SUPPLEMENTARY INFORMATION

Antimalarial Benzimidazole Derivatives Incorporating Phenolic Mannich Base Side Chains inhibit Microtubule and Hemozoin formation: Structure-Activity Relationship and In Vivo Oral Efficacy Studies

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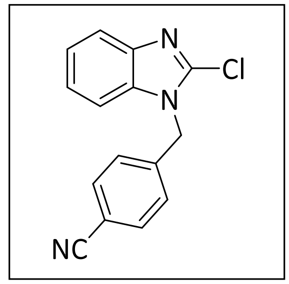
Experimental results of representative intermediates

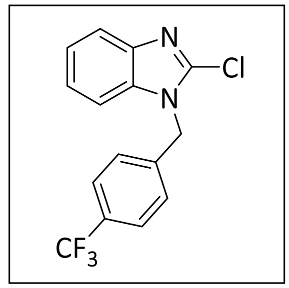
2-chloro-1-(4-cyanobenzyl)benzo[*d*]imidazole (2)

White solid (0.174 g, 99%); *R*f 0.7 (5% MeOH-DCM); mp. 149-151ºC; ^{1}H NMR (600 MHz, MeOH-d_4) δ 7.70 (d, *J* = 8.3 Hz, 2H), 7.65-7.61 (m, 1H), 7.45-7.42 (m, 1H), 7.34 (d, *J* = 8.3 Hz, 2H), 7.33-7.29 (m, 2H), 5.62 (s, 2H); ^{13}C NMR (151 MHz, MeOH-d_4) δ 142.4, 142.3, 142.0, 136.3, 133.9 (2C), 128.8 (2C), 125.1, 124.6, 119.7, 119.3, 113.1, 111.5 and 48.2; LC-MS (ESI): *m/z* 268.0 $[M+H]^+$; purity (LC-MS): 98% (t_R = 2.62 min.)



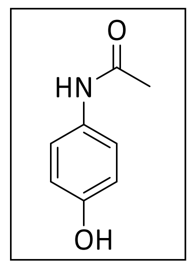
2-chloro-1-((4-trifluoromethyl)benzyl)benzo[*d*]imidazole (3)

White solid (0.200 g, 98%); *R*f 0.7 (5% MeOH-DCM); mp. 96-98ºC; ^{1}H NMR (600 MHz, MeOH-d_4) δ 7.64-7.59 (m, 3H), 7.43-7.40 (m, 1H), 7.34 (d, *J* = 8.3 Hz, 2H), 7.31-7.29 (m, 2H), 5.59 (s, 2H); ^{13}C NMR (151 MHz, MeOH-d_4) δ 142.3, 142.0, 141.3, 136.3, 131.3, 128.5 (2C), 126.9 (2C), 125.4, 125.1, 124.5, 119.7, 111.5 and 48.2; LC-MS (ESI): *m/z* 311.0 $[M+H]^+$; purity (LC-MS): 98% (t_R = 2.85 min.)



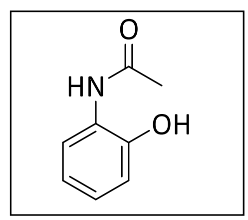
***N*-(4-hydroxyphenyl)acetamide (9a)**

Light pink solid (1.3 g, 94%); *R*f 0.3 (7% MeOH-DCM); mp. 168-170 ºC; ^{1}H NMR (600 MHz, MeOH-d_4) δ 7.35 (d, *J* = 8.8 Hz, 2H), 6.72 (d, *J* = 8.8 Hz, 2H), 2.06 (s, 3H); ^{13}C NMR (151 MHz, MeOH-d_4) δ 171.2, 155.2, 131.5, 123.2 (2C), 116.0 (2C) and 23.3; LC-MS (ESI): *m/z* 152.0 $[M+H]^+$; purity (LC-MS): 98% (t_R = 0.19 min.)



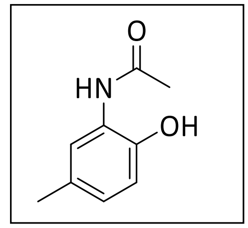
***N*-(2-hydroxyphenyl)acetamide (9c)**

White solid (1.3 g, 94%); *R*f 0.5 (7% MeOH-DCM); mp. 198-200ºC; ^{1}H NMR (600 MHz, MeOH-d_4) δ 7.56 (dd, *J* = 1.6, 7.9 Hz, 1H), 6.98 (td, *J* = 7.5, 1.6 Hz, 1H), 6.85 (dd, *J* = 1.4, 8.0 Hz, 1H), 6.79 (td, *J* = 7.6, 1.4 Hz, 1H), 2.16 (s, 3H); ^{13}C NMR (151 MHz, MeOH-d_4) δ 172.2, 149.7, 127.1, 126.8, 124.0, 120.6, 117.3 and 23.4; LC-MS (ESI): *m/z* 152.0 $[M+H]^+$; purity (LC-MS): 98% (t_R = 0.23 min.)



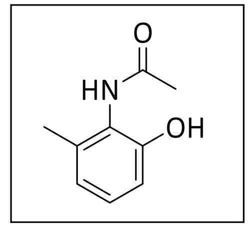
N-(2-hydroxy-5-methylphenyl)acetamide (9d)

White solid (1.2 g, 95%); *R*f 0.5 (7% MeOH-DCM); mp. 197-199ºC; ^{1}H NMR (600 MHz, MeOH-d_4) δ 7.35 (d, *J* = 2.0 Hz, 1H), 6.80 (dd, *J* = 2.2, 8.1 Hz, 1H), 6.73 (d, *J* = 8.1 Hz, 1H), 2.22 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (151 MHz, MeOH-d_4) δ 172.2, 147.4, 130.1, 127.3, 126.8, 124.3, 117.3, 23.4, and 20.7; LC-MS (ESI): *m/z* 166.0 [M+H]$^+$; purity (LC-MS): 98% (t_R = 0.64 min.)



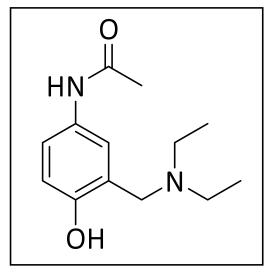
N-(2-hydroxy-6-methylphenyl)acetamide (9e)

Yellow solid (1.2 g, 95%); *R*f 0.4 (7% MeOH-DCM); mp. 164-166ºC; ^{1}H NMR (600 MHz, MeOH-d_4) δ 7.00 (t, *J* = 7.8 Hz, 1H), 6.71 (m, 2H), 2.18 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (151 MHz, MeOH-d_4) δ 172.9, 153.9, 137.6, 128.8, 124.4, 122.3, 115.0, 22.6 and 18.2; LC-MS (ESI): *m/z* 166.0 [M+H]$^+$; purity (LC-MS): 98% (t_R = 0.26 min.)



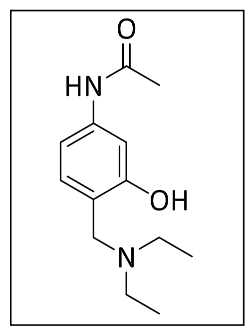
***N*-(3-((*N*,*N*-diethylamino)methyl)-4-hydroxyphenyl)acetamide (10a)**

Yellow oil (0.500 g, 64%); *R*f 0.2 (7% MeOH-DCM); ^{1}H NMR (600 MHz, DMSO-d_6) δ 9.66 (br s, 1H), 7.31 (d, *J* = 2.6 Hz, 1H), 7.26 (dd, *J* = 2.6, 8.6 Hz, 1H), 6.63 (d, *J* = 8.6 Hz, 1H), 3.70 (s, 2H), 2.58 (q, *J* = 7.1 Hz, 4H), 1.97 (s, 3H), 1.03 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 167.6, 153.1, 130.8, 122.0, 120.4, 119.7, 115.1, 54.8, 45.9 (2C), 23.7 and 10.9 (2C); LC-MS (ESI): *m/z* 237.1 [M+H]$^+$; purity (LC-MS): 98% (t_R = 0.12 min.)



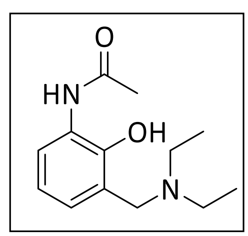
***N*-(4-((*N*,*N*-diethylamino)methyl)-3-hydroxyphenyl)acetamide (10b)**

Yellow oil (0.473 g, 61%); *R*f 0.2 (7% MeOH-DCM); ^{1}H NMR (600 MHz, MeOH-d_4) δ 6.98 (d, *J* = 1.5 Hz, 1H), 6.92-6.90 (m, 2H), 3.73 (s, 2H), 2.61 (q, *J* = 7.1 Hz, 4H), 2.07 (s, 3H), 1.09 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (151 MHz, MeOH-d_4) δ 171.5, 159.7, 140.2, 129.7, 119.5, 111.9, 108.9, 57.1, 47.4 (2C), 23.8 and 11.5 (2C); LC-MS (ESI): *m/z* 237.1 [M+H]$^+$; purity (LC-MS): 98% (t_R = 0.13 min.)

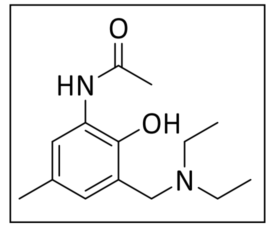


***N*-(3-((*N*,*N*-diethylamino)methyl)-2-hydroxyphenyl)acetamide (10c)**

Yellow oil (0.616 g, 79%); *R*f 0.3 (7% MeOH-DCM); ^{1}H NMR (400 MHz, MeOH-d_4) δ 7.82 (dd, *J* = 1.7, 8.1 Hz, 1H), 6.81 (d, *J* = 8.1 Hz, 1H), 6.71 (t, *J* = 7.9 Hz, 1H), 3.51 (s, 2H), 2.55 (q, *J* = 7.1 Hz, 4H), 2.18 (s, 3H), 1.08 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (101 MHz, MeOH-d_4) δ 171.6, 150.7, 128.4, 127.2, 126.9, 123.0, 122.7, 57.9, 47.3 (2C), 23.8 and 11.4 (2C); LC-MS (ESI): *m/z* 237.1 [M+H]$^+$; purity (LC-MS): 98% (t_R = 0.13 min.)

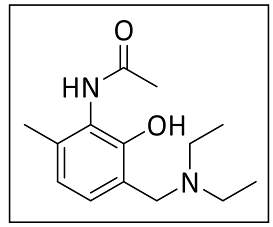


_N_-(3-((_N,N_-diethylamino)methyl)-2-hydroxy-5-methylphenyl)acetamide (10d)



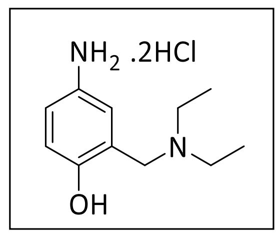
Yellow oil (0.510 g, 67%); *R*f 0.3 (7% MeOH-DCM); ^{1}H NMR (600 MHz, MeOH-d_4) δ 7.61 (d, *J* = 2.0 Hz, 1H), 6.61 (d, *J* = 2.0 Hz, 1H), 3.76 (s, 2H), 2.64 (q, *J* = 7.2 Hz, 4H), 2.20 (s, 3H), 2.14 (s, 3H), 1.11 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (151 MHz, MeOH-d_4) δ 171.6, 148.0, 128.5, 126.7, 125.9, 122.9, 122.8, 57.6, 47.4 (2C), 23.8, 20.9 and 11.5 (2C); LC-MS (ESI): *m/z* 251.1 $[M+H]^+$; purity (LC-MS): 98% (t_R = 0.15 min.)

_N_-(3-((_N,N_-diethylamino)methyl)-2-hydroxy-6-methylphenyl)acetamide (10e)



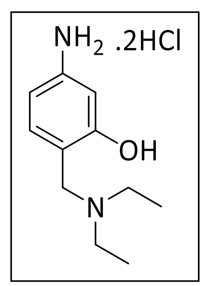
Yellow oil (0.500 g, 66%); *R*f 0.2 (7% MeOH-DCM); ^{1}H NMR (600 MHz, MeOH-d_4) δ 6.84 (d, *J* = 7.6 Hz, 1H), 6.62 (d, *J* = 7.6 Hz, 1H), 3.77 (s, 2H), 2.63 (q, *J* = 7.1 Hz, 4H), 2.15 (s, 3H), 2.14 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR (151 MHz, MeOH-d_4) δ 172.6, 155.2, 137.0, 128.1, 124.2, 121.5, 120.9, 57.4, 47.4 (2C), 22.6, 18.2 and 11.5 (2C); LC-MS (ESI): *m/z* 251.1 $[M+H]^+$; purity (LC-MS): 98% (t_R = 0.18 min.)

4-Amino-2-((_N,N_-diethylamino)methyl)phenol (11a)



Brown viscous oil (0.360 g, 88%); *R*f 0.2 (20% MeOH-DCM); ^{1}H NMR (600 MHz, MeOH-d_4) δ 7.56 (d, *J* = 2.7 Hz, 1H), 7.40 (dd, *J* = 2.7, 8.7 Hz, 1H), 7.10 (d, *J* = 8.7 Hz, 1H), 4.37 (s, 2H), 3.06 (m, 4H), 1.38 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (151 MHz, MeOH-d_4) δ 158.4, 128.5, 127.4, 123.5, 119.2, 117.8, 51.9, 48.9 (2C) and 9.2 (2C); LC-MS (ESI): *m/z* 195.1 $[M+H]^+$; purity (LC-MS): 98% (t_R = 0.12 min.)

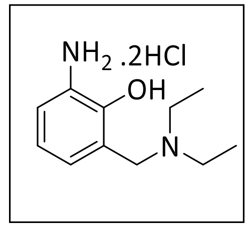
5-Amino-2-((_N,N_-diethylamino)methyl)phenol (11b)



Brown viscous oil (0.330 g, 75%); *R*f 0.2 (20% MeOH-DCM); ^{1}H NMR (600 MHz, MeOH-d_4) δ 7.61 (d, *J* = 8.1 Hz, 1H), 7.10 (d, *J* = 2.1 Hz, 1H), 7.00 (dd, *J* = 2.1, 8.1 Hz, 1H), 4.36 (s, 2H), 3.23 (m, 4H), 1.37 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (151 MHz, MeOH-d_4) δ 159.1, 135.4, 134.6, 118.9, 115.5, 111.6, 51.8, 48.8 (2C), 9.2 (2C); LC-MS (ESI): *m/z* 195.1 $[M+H]^+$; purity (LC-MS): 98% (t_R = 0.12 min.)

