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Structure-based Design, Synthesis, and Biological Evaluation of Novel Piperine-Resveratrol Hybrids as Antiproliferative Agents Targeting SIRT-2

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- Hirschfield surfaces in **5a** mapped with (a) d_{norm}; (b) Shape index, (c) full fingerprint plot; (d) H···O contacts (O-H···O and C-H…O); (e) H···C contacts (C-H···π) and (f) C···C contacts (π···π). **Figure S9**
- Hirschfield surfaces in **5c** mapped with (a) d_{norm}; (b) Shape index, (c) full fingerprint plot; (d) H···O contacts (O-H···O and C-H…O); (e) H···C contacts (C-H···π) and (f) C···C contacts (π···π). **Figure S10**
- Hirschfield surfaces in **5d** mapped with (a) d_{norm}; (b) Shape index, (c) full fingerprint plot; (d) H···O contacts (O-H···O and C-H…O); (e) H···C contacts (C-H···π) and (f) C···C contacts (π···π). **Figure S11**
- Hirschfield surfaces in **5e** mapped with (a) d_{norm}; (b) Shape index, (c) full fingerprint plot; (d) H···O contacts (O-H···O and C-H…O); (e) H···C contacts (C-H···π) and (f) C···C contacts (π···π). **Figure S12**
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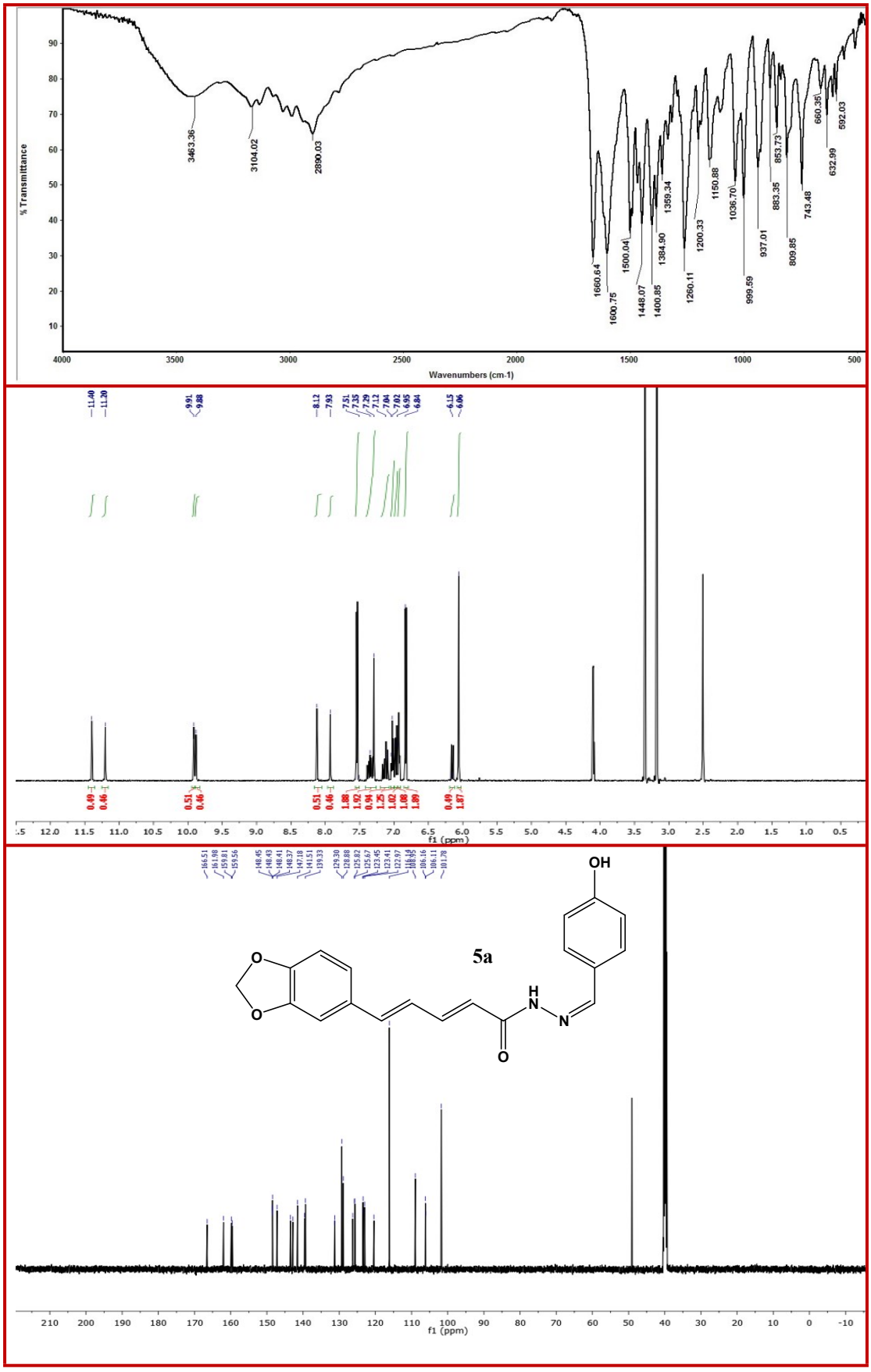
The crystallographic data and structure refinement for **5a-f** **Table S1**

Figure S1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1359.34
1260.11
1200.33
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1036.70
999.59
937.01
883.35
853.73
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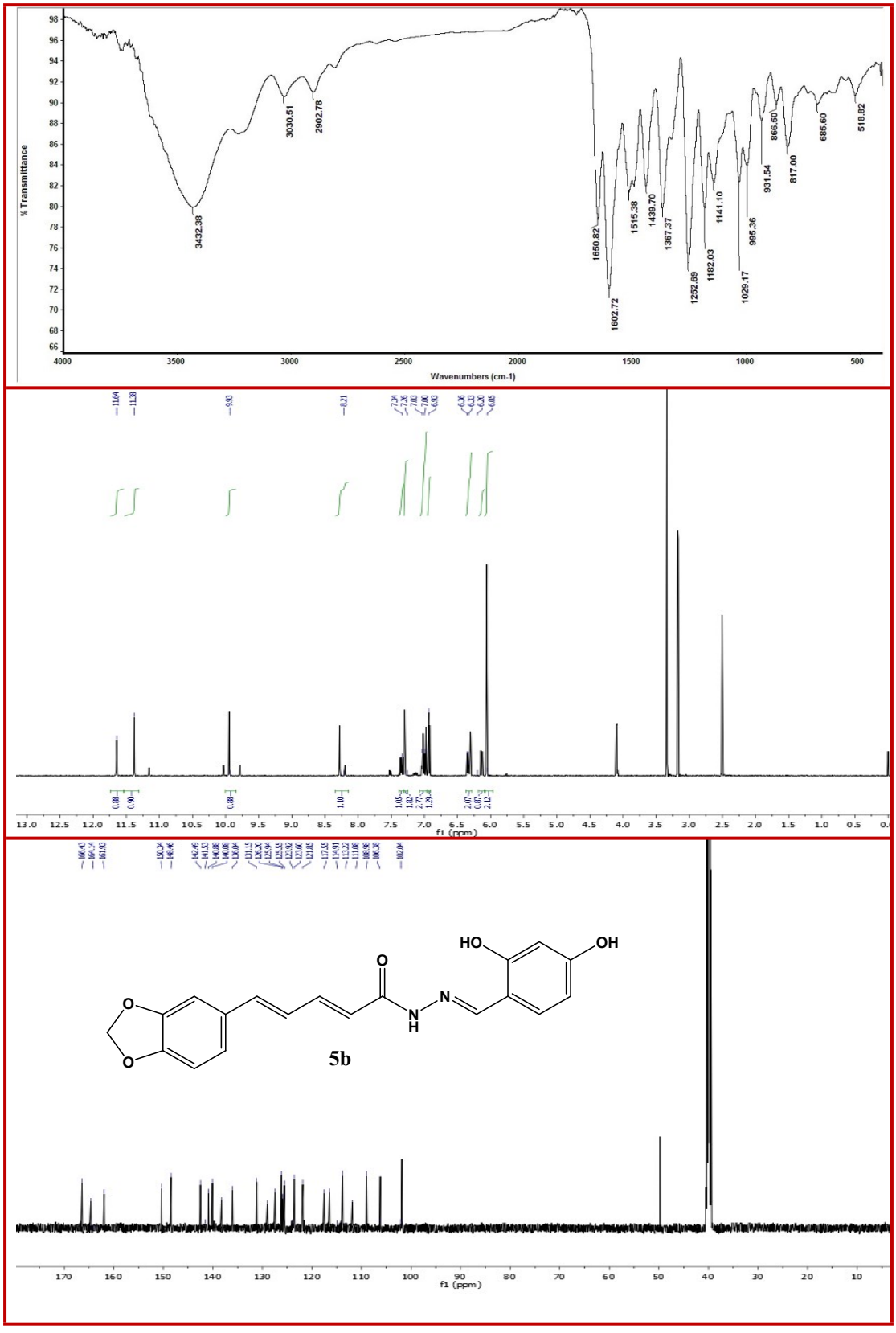
f1 (ppm)
5a
OH
O
O
H
N
N
O

