Efficient Syntheses and Antimicrobial Activities of New Thiophene Containing Pyranone and Quinolinone Derivatives by Manganese(III) Acetate. The effect of Thiophene on Ring Closure- Opening Reactions

Efficient Syntheses and Antimicrobial Activities of New Thiophene Containing Pyranone and Quinolinone Derivatives by Manganese(III) Acetate. The effect of Thiophene on Ring Closure-Opening Reactions

Mehtap Özgür[a*], Mehmet Yılmaz[b], Hiroshi Nishino[c], Eda Çinar Avar[d], Hakan Dal[e], A.Tarık Pekel[a] and Tuncer Hökelek[f]

[a]*Department of Chemistry, Ankara University, 06100 Ankara, TURKEY*

[b]*Department of Chemistry, Kocaeli University, 41380 Kocaeli, TURKEY*

[c]*Department of Chemistry, Kumamoto University, Kurokami, Kumamoto 860-8555, JAPAN*

[d]*Department of Chemistry, Gazi University, 06500 Ankara, TURKEY*

[e]*Department of Chemistry, Anadolu University, 26470 Yenibağlar, Eskişehir, TURKEY*

[f]*Department of Physics, Hacettepe University, 06800 Beytepe, Ankara, TURKEY*

ABSTRACT

The syntheses of new series of pyranones, namely fused pyranones and quinoline-based dihydrofurans accompanied by 3-alkenyl-substituted structures were described. The products were regioselectively formed Mn(III)-mediated oxidation at elevated temperature in order to obtain excellent yields. The effects on product distributions of the thiophene group together with the temperatures and reactions time were investigated. The structures of the syntheses compounds were determined on the basis of spectroscopic (IR, ^{1}H NMR, ^{13}C NMR, COSY, HSQC, HMBC and elemental analysis) and X-ray crystallographic data. In addition, the *in vitro* antimicrobial activities of the some syntheses dihydrofurans were tested against G (+) and G (-) bacteria using disc diffusion method. The results indicated that the compounds containing thiophene group showed a better antimicrobial effect than some commonly used antibiotics.

Keywords: manganese(III) acetate, dihydrofuran, 3-alkenyl–substituted coumarin, thiophene, antimicrobial activity

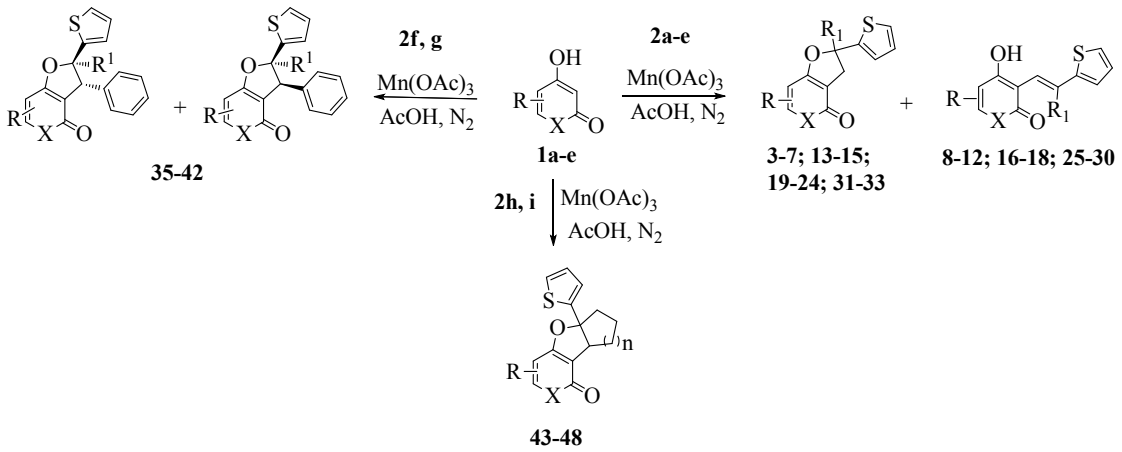
*Corresponding authors. Tel: +90 3122126720 Fax: +90 3122232395

E-mail address: myakut@ankara.edu.tr [M. Özgür]

1. Introduction

Pyranones are amongst the most abundant molecules of naturally occurring compounds and commonly used as versatile intermediates in natural product synthesis.[1] Among pyranone derivatives, coumarins and pyranocoumarines are an important class of organic compounds, and used as the building blocks of many biologically active molecules[2] exhibiting significant pharmacological activities such as anticoagulant,[3a] antitumor,[3b] anti-imflammatory,[3c] antibacterial[3d] and cytotoxic activities.[3e] Morover, 4-hydroxy-3-substituted pyranones have been used as fluorescent chemosensors,[4a] molecular switches,[4b] luminescence dyes[4c] and optical sensors[4d] owing to their conjugated features and biological activities.[5] Quinolinone and its derivatives are in another important class of heterocycles that are widely distributed in nature.[6] Dihydrofuroquinolinones and pyranoquinolinones, in particular, have found a great deal of interest since they have many applications in medicine and their biological activities were also demonstrated in literature.[7] Thiophenes, another important group of heterocyclic molecules, possess versatile applications in various fields of drug development.[8]

In this respect, here we aimed at incorporating pyranone, coumarin and quinolinone as scaffold of the target molecules in the presence of thiophene moiety. Since Mn(III)-based oxidative radical cyclization using 1,3-dicarbonyl compounds has become the most preferred way of preparing a variety of heterocycles,[9, 10] we utilized the reaction[11] in order to obtain heteroaromatic compounds containing dihydrofurans, and we found to synthesize highly functionalized dihydrofuran-fused pyranone, coumarin and quinolinone derivatives. We herein report a novel and efficient one-step synthetic protocol of biological active pyranones, dihydrofuran-fused and 3-alkenyl-substituted quinoline derivatives (**Scheme 1)**.



Scheme 1. Dihydrofuran-fused and 3-alkenyl-substituted pyranone, coumarin and quinolinone derivatives.

2. Results and discussion

2.1. Synthesis

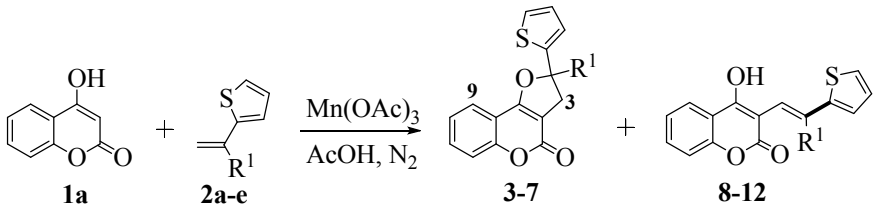
*2.1.1 Reactions of 1,1-disubstituted alkenes with **1a-e***.

We firstly examined the reaction of 4-hydroxycoumarin (**1a**) with thienyl substituted alkenes **2a-e** under different reaction conditions (**Table 1**). During the reaction at 110 °C for 5 minutes, two products were obtained. One was dihydrofuro derivatives **3-7**, and the other was 3-alkenyl-substituted compounds **8-12** (**Table 1**).

The IR spectra of compounds **3-7** showed a characteristic strong carbonyl absorption at 1720 cm^{-1}. The chemical shifts of the carbonyl groups were found at 160-161 ppm assigned to lactone carbonyl, which demonstrated that isolated compounds were angular. In addition, **H-9** proton of the angular dihydrofurocoumarin in the ^1H NMR spectrum resonated at 7.7 ppm (dd), while in the linear 2,3-dihydro-*4H*-furo[2,3-b]chromen-4-one, it is **H-5** proton appeared at 8.25 ppm (dd or d) .[12a] Besides, it was determined that **H-9** and **H-3** protons correlated with **C9a** carbon, and **H-3** protons weakly interacted with **C4** ester carbonyl in the HMBC experiment.

In the reactions, 4-hydroxy-3-alkenylcoumarins **8-12** were unexpectedly obtained in the form of E/Z isomer mixture (**Table 1)**. The existence of hydroxyl and alkenic protons in the ^1H NMR spectrum, supported the structure. Besides, in the ^1H NMR spectra of compounds **3-7**, **H-3** methylene protons showed a diastereotopic feature (^2J = 15.2-15.6 Hz as a d). These protons were not observed in the spectra of compounds **8-12.** In the reaction performed using manganese(III) acetate, it was found that more alkenyl-substituted compounds such as **8-12** were produced by increasing the temperature and prolonging the duration of the reaction. Regarding the reactions performed in acetic acid for 24 h, dihydrofurocoumarins **3-7** were formed in lower yields (Entries 7, 14) or not isolated (Entries 11, 19) and alkene derivatives **8-12** were preferentially produced.

Table 1. Reaction of 4-hydroxycoumarin (**1a**) with 1,1-disubstituted alkenes **2a-e**.[a]

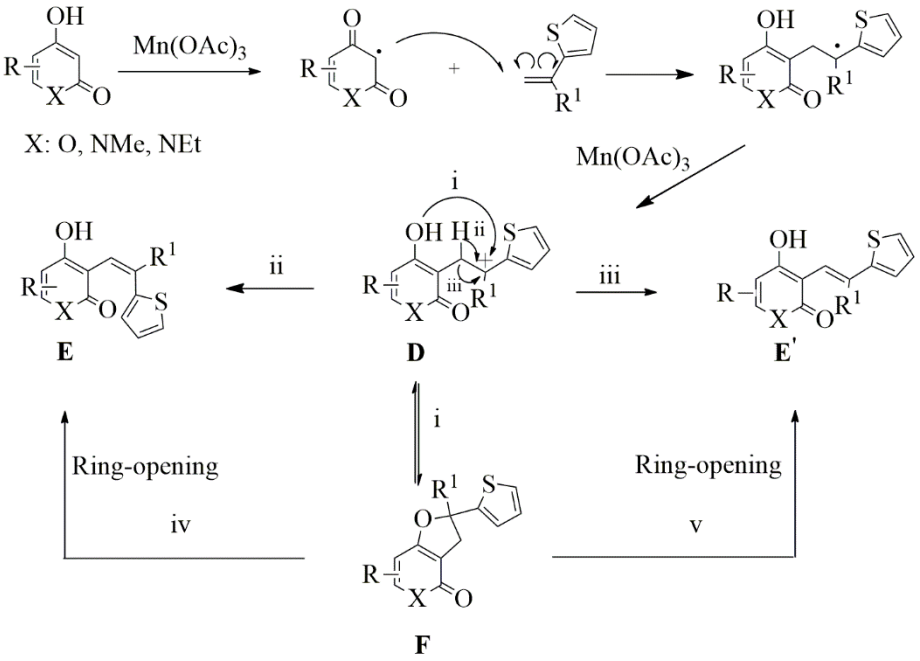


R^1: Ph (**2a**), 4-Me-C_6H_4 (**2b**), 4-F-C_6H_4 (**2c**), Me (**2d**), 2-Thienyl (**2e**)

Entry	Alkene	Temp. (°C)	Time (min.)	**3-7** (%)[b]	**8-12** (%)[b]	(**E/Z**)[c]
1	**2a**	80	1	**3** (93)	----	----
2	**2a**	80	5	**3** (89)	----	----
3	**2a**	80	10	**3** (76)	**8** (8)	1:1.70
4	**2a**	80	60	**3** (62)	**8** (23)	1:1.70
5	**2a**	70	5	**3** (86)	----	----
6	**2a**	70	60	**3** (63)	**8** (15)	1:1.70
7	**2a**	70	1440	**3** (3)	**8** (67)	1:1.70
8	**2a**	110	5	**3** (63)	**8** (27)	1:1.70
9	**2b**	80	1	**4** (94)	---	----
10	**2b**	80	5	**4** (77)	**9** (16)	1:4.25
11	**2b**	70	1440	---	**9** (68)	1:4.25
12	**2c**	80	1	**5** (97)	----	----
13	**2c**	60-70	30	**5** (68)	**10** (16)	1:1.5
14	**2c**	70	1440	**5** (9)	**10** (71)	1:1.5
15	**2d**	80	1	**6** (87)	----	----
16	**2d**	110	5	**6** (85)	**11** (10)	----
17	**2d**	70	1440	**6** (32)	**11** (14)	----
18	**2e**	80	1	**7** (57)	**12** (28)	----
19	**2e**	70	1440	----	**12** (79)	----

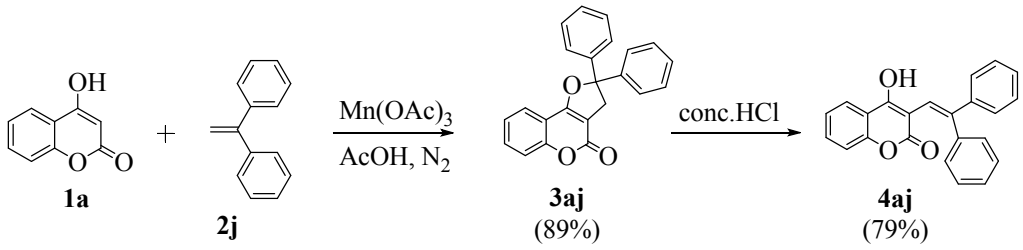
[a] All the reactions were carried out in a 1 : 2 : 3 molar ratio of alkene **2**, 4-hydroxycoumarin (**1a**) and $Mn(OAc)_3$ in AcOH.
[b] Isolated yield based on the alkene **2**.
[c] E:Z ratio determined by ^1H NMR spectrum.

This situation shows that alkenyl-substitue coumarin **8** should be formed by the ring-opening reaction of dihydrofurocoumarin **3** under acidic condition (vi and v ways). The proposed reaction mechanism for the formation of alkenyl substituted compounds **E** and **E'** is shown in **Scheme 2**. As it can be seen at the mechanism, the alkenyl-substituted compounds **E** and **E'** could be formed by two different ways. The first way would be the elimination of a proton from the **D** intermediate; secondly, after it would be formed dihydrofuran **F**, transforms into an alkene **E** and **E'** with the opening of the furan ring followed by deprotonation.



Scheme 2. The proposed mechanism for the formation of alkenyl-substituted compounds.

In literature, alkenyl-substituted products were not obtained in the reactions of 4-hydroxycoumarin (**1a)** with non-heteroaromatic alkenes.[11j-k] At the reactions that we practiced, it is thought that thiophene group would be effective in the formation of alkenyl-substituted products. With the intention of comparison, the reaction was practiced using 1,1-diphenylethene (**2j**) even in the high temperature, only dihydrofurocoumarin (**3aj**) was produced[11k] and alkenyl-substituted coumarin **4aj** was not obtained in the reaction. It was synthesized only when the obtained **3aj** was treated with the concentrated HCl (**Scheme 3**).



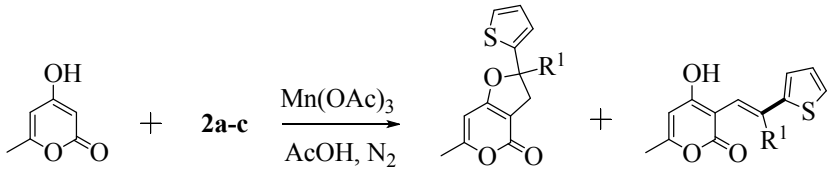
Scheme 3. Reaction of 4-hydroxycoumarin (**1a**) with **2j**.

With addition of thiophene ring to the structure, the products **8**, **11** and **12** were produced in acetic acid and effective in the yields of alkenyl-substituted compounds. This situation has the following effects; 1. Opening of the ring could occur by the electron pair over the sulfur atom at the thiophene ring and the electron pair over the oxygen at the furan ring pushing each other; 2. The enol hydrogens **8-12** and the sulfur atom at the thiophene ring could interact and constitute a more stable structure; 3. While a stronger acid was needed for the formation of **4aj**, the products **8-12,** they should be formed under the acetic

acid conditions. This might result from the redundant density of electron over the oxygen at the furan ring of **3-7**.

The reaction of 4-hydroxy-6-methyl-2*H*-pyran-2-one (**1b)** with **2a-c** gave dihydrofuropyrans **13-15** and alkenyl substituted pyrans **16-18** (**Table 2**). The ester carbonyl groups were observed at 1730 cm^{-1} in the IR spectra, and they were resonated at 160-165 ppm in ^{13}C NMR spectra, so it was determined that the dihydrofuropyrans **13-15** were the angular products. The alkenyl substituted pyrans **16-18** were obtained as an E/Z isomeric mixture. Existence of hydroxyl and alkene protons in compounds **16-18** was found by the help of ^{1}H NMR, COSY, HSQC and HMBC spectra. It was determined that **C-4** to which oxygen atom was bounded resonates at 166 ppm, **C-2** at 163 ppm and **C-6** resonates at 161 ppm in the analysis of ^{13}C NMR spectra.

Table 2. Reaction of 4-hydroxy-6-methyl-2*H*-pyran-2-one (**1b**) with **2a-c.**[a]



1b **13-15** **16-18**

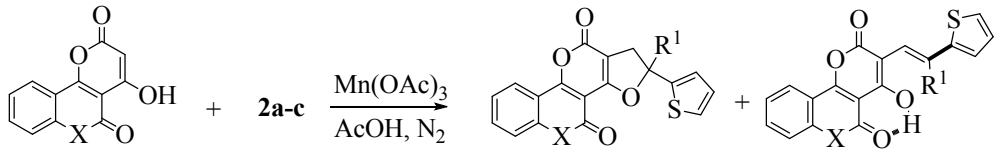
Entry	**2a-c**	Temp. °C	Time (min.)	**13-15** (%)[b]	**16-18** (%)[b]	**(E:Z)**[c]
1	**2a**	80	1	**13** (93)	---	---
2	**2a**	70	1440	**13** (28)	**16** (42)	1:1.25
3	**2a**	110	5	**13** (78)	**16** (15)	1:1.25
4	**2a**	110	10	**13** (48)	**16** (41)	1:1.25
5	**2b**	80	1	**14** (94)	---	---
6	**2b**	80	5	**14** (78)	---	---
7	**2b**	70	1440	**14** (6)	**17** (62)	1:2
8	**2c**	80	1	**15** (95)	---	---
9	**2c**	80	5	**15** (86)	---	---
10	**2c**	70	1440	**15** (17)	**18** (67)	1:1.5

[a] All the reactions were carried out in a 1 : 2 : 3 molar ratio of alkene **2**, **1b** and $Mn(OAc)_3$ in AcOH.
[b]Isolated yield based on the alkenes **2**.
[c] E/Z ratio determined by ^{1}H NMR spectrum.

As it is seen in **Table 2**, in the reactions that were practiced at 80 °C in 1 minute, the dihydrofuropyrans **13-15** were produced in high yields, while alkenyl-substituted pyrans **16-18** were obtained in high temperatures and long periods of reaction times. Even in the reactions that lasted for 24 hours, dihydrofuropyrans **13-15** were isolated.

The cyclization reactions of 4-hydroxy-2*H,5H*-pyrano[3,2-*c*]chromen-2,5-dione (**1c)** and 6-ethyl-4-hydroxy-2*H*-pyrano[3,2-*c*]quinoline-2,5-dione (**1d)** with **2a-c** resulted in the synthesis of both dihydrofurans **19-24** and alkenes **25-30** (**Table 3**). The reactions were monitored by TLC and it was determined that the alkenes **25-30** started to form after 2 minutes. Besides, in the reactions carried out at 110 °C (Entry 2 and 9), the alkenes **25** and **28** were obtained with a higher yield than the dihydrofurans **19** and **22**. The alkenyl-substituted pyranocoumarins **25-27** and pyranoquinolinones **28-30** were also isolated in E/Z isomeric mixtures.

Table 3. Reaction of **1c**, **d** with **2a-c.**



X: O (**1c**)
X: N-Et (**1d**)

X: O **19-21**
X: N-Et **22-24**

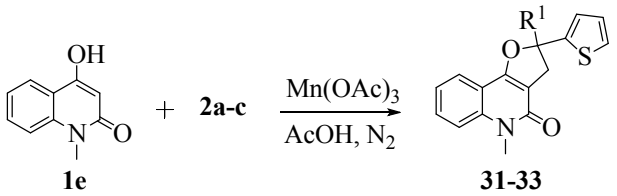
X: O **25-27**
X: N-Et **28-30**

Entry	**1c-d**	**2a-c**	Temp. (°C)	Time (min.)	**19-24** (%)[b]	**25-30** (%)[b]	**(E:Z)**[c]
1	**1c**	**2a**	80	1	**19** (51)	---	---
2	**1c**	**2a**	110	5	**19** (14)	**25** (42)	1:4
3	**1c**	**2a**	70	1440	**---**	**25** (53)	1:4
4	**1c**	**2b**	80	1	**20** (55)	---	---
5	**1c**	**2b**	70	1440	----	**26** (51)	1:3.4
6	**1c**	**2c**	80	1	**21** (62)	---	---
7	**1c**	**2c**	70	1440	----	**27** (63)	1:2
8	**1d**	**2a**	80	1	**22** (36)	---	---
9	**1d**	**2a**	110	5	**22** (22)	**28** (36)	1:2.4
10	**1d**	**2a**	70	1440	---	**28** (56)	1:2.4
11	**1d**	**2b**	80	1	**23** (38)	**29** (5)	1:8
12	**1d**	**2b**	70	1440	---	**29** (46)	1:8
13	**1d**	**2c**	80	1	**24** (39)	**30** (13)	1:3.3
14	**1d**	**2c**	70	1440	---	**30** (52)	1:3.3

[a]All the reactions were carried out in a 1 : 2 : 3 molar ratio of alkenes **2,** pyranocoumarin **1c** or pyranoquinolinone **1d** and $Mn(OAc)_3$ in AcOH.
[b]Isolated yield based on the alkenes **2**.
[c] E/Z ratio determined by ^1H NMR spectrum.

The last cyclization was examined using 1,1-disubstituted alkenes **2a-c** and 4-hydroxy-1-methyl-quinoline-2-one (**1e**). As a result, only angular dihydrofuroquinolinones **31-33** were produced (**Table 4**).

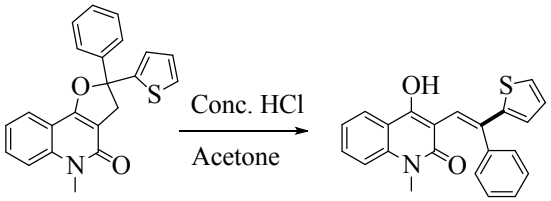
Table 4. Reaction of **1e** with **2a-c**.[a]



Entry	Alkene	Temp., °C	Time, min.	**31-33** (%)[b]
1	**2a**	60	5	**31** (81)
2	**2a**	60	1440	**31** (69)
3	**2a**	80	1	**31** (75)
4	**2a**	80	5	**31** (91)
5	**2a**	80	60	**31** (89)
6	**2a**	80	360	**31** (83)
7	**2a**	110	5	**31** (73)
8	**2b**	80	1	**32** (68)
9	**2b**	80	5	**32** (94)
10	**2c**	80	1	**33** (89)
11	**2c**	80	5	**33** (96)

[a]All the reactions were carried out in a 1 : 2 : 3 molar ratio of alkenes **2**, quinolinone **1e** and $Mn(OAc)_3$ in AcOH.
[b]Isolated yield based on the alkenes **2**.

Both angular and linear dihydrofuroquinolinones were synthesized from the reactions with non-heteroaromatic alkenes.[7b] Theoretical calculations have shown that the angular dihydrofuroquinolinones were thermodynamically stable, and linear dihydrofuroquinolinones were kinetically favored products. Although the present were examined at different temperatures and in different durations, no linear products were observed neither in short durations nor at low temperatures. This situation shows that the cyclization occurs regioselectively. Meanwhile, alkenyl substituted products were not observed. However, dihydrofuroquinolinone **31** could be converted into the corresponding vinyl-quinolinone **34** by treatment of concentrated HCl (**Scheme 4**).



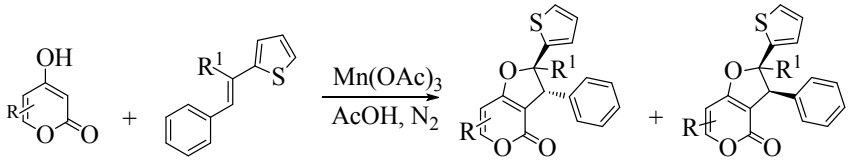
31 **34** (65%)

Scheme 4. Ring-opening reaction of dihydrofuroquinolinone **31**.

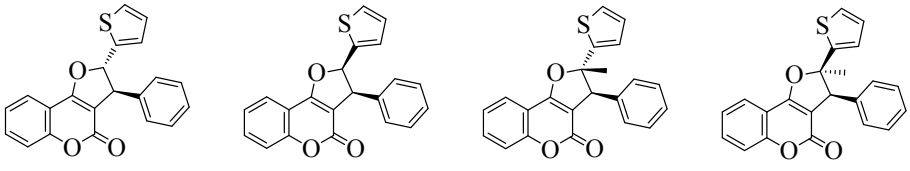
*2.1.2 Reactions of 1,2-disubstituted **2f** and 1,1,2-trisubstituted alkenes **2g** with **1a-c** and formation of dihydrofuran as a cis-trans isomer*.

When the reactions of 1,2-disubstituted **2f** and 1,1,2-trisubstituted alkenes **2g** with 4-hydroxycoumarin (**1a**) was carried out in the presence of manganese(III) acetate, two different dihydrofurocoumarins were isolated (**Table 5**). In order to characterize the structures, the IR, ^{1}H-NMR and ^{13}C-NMR spectra, HSQC and HMBC spectra were taken and it was deduced that the compounds **35** and **36** were *cis* and *trans* isomer. In the ^{1}H-NMR spectrum, the coupling constants of **H-2** and **H-3** protons were $^{3}J_{H\text{-}H}$ = 6.0 Hz in **35** and $^{3}J_{H\text{-}H}$= 9.2 Hz in **36**. By comparing with the data in the literature,[12b,c] it was determined that **35** and **36** should be "trans" and "*cis*" isomers, respectively (**Table 5).**

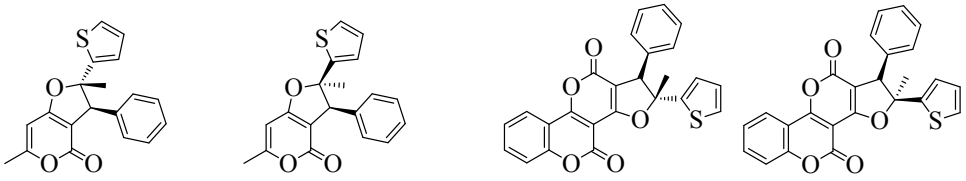
Table 5. Reactions of **1a-c** with **2f, g.**[a]



1a-c R^1: H (**2f**)
R^1: Me (**2g**)



35 (31%) **36** (8%) **37** (61%) **38** (12%)



39 (49%) **40** (27%) **41** (22%) **42** (9%)

[a] All the reactions were carried out in a 1 : 2 : 3 molar ratio of alkene **2**, **1a-c** and $Mn(OAc)_3$ in AcOH at 80 °C, 5 minutes.
[b] Isolated yield based on the alkene **2**.

When HMBC experiments of the dihydrofurocoumarins **35** and **36** were performed, it was found out that **C-2** carbon interacted with thienyl **H-3** proton and **C-3** carbon interacted with ortho protons over phenyl ring. Regarding this, it was found out that in both compounds, thienyl group should be bound to **C-2** carbon and phenyl group should be bound to **C-3** carbon.

From the reaction of **2g** with **1a-c**, two different dihydrofurans *cis* and *trans* isomer **37-42** were also produced (**Table 5**). The structure of **37** was confirmed by X-ray crystallography (**Fig. 1**). [13] According to this analysis, it was determined that phenyl and thienyl groups were in *trans* position as regards to each other.

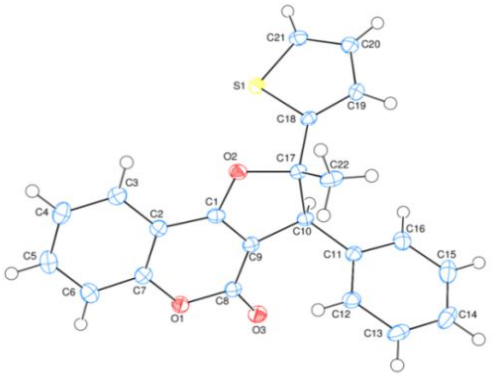
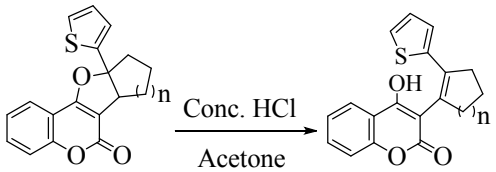


Fig. 1. The molecular entities of compound **37**, showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

*2.1.3 Reactions of cyclic alkenes **2h, i** with **1a, b** and **1e***

Finally, only dihydrofurans **43-48** were obtained from the reactions of **1a**, **b** and **1e** with cyclic alkenes **2h**, **i**. With the purpose of monitoring the formation of alkenyl substituted compounds, various experiments were carried out at high temperatures and in long durations (**Table 6**).

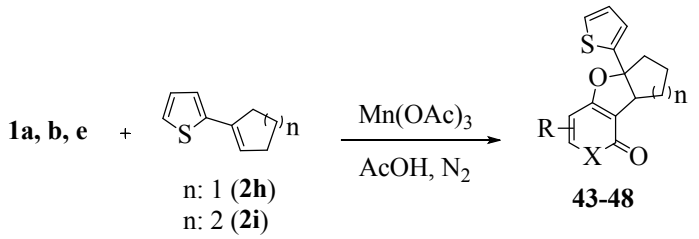
Unlike the reactions that were practiced with alkenes **2a-c**, alkenyl substituted compounds did not produce. However, the products **43** and **44** could be converted into **49** and **50** by treatment of concentrated HCl in 65% and 66% yields, respectively, as a single isomer (**Scheme 5**).

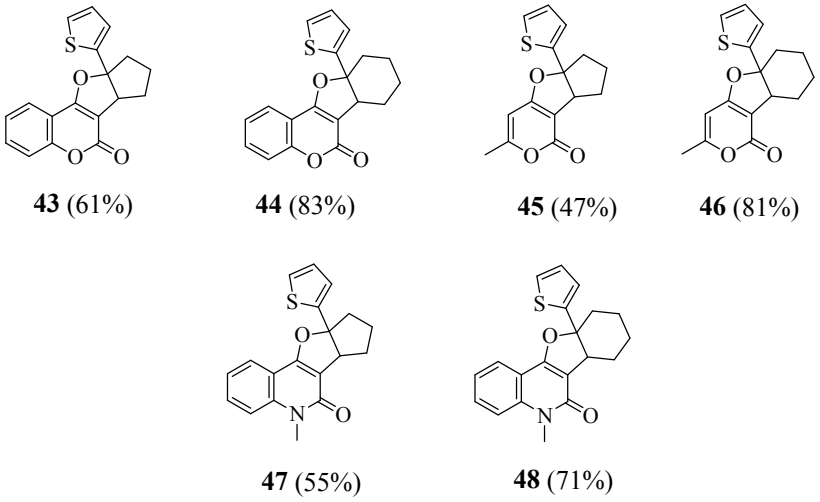


n: 1 (**43**) n: 1 (**49**) 65%
n: 2 (**44**) n: 2 (**50**) 66%

Scheme 5. Ring opening reaction of compounds **49** and **50**

Table 6. Reactions of **1a, b, e** with **2h, i**.[a]





43 (61%) **44** (83%) **45** (47%) **46** (81%)

47 (55%) **48** (71%)

[a] All the reactions were carried out in a 1 : 2 : 3 molar ratio of alkenes **2h, i**, pyranones **1a, b, e** and $Mn(OAc)_3$ in AcOH at 80 °C, 5 minutes.
[b] Isolated yield based on the alkene **2**.

2.2 Antimicrobial activity study

When the literature studies were examined, it could be clearly seen that quinolone and coumarin derivatives had antimicrobial activities. Moreover, quinolones are among the largest antimicrobial classes.[14] Quinolones are synthetic substances obtained by chemical routes different from many antibiotics obtained from living microorganisms. In this study, antimicrobial effects of some quinolone and coumarin derivatives against some gram positive and gram negative bacterial strains were determined by disk diffusion and minimum inhibitory concentration (MIC) method.[10g]

According to the results of the disk diffusion experiment in **Table 7**, the 4-methylphenylquinolinone **32** was more effective than the phenyl- **31** and 4-fluorophenyl-quinolinone **33**. Besides, the compound **3aj** showed activity against *B. licheniformis* bacteria only. In the compounds **31** and **32**, the degree of inhibition caused by the presence of nitrogen and oxygen groups also varies. It is noticed that the utilized compounds are more effective than commonly used antibiotics such as penicillin, tetracycline, ampicillin, gentamicin compared to the data in **Table 8**.

The minimum inhibitory concentrations of the compounds were studied at concentration ranges from 125 to 2000 µg/mL and the results are given in **Table 9**. It appears that the compound **32** was effective even at the concentration of 125 µg/mL on B1-coded bacteria. As a consequence, it should be noted that the compound **32** could be evaluated as an active ingredient for antibiotics.

Table 7. Zone diameters (mm) of the compounds against bacteria.

Bacteria	**3**	**4**	**5**	**3aj**	**31**	**32**	**33**
E. coli ATCC 25922	---	10	---	---	8	10	11
M. luteus M3	---	---	---	---	---	7	8
B.cereus B9	---	8	8	---	10	9	8
B.licheniformis M30	10	---	10	8	9	15, 5	11
S. Coccus	9	---	8	---	---	7	---
B. subtilis B1	---	---	10	---	---	9	---
P. aeruginosa P7	---	---	---	---	---	---	---

E.Coli: *Escherichia coli ATCC 25922*; **M3**: *Micrococcs luteus M3*; **B9**: *Bacillus cereus B9*; **M30**: *Bacillus* licheniformis M30; **S. Coccus**: *Staphylococcus aureus ATCC 6538*; **B1**: *Bacillus subtilis B1*; **P7**: *Pseudomonas aeruginosa P7*

Table 8. Zone diameters (mm) of antibiotics against bacteria[11g].

	Peniciline	**Chloram phenicol**	**Tetracycline**	**Ampicillin**	**Gentamicin**
E. coli	19	---	---	---	---
M. luteus	31	---	9	28	---
B.cereus B9	16	31	16	---	---
B.licheniformis	16	17	23	18	20
S. Coccus	---	---	---	9	---
B. subtilis	---	---	---	15	---
P. aeruginosa	---	---	---	---	16

Table 9. MIC results (μg/mL).

Bacteria	3	4	5	3aj	31	32	33
ATCC 25922	---	1000	---	---	2000	1000	2000
M3	---	---	---	---	---	2000	2000
B9	---	1000	500	---	2000	1000	2000
M30	2000	---	1000	1000	1000	500	1000
ATCC 6538	1000	---	1000	---	---	2000	---
B1	---	---	500	---	---	125	---
P7	---	---	---	---	---	---	---

3. Conclusion

As a result, the Mn(III)-based oxidation of 4-hydroxycoumarin (**1a)**, 4-hydroxy-6-methyl-2*H*-pyran-2-one (**1b**), 4-hydroxy-2*H,*5*H*-pyrano[3,2-*c*]chromen-2,5-dione (**1c**), 6-ethyl-4-hydroxy-2*H*-pyrano[3,2-*c*]quinoline-2,5-dione (**1d**) and 4-hydroxy-1-methyl-quinoline-2-one (**1e**) with thienyl-substituted alkenes **2a-i** were examined. While the radical cyclizations of 1,1-disubstituted alkenes with **1a-d** gave the dihydrofuran derivatives accompanied by 3-alkenyl-substituted structures, the reactions of **1e** gave the dihydrofuran derivatives as a sole products. The reactions of 1,2-disubstituted **2f** and 1,1,2-trisubstituted alkenes **2g** with **1a-c** was carried out, two different dihydrofuran derivatives *cis* and *trans* isomer were isolated. The structures of this compounds identified with spectroscopic method and X-ray crystallography. A similar reactions were conducted using cyclic thieny-substituted alkenes **2h-i** produced dihydrofuran derivatives. The mechanisms for the formations of the products were suggested. Apart from that, the antibacterial activities of the some synthesized compounds have been investigated and good results were obtained.

4. Experimental

4.1. Physical measurements

Melting points were determined on a Gallencamp capillary melting point instrument. IR spectra (KBr disc, $CHCl_3$) were obtained with a Matson 1000 FT-IR in the range of 400-4000 cm^{-1} with 4 cm^{-1} resolution. ^1H NMR (400 MHz), and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker Avance DPX-400 MHz and Varian Mercury-400 High performance Digital FT-NMR spectrophotometers. The mass spectra were measured on a Micromass UK LC/MS (APCI, 100-150 eV), and a Shimadzu GC-17A/GC-MS-QP5000 (EIMS, 70 eV) spectrophotometers.Elemental analyses were performed on a Leco 932 CHNS-O instrument. Crystallographic data were recorded on a Bruker Kappa APEXII CCD area-detector diffractometer using Mo K_α radiation (λ= 0.71073 Å) at T= 296(2) K. Absorption correction by multi-scan was applied[18]. Structure was solved by direct methods and refined by full-matrix least squares against F^2 using all data[19]. TLC was performed on Merck aluminium-packed silica gel plates. Purification of products was performed by column chromatography on silica gel (Merck silica gel 60, 40-60 μm) or preparative TLC on silica gel of Merck ($PF_{254\text{-}366\ nm}$).

4.2. *Materials used for syntheses*

Manganese(II) acetate tetrahydrate, $Mn(OAc)_2 \cdot 4H_2O$, was purchased from Wako Pure Chemical Ind., Ltd. Manganese(III) acetatedihydrate, $Mn(OAc)_3 \cdot 2H_2O$, was prepared according to the modified method described in theliterature.[15] All solvents, 4-hydroxycoumarin, 4-hydroxy-6-methyl-2*H*-pyran-2-one, 4-hydroxy-1-methylquinoline-2-one and other reagents were purchased from Merck. 4-Hydroxy-2*H,*5*H*-pyrano[3,2-*c*]chromen-2,5-dione (**1c**) and 6-ethyl-4-hydroxy-2*H*-pyrano[3, 2-*c*]quinoline-2,5-dione (**1d**) were prepared according to the methods reported in the literature.[16] The alkenes **2a-c**, **2e** and **2h-i** were prepared by dehydration from the carbinole prepared by Grignard reaction of aryl magnesium bromide and suitable carbonyl compounds.[17] The other alkenes **2d**,[11a] and **2f** and **2g**[11d] were prepared by Wittig reaction of suitable carbonyl compounds with phosphonium ylides.

4.3. *Syntheses*

4.3.1. General procedure for manganese(III) acetate-based oxidative cyclization

A solution of $Mn(OAc)_3 \cdot 2H_2O$ in glacial AcOH was heated under N_2 at 80° C until it dissolved. Then, a solution of **1** and alkene **2** in 5 mL glacial AcOH was added to the mixture. The reaction was monitored by TLC. When the reaction was completed, water (10 mL) was added to the mixture and extracted with $CHCl_3$ (3×20 mL). The combined organic layers were neutralized with saturated $NaHCO_3$ aqueous solution, washed with water, dried over anhydrous Na_2SO_4 and evaporated. The products were purified by column chromatography on silica gel or preparative TLC on silica gel, eluating with hexane:AcOEt mixtures.

4.3.1.1. 2-Phenyl-2-thenyl-2,3-dihydro-4H-furo[3,2-c]chromen-4-one (**3**)

Colerless solid; mp: 154-155 °C; **IR** ($\nu_{max,}$ KBr): 3104, 3093, 3069, 2974, 1716 (C=O), 1647 (C=C), 1605, 1497, 1405, 1029 (C-O-C), 729 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.82 (1H, dd, *J* = 8, 1.2 Hz, ArH), 7.59 (1H, td, *J* = 8, 1.6, ArH), 7.51 (2H, dd, *J* = 8, 1.6, ArH), 7.4-7.3 (6H, m, ArH), 7.00 (1H, dd, *J* = 3.6, 1.2 Hz, ArH), 6.97 (1H, dd, *J* = 4.8, 4 Hz, ArH), 4.05 (1H, d, *J* = 15.6 Hz, -CH_2), 3.81 (1H, d, *J* = 15.2 Hz, -CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 43.23 (C3), 95.19 (C2), 101.78 (C3a), 112.72, 117.29, 123.10, 124.32, 125.58 (CH*2), 126.69, 127.07, 127.09, 128.72, 128.81 (CH*2), 132.81, 143.60 (C ipso), 147.67 (C ipso), 155.36 (C5a), 160.43 (C4), 164.97 (C9b); **LC/MS** m/z (%): 346.99 (MH^+, 100); **Anal. Calcd. for** $C_{21}H_{14}O_3S$: C 72.81, H 4.07, S 9.2. **Found**: C 72.02, H 4.27, S 8.70.

*4.3.1.2. 2-(4-Methylphenyl)-2-(2-thenyl)-2,3-dihydro-4H-furo[3,2-c]chromen-4-one (**4**)*

Light pink solid; mp: 135-136°C; **IR** ($\nu_{max,}$ KBr): 3025, 1713 (C=O), 1647 (C=C), 1406, 1025 (C-O-C), 707 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.81 (1H, dd, *J* = 7.6, 1.6 Hz, ArH), 7.58 (1H, td, *J* = 7.8, 1.6 Hz, ArH), 7.39 (2H, d, *J* = 8.4 Hz, ArH), 7.39-7.37 (1H, m, ArH), 7.33-7.30 (2H, m, ArH), 7.2 (2H, d, *J* = 8.8 Hz, ArH), 7.00 (1H, dd, *J* = 3.6, 1.2 Hz, ArH), 6.96 (1H, dd, *J* = 5.2, 3.6 Hz, ArH), 4.00 (1H, d, *J* = 15.6 Hz, -CH_2), 3.80 (1H, d, *J* = 15.2 Hz, -CH_2), 2.36 (3H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 21.35 (Me), 43.18 (C3), 95.29 (C2), 101.80 (C3a), 112.76, 117.27, 123.11, 124.28, 125.57 (CH*2), 126.56, 126.98, 127.04, 129.45 (CH*2), 132.76, 138.64 (C ipso), 140.66 (C ipso), 147.88 (C ipso),

155.35 (C5a), 160.48 (C4), 165.00 (C9b); **LC/MS** m/z (%): 361.42 (MH^+, 100); **Anal. Calcd. for** $C_{22}H_{16}O_3S$: C 73.31, H 4.47, S 8.90. **Found**.: C 73.04, H 4.51, S 9.06.

*4.3.1.3. 2-(4-Fluorphenyl)-2-(2-thenyl)-2,3-dihydro-4H-furo[3,2-c]chromen-4-one (**5**)*

Colorless solid; mp: 115-116 °C; **IR** ($\nu_{max,}$ KBr): 3119, 3072, 2953, 1712 (C=O), 1644 (C=C), 1028 (C-O-C), 722 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$), δ (ppm): -113.65; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.80 (1H, dd, *J* = 8.0, 1.6 Hz, ArH); 7.59 (1H, td, *J* = 7.8, 1.2 Hz, ArH), 7.49 (2H, m, ArH), 7.40 (1H, d, *J* = 8.4, ArH), 7.34 (1H, dd, *J* = 4.8, 1.2 Hz, ArH), 7.31 (1H, d, *J* = 7.2 Hz, ArH), 7.08 (2H, td, *J* = 8.4, 2.0 Hz, ArH), 7.00 (1H, dd, *J* = 3.6, 1.2 Hz, ArH), 6.98 (1H, dd, *J* = 5.2, 3.6 Hz, ArH), 4.03 (1H, d, *J* = 15.2 Hz, $-CH_2$), 3.76 (1H, d, *J* = 15.2 Hz, $-CH_2$); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 43.29 (C3), 94.79 (C2), 101.72, 112.64, 115.7 (CH*2, d, ^2J = 23.1 Hz), 117.31, 123.03, 124.34, 126.67, 127.13, 127.21, 127.60(CH*2, d, ^3J = 8.4 Hz), 132.87, 139.50 (C, d, ^4J = 3.1 Hz), 147.44, 155.38 (C5a), 160.27 (C4), 162.8 (C, d, ^1J = 246.3 Hz), 164.81 (C9b); **LC/MS**, (ESI, m/z) : 365.37 (MH^+, 100); **Anal. Calcd. For** $C_{21}H_{13}FO_3S$: C 69.22, H 3.60, S 8.80. **Found**: C 70.01, H 3.81, S 8.97.

*4.3.1.4. 2-Methyl-2-(2-thenyl)-2,3-dihydro-4H-furo[3,2-c]chromen-4-one (**6**)*[2e]

Light yellow solid; mp: 79-80 °C; **IR** ($\nu_{max,}$ KBr): 3105, 1714 (C= O), 1641 (C= C), 1604, 1280, 1026 (C-O-C), 750 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.69 (1H, dd, *J* = 7.6; 1.6, ArH), 7.56 (1H, td, *J* = 8.0; 1.6 Hz, ArH), 7.38 (1H, d, *J* = 9.2, ArH), 7.30 (1H, dd, *J* = 5.2; 1.2, ArH), 7.27 (1H, dd, *J* = 7.6, 0.8 Hz, ArH), 7.12 (1H, dd, *J* = 3.6; 1.2, ArH), 7.00 (1H, dd, *J* = 5.2; 3.6 Hz, ArH), 3.57 (1H, d, *J* = 15.6 Hz, $-CH_2$), 3.34 (1H, d, *J* = 15.2 Hz, $-CH_2$), 2.01 (3H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 29.29 (CH_3), 42.11 (C3), 92.57 (C2), 101.49 (C3a), 112.84, 117.19, 123.11, 124.17, 124.27, 125.94, 127.23, 132.65, 147.84 (C-ipso), 155.28 (C5a), 160.69 (C4), 165.09 (C9b); **LC/MS** (ESI, m/z): 285.70 (MH^+, 100); **Anal. Calcd. For** $C_{16}H_{12}O_3S$: C 67.59, H 4.25, S 11.28. **Found**: C 67.41, H 3.98, S 11.33.

*4.3.1.5. 2, 2-Di(2-thenyl)-2,3-dihydro-4H-furo[3,2-c]chromen-4-one (**7**)*

Light purple solid; mp: 121-122 °C; **IR** ($\nu_{max,}$ KBr): 3086, 3003, 1720 (C=O), 1649 (C=C), 1406, 1029 (C-O-C), 748 cm^{-1}; **^{1}H NMR** ($CDCl_3$), δ (ppm):7.77 (1H, dd, *J* = 7.6, 1.6 Hz, ArH), 7.58 (1H, td, *J* = 7.6, 1.6 Hz, ArH), 7.38 (1H, dd, *J* = 8.4, 0.8 Hz, ArH), 7.35 (2H, dd, *J* = 4.8, 1.2, ArH), 7.31 (1H, td, *J* = 7.6, 1.2 Hz, ArH), 7.12 (2H, dd, *J* = 3.6, 1.2 Hz, ArH), 7.01 (2H, dd, *J* = 5.2, 4.0 Hz, ArH), 3.96 (2H, s, H3);

^{13}C NMR (100 MHz, $CDCl_3$), *δ* (ppm): 44.39 (C3), 93.25 (C2), 101.71 (C3a), 112.66, 117.26, 123.15, 124.33, 126.37 (CH*2), 126.83 (CH*2), 127.18 (CH*2), 132.85, 146.86 (C*2), 155.36 (C5a), 160.29 (C4), 164.66 (C9b); **LC/MS** (ESI, m/z): 353.70 (MH^+, 100); **Anal. Calcd. for** $C_{19}H_{12}O_3S_2$: C 64.75, H 3.43, S 18.20. **Found**: C 64.15, H 3.56 S 17.41.

*4.3.1.6 4-Hydroxy-3-[2-phenyl-2-(2-thenyl)vinyl]-2H-chromen-2-one (**8**)*

E: *Z* ratio = 1:1.70. Pale yellow solid; mp : 193-194 °C; **IR** ($\nu_{max,}$ KBr): 3078, 3005, 2978, 1658 (C=O), 1604 (C=C), 1541, 1083 (C-O-C), 700 cm^{-1}; **^{1}H NMR** (400 MHz, DMSO-d_6), *δ* (ppm): 7.91 (1H, dd, *J* = 8.0, 1.2 Hz, ArH) [7.80 (1H, dd, *J* = 8.8, 1.6 Hz, ArH)], 7.63 (1H, td, *J* = 7.8, 1.2 Hz, ArH) [7.56 (1H, td, *J* = 7.8, 1.6 Hz, ArH)], 7.46 (2H, dd, *J* = 4.8, 1.2 Hz, ArH) [7.53 (2H, dd, *J* = 5.2, 1.2 Hz, ArH)], 7.37 (1H, dd, *J* = 7.6 Hz, ArH) [7.41 (1H, dd, *J* = 7.6, 1.2 Hz, ArH)], 7.30-7.22 (5H+5H, m, ArH), 7.06 (1H, dd, *J* = 5.2, 3.6 Hz, ArH) [6.96 (1H, dd, *J* = 5.2, 3.6 Hz, ArH)], 6.91 (1H, dd, *J* = 3.6, 1.2 Hz, ArH) [6.83 (1H, dd, *J* = 3.6, 1.2 Hz, ArH)], 6.68 (1H, s, alkene) [6.40 (1H, s, alkene)]; **^{13}C NMR** (100 MHz, DMSO-d_6), *δ* (ppm): 103.21 (103.50), 116.59 (116.73), 116.77 (116.85), 117.03, 119.54, 124.13 (124.27), 124.56 (124.65), 126.70 (126.85), 127.27 (127.66), 128.35 (128.50), 128.61 (128.80), 129.01 (129.13), 129.40, 132.72 (132.91), 140.12 (140.21), 140.91, 141.91 (143.01), 146.70, 152.81 (153.01), 161.14 (161.20), 161.25 (161.76); **LC/MS** m/z (%): 347.14 (MH^+, 100); **Anal. Calcd. for** $C_{21}H_{14}O_3S$: C 72.81, H 4.07, S 9.2. **Found**: C 72.70, H 3.98, S 9.02.

*4.3.1.7 4-Hydroxy-3-[2-(4-methylphenyl)-2-(2-thenyl)vinyl]-2H-chromen-2-one (**9**)*

E:*Z* ratio = 1:4.25. Pale orange solid; mp: 145-146 °C; **IR** ($\nu_{max,}$ KBr): 3079**,** 2990, 1667 (C=O), 1609 (C=C), 1550, 1494, 1245, 1083 (C-O-C), 775, 700 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), *δ* (ppm): 7.62 (1H, dd, *J* = 8.0, 1.6 Hz, ArH), 7.50 (1H, td, *J* = 7.8, 1.6 Hz, ArH), 7.38-7.15 (7H+7H, m, ArH), 7.04 (1H, td) [6.97 (1H, dd, *J* = 5.2, 3.6 Hz)], 6.89 (1H, dd, *J* = 3.6, 1.2 Hz) [6.09 (1H, dd)], 6.62 (1H, s, alkene) [6.81 (1H, s, alkene)], 6.25 (1H, s, OH)[6.25 (1H, s, OH)], 2.37 (3H, s) [2.35 (3H, s)]; **^{13}C NMR** (100 MHz, $CDCl_3$), *δ* (ppm): 21.40 (21.38), 103.19 (103.48), 115.08 (115.12), 116.42 (116.53), 116.72, 118.75, 123.74 (123.84), 123.90 (124.03), 126.18, 127.18, 127.46 (127.67), 128.39 (128.58), 129.08 (128.90), 130.18 (130.06), 132.08 (132.27), 134.70, 139.00 (138.82), 139.77 (139.71), 145.68, 152.62 (152.77), 157.20 (158.03), 162.95 (162.84); **LC/MS** m/z (%): 361.43 (MH^+, 100); **Anal. Calcd. for** $C_{22}H_{16}O_3S$: C 73.31, H 4.47, S 8.90. **Found**: C 73.12, H 4.21, S 9.03.

*4.3.1.8 4-Hydroxy-3-[2-(4-fluorphenyl)-2-(2-thenyl)vinyl]-2H-chromen-2-one (**10**)*

E:*Z* ratio = 2:3. Pale orange solid; mp: 187-188 °C; **IR** ($\nu_{max,}$ KBr): 3104, 3074**,** 2990, 1667 (C=O), 1602 (C=C), 1494, 1213, 1153, 1083 (C-O-C), 747, 701 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$), δ (ppm): -85.00, -115.51; **^{1}H NMR**(400 MHz, CD_3COCD_3), δ (ppm): 7.85 (1H, dd, *J* = 7.6, 1.6 Hz, ArH) [7.77 (1H, dd, *J* = 7.6, 1.6 Hz, ArH)], 7.64 (1H, td, *J* = 8.4, 1.2 Hz, ArH) [7.58 (1H, td, *J* = 8.4, 1.2 Hz, ArH)], 7.47 (1H, d, *J* = 5.2, ArH) [7.37 (1H, i, *J* = 5.2, ArH)], 7.50 (2H, td, *J* = 7.0, 2.4 Hz, ArH) [7.40 (2H, td, *J* = 7.0, 2.0 Hz, ArH)], 7.34 (1H, d, *J* = 8.0 Hz, ArH) [7.30 (1H, d, *J* = 8.0 Hz, ArH)], 7.26 (1H, d, *J* = 7.6 Hz, ArH), 7.17 (2H, td, *J* = 8.4, 2.0 Hz, ArH) [7.07 (2H, td, *J* = 8.8, 2.0 Hz, ArH)], 7.04 (1H, dd, *J* = 4.8, 4.0 Hz, ArH) [6.98 (1H, t, *J* = 4 Hz, ArH)], 6.94 (1H, d, *J* = 4 Hz, ArH) [6.89 (1H, d, *J* = 3.2 Hz)], 6.66 (1H, s) [6.41 (1H, s, alkene)]; **^{13}C NMR** (100 MHz, CD_3COCD_3), δ (ppm): 103.10, 115.12 (CH*2, d, ^{2}J = 21.3Hz) [114.97 (CH*2, d, ^{2}J = 21.4Hz)], 115.98, 116.32 (116.28), 116.42, 118.57, 123.59 (123.79), 124.01 (124.07), 126.19, 126.71 (126.86), 127.71 (127.33), 129.42, 131.44 (CH*2, d, ^{3}J = 8.4 Hz) [130.68 (CH*2, d, ^{3}J = 8.4 Hz)], 132.25 (132.42), 141.14 (135.67), 146.19, 153.09, 160.92 (159.66), 162.65 (C, d, ^{1}J = 246.3 Hz); **LC/MS**, (ESI, m/z) : 365.14 (MH^+, 100); **Anal. Calcd. for** $C_{21}H_{13}FO_3S$: C 69.22, H 3.60, S 8.80. **Found**: C 69.03, H 3.42, S 8.67.

*4.3.1.9 (E)-4-Hydroxy-3-[2-(2-thenyl)-1-propenyl]-2H-chromen-2-one (**11**)*

Yellow solid; mp: 121-122 °C; **IR** ($\nu_{max,}$ KBr): 3079**,** 2990, 1667 (C=O), 1609 (C=C), 1550, 1494, 1245, 1083 (C-O-C), 775, 700 cm^{-1}; **^{1}H NMR** (400 MHz, DMSO-d_6), δ (ppm): 7.93 (1H, dd, *J* = 7.6, 1.6 Hz, ArH), 7.60 (1H, td, *J* = 7.6, 1.6 Hz, ArH), 7.45 (1H, dd, *J* = 5.2, 1.2 Hz, ArH), 7.36 (1H, d, *J* = 8.4 Hz, ArH), 7.34 (1H, td, *J* = 7.6, 1.2 Hz, ArH), 7.23 (1H, dd, *J* = 4.0, 1.2 Hz, ArH), 7.05 (1H, dd, *J* = 4.8, 3.6 Hz, ArH), 6.44 (1H, d, *J* = 1.2 Hz, alkene), 1.94 (3H, d, *J* = 1.2 Hz, CH_3); **^{13}C NMR** (100 MHz, DMSO-d_6), δ (ppm): 18.81, 102.81, 116.10, 116.84, 116.88, 124.28, 124.68, 124.82, 125.82, 128.43, 132.83, 135.08, 146.81, 152.92, 160.93, 161.89; **LC/MS** (ESI, m/z): 285.60 (MH^+, 100); **Anal. Calcd. for** $C_{16}H_{12}O_3S$: C 67.59, H 4.25, S 11.28. **Found**: C 67.41, H 4.19, S 11.07.

*4.3.1.10 3-[2,2-Di(2-thenylvinyl)]-4-hydroxy-2H-chromen-2-one (**12**)*

Purple solid; mp: 194-195 °C; **IR** ($\nu_{max,}$ KBr): 1668 (C=O), 1602 (C=C), 1492, 1217 (C-O-C), 715 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.70 (1H, dd, *J* = 7.6, 0.4 Hz, ArH), 7.53 (1H, td, *J* = 7.8, 1.2 Hz, ArH), 7.39 (1H, d, *J* = 4.8 Hz, ArH), 7.32-7.22 (4H, m, ArH), 7.09 (1H, dd, *J* = 4.4, 1.2 Hz, ArH), 7.07

(1H, dd, *J* = 4.4, 1.2 Hz, ArH), 7.00 (1H, td, *J* = 4.4, 0.8 Hz, ArH), 6.83 (1H, s, alkene), 6.50 (1H, s, OH) [disappeared after shaking with D_2O]; **^{13}C NMR** (100 MHz, $CDCl_3$), *δ* (ppm): 103.20, 115.30, 116.75, 118.56, 124.07, 124.29, 126.73, 127.56, 127.73, 127.91, 128.97, 130.20, 132.17, 132.59, 138.58, 145.30, 152.96, 158.53, 162.99: **LC/MS** (ESI, m/z): 353.70; **Anal. Calcd. for** $C_{19}H_{12}O_3S_2$: C 64.75, H 3.43, S 18.20. **Found**: C 64.51, H 3.56, S 18.01.

*4.3.1.11 2,2-Diphenyl-2,3-dihydro-4H-furo[3,2-c]chromen-4-one (**3aj**)[11l]*

Colorless solid; mp: 175-176 °C; **^{1}H NMR** (400 MHz, $CDCl_3$), *δ* (ppm): 7.71 (1H, d, *J* = 7.6 Hz, ArH), 7.64 (1H, t, *J* = 7.6 Hz, ArH), 7.51-7.35 (12H, m, ArH), 3.96 (2H, s, -CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$), *δ* (ppm): 41.8 (C3), 98.1 (C2), 102.4, 113, 2, 117.8, 123.5, 124.8, 126.6 (CH*2), 129.0 (CH*4), 129.4 (CH*4), 133.2, 144.5 (C*2), 156.1 (C5a), 166.1 (C9b), 161.3 (C4).

*4.3.1.12 3-(2,2-Diphenylvinyl)-4-hydroxy-2H-chromen-2-one (**4aj**)*

Colorless solid; mp: 204-205 °C; **IR** ($\nu_{max,}$ KBr): 3007, 2970, 1662 (C=O), 1600 (C=C), 1541, 1490, 1240, 1076, 754 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), *δ* (ppm): 7.61 (1H, dd, *J* = 8.0, 1.6 Hz, ArH), 7.51 (1H, td, *J* = 8.0, 1.6 Hz, ArH), 7.36-7.30 (11H, m, ArH), 7.20 (1H, d, *J* = 7.6, 0.8 Hz, ArH), 6.74 (1H, s, alkene), 6.44 (1H, s, OH); **^{13}C NMR** (100 MHz, $CDCl_3$), *δ* (ppm): 103.57, 115.03, 116.46, 118.69, 123.74, 123.97, 128.24 (CH*2), 128.37 (CH*2), 128.52, 129.31, 129.45 (CH*4), 132.14, 138.61, 141.71, 146.60, 152.68, 157.08, 163.03; **LC/MS** (ESI, m/z): 341.70 (MH^+, 100); **Anal. Calcd. for** $C_{23}H_{16}O_3$: C 81.16; H 4.74. **Found**: C 80.98, H 4.59.

*4.3.1.13 6-Methyl-2-phenyl-2-(2-thenyl)-2,3-dihydro-4H-furo[3, 2-c]pyran-4-one (**13**)*

Yellow oil; **IR** ($\nu_{max,}$ KBr): 3090, 2924, 1732 (C=O), 1643 (C=C), 1585, 1272 (C-O-C), 700 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), *δ* (ppm): 7.40-7.42 (2H, m, ArH), 7.38-7.32 (3H, m, ArH), 7.28 (1H, dd, *J* = 4.0, 2.4 Hz, ArH), 6.93 (2H, dd, *J* = 4.0, 1.2 Hz, ArH), 6.06 (1H, s, alkene), 3.87 (1H, d, *J* = 15.2 Hz, -CH_2), 3.63 (1H, d, *J* = 15.2 Hz, -CH_2), 2.25 (3H, d, *J* = 0.8 Hz, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$), *δ* (ppm): 20, 40 (CH_3), 41.85 (C3), 94.35 (C2), 95.68, 98.75, 125.26 (CH*2), 126.16, 126.61, 126.73, 128.30, 128.47 (CH*2), 143.43, 147.58, 161.57 (C4), 165.73 (C6), 169.35 (C7a); **LC/MS** (ESI, m/z): 311.11 (MH^+, 100); **Anal. Calcd. for** $C_{18}H_{14}O_3S$: C 69.66; H 4.55; S 10.33. **Found**: C 69.53, H 4.44, S 10.21.

*4.3.1.14 6-Methyl-2-(4-methylphenyl)-2-(2-thenyl)-2,3-dihydro-4H-furo[3,2-c]pyran-4-one (**14**)*

Yellow oil; **IR** ($\nu_{max,}$ KBr): 3090, 3030, 2960, 1732 (C=O), 1716, 1643 (C=C), 1585, 1272, 1172, 975, 700 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), *δ* (ppm): 7.31 (2H, d, *J* = 8.0 Hz, ArH), 7.27 (1H, td, *J* = 3.6 Hz, ArH), 7.17 (2H, d, *J* = 8 Hz, ArH), 6.92 (2H, d, *J* = 3.2 Hz, ArH), 6.04 (1H, s, alkene), 3.85 (1H, d, *J* = 15.2 Hz, $-CH_2$), 3.63 (1H, d, *J* = 15.2 Hz, $-CH_2$), 2.34 (3H, CH_3), 2.24 (3H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$), *δ* (ppm): 20.70 (CH_3), 21.34 (CH_3), 42.08 (C3), 94.69 (C2), 96.00 (C7), 99.04 (C3a), 125.52 (CH^*2), 126.36, 126.82, 126.99, 129.39 (CH^*2), 138.43, 140.74, 148.01, 161.91 (C4), 165.95 (C6), 169.65 (C7a); **LC/MS** (ESI, m/z): 325.31 (MH^+, 100); **Anal. Calcd. for** $C_{19}H_{16}O_3S$: C 70.35, H 4.97, S 9.88. **Found**: C 70.20, H 4.82, S 9.73.

*4.3.1.15 6-Methyl-2-(4-fluorphenyl)-2-(2-thenyl)-2,3-dihydro-4H-furo[3,2-c]pyran-4-one (**15**)*

Yellow oil; **IR** ($\nu_{max,}$ KBr): 3111, 3095, 2985, 1665 (C=O), 1631 (C=C), 1573, 1407, 1005 (C-O-C), 709 cm^{-1}**; ^{19}F NMR** (376 MHz, $CDCl_3$**)**, δ (ppm): -116.41; **^{1}H NMR** (400 MHz, $CDCl_3$), *δ* (ppm): 7.40 (2H, m, ArH), 7.31 (1H, dd, *J* = 5.2; 1.2 Hz, ArH), 7.05 (2H, td, *J* = 8.6; 2 Hz, ArH), 6.96-6.92 (2H, m, ArH), 6.07 (1H, s, alkene), 3.86 (1H, d, *J* = 15.2 Hz, $-CH_2$), 3.59 (1H, d, *J* = 14.8 Hz, $-CH_2$), 2.27 (3H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 20.68 (CH_3), 42.15 (C3), 94.15 (C2), 95.88 (C7), 98.91 (C3a), 115.62 (CH*2, d, ^{2}J = 23.1 Hz), 126.48, 127.06 (CH^*2), 127.51 (CH*2, d, ^{3}J = 8.4 Hz), 139.50 (C, d, ^{4}J = 3.1 Hz), 147.53 (C ipso), 162.65 (C, d, ^{1}J = 246.1 Hz), 161.75 (C4) , 166.16 (C6), 169.49 (C7a); **LC/MS** (ESI, m/z): 329.28 (MH^+, 100); **Anal. Calcd. for** $C_{18}H_{13}FO_3S$: C 65.84, H 3.99, S 9.77. **Found**: C 65.63, H 3.69, S 9.59.

*4.3.1.16 4-Hydroxy-6-methyl-3-[2-phenyl-2-(2-thenyl)vinyl]-2H-pyran-2-one (**16**)*

E:*Z* ratio = 1:1.25. Brown solid; mp: 190-191 °C; **IR** ($\nu_{max,}$ KBr): 3109 (O-H)**,** 3079, 3030, 2960, 1668 (C=O), 1643 (C=C), 1575, 1407, 1254, 709 cm^{-1}; **^{1}H NMR** (400 MHz, DMSO-d_6), *δ* (ppm): 11.33 (1H, s, OH), 7.45 (1H, dd, *J* = 5.2, 1.2 Hz, ArH), 7.30-7.26 (3H, m, ArH), 7.16 (2H, dd, *J* = 8.0, 1.6 Hz, ArH), 7.01 (1H, dd, *J* = 5.2, 3.6 Hz, ArH), 6.82 (1H, dd, *J* = 3.2, 1.2 Hz, ArH), 6.50 (1H, s, alkene), 5.86 (1H, d, *J* = 0.8 Hz, alkene), 2.11 (3H, CH_3); **^{13}C NMR** (100 MHz, DMSO-d_6), *δ* (ppm): 19.96, 99.69, 100.47, 117.90, 126.01, 126.19, 128.09, 128.28, 128.49 (CH^*2), 129.36 (CH^*2), 138.36, 141.04, 147.42, 161.89, 163.39, 166.02; **LC/MS** (ESI, m/z): 311.32 (MH, 100), 333.12 (M^++ Na); **Anal. Calcd. for** $C_{18}H_{14}O_3S$: C 69.66; H 4.55; S 10.33. **Found**: C 69.49, H 4.28, S 10.57.

*4.3.1.17 4-Hydroxy-6-methyl-3-[2-(4-methylphenyl)-2-(2-thenyl)vinyl]2H-pyran-2-one (**17**)*

E:*Z* ratio = 1:2. Brown solid; mp: 163-164 °C; **IR** ($\nu_{max,}$ KBr): 3116, 2996, 2917, 1666 (C=O), 1634 (C=C), 1574, 1407, 1254, 1050 (C-O-C), 975, 707 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), *δ* (ppm): 7.28 (2H, d, *J* = 7.6 Hz, ArH) [7.25 (2H, d, *J* = 8.0 Hz, ArH)], 7.24 (1H, dd, *J* = 3.6, 0.8 Hz, ArH), 7.2 (1H, d, *J* = 8.0 Hz, ArH) [7.13 (1H, d, *J* = 8.8 Hz, ArH)], 7.06-7.04 (1H, m, ArH), 6.96 (1H, dd, *J* = 5.2, 4.0 Hz, ArH) [7.39 (1H, dd, *J* = 3.6, 2.0 Hz, ArH)], 6.86 (1H, dd, *J* = 3.2, 1.2 Hz, ArH), 6.69 (1H, s, alkene) [6.51(1H, s, alkene)], 5.70 (1H, s, OH) [6.35(1H, s, OH)], 5.64 (1H, s, alkene) [5.76 (1H, s, alkene)], 2.38 (3H, CH_3) [2.37], 2.19 (3H, CH_3) [2.24]; **^{13}C NMR** (100 MHz, $CDCl_3$), *δ* (ppm): 19.84 (19.91), 21.42 (21.22), 100.09 (100.13), 100.81 (101.10), 116.62 (118.71), 125.84, 126.79, 127.40 (127.54), 128.29 (128.18), 129.09 (128.83), 130.03 (129.73), 135.00, 138.57 (138.05), 138.75 (139.14), 139.53 (140.09), 145.87, 161.53 (161.92), 162.08 (162.95), 164.79 (164.70); **LC/MS** (ESI, m/z): 325.41 (MH^+, 100); **Anal. Calcd. for** $C_{19}H_{16}O_3S$: C 70.35, H 4.97, S 9.88. **Found**: C 70.21, H 4.78, S 9.63.

*4.3.1.18 4-Hydroxy-6-methyl-3-[2-(4-fluorphenyl)-2-(2-thenyl)vinyl]-2H-pyran-2-one (**18**)*

E:*Z* ratio = 1:1.5. Brown solid; mp: 188-189 °C; **IR** ($\nu_{max,}$ KBr): 3111, 3095, 3052, 2915, 1665 (C=O), 1631 (C=C), 1573, 1407, 1219, 1005, 843, 709 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$), *δ* (ppm): -116.41; **^{1}H-NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.42-7.28 (5H, m, ArH), [7.09-7.02 (5H, m)], 6.97 (1H, td, *J* = 4.6, 1.2 Hz, ArH), 6.83 (1H, d, *J* = 3.6 Hz), 6.66 (1H, s) [6.49 (1H, s, alken)], 5.83 (1H, s, OH) [6.01 (1H, s, OH)], 5.67 (1H, s, alkene) [5.76 (1H, s, alkene)], 2.20 (3H, CH_3) [2.25 (3H, CH_3)]; **^{1}H NMR** (400 MHz, CD_3COCD_3); δ (ppm): 9.7 (1H, s, OH), 7.39 (1H, dd, *J* = 4.8, 1.2 Hz, ArH), 7.29 (2H, m), 7.06 (2H, m), 7.00 (1H, dd, *J* = 5.2, 3.6 Hz, ArH), 6.83 (1H, dd, *J* = 3.6, 1.2 Hz), 6.59 (1H, s, alkene), 5.86 (1H, d, *J* = 0.8 Hz, alkene), 2.12 (3H, CH_3); **^{13}C NMR** (100 MHz, CD_3COCD_3), *δ* (ppm): 19.02 (CH_3), 99.80 (100.11), 114.81 (CH*2, d, ^{2}J = 21.4 Hz), 117.24, 125.48, 125.94, 127.61, 131.34 (CH*2, d, ^{3}J = 8.4 Hz), 136.83 (C, d, ^{4}J = 3.1 Hz), 138.64, 146.92, 161.88, 162.42 (C, d, ^{1}J = 243.1 Hz), 162.82, 164.64; **LC/MS** (ESI, m/z): 329.36 (MH^+, 100); **Anal. Calcd. for** $C_{18}H_{13}FO_3S$: C 65.84, H 3.99, S 9.77. **Found**: C 65.61, H 3.80, S 9.67.

*4.3.1.19 2-Phenyl-2-(2-thenyl)-1,2-dihydro-4H,11H-furo[2,3:4, 5]pyrano[3,2-c]chromen-4,11-dione (**19**)*

Yellow solid; mp: 201-201 °C; **IR** ($\nu_{max,}$ KBr): 1726 (C=O), 1631 (C=C), 1558, 1273, 761, 700 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 8.13 (1H, *J* = 7.6 Hz, ArH), 7.7 (1H, t, *J* = 8.0 Hz, ArH), 7.59 (2H, d, *J* = 7.6 Hz, ArH), 7.42-7.33 (6H, m, ArH), 6.98-6.90 (2H, m, ArH), 4.00 (1H, d, *J* = 15.6 Hz, $-CH_2$), 3.79 (1H, d, *J* = 15.6 Hz, $-CH_2$); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 41.63 (C3), 95.94 (C2), 97.60, 101.75, 113.56, 117.78, 124.46, 125.87 ($CH^{*}2$), 125.96, 127.57, 127.78, 128.62, 129.16, 129.27 ($CH^{*}2$), 135.72, 143.87, 147.23, 153.75, 155.77 (C11), 157.58 (C4), 164.46 (C5a), 165.73 (C11b); **LC/MS** (ESI, m/z): 415.18 (MH^+, 100); **Anal. Calcd. for** $C_{24}H_{14}O_5S$: C 69.55, H 3.40, S 7.74. **Found:**C 68.98, H 3.71, S 6.98.

*4.3.1.20 2-(4-Methylphenyl)-2-(2-thenyl)-1,2, -dihydro-4H,11H-furo[2,3:4,5]pyrano[3,2-c]chromen-4,11-dione (**20**)*

Yellow solid; mp: 186-187 °C; **IR** ($\nu_{max,}$ KBr): 3089, 2952, 1725 (C=O), 1632 (C=C), 1559, 1274, 1104 (C-O-C), 761, 710 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 8.11 (1H, dd, *J* = 8.8, 2.0 Hz, ArH), 7.68 (1H, td, *J* = 8.8; 2.0 Hz, ArH), 7.45 (2H, d, *J* = 8.4 Hz, ArH), 7.42-7.38 (2H, m, ArH), 7.32 (1H, dd, *J* = 5.2; 1.2 Hz, ArH), 7.2 (2H, d, *J* = 8.4 Hz, ArH), 6.97 (1H, dd, *J* = 3.6, 1.2 Hz, ArH), 6.94 (1H, dd, *J* = 5.2; 3.6 Hz, ArH), 3.95 (1H, d, *J* = 15.6 Hz, $-CH_2$), 3.76 (1H, d, *J* = 15.6 Hz, $-CH_2$), 2.36 (3H, CH_3); **^{13}C NMR** (100 MHz $CDCl_3$), δ (ppm): 21.13 (Me), 41.76 (C3), 96.26 (C2), 97.08, 101.62, 112.96, 117.32, 124.27, 125.13, 125.42 ($CH^{*}2$), 126.86, 126.94, 127.01, 129.25 ($CH^{*}2$), 134.91, 138.49, 139.81, 146.91, 153.60, 155.31 (C4), 157.50 (C4), 164.13 (C5a), 165.81 (C11b); **LC/MS**, (ESI, m/z): 429.34 (MH^+, 100); **Anal. Calcd. for** ($C_{25}H_{16}O_5S$): C 70.08, H 3.76, S 7.48. **Found**: C 70.92, H 3.41, S 8.24.

*4.3.1.21 2-(4-Fluorphenyl)-2-(2-thenyl)-1,2 -dihydro-4H,11H-furo[2,3:4,5]pyrano[3,2-c]chromen-4,11-dione (**21**)*

Yellow solid; mp: 209-210 °C; **IR** ($\nu_{max,}$ KBr): 3099, 2983, 1728 (C=O), 1635 (C=C), 1560, 1160 (C-O-C), 755 cm^{-1}; **^{19}F- NMR** (376 MHz, $CDCl_3$), δ (ppm): -113.508; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 8.13 (1H, dd, *J* = 8.4; 1.6 Hz, ArH), 7.71 (1H, td, *J* = 8.0; 1.6, ArH), 7.55-7.57 (2H, m, ArH), 7.40-7.43 (2H, m, ArH), 7.3 (1H, dd, *J* = 4.8; 1.6 Hz, ArH), 7.08-7.12 (2H, m, ArH), 6.95-6.98 (2H, m, ArH), 3.99 (1H, d, *J* = 15.6 Hz, $-CH_2$), 3.75 (1H, d, *J* = 15.6 Hz, $-CH_2$); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm); 41.88 (C3),

95.71 (C2), 96.99, 101.48, 112.92, 115.58 (CH*2, d, ^2J = 22.1 Hz), 117.36, 124.30, 125.19, 127.01 (CH*2, d, ^3J = 8.4 Hz), 127.27, 127.47, 127.52, 135.03, 138.62, 146.46, 153.62, 155.30 (C11), 157.37 (C4), 161.33 (C, d, ^1J = 246.2 Hz), 163.87 (C5a), 165.67 (C11b); **LC/MS** (ESI, m/z): 433.80 (MH^{+1}, 100); **Anal. Calcd. for** ($C_{24}H_{13}FO_5S$): C 66.66, H 3.03, S 7.42. **Found**: C 66.49, H 3.21, S 7.64.

*4.3.1.22 5-Ethyl-7-hydroxy-9-phenyl-9-(2-thenyl)-5,8 9,10a-tetrahydro-6H-furo[3',2':5, 6]pyrano[3,2-c]quinolin-6-one (**22**)*

Yellow solid; mp: 175-176 °C; **IR** ($\nu_{max,}$ KBr): 3014, 1728 (C= O), 1654 (C=O), 1600 (C=C), 1556, 752, 740, 700 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 8.29 (1H, dd, *J* = 8.4; 1.2 Hz, ArH), 7.69 (1H, td, *J* = 8.4; 1.2 Hz, ArH), 7.63 (2H, dd, *J* = 7.6; 1.6 Hz, ArH), 7.41-7.32 (5H, m, ArH), 7.29 (1H, dd, *J* = 5.2, 1.2 Hz, ArH), 7.00 (1H, dd, *J* = 3.6; 1.2 Hz, ArH), 6.93 (1H, dd, *J* = 5.2; 3.6 Hz, ArH), 4.39 (2H, q, *J* = 7.2 Hz, $-CH_2$), 3.99 (1H, d, *J* = 15.6 Hz, $-CH_2$), 3.77 (1H, d, *J* = 15.6 Hz, $-CH_2$), 1.40 (3H, t, *J* = 7.2 Hz, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$), *δ* (ppm): 12.96, 37.71, 41.83, 95.69, 101.63, 101.74, 113.77, 114.66, 122.88, 125.22, 125.74 (CH*2), 126.96, 127.00, 127.04, 128.54, 128.77 (CH*2), 133.93, 139.50, 143.60, 147.55, 157.09, 158.76, 161.12, 167.13; **LC/MS** (ESI, m/z): 442.70 (MH^+, 100); **Anal. Calcd. for** $C_{26}H_{19}NO_4S$: C 70.73, H 4.34, N 3.17 S 7.26. **Found**: C 70.30, H 4.11, N 3.52, S 7.06.

*4.3.1.23 5-Ethyl-2-(4-methylphenyl)-2-(2-thenyl)-1,5-dihydro-4H-furo[2',3':4,5]pyrano[3, 2-c]quinolin-4,11(2H)-dione (**23**)*

Yellow solid; mp: 190-191 °C; **IR** ($\nu_{max,}$ KBr): 3089, 2952, 1721 (C=O), 1652 (C=O), 1610 (C=C), 1104 (C-O-C), 761 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 8.28 (1H, dd, *J* = 8.4, 1.6 Hz, ArH), 7.68 (1H, td, *J* = 7.8, 1.6 Hz, ArH), 7.49 (2H, dd, *J* = 8.8, 2.0 Hz, ArH), 7.40 (2H, d, *J* = 8.4 Hz, ArH), 7.28 (1H, dd, *J* = 5.2, 1.2 Hz, ArH), 7.20 (2H, d, *J* = 7.6), 6.99 (1H, dd, *J* = 3.6; 1.2 Hz, ArH), 6.93 (1H, dd, *J* = 5.2; 3.6 Hz, ArH), 4.39 (2H, q, *J* = 7.2 Hz, CH_2), 3.97 (1H, d, *J* = 15.2 Hz, $-CH_2$), 3.76 (1H, d, *J* = 15.2 Hz, $-CH_2$), 2.36 (3H, s, CH3), 1.39 (3H, t, *J* = 7.2 Hz, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$), *δ* (ppm): 12.73, 21.12, 37.48, 41.55, 95.56, 101.55, 102.42, 113.53, 114.43, 122.64, 124.94, 125.46 (CH*2), 126.63, 126.70, 126.78, 128.62, 129.18 (CH*2), 133.69, 138.17, 140.42, 147.54, 156.87, 158.59, 160.84, 166.92; **LC/MS** (ESI, m/z): 456.80 (MH^+, 100); **Anal. Calcd. for** $C_{27}H_{21}NO_4S$: C 71.19, H 4.65, N 3.07, S 7.04. **Found**: C 71.43, H 4.81, N 3.32, S 7.51.

*4.3.1.24 5-Ethyl-2-(4-fluorphenyl)-2-(2-thenyl)-1,5-dihydro-4H-furo[2',3':4 5]pyrano[3,2-c]quinolin-4,11(2H)-dione (**24**)*

Yellow solid; mp: 191-192 °C; **IR** ($\nu_{max,}$ KBr): 3078, 2972, 1722 (C=O), 1681 (C=O), 1651 (C=C), 1555, 1230, 941, 835 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$), δ (ppm): -113.99; **^{1}H NMR** (400 MHz, $CDCl_3$), δ(ppm): 8.30 (1H, dd, *J* = 8.0, 1.6 Hz, ArH), 7.7 (1H, td, *J* = 8.0, 1.6 Hz, ArH), 7.58 (2H, td, *J* = 8.8, 2.0 Hz, ArH), 7.42 (1H, d, *J* = 8.8 Hz, ArH), 7.35 (1H, d, *J* = 8.0 Hz, ArH), 7.31 (1H, dd, *J* = 4.8; 1.2 Hz, ArH), 7.09 (2H, td, *J* = 8.8, 2.0 Hz, ArH), 7.00 (1H, dd, *J* = 5.2, 1.2 Hz, ArH), 6.94 (1H, dd, *J* = 4.8, 4.0 Hz, ArH), 4.40 (2H, q, *J* = 7.2 Hz, CH_2), 3.99 (1H, d, *J* = 15.2 Hz, -CH_2), 3.73 (1H, d, *J* = 15.2 Hz, -CH_2), 1.40 (3H, t, *J* = 7.2 Hz, CH3); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 12.95, 37.73, 41.92, 95.24, 101.65 (C*2), 113.75, 114.70, 115.70 (CH*2, d, ^{2}J = 21.4 Hz), 122.94, 125.24, 127.02, 127.11 (CH*2, d, ^{3}J = 8.4 Hz), 127.70, 127.79, 134.03, 139.44 (CH, d, ^{4}J = 3.0 Hz), 139.51, 147.27, 157.10, 158.71, 161.19, 162.74 (C, d, ^{1}J = 246.2 Hz), 167.01; **LC/MS** (ESI, m/z): 460.70 (MH^+, 100); **Anal. Calcd. for** $C_{26}H_{18}FNO_4S$: C 67.96, H 3.95, N 3.05, S 6.98. **Found**: C 67.80, H 4.17, N 3.27, S 6.86.