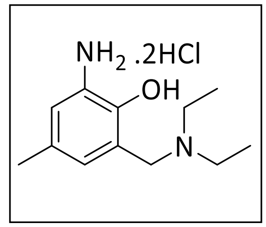
6-Amino-2-((*N,N*-diethylamino)methyl)phenol (11c)

Brown viscous oil (0.362 g, 88%); *R*f 0.6 (20% MeOH-DCM); ^{1}H NMR (600 MHz, MeOH-d_4) δ 7.61 (dd, *J* = 1.6, 7.7 Hz, 1H), 7.52 (dd, *J* = 1.6, 7.9 Hz, 1H), 7.17 (t, *J* = 7.8 Hz, 1H), 4.49 (s, 2H), 3.25 (m, 4H), 1.38 (t, *J* = 7.3 Hz, 6H); ^{13}C NMR (151 MHz, MeOH-d_4) δ 151.2, 134.7, 127.3, 123.2, 123.0, 122.2, 52.0, 48.5 (2C) and 9.1 (2C); LC-MS (ESI): *m/z* 195.1 [M+H]$^+$; purity (LC-MS): 98% (t_R = 0.13 min.)



6-Amino-2-((*N,N*-diethylamino)methyl)-4-methylphenol (11d)

Brown viscous oil (0.430 g, 86%); *R*f 0.6 (20% MeOH-DCM); ^{1}H NMR (600 MHz, MeOH-d_4) δ 7.44 (d, *J* = 1.9 Hz, 1H), 7.33 (d, *J* = 1.8 Hz, 1H), 4.43 (s, 2H), 3.24 (m, 4H), 2.35 (s, 3H), 1.37 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (151 MHz, MeOH-d_4) δ 148.6, 134.9, 133.6, 127.6, 122.7, 122.1, 52.1, 48.5 (2C), 20.4 and 9.2 (2C); LC-MS (ESI): *m/z* 209.1 [M+H]$^+$; purity (LC-MS): 98% (t_R = 0.14 min.)



6-Amino-2-((*N,N*-diethylamino)methyl)-5-methylphenol (11e)

Brown viscous oil (0.400 g, 80%); *R*f 0.6 (20% MeOH-DCM); ^{1}H NMR (600 MHz, MeOH-d_4) δ 7.56 (d, *J* = 7.9 Hz, 1H), 7.07 (d, *J* = 7.9 Hz, 1H), 4.44 (s, 2H), 3.24 (m, 4H), 2.44 (s, 3H), 1.37 (t, *J* = 7.3 Hz, 6H); ^{13}C NMR (151 MHz, MeOH-d_4) δ 150.8, 137.0, 133.8, 125.4, 122.4, 119.6, 52.1, 48.3 (2C), 17.6 and 9.1 (2C); LC-MS (ESI): *m/z* 209.1 [M+H]$^+$; purity (LC-MS): 98% (t_R = 0.15 min.)

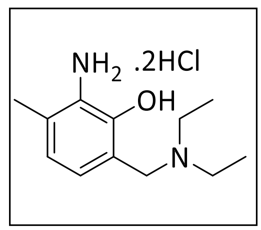
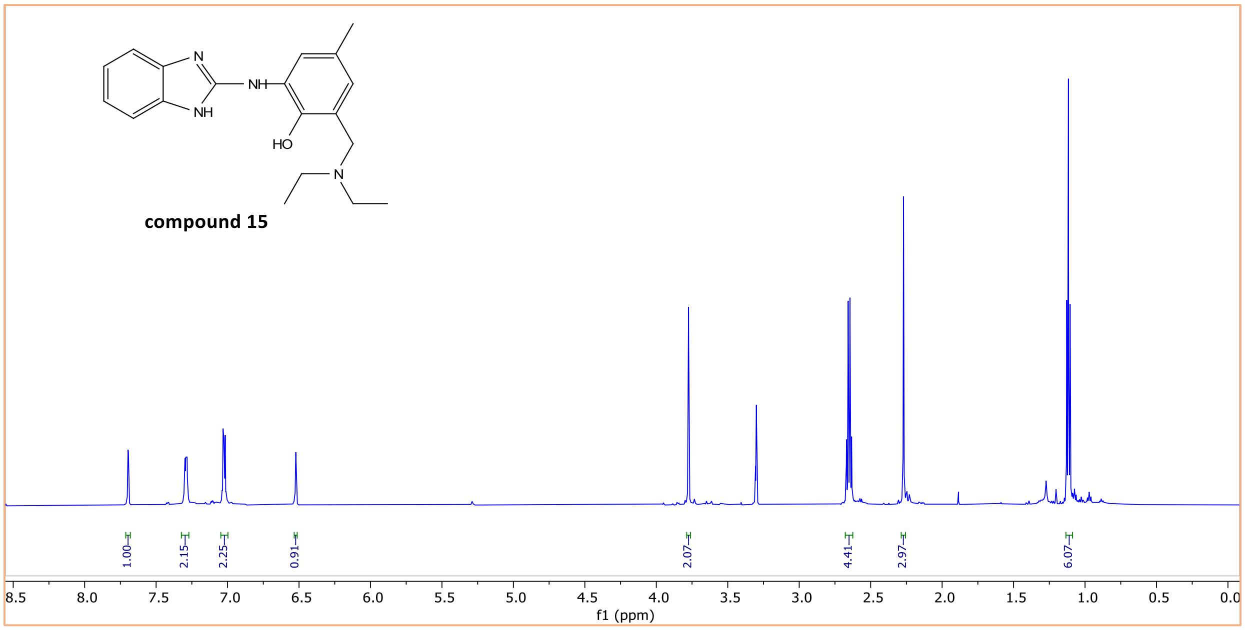
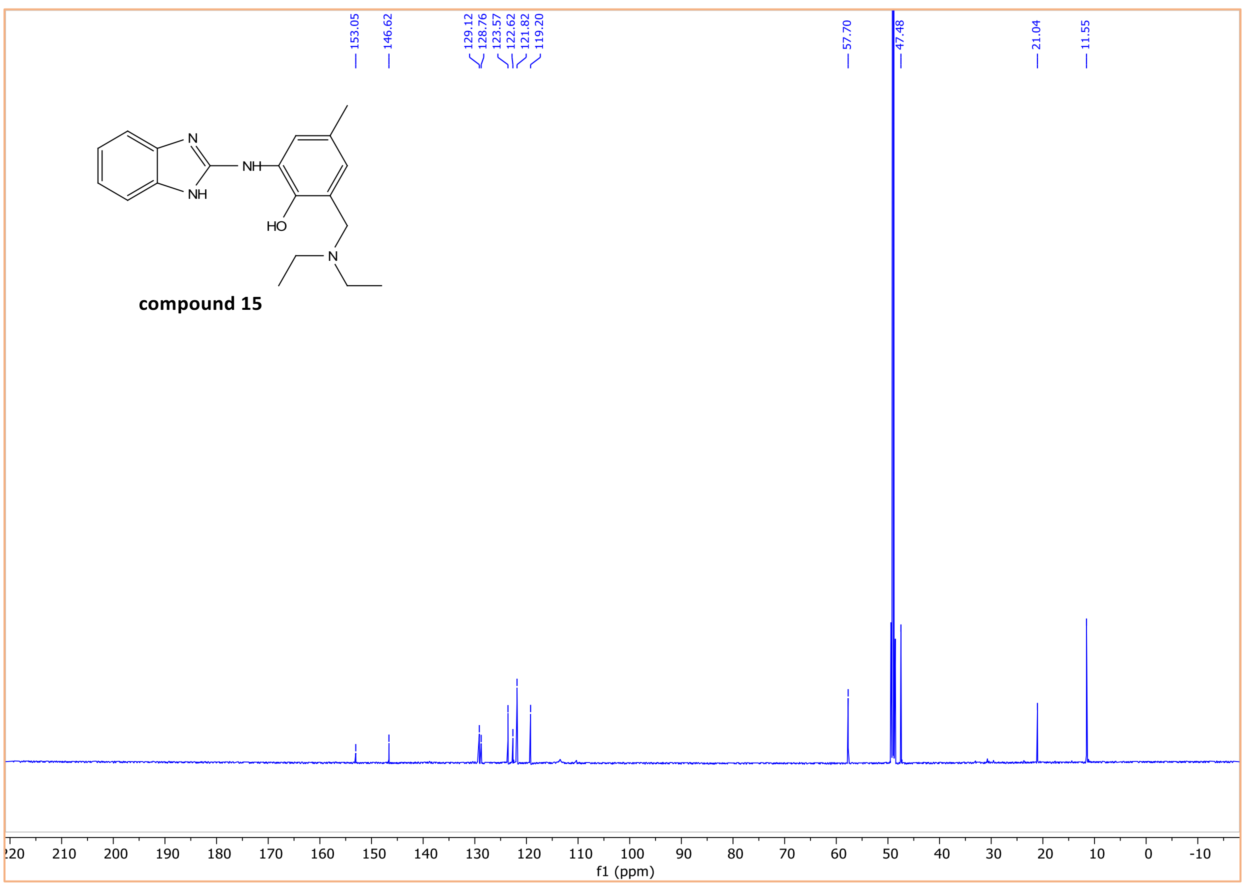
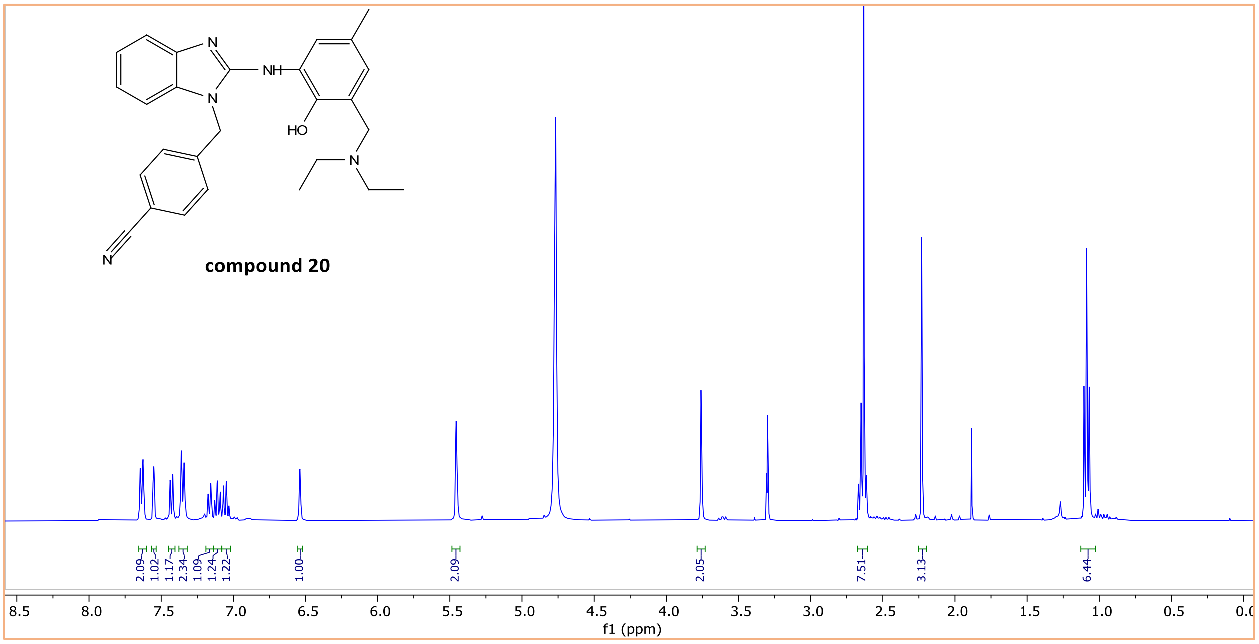


Figure S1: 1D-NMR and corresponding HPLC-MS spectra of representative target compounds



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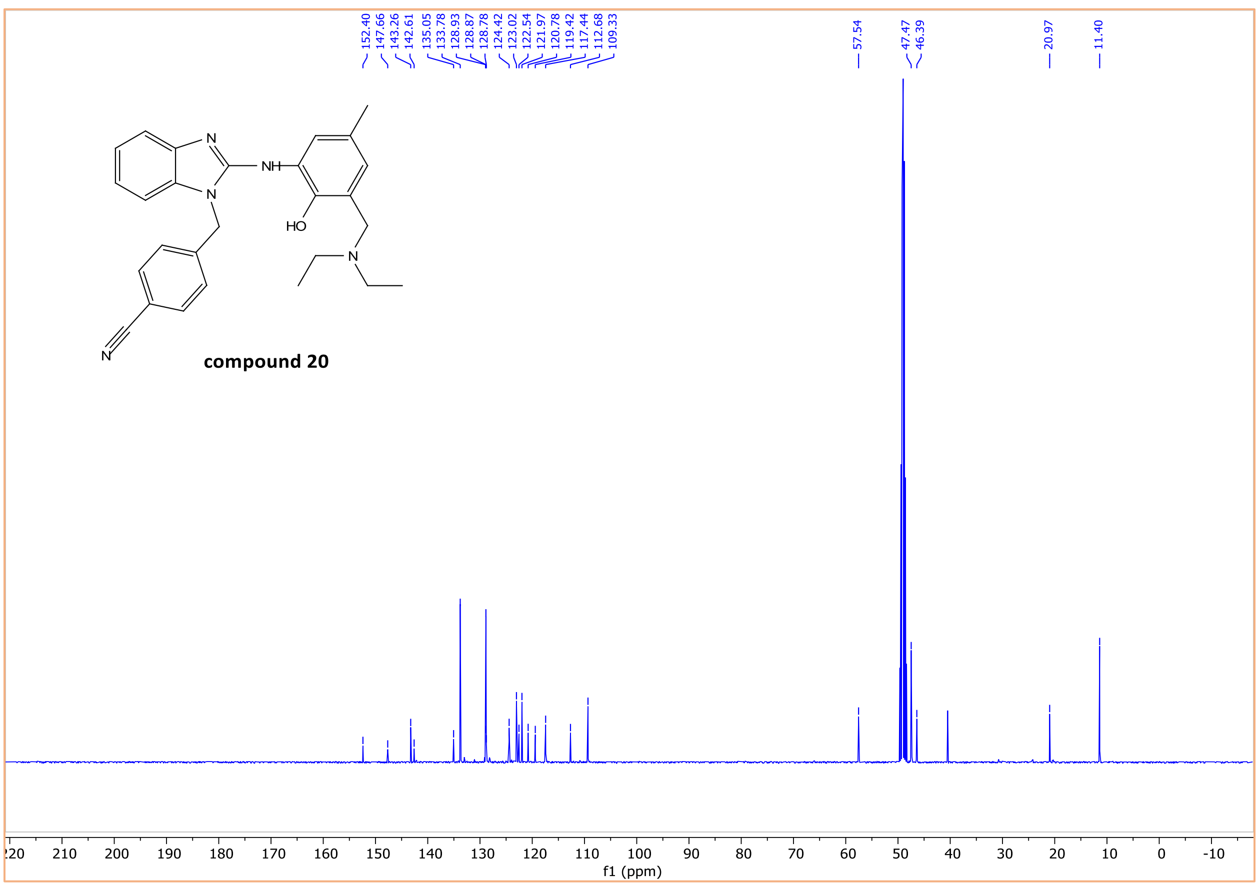
1.17
2.34
1.09
1.24
1.22
1.00
2.09
2.05
7.51
3.13
6.44
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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143.26
142.61
135.05
133.78
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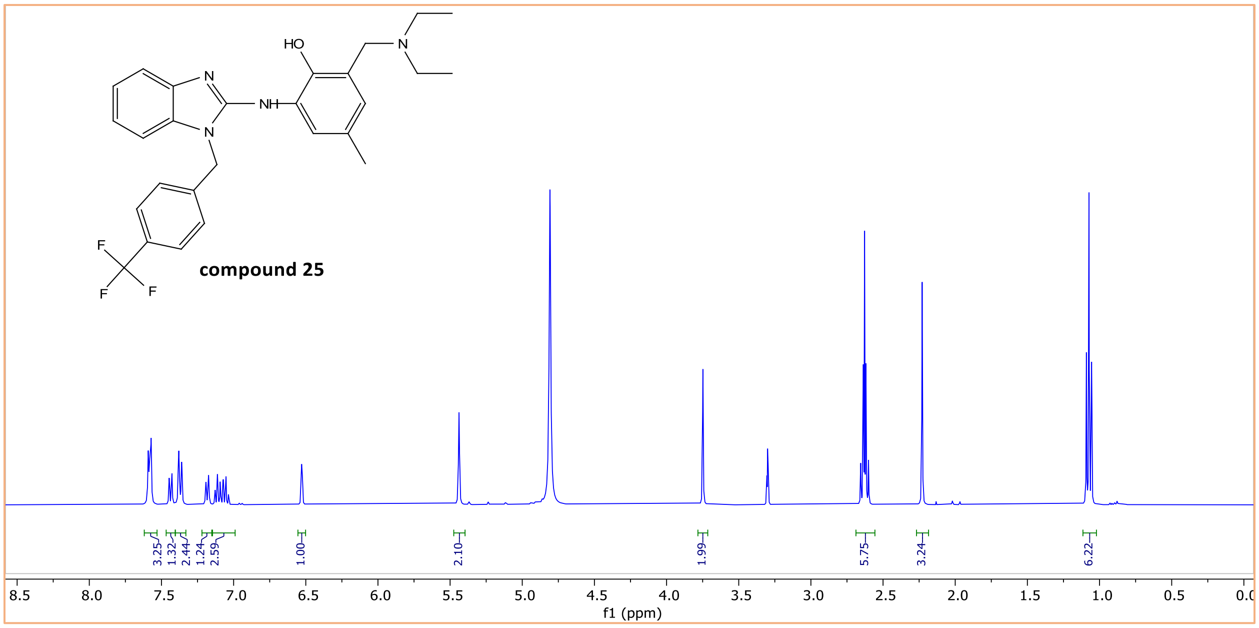
128.87
128.78
124.42
123.02
122.54
121.97
120.78
119.42
117.44
112.68
109.33
57.54
47.47
46.39
20.97
11.40
compound 20
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


