NEW STRATEGY FOR THE SYNTHESIS OF CHIRAL N-SUBSTITUTED-3,4-DIALKOXYPYRROLE FROM 2,5-DIHYDRO-2,5-DIMETHOXYFURAN

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IN
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Approval of the Graduate School of Natural and Applied Sciences.

_____

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I certify that this thesis satisfies all the requirements as a thesis for the degree of Master of Science.

_____

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Chairman of the Department

This is to certify that we have read this thesis and that in our opinion it is fully adequate, in scope and quality, as a thesis for the degree of Master of Science.

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ABSTRACT

NEW STRATEGY FOR THE SYNTHESIS OF CHIRAL N-SUBSTITUTED-3,4-DIALKOXYPYRROLE FROM 2,5-DIHYDRO-2,5-DIMETHOXYFURAN

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July 2006, 80 pages

Pyrroles are very valuable class of substances which have wide usage area in organic synthesis.

In this study, chiral 3,4-dialkoxy-N-substituted pyrrole derivatives were synthesized. These compounds are widely used as building blocks for the synthesis of natural compounds that have focused on heterocyclic rings in their structures. In addition, chiral pyrrole derivatives can be used as monomers for the synthesis of chiral conducting polymers which have received great interest due to their potential applications as electrodes for electrochemical asymmetric

synthesis, stereoselecive analyses and in many areas, such as electronics, electrochromic devices, polymeric batteries, antielectronic coatings and functional membranes.

3,4-dialkoxy-N-substituted chiral pyrrole derivatives were synthesized starting from 2,5-dimethoxy-2,5-dihydrofuran which is a commercially available, inexpensive material. After oxidation, the resultant diol were protected with alkoxy goups and then correponding 3,4-dialkoxy-N-substituted chiral pyrrole derivatives were afforded via pyrrolization reaction by using several chiral amines or aminoalcohols.

Key words : chiral, polypyrrole, 3,4-dialkoxypyrroles

ÖZ

KİRAL N-SÜBSTİTÜE 3,4-DİALKOKSİ-PİROLLERİN 2,5-DİMETOKSİ-2,5-DİHİDROFURAN'DAN BAŞLANARAK YENİ BİR YÖNTEMLE SENTEZLENMESİ

KAPAKLI, FADİLE
Yüksek Lisans, Kimya Bölümü
Tez Yöneticisi: Prof. Dr. Cihangir Tanyeli
Temmuz 2006, 80 sayfa

Piroller organik sentezde geniş kullanım alanına sahip çok değerli bileşikler sınıfıdır.

Bu çalışmada kiral N-sübstitüe 3,4-dialkoksi pirol türevleri sentezlendi. Bu bileşikler yapılarında heterosiklik halkalar bulunan doğal bileşiklerin sentezinde yaygın olarak kullanılan yapıtaşlarıdır. Ayrıca, kiral pirol türevleri potansiyel uygulamalarından dolayı büyük ilgi gören elektrokimyasal asimetrik sentez, stereoseçici analiz, elektronik, elektrokromik aletler, polimerik piller, antielektronik kaplamalar ve fonksiyonel zarlar gibi alanlarda kullanılan iletken polimerlerin sentezinde monomer olarak kullanılabilmektedir.

Kiral 3,4-dialkoksi-N-sübstitüe pirol türevleri piyasada bulunabilen , pahalı olmayan 2,5-dimetoksi-2,5-dihidrofuran ‘dan başlanarak sentezlendi. Yükseltgenme reaksiyonundan sonra elde edilen diol alkoksi gruplarıyla korundu ve ardından çeşitli kiral aminlerin veya aminoalkollerin kullanıldığı pirolleme tepkimesiyle ilgili kiral 3,4-dialkoksi-N-sübstitüe pirol türevleri elde edildi.

Anahtar kelimeler; kiral, polipirol, 3,4-dialkoksipirol

To My Family;

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I would like to express my sincere thanks to my supervisor Prof. Dr. Cihangir Tanyeli and my co-supervisor Prof. Dr. İdris Mecidoğlu Akhmedov for their support and guidance throughout this study and also for their concern and dealing whenever I need .

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CHAPTER 1

INTRODUCTION

1.1. Pyrroles

The observation that a component compound of coal tar and bone oil imparted a red color to pine splinters, which had been moistened with mineral acid, was noted by Runge in 1834 [1]. This compound was called as pyrrole and it was later isolated in a pure form through the distillation of bone oil [2].

The discovery that the pyrrole ring was an important part of haemin and of chlorophyll molecules [3, 4] created intense interest in the chemistry of pyrrole and its derivatives but the difficulties encountered in the isolation, identification and handling of pyrroles and its simple alkyl derivatives, limited the investigations for a long period and it was not until 1955 that the number of publications were increased relating pyrroles and its derivatives [5].

In the recent years, pyrroles are important in mainly two fields of study; in organic chemistry for the synthesis of pyrrole based biologically active products and as monomers for the synthesis of conducting poylmers.

1.2. Biological Importance of Pyrroles

Nitrogen–containing heterocycles are of substantial interest in organic chemistry as they are integral components of natural products, dyes, agrochemicals, and pharmaceuticals [6]. The pyrrole core represents one of the most important heterocycles because it is present in a wide variety of biologically active natural compounds.

One of these compunds is 5,6-dihydro-pyrrolo[2,1-*a*] isoquinoline frame work (**1**) which increasing attention has been devoted since its unique tricyclic structure has been found in several natural and biologically active compounds [7] including Crispine A (**2**) [8] Lettowianthine (**3**) [9] and Lamellarin D (**4**) [10] .

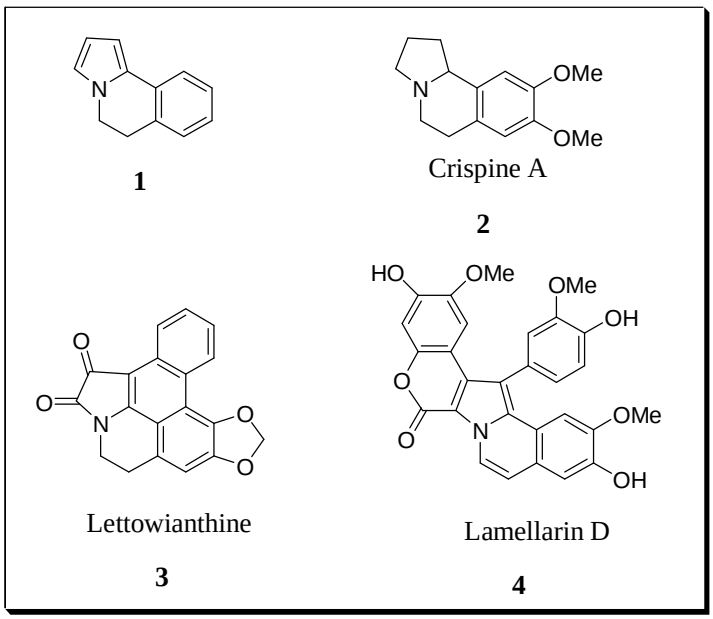

Figure 1. Some natural and biologically active compounds

Functionalized pyrroles also represent building blocks for natural tetrapyrrole pigments such as porphobilinogen and of various other natural products and their analogues.

Porphobilinogen (PBG) is the central building block for all naturally-occurring porphyrins, the chlorins and the corrin ring of vitamin B-12. In Figure 2, the structure of PBG (**5**) is presented.

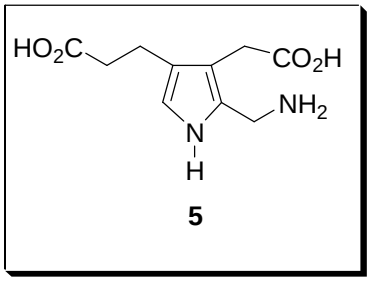

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Figure 2. Structure of porhobilinogen

A porphyrin is a heterocyclic macrocycle made from 4 pyrrole subunits linked on opposite sides (α position) through 4 methine bridges. They combine readily with metals, coordinating with them in the central cavity. Iron-, zinc-, copper-, nickel-, and cobalt-containing porphyrins are known, and many other metals can be inserted. Some iron-containing porphyrins are called hemes; and heme-containing proteins are found extensively in biochemistry, e.g., hemoglobin which have a great importance in human life. Also, since natural porphyrins sensitize cells to light, they are finding use in the emerging technique of photodynamic therapy (PDT), wherein photosensitizers that accumulate in tumorous growths can be used to eradicate cancer cells.

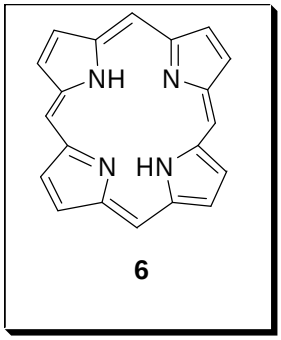

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Figure 3. Structure of porphyrin

B-12 vitamin is the most chemically complex of all the vitamins. Its structure is based on a corrin ring, which, although similar to the porphyrin ring but with one of the bridging methylene groups removed. The ring consists of 4 pyrrole subunits, joined on opposite sides by a C-CH_3 methylene link, on one side by a C-H methylene link, and with the two of the pyrroles joined directly. The nitrogen of each pyrolle is coordinated to the central cobalt atom. The structure of B-12 is shown in Figure 4 .

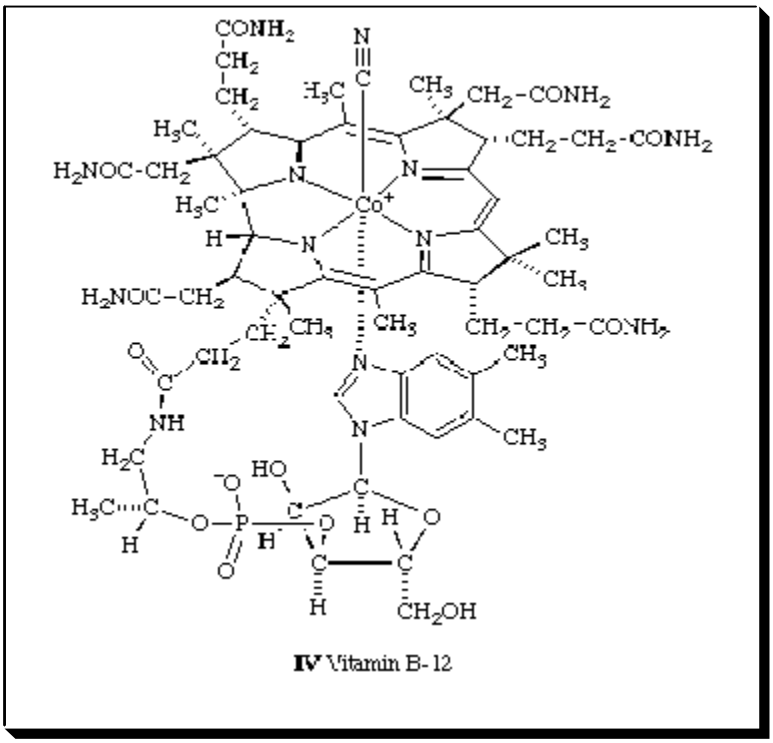

Figure 4. Structure of B-12 vitamin

1.3. 3,4-Dialkoxypyrroles

Heterocycle-based conjugated polymers, such as polypyrroles, have received significant attention due to their wide range of electrical, electrochemical and optical properties they display [11]. The heteroatom, nitrogen, within the ring has a great importance in controlling the properties of the polymers since they have intrinsic electron-donating or electron-withdrawing capabilities along with other properties which include polarizibility and hydrogen bonding [12]. These π-conjugated polymers have been found to be useful in many applications including semiconductors for field-effect transistors [13, 14] and LEDs [13,15], conductors for electrostatic charge dissipation and EMI shielding, and redox

active materials for energy storage (batteries and supercapacitors) and electrochemical devices [16].

Polypyrroles display a good conductivity in combination with high stability in its oxidized form but suffer from the occurance of undesired α-β and β-β couplings during polymerization, which deteriorate its properties [17]. In order to prevent this problem, several 3,4-disubstituted pyrroles as monomers have been synthesized and the properties of the polymers prepared from these monomers have been investigated over the past years [18,19].

One of these studies was reported by Merz and his co-workers in 1992 which includes the preparation of 3,4-dimethoxypyrrole (DMP) [18]. In addition to synthesis of the monomer, its potentiometric polymerisation was demonstrated and at the end of the experiments, it was concluded that poly(DMP) has a conductivity equal or higher than standard polypyrroles.

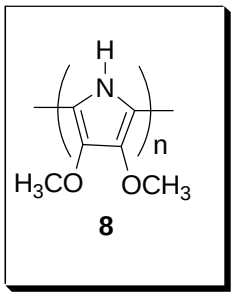

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Figure 5. Representation of poly 3,4-dimethoxypyrrole

The origin of this high conductivity is supposed to result from an enhanced chain-to-chain mobility of the charge carriers due to the substituent effect of

the methoxy groups [20]. In other words, with two methoxy groups in the 3rd- and 4th- positions of the pyrrole ring, the electron capacity is incrased which results in much more easily oxidation of DMP.

After this important results, Merz and his co-workers also studied on the investigation of the physical properties of conducting poly(3,4-dimethoxypyrrole) films in terms of thermal, mechanical and electrical conduction behaviours by uniaxial continous deformation, thermoelectric and dynamic mechanical measurements [21].

In a study which was reported by Zotti et al. in 2000 [22] electrochemically prepared poly(3,4-dimethoxypyrrole) was characterized by cyclic voltammetry, ultraviolet-visible and Fourier transform infrared spectroscopy. In the end of the investigation, it was observed that blocking the 3rd and 4th positions of the pyrrole ring allows the display of a complete potential window of conductivity during the oxidative doping process. Also it was concluded that the combination of redox-type conduction and solvation in poly(3,4-dimethoxypyrrole) gives this material unusual solvatoconductive properties. This result gave more insight into the structure-property relationship of 3,4-dimethoxy polypyrroles as well as into the mechanism of conduction within this polymers in the field of conducting polymers.

From the studies reported up to now, it can be said that 3,4-dimethoxy pyrroles play a great role in conducting polymers since the polymers prepared from these monomers allow the investigation of conductivity in a wide potential range extended both into the cathodic limit, due to the electron donor properties of the alkoxy moieties and into the anodic limit, due to protection against overoxidation along the 3rd and 4th positions. Also, the presence of alkoxy groups allows coplanarization of the rings [22].

3,4-alkylenedioxypyrroles (compound **9**, in Figure **6**) are also valuable monomers for the preparation of conducting polymers [23]. As in the case of 3,4-dialkoxypyrroles, the presence of alkylenedioxy bridge across the 3- and 4-positions of pyrroles provides decreasing of polymer oxidation potential since it adds electron density into the aromatic ring resulting in ease of oxidative polymerization and the formation of highly stable conducting polymers [24].

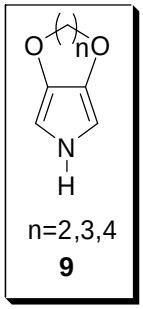


Figure 6. Representation of 3,4-alkylenedioxypyrroles

Merz and his co-workers reported a study in 1995 [25] for the synthesis of 3,4-ethylenedioxypyrrole and on the basis of this reported synthesis Reynolds prepared a small set of 3,4-alkylenedioxypyrroles [26, 27]. They investigated the properties of the resultant polymers as potential electrochromic and biostable materials.

Similarly, Groenendaal et al. [28] studied the cyclic voltammetric switching of poly 3,4-ethylenedioxypyrrole and confirmed its extremely low oxidation potential. All these results demonstrated that poly 3,4-alkylenedioxypyrroles

show unique electrochromic color changes along with potentially useful conductivity and stability properties.

Encouraged by these results, Reynolds et al. expended their studies on the synthesis of 3,4-alkylenedioxypyrroles and their subsequent functionalization [29, 30]. In the end of the experiments, they demonstrated that the derivatives prepared can serve as building blocks since they provide an immense flexibility for the synthesis of an entirely new family of electron rich monomers which can be used in preparation of conducting polymers.

1.4. Chiral Polypyrrole Polymers

Recently, pyrrole derivatives have attracted the attention focusing on the preparation of modified electrodes [31]. Among the many types of modified electrodes that have been prepared, chiral electrodes capable of performing stereoselective analyses and electrosyntheses appear to be an interesting prospect [32]. The use of electrogenerated conducting polymers like polypyrrole derivatives offers many advantages for the preparation of modified electrodes. Their electrochemical production leads to direct precipitation on the electrode surface and their high conductivity admits a fast and efficient charge transfer as well as the preparation of electrodes with a maximum density of chiral centers.

The studies started with the search for new appropriate monomers for the preparation of modified electrodes. Among the pyrrole compounds, N- or 3-substituted derivatives proved to be the most proper ones for this purpose [31]. In this manner, in 1997, Pleus and Schwientek reported the electrochemical polymerization of chiral pyrrole monomers containing (-)-ethyl L-lactate as the chiral functional group either at N- or 3-position of pyrrole [33]. They also

investigated the enantioselective properties of the modified electrode surfaces obtained upon their electropolymerization. The monomer units compound **10**, **11**, **12** and **13** that were synthesized are shown in Figure **7**.

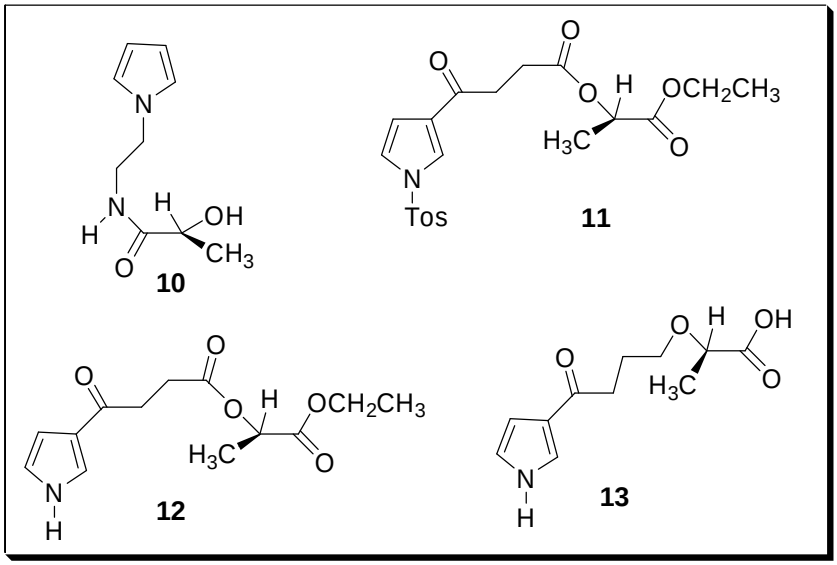


Figure 7. Structures of chiral pyrrole monomers

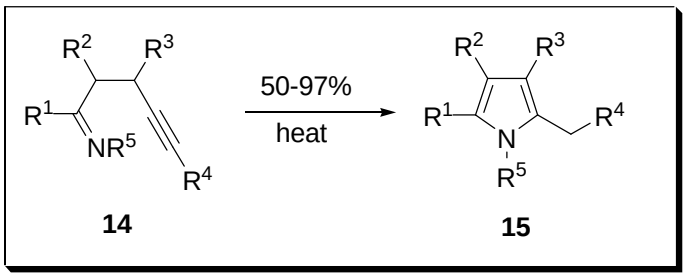
One year later, Pleus and Schwientek extended their study and reported the preparation of chiral conducting polymer films based on optically active monomers compound **10**, **11**, **12** and **13** via electropolymerization using different electrolytes [31]. At the end of the experiments, it was concluded that the coated electrodes exhibit high redox reversibility and long-term stability and can be used over a wide potential range. Also, it is mentioned that their stereoselective recognition properties are important for the future development of the electrodes as materials for performing enantioselective electrosynthesis.

It is a fact that the studies for the preparation of pyrrole based monomers which can be used for the synthesis of conducting chiral polymers are of great interest due to their potential applications as electrodes for electrochemical asymmetric synthesis and stereoselecive analyses [33, 34].

1.5. Synthesis of N-substituted Pyrrole Derivatives

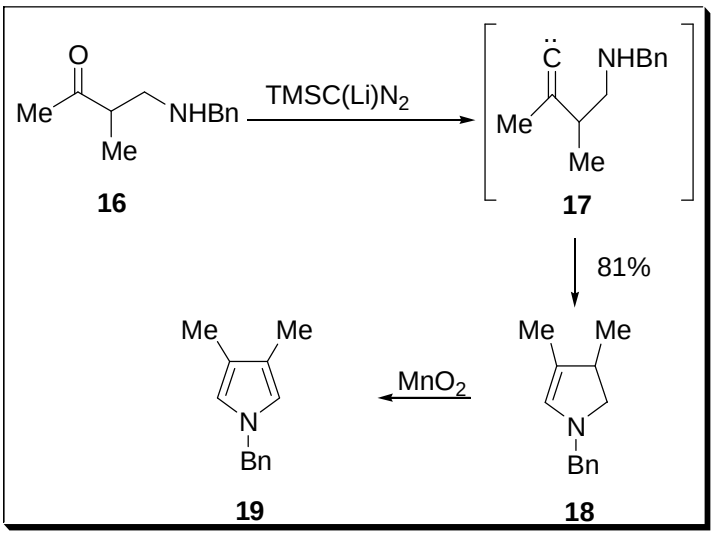
N-substituted pyrroles are important intermediates in the formation of modified polypyrrole polymers [35] which have found uses in the fields of battery, sensor, membrane, display and molecular electronics technologies [36]. Therefore, many methods for the synthesis of substituted pyrroles have been described in the literature [37].

