支撑文件

天然二氢查尔酮类衍生物的合成及降糖活性筛选

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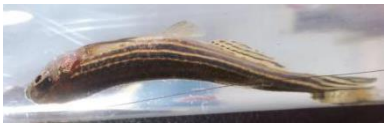
1、化合物 4n 安全性评价

表 1 化合物 **4n** 的安全性评估

化合物	组别	24 h 受试鱼死亡率/%	48 h 受试鱼死亡率/%	72 h 受试鱼死亡率/%	96 h 受试鱼死亡率/%
4n	空白组	0	0	0	0
	溶剂对照组 DMSO	0	0	0	0
	浓度 1（0.1 mg/L）	0	0	0	0
	浓度 2（1.0 mg/L）	0	5	10	20
	浓度 3（10.0 mg/L）	10	10	30	50
	浓度 4（25.0 mg/L）	20	30	60	80
	浓度 5（50.0 mg/L）	50	60	80	100

2、斑马鱼模型试验现象



3、化合物 3a-3m 实验数据

2,4-二甲氧基查尔酮 (3a): 黄色晶体; 收率 85.79%; m.p. 68.7~69.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 15.80 Hz, 1H, CH), 8.00 (d, J = 9.76 Hz, 2H, Ph-H), 7.58~7.52 (m, 3H, Ph-H, CH), 7.48 (t, J = 7.56 Hz, 2H, Ph-H), 6.53 (q, J = 6.56 Hz, 1H, Ph-H), 6.47 (s, 1H, Ph-H), 3.89 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3).

4'-甲基-2,4-二甲氧基查尔酮 (3b): 淡黄色晶体; 收率 90.15%; m.p. 85.5~86.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 15.76 Hz, 1H, CH), 7.92 (d, J = 8.20 Hz, 2H, Ph-H), 7.55 (d, J = 23.92 Hz, 1H, CH), 7.56 (s, 1H, Ph-H), 7.28 (d, J = 8.00 Hz, 2H, Ph-H), 6.53 (q, J = 8.56 Hz, 1H, Ph-H), 6.47 (d, J = 2.32 Hz, 1H, Ph-H), 3.89 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 2.42 (s, 3H, CH_3).

4'-甲氧基-2,4-二甲氧基查尔酮 (3c): 黄色晶体; 收率 95.36%; m.p. 79.5~80.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05~8.00 (m, 3H, Ph-H, CH), 7.58 (d, J = 2.00 Hz, 1H, Ph-H), 7.54 (d, J = 9.12 Hz, 1H, CH), 6.99~6.95 (m, 2H, Ph-H), 3.90 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3).

4'-氯-2,4-二甲氧基查尔酮 (3d): 黄色晶体; 收率 94.37%; m.p. 121.6~122.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 15.72 Hz, 1H, CH), 7.94 (d, J = 8.52 Hz, 2H, Ph-H), 7.56 (d, J = 8.60 Hz, 1H, Ph-H), 7.50~7.44 (m, 3H, Ph-H), 6.54 (q, J = 6.32 Hz, 1H, Ph-H), 6.48 (d, J = 2.24 Hz, 1H, Ph-H), 3.90 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3).

2,6-二甲氧基查尔酮 (3e): 淡黄色晶体; 收率 89.93%; mp 53.4-54.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.13 (d, J = 15.88 Hz, 1H, Ph-H), 8.00 (t, J = 10.40 Hz, 3H, Ph-H), 7.65 (t, J = 7.00 Hz, 1H, Ph-H), 7.57 (t, J = 7.44 Hz, 2H, Ph-H), 7.40 (t, J = 8.36 Hz, 1H, Ph-H), 6.75 (d, J = 8.44 Hz, 2H, CH_2), 3.91 (s, 6H, OCH_3).

4'-甲基-2,6-二甲氧基查尔酮 (3f): 淡黄色晶体; 收率 95.43%; mp 83.1-83.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.26 (d, J = 16.00 Hz, 1H, CH), 7.99 (d, J = 15.96 Hz, 1H, CH), 7.94 (d, J = 8.16 Hz, 2H, Ph-H), 7.30-7.26 (m, 3H, Ph-H), 6.58 (d, J = 8.40 Hz, 2H, Ph-H), 3.90 (s, 6H, OCH_3), 2.42 (s, 3H, CH_3).

4'-异丙基-2,4-二甲氧基查尔酮 (3g): 淡黄色固体; 收率 94.15%; mp 87.6-88.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.28 (d, J = 15.92 Hz, 1H, CH), 7.99 (q, J = 8.36 Hz, 3H, Ph-H, CH), 7.35-7.26 (m, 3H, Ph-H), 6.58 (d, J = 8.44 Hz, 2H, Ph-H), 3.91 (s, 6H, OCH_3), 3.01-2.95 (m, 1H, CH), 1.28 (d, J = 6.92 Hz, 6H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) 191.6, 160.3, 153.7,

136.8, 135.2, 131.4, 128.8, 126.5, 124.9, 112.9, 103.7, 55.8, 34.2, 23.7; IR (KBr) (ν_{max}, cm^{-1}): 2961, 1654, 1596, 1472, 1107, 1026; HRMS (ESI-TOF) *m/z* Calcd for $C_{20}H_{23}O_3^+$ $[M+H]^+$ 311.1642, found 311.1642.

4'-甲氧基-2,6-二甲氧基查尔酮 (3h): 淡黄色晶体; 收率 96.85%; mp 122.2-124.9 °C; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.21 (d, *J* = 15.92 Hz, 1H, CH), 8.01-7.98 (m, *2*H, Ph-H), 7.95 (d, *J* = 15.92 Hz, 1H, CH), 7.22 (t, *J* = 8.32 Hz, 1H, Ph-H), 6.94-6.91 (m, 2H, Ph-H), 6.54 (d, *J* = 8.44 Hz, 2H, Ph-H), 3.87 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3).

4'-氯-2,6-二甲氧基查尔酮 (3i): 黄色晶体; 收率 93.45%; mp 108.7-109.3 °C; ^1H NMR (400 MHz, DMSO, ppm) δ 8.13 (d, *J* = 15.80 Hz, 1H, Ph-H), 7.98 (t, *J* = 8.32 Hz, 3H, Ph-H), 7.61 (d, *J* = 8.36 Hz, 2H, Ph-H), 7.40 (t, *J* = 8.32 Hz, 1H, Ph-H), 6.74 (d, *J* = 8.48 Hz, 2H, Ph-H), 3.90 (s, 6H, OCH_3).

2,4,6-三甲氧基查尔酮 (3j): 淡黄色晶体; 收率 96.89%; mp 107.9-108.6 °C; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.26 (d, *J* = 15.84 Hz, 1H, CH), 8.00 (d, *J* = 7.12 Hz, 2H, Ph-H), 7.87 (d, *J* = 15.88 Hz, 1H, CH), 7.52 (t, *J* = 7.32 Hz, 1H, Ph-H), 7.46 (t, *J* = 7.76 Hz, 2H, Ph-H), 6.12 (s, 2H, Ph-H), 3.89 (s, 6H, OCH_3), 3.84 (s, 3H, OCH_3).