HO
N
NH
compound 25
F
F
F
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1.00
2.10
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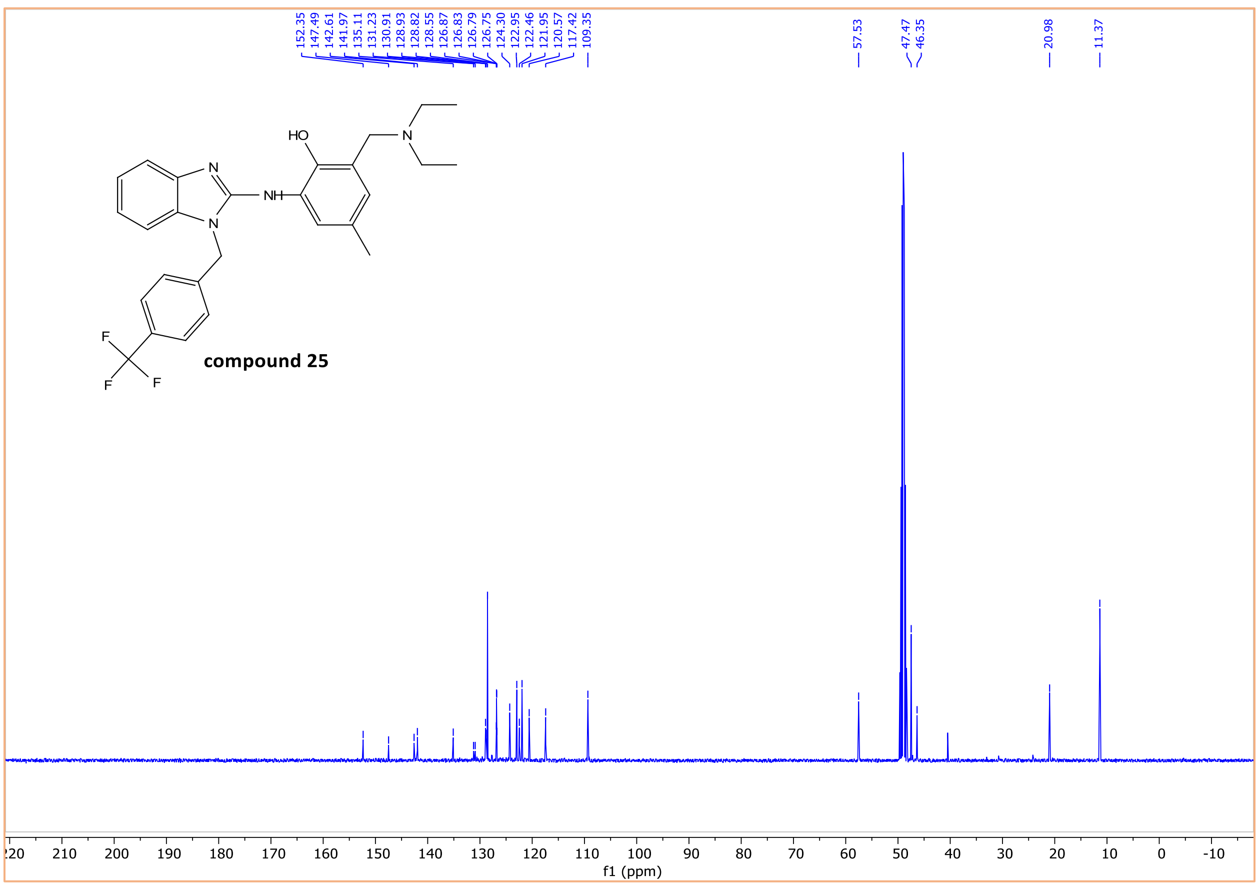
3.24
6.22
f1 (ppm)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147.49
142.61
141.97
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122.95
122.46
121.95
120.57
117.42
109.35
57.53
47.47
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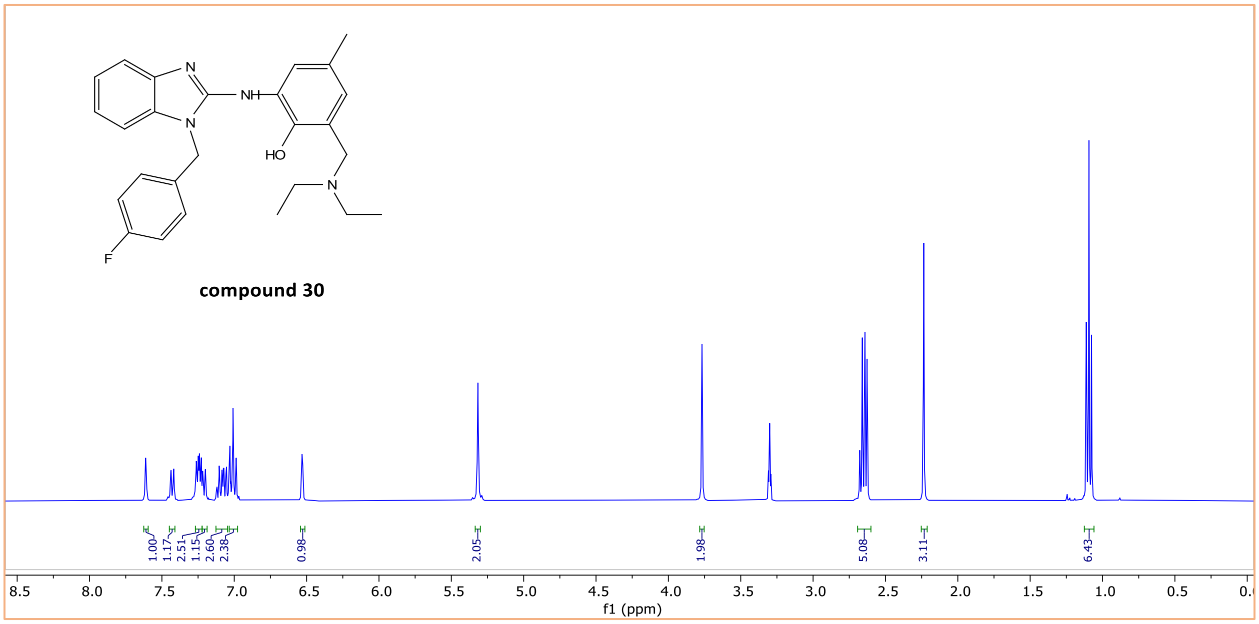
11.37
HO
N
NH
compound 25
F
F
F
f1 (ppm)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HO
N
F
compound 30
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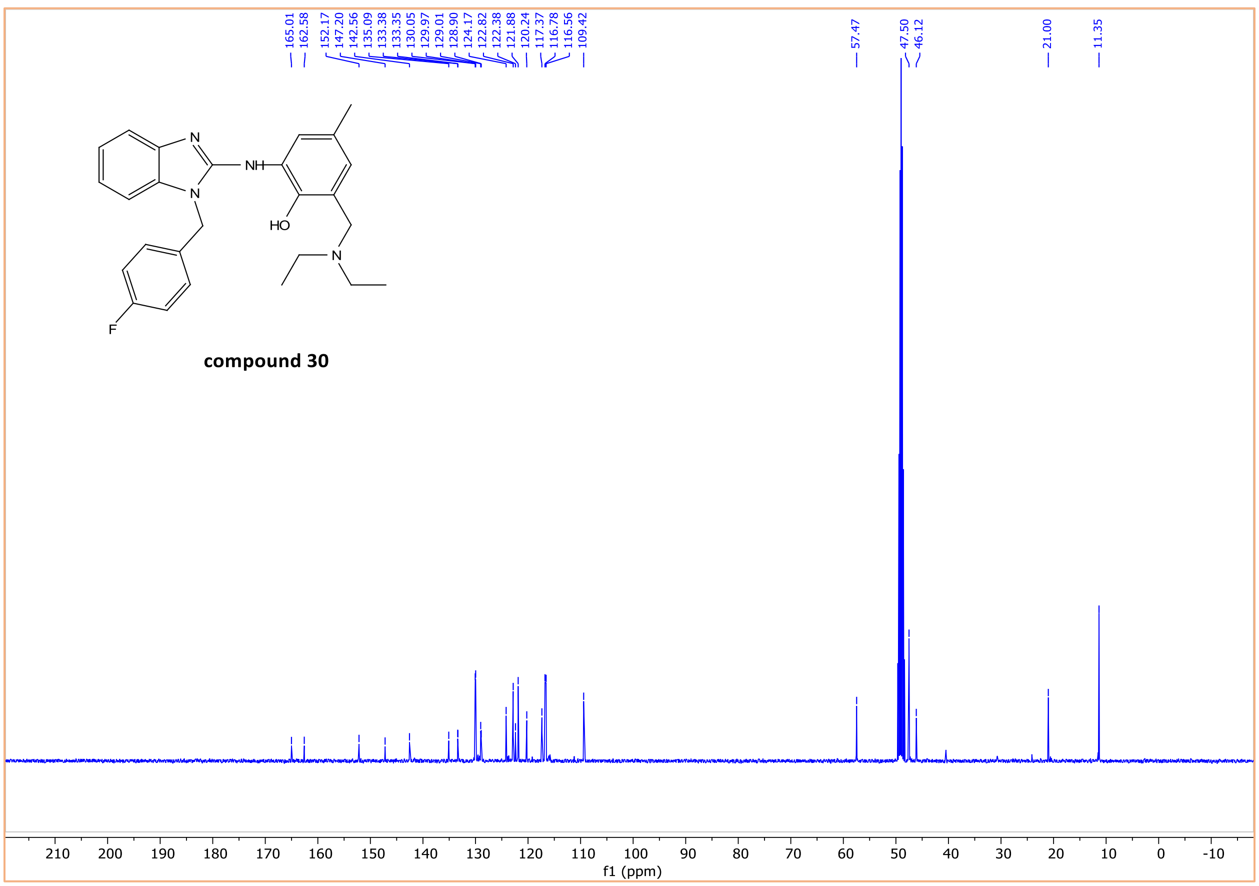
1.15
2.60
2.38
0.98
2.05
1.98
5.08
3.11
6.43
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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129.97
129.01
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122.38
121.88
120.24
117.37
116.78
116.56
109.42
57.47
47.50
46.12
21.00
11.35
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HO
N
F
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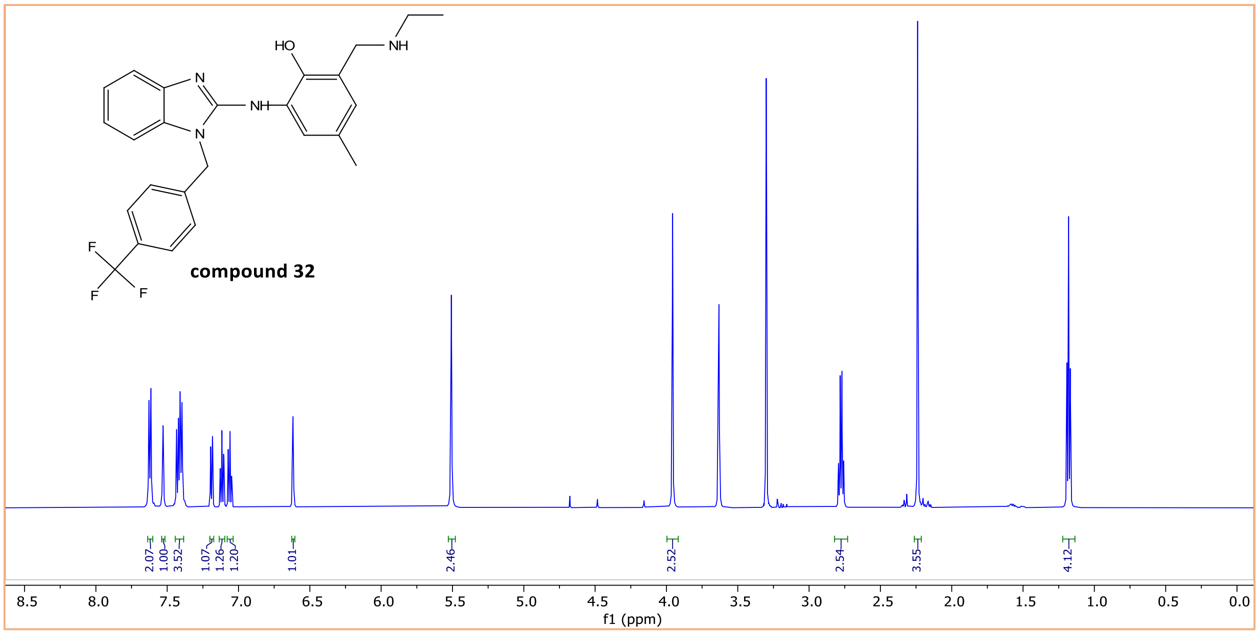
f1 (ppm)


