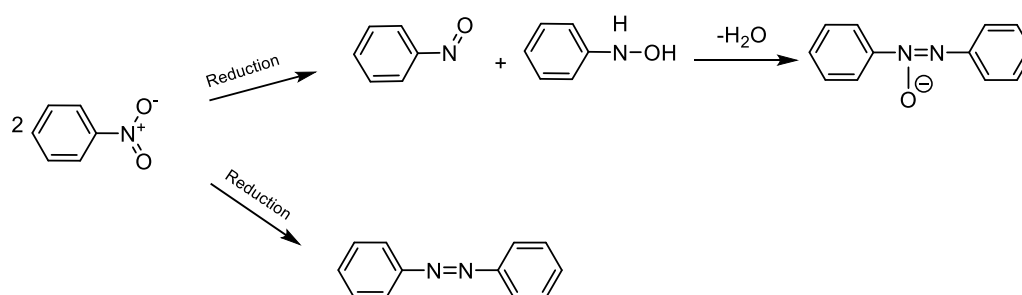
For the synthesis of unsymmetrical azobenzene derivatives, there is a conventional method invented by Mills, which is a process containing aromatic nitroso derivatives and anilines. To initially produce the nitroso compound, a number of oxidants may be employed. The literature reports the use of FeCl_3 , m-CPBA, tert-butyl hypochlorite or H_2O_2 in combination with specific metal catalysts for this step.³⁰ However, this reaction presents certain drawbacks that result in low yields. It is challenging to control the side reactions, such as the decomposition of hydroxylamine, the excessive oxidation of the nitroso to a nitro molecule, or the reaction between hydroxylamine and the nitro compound. To overcome these issues, two-phase heterogeneous systems have been developed, such as oxone in a CH_2Cl_2 and H_2O mixture. Since the nitrosoarenes are less soluble in water, these two phase systems enable the separation of N-hydroxylamine and aniline derivatives from them, thereby inhibiting the condensation process.²⁹ A general representative example of this reaction is depicted in Scheme 1.5.³⁰



Scheme 1.5 A general representative example of Mills Reaction

1.1.5.4 Reduction of Aromatic Nitro Derivatives

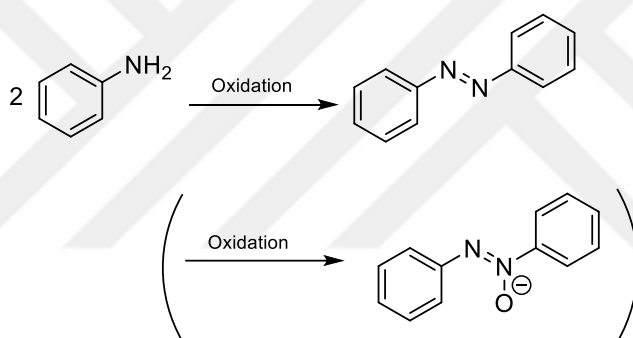
In controlled conditions, nitrobenzenes can undergo partial reduction to generate azobenzene compounds. This technique is particularly efficient for production on an extensive basis. For such a purpose, a variety of systems have been identified effective. Some inorganic salts, reducing agents such as LiAlH_4 , NaBH_4 or zinc combined with aqueous NaOH are some examples for this process.³¹ The intermediates formed during this process are azoxybenzene and nitrosobenzene. Azo compound forms by the reduction of azoxy compound which is formed by the condensation of nitro and hydroxylamino derivatives. Using two distinct nitro compound should be avoided for the inhibition of side products, therefore this approach is only suitable for the synthesis of symmetrical azo compounds. General representation of this type of reaction is given in Scheme 1.6.³²



Scheme 1.6 A general representation of reduction of aromatic nitro derivatives for azobenzene synthesis

1.1.5.5 Oxidation of Amino Compounds

Aromatic amine oxidation is another technique for obtaining symmetrical azobenzenes. Hypochlorites, peroxy compounds, chromic acid, or oxygen are utilized for this purpose. Hypochlorite is the most favored oxidizing agent among them. The azo process might encounter further oxidation, producing different kinds of azoxy molecules. Scheme 7 illustrates these reactions as a general representation.³²



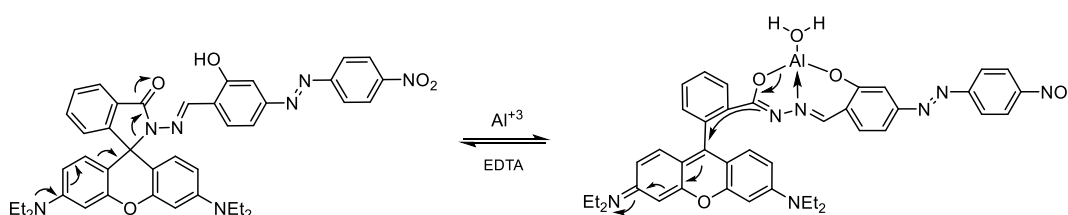
Scheme 1.7 A general representation of oxidation of amino compounds for azobenzene synthesis

1.1.6 Applications

Although the first thing that comes to mind when we think of azobenzene is the bright and useful azo dyes, their use goes far beyond this. The distinctive

photoresponsive nature of azobenzene and the phenomenon of *trans-cis* conversion have enabled the molecule to be utilised in a multitude of applications. This substance, which has been continuously studied for decades, has a wide spectrum of uses ranging from food, biochemistry, pharmaceutical sciences, solar energy systems, material sciences, optics.

With uses in biological detection, environmental monitoring, and security, azobenzene-based sensors are adaptable and offer reliable, multipurpose solutions for the detection of a variety of analytes. Azobenzene is useful for colorimetric sensors because it can undergo observable spectrum shifts. These sensors use azobenzene derivatives to bind to target analytes and change their absorption spectra. Sensors can detect several analytes and are used for a variety of metal cations and organic compounds.³³ Apart from colorimetric sensing, one method that has been studied is fluorescence-based sensing, in which azobenzene derivatives that bind to analytes like Al^{3+} and Fe^{3+} produce fluorescence (Scheme 1.8).³⁴ Lifetime-based sensing is an additional strategy that examines variations in the *cis* lifetime of azobenzene molecules. This approach offers resilience to sample variations and has the capacity to detect environmental changes such solvent polarity, acids, and metal ions. In addition, azobenzene can be added to silica or polymers to make sensors that measure humidity or detect ions. In hygroscopic polymers, azobenzene-based humidity sensors have demonstrated a strong connection between humidity and isomerization rates, revealing the possibility of low-cost sensors.³³



Scheme 1.8 : Proposed binding mode of azobenzene containing chemosensor with Al^{+3} .

In addition, the characteristics of azobenzene have influenced the development of supramolecular materials containing it. The presence of azobenzene in these materials has made them sensitive to light, pH, and environmental changes. Nanoparticles containing azobenzene, for example, have been designed to be pH sensitive and to alter morphologically under varied light conditions. By derivatizing azobenzene with amines and carboxylic acids, this pH sensitivity was attained. Furthermore, porous organic polymers bound to azobenzene have been created for the detection of CO₂ gas, which contributes significantly to global warming. Lewis acid-base interactions between azobenzene groups and CO₂ enable these materials to have strong CO₂ absorption capacities. It has been reported that the *trans-cis* isomerization of azobenzene increases regeneration efficiency by permitting the release of CO₂ under UV irradiation (Figure 1.4).³⁵

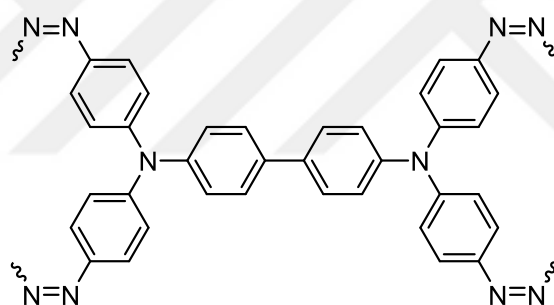


Figure 1.4 Azopolymer unit that used for CO₂ separation

Azobenzene photo-switching is also a popular feature in organic electronic devices, especially for its use in multifunctional sensing and remote-controlled systems. The distinct changes in its molecular geometry and dipole moment during photoisomerisation make it superior to other photo-switching molecules. With these

properties, it has gained a place in organic field-effect transistors (OFETs), semiconductor materials, and graphene and carbon nanotube field-effect transistors.³³

Photopharmacological treatments have been modified by the use of azobenzene derivatives as artificial photoswitches to treat eyesight loss. The development of light-controlled drugs with high sensitivity and minimal side effects has led researchers to investigate the utilisation of azobenzene, which is capable of undergoing photoisomerisation, as a means of achieving these desired characteristics. The integration of azobenzene units into drugs results in the formation of azologues, which retain the drug's parental structure. Alternatively, if a drug is modified by extending part of its structure that includes an azobenzene unit, it is referred to as an azo-extension. Both approaches have their own strategic considerations.¹⁰ These compounds (Figure 1.5), were designed to regulate the permeability of cell membranes and protein structure using light. The tactic was to change the function of cone and rod cells in the eye by modulating ion channels involved in the visual process through *trans-cis* conversion. Since the azobenzene molecule and photoreceptor cells react similarly to light, azobenzene derivatives were used to simulate this change. Red-shifted azobenzene compounds have been created as a consequence of numerous studies that reduce tissue penetration and UV radiation damage.³³ In addition to its role in restoring vision, azobenzene derivatives are also employed in the field of photopharmacology for a number of other purposes, including the modulation of neural activity, the management of pain, the treatment of bacterial infections, the management of diabetes, and the treatment of various forms of cancer.¹⁰

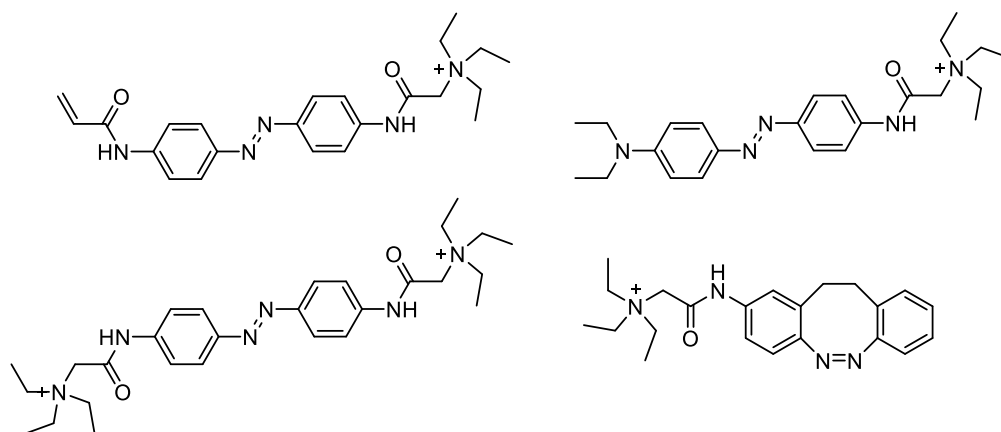
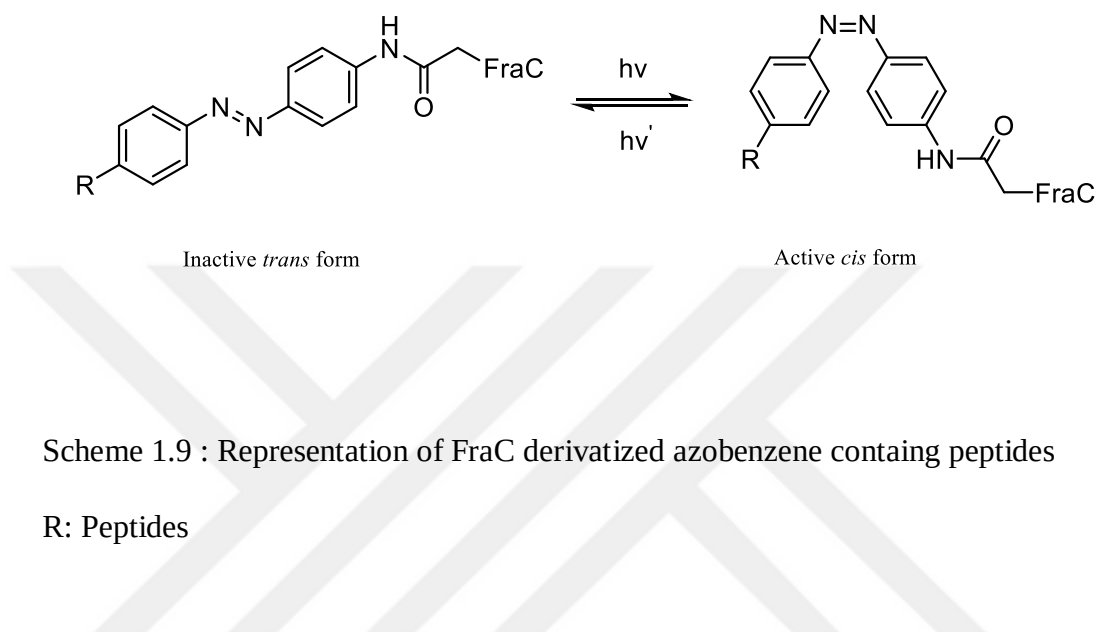


Figure 1.5 Structures of some azobenzene derivatives restoring vision loss

The ability of azobenzene to undergo photoisomerization with light has allowed it to be adapted to systems involving biomacromolecules. This has allowed the development of light-responsive systems in biomacromolecules such as DNA, peptides and proteins. This step, which is a very important development in the control of biological activities, allows the generation of conformational changes. It has been demonstrated that the folding and unfolding of α -helical structures in azobenzene-modified peptides can be controlled. Studying protein-protein interactions revealed that the *cis*-isomer stabilizes the α -helical structure and enhances cell penetration, while the *trans*-isomer decreases structural stability. Derivatives have been created for this purpose; one such example is derivatized fragaceatoxin C (FraC), which is a toxin that causes cell death, and can therefore act on cancer cells. However, the human body will suffer irreversible harm if it is not controlled and let to come into contact with healthy cells. By modifying it with an azobenzene moiety, this toxicity was eliminated, and the agent became controllable toward target cells with a *trans-cis* change (Scheme 1.9).³⁶ These photocontrollable

peptides proved to be valuable in biological applications since reversing peptide conformations using light allows cellular processes to be controlled.



Scheme 1.9 : Representation of FraC derivatized azobenzene containing peptides

R: Peptides

The *trans-cis* photoisomerization of azobenzene is also advantageous for solar thermal fuels, which use solar energy to store energy by using it in chemical bonds and releasing it as heat when required. Because of its ability to store energy, azobenzene can be used in this industry. Azobenzene-containing polymers have gained interest and made energy storage in the visible light spectrum easier due to their capacity to alter the absorption spectrum by altering its structure. When converting from *trans* to *cis* form, azobenzenes derivatized with both long chains or various aryl groups have enabled the release of heat at low temperatures.⁶ In addition to these developments in azo-polymers, azobenzene derivatives provide a novel way for creating switchable adhesives with high adherence and easy removal via light-triggered isomerization. Through two primary methods, these materials allow for contactless, remote control of adhesion. In the first, materials based on azobenzene undergo a reversible solid-to-liquid transition when exposed to radiation, which

makes them perfect for hard surfaces. The second method, which works on both hard and soft surfaces, uses azobenzene isomerization to break and rebuild supramolecular connections. In a comparable way, poly(acrylates) and other azobenzene-linked polymers have been modified to display solid-to-liquid transitions by reducing their glass transition temperature (T_g) via photoisomerization.¹⁰

Chirality induction is also one of the areas where azobenzene has been extensively studied. In this area, which is more often studied at the supramolecular level or with polymers, there are various studies in which azobenzene is incorporated into the polymer structure or included as a side chain. In a study, chiral solvent limonene is used to generate and modify supramolecular chirality in polymers containing azobenzene. The main finding of the study, which examines the relationship between temperature and achiral polymer aggregation, is that while the polymer dissolves effectively at high temperatures, chiral aggregation is caused by strong π - π stacking interactions between azobenzene units when the polymer cools. Circular dichroism (CD) signals, which become more intense as aggregation rises, can be used to identify this behavior. The study shows that it is possible to create supramolecular chirality in solid film and solution states. Chiral limonene vapors in solid films cause ordered stacking of azobenzene units, resulting in detectable CD signals that can be eliminated by heating the polymer over its glass transition temperature (T_g) and recovered by cooling while the vapors are present. Numerous repetitions of this reversible operation won't significantly weaken the chiral signal. An essential topic to consider here is the memory effect, which states that once induced, supramolecular chirality in solid films can be maintained for a long time even after solvent removal. This study offers important insights for applications in optical and data storage systems by demonstrating the potential of azobenzene-containing polymers in chiral switches and the long-term durability of their chiral structures (Figure 1.6).³⁸

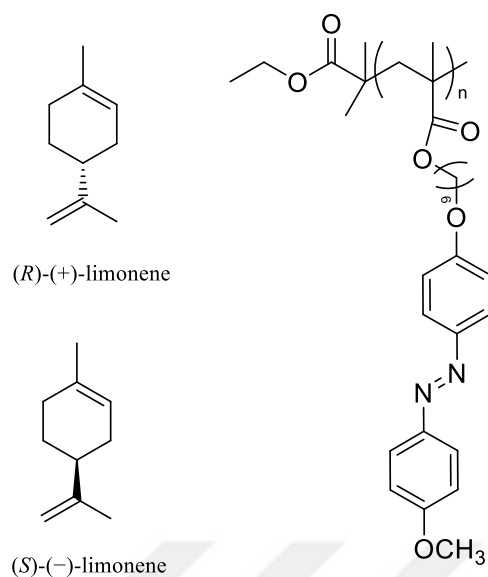


Figure 1.6 Chemical structure of azopolymer that gained chiral memory, (*R*)-(+)-limonene and (*S*)-(-)-limonene.

In another work, the induction, transfer, and regulation of supramolecular chirality in a polymer system comprising azobenzene units are investigated. A helical structure is formed as a result of the efficient transfer of chirality to achiral azo units by a single chiral group at the end of the chain. The direction of chirality is mostly determined by the distance between the achiral units and the chiral group; longer chains result in left-handed structures, whereas shorter chains induce right-handed helices. This chiral transfer is caused by the π - π stacking of azobenzene, as confirmed by CD signals. Additionally, photoisomerization and thermal reassembly of azobenzene can be used to dynamically manipulate the supramolecular structures. This study exhibits effective chirality transfer and emphasizes the utility of azobenzene containing polymers with variable chiral characteristics.³⁹

1.2 Coumarin

1.2.1 Introduction to Coumarin and its Derivatives

Coumarin, first isolated in 1820 by A. Vogel from the tonka bean and named after the French word *coumarou*, meaning tonka bean, is characterised by a 1-benzopyran-2-one core structure comprising a pyrone and benzene ring fused with a carbonyl group at position 2 (Figure 1). This compound, known in IUPAC nomenclature as 2H-chromen-2-one, represents not only itself but also a whole chemical family in which it is the parental ring. Despite its 200-year history, this substance has retained the interest of researchers since its first synthesis by W.H. Perkin in 1868. It remains a frequently studied topic, with over 1,000 structures containing it catalogued in the Cambridge Structural Database.⁴⁰

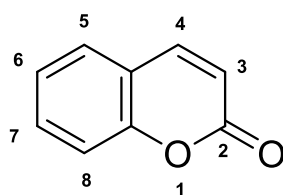


Figure 1.7 Coumarin

The attachment of various substituents to the coumarin core can have significant effects on the chemical characteristics and biological activity of coumarins. For instance, the compound's pharmacological characteristics can vary if a hydroxyl, methoxy, or isopentenyl group is present.⁴¹ While furanocoumarins and

pyranocoumarins include furan or pyran rings, respectively, which increase their biological activity, simple coumarins have substituents such a hydroxyl group at position 7 without generating extra rings. Examples of these structures depicted in Figure 2.⁴²

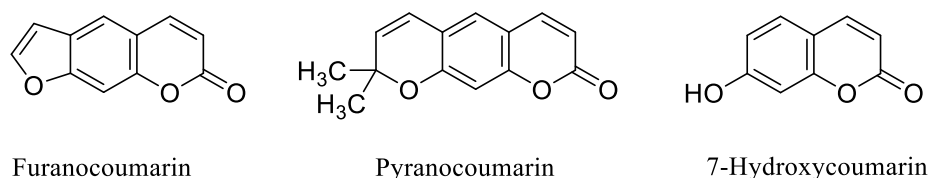
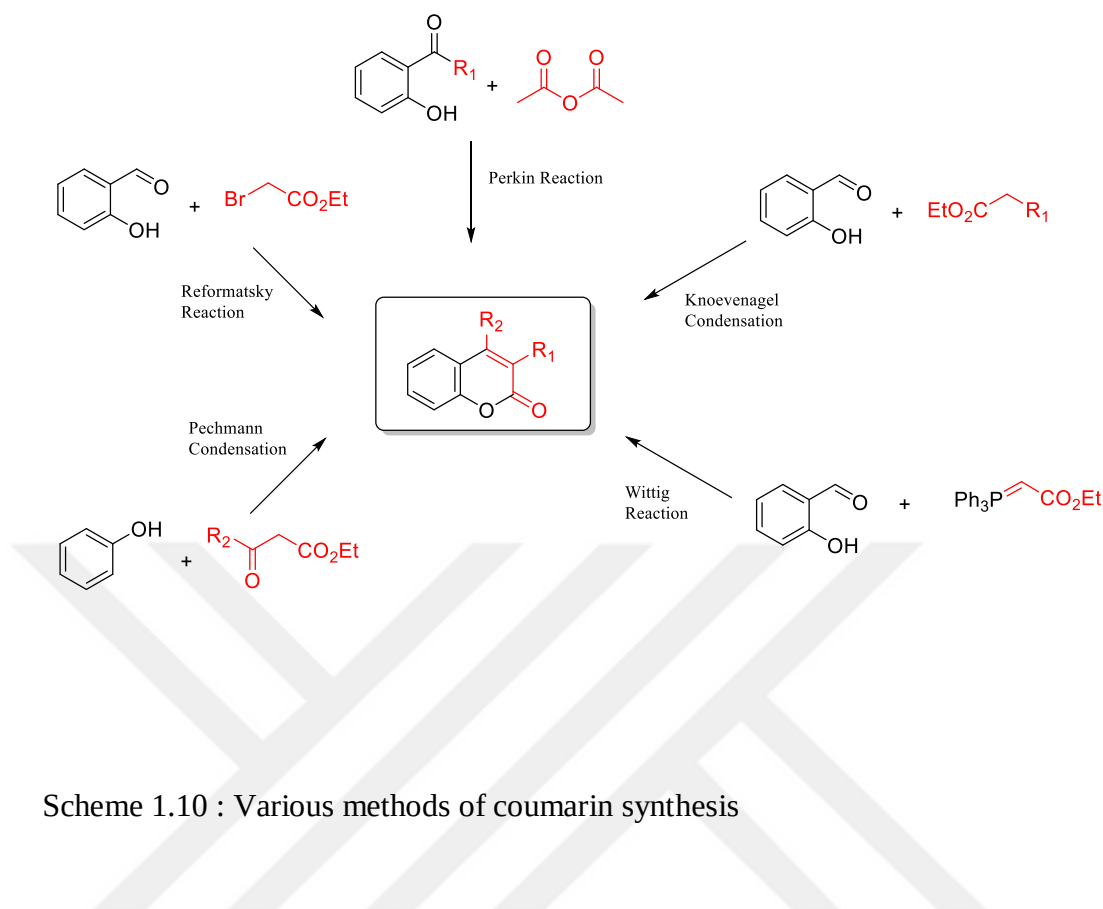


Figure 1.8 Examples of some coumarin derivatives

1.2.2 Synthesis of Coumarin Derivatives

The synthesis of coumarins is made possible by the availability and low cost of starting materials, which allows for diverse methodologies. The reactivity of the C-3 and C-4 positions allows for selective functionalization and the construction of cyclic systems. Coumarins offer a highly versatile building block for the creation of complex chemical architectures. The Knoevenagel, Perkin, Pechmann, Wittig, and Reformatsky reactions are among the traditional synthetic techniques for coumarins (Scheme 1.10).⁴³ The synthesis of coumarin derivatives is frequently achieved through the Knoevenagel reaction, which involves the condensation of 2-hydroxybenzaldehydes with active methylene group-containing coupling partners under base-mediated and heating conditions. The literature also emphasizes solvent-free, ultrasound-assisted methods that improve sustainability and reaction speeds.⁴⁴ On the other hand, the Perkin reaction, which was reported by W.H. Perkin in 1868 is the first reaction by which coumarin was synthetically obtained, allows us to obtain coumarins by condensation of salicylaldehyde and acetic anhydride. This process is

well-known for producing coumarin structures with ease and efficiency.⁴³ One of the methods for coumarin synthesis that has been investigated the most is the Pechmann reaction. The condensation of different phenols with β -ketoesters is the basis for the Pechmann reaction. It is necessary to employ a homogenous catalyst or heterogeneous catalysts for this type of reaction.⁴⁴ Another reaction used to synthesise coumarin is the Wittig Reaction. In the Wittig reaction, an aldehyde or ketone reacts with a Wittig phosphine reagent, like triphenyl phosphonium ylide, to produce the desired olefin with phosphine oxide as a byproduct. This is an especially useful process for the synthesis of natural products and pharmaceutical compounds. The reaction mechanism involves the formation of phosphorane intermediates. The scientific literature contains many examples of coumarin framework synthesis employing phosphonium ylides and aldehydes or ketones via the Wittig reaction.⁴⁵ An additional reaction used in the synthesis of coumarin is the Reformatsky reaction. The Reformatsky reaction begins with the reaction of an activated acyl halide with zinc metal, yielding a $RZnBr$ intermediate. The intermediate then forms a zinc enolate by undergoing a 1,2-addition with a ketone. After $Zn[OH(Br)]$ is eliminated, an ester is produced. Its usefulness in creating complex coumarin derivatives has been established by the synthesis of 3,4-disubstituted coumarins from α,β -unsaturated esters.⁴¹ In order to enable the more effective and sustainable synthesis of coumarins, new methods have been developed recently, such as the use of microwave and ultrasonic chemistry, creative catalysts, and environmentally friendly solvents.^{46,47}



1.2.3 Fluorescence and UV- Vis Properties of Coumarin

The parent coumarin does not fluoresce, but many substituted derivatives do. Since the 1980s, researchers have tried to make coumarin dyes emit light more efficiently. Many studies have been done to understand and improve the properties of coumarin dyes. Many coumarin dyes have been developed for use in optical brighteners, dispersed fluorescence dyes and laser dyes because they are fluorescent, can be tuned to different wavelengths and respond to the polarity of their surroundings.⁴⁰ Depending on their modification of structure and the surrounding environment, coumarin derivatives' fluorescence characteristics change significantly. The existence of electron-donating or electron-withdrawing groups, solvent effects, and

particular molecule configurations are important factors affecting these characteristics.⁴⁸ The introduction of substitutions at the coumarin backbone causes a shift in the fluorescence spectrum, with the emission maxima occurring at different wavelengths that are either blue- or redshifted. The inclusion of electron-donor groups in the 6- or 7-position, or electron-withdrawing groups in the 3- or 4-position, causes a bathochromic shift in the emission spectrum.⁴⁰ It has been demonstrated that the fluorescence characteristics of coumarin derivatives are greatly affected by the internal charge transfer (ICT) mechanism. This behaviour is caused by the excitation of a molecule, which leads to a redistribution of electron density. This results in a change in dipole moment and thereby affects the emission wavelength and intensity. Coumarin molecules exhibit a solvatochromic effect, in which the solvent's polarity affects their fluorescence properties. This demonstrates dependence on the ICT process.^{44,48} The incorporation of electron-donating or withdrawing groups affects the spectral characteristics, including shifts in absorption and emission spectra. This is due to changes in conjugation and ICT effects, which either enhance or diminish fluorescence.⁴⁸

Coumarin derivatives are useful in many different applications because of their remarkable UV-Vis absorption properties. These substances exhibit substantial UV absorption in the 280–380 nm region, which is favorable for their possible application as UV absorbers in manufactured products.⁴⁹ The recent progress in this field has enabled the manipulation of the absorption spectrum of these compounds, extending it from 300 nm to 550 nm.⁵⁰ The spectrum characteristics of phenyl rings are greatly influenced by the presence of electron-donating or withdrawing substituents, which frequently cause shifts in absorption maxima as a result of structural alterations and variations in solvent polarity. Studies employing density functional theory (DFT) and quantum chemical analysis have clarified the connection between the molecular structure of coumarin derivatives and their UV-Vis absorption properties. These investigations show that molecular shape, intramolecular hydrogen bonding, and electronic transitions have a major impact on the stability and reactivity of these compounds in their solid state. Furthermore, it

has been shown that the stability of these molecules is significantly influenced by non-covalent interactions.⁵¹

1.2.4 Applications of Coumarin Derivatives

Coumarins have been the subject of considerable interest due to their biological importance and applications. This oxygen-fused heterocycle has a range of effects, including anti-tubercular, anti-inflammatory, anticancer, anticonvulsant and neuroprotective, as well as antiviral, antifungal and anti-HIV.^{41,52} Moreover, scientists are very interested in coumarin analogues because of their prospective uses in a variety of materials, such as photosensitizers, fluorescent materials, optical brighteners, laser dyes, and food, cosmetic, and medicinal additives. The pharmaceutical industry also uses the coumarin heterocyclic ring system for medicinal compounds. Many countries employ coumarin-based medications, such as acenocoumarol, phenprocoumon, and warfarin (Figure 1.9). These discoveries improve medicinal chemistry and the biological evaluation of coumarins and their derivatives.^{48,52} Derivatives of coumarins are interesting materials with a wide range of uses. Because they can effectively switch electrical resistance and create stable thin films, they are utilized in electrical devices for memory and logic circuits. They are useful in biological and environmental monitoring because, as fluorescent probes, they can detect substances with noticeable color changes. With continued study enhancing their performance for more sophisticated applications, their potent fluorescence and charge transport capabilities make them appropriate for OLEDs, solar cells, and other optoelectronic devices in photonic technologies.^{40,48,53}

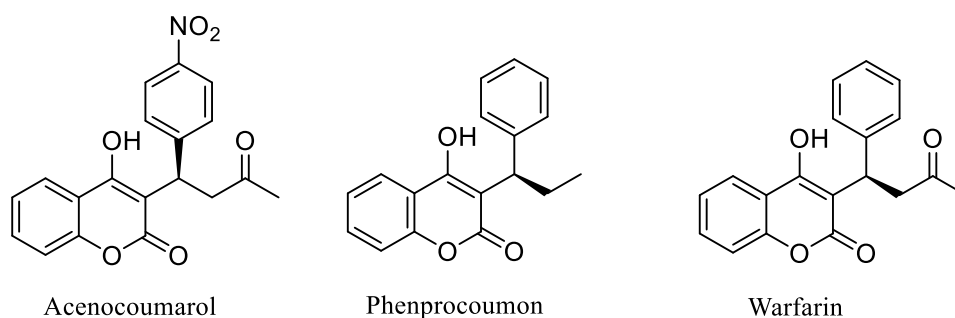


Figure 1.9 Examples of some coumarin-based medicines

1.3 Polarized Light and Circular Dichroism

1.3.1 Polarized Light

Polarization is an essential feature of light that can be seen in a variety of natural instances. It results from the geometric orientation of oscillations in the electric field of electromagnetic waves, resulting in distinct properties in how light interacts with various materials and surfaces. A variety of natural polarizers can be found in nature, affecting the polarization of light through processes like scattering, refraction, and reflection. Smooth water surfaces, leaves, ice, snow, clouds, and fog are typical examples. Reflection from certain surfaces can produce polarized light, especially when the light strikes them at specific angles.⁵⁴ The term "polarized light" describes electromagnetic radiation in which the electric field primarily oscillates in a particular direction, producing a variety of light types with important applications in many scientific and technical domains. Linearly polarized light, circularly polarized light, and elliptically polarized light are the three main forms of polarized light (Figure 1.10). The orientation and type of electric field oscillations, which are essential for applications, differentiate these groups.⁵⁴

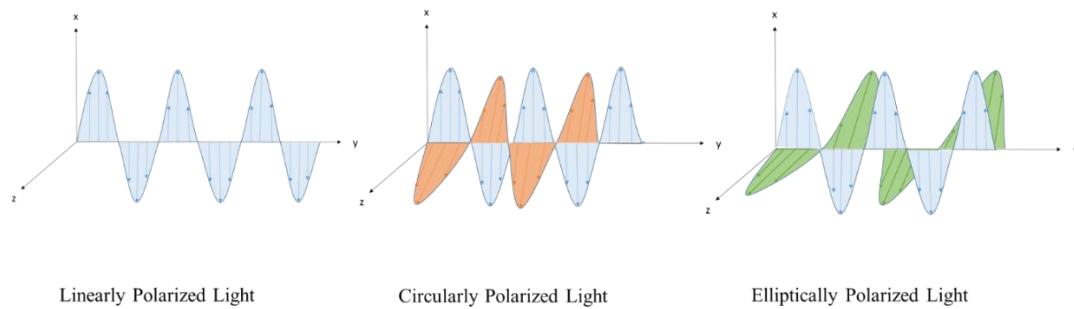


Figure 1.10 The three main forms of polarized light

In linearly polarized light, the electric field oscillates in a single plane. This indicates that as the wave propagates, the direction of the electric field remains constant. One method for generating linearly polarized light is to transmit unpolarized light through a polarizer, which effectively eliminates all but one specific polarization direction. When the electric field vector exhibits a circular pattern of rotation during wave propagation, the result is circularly polarized light. The direction of rotation determines whether the rotation is left-handed or right-handed.⁵⁴ Elliptical polarization, which is of great significance in advanced optical applications such as imaging and telecommunications, represents a combination of linear and circular polarizations. The two orthogonal electric field components have different amplitudes and/or phase shifts. This form of polarization can occur when the components are out of phase.⁵⁵ These forms of polarized light have a number of practical and scientific applications, including in optical communications, photography and more. Understanding their characteristics and how to work with them improves the efficiency of tools like optical filters, polarizers, and display technologies.

1.3.2 Circularly Polarized Light and Circular Dichroism (CD) Spectroscopy

The defining characteristic of circularly polarized light is the behavior exhibited by its electric field vector as it propagates through space. The electric field vector rotates in a circular motion as the light travels, with the direction of rotation determining its handedness.⁵⁶ If the vector rotates clockwise when viewed from the source, the light is classified as right-circularly polarized. Conversely, if it rotates counterclockwise, the light is termed left-circularly polarized.⁵⁵ The light consists of two perpendicular electromagnetic plane waves of equal amplitude, with a phase difference of 90° . When two plane waves with equal amplitudes and a phase difference of 90° are superimposed, the result is circular polarization. Quarter-wave plates oriented at an angle of 45° to the optic axis of the plate are effective at producing circularly polarized light from linearly polarized light. This process modifies the phase of one of the orthogonal components of the light wave, thereby achieving the desired circular polarization.⁵⁶ Notably, elliptically polarized light can be thought of as a specific case of circularly polarized light. When the two components' amplitudes are different, the resulting light is elliptically polarized, showing a more complicated pattern where the electric field vector's tip traces out an ellipse instead of a circle. The difference between these two types of polarization is important for a number of applications, such as spectroscopy, where chiral compounds can be studied using circular dichroism by comparing how differently left- and right-circularly polarized light is absorbed by them.⁵⁷

Circular dichroism (CD) is a spectroscopic technique that utilizes the differential absorption of left-handed and right-handed circularly polarized light by optically active chiral molecules. This phenomenon offers valuable insights into the molecular structure and conformation of various substances, particularly in the fields of biochemistry and molecular biology. The basis of CD is the principle that chiral molecules exhibit different absorption characteristics for left and right circularly polarized light. The differential absorption, often quantified as delta absorbance,

provides insight into the unique structural features of the molecule. Similar to UV-Vis absorption spectroscopy, Beer-Lambert's law is applicable here, but the distinction in the molar absorptivity of left and right circularly polarized light is taken into account (Equation 1 and 2).⁵⁷

$$\Delta A = \Delta A_L - \Delta A_R \quad (\text{Equation 1})$$

$$\Delta \epsilon = \epsilon_L - \epsilon_R = \Delta A / cl \quad (\text{Equation 2})$$

In these equations, A_L and A_R stand for absorption while ϵ_L and ϵ_R represent molar extinction coefficients for left and right circularly polarized light respectively. Pathlength is denoted as l and concentration is symbolized with c .⁵⁷

In optically active substances, the interaction with circularly polarized light can result in a phenomenon known as optical rotation, whereby the polarization plane of linearly polarized light is rotated upon passage through the material. The optical rotation degree depends on several factors, including the substance concentration and the length of the light path. In chemistry and biochemistry, this property is especially important for analyzing chiral compounds, as circularly polarized light provides crucial insights into their molecular structure and behavior. The CD spectrum is typically presented in terms of ellipticity, (θ) which quantifies the degree of ellipticity of the polarized light, offering valuable insights into the molecular conformations present.^{55,58}

From an instrumental perspective, the process of CD spectroscopy involves the use of a stable light source, such as a xenon lamp, which emits unpolarised light. Following that, the light is run through a monochromator, which separates particular wavelengths that are relevant to the chemical system being studied.⁵⁹ A polarizer is used to turn the monochromatic light into linearly polarized light. After that, a photoelastic modulator (PEM) switches the polarization state between high-frequency left- and right-circularly polarized light.⁵⁹ When this light interacts with the chiral sample, the molecules absorb the two polarization states differently, creating a measurable difference in intensity. This difference is detected and

recorded across the wavelength range, which is called CD signal.⁵⁷ A simplified instrumental representation is illustrated in Figure 1.11.

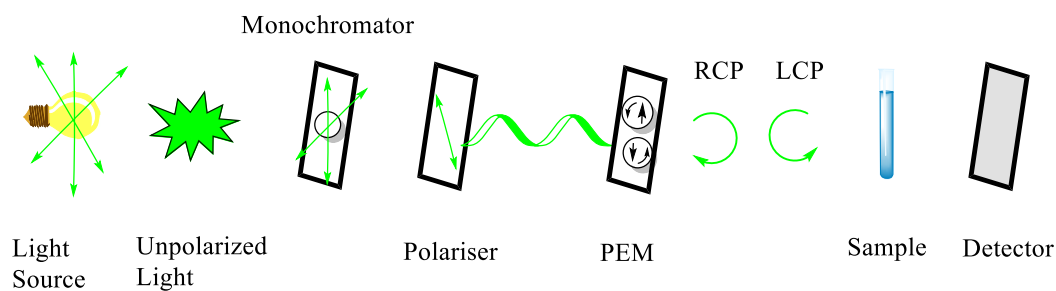


Figure 1.11 Illustration of CD spectroscopy instrumentation

1.4 Chirality

1.4.1 Discovery Of Concept Of Chirality and Chirality Types

The adventure of chirality in the scientific world started in 1848 when Louis Pasteur, one of the pioneers of stereochemistry, examined crystals of the double sodium-ammonium salt of tartaric acid (Figure 1.12) under a microscope and saw that some of the crystals' facets were oriented to the right and some to the left. He then separated the crystals with tweezers and carried out the first chiral resolution in the history of science.⁶⁰

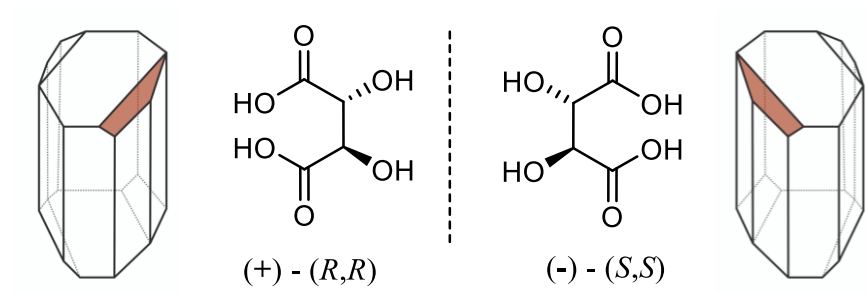


Figure 1.12 : Chemical structures of enantiomers of tartaric acid and hemihedral crystals of double sodium-ammonium tartrates

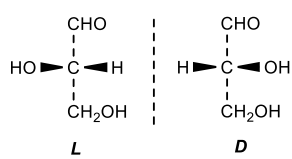
Chirality is an essential feature of living beings and therefore environment. Because nature prefers one type of chirality over another during evolution, D-sugars predominate in DNA and RNA and L-amino acids in proteins and enzymes. If an object or molecule lack planes of symmetry and inversion center, which means improper axis of rotation (S_n), it is said to be chiral. Chiral molecules are always dissymmetric (without S_n) but not always asymmetric (missing all symmetry elements except the identity), but asymmetric molecules are always chiral.⁶¹ Chirality, which can manifest at many different levels of hierarchy, is a property of an item or molecule that prevents it from being superimposed on its mirror counterpart.

Finding a stereogenic carbon/center is a common method used in practice to determine molecule chirality. A stereogenic carbon is a simple indication of chirality and is described as a sp^3 hybridized carbon bonded to four different atoms or groups of atoms. Aside from the presence of stereogenic centers, other structural factors may cause molecular chirality. For example, even without a chiral center, a molecule with two noncoplanar, asymmetrically linked rings that cannot freely rotate about the connecting bond may display chirality. This sort of chirality is referred to as planar chirality. Additionally, compounds that have a substituent arrangement around an axis that prevents the configuration from superimposing on its mirror counterpart are

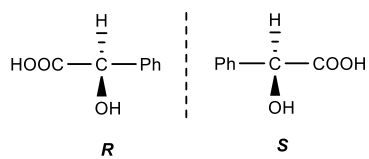
also considered to display chirality. This is known as axial chirality. Beside, the term "helicity" refers to a particular type of axial chirality in which a group of substituents are arranged spatially around a central axis that does not superimpose. Thus, molecule chirality can be classified as axis chirality (originating from spatially limited rotational axes), plane chirality (related to planar limitations), and point chirality (based on chiral carbons). Figure 13 shows examples of each of these types.⁶²



Point Chirality

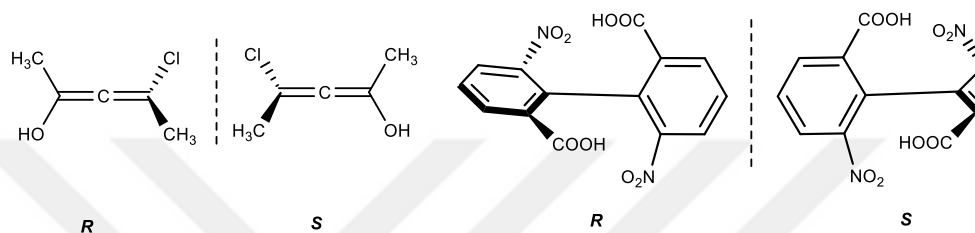


Relative Configuration

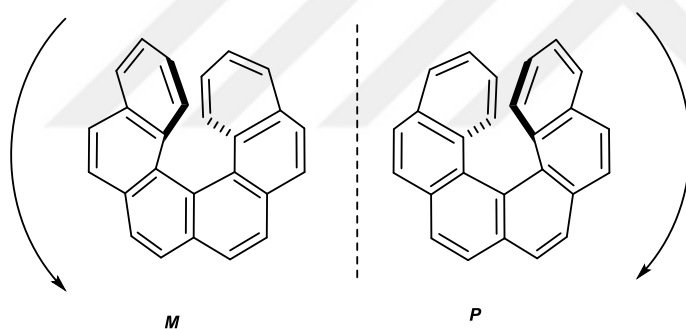


Absolute Configuration

Axial Chirality



Helical Chirality



Planar Chirality

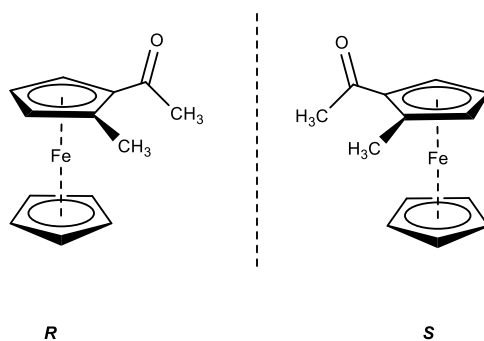


Figure 1.13 Structural examples of types of chiralities

1.4.2 Chirality Transfer and Chirality Induction

The study of chiral compounds and their interactions requires an understanding of chirality transfer and chiral induction. The phenomenon of chirality transfer in chemical processes refers to the transfer of stereochemical information from one component, such as a substrate, reagent, catalyst, or solvent, to the final product.⁶³ This type of transfer works especially well when the reaction moves through ordered transition states, where achiral and chiral molecules interact and favor one pathway over another. Typically, stereoselective molecule production has relied on control of either the substrate or the reagent, resulting in products with consistent stereochemistry.⁶⁴ This feature has important uses in asymmetric synthesis, which aims to create one enantiomer over another. In contrast, chirality induction occurs when an achiral molecule acquires chiral information under the influence of a nearby chiral object, such as a chiral catalyst or solvent.⁶⁵ While both processes involve the influence of chiral species on achiral counterparts, chirality transfer focuses on the transformation of achiral molecules into chiral ones, whereas chiral induction focuses on the electronic change of achiral molecules caused by existing chiral molecules. In terms of molecular context, chirality induction can be defined as a process involving interactions between the various components of a given molecule. In studying the interactions that induce chirality, it is crucial to understand the role of large molecular components, as well as the manner in which one molecular component affects another. Contrary to conventional belief, chirality can be observed at the atomic level.⁶⁶ Indeed, even single atomic neighbourhoods or electron clouds can exhibit chiral properties. If we apply the concept of a chiral carbon centre, which is a fundamental concept in organic chemistry, we can conclude that at least four nuclei are required for the formation of a chiral entity. However, it is now possible to think about chiral electron density clouds as real things due to the advancements in molecular modeling systems and the growing popularity of quantum chemistry

computations. It has been demonstrated that these clouds reflect the entire range of chirality properties exhibited by molecules. Even a small proportion of the cloud is clearly chiral. This leads to the question of whether these local electron clouds also control and/or represent the interaction of the whole molecule, or the parts of the molecule responsible for its chirality, with other molecules or polarised light. To address this, it has been demonstrated that for molecules in non-degenerate ground electronic states, even a minor portion of the electronic clouds encapsulates all the chiral properties of the molecule.⁶⁶ This outcome suggests that the primary information carrier in chiral molecules is the electron density clouds and their distributions. The energy of a non-degenerate electronic ground state is a unique functional of its electron density, according to the Hohenberg-Kohn Theorem⁶⁷ from density functional theory. The electron density cloud of a molecule is one of the many systems to which this can be used. This is true because the electron density cloud, which accurately depicts the nuclear distribution, and the atomic nuclei are the only components of a molecule. As a result, the electron density is responsible for all molecular attributes.⁶⁶

The process of chiral nonracemic molecules inducing optical activity in achiral solute molecules has long been recognized as significant. It has gained popularity as a method for determining the absolute configuration of transparent (non-chromophoric) chiral compounds utilizing achiral or racemic chromophores. Additionally, it has been used to investigate the molecular orientation in complexes including an achiral guest and a chiral host. Representation of this phenomena is depicted in Figure 1.14.⁶⁸

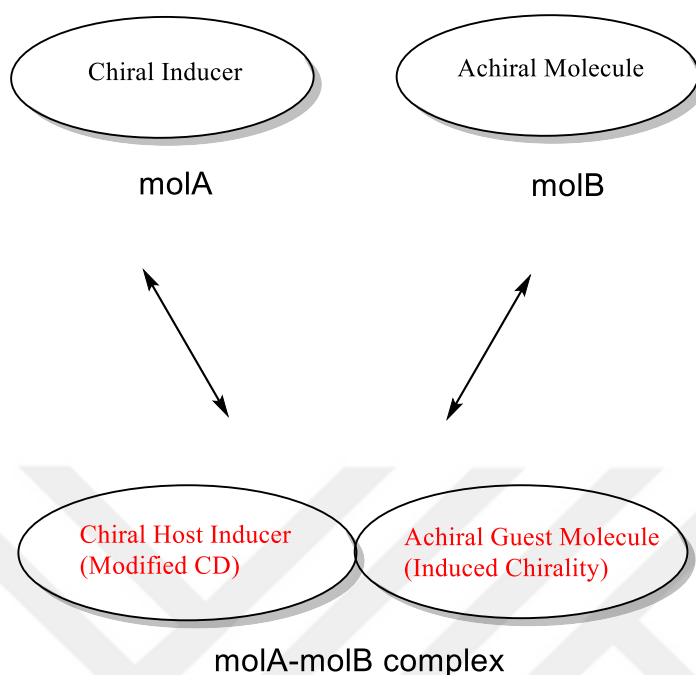


Figure 1.14 : Representation of Chirality Induction

Induced chirality in supramolecular systems is the acquisition of asymmetry by an achiral guest molecule due to information transfer and retention from a chiral host, or vice versa.⁶⁹ Conformational chirality is usually formed as a result of this asymmetry transfer and is retained in a three-dimensional optically active state by hydrogen bonds and/or steric forces. Even yet, the free, non-interacting structure is still achiral.⁶⁹ When a chiral inducer (molA) and an achiral molecule (molB) interact, induced circular dichroism (ICD) appears in molB's absorption bands. The observed result is caused by the arrangement of chiral electric dipole transition moments between the chromophores of the achiral (guest) and chiral (host) molecules, or by the existence of a dominant chiral structure in the achiral molecule.⁶⁸ Chiral induction is often influenced by steric or electronic chiral fields that serve to restrict the 3D optically active form within these chiral environments.⁶⁹ Furthermore,

although it is common to see the induction of CD in achiral molecules molB, the opposite phenomena is not as well recognized. Because of changes in the molA-molB complex, the chiral inducer molA's CD may also change.⁶⁸ The inductor's electrical and conformational properties change as a result of this inverse chirality adjustment, in which its contact with the newly optically active guest affects its own chirality.⁶⁹ If the electronic transitions of molA and molB are sufficiently distinct from one another, it is conceivable to witness both the modified CD of molA and the ICD of molB. This requirement is difficult to fulfill, though, because transitions in the short-wavelength area overlap. It becomes feasible to identify ICD in achiral molecules when molB absorbs at higher wavelengths than molA. The complexation of an azo chromophore with cyclodextrin⁷⁰ and the interaction of a 1,8-naphthyridine derivative with guanine in DNA⁷¹ serve as examples of this. Researchers use a variety of methodologies to obtain insight into the changes in conformation and mechanisms that cause chirality induction, including observing changes in the system's physical and chemical properties. Depending on the chiral steric and electronic fields, these could include spectroscopic shifts, changes in binding constants, color changes, and the development of chiral macroscale structures.⁶⁹

The phenomenon of induced chirality is observed when a product formed by coupling a chiral sample to an achiral chromophore exhibits a non-zero rotational strength.⁶³ The electric and magnetic dipole transition moments in this complex with induced chirality are produced by the combination of the dipole moments of the chiral and achiral units. There are two theories that try to describe this induced chirality. One of them is the 'CD Stealing' Perturbation theory. According to this theory, the rotational strength of the chiral sample is directly transferred to the central core of the chromophore. The electric dipole moment of the chromophore and the magnetic dipole moment of the chiral sample are coupled by dipolar coupling and the rotational strength depends on both. The geometry is therefore crucial for this mechanism to take place, as the electric and magnetic dipole moments of the structures must be aligned in order to observe a non-zero rotational force. The other theory used to explain induced chirality is the Kuhn-Kirkwood coupled oscillator.

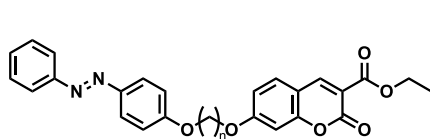
This mechanism is used to describe the allowed electric dipole transition of the achiral chromophore. According to this mechanism, the alignment of the electric dipole transition moments of the chiral and achiral parts is the factor that determines the rotational strength of the system. Additionally, geometry plays a significant role in this mechanism, as the alignment must be non-coplanar.⁷²

Understanding these processes is essential for applications as chirality has a major influence on the functionality and activity of compounds. Investigations into techniques such as using chiral ligands or light to generate chirality have resulted in improvements in materials science. These include using achiral monomers to create chiral polydiacetylene films, fabrication of asymmetric polymers by using circularly polarized light,⁷³ and obtaining stable chirality induction in solid films of azobenzene containing polymers.³⁸

CHAPTER 2

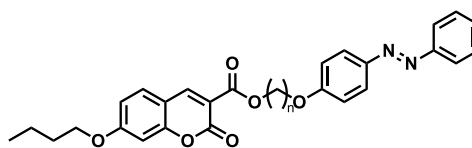
AIM OF THE STUDY

In our laboratory, it was observed that coumarin derivatives with a flexible chiral side chain exhibited varying CD spectra in different solvents, which was attributed to solvent-dependent conformational changes of the side chain.⁷⁴ To explore this phenomenon further, coumarin was modified to include a fixed chiral moiety (*D*-(-)-ribose) and a photoresponsive azobenzene side chain. The azobenzene unit can undergo light-induced *trans-cis* isomerization ($\lambda = 365$ nm), enabling structural and conformational changes within the system.⁴ In pursuit of this goal, it was observed that the light-triggered conformation change of azobenzene affects the fluorescence of the coumarin unit. To elucidate this intriguing observation, additional new coumarin-azobenzene derivatives will be synthesized and investigated, providing an extensive insight into the relationship between molecular structure and photophysical properties. For both parts of this study, the substituents of the synthesized new coumarin derivatives were provided at positions 3- and 7- of coumarin. This dual approach, incorporating both fluorescence and CD responses, facilitates a comprehensive understanding of the interacting dynamics between light-responsive azobenzene, coumarin, and chiral units. Within this scope, the following compounds are designed and synthesized.



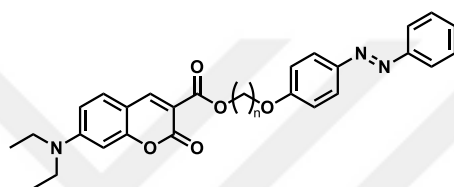
AzoCoum-1

AzoCoum-1a n = 3
AzoCoum-1b n = 8



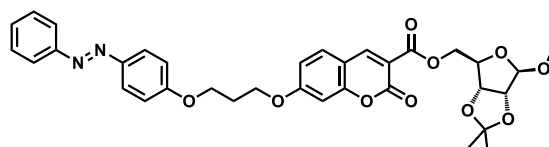
AzoCoum-2

AzoCoum-2a n = 3
AzoCoum-2b n = 8

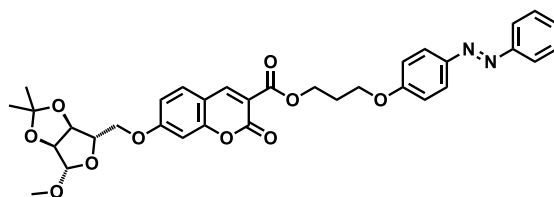


AzoCoum-3

AzoCoum-3a n = 3
AzoCoum-3b n = 8



AzoCoumR-1



AzoCoumR-2

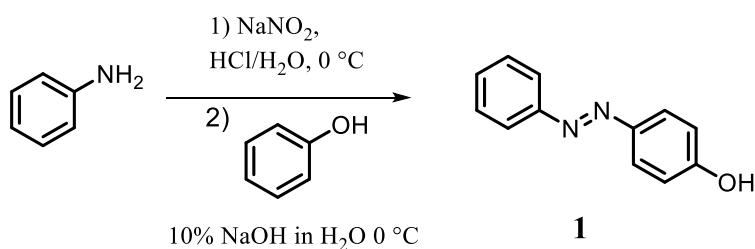
CHAPTER 3

RESULTS AND DISCUSSIONS

3.1 Synthesis

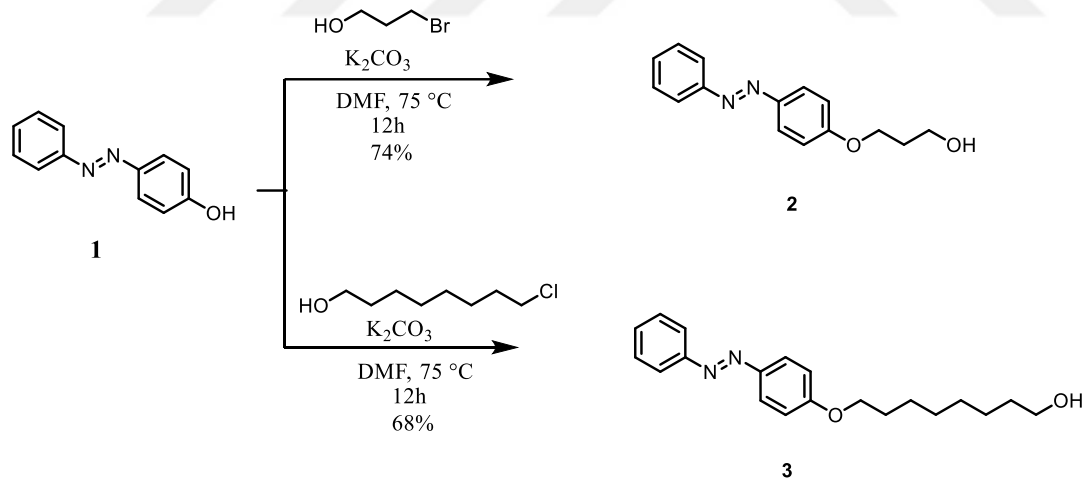
3.1.1 Synthesis of Azobenzene Cores

The 4-hydroxyazobenzene moiety, **1**, which is present in the backbone of all synthesized compounds, was obtained in 90 % yield from the reaction of corresponding diazonium salt obtained from aniline, and phenol by following procedure described in detail in the introduction section.²⁷ It was characterized by ¹H NMR and IR spectroscopy, and IR spectrum of **1** shows a peak at 1582 cm⁻¹, which is characteristic to diazo bond (-N=N-), and is consistent with the literature.²⁶ Compound was used for the next steps.



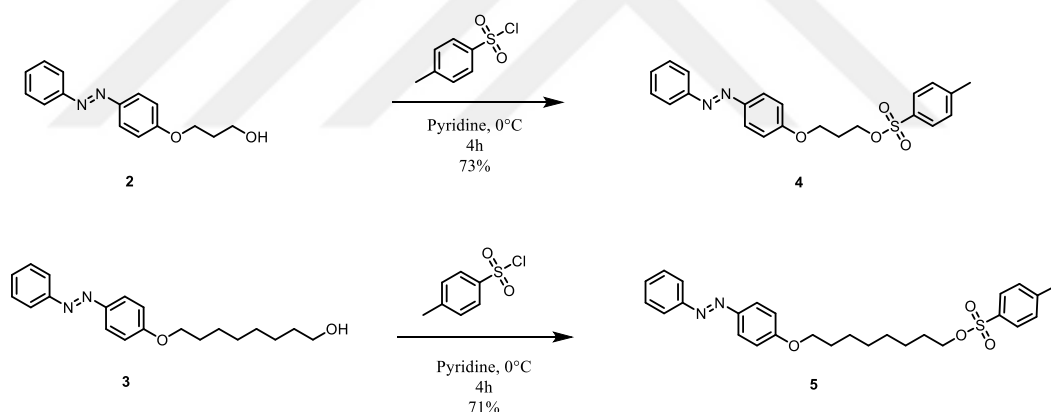
Scheme 3.1 Synthesis of 4 –Hydroxyazobenzene

In order to functionalize the 4-hydroxyazobenzene for subsequent incorporation to coumarin, two different side chains were treated with azobenzene derivative **1** to get compounds **2** and **3**. In the first reaction, 4-hydroxyazobenzene was treated with 3-bromo-1-propanol under suitable conditions to form a compound bearing a hydroxyl-terminated propyl side chain. This reaction introduces a flexible alkyl spacer, allowing for future attachment to coumarin via the hydroxyl group. In a separate experiment, 4-hydroxyazobenzene was reacted with 8-chloro-1-octanol to synthesize another derivative with a hydroxyl-terminated octyl side chain. The longer alkyl chain was designed to explore the effects of spacer length on the overall photophysical and chiroptical properties of the final coumarin-azobenzene conjugates (Scheme 3.2). Compounds **2** and **3** were obtained in 74% and 68% yields, respectively. Both compounds were characterized with ^1H NMR and IR spectroscopy (Appendices A and B), which are consistent with literature.⁷⁵



Scheme 3.2 : Synthesis of Compounds **2** and **3**

These above mentioned two reactions produced derivatives of azobenzene with terminal hydroxyl groups, which are essential for the next synthesis step in which these units are attached to coumarin. Employing tosyl chloride (TsCl) and pyridine as a base, the hydroxyl groups were transformed into tosyl (tosylate) groups to prepare the hydroxyl-functionalized azobenzene derivatives for further reactions. Because it can activate the hydroxyl groups by turning them into good leaving groups, the tosylation step was chosen to make it easier to use them in nucleophilic substitution reactions in the following synthetic steps. Yields were calculated as 73% and 71% respectively. Characterizations were done by NMR spectroscopy for compound **4** and results are consistent with literature⁷⁵ while for Compound **5**, NMR, IR spectroscopies and HRMS are used (Appendices A,B and C).



