Supplementary data

To target or not to target *Schistosoma mansoni* cyclic nucleotide phosphodiesterase 4A?

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Table S1. Overview of the PDE4NPD toolbox and inhibitor selectivity for human (h) or parasite PDEs.

Table S2. SmPDE4A inhibition of roflumilast analogues.

Fig S1. Correlation plot of the inhibition of the PDE Toolbox compounds of the enzymatic activities of purified SmPDE4A_CD (catalytic domain) and SmPDE4A_FL (full length).

Fig S2. Binding of the substrate cAMP (A) and its hydrolyzed product AMP (B) in the binding pockets of SmPDE4A_CD, as observed in the chain A and chain B of the X-ray structure 6FG5.

Fig S3-S257. Chemical characterization of final compounds.

Experimental section

All starting materials were obtained from commercial suppliers and used without purification. Anhydrous THF and DMF were obtained by passing through an activated alumina column prior to use. TLC analyses were performed using Merck F_{254} aluminum-backed silica plates and visualized with 254 nm UV light. Flash column chromatography was executed using Biotage Isolera equipment. All HRMS spectra were recorded on a Bruker microTOF mass spectrometer using ESI in positive-ion mode. All NMR spectra were recorded on either a Bruker Avance 250, Bruker Avance 300, Bruker Avance 500, or Bruker Avance 600 spectrometer. The peak multiplicities are defined as follows: s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; dd, doublet of doublets; dt, doublet of triplets; td, triplet of doublets; br, broad; m, multiplet; app, apparent. The spectra were referenced to the internal solvent peak as follows: CDCl$_3$ (δ = 7.26 ppm in ^{1}H NMR, δ = 77.16 ppm in ^{13}C NMR), DMSO-d_6 (δ = 2.50 ppm in ^{1}H NMR, δ = 39.52 ppm in ^{13}C NMR). IUPAC names were adapted from ChemBioDraw Ultra 19.0. Purities were measured with the aid of analytical LC-MS using a Shimadzu LC-20AD liquid chromatography pump system with a Shimadzu SPDM20A diode array detector with the MS detection performed with a Shimadzu LCMS-2010EV mass spectrometer operating in positive ionization mode. The column used was an Xbridge (C18) 5 µm column (100 mm × 4.6 mm). The following solutions are used for the eluents. Solvent A: H_2O/HCOOH 999:1, and solvent B: MeCN/HCOOH 999:1. The eluent program used is as follows: flow rate: 1.0 mL/min, start with 95% A in a linear gradient to 10% A over 4.5 min, hold 1.5 min at 10% A, in 0.5 min in a linear gradient to 95% A, hold 1.5 min at 95% A, total run time: 8.0 min. Compound purities were calculated as the percentage peak area of the analyzed compound by UV detection at 254 nm. Given that many compounds were made by undergraduate students and re-purification was usually necessary, yields are not representative and are therefore omitted from the procedures.

General procedure for all compounds: under an N$_2$ atmosphere in a dry flask, oxalyl chloride (4.8 mmol, 1.2 eq.) was added dropwise to a mixture of carboxylic acid A (4.0 mmol, 1.0 eq.) and DMF (100 µL) in THF (20 mL) at 0°C. The mixture was allowed to reach room temperature and stirred for an additional 30 min to obtain the corresponding acyl chloride. In another dry flask with N$_2$ insert, NaH (60% dispersion in mineral oil, 10.0 mmol, 2.5 eq.) was added in small portions to amine/aniline B (10.0 mmol, 2.5 eq.) in DMF (20 mL) at 0°C. The suspension was allowed to reach room temperature and stirred for an additional 30 min. To this mixture, the crude acyl chloride solution was added dropwise at 0°C. The reaction mixture was allowed to reach room temperature and stirred for an additional 30 min. After quenching with a saturated NH$_4$Cl solution (150 mL), the aqueous suspension was extracted with EtOAc for three times. The combined organic layers were washed with brine, dried over Na$_2$SO$_4$ and concentrated *in vacuo*. The crude product was purified using flash column chromatography. All compounds were analyzed using LCMS, ^{1}H NMR, ^{13}C NMR and HRMS and had purity >95% (area% on LC at 254 nm).
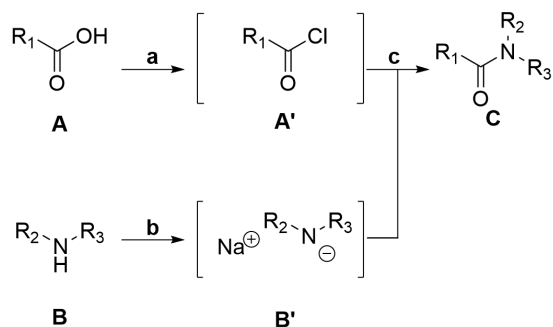
Scheme 1. General synthetic route of the roflumilast analogue library. Reagents and conditions: a: acid A, THF, (COCl)$_2$, *cat*. DMF, 0°C to RT, 30 min; b: amine/aniline B, NaH, DMF, 0°C to RT, 30 min; c: A', B', 0°C to RT, 30 min; d: C, *m*-CPBA, DCM, RT, 30 min.
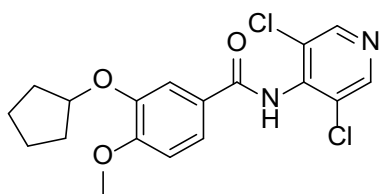

3-(Cyclopentyloxy)-*N*-(3,5-dichloropyridin-4-yl)-4-methoxybenzamide (NPD-0005).

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.56 (s, 2H), 7.69 (s, 1H), 7.52 - 7.48 (m, 2H), 6.94 (d, *J* = 8.3 Hz, 1H), 4.87 (tt, *J* = 6.3, 3.2 Hz, 1H), 3.93 (s, 3H), 2.04 - 1.80 (m, 6H), 1.67 - 1.59 (m, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.3, 154.2, 148.2, 148.0, 140.7, 128.8, 125.0, 120.7, 114.3, 111.0, 80.9, 56.3, 32.9, 24.2. LC-MS: t_R= 4.52 min, purity: >99%, M/z [M+H]$^+$: 381; HRMS calcd. for C$_{18}$H$_{18}$Cl$_2$N$_2$O$_3$ [M+H]$^+$ = 381.0767, found 381.0784. Spectral data are in agreement with a previous report. [1]
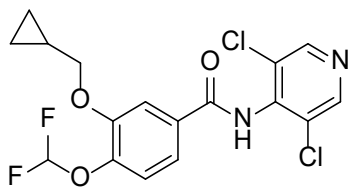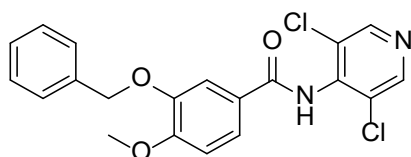

3-(Cyclopropylmethoxy)-*N*-(3,5-dichloropyridin-4-yl)-4-(difluoromethoxy)benzamide (NPD-0006)

^{1}H NMR (600 MHz, CDCl$_3$) δ 8.58 (s, 2H), 7.70 (s, 1H), 7.59 (s, 1H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.29 (d, *J* = 8.2 Hz, 1H), 6.75 (t, *J* = 74.8 Hz, 1H), 3.97 (d, *J* = 6.9 Hz, 2H), 1.36 - 1.28 (m, 1H), 0.70 - 0.66 (m, 2H), 0.40 - 0.36 (m, 2H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 163.8, 151.1, 148.4, 144.0, 139.9, 130.9, 129.0, 122.5, 120.0, 117.5, 115.8 (t, *J* = 256.7 Hz), 74.4, 10.2, 3.5. LC-MS: t_R= 4.65 min, purity: 99%, M/z [M+H]$^+$: 403; HRMS calcd. for C$_{17}$H$_{14}$Cl$_2$F$_2$N$_2$O$_3$ [M+H]$^+$ = 403.0422, found 403.0417. Spectral data are in agreement with a previous report. [2]
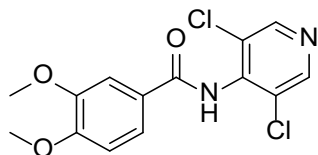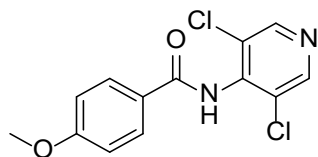
N-(3,5-Dichloropyridin-4-yl)-3,4-dimethoxybenzamide (NPD-0446)

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.48 (s, 1H), 8.77 (s, 2H), 7.70 (dd, J = 8.4, 2.1 Hz, 1H), 7.59 (d, J = 2.1 Hz, 1H), 7.14 (d, J = 8.5 Hz, 1H), 3.87 (s, 3H), 3.85 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.3, 152.3, 148.5, 148.3, 141.6, 130.8, 124.7, 121.6, 111.1, 111.0, 55.8, 55.6. LC-MS: t_R= 3.51 min, purity: >99%, M/z [M+H]$^+$: 327; HRMS calcd. for C$_{14}$H$_{12}$Cl$_2$N$_2$O$_3$ [M+H]$^+$ = 327.0298, found 327.0309. Spectral data are in agreement with a previous report. [3]


3-(Benzyloxy)-N-(3,5-dichloropyridin-4-yl)-4-methoxybenzamide (NPD-0546)

^{1}H NMR (500 MHz, DMSO-d_6 + 1 drop of CDCl$_3$) δ 10.35 (s, 1H), 8.61 (s, 2H), 7.71 - 7.66 (m, 2H), 7.47 - 7.43 (m, 2H), 7.38 - 7.33 (m, 2H), 7.32 - 7.27 (m, 1H), 7.07 - 7.02 (m, 1H), 5.13 (s, 2H), 3.86 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6 + 1 drop of CDCl$_3$) δ 164.2, 152.5, 147.9, 147.3, 141.4, 136.5, 130.7, 128.2, 127.75, 127.68, 124.7, 122.0, 112.9, 110.8, 70.1, 55.6. LC-MS: t_R= 4.52 min, purity: >99%, M/z [M+H]$^+$: 403; HRMS calcd. for C$_{20}$H$_{16}$Cl$_2$N$_2$O$_3$ [M+H]$^+$ = 403.0611, found 403.0609. Spectral data are in agreement with a previous report. [4]

N-(3,5-Dichloropyridin-4-yl)-4-methoxybenzamide (NPD-0548)

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.49 (s, 1H), 8.76 (s, 2H), 8.02 (d, J = 8.9 Hz, 2H), 7.12 (d, J = 8.9 Hz, 2H), 3.87 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.3, 162.5, 148.3, 141.6, 130.9, 130.0, 124.8, 113.9, 55.6. LC-MS: t_R= 3.73 min, purity: >99%, M/z [M+H]$^+$: 297; HRMS calcd. for C$_{13}$H$_{10}$Cl$_2$N$_2$O$_2$ [M+H]$^+$ = 297.0192, found 297.0201.
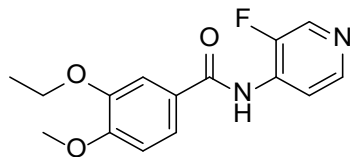
3-Ethoxy-N-(3-fluoropyridin-4-yl)-4-methoxybenzamide (NPD-1177)

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.28 (s, 1H), 8.58 (d, J = 2.8 Hz, 1H), 8.38 (d, J = 5.3 Hz, 1H), 7.87 (dd, J = 6.7, 5.3 Hz, 1H), 7.63 (dd, J = 8.4, 2.1 Hz, 1H), 7.54 (d, J = 2.1 Hz, 1H), 7.10 (d, J = 8.5 Hz, 1H), 4.09 (q, J = 7.0 Hz, 2H), 3.85 (s, 3H), 1.36 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.2, 152.4, 151.4 (d, J = 255.1 Hz), 147.6, 146.3 (d, J = 5.0 Hz), 138.2 (d, J = 21.8 Hz), 133.7 (d, J = 9.5 Hz), 125.4, 121.8, 118.7 (app s), 112.1, 111.0, 63.9, 55.7, 14.7. LC-MS: t_R= 3.26 min, purity: >99%, M/z [M+H]$^+$: 291; HRMS calcd. for $C_{15}H_{15}FN_2O_3$ [M+H]$^+$ = 291.1139, found 291.1150.
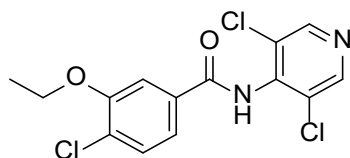
4-Chloro-*N*-(3,5-dichloropyridin-4-yl)-3-ethoxybenzamide (NPD-1178)

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.73 (s, 1H), 8.77 (s, 2H), 7.71 - 7.65 (m, 1H), 7.66 - 7.61 (m, 2H), 4.22 (q, J = 7.0 Hz, 2H), 1.40 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.3, 154.4, 148.8, 141.6, 133.0, 131.1, 130.6, 126.1, 121.3, 113.1, 65.1, 15.0. LC-MS: t_R= 4.60 min, purity: 99%, M/z [M+H]$^+$: 345; HRMS calcd. For $C_{14}H_{11}Cl_3N_2O_2$ [M+H]$^+$ = 344.9959, found 344.9958.
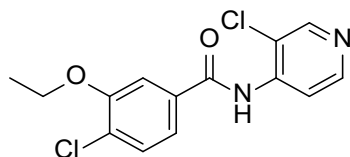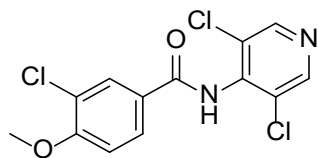

4-Chloro-*N*-(3-chloropyridin-4-yl)-3-ethoxybenzamide (NPD-1179)

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.25 (s, 1H), 8.70 (s, 1H), 8.52 (d, J = 5.3 Hz, 1H), 7.83 (d, J = 5.3 Hz, 1H), 7.67 (d, J = 1.7 Hz, 1H), 7.63 (d, J = 8.2 Hz, 1H), 7.57 (dd, J = 8.2, 1.8 Hz, 1H), 4.22 (q, J = 7.0 Hz, 2H), 1.40 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.1, 154.3, 150.2, 149.1, 142.8, 133.9, 130.5, 126.0, 125.2, 121.4, 120.7, 113.2, 65.1, 15.0. LC-MS: t_R= 4.64 min, purity: >99%, M/z [M+H]$^+$: 311; HRMS calcd. For $C_{14}H_{12}Cl_2N_2O_2$ [M+H]$^+$ = 311.0349, found 311.0351.

3-Chloro-*N*-(3,5-dichloropyridin-4-yl)-4-methoxybenzamide (NPD-1180)

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.63 (s, 1H), 8.75 (s, 2H), 8.11 (s, 1H), 8.01 (d, J = 8.7 Hz, 1H), 7.34 (d, J = 8.8 Hz, 1H), 3.96 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.2, 157.8, 148.4, 141.2, 130.7, 129.5, 128.9, 125.5, 121.2, 112.7, 56.7. LC-MS: t_R= 4.18 min, purity: 98%, M/z [M+H]$^+$: 331; HRMS calcd. For $C_{13}H_9Cl_3N_2O_2$ [M+H]$^+$ = 330.9802, found 330.9810.
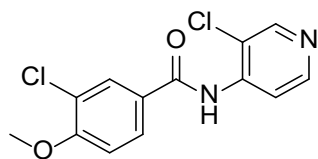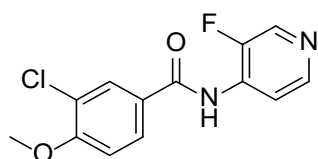
3-Chloro-*N*-(3-chloropyridin-4-yl)-4-methoxybenzamide (**NPD-1181**)

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.17 (s, 1H), 8.68 (s, 1H), 8.50 (d, *J* = 5.4 Hz, 1H), 8.09 (d, *J* = 2.2 Hz, 1H), 8.00 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.84 (dd, *J* = 5.6, 0.5 Hz, 1H), 7.33 (d, *J* = 8.7 Hz, 1H), 3.97 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.3, 158.1, 150.2, 149.0, 142.9, 130.1, 129.4, 126.7, 125.1, 121.5, 120.5, 113.0, 57.1. LC-MS: t$_R$= 4.13 min, purity: >99%, M/z [M+H]$^+$: 297; HRMS calcd. For C$_{13}$H$_{10}$Cl$_2$N$_2$O$_2$ [M+H]$^+$= 297.0192, found 297.0197.

3-Chloro-*N*-(3-fluoropyridin-4-yl)-4-methoxybenzamide (**NPD-1182**)

^{1}H NMR (500 MHz, CDCl$_3$) δ 10.45 (s, 1H), 8.59 (d, *J* = 2.9 Hz, 1H), 8.38 (d, *J* = 5.3 Hz, 1H), 8.09 (d, *J* = 2.2 Hz, 1H), 7.98 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.88 (dd, *J* = 6.7, 5.3 Hz, 1H), 7.31 (d, *J* = 8.8 Hz, 1H), 3.96 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.2, 157.6, 151.3 (d, *J* = 255.7 Hz), 146.3 (d, *J* = 5.1 Hz), 138.2 (d, *J* = 21.8 Hz), 133.4 (d, *J* = 9.2 Hz), 129.8, 129.1, 126.3, 120.9, 118.6 (app s), 112.5, 56.6. LC-MS: t$_R$= 3.53 min, purity: >99%, M/z [M+H]$^+$: 281; HRMS calcd. For C$_{13}$H$_{10}$ClFN$_2$O$_2$ [M+H]$^+$= 281.0488, found 281.0490.
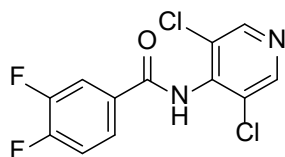
***N*-(3,5-Dichloropyridin-4-yl)-3,4-difluorobenzamide** (**NPD-1183**)

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.82 (s, 1H), 8.79 (s, 2H), 8.11-8.00 (m, 1H), 7.96-7.89 (m, 1H), 7.75-7.62 (m, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.8 (d, *J* = 2.0 Hz), 152.2 (dd, *J* = 252.3, 12.6 Hz), 149.7 (dd, *J* = 249.8, 12.7 Hz), 148.4, 140.9, 130.7, 130.0 (dd, *J* = 4.7, 3.4 Hz), 125.7 (dd, *J* = 7.7, 3.5 Hz), 118.2 (d, *J* = 17.7 Hz), 117.4 (d, *J* = 18.6 Hz). LC-MS: t$_R$= 4.15 min, purity: >99%, M/z [M+H]$^+$: 303; HRMS calcd. For C$_{12}$H$_6$Cl$_2$F$_2$N$_2$O [M+H]$^+$= 302.9898, found 302.9908.
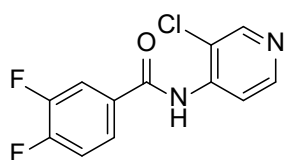
N-(3-Chloropyridin-4-yl)-3,4-difluorobenzamide (NPD-1184)

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.33 (s, 1H), 8.70 (d, J = 0.5 Hz, 1H), 8.52 (d, J = 5.3 Hz, 1H), 8.11-8.00 (m, 1H), 7.93-7.85 (m, 1H), 7.83 (dd, J = 5.4, 0.5 Hz, 1H), 7.75-7.58 (m, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.6 (d, J = 2.0 Hz), 152.0 (dd, J = 252.0, 12.7 Hz), 149.8, 149.2 (dd, J = 247.2, 13.1 Hz), 148.7, 142.3, 130.9 (dd, J = 5.3, 3.4 Hz), 125.8 (dd, J = 7.7, 3.5 Hz), 124.8, 120.2, 118.0 (d, J = 17.8 Hz), 117.6 (d, J = 18.6 Hz). LC-MS: t_R= 4.01 min, purity: >99%, M/z [M+H]$^+$: 269; HRMS calcd. For $C_{12}H_7ClF_2N_2O$ [M+H]$^+$= 269.0288, found 269.0299.
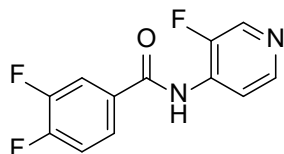
**3,4-Difluoro-N-(3-fluoropyridin-4-yl)benzamide (NPD-1185)**

^{1}H NMR (250 MHz, CDCl$_3$) δ 8.49 (d, J = 2.3 Hz, 1H), 8.45 (d, J = 6.2 Hz, 1H), 8.41 (d, J = 5.4 Hz, 1H), 8.16 (s, 1H), 7.84 - 7.71 (m, 1H), 7.71 - 7.59 (m, 1H), 7.40 - 7.27 (m, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.9 (d, J = 2.1 Hz), 151.2 (d, J = 255.6 Hz), 152.0 (dd, J = 251.9, 12.6 Hz), 149.1 (dd, J = 246.9, 13.0 Hz), 146.4 (d, J = 5.3 Hz), 138.3 (d, J = 21.6 Hz), 133.1 (d, J = 9.4 Hz), 130.9 (dd, J = 5.3, 3.4 Hz), 125.9 (dd, J = 7.6, 3.4 Hz), 118.5 (app s), 117.8 (d, J = 17.7 Hz), 117.8 (d, J = 18.6 Hz). LC-MS: t_R= 3.50 min, purity: >99%, M/z [M+H]$^+$: 253; HRMS calcd. For $C_{12}H_7F_3N_2O$ [M+H]$^+$= 253.0583, found 253.0593.
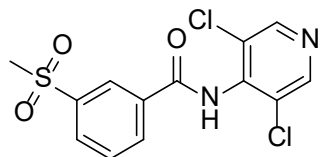
N-(3,5-Dichloropyridin-4-yl)-3-(methylsulfonyl)benzamide (NPD-1186)

^{1}H NMR (500 MHz, DMSO-d_6 + 1 drop of CDCl$_3$) δ 10.96 (s, 1H), 8.69 (s, 2H), 8.57 (d, J = 8.7 Hz, 1H), 8.33 (d, J = 7.8 Hz, 1H), 8.18 (d, J = 7.9 Hz, 1H), 7.83 (t, J = 7.8 Hz, 1H), 3.26 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6 + 1 drop of CDCl$_3$) δ 163.8, 148.6, 148.2, 141.7, 134.2, 133.4, 131.1, 131.0, 130.4, 126.9, 44.0. LC-MS: t_R= 3.81 min, purity: >99%, M/z [M+H]$^+$: 345; HRMS calcd. For $C_{13}H_{10}Cl_2N_2O_3S$ [M+H]$^+$= 344.9862, found 344.9852.
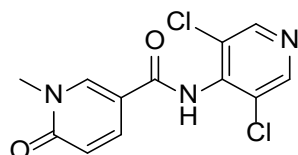
N-(3,5-Dichloropyridin-4-yl)-1-methyl-6-oxo-1,6-dihydropyridine-3-carboxamide (NPD-1187)

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.41 (s, 1H), 8.74 (s, 2H), 8.57 (d, J = 2.6 Hz, 1H), 7.98 (dd, J = 9.5, 2.7 Hz, 1H), 6.50 (d, J = 9.5 Hz, 1H), 3.53 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 162.6, 162.3, 148.8, 144.3, 141.6, 138.2, 130.9, 118.6,

111.1, 38.0. LC-MS: t_R= 2.69 min, purity: >99%, M/z [M+H]$^+$: 298; HRMS calcd. For $C_{12}H_9Cl_2N_3O_2$ [M+H]$^+$= 298.0145, found 298.0152.
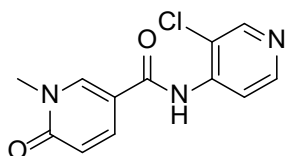
N-(3-Chloropyridin-4-yl)-1-methyl-6-oxo-1,6-dihydropyridine-3-carboxamide acetate (NPD-1188)

^{1}H NMR (250 MHz, DMSO-d_6) δ 8.66 (s, 1H), 8.60 (d, J = 2.6 Hz, 1H), 8.48 (d, J = 5.4 Hz, 1H), 7.94 (dd, J = 9.5, 2.7 Hz, 1H), 7.82 (d, J = 5.4 Hz, 1H), 6.48 (d, J = 9.6 Hz, 1H), 1.89 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 172.3, 163.0, 161.8, 149.7, 148.6, 143.9, 142.5, 138.1, 123.9, 119.4, 118.0, 111.4, 37.5. LC-MS: t_R= 2.29 min, purity: 95%, M/z [M+H]$^+$: 264; HRMS calcd. For $C_{12}H_{10}ClN_3O_2$ [M+H]$^+$= 264.0534, found 264.0545.
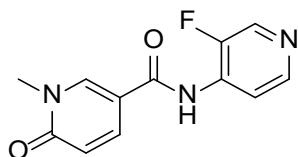
N-(3-Fluoropyridin-4-yl)-1-methyl-6-oxo-1,6-dihydropyridine-3-carboxamide (NPD-1189)

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.20 (s, 1H), 8.61- 8.55 (m, 2H), 8.36 (d, J = 5.3 Hz, 1H), 7.94- 7.87 (m, 2H), 6.46 (d, J = 9.5 Hz, 1H), 3.51 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.3, 161.8, 150.8 (d, J = 255.1 Hz), 146.4 (d, J = 5.1 Hz), 143.9, 138.3, 138.1 (d, J = 21.7 Hz), 133.4 (d, J = 9.0 Hz), 118.0 (app s), 117.8, 111.3, 37.5. LC-MS: t_R= 1.94 min, purity: >99%, M/z [M+H]$^+$: 248; HRMS calcd. For $C_{12}H_{10}FN_3O_2$ [M+H]$^+$= 248.0830, found 248.0840.
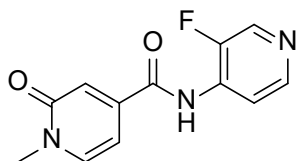
N-(3-Fluoropyridin-4-yl)-1-methyl-2-oxo-1,2-dihydropyridine-4-carboxamide (NPD-1190)

^{1}H NMR (250 MHz, DMSO-d_6) δ 8.55 (d, J = 2.9 Hz, 1H), 8.35 (d, J = 5.3 Hz, 1H), 7.93 - 7.78 (m, 2H), 6.94 (d, J = 1.6 Hz, 1H), 6.60 (dd, J = 7.0, 2.0 Hz, 1H), 3.47 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.5, 161.7, 151.5 (d, J = 255.8 Hz), 146.2 (d, J = 5.1 Hz), 144.9, 140.2, 138.1 (d, J = 21.9 Hz), 134.4 (app s), 118.8, 118.4 (app s), 103.2, 36.9. LC-MS: t_R= 2.00 min, purity: >99%, M/z [M+H]$^+$: 248; HRMS calcd. For $C_{12}H_{10}FN_3O_2$ [M+H]$^+$= 248.0830, found 248.0829.
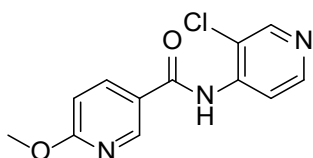
N-(3-Chloropyridin-4-yl)-6-methoxynicotinamide (NPD-1191)

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.20 (s, 1H), 8.81 (d, J = 2.1 Hz, 1H), 8.68 (s, 1H), 8.51 (d, J = 5.4 Hz, 1H), 8.24 (dd, J = 8.7, 2.5 Hz, 1H), 7.89 (d, J = 5.4 Hz, 1H), 6.98 (d, J = 8.7 Hz, 1H), 3.95 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 166.3, 164.5, 150.2, 149.1, 148.5, 142.7, 139.4, 124.7, 123.4, 120.1, 110.9, 54.3. LC-MS: t_R= 3.37 min, purity: >99%, M/z [M+H]$^+$: 264; HRMS calcd. For $C_{12}H_{10}ClN_3O_2$ [M+H]$^+$= 264.0534, found 264.0535.
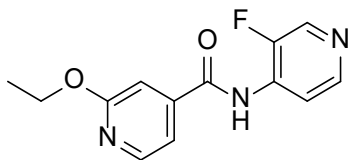
2-Ethoxy-N-(3-fluoropyridin-4-yl)isonicotinamide (NPD-1192)

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.69 (s, 1H), 8.61 (d, J = 2.8 Hz, 1H), 8.40 (d, J = 5.3 Hz, 1H), 8.34 (dd, J = 5.3, 0.8 Hz, 1H), 7.91 (dd, J = 6.7, 5.3 Hz, 1H), 7.40 (dd, J = 5.3, 1.5 Hz, 1H), 7.27 (dd, J = 1.5, 0.8 Hz, 1H), 4.36 (q, J = 7.0 Hz, 2H), 1.33 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.4, 163.7, 151.2 (d, J = 256.2 Hz), 147.9, 146.4 (d, J = 5.3 Hz), 143.9, 138.3 (d, J = 21.7 Hz), 132.9 (d, J = 9.3 Hz), 118.6 (app s), 115.0, 109.4, 61.8, 14.5. LC-MS: t_R= 3.39 min, purity: >99%, M/z [M+H]$^+$: 262; HRMS calcd. For $C_{13}H_{12}FN_3O_2$ [M+H]$^+$= 262.0986, found 262.0989.

**N-(3-Chloropyridin-4-yl)-3-ethoxy-4-methoxybenzamide (NPD-1193)**

^{1}H NMR (250 MHz, DMSO-d_6) δ 9.94 (s, 1H), 8.67 (s, 1H), 8.49 (d, J = 5.4 Hz, 1H), 7.86 (d, J = 5.4 Hz, 1H), 7.64 (dd, J = 8.4, 2.1 Hz, 1H), 7.54 (d, J = 2.1 Hz, 1H), 7.11 (d, J = 8.5 Hz, 1H), 4.09 (q, J = 7.0 Hz, 2H), 3.85 (s, 3H), 1.36 (t, J = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.4, 152.8, 150.1, 149.0, 148.1, 143.1, 125.8, 124.8, 122.0, 120.2, 112.4, 111.6, 64.3, 56.2, 15.2. LC-MS: t_R= 3.83 min, purity: >99%, M/z [M+H]$^+$: 307; HRMS calcd. For $C_{15}H_{15}ClN_2O_3$ [M+H]$^+$= 307.0844, found 307.0852.
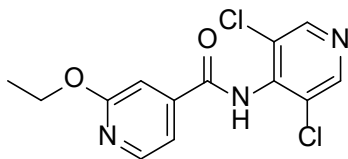
N-(3,5-Dichloropyridin-4-yl)-2-ethoxyisonicotinamide (NPD-1194)

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.95 (s, 1H), 8.79 (s, 2H), 8.39 (dd, J = 5.3, 0.6 Hz, 2H), 7.45 (d, J = 5.3, 1.5 Hz, 1H), 7.35 - 7.28 (m, 1H), 4.38 (q, J = 7.0 Hz, 2H), 1.35 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.3, 163.7,

148.9, 148.7, 143.3, 141.0, 131.1, 115.2, 109.5, 62.3, 14.9. LC-MS: t_R= 4.01 min, purity: >99%, M/z [M+H]$^+$: 312; HRMS calcd. For $C_{13}H_{11}Cl_2N_3O_2$ [M+H]$^+$= 312.0301, found 312.0296.
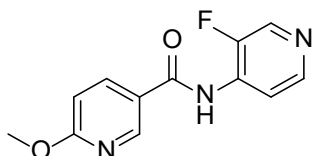
N-(3-Fluoropyridin-4-yl)-6-methoxynicotinamide (NPD-1195)

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.51 (s, 1H), 8.78 (dd, J = 2.5, 0.8 Hz, 1H), 8.59 (d, J = 2.8 Hz, 1H), 8.38 (d, J = 5.3 Hz, 1H), 8.22 (dd, J = 8.7, 2.5 Hz, 1H), 7.93 (dd, J = 6.7, 5.3 Hz, 1H), 6.96 (dd, J = 8.7, 0.7 Hz, 1H), 3.93 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 166.2, 164.8, 151.5 (d, J = 255.5 Hz), 148.7, 146.8 (d, J = 5.2 Hz), 139.5, 138.6 (d, J = 21.5 Hz), 133.8 (d, J = 9.3 Hz), 123.5, 118.7 (app s), 110.8, 54.3. LC-MS: t_R= 2.83 min, purity: >99%, M/z [M+H]$^+$: 248; HRMS calcd. For $C_{12}H_{10}FN_3O_2$ [M+H]$^+$= 248.0830, found 248.0830.
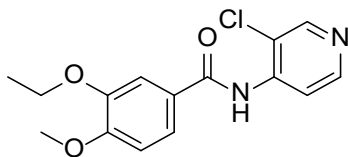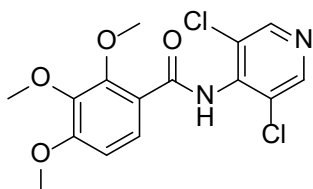

**N-(3,5-Dichloropyridin-4-yl)-2,3,4-trimethoxybenzamide (NPD-1196)**

^{1}H NMR (500 MHz, CDCl$_3$) δ 10.01 (s, 1H), 8.56 (s, 2H), 7.99 (d, J = 9.0 Hz, 1H), 6.84 (d, J = 9.0 Hz, 1H), 4.16 (s, 3H), 3.95 (s, 3H), 3.92 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 162.0, 157.8, 152.7, 148.0, 141.8, 140.9, 129.5, 127.7, 117.2, 108.0, 62.5, 61.2, 56.4. LC-MS: t_R= 4.27 min, purity: >99%, M/z [M+H]$^+$: 357; HRMS calcd. For $C_{15}H_{14}Cl_2N_2O_4$ [M+H]$^+$= 357.0403, found 357.0403. Spectral data are in agreement with a previous report. [3]
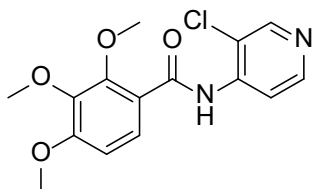
N-(3-Chloropyridin-4-yl)-2,3,4-trimethoxybenzamide (NPD-1197)

^{1}H NMR (500 MHz, CDCl$_3$) δ 11.08 (s, 1H), 8.74 (d, J = 5.8 Hz, 1H), 8.58 (s, 1H), 8.44 (d, J = 5.8 Hz, 1H), 8.00 (d, J = 9.0 Hz, 1H), 6.85 (d, J = 9.1 Hz, 1H), 4.15 (s, 3H), 3.95 (s, 3H), 3.91 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 163.7, 158.1, 152.7, 147.7, 147.6, 144.0, 141.7, 127.7, 120.1, 117.4, 115.1, 108.0, 62.5, 61.2, 56.3. LC-MS: t_R= 4.06 min, purity: >99%, M/z [M+H]$^+$: 323; HRMS calcd. For $C_{15}H_{15}ClN_2O_4$ [M+H]$^+$= 323.0793, found 323.0795.
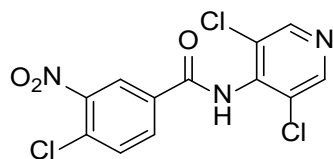
4-Chloro-*N*-(3,5-dichloropyridin-4-yl)-3-nitrobenzamide (NPD-1198)

^{1}H NMR (500 MHz, CDCl$_3$ + 1 drop of DMSO-*d$_6$*) δ 10.44 (s, 1H), 8.70 (s, 1H), 8.51 (s, 2H), 8.21 (d, *J* = 9.5 Hz, 1H), 7.63 (d, *J* = 9.5 Hz, 1H). ^{13}C NMR (126 MHz, CDCl$_3$ + 1 drop of DMSO-*d$_6$*) δ 162.4, 148.1, 147.6, 140.7, 133.3, 132.6, 132.1, 130.77, 130.75, 125.5. LC-MS: t_R= 4.31 min, purity: >99%, M/z [M+H]$^+$: 346; HRMS calcd. For C$_{12}$H$_6$Cl$_3$N$_3$O$_3$ [M+H]$^+$= 345.9548, found 345.9547.
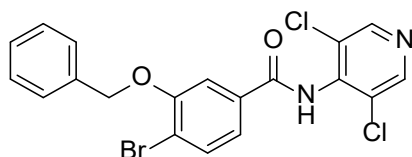
3-(Benzyloxy)-4-bromo-*N*-(3,5-dichloropyridin-4-yl)benzamide (NPD-1199)

^{1}H NMR (500 MHz, CDCl$_3$) δ 9.82 (s, 1H), 8.45 (s, 2H), 7.62 - 7.53 (m, 2H), 7.49 -7.43 (m, 1H), 7.42 - 7.35 (m, 2H), 7.32 - 7.19 (m, 3H), 5.12 (s, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.5, 154.9, 148.0, 140.7, 135.8, 133.1, 133.0, 130.5, 128.4, 127.9, 127.0, 121.4, 116.9, 113.2, 70.6. LC-MS: t_R= 5.07 min, purity: >99%, M/z [M+H]$^+$: 453; HRMS calcd. For C$_{19}$H$_{13}$BrCl$_2$N$_2$O$_2$ [M+H]$^+$= 450.9610, found 450.9621.
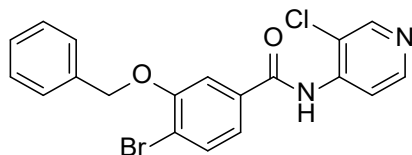
3-(Benzyloxy)-4-bromo-*N*-(3-chloropyridin-4-yl)benzamide (NPD-1200)

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.65 - 8.56 (m, 2H), 8.56 - 8.46 (m, 2H), 7.73 (d, *J* = 8.2 Hz, 1H), 7.53 - 7.47 (m, 3H), 7.44 - 7.39 (m, 2H), 7.37 - 7.33 (m, 1H), 7.30 (dd, *J* = 8.2, 2.0 Hz, 1H), 5.28 (s, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.7, 155.9, 148.3, 148.0, 142.3, 135.7, 134.1, 133.8, 128.9, 128.4, 127.1, 120.1, 119.7, 118.5, 114.4, 112.7, 71.1. LC-MS: t_R= 5.17 min, purity: >99%, M/z [M+H]$^+$: 417; HRMS calcd. For C$_{19}$H$_{14}$BrClN$_2$O$_2$ [M+H]$^+$= 417.0000, found 417.0006.
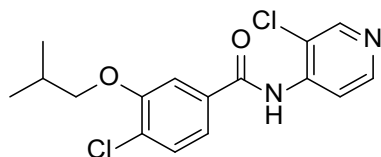
4-Chloro-*N*-(3-chloropyridin-4-yl)-3-isobutoxybenzamide (NPD-1201)

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.62 - 8.56 (m, 3H), 8.50 (d, *J* = 5.7 Hz, 1H), 7.53 - 7.47 (m, 2H), 7.31 (dd, *J* = 8.2, 2.0 Hz, 1H), 3.88 (d, *J* = 6.5 Hz, 2H), 2.19 (app hept, *J* = 6.6 Hz, 1H), 1.08 (d, *J* = 6.7 Hz, 6H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.8,

155.6, 148.4, 148.1, 142.3, 133.0, 130.7, 128.6, 120.1, 118.5, 114.4, 112.5, 75.7, 28.4, 19.3. LC-MS: t_R= 5.34 min, purity: 98%, M/z [M+H]+: 339; HRMS calcd. For $C_{16}H_{16}Cl_2N_2O_2$ [M+H]+= 339.0662, found 339.0670.
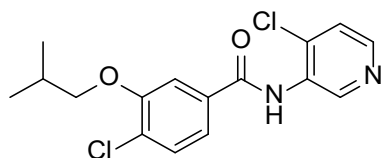
4-Chloro-*N*-(4-chloropyridin-3-yl)-3-isobutoxybenzamide (NPD-1202)

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.44 (s, 1H), 8.71 (s, 1H), 8.47 (d, *J* = 5.2 Hz, 1H), 7.71 (s, 2H), 7.68 - 7.56 (m, 2H), 3.96 (d, *J* = 6.3 Hz, 2H), 2.12 (app hept, *J* = 6.5 Hz, 1H), 1.05 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.7, 154.0, 149.6, 148.2, 139.7, 133.4, 132.2, 130.0, 125.4, 124.7, 120.8, 112.7, 74.8, 27.8, 19.0. LC-MS: t_R= 4.95 min, purity: >99%, M/z [M+H]+: 339; HRMS calcd. For $C_{16}H_{16}Cl_2N_2O_2$ [M+H]+= 339.0662, found 339.0675.
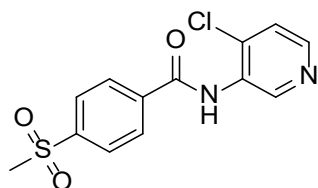
***N*-(4-Chloropyridin-3-yl)-4-(methylsulfonyl)benzamide (NPD-1203)**

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.71 (s, 1H), 8.72 (s, 1H), 8.48 (d, *J* = 5.3 Hz, 1H), 8.23 (d, *J* = 8.5 Hz, 2H), 8.12 (d, *J* = 8.5 Hz, 2H), 7.72 (d, *J* = 5.3 Hz, 1H), 3.31 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.7, 149.5, 148.5, 143.7, 139.8, 137.8, 131.9, 128.9, 127.4, 124.9, 43.3. LC-MS: t_R= 2.90 min, purity: 96%, M/z [M+H]+: 311; HRMS calcd. For $C_{13}H_{11}ClN_2O_3S$ [M+H]+= 311.0252, found 311.0257.
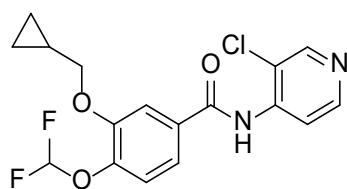
***N*-(3-Chloropyridin-4-yl)-3-(cyclopropylmethoxy)-4-(difluoromethoxy)benzamide (NPD-1204)**

