**Supplementary Materials**

# Design and Synthesis of Lactams Derived from Mucochloric and Mucobromic Acids as *Pseudomonas aeruginosa* Quorum Sensing Inhibitors

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**Table S1.** Growth inhibition (OD 600 reduction) at different concentrations.

| | % reduction of bacterial growth | | |
|---|---|---|---|
| **Compound** | **250 μM** | **125 μM** | **62.5 μM** |
| **9** | 23.5 ± 1.0 | 11.8 ± 1.8 | 0 |
| **10** | 22.5 ± 0.5 | 9.1 ± 0.5 | 0 |
| **11** | 18.1 ± 3.4 | 12.0 ± 2.5 | 0 |
| **12** | 27.0 ± 5.7 | 9.2 ± 2.6 | 0 |
| **13** | 21.3 ± 3.6 | 6.1 ± 0.8 | 0 |
| **14** | 13.6 ± 3.3 | 11.6 ± 3.3 | 0 |
| **15** | 0 | 0 | 0 |
| **16** | 0 | 0 | 0 |
| **19** | 6.83 ± 0.6 | 0 | 0 |
| **20** | 4.10 ± 3.7 | 0 | 0 |
| **21** | 3.00 ± 3.26 | 0 | 0 |
| **22** | 25.2 ± 1.8 | 14.7 ± 0.89 | 0 |
| **23** | 21.2 ± 2.1 | 15.9 ± 0.008 | 9.06 ± 0.001 |
| **24** | 15.9 ± 3.0 | 12.5 ± 4.1 | 3.30 ± 0.005 |
| **25** | 14.7 ± 0.6 | 0 | 0 |
| **26** | 0 | 0 | 0 |
| **27** | 0 | 0 | 0 |
| **29** | 0 | 0 | 0 |
| **30** | 13.4 ± 1.7 | 5.9 ± 1.0 | 0 |
| **31** | 12.3 ± 6.5 | 4.7 ± 6.2 | 0 |
| **32** | 12.0 ± 4.5 | 7.5 ± 5 | 0 |
| **33** | 7.5 ± 2.5 | 5.2 ± 5.8 | 0 |
| **34** | 5.5 ± 3.9 | 0 | 0 |
| **35** | 6.0 ± 4.4 | 0 | 0 |
| **36** | 7.8 ± 0.5 | 3.9 ± 2.1 | 0 |
| **37** | 7.7 ± 5.4 | 7.0 ± 1.2 | 0 |
| **38** | 4.6 ± 3.4 | 0 | 0 |
| **39** | 0 | 0 | 0 |
| **40** | 0 | 0 | 0 |
| **41** | 0 | 0 | 0 |
| **42** | 0 | 0 | 0 |
| **TP-5** | 0 | | |
| **5** | 86.5 ± 2.6 | 53.2 ± 4.5 | 44.2 ± 1.6 |

**Table S2.** Docking of lactams to the LasR receptor protein of *P. aeruginosa*.

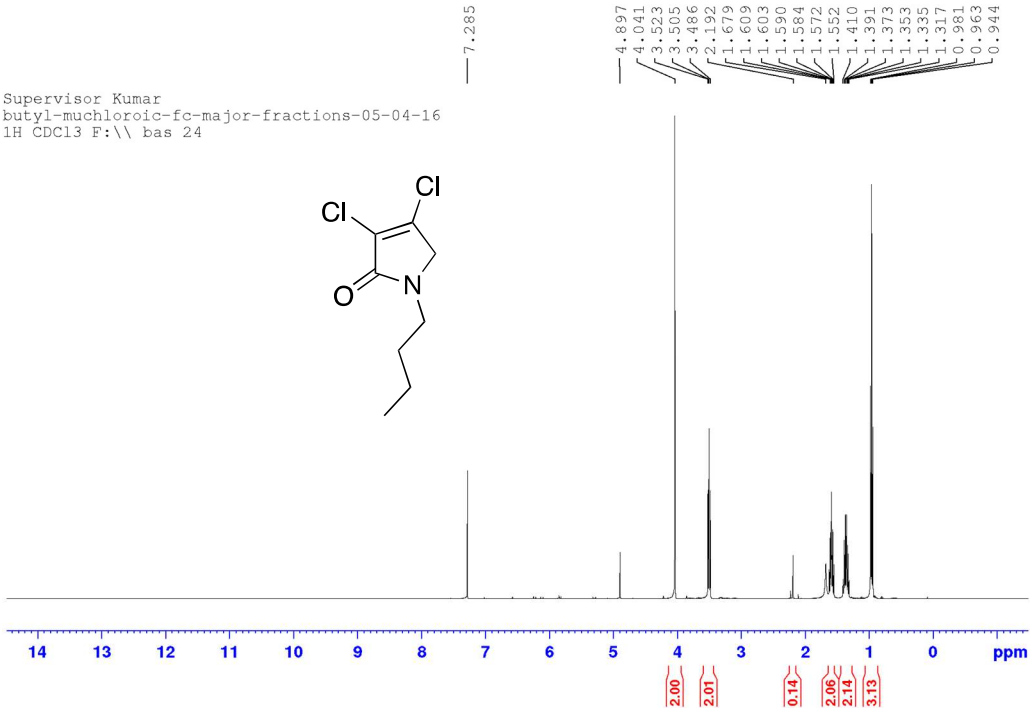
| Entry | GoldScore | [a]Pose No. | H-bond interactions | electrostatic interactions | [b]Hydrophobic and π interactions |
|---|---|---|---|---|---|
| **9** | 48.12 | 1 | Arg61, Trp60 | Tyr64[d] | Ala105, Ala127, Leu36, Phe101, Trp88, Val76 |
| **10** | 53.36 | 1 | Arg61 | Tyr64[d] | Ala105, Ala127, Leu36, Leu110, Trp88, Val76 |
| **11** | 53.33 | 1 | Arg61 | TYR64 [d] | Ala70, Ala50, Ile52, Val76 |
| **12** | 48.00 | 3 | Trp60, Tyr56 | — | Leu36, Phe101, Trp88, Tyr64 |
| **13** | 53.6 | 1 | Arg61, Trp60 | Leu110[c] | Leu36, Trp88, Tyr56, Tyr93, |
| **14** | 52.26 | 1 | Leu110, Trp60, | — | Ala105, Ala127, Leu36, Phe101, Trp88, Val76, |
| **15** | 58.90 | 6 | Arg61, TRP60, TYR93 | Leu110[c], Trp88, Tyr64[e] | Ile92, Leu36, Tyr56 |
| **16** | 58.33 | 1 | Arg61, Leu110 | Asp73[d], Trp88, Tyr64[e] | Leu36, Tyr56, Val76 |
| **19** | 54.25 | 1 | Arg61 | Asp73[d], Tyr64[e] | Ala127, Leu36, Val76 |
| **20** | 52.67 | 1 | Arg61 | Asp73[d], Tyr64[e] | Ala127, Leu36, Val76 |
| **21** | 50.47 | 15 | Arg61 | Asp73[d], Tyr64[e] | Ala127, Leu36, Val76 |
| **22** | 43.31 | 1 | Trp60 | — | Ala127, Trp88, Val76 |
| **23** | 51.06 | 4 | Trp60 | — | Ala105, Ala127, Leu36, Leu110, Phe101, Trp88, Tyr64 |
| **24** | 52.39 | 1 | Arg61 | Asp73[d], Tyr64[e] | Ala127, Leu36, Val76 |
| **25** | 55.22 | 12 | Trp60, Arg61, ,Tyr93 | Leu110[c], Tyr64[e] | Trp88, Tyr56, Leu36 |
| **26** | 57.87 | 7 | Arg61, Trp60 | Trp88[e] | Ala127, Leu36, Tyr93, Val76 |
| **27** | 59.58 | 1 | Arg61, Leu110, Tyr93 | Asp73[d] | Ala127, Leu36, Tyr56 |
| ***29*** | *52.32* | 1 | Arg61, Trp60 | — | Ala50, , Ala70, Ala105, Leu110, Trp88, Tyr47 |
| ***30*** | 62.25 | 1 | Arg61, THR 115 | Asp65[c], Asp73[d] | Ala50, , Ala70, Ala105, Tyr47, Trp88, Leu110, |
| **31** | 60.95 | 7 | Arg61, Leu110 | Tyr64[e] | Ala105, Ala127, Leu36, Trp88, |
| **32** | 65.87 | 1 | Trp60 | — | Leu36, Leu40, Leu125, Trp88, Tyr64, , Tyr47 |
| **33** | 73.79 | 1 | Arg61 | Leu110[c] | Leu36, Leu40, Leu125, Tyr64, Tyr93, Ile92, Tyr47 |
| **34** | 74.59 | 1 | Trp60 | — | Ala50, Ala127, Leu36, Leu40 Trp88, Tyr64, |

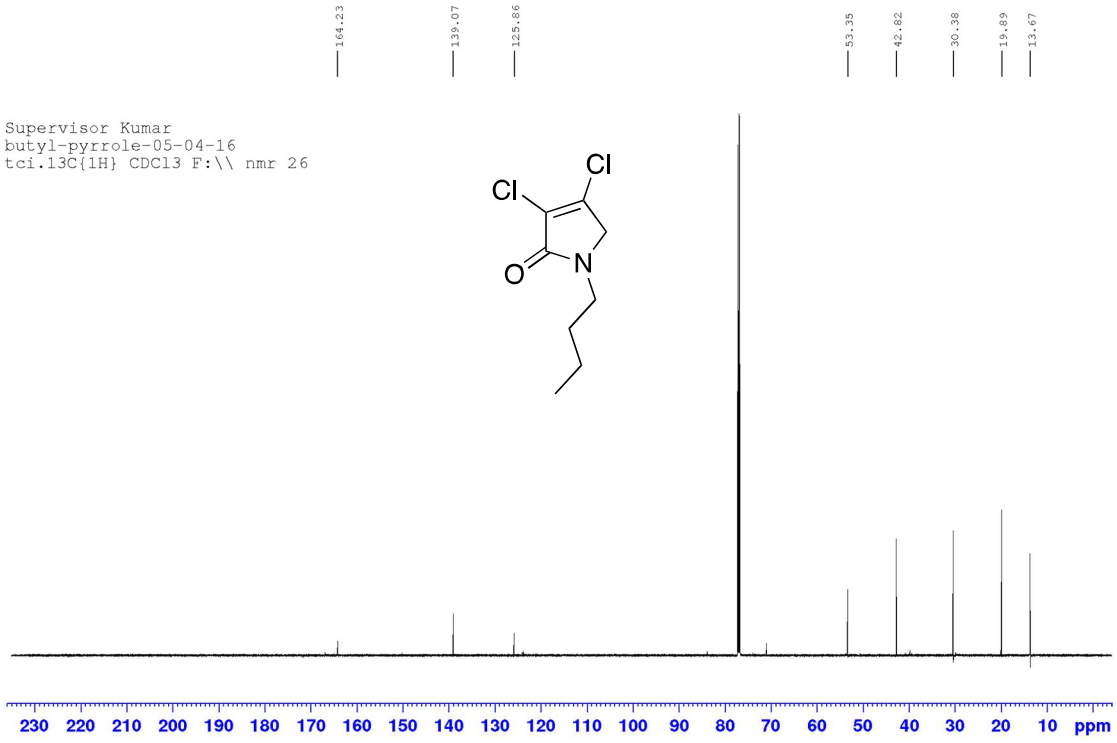
| | | | | | |
|---|---|---|---|---|---|
| **35** | 79.83 | 1 | Arg61 | Leu110[c] | Ala50, Ala70, Leu36, Leu40, Ile92, Tyr47, Tyr56, Tyr93, Val76 |
| **36** | 66.85 | 1 | Thr115, Arg61 | Leu110[c], Thr75[f] | Ala50, Ala70, Ala105, Leu36, Tyr47, Tyr56, Tyr64, Val76 |
| **37** | 74.03 | 1 | Arg61, Trp60, Tyr93 | Leu110[c] | Ala50, Ala127, Leu40, Leu36, Tyr64, Val76 |
| ***38*** | 64.20 | 1 | Arg61 | Leu110[c] | Ala50, Leu40, , Leu36, Leu125, Ile92, Tyr47, Trp88, Tyr93, Tyr56 |
| **39** | 62.76 | 1 | Trp60 | Asp73[d] | Ala127, Leu36, Leu40, Leu125, Trp88, Tyr47, Tyr64 |
| **40*** | 68.74 | 1 | Trp60 | — | Ala127, Cys79, Leu36, Leu125, Trp88, Tyr47, Tyr64, , Val76 |
| **41*** | 73.63 | 1 | Tyr64 | Arg61[f], Leu110[c] | Ile92, Leu36, Leu125, Leu40, Tyr47, Tyr56, Tyr93, Val76 |
| **42** | 79.36 | 5 | Trp60, Tyr64 | Asp73[d], Leu110[c], Leu125[c] | Ala50, Leu36, Leu140, Tyr56, Tyr93, |
| **5** | 43.27 | 1 | Arg61, Trp60 | Asp73[d], Tyr64[e] | Ala105, Leu36, leu110, Phe101, Trp60 |
| **3**[g] | 68.32 | 2 | Asp37, Ser129, Trp60, Tyr56 | — | Ala127, Cys79, Leu125 |
| **3**[h] | — | | Tyr56, Trp60, Asp73 | — | Trp88 |

[a]The highest-ranked pose of the largest cluster was selected for analysis.
[b]Hydrophobic interactions include π-π stacked and T-shaped, alkyl and π-alkyl and π-sigma; other interactions include [c]halogen and [d]π-anion and [e] π-lone pair;[f] unfavorable interaction; [g] Docked OdDHL, [h] OdDHL crystal structure.

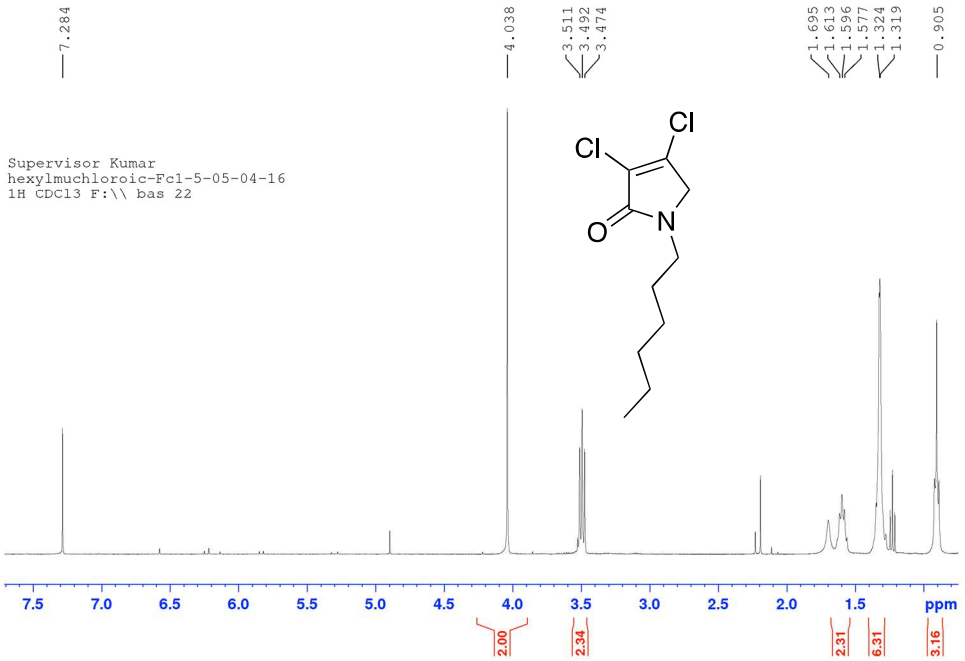
**Spectra Data** $^{1}$H NMR and $^{13}$C NMR Spectra

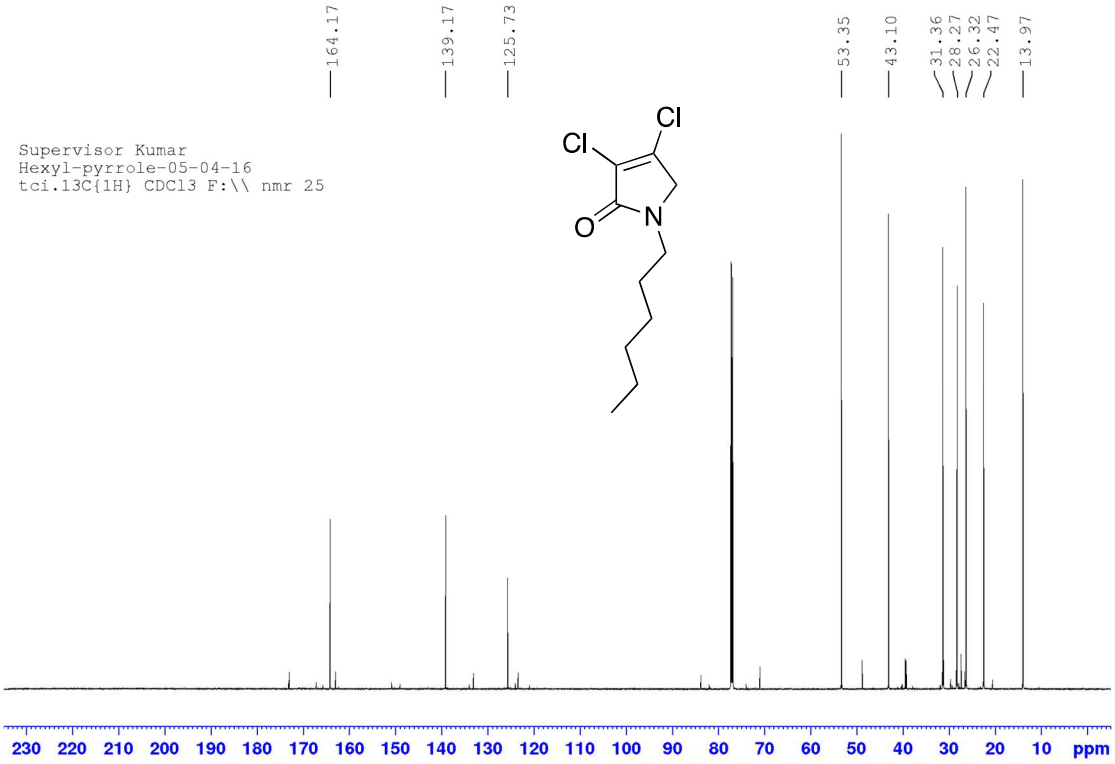
**1) 1-butyl-3,4-dichloro-1,5-dihydro-2*H*-pyrrol-2-one (Compound 9)**