HO
NH
N
NH
N
F
F
F
compound 32
2.07
1.00
3.52
1.07
1.26
1.20
1.01
2.46
2.52
2.54
3.55
4.12
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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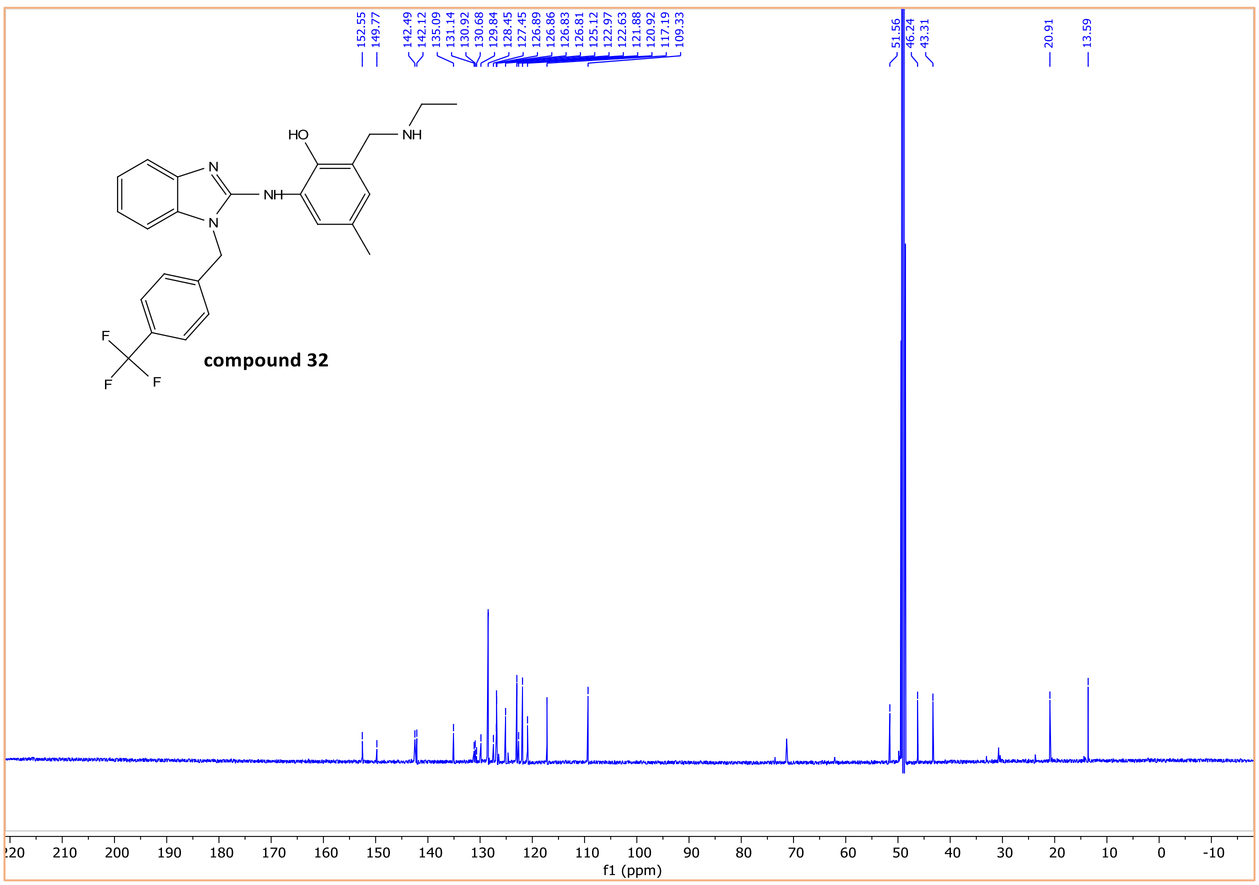
f1 (ppm)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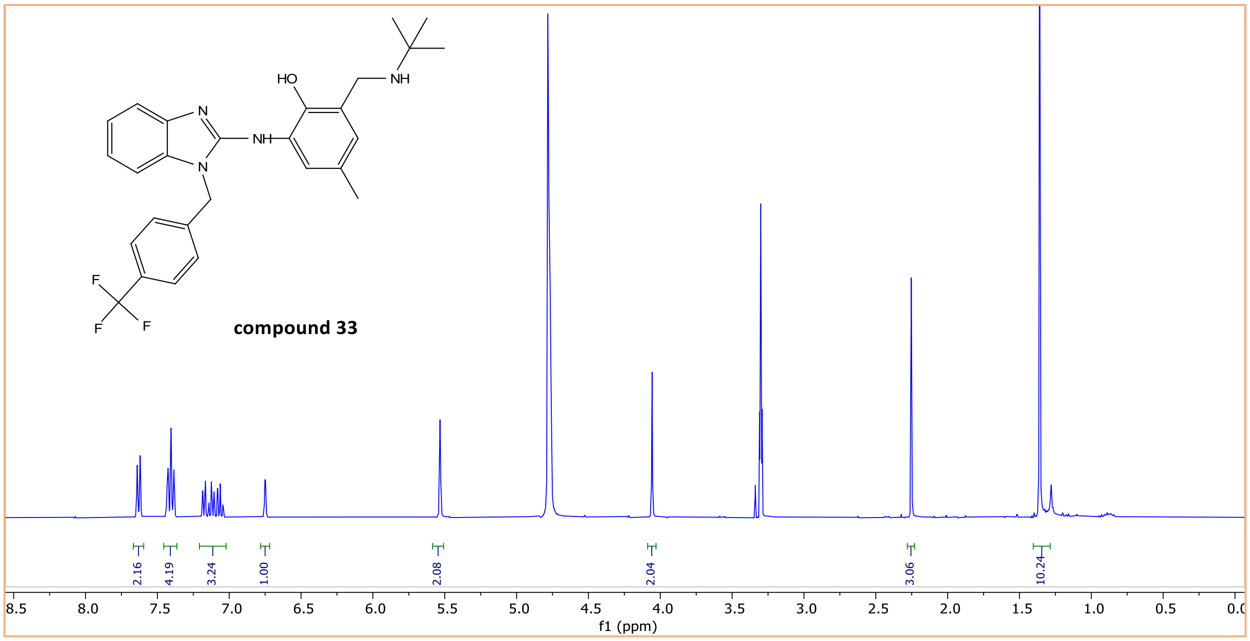
126.86
126.83
126.81
125.12
122.97
122.63
121.88
120.92
117.19
109.33
51.56
46.24
43.31
20.91
13.59
HO
NH
N
NH
N
F
F
F
compound 32
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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NH
F
F
F
compound 33
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4.19
3.24
1.00
2.08
2.04
3.06
10.24
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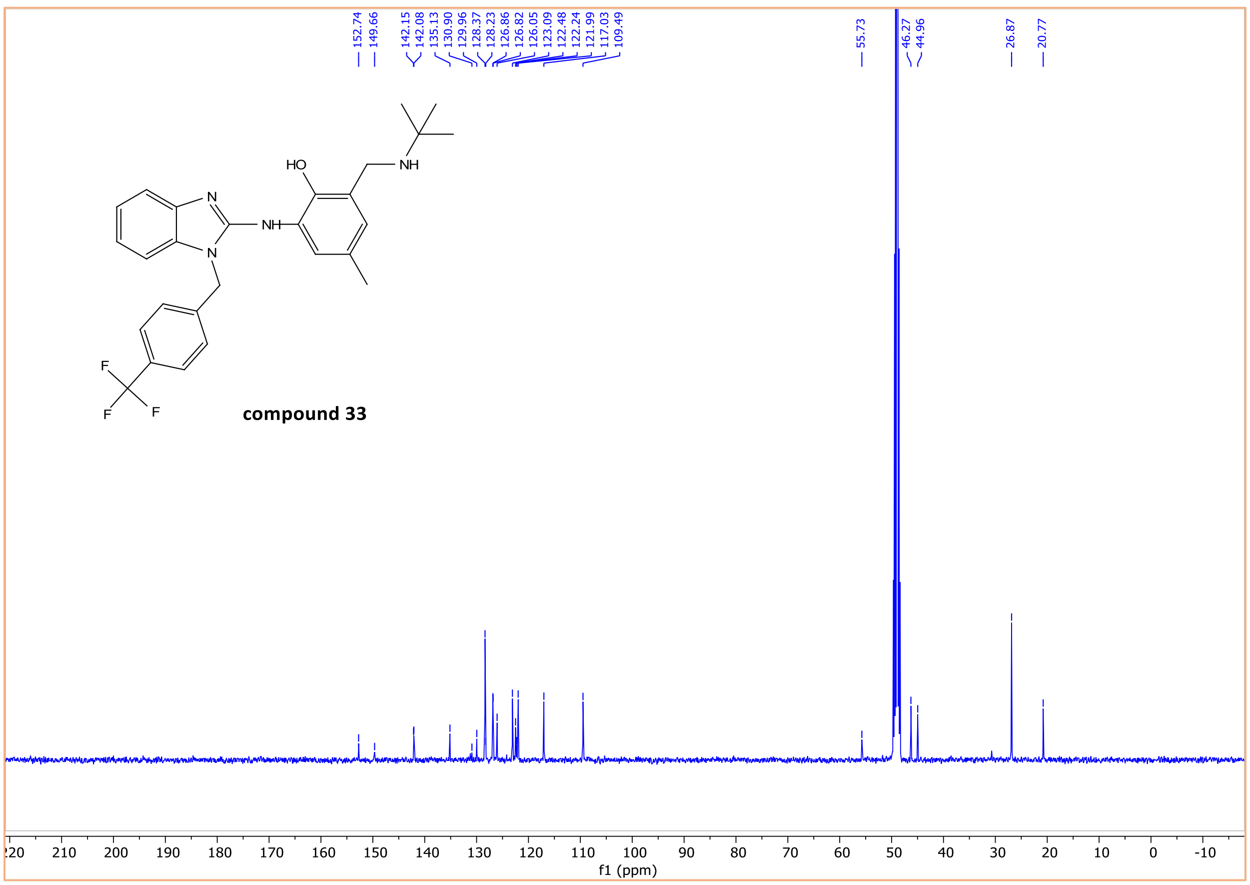
f1 (ppm)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122.48
122.24
121.99
117.03
109.49
55.73
46.27
44.96
26.87
20.77
HO
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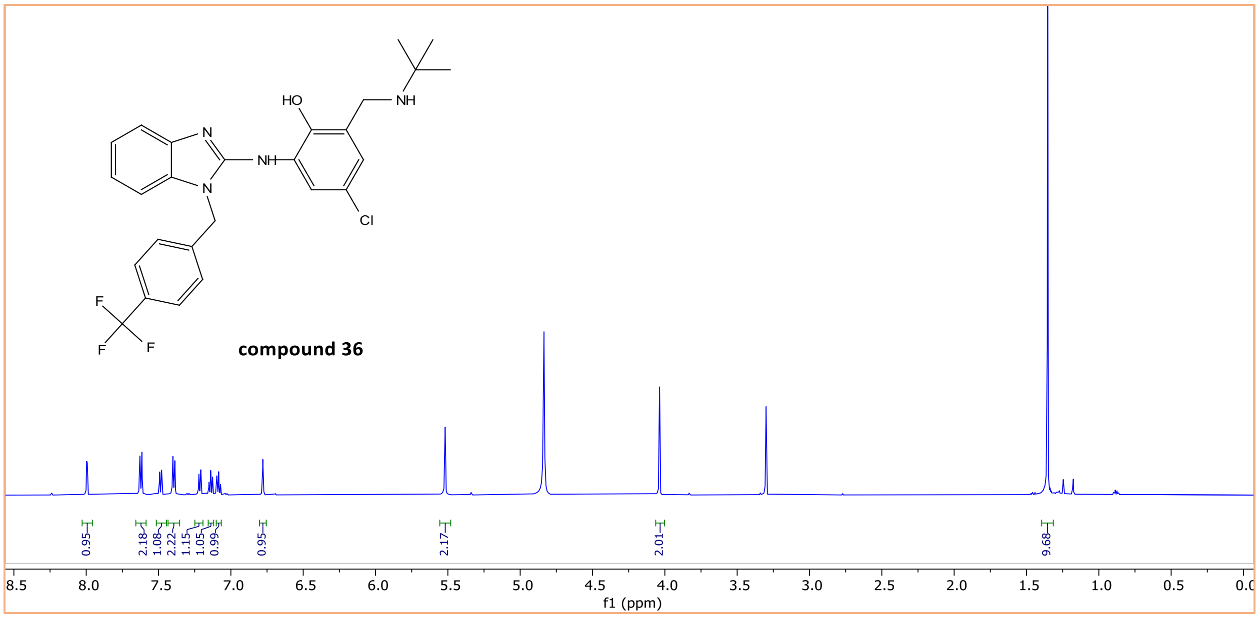
N
NH
F
F
F
compound 33
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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N
Cl
F
F
F
compound 36
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2.18
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1.05
0.99
0.95
2.17
2.01
9.68
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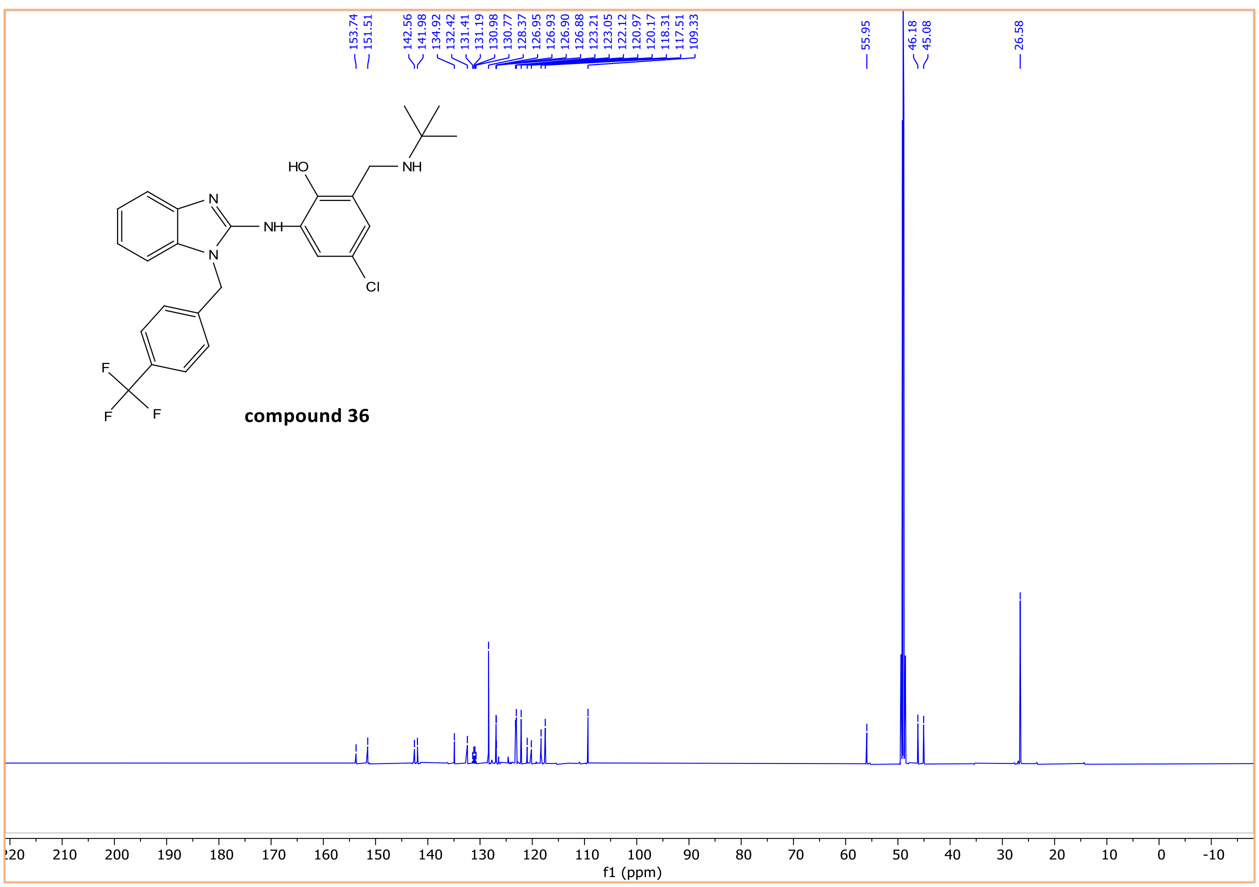
f1 (ppm)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126.90