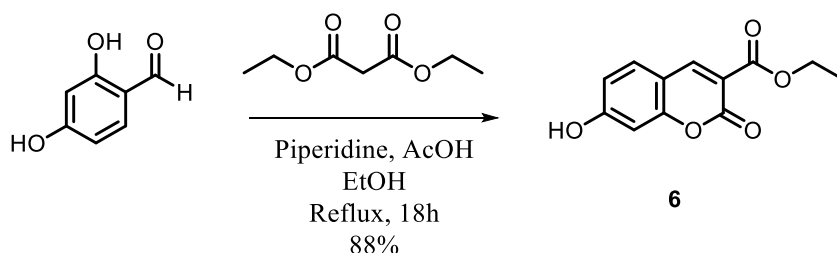
Scheme 3.3 : Synthesis of Compounds **4** and **5**

3.1.2 Synthesis of Coumarin Units and Coupling with Azobenzene Cores

3.1.2.1 Synthesis of AzoCouv-1 Derivatives

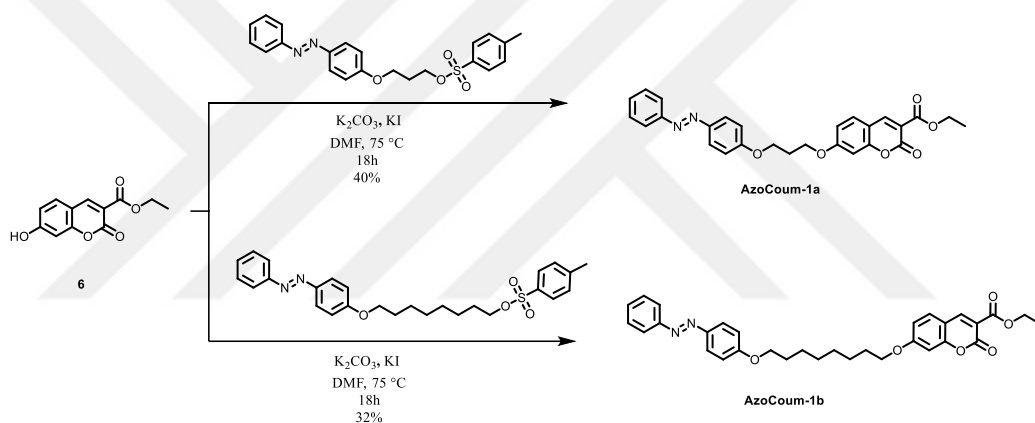
Ethyl 7-hydroxycoumarin-3-carboxylate (**6**) was the first coumarin derivative used in this study. It served as a flexible framework for examining chiroptical responses and fluorescence modulation. This coumarin derivative was essential to the investigation because it gave the azobenzene side chains the structural support they needed as a chromophore to attach and provided a platform for examining light-induced changes in fluorescence and CD responses.

The synthesis of ethyl 7-hydroxycoumarin-3-carboxylate was accomplished through a Knoevenagel condensation⁴³, in which 2,4-dihydroxybenzaldehyde and diethyl malonate were reacted in the presence of piperidine as a base and acetic acid as a catalyst, under reflux conditions in ethanol. This process yielded a high-purity coumarin derivative (88%), suitable for further functionalization (Scheme 3.4).



Scheme 3.4 : Synthesis of Compound **6**

Tosylated azo derivatives were linked to the 7-position of the coumarin scaffold via nucleophilic substitution in the presence of K_2CO_3 as a base, KI to promote tosyl group departure, and DMF as the solvent at 75°C (Scheme 3.5). This reaction facilitated the efficient coupling of photoresponsive azo side chains to the coumarin unit, yielding hybrid compounds with fluorescent and photoresponsive properties. The new compounds, **AzoCouv-1a** and **AzoCouv-1b**, were obtained in yields of 40% and 32%, respectively. Their structures were fully characterized using ^1H , ^{13}C NMR, IR Spectroscopy, and HRMS (Appendices A, B and C).

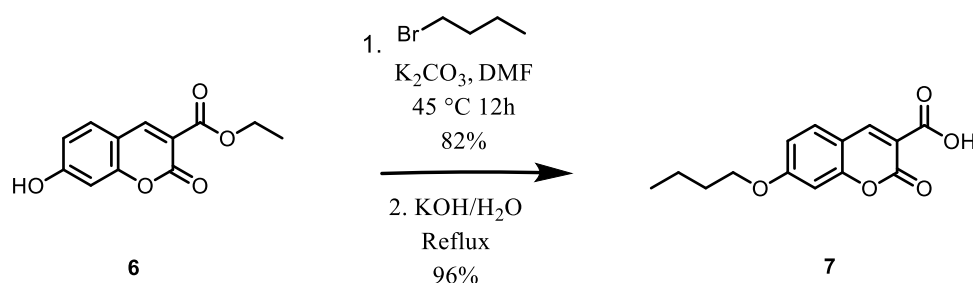


Scheme 3.5 : Synthesis of **AzoCouv-1a** and **AzoCouv-1b**

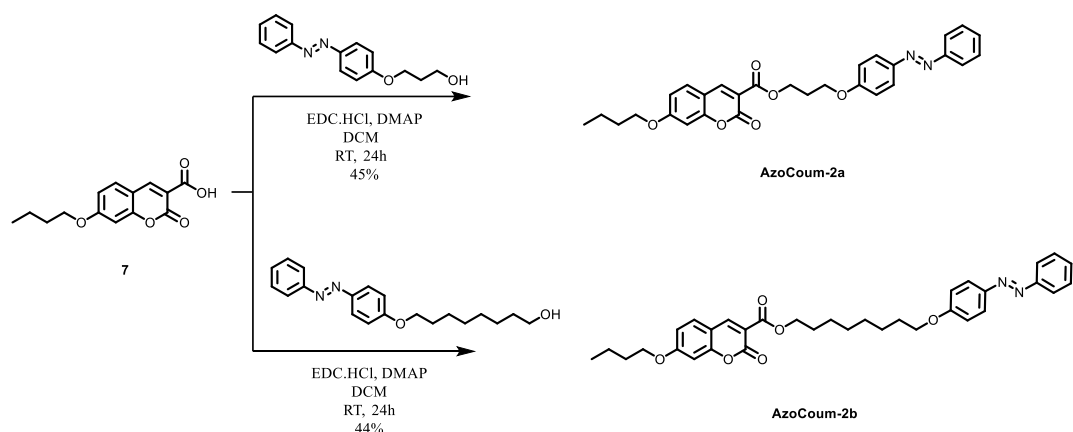
3.1.2.2 Synthesis of AzoCouv-2 Derivatives

A separate modification was made in order to distinguish the contribution of the 7th position and further investigate the positional consequences. By treating ethyl 7-hydroxycoumarin-3-carboxylate (compound **6**) with 1-bromobutane, the hydroxyl group at the coumarin unit's 7-position was capped with an alkyl chain.⁷⁶ By

protecting the 7-position, this step made sure that functionalization would only be allowed in the 3-position going forward. Following this, the ethyl ester at the 3-position was hydrolyzed in alkaline conditions and subsequently acidified, leading in the production of a carboxylic acid group (Scheme 3.6).⁷⁶ Later on, this group was used as a reactive handle for further derivatization. Aliphatic azo alcohols (Compounds **2** and **3**) were then used to functionalize the hydrolyzed coumarin derivative, attaching the photoresponsive side chains at the 3-position by using EDC.HCl (1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride) as a coupling agent (Scheme 3.7). Another new compounds, **AzoCoum-2a** and **AzoCoum-2b**, were obtained in yields of 45% and 44%, respectively. Their structures were fully characterized using ¹H, ¹³C NMR, IR Spectroscopy, and HRMS (Appendices A, B and C). A methodical examination of the impact of azobenzene side chains at various locations on the fluorescence and CD responses of the coumarin system was made possible by this established change.



Scheme 3.6 : Synthesis of Compound **7**

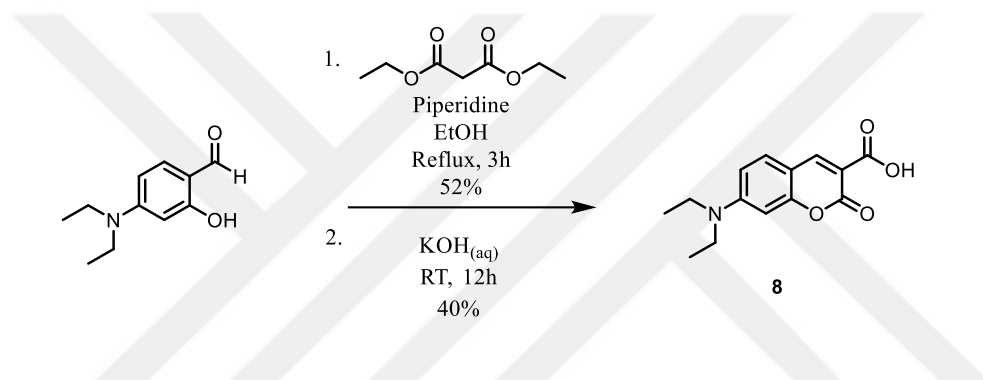


Scheme 3.7 : Synthesis of **AzoCouv-2a** and **AzoCouv-2b**

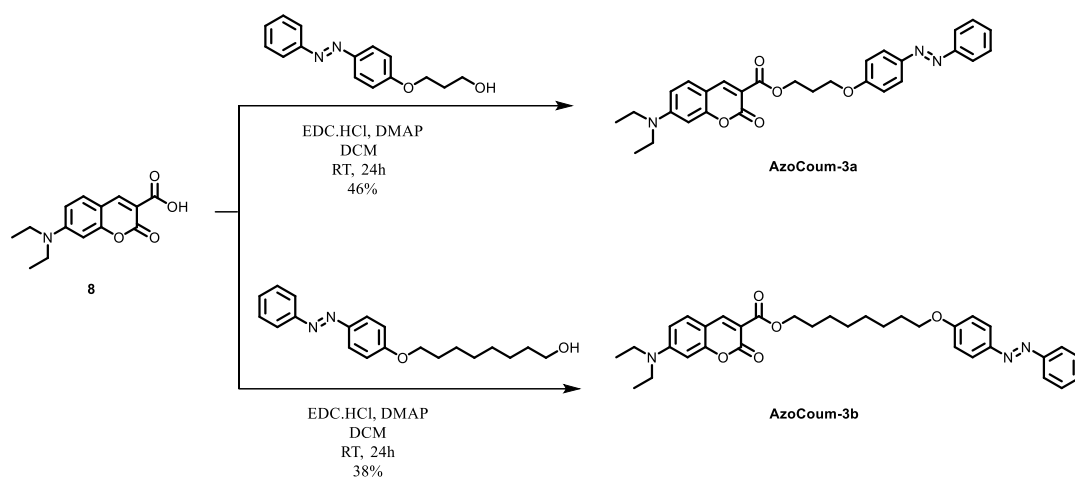
3.1.2.3 Synthesis of AzoCouv-3 Derivatives

To broaden the understanding of the impact of substituents located at the 7-position on the characteristics of fluorescence behavior, in the presence of photoresponsive azobenzene side chain, another synthetic procedure was initiated that yielded another coumarin derivative. Ethyl 7-(diethylamino)coumarin-3-carboxylate was chosen to investigate this incident. The diethylamino group serves as a strong electron-donating substituent in this compound. In the presence of piperidine as a base, 4-(diethylamino)-2-hydroxybenzaldehyde reacted with diethyl malonate to initiate the synthesis. Following the Knoevenagel condensation, the reaction was conducted in ethanol under reflux.⁷⁷ This led to the generation of a coumarin derivative with improved electron-donating capabilities at the 7th position, which is ethyl 7-(diethylamino)coumarin-3-carboxylate. To enable further functionalization, the ethyl ester group at the 3-position was hydrolyzed under basic conditions and then acidified to generate the corresponding carboxylic acid (Scheme 3.8). The

hydrolyzed coumarin derivative was subsequently functionalized using aliphatic azo alcohols (Compounds **2** and **3**), to obtain new compounds, in which the photoresponsive azobenzene side chains were attached to the 3- position. Using EDC.HCl coupling conditions again, **AzoCoum-3a** and **AzoCoum-3b** products obtained with the yields of 45% and 38% (Scheme 3.9). The characterization of the compounds was conducted using a variety of methods, including ^1H , ^{13}C NMR, IR spectroscopy, and HRMS. All spectra are provided in detail in Appendices A, B, and C.



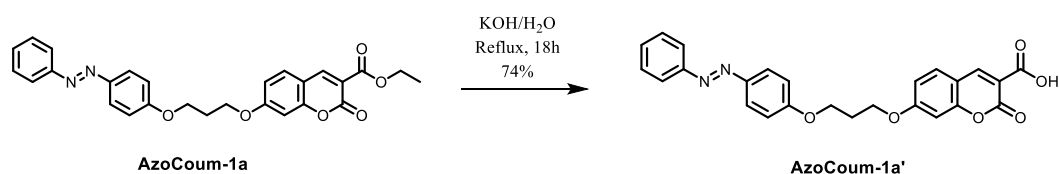
Scheme 3.8 : Synthesis of Compound **8**



Scheme 3.9 : Synthesis of **AzoCoum-3a** and **AzoCoum-3b**

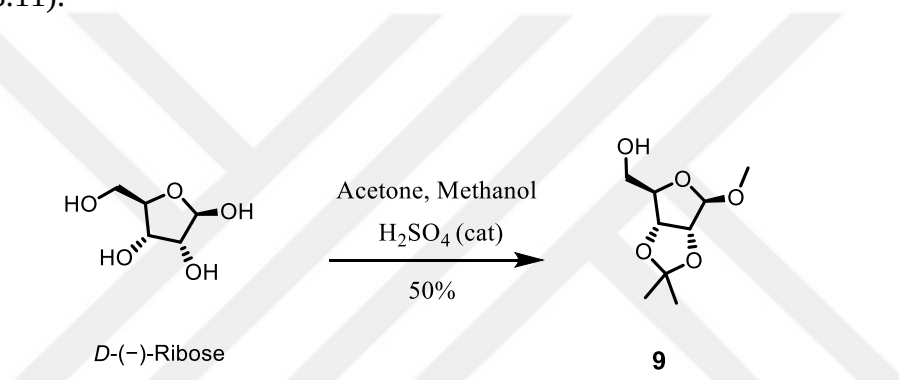
3.1.2.4 Synthesis of AzoCoumR Derivatives

To introduce chirality into the system, firstly we utilized **AzoCoum-1a**, the coumarin derivative previously synthesized with a 3-carbon aliphatic chain at the 7-position. The ethyl ester group at the 3-position of **AzoCoum-1a** was hydrolyzed under basic conditions and acidified to produce the corresponding carboxylic acid, **AzoCoum-1a'** (Scheme 3.10)



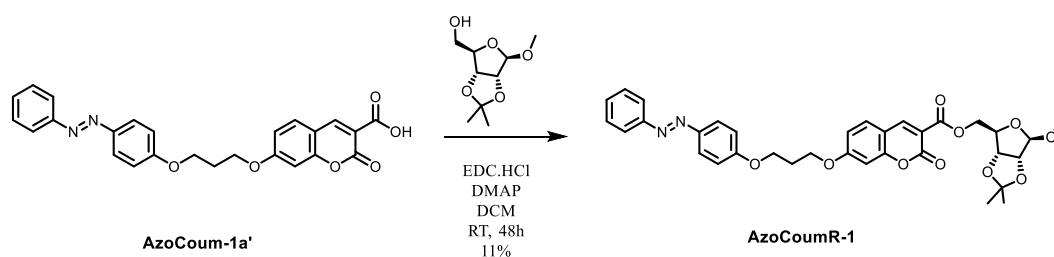
Scheme 3.10 : Synthesis of **AzoCoum-1a'**

This new carboxylic acid characterized with NMR and IR spectroscopy and was kept for coupling with a selectively protected *D*-(-)-ribose derivative as a chiral unit in desired compound. The *D*-(-)-ribose derivative was prepared by selectively protecting its hydroxyl groups to control its reactivity during the coupling reaction. Specifically, the hydroxyl groups at the C-2 and C-3 positions of ribose were protected as acetals, while the hydroxyl group at the C-1 position was methylated. This selective protection left the hydroxyl group at the C-5 position unprotected and available for reaction. The protection reaction was achieved in a single step by reacting *D*-(-)-ribose with acetone and methanol in the presence of catalytic H_2SO_4 (Scheme 3.11).⁷⁸



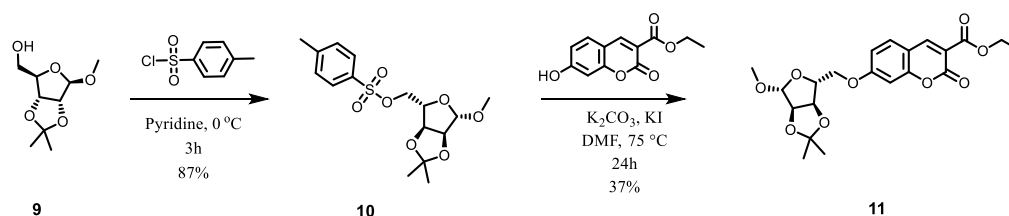
Scheme 3.11 : Synthesis of Compound **9**

Afterwards, the carboxylic acid group of **AzoCoum-1a'** was coupled with the unprotected primary hydroxyl group at position C-5, by using EDC.HCl as coupling agent, adding chirality to the system, with the yield of 11% (Scheme 3.12). The resulting chiral coumarin-azobenzene derivative, **AzoCoumR-1** was designed for further exploration of its chiroptical properties and its potential to modulate circular dichroism (CD) signals. A range of techniques, including ^1H , ^{13}C NMR, IR spectroscopy, and HRMS, were used to characterize the molecule. The corresponding spectra are provided in Appendices A, B, and C.



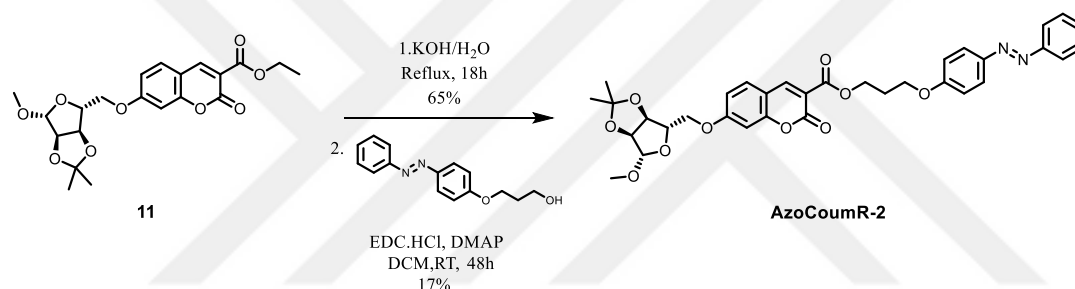
Scheme 3.12 : Synthesis of **AzoCoumR-1**

In order to further investigate the influence of the positional arrangement of the chiral unit and azobenzene side chain on the chiroptical properties, a new coumarin derivative was synthesized. In this derivative, the selectively protected *D*-(-)-ribose unit was attached to the 7-position of ethyl 7-hydroxycoumarin-3-carboxylate. Initially, the *D*-(-)-ribose derivative was tosylated to introduce a good leaving group. This was accomplished using tosyl chloride in pyridine, yielding a 87% yield of the tosylated ribose derivative.⁷⁹ Subsequently, the tosylated ribose derivative was subjected to a reaction with ethyl 7-hydroxycoumarin-3-carboxylate in the presence of K_2CO_3 , KI, and DMF at 75°C for a duration of 24 hours. This reaction resulted in the formation of the desired coumarin derivative, featuring the chiral sugar unit at the 7-position, with a yield of 37% (Scheme 3.13).



Scheme 3.13 : Synthesis of compounds **10** and **11**

Subsequently, the ethyl ester at the 3-position of the compound was hydrolyzed under basic conditions and then acidified to generate the carboxylic acid of **11**. Utilizing EDC·HCl coupling, a 3-carbon aliphatic azobenzene alcohol (**2**) was attached to this position, resulting in a new coumarin-based compound, **AzoCoumR-2**, where the azobenzene and chiral units were swapped in their positions. This final step resulted in the desired compound, with a 17% yield (Scheme 3.14). A series of techniques was employed, including ^1H , ^{13}C NMR, IR spectroscopy, and HRMS, to characterize the molecule. Raw data is given in Appendices A, B, and C. This structural modification enabled the exploration of the effects of the positional arrangement of the chiral sugar and azobenzene moieties on the chiroptical properties.



Scheme 3.14 : Synthesis of compounds **AzoCoumR-2**

3.2 Photophysical Studies

In our photophysical studies, we employed UV-Vis and Fluorescence spectroscopy. Each compound was subjected to these studies in four different solvents in order to investigate the solvent-dependent properties. CD measurements will be reported in a different subsection. In this section, we separated compounds into four different categories;

- i. Azobenzene side chain bonded to 7th position of 7-hydroxycoumarin derivative
(**AzoCoun-1a** and **Azocoun-1b**)
- ii. Azobenzene side chain bonded to 3rd position of 7-hydroxycoumarin derivative
(**AzoCoun-2a** and **AzoCoun-2b**)
- iii. Azobenzene bonded to 3rd position of 7-(diethylamino)coumarin derivative
(**AzoCoun-3a** and **AzoCoun-3b**)
- iv. Chiral sugar incorporated azobenzene-coumarin conjugates
(**AzoCounR-1** and **AzoCounR-2**)

3.2.1 UV-Vis and Fluorescence Studies

For the first set of compounds, solutions of compounds **AzoCoun-1a** and **Azocoun-1b** were prepared in DCM, MeCN, THF and MeOH. Before we start measuring the UV-vis spectra of these compounds, we record UV-Vis spectra of fragments, compounds **2** and **7**. Each spectrum of these compounds was plotted on a single figure (Figure 3.1) in order to distinguish absorption regions of each fragment for **AzoCoun-1a** and **Azocoun-1b**. Aliphatic azo-alcohol (compound **3**) shows an absorption peak $\lambda_{\max} = 320$ nm for $\pi \rightarrow \pi^*$ and $\lambda_{\max} = 450$ nm for $n \rightarrow \pi^*$ transition. The $n \rightarrow \pi^*$ transitions are not allowed (probability is low since the symmetry is not allowed). This can be seen in the Figure 3.2 that $\pi \rightarrow \pi^*$ transitions have more prominent absorption peaks than $n \rightarrow \pi^*$ transitions. On the same figure, 7-hydroxycoumarin derivative was also drawn, which shows $\lambda_{\max} = 356$ nm. The combination (addition) of these two spectra results in a spectrum that corresponds to

the spectra of **AzoCouv-1a**, **Azocouv-1b**, **AzoCouv-2a**, **AzoCouv-2b**, **AzoCouvR-1** and **AzoCouvR-2** (*vide infra*).

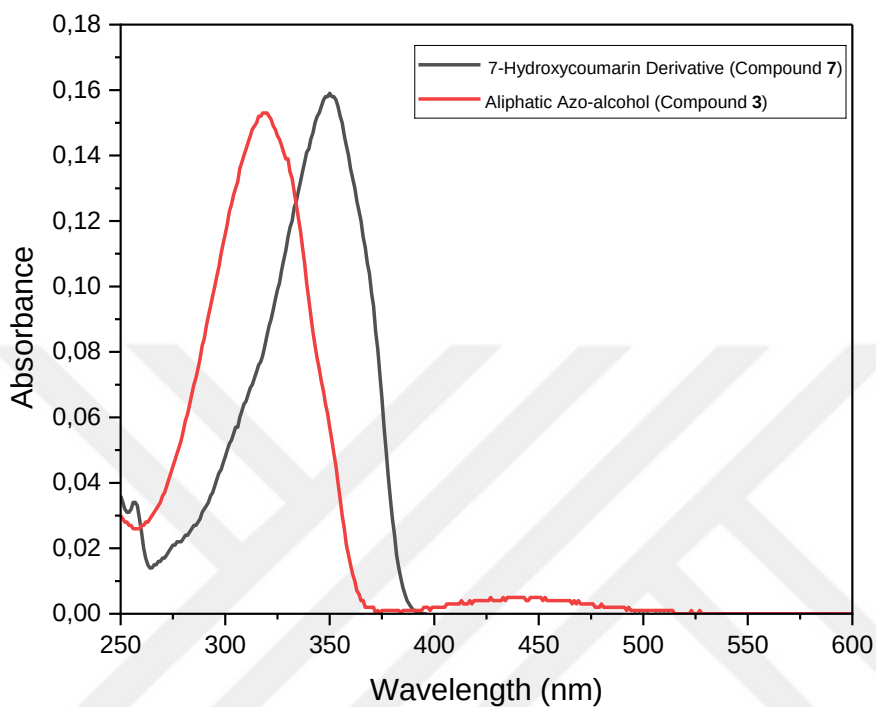


Figure 3.1 : UV-Vis spectra of compounds **2** and **7** in DCM (10^{-7} M)

In order to elaborate if the azobenzene side chain could undergo *trans* - *cis* transformation upon irradiation, aliphatic azo-alcohol (compound **2**) dissolved in DCM and irradiated with a 365 nm light source. With that, we observed that the absorption peak at around 350 nm decreased upon irradiation (Figure 3.2). This shows that the compound transformed from *trans* configuration to *cis* configuration. The light source we used, has a line-like shape with a spectral width =10 nm. The irradiating light source spectra overlaps with aliphatic azo-alcohol (compound **2**) in a small region; therefore the rapid conversion from *trans* to *cis* form is not observed. That is why even after 20 minutes of irradiation, still *trans* azobenzene was present

in the solution. Also, it should be noted that, irradiation of 7-butoxycoumarin unit with a 365 nm, did not affect the UV-Vis spectrum of the compound.

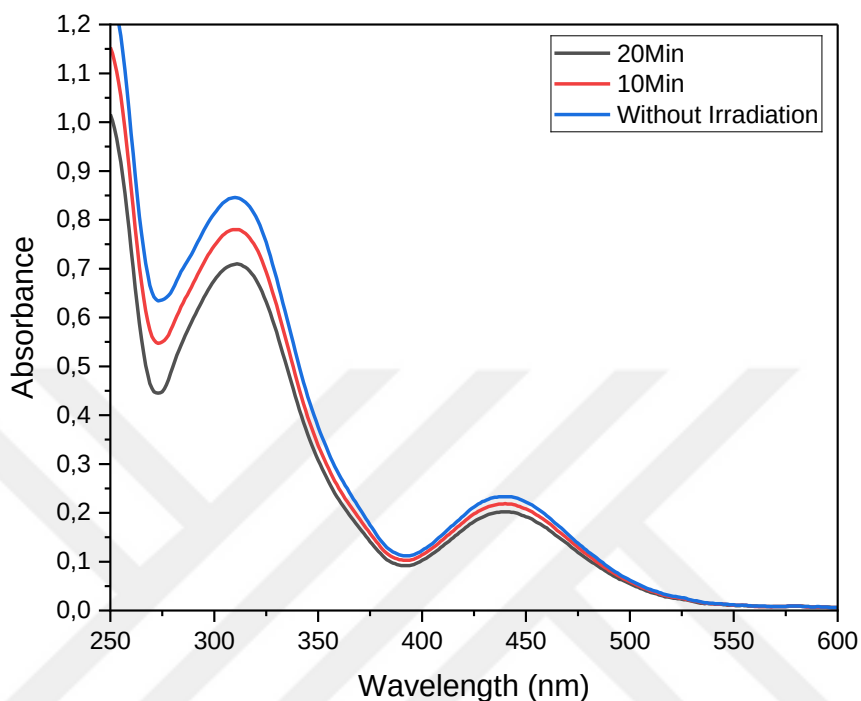


Figure 3.2 : UV-Vis spectra of aliphatic azo-alcohol (compound 2) upon irradiation in DCM (10^{-5} M)

With these results in hand, we started our studies with **AzoCouv-1a**, which azobenzene side chain connected to 7th position of the coumarin unit. This compound was a precursor for our chiral final compounds **AzoCouvR-1** and **AzoCouvR-2**. Before proceeding to studies of chiral compounds, **AzoCouv-1a** was studied with UV-Vis spectrum showing $\lambda_{\text{max}} = 348$, with shoulder at around 315 nm. After irradiation with 365 nm for 10 minutes, 20 minutes and 30 minutes, the absorption decreased. Expectedly, this shows that the *trans* azobenzene unit transformed into the *cis* azobenzene unit (Figure 3.3). In order to investigate if coumarin's fluorescence properties are changing during *trans-cis* isomerization, the

emission and excitation spectra of the **AzoCoum-1a** with exposure to the light ($\lambda = 365$ nm) were recorded. Although λ_{max} of excitation was similar to the UV-Vis spectra, as the compound was exposed to light, the excitation intensity increased. As to fluorescence spectra, a similar trend to excitation spectra was observed (Figure 3.3). Surprisingly, since the solution concentration did not change, this observation was unexpected.

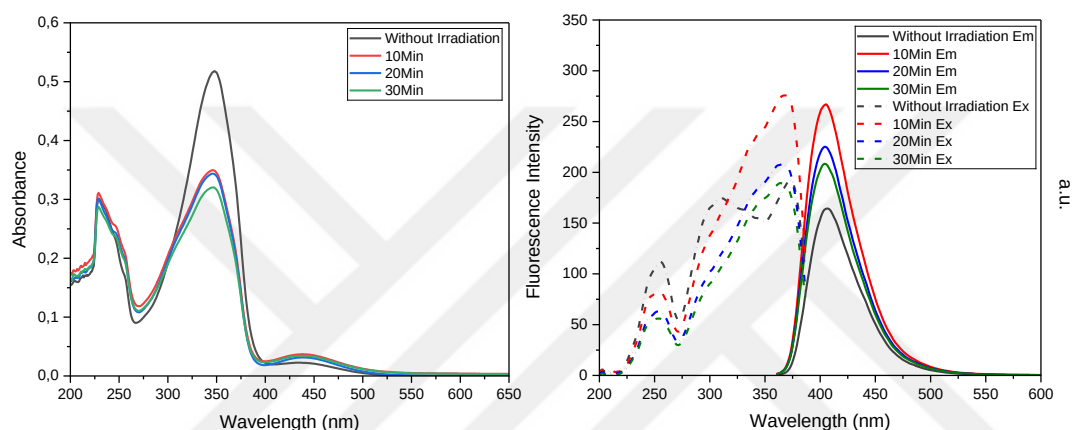


Figure 3.3 : UV-Vis and fluorescence spectra of **AzoCoum-1a** in DCM (10^{-5} M)

With this surprising observation in hand, in order to conclude if this observed phenomenon occurred due to the charge transfer, we ran the same experiments within the different solvents, i.e., THF, MeCN and MeOH. Charge transfer is known to be affected by solvent polarity.⁸⁰ Same phenomena as in DCM were observed for these different solvents (Appendices D and E). This excludes the possibility of photo-induced charge transfer affecting the fluorescence spectrum to some extent. If photoinduced charge transfer is a factor in these observations, the distance between azobenzene and coumarin unit should also be affected.

To test this approach, a derivative called **AzoCoum-1b** was constructed, in which an 8-carbon linker separated the azobenzene and coumarin units. The purpose of the

longer chain was to test whether the fluorescence behavior is changed by the greater separation between the coumarin core and the photoresponsive azobenzene unit. Through this alteration, we were able to investigate whether the azobenzene group's close proximity promotes or inhibits charge transfer processes or any conformational changes that affect the molecule's photophysical characteristics. We compared the optical responses of **AzoCouv-1a** and **AzoCouv-1b** to acquire a better understanding of how the relative position of the azobenzene side chain influences coumarin fluorescence. For this purpose, we applied the same procedure, in which the 365 nm light irradiation was performed for 10 minutes, 20 minutes, and 30 minutes, and UV-Vis and fluorescence studies operated in DCM (Figure 3.4). Analyzing **Azocouv-1b**'s excitation and emission spectra revealed a rise in fluorescence intensity upon azobenzene isomerization, which is consistent with the trend reported in **AzoCouv-1a**, the 3-carbon-linked analog. However, compared to the 3-carbon analog, the 8-carbon-linked system's fluorescence amplification was observed to be proportionately smaller. Conversely, the fluorescence intensity of the 8-carbon-linked compound was notably higher than that of **AzoCouv-1a** before isomerization. To check solvent-dependency, we also performed these analyses again in THF, MeCN, and MeOH, and results were consistent with DCM (Appendices D and E).

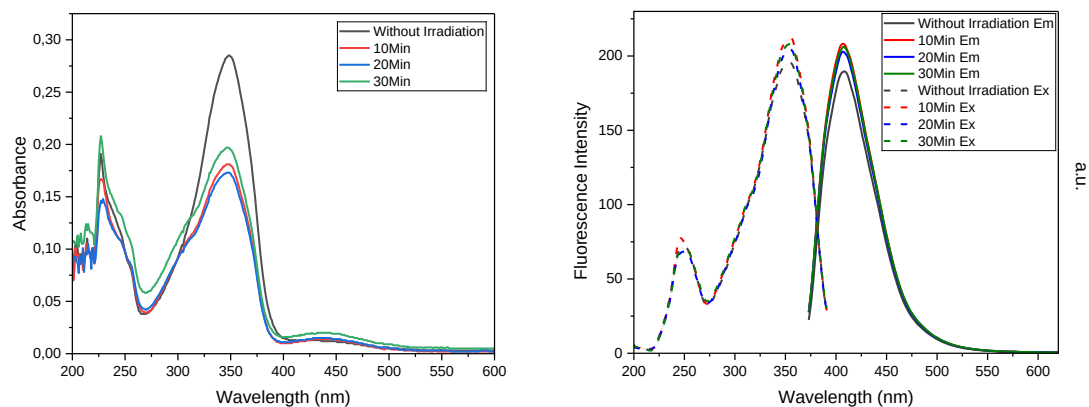


Figure 3.4 : UV-Vis and fluorescence spectra of **AzoCoun-1b** in DCM (10^{-5} M)

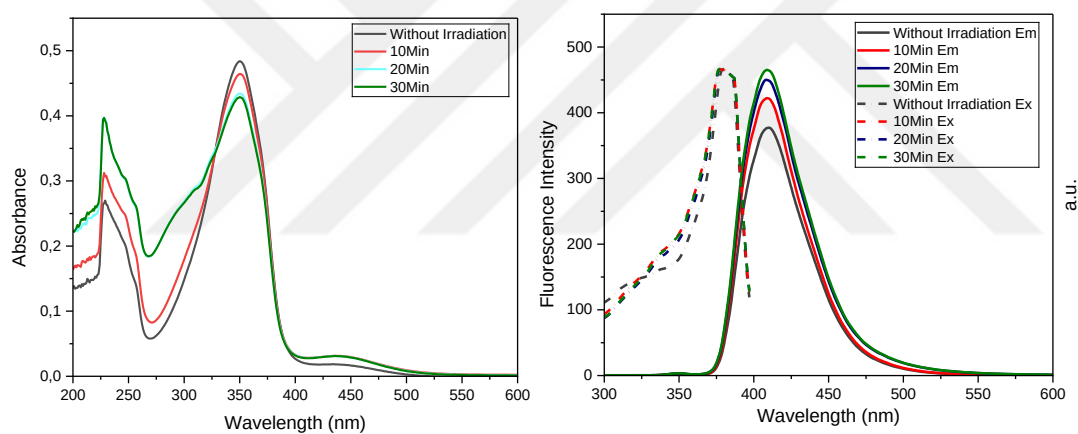


Figure 3.5 : UV-Vis and fluorescence spectra of **AzoCoun-2a** in DCM (10^{-5} M)

In order to further explore the positional effects of substituents on fluorescence enhancement, two new derivatives were synthesized: **AzoCoum-2a** and **AzoCoum-2b**. In these compounds, the 7th position of the coumarin core was capped with a butyl group, effectively removing any potential interaction at this position. This design serves to isolate the role of the azobenzene-coumarin interaction at a singular position, thereby facilitating a more comprehensive understanding of its influence. This approach enabled us to concentrate specifically on the impact of azobenzene side chains attached to the 3-position via linkers of varying lengths (3-carbon and 8-carbon aliphatic azo alcohols). With this, **AzoCoum-2a** and **AzoCoum-2b** dissolved in DCM and UV-Vis ($\lambda_{\text{max}} = 350$ nm for both), and fluorescence study was performed in the same manner mentioned above. Results are shown in Figure 3.5 and Figure 3.6, which are consistent with **AzoCoum-1a** and **AzoCoum-1b**.

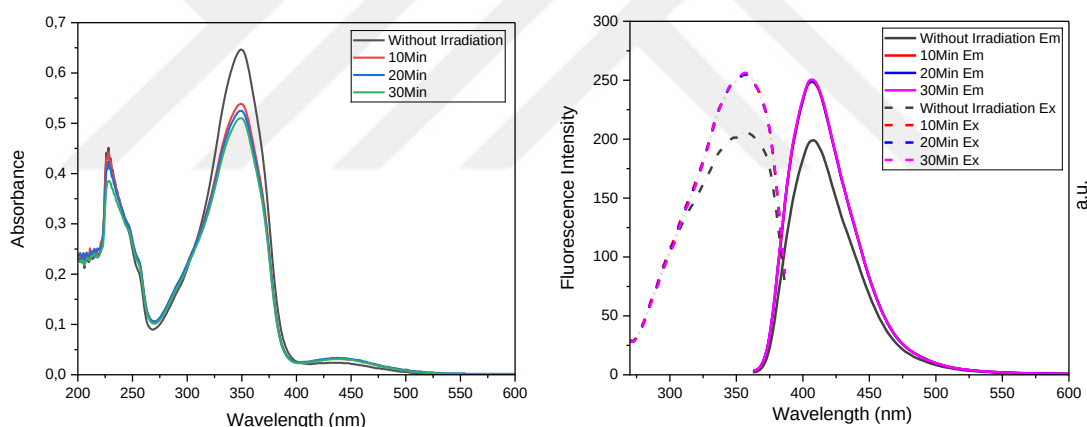


Figure 3.6 : UV-Vis and fluorescence spectra of **AzoCoum-2b** in DCM (10^{-5} M)

The results demonstrated a consistent enhancement in fluorescence intensity upon the *trans*-to-*cis* isomerization of the azobenzene unit across other solvents: THF, MeCN and MeOH, each with varying polarity (Appendix E). The fluorescence intensity of both **AzoCoum-2a** and **AzoCoum-2b** exhibited variation depending on the solvent, as expected. This variability can be attributed to differences in solvent

polarity, which can alter the electronic environment around the coumarin core and azobenzene unit, affecting their individual and combined photophysical properties. While both compounds exhibited fluorescence enhancement, the magnitude of the increase was notably different. The 3-carbon-linked **AzoCoum-2a** demonstrated a more dramatic enhancement compared to the 8-carbon-linked **AzoCoum-2b** in all solvents. This observation indicates that the increased proximity of the azobenzene unit to the coumarin core in **AzoCoum-2a** enables more efficient electronic interaction or energy transfer, thereby amplifying the fluorescence response upon isomerization. Despite the observed differences in fluorescence intensities within each solvent, the overall trend of fluorescence enhancement was the same.

With all these results in mind (*vide supra*), it was decided that the coumarin absorption should be shifted to the bathochromic region compared to the azobenzene absorption region. This shifting, in turn, will create an absorption spectrum on which the chromophore units will have separated absorptions. With this, we could control *trans-cis* isomerization better without disturbing the coumarin unit's absorption region so that *trans-cis* isomerization interfering with coumarin unit absorption will have a minimum value. For this purpose, we synthesized **AzoCoum-3a** and **AzoCoum-3b**. Installing the diethylamino group at the 7th position of the coumarin shifted the absorption of the coumarin unit to the red region. This choice separated the coumarin chromophore from the azobenzene chromophore in the UV-Vis spectrum (Figure 3.7). Irradiating the compound in DCM at 365 nm led to a disappearance of the absorption at 340 nm (azobenzene region). This shows the *trans*-azobenzene side chain converted into its *cis* form. The same pattern was observed for different solvents (Appendix D).

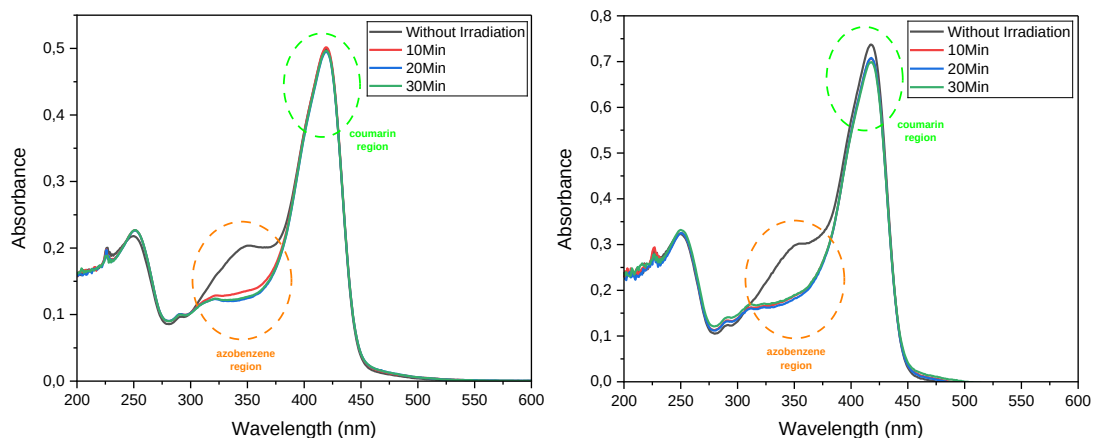


Figure 3.7 : UV-Vis spectra of **AzoCoun-3a** and **AzoCoun-3b** in DCM (10^{-5} M)

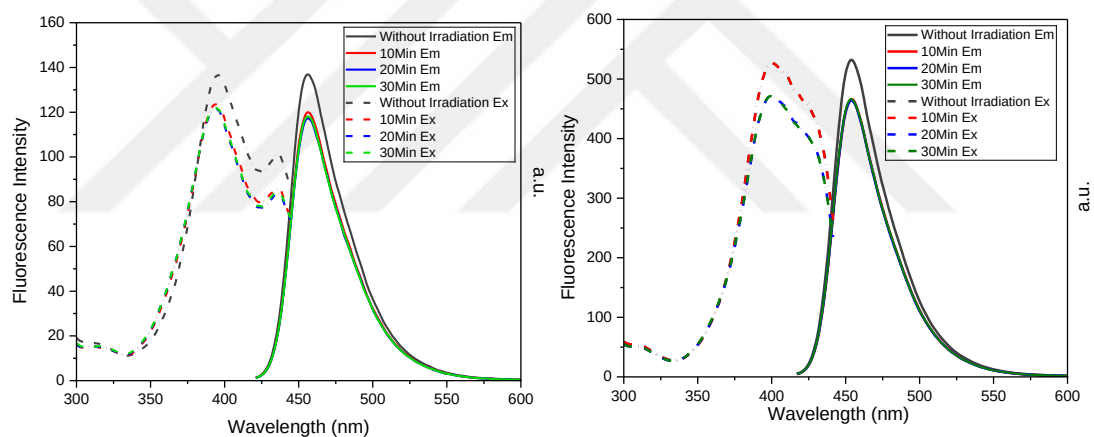


Figure 3.8 : Fluorescence spectra of **AzoCoun-3a** and **AzoCoun-3b** in DCM (10^{-5} M)

As to the emission properties of these compounds with azobenzene in *trans* form and *cis* form, the spectra were recorded without and after irradiation. When compounds were excited with light of $\lambda_{\text{max}} = 398$ nm, we observed fluorescence at around 455 nm. Contrary to previous observations, azobenzene in the *cis* form

caused a decrease in fluorescence intensity (Figure 3.8). To elaborate on this observed abnormal effect of *trans-cis* isomerization of these compounds, one needs to investigate this phenomenon theoretically.

Another compound, **AzoCoumR-1**, was synthesized by modification of **AzoCoum-1a** through the hydrolysis of ethyl ester part at 3rd position of the coumarin unit and reacting with protected D-(-)-ribose to introduce chirality into the system. The photophysical behavior of this compound was analyzed using UV-Vis and fluorescence spectroscopy in four different solvents similar to other compounds. Results for DCM measurements are shown in Figure 3.9, other measurements employing different solvents, i.e., THF, MeCN and MeOH, was added to Appendices D and E. During the *trans-cis* isomerization process, which was monitored via UV-Vis, an increase in fluorescence intensity was observed. This behavior matched that of **AzoCoum-1a**, its non-chiral counterpart. This outcome was expected, as the chromophoric units and molecular backbone of both compounds are identical, with the only distinction being the incorporation of the ribose unit. However, while the fluorescence trend during isomerization exhibited consistency with **AzoCoum-1a**, the overall fluorescence intensity of the ribose-containing derivative was notably lower. This reduced intensity can be attributed to the presence of the ribose unit, which may introduce additional non-radiative decay pathways or influence the local electronic environment, thereby reducing the quantum yield of fluorescence compared to the simpler, sugar-free analog. These findings highlight the slight but measurable impact of structural alterations on fluorescence characteristics, emphasizing the significance of the chromophore environment and substituent effects in photophysical research.

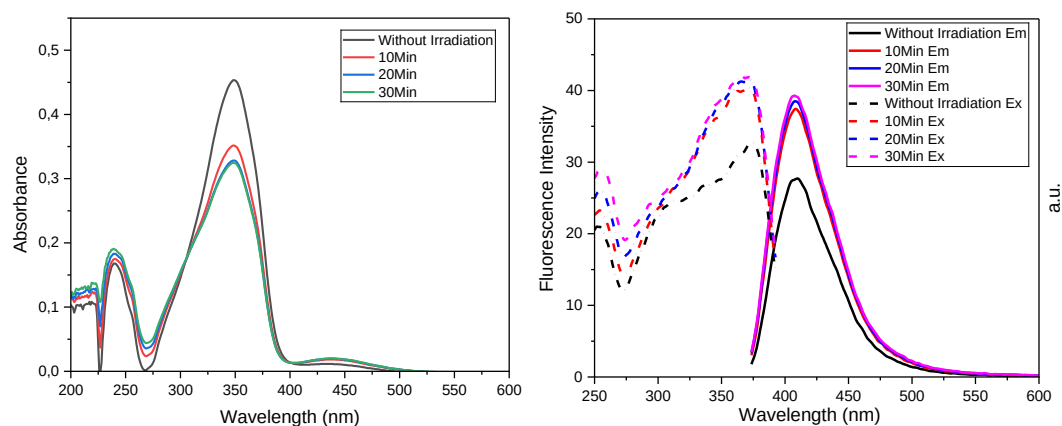


Figure 3.9 : UV-Vis and fluorescence spectra of **AzoCounR-1** in DCM (10^{-5} M)

The compound **AzoCounR-2**, featuring a protected *D*-(-)-ribose unit at the 7th position of coumarin unit and an azobenzene moiety linked via a propyl chain at the 3rd position, was synthesized to investigate the effect of the positional changes of the chiral unit on both fluorescence and chiroptical properties. To this end, a series of UV-Vis and fluorescence studies were conducted in four distinct solvents, a practice that has been standard for other compounds to monitor their photophysical behavior and evaluate the impact of incorporating the chiral unit. UV-Vis and fluorescence studies results are given in Figure 3.10 for DCM. For other solvents, results are added to Appendices D and E. The results obtained from these studies indicated that the *trans-cis* isomerization of the azobenzene moiety, as monitored through UV-Vis spectroscopy, led to an enhancement in fluorescence intensity. This finding is consistent with the observations reported for previous analogs, such as **AzoCoun-2a**, which has butyl group at its 7th position. However, the fluorescence intensity of **AzoCounR-2** in all solvents was higher compared to its other chiral counterpart, **AzoCounR-1**, likely due to the absence of the bulky chiral moiety influencing the environment around the coumarin unit is. Despite the overall higher fluorescence intensities, the same trend of fluorescence enhancement upon *trans-cis* isomerization was observed, consistent with the behavior of other azobenzene-functionalized

coumarin derivatives. This observation indicates that the proximity and orientation of the azobenzene unit relative to the coumarin chromophore, in addition to the ribose substitution, play a key role in determining the photophysical properties of the compound. These findings underscore the significance of structural modifications, such as positional swapping of functional groups, in the regulation of fluorescence and the elucidation of molecular interactions within these systems.

While these studies primarily served as a preparatory investigation to determine if the chiral unit would influence Circular Dichroism (CD) properties, they did also contribute to enhanced fluorescence behavior. By altering the position of the chiral unit, the study aimed to elucidate its role in the optical and chiroptical behavior of the system. This investigation provided critical insights into the positional dependency of chiral and azobenzene units on CD responses.

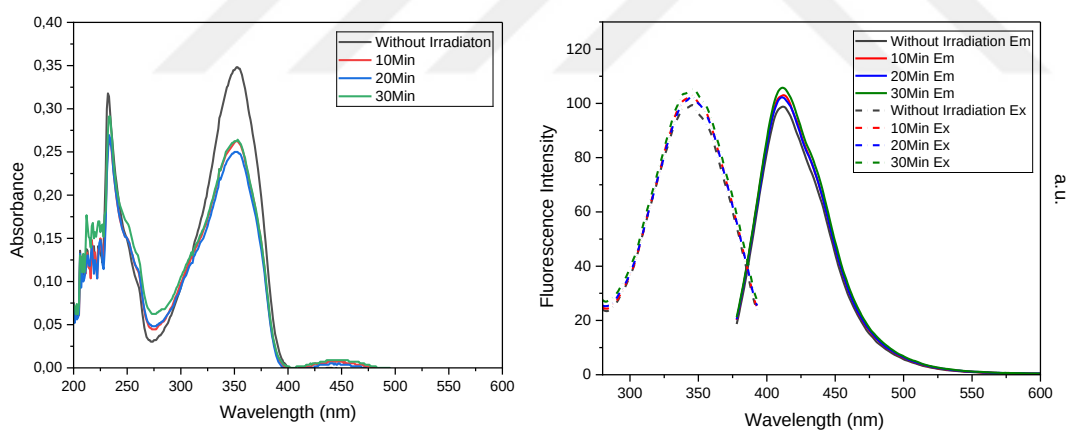


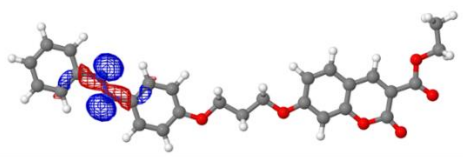
Figure 3.10 : UV-Vis and fluorescence spectra of **AzoCoumR-2** in DCM (10^{-5} M)

3.3 Computational Studies

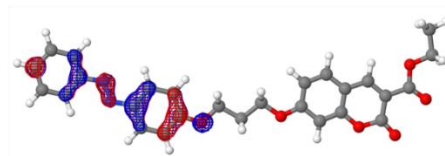
The geometries of all the above-mentioned compounds were optimized at the B3LYP/6-31g(d) level of theory as implemented in Gaussian 09.⁸¹ The *cis* forms of these compounds were also optimized at the same level. In order to shine light on the fluorescence properties observed above, we also performed population analysis and time-dependent DFT calculations.

To minimize the computation time for 7-butoxycoumarin compounds (**AzoCoun-2a** and **AzoCoun-2b**), butyl group at the 7th position of these derivatives was replaced with the methyl group. Optimization shows that the compounds did not aggregate within themselves. This shows that there is no force to stack the coumarin unit with the azobenzene unit. The basic assumption in our calculations is that the octyl linker will not affect the photophysical properties. It was given that no interaction between azo and coumarin units was observed for calculations for propyl linker unit. The same trend was observed for **AzoCoun-1a** and **AzoCoun-3a**.

On these optimized geometries, population analysis was done at the B3LYP/6-31g(d) level. The visualization of molecular orbitals were done by using Jmol.⁸² For azobenzene unit at its *trans* form, attached to 7th (Figure 3.11) and 3rd (Figure 3.12) position of coumarin, resulted in the same frontier orbitals, that is HOMO-1 is located on nonbonding orbitals of azo units, HOMO is located on π MO of azo unit, LUMO is located on coumarin and LUMO+1 is located on the π^* MO of azo unit. The calculation results are obtained in Hartree and converted to eV. With this conversion, it is more clearly seen that the frontier molecular orbitals of **AzoCoun-1a** and **AzoCoun-2a**, where the coumarin of the azobenzene unit is located at the 7th and 3rd position, respectively, are not only located at the same places but also have similar energies.



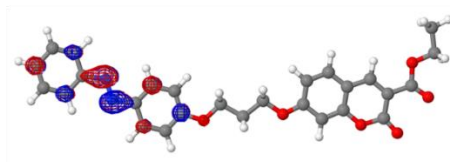
HOMO-1 (123) (E= -6.117 eV).



HOMO (124) (E=-5.880 eV)

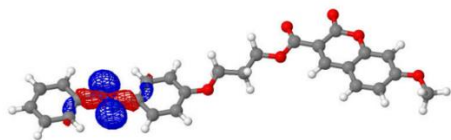


LUMO (125) (E=-2.225 eV).

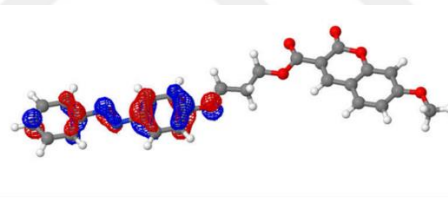


LUMO+1 (126) (E=-2.130 eV)

Figure 3.11 : Frontier molecular orbitals of *trans*-**AzoCoum-1a**



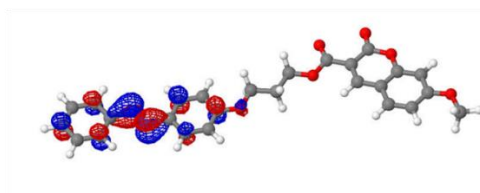
HOMO-1 (119) (E=-6.014 eV)



HOMO (120) (E=-5.760 eV)



LUMO (121) (E=-2.272 eV)



LUMO+1 (122) (E=-2.026 eV)

Figure 3.12 : Frontier molecular orbitals of *trans*-**AzoCoum-2a**

For the *cis* form of these compounds (**AzoCouv-1a** and **AzoCouv-2a**), HOMO LUMO and LUMO+1 stayed in the same order, while HOMO-1 is now located on coumarin for both. This could be easily understood due to the conjugation being disrupted for the *cis* form, on the azobenzene unit (Figure 3.13 and Figure 3.14). The frontier orbital energy resemblance that we observed in the *trans* form was also observed in the *cis* form of these substances; that is, as we expected, the frontier orbitals of both substances have similar energies.

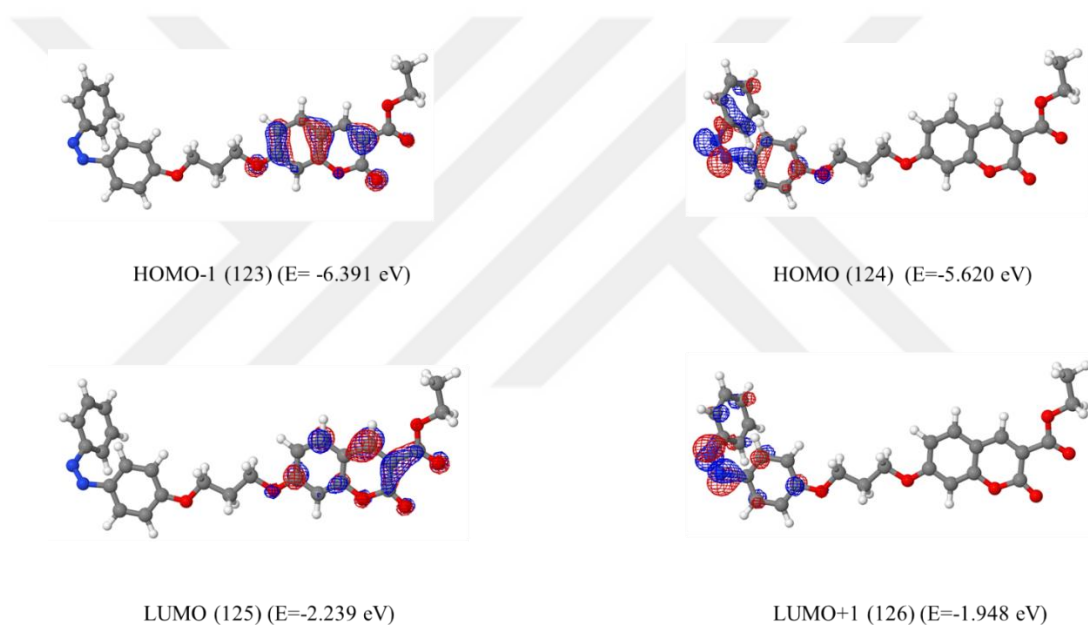


Figure 3.13 : Frontier molecular orbitals of *cis*-**AzoCouv-1a**

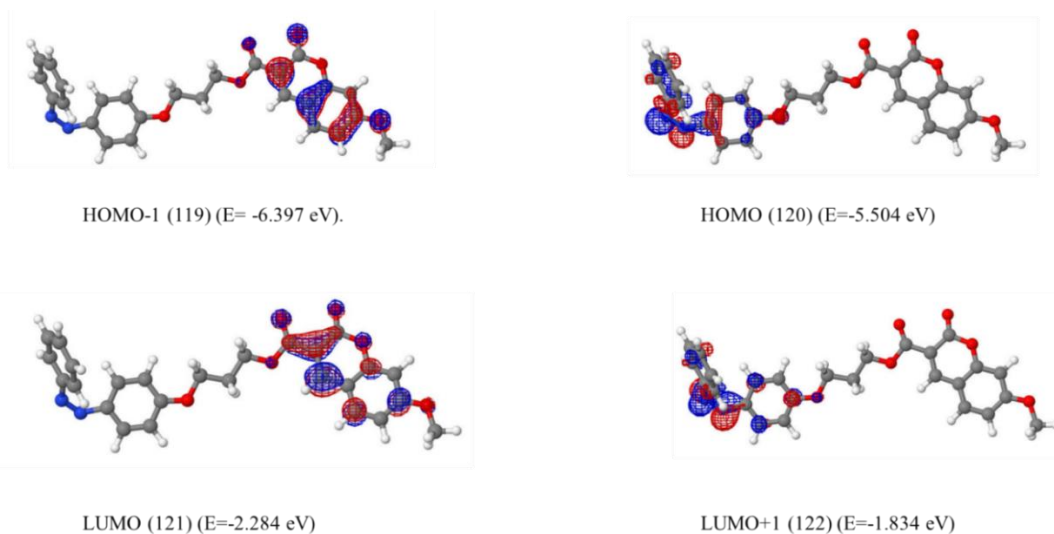


Figure 3.14 : Frontier molecular orbitals of *cis*-**AzoCoum-2a**

For the 7-(diethylamino)coumarin derivative compound (**AzoCoum-3a**), the coumarin unit has more contribution to the frontier molecular orbitals that the HOMO and LUMO+1 are located on coumarin, while HOMO-1 and LUMO are located on the azobenzene unit for the *trans* form (Figure 3.15). In the *cis* form, the contribution of chromophores to the molecular orbitals exchanged, that is, HOMO-1 and LUMO are located on coumarin while HOMO and LUMO+1 are located on the azobenzene unit (Figure 3.16).

