

Université de Montréal

**Synthèse des matériaux électroactifs à base de thiophènes et de  
bipyrroles dissymétriques.**

Par

Tshitundu Tshibaka

Département de Chimie

Faculté des Arts et Sciences

Mémoire présenté à la Faculté des Études Supérieures

En vue de l'obtention du grade de

Maîtrise es science (M. Sc.)

En chimie

Juillet 2011

© Tshitundu Tshibaka, 2011

Université de Montréal

Juillet 2011

Université de Montréal  
Faculté des études supérieures

Ce mémoire intitulé :

**Synthèse des matériaux électroactifs à base de thiophènes et de  
bipyrroles dissymétriques.**

Présenté par :

Tshitundu Tshibaka

A été évalué par un jury composé des personnes suivantes :

Joëlle Pelletier  
(présidente du jury)

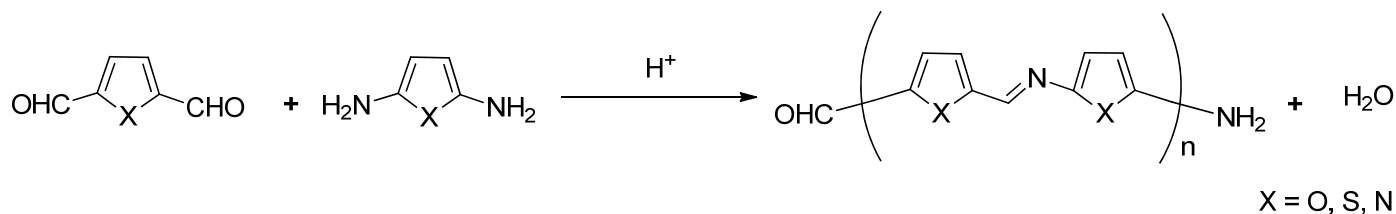
Yvan Guindon  
(membre du jury)

William D. Lubell  
(directeur de recherche)

À mes parents Faustin Tshibaka et Élisabeth Ntumba

## SOMMAIRE

Le couplage des aldéhydes aryliques et des amines pour donner les azométhines est une alternative intéressante pour la synthèse des comonomères conjugués. Contrairement aux techniques de couplage classiques qui conduisent à des mélanges de produits, il est possible, par cette méthode, d'obtenir sélectivement des composés ciblés et dissymétriques tout en contrôlant la stœchiométrie des réactifs et les solvants.



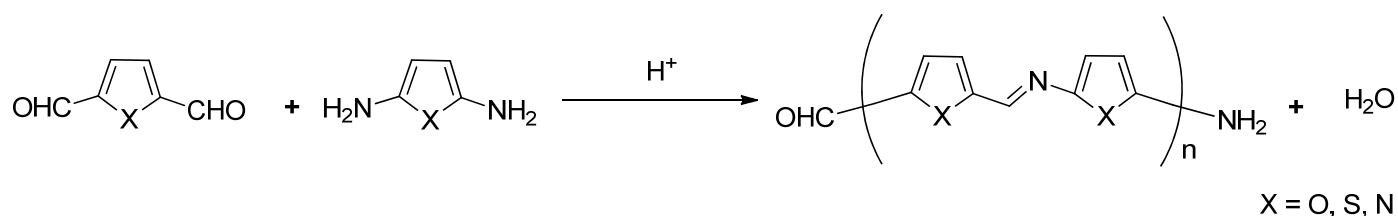
Dans le cadre de nos recherches sur les matériaux fonctionnels ayant des propriétés électrochromiques améliorées, nous avons planifié de conjuguer des thiophènes et des bipyrrroles dissymétriques par les liaisons azométhines. Tout d'abord des analogues des 4-méthoxy-2,2'-bipyrrroles **1-2** (chapitre 2) et **3-6** (chapitre 3) ont été synthétisés par une voie générale à partir de 4-hydroxyproline et convertis ensuite en dialdéhydes **8-13** (chapitre 3) qui, à leur tour, ont subi des condensations avec différents aminothiophènes pour donner les azométhines conjugués **17-23** (chapitre 3).

## MOTS CLÉS

Prodigiosine, polymères conducteurs, azométhine, 2,2'-bipyrrrole, réaction de Vilsmeier, 4-alkoxybipyrrrole, électrochimie, électrochromisme, rayon X.

## ABSTRACT

The condensation of amine and aldehyde functional groups is an attractive strategy for the synthesis of conjugated, conductive polymers. Unlike conventional coupling techniques that give a mixture of products, selective product formation affording unsymmetric products is possible by controlling the reagent stoichiometry and solvents.



A series of such polymers **17-23** (chapter 3) were synthesized by the dehydration of aminothiophenes and a series of asymmetric bisaldehydes **8-13** (chapter 3) featuring an asymmetric 4-methoxy-2,2'-bipyrrole core. The latter was constructed by a general route from 4-hydroxyproline providing derivatives **1-2** (chapter 2) and **3-6** (chapter 3), which were diformylated in the last step to afford the bisaldehyde monomers **8-13** (chapter 3). In the search for functional materials, the electrochromic properties of polymers **17-23** (chapter 3) were evaluated.

## KEY WORDS

Prodigiosin, conductive polymers, azomethine, 2,2'-bipyrrole, Vilsmeier reaction, 4-alkoxyproline, electrochemistry, electrochromism, X-ray

## **TABLE DES MATIÈRES**

SOMMAIRE	IV
MOTS CLÉS	IV
ABSTRACT	V
KEY WORDS	V
TABLE DES MATIÈRES	VI
LISTE DES FIGURES	IX
LISTE DES SCHÉMAS	XI
LISTE DES TABLEAUX	XIII
LISTE DES ABRÉVIATIONS	XIV
REMERCIEMENTS	XVI

## **CHAPITRE 1 : INTRODUCTION**

1.1 2,2'-bipyrroles	2
1.2 Synthèses des 2,2'-bipyrroles	3
1.2.1 Les 2, 2'-bipyrroles symétriques	3
1.2.2 Les 2,2-bipyrroles comme sous unités des Prodigiosines	5
1.2.3 Les 2,2'-bipyrroles dissymétriques	8
1.3 Polymères conducteurs	12
1.4. Les polyazométhines	14
1.4.1 Liaison azométhine	14

1.4.2 Azométhines précédemment synthétisées	15
1.5 Relation entre la structure et les propriétés	18
1.6 Notre intérêt de recherche	19
1.7 Références	21

## CHAPITRE 2 :

**Article 1 :** Tshibaka, T.; Roche, I. U.; Dufresne, S.; Lubell, W. D.; Skene, W. G. « Unsymmetric Electronic Push-Pull Bipyrrroles – Synthesis, Spectroelectrochemical, and Photophysical Investigation » *J. Org. Chem.* **2009**, 74, 9497-9500.

2.1 Introduction	26
2.2 Abstract	27
2.3 Introduction	29
2.4 Synthesis	30
2.5. Electrochemistry	32
2.6 Spectroscopy	36
2.7 Experimental Section	39
2.8 References	41
2.9 Contribution des co-auteurs pour l'article 1	44

## CHAPITRE 3 :

**Article 2 :** Tshibaka, T.; Bishop, s.; Roche, I. U.; Dufresne, S.; Lubell, W. D.; Skene, W. G. « Conjugated 4-methoxybipyrrole thiophene azomethines: synthesis, opto-electronic properties and crystallographic characterization » *Chem. Eur. J.* **2011**, 17, 10789-10888

3.1 Introduction	46
3.2 Abstract	49
3.3 Introduction	50
3.4 Experimental Section	52
3.5 Crystal Structure Determination	63
3.6 Results and Discussion	64
3.6.1 Synthesis	64
3.6.2 X-ray Crystallography	74
3.6.3 Electrochemistry	80
3.6.4 Chemical Oxidation	85
3.7 Conclusion	87
3.8 References	88
3.9 Contribution des co-auteurs pour l'article 2	92
<b>CHAPITRE 4 : CONCLUSION</b>	
4.1 Conclusion	94
4.2 Références	98
<b>Annexe</b>	
Données spectrales des chapitres 2 et 3	99



## LISTE DES FIGURES

### CHAPITRE 1

- Figure 1.** Structure de produits naturels contenant le 2,2'-bipyrrole 2
- Figure 2.** bipyrroles synthétisés par la réaction de Paal Knorr 11

### CHAPITRE 2

- Figure 1.** Cyclic voltammogram of **2** recorded in deaerated and anhydrous dichloromethane with 0.1 M TBAPF<sub>6</sub> supporting electrolyte at a sweep rate of 100 mV/sec. 33
- Figure 2.** Change in absorption of **1** with 0, 1, 5, and 4 min at a potential of + 850 mV followed by 2.5, 5, and 8 min at a potential of - 200 mV. 35
- Figure 3.** Normalized absorption spectra of **3** recorded in acetonitrile, dichloromethane, 4: 1 methanol/ethanol. 36
- Figure 4.** Normalized transient absorption spectra of **4** and xanthone reference measured at 1  $\mu$ s after the laser pulse at 266 nm in deaerated and anhydrous acetonitrile. 37

### CHAPITRE 3

- Figure 1.** Front view of **20** and seen along the *c* axis 73
- Figure 2.** Intermolecular interactions of **20** 74
- Figure 3.** Crystal packing of **20** with solvent molecules omitted for clarity 74

**Figure 4.** Cyclic voltammogram of **20** measured at scan rates between 200 and 900 mV and Randles-Sevcik plot of the first and second oxidation peaks of **20** relative to ferrocene measured in dichloromethane 80

**Figure 5.** Absorbance spectra change of **20** upon applying an oxidation potential of 0.4 V for 0 to 5 min. and color change of **20** before and after electrochemical oxidation. 81

**Figure 5.** Absorbance spectra change of **22** and color change of **22** before and after electrochemical oxidation. 81

**Figure 6.** Absorbance of **20** with added TFA followed by the addition of Et<sub>3</sub>N and Change in color of **20** with the addition of increasing amounts of TFA followed by the addition of triethylamine. 86

# LISTE DES SCHÉMAS

## CHAPITRE 1

<b>Schéma 1</b> : Synthèse de 2,2'-bipyrroles par la réaction d'Ullmann	3
<b>Schéma 2</b> : Synthèse des 2,2'-bipyrroles symétriques	4
<b>Schéma 3</b> : Synthèse de 2,2'-bipyrroles par désulfuration des thienodipyrroles	5
<b>Schéma 4</b> : Synthèse de 2,2'-bipyrroles par déshydrogénation catalytique du 2,2'-pyrrolinylpyrrole	6
<b>Schéma 5</b> : formation de 2,2'-bipyrroles par catalyse de palladium II	6
<b>Schéma 6</b> : Synthèse de 2,2'-bipyrroles par couplage oxydatif entre un pyrrole et un intermédiaire iminohydroperoxyde et par cyclisation d'un vinyl tricarbonyle.	7
<b>Schéma 7</b> : Synthèse de 2,2'-bipyrroles par couplage entre un boronopyrrole et un pyrrolyltriflate	8
<b>Schéma 8</b> : Synthèse de 2,2'-bipyrrole par réaction des cyclopropanes donneurs-accepteurs avec les 2-cyanopyrroles	9
<b>Schéma 9</b> : Formation de 2,2'-bipyrrole par la réaction d'aza-Nazarov	9
<b>Schéma 10</b> : synthèses des 2,2'-bipyrroles par la réaction de Paal-Knorr	10
<b>Schéma 11</b> : Formation de la liaison azométhine	14
<b>Schéma 12</b> : Mécanisme de formation d'une imine catalysée par un acide.	15
<b>Schéma 13</b> : Formation de la liaison imine suivie d'une estérification	16
<b>Schéma 14</b> : Les comonomères dissymétriques obtenus par la formation des liaisons azométhines	17

**CHAPITRE 2**

<b>Scheme 1.</b> Synthesis of bipyrrroles <b>3</b> and <b>4</b>	30
---	----

**CHAPITRE 3**

<b>Scheme 1.</b> <i>N</i> <sup>7</sup> -Modification of bipyrrrole <b>2</b> .	64
---	----

<b>Scheme 2.</b> Vilsmeier-Haack formylation of methoxybipyrrrole <b>1</b> .	65
--	----

<b>Scheme 3.</b> Vilsmeier-Haack formylations of 1-phenylsulfonyl methoxybipyrrroles <b>2-6</b> .	66
---	----

<b>Scheme 4.</b> Condensations of methoxybipyrrroles <b>8</b> and <b>9</b> with amino thiophene <b>16</b> .	68
---	----

<b>Scheme 4.</b> Condensations of methoxybipyrrroles <b>8</b> and <b>9</b> with amino thiophene <b>19</b> .	70
---	----

<b>Scheme 5.</b> Condensation of methoxybipyrrroles <b>12</b> with amino thiophene <b>19</b> .	71
--	----

<b>Scheme 6.</b> Condensation of methoxybipyrrroles <b>11</b> with amino thiophene <b>19</b>	72
--	----

## LISTE DES TABLEAUX

### CHAPITRE 1

<b>Tableau 1.</b> Rendements de 2,2-bipyrroles synthétisés par déshydrogénation catalytique du 2,2'-pyrrolinylpyrrole	6
---	---

### CHAPITRE 2

<b>Table 1.</b> Electrochemical data of bipyrroles measured in anhydrous and deaerated dichloromethane with 0.1 M TBAPF <sub>6</sub> .	34
--	----

### CHAPITRE 3

<b>Table 1.</b> Details of Crystal Structure Determination for <b>20</b>	77
<b>Table 2.</b> Spectroscopic and electrochemical data of neutral and corresponding radical cations of unsymmetric bipyrrole azomethines	79

## LISTE DES ABREVIATIONS

AcOEt	acetate d'éthyle
Bn	benzyle
Bu	butyle
°C	degré Celsius
Cald	Calculated
CCM	chromatographie sur couche mince
COSY	<i>correlation spectroscopy</i>
$\delta$	déplacement chimique en partie par million
d	doublet
dd	doublet de doublet
DCM	dichlorométhane
DMF	diméthylformamide
DMSO	diméthyl sulfoxyde
Et	éthyle
ES-MS	<i>Electron Spray Mass Spectroscopy</i>
Hz	Hertz
$J$	constante de couplage
KHMDS	hexaméthylidisilazane de potassium
LCMS	<i>Liquid Chromatography Mass Spectroscopy</i>
m	multiplet
M	molaire (mole/litre)
Me	méthyle

mg	milligramme
MHZ	mégahertz
min	minutes
mL	millilitre
mmol	millimole
m.p.	<i>Melting Point</i>
NaHMDS	hexaméthylidisilazane de sodium
NMR	<i>nuclear magnetic resonance</i>
NOESY	<i>nuclear overhauser effect spectroscopy</i>
p.f.	point de fusion
Ph	phenyl
PhF	9-(9-phénylfluorényle)
rt	<i>Room temperature</i>
s	seconde
t	triplet
THF	tétrahydrofurane

## REMERCIEMENTS

Je tiens d'abord à remercier le professeur William D. Lubell pour m'avoir permis d'effectuer mes études de maîtrise dans son groupe de recherche. Je le remercie de la confiance qu'il m'a témoignée durant mes études. Sa passion pour la chimie, ses connaissances et son sens critique ont grandement contribué à faire de moi le scientifique que je suis aujourd'hui.

Je remercie aussi tous les membres du groupe de recherche, anciens et présents, avec qui j'ai eu la chance de travailler et de qui j'ai beaucoup appris. Notamment, Benoit Jolicoeur pour ses conseils ainsi que les docteurs David Sabatino et Tarek Kassem qui ont partagé agréablement mon quotidien au D-636.

Je remercie également les techniciens des laboratoires de résonance magnétique nucléaire et de spectrométrie de masse ainsi que Lyne Laurin et surtout Mildred Bien-Aimé pour leur assistance aux tâches administratives.

Enfin, je tiens à remercier de tout cœur mes parents et mes frères Judith, Wivine, JC, Meta, Sylvain, Virginie et Mamy pour leur appui inconditionnel. Merci pour votre support moral mais surtout pour votre amour. Merci à ma fiancée Clarisse-Angel pour sa patience, son assistance et son amour.

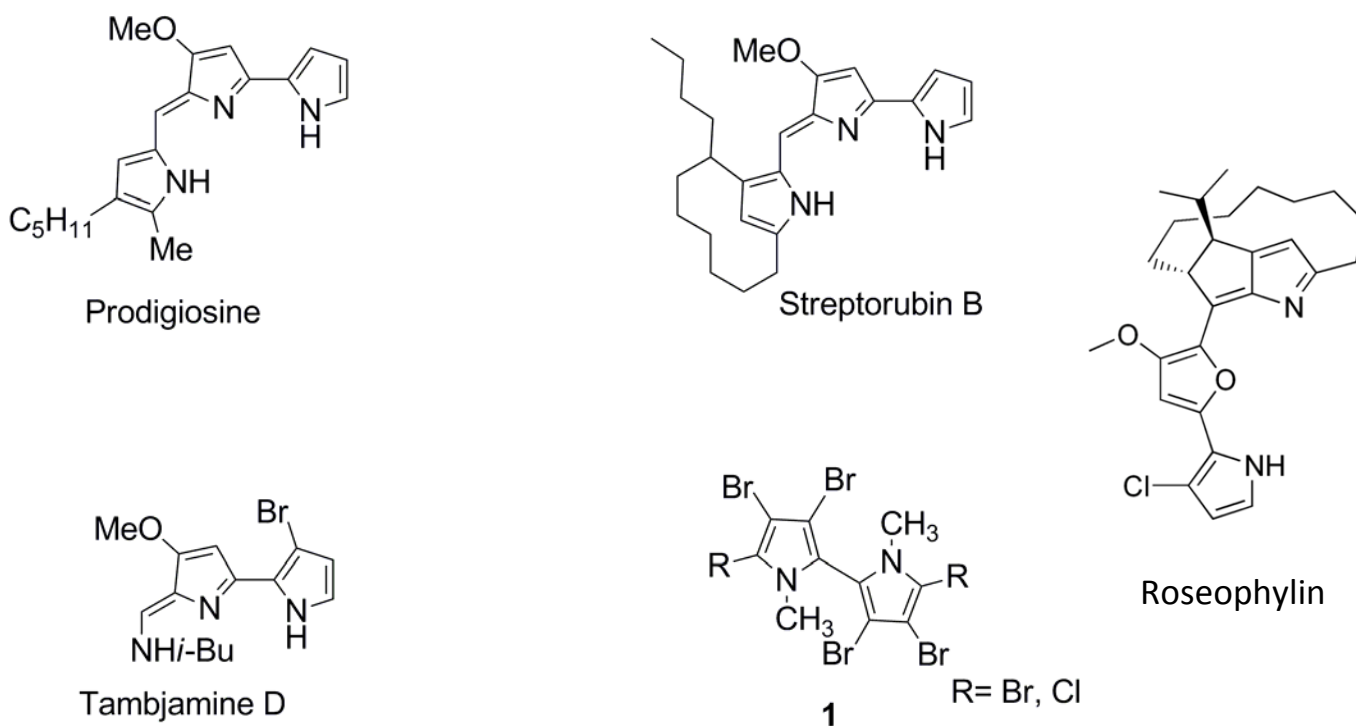


## **Chapitre 1**

### **Introduction**

## 1.1 2,2'-Bipyrroles

L'abondance de pyrroles dans les produits naturels, pharmaceutiques et les nouveaux matériaux est à l'origine de l'intérêt grandissant porté à cette classe de composés. Dans cette famille, les 2,2'-bipyrroles jouissent d'un intérêt certain lié à la présence de ces motifs dans des produits naturels d'importance tels que les dérivés de prodigiosine<sup>2</sup> ou de Tambjamines (Fig.1). Récemment, la présence d'un certain nombre des bipyrroles halogénés **1** (Fig. 1) ont également été découverts<sup>3</sup> dans les œufs d'oiseaux des océans Pacifique et Atlantique. Les 2,2'-bipyrroles sont utilisés comme précurseurs dans la synthèse des prodigiosines<sup>2a</sup>, des porphyrines<sup>4</sup> et des polymères nano-conducteurs<sup>5</sup>.



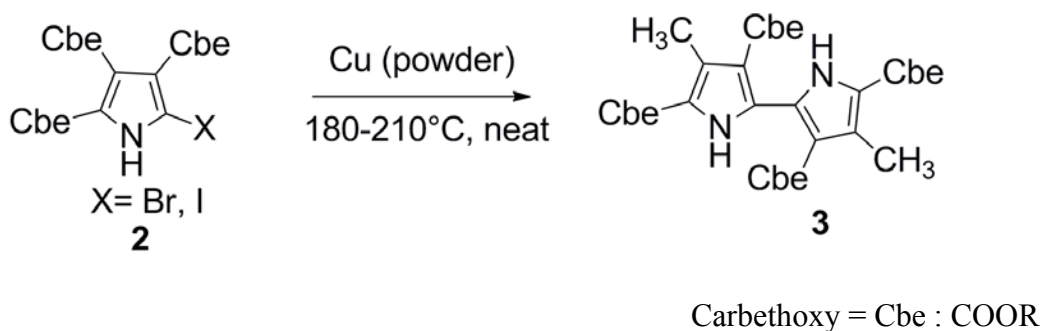
**Figure 1** : Structure de produits naturels contenant un 2,2'-bipyrrole

## 1.2 Synthèses des 2,2'-bipyrroles

### 1.2.1 Les 2, 2'-bipyrroles symétriques

Les premières synthèses de bipyrroles reportées dans la littérature utilisaient des conditions de réaction drastiques et les produits de ces réactions étaient souvent polysubstitués et symétriques<sup>6</sup>. Il existe diverses méthodes de synthèse des 2,2'-bipyrroles symétriques, la plupart étant des réactions de couplage faisant intervenir les métaux de transition.

En 1953, la réaction d'Ullmann a été utilisée pour effectuer l'homocouplage du 2-bromo ou 2-iodo-pyrroles dans la synthèse des 2,2'-bipyrroles<sup>7</sup>. Cette synthèse est réalisée à des températures élevées et sans solvant en utilisant le cuivre comme catalyseur. Cependant cette réaction exige la présence d'au moins deux groupements carboxyliques sur chaque pyrrole (schéma 1). L'utilisation d'un solvant tel que le *N,N*-diméthylformamide permet toutefois de réduire considérablement la température de cette réaction<sup>8</sup>.



**Schéma 1** : Synthèse de 2,2'-bipyrroles par la réaction d'Ullmann<sup>7</sup>

D'autres stratégies développées plus tard permettent d'obtenir des 2,2'-bipyrroles symétriques. Parmi elles, on peut citer quelques exemples tels que le couplage oxydatif du stannylate de 2-triméthyle pyrrole utilisant le cuivre II comme catalyseur<sup>9</sup>, le couplage des pyrroles catalysé par le bis(trifluoroacétate) de l'iodophenyle<sup>10</sup>, le couplage des lithiopyrroles catalysés par le nickel<sup>11</sup> ainsi que la réaction sous pression des dioximes en présence d'acétylène<sup>12</sup> (réaction de Trofimov<sup>13</sup>) (schéma 2).

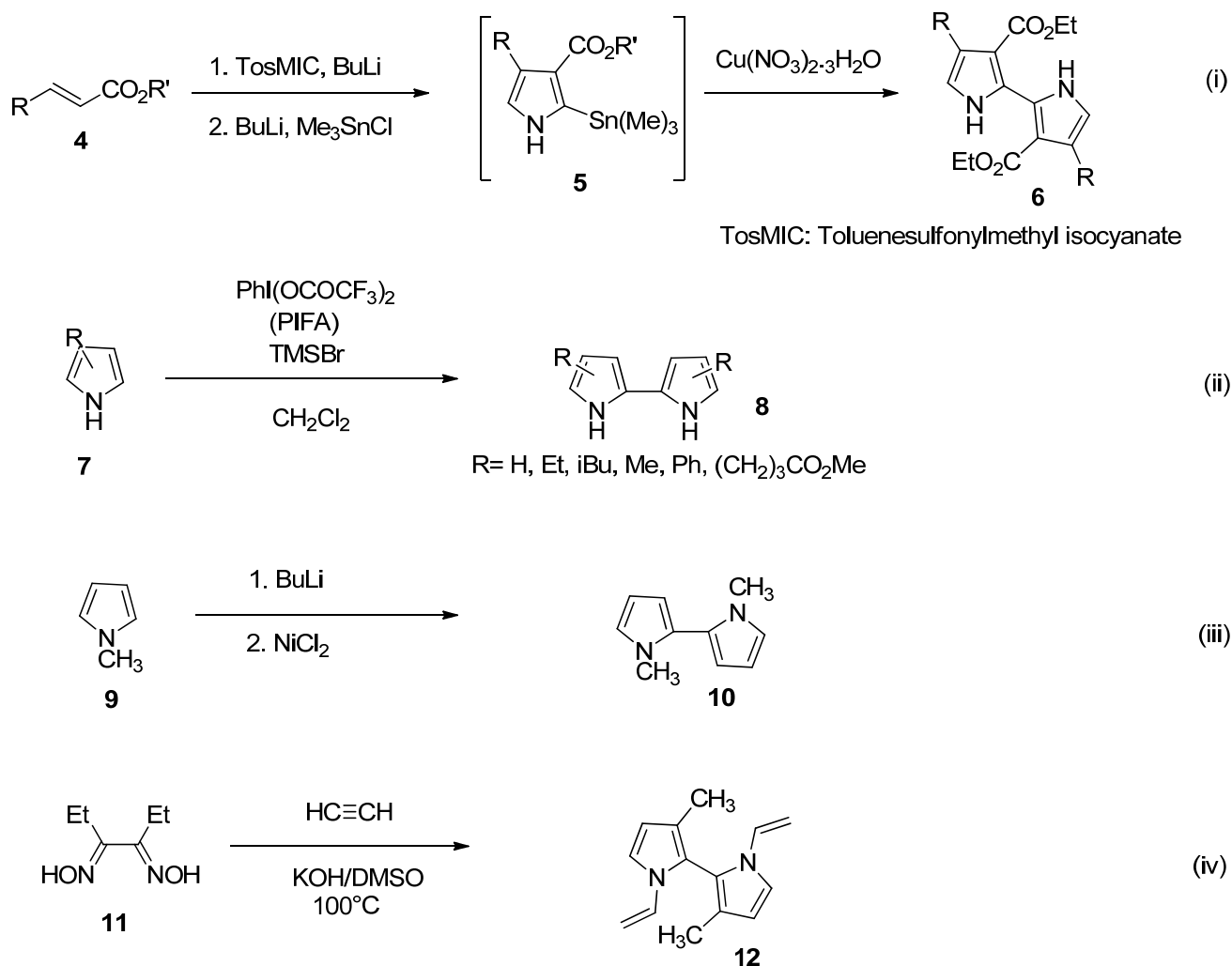
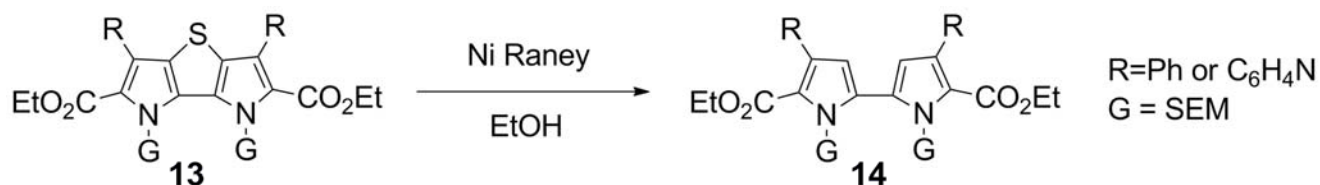


Schéma 2 : Synthèse des 2,2'-bipyrroles symétriques<sup>9,10,11,12</sup>

Une autre méthode de synthèse symétrique est celle réalisée par la désulfuration des thienodipyrroles suivie d'une déprotection du bipyrrrole obtenu<sup>14</sup> (schéma 3).



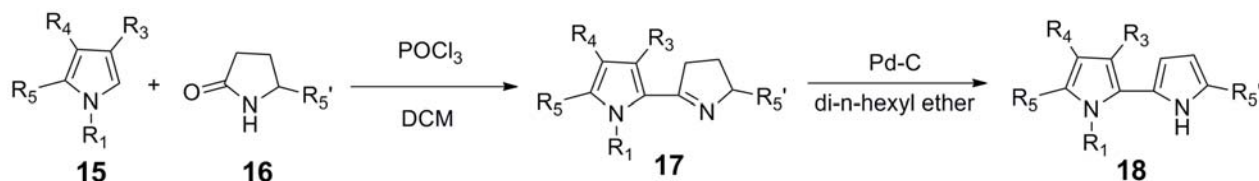
**Schéma 3** : Synthèse de 2,2'-bipyrrroles par désulfuration des thienodipyrroles<sup>14</sup>

### 1.2.2 Les 2,2'-bipyrrroles comme sous-unités des Prodigiosines

Quelques stratégies de synthèse du 2,2'-bipyrrrole ont également été développées dans l'objectif de synthétiser la sous-unité 5-carboxaldéhyde-4-méthoxy-2,2'-bipyrrrole contenue dans la prodigiosine.

Au début des années soixante, dans leur effort de réaliser la première synthèse totale de la Prodigiosine, le groupe de Rapoport a préparé des bipyrrroles dissymétriques et moins substitués. Pour ce faire, ils ont utilisé la déshydrogénation catalytique du 2,2'-pyrrolidinylpyrrole préparé à partir du pyrrole et de 1-pyrroline<sup>2a,6,15a-b</sup>. Pour surmonter les problèmes de rendement rencontrés lors de deux étapes de cette réaction (condensation et déshydrogénation), le 2,2'-bipyrrrole a ensuite été synthétisé par condensation de type Vilsmeier entre un pyrrole **15** et un 2-pyrrolidinone **16** suivi de la déshydrogénation du 2,2'-pyrrolinylpyrrole **17** formé (schéma 4). La présence des groupements esters sur les pyrroles rend

encore problématique l'étape de la condensation car ils rendent ces derniers moins nucléophiles<sup>15b</sup>.

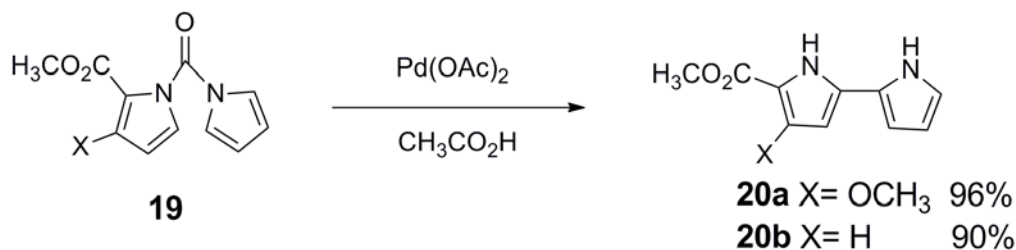


**Schéma 4** : Synthèse de 2,2'-bipyrroles par déshydrogénation catalytique du 2,2'-pyrrolinylpyrrole<sup>15b</sup>

**Tableau 1** : rendements de 2,2-bipyrroles synthétisés par déshydrogénation catalytique du 2,2'-pyrrolinylpyrrole<sup>15b</sup>

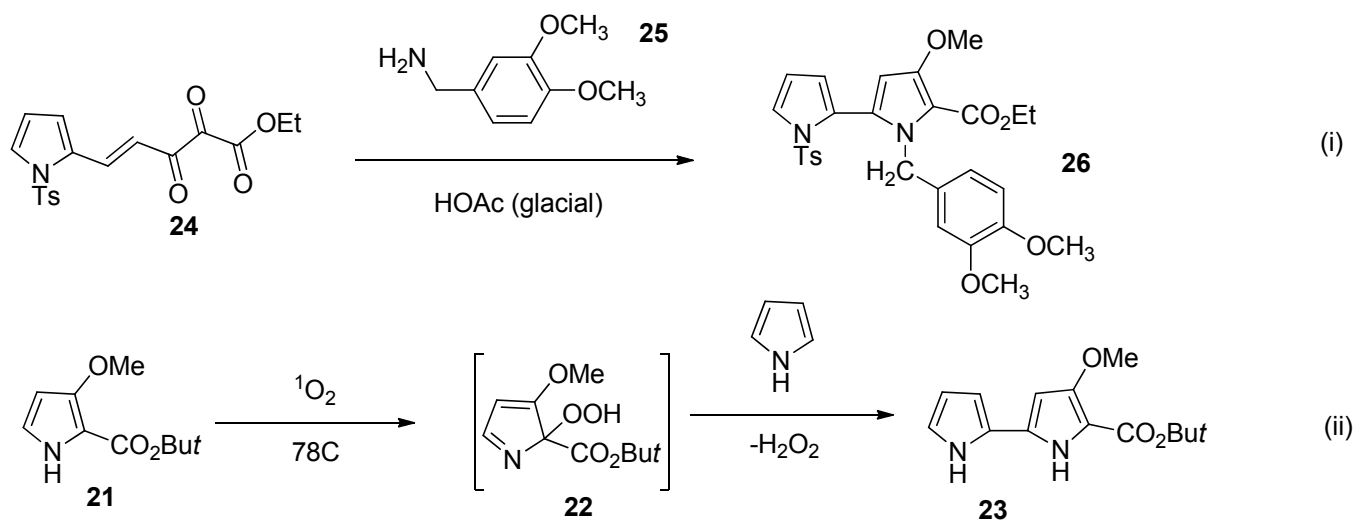
18	R1	R3	R4	R5	R5'	Rendement (%)
A	H	H	H	CH3	H	29
B	H	H	H	H	CH3	29
C	H	H	H	CH3	CH3	24
D	H	H	CH3	H	H	22
E	H	CH3	H	H	H	25
F		CH3	CO2C2H5	H	H	46
G	H	H	H	H	CO2CH3	79
H	CH3	H	H	H	CO2CH3	45

Boger et son équipe<sup>16</sup> ont utilisé le couplage oxydatif intramoléculaire de 1,1'-carbonyldipyrroles **19** catalysé par le palladium II suivi de la méthanolyse du 1,1'-carbonyl-2,2'-bipyrrole formé (schéma 5).



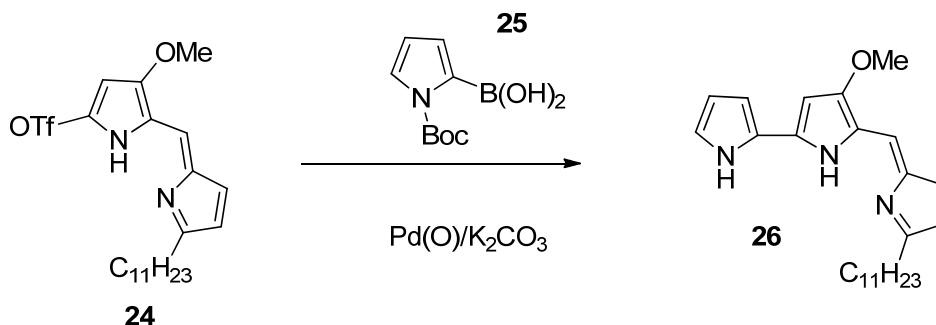
**Schéma 5** : formation de 2,2'-bipyrroles par catalyse de palladium II<sup>16</sup>

Wasserman et ses collaborateurs ont par ailleurs développé deux méthodes pour synthétiser la sous-unité 2,2'-bipyrrole des Prodigiosines. D'abord, ils ont utilisé l'amination d'un tricarbonyle vinylique **24** suivi d'une déprotection<sup>17</sup> (schéma 6). Par la suite, ils ont effectué le couplage oxydatif intermoléculaire entre un pyrrole et un intermédiaire iminohydroperoxide **22** produit lors de l'oxydation de l'ester *tert*-butylique du 3-méthoxypyrrole par l'oxygène à l'état singulet<sup>18</sup> (schéma 6)



**Schéma 6 :** Synthèse de 2,2'-bipyrroles par couplage oxydatif entre un pyrrole et un intermédiaire iminohydroperoxide<sup>17</sup> et par cyclisation d'un tricarbonyle vinylique<sup>18</sup>.

Dans le but de synthétiser l'undecylprodigiosine, un dérivé de prodigiosine, le 2,2'-bipyrrolo-pyrrométhène **26** a été synthétisé par couplage de Suzuki entre un acide boronique de pyrrole **25** et un triflate de pyrrolyle **24**<sup>19</sup>(schéma 7).

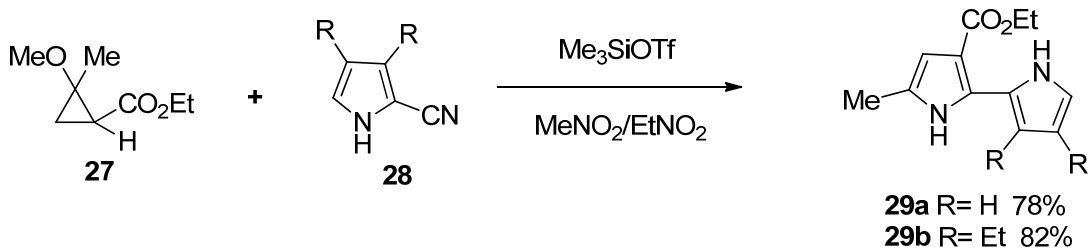


**Schéma 7** : Synthèse de 2,2'-bipyrroles par couplage entre un boronopyrrole et un triflate de pyrrolyle<sup>19</sup>

### 1.2.3 Les 2,2'-bipyrroles dissymétriques

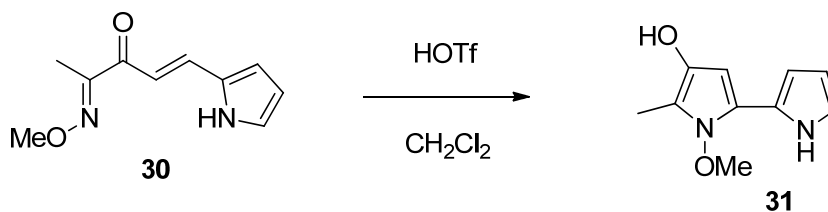
Récemment, des nouvelles stratégies capables d'apporter de la diversité et de produire des bipyrroles non symétriques ont été développées. En 2004, B.L. Pangenkopf et coll.<sup>20</sup> ont utilisé les réactions de cyclopropanes donneurs-accepteurs **27** avec les 2-cyanopyrroles **28** en présence du triflate de triméthylsilyle. La cyclisation, la tautomerisation, et la déshydratation qui s'ensuit produit les 2,2'-bipyrroles désirés (schéma 8).





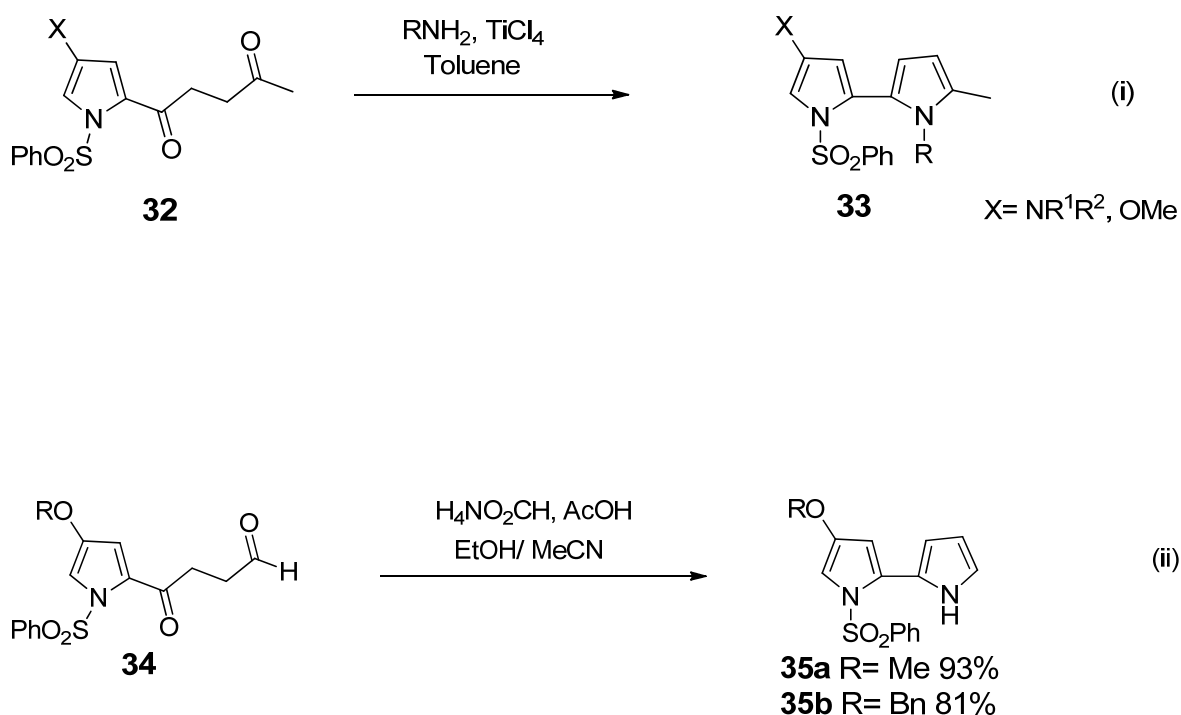
**Schéma 8** : Synthèse de 2,2'-bipyrrole par réaction des cyclopropanes donneurs-accepteurs avec les 2-cyanopyrroles

Dans leurs efforts vers la synthèse des 3-hydroxypyrroles, E. U. Wurthwein et son groupe<sup>21</sup> ont utilisé la réaction de cyclisation d'Aza-Nazarov d'un azadione **30** en présence d'un acide organique fort pour former le 2,2'-bipyrrole **31** (schéma 9).

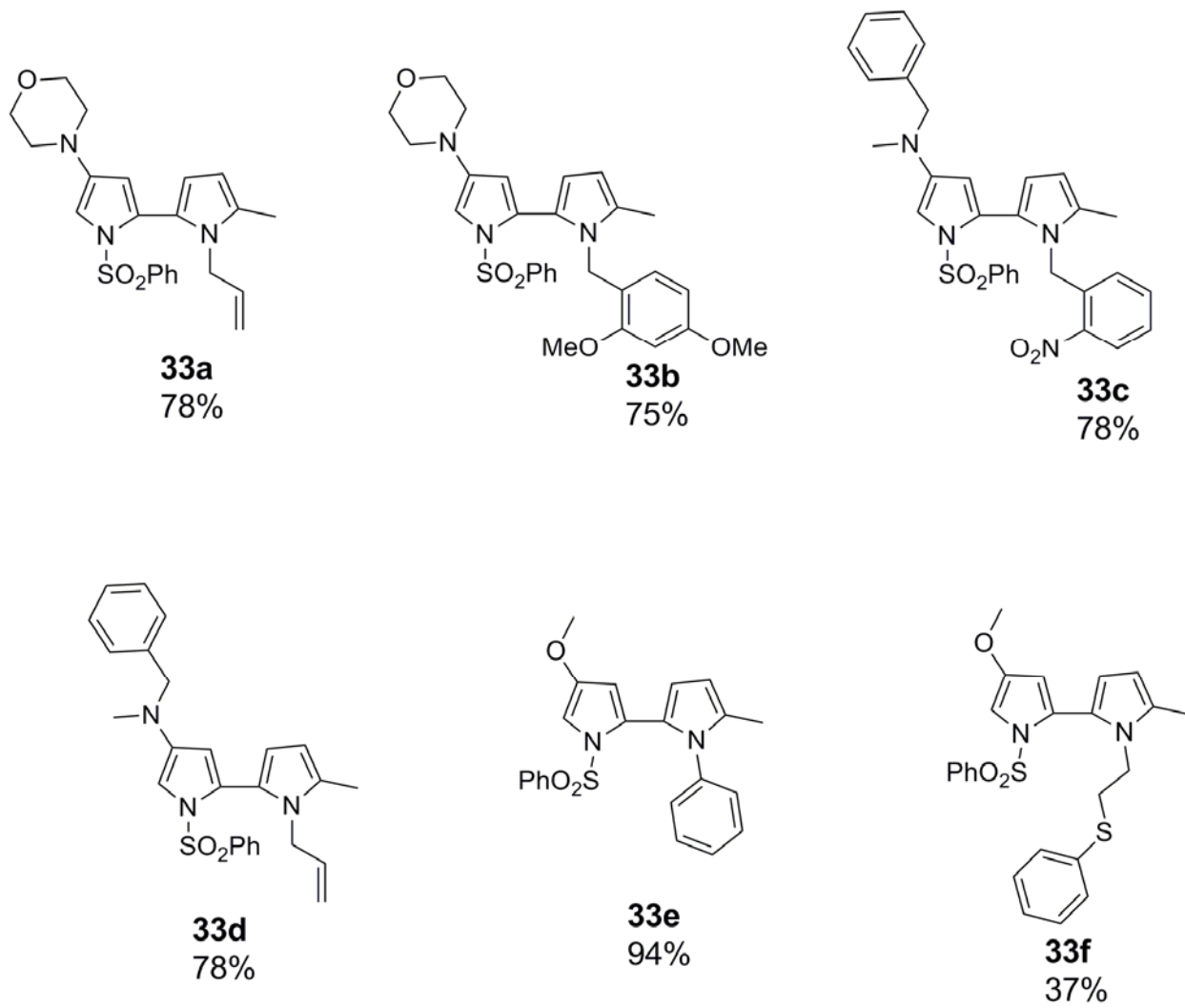


**Schéma 9** : Formation de 2,2'-bipyrrole par la réaction d'aza-Nazarov<sup>21</sup>

Récemment, le groupe Lubell a développé une nouvelle stratégie permettant de synthétiser des 4-alkoxy et 4-amino-2,2'-bipyrroles à partir de 4-hydroxyproline<sup>22,23,24,25</sup>. Les étapes clés de cette méthode comprennent la synthèse d'une cétone homoallylique par la réaction entre un ester méthylique de la proline et un excès de bromure de vinylmagnésium, une oxydation d'oléfine par le protocole d'oxydation de *Tsuji-Wacker* ou par le système OsO<sub>4</sub>/NaIO<sub>4</sub> et, à la fin de la séquence, une condensation de *Paal-Knorr* conduisant au bipyrrole désiré (schéma 10).



**Schéma 10** : synthèses des 2,2'-bipyrroles par la réaction de Paal-Knorr<sup>22-25</sup>



**Figure 2.** bipyrroles synthétisés par la réaction de Paal Knorr<sup>23</sup>

### 1.3 Polymères conducteurs

Jusqu'il y a 40 ans, l'idée qu'un polymère organique puisse être un conducteur d'électricité était considérée comme absurde. Cette perception a changé lorsqu'un étudiant gradué de l'institut de Technologie de Tokyo a obtenu un mince film argenté ayant une conductivité d'à peu près  $10^{-3}$  Sm (similaire aux semi conducteurs) alors qu'il tentait de synthétiser du polyacéthylène.

Les années 80 marquèrent l'émergence des polyhétérocycles. Bien que la conductivité de ces derniers soit moins grande, ces composés présentent l'avantage d'être plus stables à température ambiante par rapport aux polyacéthylènes. De plus, leurs propriétés (couleur, solubilité, réactivité face aux agents oxydants et réducteurs,..) peuvent être contrôlées par simples modifications des groupements attachés au polymère.

Il existe de nombreuses voies de synthèse des polymères conducteurs. La méthode de polymérisation anodique (chimique et électrochimique) est celle qui est utilisée le plus souvent. Elle présente de nombreux avantages tels que l'absence de catalyseur. Elle permet également le dépôt direct des polymères formés sur la surface de l'électrode donnant ainsi la possibilité de les caractériser *in situ* par électrochimie ou par spectroscopie. Cependant cette méthode souffre de problèmes de régio-selectivité.

Parmi les autres méthodes employées, citons par exemple la polymérisation utilisant la métathèse par ouverture de cycle<sup>26,27</sup>, la réaction de *Wessling*<sup>28</sup>, les réactions de *Wittig* et ses dérivés<sup>29,30</sup>, la réaction de *Knoevenagel*<sup>31,32</sup> ou encore le réaction de *McMurry*<sup>33,34,35</sup>.

Malgré que ces différentes méthodes permettent d'obtenir les composés désirés, elles présentent de problèmes de purification dus essentiellement à la présence de métaux ou de produits secondaires en grande quantité (réaction de Wittig). Ces méthodes aboutissent également à des

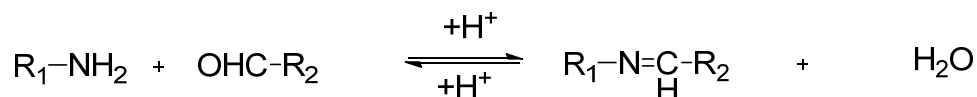
défauts de structures (saturation du squelette carboné par exemple) pouvant altérer les propriétés électroniques du polymère<sup>36</sup>.