126.88
123.21
123.05
122.12
120.97
120.17
118.31
117.51
109.33
55.95
46.18
45.08
26.58
HO
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NH
N
Cl
F
F
F
compound 36
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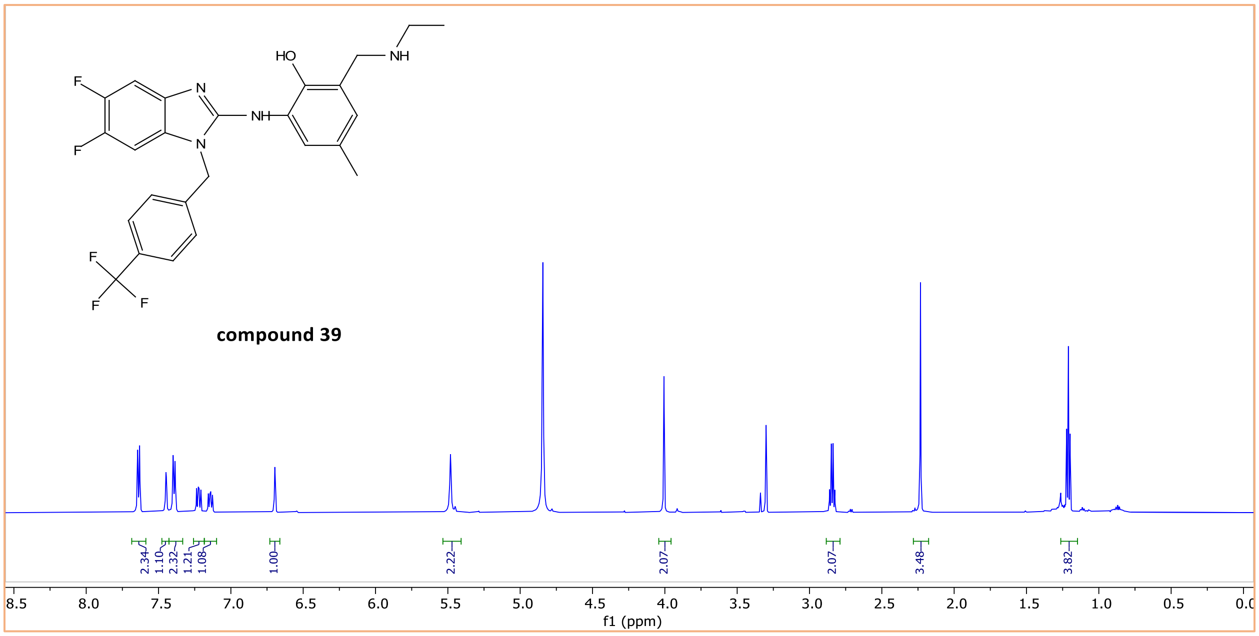
f1 (ppm)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3.82
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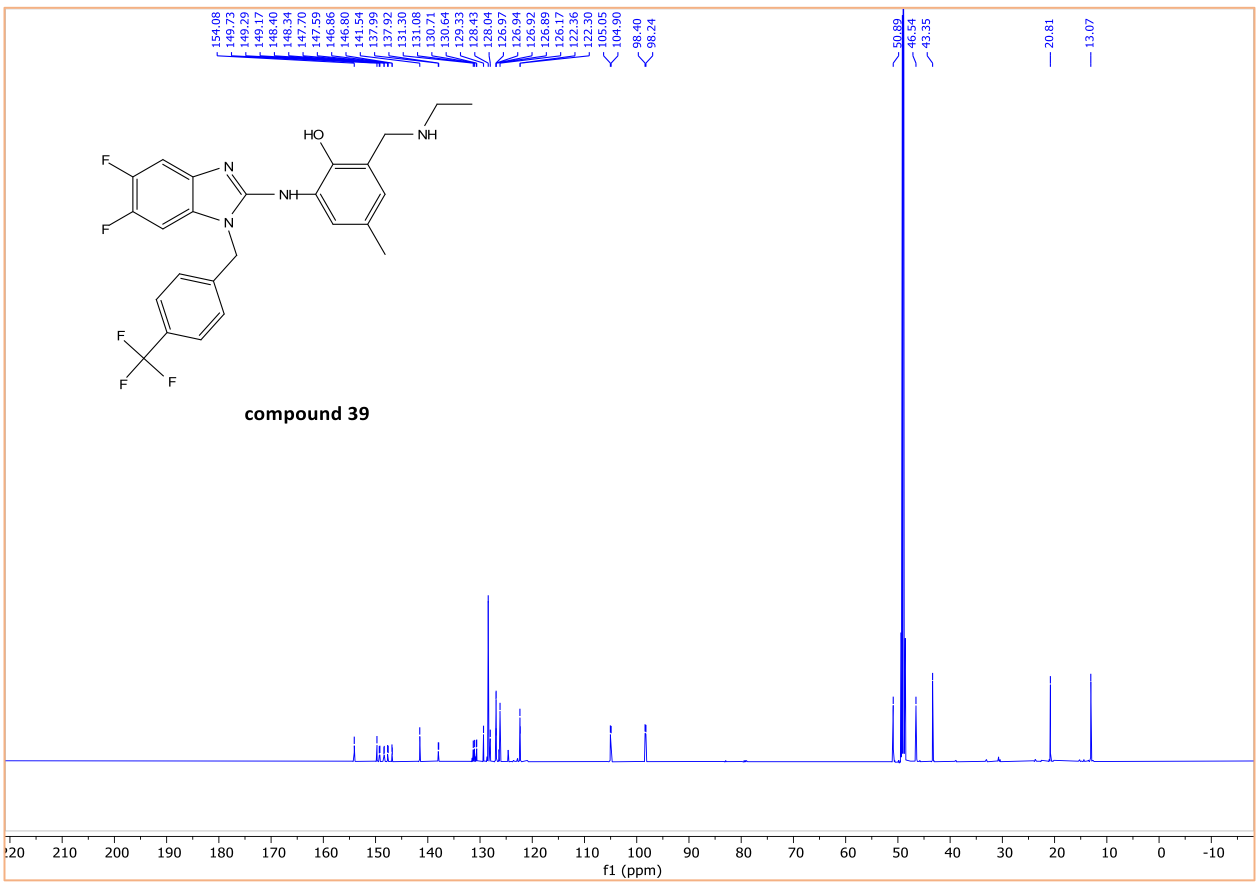
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130.71
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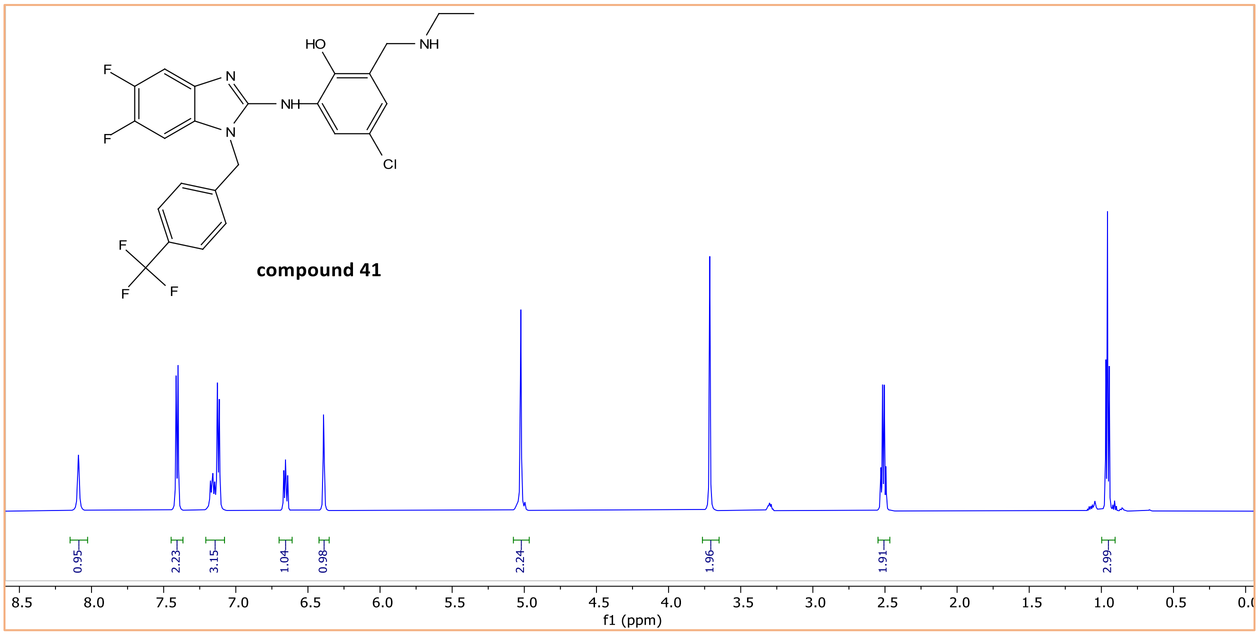
129.33
128.43
128.04
126.97
126.94
126.92
126.89
126.17
122.36
122.30
105.05
104.90
98.40
98.24
50.89
46.54
43.35
20.81
13.07
HO
NH
F
F
N
NH
N
F
F
F
compound 39
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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F
F
N
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NH
Cl
F
F
F
compound 41
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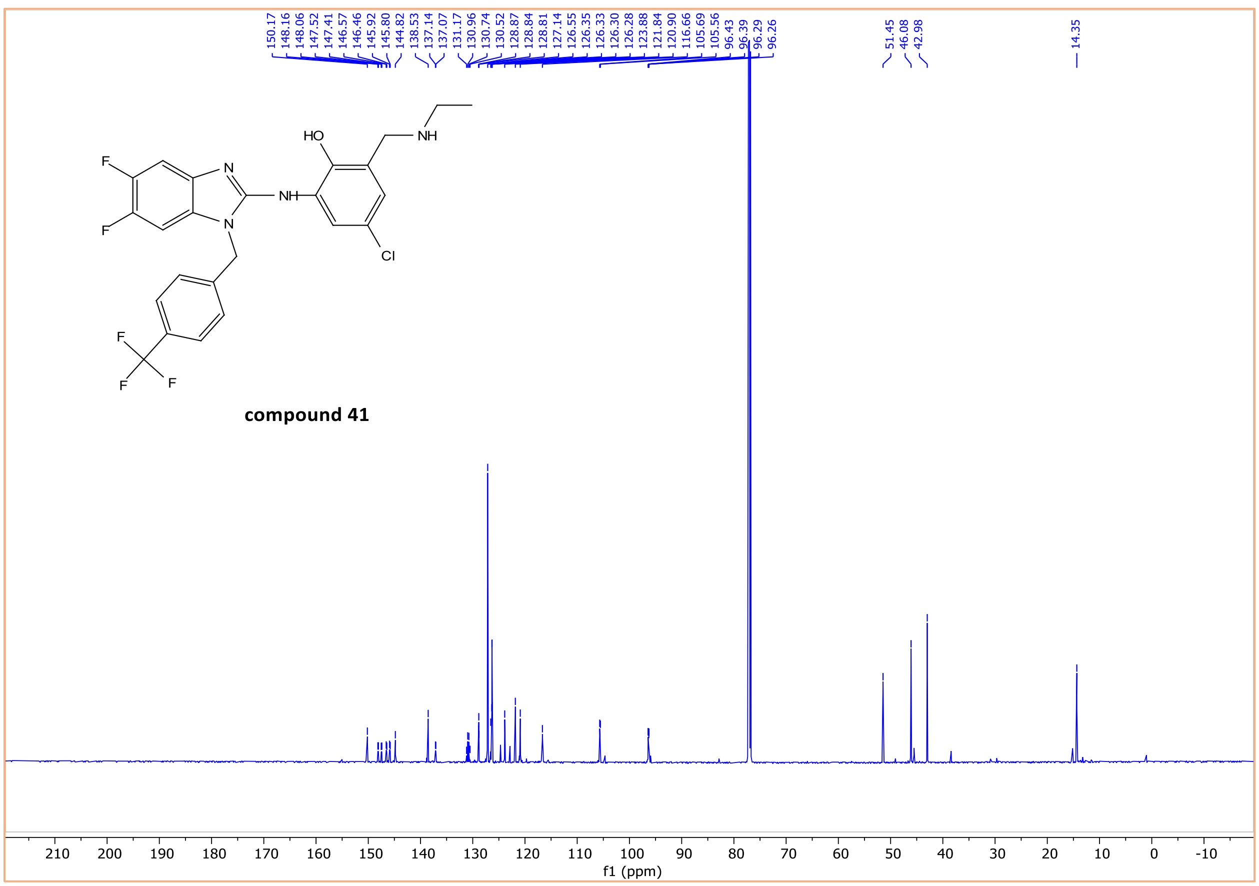
2.23
3.15
1.04
0.98
2.24
1.96
1.91
2.99
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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121.84
120.90
116.66
105.69
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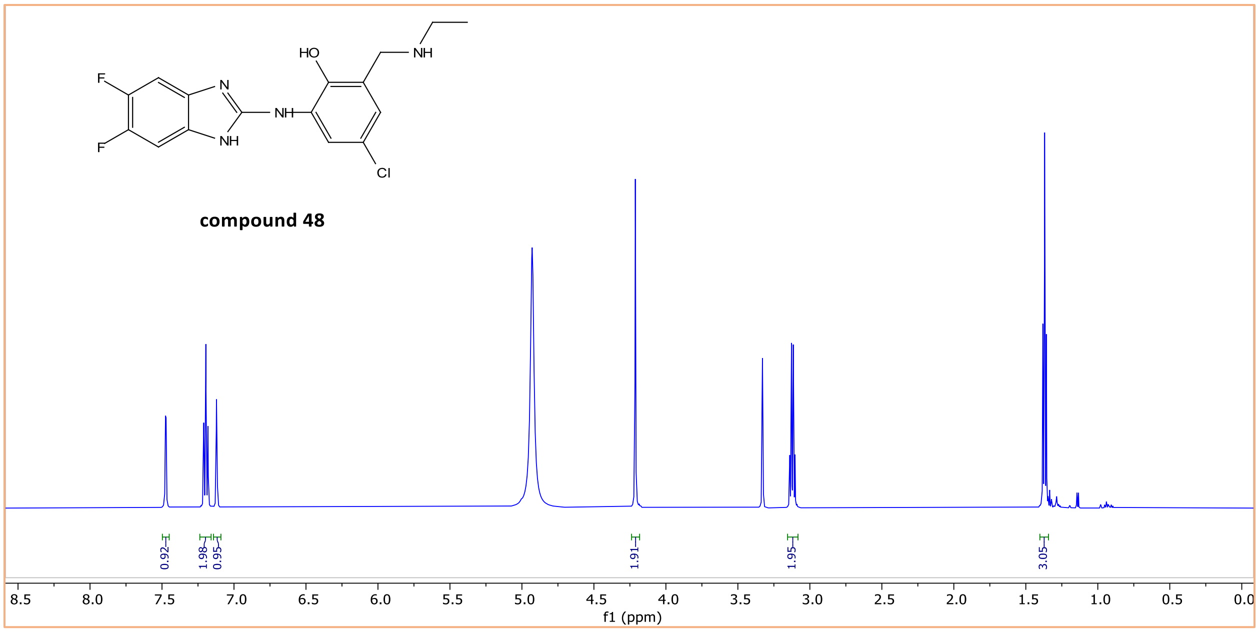
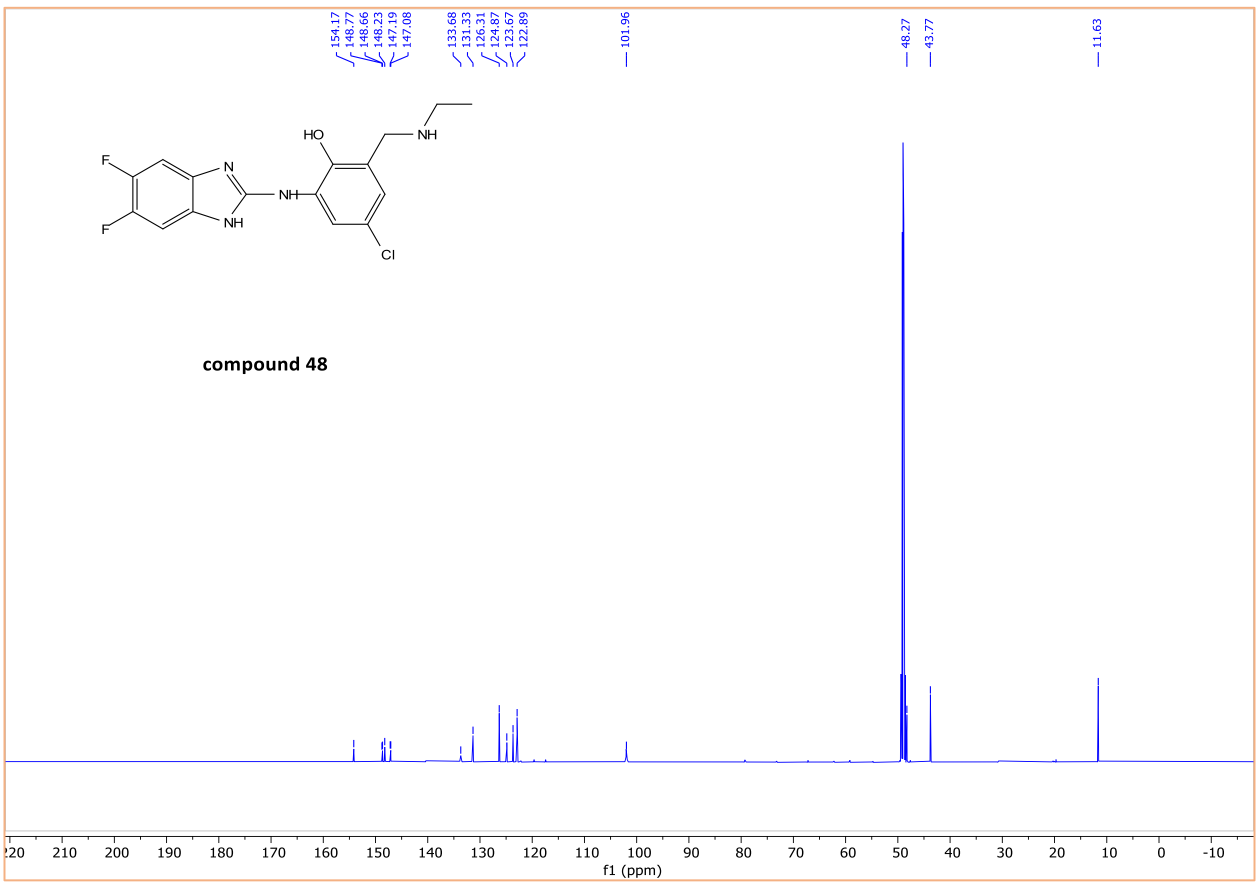
96.39
96.29
96.26
51.45
46.08
42.98
14.35
HO
NH
F
F
N
N
NH
Cl
F
F
F
compound 41
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

