10.1071/CH13254_AC

Australian Journal of Chemistry 2013, 66(12), 1594-1599

Supplementary Material

$Al(OTf)_3$ Catalysed Friedel-Crafts Michael Type Addition of Indoles to *α,β*-Unsaturated Ketones with PEG-200 as Recyclable Solvent

Al triflate Catalysed Addition of Indoles to Ketones

Mukut Gohain,[A] Jc Jacobs,[A] Charlene Marais,[A] and Barend C.B. Bezuidenhoudt[A,B]

[A]Department of Chemistry, University of the Free State, PO Box 339, Bloemfontein 9300, South Africa.

[B]Corresponding author. E-mail: bezuidbc@ufs.ac.za

Experimental

General procedure for Microwave heating

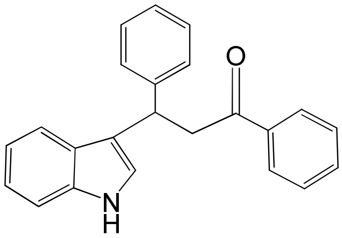
Indole **1** (1 mmol) was added to a solution of α,β-unsaturated ketone **2** (1.15 mmol) in polyethylene glycol-200 (2 mL) contained in a 35 ml microwave vial. Al(OTf)3 (2.5 mol%) was added and the vial sealed with a septum and stirred at 80 ^{o}C (300 Watt, power cycling method, CEM microwave, Model: DISCOVER-SP W/ACTIVENT) for the time period indicated in Table 2. After completion of the reaction (TLC), ice cold water (10 mL) was slowly added to the reaction mixture by dropping funnel over a 10 minute period and the mixture allowed to stir until solid precipitation was completed (monitored by TLC). Afterwards another batch of ice cold water (10mL) was added and stirring continued for another 10 minutes. The solid was filtered off and the water removed from the PEG by vacuum distillation on a rotary evaporator at 80 ^{0}C. The solid obtained by filtration was further purified by recrystallization from aqueous ethanol (30% v/v) or by FCC.

General procedure for Conventional Heating

Indole **1** (1 mmol) was added to a solution of α,β-unsaturated ketone **2** (1.15 mmol) in polyethylene glycol-200 (2 mL) and Al(OTf)3 (2.5 mol%) added. The reaction mixture was heated to 80^{o}C and stirred for the time indicated in tables 1 and 2. After completion of the reaction (TLC) the products were isolated as described under the microwave method. The physical data of the compounds were identical to those previously published (see references in Table 2).

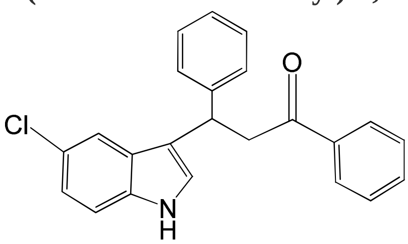
NMR Data

3-(1H-Indol-3-yl)-1,3-diphenylpropan-1-one (3aa)[19]



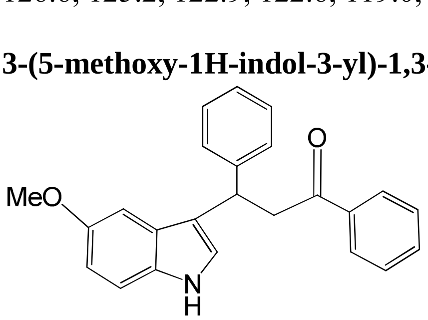
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 (br, s, 1H), 7.97 – 7.91 (m, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.48 – 7.33 (m, 6H) , 7.27 (d, *J* = 9.4 Hz, 2H), 7.17 (dd, *J* = 14.6, 7.3 Hz, 2H), 7.03 (dd, *J* = 8.9, 5.0 Hz, 2H), 5.09 (t, *J* = 7.2 Hz, 1H), 3.84 (dd, *J* = 16.7, 6.8 Hz, 1H), 3.75 (dd, *J* = 16.7, 7.6 Hz, 1H).
^{13}C NMR (150 MHz, $CDCl_3$) δ 198.7, 144.3, 137.2, 136.7, 133.15, 128.7, 128.6, 128.2, 127.9, 126.7, 126.4, 122.3, 121.5, 119.6, 119.5 119.4, 111.3, 45.3, 38.3.

3-(5-chloro-1*H*-indol-3-yl)-1,3-diphenylPropan-1-one (3ba)[27]:



^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09 (br, s, 1H), 7.99 – 7.93 (m, 2H), 7.60 – 7.55 (m, 1H), 7.49 – 7.44 (m, 2H), 7.41 (d, *J* = 2.0 Hz, 1H), 7.38 – 7.27 (m, 4H), 7.23 – 7.18 (m, 2H), 7.10 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.00 (d, *J* = 2.1 Hz, 1H), 5.03 (t, *J* = 7.2 Hz, 1H), 3.81 (dd, *J* = 16.8, 7.3 Hz, 1H), 3.72 (dd, *J* = 16.8, 7.2 Hz, 1H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 198.6, 143.9, 137.1, 135.0, 133.3, 128.7, 128.7, 128.2, 127.8, 126.6, 125.2, 122.9, 122.6, 119.0, 118.9, 112.3, 77.4, 76.9, 45.3, 38.1.

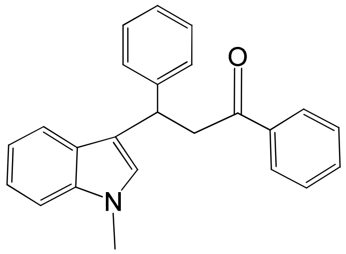
3-(5-methoxy-1H-indol-3-yl)-1,3-diphenylpropan-1-one (3da)[27]:



^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 – 7.95 (m, 2H), 7.92 (br, s, 1H), 7.59 – 7.54 (m, 1H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.38 (d, *J* = 7.3 Hz, 2H), 7.32 – 7.25 (m, 1H), 7.20 (dd, *J* = 15.7, 8.1 Hz, 2H),

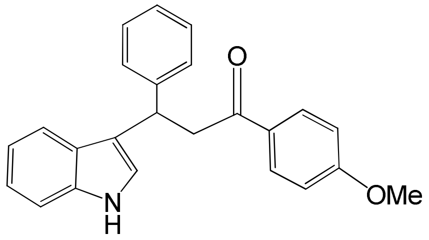
6.97 (d, *J* = 2.1 Hz, 1H), 6.87 (d, *J* = 2.3 Hz, 1H), 6.83 (dd, *J* = 8.7, 2.4 Hz, 1H), 5.05 (t, *J* = 7.2 Hz, 1H), 3.82 (dd, *J* = 16.7, 6.8 Hz, 1H), 3.78 – 3.72 (m, 2H).
^{13}C NMR (150 MHz, $CDCl_3$) δ 198.8, 153.9, 144.3, 137.2, 133.2, 131.8, 128.7, 128.6, 128.2, 127.9, 127.2, 126.4, 122.3, 119.1, 112.3, 111.9, 101.6, 55.9, 45.2, 38.3.

3-(1-methyl-1*H*-indol-3-yl)-1,3-diphenylpropan-1-one (**3ea**)[23]:



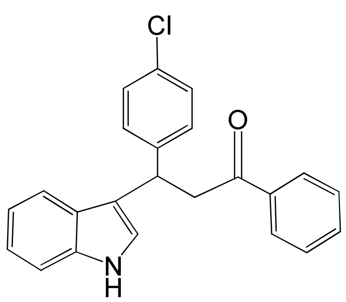
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 – 7.94 (m, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.50-7.43 (m, 3H), 7.39 (d, *J* = 7.3 Hz, 2H), 7.31 – 7.27 (m, 2H), 7.24 – 7.17 (m, 1H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.87 (s, 1H), 5.10 (t, *J* = 7.2 Hz, 1H), 3.84 (dd, *J* = 16.8, 6.7 Hz, 1H), 3.78 (dd, *J* = 16.8, 7.8 Hz, 1H), 3.74 (s, 3H).
^{13}C NMR (150 MHz, $CDCl_3$) δ 198.6, 144.5, 137.4, 137.2, 133.1, 128.7, 128.6, 128.2, 127.9, 127.1, 126.4, 121.8, 119.7, 118.9, 117.9, 109.3, 45.5, 38.2, 32.8.

3-(1*H*-indol-3-yl)-1-(4-methoxyphenyl)-3-phenylpropan-1-one (3ac)[23]:



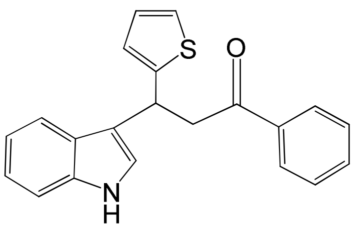
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (br, s, 1H), 7.97 – 7.93 (m, 2H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.37 (d, *J* = 7.4 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 1H), 7.30 – 7.25 (m, 2H), 7.20 – 7.15 (m, 2H), 7.06 – 6.98 (m, 2H), 6.95 – 6.90 (m, 2H), 5.09 (t, *J* = 7.2 Hz, 1H), 3.87 (s, 3H), 3.79 (dd, *J* = 16.5, 6.9 Hz, 1H), 3.69 (dd, *J* = 16.5, 7.6 Hz, 1H).
^{13}C NMR (150 MHz, $CDCl_3$) δ 197.2, 163.5, 144.5, 136.7, 130.5, 130.3, 128.5, 128.0, 126.8, 126.4, 122.2, 121.6, 119.7, 119.5, 119.5, 113.8, 111.2, 55.6, 45.0, 38.5.