*4.3.1.25 4-Hydroxy-3-[2-phenyl-2-(2-thenyl)vinyl]2H,5H-pyrano[3,2-c]chromen-2, 5-dione (**25**)*

E:*Z* ratio = 1:4. Orange solid; mp: 229-231 °C; **IR** ($\nu_{max,}$ KBr): 3438, 3144, 3082, 2925, 1727 (C=O), 1681 (C=C), 1414, 1106 (C-O-C), 771, 694 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 10.89 (1H, s) [11.07 (1H, s)], 8.08 (1H, dd, *J* = 8.4, 1.6 Hz, ArH), 7.72 (1H, td, *J* = 8.8, 1.6 Hz, ArH), 7.44-7.49 (2H, m, ArH), 7.36-7.27 (6H, m, ArH), 6.96 (1H, dd, *J* = 5.2, 3.6 Hz, ArH), 6.87 (1H, d, *J* = 3.6 Hz, ArH), 6.70 (1H, s, alkene) [6.45 (1H, s, alkene)]; **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm); 96.71, 103.16, 114.04 (113.09), 116.57, 117.39 (117.45), 124.29 (124.38), 125.73 (125.45), 126.09 (126.15), 126.90 (126.37), 127.36 (126.70), 127.99 (CH*2) (128.32), 128.04 (128.60), 129.12 (CH*2) (128.70), 134.99 (135.0), 140.23, 141.80, 146.43, 152.28, 158.87, 160.83, 161.20, 163.00; **LC/MS** (ESI, m/z): 415.42 (MH^+, 100); **Anal. Calcd. for** $C_{24}H_{14}O_5S$: C 69.55, H 3.40, S 7.74. **Found:** C 69.65, H 3.51, S 7.80.

*4.3.1.26 4-Hydroxy-3-[2-(4-methylphenyl)-2-(2-thenyl)vinyl]2H, 5H-pyrano[3,2-c]chromen-2 5-dione (**26**)*

E:*Z* ratio = 1:3.4. Orange solid; mp: 232-233 °C; **IR** ($\nu_{max,}$ KBr): 3099. 3025, 1737 (C=O), 1683 (C=C), 1589, 1415, 1106 (C-O-C), 762, 702 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ(ppm): 10.89 (1H, s, OH) [11.03

(1H, s, OH)], 8.10 (1H, dd, *J* = 8.4, 1.6 Hz, ArH), 7.73 (1H, td, *J* = 7.6, 1.6 Hz, ArH), 7.44-7.49 (2H, m, ArH), 7.25 (1H, *J* = 0.8 Hz, ArH), 7.21 (2H, d, *J* = 8.4, ArH) [7.34 (2H, d, *J* = 8.4 Hz, ArH)], 7.09 (2H, d, *J* = 8.4, ArH) [7.16 (2H, d, *J* = 8.4 Hz, ArH)], 6.97 (1H, dd, *J* = 5.2; 3.6 Hz, ArH), 6.89 (1H, dd, *J* = 5.2, 1.2 Hz, ArH), 6.67 (1H, s, alkene) [6.44 (1H, s, alkene)], 2.33 (3H, CH_3) [2.39 (3H, CH_3)]; **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 21.36 (Me), 96.81, 103.40, 113.66, 117.38, 124.28, 125.64, 126.07 (126.27), 126.79, 127.31, 128.73 (CH^*2) (128.58), 128.98 (CH^*2), 134.93, 137.29, 137.75, 141.48, 143.90, 146.66, 152.26, 158.86, 160.75, 161.10, 163.03; **LC/MS** (ESI, m/z): 429.85 (MH^+), 451.86 (M+ Na, 100); **Anal. Calcd. for** ($C_{25}H_{16}O_5S$): C 70.08, H 3.76, S 7.48. **Found**: C 70.22, H 3.51, S 7.81.

*4.3.1.27 4-Hydroxy-3-[2-(4-fluorphenyl)-2-(2-thenyl)vinyl]-2H, 5H-pyrano[3,2-c]chromen-2,5-dione (**27**)*

E:*Z* ratio = 1:2. Orange solid; mp: 214-215 °C; **IR** ($\nu_{max,}$ KBr): 2965, 1758, 1724, 1702, 1673, 1099, 768 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$)**,** *δ* (ppm): -113.90, -114.10; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm):10.98 (1H, s, OH) [11.05 (1H, s, OH)], 8.10 (1H, dd, *J* = 8.0; 2.0 Hz, ArH) [8.15 (1H, dd, *J* = 8.0; 2.0 Hz, ArH)], 7.75 (1H, td, *J* = 8.0, 2.0 Hz; ArH), 7.40-7.50 (3H, m, ArH), 7.27-7.32 (2H, m, ArH), 6.96-7.05 (3H, m, ArH), 6.85 (1H, dd, *J* = 3.6, 0.8 Hz, ArH) [6.93 (1H, dd, *J* = 3.6, 1.2 Hz, ArH)], 6.70 (1H, s, alkene) [6.41 (1H, s, alkene)]; **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 76.94, 96.89, 103.15 (103.61), 113.28 (113.36), 114.53, 115.30 (CH, d, ^{2}J = 21.3 Hz) [115.14 (CH, d, ^{2}J = 21.3 Hz)], 116.66, 117.67 (117.70), 124.53 (124.61), 126.15, 126.38 (126.80), 127.06 (127.01), 127.67 (128.85), 131.11 (CH, d, ^3J = 7.7 Hz) [130.60 (CH, d, ^3J = 8.4 Hz)], 135.36 (135.38), 136.43 (C, d, ^4J = 3.8 Hz) (136.89), 140.94 (140.15), 146.51 (142.25), 152.55 (152.64), 159.01 (159.09), 161.18 (161.31), 161.60 (162.23), 162.69 (C, d, ^1J = 245.4) [163.19 (C, d, ^1J = 246.1)], 163.26 (163.32); **LC/MS** (ESI, m/z): 433.62 (MH^+, 100); **Anal. Calcd. for** ($C_{24}H_{13}FO_5S$): C 66.66, H 3.03, S 7.42. **Found**: C 66.48, H 3.18, S 7.29.

*4.3.1.28 6-Ethyl-4-hydroxy-3-[2-phenyl-2-(2-thenyl)vinyl]-2H, 5H-pyrano[3,2-c]quinolin-2,5-dione (**28**)*

E:*Z* ratio = 1:2.4. Orange solid; mp: 198-199 °C; **IR** ($\nu_{max,}$ KBr): 3465 (O-H)**,** 3065 (Ar-H), 2983 (R-H), 1742 (C= O), 1668 (C=O), 1615 (C=C), 1548, 1106 (C-O-C), 758 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 13.28 (1H, s, OH) [13.44 (1H, s, OH)], 8.26 (1H, d, *J* = 7.6, ArH), 7.71-7.78 (1H, m, ArH), 7.48 (1H, d, *J* = 8.4 Hz, ArH) [7.51 (1H, d, *J* = 8.4 Hz, ArH)], 7.38-7.45 (1H, m, ArH), 7.32-7.36 (3H, m, ArH),

7.25-7.29 (2H, m, ArH), 7.23 (1H, d, *J* = 5.2 Hz, ArH), 6.92-6.96 (1H, m, ArH), 6.86 (1H, d, *J* = 3.6, ArH), 6.75 (1H, s, alkene) [6.50 (1H, s, alkene)], 4.37 (2H, q, *J* = 7.2 Hz) [4.41 (2H, q, *J* = 7.2 Hz)], 1.38 (3H, t, *J* = 7.2 Hz, N-CH_3) [(3H, t, *J* = 7.2 Hz, N-CH_3)]; **^{13}C NMR** (100 MHz, $CDCl_3$), *δ* (ppm): 12.75 (12.79), 37.65, 99.92, 102.18, 113.99 (114.06), 114.77 (114.54), 115.03 (114.83), 123.95 (124.01), 124.88 (124.98), 125.28, 126.45 (126.51), 127.23, 127.73, 127.85 (CH^*2), 129.22 (CH^*2), 133.70 (133.78), 137.56 (137.68), 140.56, 140.90, 146.88, 157.50, 159.97, 162.74 (162.83), 164.07 (164.77); **LC/MS** (ESI, m/z): 442.34 (MH^+, 100); **Anal. Calcd. for** $C_{26}H_{19}NO_4S$: C 70.73, H 4.34, N 3.17 S 7.26. **Found**: C 71.49, H 4.81, N 3.61, S 7.46.

*4.3.1.29 6-Ethyl-4-hydroxy-3-[2-(4-methylphenyl)-2-(2-thenyl)vinyl]-2H-pyrano[3,2-c] quinolin-2,5(6H)-dione (**29**)*

E:*Z* ratio = 1:8. Orange solid; mp: 236-237 °C; **IR** ($\nu_{max,}$ KBr): 3071, 2920 (R-H), 1735 (C=O), 1661 (C=O), 1421 (C=C), 759 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 13.28 (1H, s, OH) [13.44 (1H, s, OH)], 8.26 (1H, dd, *J* = 7.6, 1.2 Hz, ArH), 7.74 (1H, td, *J* = 7.6, 1.6 Hz, ArH), 7.48 (1H, d, *J* = 8.4 Hz, ArH), 7.40 (1H, d, *J* = 8.0, 0.8 Hz, ArH), 7.29 (2H, d, *J* = 8.0 Hz, ArH), 7.21 (1H, d, *J* = 1.2 Hz, ArH), 7.07 (2H, d, *J* = 7.6 Hz, ArH), 6.95 (1H, dd, *J* = 5.2, 3.6 Hz, ArH), 6.89 (1H, dd, *J* = 3.6, 1.2 Hz, ArH), 6.72 (1H, s, alkene), 4.38 (2H, q, *J* = 7.2 Hz), 2.32 (3H, s) [2.38 (3H, s)], 1.46 (3H, t, *J* = 7.2 Hz, N-CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$), *δ* (ppm): 13.01, 21.62, 37.89, 100.19, 102.65, 114.26, 114.87, 115.00, 124.18, 125.12, 125.45, 126.60, 127.43, 128.86 (CH^*2), 129.30 (CH^*2), 133.90, 137.60, 137.78, 137.83, 141.03, 147.35, 157.68, 160.10, 162.99, 164.31; **LC/MS** (ESI, m/z): 456.70 (MH^+, 100; **Anal. Calcd. for** $C_{27}H_{21}NO_4S$: C 71.19, H 4.65, N 3.07, S 7.04. **Found**: C 71.31, H 4.71, N 3.29, S 7.31.

*4.3.1.30 6-Ethyl-3-[2-(4-fluorphenyl)-2-(2-thenyl)vinyl]-4-hydroxy-2H-pyrano[3,2-c]quinolin-2,5(6H)-dione (**30**)*

E:*Z* ratio = 1:3.3. Orange solid; mp: 249-250 °C; **IR** ($\nu_{max,}$ KBr): 3671, 2987 (R-H), 1736 (C= O), 1668 (C= O), 1504, 1219, 757 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$**)**, *δ* (ppm): -114.53, -114.66; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 13.37 (1H, s, OH) [13.48 (1H, s, OH)], 8.25 (1H, dd, *J* = 8.0 Hz, ArH) [8.31 (1H, dd, *J* = 7.6 Hz, ArH)], 7.74 (1H, t, *J* = 8.8 Hz, ArH), 7.50-7.38 (2H, m, ArH), 7.33-7.30 (2H, m, ArH), 7.24 (1H, d, *J* = 4.4 Hz, ArH), 7.00-6.93 (3H, m, ArH), 6.84 (1H, d, *J* = 4.0 Hz, ArH), 6.73 (1H, s, alkene) [6.44 (1H, s, alkene)], 4.38 (2H, q, *J* = 7.6 Hz, CH_2), 1.38 (3H, t, *J* = 8.0 Hz, -CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$),

δ (ppm): 12.77, 37.71, 99.86, 101.94, 102.43, 113.97, 114.67, 114.79, 114.83, 115.00, 115.32, 117.47, 124.03, 124.90, 124.99, 125.47, 126.22, 126.38, 126.59, 127.31, 128.39, 130.31, 130.40, 130.90, 130.98, 133.82, 136.55, 136.52, 137.62, 137.71, 138.93, 139.75, 142.57, 146.73, 157.59, 157.72, 159.96, 160.01, 161.08, 162.74, 162.84, 163.53, 164.03, 164.19, 164.83; **LC/MS** (ESI, m/z): 460.13 (MH^+, 100); **Anal. Calcd. for** $C_{26}H_{18}FNO_4S$: C 67.96, H 3.95, N 3.05, S 6.98; **Found**: C 70.13, H 4.09, N 3.25, S 7.06.

*4.3.1.31 5-Methyl-2-phenyl-2-thenyl-3, 5-dihydrofuro[3,2-c]quinolin-4H-one (**31**)*

Colorless solid; mp: 181-182 °C; **IR** ($\nu_{max,}$ KBr): 3107, 3001, 2918, 1656 (C=O), 1639 (C=C), 1598, 1240, 1107, 742 cm^{-1}; **^{1}H-NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.95 (1H, dd, *J* = 8.0; 1.6 Hz, ArH), 7.59 (1H, td, *J* = 7.8; 1.6 Hz, ArH), 7.52 (1H, dd, *J* = 8.4; 1.6 Hz, ArH), 7.38 (1H, dd, *J* = 8.4, 0.8 Hz, ArH), 7.25-7.36 (6H, m, ArH), 7.09 (1H, dd, *J* = 3.6, 1.2 Hz, ArH), 6.94 (1H, d, *J* = 5.2, 4.0 Hz, ArH), 4.1 (1H, d, *J* = 15.6 Hz, H3), 3.87 (1H, d, *J* = 15.6 Hz, H3), 3.70 (3H, s, N-CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 29.38 (CH_3), 44.50 (C3), 93.60 (C2), 107.70, 112.76, 114.82, 122.00, 123.47, 125.68 (CH*2), 126.12, 126.50, 126.90, 128.33, 128.65 (CH*2), 131.38, 141.01, 144.47 (C ipso), 148.83 (C ipso), 160.95 (C4), 161.22 (C9b); **LC/MS** (ESI, m/z): 360.01 (MH^+, 100); **Anal. Calcd. for** $C_{22}H_{17}NO_2S$: C 73.51, H 4.77, N 3.90, S 8.92. **Found**: C 72.68, H 4.86, N 3.75, S 8.26.

*4.3.1.32 5-Methyl-2-(4-methylphenyl)-2-thenyl-3,5-dihydrofuro[3,2-c]quinolin-4H-one (**32**)*

Colorless solid; mp: 144-145 °C; **IR** ($\nu_{max,}$ KBr): 3084 (Ar-H), 2979 (R-H), 1657 (C=O), 1635 (C=C), 1597, 1450, 1240, 1106, 754, 698 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.94 (1H, dd, *J* = 8.0, 1.6 Hz, ArH), 7.59 (1H, td, *J* = 8.0, 1.6 Hz, ArH), 7.42 (2H, d, *J* = 8.0 Hz, ArH), 7.38 (1H, d, *J* = 8.4 Hz, ArH), 7.28-7.24 (2H, m, ArH), 7.17 (2H, d, *J* = 8.0 Hz, ArH), 7.0 (1H, dd, *J* = 3.6, 1.2 Hz, ArH), 6.94 (1H, dd, *J* = 5.2, 3.2 Hz, ArH), 4.07 (1H, d, *J* = 15.6 Hz, H3), 3.87 (1H, d, *J* = 15, 6 Hz, H3), 3.7 (3H, s, N-CH_3), 2.34 (3H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 21.09 (CH_3), 29.11 (CH_3), 44.19 (C3), 93.37 (C2), 107.54, 112.53, 114.54, 121.70, 123.24, 125.41 (CH*2), 125.75, 126.15, 126.62, 129.05 (CH*2), 131.08, 137.91, 140.73, 141.26, 148.78, 160.68 (C4), 160.98 (C9b); **LC/MS** (ESI, m/z):374.41 (M^+, 100); **Anal. Calcd. for** $C_{23}H_{19}NO_2S$: C 73.97, H 5.13, N 3.75, S 8.79. **Found**: C 74.13, H 5.42, N 3.16, S 7.99.

*4.3.1.33 5-Methyl-2-(4-fluorphenyl)-2-thenyl-3,5-dihydrofuro[3,2-c]quinolin-4H-one (**33**)*

Colorless solid; mp: 143-144 °C; **IR** ($\nu_{max,}$ KBr): 3084 (Ar-H), 2979 (R-H), 1657 (C=O), 1635 (C=C), 1597, 1240 (C-O-C), 1106, 754 cm^{-1}; **^{19}F NMR** (376 MHz, $CDCl_3$), δ (ppm): -114.42; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.92 (1H, dd, *J* = 8.0, 1.6 Hz, ArH), 7.61 (1H, td, *J* = 7.8; 1.6 Hz, ArH), 7.52-7.49 (2H, m, ArH), 7.39 (1H, d, *J* = 8.8 Hz, ArH), 7.30-7.25 (2H, m, ArH), 7.07-7.03 (2H, m, ArH), 7.00 (1H, dd, *J* = 3.6, 1.2 Hz, ArH), 6.95 (1H, dd, *J* = 5.2, 3.6 Hz, ArH), 4.09 (1H, d, *J* = 15.6 Hz, H3), 3.82 (1H, d, *J* = 15.6 Hz, H3), 3.71 (3H, s, N-CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 29.38 (CH_3), 44.55 (C3), 93.14 (C2), 107.65, 112.63, 114.85, 115.55 (CH, d, ^{2}J = 21.4 Hz), 122.04, 123.40, 126.18, 126.88, 126.97, 127.60 (CH, d, ^{3}J = 8.3 Hz), 129.81 (CH, d, ^{3}J = 8.4 Hz), 131.46, 132.86, 140.31 (C, d, ^{4}J = 3.0 Hz), 141.01, 148.53, 160.77 (C4), 161.13 (C9b), 162.64 (C, d, ^{1}J = 246.1); **LC/MS** (ESI, m/z): 378.42 (MH^+, 100); **Anal. Calcd. for** $C_{22}H_{16}FNO_2S$: C 70.01, H 4.27, N 3.71, S 8.50. **Found**: C 70.11, H 4.29, N 3.80, S 8.55.

*4.3.1.34 4-Hydroxy-1-methyl-3-[2-phenyl-2-(2-thenyl)vinyl]quinolin-2(1H)-one (**34**)*

E:*Z* ratio = 1:2.17. Yellow solid; mp: 204-205 °C; **IR** ($\nu_{max,}$ KBr): 3109, 3075, 1617 (C=O), 1575 (C=C), 1161 (C-O-C), 754 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm):7.74 (1H, dd, *J* = 7.6; 1.6 Hz, ArH) [7.89 (1H, td, *J* = 8.0, 1.6 Hz, ArH)], 7.52 (1H, td, *J* = 7.8; 1.6 Hz, ArH) [7.57(1H, td, *J* = 7.2; 1.6 Hz, ArH)], 7.43-7.40 (6H, m, ArH) [7.36-7.29 (6H, m, ArH)], 7.26 (1H, dd, *J* = 3.2; 1.6 Hz, ArH), 7.14 (1H, t, *J* = 8.0 Hz, ArH) [7.20 (1H, t, *J* = 8.0 Hz, ArH)], 7.05 (1H, s, alkene) [6.80 (1H, s, alkene)], 6.97 (1H, td, *J* = 5.2, 1.2 Hz, ArH), 6.89 (1H, dd, *J* = 3.6, 1.2 Hz, ArH), 5.85 (1H, s, OH) [6.12 (1H, s, OH)], 3.72 (3H, s, N-CH_3) [3.74 (3H, s, N-CH_3)]; **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 29.74 (CH_3), 108.58, 113.96 (114.08), 115.53, 119.72 (122.11), 121.84 (121.95), 124.38 (124.56), 125.96, 127.01, 127.57 (127.65), 128.29 (128.36), 128.80 (128.63), 129.38 (129.44), 129.52 (130.06), 131.18 (131.39), 138.45 (138.02), 138.88, 139.33 (139.51), 140.32 (142.59), 146.29, 154.11 (154.94), 163.39; **LC/MS** (ESI, m/z): 360.70 (MH^+, 100); **Anal. Calcd. for** ($C_{22}H_{17}NO_2S$): C 73.51, H 4.77, N 3.90, S 8.92; **Found**: C 73.61, H 4.83, N 3.97, S 9.01.

*4.3.1.35 3-Phenyl-2-thenyl-2,3-dihydro-4H-furo[3,2-c]chromen-4-one (**35**)*

Colorless solid; mp: 153-154°C; **IR** ($\nu_{max,}$ KBr): 3025 (Ar-H), 1718 (C=O), 1641 (C=C), 1496, 1406, 1035 (C-O-C), 700 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.77 (1H, dd, *J* = 8.0, 1.6 Hz, ArH), 7.61 (1H, td, *J* = 8.2, 1.6 Hz, ArH), 7.43-7.27 (8H, m, ArH), 7.18 (1H, d, *J* = 2.8 Hz, ArH), 7.05 (1H, dd, *J* = 4.8, 3.6 Hz, ArH), 6.05 (1H, d, *J* = 6.4 Hz, H2), 4.83 (1H, d, *J* = 6.0 Hz, H3); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm):54.94 (C3), 91.93 (C3), 104.96, 112.69, 117.32, 123.37, 124.29, 126.85, 127.21, 127.42, 127.57, 128.11, 128.59, 129.00, 129.36, 133.05, 139.91, 141.67, 155.72 (C5a), 159.82 (C4), 166.12 (C9b); **LC/MS** (ESI, m/z): 346.97 (MH^+, 100); **Anal. Calcd. for** ($C_{21}H_{14}O_3S$): C 72.81, H 4.07, O 13.86, S 9.26. **Found**: C 72.41, H 4.27, S 8.20.

*4.3.1.36 3-Phenyl-2-thenyl-2,3-dihydro-4H-furo[3, 2-c]chromen-4-one (**36**)*

Light yellow solid; mp: 131-132°C; **IR** ($\nu_{max,}$ KBr): 3028 (Ar-H), 1710 (C= O), 1635 (C= C), 1409, 1026 (C-O-C), 788 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.8 (1H, dd, *J* = 8.0, 1.6 Hz, ArH), 7.63 (1H, td, *J* = 7.8, 1.6 Hz, ArH), 7.45 (1H, dd, *J* = 8.4, 0.8 Hz, ArH), 7.35 (1H, td, *J* = 7.6, 1.2 Hz, ArH), 7.16-7.13 (4H, m, ArH), 6.96-6.94 (2H, m, ArH), 6.85-6.83 (1H, m, ArH), 6.82 (1H, dd, *J* = 5.2, 4.0 Hz, ArH), 6.52 (1H, d, *J* = 9.2, H2), 4.86 (1H, d, *J* = 9.2 Hz, H3); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 51.00 (C3), 89.00 (C2), 106.00, 112.50, 117.00, 123.42, 124.37, 126.35, 127.17, 127.57, 127.98, 128.59 (CH^*2), 128.98 (CH^*2), 133.13, 135.79, 137.27, 155.55 (C5a), 159.88 (C4), 167.01 (C9b); **LC/MS**, (ESI, m/z) : 347.70 (MH^+, 100); **Anal. Calcd. for** ($C_{21}H_{14}O_3S$): C 72.81, H 4.07, O 13.86, S 9.26. **Found**: C 73.12, H 4.31, S 8.46.

*4.3.1.37 (2S, 3S)-2-Methyl-3-phenyl-2-(2-thenyl)-4H-furo[3,2-c]chromen-4-one (**37**)*

Colorless solid; mp: 137-138 °C; **IR** ($\nu_{max,}$ KBr): 3028 (Ar-H), 2989 (R-H), 1722 (C=O), 1647 (C=C), 1406, 1029, 727 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.80 (1H, dd, *J* = 8.0, 1.6 Hz, ArH), 7.60 (1H, td, *J* = 7.8, 1.6 Hz, ArH), 7.42 (1H, d, *J* = 8.4 Hz, ArH), 7.35-7.30 (4H, m, ArH), 7.27 (1H, dd, *J* = 5.2, 1.2 Hz, ArH), 7.17 (2H, dd, *J* = 8.4, 1.6 Hz, ArH), 7.13 (1H, dd, *J* = 3.6, 1.2 Hz, ArH), 7.00 (1H, dd, *J* = 5.2, 4.0 Hz, ArH), 4.93 (1H, s, H3), 1.48 (3H, s, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 26.07 (CH_3), 58.15 (C3), 95.84 (C2), 104.51, 112.71, 117.33, 123.36, 123.69, 124.34, 125.48, 127.29, 128.28, 128.87 (CH^*2), 129.01 (CH^*2), 133.06, 136.40, 149.70, 155.61 (C5a), 159.99 (C4), 166.02 (C9b); **LC/MS**, (ESI,

m/z) : 361.41 (MH^+, 100); **Anal. Calcd. for** ($C_{22}H_{16}O_3S$): C 73.31, H 4.47, S 8.90. **Found**: C 73.02, H 4.51, S 9.06.

*4.3.1.38 2-Methyl-3-phenyl-2-(2-thenyl)-4H-furo[3,2-c]chromen-4-one (**38**)*

Light yellow solid; mp: 161-162 °C; **IR** ($\nu_{max,}$ KBr): 3099 (Ar-H), 2918 (R-H), 1718 (C=O), 1633 (C=C), 1573, 1408, 825, 759 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.86 (1H, dd, *J* = 7.6, 1.6 Hz, ArH), 7.64 (1H, td, *J* = 7.8, 1.6 Hz, ArH), 7.44 (1H, d, *J* = 8.0 Hz), 7.38 (1H, t, *J* = 7.6 Hz), 7.08-7.06 (3H, m, ArH), 7.02 (1H, dd, *J* = 5.2, 0.8 Hz), 6.89 (2H, m, ArH), 6.70 (1H, dd, *J* = 5.2, 3.6 Hz), 6.56 (1H, dd, *J* = 3.6, 0.8 Hz), 4.63 (1H, s), 2.11 (3H, s); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 30.43 (CH_3), 58.64 (C3), 97.31 (C2), 104.94, 112.72, 117.36, 123.36, 124.31, 125.03, 125.12, 126.74, 127.61, 128.22 (CH^*2), 128.61 (CH^*2), 133.04, 136.73, 143.60, 155.59 (C5a), 160.08 (C4), 165.76 (C9b); **LC/MS**, (ESI, m/z): 361.61 (MH^+, 100); **Anal. Calcd. for** ($C_{22}H_{16}O_3S$): C 73.31, H 4.47, S 8.90. **Found**: C 72.90, H 4.60, S 8.32.

*4.3.1.39 2, 6-Dimethyl-3-phenyl-2-(2-thenyl)-2,3-dihydro-4H-furo[3,2-c]piran-4-one (**39**)*

Light yellow oil; **IR** ($\nu_{max,}$ KBr): 3089 (Ar-H), 2989 (R-H), 1716 (C=O), 1637 (C=C), 1571, 1446, 1259, 977, 723 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.35-7.25 (4H, m, ArH), 7.13 (2H, d, *J* = 6.8, ArH), 7.06 (1H, d, *J* = 3.2, Hz, ArH), 6.99 (1H, dd, *J* = 5.2; 3.6, ArH), 6.06 (1H, s, alkene), 4.77 (1H, s, H3), 2.29 (3H, CH_3), 1.35 (3H, s, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 20.82 (CH_3), 25.80 (CH_3), 57.13 (C3), 95.11 (C2), 95.93, 101.62, 123.67, 125.40, 127.23, 128.12, 128.83 (CH^*2), 128.89(CH^*2), 136.51, 149.67, 161.51 (C4), 166.61 (C6), 170.57 (C7a); **LC/MS**, (ESI, m/z): 325.37 (MH^+, 100); **Anal. Calcd. for** ($C_{19}H_{16}O_3S$): C 70.35, H 4.97, S 9.88. **Found**: C 70.17, H 4.80, S 9.71.

*4.3.1.40 2, 6-Dimethyl-3-phenyl-2-(2-thenyl)-2, 3-dihydro-4H-furo[3, 2-c]piran-4-one (**40**)*

Light yellow oil; **IR** ($\nu_{max,}$ KBr): 3089 (Ar-H), 2989 (R-H), 1716 (C=O), 1637 (C=C), 1571, 1446, 1259, 977, 696 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.07-7.05 (3H, m, ArH), 6.99 (1H, dd, *J* = 4.8, 1.2 Hz, ArH), 6.86-6.83 (2H, m, ArH), 6.68 (1H, dd, *J* = 5.2; 3.6, ArH), 6.49 (1H, dd, *J* = 3.2, 1.2 Hz, ArH), 6.13 (1H, s, alkene), 4.46 (1H, s, H3), 2.33 (3H, CH_3), 2.00 (3H, s, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 20.85 (CH_3), 30.23 (CH_3), 57.62 (C3), 95.92 (C2), 96.64, 102.21, 124.86, 124.94, 126.69, 127.47, 128.13 (CH^*2), 128.57 (CH^*2), 136.93, 143.71, 161.63 (C4), 166.54 (C6), 170.38 (C7a); **LC/MS**, (ESI,

m/z) : 325.37 (MH^+, 100); **Anal. Calcd. for** ($C_{19}H_{16}O_3S$): C 70.35, H 4.97, S 9.88. **Found**: C 70.11, H 4.78, S 9.73.

*4.3.1.41 2-Methyl-1-phenyl-2-(2-thenyl)-1,2-dihydro-4H,11H-furo[2,3:4,5]pyrano[3,2-c]chromen-4, 11-dione (**41**)*

White solid; mp: 231-232 °C; **IR** ($\nu_{max,}$ KBr): 3096, 3010, 1724 (C= O), 1624 (C= C), 1558, 1224, 761, 725 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 8.15 (1H, d, *J* = 8.4 Hz, ArH), 7.72 (2H, t, *J* = 8.4 Hz, ArH), 7.43 (1H, d, *J* = 8.4 Hz, ArH), 7.40-7.37 (3H, m, ArH), 7.31 (1H, dd, *J* = 5.2 Hz, ArH), 7.20-7.17 (3H, m, ArH), 7.01 (1H, t, *J* = 4.4 Hz, ArH), 4.87 (1H, s, H3), 1.53 (3H, s, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 26.07 (CH_3), 56.99 (C3), 97.11 (C2), 97.24, 104.82, 113.23, 117.59, 124.15, 124.68, 125.44, 125.66, 127.25, 128.52, 128.78 (CH^*2), 129.13 (CH^*2), 135.35, 135.81, 148.95, 153.91, 155.77 (C11), 157.25 (C4), 164.91 (C5a), 166.95 (C11b); **LC/MS**, (ESI, m/z): 429.40 (MH^+, 100); **Anal. Calcd. for** ($C_{25}H_{16}O_5S$): C 70.08, H 3.76, S 7.48. **Found**.: C 70.40, H 4.01, S 6.98.

*4.3.1.42 2-Methyl-1-phenyl-2-(2-thenyl)-1,2-dihydro-4H,11H-furo[2,3:4,5]pyrano[3,2-c]chromen-4,11-dione (**42**)*

Colorless solid; mp: 207-208 °C; **IR** ($\nu_{max,}$ KBr): 3096, 3010, 1726 (C=O), 1625 (C=C), 1554, 1224, 759, 692 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 8.16 (1H, dd, *J* = 8.4, 1.6 Hz, ArH), 7.72 (1H, td, *J* = 8.0, 1.6 Hz, ArH), 7.45-7.40 (2H, m, ArH), 7.11-7.10 (3H, m, ArH), 7.01 (1H, dd, *J* = 4.4, 3.0, ArH), 6.91-6.89 (2H, m, ArH), 6.68 (1H, dd, *J* = 4.8, 3.6 Hz, ArH), 6.56 (1H, dd, *J* = 3.2, 1.2 Hz, ArH), 4.60 (1H, s, H3), 2.14 (3H, s, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 30.49 (CH_3), 55.56 (C3), 97.07 (C2), 98.58, 104.80, 113.25, 117.61, 124.70, 125.26, 125.36, 125.42, 126.71, 127.87, 128.34 (CH^*2), 128.56 (CH^*2), 135.33, 135.99, 142.71, 153.97, 155.69 (C11), 157.28 (C4), 164.90 (C5a), 166.85 (C11b); **LC/MS**, (ESI, m/z) : 429.80 (MH^+, 100); **Anal. Calcd. for** ($C_{25}H_{16}O_5S$): C 70.08, H 3.76, S 7.48. **Found**: C 70.31, H 3.51, S 6.99.

*4.3.1.43 9a-(2-Thenyl)-7,8,9,9a-tetrahydro-6H,6H-cyclopenta[4, 5]furo[3,2-c]chromen-6-one (**43**)*

Light yellow solid; mp: 125-126 °C; **IR** ($\nu_{max,}$ KBr): 3107, 2966, 1708 (C=O), 1643 (C=C), 1604, 1404, 1325, 893, 750 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.70 (1H, dd, *J* = 7.6, 1.2 Hz), 7.57 (1H, td,

J = 7.8, 1.6 Hz, ArH), 7.38 (1H, d, *J* = 8.8 Hz), 7.30 (2H, m), 7.10 (1H, dd, *J* = 3.6, 1.2 Hz), 7.00 (1H, dd, *J* = 5.2, 4.0 Hz), 4.01 (1H, d, *J* = 7.6 Hz), 2.67 (1H, dd, *J* = 14.0, 6.0 Hz), 2.28 (1H, td, *J* = 13.6, 6.4 Hz), 2.19-2.08 (2H, m), 1.97-1.94 (1H, m), 1.76-1.70 (1H, m); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 25.07, 32.70, 42.55, 53.05, 103.19, 105.02, 112.64, 117.20, 123.32, 124.08, 124.16, 125.89, 127.31, 132.63, 146.14, 155.27, 160.76 (C6), 165.66 (C10a); **LC/MS**, (ESI, m/z): 311.34 (MH^+, 100); **Anal. Calcd. for** $C_{18}H_{14}O_3S$: C 69.66, H 4.55, S 10.33. **Found**: C 69.02, H 4.67, S 9.06.

*4.3.1.44 10a-(2-Thenyl)-6b,7 8 9 10,10a-hexahydro-6H-benzofuro[3, 2-c]chromen-6-one (**44**)*

Light yellow oil; **IR** ($\nu_{max,}$ KBr): 2937, 2860, 1720 (C=O), 1639 (C=C), 1604, 1404, 1028 (C-O-C), 754 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.70 (1H, dd, *J* = 7.6, 1.6 Hz), 7.54 (1H, td, *J* = 8.0, 1.6 Hz, ArH), 7.36 (1H, d, *J* = 7.6 Hz, ArH), 7.29-7.25 (2H, m, ArH), 7.16 (1H, dd, *J* = 3.6, 1.2 Hz), 7.00 (1H, dd, *J* = 5.2, 3.6 Hz), 3.85 (1H, t, *J* = 6.4 Hz), 2.30-2.27 (2H, m), 2.25-2.28 (1H, m), 1.99-1.93 (1H, m), 1.68-1.63 (1H, m), 1.60-1.49 (3H, m); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 19.09, 19.26, 23.73, 34.23, 46.65, 94.22, 105.66, 113.06, 117.13, 123.05, 124.14, 124.50, 125.72, 127.19, 132.60, 147.64, 155.28, 160.61 (C6), 165.59 (C11a); **LC/MS** (ESI, m/z): 325.37 (MH^+, 100); **Anal. Calcd. for** $C_{19}H_{16}O_3S$: C70.35, H 4.97, S 9.88. **Found**: C 70.09, H 4.71, S 9.73.

*4.3.1.45 3-Methyl-5a-(2-thenyl)-5a, 7, 8, 8a-tetrahydro-1H,6H-cyclopenta[4,5]furo[3 2-c]pyran-1-one (**45**)*

Light yellow oil; **IR** ($\nu_{max,}$ KBr): 3089, 2968, 1710 (C=O), 1637 (C=C), 1577, 1446, 1278, 977, 920, 700 cm^{-1}; **^{1}H NMR**(400 MHz, $CDCl_3$), δ (ppm): 7.25 (1H, dd, *J* = 5.2, 1.2 Hz), 7.00 (1H, dd, *J* = 4.0, 1.2 Hz), 6.95 (1H, dd, *J* = 5.2, 3.6 Hz), 5.90 (1H, s), 3.83 (1H, d, *J* = 8.0 Hz), 2.50 (1H, dd, *J* = 14.4, 6.0 Hz), 2.22 (3H, s), 2.15 (1H, td, *J* = 12.8, 6.4 Hz), 2.06-1.95 (2H, m), 1.89-1.85 (1H, m), 1.67-1.60 (1H, m); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 20.63, 24.92, 32.59, 42.37, 51.93, 95.71, 102.42, 102.48, 123.89, 125.70, 127.23, 146.23, 162.15, 165.61, 170.28; **LC/MS** (ESI, m/z) : 275.60 (MH^+, 100); **Anal. Calcd. for** $C_{15}H_{14}O_3S$: C 65.67, H 5.14, S 11.69. **Found**: C 65.41, H 4.97, S 11.57.

*4.3.1.46 3-Methyl-5a-(2-thenyl)-5a,6,7, 8, 9,9a-hexahydro-1H-pyrano[4, 3-b]benzofuran-1-one (**46**)*

Light yellow oil; **IR** ($\nu_{max,}$ KBr): 3091, 2937, 1708 (C=O), 1633 (C=C), 1575, 1446, 979, 748, 700 cm^{-1}; **^{1}H NMR**(400 MHz, $CDCl_3$), δ (ppm): 7.28 (1H, dd, *J* = 4.8, 1.2 Hz, ArH), 7.11 (1H, dd, *J* = 3.6, 1.2 Hz, ArH), 6.99 (1H, dd, *J* = 4.8, 3.6 Hz, ArH), 5.95 (1H, s), 3.70 (1H, t, *J* = 5.2 Hz), 2.25 (3H, s), 2.21-2.11 (3H, m), 1.90-1.84 (1H, m), 1.58-1.65 (1H, m), 1.46-1.56 (3H, m); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 19.01, 19.24, 20.68, 23.53, 34.11, 45.56, 93.46, 96.28, 102.77, 124.37, 125.58, 127.10, 147.61, 162.07, 165.78, 170.19; **LC/MS**, (ESI, m/z) : 289.61 (M^++H, 100); **Anal. Calcd. for** $C_{16}H_{16}O_3S$: C 66.64, H 5.59, S 11.12. **Found**: C 66.46, H 5.37, S 11.01.

*4.3.1.47 5-Methyl-9a-(2-thenyl)-5,6b, 7, 8,9,9a-hexahydro-6H-cyclopenta[4, 5]furo[3, 2-c]quinolin-6-one (**47**)*

Light yellow oil; **IR** ($\nu_{max,}$ KBr): 2972, 2939, 1658 (C=O), 1637 (C=C), 1597, 1068 (C-O-C), 702 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.80 (1H, dd, *J* = 7.6, 1.6 Hz, ArH), 7.56 (1H, td, *J* = 8.0, 1.6 Hz, ArH), 7.36 (1H, d, *J* = 8.4 Hz, ArH), 7.25-7.20 (2H, m), 7.07 (1H, dd, *J* = 4.0, 1.2 Hz), 6.96 (1H, dd, *J* = 5.2, 3.6 Hz, ArH), 4.06 (1H, dd, *J* = 8.0, 2.0 Hz), 3.69 (3H, s), 2.63 (1H, dd, *J* = 13.6, 6.0 Hz), 2.25 (1H, td, *J* = 13.6, 6.0 Hz), 2.17-2.09 (2H, m), 1.92-1.89 (1H, m), 1.73-1.69 (1H, m); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 25.20, 29.21, 32.88, 42.86, 54.33, 101.34, 110.88, 112.57, 114.70, 121.79, 123.42, 123.68, 125.25, 127.13, 131.18, 140.92, 147.55, 161.40 (C6), 161.68 (C10a); **LC/MS**, (ESI, m/z): 324.70 (M^++H, 100); **Anal. Calcd. for** $C_{19}H_{17}NO_2S$: C70.56, H 5.30, N 4.33, S 9.91. **Found**: C 70.29, H 5.12, N 4.03, S 9.86.

*4.3.1.48 5-Methyl-10a-(2-thenyl)-6b,7, 8,9,10,10a-hexahydrobenzofuro[3,2-c]quinolin-6(5H)-one (**48**)*

Light yellow oil; **IR** ($\nu_{max,}$ KBr): 3093, 3062, 2939, 1649 (C=O), 1631 (C=C), 1593, 1305, 1157, 1101 (C-O-C), 742, 711 cm^{-1}; **^{1}H NMR**(400 MHz, $CDCl_3$), δ (ppm): 7.84 (1H, dd, *J* = 8.0, 1.2 Hz, ArH), 7.56 (1H, td, *J* = 7.8, 1.6 Hz, ArH), 7.35 (1H, d, *J* = 8.4 Hz, ArH), 7.24-7.20 (2H, m), 7.12 (1H, dd, *J* = 4.0, 1.2 Hz, ArH), 6.95 (1H, dd, *J* = 5.2, 3.6 Hz, ArH), 3.87 (1H, t, *J* = 5.6 Hz), 3.68 (3H, s), 2.32 (1H, dt, *J* = 14.4, 6.4 Hz, ArH), 2.26-2.04 (3H, m), 1.67-1.59 (2H, m), 1.56-1.50 (2H, m); **^{13}C NMR** (100 MHz, $CDCl_3$), δ

(ppm): 19.34, 19.48, 24.53, 29.12, 34.56, 47.75, 92.44, 111.98, 113.11, 114.68, 121.77, 123.43, 123.74, 124.90, 126.94, 131.14, 140.92, 149.62, 161.47, 161.48; **LC/MS**, (ESI, m/z) : 338.72 (MH^+, 100); **Anal. Calcd. for** $C_{20}H_{19}NO_2S$: C71.19, H 5.68, N 4.15, S 9.50. **Found**: C 71.01, H 5.43, N 3.98, S 9.36.

*4.3.1.49 4-Hydroxy-3-[2-(2-thenyl)cyclopent-1-en-1-yl]-2H-chromen-2-one (**49**)*

Colorless solid; mp: 198-200 °C; **IR** ($\nu_{max,}$ KBr): 3101, 3077, 2948, 1665 (C= O), 1601 (C= C), 1557, 1495, 1107, 754; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.90 (1H, dd, *J* = 8.0, 1.6 Hz), 7.67 (1H, td, *J* = 7.8, 1.6 Hz, ArH), 7.39-7.35 (2H, m, ArH), 7.26 (1H, dd, *J* = 5.2, 1.2 Hz), 7.02 (1H, dd, *J* = 3.6, 1.2 Hz), 6.95 (1H, dd, *J* = 5.2, 3.6 Hz, ArH), 3.00-2.88 (4H, m), 2.65-2.61 (2H, m); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 22.31, 37.19, 37.34, 103.20, 114.68, 116.70, 123.75, 124.02, 126.53, 126.59, 126.76, 126.95, 132.48, 137.51, 137.59, 153.25, 159.31, 160.96; **LC/MS** (ESI, m/z): 311.60 (MH^+, 100); **Anal. Calcd. for** $C_{18}H_{14}O_3S$: C 69.66, H 4.55, S 10.33. **Found**: C 69.02, H 4.67, S 9.06.

*4.3.1.50 4-Hydroxy-3-[2-(2-thenyl)cyclohexen-1-yl]-2H-chromen-2-one (**50**)*

Colorless solid; mp: 162-163 °C; **IR** ($\nu_{max,}$ KBr): 3210, 2940, 2920, 1678 (C=O), 1603, 1633, 1177 (C-O-C), 757, 699 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$), δ (ppm): 7.75 (1H, dd, *J* = 8.0, 1.6 Hz), 7.54 (1H, td, *J* = 8.4, 1.6 Hz, ArH), 7.35 (1H, d, *J* = 8.4 Hz), 7.26 (1H, td, *J* = 8.0, 0.8 Hz, ArH), 7.09 (1H, dd, *J* = 5.2, 1.6 Hz), 7.03 (1H, dd, *J* = 3.6, 1.6 Hz), 6.86 (1H, dd, *J* = 4.8, 4.0 Hz), 6.43 (1H, s, OH), 2.78-2.20 (2H, m), 2.58-2.52 (1H, m), 2.05-1.97 (2H, m), 1.86-1.76 (3H, m); **^{13}C NMR** (100 MHz, $CDCl_3$), δ (ppm): 22.22, 22.91, 29.63, 31.12, 107.62, 114.77, 116.62, 123.70, 123.87, 124.84, 125.61, 125.75, 126.57, 132.23, 134.33, 142.03, 153.15, 158.39, 161.52; **LC/MS** (ESI, m/z): 325.80 (MH^+, 100); **Anal. Calcd. for** $C_{19}H_{16}O_3S$: C70.35, H 4.97, S 9.88. **Found**: C 70.03, H 4.71, S 9.69.

4.4. *Evaluation of in vitro antimicrobial activity*

Escherichia coli ATCC 25922, *Micrococcus luteus* M3, *Bacillus cereus* B9, *Bacillus licheniformis* M30, *Staphylococcus aureus* ATCC 6538, *Bacillus subtilis* B1, *Pseudomonas aeruginosa* P7 were the test microorganisms used in the study. Muller-Hinton agar was sterilized at 121 °C, 1.5 atm for 15 min, and poured into each sterile petri dish (20 mL). These petri dishes were seeded with 500 µL of bacteria, that had been previously awakened in a Nutrient-Broth medium at 37 °C for 48 hours, and spread.Bacteria were allowed to grown on solid medium and the prepared sterile discs were placed on the medium. 5

mg/mL of the compounds to be investigated for antimicrobial activity were filtered with a pore size of 0.45 mm and dissolved in DMSO. 50 mL of componds were dropped onto discs and petri dishes were incubated at 37 ^{o}C for 24 hours. Finally, the measurements obtained.

Conflicts of interest

There are no conflicts of interest to declare.

Acknowledgments

This work was supported by a research grant from the Scientific and Technical Research Council of Turkey (TBAG-2380, 103T124) and Ankara University BAP (10B4240006).

Appendix A. Supplementary data

NMR spectra of synthesized compounds; ORTEP view, crystallographic data and explanations for compounds **37** (PDF).

References

1. (a) B. R McDonald, K.A. Scheidt, *Acc. Chem. Res.,* 2015, **48**, 1172-1183; (b) T. Narender, S. Sarkar, V. Kand, J.K. Kumar, *Tetrahedron Lett.,* 2010, **51**, 6576-6579.

2. (a) M. A. Musa, J.S. Cooperwood and M.O.F. Khan, *Curr. Med. Chem.,* 2008, **15**, 2664-2679; (b) J. Moreau, C. Hubert, J. Batany, L. Toupet, T. Roisnel, J.P. Hurvois and J.L. Renaud, *J. Org. Chem.,* 2009, **74**, 8963-8973; (c) P. Borah, P.S. Naidu and P.J. Bhuyan, *Tetrahedron Lett.,* 2012, **53**, 5034-5037; (d) P. Borah, P.S. Naidu, S.nMajumder and P.J. Bhuyan, *RSC Adv.,* 2013, **3**, 20450-20455; (e) R. Grigg, M. Nurnabi, and A. Sarkar, *Tetrahedron,* 2004, **60**, 3359-3373; (f) D. Yu, M. Suzuki, L. Xie , S.L. Morris-Natschke and K.H. Lee, *Medicinal Res. Rev.,* 2003, **23**, 322-345; (g) R. Gali, J. Banothu, M. Porika, R. Velpula, R. Bavantula and S. Abbagani *RSC Adv.,* 2014, **4**, 53812-53819.

3. (a) K. Pam, Z. Zhang, S. Shen, L. Ma, L. Hu, *Tetrahedron,* 2013, **69**, 10933-10939; (b) J.C Jung., J.H. Lee, S. Oh, J.G. Lee, O.S. Park, *Bioorg. Med. Chem. Lett.,* 2004, **14**, 5527-5531; (c) J. Groverand, S.M. Jachak, *RSC Adv.,* 2015, **5**, 38892-38905; (d) L.C. Rao, N.S. Kumar, V. Dileepkumar, U.S.N. Murthyand, H.M. Meshram, *RSC Adv.,* 2015, **5**, 28958-28964; (e) R. Gondru, J. Banothu, R.K. Thatipamula, R. Bavantula, *RSC Adv.,* 2015, **5**, 33562-33569; (f) S. Stanchev, G. Momekov, F. Jensenand, I. Manolov, *Eur. J. Med. Chem.*, 2008, **43**, 694-706.

4. (a) S. Qiu, X. Li, W. Xiong, L. Xie, L. Guo, Z. Lin, B. Qiuand, G. Chen, *Biosens Bioelectron,* 2013, **41**, 403-408; (b) S.H. Su and D.Y. Yang, *ARKIVOC*, 2012, 253-263; (c) S.B Phadtare, K.J. Jaragand and G.S. Shankarling, *Dyes and Pigments*, 2013, **97**, 105-112; (d) M. Saleemand, K.H. Lee, *RSC Adv.,* 2015, **5**, 72150-72287.

5. (a) K.A Nolan., J.R. Doncaster, M.S. Dunstan, K.A. Scott, A.D. Frenkel, D. Siegel, D. Ross, J. Barnes, C. Levy, R.C. Whitehead, I.J. Stratfordand, R.A.Bryce, *J. Med. Chem.,* 2009, **52**, 7142-7156; (b) S. Stanchev, V. Hadjimitova, T. Traykov, T. Boyanovand, I. Manolov, *Eur. J. Med.Chem.,* 2009, **44**, 3077-3082; (c) I. Manolov, C.M. Moessmerand, N. Danchev, *Eur J. Med. Chem*., 2006, **41**, 882-890.

6. (a) S.M. Prajapati, K.D. Patel, R. H. Vekariya, S. N. Panchaland, H. D. Patel, *RSC Adv.,* 2014, **4**, 24463-24476; (b) A Marella., O.P. Tanwar, R. Saha, M.R. Ali, S. Srivastava, M. Akhter, M. Shaquiquzzamanand, M. M. Alam, *Saudi Pharma J.,* 2013, **21**, 1-12; (c) R. Musiol, T. Magdziarzand, A. Kurczyk, *Formatex*, 2011, **b1**, 72-83; (d) J. Michael, *Nat. Prod. Rep.,* 2004, **21**, 650-668.

7. (a) D.K. Barange, V. Kavala, C.W. Kuo, P.M. Leiand, C.F. Yao, *Tetrahedron*, 2011, **67**, 2870-2877; (b) G. Bar, A.F. Parsons, C.B. Thomas, *Tetrahedron*, 2001, **57**, 4719-4728; (c) I. Butenschön, K. Möllerand, W. Hansel, *J. Med. Chem.,* 2001, **44**, 1249-1256; (d) J.P.Michael, *Nat. Prod. Rep.,* 2002, **19**, 742-760; (e) P. Fossa, L. Mosti, G. Menozzi, C. Marzano, F. Baccichettiand, F. Bordin, *Bioorg. Med. Chem.,* 2002, **10**, 743-751; (f) J. P. Michael, *Nat. Prod. Rep.,* 2003, **20**, 476-493.

8. (a) C. Medower, L. Wen, W.W. Johnson, *Chem. Res. Toxicol.,* 2008, **21**, 1570-1577; (b) G.,Wu S.C. Vashishthaand, J.C.L. Erve, *Chem. Res. Toxicol.,* 2010, **23**, 1393-1404; (c) D. Gramec, L.P. Masicand, M. S. Dolenc, *Chem. Res. Toxicol.,* 2014, **27**, 1344-1358.

9. (a) M. Mondal, U. Bora, *RSC Adv.,* 2013, **3**, 18716-18754; (b) A.S. Demir and M. Emrullaoglu, *Curr. Org. Chem.,* 2007, **4**, 223-237; (c) D. Ergüntürk, M. B. Gürdere, Y.Budak, M. Ceylan, *Synth Commun*., 2017, **47**, 1501–1506; (d) R. Caliskan, A. T. Pekel, W. H. Watson, M. Balci, *Tetrahedron Lett.*, 2005, **46**, 6227-6230. (e) Deliomeroglu M. K.; Dengiz C.; Calıskan R.; Balci M. *Tetrahedron,* 2012, **68**, 5838-5844; (f) R.Çalışkan, N. Nohut, Ö. Yılmaz, E. Sahin, M. Balci, *Tetrahedron*, 2017, **73**, 291-297; (g) W. Yuan, Y. Wei, M. Shi, *Tetrahedron*, 2011, **67**, 7139-7142; (h) M. Furuta, K. Hanaya, T. Sugai, M. Shoji, *Tetrahedron*, 2017, **73**, 2316-2322; (i) E. I. Heiba, R. M. Dessau, *J. Org. Chem.*, 1974, **39**, 3456-3457.

10. (a) T. Huynh, V. Nguyen, and H. Nishino, *Tetrahedron*, 2017, **58**, 3619-3622; (b) C. Matsumoto, K. Yasutake, H. Nishino, *Tetrahedron*, 2016, **72**, 6963-6972; (c) C. Akazaki, S. Kawabata, H. Nishino, Molbank, 2016, **4**, M913, doi:10.3390/M913; (d) Ito Y, Yoshinaga T, and Nishino H. *Tetrahedron*, 2010, **66**, 2683-2694. (e) M. A. Haque, H. Nishino, *J. Heterocycl. Chem.,* 2014, **51**, 579-585; (f) Y. Maemura, Y. Tanoue, H. Nishino, *Heterocycles,* 2012, **85**, 2491-2503; (g) M. A. Haque, H. Nishino, *Heterocycles,* 2011, **83**, 1783-1805; (h) Y. Ito, S. Jogo, N. Fukuda, R. Okumura, H. Nishino, *Synthesis,* 2011, **9**, 1365-1374; (i) Y. Ito, Y. Tomiyasu, T. Kawanabe, K. Uemura, Y. Ushimizu, H. Nishino, *Org. Biomol. Chem*., 2011, **9**, 1491−1507; (j) H. Nishino, *Bull. Chem. Soc. Jpn.*, 1986, **59**, 1733-1739; (k) J. Sasaki, M. Kobayashi, Y. Ibe, H. Nishino, *Heterocycles*, 2019, **99,** in press, DOI: 10.3987/COM-18-S(F)62.

11. (a) R. Matsumoto , H. Nishino, *Synth. Commun.,* 2015, **45**, 1807-1816; (b) E. Biçer, M. Yılmaz, M., E.V. Burgaz and A.T. Pekel, *Helv. Chim. Acta.,* 2013, **96**, 135-141; (c) N. Kikue, T. Takahashi, H. Nishino, *Heterocycles*, 2015, **90**, 540-562; (d) M. Yılmaz, E.V. Burgaz, M. Yakut and E. Biçer, *J. Chin. Chem., Soc.,* 2014, **61**, 1101-1107; (e) E. Loğoğlu, M. Yılmaz, H. Katircioğlu, M. Yakut and S. Mercan, *Med. Chem. Res.,* 2010, **19**, 490-497; (f) A. Ustalar, M. Yılmaz, A. Osmani and S.A. Keçeli, *Turk. J. Chem.*, 2017, **41**, 80-88; (g) A. Ustalar, M. Yılmaz, *Tetrahedron Lett.,* 2017, **58**, 516-519; (h) O. Alagöz, M. Yılmaz, A.T. Pekel, C. Graiffand, R. Maggi, *RSC Adv.,* 2014, **4**, 14644-14654; (i) H. Aslan, D. A. Akpınar, A. Öktemer, M. Yakut and A. Alagöz, *Helv. Chim. Acta.,* 2014, **97**, 652-663; (j) H. Nishino, R.

Kumabe, R. Hamada, M. Yakut, *Tetrahedron*, 2014, **70**, 1437-1450; (k) M. Yılmaz, M. Yakut, and A. T. Pekel, *Synth. Commun.*, 2008, **38**, 914-927; (l) M. Özgür, M. Yılmaz, A.T. Pekel, *Commun.Fac.Sci.Univ.Ank.Series B*, 2017, **59**, 1-11; (m) H. Aslan, F. Eroğlu, M. Özgür, *Commun.Fac.Sci.Univ.Ank.Series B*, 2018, **60**, 17-24.

12. (a) K. Kobayashi, K. Sakashita, H. Akamatsu, K. Tanaka, M. Uchida, T. Uneda, T. Kitamura, O. Morikawa, H. Konishi, *Heterocycles*, 1999, **51**, 2881-2892; (b) C.B. Miao, R. Liu, Y.F. Sun, Q.X. Sun and H.T. Yang, *Tetrahedron Lett.*, 2017, **58**, 541-545; (c) M. Yilmaz, A. Ustalar, B. Uçan, and A.T. Pekel, *ARKIVOC*, 2016, **vi**, 79-91.

13. **CCDC-**1579314 contain the supplementary crystallographic data for the structure of compound **37**. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

14. M. Özyanık, S. Demirci, H. Bektaş, N. Demirbaş, A. Demirbaş, Ş. Karaoğlu, *Turk. J. Chem.*, 2012, **36**, 233-246.

15. A. Güvenç, A.T. Pekel, M. Koçkar, *Chem. Eng. J.,* 2004, **99**, 257-263.

16.(a) E. Ziegler. *Monath. Chem.,* 1961, **92**, 927-933; (b) K. Thomas, A..Rudolf, H. Peter, S.Wolfgang, *Journal für Practische Chemie*, 1994, **336**, 596-601.

17. (a) M.Yilmaz, *Tetrahedron*, 2011, **67**, 8255-8263; (b) V. Teresa, A. Belen, B. Rafael, A.Gregorio, *Chem. Ber.*, 1991, **124**, 1203 – 1206.18. Bruker (2012). *SADABS*. Bruker AXS Inc. Madison, Wisconsin, USA.

19. G. M. Sheldrick, *Acta Cryst,* 2008, **A64**, 112-122.

Scheme Captions

Scheme 1. Dihydrofuran-fused and 3-alkenyl-substituted pyranone, coumarin and quinolinone derivatives.

Scheme 2. The proposed mechanism for the formation of alkenyl-substituted compounds.

Scheme 3. Reaction of 4-hydroxycoumarin (**1a**) with **2j**.

Scheme 4. Ring-opening reaction of dihydrofuroquinolinone **31**.

Scheme 5. Ring opening reaction of compounds **49** and **50**

Table Captions

Table 1. Reaction of 4-hydroxycoumarin (**1a**) with 1,1-disubstituted alkenes **2a-e**.[a]

Table 2. Reaction of 4-hydroxy-6-methyl-2*H*-pyran-2-one (**1b**) with **2a-c.**[a]

Table 3. Reaction of **1c**, **d** with **2a-c.**

Table 4. Reaction of **1e** with **2a-c**.[a]

Table 5. Reactions of **1a-c** with **2f, g.**[a]

Table 6. Reactions of **1a, b, e** with **2h, i**.[a]

Table 7. Zone diameters (mm) of the compounds against bacteria.

Table 8. Zone diameters (mm) of antibiotics against bacteria[11g].

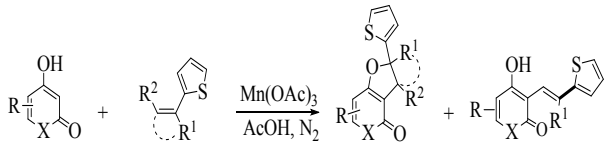
Table 9. MIC results (μg/mL).

Figure Caption

Fig. 1. The molecular entities of compound **37**, showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

Table of Contents

The syntheses, spectroscopic properties, and antimicrobial activities of new pyranones and quinoline-based dihydrofurans accompanied by 3-alkenyl-substituted structures were investigated.



Efficient Syntheses and Antimicrobial Activities of New Thiophene Containing Pyranone and Quinolinone Derivatives by Manganese(III) Acetate. The effect of Thiophene on Ring Closure-Opening Reactions

Mehtap Özgür[a*], Mehmet Yılmaz[b], Hiroshi Nishino[c], Eda Çinar Avar[d], Hakan Dal[e], A.Tarık Pekel[a], Tuncer Hökelek[f]

[a]Department of Chemistry, Ankara University, 06100 Ankara, TURKEY

[b]Department of Chemistry, Kocaeli University,41380 Kocaeli, TURKEY

[c]Department of Chemistry, Kumamoto University, Kurokami, Kumamoto 860-8555, JAPAN

[d]Department of Chemistry, Gazi University, 06500 Ankara, TURKEY

[e]Department of Chemistry, Anadolu University, 26470 Yenibağlar, Eskişehir, TURKEY

[f]Department of Physics, Hacettepe University, 06800 Beytepe, Ankara, TURKEY

*Corresponding author: mehtapyakut@gmail.com, Phone Number: +90 0312-212-67-20

Supplementary Materials

Contents

X-ray Crystallography data

The colourless block shaped crystals of the title compound **37** was crystallized from Hexane/Ethylacetate.at room temperature. Crystallographic data were recorded on a Bruker Kappa APEXII CCD area-detector diffractometer using Mo K_α radiation (λ=0.71073 Å) at T=296(2) K. Absorption correction by multi-scan [1] was applied. Structure was solved by direct methods and refined by full-matrix least squares against F^2 using all data [2]. All non-H atoms were refined anisotropically. Methine H atom was located in a difference Fourier map and refined freely. The remaining C-bound H-atoms were positioned geometrically with C---H = 0.93 and 0.96 Å for aromatic and methyl H-atoms, respectively, and constrained to ride on their parent atoms, with U_{iso} (H) = k x U_{eq}(C), where k = 1.5 for methyl H-atoms and k = 1.2 for aromatic H-atoms.

Crystal structure

In the molecule of the compound **37** (Fig. 1), the bond lengths and angles (Table 2) are generally within normal ranges. The benzene, A (C2-C7) and D (C11-C16), and the thiophene, E (S1/C18-C21), rings are planar, and they are oriented at dihedral angles of A/B = 62.67(4)°, A/E = 60.75(4)° and B/E = 24.44(4)°. But, ring B (C1/C2/C7/O1/C8/C9) is in flattened-boat conformation with puckering parameters of φ = -61.4(3)°, θ = 74.5(3)° and Q_T = 0.244(4) Å [**3**]. The furan, C (C1/C9/C10/C17/O2), ring is in envelope conformation with atom C10 at the flap position, and it is -1.1519(11) Å away from the best least-squares plane of the other four atoms. Atoms C10 and C17 are the chiral centres with chilarity S. In the crystal structure, intermolecular C-H … O hydrogen bonds (Table 3) link the molecules into infinite chains along the b-axis (Fig. 2), additional π … π contacts between the parallel benzene rings, A, Cg1 … $Cg1^i$ (where Cg1 is the centroid of ring A) may further stabilize the structure, with centroid-to-centroid distance of 3.6131(7) Å. A weak C-H … π interaction (Table 3) is also observed.

References

[1] Bruker (2012). *SADABS*. Bruker AXS Inc. Madison, Wisconsin, USA.

[2] Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112--122.

[3] Cremer, D & Pople, J.A. (1975). J. Amer. Chem. Soc. **97**, 1354-1358.

CCDC-1579314

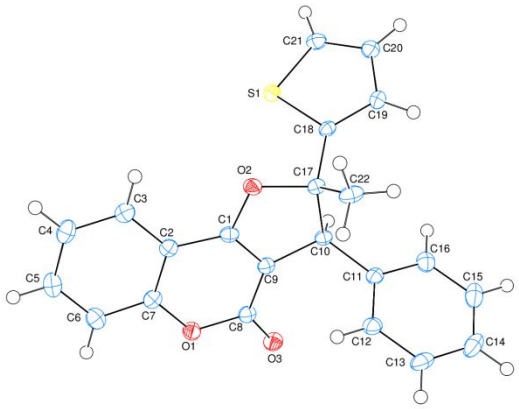


Figure 1. The molecular entities of the title compound, showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

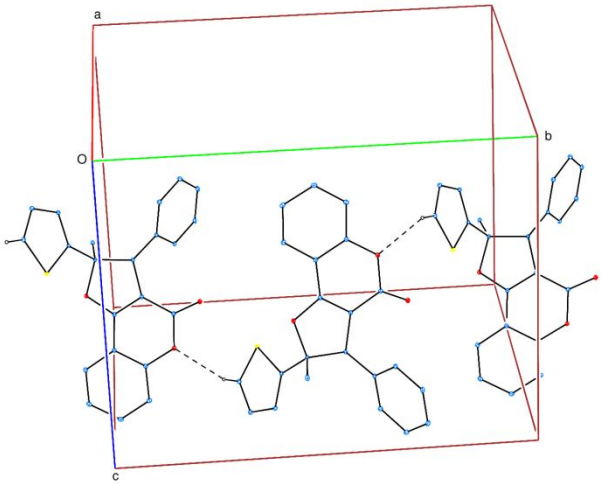


Figure 2. A partial packing diagram of the title compound. Intermolecular C-H …O hydrogen bonds are shown as dashed lines. Nonbonding H atoms have been omitted for clarity.

Table 1. Crystallographic data.	
Empirical Formula	$C_{22}H_{16}O_3S$
Fw	360.41
Crystal System	monoclinic
Space Group	*P* 2_1/c
a (Å)	9.9226 (2)
b (Å)	15.7155 (3)
c (Å)	11.5782 (2)
α (°)	90
β (°)	108.572 (3)
γ (°)	90
V (Å^3)	1711.47 (6)
Z	4
μ (MoKα) (mm^{-1})	0.21
ρ (calcd) (g cm^{-3})	1.399
Number of Reflections Total	16080
Number of Reflections Unique	4292
Number of Reflections Observed [$I > 2\sigma(I)$]	3772
R_{int}	0.019
$2\theta_{max}$ (°)	56.8
T_{min} / T_{max}	0.926 / 0.977
Number of Parameters	239
R [$F^2 > 2\sigma(F^2)$]	0.032
wR	0.084
S	1.03
$\Delta\rho_{max}$(e Å^{-3})	0.35
$\Delta\rho_{min}$(e Å^{-3})	−0.27

Table 2. The Selected Bond Lengths (Å) and Angles (deg).	
O1– C7	1.3749 (14)
O1– C8	1.3967 (14)
O2– C1	1.3414 (14)
O2– C17	1.4890 (14)
O3– C8	1.2068 (14)
S1– C18	1.7243 (11)
S1– C21	1.7114 (12)
C7– O1– C8	123.15 (9)
C1– O2– C17	107.94 (8)
O1– C8– O3	116.75 (10)
O3– C8– C9	128.05 (11)
O2–C17–C10	105.07 (8)
C18–S1– C21	91.93 (6)
S1–C18–C17	119.87 (8)
O2–C17–C18	105.77 (8)

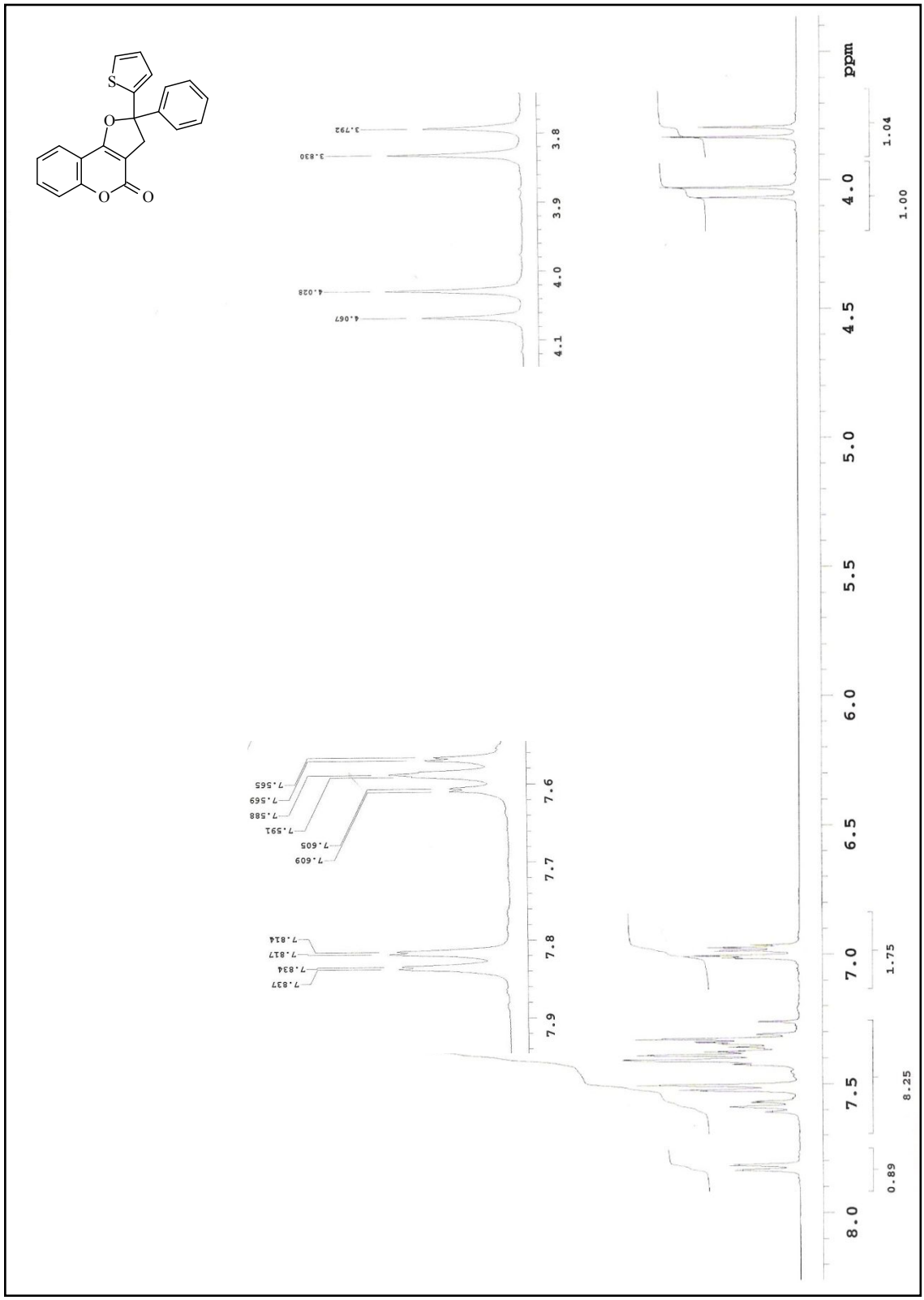
Table 3 Hydrogen-bond geometry (Å,°)

D-H ...A	**D-H**	**H ...A**	**D ...A**	**D-H ...A**
C21—H21···O1^{i}	0.93	2.43	3.2052 (16)	141
C13—H13···*Cg*1^{ii}	0.93	3.08	4.0018 (15)	173

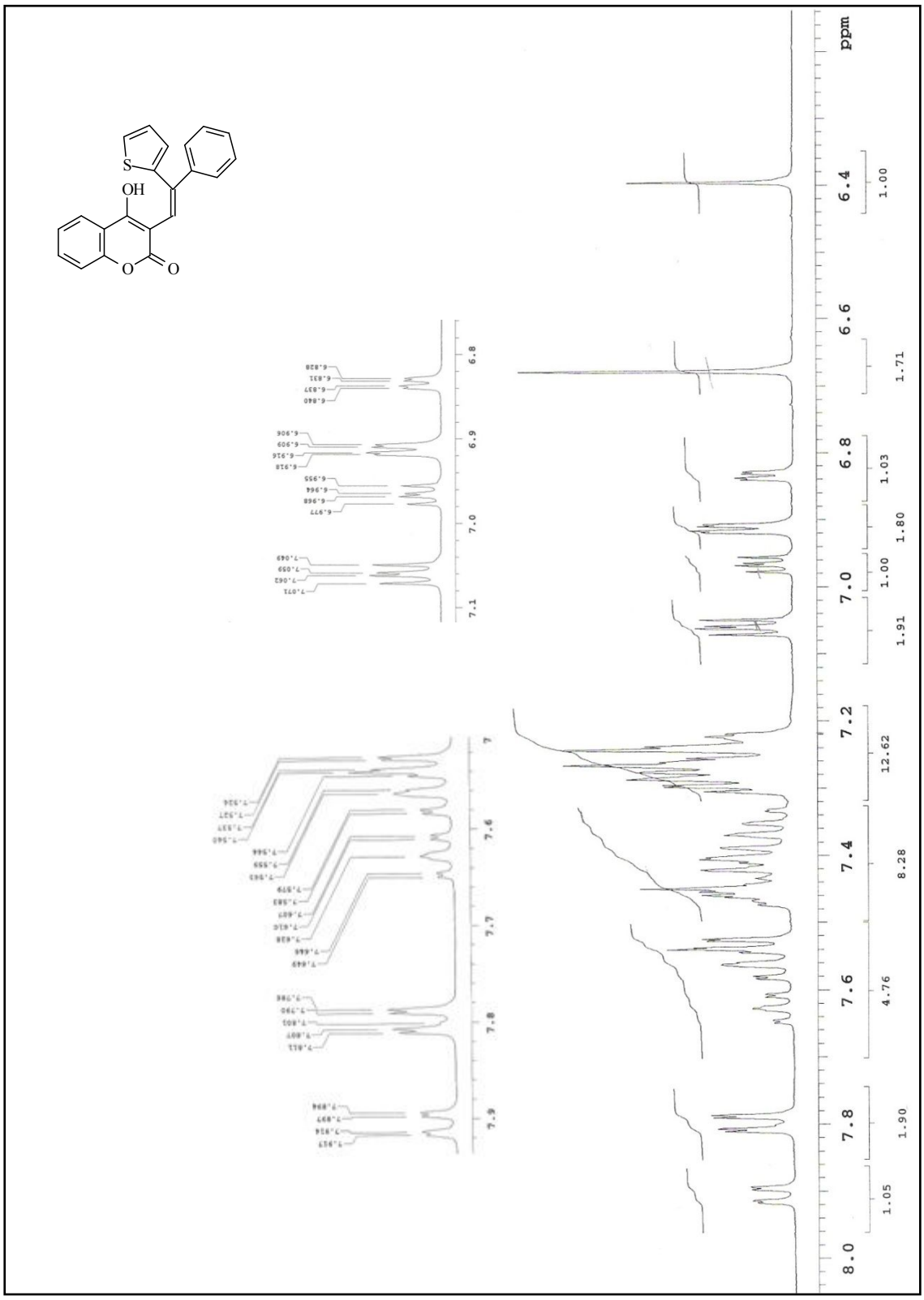
Symmetry codes: (i) −*x*+1, *y*+1/2, −*z*+1/2; (ii) −*x*+2, *y*+1/2, −*z*+3/2. Cg1 is the centroid of ring A (C2-C7).