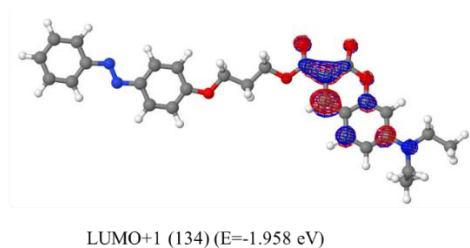
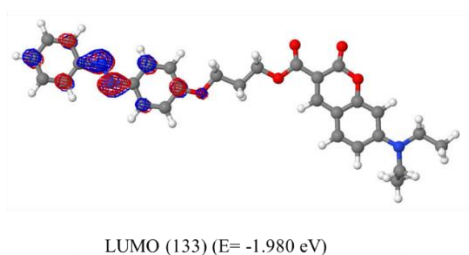
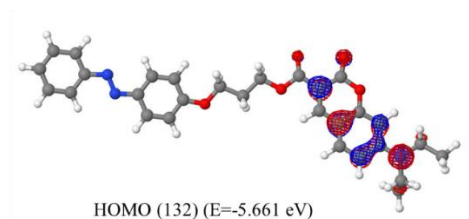
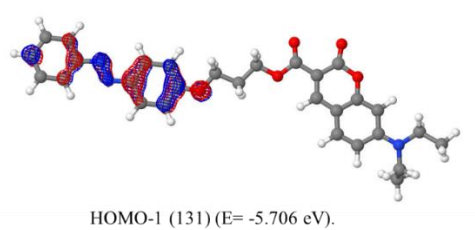


Figure 3.15 : Frontier molecular orbitals of *trans*-AzoCoum-3a

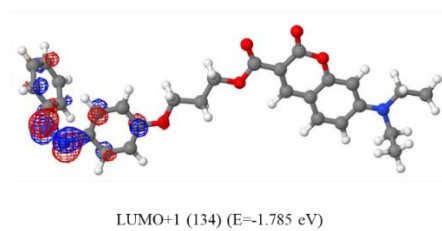
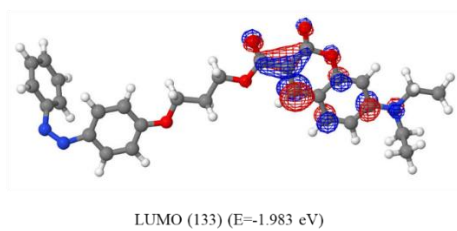
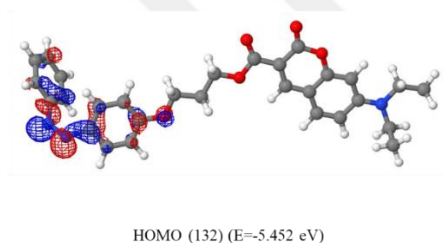
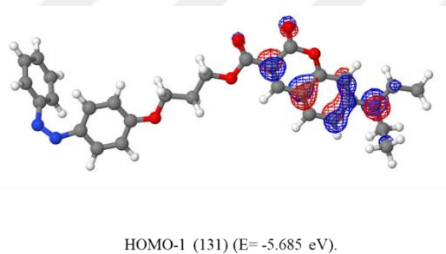


Figure 3.16 : Frontier molecular orbitals of *cis*-AzoCoum-3a

Time-Dependent DFT calculations were run for these compounds. Table 3.1 shows the corresponding transitions with their probabilities (oscillator strength). The calculations were performed at the CAM-B3LYP/6-31g(d) level of theory as implemented in Gaussian 09. Due to the computational cost, we calculated three vertical excitations. The results are tabulated in Table 3.1. Vertical transitions show that the transitions are isolated; that means transitions from the azobenzene unit to the coumarin unit or vice versa are not observed. This is consistent with the experimental observations. As we irradiated *trans*-azobenzene compounds (**AzoCouv-1a**, **AzoCouv-2a**, and **AzoCouv-3a**) with 365 nm UV light to convert them into *cis* form, there is no change on the UV-Vis spectrum for the corresponding coumarin region. The same is valid for the amino compounds' coumarin region. These results implies that there is no effect of *cis* and *trans* isomerization on fluorescence.

Table 3.1 : Transitions with their oscillator strengths for calculated wavelengths

Compound/td	<i>trans</i>				<i>cis</i>			
	λ (nm)	f (oscillator strength)	Transition	Transition Type (Most Contribution)	λ (nm)	f (oscillator strength)	Transition	Transition Type (Most Contribution)
AzoCouv-1a	448	0.0000	122-126		467	0.0415	124-126	HOMO->LUMO+1
	320	1.2631	124-126	HOMO->LUMO+1	302	0.6403	123-125	HOMO-1->LUMO
	302	0.3789	123-125	HOMO-1->LUMO	280	0.0010	118-125	
AzoCouv-2a	476	0.0000	119-122	HOMO-1->LUMO+1	485	0.0585	120-122	HOMO->LUMO+1
	383	0.0006	120-121	HOMO->LUMO	415	0.0001	120-121	HOMO->LUMO
	351	0.0000	119-121	HOMO-1->LUMO	328	0.0010	114-121	
AzoCouv-3a	497	0.0000	130-133		510	0.0491	132-134	HOMO->LUMO+1
	354	1.4709	132-133	HOMO->LUMO	348	0.1285	132-133	HOMO->LUMO
	346	0.2389	131-134	HOMO-1->LUMO+1	347	0.6462	131-133	HOMO-1->LUMO

With the theoretical calculations in hand, we attempted to explain the increase for **AzoCouv-1a** and **AzoCouv-2a** and the decrease for **AzoCouv-3a**. Theoretical calculations show that the *trans-cis* azobenzene conversion does not have any effect on vertical excitations and, thus, on fluorescence. When we closely examined our experimental results, we realized that, in the excitation wavelength, the *trans*-

azobenzene unit has an absorption. In the *cis* form, that absorption vanishes; thus more photons are available for exciting coumarin units.

On the other hand, for the *trans* form, the number of photons reaching to the coumarin moiety is less than that of the *cis* form, which leads to a lower fluorescence intensity compared to the *cis* form. As a result, as the *trans*-azobenzene converted to the *cis* form, a fluorescence increase was observed for **AzoCoum-1a** and **AzoCoum-2a**.

As to **AzoCoum-3a**, a fluorescence intensity decrease should be explained differently due to the fact that the excitation wavelength is not in the region of the azobenzene absorption band. As we converted *trans*-azobenzene into the *cis* form, the $n \rightarrow \pi^*$ band (around 410-450 nm) increased. That region falls into the emitting region of 7-(diethylamino)coumarin unit. This shows that coumarin fluorescence, $n \rightarrow \pi^*$ region absorbs these photons. This, in turn, leads to a decrease in fluorescence of **AzoCoum-3a** and **AzoCoum-3b**.

The procedures utilized for the sugar-incorporated derivatives, **AzoCoumR-1** and **AzoCoumR-2**, are analogous to those employed in computational studies. In accordance with predictions, the placements of frontier orbitals for both *trans* and *cis* isomers of these compounds, **AzoCoumR-1** (Figure 3.17 and Figure 3.18) and **AzoCoumR-2** (Figure 3.19 and Figure 3.20) demonstrate similarity to their sugar-free analogues. This observation accounts for the finding that, despite the incorporation of the protected *D*-(-)-ribose resulting in a decrease in overall fluorescence intensity, it did not exert an effect on the fluorescence enhancement behavior.

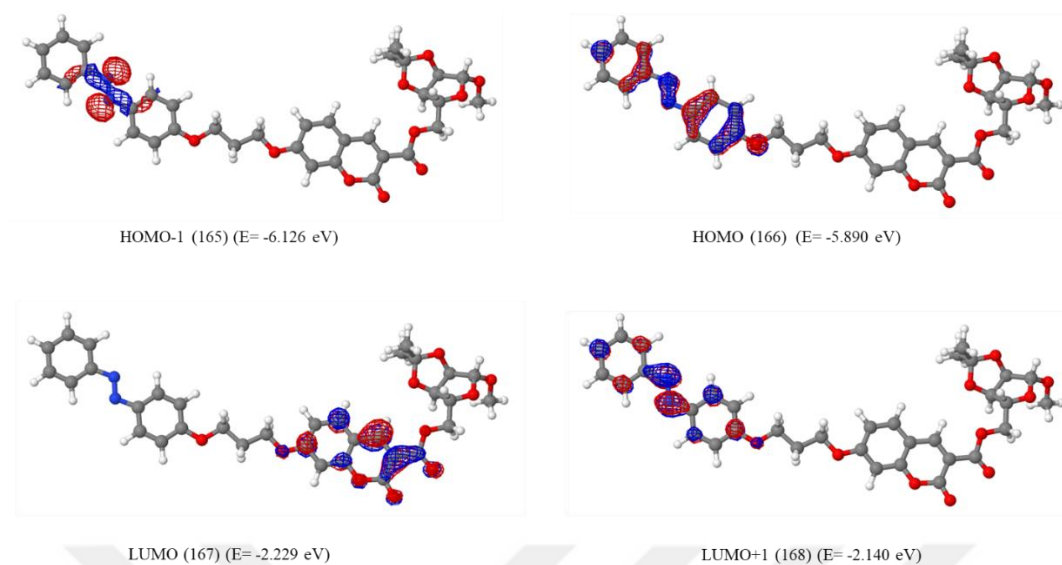


Figure 3.17 : Frontier molecular orbitals of *trans*-AzoCoumR-1

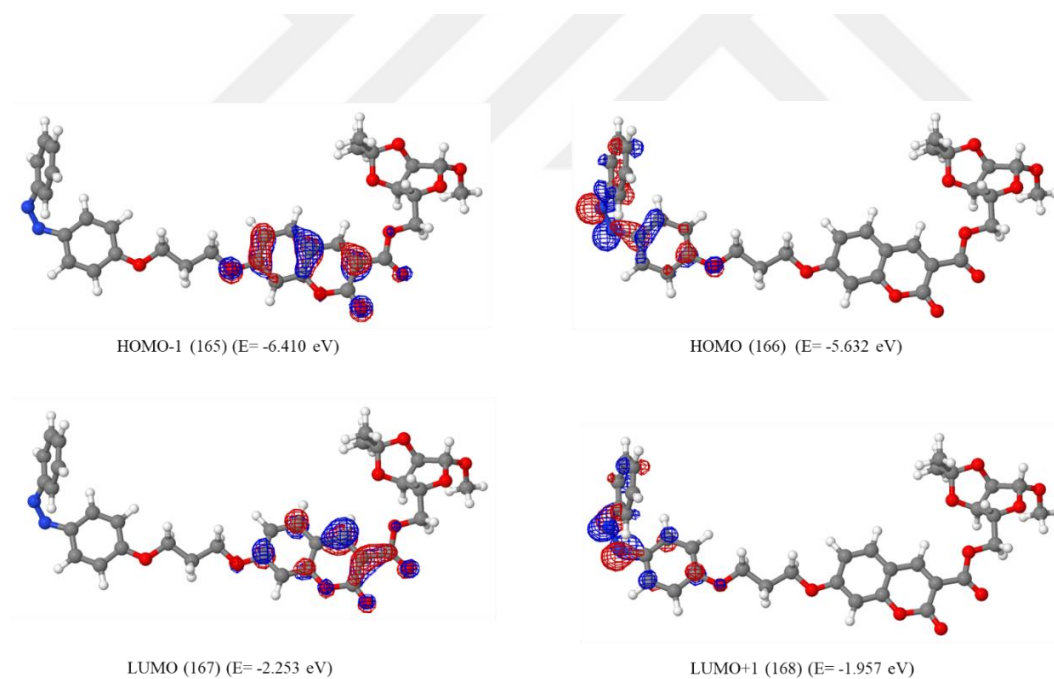


Figure 3.18 : Frontier molecular orbitals of *cis*-AzoCoumR-1

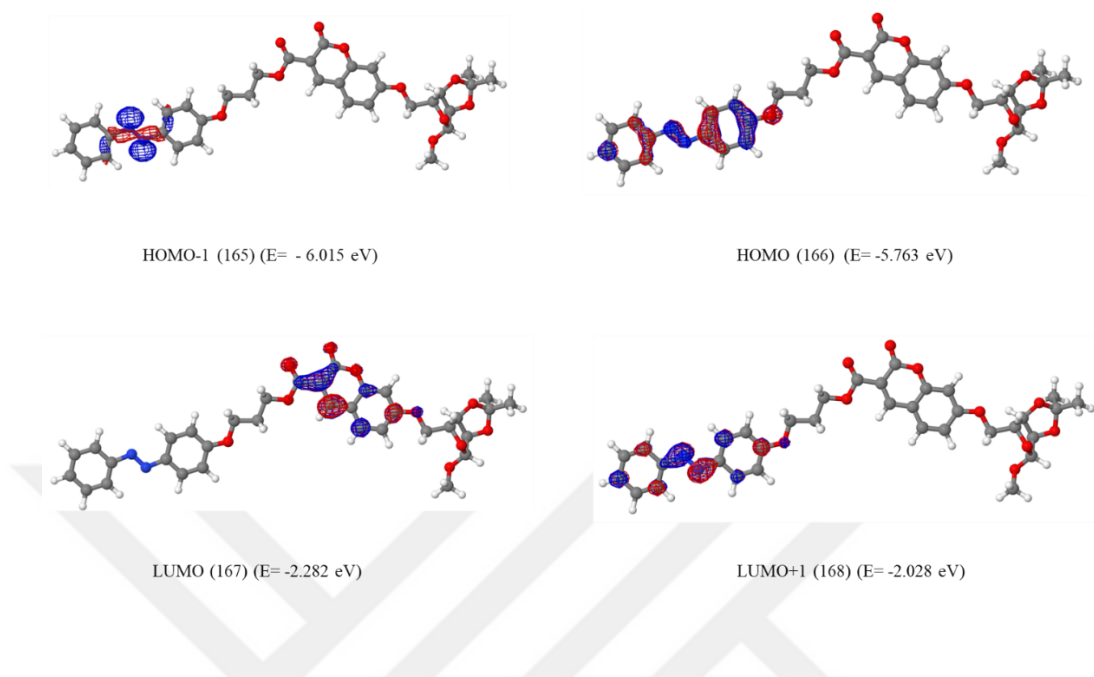


Figure 3.19 : Frontier molecular orbitals of *trans*-AzoCouvR-2

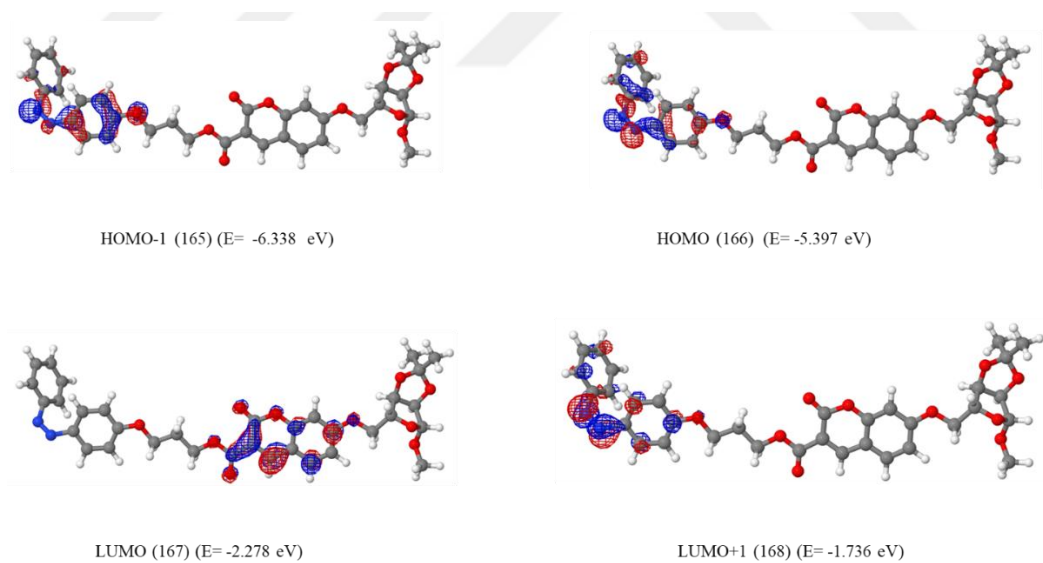


Figure 3.20 : Frontier molecular orbitals of *cis*-AzoCouvR-2

3.4 Circular Dichroism Studies

As a chiral moiety, we chose *D*-(-)-ribose because of its abundance and ease of further functionalization. As expected, *D*-(-)-ribose was easily protected in acetone and methanol, leaving the primary alcohol group intact. This alcohol group was attached to the coumarin unit at either the 3rd or 7th position of the coumarin. The sugar moiety provided chiral centers to our molecules. As known from previous studies, coumarin units exhibit CD signals upon the attachment of a chiral unit.^{63,74} Based on this understanding, we synthesized **AzoCouvR-1** and **AzoCouvR-2**. Both compounds showed positive CD signals in different solvents, including DCM, MeCN, THF, and MeOH (Figure 3.21).

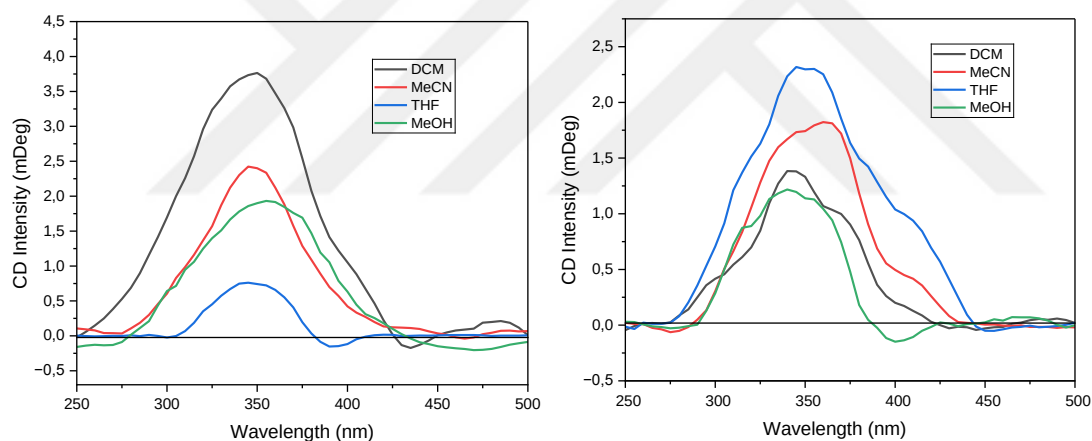


Figure 3.21 : CD spectra of **AzoCouvR-1** and **AzoCouvR-2** in different solvents (5×10^{-5} M)

As to irradiation of the compound **AzoCoumR-1**, which is the chiral moiety attached to 3rd position, the CD changes were observed upon shining light at 365 nm. In DCM, this change was seen as decrease in CD signal intensity with small fluctuations in λ_{max} compared to the *trans* form (Figure 3.22). In MeCN, the decrease was more than that in DCM. Interestingly, in THF, as we irradiated (*trans* isomer converted into *cis* one), the CD signal reversed (Figure 3.22). Irradiating for 30 minutes, brought the signal back into the positive region. For MeOH, the CD behavior of the compound resembles that of in DCM and MeCN. For other CD results one can check Appendix F.

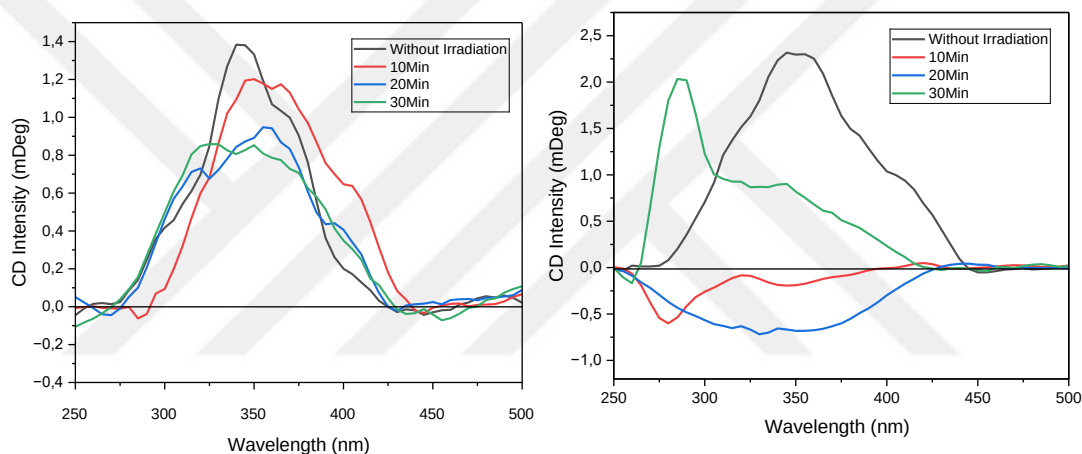


Figure 3.22 : CD spectra of **AzoCoumR-1** in DCM and THF upon irradiation (365 nm) (5×10^{-5} M)

AzoCoumR-2, which has sugar moiety at 7th position of coumarin, has positive CD signal in DCM, MeCN, THF and MeOH. Upon irradiation, like in the case of **AzoCoumR-1**, in DCM and MeCN, except the CD intensity, no significant change was observed. On the other hand, in THF and MeOH, the band around 400 nm had negative CD signal which increased in absolute value upon irradiation. In Figure

3.23, DCM and THF studies are tabulated, other solvent measurement results are given in Appendix F.

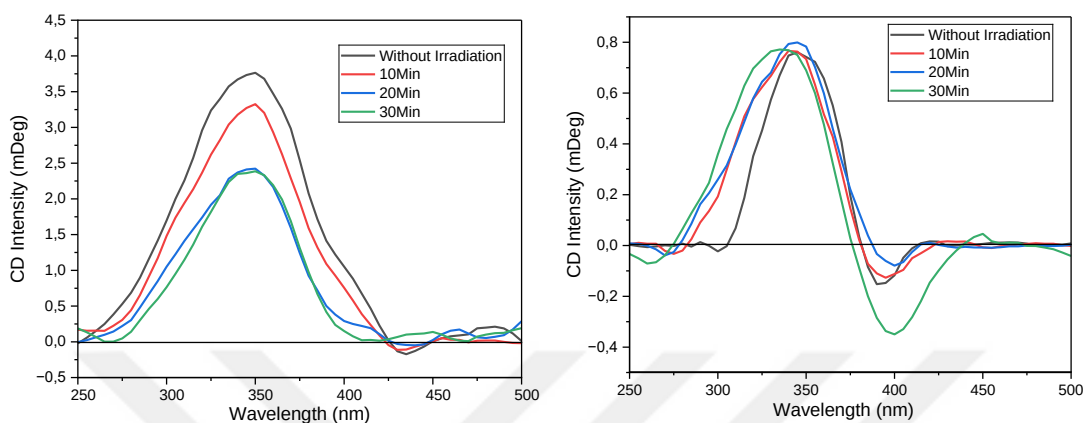


Figure 3.23 : CD spectra of **AzoCouvR-2** in DCM and THF upon irradiation
(365 nm) (5×10^{-5} M)

With the CD studies, it was shown that, a change on the side chain, affected the chiroptical signal of the coumarin. This signals showed variance depending on the solvent. This is in accordance with our proposed explanation for CD variance in the solvents of the compound, that is, side chain conformation affects the chiroptical features of coumarin.⁷⁴ It is obvious that *trans* to *cis* change is a configuration change, however, in the azobenzene unit this is a dynamic process, therefore one can see this as locked conformation. With the chiral unit, at 3rd position has more effect on CD spectrum of the compounds than at 7th position. This is also consistent with our previous observations in which chiral moiety (aminoacid) was bonded to 3rd position of coumarin.⁷⁴

3.5 Calculated CD Spectrum

The time-dependent density functional theory (TD-DFT) calculations were conducted using the CAM-B3LYP/6-31G(d) level of theory, provided the theoretical wavelengths, electronic states, and rotatory strengths (R) for both the *trans* and *cis* isomers of compounds **AzoCoumR-1** and **AzoCoumR-2**. With these calculations, it was aimed to predict their circular dichroism (CD) response, compare with experimental results, and assess how structural variations influence electronic transitions (Table 3.2). However, it should be noted that some disparities between theoretical and experimental findings underscore the complex nature of solvent effects and the limitations of gas-phase DFT calculations. Moreover, due to the nature of theoretical calculations, calculations are not exact, therefore they are used qualitatively in this thesis.

For **AzoCoumR-1**, in the *trans* isomer, weak rotatory strengths (R) are observed at longer wavelengths, with a minor positive R at 449 nm ($R = 0.0109$ au) and a negative R at 321 nm ($R = -0.0288$ au). Upon isomerization to the *cis* form, a substantial change in optical activity is observed, with a strong positive R at 467 nm ($R = 0.5046$ au), indicative of a significant change in the chiral environment induced by the *cis* configuration. These changes suggest that the *cis*-**AzoCoumR-1** experiences an enhancement in asymmetry, particularly in electronic transitions involving the azobenzene unit.

In contrast, the positional rearrangement of **AzoCoumR-2** leads to distinct CD characteristics. The *trans* isomer displays relatively weak R values across the spectrum, including a slightly negative R at 305 nm ($R = -0.0488$ au). Conversely, the *cis* isomer demonstrates a pronounced inversion at 467 nm ($R = -0.5511$ au), exhibiting strong positive R values at shorter wavelengths, such as 278 nm ($R =$

0.2632 au). This observation indicates that the positional exchange of azobenzene and *D*-(-)-ribose significantly impacts the electronic transitions and the chiral environment, particularly in the *cis* configuration.

Table 3.2 : Rotatory strengths of **AzoCoumR-1** and **AzoCoumR-2** at calculated wavelengths

Compound/Isomer	<i>trans</i>			<i>cis</i>		
	Wavelength	State	R(au)	Wavelength	State	R(au)
AzoCoumR-1	449	1	0.0109	467	1	0.5046
	321	2	-0.0288	302	2	-0.0263
	302	3	0.0093	278	3	-0.3914
AzoCoumR-2	448	1	0.0007	467	1	-0.5511
	321	2	0.0306	305	2	0.0265
	305	3	-0.0488	278	3	0.2632

These results demonstrate that *trans-cis* isomerization affects the CD response of both compounds, confirming that the change in geometry and electronic structure upon isomerization influences the chiroptical properties. In addition, the differences between **AzoCoumR-1** and **AzoCoumR-2** highlight the critical role of positional arrangements of the chromophores in determining the magnitude and direction of rotatory strengths. These findings underscore the sensitivity of CD responses to molecular geometry and the spatial arrangement of chromophores, providing insights into the potential for tuning chiroptical properties through structural modifications.

CHAPTER 4

CONCLUSIONS

In this study, eight new coumarin-conjugated azobenzene derivatives were successfully synthesized to explore their optical and chiroptical properties. The structural adjustments were focused on the positional variations of the azobenzene and *D*-(-) ribose units on the coumarin core, notably at the 3- and 7-positions, and the distance between coumarin core and azobenzene unit. Their effects on fluorescence and circular dichroism (CD) signals were carefully studied. A key finding was that the substitution of amino or butoxy units at the 7th position of coumarin core led to distinct fluorescence behaviors, that is, as *trans-cis* isomerization occurred, fluorescence enhancement was observed when the 7th position of coumarin unit was capped with butoxy, while a decrease in fluorescence was observed in 7-(diethylamino)coumarin derivatives. Theoretical studies and experiments in various solvents allow us to conclude that there is no charge transfer and chromophoric units act independently. Additionally, computational studies showed that fluorescence does not directly impacted by the *trans-cis* isomerization of azobenzene. Experimental findings revealed that azobenzene absorbs at the excitation wavelength in the *trans* form, lowering the amount of photons that reach to the coumarin unit; in contrast, this absorption disappears in the *cis* form, increasing fluorescence for **AzoCouv-1** and **AzoCouv-2** derivatives. In contrast, **AzoCouv-3** derivatives undergoes fluorescence quenching as a result of the *trans-cis* conversion, which increases the $n \rightarrow \pi^*$ absorption in the emission region of the 7-(diethylamino)coumarin unit.

Circular dichroism (CD) studies of chiral coumarin derivatives, **AzoCouvR-1** and **AzoCouvR-2**, demonstrated clear chirality induction on the coumarin unit. In addition, the *trans-cis* isomerization of the azobenzene directly influenced the chiral

environment, leading to significant changes in the CD responses across different solvents. Upon *trans-cis* isomerization of the azobenzene unit, **AzoCoumR-1** and **AzoCoumR-2**, positional isomers with different azobenzene and *D*-(-)-ribose placements, showed notably distinct CD responses. **AzoCoumR-1**, which has the chiral moiety attached to 3rd position, showed more significant changes upon isomerization and solvent and exhibited CD signal sign reversion in THF, while for **AzoCoumR-2**, except the CD intensity, no significant change was observed. Computational studies supported the experimental findings. With these studies, it was shown that, a change on the side chain affect the chiroptical properties of coumarin, and specifically, CD responses of both compounds are impacted by *trans-cis* isomerization. It indicates that the chiroptical properties are influenced by the change in geometry and electronic structure that occurs during isomerization. If one wants to use coumarin to detect chirality through weak interactions, the best position to attach the chiral recognizing unit is 3rd position.

CHAPTER 5

EXPERIMENTAL

5.1 General Information

All reagents and solvents were sourced from Sigma Aldrich and used without further purification. Reaction progress was monitored via thin layer chromatography (TLC) using Merck Silica Gel 60 F254 plates and visualized under 254 nm UV light.

The instruments that are indicated below were used to perform a structural evaluation of the synthesized compounds.

Melting points were determined using a Stuart SMP11 instrument, and the values reported are uncorrected.

^1H and ^{13}C nuclear magnetic resonance spectra of the compounds obtained using a Bruker Avance III Ultrashield 400 MHz spectrometer in deuterated solvents. Chemical shifts (in ppm) were referenced to tetramethylsilane (TMS). Spin multiplicities are denoted as s (singlet), d (doublet), dd (doublet of doublets), t (triplet), and m (multiplet), with coupling constants (J) reported in Hz. Detailed NMR spectra, including ^1H , ^{13}C , and other NMR techniques, are provided in Appendix A and were processed with the MestReNova program.

Infrared (IR) spectra were recorded with Thermo Scientific Nicolet iS10 ATR-IR spectrometer. Peak positions are reported in cm^{-1} . The IR spectra are available in Appendix B and were processed using OriginPro 2024.

High-Resolution Mass Spectra (HRMS) were acquired in positive mode (ES^+) using a Time of Flight mass analyzer. The HRMS data are presented in Appendix C.

UV-Vis measurements were performed using Shimadzu UV-2450 spectrophotometer and carried out in DCM, MeCN, THF, and MeOH (all of gradient grade). The UV absorption spectra can be found in Appendix D and were processed with OriginPro 2024.

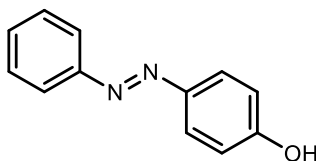
Fluorescence measurements were recorded using a Perkin Elmer LS55 spectrofluorometer and carried out in DCM, MeCN, THF, and MeOH (all of gradient grade). The fluorescence spectra are provided in Appendix E and were processed with OriginPro 2024.

Circular Dichroism (CD) Measurements were conducted with a Jasco J-1500 CD spectrometer, with baseline corrections made using the corresponding solvent. The CD spectra in DCM, MeCN, THF, and MeOH (all of gradient grade) are included in Appendix F and were processed with OriginPro 2024.

All computational studies were performed using Gaussian 09. Initial structure optimizations were carried out using the B3LYP/6-31g(d) level of theory. The final XYZ coordinates of the optimized structures are provided in Appendix G.

5.2 Synthesis of Compounds

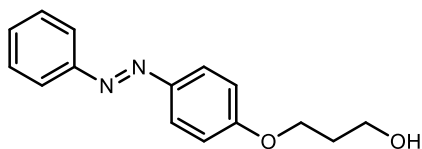
5.2.1 Synthesis of (*E*)-4-(phenyldiazenyl)phenol²⁷



Aniline (5.0 g, 53.7 mmole) was dissolved in 20 mL concentrated HCl and 20 mL of distilled water in a round bottom flask placed in a ice bath. Solution of sodium nitrite (5.0 g, 72.5 mmole) in 20 mL of water was added to the former stirring solution for diazotization to occur. In another flask, a solution of phenol (5.8 g, 61.6 mmole) in 50 mL of 10 % NaOH was prepared. This solution also was cooled to 5 °C by immersion in ice bath. After 30 minutes, the phenol solution was strongly stirred along with the slow addition of cold diazonium salt solution. Dark orange-yellow solid product was soon appered and precipitated. Mixture was filtered through a funnel and solid product on filter paper was washed several times with cold water and dried for isolation. (9.0 g, 90%). IR: 1470 cm⁻¹ (N=N), 2800-3200 cm⁻¹ (OH).

¹H NMR (400 MHz, CDCl₃): δ(ppm) = 7.88(d, *J*=4.6 Hz, 2H), 7.86(d, *J*=3.0 Hz, 2H), 7.50(m, 2H), 7.44 (m, 1H), 6.94 (d, *J*=8.77 Hz, 2H).

5.2.2 Synthesis of (*E*)-3-(4-(phenyldiazenyl)phenoxy)propan-1-ol⁷⁵

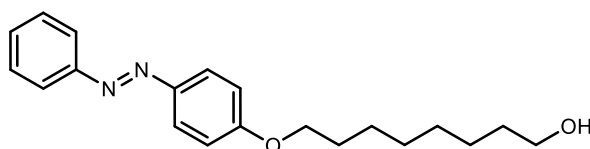


2

4-hydroxy azobenzene (**1**) (1.98 g, 9.98 mmole) and 3-bromo-1-propanol (1.08 mL, 12.0 mmole) were dissolved in 30 mL of DMF. K₂CO₃ (2.1 g, 15.0 mmol) was added to this solution and the solution was stirred at 75 °C for 12 hours. After cooling to the RT, the solution was poured into 50 mL of cold water and extracted with 50 mL of chloroform. The organic phase washed with 30 mL of 1M HCl and 30 mL of brine solution, then dried over anhydrous MgSO₄. Solvent evaporated under vacuum and orange solid product isolated. (Silica, EtOAc/Hex 1:3-1) (1.90 g, 74%) IR: 1494 cm⁻¹ (N=N), 2800-3300 cm⁻¹ (OH).

¹H NMR (100 MHz, CDCl₃): δ(ppm) = 7.90(dd, *J*= 9.08, 8.9 Hz 4H), 7.50(t, *J*=7.5 Hz 2H), 7.44(t, *J*=7.2 1H), 7.02 (d, *J*=9.1 2H), 4.20 (t, *J*=5.9 Hz, 2H), 3.90(t, *J*=5.2 2H), 2.09(m, 2H), 1.64(s, 1H).

5.2.3 Synthesis of (*E*)-8-(4-(phenyldiazenyl)phenoxy)octan-1-ol



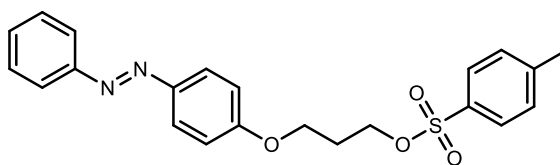
3

The same procedure with the synthesis of (*E*)-3-(4-(phenyldiazenyl)phenoxy)propan-1-ol (compound 2) was applied with 8-chloro-1-octanol as starting material. Orange solid product obtained. (Silica, EtOAc/Hex 1:3-1) (0.67 g, 68%) (M.p.:91.3°C) IR: 1472 cm⁻¹ (N=N), 2800-3280 cm⁻¹ (OH).

¹H NMR (400 MHz, CDCl₃): δ(ppm) = 7.91 (dd, *J*= 8.9, 2.2 Hz, 2H), 7.85 (m, 2H), 7.50 (td, *J*=8.0 Hz, 2H), 7.43 (m, 1H), 7.00 (dd, *J*=9.1, 2.0 Hz, 2H), 4.05 (t, *J*=6.32 Hz, 2H), 3.65 (q, *J*=6.3, 2H), 1.8(m, 2H), 1.5 (m, 2H), 1.37 (m, 8H).

¹³C NMR (100 MHz, CDCl₃): δ(ppm) 160.38, 151.42, 145.57, 128.97, 127.70, 123.39, 121.20, 113.33, 31.49, 27.98, 27.81, 24.60, 24.33

5.2.4 Synthesis of (*E*)-3-(4-(phenyldiazenyl)phenoxy)propyl 4-methylbenzenesulfonate⁷⁵



4

Compound 2 (0.82 g, 3.20 mmole) dissolved in 5 mL of pyridine, cooled to 0 °C in ice bath for 30 minutes, then tosyl chloride (0.70 g, 3.70 mmole) was added slowly to the stirring solution. The solution was kept in ice bath for 3 hours while reaction was proceeding. After 3 hours, 30 mL of ice-water was added to quench the reaction. Precipitated solid filtered and washed several times with cold water. After collecting the solid on the filter paper dissolved in DCM and extracted with 0.1M, 30 mL of H₂SO₄. The mixture was dried over MgSO₄ and the solvent was evaporated under

vacuum. Brownish-orange solid product isolated purely. (0.95 g, 73%)) IR: 1466 cm^{-1} (N=N), 1746 cm^{-1} (C=O), 2939 cm^{-1} (Methyl group of p-toluene from tosyl group).

^1H NMR (400 MHz, CDCl_3): $\delta(\text{ppm}) = 7.80$ (m, 3H), 7.45 (m, 3H), 7.23 (d, $J=7.52$ Hz, 2H), 6.85 (d, $J=8.84$, 2H), 4.26 (t, $J=6.48$ Hz, 2H), 4.02 (t, $J=5.56$, 2H), 2.35(s, 3H), 2.15 (t, $J=5.36$, 2H), 1.37 (m, 8H).

5.2.5 Synthesis of (*E*)-8-(4-(phenyldiazenyl)phenoxy)octyl 4-methylbenzenesulfonate



5

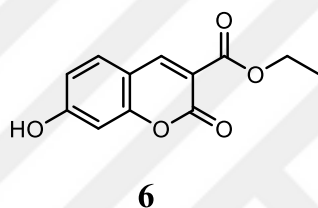
The same procedure with the synthesis of (*E*)-3-(4-(phenyldiazenyl)phenoxy)propyl 4-methylbenzenesulfonate was applied with (*E*)-8-(4-(phenyldiazenyl)phenoxy)octan-1-ol (compound **3**) as starting material. (0.71 g, 71%) (M.p.:101.8 °C) IR: 1463 cm^{-1} (N=N), 1603 cm^{-1} (C=O), 2939 cm^{-1} (Methyl group of p-toluene from tosyl group).

^1H NMR (400 MHz, CDCl_3): $\delta(\text{ppm}) = 7.90$ (m, 4H), 7.80 (d, $J=8.16$, 2H), 7.49 (m, 4H), 7.35 (d, $J=8.72$, 1H), 7.00 (d, $J=9.12$ Hz, 2H), 4.02 (t, $J=6.50$, 4H), 2.95(s, 3H), 1.80 (m, 3H), 1.30 (m, 10H).

^{13}C NMR (100 MHz, CDCl_3): $\delta(\text{ppm})$ 161.66, 152.73, 146.80, 144.66, 133.25, 130.29, 129.73, 129.15, 127.91, 124.60, 122.43, 114.57, 70.61, 68.19, 29.12, 28.84, 28.81, 25.87, 25.25, 21.65

HRMS (ESI/MS) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{27}\text{H}_{33}\text{N}_2\text{O}_4\text{S}^+$ 481.2161, found 481.2161

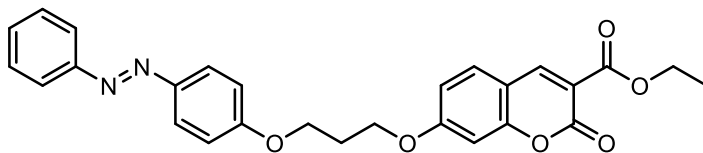
5.2.6 Synthesis of ethyl 7-hydroxy-2-oxo-2H-chromene-3-carboxylate⁴⁴



2,4-dihydroxybenzaldehyde (1.21 g, 8.77 mmole) and diethyl malonate (1.46 mL, 9.57 mmole) were dissolved in 15 mL EtOH. Piperidine (0.37 mL) and acetic acid (0.15 mL) were added to this stirring solution and reaction carried on under reflux conditions for 18 hours. EtOH was evaporated under vacuum and oilish residue poured into ice-water mixture. Precipitated solid was filtered and recrystallized from EtOH. White crystals filtered and dried to give the compound. (1.80 g, 88%)

^1H NMR (400 MHz, $\text{DMSO}-d_6$): $\delta(\text{ppm})$ = 8.57 (s, 1H), 7.66 (d, $J=8.20$, 2H), 6.63-6.75 (m, 2H), 4.15 (q, $J=7.88$, 2H), 1.20 (t, $J=6.20$, 3H)

5.2.7 Synthesis of AzoCouv-1a



AzoCouv-1a

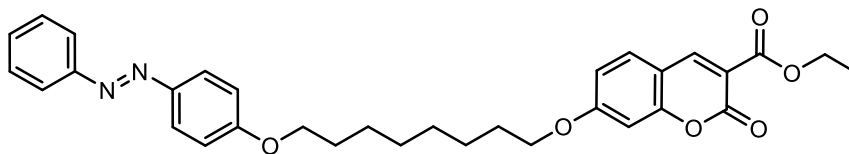
Ethyl 7-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (compound **6**) (0.50 g, 2.20 mmole) and K_2CO_3 (0.35 g, 2.53 mmole) dissolved in 25 mL of DMF under slow heating to 60 °C. After an hour, (*E*)-3-(4-(phenyldiazenyl)phenoxy)propyl 4-methylbenzenesulfonate (compound **4**) (0.90 g, 2.20 mmole) and KI (0.28 g, 1.68 mmole) added to the mixture and heat raised to 75 °C. After 18 hours, reaction mixture was cooled to the RT, then poured into 50 mL of cold water. After precipitation finished, it was filtered and solid washed several times with cold water. Compound recrystallized from EtOH, dark orange solid dried and isolated. (0.42 g, 40%) (M.p.: 107.9 °C) IR: 1468 cm^{-1} (N=N), 1750 cm^{-1} (C=O), 2881 cm^{-1} (C-H).

^1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 8.50 (s, 1H), 7.89 (dd, $J = 9.32, 7.56$, 4H), 7.50 (m, 4H), 7.02 (d, $J = 8.74$, 2H), 6.91 (dd, $J = 1.84$ Hz, 1H), 6.85 (s, 1H), 4.40 (q, $J = 7.28, 6.84$, 2H), 4.27 (q, $J = 7.92, 8.28$, 4H), 2.35 (m, 2H), 1.40 (t, $J = 6.6$, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 188.28, 164.33, 163.46, 161.15, 157.53, 152.75, 148.97, 147.09, 130.80, 130.44, 129.02, 124.81, 122.57, 114.76, 113.81, 111.70, 101.08, 65.18, 64.29, 61.73, 28.87, 14.37.

HRMS (TOF/MS) m/z : $[M + H]^+$ Calcd for $C_{27}H_{25}N_2O_6^+$ 473.1714, found 473.1713.

5.2.8 Synthesis of AzoCouv-1b



AzoCouv-1b

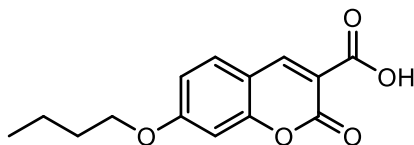
The same procedure with the synthesis of AzoCouv-1a was applied with (*E*)-8-(4-(phenyldiazenyl)phenoxy)octyl 4-methylbenzenesulfonate (compound 5) as a starting material. (0.095 g, 32%) (M.p.:114.6 °C) IR: 1473 cm⁻¹(N=N), 1745 cm⁻¹ (C=O), 2853,2936 cm⁻¹ (C-H).

¹H NMR (400 MHz, CDCl₃): δ(ppm) = 8.50 (s, 1H), 7.89 (dd, *J*=7.68, 8.92, 4H), 7.48 (m, 4H), 7.00 (d, *J*=8.96, 2H), 6.87 (m, 1H), 6.79 (d, *J*=2.12, 1H), 4.39(q, *J*=7.08, 7.06, 2H), 4.04(m, 4H), 1.83 (m, 4H), 1.41 (m, 11H).

¹³C NMR (100 MHz, CDCl₃): δ(ppm) 164.73, 163.51, 161.64, 157.60, 157.25, 152.76, 149.04, 146.86, 130.66, 130.32, 129.02, 124.74, 122.52, 114.68, 114.03, 113.88, 111.47, 100.76, 68.90, 68.25, 61.69, 29.24, 29.21, 29.15, 28.85, 25.94, 25.86, 14.29.

HRMS (TOF/MS) *m/z*: [M + H]⁺ Calcd for C₃₂H₃₅N₂O₆⁺ 543.2495, found 543.2495.

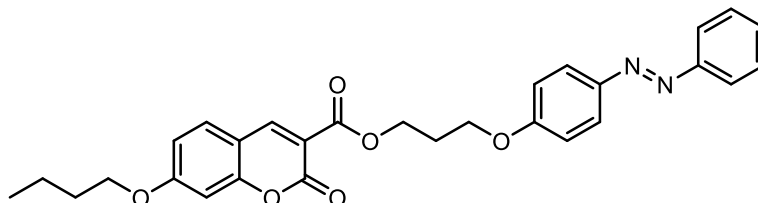
5.2.9 Synthesis of 7-butoxy-2-oxo-2H-chromene-3-carboxylic acid⁷⁶



7

Ethyl 7-hydroxy-2-oxo-2H-chromene-3-carboxylate (compound **6**) (0.23 g, 1.00 mmole) and K₂CO₃ (0.20 g, 1.50 mmole) were dissolved in 7 mL of dry DMF and allowed to stir for an hour with heating to 45 °C. (Temperature should not be above 60 °C.) After an hour, 1-bromobutane (0.13 mL, 1.20 mmole) added portionwise to the reaction medium. Reaction allowed to proceed for 12 hours and after controlling with TLC (EtOAc/Hex 1:1), the reaction was finished and cooled to the RT. After cooling, reaction mixture poured into ice-water mixture and filtered. Washed with water several times and dried. The obtained white solid (0.24 g, 0.82 mmole 82%), dissolved in 5 mL of 60% EtOH-water solution with KOH (0.08 g, 1.38 mmole). The reaction allowed to proceed for 5 hours at 50°C and then additional 1 hour at RT. After completion of the reaction, EtOH was removed under vacuo and the residual solution was acidified to pH = 1 with dilute HCl solution in ice bath. The precipitated solid was filtered and dried to provide white solid product. (0.21 g, 96%)
¹H NMR (400 MHz, DMSO-*d*₆): δ(ppm) = 8.72 (s, 1H), 7.82 (d, *J*=8.60, 1H), 6.98-7.01 (m, 2H), 4.11 (t, *J*=6.48, 2H), 1.76 (m, 2H), 1.44 (m, 2H), 0.93 (t, *J*=7.28, 3H).

5.2.10 Synthesis of AzoCoum-2a



AzoCoum-2a

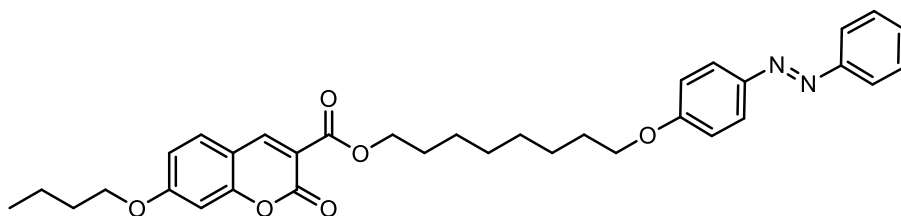
DMAP (0.09 g, 0.76 mmole) and EDC.HCl (0.55 g, 2.85 mmole) were successively added to a stirring solution of 7-butoxy-2-oxo-2*H*-chromene-3-carboxylic acid (compound **7**) (0.50 g, 1.90 mmole) and (*E*)-3-(4-(phenyldiazenyl)phenoxy)propan-1-ol (compound **2**) (0.48 g, 1.90 mmole) in 20 mL anhydrous DCM. The mixture was stirred at RT for 24 hours under argon atmosphere. After that, in DCM, extraction was performed with saturated NaHCO₃ solution, water, and brine respectively and Na₂SO₄ was used as a drying agent. Solvent removed under vacuum and the solid product recrystallized from EtOH. Yellow crystals were isolated. (0.42 g, 45%) (M.p.: 98.0 °C) IR: 1471 cm⁻¹(N=N), 1724 cm⁻¹ (C=O), 2872,2959 cm⁻¹ (C-H).

¹H NMR (400 MHz, CDCl₃): δ(ppm) = 8.50 (s, 1H), 7.90 (m, 4H), 7.50 (m, 4H), 7.04 (d, *J*=9.04 Hz, 2H), 6.86 (dd, *J*=6.32, 3.14 Hz, 1H), 6.79 (d, *J*=2.40, 1H), 4.56 (t, *J*= 6.20 Hz 2H), 4.26 (t, *J*= 5.88 Hz 2H), 4.04 (t, *J*= 6.64 Hz 2H), 2.30 (m, 2H), 1.80 (m, 2H), 1.50 (m, 2H), 0.99 (t, *J*=7.12, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 164.90, 163.70, 161.30, 157.69, 157.14, 152.76, 149.31, 147.05, 130.75, 130.36, 129.03, 124.78, 123.14, 122.75, 122.56, 114.79, 114.06, 113.61, 111.43, 100.80, 68.69, 64.74, 62.33, 30.88, 28.58, 19.14, 13.77.

HRMS (TOF/MS) *m/z*: [M + H]⁺ Calcd for C₂₉H₂₉N₂O₆⁺ 501.2026, found 501.2025.

5.2.11 Synthesis of AzoCoum-2b



AzoCoum-2b

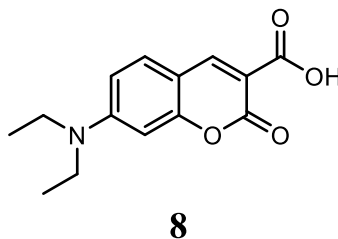
The same procedure with the synthesis of **AzoCoum-2a** was applied with the difference of usage of (*E*)-8-(4-(phenyldiazenyl)phenoxy)octan-1-ol (compound **3**) as a starting material. (0.40 g, 44%) (M.p.: 82 °C)) IR: 1472 cm⁻¹(N=N), 1748 cm⁻¹ (C=O), 2855,2939 cm⁻¹ (C-H).

¹H NMR (400 MHz, CDCl₃): δ(ppm) = 8.49 (s, 1H), 7.90 (m, 4H), 7.50 (m, 4H), 7.00 (d, *J*=9.05 Hz, 2H), 6.86 (dd, *J*= 6.44, 2.56 Hz, 1H), 6.78 (d, *J*=2.40, 1H), 4.33 (t, *J*= 6.60 Hz 2H), 4.04 (m, 4H), 1.79 (m, 5H), 1.45 (m, 11H), 0.98 (t, *J*=7.32, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 164.77, 163.65, 161.70, 157.62, 157.19, 152.80, 148.95, 146.86, 130.64, 130.28, 129.01, 124.74, 122.53, 114.70, 114.00, 111.46, 100.79, 68.67, 68.31, 65.74, 30.88, 29.19, 29.15, 29.12, 28.60, 25.92, 25.82, 19.13, 14.12, 13.76.

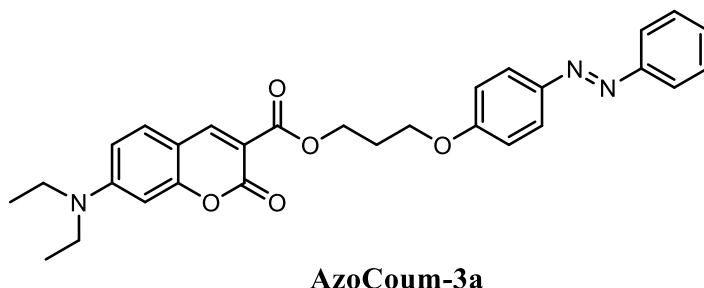
HRMS (TOF/MS) *m/z*: [M + H]⁺ Calcd for C₃₄H₃₉N₂O₆⁺ 571.2808, found 501.2807.

5.2.12 Synthesis of 7-(diethylamino)-2-oxo-2H-chromene-3-carboxylic acid⁷⁷



4-diethylaminosalicylaldehyde (0.96 g, 5.00 mmole) was dissolved in 3.3 mL of EtOH. Diethyl malonate (1 mL, 6.5 mmole) and 0.4 mL of piperidine were added to this solution and reaction mixture refluxed for 3 hours. After evaporation of EtOH, reaction medium diluted with 50 mL water and extracted with EtOAc (50 mL x3). It was dried over MgSO₄ and solvent removed under vacuum. Viscous product was purified with column chromatography (Silica, EtOAc/Hex 1:5-1) and yellow crystals obtained (0.75 g, 52%). Afterwards, to a solution of this ester product (0.29 g, 1.0 mmole) in 10 mL of EtOH, was added 10 mL of 0.5M NaOH. The reaction allowed to proceed at RT for 12 hours and after the completion of the reaction, EtOH was evaporated. After adding 5 mL of water to remaining solution, acidification was performed with 1M HCl until pH = 4. Then with the completion of the precipitation, solid was filtered and washed with water for a few times. Orange solid product was isolated. (0.1 g, 40%) ¹H NMR (400 MHz, CDCl₃): δ(ppm) = 8.66 (s, 1H), 7.45 (d, *J*=9.0 Hz, 1H), 6.71 (dd, *J*=6.58, 4.76, 1H), 6.53 (d, *J*=2.6 Hz, 1H), 3.49 (q, *J*=7.12, 4H), 1.26 (t, *J*=6.68, 6H).

5.2.13 Synthesis of AzoCoum-3a



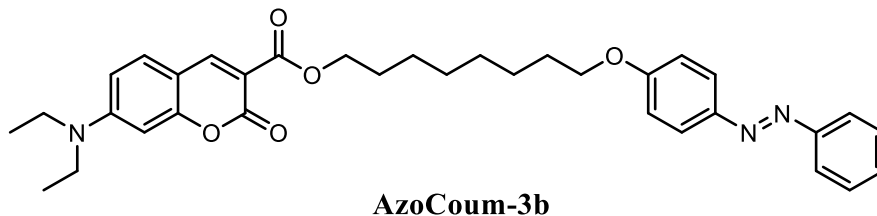
EDC.HCl (0.15 g, 0.76 mmole) and DMAP (0.03 g, 0.25 mmole) were added to a stirring solution of 7-(diethylamino)-2-oxo-2*H*-chromene-3-carboxylic acid (compound **8**) (0.14 g, 0.51 mmole) and (*E*)-3-(4-(phenyldiazenyl)phenoxy)propan-1-ol (compound **2**) (0.13 g, 0.51 mmole) in 10 mL anhydrous DCM. The mixture was stirred at RT for 24 hours under argon atmosphere. After that, in DCM, extraction was performed with saturated NaHCO₃ solution, water, and brine respectively and Na₂SO₄ was used as a drying agent. Solvent removed under vacuum and the yellow solid product were isolated after column chromatography (Silica, EtOAc/Hex 1:3-1). (0.12 g, 45%) (M.p.:115.0 °C) IR: 1214 cm⁻¹ (C-N (aromatic)), 1189 cm⁻¹ (C-N (aliphatic)), 1465 cm⁻¹ (N=N), 1725 cm⁻¹ (C=O).

¹H NMR (400 MHz, CDCl₃): δ(ppm) = 8.40 (s, 1H), 7.88 (m, 4H), 7.45 (m, 3H), 7.33(d, *J*=9.32 Hz, 1H), 6.58 (dd, *J*= 6.56, 2.32 Hz, 1H), 6.45 (d, *J*=2.36, 1H), 4.53 (t, *J*= 5.60 Hz 2H), 4.26 (t, *J*= 6.32 Hz 2H), 3.43 (q, *J*= 6.96, 7.16 Hz 4H), 2.30 (m, 2H), 1.23 (m, 6H).

¹³C NMR (100 MHz, CDCl₃) δ 164.30, 161.27, 158.45, 158.04, 152.84, 152.69, 149.23, 146.92, 130.97, 130.16, 128.87, 124.64, 122.42, 114.71, 109.43, 108.63, 107.59, 96.64, 64.82, 61.70, 44.97, 28.58, 12.31.

HRMS (TOF/MS) *m/z*: [M + H]⁺ Calcd for C₂₉H₃₀N₃O₅⁺ 500.2185, found 500.2185.

5.2.14 Synthesis of AzoCoum-3b



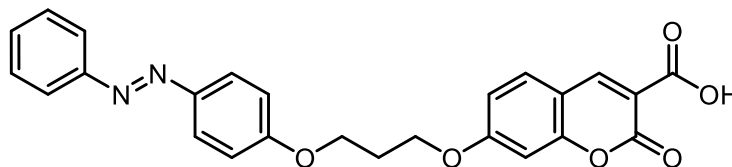
The same procedure with the synthesis of **AzoCoum-3a** was applied with the difference of usage of (*E*)-8-(4-(phenyldiazenyl)phenoxy)octan-1-ol (compound **3**) as a starting material. (0.11 g, 38%). (M.p.:84.3 °C) IR: 1215 cm⁻¹ (C-N (aromatic)), 1190 cm⁻¹ (C-N (aliphatic)), 1471 cm⁻¹(N=N), 1747 cm⁻¹ (C=O).

¹H NMR (400 MHz, CDCl₃): δ(ppm) = 8.42 (s, 1H), 7.90 (m, 4H), 7.46 (m, 3H), 7.34(d, *J*=8.84 Hz, 1H), 7.00 (d, *J*=8.82 Hz, 2H), 6.58 (dd, *J*=6.36, 2.36, 1H), 6.45 (d, *J*= 2.2 Hz 1H), 4.31 (t, *J*= 6.48 Hz 2H), 4.04 (t, *J*= 6.56 Hz 2H), 3.43 (q, *J*= 7.12, 7.24, 4H), 1.80(m, 4H), 1.44 (m, 4H), 1.23 (m, 6H).

¹³C NMR (100 MHz, CDCl₃) δ 164.39, 161.72, 158.48, 158.29, 152.84, 152.79, 149.15, 146.83, 131.02, 130.29, 129.03, 124.75, 122.53, 114.71, 109.47, 109.02, 107.68, 96.73, 68.33, 65.27, 45.09, 29.22, 29.17, 28.69, 25.93, 25.87, 12.44.

HRMS (TOF/MS) *m/z*: [M + H]⁺ Calcd for C₃₄H₄₀N₃O₅⁺ 570.2968, found 570.2968.

5.2.15 Synthesis of AzoCouv-1a'



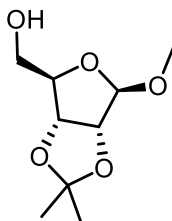
AzoCouv-1a'

AzoCouv-1a was dissolved in 15 mL of 60% EtOH solution and KOH (0.04 g, 0.70 mmole) was added to this stirring solution. The mixture refluxed for 18 hours. After cooling to the RT and removal of EtOH, acidification was performed with 1M HCl until orange precipitate formation. The orange solid was filtered and washed a few times with small amount of water. (0.14 g, 74%) (M.p.:125.2 °C) IR: 1469 cm⁻¹ (N=N), 1737 cm⁻¹ (C=O), 2934 cm⁻¹ (C-H), 2600-3065 cm⁻¹ (O-H)

¹H NMR (400 MHz, CDCl₃): δ(ppm) = 8.66 (s, 1H), 7.90 (dd, *J*=10.8, 7.48, 4H), 7.64 (d, *J*= 9.20 1H), 7.49 (m, 4H), 7.02 (m, 2H), 6.96 (d, *J*=2.28, 1H), 4.34 (t, *J*=5.80, 2H), 4.27(t, *J*=5.36, 2H), 2.40 (m, 2H).

