

Synthesis and Anticancer Activity of Prodigiosenes bearing C-Ring Esters and Amides

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NCI data reported using drug concentration values

Compound	Mean GI ₅₀ ^a (μM)	Mean TGI ^b (μM)	Mean LC ₅₀ ^c (μM)	tPSA (Å ²)
Prodigiosin	0.014	2.1	0.22	45.65
Prodigiosin-Me	0.015	0.14	1.1	45.65
10	0.85	4.9	45	98.25
11	3.5	15	51	98.25
12	0.54	5.4	30	71.95
13	0.37	2.5	28	98.25
14	0.35	2.0	17	71.95
15	0.2	2.3	20	71.95
15a	0.32	1.8	16	71.95
15b	0.091	1.0	5.9	71.95
15c	0.22	1.2	5.5	71.95
15d	1.4	3.0	6.0	74.75
15e	2.4	8.7	46	74.75
15f	0.48	11	65	65.96

Table 15. Mean *in vitro* activity of prodigiosin (**1**) and prodigosenes **2b-d**, **3-11** over 60 cancer cell lines; (<http://dtp.cancer.gov>); ^aGI₅₀ = half maximal growth inhibition concentration; ^bTGI = total growth inhibition concentration; ^cLC₅₀ = half maximal lethal concentration.

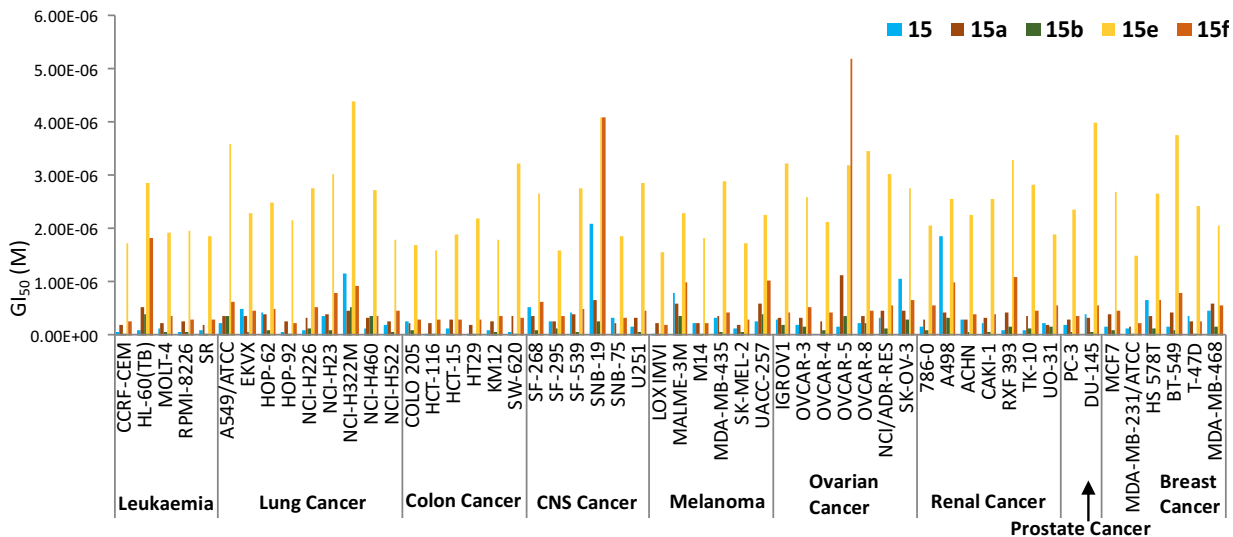


Figure 1S: GI₅₀ concentrations (half maximal growth inhibition concentrations) of prodigiosenes 15, 15a, 15b, 15e and 15f against the NCI-60 human cancer cell lines representing 9 different cancer types; see <http://http.dtp.cancer.gov>

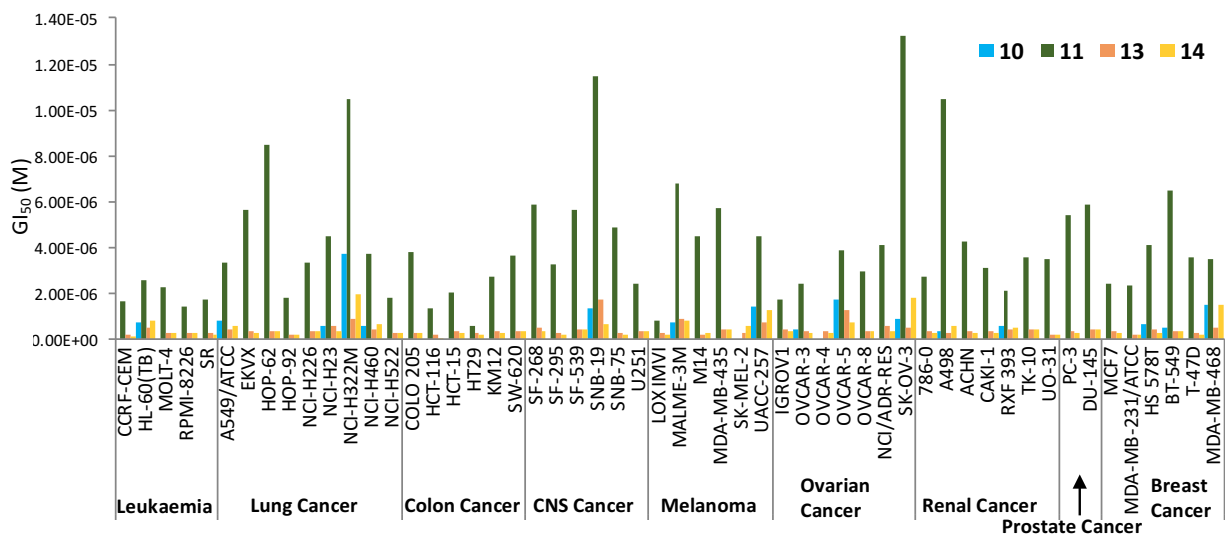
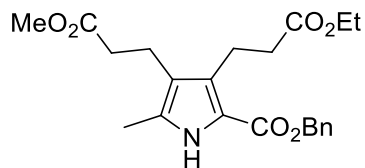


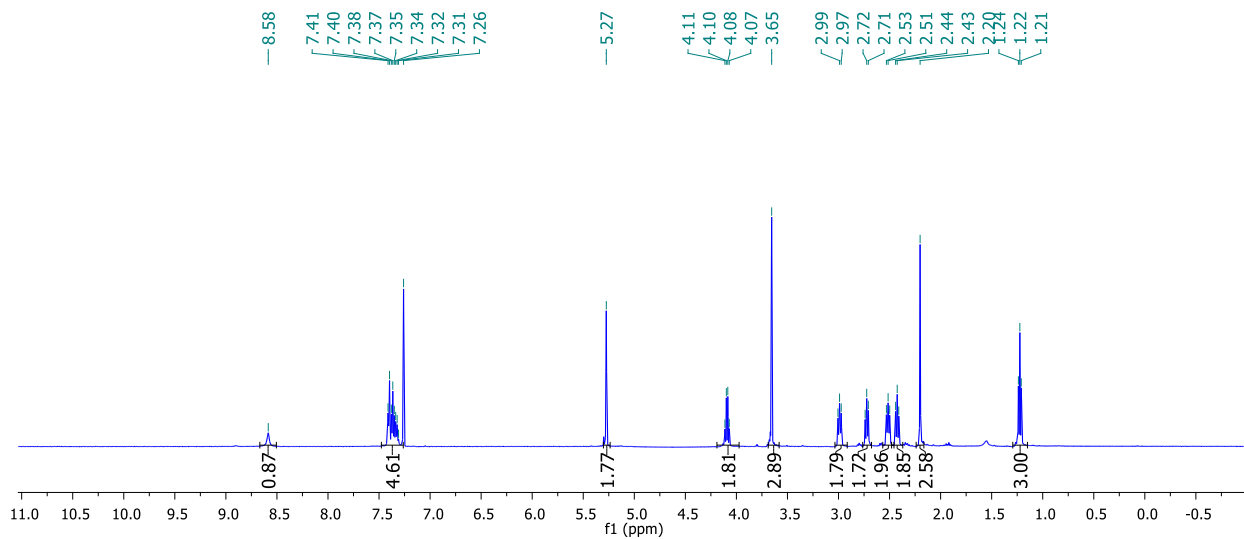
Figure 2S: GI₅₀ concentrations (half maximal growth inhibition concentrations) of prodigiosenes 10, 11, 13 and 14 against the NCI-60 human cancer cell lines representing 9 different cancer types; see <http://http.dtp.cancer.gov>