Recently, some reactions that were previously used to synthesize furans have been successfully adapted to the preparation of pyrroles. Thus, the imines compound **14** ,which are formed from the corresponding ketones and primary amines, spontaneously cyclise to pyrroles [38].



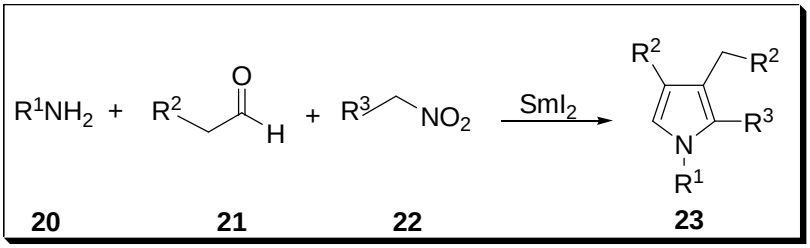
Scheme 1. Synthesis of compound **15**

Another cyclisation reaction is shown in Scheme **2** [39]. Trimethylsilyldiazomethyllithium is used to generate a vinylidene carbene compound **17** from which the five membered ring is generated by intramolecular N-H insertion.



Scheme 2. Synthesis of compound **19**

In the literature, there are also three-component pyrrole syntheses one of which is illustrated in Scheme **3** [40].



Scheme 3. Synthesis of compound **23**

The samarium(II) iodide catalysed condensation of alkylamines, aldehydes and nitroalkanes gave 1,2,3,4-tetrasubstituted pyrroles in moderate to good yields.

1.6. Aim of the Study

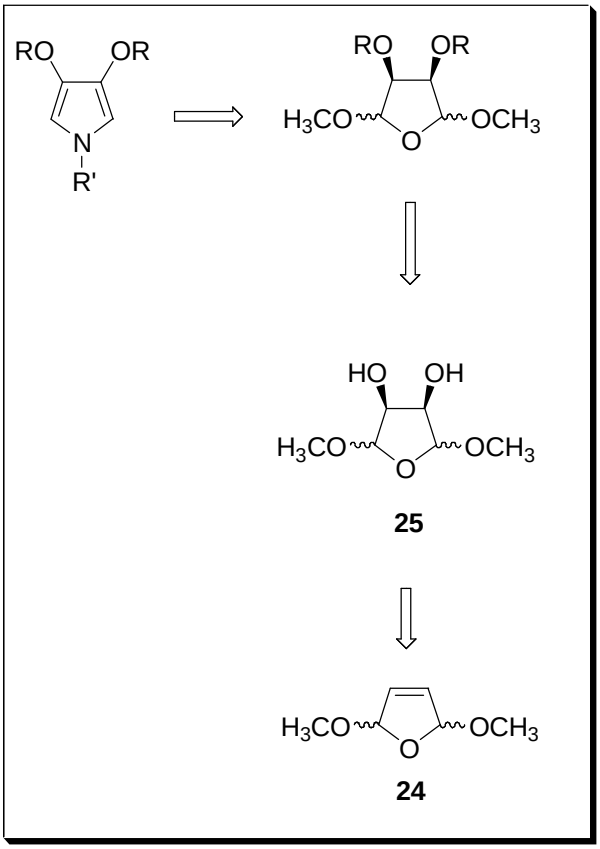
Pyrroles play a great role in the class of substances which have wide usage area; either as starting materials for many biologically active natural compounds or as monomers for the preparation of conducting polymers.

Recently, 3,4-dialkoxy pyrroles have received great attention in the field of conducting polymers since the presence of alkoxy substituents in 3^{rd} and 4^{th} positions increase the electron capacity of the ring which results in much more easily oxidation of the pyrrole. Also it prevents the occurance of undesired α-β and β-β couplings during polymerization, which deteriorate its properties.

Chiral polypyrroles are important for the preparation of chiral modified electrodes. They are capable of performing stereoselective analyses and electrosyntheses which appears to be an interesting prospect.

In this study our aim is to synthesize chiral N-substituted-3,4-dialkoxypyrrole derivatives which are new in the literature to enable their application not only in the preparation of conducting polymers as valuable monomers but also in electrochemical asymmetric synthesis and stereoselective analyses owing to presence of chirality.

The aim of the work is shown retrosynthetically in Scheme **4**.



Scheme 4. Retrosynthesis of the Work

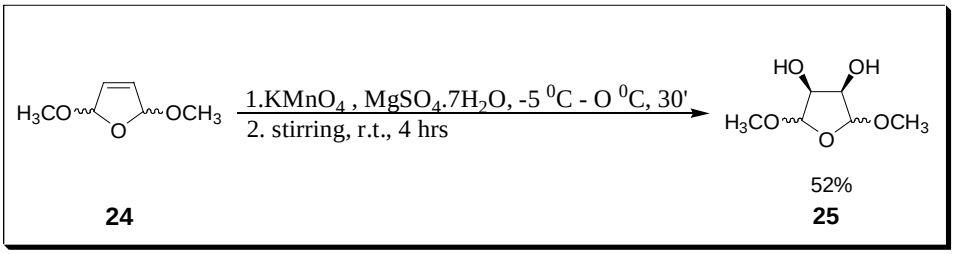
As shown in the Scheme 4, 2,5-dimethoxy-2,5-dihydrofuran was chosen as the starting material which is an inexpensive, commercially available material. After oxidation, protection of the resultant diol was performed by using corresponding dialkylsulfate and in the last step, chiral N-substituted 3,4-dialkoxypyrrole derivatives were afforded via pyrrolization reaction by using several chiral amines or aminoalcohols.

CHAPTER 2

RESULTS and DISCUSSION

2.1. Synthesis of 2,5-dimethoxy-tetrahydrofuran-3,4-diol

For the synthesis of 2,5-dimethoxy-tetrahydrofuran-3,4-diol, the procedure which was described by Villacampa et al. in 1992 [41] was applied. The oxidation of 2,5-dimethoxy-2,5-dihydrofuran, which is protected form of malealdehyde, with potassium permanganate and heptahydrated magnesium sulfate afforded compound **25** with a yield of 52% as a pure, pale yellow oil.



Scheme 5. Synthesis of 2,5-dimethoxy-tetrahydrofuran-3,4-diol, **25**

Since compound **25** is a mixture of diastreoisomers as shown in the Figure **8**, there are 3 singlet peaks correponding to methoxy protons in the spectrum.

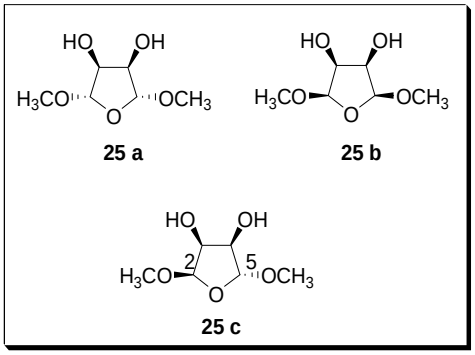
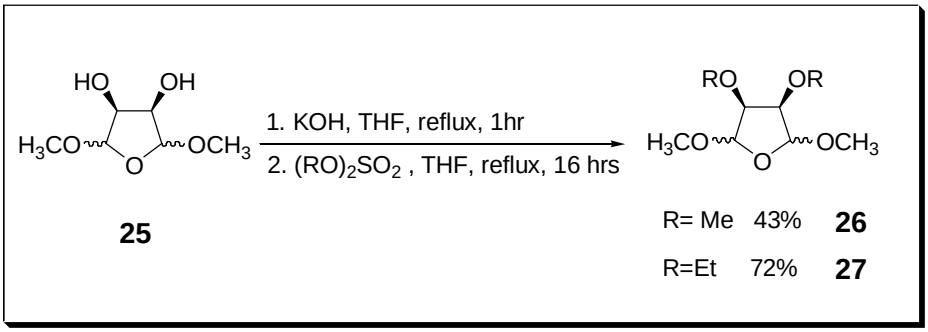


Figure 8. Diastereomeric Mixtures of compound **25**

In the ^{1}H-NMR spectrum, methoxy protons for compound **25a** and **25b** give a singlet at 3.42 ppm. However, methoxy protons for compound **25c** give two singlet peaks at different ppm values. Methoxy protons attached to C-5 give a singlet at 3.49 ppm while the methoxy protons attached to C-2 give a singlet at 3.39 ppm. This difference also observed in the ^{13}C-NMR spectrum. The other signals in ^{1}H and ^{13}C NMR spectra of the compound **25** are in accordance with the data given in the literature [41].

2.2. Synthesis of 3,4-dialkoxy-2,5-dimethoxy-tetrahydrofuran

Both 2,3,4,5-tetramethoxy-tetrahydrofuran and 3,4-diethoxy-2,5-dimethoxy-tetrahydrofuran were synthesized by following the procedure in a study which was reported by Merz and Meyer in 1999 [42]. In the synthesis, after refluxing compound **25** with KOH for one hour, corresponding dialkylsulfate was added. At the end of the workup and chromatography, compound **26** was obtained in 43% while compound **27** was obtained in 72% yield.



Scheme 6. Synthesis of compound **26** and **27**

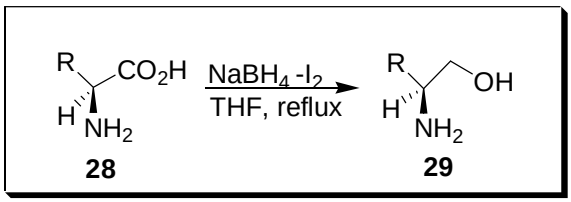
In the ^{1}H-NMR spectrum of the 2,3,4,5-tetramethoxy-tetrahydrofuran, four methoxy group protons exhibit as a doublet of doublet at 3.44 ppm (J= 2.5, 13.7 Hz) when methoxy groups give a singlet at 3.43 ppm in the ^{1}H-NMR spectra of the 3,4-diethoxy-2,5-dimethoxy-tetrahydrofuran.

In the ^{13}C-NMR spectrum of compound **26** , there are two signals for methoxy carbons, one for the methoxy carbons next to C-2 and C-5 at 55.6 ppm, and the other for the methoxy carbons next to the C-3 and C-4 at 58.5 ppm. In the ^{13}C-NMR spectrum of compound **27**, there is one signal at 55.6 ppm for the presence of methoxy carbons.

The other signals in ^{1}H and ^{13}C-NMR spectra of the compound **26** and **27** are in the range expected for the proposed structure.

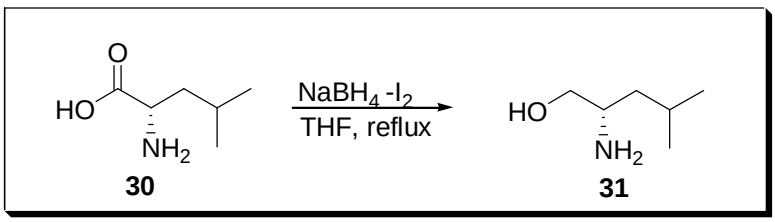
2.3. Synthesis of L-Leucinol

In the study reported by Meyers and Drauz in 1993 [43] several amino acids with sodium borohydride-iodine in THF afforded the corresponding amino alcohols as crude products.



Scheme 7. Reduction synthesis of aminoacids

For the synthesis of L-Leucinol, the same procedure in the study was applied and the target compound **31** was obtained with a yield of 97% as a crude product.

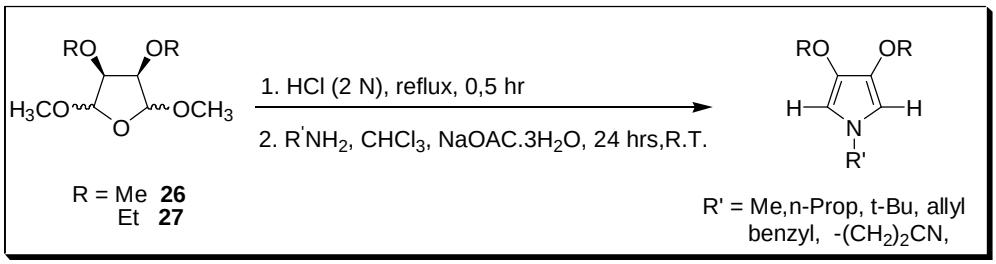


Scheme 8. Synthesis of L-Leucinol, **31**

The product was identified by using ^{1}H and ^{13}C-NMR spectroscopy. Presence of new methylene protons in ^{1}H-NMR spectra and disappearance of the carbonyl carbon in the ^{13}C-NMR spectra were observed which confirm the structure of L-Leucinol. Also, the other signals in both spectras are in the expected range and in accordance with the proposed structure.

2.4. Synthesis of Chiral N-substituted-3,4-Dialkoxypyrrole Derivatives

In the study of Merz and Meyer in 1999 [42], N-substituted 3,4-dialkoxypyrroles were prepared in good yields by using different primary amines. In the preparation firstly 3,4-dialkoxy-2,5-dimethoxy-tetrahydrofuran is hydrolyzed with HCl. Then with the addition of $NaOAc.3H_2O$ and hydrochloride of the corresponding primary amine, the target N-substituted pyrrole is obtained.

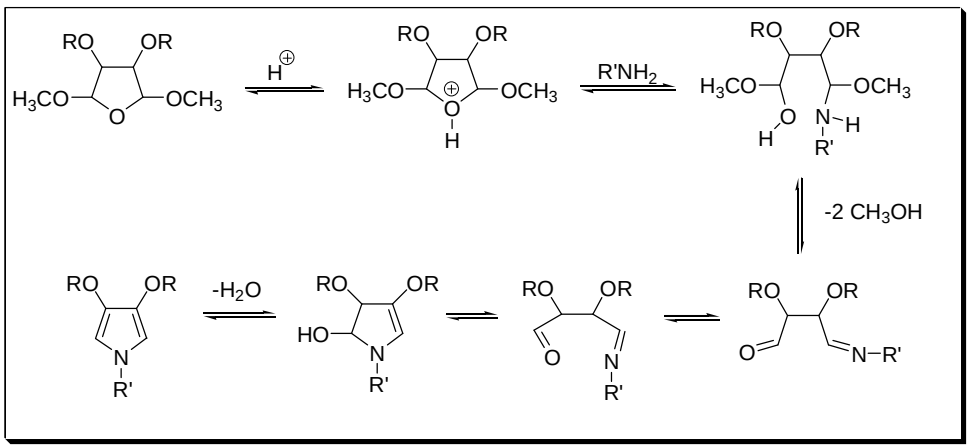


Scheme 9. Synthesis of N-substituted-3,4-Dialkoxypyrrole Derivatives

Concerning the high yield, it is tried to extend this chemistry, by searching whether it is possible to obtain chiral N-substituted-3,4-dialkoxypyrrole derivatives by using the same procedure. For this purpose 2,3,4,5-tetramethoxy-tetrahydrofuran was chosen as the starting material and 3,4-dimethoxy-1-(1-

phenylethyl)-1*H*-pyrrole was the target compound that was planned to be afforded. Unfortunately, production of 3,4-dimethoxy-1-(1-phenylethyl)-1*H*-pyrrole could be achieved only with a very low yield when the same procedure applied. Then, it is decided to modify this procedure and to prepare the target compound by stirring the mixture at reflux instead of room temperature for 24 hours after the hydrolysis of 2,3,4,5-tetramethoxy-tetrahydrofuran. In the first attempt, 3,4-dimethoxy-1-(1-pnenylethyl)-1*H*-pyrrole was successfully performed with a yield of 78% and the same procedure was applied for the synthesis of other chiral N-substituted-3,4-dialkoxypyrrole derivatives.

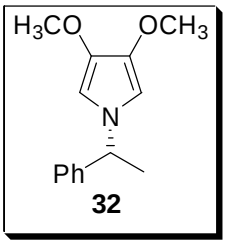
The mechanism which is proposed for the synthesis of N-substituted-3,4-dialkoxypyrrole derivatives is presented in Scheme **10** [44]



Scheme 10. Mechanism for the synthesis of N-substituted 3,4-dialkoxypyrrole

2.4.1. Synthesis of (*R*)-3,4-dimethoxy-1-(1-phenylethyl)-1*H*-pyrrole

Our improved procedure was applied for the synthesis of compound **32**. *R* (+)-α-methylbenzyl amine and 2,3,4,5-tetramethoxy- tetrahydrofuran were chosen as the starting materials and the target compound was afforded with a yield of 78%



32

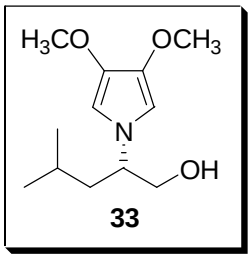
Figure 9

For the characterization of compound **32**, ^{1}H and ^{13}C-NMR spectroscopy were used. Characteristic pyrrole protons appear as a singlet at 6.18 ppm while the other signals were observed in the expected range in the ^{1}H-NMR spectrum. Also the carbon signals are in accordance with the proposed structure in addition to characteristic pyrrole carbons which give signals at 137.5 and 101.3 ppm.

2.4.2. Synthesis of (*S*)-2-(3,4-dimethoxy-1*H*-pyrrol-1-yl)-methylpentan-1-ol

The target compound **33** was prepared by the reaction of 2,3,4,5-tetramethoxy-tetrahydrofuran with L-Leucinol which has already given the synthesis from L-

Leucine. In the reaction, aminoalcohol was the source of chirality to synthesize chiral product which was obtained as a colorless oil in 52% yield.



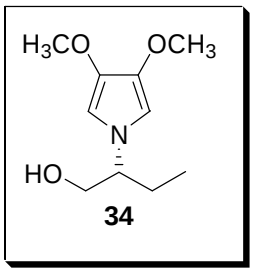
33

Figure 10

In the ^{1}H-NMR spectrum of (S)-2-(3,4-dimethoxy-1*H*-pyrrol-1-yl)-methylpentan-1-ol, characteristic pyrrole protons exhibit as a singlet at 6.16 ppm while the pyrrole ring carbons give signals at 137.4 and 100.9 ppm in ^{13}C-NMR spectrum. Also, it should be mentioned that methyl protons in the structure were observed as a quartet in both ^{1}H–NMR spectra of L-Leucinol and (S)-2-(3,4-dimethoxy-1*H*-pyrrol-1-yl)-methylpentan-1-ol which is possible due to presence of stereogenic center.

2.4.3. Synthesis of (*R*)-2-(3,4-dimethoxy-1*H*-pyrrol-1-yl)butan-1-ol

2,3,4,5-Tetramethoxy-tetrahydrofuran and (*R*)-(-)-2-Amino-1-butanol were the starting materials for the preparation of the compound **34**. After workup and chromatography, (*R*)-2-(3,4-dimethoxy-1*H*-pyrrol-1-yl)butan-1-ol was obtained with a yield of 57%.



34

Figure 11

In ^{1}H and ^{13}C-NMR spectra of (*R*)-2-(3,4-dimethoxy-1*H*-pyrrol-1-yl)butan-1-ol, characteristic pyrrole ring protons and carbons were observed in the range which confirm the proposed structure.

2.4.4. Synthesis of (*R*)-3,4-diethoxy-1-(1-phenylethyl)-1*H*-pyrrole

In the literature, it is known that different alkoxy groups in the pyrrole ring have different effects in the synthesis of polypyrrole conducting polymers. In this manner, synthesized 3,4-diethoxy-2,5-dimethoxy-tetrahdrofuran was used as starting compound with different amine or aminoalcohols to get chiral N-substituted-3,4-diethoxy-pyrrole derivatives.

As in the case of (*R*)-3,4-dimethoxy-1-(1-phenylethyl)-1*H*-pyrrole, *R*(+)-α-methylbenzyl amine was used as the source of chirality. Our improved procedure was applied and the target compound **35** was obtained with 67% yield.

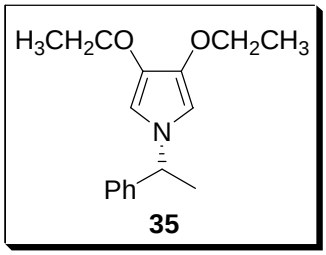


Figure 12

The characterization of compound **35** was identified with ^{1}H and ^{13}C-NMR spectroscopy. The signals in both ^{1}H and ^{13}C-NMR spectra confirm the structure of (R)-3,4-diethoxy-1-(1-pnenylethyl)-1*H*-pyrrole which are in the expected range.

2.4.5. Synthesis of (*R*)-2-(3,4-diethoxy-1*H*-pyrrol-1-yl)butan-1-ol

The target compound **36** was obtained by the reaction of 3,4-diethoxy-2,5-dimethoxy tetrahydrofuran with (*R*)-(-)-2-Amino-1-butanol with a yield of 58% yield

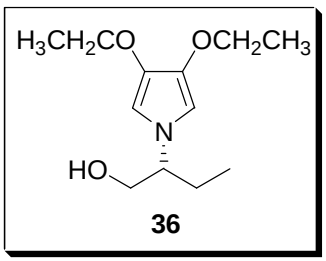
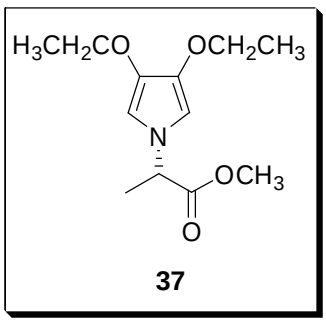


Figure 13

In the ^{1}H-NMR spectrum of 2-(3,4-diethoxy-1-*H*-pyrrol-1-yl)butan-1-ol, characteristic pyrrole ring protons show a singlet at 6.15 ppm while the other protons were observed in the expected range. In the ^{13}C-NMR spectrum, pyrrole ring carbons give signals at 136.4 and 101.6 ppm in addition to other carbon signals which are in accordance with the proposed structure.