^{1}H NMR (500 MHz, CDCl₃) δ 8.58 (s, 1H), 8.52 (d, *J* = 5.5 Hz, 2H), 8.48 (d, *J* = 5.6 Hz, 1H), 7.57 (d, *J* = 2.1 Hz, 1H), 7.38 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.30 (d, *J* = 8.3 Hz, 1H), 6.74 (t, *J* = 74.7 Hz, 1H), 3.97 (d, *J* = 7.0 Hz, 2H), 1.37 - 1.28 (m, 1H), 0.71 - 0.66 (m, 2H), 0.41 - 0.37 (m, 2H). ^{13}C NMR (126 MHz, CDCl₃) δ 164.7, 151.2, 149.4, 149.1, 143.9, 141.4, 131.9, 122.5, 120.0, 119.0, 115.7 (t, *J* = 262.0 Hz), 114.3, 114.0, 74.3, 10.1, 3.5. LC-MS: t_R= 4.68 min, purity: >99%, M/z [M+H]+: 369; HRMS calcd. For $C_{17}H_{15}ClF_2N_2O_3$ [M+H]+= 369.0812, found 369.0806.
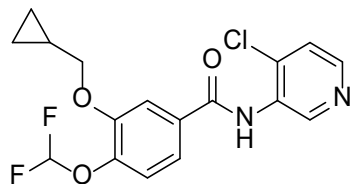
N-(4-Chloropyridin-3-yl)-3-(cyclopropylmethoxy)-4-(difluoromethoxy)benzamide (**NPD-1205**)

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.37 (s, 1H), 8.68 (s, 1H), 8.46 (d, J = 5.3 Hz, 1H), 7.74 - 7.68 (m, 2H), 7.64 (dd, J = 8.4, 2.0 Hz, 1H), 7.40 - 7.08 (m, 2H), 3.99 (d, J = 7.0 Hz, 2H), 1.28 (m, 1H), 0.62 - 0.57 (m, 2H), 0.40 - 0.35 (m, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.7, 149.6, 149,6 (confirmed by HMBC), 148.2, 142.7 (t, J = 3.1 Hz), 140.0, 132.2, 131.2, 124.8, 120.7, 120.3, 116.5 (t, J = 258.3 Hz), 113.6, 73.3, 10.0, 3.1. LC-MS: t_R= 4.38 min, purity: >99%, M/z [M+H]$^+$: 369; HRMS calcd. For $C_{17}H_{15}ClF_2N_2O_3$ [M+H]$^+$= 369.0812, found 369.0805.
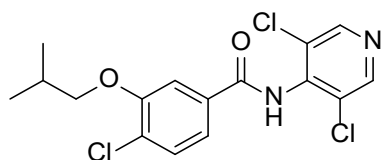
4-Chloro-N-(3,5-dichloropyridin-4-yl)-3-isobutoxybenzamide (**NPD-1206**)

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.59 – 8.50 (m, 3H), 8.46 (dd, J = 5.7, 3.0 Hz, 1H), 7.51 - 7.45 (m, 2H), 7.32 – 7.26 (m, 1H), 3.89 – 3.83 (m, 2H), 2.25 – 2.10 (m, 1H), 1.09 – 1.04 (m, 6H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 166.2, 157.7, 150.7, 142.0, 134.4, 132.7, 131.1, 130.7, 121.7, 115.0, 77.9, 30.6, 21.5. LC-MS: t_R= 5.22 min, purity: 99%, M/z [M+H]$^+$: 373; HRMS calcd. For $C_{16}H_{15}Cl_3N_2O_2$ [M+Na]$^+$= 395.0091, found 395.0073.
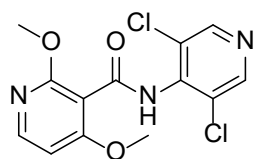
N-(3,5-Dichloropyridin-4-yl)-2,4-dimethoxynicotinamide (**NPD-1472**)

^{1}H NMR (300 MHz, DMSO-d_6) δ 9.97 (s, 1H), 8.73 (s, 2H), 8.21 (d, J = 8.3 Hz, 1H), 6.56 (d, J = 8.3 Hz, 1H), 4.08 (s, 3H), 3.97 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 164.8, 161.5, 160.4, 148.1, 143.9, 141.5, 130.7, 106.6, 102.7, 54.2, 54.1. LC-MS: t_R= 4.58 min, purity: >99%, M/z [M+H]$^+$: 328; HRMS calcd. For $C_{13}H_{11}Cl_2N_3O_3$ [M+H]$^+$= 328.0250, found 328.0254.
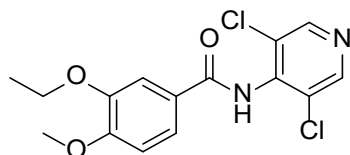
N-(3,5-Dichloropyridin-4-yl)-3-ethoxy-4-methoxybenzamide (**NPD-2976**)

^{1}H NMR (600 MHz, DMSO-d_6) δ 10.42 (s, 1H), 8.74 (s, 2H), 7.67 (dd, J = 8.5, 2.1 Hz, 1H), 7.56 (d, J = 2.1 Hz, 1H), 7.12 (d, J = 8.4 Hz, 1H), 4.09 (q, J = 7.0 Hz, 2H), 3.85 (s, 3H), 1.36 (t, J = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 164.2, 152.4, 148.2, 147.7, 141.7 (confirmed by HMBC), 130.7, 124.8, 121.6, 112.0, 111.2, 63.9, 55.7, 14.7. LC-MS: t_R= 3.81 min, purity: >99%, M/z [M+H]$^+$: 341; HRMS calcd. For $C_{15}H_{14}Cl_2N_2O_3$ [M+H]$^+$= 341.0454, found 341.0457. Spectral data are in agreement with a previous report. [4]
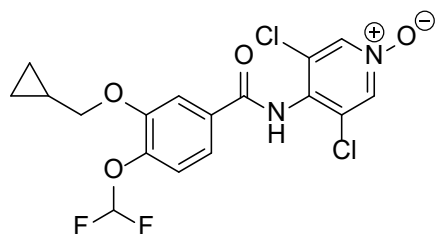
3,5-Dichloro-4-(3-(cyclopropylmethoxy)-4-(difluoromethoxy)benzamido)pyridine 1-oxide (**NPD-2980**)

To a stirred, ice-cooled (0 °C) solution of **NPD-0006** (0.15 g, 0.37 mmol) in DCM (15 mL) was added portion-wise m-CPBA (0.11 g, 0.48 mmol). The reaction mixture was warmed to room temperature and stirred overnight. Saturated aq. NaHCO$_3$ (10 mL) was slowly added and the mixture was extracted with DCM (3 x 15 mL). The combined organic layers were washed with brine (50 mL), dried over Na$_2$SO$_4$, filtered and concentrated *in vacuo*. The crude product was purified with flash column chromatography using a gradient elution of EtOAc in cyclohexane (30% to 80%) to 5:1 as eluents to yield the title compound as a white solid. ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.25 (s, 2H), 7.82 (s, 1H), 7.58 (s, 1H), 7.46 (d, J = 8.3 Hz, 1H), 7.28 (d, J = 8.2 Hz, 1H), 6.74 (t, J = 74.8 Hz, 1H), 3.96 (d, J = 6.9 Hz, 2H), 1.36 - 1.27 (m, 1H), 0.70 - 0.65 (m, 2H), 0.40 - 0.36 (m, 2H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 164.4, 151.1, 144.1, 138.5, 131.8, 131.4, 130.6, 122.5, 119.9, 115.8 (t, J = 264.3 Hz), 114.3, 74.4, 10.1, 3.4. LC-MS: t_R= 4.01 min, purity: 98%, M/z [M+H]$^+$: 419; HRMS calcd. For $C_{17}H_{14}Cl_2F_2N_2O_4$ [M+H]$^+$= 419.0371, found 419.0364. Spectral data are in agreement with a previous report. [5]
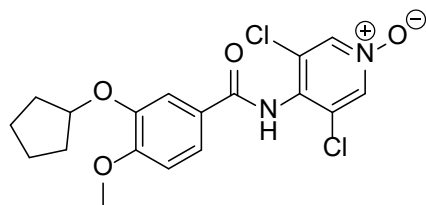
3,5-Dichloro-4-(3-(cyclopentyloxy)-4-methoxybenzamido)pyridine 1-oxide (**NPD-2981**)

Prepared from **NPD-0005** (0.15 g, 0.39 mmol) with m-CPBA (0.12 g, 0.51 mmol) as described for **NPD-2980** to give the title compound as a white solid. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.28 (s, 2H), 7.74 (s, 1H), 7.59 - 7.43 (m, 2H), 6.93 (d, J = 7.8 Hz, 1H), 4.87 (s, 1H), 3.93 (s, 3H), 2.07 - 1.78 (m, 6H), 1.63 (app s, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.6, 154.4, 148.2, 138.5, 134.4, 131.0, 124.5, 120.8, 114.3, 111.0, 80.9, 56.3, 32.9, 24.2. LC-MS: t_R= 3.74 min, purity: 97%,

M/z [M+H]$^+$: 397; HRMS calcd. For $C_{18}H_{18}Cl_2N_2O_4$ [M+H]$^+$= 397.0716, found 397.0705. Spectral data are in agreement with a previous report. [1]
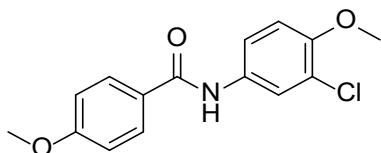
N-(3-Chloro-4-methoxyphenyl)-4-methoxybenzamide (**NPD-2991**)

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.82 (d, J = 8.5 Hz, 2H), 7.71 - 7.65 (m, 2H), 7.50 (dd, J = 8.8, 2.1 Hz, 1H), 6.96 (d, J = 8.6 Hz, 2H), 6.91 (d, J = 8.8 Hz, 1H), 3.90 (s, 3H), 3.87 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 165.3, 162.7, 152.1, 131.7, 129.0, 126.8, 122.9, 122.6, 120.1, 114.1, 112.4, 56.5, 55.6. LC-MS: t_R= 4.32 min, purity: >99%, M/z [M+H]$^+$: 292; HRMS calcd. For $C_{15}H_{14}ClNO_3$ [M+H]$^+$= 292.0735, found 292.0728.
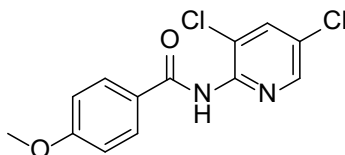
N-(3,5-Dichloropyridin-2-yl)-4-methoxybenzamide (**NPD-2992**)

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.38 (d, J = 1.7 Hz, 1H), 8.30 (s, 1H), 7.90 (d, J = 8.7 Hz, 2H), 7.78 (d, J = 2.1 Hz, 1H), 6.99 (d, J = 8.7 Hz, 2H), 3.88 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.4, 163.2, 146.6, 145.6, 137.7, 129.7, 127.9, 126.0, 123.0, 114.2, 55.7. LC-MS: t_R= 4.00 min, purity: >99%, M/z [M+H]$^+$: 297; HRMS calcd. For $C_{13}H_{10}Cl_2N_2O_2$ [M+H]$^+$= 297.0192, found 297.0186.
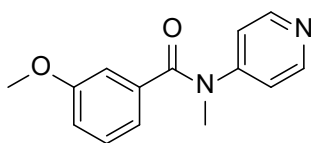
3-Methoxy-N-methyl-N-(pyridin-4-yl)benzamide (**NPD-2993**)

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.44 (d, J = 4.6 Hz, 2H), 7.13 (t, J = 7.9 Hz, 1H), 6.96 (d, J = 6.0 Hz, 2H), 6.92 (s, 1H), 6.88 (dd, J = 8.2, 2.4 Hz, 1H), 6.83 (d, J = 7.6 Hz, 1H), 3.71 (s, 3H), 3.51 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.7, 159.5, 152.2, 150.6, 136.3, 129.4, 121.1, 120.2, 116.8, 113.9, 55.4, 37.5. LC-MS: t_R= 2.48 min, purity: >99%, M/z [M+H]$^+$: 243; HRMS calcd. For $C_{14}H_{14}N_2O_2$ [M+H]$^+$= 243.1128, found 243.1130.
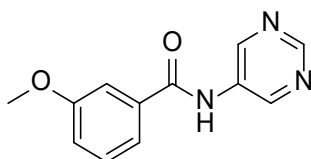
3-Methoxy-*N*-(pyrimidin-5-yl)benzamide (NPD-2994)

^{1}H NMR (600 MHz, CDCl$_3$) δ 9.20 (s, 2H), 9.01 (s, 1H), 8.17 (s, 1H), 7.48 - 7.39 (m, 3H), 7.13 (ddd, *J* = 7.9, 2.5, 1.1 Hz, 1H), 3.88 (s, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 166.0, 160.3, 153.8, 148.2, 134.8, 133.9, 130.2, 119.1, 119.0, 112.9, 55.7. LC-MS: t_R= 3.06 min, purity: >99%, M/z [M+H]$^+$: 230; HRMS calcd. For C$_{12}$H$_{11}$N$_3$O$_2$ [M+H]$^+$= 230.0924, found 230.0916.
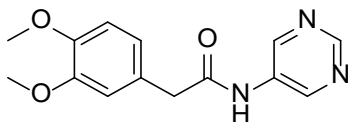
2-(3,4-Dimethoxyphenyl)-*N*-(pyrimidin-5-yl)acetamide (NPD-2995)

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.97 - 8.88 (m, 3H), 7.41 (s, 1H), 6.92 - 6.85 (m, 2H), 6.82 (s, 1H), 3.91 - 3.87 (m, 6H), 3.73 (s, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 170.2, 154.3, 149.7, 149.0, 147.8, 133.3, 125.9, 121.9, 112.4, 111.9, 56.11, 56.07, 44.1. LC-MS: t_R= 2.78 min, purity: >99%, M/z [M+H]$^+$: 274; HRMS calcd. For C$_{14}$H$_{15}$N$_3$O$_3$ [M+H]$^+$= 274.1186, found 274.1190.
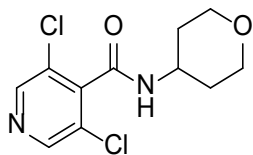
3,5-Dichloro-*N*-(tetrahydro-2*H*-pyran-4-yl)isonicotinamide (NPD-2996)

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.52 (s, 2H), 5.80 (d, *J* = 7.3 Hz, 1H), 4.31 - 4.22 (m, 1H), 3.98 (s, 2H), 3.58 - 3.49 (m, 2H), 2.08 - 2.02 (m, 2H), 1.66 - 1.53 (m, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 161.4, 147.9, 142.2, 129.1, 66.7, 46.7, 32.9. LC-MS: t_R= 2.78 min, purity: >99%, M/z [M+H]$^+$: 275; HRMS calcd. For C$_{11}$H$_{12}$Cl$_2$N$_2$O$_2$ [M+H]$^+$= 275.0349, found 275.0338.
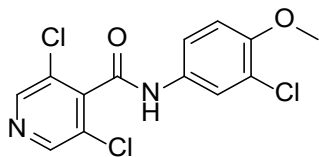
3,5-Dichloro-*N*-(3-chloro-4-methoxyphenyl)isonicotinamide (NPD-2997)

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.56 (s, 2H), 7.68 - 7.64 (m, 1H), 7.59 (s, 1H), 7.52 - 7.46 (m, 1H), 6.94 (d, *J* = 8.8 Hz, 1H), 3.92 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 160.1, 153.1, 148.0, 141.8, 129.9, 129.2, 123.3, 123.0, 120.5, 112.4, 56.6. LC-MS: t_R= 4.26 min, purity: >99%, M/z [M+H]$^+$: 331; HRMS calcd. For C$_{13}$H$_9$Cl$_3$N$_2$O$_2$ [M+H]$^+$= 330.9802, found 330.9799.
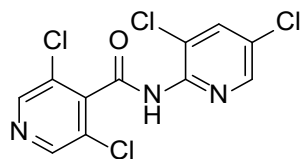
3,5-Dichloro-*N*-(3,5-dichloropyridin-2-yl)isonicotinamide (NPD-2998)

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.52 (s, 2H), 8.42 (s, 1H), 7.75 (s, 2H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 149.0, 147.5, 145.1, 144.2, 137.9, 128.5. Note: not all Carbon signals visible in spectrum. LC-MS: t_R= 4.07 min, purity: >99%, M/z [M+H]$^+$: 338; HRMS calcd. For C$_{11}$H$_5$Cl$_4$N$_3$O [M+H]$^+$= 335.9259, found 335.9260.
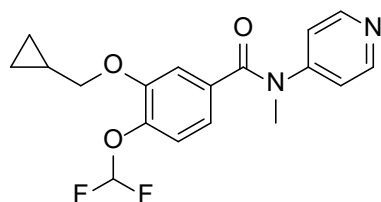
3-(Cyclopropylmethoxy)-4-(difluoromethoxy)-*N*-methyl-*N*-(pyridin-4-yl)benzamide (NPD-2999)

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.47 (d, *J* = 5.3 Hz, 2H), 7.04 - 6.98 (m, 4H), 6.85 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.62 (t, *J* = 74.9 Hz, 1H), 3.74 (d, *J* = 7.0 Hz, 2H), 3.52 (s, 3H), 1.22 - 1.10 (m, 1H), 0.66 - 0.57 (m, 2H), 0.34 - 0.28 (m, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 169.9, 152.7, 150.3, 149.8, 142.3, 132.8, 122.0, 121.9, 119.9, 115.8 (t, *J* = 260.5 Hz), 115.0, 74.1, 37.7, 10.0, 3.4. LC-MS: t_R= 3.60 min, purity: >99%, M/z [M+H]$^+$: 349; HRMS calcd. For C$_{18}$H$_{18}$F$_2$N$_2$O$_3$ [M+H]$^+$= 349.1358, found 349.1363.
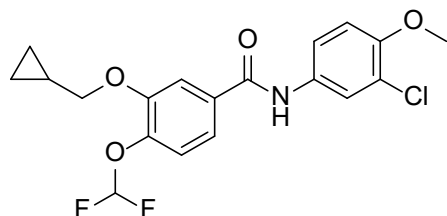
N-(3-Chloro-4-methoxyphenyl)-3-(cyclopropylmethoxy)-4-(difluoromethoxy)benzamide (NPD-3000)

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.73 - 7.66 (m, 2H), 7.53 (s, 1H), 7.49 (d, *J* = 8.6 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.23 (d, *J* = 8.2 Hz, 1H), 6.93 (d, *J* = 8.8 Hz, 1H), 6.72 (t, *J* = 75.0 Hz, 1H), 3.94 (d, *J* = 6.9 Hz, 2H), 3.91 (s, 3H), 1.31 (m, 1H), 0.67 (app d, *J* = 7.6 Hz, 2H), 0.37 (app d, *J* = 4.5 Hz, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.7, 152.4, 151.0, 143.1, 133.0, 131.3, 123.0, 122.8, 122.3, 120.2, 118.8, 115.9 (t, *J* = 260.4 Hz), 113.9, 112.4, 74.3, 56.5, 10.2, 3.4. LC-MS: t_R= 5.00 min, purity: >99%, M/z [M+H]$^+$: 398; HRMS calcd. For C$_{19}$H$_{18}$ClF$_2$NO$_4$ [M+H]$^+$= 398.0965, found 398.0955.

3-(Cyclopropylmethoxy)-4-(difluoromethoxy)-*N*-(pyrimidin-5-yl)benzamide (**NPD-3001**)

^{1}H NMR (500 MHz, CDCl$_3$) δ 9.16 (s, 2H), 9.02 (s, 1H), 8.18 (s, 1H), 7.56 (s, 1H), 7.40 (d, *J* = 8.1 Hz, 1H), 7.24 (d, *J* = 8.1 Hz, 1H), 6.74 (t, *J* = 74.8 Hz, 1H), 3.95 (d, *J* = 6.9 Hz, 2H), 1.31 (tt, *J* = 12.7, 7.8 Hz, 1H), 0.67 (app q, *J* = 7.6 Hz, 2H), 0.37 (app q, *J* = 4.7 Hz, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 165.2, 154.6, 151.1, 148.4, 143.7 (t, *J* = 3.2 Hz), 133.5, 131.6, 122.3, 119.2, 115.8 (t, *J* = 264.2 Hz), 114.0, 74.4, 10.1, 3.4. LC-MS: t$_R$= 4.09 min, purity: >99%, M/z [M+H]$^+$: 336; HRMS calcd. For C$_{16}$H$_{15}$F$_2$N$_3$O$_3$ [M+H]$^+$= 336.1154, found 336.1145.
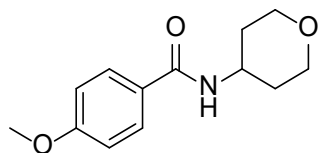
4-Methoxy-*N*-(tetrahydro-2*H*-pyran-4-yl)benzamide (**NPD-3002**)

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.66 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 8.0 Hz, 2H), 5.90 (d, *J* = 6.2 Hz, 1H), 4.17 - 4.07 (m, 1H), 3.93 (app d, *J* = 10.2 Hz, 2H), 3.78 (s, 3H), 3.46 (app t, *J* = 11.7 Hz, 2H), 1.93 (app d, *J* = 12.5 Hz, 2H), 1.49 (app q, *J* = 11.8 Hz, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 166.5, 162.4, 128.8, 126.9, 113.9, 67.1, 55.6, 46.3, 33.5. LC-MS: t$_R$= 3.01 min, purity: >99%, M/z [M+H]$^+$: 236; HRMS calcd. For C$_{13}$H$_{17}$NO$_3$ [M+H]$^+$= 236.1281, found 236.1272.
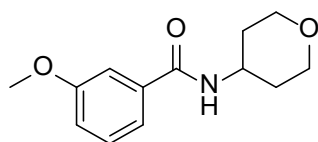
3-Methoxy-*N*-(tetrahydro-2*H*-pyran-4-yl)benzamide (**NPD-3003**)

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.30 - 7.25 (m, 2H), 7.24 - 7.18 (m, 1H), 6.98 (d, *J* = 8.1 Hz, 1H), 6.04 - 5.93 (m, 1H), 4.21 - 4.08 (m, 1H), 3.94 (app d, *J* = 10.6 Hz, 2H), 3.79 (s, 3H), 3.48 (app t, *J* = 11.7 Hz, 2H), 1.95 (app d, *J* = 12.6 Hz, 2H), 1.51 (app q, *J* = 11.9 Hz, 2H).^{13}C NMR (151 MHz, CDCl$_3$) δ 166.8, 160.0, 136.2, 129.7, 118.7, 117.7, 112.5, 67.0, 55.6, 46.4, 33.3. LC-MS: t$_R$= 3.10 min, purity: >99%, M/z [M+H]$^+$: 236; HRMS calcd. For C$_{13}$H$_{17}$NO$_3$ [M+H]$^+$= 236.1281, found 236.1271.
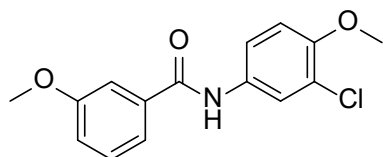
N-(3-Chloro-4-methoxyphenyl)-3-methoxybenzamide (**NPD-3004**)

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.86 (s, 1H), 7.68 (s, 1H), 7.50 (d, J = 8.8 Hz, 1H), 7.41 (s, 1H), 7.39 - 7.32 (m, 2H), 7.07 (s, 1H), 6.90 (d, J = 8.8 Hz, 1H), 3.89 (s, 3H), 3.85 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 165.5, 160.0, 152.1, 136.1, 131.4, 129.8, 122.8, 122.5, 120.0, 118.6, 118.1, 112.4, 112.2, 56.4, 55.5. LC-MS: t_R= 4.39 min, purity: >99%, M/z [M+H]$^+$: 292; HRMS calcd. For C$_{15}$H$_{14}$ClNO$_3$ [M+H]$^+$= 292.0735, found 292.0721.
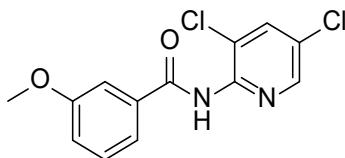
N-(3,5-Dichloropyridin-2-yl)-3-methoxybenzamide (**NPD-3005**)

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.38 (s, 2H), 7.79 (s, 1H), 7.49 (s, 1H), 7.45 (d, J = 7.5 Hz, 1H), 7.41 (t, J = 7.7 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 3.88 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.8, 160.2, 146.3, 145.7, 137.7, 135.3, 130.1, 128.2, 123.1, 119.3, 118.9, 113.0, 55.7. LC-MS: t_R= 4.06 min, purity: >99%, M/z [M+H]$^+$: 297; HRMS calcd. For C$_{13}$H$_{10}$Cl$_2$N$_2$O$_2$ [M+H]$^+$= 297.0192, found 297.0182.
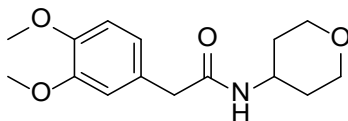
2-(3,4-Dimethoxyphenyl)-N-(tetrahydro-2H-pyran-4-yl)acetamide (**NPD-3006**)

^{1}H NMR (500 MHz, CDCl$_3$) δ 6.85 (d, J = 7.9 Hz, 1H), 6.80 - 6.75 (m, 2H), 5.29 (d, J = 7.4 Hz, 1H), 4.03 - 3.93 (m, 1H), 3.91 - 3.86 (m, 8H), 3.50 (s, 2H), 3.44 (app t, J = 11.6 Hz, 2H), 1.82 (app d, J = 12.7 Hz, 2H), 1.33 (app q, J = 11.7 Hz, 2H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 170.7, 149.4, 148.5, 127.3, 121.7, 112.5, 111.7, 66.8, 56.1, 56.1, 45.8, 43.6, 33.1. LC-MS: t_R= 2.78 min, purity: >99%, M/z [M+H]$^+$: 280; HRMS calcd. For C$_{15}$H$_{21}$NO$_4$ [M+H]$^+$= 280.1543, found 280.1531.
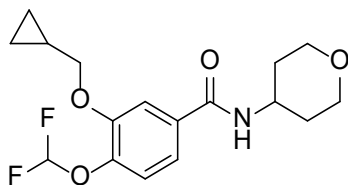
3-(Cyclopropylmethoxy)-4-(difluoromethoxy)-N-(tetrahydro-2H-pyran-4-yl)benzamide (**NPD-3007**)

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.46 (s, 1H), 7.23 − 7.14 (m, 2H), 6.69 (t, J = 75.1 Hz, 1H), 5.95 (d, J = 6.7 Hz, 1H), 4.24 − 4.12 (m, 1H), 4.00 (app d, J = 10.8 Hz, 2H), 3.93 (app d, J = 6.8 Hz, 2H), 3.53 (app t, J = 11.7 Hz, 2H), 2.00 (app d, J = 12.0 Hz, 2H), 1.65 - 1.54 (m, 2H), 1.36 - 1.22 (m, 1H), 0.66 (app d, J = 7.0 Hz, 2H), 0.36 (app s, 2H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 165.9, 150.8, 142.9 (t, J = 3.1 Hz), 122.3, 118.7, 115.9 (t, J = 261.1 Hz), 113.9, 74.3, 66.9, 46.6, 33.3, 10.2,

3.4. LC-MS: t_R= 4.15 min, purity: >99%, M/z [M+H]$^+$: 342; HRMS calcd. For $C_{17}H_{21}F_2NO_4$ [M+H]$^+$= 342.1511, found 342.1509.
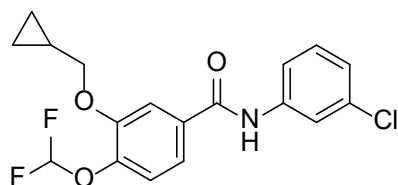
N-(3-Chlorophenyl)-3-(cyclopropylmethoxy)-4-(difluoromethoxy)benzamide (**NPD-3075**)

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.80 (s, 1H), 7.76 (app t, J = 2.0 Hz, 1H), 7.53 (d, J = 2.0 Hz, 1H), 7.49 - 7.45 (m, 1H), 7.34 - 7.27 (m, 2H), 7.24 (d, J = 8.2 Hz, 1H), 7.14 (ddd, J = 8.0, 1.9, 0.9 Hz, 1H), 6.72 (t, J = 74.9 Hz, 1H), 3.94 (d, J = 7.0 Hz, 2H), 1.35 - 1.27 (m, 1H), 0.69 - 0.65 (m, 2H), 0.39 - 0.35 (m, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.8, 151.0, 143.3, 138.9, 135.0, 132.9, 130.3, 124.9, 122.4, 120.4, 118.8, 118.2, 115.9 (t, J = 263.6 Hz), 113.9, 74.3, 10.1, 3.4. LC-MS: t_R= 5.18 min, purity: >99%, M/z [M+H]$^+$: 368; HRMS calcd. For $C_{18}H_{16}ClF_2NO_3$ [M+H]$^+$= 368.0860, found 368.0854.
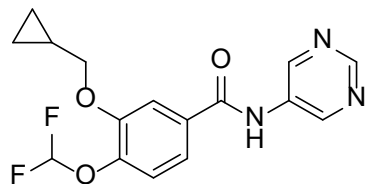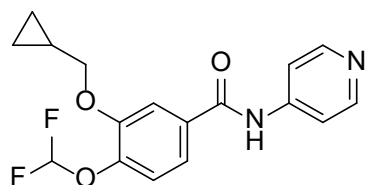

3-(Cyclopropylmethoxy)-4-(difluoromethoxy)-N-(pyridin-4-yl)benzamide (**NPD-3076**)

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.55 (d, J = 5.1 Hz, 2H), 8.14 (s, 1H), 7.61 (d, J = 5.1 Hz, 2H), 7.53 (s, 1H), 7.35 (d, J = 8.2 Hz, 1H), 7.24 (d, J = 8.2 Hz, 1H), 6.73 (t, J = 74.8 Hz, 1H), 3.94 (d, J = 6.9 Hz, 2H), 1.31 (m, 1H), 0.67 (app d, J = 7.3 Hz, 2H), 0.37 (app d, J = 4.4 Hz, 2H). ^{13}C NMR (151 MHz, DMSO-d_6) δ 165.3, 151.1, 150.9, 145.1, 143.1 (t, J = 3.1 Hz), 132.4, 122.3, 119.1, 115.8 (t, J = 264.7 Hz), 114.0, 114.0, 74.3, 10.1, 3.4. LC-MS: t_R= 3.54 min, purity: >99%, M/z [M+H]$^+$: 335; HRMS calcd. For $C_{17}H_{16}F_2N_2O_3$ [M+H]$^+$= 335.1202, found 335.1209.
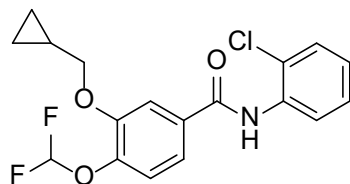
N-(2-Chlorophenyl)-3-(cyclopropylmethoxy)-4-(difluoromethoxy)benzamide (**NPD-3080**)

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.52 (dd, J = 8.3, 1.5 Hz, 1H), 8.40 (s, 1H), 7.59 (d, J = 2.0 Hz, 1H), 7.44 - 7.38 (m, 2H), 7.36 - 7.32 (m, 1H), 7.27 (d, J = 8.2 Hz, 1H), 7.10 (app td, J = 7.8, 1.5 Hz, 1H), 6.73 (app t, J = 74.9 Hz, 1H), 3.97 (d, J = 7.0 Hz, 2H), 1.37 - 1.29 (m, 1H), 0.71 - 0.65 (m, 2H), 0.42 - 0.36 (m, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.4, 151.0, 143.4, 134.6, 133.1, 129.2, 128.1, 125.1, 123.2, 122.5, 121.6, 118.9, 115.9 (t, J = 261.6 Hz), 114.0, 74.2, 10.2, 3.4. LC-MS: t_R=

5.08 min, purity: >99%, M/z [M+H]⁺: 368; HRMS calcd. For $C_{18}H_{16}ClF_2NO3$ [M+H]⁺= 368.0860, found 368.0851. Spectral data are in agreement with a previous report. [6]
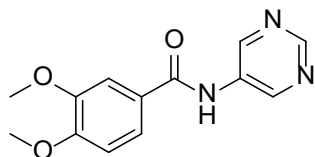
3,4-Dimethoxy-*N*-(pyrimidin-5-yl)benzamide (**NPD-3081**)

¹H NMR (500 MHz, CDCl₃) δ 9.11 (s, 2H), 9.00 (s, 1H), 8.01 (s, 1H), 7.50 (s, 1H), 7.44 (d, *J* = 8.3 Hz, 1H), 6.92 (d, *J* = 8.2 Hz, 1H), 3.95 (app s, 6H). ¹³C NMR (126 MHz, CDCl₃) δ 165.7, 154.3, 152.9, 149.5, 148.2, 133.8, 125.9, 120.0, 110.9, 110.5, 56.3, 56.3. LC-MS: t_R= 2.82 min, purity: 97%, M/z [M+H]⁺: 260; HRMS calcd. For $C_{13}H_{13}N_3O_3$ [M+H]⁺= 260.1030, found 260.1024.
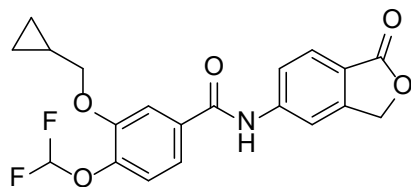
3-(Cyclopropylmethoxy)-4-(difluoromethoxy)-*N*-(1-oxo-1,3-dihydroisobenzofuran-5-yl)benzamide (**NPD-3083**)

¹H NMR (500 MHz, CDCl₃) δ 8.23 (s, 2H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.55 (s, 1H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.29 - 7.24 (m, 1H), 6.73 (t, *J* = 74.8 Hz, 1H), 5.32 (s, 2H), 3.96 (d, *J* = 6.9 Hz, 2H), 1.32 (m, 1H), 0.68 (app q, *J* = 5.4 Hz, 2H), 0.38 (app q, *J* = 4.8 Hz, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 170.7, 165.0, 150.9, 148.6, 143.4 (t, *J* = 3.1 Hz), 143.2, 132.4, 126.7, 122.3, 121.3, 120.6, 119.0, 115.7 (t, *J* = 261.1 Hz), 113.8, 112.7, 74.2, 69.6, 10.0, 3.3. LC-MS: t_R= 4.55 min, purity: 98%, M/z [M+H]⁺: 390; HRMS calcd. For $C_{20}H_{17}F_2NO_5$ [M+H]⁺= 390.1148, found 390.1140.
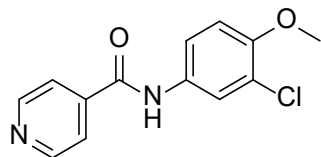
***N*-(3-chloro-4-methoxyphenyl)isonicotinamide** (**NPD-3085**)

¹H NMR (500 MHz, CDCl₃) δ 8.80 (d, *J* = 3.5 Hz, 2H), 7.83 (s, 1H), 7.70 (app s, 3H), 7.52 (d, *J* = 8.6 Hz, 1H), 6.94 (d, *J* = 8.7 Hz, 1H), 3.92 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 163.7, 152.7, 151.0, 141.8, 130.7, 123.1, 122.9, 120.9, 120.3, 112.3, 56.5. LC-MS: t_R= 3.33 min, purity: >99%, M/z [M+H]⁺: 263; HRMS calcd. For $C_{13}H_{11}ClN_2O_2$ [M+H]⁺= 263.0582, found 263.0586.
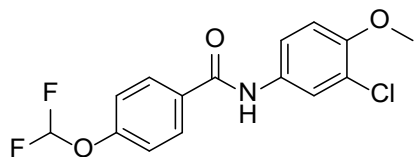
N-(3-Chloro-4-methoxyphenyl)-4-(difluoromethoxy)benzamide (NPD-3086)

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.87 (d, J = 7.7 Hz, 2H), 7.76 (s, 1H), 7.67 (s, 1H), 7.49 (d, J = 8.8 Hz, 1H), 7.20 (d, J = 7.8 Hz, 2H), 6.91 (d, J = 8.8 Hz, 1H), 6.59 (t, J = 73.1 Hz, 1H), 3.90 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.6, 153.8 (t, J = 2.7 Hz), 152.2, 131.5, 131.2, 129.0, 123.0, 122.6, 120.2, 119.3, 115.4 (t, J = 261.5 Hz), 112.2, 56.4. LC-MS: t_R= 4.57 min, purity: >99%, M/z [M+H]$^+$: 328; HRMS calcd. For C$_{15}$H$_{12}$ClF$_2$NO$_3$ [M+H]$^+$= 328.0547, found 328.0540.
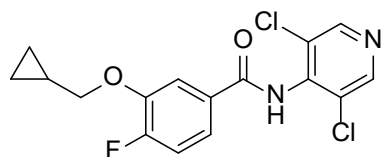
3-(Cyclopropylmethoxy)-N-(3,5-dichloropyridin-4-yl)-4-fluorobenzamide (NPD-3093)

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.57 (s, 2H), 7.68 (s, 1H), 7.59 (dd, J = 8.0, 2.1 Hz, 1H), 7.46 (ddd, J = 8.3, 4.0, 2.2 Hz, 1H), 7.20 (dd, J = 10.5, 8.4 Hz, 1H), 3.96 (d, J = 7.0 Hz, 2H), 1.38 - 1.29 (m, 1H), 0.71 - 0.65 (m, 2H), 0.38 (app q, J = 4.8 Hz, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 163.8, 155.8 (d, J = 254.3 Hz), 148.5, 147.9 (d, J = 10.9 Hz), 139.9, 129.2 (d, J = 3.2 Hz), 128.9, 120.3 (d, J = 8.2 Hz), 116.5 (d, J = 19.5 Hz), 115.2 (d, J = 3.2 Hz), 74.6, 10.2, 3.5. LC-MS: t_R= 4.52 min, purity: 96%, M/z [M+H]$^+$: 355; HRMS calcd. For C$_{16}$H$_{13}$Cl$_2$FN$_2$O$_2$ [M+H]$^+$= 355.0411, found 355.0398.
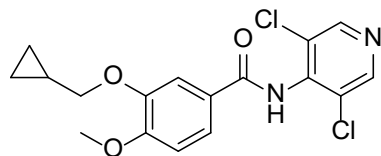
3-(Cyclopropylmethoxy)-N-(3,5-dichloropyridin-4-yl)-4-methoxybenzamide (NPD-3094)

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.57 (s, 2H), 7.73 - 7.48 (m, 3H), 6.97 (d, J = 7.9 Hz, 1H), 4.05 - 3.85 (m, 5H), 1.45 - 1.33 (m, 1H), 0.69 (app d, J = 7.2 Hz, 2H), 0.47 - 0.31 (m, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 164.3, 153.6, 148.9, 148.4, 140.3, 128.7, 125.1, 121.0, 112.9, 110.8, 74.3, 56.3, 10.3, 3.6. LC-MS: t_R= 4.17 min, purity: 98%, M/z [M+H]$^+$: 367; HRMS calcd. For C$_{17}$H$_{16}$Cl$_2$N$_2$O$_3$ [M+H]$^+$= 367.0611, found 367.0593.
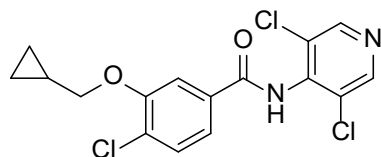
4-Chloro-3-(cyclopropylmethoxy)-N-(3,5-dichloropyridin-4-yl)benzamide (NPD-3096)

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.58 (s, 2H), 7.69 (s, 1H), 7.56 - 7.48 (m, 2H), 7.40 (dd, *J* = 8.1, 1.6 Hz, 1H), 3.98 (d, *J* = 6.8 Hz, 2H), 1.39 - 1.30 (m, 1H), 0.68 (app q, *J* = 5.5 Hz, 2H), 0.41 (app q, *J* = 5.1 Hz, 2H). ^{13}C NMR (126 MHz, CDCl$_3$) δ 163.9, 155.3, 148.5, 139.8, 132.3, 130.7, 129.0, 128.6, 119.7,113.3, 74.3, 10.1, 3.5. LC-MS: t_R= 4.81 min, purity: >99%, M/z [M+H]$^+$: 371; HRMS calcd. For C$_{16}$H$_{13}$Cl$_3$N$_2$O$_2$ [M+H]$^+$= 371.0115, found 371.0101.
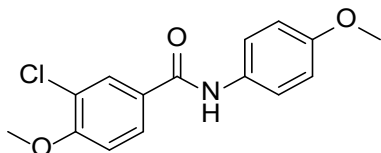
3-Chloro-4-methoxy-*N*-(4-methoxyphenyl)benzamide (**NPD-3286**)

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.89 (d, *J* = 2.1 Hz, 1H), 7.78 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.63 (s, 1H), 7.51 (d, *J* = 8.7 Hz, 2H), 6.99 (d, *J* = 8.5 Hz, 1H), 6.91 (d, *J* = 8.9 Hz, 2H), 3.97 (s, 3H), 3.82 (s, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 164.0, 157.7, 156.7, 130.8, 129.1, 128.0, 127.2, 122.8, 122.2, 114.3, 111.6, 56.4, 55.5. LC-MS: t_R= 4.25 min, purity: >99%, M/z [M+H]$^+$: 292; HRMS calcd. For C$_{15}$H$_{14}$ClNO$_3$ [M+H]$^+$= 292.0735, found 292.0729.
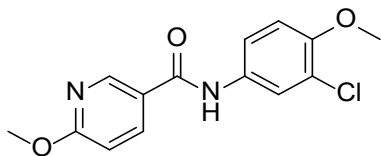
***N*-(3-Chloro-4-methoxyphenyl)-6-methoxynicotinamide** (**NPD-3287**)

^{1}H NMR (600 MHz, CDCl$_3$) δ 8.70 (s, 1H), 8.09 (d, *J* = 8.3 Hz, 1H), 7.70 (s, 1H), 7.64 (s, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 6.95 (d, *J* = 8.7 Hz, 1H), 6.86 (d, *J* = 8.5 Hz, 1H), 4.03 (s, 3H), 3.93 (s, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 166.4, 163.9, 152.4, 146.5, 138.0, 131.3, 123.9, 123.2, 122.8, 120.3, 112.4, 111.3, 56.6, 54.3. LC-MS: t_R= 4.06 min, purity: 99%, M/z [M+H]$^+$: 293; HRMS calcd. For C$_{14}$H$_{13}$ClN$_2$O$_3$ [M+H]$^+$= 293.0687, found 293.0676.
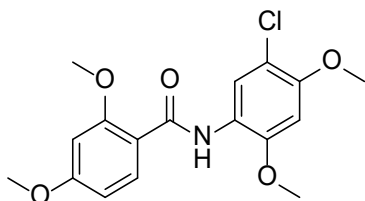
***N*-(5-Chloro-2,4-dimethoxyphenyl)-2,4-dimethoxybenzamide** (**NPD-3288**)