NMR Spectra

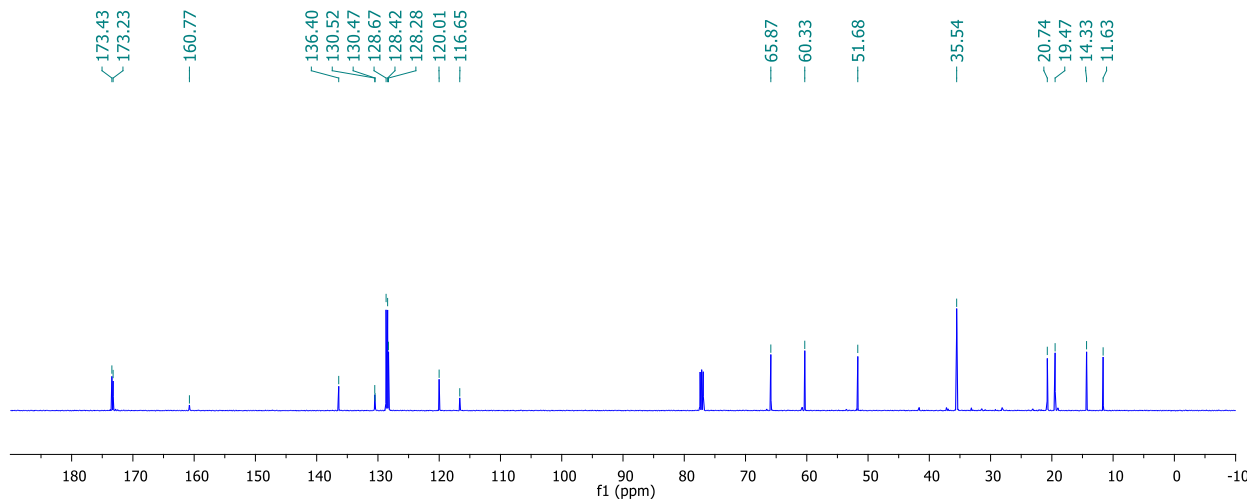
Benzyl 3-(3-ethoxy-3-oxopropyl)-4-(3-methoxy-3-oxopropyl)-5-methyl-1H-pyrrole-2-carboxylate (1)



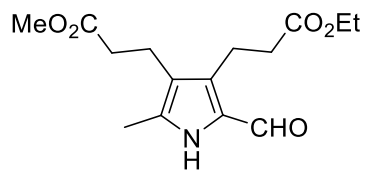
^1H NMR; 300 MHz, CDCl_3



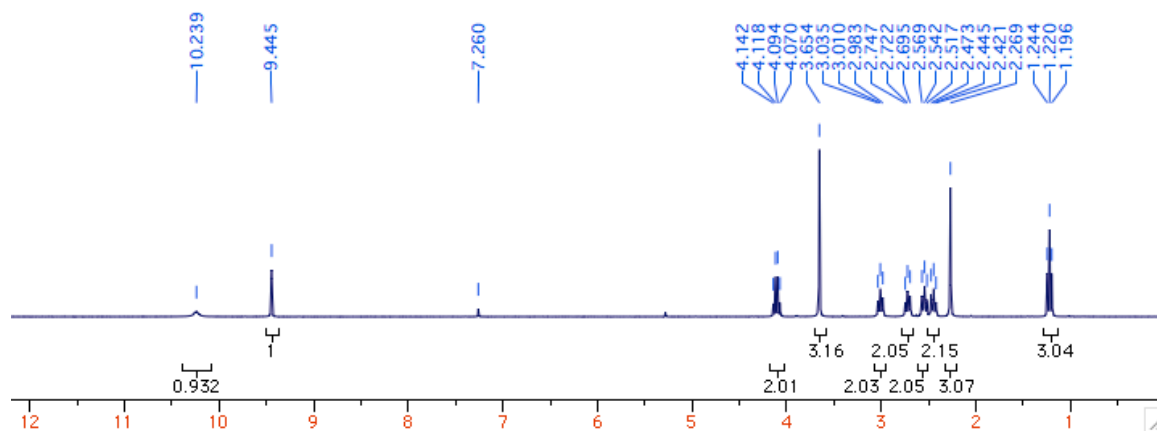
^{13}C NMR; 125 MHz, CDCl_3



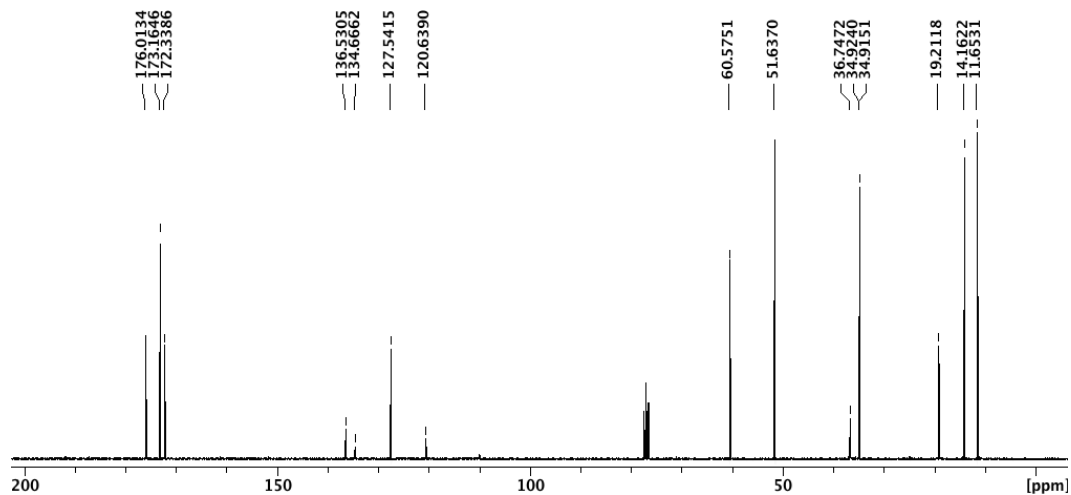
4-[(Methoxycarbonyl)ethyl]-3-[2-(ethoxycarbonyl)ethyl]-5-methyl pyrrole-2-carboxaldehyde (3)



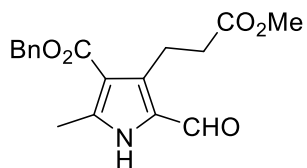
¹H NMR; 300 MHz, CDCl₃



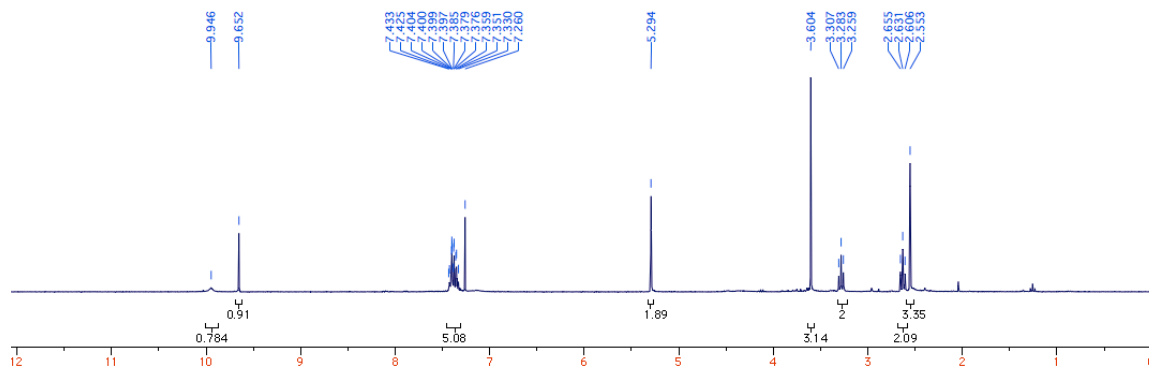
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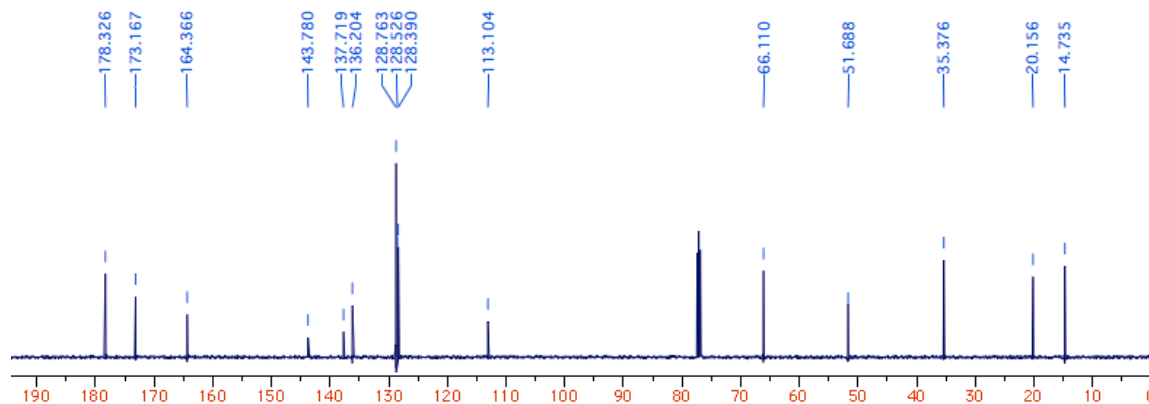
4-(Benzylmethanoate)-3[(methoxycarbonyl)ethyl]-5-methyl pyrrole-2-carboxaldehyde (4)