## 1.4. Les polyazométhines

### 1.4.1 Liaison azométhine

La liaison azométhine, aussi appelé imine, sert à protéger un aldéhyde ou une amine car étant facilement réversible. Elle est utilisée dans la synthèse de polymères conjugués essentiellement pour deux raisons.

Le sous-produit de la réaction de condensation entre une amine et un aldéhyde est l'eau (schéma 11). Cela confère un caractère `` chimie verte`` et donc un avantage par rapport aux préoccupations de l'heure concernant la sauvegarde de l'environnement. En plus, cette liaison est encore plus robuste et presque irrésistible lorsque les réactifs aryles conjugués sont utilisés. Ainsi la résistance chimique de ces liaisons permet de synthétiser des oligomères et des polymères stables sous conditions ambiantes.

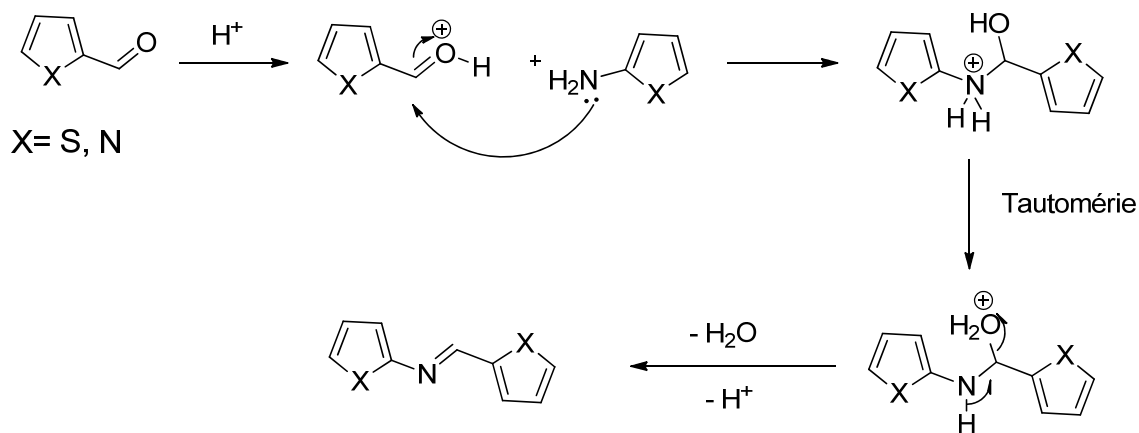


**Schéma 11** : Formation de la liaison azométhine

Les conditions réactionnelles pour la synthèse des azométhines ne sont pas exigeantes et dépendent de la réactivité de l'amine. La réaction peut se faire sans assistance des catalyseurs métalliques évitant ainsi la contamination due aux résidus métalliques nécessitant des lourdes purifications et entraînant une altération des propriétés physiques du produit final<sup>37-41</sup>.

Un autre avantage à utiliser les liaisons azométhines est le fait qu'elles sont isoélectroniques<sup>42,43</sup> à leurs analogues carbonés, les rendant ainsi adaptées à des utilisations comme matériaux conducteurs<sup>44</sup>.

La réactivité de l'amine sur l'aldéhyde détermine l'utilisation ou non d'un acide de Lewis comme le  $\text{TiCl}_4$ . Si l'amine n'est pas trop désactivée, un simple ajout d'acide fort tel le TFA (schéma 12) suffit pour activer la réaction. Si par contre l'amine est moins réactive, il est alors nécessaire d'ajouter le  $\text{TiCl}_4$  qui force la déshydratation et déplace ainsi l'équilibre vers la formation de l'imine. Le titane coordonne l'atome d'oxygène du carbonyle préparant ainsi le carbonyle à la réaction avec l'amine, suivie du transfert de l'oxygène à l'atome de titane<sup>45-46</sup>.

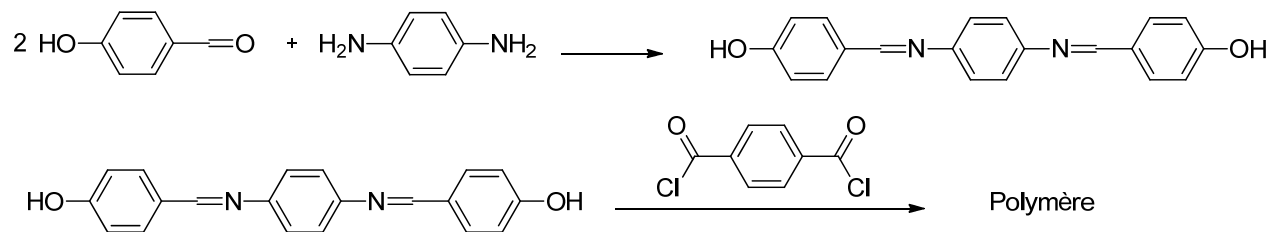


**Schéma 12** : Mécanisme de formation d'une imine catalysée par un acide.

### 1.4.2 Azométhines décrits dans la littérature

Il existe relativement peu d'exemples de synthèse de polyazométhines dans la littérature en comparaison avec les autres classes de polymères conjugués, dû en grande partie au nombre limité des précurseurs diamino aryles stables existants.

Des dérivés benzéniques peuvent être synthétisés à partir des précurseurs diamino benzéniques. Tout d'abord le monomère contenant la liaison imine est formé puis on le polymérise. La polymérisation se fait par voie radicalaire<sup>47</sup>, par estérification<sup>48</sup> (schéma 13) ou par polymérisation anodique<sup>49</sup>.



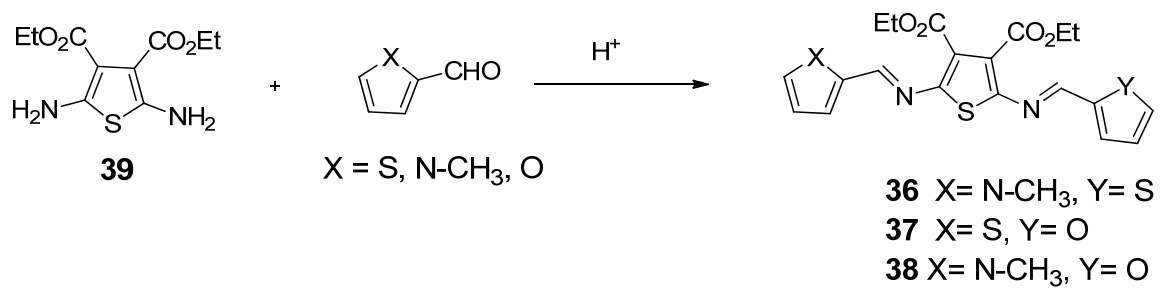
**Schéma 13:** Formation de la liaison imine suivie d'une estérification.

Cependant les précurseurs homoaryliques utilisés dans ces réactions sont problématiques à cause de leur oxydation indésirable à température ambiante. En plus les polyazométhines formés souffrent de problèmes de solubilité, de décomposition oxydative, de formation de radical cation irréversible ainsi que des propriétés conductrices et électriques pauvres<sup>50</sup>.

Récemment, Skene et son équipe<sup>50</sup> ont synthétisé des oligomères de 4 et 5 unités de thiophène en utilisant le 2,5-diaminothiophène **39** (schéma 14) comme précurseur. Cette molécule est largement reconnue à cause de ses propriétés conductrices et électroniques en plus d'être stable à la température ambiante (grâce aux groupements électroattracteurs aux positions 3 et 4). Les polyazométhines qui en découlent sont stables, leurs radicaux cationiques sont réversibles et leurs propriétés conductrices et électriques sont très bonnes.

Pour faire suite à ces travaux, d'autres analogues conjugués et non symétriques **36-38** comprenant des thiophènes, des pyrroles et des furanes ont été produits<sup>51</sup> (schéma 14).





**Schéma 14** : Les comonomères dissymétriques obtenus par la formation des liaisons azométhines<sup>51</sup>.

## 1.5 Relation entre la structure et les propriétés

Dans le développement des polymères conjugués l'objectif recherché est une augmentation de conductivité, corrélée avec une diminution du potentiel d'oxydation et un décalage bathochromique du maximum d'absorption (conséquence de la réduction de l'écart énergétique entre l'HOMO et la LUMO).

Le degré de conjugaison augmente avec la longueur du polymère et provoque ainsi un déplacement bathochromique sur les spectres d'absorption et de fluorescence. Elle provoque également la diminution de la bande interdite<sup>50</sup>.

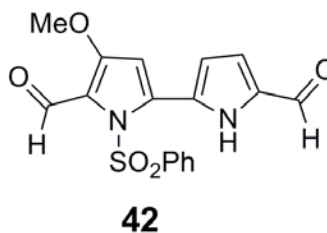
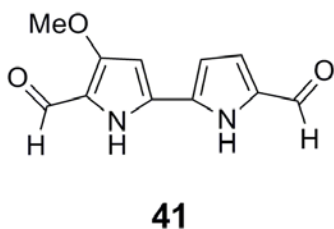
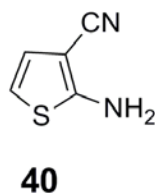
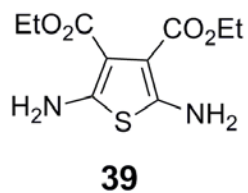
Les oligomères conjugués possédant des groupements électroniques donneurs et accepteurs en bouts de chaînes sont particulièrement intéressants car leurs propriétés spectrochimiques et électrochimiques sont influencées de façon significative par la nature de ces substituants. En effet, un groupement attracteur (resp. donneur) attire (resp. repousse) les électrons induisant un effet sur l'ensemble de la molécule grâce à la conjugaison. Ces effets peuvent être additifs si une molécule possède un groupement donneur à une extrémité et un groupement attracteur à l'autre; on parlera alors d'effet "push-pull". Si par contre une molécule possède deux groupements attracteurs (resp. donneurs), cet effet sera appelé l'effet "pull-pull" (resp. "push-push").

Les groupements esters sont connus pour influencer sélectivement la LUMO alors que les groupements amino agissent plus sur la HOMO. Les deux, mis ensemble, provoquent la diminution de la bande interdite et stabilisent le polymère<sup>25,50</sup>. En général les groupes électrodonneurs contribuent à diminuer les potentiels d'oxydation alors que les groupes électroattracteurs les rendent plus positifs. La tendance est inversée en ce qui concerne le potentiel de réduction.

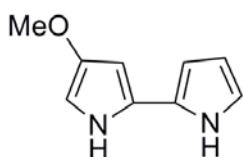
## 1.6 Notre intérêt de recherche

Ces travaux de maîtrise sont effectués dans le cadre d'une collaboration entre les laboratoires des professeurs Skene et Lubell. Ils s'inscrivent dans la recherche de nouveaux types de polymères basés sur la formation des liens imines. Dans la perspective d'améliorer les propriétés des polyazométhines et de les utiliser dans les matériaux conducteurs, nous nous sommes intéressés à synthétiser des oligomères dissymétriques constitués des thiophènes et des 4-méthoxy-2,2'-bipyrroles.

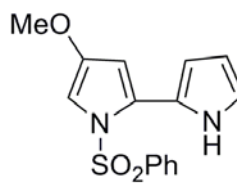
Les molécules choisies comme précurseurs pour ces polymères conjugués sont d'une part l'ester 3,4-diéthyle du 2,5-diaminothiophène **39** et le 2-amino-3-cyanothiophène **40** et d'autre part le 4-(Méthoxy)-5,5'-bisformyl-2,2'-bipyrrole **41** et le 4-(Méthoxy)-1-benzenesulfonyl-5,5'-bisformyl-2,2'-bipyrrole **42**.



Les deux thiophènes sont des molécules qu'on retrouve déjà dans la littérature et sont connus pour être des précurseurs de choix pour la formation des liens imines avec les aldéhydes aryliques. Ainsi nos deux principales cibles sont les synthèses des aldéhydes **41** et **42**. Ces derniers seront synthétisés par la réaction de Vilsmeier sur le 4-méthoxy-2,2'-bipyrrole **43** et son analogue sulfoné **35a** qui seront préparé à partir de la 4-hydroxyproline en 8 étapes.



**43**



**35a**

Ce mémoire sera divisé en deux parties présentées sous forme d'articles. Dans la première partie nous présentons la synthèse des bipyrroles dissymétriques et l'investigation des effets de substituants (cétone de trichlorométhyle, ester, méthoxy, sulfonamide) sur l'électrochromisme et leurs potentiels d'oxydation. Des études électrochimiques et spectroélectrochimiques seront également présentées et les relations structure-propriété établies.

La deuxième partie sera consacrée à la synthèse des azométhines conjugués et à l'étude de leurs propriétés.

## 1.7 Références

1. Bonnet, R.; Cannon, J. R.; Clark, M.; Johnson, A. W.; Parker, L. F. J.; Smith, E. L. ; Todd, A. *J. Chem. Soc.*, **1957**, 1158.
2. (a) Rapoport, H.; Holden, K. G. *J. Am. Chem. Soc.* **1962**, 84, 635-642; (b) Wasserman, H. H.; McKeon, J. E.; Smith, L.; Forgione, P. *J. Am. Chem. Soc.* **1960**, 32, 506
3. Gribble, G. W.; Blank, D. H.; Jasinski, J. P. *Chem. Commun.* **1999**, 21, 2195 - 21-96
4. Sessler, J. L.; Aguilar, A.; Sanchez-Garcia, D.; Seidel, D.; Kohler, T.; Arp, F.; Lynch, V. *M. Org. Lett.* **2005**, 7, 1887-1890
5. Tran, H. D.; Wang, Y.; D'Arcy, J. M.; Kaner, R. B. *ACS Nano* **2008**, 2, 1841-1848
6. Rapoport, H.; Castagnoli, N. *J. Am. Chem. Soc.* **1962**, 84, 2178-2181.
7. Webb, J. L. A.; Threlkeld, R. R. *J. Org. Chem.* **1953**, 18, 1406-1412.
8. Grigg, R.; Johnson, A. W.; Wasley, J. W. F. *J. Chem. Soc.* **1963**, 359-366.
9. Sanchez-Garcia, D.; Borell, J. I.; Nonell, S. *Org. Lett.* **2009**, 11, 77-79
10. Dohi, T.; Morimoto, K.; Maruyama, A.; Kita, Y. *Org. Lett.* **2006**, 8, 2007-2010
11. Gribble, G. W.; Blank, D. H.; Jasinski, J. P. *Chem. Comm.* **1999**, 2195-2196
12. Zaitsev, A. B.; Schmidt, E. Y.; Vasil'tsov, A. M.; Mikhaleva, A. I.; Petrova, O. V.; Afonin, A. V.; Zorina, N. V. *Chem.Hetrocycl. Compd.* **2006**, 42, 34-41.
13. Bergauer, M.; Hubner, H.; Gmeiner, P. *Tetrahedron* **2004**, 60, 1197- 1204.
14. Arad, O.; Morros, J.; Batllori, X.; Teixido, J.; Nonell, S.; Borrell, J. I. *Org. Lett.* **2006**, 8, 847-850.
15. (a) Fuhlhage, D. W.; VanderWerf, C. A. *J. Am. Chem. Soc.* **1958**, 80, 6249; (b) Rapoport, H.; Bodner, J. *J. Org. Chem.* **1964**, 29, 2727-2731.
16. Boger, D. L.; Patel, M. *J. Org. Chem.* **1988**, 53, 1405-1415.

17. Wasserman, H. H.; Lombardo, L. J. *Tetrahedron Lett.* **1989**, 30, 1725-1728.
18. Wasserman, H. H.; Xia, M. D.; Wang, J. J.; Petersen, A. K.; Jorgensen, M.; Power, P.; Parr, J. *Tetrahedron* **2004**, 60, 7419-7425.
19. (a) D'allessio, R.; Rossi, A. *Synlett* **1996**, 513-514. (b) Fürstner, A.; Grabowski, J.; Lehmann, C. W.; Kataoka, T.; Nagai, K. *ChemBiochem.* **2001**, 2, 60-68.
20. Yu, M.; Pantos, G. D.; Sessler, J. L.; Pagenkopf, B. L. *Org. Lett.* **2004**, 6, 1057-1059.
21. Dieker, J.; Frohlich, R.; Wurthwein, E.-U. *Eur. J. Org. Chem.* **2006**, 5339-5365.
22. Marcotte, F. A.; Lubell, W. D. *Org. Lett.* **2002**, 4, 2601-2603.
23. Jolicoeur, B.; Lubell, W. D. *Org. Lett.* **2006**, 8, 6107-6110.
24. Jolicoeur, B.; Lubell, W. D. *Can. J. Chem.* **2008**, 86, 213-218.
25. Tshibaka, T.; Lubell, W. D. *J. Org. Chem.* **2009**, 74, 9497-9500.
26. Pron, A.; Rannou, P. *Progress in polymer science* **2001**, 27, 135-190.
27. Edwards, J.H; Feast, W. J. *Polymer* **1980**, 21, 595-596
28. Wessling, R. A.; Zimmerman, R. G.; (Dow Chemical Co.) US 3,401,152, **1968**, p 4 pp
29. Drury, A.; Maier, S.; Ruther, M.; Blau, W.J. *J. Mater. Chem.* **2003**, 13, 485-490.
30. Jestin, I.; Frere, P.; Mercier, N.; Levillain, E.; Stievenard, D.; Roncali, J. *J. Am. Chem. Soc.* **1998**, 120, 8150-8158.
31. Egbe, D. A. M.; Kietzke, T.; Carbonnier, B.; Muhlbacher, D.; Horhold, H. H.; Neher, D.; Pakula, T. *Macromolecules* **2004**, 37, 8863-8873.
32. Thompson, B. C; Kim, Y. G.; McCarley, T. D.; Reynolds, J. R. *J. Am. Chem. Soc.* **2006**, 128, 12714-12725
33. McMurry, J. E. *Chem. Rev.* **1989**, 89, 1513-1524

34. Elandaloussi, E. H.; Frere, P.; Richomm, P.; Orduna, J.; Garin, J.; Roncali, J. *J. Am. Chem. Soc.* **1997**, 119, 10774-10784
35. Goldoni, F.; Jansen, R. A. J.; Meier, E. W. *J. Polym. Sci., Part A: Polym. Chem.* **1999**, 37, 4629-4639.
36. Bourgeaux, M. these de doctorat: Thiophènes azométhines : études de composés modèles pour des matériaux fonctionnels. **2008**
37. Schwendeman, I.; Hwang, J.; Welsh, D. M.; Tanner, D. B.; Reynolds, J. R. *Adv. Mater.* **2001**, 13, 634-637.
38. Mayor, M. S.; Nelson, T. L.; O'Sullivan, C.; Lavigne, J. J. *Org. Lett.* **2007**, 9, 3217-3220.
39. Kraft, A.; Grimsdale, A. C.; Holmes, A. B. *Angew. Chem. Int. Ed.* **1998**, 37, 402-428.
40. Lavastre, O.; Illitchev, I.; Jegou, G.; Dixneuf, P. H. *J. Am. Chem. Soc.* **2002**, 124, 5278-5279.
41. Leclerc, M. *J. Polym. Sci. Part A : Polym. Chem.* **2001** 39, 2867-2873.
42. Wang, C.; Shieh, S.; LeGoff, E.; Kanatzidis, M. G. *Macromolecules* **1996**, 29, 3147-3156
43. Yang, C.-J.; Jenekhe, S. A. *Chem. Mater.* **1991**, 3, 878-887.
44. Kiriy, N.; Bocharova, V.; Kiriy, A.; Stamm, M.; Krebs, F. C.; Adler, H.-J. *Chem. Mater.* **2004**, 16, 4765-4771.
45. Weingarten, H.; Chupp, J. P. White, W. A.; *J. Org. Chem.* **1967**, 32, 3245-3249.
46. White, W.A.; Weingarten, H. *J. Org. Chem.* **1967**, 32, 213-214.
47. Mandal, B. K.; Takahashi, T.; Maeda, M.; Kumar, S.; Blumstein, A.; Tripathy, S. *Makromolekulare Chemie* **1991**, 192, 1009-1016.

48. Sek, D. *Eur. Polym. J.* **1984**, 20, 805-809.
49. Sylla, M.; Manaila-Maximean, D.; Albu, A. M.; Delaunay, J. *Polymer* **2000**, 41, 3507-3511.
50. Bourgeaux, M.; Skene, W. G. *J. Org. Chem.* **2007**, 72, 8882-8892.
51. Dufresne, S.; Skene, W. G. *J. Org. Chem.* **2008**, 73, 3859-3866.



## Chapitre 2

### Article 1:

Tshibaka, T.; Roche, I. U.; Dufresne, S.; Lubell, W. D.; Skene, W. G. « Unsymmetric Electronic Push-Pull Bipyrrroles – Synthesis, Spectroelectrochemical, and Photophysical Investigation » *J. Org. Chem.* **2009**, 74, 9497-9500.

## 2.1 Introduction

Le potentiel des hétérocycles à former des radicaux ioniques stables et à être polymérisés en matériaux fonctionnels avec des potentiels d'oxydation faibles leur permettent de jouer un rôle majeur dans le développement de l'électronique plastique. En dépit de leurs propriétés prometteuses, les pyrroles sont moins utilisés dans les matériaux fonctionnels et dans les dispositifs. Dans ce chapitre 2, présenté sous forme d'article, les analogues de 4-méthoxy-2, 2'-bipyrroles **1-4** ( voir article 1) ont été synthétisés à partir de 4-hydroxyproline et leurs relations structure-propriété ont été caractérisées spectroscopiquement, électrochimiquement et spectroélectrochimiquement. L'influence du groupement méthoxy et ceux des groupements électro-accepteurs (cétone de trichlorométhyle, ester et sulfonamide) sur les potentiels d'oxydation et des propriétés spectroscopiques ont également été établis.

# Unsymmetric Electronic Push-Pull Bipyrroles – Synthesis, Spectroelectrochemical, and Photophysical Investigation

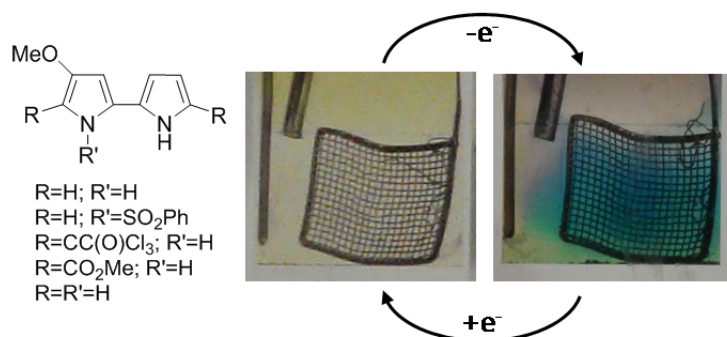
Tshitundu Tshibaka<sup>1</sup>, Ivan Ulliel<sup>2</sup>, Stéphane Dufresne<sup>2</sup> and William D. Lubell\*<sup>1</sup>, and W. G. Skene\*<sup>2</sup>

<sup>1</sup>Département de Chimie, Pavillon Roger Gaudry, Université de Montréal, CP 6128, succ. Centre-ville, Montréal, Québec, CANADA, H3C 3J7.

<sup>2</sup>Centre for Self-Assembled Chemical Structures

Département de Chimie, Pavillon J. A. Bombardier, Université de Montréal, CP 6128, succ. Centre-ville, Montréal, Québec, CANADA, H3C 3J7.

## 2.2 Abstract



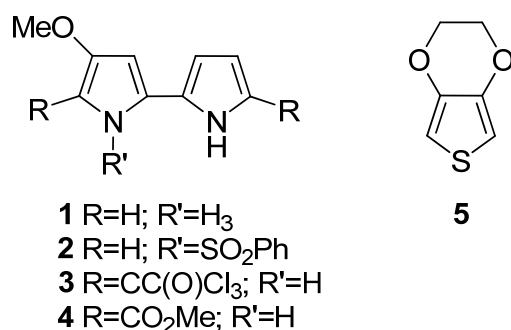
---

The electrochromic and photophysical behavior of new unsymmetric bipyrroles were observed as intense color changes of the oxidized products relative to the neutral form. The color of the oxidized form and the oxidation potential were both tunable contingent on electronic group and substitution.

---

## 2.3 Introduction

Heterocycles play major roles in plastic electronics due in part to their capacity to be polymerized into functional materials with low oxidation potentials and stable radical ionic intermediates. Thiophenes such as EDOT (3,4-Ethylenedioxy Thiophène) (**5**) have been widely used because of their electronic and conductive properties.<sup>1,2</sup> The stability of their electrochemically induced polarons and bipolarons accompanied by significant color changes in the visible have led to their use as displays in consumer electronics including tinted windows, goggles, and personal portable devices.<sup>3-5</sup>



**Chart 1.** Bipyrroles prepared and investigated and representative analogues.

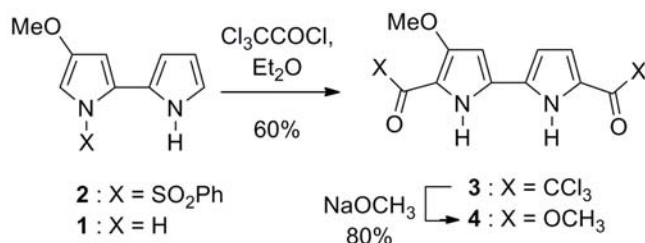
Demands on device performance for increased fast switching times and electrochromic materials capable of producing a gamut of colors have driven the search for new heterocycle comonomers to improve performance and expand the color palette. Comonomers have typically consisted of dyads and triads containing electron rich and deficient aryl groups sandwiched between polymerizable end groups, such as EDOT.<sup>2,6</sup> Although color and oxidation potential may be tuned by incorporating such electron donor and acceptor units, the overall properties of such devices remain typically governed by the terminal EDOT moieties.<sup>7</sup>

Pyrroles represent viable alternatives for addressing challenges in organic electronics. Although they possess low oxidation potentials similar to their thiophene analogues, pyrroles may exhibit different spectroscopic and photophysical properties due to the nitrogen heteroatom.<sup>8,9</sup> The nitrogen in the heterocycle contributes to decreasing the oxidation potential ( $E_{pa}$ ) as seen with the  $E_{pa}$  of 2,2'-bipyrrole, which is 650 mV lower than the corresponding bithiophene.<sup>10</sup> One advantage of pyrroles is their higher HOMO-LUMO energy gaps relative to their thiophene counterparts. In spite of their properties, pyrroles have been less widely used as thiophenes in functional materials and devices.<sup>11</sup>

In the context of a program on comonomer research,<sup>12-15</sup> we have been investigating pyrrole derivatives to characterize their oxidation potential for potential use in tuneable spectroelectrochemical color devices. Unsymmetric bipyrroles have been targeted to examine substituent effects on electrochromic behavior. The bipyrroles **1-4** (Chart 1) were synthesized and their structure-property relationships characterized spectroscopically, electrochemically, and spectroelectrochemically. These compounds may be ideal electrochromes because their anodically induced intermediates and significant color changes can be produced at low potentials. Structure-property relationships have been studied to determine the effect of the electron donating methoxy and different electron withdrawing groups (trichloromethylketone, ester and sulfonamide) on the oxidation potentials and spectroscopic properties of the neutral and radical cation species.

## 2.4 Synthesis

2,2-Bipyrrole<sup>16</sup> has served as a precursor for synthesis of prodigiosin natural products<sup>17</sup>, expanded porphyrins,<sup>18-20</sup> and conducting polymers with nanofiber morphology.<sup>21</sup> Oxidative couplings of 1,1'-carbonyldipyrroles,<sup>22</sup> 2-trimethylstannylated pyrroles<sup>23</sup> and pyrrole,<sup>24</sup> dehalogen coupling of halogenated pyrroles, and desulfurization of thienodipyrroles,<sup>25</sup> all have been used to assemble symmetric  $\alpha$ -linked bipyrroles. Among the few methods for preparing unsymmetrical bipyrroles, such as the reaction of donor-acceptor cyclopropanes with 2-cyanopyrroles,<sup>26</sup> the synthesis of 4-alkoxy and 4-amino-2,2'-bipyrroles from hydroxyproline provides less common products that possess electron donating substituents.<sup>27</sup> The acylation of the 4-methoxy-2,2'-bipyrrole **1** was explored to study captodative effects on radicals from the monomer.



**Scheme 1.** Synthesis of bipyrroles **3** and **4**.

4-Methoxy-2,2' bipyrrole **1** and its sulfonamide **2** were both prepared from hydroxyproline as described.<sup>28,29</sup>

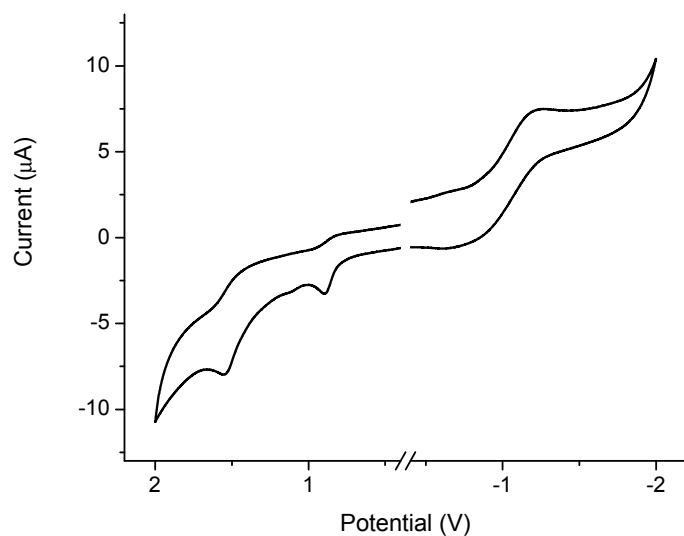
4-Methoxy-5,5'-bistrichloroacetyl-2,2'-bipyrrole (**3**) was synthesized by a double acylation of **1** using trichloroacetyl chloride in diethyl ether (scheme 1).<sup>28</sup> After 15 min, TLC analysis showed complete consumption of starting material and the formation of monoacylated bipyrrole (Rf =

0.6, hexane/ethyl acetate, 3:1), which underwent more slowly the second acylation. After 2 h, the reaction mixture was quenched and purified by column chromatography to afford dione **3** as a yellow solid in 60% yield. Dimethyl ester **4** was synthesized by treating dione **3** in a haloform reaction with sodium methoxide in methanol in 90% yield after column chromatography on silica gel.

## 2.5. Electrochemistry

Comonomers **1-4** all underwent both oxidation and reduction processes (Figure 1) demonstrating their n- and p-type behavior. One discrete reduction process corresponding to the formation of the radical anion was observed in all cases. Similarly, the oxidation process was also a one-electron process resulting in the radical cation. Only a single one-electron transfer process was observed with dione **3** and diester **4** as a result of their high  $E_{pa}$ , and the limited oxidation window of the solvent. On the other hand, a second one-electron process corresponding to formation of the dication was observed for 4-methoxy-2,2'-bipyrrole **1** and its sulfonamide **2**. In all cases, the observed electrochemical processes were pseudo-reversible demonstrating the reactivity of the produced intermediates, which is not surprising in light of unsubstituted terminal positions susceptible to cross-coupling and polymerization by way of radical cation intermediates.





**Figure 3.** Cyclic voltammogram of **2** recorded in deaerated and anhydrous dichloromethane with 0.1 M TBAPF<sub>6</sub> ( tetrabutylammonium hexafluorophosphate) supporting electrolyte at a sweep rate of 100 mV/sec.

The methoxy group lowered the oxidation potential as seen by the 150 mV decrease in  $E_{pa}$  of **1** compared the parent heterocycle, 2,2'-bipyrrole (Table 1).<sup>28-30</sup> The introduction of electron acceptor groups gave more positive  $E_{pa}$  values as a result of the electronic push-pull effect. The most pronounced effect was exhibited by dione **3** possessing three times greater  $E_{pa}$  than 4-methoxy-2,2'-bipyrrole (**1**). Tuning of the  $E_{pa}$  of bipyrroles has thus been demonstrated.

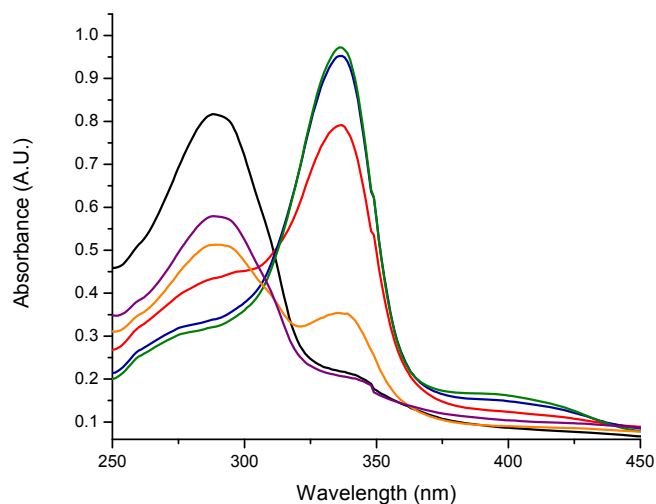
The HOMO and LUMO values were calculated from the measured oxidation and reduction potentials, respectively, according to standard means (Table 1).<sup>31</sup> The  $E_g$  was calculated from these values and illustrated the HOMO to be affected more by the electronic groups than the LUMO. The collective affect of the HOMO and LUMO

resulted in an energy gap energies variation of 1 eV, while the bipyrrroles **1-4** are air stable.

**Table 1.** Electrochemical data of bipyrrroles measured in anhydrous and deaerated dichloromethane with 0.1 M TBAPF<sub>6</sub>.

Compound	$\lambda_{\text{abs}}$ (nm) <sup>a</sup>	$\lambda_{\text{fl}}$ (nm) <sup>a</sup>	$\Phi_{\text{fl}}$ <sup>a</sup>	$\lambda_{\text{TT}}$ (nm) <sup>b</sup>	$E_{\text{pa}}^1$ (mV)	$E_{\text{pa}}^2$ (mV)	$E_{\text{pc}}$ (mV)	HOMO <sup>b</sup>	LUMO <sup>b</sup>	$E_{\text{g}}$	$R^{++}$ (nm) <sup>c</sup>
<b>1</b>	291	350	0.01	380	450	1600	-1.4	-4.9	-3.0	1.9	335 (403)
<b>2</b>	260	370	0	380	890	1550	-1.1	-5.3	-3.3	2.0	378 (559)
<b>3</b>	400	420	0.01	450	1350	-	-1.4	-5.8	-3.0	2.8	380 (591, 342)
<b>4</b>	333	393	0.92	410	980	-	-1.2	-5.4	-3.2	2.2	380

<sup>a</sup>Measured in dichloromethane. <sup>b</sup>Relative to the vacuum level. <sup>c</sup>Refers to the radical cation absorption obtained by applying a potential equivalent to  $E_{\text{pa}}^1$ .

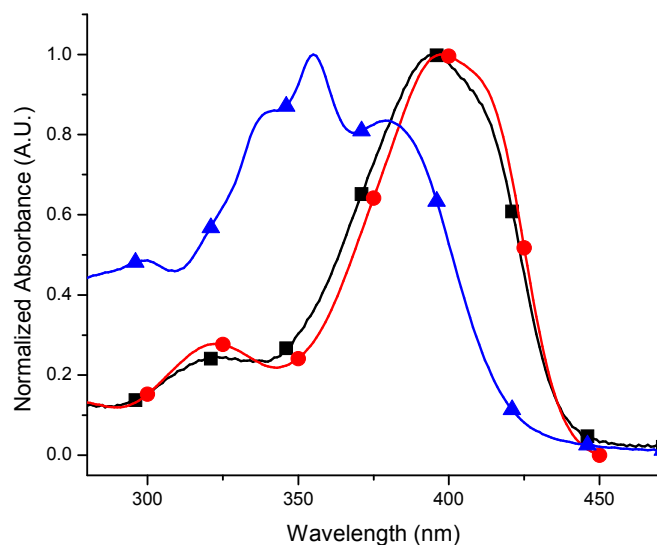


**Figure 4.** Change in absorption of **1** with 0 (black), 1 (red), 5 (blue), and 4 (green) min at a potential of + 850 mV followed by 2.5 (orange), 5 (purple), and 8 (black) min at a potential of - 200 mV.

The electrochromic properties of the bipyrrroles were of particular interest for assessing the effect of the electronic groups on the color of the radical cation. The anodically produced radical cation was spectroscopically characterized when produced by applying a potential to the neutral bipyrrrole (Figure 2). Two new absorptions occurred upon electrochemical oxidation of methoxybipyrrrole **1**. The isobestic point at 310 nm confirmed that the oxidation process was reversible and that there were only two species present: the neutral form and radical cation. In all cases, the radical cation absorbed at longer wavelength than the corresponding neutral form. Both the absorptions of the transients of **1** and **3** are bathochromically shifted by only 50 nm. This implied that the radical cation was only slightly more stable than the neutral form. Conversely, the intermediates from **2** and **4** were considerably more stable than their

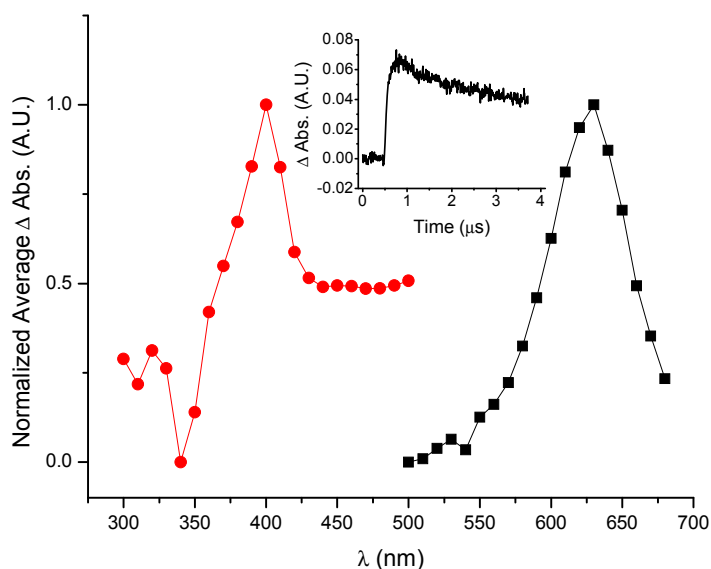
## 2.6 Spectroscopy

The absorption and fluorescence of the new bipyrrroles were investigated further by examining the effect of the electronic groups on the spectroscopic properties (summarized in Table 1). Significant absorption and fluorescence bathochromic shifts resulted from energy gap narrowing and intramolecular electronic effects, as evidenced by the absorbance at 580 nm of **1**, which occurred only in polar solvents versus an absorption at 260 nm in less polar solvents (see Supporting Information). Similarly, dione **3** exhibited solvent dependent absorption. The negative solvatochromism (Figure 3) implies that the ground state of **3** is highly polar as a result of efficient electron push-pull effect.



**Figure 3.** Normalized absorption spectra of **3** recorded in acetonitrile (●), dichloromethane (■), 4: 1 methanol/ethanol (▲).

Except for diester **4**, which fluoresces strongly ( $\Phi_f > 0.8$ ), contingent somewhat on solvent polarity, the bipyrroles did not exhibit fluorescence regardless of the solvent. When laser flash photolysis was used to determine the cause of the weak fluorescence, the bipyrroles all exhibited transient absorption spectra (Figure 4). The observed intermediates were assigned to the triplet owing to their first order decay (Inset Figure 4) concomitant signal suppression with the common triplet quencher, 1,3-cyclohexadiene. The stabilization effect of the heterocyclic nitrogen is further evidenced by the observed transients that are bathochromically shifted relative to bithiophene ( $\lambda_{TT} = 370$  nm).<sup>32</sup>



**Figure 4.** Normalized transient absorption spectra of **4** (●) and xanthone reference (■) measured at 1  $\mu$ s after the laser pulse at 266 nm in deaerated and anhydrous acetonitrile.

Unsymmetric bipyrroles **1-4** possessing an electron donating and accepting groups were synthesized and shown to be inherently both p- and n-type materials, with tunable oxidation and reduction potentials across a range of 900 mV. Their electrochromic push-pull nature gave

significant color changes in the visible spectrum demonstrating that bipyrrroles are suitable precursors for functional electrochromic materials. The unsymmetric bipyrrroles exhibited advantageous properties, including their  $E_{pa}$ , the modulation of the absorption of their radical cation with structure, and their tolerance to ambient conditions, properties not readily possible with symmetric bipyrrrole and thiophene analogues. Unsymmetric bipyrrroles are therefore interesting comonomers for the preparation of electrochromic materials.

## 2.7 Experimental Section

**4-Methoxy-5,5'-bistrichloroacetyl-2,2'-bipyrrole (3).**<sup>33,34</sup> Trichloroacetyl chloride (0.6 mL, 5 mmol, 8 equiv.) was added to a solution of bipyrrole **2** (105 mg, 0.65 mmol, 100 mol%) in dry diethyl ether (8 mL) under argon at rt. The mixture was stirred at 60°C for 8 h, diluted with saturated NaHCO<sub>3</sub> and extracted with ethyl acetate. The combined organic layer was washed with H<sub>2</sub>O and brine, dried with MgSO<sub>4</sub>, filtered and concentrated in vacuo to give a yellow solid, which was purified by column chromatography (silica gel, hexane/ethyl acetate, 4:1) to afford dione **3** (174 mg, 60%) as a yellow solid: m.p. 234 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ: 10.1 (s, 1H), 9.6 (s, 1H), 7.5 (s, 1H), 6.7 (s, 1H), 6.3 (s, 1H), 4.0 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ: 173.5, 172.1, 155.7, 131.3, 130.9, 124.7, 122.7, 112.7, 110.9, 95.9, 95.3, 95.0, 58.7. HR-MS calcd. For C<sub>13</sub>H<sub>9</sub>Cl<sub>6</sub>N<sub>2</sub>O<sub>3</sub> ([M + H<sup>+</sup>]): 450.8739; found: 450.8741.

**4-(Methoxy)bismethyl-2,2'-bipyrrole-5,5'-carboxylate (4).**<sup>35</sup> In dry methanol (7 mL), sodium (0.28 mg, 0.01 mmol, 0.28 equiv.) was dissolved and bis-trichloroacetylketone **3** (20 mg, 0.04 mmol, 1 equiv.) was added to the reaction mixture, which was stirred at room temperature for 1 h. The volatiles were evaporated and the resulting solid was dissolved in ethyl acetate (8 mL). The solution was washed with 3 N hydrochloric acid (2 mL) and a saturated sodium hydrogen carbonate solution (2 mL). The organic layer was dried (MgSO<sub>4</sub>) and concentrated to a residue that was purified by column chromatography (Silica gel, hexane/ethyl acetate, 1:1). Evaporation of the collected fractions yielded bipyrrole diester **4** as a brown solid (11 mg) in 90% yield; m.p. 168°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ: 10.55 (s, 1H), 10.06 (s, 1H), 6.95 (s, 1H), 6.50 (s, 1H), 6.16 (d, *J* = 2.2 Hz, 1H), 3.92 (s, 3H), 3.90 (s, 3H), 3.89 (s, 3H). <sup>13</sup>C NMR

(100 MHz, CDCl<sub>3</sub>): 162.52, 162.5, 154.4, 129.5, 127.7, 123.3, 117.4, 109.0, 107.5, 94.0, 58.6, 52.2, 52.1. HR-MS calcd. for C<sub>13</sub>H<sub>15</sub>N<sub>2</sub>O<sub>5</sub> ([M + H<sup>+</sup>]): 279.0976; found: 279.0983.



## 2.8 References

- (1) Daugaard, A. E.; Hvilsted, S. r.; Hansen, T. S.; Larsen, N. B. *Macromolecules* **2008**, *41*, 4321-4327.
- (2) Sonmez, G. *Chem. Commun.* **2005**, 5251-5259.
- (3) Tehrani, P.; Hennerdal, L.-O.; Dyer, A. L.; Reynolds, J. R.; Berggren, M. *J. Mater. Chem.* **2009**, *19*, 1799-1802.
- (4) Barbosa, P. C.; Silva, M. M.; Smith, M. J.; Gonçalves, A.; Fortunato, E. *Thin Solid Films* **2008**, *516*, 1480-1483.
- (5) Grenier, A. L. D. C. R. G.; Reynolds, J. R. *Adv. Funct. Mater.* **2007**, *17*, 1480-1486.
- (6) Tarkuc, S. m.; Ak, M. n.; Onurhan, E.; Toppare, L. *J. Macromol. Sci. A* **2008**, *45*, 164 - 171.
- (7) Houpis, I. N.; Shields, D.; Nettekoven, U.; Schnyder, A.; Bappert, E.; Weerts, K.; Canters, M.; Vermuelen, W. *Org. Proc. Res. Develop.* **2009**, *13*, 598-606.
- (8) MacDiarmid, A. G. *Angew. Chem. Int. Ed.* **2001**, *40*, 2581-2590.
- (9) Heeger, A. J. *J. Phys. Chem. B* **2001**, *105*, 8475-8491.
- (10) Meerholz, K.; Heinze, J. *Electrochem. Acta* **1996**, *41*, 1839-1854.
- (11) Walczak, R. M.; Reynolds, J. R. *Adv. Mater.* **2006**, *18*, 1121-1131.
- (12) Hansford, K. A.; Guarin, S. A. P.; Skene, W. G.; Lubell, W. D. *J. Org. Chem.* **2005**, *70*, 7996 -8000.
- (13) Dufresne, S.; Skene, W. G. *J. Org. Chem.* **2008**, *73*, 3859-3866.
- (14) Bourgeaux, M.; Skene, W. G. *J. Org. Chem.* **2007**, *72*, 8882-8892.
- (15) Dufresne, S.; Bourgeaux, M.; Skene, W. G. *J. Mater. Chem.* **2007**, *17*, 1166-1177.
- (16) Rapoport, H.; Castagnoli, N. *J. Am. Chem. Soc* **2002**, *84*, 2178-2181.

- (17) Rapoport, H.; Willson, C. D. *J. Am. Chem. Soc.* **2002**, *84*, 630-635.
- (18) Sessler, J. L.; Aguilar, A.; Sanchez-Garcia, D.; Seidel, D.; Kohler, T.; Arp, F.; Lynch, V. M. *Org. Lett.* **2005**, *7*, 1887-1890.
- (19) Katayev, E. A.; Boev, N. V.; Khrustalev, V. N.; Ustynyuk, Y. A.; Tananaev, I. G.; Sessler, J. L. *J. Org. Chem.* **2007**, *72*, 2886-2896.
- (20) Mori, M.; Okawa, T.; Iizuna, N.; Nakayama, K.; Lintuluoto, J. M.; Setsune, J.-i. *J. Org. Chem.* **2009**, *74*, 3579-3582.
- (21) Tran, H. D.; Wang, Y.; D'Arcy, J. M.; Kaner, R. B. *ACS Nano* **2008**, *2*, 1841-1848.
- (22) Boger, D. L.; Patel, M. *J. Org. Chem.* **2002**, *52*, 2319-2323.
- (23) Sánchez-García, D.; Borrell, J. I.; Nonell, S. *Org. Lett.* **2008**, *11*, 77-79.
- (24) Dohi, T.; Morimoto, K.; Maruyama, A.; Kita, Y. *Org. Lett.* **2006**, *8*, 2007-2010.
- (25) Arad, O.; Morros, J.; Batllori, X.; Teixido, J.; Nonell, S.; Borrell, J. I. *Org. Lett.* **2006**, *8*, 847-850.
- (26) Yu, M.; Pantos, G. D.; Sessler, J. L.; Pagenkopf, B. L. *Org. Lett.* **2004**, *6*, 1057-1059.
- (27) Jolicoeur, B.; Lubell, W. D. *Org. Lett.* **2006**, *8*, 6107-6110.
- (28) Guyard, L.; Hapiot, P.; Neta, P. *J. Phys. Chem. B* **1997**, *101*, 5698-5706.
- (29) Andrieux, C. P.; Hapiot, P.; Audebert, P.; Guyard, L.; Dinh An, M. N.; Groenendaal, L.; Meijer, E. W. *Chem. Mater.* **1997**, *9*, 723-729.
- (30) Beck, F.; Oberst, M.; Jansen, R. *Electrochim. Acta* **1900**, *35*, 1841-1848.
- (31) Bard, A. J.; Faulkner, L. R. *Electrochemical Methods: Fundamentals and Applications*; 2nd ed.; John Wiley & Sons, 2001.
- (32) Evans, C. H.; Scaiano, J. C. *J. Am. Chem. Soc.* **1990**, *112*, 2694-2701.

(33) Harbuck, J. W.; Rapoport, H. *The Journal of Organic Chemistry* **2002**, *37*, 3618-3622.(34)

Tanada, M.; Shibata, Y.; Maeda, M.; Sasak, S. *Heterocycles* **2004**, *63*, 29-39.

(34) Tanada, M.; Shibata, Y.; Maeda, M.; Sasak, S. *Heterocycles* **2004**, *63*, 29-39.