2.4.6. Synthesis of (*S*)-methyl-2-(3,4-diethoxy-1*H*-pyrrol-1-yl)propanoate

In order to check the validity of our improved procedure for the synthesis of chiral N-substituted-3,4-dialkoxy-pyrroles by using HCl salt of aminoacid ester derivatives, hydrochloride salt of L-Alanine methyl ester was chosen as the starting material which is a commercially available material. In the end of the workup and chromatography, compound **37** was obtained in 54% yield.



37

Figure 14

In ^{1}H-NMR spectrum of (*S*)-methyl-2-(3,4-diethoxy-1*H*-pyrrol-1-yl)propanoate, characteristic pyrrole ring protons are observed at 6.09 ppm as a singlet. The other protons are in accordance with the proposed structure. In ^{13}C-NMR spectrum, in addition to pyrrole ring carbons at 137.1 and 102.2 ppm, the

presence of signal at 171.9 ppm which corresponds to carbonyl carbon confirms the proposed structure of compound **37**.

2.4.7. Synthesis of (*R*)-1-(3,4-diethoxy-1*H*-pyrrol-1-yl)propan-2-ol, (*R*)-2-(3,4-diethoxy-1*H*-pyrrol-1-yl)propan-1-ol and (*R*)-2-(3,4diethoxy-1*H*-pyrrol-1-yl)-3-phenylpropan-1-ol

Corresponding aminoalcohols; (*R*)-(-)-1-Amino-2-propanol, (*R*)-(-)-2-Amino-1-propanol and (*R*)(+)-2-Amino-3-phenyl-1-propanol were used for the synthesis of compound **38**, compound **39** and compound **40**, respectively, by applying the same procedure.

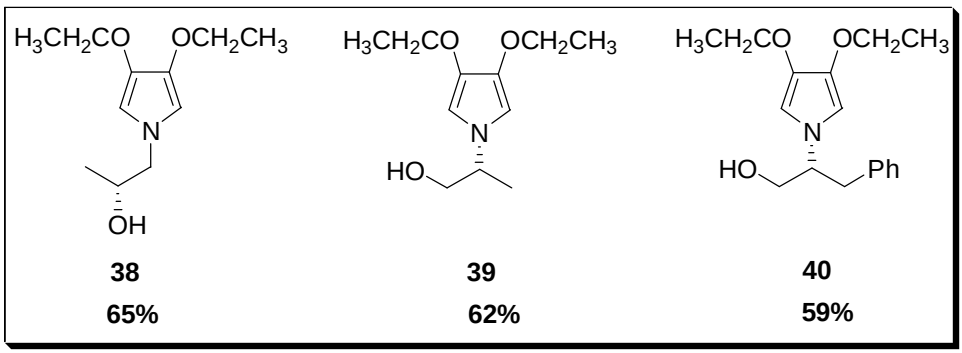


Figure 15

Compounds **38**, **39** and **40** were identified by ^{1}H and ^{13}C-NMR spectroscopy. In the ^{1}H-NMR spectrum, characteristic pyrrole ring protons of compound **38** exhibit as a singlet at 6.06 ppm. In the case of compound **39**, pyrrole ring protons give a singlet at 6.18 ppm while the ones of compound **40** show a singlet at 6.04 ppm. The other protons are observed in the expected range which

confirm the structures of compounds and also carbon signals are in accordance with the proposed structures of compounds **38**, **39** and **40.**

The structures of synthesized chiral N-substituted-3,4-dialkoxy-pyrrole derivatives are shown in Table 1 and Table 2 with their compound's number, yield and $[\alpha]_D^{20}$ values.

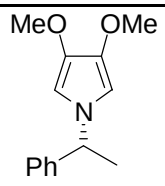
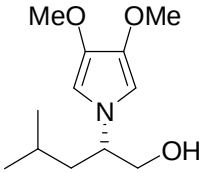
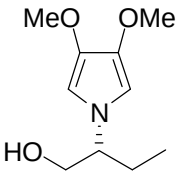
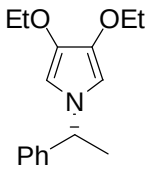
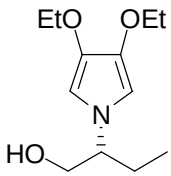
compound	compound number	yield	alpha
	**32**	78%	-24.97
	**33**	52%	-11.98
	**34**	57%	+14.67
	**35**	67%	-21.80
	**36**	58%	+10.54

Table 1

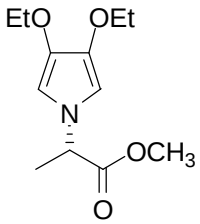
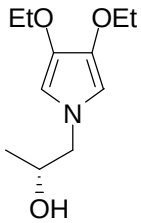
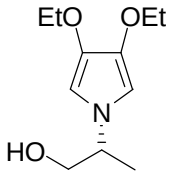
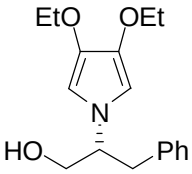
compound	compound number	yield	alpha
	**37**	54%	-25.20
	**38**	65%	23.56
	**39**	62%	6.46
	**40**	59%	+46.57

Table 2

2.5. Cyclic Voltammetry Study of (*R*)-3,4-Dimethoxy-1-(1-phenylethyl)-1*H*-pyrrole

Studies for the preparation of chiral conducting polymers has not been completed yet. But the preliminary studies implied the possible use of these synthesized pyrrole derivatives as valuable monomers for the synthesis of conducting polymers which can have wide range of applictions due to their electrical, electrochemical and optical properties.

The representative CV of (*R*)-3,4-dimethoxy-1-(1-phenylethyl)- 1*H*-pyrrole is shown in Figure **16**.

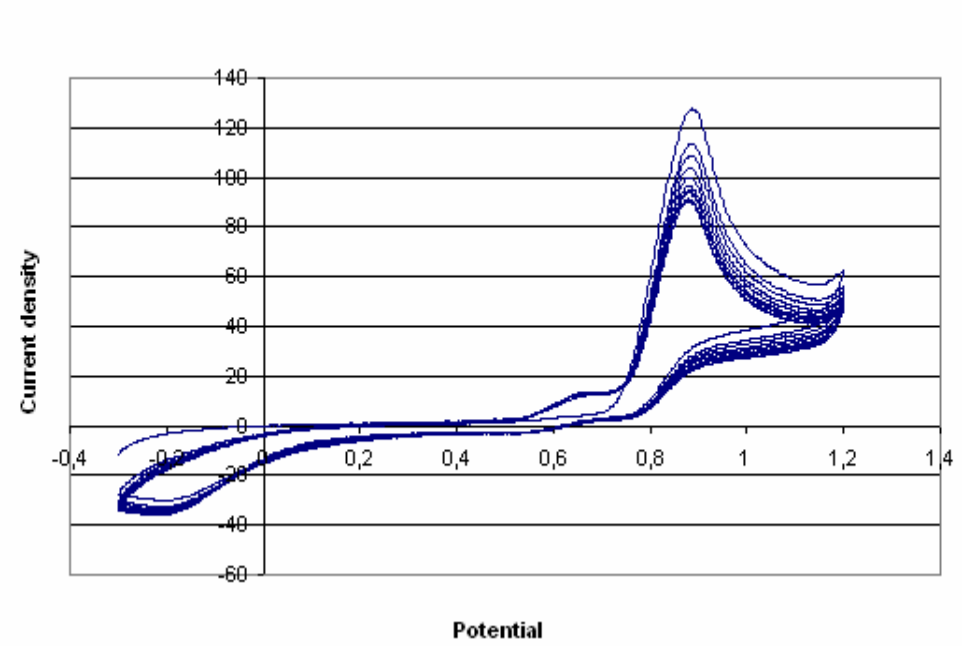


Figure 16

CV of (*R*)-3,4-dimethoxy-1-(1-phenylethyl)- 1*H*-pyrrole was taken in acetonitrile as solvent and tetrabutylammoniumtetrafluoroborate was used as supporting electrode.

CHAPTER 3

EXPERIMENTAL

In this study structure characterizations of the compounds were done with the instruments as written.

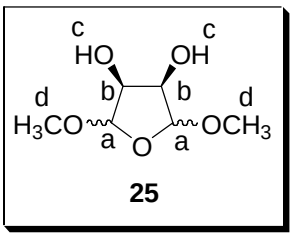
^{1}H-NMR and ^{13}C-NMR spectra were recorded in $CDCl_3$ on Bruker Spectrospin Avance DPX 400 spectrometer. Chemical shifts are given in ppm from tetramethylsilane. Spin multiplicities are mentioned as: s (singlet), br s (broad singlet), d (doublet), dd (doublet of doublet), dt (doublet of triplet), t (triplet), p (pentet), sxt (sextet), m (multiplet).

Flash column chromatography was performed by using thick-walled glass columns with a flash grade (Merck Silica Gel 60).Reactions were monitored by thin layer chromatography using precoated silica gel plates (Merck Silica Gel PF-254), visualized by UV-light and polymolybden phosphoric acid, in ethanol as appropriate.

All extracts were dried over anhydrous magnesium sulphate and solutions were concentrated under vacuum by using rotary evaporator.

3.1 Synthesis of 2,5-dimethoxy-tetrahydrofuran-3,4-diol (25)

A solution of 2,5-dimethoxy-2,5-dihydrofuran (10 g, 0.077 mol) (cis-trans mixture) in ethanol (77 mL) was placed in a 500 mL round bottomed flask equipped with a mechanical stirrer, an additional funnel and a thermometer. The reaction was cooled to -5 ^{o}C and a solution of potassium permanganate (12.14 g, 0.077 mol) and heptahydrated magnesium sulfate (17.29 g, 0.070 mol) in water (197 mL) was added over 30 minutes with simultaneous addition of crushed ice in order to maintain an internal temperature of -5 ^{o}C to 0 ^{o}C. The suspension was stirred at room temperature for 4 hours, left standing overnight and filtered through a layer of silica gel. The filtrate was evaporated to 15 mL and extracted with 1-butanol (5 x 15 mL). The extracts were dried over anhydrous sodium sulfate and evaporated, to yield the desired compound, as a mixture of cis-trans streoisomers, pale yellow oil. (5.76 g, 52%) [41].



25

Figure 17

^{1}H-NMR ($CDCl_3$)

δ (ppm): 4.94 (s, 2H, H_a), 4.16 (s, 2H, H_b), 3.92 (bs, 2H, H_c), 3.49 (s, 3H, H_d), 3.42 (s, 6H, H_d), 3.39 (s, 3H, H_d)

^{13}C-NMR ($CDCl_3$)

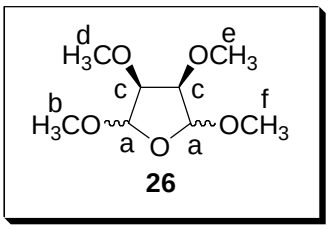
δ (ppm): 109.6, 108.1, 102.6, 75.3, 73.8, 70.6, 56.5, 55.6, 55.5

3.2. General Procedure for the Synthesis of 3,4-dialkoxy-2,5-dimethoxy-tetrahydrofuran

A stirred mixture of -2,5-dimethoxy-tetrahydrofuran-3,4-diol (6.09 mmol) and powdered KOH (0.038 mol) in dry THF (12 mL) was heated at reflux for one hour. Within 3 hours, a solution of the corresponding dialkylsulfate (18.27 mmol) in dry THF (7 mL) was added. Stirring and heating were continued for 16 h and water (5 mL) was added. After 1 h, the mixture was diluted with water (28 mL) and extracted with diethylether (15 mL) and CH_2Cl_2 (3 x 10 mL). By drying over $MgSO_4$, filtering, evaporating *in vacuo*, and purifying with flash chromatography , using 1:2 EtOAc: hexane as eluent, (3S,4R)-3,4-dialkoxy-2,5-dimethoxy-tetrahydrofuran were obtained.

3.2.1. 2,3,4,5-Tetramethoxy-tetrahydrofuran (26):

Colorless oil; 43 % yield , compound **26**



26

Figure 18

^{1}H-NMR ($CDCl_3$)

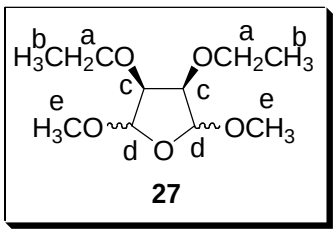
δ (ppm): 4.98 (bs, 2H, H_a), 3.82 (bs, 2H, H_c), 3.46 (s, 3H, H_b or H_f), 3.43 (s, 3H, H_b or H_f), 3.43 (s, 3H, H_d or H_e), 3.42 (s, 3H, H_d or H_e)

^{13}C-NMR ($CDCl_3$)

δ (ppm): 106.9, 83.3, 58.5, 55.6

3.2.2. 3,4-Diethoxy-2,5-dimethoxy-tetrahydrofuran (27):

Colorless oil; 72% yield, compound **27**



27

Figure 19

^{1}H-NMR ($CDCl_3$)

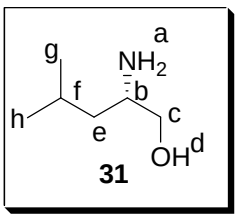
δ (ppm): 4.98 (bs, 2H, H_d), 3.90 (bs, 2H, H_c), 3.65-3.56 (m, 4H, H_a), 3.43 (s, 6H, H_e), 1.24 (t, J=7.0 Hz, 6H, H_b)

^{13}C-NMR ($CDCl_3$)

δ (ppm): 107.7, 81.8, 66.3, 55.6, 15.3

3.3. Synthesis of L-Leucinol (31):

To the solution of sodium borohydride (0.692 gr, 18.32 mmol) and anhydrous THF (20 mL), L-Leucine (1 gr, 7.63 mmol) was added in one portion and the mixture was cooled to 0 ^{0}C in an ice bath under argon atmosphere. After dissolving I_2 (1.936 gr, 7.63 mmol) in anhydrous THF (5 mL), the solution was added slowly and dropwise to the mixture over 30 minutes resulting in vigorous evolution of hydrogen. When the gas evolution ceased, the mixture was heated at reflux for 18 hours and then cooled to room temperature. Methanol (70 mL) was added cautiously until the mixture was became clear. After stirring 30 min., the solvent was removed by rotary evaporation leaving a white paste which was dissolved by addition of 20 % KOH (15 mL). The solution was stirred for 4 hours and extracted with CH_2Cl_2 (3 x 10 mL). The combined extracts were dried over sodium sulfate and concentrated *in vacuo* to get L-Leucinol. Clear oil, (0.869 gr, 97%) [42].



31

Figure 20

^{1}H-NMR ($CDCl_3$)

δ (ppm): 3.56 (dd, 1H, *J*=2.8, 10.9 Hz, H_c), 3.26 (t, 1H, *J*=9.2 Hz, H_c), 2.89 (bs, 4H, H_a, H_b, H_d), 1.70 (m, 1H, J=4.3 Hz, H_f), 1.20 (t, 2H, J=7.0 Hz, H_e), 0.93 (d, 3H, J=6.5, Hz, H_g or H_h), 0.90 (d, 3H, J=6.5 Hz, H_g or H_h)

^{13}C-NMR ($CDCl_3$)

δ (ppm): 67.1, 50.6, 43.8, 24.7, 23.3, 22.2

3.4. General Procedure for the Synthesis of chiral N-substituted 3,4-dialkoxypyrrole derivatives

3,4-dialkoxy-2,5-dimethoxy-tetrahydrofuran (1 mmol) and HCl (0.1 N, 3.5 mL) were stirred at 75 ^{o}C for half an hour. The reaction mixture was allowed to warm to room temperature before addition of $NaOAc.3H_2O$ (1 g, 7.1 mmol), amine or aminoalcohol (5 mmol) and $CHCl_3$ (15 mL). Heating and stirring were continued at reflux for 24 h. For workup; the reaction mixture was washed with $NaHCO_3$ and inorganic phase washed with $CHCl_3$ (3 x 10 mL). Then organic extracts were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The mixture was purified with flash chromatography , using EtOAc: hexane as eluent in order to get corresponding N-substituted 3,4-dialkoxy chiral pyrrole derivatives.

3.4.1. (*R*)-3,4-dimethoxy-1-(1-phenylethyl)-1*H*-pyrrole (32):

Colorless oil, (0.180 gr, 78 %), $[\alpha]_D^{20}$= -24.97 (*c* 3.5 , MeOH)

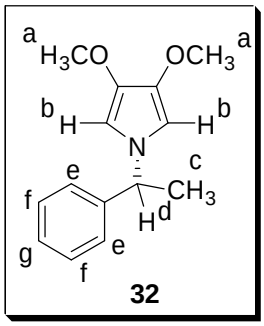


Figure 21

^{1}H-NMR ($CDCl_3$)

δ (ppm): 7.30 (t, J=7.5 Hz, 2H, H_f), 7.25 (d, J= 6.8 Hz, 1H, H_g), 7.07 (d, J=7.6 Hz, 2H, H_e), 6.18 (s, 2H, H_b), 5.02 (q, J=7.0 Hz, 1H, H_d), 3.72 (s, 6H, H_a), 1.74 (d, J=7.1 Hz, 3H, H_c)

^{13}C-NMR ($CDCl_3$)

δ (ppm): 143.8, 137.49, 128.6, 127.4, 125.8, 101.4, 58.5, 58.46, 21.6

3.4.2. (*S*)-2-(3,4-dimethoxy-1*H*-pyrrol-1-yl)-4-methylpentan-1-ol (33):

Colorless oil, (0.118 gr, 52 %), $[\alpha]_D^{20}$= -11.98 (*c* 0.53 , MeOH)

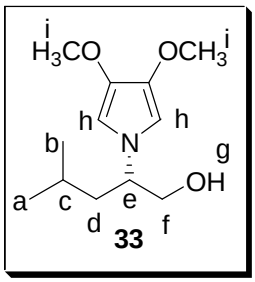


Figure 22

^{1}H-NMR ($CDCl_3$)

δ (ppm): 6.16 (s, 2H, H_h), 3.82-3.60 (m, 3H, H_e, H_f), 3.74 (s, 6H), 1.64 (m, 1H, H_c), 1.41 (m, 2H, H_d), 0.92 (d, J= 6.3, Hz, 3H, H_b or H_a), 0.88 (d, J=6.4 Hz, 3H, H_b or H_a)

^{13}C-NMR ($CDCl_3$)

δ (ppm): 137.4, 100.9, 66.6, 60.9, 58.5, 40.1, 24.6, 23.1, 22.0

3.4.3. (*R*)-2-(3,4-dimethoxy-1*H*-pyrrol-1-yl)butan-1-ol (34):

Colorless oil, (0.113 gr, 57%), $[\alpha]_D^{20}$= +14.67 (*c* 1.52 , MeOH)

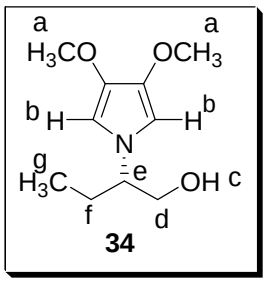


Figure 23

^{1}H-NMR ($CDCl_3$)

δ (ppm): 6.15 (s, 2H, H_b), 3.73 (s, 6H, H_a3.71-3.64 (m, 2H, H_d), 3.60-3.56 (m, 1H, H_e), 1.65 (dq, J=7.5, 29.6 Hz, 2H, H_f), 1.48 (bs, 1H, H_c), 0.85 (t, J=7.4 Hz, 3H, H_g)

^{13}C-NMR ($CDCl_3$)

δ (ppm): 137.5, 100.7, 66.0, 64.6, 58.5, 24.5, 10.6

3.4.4. (*R*)-3,4-diethoxy-1-(1-phenylethyl)-1*H*-pyrrole (35):

Colorless oil, (0. 174gr, 67%), $[\alpha]_D^{20}$= -21.8 (*c* 3.2 , MeOH)

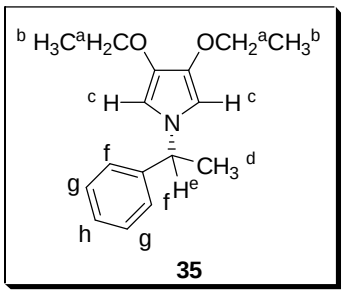


Figure 24

^{1}H-NMR ($CDCl_3$)

δ (ppm): 7.23-7.14 (m, 3 H, H_g, H_h), 6.98 (d, J= 7.3 Hz, 2H, H_f), 6.10 (s, 2H, H_c), 4.94 (q, J=7.0 Hz, 1H, H_e), 3.83 (q, J=7.0 Hz, 4H, H_a), 1.66 (d, J= 6.9 Hz, 3H, H_d), 1.29 (t, J= 7.0 Hz, 6 H, H_b)

^{13}C-NMR ($CDCl_3$)

δ (ppm): 141.3, 136.4, 128.2, 127.3, 126.0, 102.1, 66.7, 58.3, 21.6, 15.1

3.4.5. (*R*)-2-(3,4-diethoxy-1*H*-pyrrol-1-yl)butan-1-ol (36):

Colorless oil, (0.131 gr, 58 %), $[\alpha]_D^{20}$= +10.54 (*c* 1.03 ,MeOH)

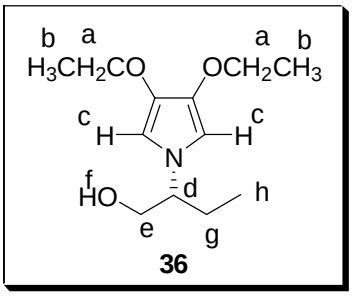


Figure 25

^{1}H-NMR ($CDCl_3$)