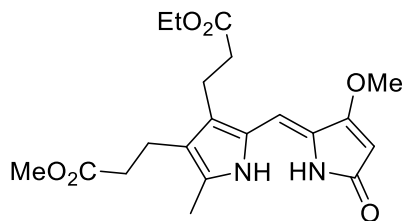
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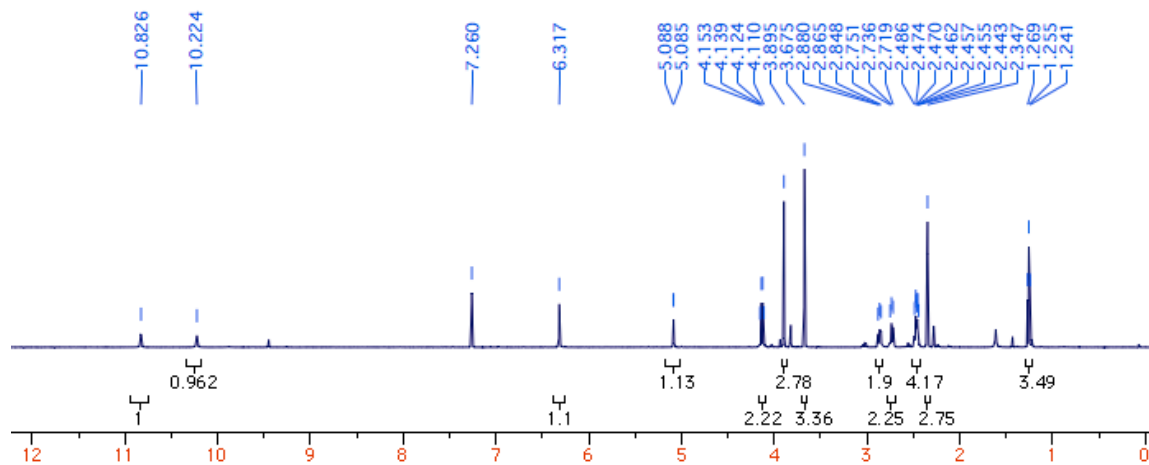
^{13}C NMR; 125 MHz, CDCl_3



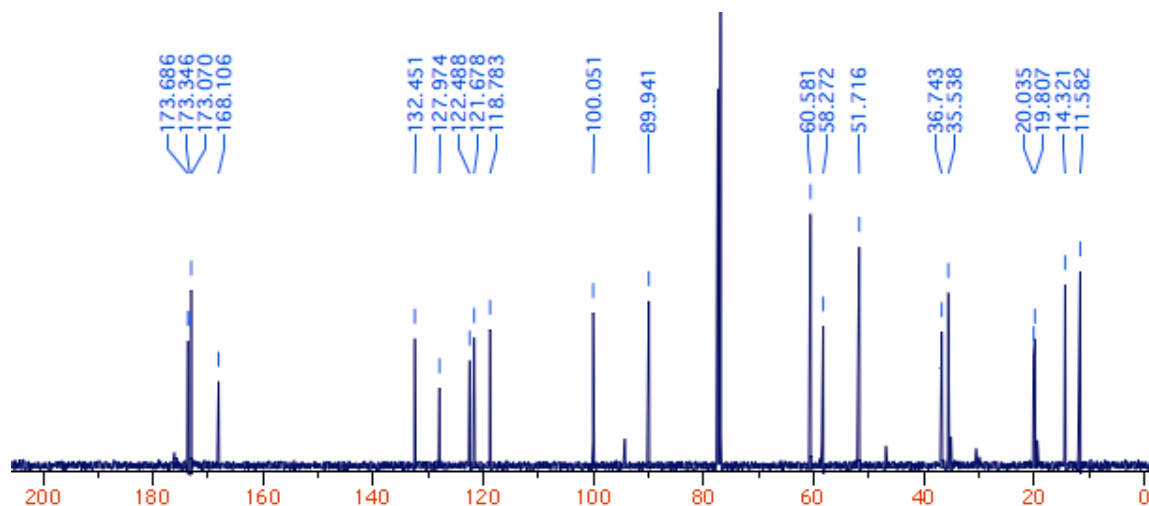
(Z)-Ethyl 3-(4-(3-methoxy-3-oxopropyl)-2-((3-methoxy-5-oxo-1H-pyrrol-2(5H)-ylidene)methyl)-5-methyl-1H-pyrrol-3-yl)propanoate (5)



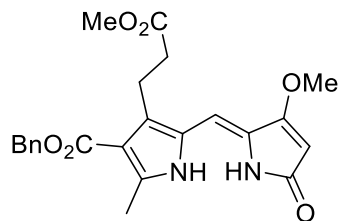
^1H NMR; 500 MHz, CDCl_3



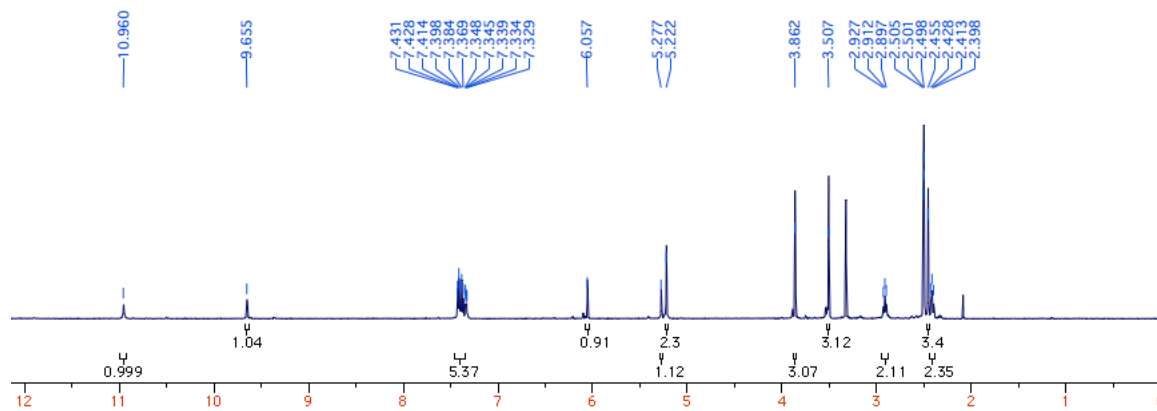
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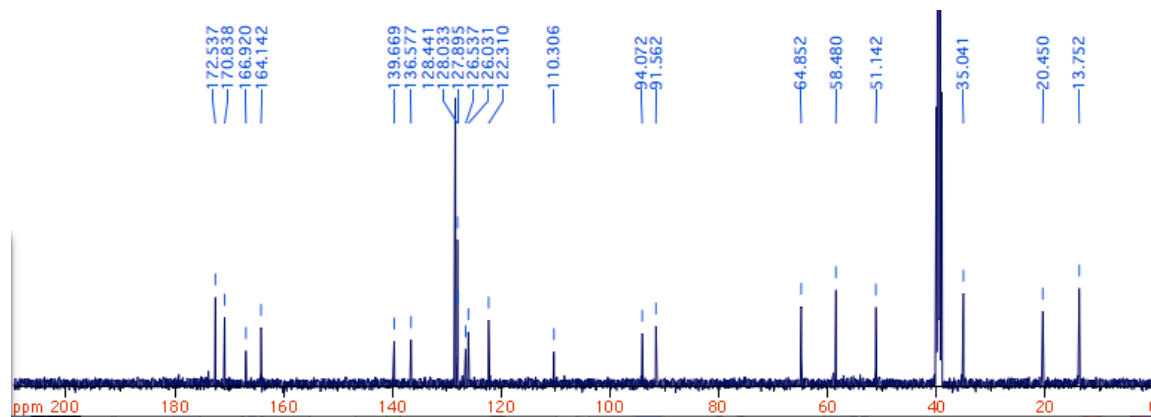
(Z)-Benzyl 4-(3-(3-methoxy-3-oxopropyl)-2-(3-methoxy-5-oxo-1H-pyrrole-2(5H)-ylidene)methyl)-5-methyl-1H-pyrrol-3-yl)formate (6)



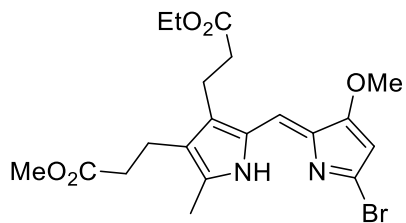
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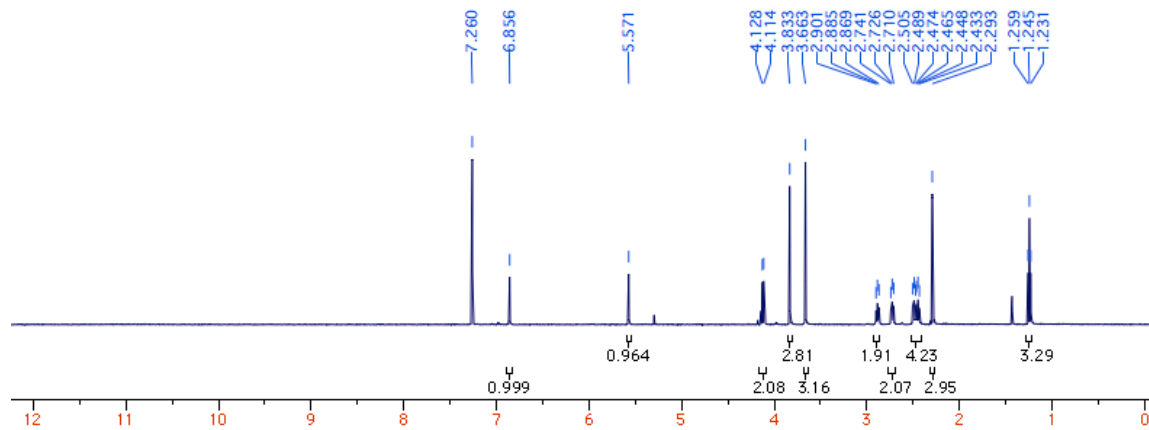
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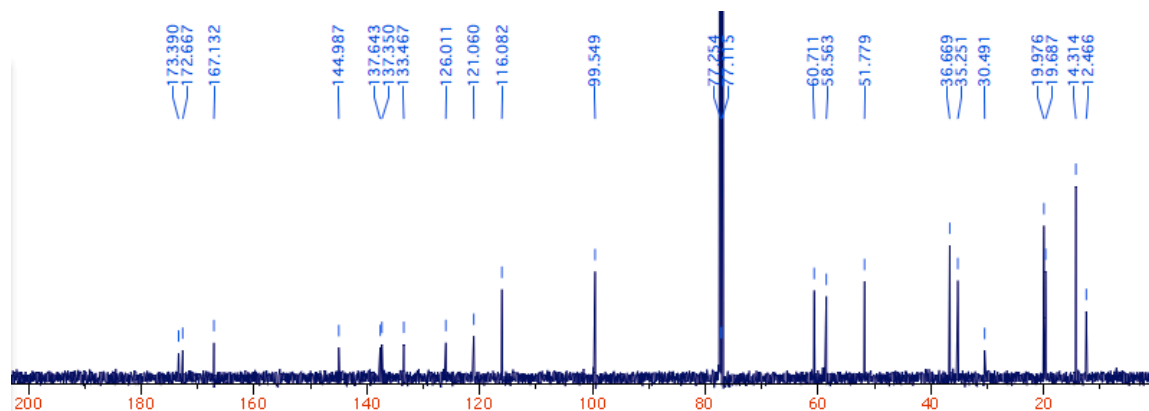
(Z)-Ethyl 3-(2-((5-bromo-3-methoxy-2H-pyrrol-2-ylidene)methyl)-4-(3-methoxy-oxopropyl)-5-methyl-1H-pyrrol-3-yl)propanoate (7)