(35) Schmuck, C.; Bickert, V.; Merschky, M; Geiger, L.; Rupprecht, D.; Dudaczek, J.; Wich, P.; Rehm, T.; Machon, U. *Eur. J. Org. Chem.* **2008**, 324-329.

## **2.9 Contribution des co-auteurs pour l'article 1**

J'ai effectué l'ensemble de réactions et de la caractérisation des molécules présentées dans cet article. J'ai aussi participé à la rédaction de l'article en écrivant une partie de l'introduction, la synthèse et la partie expérimentale.

Stéphane Dufresne et Ivan Ulliel Roche ont effectué les analyses électrochimiques des composés.

A part leur contribution à l'écriture, les professeurs William D. Lubell et William Skene ont supervisé la recherche et la rédaction de l'article.

## **Chapitre 3**

### **Article 2 :**

Tshibaka, T.; Bishop, s.; Roche, I. U.; Dufresne, S.; Lubell, W. D.; Skene, W. G. « Conjugated 4-methoxybipyrrole thiophene azomethines: synthesis, opto-electronic properties and crystallographic characterization » *Chem. Eur. J.* **2011**, 17, 10789- 10888.

### **3.1 Introduction**

Le chapitre 3, présenté sous forme d'article, montre les résultats de la synthèse des oligomères conjugués à partir des dialdéhydes pyrroliques et des aminothiophènes. On y retrouve également les études spectroscopiques et électrochimiques qui démontrent le potentiel d'utiliser ces comonomères conjugués dans les matériaux conducteurs.

**Conjugated 4-methoxybipyrrole thiophene azomethines: synthesis, opto-electronic  
properties and crystallographic characterization**

Tshitundu Tshibaka,<sup>2</sup> Sophie Bishop,<sup>1</sup> Ivan Ulliel Roche,<sup>1,3</sup> Stéphane Dufresne,<sup>1</sup>  
William D. Lubell\*<sup>2</sup>, and W. G. Skene\*<sup>1</sup>

<sup>1</sup>Laboratoire de caractérisation photophysique des matériaux conjugués,<sup>2</sup>Département de Chimie,  
Université de Montréal, CP 6128, succ. Centre-ville, Montréal, Québec, CANADA, H3C 3J7.

<sup>3</sup>Current Address:

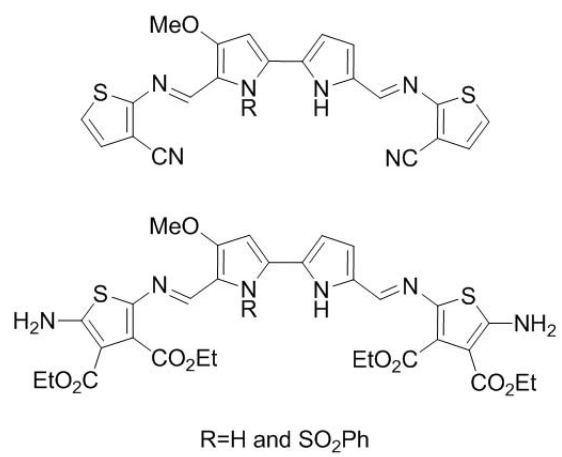
École Nationale Supérieure de Chimie et Physique de Bordeaux (ENSCP)

16 avenue Pey Berland

33600 Pessac

France

## Graphical Abstract





### 3.2 Abstract

In the search of functional materials with improved electrochromic properties, thiophenes and asymmetric bipyrrroles have been conjugated with azomethine units. 4-Methoxy-2,2'-bipyrrroles **3-6** were first synthesized by a general route from 4-hydroxyproline and converted subsequently to dialdehydes **8-15**, which underwent condensations with different aminothiophenes to provide azomethine conjugates **14-18** and **20-22**. The crystallization and X-ray analysis of **20** showed the heterocycles and azomethine bonds were all co-planar with the heterocycles adopting an anti-parallel arrangement. These configurations result in extended conjugation and enhanced optoelectronic properties of the azomethines. Oxidation potential ( $E_{pa}$ ) was tailored contingent on substitution of the terminal thiophenes and central pyrroles of the azomethines. The combined low  $E_{pa}$  and extended azomethine degree of conjugation resulted in stark color transitions occurring between their neutral and oxidized states. Reversible color formation was induced both electrochemically and by doping/dedoping with trifluoroacetic acid/triethylamine.

### 3.3 Introduction

Plastic electronics including, light emitting devices (OLED), photovoltaic devices (OPVD), and organic field effect transistors (OFET),<sup>1-6</sup> all have made extensive application of thiophene-based materials. Thiophenes offer low oxidation potentials ( $E_{pa}$ ) and reversible oxidation.<sup>7</sup> Conjugated systems containing thiophenes have been employed in electrochromic devices, because they may display sharp color changes within the visible spectrum upon electrochemical oxidation.<sup>8</sup>

Complementing thiophenes, pyrroles have been employed as components of conducting polymers, such as polypyrrole, which is used in sensors, due to their simple polymerization, stability, and good electrical conductivity.<sup>9,10,11</sup> Contingent on the structure of the pyrrole monomer,<sup>12,13</sup> conductivity and ease of synthesis may be altered. For example, poly(3,4-dimethoxypyrrole) has higher conductivity and is easier to synthesize than its un-substituted and alkyl-substituted counterparts.<sup>14,15</sup> In this light, bipyrroles represent interesting starting points for constructing conducting polymers; however, to the best of our knowledge, only symmetric bipyrroles<sup>9,16</sup> have been studied, likely due to a dearth of methods for preparing unsymmetrical bipyrroles.<sup>17-20</sup>

Functional materials with multiple color states and a large palette of colors are required to meet the requirements for new electrochromic devices. Enhanced properties for improved color transitions have arrived from incorporating unsaturated linkages into conjugated materials, which may exhibit extended degrees of conjugation through coplanar aryl units.<sup>8,21-26</sup> For example, vinyl links have shown promise for preparing new functional materials; however, their synthesis by Gilch and Horner-Emmons protocols,

often requires rigorous reaction conditions (i.e., anhydrous solvent and inert atmosphere), lacks atom economy and necessitates tedious product purification.<sup>21,22</sup> On the other hand, azomethines (-N=CH-) are isoelectronic to their vinyl counterparts,<sup>27</sup> however, their synthesis is relatively straightforward and efficient, involving condensation of amine and aldehyde components to produce the conjugate and water, facilitating purification.<sup>28-30</sup>

In spite of their practical synthesis, conjugated materials incorporating azomethines and heterocycles have not been pursued, likely because homoaryl azomethine counterparts exhibited properties incompatible for devices, such as poor electrochromic behavior and high  $E_{pa}$ .<sup>31-35</sup> Seeking new materials for electrochromic applications, we have studied heterocycle-azomethine conjugates exhibiting stark color transitions between neutral and oxidized forms at low  $E_{pa}$ . In particular, thiophenes and asymmetric bipyrrroles have been conjugated with azomethine units. The synthesis of these novel conjugated systems is now reported as well as their characterization by X-ray crystallography and their electrochemical, spectroelectrochemical, and spectrochemical properties. Offering promise for use in functional electrochromic materials, these heterocycle-azomethine conjugates exhibit dramatic visible color changes upon electrochemical and chemical oxidization.

### 3.4 Experimental Section

#### General Protocols

Unless noted otherwise, all reactions were performed under argon atmosphere, using anhydrous conditions and flame-dried glassware. Anhydrous solvents (tetrahydrofuran, toluene and methylene chloride) were obtained by passage through solvent filtration systems (GlassContour, Irvine, CA). 4-Methoxy-2,2'-bipyrrrole **1** and its sulfonamide **2**, both were prepared from hydroxyproline as previously described.<sup>19,20</sup> Chromatography was performed on silica gel (Silicycle; 230-400 mesh). Melting points are uncorrected. NMR spectra were recorded on Bruker AV 400-MHz and AV 300-MHz spectrometers. Chemical shifts are reported in ppm ( $\delta$  units) downfield from internal tetramethylsilane ( $(\text{CH}_3)_4\text{Si}$ ), or relative to peaks for residual solvent:  $\text{CHCl}_3$ ,  $(\text{CH}_3)_2\text{CO}$  and DMSO. Accurate mass measurements were performed by the Centre Régional de Spectrométrie de Masse de l'Université de Montréal on a LC-MSD-TOF instrument from Agilent technologies in positive electrospray mode. Either protonated molecular ions  $(\text{M}+\text{H})^+$  or sodium adducts  $(\text{M}+\text{Na})^+$  were used for empirical formula confirmation.

Absorption measurements were performed on a Cary-500 spectrometer and fluorescence studies were carried out on an Edinburgh Instruments FLS-920 fluorimeter after deaerating the samples thoroughly with nitrogen for 20 minutes. Compounds were dissolved in anhydrous, deaerated dichloromethane at  $10^{-5}\text{M}$ .

Cyclic voltammetry measurements were performed on a Bio Analytical Systems EC Epsilon potentiostat. Compounds were dissolved in anhydrous, deaerated dichloromethane at  $10^{-4}\text{M}$  along with sufficient  $\text{NBu}_4\text{PF}_6$  as supporting electrolyte for

satisfactory conductivity. A platinum button electrode was used as the working electrode. Platinum wire and silver wire electrodes were employed as auxiliary and reference electrodes, respectively.

Spectroelectrochemical measurements were performed by combining a Bio Analytical Systems EC Epsilon potentiostat with a Cary-500 spectrometer, using a thin optical path length cuvette with a platinum gauze wire as the working electrode, a platinum counter electrode, and saturated Ag/AgCl or silver wire Ag/Ag<sup>+</sup> reference electrode, applying a potential greater than the E<sub>pa</sub> of the given compound. The spectroelectrochemical cell was provided by CH Instruments Japan (CHI140A) with a spectroscopic height of 6.5 mm and an optical path length of 1 mm.

#### **Representative method A for bipyrrrole *N*-alkylation**

#### **4 - Methoxy-1-phenylsulfonyl-1'-allyl-2,2'-bipyrrrole (3)**

A solution of 4-(methoxy)-1-benzenesulfonyl-2,2'-bipyrrrole **2** (15 mg, 0.04 mmol, 1 equiv.) in THF (1 mL) was added dropwise to a 0°C solution of potassium *t*-butoxide (15 mg, 0.13 mmol, 3.2 equiv.) and 18-crown-6 (2 mg, 0.008 mmol, 0.1 equiv.) in THF (1 mL), stirred for 30 min, and treated with allyl iodide (11 μL, 1.2 mmol, 1.2 equiv.). The ice bath was removed and the solution was allowed to warm to room temperature, with stirring overnight. The reaction mixture was partitioned between water (3 mL) and EtOAc (5 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 mL). The organic layers were combined, washed with brine, dried over MgSO<sub>4</sub>, filtered, and concentrated under vacuum to a residue that was purified by column chromatography on silica gel eluting with 50% EtOAc/hexanes (R<sub>f</sub>: 0.3). Evaporation of the collected fractions gave the allyl bipyrrrole **3** as a green oil (9 mg, 52 %): <sup>1</sup>H NMR

(300 MHz, CDCl<sub>3</sub>)  $\delta$  : 7.56-7.52 (m, 5H), 6.91 (d,  $J$  = 2.1 Hz, 1H), 6.74 (t,  $J$  = 2.4 Hz, 1H), 6.14 (t,  $J$  = 3.6 Hz, 1H), 6.00 (d,  $J$  = 2.1 Hz, 1H), 5.89-5.87 (m, 2H), 5.12 (d,  $J$  = 1.5 Hz, 1H), 5.03 (d,  $J$  = 1.5 Hz, 1H), 4.22 (m, 2H), 3.75 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  : 151.2, 139.1, 135.2, 134.4, 129.5 (2C), 128.2 (2C), 126.4, 123.0, 122.4, 118.1, 113.9, 111.9, 108.3, 103.9, 58.4, 50.5. HR-MS calcd. for C<sub>18</sub>H<sub>19</sub>N<sub>2</sub>O<sub>3</sub>S ([M+H<sup>+</sup>]) 343.1110, found 343.1121.

**4-Methoxy-1-phenylsulfonyl-1'-butyl-2,2'-bipyrrole (4)** was obtained using Method A from 4-(methoxy)-1-benzenesulfonyl-2,2'-bipyrrole (**2**, 30 mg, 0.1 mmol) and 1-iodobutane (17  $\mu$ L, 0.14 mmol) as a brown oil (31 mg, 86%), after chromatography using 20% EtOAc/Hex. (R<sub>f</sub> : 0.5): <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  : 7.56-7.41 (m, 5H), 6.93 (t,  $J$  = 1.5 Hz, 1H), 6.77 (d,  $J$  = 0.9 Hz, 1H), 6.12 (d,  $J$  = 2.1 Hz, 1H), 6.02 (d,  $J$  = 1.5 Hz, 1H), 5.81 (t,  $J$  = 1.2 Hz, 1H), 3.77 (s, 3H), 3.69-3.65 (m, 2H), 1.58 (m, 2H), 1.21 (m, 2H), 0.88-0.84 (m, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  : 151.2, 139.1, 134.3, 129.5 (2C), 128.3 (2C), 126.9, 122.8, 122.5, 113.5, 111.9, 107.8, 103.9, 58.5, 47.9, 33.9, 20.9, 14.4. HR-MS calcd. for C<sub>19</sub>H<sub>23</sub>N<sub>2</sub>O<sub>3</sub>S ([M+H<sup>+</sup>]) 359.1423, found 359.1425.

**4-Methoxy-1-phenylsulfonyl-1'-octyl-2,2'-bipyrrole (5)** was obtained using Method A from 4-(methoxy)-1-benzenesulfonyl-2,2'-bipyrrole (**2**, 25 mg, 0.08 mmol) and 1-iodooctane (22  $\mu$ L, 0.12 mmol) as a brown oil (26 mg, 76%), after chromatography using 20% EtOAc/Hex.: R<sub>f</sub> 0.53; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$ : 7.55-7.41 (m, 5H), 6.93 (t,  $J$  = 1.5 Hz, 1H), 6.77 (d,  $J$  = 0.9 Hz, 1H), 6.12 (d,  $J$  = 2.1 Hz, 1H), 6.01 (d,  $J$  = 1.5 Hz, 1H), 5.82 (t,  $J$  = 1.2 Hz, 1H), 3.77 (s, 3H), 3.66 (m, 2H), 1.58 (m, 2H), 1.23 (m, 10H), 0.90-0.88 (m, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  : 151.2, 139.1, 134.4, 129.6 (2C), 128.3 (2C), 126.9, 122.8, 122.3, 113.4, 111.8, 107.7, 103.9, 58.3, 48.2, 32.5, 31.7, 29.9,

29.9, 27.5, 23.3, 14.9. HR-MS calcd. for  $C_{23}H_{31}N_2O_3S$  ( $[M+H^+]$ ) 415.2050, found 415.2051.

**4-Methoxy-1,1'-biphenylsulfonyl-2,2'-bipyrrole (6)** was prepared using Method A from 4-(methoxy)-1-benzenesulfonyl-2,2'-bipyrrole (**2**, 25 mg, 0.08 mmol) and benzenesulfonyl chloride (49  $\mu$ L, 0.23 mmol) as a white solid (18 mg, 50 %) after chromatography using 50% EtOAc/Hex. :  $R_f$  : 0.79;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.62 (m, 6H), 7.48 (m, 5H), 6.94 (d,  $J=2$  Hz, 1H), 6.31 (t,  $J=1.2$  Hz, 1H), 5.99 (d,  $J=1.6$  Hz, 1H), 5.77 (s, 1H), 3.78 (s, 3H) ;  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  : 149.2, 138.4, 138.4, 133.5, 133.3, 128.7 (2C), 128.6 (2C), 127.1 (2C), 126.9 (2C), 123.9, 122.2, 121.6, 118.9, 11.4, 110.7, 103.4, 57.3. HR-MS calcd. for  $C_{21}H_{19}N_2O_5S_2$  ( $[M+H^+]$ ) 443.0730, found 443.0730.

### Representative Method B

#### 4-(Methoxy)-1-benzenesulfonyl-5,5'-bisformyl-2,2'-bipyrrole (9)

Phosphoryl chloride (49  $\mu$ L, 0.52 mmol, 4 equiv.) was added to dimethylformamide (0.1 mL, 1.3 mmol, 10 equiv.) at 5-10  $^{\circ}C$  and stirred for 30 min. A solution of 4-(methoxy)-1-benzenesulfonyl-2,2'-bipyrrole (**2**, 40 mg, 0.13 mmol, 1 equiv.) in 1.6 mL of dichloromethane was cooled to  $-15$   $^{\circ}C$ , and treated drop-wise with the preformed solution of Vilsmeier reagent. The reaction mixture was stirred at  $-15$   $^{\circ}C$  for 30 min, at  $0^{\circ}C$  for 9h, at room temperature overnight, treated with a saturated aqueous sodium acetate solution (3 mL) and heated to a reflux for 2h. The layers were separated and the aqueous layer was extracted with EtOAc. The organic layers were combined, washed with brine, dried ( $MgSO_4$ ), and concentrated to a residue that was purified by

chromatography on silica (60% EtOAc in hexanes). Evaporation of the collected fractions yielded dialdehyde **9** as a green oil (43 mg) in 90% yield:  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  : 10.17 (m, 2H), 9.62 (s, 1H), 7.55 (m, 1H), 7.37 (m, 4H), 7.00 (dd,  $J = 1.5, 2.5$  Hz, 1H), 6.53 (dd,  $J = 1.5, 2.5$  Hz, 1H), 6.32 (s, 1H), 3.88 (s, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  : 180.7, 179.7, 159.1, 136.3, 134.7, 134.5, 134.3, 129.2, 128.2, 127.1, 121.1, 120.4, 115.2, 107.1, 59.0. HR-MS calcd. for  $\text{C}_{17}\text{H}_{15}\text{N}_2\text{O}_5\text{S}$  ( $[\text{M}+\text{H}^+]$ ) 359.0696, found 359.0708.

**4-(Methoxy)-5,5'-bisformyl-2,2'-bipyrrole (8)** was prepared according to method B from bipyrrole **1** (40 mg, 0.24 mmol) without purification by chromatography. Dialdehyde **8** was obtained as a green oil (26 mg, 50%):  $R_f$  : 0.54 (50%EtOAc/Hex.);  $^1\text{H}$  NMR (300 MHz,  $(\text{CD}_3)_2\text{CO}$ )  $\delta$  : 9.56 (s, 1H), 9.53 (s, 1H), 7.07 (d,  $J = 4$  Hz, 1H), 6.93 (m, 2H), 6.85 (br, 1H), 6.65 (s, 1H), 3.91 (s, 3H). HR-MS calcd. for  $\text{C}_{11}\text{H}_{11}\text{N}_2\text{O}_3$  ( $[\text{M}+\text{H}^+]$ ) 219.0764, found 219.0754.

**4-Methoxy-1-phenylsulfonyl-1'-allyl-5-formyl-2,2'-bipyrrole (14)** was prepared according to method B from bipyrrole **3** (7 mg, 0.03 mmol) as a green oil (4 mg, 53%):  $R_f$  : 0.3 (50% EtOAc/Hex.);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$ : 10.23 (s, 1H), 7.59-7.41 (m, 5H), 6.92 (s, 1H), 6.25 (t,  $J = 3.2$  Hz, 1H), 6.17 (t,  $J = 2$  Hz, 1H), 6.08 (s, 1H), 5.89 (m, 1H), 5.16 (d,  $J = 10.4$  Hz, 1H), 5.08 (d,  $J = 16.8$  Hz, 1H), 4.56 (d,  $J = 5.6$  Hz, 2H), 3.87 (s, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 181.5, 160.2, 137.4, 136.6, 135.1, 134.7, 129.7 (2C), 128.4 (2C), 125.7, 123.1, 121.1, 118.7, 114.8, 109.1, 107.9, 59.7, 51.6. HR-MS calcd. for  $\text{C}_{19}\text{H}_{19}\text{N}_2\text{O}_4\text{S}$  ( $[\text{M}+\text{H}^+]$ ) 371.1060, found 371.1070.



**4-(Methoxy)-1-benzenesulfonyl-1'-butyl-5,5'-bisformyl-2,2'-bipyrrole (10)** and **4-(methoxy)-1-benzenesulfonyl-1'-butyl-5,4'-bisformyl-2,2'-bipyrrole (11)** were both prepared according to method B from bipyrrole **4** (27 mg, 0.08 mmol) and separated during purification by column chromatography on silica gel (40% EtOAc in hexane). First to elute was 5,5'-dialdehyde **10** as a brown oil (7 mg, 23%):  $R_f$ : 0.27;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 10.28 (s, 1H), 9.67 (s, 1H), 7.63 -7.43 (m, 5H), 6.98 (d,  $J = 4.2$  Hz, 1H), 6.22 (s, 1H), 6.18 (d,  $J = 4.2$  Hz, 1H), 4.33 (br, 2H), 3.90 (s, 3H), 1.58 (m, 2H), 1.18 (m, 2H), 0.83 (m, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 181.4, 180.3, 159.6, 137.6, 135.7, 134.4, 133.3, 131.9, 130.0 (2C), 128.3 (2C), 124.1, 121.5, 114.6, 108.9, 59.7, 47.9, 34.2, 20.5, 14.6. HR-MS calcd. for  $\text{C}_{21}\text{H}_{23}\text{N}_2\text{O}_5\text{S}$  ( $[\text{M}+\text{H}^+]$ ) 415.1322, found 415.1329. Second to elute was 5,4'-dialdehyde **11** as a yellow oil (19 mg, 61%);  $R_f$  0.17;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 10.2 (s, 1H), 9.8 (s, 1H), 7.62-7.43 (m, 6H), 6.54 (d,  $J = 1.8$  Hz, 1H), 6.18 (s, 1H), 4.08 (t,  $J = 6.9$  Hz, 2H), 3.88 (s, 3H), 1.68 (m, 2H), 1.28 (m, 2H), 0.90 (t,  $J = 7.2$  Hz, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$ : 185.8, 181.4, 159.9, 137.2, 135.7, 134.2, 132.2, 130.0 (2C), 128.3 (2C), 126.3, 126.08, 121.3, 112.6, 109.1, 59.5, 49.6, 33.3, 20.7, 14.3. HR-MS calcd. for  $\text{C}_{21}\text{H}_{23}\text{N}_2\text{O}_5\text{S}$  ( $[\text{M}+\text{H}^+]$ ) 415.1322, found 415.1330.

**4-(Methoxy)-1-benzenesulfonyl-5,5'-bisformyl-1'-octyl-2,2'-bipyrrole (12)** and **4-(methoxy)-1-benzenesulfonyl-5,4'-bisformyl-1'-octyl-2,2'-bipyrrole (13)** were prepared according to method B from bipyrrole **5** (21 mg, 0.05 mmol) and separated during purification by column chromatography on silica gel (40% EtOAc-hexane). First to elute was 5,5'-dialdehyde **12** as a clear oil (5 mg, 21%):  $R_f$  0.32;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$ : 10.28 (s, 1H), 9.67 (s, 1H), 7.65 - 7.42 (m, 5H), 6.98 (d,  $J = 3.9$  Hz, 1H), 6.21 (s, 1H), 6.18 (d,  $J = 3.8$  Hz, 1H), 4.32 (br, 2H), 3.90 (s, 3H), 1.58 (m, 2H), 1.24 (m,

10H), 0.86 (m, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  : 181.3, 180.6, 159.3, 137.7, 135.4, 134.3, 133.4, 132.0, 129.9 (2C), 128.4 (2C), 123.8, 121.5, 114.7, 109.0, 59.9, 48.1, 32.6, 31.9, 30.0, 29.9, 27.5, 23.4, 14.9; HR-MS calcd. for  $\text{C}_{25}\text{H}_{31}\text{N}_2\text{O}_5\text{S}$  ( $[\text{M}+\text{H}^+]$ ) 471.1948, found 471.1951. Second to elute was 5,4'-dialdehyde **13** as an orange oil (12 mg, 50%);  $R_f$  : 0.22;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  : 10.11 (s, 1H), 9.78 (s, 1H), 7.83 (d,  $J=1.5\text{Hz}$ , 1H), 7.75 (m, 1H), 7.61 (m, 4H), 6.61 (s, 1H), 6.55 (d,  $J=1.5\text{Hz}$ , 1H), 4.12 (m, 2H), 3.88 (s, 3H), 0.83-1.71 (m, 15 H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  : 185.7, 181.3, 159.7, 137.2, 135.6, 134.1, 132.4, 130.0 (2C), 128.2 (2C), 126.3, 126.2, 121.3, 112.5, 109.1, 59.7, 49.9, 32.5, 31.1, 29.9, 29.8, 27.3, 23.4, 14.9. HR-MS calcd. for  $\text{C}_{25}\text{H}_{31}\text{N}_2\text{O}_5\text{S}$  ( $[\text{M}+\text{H}^+]$ ) 471.1948, found 471.1950.

**4-Methoxy-1,1'-diphenylsulfonyl-5-formyl-2,2'-bipyrrole (15)** was prepared according to method B from bipyrrole **6** (15 mg, 0.03 mmol). Purification by column chromatography on silica gel (50% EtOAc-hexane) afforded **15** as a brown solid (15 mg, 94%);  $R_f$  0.27; m.p. 156-158°C;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  : 10.22 (s, 1H), 7.75-7.45 (m, 11H), 6.40 (t,  $J = 3.3\text{ Hz}$ , 1H), 6.22 (m, 1H), 5.91 (d,  $J = 0.6\text{ Hz}$ , 1H), 3.81 (s, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  : 181.2, 158.6, 139.4, 138.8, 135.1, 135.0, 131.9, 130.1 (2C), 129.9 (2C), 128.5 (2C), 128.2 (2C), 126.3, 123.8, 121.1, 119.3, 112.2, 108.6, 59.5; HR-MS calcd. for  $\text{C}_{22}\text{H}_{19}\text{N}_2\text{O}_6\text{S}_2$  ( $[\text{M}+\text{H}^+]$ ) 471.0679, found 471.0690.

**5'-((Dimethylamino)methylene)-4-methoxy-1*H*,5'*H*-[2,2'-bipyrrole]-5-carbaldehyde (7)** was prepared according to method B from bipyrrole **1** (16 mg, 0.05 mmol). The hydrolysis with saturated aqueous sodium acetate solution was stopped after 30 min and **7** was isolated by extraction with ethyl acetate. The organic extracts were dried over  $\text{MgSO}_4$ , filtered and evaporated to a green solid (20 mg, 80%); m.p. 205-208 °C;  $^1\text{H}$

NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  : 9.82 (s, 1H), 7.50 (s, 1H), 6.96 (d,  $J$  = 3.9 Hz, 1H), 6.75 (d,  $J$  = 3.9 Hz, 1H), 6.18 (s, 1H), 3.95 (s, 3H), 3.91 (s, 3H), 3.50 (s, 3H); <sup>13</sup>C NMR (100 MHz, (CDCl<sub>3</sub>)  $\delta$  : 180.9, 165.6, 143.9, 143.5, 137.0, 128.8, 117.8, 115.0, 110.9, 94.9, 59.6, 49.7, 44.3. HR-MS calcd. for C<sub>13</sub>H<sub>16</sub>N<sub>3</sub>O<sub>2</sub> ([M+H<sup>+</sup>]) 246.1237, found 246.1230.

### Representative procedure C

#### **Tetra-ethyl-5,5'-((4-methoxy-1*H*,1'*H*-[2,2'-bipyrrole]-5,5'-**

#### **diyl)bis(methanylydene))bis(azanylylidene))bis(2-aminothiophene-3,4-**

**dicarboxylate) (20).** A solution of 2,5-diaminothiophene-3,4-dicarboxylic acid diethylester (**19**, 76 mg, 0.29 mmol, 2.2 equiv.) in absolute ethanol (31 mL) was treated with 4-methoxy-5,5'-bisformyl-2,2'-bipyrrole (**8**, 29 mg, 0.13 mmol, 1 equiv.) followed by a catalytic amount of trifluoroacetic acid, heated at reflux for 3 h, cooled, and evaporated to an orange film, which was purified by column chromatography on silica gel (60% EtOAc-hexane) to afford conjugated tetracycle **20** as an orange film (60 mg, 65%);  $R_f$  : 0.44 ; <sup>1</sup>H NMR (300 MHz, DMSO)  $\delta$  : 11.76 (br, 1H), 11.35 (br, 1H), 7.82 (s, 1H), 7.81 (s, 2H), 7.66 (m, 3H), 6.75 (m, 2H), 6.53 (s, 1H), 4.30 (m, 4H), 4.16 (m, 4H), 3.84 (s, 3H), 1.19 (m, 12H); <sup>13</sup>C NMR (100 MHz, (CD<sub>3</sub>)<sub>2</sub>CO)  $\delta$  : 166.6, 166.4, 164.8, 164.7, 160.9, 160.1, 155.9, 144.5, 140.2, 136.7 135.1, 132.1, 130.8, 129.7, 127.2, 124.8, 120.0, 120.0, 116.5, 111.9, 111.6, 101.5, 62.0, 61.9, 60.7, 60.6, 59.2, 32.0, 30.9, 15.5, 15.3. HR-MS calcd. for C<sub>31</sub>H<sub>35</sub>N<sub>6</sub>O<sub>9</sub>S<sub>2</sub> ([M+H<sup>+</sup>]) 699.1901, found 699.1901.

#### **2,2'-((4-methoxy-1-(phenylsulfonyl)-1*H*,1'*H*-[2,2'-bipyrrole]-**

#### **5,5' diyl)bis(methanylylidene))bis(azanylylidedene)bis(thiophene-3-carbonitrile) (18)**

was prepared by a modification of method C from 4-(methoxy)-1-benzenesulfonyl-5,5'-

bisformyl-2,2'-bipyrrole (**9**, 10 mg, 0.03 mmol) and 2-amino-3-cyanothiophene (**17**, 8 mg, 0.40 mmol) by stirring for 30 min at room temperature. Purification by column chromatography on silica gel (50% EtOAc-hexane) afforded conjugated tetracycle **18** as a brown solid (16 mg, 91%);  $R_f$ : 0.41;  $^1\text{H}$  NMR (300 MHz, DMSO- $d_6$ )  $\delta$ : 12.43 (br, 1H), 8.80 (s, 1H), 8.48 (s, 1H), 7.74 (m, 1H), 7.58 (m, 2H), 7.42 (m, 4H), 7.33 (m, 2H), 7.08 (s, 1H), 6.94 (s, 1H), 6.69 (s, 1H), 3.86 (s, 3H);  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta$ : 165.8, 165.0, 158.8, 151.6, 150.9, 136.0, 135.5, 135.1, 134.1, 132.1, 129.7 (2), 129.0, 127.9, 126.7 (2), 121.6, 121.5, 117.4, 116.3, 115.3, 115.3, 109.5 (2), 102.4, 102.3, 59.3. HR-MS calcd. for  $\text{C}_{27}\text{H}_{19}\text{N}_6\text{O}_3\text{S}_3$  ( $[\text{M}+\text{H}^+]$ ) 571.0675, found 571.0679.

**Tetra-ethyl-5,5'-((4-methoxy-1-(phenylsulfonyl)-1*H*,1'*H*-[2,2'-bipyrrole]-5,5'-diyl)bis(methanylydene))bis(azanylylidene))bis(2-aminothiophene-3,4-dicarboxylate) (**21**)** was prepared according to method C from 4-(methoxy)-1-benzenesulfonyl-5,5'-bisformyl-2,2'-bipyrrole (**9**, 12 mg, 0.03 mmol) and 2,5-diaminothiophene-3,4-dicarboxylic acid diethylester (**19**, 19 mg, 0.07 mmol). Purification by column chromatography on silica gel (50% EtOAc-hexane) afforded conjugated **22** as an orange film (8 mg, 28%) which displayed the same physical and spectral properties as **20**, which was observed to contain a trace of **21** by HR-MS: calcd. for  $\text{C}_{37}\text{H}_{39}\text{N}_6\text{O}_{11}\text{S}_3$  ( $[\text{M}+\text{H}^+]$ ) 839.1833, found 839.1807).

**2,2'-((4-methoxy-1*H*,1'*H*-[2,2'-bipyrrole]-5,5'-diyl)bis(methanylylidene))bis(azanylylidenene)bis(thiophene-3-carbonitrile) (**17**)** was prepared according to method C from 4-(methoxy)-5,5'-bisformyl-2,2'-bipyrrole (**8**, 40 mg, 0.18 mmol) and 2-amino-3-cyanothiophene (**17**, 50 mg, 0.40 mmol). Purification by column chromatography on silica gel (50% EtOAc-hexane) afforded conjugated tetracycle **17** as

an orange film (19 mg, 37%):  $R_f$  0.7;  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  : 10.0 (br, 1H), 9.57 (br, 1H), 8.24 (s, 1H), 8.21 (s, 1H), 7.1 (d,  $J=5.7$  Hz, 1H), 7.03 (d,  $J=5.7$  Hz, 1H), 6.98 (d,  $J=5.7$  Hz, 1H), 6.89 (s, 1H), 6.86 (m, 1H), 6.68 (d,  $J=3.9$  Hz, 1H), 6.28 (s, 1H), 3.93 (s, 3H);  $^{13}\text{C NMR}$  (100 MHz,  $(\text{CD}_3)_2\text{CO}$ )  $\delta$  : 166.6, 164.9, 158.0, 150.2, 144.9, 131.7, 131.4, 130.9, 127.7, 127.5, 122.2, 120.5, 118.8, 117.0, 115.4, 114.9, 111.8, 102.8, 100.8, 95.2, 58.0. HR-MS calcd. for  $\text{C}_{21}\text{H}_{14}\text{N}_6\text{OS}_2$  ( $[\text{M}^+]$ ) 431.0743, found 431.0747.

**2,2'-((4-methoxy-1-(phenylsulfonyl)-1*H*,1'*H*-[2,2'-bipyrrole]-**

**5,5'-diyl)bis(methanylylidene))bis(azanylylidenene)bis(thiophene-3-carbonitrile) (18)**

was prepared by a modification of method C from 4-(methoxy)-1-benzenesulfonyl-5,5'-bisformyl-2,2'-bipyrrole (**9**, 10 mg, 0.03 mmol) and 2-amino-3-cyanothiophene (**17**, 8 mg, 0.40 mmol) by stirring for 30 min at room temperature. Purification by column chromatography on silica gel (50% EtOAc-hexane) afforded conjugated tetracycle **18** as a brown solid (16 mg, 91%);  $R_f$  : 0.41;  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ )  $\delta$  : 12.43 (br, 1H), 8.80 (s, 1H), 8.48 (s, 1H), 7.74 (m, 1H), 7.58 (m, 2H), 7.42 (m, 4H), 7.33 (m, 2H), 7.08 (s, 1H), 6.94 (s, 1H), 6.69 (s, 1H), 3.86 (s, 3H). HR-MS calcd. for  $\text{C}_{27}\text{H}_{19}\text{N}_6\text{O}_3\text{S}_3$  ( $[\text{M}+\text{H}^+]$ ) 571.0675, found 571.0679.

**Tetra-ethyl-5,5'-((4-methoxy-1-octyl-1*H*,1'*H*-[2,2'-bipyrrole]-5,5'-diyl)bis**

**(methanylydene))bis(azanylylidene))bis(2-aminothiophene-3,4-dicarboxylate) (22)**

was prepared by a modification of method C from bipyrrole **12** (3.6 mg, 0.008 mmol) and 2,5-diaminothiophene-3,4-dicarboxylic acid diethylester (**19**, 4.3 mg, 0.017 mmol) by stirring for 1h at room temperature. Purification by column chromatography on silica gel (60% EtOAc-hexane) afforded conjugated tetracycle **22** as an orange film (2 mg, 28%):  $R_f$  0.61;  $^1\text{H NMR}$  (700 MHz,  $\text{CDCl}_3$ )  $\delta$  : 8.92 (br, 1H), 7.89 (s, 1H), 7.83 (s, 1H), 6.65 (d,

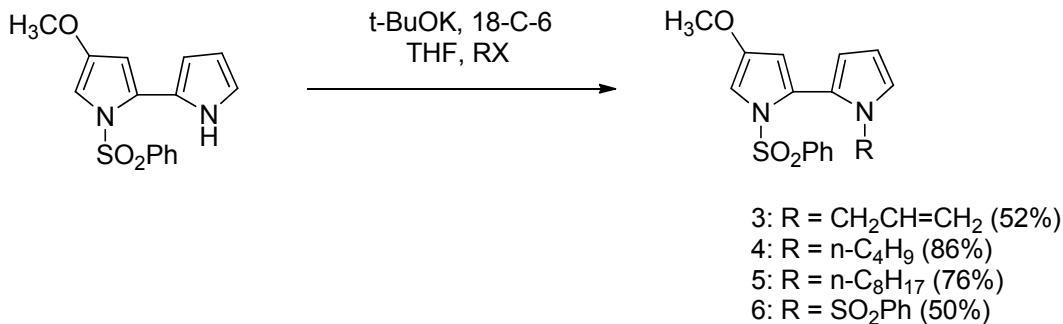
$J = 4.2\text{ Hz}$ , 1H), 6.42 (s, 1H), 6.27 (s, 2H), 6.19 (s, 2H), 6.06 (s, 1H), 4.62 (m, 2H), 4.37 (m, 4H), 4.28 (m, 4H), 3.91 (s, 3H), 0.9-1.43 (m, 27H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  : 166.0, 165.7, 164.5, 164.5, 158.6, 158.1, 144.2, 139.9, 136.0, 132.5, 131.1, 128.9, 126.6, 126.6, 124.8, 120.4, 120.4, 116.5, 103.2, 103.1, 95.7, 95.7, 61.4, 61.3, 60.2, 60.1, 58.1, 46.6, 31.9, 31.1, 29.7, 29.4, 29.3, 26.4, 22.7, 14.4, 14.3, 14.2, 14.1. HR-MS calcd for  $\text{C}_{39}\text{H}_{50}\text{N}_6\text{O}_9\text{S}_2$  ( $[\text{M}+\text{H}^+]$ ) 811.3107, found 811.3114.

### 3.5 Crystal Structure Determination

Diffraction data for **20** was collected on a Bruker FR591 diffractometer using graphite-monochromatized CuK $\alpha$  radiation with 1.54178 Å. The structures were solved by direct methods (SHELXS97). All non-hydrogen atoms were refined based on Fobs2 (SHELXS97), while hydrogen atoms were refined on calculated positions with fixed isotropic U, using riding model techniques.

## 3.6 Results and Discussion

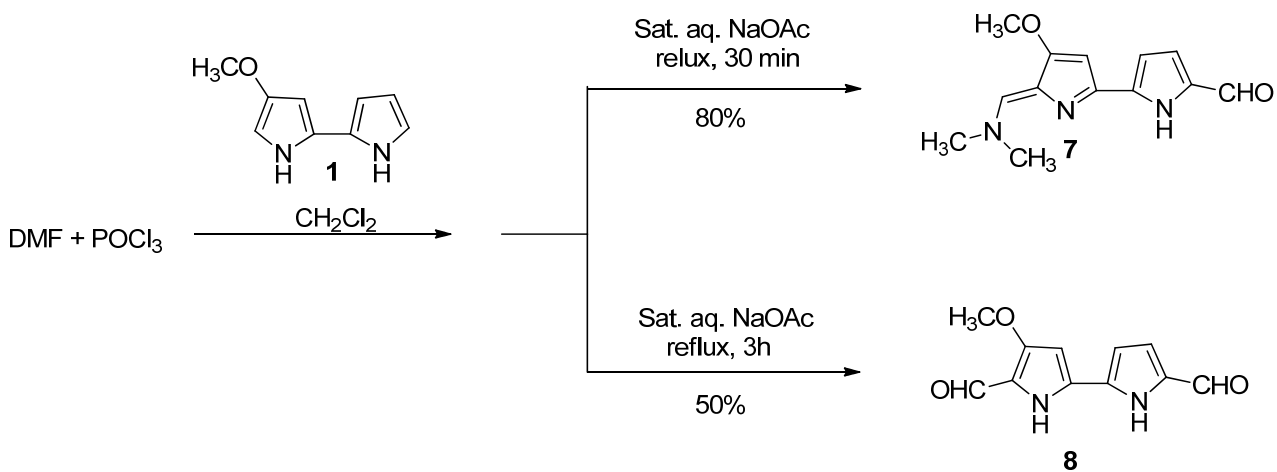
### 3.6.1 Synthesis



**Scheme 1.** *N*<sup>7</sup>-Modification of bipyrrole **2**.

4-Methoxy-2,2'-bipyrrole **1** and its sulfonamide **2**, both were prepared from hydroxyproline as described.<sup>19,20</sup> To explore the influence of a 1'-nitrogen substituent on the opto-electronic properties of bipyrrole analogs, the anion of the pyrrole nitrogen of **2** was generated with potassium *tert*-butoxide and 18-crown-6-ether in THF and respectively, alkylated in reactions with a set of alkyl iodides (allyl iodide, butyl iodide, octyl iodide) and sulfonylated with benzenesulfonyl chloride.<sup>18,19</sup> 4-Methoxy-1-phenylsulfonyl-1'-allyl-2,2'-bipyrrole (**3**), its 1'-butyl and 1'-octyl counterparts **4** and **5** and 4-methoxy-1,1'-biphenylsulfonyl-2,2'-bipyrrole (**6**) were isolated respectively after chromatography on silica gel in 52%, 86%, 76% and 50% yields, respectively (Scheme 1).



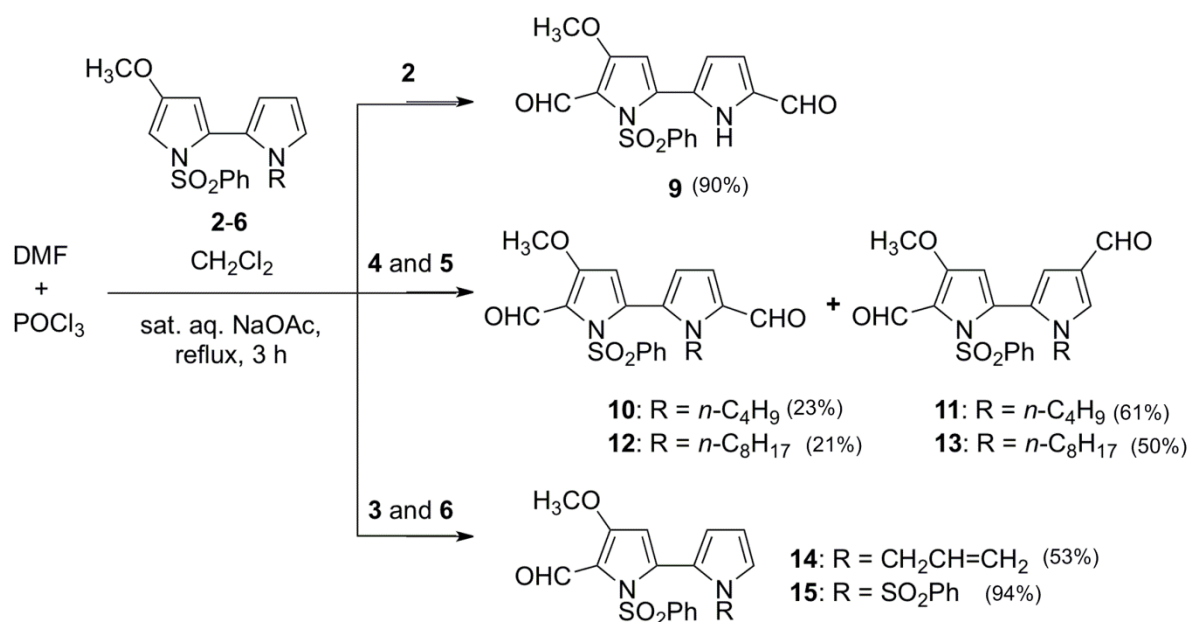


**Scheme 2.** Vilsmeier-Haack formylation of methoxybipyrrole **1**.

A series of mono- and bis-formyl analogs was then prepared by treating bipyrroles **1-6** under Vilsmeier-Haack formylation conditions<sup>36</sup> (Schemes 2 and 3). The Vilsmeier reagent was prepared in the neat by treating dimethylformamide with phosphoryl chloride and then added slowly to the respective bipyrrole in dichloromethane at  $-15^{\circ}\text{C}$ . The reaction mixture was then let warm to room temperature with stirring overnight. In the reaction of the parent 4-methoxy-2,2'-bipyrrole **1**, the workup with aqueous sodium acetate at reflux afforded enamine **7** in 80 % yield (Scheme 2). On the other hand, bipyrrole dialdehyde **8** was isolated in 50% yield without need of further purification by modification of the hydrolysis protocol by treating the reaction mixture with an aqueous solution of sodium acetate at reflux for 2h. The same reaction and work-up conditions used to prepare **8** were applied on sulfonamides **2-6** (Scheme 3).

Treatment of 1-phenylsulfonyl methoxybipyrrole **2** under the formylation and workup conditions used to prepare **8** provided 4-(methoxy)-1-benzenesulfonyl-5,5'-bisformyl-2,2'-bipyrrole **9** in 70% yield. Similarly, bis-formylation was observed with 1'-alkyl (butyl and octyl) bipyrroles **4** and **5**; however, mixtures of 5,5'- and 5,4'-

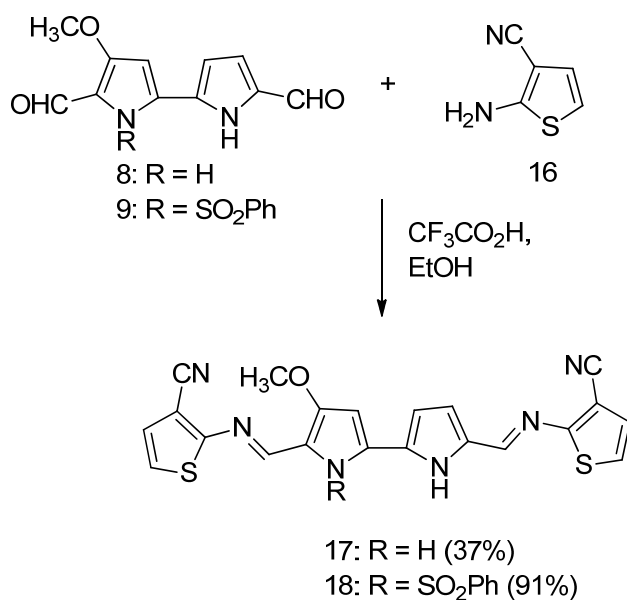
regioisomers were obtained, with a preference for the latter (1:3 ratio). The 5,5'- and 5,4'-regioisomers were separable by chromatography such that 5,4'-substituted bipyrroles **11** and **13** were isolated in 61% and 50% yields, respectively, along with their 5,5'-counterparts **10** and **12** in 23% and 21% yields. 5,4'-Bisformyl-2,2'-bipyrroles **11** and **13** were, however, unstable and observed by thin layer chromatography to degrade after a few hours at ambient atmosphere. Finally, selective mono-formylation of the 5-position of the 1-phenylsulfonyl methoxypyrrole ring was observed when the same formylation and work-up conditions were applied on 1-phenylsulfonyl 1'-allylbipyrrole (**3**) and bis-sulfonamide **6** to respectively provide 5-formyl bipyrroles **14** and **15** in 53% and 94% yields, respectively (Scheme 3).



**Scheme 3.** Vilsmeier-Haack formylations of 1-phenylsulfonyl methoxybipyrroles **2-6**.

The position of bipyrrole formylation was determined by COSY and NOESY spectroscopy (see Supporting Information). For example, in the NOESY spectrum of 5,5'-dialdehyde **9**, through space transfers of magnetization were observed, respectively, between the pyrrole 3-position proton (6.31 ppm) and the methoxy group singlet (3.9 ppm), between the 5-position aldehyde proton (10.17 ppm) and both the methoxy group singlet and the sulphonamide aromatic protons (7.37 ppm), and between the pyrrole 4'-position proton (6.99 ppm) and the 5'-position aldehyde proton (9.62 ppm). In the COSY spectrum of **9**, a through-bond coupling was observed between the pyrrole protons at the 3'- and 4'-positions (6.53 ppm and 6.99 ppm). Similarly, in the NOESY spectrum of 5,5'-dialdehyde **10**, transfer of magnetization was respectively observed between the 5-position aldehyde proton (10.28 ppm) with the sulphonamide aromatic protons (7.5 ppm) and methoxy singlet (3.89 ppm), as well as between the 5'-position aldehyde proton (9.67 ppm) and both the pyrrole 4'-proton (6.99 ppm) and the butyl chain methylene proton signals (4.33 ppm). On the other hand, in the COSY spectrum of 5,4'-dialdehyde **11**, a through-bond coupling was observed between the 5-position aldehyde proton (10.27 ppm) and the pyrrole 3-position proton (6.18 ppm). In the NOESY spectrum of **11**, through-space transfer of magnetization was observed between the 4'-position aldehyde proton (9.79 ppm) and both the 3- and 5-position pyrrole protons (6.98 and 6.55 ppm). The COSY and NOESY spectra of *N*<sup>2</sup>-octyl bipyrroles **12** and **13** exhibited similar couplings and through-space transfer of magnetization as seen in spectra of **10** and **11**, respectively. For aldehyde **15**, the COSY spectrum exhibited coupling between the 3',4' and 5'-pyrrole protons (6.22, 6.39 and 7.60) establishing the absence of a formyl group on the pyrrole B-ring. In addition, coupling was observed between the 5-position

aldehyde proton (10.22 ppm) with the pyrrole 3-position proton (5.93 ppm). The NOESY spectrum of **15** supported the assignment exhibiting through-space transfer of magnetization between the methoxy singlet (3.81 ppm) and pyrrole 3-position proton (5.93 ppm). For aldehyde **14**, the assignment of the aldehyde to the 5-position was based on its chemical shift (10.24 ppm), which in the case of dialdehydes **9-13**, appeared always further downfield relative to that of aldehydes on the pyrrole B-ring.