Figure S2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Wavenumbers (cm-1)
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1141.10
1029.17
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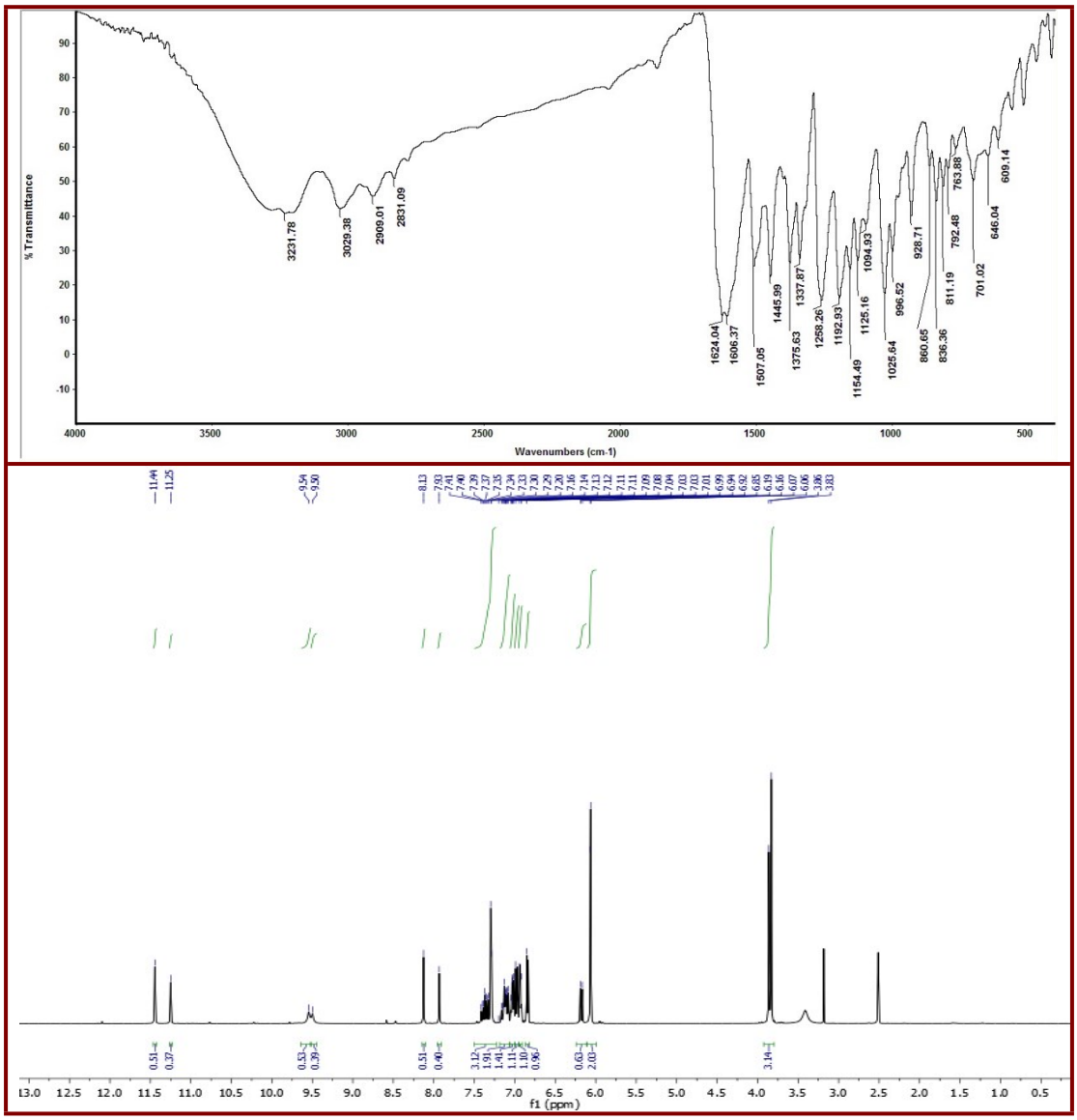
685.60
518.82
f1 (ppm)
HO
OH
O
N
H
5b

Figure S3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1337.87
1258.26
1192.93
1154.49
1125.16
1094.93
1025.64
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f1 (ppm)