3-(4-chlorophenyl)-3-(1*H*-indol-3-yl)-1-phenylpropan-1-one (3ad)[23]:



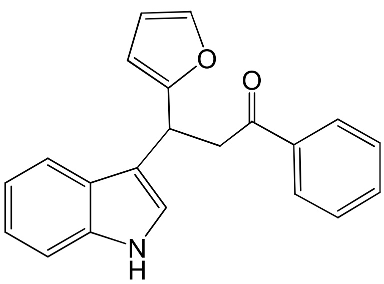
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (br, s, 1H), 7.97 – 7.91 (m, 2H), 7.60 – 7.54 (m, 1H), 7.48 – 7.34 (m, 4H), 7.32 – 7.21 (m, 4H), 7.20 – 7.17 (m, 1H), 7.08 – 6.(m, 2H), 5.07 (t, *J*= 7.2 Hz , 1H)3.82 (dd, *J* = 16.8, 6.3 Hz, 1H), 3.72 (dd, *J* = 16.8, 8.1 Hz, 1H).
^{13}C NMR (150 MHz, $CDCl_3$) δ 198.4, 142.9, 137.1, 136.8, 133.3, 132.1, 129.4, 128.8, 128.7, 128.2, 126.6, 122.5, 121.5, 119.7, 119.6, 119.1, 111.3, 45.1, 37.7.

3-(1*H*-indol-3-yl)-1-phenyl-3-(2-thienyl)-Propan-1-one (**3ah**)[26]:



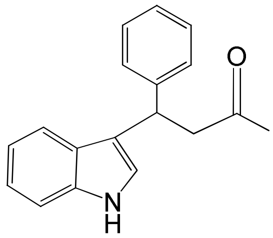
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (br, s, 1H), 7.96 (d, *J* = 7.5 Hz, 2H), 7.61 – 7.54 (m, 2H), 7.50 – 7.43 (m, 2H), 7.36 (d, *J* = 8.2 Hz, 1H), 7.21 – 7.08 (m, 4H), 6.96 – 6.89 (m, 2H), 5.39 (t, *J* = 7.0 Hz, 1H), 3.86 (dd, *J* = 7.0, 1.6 Hz, 2H).
^{13}C NMR (150 MHz, $CDCl_3$) δ 198.8, 144.6, 137.0, 136.3, 135.6, 133.1, 133.0, 128.9, 128.8, 128.5, 128.5, 128.2, 127.9, 127.7, 126.1, 122.1, 120.7, 119.8, 114.7, 111.3, 44.6, 36.9.

3-(2-furanyl)-3-(1*H*-indol-3-yl)-1-phenylpropan-1-one (3ai)[27]:



^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (br, s, 1H), 7.96 (dd, *J* = 8.3, 1.1 Hz, 2H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.57 – 7.53 (m, 1H), 7.38 – 7.32 (m, 2H), 7.21 – 7.18 (m, 1H), 7.13 – 7.09 (m, 2H), 6.28 (dd, *J* = 3.1, 1.9 Hz, 1H), 6.10 (d, *J* = 3.2 Hz, 1H), 5.17 (t, *J* = 7.0 Hz, 1H), 3.91 (dd, *J* = 16.9, 7.4 Hz, 1H), 3.72 (dd, *J* = 16.9, 6.8 Hz, 1H).
^{13}C NMR (150 MHz, $CDCl_3$) δ 198.3, 157.0, 141.3, 137.1, 136.6, 133.2, 128.7, 128.2, 126.3, 122.3, 122.2, 119.7, 119.5, 116.8, 111.4, 110.3, 105.8, 43.2, 32.2.

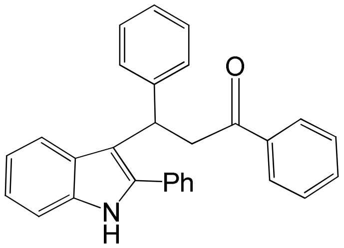
4-(1*H*-indol-3-yl)-butan-2-one (3al):



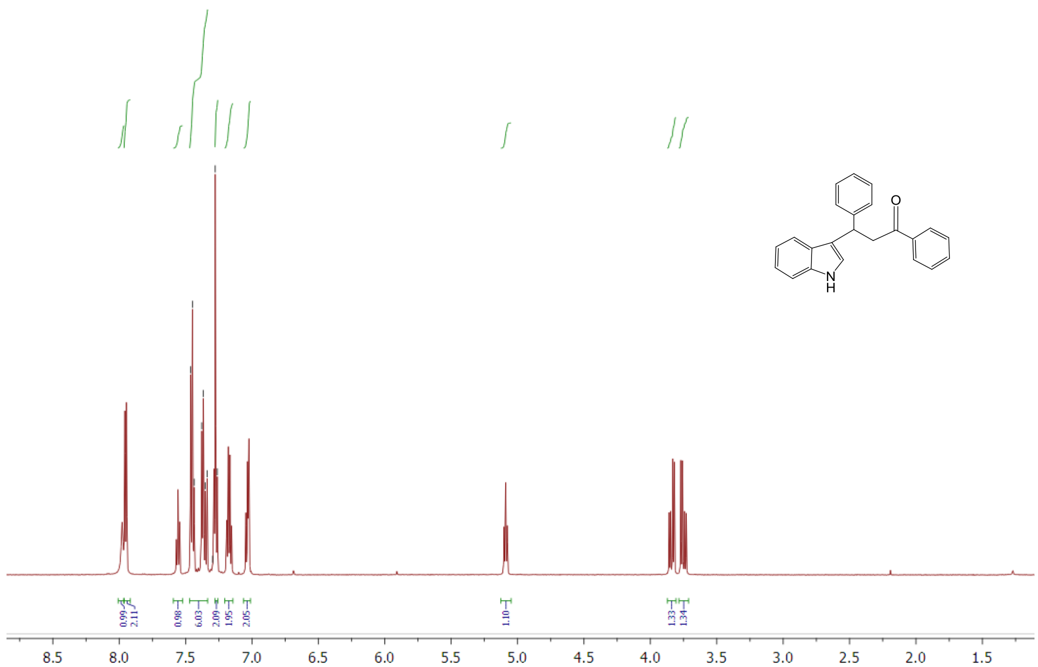
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 (br, s, 1H), 7.61 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.24 – 7.20 (m, 1H), 7.17 – 7.13 (m, 1H), 7.02 – 7.00 (m, 1H), 3.09 – 3.04 (m, 2H), 2.87 (t, *J* = 7.5 Hz, 2H), 2.17 (s, 3H).

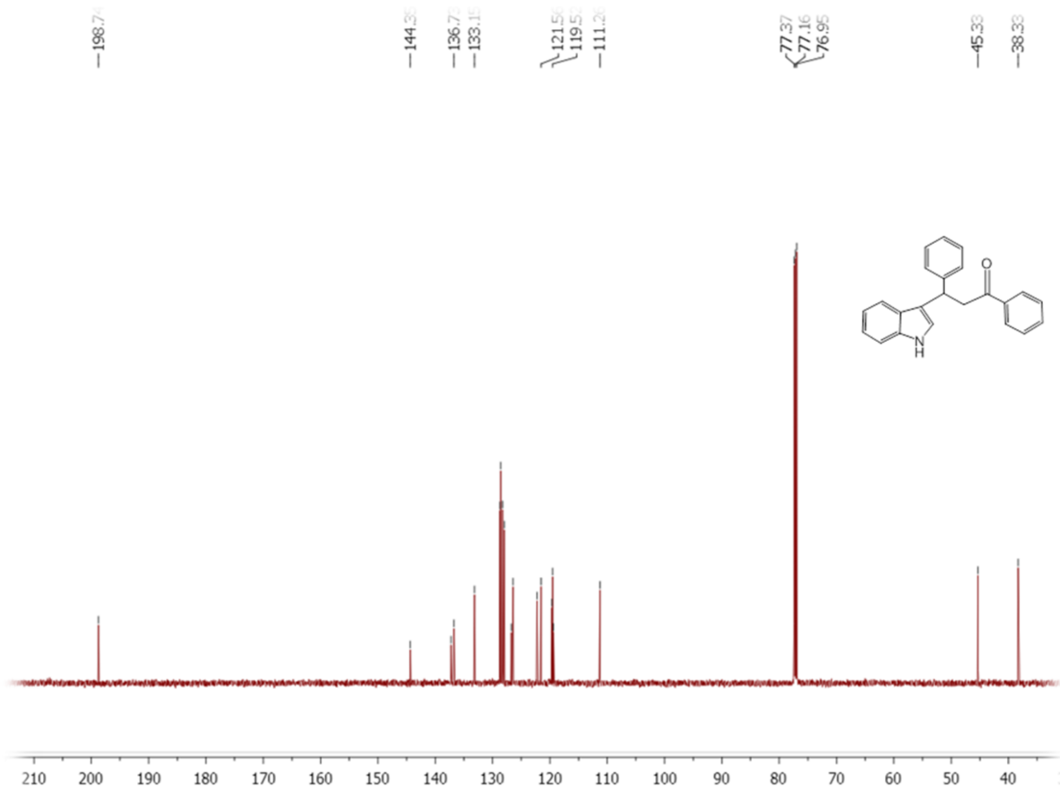
^{13}C NMR (150 MHz, $CDCl_3$) δ 209.0, 136.4, 127.3, 122.2, 121.6, 119.4, 118.8, 115.3, 111.3, 44.2, 30.2, 19.5.