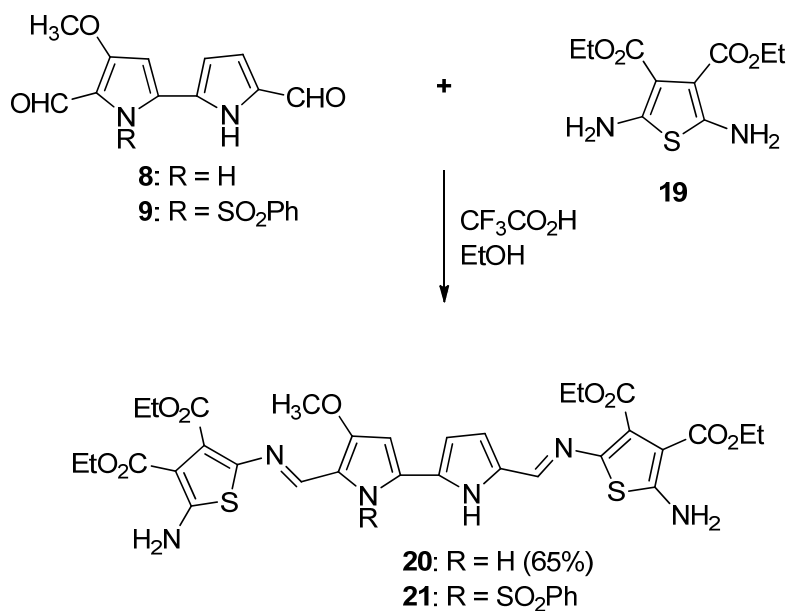


**Scheme 4.** Condensations of methoxybipyrroles **8** and **9** with amino thiophene **16**.

Asymmetric azomethine comonomers were next pursued by linking the 4-methoxy-2,2'-bipyrrole cores by way of imine bridges to two different amino thiophenes (Schemes 4-6). For these syntheses, 2-amino-3-cyanothiophene **16** and 2,5-diaminothiophene-3,4-dicarboxylic acid diethyl ester **19** were selected because of their previous application in condensations to form comonomers<sup>28,37,38</sup> and prepared as previously described.<sup>39,40</sup> The electron-withdrawing groups at the 3- and 4-positions of **16** and **19** deactivate the electron-rich amines at the 2- and 5-positions, conferring greater stability. Amine **16** and

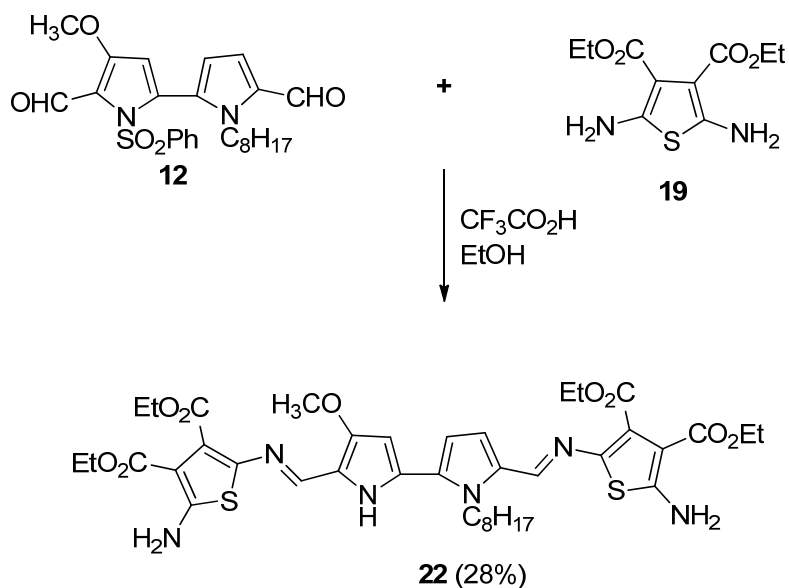
diamine **19** have the respective utility to end-cap the conjugated system and to allow for additional condensations to make longer comonomers.

The imine bridges were effectively assembled by dehydration of the respective bis-formyl bipyrrrole and aminothiophene in ethanol containing catalytic trifluoroacetic acid (TFA) at reflux. Initially, the amino cyanothiophene **16** was employed in condensations under these conditions with the parent methoxybipyrrrole **8** and its 1-phenylsulfonyl counterpart **9** to afford respectively the conjugated azomethine tetracycles **17** and **18**. In the case of the parent **8**, azomethine comonomer **17** was obtained after isolation by chromatography on silica gel in 37% yield. On the other hand, the reaction between 1-phenylsulfonyl methoxybipyrrrole **9** and **16** did not provide product on heating at reflux with and TFA in EtOH. At room temperature, however, the condensation of **9** and **16** went smoothly to yield azomethine tetracycle **17** in 91 % yield after purification by chromatography on silica gel. Although the azomethane link appeared robust during the synthesis and analysis of the conjugated systems, certain products showed the appearance of new signals in their NMR spectra after storage over time, which may be due to various modes of decomposition.



**Scheme 4.** Condensations of methoxybipyrroles **8** and **9** with amino thiophene **19**.

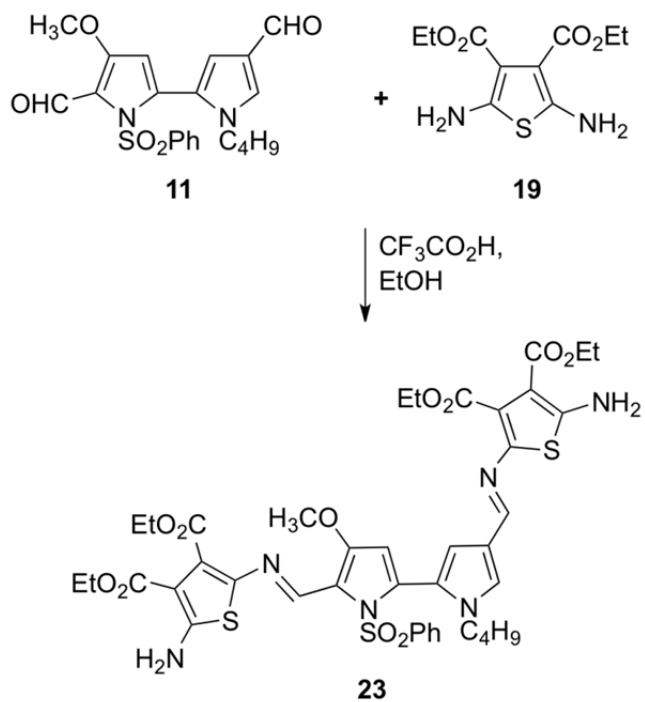
Diaminothiophene **19** was subsequently reacted with methoxybipyrrole **8** in ethanol containing catalytic TFA at reflux to provide conjugated azomethine tetracycle **20** in 65% yield after chromatography on silica gel. Attempts to perform the same condensation using the *N*-phenylsulfonyl analog **9** provided a condensation product in 28% yield after chromatography. Although the ion corresponding to azomethine tetracycle **21** was observed in the mass spectrometric analysis, inspection of the proton NMR spectrum demonstrated loss of the phenylsulfonyl group to provide **20**. Analysis of samples on silica plate suggested that the phenylsulfonyl group was likely removed from **21** during purification on silica gel.



**Scheme 5.** Condensation of methoxybipyrroles **12** with amino thiophene **19**.

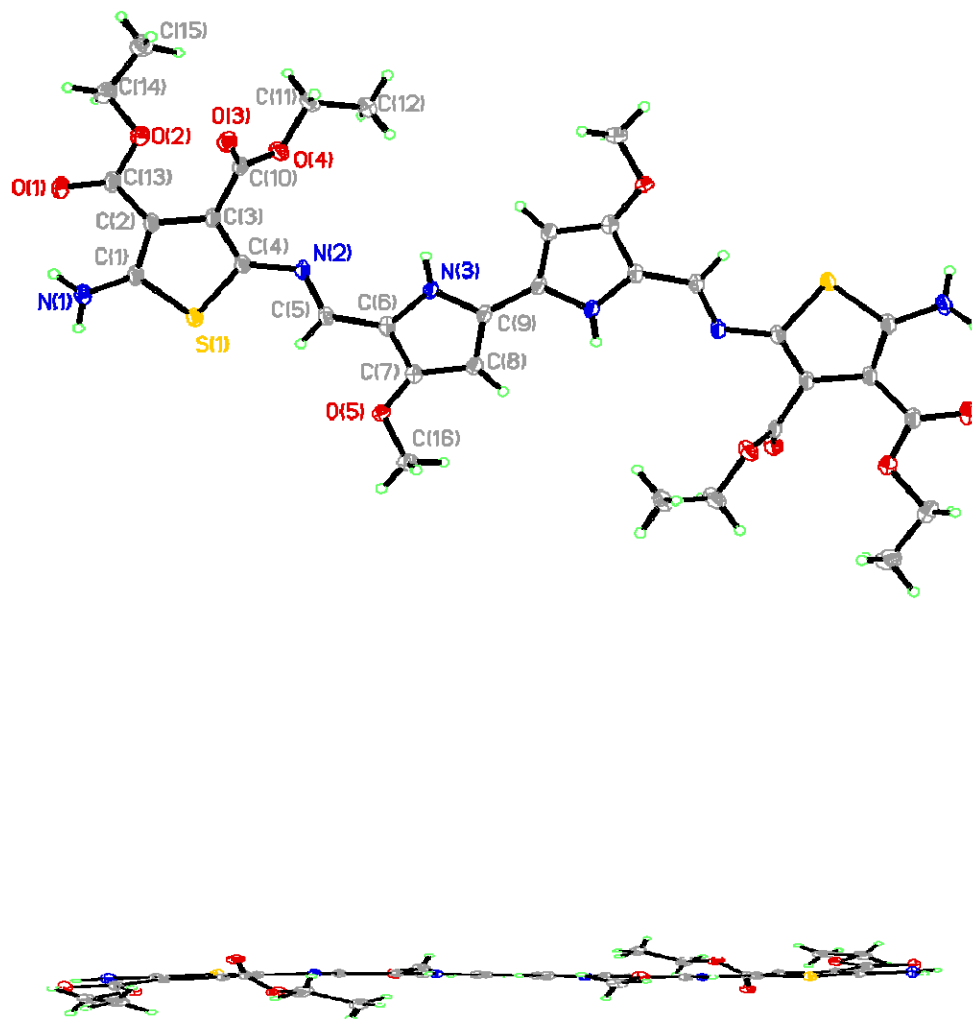
Attempts were less successful to produce conjugated tetracycles from bipyrroles **10-13** possessing a 1'-alkyl substituent. No condensation product could be isolated from the reaction of 5,5'-bisformyl-1'-butylbipyrrole **10** and diaminothiophene **19** with TFA in ethanol at reflux. On the other hand, 5,5'-bisformyl-1'-octylbipyrrole **12** reacted with thiophene **19** and TFA in ethanol at room temperature to afford azomethine tetracycle **22** as a brown film in 28 % yield (Scheme 5). Analysis of azomethine tetracycle **22** by proton NMR spectroscopy indicated that loss of the phenylsulfonamide had occurred in a similar way as described for **21** above. Temperature had an effect on the condensation of the 5,4'-bisformyl-1'-alkylbipyrroles **11** and **13**. From ethanol at reflux, no product was obtained in the condensation of thiophene **19** with 1'-*n*-octylbipyrrole **13**. On the contrary, the desired conjugated tetracycle **23** was isolated after chromatography on silica gel in 53% yield from condensation of 5,4'-bisformyl-1'-butylbipyrrole **11** with **19** using TFA in EtOH at room temperature. Conjugated tetracycle **23** proved, however, to be

unstable and degraded as observed by thin layer chromatography, after sitting overnight under vacuum.

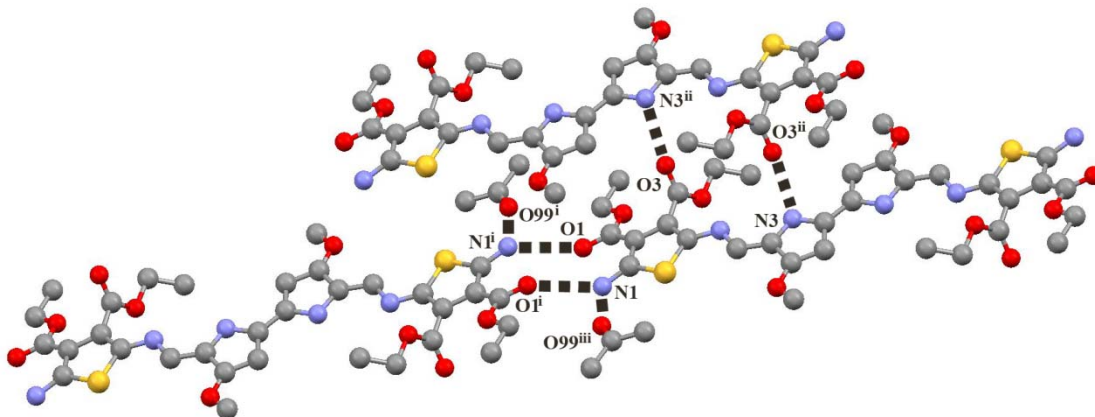


**Scheme 6.** Condensation of methoxybipyrroles **11** with amino thiophene **19**

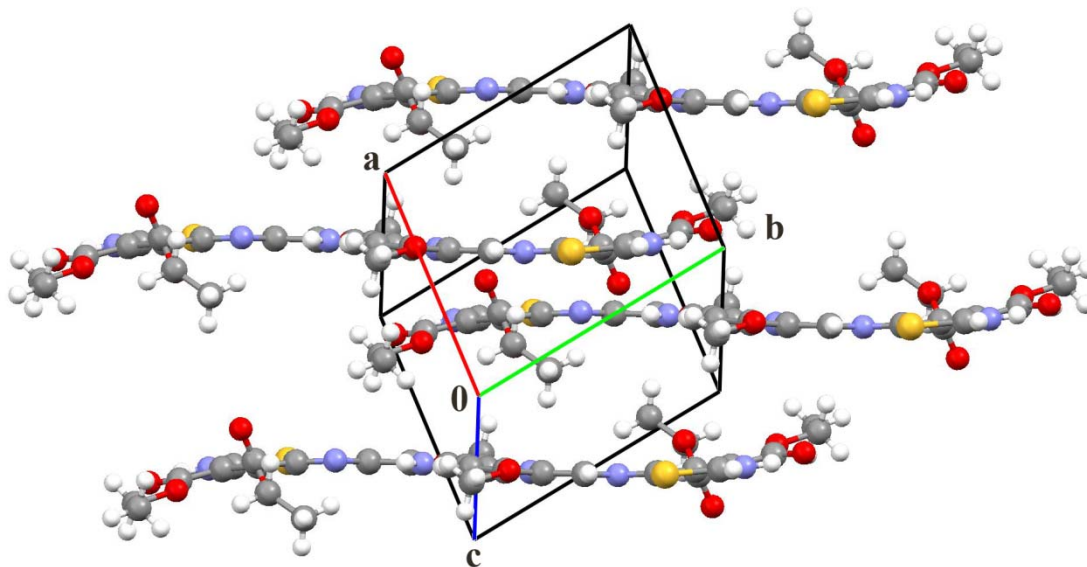




**Figure 1.** Front view of **20** (top) and seen along the *c* axis (bottom).



**Figure 2.** Intermolecular interactions of **20** (symmetry codes: (i)  $-x, 2-y, -z$ ; (ii)  $1-x, 1-y, 1-z$ ; (iii)  $x, y, 1+z$ ).



**Figure 3.** Crystal packing of **20** with solvent molecules omitted for clarity.

### 3.6.2 X-ray Crystallography

Although only one isomer was detected by  $^1\text{H}$  NMR spectroscopy of the azomethine analogs, assignment of *E* or *Z* configuration was not possible. Unequivocal assignment of the imine geometry was made possible by X-ray crystallography on a single crystal of

tetracycle **20**, which crystallized from slow evaporation of acetone. The crystal structure confirmed that **20** adopted the imine *E*-isomer. The methoxy group breaks the symmetry of tetracycle **20** and resulted in disordering within the crystal structure. The structure was solved without specific assignment of the position of the methoxy group; instead, the resolution was refined by placing its occupancy factor to 50 %. The data nonetheless confirm the correct structure for **20** and illustrate a coplanar orientation of the heteroatoms in an anti-parallel arrangement (Figure 1), consistent with previous azomethine structures.<sup>27,28,41</sup>

The terminal heterocycles of **20** were slightly twisted by 9.36° from the mean plane described by the central planar bipyrrrole and the two azomethine bonds to which they are connected. The observed mean plane angles are in agreement with other heterocyclic azomethines and are in contrast to homoaryl azomethine structures, in which mean planes are highly twisted by 65°.<sup>42</sup> The C=N, N-aryl, and CH-aryl bond distances for **20** were respectively, 1.299(3) Å, 1.389(3) Å and 1.439(3) Å on both side. The observed coplanarity of the aryl groups and the azomethine bonds confirm the high degree of  $\pi$ -conjugation of the azomethine, as per the spectroscopic data.

Intermolecular interactions between the molecules in the solid state were apparent in the crystallographic data. For example, hydrogen bonds were observed between two terminal aminothiophenes and the carbonyl forming an acceptor-donor-acceptor motif, as seen in Figure 2. The distances for N1-H1A...O1<sup>i</sup>, N1-H1B...O99<sup>iii</sup> and N3-H3A...O3<sup>ii</sup> were 2.309 Å, 2.015 Å and 2.194 Å. The angles of these hydrogen bridges were 136° 164° and 154°, which were consistent with hydrogen bonding. Every molecule was well-aligned in one direction within the 3D arrangement (Figure 3). No regular  $\pi$ -

stacking was found, because hydrogen bonding shifted the direction of the  $\pi$ -stacking. Linear and coplanar configurations were adopted by the comonomers, because of the contributions of such interactions.

**Table 1.** Details of Crystal Structure Determination for **20**.

Formula	C <sub>31</sub> H <sub>36</sub> N <sub>6</sub> O <sub>9</sub> S <sub>2</sub>
CCSD no.	CCDC 831157
<i>Mw</i> (g/mol); F(000)	816.93 g/mol ; 432
Crystal color and form	Red plate
Crystal size (mm)	0.10 x 0.07 x 0.04
<i>T</i> (K); <i>d</i> <sub>calcd.</sub> (g/cm <sup>3</sup> )	150 (2) ; 1.279
Crystal System	Triclinic
Space Group	P-1
Unit Cell: <i>a</i> (Å)	8.227 (10)
<i>b</i> (Å)	10.295 (10)
<i>c</i> (Å)	13.617 (18)
<i>α</i> (°)	73.85 (3)
<i>β</i> (°)	87.18 (5)
<i>γ</i> (°)	73.37 (3)
<i>V</i> (Å <sup>3</sup> ); <i>Z</i>	1061 (2) ; 1

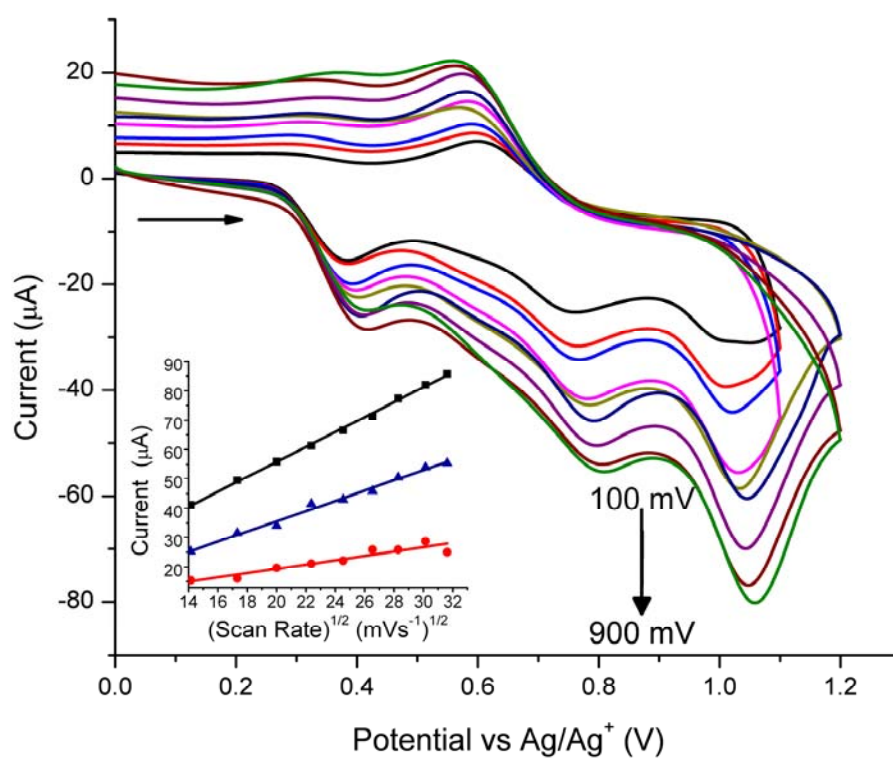
$\theta$ range (°); completeness	3.38 - 71.11 ; 0.955
Reflections: collected / independent; $R_{\text{int}}$	13056 / 3938 ; 0.0322
$\mu$ (mm <sup>-1</sup> )	1.666
Abs. Corr.	Semi-empirical
$R_1(F)$ ; $wR(F^2)$ [ $I > 2\sigma(I)$ ]	0.0492; 0.1474
$R_1(F)$ ; $wR(F^2)$ (all data)	0.0560; 0.1537
GoF( $F^2$ )	1.050
Max. residual e <sup>-</sup> density	0.453 e <sup>-</sup> · Å <sup>-3</sup>

**Table 2.** Spectroscopic and electrochemical data of neutral and corresponding radical cations of unsymmetric bipyrrole azomethines.

<b>Compound</b>	$\lambda_{\text{abs}}$ (nm)	$R^{++}$ (nm) <sup>1</sup>	$E_{\text{pa}}$ (V) <sup>2</sup>	$E_{\text{pc}}$ (V) <sup>2</sup>	$E_{\text{g}}$ (eV) <sup>3</sup>
<b>20</b>	520	560 (605)	0.4; 0.8	-1.3	1.1
<b>22</b>	480	540 (610)	0.3; 0.7	-1.3	1.1
<b>17</b>	520	785	0.8	-1.1	1.4
<b>18</b>	480	540	1.1	-1.2	1.8

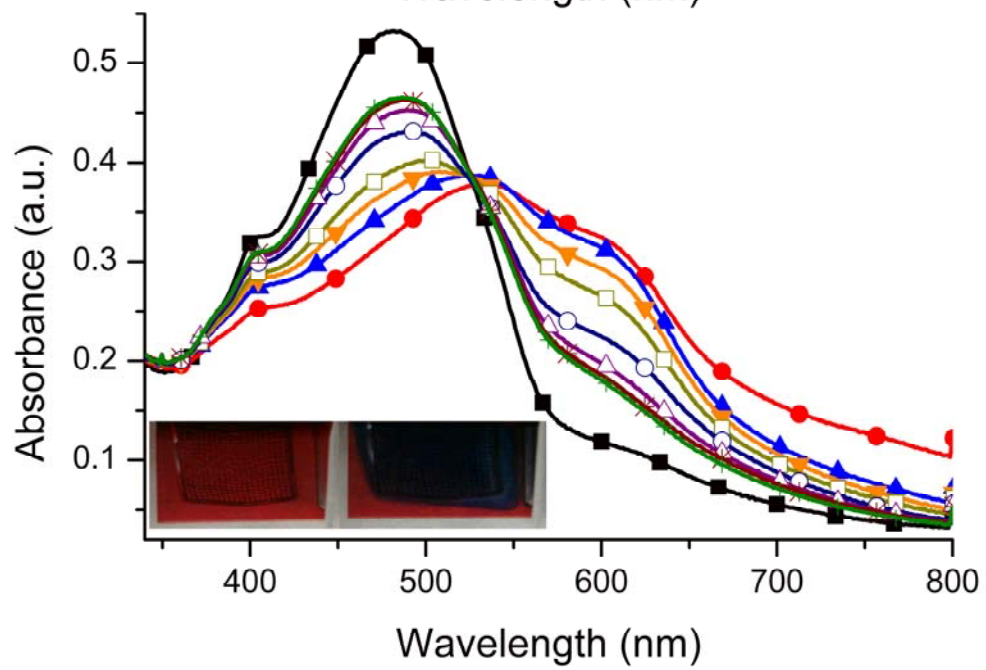
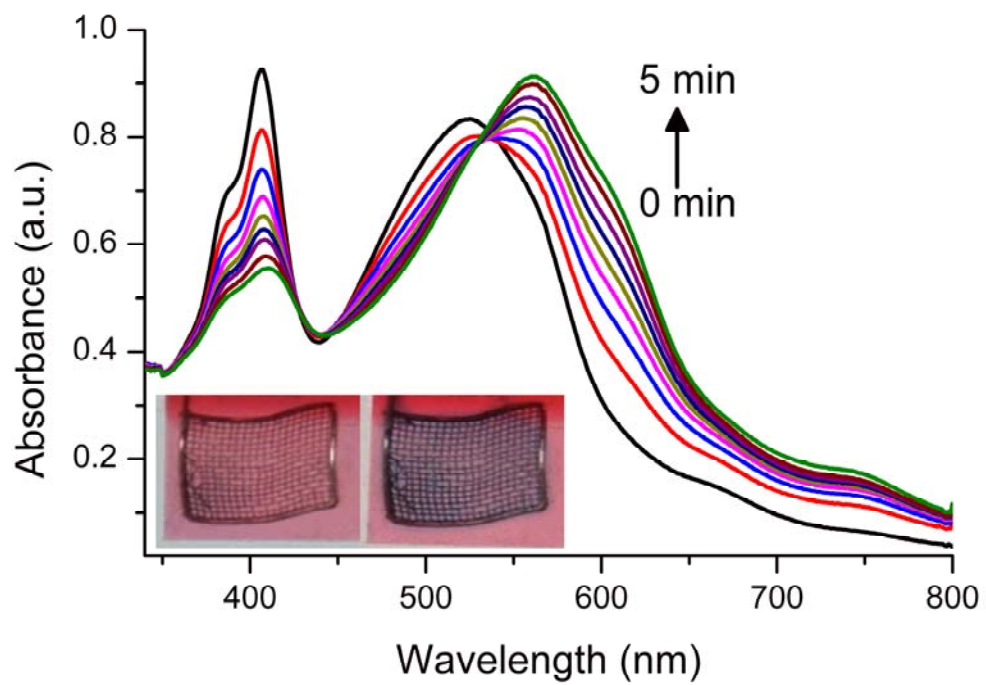
<sup>1</sup> Absorbance of radical cation. <sup>2</sup> Potentials vs. Ag/Ag<sup>+</sup>, corrected using ferrocene (0.435V) as an internal reference.<sup>43</sup> <sup>3</sup> Electrochemical energy-gap taken as the difference between the measured HOMO and LUMO values.

### 3.6.3 Electrochemistry



**Figure 4.** Cyclic voltammogram of **20** measured at scan rates between 200 and 900  $\text{mV}/\text{s}$ . Inset: Randles-Sevcik plot of the first (●) and second (▲) oxidation peaks of **20** relative to ferrocene (■) measured in dichloromethane.





**Figure 5.** Top: Absorbance spectra change of **20** upon applying an oxidation potential of 0.4 V for 0 to 5 min. Inset: Color change of **20** before (left) and after (right) electrochemical oxidation. Bottom: Absorbance spectra change of **22** upon applying an oxidation potential of 0.5 V for 0 (■) and 3 min (●) followed by applying a potential of -0.1 V for 0 (▼), 1 (□), 4 min (○) followed by -0.25 V applied for 1 (△), 2 (\*), and 3 min (+). Inset: Color change of **22** before (left) and after (right) electrochemical oxidation.

The electrochemical oxidation of the azomethines was investigated by cyclic voltammetry in anhydrous and deaerated dichloromethane. The anodic behavior of tetracycles **20** and **22** was investigated at different scan speeds. The number of electrons involved in the anodic processes was assigned and the reversibility of the resulting intermediates was unequivocally determined. In contrast to analogous aminothiophene azomethines, which exhibited reversible radical cation formation,<sup>28,29</sup> the first oxidation of **20** and **22** was irreversible (Figure 4), most likely due to the unsubstituted pyrrole positions in the reactive radical cation, which may have undergone cross-coupling. The cathodic current associated with the second oxidation process was much smaller than its corresponding anodic current, which when taken together with the change in  $E_{pa}$  as a function of scan speed, confirmed that the second oxidation process was pseudo-reversible. The Randels-Sevcik relationship was used to determine the number of electrons participating in the anodic processes. The peak current at different scan rates, relative to ferrocene as internal reference, was employed to derive the number of electrons participating in the oxidation processes according to:  $i_p = (2.69 \times 10^5) n^{3/2} A D^{1/2} C v^{1/2}$ , where  $i_p$  is the peak current;  $n$ , the number of electrons involved in the oxidation process;  $D$ , the diffusion coefficient;  $A$ , the electrode surface

area;  $C$ , the concentration; and  $v$ , the scan rate. Ferrocene ( $E_{pa} = 0.46$  vs. SCE in dichloromethane) was also used as an internal reference for determining the diffusion coefficient concomitant with other parameters of the Randles-Sevcik equation.<sup>43</sup> Azomethine **20** underwent two oxidation processes: one at ca. 0.4 and another at ca. 0.7 V. The oxidation of **20** was determined to proceed by a sequential one-electron process, by taking into account the different diffusion rates, which correlated with formation of the radical cation and dication (Figure 4).

The double oxidation was also observed for **22**. Conversely, both **17** and **18** underwent a single oxidation process. The oxidation potentials measured for the azomethines at similar scan speeds are summarized in Table 2. From the tabulated data, it is obvious that the first oxidation potentials of **20** and **22**, corresponding to the radical cation, are lower than for **17** and **18**. This is a result of the strong electron donating character of the terminal amine that decreases the oxidation potential. The second one-electron oxidation affording the dication of **17** and **18** is not visible, which is assumed be a result of their higher  $E_{pa}$  relative to **20** and **22**, implying that dication oxidation occurs beyond the working solvent redox window. By tailoring the N-pyrrole and terminal-thiophene substitutions with varying electronic groups, we were thus able to adjust the potential at which the radical cation was formed. It should be noted that the exact heterocycle that is oxidized to form the radical cation and further oxidized leading to the dication cannot be determined. However, the semi-empirically calculated SOMO levels for **20** (see Figures 6 and 7 in Supporting Information) show the radical cation and dication are not localized on a specific heterocycle; instead, they are evenly distributed across the tetracycle.

The HOMO and LUMO energy values can be determined from the redox onsets ( $E^{\text{onset}}$ ) according to:  $\text{HOMO} = - (E_{\text{pa}}^{\text{onset}} + 4.4)$  and  $\text{LUMO} = - (E_{\text{pc}}^{\text{onset}} + 4.4)$  (Table 2). The energy-gap ( $E_g$ ) calculated from the energy levels was ca. 1.5 eV and illustrated that the compounds were air stable and did not spontaneously oxidize or decompose under ambient conditions.

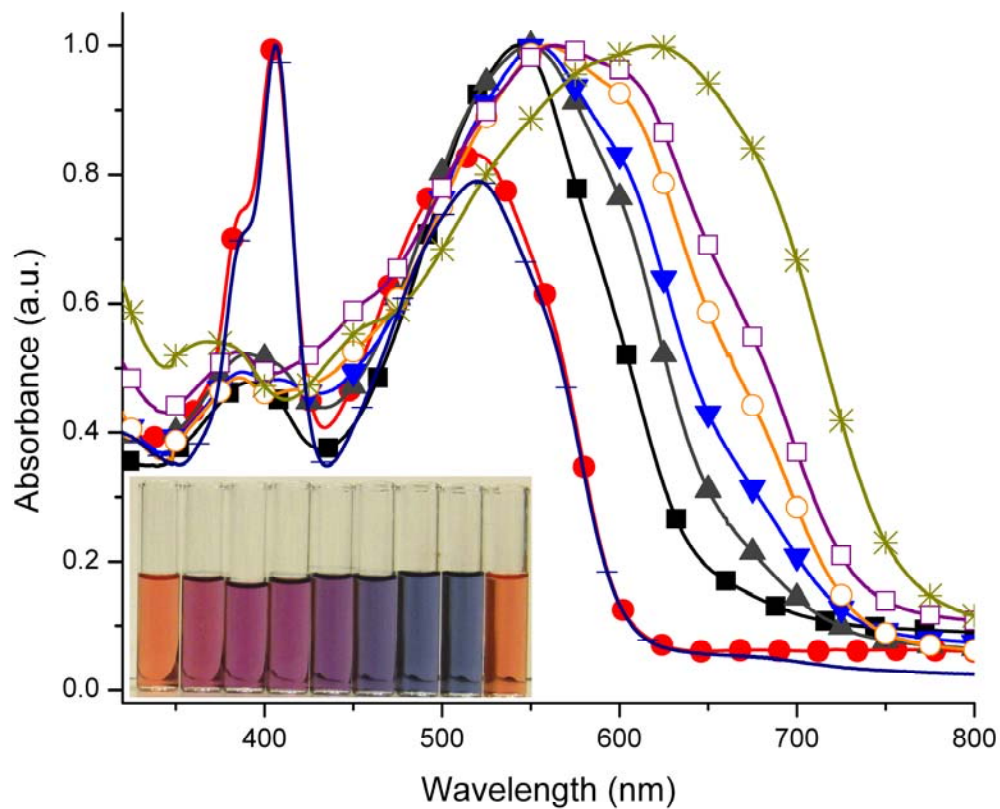
The spectroelectrochemistry of the azomethines was investigated for assessing the spectroscopic properties of the electrochemically induced radical cation intermediates. Upon applying potentials slightly greater than the first  $E_{\text{pa}}$ , both **20** and **22** underwent stark color changes (Figure 5 inset). The initial red color of neutral **20** ( $\lambda_{\text{max}} = 520$  nm) bleaches concomitant with a new absorbance of the blue radical cation, visible at 560 nm. Similarly, the radical cation of **22** was also blue and bathochromically shifted 60 nm from the neutral absorbance; however, **22** had a strong shoulder absorbance at 610 nm. The clear isosbestic point seen for both **20** and **22** confirmed the interdependence of the neutral and oxidized states, demonstrating that oxidation of these azomethines gave rise to a single product, which was assigned to the radical cation based on the cyclic voltammetric measurements. The spectroelectrochemical data demonstrated that the azomethines undergo reversible stark visible color changes upon radical cation formation.

The stability of the oxidized intermediate under the spectroelectrochemical conditions was examined by applying a negative potential to neutralize the anodically induced intermediate of **22** (Figure 5). The absorbance spectrum of the reduced intermediate was identical to that of the original neutral **22**; however, the intensity of the neutralized radical cation was somewhat lower than that of the original **22**, likely because of cross-coupling of the radical cation, as noted previously in the cyclic voltammetric

studies. The clear isosbestic point and the persistent absorbance at 520 nm confirmed the lack of azomethine decomposition and illustrated the robustness of the azomethine-linked heterocyclic systems.

#### 3.6.4 Chemical Oxidation

Azomethines have been misperceived to be susceptible to decomposition.<sup>44</sup> On the contrary, azomethines **17**, **18**, **20**, and **22**, all exhibited spectroelectrochemical properties indicative of their stability during reversible oxidation. Chemical doping of **20** was next performed, because significant spectroscopic changes between the neutral and oxidized forms of this azomethine were observed when electrochemically oxidized. Chemical doping affords the means to investigate the stability of both the doped products and neutral azomethines via dissipation and/or irreversible color formation, because of diffusion controlled kinetics, in contrast to the spectroelectrochemical measurements. For example, the chemical doping of **20** with increasing amounts of TFA was contingent on the number of equivalents of added acid and the apparent color shift from 520 to 625 nm was observed as the neutral species converted to the radical cation and finally to the dication (Figure 6). Moreover, the doped intermediate could be neutralized with excess of triethylamine to restore the original color of neutral **20**. The robustness of azomethine **20** was illustrated by performing multiple doping/dedoping cycles without significant color variation.



**Figure 6.** Absorbance of **20** with added TFA 0 (●), 1 (■), 2 (▲), 5 (▼), 10 (△), 20 (○), 40 (□), 100 (\*) equivalents followed by the addition of 100 eq of Et<sub>3</sub>N (-). Inset: Change in color of **20** with the addition of increasing amounts of 0-100 equivalents trifluoroacetic acid (from left to right) followed by the addition of 100 equivalents of triethylamine (right).

### 3.7 Conclusion

Conjugated azomethines were synthesized, which incorporated thiophene and bipyrrrole units. They were oxidized at low potentials and switched reversibly between oxidized and neutral states giving rise to stark color transitions. The heterocyclic conjugated azomethines, such as **20** and **22** exhibited enhanced spectroscopic and electrochemical properties, which could be tuned by modification of pendant groups. In light of the stark color states exhibited by the bipyrrrole-thiophenoazomethine analogs, resounding evidence was obtained to demonstrate that robust conjugated azomethines may be prepared for employment in functional materials for potential electrochromic applications.

### 3.8 References

1. Beaujuge, P. M.; Reynolds, J. R., *Chem. Rev.* **2010**, *110*, 268-320.
2. Mortimer, R. J.; Dyer, A. L.; Reynolds, J. R., *Displays* **2006**, *27*, 2-18.
3. Ma, H.; Yip, H.-L.; Huang, F.; Jen, A. K. Y., *Adv. Funct. Mater.* **2010**, *20*, 1371-1388.
4. Bredas, J.-L.; Durrant, J. R., *Acc. Chem. Res.* **2009**, *42*, 1689-1690.
5. Grimsdale, A. C.; Leok Chan, K.; Martin, R. E.; Jokisz, P. G.; Holmes, A. B., *Chem. Rev.* **2009**, *109*, 897-1091.
6. Lee, K.; Nair, P. R.; Scott, A.; Alam, M. A.; Janes, D. B., *J. Appl. Phys* **2009**, *105*, 102046-13.
7. Roncali, J., *Acc. Chem. Res.* **2009**, *42*, 1719-1730.
8. Monk, P. M. S.; Mortimer, R. J.; Rosseinsky, D. R., *Electrochromism and Electrochromic Devices*. Cambridge University Press: Cambridge, **2007**.
9. Broncova, G.; Anikin, S.; Lange, U.; Matejka, P.; Krondak, M.; Kral, V.; Mirsky, V. M. *J. Solid State Electrochem.* **2010**, *14*, 1035-1044.
10. Maksymiuk, K. *Electroanalysis* **2006**, *18*, 1537
11. Hung, S. L.; Wen, T. C.; Gopalan, A. *Mater. Lett.* **2002**, *55*, 165
12. Chen, Y.; Imrie, C. T.; Cooper, J. M.; Glidle, A.; Morris, D. G.; Ryder, K. S. *Polym. Int.* **1998**, *47*, 43



13. Zotti, G.; Zecchin, S.; Schiavon, G.; Vercelli, B. *Chem. Mater.* **2003**, *15*, 4642
14. Gassner, F.; Graf, S.; Merz, A. *Synth. Met.* **1997**, *87*, 75
15. Zotti, G.; Zecchin, S.; Schiavon, G.; Groenendaal, L. B. *Chem. Mater.* **2000**, 2996-3005.
16. Merz, A.; Anikin, S.; Lieser, B.; Hienze, J.; John, H. *Chem. Eur. J.* **2003**, *9*, 449-455
17. Yu, M.; Pantos, G. D.; Sessler, J. L.; Pagenkopf, B. L. *Org. Lett.* **2004**, *6*, 1057-1059
18. Jolicoeur, B.; Lubell, W. D. *Org. Lett.* **2006**, *8*, 6107-6110.
19. Jolicoeur, B.; Lubell, W. D. *Can. J. Chem.* **2008**, *86*, 213-218
20. Tshibaka, T.; Roche, I. U.; Dufresne, S.; Lubell, W.D.; Skene, W. G. *J. Org. Chem.* **2009**, *74*, 9497-9500.
21. Yu, N.; Zhu, R.; Peng, B.; Huang, W.; Wei, W., *J. Appl. Polym. Sci.* **2008**, *108*, 2438-2445.
22. Morin, J.-F.; Drolet, N.; Tao, Y.; Leclerc, M., *Chem. Mater.* **2004**, *16*, 4619-4626.
23. Roncali, J.; Blanchard, P.; Frère, P., *J. Mater. Chem.* **2005**, *16*, 1589-1610.
24. Groves, C.; Reid, O. G.; Ginger, D. S., *Acc. Chem. Res.* **2010**, *43*, 612-620.
25. Shrotriya, G. L. V.; Huang, Y. Y. J.; Yang, Y., *J. Mater. Chem.* **2007**, *17*, 3126-3140.

26. Mei, J.; Heston, N. C.; Vasilyeva, S. V.; Reynolds, J. R., *Macromolecules* **2009**, *42*, 1482-1487.
27. Yang, C.-J.; Jenekhe, S. A., *Chem. Mater.* **1991**, *3*, 878-887.
28. Dufresne, S.; Bolduc, A.; Skene, W. G., *J. Mater. Chem.* **2010**, *20*, 4861-4866.
29. Bolduc, A.; Dufresne, S.; Skene, W. G., *J. Mater. Chem.* **2010**, *20*, 4820-4826.
30. Barik, S.; Skene, W. G. *Polym. Chem.* **2011**, 10.1039/C0PY00394H. Barik, S.; Skene, W. G. *Macromolecules* **2010**, *43*, 10435-10441
31. Suematsu, K.; Nakamura, K.; Takeda, J., *Colloid. Polym. Sci.* **1983**, *261*, 493-501.
32. Morgan, P. W.; Kwolek, S. L.; Pletcher, T. C., *Macromolecules* **1987**, *20*, 729-739.
33. Destri, S.; Pasini, M.; Pelizzi, C.; Porzio, W.; Predieri, G.; Vignali, C., *Macromolecules* **1998**, *32*, 353-360.
34. Zotti, G.; Randi, A.; Destri, S.; Porzio, W.; Schiavon, G., *Chem. Mater.* **2002**, *14*, 4550-4557.
35. Kiriya, N.; Bocharova, V.; Kiriya, A.; Stamm, M.; Krebs, F. C.; Adler, H.-J., *Chem. Mater.* **2004**, *16*, 4765-4771.
36. Schmuck, C.; Bickert, V.; Merschky, M.; Geiger, L.; Rupprecht, D.; Dudaczek, J.; Wich, P.; Rehm, T.; Machon, U. *Eur. J. Org. Chem.* **2008**, *2*, 324-329
37. Dufresne, S.; Skene, W.G. *J. Org. Chem.* **2008**, *73* (10), 3859-3866.

38. Bourgeaux, M.; Skene, W.G. *J. Org. Chem.* **2007**, *72*, 8882-8892.
39. Gewalt, V.K.; Kleinert, M.; Thiele, B.; Hentschel, M. *J. Prak. Chem.* **1972**, 303-314.
40. Bourgeaux, M.; Vomscheid, S.; Skene, W. G. *Synth. Commun.* **2007** *37* 3551-3558
41. Dufresne, S.; Skalski, T.; Skene, W. G., *Can. J. Chem.* **2011**, *89*, 173-180.
42. Skene, W. G.; Dufresne, S., *Org. Lett.* **2004**, *6*, 2949-2952.
43. Connelly, N. G.; Geiger, W. E., *Chem. Rev.* **1996**, *96*, 877-910.
44. Park, S. B.; Kim, H.; Zin, W. C.; Jung, J. C. *Macromolecules* **1993**, *26*, 1627. Du, J.; Fan, J.; Peng, X.; Sun, P.; Wang, J.; Li, H.; Sun, S. *Org. Lett.* **2010**.

### **3.9 Contribution des co-auteurs pour l'article 2**

J'ai effectué l'ensemble de réactions et de la caractérisation des molécules présentées dans cet article. J'ai aussi participé à la rédaction de l'article en écrivant une partie de l'introduction, la synthèse et la partie expérimentale.

Stéphane Dufresne, Sophie Bishop et Ivan Ulliel Roche ont effectué les analyses électrochimiques des composés.

A part leur contribution à l'écriture, les professeurs William D. Lubell et William Skene ont supervisé la recherche et la rédaction de l'article.

**Chapitre 4**  
**conclusion**

## 4.1 Conclusion

Ces travaux ont été consacrés à la synthèse des analogues de 4-méthoxy-2,2'-bipyrrole et d'un nouveau type de polymère basé sur la formation des liens imines dans le but de les utiliser dans les matériaux conducteurs.

Notre premier objectif a été la synthèse d'une série d'analogues du 4-méthoxy-2,2'-bipyrrole qui devaient servir de comonomères aux thiophènes (l'ester 3,4-diéthylique du 2,5-diaminothiophène et le 2-amino-3-cyanothiophène) dans la synthèse des azométhines dissymétriques. Le 4-méthoxy-1-benzène sulfonyl-2,2'-bipyrrole **35a** a été synthétisé en 11 étapes à partir de la 4-hydroxyproline avec un rendement total de 10%. L'alkylation (allyl, butyl, octyl, et sulfonyl) de **35a** à la position 1' a permis d'obtenir d'autres analogues de bipyrroles. La déprotection du groupement sulfonyl de **35a** grâce au magnésium a permis de recueillir le 4-méthoxy-2,2'-bipyrrole **43** avec un rendement de 60%.

Dans le but de déterminer le potentiel de ces bipyrroles pour être utilisés dans les matériaux conducteurs, le 4-méthoxy-5,5'-trichloroacétyl-2,2'-bipyrrole **3** et l'ester 5,5'-diméthylque du 4-méthoxy-2,2'-bipyrrole **4** ont également été synthétisés, puis leurs potentiels d'oxydation et leurs relations structure-propriété ainsi que ceux de **35a** et **43** ont été déterminés spectroscopiquement, électrochimiquement et spectroélectrochimiquement. Ces études ont démontré que le groupement méthoxy abaisse le potentiel d'oxydation des bipyrroles et que les groupements électroattracteurs influencent (abaissent) sélectivement le niveau d'énergie de la HOMO. L'effet "push-pull" a également été observé, provoquant des changements significatifs de couleur dans le spectre du visible et, démontrant ainsi que ces bipyrroles sont des précurseurs intéressants pour les matériels électrochromiques fonctionnalisés.

Une fois le potentiel des bipyrroles établi, nous sommes passés à l'étape de la synthèse des oligomères dissymétriques à base de thiophènes et des bipyrroles. Pour ce faire, les bipyrroles ont été traités dans les conditions de la réaction de Vilsmeier-Haack afin d'obtenir les aldéhydes susceptibles de former les liens imines avec les aminothiophènes.

Les réactions de **43** et **35a** produisent respectivement les 5,5'-dialdéhydes **41** et **42** alors que celles de N'-butyl et N'-octylbipyrroles aboutissent à la formation de deux isomères, soit les 5,5'-dialdéhydes et les 5,4'-dialdéhydes. Le N'-allyl et le N,N'-disulfonylbipyrrole réagissent dans les mêmes conditions en ne formant qu'un produit monoformylé à position 5 du bipyrrole.

Les tentatives de former les tétramères avec les isomères 5,4'-diformylbipyrroles **11** et **13** ont tous échoué à cause de la dégradation du produit formé ou du manque de stabilité du réactif de départ. Les oligomères ont donc été synthétisés en utilisant les 5,5'-dialdéhydes et les aminothiophènes. Les RMN-<sup>1</sup>H et <sup>13</sup>C ainsi que le spectre de masse indiquent la perte du groupement sulfonyle dans les oligomères lorsque l'ester 3,4-diéthylique du 2,5-diaminothiophène est utilisé comme réactif. Nous ne sommes toutefois pas capables de déterminer si la perte se fait pendant la réaction ou lors de la purification sur silice. Les réactions faites parfois à reflux, en milieux acide et la purification sur silice démontrent à quel point la liaison imine est très stable grâce à la conjugaison.