^{1}H NMR (300 MHz, CDCl$_3$) δ 9.87 (s, 1H), 7.98 (d, *J* = 9.0 Hz, 1H), 7.72 (d, *J* = 2.5 Hz, 1H), 7.58 (dd, *J* = 8.9, 2.5 Hz, 1H), 6.92 (d, *J* = 8.9 Hz, 1H), 6.83 (d, *J* = 9.0 Hz, 1H), 4.07 (s, 3H), 3.93 (s, 3H), 3.92 - 3.88 (m, 6H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 162.8, 157.0, 152.3, 151.8, 141.9, 132.4, 127.1, 122.7, 122.6, 119.8, 118.8, 112.5, 108.0, 62.1, 61.2, 56.6, 56.3. LC-MS: t_R= 4.61 min, purity: >99%, M/z [M+H]$^+$: 352; HRMS calcd. For C$_{17}$H$_{18}$ClNO$_5$ [M+H]$^+$= 352.0946, found 352.0945.
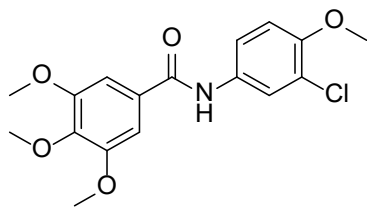
N-(3-Chloro-4-methoxyphenyl)-3,4,5-trimethoxybenzamide (**NPD-3289**)

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.68 (s, 1H), 7.66 (d, *J* = 2.5 Hz, 1H), 7.53 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.06 (s, 2H), 6.93 (d, *J* = 8.9 Hz, 1H), 3.92 (app s, 6H), 3.91 (s, 3H), 3.90 (s, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 165.5, 153.5, 152.3, 141.5, 131.5, 130.2, 123.0, 122.8, 120.2, 112.4, 104.6, 61.1, 56.6. Note: Carbon signals of the two non-equivalent methoxy groups overlap. LC-MS: t$_R$= 4.23 min, purity: >99%, M/z [M+H]$^+$: 352; HRMS calcd. For C$_{17}$H$_{18}$ClNO$_5$ [M+H]$^+$= 352.0946, found 352.0940.
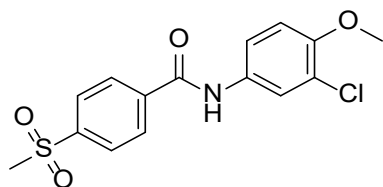
N-(3-Chloro-4-methoxyphenyl)-4-(methylsulfonyl)benzamide (**NPD-3290**)

^{1}H NMR (300 MHz, CDCl$_3$ + DMSO-*d$_6$*) δ 10.16 (s, 1H), 8.14 (d, *J* = 8.4 Hz, 2H), 7.96 (d, *J* = 8.4 Hz, 2H), 7.83 (d, *J* = 2.4 Hz, 1H), 7.62 - 7.57 (m, 1H), 6.89 (d, *J* = 8.9 Hz, 1H), 3.82 (s, 3H), 3.07 (s, 3H). ^{13}C NMR (151 MHz, CDCl$_3$ + DMSO-*d$_6$*) δ 163.2, 150.6, 142.0, 138.8, 131.4, 127.9, 126.3, 122.0, 120.7, 119.5, 111.2, 55.3, 43.3. LC-MS: t$_R$= 3.83 min, purity: 97%, M/z [M+H]$^+$: 340; HRMS calcd. For C$_{15}$H$_{14}$ClNO$_4$S [M+H]$^+$= 340.0405, found 340.0400.
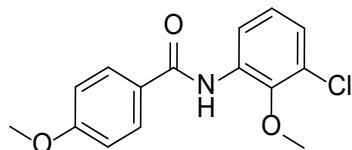
N-(3-Chloro-2-methoxyphenyl)-4-methoxybenzamide (**NPD-3291**)

^{1}H NMR (300 MHz, CDCl$_3$) δ 8.48 (s, 1H), 8.43 (dd, *J* = 5.8, 4.0 Hz, 1H), 7.86 (d, *J* = 8.8 Hz, 2H), 7.11 (s, 1H), 7.10 (d, *J* = 1.9 Hz, 1H), 7.01 (d, *J* = 8.8 Hz, 2H), 3.95 (s, 3H), 3.89 (s, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 165.0, 162.9, 145.2, 133.5, 129.1, 127.0, 126.9, 125.5, 125.0, 119.0, 114.3, 61.1, 55.7. LC-MS: t$_R$= 4.65 min, purity: >99%, M/z [M+H]$^+$: 292; HRMS calcd. For C$_{15}$H$_{14}$ClNO$_3$ [M+H]$^+$= 292.0735, found 292.0726.
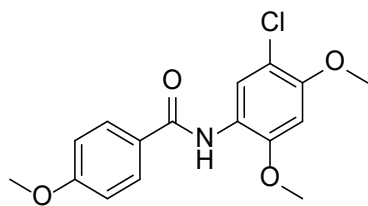
N-(5-Chloro-2,4-dimethoxyphenyl)-4-methoxybenzamide (NPD-3292)

^{1}H NMR (300 MHz, CDCl$_3$) δ 8.60 (s, 1H), 8.25 (s, 1H), 7.86 (d, J = 8.8 Hz, 2H), 7.01 (d, J = 8.8 Hz, 2H), 6.58 (s, 1H), 3.97 (s, 3H), 3.93 (s, 3H), 3.90 (s, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 164.6, 162.6, 151.4, 147.9, 129.0, 127.4, 122.0, 121.7, 114.14, 114.11, 96.8, 56.9, 56.4, 55.6. LC-MS: t$_R$= 4.46 min, purity: >99%, M/z [M+H]$^+$: 322; HRMS calcd. For C$_{16}$H$_{16}$ClNO$_4$ [M+H]$^+$= 322.0841, found 322.0840.
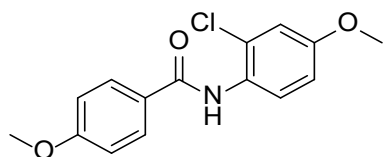
N-(2-Chloro-4-methoxyphenyl)-4-methoxybenzamide (NPD-3293)

^{1}H NMR (300 MHz, CDCl$_3$) δ 8.38 (d, J = 9.1 Hz, 1H), 8.14 (s, 1H), 7.88 (d, J = 8.8 Hz, 2H), 7.04 - 6.94 (m, 3H), 6.88 (dd, J = 9.1, 2.8 Hz, 1H), 3.88 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 164.8, 162.8, 156.3, 129.1, 128.4, 127.1, 124.3, 123.0, 114.7, 114.2, 113.4, 55.9, 55.6. LC-MS: t$_R$= 4.26 min, purity: >99%, M/z [M+H]$^+$: 292; HRMS calcd. For C$_{15}$H$_{14}$ClNO$_3$ [M+H]$^+$= 292.0735, found 292.0728.
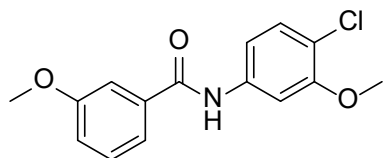
N-(4-Chloro-3-methoxyphenyl)-3-methoxybenzamide (NPD-3294)

^{1}H NMR (300 MHz, CDCl$_3$) δ 7.81 (s, 1H), 7.72 (d, J = 2.2 Hz, 1H), 7.43 (s, 1H), 7.39 (app d, J = 7.2 Hz, 2H), 7.32 (d, J = 8.5 Hz, 1H), 7.10 (m, 1H), 6.90 (dd, J = 8.5, 2.3 Hz, 1H), 3.95 (s, 3H), 3.88 (s, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 165.7, 160.2, 155.5, 137.9, 136.2, 130.2, 130.0, 118.7, 118.4, 117.9, 112.6, 112.3, 104.7, 56.4, 55.7. LC-MS: t$_R$= 4.46 min, purity: >99%, M/z [M+H]$^+$: 292; HRMS calcd. For C$_{15}$H$_{14}$ClNO$_3$ [M+H]$^+$= 292.0735, found 292.0725.
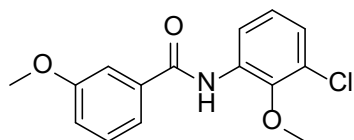
N-(3-Chloro-2-methoxyphenyl)-3-methoxybenzamide (NPD-3295)

^{1}H NMR (300 MHz, CDCl$_3$) δ 8.38 (d, J = 9.1 Hz, 1H), 8.21 (s, 1H), 7.51 - 7.45 (m, 1H), 7.42 (app d, J = 6.6 Hz, 2H), 7.10 (m, 1H), 6.98 (d, J = 2.8 Hz, 1H), 6.89 (dd, J = 9.1, 2.8 Hz, 1H), 3.89 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 165.2, 160.2, 156.5, 136.4, 130.0, 128.2, 124.4, 123.1, 118.8, 118.3, 114.7, 113.5, 112.7, 55.9, 55.6. LC-MS: t_R= 4.33 min, purity: >99%, M/z [M+H]$^+$: 292; HRMS calcd. For C$_{15}$H$_{14}$ClNO$_3$ [M+H]$^+$= 292.0735, found 292.0732.
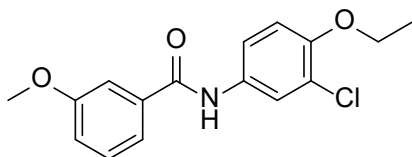
N-(3-Chloro-4-ethoxyphenyl)-3-methoxybenzamide (NPD-3296)

^{1}H NMR (300 MHz, CDCl$_3$) δ 7.71 (s, 1H), 7.68 (d, J = 2.6 Hz, 1H), 7.49 (dd, J = 8.9, 2.6 Hz, 1H), 7.44 - 7.40 (m, 1H), 7.40 - 7.33 (m, 2H), 7.08 (m, 1H), 6.92 (d, J = 8.9 Hz, 1H), 4.11 (q, J = 7.0 Hz, 2H), 3.87 (s, 3H), 1.47 (t, J = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 165.6, 160.1, 151.7, 136.3, 131.5, 129.9, 123.3, 122.9, 120.1, 118.7, 118.2, 113.9, 112.6, 65.3, 55.6, 14.9. LC-MS: t_R= 4.61 min, purity: >99%, M/z [M+H]$^+$: 306; HRMS calcd. For C$_{16}$H$_{16}$ClNO$_3$ [M+H]$^+$= 306.0891, found 306.0881.
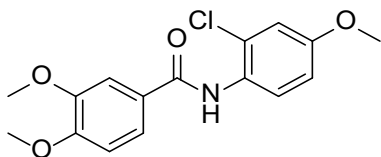
N-(2-Chloro-4-methoxyphenyl)-3,4-dimethoxybenzamide (NPD-3297)

^{1}H NMR (300 MHz, CDCl$_3$) δ 8.59 (s, 1H), 8.29 (s, 1H), 7.45 (s, 1H), 7.42 - 7.34 (m, 2H), 7.15 - 7.02 (m, 1H), 6.56 (s, 1H), 3.94 (s, 3H), 3.91 (s, 3H), 3.88 (s, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 164.9, 160.1, 151.6, 148.0, 136.6, 129.9, 121.8, 121.7, 118.8, 118.0, 114.1, 112.7, 96.7, 56.9, 56.4, 55.6. LC-MS: t_R= 4.53 min, purity: >99%, M/z [M+H]$^+$: 322; HRMS calcd. For C$_{16}$H$_{16}$ClNO$_4$ [M+H]$^+$= 322.0841, found 322.0835.
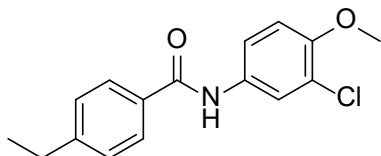
N-(3-Chloro-4-methoxyphenyl)-4-ethylbenzamide (NPD-3298)

^{1}H NMR (300 MHz, CDCl$_3$) δ 7.77 (d, J = 8.1 Hz, 2H), 7.69 (d, J = 2.4 Hz, 2H), 7.52 (dd, J = 8.9, 2.5 Hz, 1H), 7.31 (d, J = 8.1 Hz, 2H), 6.92 (d, J = 8.9 Hz, 1H), 3.90 (s, 3H), 2.72 (q, J = 7.6 Hz, 2H), 1.27 (t, J = 7.6 Hz, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 165.7, 152.2, 148.9, 132.1, 131.7, 128.4, 127.2, 122.9, 122.7, 120.1, 112.4, 56.6, 29.0, 15.4. LC-MS: t_R= 4.74 min, purity: >99%, M/z [M+H]$^+$: 290; HRMS calcd. For C$_{16}$H$_{16}$ClNO$_2$ [M+H]$^+$= 290.0942, found 290.0933.
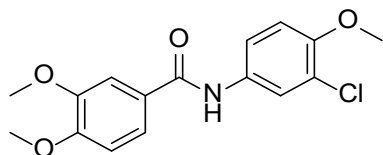
N-(3-Chloro-4-methoxyphenyl)-3,4-dimethoxybenzamide (NPD-3299)

^{1}H NMR (600 MHz, CDCl$_3$) δ 7.70 (s, 1H), 7.67 (d, J = 2.5 Hz, 1H), 7.52 (dd, J = 8.8, 2.5 Hz, 1H), 7.48 (d, J = 1.8 Hz, 1H), 7.37 (dd, J = 8.3, 1.8 Hz, 1H), 6.94 - 6.89 (m, 2H), 3.95 (s, 6H), 3.90 (s, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 165.3, 152.3, 152.1, 149.4, 131.7, 127.3, 123.0, 122.7, 120.1, 119.5, 112.4, 110.8, 110.5, 56.6, 56.2. Note: Two methoxy group carbon signals overlap. LC-MS: t_R= 4.07 min, purity: >99%, M/z [M+H]$^+$: 322; HRMS calcd. For C$_{16}$H$_{16}$ClNO$_4$ [M+H]$^+$= 322.0841, found 322.0841.
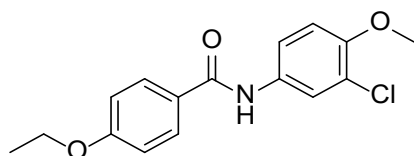
N-(3-Chloro-4-methoxyphenyl)-4-ethoxybenzamide (NPD-3300)

^{1}H NMR (300 MHz, CDCl$_3$) δ 7.81 (d, J = 8.8 Hz, 2H), 7.70 - 7.63 (m, 2H), 7.50 (dd, J = 8.9, 2.5 Hz, 1H), 6.98 - 6.89 (m, 3H), 4.10 (q, J = 7.0 Hz, 2H), 3.90 (s, 3H), 1.45 (t, J = 7.0 Hz, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 165.3, 162.1, 152.1, 131.8, 129.0, 126.7, 122.9, 122.7, 120.1, 114.6, 112.4, 63.9, 56.6, 14.8. LC-MS: t_R= 4.52 min, purity: >99%, M/z [M+H]$^+$: 306; HRMS calcd. For C$_{16}$H$_{16}$ClNO$_3$ [M+H]$^+$= 306.0891, found 306.0884.
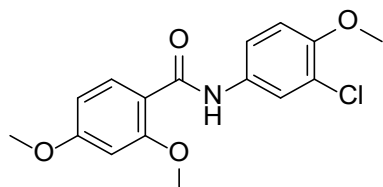
N-(3-Chloro-4-methoxyphenyl)-2,4-dimethoxybenzamide (NPD-3301)

^{1}H NMR (300 MHz, CDCl$_3$) δ 9.59 (s, 1H), 8.24 (d, J = 8.8 Hz, 1H), 7.67 (d, J = 2.5 Hz, 1H), 7.60 (d, J = 2.4 Hz, 1H), 6.91 (d, J = 2.4 Hz 1H), 6.65 (dd, J = 8.8, 2.3 Hz, 1H), 6.53 (d, J = 2.1 Hz, 1H), 4.03 (s, 3H), 3.90 (s, 3H), 3.88 (s, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 164.0, 163.2, 158.7, 151.7, 134.4, 132.4, 122.9, 122.5, 120.1, 114.6, 112.4, 105.9, 98.9, 56.6, 56.4, 55.8. LC-MS: t_R= 4.59 min, purity: >99%, M/z [M+H]$^+$: 322; HRMS calcd. For C$_{16}$H$_{16}$ClNO$_4$ [M+H]$^+$= 322.0841, found 322.0838.
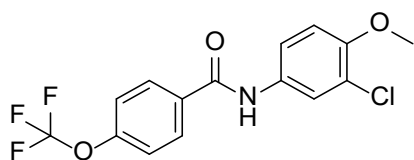
N-(3-Chloro-4-methoxyphenyl)-4-(trifluoromethoxy)benzamide (**NPD-3302**)

^{1}H NMR (300 MHz, CDCl$_3$) δ 7.89 (d, J = 8.7 Hz, 2H), 7.74 (s, 1H), 7.67 (d, J = 2.4 Hz, 1H), 7.49 (dd, J = 8.8, 2.4 Hz, 1H), 7.31 (d, J = 8.4 Hz, 2H), 6.92 (d, J = 8.9 Hz, 1H), 3.90 (s, 3H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 164.3, 152.4, 151.8, 133.1, 131.1, 128.9, 123.0, 122.7, 120.9, 120.1, 119.5 (q, J = 260.4 Hz), 112.3, 56.4. LC-MS: t_R= 4.86 min, purity: >99%, M/z [M+H]$^+$: 346; HRMS calcd. For C$_{15}$H$_{11}$ClF$_3$NO$_3$ [M+H]$^+$= 346.0452, found 346.0456.
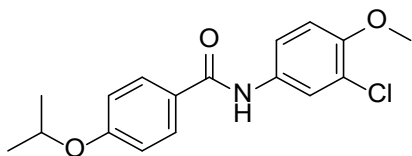
N-(3-Chloro-4-methoxyphenyl)-4-isopropoxybenzamide (**NPD-3303**)

^{1}H NMR (300 MHz, CDCl$_3$) δ 7.80 (d, J = 8.8 Hz, 2H), 7.68 (d, J = 2.5 Hz, 1H), 7.63 (s, 1H), 7.50 (dd, J = 8.8, 2.5 Hz, 1H), 6.98 - 6.89 (m, 3H), 4.64 (hept, J = 6.1 Hz, 1H), 3.90 (s, 3H), 1.37 (d, J = 6.1 Hz, 6H). ^{13}C NMR (151 MHz, CDCl$_3$) δ 165.3, 161.2, 152.1, 131.8, 129.0, 126.4, 122.9, 122.7, 120.1, 115.6, 112.4, 70.3, 56.6, 22.1. LC-MS: t_R= 4.72 min, purity: >99%, M/z [M+H]$^+$: 320; HRMS calcd. For C$_{17}$H$_{18}$ClNO$_3$ [M+H]$^+$= 320.1048, found 320.1036.
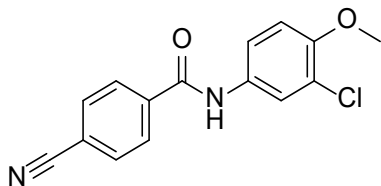
N-(3-Chloro-4-methoxyphenyl)-4-cyanobenzamide (**NPD-3304**)

^{1}H NMR (300 MHz, CDCl$_3$) δ 7.96 (d, J = 8.3 Hz, 2H), 7.79 (d, J = 8.4 Hz, 2H), 7.75 (s, 1H), 7.68 (d, J = 2.3 Hz, 1H), 7.50 (dd, J = 8.8, 2.2 Hz, 1H), 6.94 (d, J = 8.9 Hz, 1H), 3.91 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 163.9, 151.1, 138.7, 132.5, 132.4, 128.5, 122.0, 120.5, 120.3, 118.4, 113.9, 112.8, 56.2. LC-MS: t_R= 4.20 min, purity: >99%, M/z [M+H]$^+$: 287; HRMS calcd. For C$_{15}$H$_{11}$ClN$_2$O$_2$ [M+H]$^+$= 287.0582, found 287.0570.

Table S1. Overview of the PDE4NPD toolbox and inhibitor selectivity for human (h) or parasite PDEs

Tool	Compound ID	Name	PDE selectivity	Literature
NPD-0013	VUF14752	IBMX	non-selective	[7]
NPD-0014	VUF14753	Caffeine	non-selective	[8]
NPD-0015	VUF14754	Dipyradamole	non-selective	[9]
NPD-0009	VUF14748	Vinpocetine	hPDE1	[10]
NPD-0031	VUF14680		hPDE1	[11]
NPD-0017	VUF14759	BAY 60-7550	hPDE2	[12]
NPD-0010	VUF14749	Trequinsin	hPDE3	[13]
NPD-0011	VUF14750	Amrinone	hPDE3	[14]
NPD-0018	VUF14760	Milrinone	hPDE3	[12]
NPD-0027	VUF14810	Cilostamide	hPDE3	[15]
NPD-0005	VUF14664	piclamilast	hPDE4	[16]
NPD-0006	VUF14665	roflumilast	hPDE4	[12]
NPD-0007	VUF14672		hPDE4	[17]
NPD-0034	VUF14910	etazolate	hPDE4	[18]
NPD-0072	VUF14761	Rolipram	hPDE4	[12]
NPD-0029	VUF14834		hPDE4/7	[19]
NPD-0001	VUF14656	PPS54019	hPDE4/TbrPDEB1	[20]
NPD-0340	VUF13524		hPDE4/TbrPDEB1	[21]
NPD-0339	VUF11842		hPDE4/TbrPDEB1	[12]
NPD-0002	VUF14661		hPDE5	[22]
NPD-0003	VUF14662	Sildenafil	hPDE5	[12]
NPD-0004	VUF14789		hPDE5	[23]
NPD-0022	VUF14786	Tadalafil	hPDE5	[12]
NPD-0030	VUF14837	Vardenafil	hPDE5	[12]
NPD-0025	VUF14808	Zaprinast	hPDE5/PDE6	[24]
NPD-0020	VUF14782	BRL-50481	hPDE7	[25]
NPD-0078	MR 1.51		hPDE7	[26]
NPD-0082	AGF2.20		hPDE7	[27]
NPD-1091	WP5.11b		hPDE8	[28]
NPD-1092	WP5.19R		hPDE8	[28]
NPD-1100	VSP2.34		hPDE8	[28]
NPD-0012	VUF14751	BAY73-6691	hPDE9	[12]
NPD-0019	VUF14763	BIPPO	PfPDEalpha	[29]
NPD-0024	VUF14792		PfPDEalpha	[29]
NPD-0008	VUF14680	PPS58083	TbrPDEB1	[30]
NPD-0016	VUF14755	Papaverine	hPDE10	[12]
NPD-0026	VUF14809	TC-E 5005	hPDE10	[31]

NPD-0028   VUF14811   PF-2545920   hPDE11   [32]

Table S2. SmPDE4A inhibition of roflumilast analogues

Comp	SmPDE4A pK_i[a] or inhibition at 10 µM	Comp	SmPDE4A pK_i[a] or inhibition at 10 µM	Comp	SmPDE4A pK_i[a] or inhibition at 10 µM
NPD-1177	44%	NPD-1201	1%	NPD-3083	3%
NPD-1178	48%	NPD-1202	0%	NPD-3085	1%
NPD-1179	50%	NPD-1203	10%	NPD-3086	41%
NPD-1181	22%	NPD-1206	14%	NPD-3093	5.6 ± 0.0[a]
NPD-1182	22%	NPD-1472	5%	NPD-3286	7%
NPD-1183	15%	NPD-2976	46%	NPD-3287	20%
NPD-1184	22%	NPD-2981	6.4 ± 0.1	NPD-3288	0%
NPD-1185	18%	NPD-2991	5.2 ± 0.2[a]	NPD-3289	0%
NPD-1186	19%	NPD-2992	4%	NPD-3290	0%
NPD-1187	20%	NPD-2993	24%	NPD-3291	0%
NPD-1188	13%	NPD-2994	7%	NPD-3292	0%
NPD-1189	8%	NPD-2995	3%	NPD-3293	2%
NPD-1190	9%	NPD-2996	21%	NPD-3294	0%
NPD-1191	8%	NPD-2997	27%	NPD-3295	8%
NPD-1192	6%	NPD-2998	11%	NPD-3296	6%
NPD-1193	7%	NPD-2999	26%	NPD-3297	0%
NPD-1194	0%	NPD-3001	15%	NPD-3298	6.1 ± 0.0[a]
NPD-1195	0%	NPD-3002	21%	NPD-3299	0%
NPD-1196	1%	NPD-3003	4%	NPD-3300	5.8 ± 0.0[a]
NPD-1197	10%	NPD-3004	5.0 ± 0.0[a]	NPD-3301	16%
NPD-1198	6%	NPD-3005	18%	NPD-3302	42%
NPD-1199	28%	NPD-3006	16%	NPD-3303	27%
NPD-1200	0%	NPD-3007	34%	NPD-3304	18%

[a] Partial curve
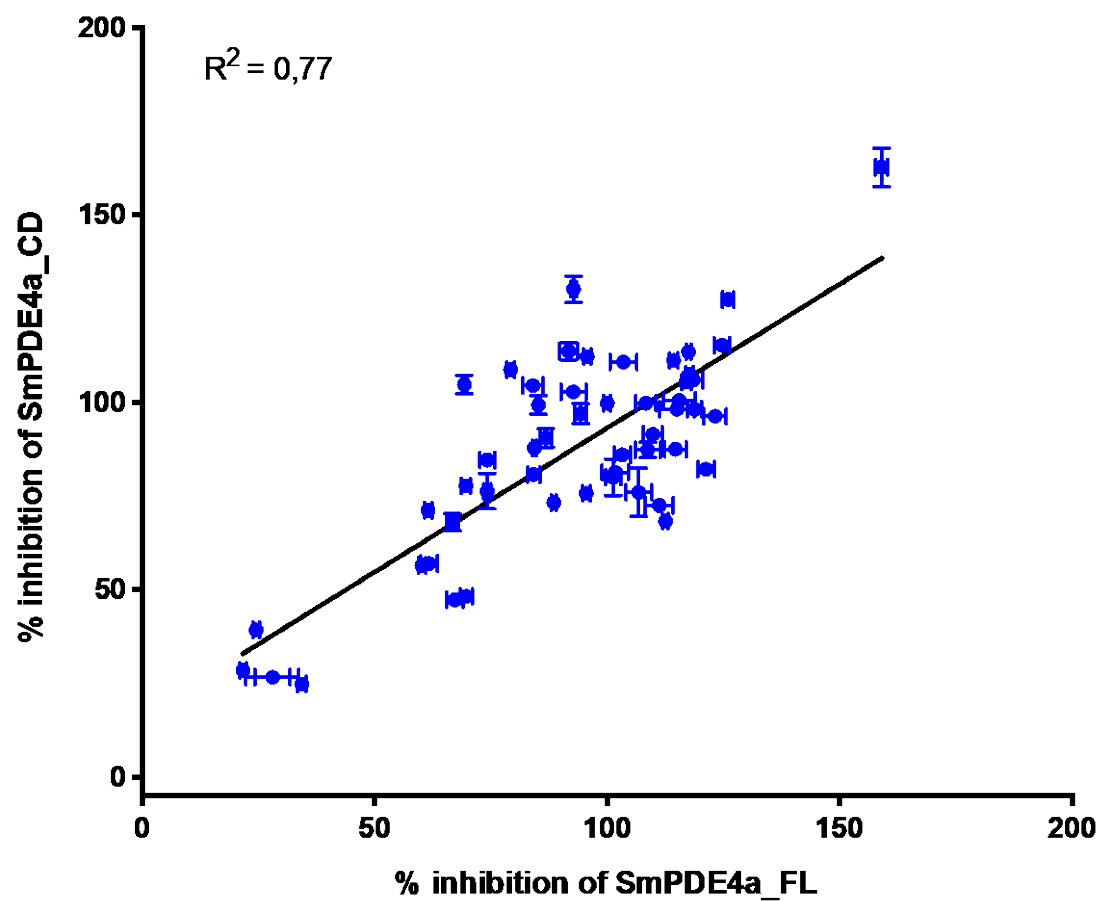
Fig S1. Correlation plot of the inhibition of the PDE Toolbox compounds of the enzymatic activities of purified SmPDE4A_CD (catalytic domain) and SmPDE4A_FL (full length).
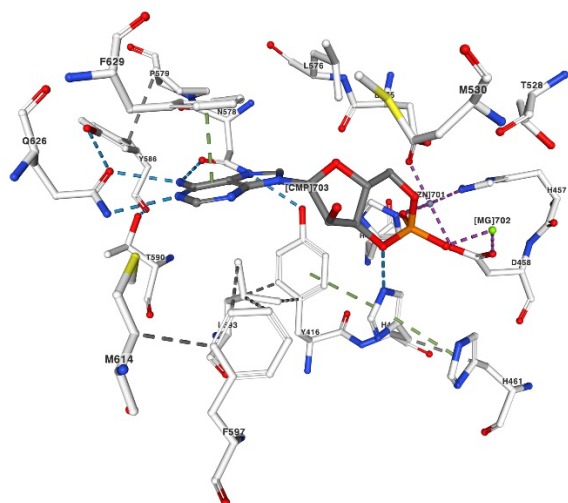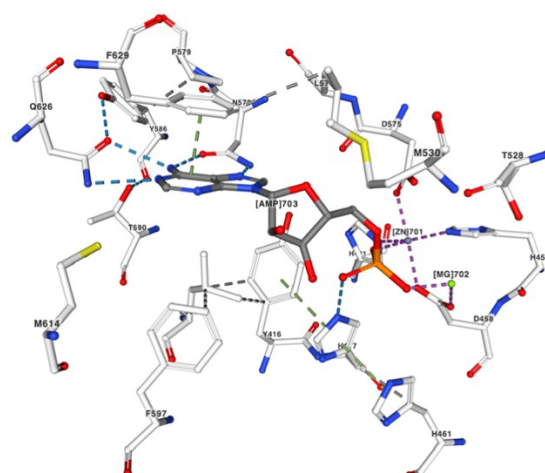
Fig S2. Binding of the substrate cAMP (A) and its hydrolyzed product AMP (B) in the binding pockets of SmPDE4A_CD, as observed in the chain A and chain B of the X-ray structure 6FG5. Binding pocket residues are visualized with NGL Viewer [33] implemented at the RCSB PDB website.

Crystallographic data

The coordinates of the 2 obtained x-ray structures of SmPDE4A_CD can be obtained from the Protein Data Bank with the IDs 6FG5 (apo structure) and 6EZU (co-crystal with cAMP and AMP). Full validation reports for both structures can be found at https://files.rcsb.org/pub/pdb/validation_reports/fg/6fg5/6fg5_full_validation.pdf for 6FG5 and at https://files.rcsb.org/pub/pdb/validation_reports/ez/6ezu/6ezu_full_validation.pdf for 6EZU. For both structures the data and refinement statistics are reported in the tables below.

6FG5:

Property	Value	Source
Space group	P 31 2 1	Depositor
Cell constants a, b, c, α, β, γ	81.80Å 81.80Å 256.13Å 90.00° 90.00° 120.00°	Depositor
Resolution (Å)	47.50 – 2.35 47.50 – 2.35	Depositor EDS
% Data completeness (in resolution range)	100.0 (47.50-2.35) 96.1 (47.50-2.35)	Depositor EDS
R_{merge}	0.07	Depositor
R_{sym}	(Not available)	Depositor
$< I/\sigma(I) >$ [1]	1.67 (at 2.34Å)	Xtriage
Refinement program	REFMAC 5.8.0189	Depositor
R, R_{free}	0.203 , 0.245 0.205 , (Not available)	Depositor DCC
R_{free} test set	No test flags present.	wwPDB-VP
Wilson B-factor (Å²)	50.1	Xtriage
Anisotropy	0.236	Xtriage
Bulk solvent k_{sol}(e/Å³), B_{sol}(Å²)	0.31 , 26.2	EDS
L-test for twinning [2]	$< \|L\| > = 0.49, < L^2 > = 0.33$	Xtriage
Estimated twinning fraction	0.026 for -h,-k,l	Xtriage
F_o,F_c correlation	0.95	EDS
Total number of atoms	5411	wwPDB-VP
Average B, all atoms (Å²)	57.0	wwPDB-VP

6EZU:

Property	Value	Source
Space group	P 31 2 1	Depositor
Cell constants a, b, c, α, β, γ	81.55Å 81.55Å 255.87Å 90.00° 90.00° 120.00°	Depositor
Resolution (Å)	85.44 – 2.04 47.41 – 2.04	Depositor EDS
% Data completeness (in resolution range)	99.9 (85.44-2.04) 100.0 (47.41-2.04)	Depositor EDS
R_{merge}	0.07	Depositor
R_{sym}	(Not available)	Depositor
$< I/\sigma(I) >$ [1]	1.84 (at 2.05Å)	Xtriage
Refinement program	REFMAC 5.8.0189	Depositor
R, R_{free}	0.199 , 0.233 0.205 , 0.236	Depositor DCC
R_{free} test set	3042 reflections (4.76%)	wwPDB-VP
Wilson B-factor (Å^2)	49.4	Xtriage
Anisotropy	0.254	Xtriage
Bulk solvent k_{sol}(e/Å^3), B_{sol}(Å^2)	0.32 , 44.8	EDS
L-test for twinning[2]	$< \lvert L \rvert > = 0.50, < L^2 > = 0.34$	Xtriage
Estimated twinning fraction	0.022 for -h,-k,l	Xtriage
F_o,F_c correlation	0.96	EDS
Total number of atoms	5340	wwPDB-VP
Average B, all atoms (Å^2)	61.0	wwPDB-VP

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Method File   : Method SCAN ACID standard.lcm
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PDA Graph

PeakTable

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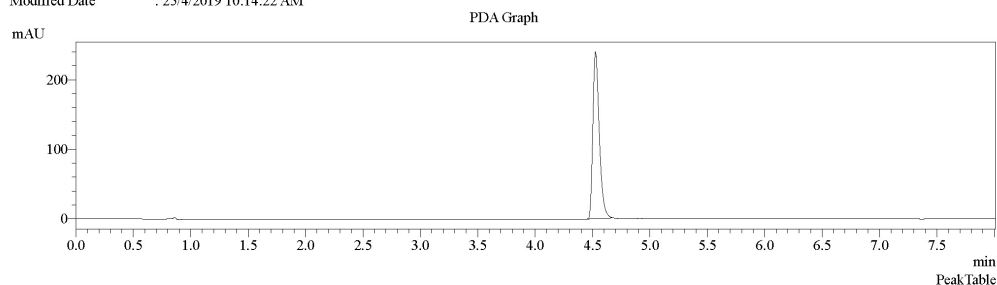
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MS Chromatogram
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MS Spectrum Graph

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MS Spectrum Table

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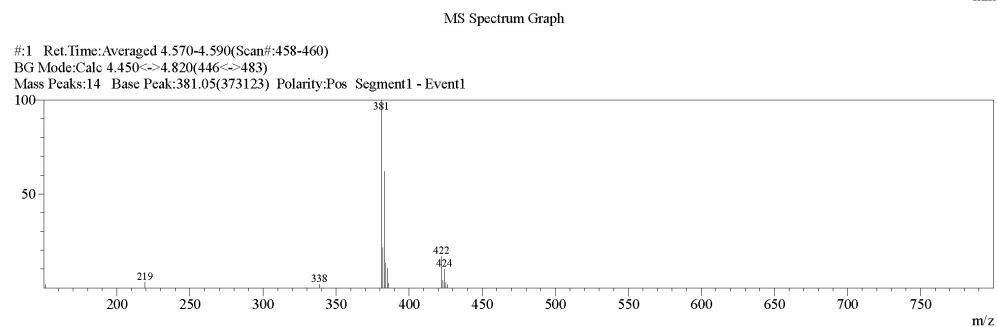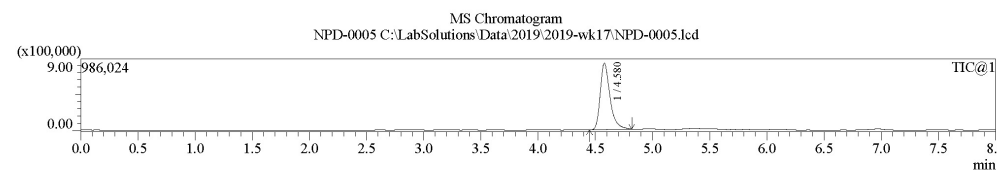
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1	150.90	6333	1.70				8	385.05	38470	10.31			
2	219.10	10740	2.88				9	386.15	8921	2.39			
3	338.30	6050	1.62				10	422.10	61998	16.62			
4	381.05	373123	100.00				11	423.05	14621	3.92			
5	382.00	79416	21.28				12	424.10	36514	9.79			
6	383.05	231440	62.03				13	425.15	9774	2.62			
7	384.05	49370	13.23				14	426.05	6295	1.69			

Figure S3 LCMS spectrum of compound NPD-0005
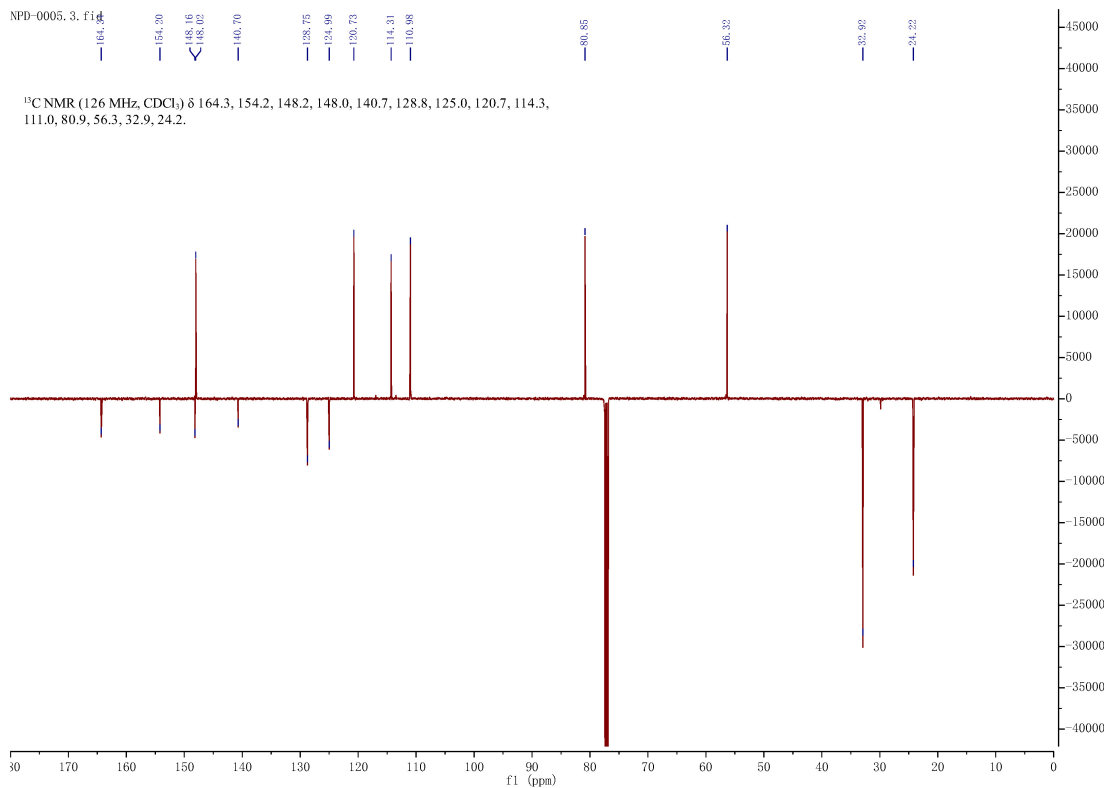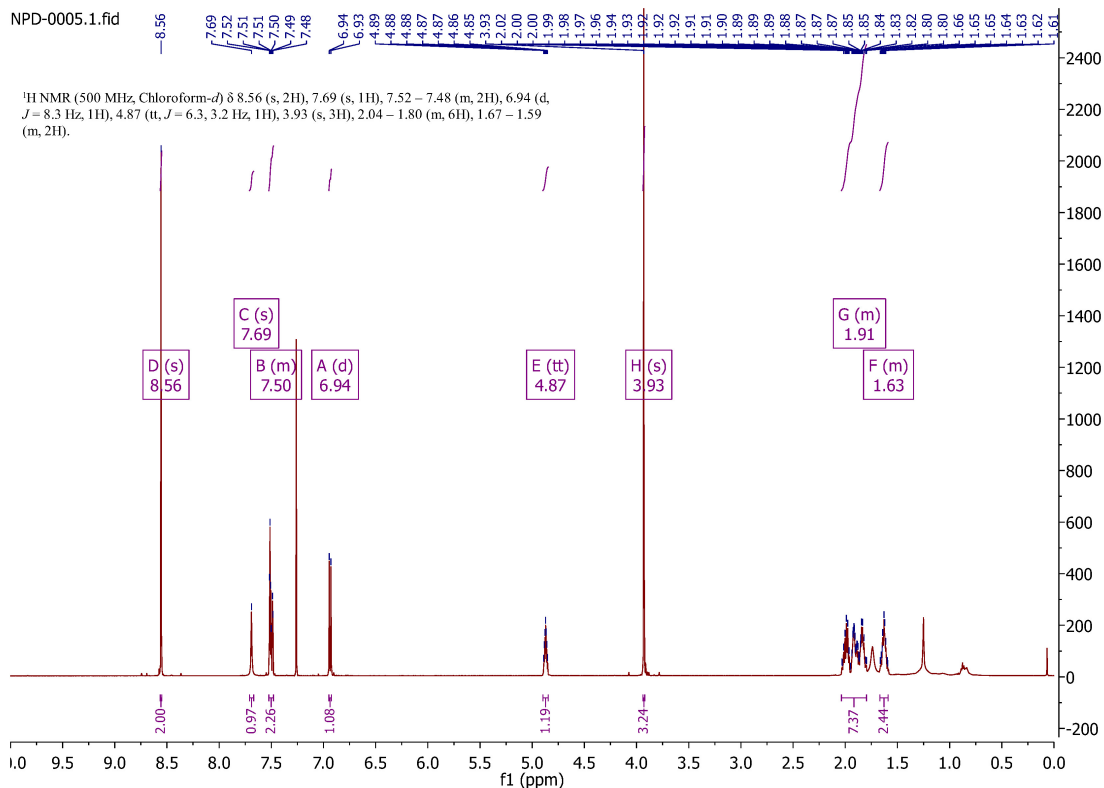
37

NPD-0005.1.fid

¹H NMR (500 MHz, Chloroform-*d*) δ 8.56 (s, 2H), 7.69 (s, 1H), 7.52 – 7.48 (m, 2H), 6.94 (d, *J* = 8.3 Hz, 1H), 4.87 (tt, *J* = 6.3, 3.2 Hz, 1H), 3.93 (s, 3H), 2.04 – 1.80 (m, 6H), 1.67 – 1.59 (m, 2H).