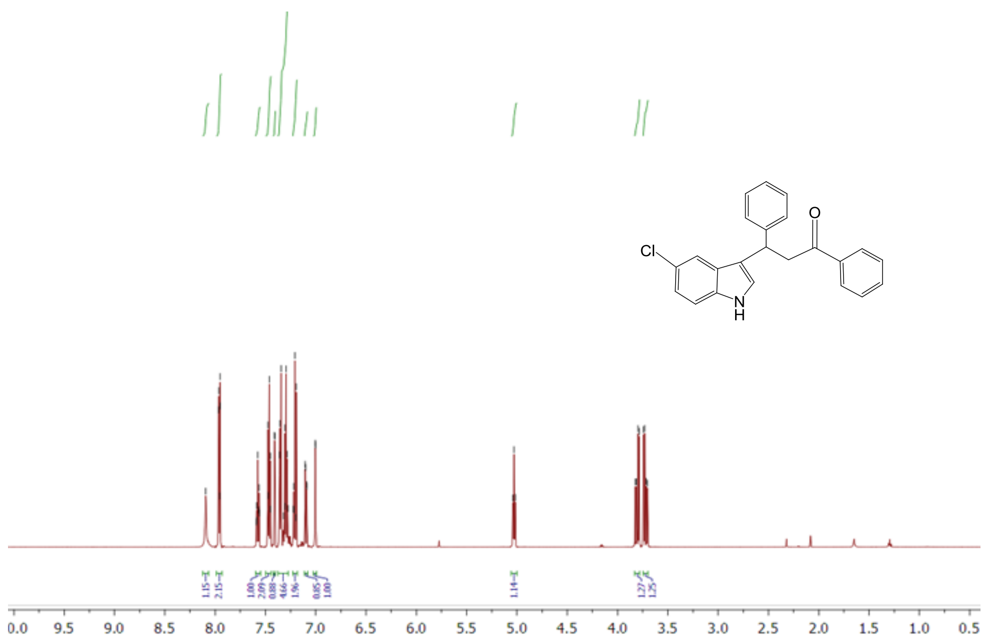
1,3-diphenyl-3-(2-phenyl-1*H*-indol-3-yl)-propan-1-one (3an)[31]

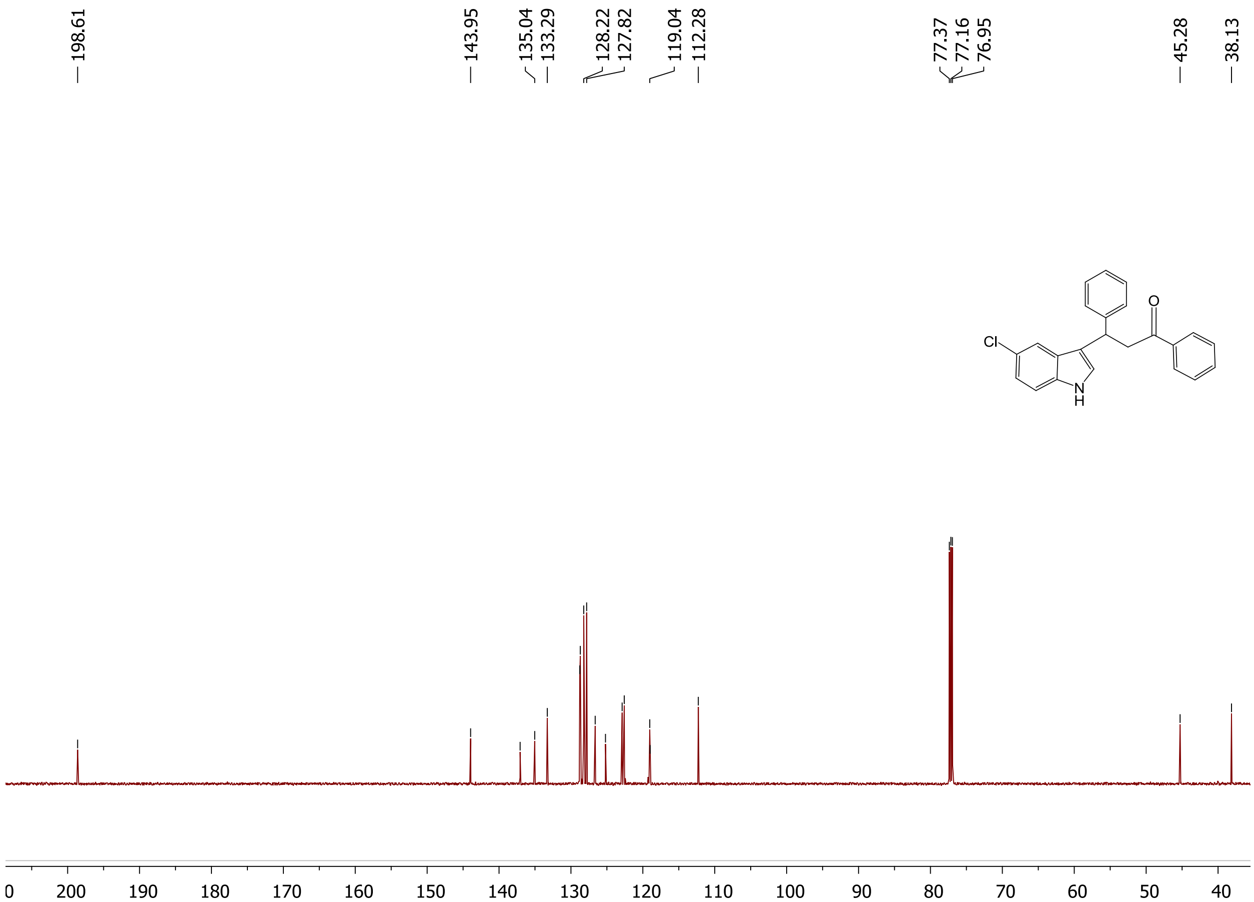


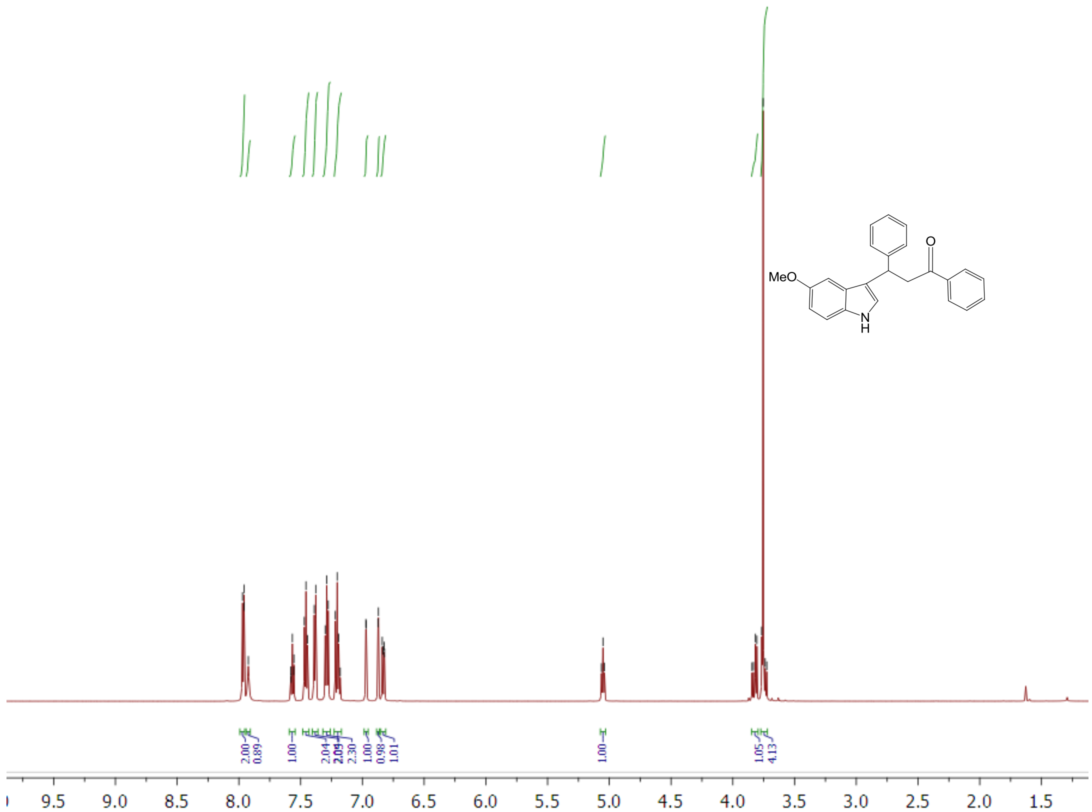
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10 (br, s, 1H), 7.89 – 7.81 (m, 2H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.56 – 7.48 (m, 3H), 7.46 – 7.34 (m, 8H), 7.30 – 7.26 (m, 2H), 7.24 – 7.18 (m, 2H), 7.15 – 7.08 (m, 1H), 5.36 (t, *J* = 6.9 Hz, 1H), 4.02 (dd, *J* = 17.0, 7.3 Hz, 1H), 3.93 (dd, *J* = 17.0, 6.6 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.8, 144.6, 137.0, 136.3, 135.6, 133.1, 133.0, 128.9, 128.8, 128.5, 128.5, 128.2, 127.9, 127.7, 126.1, 122.1, 120.7, 119.8, 114.7, 111.3, 44.6, 36.9.