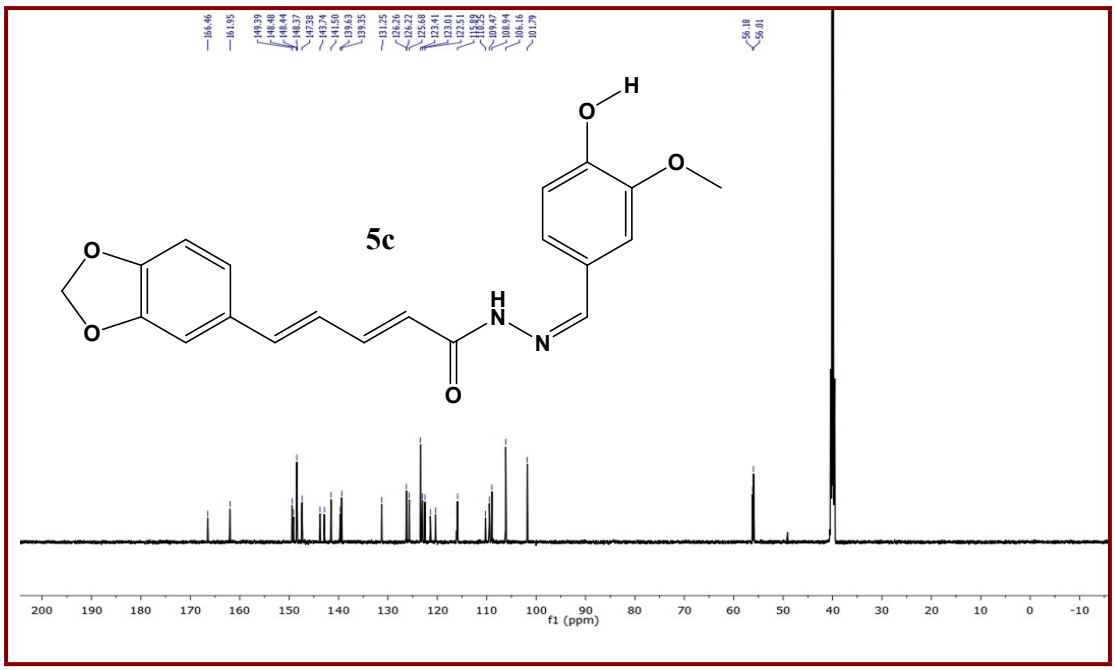
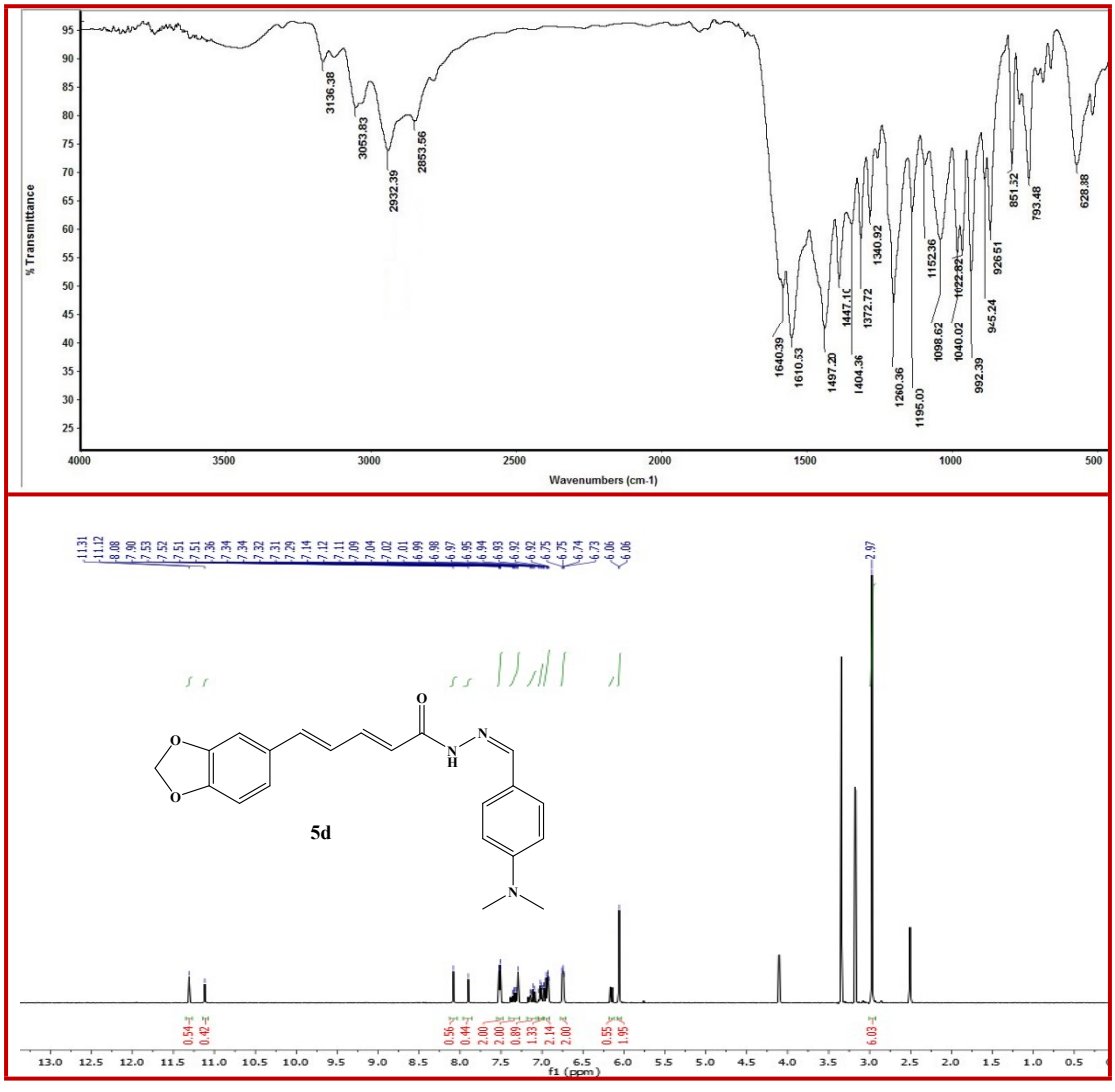

5c
f1 (ppm)

Figure S4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1404.36
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1340.92
1260.36
1195.03
1152.36
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1040.02
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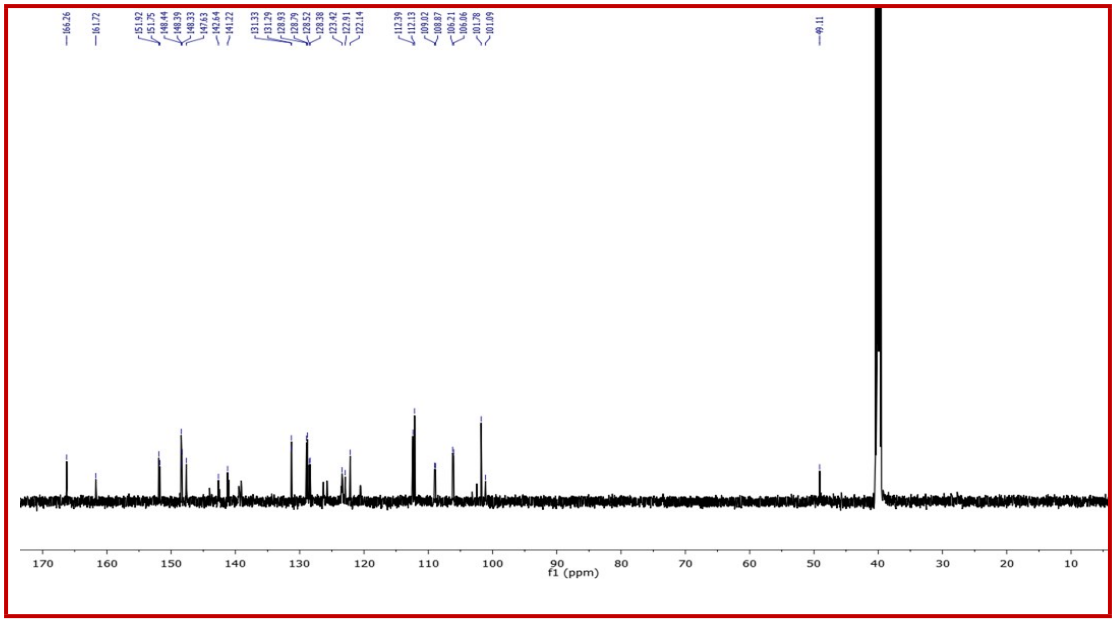
851.32
793.48
628.88
5d
f1 (ppm)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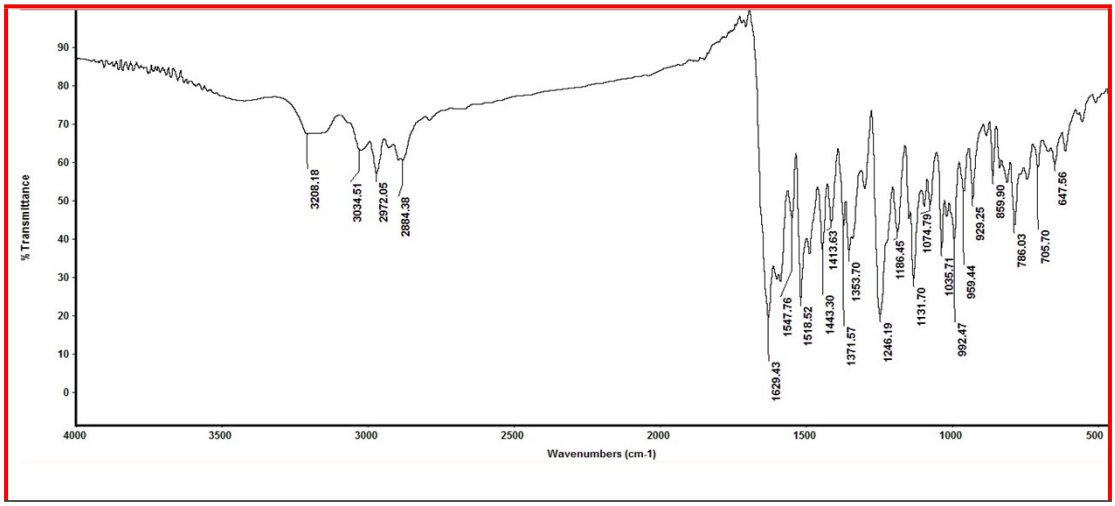
161.72
151.92
151.75
148.44
148.39
148.33
147.63
142.64
141.22
131.33
131.30
128.43
128.29
128.52
128.38
123.42
122.91
122.14
112.39
112.13
109.02
108.87
106.21
100.46
101.28
101.09
49.11
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