Figure S4 ¹H NMR spectrum of compound NPD-0005

NPD-0005.3.fid

¹³C NMR (126 MHz, CDCl₃) δ 164.3, 154.2, 148.2, 148.0, 140.7, 128.8, 125.0, 120.7, 114.3, 111.0, 80.9, 56.3, 32.9, 24.2.

Figure S5 ¹³C NMR spectrum of compound NPD-0005

PDA Graph
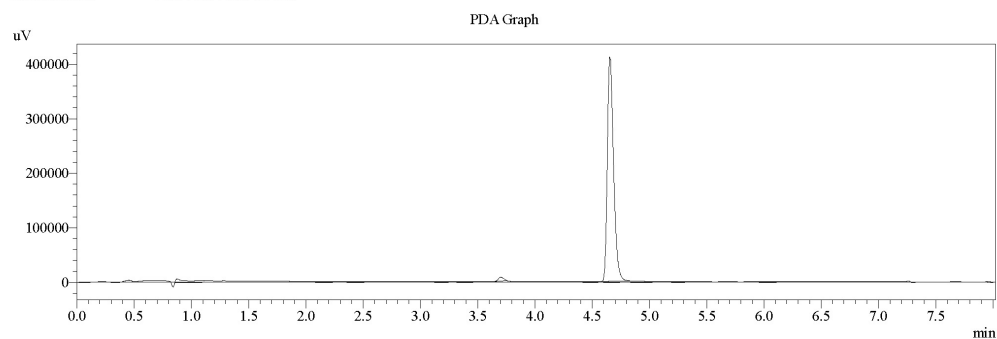
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.697	22427	1.427
2		4.650	1549438	98.573

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.690-4.710(Scan#:470-472)
Mass Peaks:22 Base Peak:403.05(245047) Polarity:Pos Segment1 - Event1
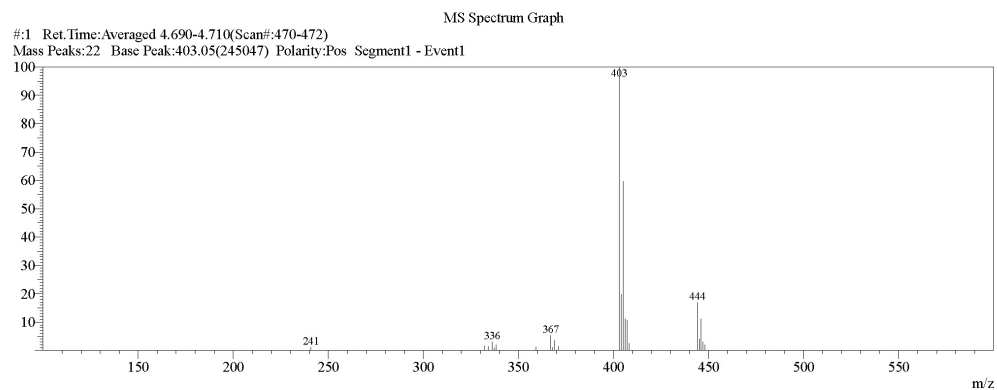
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.580<->4.910(459<->492)
Mass Peaks:22 Base Peak:403.05(245047) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	240.90	2748	1.12				12	403.05	245047	100.00			
2	332.25	4102	1.67				13	404.10	48852	19.94			
3	334.15	3658	1.49				14	405.05	146051	59.60			
4	336.15	7441	3.04				15	406.00	27547	11.24			
5	337.15	2468	1.01				16	407.05	26258	10.72			
6	338.20	4864	1.98				17	408.10	6298	2.57			
7	359.35	3002	1.23				18	444.10	41602	16.98			
8	367.05	12833	5.24				19	445.25	10121	4.13			
9	368.15	2868	1.17				20	446.15	27620	11.27			
10	369.10	8749	3.57				21	447.15	7595	3.10			
11	371.15	3473	1.42				22	448.10	4990	2.04			

Figure S6 LCMS spectrum of compound NPD-0006

YAZH04-022/3

7.70
7.59
7.48
7.46
7.30
7.29
7.26
6.87
6.75
6.62
8.58
3.97
3.96
1.35
1.34
1.33
1.33
1.32
1.31
1.31
1.30
1.29
0.69
0.68
0.67
0.66
0.39
0.38
0.38
0.37

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.58 (s, 2H), 7.70 (s, 1H), 7.59 (s, 1H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.29 (d, *J* = 8.2 Hz, 1H), 6.75 (t, *J* = 74.8 Hz, 1H), 3.97 (d, *J* = 6.9 Hz, 2H), 1.36 – 1.28 (m, 1H), 0.70 – 0.66 (m, 2H), 0.40 – 0.36 (m, 2H).

E (s) 8.58	G (s) 7.59					A (d) 3.97		D (m) 0.38
F (s) 7.70	I (d) 7.29	J (t) 6.75				B (m) 1.32	C (m) 0.68
H (d) 7.47						

1.99
0.93
1.04
1.05
0.99
1.19
2.00
1.03
1.96
1.97
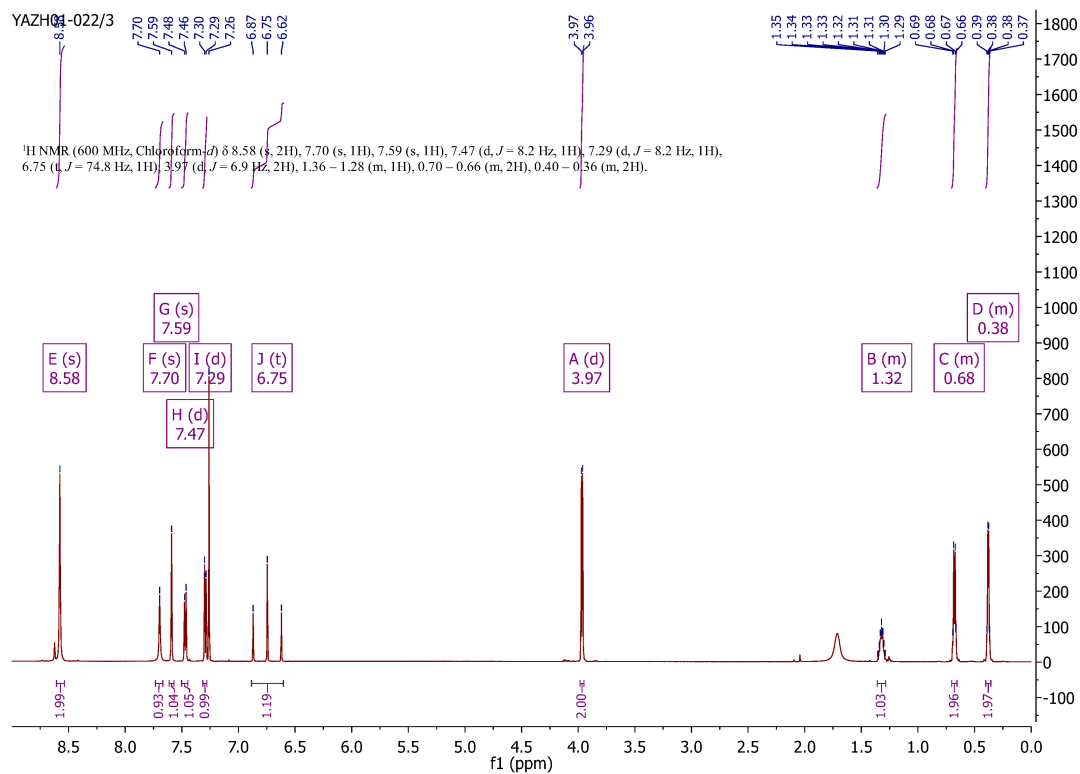
Figure S7 ^{1}H NMR spectrum of compound NPD-0006

163.76
151.11
148.38
144.04
139.93
130.95
128.99
122.50
120.03
117.52
115.79
114.40
114.05
74.38
10.16
3.45

^{13}C NMR (151 MHz, Chloroform-*d*) δ 163.8, 151.1, 148.4, 144.0, 139.9, 130.9, 129.0, 122.5, 120.0, 117.5, 115.8 (t, *J* = 262.8 Hz), 74.4, 10.2, 3.5.
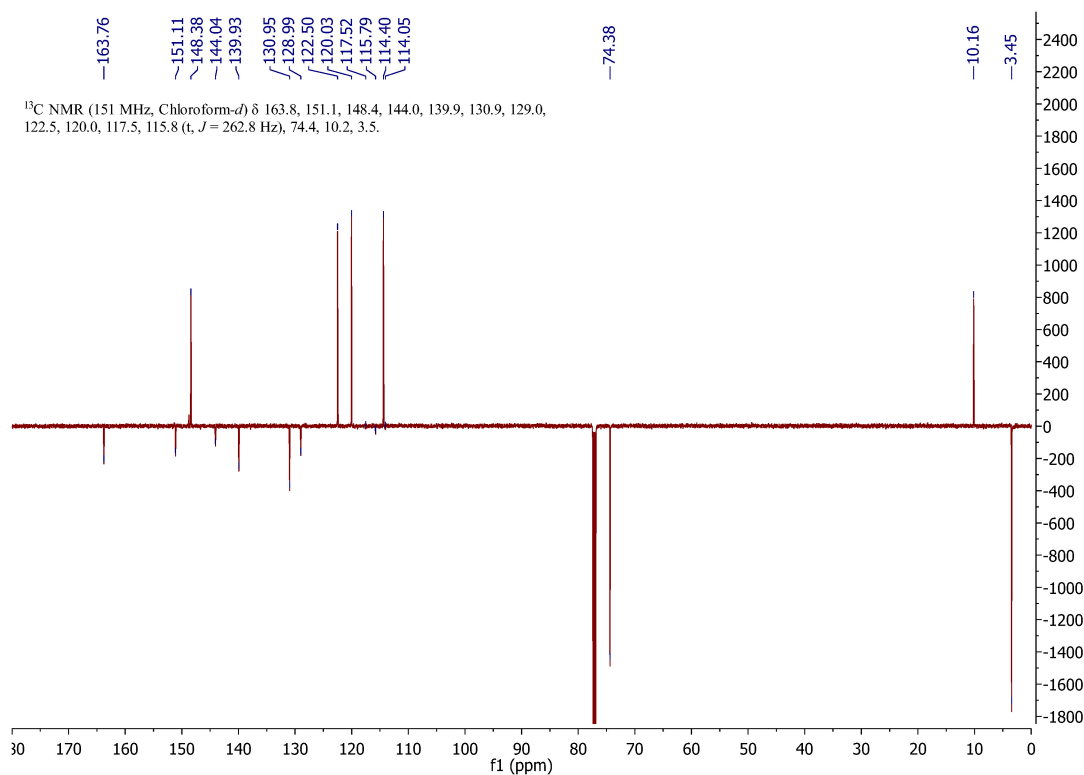
Figure S8 ^{13}C NMR spectrum of compound NPD-0006

40

PDA Graph

mAU

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.511	13845926	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 3.550-3.570(Scan#:356-358)
Mass Peaks:12 Base Peak:326.95(850318) Polarity:Pos Segment1 - Event1
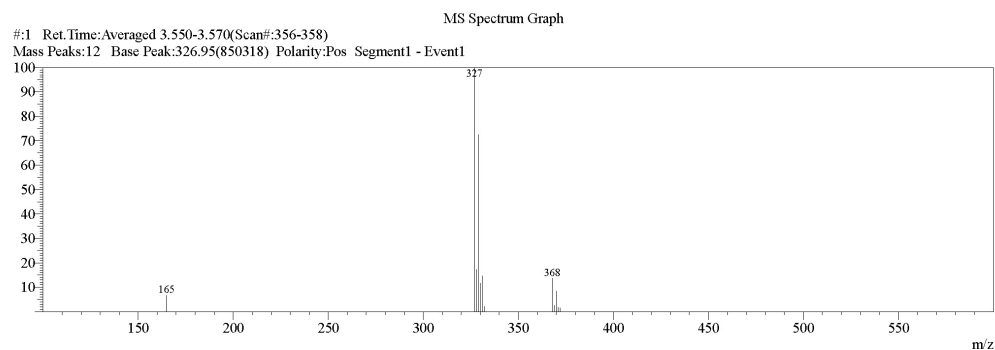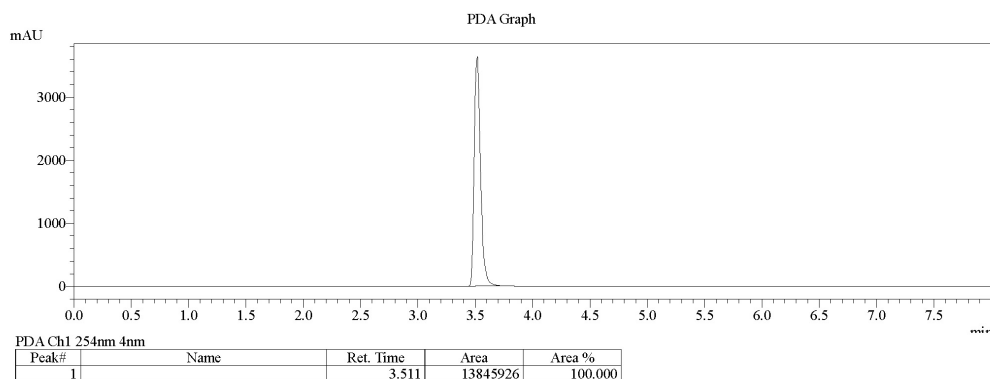
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.450<->3.950(346<->396)
Mass Peaks:12 Base Peak:326.95(850318) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	165.00	56320	6.62				7	332.00	18582	2.19			
2	326.95	850318	100.00				8	368.00	115503	13.58			
3	328.00	147851	17.39				9	369.05	22429	2.64			
4	329.00	617151	72.58				10	370.05	71128	8.36			
5	329.95	99378	11.69				11	371.05	16009	1.88			
6	331.00	124143	14.60				12	372.05	12762	1.50			

Figure S9 LCMS spectrum of compound NPD-0446

41

VUF14667.1.fid

¹H NMR (500 MHz, DMSO-d_6) δ 10.48 (s, 1H), 8.77 (s, 2H), 7.70 (dd, J = 8.4, 2.1 Hz, 1H), 7.59 (d, J = 2.1 Hz, 1H), 7.14 (d, J = 8.5 Hz, 1H), 3.87 (s, 3H), 3.85 (s, 3H).

G (s)
10.48

F (s)
8.77

D (d)
7.59

C (d)
7.14

E (dd)
7.70

B (s)
3.85

A (s)
3.87
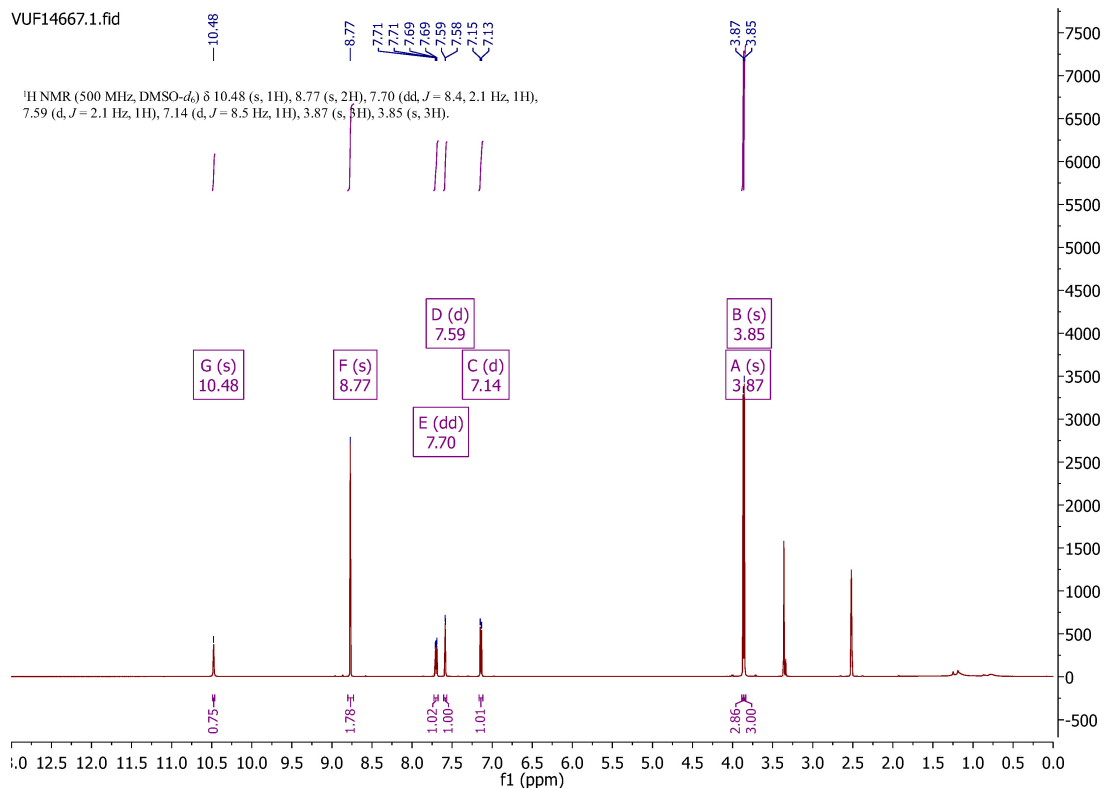
Figure S10 ¹H NMR spectrum of compound NPD-0446

VUF14667-2.1

¹³C NMR (126 MHz, DMSO) δ 164.3, 152.3, 148.5, 148.3, 141.6, 130.8, 124.7, 121.6, 111.1, 111.0, 55.8, 55.6.
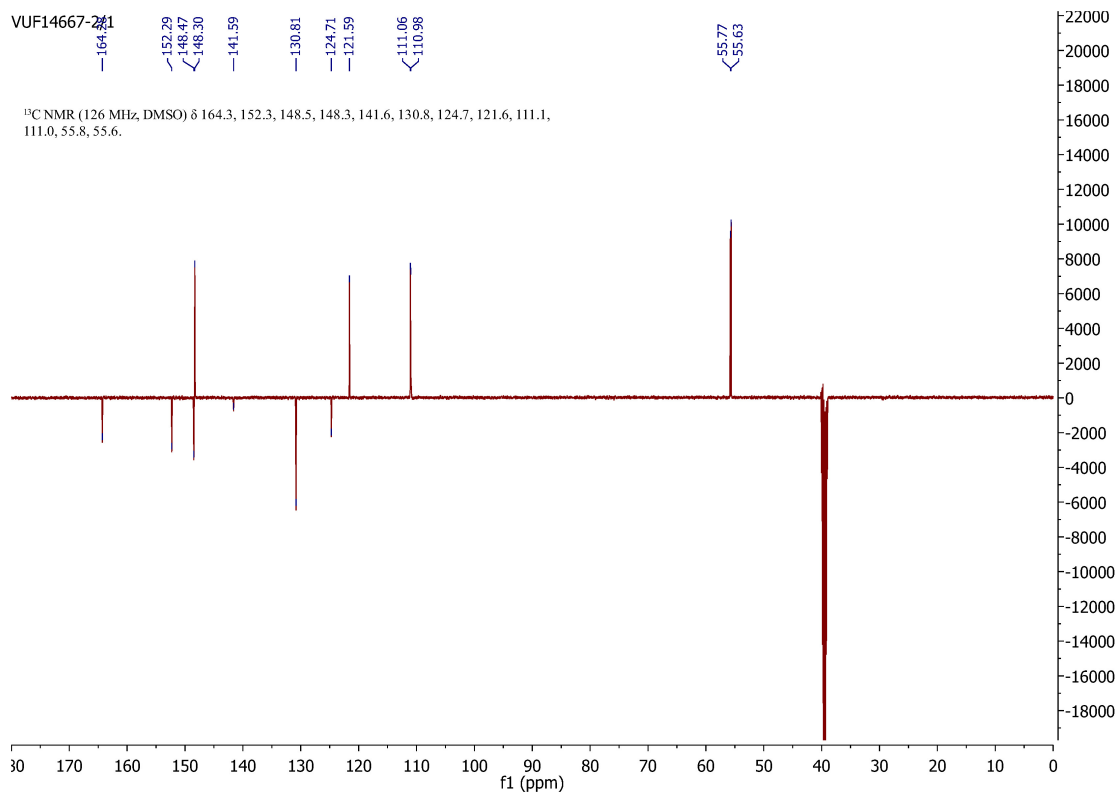
Figure S11 ¹³C NMR spectrum of compound NPD-0446

42

Acquired by   : Admin
Date Acquired   : 1/26/2016 5:05:32 PM
Sample Name   : Fatih compound 62
Sample ID   :
Tray#   : 1
Vial#   : 5
Injection Volume   : 1
Data File   : C:\LabSolutions\Methods\FAR Pract Fatih compound 62.lcd
Background File   : Blanco-2 26012016.lcd
Method File   : Method SCAN ACID standard.lcm
Report Format   : DefaultLCMS.lcr
Tuning File   : C:\LabSolutions\Tuning File\Tuning-ESI-pos-neg01072015.lct
Processed by   : Admin
Modified Date   : 1/27/2016 9:06:35 AM

PDA Graph
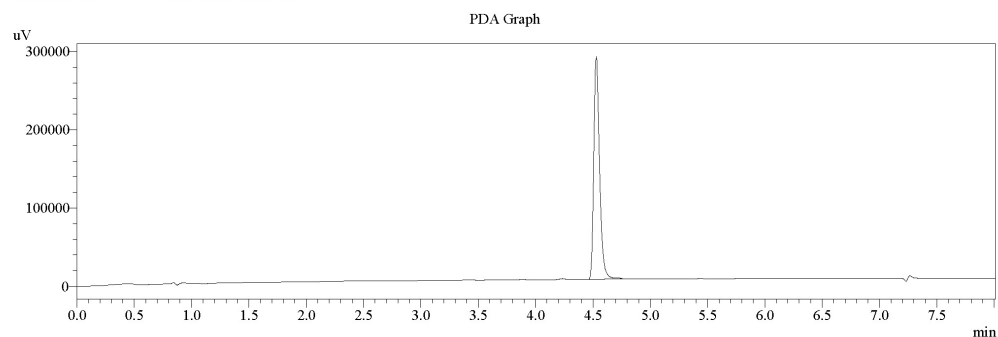
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.524	989667	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.650-4.680(Scan#:465-468)
Mass Peaks:6 Base Peak:403.02(1149896) Polarity:Pos Segment1 - Event1
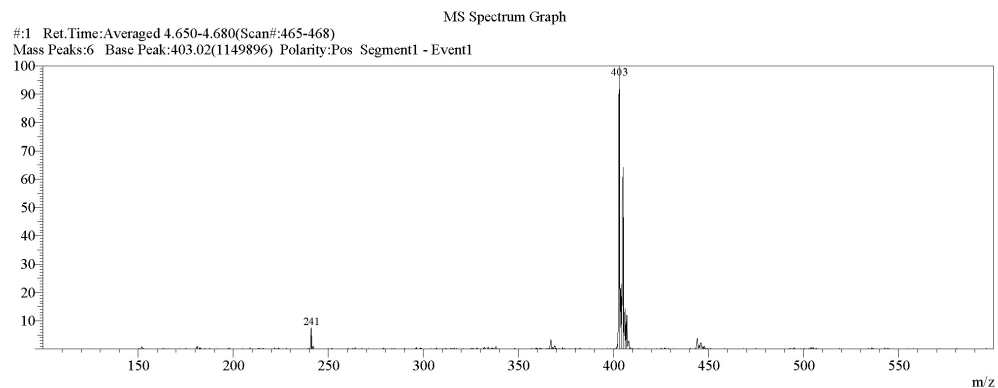
MS Spectrum Table

#:1 Ret.Time:
BG Mode:None
Mass Peaks:6 Base Peak:403.02(1067212) Polarity:Pos Segment1 - Event

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	241.07	73936	6.93				4	405.01	707412	66.29			
2	403.02	1067212	100.00				5	406.08	142461	13.35			
3	404.08	229993	21.55				6	407.01	121379	11.37			

Figure S12 LCMS spectrum of compound NPD-0546
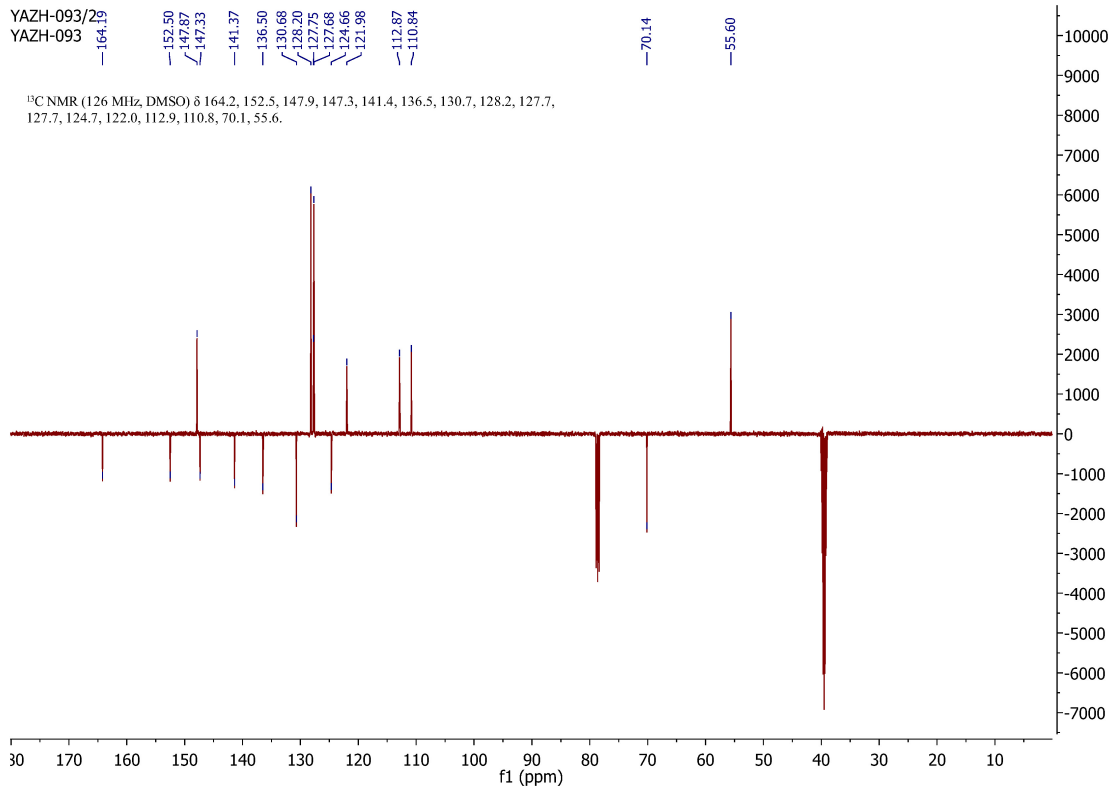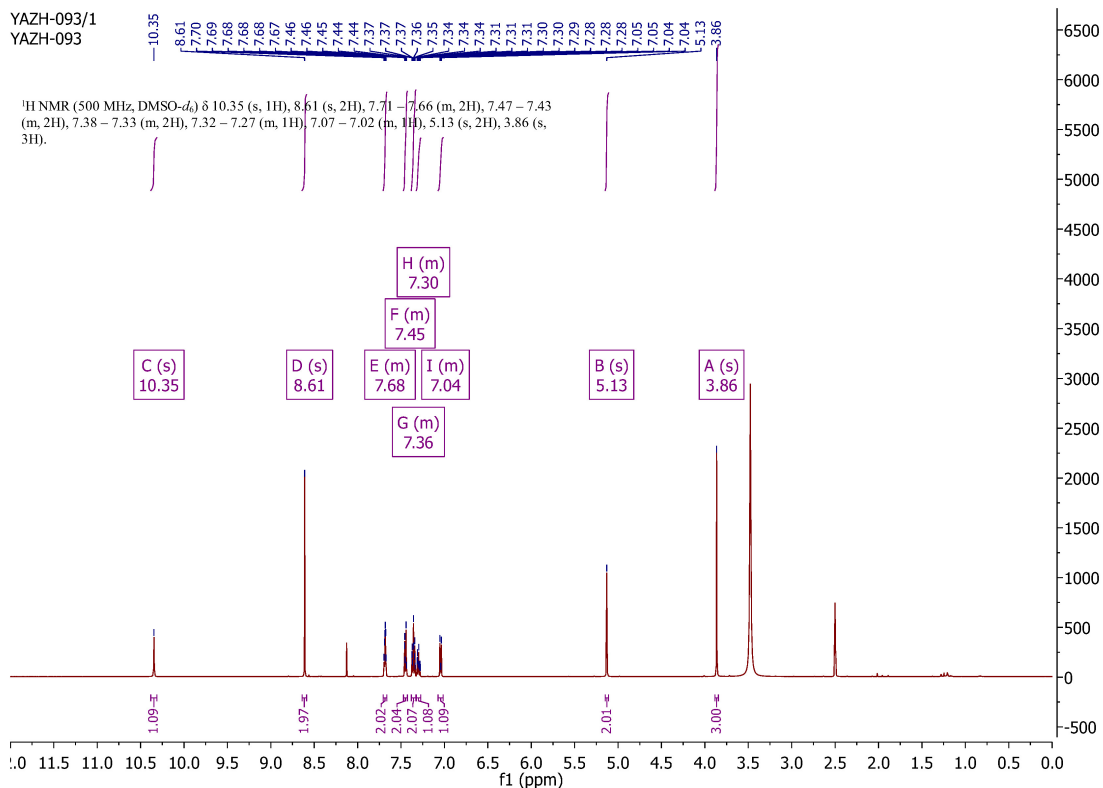
43

YAZH-093/1
YAZH-093

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.35 (s, 1H), 8.61 (s, 2H), 7.71 – 7.66 (m, 2H), 7.47 – 7.43 (m, 2H), 7.38 – 7.33 (m, 2H), 7.32 – 7.27 (m, 1H), 7.07 – 7.02 (m, 1H), 5.13 (s, 2H), 3.86 (s, 3H).

H (m)
7.30

F (m)
7.45

C (s)
10.35

D (s)
8.61

E (m)
7.68

I (m)
7.04

B (s)
5.13

A (s)
3.86

G (m)
7.36

Figure S13 ^{1}H NMR spectrum of compound NPD-0546

YAZH-093/2
YAZH-093

^{13}C NMR (126 MHz, DMSO) δ 164.2, 152.5, 147.9, 147.3, 141.4, 136.5, 130.7, 128.2, 127.7, 127.7, 124.7, 122.0, 112.9, 110.8, 70.1, 55.6.

Figure S14 ^{13}C NMR spectrum of compound NPD-0546

44

PDA Graph

mAU

PDA Ch1 230nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.726	4222080	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 3.780-3.800(Scan#:379-381)
Mass Peaks:11 Base Peak:297.00(756618) Polarity:Pos Segment1 - Event1
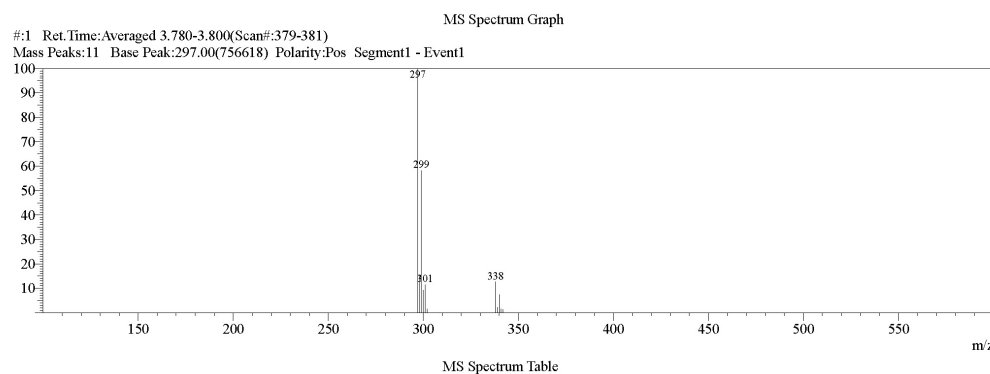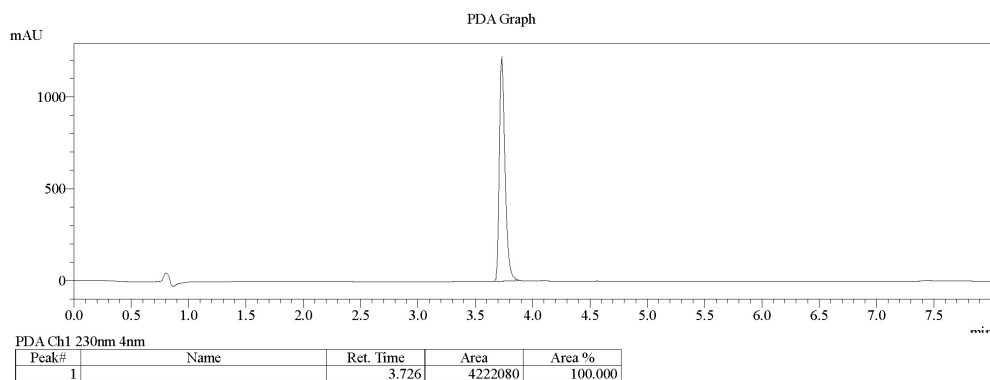
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.680<->4.090(369<->410)
Mass Peaks:11 Base Peak:297.00(756618) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	297.00	756618	100.00				7	338.00	95139	12.57			
2	298.00	113869	15.05				8	339.05	16956	2.24			
3	299.00	440277	58.19				9	340.05	55883	7.39			
4	300.00	70642	9.34				10	341.05	11650	1.54			
5	300.95	87257	11.53				11	341.95	9945	1.31			
6	302.00	11893	1.57										

Figure S15 LCMS spectrum of compound NPD-0548

45

VUF14666.1.fid

−10.49 −8.76 ⟨8.03 ⟨8.01 ⟨7.13 ⟨7.11 −3.87

¹H NMR (500 MHz, DMSO-*d₆*) δ 10.49 (s, 1H), 8.76 (s, 2H), 8.02 (d, *J* = 8.9 Hz, 2H), 7.12 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H).

D (s)
8.76

E (s)
10.49

C (d)
8.02

B (d)
7.12

A (s)
3.87

0.89
1.78
2.02
2.02
3.00

Figure S16 ¹H NMR spectrum of compound NPD-0548

VUF14666-2/15

164.2 162.5 −148.28 −141.60 ⟨130.86 ⟨130.00 ⟨124.80 −113.92 −55.57

¹³C NMR (126 MHz, DMSO) δ 164.3, 162.5, 148.3, 141.6, 130.9, 130.0, 124.8, 113.9, 55.6.

Figure S17 ¹³C NMR spectrum of compound NPD-0548

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.258	710577	100.000

MS Spectrum Graph

#:1   Ret.Time:Averaged 3.320-3.340(Scan#:333-335)
Mass Peaks:6   Base Peak:291.00(1921412) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1   Ret.Time:
BG Mode:Calc 3.190<->3.560(320<->357)
Mass Peaks:6   Base Peak:291.00(1921412) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	179.00	50991	2.65				4	292.05	369332	19.22			
2	224.10	45000	2.34				5	293.05	44757	2.33			
3	291.00	1921412	100.00				6	332.10	56581	2.94			

Figure S18 LCMS spectrum of compound NPD-1177

47

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.28 (s, 1H), 8.58 (d, J = 2.8 Hz, 1H), 8.38 (d, J = 5.3 Hz, 1H), 7.87 (dd, J = 6.7, 5.3 Hz, 1H), 7.63 (dd, J = 8.4, 2.1 Hz, 1H), 7.54 (d, J = 2.1 Hz, 1H), 7.10 (d, J = 8.5 Hz, 1H), 4.09 (q, J = 7.0 Hz, 2H), 3.85 (s, 3H), 1.36 (t, J = 7.0 Hz, 3H).

A (s)
10.28

B (d)
8.58

C (d)
8.38

D (dd)
7.87

E (dd)
7.63

F (d)
7.54

G (d)
7.10

H (q)
4.09

I (s)
3.85

J (t)
1.36

Figure S19 ^{1}H NMR spectrum of compound NPD-1177

YAZH-005.3.fid

^{13}C NMR (126 MHz, DMSO-d_6) δ 165.2, 152.4, 151.4 (d, , J = 255.1 Hz), 147.6, 146.3 (d, J = 5.0 Hz), 138.2 (d, J = 21.8 Hz), 133.7 (d, J = 9.5 Hz), 125.4, 121.8, 118.7 (app s), 112.1, 111.0, 63.9, 55.7, 14.7.

Figure S20 ^{13}C NMR spectrum of compound NPD-1177

48

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.368	5235	1.147
2		4.601	451033	98.853

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.670-4.690(Scan#:468-470)
Mass Peaks:20 Base Peak:345.00(212441) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.550<->4.900(456<->491)
Mass Peaks:20 Base Peak:345.00(212441) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	173.00	3126	1.47				11	348.00	32728	15.41			
2	182.90	8434	3.97				12	348.95	63089	29.70			
3	223.95	4605	2.17				13	350.00	11665	5.49			
4	308.95	8497	4.00				14	350.80	6922	3.26			
5	310.10	2352	1.11				15	386.05	40483	19.06			
6	310.80	5736	2.70				16	386.95	6898	3.25			
7	334.20	2461	1.16				17	387.90	39119	18.41			
8	345.00	212441	100.00				18	389.15	7650	3.60			
9	345.90	33033	15.55				19	390.05	6968	3.28			
10	346.95	185495	87.32				20	391.05	2142	1.01			

Figure S21 LCMS spectrum of compound NPD-1178

¹H NMR (250 MHz, DMSO-d_6) δ 10.73 (s, 1H), 8.77 (s, 2H), 7.71 – 7.65 (m, 1H), 7.66 – 7.61 (m, 2H), 4.22 (q, J = 7.0 Hz, 2H), 1.40 (t, J = 7.0 Hz, 3H).

A (s)
10.73

B (s)
8.77

C (m)
7.68

D (m)
7.63

E (q)
4.22

F (t)
1.40

f1 (ppm)

Figure S22 ¹H NMR spectrum of compound NPD-1178

¹³C NMR (120 MHz, DMSO) δ 164.30, 154.39, 148.82, 141.55, 133.00, 131.12, 130.62, 126.13, 121.32, 113.08, 65.11, 14.97.

f1 (ppm)

Figure S23 ¹³C NMR spectrum of compound NPD-1178

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.210	3214	0.297
2		4.639	1076423	99.535
3		5.231	1810	0.167

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.700-4.720(Scan#:471-473)
Mass Peaks:9 Base Peak:310.90(1130445) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.560<->4.960(457<->497)
Mass Peaks:9 Base Peak:310.90(1130445) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	310.90	1130445	100.00				6	316.10	17698	1.57			
2	312.00	212987	18.84				7	352.00	84880	7.51			
3	312.95	792980	70.15				8	353.00	18323	1.62			
4	314.00	111042	9.82				9	354.00	55399	4.90			
5	315.00	129351	11.44										

Figure S24 LCMS spectrum of compound NPD-1179

¹H NMR (250 MHz, DMSO-d_6) δ 10.25 (s, 1H), 8.70 (s, 1H), 8.52 (d, J = 5.3 Hz, 1H), 7.83 (d,
J = 5.3 Hz, 1H), 7.67 (d, J = 1.7 Hz, 1H), 7.63 (d, J = 8.2 Hz, 1H), 7.57 (dd, J = 8.2, 1.8 Hz,
1H), 4.22 (q, J = 7.0 Hz, 2H), 1.40 (t, J = 7.0 Hz, 3H).

Figure S25 ¹H NMR spectrum of compound NPD-1179

YAZH-007/1
YAZH-007

¹³C NMR (126 MHz, DMSO) δ 165.12, 154.27, 150.21, 149.10, 142.82, 133.90, 130.51, 125.97, 125.23,
121.36, 120.65, 113.23, 65.09, 14.96.

Figure S26 ¹³C NMR spectrum of compound NPD-1179

PDA Graph

uV

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.368	3970	1.836
2		4.183	212236	98.164

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.260-4.280(Scan#:427-429)
Mass Peaks:29 Base Peak:332.95(98731) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.140<->4.430(415<->444
Mass Peaks:29 Base Peak:332.95(98731) Polarity:Pos Segment1 - Event

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	164.00	1285	1.30				15	325.15	1409	1.43			
2	168.85	5260	5.33				16	328.75	1447	1.47			
3	183.00	2007	2.03				17	330.90	89102	90.25			
4	196.15	1366	1.38				18	332.00	18499	18.74			
5	199.95	1394	1.41				19	332.95	98731	100.00			
6	204.75	1083	1.10				20	333.85	14089	14.27			
7	223.85	4249	4.30				21	334.95	28552	28.92			
8	275.85	1686	1.71				22	335.90	6508	6.59			
9	281.85	1477	1.50				23	337.00	2904	2.94			
10	294.20	1034	1.05				24	357.00	1712	1.73			
11	294.80	4317	4.37				25	371.95	8292	8.40			
12	296.20	1779	1.80				26	373.00	2227	2.26			
13	296.80	2477	2.51				27	374.00	8706	8.82			
14	303.80	1057	1.07				28	374.95	1519	1.54			

Figure S27 LCMS spectrum of compound NPD-1180

1H NMR (250 MHz, DMSO-d_6) δ 10.63 (s, 1H), 8.75 (s, 2H), 8.11 (s, 1H), 8.01 (d, J = 8.7 Hz, 1H), 7.34 (d, J = 8.8 Hz, 1H), 3.96 (s, 3H).