¹³C NMR (100 MHz, CDCl₃) δ 164.31, 163.46, 161.12, 157.53, 152.73, 148.95, 147.15, 130.76, 130.45, 129.05, 124.78, 122.58, 114.70, 114.23, 113.83, 111.75, 101.02, 65.21, 64.26, 61.74, 28.92, 14.29.

5.2.16 Synthesis of ((3R,4R,6R,6R)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol⁷⁸

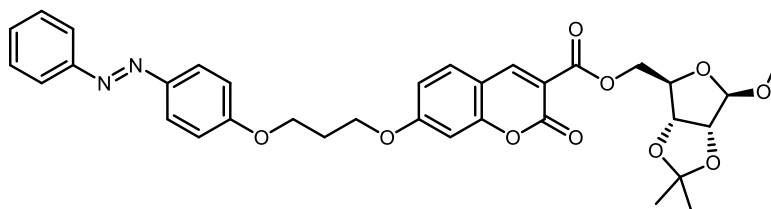


9

D-(-)-ribose (1.00 g, 6.60 mmole) in 5 mL of acetone and 5 mL of MeOH was slowly added 0.5 mL of H₂SO₄. The mixture was allowed to stir for 48 hours under argon atmosphere at RT. The reaction was quenched with saturated NaHCO₃ and concentrated under vacuum. After that, the resulting residue was dissolved in EtOAc and washed with water. It was dried over Na₂SO₄ and the solvent was removed to obtain the pale yellow oil product. (0.67 g, 50%)

¹H NMR (400 MHz, CDCl₃): δ(ppm) = 4.99 (s, 1H), 4.84 (d, *J* = 5.9 Hz, 1H), 4.59 (d, *J* = 5.92 Hz, 1H), 3.69-3.59 (m, 2H), 3.44 (s, 3H), 1.49 (s, 3H), 1.30 (s, 3H).

5.2.17 Synthesis of AzoCoumR-1



AzoCoumR-1

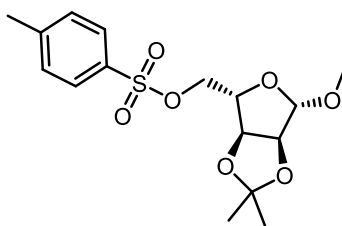
EDC.HCl (0.06 g, 0.32 mmole) and DMAP (0.01 g, 0.08 mmole) were added to a stirring solution of **AzoCoug-1a'** (0.09 g, 0.21 mmole) and ((3R,4R,6R,6R)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (compound **9**) (0.04 g, 0.21 mmole) in 5 mL of DCM. Reaction allowed to proceed under argon atmosphere at RT for 24 hours. Afterwards, extraction was performed in DCM with saturated NaHCO₃ solution, water, and brine respectively and Na₂SO₄ was used as a drying agent. Solvent removed under vacuum and white solid product was obtained after column chromatography (Silica, EtOAc/Hex 1:4-1). (0.014 g, 11%) (M.p.:106.7 °C) IR: 1251 cm⁻¹ (O-CH₂-sugar), 1469 cm⁻¹ (N=N), 1765 cm⁻¹ (C=O), 2932 cm⁻¹ (C-H).

¹H NMR (400 MHz, CDCl₃): δ(ppm) = 8.54 (s, 1H), 7.90 (m, 4H), 7.49 (m, 4H), 7.03(dd, *J*=4.56, 2.36 Hz, 2H), 6.91 (dd, *J*=6.28, 2.4 Hz, 1H), 6.85 (d, *J*= 2.36, 1H), 5.01 (s, 1H), 4.81 (d, *J*= 5.76 Hz 1H), 4.65 (d, *J*= 5.80 Hz 1H), 4.52 (t, *J*= 6.80, 1H), 4.30(m, 6H), 3.34 (s, 3H), 2.36 (m, 2H), 1.49(s, 3H), 1.33 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 164.54, 162.81, 161.13, 157.69, 152.79, 149.19, 147.23, 130.91, 130.45, 129.05, 124.80, 122.60, 114.74, 113.90, 112.64, 111.71, 109.74, 101.10, 85.33, 84.30, 81.90, 65.58, 65.31, 64.31, 55.07, 28.96, 26.49, 25.05.

HRMS (TOF/MS) *m/z*: [M + H]⁺ Calcd for C₃₄H₃₅N₂O₁₀⁺ 631.2292, found 631.2292.

5.2.18 Synthesis of ((3S,4S,6S,6S)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl 4-methylbenzenesulfonate⁷⁹

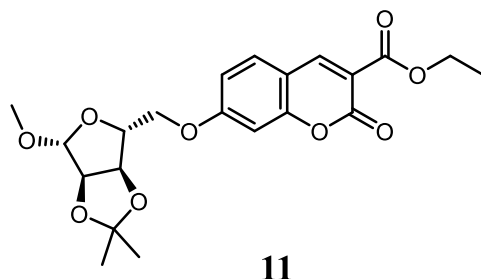


10

((3R,4R,6R,6R)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methanol (compound **9**) (0.40 g, 1.96 mmole) was dissolved in 1 mL of pyridine and placed in a ice bath. After cooling the mixture to 0 °C, tosyl chloride (0.55 g, 2.74 mmole) was added portionwise and the reaction was allowed to proceed for 3 hours. Ice-water mixture (40 mL) was added to the reaction mixture for quenching and filtered. White precipitate collected on filter paper washed with cold water for several times. White solid product was dried and isolated. (0.61 g, 87%)

¹H NMR (400 MHz, CDCl₃): δ(ppm) = 7.80 (dt, *J*=8.3 Hz, 2H), 7.36 (d, *J*=8.0 Hz, 2H), 4.93 (s, 1H), 4.56(d, *J*=6.12, 1H), 4.53(d, *J*=6.0, 1H), 4.32 (t, *J*=7.5 Hz, 1H), 4.01 (m, 2H), 3.23 (s, 3H), 2.46 (s, 3H), 1.45 (s, 3H), 1.28 (s, 3H)

5.2.19 Synthesis of Ethyl 7-(((3R,4R,6R,6R)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)-2-oxo-2H-chromene-3-carboxylate



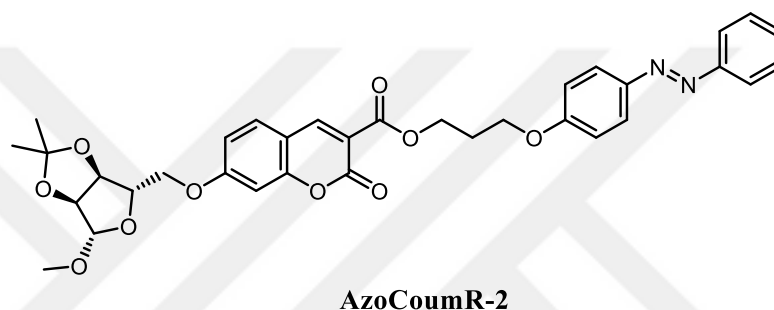
Ethyl 7-hydroxy-2-oxo-2*H*-chromene-3-carboxylate (compound **6**) (0.35 g, 1.49 mmole) and K₂CO₃ (0.24 g, 1.74 mmole) were dissolved in 10 mL of DMF and heated to 65 °C. After 30 minutes, ((3*S*,4*S*,6*S*,6*S*)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)methyl-4-methylbenzenesulfonate (compound **10**) (0.45 g, 1.24 mmole) and KI (0.20 g, 1.20 mmole) were added to reaction mixture and the mixture heated to 75 °C. After 24 hours, reaction mixture allowed to cool to the RT and poured into 50 mL of cold water. Extraction was performed with chloroform and brine solution, respectively. It was dried over MgSO₄ and solvent removed under vacuum. The white solid product isolated after performing column chromatography (Silica, EtOAc/Hex 1:3-1). (0.19 g, 37%) (M.p: 72.4 °C) IR: 2849 cm⁻¹ (O-CH₃), 2915 cm⁻¹ (C-H), 1755 cm⁻¹ (C=O), 1274 cm⁻¹ (O-CH₂-sugar)

¹H NMR (400 MHz, CDCl₃): δ(ppm) = 8.50 (s, 1H), 7.51 (d, *J*=8.64, 1H), 6.92 (dd, *J*= 6.20, 6.16, 1H), 6.82(d, *J*=2.32, 1H), 5.03 (s, 1H), 4.78 (d, *J*=5.72, 1H), 4.65(d, *J*=6.08, 1H), 4.55(m, 1H), 4.40 (q, *J* = 7.28, 7.0 Hz, 2H), 4.05 (m, 2H), 3.34 (s, 3H), 1.47 (m, 9H)

^{13}C NMR (100 MHz, CDCl_3) δ 148.68, 141.58, 130.77, 113.90, 112.80, 111.99, 109.51, 101.00, 85.09, 84.11, 81.95, 76.68, 69.09, 61.76, 55.07, 29.48, 26.43, 24.98, 14.27.

HRMS (TOF/MS) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{21}\text{H}_{25}\text{O}_9$ 421.1499, found 421.1500.

5.2.20 Synthesis of AzoCoumR-2



EDC.HCl (0.09 g, 0.48 mmole) and DMAP (0.02 g, 0.16 mmole) were added to a stirring solution of 7-(((3R,4R,6R,6R)-6-methoxy-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)-2-oxo-2H-chromene-3-carboxylic acid (compound **11'**) (0.08 g, 0.32 mmole) and (*E*)-3-(4-(phenyldiazenyl)phenoxy)propan-1-ol (compound **2**) (0.04 g, 0.15 mmole) in 15 mL of anhydrous DCM. After 48 hours, extraction was performed in DCM with saturated NaHCO_3 , water and brine, respectively. After drying over Na_2SO_4 , the compound was purified with preparative thin layer chromatography to yield orange solid product. (EtOAc/Hex 1:6) (0.035 g, 17%). (M.p.: 112.6 °C) IR: 1249 cm^{-1} (O-CH₂-sugar), 1473 cm^{-1} (N=N), 1745 cm^{-1} (C=O), 2936 cm^{-1} (C-H).

^1H NMR (400 MHz, CDCl_3): δ (ppm) = 8.50 (s, 1H), 7.90 (m, 4H), 7.49 (m, 4H), 7.04 (dd, $J=4.44$, 2.20 Hz, 2H), 6.9 (m, 1H), 6.82 (d, $J=2.36$, 1H), 5.04 (s, 1H), 4.79

(d, $J = 5.64$ Hz, 1H), 4.65 (d, $J = 5.88$ Hz 1H), 4.57 (m, 2H), 4.17(m, 5H), 3.43 (s, 3H), 2.31 (m, 2H), 1.52 (s, 3H), 1.35 (s, 3H).

^{13}C NMR (100 MHz, CDCl_3) δ 166.22, 165.94, 164.14, 163.39, 160.84, 157.76, 152.76, 151.26, 150.27, 130.89, 130.25, 129.04, 124.78, 122.56, 114.78, 113.95, 112.80, 109.48, 100.98, 85.07, 84.08, 81.92, 69.12, 65.32, 61.06, 55.10, 29.71, 26.42, 24.96.

HRMS (TOF/MS) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{34}\text{H}_{35}\text{N}_2\text{O}_{10}^+$ 631.2292, found 631.2292.



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APPENDICES

A. NMR Spectra

NMR spectra of all compounds were acquired at Bruker Avance III Ultrashield 400 MHz. Solvents that were used in all measurements were CDCl_3 and $\text{DMSO}-d_6$.



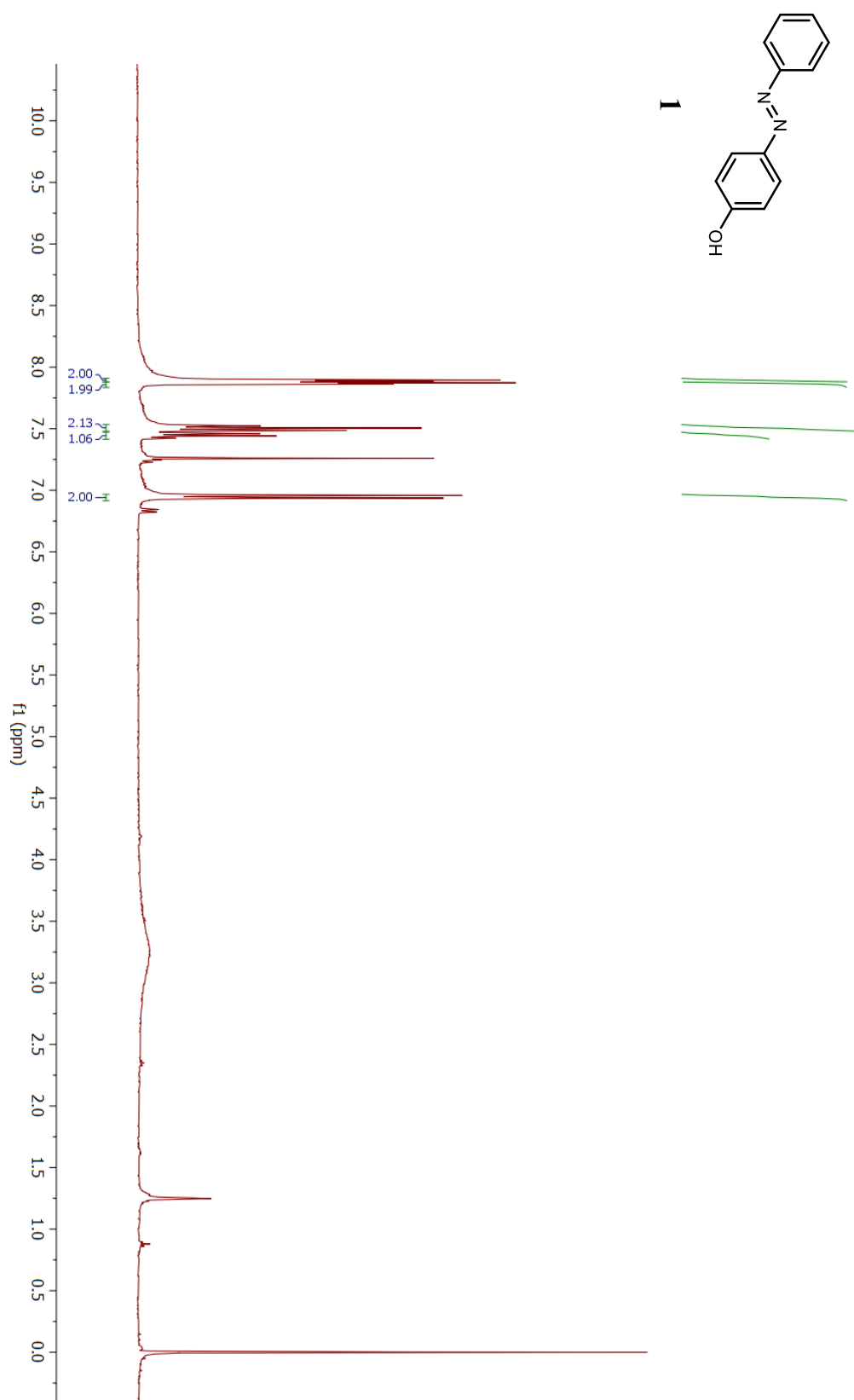


Figure A.1 : ^1H NMR of compound **1**

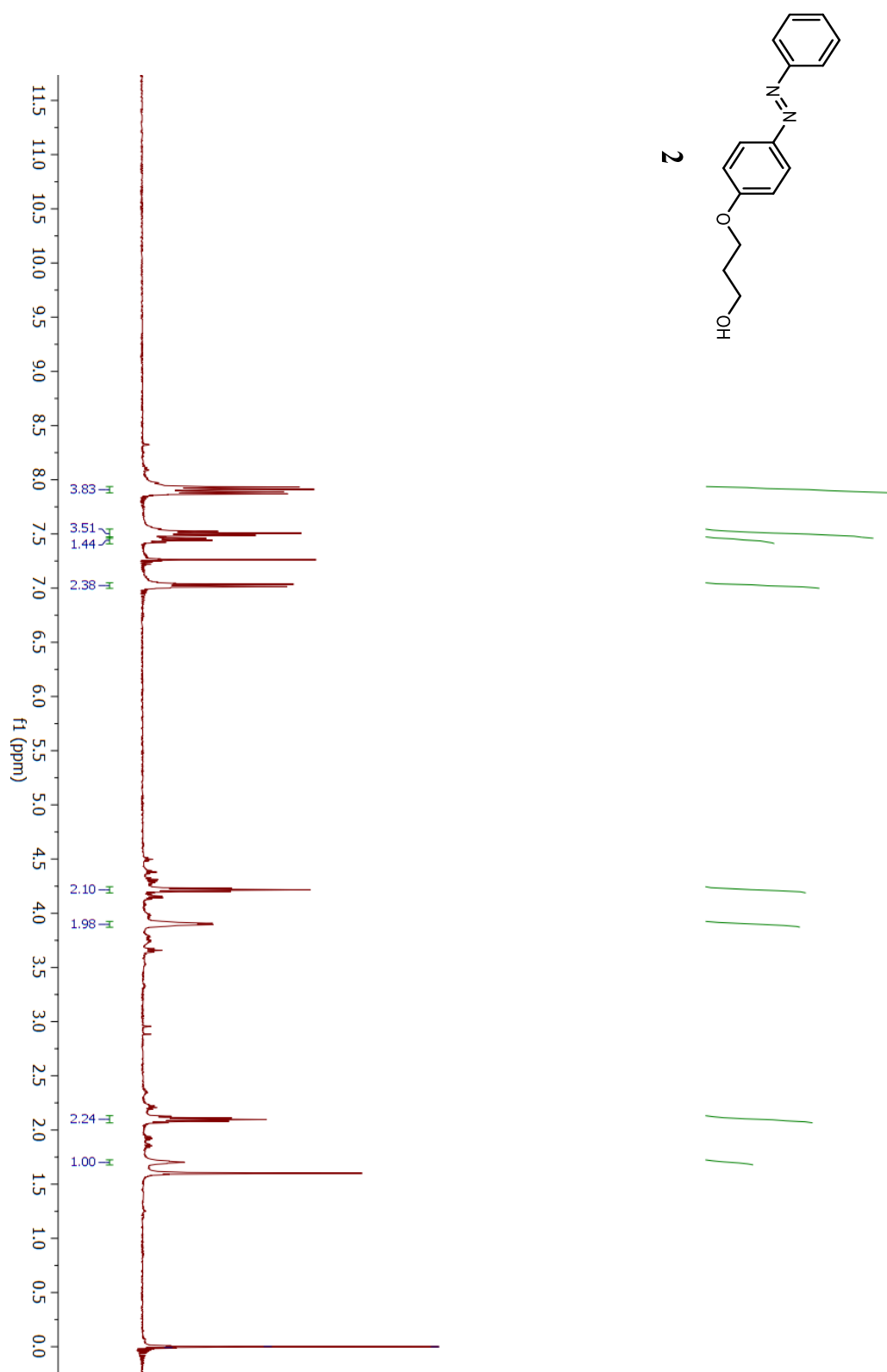


Figure A.2 : ¹H NMR of compound **2**

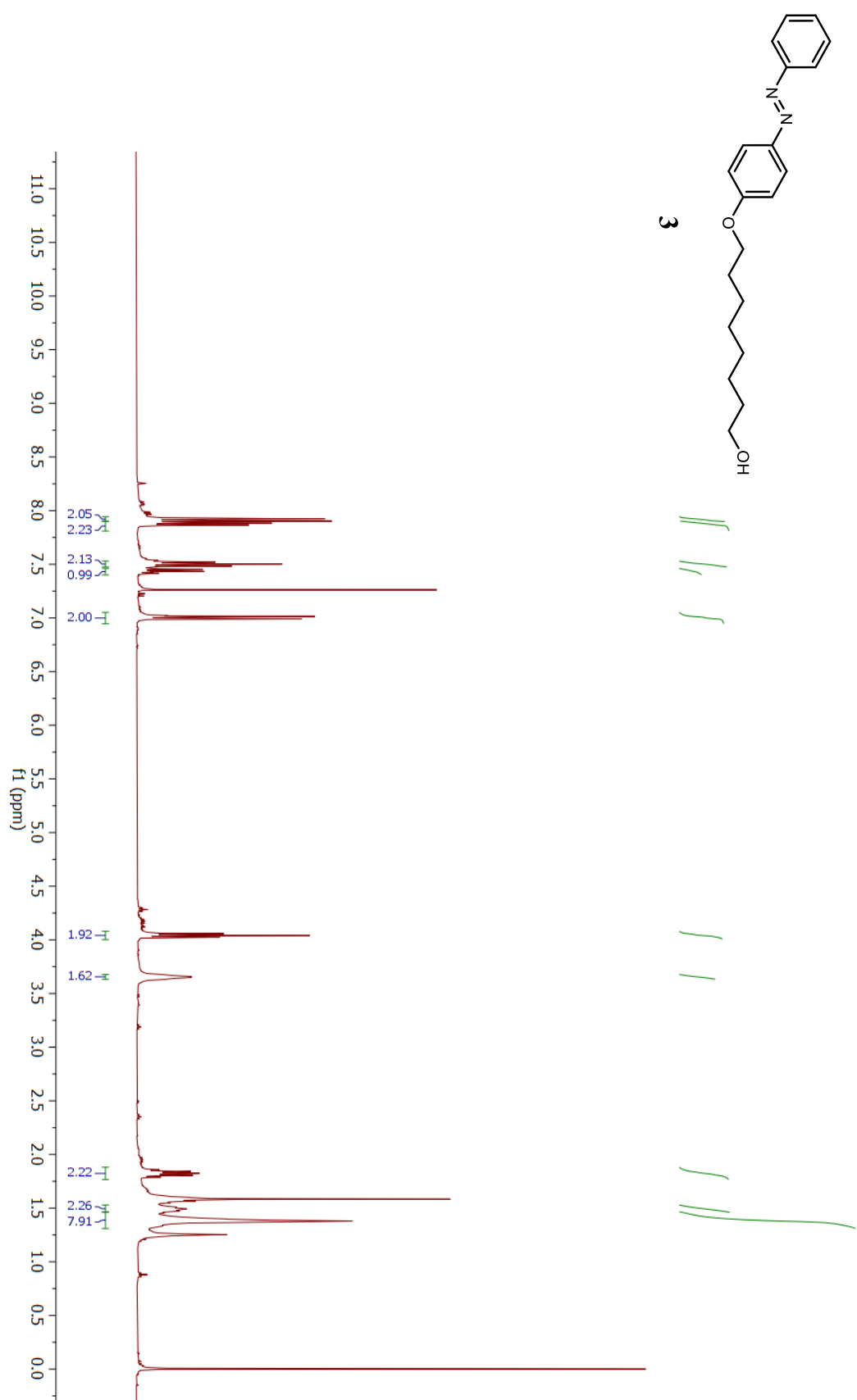


Figure A.3 : ¹H NMR of compound **3**

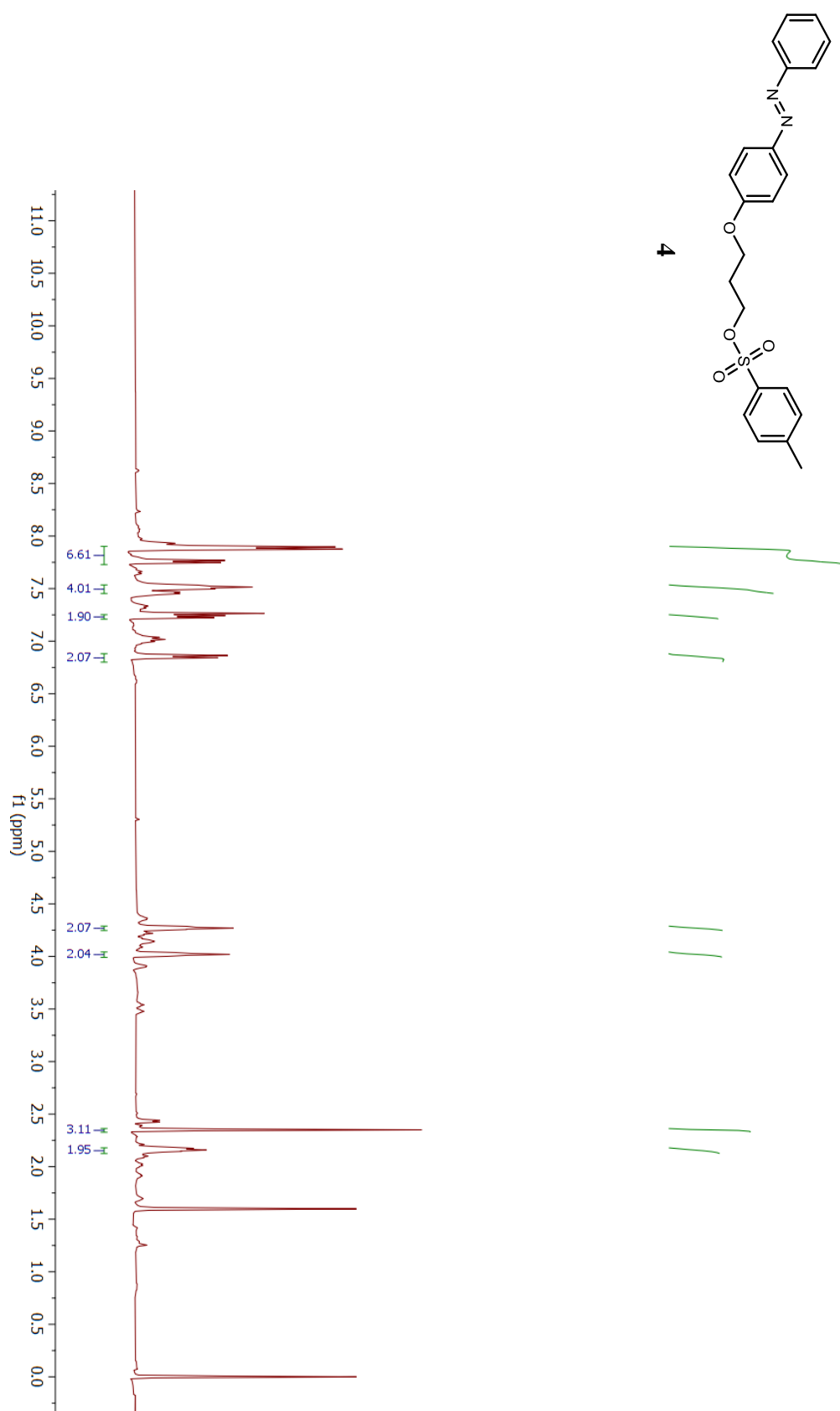


Figure A.4 : ^1H NMR of compound **4**

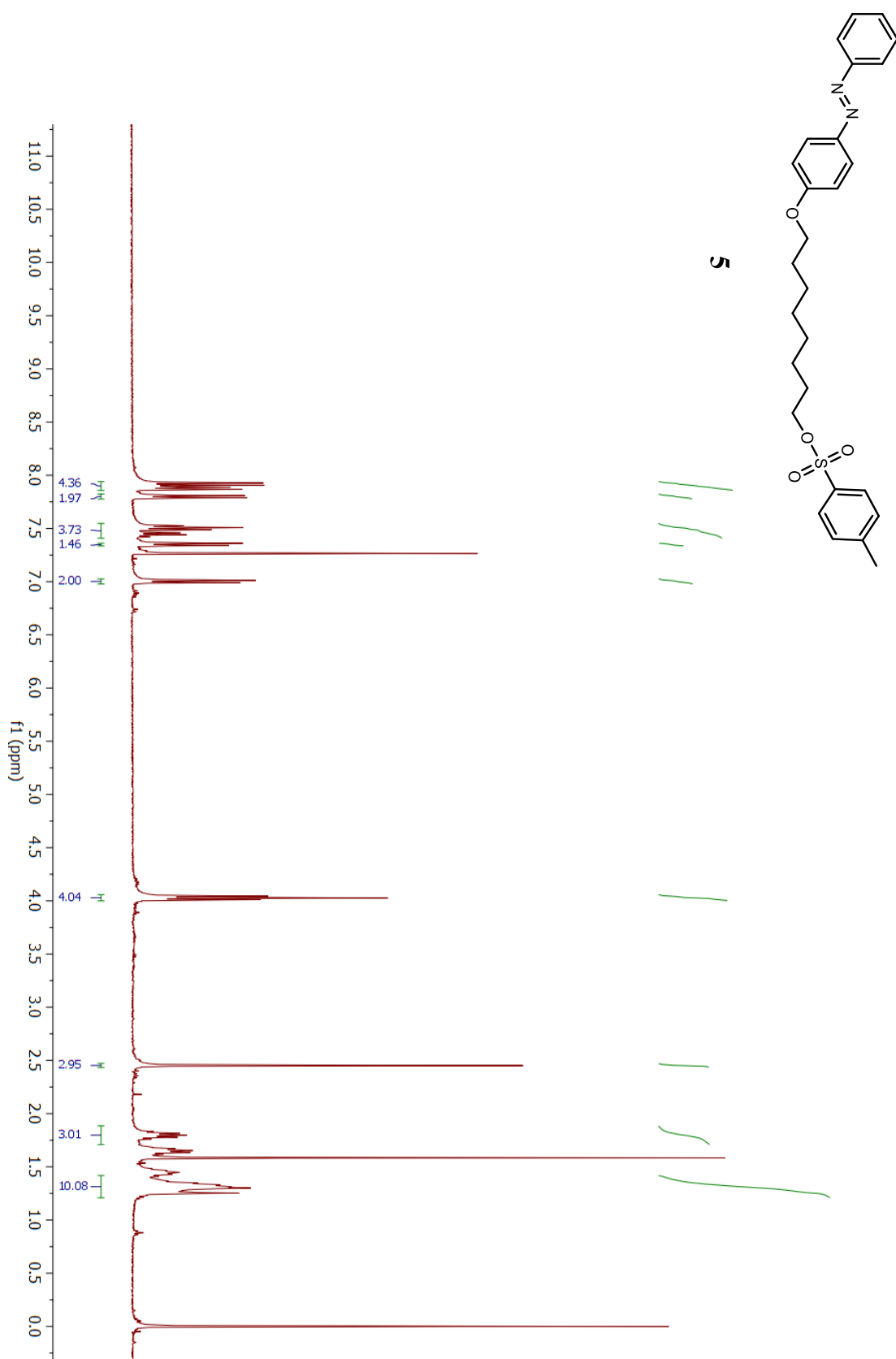


Figure A.5 : ¹H NMR of compound 5



121

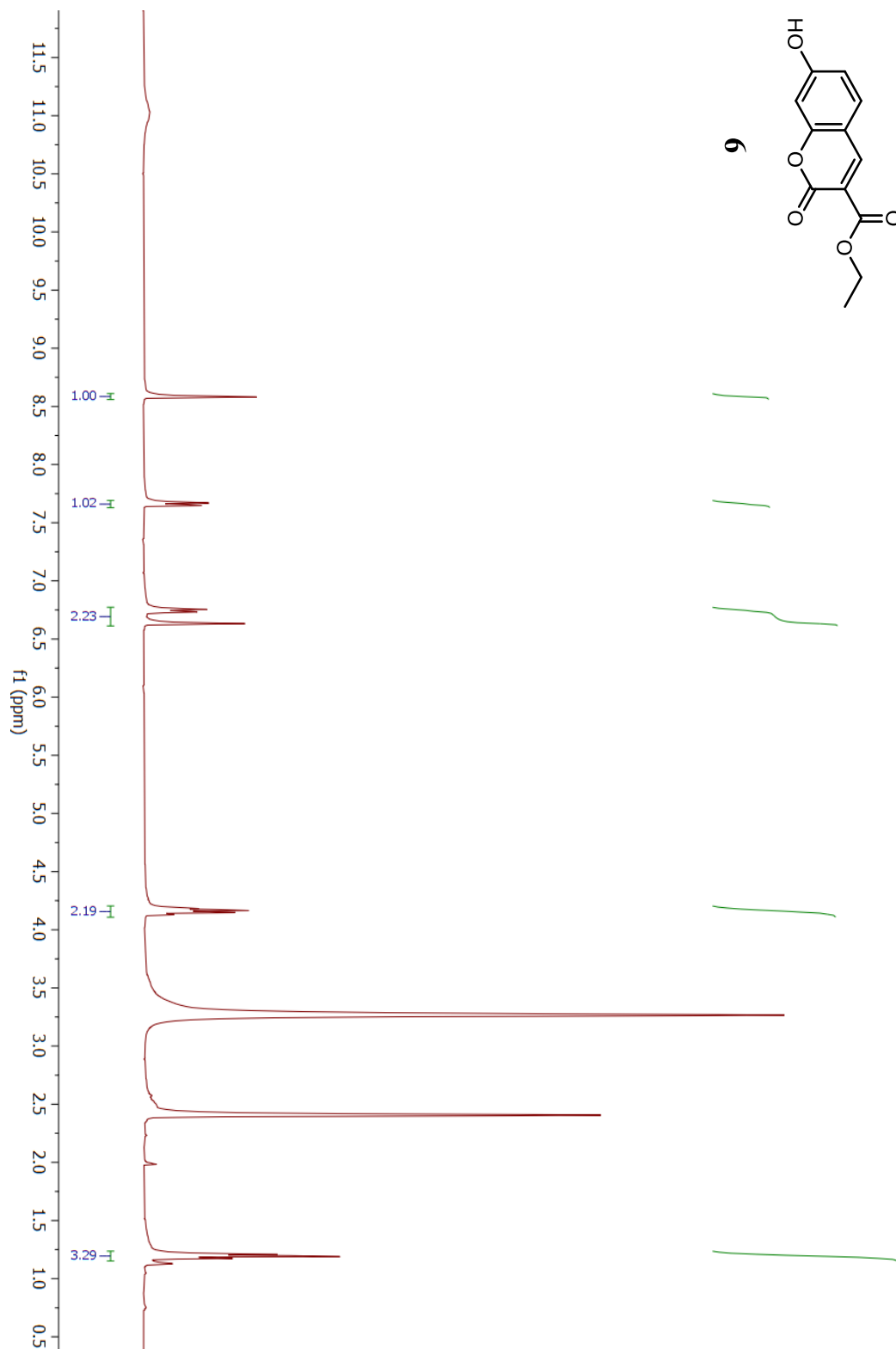


Figure A.7 : ^1H NMR of compound **6**

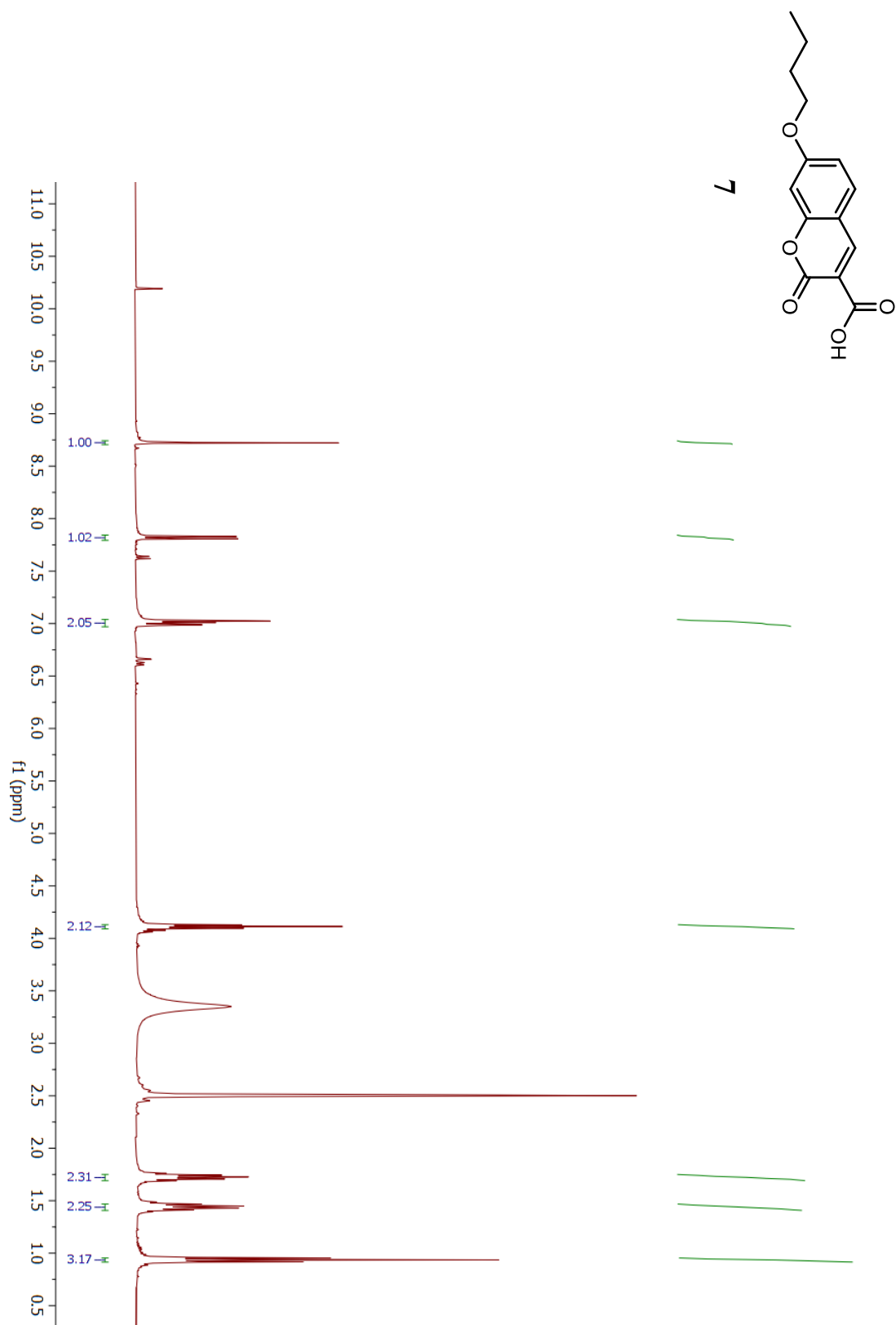


Figure A.8 : ¹H NMR of compound 7

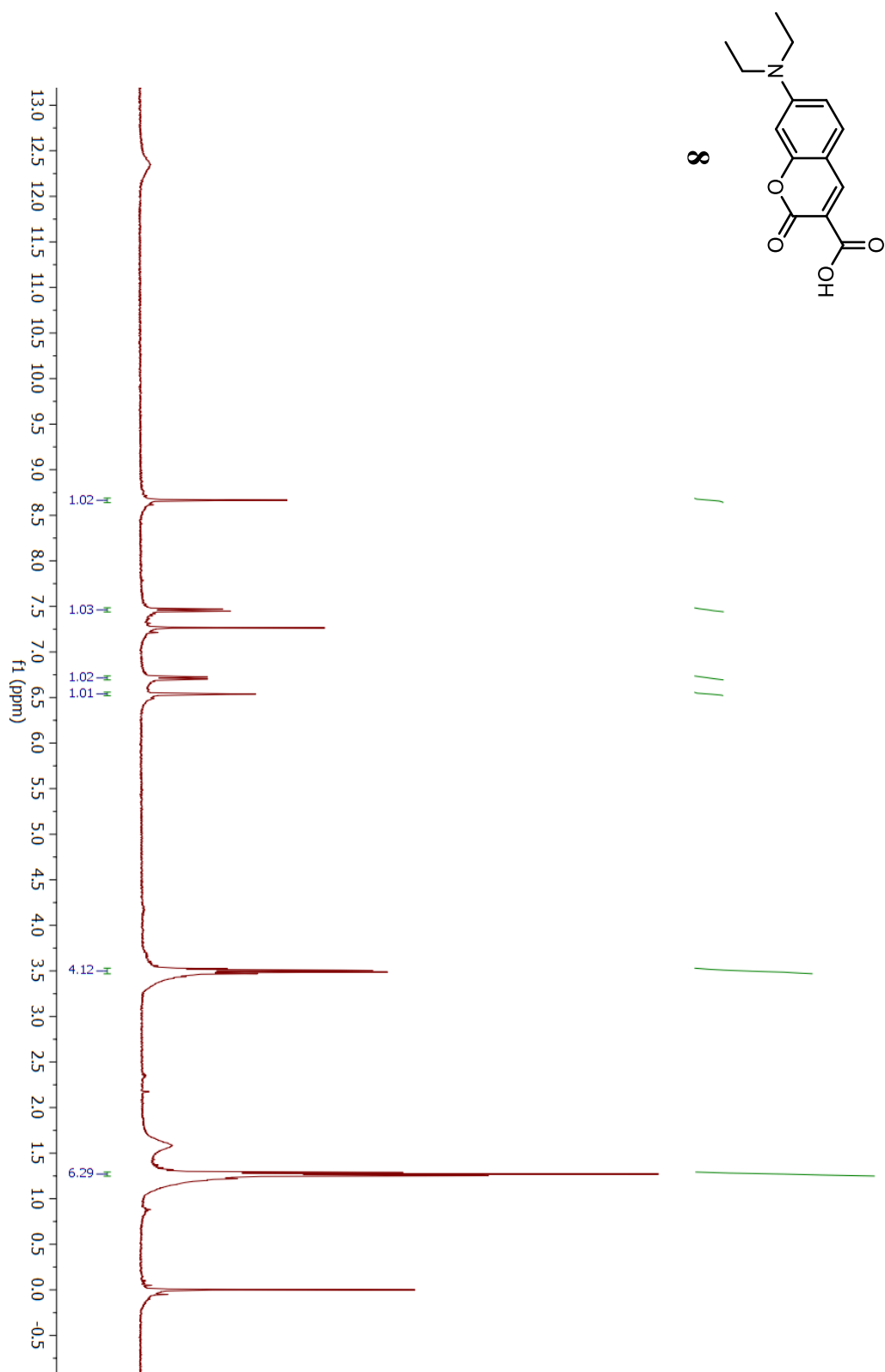


Figure A.9 : ^1H NMR of compound **8**

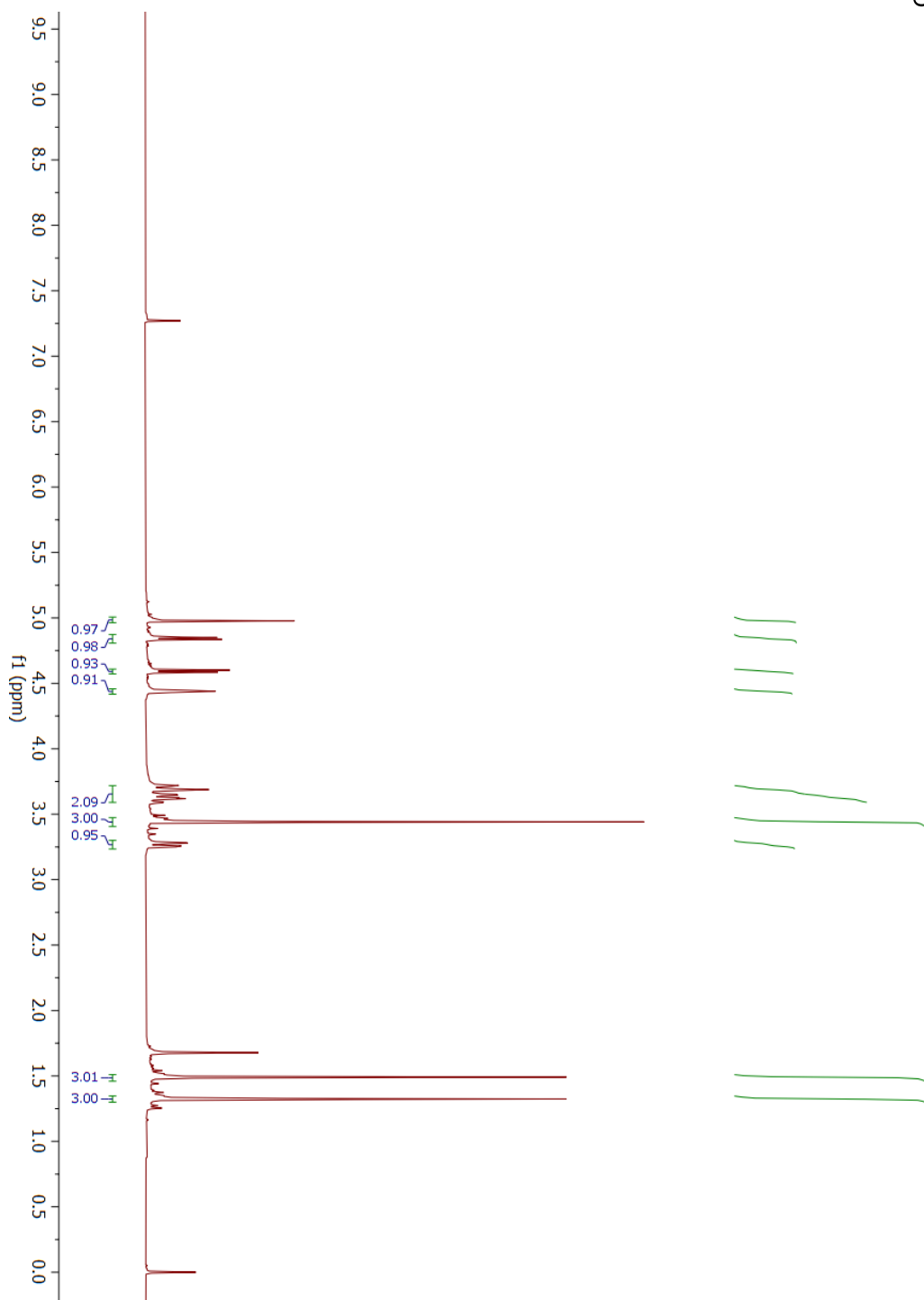
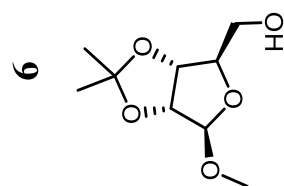


Figure A.10 : ¹H NMR of compound **9**

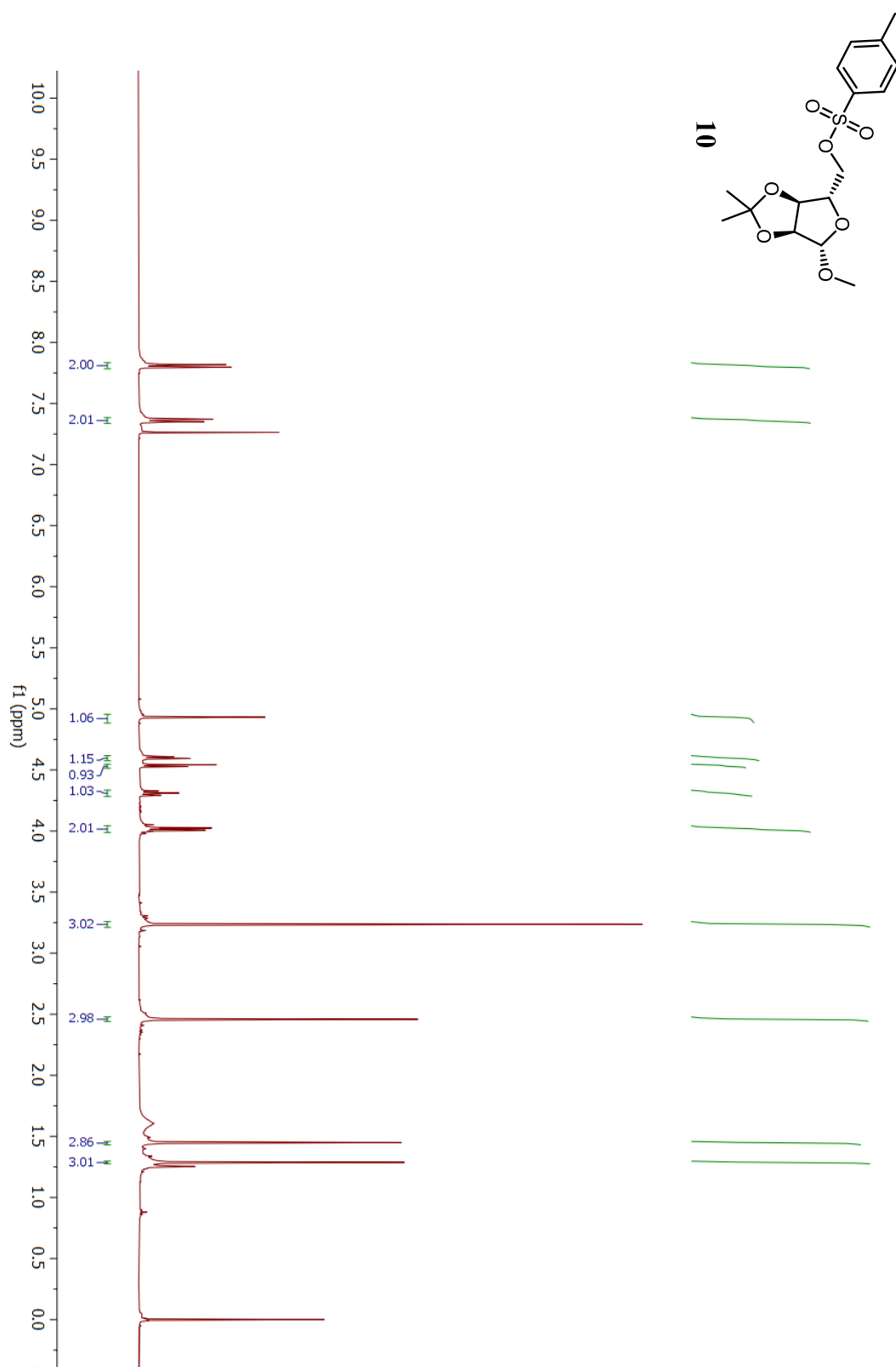


Figure A.11 : ¹H NMR of compound **10**

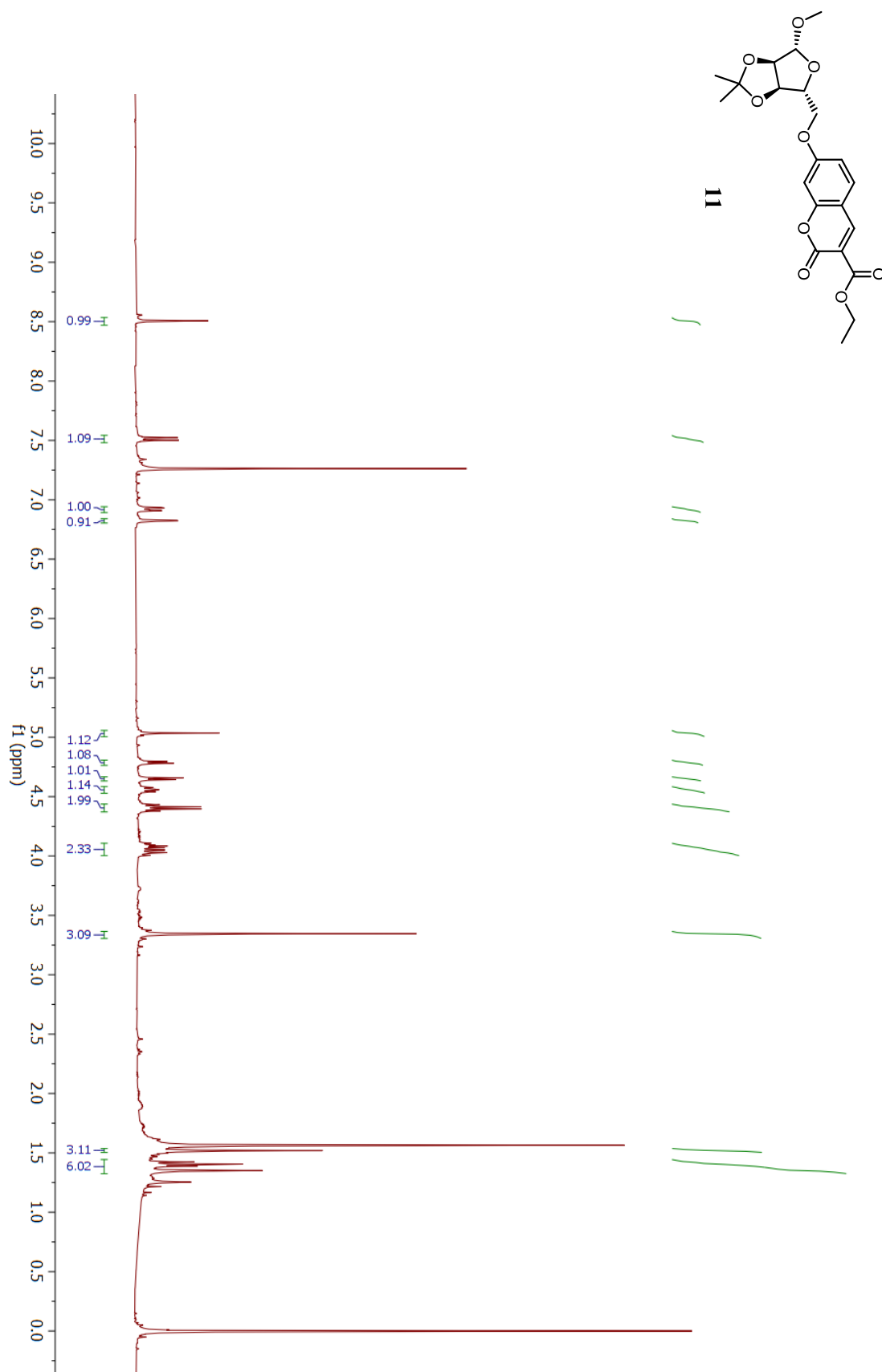
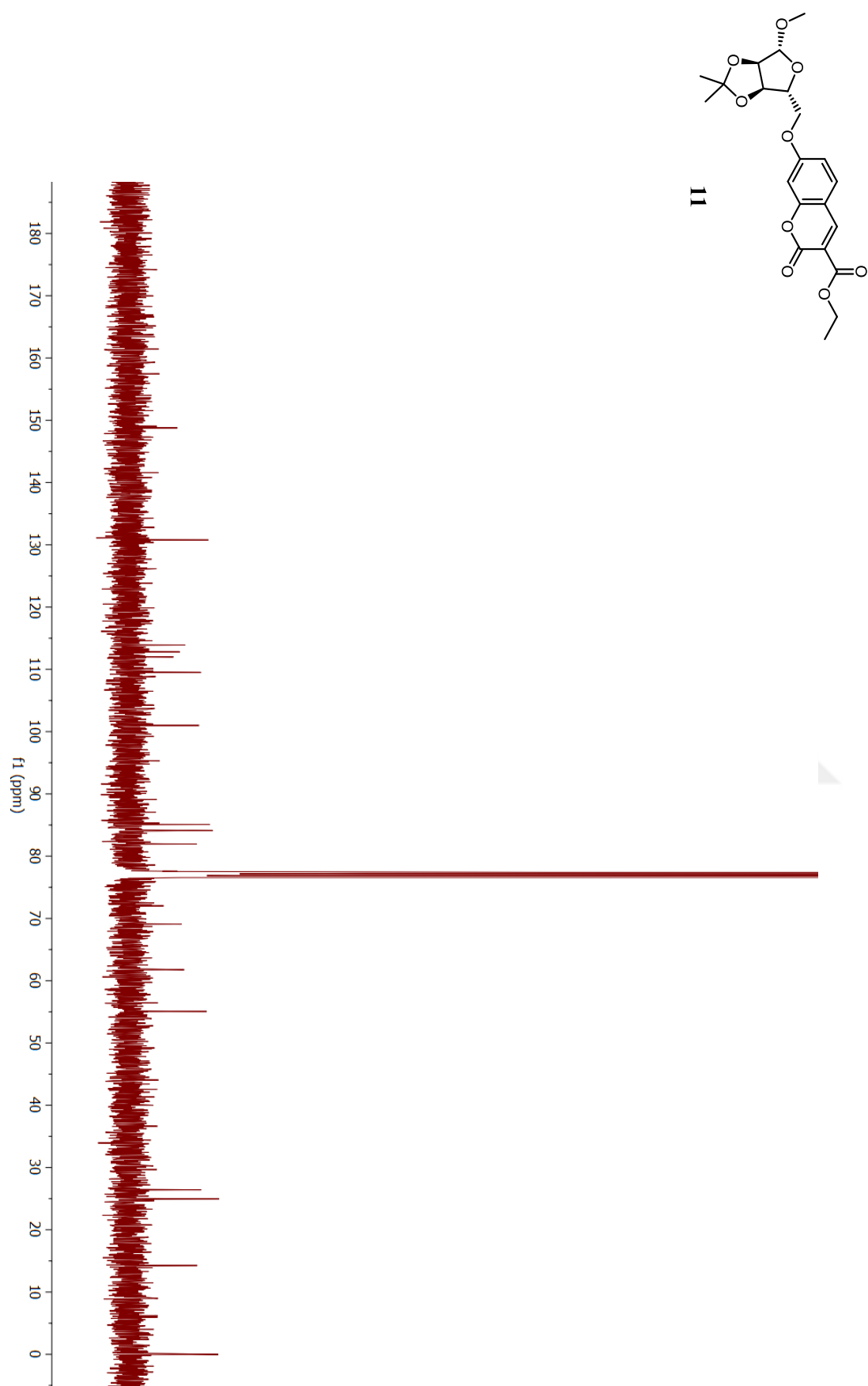