δ (ppm): 6.15 (s, 2H, H_c), 3.92 (q, J= 7.0 Hz, 4H, H_a), 3.68-3.63 (m, 2H, H_e), 3.61- 3.54 (m, 1H, H_d), 1.65 (dq, 2H, J=7.0, 28.4 Hz, H_g), 1.47 (bs, 1H, H_f), 1.37 (t, J=7.0 Hz, 6H, H_b), 0.85 (t, J=7.4 Hz, 3H, H_h)

^{13}C-NMR ($CDCl_3$)

δ (ppm): 136.4, 101.6, 68.1, 66.0, 64.0, 24.5, 15.3, 10.8

3.4.6. (*S*)-methyl 2-(3,4-diethoxy-1*H*-pyrrol-1-yl)propanoate (37):

Colorless oil, (0.147 gr, 61 %), $[\alpha]_D^{20}$= -25.2 (*c* 1.45 , MeOH)

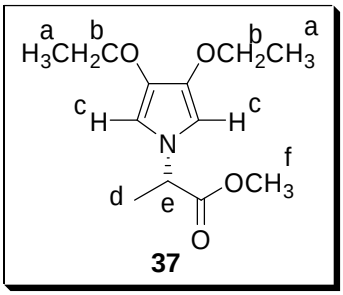


Figure 26

^{1}H-NMR ($CDCl_3$)

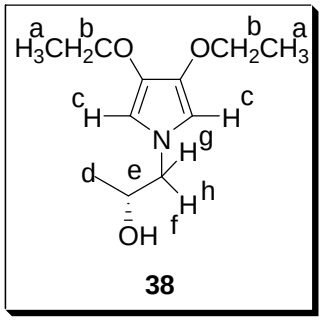
δ (ppm): 6.09 (s, 2H, H_c), 4.39 (q, J= 7.2 Hz, 1H, H_e), 3.84 (q, J= 7.0 Hz, 4H, H_b), 3.63 (s, 3H, H_f), 1.55 (d, J=7.3 Hz, 3H, H_d), 1.30 (t, J= 7.0 Hz, 6H, H_a)

^{13}C-NMR ($CDCl_3$)

δ (ppm): 171.9, 137.1, 102.2, 66.7, 57.3, 52.4, 17.6, 15.0

3.4.7. (*R*)-1-(3,4-diethoxy-*1H*-pyrrol-1-yl)propan-2-ol (38):

Colorless oil, (0.138 gr, 65 %), $[\alpha]_D^{20}$= -23.56 (*c* 1.43 , MeOH)



38

Figure 27

^{1}H-NMR ($CDCl_3$)

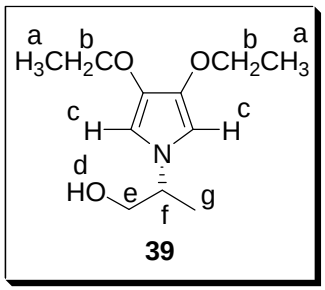
δ (ppm): 6.06 (s, 2H, H_c), 3.89-3.82 (m, 5H, H_b, H_e), 3.62 (dd, A part of AB system, J=3.6, 14.1 Hz, 1H, H_g), 3.43 (dd, B part of AB system, J=8.0, 14.1 Hz, 1H, H_h), 1.70 (bs, 1H, H_f), 1.30 (t, J= 7.0 Hz, 6H, H_a), 1.09 (d, J=6.2 Hz, 3H, H_d)

^{13}C-NMR ($CDCl_3$)

δ (ppm): 136.7, 103.8, 68.0, 66.9, 57.9, 19.9, 15.0

3.4.8. (*R*)-2-(3,4-diethoxy-1*H*-pyrrol-1-yl)propan-1-ol (39):

Colorless oil, (0.132 gr, 62 %), $[\alpha]_D^{20}$= -6.46 (*c* 1.47, MeOH)



39

Figure 28

^{1}H-NMR ($CDCl_3$)

δ (ppm): 6.18 (s, 2H, H_c), 3.93-3.87 (m, 5H, H_b, H_f), 3.70-3.57, (m, 2H, H_e), 1.54 (bs, 1H, H_d), 1.37 (t, J= 6.2 Hz, 9H, H_a, H_g)

^{13}C-NMR ($CDCl_3$)

δ (ppm): 136.5, 101.5, 67.4, 66.8, 57.5, 16.8, 15.0

3.4.9. (*R*)-2-(3,4-diethoxy-1*H*-pyrrol-1-yl)-3-phenylpropan-1-ol (40):

Colorless oil, (0.170 gr, 59 %), $[\alpha]_D^{20}$= +46.57 (*c* 0.35 , MeOH)

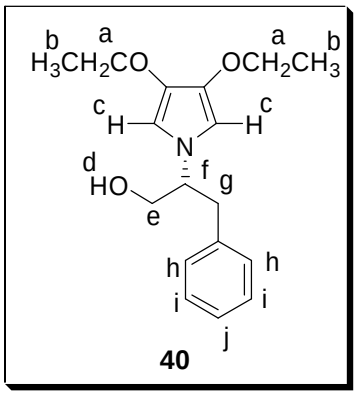


Figure 29

^{1}H-NMR ($CDCl_3$)

δ (ppm): 7.19-7.10 (m, 3H, H_i, H_j), 6.94 (d, J= 6.9 Hz, 2H, H_h), 6.04 (s, 2H, H_c), 3.82 (q, J= 6.7, 13.6 Hz, 6H, H_a, H_e), 3.70-3.67 (m, 1H, H_f), 2.89-2.86 (m, 2H,H_g), 1.52 (bs, 1H, H_d), 1.28 (t, J= 7.02 Hz, 6H,H_b)

^{13}C-NMR ($CDCl_3$)

δ (ppm): 137.3, 136.7, 128.9, 128.6, 128.5, 101.9, 66.8, 65.1, 64.1, 38.3, 15.0

CHAPTER 4

CONCLUSION

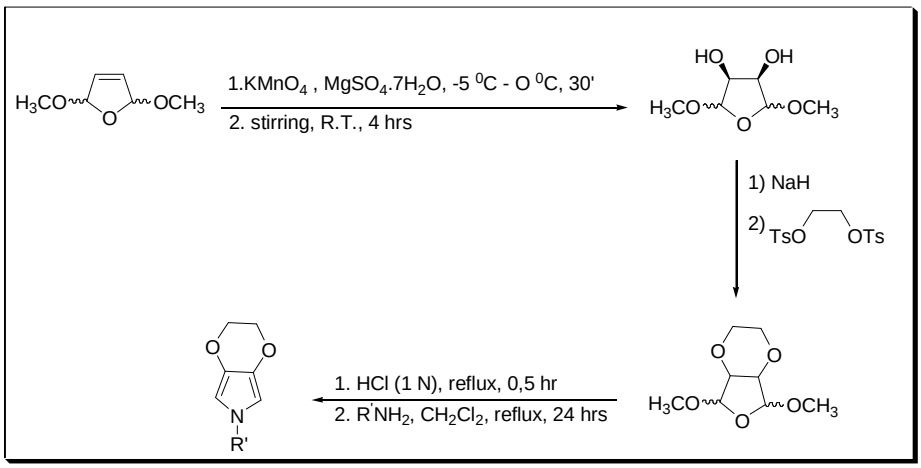
Pyrroles are an important class of heterocyclic compounds having different biological activities [45] and occur in numerous pharmacologically active natural and unnatural products in addition to their usage as monomers for the synthesis of conducting polymers.

In our study, several chiral N-substituted-3,4-dialkoxy-pyrrole derivatives were synthesized in modarate to good yields. They can be used as valuable monomers not only due to presence of alkoxy groups which enables lower oxidation potential and prevents the occurance of undesired α-β and β-β couplings during polymerization but also due to the chiral moiety which provides their potential application in electrochemical asymmetric synthesis and stereoselecive analyses.

The studies for the preparation of chiral conducting polymers hasn't been completed yet, but preliminary studies implied the possible use of these pyrrole derivatives as valuable monomers for the synthesis of conducting polymes.

In addition to these studies, the synthesis of chiral N-substituted-3,4-ethylenedioxypyrroles is in progress. Recently, the synthesis of 3,4-alkylenedioxypyrroles have received great attention since the polymers

prepared from these monomers might prove especially useful for the synthesis of very easily oxidized electroactive conjugated polymers [29]. In the literature, 3,4-ethylenedioxypyrroles are synthesized in five steps starting from a known intermediate which is already synthesized by two steps [29]. Our aim is to obtain chiral N-substituted-3,4-ethylenedioxypyrrole derivatives in a shorter pathway by starting from 2,5-dimethoxy-2,5-dihydrofuran as shown in the Scheme **11.**



Scheme 11 Proposed pathway for the synthesis of N-substituted-3,4-ethylenedioxypyrrole

Actually, there is no problem in the first and the third steps which are also used for the synthesis of N-substituted-3,4-dialkoxypyrrole derivatives, only the validity of the second step is in consider.