D (s)
10.63

C (s)
8.75

B (d)
8.01

E (s)
8.11

A (d)
7.34

F (s)
3.96

f1 (ppm)

Figure S28 ^{1}H NMR spectrum of compound NPD-1180

^{13}C NMR (126 MHz, DMSO) δ 163.2, 157.8, 148.4, 141.2, 130.7, 129.5, 128.9, 125.5, 121.2, 112.7, 56.7.

f1 (ppm)

Figure S29 ^{13}C NMR spectrum of compound NPD-1180

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.125	275772	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.180-4.200(Scan#:419-421)
Mass Peaks:9 Base Peak:296.95(379046) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.050<->4.410(406<->442)
Mass Peaks:9 Base Peak:296.95(379046) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	169.00	6886	1.82				6	300.95	41810	11.03			
2	296.95	379046	100.00				7	301.95	7970	2.10			
3	298.00	59840	15.79				8	337.90	15932	4.20			
4	299.00	239611	63.21				9	339.95	10560	2.79			
5	300.00	32198	8.49										

Figure S30 LCMS spectrum of compound NPD-1181

55

YAZH-013.1.fid
1H_proton DMSO {D:\NMRDATA} ZhengYZZ 19

1H NMR (250 MHz, DMSO-d_6) δ 10.17 (s, 1H), 8.68 (s, 1H), 8.51 (d, J = 5.4 Hz, 1H), 8.09 (d, J = 2.2 Hz, 1H), 8.00 (dd, J = 8.6, 2.3 Hz, 1H), 7.84 (dd, J = 5.4, 0.5 Hz, 1H), 7.33 (d, J = 8.7 Hz, 1H), 3.97 (s, 3H).

E (d) 8.50
F (s) 8.68   B (dd) 7.83
G (s) 10.16   D (d) 8.09   A (d) 7.33   H (s) 3.96
C (dd) 7.99

Figure S31 ^{1}H NMR spectrum of compound NPD-1181

YAZH-013/1
YAZH-013

13C NMR (126 MHz, DMSO) δ 164.33, 158.10, 150.15, 149.03, 142.85, 130.05, 129.36, 126.66, 125.06, 121.49, 120.51, 112.99, 57.06.
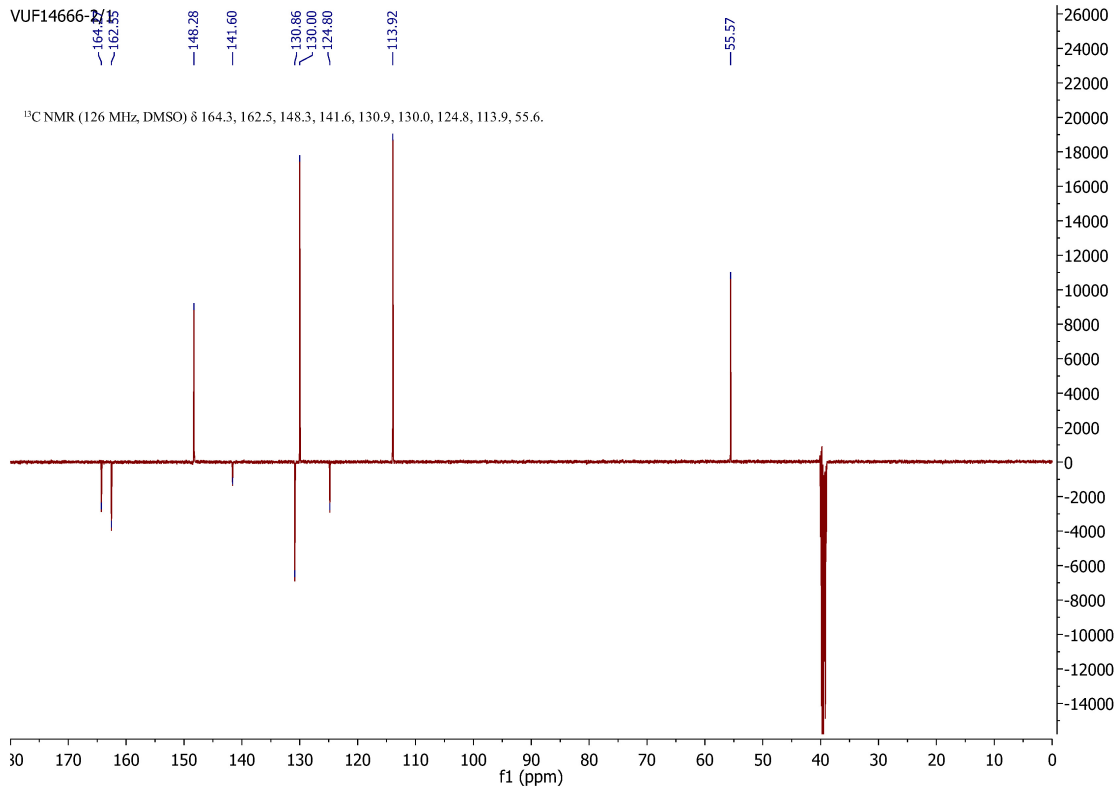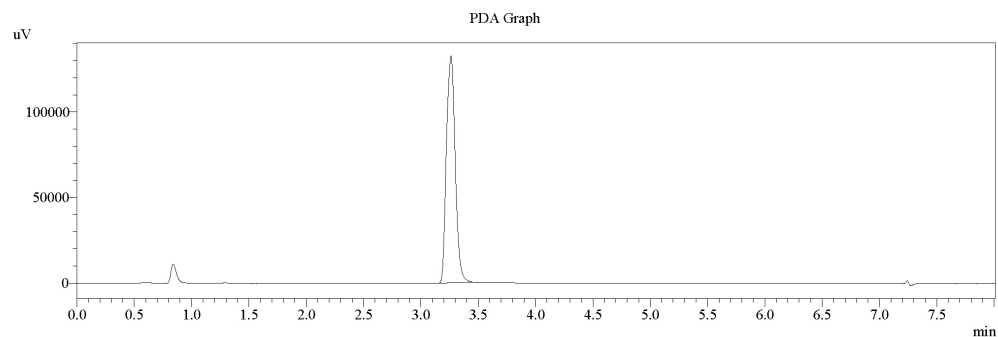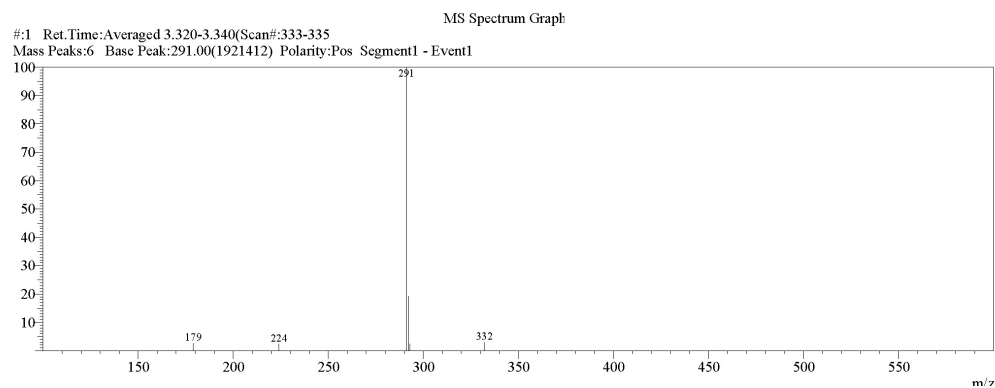
Figure S32 ^{13}C NMR spectrum of compound NPD-1181

56

Acquired by   : Admin
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Sample ID   :
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Background File   : blanco 10052019.lcd
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Processed by   : Admin
Modified Date   : 10/5/2019 4:20:45 PM

PDA Graph

mAU

PDA Ch1 254nm 4nm
PeakTable

Peak#	Name	Ret. Time	Area	Area %
1		3.530	12764741	100.000

MS Chromatogram
YAZH-014 C:\LabSolutions\Data\2019\2019-wk19\YAZH-014.lcd

(x1,000,000)
3.00 3,079,954   TIC@1

MS Spectrum Graph

#:1 Ret.Time:Averaged 3.580-3.600(Scan#:359-361)
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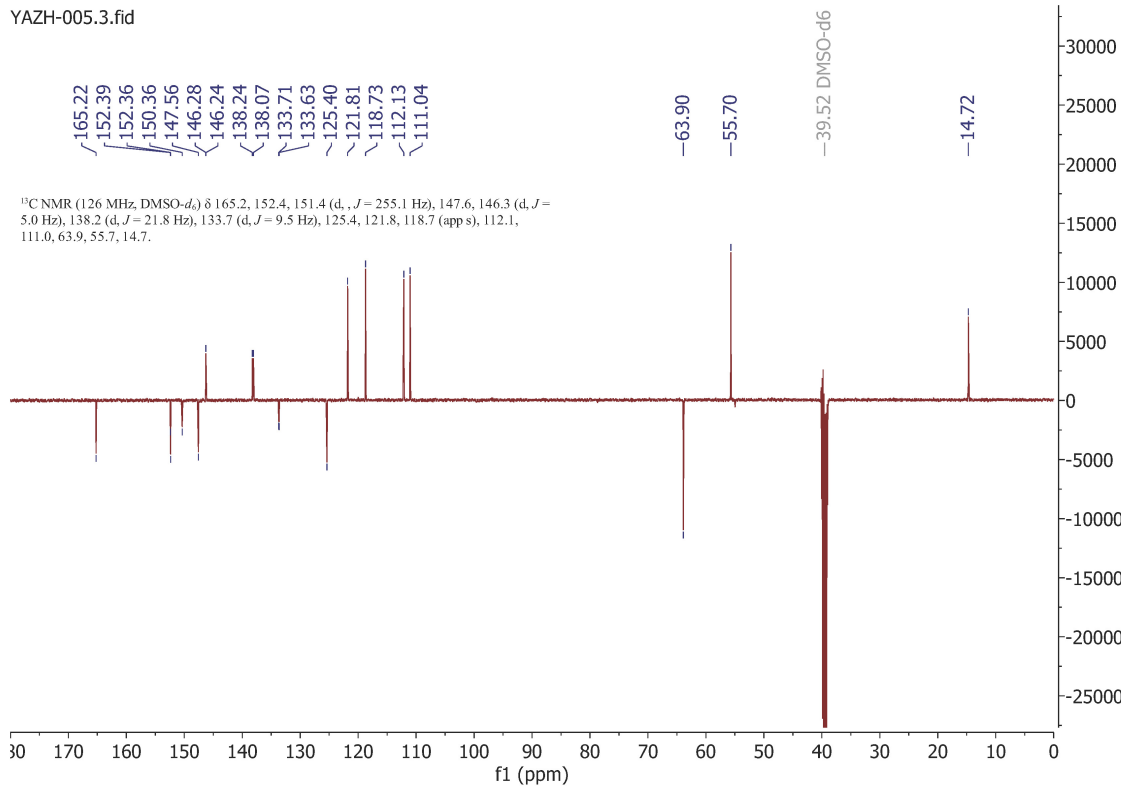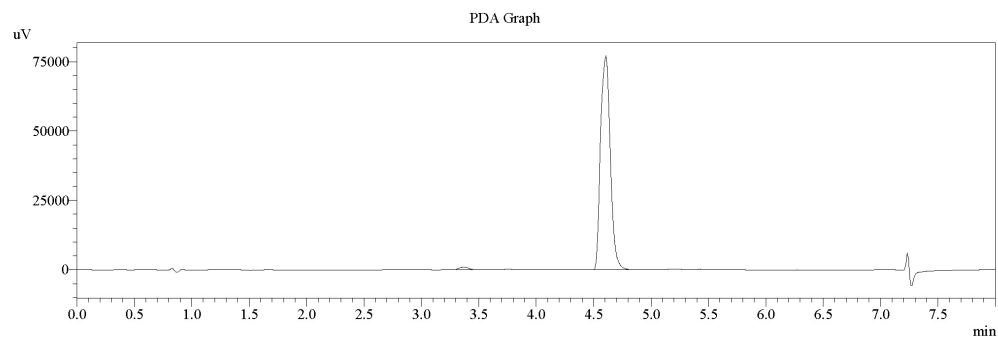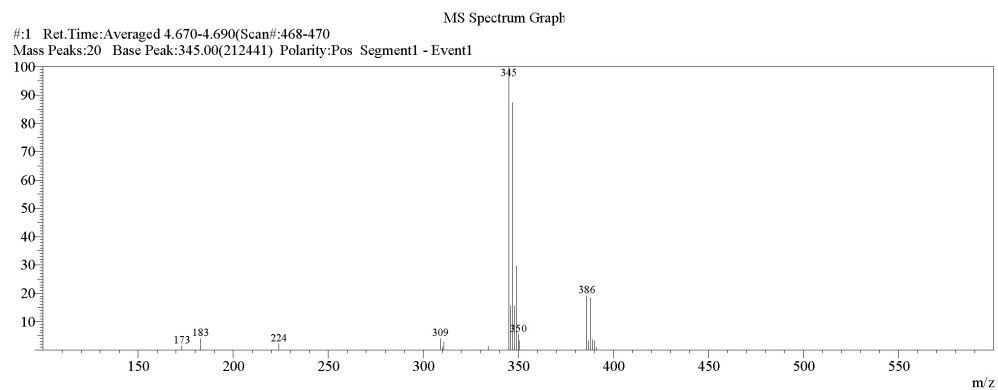Mass Peaks:8 Base Peak:281.00(1768940) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.450<->3.870(346<->388)
Mass Peaks:8 Base Peak:281.00(1768940) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	169.00	18379	1.04				5	284.05	104172	5.89			
2	281.00	1768940	100.00				6	322.05	94099	5.32			
3	282.00	304788	17.23				7	323.05	18549	1.05			
4	283.00	629665	35.60				8	324.05	33808	1.91			

Figure S33 LCMS spectrum of compound NPD-1182

57

YAZH-014.1.fid
1H_proton DMSO {D:\NMRDATA} ZhengYZZ

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.45 (s, 1H), 8.59 (d, J = 2.9 Hz, 1H), 8.38 (d, J = 5.3 Hz, 1H), 8.09 (d, J = 2.2 Hz, 1H), 7.98 (dd, J = 8.7, 2.3 Hz, 1H), 7.88 (dd, J = 6.7, 5.3 Hz, 1H), 7.31 (d, J = 8.8 Hz, 1H), 3.96 (s, 3H).

E (d)
8.38

C (dd)
7.98

G (s)
10.45

B (d)
8.09

A (d)
7.31

H (s)
3.96

D (dd)
7.88

F (d)
8.59

Figure S34 ^{1}H NMR spectrum of compound NPD-1182

YAZH-014.3.fid

^{13}C NMR (126 MHz, DMSO-d_6) δ 164.2, 157.6, 151.3 (d, J = 255.7 Hz), 146.3 (d, J = 5.1 Hz), 138.2 (d, J = 21.8 Hz), 133.4 (d, J = 9.2 Hz), 129.8, 129.1, 126.3, 120.9, 118.6, 112.5, 56.6.
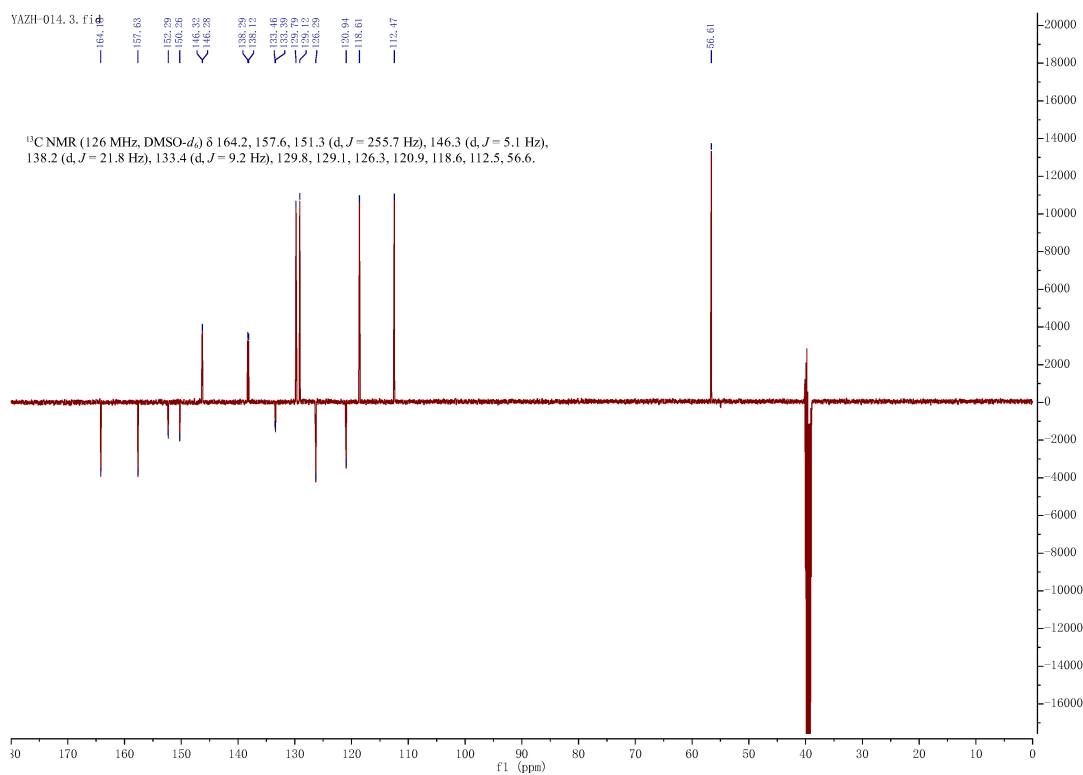
Figure S35 ^{13}C NMR spectrum of compound NPD-1182

58

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.146	301413	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.220-4.240(Scan#:423-425
Mass Peaks:15   Base Peak:302.95(262596) Polarity:Pos Segment1 - Event1
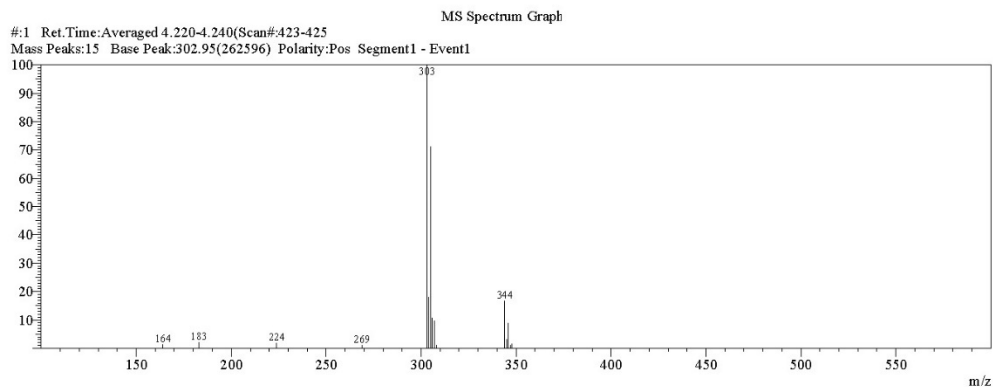
#:1 Ret.Time:
BG Mode:Calc 4.100<-->4.450(411<-->446)
Mass Peaks:15   Base Peak:302.95(262596) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	164.00	3498	1.33				9	306.95	25124	9.57			
2	182.95	5134	1.96				10	308.05	2683	1.02			
3	223.90	4892	1.86				11	343.95	43986	16.75			
4	268.85	2932	1.12				12	345.15	8229	3.13			
5	302.95	262596	100.00				13	345.90	23230	8.85			
6	303.95	46888	17.86				14	347.00	2967	1.13			
7	304.95	186816	71.14				15	348.00	3792	1.44			
8	305.85	27745	10.57										

Figure S36 LCMS spectrum of compound NPD-1183

59

YAZH-015.1.fid
1H_proton DMSO {D:\NMRDATA} ZhengYZz 21

E (s)
10.82

D (s)
8.79

B (m)
7.93

A (m)
7.68

C (m)
8.05

0.95

1.84

0.99
0.99
1.00
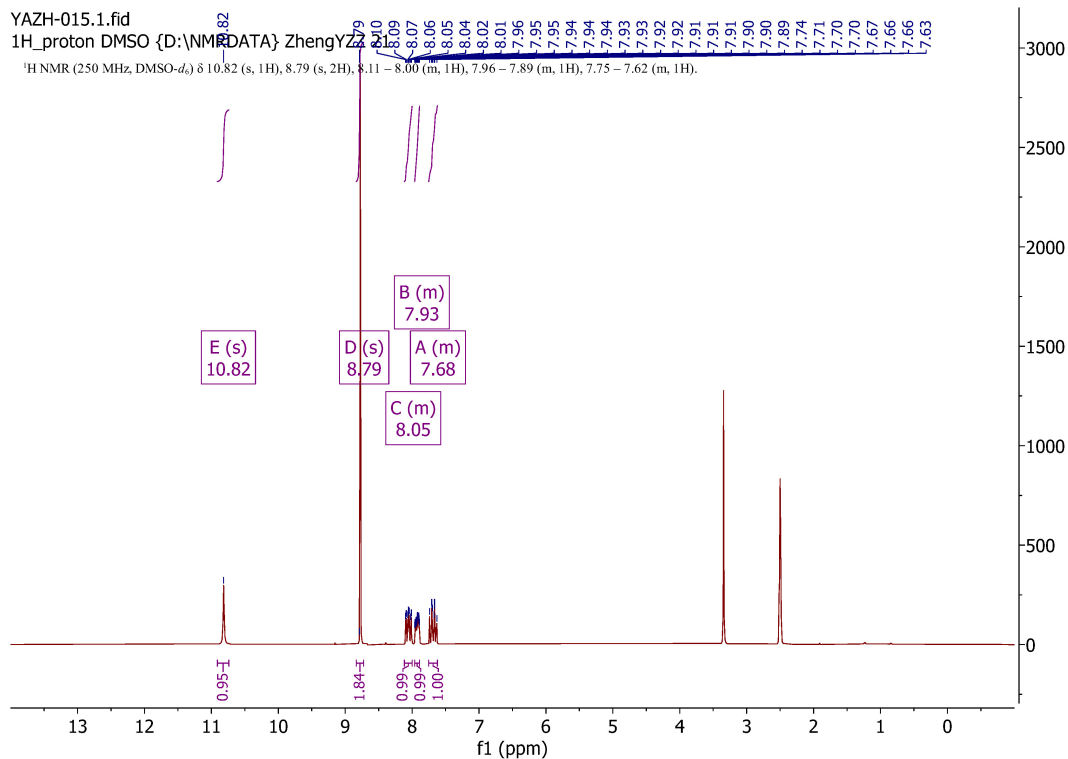
Figure S37 ^{1}H NMR spectrum of compound NPD-1183

YAZH-015.3.fid
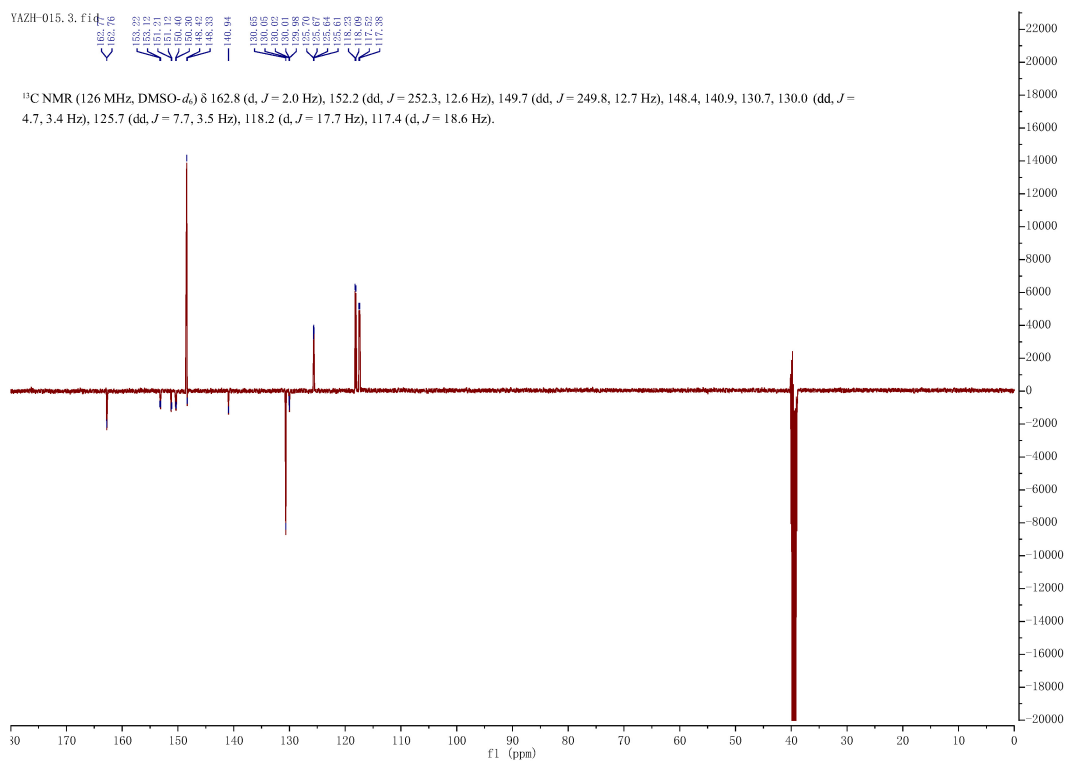
Figure S38 ^{13}C NMR spectrum of compound NPD-1183
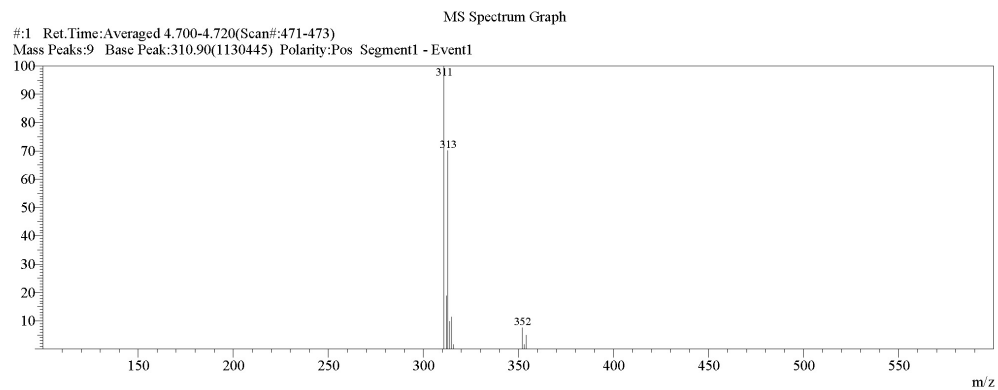
60

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Sample ID   :
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Injection Volume   : 1
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Background File   : blanco 16102016.lcd
Method File   : Method SCAN ACID standard.lcm
Report Format   : DefaultLCMS.lcr
Tuning File   : C:\LabSolutions\Tuning File\Tuning-ESI-pos-neg01072015.lct
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uV
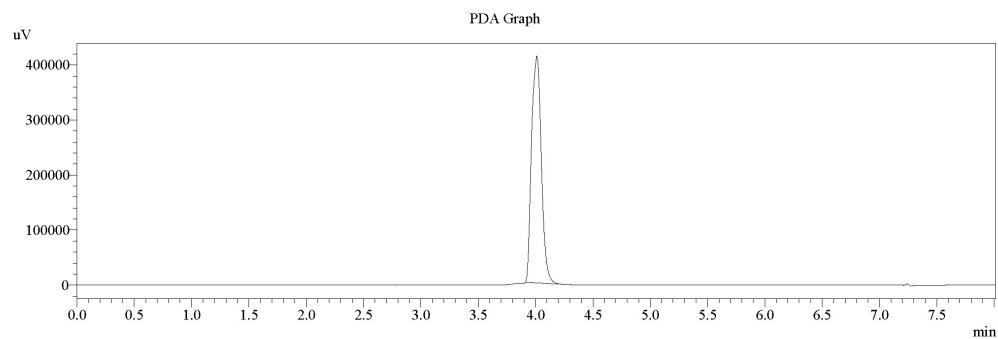
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.006	2450571	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.080-4.100(Scan#:409-411)
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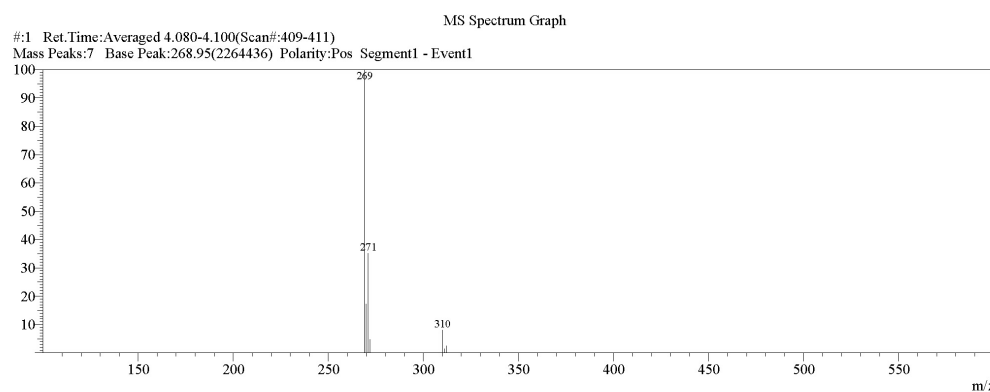
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.920<->4.510(393<->452)
Mass Peaks:7 Base Peak:268.95(2264436) Polarity:Pos Segment1 - Event
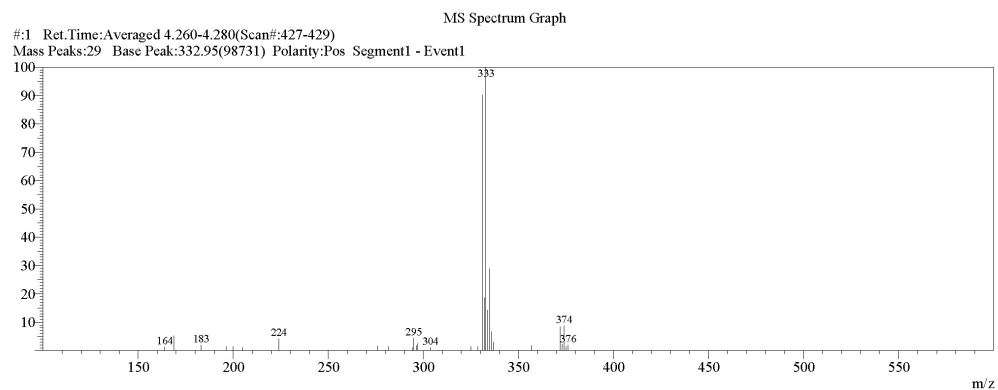
#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	268.95	2264436	100.00				5	310.00	182863	8.08			
2	269.95	390369	17.24				6	311.05	33790	1.49			
3	270.95	795370	35.12				7	312.00	55214	2.44			
4	272.00	109158	4.82										

Figure S39 LCMS spectrum of compound NPD-1184

YAZH-016.1.fid
1H_proton DMSO {D:\NMRDATA\ ZhangYZZ 22

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.33 (s, 1H), 8.70 (d, J = 0.5 Hz, 1H), 8.52 (d, J = 5.3 Hz, 1H), 8.11 − 8.00 (m, 1H), 7.93 − 7.85 (m, 1H), 7.83 (dd, J = 5.4, 0.5 Hz, 1H), 7.75 − 7.58 (m, 1H).

G (dd)
7.83

C (m)
8.05

D (s)
10.33

A (d)
8.52

B (m)
7.66

E (d)
8.70

F (m)
7.89

0.95

0.93
1.00
1.01
1.00
1.00
1.03

Figure S40 ^{1}H NMR spectrum of compound NPD-1184

^{13}C NMR (126 MHz, DMSO-d_6) δ 163.6 (d, J = 2.0 Hz), 152.0 (dd, J = 252.0, 12.7 Hz), 149.8, 149.2 (dd, J = 247.2, 13.1 Hz), 148.7, 142.3, 130.9 (dd, J = 5.3, 3.4 Hz), 125.8 (dd, J = 7.7, 3.5 Hz), 124.8, 120.2, 118.0 (d, J = 17.8 Hz), 117.6 (d, J = 18.6 Hz).

Figure S41 ^{13}C NMR spectrum of compound NPD-1184

PDA Graph

uV

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.498	548298	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 3.570-3.590(Scan#:358-360)
Mass Peaks:5 Base Peak:252.95(874331) Polarity:Pos Segment1 - Event1
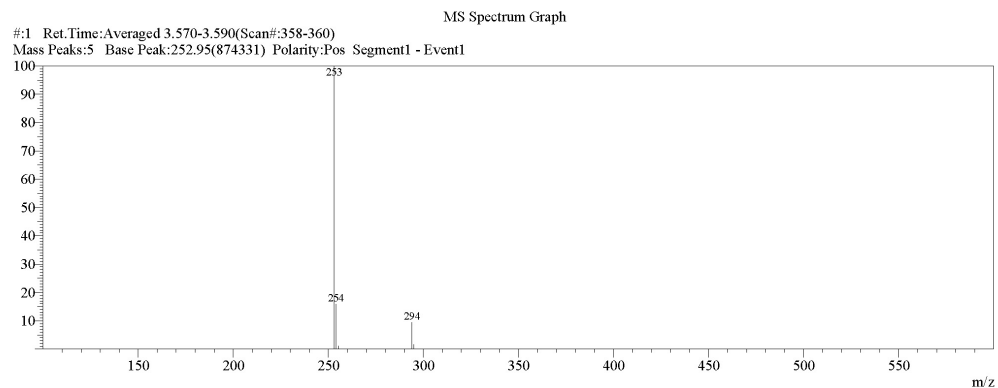
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.450<->3.780(346<->379)
Mass Peaks:5 Base Peak:252.95(874331) Polarity:Pos Segment1 - Event

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	252.95	874331	100.00				4	294.00	82311	9.41			
2	254.00	138589	15.85				5	294.90	14439	1.65			
3	255.25	9793	1.12										

Figure S42 LCMS spectrum of compound NPD-1185

¹H NMR (250 MHz, Chloroform-*d*) δ 8.49 (d, *J* = 2.3 Hz, 1H), 8.45 (d, *J* = 6.2 Hz, 1H), 8.41 (d, *J* = 5.4 Hz, 1H), 8.16 (s, 1H), 7.84 − 7.71 (m, 1H), 7.71 − 7.59 (m, 1H), 7.40 − 7.27 (m, 1H).

Figure S43 ¹H NMR spectrum of compound NPD-1185

¹³C NMR (126 MHz, DMSO-*d₆*) δ 163.9 (d, *J* = 2.1 Hz), 151.2 (d, *J* = 255.6 Hz), 152.0 (dd, *J* = 251.9, 12.6 Hz), 149.1 (dd, *J* = 246.9, 13.0 Hz), 146.4 (d, *J* = 5.3 Hz), 138.3 (d, *J* = 21.6 Hz), 133.1 (d, *J* = 9.4 Hz), 130.9 (dd, *J* = 5.3, 3.4 Hz), 125.9 (dd, *J* = 7.6, 3.4 Hz), 118.5 , 117.8 (d, *J* = 17.7 Hz), 117.8 (d, *J* = 18.6 Hz).
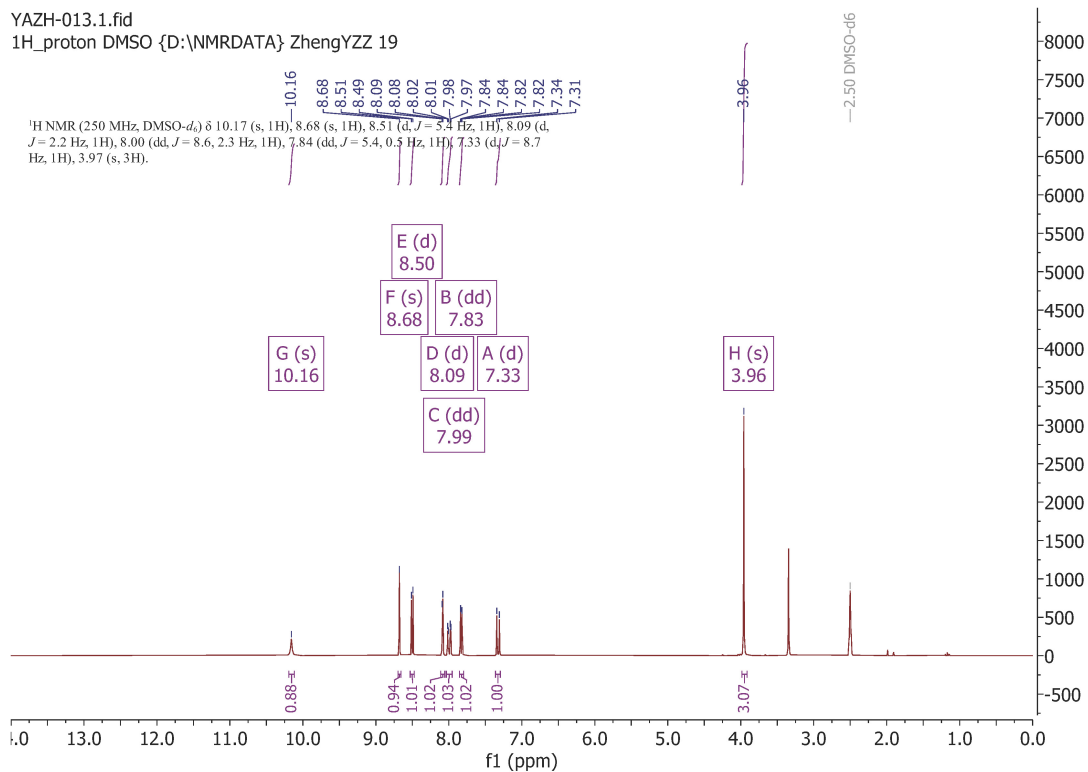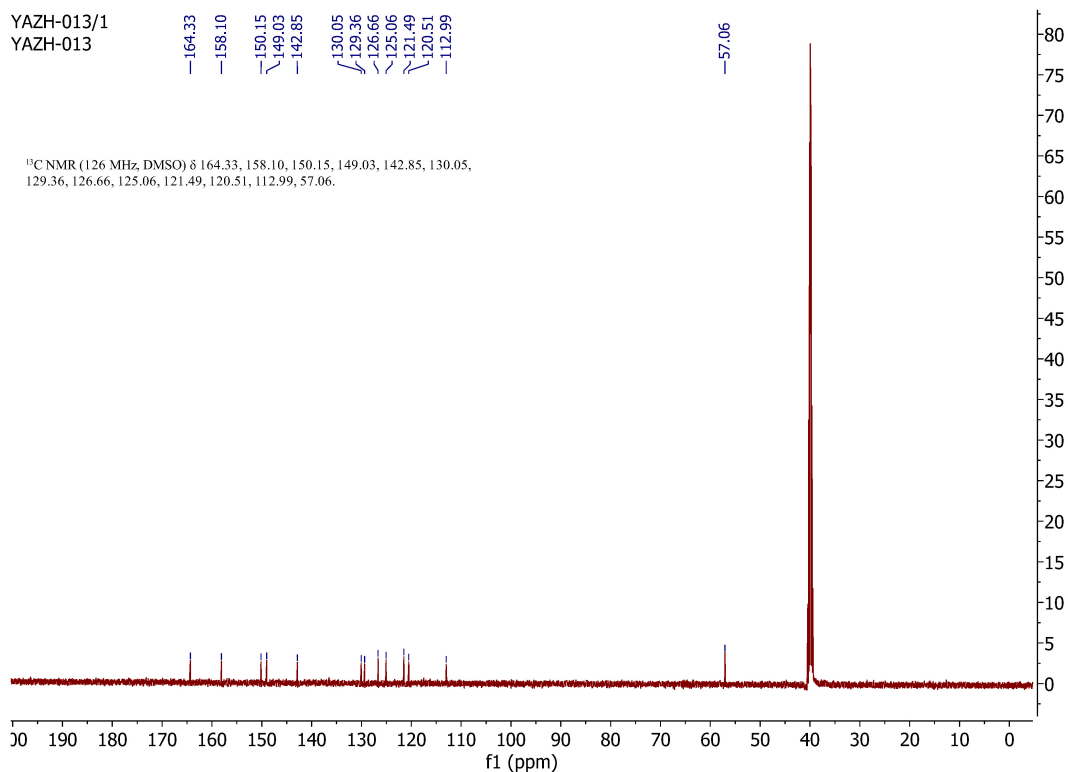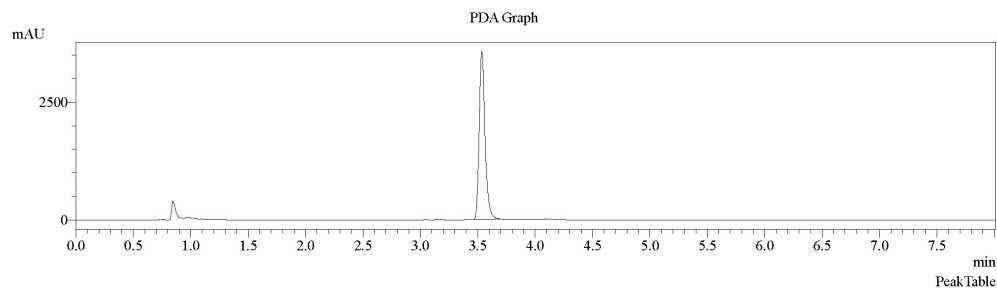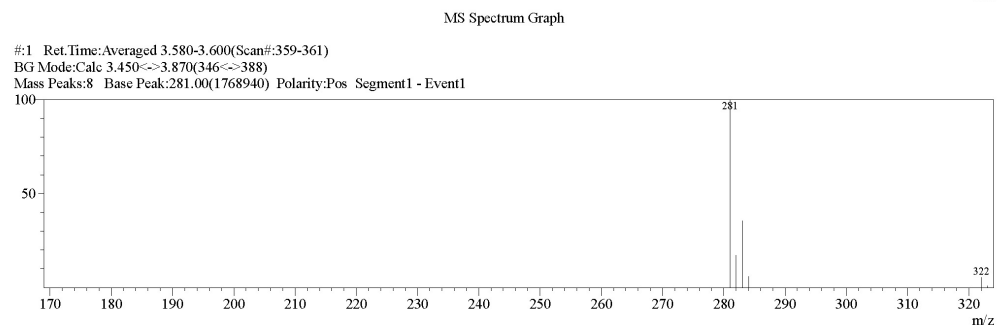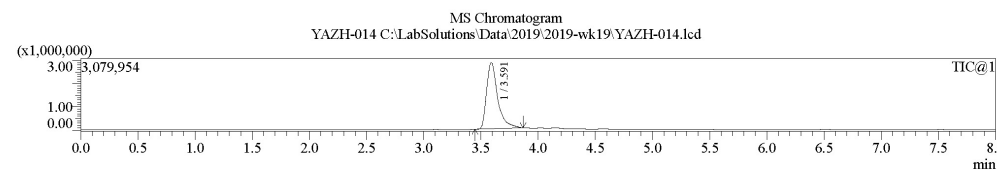
Figure S44 ¹³C NMR spectrum of compound NPD-1185