Figure A.12 : ¹H NMR of compound **11**



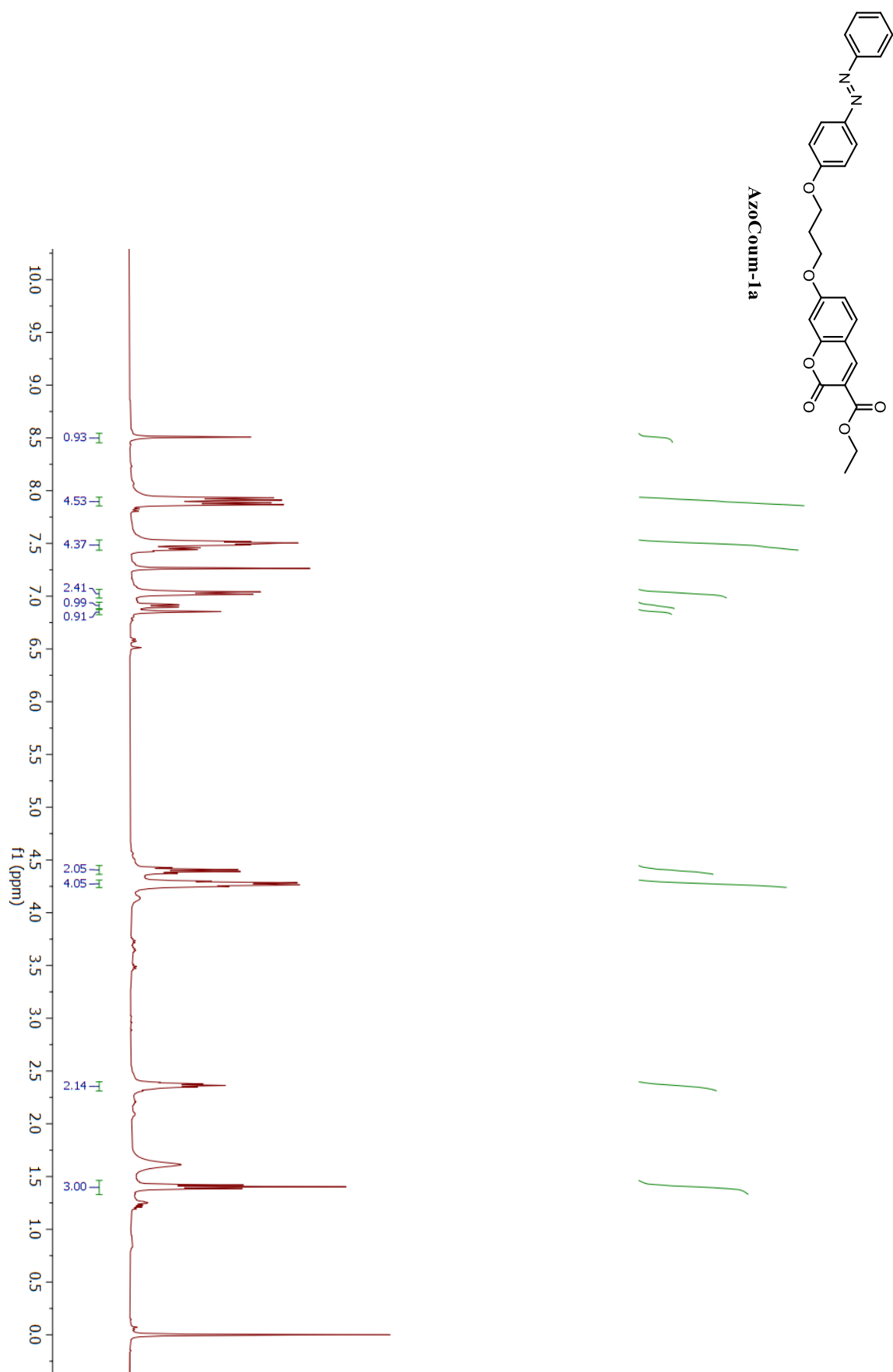


Figure A.14 : ¹H NMR of AzoCounm-1a

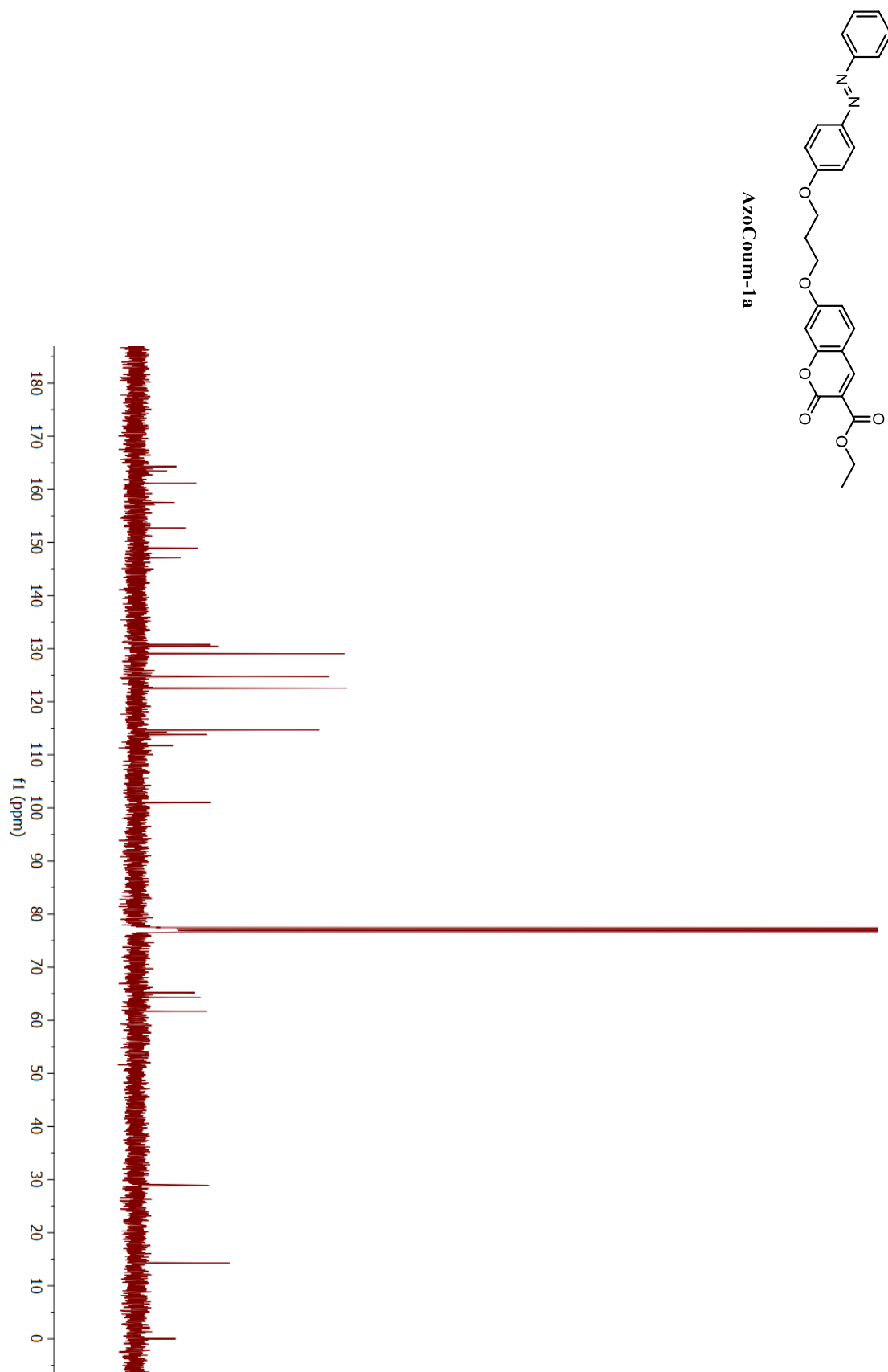


Figure A.15 : ^{13}C NMR of **AzoCoun-1a**

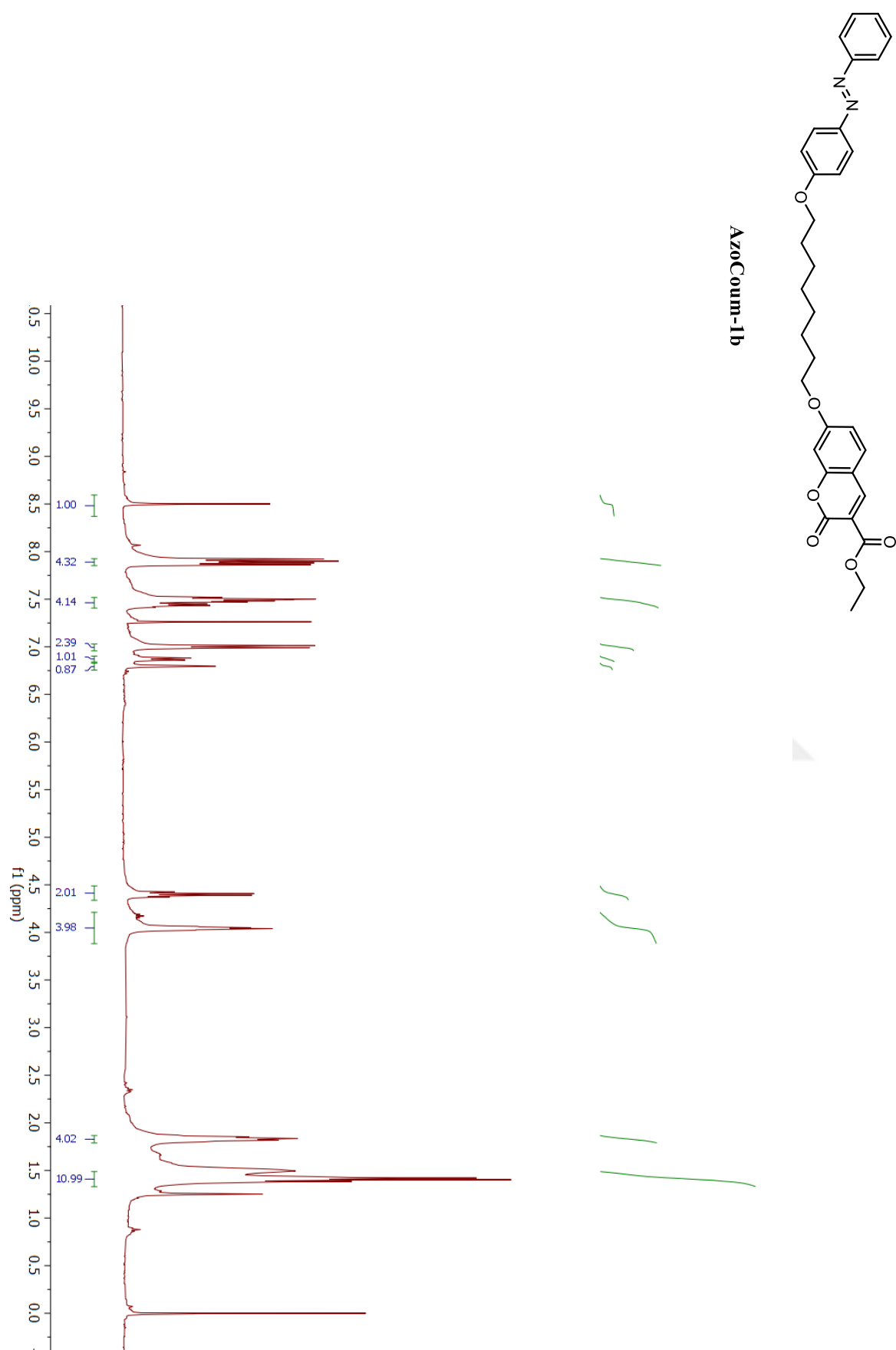


Figure A.16 : ¹H NMR of AzoCoun-1b

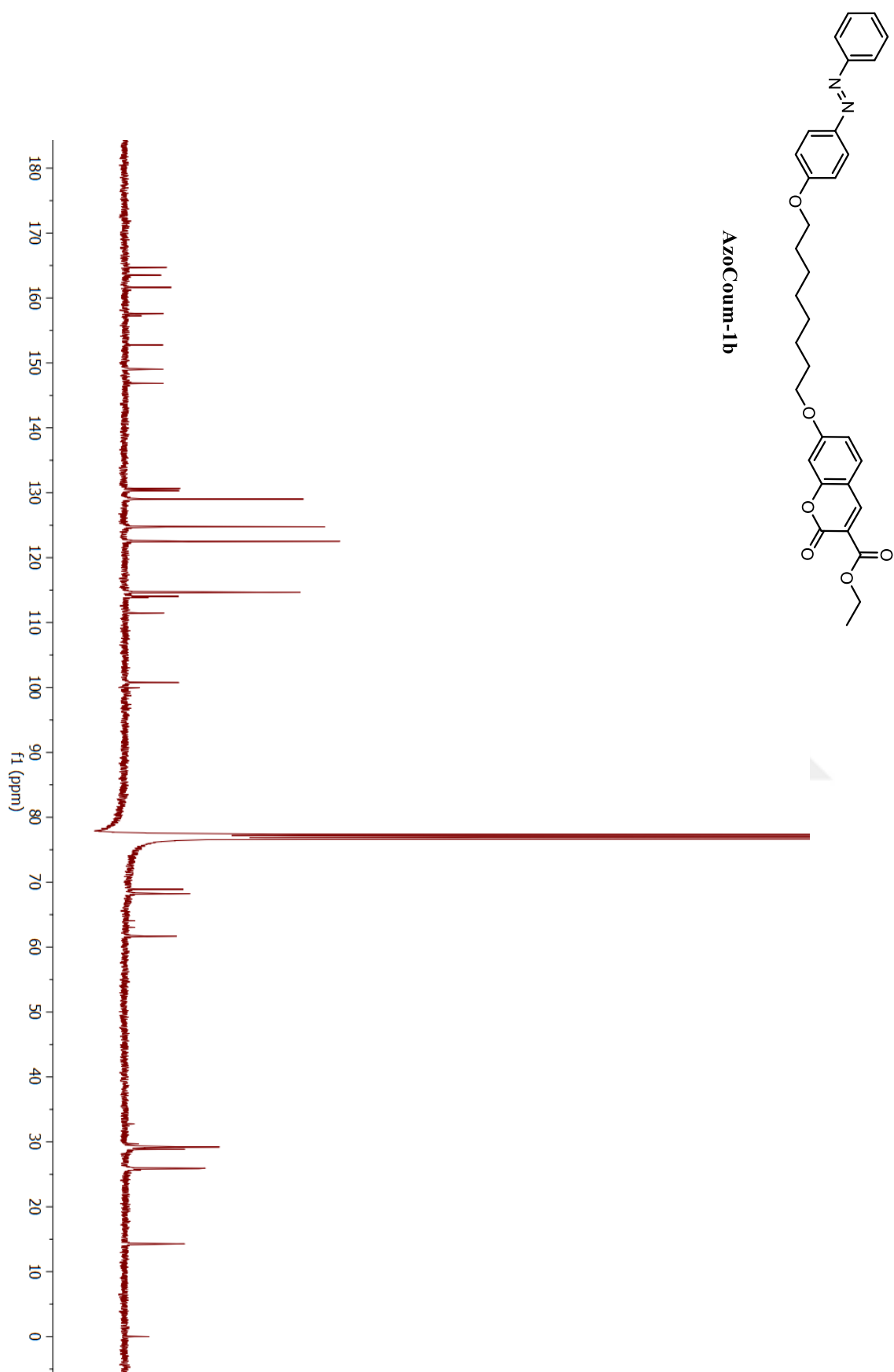


Figure A.17 : ¹³C NMR of AzoCoun-1b

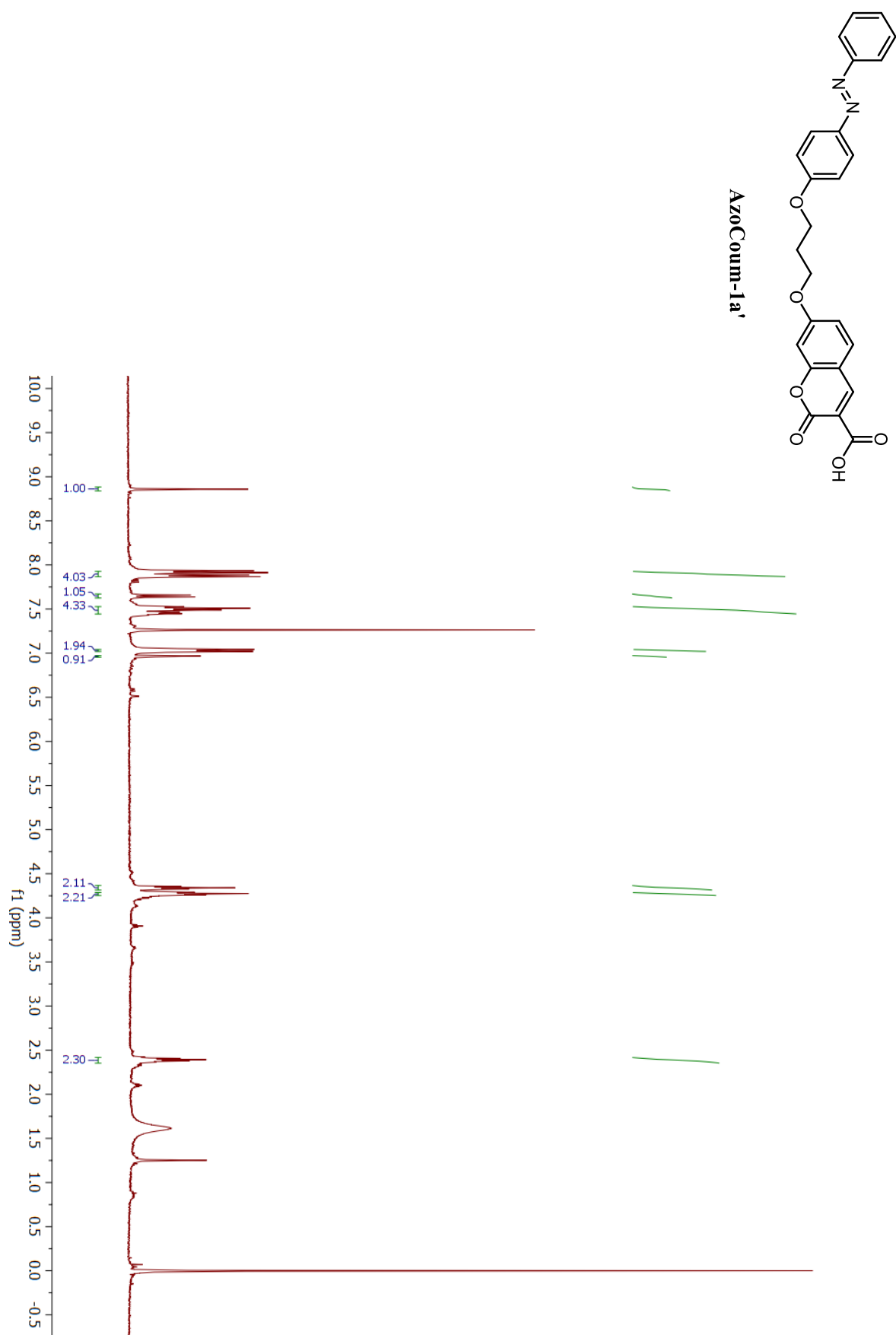


Figure A.18 : ¹H NMR of AzoCounm-1a'

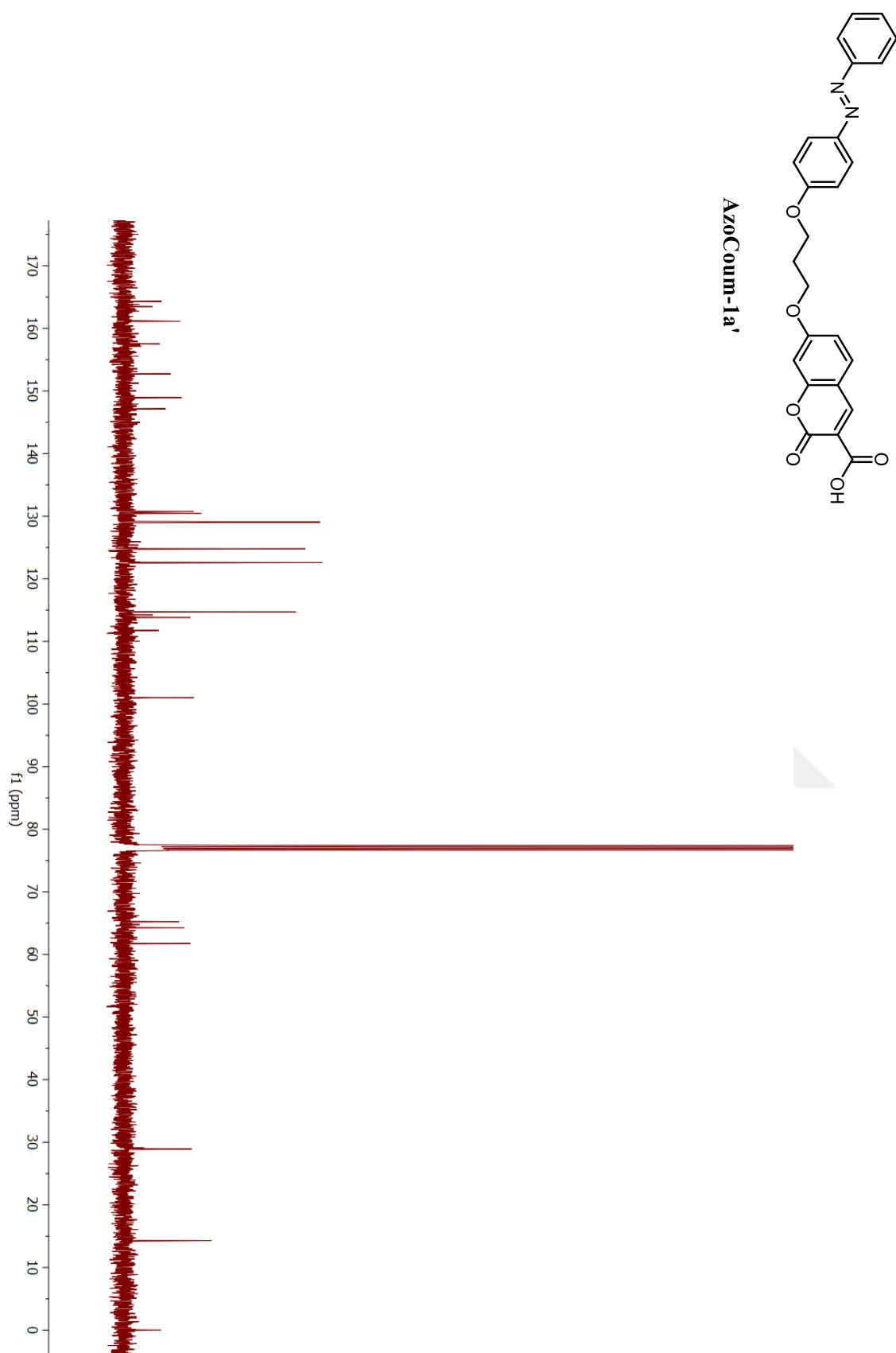


Figure A.19 : ¹³C NMR of **AzoCoug-1a'**

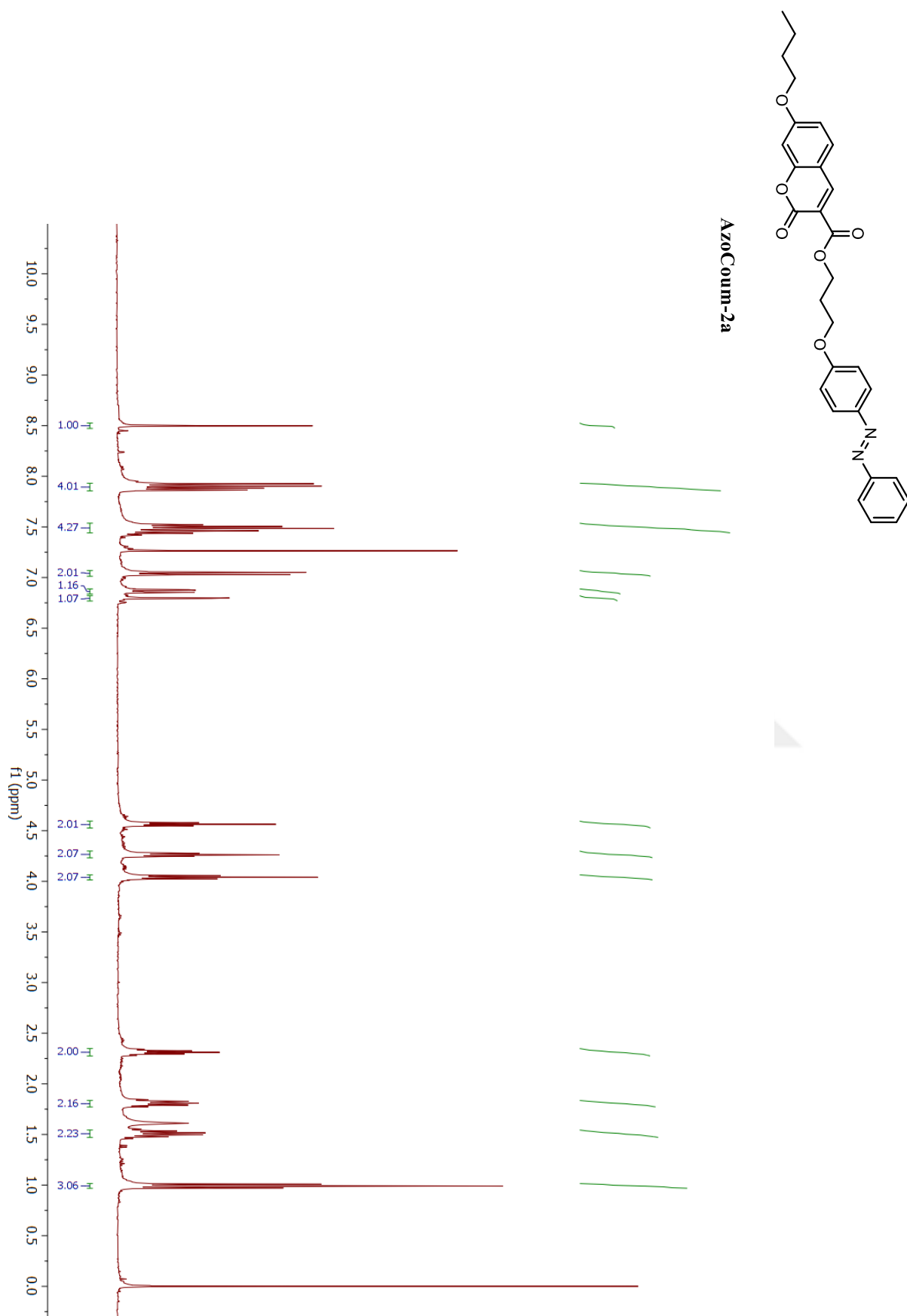


Figure A.20 : ^1H NMR of AzoCoum-2a

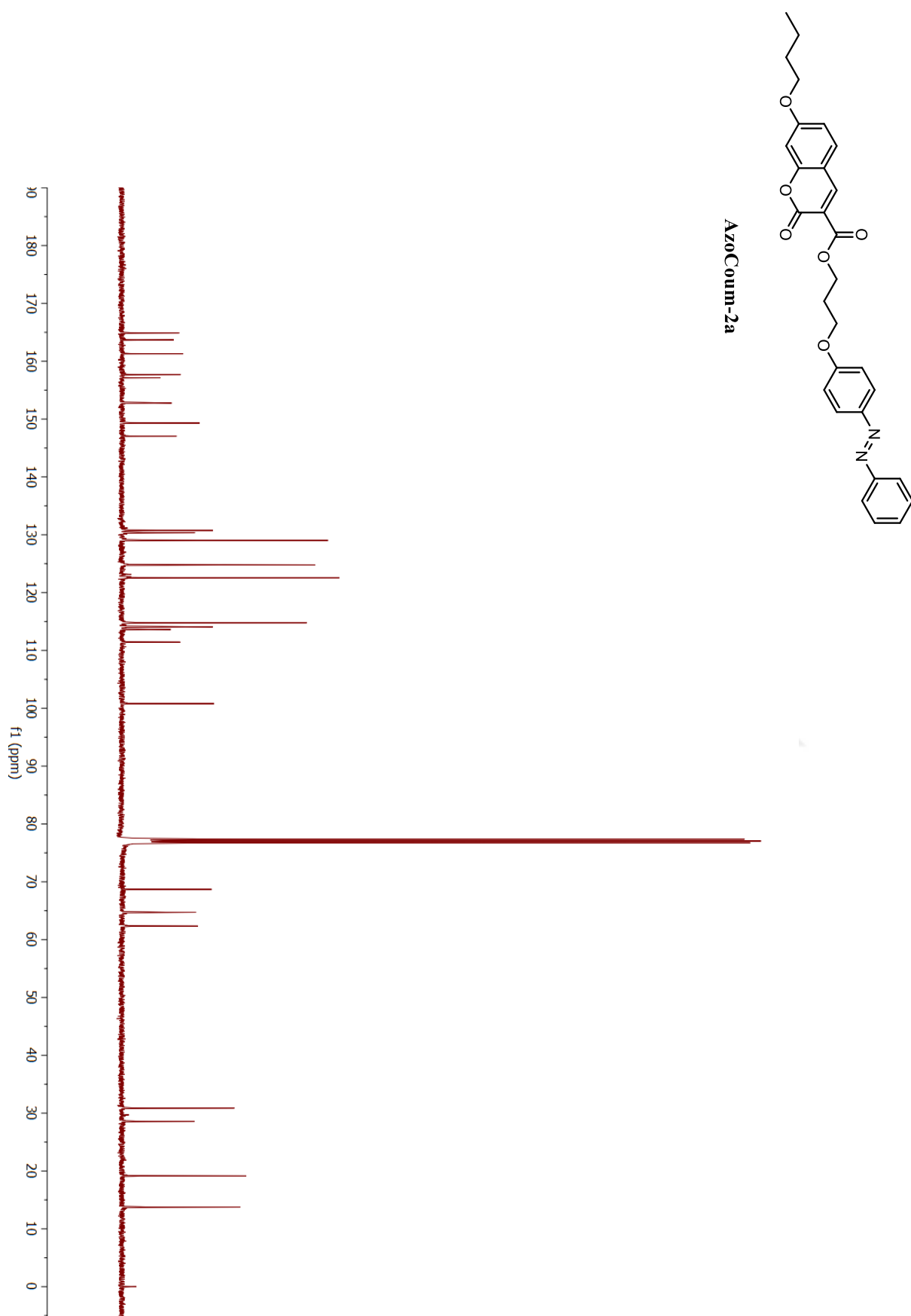


Figure A.21 : ¹³C NMR of AzoCoun-2a

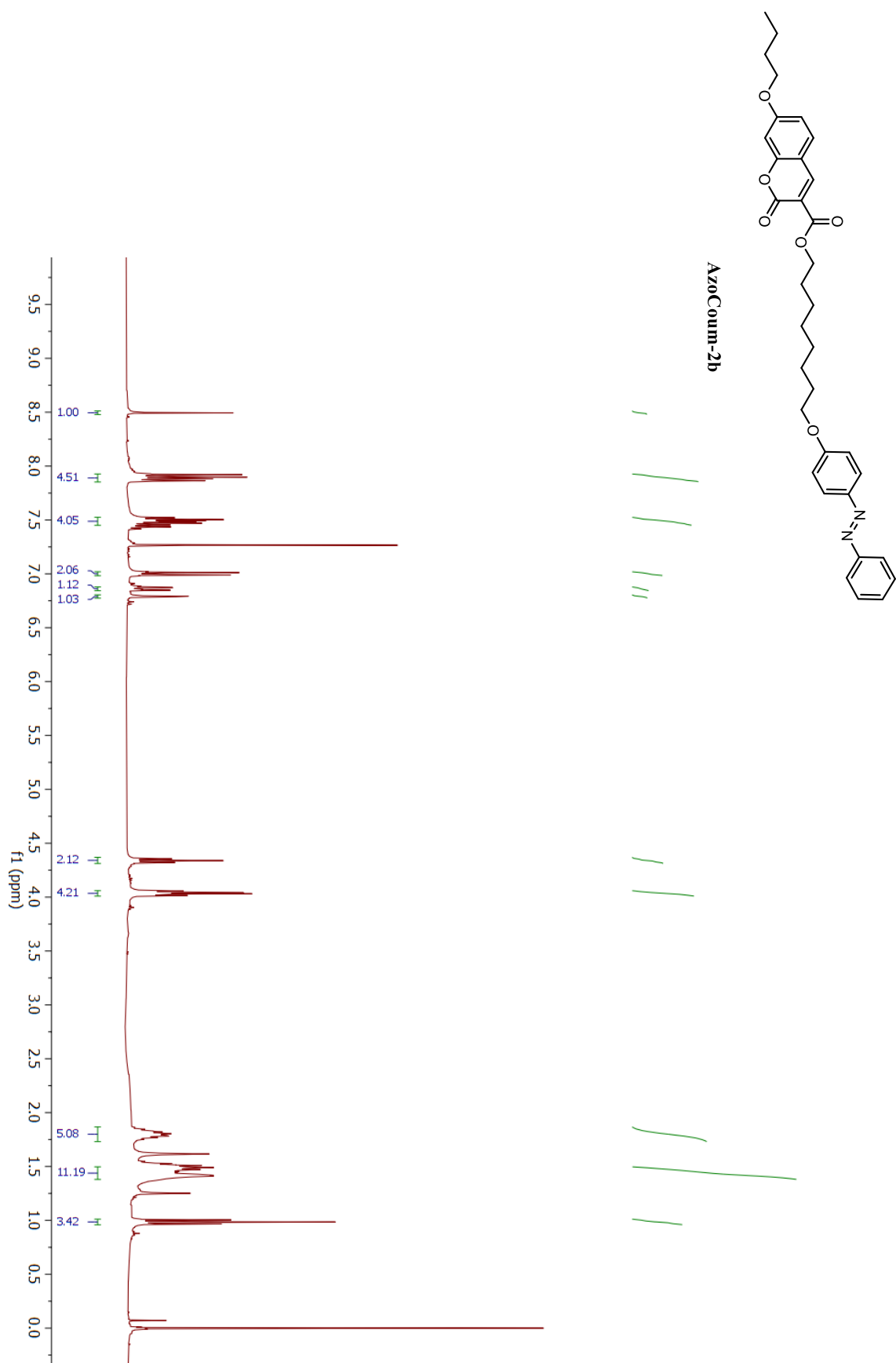


Figure A.22 : ¹H NMR of AzoCoun-2b

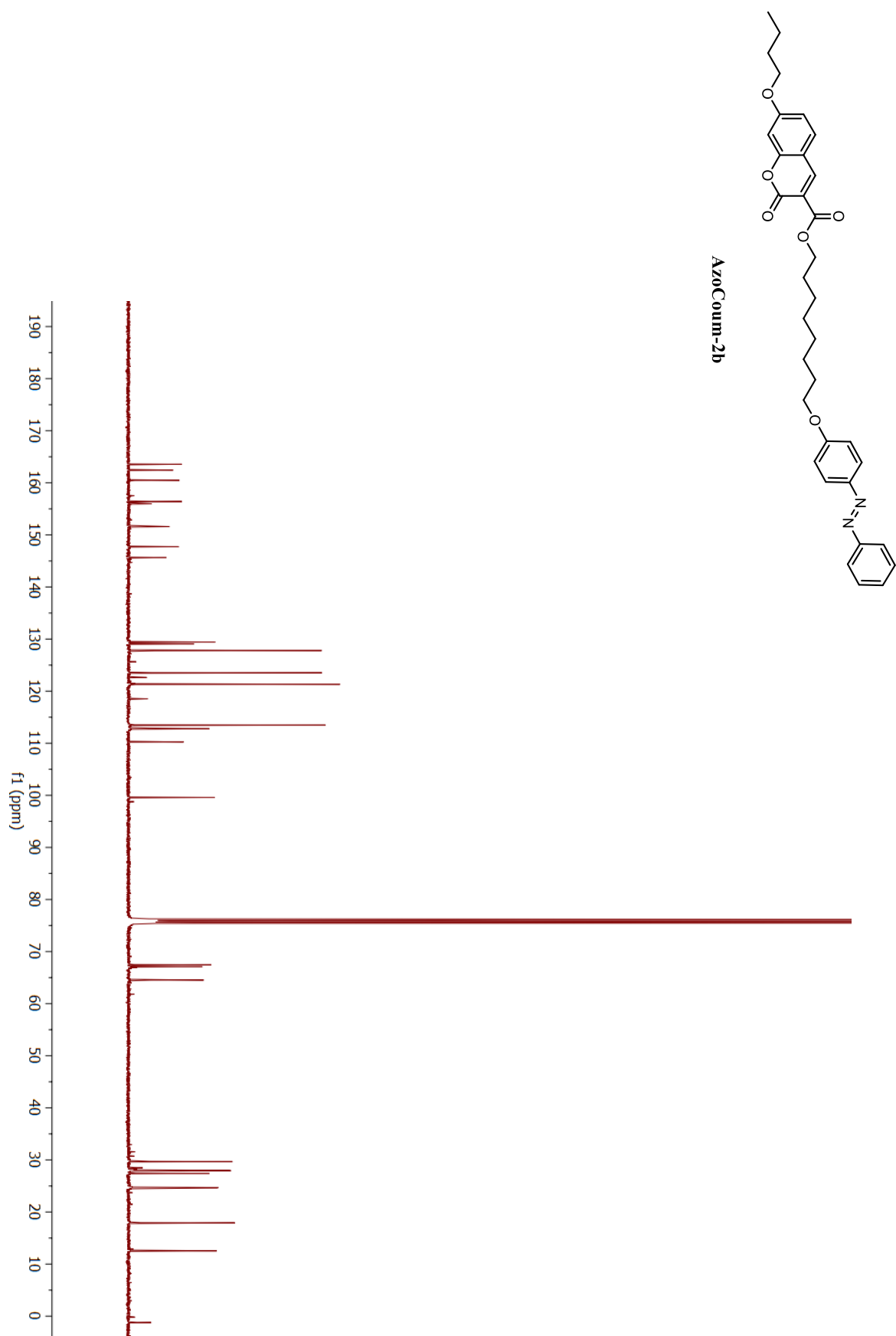


Figure A.23 : ^{13}C NMR of **AzoCoun-2b**

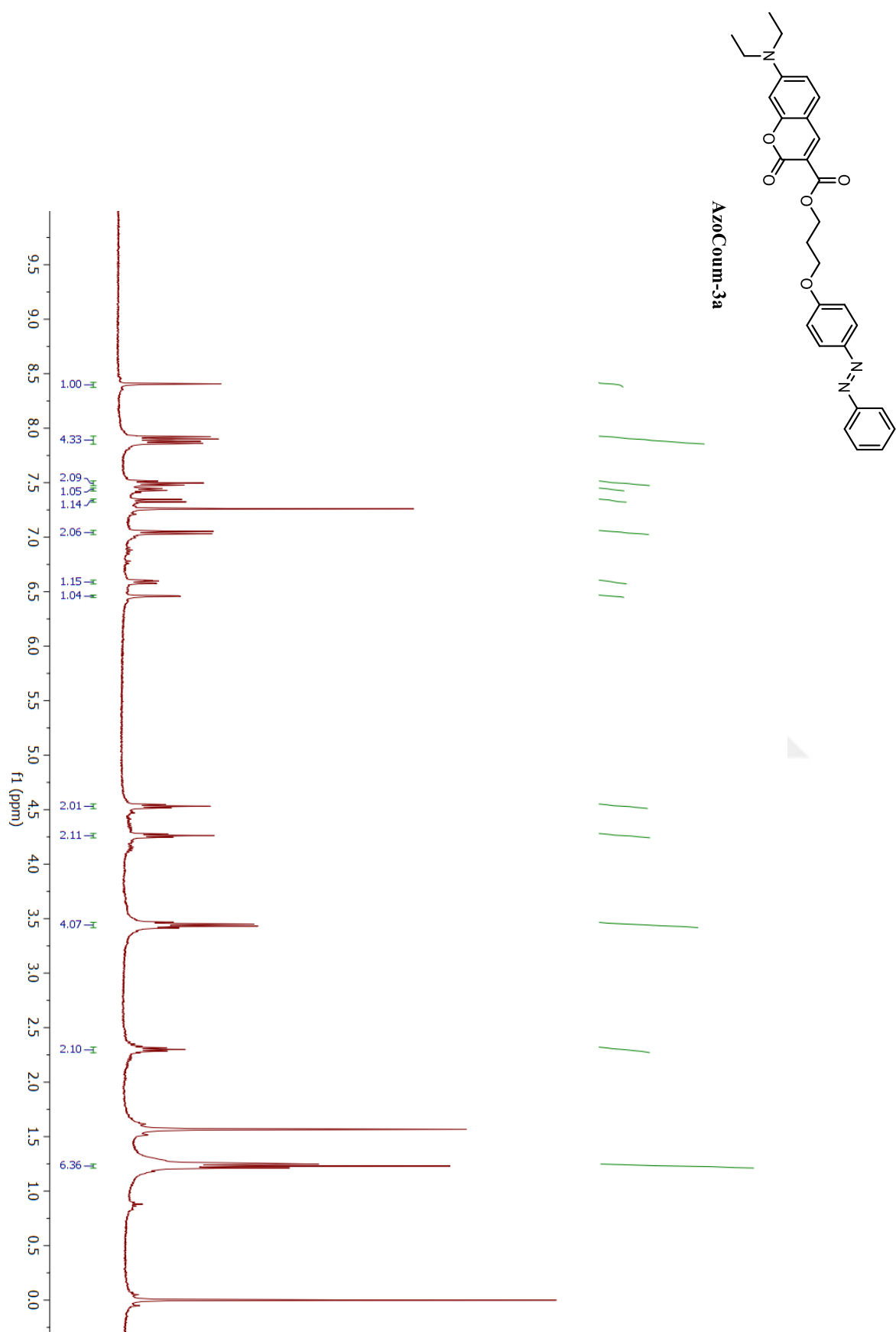


Figure A.24 : ¹H NMR of AzoCoun-3a

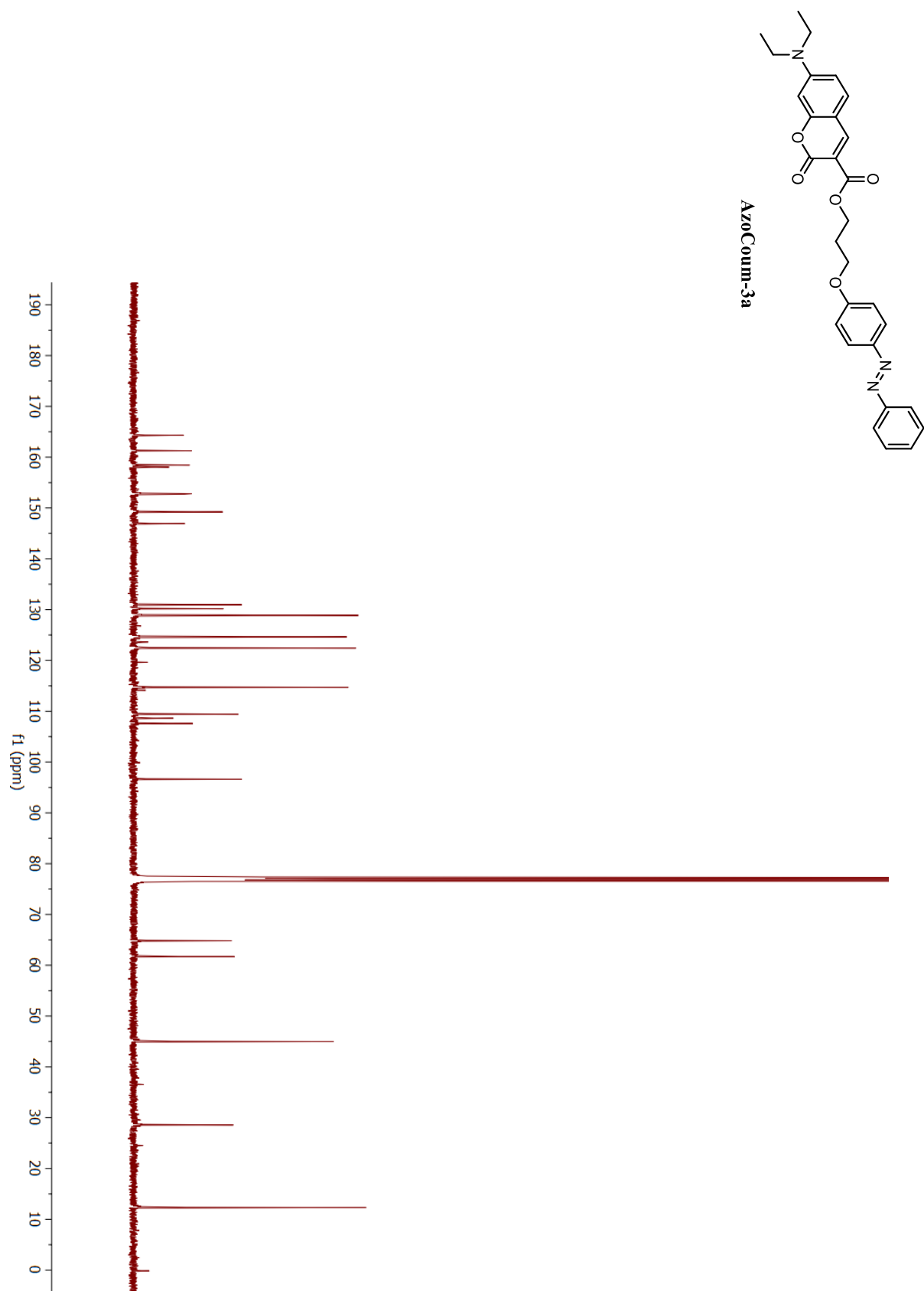


Figure A.25 : ^{13}C NMR of AzoCoun-3a

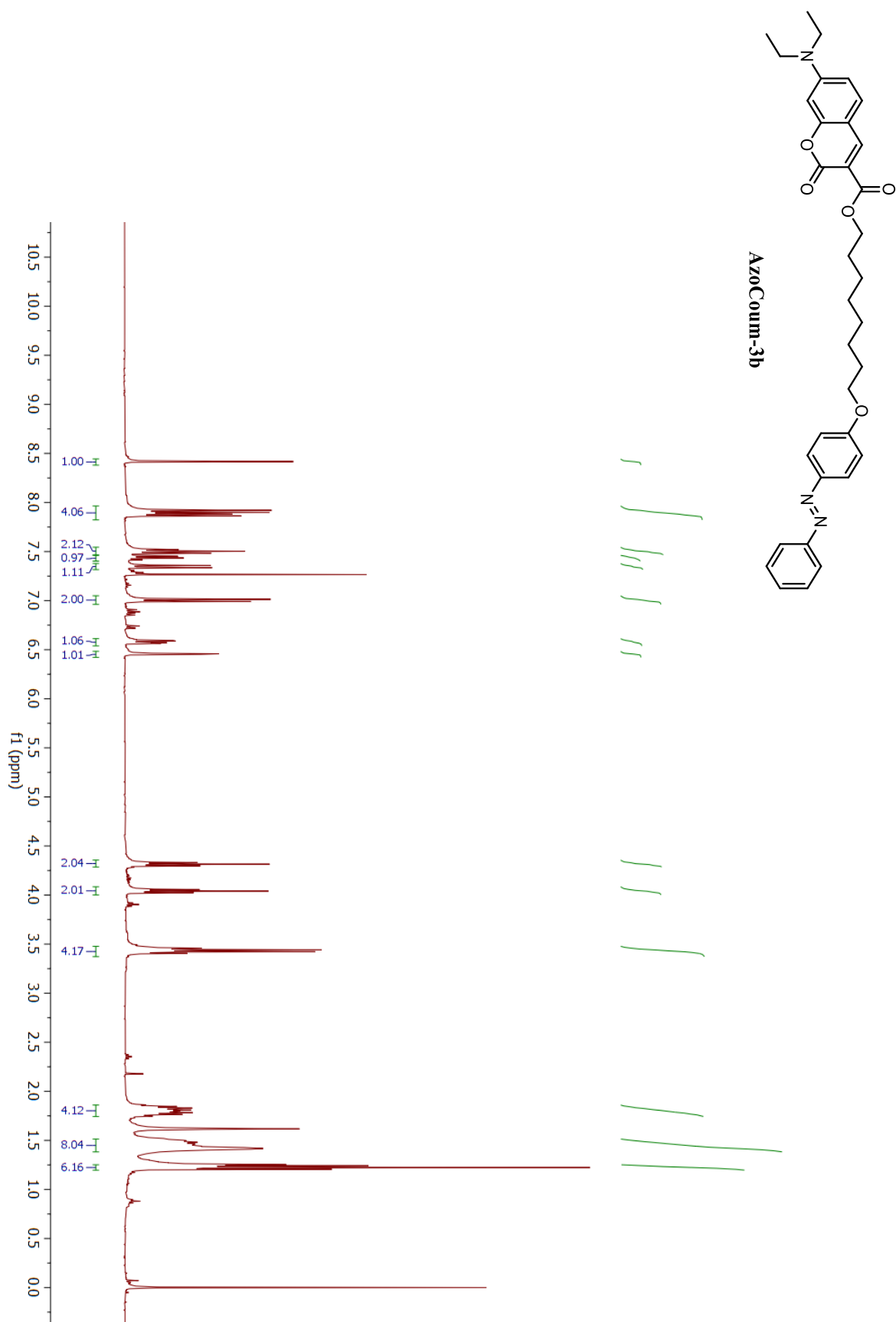


Figure A.26 : ¹H NMR of AzoCoun-3b

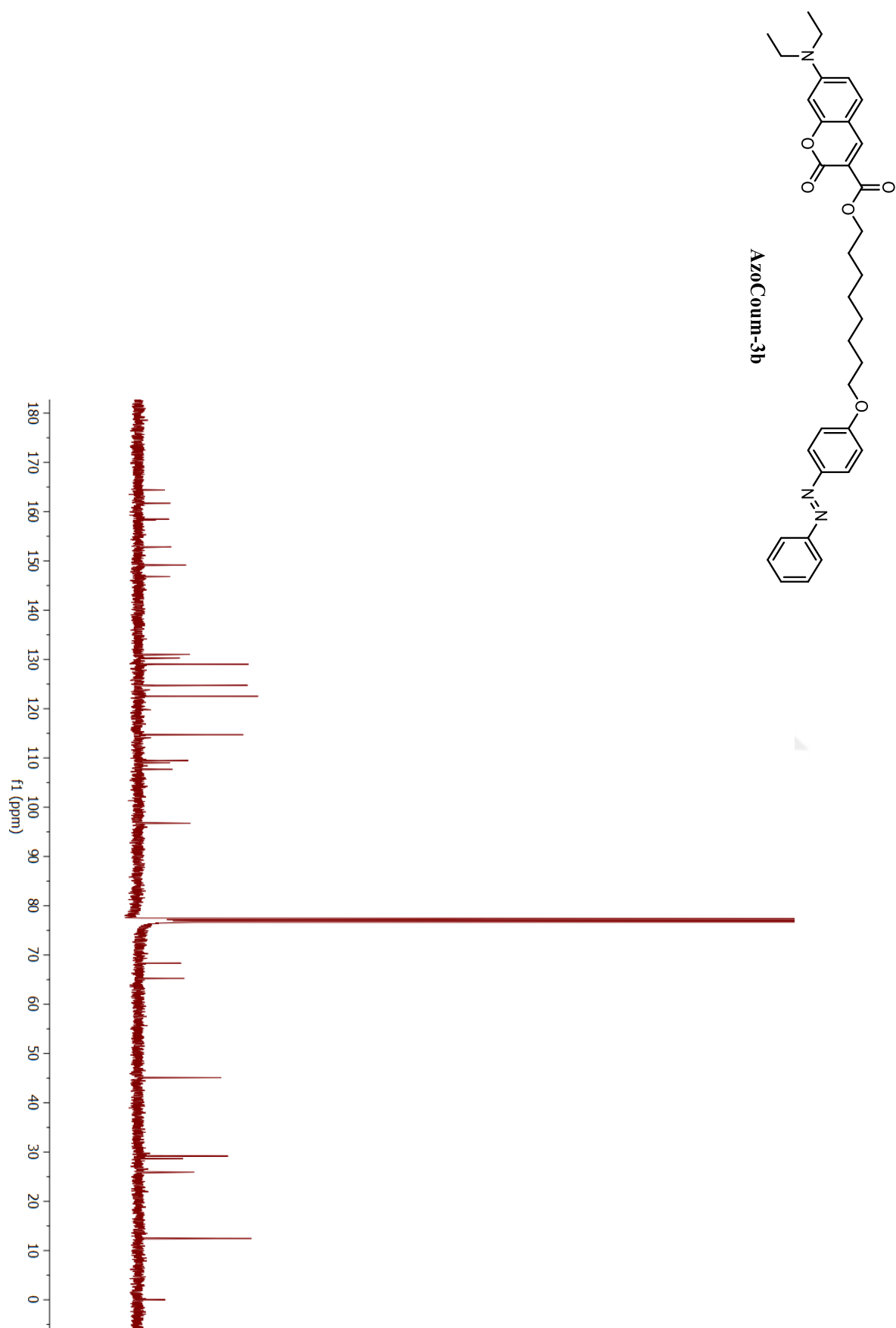


Figure A.27 : ¹³C NMR of AzoCoun-3b

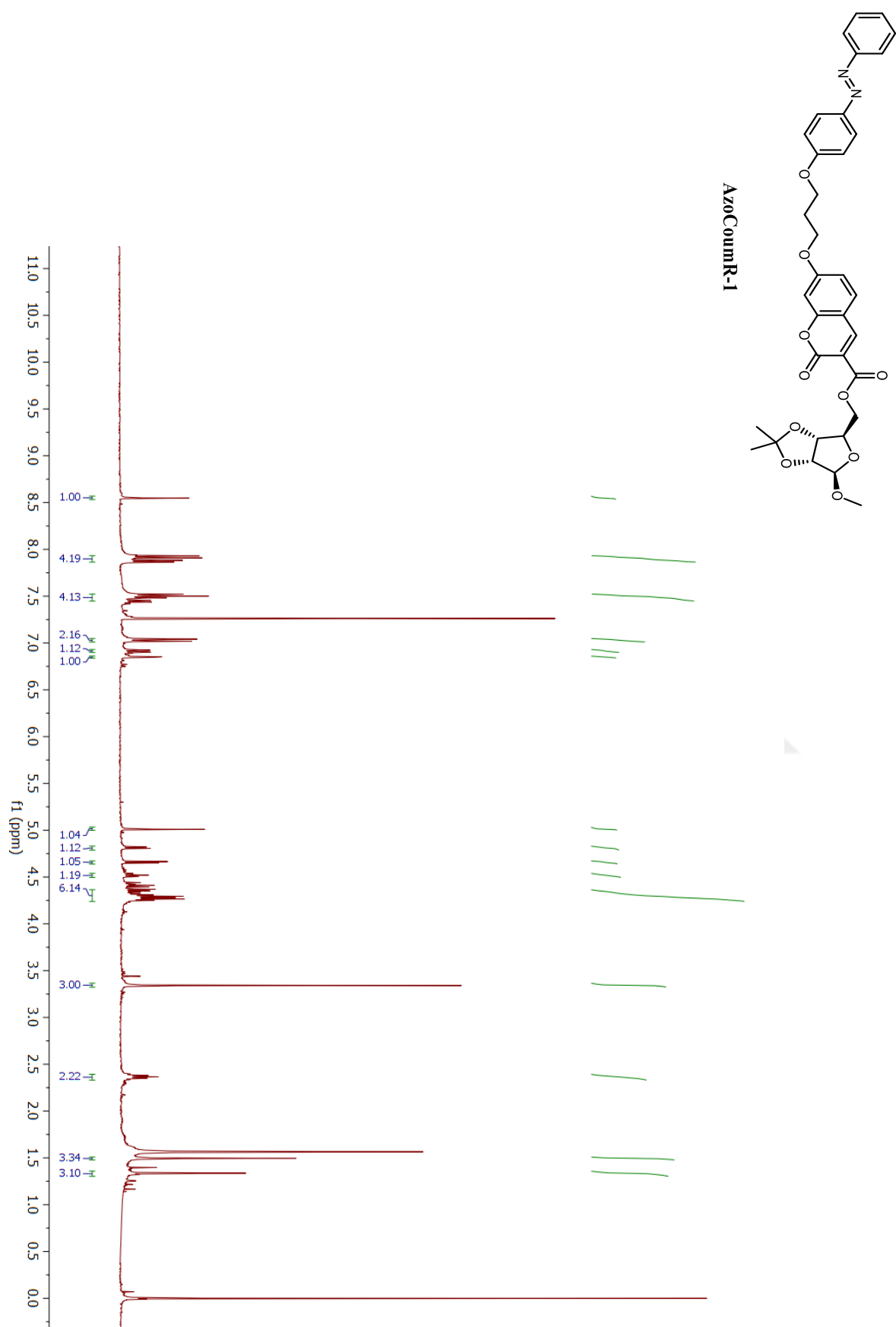


Figure A.28 : ¹H NMR of AzoCounR-1

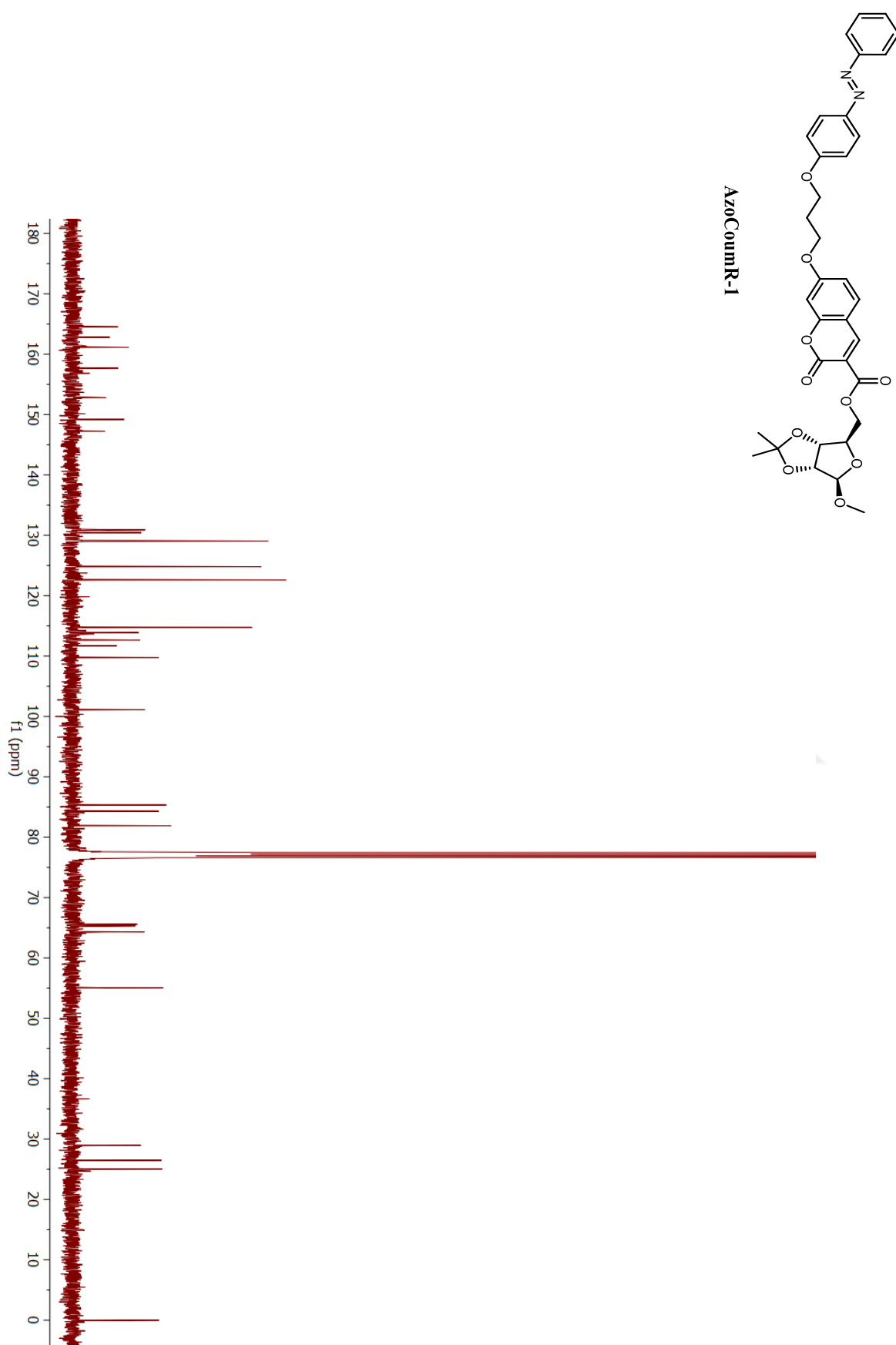


Figure A.29 : ^{13}C NMR of AzoCounR-1

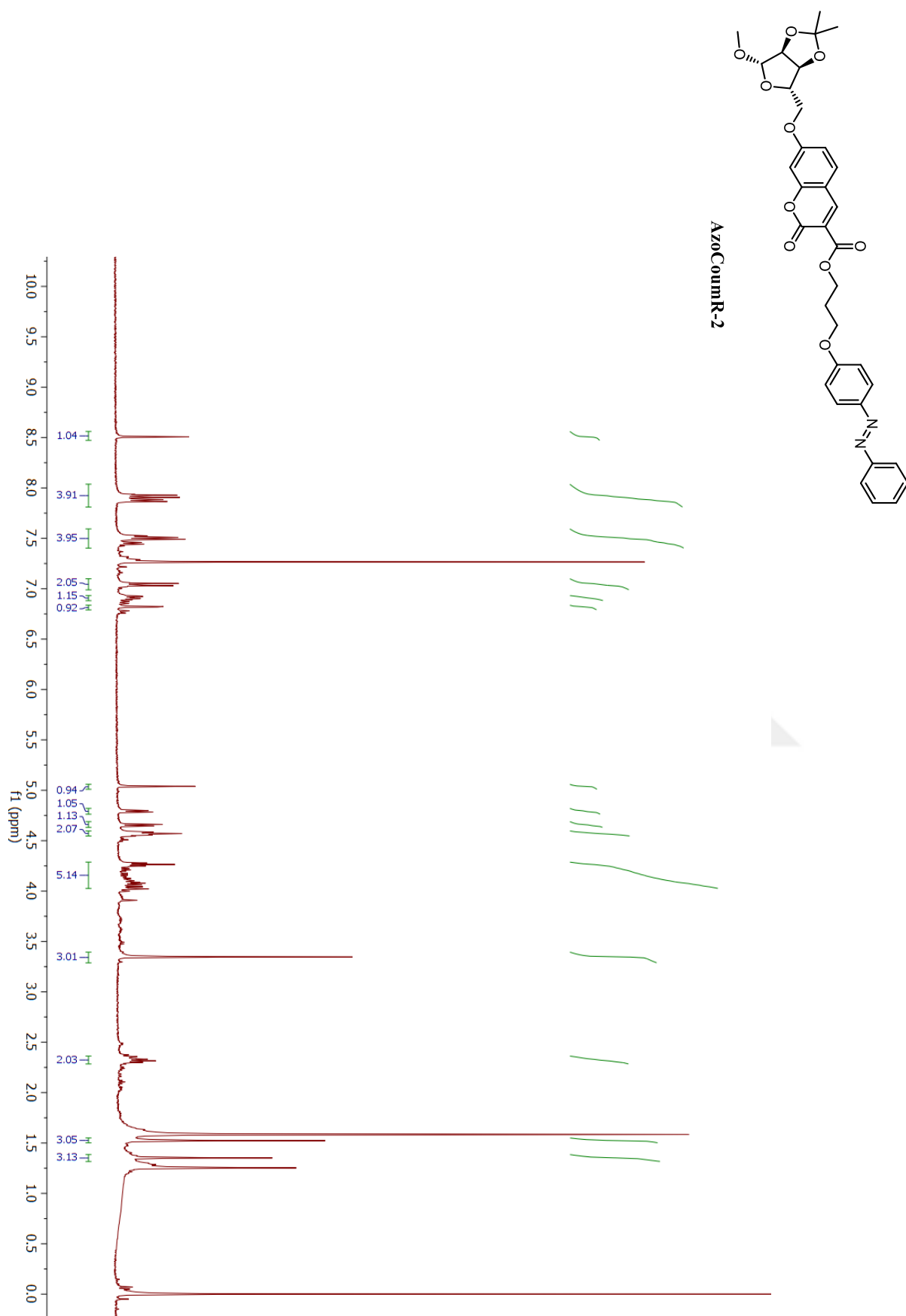


Figure A.30 : ¹H NMR of AzoCounR-2

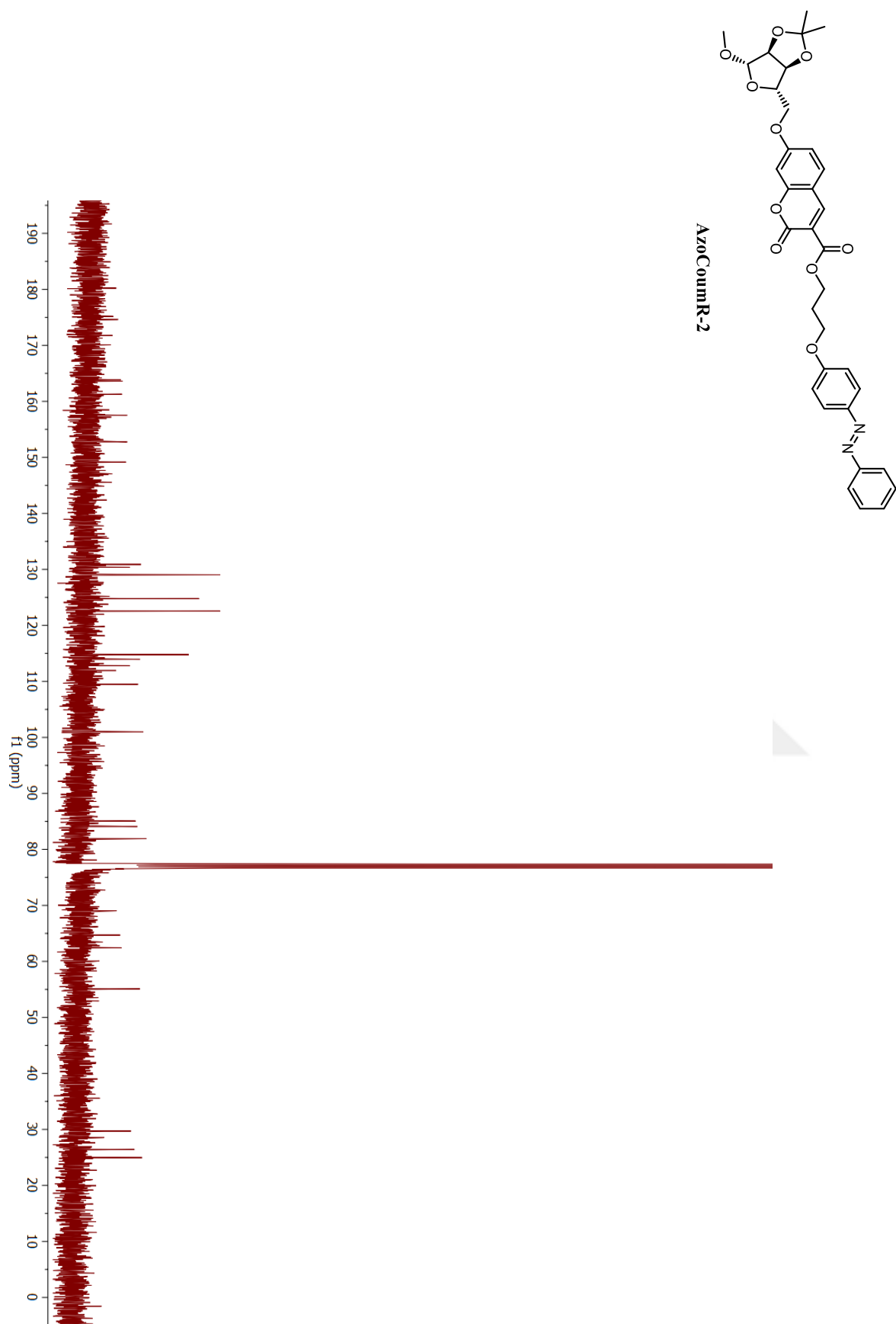


Figure A.31 : ^{13}C NMR of AzoCounR-2

B. Infrared (IR) Spectra

The IR spectra measurements were recorded using Thermo Scientific Nicolet iS10 ATR-IR spectrometer.