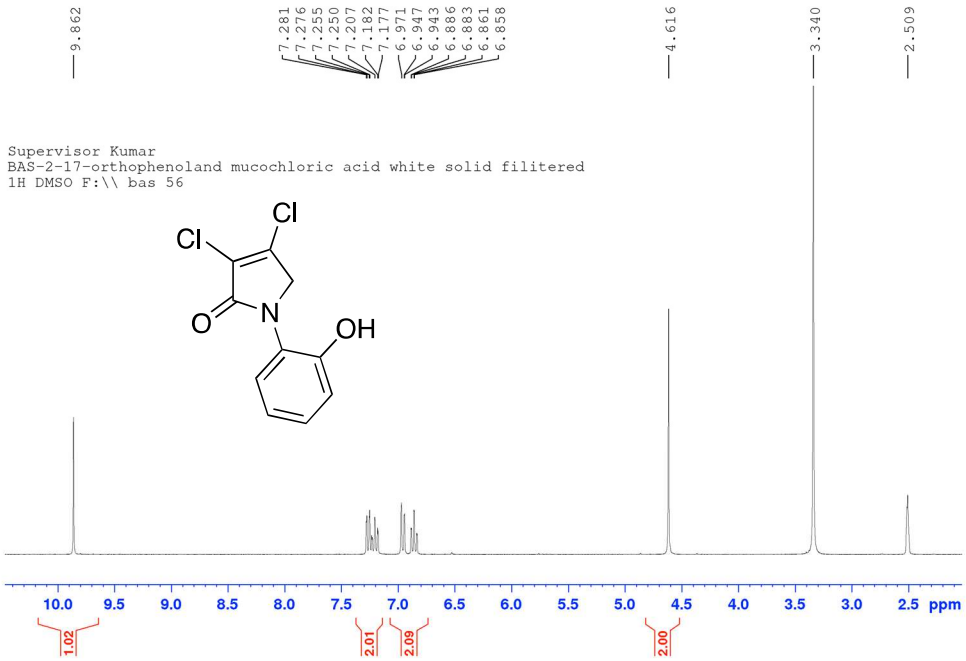



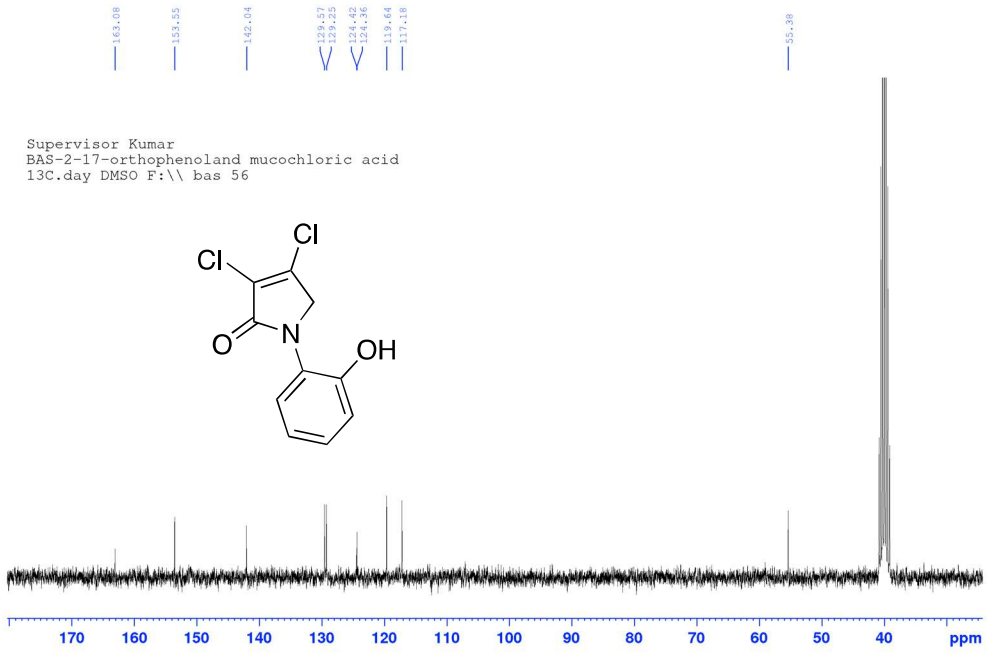
## 2) 3,4-dichloro-1-hexyl-1,5-dihydro-2*H*-pyrrol-2-one (Compound 10)



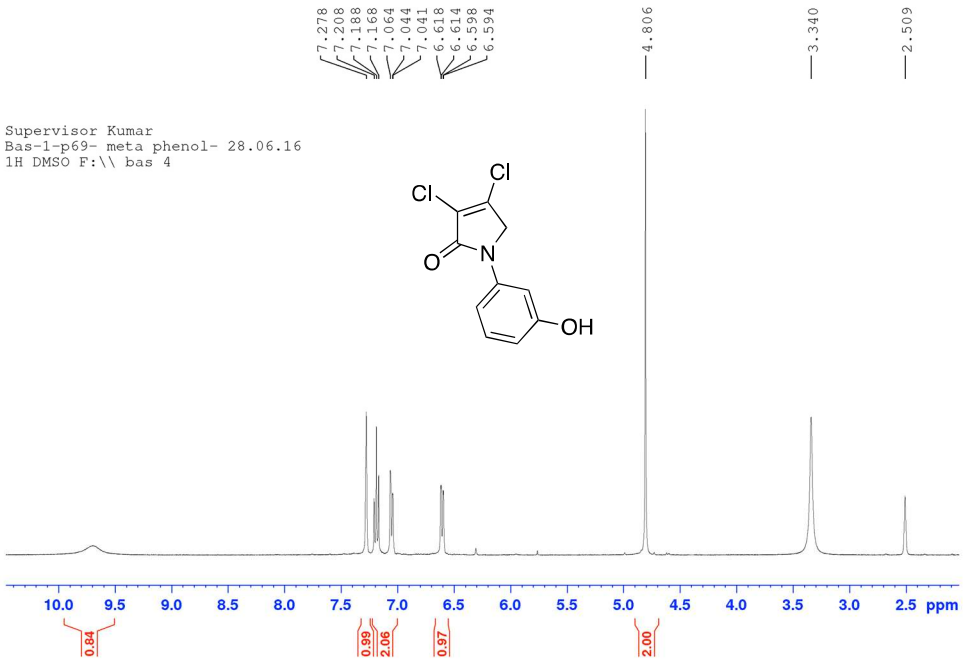



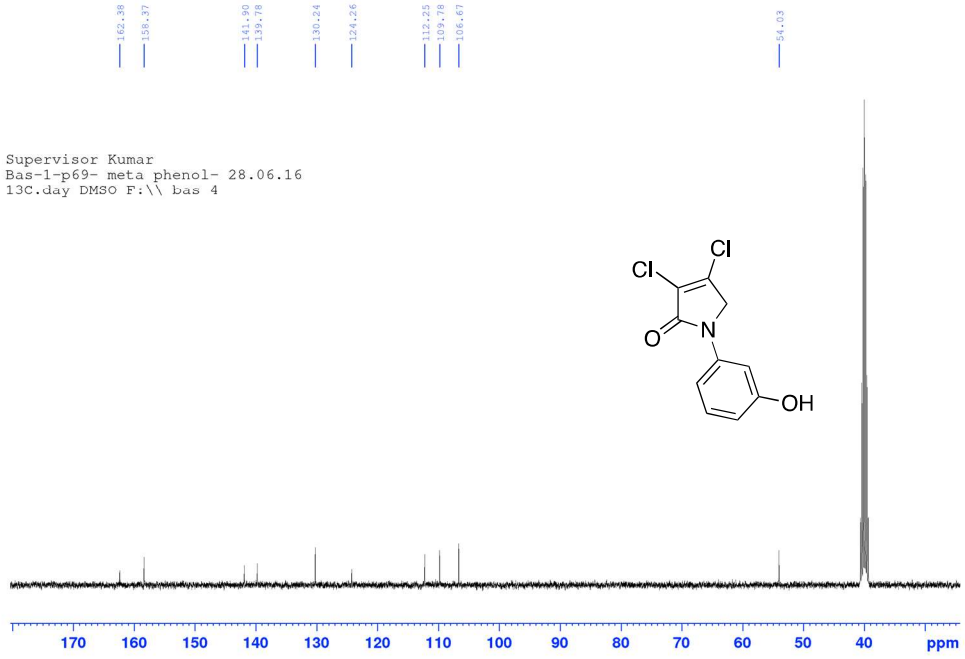
## 3) 3,4-dichloro-1-(2-hydroxyphenyl)-1,5-dihydro-2H-pyrrol-2-one (Compound 12)



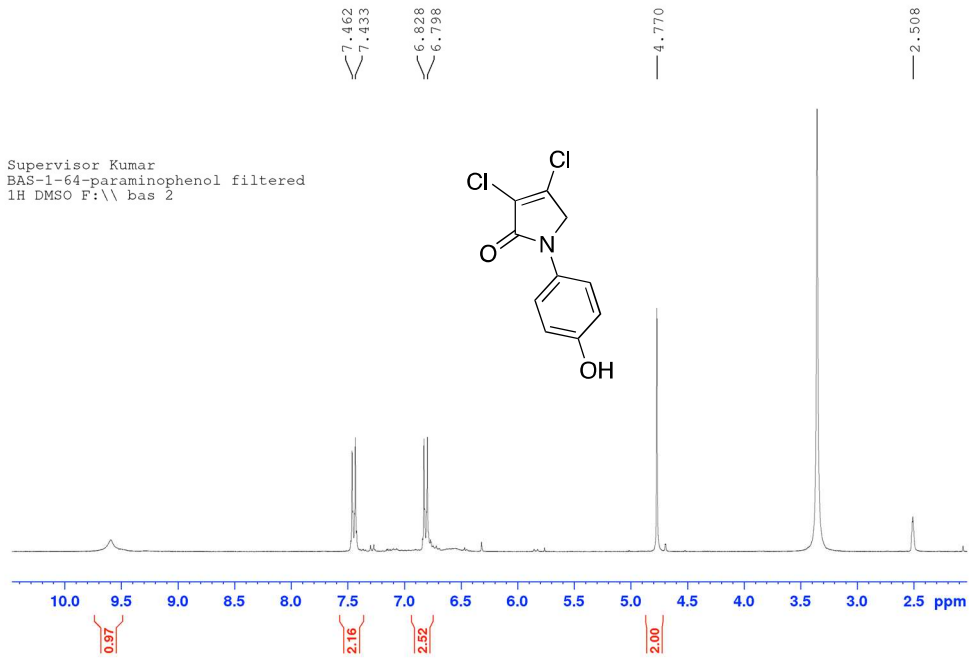



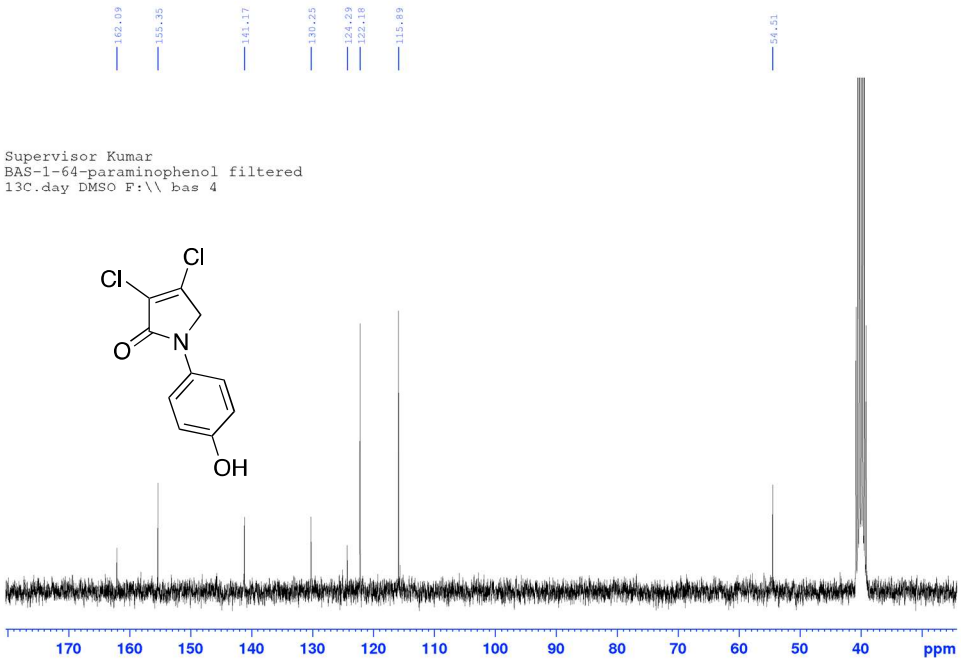
**4) 3,4-dichloro-1-(3-hydroxyphenyl)-1,5-dihydro-2*H*-pyrrol-2-one (Compound 13)**



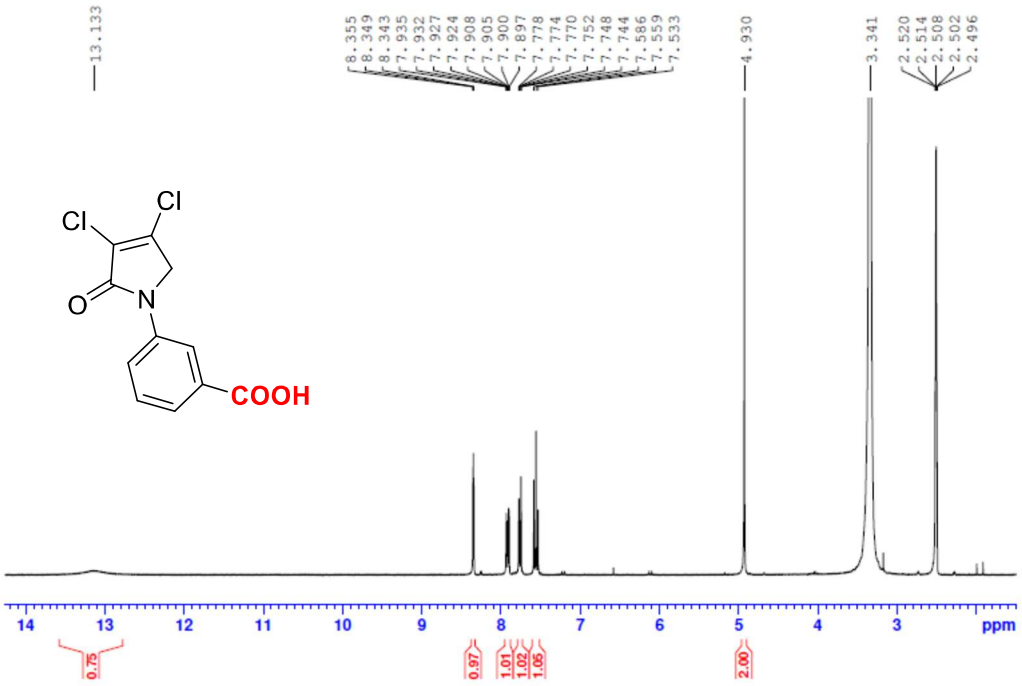



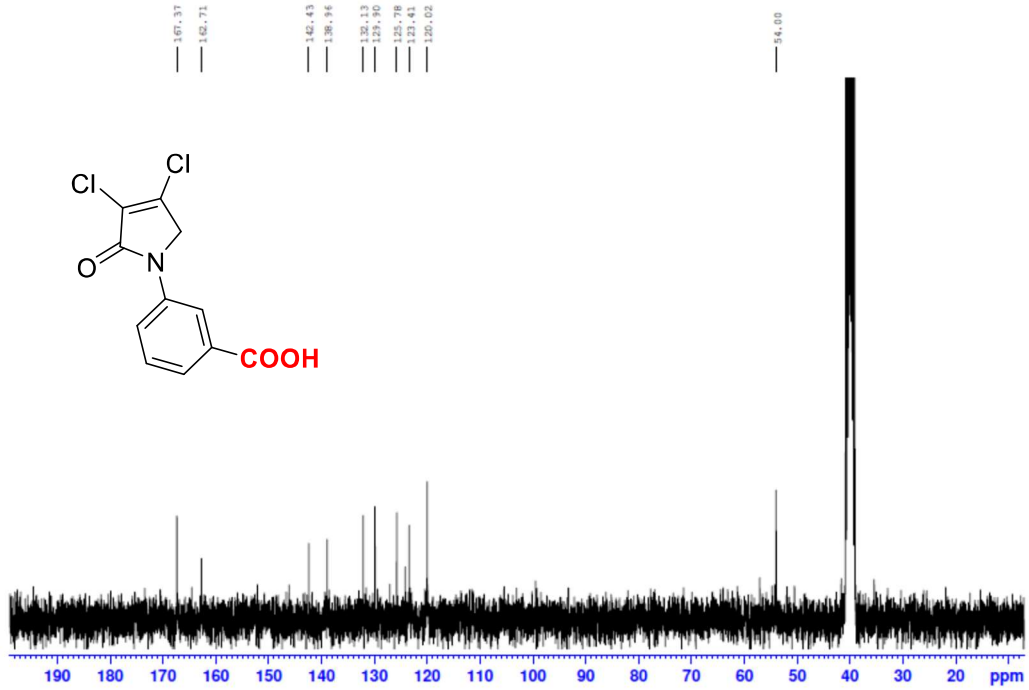
## 5) 3,4-dichloro-1-(4-hydroxyphenyl)-1,5-dihydro-2*H*-pyrrol-2-one (Compound 14)