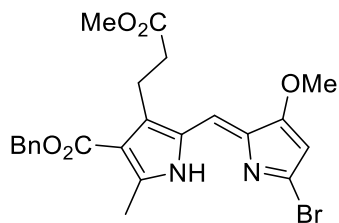
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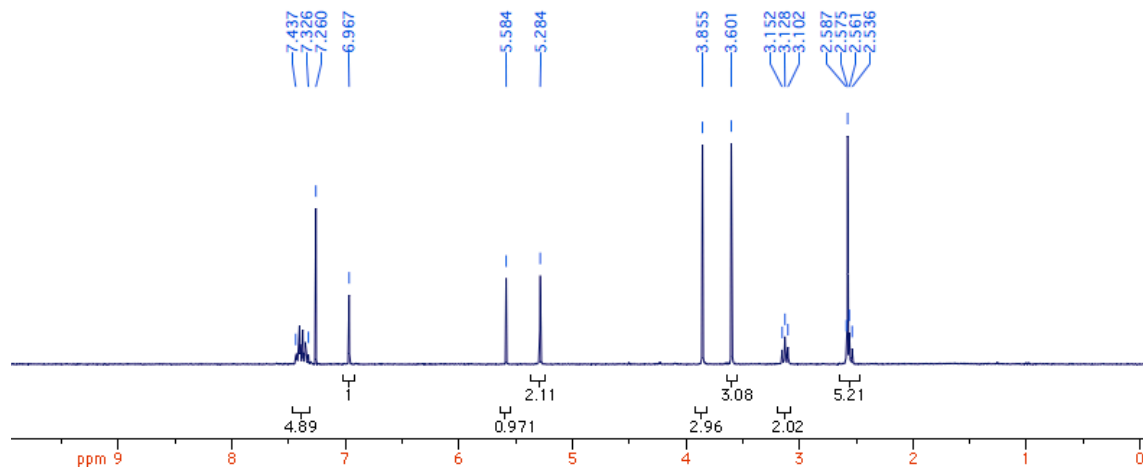
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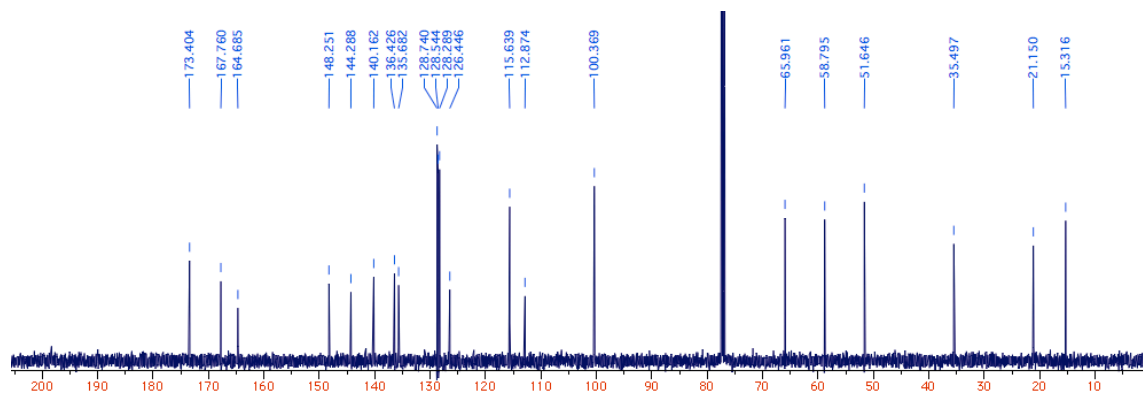
(Z)-Benzyl 4-(2-((5-bromo-3-methoxy-2H-pyrrol-2-ylidene)methyl)-3-(3-methoxy-3-oxopropyl)-5-methyl-1H-pyrrol-3-yl)formate (8)



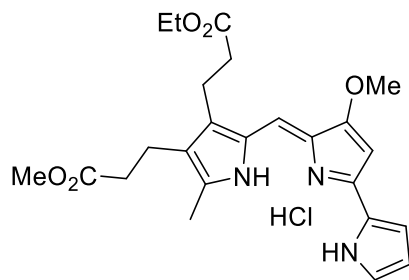
$^1\text{H NMR}$; 500 MHz, CDCl_3



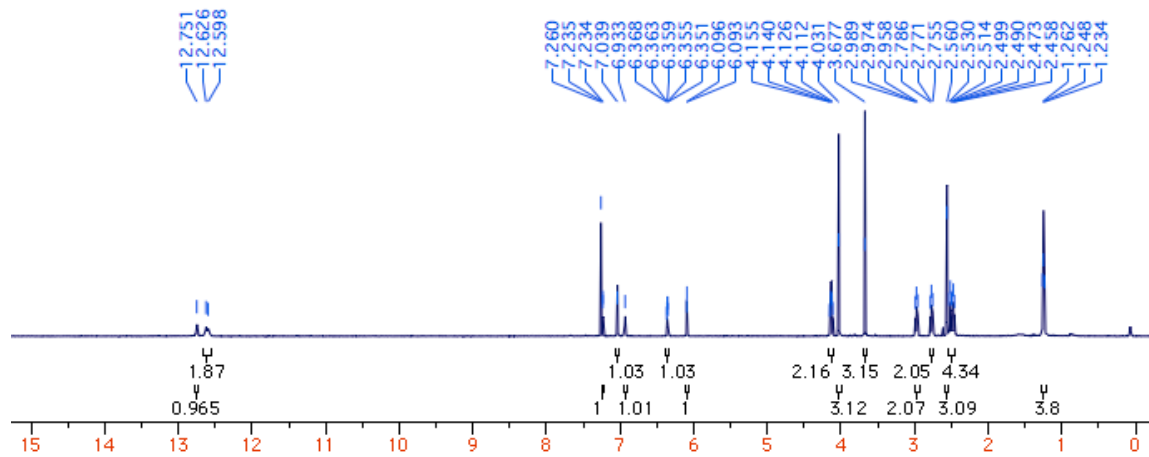
$^{13}\text{C NMR}$; 125 MHz, CDCl_3



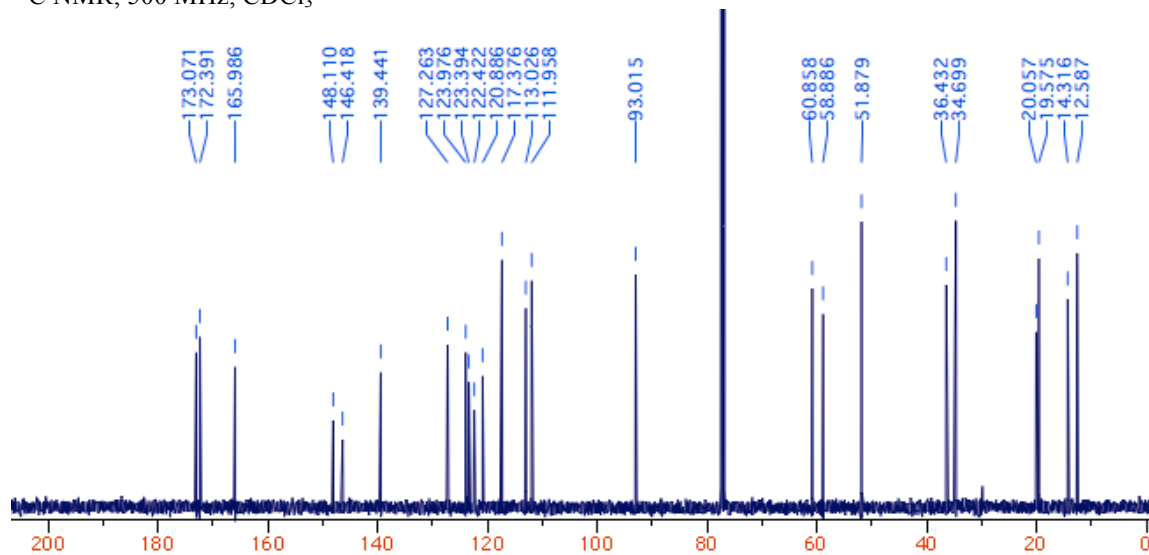
(Z)-Ethyl 3-(2-((4-methoxy-1H-1H'-[2,2'-bipyrrol]-5-yl)methylene)-4-(3-methoxy-3-oxopropyl)-5-methyl-2H-pyrrol-3-yl)propanoate hydrochloride (9•HCl)