^{1}H-NMR of COMPOUNDS

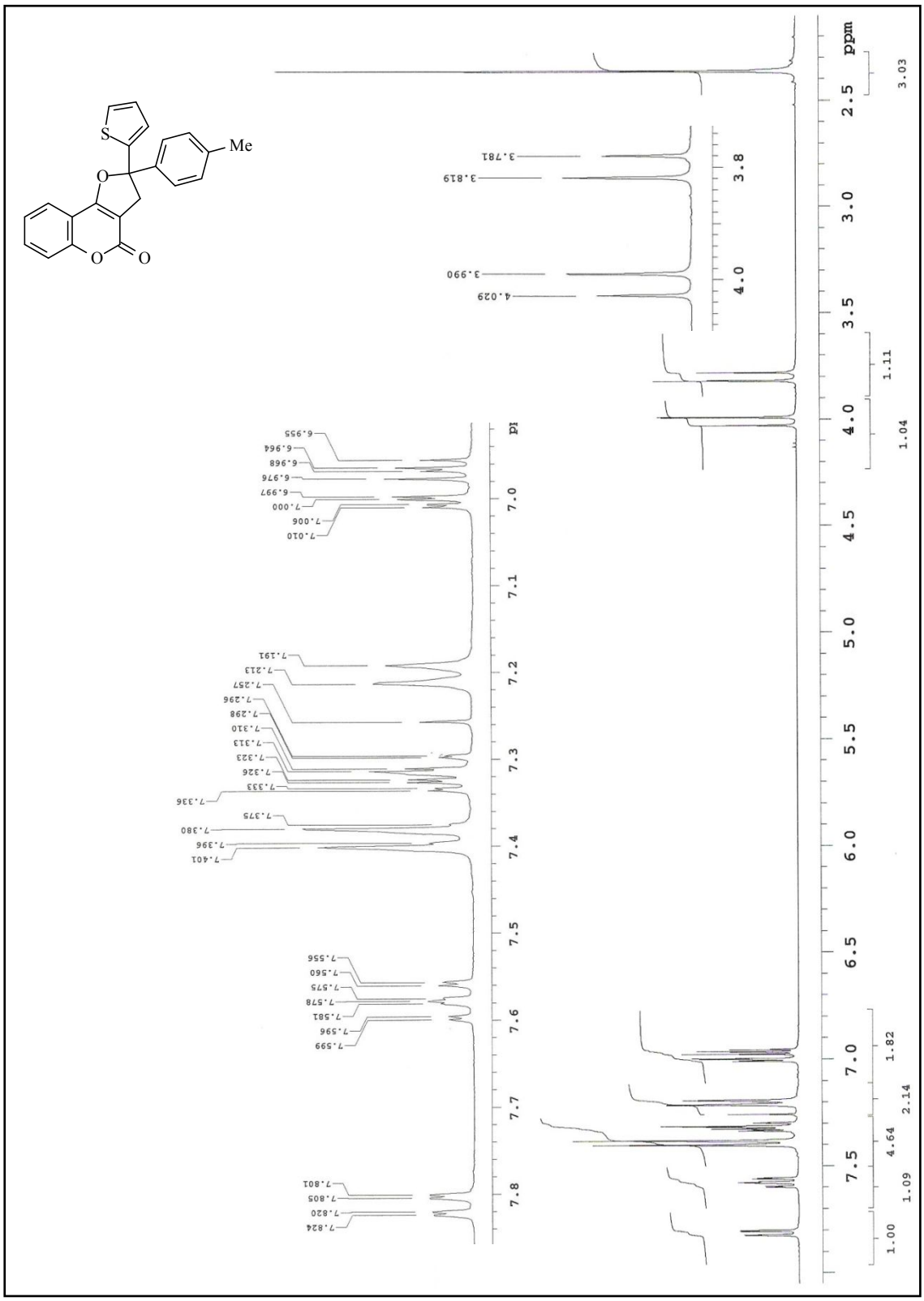
2.1 ^{1}H-NMR spectra of **3**



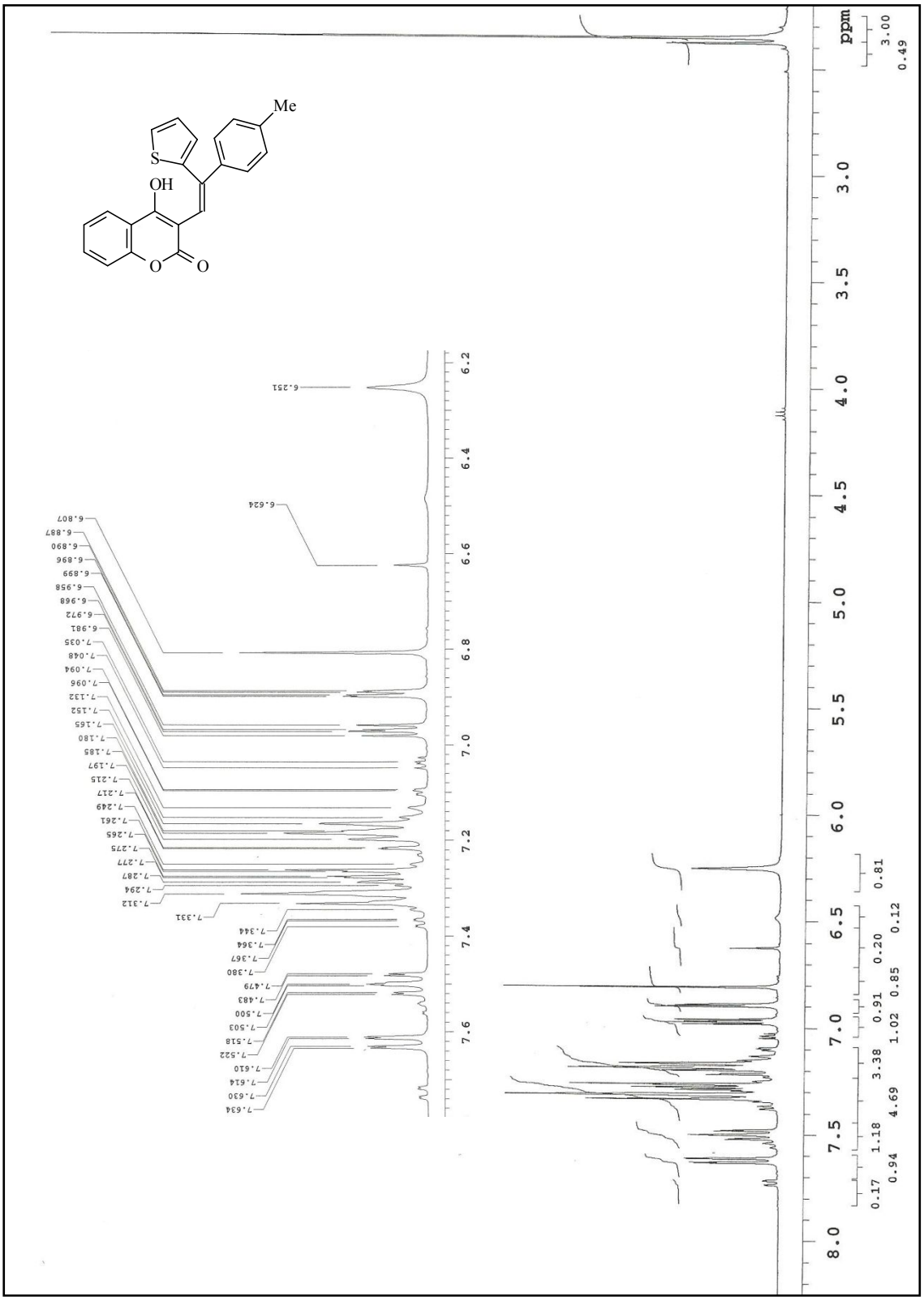
2.2 ^{1}H-NMR spectra of **8**



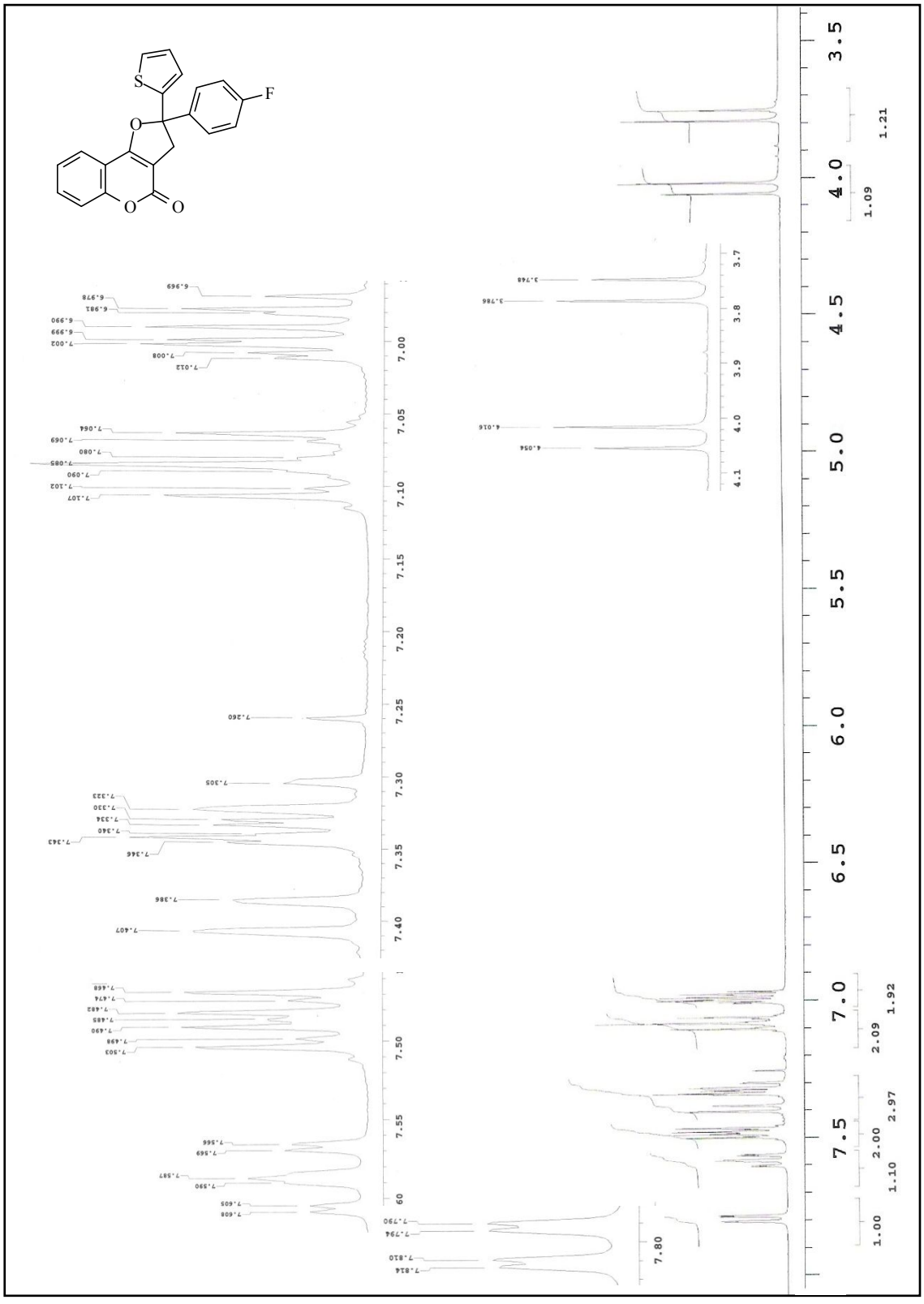
2.3 ^{1}H-NMR spectra of **4**



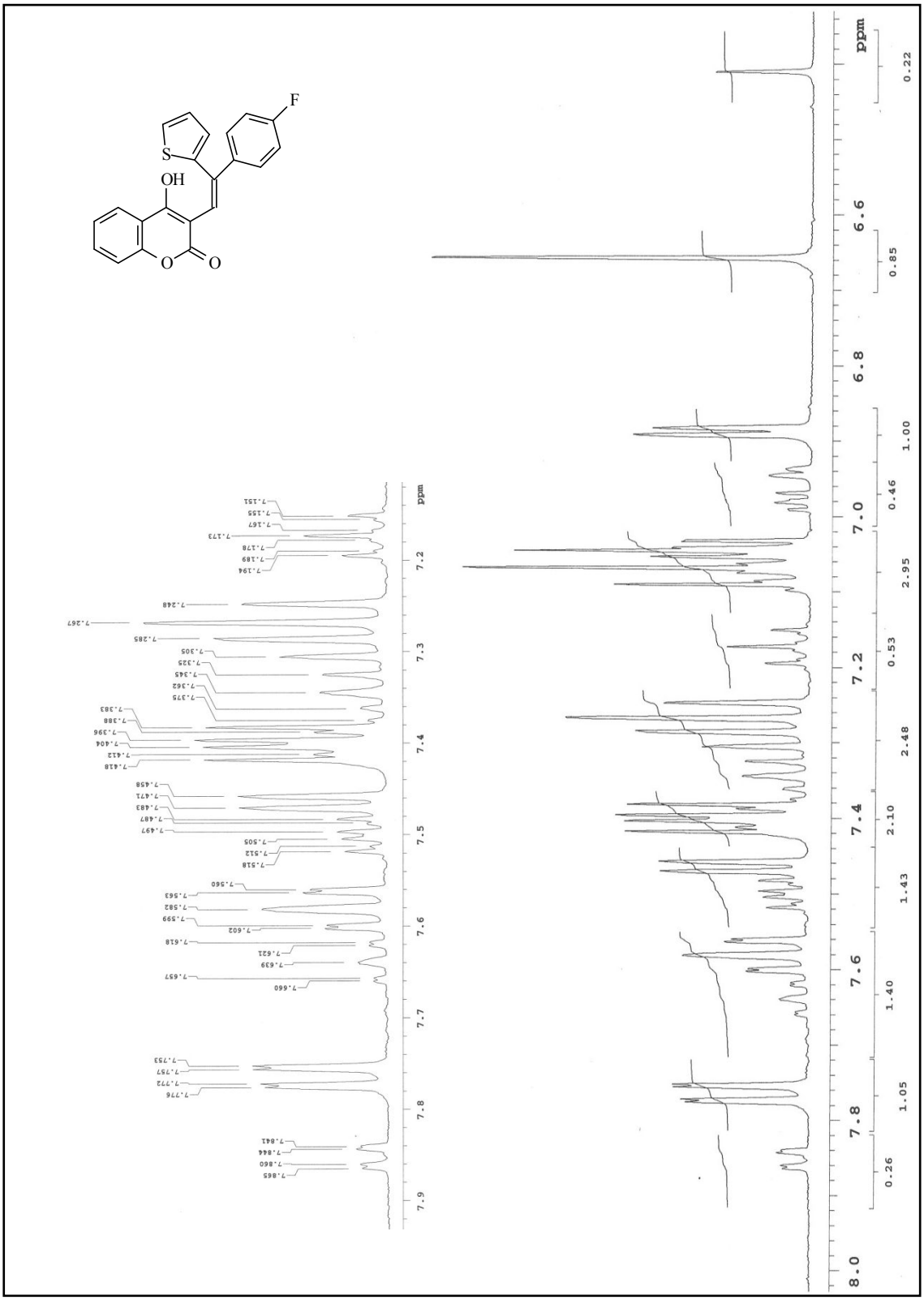
2.4 ^{1}H-NMR spectra of **9**



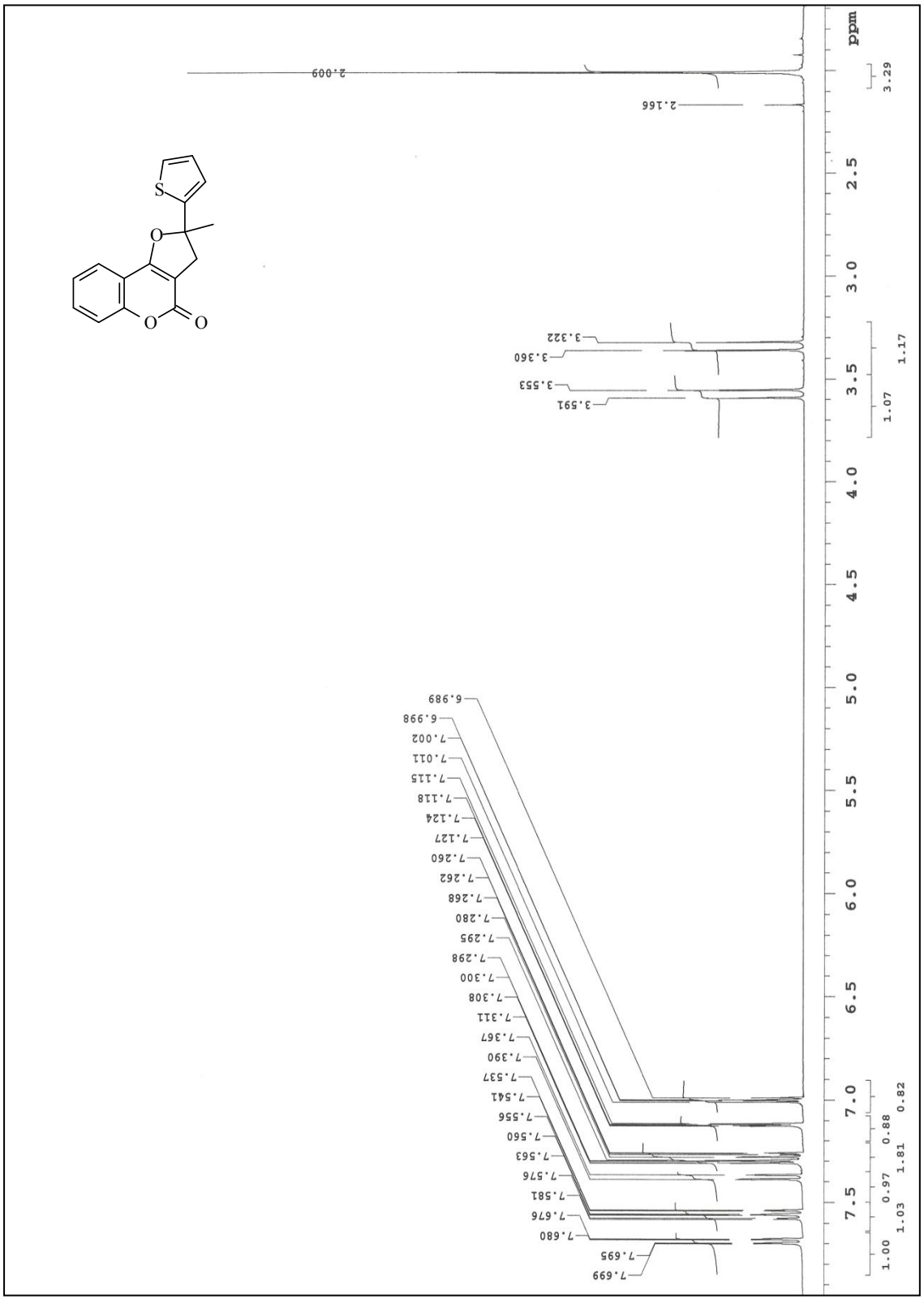
2.5 ^{1}H-NMR spectra of **5**



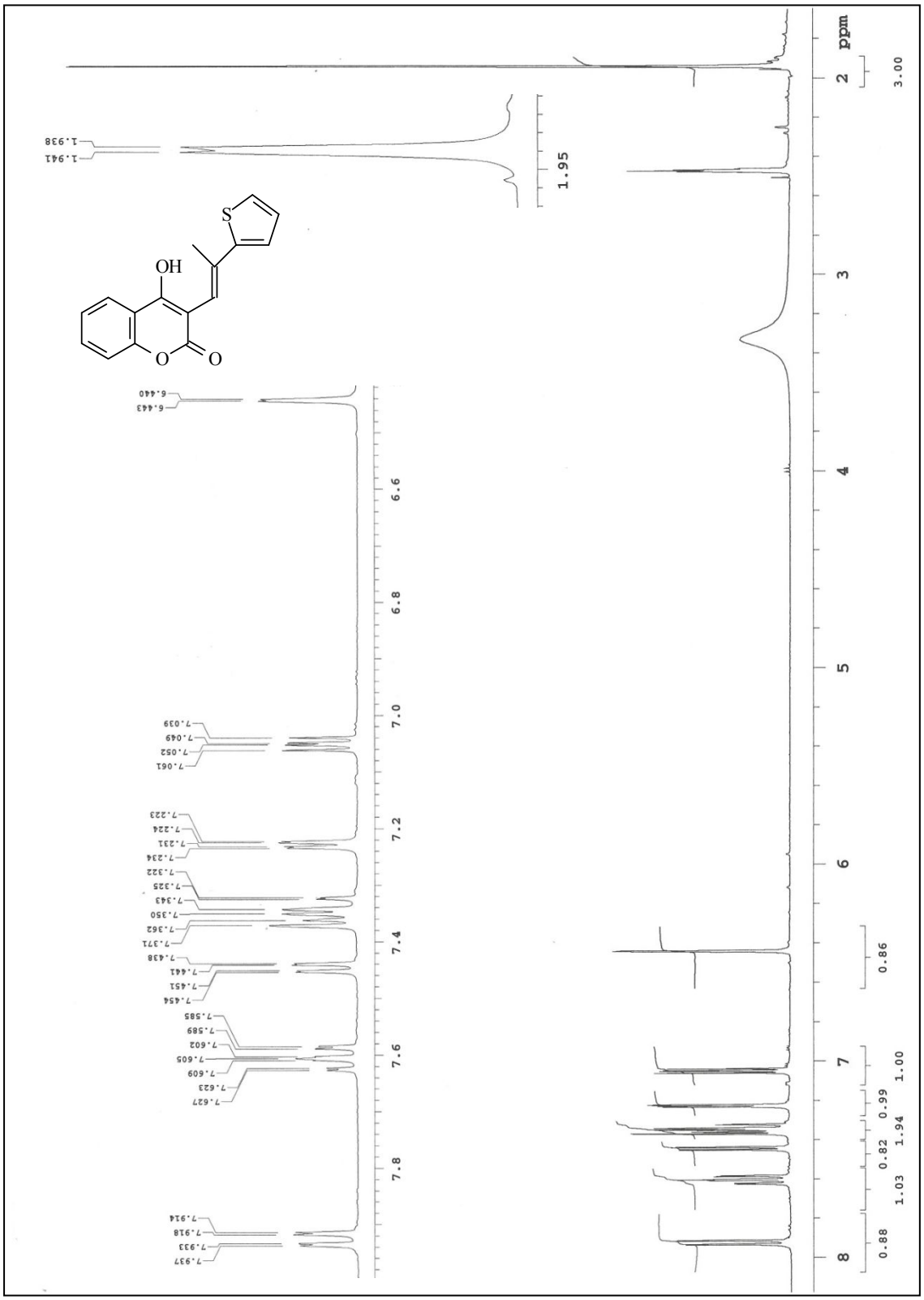
2.6 ^{1}H-NMR spectra of **10**



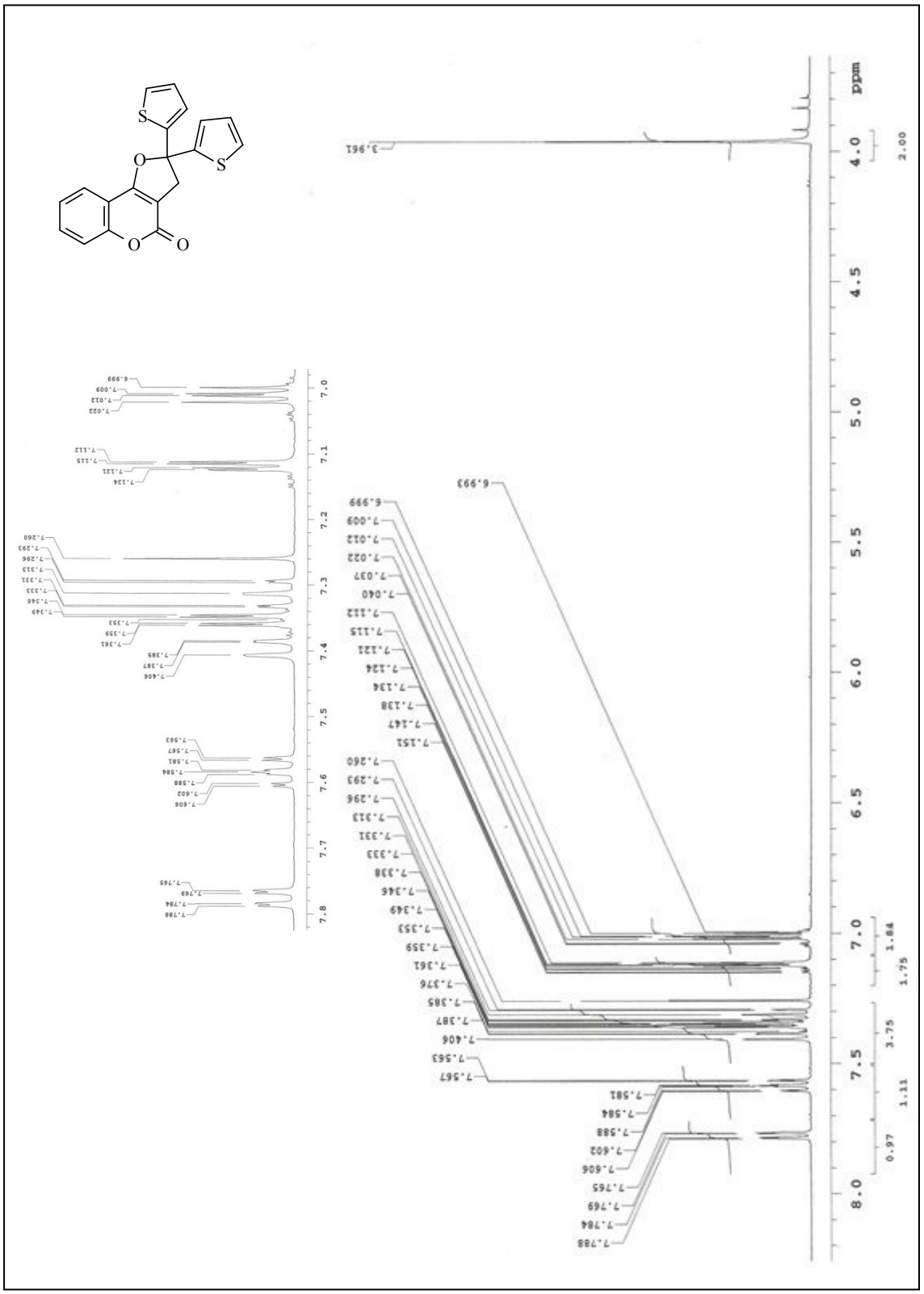
2.7 ^{1}H-NMR spectra of **6**



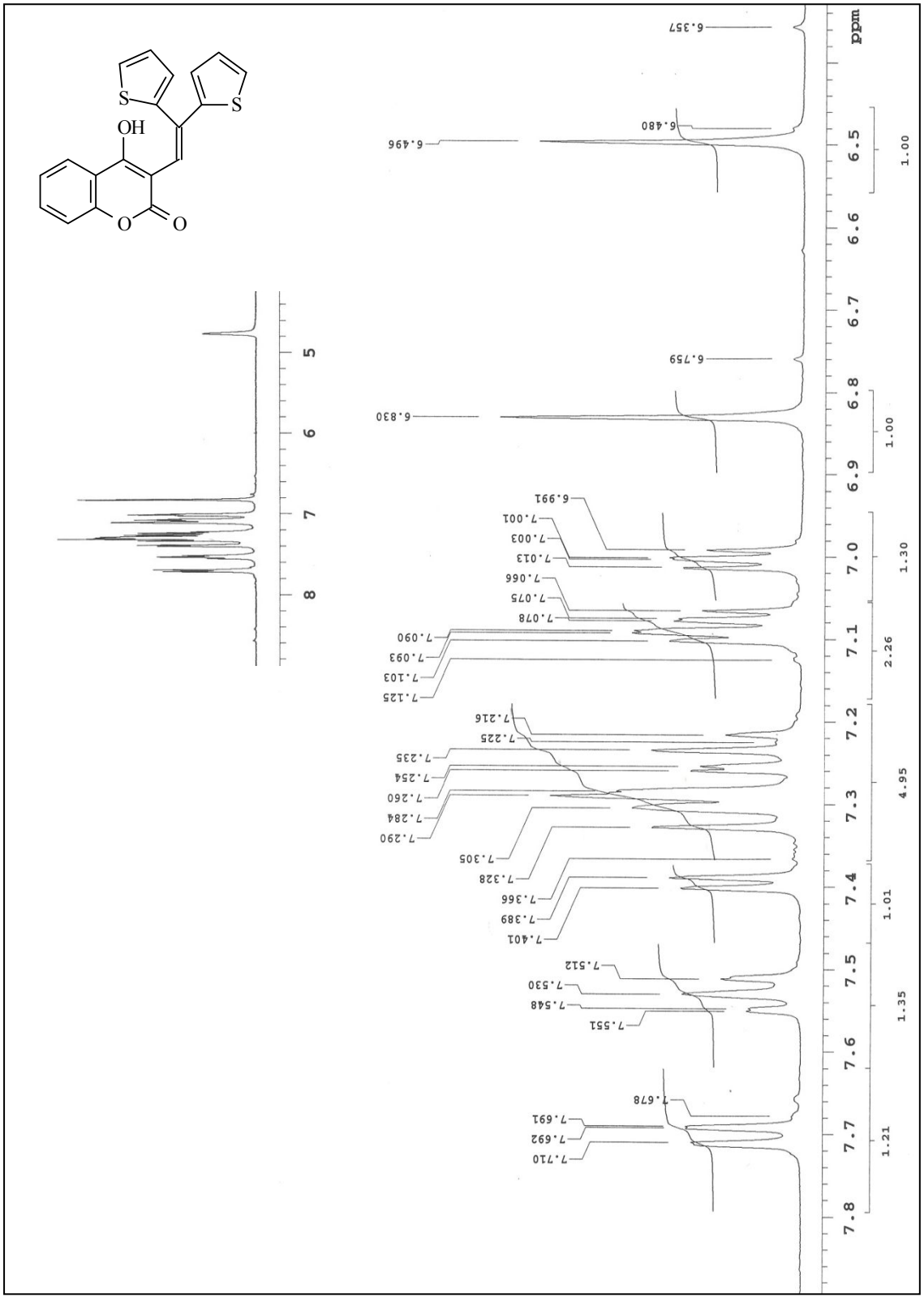
2.8 ^{1}H-NMR spectra of **11**



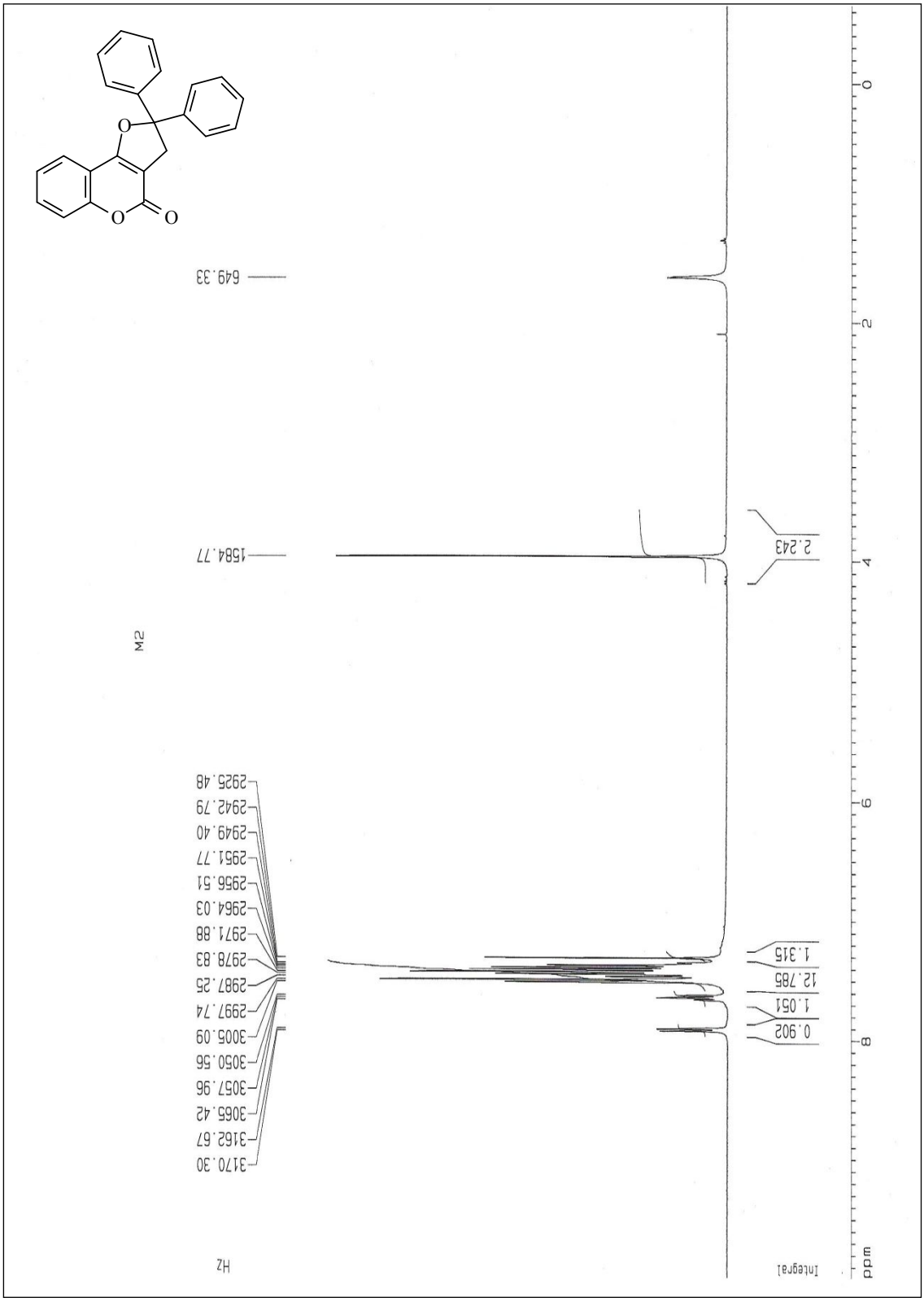
2.9 ^{1}H-NMR spectra of **7**



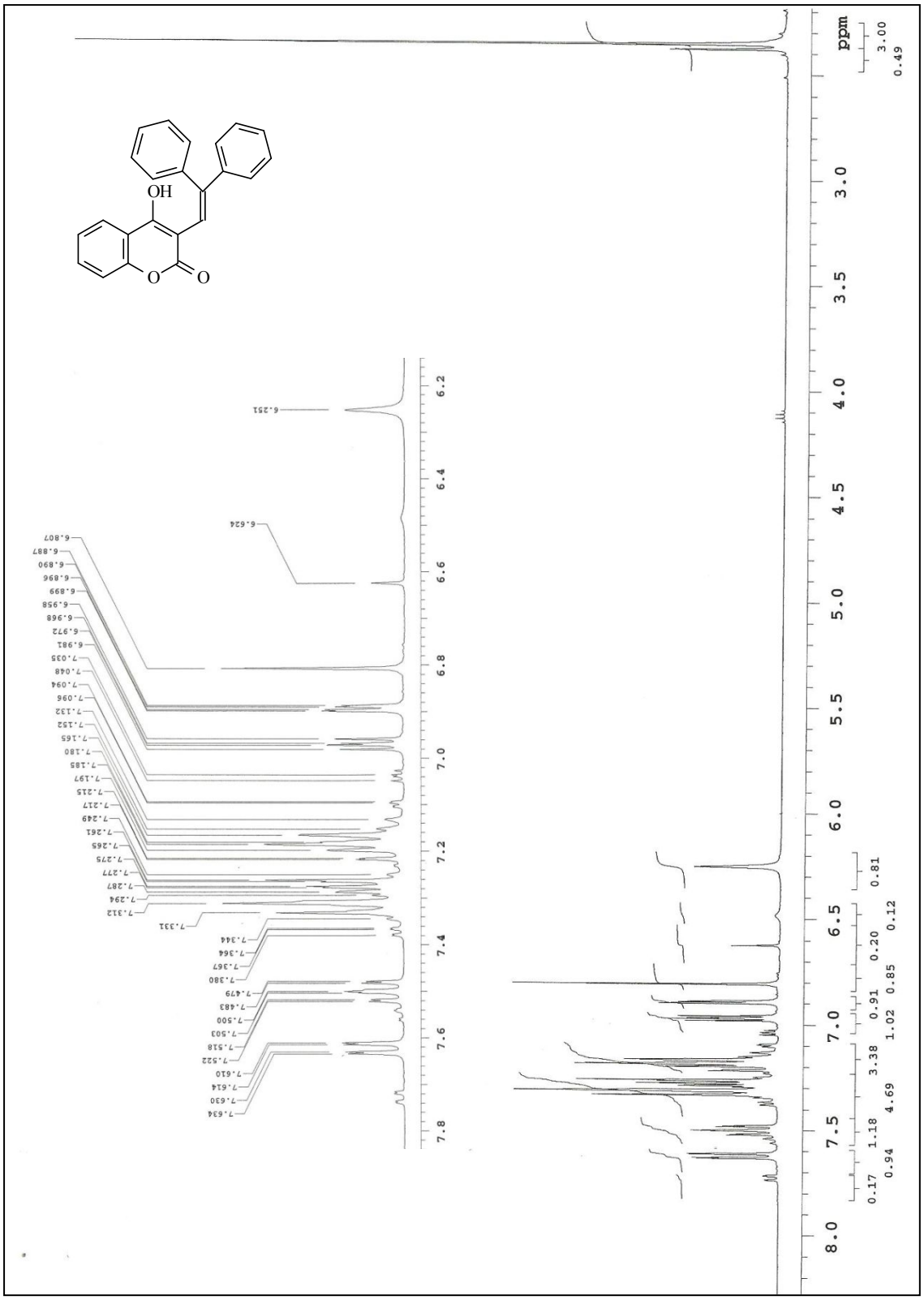
2.10 ^{1}H-NMR spectra of **12**



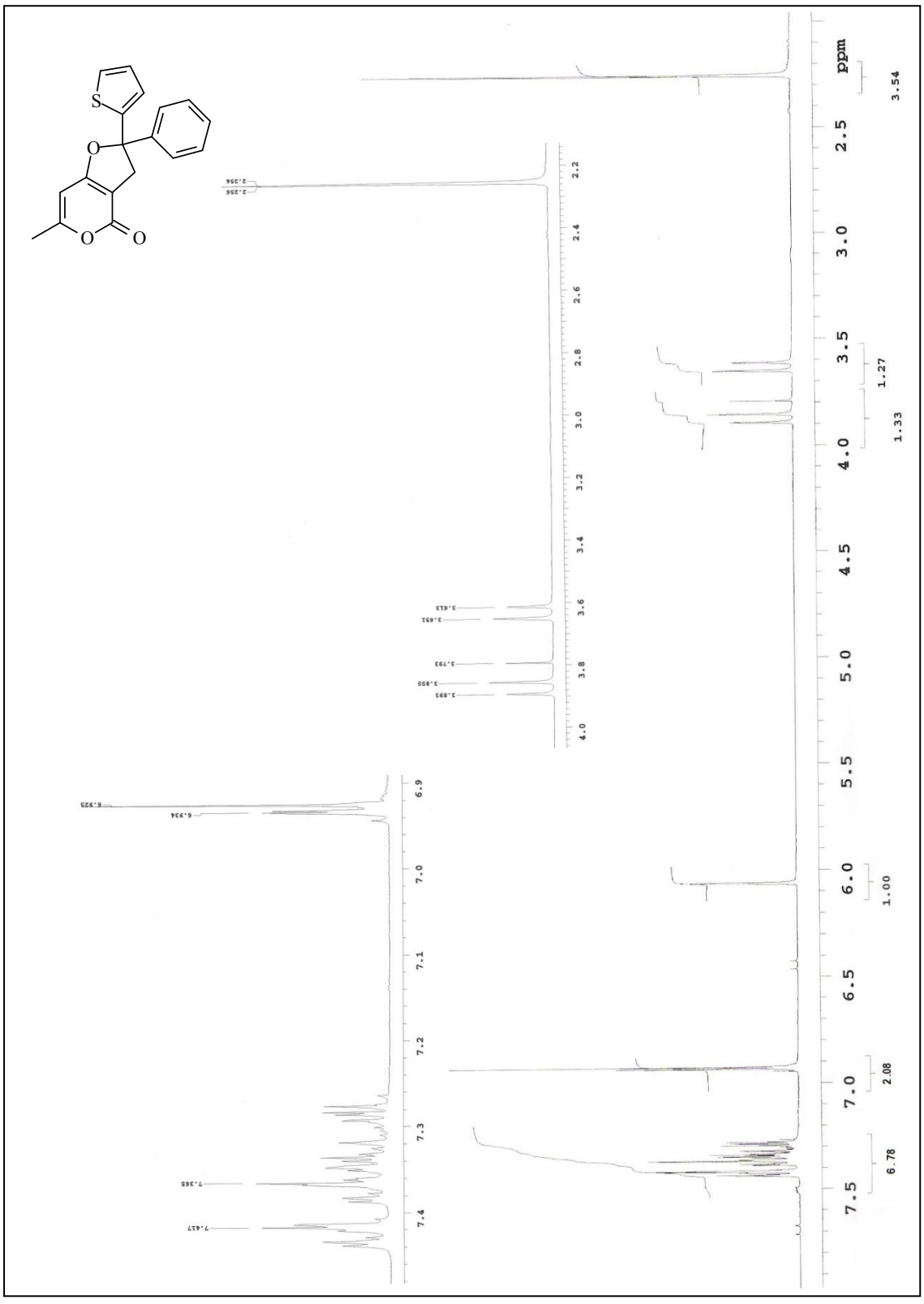
2.11 ^{1}H-NMR spectra of **3aj**



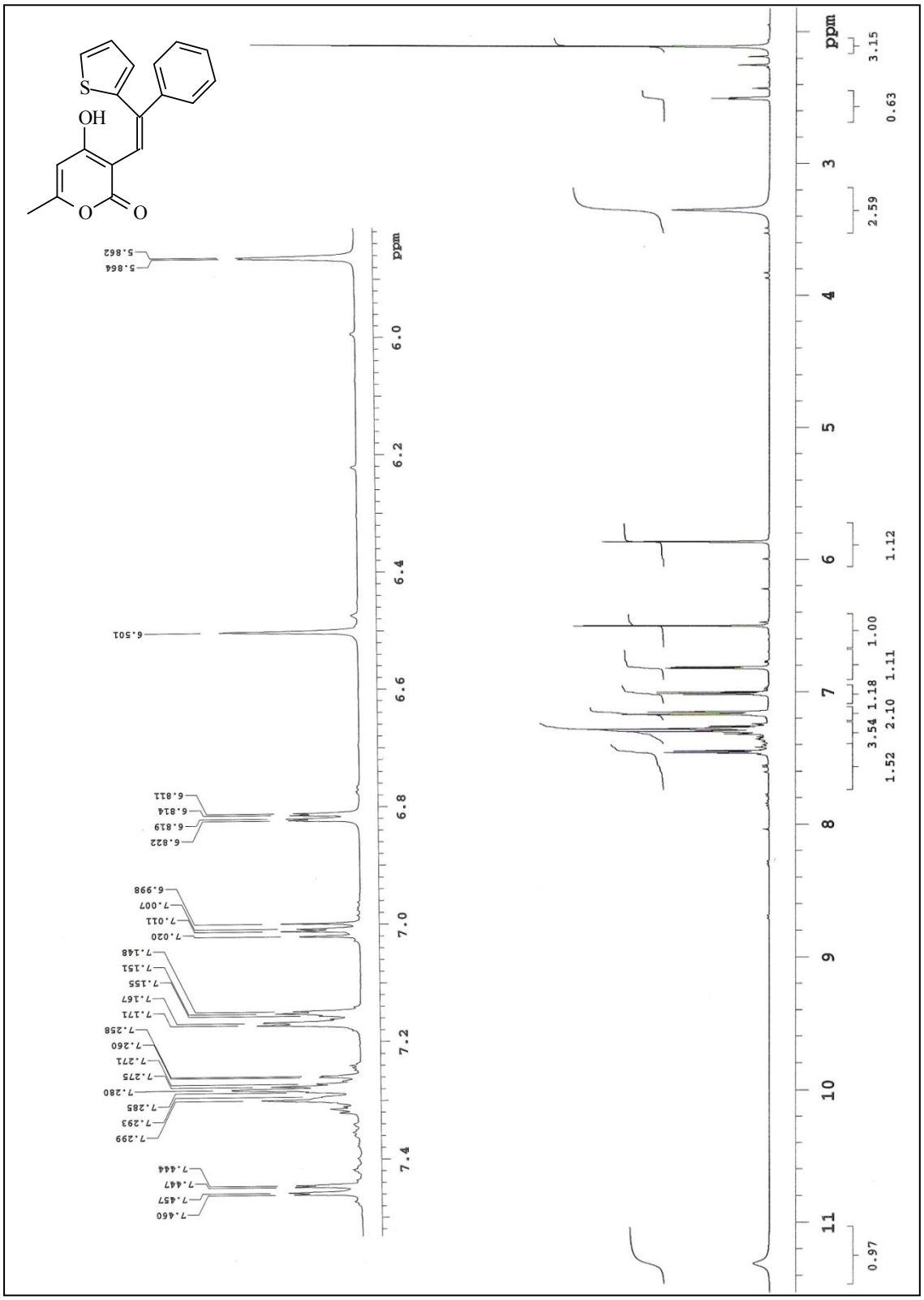
2.12 ^{1}H-NMR spectra of **4aj**



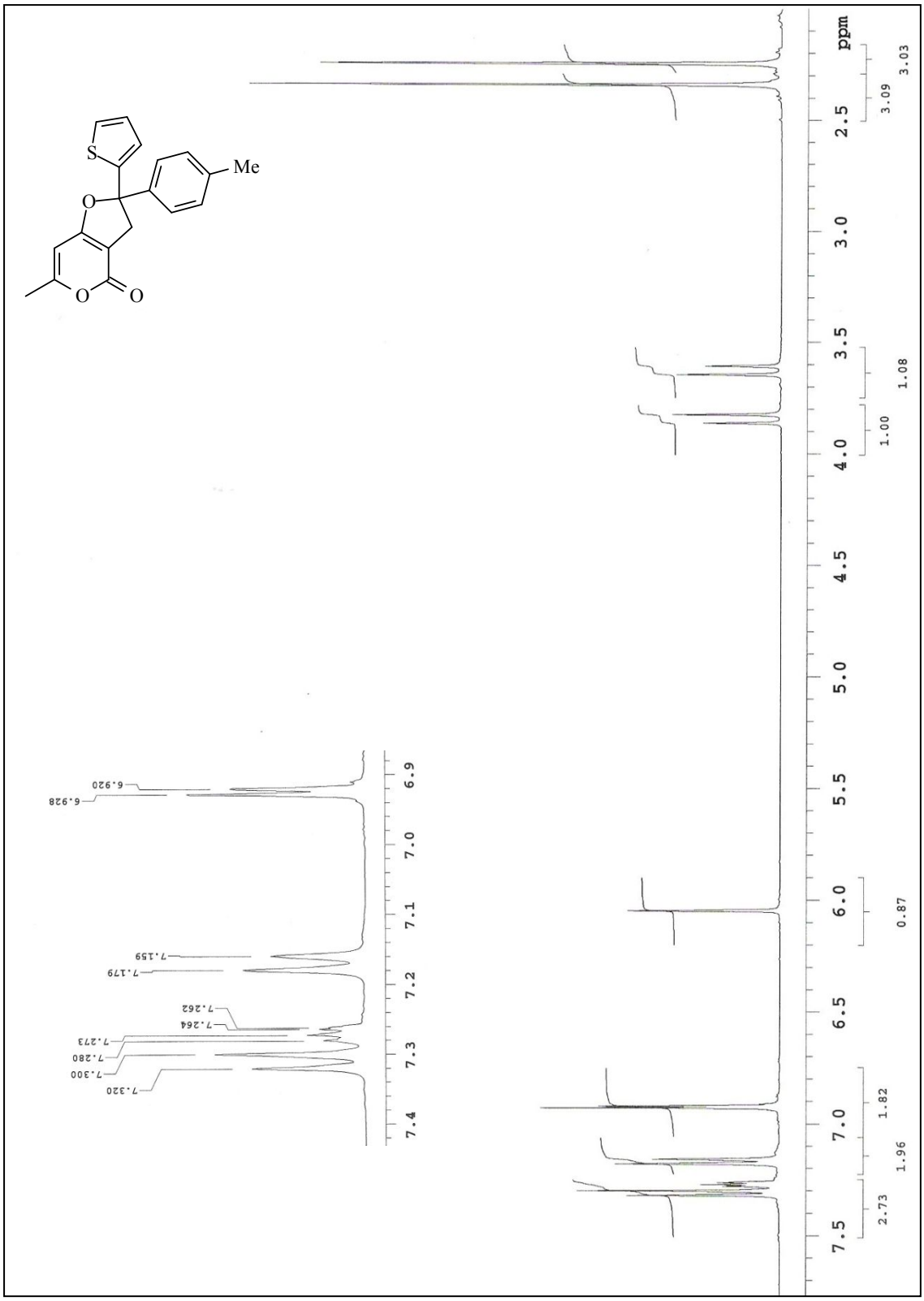
2.13 ^{1}H-NMR spectra of **13**



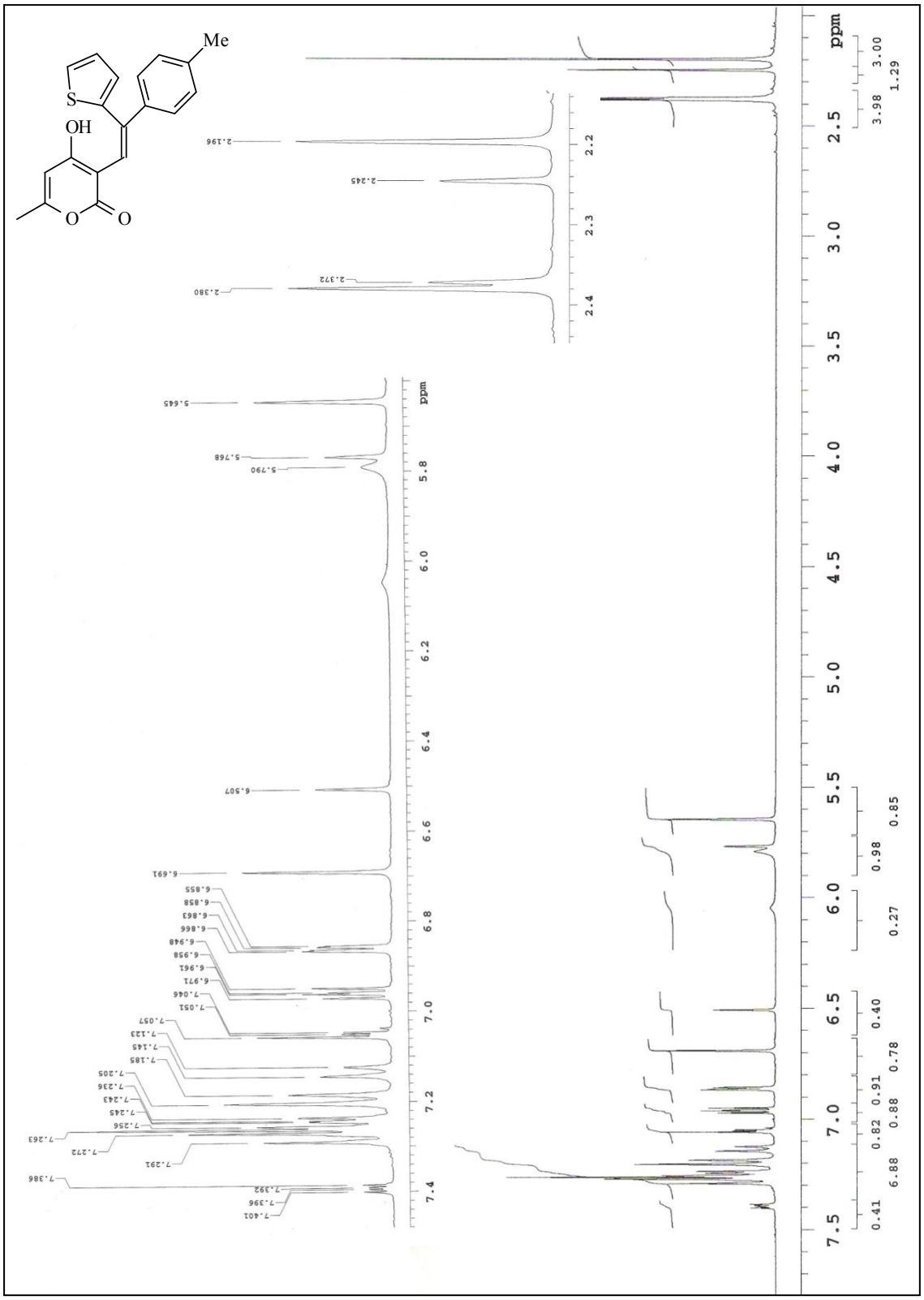
2.14 ^{1}H-NMR spectra of **16**



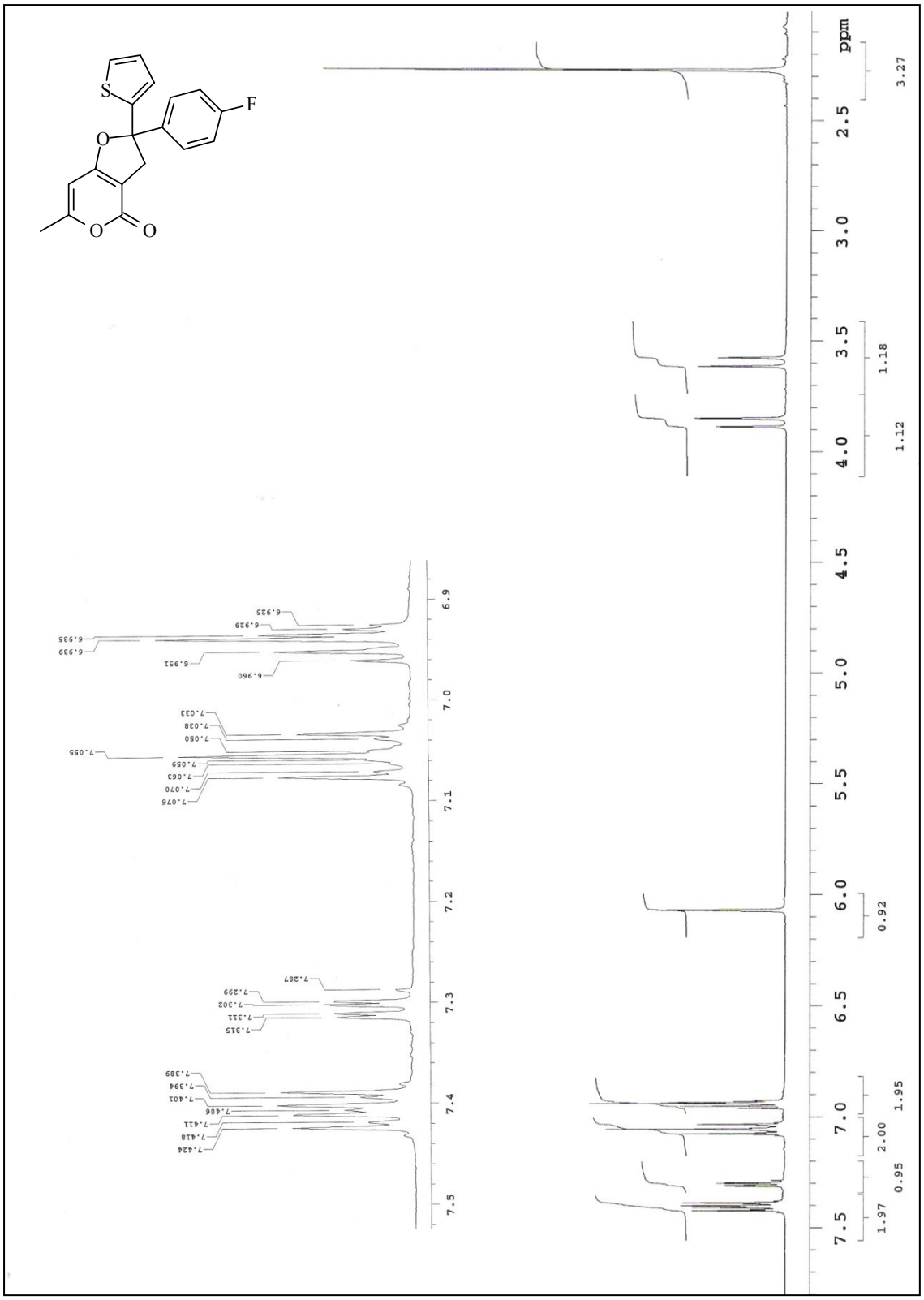
2.15 ^{1}H-NMR spectra of **14**



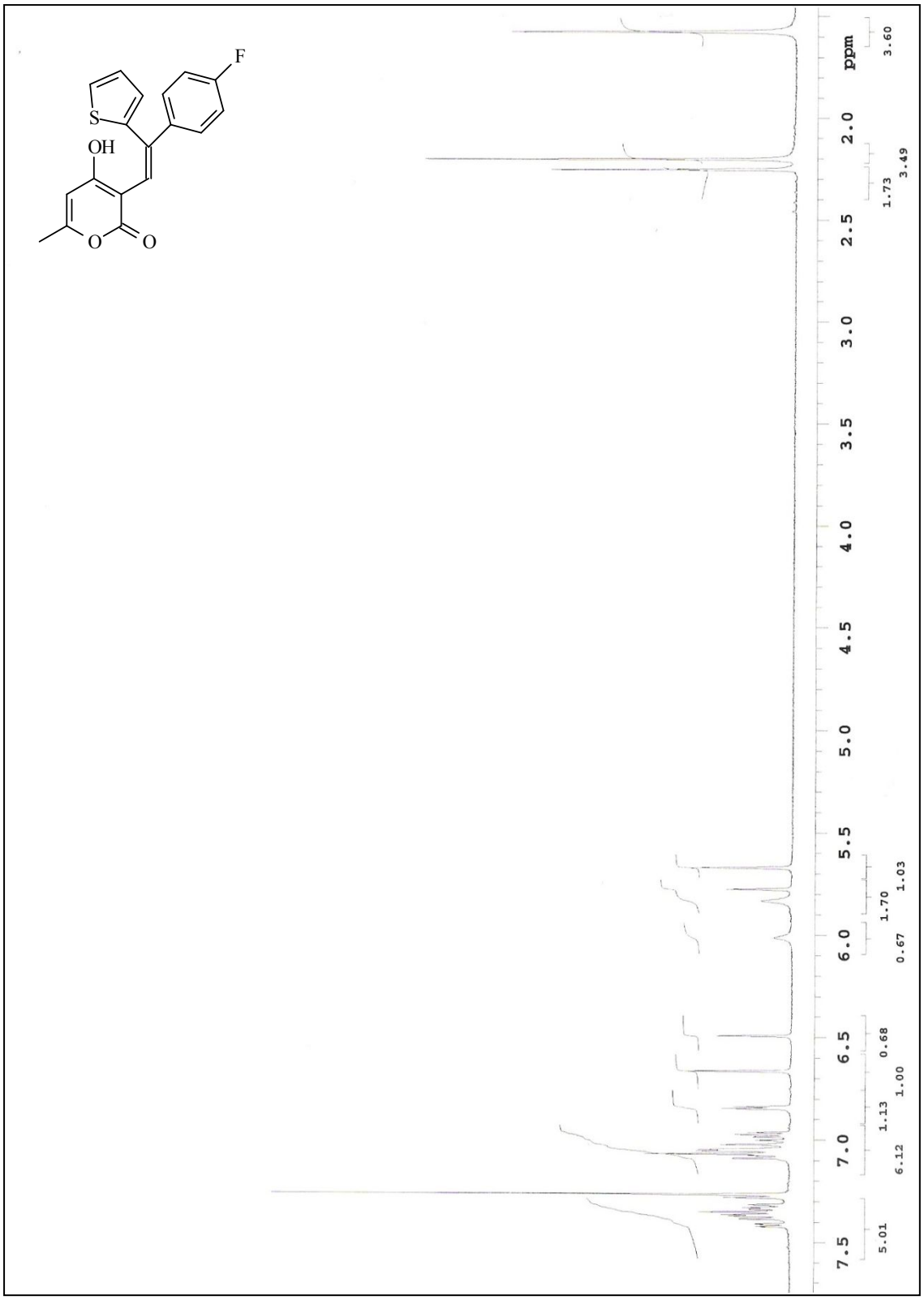
2.16 ^{1}H-NMR spectra of **17**



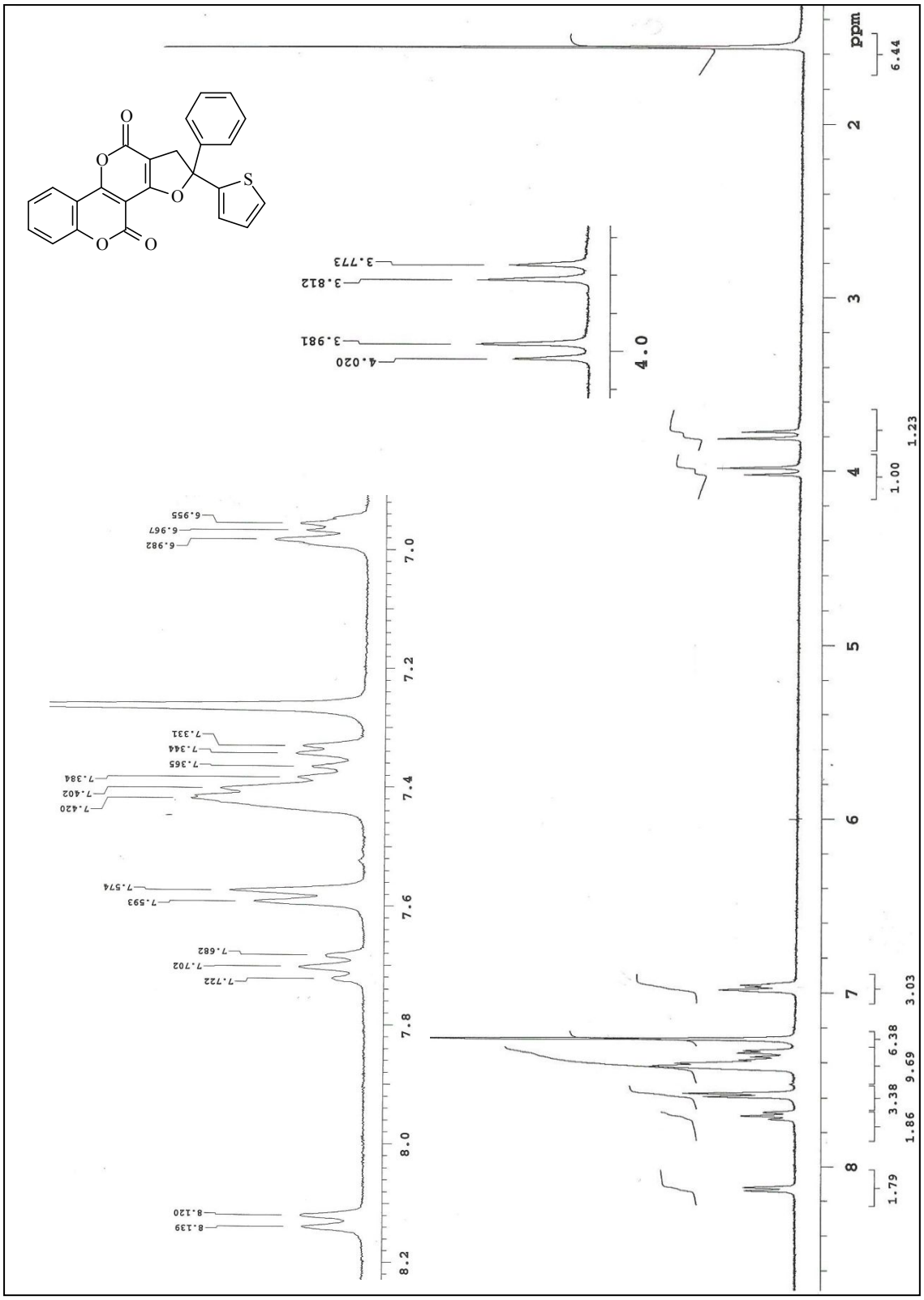
2.17 ^{1}H-NMR spectra of **15**



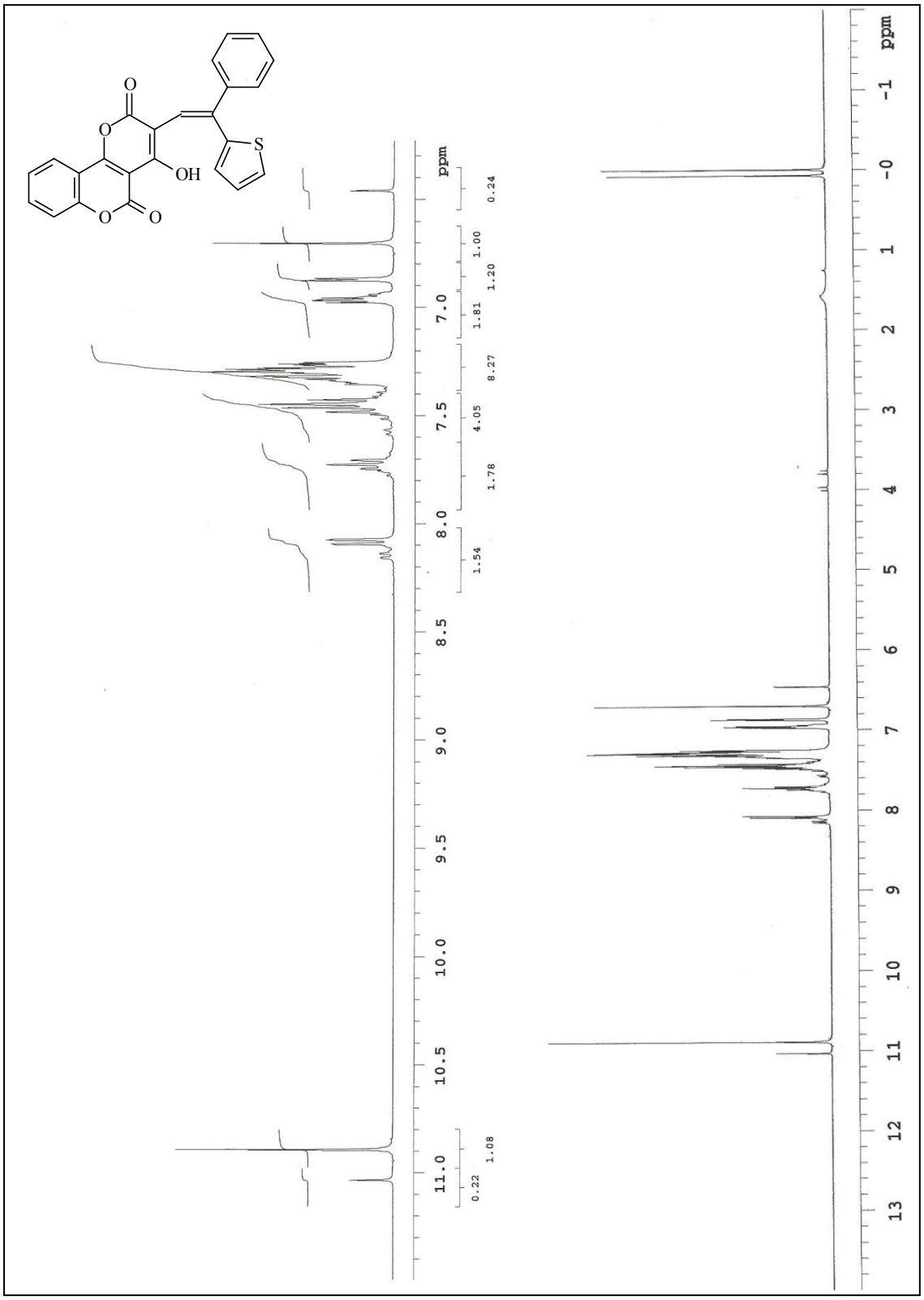
2.18 ^{1}H-NMR spectra of **18**



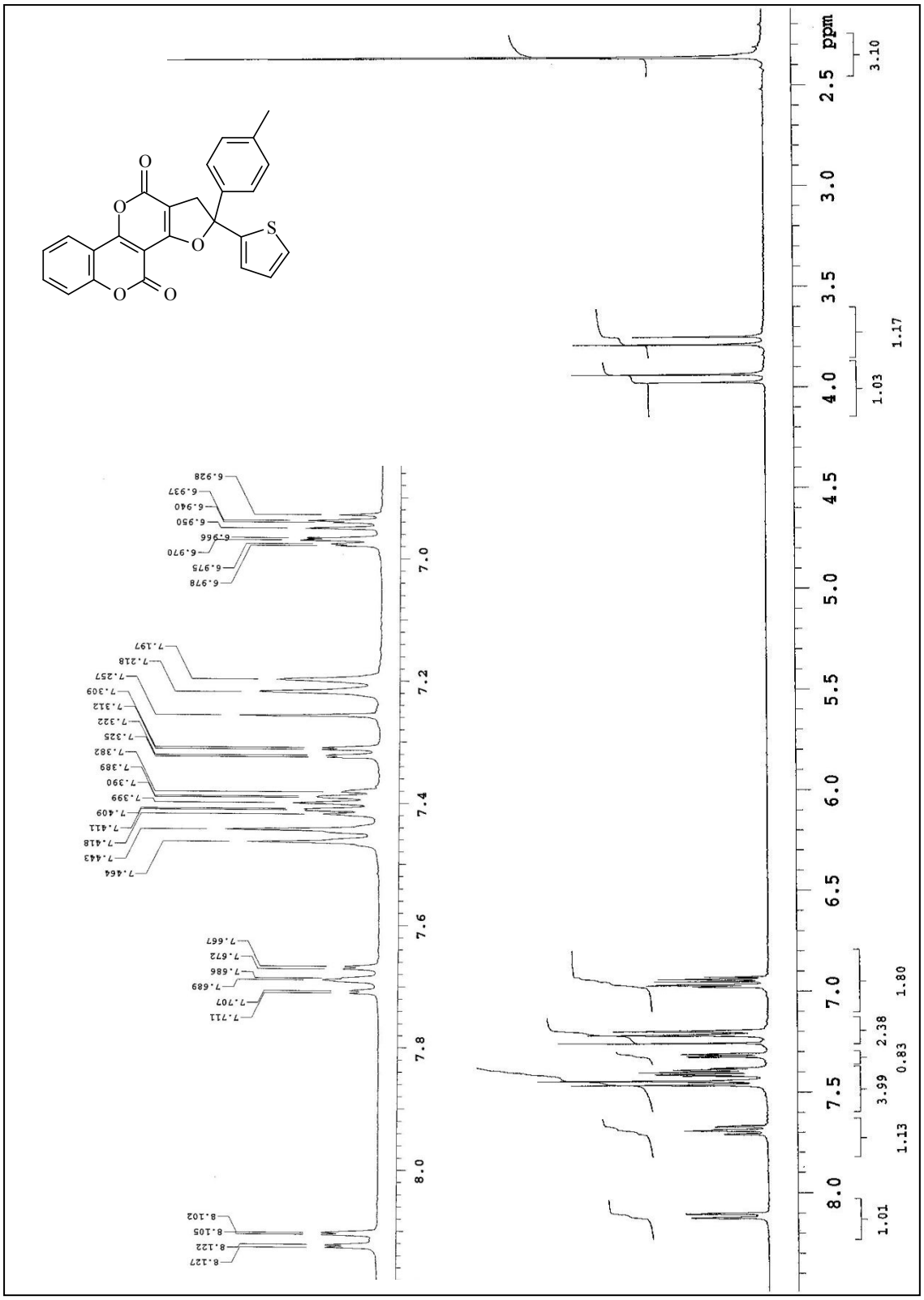
2.19 ^{1}H-NMR spectra of **19**



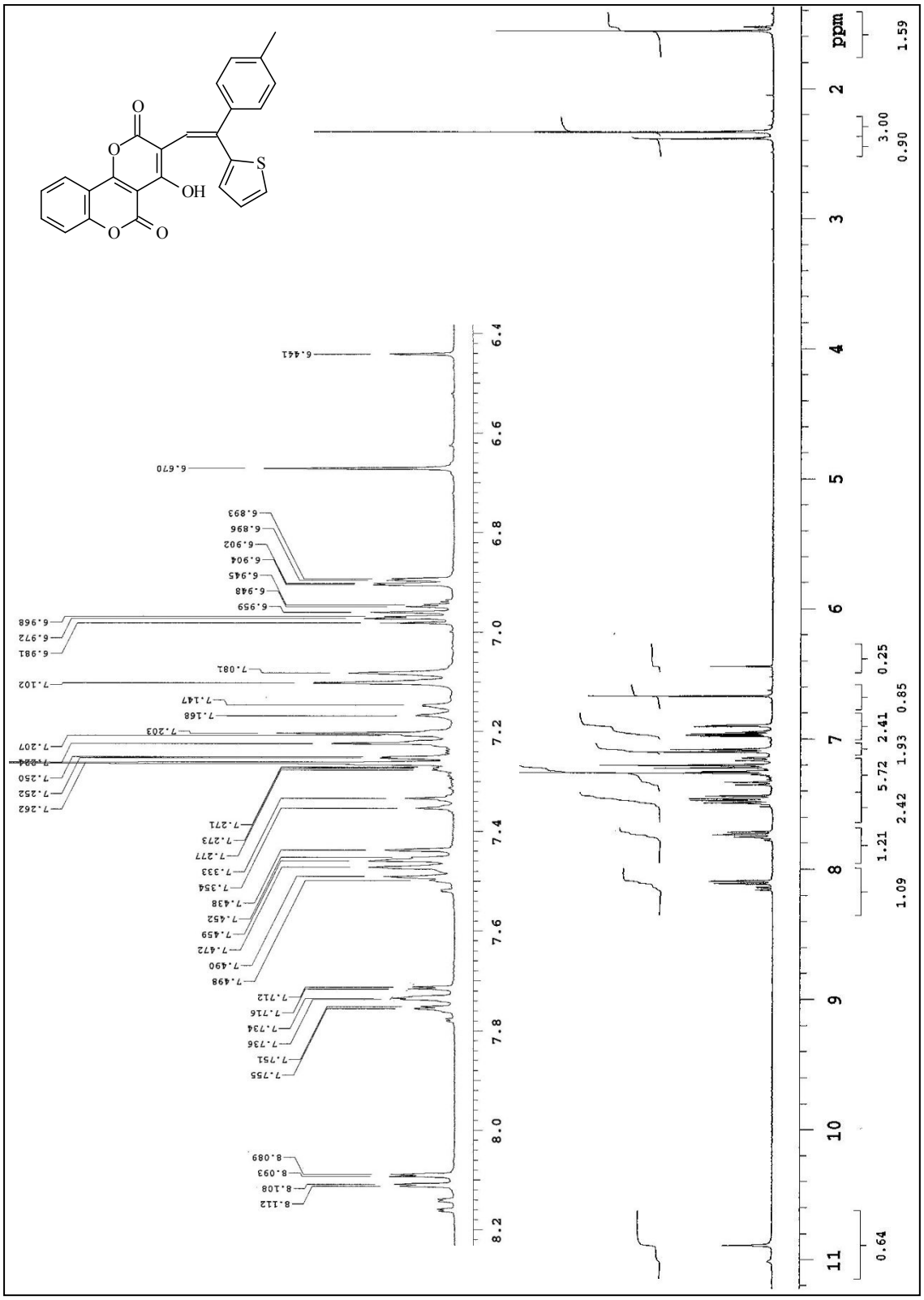
2.20 ^{1}H-NMR spectra of **25**



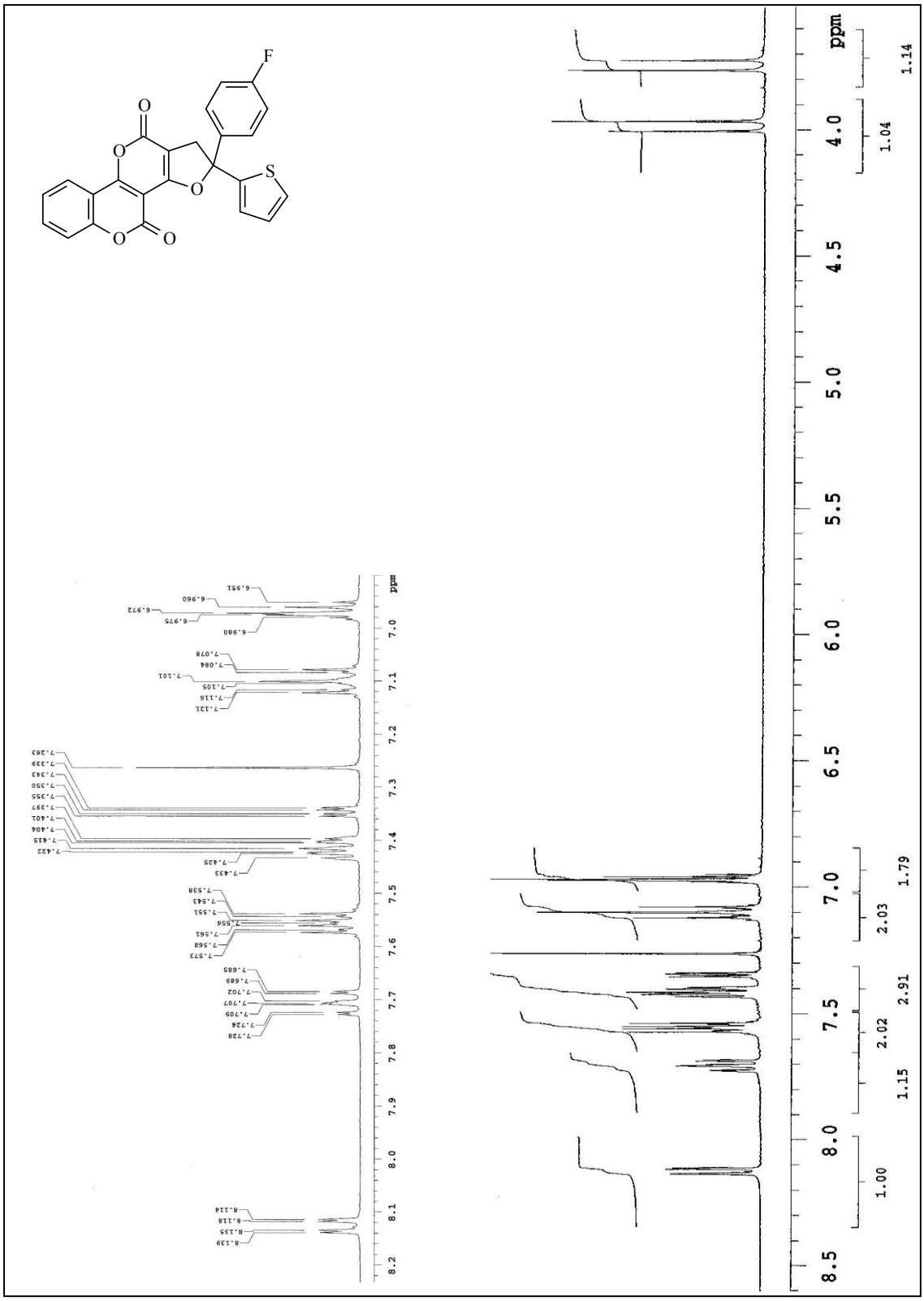
2.21 ^{1}H-NMR spectra of **20**



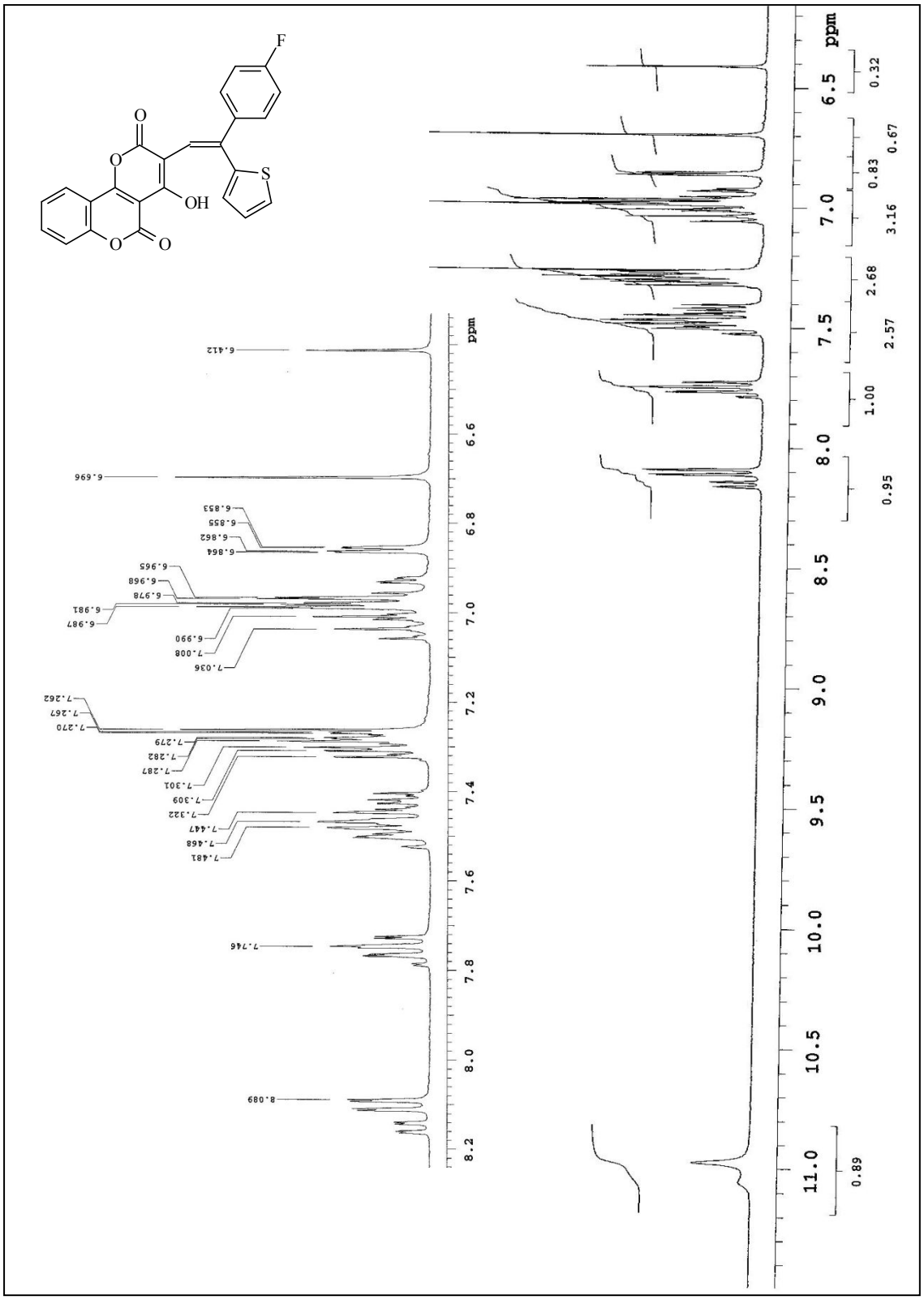
2.22 ^{1}H-NMR spectra of **26**



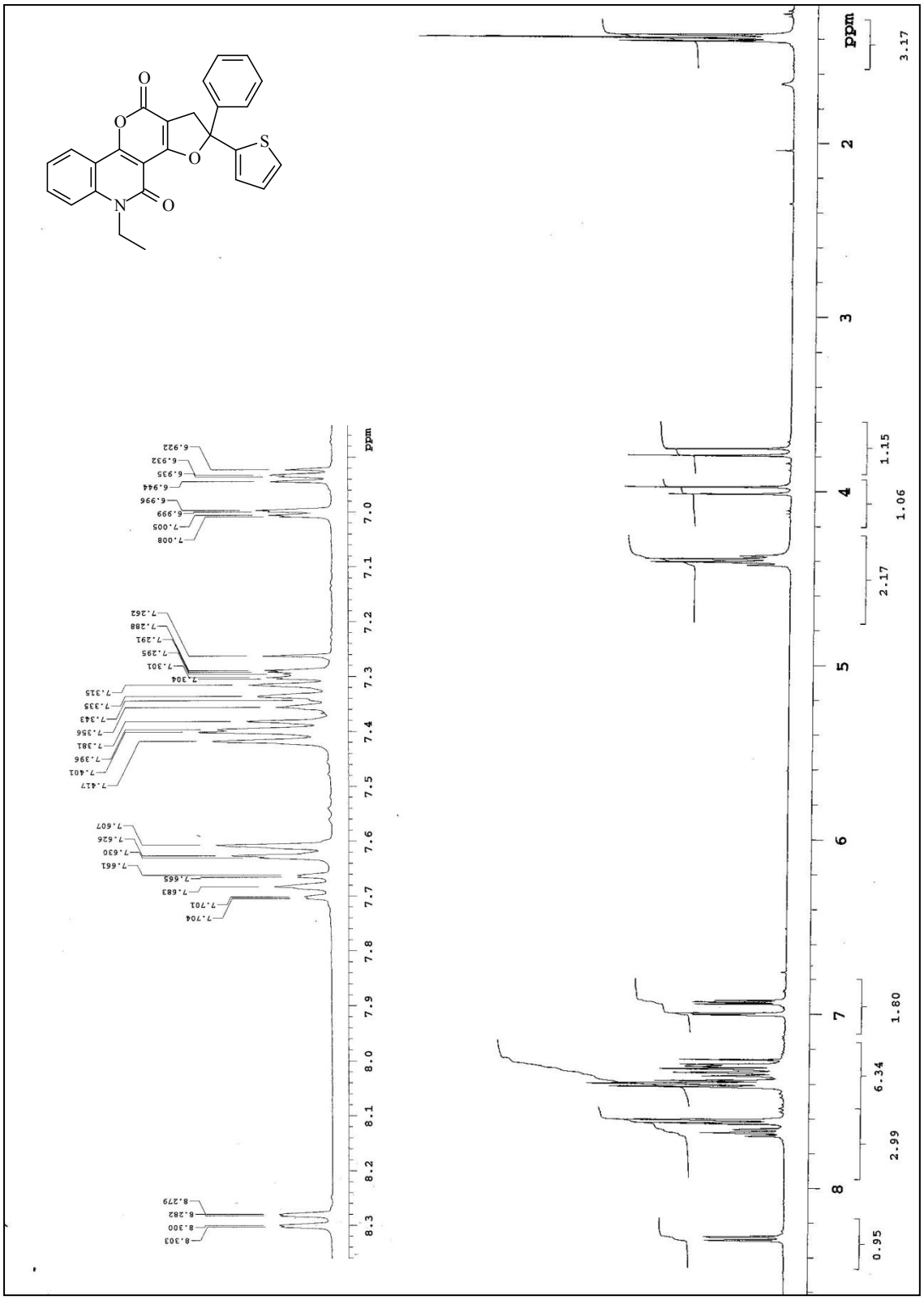
2.23 ^{1}H-NMR spectra of **21**



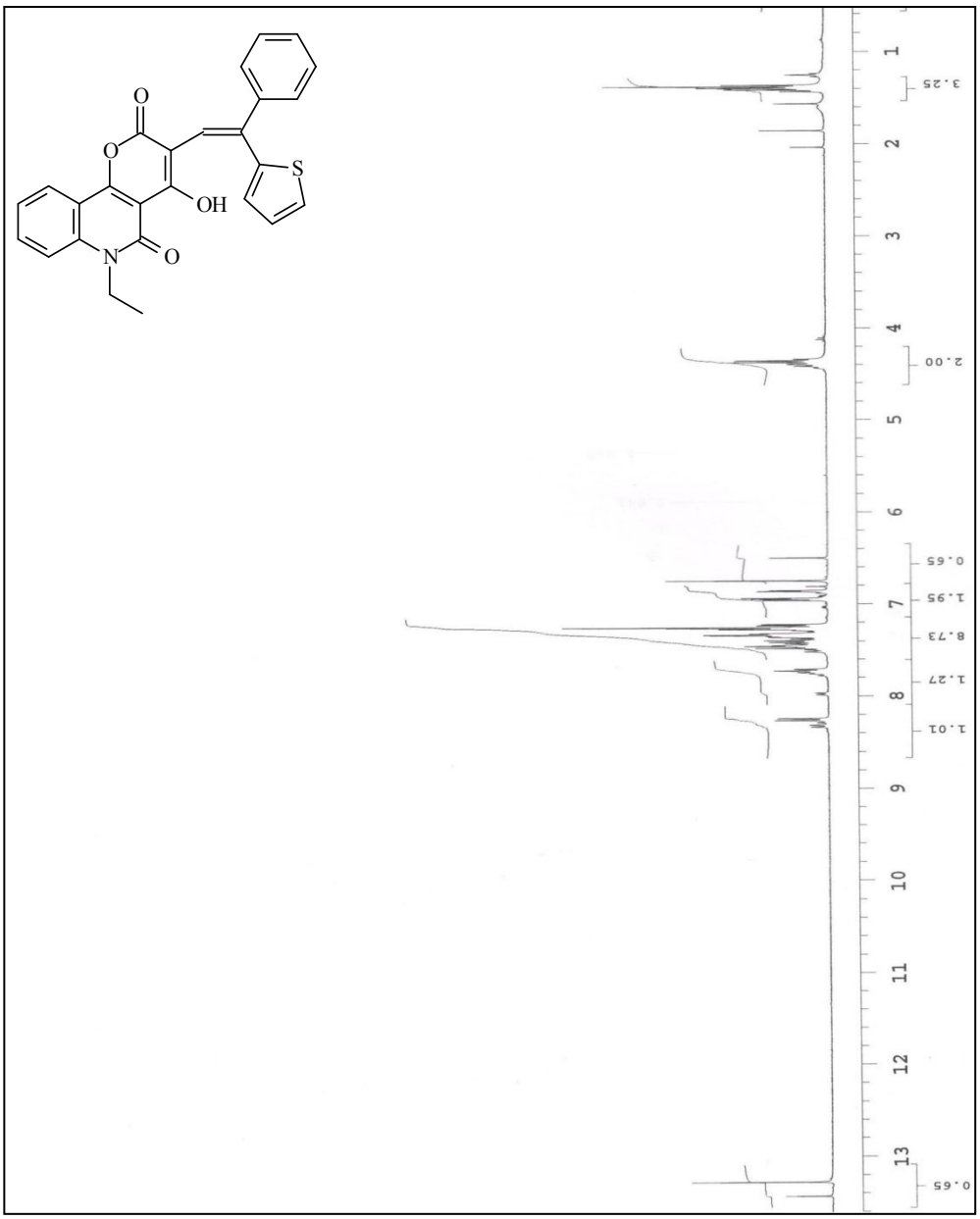
2.24 ^{1}H-NMR spectra of **27**



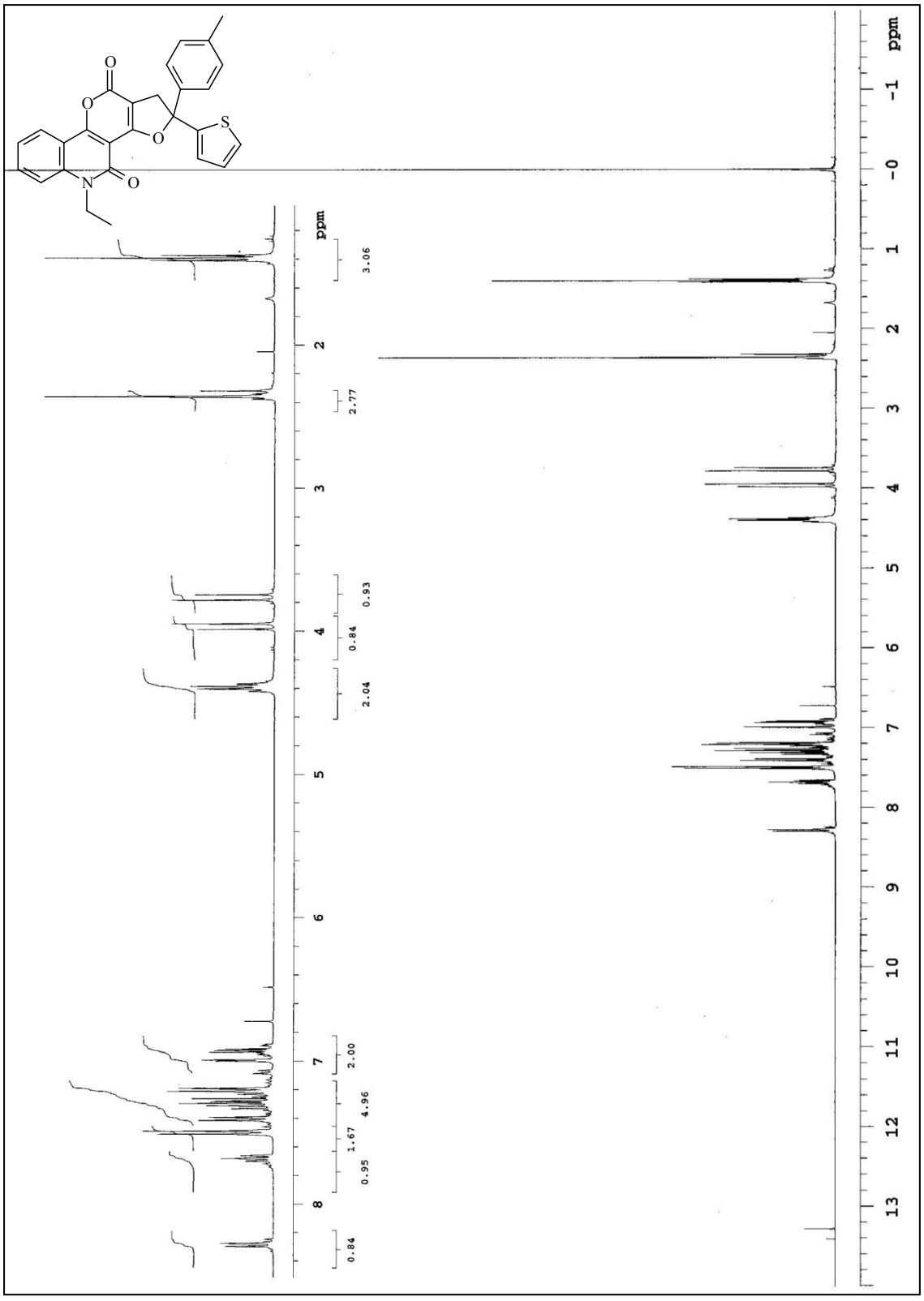
2.25 ^{1}H-NMR spectra of **22**



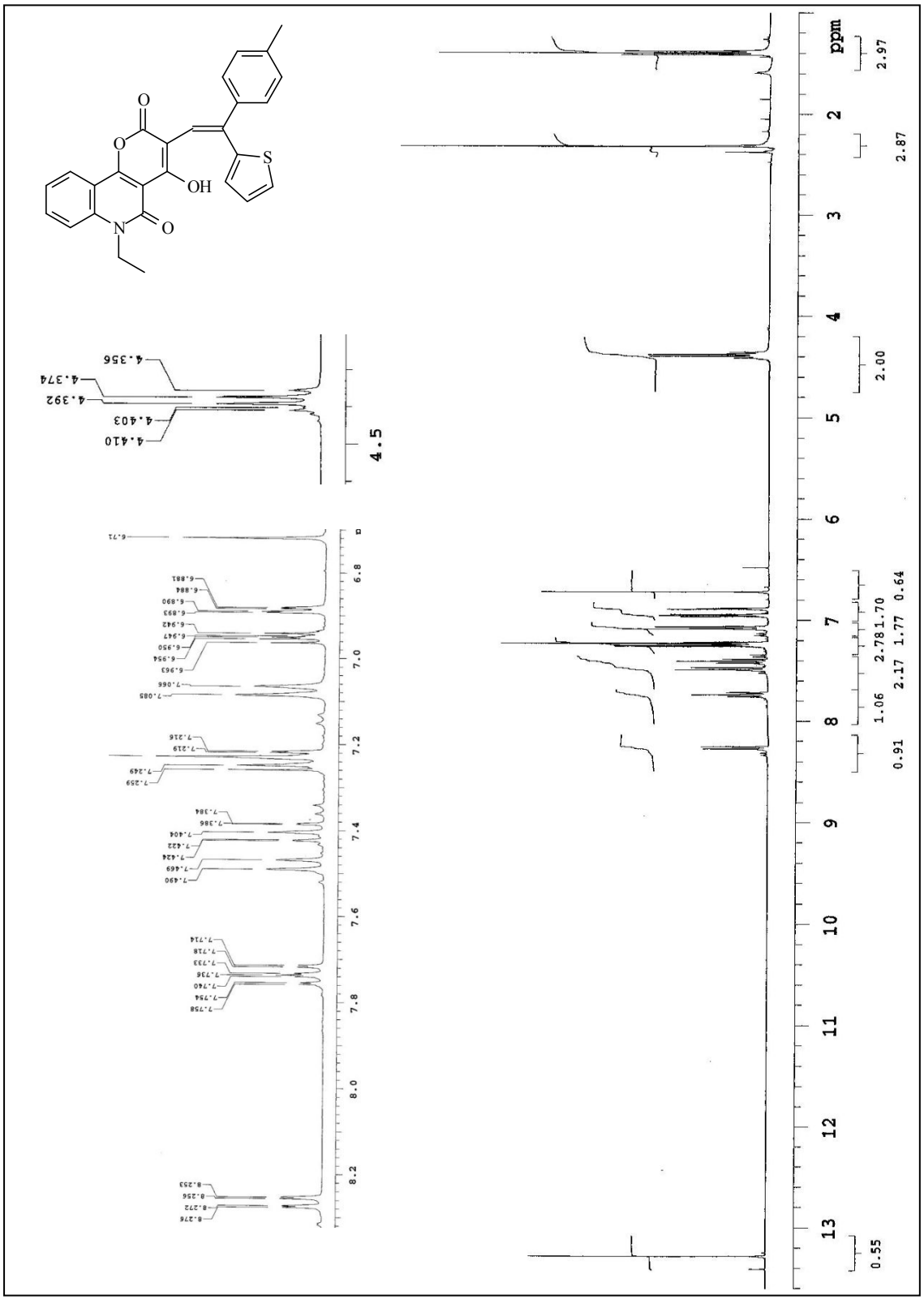
2.26 ^{1}H-NMR spectra of **28**



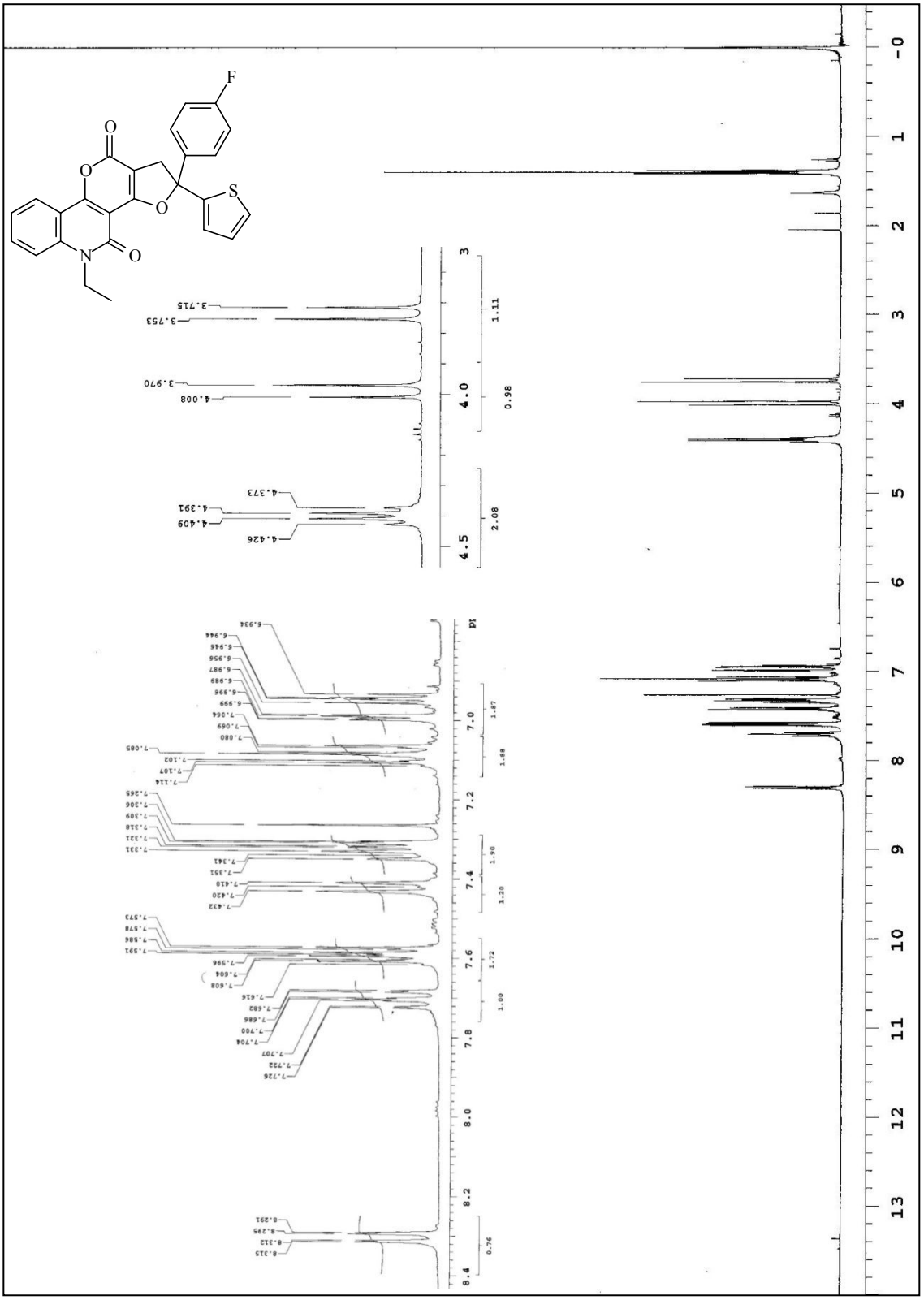
2.27 ^{1}H-NMR spectra of **23**



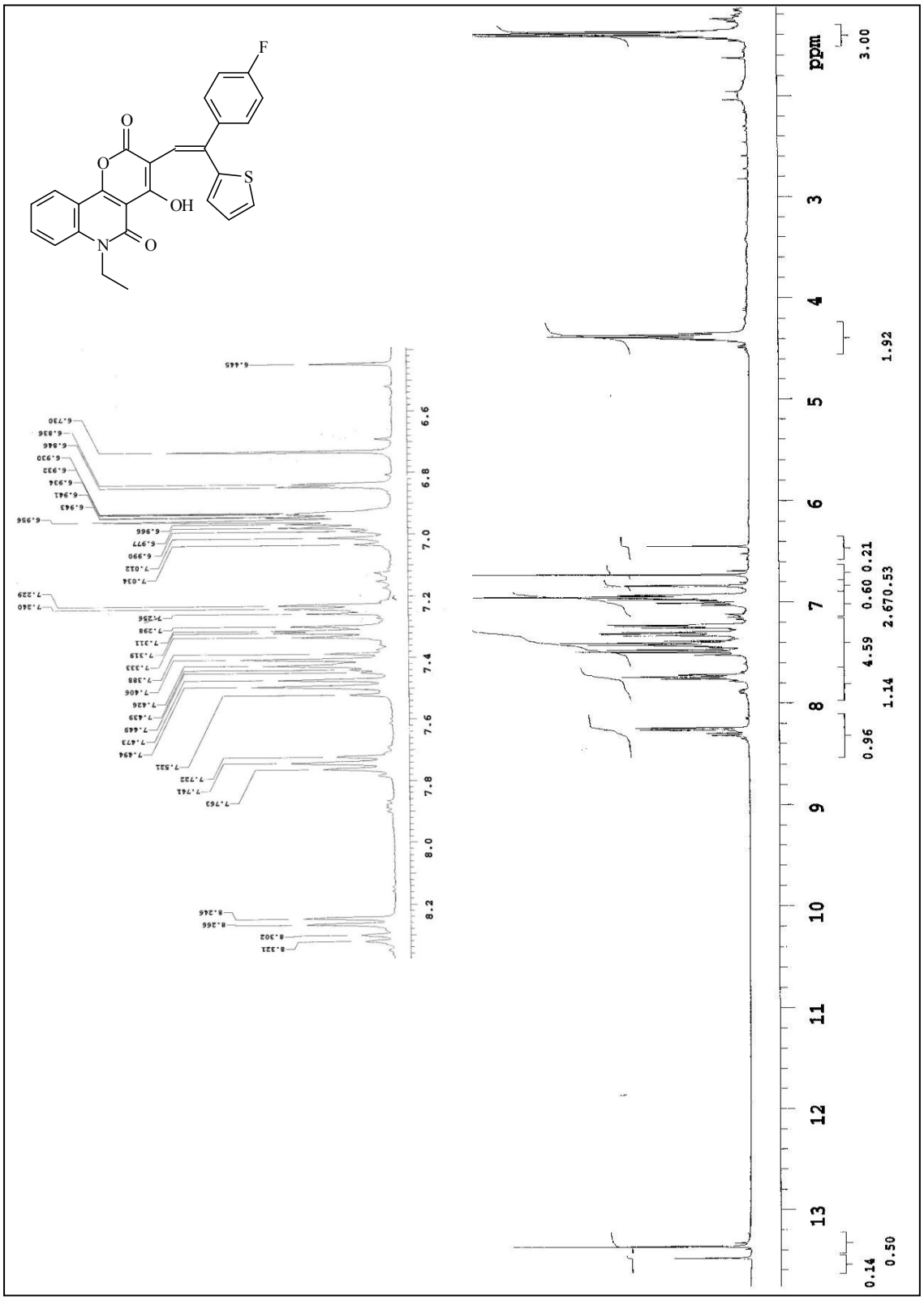
2.28 ^{1}H-NMR spectra of **29**



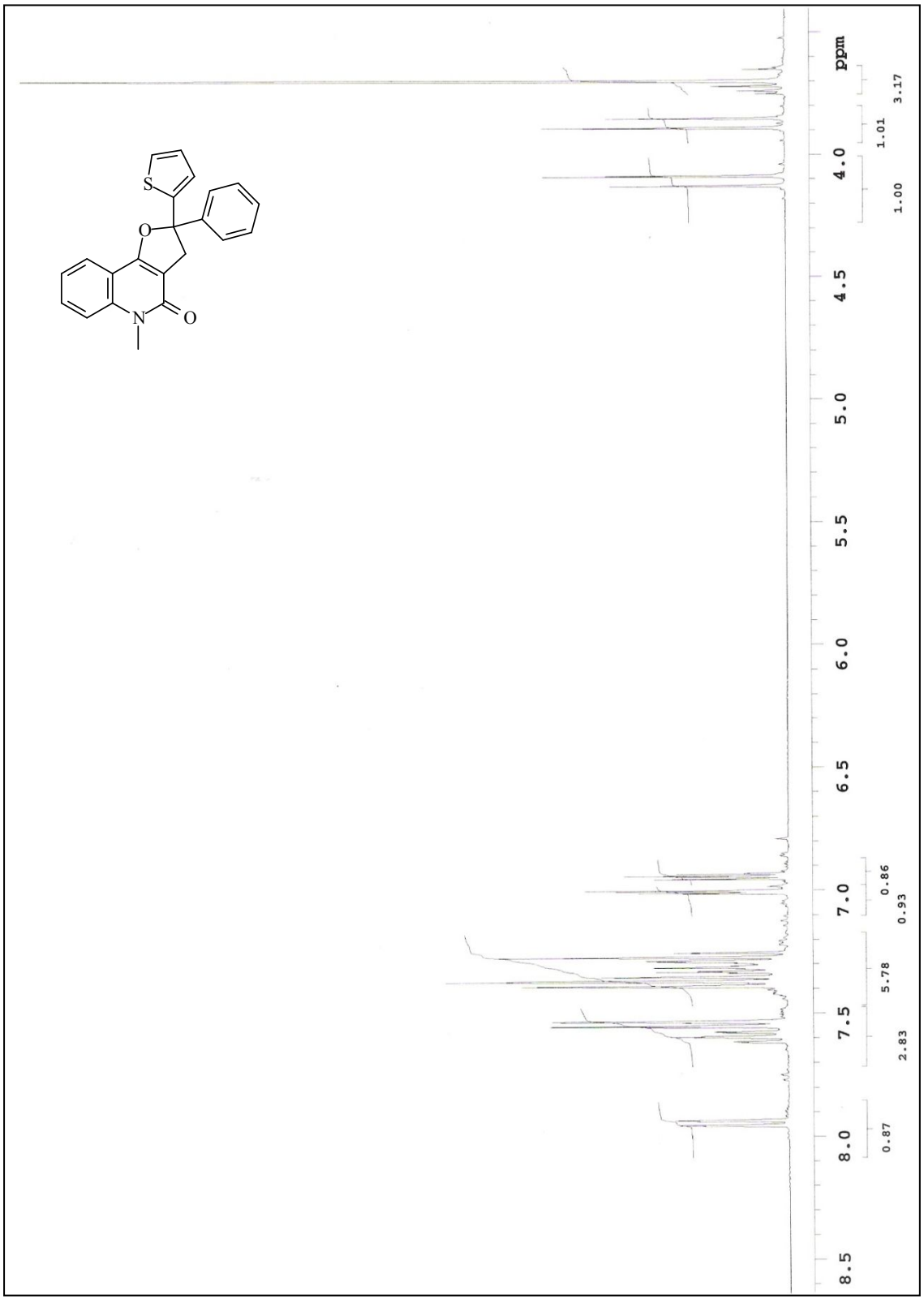
2.29 ^{1}H-NMR spectra of **24**



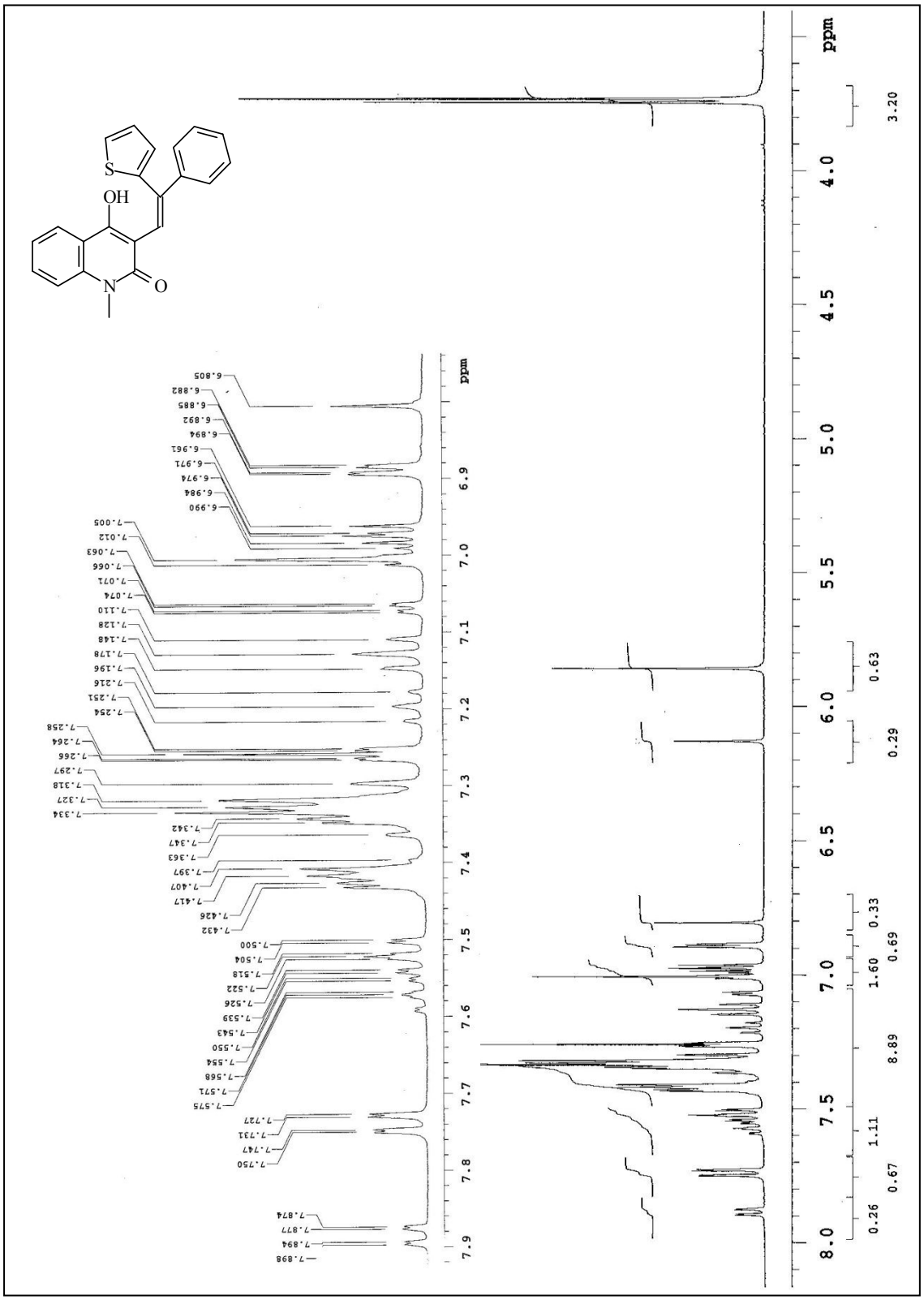
2.30 ^{1}H-NMR spectra of **30**



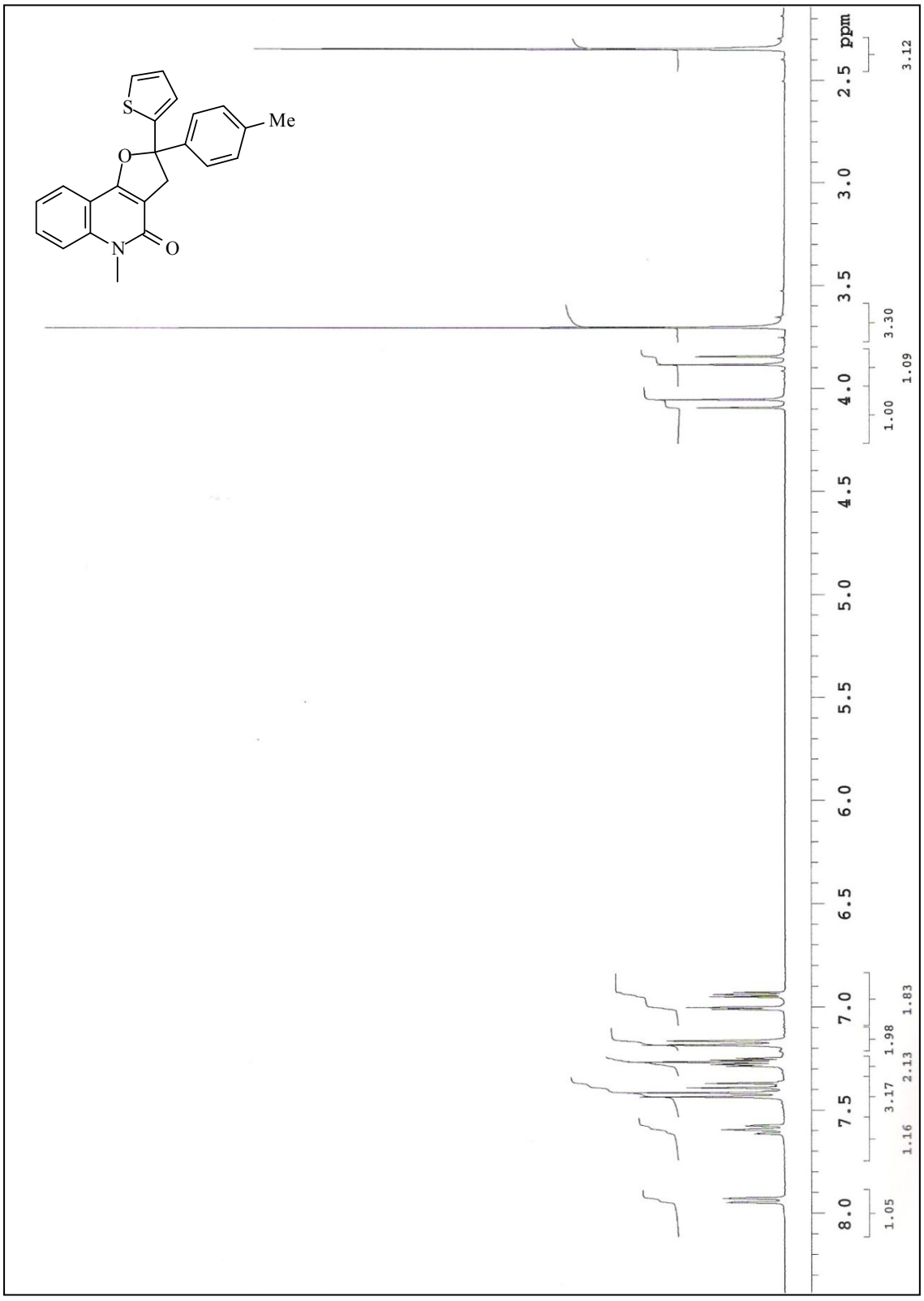
2.31 ^{1}H-NMR spectra of **31**



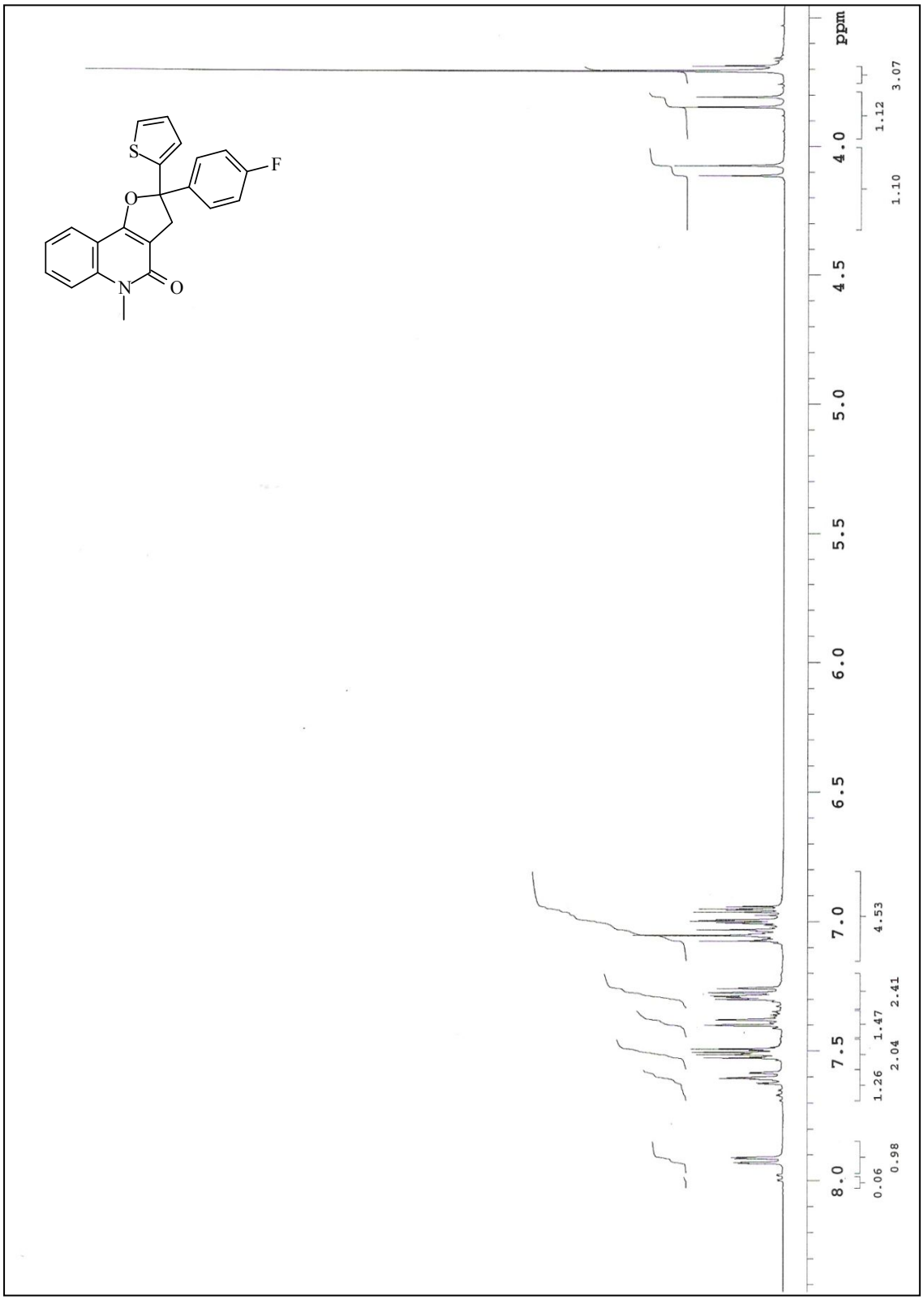
2.32 ^{1}H-NMR spectra of **34**



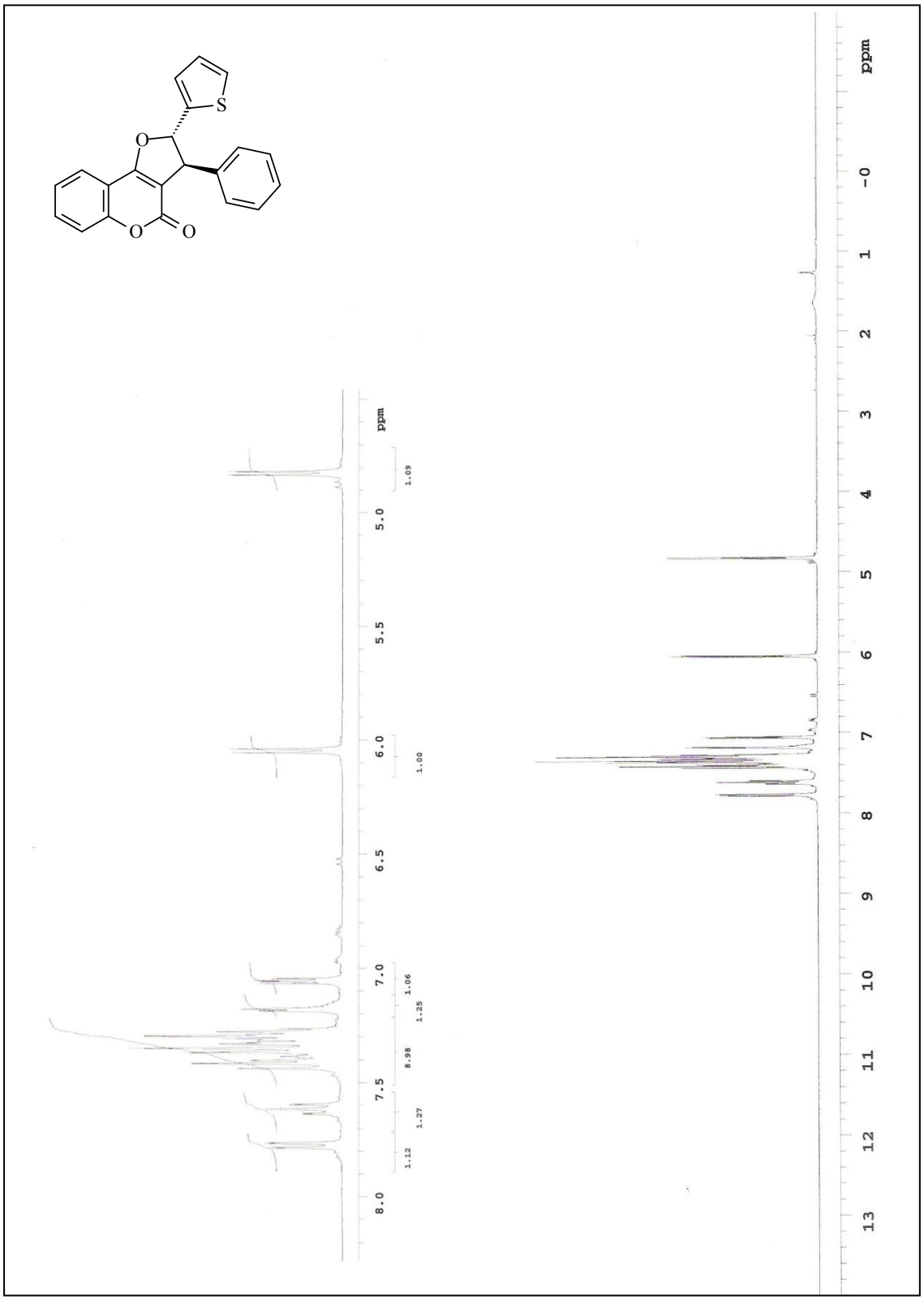
2.33 ^{1}H-NMR spectra of **32**



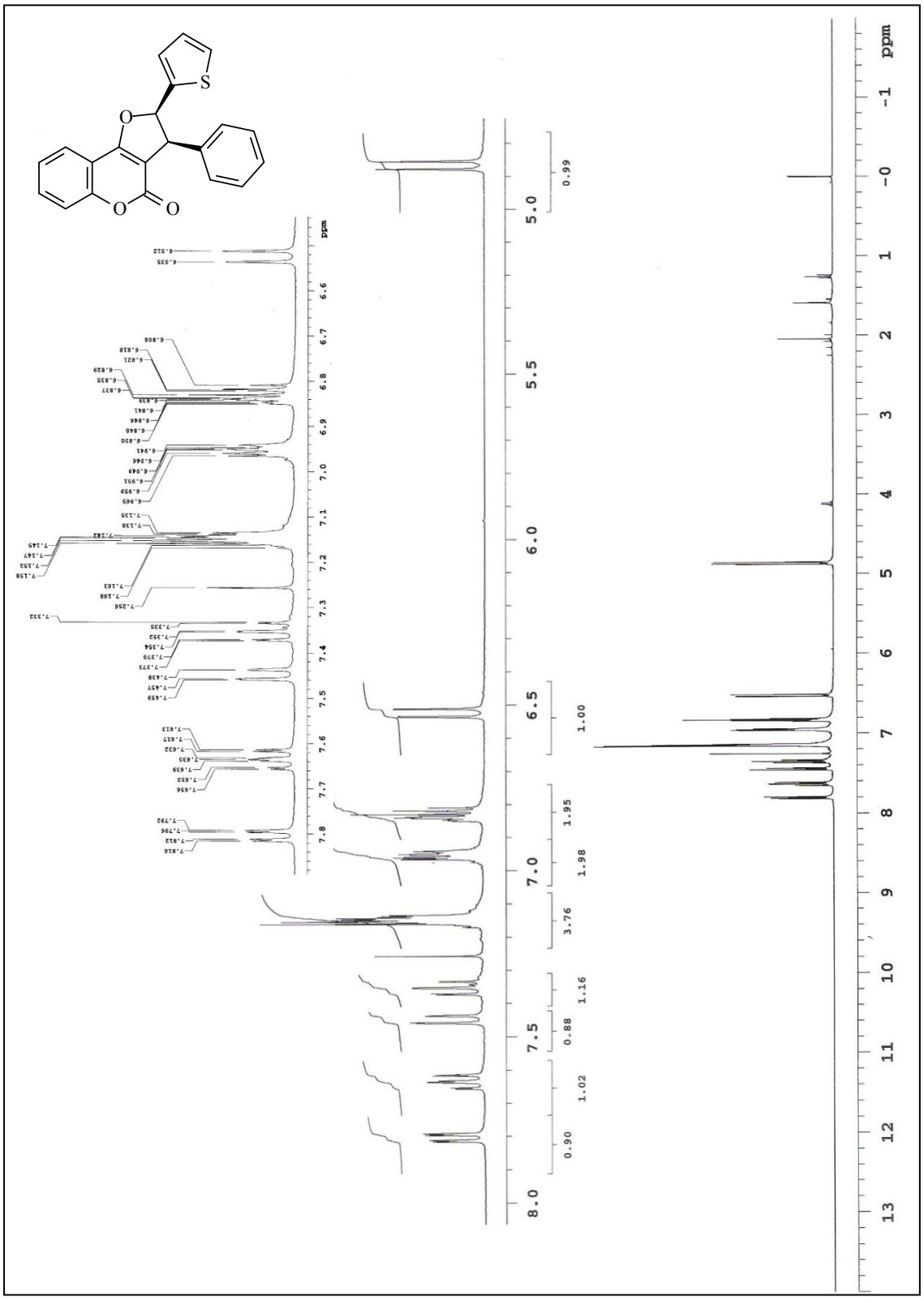
2.34 ^{1}H-NMR spectra of **33**



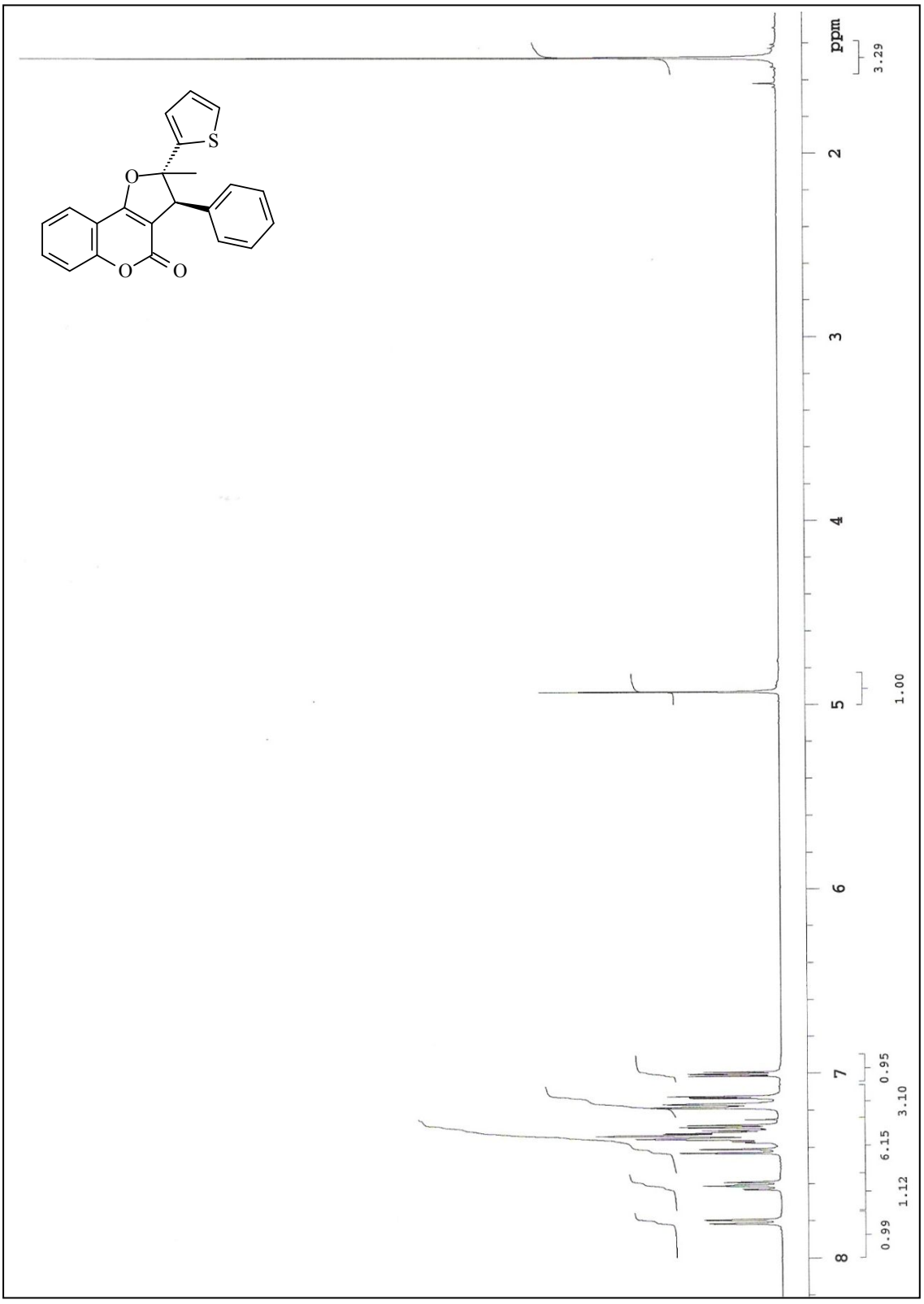
2.35 ^{1}H-NMR spectra of **35**



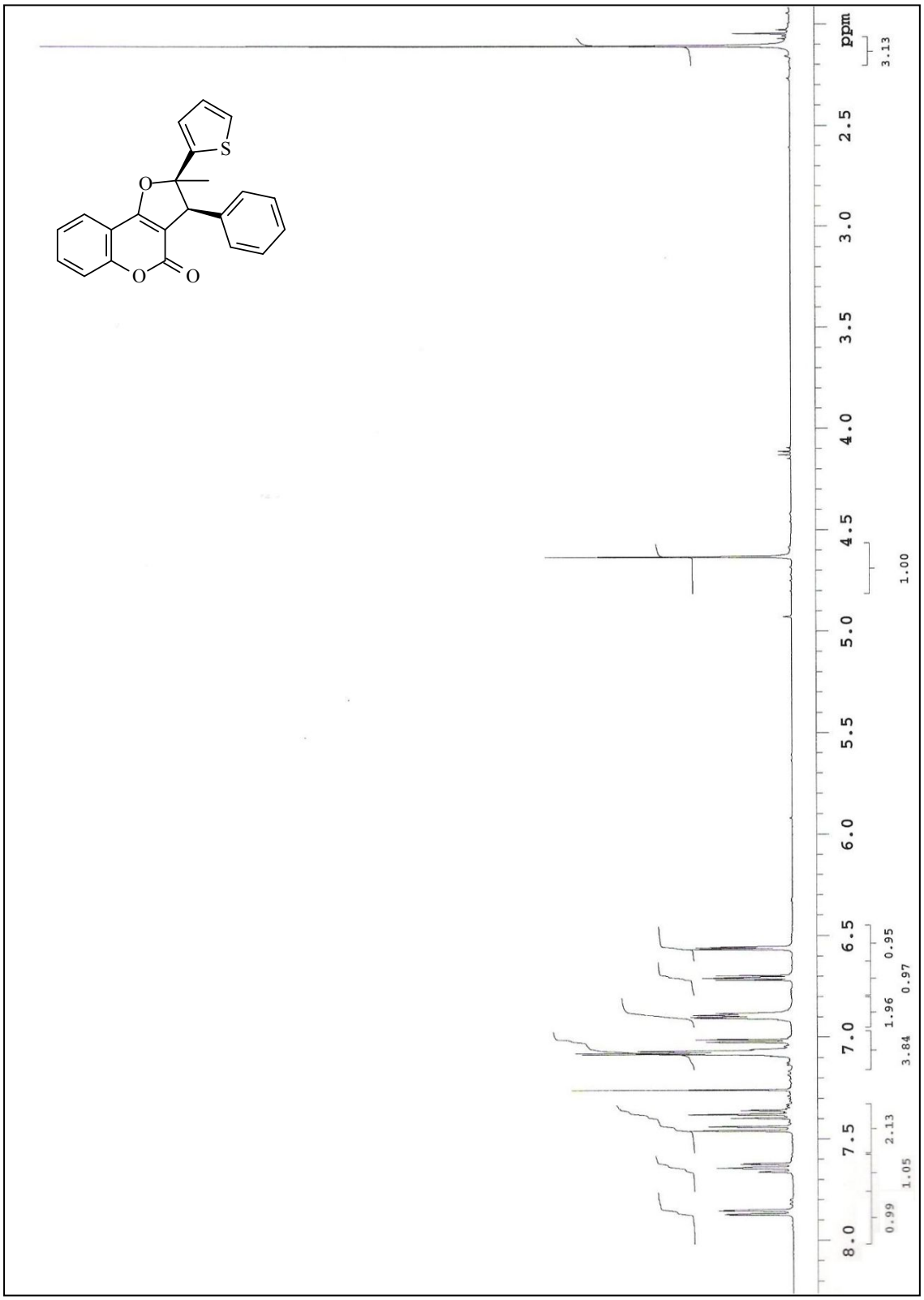
2.36 ^{1}H-NMR spectra of **36**



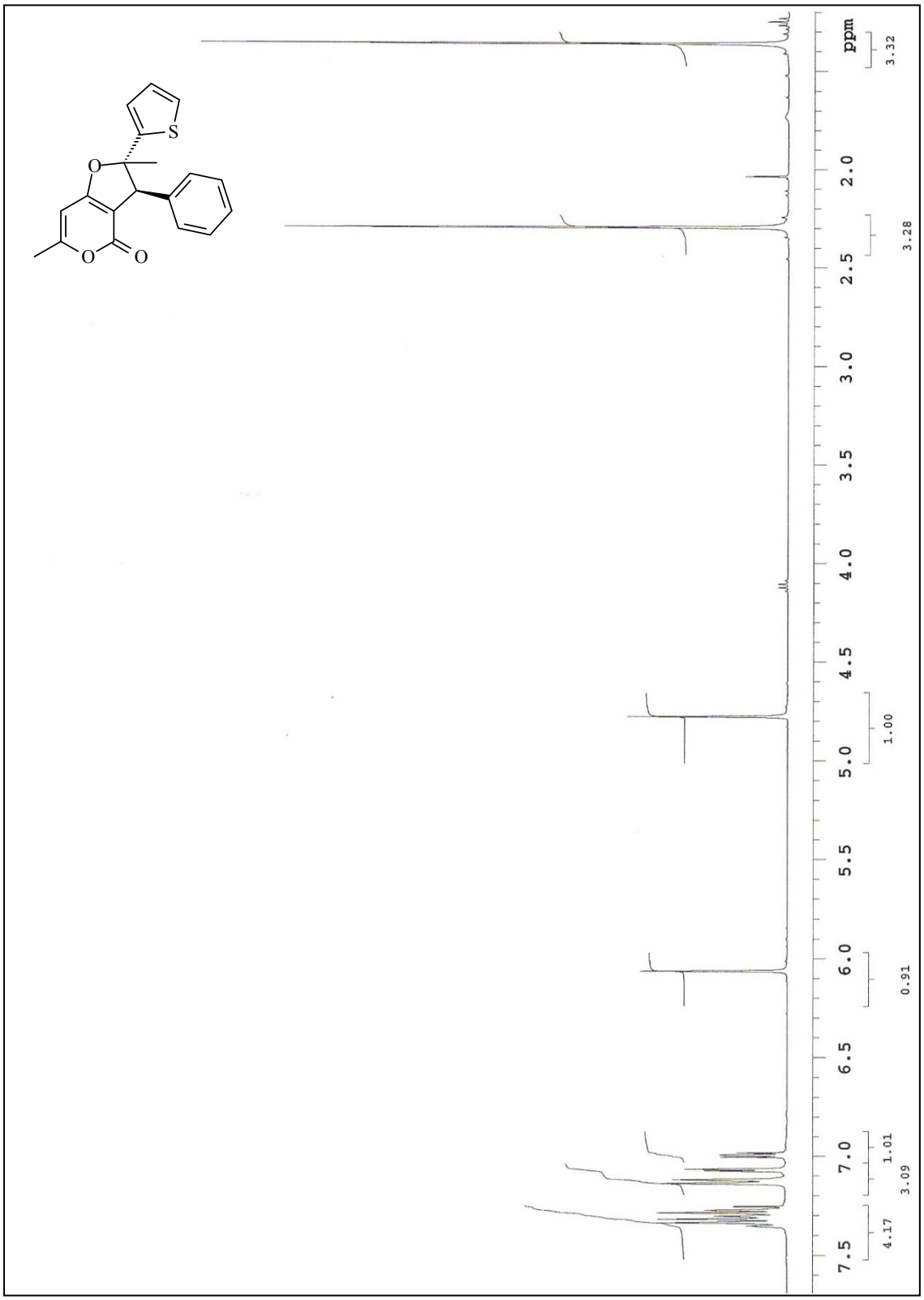
2.37 ^{1}H-NMR spectra of **37**



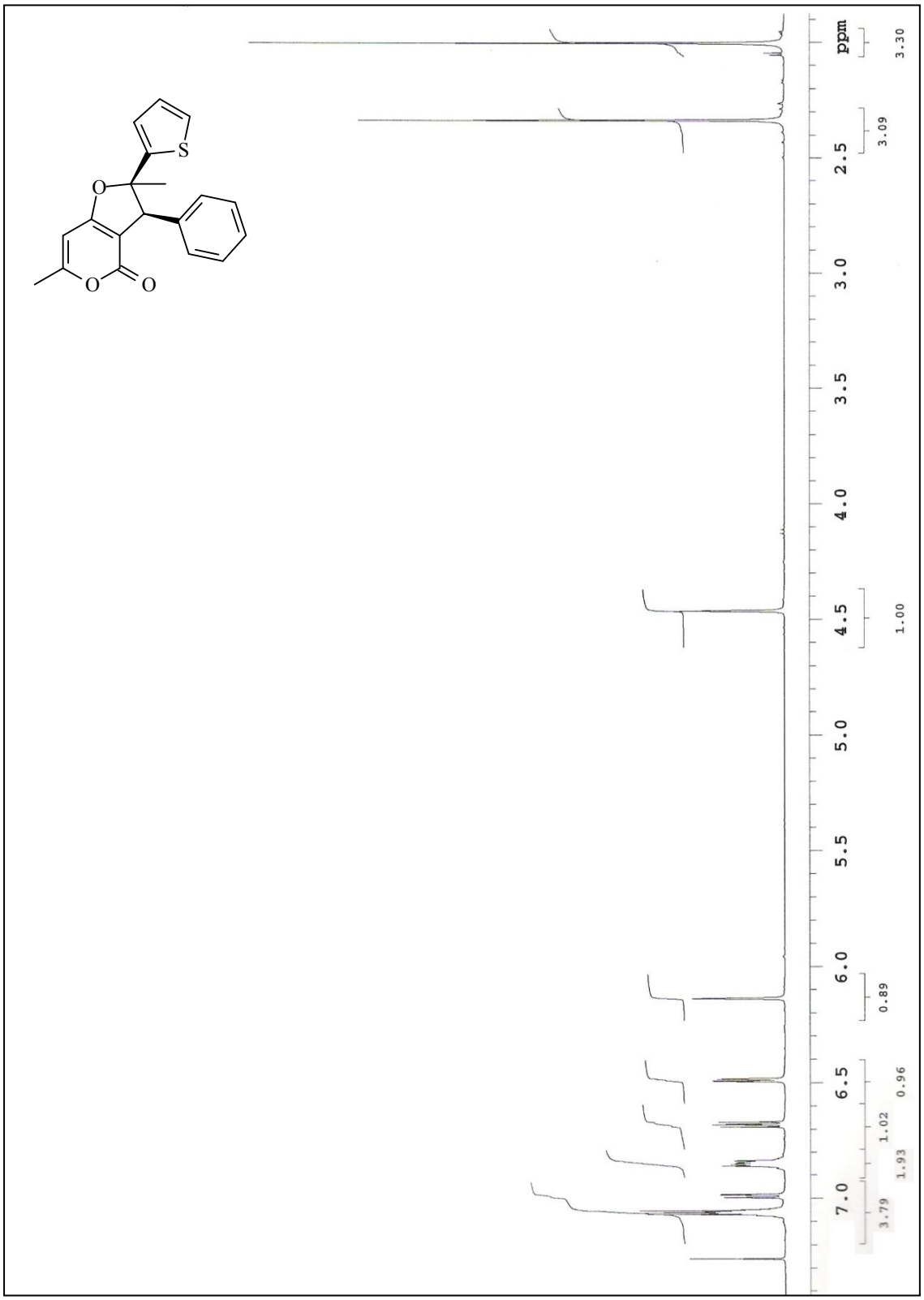
2.38 ^{1}H-NMR spectra of **38**



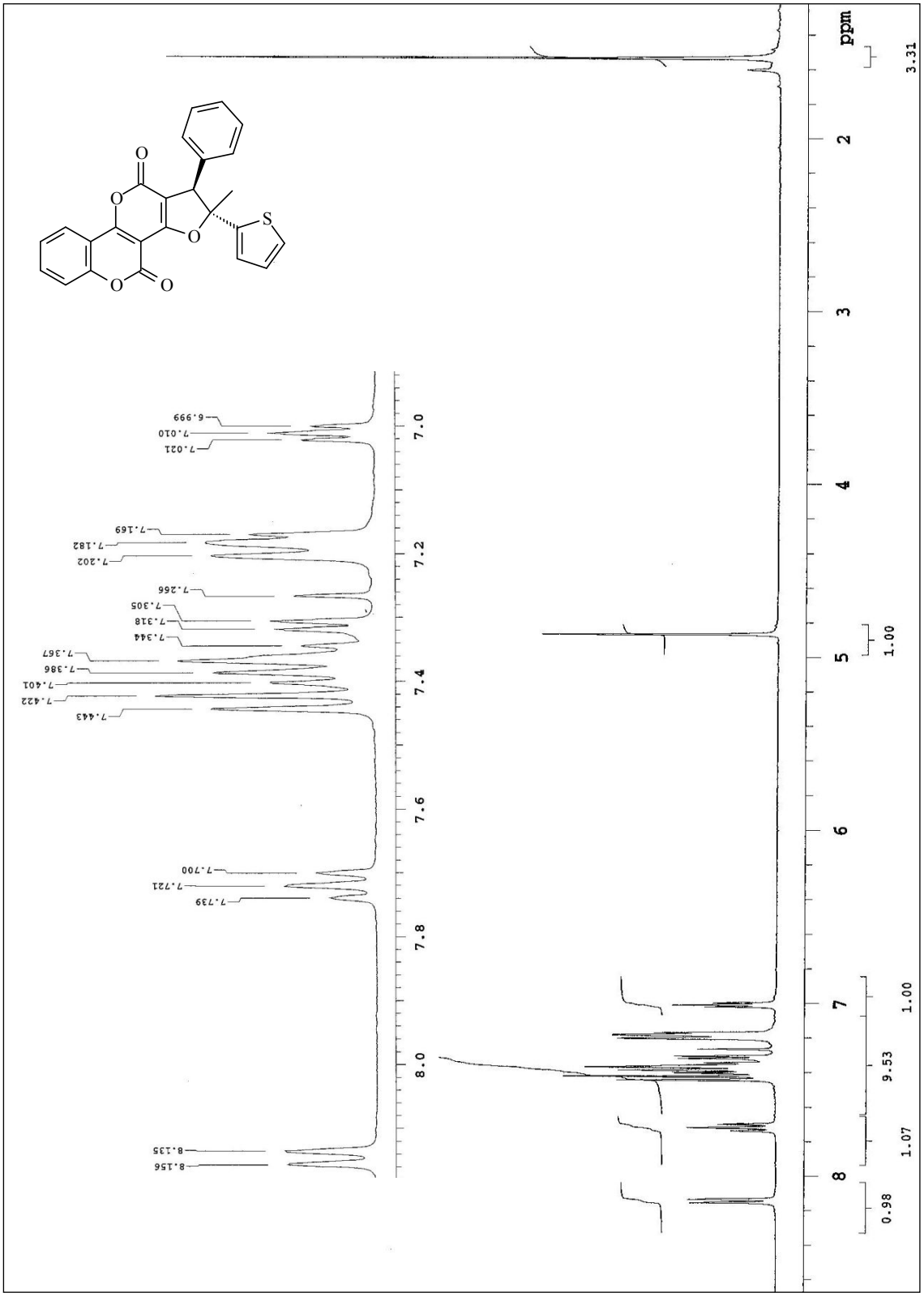
2.39 ^{1}H-NMR spectra of **39**



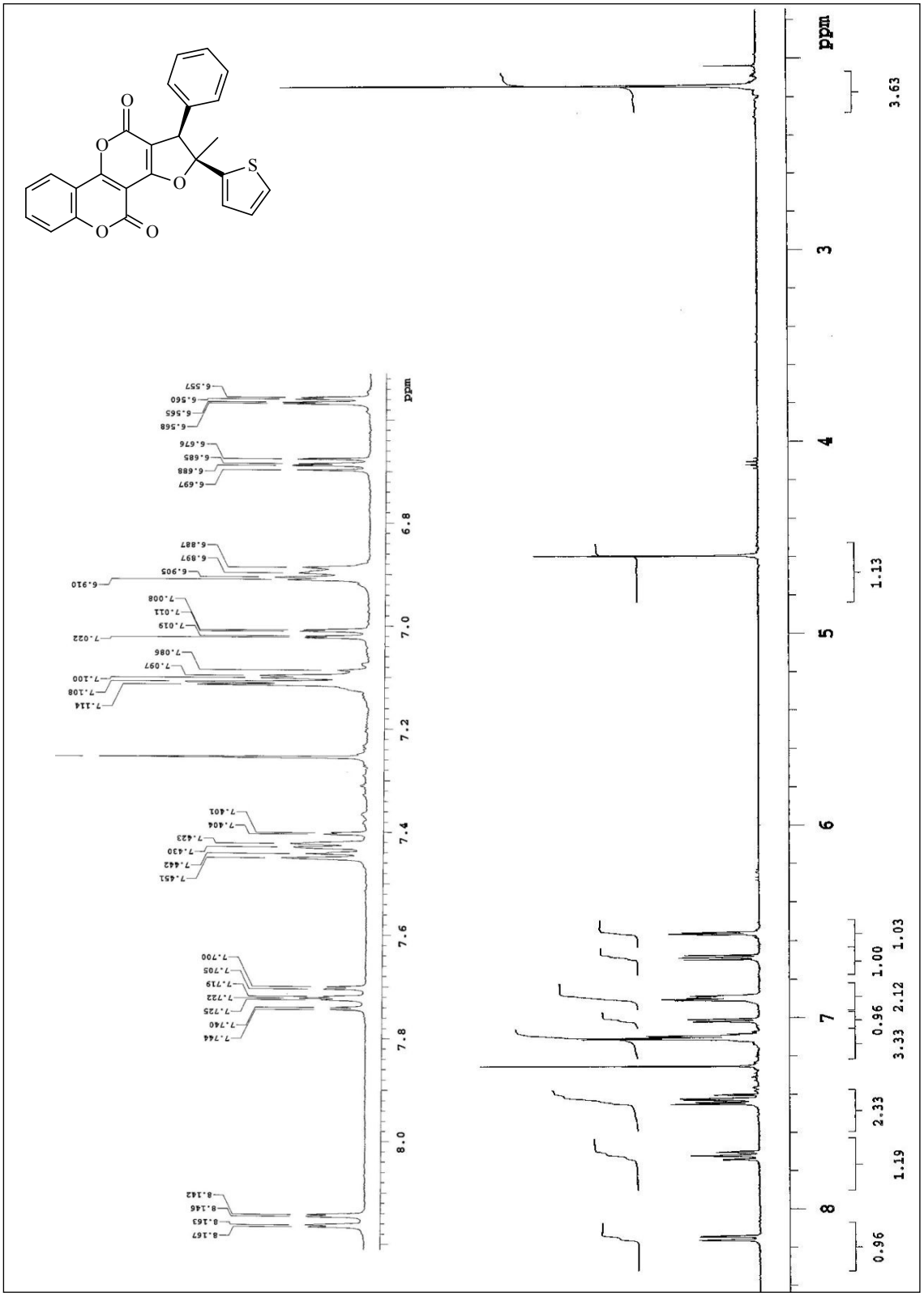
2.40 ^{1}H-NMR spectra of **40**



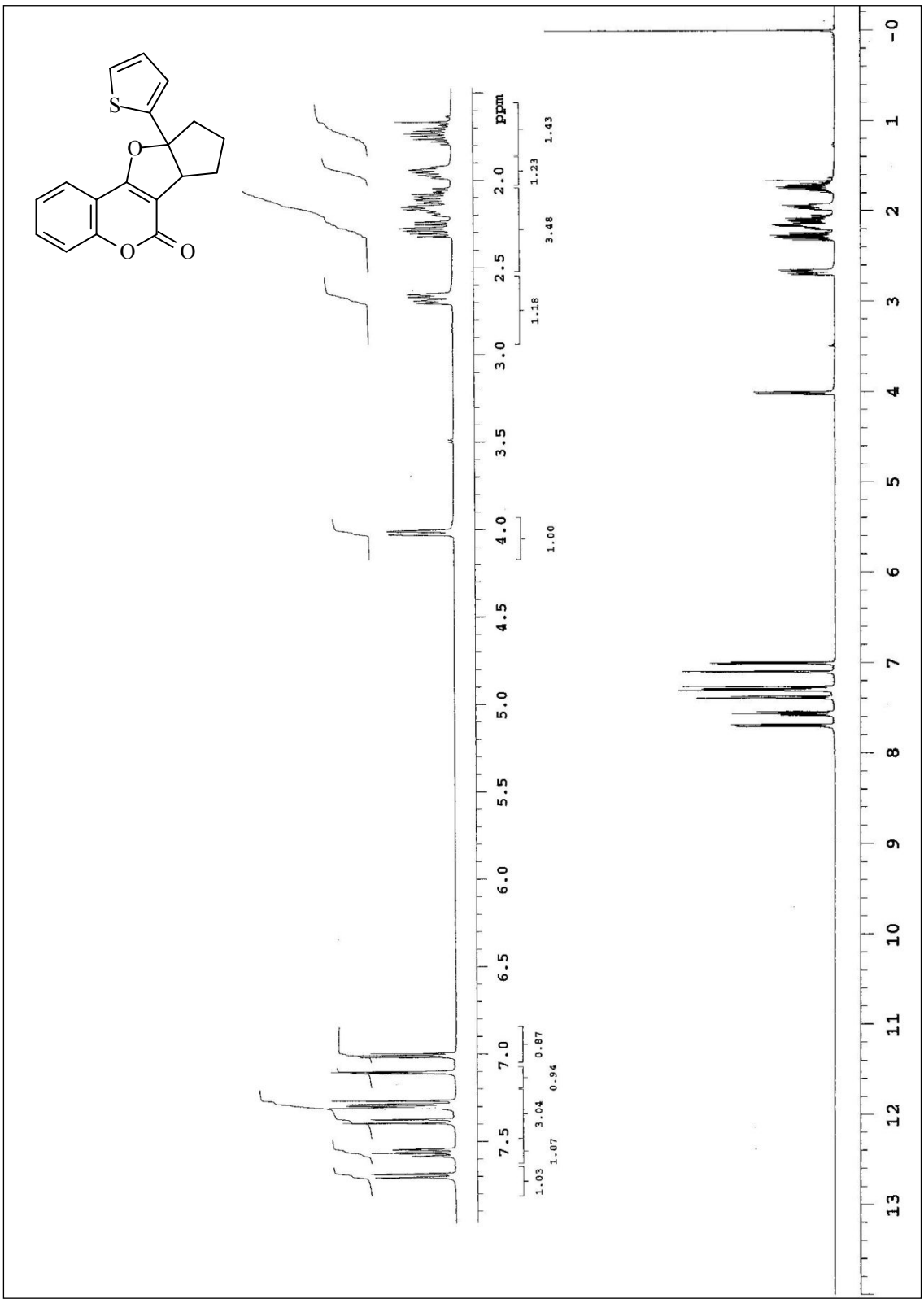
2.41 ^{1}H-NMR spectra of **41**



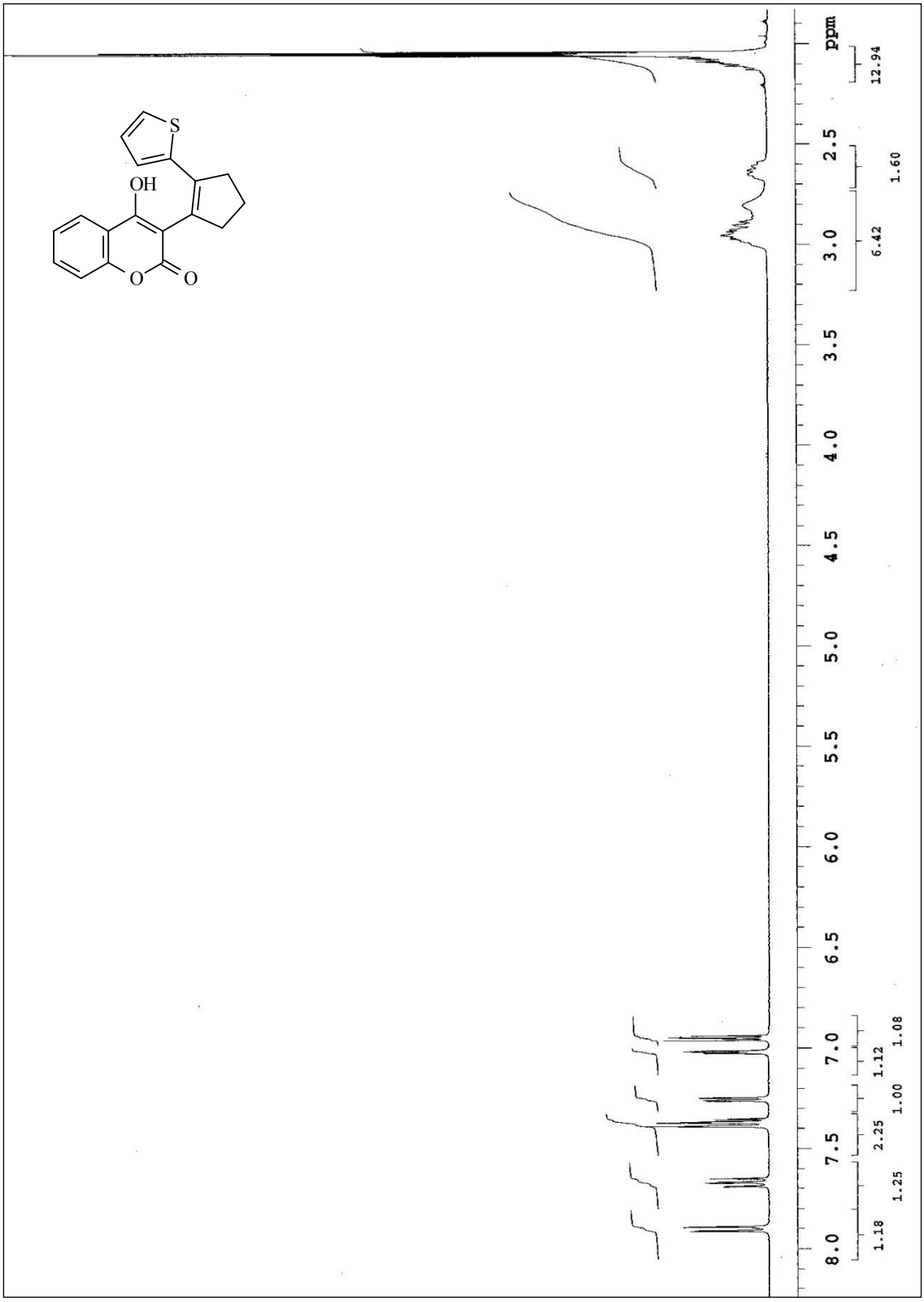
2.42 ^{1}H-NMR spectra of **42**



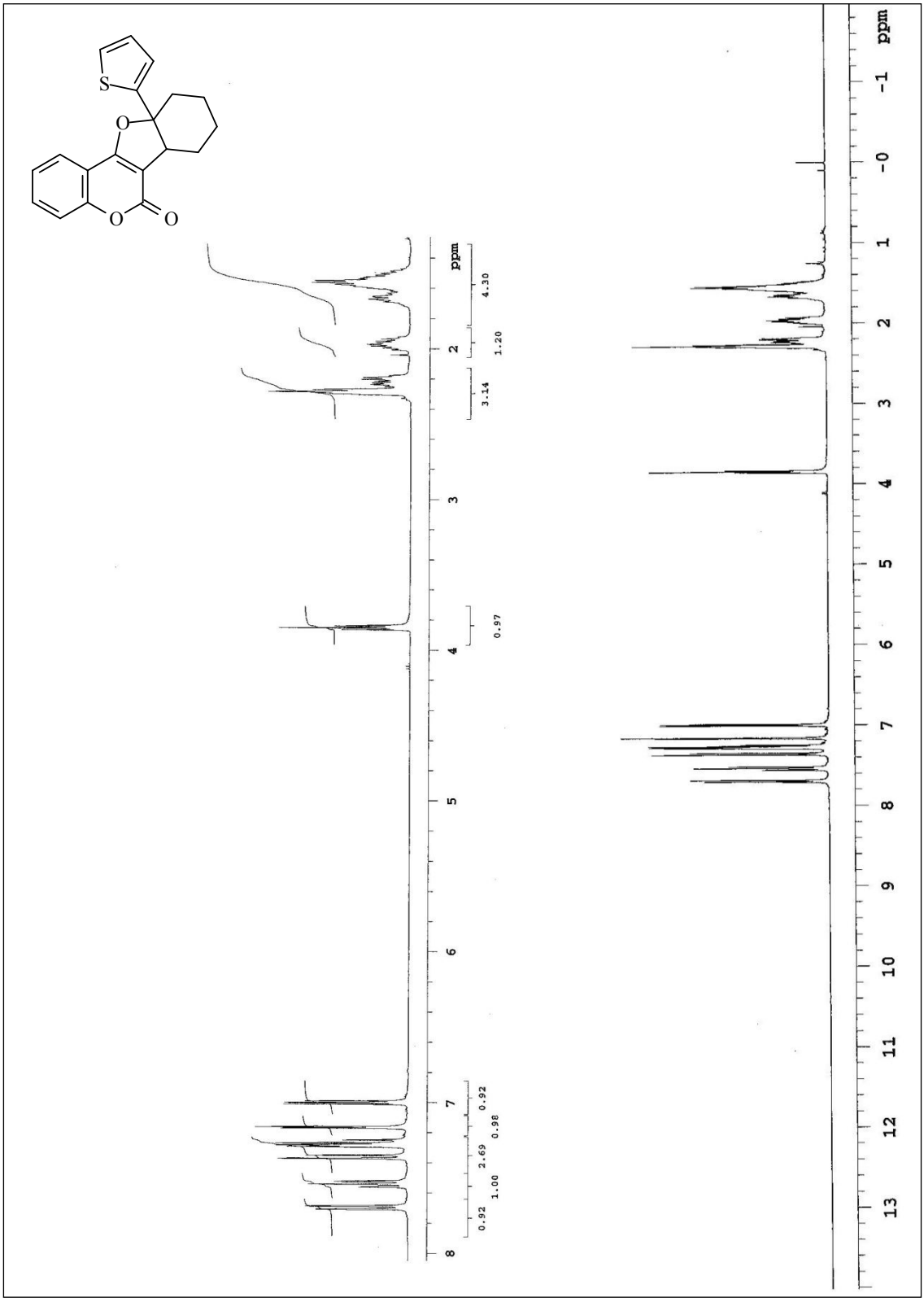
2.43 ^{1}H-NMR spectra of **43**



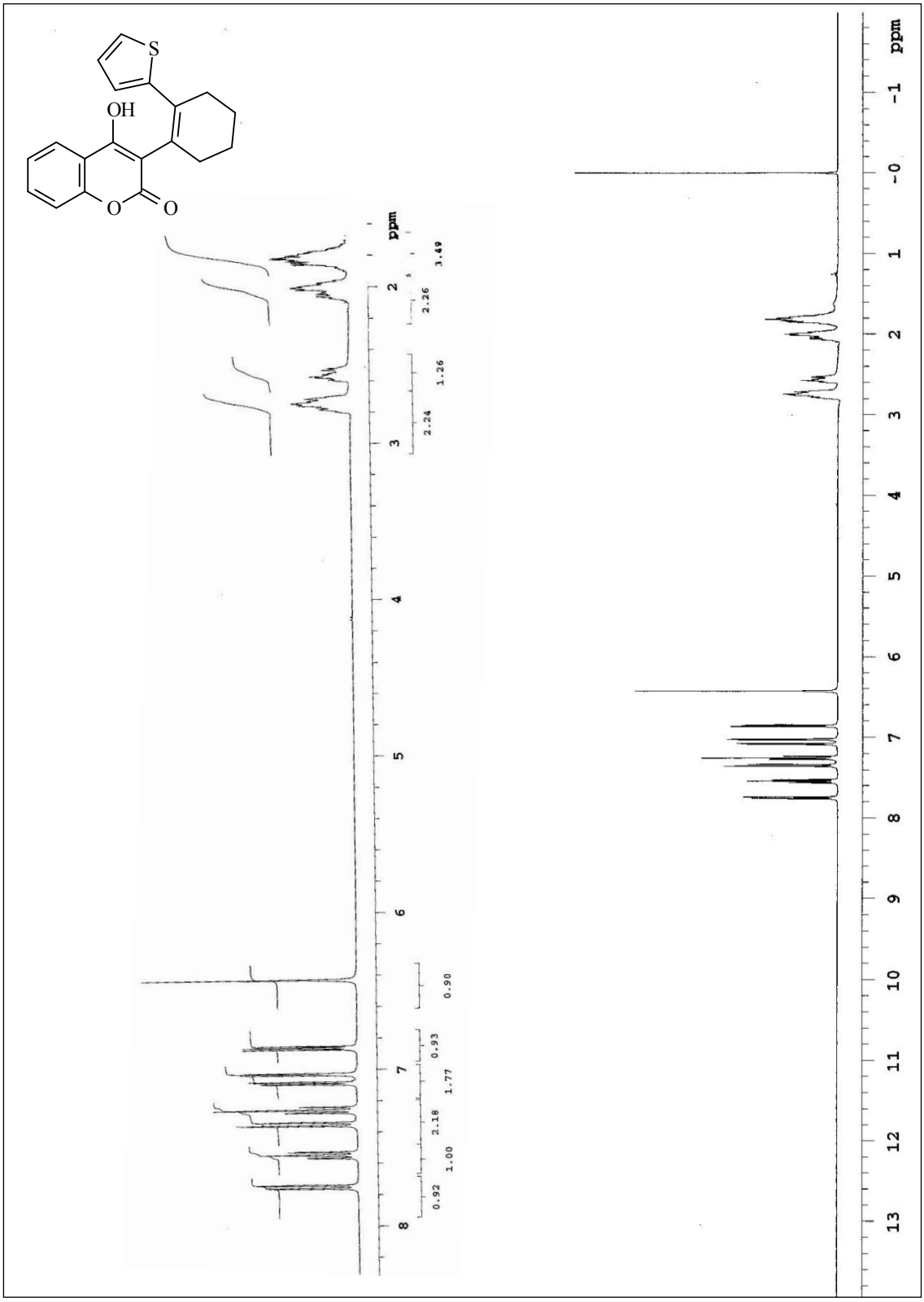
2.44 ^{1}H-NMR spectra of **49**



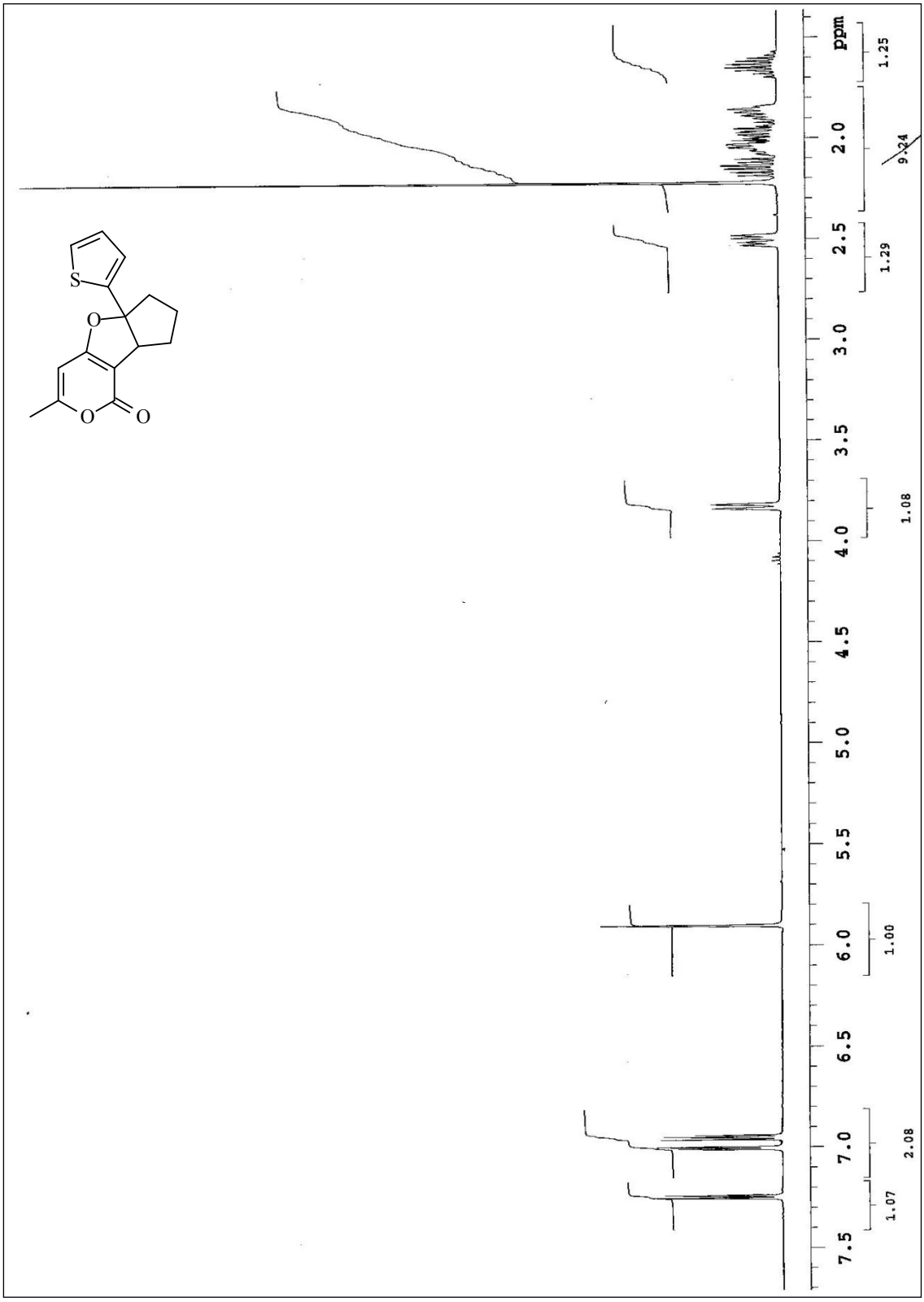
2.45 ^{1}H-NMR spectra of **44**



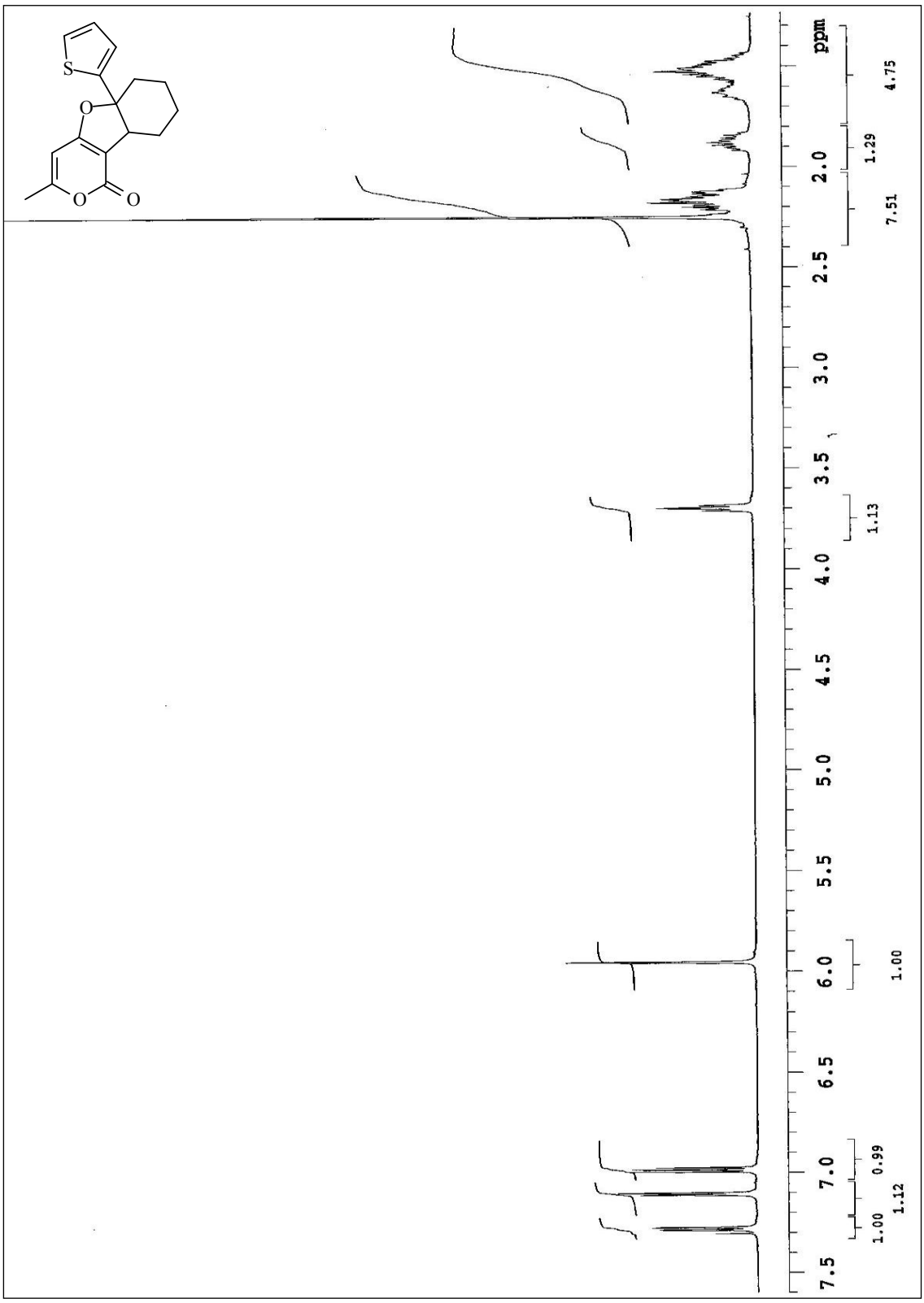
2.46 ^{1}H-NMR spectra of **50**



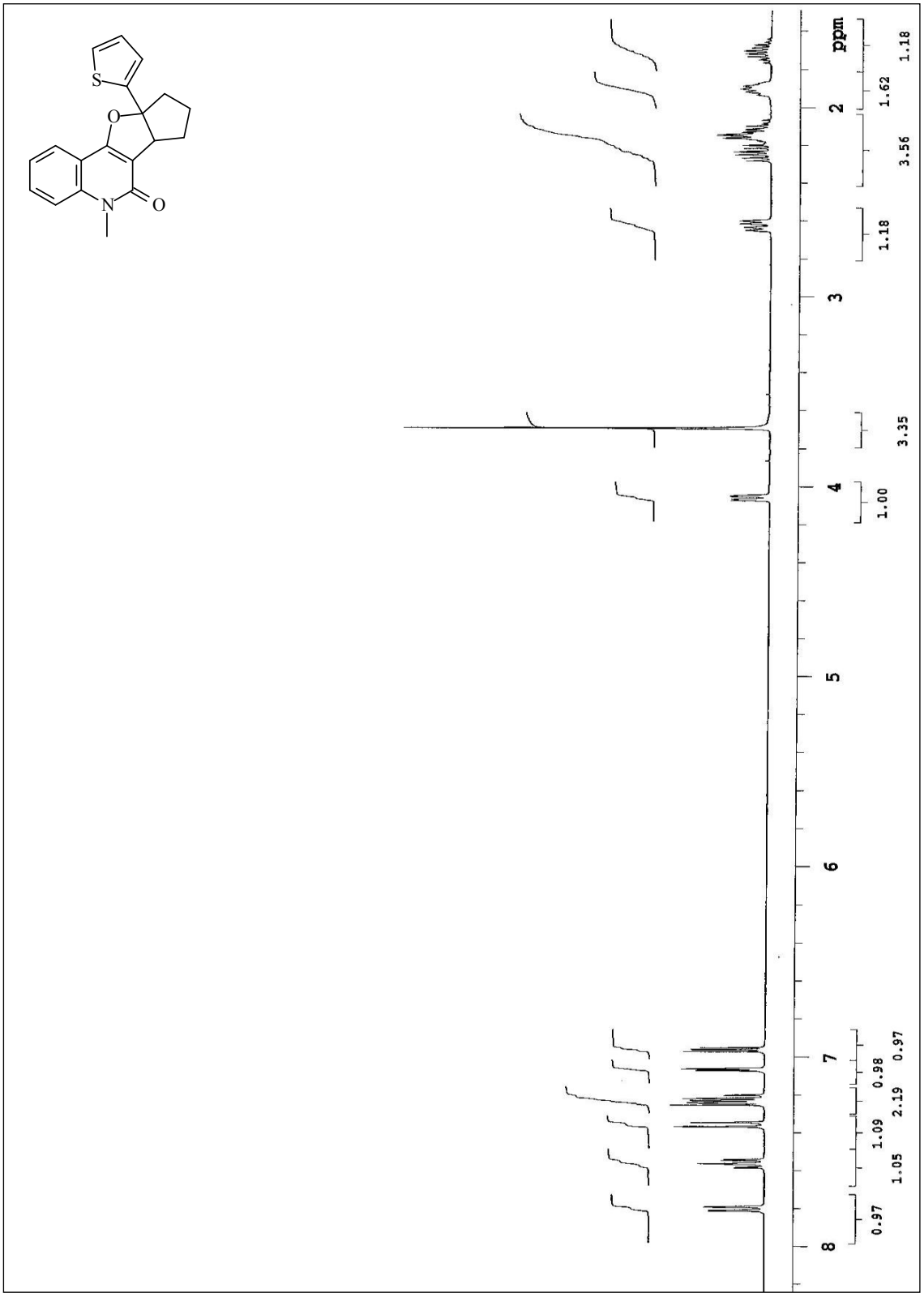
2.47 ^{1}H-NMR spectra of **45**



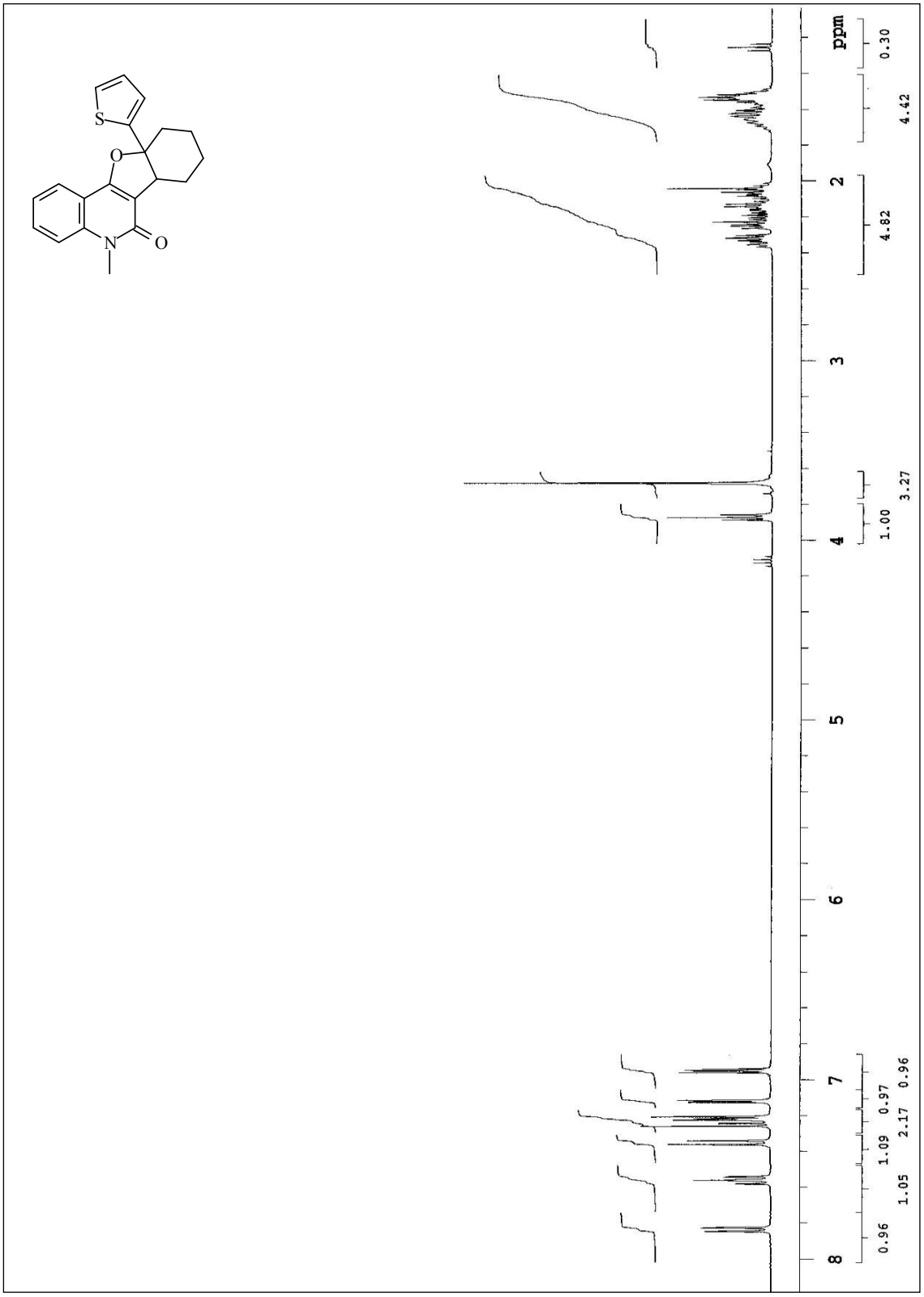
2.48 ^{1}H-NMR spectra of **46**



2.49 ^{1}H-NMR spectra of **47**

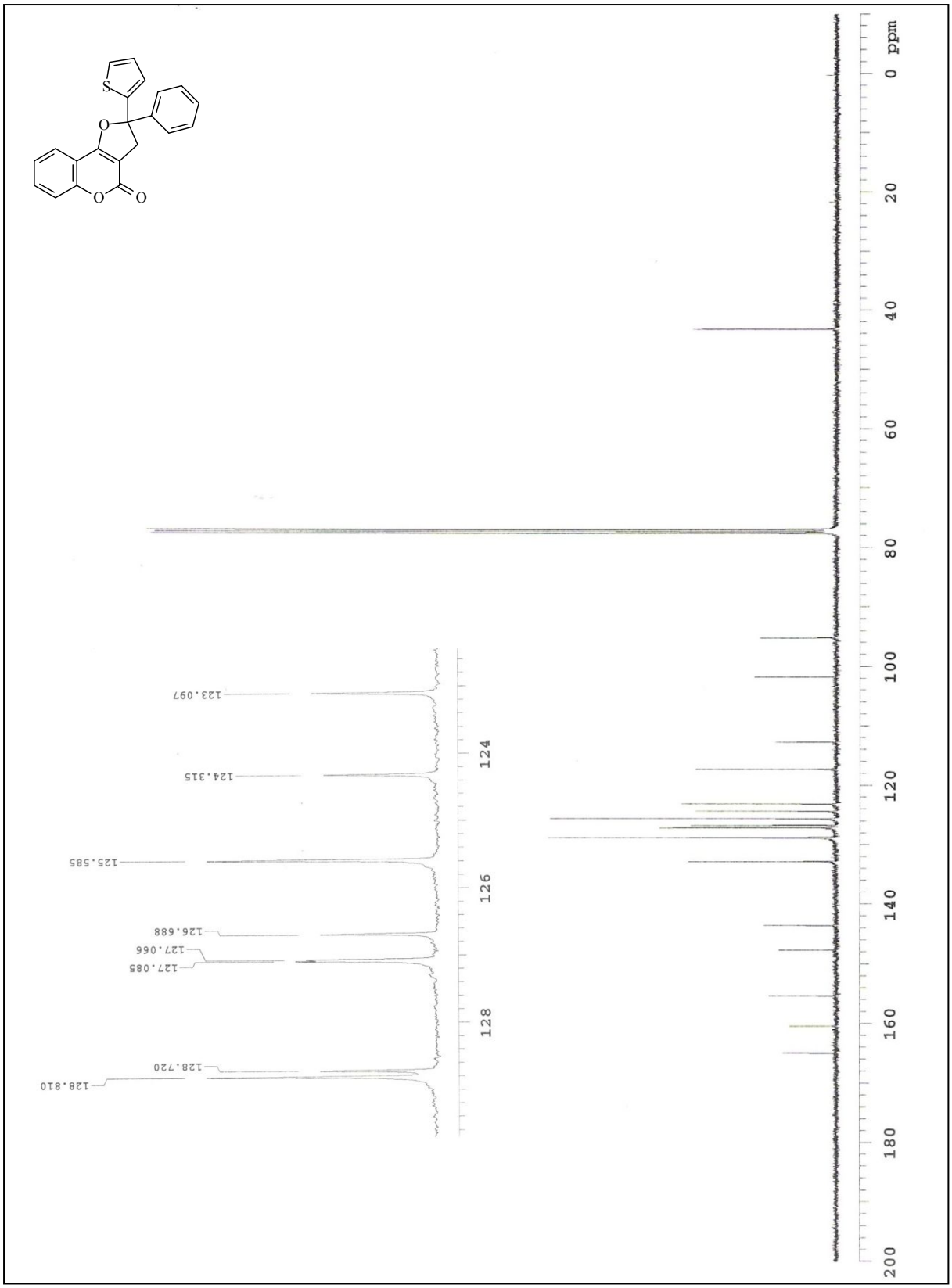


2.50 ^{1}H-NMR spectra of **48**

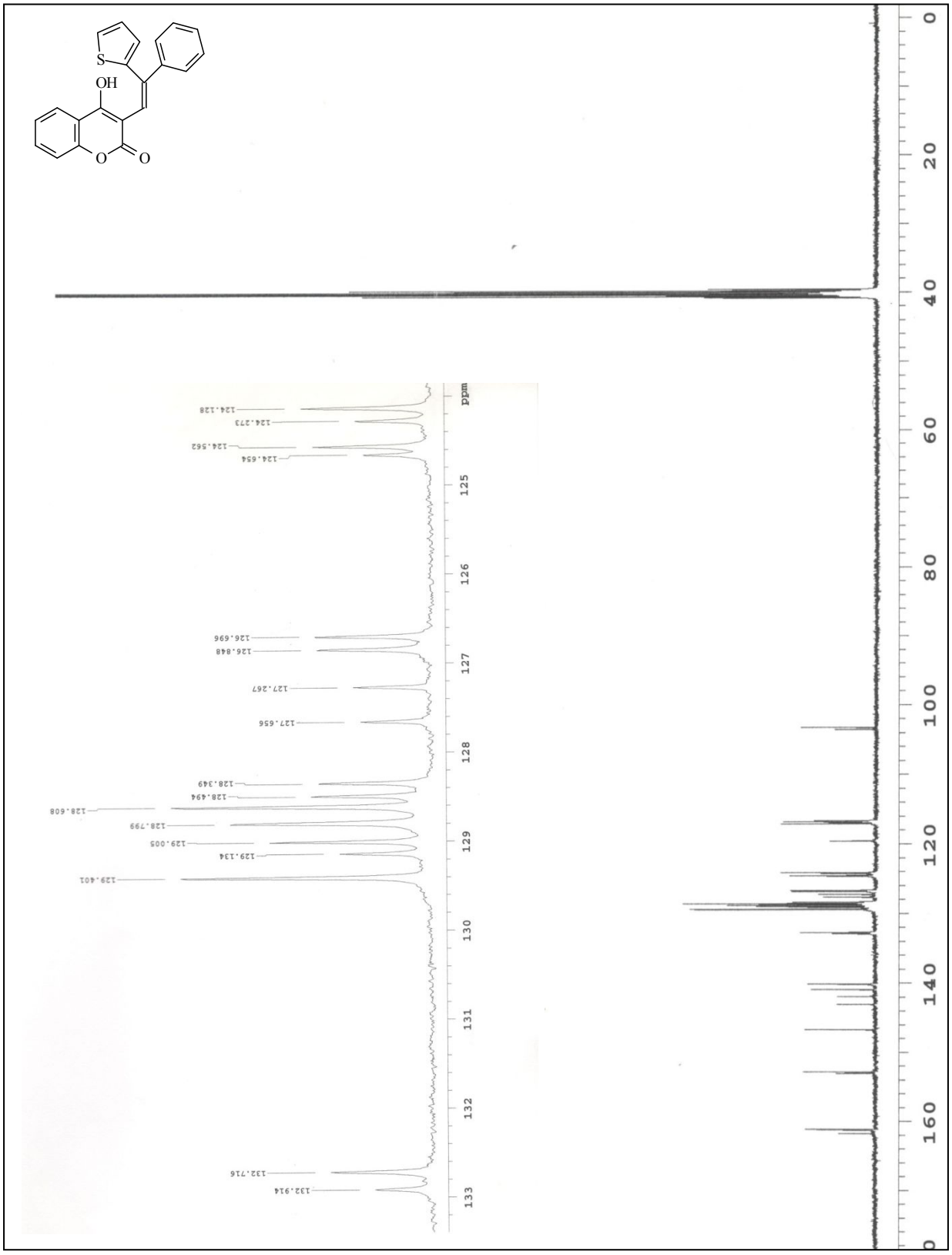


^{13}C-NMR of COMPOUNDS

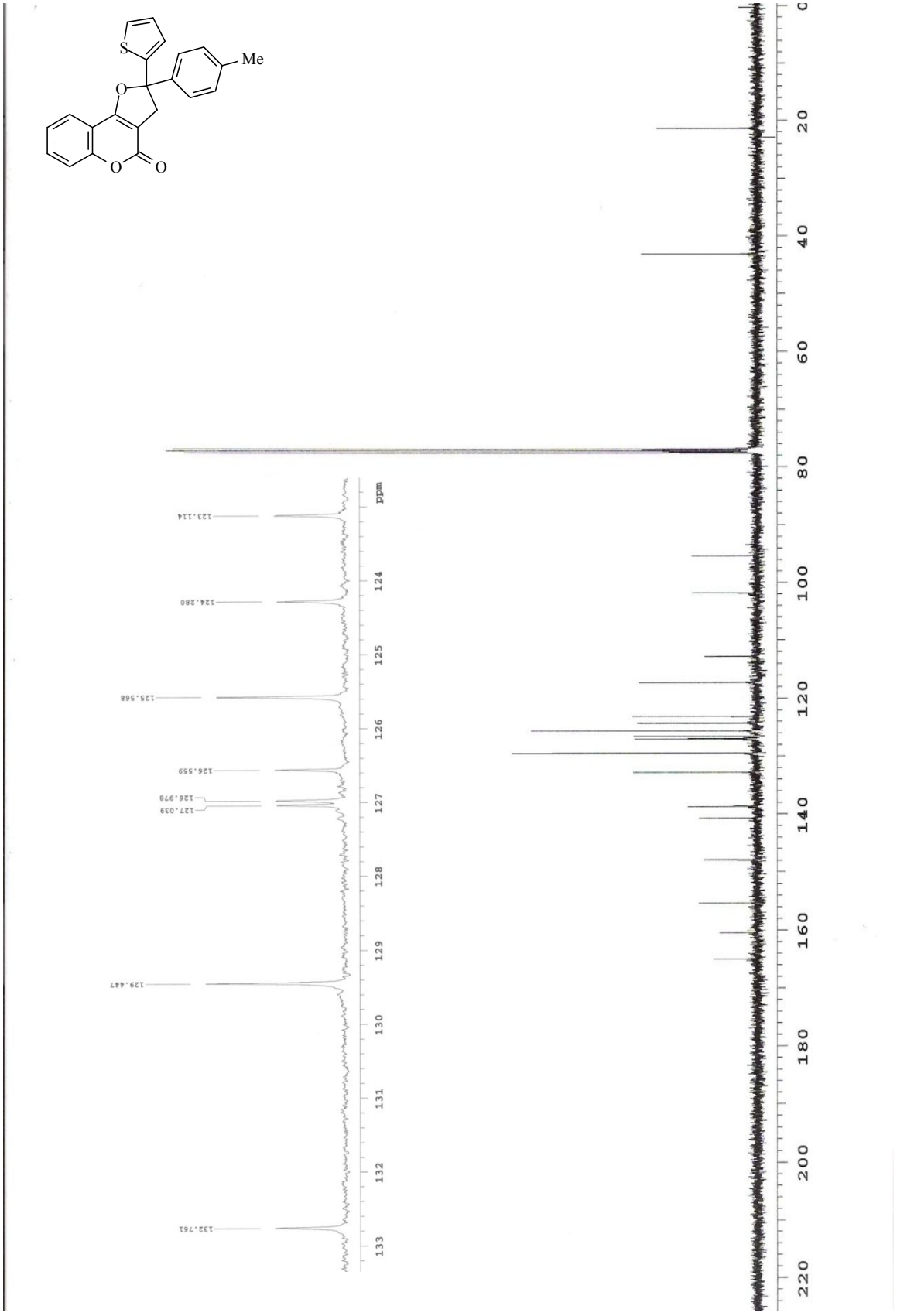
3.1 ^{13}C-NMR spectra of **3**



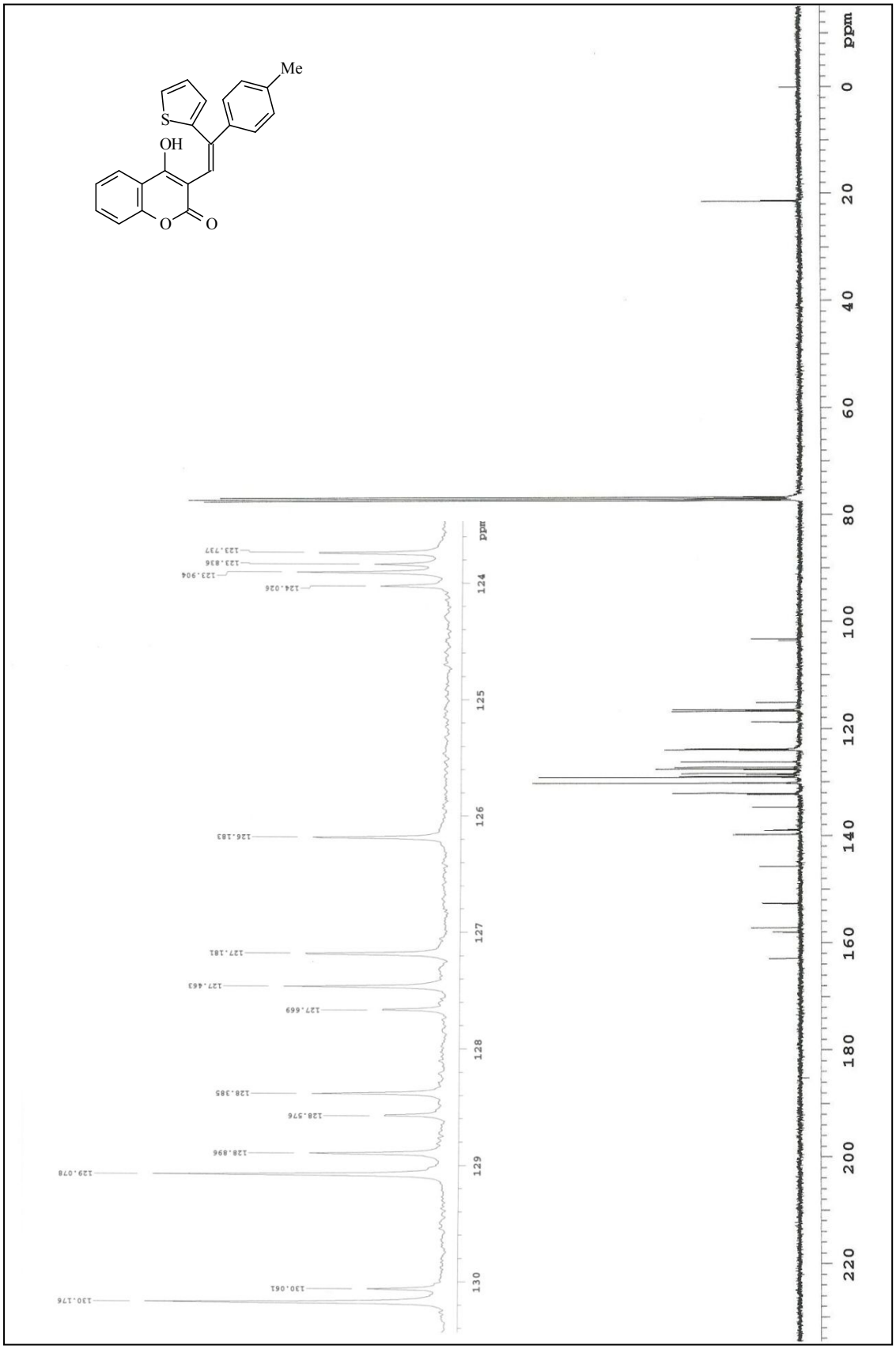
3.2 ^{13}C-NMR spectra of **8**



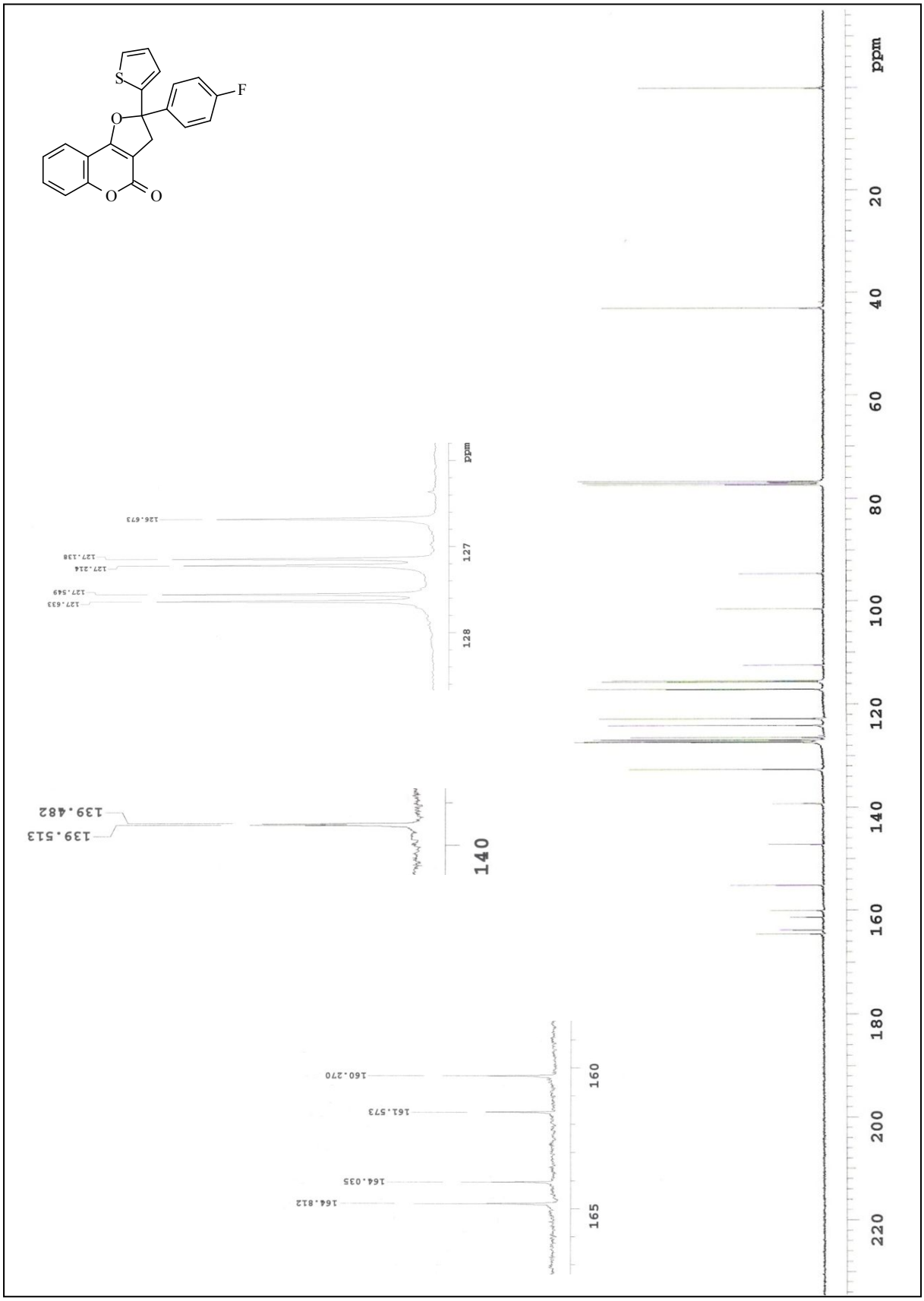
3.3 ^{13}C-NMR spectra of **4**



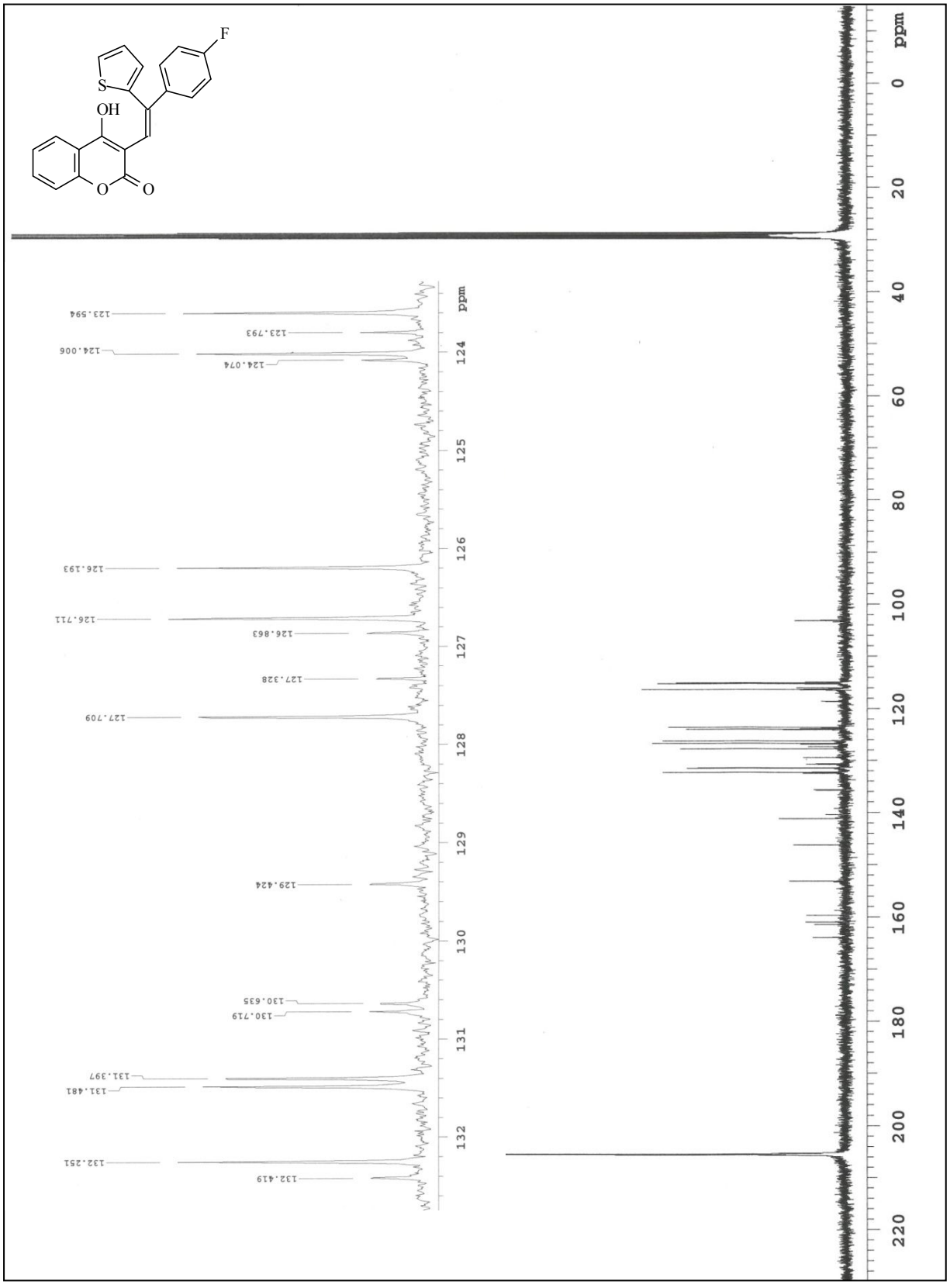
3.4 ^{13}C-NMR spectra of **9**



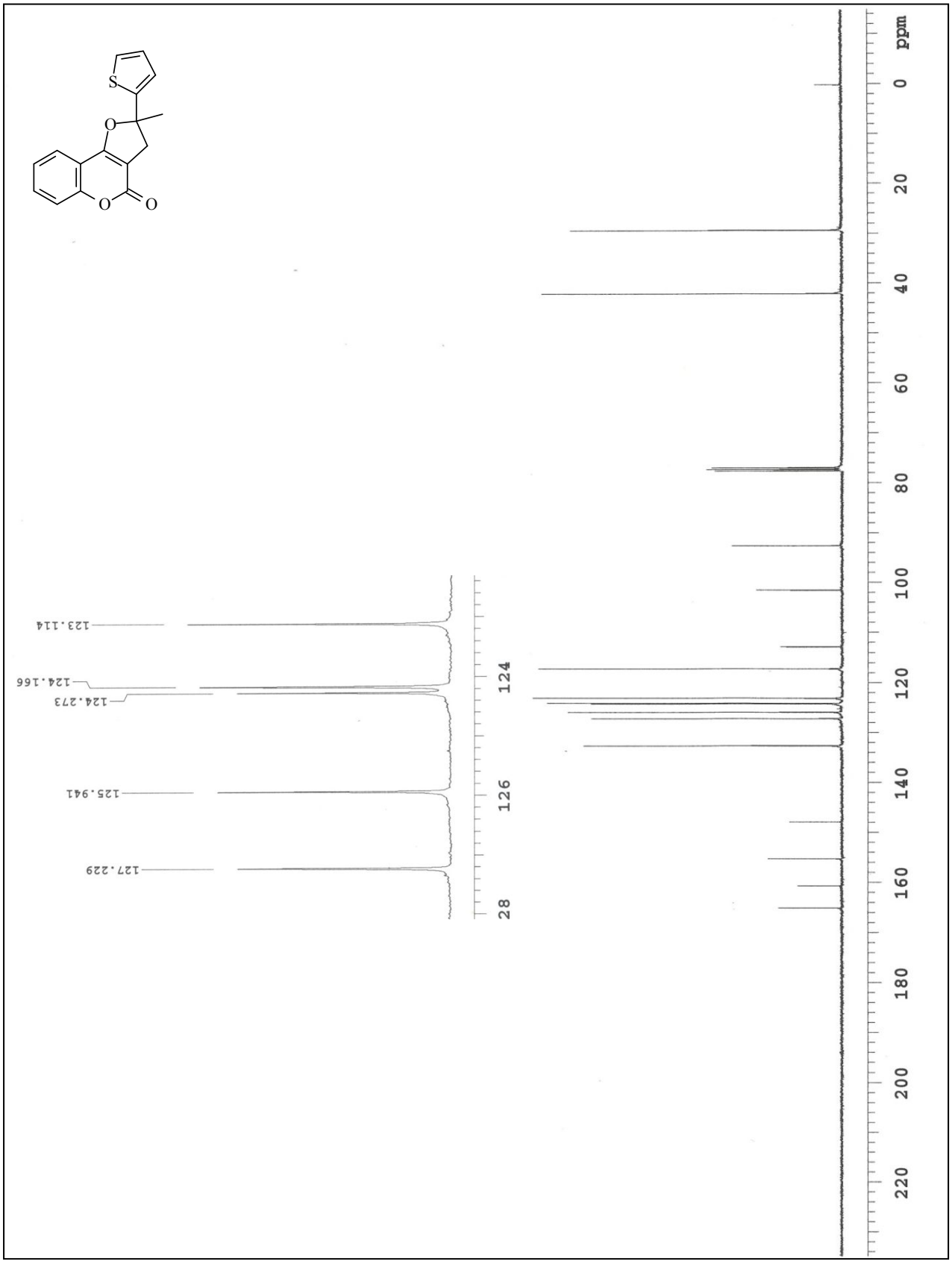
3.5 ^{13}C-NMR spectra of **5**



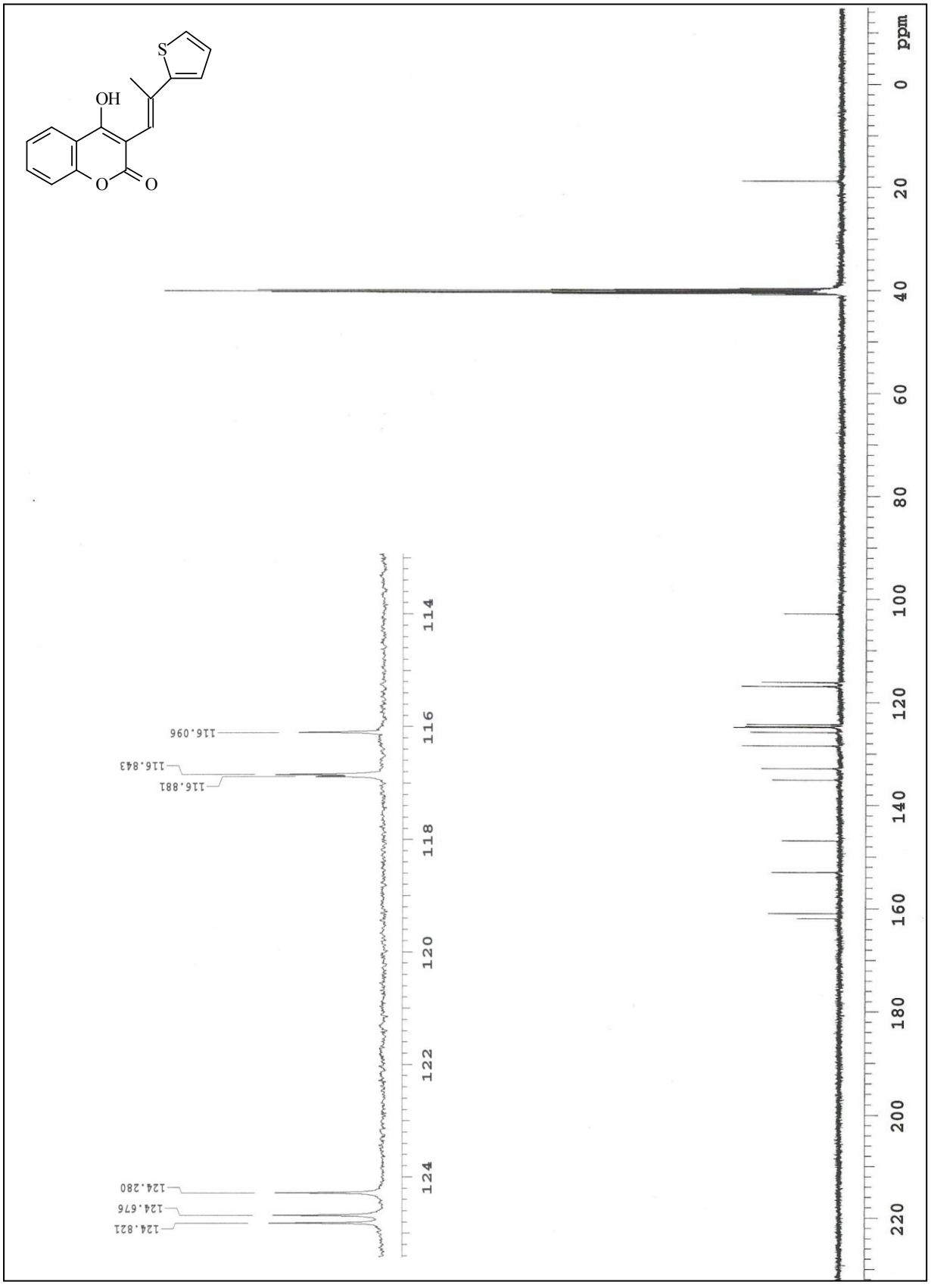
3.6 ^{13}C-NMR spectra of **10**



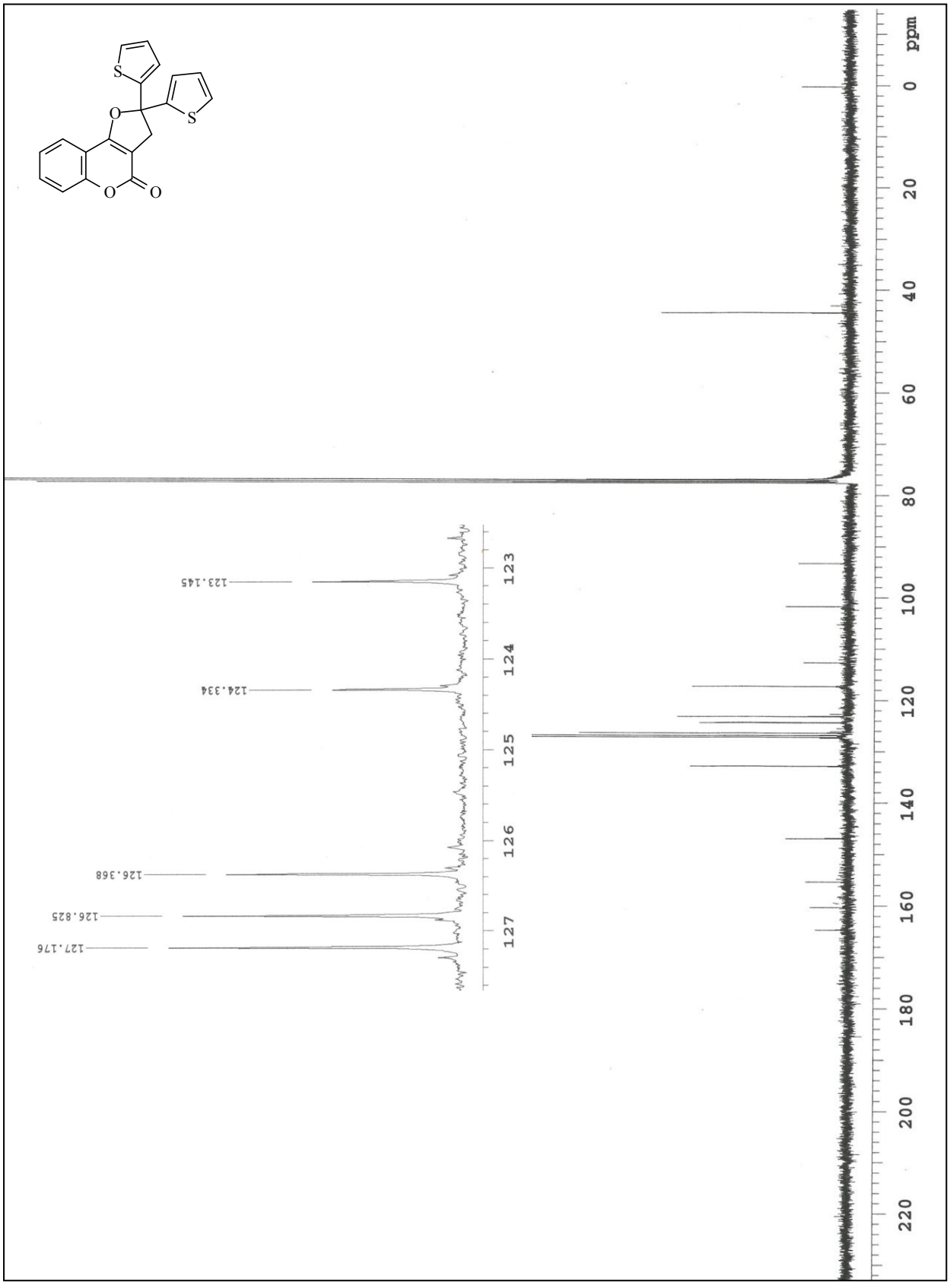
3.7 ^{13}C-NMR spectra of **6**



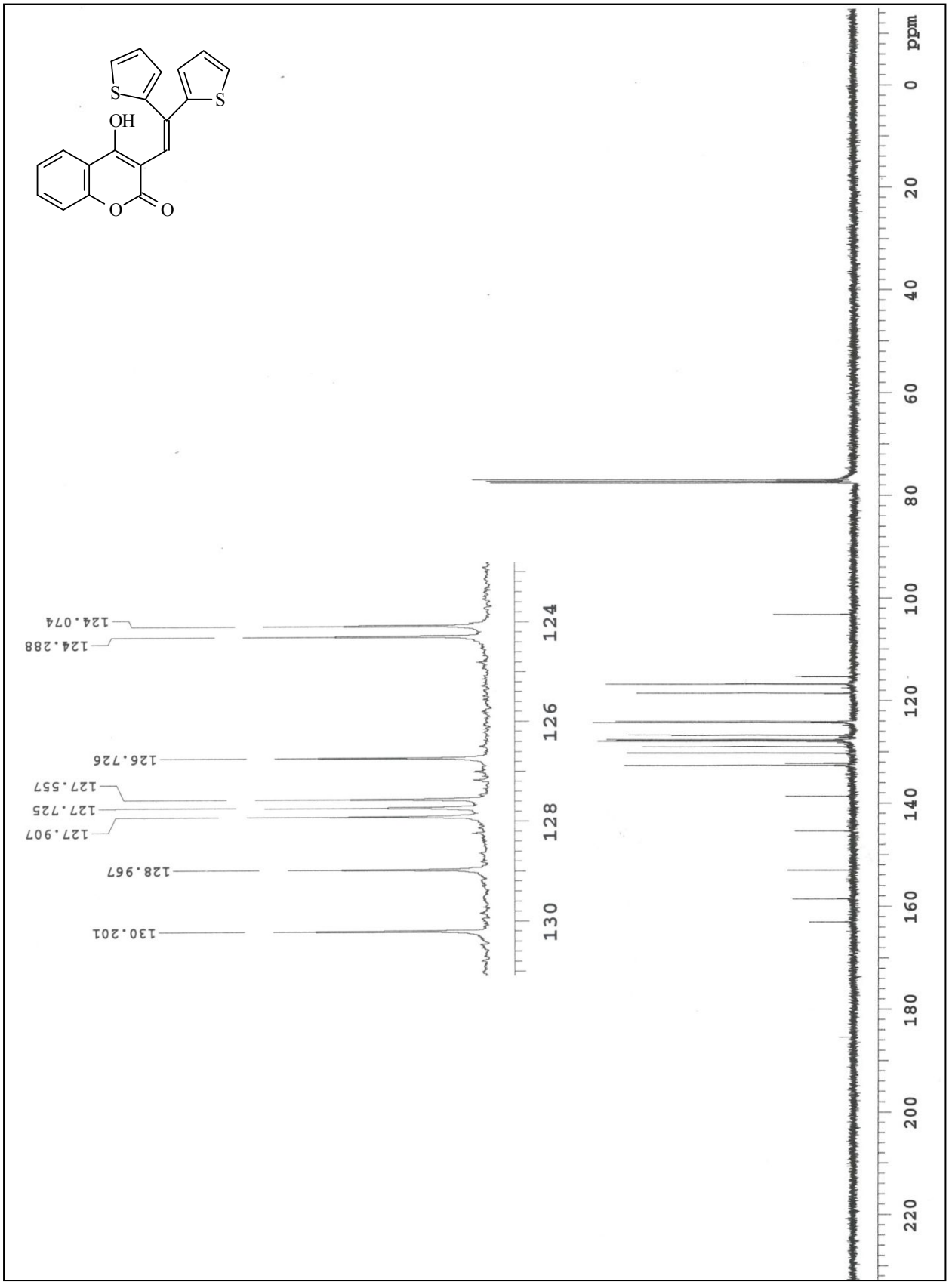
3.8 ^{13}C-NMR spectra of **11**



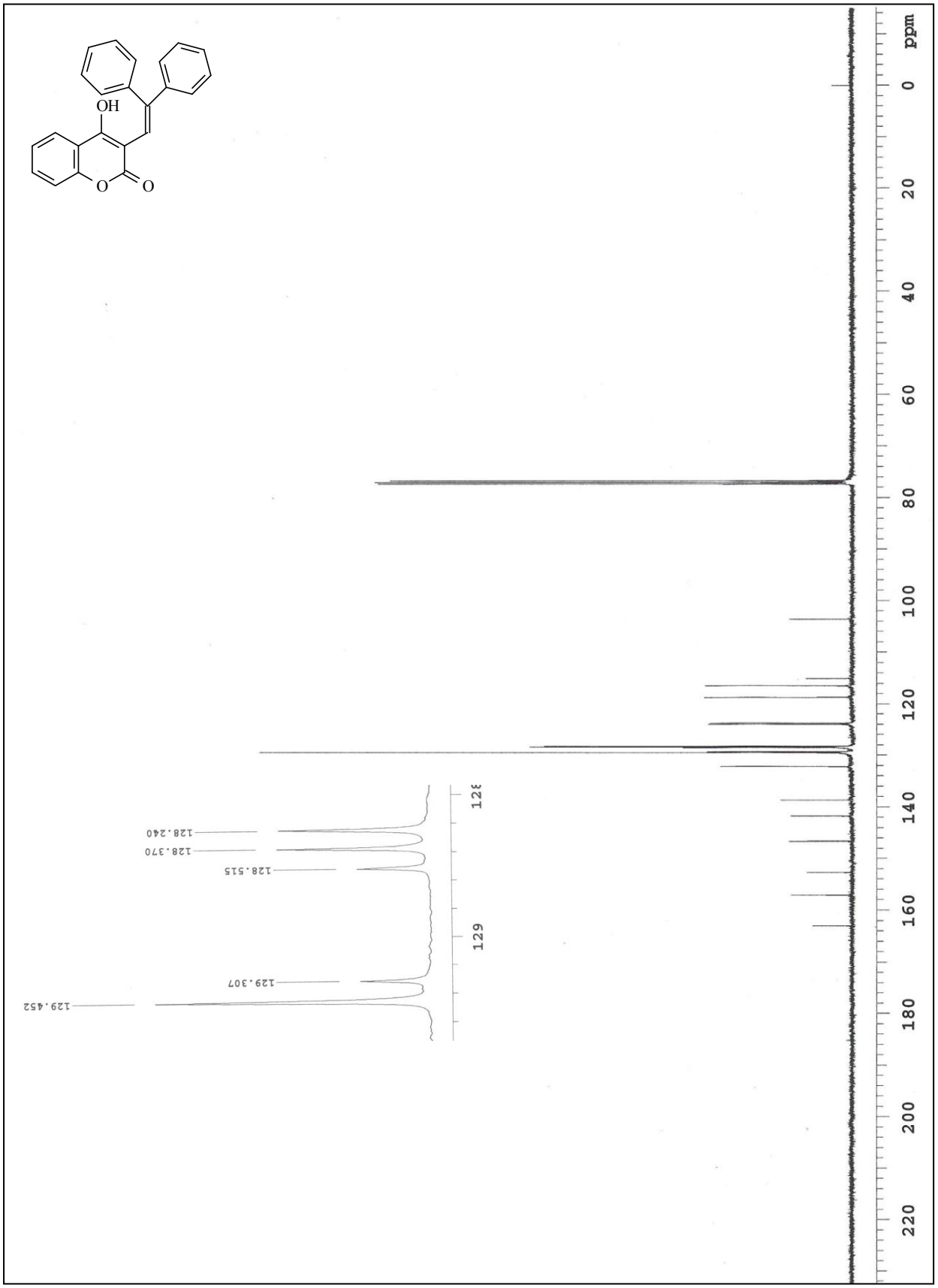
3.9 ^{13}C-NMR spectra of **7**



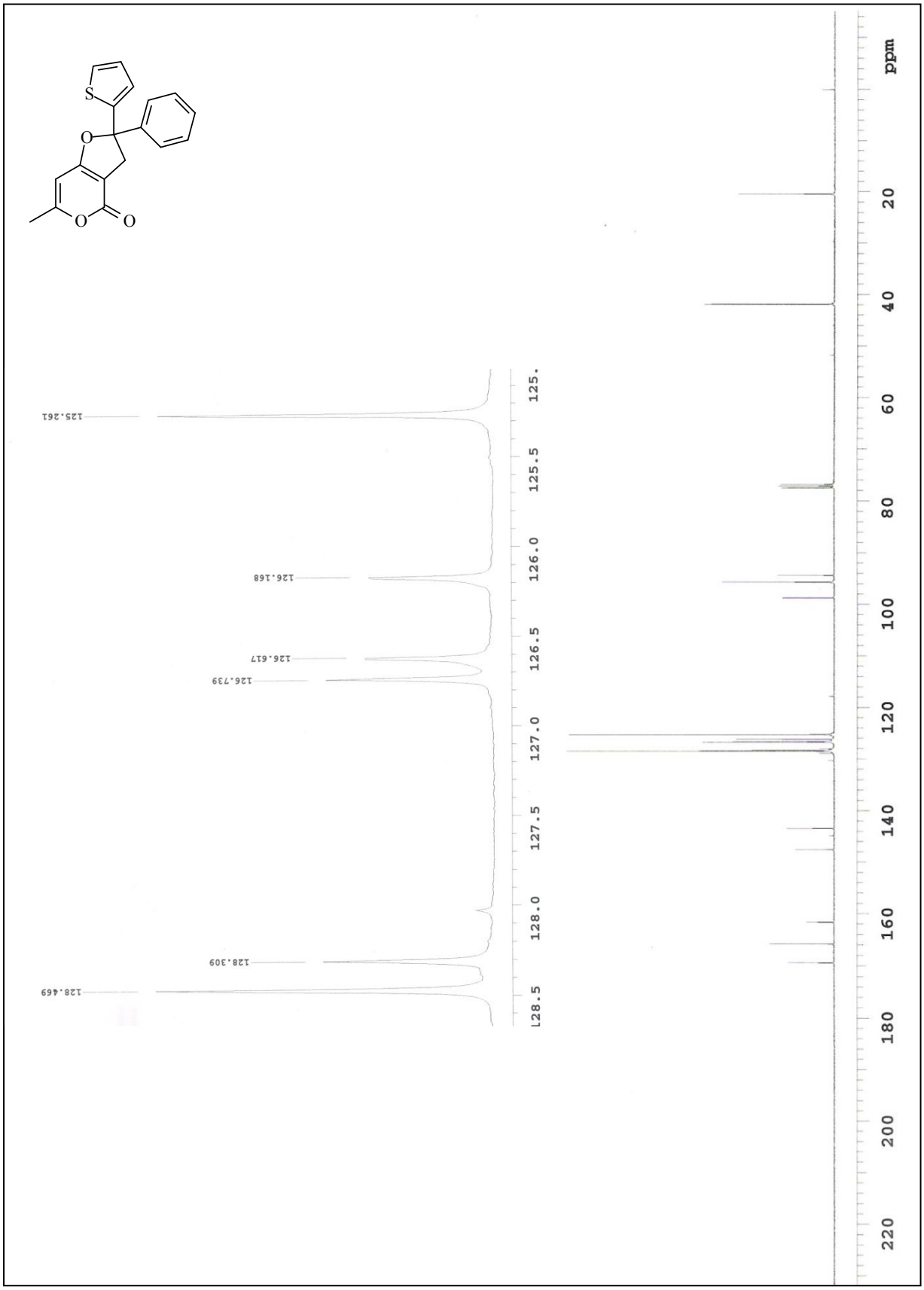
3.10 ^{13}C-NMR spectra of **12**



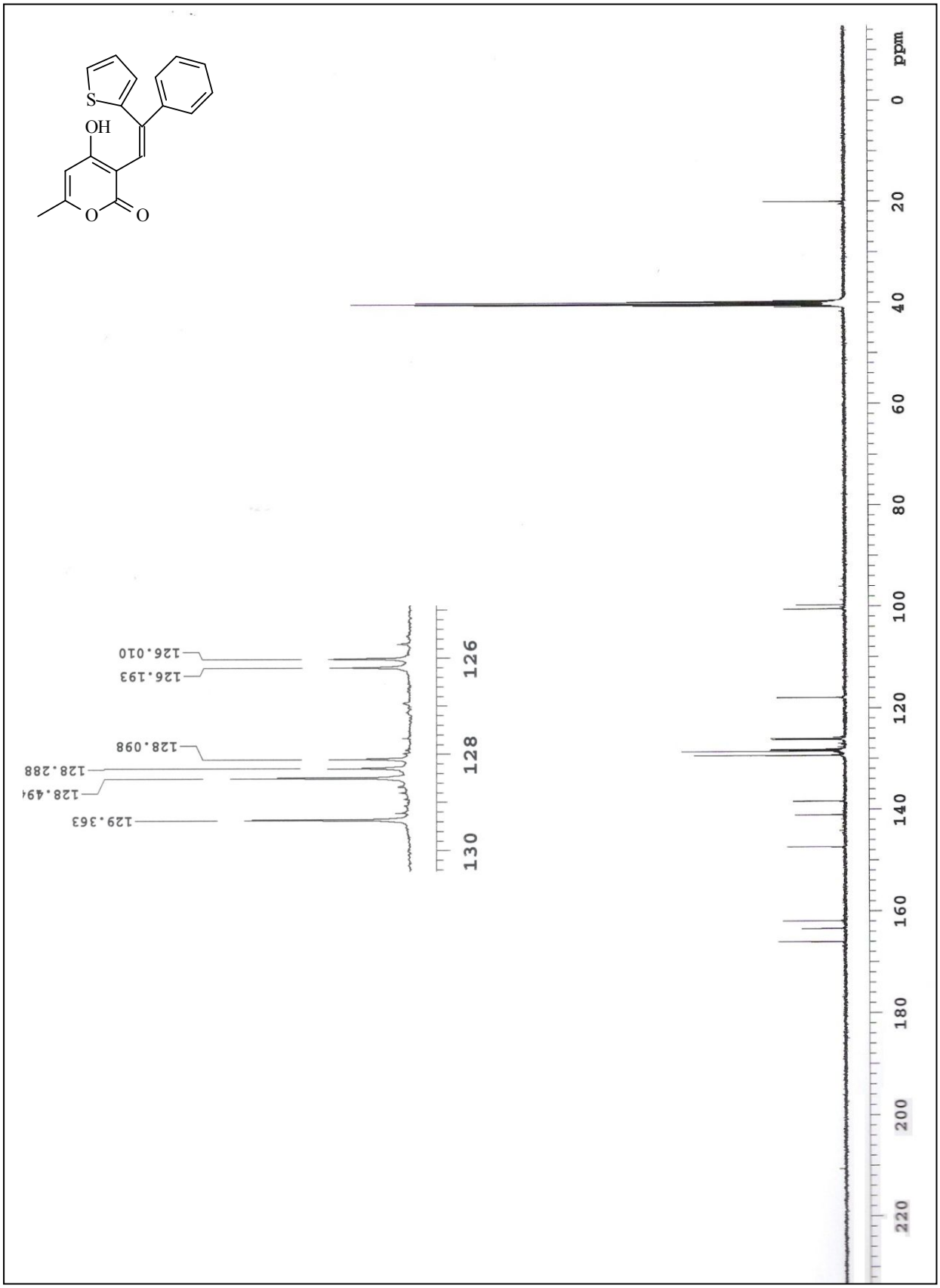
3.11 ^{13}C-NMR spectra of **4aj**



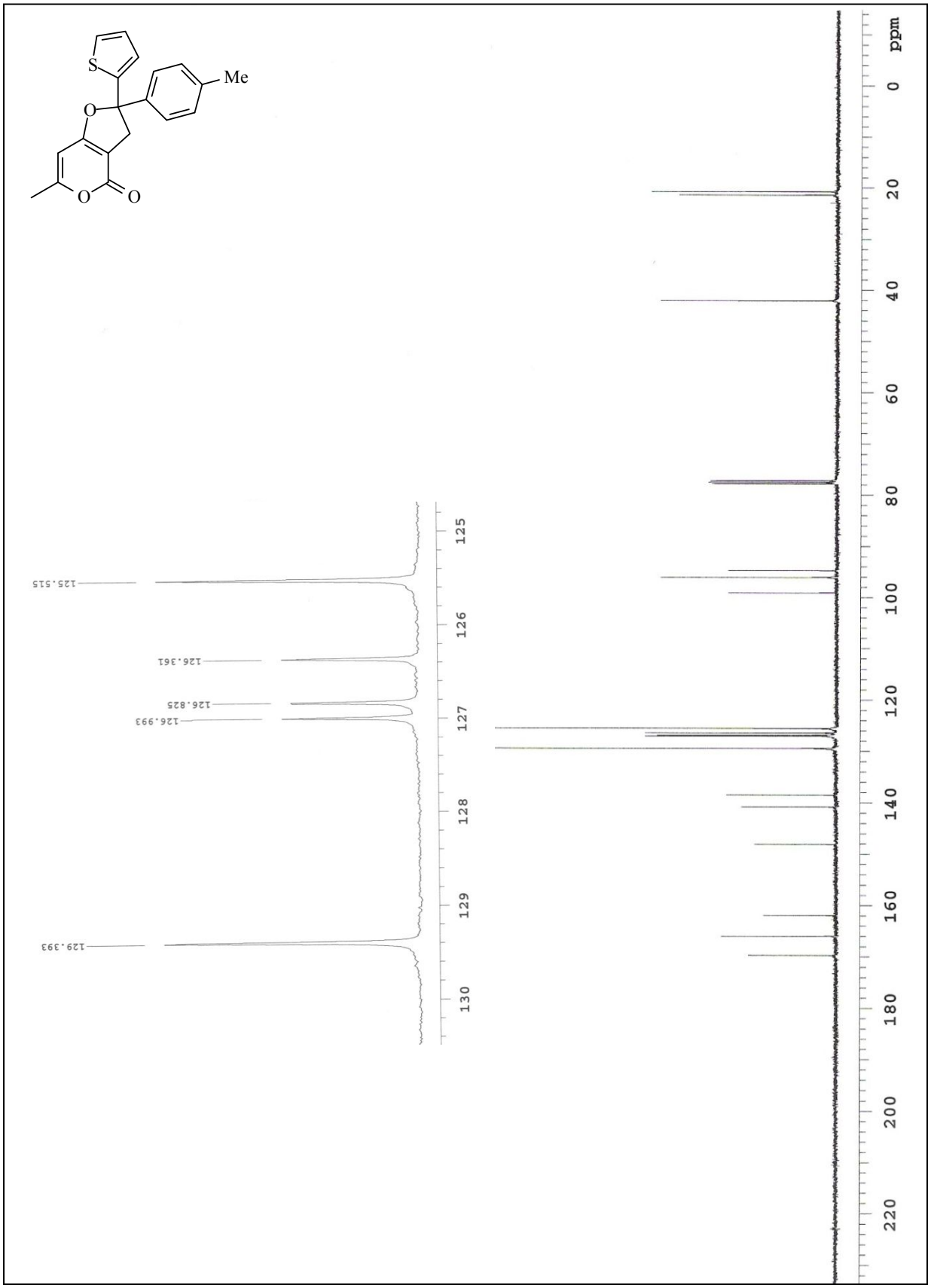
3.12 ^{13}C-NMR spectra of **13**



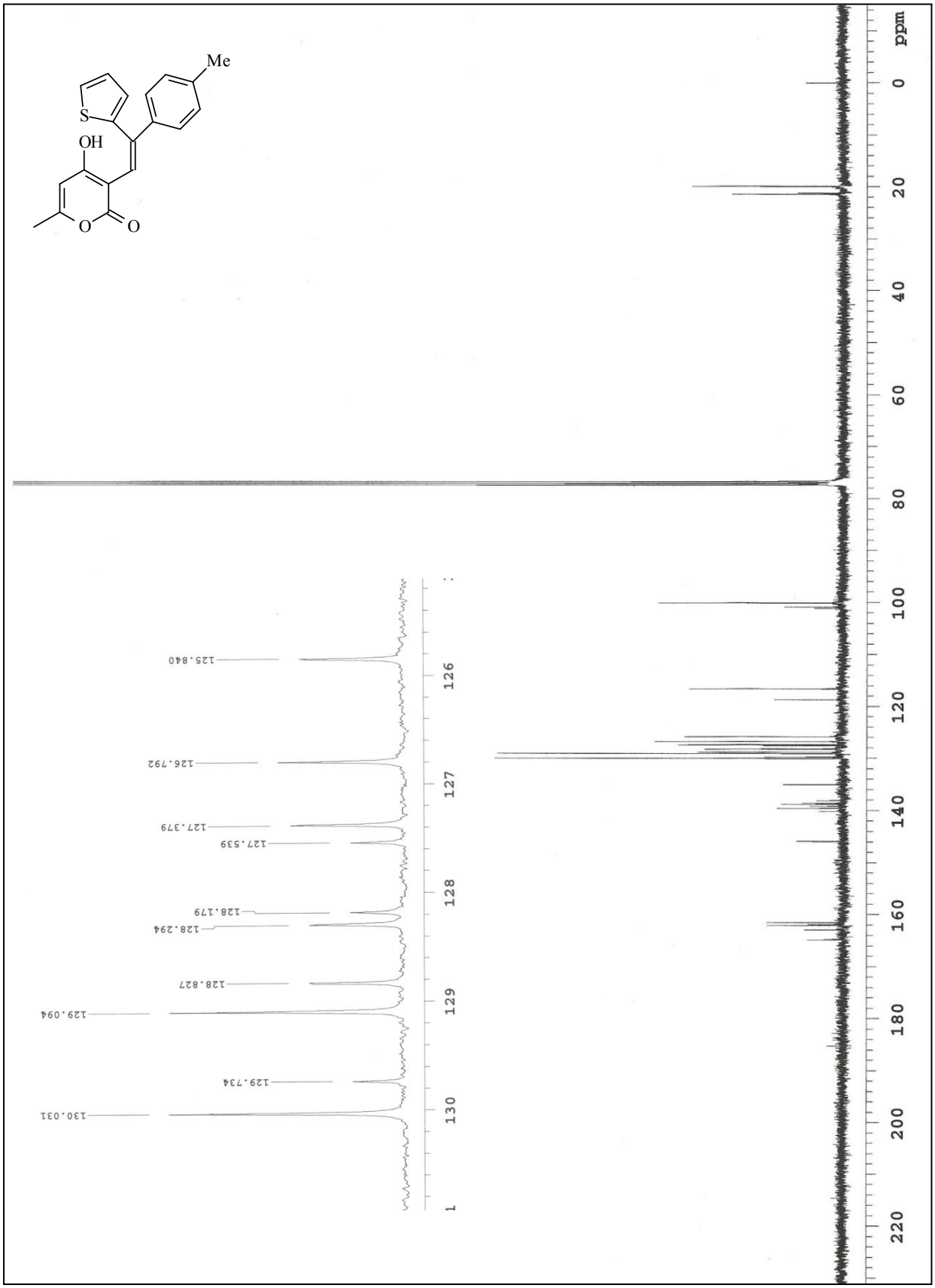
3.13 ^{13}C-NMR spectra of **16**



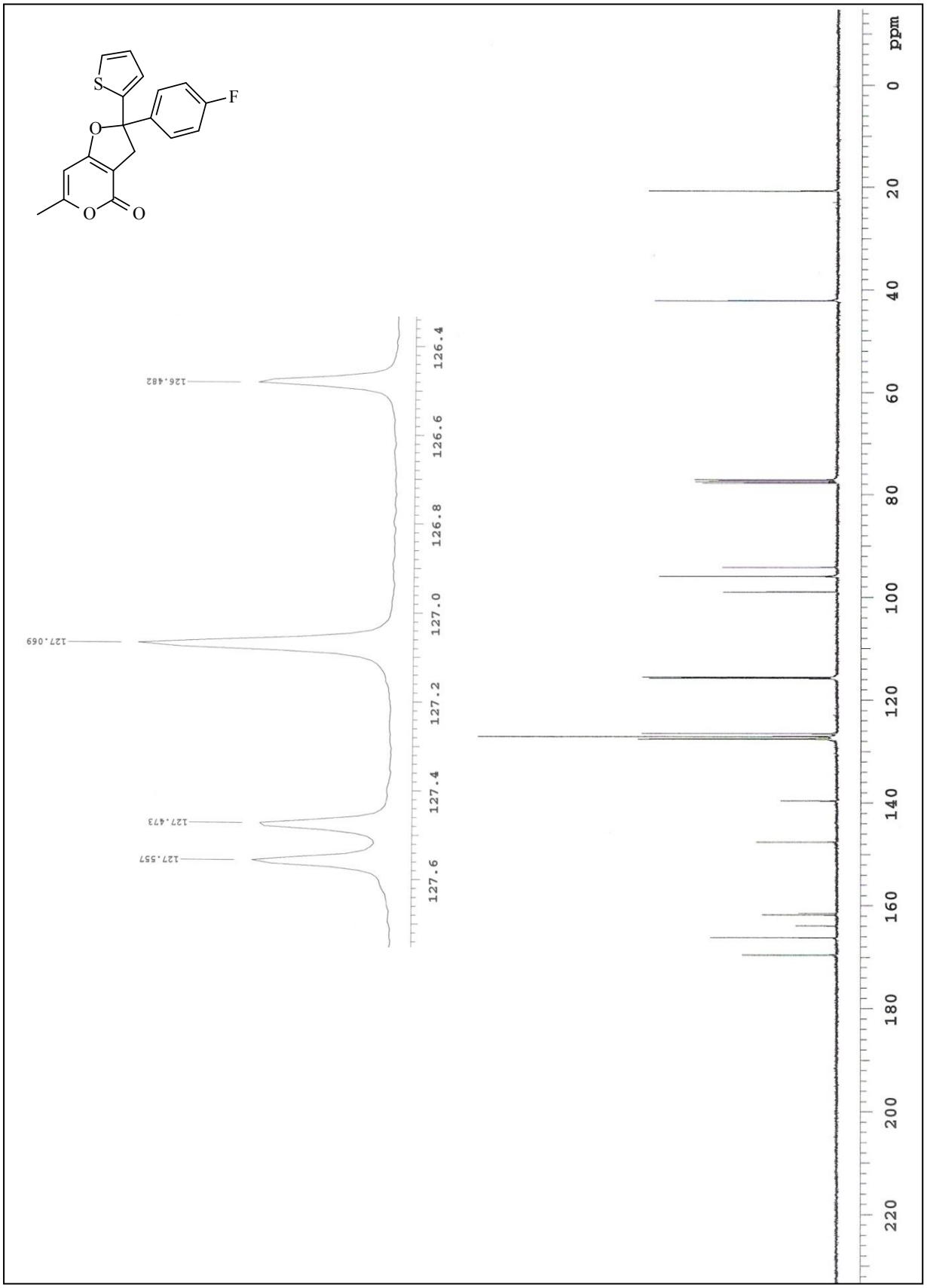
3.14 ^{13}C-NMR spectra of **14**



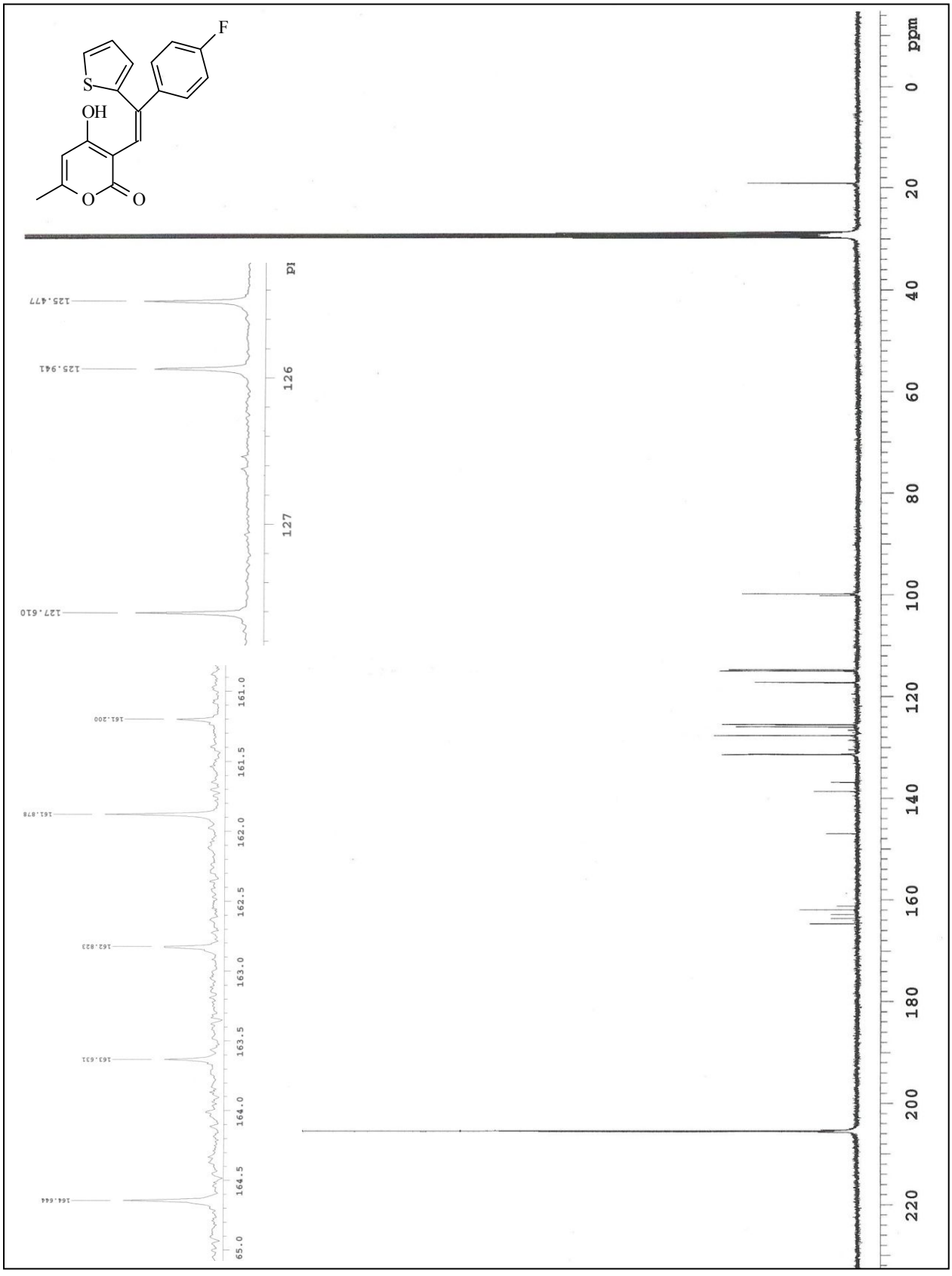
3.15 ^{13}C-NMR spectra of **17**



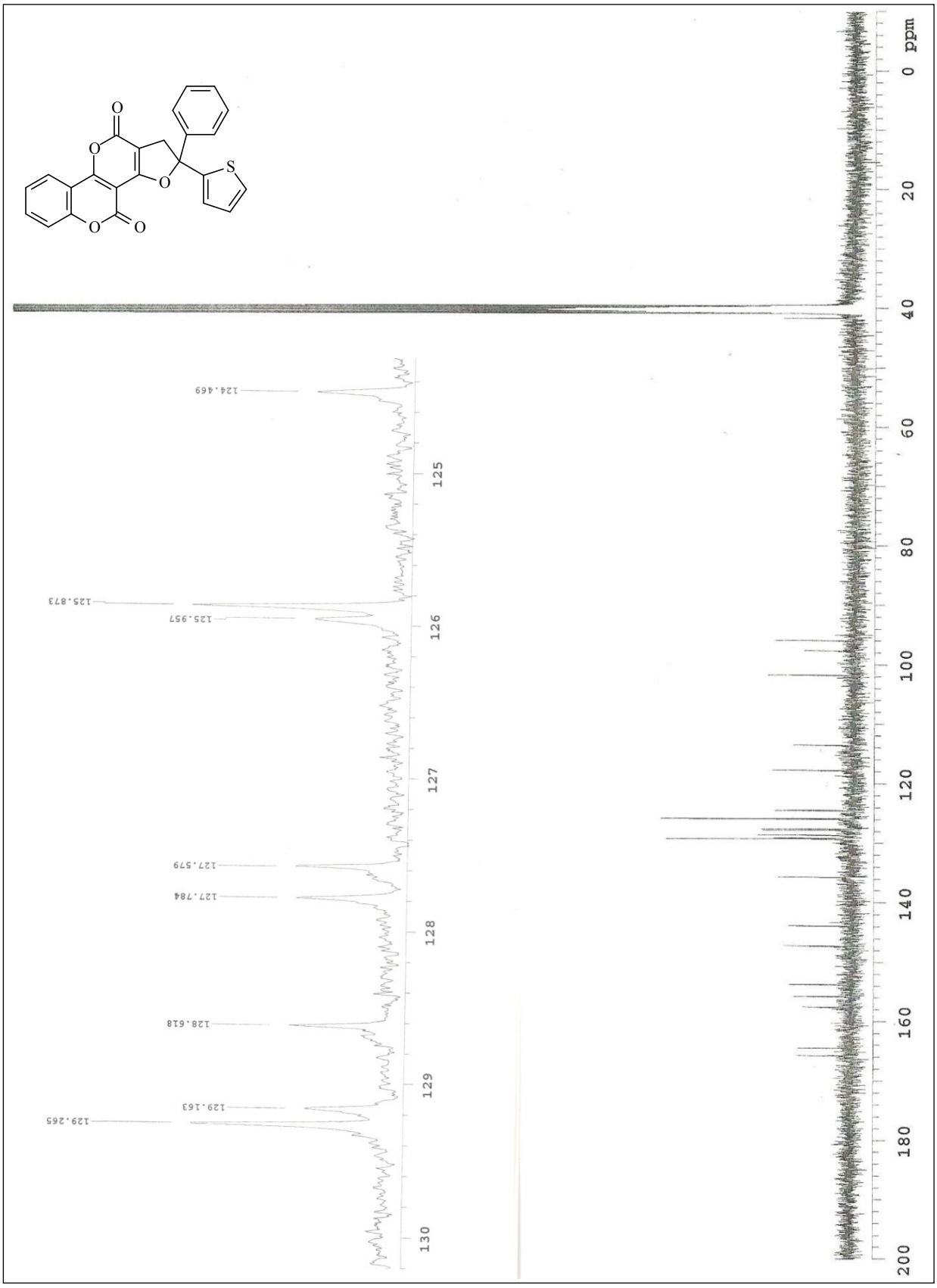
3.16 ^{13}C-NMR spectra of **15**



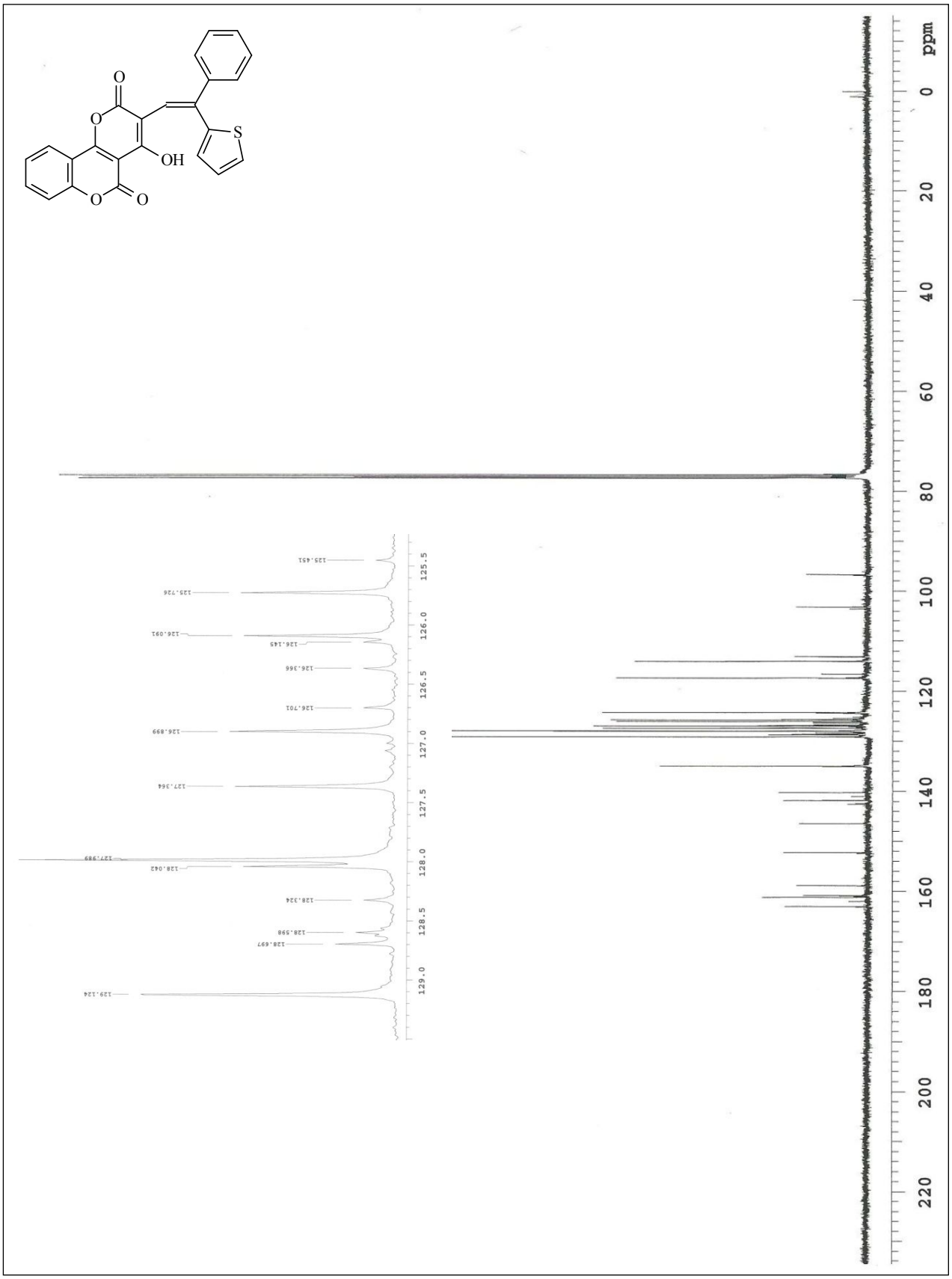
3.17 ^{13}C-NMR spectra of **18**



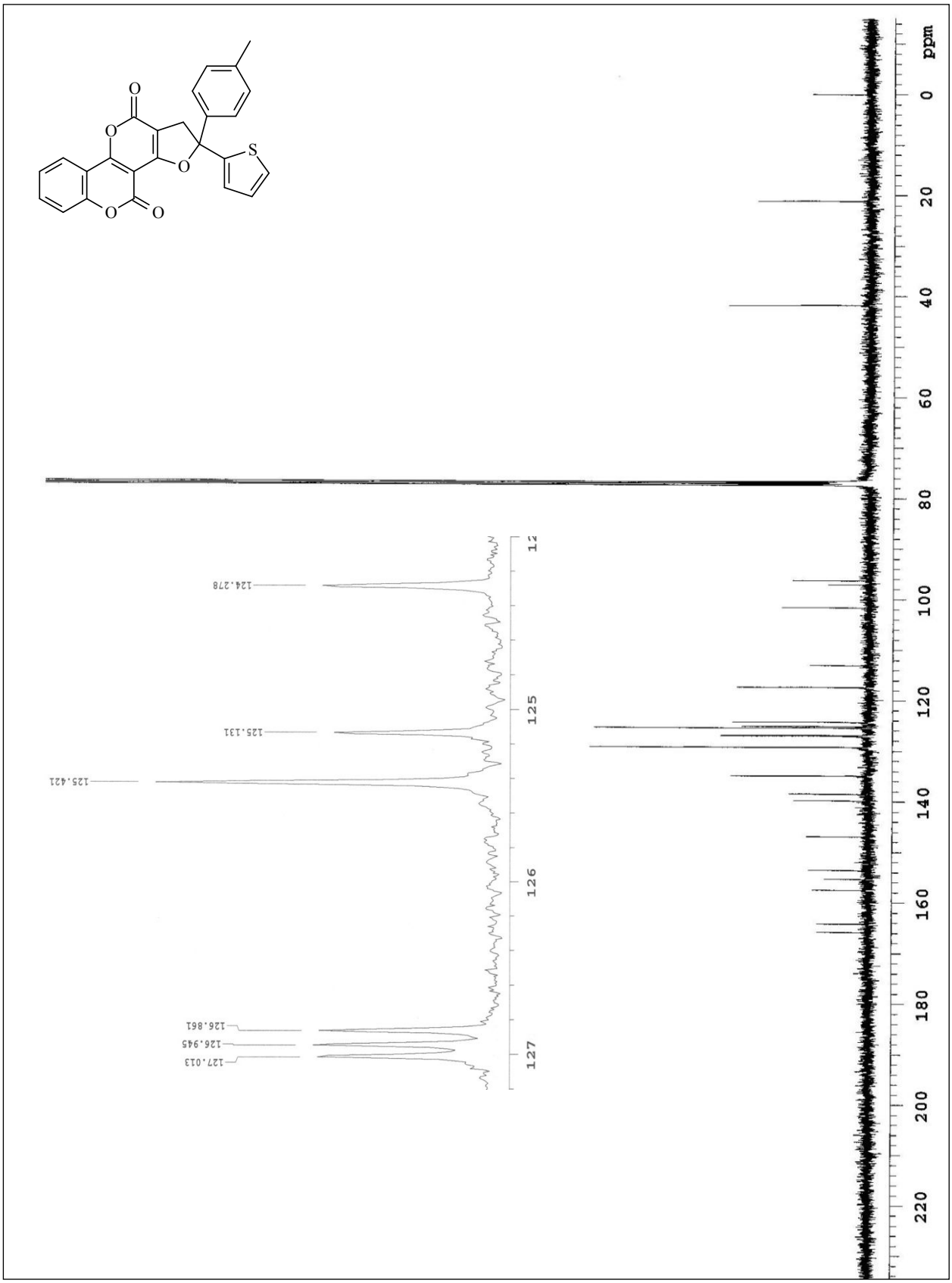
3.18 ^{13}C-NMR spectra of **19**



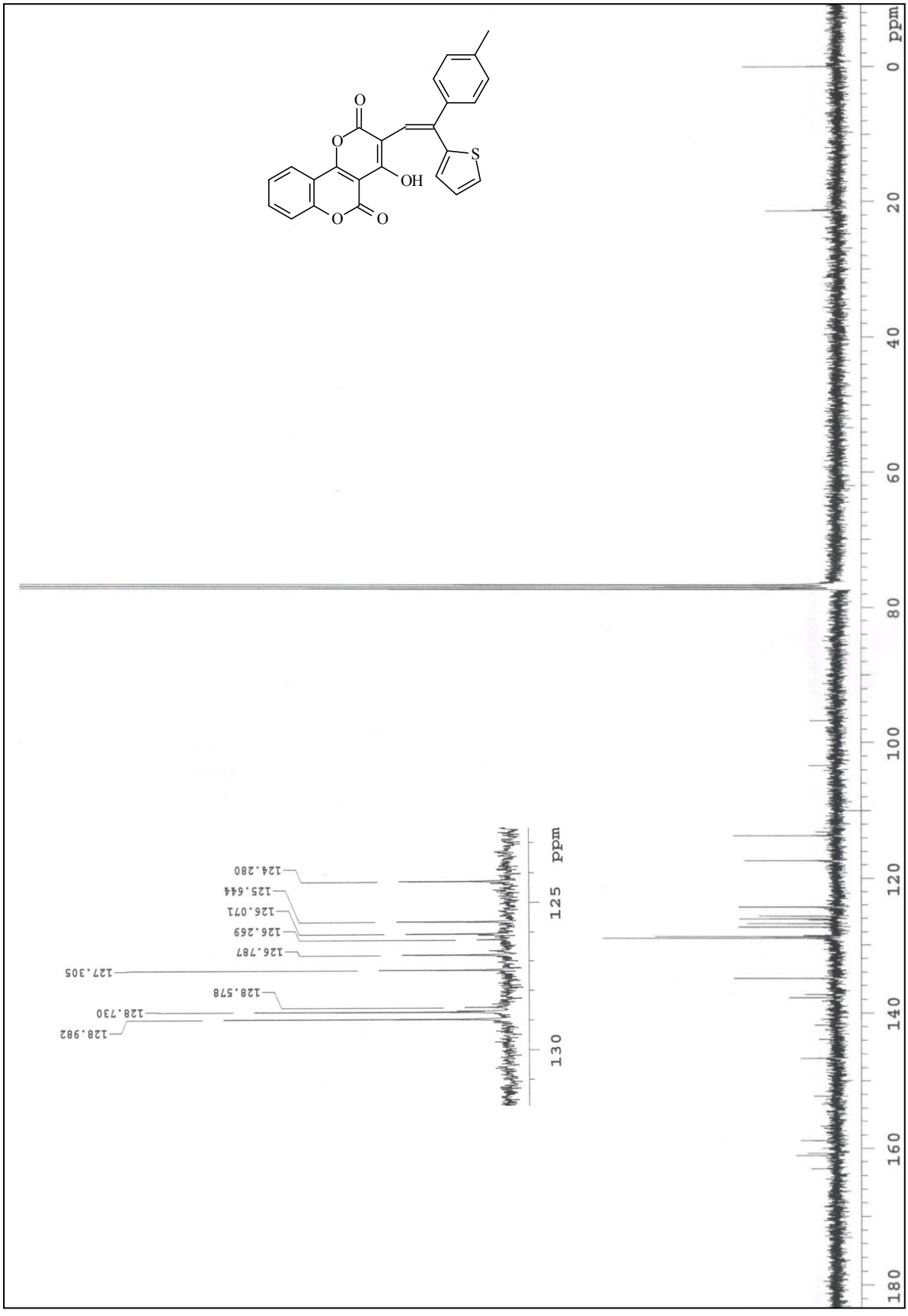
3.19 ^{13}C-NMR spectra of **25**



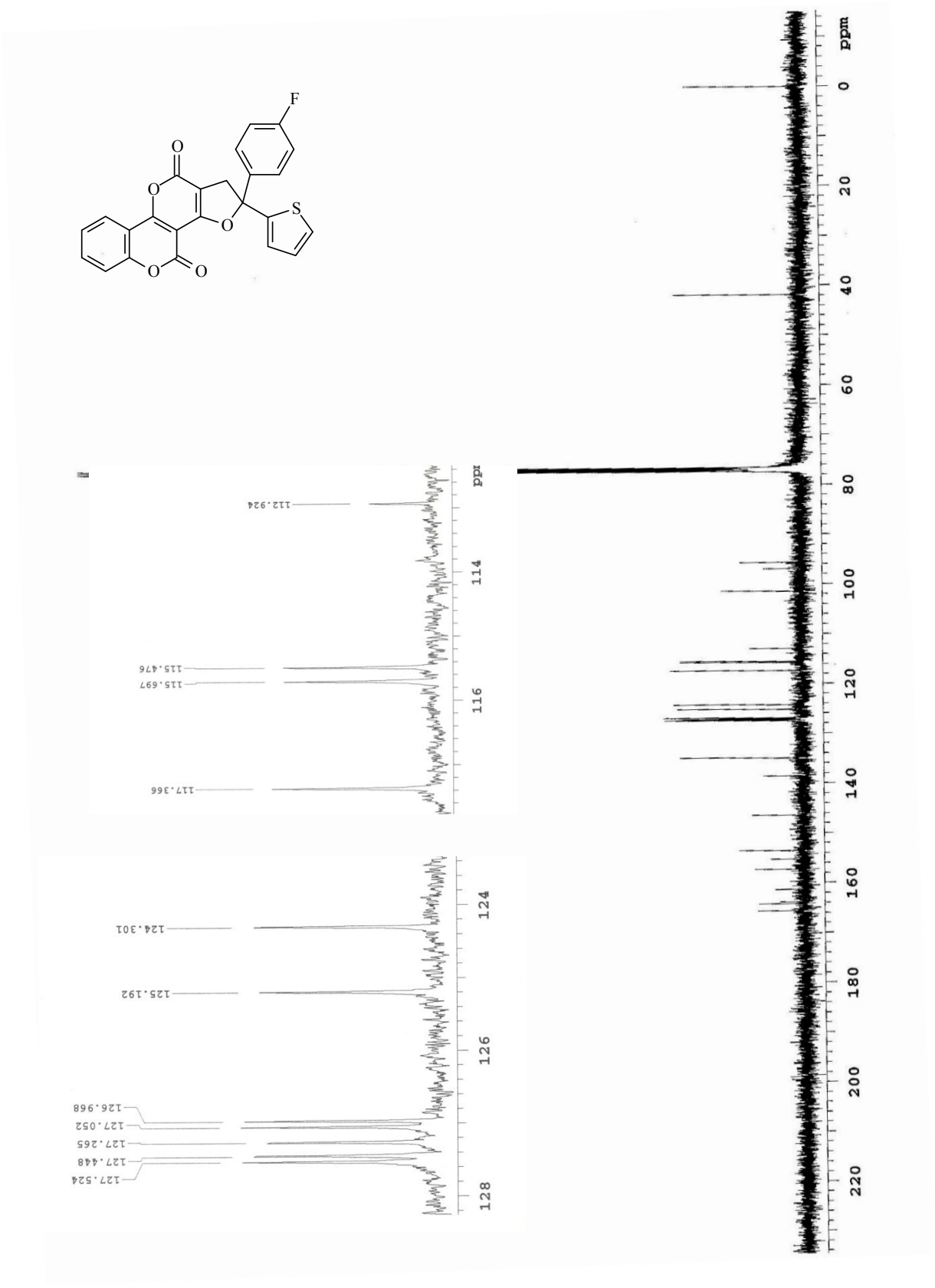
3.20 ^{13}C-NMR spectra of **20**



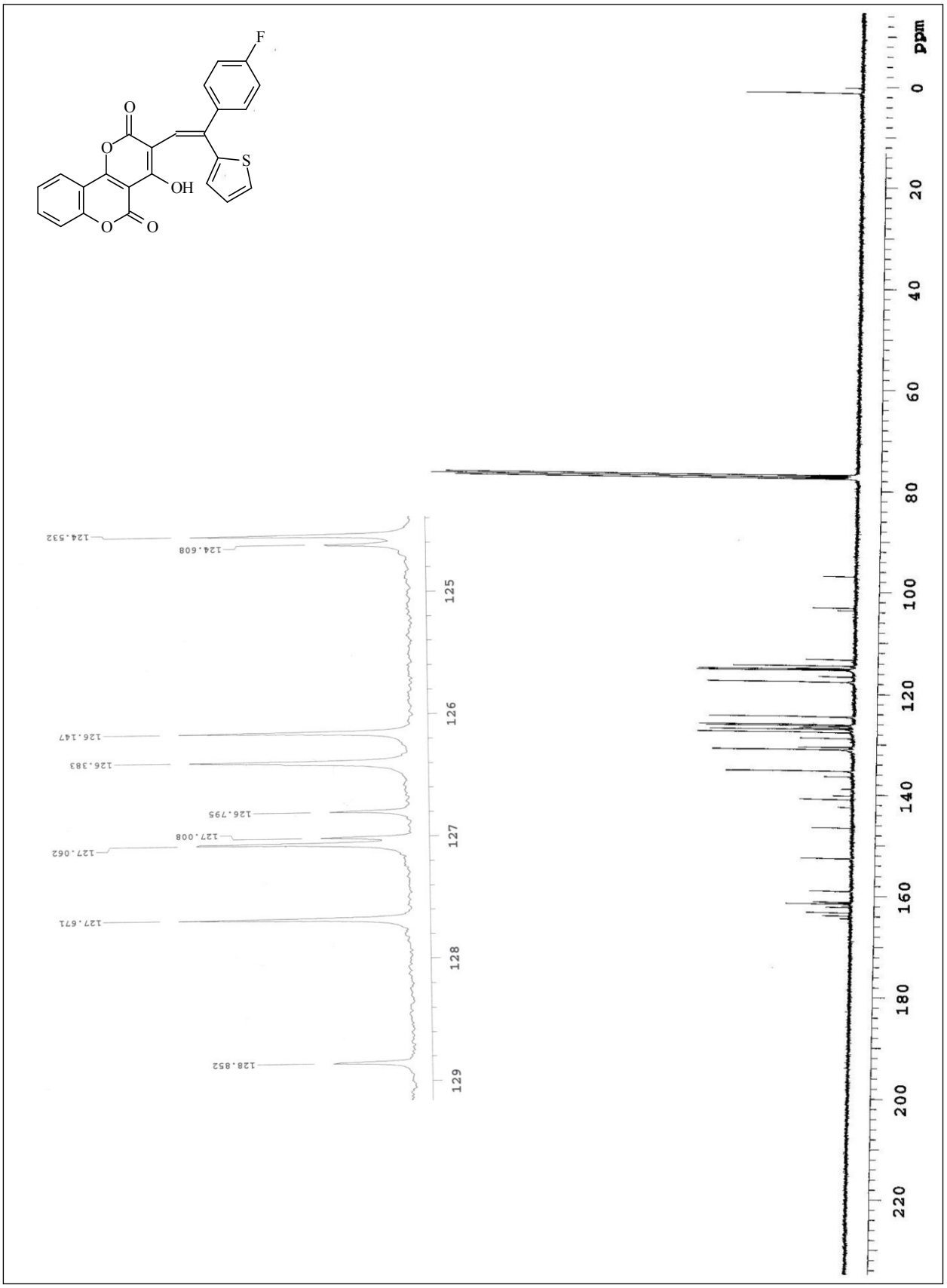
3.21 ^{13}C-NMR spectra of **26**