APPENDIX A

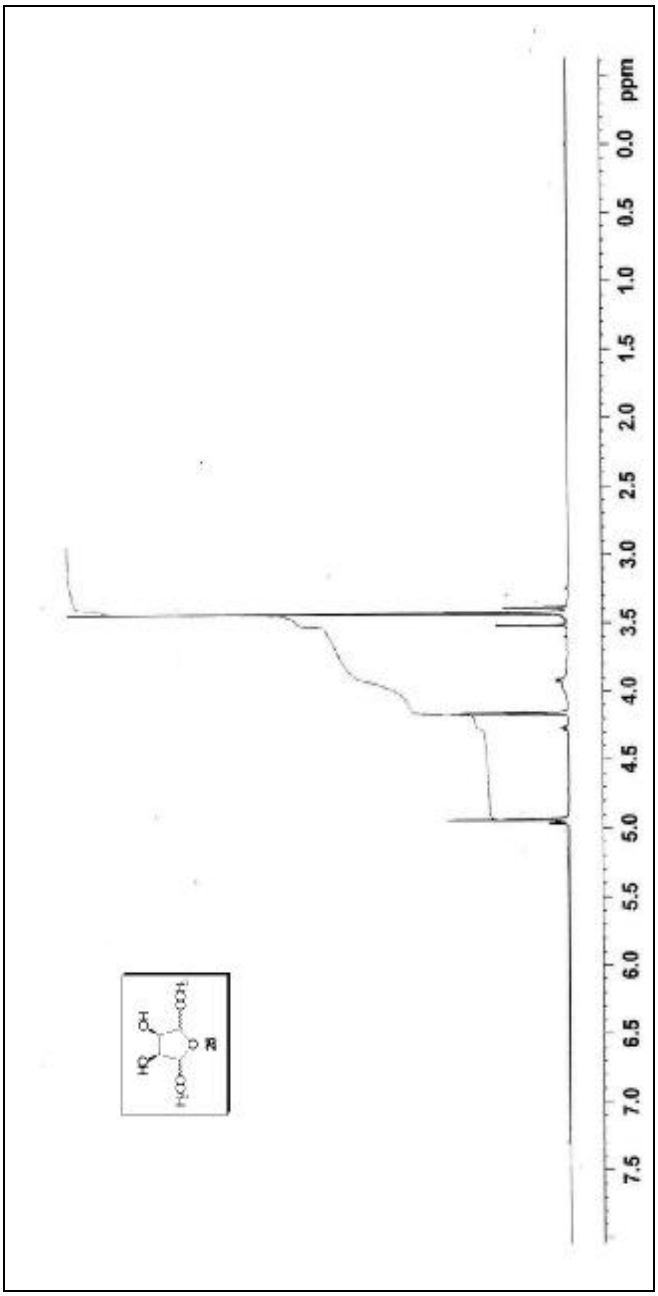


Figure 30. ^{1}H-NMR spectrum of compound **25**

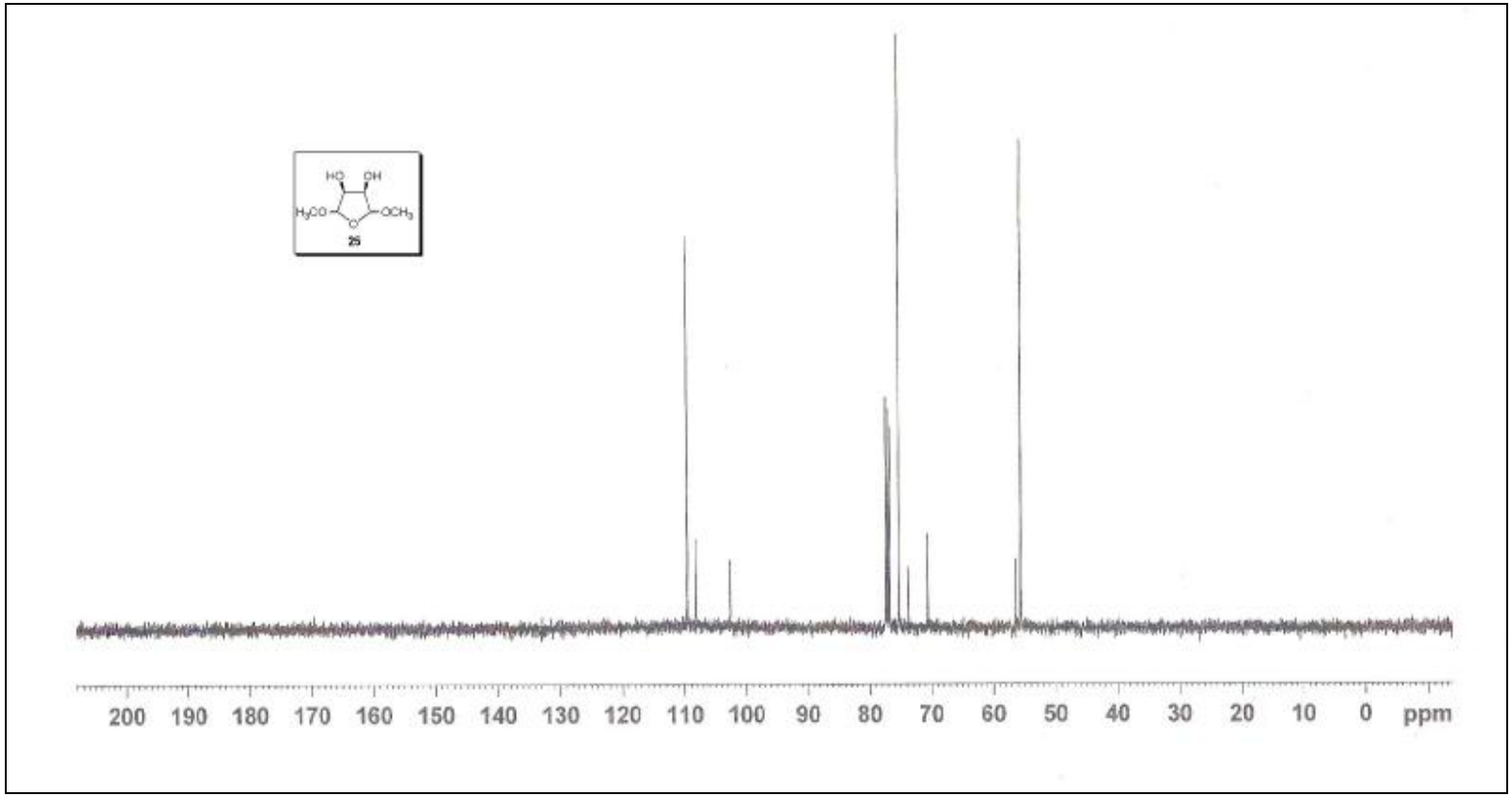


Figure 31. ^{13}C-NMR spectrum of compound **25**

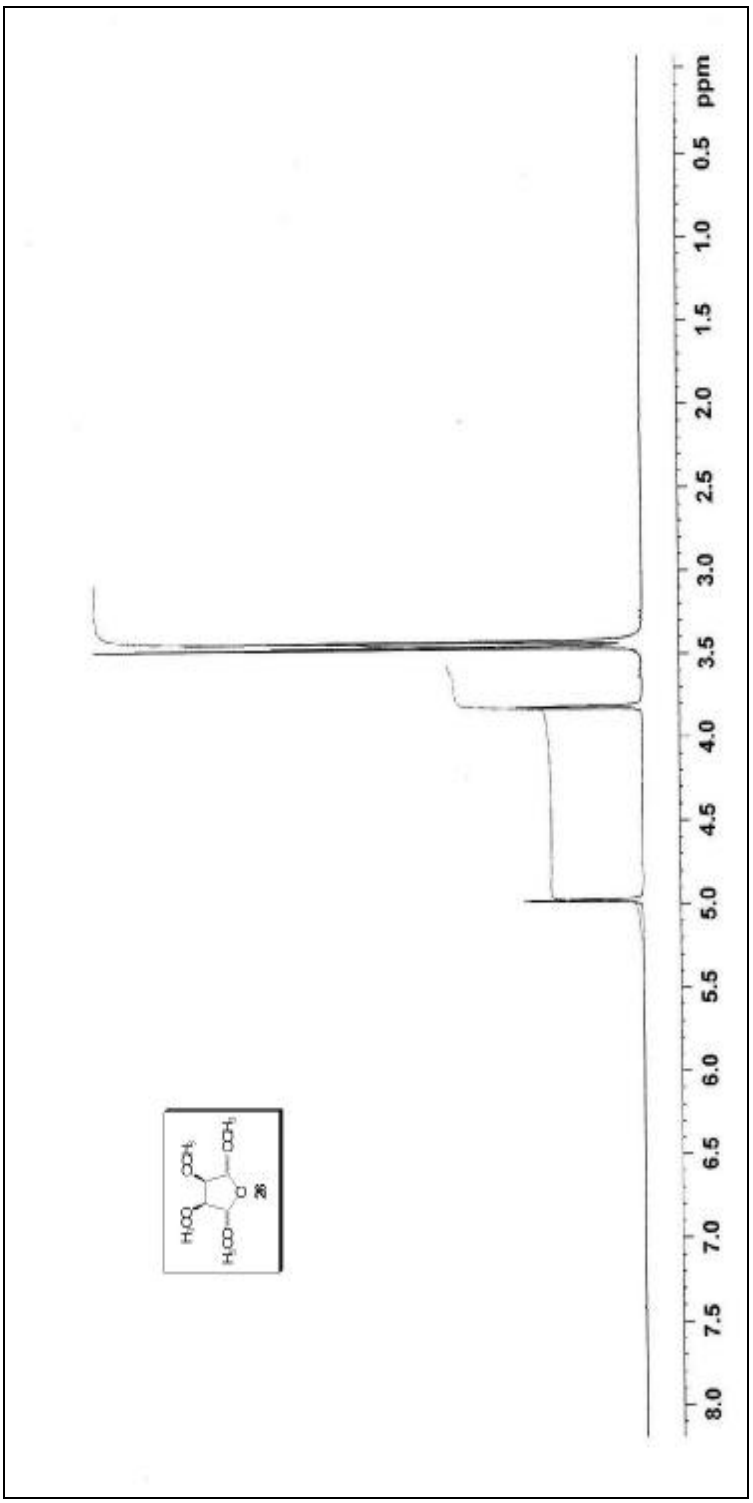


Figure 32. ^{1}H-NMR spectrum of compound **26**

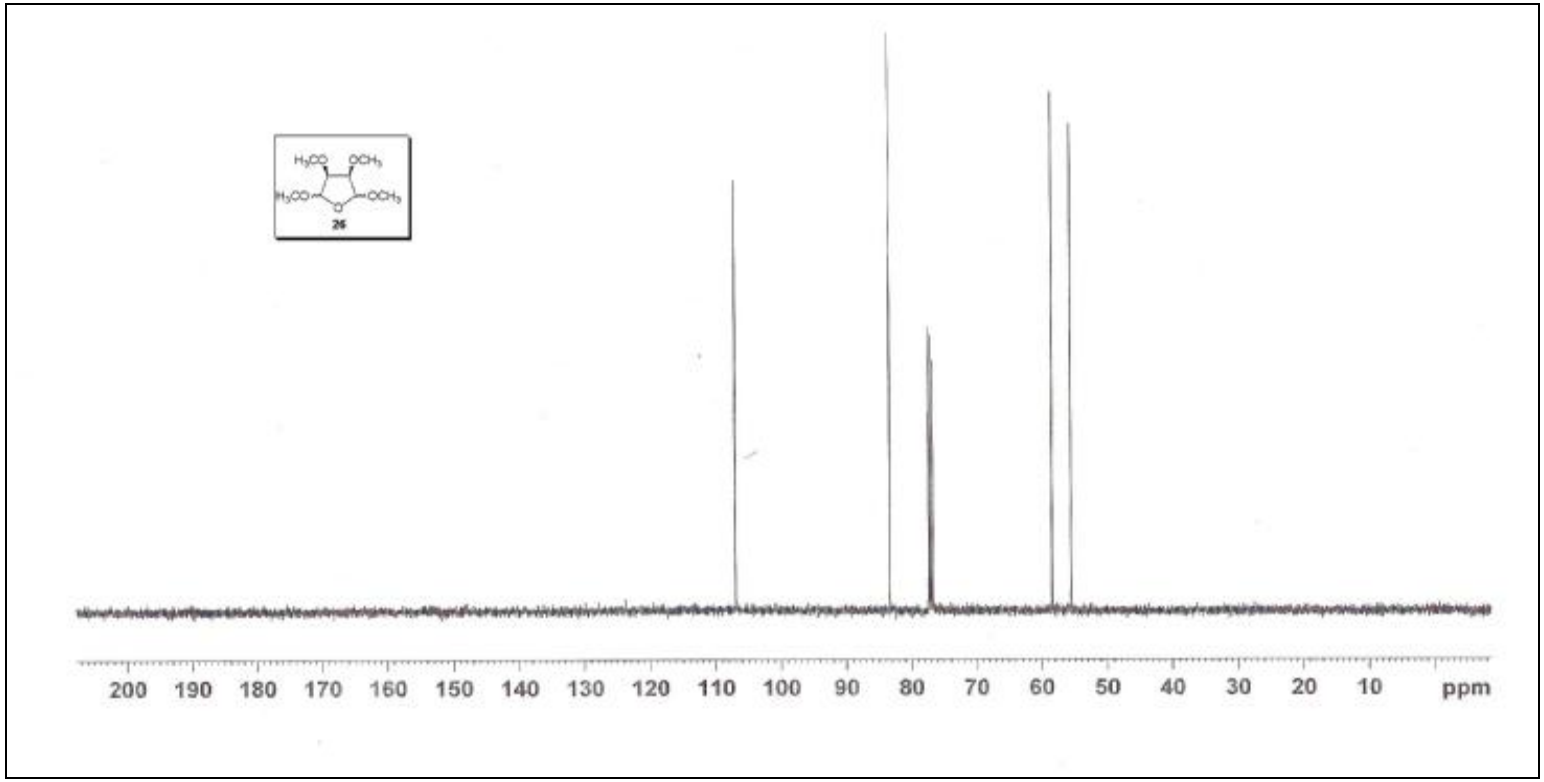


Figure 33. ^{13}C-NMR spectrum of compound **26**

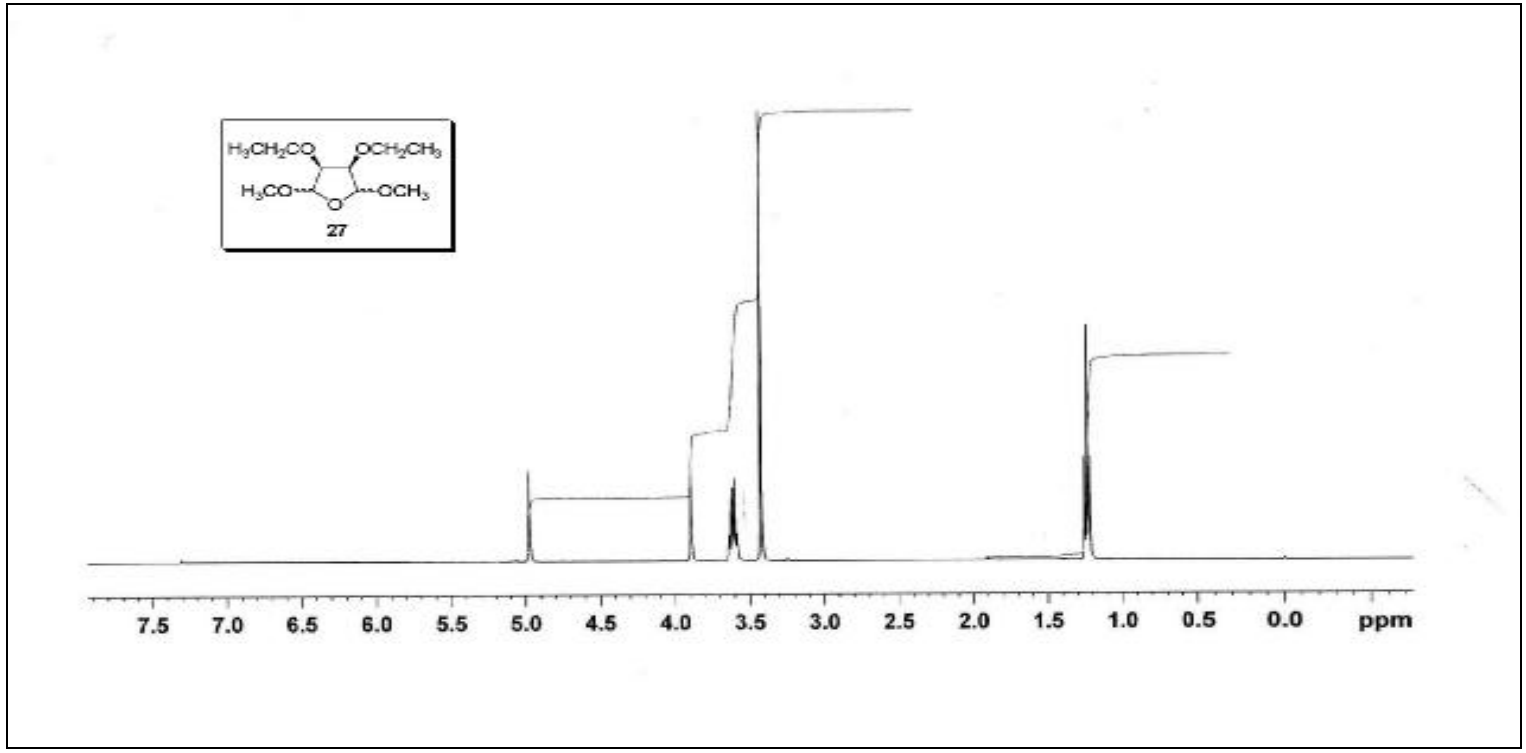


Figure 34 ^{1}H-NMR spectrum of compound **27**

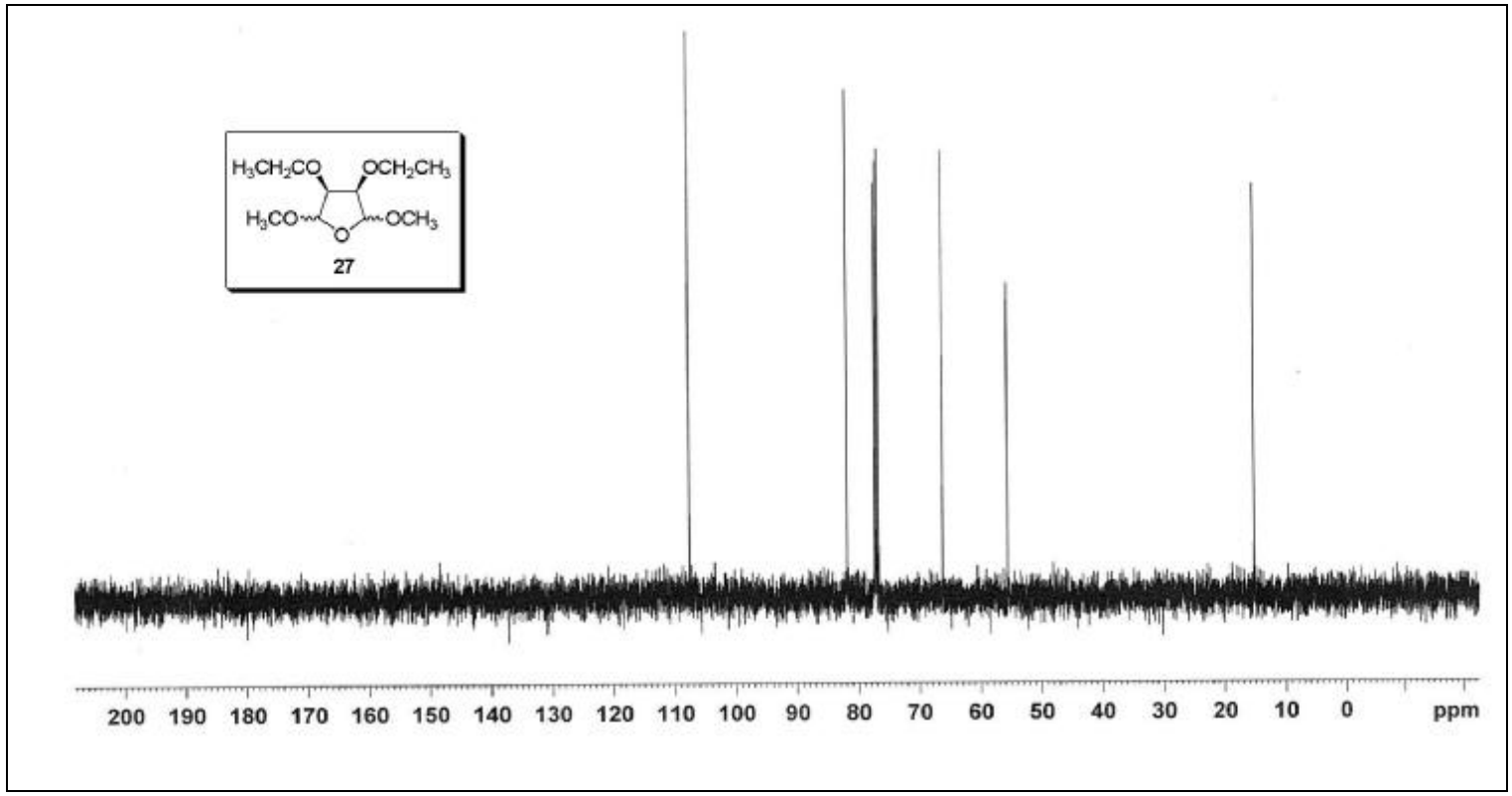


Figure 35. ^{13}C-NMR spectrum of compound **27**