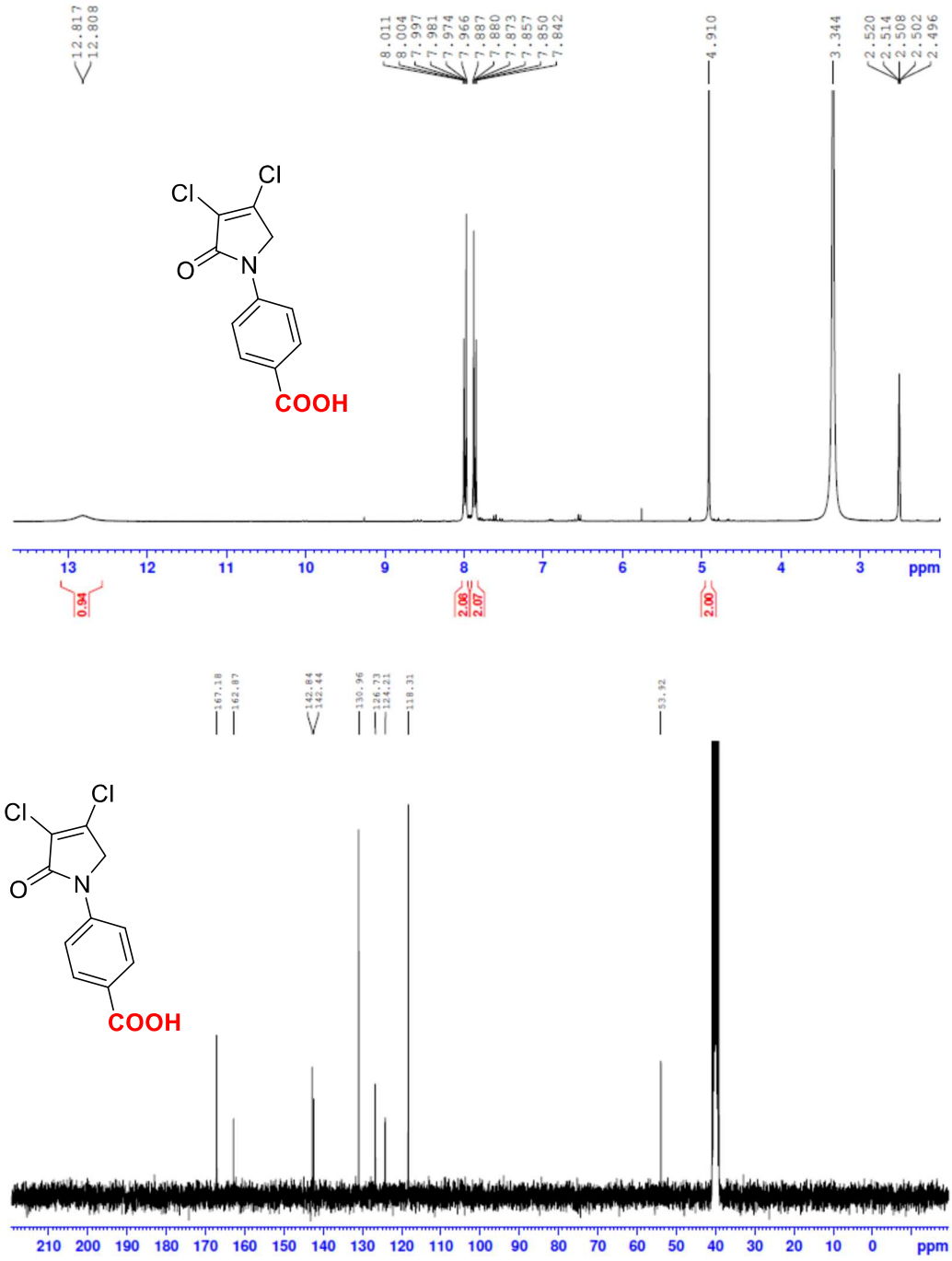



**6) N-(3-carboxyphenyl)-3,4-dibromo-1,5-dihydro-2H-pyrrol-2-one (DHP phenyl acid-2) (Compound 15)**

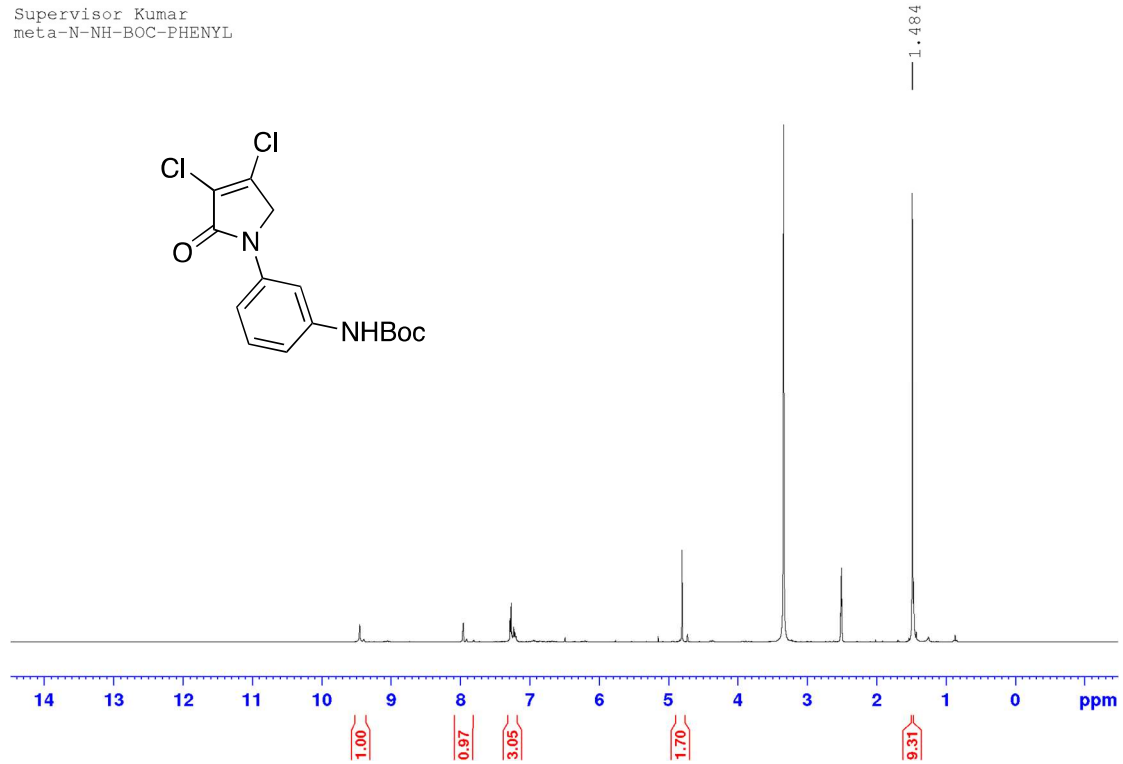


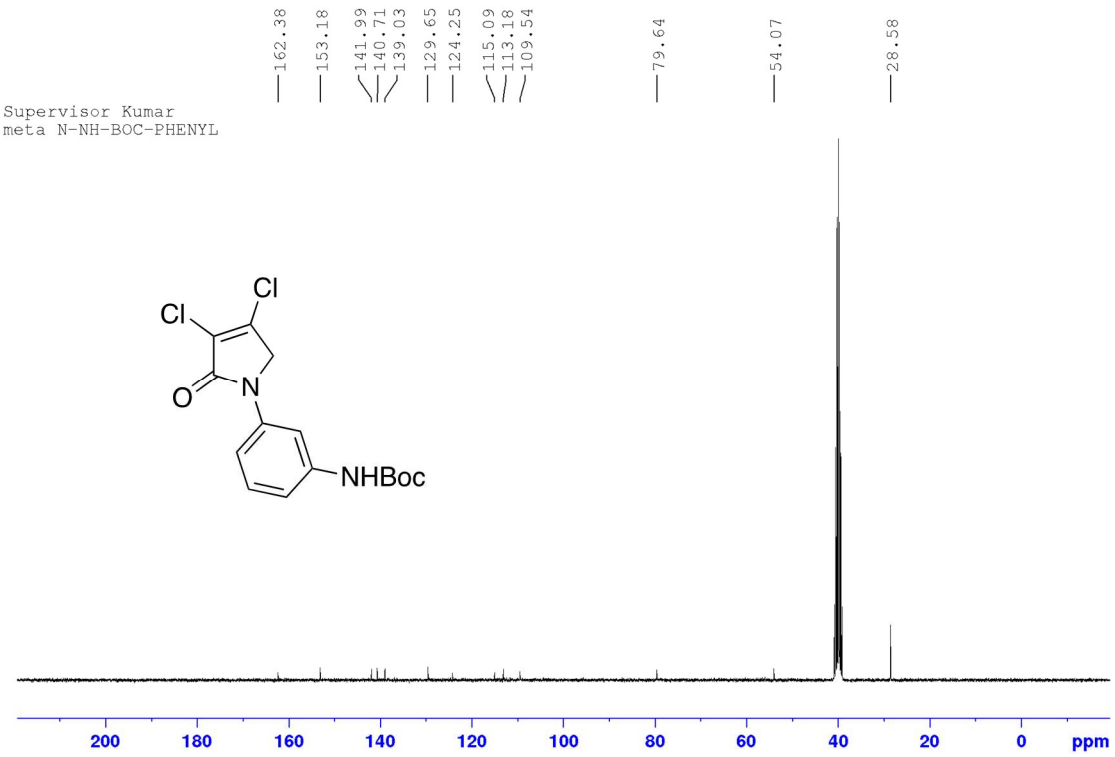



**7) N-(4-carboxyphenyl)-3,4-dichloro-1,5-dihydro-2H-pyrrol-2-one (DHP phenyl acid-1) (Compound 16)**

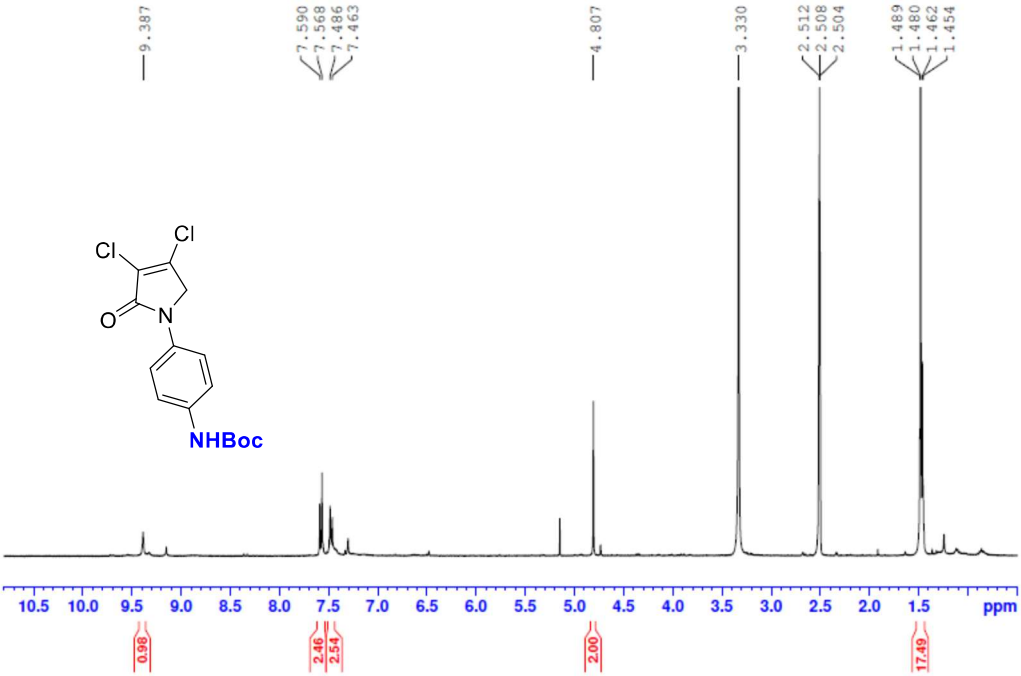


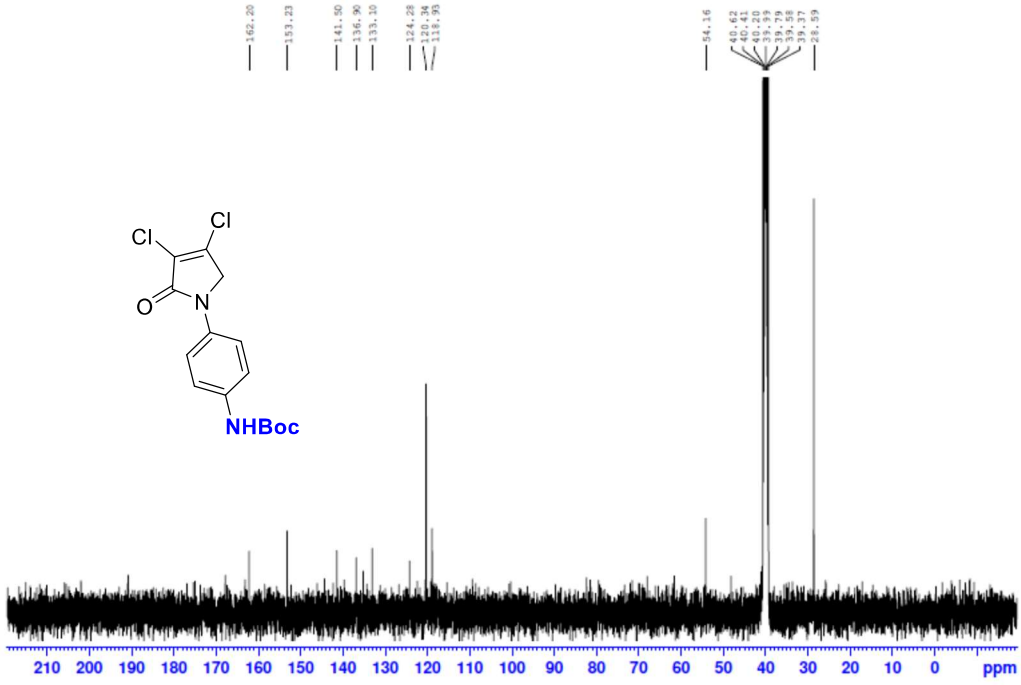
**8) N-(3-tert-butylphenylcarbamate)-3,4-dichloro-1,5-dihydro-2H-pyrrol-2-one (Compound 17)**



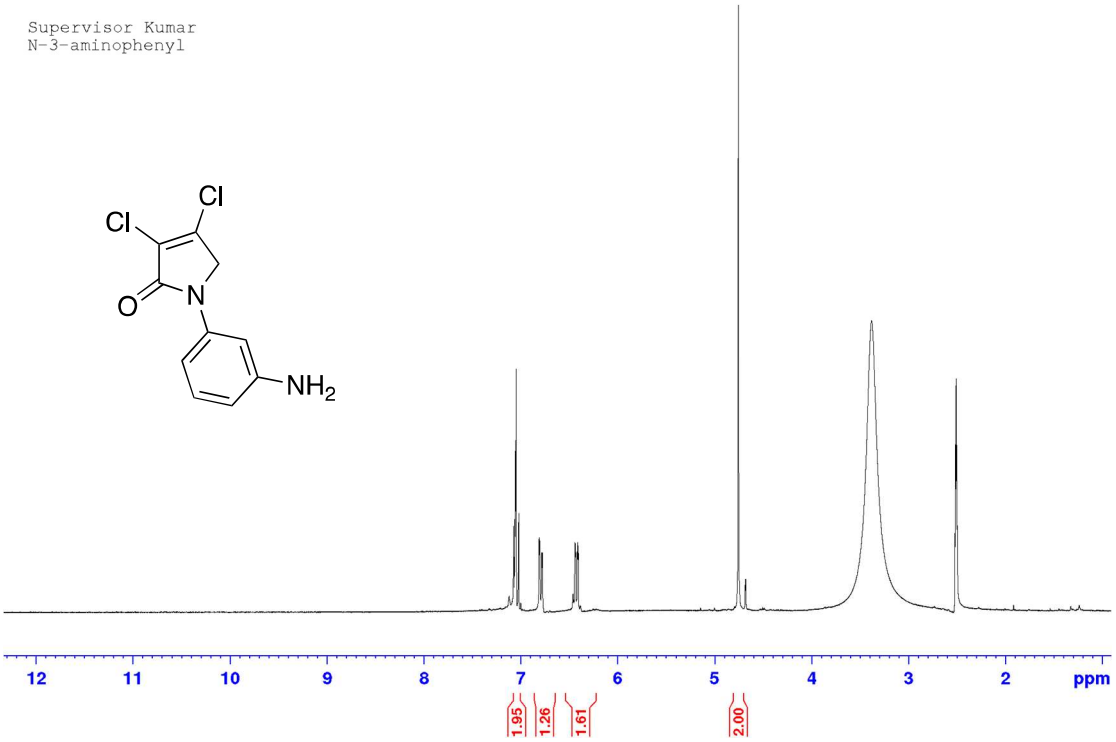



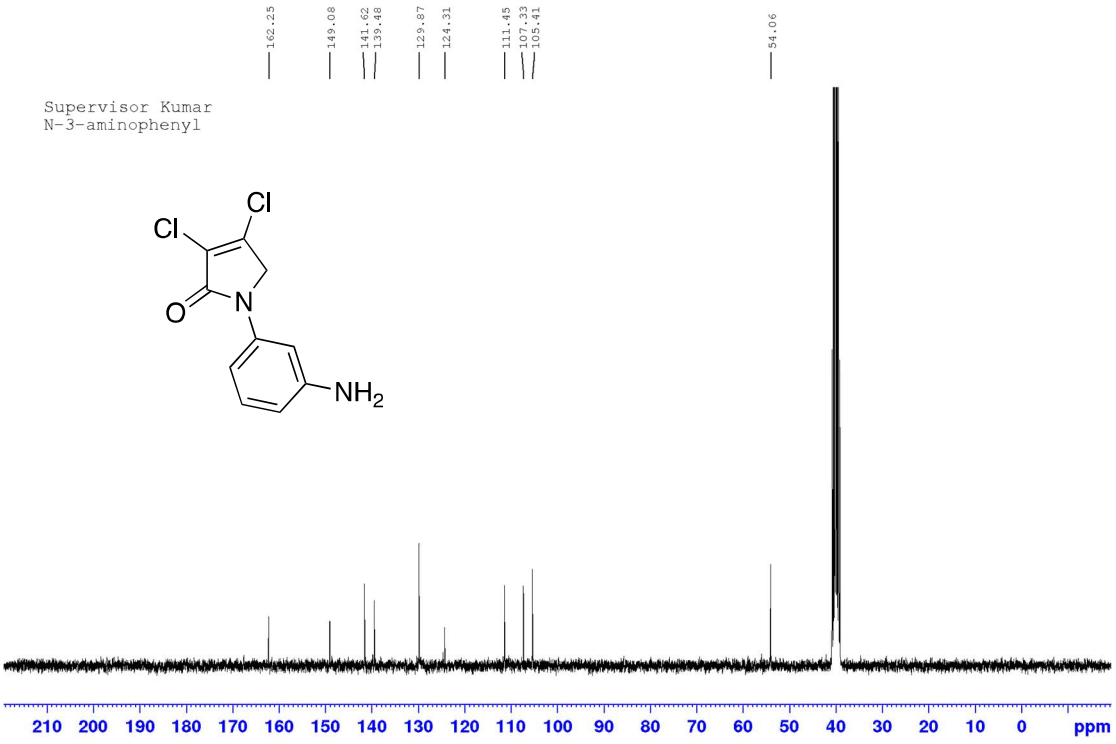
**9) N-(4′-tert-butylphenylcarbamate)-3,4-dichloro-1,5-dihydro-2H-pyrrol-2-one (Compound 18)**



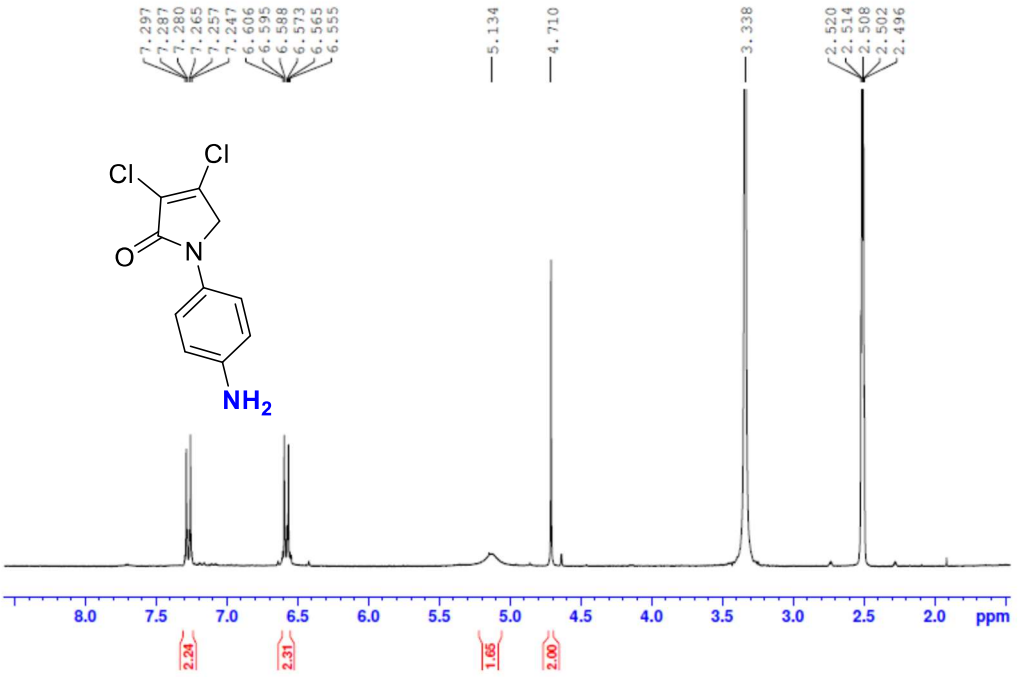



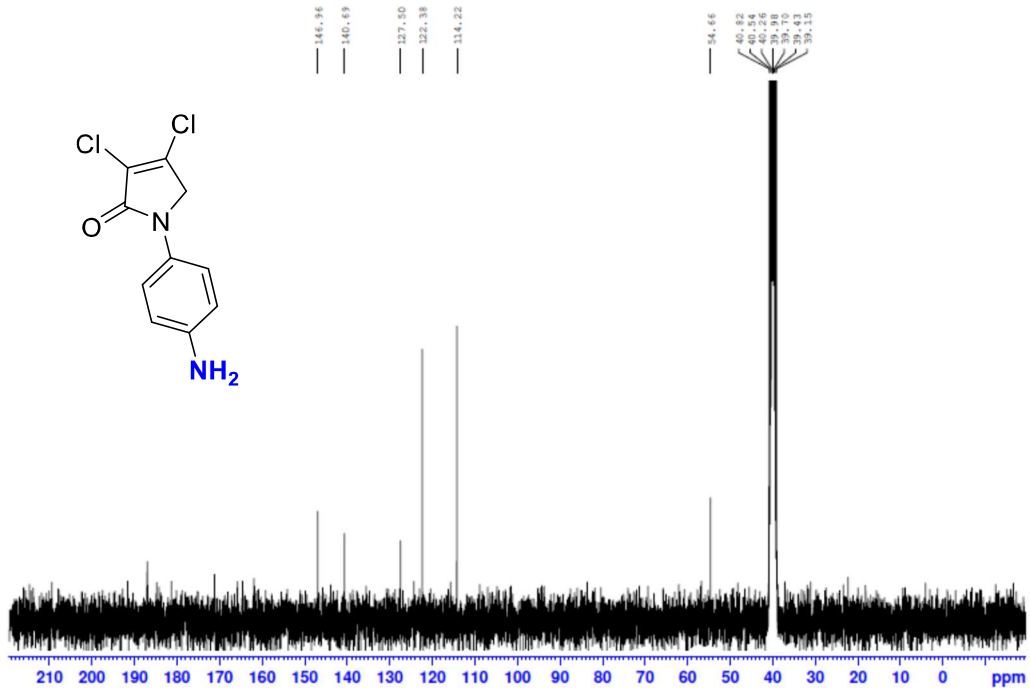
**10) N-(3-aminophenyl)-3,4-dichloro-1,5-dihydro-2H-pyrrol-2-one (compound 19)**