Figure S5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70
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20
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1547.76
1518.52
1443.30
1413.63
1371.57
1353.70
1246.19
1186.45
1131.70
1074.79
1035.71
992.47
969.44
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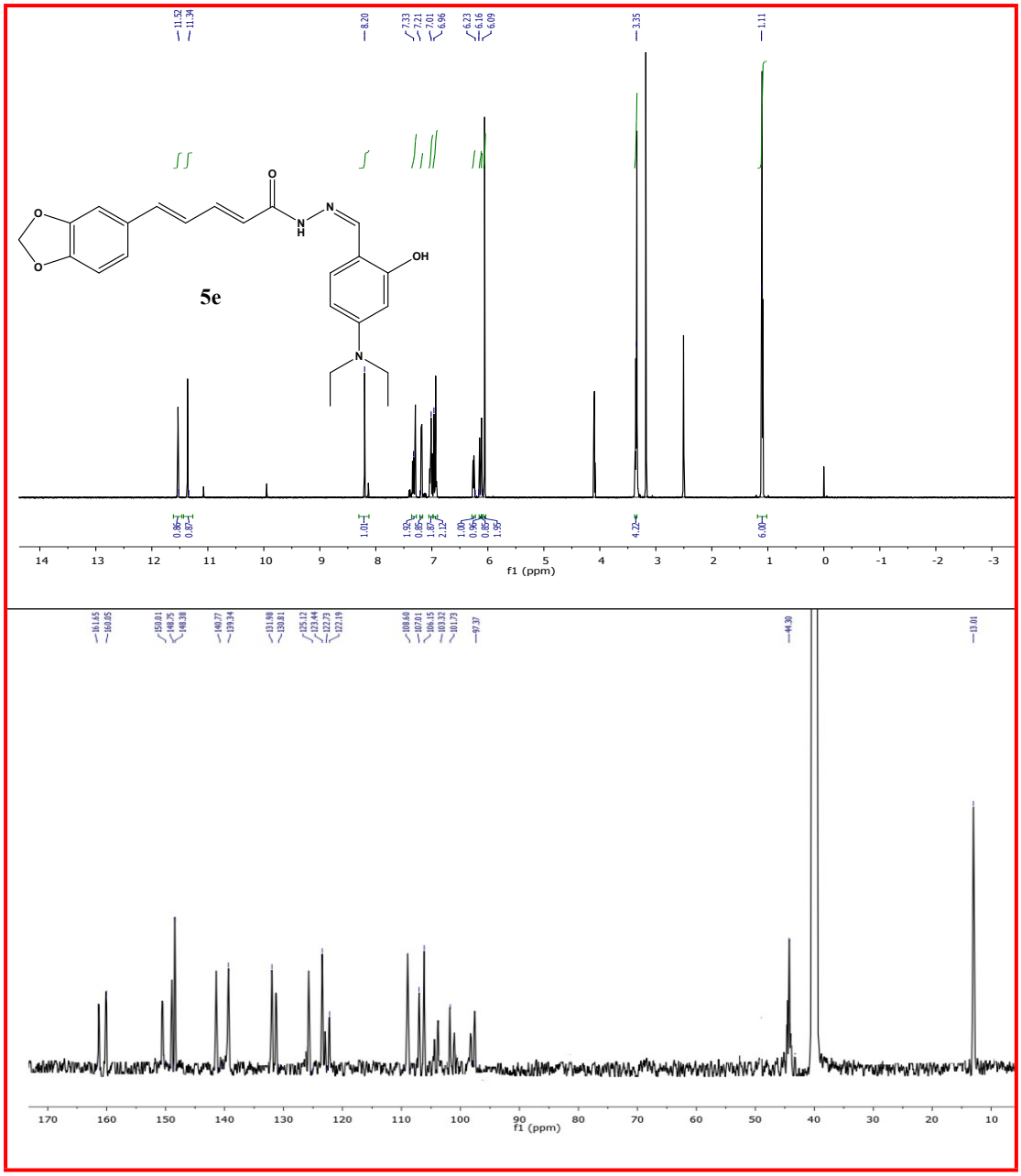
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers (cm-1)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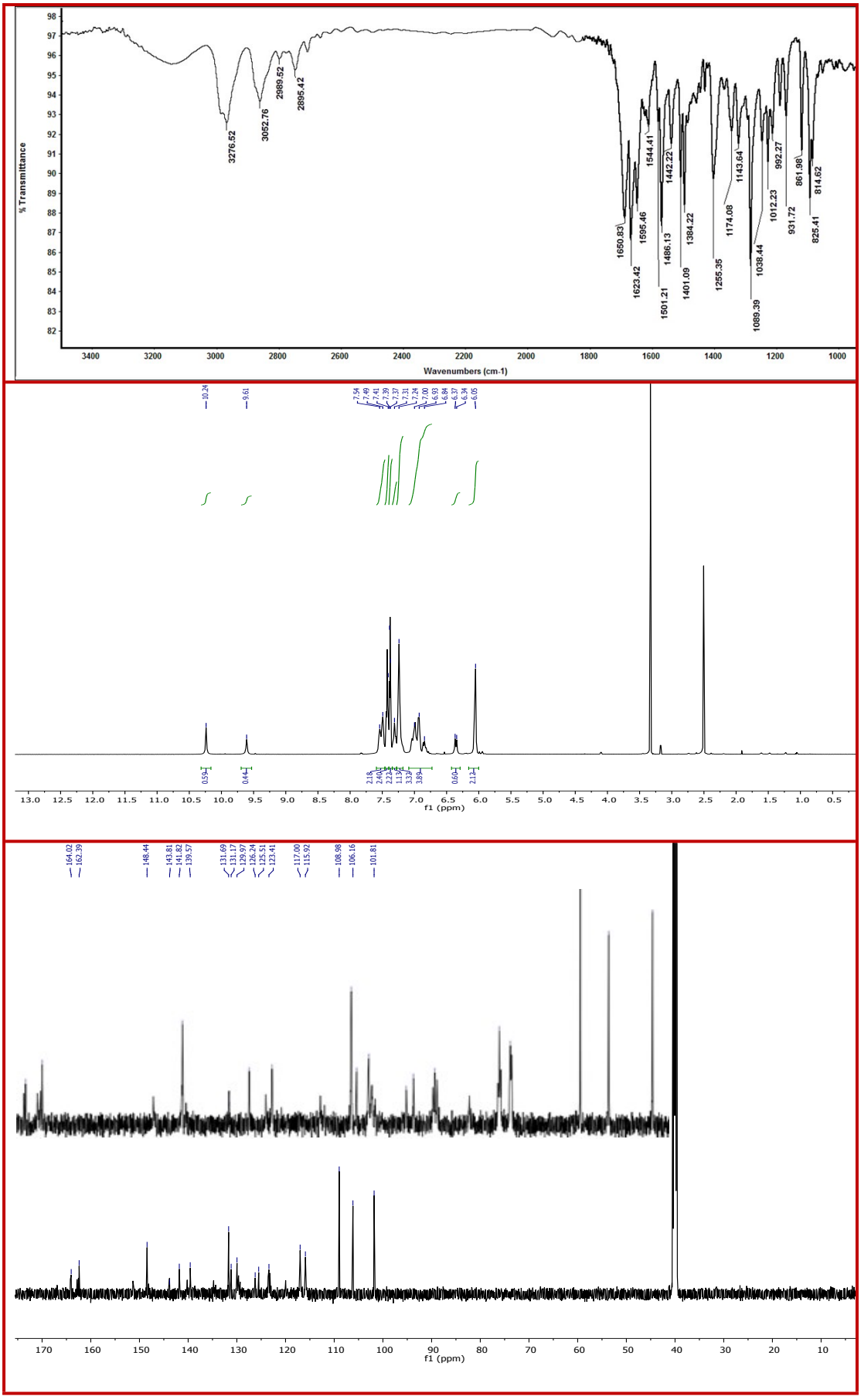
11.34
8.20
7.33
7.21
7.01
6.96
6.23
6.16
6.09
3.35
1.11
O
O
O
N
N
H
OH
N
5e
f1 (ppm)
161.65
160.05
150.01
148.75
148.38
140.77
139.34
131.98
130.81
125.12
123.44
122.73
122.19
108.60
107.01
106.15
103.32
101.73
97.37
44.30
13.01
f1 (ppm)