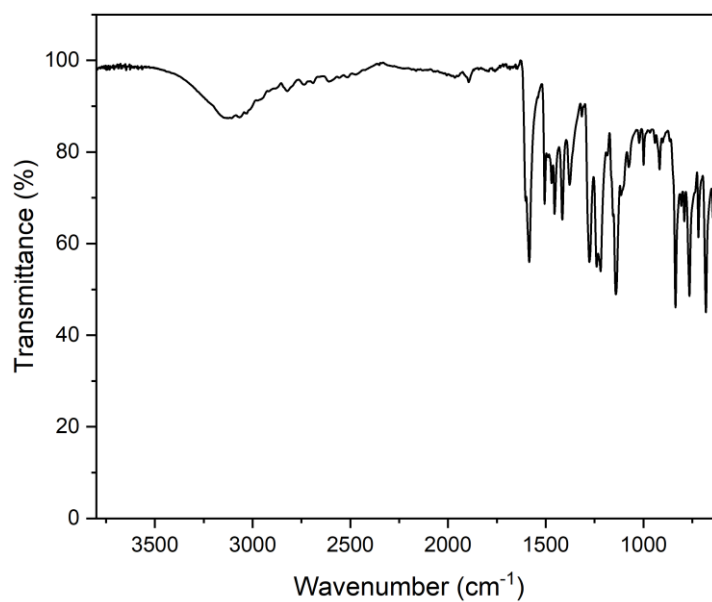


Figure B.1 : IR spectrum of compound 1

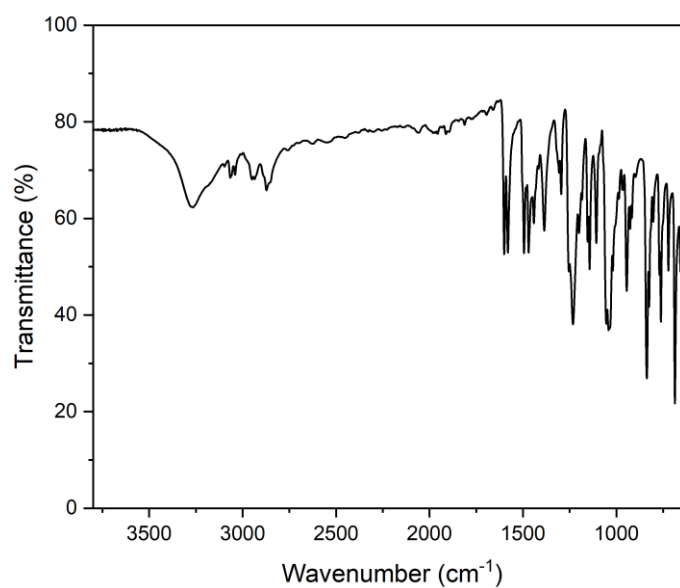


Figure B.2 : IR spectrum of compound 2

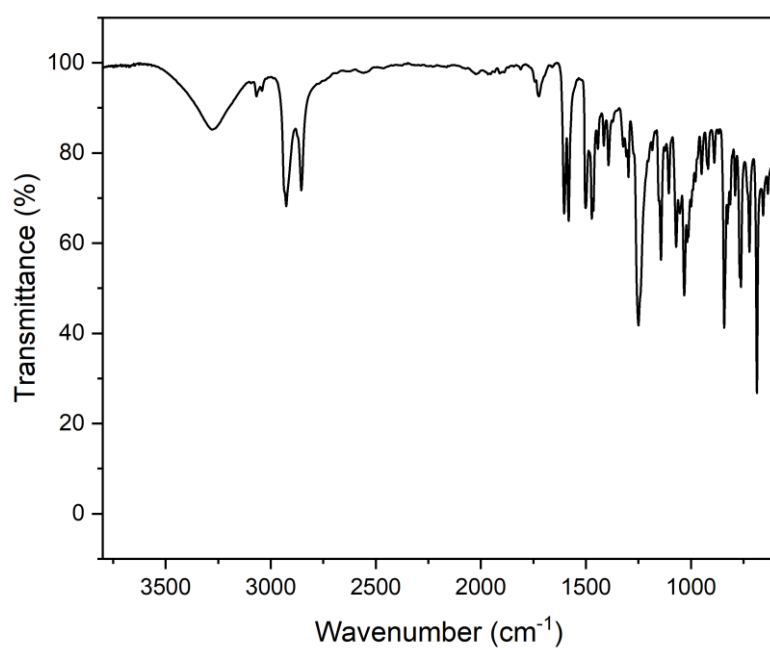


Figure B.3 : IR spectrum of compound **3**

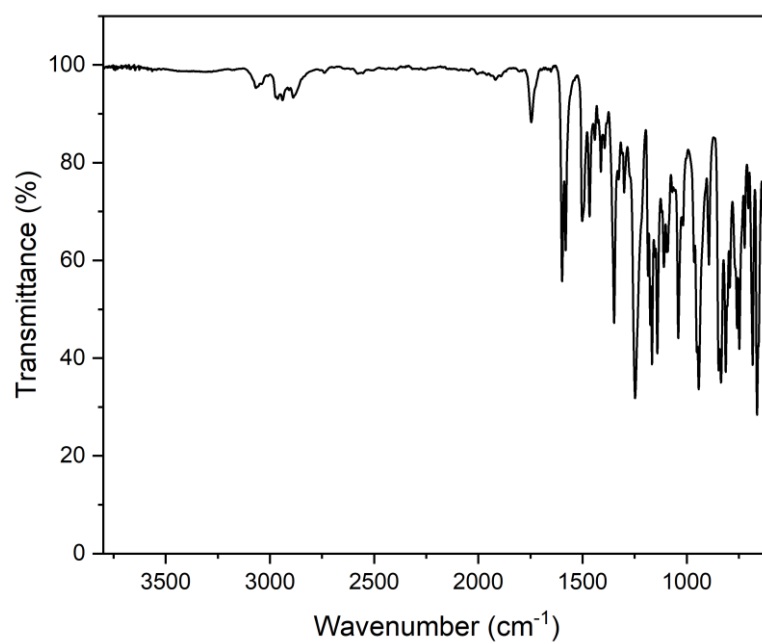


Figure B.4 : IR spectrum of compound **4**

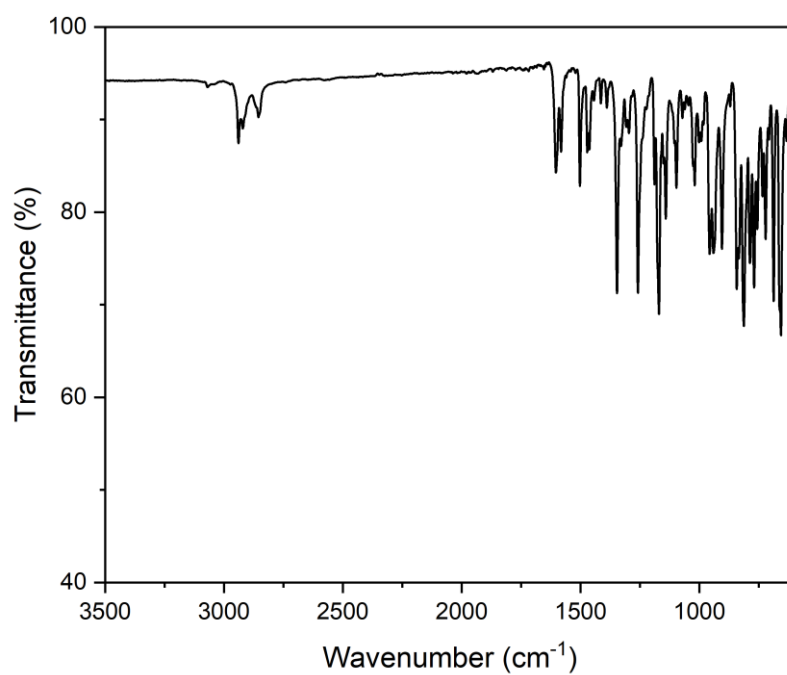


Figure B.5 : IR spectrum of compound **5**

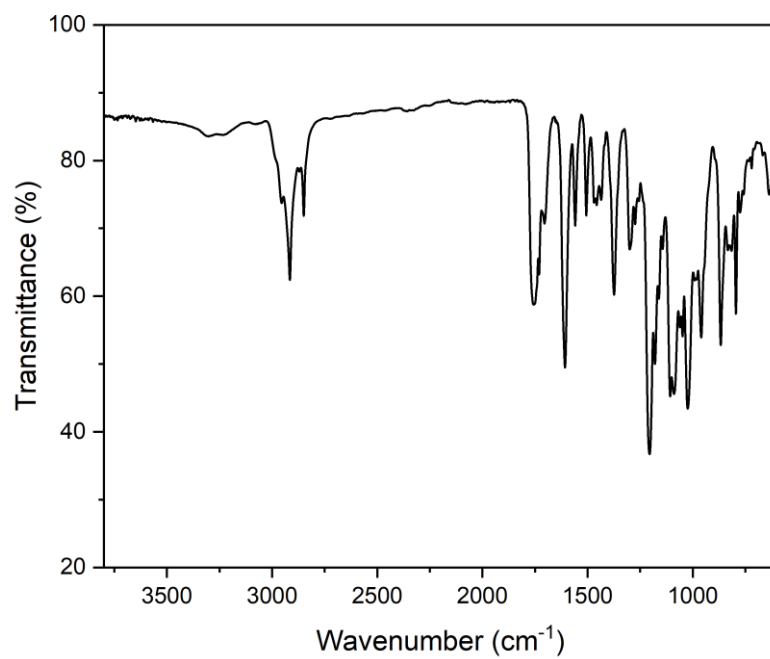


Figure B.6 : IR spectrum of compound **11**

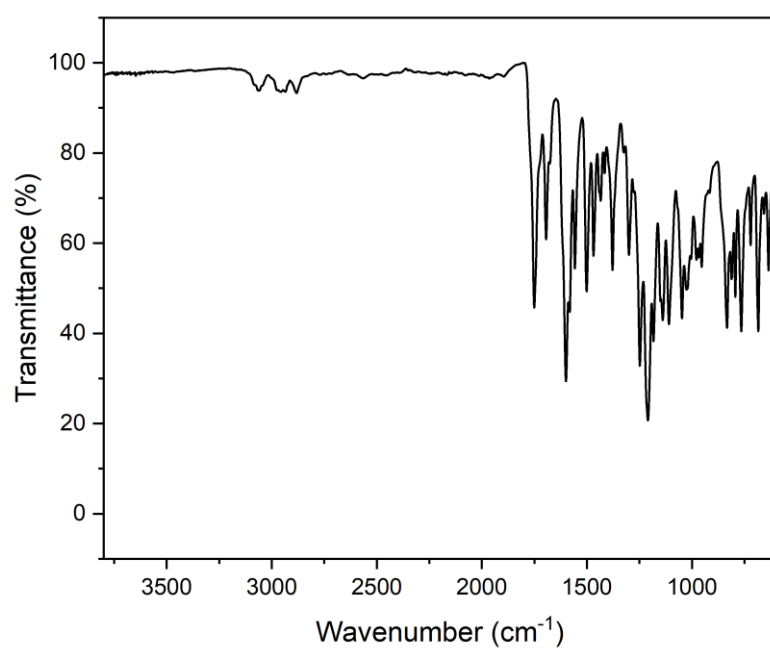


Figure B.7 : IR spectrum of **AzoCoun-1a**

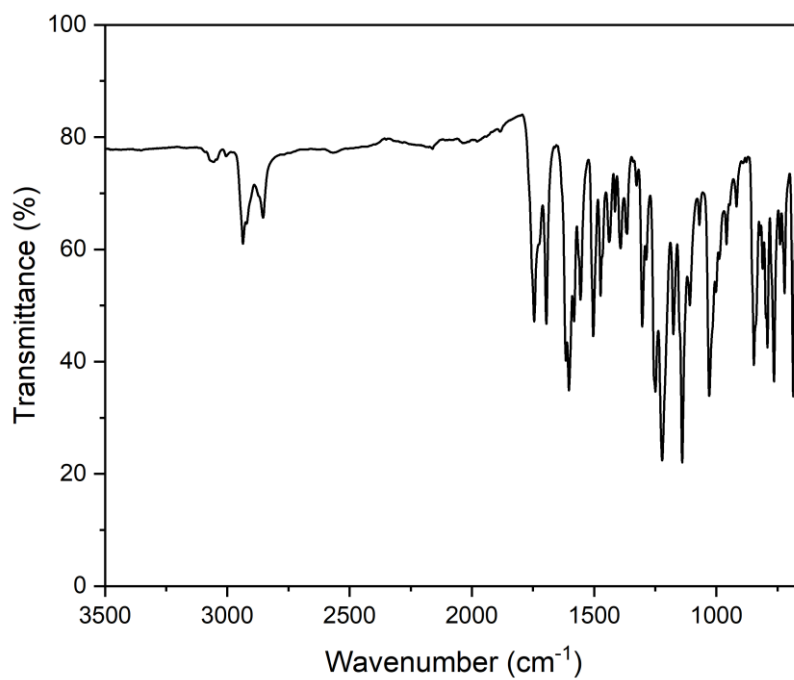


Figure B.8 : IR spectrum of **AzoCoun-1b**

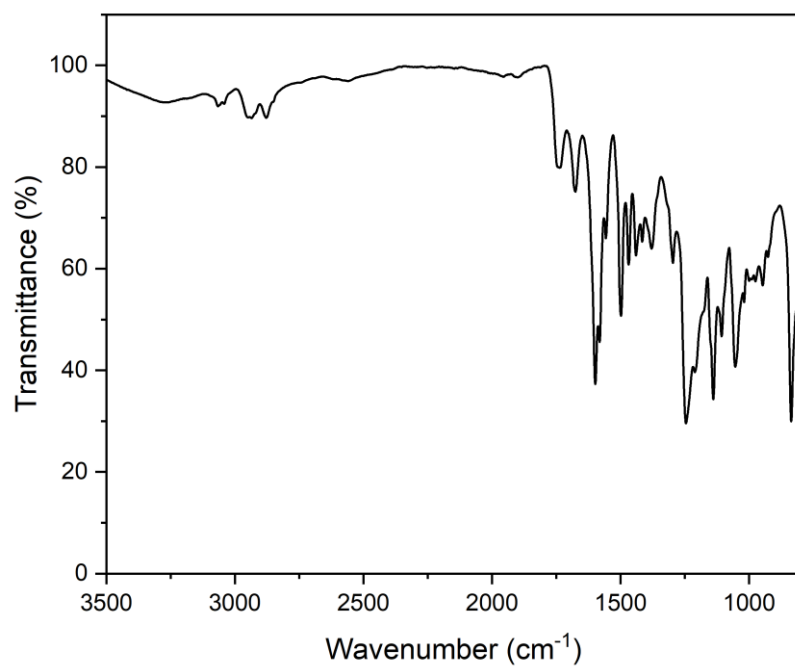


Figure B.9 : IR spectrum of **AzoCouv-1a'**

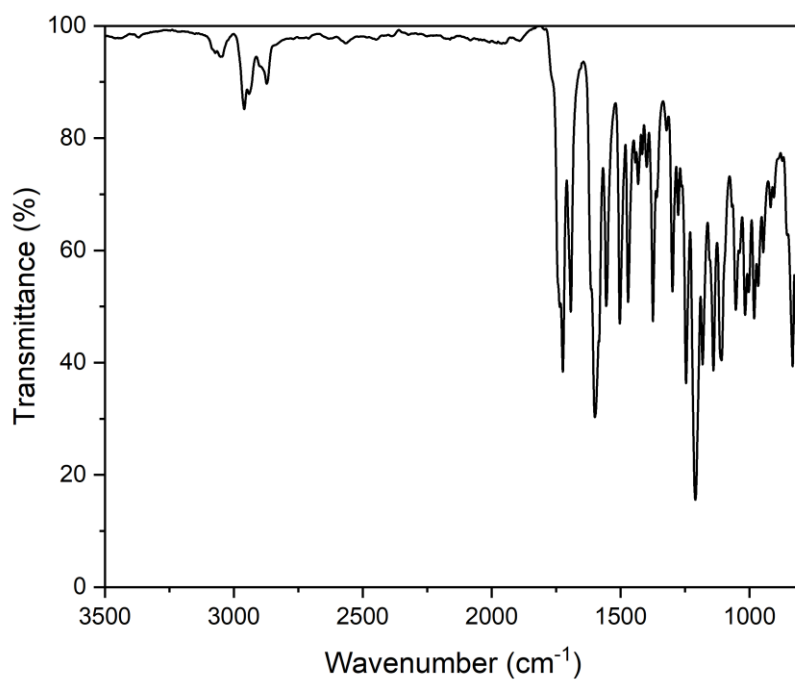


Figure B.10 : IR spectrum of **AzoCouv-2a**

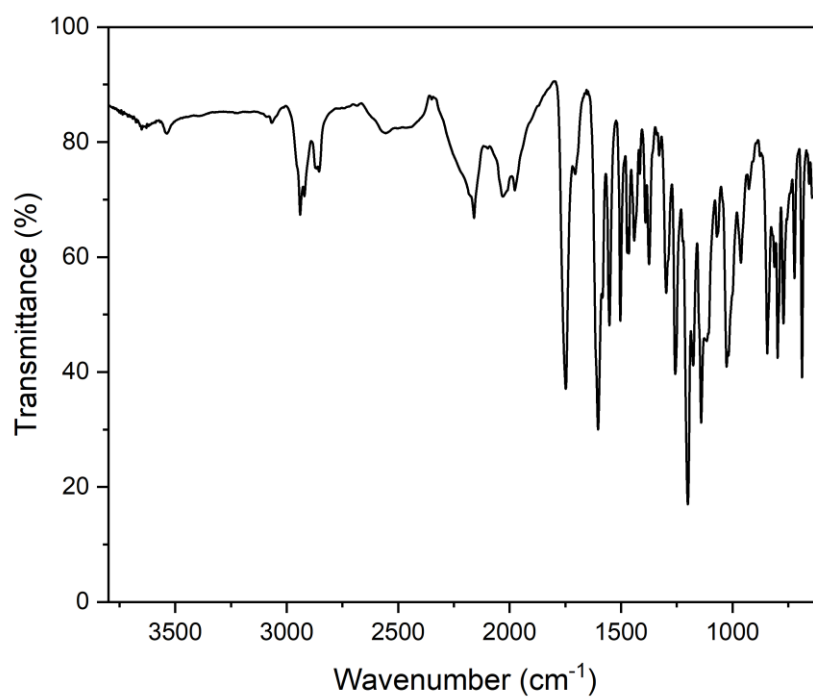


Figure B.11 : IR spectrum of **AzoCouv-2b**

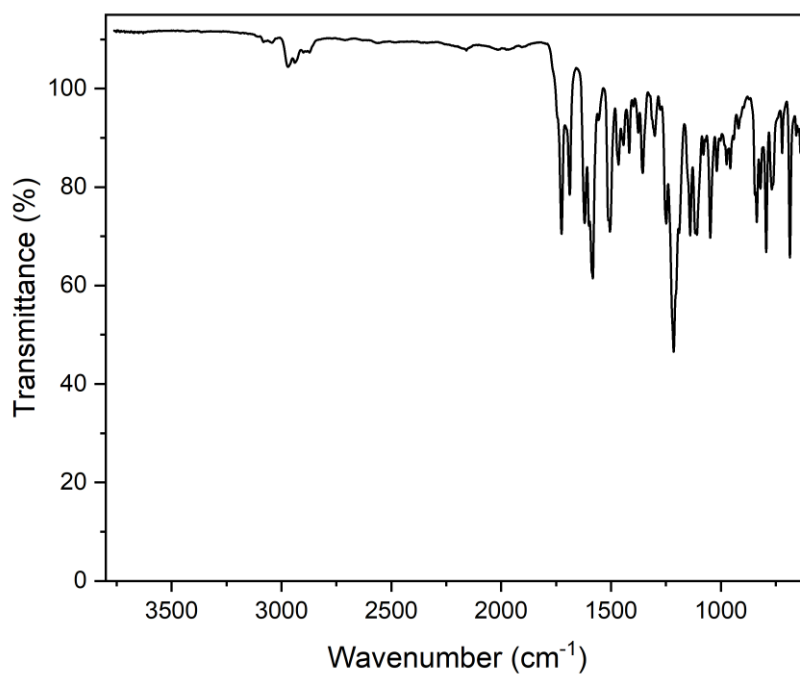


Figure B.12 : IR spectrum of **AzoCouv-3a**

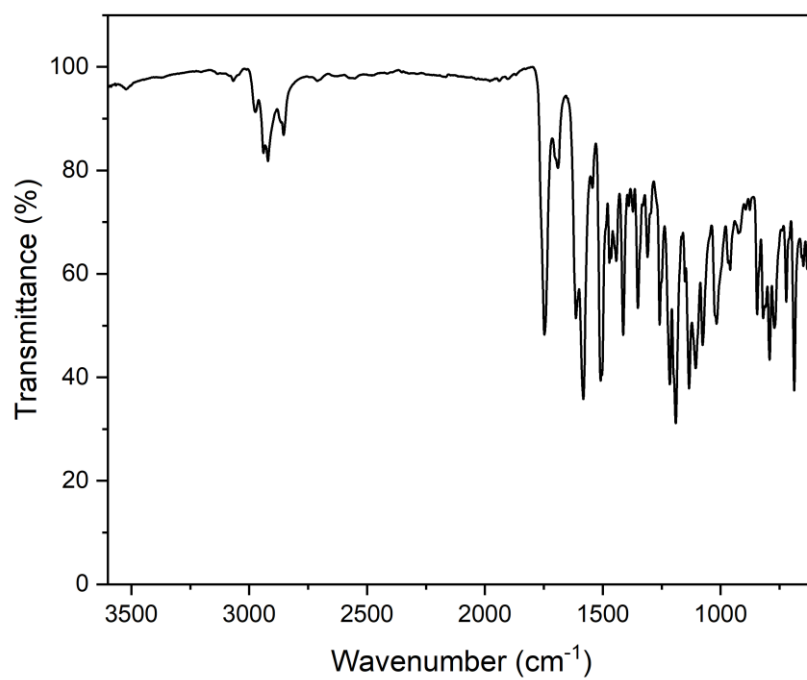


Figure B.13 : IR spectrum of **AzoCoum-3b**

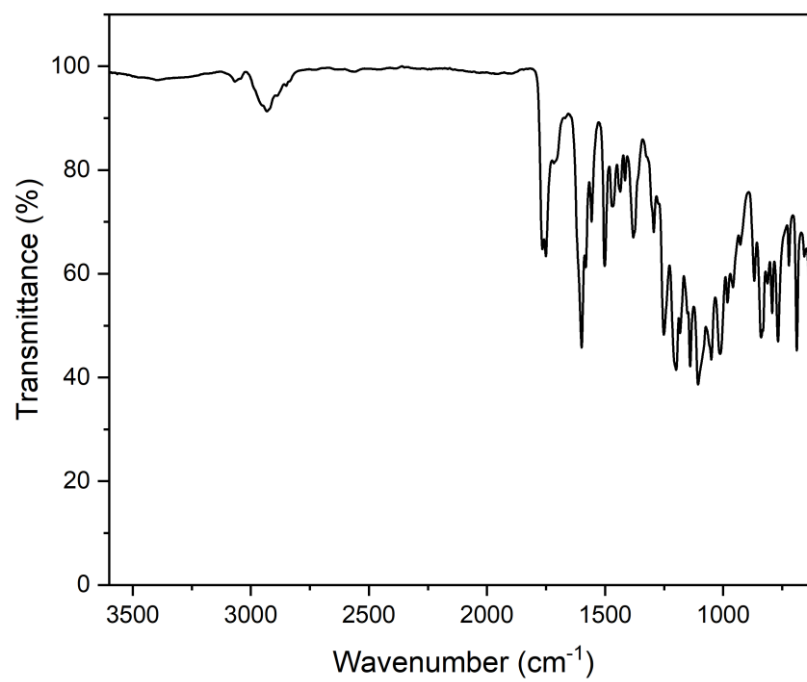


Figure B.14 : IR spectrum of **AzoCoumR-1**

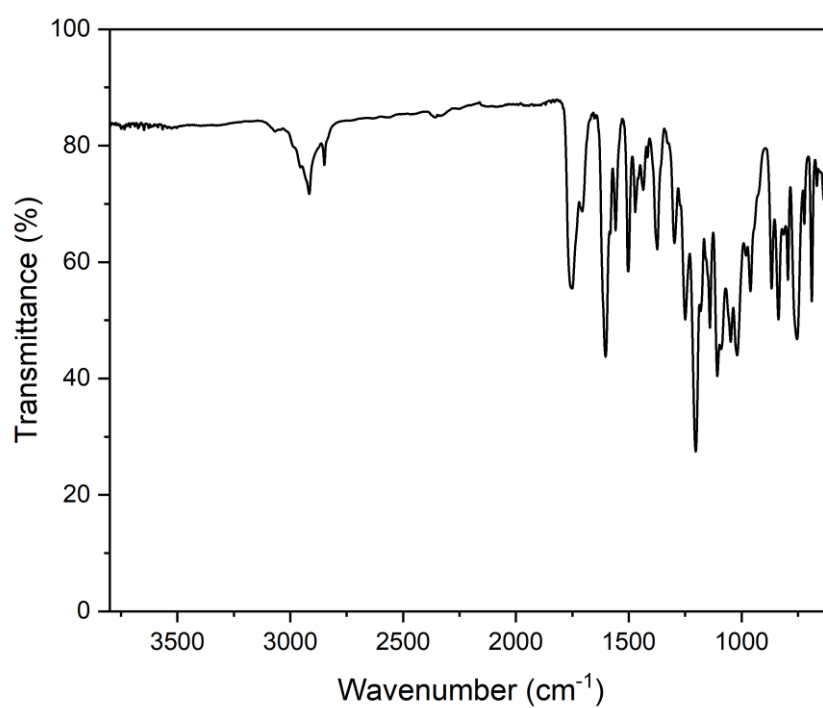


Figure B.15 : IR spectrum of **AzoCoumR-2**

C. High-Resolution Mass Spectra (HRMS)

High-Resolution Mass Spectra (HRMS) analyses were obtained using the Time of Flight mass analyzer in positive mode on (ES+).

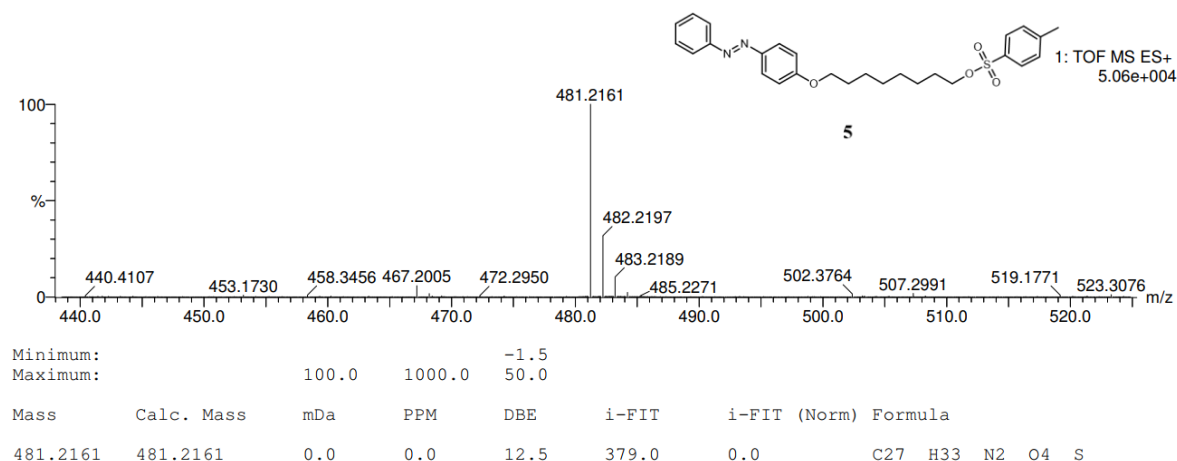


Figure C.1 : HRMS spectrum of compound **5**

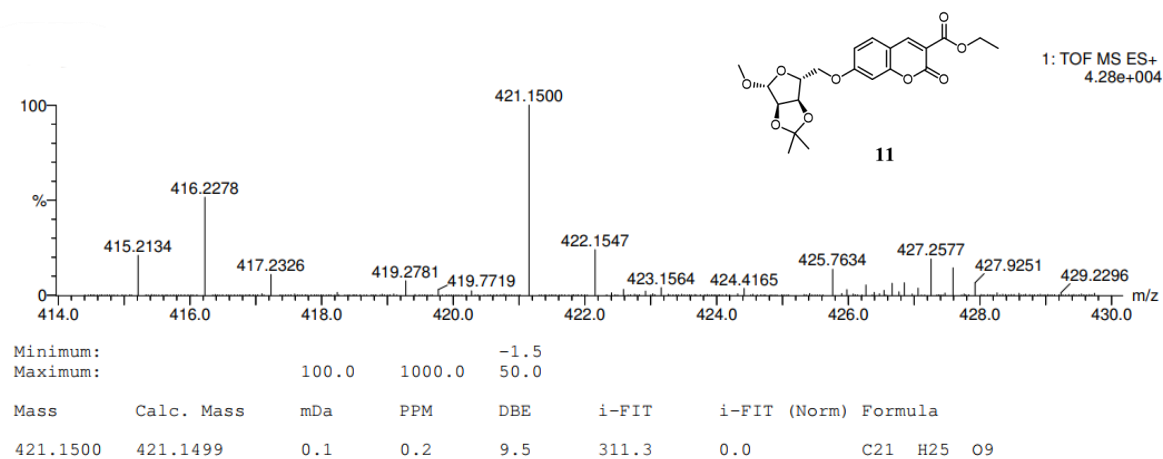


Figure C.2 : HRMS spectrum of compound **11**

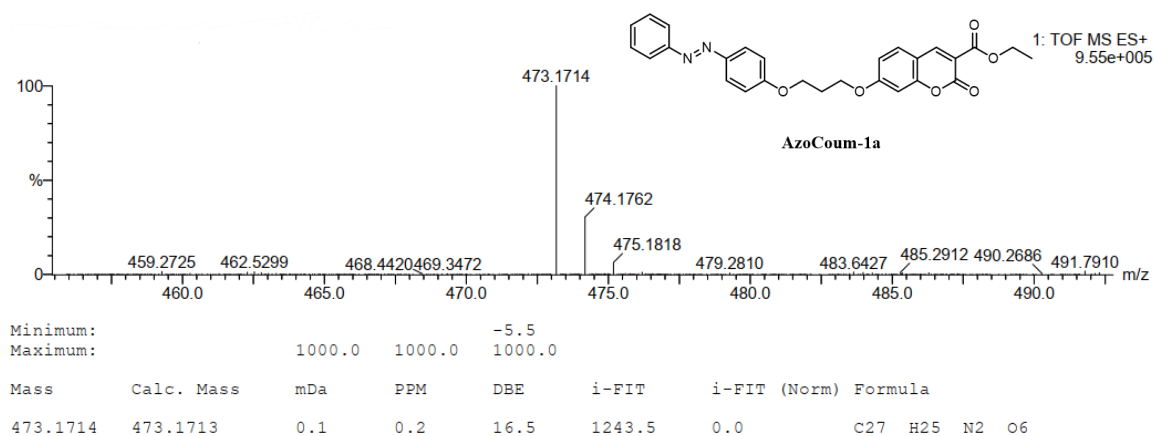


Figure C.3 : HRMS spectrum of **AzoCoun-1a**

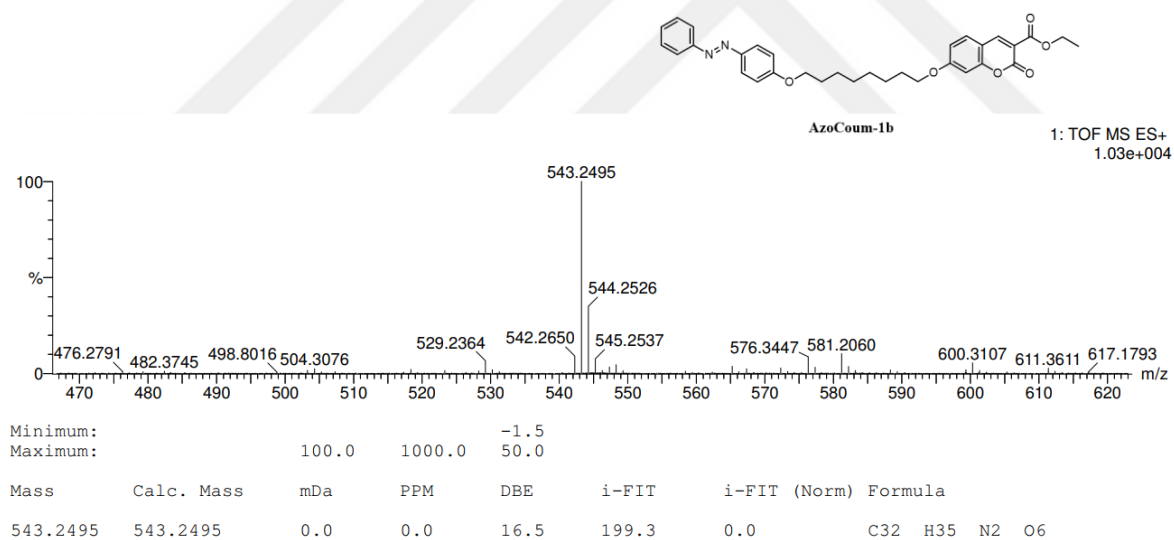


Figure C.4 : HRMS spectrum of **AzoCoun-1b**

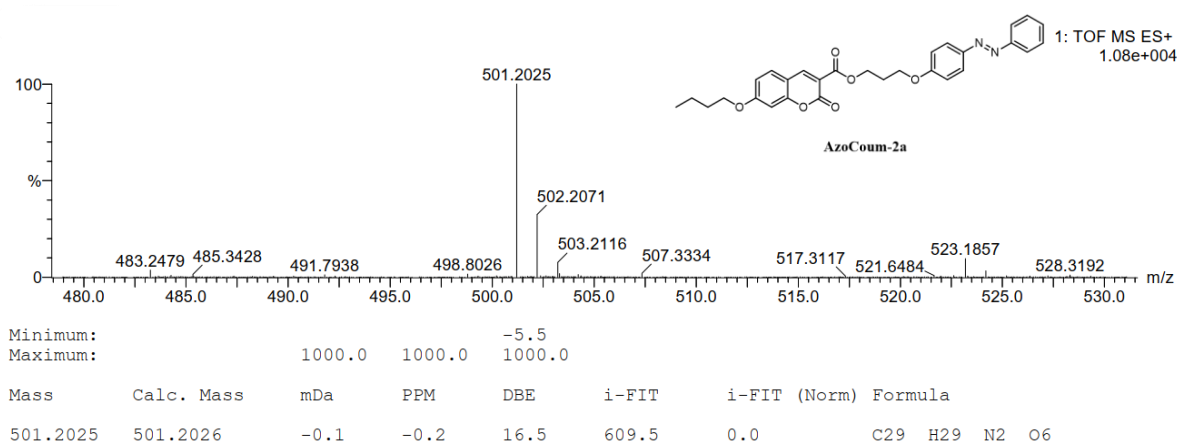


Figure C.5 : HRMS spectrum of **AzoCoum-2a**

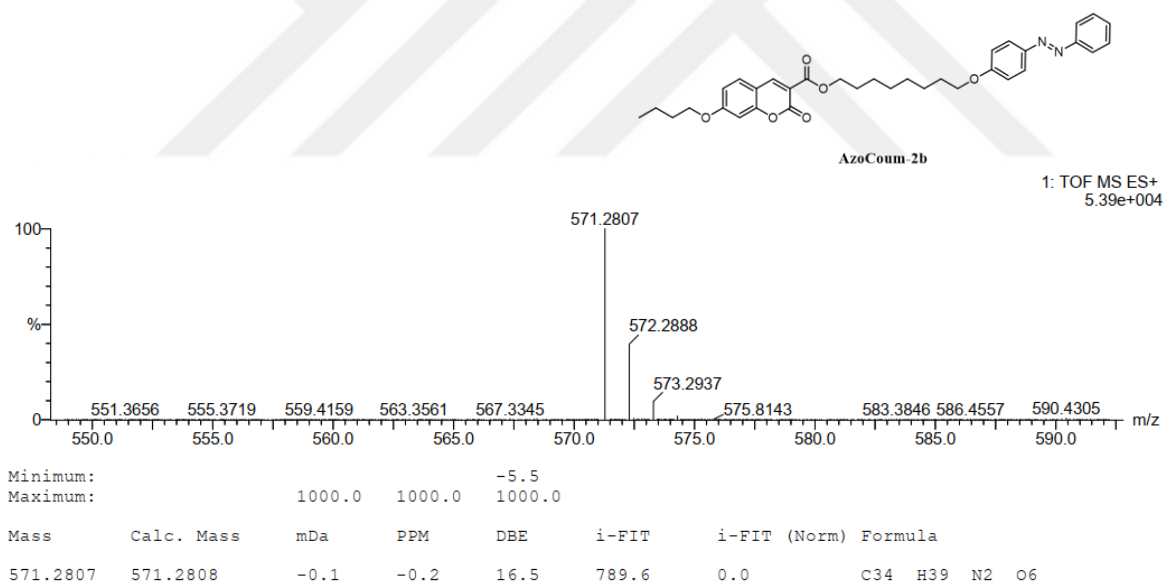


Figure C.6 : HRMS spectrum of **AzoCoum-2b**

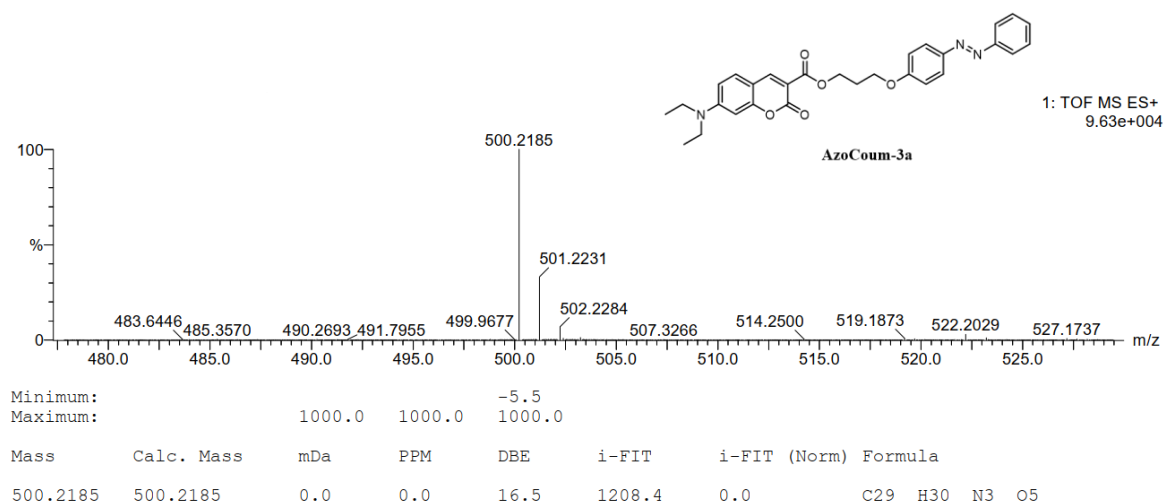


Figure C.7 : HRMS spectrum of **AzoCoun-3a**

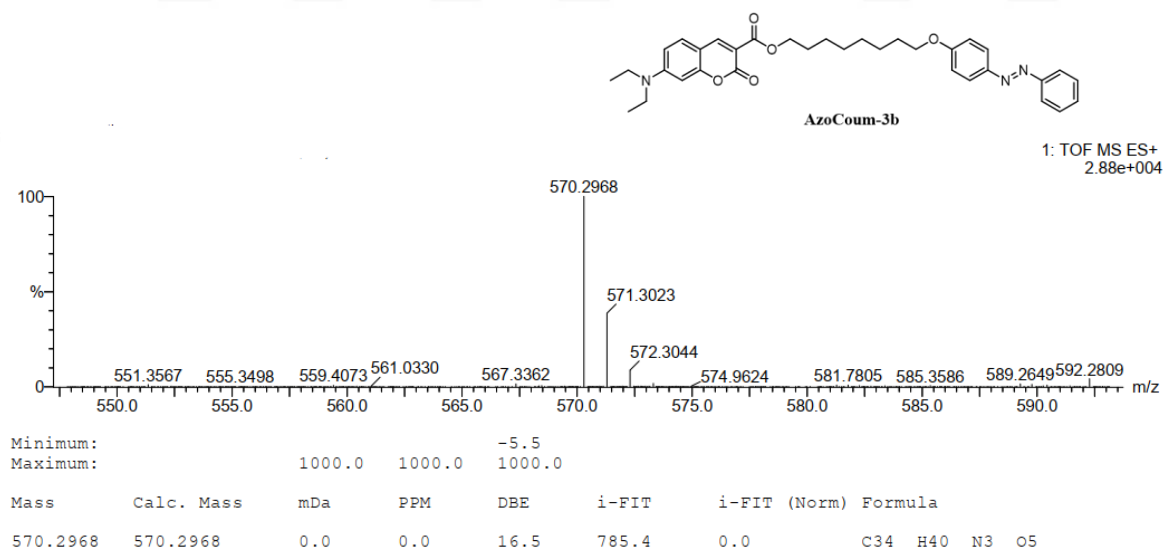


Figure C.8 : HRMS spectrum of **AzoCoun-3b**

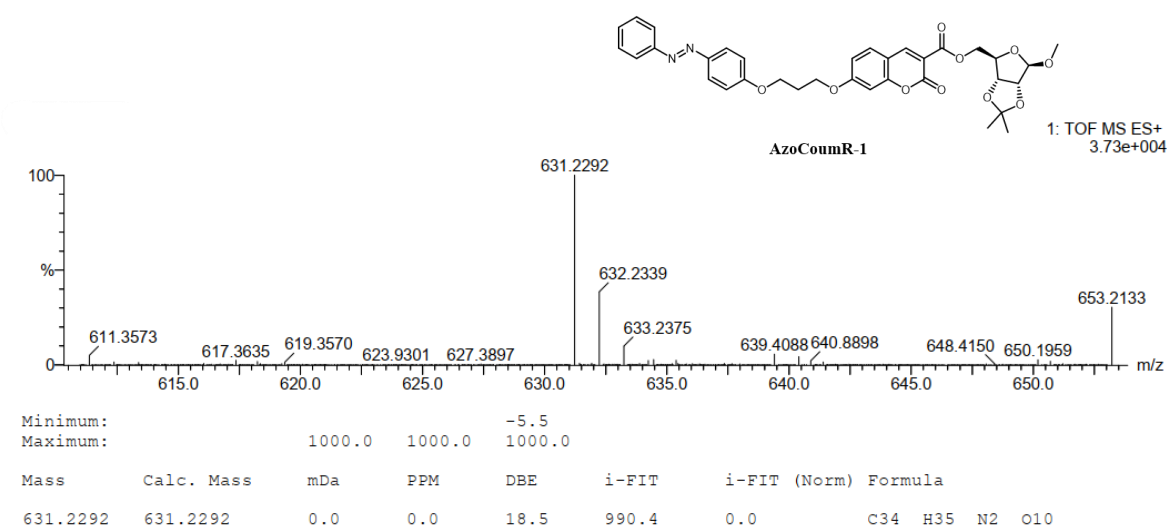


Figure C.9 : HRMS spectrum of **AzoCounR-1**

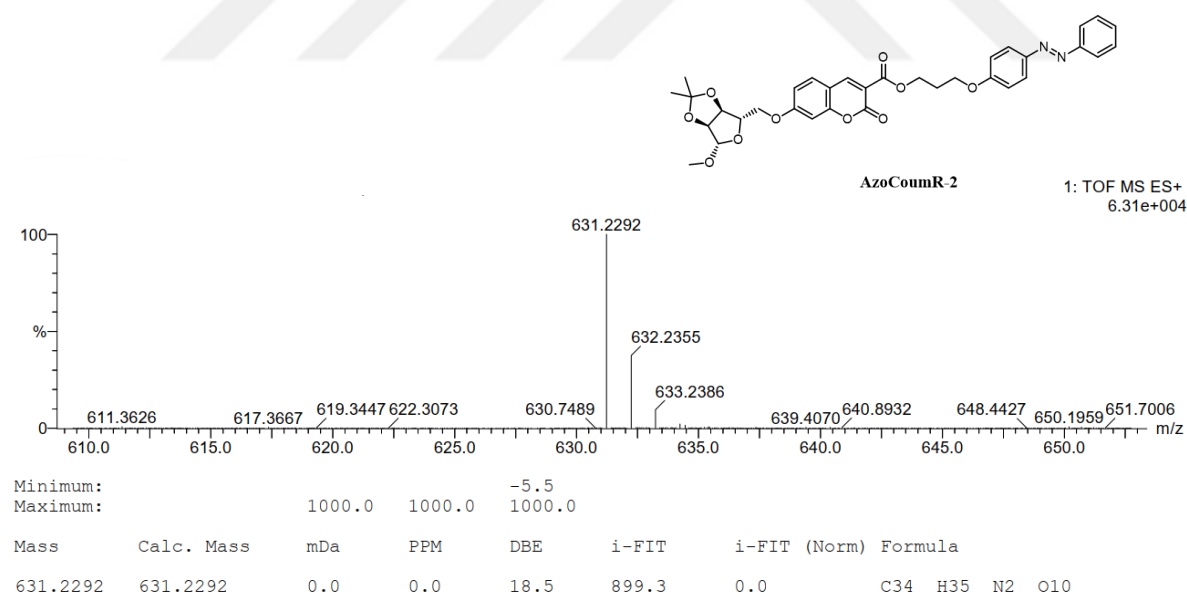


Figure C.10 : HRMS spectrum of **AzoCounR-2**



D. UV-Vis Spectra

UV-Vis measurements were performed using Shimadzu UV-2450 spectrophotometer.