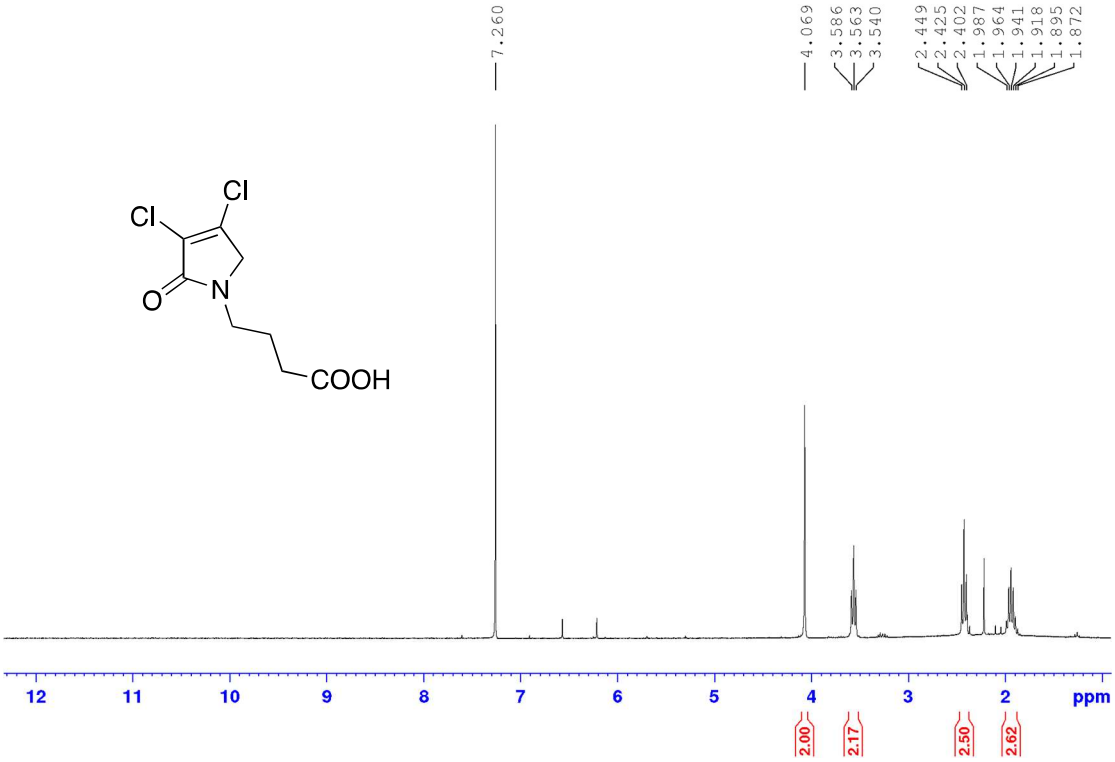



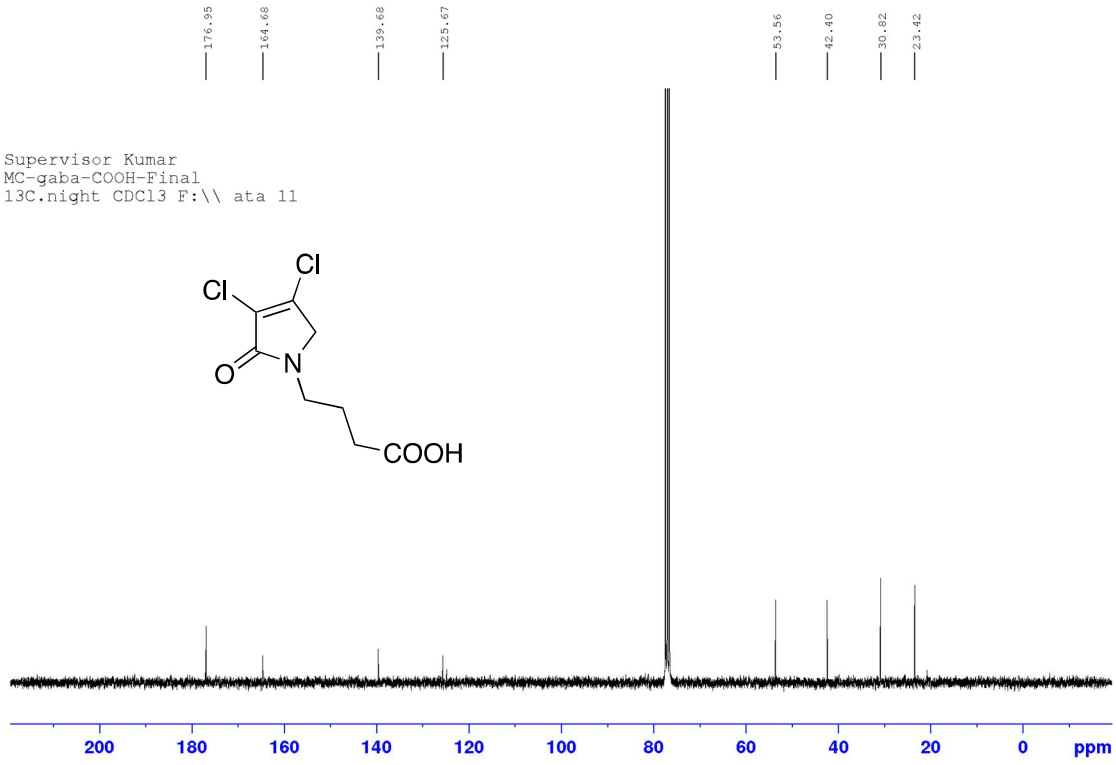
**11) N-(4-aminophenyl)-3,4-dichloro-1,5-dihydro-2H-pyrrol-2-one (Compound 20)**



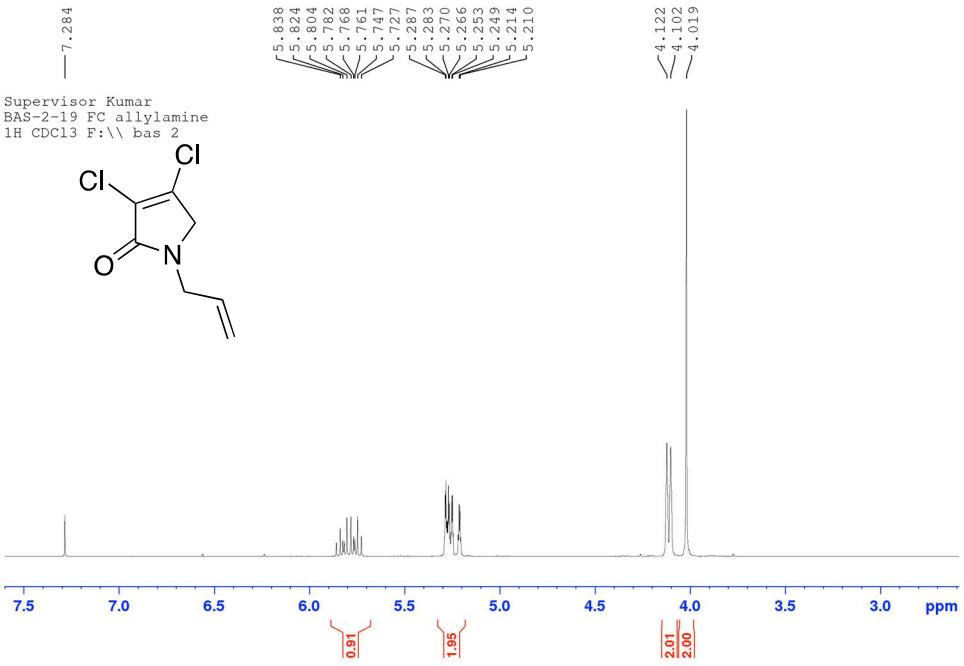



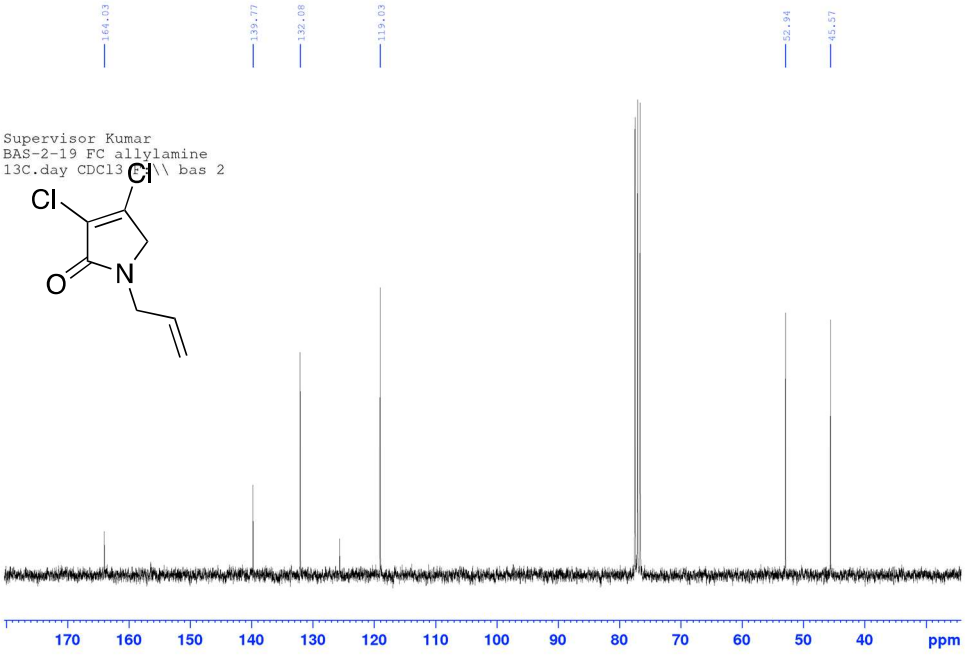
**12) 4-(3,4-dichloro-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)butanoic acid (Compound 21)**



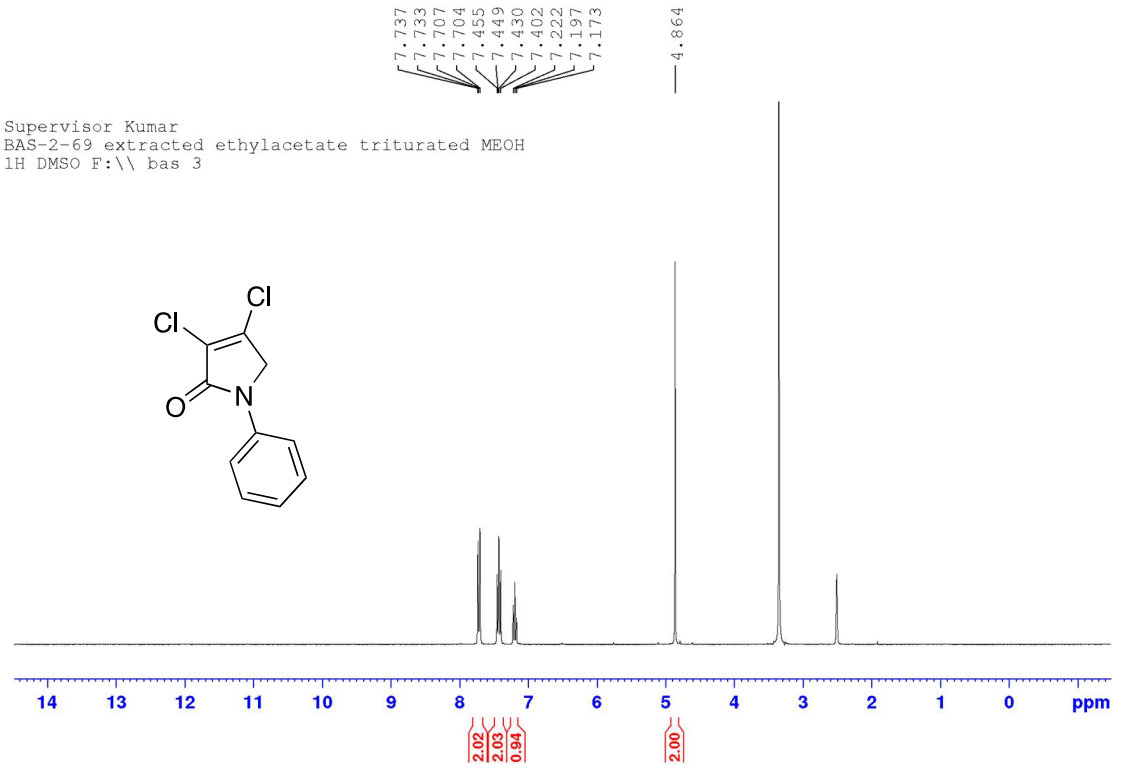



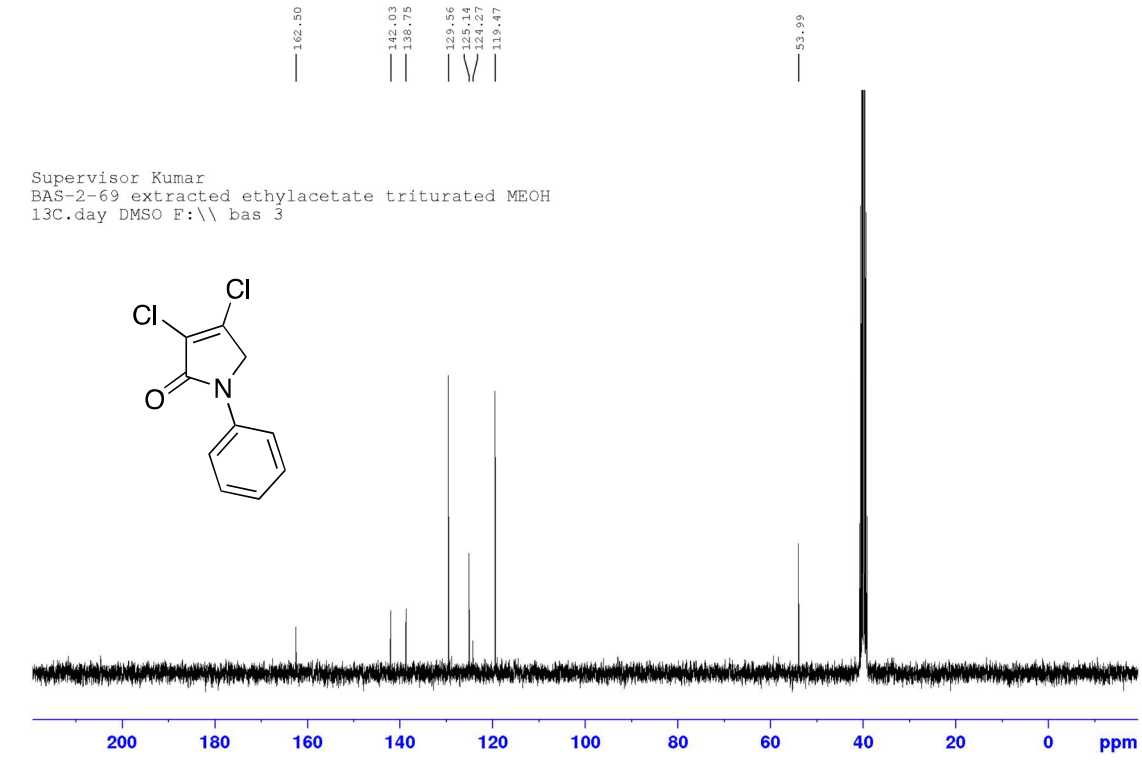
## 13) 1-allyl-3,4-dichloro-1,5-dihydro-2*H*-pyrrol-2-one (Compound 22)



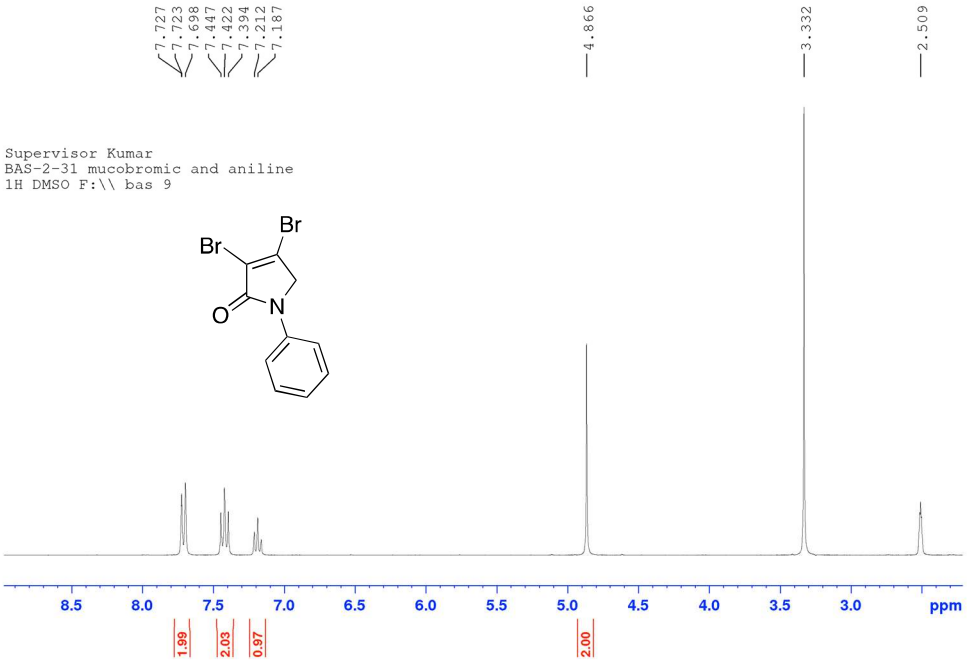



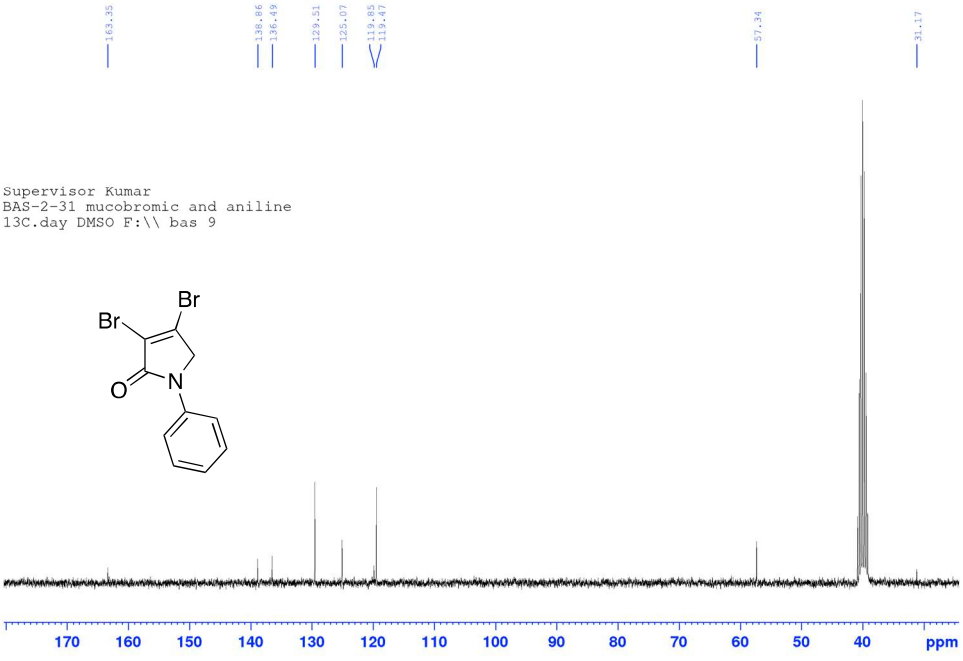
## 14) 3,4-dichloro-1-phenyl-1,5-dihydro-2*H*-pyrrol-2-one (Compound 23)