Figure S6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Wavenumbers (cm-1)
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1650.83
1623.42
1595.46
1544.41
1501.21
1486.13
1442.22
1401.09
1384.22
1255.35
1174.08
1143.64
1089.39
1038.44
1012.23
992.27
931.72
861.98
825.41
814.62
f1 (ppm)
f1 (ppm)

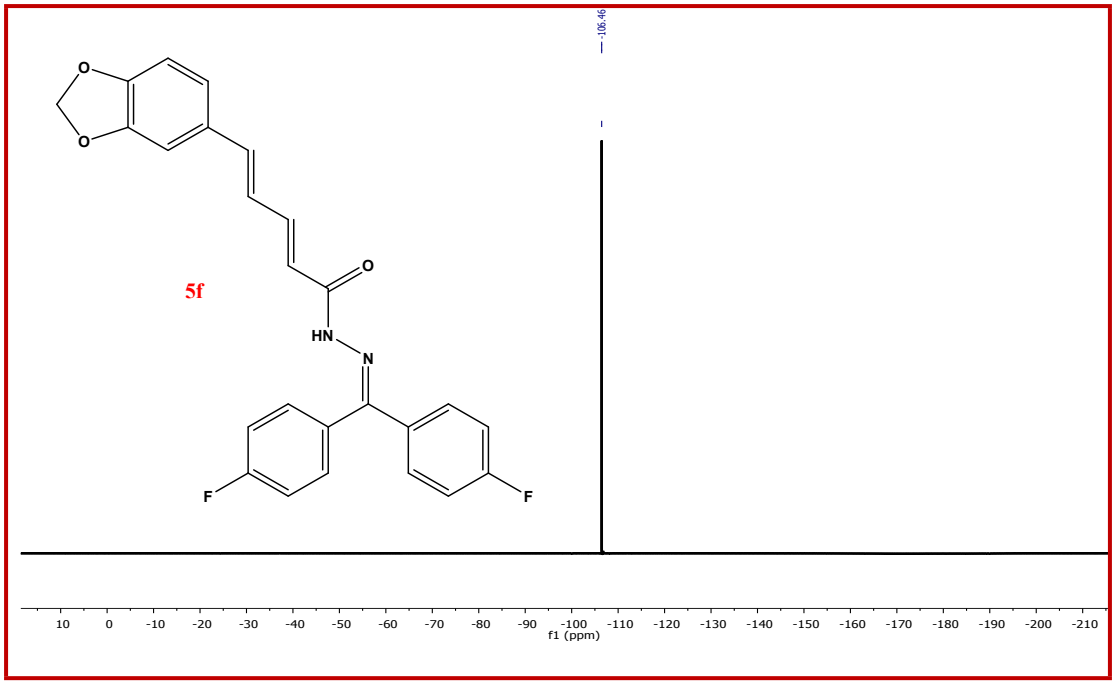
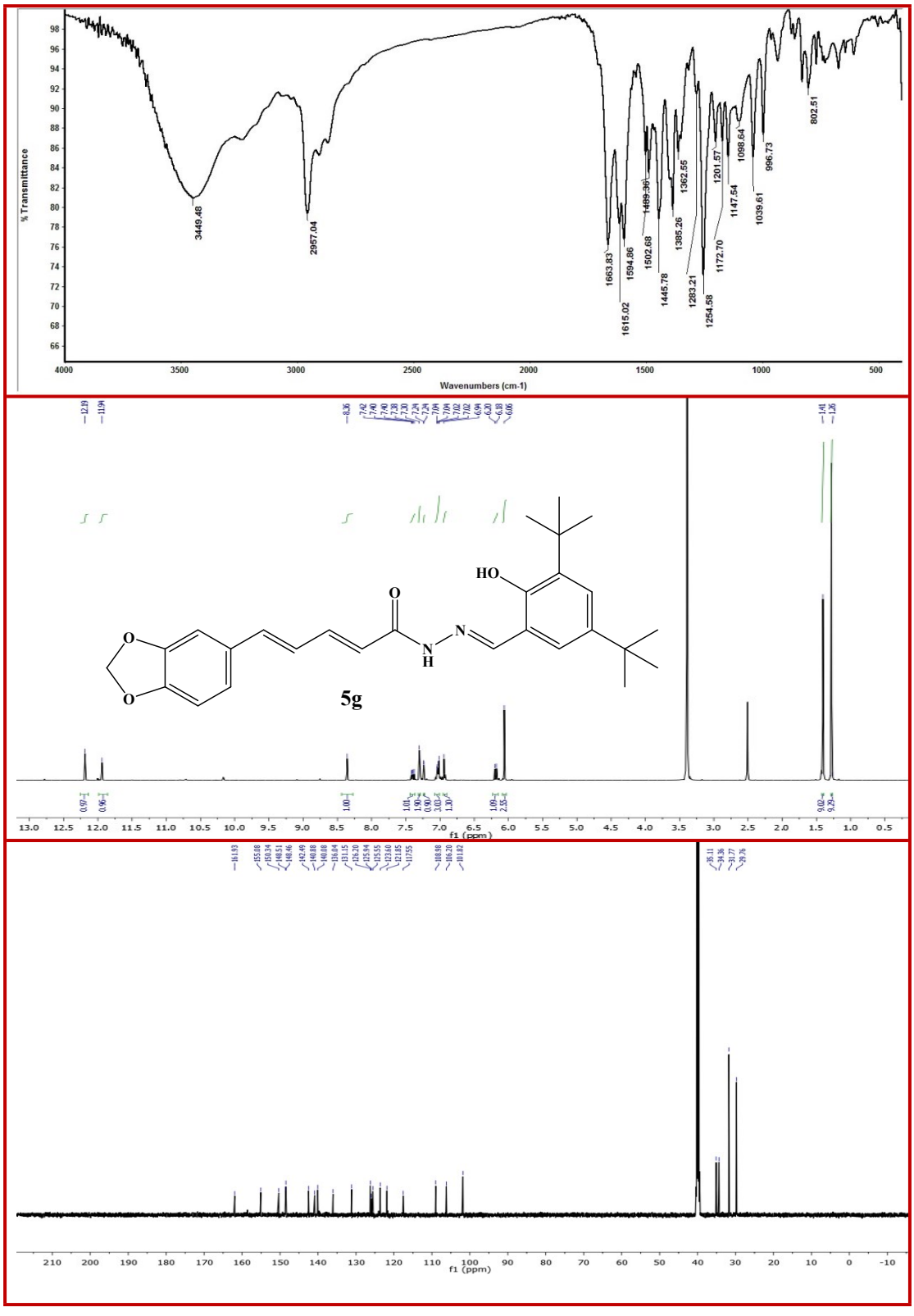