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Sample ID :
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Vial# : 37
Injection Volume : 3
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Background File : blanco 10052019.lcd
Method File : Method SCAN ACID standard.lcm
Report Format : DefaultLCMS.lcr
Tuning File : C:\LabSolutions\Tuning\Tuning-ESI-pos-neg01072015a.lct
Processed by : Admin
Modified Date : 10/5/2019 4:21:59 PM

PDA Graph

PeakTable

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.281	21243	0.502
2		3.808	4200066	99.252
3		4.153	10397	0.246

MS Chromatogram
YAZH-018 C:\LabSolutions\Data\2019\2019-wk19\YAZH-018.lcd

MS Spectrum Graph

#:1 Ret.Time:Averaged 3.860-3.880(Scan#:387-389)
BG Mode:Calc 3.730<->4.130(374<->414)
Mass Peaks:9 Base Peak:341.00(627181) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.730<->4.130(374<->414)
Mass Peaks:9 Base Peak:341.00(627181) Polarity:Pos Segment1 - Event1

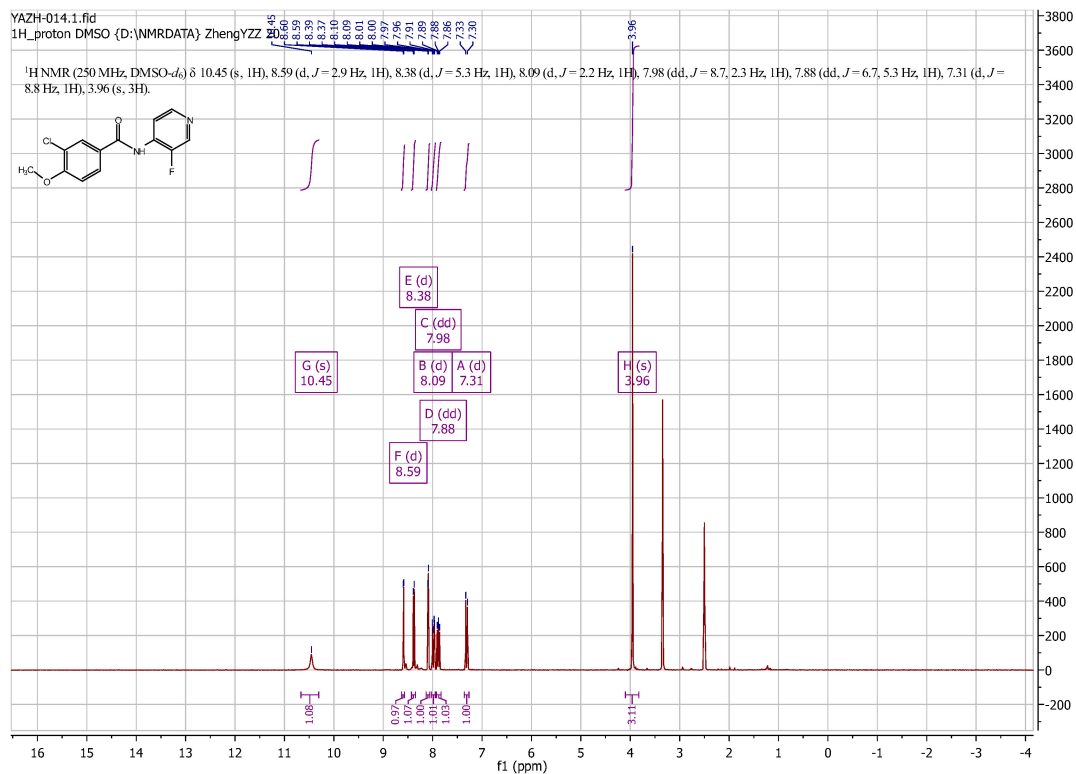| #	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	179.00	23933	3.82				6	345.05	66619	10.62			
2	341.00	627181	100.00				7	346.05	11028	1.76			
3	342.05	105030	16.75				8	382.00	40100	6.39			
4	343.00	394560	62.91				9	384.05	27033	4.31			
5	344.05	65299	10.41										

Figure S45 LCMS spectrum of compound NPD-1186

Figure S46 ¹H NMR spectrum of compound NPD-1186

¹H NMR (500 MHz, DMSO-*d₆*) δ 10.96 (s, 1H), 8.69 (s, 2H), 8.57 (d, *J* = 8.7 Hz, 1H), 8.33 (d, *J* = 7.8 Hz, 1H), 8.18 (d, *J* = 7.9 Hz, 1H), 7.83 (t, *J* = 7.8 Hz, 1H), 3.26 (s, 3H).

Figure S47 ¹³C NMR spectrum of compound NPD-1186

¹³C NMR (126 MHz, DMSO) δ 163.80, 148.61, 148.16, 141.72, 134.23, 133.41, 131.10, 130.99, 130.35, 126.91, 44.04.

66

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		2.693	1518425	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 2.770-2.790(Scan#:278-280)
Mass Peaks:11 Base Peak:297.95(344189) Polarity:Pos Segment1 - Event1

#:1 Ret.Time:
BG Mode:Calc 2.640<->3.010(265<->302)
Mass Peaks:11 Base Peak:297.95(344189) Polarity:Pos Segment1 - Event

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	297.95	344189	100.00				7	338.90	52191	15.16			
2	299.00	47397	13.77				8	339.95	4878	1.42			
3	299.95	195121	56.69				9	340.95	27680	8.04			
4	300.95	30774	8.94				10	341.95	5631	1.64			
5	301.90	37966	11.03				11	342.90	3658	1.06			
6	303.05	5665	1.65										

Figure S48 LCMS spectrum of compound NPD-1187

YAZH-022.1.fid
1H_proton DMSO {D:\NMRDATA} ZhengYZZ 23

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.41 (s, 1H), 8.74 (s, 2H), 8.57 (d, J = 2.6 Hz, 1H), 7.98 (dd, J = 9.5, 2.7 Hz, 1H), 6.50 (d, J = 9.5 Hz, 1H), 3.53 (s, 3H).

E (s)
10.41

D (s)
8.74

C (d)
8.57

B (dd)
7.98

A (d)
6.50

F (s)
3.53

Figure S49 ^{1}H NMR spectrum of compound NPD-1187

YAZH-022/1
YAZH-022

^{13}C NMR (126 MHz, DMSO) δ 162.62, 162.25, 148.76, 144.32, 141.60, 138.17, 130.91, 118.60, 111.06, 99.99, 37.96.

Figure S50 ^{13}C NMR spectrum of compound NPD-1187

68

PDA Graph

uV

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		2.286	1098596	95.233
2		3.469	19853	1.721
3		3.897	35139	3.046

MS Spectrum Graph

#:1 Ret.Time:Averaged 2.350-2.370(Scan#:236-238)
Mass Peaks:5 Base Peak:264.00(981666) Polarity:Pos Segment1 - Event1
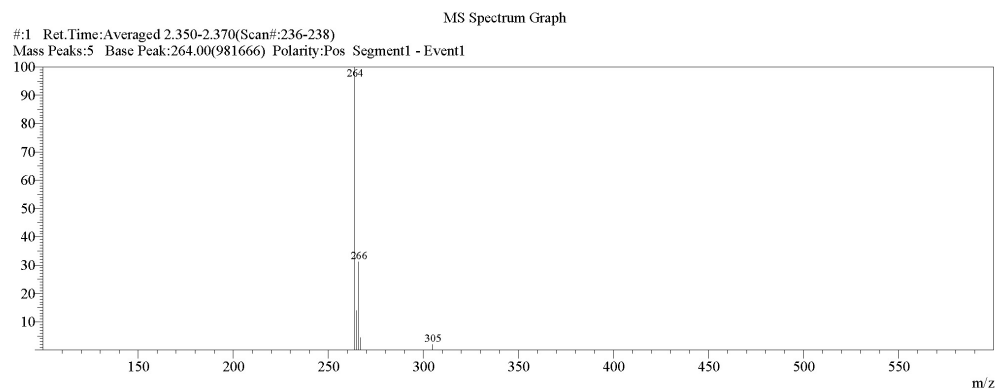
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 2.230<->2.610(224<->262)
Mass Peaks:5 Base Peak:264.00(981666) Polarity:Pos Segment1 - Event

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	264.00	981666	100.00				4	266.95	42805	4.36			
2	265.00	137234	13.98				5	304.95	19192	1.96			
3	266.00	305677	31.14										

Figure S51 LCMS spectrum of compound NPD-1188

^{1}H NMR (250 MHz, DMSO-d_6) δ 8.66 (s, 1H), 8.60 (d, J = 2.6 Hz, 1H), 8.48 (d, J = 5.4 Hz, 1H), 7.94 (dd, J = 9.5, 2.7 Hz, 1H), 7.82 (d, J = 5.4 Hz, 1H), 6.48 (d, J = 9.6 Hz, 1H), 1.89 (s, 3H).

B (d)
8.60

E (d)
7.82

A (s)
8.66

D (dd)
7.94

F (d)
6.48

H (s)
1.89

C (d)
8.48
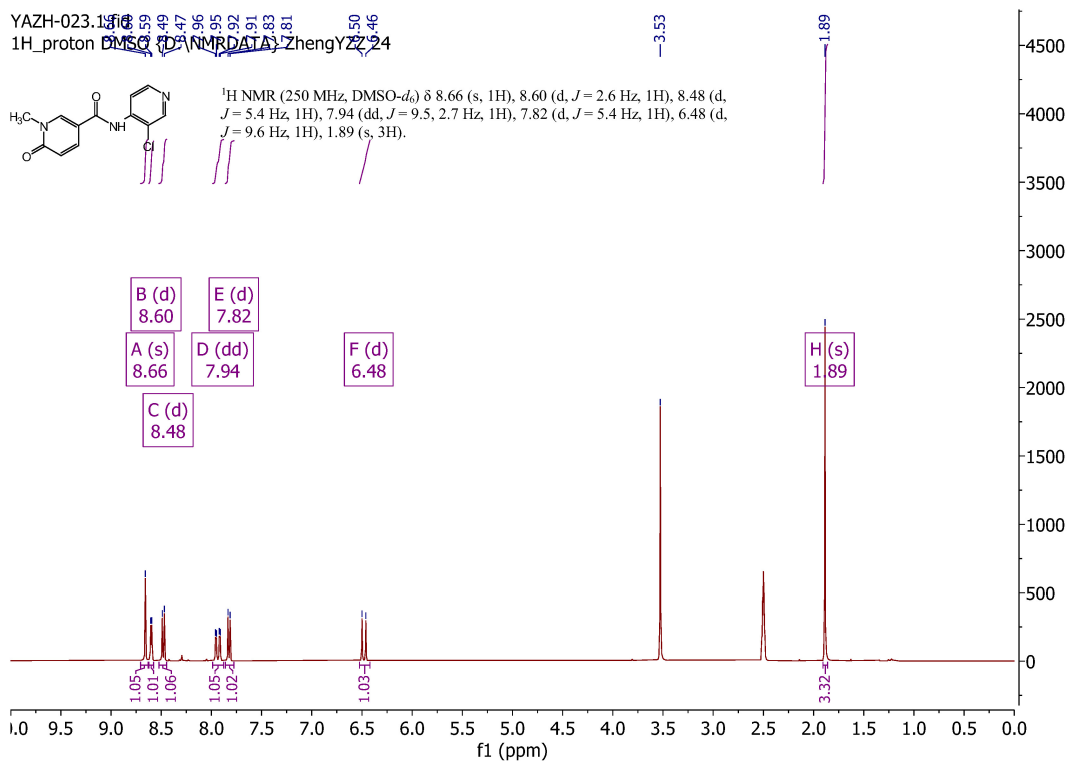
Figure S52 ^{1}H NMR spectrum of compound NPD-1188

^{13}C NMR (126 MHz, DMSO) δ 172.3, 163.0, 161.8, 149.7, 148.6, 143.9, 142.5, 138.1, 123.9, 119.4, 118.0, 111.4, 37.5, 21.4.
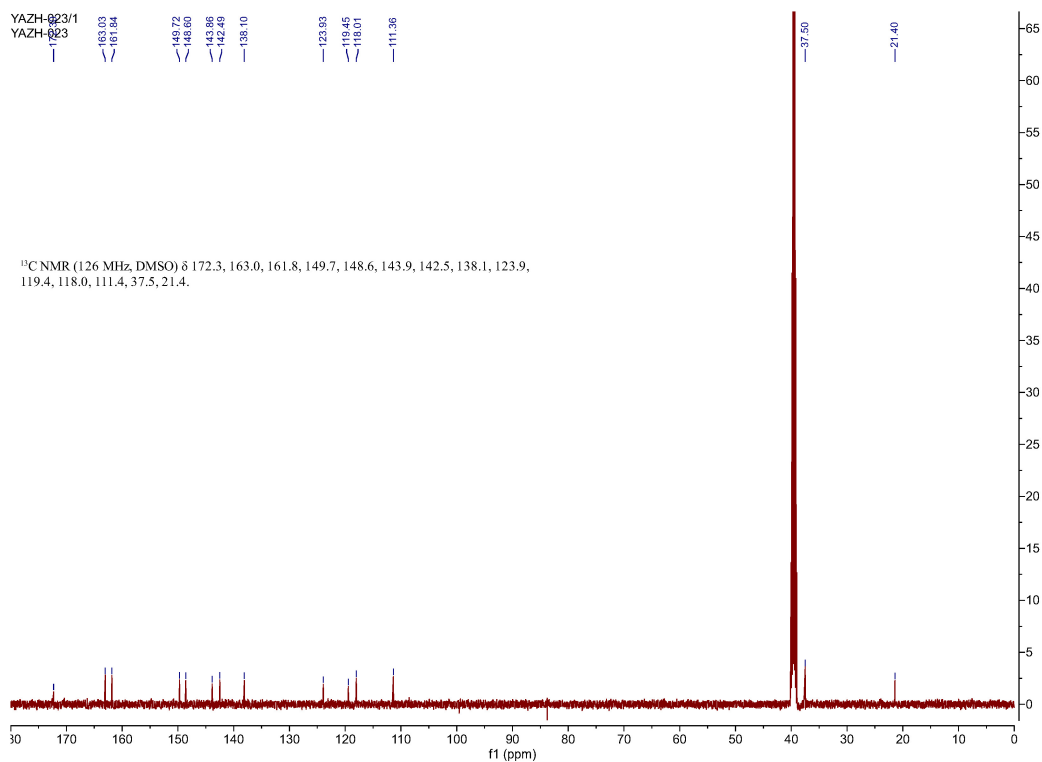
Figure S53 ^{13}C NMR spectrum of compound NPD-1188

Medicinal Chemistry
Vrije Universiteit Amsterdam

PDA Graph

mAU
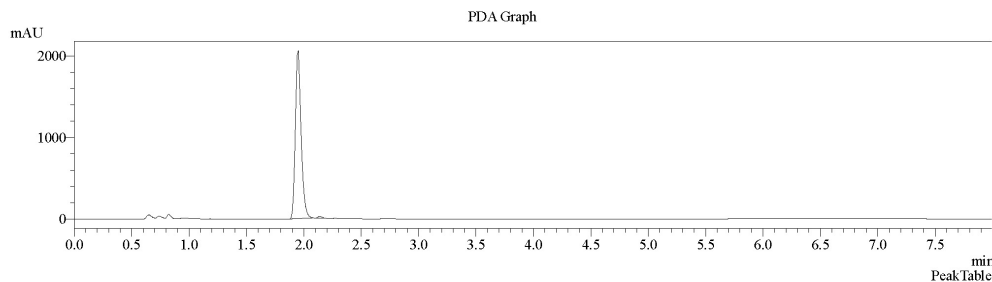
PDA Ch1 254nm 4nm
PeakTable

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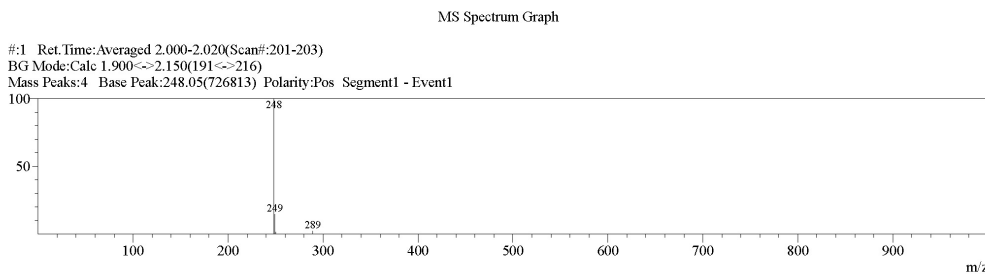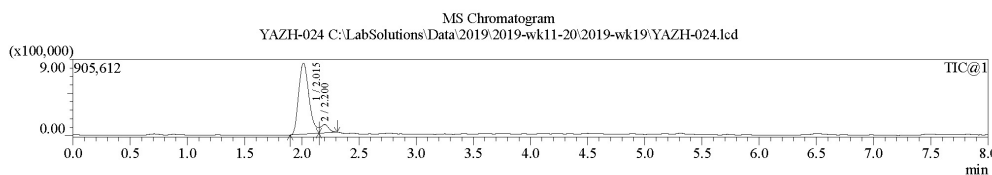
MS Chromatogram
YAZH-024 C:\LabSolutions\Data\2019\2019-wk11-20\2019-wk19\YAZH-024.lcd

(x100,000)

MS Spectrum Graph

#:1   Ret.Time:Averaged 2.000-2.020(Scan#:201-203)
BG Mode:Calc 1.900<->2.150(191<->216)
Mass Peaks:4   Base Peak:248.05(726813) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1   Ret.Time:
BG Mode:Calc 1.900<->2.150(191<->216)
Mass Peaks:4   Base Peak:248.05(726813) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	248.05	726813	100.00				3	250.05	11223	1.54			
2	249.00	107663	14.81				4	289.05	17644	2.43			

Figure S54 LCMS spectrum of compound NPD-1189

YAZH-024.1.fid
1H_proton DMSO {D:\NMRDATA} ZhengYZZ 25

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.20 (s, 1H), 8.61 − 8.55 (m, 2H), 8.36 (d, J = 5.3 Hz, 1H), 7.94 − 7.87 (m, 2H), 6.46 (d, J = 9.5 Hz, 1H), 3.51 (s, 3H).

A (s)	B (m)	C (d)	D (m)	E (d)	F (s)
10.20	8.58	8.36	7.91	6.46	3.51

Figure S55 ^{1}H NMR spectrum of compound NPD-1189

YAZH-024/3

^{13}C NMR (126 MHz, DMSO-d_6) δ 163.3 , 161.8 , 150.8 (d, J = 255.1 Hz), 146.4 (d, J = 5.1 Hz), 143.9 , 138.3 , 138.1 (d, J = 21.7 Hz), 133.4 (d, J = 9.0 Hz), 118.0 , 117.8 , 111.3 , 37.5 .
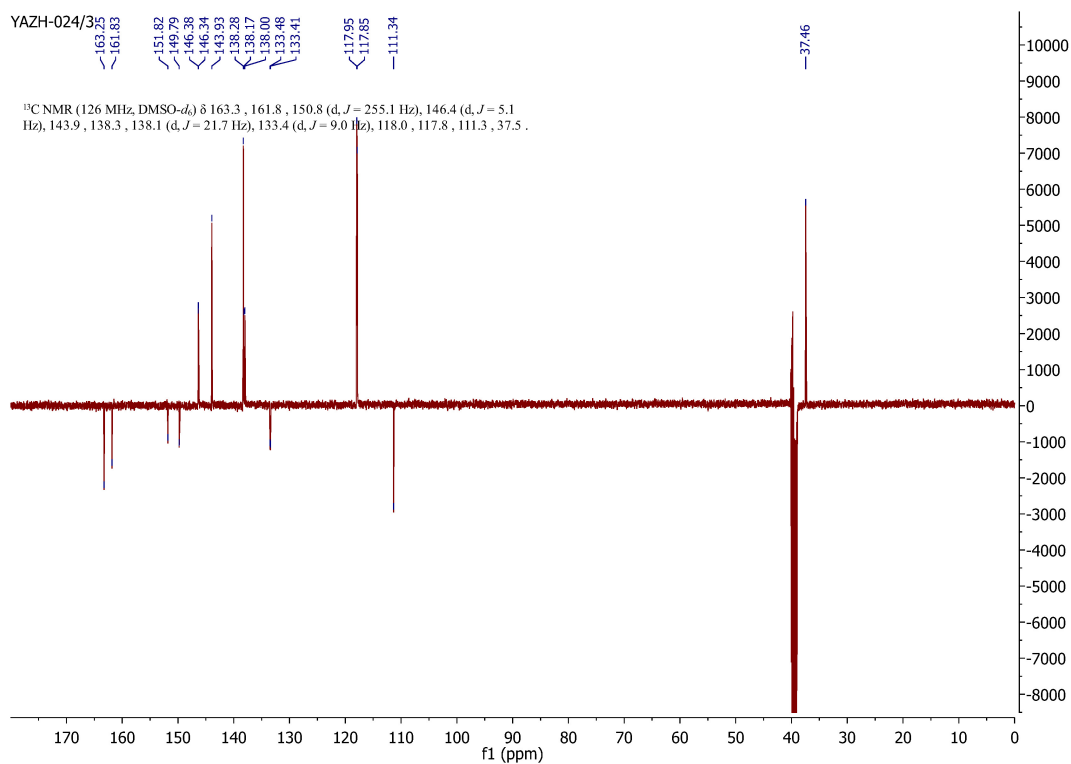
Figure S56 ^{13}C NMR spectrum of compound NPD-1189

72

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Sample ID :
Tray# : 1
Vial# : 29
Injection Volume : 3
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Background File : blanco 10052019.lcd
Method File : Method SCAN ACID standard.lcm
Report Format : DefaultLCMS.lcr
Tuning File : C:\LabSolutions\Tuning\Tuning-ESI-pos-neg01072015a.lct
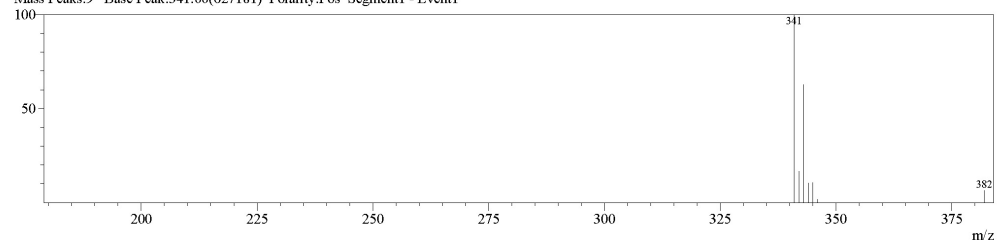Processed by : Admin
Modified Date : 10/5/2019 5:00:29 PM

PDA Graph

mAU

PeakTable
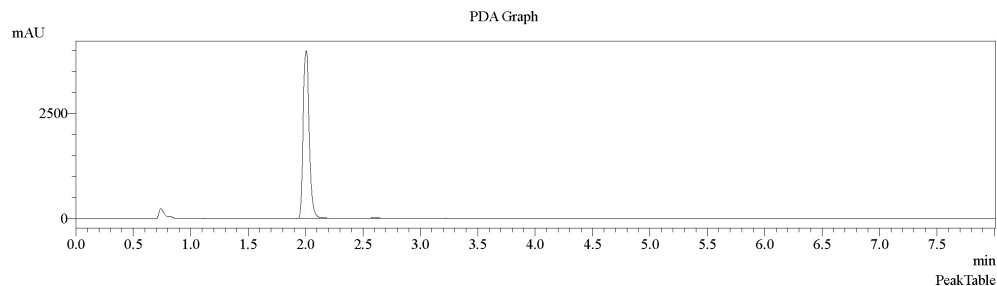
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		2.001	14532492	99.441
2		2.598	81620	0.559

MS Chromatogram
YAZH-029 C:\LabSolutions\Data\2019\2019-wk19\YAZH-029.lcd

(x1,000,000)
1.40 1,420,616   TIC@1

MS Spectrum Graph

#:1 Ret.Time:Averaged 2.050-2.070(Scan#:206-208)
BG Mode:Calc 1.940<->2.340(195<->235)
Mass Peaks:4 Base Peak:248.00(1149468) Polarity:Pos Segment1 - Event1
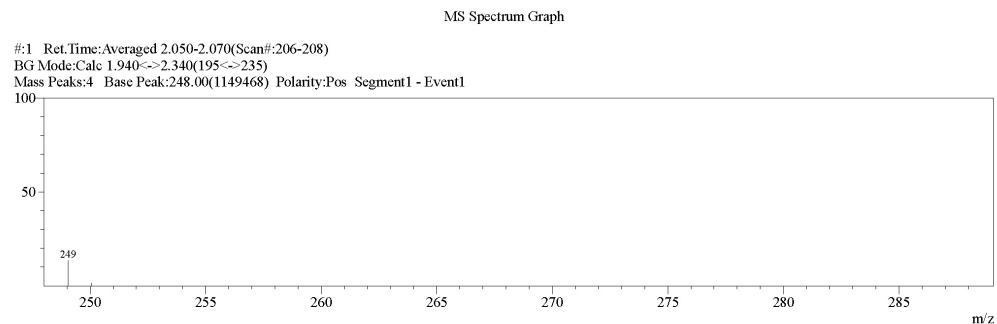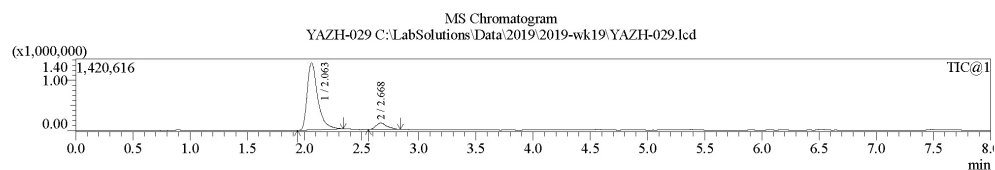
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 1.940<->2.340(195<->235)
Mass Peaks:4 Base Peak:248.00(1149468) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	248.00	1149468	100.00				3	250.05	16702	1.45			
2	249.05	154747	13.46				4	289.10	32360	2.82			

Figure S57 LCMS spectrum of compound NPD-1190

YAZH-029.1.fid
1H_proton DMSO {D:\NMRDATA} ZhengYZZ-27

^{1}H NMR (250 MHz, DMSO-d_6) δ 8.55 (d, J = 2.9 Hz, 1H),
8.35 (d, J = 5.3 Hz, 1H), 7.93 − 7.78 (m, 2H), 6.94 (d, J = 1.6
Hz, 1H), 6.60 (dd, J = 7.0, 2.0 Hz, 1H), 3.47 (s, 3H).

B (d)
10.64

E (dd)
8.89

A (d)
10.84

C (m)
10.15

D (d)
9.23

G (s)
5.76

Figure S58 ^{1}H NMR spectrum of compound NPD-1190

YAZH-029/39

^{13}C NMR (126 MHz, DMSO-d_6) δ 164.5 , 161.7 , 151.5 (d, J = 255.8 Hz), 146.2 (d, J = 5.1
Hz), 144.9 , 140.2 , 138.1 (d, J = 21.9 Hz), 134.4 , 118.8 , 118.4 , 103.2 , 36.9 .

Figure S59 ^{13}C NMR spectrum of compound NPD-1190

74

PDA Graph

uV

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.366	967925	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 3.430-3.450(Scan#:344-346)
Mass Peaks:6 Base Peak:263.95(1119848) Polarity:Pos Segment1 - Event1

#:1 Ret.Time:
BG Mode:Calc 3.290<->3.650(330<->366)
Mass Peaks:6 Base Peak:263.95(1119848) Polarity:Pos Segment1 - Event

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	263.95	1119848	100.00				4	267.05	47817	4.27			
2	265.00	175976	15.71				5	305.05	50223	4.48			
3	266.00	368548	32.91				6	306.95	11456	1.02			

Figure S60 LCMS spectrum of compound NPD-1191

75

YAZH-031.1.fid
1H_proton DMSO {D:\NMRDATA} ZhengYZZ-28

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.20 (s, 1H), 8.81 (d, J = 2.1 Hz, 1H), 8.68 (s, 1H), 8.51 (d, J = 5.4 Hz, 1H), 8.24 (dd, J = 8.7, 2.5 Hz, 1H), 7.89 (d, J = 5.4 Hz, 1H), 6.98 (d, J = 8.7 Hz, 1H), 3.95 (s, 3H).

G (s)
10.20

F (d)
8.81

C (dd)
8.24

D (d)
8.51

B (d)
7.89

A (d)
6.98

H (s)
3.95

E (s)
8.68

Figure S61 ^{1}H NMR spectrum of compound NPD-1191

YAZH-031/1
YAZH-031

^{13}C NMR (126 MHz, DMSO) δ 166.27, 164.49, 150.17, 149.08, 148.52, 142.72, 139.37, 124.70, 123.39, 120.14, 110.88, 54.34.

Figure S62 ^{13}C NMR spectrum of compound NPD-1191

76

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.388	529345	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 3.460-3.480(Scan#:347-349)
Mass Peaks:5 Base Peak:262.05(1018880) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.330<->3.700(334<->371)
Mass Peaks:5 Base Peak:262.05(1018880) Polarity:Pos Segment1 - Event

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	262.05	1018880	100.00				4	303.05	91380	8.97			
2	263.05	175193	17.19				5	304.05	20228	1.99			
3	264.05	20439	2.01										

Figure S63 LCMS spectrum of compound NPD-1192

YAZH-035.1.fid
1H_proton DMSO {D:\NMRDATA} ZhengYZZ 30

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.69 (s, 1H), 8.61 (d, J = 2.8 Hz, 1H), 8.40 (d, J = 5.3 Hz, 1H), 8.34 (dd, J = 5.3, 0.8 Hz, 1H), 7.91 (dd, J = 6.7, 5.3 Hz, 1H), 7.40 (dd, J = 5.3, 1.5 Hz, 1H), 7.27 (dd, J = 1.5, 0.8 Hz, 1H), 4.36 (q, J = 7.0 Hz, 2H), 1.33 (t, J = 7.0 Hz, 3H).

G (s)
10.69

B (d)
8.40

E (dd)
7.40

A (d)
8.61

D (dd)
7.91

C (dd)
8.34

F (dd)
7.27

H (q)
4.36

I (t)
1.33

Figure S64 ^{1}H NMR spectrum of compound NPD-1192

YAZH-035/$

^{13}C NMR (126 MHz, DMSO-d_6) δ 164.4 , 163.7 , 151.2 (d, J = 256.2 Hz), 147.9 , 146.4 (d, J = 5.3 Hz),
143.9 , 138.3 (d, J = 21.7 Hz), 132.9 (d, J = 9.3 Hz), 118.6 , 115.0 , 109.4 , 61.8 , 14.5 .

Figure S65 ^{13}C NMR spectrum of compound NPD-1192

78

PDA Graph

uV

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.828	358888	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 3.890-3.910(Scan#:390-392)
Mass Peaks:6 Base Peak:307.05(1032243) Polarity:Pos Segment1 - Event1

m/z

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.750<->4.170(376<->418)
Mass Peaks:6 Base Peak:307.05(1032243) Polarity:Pos Segment1 - Event

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	179.00	27516	2.67				4	309.00	375372	36.36			
2	307.05	1032243	100.00				5	310.05	56840	5.51			
3	308.05	187211	18.14				6	348.10	21337	2.07			

Figure S66 LCMS spectrum of compound NPD-1193

YAZH-036.2.fid
1H_proton DMSO {D:\NMRDATA} ZhengYZZ 56

^{1}H NMR (250 MHz, DMSO-d_6) δ 9.94 (s, 1H), 8.67 (s, 1H), 8.49 (d, J = 5.4 Hz, 1H), 7.86 (d, J = 5.4 Hz, 1H), 7.64 (dd, J = 8.4, 2.1 Hz, 1H), 7.54 (d, J = 2.1 Hz, 1H), 7.11 (d, J = 8.5 Hz, 1H), 4.09 (q, J = 7.0 Hz, 2H), 3.85 (s, 3H), 1.36 (t, J = 6.9 Hz, 3H).

G (s)
9.94

F (s)
8.67

C (dd)
7.64

A (d)
8.49
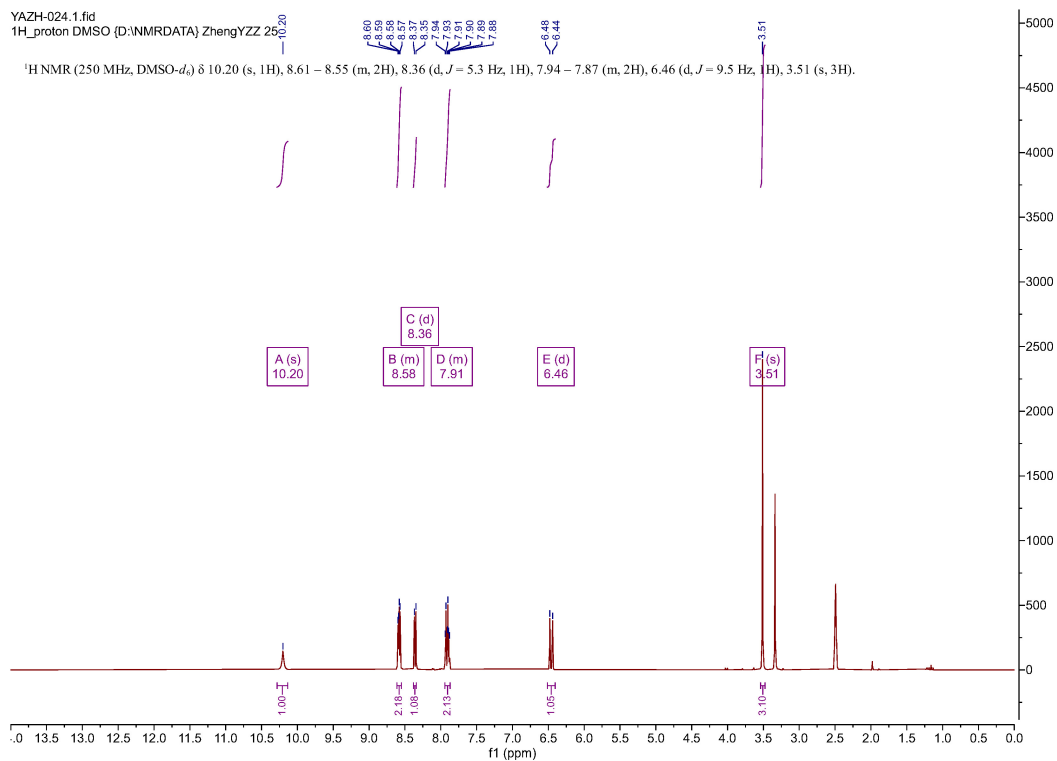
B (d)
7.86

E (d)
7.11

D (d)
7.54

I (s)
3.85

H (q)
4.09

J (t)
1.36

Figure S67 ^{1}H NMR spectrum of compound NPD-1193

YAZH-036/1
YAZH-036

^{13}C NMR (126 MHz, DMSO) δ 165.39, 152.84, 150.06, 149.02, 148.09, 143.05, 125.83, 124.79, 121.96, 120.15, 112.39, 111.56, 64.33, 56.15, 15.15.

Figure S68 ^{13}C NMR spectrum of compound NPD-1193

80

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.008	570367	100.000

MS Spectrum Graph

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Mass Peaks:10   Base Peak:311.95(1102667) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1   Ret.Time:
BG Mode:Calc 3.940<->4.290(395<->430
Mass Peaks:10   Base Peak:311.95(1102667) Polarity:Pos Segment1 - Event

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	284.00	27661	2.51				6	315.00	124002	11.25			
2	286.10	11507	1.04				7	316.00	133888	12.14			
3	311.95	1102667	100.00				8	316.90	20365	1.85			
4	313.00	169450	15.37				9	353.00	55551	5.04			
5	314.00	808420	73.31				10	355.05	39760	3.61			

Figure S69 LCMS spectrum of compound NPD-1194

8.79
8.40
8.40
8.38
8.38
7.47
7.46
7.45
7.44
7.32
7.32
7.32
7.32
10.95
4.43
4.40
4.37
4.34
1.38
1.35
1.32

1H NMR (250 MHz, DMSO-d_6) δ 10.95 (s, 1H), 8.79 (s, 2H), 8.39 (dd, J = 5.3, 0.6 Hz, 2H), 7.45 (d, J = 5.3, 1.5 Hz, 1H), 7.35 − 7.28 (m, 1H), 4.38 (q, J = 7.0 Hz, 2H), 1.35 (t, J = 7.0 Hz, 3H).

D (s) 8.79		C (m) 7.32
E (s) 10.95	A (dd) 8.39	B (d) 7.45
	F (q) 4.38	G (t) 1.35

0.93
1.90
1.61
1.01
1.01
2.05
3.07

14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 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
f1 (ppm)

Figure S70 ^{1}H NMR spectrum of compound NPD-1194

164.29
163.67
148.87
148.69
143.34
140.98
131.09
115.17
109.54
62.30
14.90

13C NMR (126 MHz, DMSO) δ 164.29, 163.67, 148.87, 148.69, 143.34, 140.98, 131.09, 115.17, 109.54, 62.30, 14.90.

00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Figure S71 ^{13}C NMR spectrum of compound NPD-1194

PDA Graph
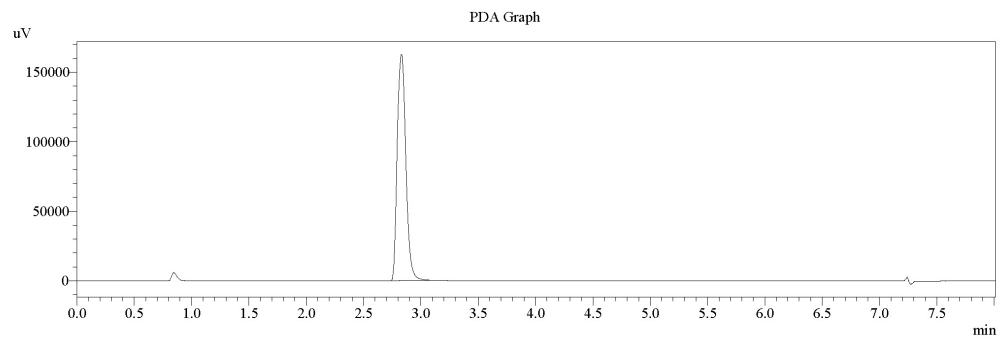
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
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MS Spectrum Graph

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MS Spectrum Table

#:1 Ret.Time:
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Mass Peaks:4 Base Peak:247.95(1162640) Polarity:Pos Segment1 - Event

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1	247.95	1162640	100.00				3	249.95	17045	1.47			
2	249.05	162346	13.96				4	288.95	38528	3.31			

Figure S72 LCMS spectrum of compound NPD-1195

83

YAZH-067.1.fid
1H_proton DMSO {D:\NMRDATA} Zheng YZZ 479

^{1}H NMR (250 MHz, DMSO-d_6) δ 10.51 (s, 1H), 8.78 (dd, J = 2.5, 0.8 Hz, 1H), 8.59 (d, J = 2.8 Hz, 1H), 8.38 (d, J = 5.3 Hz, 1H), 8.22 (dd, J = 8.7, 2.5 Hz, 1H), 7.93 (dd, J = 6.7, 5.3 Hz, 1H), 6.96 (dd, J = 8.7, 0.7 Hz, 1H), 3.93 (s, 3H).

| D (dd) 8.22 |
| B (d) 8.59 |

| G (s) 10.51 | A (dd) 8.78 | E (dd) 7.93 | F (dd) 6.96 | H (s) 3.93 |

| C (d) 8.38 |

f1 (ppm)

Figure S73 ^{1}H NMR spectrum of compound NPD-1195

YAZH-067.1.fid
YAZH-067.1.fid

^{13}C NMR (126 MHz, DMSO-d_6) δ 166.2 , 164.8 , 151.5 (d, J = 255.6 Hz), 148.7 , 146.8 (d, J = 5.2 Hz), 139.5 , 138.6 (d, J = 21.6 Hz), 133.8 (d, J = 9.3 Hz), 123.5 , 118.7 , 110.7 , 54.3 .

f1 (ppm)

Figure S74 ^{13}C NMR spectrum of compound NPD-1195

84

PDA Graph

uV

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.271	2209356	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.360-4.420(Scan#:436-442)
Mass Peaks:6   Base Peak:357.02(2049230) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:None
Mass Peaks:6   Base Peak:357.02(2015727) Polarity:Pos Segment1 - Event

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	194.94	182373	9.05				4	359.01	1331645	66.06			
2	357.02	2015727	100.00				5	359.94	226471	11.24			
3	358.01	398416	19.77				6	360.94	214688	10.65			

Figure S75 LCMS spectrum of compound NPD-1196

85

YAZH-095/1
YAZH-095

^{1}H NMR (500 MHz, Chloroform-*d*) δ 10.01 (s, 1H), 8.56 (s, 2H), 7.99 (d, *J* = 9.0 Hz, 1H), 6.84 (d, *J* = 9.0 Hz, 1H), 4.16 (s, 3H), 3.95 (s, 3H), 3.92 (s, 3H).