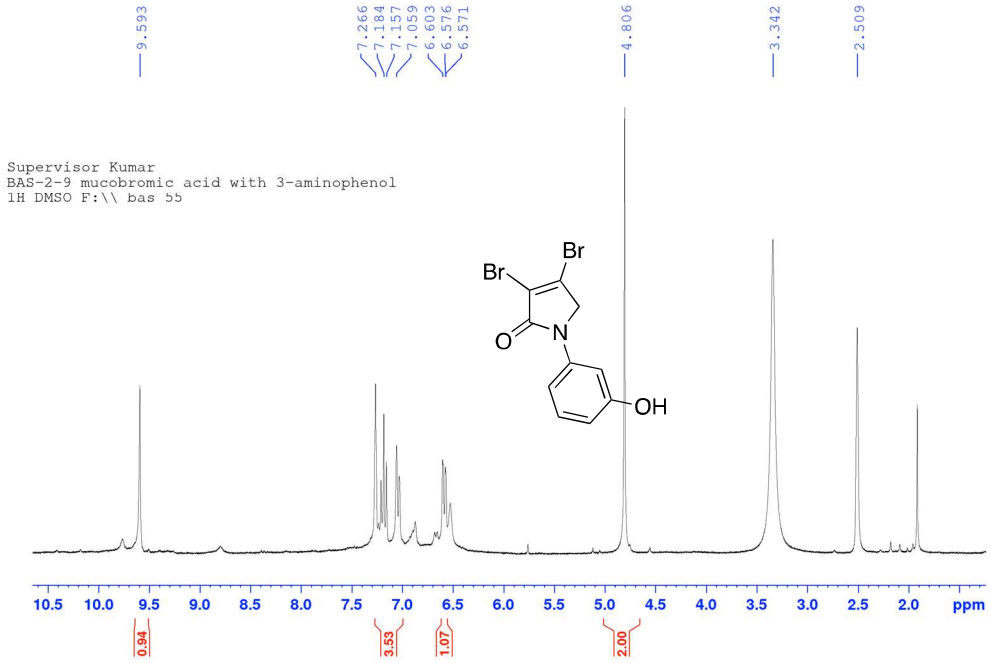



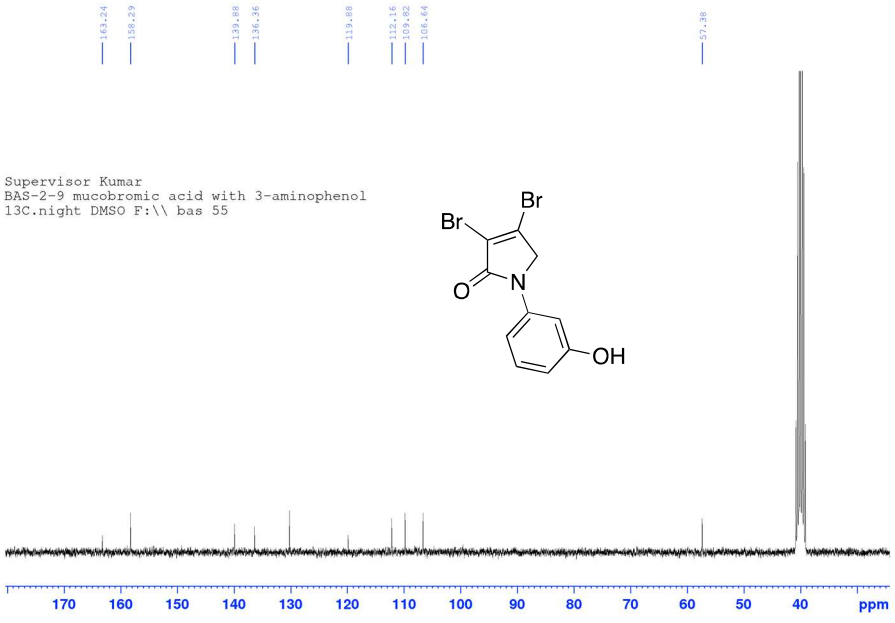
## 15) 3,4-dibromo-1-phenyl-1,5-dihydro-2*H*-pyrrol-2-one (Compound 24)



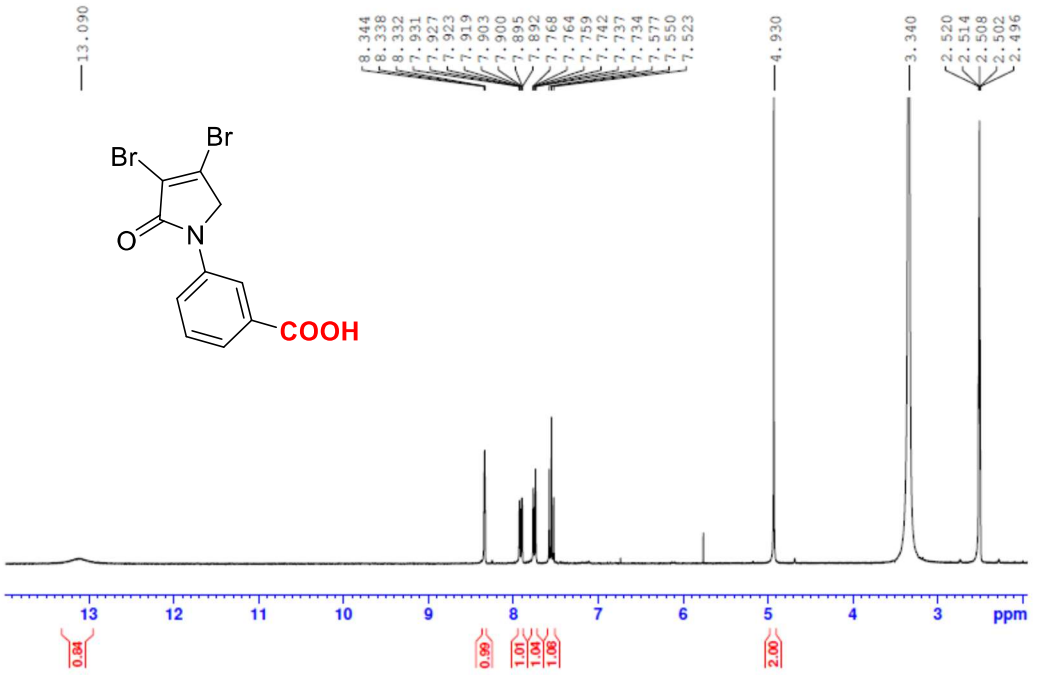



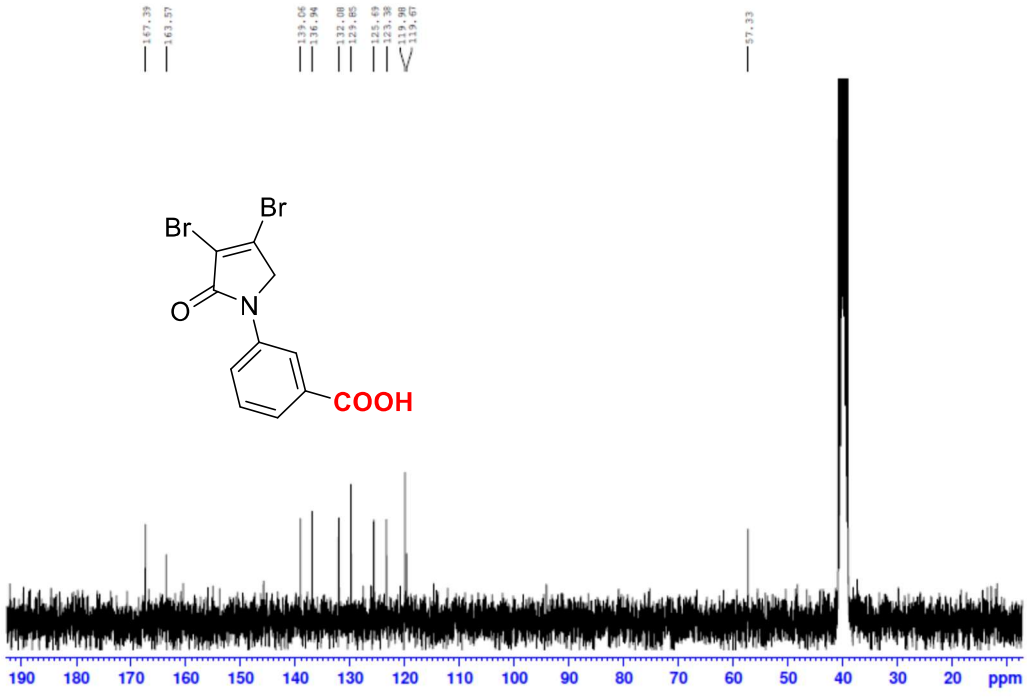
## 16) 3,4-dibromo-1-(3-hydroxyphenyl)-1,5-dihydro-2*H*-pyrrol-2-one (Compound 25)



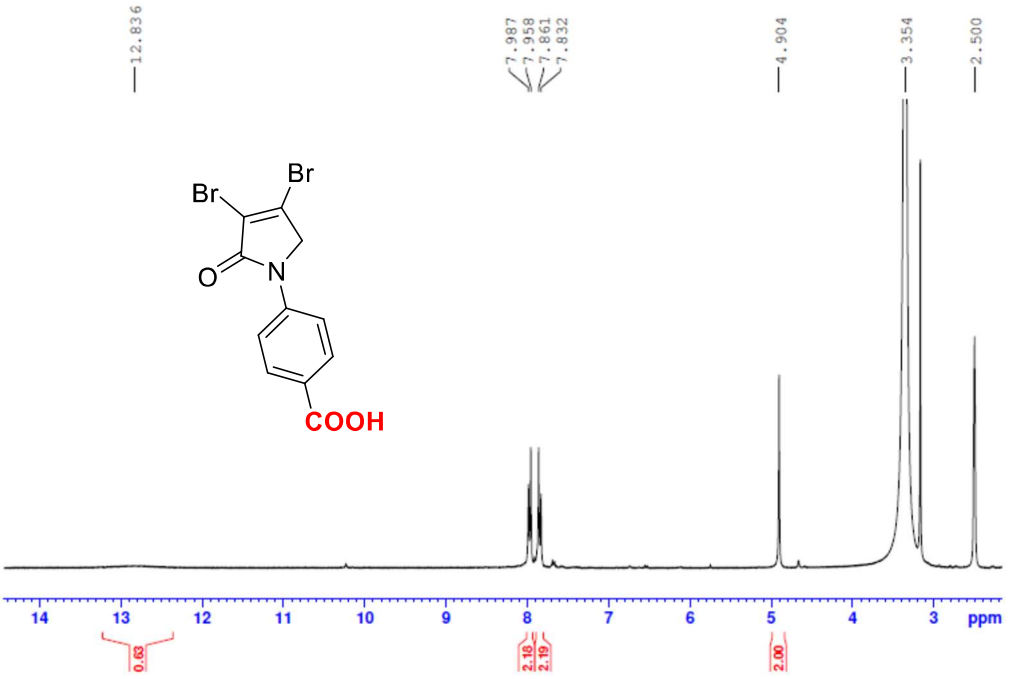



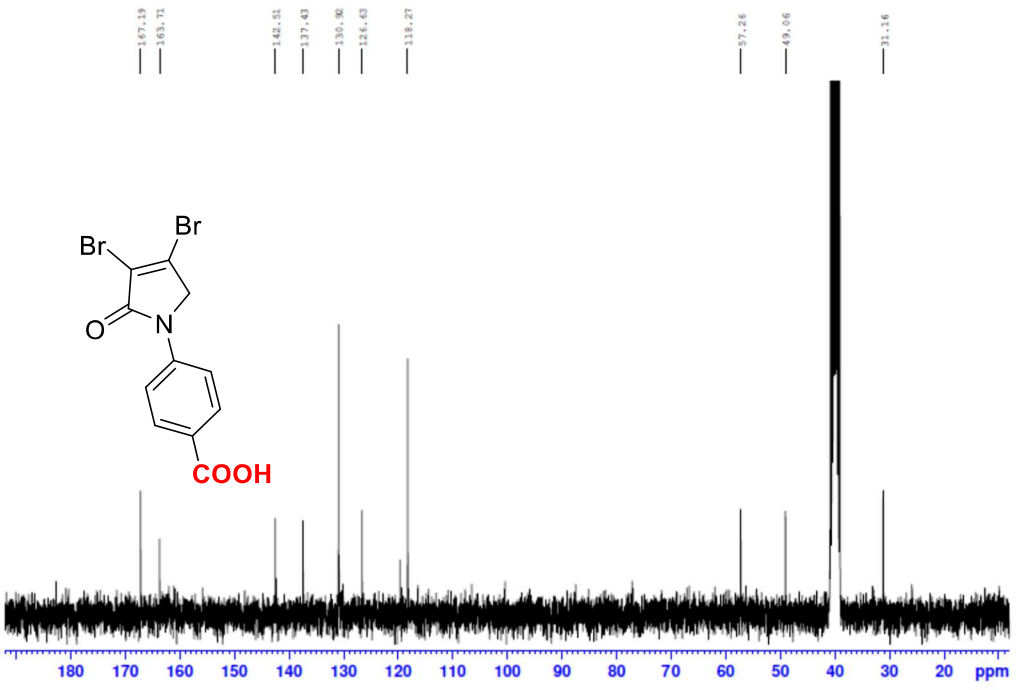
**17) N-(3-carboxyphenyl)-3,4-dichloro-1,5-dihydro-2H-pyrrol-2-one (Compound 26)**



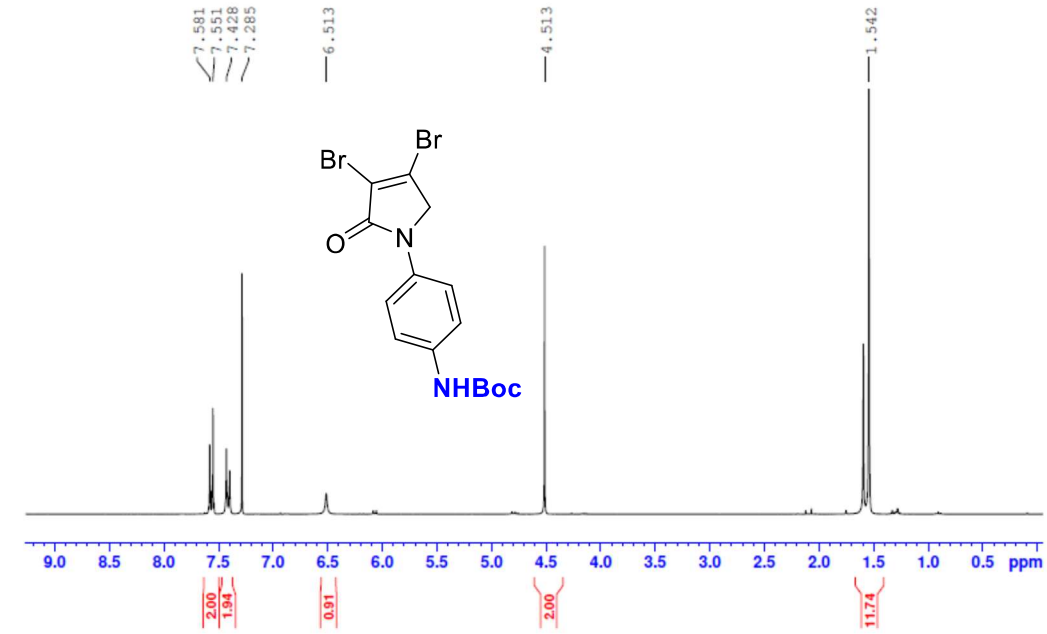



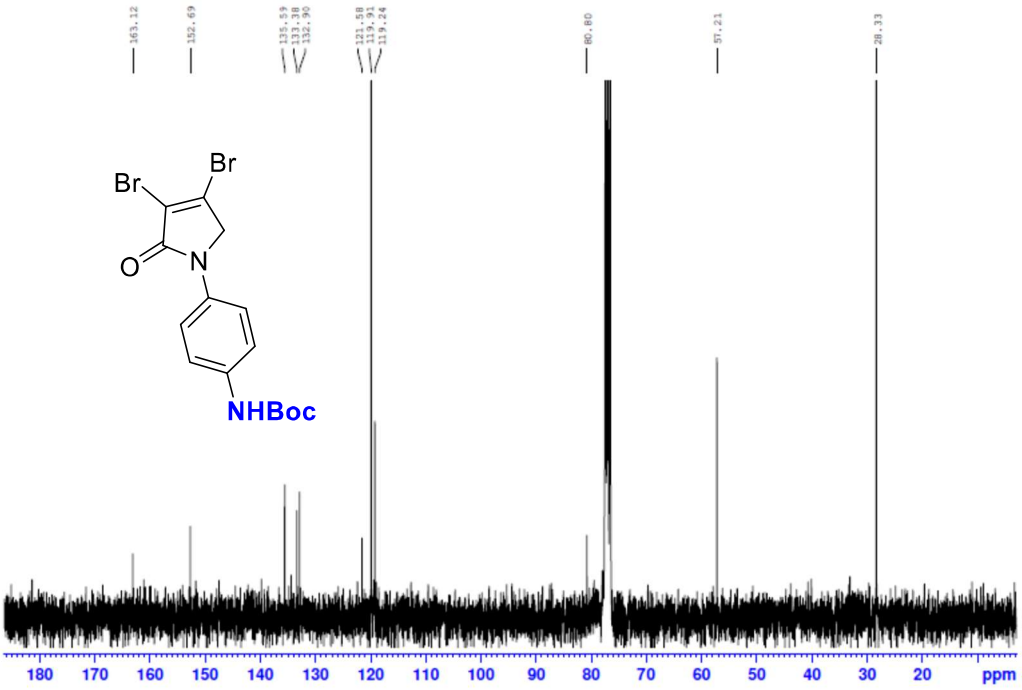
**18) N-(4-carboxyphenyl)-3,4-dichloro-1,5-dihydro-2H-pyrrol-2-one (Compound 27)**