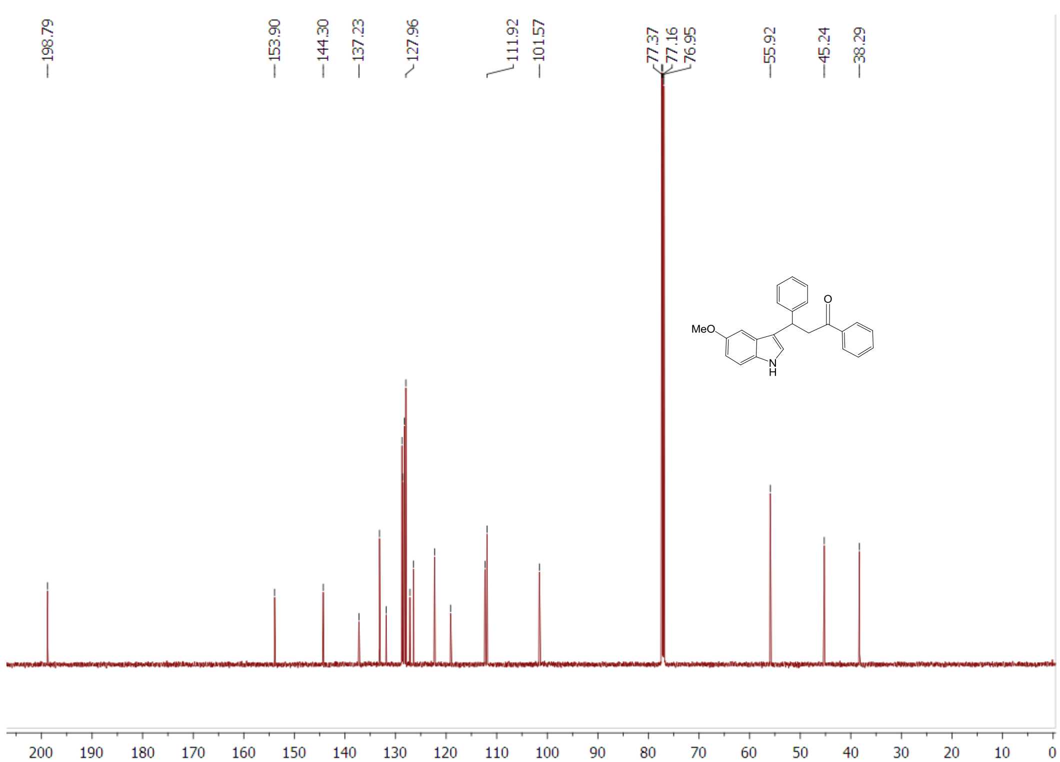

O
N
H
0.99
2.11
0.98
6.03
2.09
1.95
2.05
1.10
1.33
1.34
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

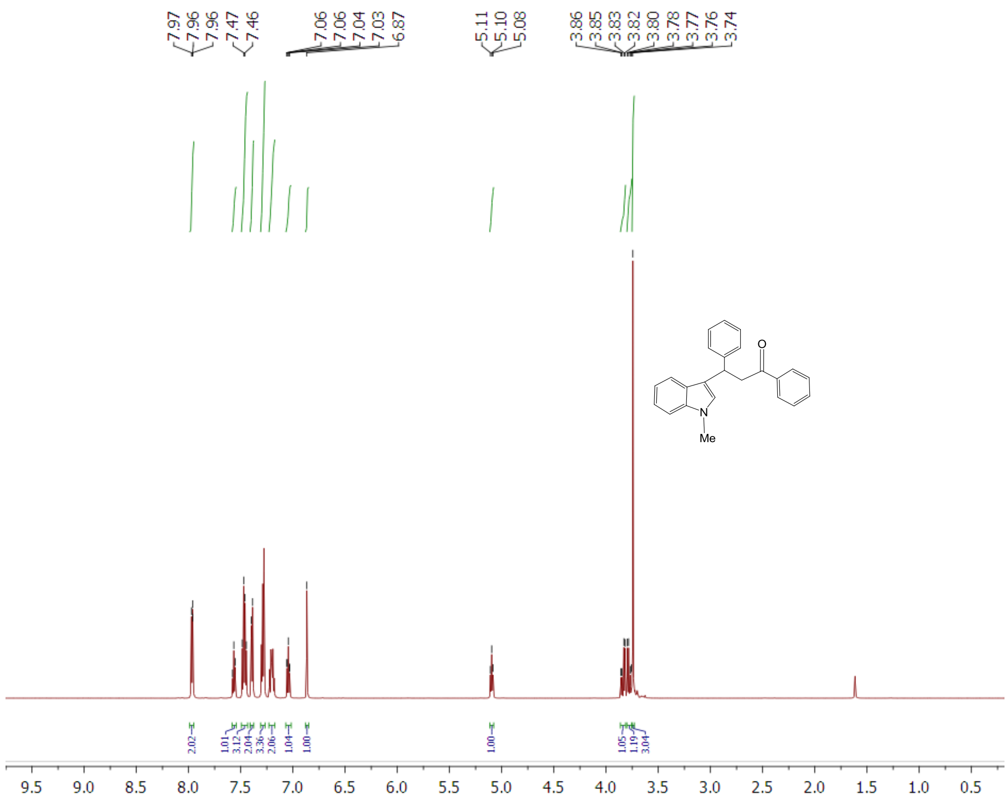

198.74
144.35
136.73
133.15
121.56
119.53
111.26
77.37
77.16
76.95
45.33
38.33
O
N
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40