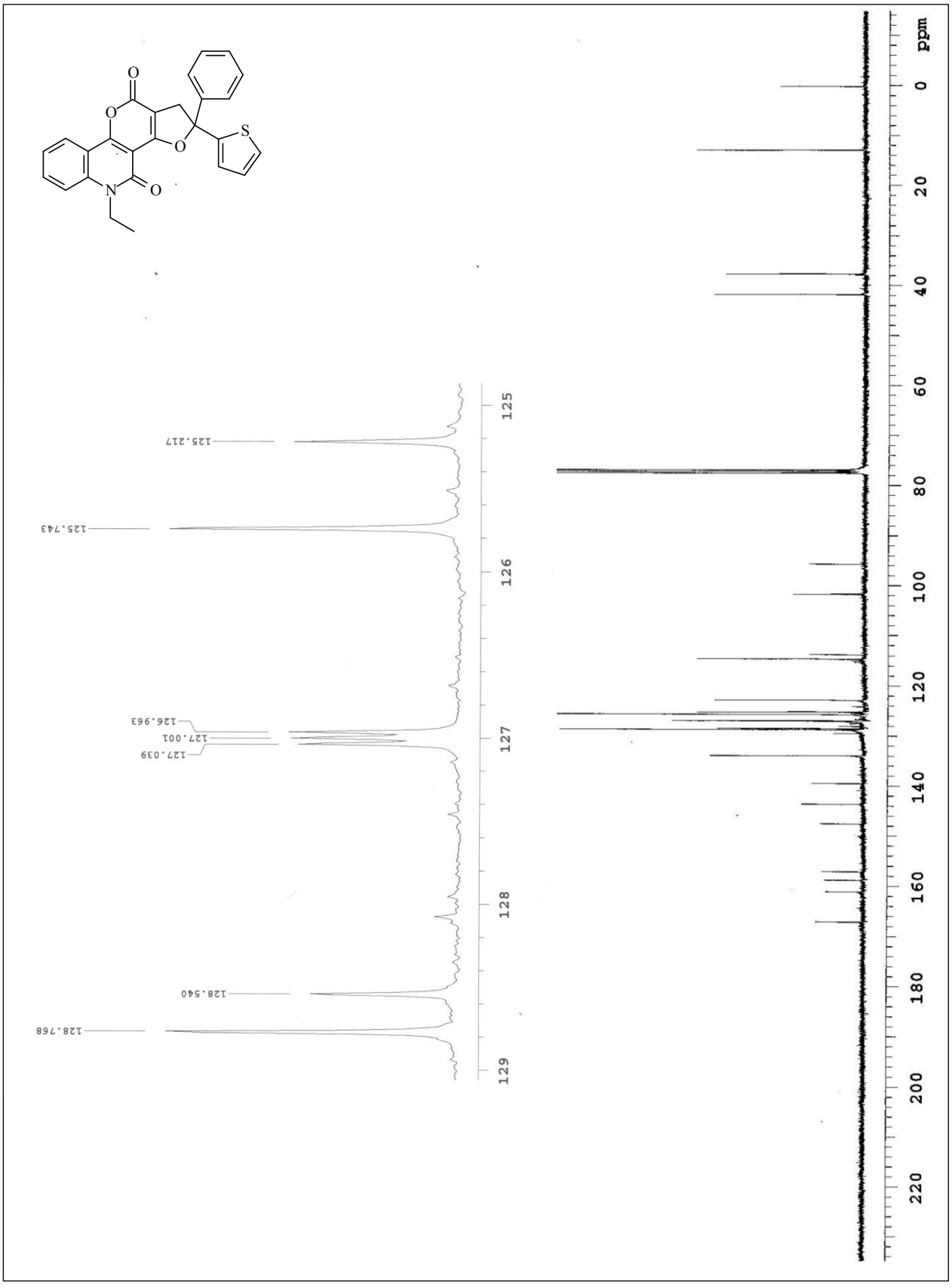
3.22 ^{13}C-NMR spectra of **21**



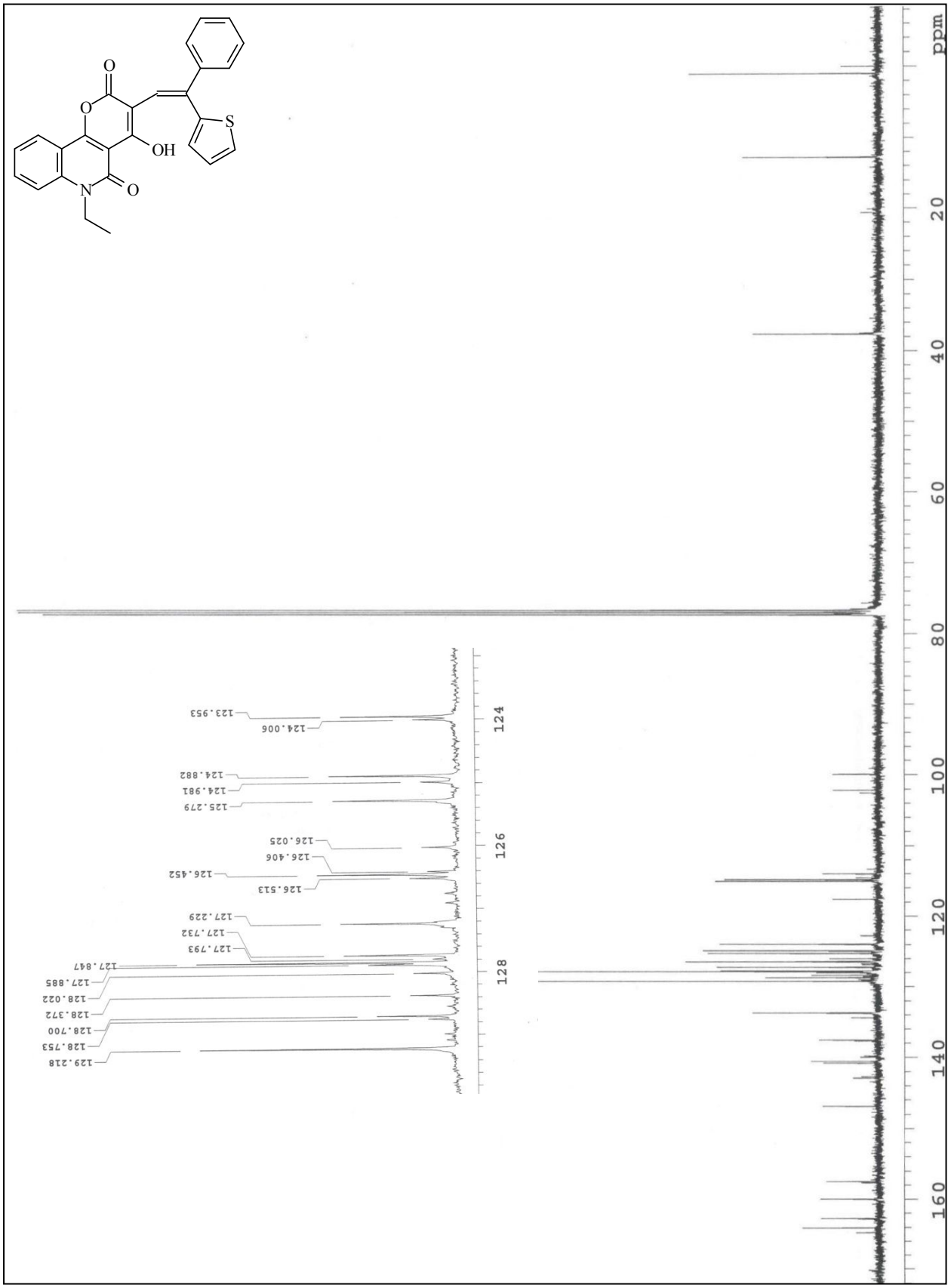
3.23 ^{13}C-NMR spectra of **27**



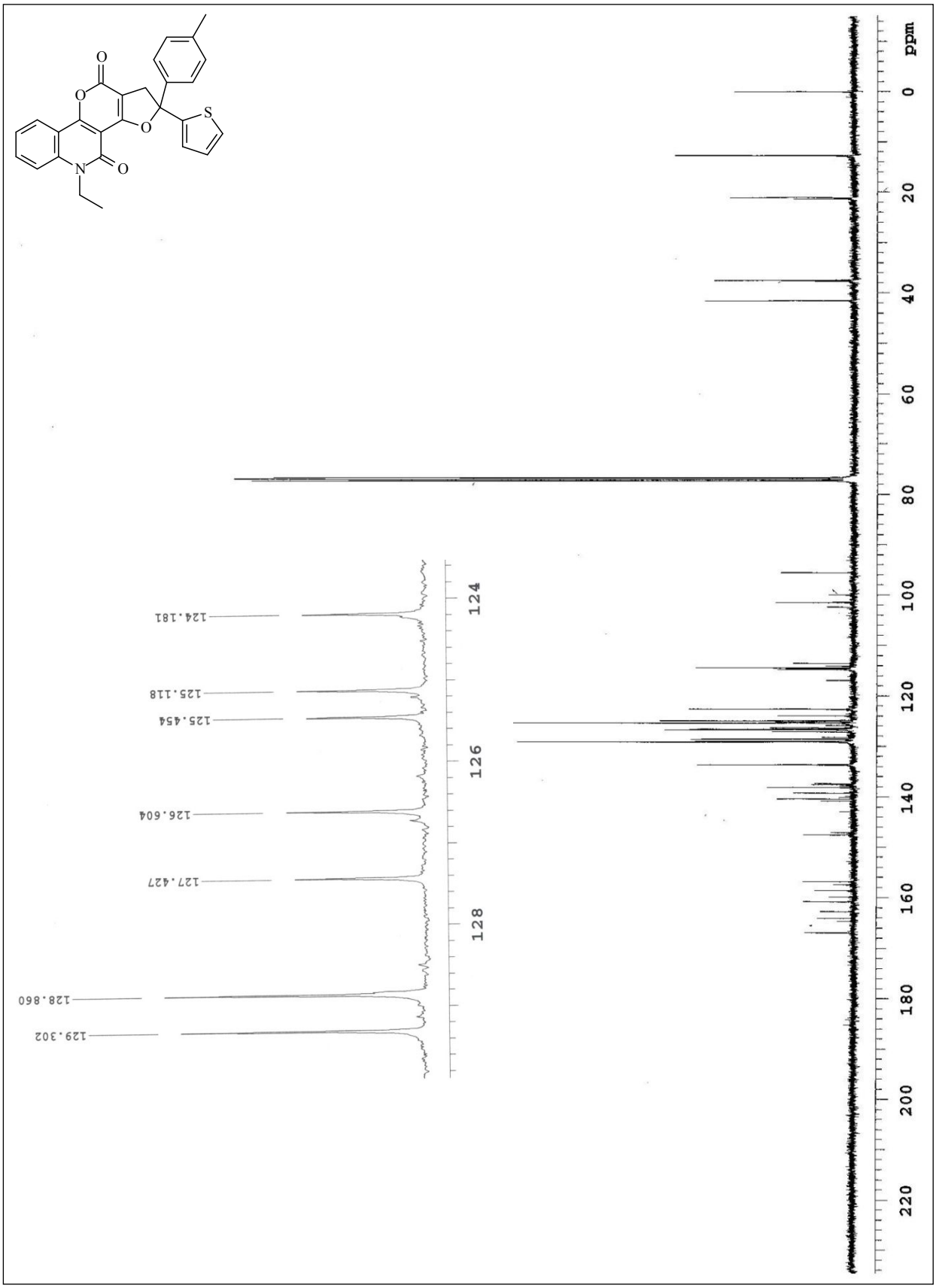
3.24 ^{13}C-NMR spectra of **22**



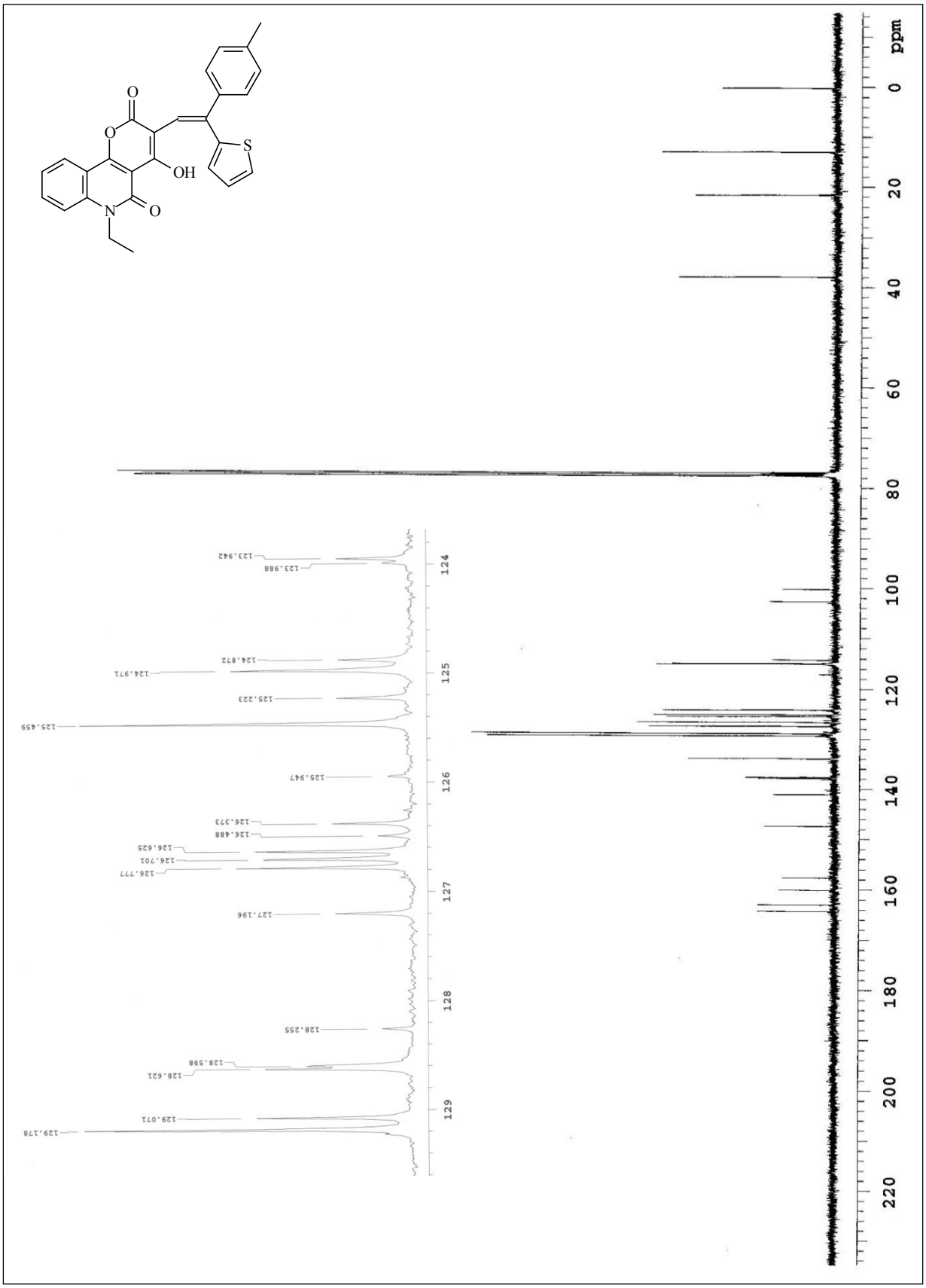
3.25 ^{13}C-NMR spectra of **28**



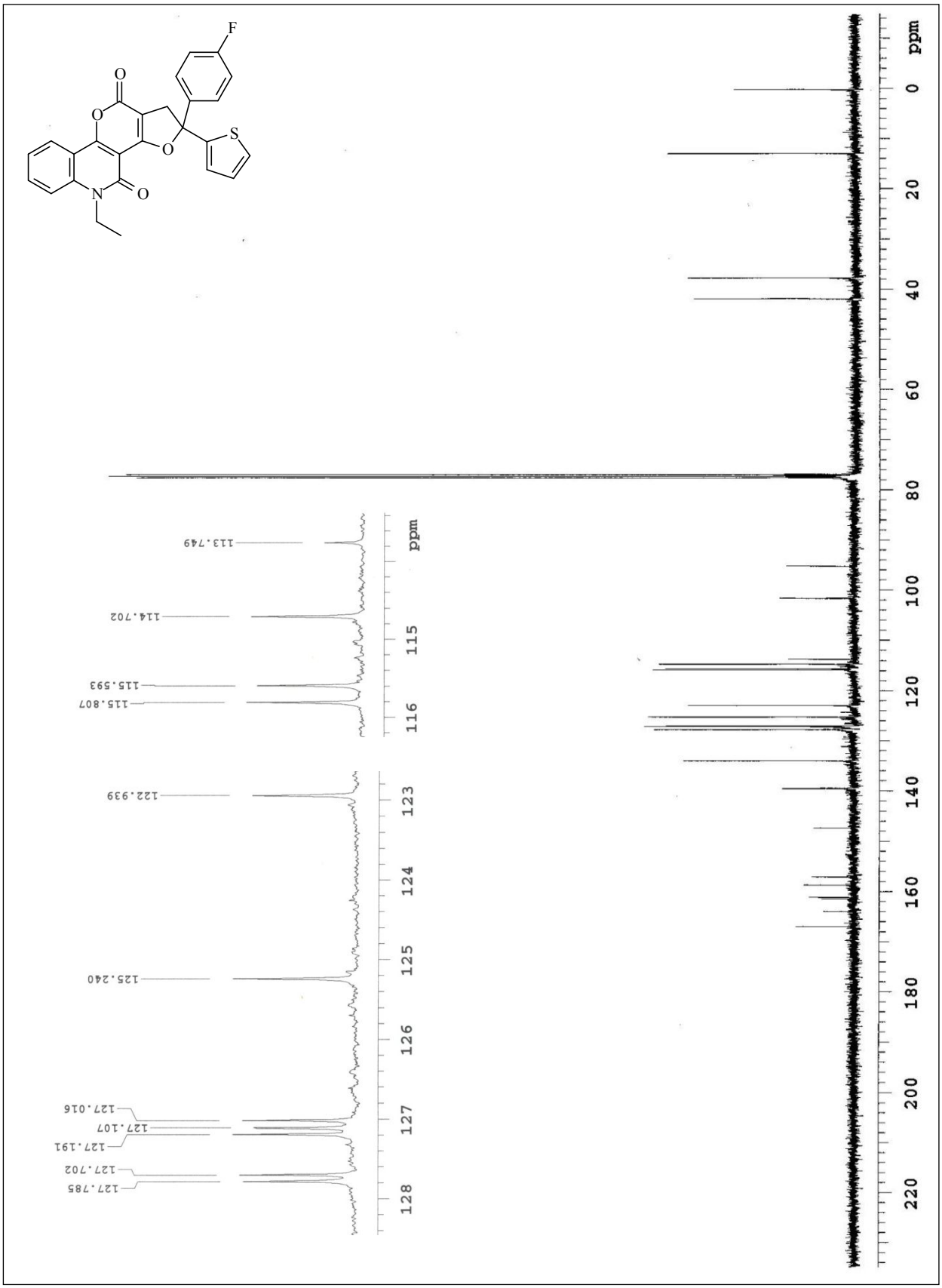
3.26 ^{13}C-NMR spectra of **23**



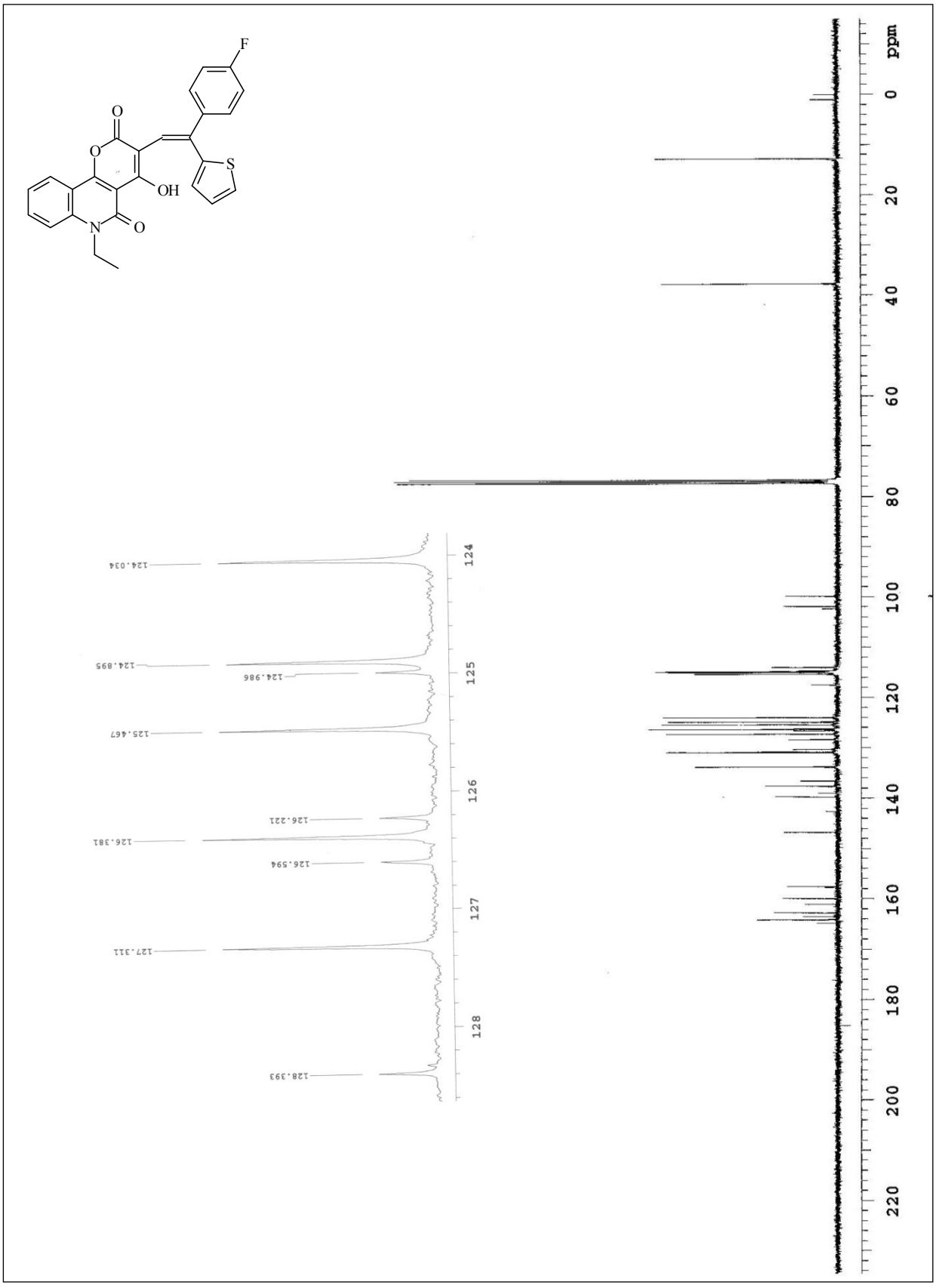
3.27 ^{13}C-NMR spectra of **29**



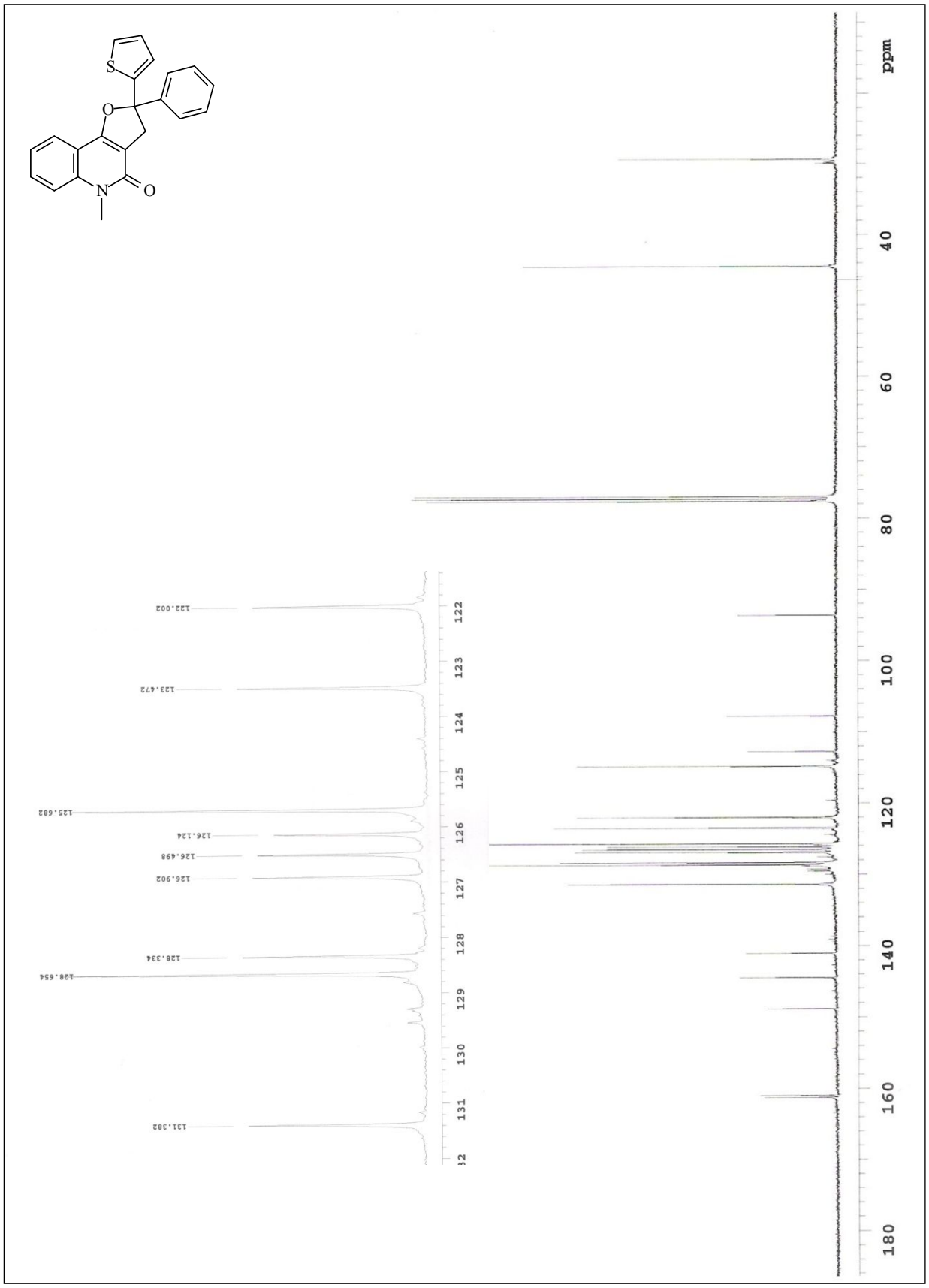
3.28 ^{13}C-NMR spectra of **24**



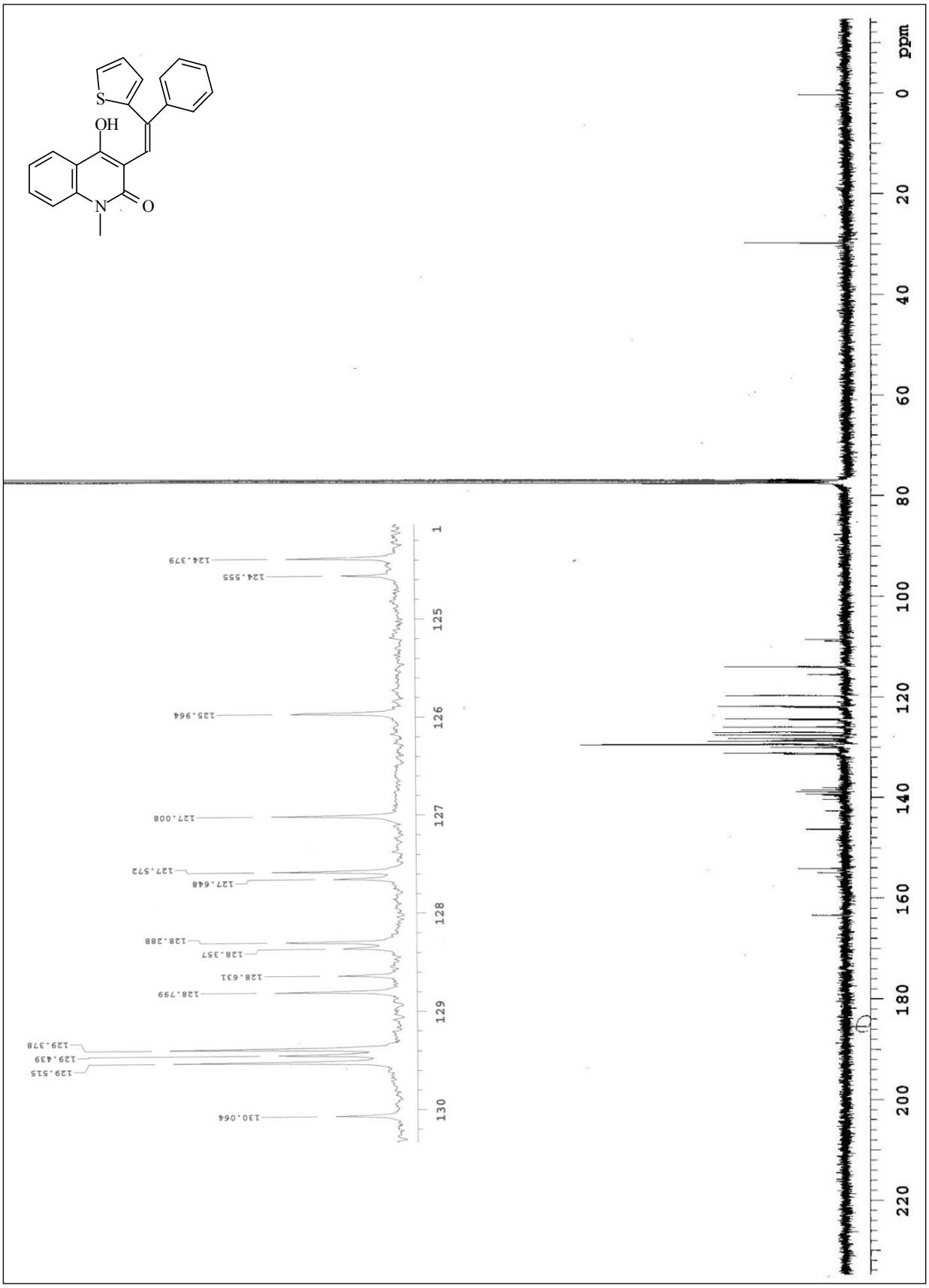
3.29 ^{13}C-NMR spectra of **30**



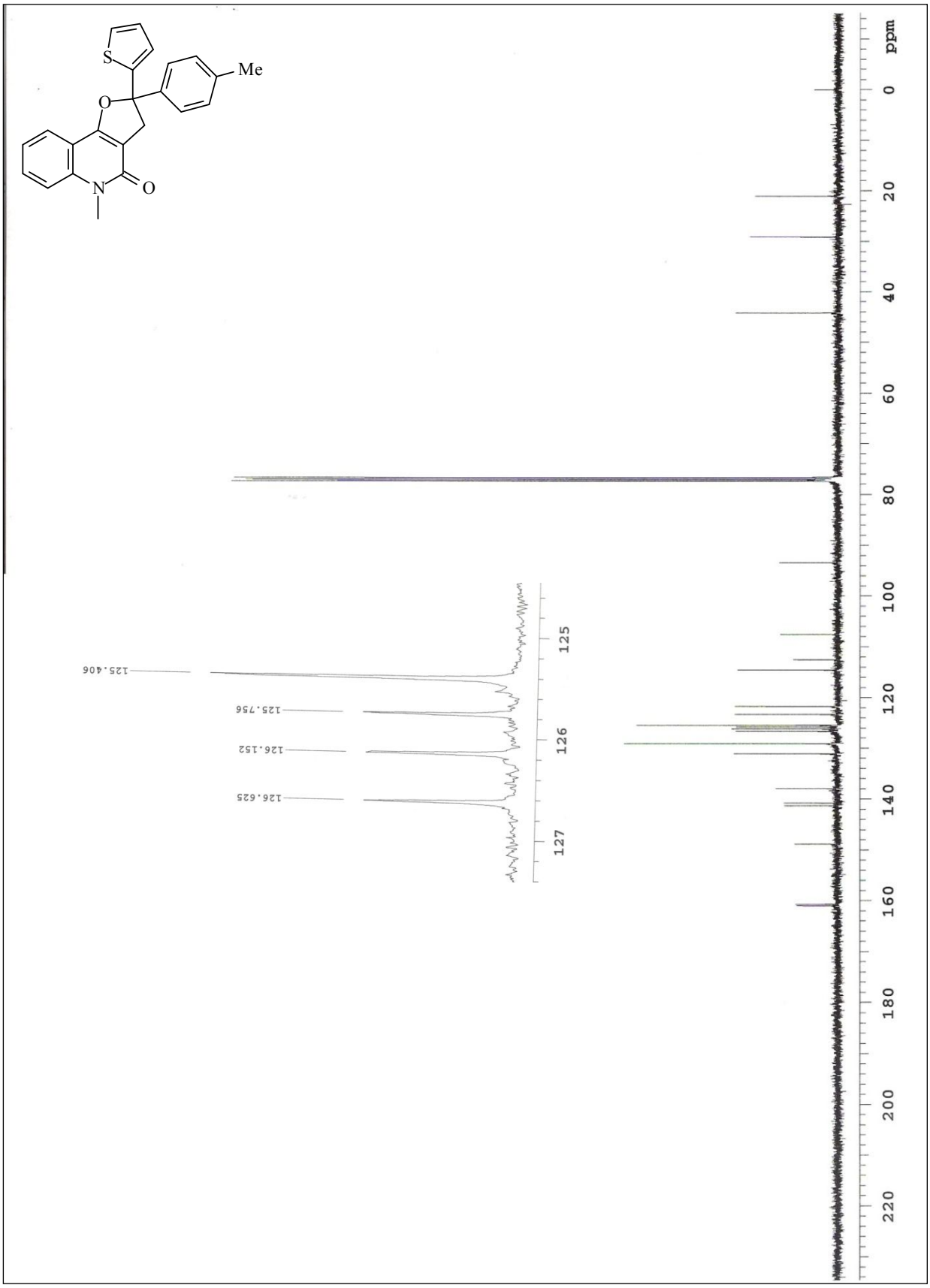
3.30 ^{13}C-NMR spectra of **31**



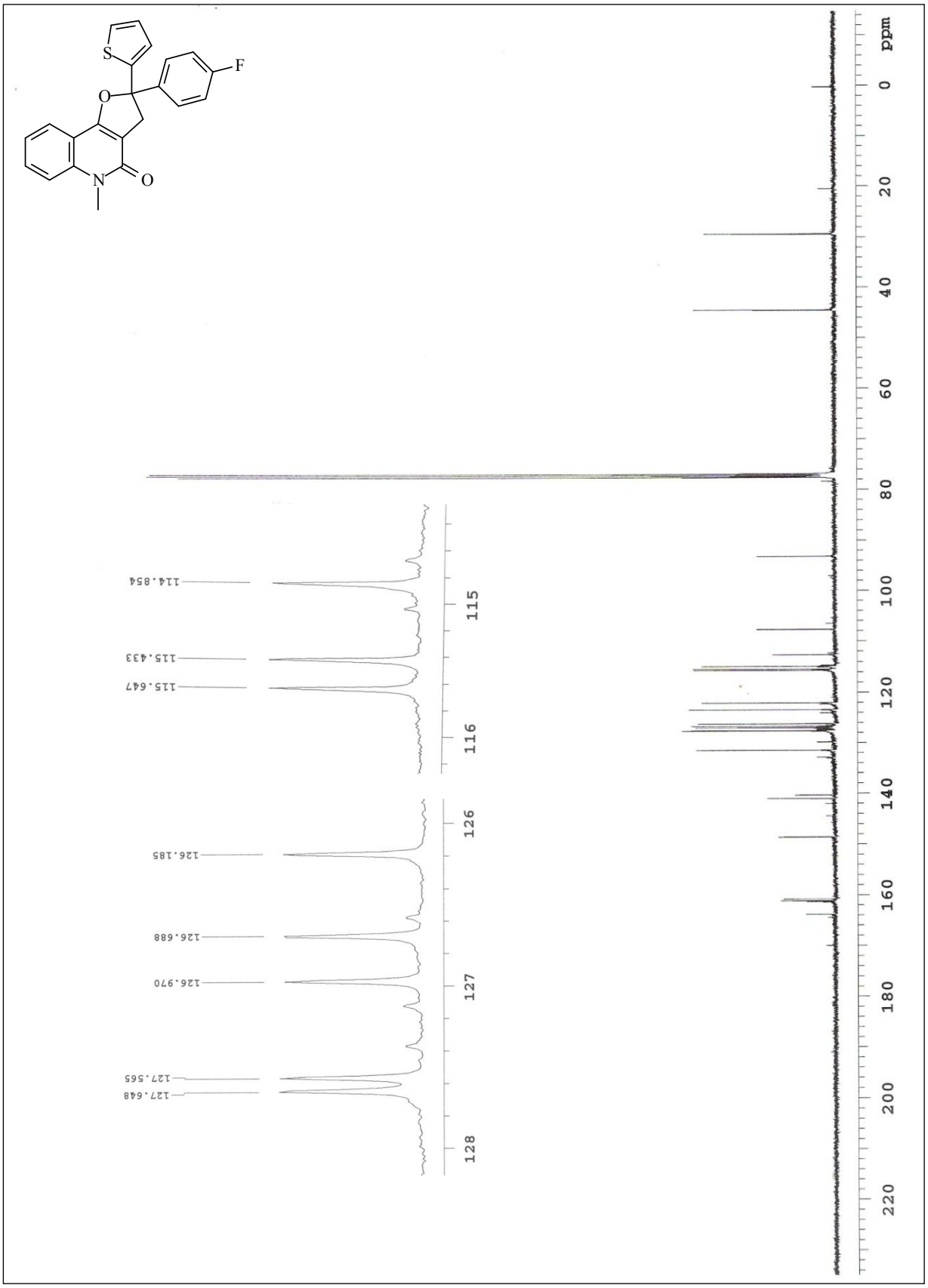
3.31 ^{13}C-NMR spectra of **34**



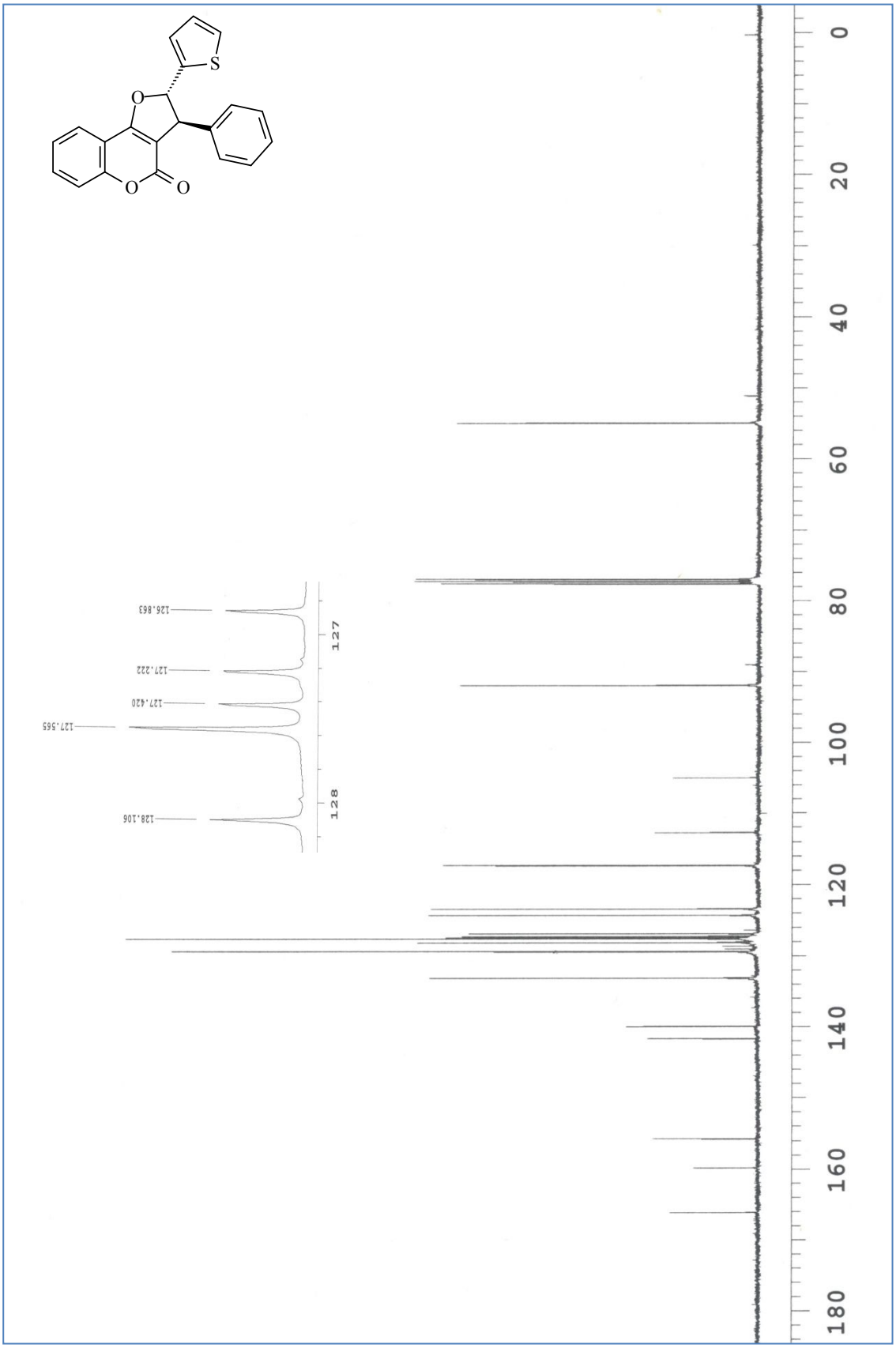
3.32 ^{13}C-NMR spectra of **32**



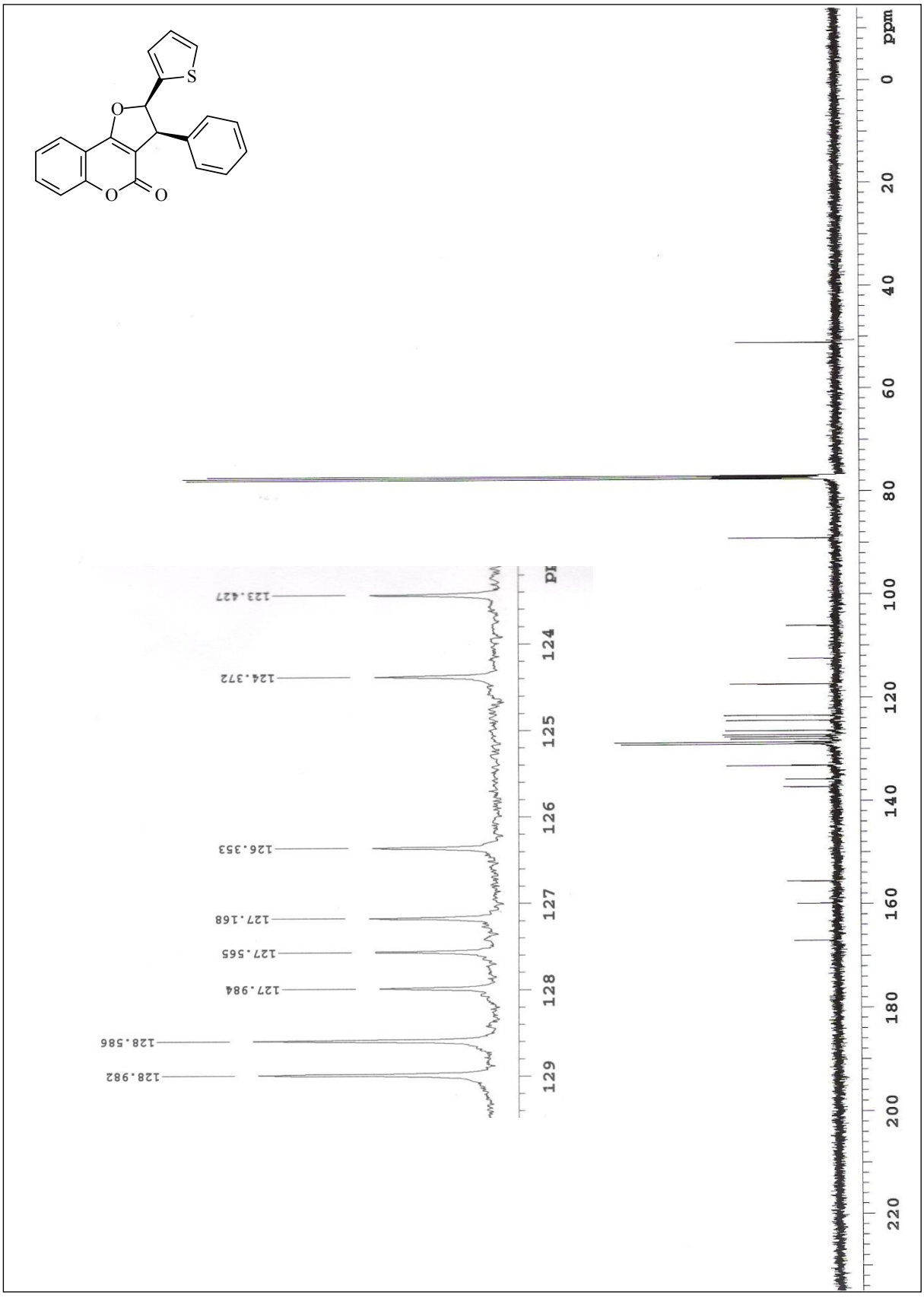
3.33 ^{13}C-NMR spectra of **33**



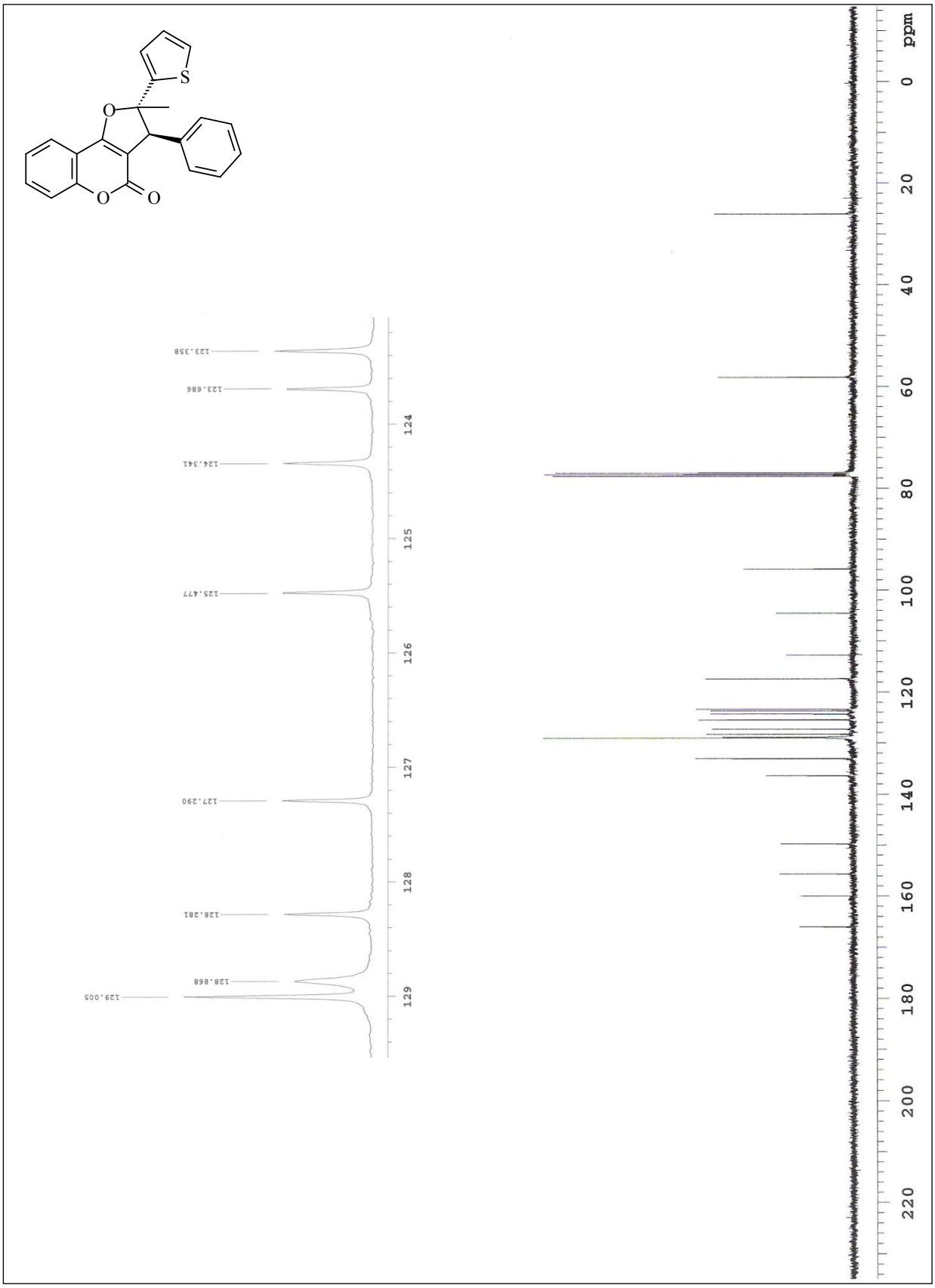
3.34 ^{13}C-NMR spectra of **35**



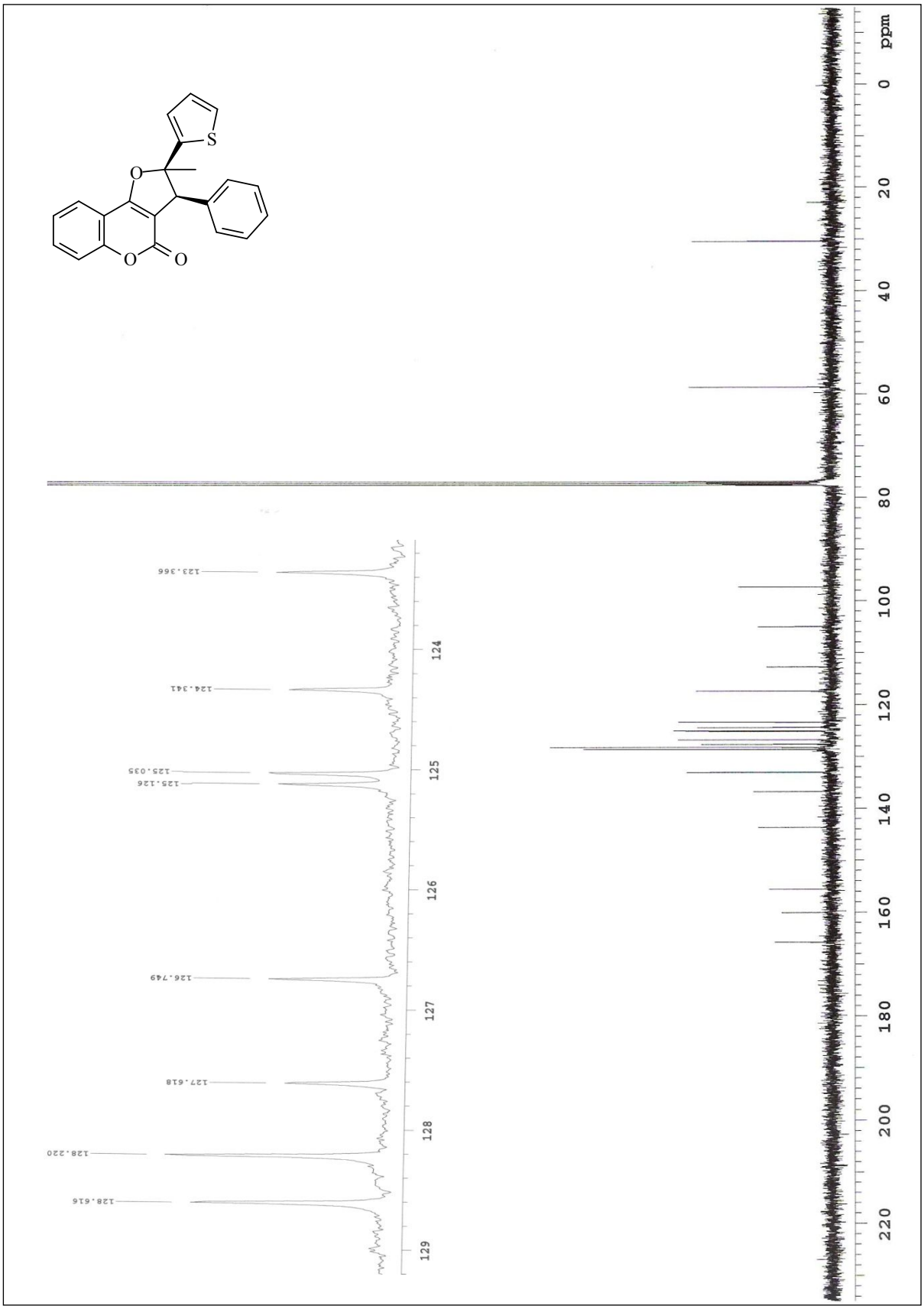
3.35 ^{13}C-NMR spectra of **36**



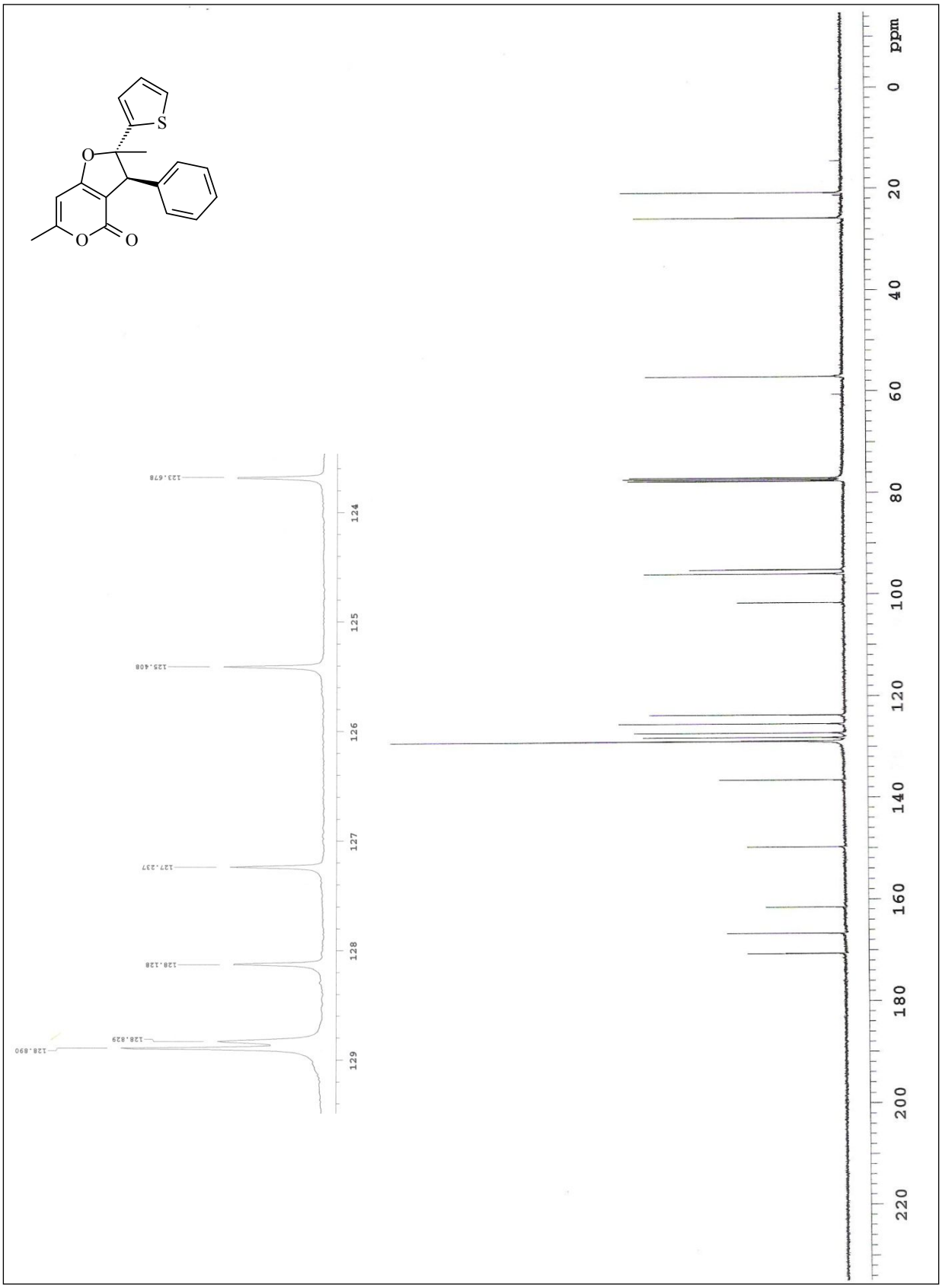
3.36 ^{13}C-NMR spectra of **37**



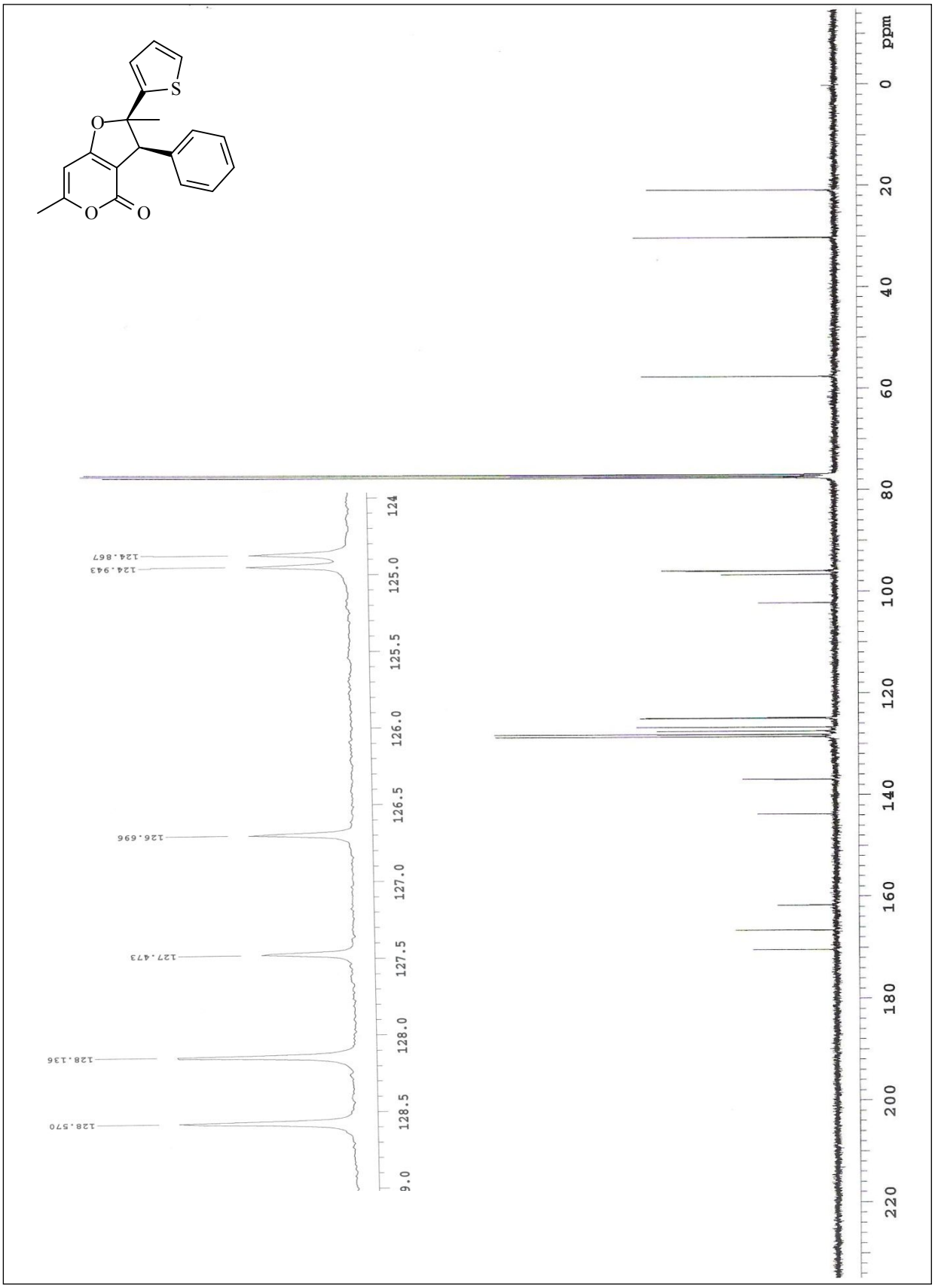
3.37 ^{13}C-NMR spectra of **38**



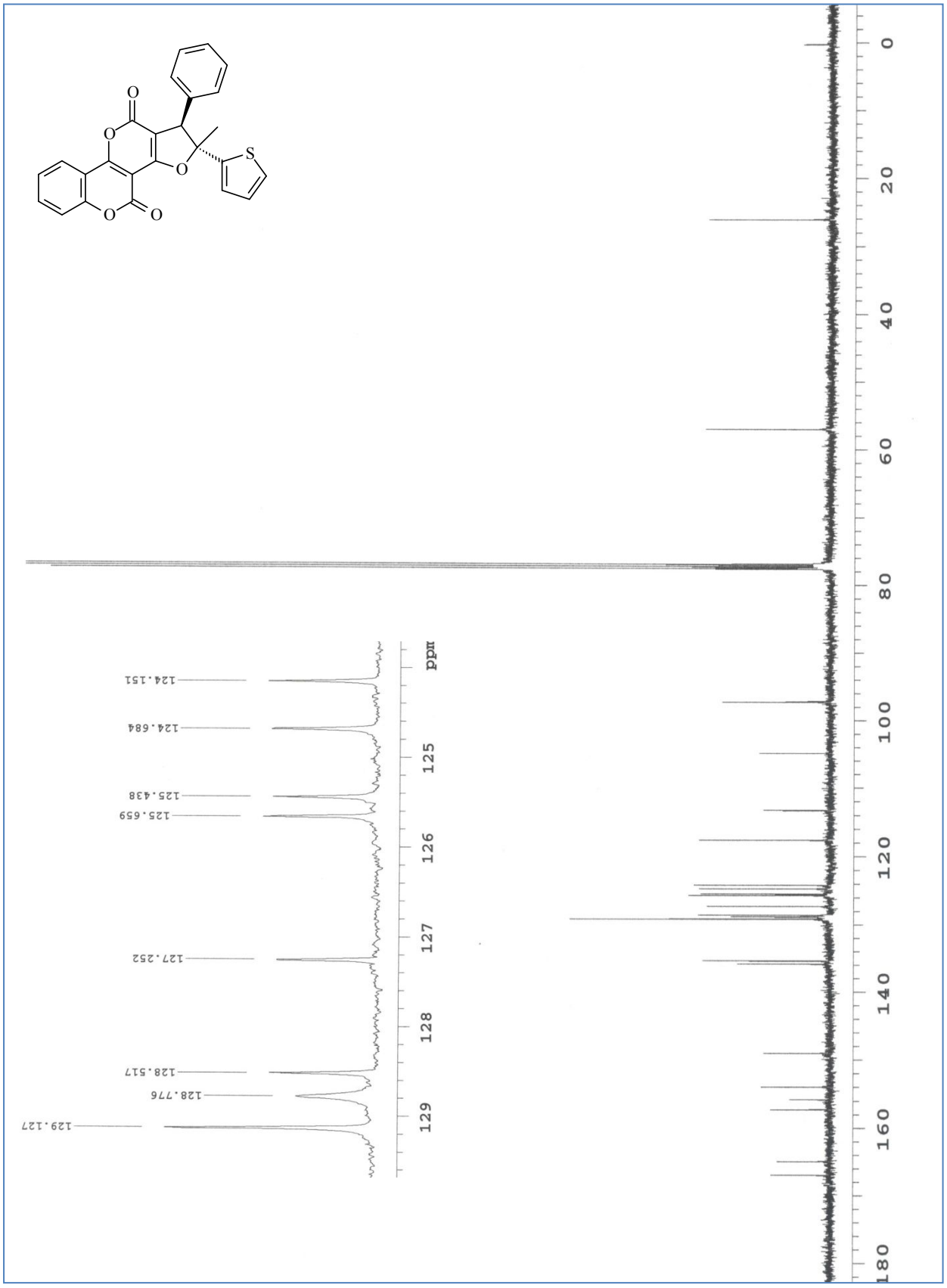
3.38 ^{13}C-NMR spectra of **39**



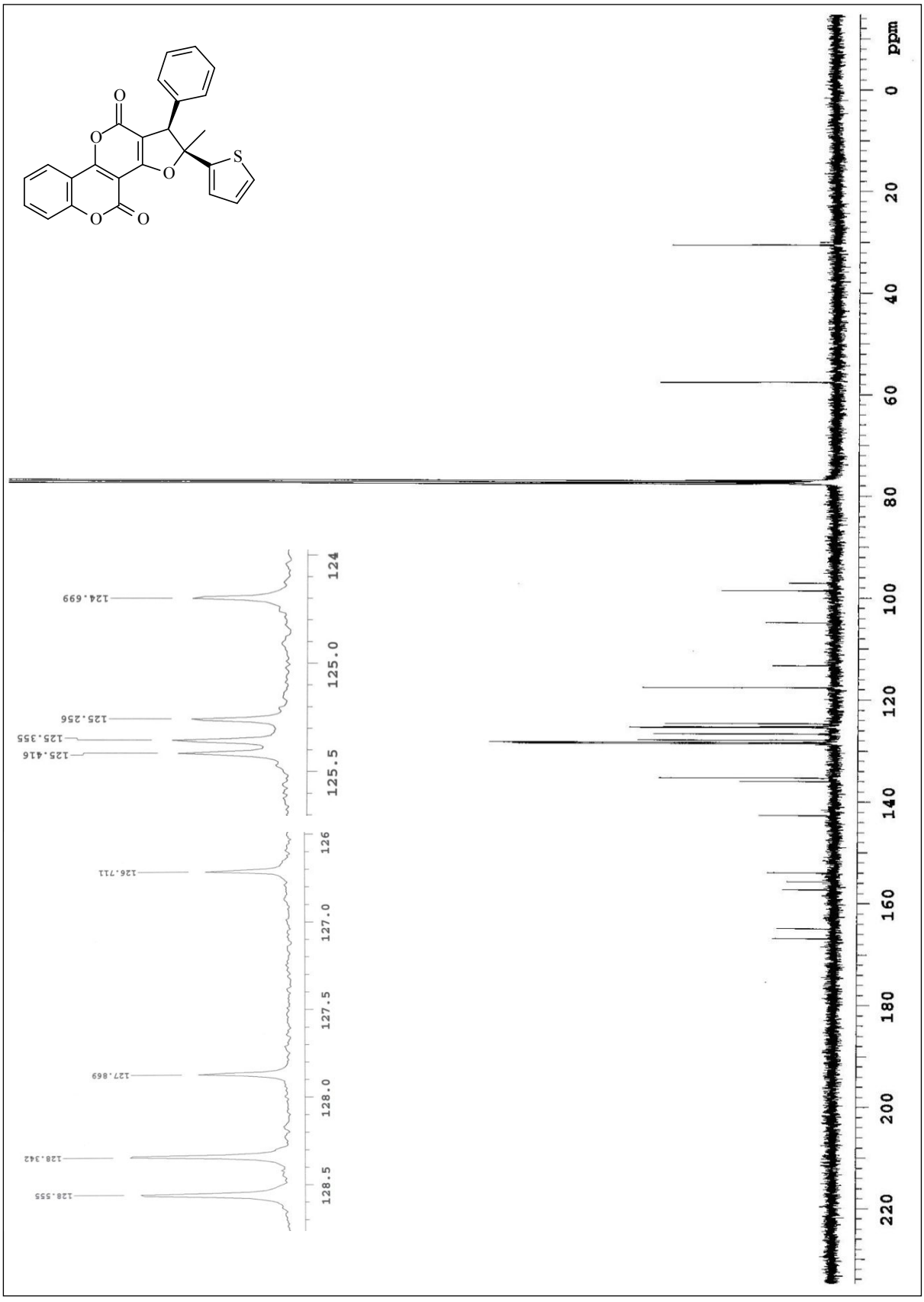
3.39 ^{13}C-NMR spectra of **40**



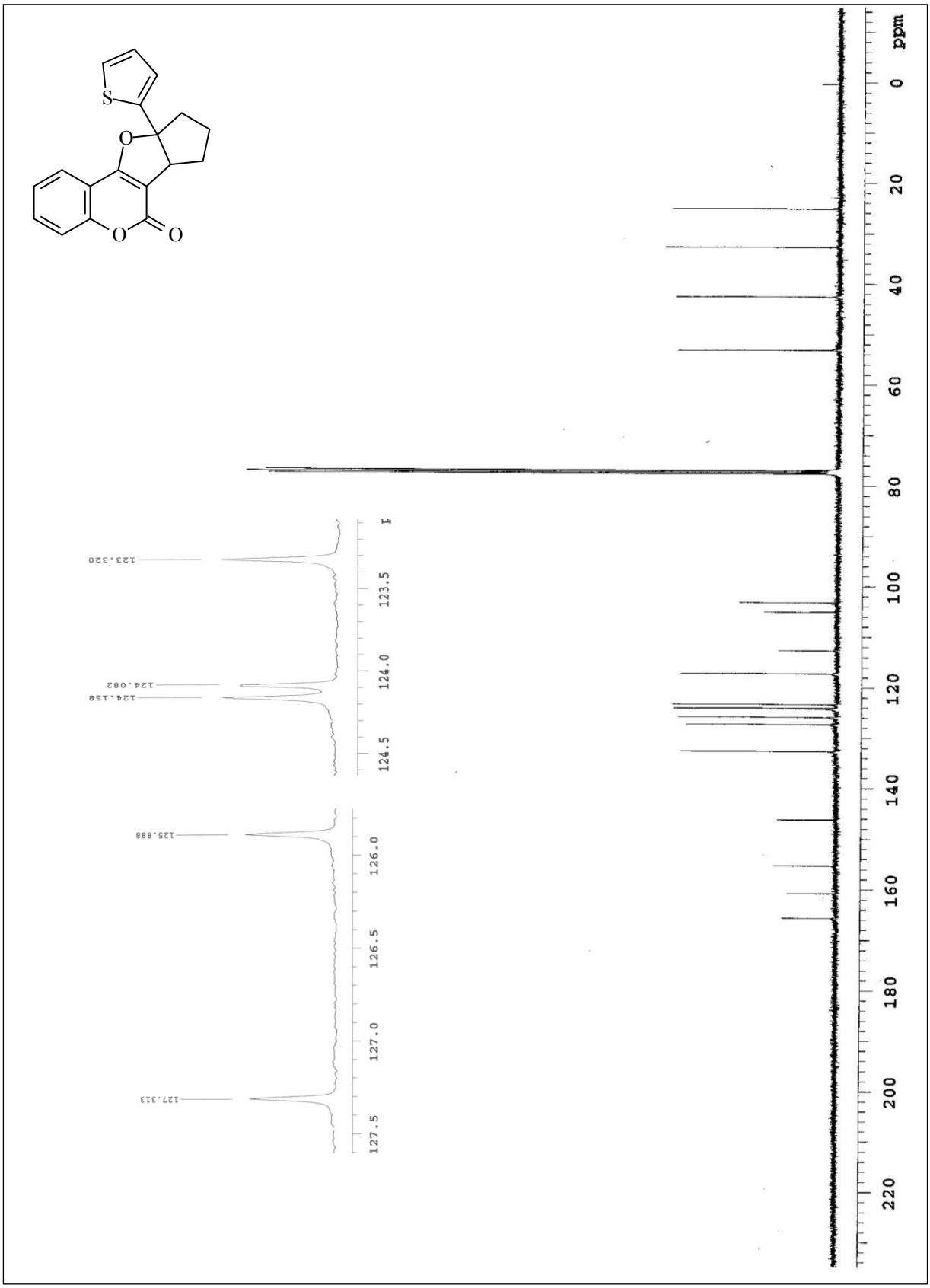
3.40 ^{13}C-NMR spectra of **41**



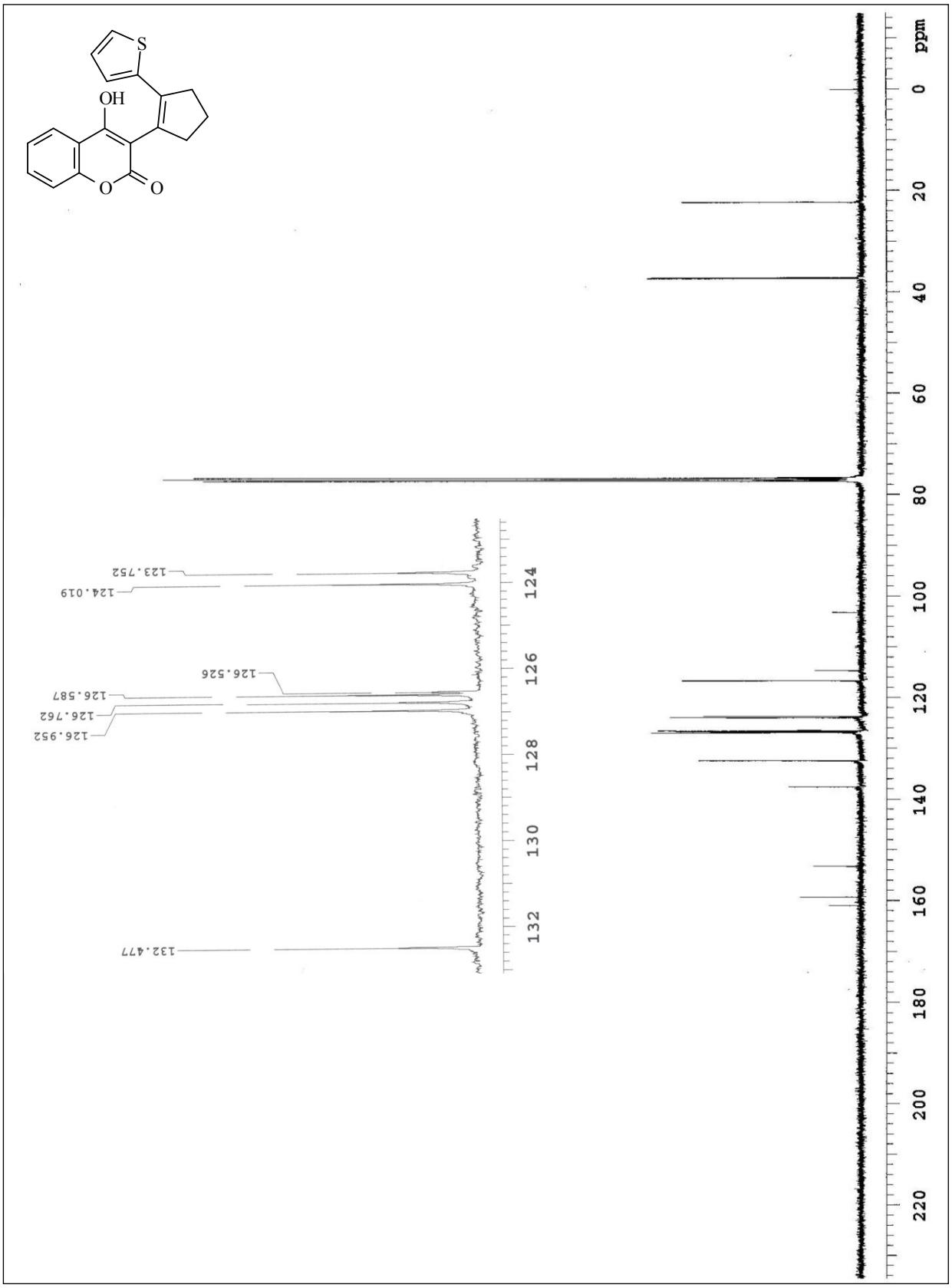
3.41 ^{13}C-NMR spectra of **42**



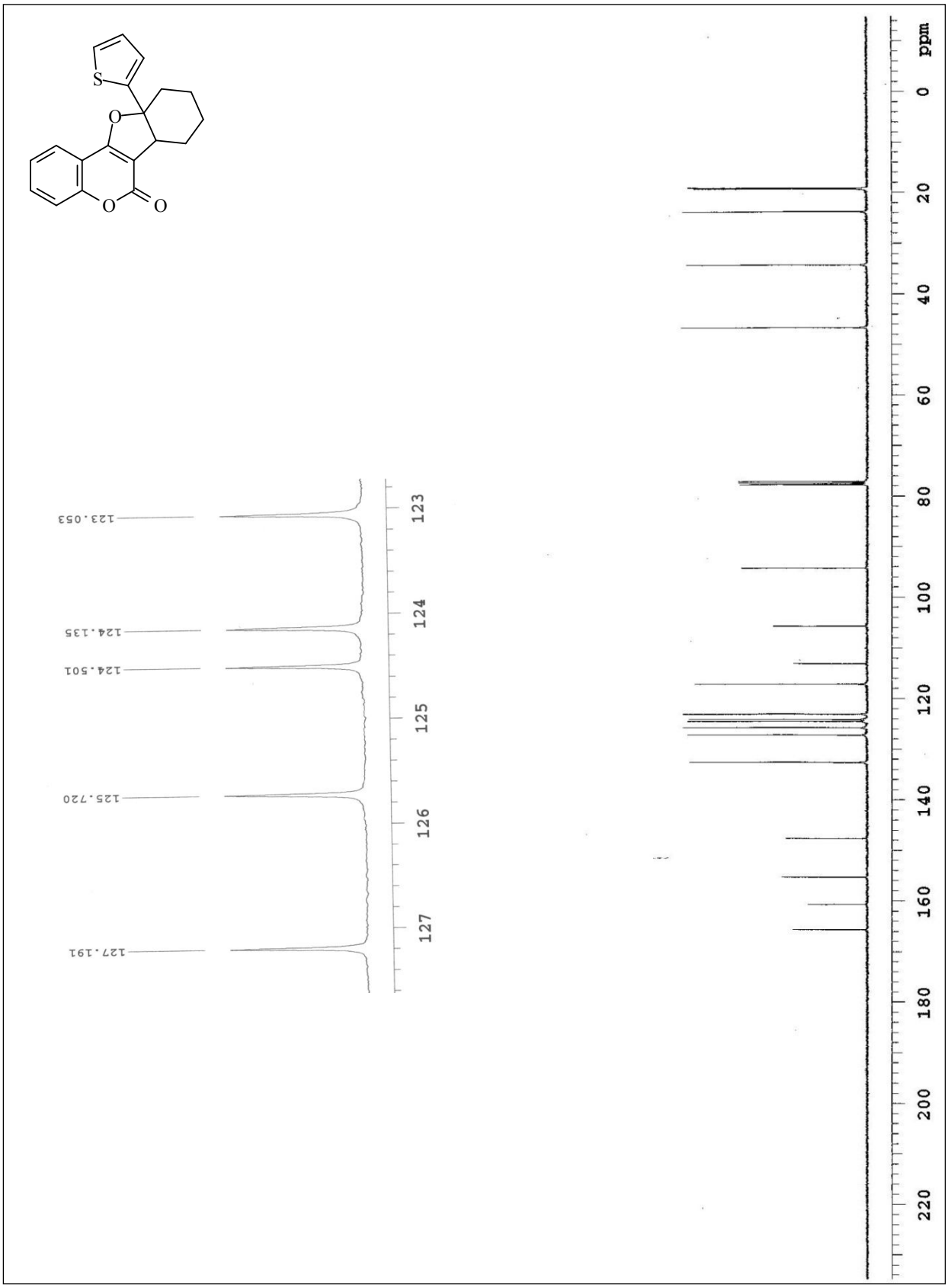
3.42 ^{13}C-NMR spectra of **43**



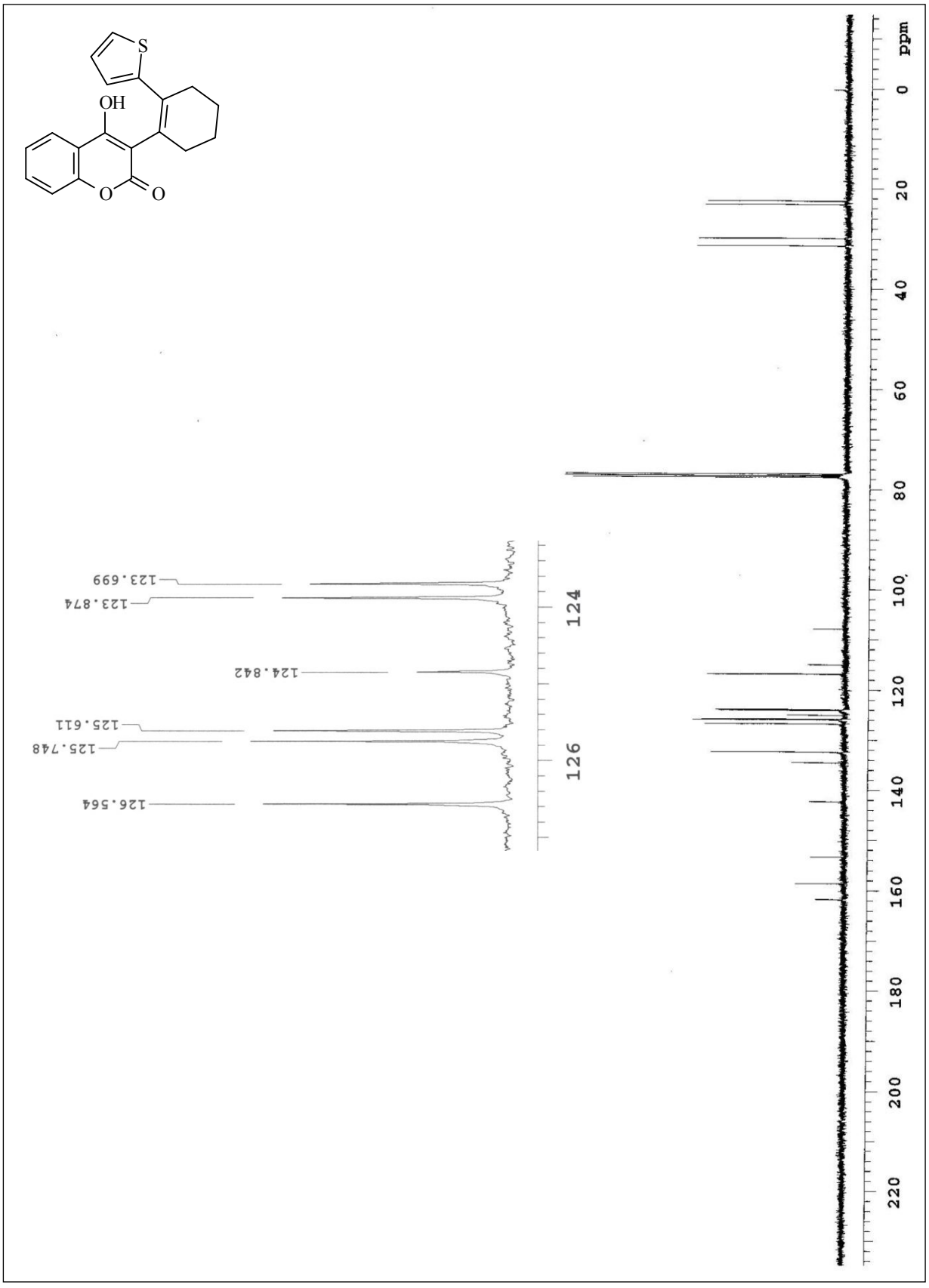
3.43 ^{13}C-NMR spectra of **49**



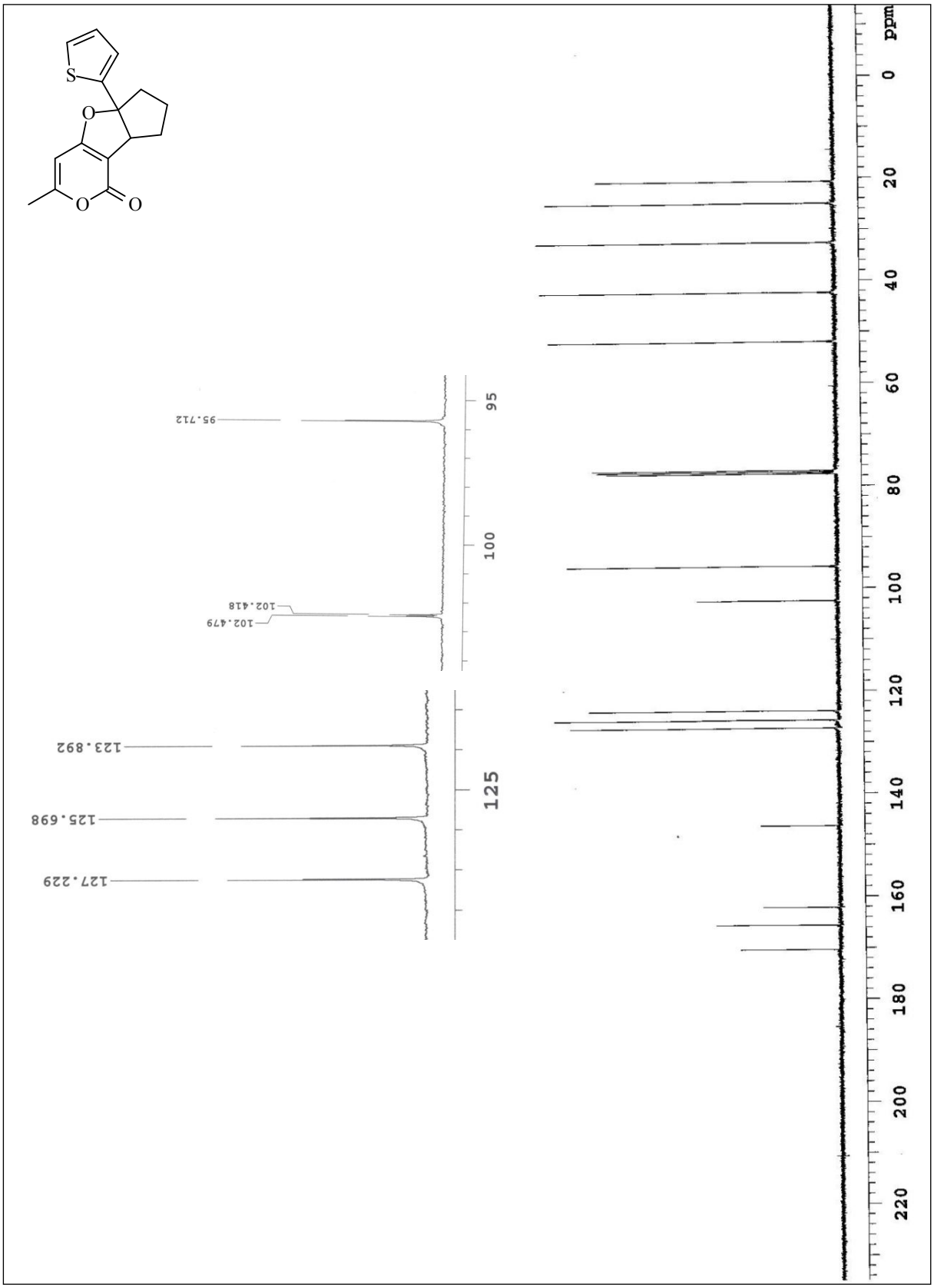
3.44 ^{13}C-NMR spectra of **44**



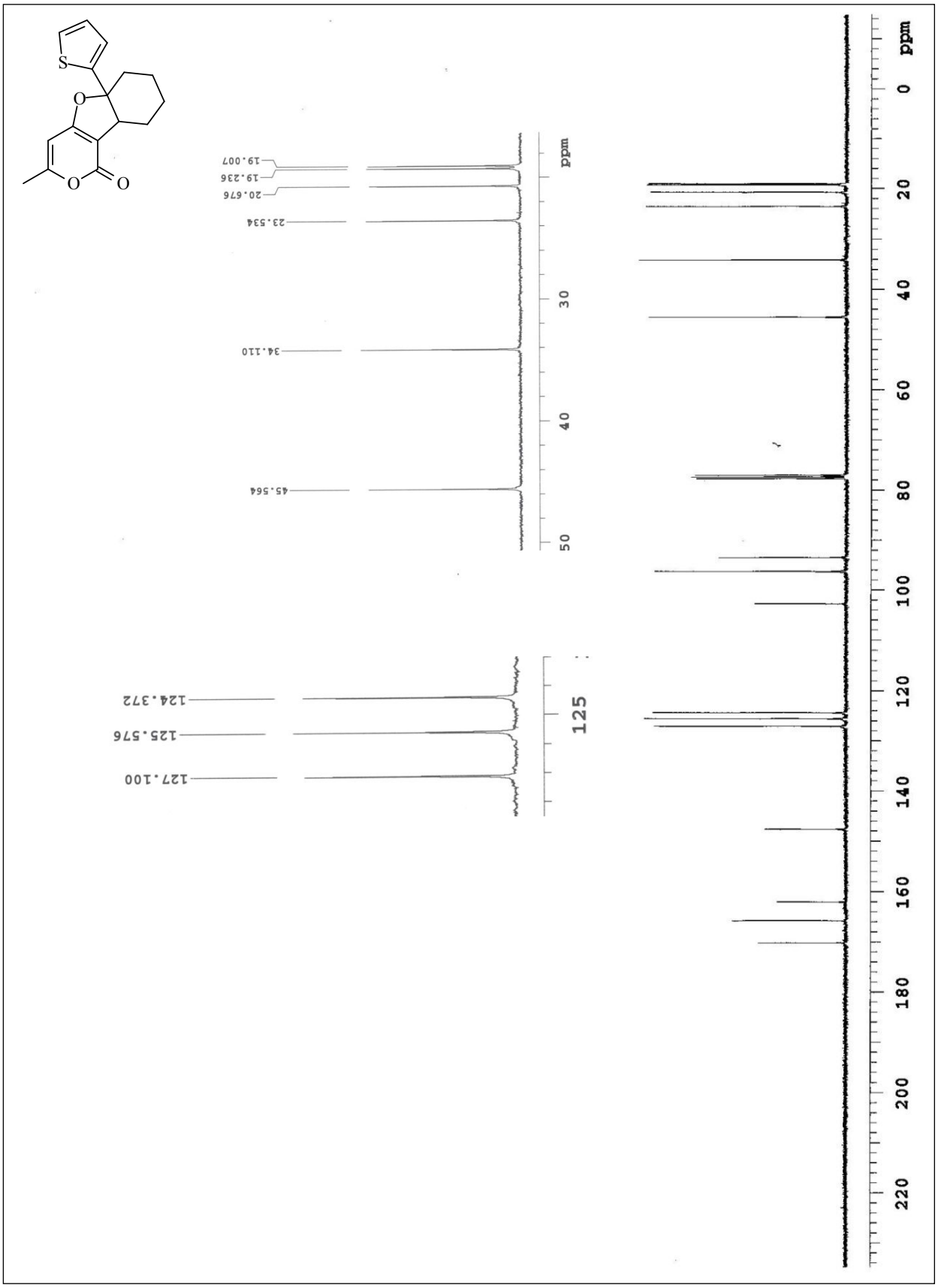
3.45 ^{13}C-NMR spectra of **50**



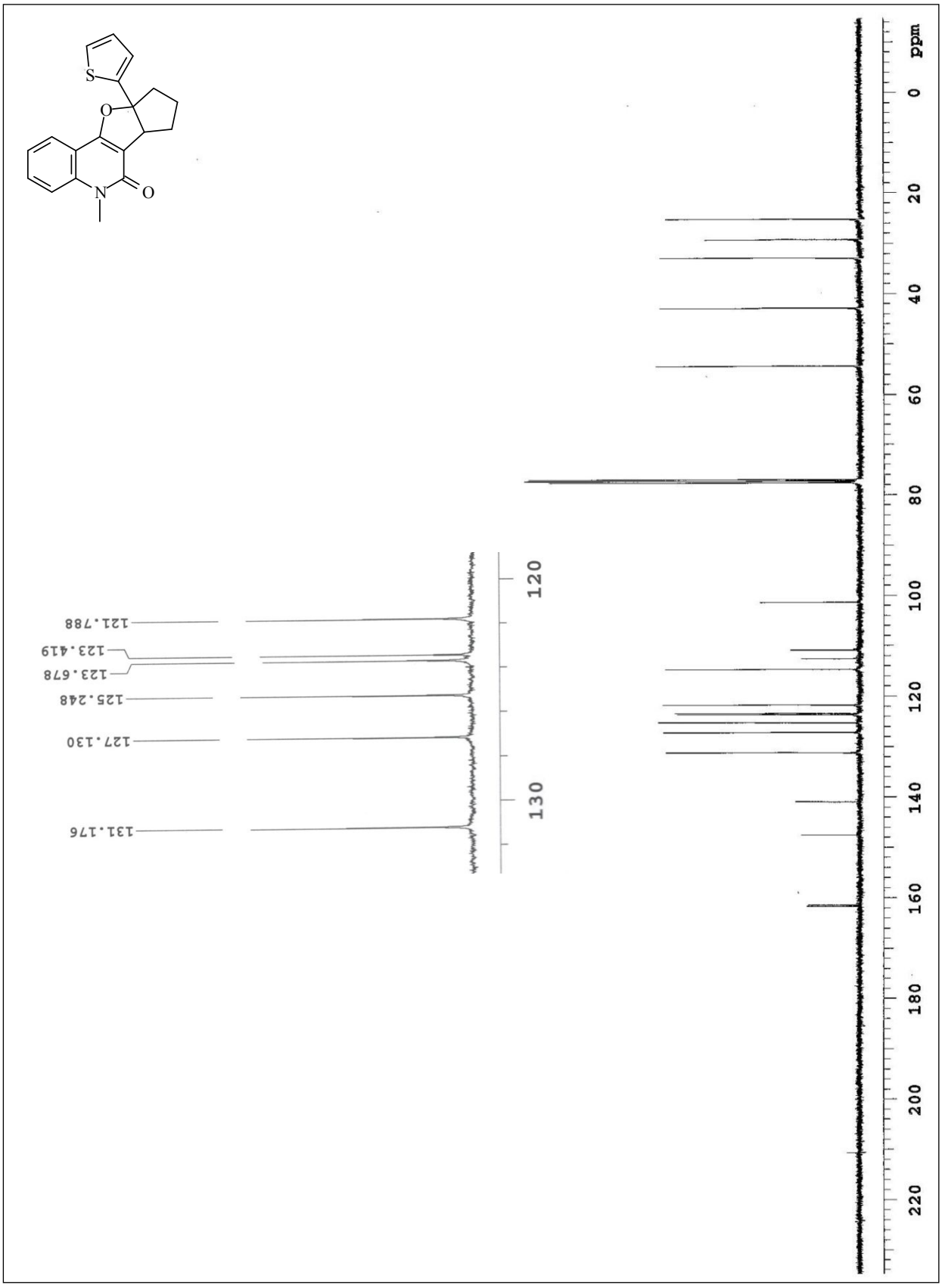
3.46 ^{13}C-NMR spectra of **45**



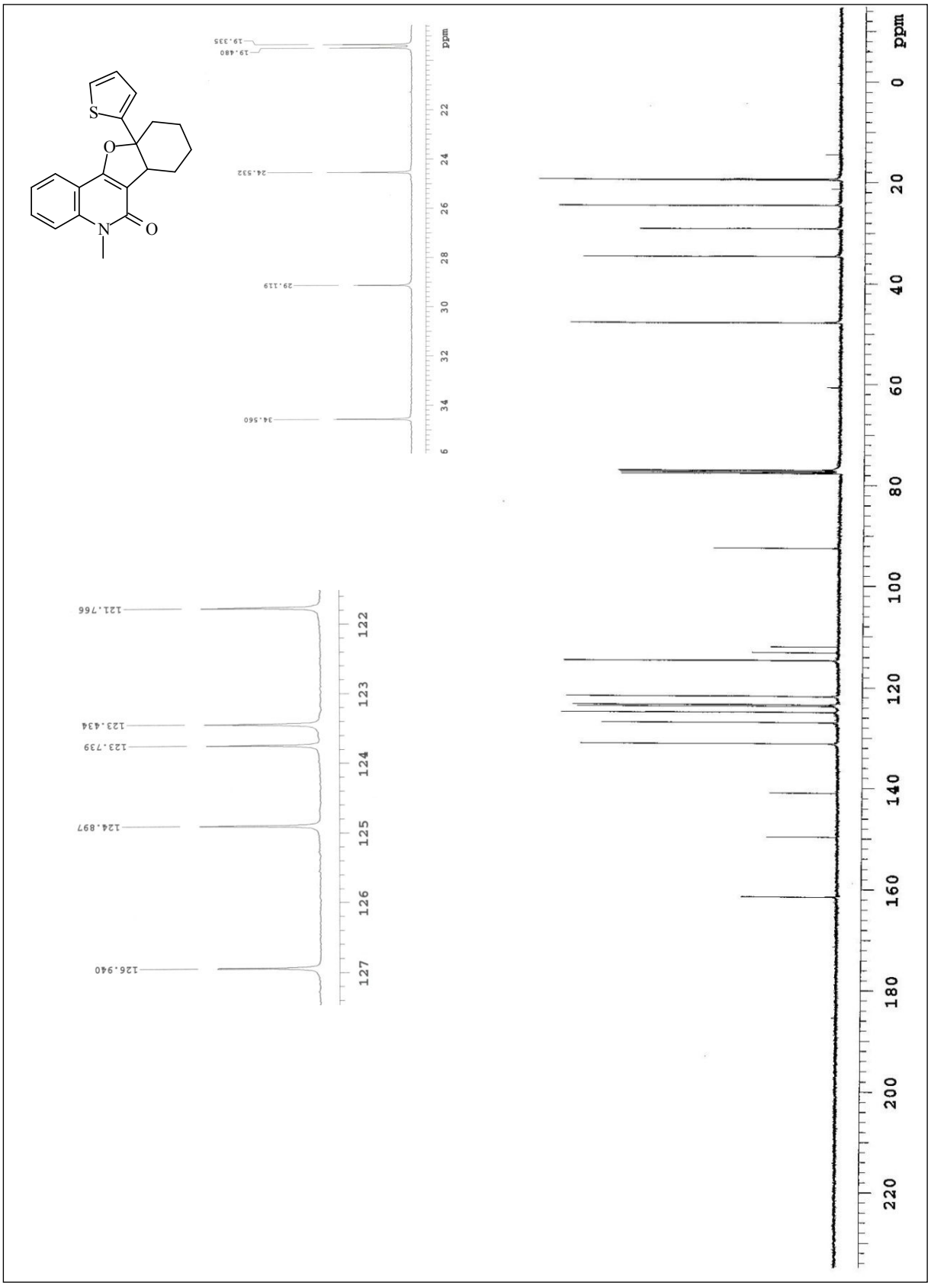
3.47 ^{13}C-NMR spectra of **46**



3.48 ^{13}C-NMR spectra of **47**

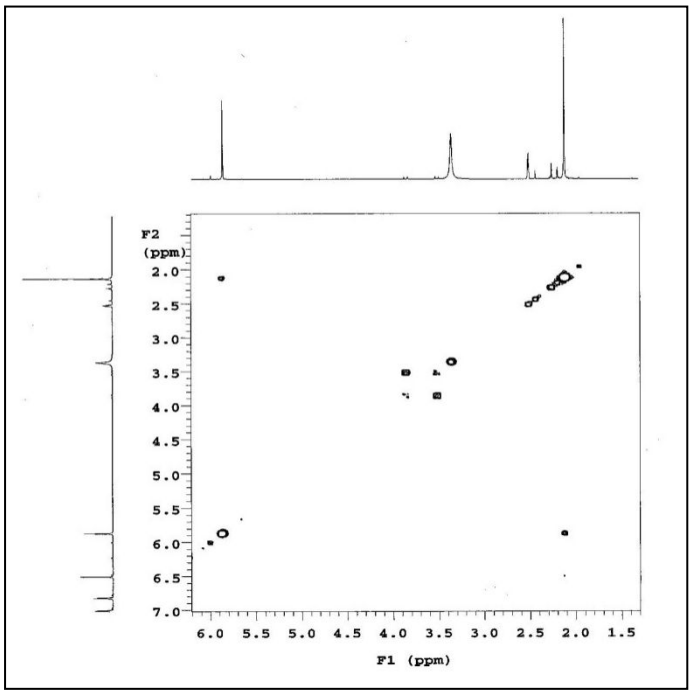


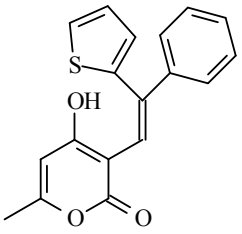
3.49^{13}C-NMR spectra of **48**

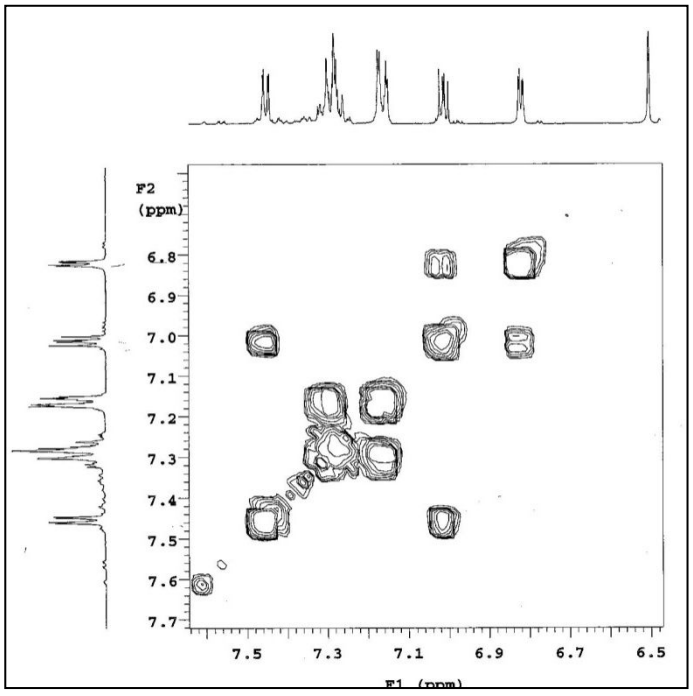


4. COSY Spectra of Compound

4.1 COSY spectra of **16**

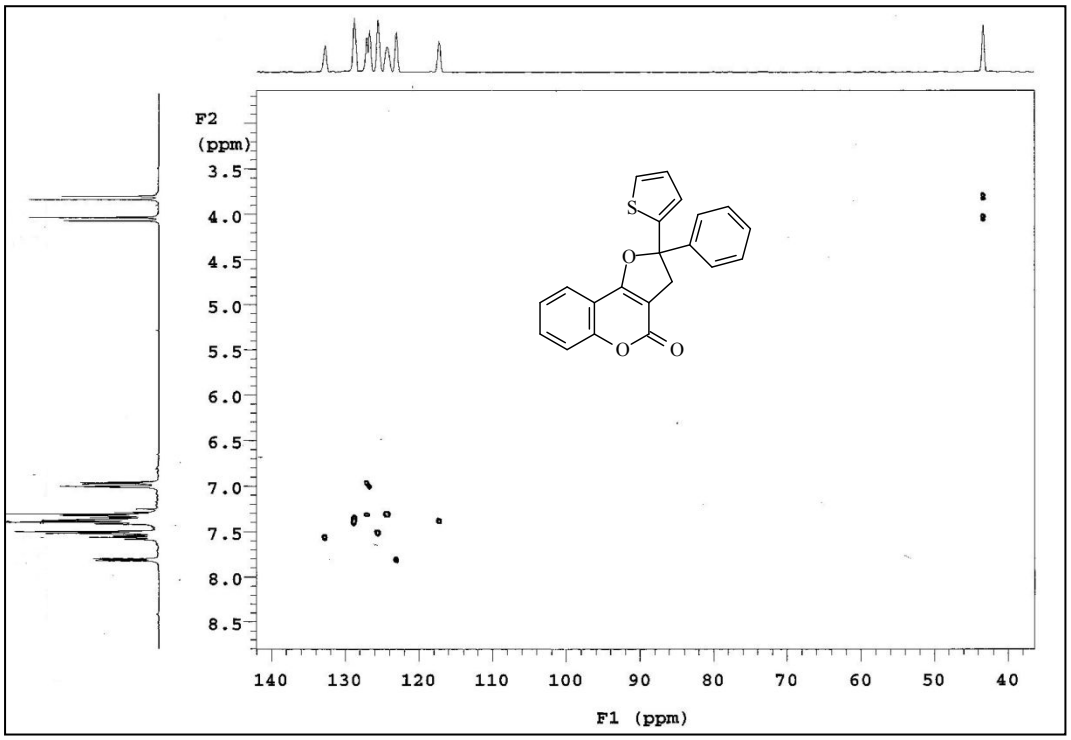


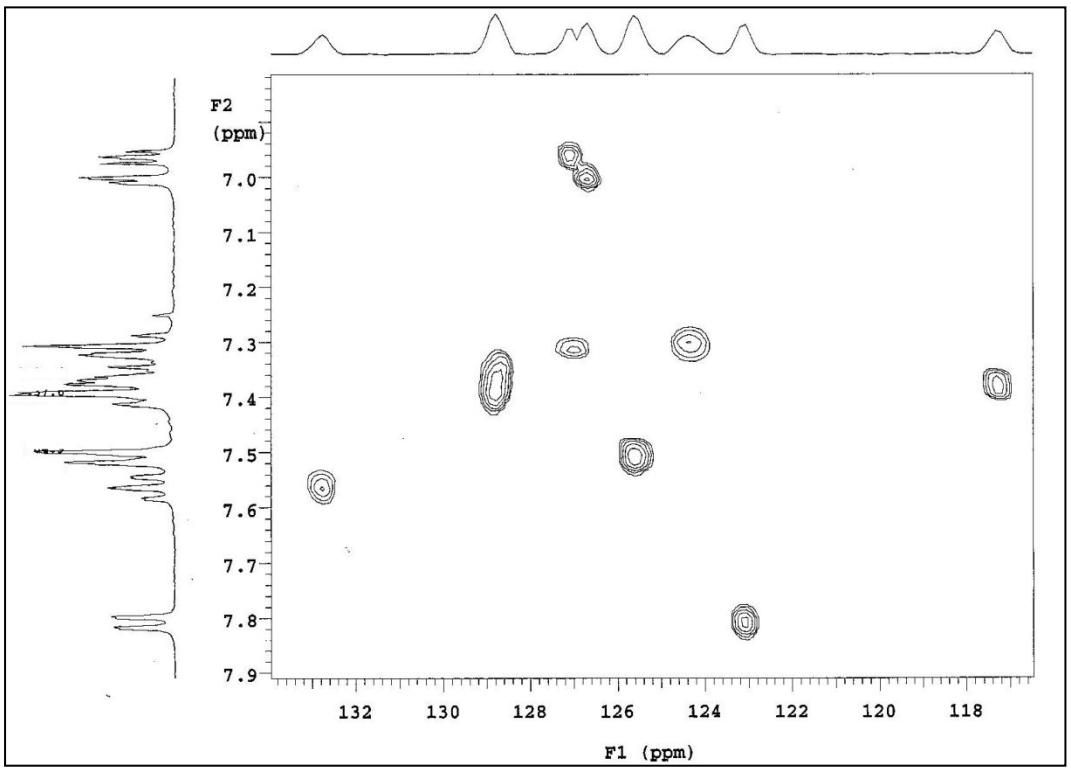




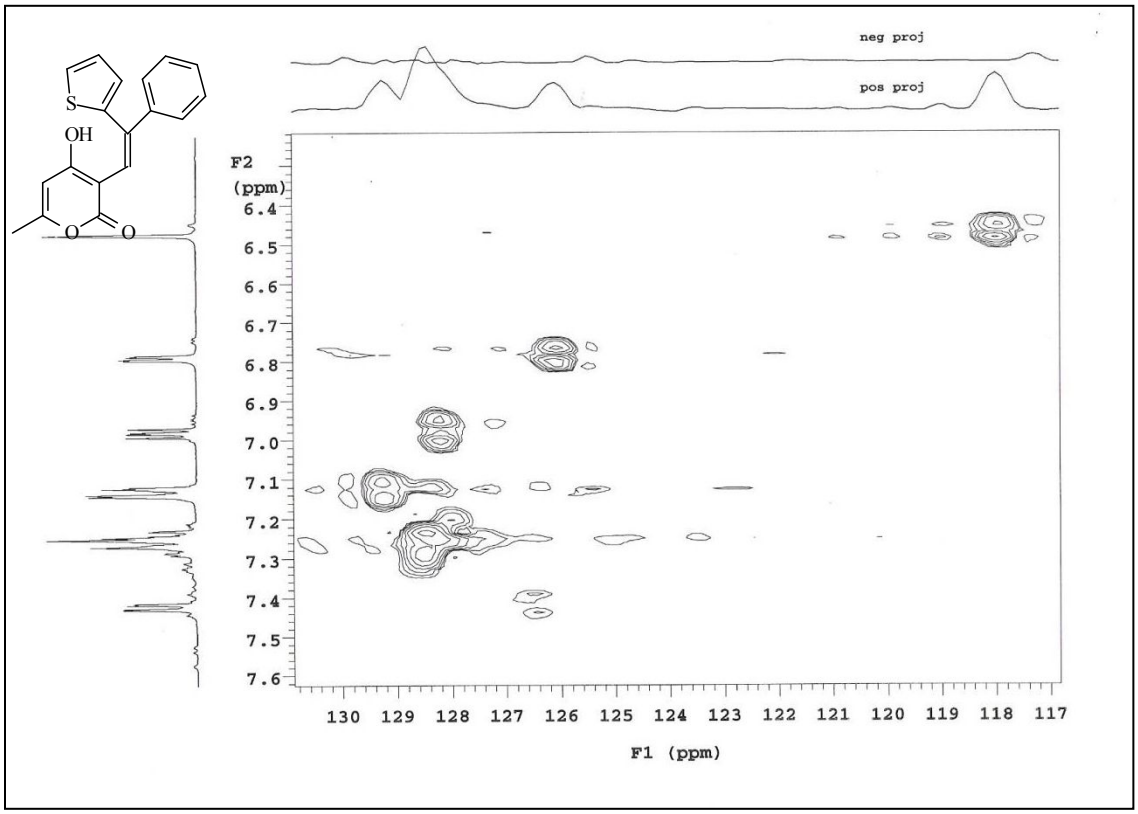
5. HSQC Spectra of Compounds

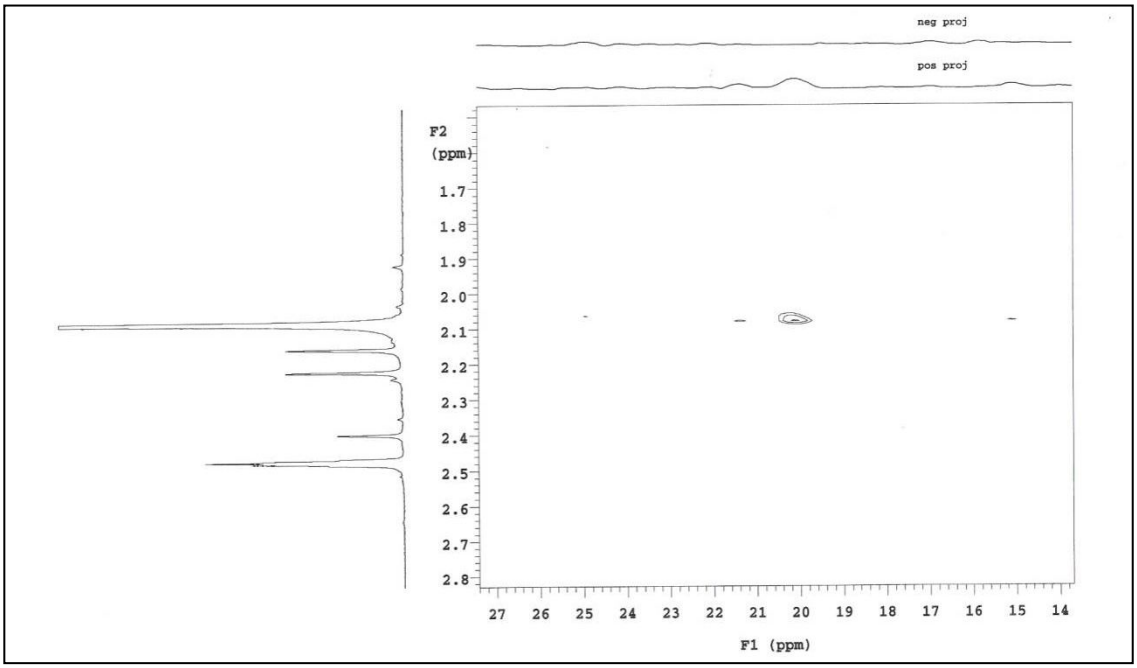
5.1 HSQC spectra of **3**



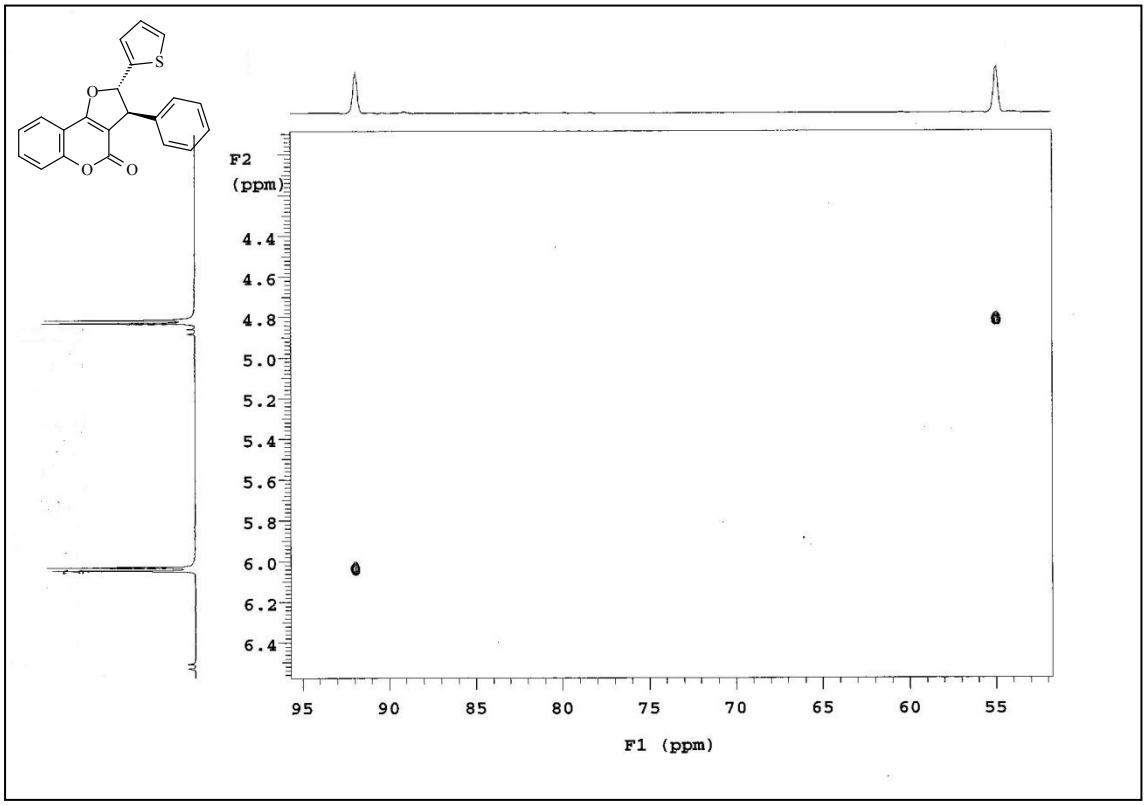


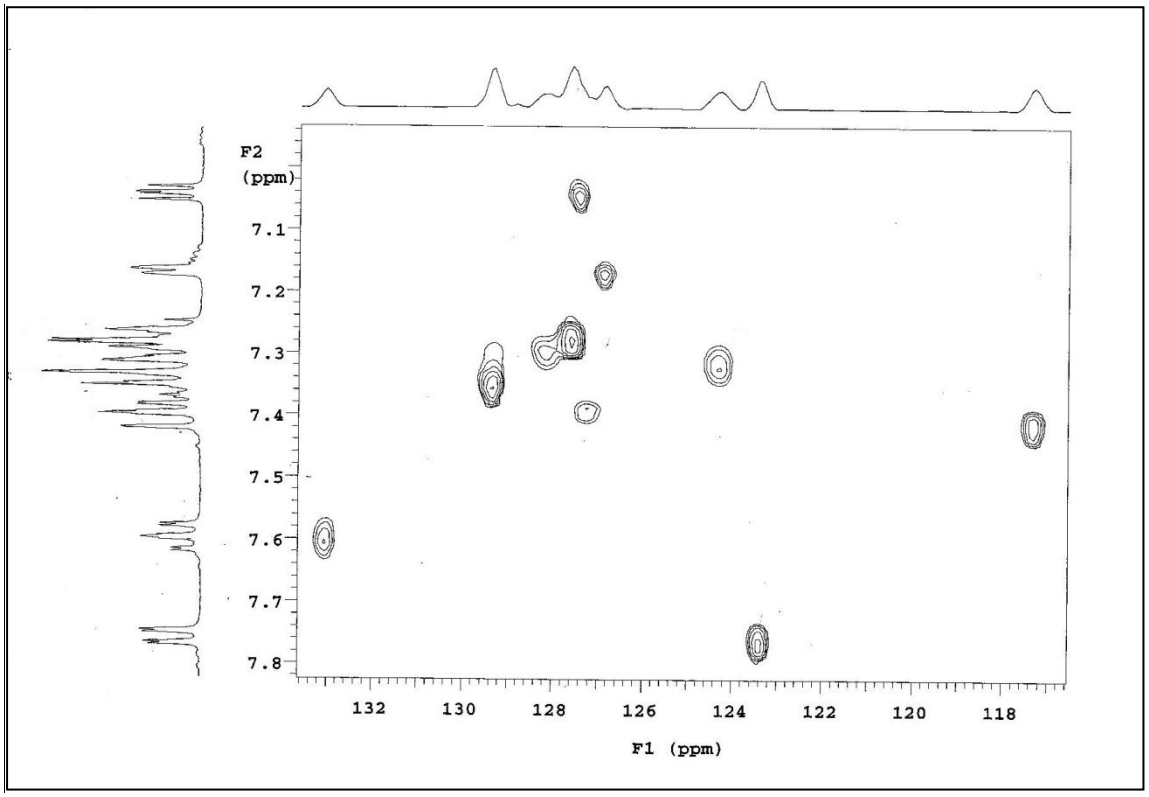
5.2 HSQC spectra of **16**



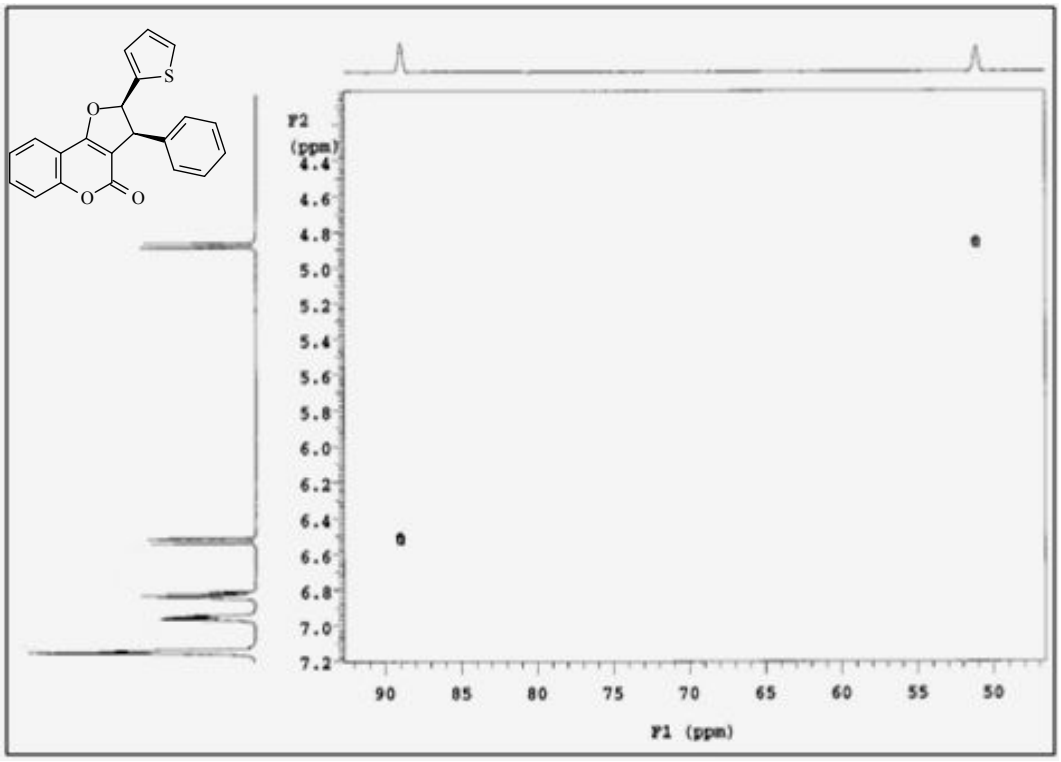


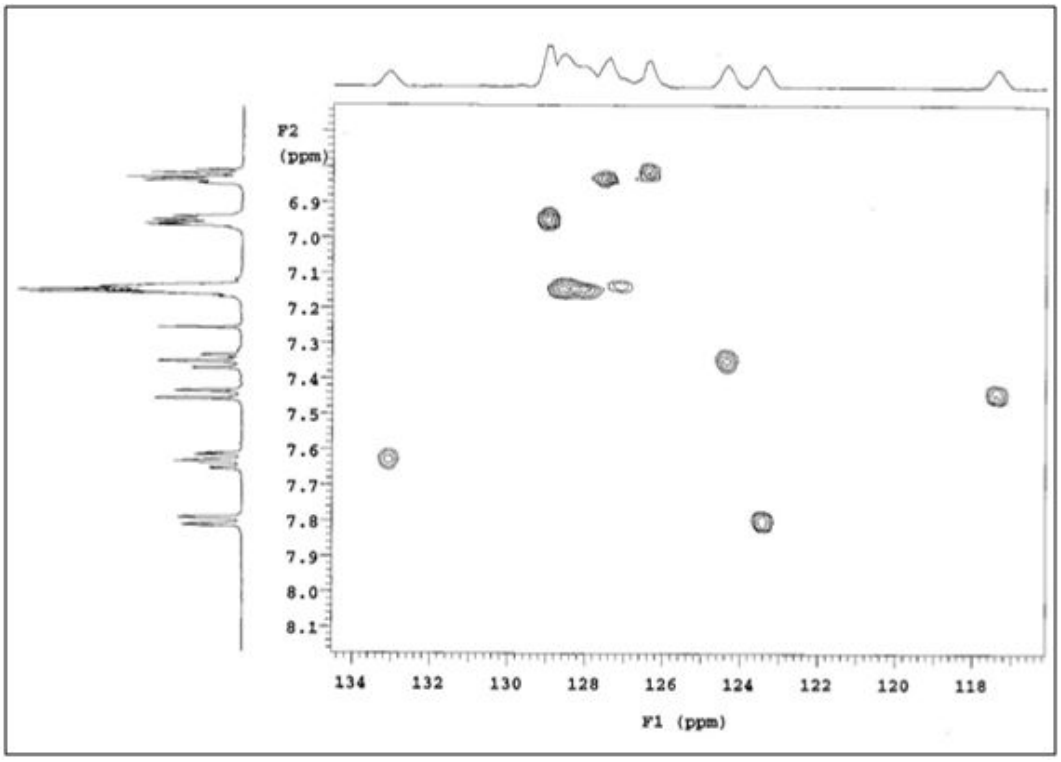
5.3 HSQC spectra of **35**



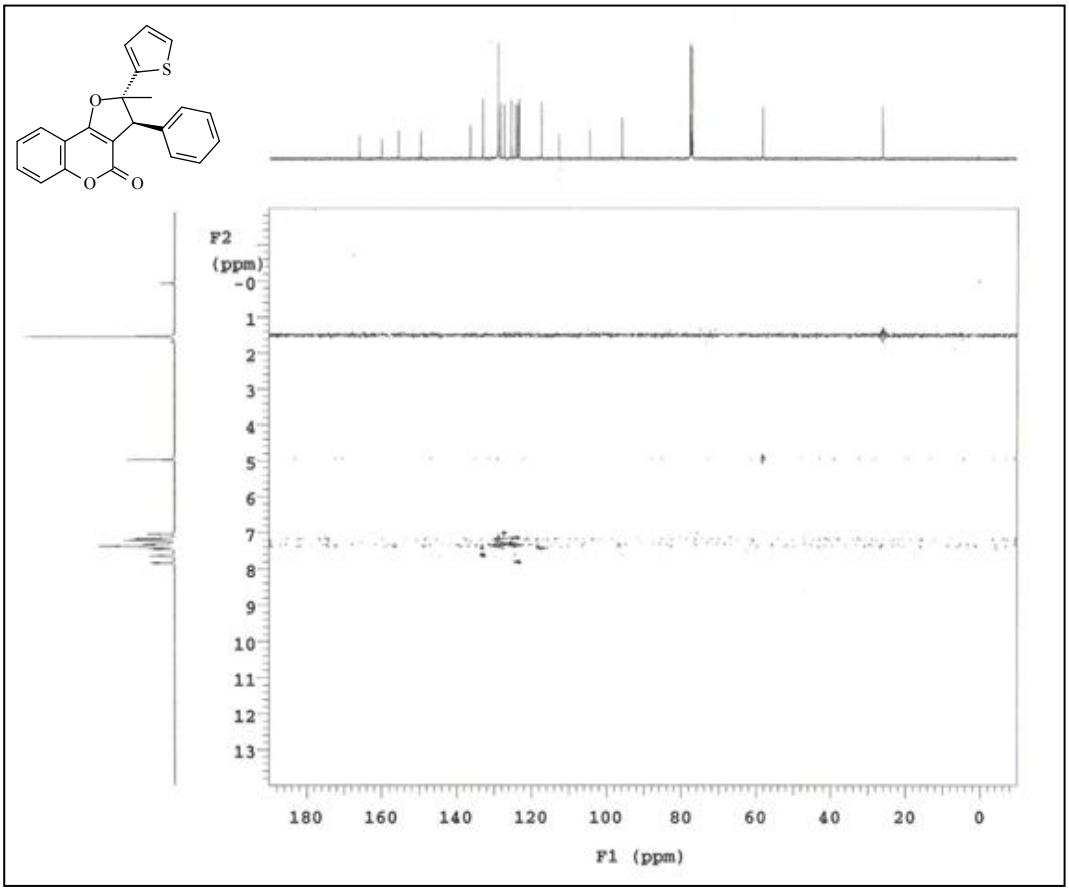


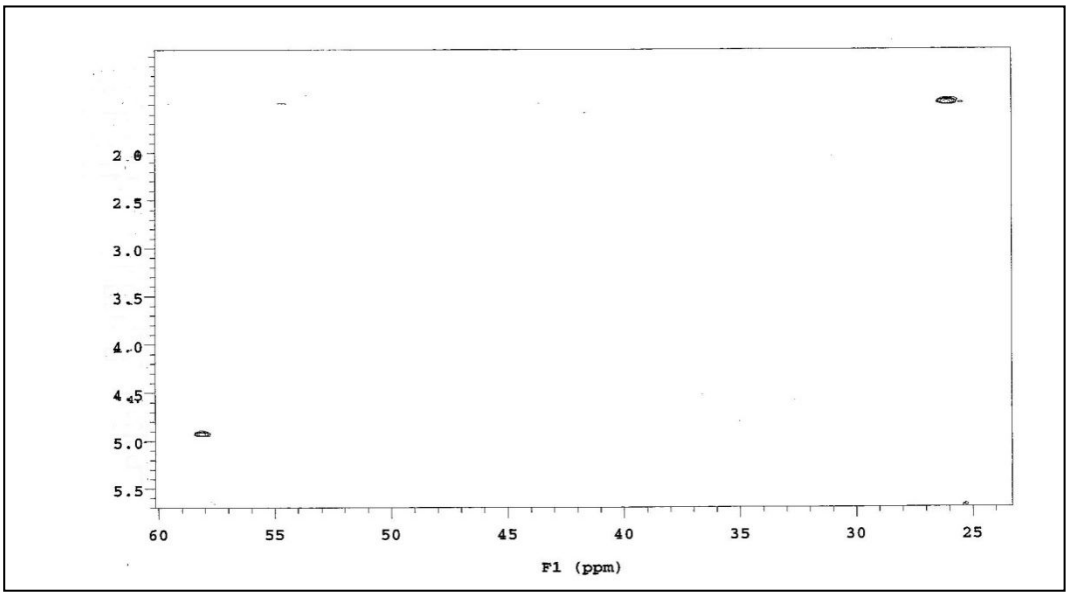
5.4 HSQC spectra of **36**



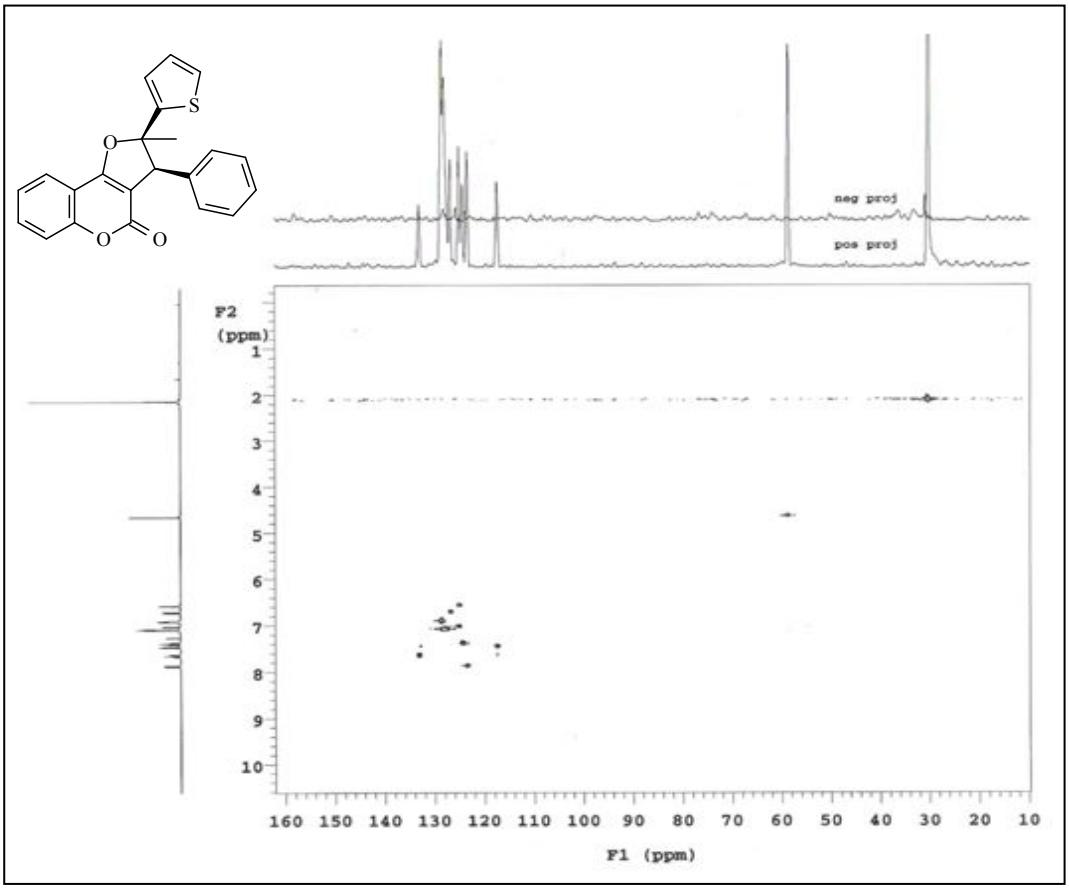


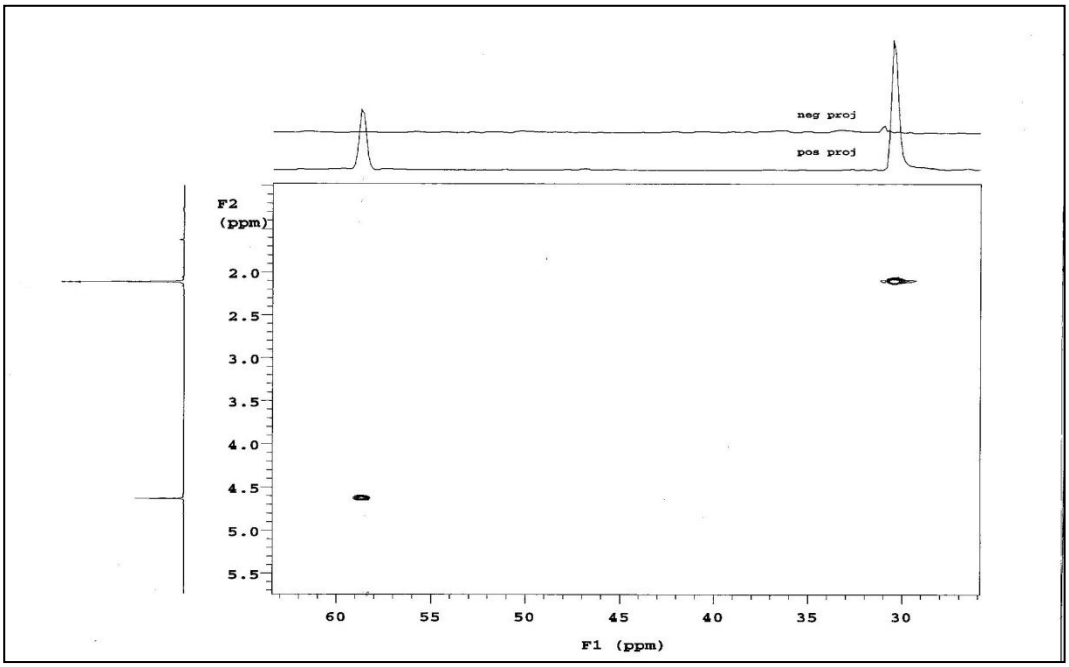
5.5 HSQC spectra of **37**



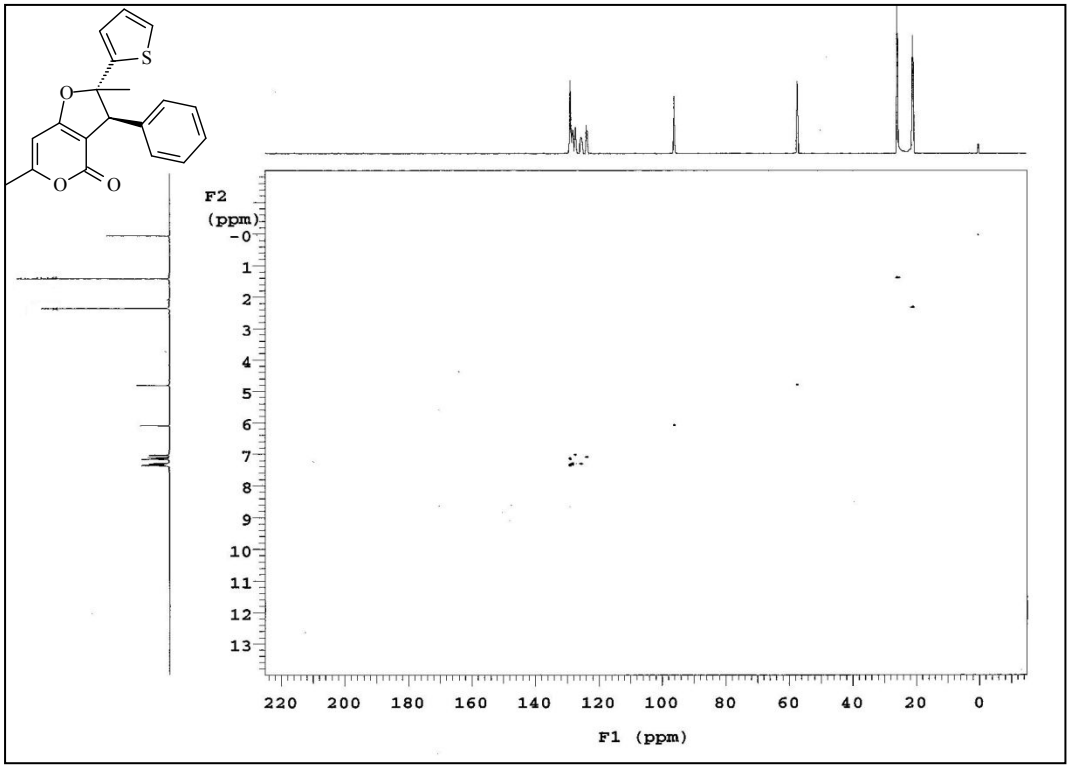


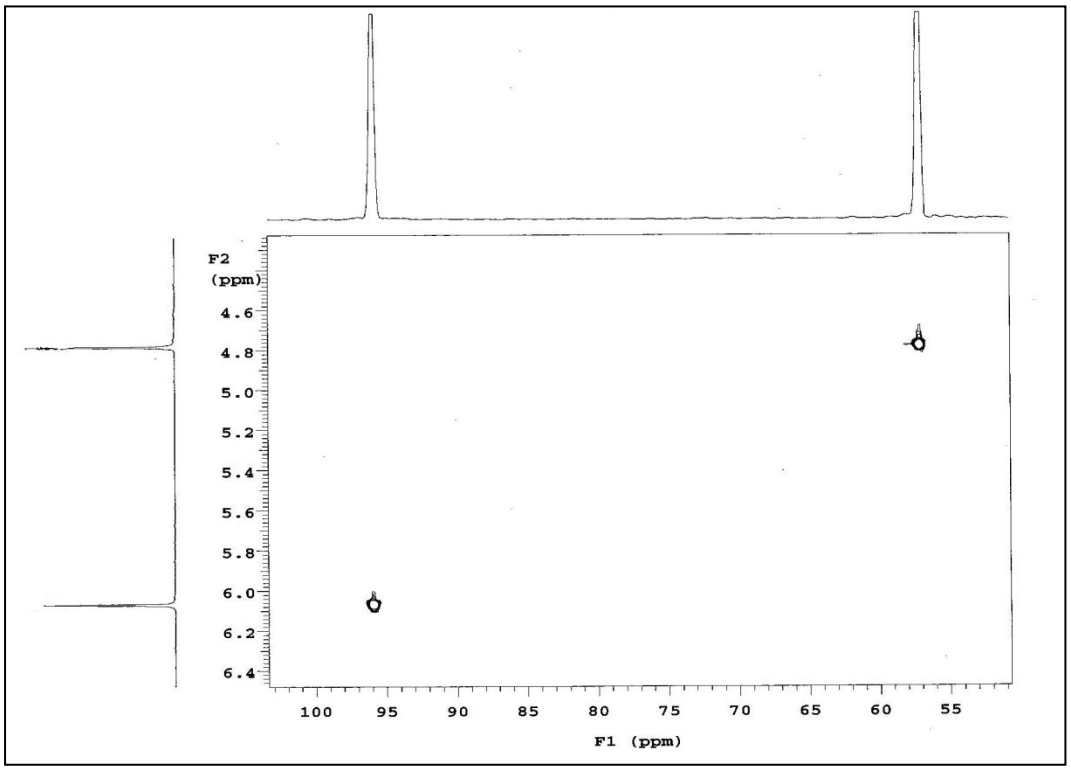
5.6 HSQC spectra of **38**



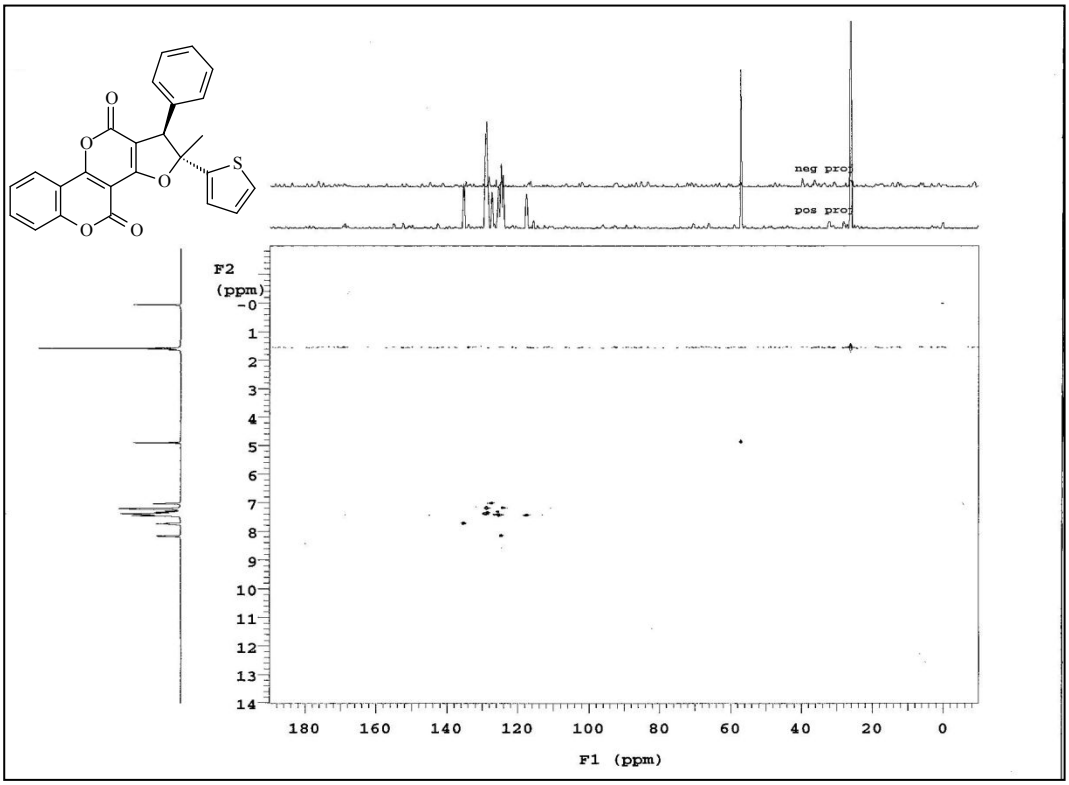


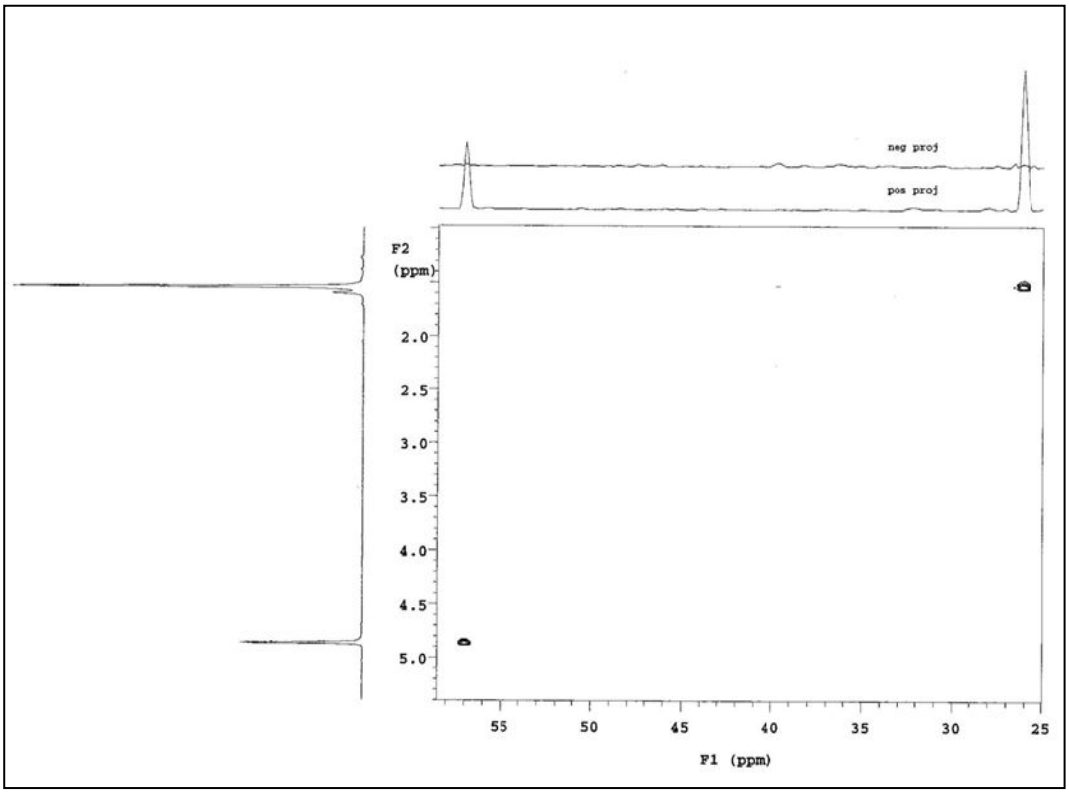
5.7 HSQC spectra of **39**



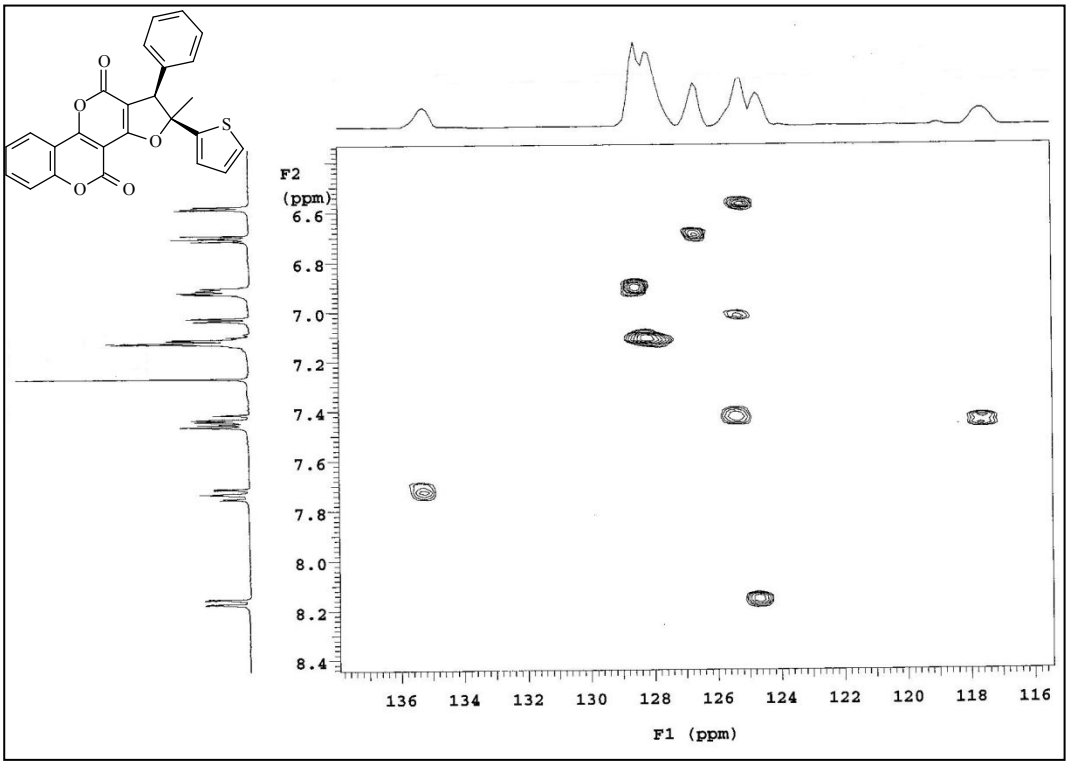


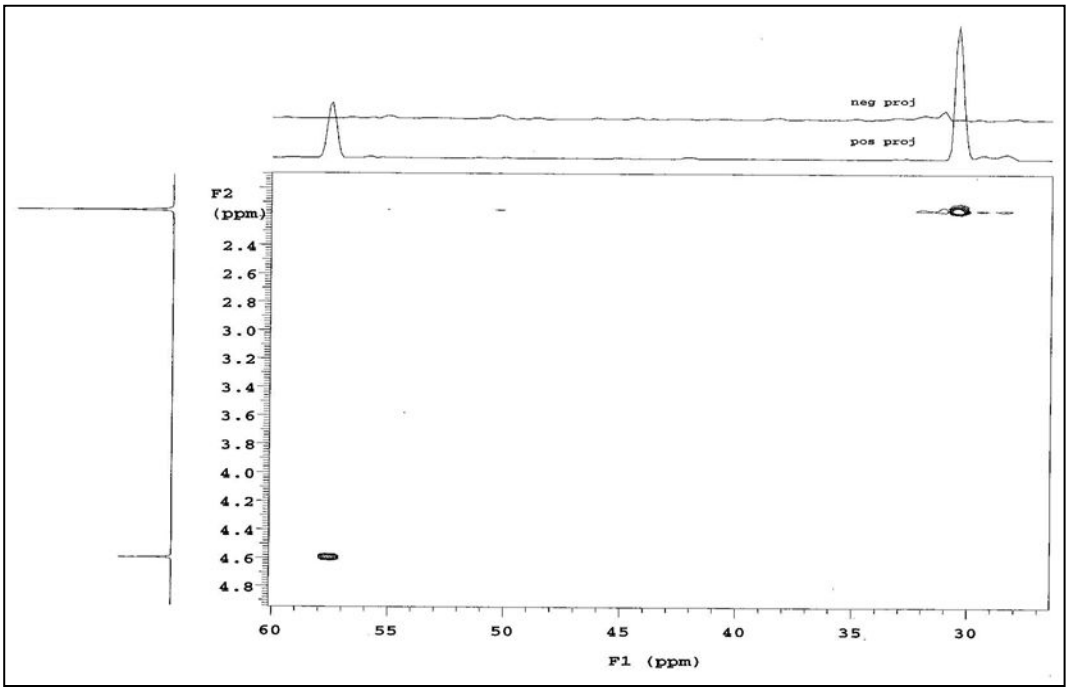
5.8 HSQC spectra of **41**





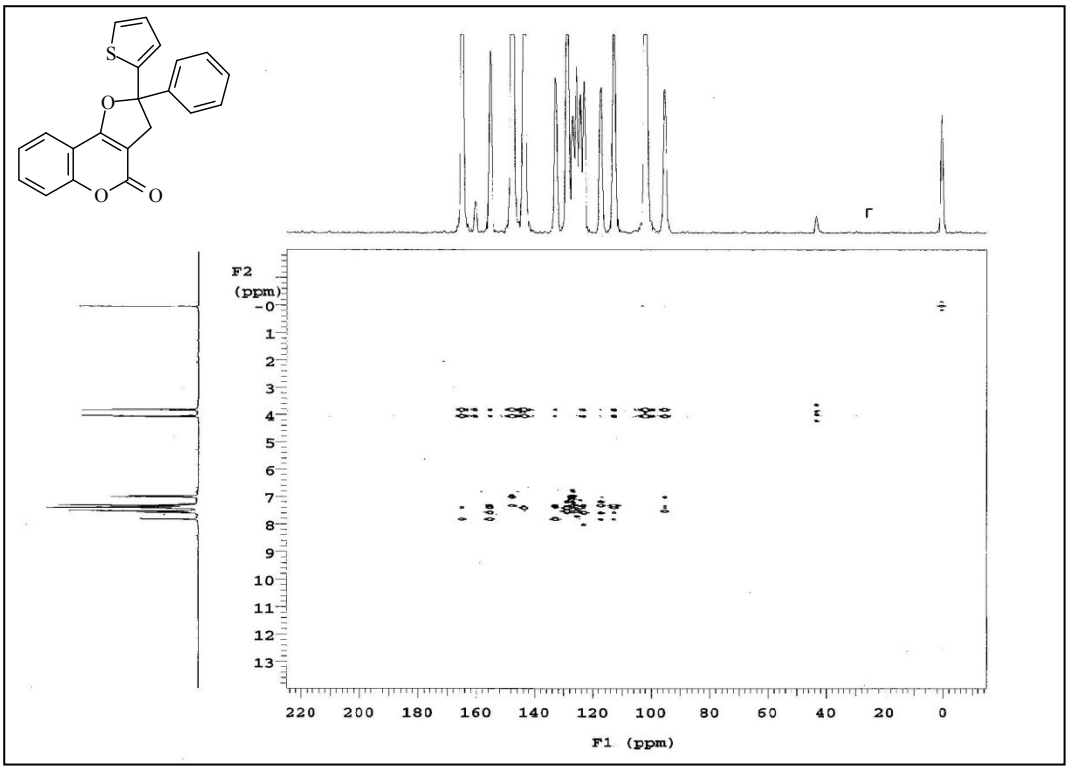
5.9 HSQC spectra of **42**

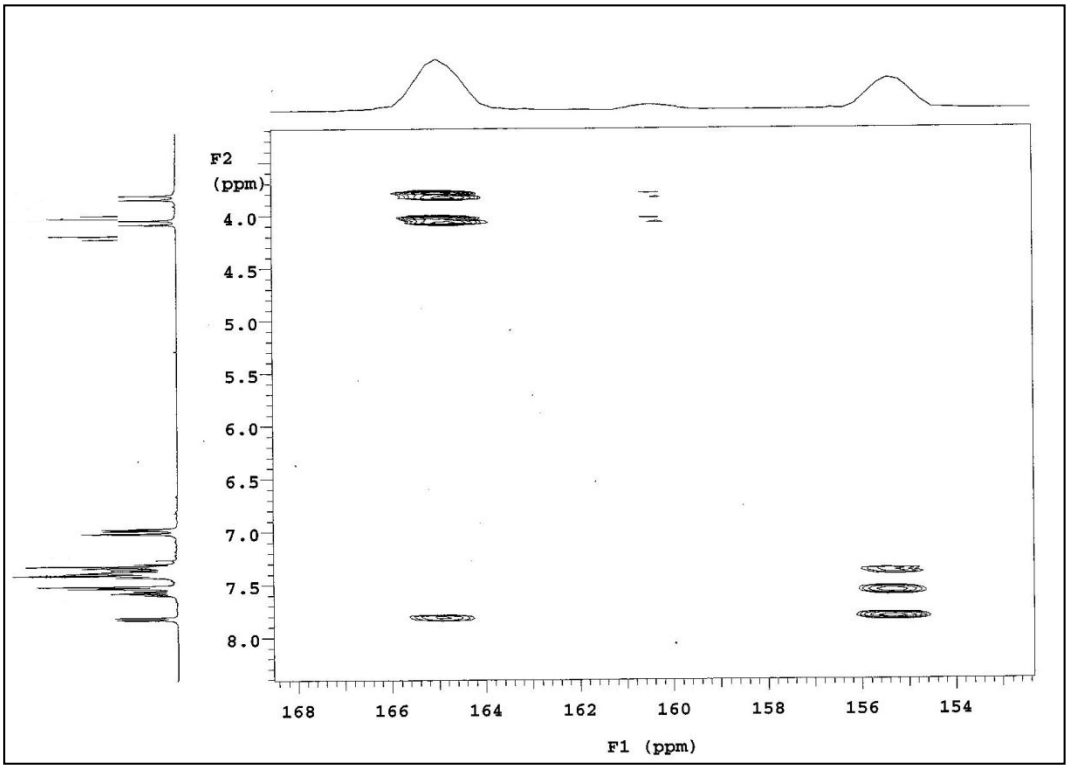




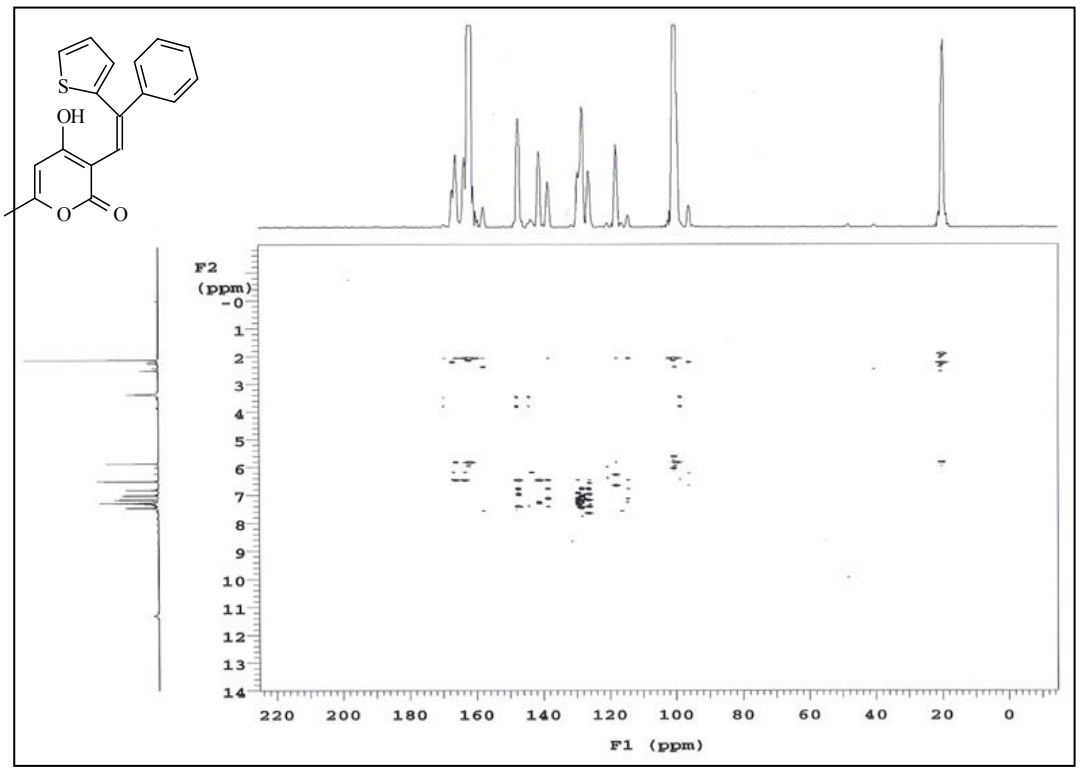
6. HMBC Spectra of COMPOUNDS

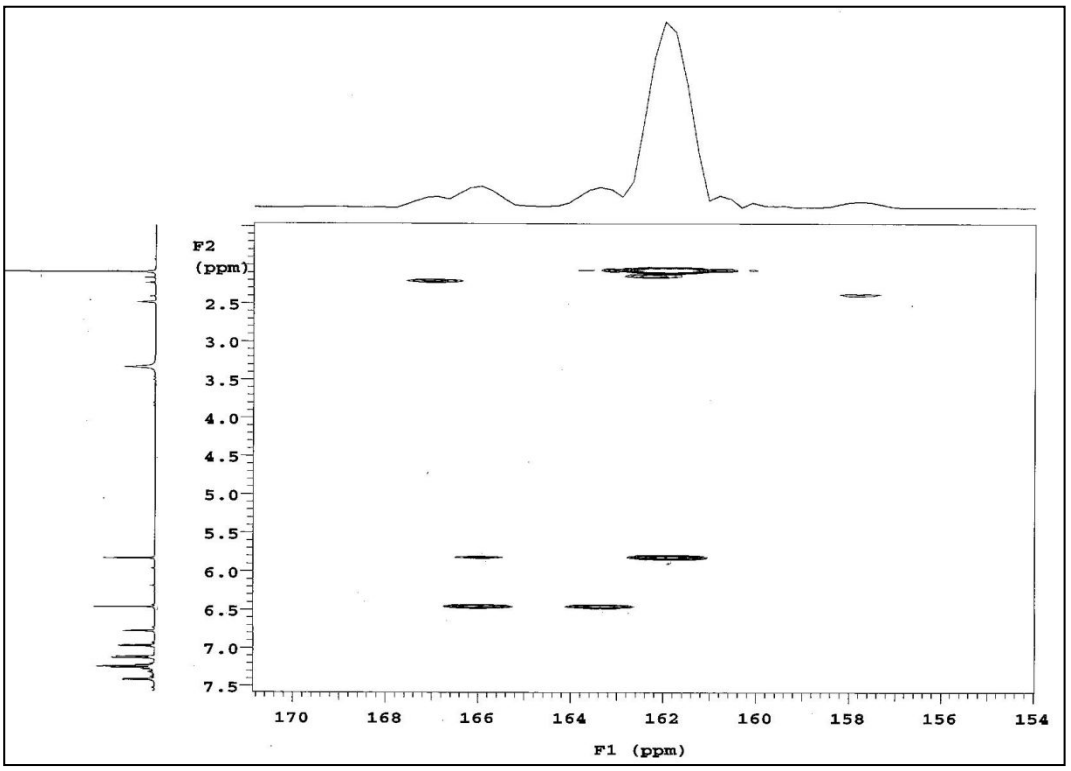
6.1 HMBA spectra of **3**



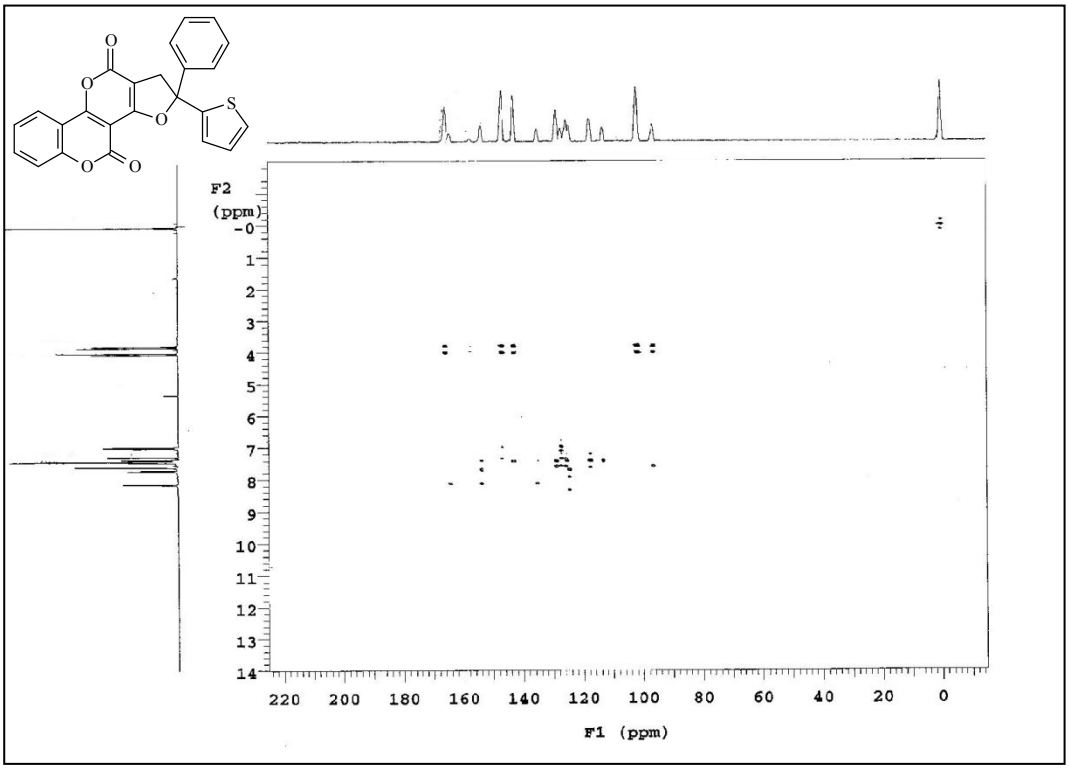


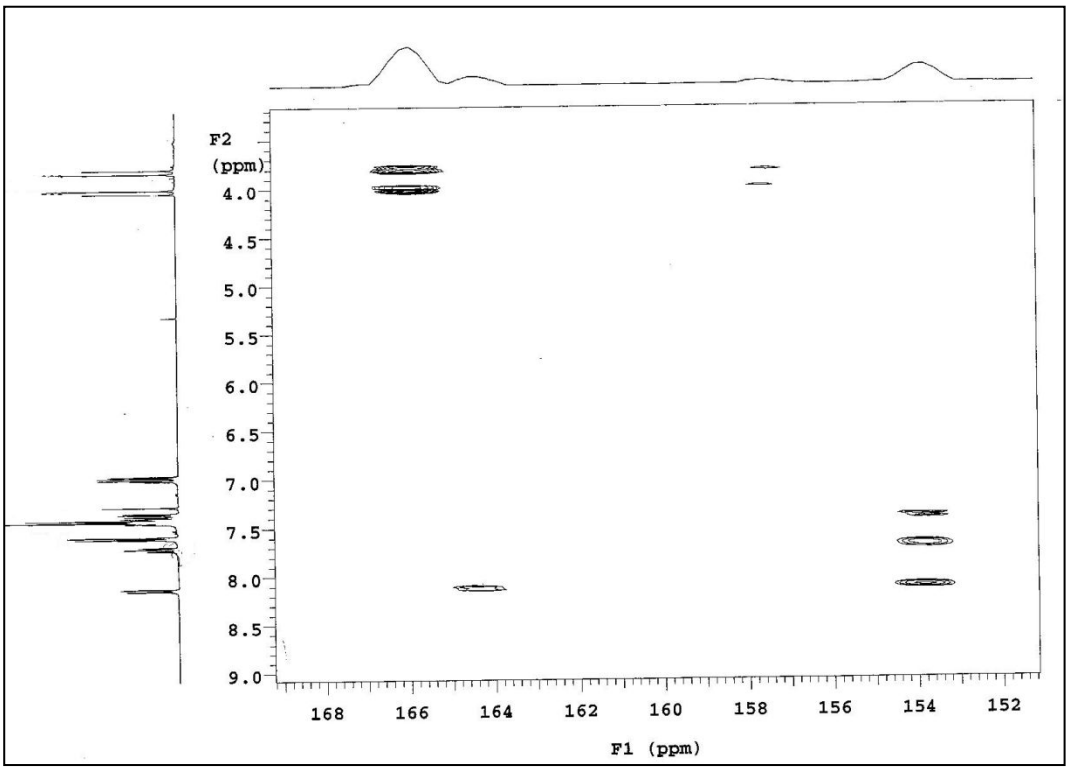
6.2 HMBC spectra of **16**



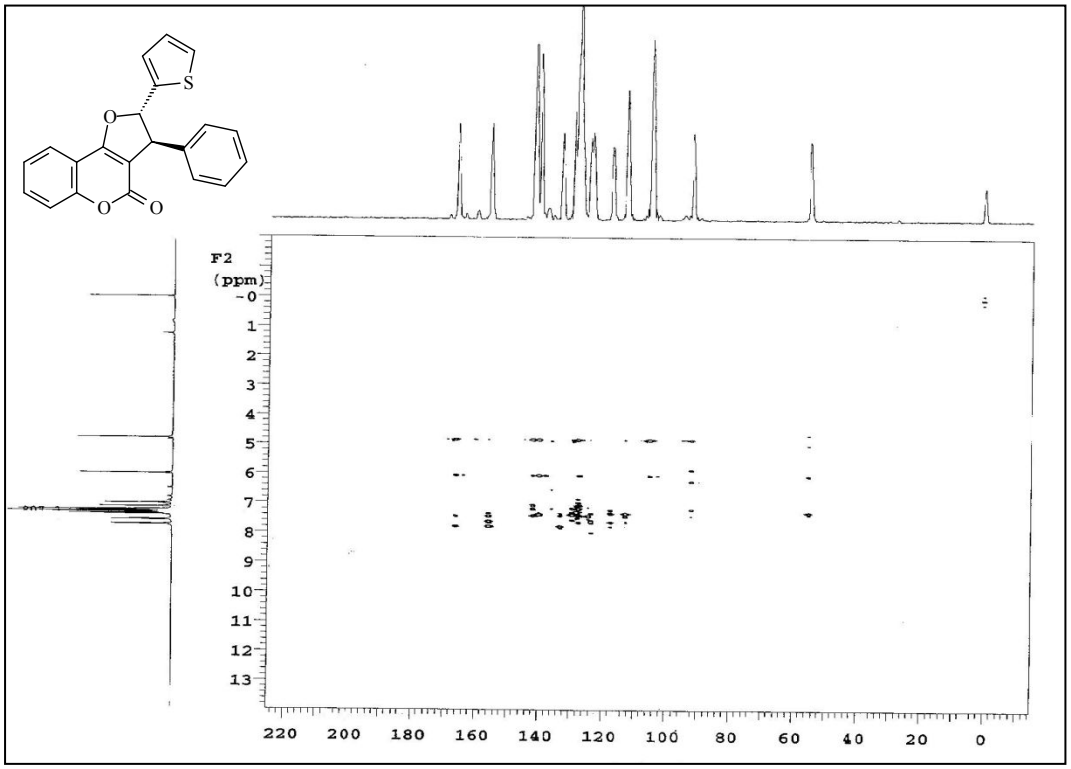


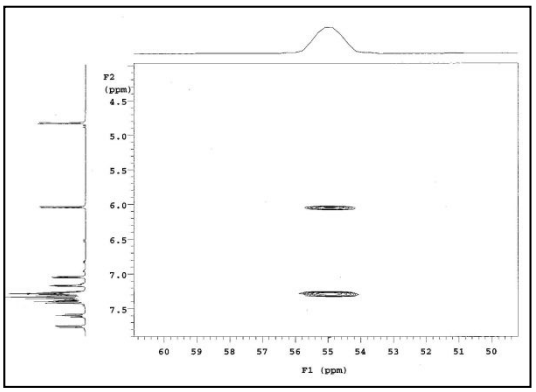
6.3 HMBC spectra of **19**

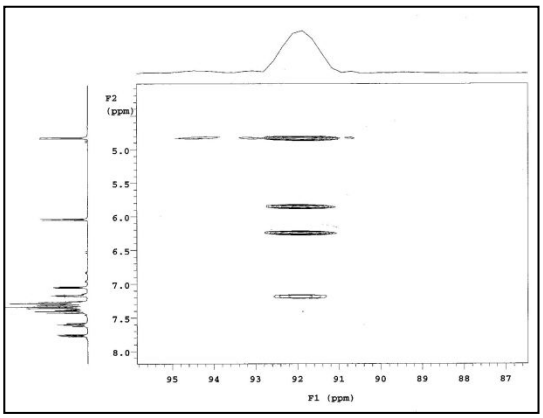




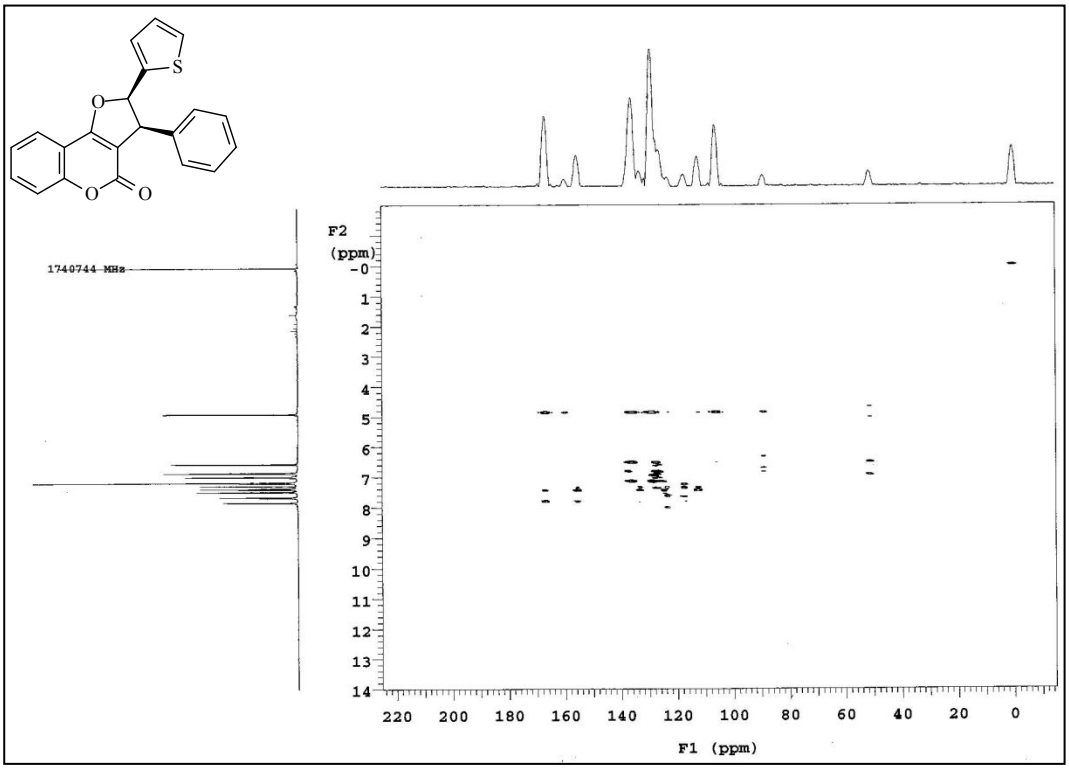
6.4 HMBC spectra of **35**

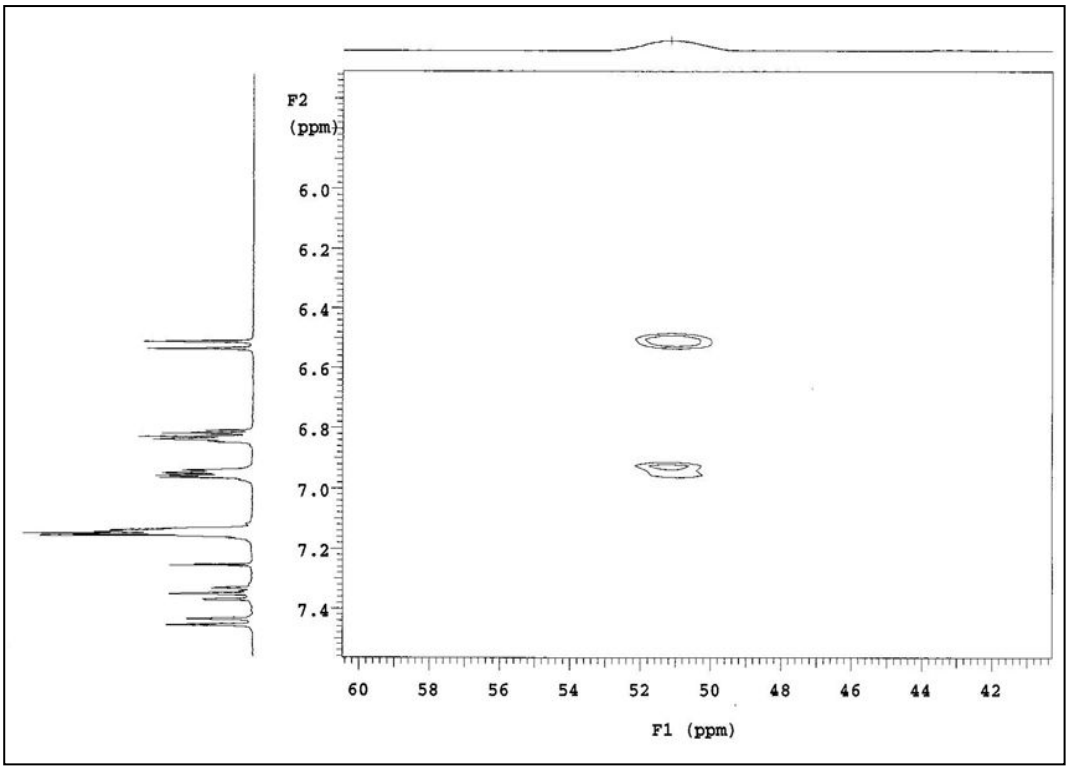




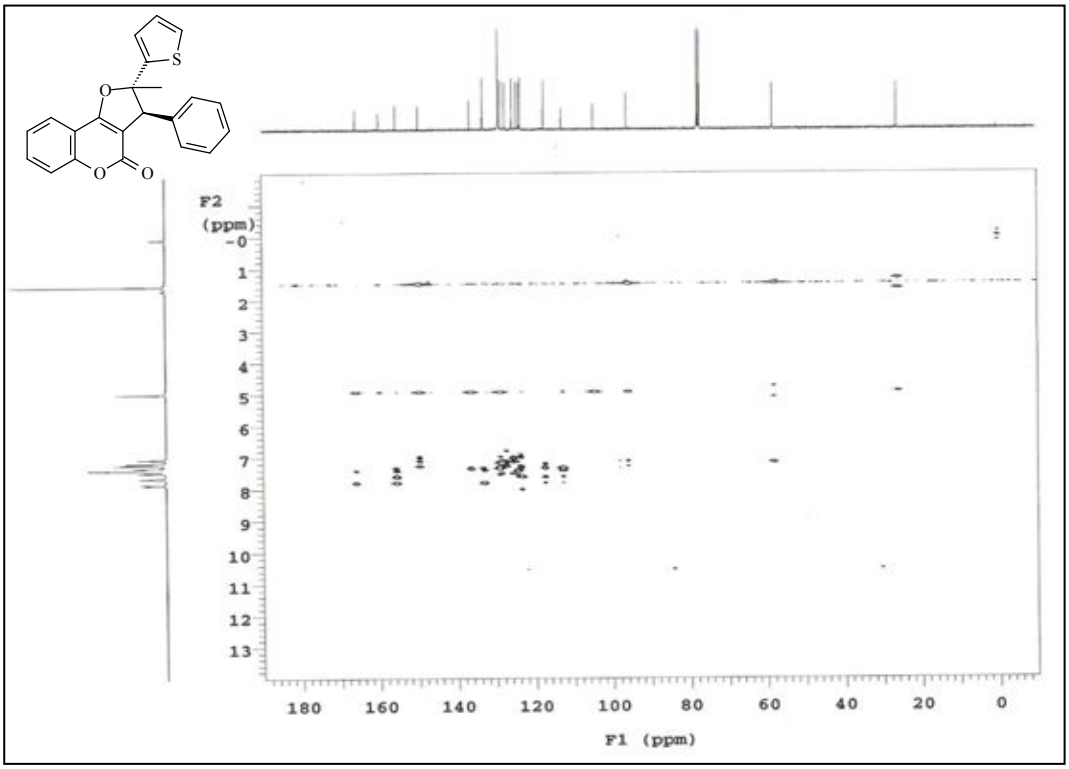


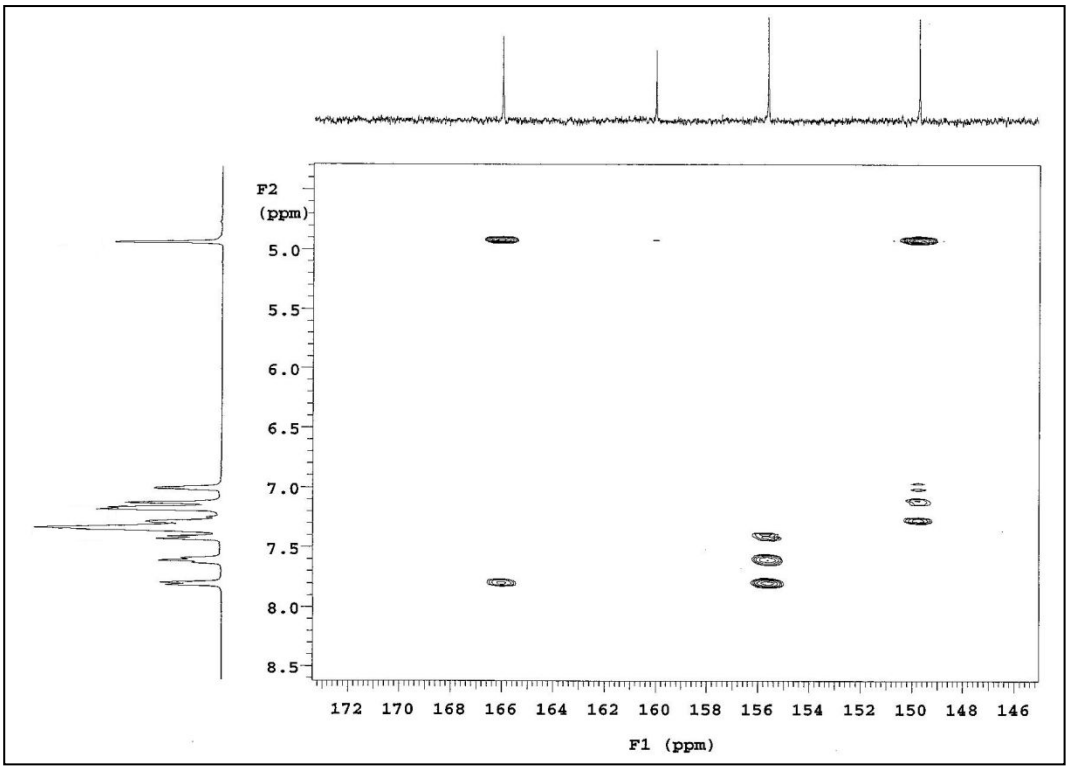
6.5 HMBC spectra of **36**



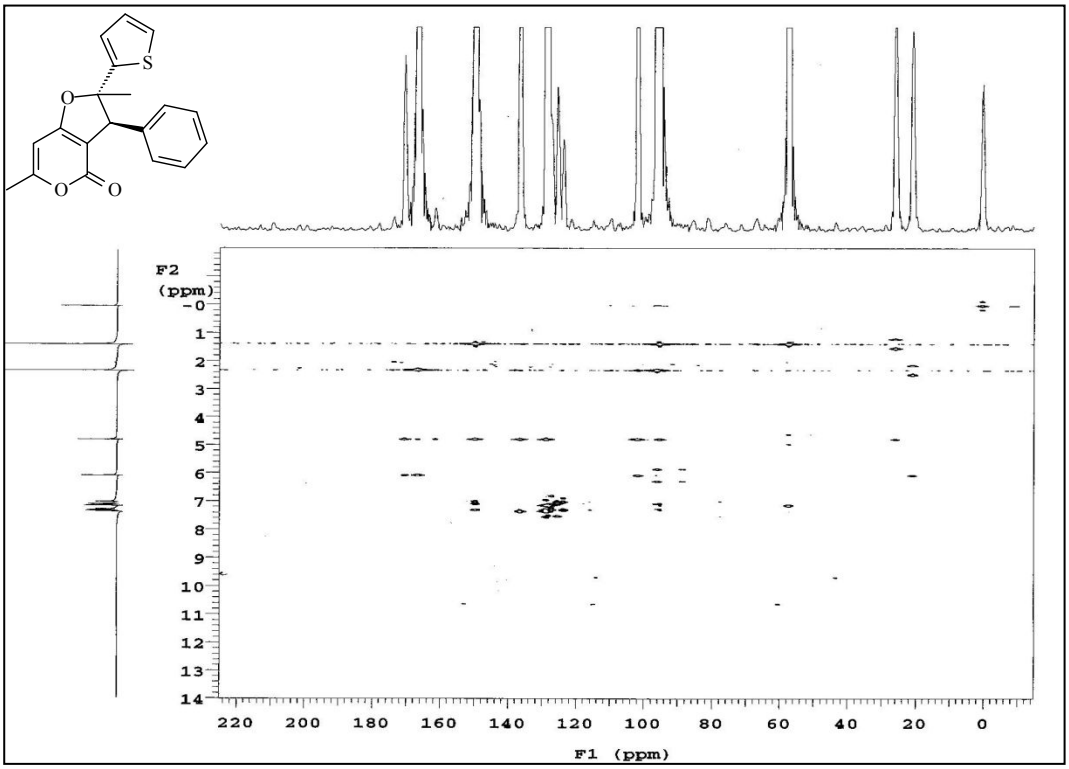


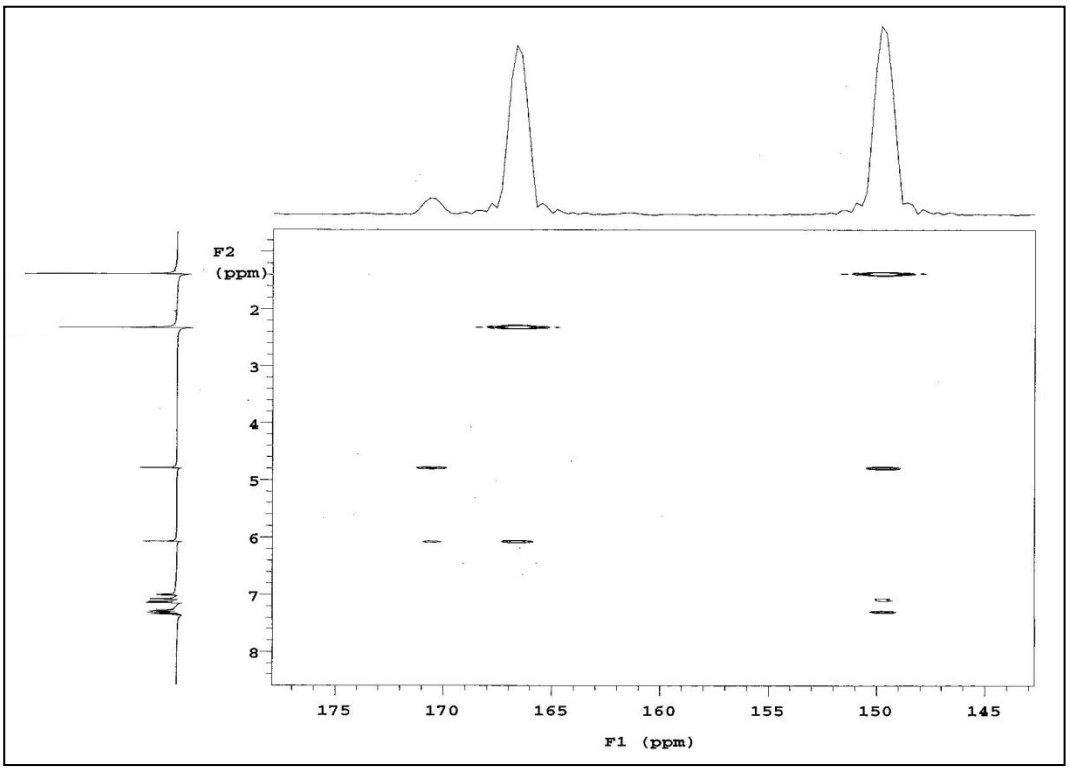
6.6 HMBC spectra of **37**



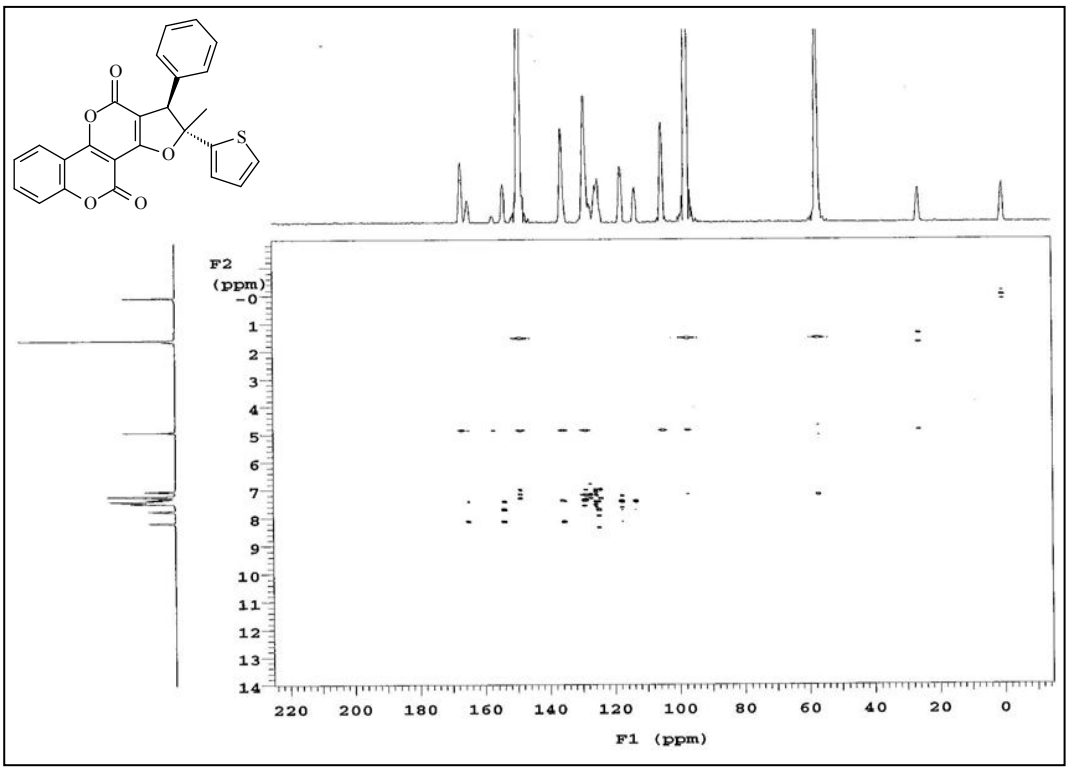


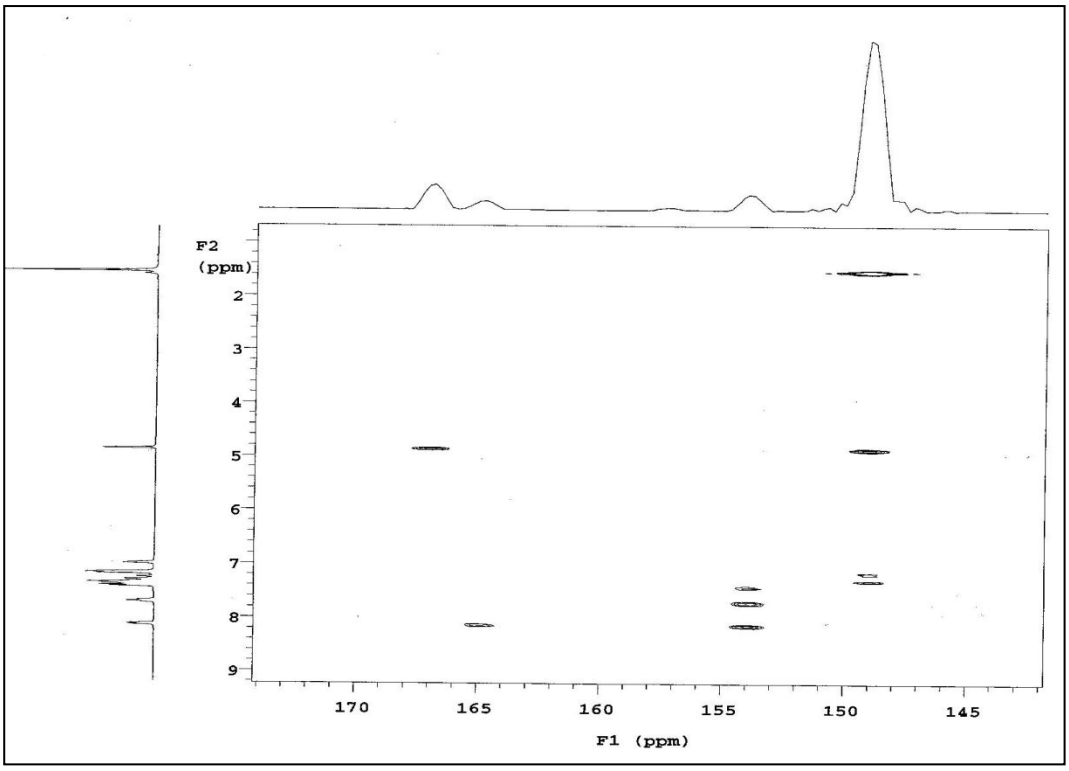
6.7 HMBC spectra of **39**





6.8 HMBC spectra of **39**





```
data_md501_0m

_iucr_refine_instructions_details
;
TITL md501_0m in P 21/c
CELL  0.71073   9.9226  15.7155  11.5782   90.000  108.572   90.000
ZERR    4.00   0.0002   0.0003   0.0002    0.000    0.003    0.000
LATT   1
SYMM  - X, 1/2 + Y, 1/2 - Z
SFAC  C    H    O    S
UNIT  88   64   12   4
MERG   2
FMAP   2
PLAN   20
SIZE    0.16   0.25   0.32
ACTA
BOND   $H
CONF
LIST   4
L.S.  10
TEMP    20.00
WGHT    0.036900    0.832700
FVAR      0.18359
H10   2    0.342282   -0.061688    0.366198    11.00000    0.01588
MOLE    1
S1    4    0.422148    0.145520    0.357393    11.00000    0.01945    0.02135 =
      0.02482   -0.00592    0.01208   -0.00720
O1    3    0.340548   -0.151448    0.023621    11.00000    0.02272    0.01652 =
      0.02247    0.00017    0.01058    0.00309
O2    3    0.217328    0.061095    0.163562    11.00000    0.02542    0.01318 =
      0.01633    0.00052    0.00607    0.00191
O3    3    0.356454   -0.222493    0.193090    11.00000    0.02325    0.01575 =
      0.02590    0.00217    0.00902    0.00421
C9    1    0.279346   -0.078675    0.181215    11.00000    0.01375    0.01497 =
      0.01890   -0.00031    0.00517    0.00002