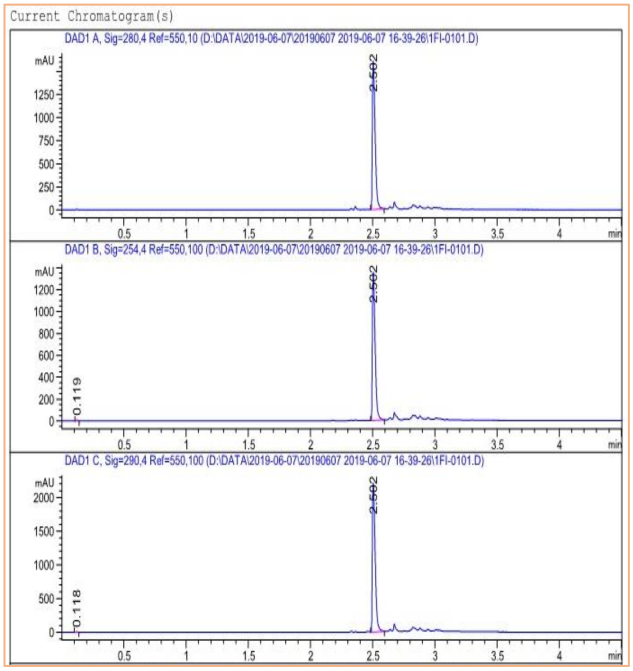


compound 48

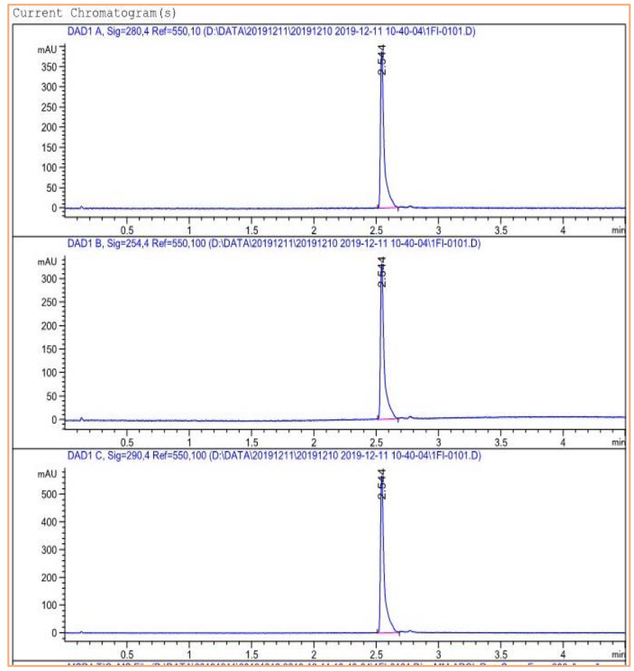


compound 48

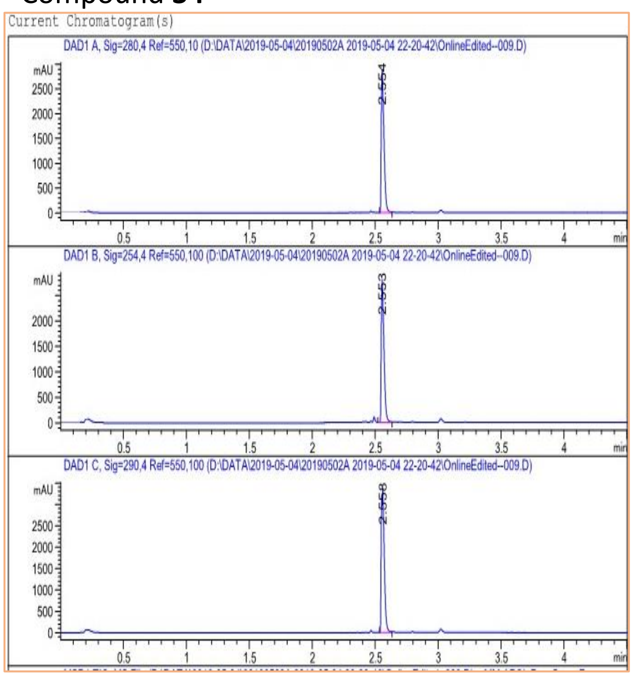
Compound **32**



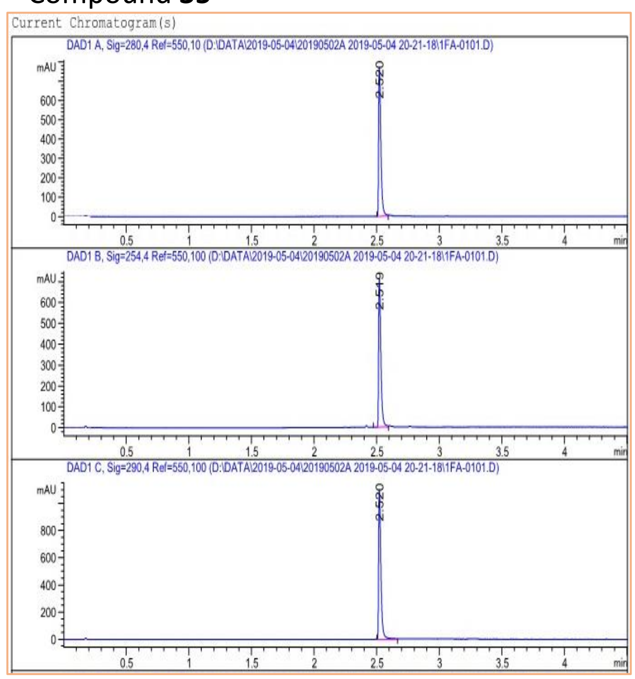
Compound **33**



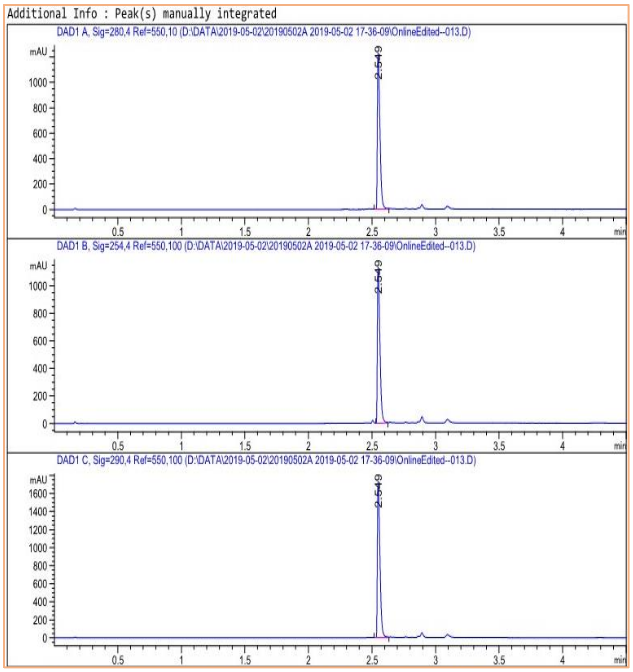
Compound **34**



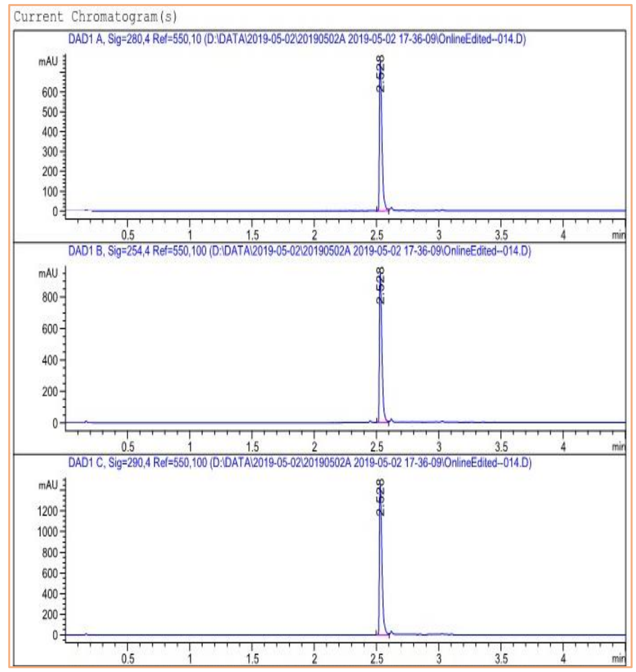
Compound **35**



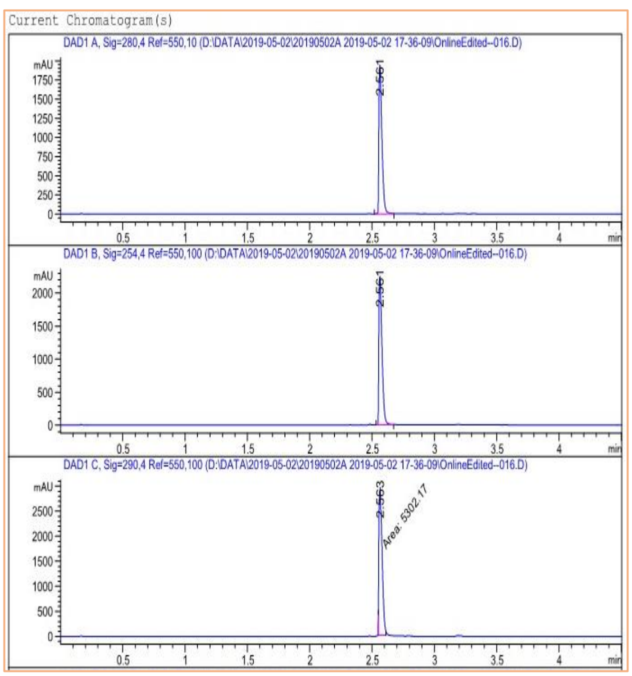
Compound **36**



Compound **39**



Compound **41**



Compound **48**

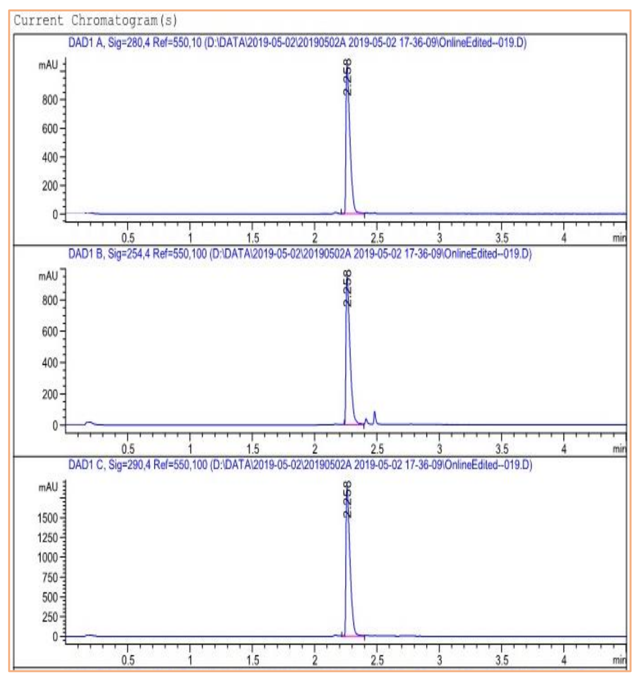


Table S1: β-hematin inhibition activity (βHIA) and cytotoxicity (HepG2) and of the selected compounds

Compound	βHIA (IC_{50}, μM)	HepG2 (EC_{50}, μM)[a]	Compound	βHIA (IC_{50}, μM)	HepG2 (EC_{50}, μM)[a]
12	631.6		**32**	137.8	27.36
13	486.2		**33**	96.7	1.09
14	74.6		**34**	21.1	35.47
15	39.5		**35**	33.3	14.01
16	159.3		**36**	32.4	8.21
17	1079		**37**	34.5	20.74
18	131.8		**38**	79.3	25.0
19	159.4		**39**	30.7	1.00
20	126.6		**40**	16.3	49.14
21	133.9		**41**	18.1	6.88
22	140.0		**42**	16.3	22.65
23	90.9		**43**	17.3	
24	236.9		**44**	12.7	
25	65.3	1.26	**45**	8.13	
26	91.4		**46**	8.45	
27	399.2		**47**	8.11	
28	148.5		**48**	7.15	
29	250.4		**49**	11.5	
30	123.2		**50**	10.3	
31	142.3		**51**	12.6	
Amodiaquine	13.16		Amodiaquine	13.16	
Emetine		4.45	Emetine		4.45

[a]Emetine was used as control and showed 94.7% toxicity at 2 μM
Blank spaces = Not tested

Table S2: LC-MS/MS analytical conditions for PK analysis

Instrument	AB SCIEX 5500 QTRAP equipped with a Turbo V™ ion source coupled to an Agilent 1260 HPLC