-106.46
O
O
O
HN
N
F
F
5f
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

Figure S7


% Transmittance
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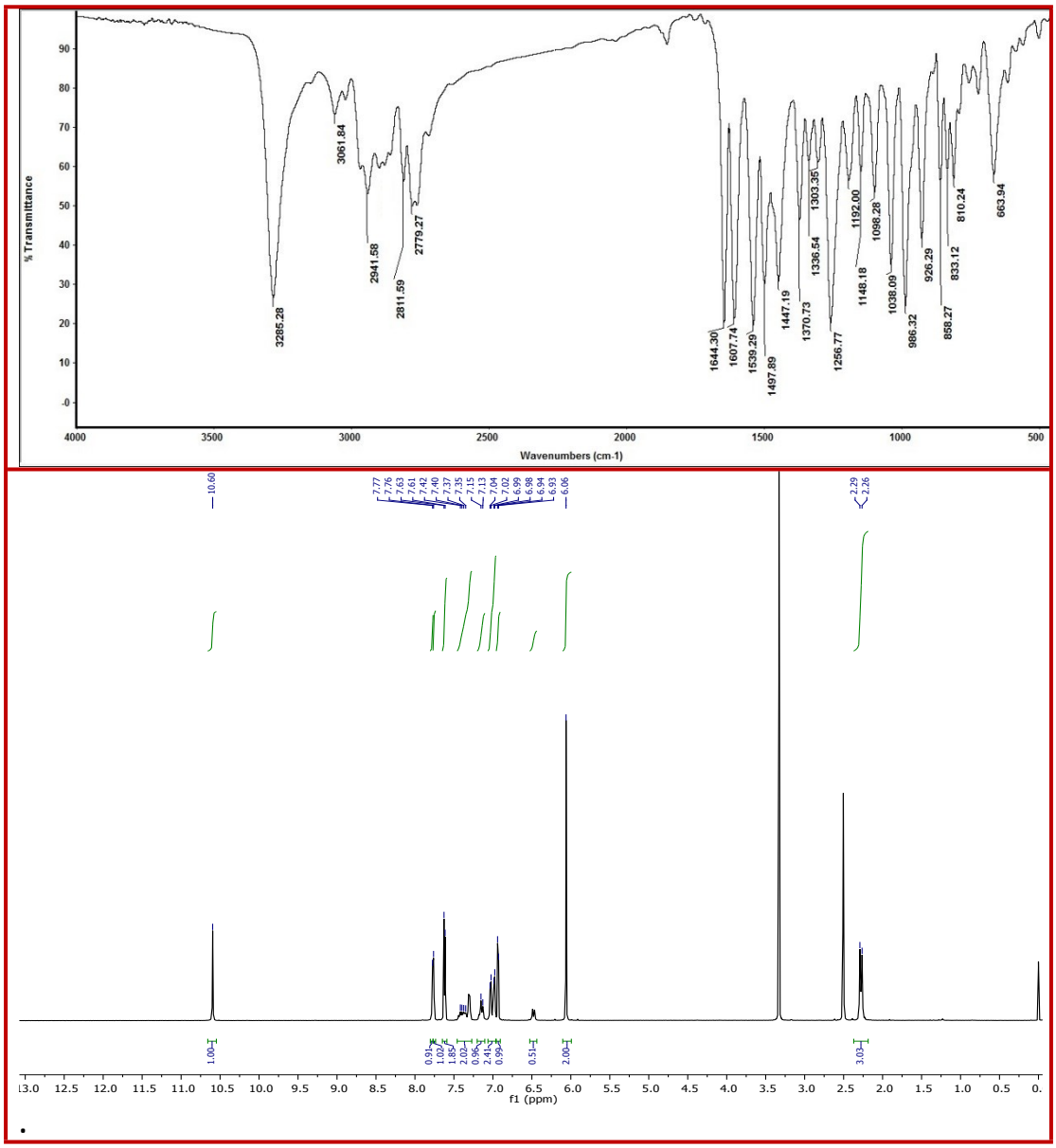
1615.02
1594.86
1502.68
1489.30
1445.78
1385.26
1362.55
1283.21
1254.58
1201.57
1172.70
1147.54
1098.64
1039.61
996.73
802.51
HO
O
N
H
O
O
5g
f1 (ppm)

Figure S8


% Transmittance
Wavenumbers (cm-1)
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2941.58
2811.59
2779.27
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1539.29
1497.89
1447.19
1370.73
1336.54
1303.35
1256.77
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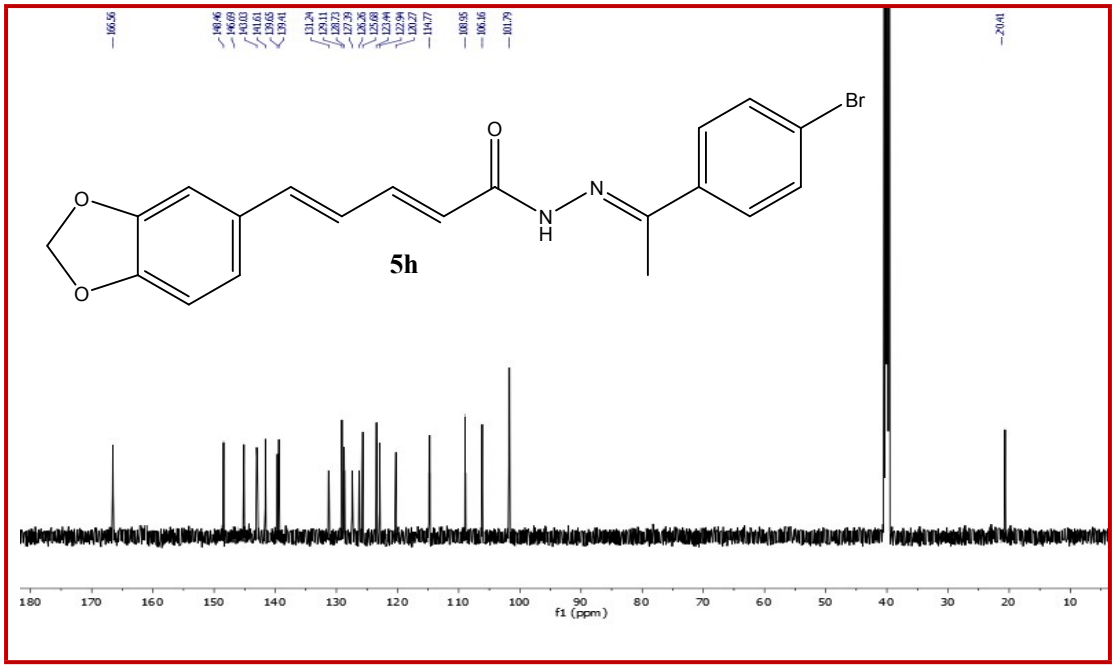
833.12
810.24
663.94
f1 (ppm)