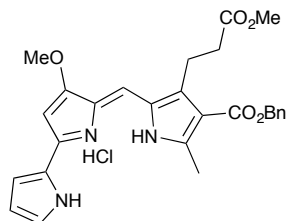
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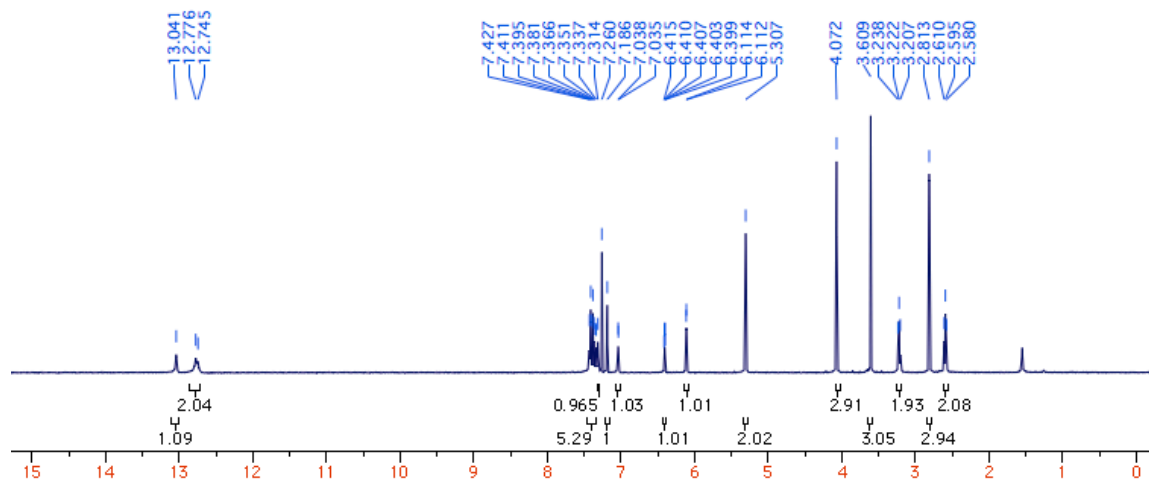
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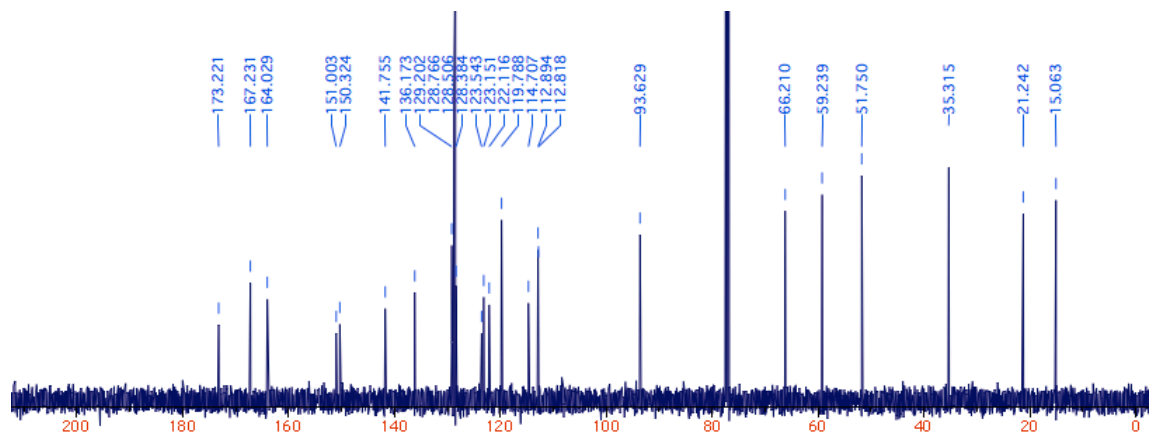
(Z)-Benzyl 4-(2-((4-methoxy-1H,1H'-[2,2'-bipyrrol]-5-yl)methylene)-3-(3-methoxy-3-oxopropyl)-5-methyl-2H-pyrrol-3-yl)formate (10•HCl)



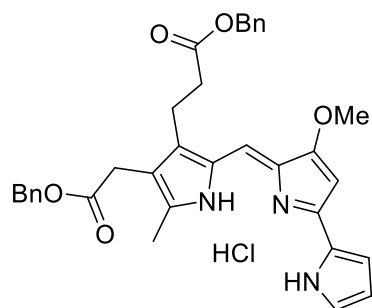
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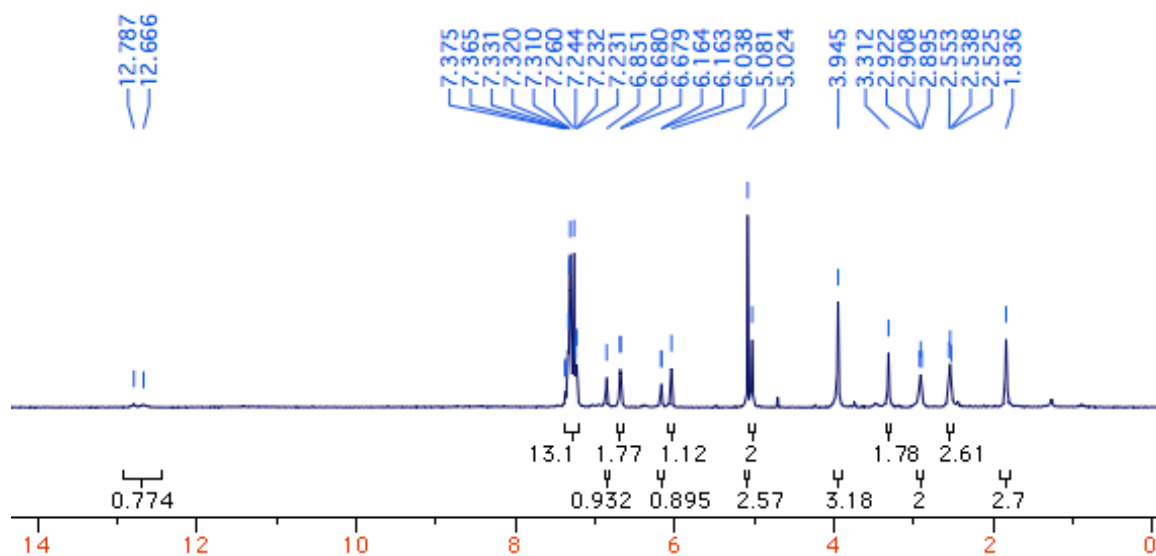
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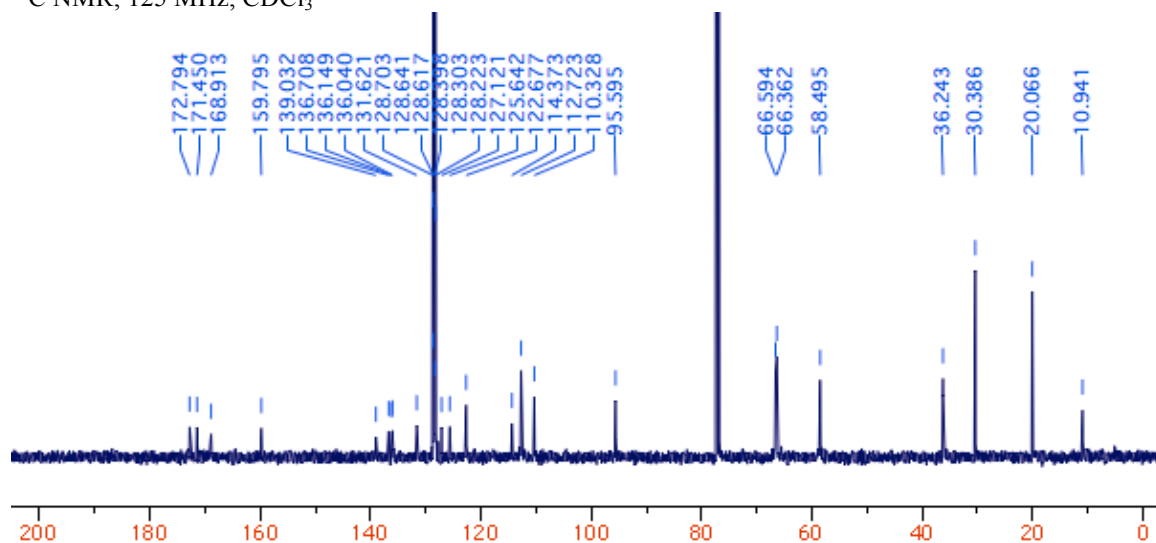
(Z)-Methyl 3-(2-((4-methoxy-1H,1'H-[2,2'-bipyrrol]-5-yl)methylene)-4-(2-methoxy-2-oxoethyl)-5-methyl-2H-pyrrol-3-yl)propanoate (13•HCl)