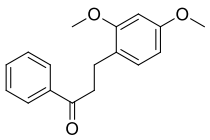
4'-甲基-2,4,6-三甲氧基查尔酮 (3k): 黄色晶体; 收率 95.30%; mp 120.1-121.3 °C; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 8.25 (d, *J* = 15.88 Hz, 1H, CH), 7.92 (d, *J* = 8.16 Hz, 2H, Ph-H), 7.88 (d, *J* = 15.88 Hz, 1H, CH), 7.28 (s, 1H, Ph-H), 7.26 (s, 1H, Ph-H), 6.12 (s, 2H, Ph-H), 3.89 (s, 6H, OCH_3), 3.84 (s, 3H, OCH_3), 2.42 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) 191.7, 163.0, 161.7, 142.6, 136.7, 135.6, 129.1, 128.6, 122.0, 106.6, 90.5, 55.8, 55.4, 21.6; IR (KBr) (ν_{max}, cm^{-1}): 3017, 2977, 2938, 2838, 1648, 1604, 1560, 997, 950, 820, 753; HRMS (ESI-TOF) *m/z* Calcd for $C_{19}H_{21}O_4^+$ $[M+H]^+$ 313.1434, found 313.1431.

4'-异丙基-2,4,6-三甲氧基查尔酮 (3l): 黄色晶体; 收率 90.85%; mp 86.0-87.0 °C; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.97 (t, *J* = 7.24 Hz, 2H, Ph-H), 7.62 (t, *J* = 7.4 Hz, 1H, Ph-H), 7.51 (t, *J* = 7.8 Hz, 2H, Ph-H), 7.26 (q, *J* = 5.96 Hz, 4H, Ph-H), 7.20-7.15 (m, 1H, Ph-H), 3.37 (t, *J* = 7.52 Hz, 2H, CH_2), 2.93 (t, *J* = 7.56 Hz, 2H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) 191.7, 163.0, 161.7, 153.4, 137.1, 135.5, 128.7, 126.5, 122.0, 106.6, 90.5, 55.8, 55.4, 34.2, 23.8; IR (KBr) (ν_{max}, cm^{-1}): 2964, 1648, 1606, 1061, 1029; HRMS (ESI-TOF) *m/z* Calcd for $C_{21}H_{25}O_4^+$ $[M+H]^+$ 341.1747, found 341.1743.

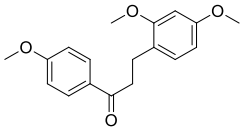
4'-甲氧基-2,4,6-三甲氧基查尔酮 (3m): 黄色固体; 收率 90.13%; mp 155.7-155.9 °C; ^1H

NMR (400 MHz, $CDCl_3$, ppm) δ 8.23 (d, J = 15.84 Hz, 1H, CH), 8.02 (d, J = 8.92 Hz, 2H, Ph-H), 7.88 (d, J = 15.84 Hz, 1H, CH), 6.95 (d, J = 8.92 Hz, 2H, Ph-H), 6.12 (s, 2H, Ph-H), 3.89 (s, 6H, OCH_3), 3.86 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3).

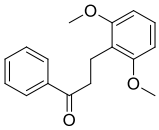
4、目标化合物 4a, 4c, 4e, 4f, 4h-4j, 4m 实验数据



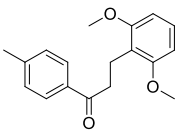
2,4-二甲氧基二氢查尔酮 (4a): 黄色液体; 收率为 68%; ^{1}H NMR (DMSO, 400 MHz, TMS) δ: 7.61 (t, J = 7.24 Hz, 1H, Ph-H), 7.50 (t, J = 7.48 Hz, 2H, Ph-H), 7.07 (d, J = 8.20 Hz, 1H, Ph-H), 6.52 (s, 1H, Ph-H), 6.42 (d, J = 8.02 Hz, 1H, Ph-H), 3.76 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 3.20 (t, J = 7.48 Hz, 2H, CH_2), 2.82 (t, J = 7.48 Hz, 2H, CH_2).



4'-甲氧基-2,4-二甲氧基二氢查尔酮 (4c): 白色晶体; 收率为 74%; 熔点: 61.1~61.9 ^{o}C; ^{1}H NMR (400 MHz, DMSO, ppm) δ: 7.93 (d, J = 8.76 Hz, 2H, Ph-H), 7.06 (d, J = 8.24 Hz, 1H, Ph-H), 7.02 (d, J = 8.8 Hz, 2H, Ph-H), 6.51 (s, 1H, Ph-H), 6.42 (q, J = 6.04 Hz, 1H, Ph-H), 3.83 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 3.13 (t, J = 7.4 Hz, 2H, CH_2), 2.79 (t, J = 7.76 Hz, 2H, CH_2).

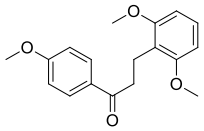


2,6-二甲氧基二氢查尔酮 (4e): 白色晶体; 收率为 71%; 熔点: 89.2-89.5 ^{o}C; ^{1}H NMR (400 MHz, DMSO, ppm) δ: 7.95 (d, J = 7.32 Hz, 2H, Ph-H), 7.62 (t, J = 7.4 Hz, 1H, Ph-H), 7.51 (t, J = 7.68 Hz, 2H, Ph-H), 7.15 (t, J = 8.36 Hz, 1H, Ph-H), 6.62 (d, J = 8.36 Hz, 2H, Ph-H), 3.73 (s, 6H, OCH_3), 3.04 (t, J = 7.12 Hz, 2H, CH_2), 2.87 (t, J = 8.56 Hz, 2H, CH_2).

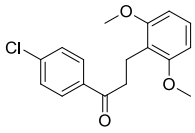


4'-甲基-2,6-二甲氧基二氢查尔酮 (4f): 白色晶体; 收率为 73%; 熔点: 93.5~93.8 ^{o}C; ^{1}H

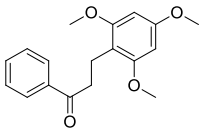
NMR (400 MHz, DMSO, ppm) δ: 7.85 (d, J = 8.12 Hz, 2H, Ph-H), 7.31 (d, J = 7.92 Hz, 2H, Ph-H), 7.15 (t, J = 8.36 Hz, 1H, Ph-H), 6.62 (d, J = 8.36 Hz, 2H, Ph-H), 3.74 (s, 6H, OCH_3), 3.00 (t, J = 6.92 Hz, 2H, CH_2), 2.85 (t, J = 8.68 Hz, 2H, CH_2), 2.36 (s, 3H, CH_3).



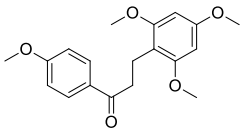
4'-甲氧基-2,6-二甲氧基二氢查尔酮 (4h): 白色晶体; 收率为 74%; 熔点: 110.5~110.8 ^{o}C; ^{1}H NMR (400 MHz, DMSO, ppm) δ: 7.95-7.92 (m, 2H, Ph-H), 7.15 (t, J = 8.32 Hz, 1H, Ph-H), 7.04-7.01 (m, 2H, Ph-H), 6.62 (d, J = 8.36 Hz, 2H, Ph-H), 3.83 (s, 3H, OCH_3), 3.75 (s, 6H, OCH_3), 2.98-2.94 (m, 2H, CH_2), 2.89-2.83 (m, 2H, CH_2).



4'-氯-2,6-二甲氧基二氢查尔酮 (4i): 白色晶体; 收率为 76%; 熔点: 108.9~109.5 ^{o}C; ^{1}H NMR (400 MHz, DMSO, ppm) δ: 7.96-7.94 (m, 2H, Ph-H), 7.59-7.56 (m, 2H, Ph-H), 7.15 (t, J = 8.36 Hz, 1H, Ph-H), 6.61 (d, J = 8.36 Hz, 2H, Ph-H), 3.73 (s, 6H, OCH_3), 3.03 (t, J = 7.04 Hz, 2H, CH_2), 2.86 (t, J = 8.56 Hz, 2H, CH_2).