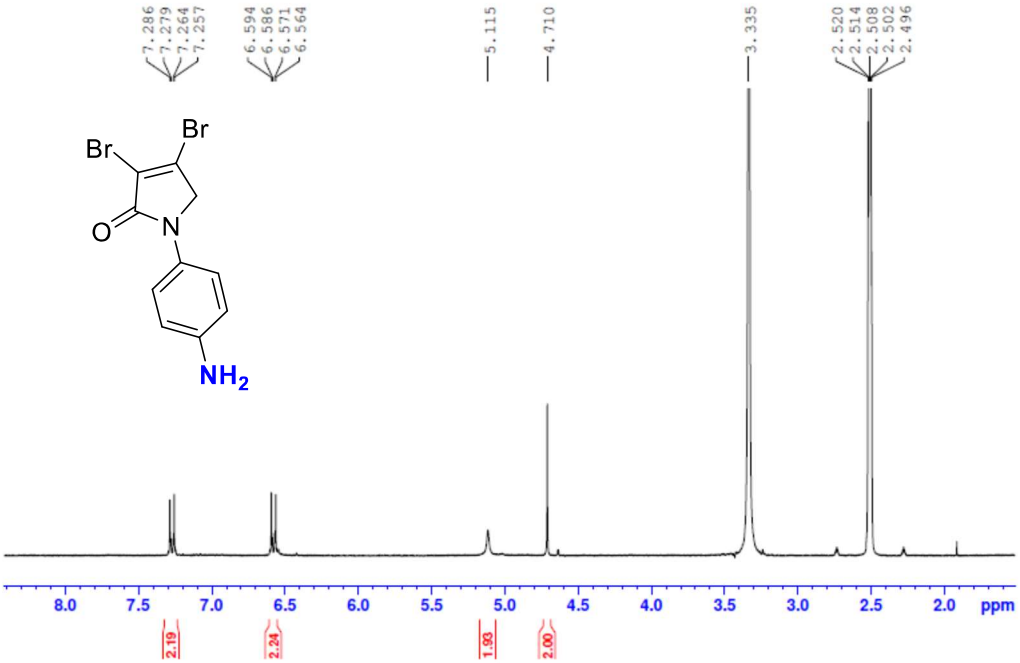



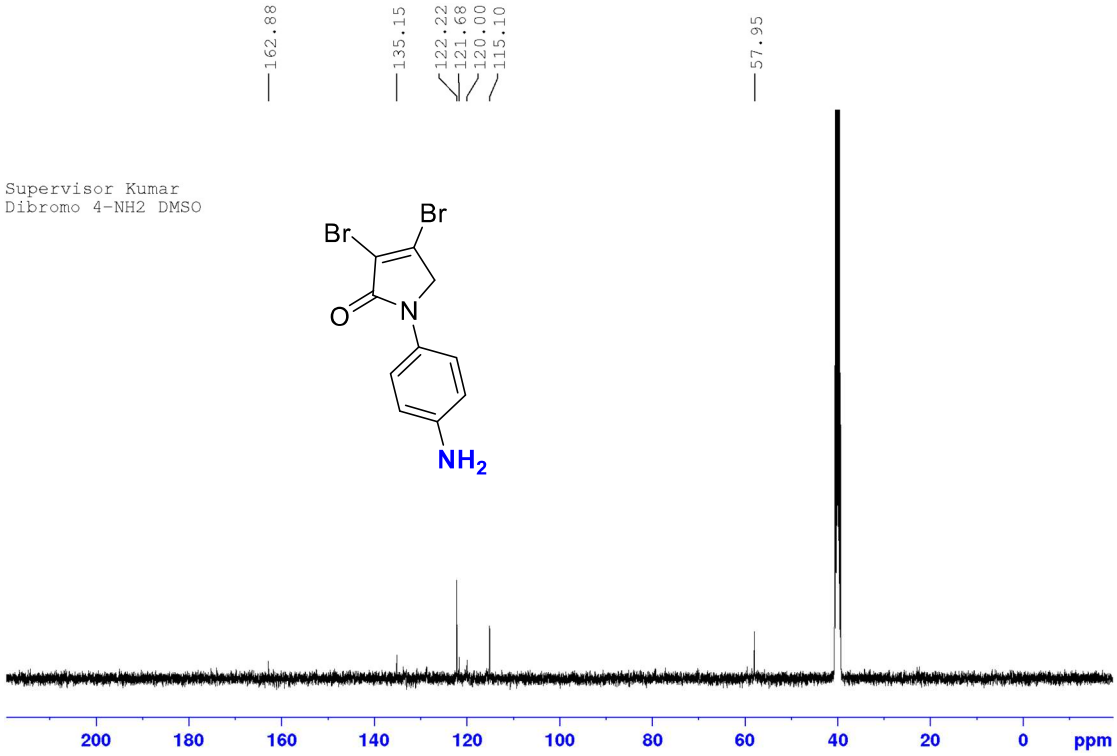
**19) N-(4′-tert-butylphenylcarbamate)-3,4-dibromo-1,5-dihydro-2H-pyrrol-2-one (Compound 28)**



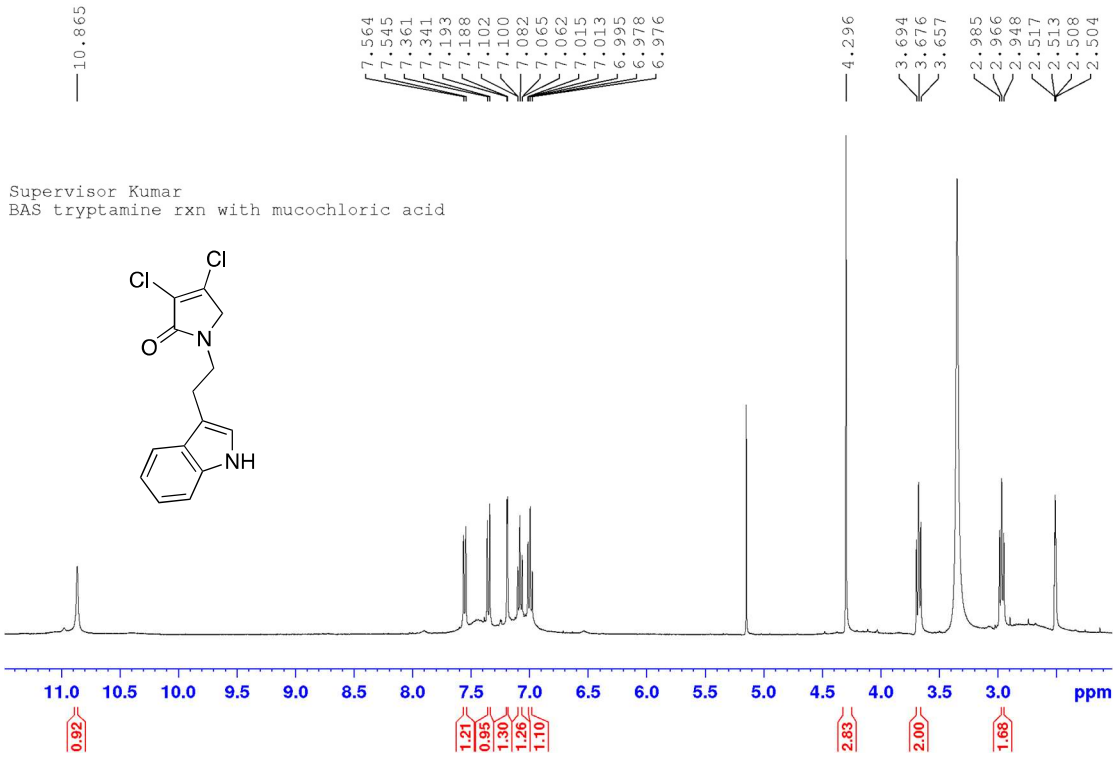



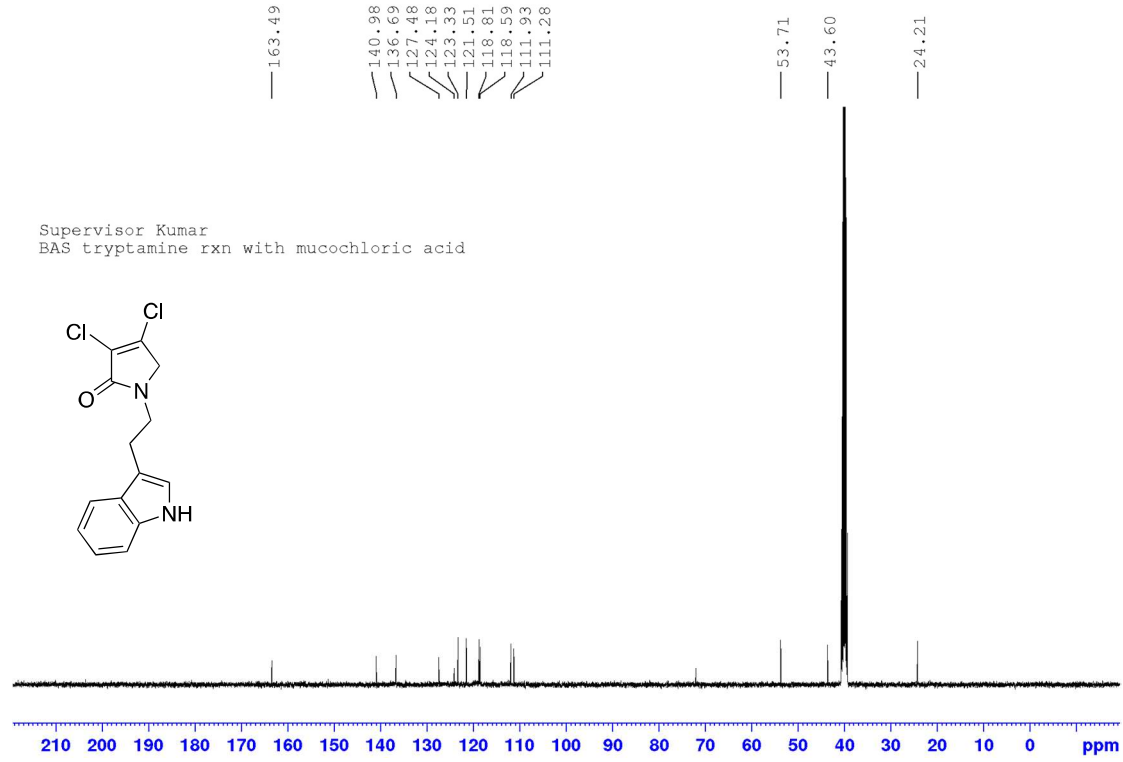
**20) N-(4-aminophenyl)-3,4-dibromo-1,5-dihydro-2H-pyrrol-2-one (DHP phenyl amine-2) (Compound 29)**



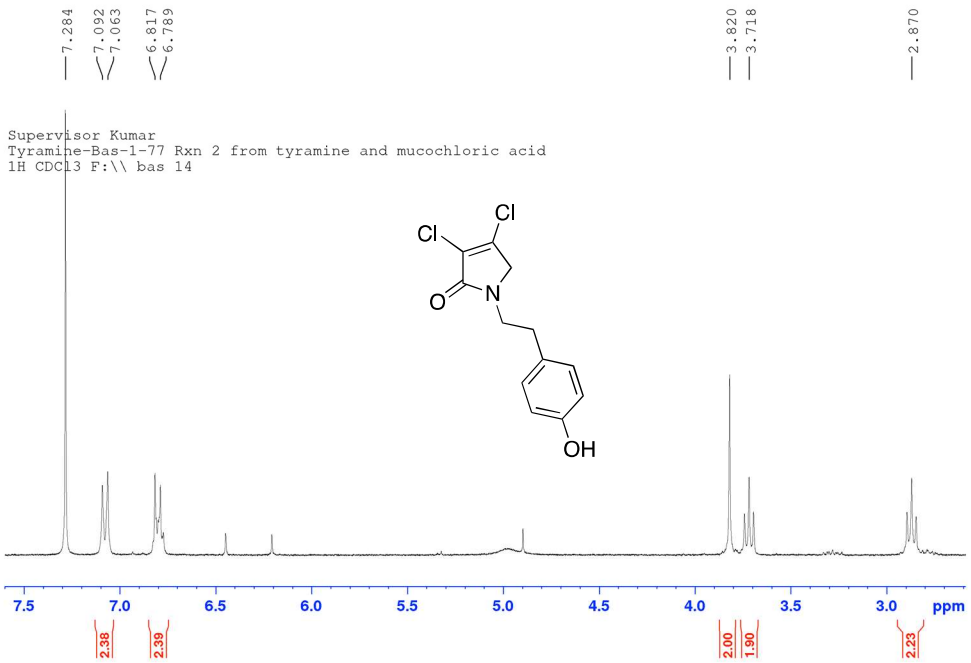



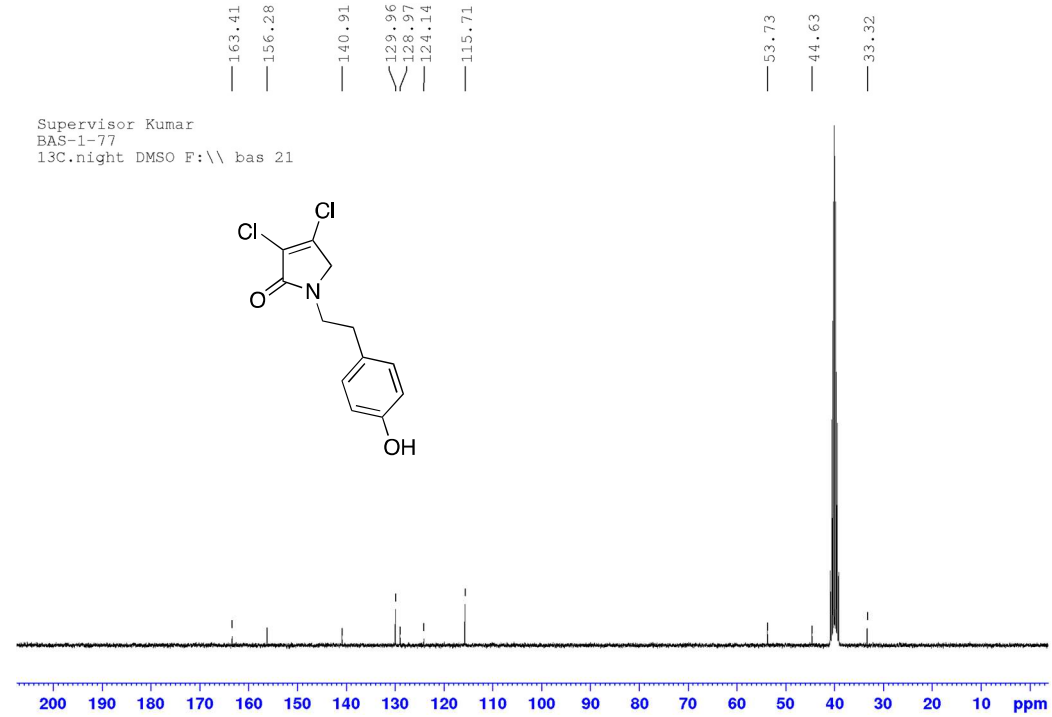
21) 3,4-dichloro-1-(4-hydroxyphenethyl)-1,5-dihydro-2*H*-pyrrol-2-one (Compound 30)



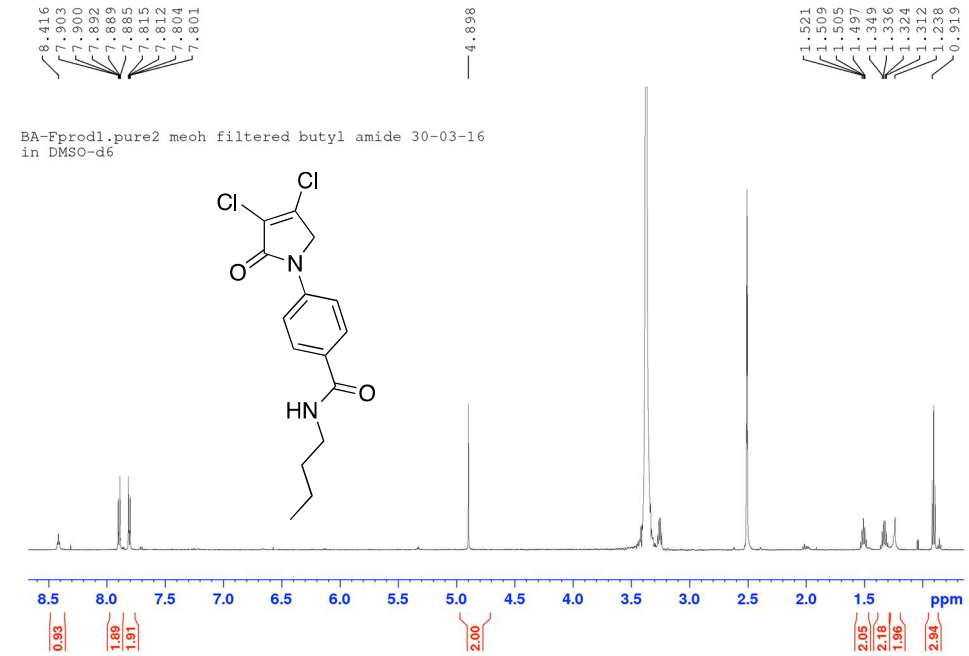



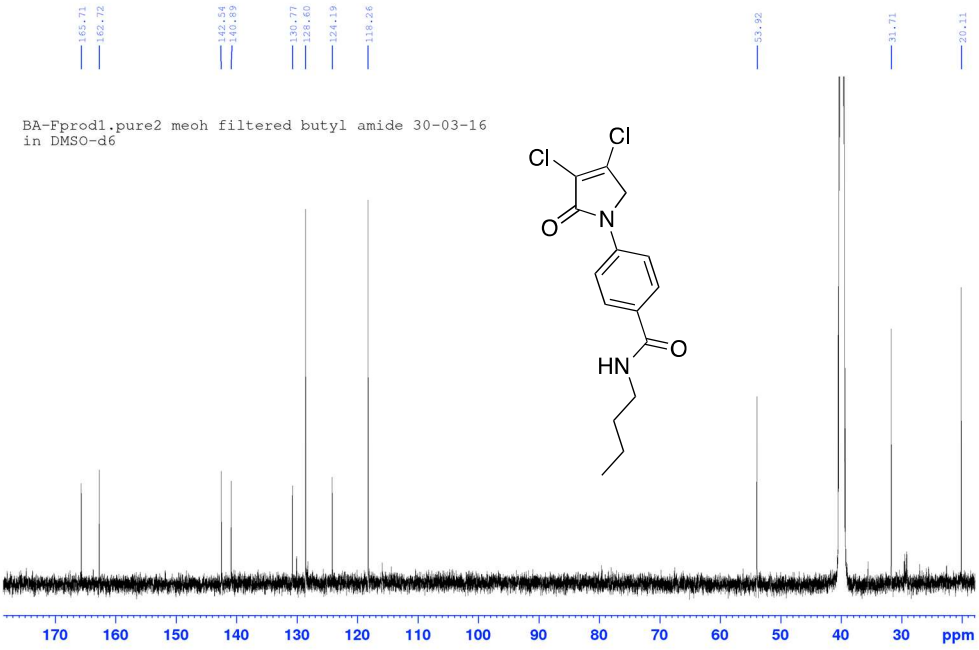
## 22) 1-(2-(1*H*-indol-3-yl)ethyl)-3,4-dichloro-1,5-dihydro-2*H*-pyrrol-2-one (Compound 31)