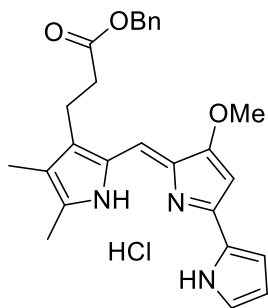
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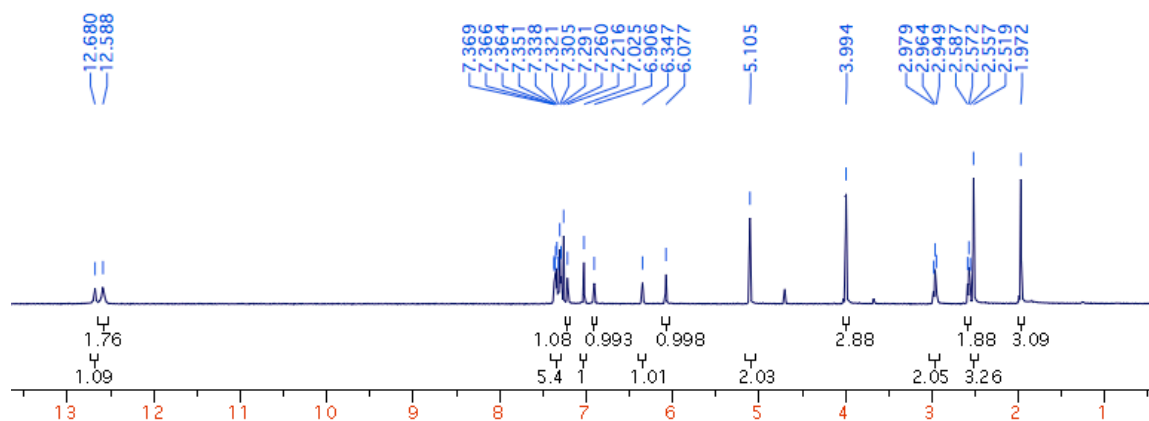
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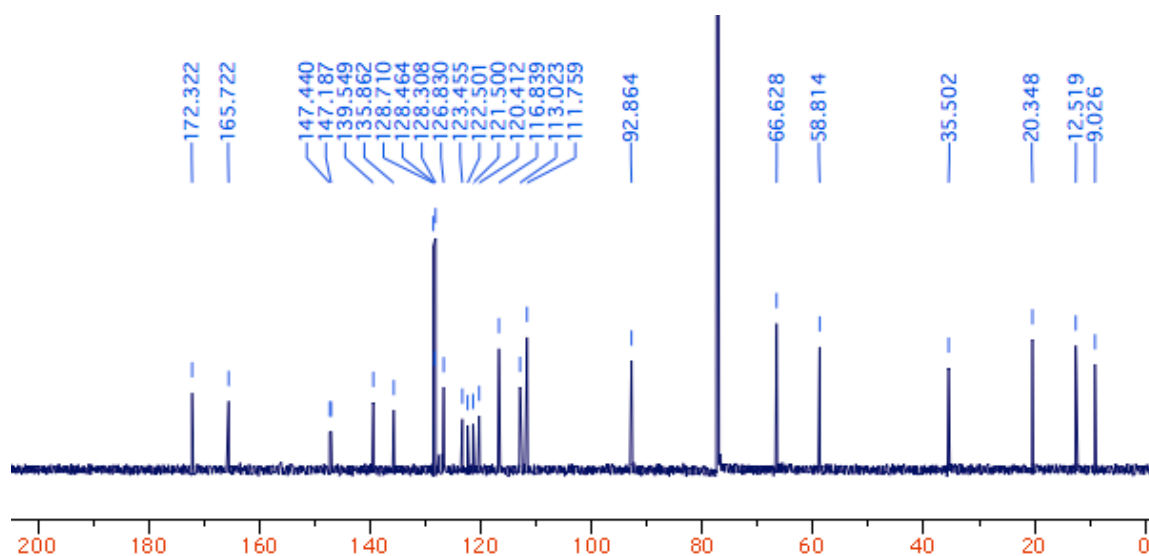
(Z)-Methyl 3-(2-((4-methoxy-1H,1'H-[2,2'-bipyrrol]-5-yl)methylene)-4,5-dimethyl-2H-pyrrol-3-yl)propanoate (14•HCl)



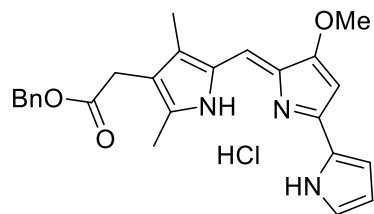
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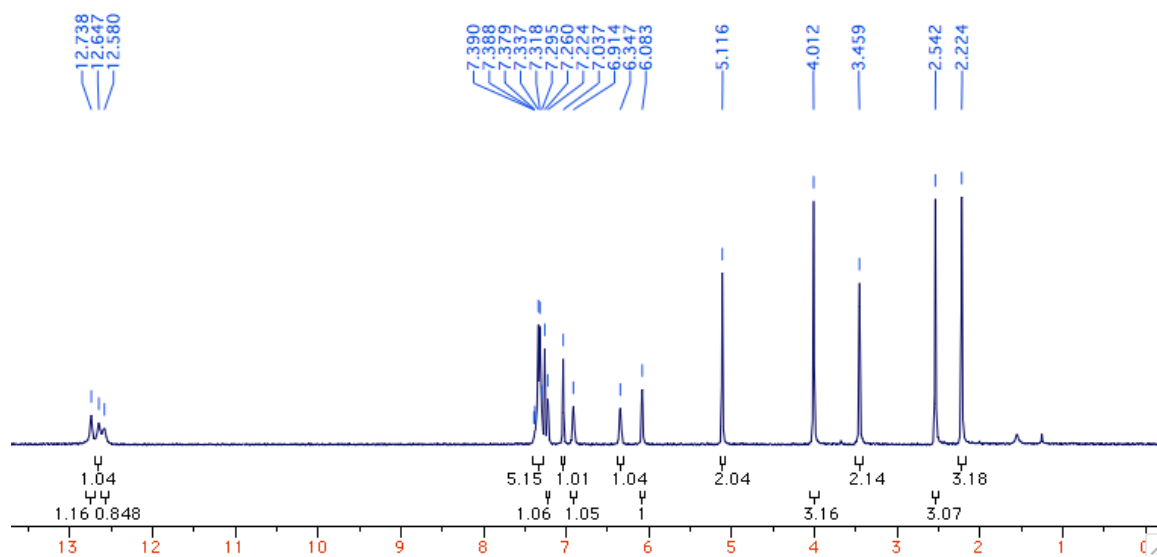
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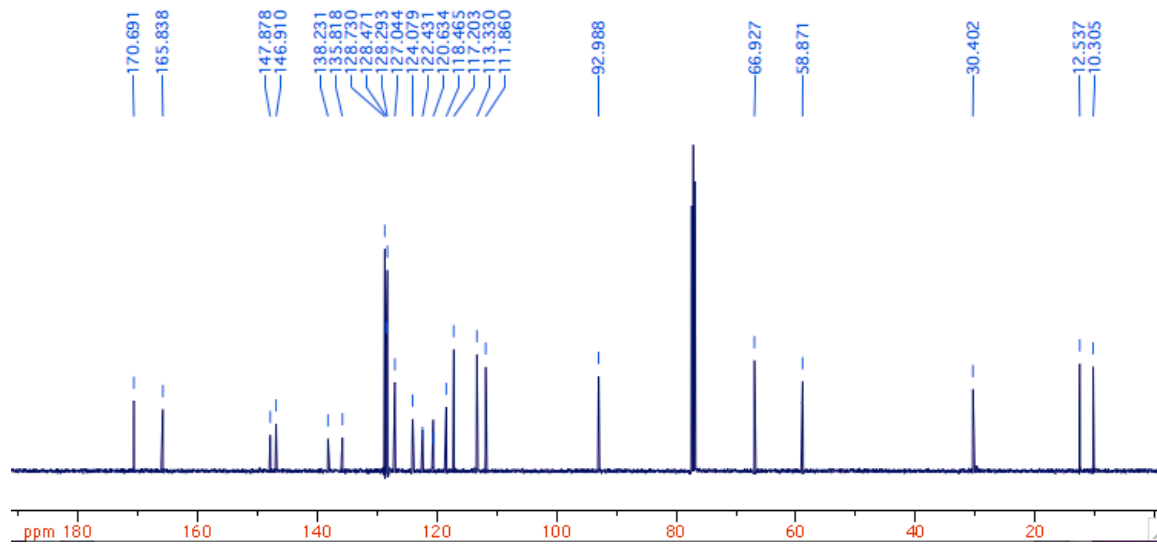
(Z)-Benzyl 2-(2-((4-methoxy-1H,1H'-[2,2'-bipyrrol]-5-yl)methylene)-3,5-dimethyl-2H-pyrrol-4-yl)acetate (15a•HCl)