Figure S76 ^{1}H NMR spectrum of compound NPD-1196

YAZH-095.2.fid
YAZH-095

^{13}C NMR (126 MHz, CDCl₃) δ 162.0, 157.8, 152.7, 148.0, 141.8, 140.9, 129.5, 127.7, 117.2, 108.0, 62.5, 61.2.

Figure S77 ^{13}C NMR spectrum of compound NPD-1196

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Sample ID :
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Vial# : 3
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Method File : Method SCAN ACID standard.lcm
Report Format : DefaultLCMS.lcr
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Processed by : Admin
Modified Date : 13/5/2019 10:57:10 AM

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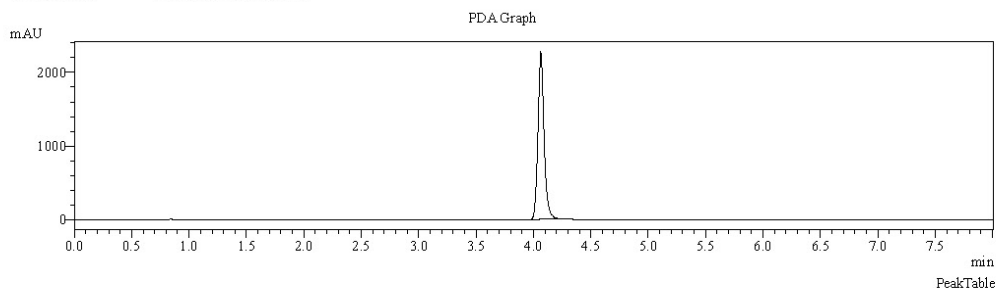
Peak#	Name	Ret. Time	Area	Area %
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MS Chromatogram
VUF15577 C:\LabSolutions\Data\2019\2019-wk20\VUF15577.lcd

MS Spectrum Graph

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Mass Peaks:6 Base Peak:323.05(2105968) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#1 Ret.Time:
BG Mode:Calc 3.980<->4.450(399<->446)
Mass Peaks:6 Base Peak:323.05(2105968) Polarity:Pos Segment1 - Event1
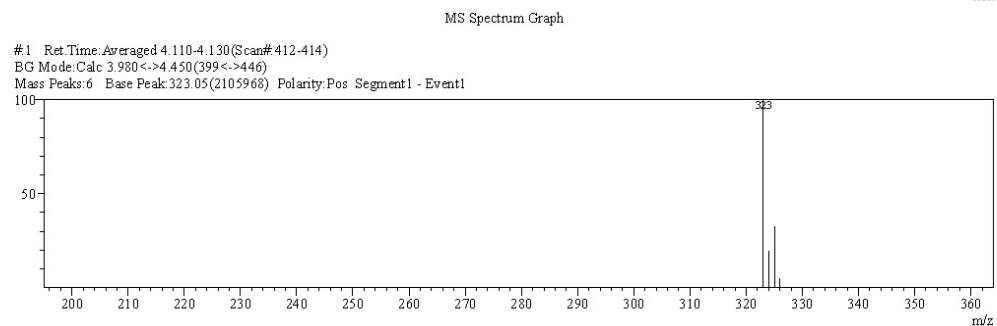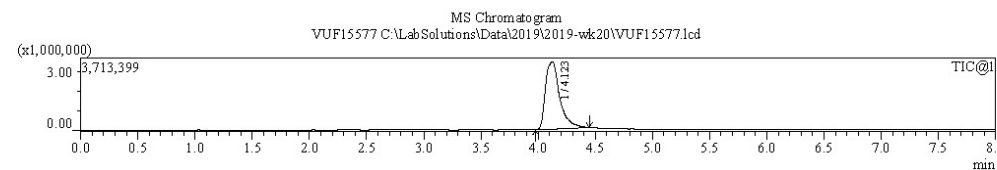
#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	195.00	68515	3.25				4	325.05	682617	32.41			
2	323.05	2105968	100.00				5	326.05	104359	4.96			
3	324.05	412686	19.60				6	364.05	58990	2.80			

Figure S78 LCMS spectrum of compound NPD-1197

YAZH-096.1.fid
YAZH-096
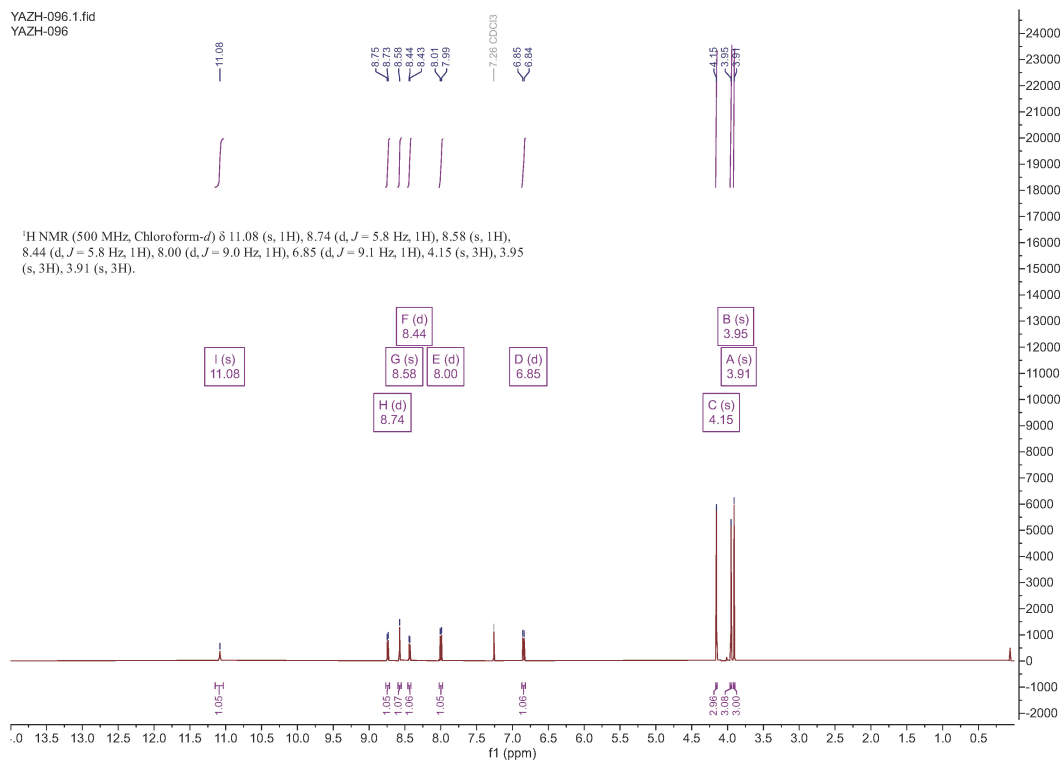
Figure S79 ¹H NMR spectrum of compound NPD-1197

YAZH-096/2
YAZH-096
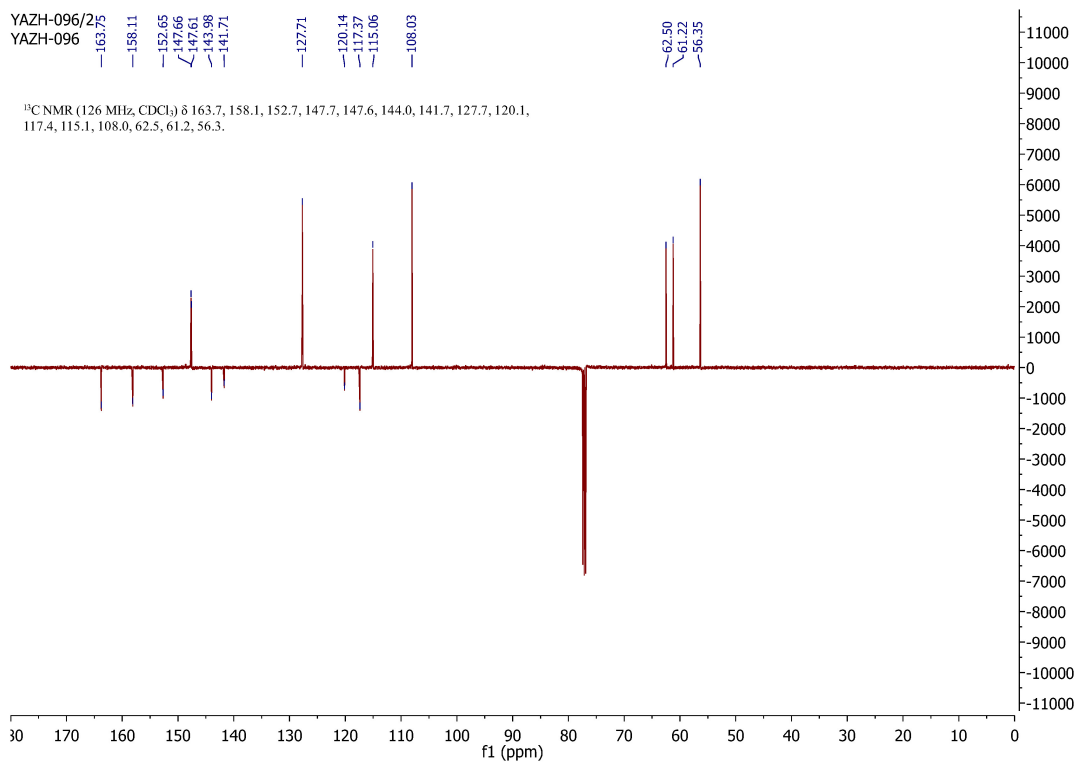
Figure S80 ¹³C NMR spectrum of compound NPD-1197

88

PDA Graph
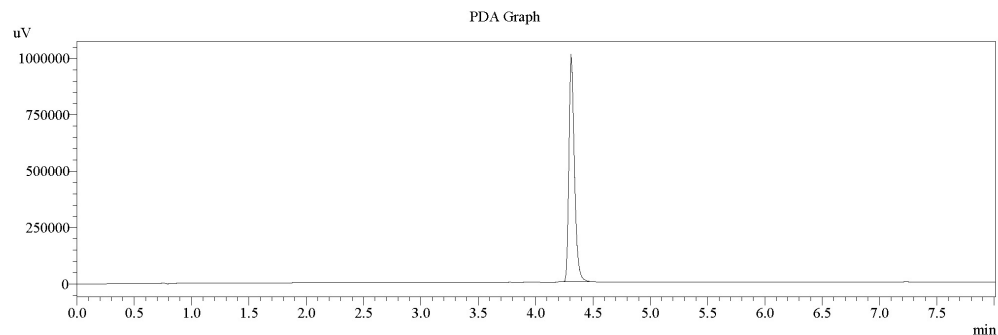
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.306	3356031	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.410-4.450(Scan#:441-445)
Mass Peaks:7   Base Peak:345.83(887348) Polarity:Pos Segment1 - Event1
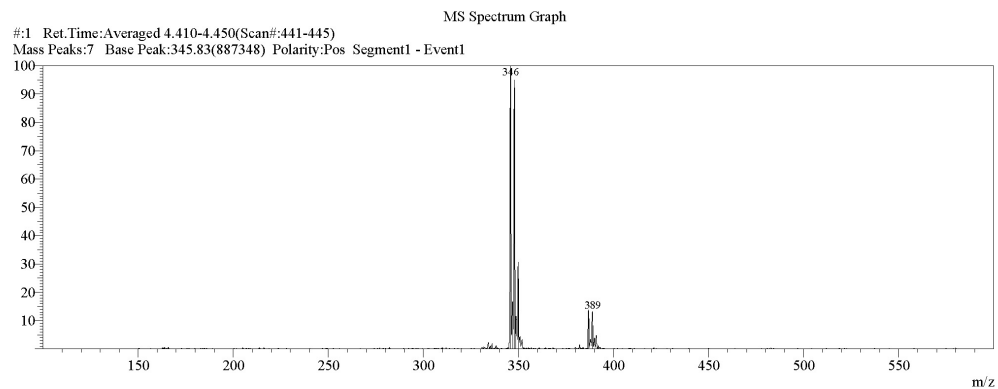
MS Spectrum Table

#:1 Ret.Time:
BG Mode:None
Mass Peaks:7 Base Peak:345.83(804222) Polarity:Pos Segment1 - Event

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	345.83	804222	100.00				5	349.89	231288	28.76			
2	346.96	125677	15.63				6	386.91	105571	13.13			
3	347.89	786867	97.84				7	388.97	109803	13.65			
4	348.76	99929	12.43										

Figure S81 LCMS spectrum of compound NPD-1198

89

YAZH-097/1
YAZH-097

1H NMR (500 MHz, Chloroform-*d*) δ 10.44 (s, 1H), 8.74 – 8.67 (m, 1H), 8.52 (d, *J* = 1.0 Hz, 2H), 8.24 – 8.19 (m, 1H), 7.63 (dd, *J* = 8.4, 1.1 Hz, 1H).

E (s)
10.44

B (m)
8.21

C (d)
8.52

A (dd)
7.63

D (m)
8.70

Figure S82 1H NMR spectrum of compound NPD-1198

YAZH-097/2
YAZH-097

13C NMR (126 MHz, CDCl3) δ 162.4, 148.1, 147.6, 140.7, 133.3, 132.6, 132.1, 130.8, 130.8, 125.5.

Figure S83 13C NMR spectrum of compound NPD-1198
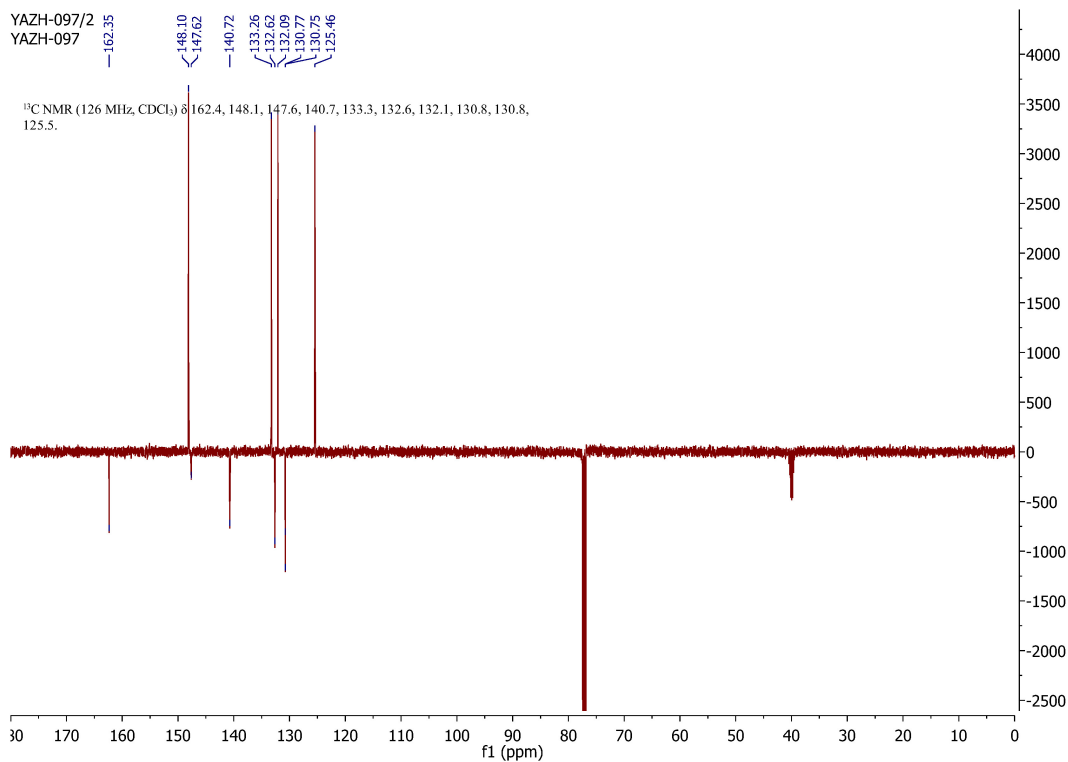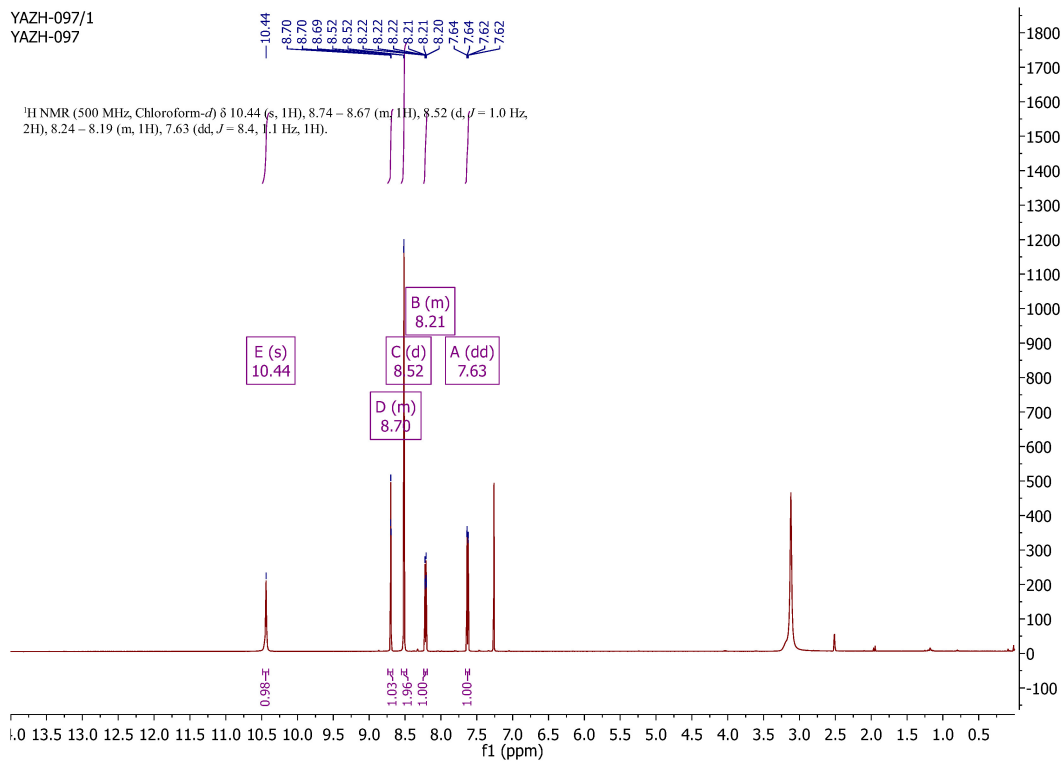
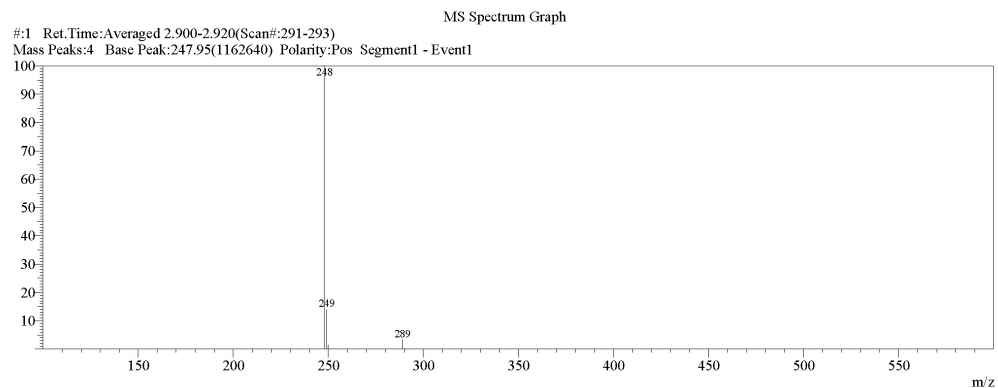Acquired by   : Admin
Date Acquired   : 1/26/2016 7:23:57 PM
Sample Name   : Jay compound 74
Sample ID   :
Tray#   : 1
Vial#   : 21
Injection Volume   : 1
Data File   : C:\LabSolutions\Methods\FAR Pract Jay compound 74.lcd
Background File   : Blanco-2 26012016.lcd
Method File   : Method SCAN ACID standard.lcm
Report Format   : DefaultLCMS.lcr
Tuning File   : C:\LabSolutions\Tuning File\Tuning-ESI-pos-neg01072015.lct
Processed by   : Admin
Modified Date   : 1/27/2016 9:50:12 AM

PDA Graph
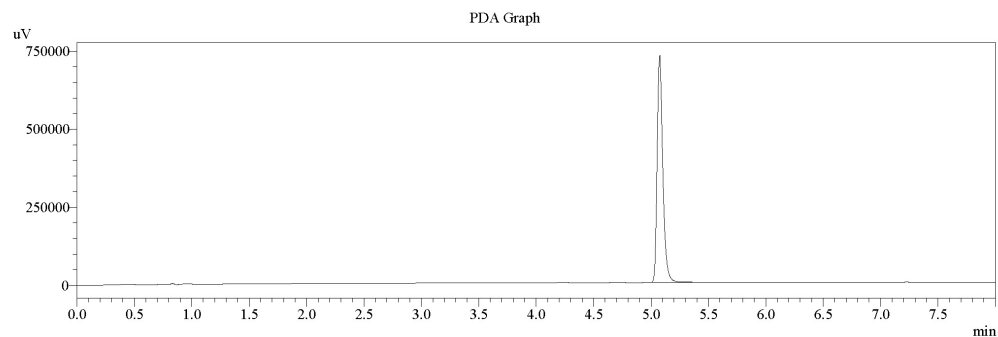
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		5.070	2494903	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 5.170-5.240(Scan#:517-524)
Mass Peaks:8   Base Peak:452.95(634766) Polarity:Pos Segment1 - Event1

MS Spectrum Table
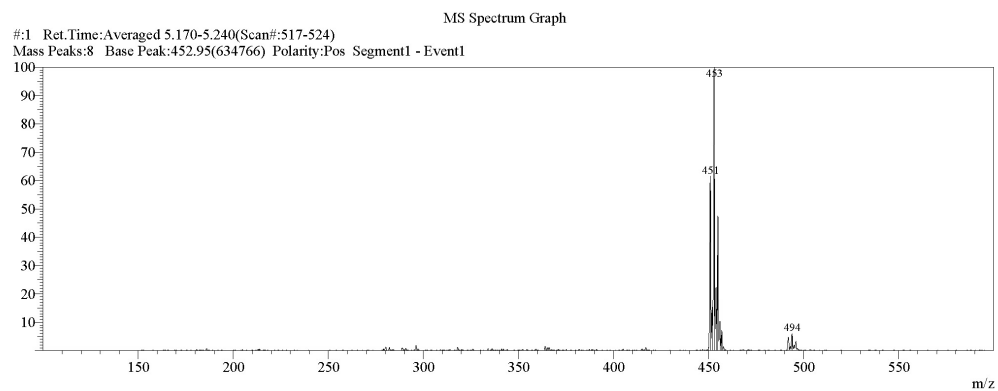
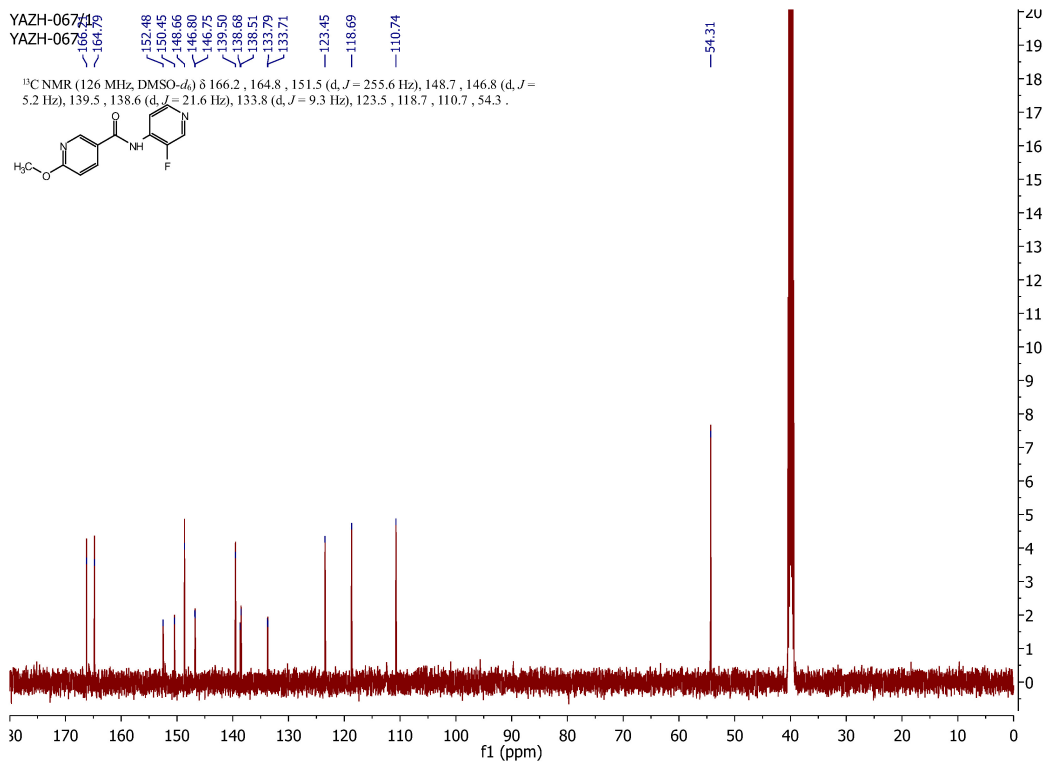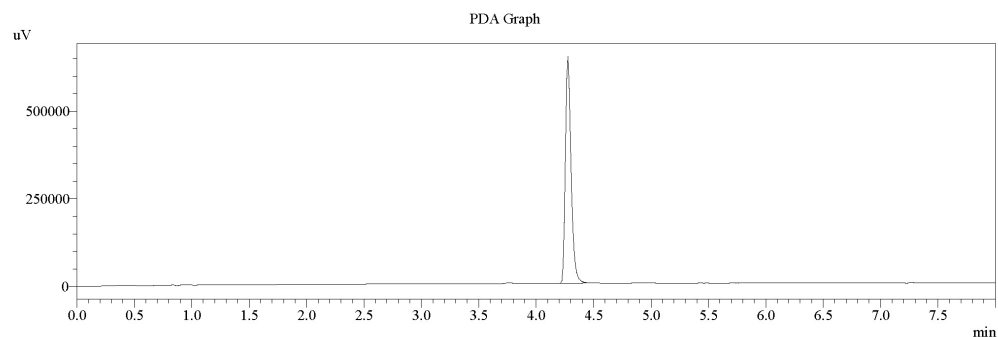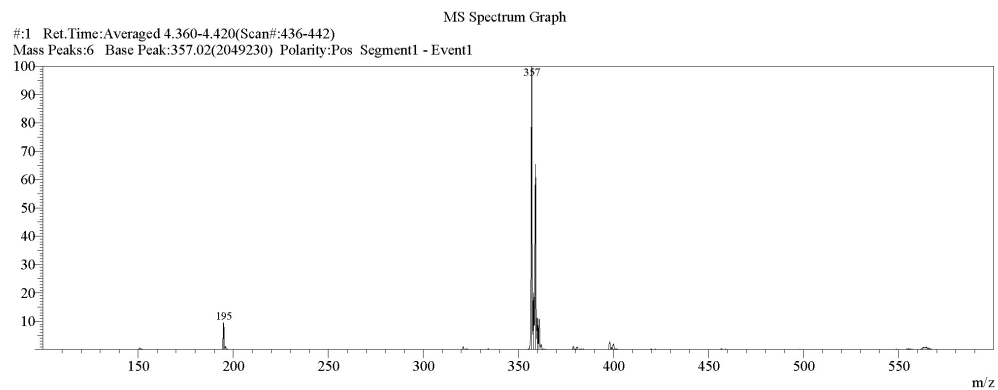#:1 Ret.Time:
BG Mode:None
Mass Peaks:8   Base Peak:452.95(593061) Polarity:Pos Segment1 - Event

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	450.95	374414	63.13				5	454.94	261926	44.17			
2	452.01	85256	14.38				6	456.01	55285	9.32			
3	452.95	593061	100.00				7	457.01	38313	6.46			
4	453.94	131388	22.15				8	493.95	37433	6.31			

Figure S84 LCMS spectrum of compound NPD-1199

¹H NMR (500 MHz, Chloroform-*d*) δ 9.82 (s, 1H), 8.45 (s, 2H), 7.62 – 7.53 (m, 2H), 7.49 – 7.43 (m, 1H), 7.42 – 7.35 (m, 2H), 7.32 – 7.19 (m, 3H), 5.12 (s, 2H).

Figure S85 ¹H NMR spectrum of compound NPD-1199

¹³C NMR (126 MHz, CDCl₃) δ 164.5, 154.9, 148.0, 140.7, 135.8, 133.2, 133.1, 130.5, 128.4, 127.9, 127.0, 121.4, 117.0, 113.2, 70.7.

Figure S86 ¹³C NMR spectrum of compound NPD-1199

PDA Graph

uV
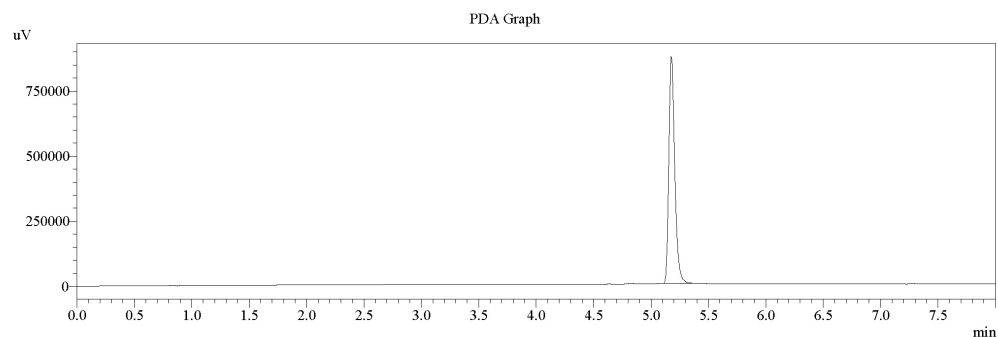
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		5.173	3089682	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 5.270-5.320(Scan#:527-532)
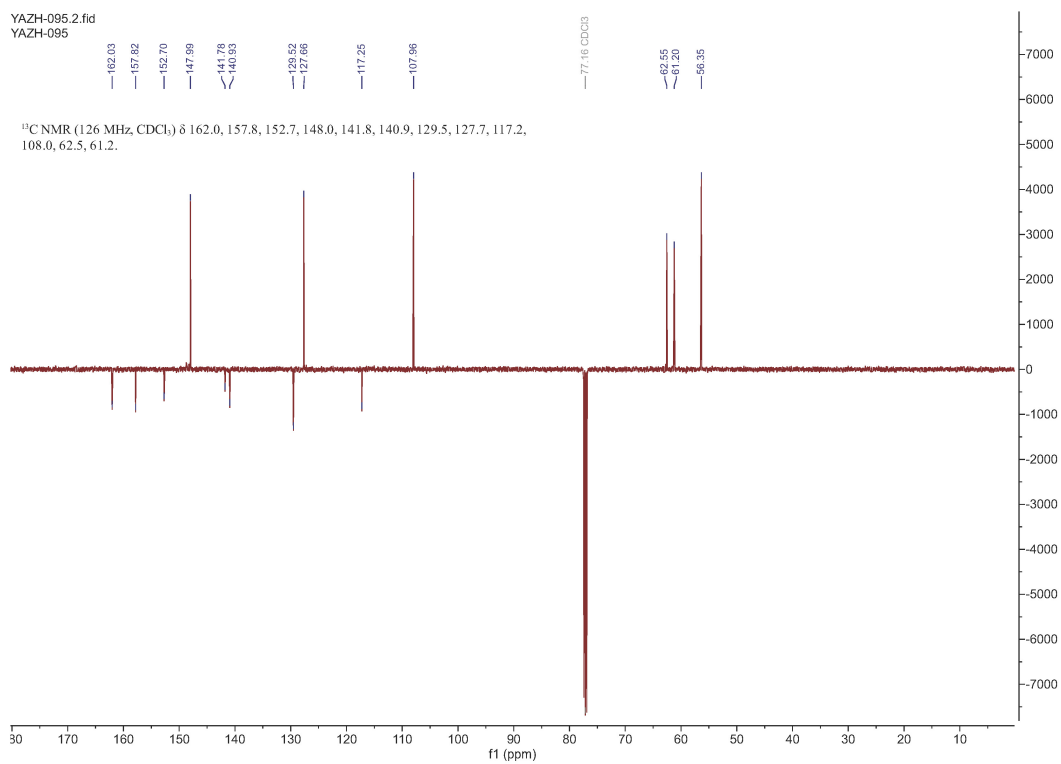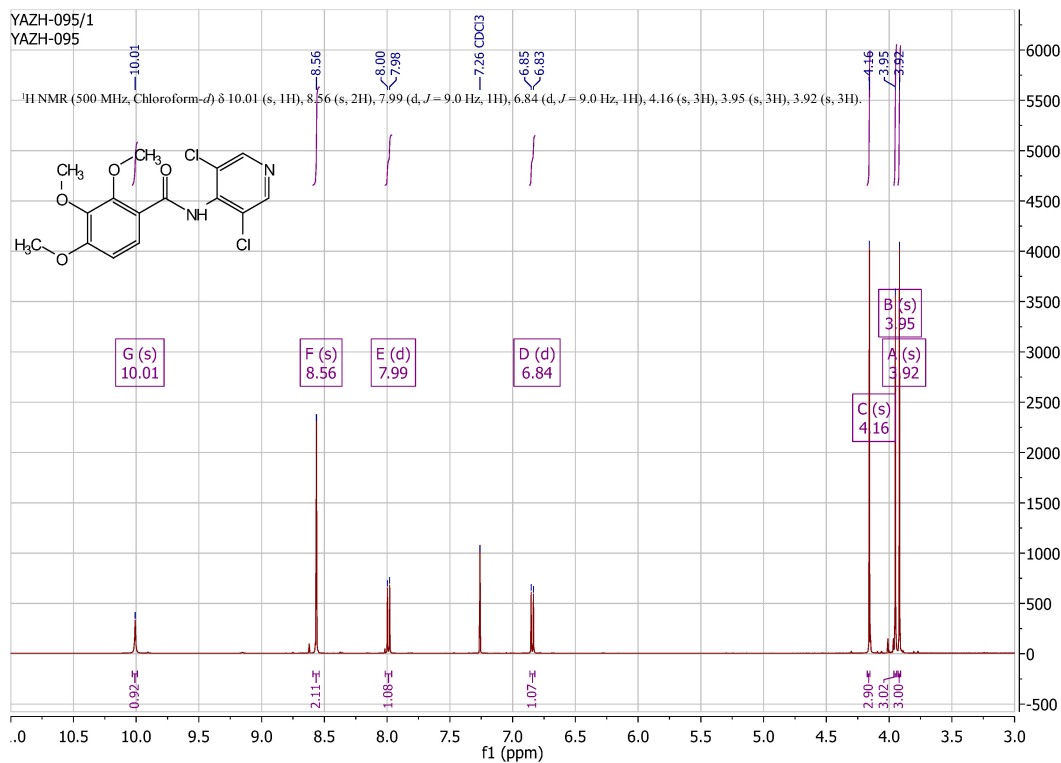Mass Peaks:5 Base Peak:418.99(3440008) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:None
Mass Peaks:5 Base Peak:418.99(3179486) Polarity:Pos Segment1 - Event

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	417.00	2499700	78.62				4	419.99	745467	23.45			
2	417.93	561811	17.67				5	420.92	888480	27.94			
3	418.99	3179486	100.00										

Figure S87 LCMS spectrum of compound NPD-1200

93
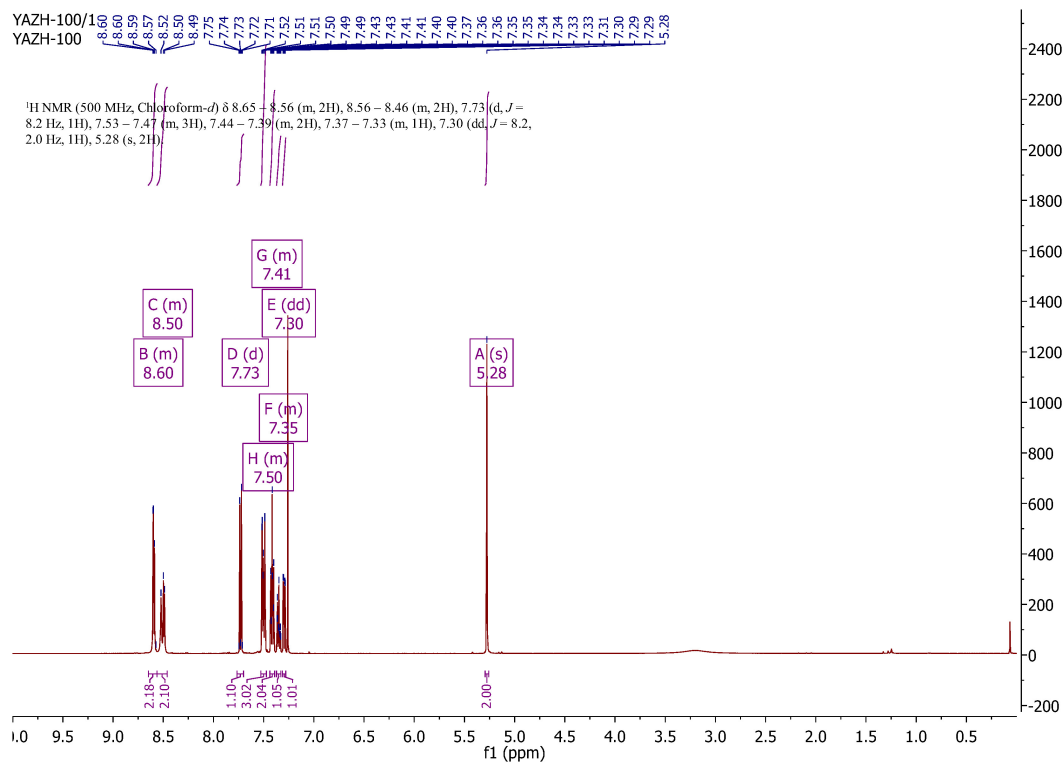
Figure S88 ¹H NMR spectrum of compound NPD-1200
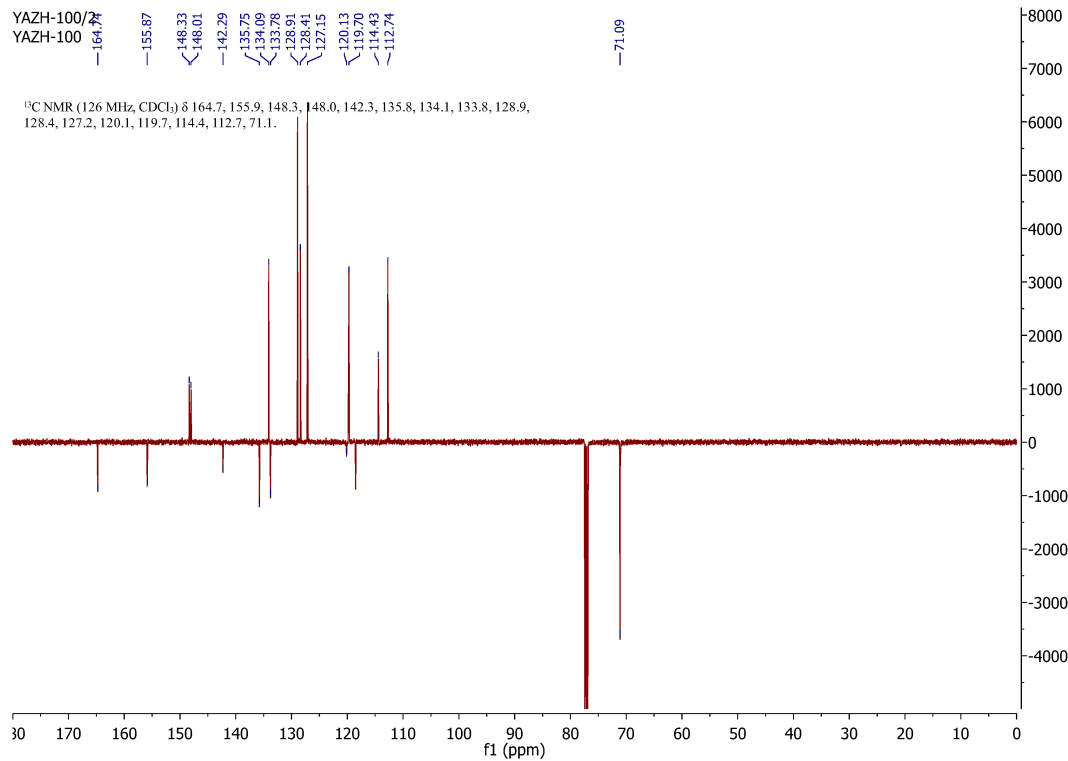
Figure S89 ¹³C NMR spectrum of compound NPD-1200

94

PDA Graph
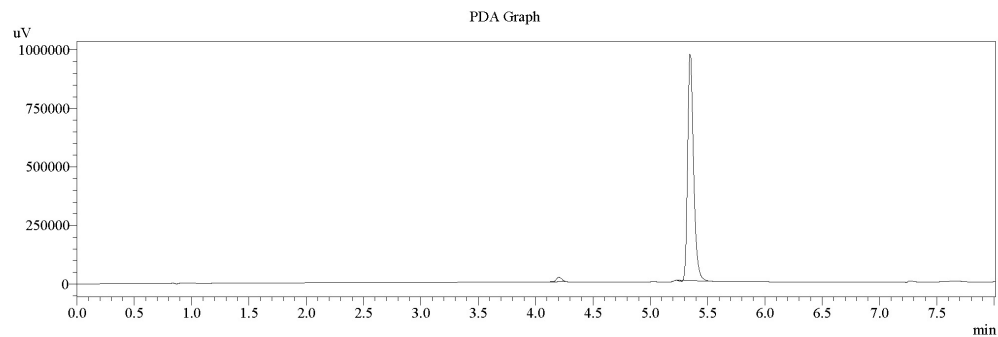
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.199	65625	1.850
2		5.344	3481795	98.150

MS Spectrum Graph

#:1 Ret.Time:Averaged 5.450-5.480(Scan#:545-548)
Mass Peaks:5 Base Peak:338.98(5223922) Polarity:Pos Segment1 - Event1
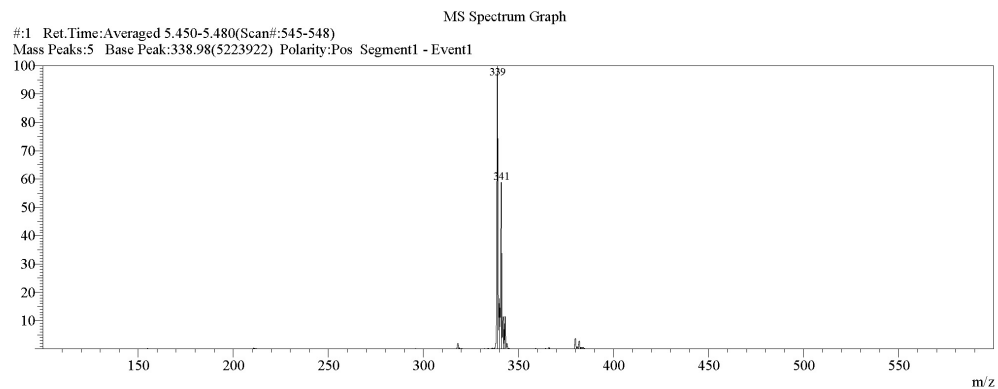
MS Spectrum Table

#:1 Ret.Time:
BG Mode:None
Mass Peaks:5 Base Peak:338.98(4826833) Polarity:Pos Segment1 - Event

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	338.98	4826833	100.00				4	342.04	543457	11.26			
2	340.04	867402	17.97				5	343.04	515410	10.68			
3	341.04	2801323	58.04										

Figure S90 LCMS spectrum of compound NPD-1201

95

8.60
8.60
8.59
8.58
8.50
8.49
7.51
7.51
7.50
7.32
7.31
7.30
7.30

3.89
3.88

2.23
2.22
2.21
2.18
2.17
2.15

1.09
1.08
1.07

^{1}H NMR (500 MHz, Chloroform-d) δ 8.62 – 8.56 (m, 3H), 8.50 (d, J = 5.7 Hz, 1H), 7.53 – 7.47 (m, 2H), 7.31 (dd, J = 8.2, 2.0 Hz, 1H), 3.88 (d, J = 6.5 Hz, 2H), 2.19 (hept, J = 6.6 Hz, 1H), 1.08 (d, J = 6.7 Hz, 6H).