166.56
148.46
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140.03
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139.41
131.24
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128.73
127.39
126.26
125.68
123.44
122.94
120.27
114.77
108.95
106.16
101.79
20.41
O
O
O
N
H
N
Br
5h
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

Figure S9

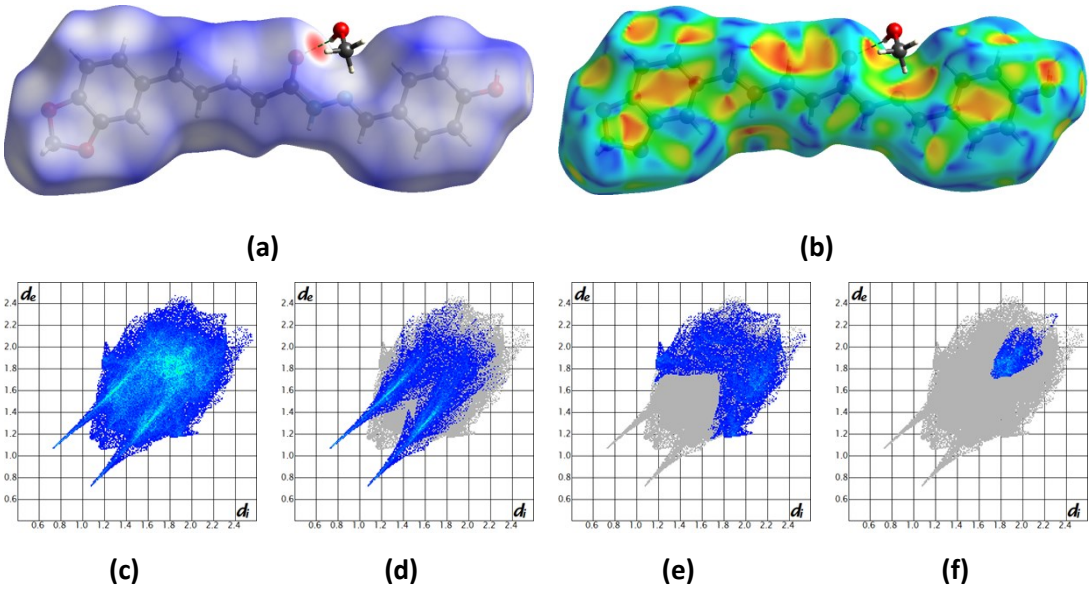

Figure S10

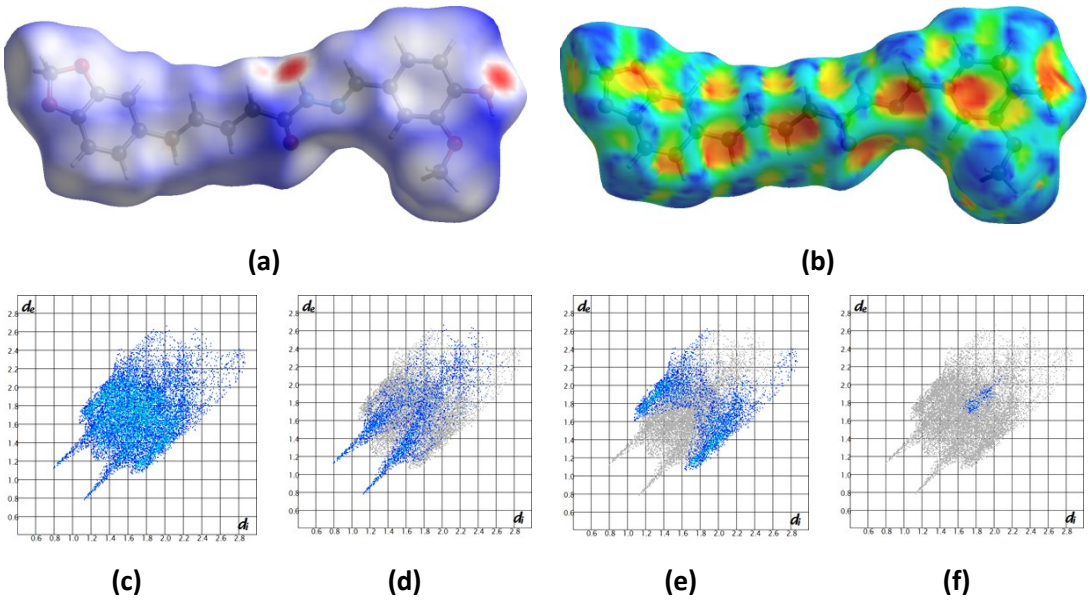

Figure S11

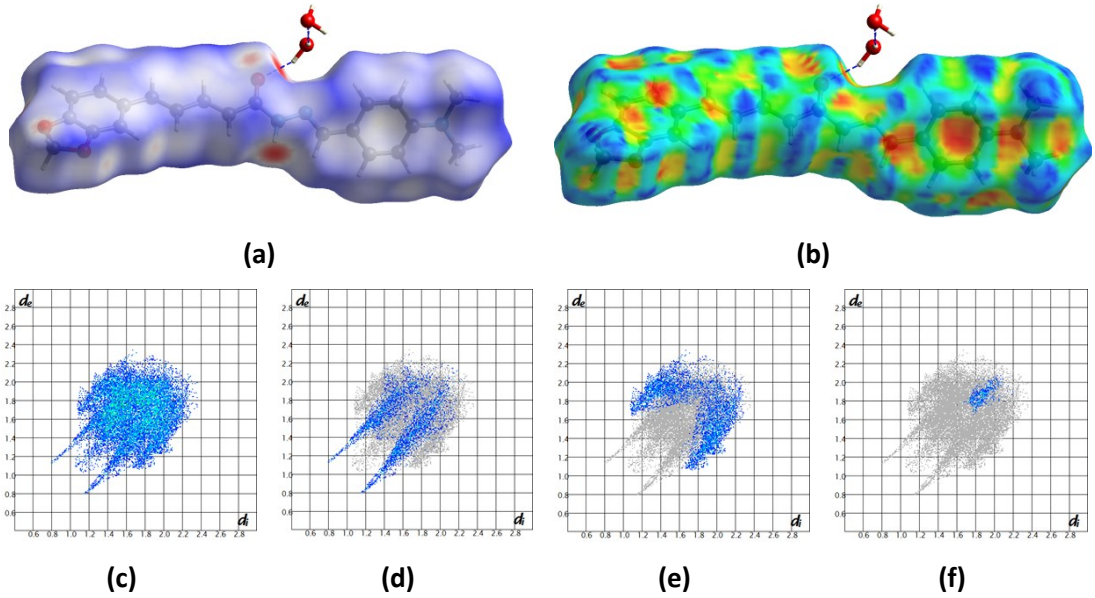

Figure S12

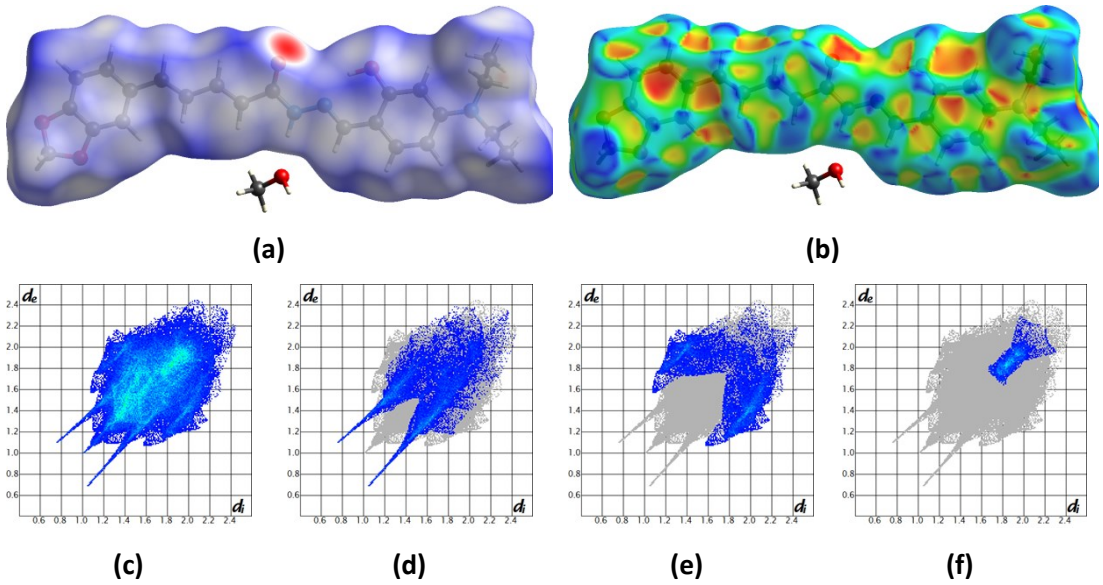

Figure S13

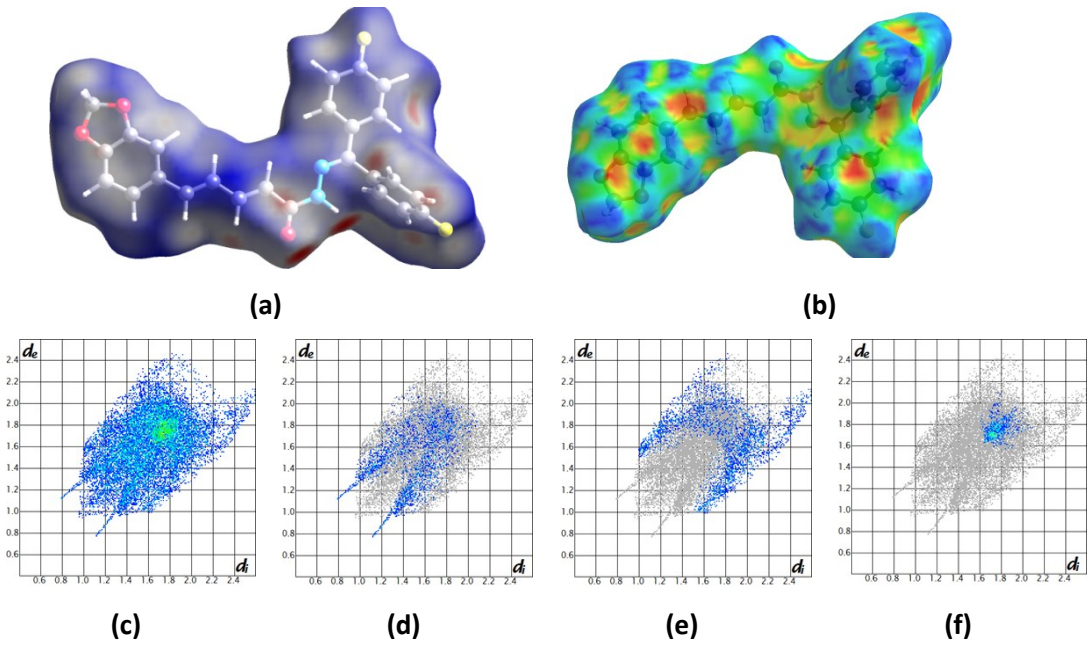

Table S1

	5a	**5b**	**5c**	**5d**	**5e**	**5f**
Empirical formula	$C_{20}H_{20}N_2O_5$	$C_{20}H_{20}N_2O_6$	$C_{20}H_{18}N_2O_5$	$C_{21}H_{24.75}N_3O_{4.42}$	$C_{24}H_{29}N_3O_5$	$C_{25}H_{18}F_2N_2O_3$
Formula weight	368.38	384.38	366.36	389.87	439.50	432.41
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic	Monoclinic	Triclinic
Space group	*$P2_1/c$*	*$P2_1/c$*	*$P2_1/c$*	*$P2_1/c$*	*$P2_1/c$*	*P-1*
Unit cell dimensions						
a (Å)	10.9249(5)	6.6192(6)	18.1988(7)	13.6957(16)	11.298(3)	5.329(3)
b (Å)	6.5740(3)	19.7039(17)	4.8105(2)	6.3687(7)	13.398(3)	10.708(5)
c (Å)	25.7341(11)	14.2723(13)	22.1672(8)	24.058(3)	15.678(4)	15.496(7)