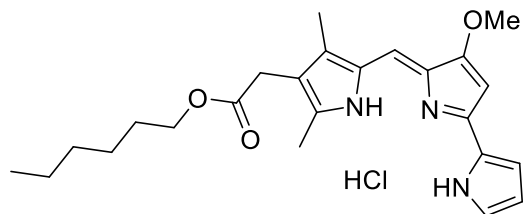
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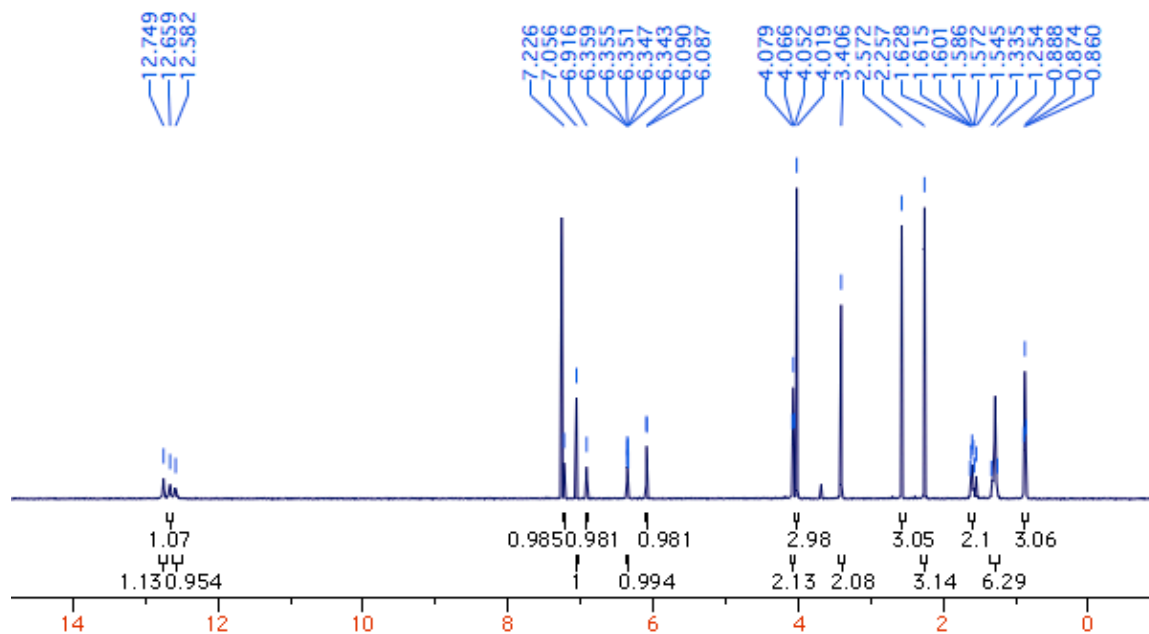
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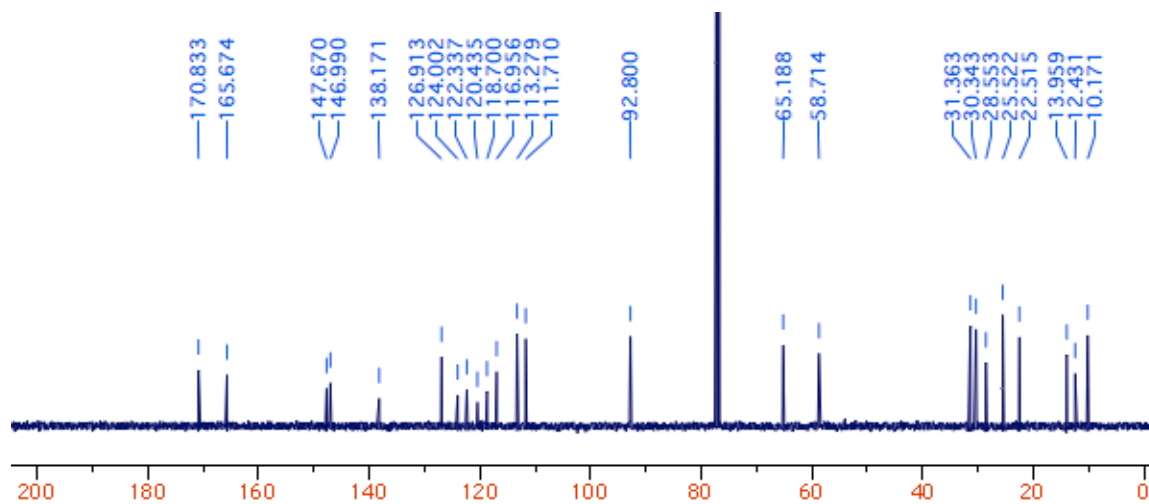
(Z)-Hexyl 2-(2-((4-methoxy-1H,1H'-[2,2'-bipyrrrol]-5-yl)methylene)-3,5-dimethyl-2H-pyrrol-4-yl)acetate (15b•HCl)



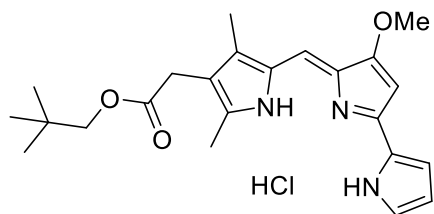
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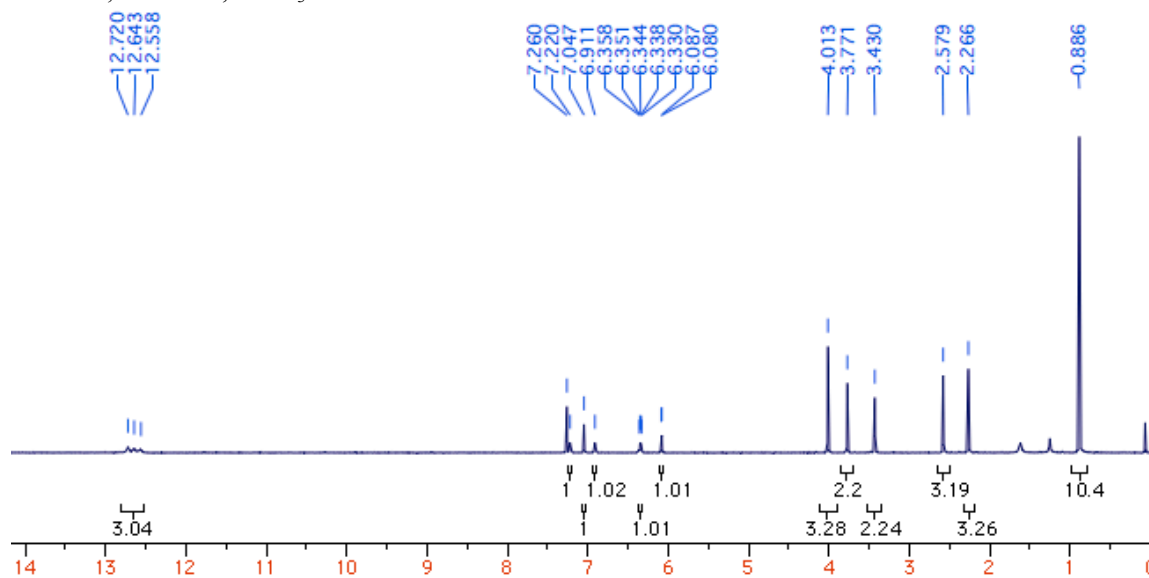
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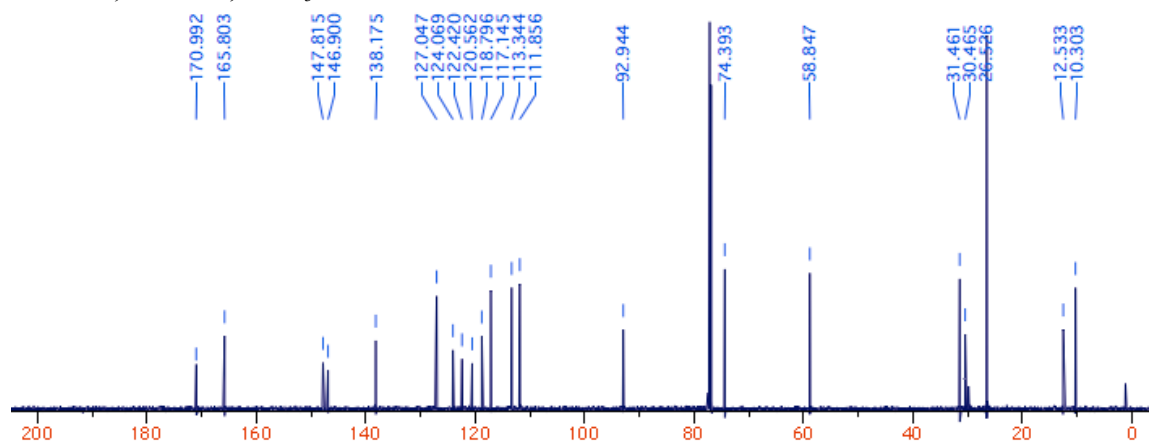
(Z)-Neopentyl 2-(2-((4-methoxy-1H,1H'-[2,2'-bipyrrol]-5-yl)methylene)-3,5-dimethyl-2H-pyrrol-4-yl)acetate hydrochloride (15c•HCl)