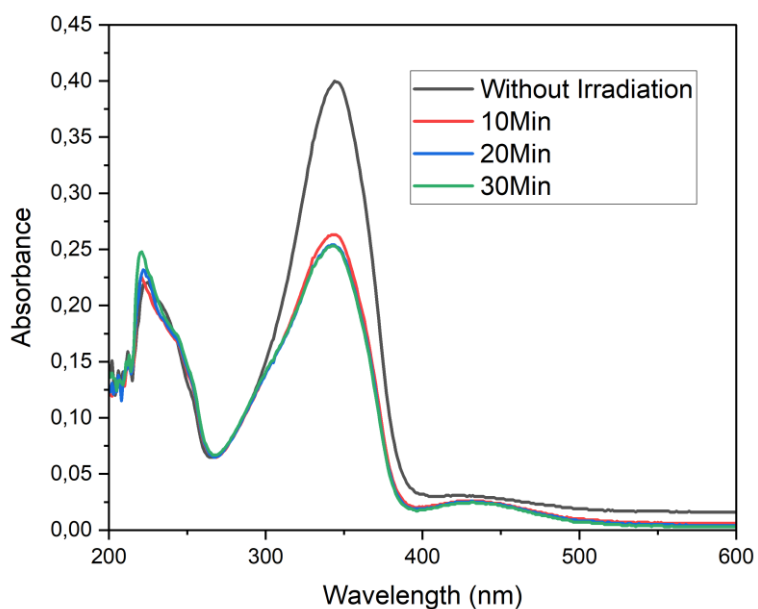


Figure D.1 : UV-Vis Spectra of **AzoCoum-1a** upon irradiation in MeCN (10^{-5} M)

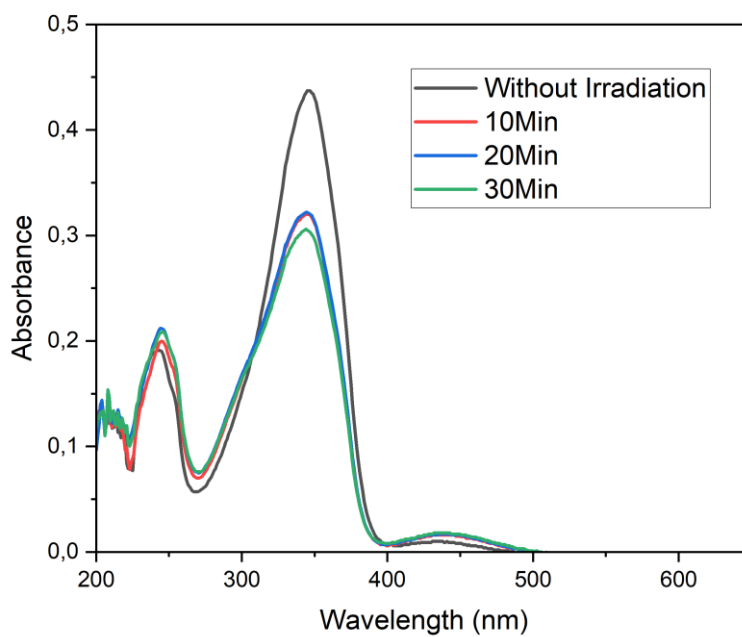


Figure D.2 : UV-Vis Spectra of **AzoCoum-1a** upon irradiation in THF (10^{-5} M)

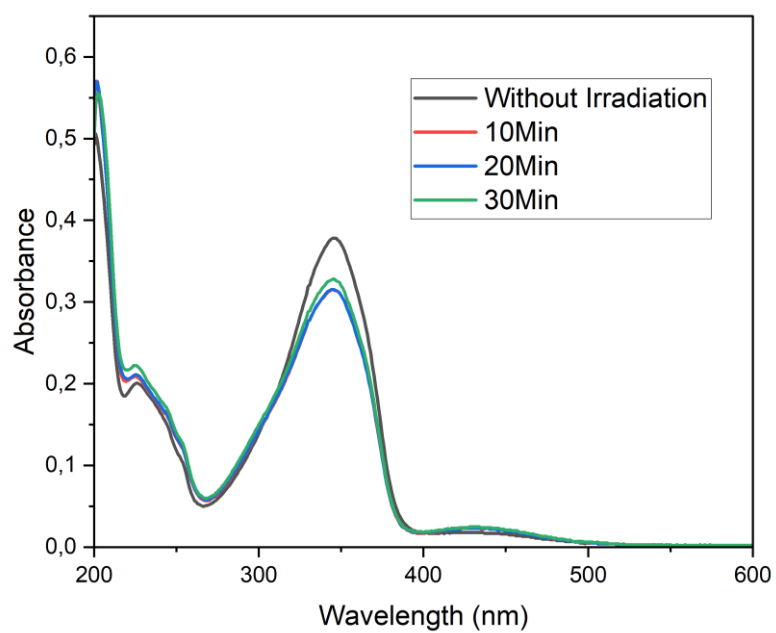


Figure D.3 : UV-Vis Spectra of **AzoCoum-1a** upon irradiation in MeOH (10^{-5} M)

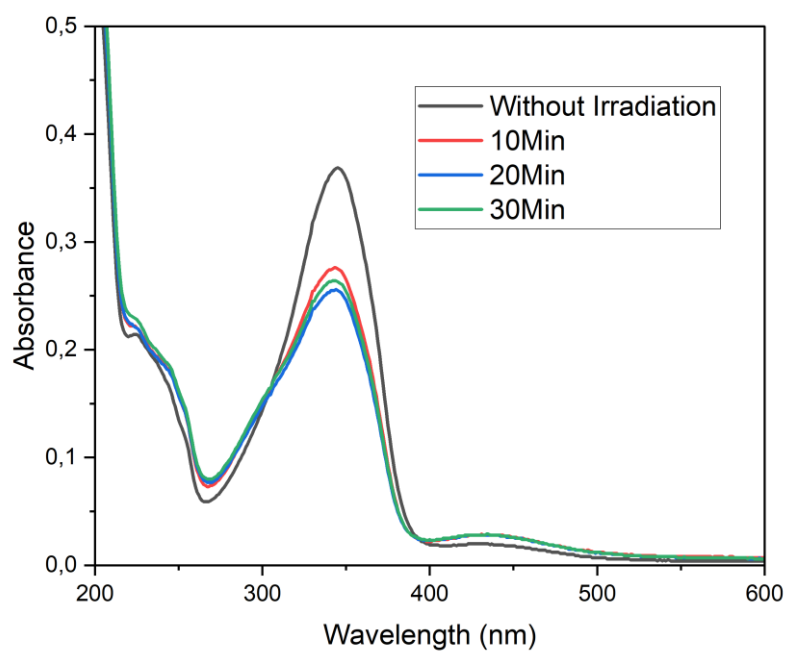


Figure D.4 : UV-Vis Spectra of **AzoCoum-1b** upon irradiation in MeCN (10^{-5} M)

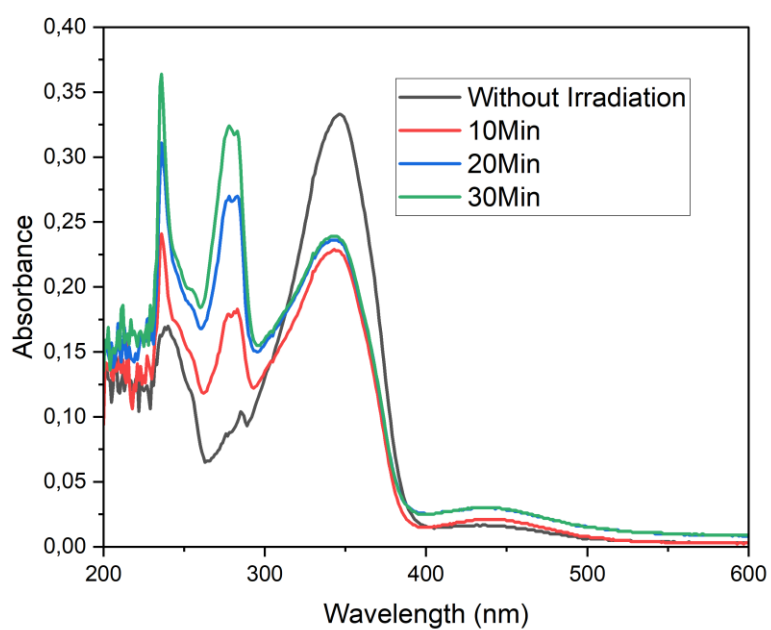


Figure D.5 : UV-Vis Spectra of **AzoCoul-1b** upon irradiation in THF (10^{-5} M)

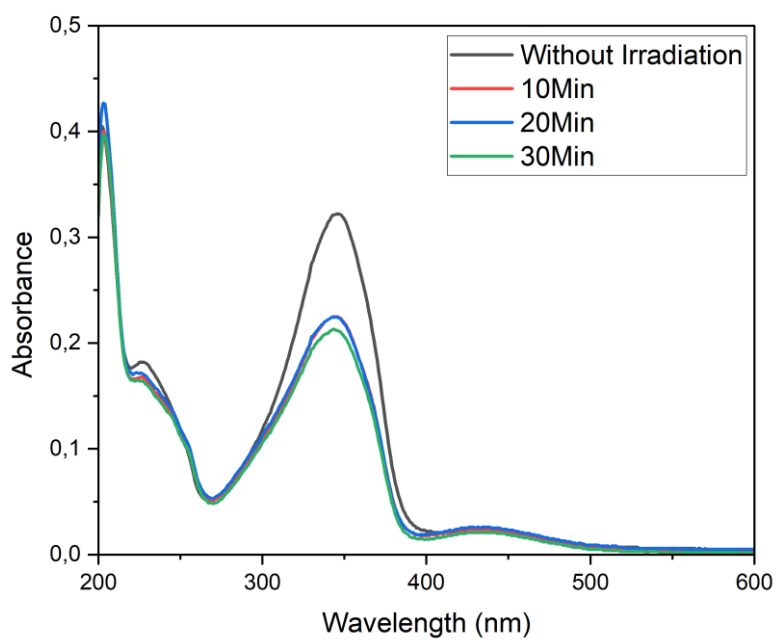


Figure D.6 : UV-Vis Spectra of **AzoCoul-1b** upon irradiation in MeOH (10^{-5} M)

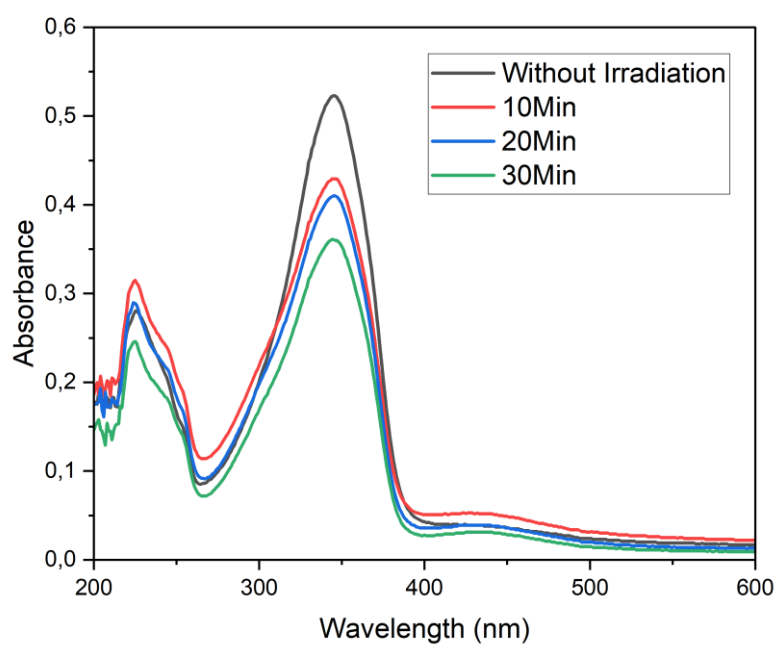


Figure D.7 : UV-Vis Spectra of **AzoCoum-2a** upon irradiation in MeCN (10^{-5} M)

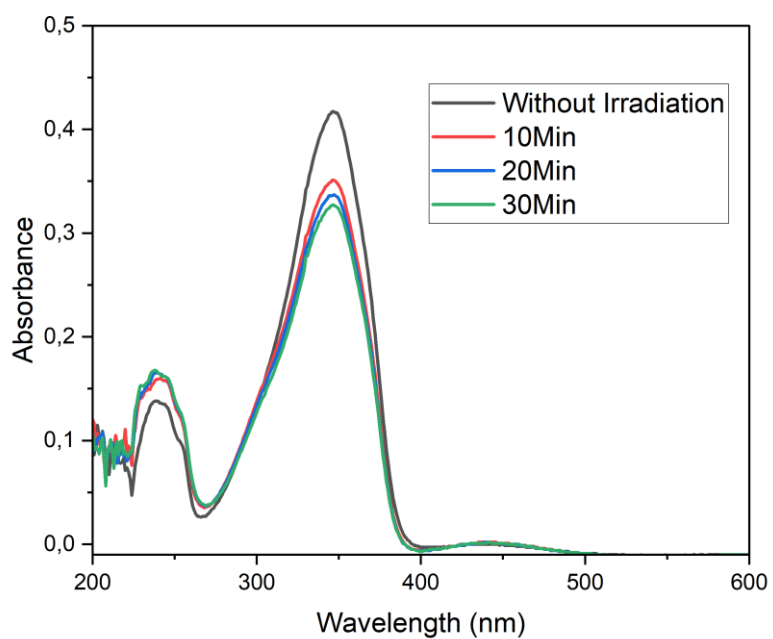


Figure D.8 : UV-Vis Spectra of **AzoCoum-2a** upon irradiation in THF (10^{-5} M)

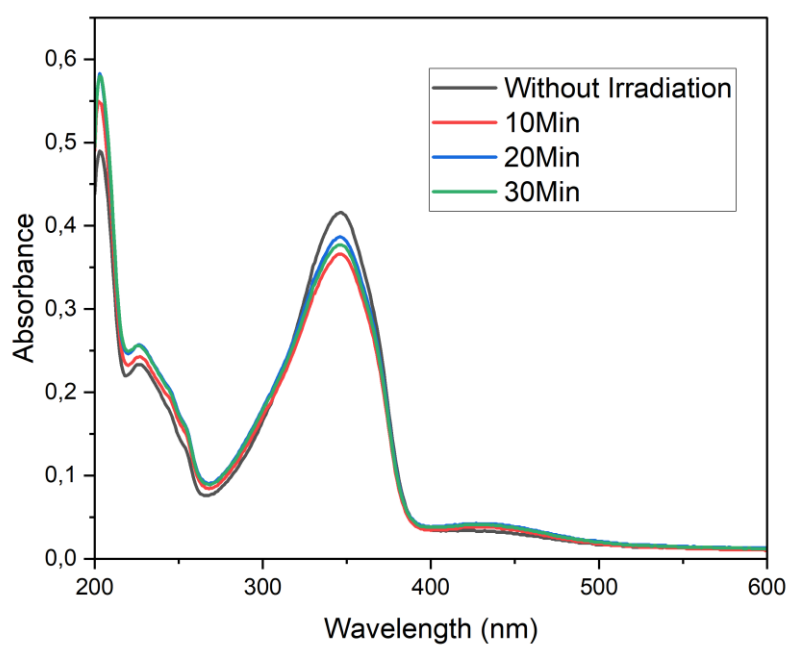


Figure D.9 : UV-Vis Spectra of **AzoCoum-2a** upon irradiation in MeOH (10^{-5} M)

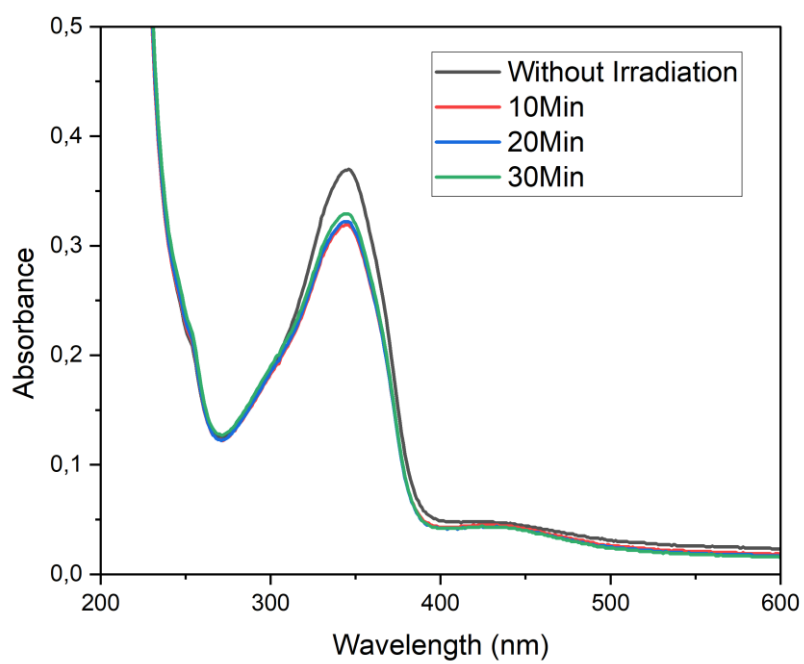


Figure D.10 : UV-Vis Spectra of **AzoCoum-2b** upon irradiation in MeCN (10^{-5} M)

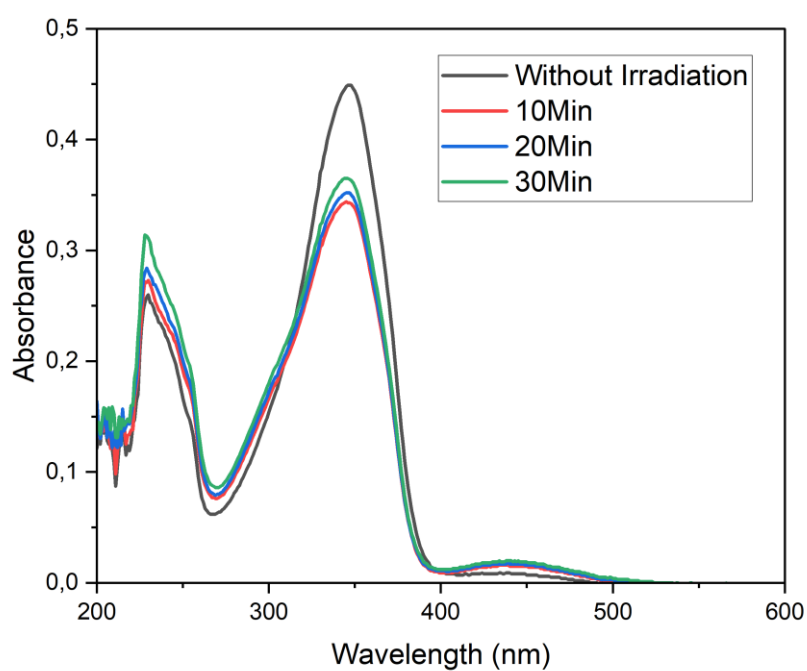


Figure D.11 : UV-Vis Spectra of **AzoCoum-2b** upon irradiation in THF (10^{-5} M)

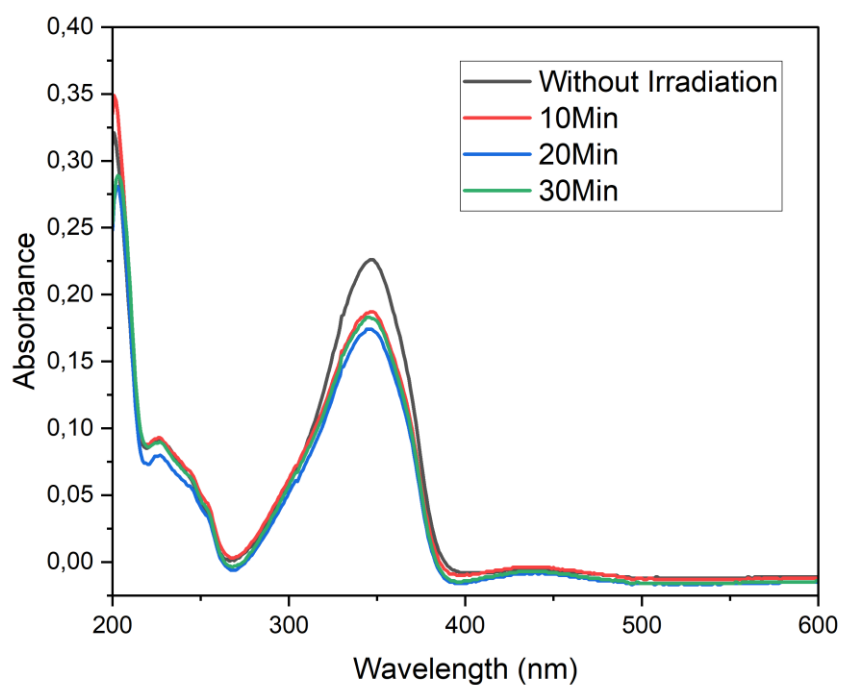


Figure D.12 : UV-Vis Spectra of **AzoCoum-2b** upon irradiation in MeOH (10^{-5} M)

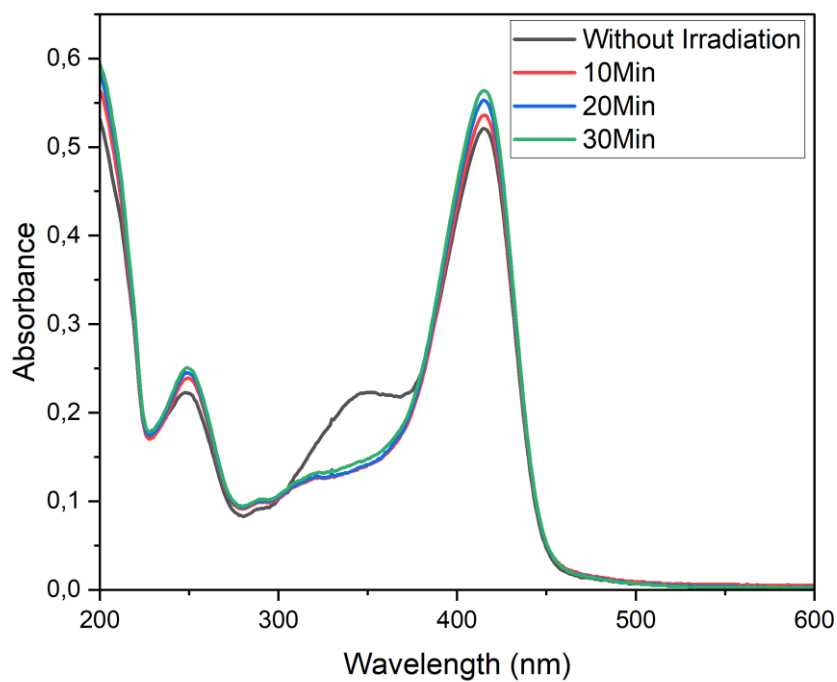


Figure D.13 : UV-Vis Spectra of **AzoCoum-3a** upon irradiation in MeCN (10^{-5} M)

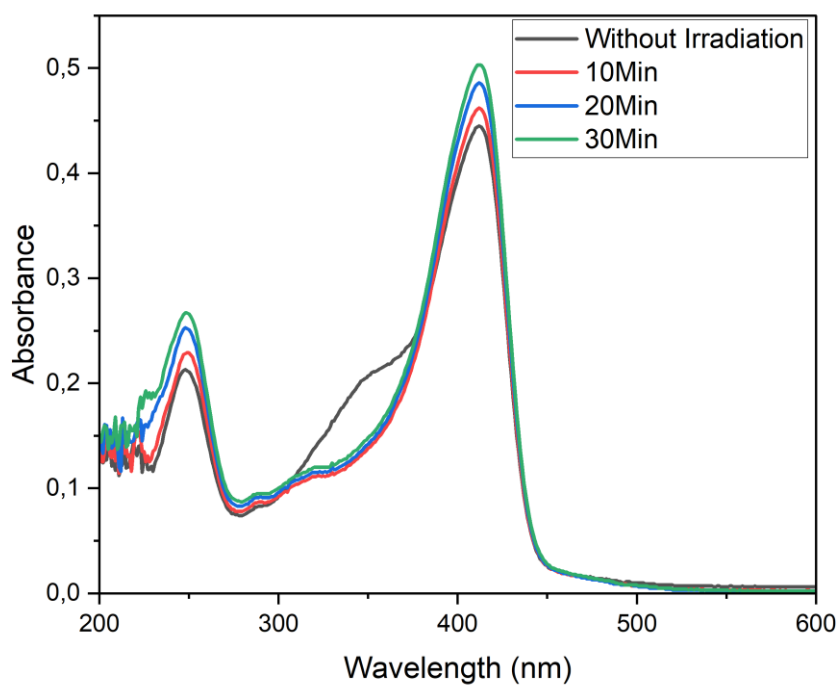


Figure D.14 : UV-Vis Spectra of **AzoCoum-3a** upon irradiation in THF (10^{-5} M)

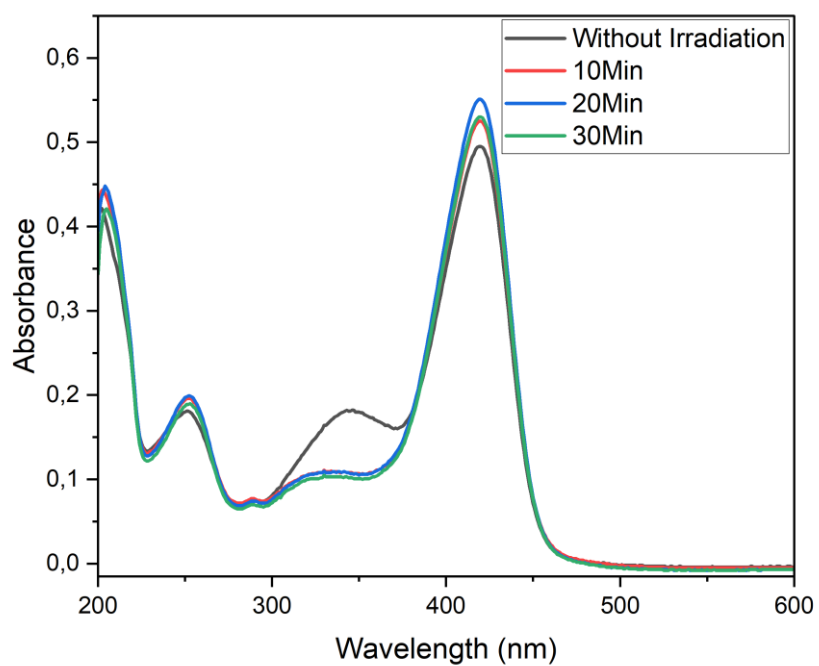


Figure D.15 : UV-Vis Spectra of **AzoCoum-3a** upon irradiation in MeOH (10^{-5} M)

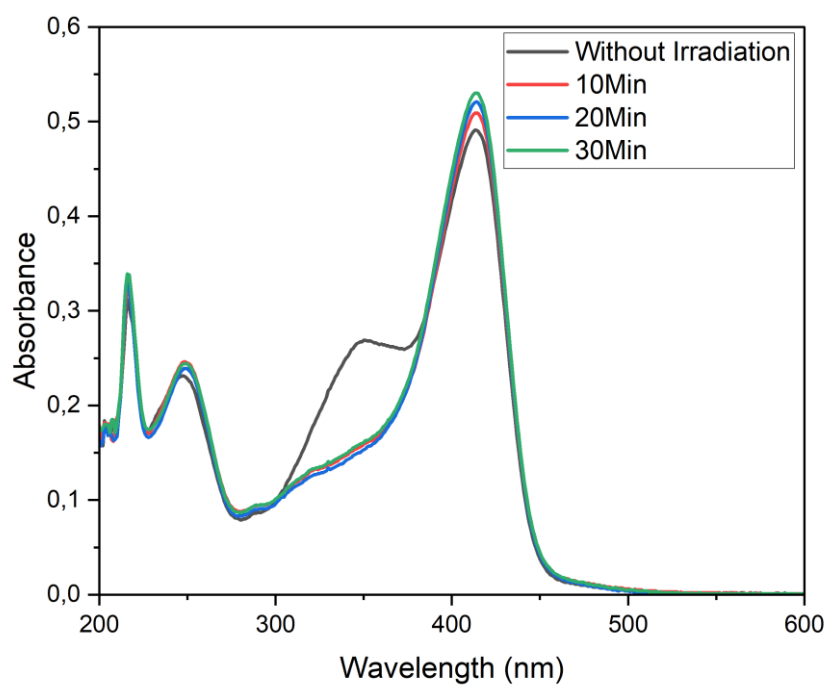


Figure D.16 : UV-Vis Spectra of **AzoCoum-3b** upon irradiation in MeCN (10^{-5} M)

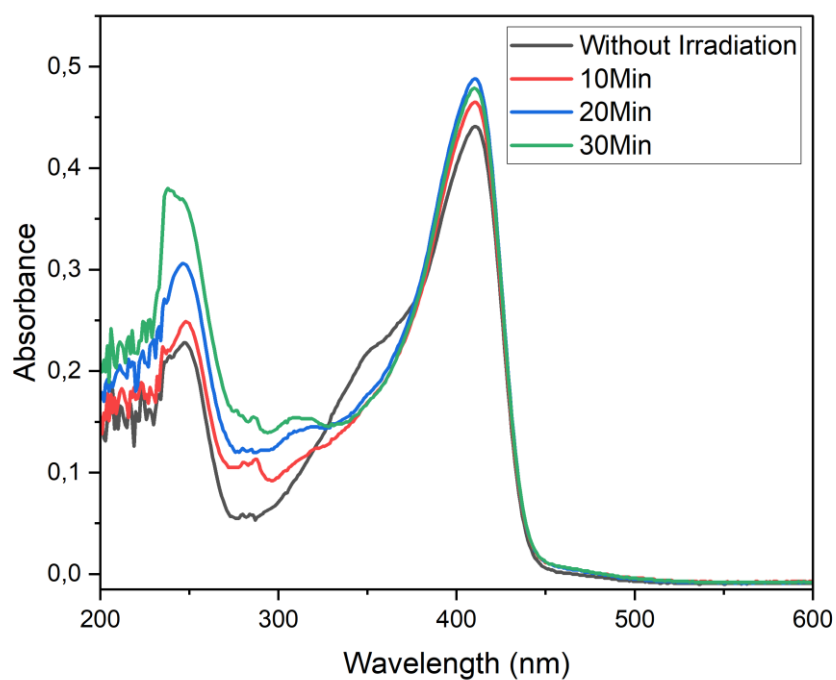


Figure D.17 : UV-Vis Spectra of **AzoCoum-3b** upon irradiation in THF (10^{-5} M)

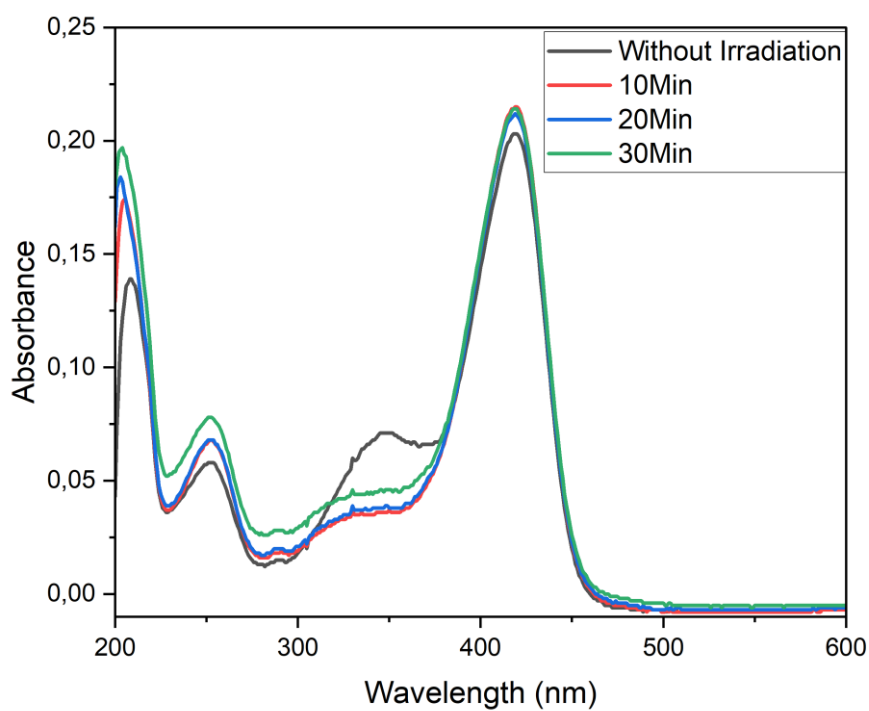


Figure D.18 : UV-Vis Spectra of **AzoCoum-3b** upon irradiation in MeOH (10^{-5} M)

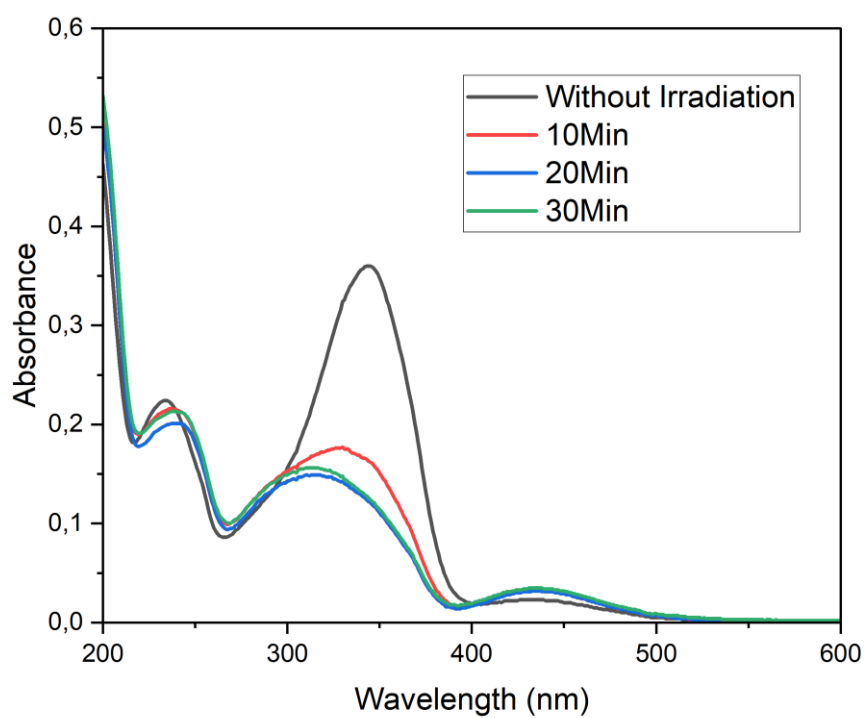


Figure D.19 : UV-Vis Spectra of **AzoCoumR-1** upon irradiation in MeCN (10^{-5} M)

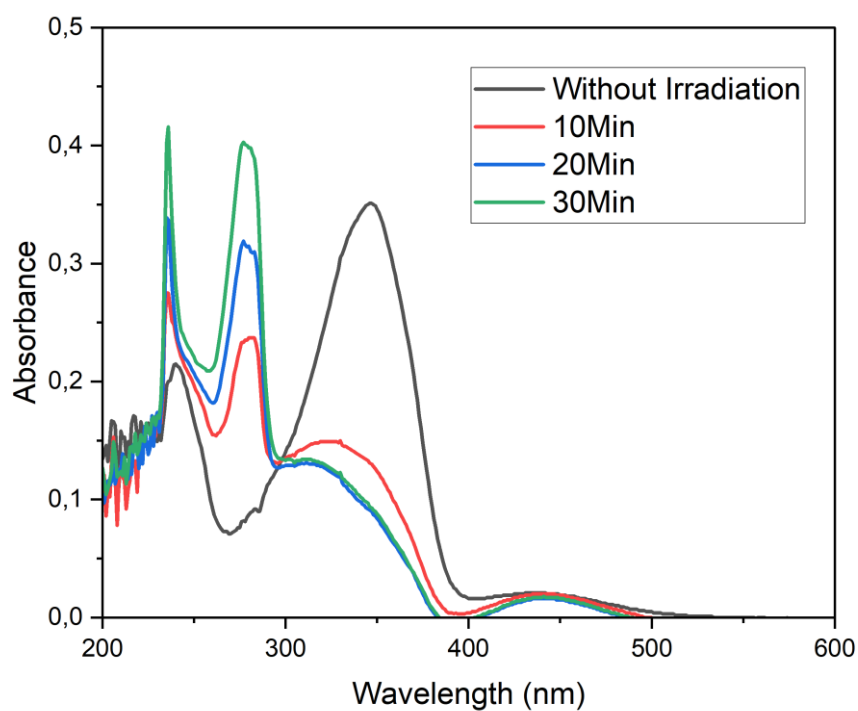


Figure D.20 : UV-Vis Spectra of **AzoCoumR-1** upon irradiation in THF (10^{-5} M)

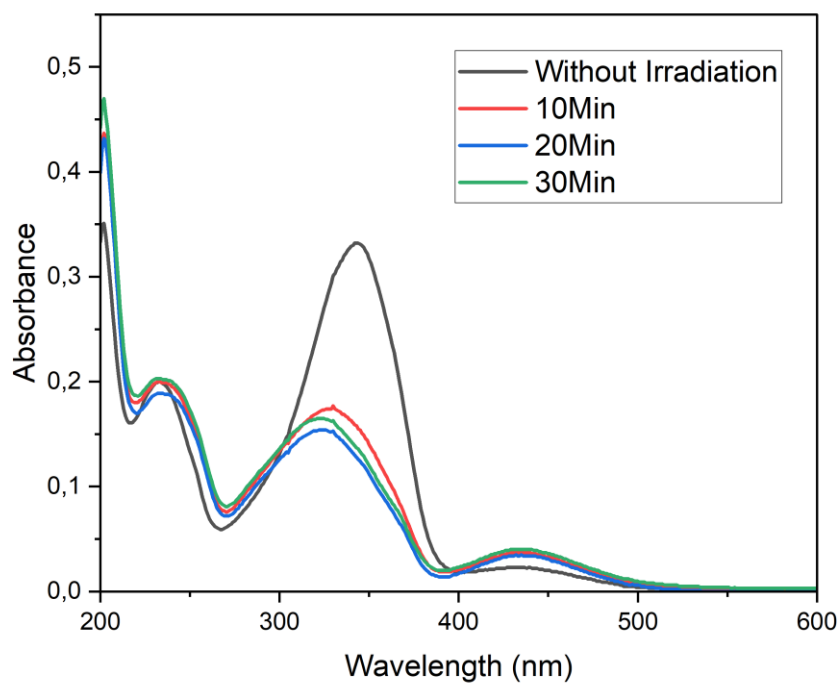


Figure D.21 : UV-Vis Spectra of **AzoCoumR-1** upon irradiation in MeOH (10^{-5} M)

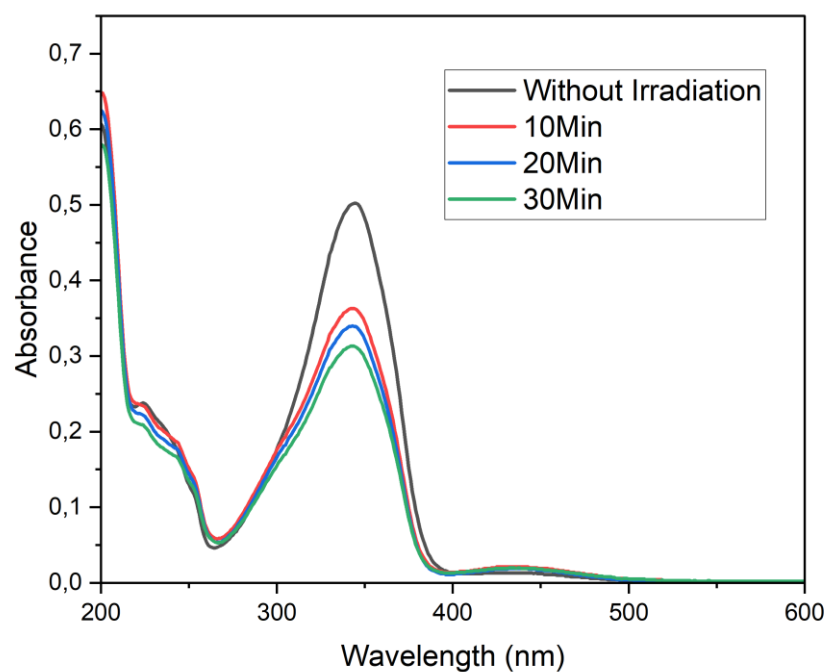


Figure D.22 : UV-Vis Spectra of **AzoCoumR-2** upon irradiation in MeCN (10^{-5} M)

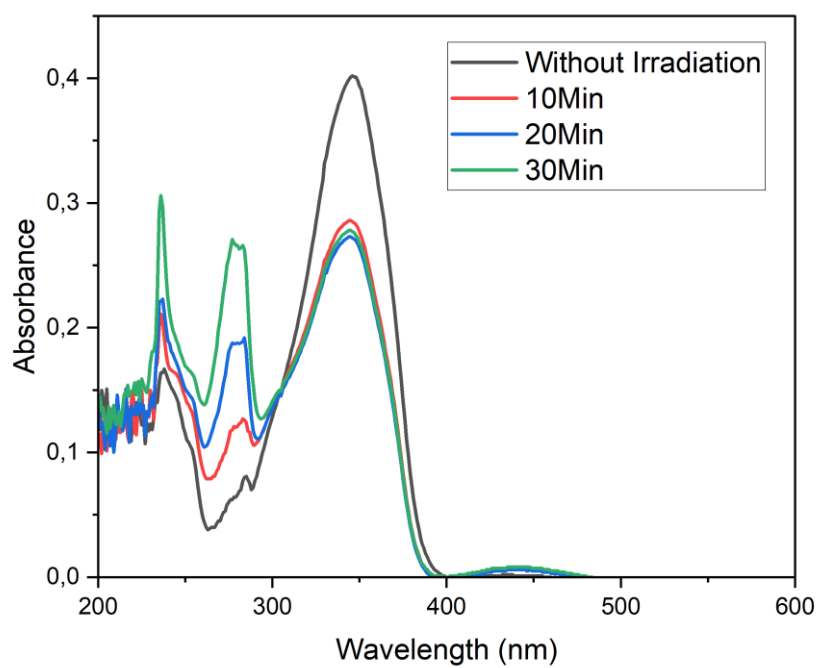


Figure D.23 : UV-Vis Spectra of **AzoCoumR-2** upon irradiation in THF (10^{-5} M)

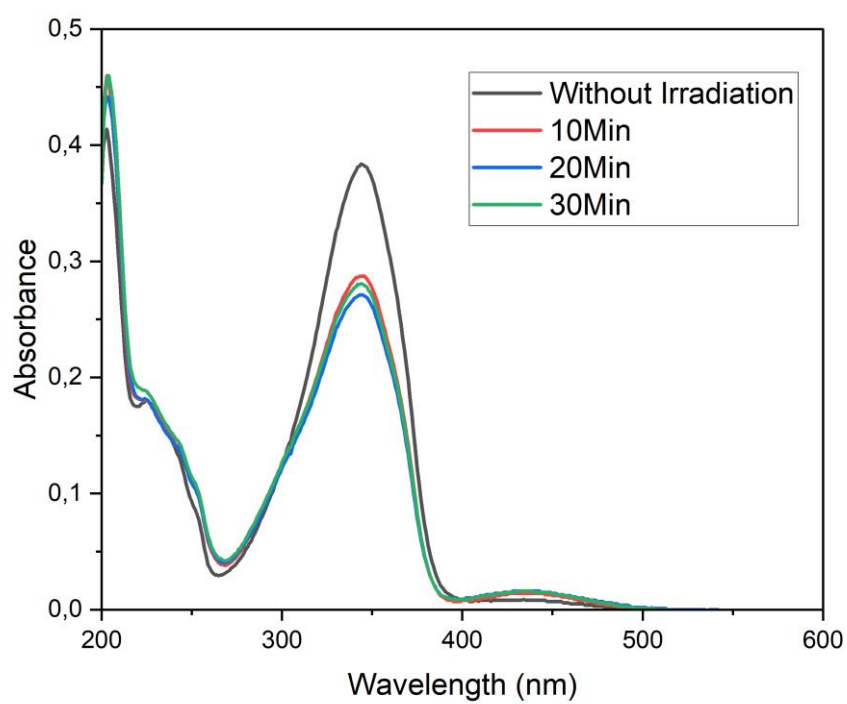


Figure D.24 : UV-Vis Spectra of **AzoCoumR-2** upon irradiation in MeOH (10^{-5} M)

E. Fluorescence Spectra

Fluorescence measurements were recorded using a Perkin Elmer LS55 spectrofluorometer.

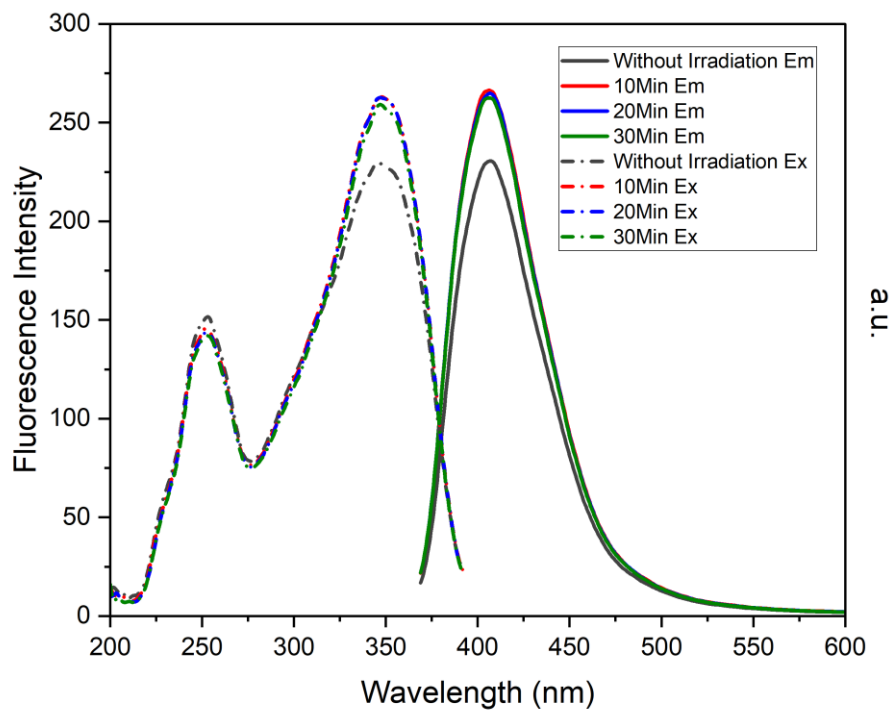


Figure E.1 : Fluorescence Spectra of **AzoCoum-1a** upon irradiation in MeCN (10^{-5} M)

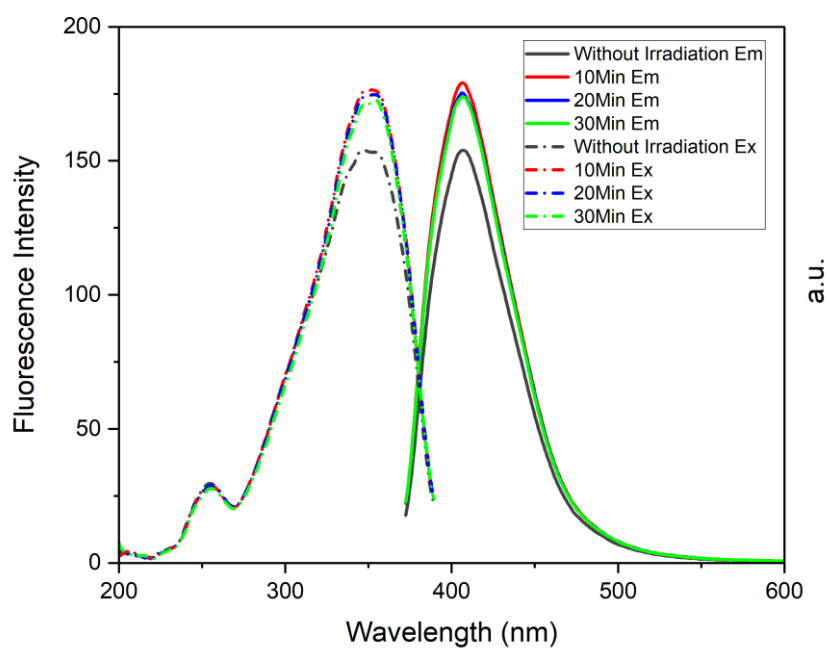


Figure E.2 : Fluorescence Spectra of **AzoCoum-1a** upon irradiation in THF (10^{-5} M)

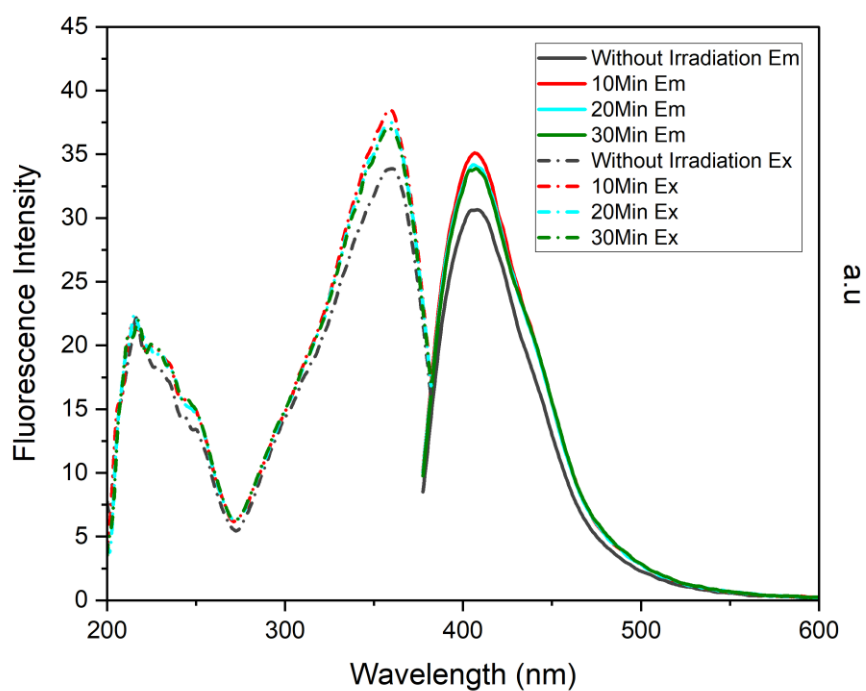


Figure E.3 : Fluorescence Spectra of **AzoCoum-1a** upon irradiation in MeOH (10^{-5} M)

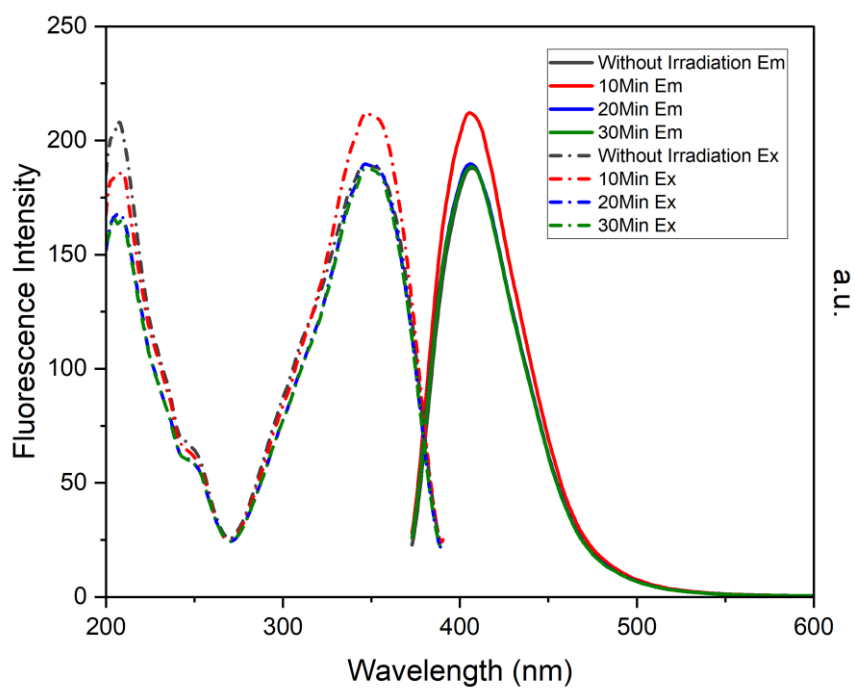


Figure E.4 : Fluorescence Spectra of **AzoCoum-1b** upon irradiation in MeCN (10^{-5} M)

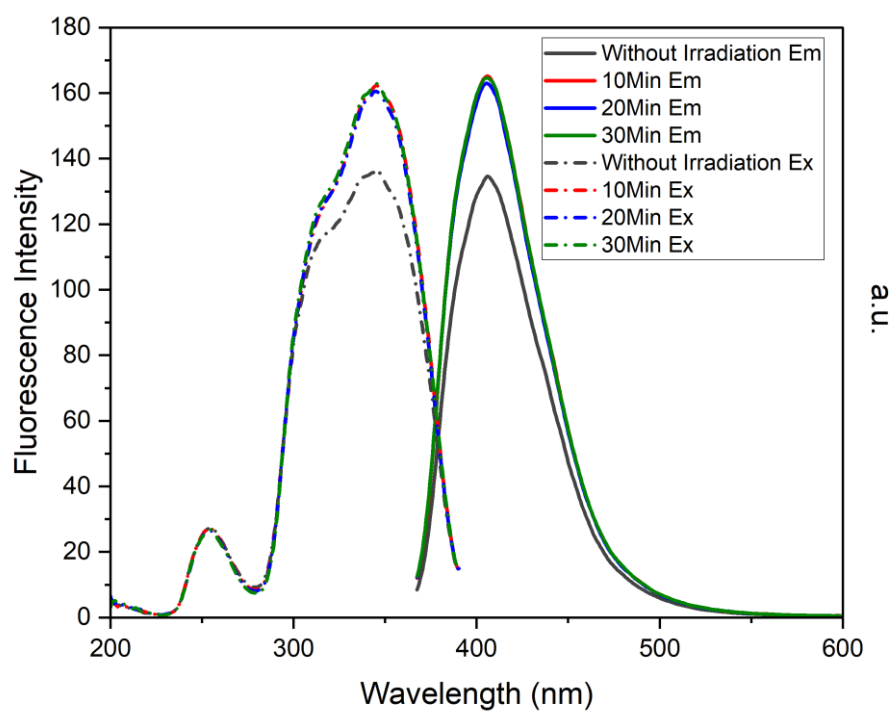


Figure E.5 : Fluorescence Spectra of **AzoCoum-1b** upon irradiation in THF (10^{-5} M)

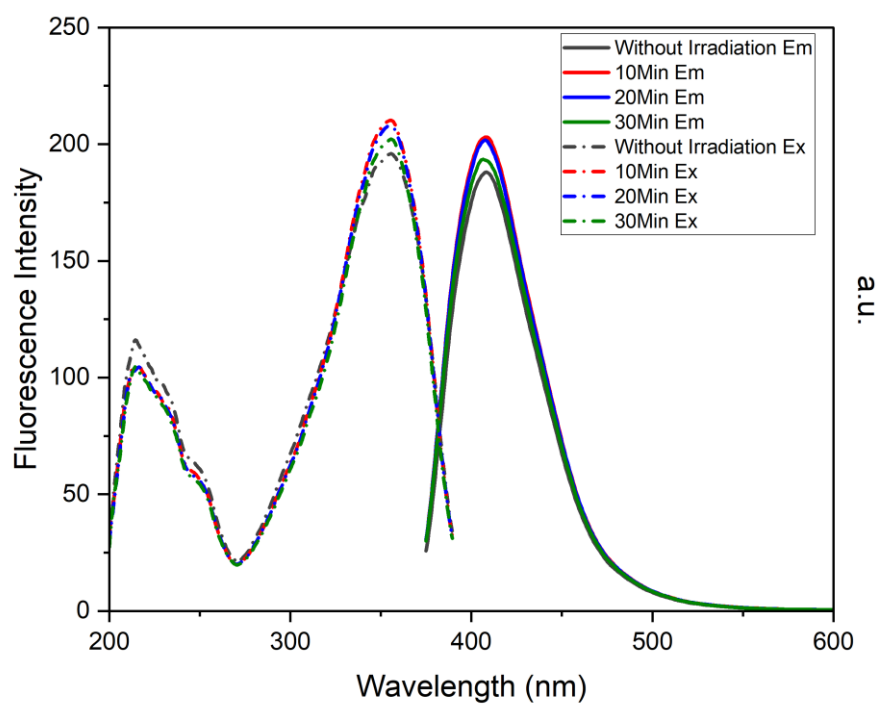


Figure E.6 : Fluorescence Spectra of **AzoCoum-1b** upon irradiation in MeOH (10^{-5} M)

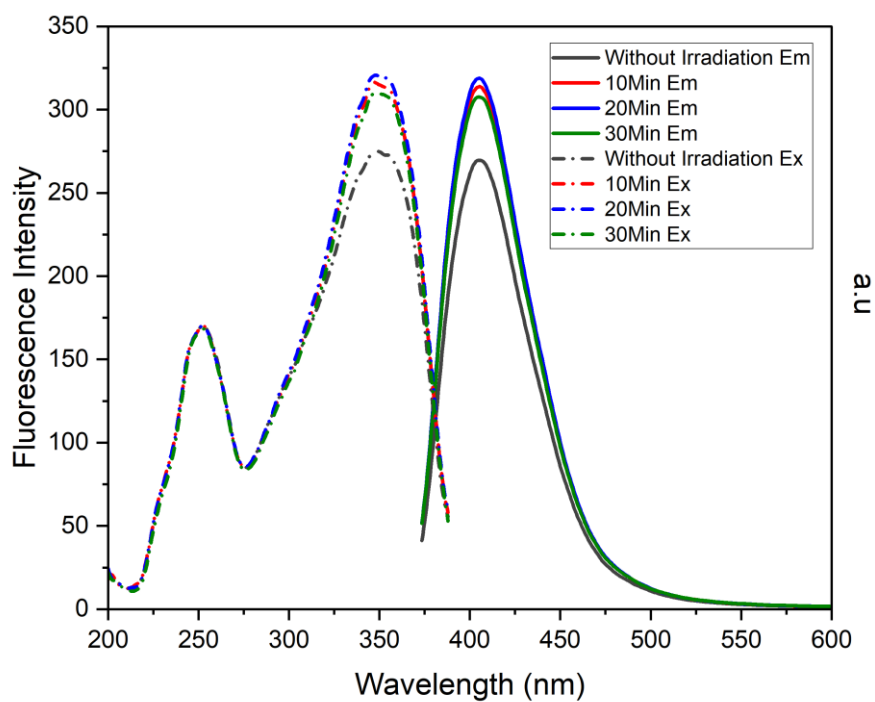


Figure E.7 : Fluorescence Spectra of **AzoCoum-2a** upon irradiation in MeCN (10^{-5} M)

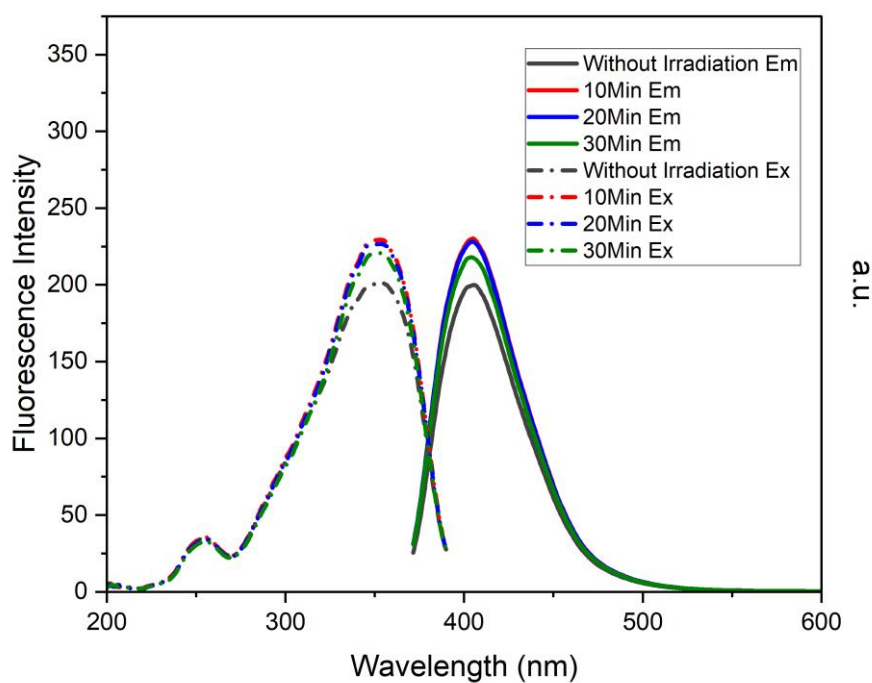


Figure E.8 : Fluorescence Spectra of **AzoCoum-2a** upon irradiation in THF (10^{-5} M)

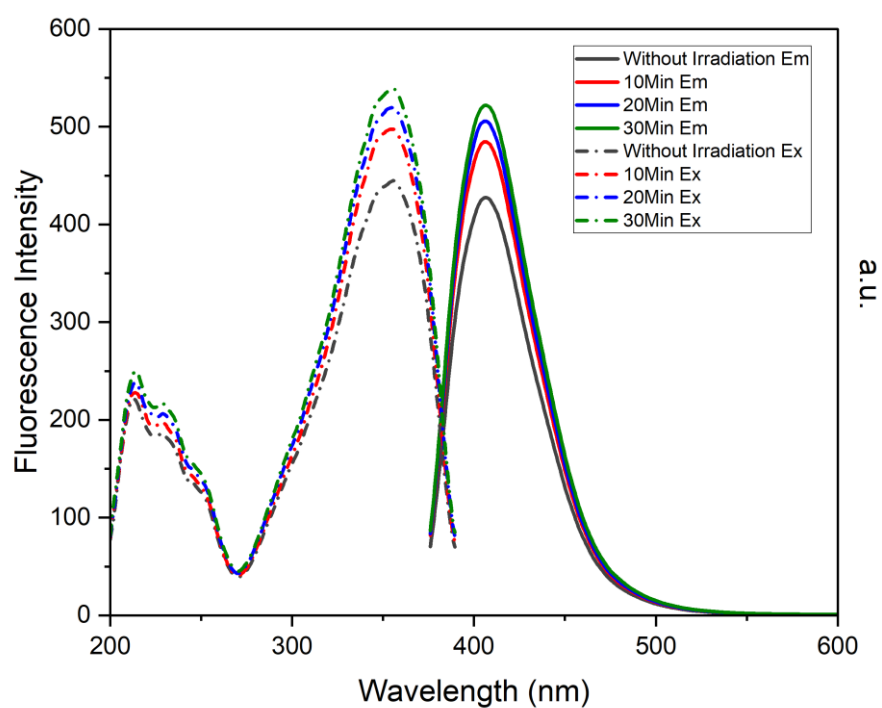


Figure E.9 : Fluorescence Spectra of **AzoCoum-2a** upon irradiation in MeOH (10^{-5} M)

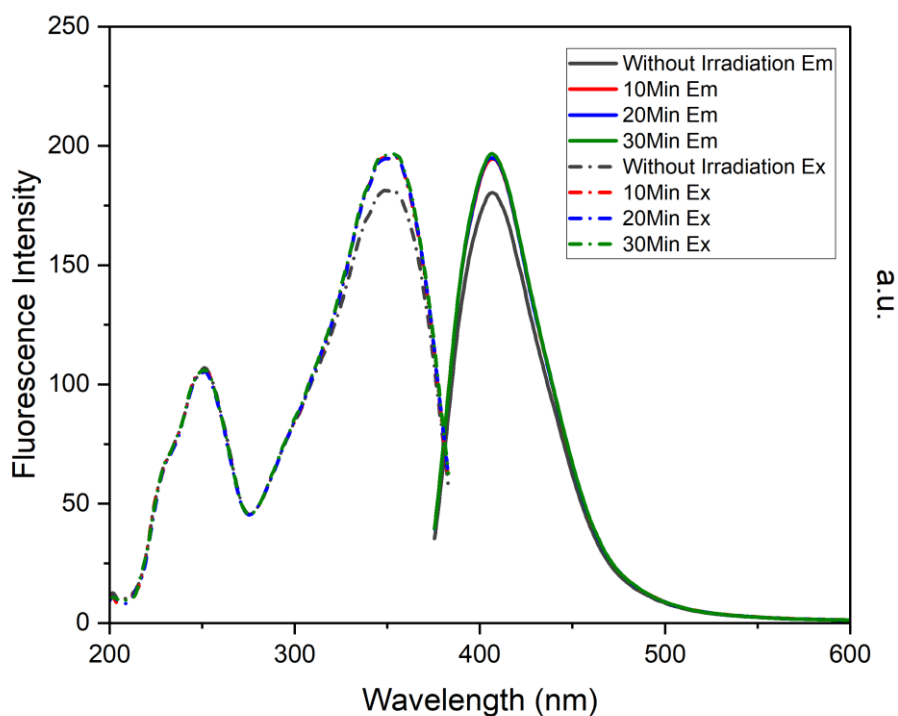


Figure E.10 : Fluorescence Spectra of **AzoCoum-2b** upon irradiation in MeCN (10^{-5} M)

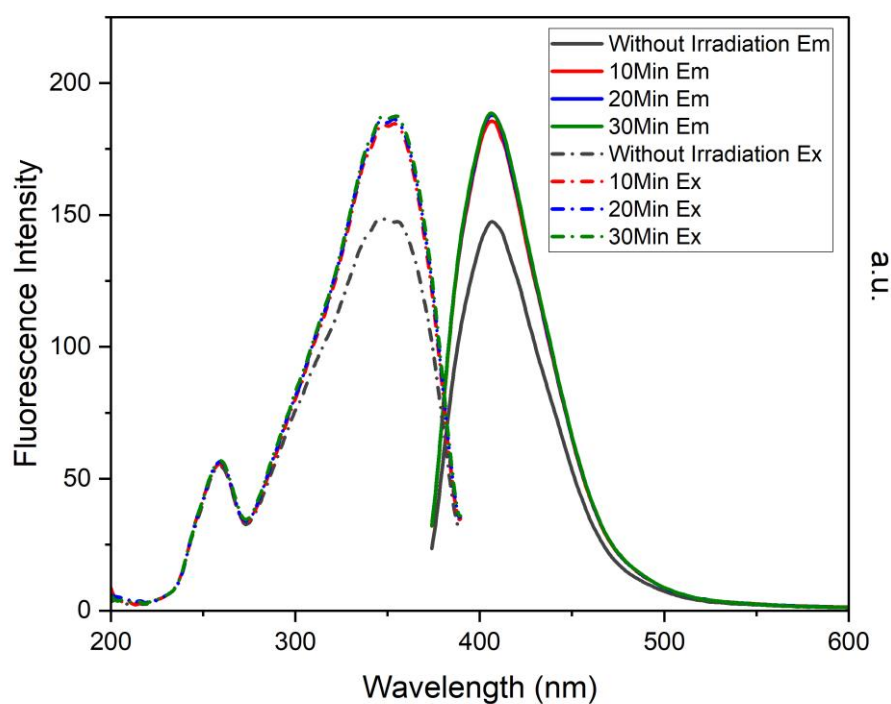


Figure E.11 : Fluorescence Spectra of **AzoCoum-2b** upon irradiation in THF (10^{-5} M)