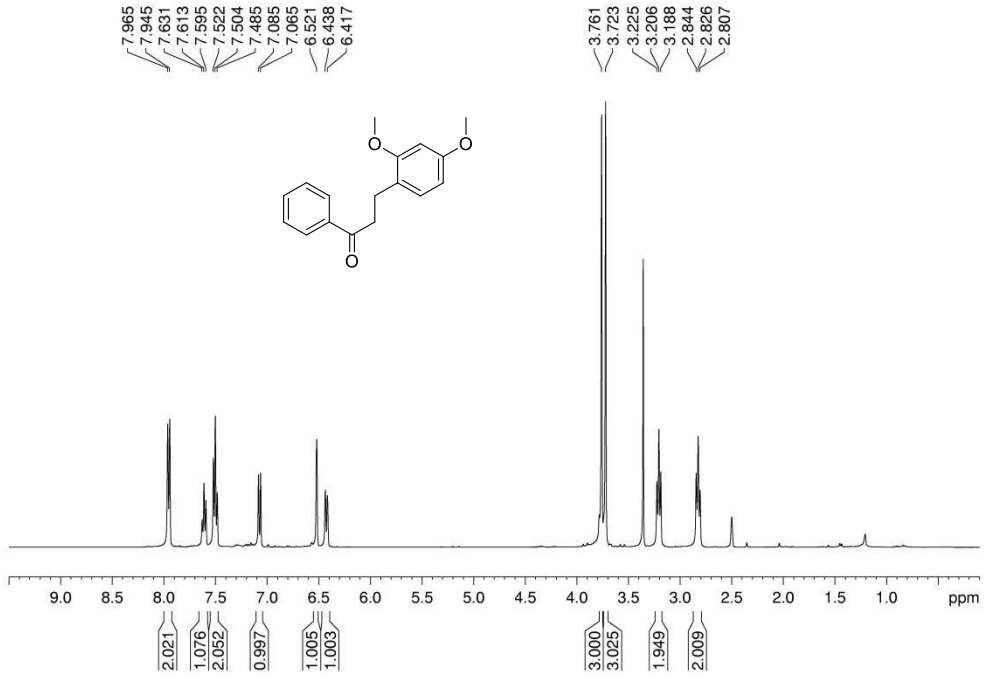
2,4,6-三甲氧基二氢查尔酮 (4j): 白色晶体; 收率为 70%; 熔点: 82.6~83.4 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ: 7.99 (d, J = 7.08 Hz, 2H, Ph-H), 7.53 (t, J = 7.32 Hz, 1H, Ph-H), 7.43 (t, J = 7.76 Hz, 2H, Ph-H), 6.13 (s, 2H, Ph-H), 3.81 (s, 3H, OCH_3), 3.77 (s, 6H, OCH_3), 3.12-3.06 (m, 2H, CH_2), 3.02-2.97 (m, 2H, CH_2).



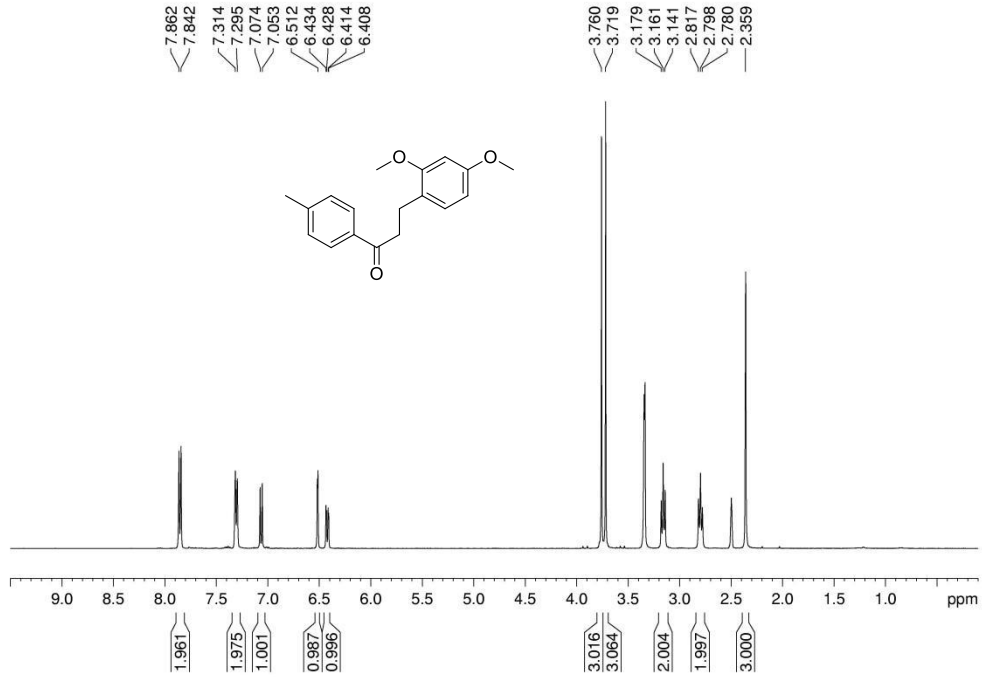
4'-甲氧基-2,4,6-三甲氧基二氢查尔酮 (4m): 白色晶体; 收率为 78%; 熔点: 117.7~118.3 ^{o}C; yield 15.3%; ^{1}H NMR (400 MHz, DMSO, ppm) δ: 7.92 (d, J = 8.76 Hz, 2H, Ph-H), 7.03 (d, J = 8.8 Hz, 2H, Ph-H), 6.21 (s, 2H, Ph-H), 3.83 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 3.73 (s, 6H, OCH_3), 2.92 (t, J = 7.12 Hz, 2H, CH_2), 2.76 (t, J = 8.8 Hz, 2H, CH_2).

5、目标化合物 4a-4n ^{1}H NMR 和 ^{13}C NMR 谱图

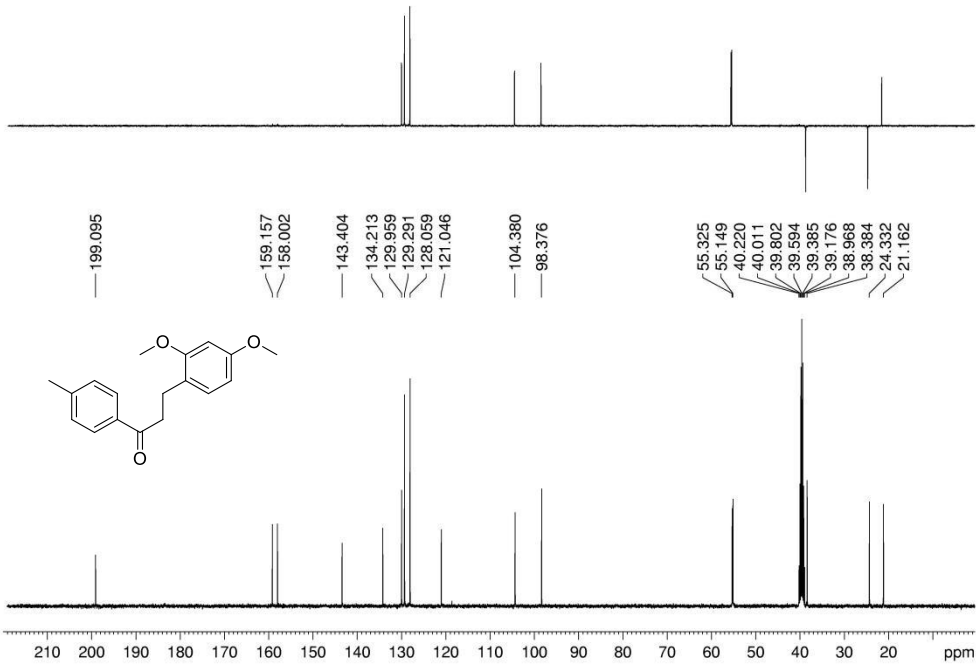
4a ^{1}H NMR (400 MHz, DMSO)