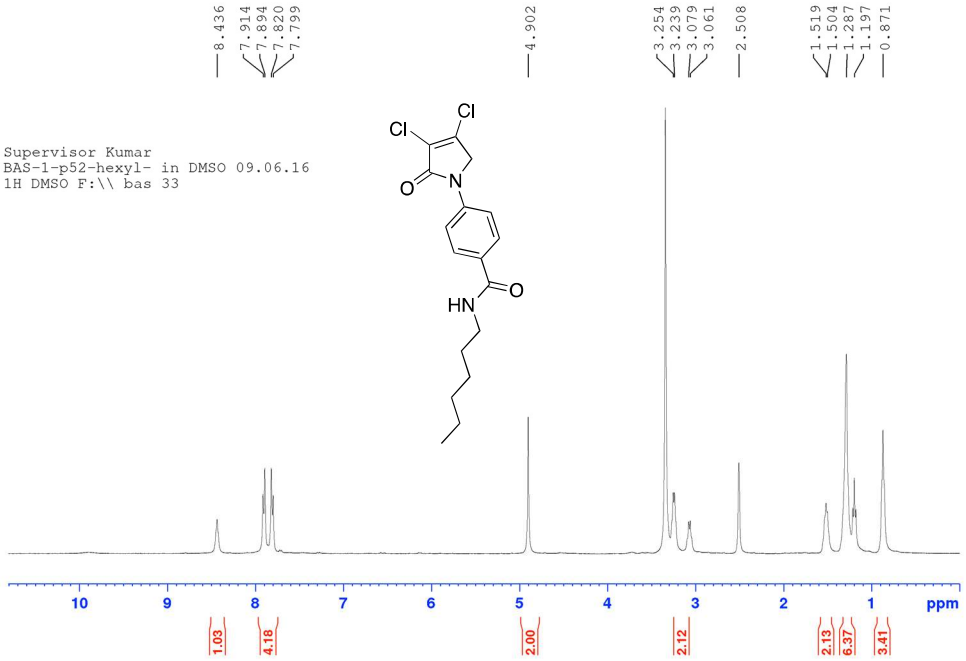



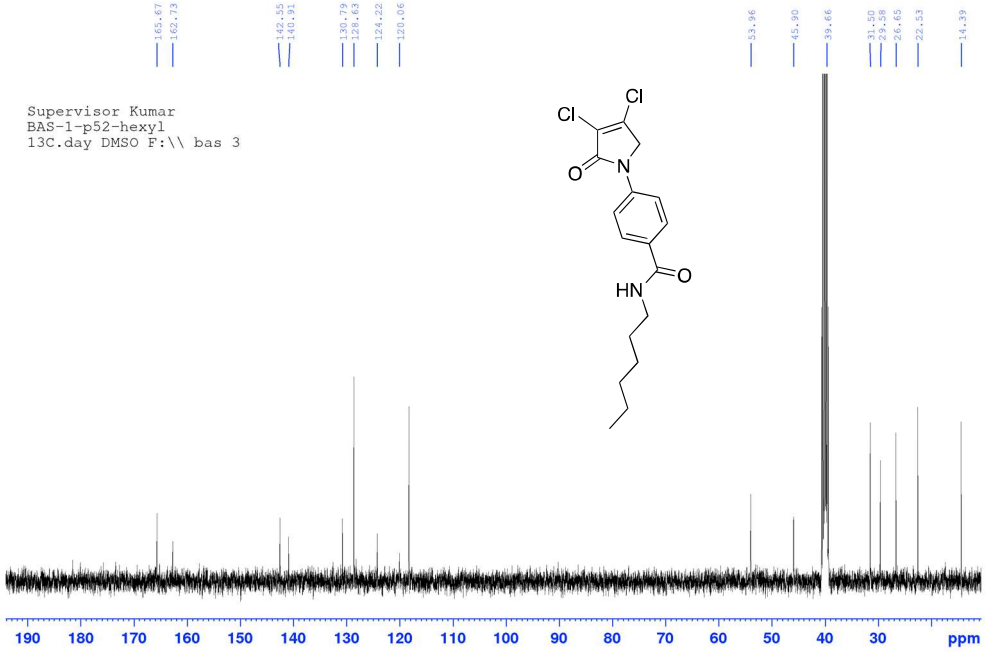
## 23) *N*-butyl-4-(3,4-dichloro-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)benzamide (Compound 32)



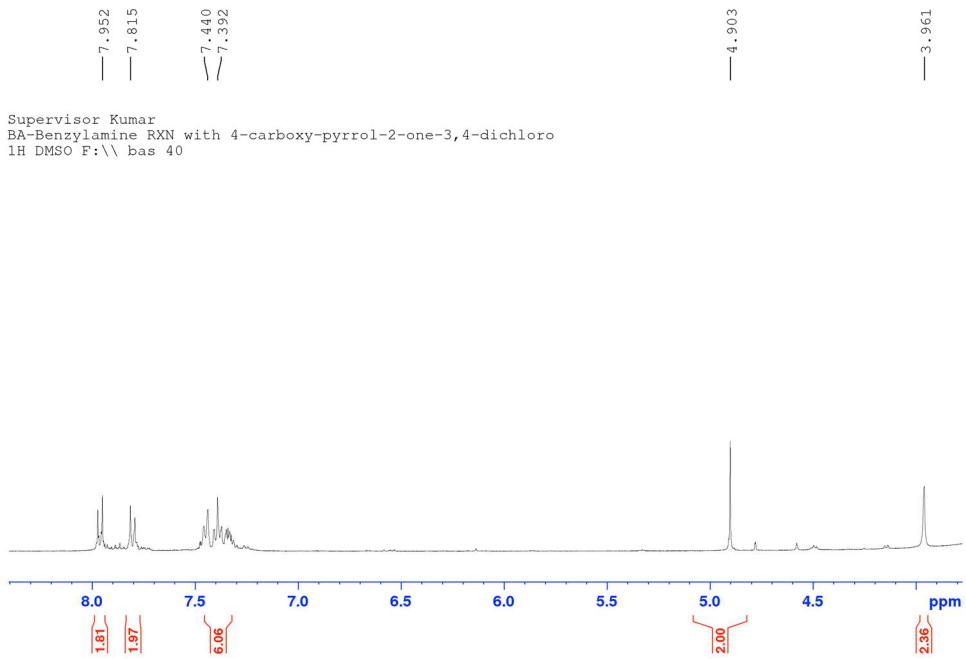



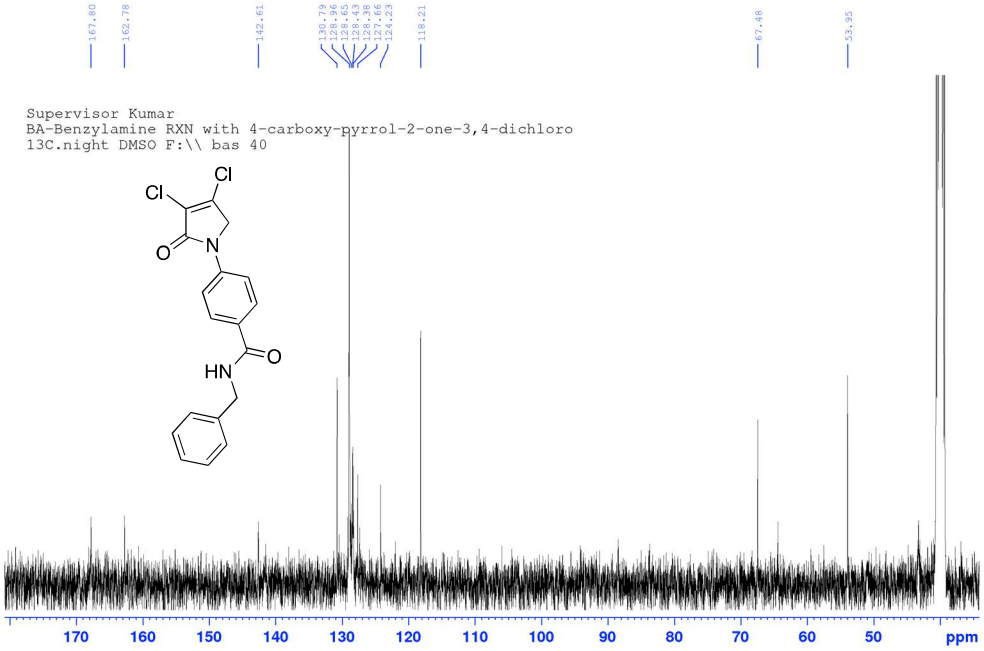
**24) *N*-hexyl-4-(3,4-dichloro-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)benzamide (Compound 33)**



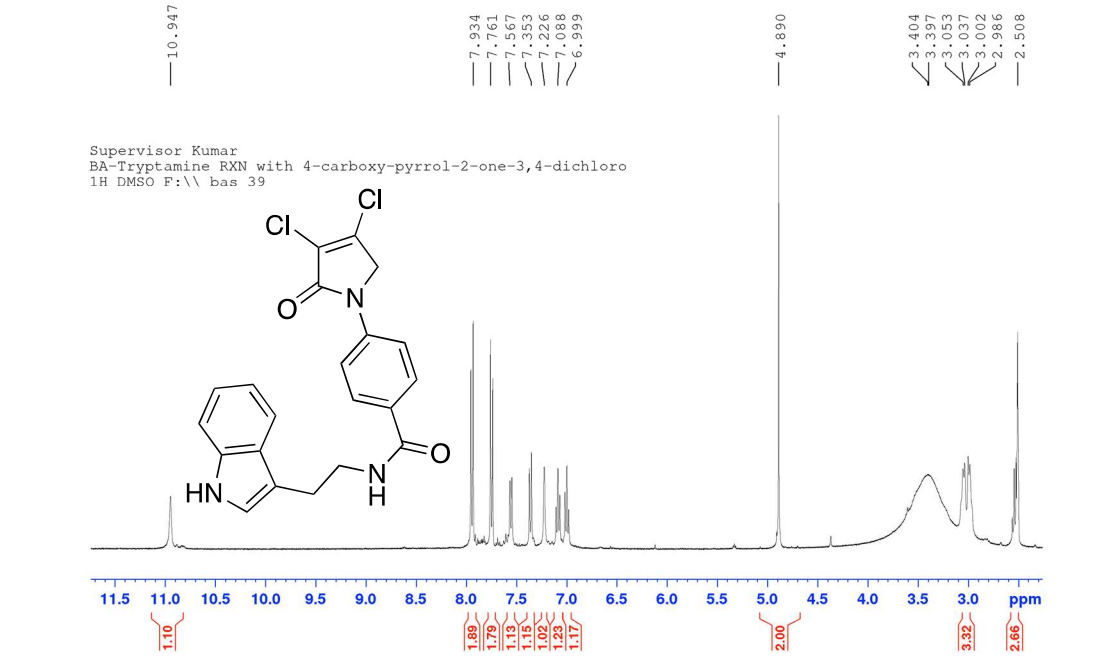



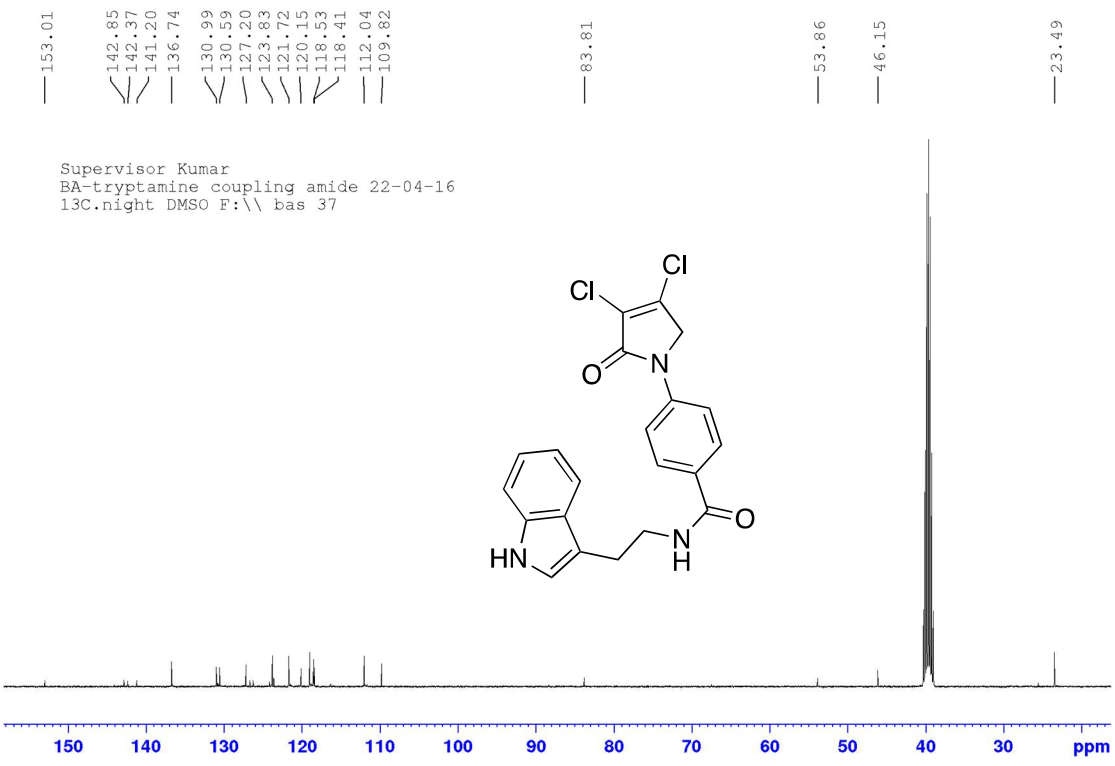
## *25) N*-benzyl-4-(3,4-dichloro-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)benzamide (Compound 34)



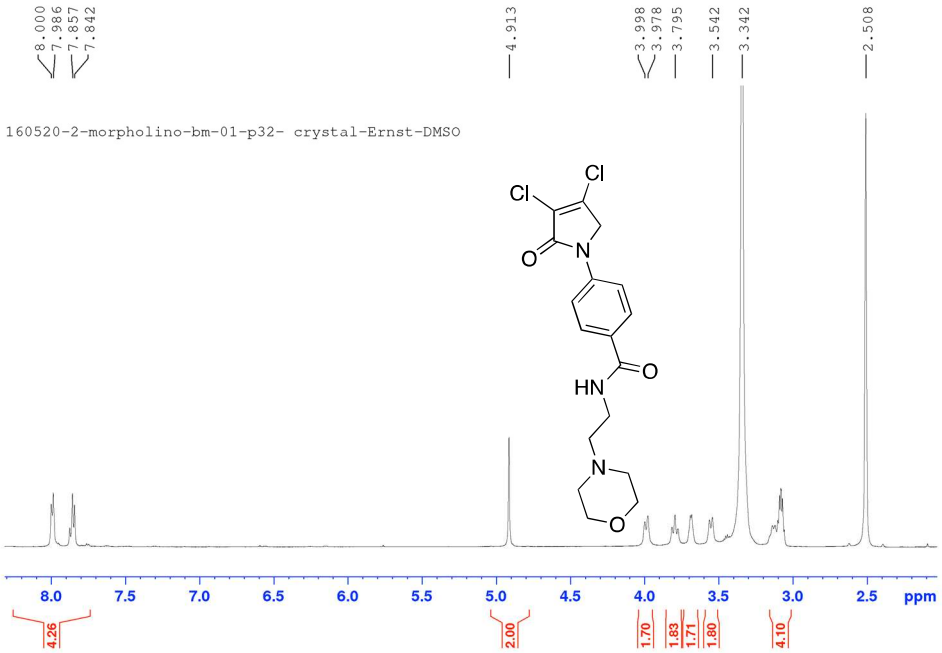



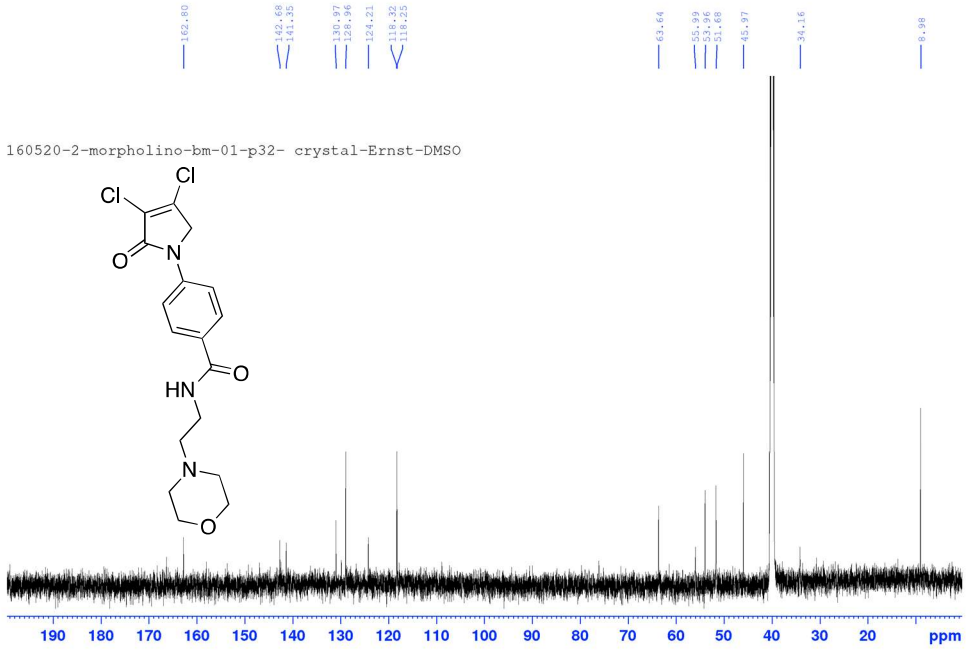
**26) *N*-(2-(1*H*-indol-3-yl)ethyl)-4-(3,4-dichloro-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)benzamide (Compound 35)**



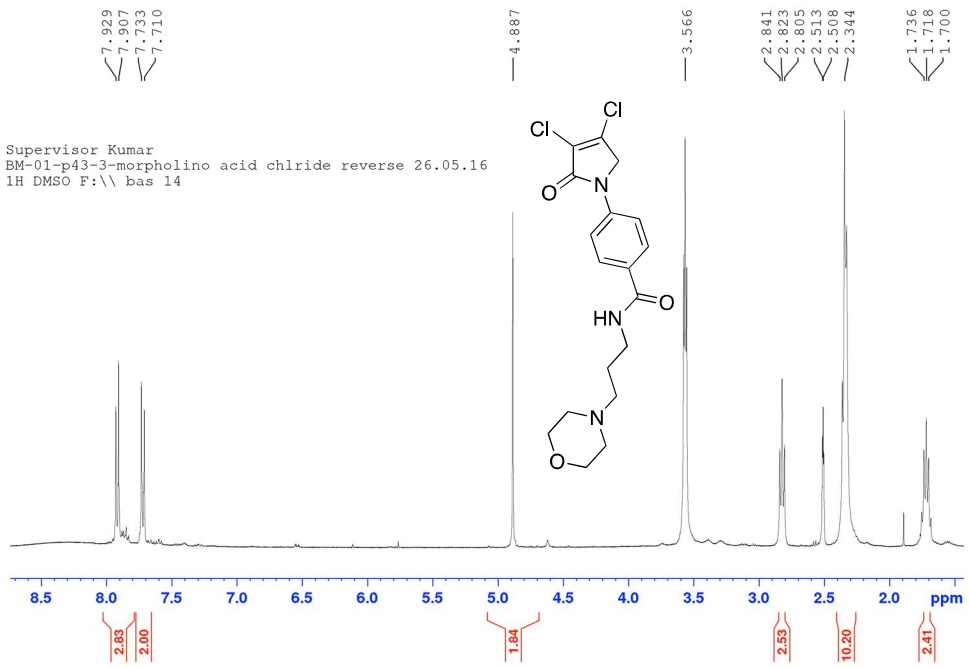



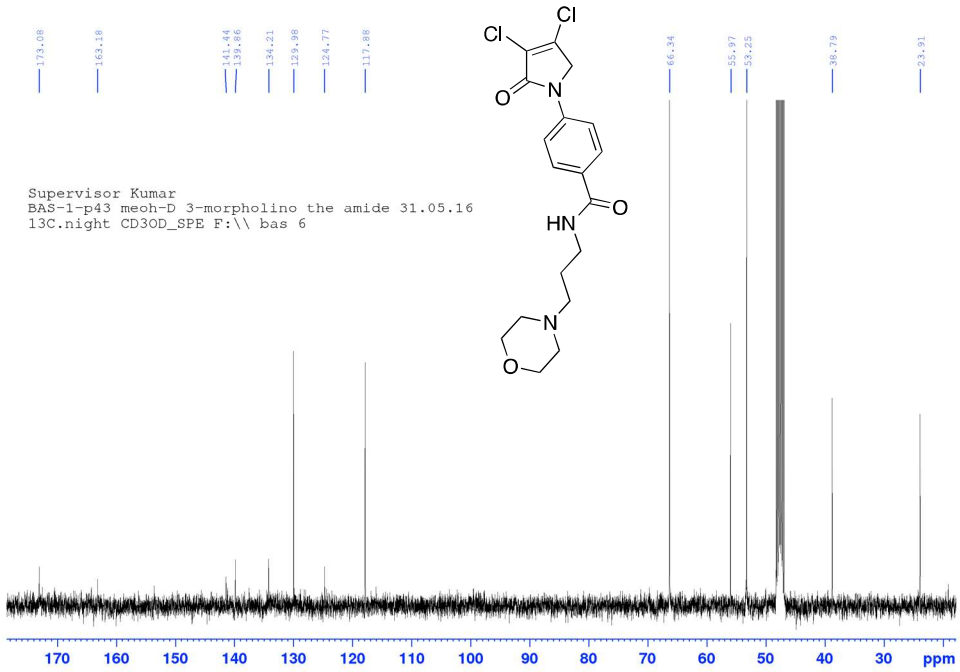
## 27) 4-(3,4-dichloro-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)-*N*-(2-morpholinoethyl)benzamide (Compound 36)