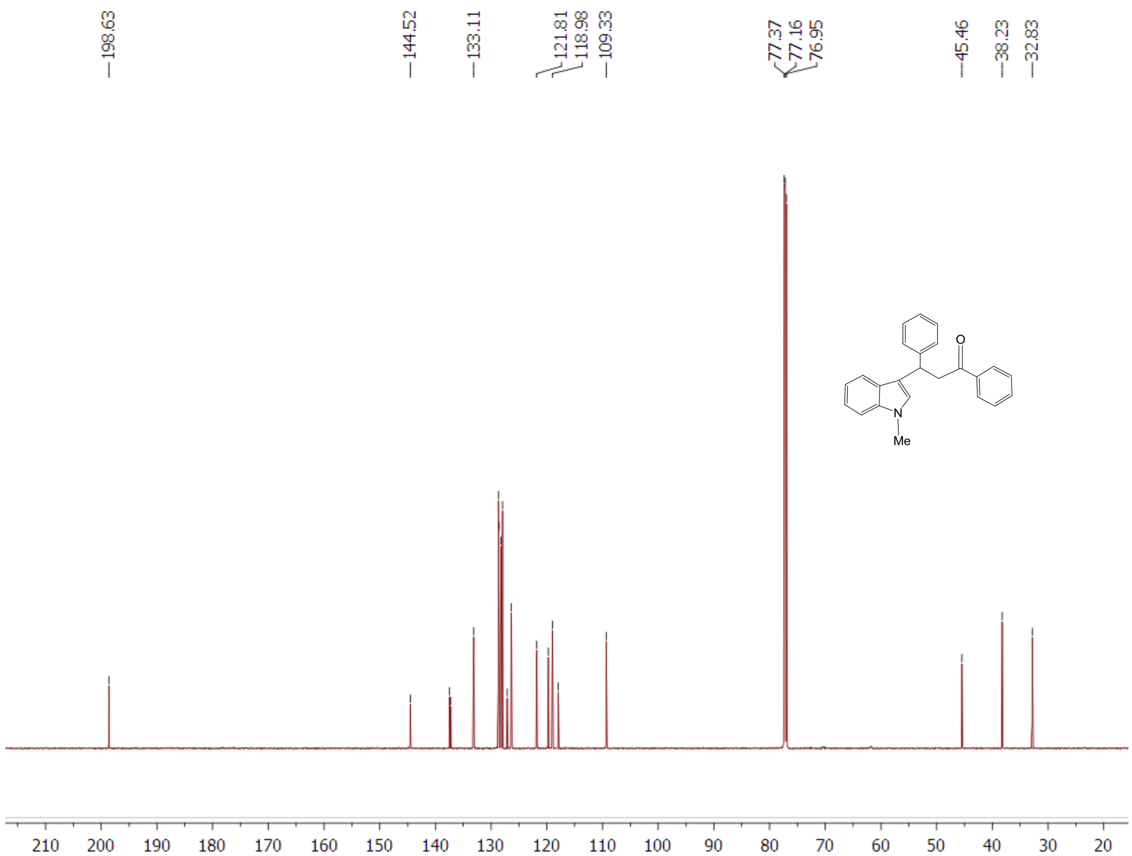

Cl
O
N
H
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5

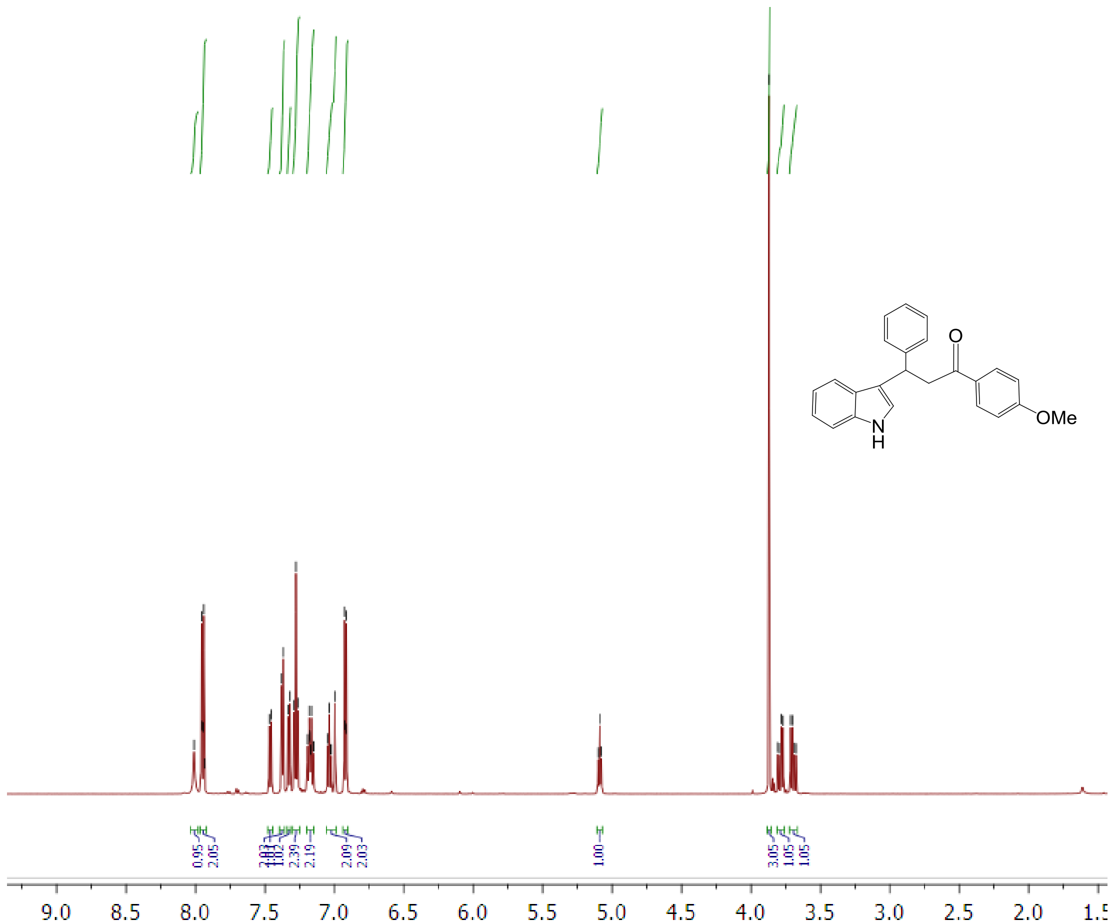

198.61
143.95
135.04
133.29
128.22
127.82
119.04
112.28
77.37
77.16
76.95
45.28
38.13
Cl
O
N
H
0 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40

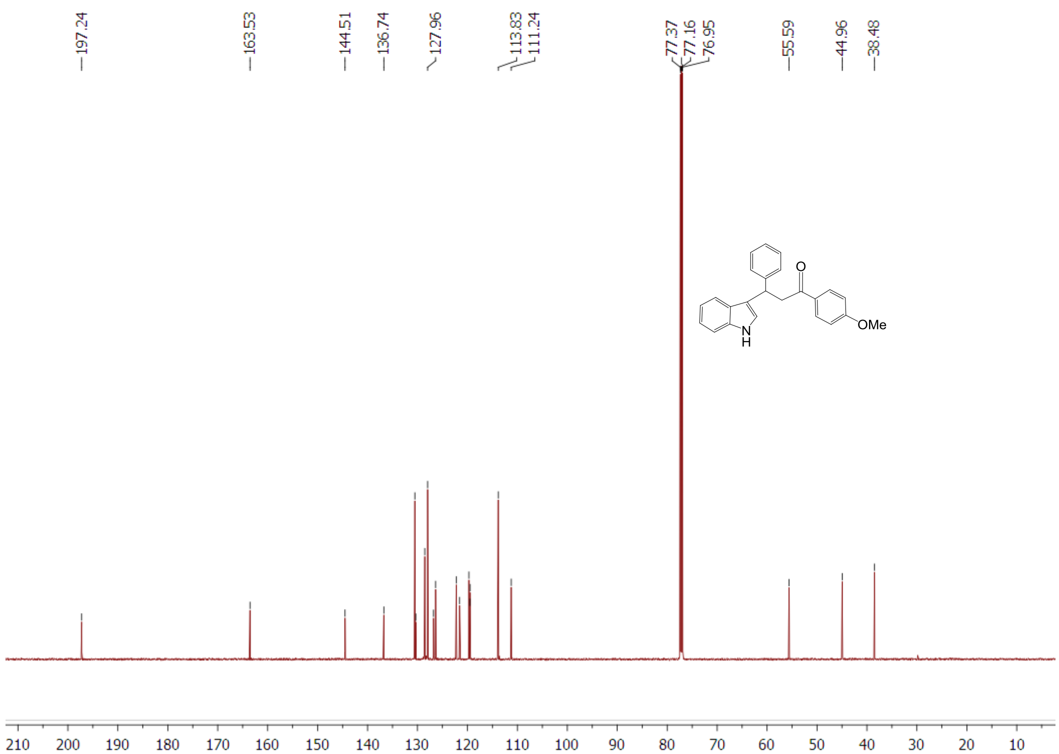

MeO
O
N
H
2.00
0.89
1.00
2.04
2.04
2.05
2.30
1.00
0.98
1.01
1.00
1.05
4.13
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

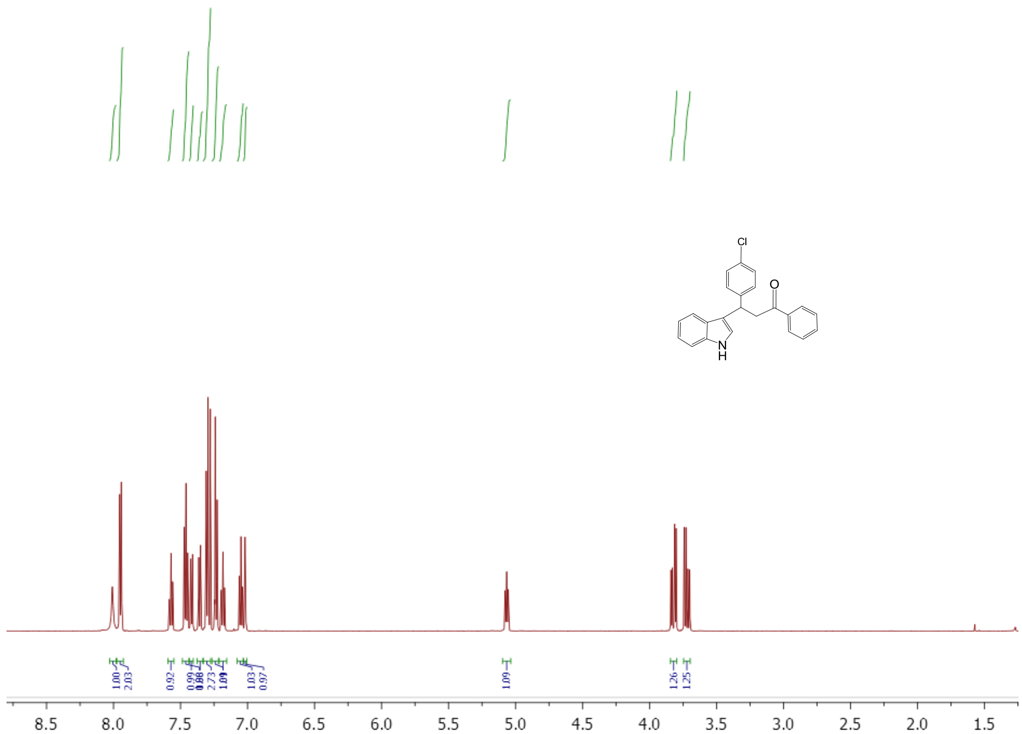

198.79
153.90
144.30
137.23
127.96
111.92
101.57
77.37
77.16
76.95
55.92
45.24
38.29
MeO
O
N
H
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