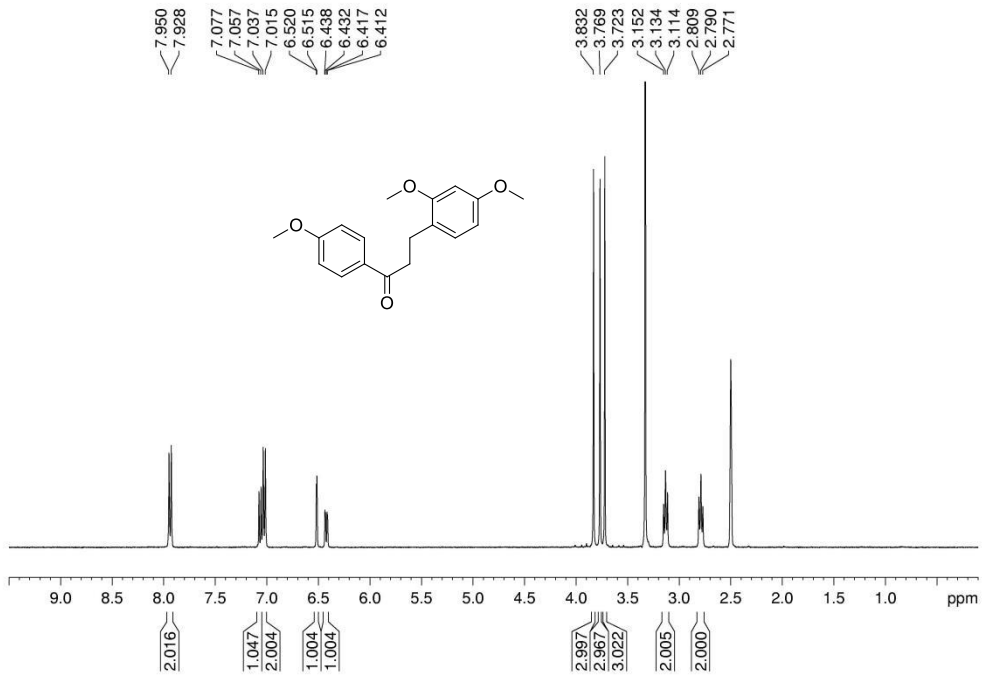
4b ^{1}H NMR (400 MHz, DMSO)



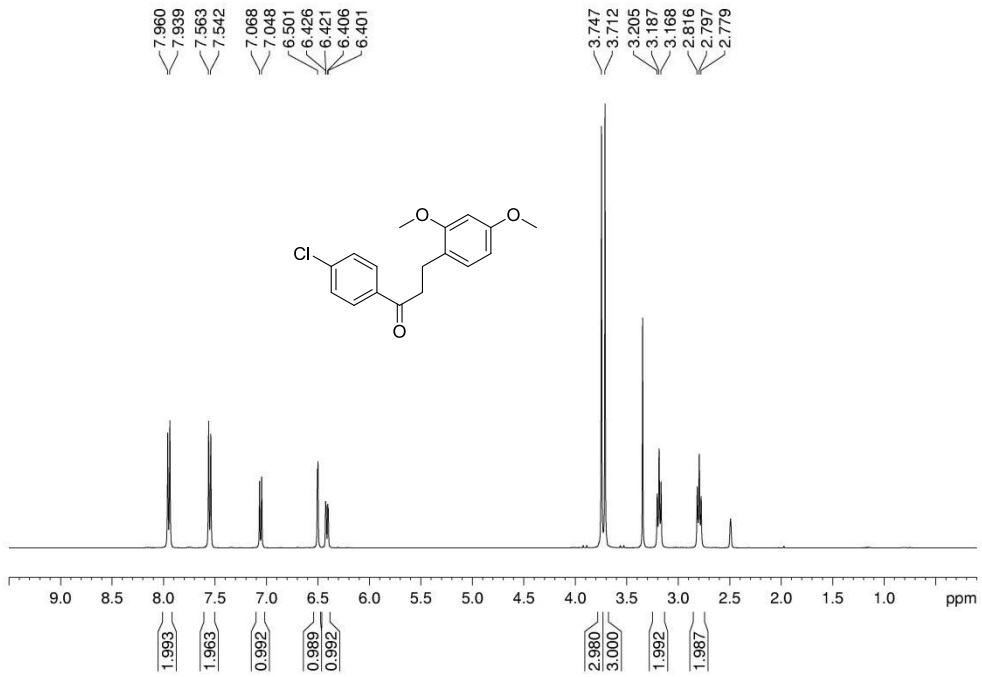
4b ^{13}C NMR (100 MHz, DMSO)



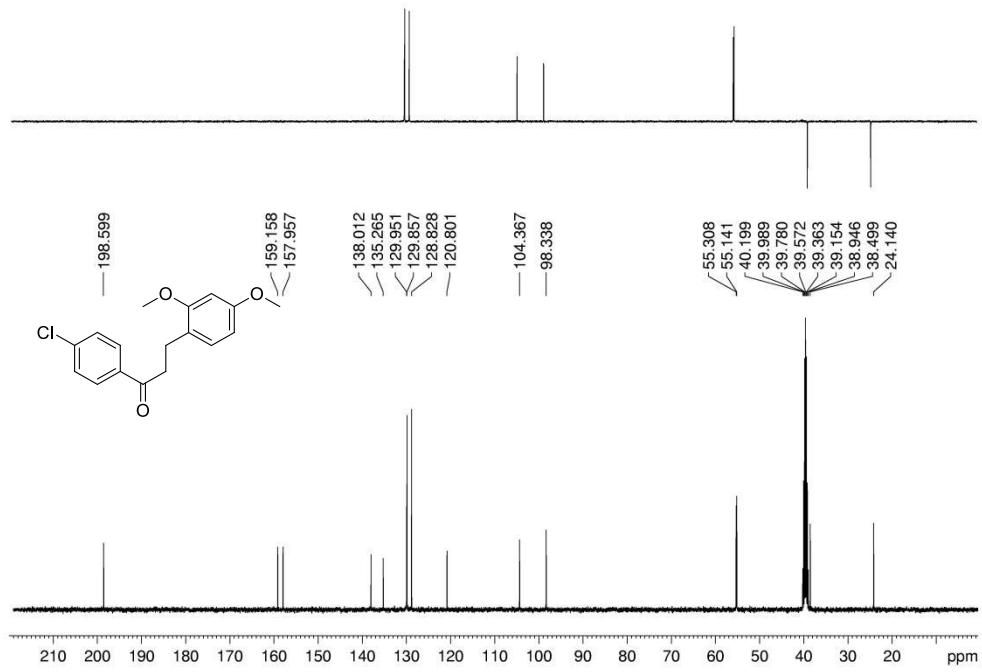
4c ^{1}H NMR (400 MHz, DMSO)