Detection	Positive electrospray ionization under MRM scans
Column	Kinetex C18, 50x2.1mm, 2.6µm
LC Conditions	Gradient 0.4mL/min, 7 min run, injection volume 5µL, column temperature 40℃, sample tray temperature 8℃
Mobile Phase	A: 0.1% formic acid; B 0.1% formic acid in acetonitrile
Software	Analyst 1.6.3 software for instrument control, data acquisition and analysis

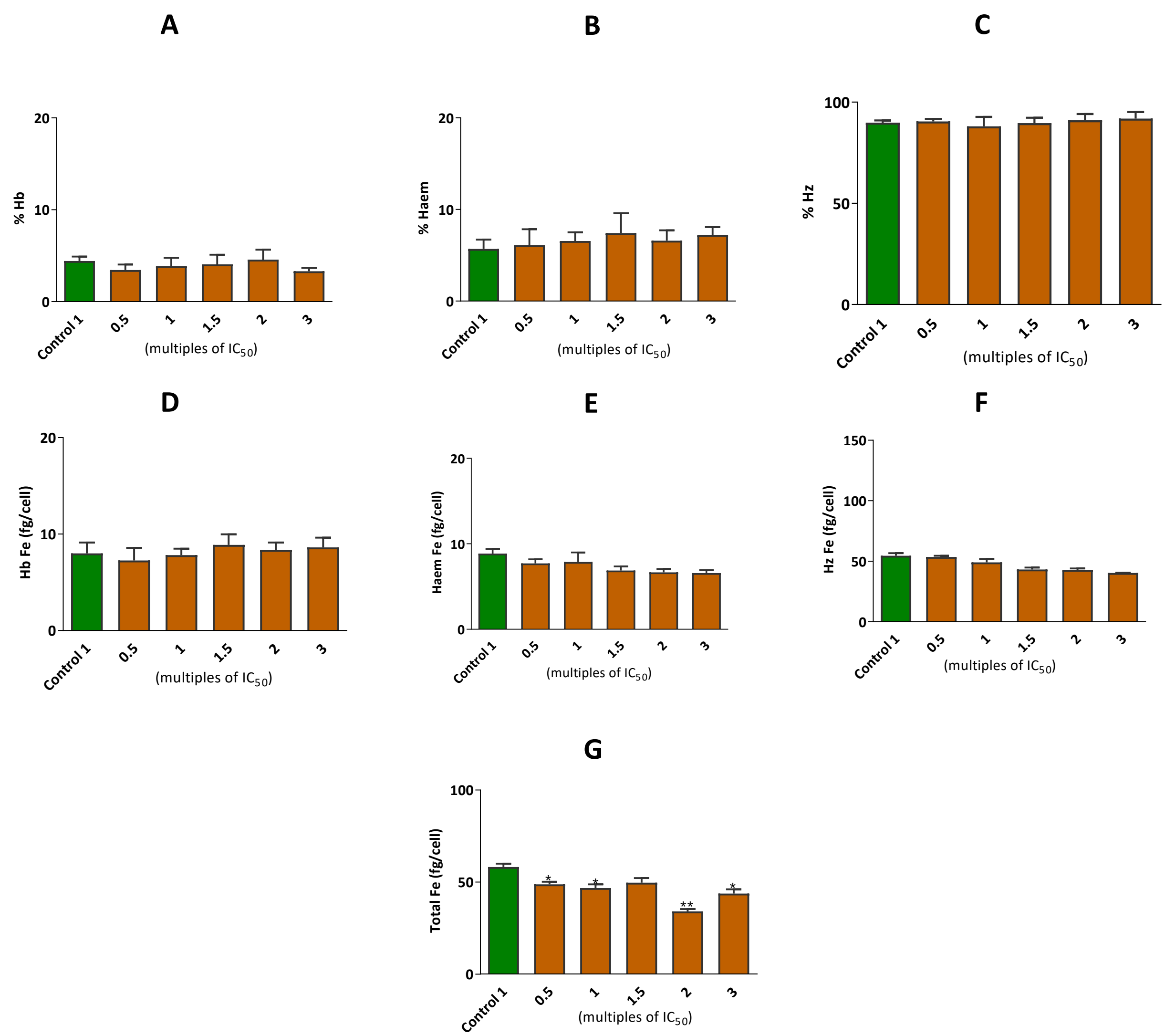


Figure S2: Heme species in synchronized control and compound **35** treated *Pf*NF54 parasites. Heme fractionation profile of **35** showing percent hemoglobin (A), haem (B) and hemozoin (C) at multiples of its IC_{50}. The absolute amount of hemoglobin (Hb) Fe, "free" heme Fe and hemozoin (Hz) Fe are depicted in (D), (E) and (F) at multiples of its IC_{50}. Plot G represents total Fe at multiples of its IC_{50}. Significance levels are shown with asterisks, where $p < 0.05$ (*), $p < 0.01$ (**), and $p < 0.001$ (***).

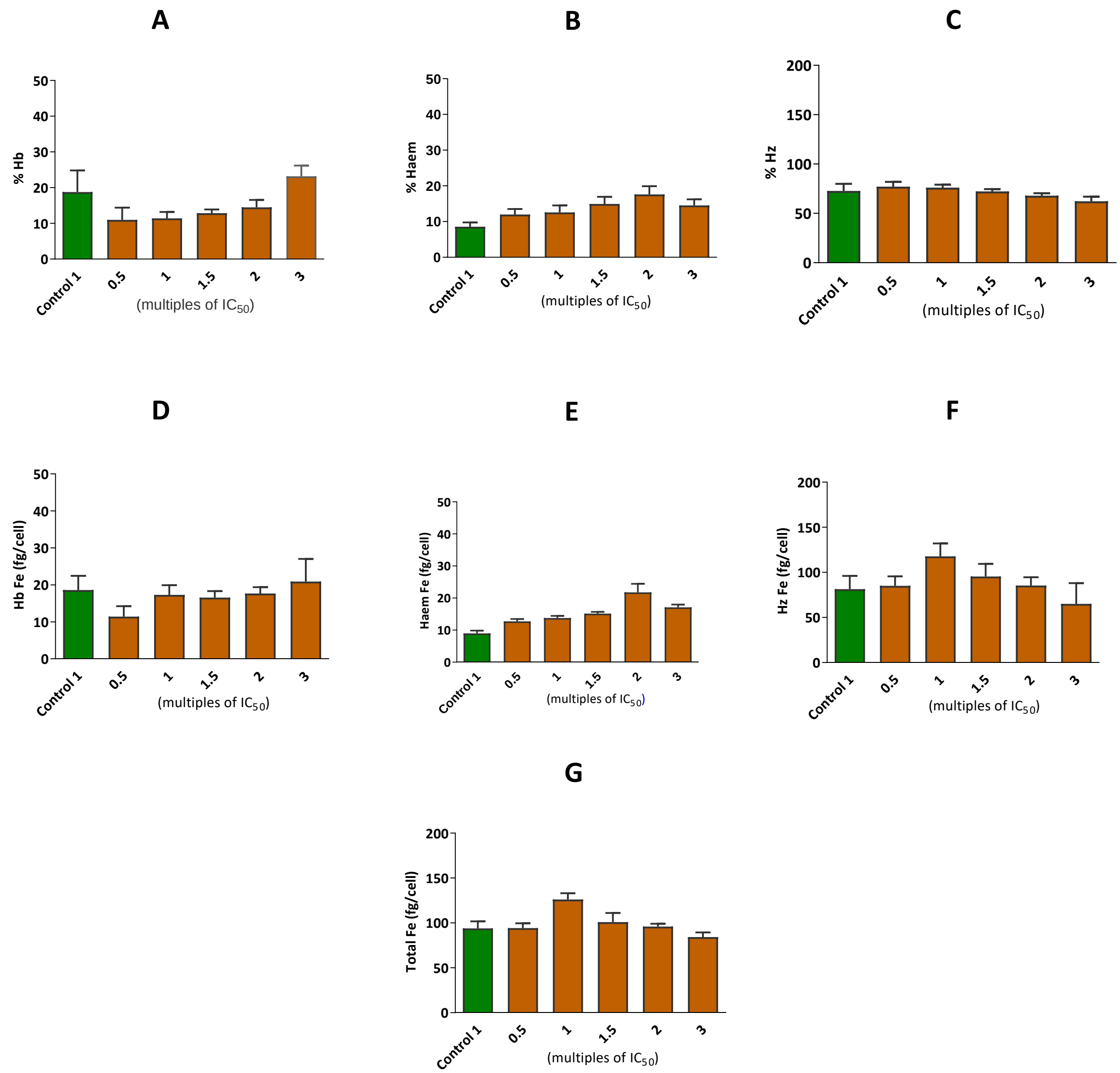


Figure S3: Heme species in synchronized control and compound **41** treated *Pf*NF54 parasites Heme fractionation profile of **41** showing percent hemoglobin (A), haem (B) and hemozoin (C) at multiples of its IC_{50}. The absolute amount of hemoglobin (Hb) Fe, "free" heme Fe and hemozoin (Hz) Fe are depicted in (D), (E) and (F) at multiples of its IC_{50}. Plot G represents total Fe at multiples of its IC_{50}. Significance levels are shown with asterisks, where $p < 0.05$ (*), $p < 0.01$ (**), and $p < 0.001$ (***).