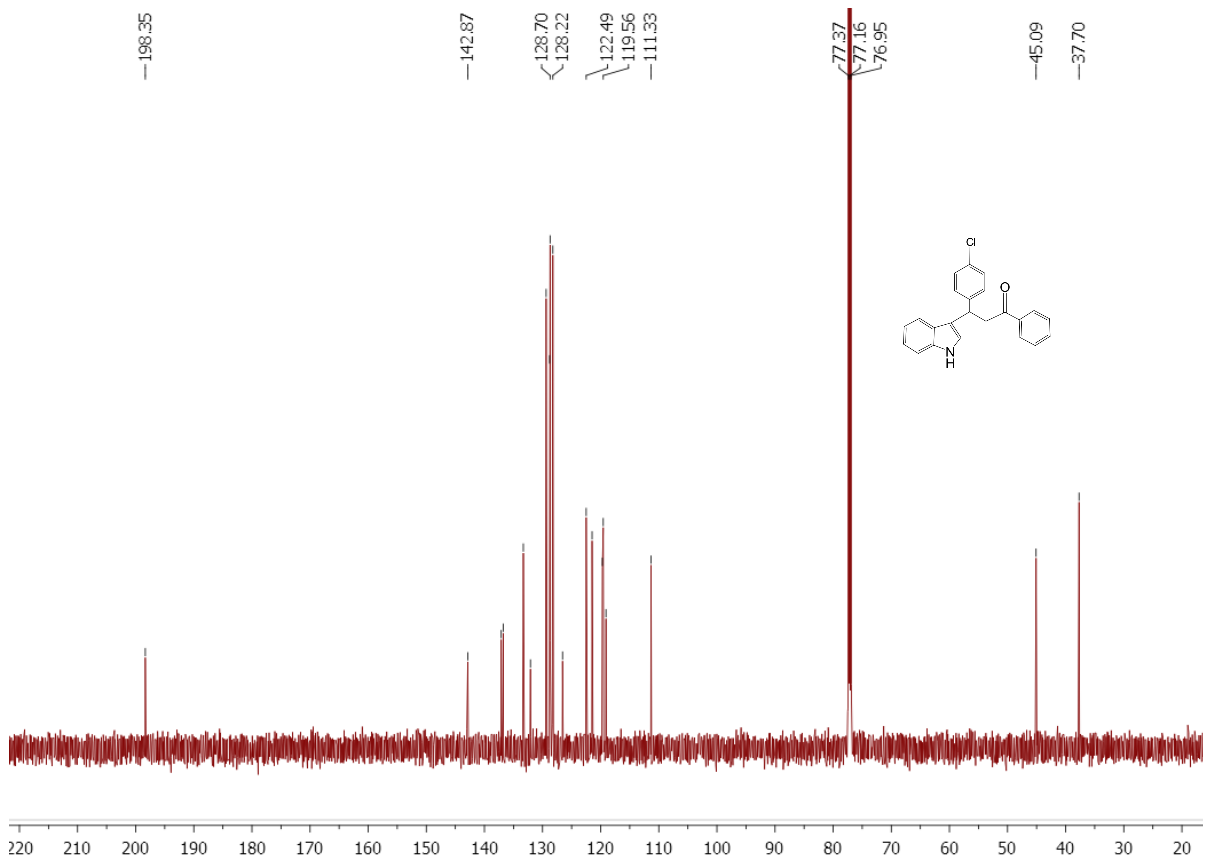

7.97
7.96
7.96
7.47
7.46
7.06
7.06
7.04
7.03
6.87
5.11
5.10
5.08
3.86
3.85
3.83
3.82
3.80
3.78
3.77
3.76
3.74
O
N
Me
2.02
1.01
3.12
2.04
3.36
2.06
1.04
1.00
1.00
1.05
1.19
3.04
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5

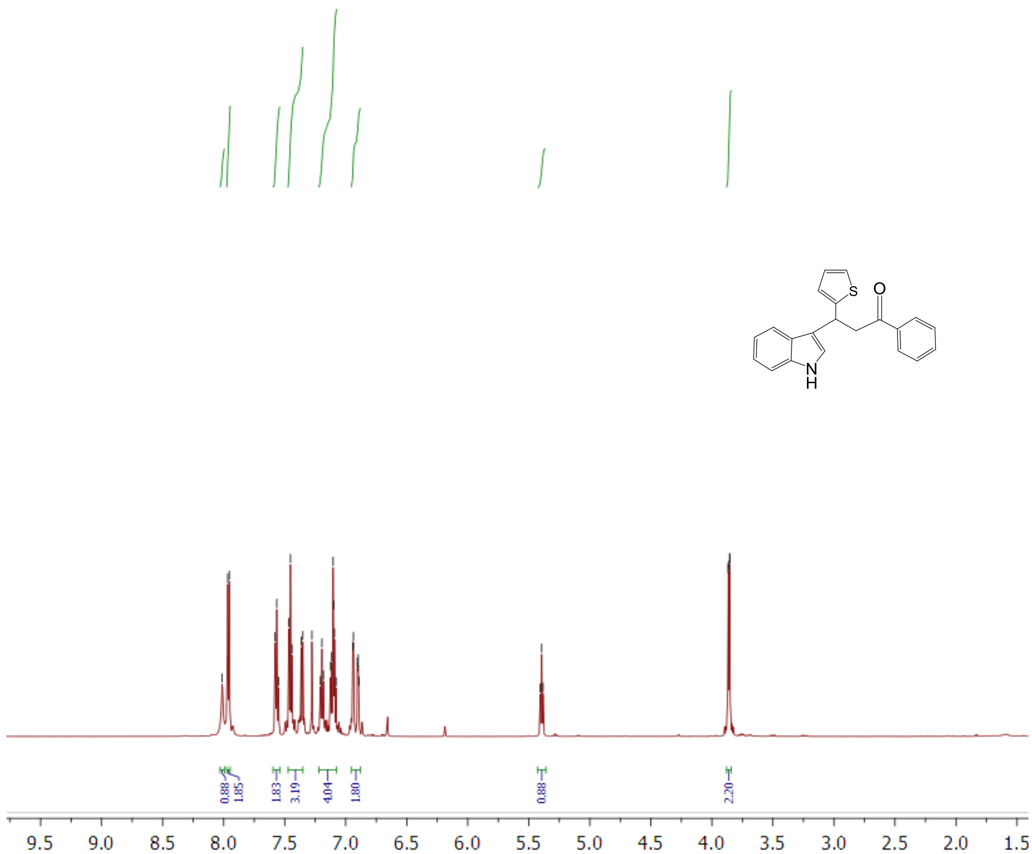

198.63
144.52
133.11
121.81
118.98
109.33
77.37
77.16
76.95
45.46
38.23
32.83
O
N
Me
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20


O
OMe
N
H
0.95
2.05
1.02
2.39
2.19
2.09
2.03
1.00
3.05
1.05
1.05
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0

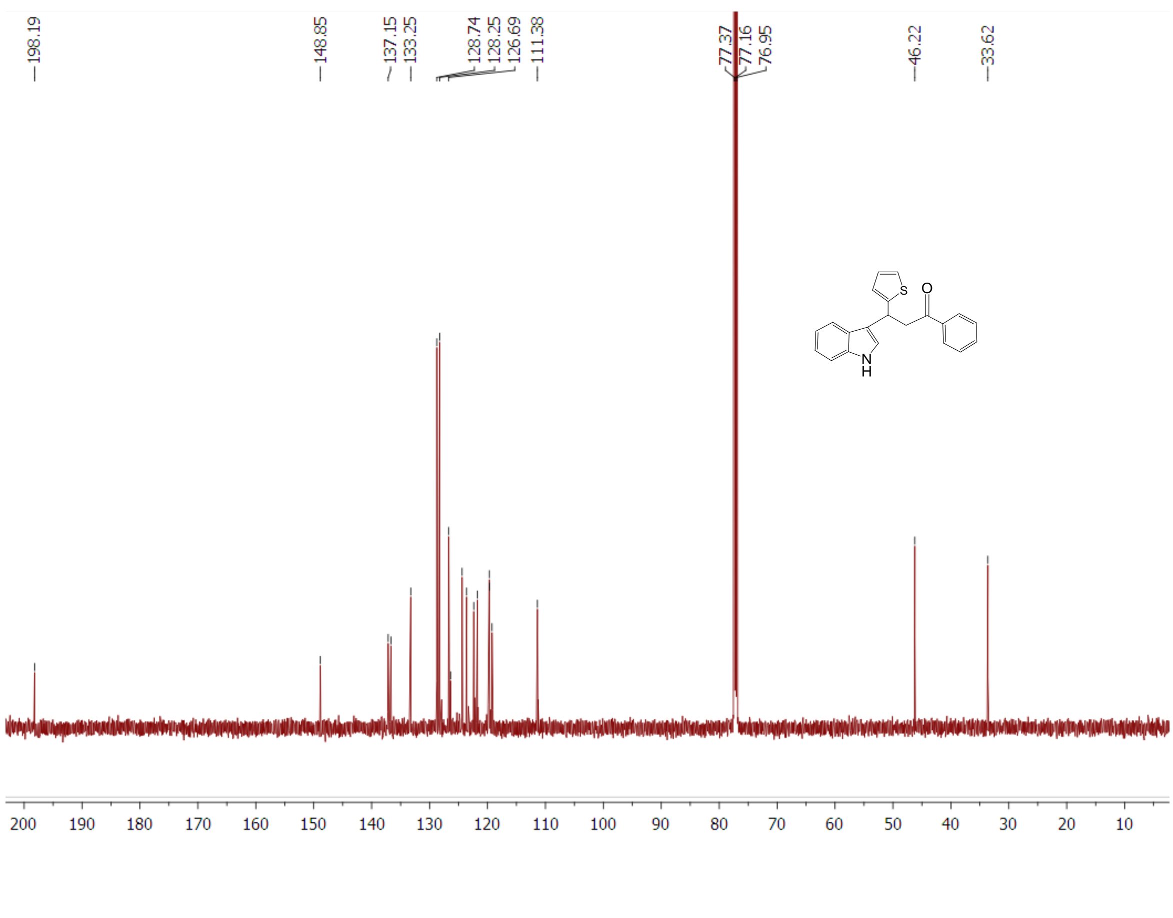

197.24
163.53
144.51
136.74
127.96
113.83
111.24
77.37
77.16
76.95
55.59
44.96
38.48
O
OMe
N
H
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10