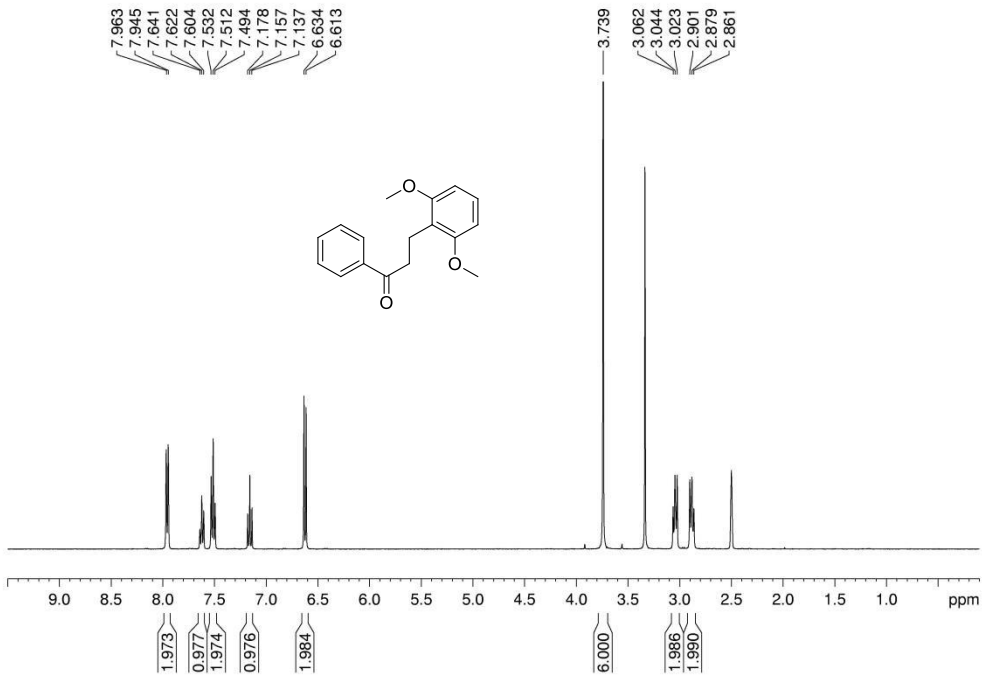
4d ^{1}H NMR (400 MHz, DMSO)



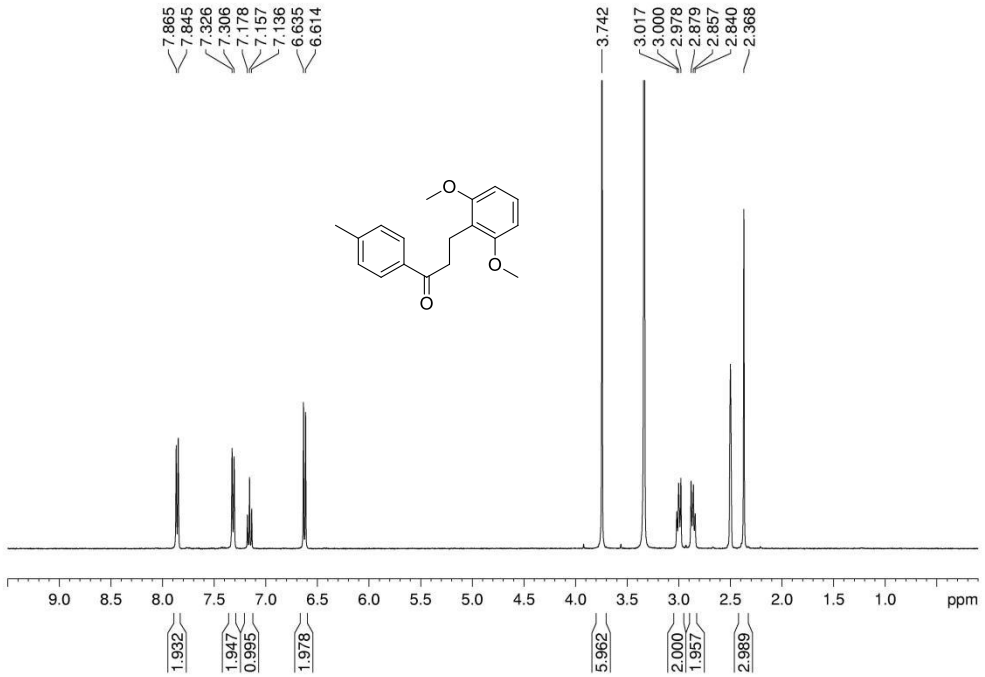
4d ^{13}C NMR (100 MHz, DMSO)



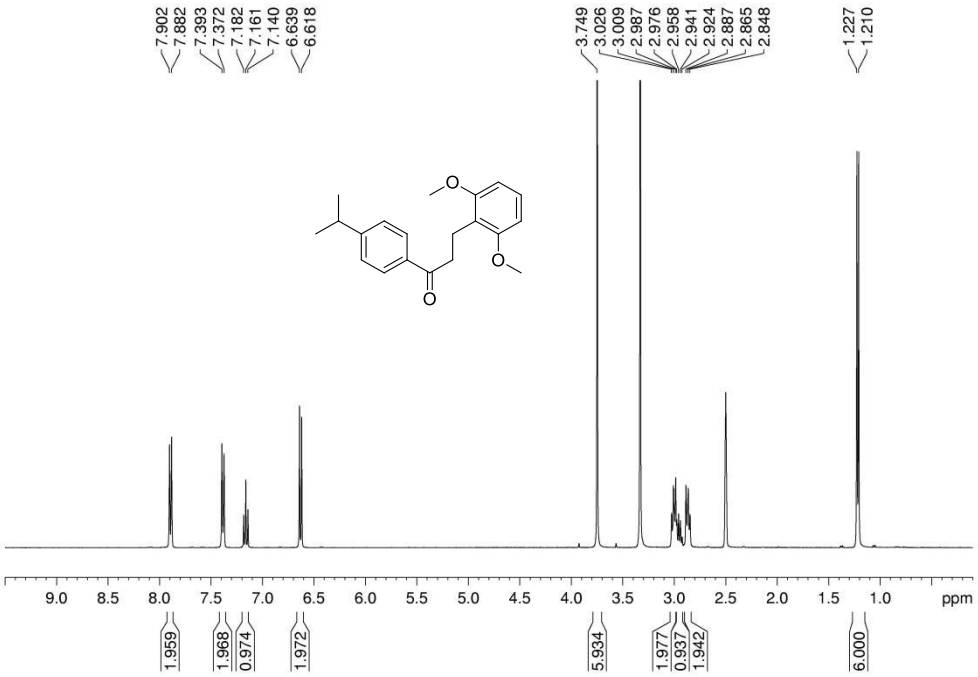
4e ^{1}H NMR (400 MHz, DMSO)