L'analyse par rayon X de **20** montre que l'imine adopte une configuration E et que les hétéroatomes adoptent une orientation coplanaire dans un arrangement antiparallèle. La coplanarité des groupements aryles et des liens azométhines confirme le haut degré de conjugaison dans la molécule. Les oligomères ayant les groupements amines terminaux possèdent des potentiels d'oxydation bas à cause de leur caractère donneur très fort.

Que ça soit dans le cas des 4-méthoxybipyrroles ou des azométhines conjugués, les processus électrochimiques observés étaient pseudo réversibles démontrant la réactivité des intermédiaires qui, sans surprise, sont susceptibles de se coupler et de polymériser par la voie des intermédiaires radicalaires cationiques à cause des positions non substituées sur les noyaux pyrroliques. Afin de surmonter ce problème, nous nous proposons de synthétiser des bipyrroles dont les sites réactifs seront bloqués.

Une des approches que nous allons explorer est la synthèse du 4-méthoxy-3',4'-diméthyle-2,2'-bipyrrole. Pour ce faire on utilisera la même méthodologie employée

précédemment mais en utilisant cette fois-ci le bromure de 1-propenylmagnésium à l'étape de la formation de la cétone homoallylique de la proline. Toutefois cette stratégie ne permettra pas de bloquer la position 3 du bipyrrrole qui restera ouverte et donc susceptible de faire des réactions de couplage. Une autre méthode pouvant être explorée et qui permettra de réduire les sites de couplages est la méthylation de la position 5' du bipyrrrole. Cela est possible lorsque, à l'étape de l'oxydation de l'oléfine, on remplace le système OsO<sub>4</sub>/NaIO<sub>4</sub> par les conditions de Tsuji-Wacker formant ainsi une cétone au lieu et place d'un aldéhyde<sup>1,2</sup>. Le traitement du 1,4-dicarbonyle dans les conditions de Paal Knorr permettra ainsi d'obtenir un bipyrrrole alkylé à la position 5'.

La stratégie employée dans ce mémoire permet de diversifier les substituants en position 4 du bipyrrrole. Les 4-méthoxy-2,2'-bipyrrroles sont retrouvés dans des produits naturels ayant des activités biologiques tels que les prodigiosines et les tambjamines.

Outre les propriétés antibactériennes, antifongiques, immunosuppressives et cytotoxiques que possèdent l'Undecylprodigiosine ou la Prodigiosine, le développement de ces produits naturels en tant que médicaments est freiné par les effets secondaires dont le groupement méthoxy à la position 6 de la molécule (position 4 du bipyrrrole) semble être responsable<sup>3</sup>. Ainsi, dans le but de contrer ces effets et dans celui d'améliorer le profil pharmacologique de ces produits, l'utilisation de notre méthodologie pourrait permettre la synthèse des analogues de prodigiosines ayant des substituants divers<sup>4</sup>.

Le composé **7** (2<sup>e</sup> article de la mémoire), qui est un intermédiaire isolé lors du traitement du 4-méthoxy-2,2'-bipyrrrole **1** par la réaction de Vilsmeier, a également le potentiel d'être utilisé comme précurseur dans la synthèse des analogues des tambjamines. En effet, des réactions de transaminations sur l'intermédiaire combinées aux ajouts ou à des modifications de substituants devraient permettre la synthèse des analogues dont les propriétés biologiques pourraient s'avérer intéressantes.

En bref, en considérant les possibilités offertes par cette méthode pour générer des bipyrrroles dissymétriques possédant des substituants capables de modifier leurs propriétés et l'intérêt croissant de ces types d'intermédiaires pour la synthèse des produits



naturels ayant des activités biologiques intéressantes, cette approche devrait être d'intérêt général et utile pour la communauté scientifique engagée dans la chimie médicinale et dans la chimie des matériaux.

Les travaux présentés dans ce mémoire devraient contribuer à l'avancement des méthodes de synthèse de 2,2-bipyrroles et des azométhines en plus de fournir des possibilités de substitutions sur leurs squelettes. La plupart des composés présentés dans ce mémoire ont été soumis à des études électrochimiques et électrospectroscopiques montrant leur potentiel à être utilisés dans les matériaux conducteurs. Ces molécules seront également soumises au centre de criblage à haut débit de l'Institut de Recherche en Immunologie et Cancérologie (IRIC) afin de déterminer leur activité avec différents systèmes et modèles biologiques.

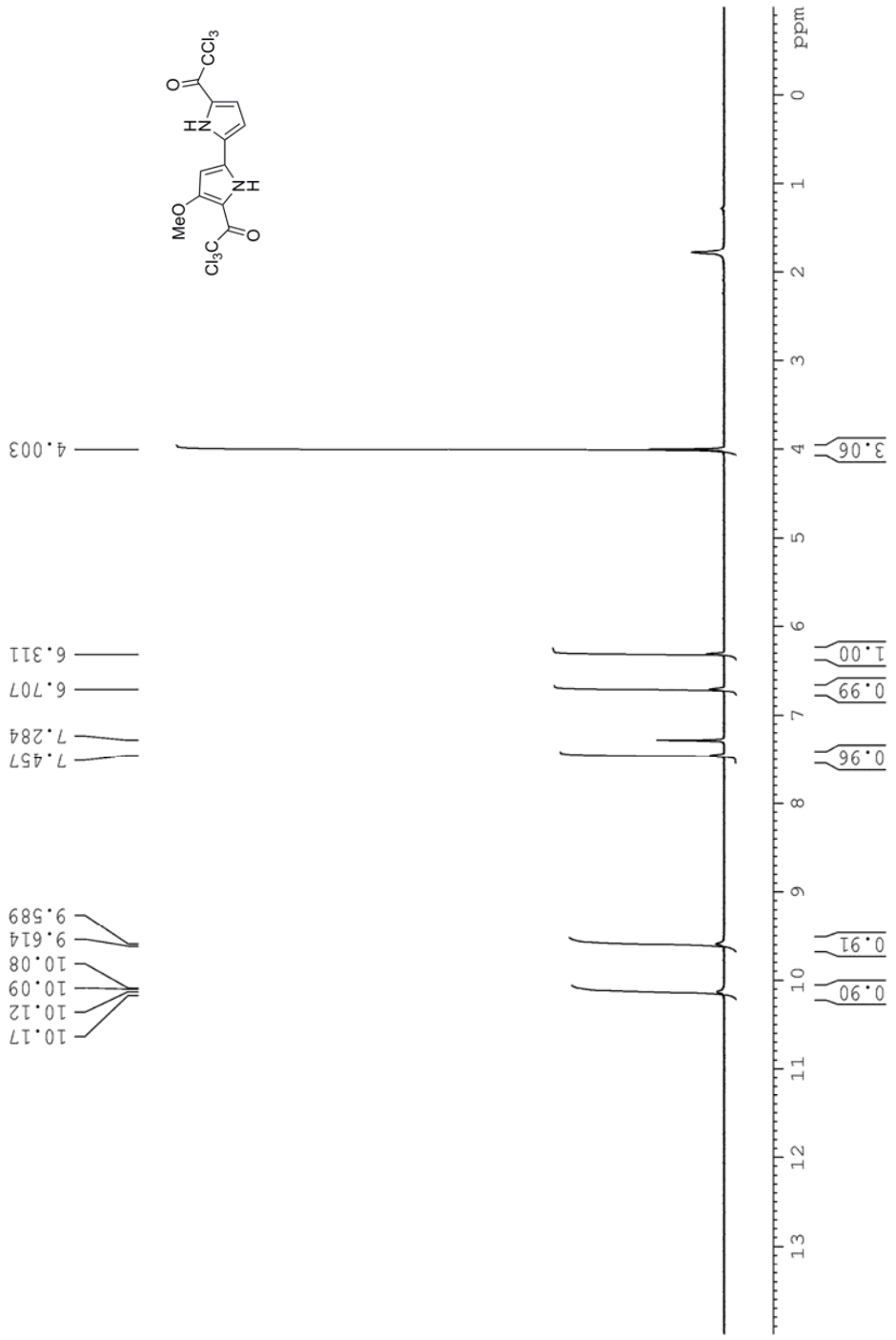
## 4.2 Références

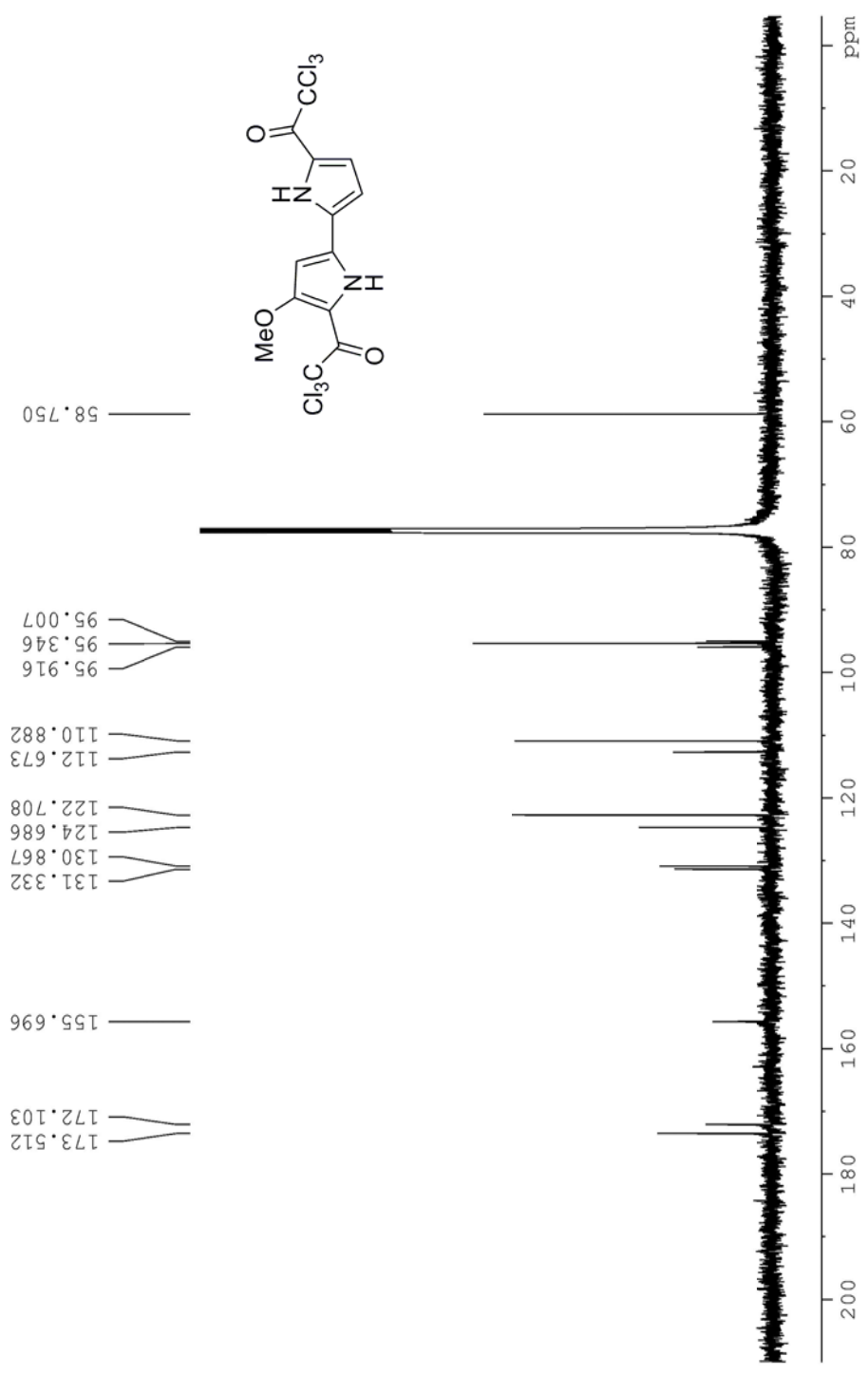
1. Jolicoeur, B.; Lubell, W. D. *Org. Lett.* **2006**, 8, 6107-6110.
2. Hansford, K. A.; Zanzarova, V.; Dorr, A.; Lubell, W. D. *J. Comb. Chem.* **2004**, 6, 893-898
3. Songia, S.; Mortellaro, A.; Taverna, S.; Fornasiero, C.; Scheiber, E. A.; Erba, E.; Colotta, F.; Mantovani, A.; Isetta, A. M.; Golay, J. *J. Immunol.* **1997**, 158, 3987.
4. Jolicoeur, B.; Lubell, W. D. *Can. J. Chem.* **2008**, 86, 216-218.

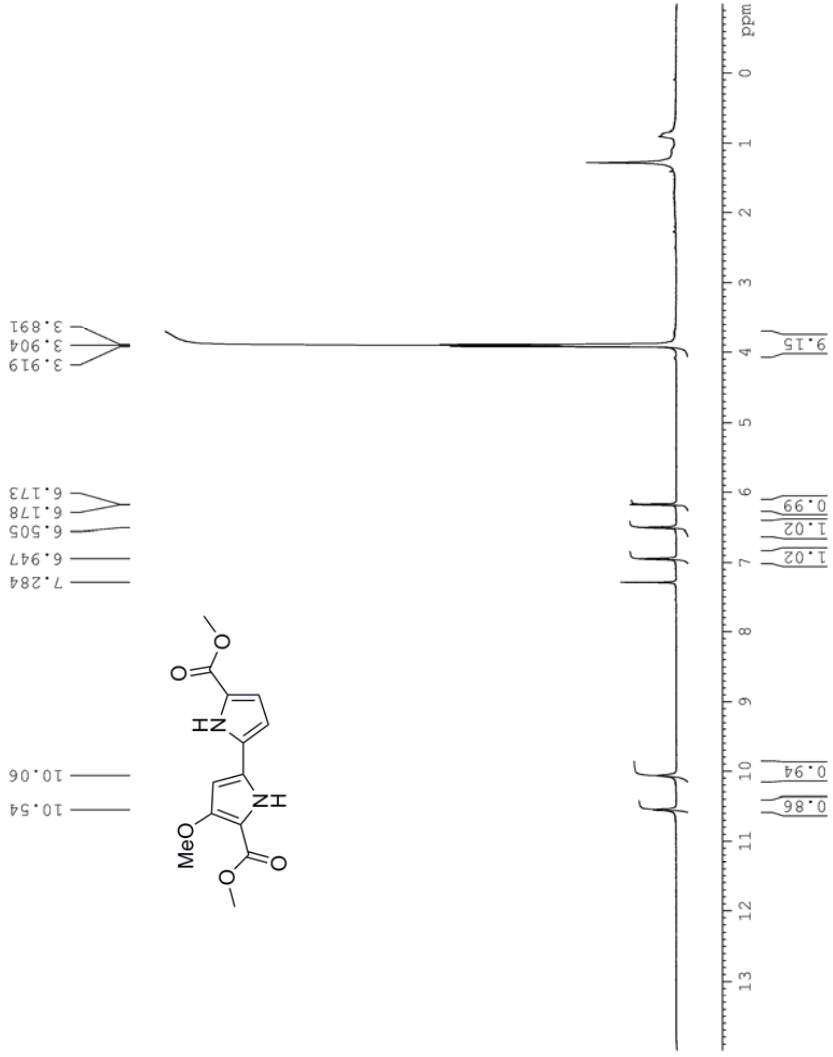
## **Annexe**

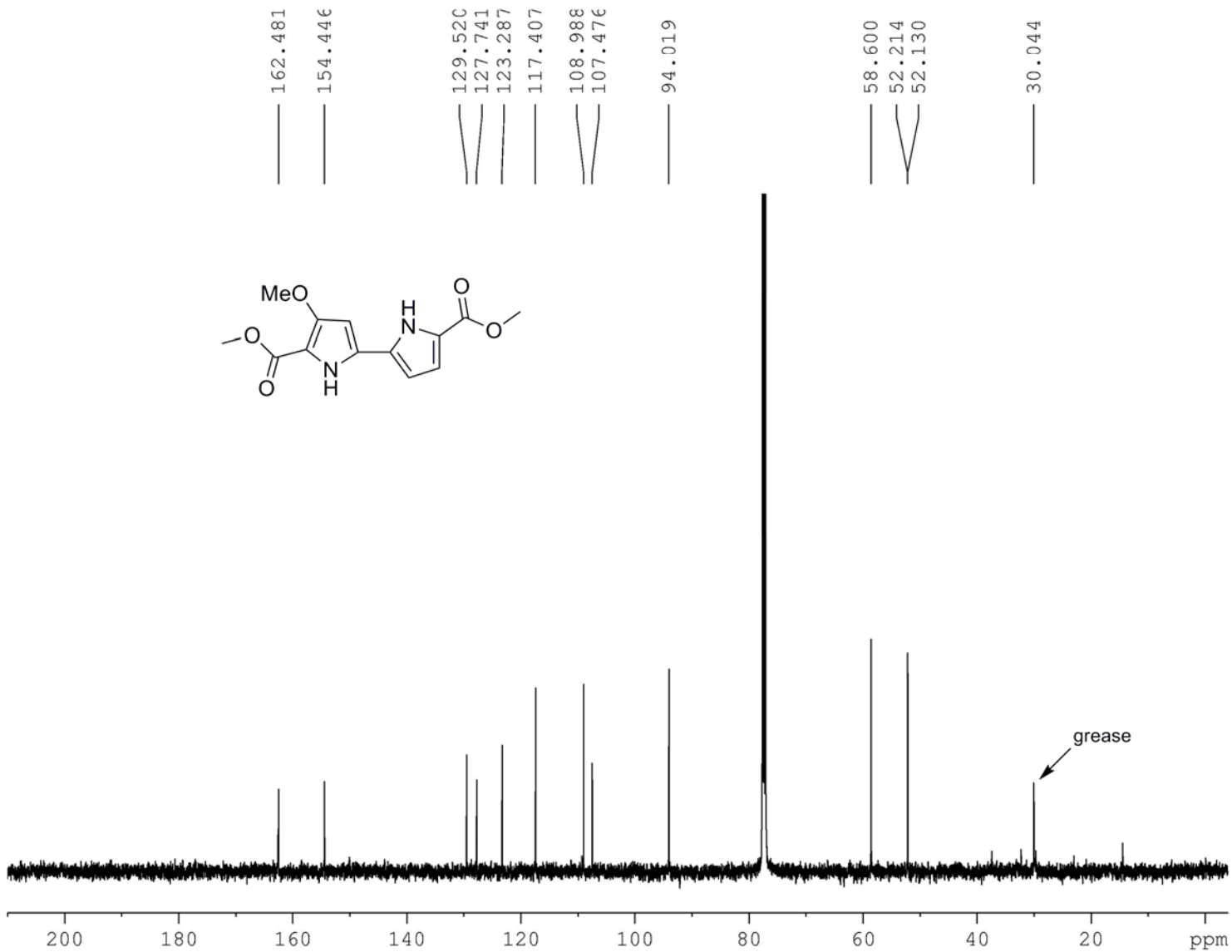
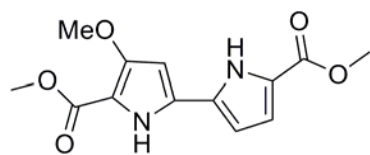
### **Données spectrales des chapitres 2 et 3**

## **Chapitre 2**

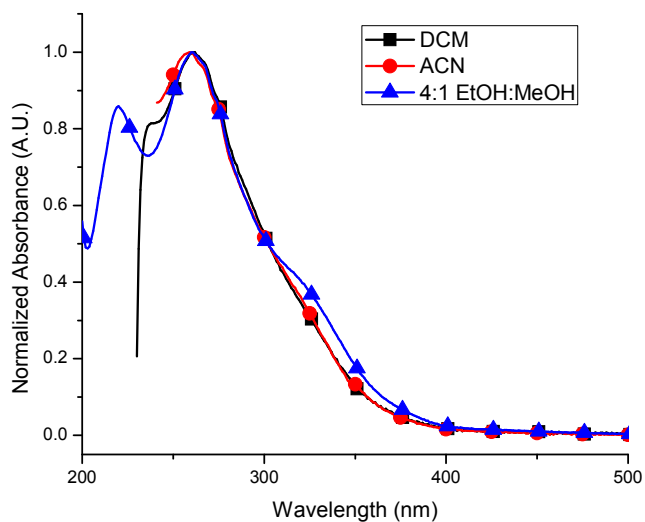




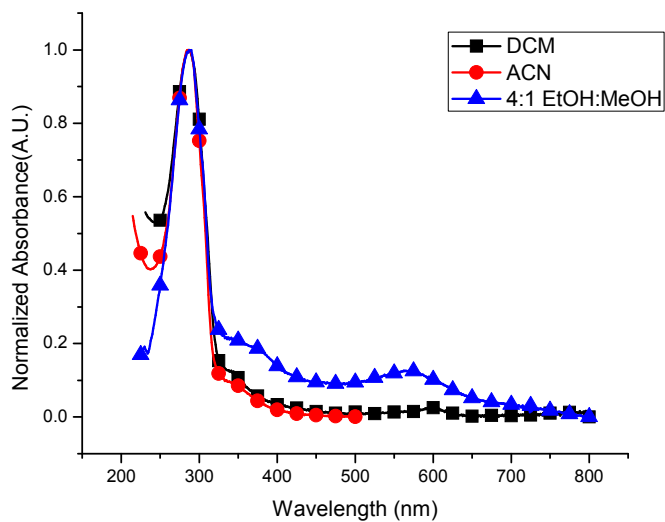




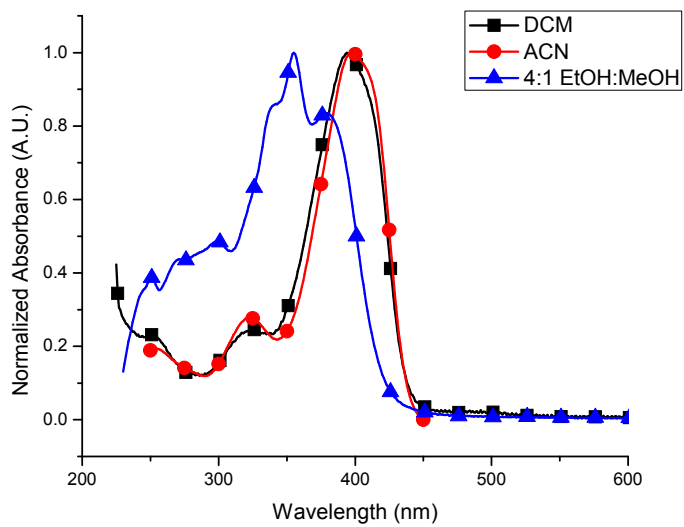




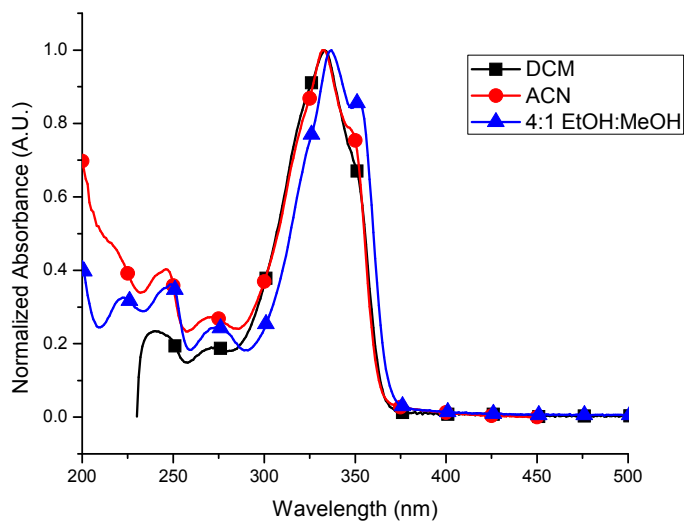
**Figure 5.** Absorption spectra of **2** measured in different solvents.



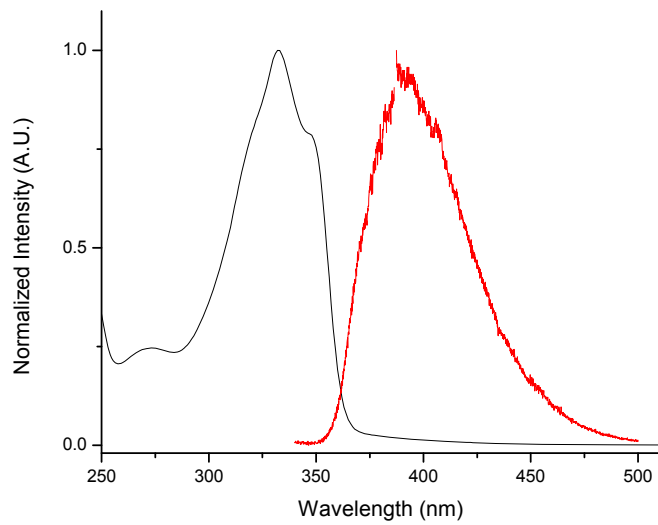
**Figure 2.** Absorption spectra of **1** measured in different solvents.



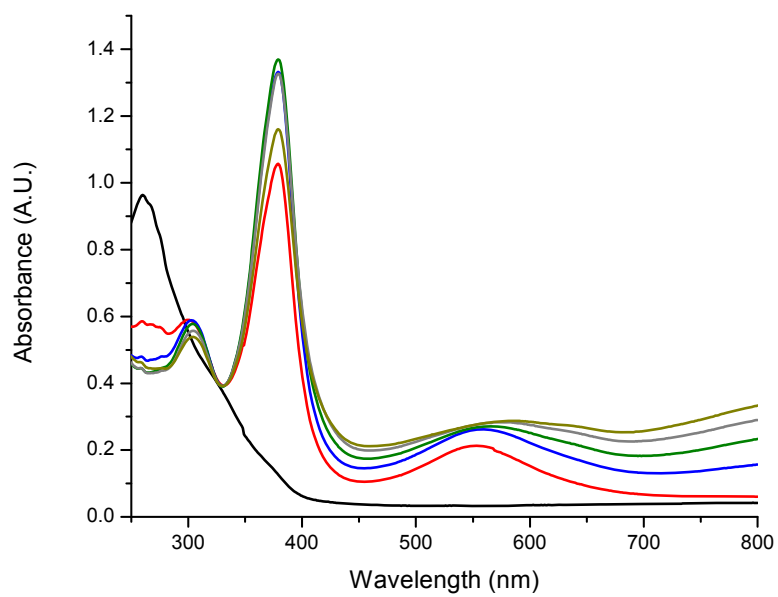
**Figure 3.** Absorption spectra of **3** measured in different solvents.



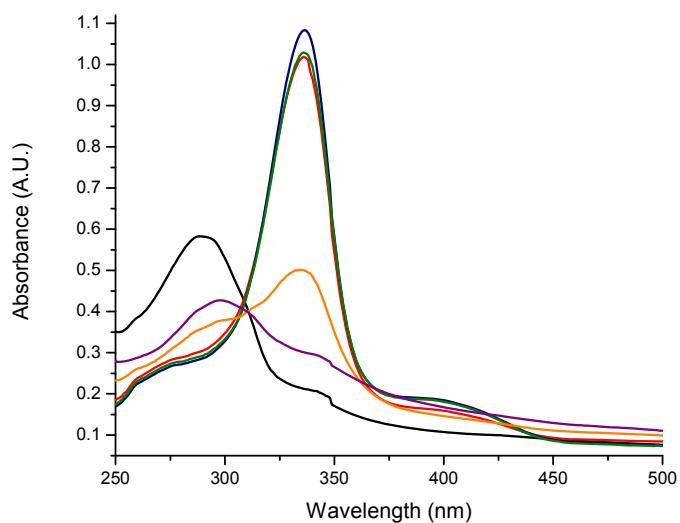
**Figure 4.** Absorption spectra of **4** measured in different solvents.



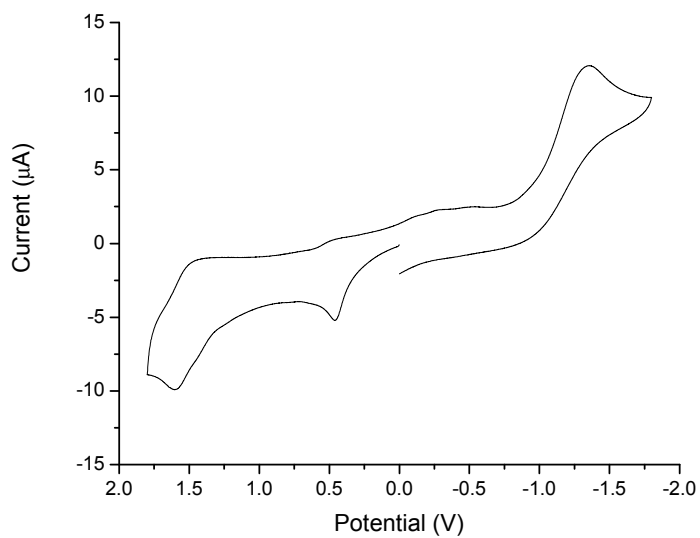
**Figure 6.** Normalized absorption and fluorescence of **4** recorded in anhydrous and deaerated dichloromethane.



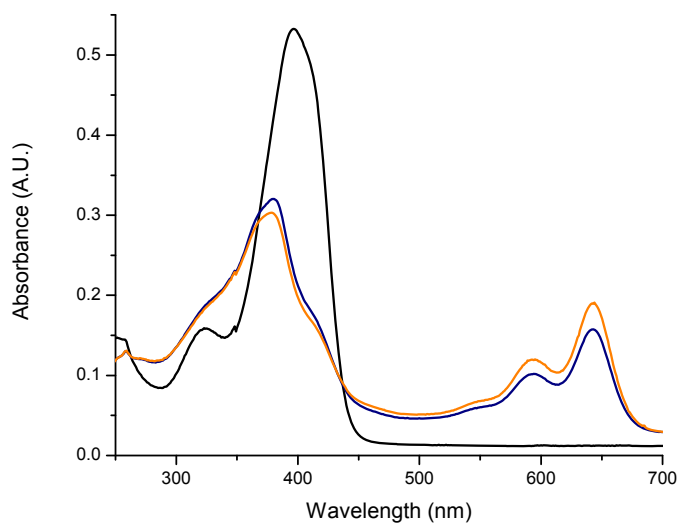
**Figure 6.** Change in absorption of **1** with 0 (black), 1 (red), 2 (blue), 4 (green), 7 (gray), and 10 (beige) of oxidation at 1 V in deaerated and anhydrous acetonitrile.



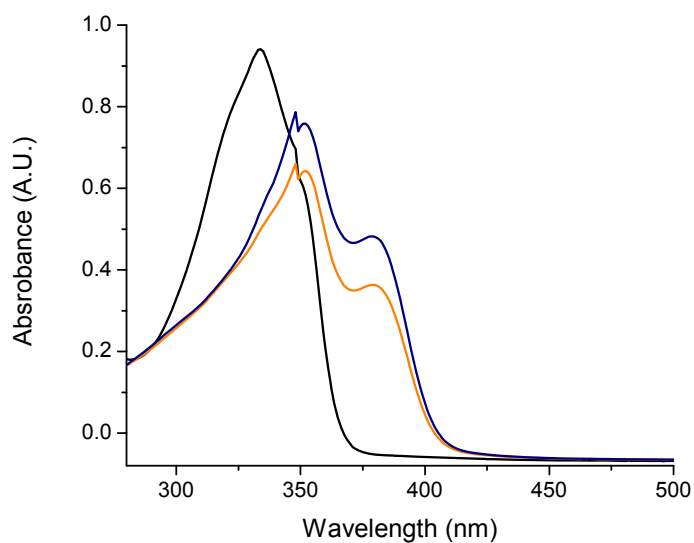
**Figure 7.** Change in absorption of **2** with 0 (black), 1 (red), 4 (blue), and 10 (green) min at a potential of + 1.7 V followed by 2 (orange) and 10 (purple) min at a potential of -200 mV.



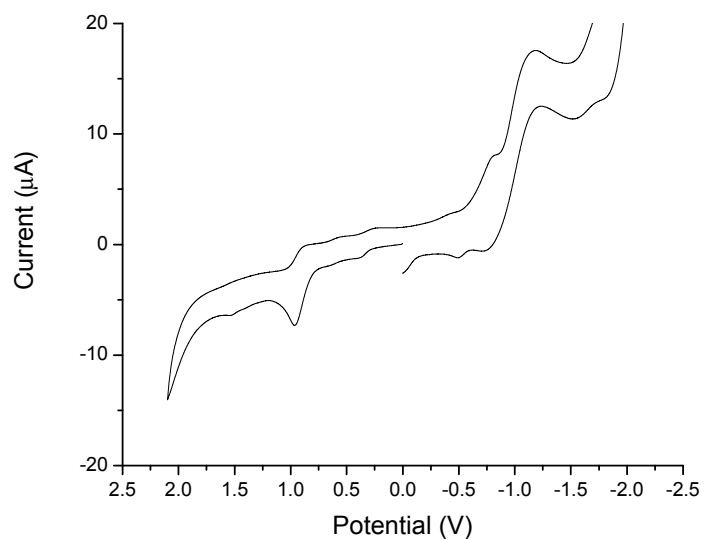
**Figure 8.** Cyclic voltammogram of **2** recorded in deaerated and anhydrous dichloromethane with 0.1 M TBAPF<sub>6</sub> supporting electrolyte at a sweep rate of 100 mV/sec.



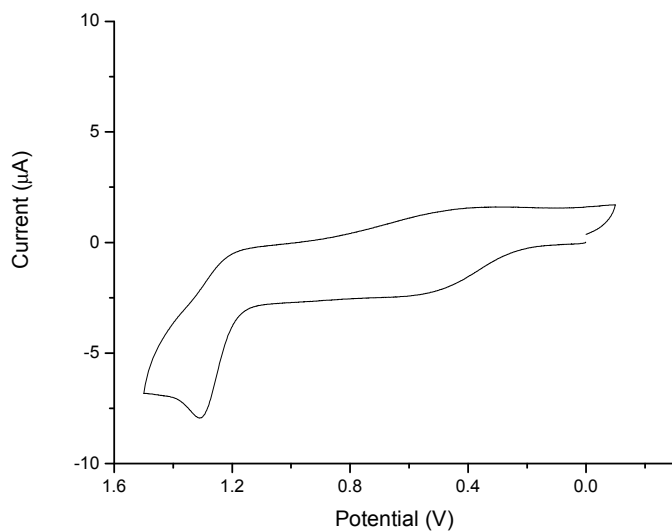
**Figure 9.** Change in absorption of **3** with 0 (black), 5 (blue), and 10 (orange) min at a potential of 1.4 V.



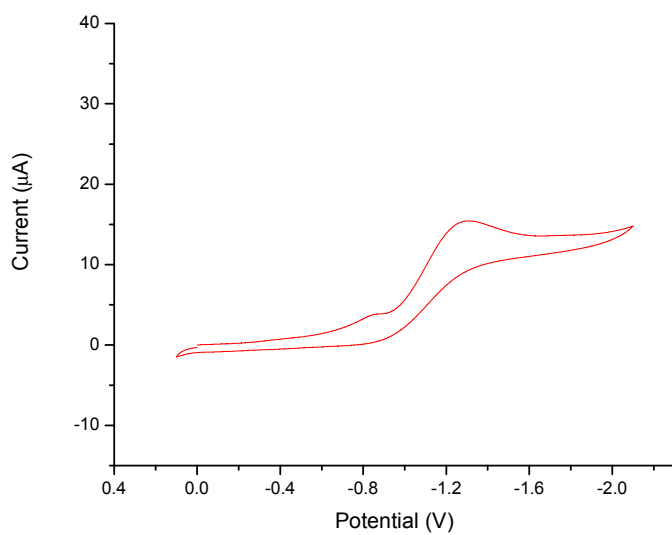
**Figure 10.** Change in absorption of **4** with 0 (black), 4 (orange), and 20 (blue) min at a potential of + 1.1 V.



**Figure 11.** Cyclic voltammogram of **4** recorded in deaerated and anhydrous dichloromethane with 0.1 M TBAPF<sub>6</sub> supporting electrolyte at a sweep rate of 100 mV/sec.



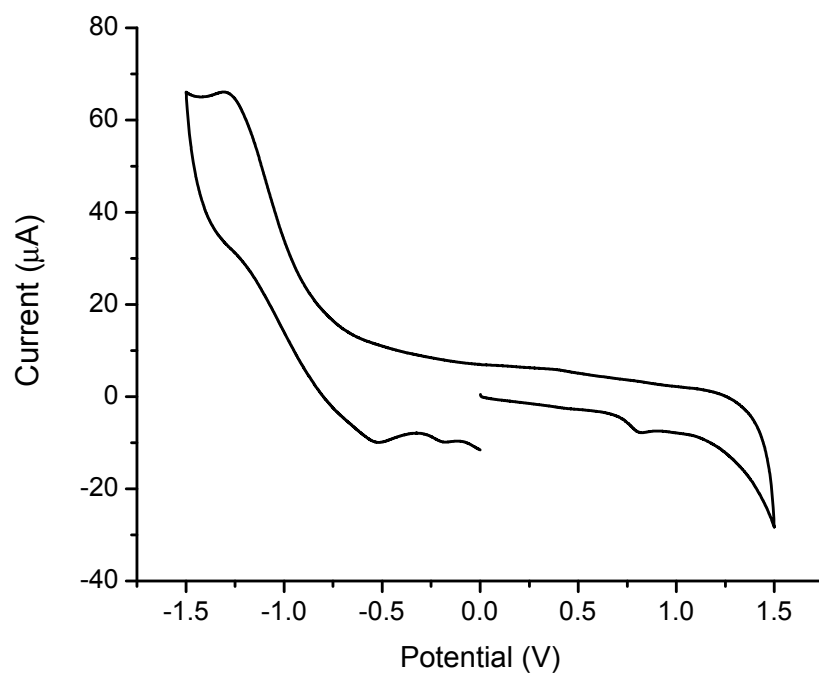
**Figure 12.** Cyclic voltammogram of **3** recorded in deaerated and anhydrous dichloromethane with 0.1 M TBAPF<sub>6</sub> supporting electrolyte at a sweep rate of 100 mV/sec.



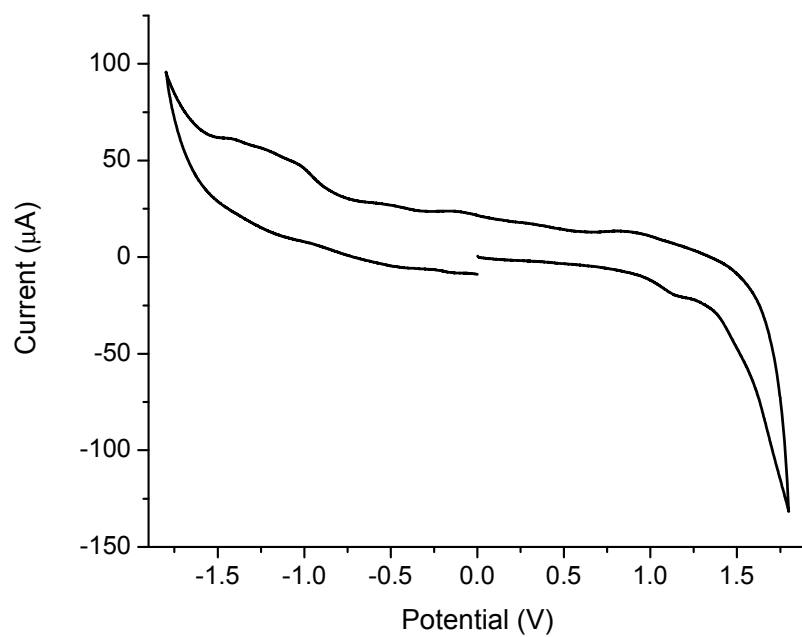
**Figure 13.** Cyclic voltammogram of **3** recorded in deaerated and anhydrous dichloromethane with 0.1 M TBAPF<sub>6</sub> supporting electrolyte at a sweep rate of 100 mV/sec.



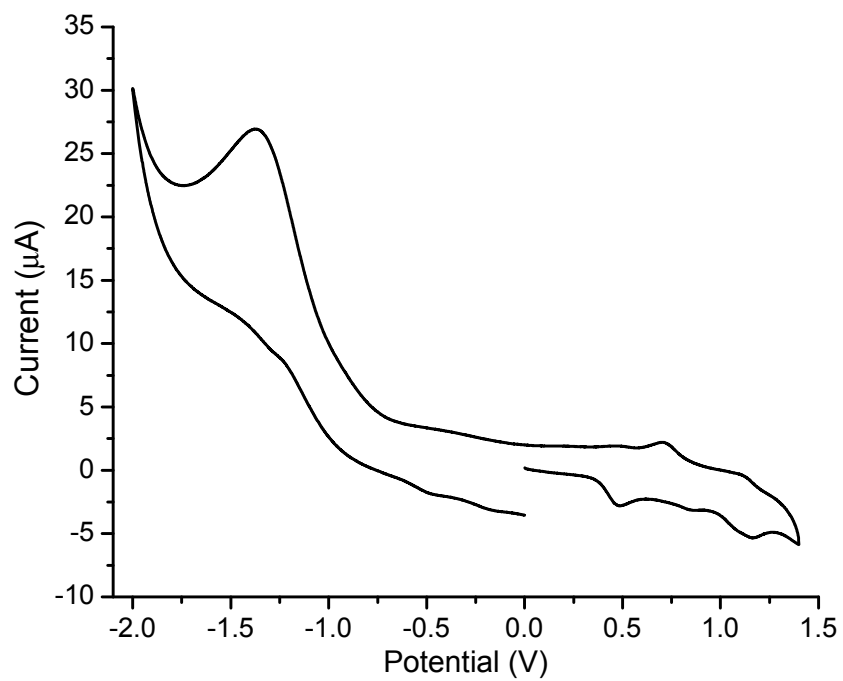
## **Chapitre 3**



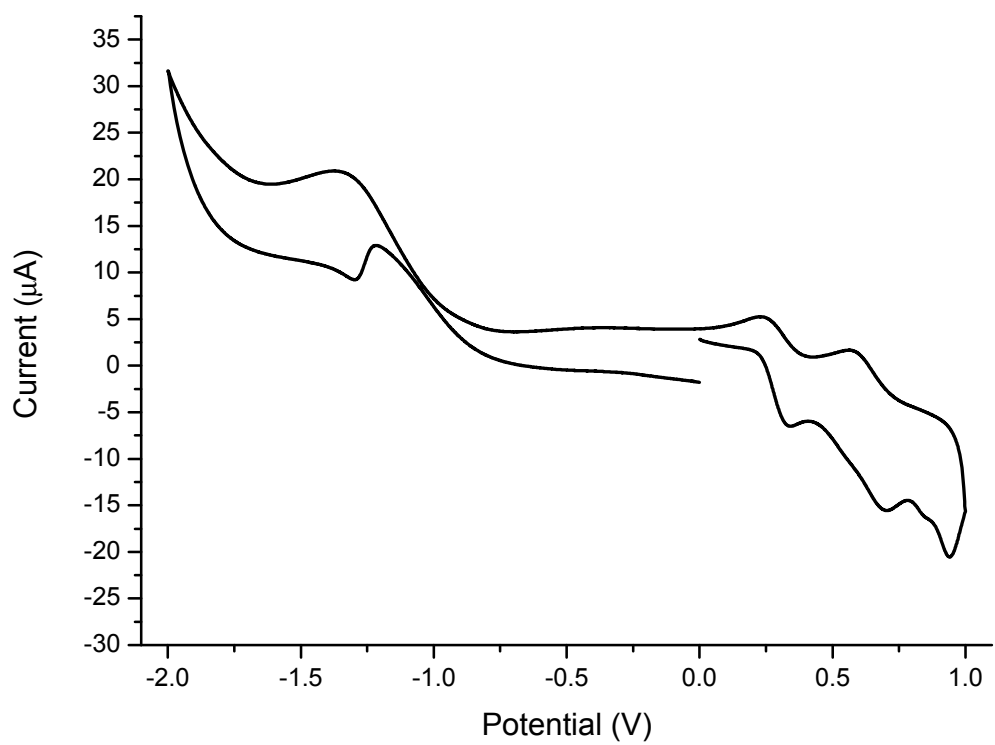
**Figure 7. Cyclic voltammogram of 17 in dichloromethane with 0.1 M TBAPF<sub>6</sub>.**



**Figure 8. Cyclic voltammogram of 18 in dichloromethane with 0.1 M TBAPF<sub>6</sub>.**



**Figure 9.** Cyclic voltammetry of 20 in dichloromethane with 0.1 M TBAPF<sub>6</sub>.



**Figure 4.** Cyclic voltammogram of 22 in dichloromethane with 0.1 M TBAPF<sub>6</sub>.

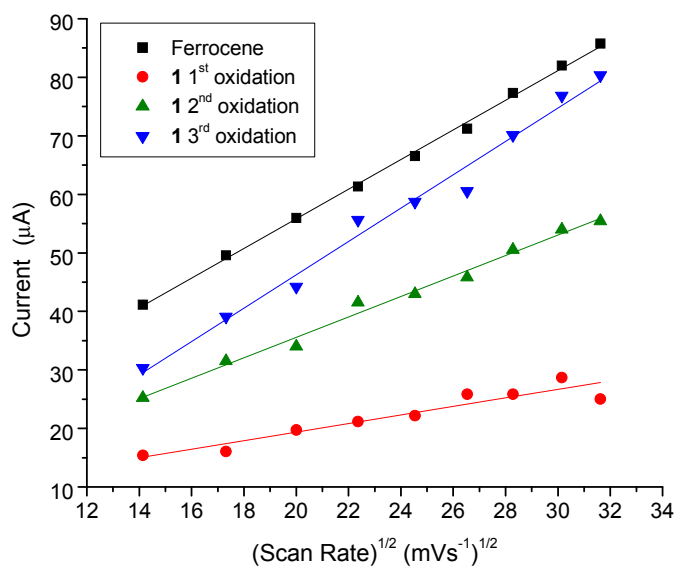
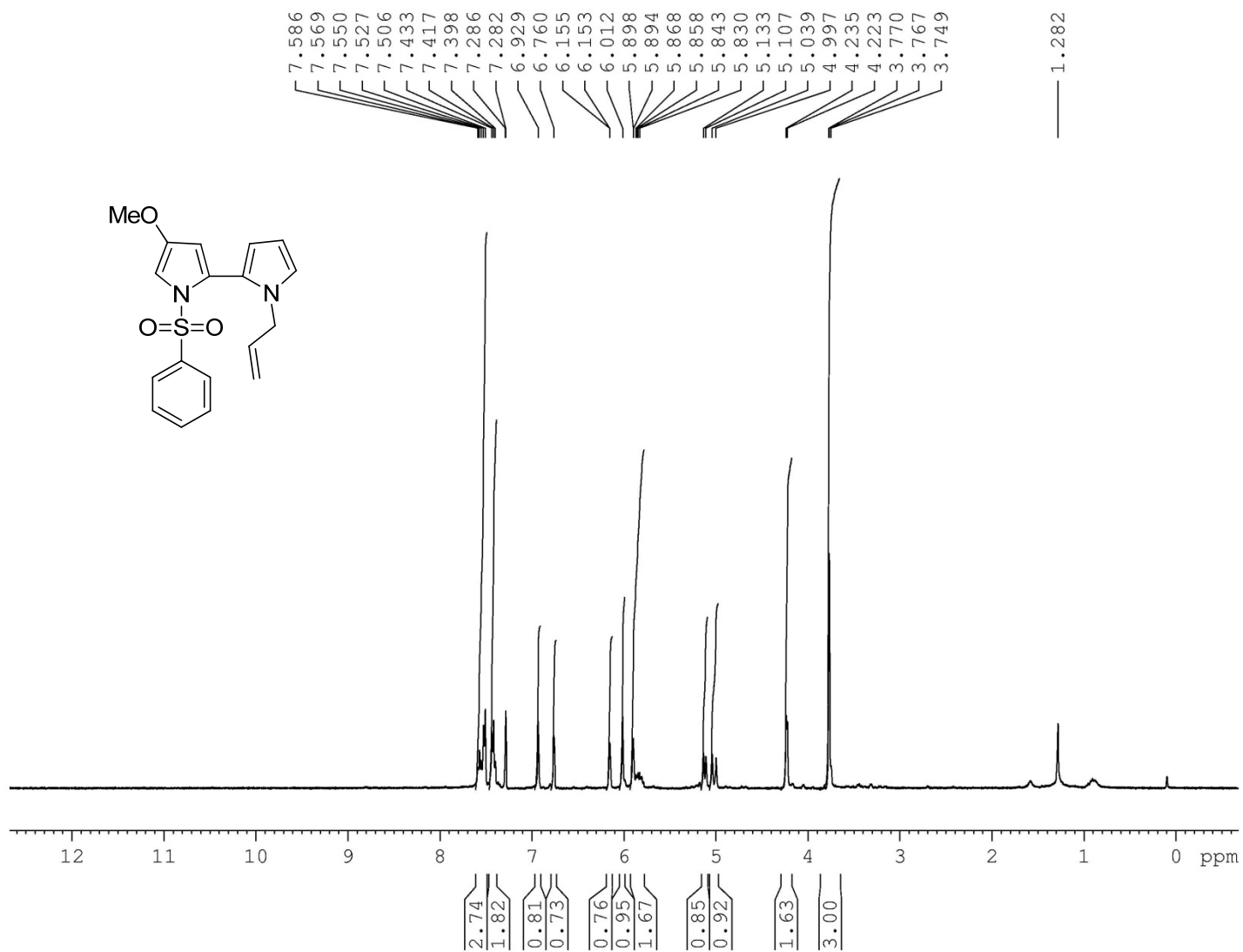
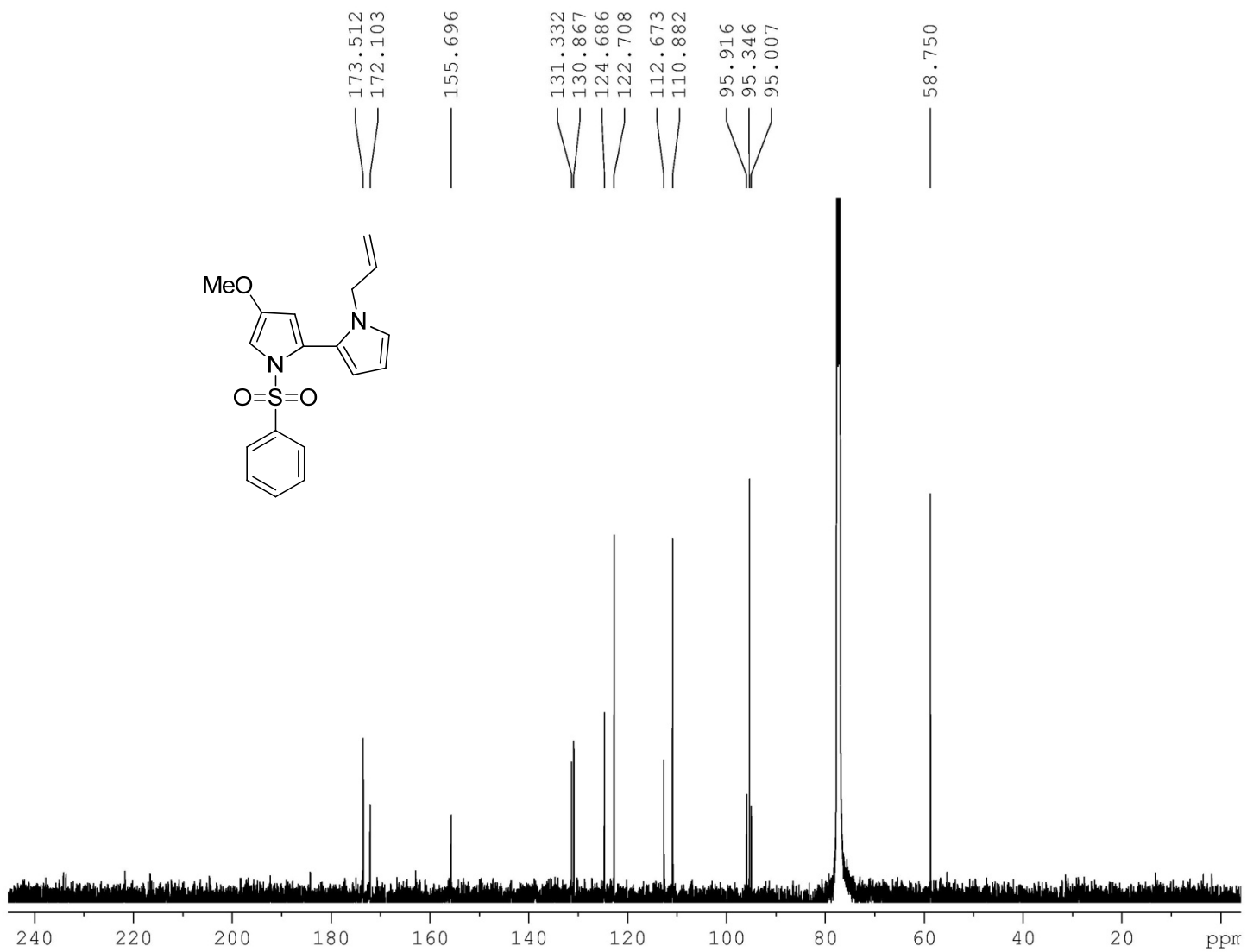


Figure 5. Randles-Sevcik plot of 20 and ferrocene measured in dichloromethane.