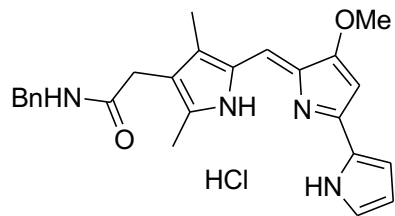
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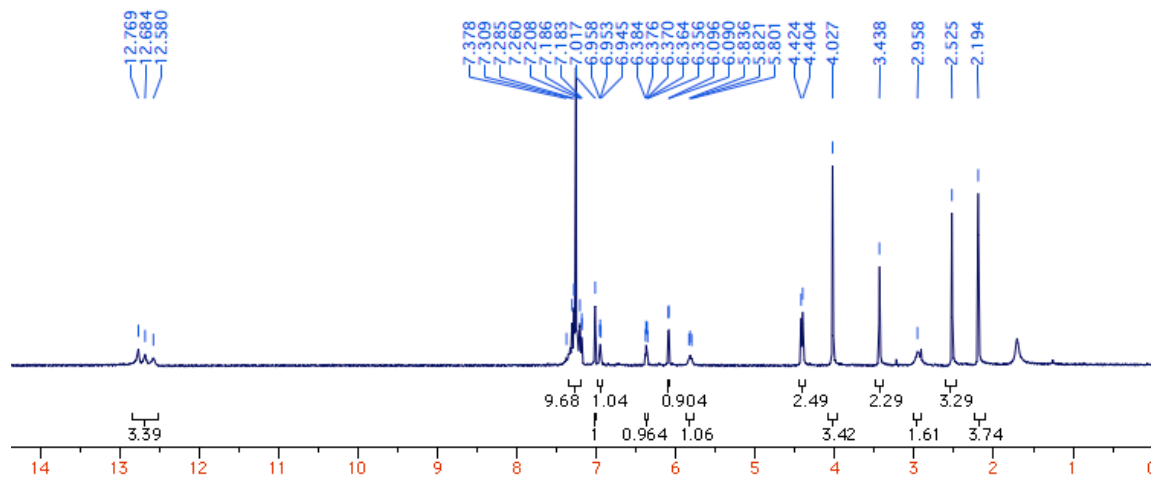
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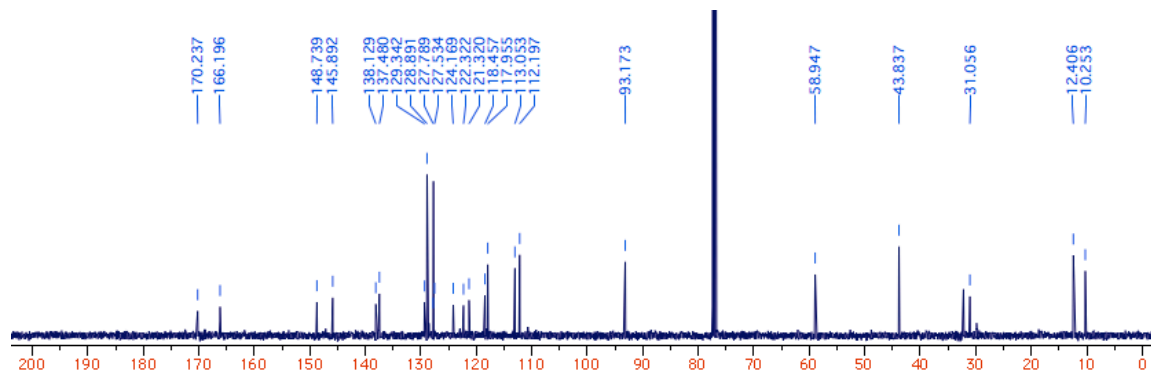
(Z)-Benzyl 2-(2-((4-methoxy-1H,1H'-[2,2'-bipyrrol]-5-yl)methylene)-3,5-dimethyl-2H-pyrrol-4-yl)acetamide hydrochloride (15d•HCl)



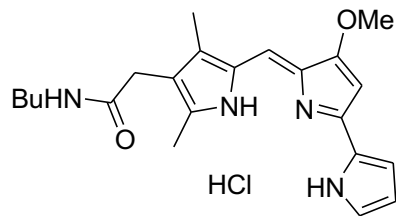
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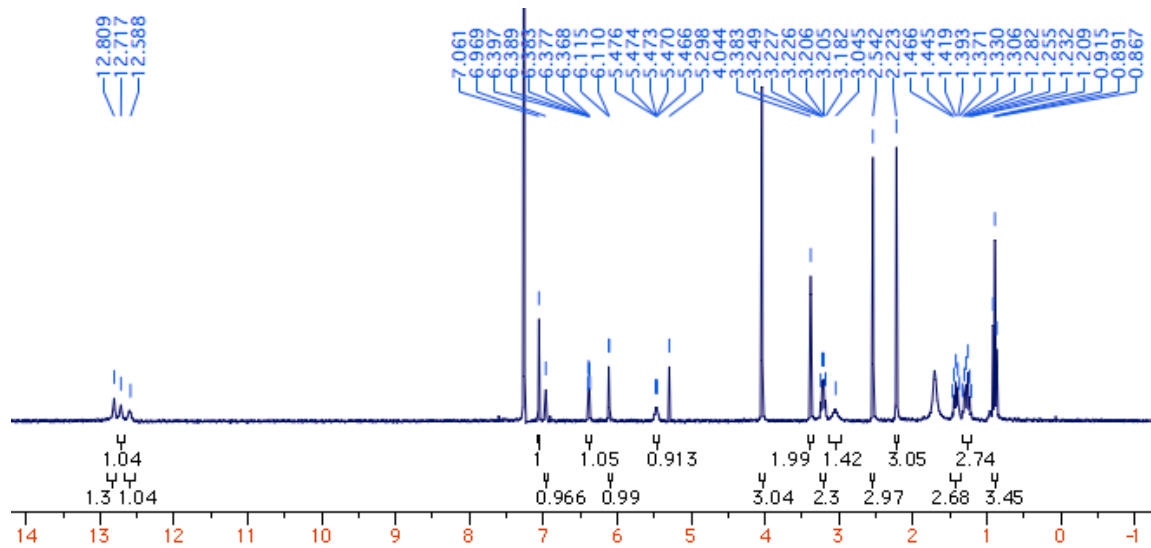
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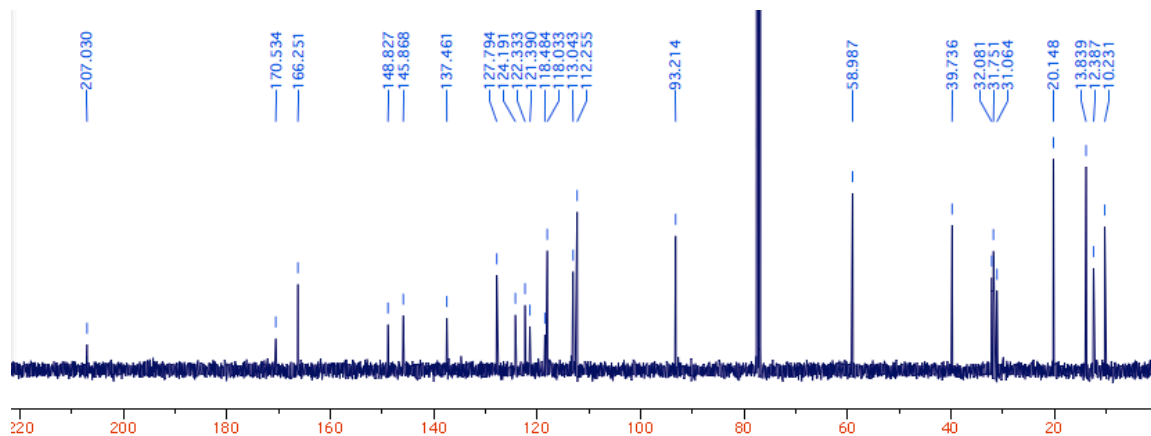
(Z)-Butyl 2-(2-((4-methoxy-1H,1H'-[2,2'-bipyrrol]-5-yl)methylene)-3,5-dimethyl-2H-pyrrol-4-yl)acetamide hydrochloride (15e•HCl)



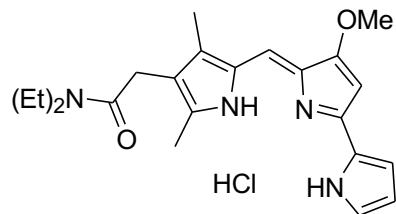
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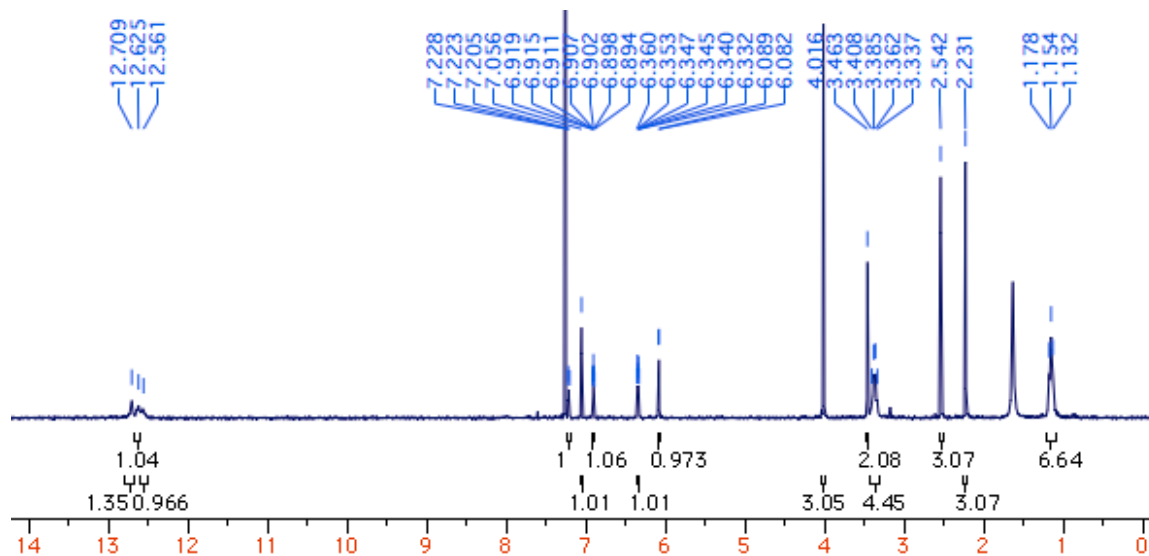
¹³C NMR; 125 MHz, CDCl₃



(Z)-N,N-Diethyl 2-(2-((4-methoxy-1H,1H'-[2,2'-bipyrrol]-5-yl)methylene)-3,5-dimethyl-2H-pyrrol-4-yl)acetamide hydrochloride (15f•HCl)



^1H NMR; 300 MHz, CDCl_3



^{13}C NMR; 125 MHz, CDCl_3