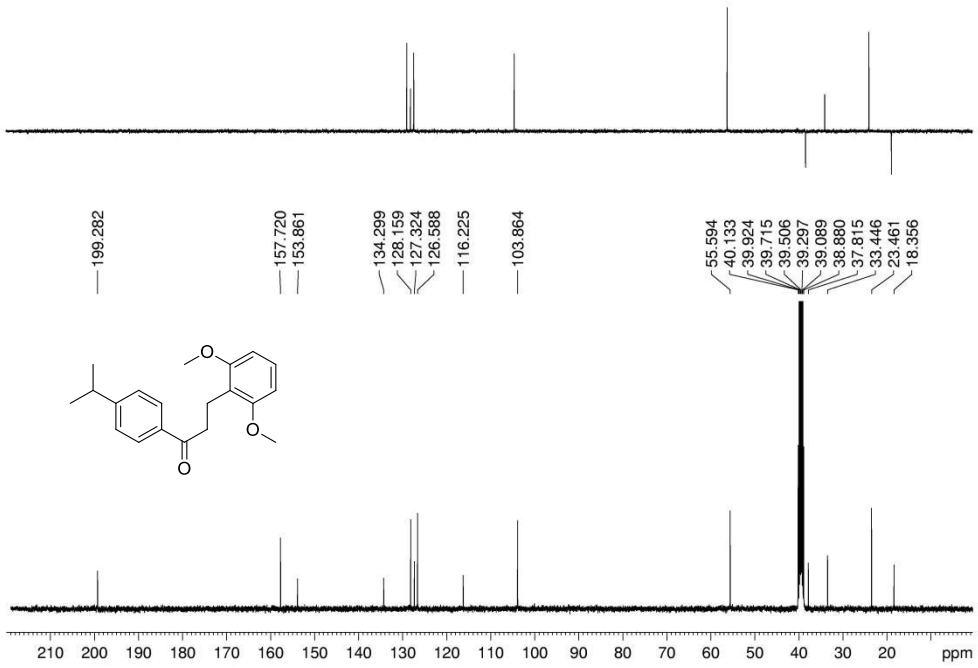
4f ^{1}H NMR (400 MHz, DMSO)



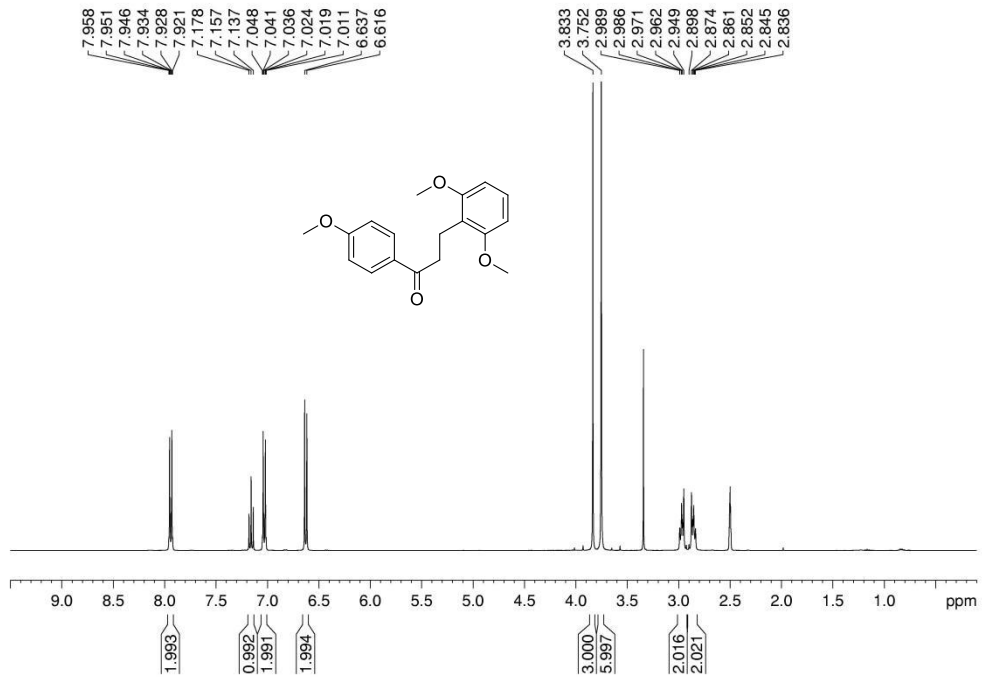
4g ^{1}H NMR (400 MHz, DMSO)



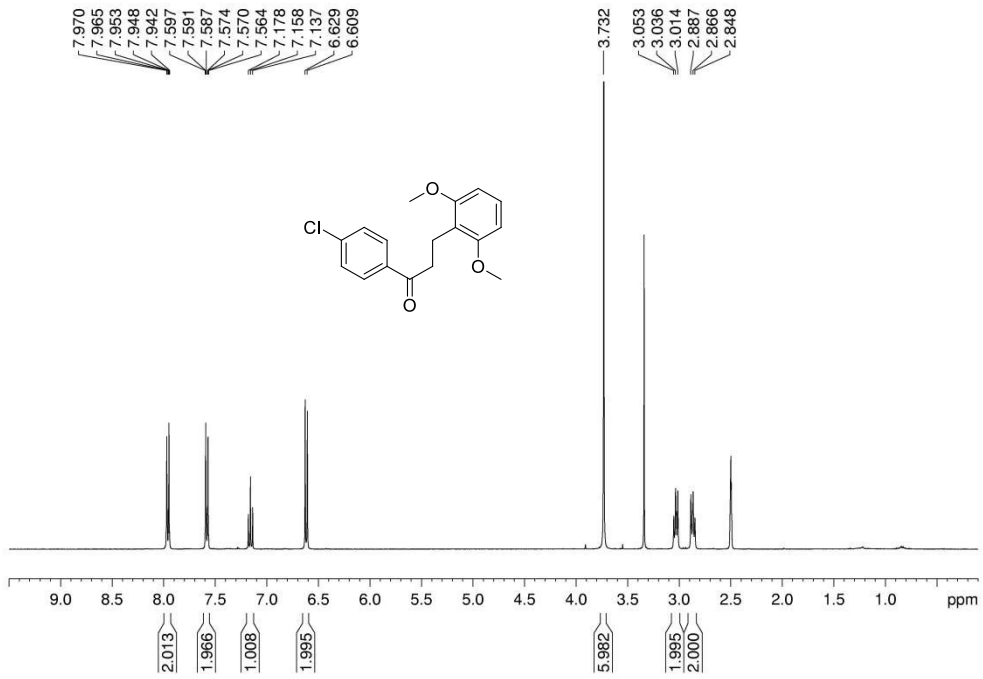
4g ^{13}C NMR (100 MHz, DMSO)