C10   1    0.252070   -0.061865    0.299583    11.00000    0.01459    0.01268 =
      0.01739    0.00000    0.00415    0.00063
C4    1    0.318005    0.071437   -0.172410    11.00000    0.02040    0.02666 =
      0.02247    0.00716    0.00575    0.00007
AFIX  43
H4    2    0.316600    0.121114   -0.216427    11.00000   -1.20000
AFIX   0
C8    1    0.327908   -0.155387    0.140245    11.00000    0.01410    0.01689 =
      0.02086   -0.00081    0.00601   -0.00010
C16   1    0.167854   -0.136743    0.455565    11.00000    0.02280    0.02049 =
```

```
      0.02244   0.00220   0.00900   0.00408
AFIX  43
H16   2   0.238535  -0.108240   0.515577   11.00000  -1.20000
AFIX   0
C7    1   0.328587  -0.076981  -0.041201   11.00000   0.01393   0.01902 =
      0.02009   0.00126   0.00430   0.00013
C2    1   0.291096  -0.000432   0.001867   11.00000   0.01350   0.01870 =
      0.01648   0.00004   0.00209  -0.00136
C1    1   0.261791  -0.006521   0.114915   11.00000   0.01329   0.01528 =
      0.01786  -0.00160   0.00261  -0.00055
C18   1   0.277427   0.093048   0.375200   11.00000   0.01237   0.01260 =
      0.01995   0.00062   0.00580  -0.00027
C19   1   0.259045   0.113045   0.483533   11.00000   0.02157   0.01988 =
      0.02089  -0.00085   0.01046  -0.00424
AFIX  43
H19   2   0.185929   0.091394   0.508964   11.00000  -1.20000
AFIX   0
C17   1   0.193151   0.033070   0.278229   11.00000   0.01591   0.01336 =
      0.01740   0.00034   0.00479  -0.00033
C21   1   0.459675   0.192919   0.497176   11.00000   0.02124   0.01750 =
      0.02234  -0.00342   0.00492  -0.00457
AFIX  43
H21   2   0.536140   0.229340   0.530266   11.00000  -1.20000
AFIX   0
C11   1   0.154173  -0.123950   0.333287   11.00000   0.01689   0.01224 =
      0.02201   0.00076   0.00822   0.00246
C3    1   0.287135   0.074533  -0.064456   11.00000   0.01889   0.01906 =
      0.02009   0.00145   0.00380  -0.00017
AFIX  43
H3    2   0.263879   0.126001  -0.035954   11.00000  -1.20000
AFIX   0
C13   1  -0.042153  -0.223028   0.278030   11.00000   0.02131   0.01385 =
      0.04047  -0.00227   0.01181  -0.00154
AFIX  43
H13   2  -0.112341  -0.252090   0.218319   11.00000  -1.20000
AFIX   0
C22   1   0.034647   0.040664   0.256682   11.00000   0.01445   0.01487 =
      0.03096  -0.00105   0.00281   0.00000
AFIX  33
H22A  2  -0.015352   0.001401   0.194200   11.00000  -1.50000
H22B  2   0.004158   0.097624   0.231513   11.00000  -1.50000
H22C  2   0.014804   0.027773   0.330694   11.00000  -1.50000
AFIX   0
C6    1   0.356517  -0.080763  -0.151413   11.00000   0.01854   0.02674 =
      0.02217  -0.00144   0.00722   0.00275
AFIX  43
```

```
H6    2    0.378126   -0.132214   -0.181104    11.00000   -1.20000
AFIX   0
C14   1   -0.027994   -0.235035    0.400019    11.00000    0.02738    0.01776 =
      0.04807    0.00781    0.02298    0.00272
AFIX  43
H14   2   -0.088656   -0.272034    0.422206    11.00000   -1.20000
AFIX   0
C12   1    0.048349   -0.167654    0.244893    11.00000    0.02148    0.01474 =
      0.02436   -0.00130    0.00891    0.00047
AFIX  43
H12   2    0.038130   -0.159723    0.162939    11.00000   -1.20000
AFIX   0
C15   1    0.076716   -0.191763    0.488595    11.00000    0.03157    0.02628 =
      0.03149    0.00908    0.01900    0.00771
AFIX  43
H15   2    0.086131   -0.199515    0.570428    11.00000   -1.20000
AFIX   0
C5    1    0.351309   -0.005892   -0.215800    11.00000    0.01938    0.03341 =
      0.01912    0.00334    0.00684    0.00219
AFIX  43
H5    2    0.370391   -0.007222   -0.289384    11.00000   -1.20000
AFIX   0
C20   1    0.364240    0.170890    0.553913    11.00000    0.02733    0.01971 =
      0.01822   -0.00195    0.00745   -0.00389
AFIX  43
H20   2    0.367094    0.191214    0.630094    11.00000   -1.20000
HKLF    4

REM  md501_0m in P 21/c
REM R1 =  0.0322 for   3772 Fo > 4sig(Fo)  and  0.0381 for all   4292 data
REM    239 parameters refined using      0 restraints

END

WGHT      0.0369      0.8327
REM Highest difference peak  0.354,  deepest hole -0.265,  1-sigma level  0.045
Q1    1   0.2374  0.0651  0.3278  11.00000  0.05    0.35
Q2    1   0.2898 -0.1171  0.1570  11.00000  0.05    0.35
Q3    1   0.2807 -0.0014  0.0575  11.00000  0.05    0.35
Q4    1   0.3327  0.1150  0.3624  11.00000  0.05    0.35
Q5    1   0.2625 -0.0755  0.2339  11.00000  0.05    0.33
Q6    1   0.3250 -0.0818 -0.1042  11.00000  0.05    0.33
Q7    1   0.2002 -0.0943  0.3168  11.00000  0.05    0.33
Q8    1   0.3108  0.1409  0.5222  11.00000  0.05    0.33
Q9    1   0.2454 -0.0515  0.1366  11.00000  0.05    0.32
Q10   1   0.2902 -0.0397  0.1633  11.00000  0.05    0.32
```

```
Q11   1   0.2172 -0.0147  0.2910  11.00000  0.05    0.31
Q12   1   0.2991 -0.0386 -0.0220  11.00000  0.05    0.30
Q13   1   0.2777  0.0356 -0.0346  11.00000  0.05    0.30
Q14   1   0.1162  0.0368  0.2690  11.00000  0.05    0.29
Q15   1   0.1642 -0.1329  0.3920  11.00000  0.05    0.29
Q16   1   0.0909 -0.1455  0.2966  11.00000  0.05    0.29
Q17   1   0.4052  0.1912  0.5155  11.00000  0.05    0.28
Q18   1   0.1191 -0.1665  0.4635  11.00000  0.05    0.27
Q19   1   0.4470  0.1725  0.4376  11.00000  0.05    0.27
Q20   1   0.0072 -0.1932  0.2649  11.00000  0.05    0.26
;

_audit_creation_method            SHELXL-97
_chemical_name_systematic
;
 ?
;
_chemical_name_common             ?
_chemical_melting_point           ?
_chemical_formula_moiety          'C22 H16 O3 S'
_chemical_formula_sum
 'C22 H16 O3 S'
_chemical_formula_weight          360.41

loop_
 _atom_type_symbol
 _atom_type_description
 _atom_type_scat_dispersion_real