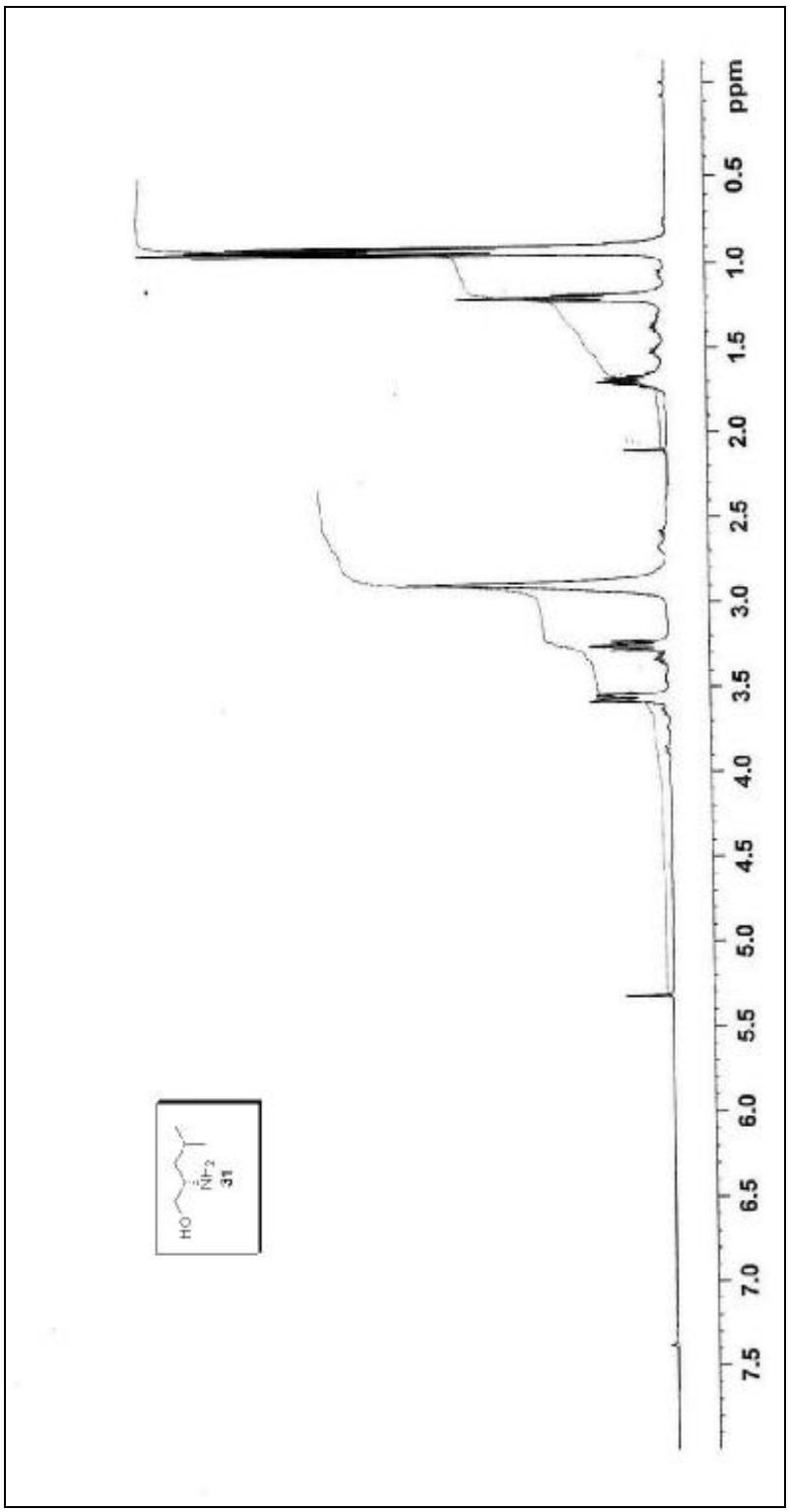


Figure 36. ^{1}H-NMR spectrum of compound **31**

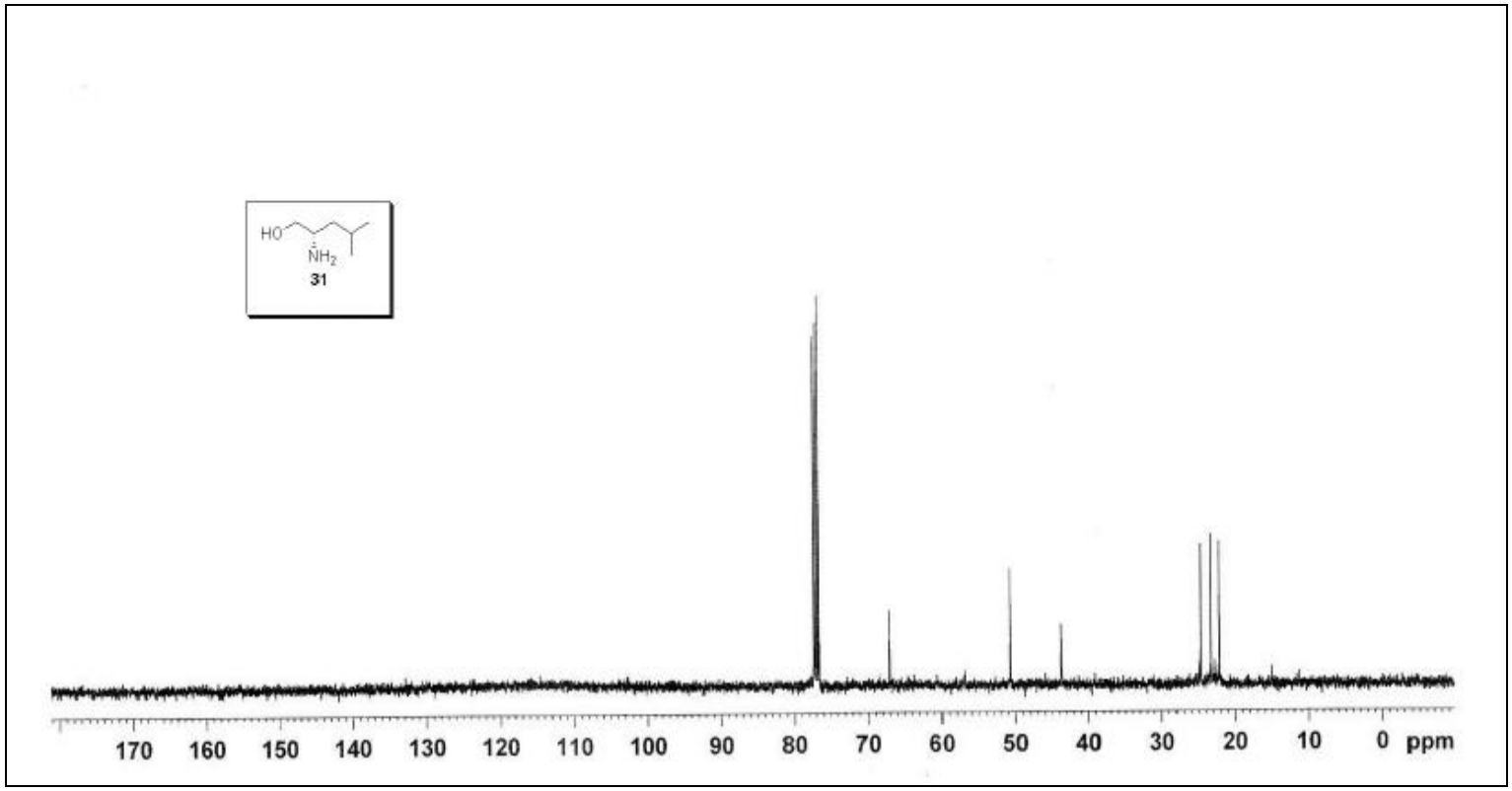


Figure 37. ^{13}C-NMR spectrum of compound **31**

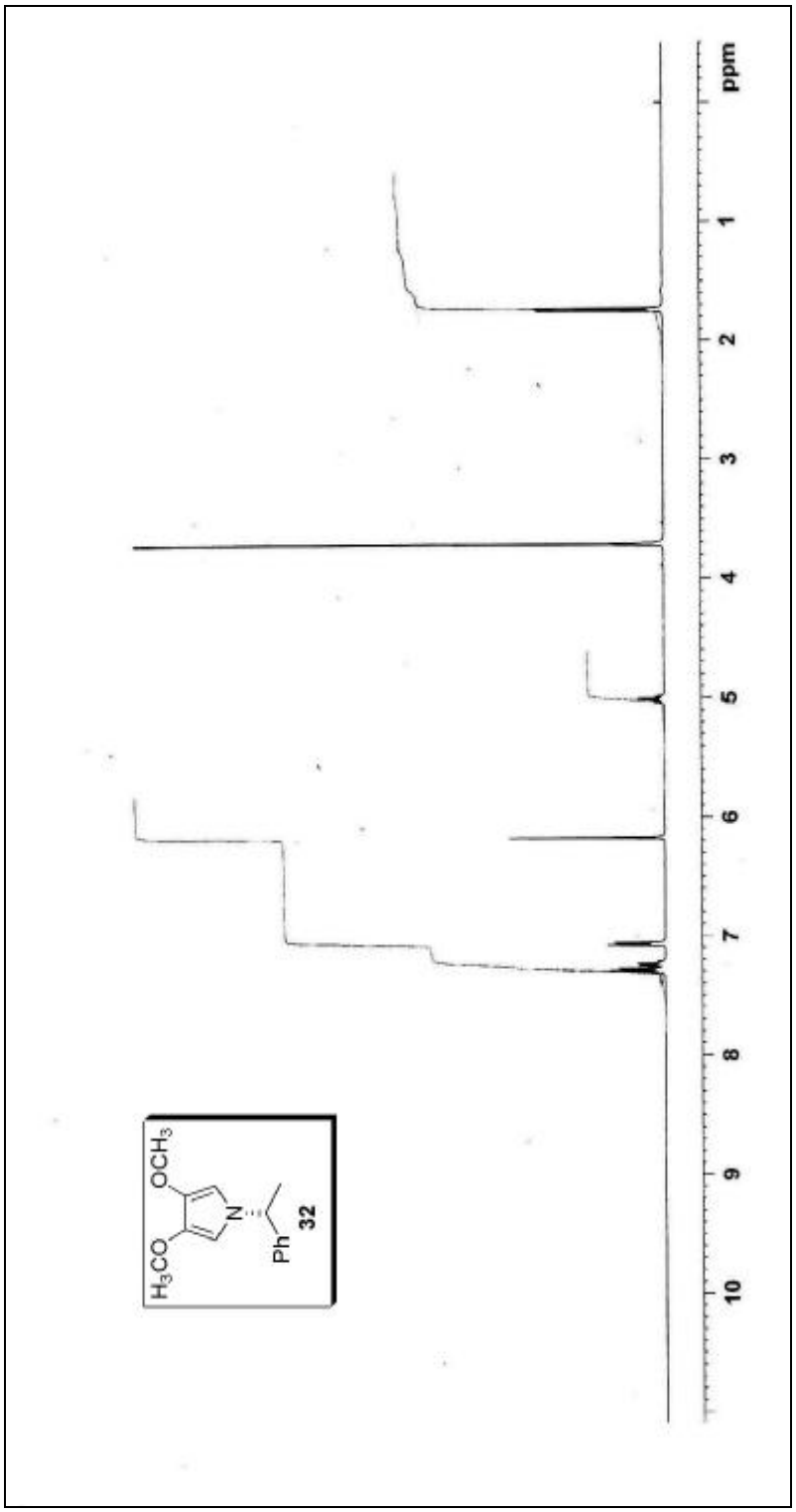


Figure 38. ^{1}H-NMR spectrum of compound **32**

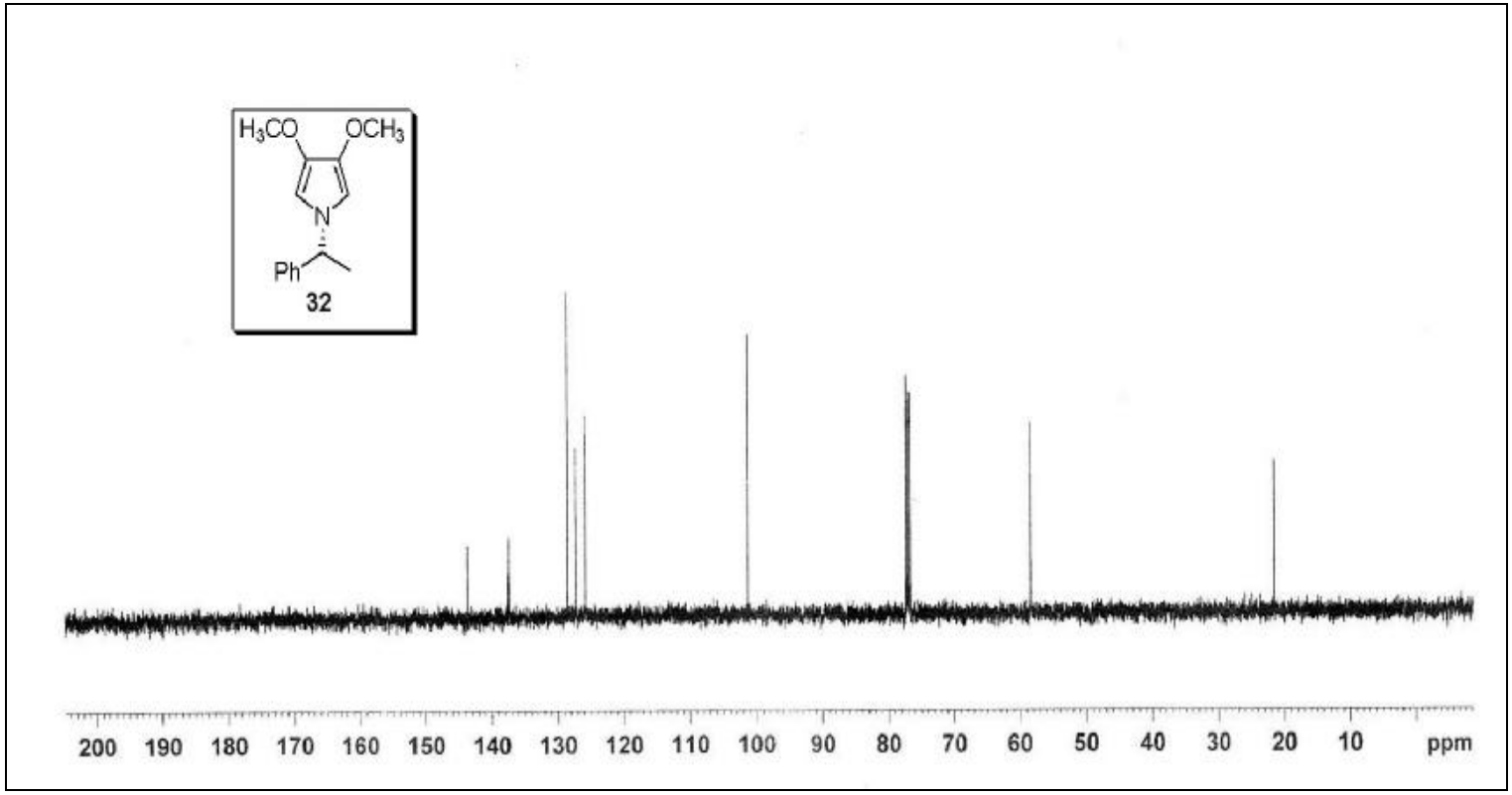


Figure 39. ^{13}C-NMR spectrum of compound **32**

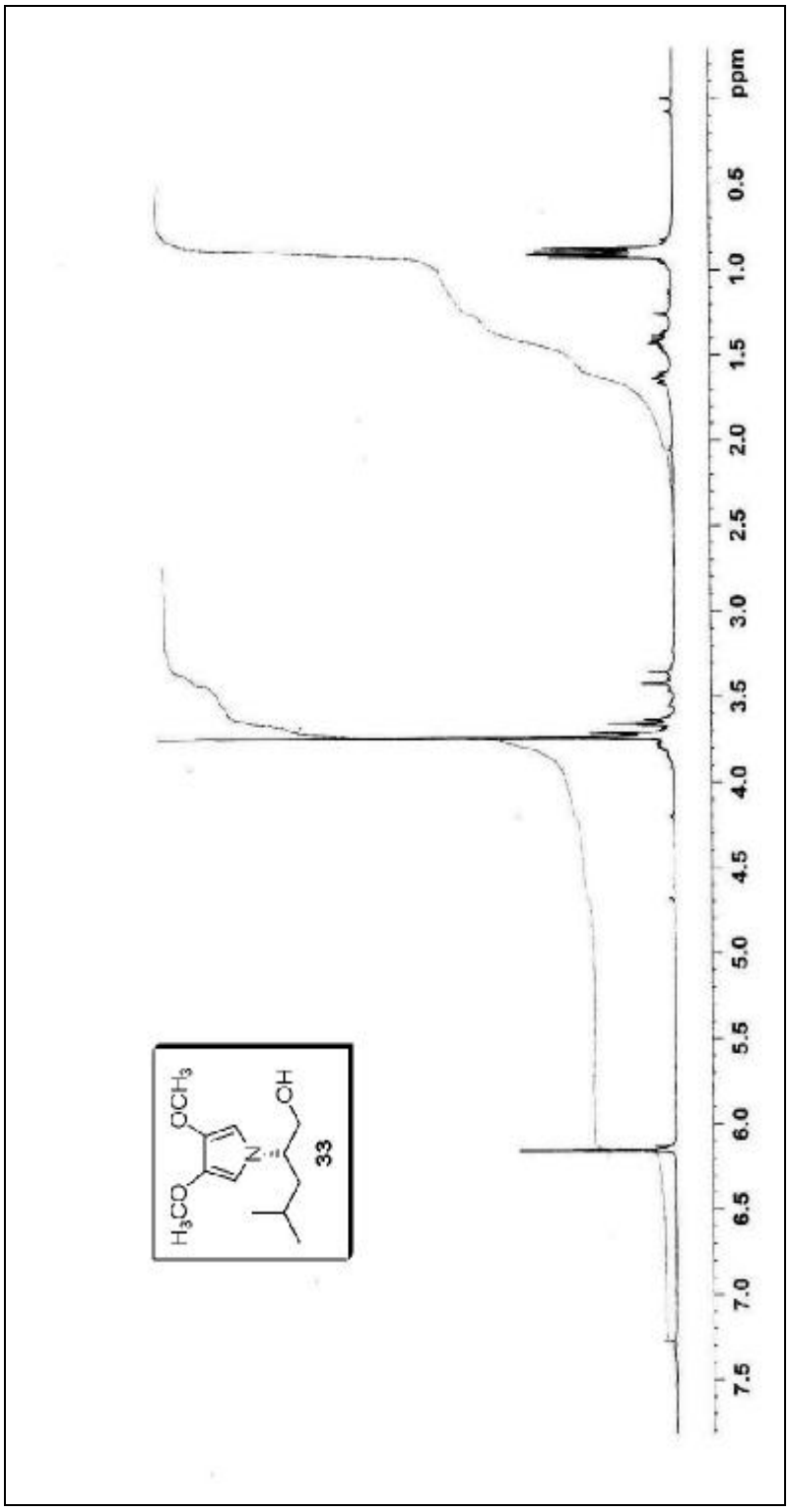


Figure 40. ^{1}H-NMR spectrum of compound **33**

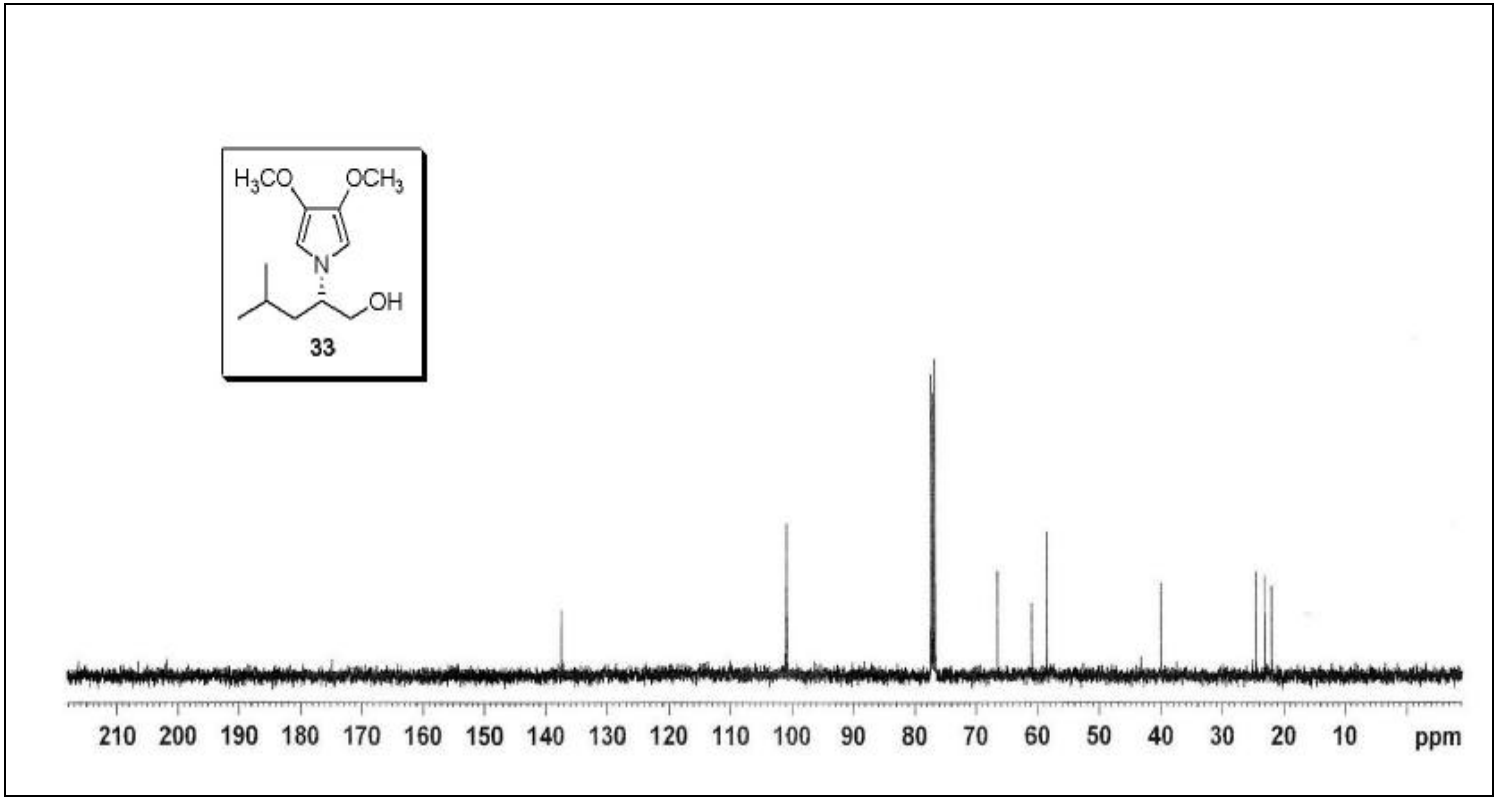
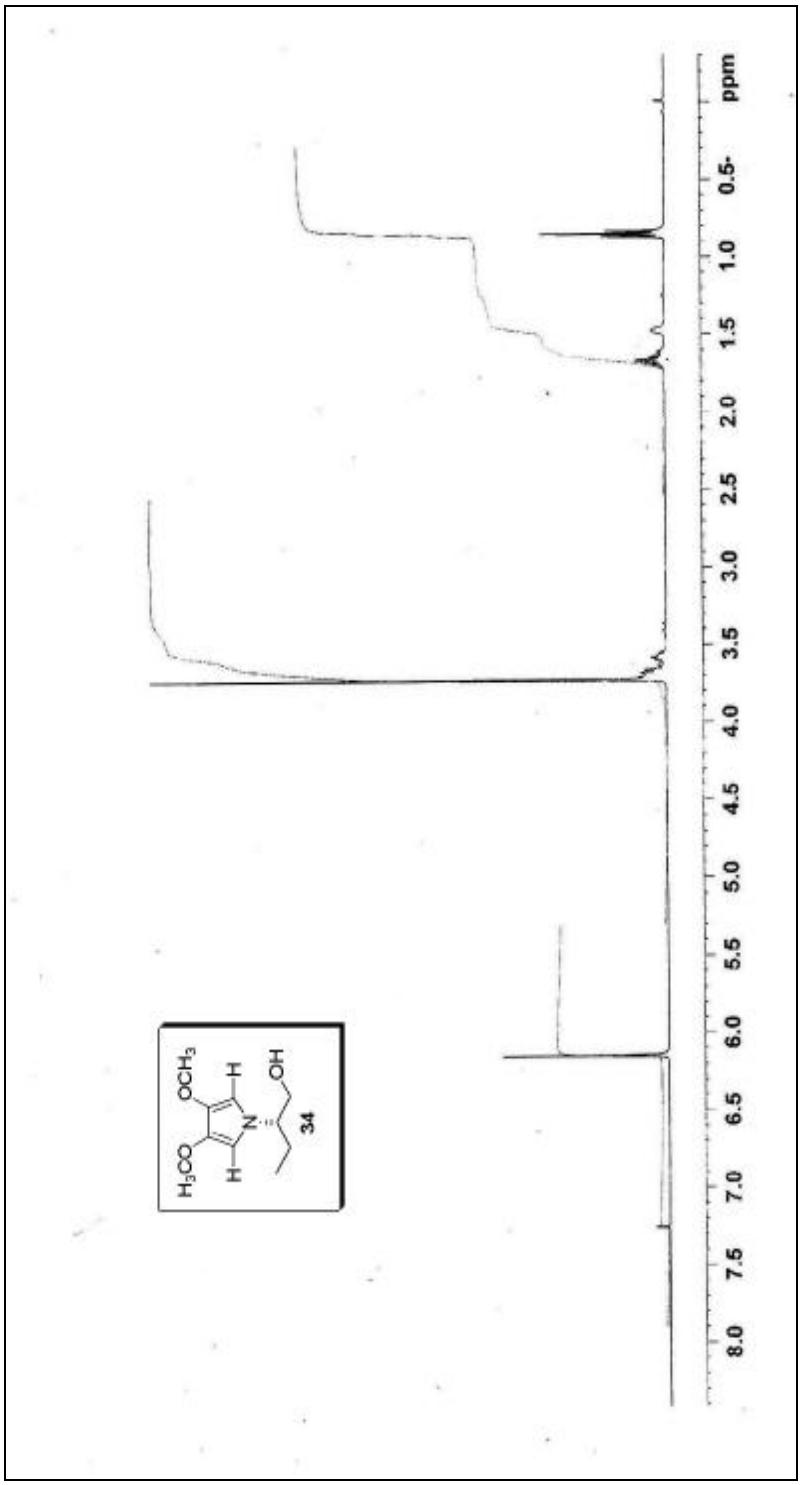