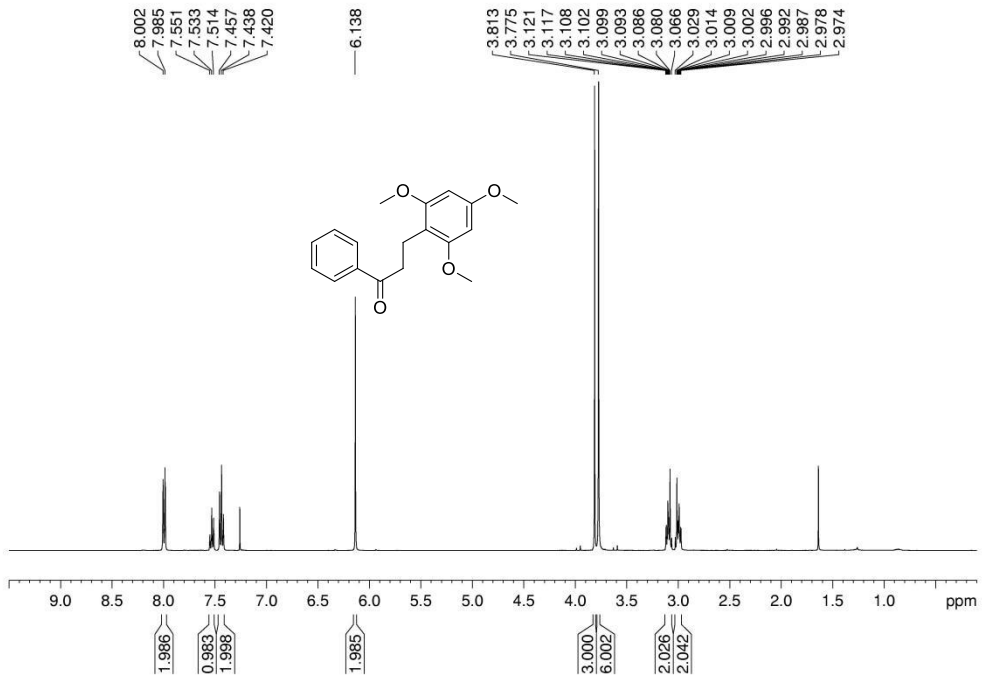
4h ^{1}H NMR (400 MHz, DMSO)



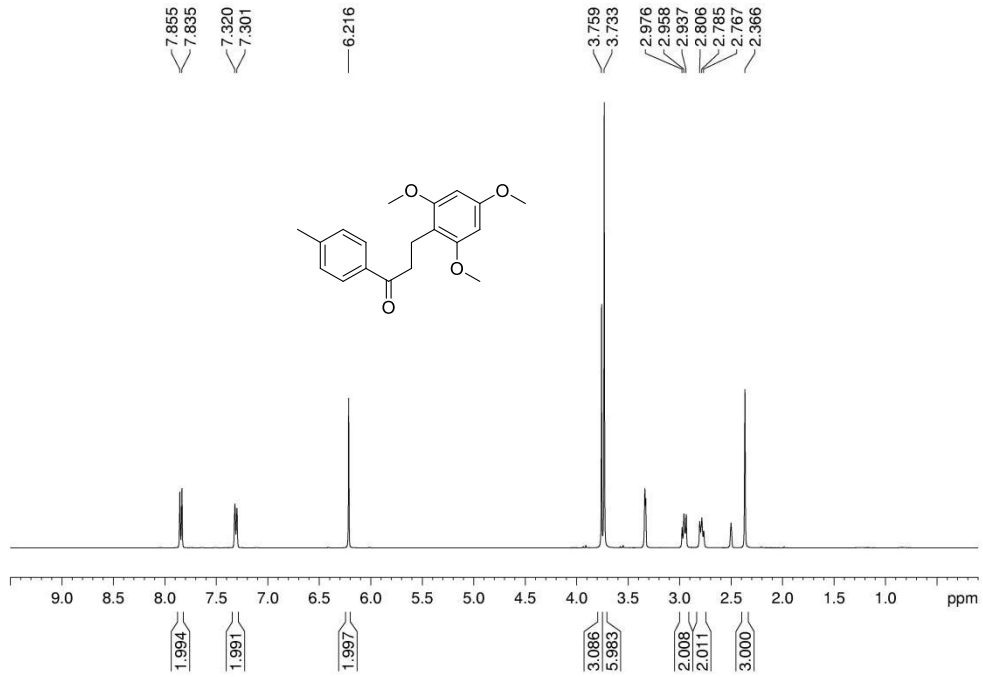
4i ^{1}H NMR (400 MHz, DMSO)



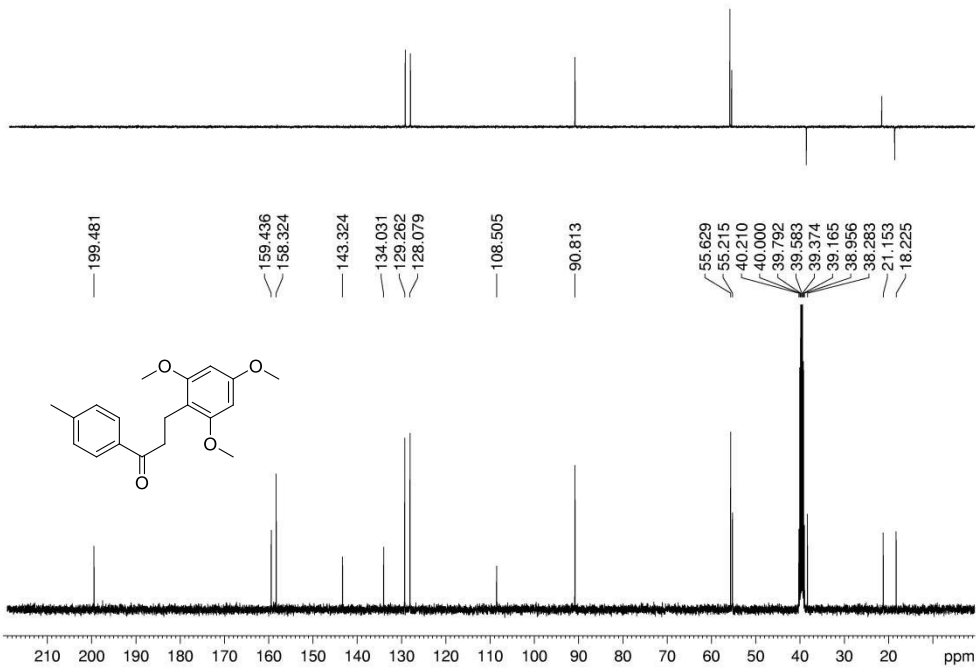
4j ^{1}H NMR (400 MHz, $CDCl_3$)



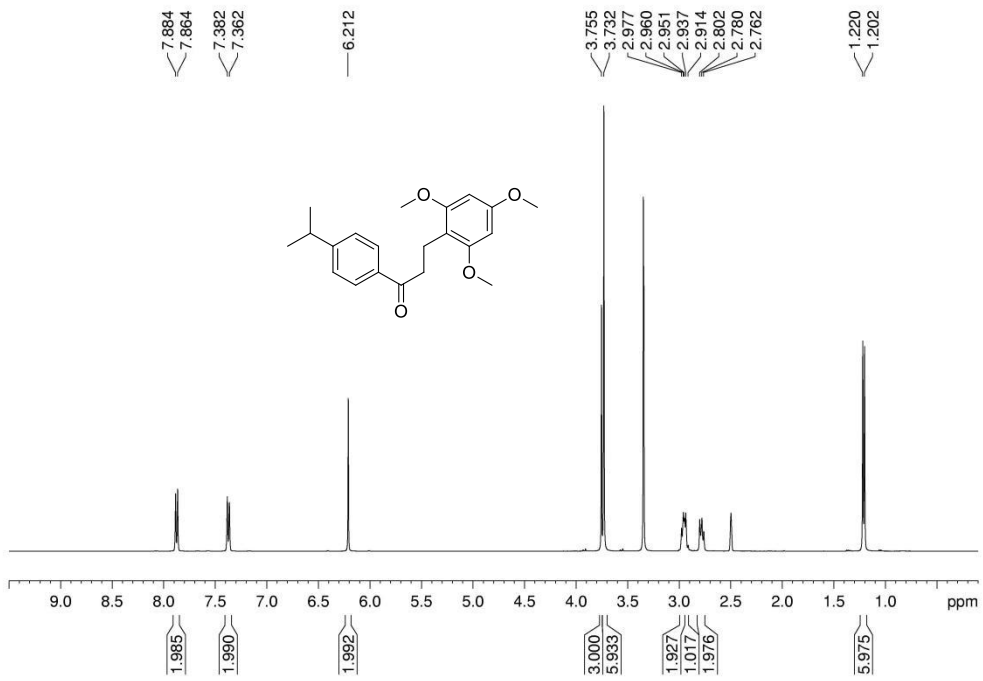
4k ^{1}H NMR (400 MHz, DMSO)