 _atom_type_scat_dispersion_imag
 _atom_type_scat_source
'C'  'C'   0.0033   0.0016
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
'H'  'H'   0.0000   0.0000
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
'O'  'O'   0.0106   0.0060
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'
'S'  'S'   0.1246   0.1234
'International Tables Vol C Tables 4.2.6.8 and 6.1.1.4'

_symmetry_cell_setting            monoclinic
_symmetry_space_group_name_H-M    'P 21/c'
_symmetry_space_group_name_Hall   '-P 2ybc'


loop_
 _symmetry_equiv_pos_as_xyz
```

```
'x, y, z'
'-x, y+1/2, -z+1/2'
'-x, -y, -z'
'x, -y-1/2, z-1/2'

_cell_length_a                 9.9226(2)
_cell_length_b                 15.7155(3)
_cell_length_c                 11.5782(2)
_cell_angle_alpha               90.00
_cell_angle_beta                108.572(3)
_cell_angle_gamma               90.00
_cell_volume                   1711.47(6)
_cell_formula_units_Z           4
_cell_measurement_temperature    296(2)
_cell_measurement_reflns_used    8525
_cell_measurement_theta_min      2.26
_cell_measurement_theta_max      28.39

_exptl_crystal_description       block
_exptl_crystal_colour            colourless
_exptl_crystal_size_max          0.32
_exptl_crystal_size_mid          0.25
_exptl_crystal_size_min          0.16
_exptl_crystal_density_meas      ?
_exptl_crystal_density_diffrn    1.399
_exptl_crystal_density_method    'not measured'
_exptl_crystal_F_000             752
_exptl_absorpt_coefficient_mu    0.209
_exptl_absorpt_correction_type   multi-scan
_exptl_absorpt_correction_T_min  0.9263
_exptl_absorpt_correction_T_max  0.9774
_exptl_absorpt_process_details   'SADABS; Bruker, 2012'

_exptl_special_details
;
 ?
;

_diffrn_ambient_temperature      296(2)
_diffrn_radiation_wavelength     0.71073
_diffrn_radiation_type           MoK\a
_diffrn_radiation_source         'fine-focus sealed tube'
_diffrn_radiation_monochromator  graphite
_diffrn_measurement_device_type  'Bruker APEX-II CCD'
_diffrn_measurement_method       '\f and \w scans'
_diffrn_detector_area_resol_mean  ?
```

```
_diffrn_standards_number         ?
_diffrn_standards_interval_count  ?
_diffrn_standards_interval_time   ?
_diffrn_standards_decay_%         ?
_diffrn_reflns_number            16080
_diffrn_reflns_av_R_equivalents   0.0193
_diffrn_reflns_av_sigmaI/netI     0.0188
_diffrn_reflns_limit_h_min       -13
_diffrn_reflns_limit_h_max        13
_diffrn_reflns_limit_k_min       -16
_diffrn_reflns_limit_k_max        21
_diffrn_reflns_limit_l_min       -15
_diffrn_reflns_limit_l_max        13
_diffrn_reflns_theta_min          2.17
_diffrn_reflns_theta_max          28.42
_reflns_number_total             4292
_reflns_number_gt                3772
_reflns_threshold_expression      I>2\s(I)

_computing_data_collection        'APEX2 (Bruker, 2007)'
_computing_cell_refinement        'SAINT (Bruker, 2007)'
_computing_data_reduction         'SAINT'
_computing_structure_solution     'SHELXS97 (Sheldrick, 2008)'
_computing_structure_refinement   'SHELXL97 (Sheldrick, 2008)'
_computing_molecular_graphics     'Ortep-3 for Windows (Farrugia, 1997)'
_computing_publication_material
'WinGX publication routines (Farrugia, 1999) and PLATON (Spek, 2003)'

_refine_special_details
;
 Refinement of F^2^ against ALL reflections.  The weighted R-factor wR and
 goodness of fit S are based on F^2^, conventional R-factors R are based
 on F, with F set to zero for negative F^2^. The threshold expression of
 F^2^ > 2sigma(F^2^) is used only for calculating R-factors(gt) etc. and is
 not relevant to the choice of reflections for refinement.  R-factors based
 on F^2^ are statistically about twice as large as those based on F, and R-
 factors based on ALL data will be even larger.
;

_refine_ls_structure_factor_coef  Fsqd
_refine_ls_matrix_type            full
_refine_ls_weighting_scheme       calc
_refine_ls_weighting_details
 'calc w=1/[\s^2^(Fo^2^)+(0.0369P)^2^+0.8327P] where P=(Fo^2^+2Fc^2^)/3'
_atom_sites_solution_primary      direct
_atom_sites_solution_secondary    difmap
```

```
_atom_sites_solution_hydrogens    geom
_refine_ls_hydrogen_treatment     mixed
_refine_ls_extinction_method      none
_refine_ls_extinction_coef        ?
_refine_ls_number_reflns          4292
_refine_ls_number_parameters      239
_refine_ls_number_restraints      0
_refine_ls_R_factor_all           0.0381
_refine_ls_R_factor_gt            0.0322
_refine_ls_wR_factor_ref          0.0841
_refine_ls_wR_factor_gt           0.0802
_refine_ls_goodness_of_fit_ref    1.030
_refine_ls_restrained_S_all       1.030
_refine_ls_shift/su_max           0.000
_refine_ls_shift/su_mean          0.000

loop_
 _atom_site_label
 _atom_site_type_symbol
 _atom_site_fract_x
 _atom_site_fract_y
 _atom_site_fract_z
 _atom_site_U_iso_or_equiv
 _atom_site_adp_type
 _atom_site_occupancy
 _atom_site_symmetry_multiplicity
 _atom_site_calc_flag
 _atom_site_refinement_flags
 _atom_site_disorder_assembly
 _atom_site_disorder_group
S1 S 0.42215(3) 0.145520(19) 0.35739(3) 0.02068(8) Uani 1 1 d . . .
O1 O 0.34055(9) -0.15145(5) 0.02362(8) 0.01977(18) Uani 1 1 d . . .
O2 O 0.21733(9) 0.06109(5) 0.16356(7) 0.01845(17) Uani 1 1 d . . .
O3 O 0.35645(9) -0.22249(5) 0.19309(8) 0.02135(18) Uani 1 1 d . . .
C1 C 0.26179(11) -0.00652(7) 0.11491(10) 0.0160(2) Uani 1 1 d . . .
C2 C 0.29110(11) -0.00043(7) 0.00187(10) 0.0169(2) Uani 1 1 d . . .
C3 C 0.28714(12) 0.07453(8) -0.06446(11) 0.0199(2) Uani 1 1 d . . .
H3 H 0.2639 0.1260 -0.0360 0.024 Uiso 1 1 calc R . .