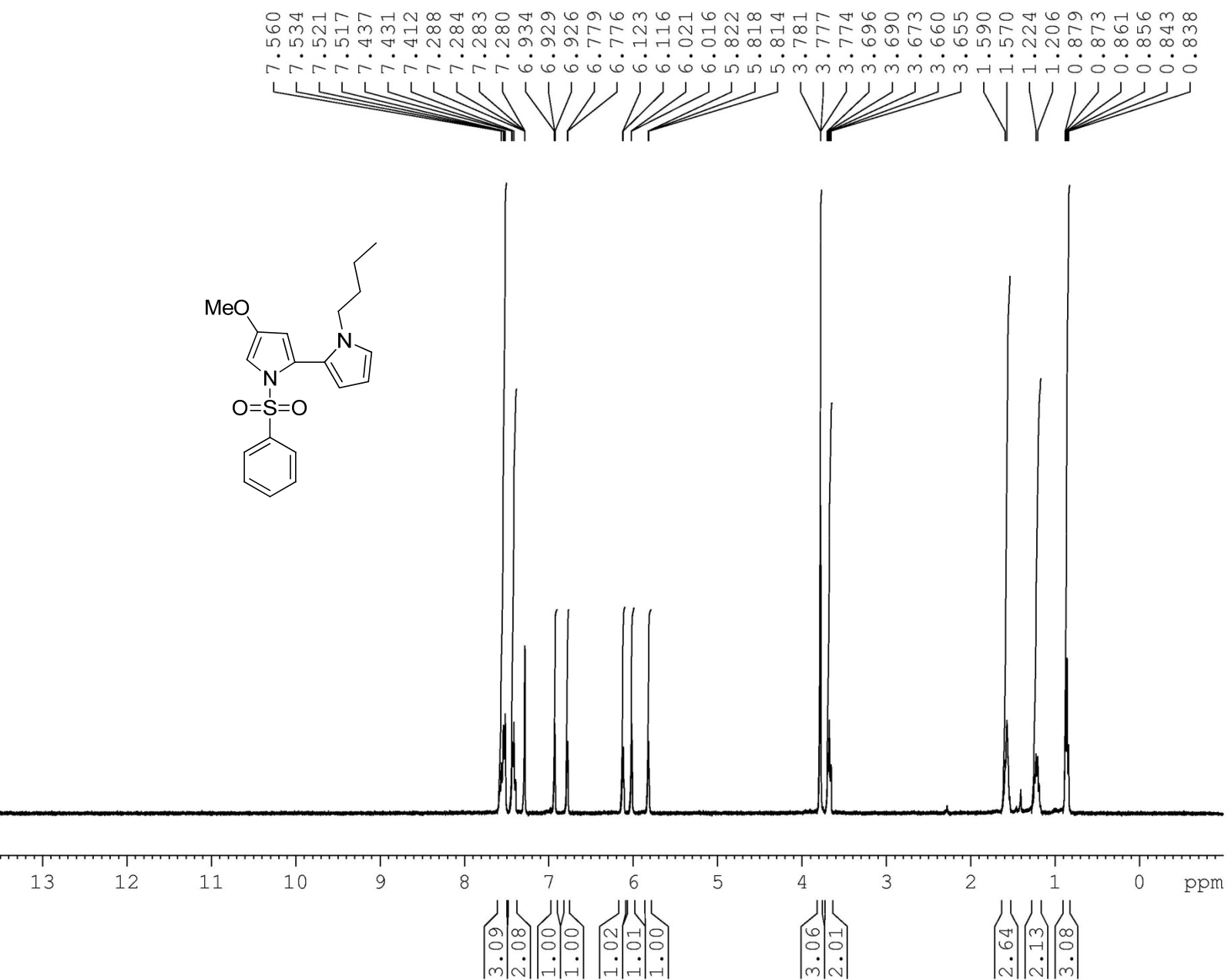


**Figure 7.** NMR H spectra of **3**



**Figure 8.** NMR  $^{13}\text{C}$  spectra of **3**





**Figure 9.** NMR H spectra of 4

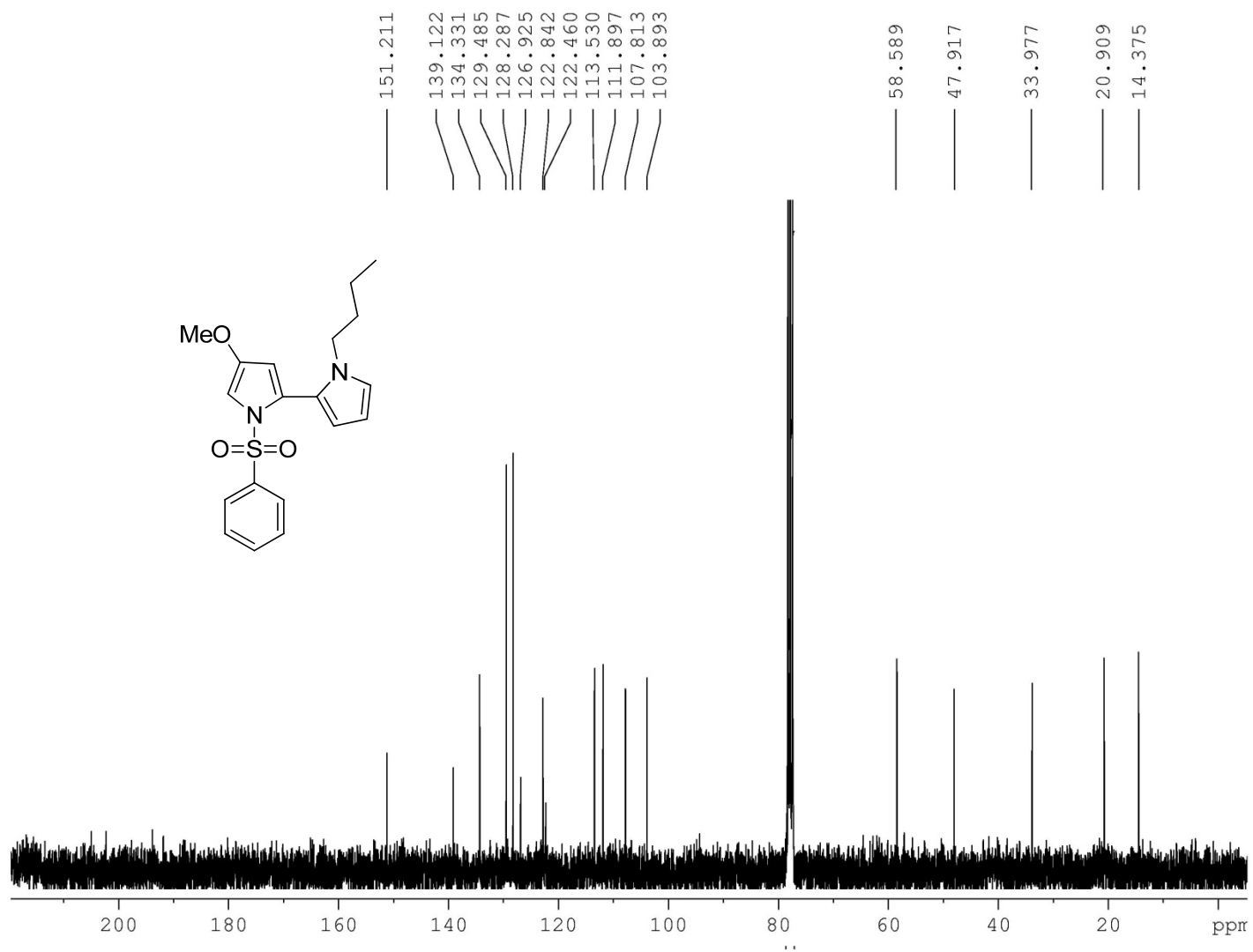
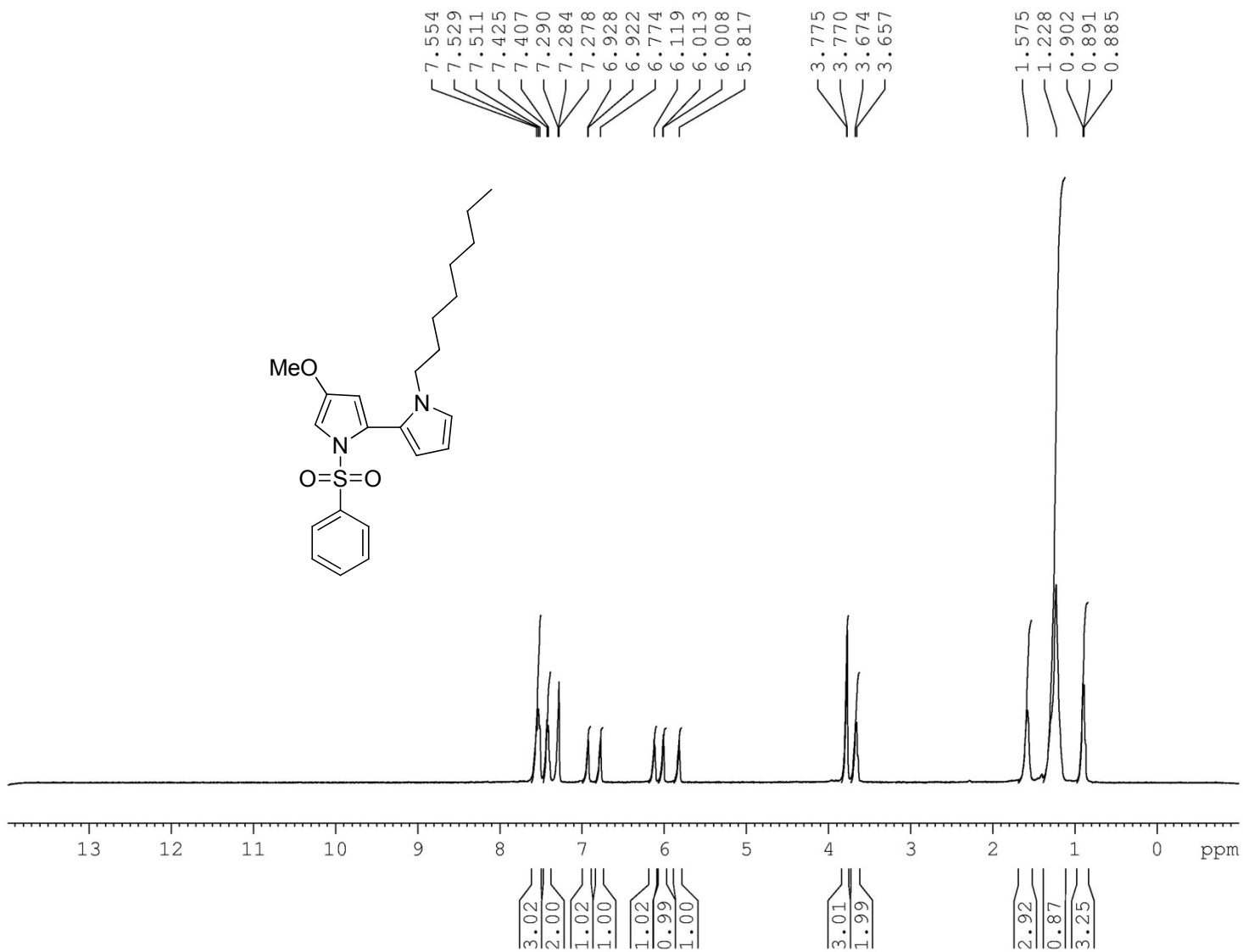


Figure 10. NMR <sup>13</sup>C spectra of 4



**Figure 11.** NMR H spectra of **5**

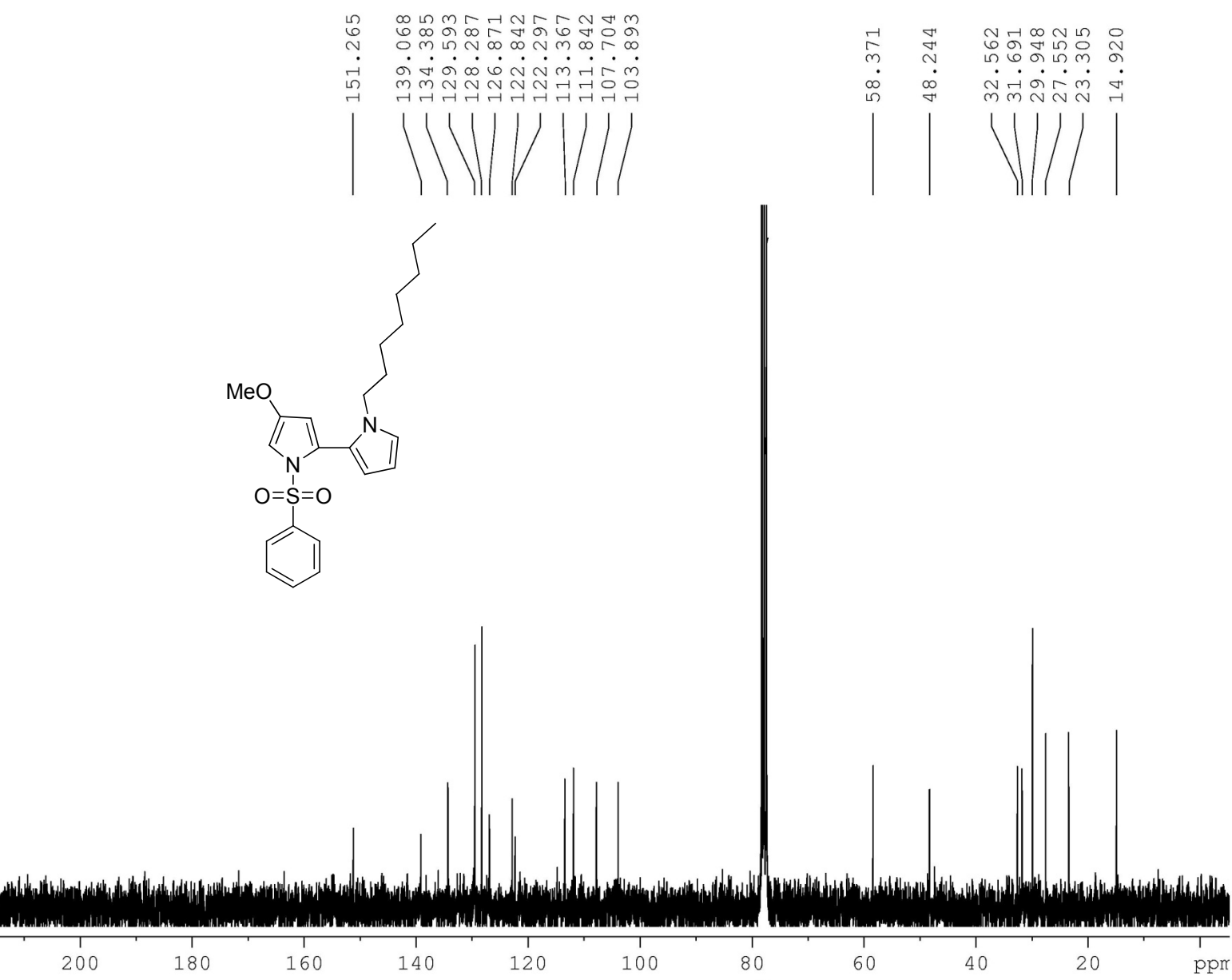


Figure 12. NMR <sup>13</sup>C spectra of 5

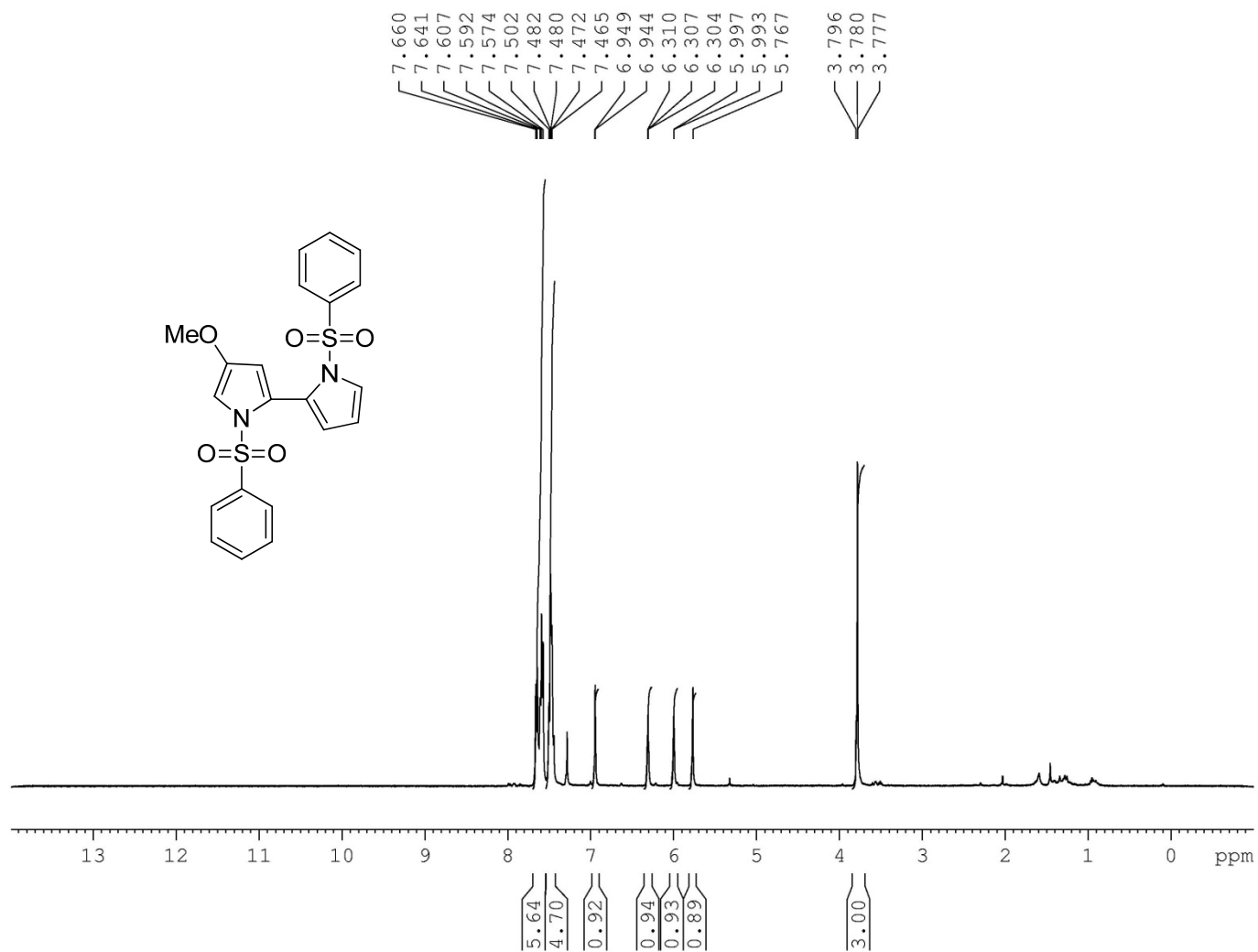


Figure 13. NMR H spectra of 6

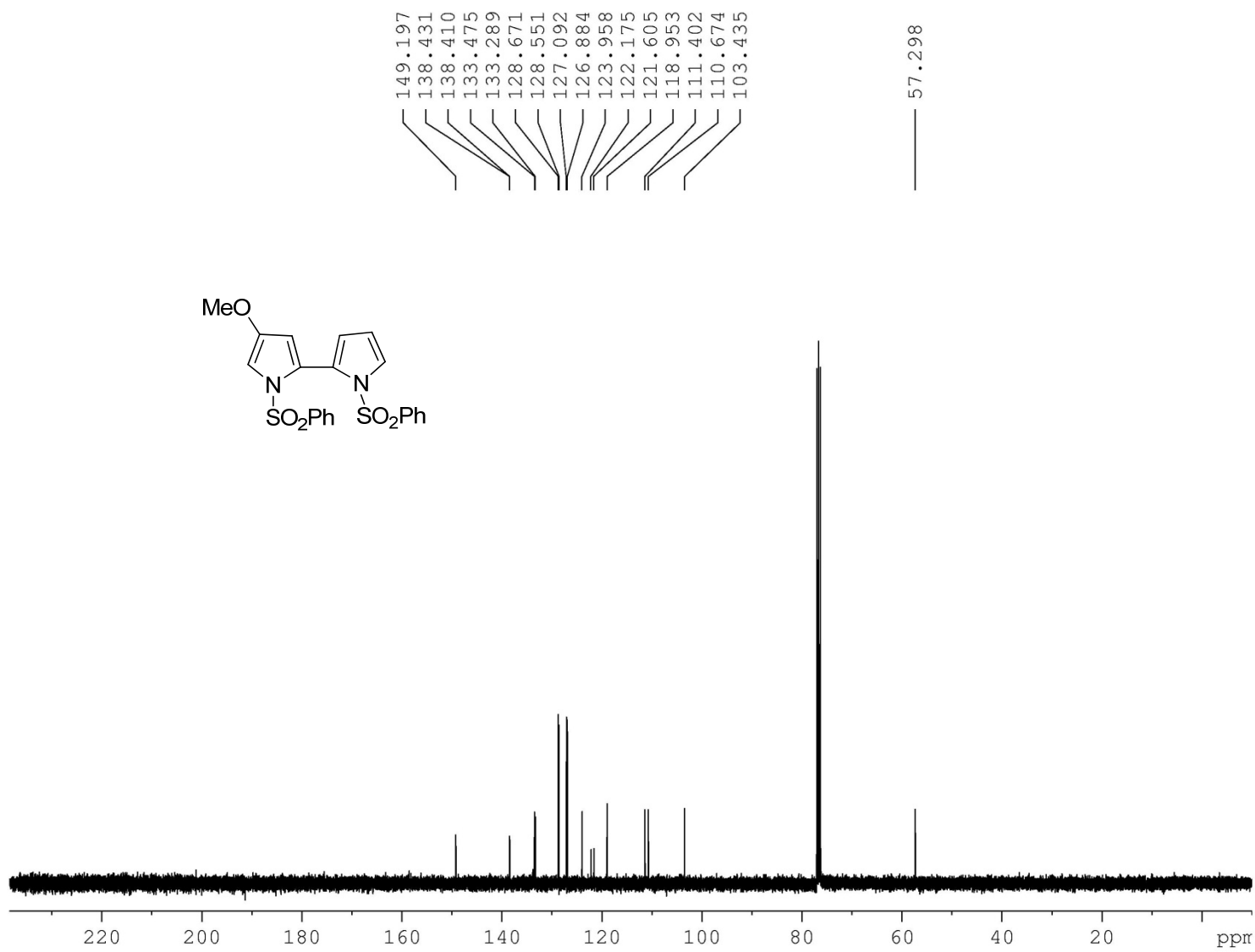
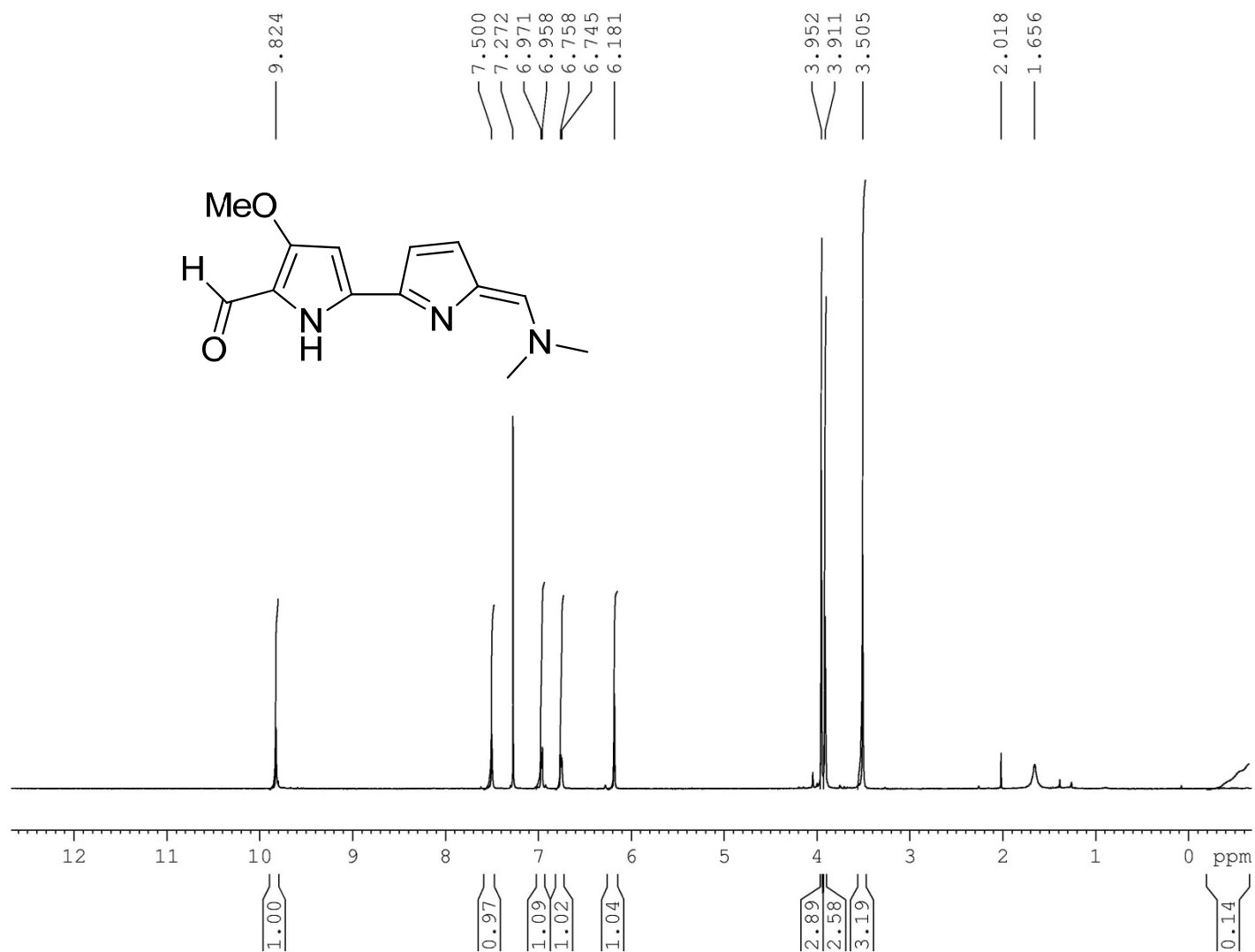


Figure 14. NMR  $^{13}\text{C}$  spectra of 6



**Figure 15.** NMR H spectra of 7

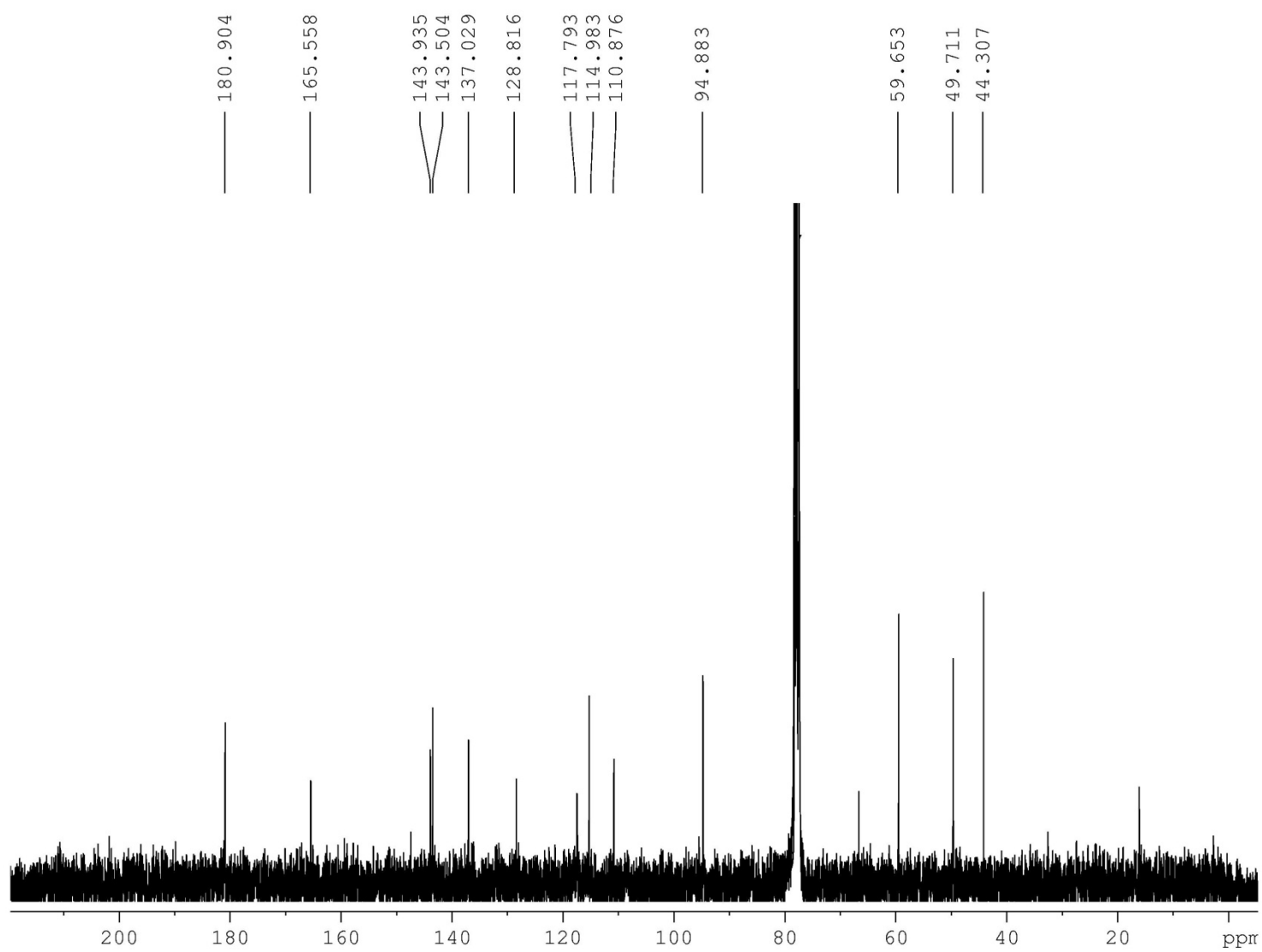
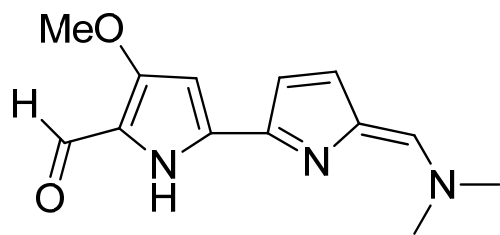
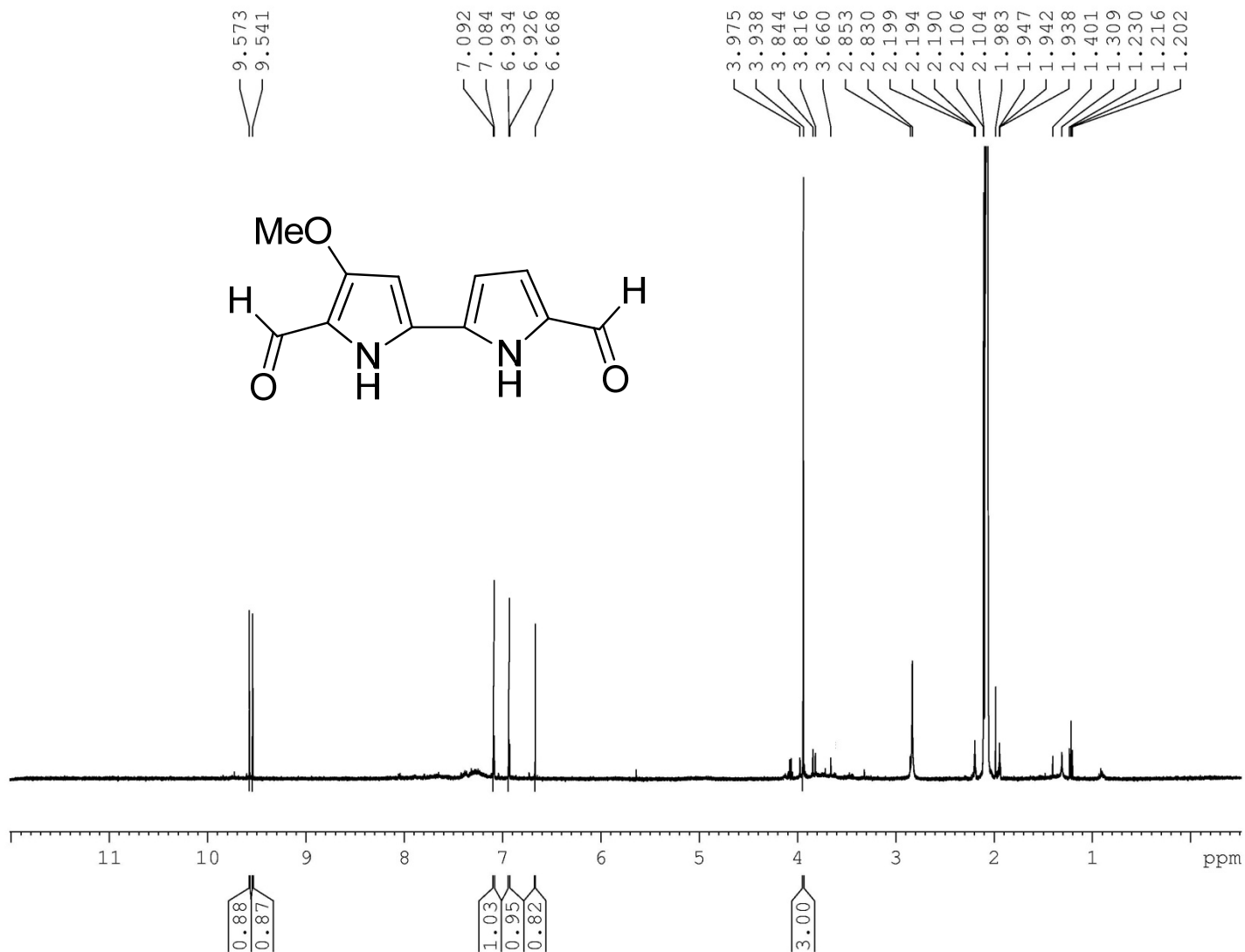
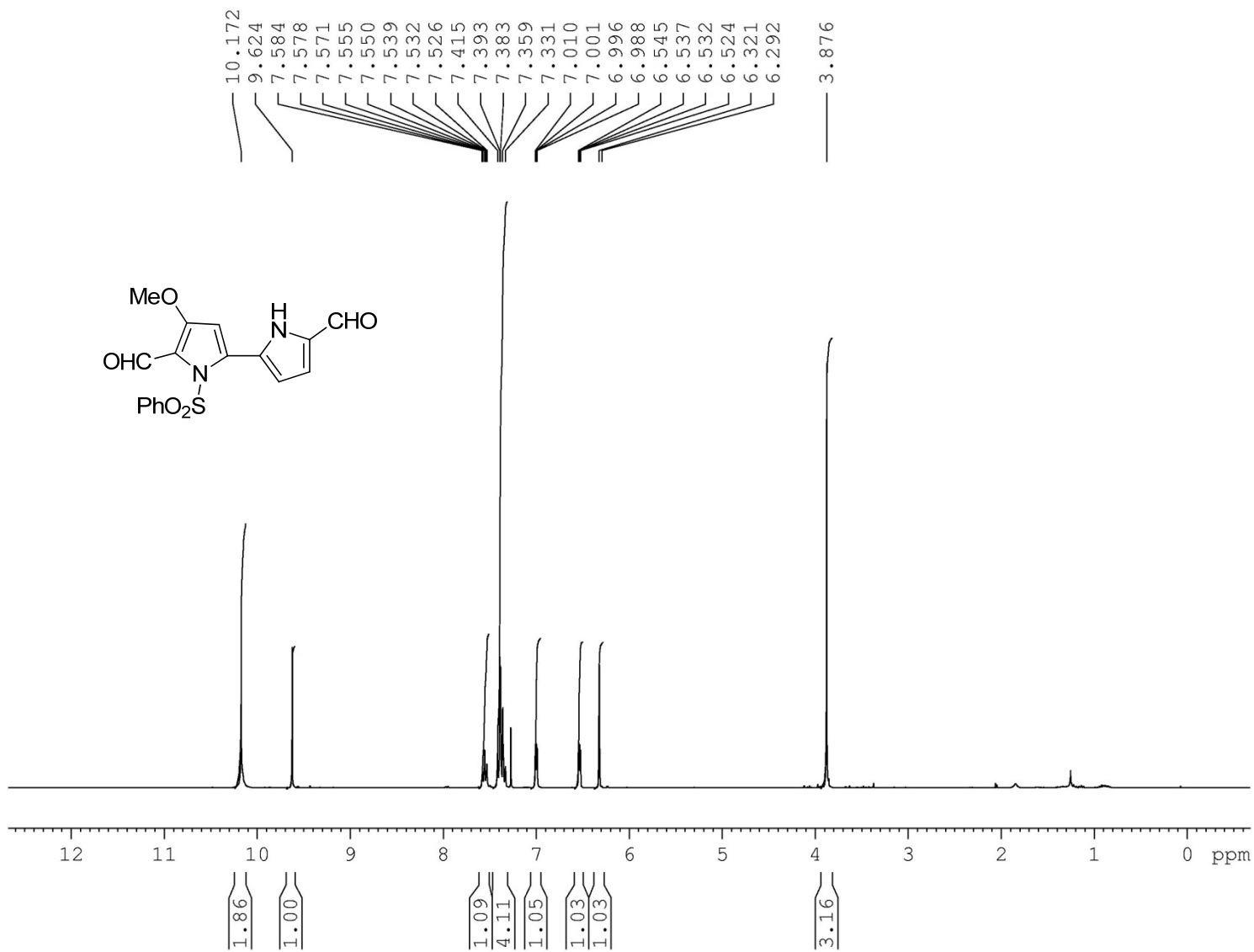


Figure 16. NMR  $^{13}\text{C}$  spectra of 7





**Figure 17.** NMR H spectra of **8**



**Figure 18.** NMR H spectra of **9**

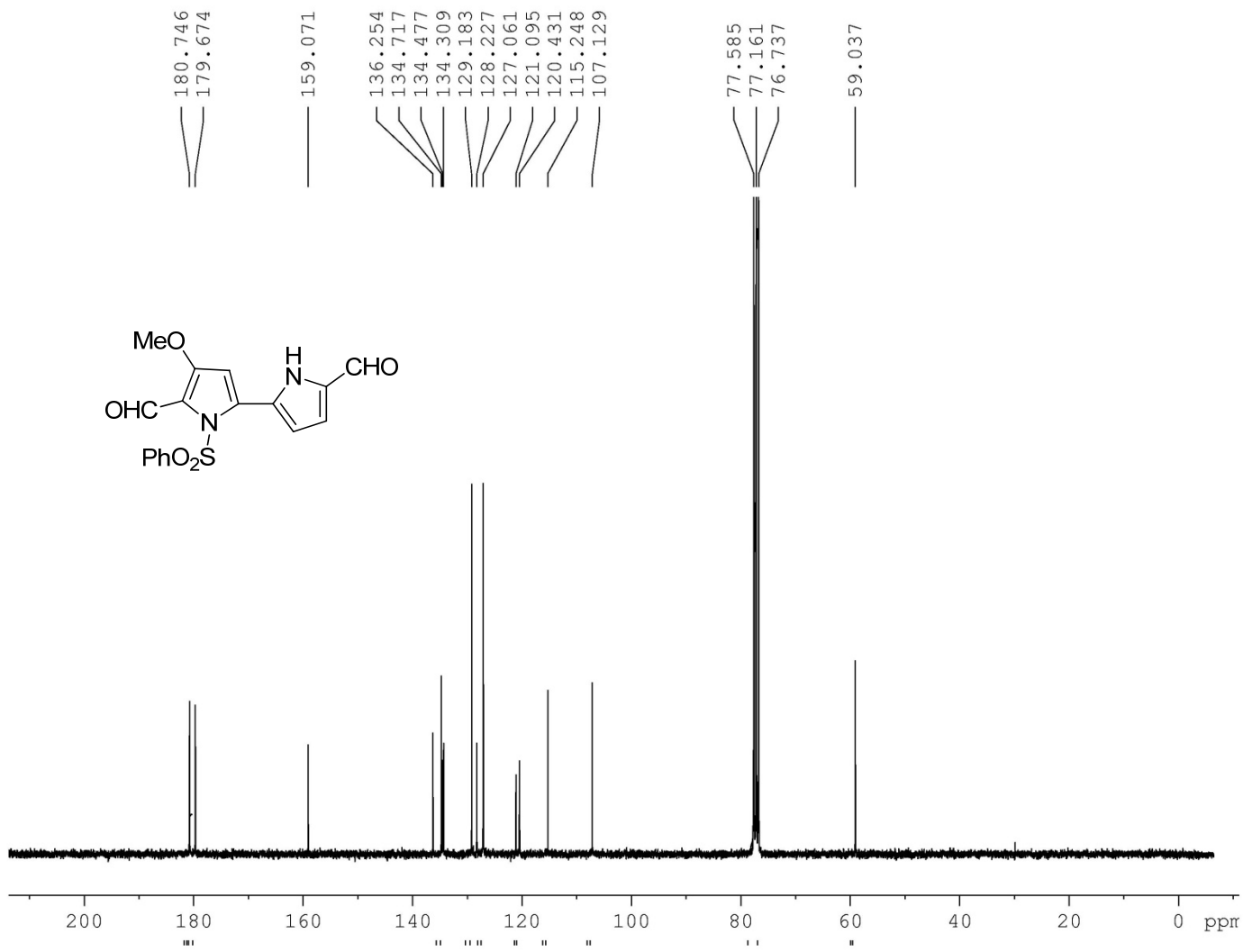
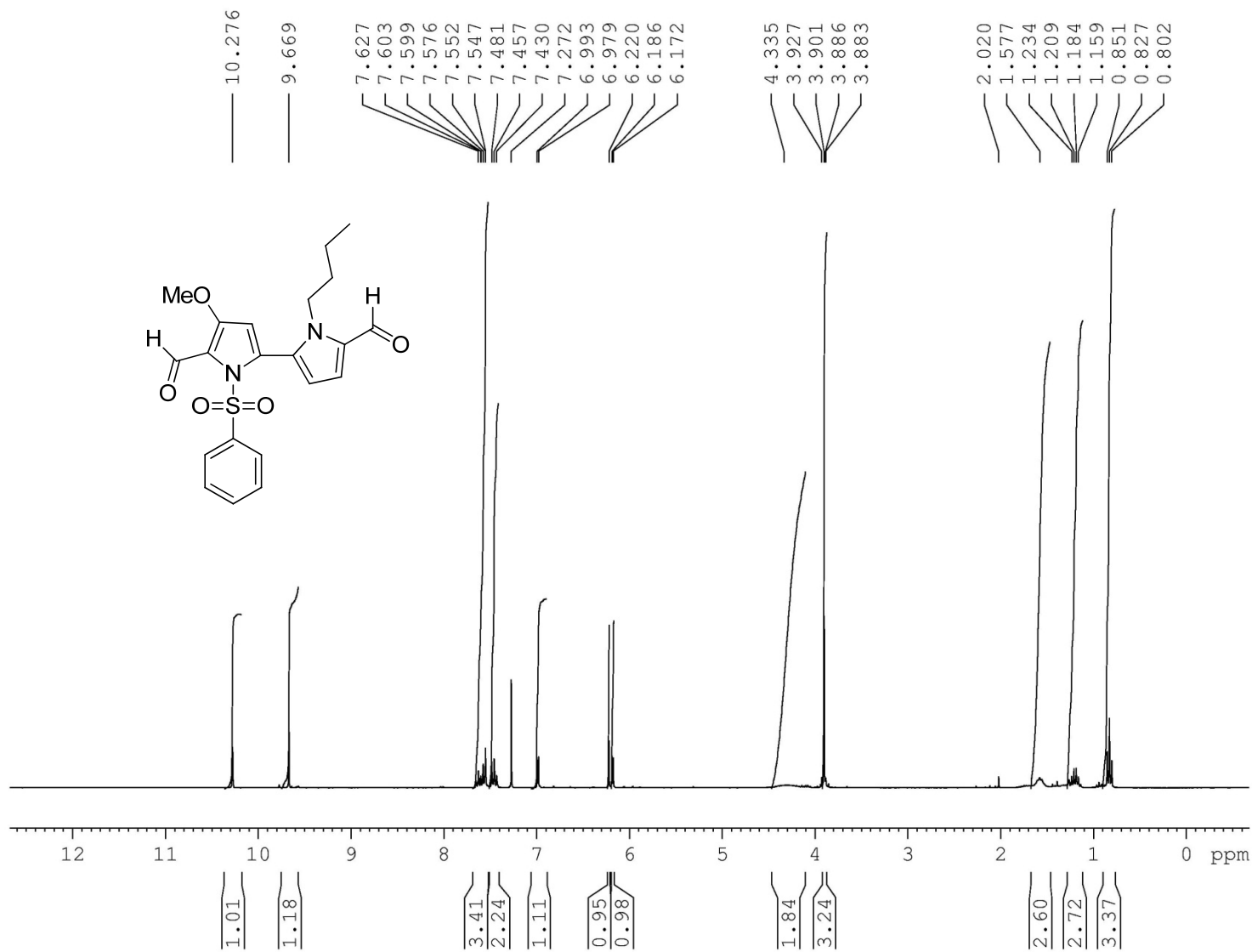