Figure 41. ^{13}C-NMR spectrum of compound **33**



igure 42. ^{1}H-NMR spectrum of compound **34**

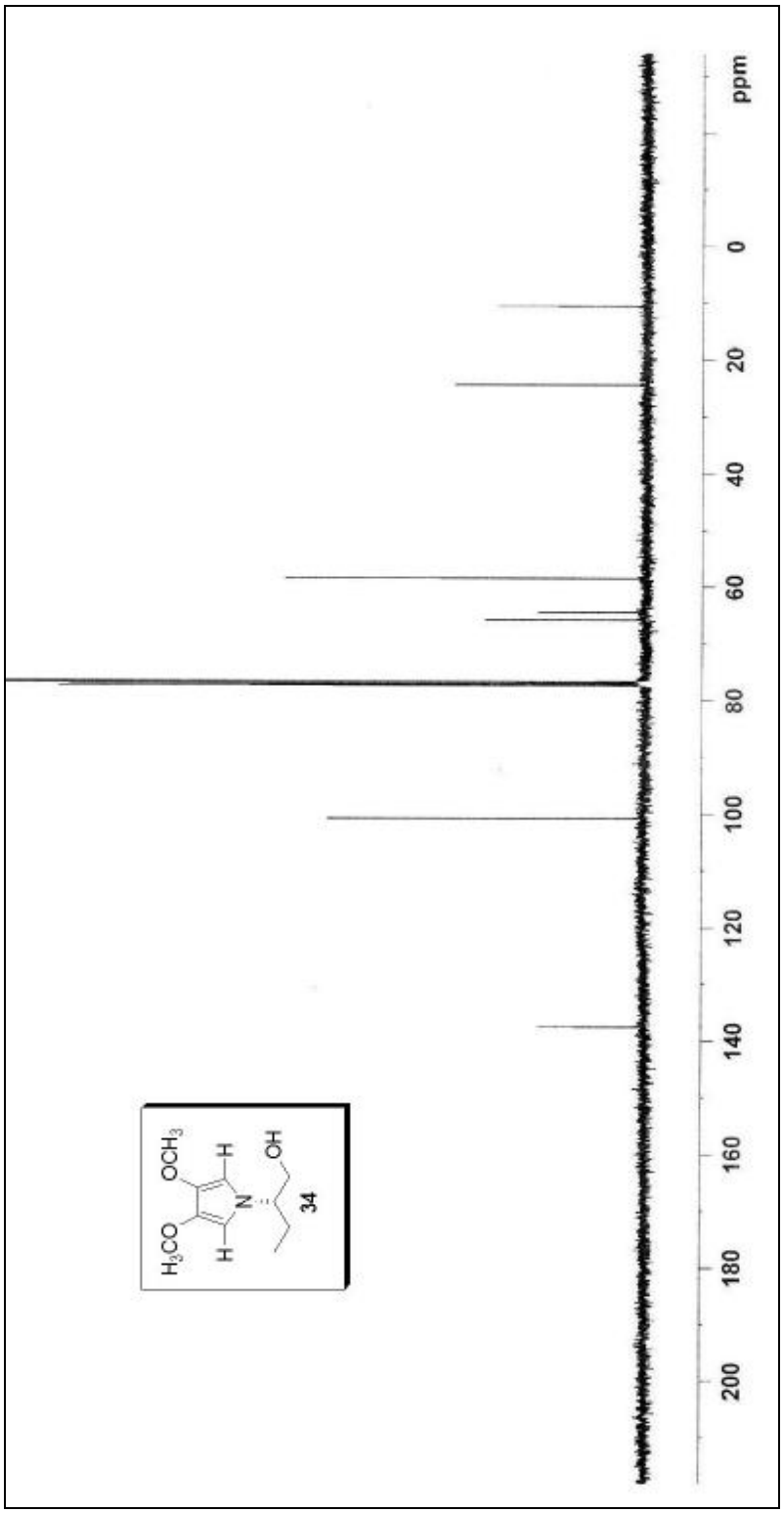


Figure 43. ^{13}C-NMR spectrum of compound **34**

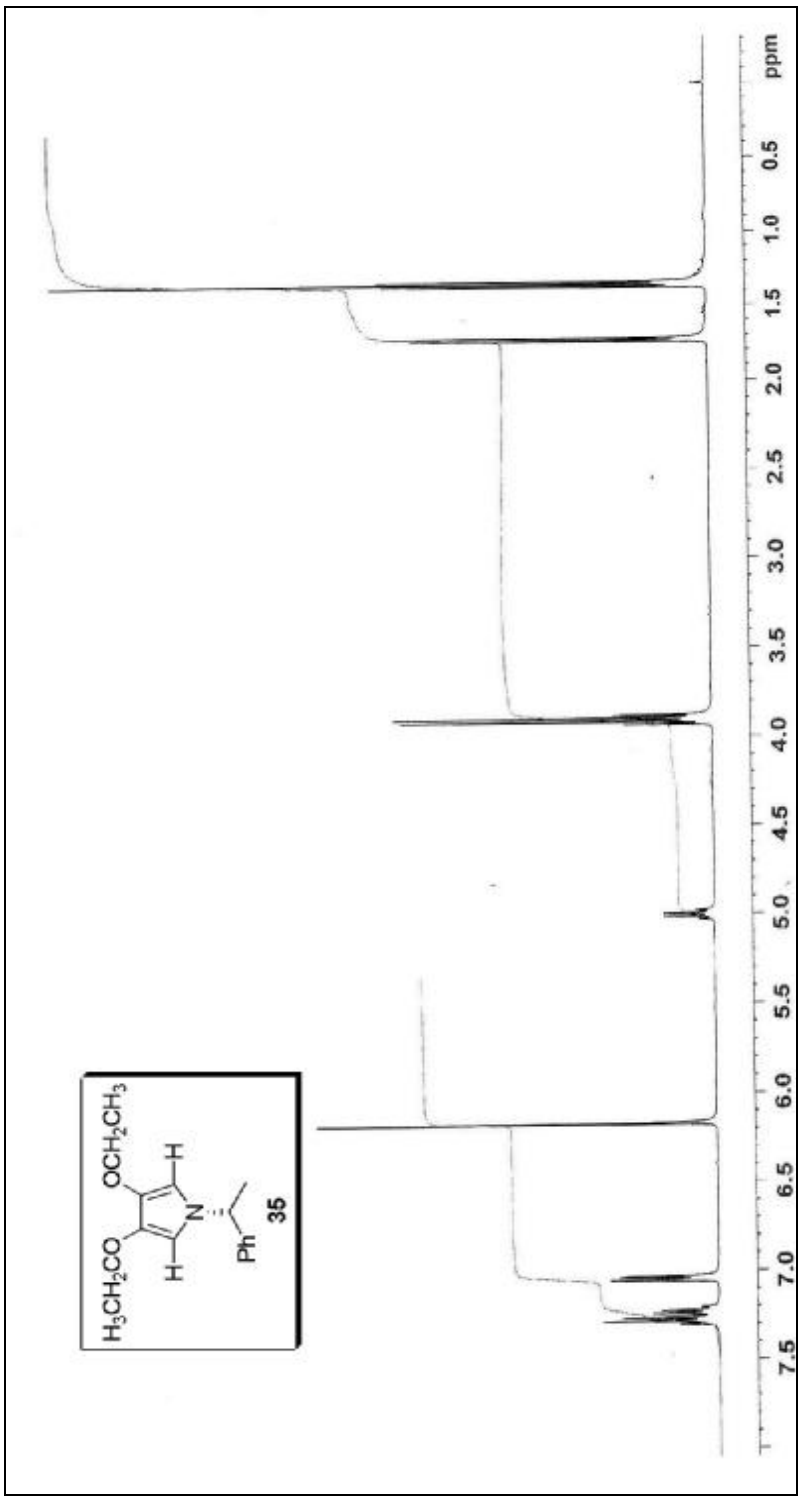


Figure 44. ^{1}H-NMR spectrum of compound **35**

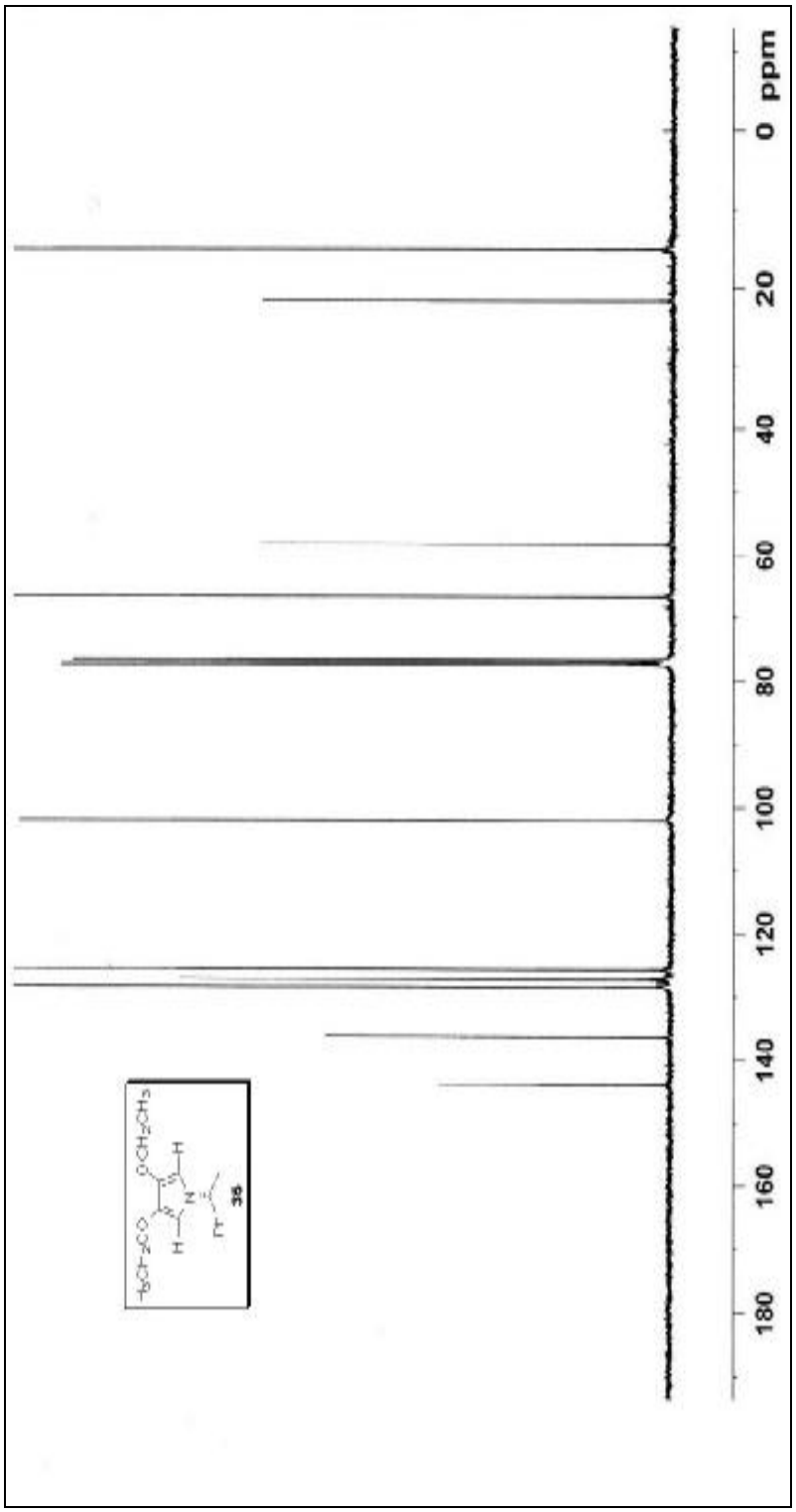
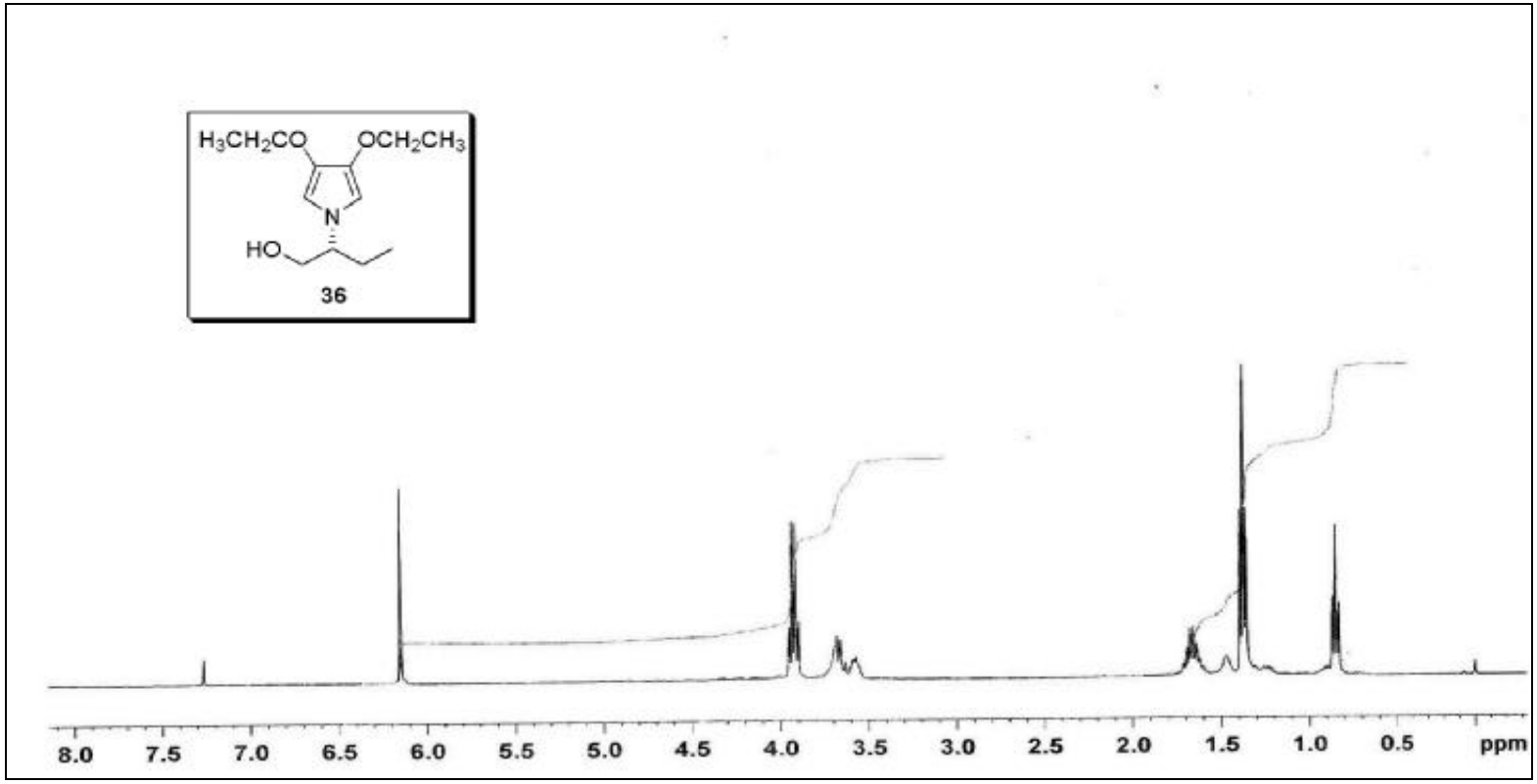
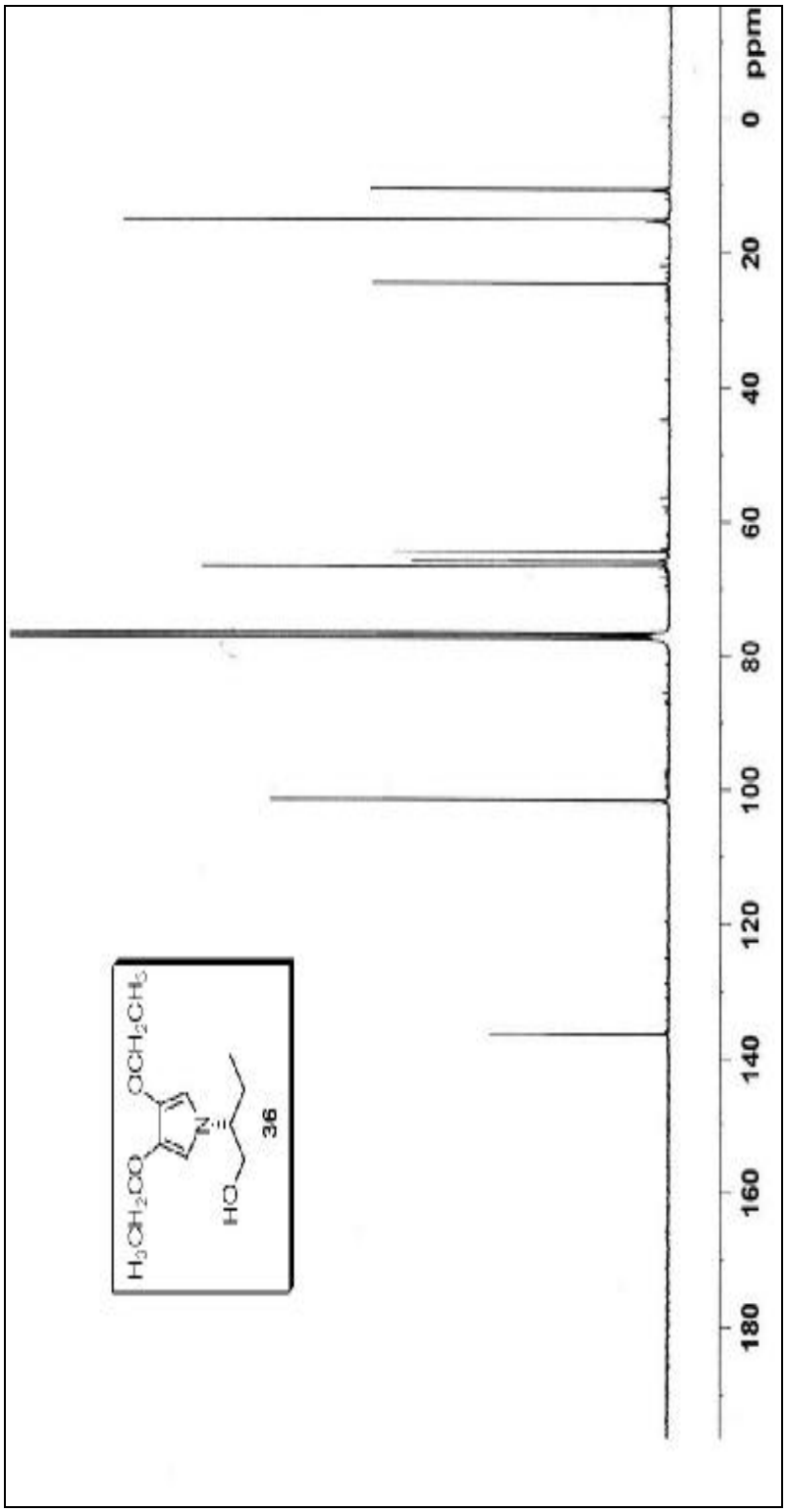


Figure 45. ^{13}C-NMR spectrum of compound **35**



igure 46. ^{1}H-NMR spectrum of compound **36**



igure 47. ^{13}C-NMR spectrum of compound **36**

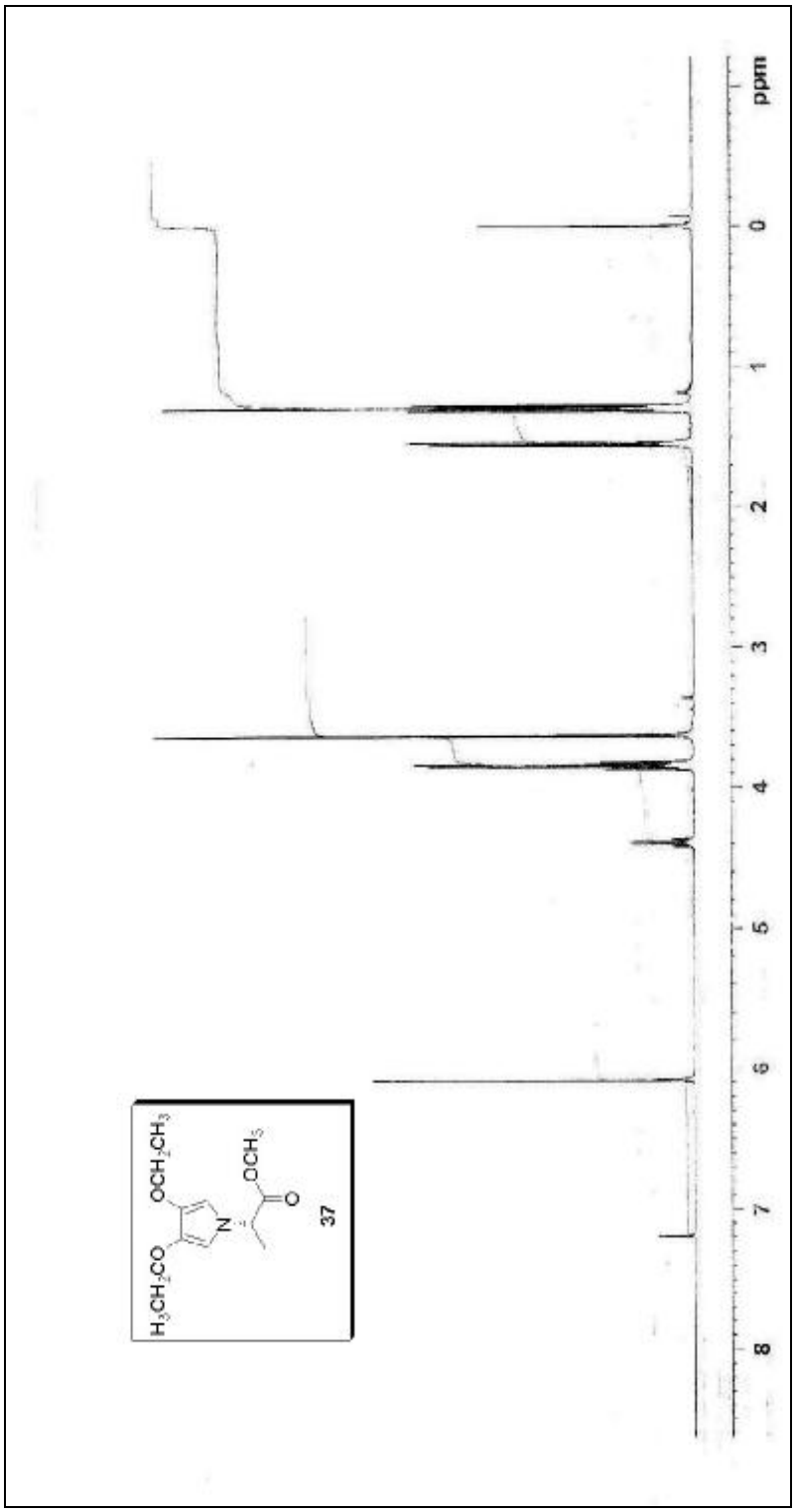


Figure 48. ^{1}H-NMR spectrum of compound **37**

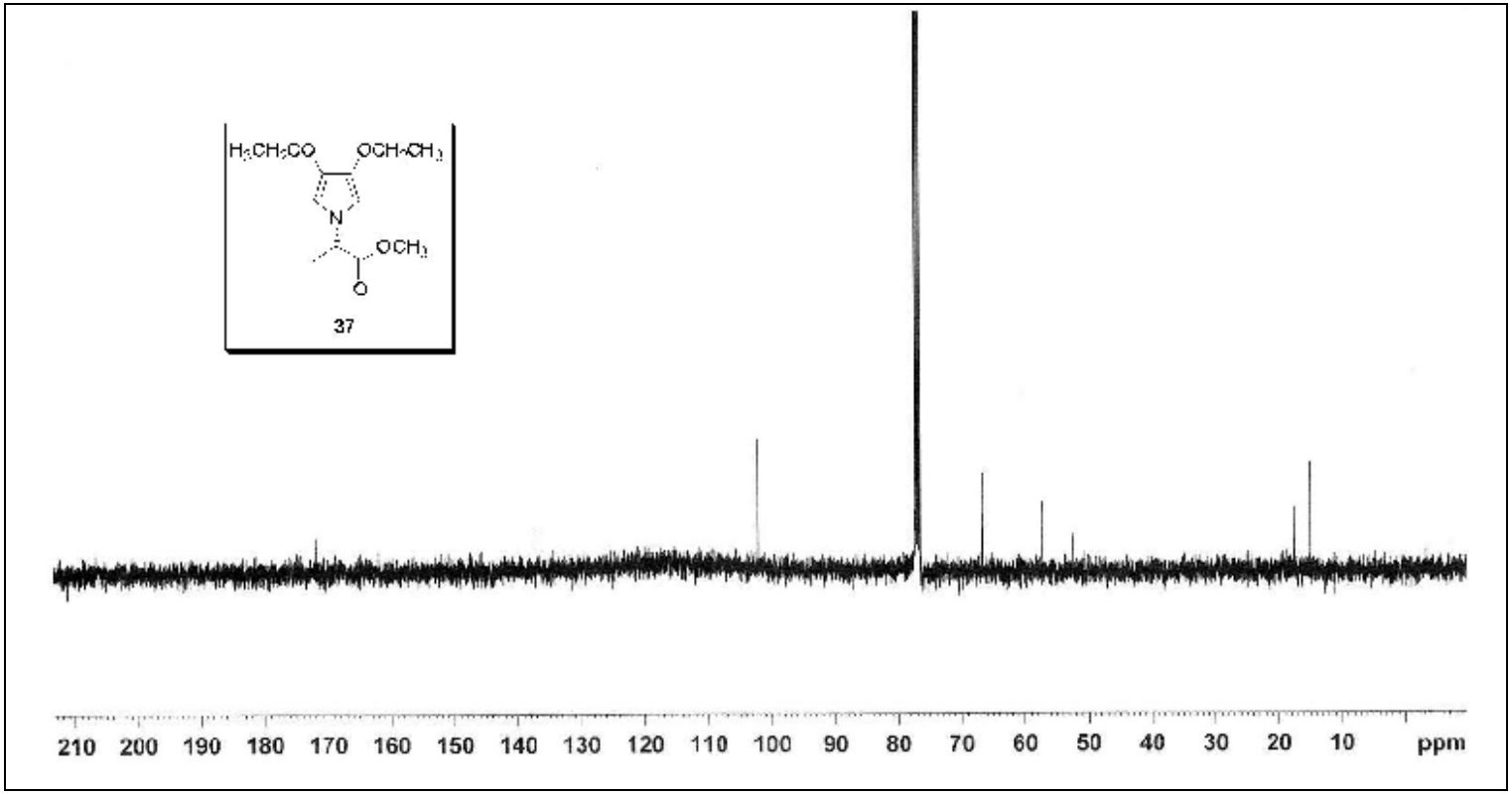
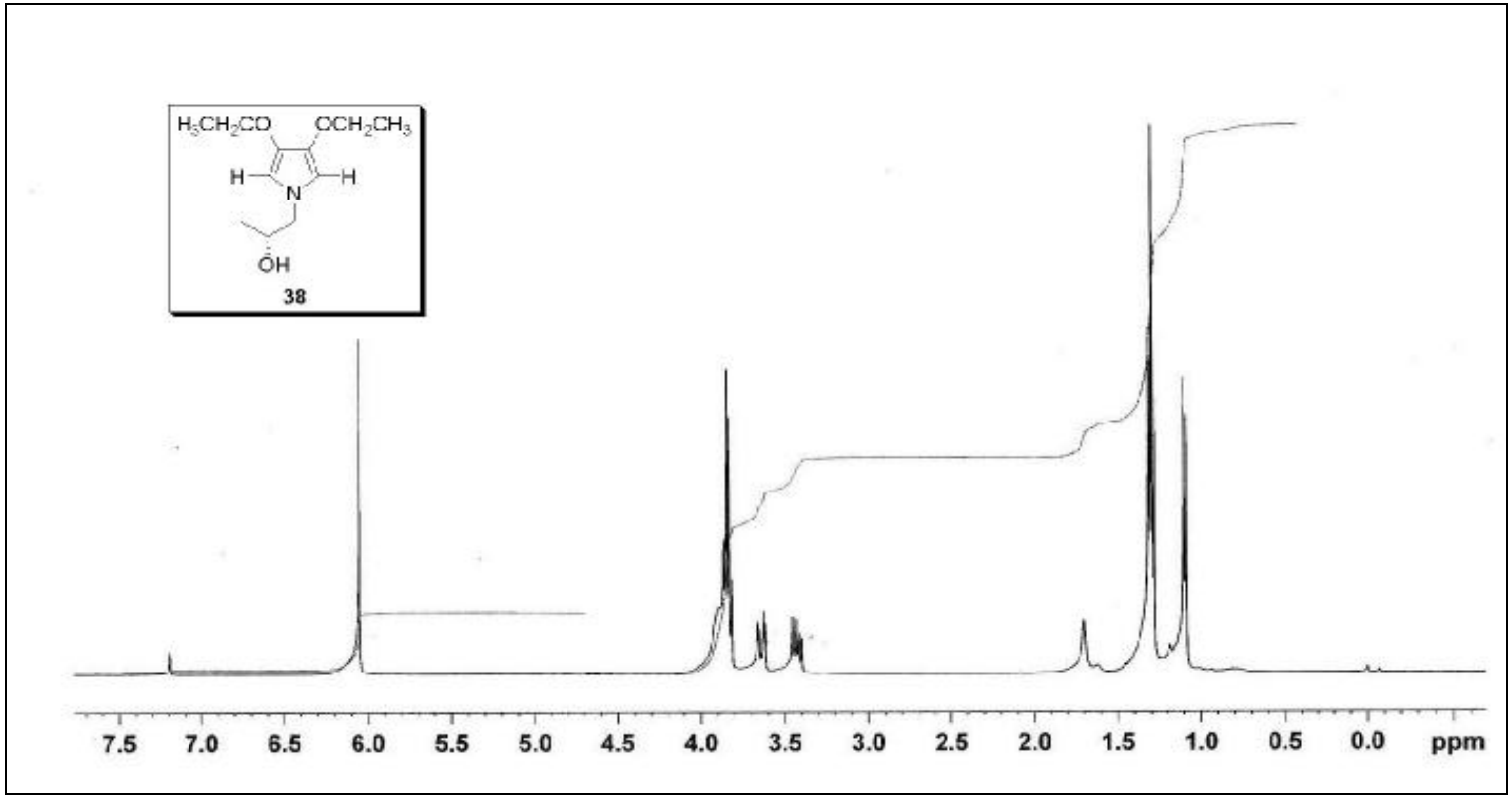