C4 C 0.31800(13) 0.07144(8) -0.17241(11) 0.0234(3) Uani 1 1 d . . .
H4 H 0.3166 0.1211 -0.2164 0.028 Uiso 1 1 calc R . .
C5 C 0.35131(13) -0.00589(9) -0.21580(11) 0.0238(3) Uani 1 1 d . . .
H5 H 0.3704 -0.0072 -0.2894 0.029 Uiso 1 1 calc R . .
C6 C 0.35652(12) -0.08076(8) -0.15141(11) 0.0223(2) Uani 1 1 d . . .
H6 H 0.3781 -0.1322 -0.1811 0.027 Uiso 1 1 calc R . .
C7 C 0.32859(12) -0.07698(7) -0.04120(11) 0.0179(2) Uani 1 1 d . . .
C8 C 0.32791(11) -0.15539(7) 0.14024(11) 0.0172(2) Uani 1 1 d . . .
```

C9 C 0.27935(11) -0.07868(7) 0.18122(10) 0.0159(2) Uani 1 1 d . . .
C10 C 0.25207(11) -0.06187(7) 0.29958(10) 0.0151(2) Uani 1 1 d . . .
H10 H 0.3423(15) -0.0617(9) 0.3662(12) 0.016(3) Uiso 1 1 d . . .
C11 C 0.15417(12) -0.12395(7) 0.33329(11) 0.0166(2) Uani 1 1 d . . .
C12 C 0.04835(12) -0.16765(7) 0.24489(11) 0.0198(2) Uani 1 1 d . . .
H12 H 0.0381 -0.1597 0.1629 0.024 Uiso 1 1 calc R . .
C13 C -0.04215(13) -0.22303(8) 0.27803(13) 0.0247(3) Uani 1 1 d . . .
H13 H -0.1123 -0.2521 0.2183 0.030 Uiso 1 1 calc R . .
C14 C -0.02799(14) -0.23503(8) 0.40002(14) 0.0285(3) Uani 1 1 d . . .
H14 H -0.0887 -0.2720 0.4222 0.034 Uiso 1 1 calc R . .
C15 C 0.07672(14) -0.19176(9) 0.48859(13) 0.0277(3) Uani 1 1 d . . .
H15 H 0.0861 -0.1995 0.5704 0.033 Uiso 1 1 calc R . .
C16 C 0.16785(13) -0.13674(8) 0.45556(12) 0.0215(2) Uani 1 1 d . . .
H16 H 0.2385 -0.1082 0.5156 0.026 Uiso 1 1 calc R . .
C17 C 0.19315(12) 0.03307(7) 0.27823(10) 0.0157(2) Uani 1 1 d . . .
C18 C 0.27743(11) 0.09305(7) 0.37520(10) 0.0148(2) Uani 1 1 d . . .
C19 C 0.25905(13) 0.11304(8) 0.48353(11) 0.0199(2) Uani 1 1 d . . .
H19 H 0.1859 0.0914 0.5090 0.024 Uiso 1 1 calc R . .
C20 C 0.36424(13) 0.17089(8) 0.55391(11) 0.0217(2) Uani 1 1 d . . .
H20 H 0.3671 0.1912 0.6301 0.026 Uiso 1 1 calc R . .
C21 C 0.45968(13) 0.19292(8) 0.49718(11) 0.0208(2) Uani 1 1 d . . .
H21 H 0.5361 0.2293 0.5303 0.025 Uiso 1 1 calc R . .
C22 C 0.03465(12) 0.04066(7) 0.25668(12) 0.0211(2) Uani 1 1 d . . .
H22A H -0.0154 0.0014 0.1942 0.032 Uiso 1 1 calc R . .
H22B H 0.0042 0.0976 0.2315 0.032 Uiso 1 1 calc R . .
H22C H 0.0148 0.0278 0.3307 0.032 Uiso 1 1 calc R . .

loop_
 _atom_site_aniso_label
 _atom_site_aniso_U_11
 _atom_site_aniso_U_22
 _atom_site_aniso_U_33
 _atom_site_aniso_U_23
 _atom_site_aniso_U_13
 _atom_site_aniso_U_12
S1 0.01945(14) 0.02135(15) 0.02482(16) -0.00592(11) 0.01208(11) -0.00720(11)
O1 0.0227(4) 0.0165(4) 0.0225(4) 0.0002(3) 0.0106(3) 0.0031(3)
O2 0.0254(4) 0.0132(4) 0.0163(4) 0.0005(3) 0.0061(3) 0.0019(3)
O3 0.0232(4) 0.0158(4) 0.0259(4) 0.0022(3) 0.0090(3) 0.0042(3)
C1 0.0133(5) 0.0153(5) 0.0179(5) -0.0016(4) 0.0026(4) -0.0005(4)
C2 0.0135(5) 0.0187(5) 0.0165(5) 0.0000(4) 0.0021(4) -0.0014(4)
C3 0.0189(5) 0.0191(6) 0.0201(6) 0.0015(4) 0.0038(4) -0.0002(4)
C4 0.0204(5) 0.0267(6) 0.0225(6) 0.0072(5) 0.0058(5) 0.0001(5)
C5 0.0194(5) 0.0334(7) 0.0191(6) 0.0033(5) 0.0068(5) 0.0022(5)
C6 0.0185(5) 0.0267(6) 0.0222(6) -0.0014(5) 0.0072(5) 0.0028(5)
C7 0.0139(5) 0.0190(5) 0.0201(5) 0.0013(4) 0.0043(4) 0.0001(4)

```
C8 0.0141(5) 0.0169(5) 0.0209(5) -0.0008(4) 0.0060(4) -0.0001(4)
C9 0.0138(5) 0.0150(5) 0.0189(5) -0.0003(4) 0.0052(4) 0.0000(4)
C10 0.0146(5) 0.0127(5) 0.0174(5) 0.0000(4) 0.0041(4) 0.0006(4)
C11 0.0169(5) 0.0122(5) 0.0220(6) 0.0008(4) 0.0082(4) 0.0025(4)
C12 0.0215(5) 0.0147(5) 0.0244(6) -0.0013(4) 0.0089(5) 0.0005(4)
C13 0.0213(6) 0.0138(5) 0.0405(7) -0.0023(5) 0.0118(5) -0.0015(4)
C14 0.0274(6) 0.0178(6) 0.0481(8) 0.0078(6) 0.0230(6) 0.0027(5)
C15 0.0316(7) 0.0263(7) 0.0315(7) 0.0091(5) 0.0190(6) 0.0077(5)
C16 0.0228(6) 0.0205(6) 0.0224(6) 0.0022(5) 0.0090(5) 0.0041(4)
C17 0.0159(5) 0.0134(5) 0.0174(5) 0.0003(4) 0.0048(4) -0.0003(4)
C18 0.0124(5) 0.0126(5) 0.0199(5) 0.0006(4) 0.0058(4) -0.0003(4)
C19 0.0216(5) 0.0199(6) 0.0209(6) -0.0009(5) 0.0105(5) -0.0042(4)
C20 0.0273(6) 0.0197(6) 0.0182(6) -0.0019(4) 0.0074(5) -0.0039(5)
C21 0.0212(5) 0.0175(6) 0.0223(6) -0.0034(4) 0.0049(5) -0.0046(4)
C22 0.0144(5) 0.0149(5) 0.0310(6) -0.0010(5) 0.0028(5) 0.0000(4)

_geom_special_details
;
 All esds (except the esd in the dihedral angle between two l.s. planes)
 are estimated using the full covariance matrix.  The cell esds are taken
 into account individually in the estimation of esds in distances, angles
 and torsion angles; correlations between esds in cell parameters are only
 used when they are defined by crystal symmetry.  An approximate (isotropic)
 treatment of cell esds is used for estimating esds involving l.s. planes.
;

loop_
 _geom_bond_atom_site_label_1
 _geom_bond_atom_site_label_2
 _geom_bond_distance
 _geom_bond_site_symmetry_2
 _geom_bond_publ_flag
S1 C18 1.7243(11) . ?
S1 C21 1.7114(12) . ?
O1 C7 1.3749(14) . ?
O1 C8 1.3967(14) . ?
O2 C1 1.3414(14) . ?
O2 C17 1.4890(14) . ?
O3 C8 1.2068(14) . ?
C2 C1 1.4316(16) . ?
C2 C3 1.4000(16) . ?
C3 H3 0.9300 . ?
C4 C3 1.3793(17) . ?
C4 C5 1.3944(19) . ?
C4 H4 0.9300 . ?
C5 H5 0.9300 . ?
```

```
C6 C5 1.3850(18) . ?
C6 H6 0.9300 . ?
C7 C6 1.3907(17) . ?
C7 C2 1.3973(16) . ?
C9 C1 1.3492(16) . ?
C9 C8 1.4339(15) . ?
C9 C10 1.5025(16) . ?
C10 C11 1.5130(15) . ?
C10 C17 1.5927(15) . ?
C10 H10 0.978(14) . ?
C11 C12 1.3918(16) . ?
C12 H12 0.9300 . ?
C13 C12 1.3894(17) . ?
C13 C14 1.387(2) . ?
C13 H13 0.9300 . ?
C14 C15 1.384(2) . ?
C14 H14 0.9300 . ?
C15 H15 0.9300 . ?
C16 C15 1.3900(18) . ?
C16 C11 1.3931(17) . ?
C16 H16 0.9300 . ?
C17 C22 1.5166(15) . ?
C18 C17 1.5001(15) . ?
C18 C19 1.3605(16) . ?
C19 C20 1.4276(16) . ?
C19 H19 0.9300 . ?
C20 H20 0.9300 . ?
C21 C20 1.3581(17) . ?
C21 H21 0.9300 . ?
C22 H22A 0.9600 . ?