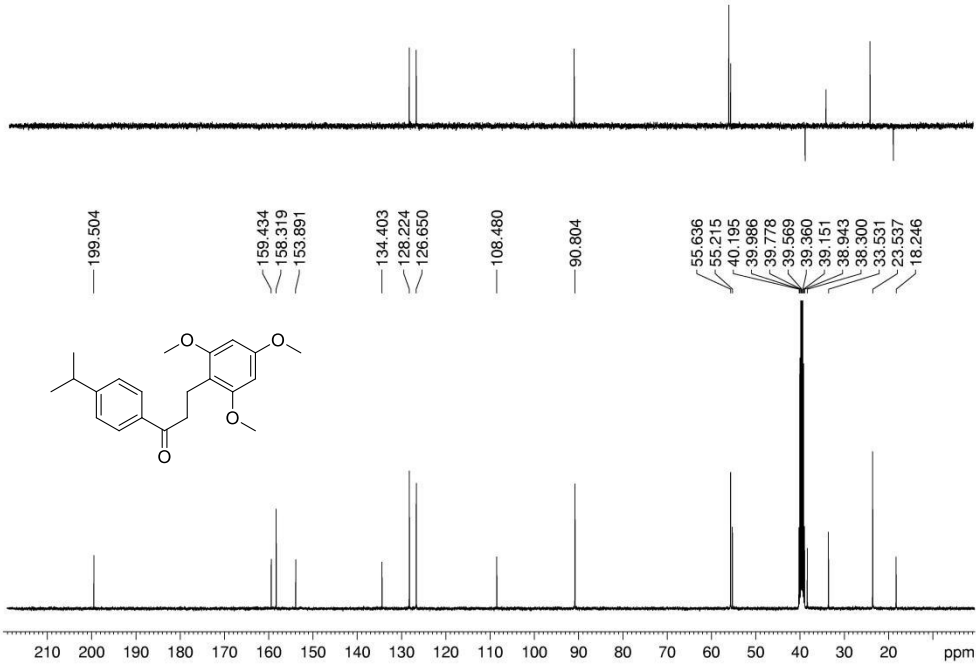
4k ^{13}C NMR (100 MHz, DMSO)



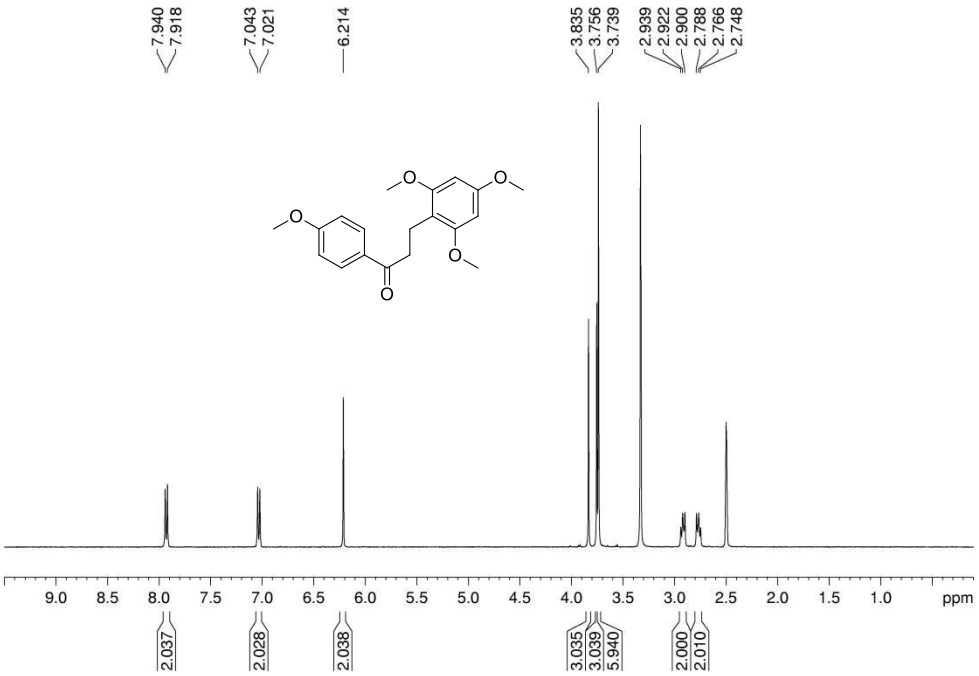
4l ^{1}H NMR (400 MHz, DMSO)



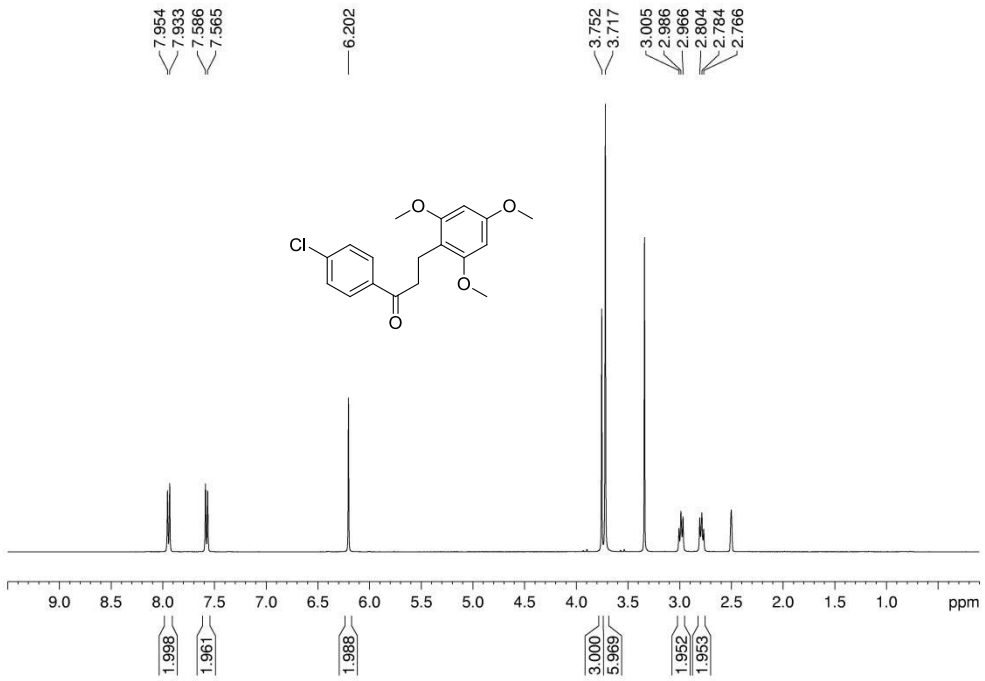
4l ^{13}C NMR (100 MHz, DMSO)



4m ^{1}H NMR (400 MHz, DMSO)



4n ^{1}H NMR (400 MHz, DMSO)



4n ^{13}C NMR (100 MHz, DMSO)