Figure 49. ^{13}C-NMR spectrum of compound **37**



igure 50. ^{1}H-NMR spectrum of compound **38**

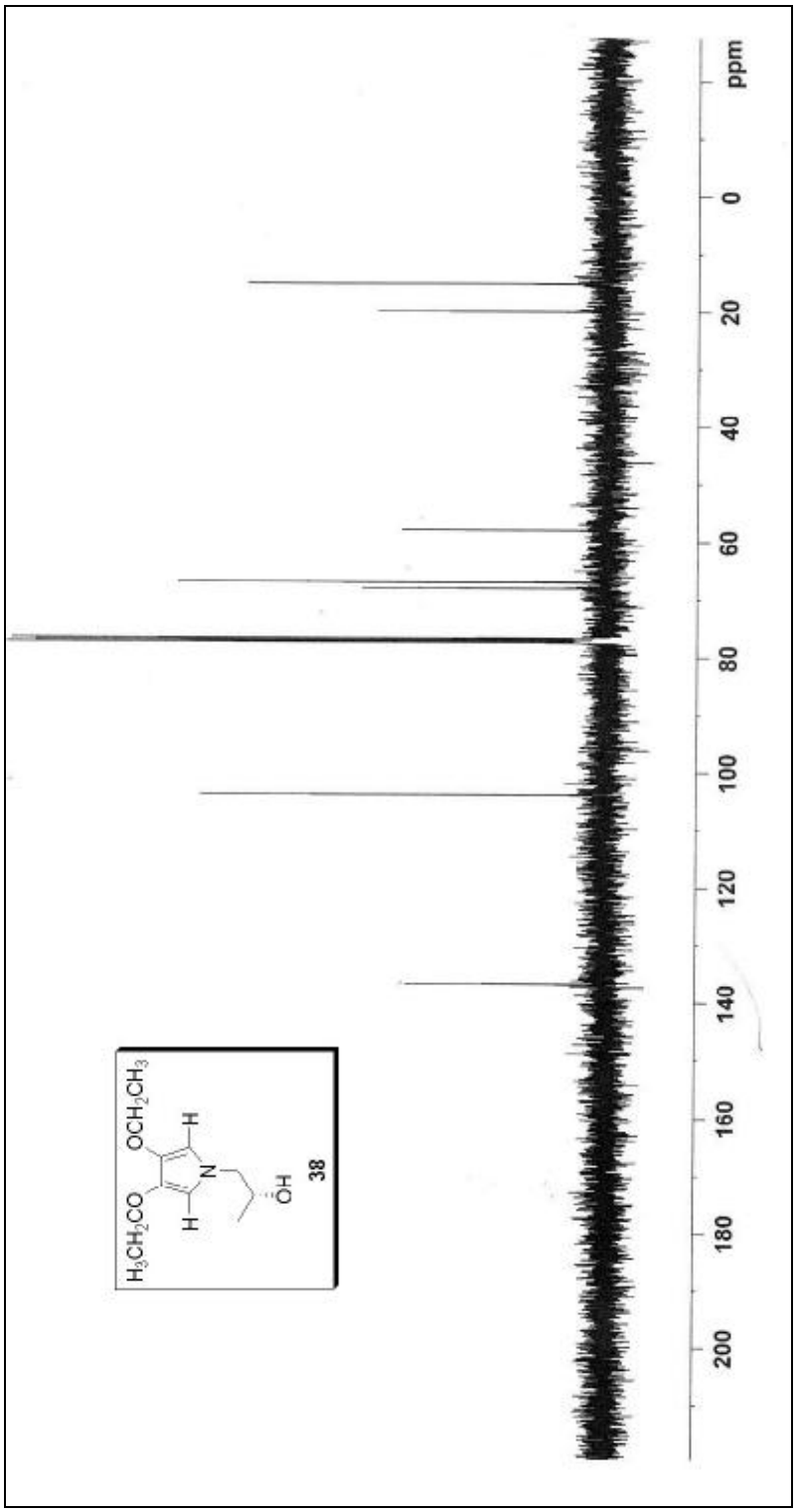


Figure 51. ^{13}C-NMR spectrum of compound **38**

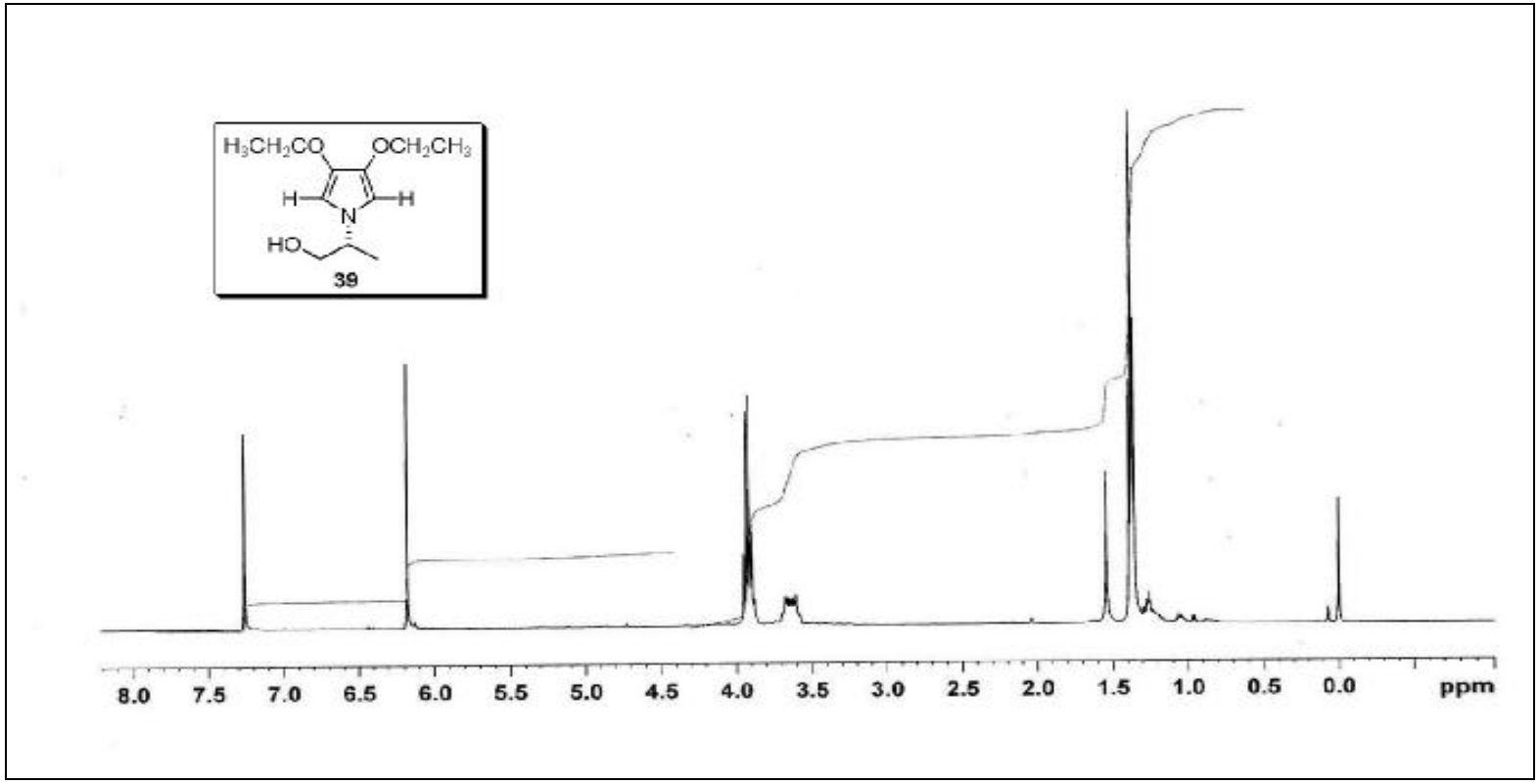


Figure 52. ^{1}H-NMR spectrum of compound **39**

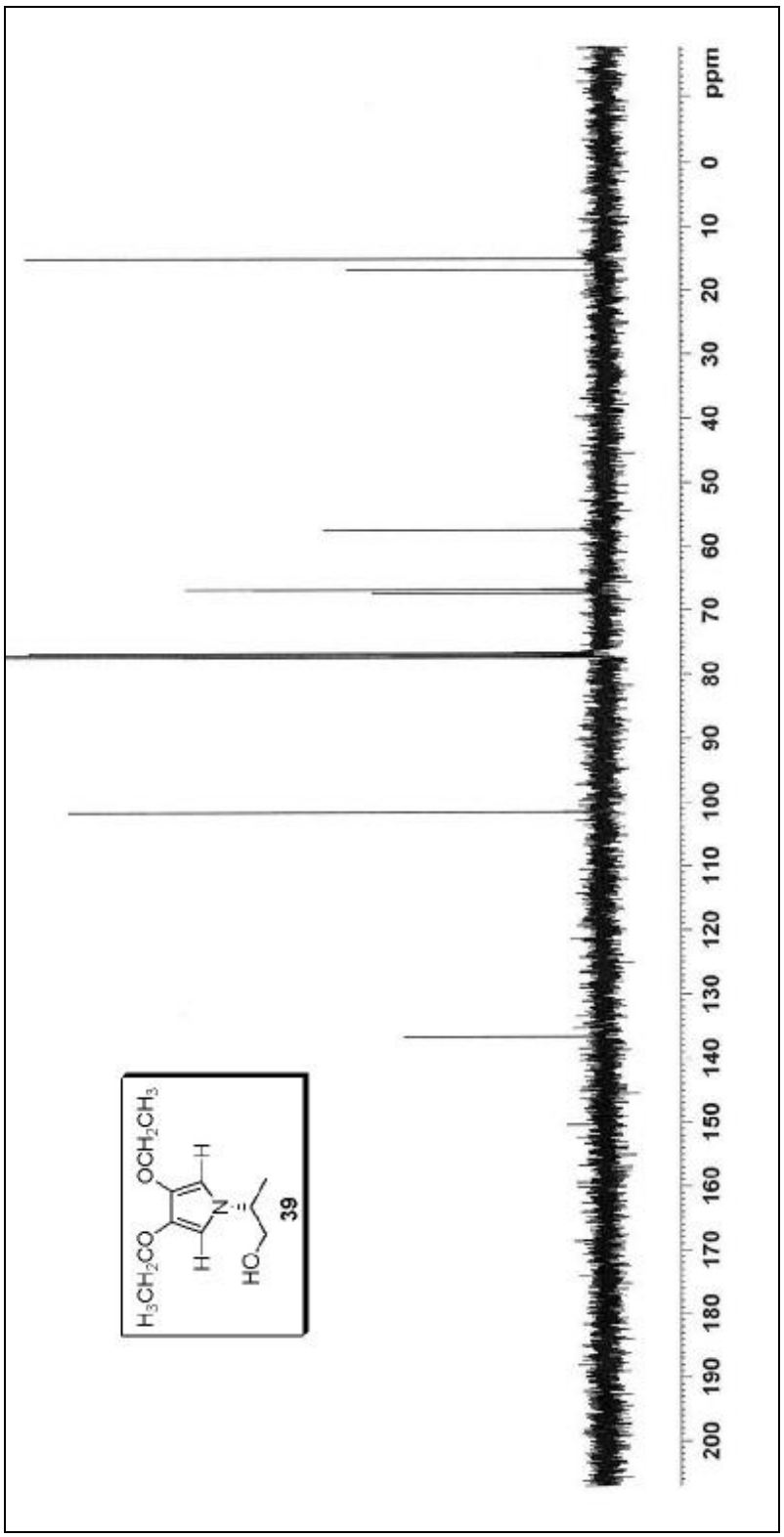


Figure 53. ^{13}C-NMR spectrum of compound **39**

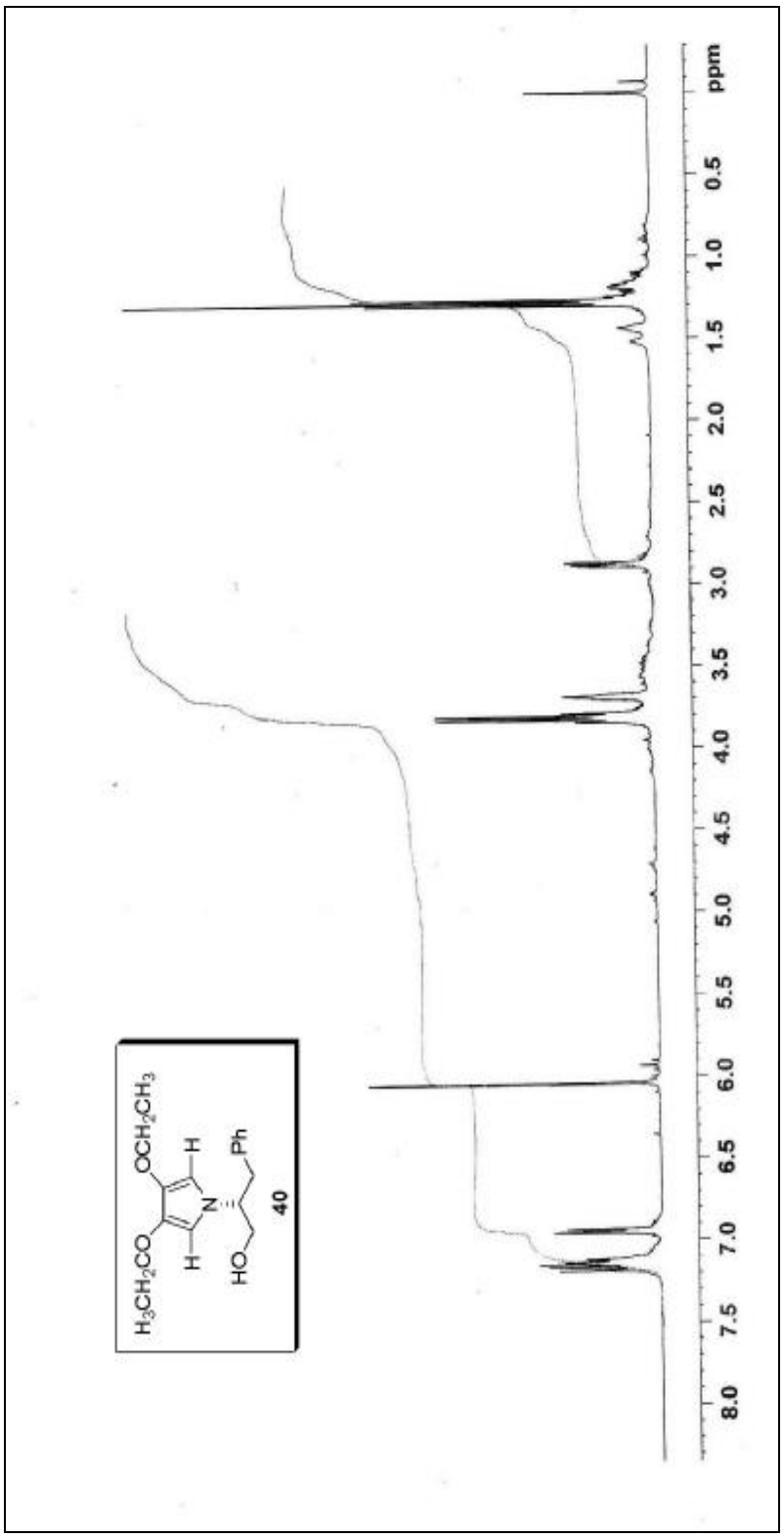


Figure 54. ^{1}H-NMR spectrum of compound **40**

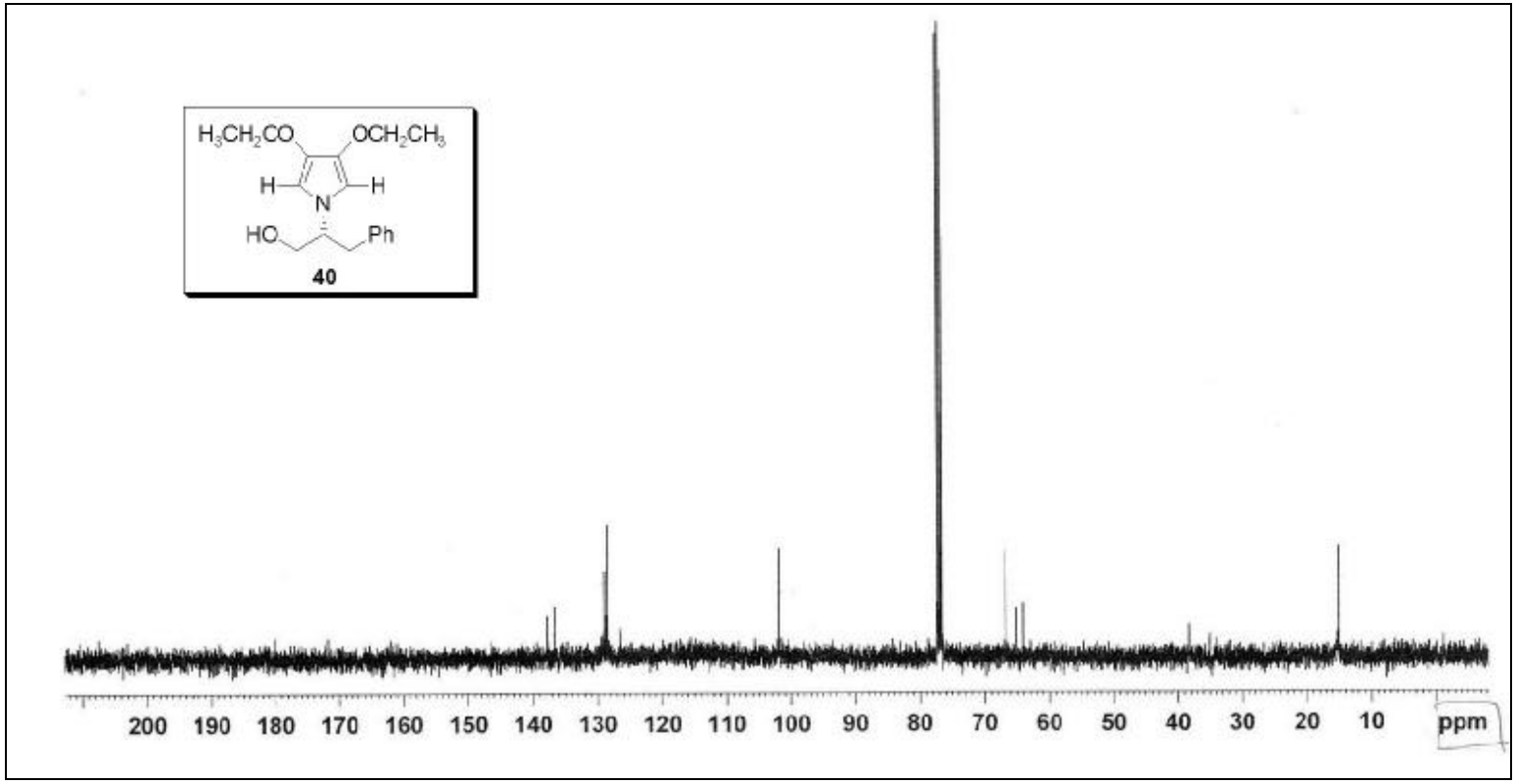


Figure 55. ^{13}C-NMR spectrum of compound **40**

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2**.** U. S. Patent 2 478456 ; *Chem. Abstr.* **1950**, *44,* 665 .

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