Cl
O
N
H
1.00
2.03
0.92
2.73
1.03
0.97
1.09
1.26
1.25
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5

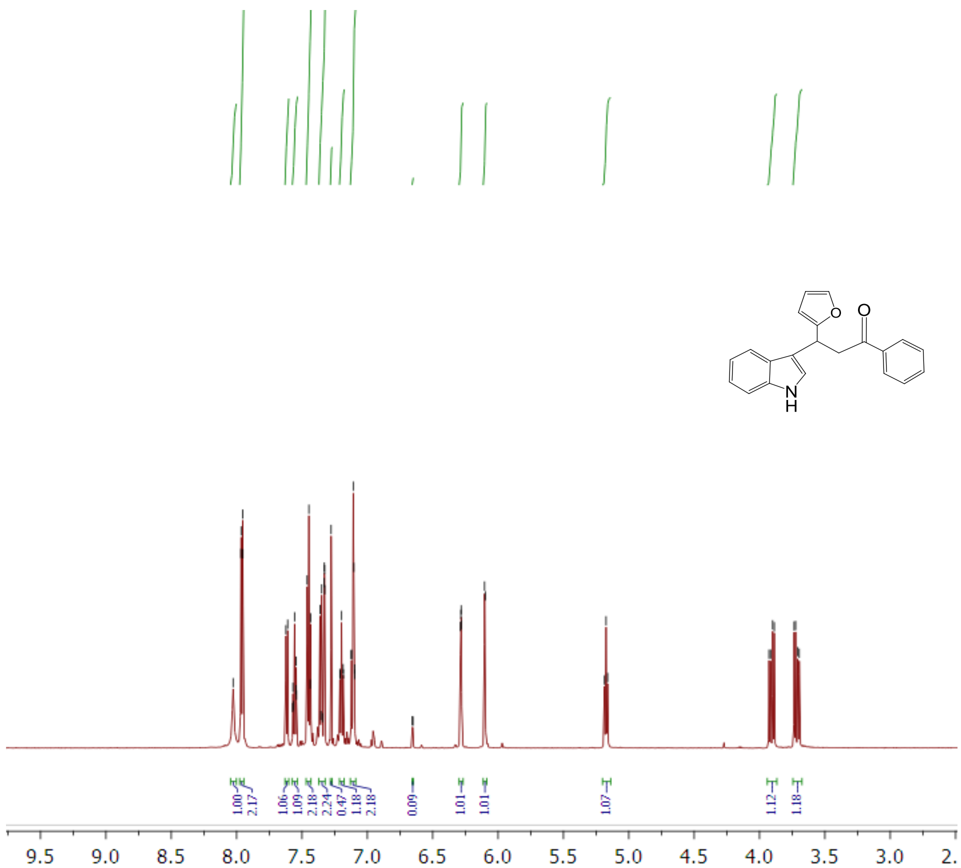

198.35
142.87
128.70
128.22
122.49
119.56
111.33
77.37
77.16
76.95
45.09
37.70
Cl
O
H
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20



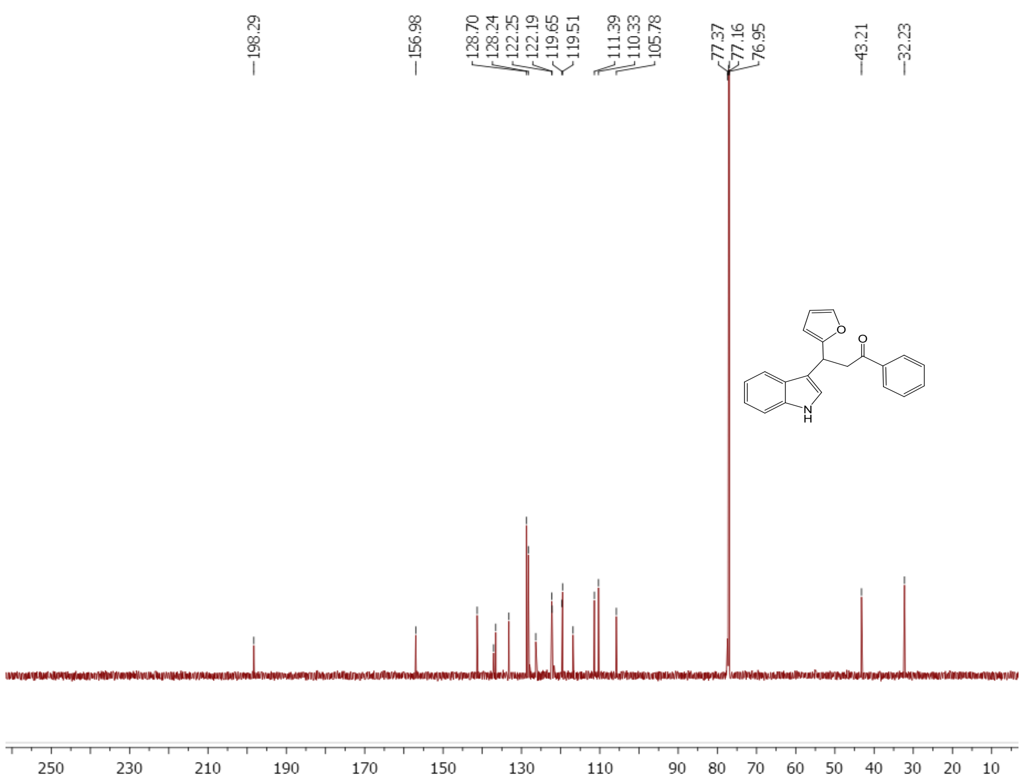
S
O
N
H
0.88
1.85
1.83
3.19
4.04
1.80
0.88
2.20
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5



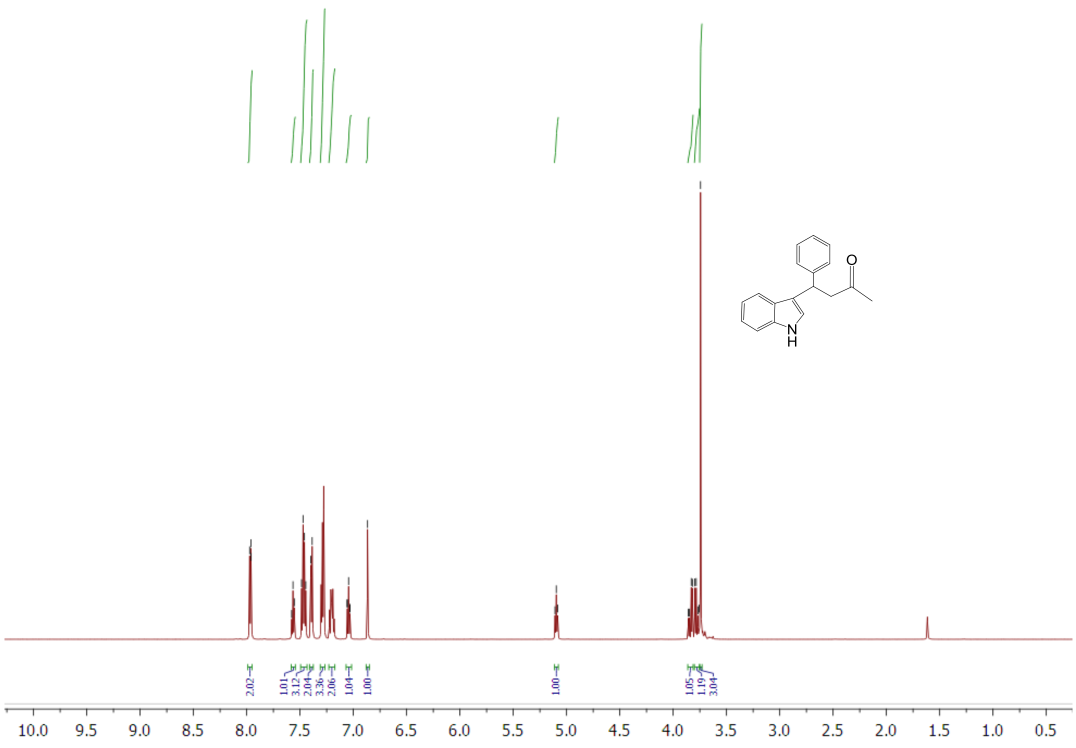
198.19
148.85
137.15
133.25
128.74
128.25
126.69
111.38
77.37
77.16
76.95
46.22
33.62
S
O
N
H
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10