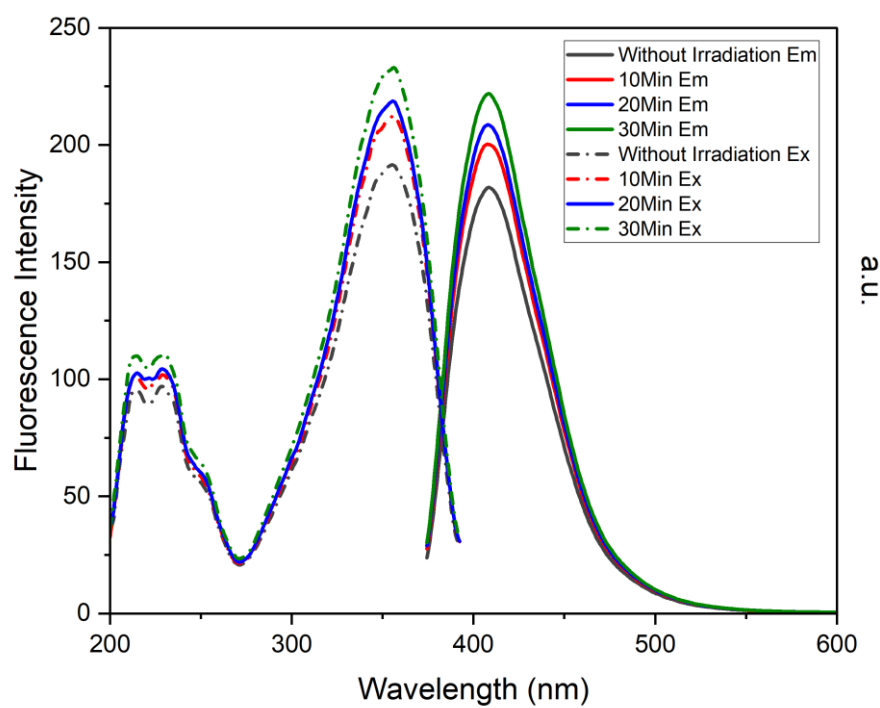


Figure E.12 : Fluorescence Spectra of **AzoCoum-2b** upon irradiation in MeOH (10^{-5} M)

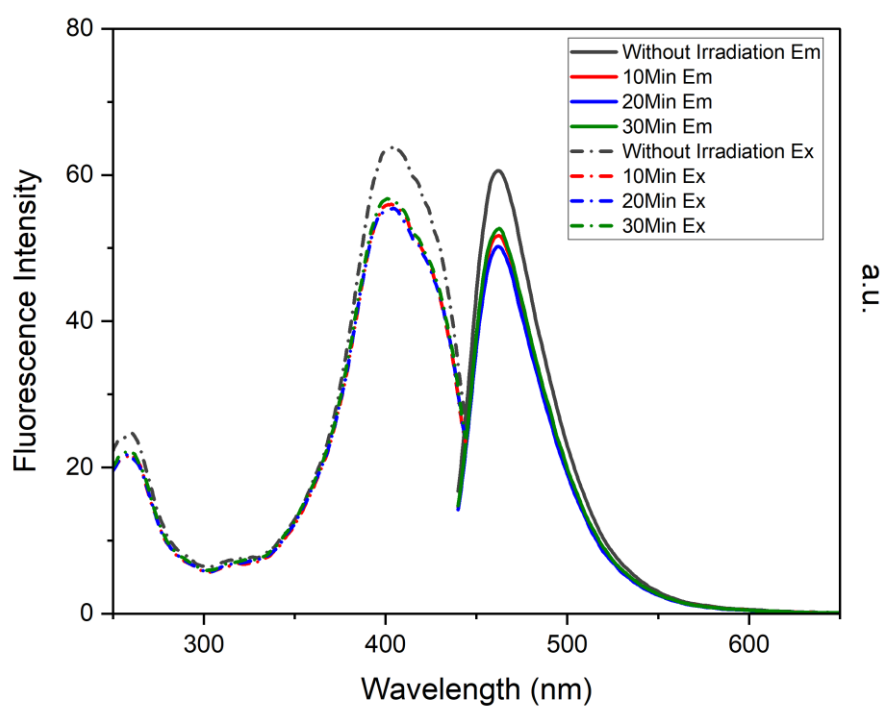


Figure E.13 : Fluorescence Spectra of **AzoCoum-3a** upon irradiation in MeCN (10^{-5} M)

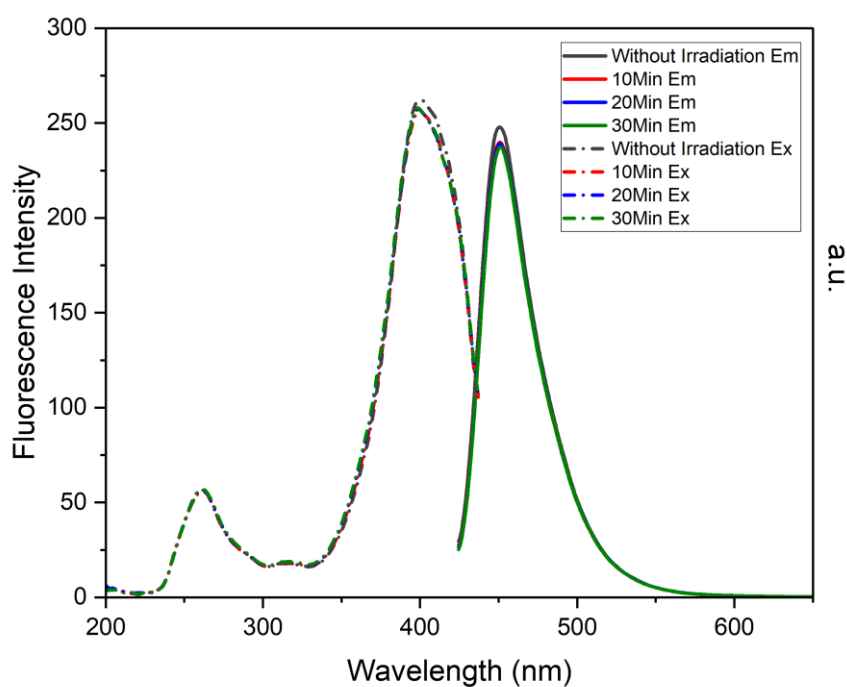


Figure E.14 : Fluorescence Spectra of **AzoCoum-3a** upon irradiation in THF (10^{-5} M)

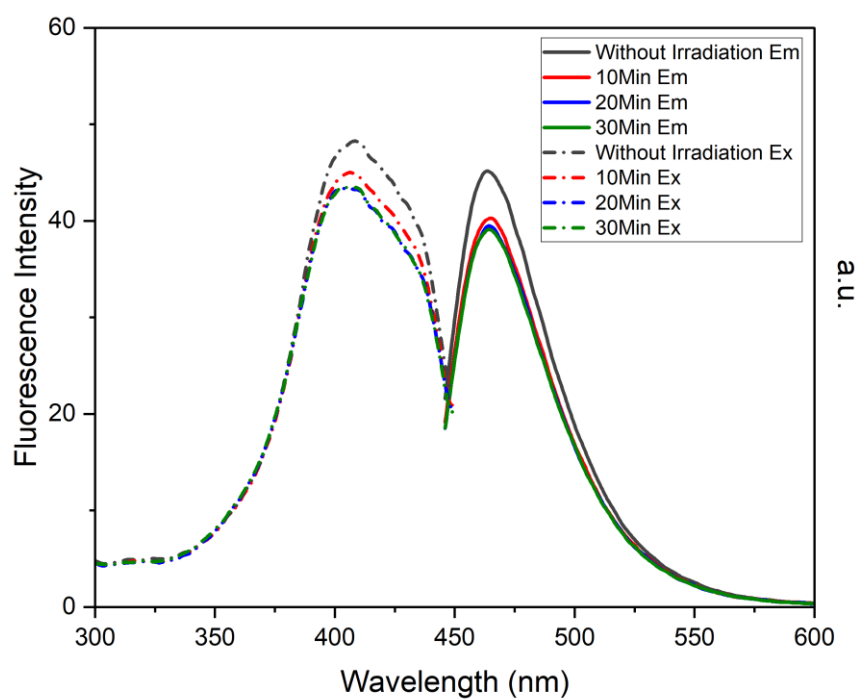


Figure E.15 : Fluorescence Spectra of **AzoCoum-3a** upon irradiation in MeOH (10^{-5} M)

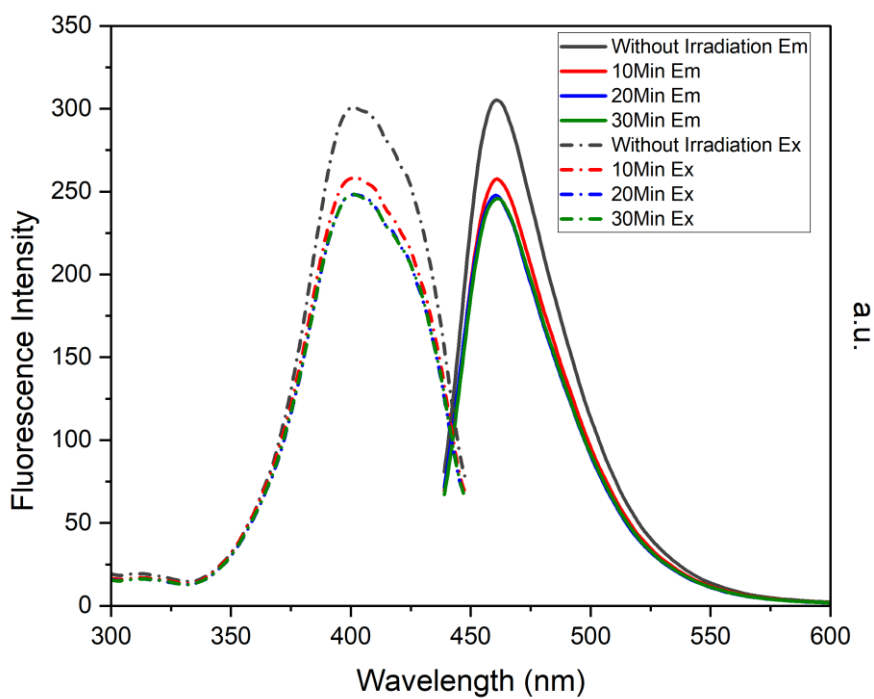


Figure E.16 : Fluorescence Spectra of **AzoCoum-3b** upon irradiation in MeCN (10^{-5} M)

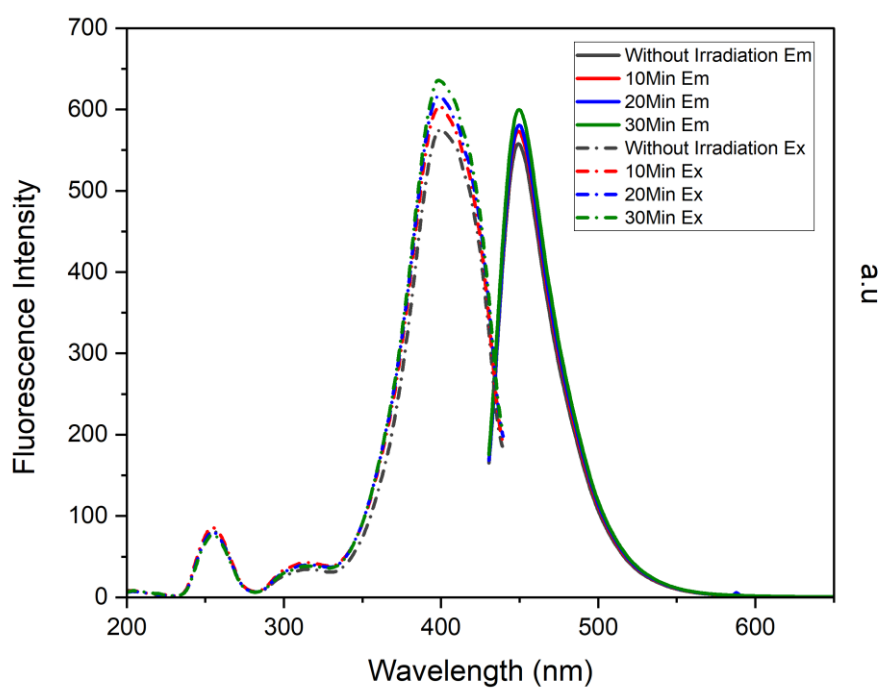


Figure E.17 : Fluorescence Spectra of **AzoCoum-3b** upon irradiation in THF (10^{-5} M)

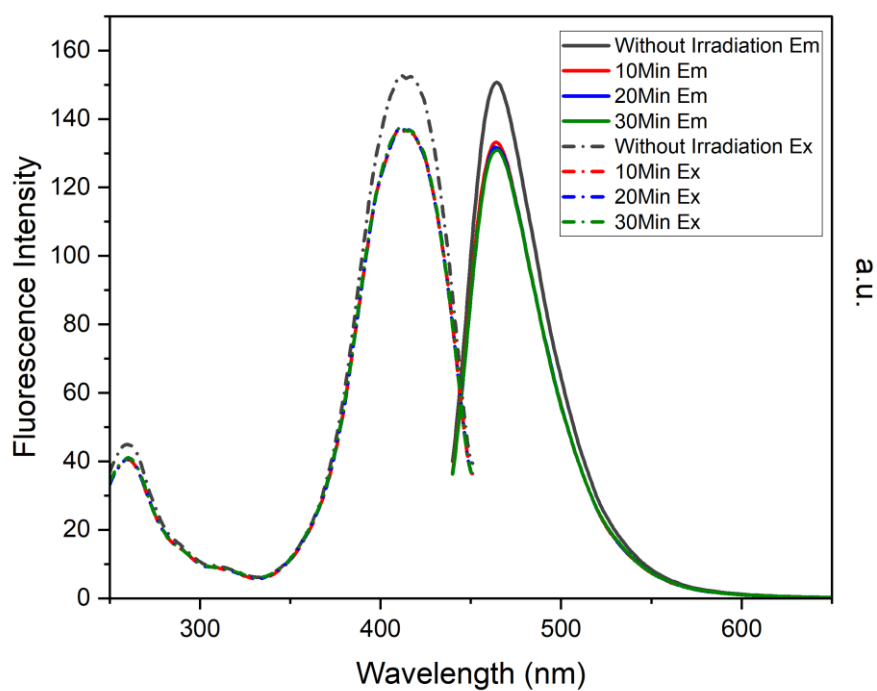


Figure E.18 : Fluorescence Spectra of **AzoCoum-3b** upon irradiation in MeOH (10^{-5} M)

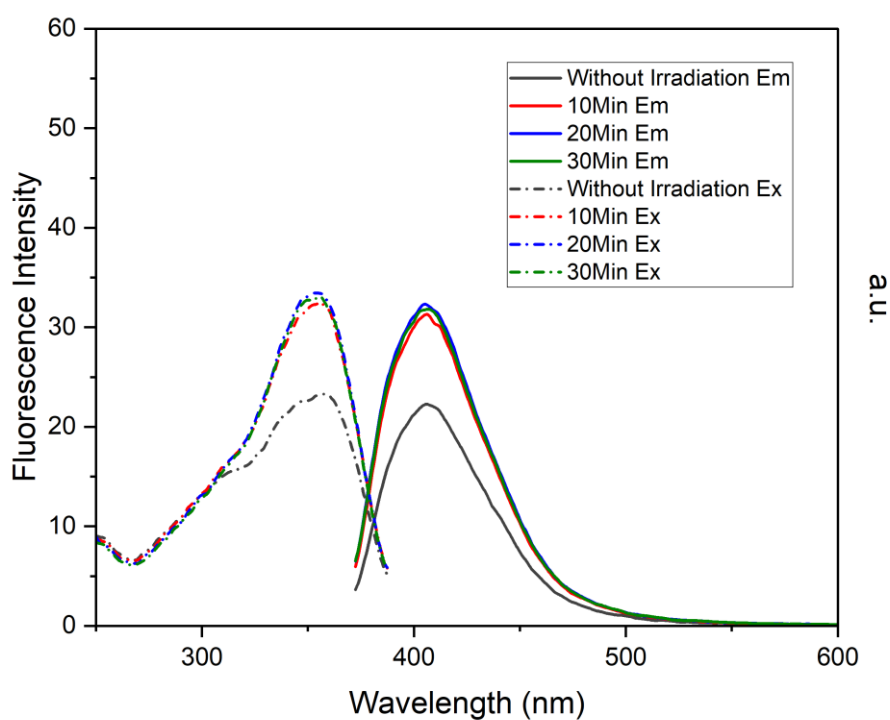


Figure E.19 : Fluorescence Spectra of **AzoCoumR-1** upon irradiation in MeCN (10^{-5} M)

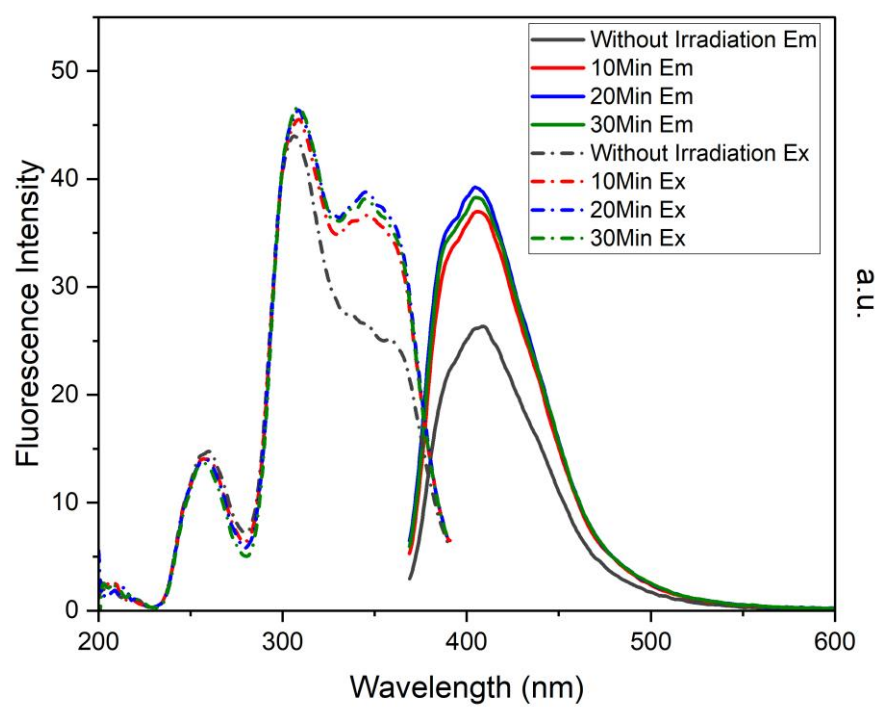


Figure E.20 : Fluorescence Spectra of **AzoCoumR-1** upon irradiation in THF (10^{-5} M)

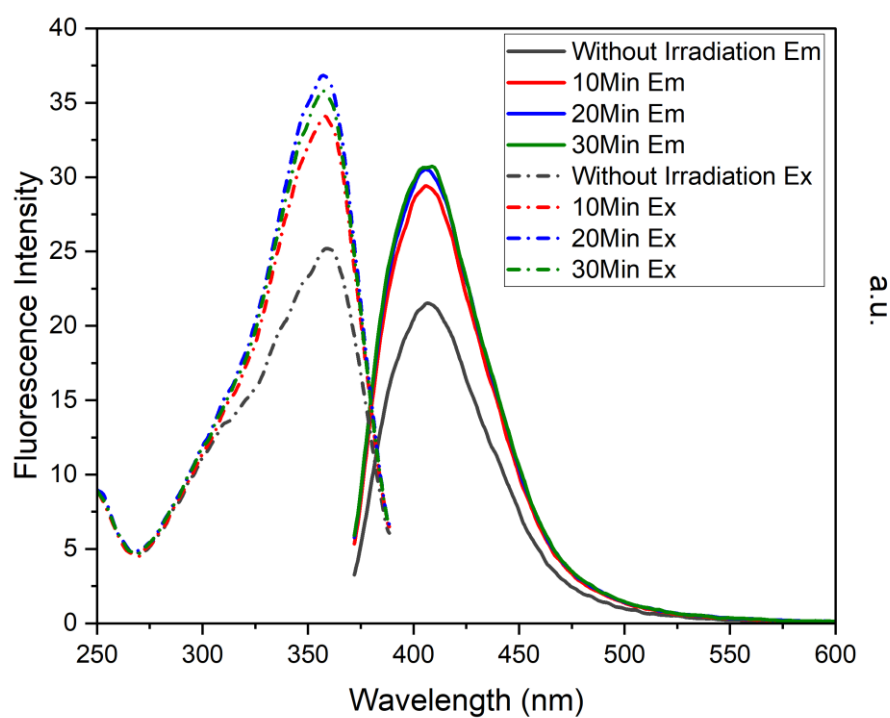


Figure E.21 : Fluorescence Spectra of **AzoCoumR-1** upon irradiation in MeOH (10^{-5} M)

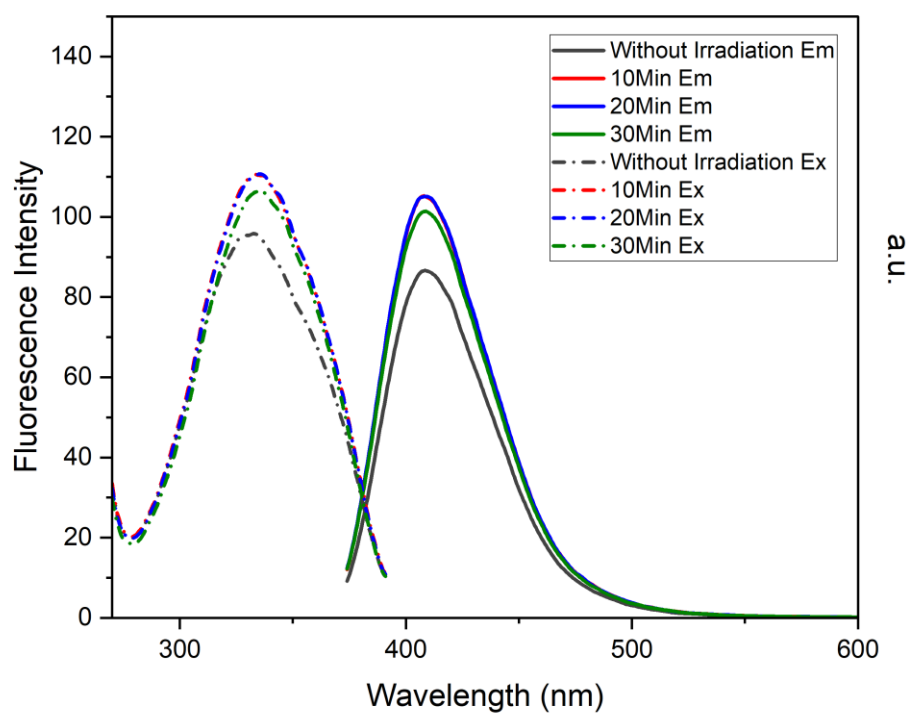


Figure E.22 : Fluorescence Spectra of **AzoCoumR-2** upon irradiation in MeCN (10^{-5} M)

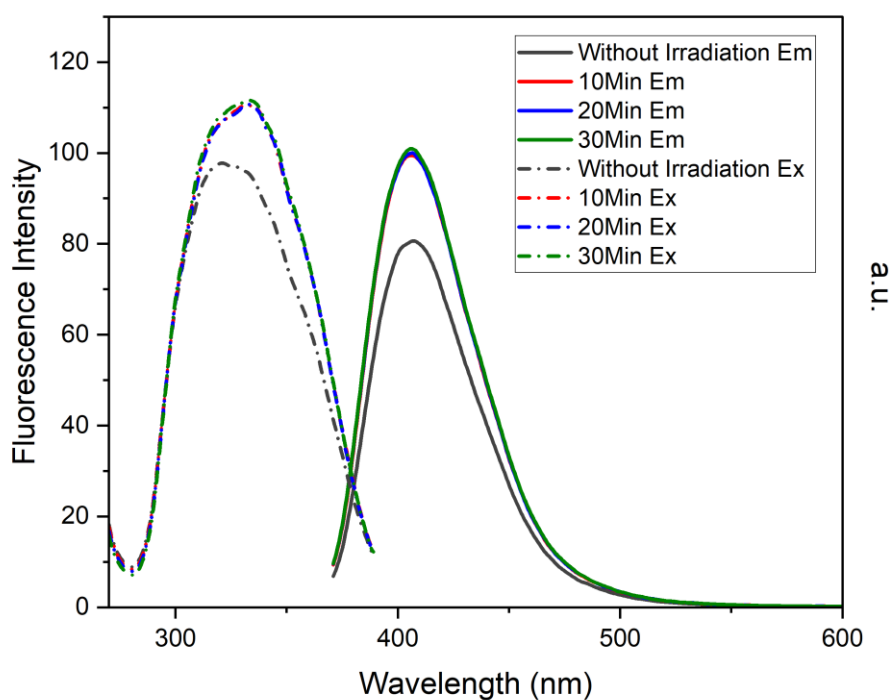


Figure E.23 : Fluorescence Spectra of **AzoCoumR-2** upon irradiation in THF (10^{-5} M)

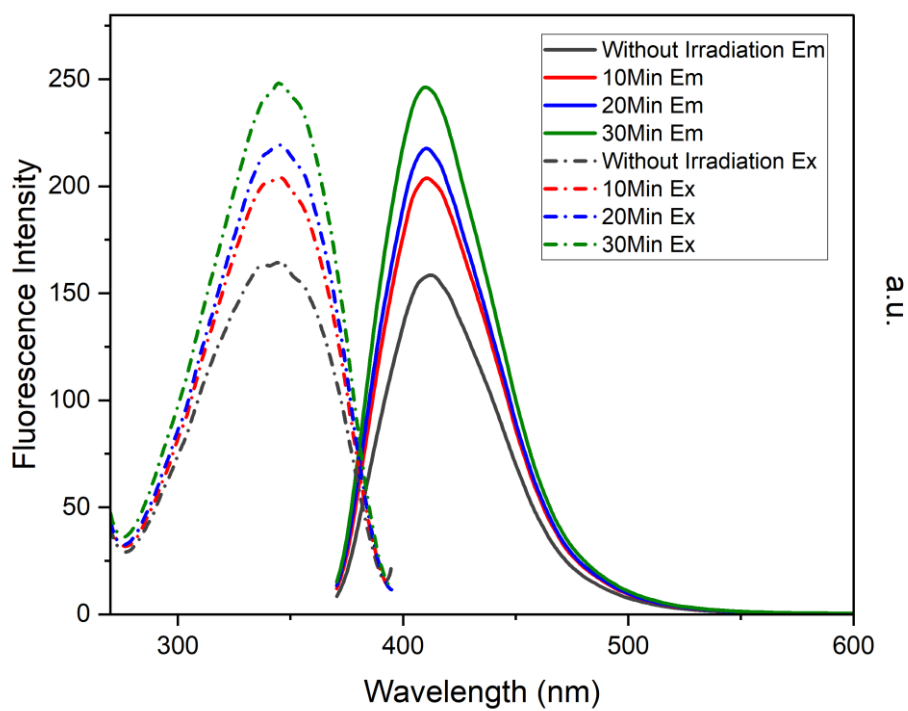


Figure E.24 : Fluorescence Spectra of **AzoCoumR-2** upon irradiation in MeOH (10^{-5} M)

F. Circular Dichroism (CD) Spectra

Circular Dichroism (CD) Measurements were conducted with a Jasco J-1500 CD spectrometer.

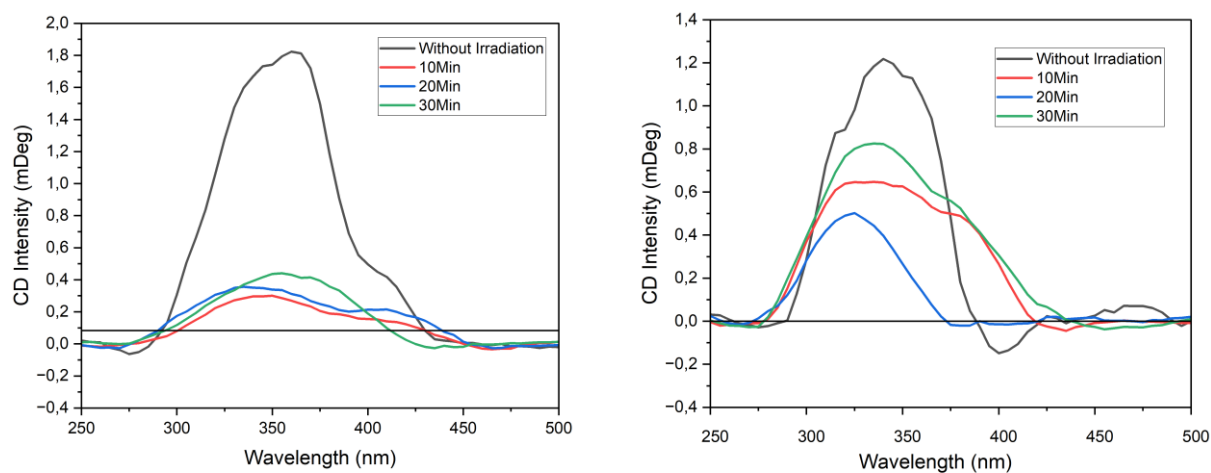


Figure F.1 : CD spectra of **AzoCouvR-1** in MeCN and MeOH upon irradiation (365 nm) (5×10^{-5} M)

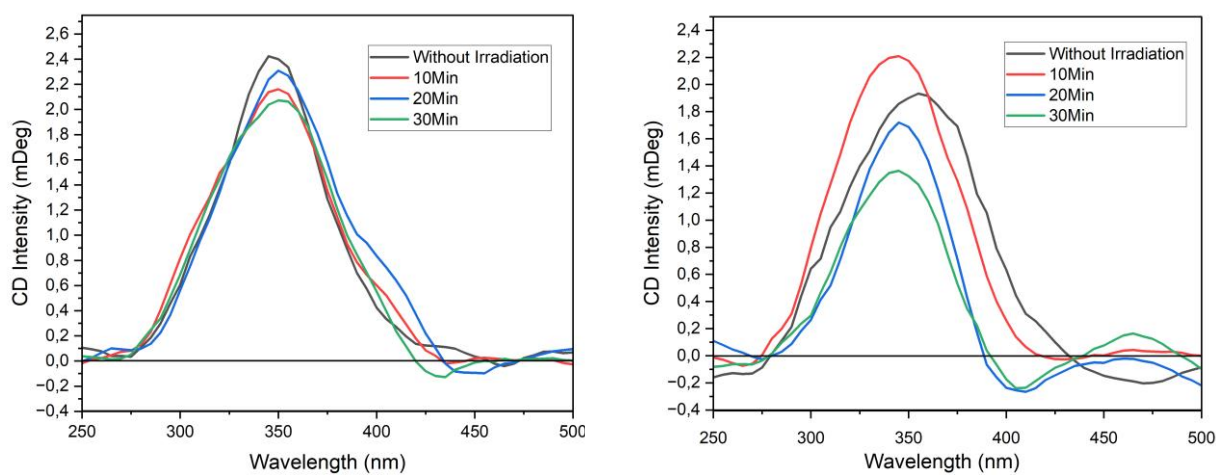


Figure F.2 : CD spectra of **AzoCouvR-2** in MeCN and MeOH upon irradiation (365 nm) (5×10^{-5} M)



G. XYZ Coordinates of Optimized Structures

For *trans*-AzoCoum-1a

Coordinates (Angstroms)

X	Y	Z
6.47853	-1.923249	-0.001464
7.837341	-1.533737	-0.001914
8.644774	-2.422309	-0.00274
8.076116	-0.080187	-0.000947
7.023525	0.789621	0.00013
5.668331	0.342498	0.00045
4.5508	1.196849	0.001541
3.259218	0.694832	0.001788
3.060927	-0.702872	0.00093
4.154102	-1.576541	-0.000151
5.439876	-1.051585	-0.000382
1.842593	-1.299031	0.0011
0.664373	-0.491358	0.001907
-0.526334	-1.441165	0.001621
-1.853079	-0.691122	0.00242
-2.88574	-1.671301	0.002284
-8.676871	0.785069	-0.00025
-8.314267	-0.424091	-0.000605

-10.080767	0.984433	-0.000902
-10.497329	2.322495	-0.000583
-11.855479	2.636031	-0.001165
-12.804969	1.61279	-0.002063
-12.391209	0.274339	-0.002382
-11.038427	-0.04501	-0.001809
-6.916758	-0.628665	0.000217
-6.49393	-1.968326	-0.000435
-5.144915	-2.286836	0.000238
-4.186174	-1.262194	0.001622
-4.596617	0.082018	0.002359
-5.952086	0.390694	0.001642
9.485146	0.411428	-0.001177
10.480867	-0.276249	-0.002126
9.525765	1.772327	-0.000213
10.84891	2.351843	-0.000399
10.686123	3.860325	0.000434
7.223413	1.856349	0.000783
4.711335	2.27178	0.002199
2.418036	1.376624	0.002646
3.996472	-2.648638	-0.000808
0.655372	0.153659	0.892071
0.654922	0.154771	-0.887444
-0.475326	-2.087704	-0.880994

-0.474884	-2.088782	0.883422
-1.94246	-0.050268	0.891929
-1.943076	-0.049388	-0.886383
-9.736205	3.096974	0.00012
-12.17232	3.675358	-0.000916
-13.864807	1.853062	-0.002515
-13.132535	-0.520599	-0.003078
-10.699019	-1.07476	-0.002046
-7.251133	-2.746414	-0.001514
-4.804687	-3.317318	-0.000295
-3.868607	0.885484	0.003553
-6.284772	1.4228	0.002199
11.390499	1.995861	0.881827
11.389864	1.996759	-0.883373
11.67111	4.339675	0.000303
10.140744	4.196837	-0.887419
10.141418	4.19594	0.889039

For *cis*-AzoCoum-1a

Coordinates (Angstroms)

X	Y	Z
-7.325824	-1.475377	0.56249
-7.541124	-0.068317	0.184444

-6.478944	0.731527	-0.124878
-5.133298	0.257788	-0.080127
-4.005509	1.041479	-0.384148
-2.72397	0.518734	-0.31561
-2.546966	-0.828	0.068784
-3.650707	-1.630769	0.377943
-4.926188	-1.086712	0.300928
-5.975587	-1.890823	0.602805
-8.937644	0.456944	0.159338
-9.924102	-0.123197	0.552587
-8.975958	1.712585	-0.365063
-1.339899	-1.438827	0.168694
-0.153636	-0.706307	-0.141836
1.020119	-1.657253	0.053407
2.353199	-0.991462	-0.266855
3.368407	-1.963797	-0.043758
4.668686	-1.625903	-0.280276
5.609885	-2.644608	-0.062073
6.954123	-2.407316	-0.299119
7.400801	-1.134965	-0.695777
6.455863	-0.126969	-0.926404
5.096629	-0.369821	-0.731104
8.792022	-1.040896	-1.021114
9.500481	-0.029727	-0.819297

9.084738	1.105938	-0.046468
9.363134	2.373571	-0.574626
9.102164	3.515435	0.180639
8.6157	3.39912	1.485175
8.386219	2.132067	2.028421
8.610091	0.985894	1.268374
-8.147319	-2.309011	0.830456
-10.283485	2.325545	-0.406884
-10.119596	3.709966	-1.005553
-6.663204	1.762464	-0.409919
-4.149916	2.077725	-0.678373
-1.874601	1.146058	-0.555756
-3.509086	-2.664217	0.671536
-0.069731	0.166471	0.521119
-0.200523	-0.344022	-1.178698
0.888485	-2.53282	-0.591201
1.031268	-2.013564	1.089047
2.522582	-0.115824	0.377333
2.380893	-0.650868	-1.312517
5.257009	-3.616948	0.266386
7.68664	-3.199284	-0.175328
6.773989	0.847486	-1.279402
4.386154	0.423699	-0.932384
9.77836	2.445042	-1.575731

9.299158	4.496786	-0.24255
8.433212	4.288896	2.081224
8.029381	2.034967	3.050418
8.433093	0.001511	1.689725
-10.690114	2.361387	0.608922
-10.948889	1.694919	-1.005037
-11.093228	4.209298	-1.056715
-9.709232	3.65315	-2.019064
-9.45032	4.325241	-0.39515

For *trans*-AzoCoum-2a

Coordinates (Angstroms)

X	Y	Z
-7.307835	1.738462	-0.00084
-6.030781	2.341054	-0.000694
-6.00824	3.541681	-0.001057
-4.893054	1.405716	-0.000202
-5.110683	0.056762	0.00008
-6.423433	-0.500084	-0.00009
-6.700843	-1.879864	0.000193
-8.002583	-2.353123	0.000023
-9.07352	-1.432308	-0.000443
-8.827055	-0.054252	-0.000734

-7.514554	0.397914	-0.000558
-10.380339	-1.787654	-0.00065
-10.720337	-3.170008	-0.00031
-3.513189	1.966893	0.00001
-3.214244	3.139152	0.000179
-2.579539	0.970416	0.000446
-1.211604	1.417467	0.00094
-0.331625	0.175241	0.000926
1.148597	0.537764	0.0015
1.882434	-0.684915	0.00162
7.44667	-0.930587	-0.000155
8.118078	0.138603	-0.000055
6.04547	-0.755785	0.000346
5.280396	-1.934067	0.000022
3.895386	-1.881119	0.000431
3.243711	-0.637867	0.001203
3.998764	0.548116	0.00159
5.387133	0.483978	0.001149
9.524414	-0.042948	-0.000496
10.282307	1.135877	-0.000511
11.674923	1.076825	-0.000934
12.317981	-0.162147	-0.001333
11.562741	-1.342098	-0.00131
10.173747	-1.290049	-0.000894

-4.257379	-0.613937	0.000448
-5.871543	-2.582403	0.00055
-8.186983	-3.420158	0.000245
-9.65249	0.647807	-0.001089
-11.810539	-3.204277	-0.000485
-10.339764	-3.67581	-0.896149
-10.340065	-3.675294	0.895947
-1.039178	2.043319	-0.881616
-1.039681	2.042916	0.883885
-0.552738	-0.435402	0.883595
-0.552172	-0.434982	-0.882174
1.407606	1.130963	-0.887281
1.406937	1.130738	0.890634
5.802748	-2.88595	-0.000586
3.292759	-2.783669	0.000156
3.51162	1.516546	0.002275
5.982636	1.390229	0.001438
9.754681	2.084954	-0.000192
12.256702	1.994509	-0.000949
13.40356	-0.212666	-0.001658
12.065838	-2.305692	-0.001617
9.572465	-2.192315	-0.000871

For *cis*-AzoCoum-2a

Coordinates (Angstroms)

X	Y	Z
6.721013	1.842625	-0.256622
5.42194	2.351759	-0.472624
5.346694	3.511437	-0.775487
4.328347	1.379714	-0.304961
4.604379	0.080908	0.016458
5.937572	-0.383693	0.216852
6.274015	-1.70724	0.556431
7.591859	-2.090308	0.743676
8.618848	-1.132802	0.591539
8.313189	0.191134	0.254379
6.985584	0.552893	0.070586
9.936608	-1.400841	0.751613
10.336081	-2.722874	1.096766
2.926235	1.850578	-0.481486
2.56631	2.99619	-0.627785
2.051612	0.802578	-0.448557
0.66394	1.160374	-0.581175
-0.136921	-0.133752	-0.551955
-1.633505	0.124173	-0.678376
-2.280406	-1.14588	-0.652938

-7.80792	-1.808852	-1.129767
-8.753978	-1.14287	-0.653007
-6.422847	-1.522933	-0.907299
-5.573089	-2.641097	-0.85141
-4.201291	-2.483514	-0.739178
-3.639177	-1.196556	-0.746471
-4.473185	-0.075846	-0.863635
-5.855832	-0.242071	-0.931746
-8.600275	-0.12733	0.349477
-7.952899	-0.370416	1.570324
-7.984531	0.5965	2.573033
-8.642538	1.811902	2.365699
-9.299335	2.045429	1.154946
-9.303454	1.069709	0.159728
3.783112	-0.619835	0.12818
5.478015	-2.438094	0.672655
7.822121	-3.115867	1.004256
9.105262	0.921522	0.138695
11.424024	-2.691576	1.168405
9.916133	-3.028234	2.062971
10.042513	-3.444167	0.324286
0.387766	1.834624	0.237457
0.5243	1.709823	-1.51846
0.184948	-0.78575	-1.371751

0.056793	-0.668336	0.384984
-1.996491	0.748127	0.151219
-1.864825	0.64497	-1.618917
-6.016062	-3.631846	-0.88877
-3.537896	-3.339768	-0.670574
-4.060715	0.925731	-0.90198
-6.490052	0.632349	-1.024371
-7.442191	-1.314473	1.730992
-7.490534	0.400216	3.521038
-8.657355	2.564505	3.149008
-9.82721	2.981323	0.992478
-9.841669	1.220085	-0.771649

For *trans*-AzoCoum-3a

Coordinates (Angstroms)

X	Y	Z
-6.987515	-1.899979	-0.295353
-8.068581	-0.965423	-0.215624
-7.737241	0.4027	-0.081535
-6.408229	0.805447	-0.058702
-5.341385	-0.111467	-0.152539
-5.67751	-1.477362	-0.269449
-6.164677	2.134564	0.068561

-4.869095	2.701784	0.11582
-3.76046	1.743104	0.014632
-4.019403	0.402576	-0.111026
-4.819433	3.896828	0.235283
-9.384263	-1.378878	-0.280783
-9.71972	-2.799981	-0.162313
-10.439923	-0.367538	-0.10336
-11.867039	-0.849655	-0.356051
-9.665848	-3.34402	1.271354
-2.368478	2.260349	0.051876
-2.029052	3.420268	0.122887
-1.462697	1.235986	-0.006311
-0.083691	1.639977	0.020355
0.755694	0.370478	-0.025106
2.24757	0.678651	0.003453
2.935871	-0.570188	-0.044749
4.297034	-0.576782	-0.035049
4.899484	-1.843657	-0.090552
6.281093	-1.951564	-0.086506
7.092131	-0.805834	-0.027183
6.483124	0.457782	0.028898
5.098487	0.577036	0.025212
8.484855	-1.036586	-0.029988
9.199398	0.003035	0.02391

10.597096	-0.236444	0.019428
11.402971	0.908472	0.081156
12.791922	0.791848	0.082115
13.383476	-0.471069	0.021162
12.580263	-1.617195	-0.040721
11.194625	-1.507697	-0.041948
-7.183597	-2.960306	-0.378246
-8.486736	1.175078	0.014528
-4.877505	-2.210558	-0.335987
-3.185015	-0.288034	-0.181527
-10.718723	-2.944824	-0.574844
-9.054837	-3.372554	-0.814869
-10.379176	0.066796	0.907069
-10.235599	0.448216	-0.805622
-12.537492	0.011157	-0.263739
-11.988585	-1.257312	-1.365185
-12.198676	-1.600175	0.368314
-9.919372	-4.410464	1.283148
-8.667993	-3.224509	1.705414
-10.378447	-2.819829	1.917912
0.11663	2.295493	-0.834766
0.102801	2.223468	0.928848
0.504466	-0.268849	0.828737
0.52329	-0.194654	-0.934875

2.537568	1.299814	-0.856155
2.519407	1.221573	0.920061
4.261497	-2.720375	-0.136436
6.765622	-2.922318	-0.129391
7.113913	1.338628	0.074995
4.649727	1.562868	0.069208
10.914826	1.877344	0.127622
13.411034	1.683504	0.130152
14.466057	-0.566357	0.021593
13.043152	-2.599607	-0.088319
10.556658	-2.383086	-0.089633

For *cis*-AzoCoum-3a

Coordinates (Angstroms)

X	Y	Z
-6.653686	-1.686392	0.670389
-7.674046	-0.693793	0.522158
-7.26394	0.611253	0.165352
-5.916779	0.904454	-0.003166
-4.908543	-0.067809	0.156007
-5.324316	-1.372955	0.496872
-5.597347	2.178982	-0.34296
-4.274513	2.634058	-0.556188

-3.226561	1.618431	-0.385915
-3.562457	0.332989	-0.047307
-4.155476	3.79241	-0.854421
-9.006012	-0.993499	0.733344
-9.445821	-2.390401	0.793596
-10.00246	0.063584	0.492575
-11.425895	-0.25762	0.944232
-9.518692	-3.086513	-0.571768
-1.810486	2.019292	-0.587056
-1.401838	3.131106	-0.837075
-0.972204	0.945951	-0.451601
0.424243	1.239439	-0.623195
1.180653	-0.072983	-0.47027
2.683257	0.118453	-0.634364
3.289335	-1.16334	-0.479897
4.643628	-1.269635	-0.581748
5.163752	-2.566826	-0.442313
6.527789	-2.782309	-0.551931
7.412931	-1.706209	-0.736908
6.88778	-0.416597	-0.892017
5.512465	-0.196974	-0.827325
8.784168	-2.061418	-0.943305
9.75886	-1.380159	-0.553642
9.654686	-0.25776	0.334708

10.39193	0.887911	0.007167
10.437472	1.963832	0.892007
9.79592	1.883119	2.130454
9.102915	0.719913	2.476476
9.022172	-0.346975	1.583967
-6.91173	-2.705274	0.925615
-7.965669	1.415881	-0.000535
-4.571486	-2.147439	0.621144
-2.77232	-0.401948	0.069765
-8.783133	-2.939237	1.46831
-10.424448	-2.41304	1.273978
-9.674092	0.952521	1.041491
-10.013427	0.339842	-0.573963
-12.038824	0.638375	0.800953
-11.887623	-1.06333	0.364955
-11.465367	-0.52106	2.00647
-9.847302	-4.125474	-0.452577
-10.230109	-2.580555	-1.23399
-8.542448	-3.090788	-1.066975
0.578545	1.689721	-1.610119
0.731066	1.980069	0.124222
0.979275	-0.503568	0.517226
0.826924	-0.792208	-1.217592
2.921662	0.528666	-1.626403

3.076316	0.813268	0.121901
4.473637	-3.387618	-0.274936
6.937399	-3.785976	-0.487796
7.54889	0.420985	-1.084137
5.132209	0.808145	-0.968297
10.917178	0.91985	-0.943034
10.991863	2.858741	0.62226
9.84907	2.714078	2.828248
8.620035	0.642871	3.447131
8.484656	-1.250704	1.852586

For *trans*-AzoCoumR-1

Coordinates (Angstroms)

X	Y	Z
-6.27713	2.08504	0.039418
-7.586924	1.673792	0.400693
-8.402986	2.964498	0.534584
-7.667569	3.874791	-0.279555
-6.291664	3.508455	-0.207478
-9.775882	2.676985	-0.115679
-9.684361	1.362998	-0.670629
-8.331738	0.914793	-0.723351
-8.340189	-0.59793	-0.565929

-6.965534	-1.003084	-0.639174
-6.683011	-2.267679	-0.213964
-7.535995	-3.05551	0.122647
-10.874833	2.774523	0.735777
-10.948107	1.815516	1.784825
-5.65042	3.795789	-1.557177
-5.592795	4.219681	0.953051
-5.210531	-2.491507	-0.203359
-4.713334	-3.872961	-0.106407
-3.311342	-4.006326	-0.026427
-2.449648	-2.958665	-0.064363
-2.926065	-1.634217	-0.188043
-4.339093	-1.440571	-0.253604
-1.092069	-3.237007	0.021698
-0.175277	-2.180529	-0.019785
-0.621744	-0.847552	-0.147433
-1.981601	-0.59236	-0.226948
1.128786	-2.542047	0.071137
2.143339	-1.537624	0.023153
3.48123	-2.252292	0.16153
4.656795	-1.284582	0.095546
5.840427	-2.05842	0.261068
7.051558	-1.434013	0.220048
8.168758	-2.265142	0.393706

9.443346	-1.721386	0.364134
9.633623	-0.344386	0.160978
8.511397	0.480909	-0.009942
7.22868	-0.054259	0.019503
10.975427	0.096211	0.146992
11.129226	1.333743	-0.049225
12.478475	1.769711	-0.061775
12.665552	3.138479	-0.29742
13.950871	3.676518	-0.333465
15.056677	2.848689	-0.132398
14.872342	1.480346	0.104983
13.59335	0.93743	0.141343
-5.350787	-4.891177	-0.10121
-9.965032	3.409537	-0.907417
-4.728897	-0.429246	-0.331099
-2.334728	0.431043	-0.321449
0.082541	-0.025694	-0.182429
-0.743856	-4.258654	0.11783
-5.679913	4.868632	-1.770333
-4.606663	3.46745	-1.556347
-6.190181	3.263232	-2.344403
-4.556279	3.878314	1.03681
-5.596803	5.3027	0.794645
-6.100275	4.003274	1.89839

-8.918224	-1.08081	-1.359855
-8.770479	-0.893834	0.395993
-7.540904	1.081005	1.320928
-8.508159	3.342666	1.558321
-7.87066	1.184709	-1.683856
2.081434	-0.991854	-0.929214
1.99462	-0.816782	0.839602
3.508243	-2.79108	1.114743
3.579	-2.996516	-0.636091
4.68081	-0.76059	-0.871166
4.589743	-0.525673	0.889179
11.786788	3.757827	-0.450189
14.089544	4.73835	-0.517478
16.06042	3.264329	-0.159182
15.735034	0.838016	0.26209
13.43081	-0.119006	0.323329
10.320433	-2.347586	0.495983
8.007827	-3.327167	0.548115
6.375909	0.601951	-0.113619
8.664712	1.543142	-0.165224
-11.844329	2.064774	2.356556
-11.036866	0.797692	1.392344
-10.078984	1.86832	2.458171

For *cis*-AzoCoumR-1

Coordinates (Angstroms)

X	Y	Z
5.937871	1.972644	-0.319744
7.261793	1.497759	-0.511687
8.120436	2.747212	-0.737576
7.343827	3.766395	-0.113054
5.969844	3.4159	-0.260815
9.426282	2.52385	0.058688
9.251057	1.299011	0.774078
7.88854	0.87816	0.760431
7.873955	-0.642066	0.796917
6.488393	-1.014227	0.818364
6.210844	-2.329436	0.588886
7.069536	-3.168855	0.449318
9.573896	3.352431	0.759296
10.592754	2.484378	-0.703503
10.718871	1.392442	-1.607661
5.220936	3.889989	0.975947
5.394722	3.978177	-1.562573
4.737981	-2.539706	0.515239
4.221498	-3.914698	0.603717
2.823098	-4.044574	0.469112

1.980339	-2.995754	0.293354
2.474414	-1.673612	0.230119
3.88486	-1.485945	0.347341
0.623896	-3.270387	0.180126
-0.273722	-2.211628	0.002377
0.190936	-0.880403	-0.063663
1.549279	-0.629527	0.048795
-1.578482	-2.569005	-0.09663
-2.573415	-1.559223	-0.271832
-3.918537	-2.270023	-0.345195
-5.074009	-1.291583	-0.520424
-6.267111	-2.065199	-0.581635
-7.461295	-1.425909	-0.744042
-8.58905	-2.258248	-0.825494
-9.845274	-1.705487	-1.014964
-10.017185	-0.311337	-1.061844
-8.88713	0.513406	-0.99548
-7.61412	-0.036896	-0.849085
-11.339115	0.141974	-1.37407
-11.859069	1.180266	-0.90866
-11.295995	1.954312	0.160863
-10.946899	1.386169	1.395366
-10.570496	2.211301	2.453159
-10.52244	3.598239	2.288166

-10.884201	4.162404	1.062257
-11.297046	3.347365	0.009814
4.839286	-4.92813	0.788775
4.288453	-0.478772	0.289752
1.91631	0.392055	-0.002919
-0.498164	-0.056565	-0.201732
0.262043	-4.290572	0.23064
5.259941	4.981163	1.047817
4.172934	3.579727	0.92387
5.675183	3.459627	1.872062
4.358747	3.649494	-1.691718
5.419491	5.072337	-1.549135
5.97296	3.626249	-2.422666
8.381683	-1.026718	1.686696
8.366029	-1.065094	-0.084799
7.276533	0.791768	-1.349568
8.321204	2.988292	-1.788114
7.352273	1.272547	1.634981
-2.543184	-0.855828	0.572469
-2.373449	-0.99467	-1.193624
-3.911426	-2.976061	-1.182425
-4.071603	-2.851588	0.570207
-5.124076	-0.586521	0.322557
-4.957584	-0.705375	-1.444084

-10.985557	0.30917	1.523601
-10.312155	1.768123	3.411325
-10.222239	4.235594	3.115153
-10.865888	5.241095	0.931704
-11.61967	3.77227	-0.9363
-10.719417	-2.340704	-1.122208
-8.447891	-3.33256	-0.763982
-6.755498	0.62394	-0.817932
-8.992809	1.589315	-1.077883
11.67064	1.537632	-2.122628
10.731957	0.434191	-1.078993
9.914122	1.379944	-2.35831

For *trans*-AzoCouvR-2

Coordinates (Angstroms)

X	Y	Z
-3.478809	2.04078	-0.350236
-4.838602	1.77745	-0.448822
-5.266788	0.45376	-0.600874
-4.331885	-0.603117	-0.652595
-2.980351	-0.317628	-0.552351
-2.520314	1.003831	-0.399967
-1.146013	1.370247	-0.297409

-0.748823	2.669795	-0.155457
-1.564983	4.928248	0.040762
-1.748837	3.749279	-0.094046
-3.09412	3.333205	-0.204336
0.693332	3.032104	-0.065257
1.150537	4.150269	-0.001586
1.478996	1.915401	-0.067872
2.894775	2.165789	-0.00225
3.591287	0.812645	-0.019858
5.107454	0.957498	0.031731
5.653754	-0.359614	0.010884
11.115027	-1.444206	0.104243
11.942071	-0.491218	0.147623
9.757127	-1.058089	0.08551
8.823334	-2.106585	0.035045
7.462722	-1.844408	0.011546
7.006194	-0.517384	0.038415
7.930899	0.540295	0.089894
9.293529	0.266561	0.112893
13.30338	-0.888491	0.165721
14.235084	0.157361	0.212233
15.601319	-0.11843	0.233334
16.043877	-1.442043	0.208119
15.11457	-2.489328	0.161741

13.750944	-2.221063	0.140465
-9.591634	-2.843106	-0.110729
-9.924111	-1.781594	0.948244
-9.316745	-0.46748	0.388021
-8.664329	-0.879996	-0.9404
-9.262738	-2.133885	-1.295672
-11.322692	-1.550551	0.98295
-11.556316	-0.142685	0.871531
-10.440476	0.365883	0.140106
-12.814002	0.073757	0.045617
-11.625289	0.496432	2.261238
-8.5174	-3.611315	0.37643
-7.143703	-1.0323	-0.858818
-6.608078	0.283033	-0.692234
-8.190933	-4.720961	-0.452668
-5.560818	2.584469	-0.410972
-4.660092	-1.628411	-0.769119
-2.254126	-1.125264	-0.591918
-0.391897	0.590711	-0.336563
3.187628	2.790573	-0.853474
3.116157	2.731355	0.909614
3.258318	0.213164	0.834944
3.314736	0.266263	-0.928751
5.476627	1.531181	-0.830521

5.422654	1.480631	0.946068
9.196105	-3.126167	0.014526
6.730842	-2.644757	-0.027856
7.59488	1.570766	0.11203
10.018882	1.07174	0.152115
13.861754	1.176896	0.231008
16.318616	0.696939	0.269317
17.108201	-1.661104	0.224453
15.461503	-3.519326	0.142198
13.016745	-3.018099	0.104652
-10.44959	-3.480655	-0.354498
-9.540096	-2.074858	1.930677
-8.608115	0.021779	1.065539
-8.913681	-0.15915	-1.723308
-13.680599	-0.357074	0.555824
-12.988849	1.143447	-0.102708
-12.69474	-0.408012	-0.928011
-11.767665	1.578106	2.175127
-12.457106	0.073781	2.833268
-10.699121	0.315289	2.817024
-6.860092	-1.67714	-0.01922
-6.776899	-1.48236	-1.789391
-7.369697	-5.248971	0.037072
-9.049045	-5.401683	-0.552127

-7.877556 -4.398843 -1.4529

For *cis*-AzoCoumR-2

Coordinates (Angstroms)

X	Y	Z
13.455161	2.219454	-0.457795
13.354742	3.521624	0.02862
12.650077	3.779881	1.207098
12.040836	2.726414	1.894042
12.106007	1.426566	1.39649
12.801472	1.171892	0.204733
13.052587	-0.160185	-0.264862
12.164226	-1.024382	-0.441866
8.572377	-1.734307	0.047387
9.963388	-1.821197	0.047306
10.757739	-0.762848	-0.407895
10.127994	0.373778	-0.951481
8.745535	0.449946	-0.995398
7.955207	-0.592075	-0.47971
6.609553	-0.400851	-0.556266
5.738306	-1.419624	-0.07043
4.311552	-0.929727	-0.284095
3.288973	-1.951568	0.192114

0.319404	0.643456	-0.773857
1.98824	-1.380102	-0.047376
1.058222	-3.263889	0.772947
0.942801	-2.1488	0.293917
-1.868547	0.268566	-0.69495
-2.957301	-0.496422	-0.4287
-4.208646	0.051796	-0.676189
-5.350628	-0.712782	-0.41147
-5.235898	-2.023603	0.101103
-3.97778	-2.550597	0.340642
-2.811515	-1.805567	0.083253
-1.486444	-2.281034	0.298902
-0.38492	-1.520221	0.026861
-0.536956	-0.154988	-0.497377
-10.735178	-0.392991	0.449262
-10.292645	0.987988	0.952776
-9.056842	1.343783	0.082596
-8.887588	0.138888	-0.856762
-10.141048	-0.557998	-0.828713
-11.26607	1.96193	0.614579
-10.608895	3.057536	-0.029804
-9.458835	2.48867	-0.656844
-11.528228	3.603114	-1.110403
-10.192953	4.110497	1.001404

-7.756373	-0.806696	-0.446688
-6.53188	-0.106552	-0.682284
-10.291235	-1.349638	1.381342
-10.743882	-2.669261	1.100462
14.030489	1.99687	-1.35179
13.844207	4.333295	-0.50304
12.588926	4.792362	1.596129
11.508211	2.917852	2.821889
11.632497	0.607867	1.92889
7.986719	-2.561421	0.43128
10.456939	-2.716904	0.412682
10.720975	1.185278	-1.357312
8.245504	1.311918	-1.425734
5.919603	-2.358004	-0.614844
5.936479	-1.604745	0.995589
4.165982	0.013484	0.253253
4.154984	-0.72181	-1.348015
3.389973	-2.173011	1.260676
3.368042	-2.900959	-0.349175
-4.303281	1.056754	-1.070369
-6.117627	-2.617435	0.30738
-3.880231	-3.558766	0.734319
-1.32704	-3.28214	0.691047
-11.819422	-0.462913	0.302561

-10.097476	0.969245	2.030005
-8.149152	1.551119	0.660128
-8.719956	0.480211	-1.881526
-12.445455	3.997533	-0.663218
-11.03003	4.407725	-1.659236
-11.784548	2.800256	-1.806099
-9.654752	4.928593	0.51275
-11.074511	4.517782	1.506181
-9.535468	3.672113	1.759784
-7.846141	-1.088508	0.608741
-7.804892	-1.714359	-1.060566
-10.361335	-3.309741	1.898259
-11.842787	-2.714657	1.097294
-10.372514	-3.024739	0.131928