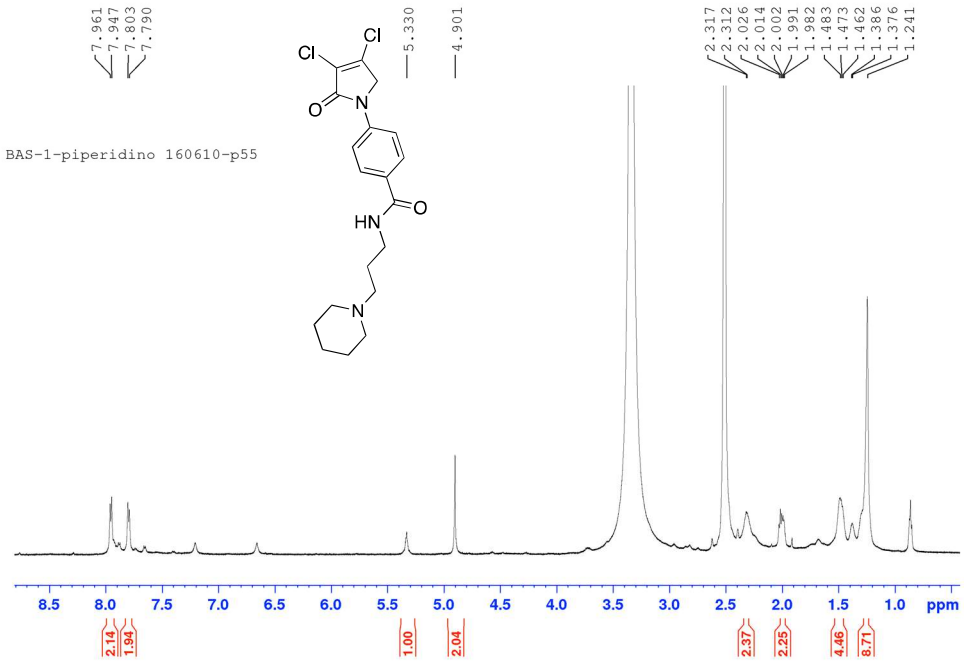



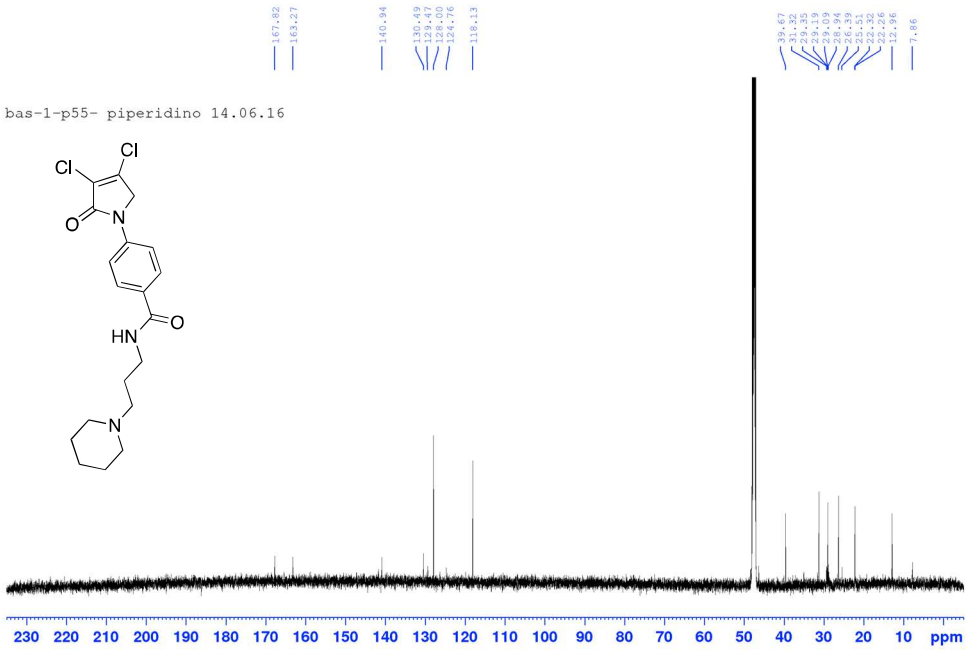
## 28) 4-(3,4-dichloro-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)-*N*-(3-morpholinopropyl)benzamide (Compound 37)



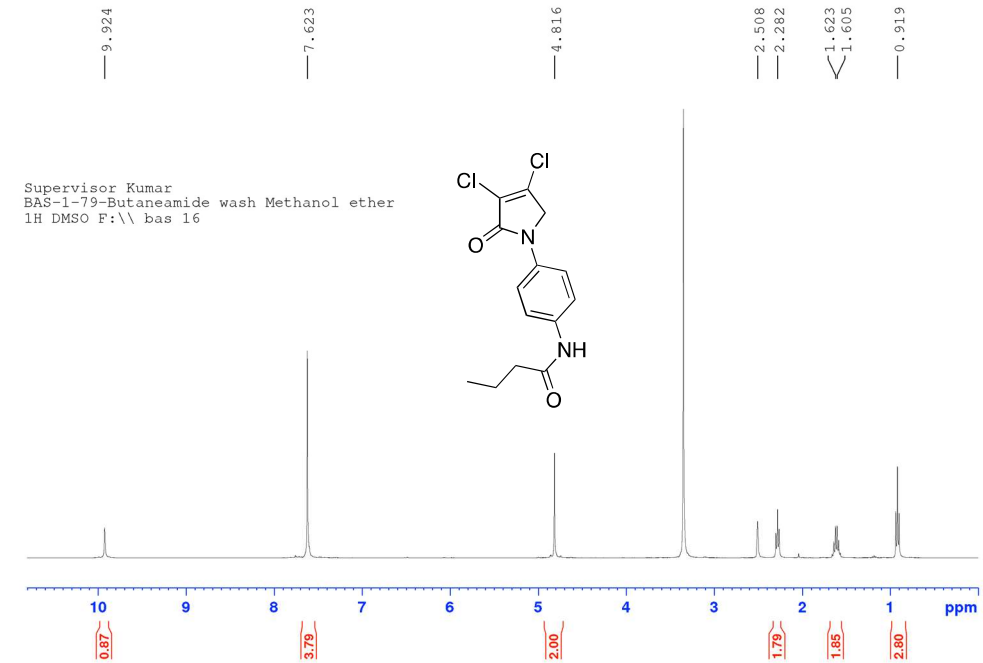



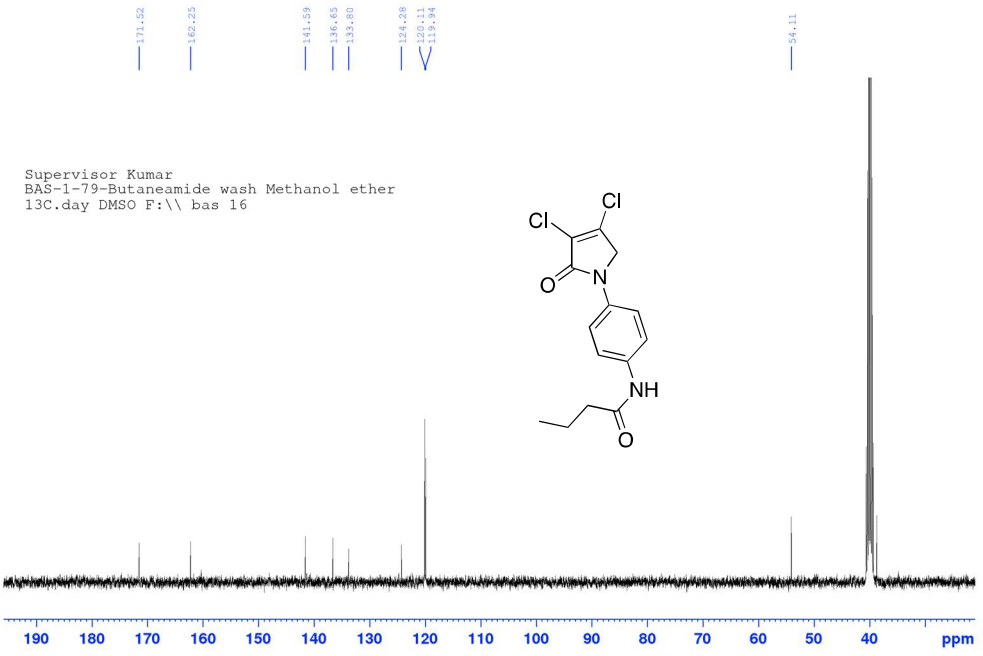
**29) 4-(3,4-dichloro-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)-*N*-(3-(piperidin-1-yl)propyl)benzamide (Compound 38)**



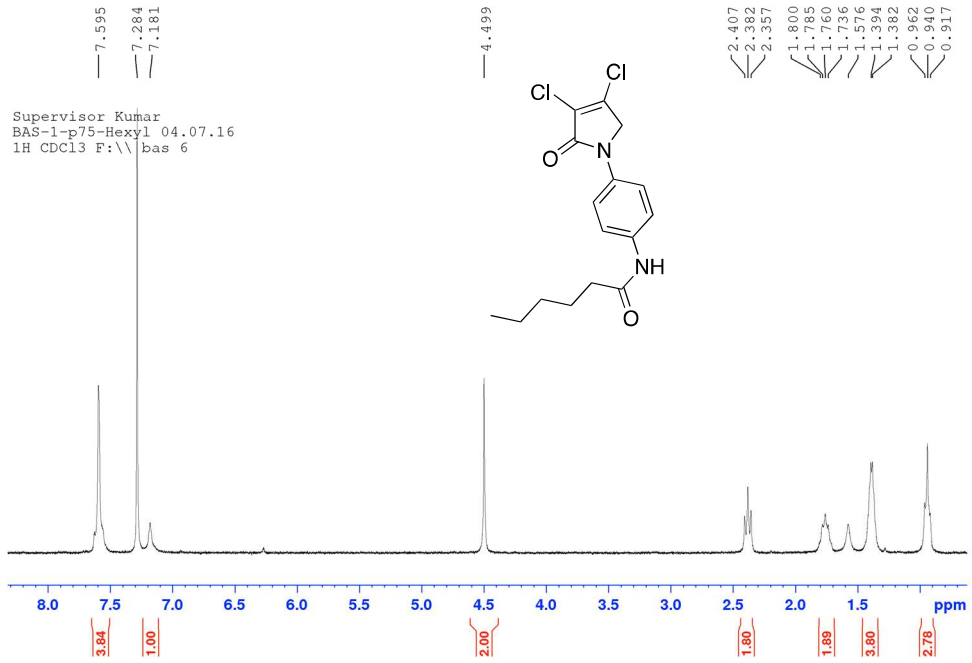



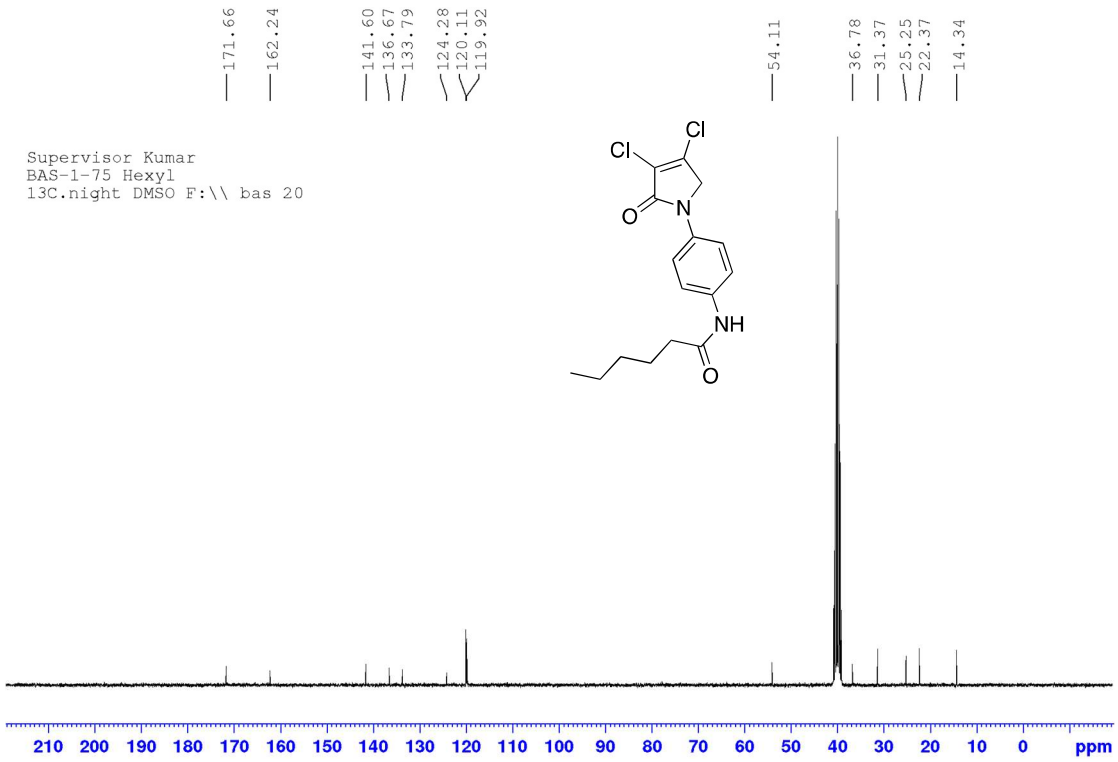
**30) *N*-(4-(3,4-dichloro-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)phenyl)butyramide (Compound 39)**



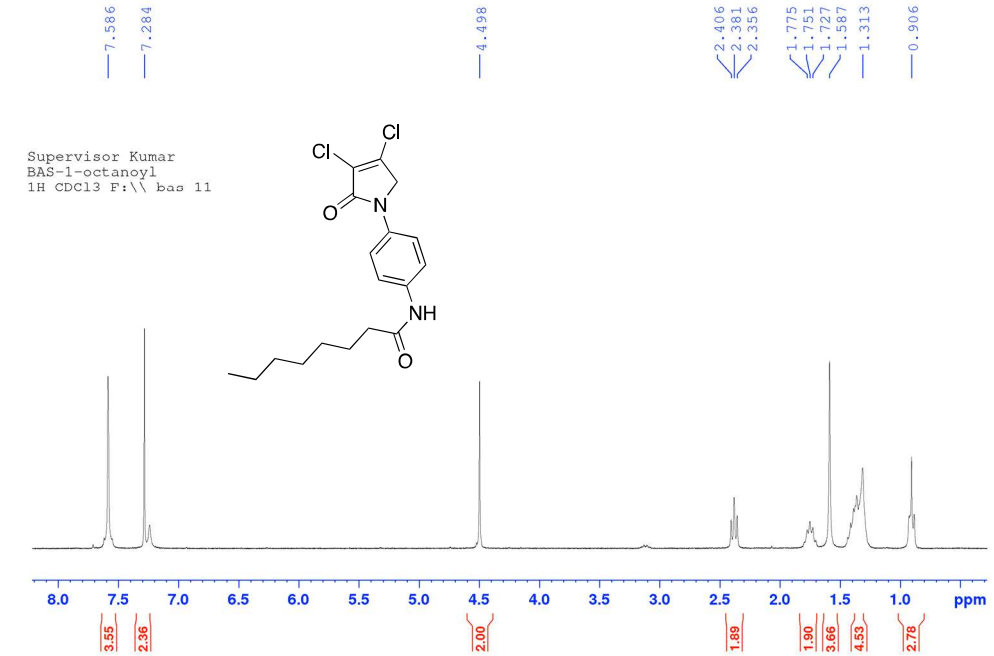



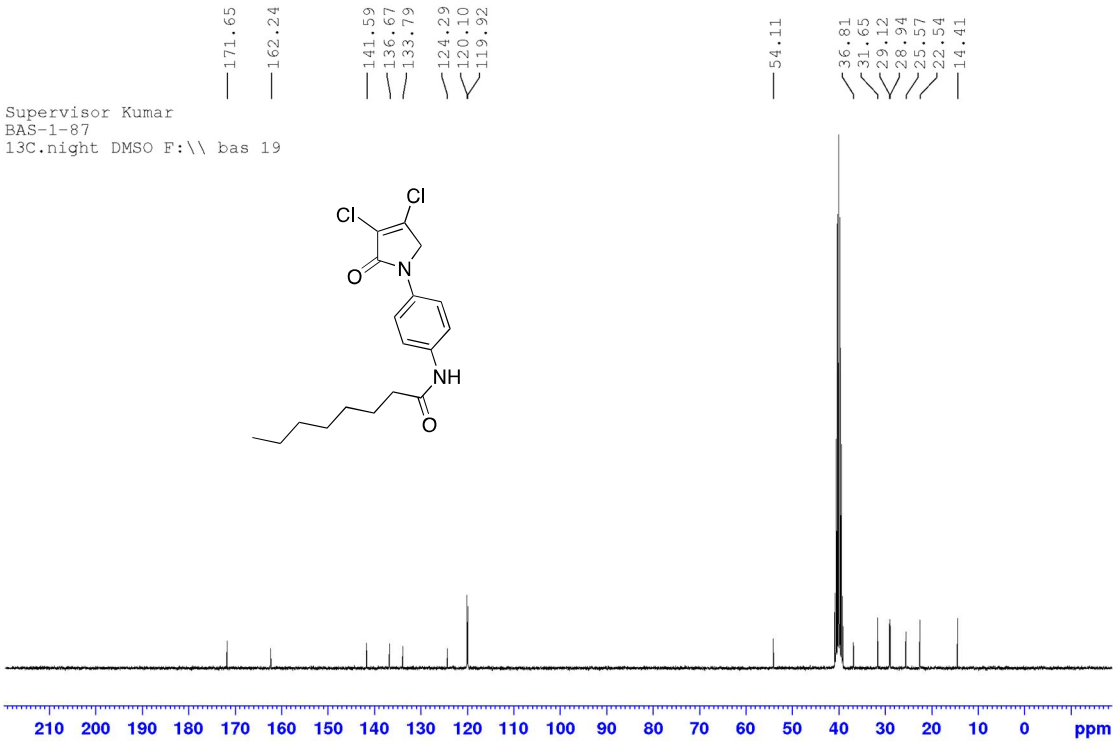
**31) *N*-(4-(3,4-dichloro-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)phenyl)hexanamide (Compound 40)**



## 32) N-(4-(3,4-dichloro-2-oxo-2,5-dihydro-1H-pyrrol-1-yl)phenyl)octanamide (Compound 41)



**33) 2-(4-bromophenyl)-*N*-(4-(3,4-dichloro-2-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)phenyl)acetamide (Compound 42)**