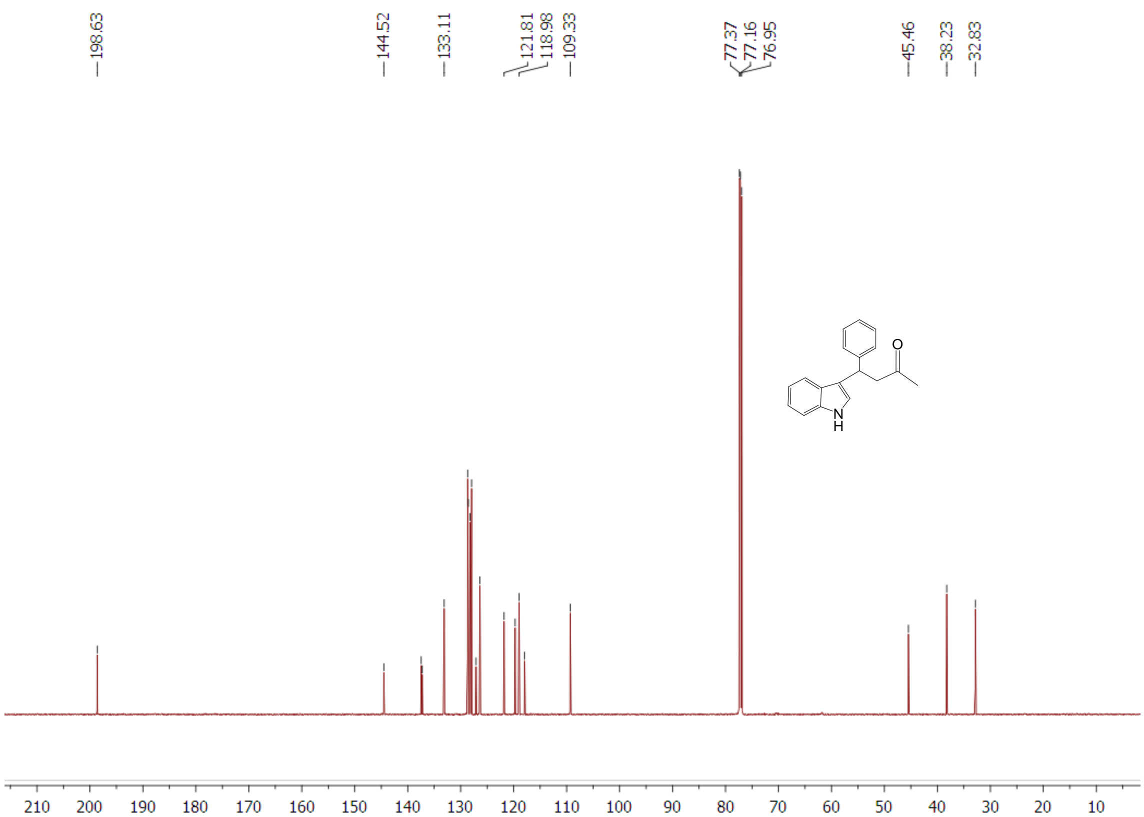


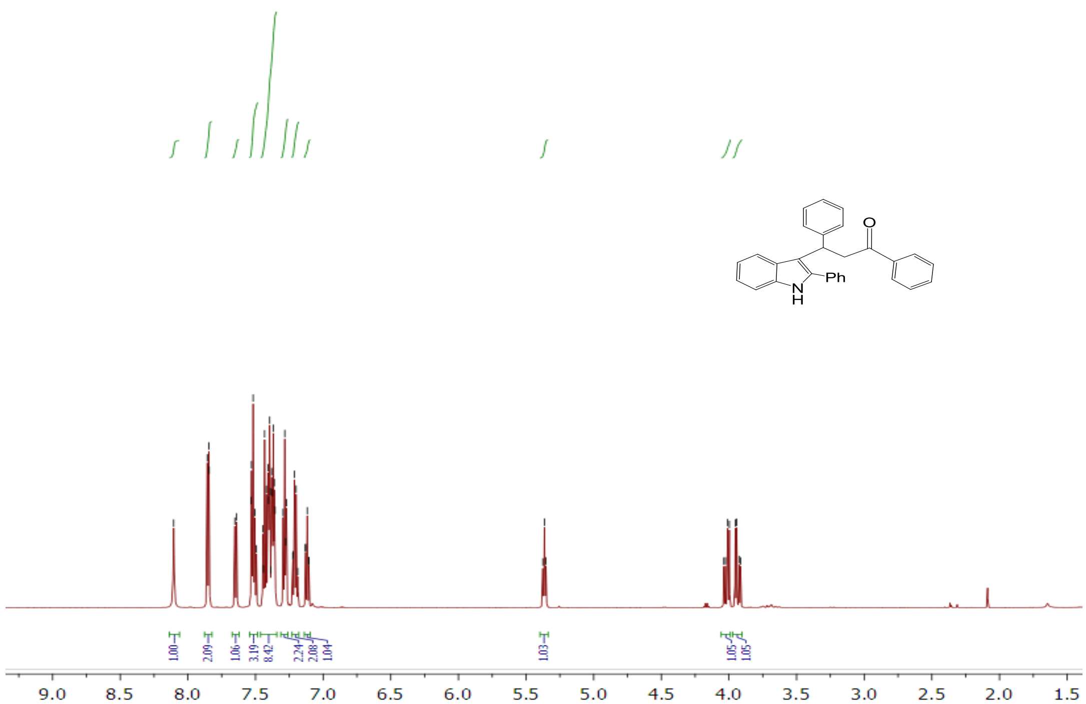
O
N
H
1.00
2.17
1.06
1.09
2.18
2.24
0.47
1.18
2.18
0.09
1.01
1.01
1.07
1.12
1.18
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.

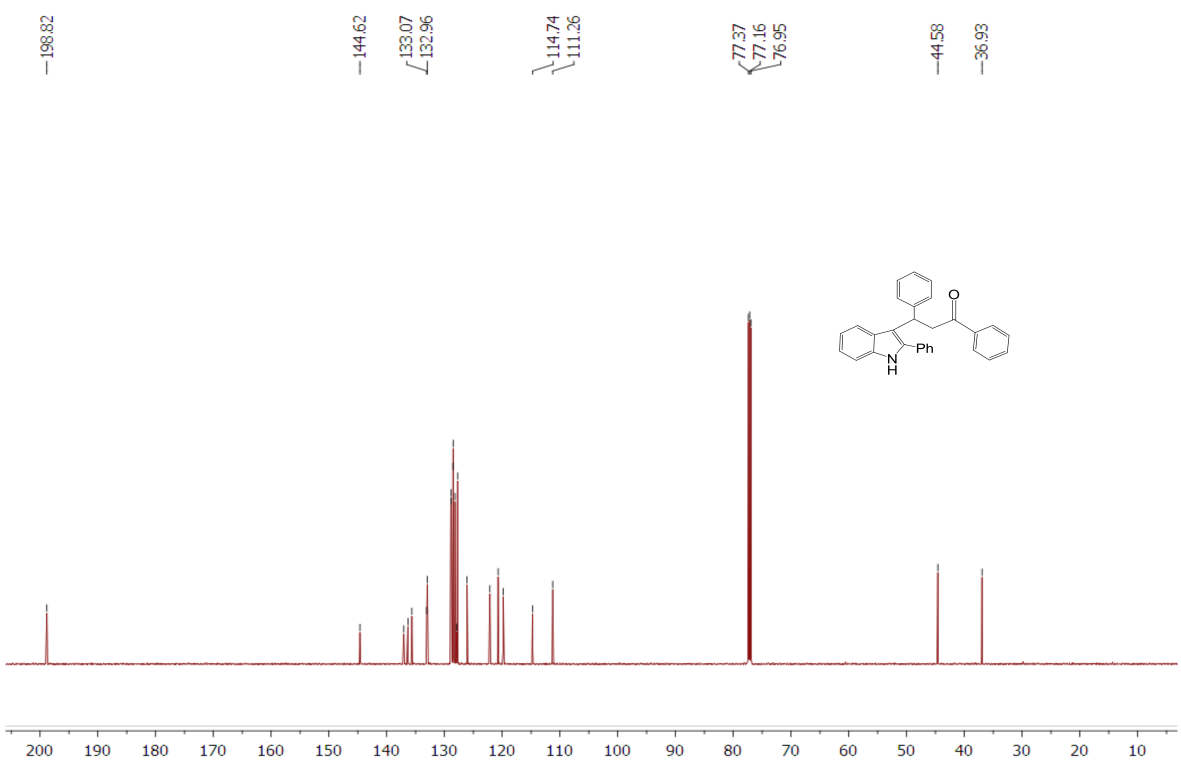


198.29
156.98
128.70
128.24
122.25
122.19
119.65
119.51
111.39
110.33
105.78
77.37
77.16
76.95
43.21
32.23
O
N
H
250 230 210 190 170 150 130 110 90 80 70 60 50 40 30 20 10


2.02
1.01
3.12
2.04
3.36
2.06
1.04
1.00
1.00
1.05
1.19
3.04
N
H
O
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5


198.63
144.52
133.11
121.81
118.98
109.33
77.37
77.16
76.95
45.46
38.23
32.83
N
H
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10


Ph
N
H
O
1.00
2.09
1.06
3.19
8.42
2.24
2.08
1.04
1.03
1.05
1.05
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5


198.82
144.62
133.07
132.96
114.74
111.26
77.37
77.16
76.95
44.58
36.93
Ph
N
H
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10