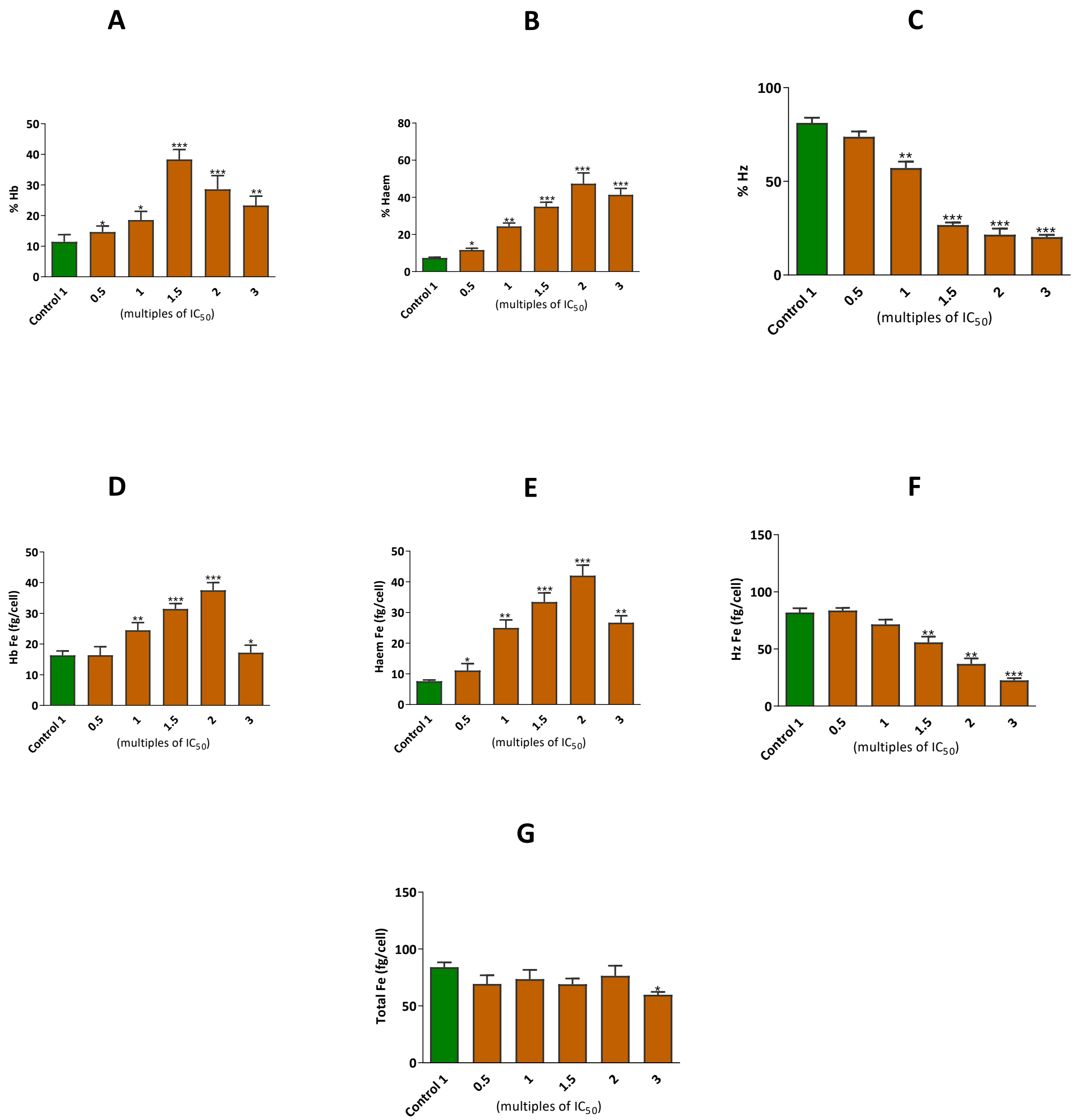


Figure S4: Heme species in synchronized control and compound **44** treated *Pf*NF54 parasites Heme fractionation profile of **44** showing percent hemoglobin (A), haem (B) and hemozoin (C) at multiples of its IC_{50}. The absolute amount of hemoglobin (Hb) Fe, "free" heme Fe and hemozoin (Hz) Fe are depicted in (D), (E) and (F) at multiples of its IC_{50}. Plot G represents total Fe at multiples of its IC_{50}. Significance levels are shown with asterisks, where $p < 0.05$ (*), $p < 0.01$ (**), and $p < 0.001$ (***).

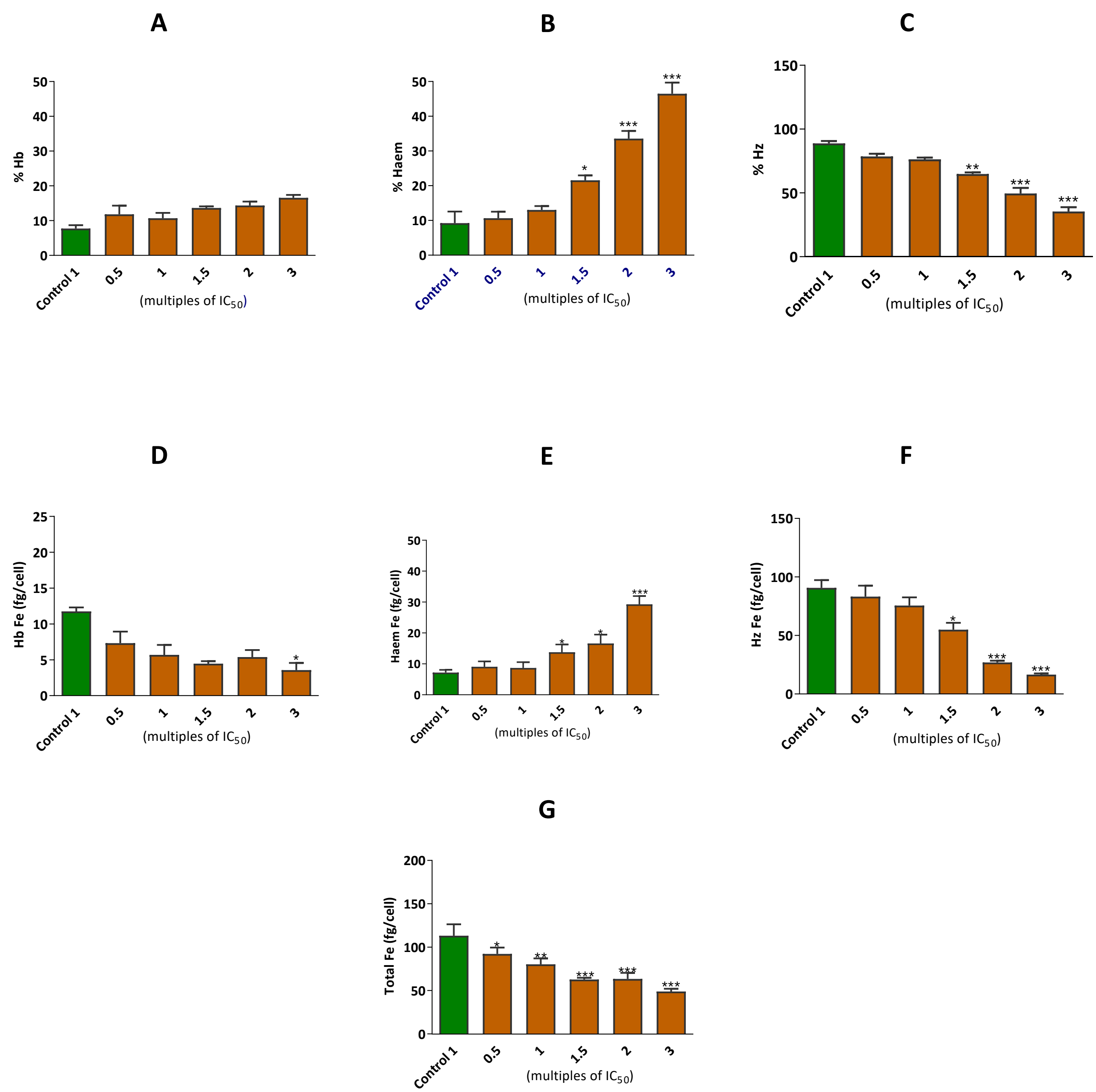


Figure S5: Heme species in synchronized control and compound **48** treated *Pf*NF54 parasites Heme fractionation profile of **48** showing percent hemoglobin (A), haem (B) and hemozoin (C) at multiples of its IC_{50}. The absolute amount of hemoglobin (Hb) Fe, "free" heme Fe and hemozoin (Hz) Fe are depicted in (D), (E) and (F) at multiples of its IC_{50}. Plot G represents total Fe at multiples of its IC_{50}. Significance levels are shown with asterisks, where $p < 0.05$ (*), $p < 0.01$ (**), and $p < 0.001$ (***).

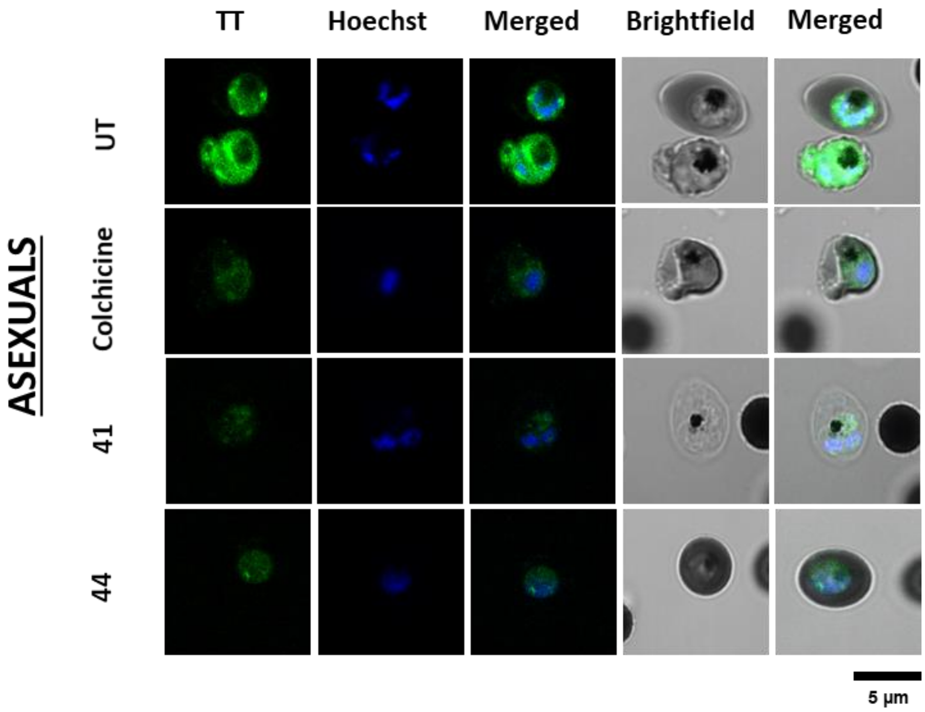


Figure S6: Live cell confocal imaging of asexual trophozoites of *Plasmodium falciparum.* Cells are labelled with Tubulin Tracker® (TT, green) and Hoescht 3324 nuclear stain (blue). Brightfield images are shown on right side of each image. UT = Untreated. Scale represents 5 μm.

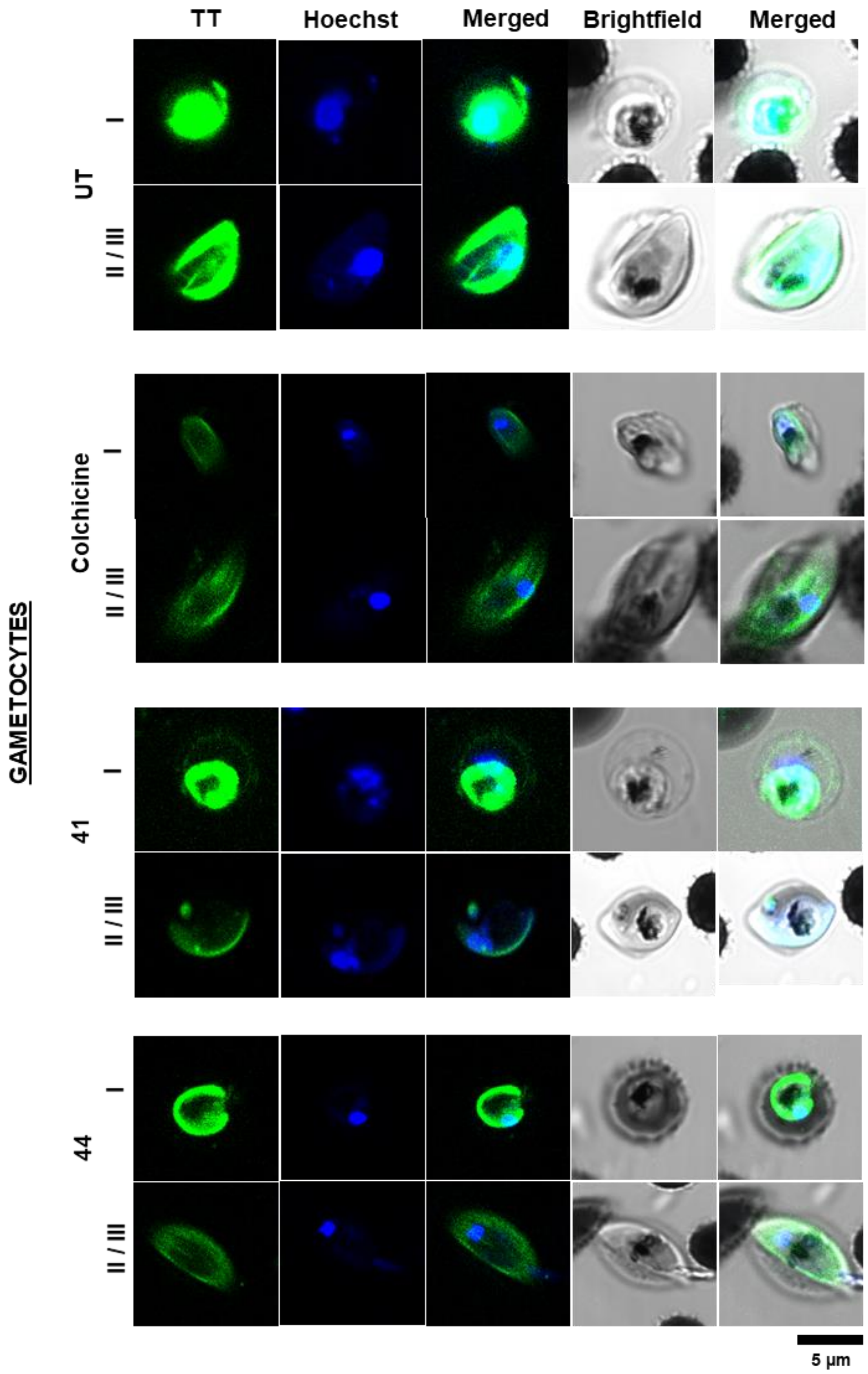


Figure S7: Live cell confocal imaging of stage I-III gametocytes of *Plasmodium falciparum.* Cells are labelled with Tubulin Tracker® (TT, green) and Hoescht 3324 nuclear stain (blue). Brightfield images are shown on right side of each image. UT = Untreated. Scale represents 5 µm.