Figure 19. NMR <sup>13</sup>C spectra of 9



**Figure 20.** NMR H spectra of **10**

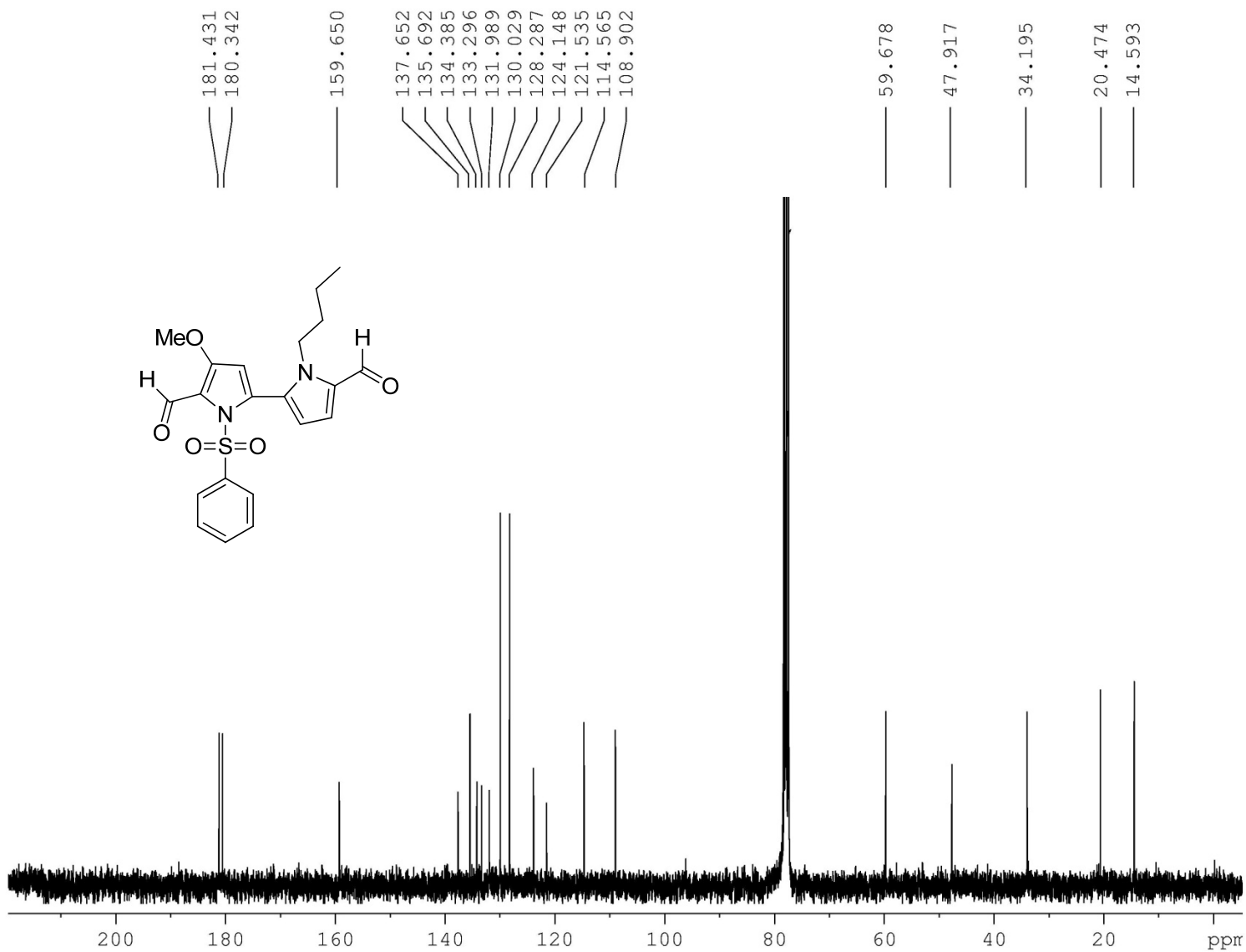
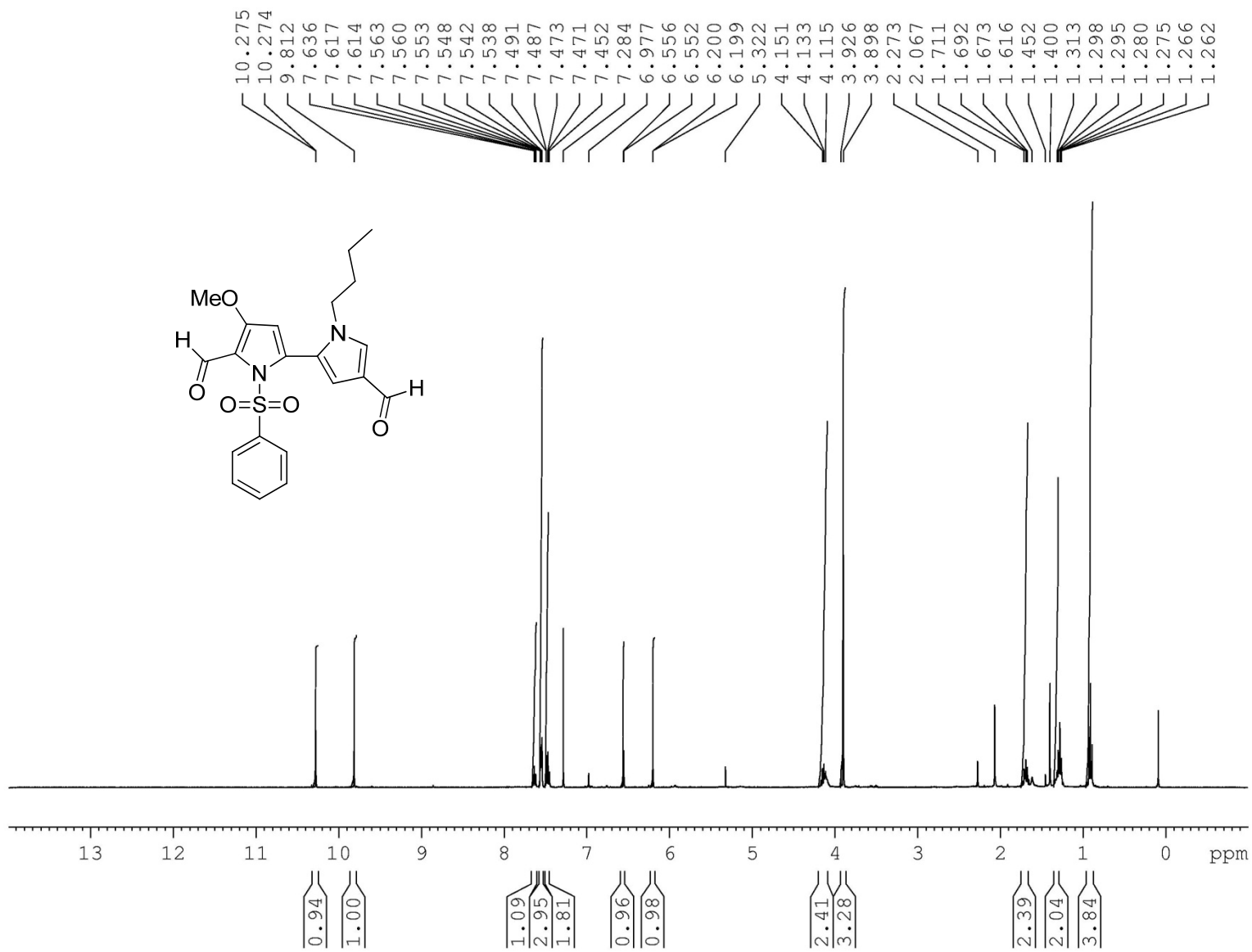


Figure 21. NMR  $^{13}\text{C}$  spectra of 10



**Figure 22.** NMR H spectra of 11

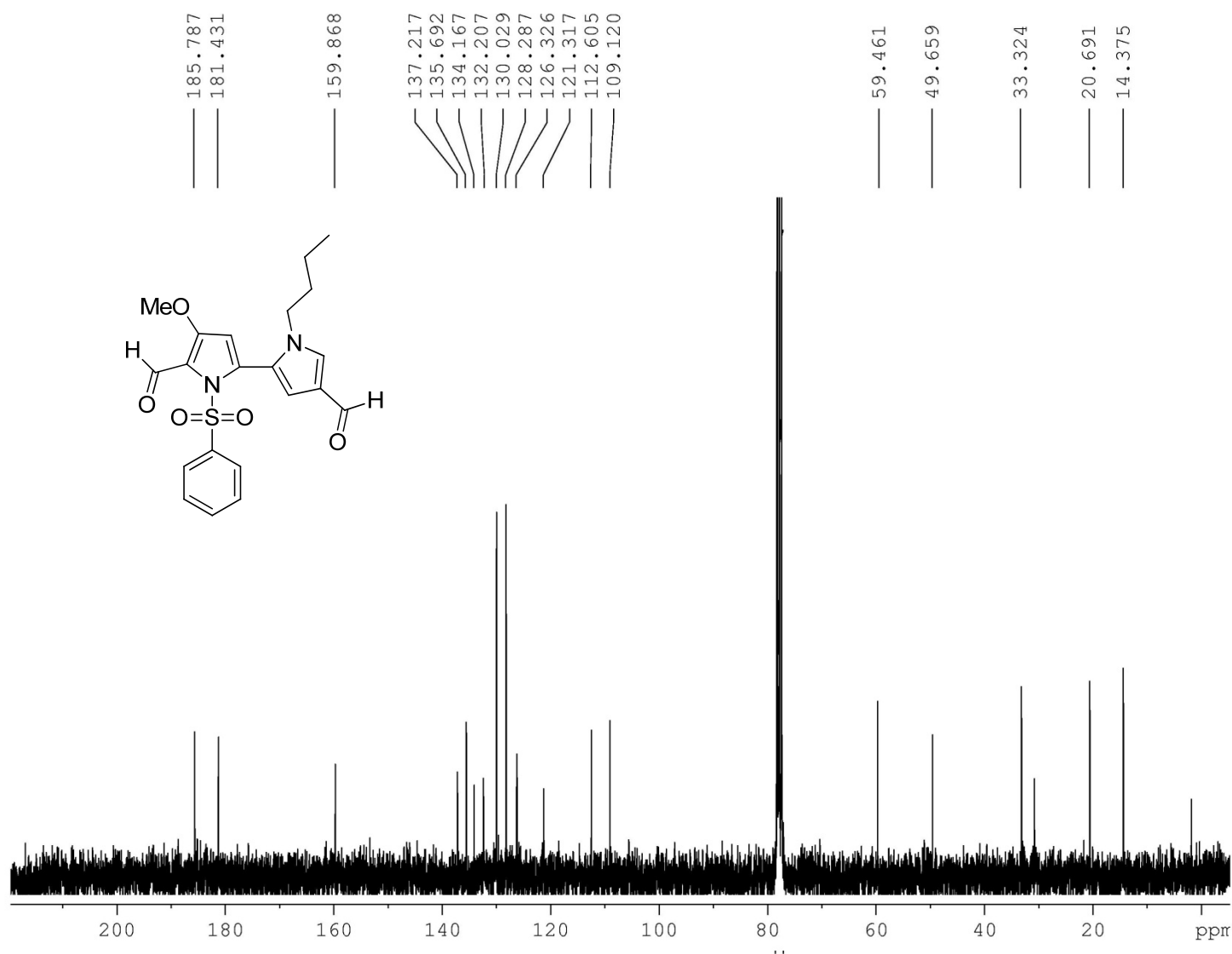
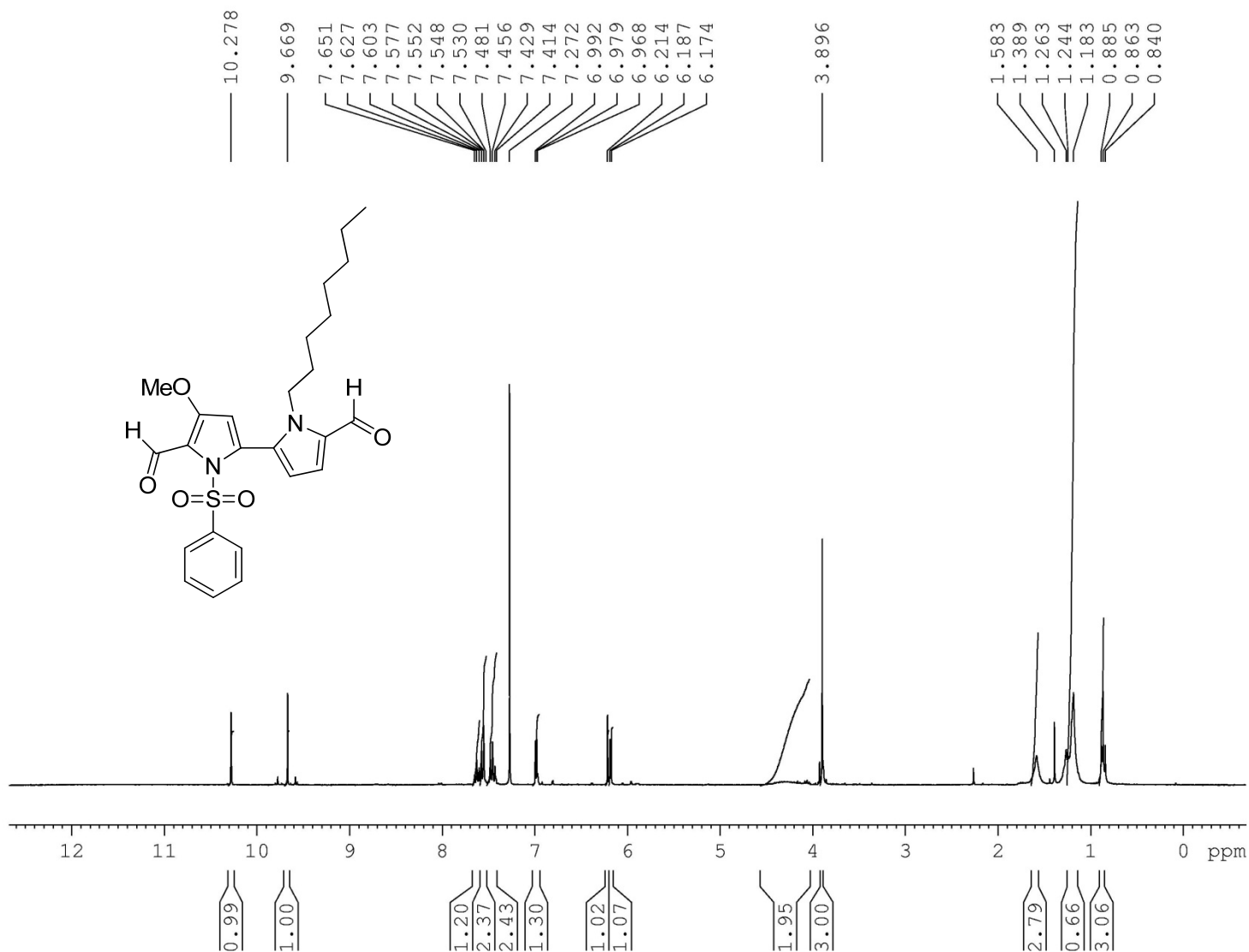


Figure 23. NMR  $^{13}\text{C}$  spectra of 11



**Figure 24.** NMR H spectra of **12**



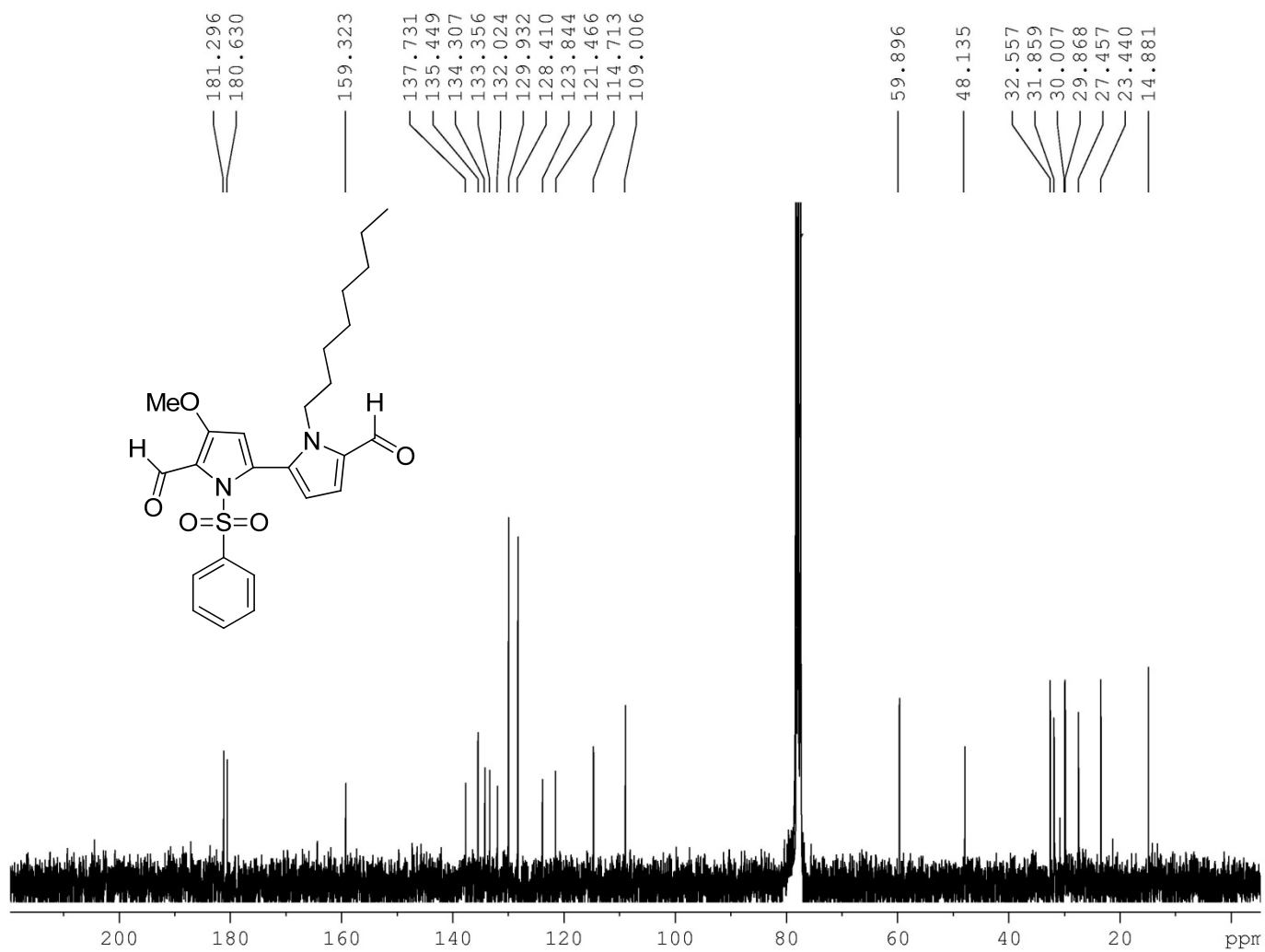
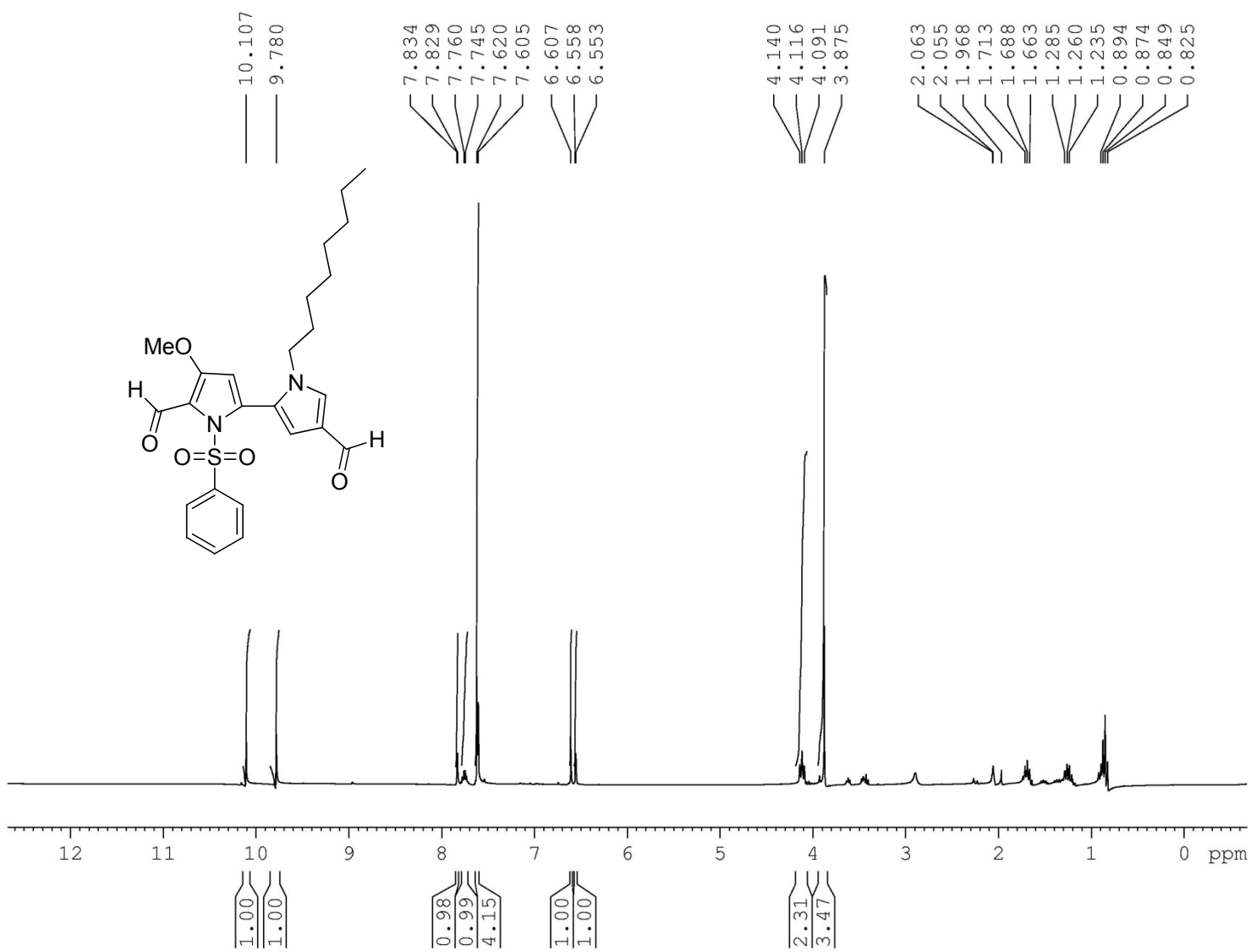


Figure 25. NMR <sup>13</sup>C spectra of 12



**Figure 26.** NMR H spectra of **13**

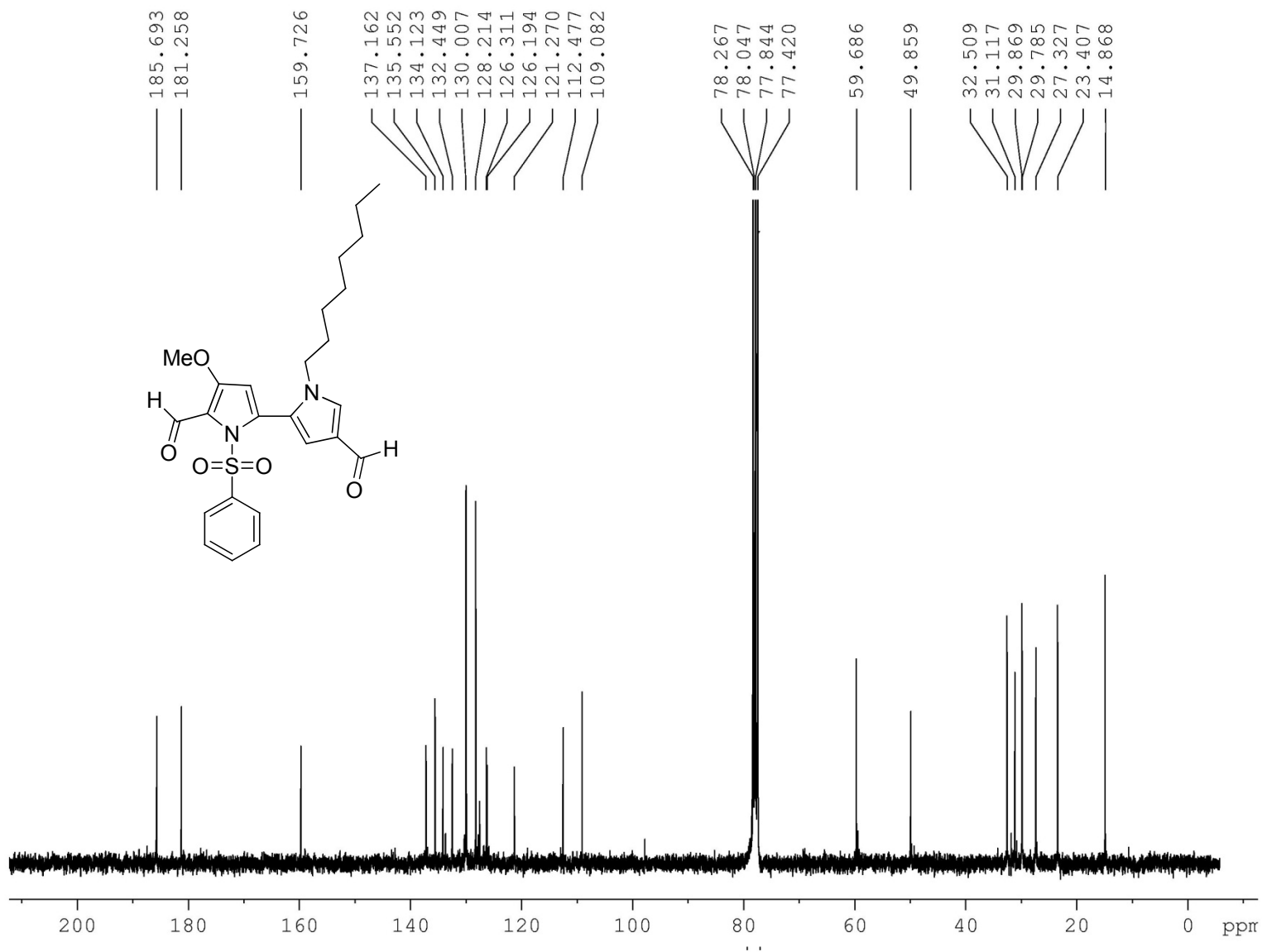
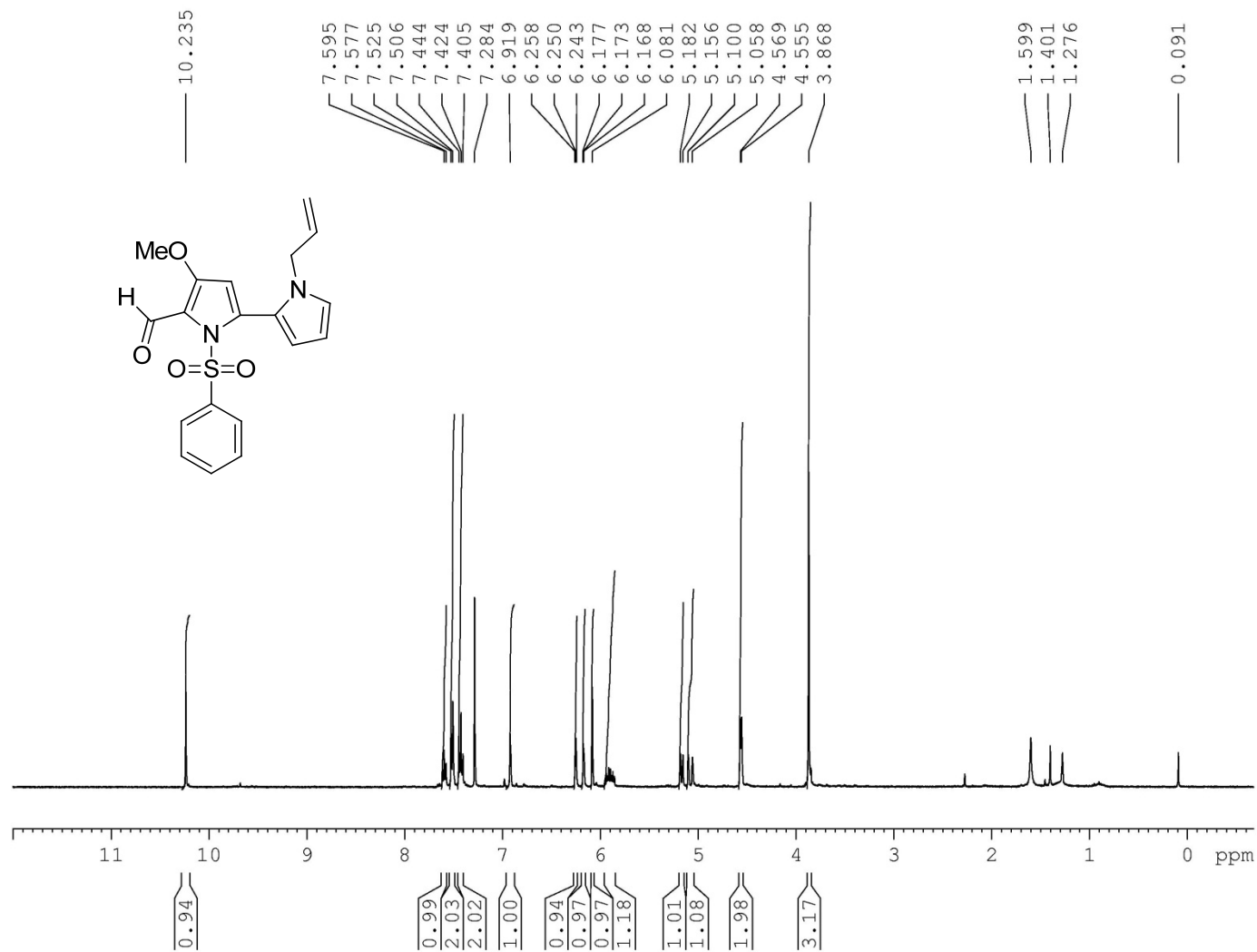


Figure 27. NMR  $^{13}\text{C}$  spectra of 13



**Figure 28.** NMR H spectra of 14

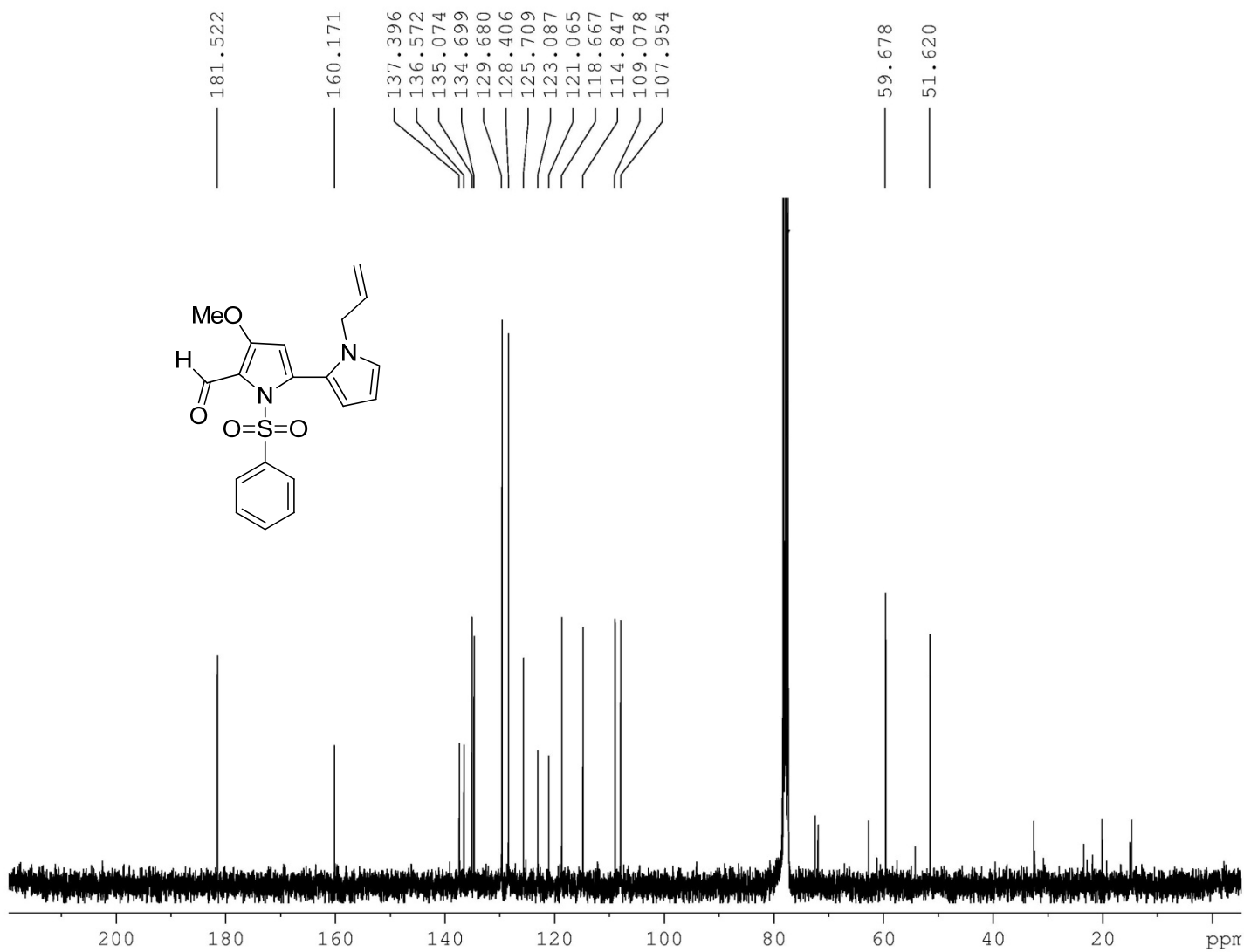


Figure 29. NMR <sup>13</sup>C spectra of 14

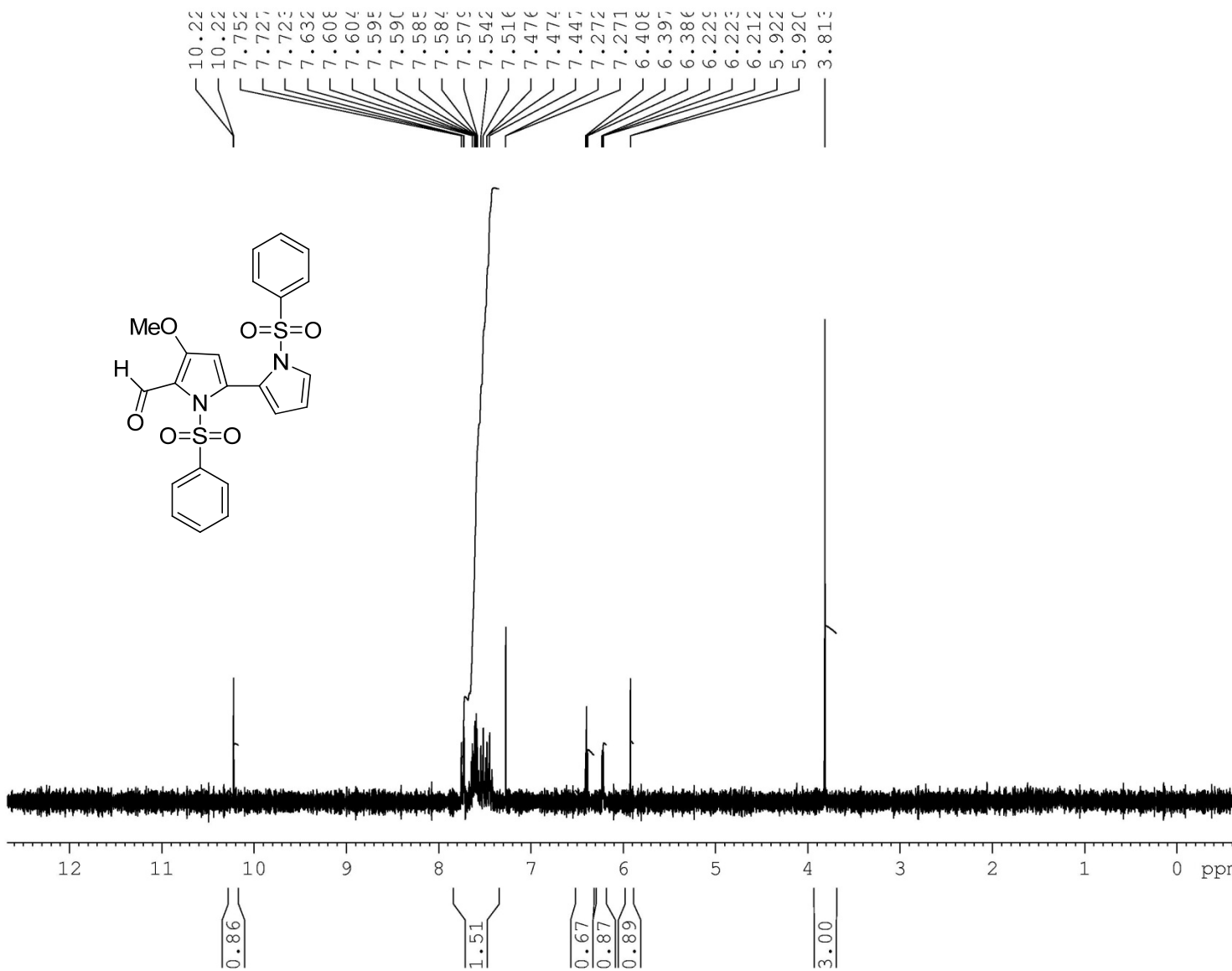


Figure 30. NMR H spectra of 15

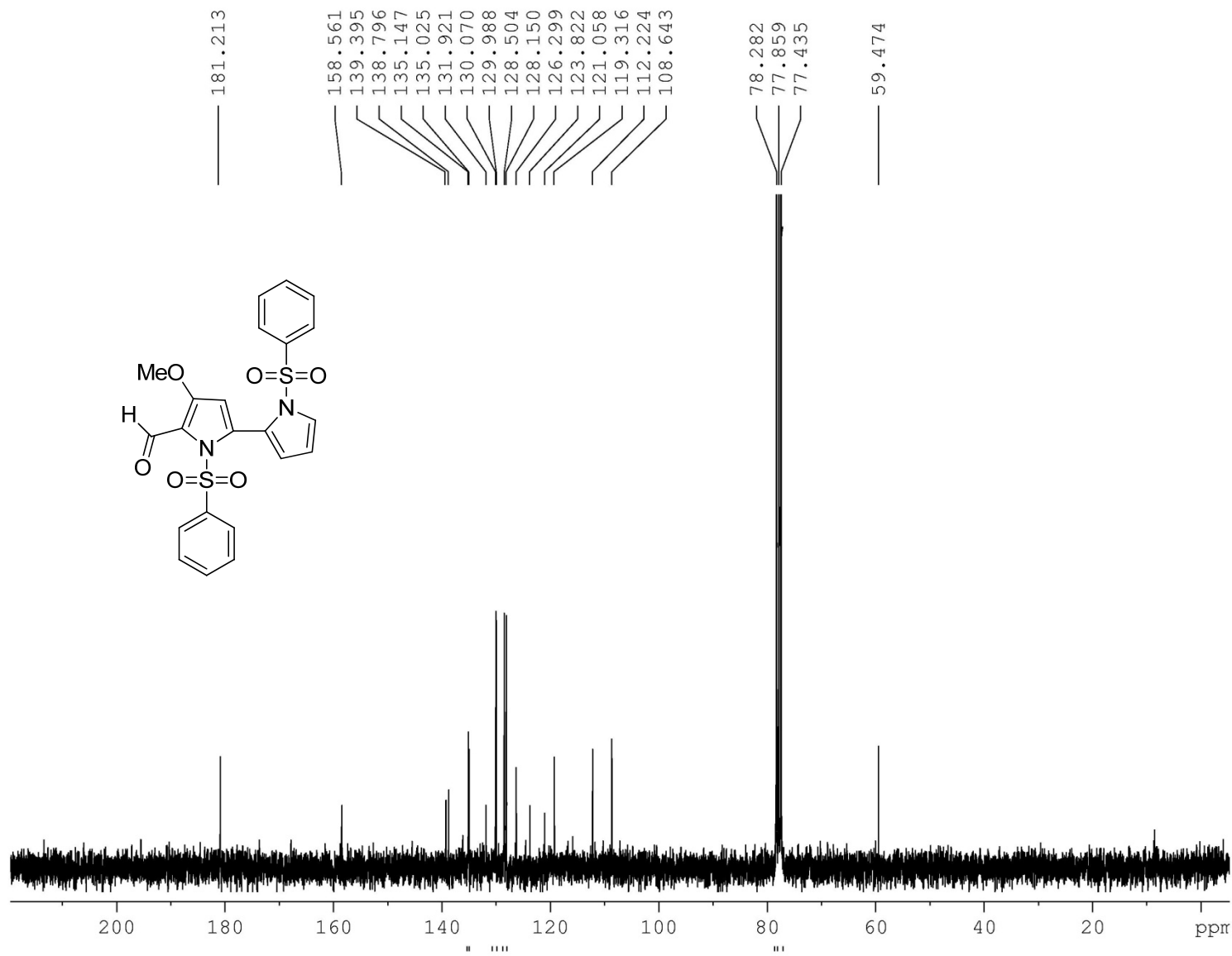
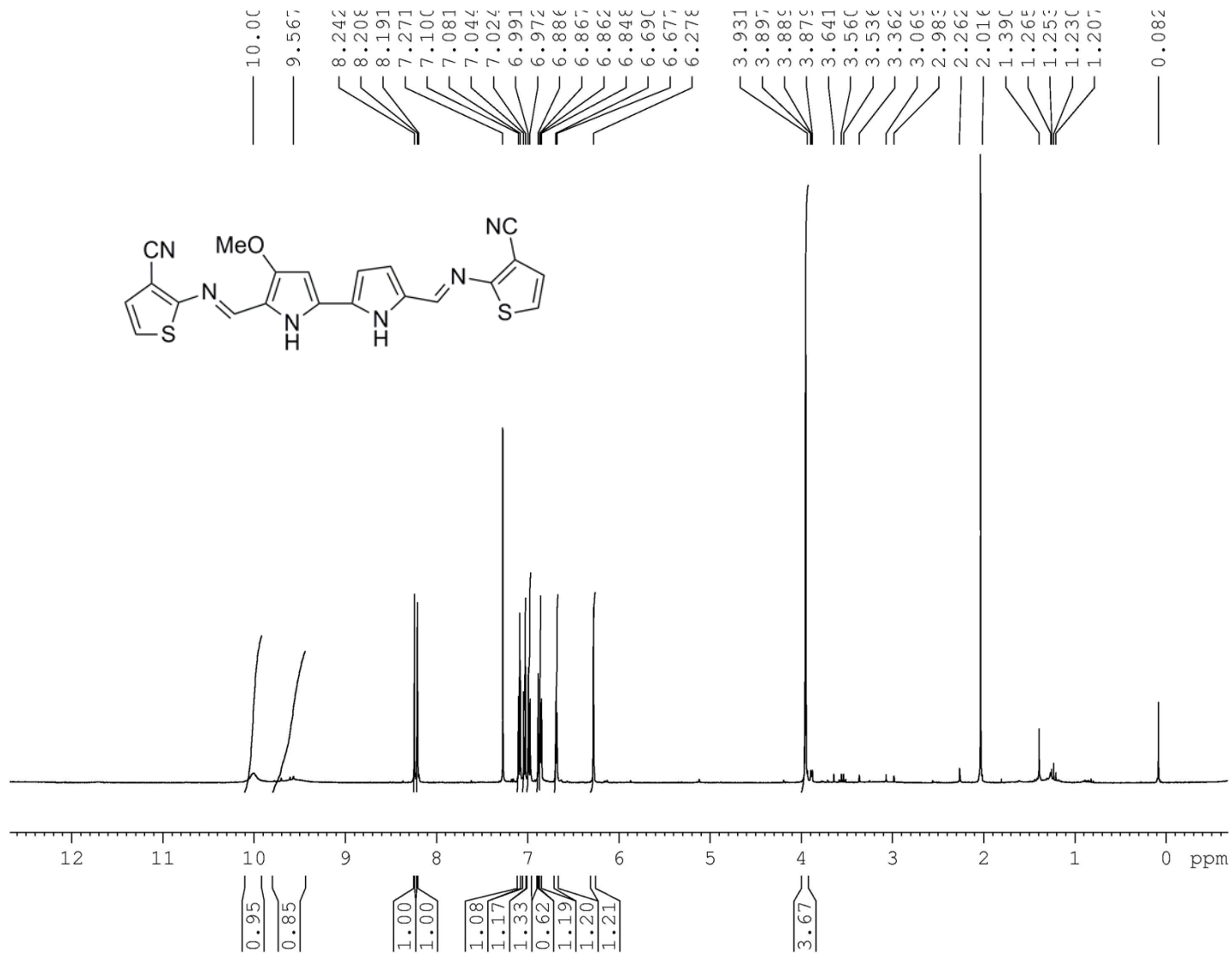