C22 H22B 0.9600 . ?
C22 H22C 0.9600 . ?

loop_
 _geom_angle_atom_site_label_1
 _geom_angle_atom_site_label_2
 _geom_angle_atom_site_label_3
 _geom_angle
 _geom_angle_site_symmetry_1
 _geom_angle_site_symmetry_3
 _geom_angle_publ_flag
C21 S1 C18 91.93(6) . . ?
C7 O1 C8 123.15(9) . . ?
C1 O2 C17 107.94(8) . . ?
O2 C1 C2 121.38(10) . . ?
O2 C1 C9 115.28(10) . . ?
```

C9 C1 C2 123.32(10) . . ?
C3 C2 C1 125.41(11) . . ?
C7 C2 C1 115.05(10) . . ?
C7 C2 C3 119.53(11) . . ?
C2 C3 H3 120.3 . . ?
C4 C3 C2 119.46(11) . . ?
C4 C3 H3 120.3 . . ?
C3 C4 C5 120.25(12) . . ?
C3 C4 H4 119.9 . . ?
C5 C4 H4 119.9 . . ?
C4 C5 H5 119.4 . . ?
C6 C5 C4 121.26(12) . . ?
C6 C5 H5 119.4 . . ?
C5 C6 C7 118.26(12) . . ?
C5 C6 H6 120.9 . . ?
C7 C6 H6 120.9 . . ?
O1 C7 C2 121.64(10) . . ?
O1 C7 C6 117.18(11) . . ?
C6 C7 C2 121.18(11) . . ?
O1 C8 C9 115.19(10) . . ?
O3 C8 O1 116.75(10) . . ?
O3 C8 C9 128.05(11) . . ?
C1 C9 C8 120.96(11) . . ?
C1 C9 C10 110.06(10) . . ?
C8 C9 C10 128.81(10) . . ?
C9 C10 C11 116.03(9) . . ?
C9 C10 C17 100.78(9) . . ?
C9 C10 H10 109.5(8) . . ?
C11 C10 C17 114.21(9) . . ?
C11 C10 H10 107.5(8) . . ?
C17 C10 H10 108.6(8) . . ?
C12 C11 C10 121.64(11) . . ?
C12 C11 C16 118.85(11) . . ?
C16 C11 C10 119.50(10) . . ?
C11 C12 H12 119.7 . . ?
C13 C12 C11 120.57(12) . . ?
C13 C12 H12 119.7 . . ?
C12 C13 H13 119.9 . . ?
C14 C13 C12 120.11(12) . . ?
C14 C13 H13 119.9 . . ?
C13 C14 H14 120.1 . . ?
C15 C14 C13 119.76(12) . . ?
C15 C14 H14 120.1 . . ?
C14 C15 C16 120.17(12) . . ?
C14 C15 H15 119.9 . . ?
C16 C15 H15 119.9 . . ?

```
C11 C16 H16 119.7 . . ?
C15 C16 C11 120.53(12) . . ?
C15 C16 H16 119.7 . . ?
O2 C17 C18 105.77(8) . . ?
O2 C17 C22 106.45(9) . . ?
O2 C17 C10 105.07(8) . . ?
C18 C17 C22 112.05(9) . . ?
C18 C17 C10 112.51(9) . . ?
C22 C17 C10 114.17(9) . . ?
C17 C18 S1 119.87(8) . . ?
C19 C18 S1 111.17(8) . . ?
C19 C18 C17 128.95(10) . . ?
C18 C19 C20 112.64(11) . . ?
C18 C19 H19 123.7 . . ?
C20 C19 H19 123.7 . . ?
C19 C20 H20 123.8 . . ?
C21 C20 C19 112.45(11) . . ?
C21 C20 H20 123.8 . . ?
S1 C21 H21 124.1 . . ?
C20 C21 S1 111.79(9) . . ?
C20 C21 H21 124.1 . . ?
C17 C22 H22A 109.5 . . ?
C17 C22 H22B 109.5 . . ?
C17 C22 H22C 109.5 . . ?
H22A C22 H22B 109.5 . . ?
H22A C22 H22C 109.5 . . ?
H22B C22 H22C 109.5 . . ?

loop_
 _geom_torsion_atom_site_label_1
 _geom_torsion_atom_site_label_2
 _geom_torsion_atom_site_label_3
 _geom_torsion_atom_site_label_4
 _geom_torsion
 _geom_torsion_site_symmetry_1
 _geom_torsion_site_symmetry_2
 _geom_torsion_site_symmetry_3
 _geom_torsion_site_symmetry_4
 _geom_torsion_publ_flag
C21 S1 C18 C17 -177.70(9) . . . . ?
C21 S1 C18 C19 1.01(9) . . . . ?
C18 S1 C21 C20 -1.13(10) . . . . ?
C8 O1 C7 C2 -5.34(16) . . . . ?
C8 O1 C7 C6 174.17(10) . . . . ?
C7 O1 C8 O3 -171.81(10) . . . . ?
C7 O1 C8 C9 9.40(15) . . . . ?
```

C17 O2 C1 C2 178.54(9) . . . . ?
C17 O2 C1 C9 -2.88(12) . . . . ?
C1 O2 C17 C10 7.62(11) . . . . ?
C1 O2 C17 C18 126.83(9) . . . . ?
C1 O2 C17 C22 -113.82(10) . . . . ?
C3 C2 C1 O2 4.68(17) . . . . ?
C3 C2 C1 C9 -173.79(11) . . . . ?
C7 C2 C1 O2 -176.46(10) . . . . ?
C7 C2 C1 C9 5.08(16) . . . . ?
C1 C2 C3 C4 179.90(11) . . . . ?
C7 C2 C3 C4 1.08(17) . . . . ?
C5 C4 C3 C2 0.72(18) . . . . ?
C3 C4 C5 C6 -1.04(19) . . . . ?
C7 C6 C5 C4 -0.47(18) . . . . ?
O1 C7 C2 C1 -2.09(15) . . . . ?
O1 C7 C2 C3 176.85(10) . . . . ?
C6 C7 C2 C1 178.43(10) . . . . ?
C6 C7 C2 C3 -2.64(17) . . . . ?
O1 C7 C6 C5 -177.20(10) . . . . ?
C2 C7 C6 C5 2.31(17) . . . . ?
C8 C9 C1 O2 -179.33(10) . . . . ?
C8 C9 C1 C2 -0.78(17) . . . . ?
C10 C9 C1 O2 -3.62(13) . . . . ?
C10 C9 C1 C2 174.94(10) . . . . ?
C1 C9 C8 O1 -6.30(15) . . . . ?
C1 C9 C8 O3 175.07(11) . . . . ?
C10 C9 C8 O1 178.87(10) . . . . ?
C10 C9 C8 O3 0.2(2) . . . . ?
C1 C9 C10 C11 131.66(10) . . . . ?
C1 C9 C10 C17 7.78(11) . . . . ?
C8 C9 C10 C11 -53.06(15) . . . . ?
C8 C9 C10 C17 -176.94(11) . . . . ?
C9 C10 C11 C12 -28.12(15) . . . . ?
C9 C10 C11 C16 153.18(10) . . . . ?
C17 C10 C11 C12 88.48(13) . . . . ?
C17 C10 C11 C16 -90.23(13) . . . . ?
C9 C10 C17 O2 -9.00(10) . . . . ?
C9 C10 C17 C18 -123.60(10) . . . . ?
C9 C10 C17 C22 107.26(11) . . . . ?
C11 C10 C17 O2 -134.12(9) . . . . ?
C11 C10 C17 C18 111.28(11) . . . . ?
C11 C10 C17 C22 -17.86(14) . . . . ?
C10 C11 C12 C13 -178.66(10) . . . . ?
C16 C11 C12 C13 0.05(17) . . . . ?
C14 C13 C12 C11 0.21(18) . . . . ?
C12 C13 C14 C15 -0.09(19) . . . . ?

```
C13 C14 C15 C16 -0.29(19) . . . . ?
C15 C16 C11 C10 178.30(11) . . . . ?
C15 C16 C11 C12 -0.44(17) . . . . ?
C11 C16 C15 C14 0.57(19) . . . . ?
S1 C18 C17 O2 -24.36(11) . . . . ?
S1 C18 C17 C10 89.81(10) . . . . ?
S1 C18 C17 C22 -139.95(9) . . . . ?
C19 C18 C17 O2 157.18(11) . . . . ?
C19 C18 C17 C10 -88.64(14) . . . . ?
C19 C18 C17 C22 41.60(16) . . . . ?
S1 C18 C19 C20 -0.65(13) . . . . ?
C17 C18 C19 C20 177.91(11) . . . . ?
C18 C19 C20 C21 -0.20(16) . . . . ?
S1 C21 C20 C19 0.96(14) . . . . ?

loop_
_geom_hbond_atom_site_label_D
_geom_hbond_atom_site_label_H
_geom_hbond_atom_site_label_A
_geom_hbond_distance_DH
_geom_hbond_distance_HA
_geom_hbond_distance_DA
_geom_hbond_angle_DHA
_geom_hbond_site_symmetry_A
_geom_hbond_publ_flag
#
#D   H   A   D - H  H...A   D...A    D - H...A  symm(A)
#
C21  H21  O1  0.93  2.4300  3.2052(16)  141  2_655  yes
C13  H13  Cg1 0.93  3.0773  4.0018(15)  173  2_756  yes

_diffrn_measured_fraction_theta_max    0.997
_diffrn_reflns_theta_full              28.42
_diffrn_measured_fraction_theta_full   0.997
_refine_diff_density_max    0.354
_refine_diff_density_min   -0.265
_refine_diff_density_rms    0.045
```