α (°)	90	90	90	90	90	83.878(9)
β (°)	94.790(3)	99.079(5)	112.874(3)	104.090(6)	107.247(4)	87.608(9)
γ (°)	90	90	90	90	90	82.240(9)
Volume ($Å^3$)	1841.78(14)	1838.1(3)	1788.03(13)	2035.3(4)	2266.5(10)	870.8(7)
Z	4	4	4	4	4	4
Calc. density (Mg/m^3)	1.329	1.389	1.361	1.272	1.288	1.649
F(000)	776	808	768	828.0	936	448
Crystal size (mm)	0.12 x 0.1 x 0.1	0.13 x 0.12 x 0.1	0.12 x 0.1 x 0.1	0.12 × 0.04 × 0.03	0.15 x 0.15 x 0.1	0.20×0.12×0.10
θ range (°)	3.447 - 64.989	3.856 - 64.992	2.635 - 65.921	6.808-115.404	1.887 - 26.372	2.23 -25.00
Reflections collected	10352	10609	14927	9153	17545	6085
Independent reflections	3035	2973	3069	2692	4630	3045
Number of parameters/R_{int}	248 /0.0865	258/0.0552	247/0.0601	273/0.0786	295/0.0604	290/0.0520
Goof %	1.026	1.074	1.072	1.029	1.037	1.052
Final *R* indices [$I > 2\sigma(I)$]	*R1 = 0.0925* *wR2 = 0.2368*	R_1 = 0.0461 wR_2 =0.1239	R_1=0.0490 wR_2=0.1431	R_1 =0.0706 wR_2 =0.1880	R_1 = 0.0475 wR_2 =0.1263	R_1 = 0.0623 wR_2 = 0.1690
R indices (all data)	*R1 = 0.1011* *wR2 = 0.2530*	R_1 =0.0507 wR_2 =0.1332	R_1=0.0687 wR_2=0.1575	R_1 =0.1081 wR_2 =0.2150	R_1 = 0.0948 wR_2 = 0.1535	R_1 = 0.0965 wR_2 = 0.1941
Max. diff. peak and hole ($eÅ^{-3}$)	*0.332, -0.362*	0.285, -0.225	0.215, -0.171	0.23, -0.19	0.257, -0.164	0.241, -0.241