Figure 31. NMR  $^{13}\text{C}$  spectra of 15



**Figure 32.** NMR H spectra of 17



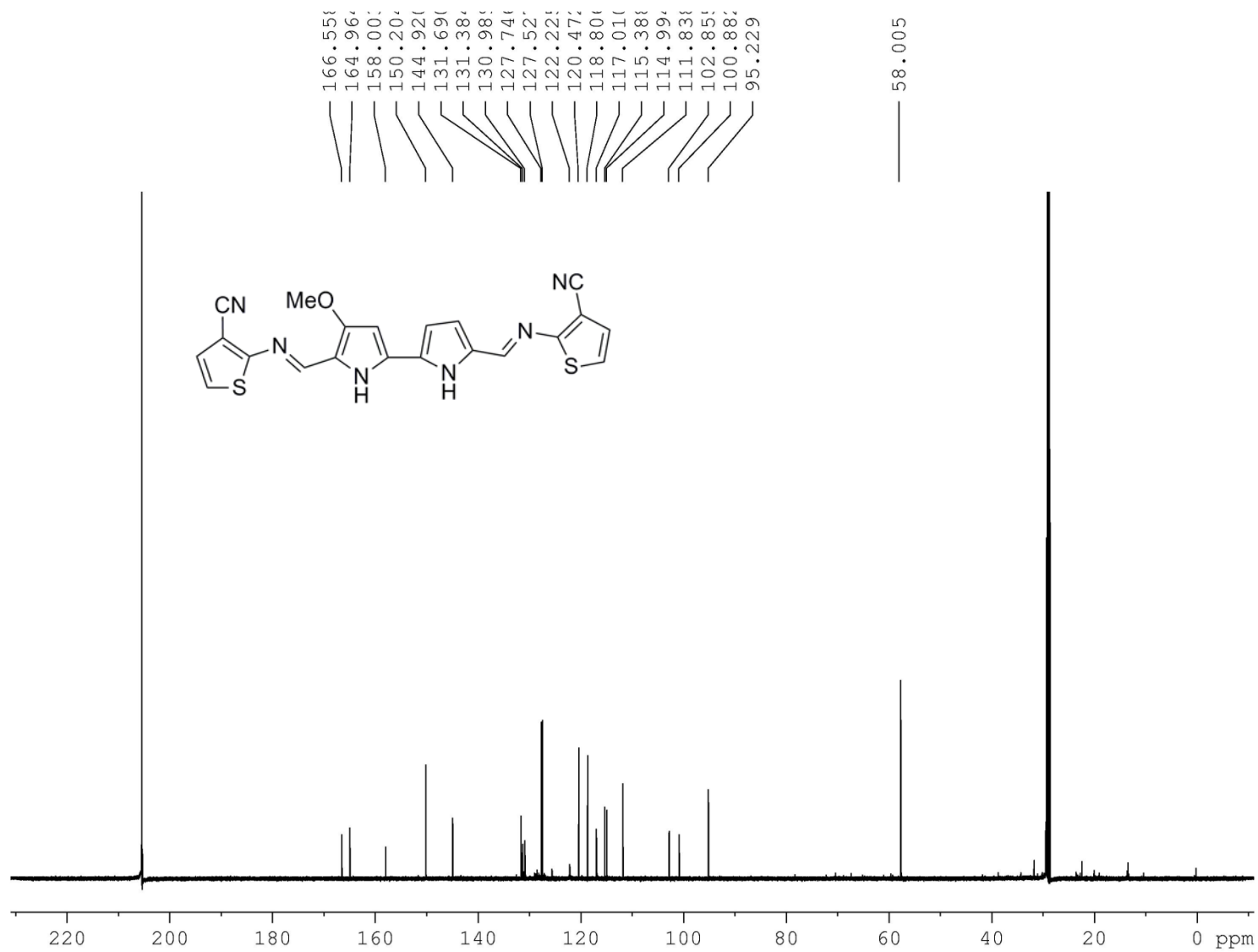


Figure 33. NMR  $^{13}\text{C}$  spectra of 17

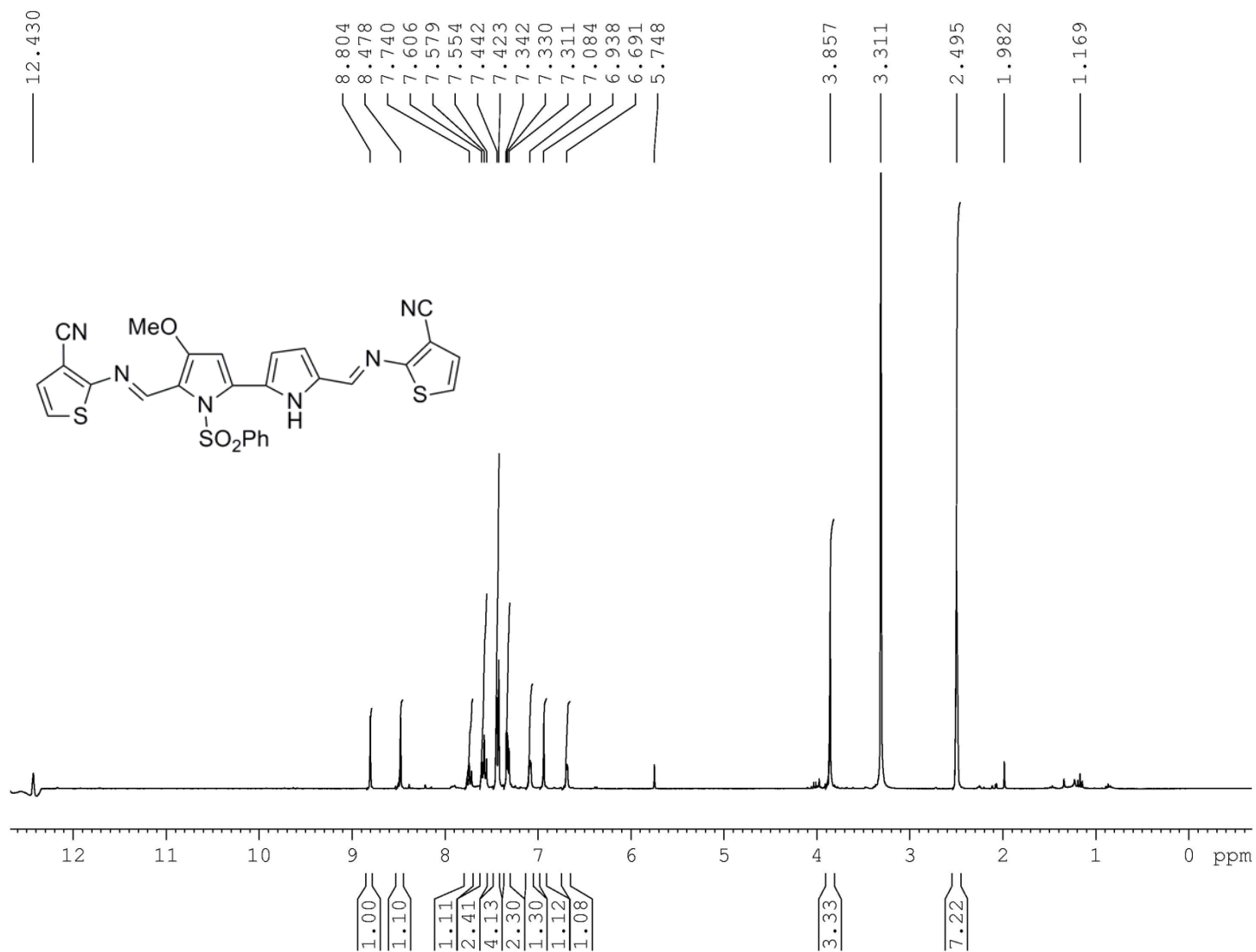
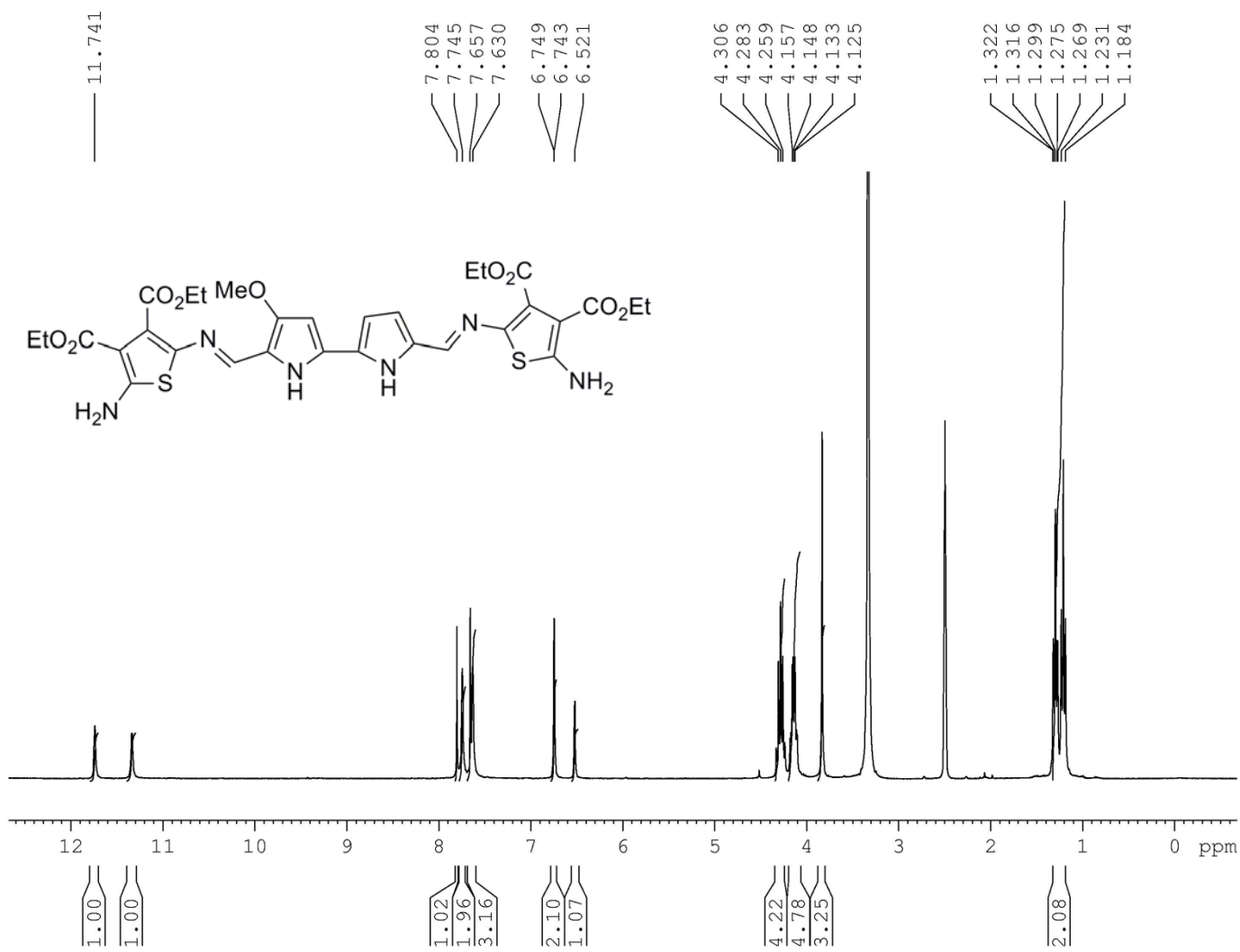


Figure 34. NMR H spectra of **18**



**Figure 35.** NMR H spectra of **20**

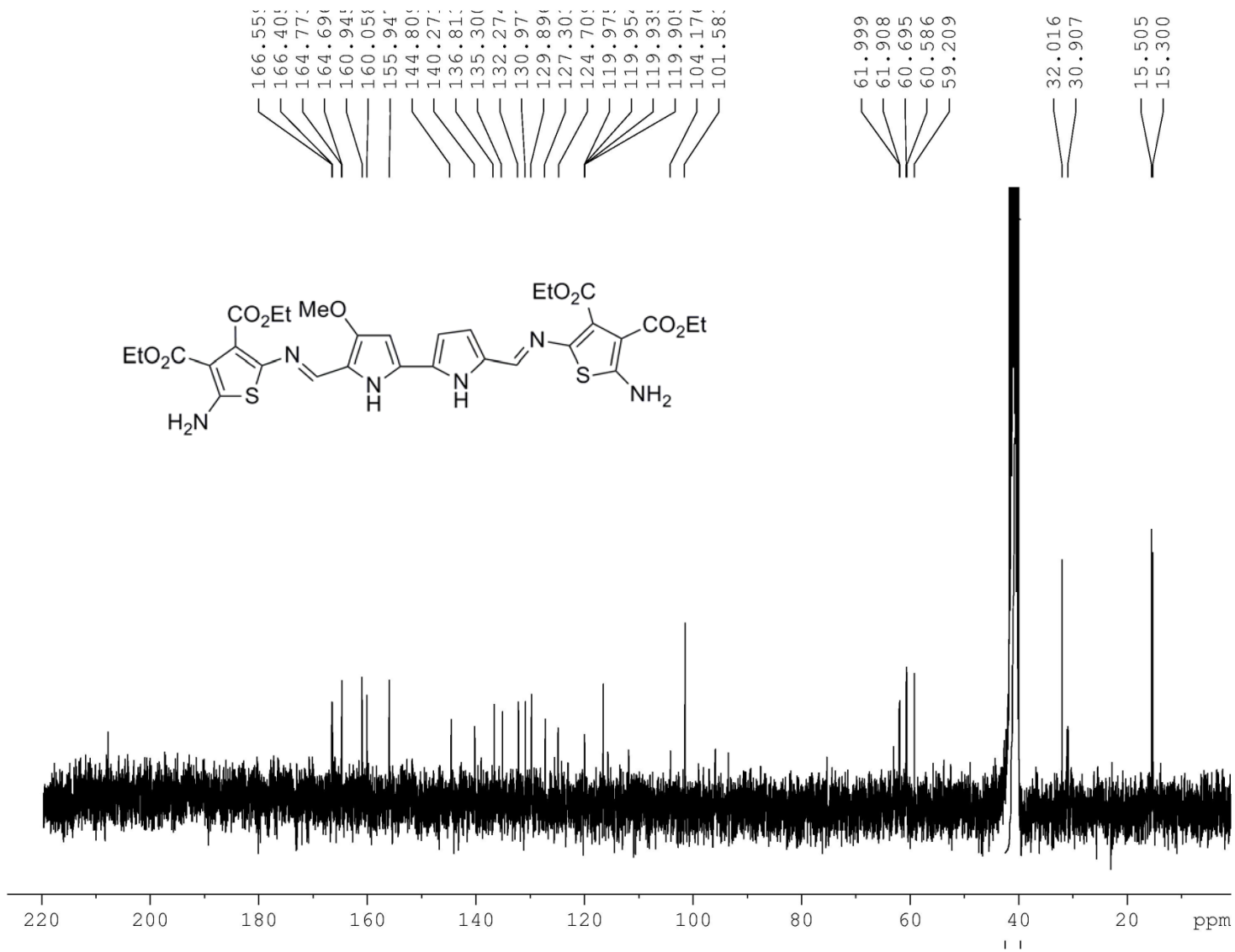


Figure 36. NMR <sup>13</sup>C spectra of 20

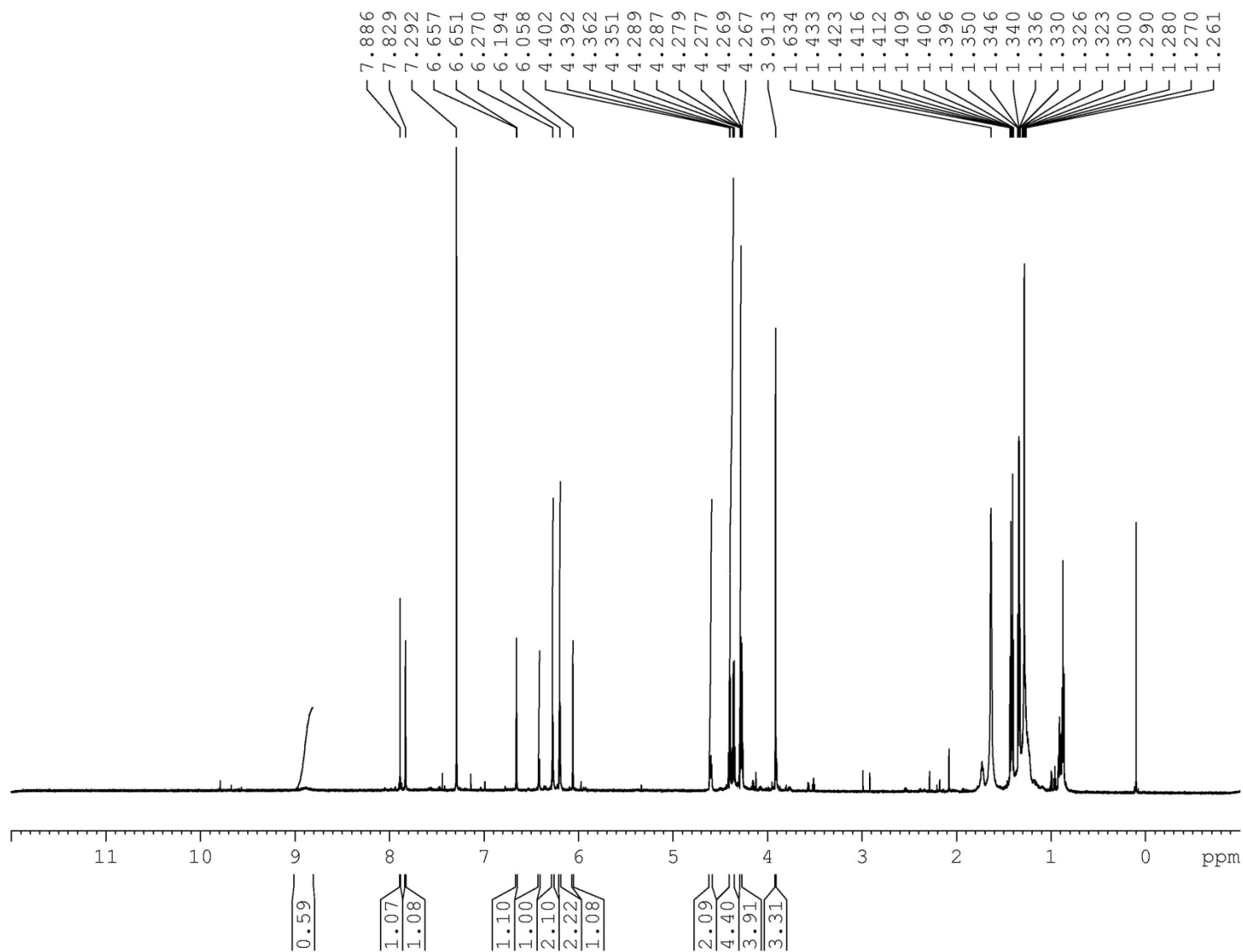
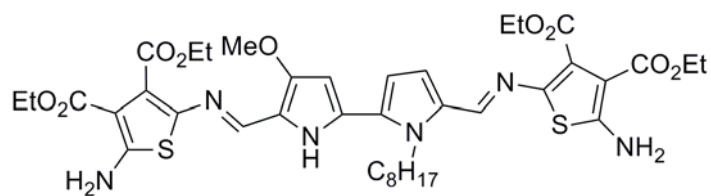


Figure 37. NMR H spectra of 22

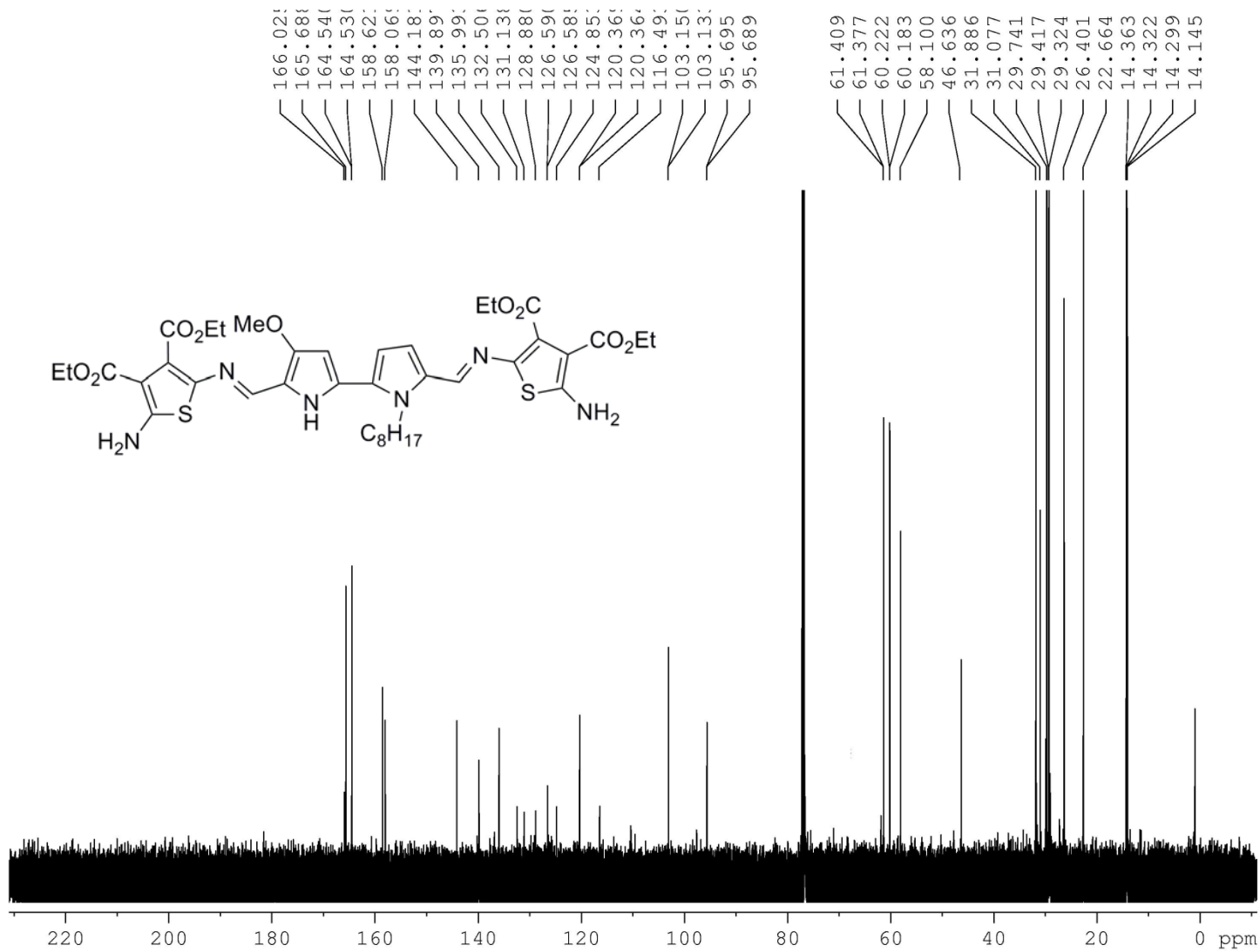
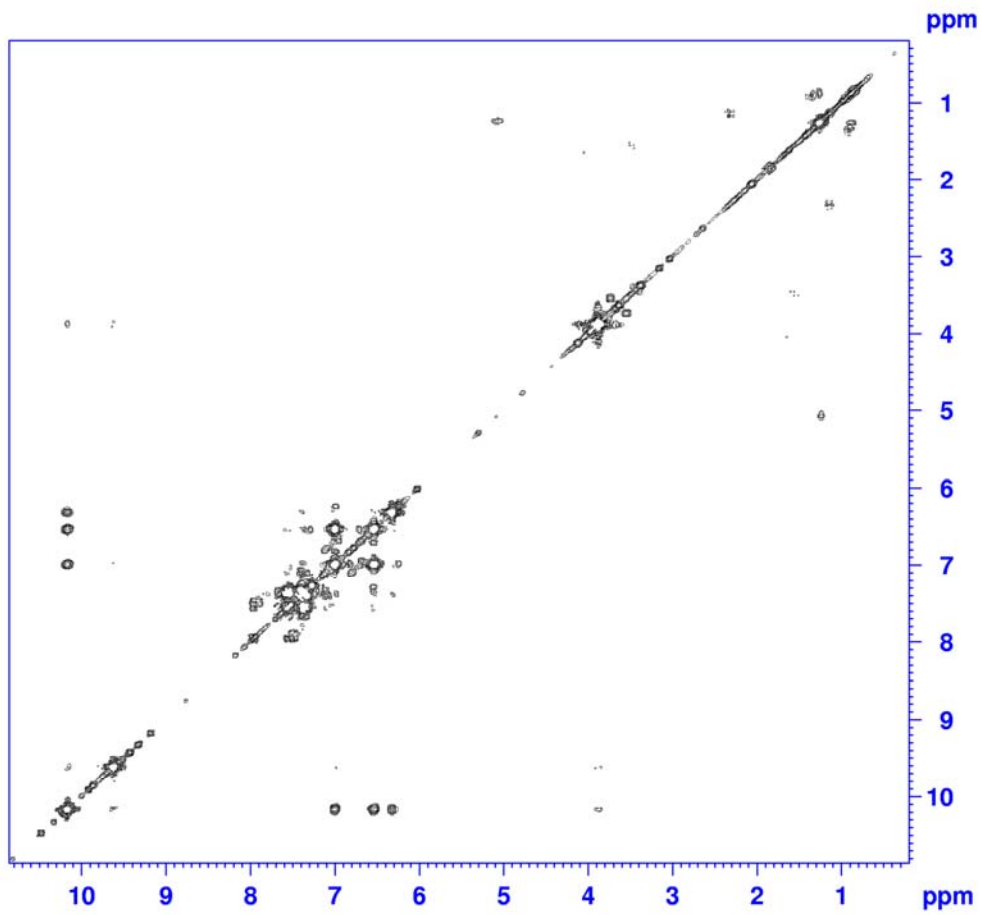
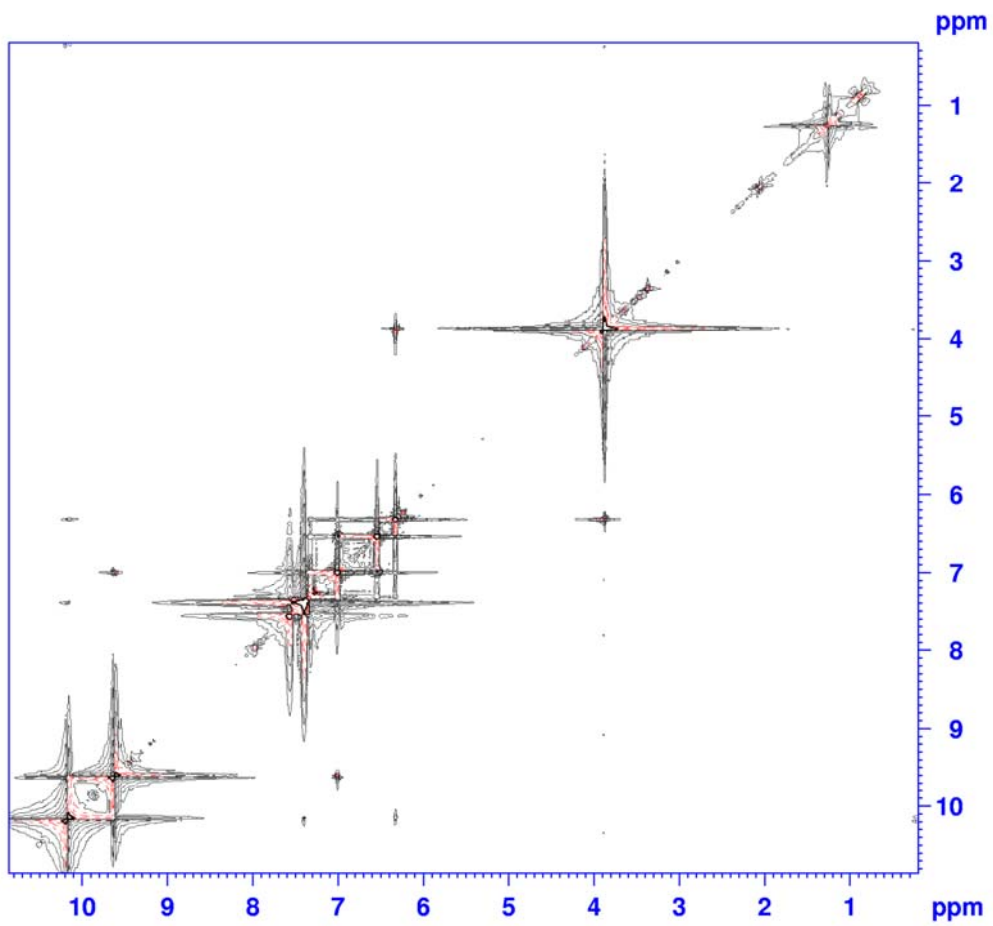


Figure 38. NMR  $^{13}\text{C}$  spectra of 22

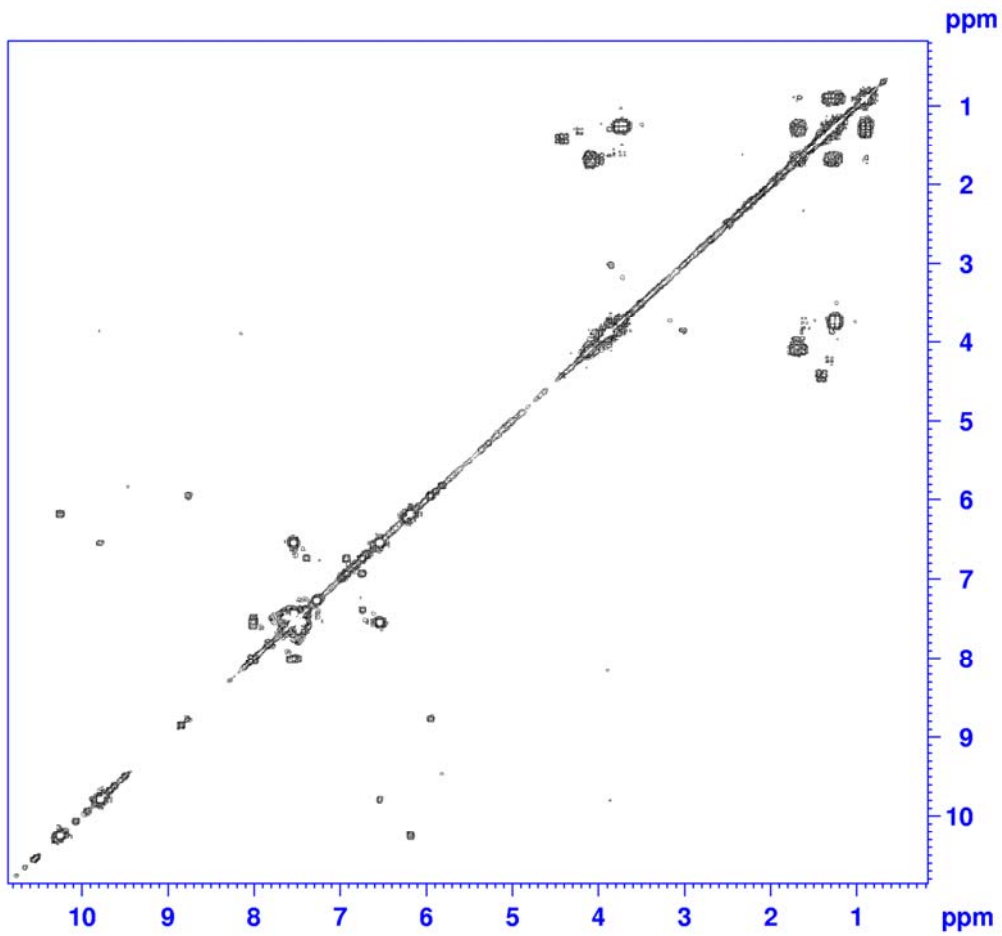


**Figure 39.** COSY spectrum of **9**

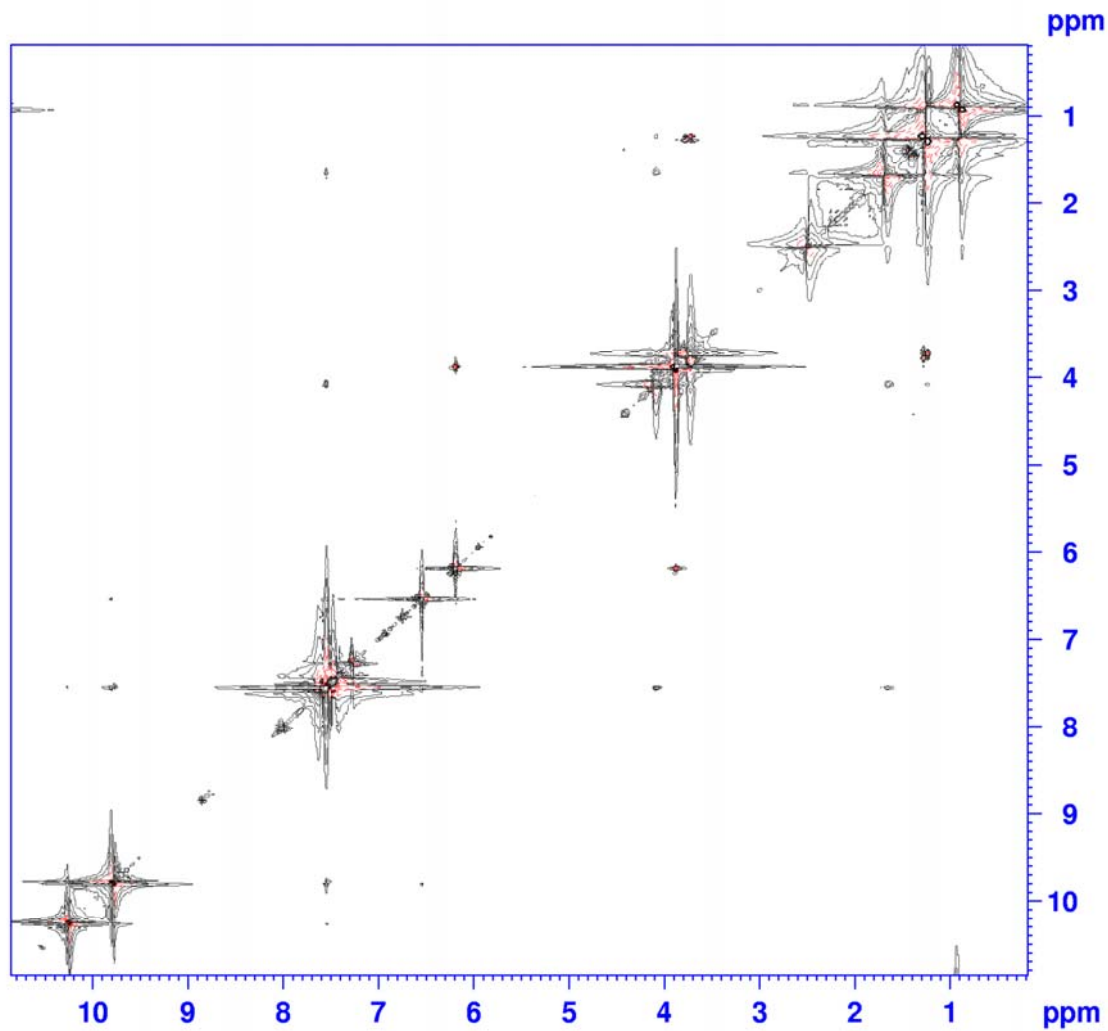


**Figure 40.** NOESY spectrum of **9**

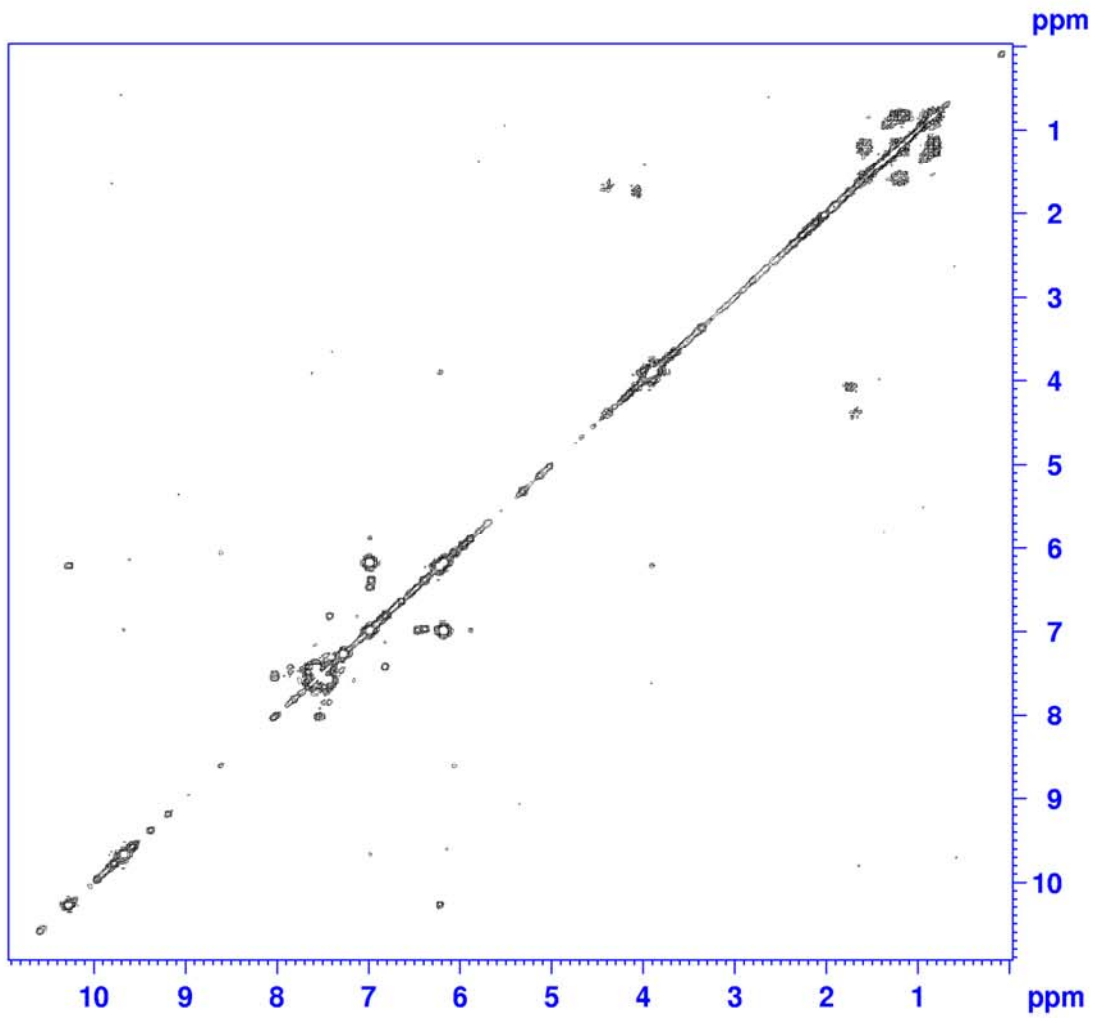




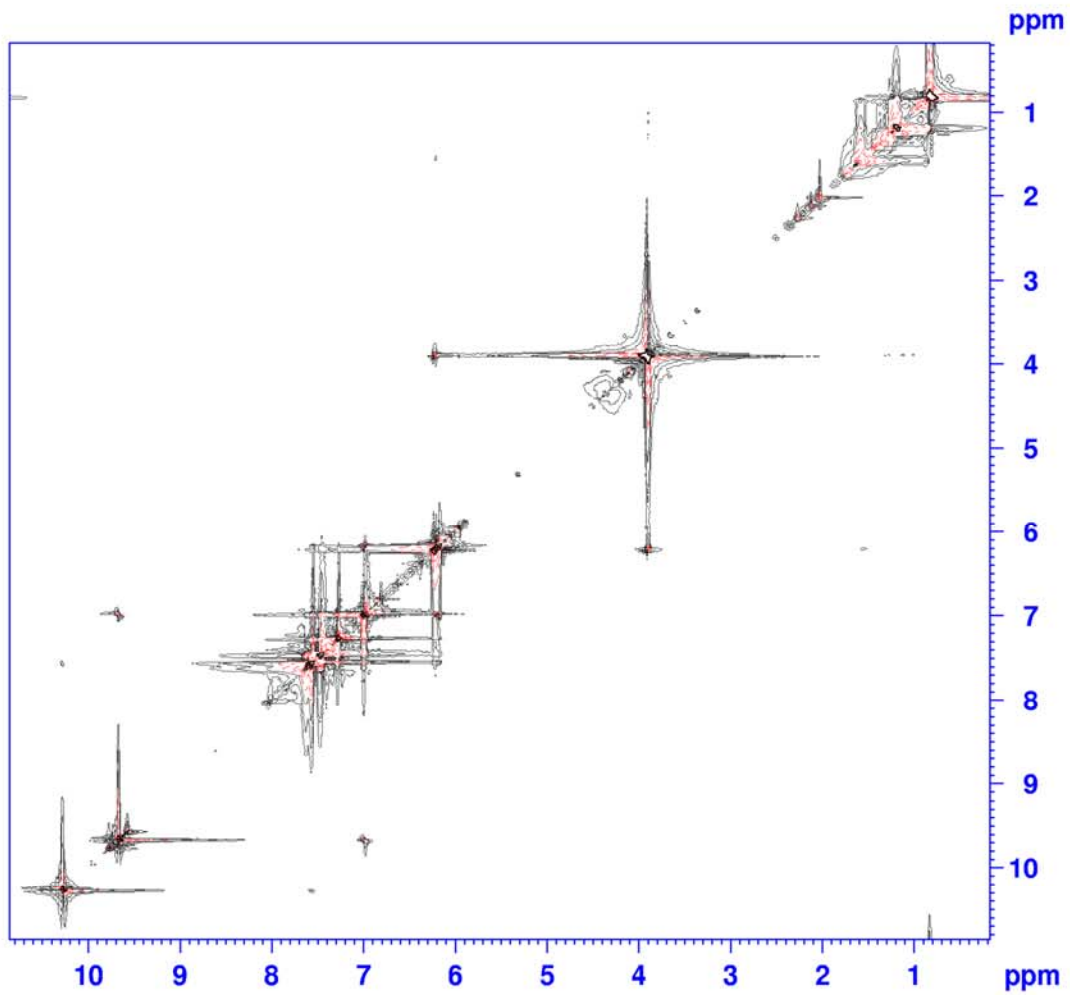
**Figure 41.** COSY spectrum of **10**



**Figure 42.** NOESY spectrum of **10**



**Figure 43.** COSY spectrum of **11**



**Figure 44.** NOESY spectrum of **11**

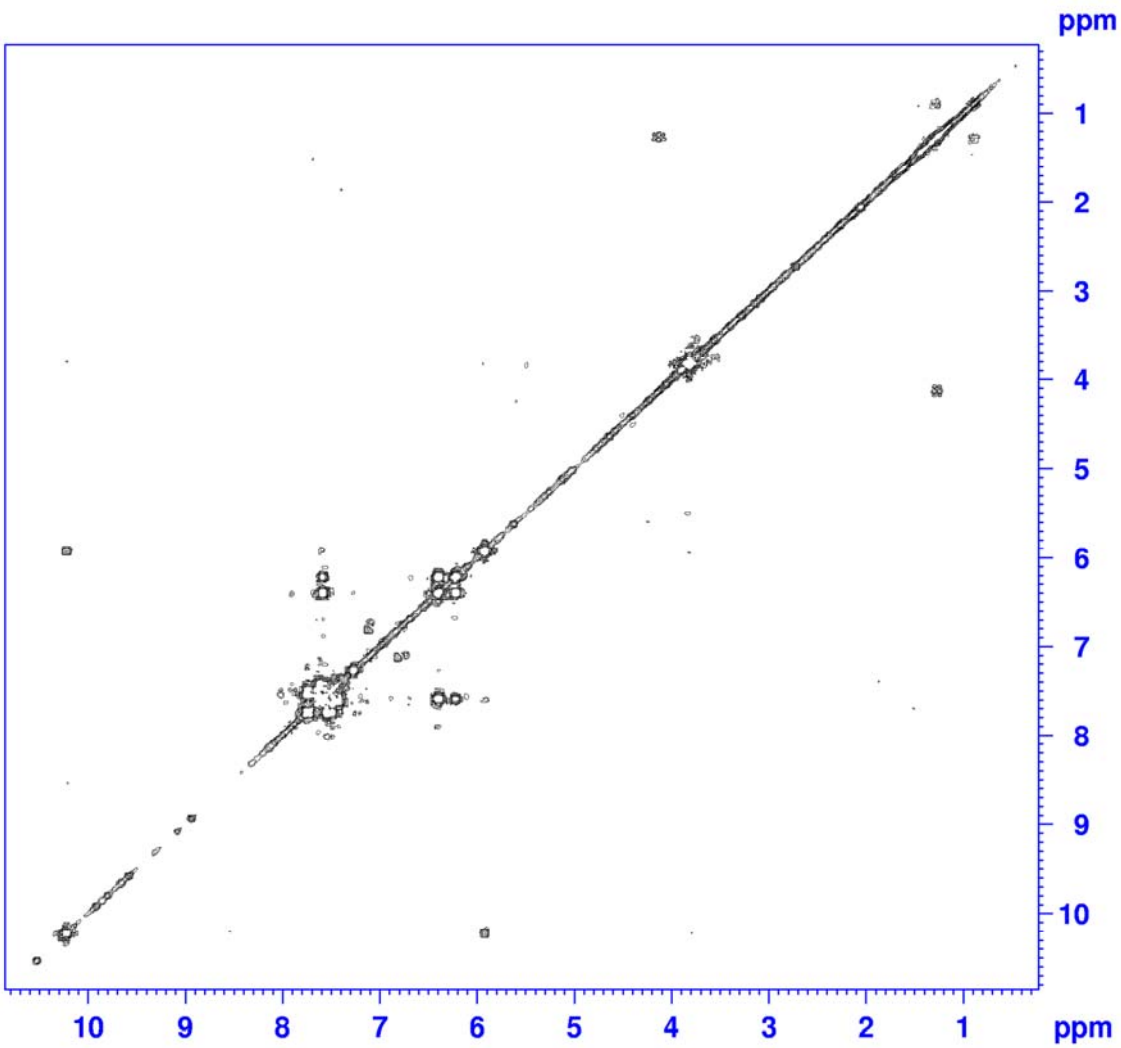
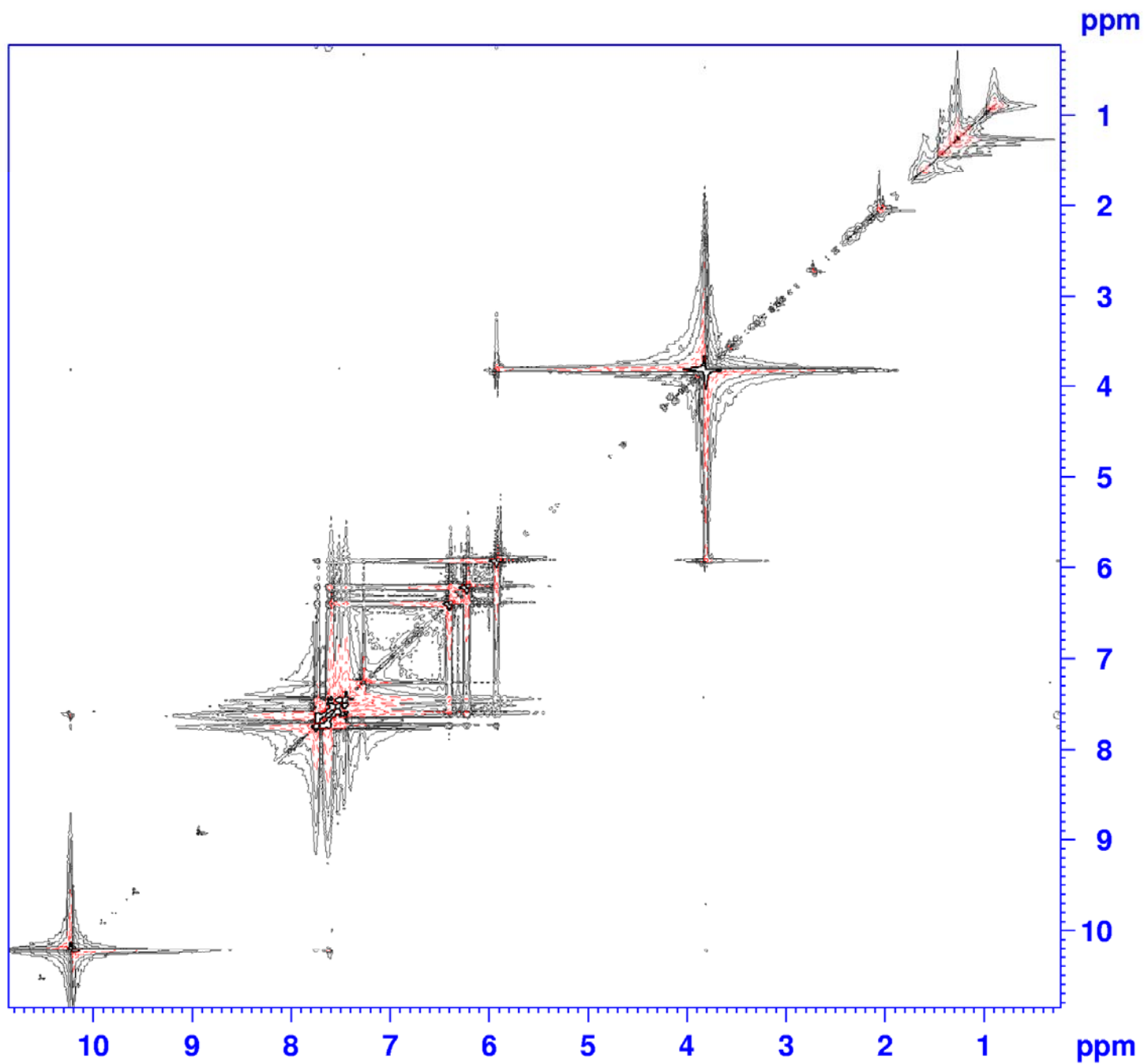


Figure 45. COSY spectrum of **15**



**Figure 46.** NOESY spectrum of **15**