B (d)
8.50

D (dd)
7.31

A (m)
8.59

C (m)
7.51

E (d)
3.88

F (hept)
2.19

G (d)
1.08

3.02
0.99

2.02
0.99

1.97

0.96

6.05

f1 (ppm)

Figure S91 ^{1}H NMR spectrum of compound NPD-1201

164.8
155.60
148.42
148.12
142.29
132.99
130.65
128.59
120.12
118.49
114.42
112.49
75.65
28.36
19.28

^{13}C NMR (126 MHz, CDCl$_3$) δ 164.8, 155.6, 148.4, 148.1, 142.3, 133.0, 130.7, 128.6, 120.1, 118.5, 114.4, 112.5, 75.7, 28.4, 19.3.

f1 (ppm)

Figure S92 ^{13}C NMR spectrum of compound NPD-1201

96

Medicinal Chemistry
Vrije Universiteit Amsterdam

Chromatogram
YAZH-103 C:\LabSolutions\Data\2019\2019-wk18\YAZH-103.lcd

1 PDA Multi 1 / 254nm 4nm
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.951	6511021	100.000

MS Chromatogram
YAZH-103 C:\LabSolutions\Data\2019\2019-wk18\YAZH-103.lcd

MS Spectrum Graph

#:1 Ret.Time:Averaged 5.000-5.020(Scan#:501-503)
Mass Peaks:13 Base Peak:339.05(2246230) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.870<->5.510(488<->552)
Mass Peaks:13 Base Peak:339.05(2246230) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	246.95	28892	1.29				8	344.05	44618	1.99			
2	303.05	55544	2.47				9	380.10	262473	11.69			
3	339.05	2246230	100.00				10	381.10	60800	2.71			
4	340.05	398781	17.75				11	382.10	187956	8.37			
5	341.00	1515279	67.46				12	383.05	33808	1.51			
6	342.00	262388	11.68				13	384.05	28437	1.27			
7	343.00	226478	10.08										

Figure S93 LCMS spectrum of compound NPD-1202

10.44
8.71
8.48
8.47
7.71
7.65
7.64
7.62
7.61
3.96
3.95
2.15
2.14
2.13
2.12
2.10
2.09
2.08
1.06
1.04

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.44 (s, 1H), 8.71 (s, 1H), 8.47 (d, J = 5.2 Hz, 1H), 7.71 (s, 2H), 7.68 – 7.56 (m, 2H), 3.96 (d, J = 6.3 Hz, 2H), 2.12 (hept, J = 6.5 Hz, 1H), 1.05 (d, J = 6.6 Hz, 6H).

G (s)
8.71

E (s)
7.71

H (s)
10.44

F (d)
8.47

D (m)
7.63

C (d)
3.96

B (hept)
2.12

A (d)
1.05

0.76
1.05
1.02
1.99
2.12
2.20
1.17
6.00
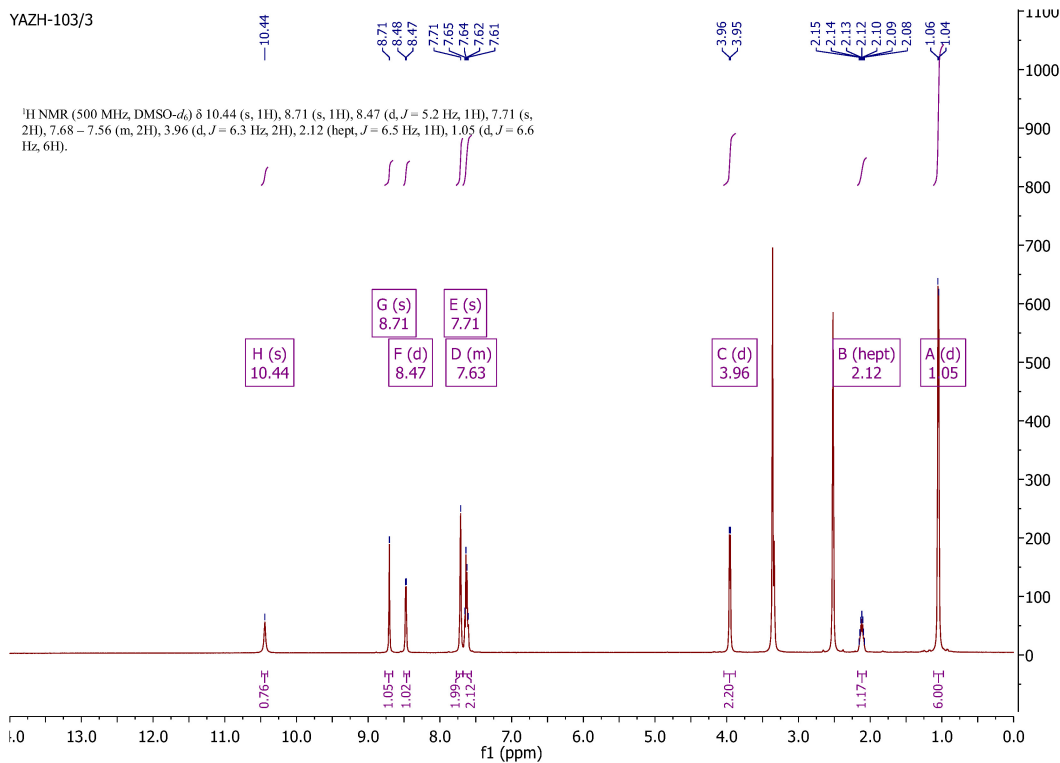
Figure S94 ^{1}H NMR spectrum of compound NPD-1202

164.68
154.00
149.59
148.21
139.66
133.39
132.22
130.01
125.39
124.75
120.82
112.65
74.83
27.82
18.98

^{13}C NMR (126 MHz, DMSO) δ 164.7, 154.0, 149.6, 148.2, 139.7, 133.4, 132.2, 130.0, 125.4, 124.7, 120.8, 112.7, 74.8, 27.8, 19.0.
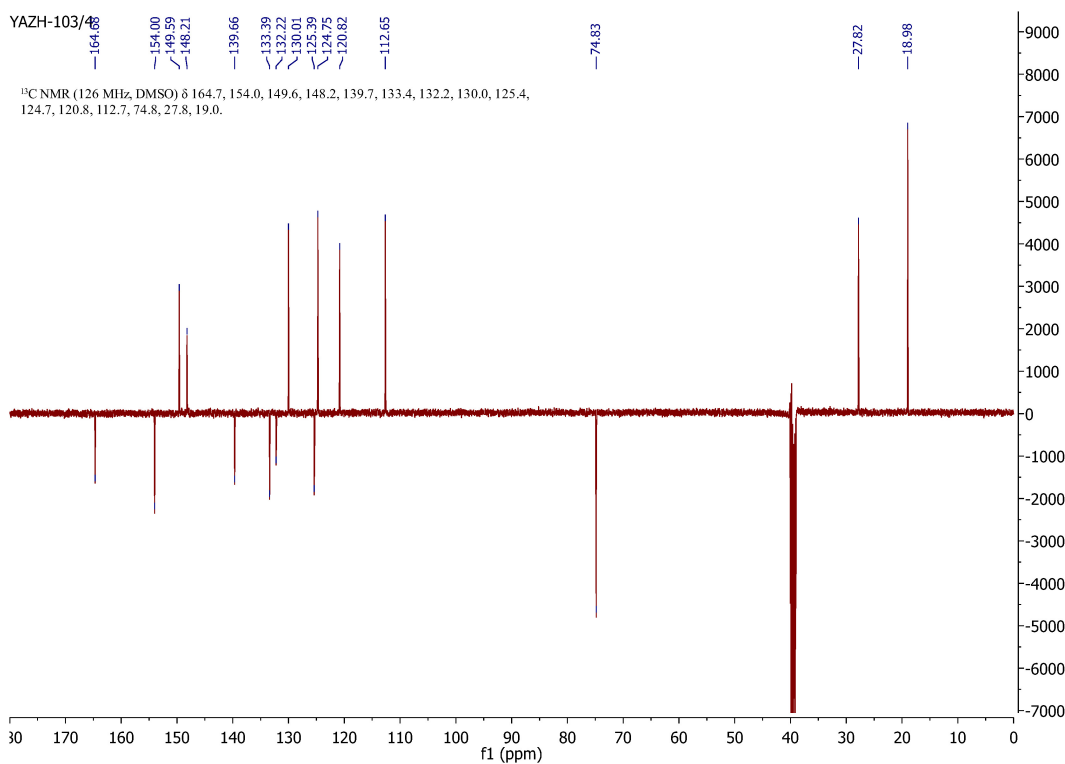
Figure S95 ^{13}C NMR spectrum of compound NPD-1202

PDA Graph
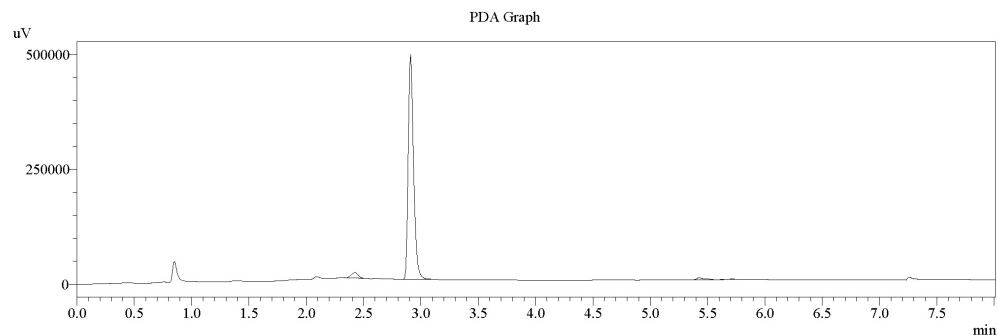
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		2.419	45731	2.788
2		2.904	1567771	95.589
3		5.422	20848	1.271
4		5.708	5769	0.352

MS Spectrum Graph

#:1 Ret.Time:Averaged 3.020-3.060(Scan#:302-306)
Mass Peaks:5 Base Peak:310.96(858231) Polarity:Pos Segment1 - Event1
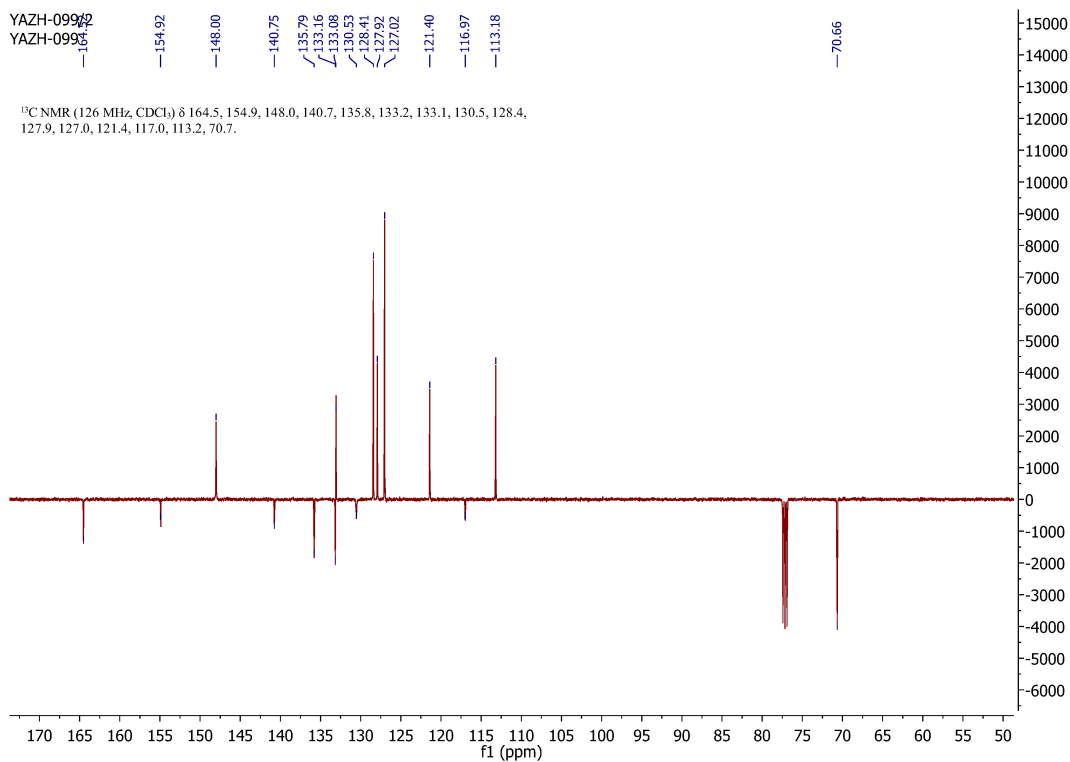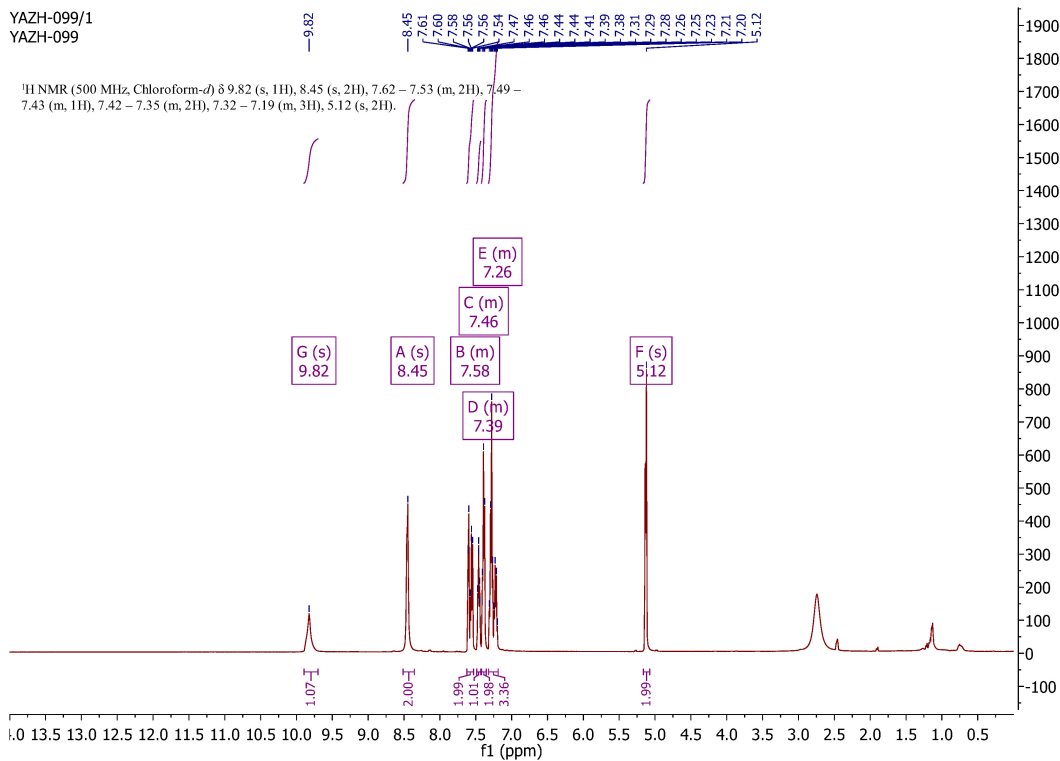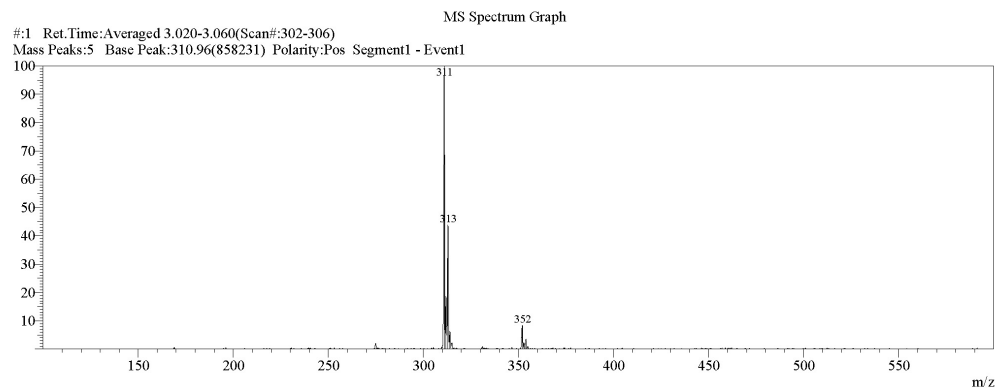
MS Spectrum Table

#:1 Ret.Time:
BG Mode:None
Mass Peaks:5 Base Peak:310.96(779830) Polarity:Pos Segment1 - Event

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	310.96	779830	100.00				4	313.95	43430	5.57			
2	311.89	138952	17.82				5	352.02	70113	8.99			
3	312.95	320056	41.04										

Figure S96 LCMS spectrum of compound NPD-1203
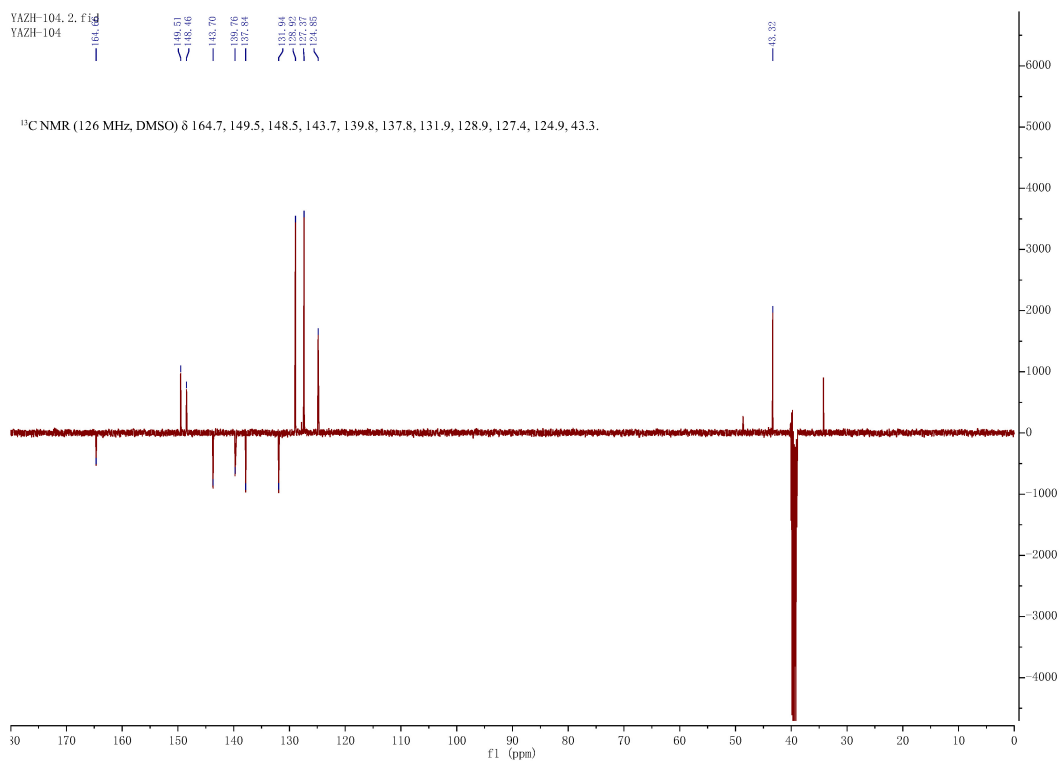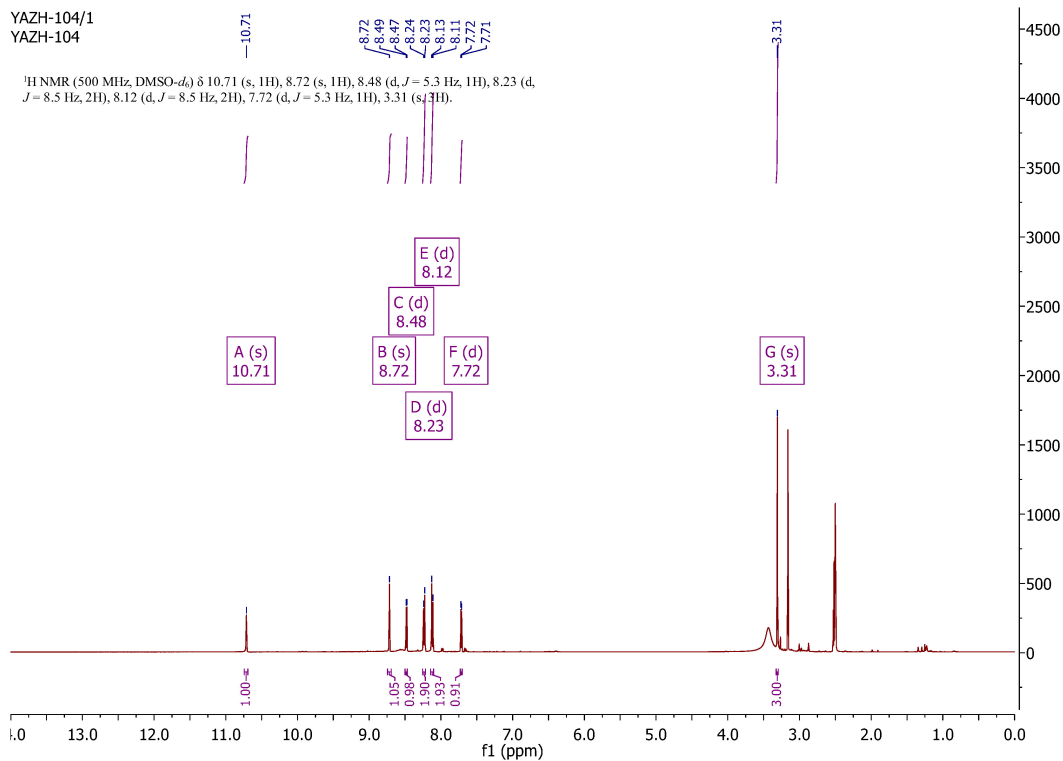
99

10.71

8.72
8.49
8.47
8.24
8.23
8.13
8.11
7.72
7.71

3.31

¹H NMR (500 MHz, DMSO-d_6) δ 10.71 (s, 1H), 8.72 (s, 1H), 8.48 (d, J = 5.3 Hz, 1H), 8.23 (d, J = 8.5 Hz, 2H), 8.12 (d, J = 8.5 Hz, 2H), 7.72 (d, J = 5.3 Hz, 1H), 3.31 (s, 3H).

| E (d) |
| 8.12 |

| C (d) |
| 8.48 |

| A (s) | | B (s) | F (d) | | G (s) |
| 10.71 | | 8.72 | 7.72 | | 3.31 |

| D (d) |
| 8.23 |

1.00

1.05
0.98
1.90
1.93
0.91

3.00

Figure S97 ¹H NMR spectrum of compound NPD-1203

164.66

149.51
148.46

143.70

139.76
137.84

131.94
128.92
127.37
124.85

43.32

¹³C NMR (126 MHz, DMSO) δ 164.7, 149.5, 148.5, 143.7, 139.8, 137.8, 131.9, 128.9, 127.4, 124.9, 43.3.

Figure S98 ¹³C NMR spectrum of compound NPD-1203

PDA Graph
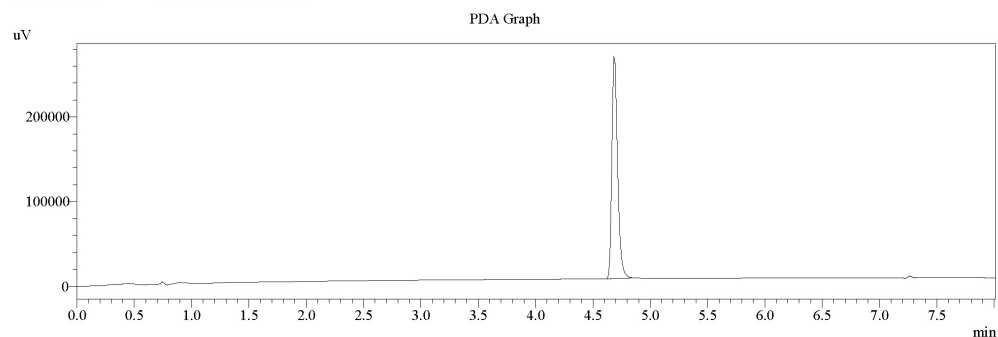
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.681	907011	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.790-4.850(Scan#:479-485)
Mass Peaks:4 Base Peak:369.00(2431561) Polarity:Pos Segment1 - Event1
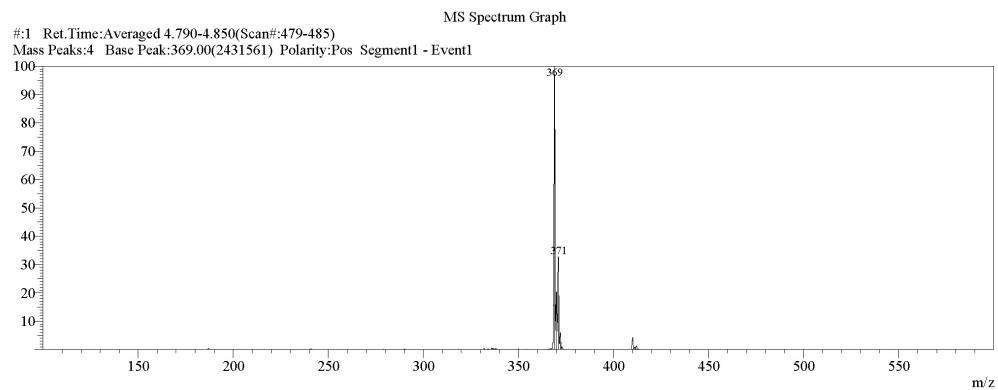
MS Spectrum Table

#:1 Ret.Time:
BG Mode:None
Mass Peaks:4 Base Peak:369.00(2276897) Polarity:Pos Segment1 - Event

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	369.00	2276897	100.00				3	371.06	734239	32.25			
2	369.93	458155	20.12				4	372.06	124487	5.47			

Figure S99 LCMS spectrum of compound NPD-1204

101

YAZH-106.1.fid
YAZH-106

¹H NMR (500 MHz, Chloroform-*d*) δ 8.58 (s, 1H), 8.52 (d, *J* = 5.5 Hz, 2H), 8.48 (d, *J* = 5.6 Hz, 1H), 7.57 (d, *J* = 2.1 Hz, 1H), 7.38 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.30 (d, *J* = 8.2 Hz, 1H), 6.74 (t, *J* = 74.7 Hz, 1H), 3.97 (d, *J* = 7.0 Hz, 2H), 1.37 − 1.28 (m, 1H), 0.71 − 0.66 (m, 2H), 0.41 − 0.37 (m, 2H).

F (d) 8.52	I (dd) 7.38			C (m) 0.68
E (s) 8.58	H (d) 7.57	D (t) 6.74	A (d) 3.97	K (m) 1.32	B (m) 0.39
G (d) 8.48	J (d) 7.30			
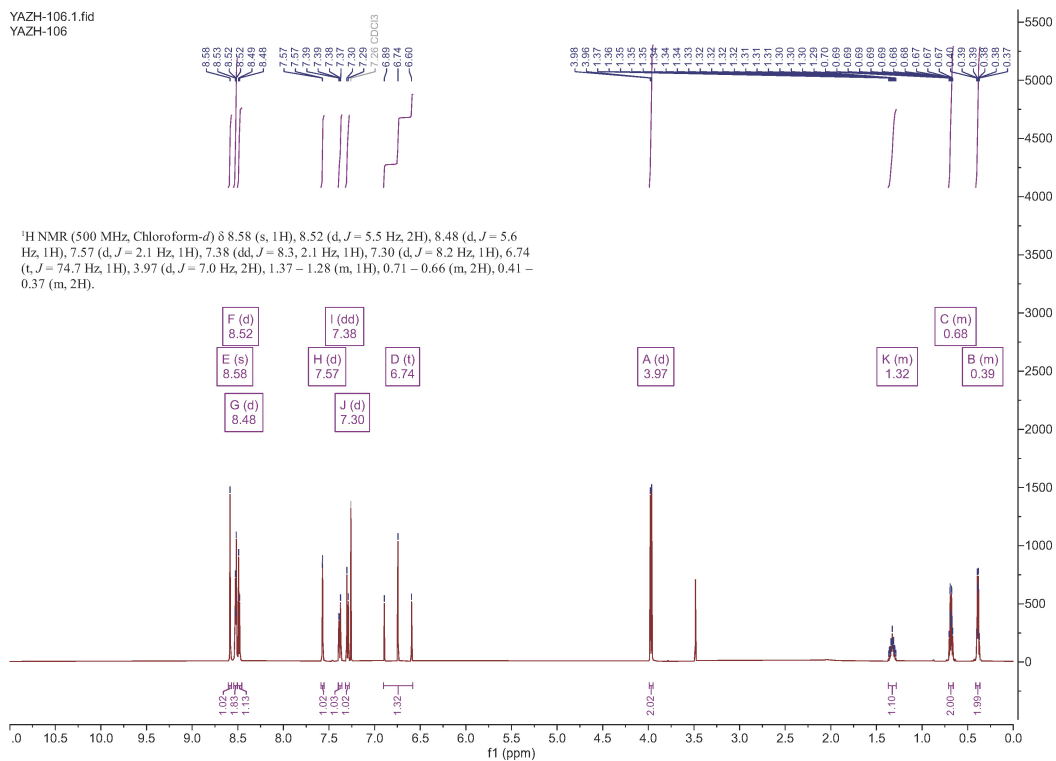
Figure S100 ¹H NMR spectrum of compound NPD-1204

YAZH-106.2.fid
YAZH-106

¹³C NMR (126 MHz, Chloroform-*d*) δ 164.7, 151.2, 149.4, 149.1, 143.9, 141.4, 131.9, 122.5, 120.0, 119.0, 115.7 (t, *J* = 262.0 Hz), 114.3, 114.0, 74.3, 10.1, 3.5.
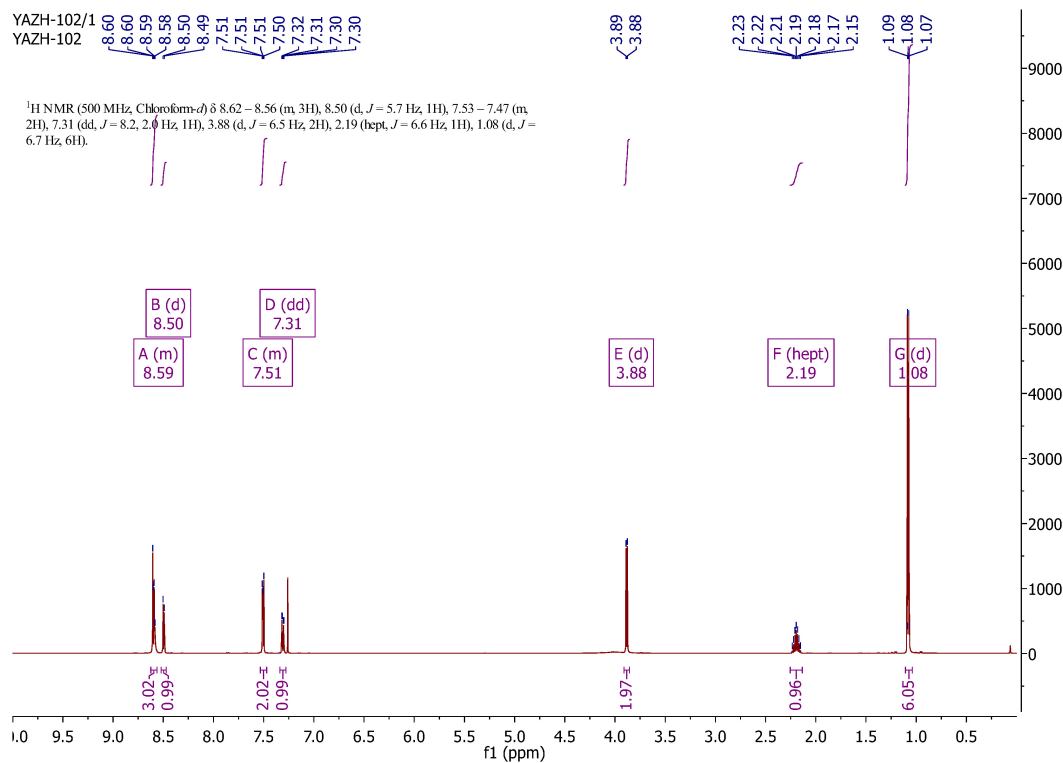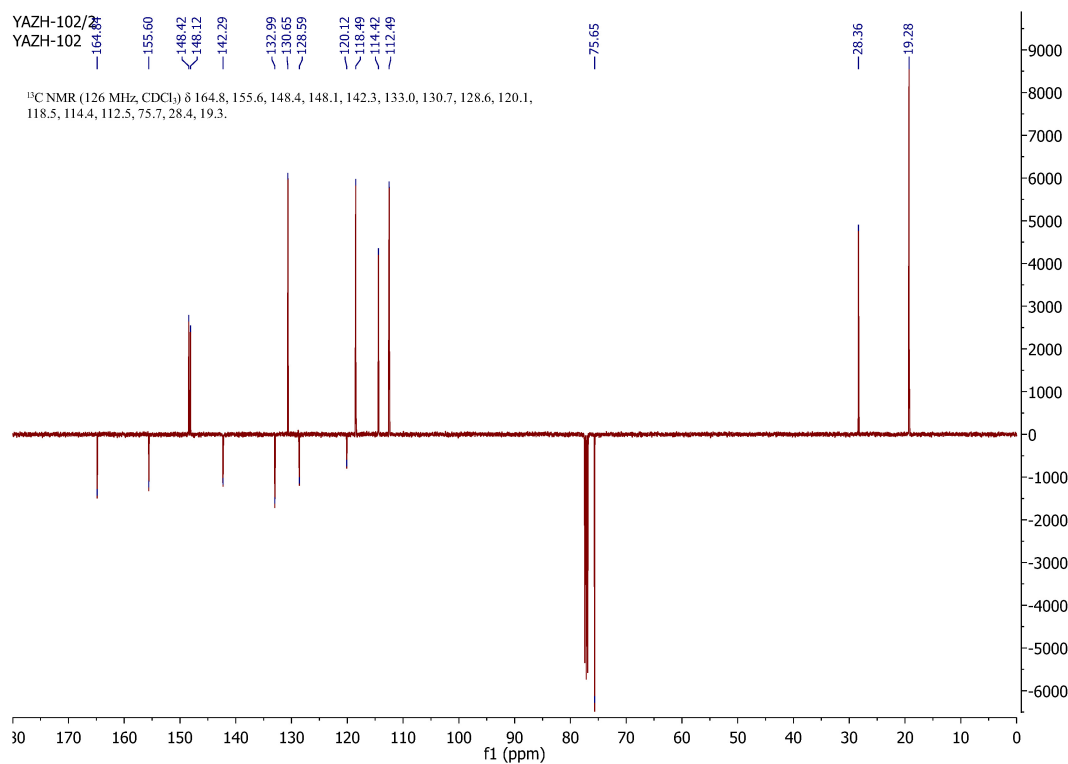

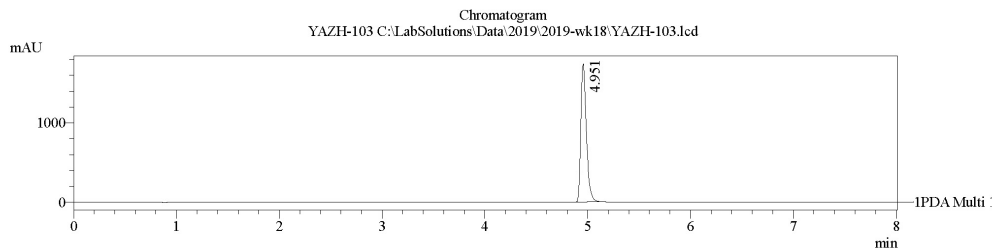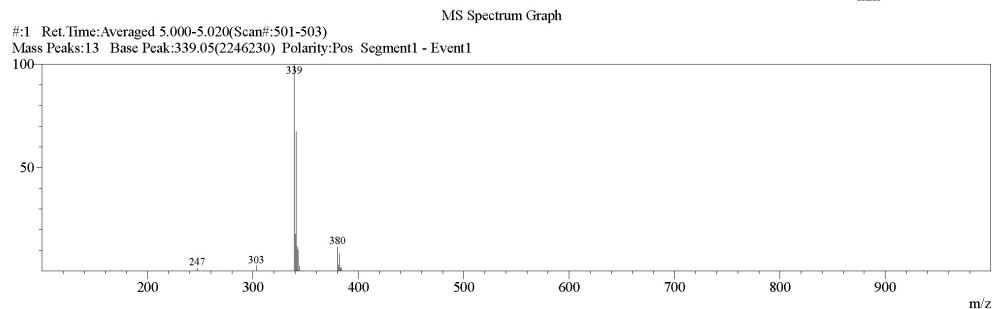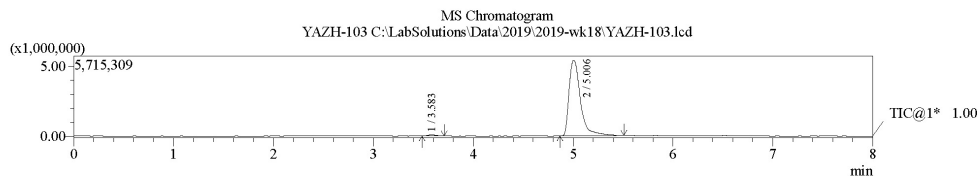**Figure S101 ¹³C NMR spectrum of compound NPD-1204**

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Sample ID   :
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Vial#   : 9
Injection Volume   : 3
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Background File   : blanco 03052019.lcd
Method File   : Method SCAN ACID standard.lcm
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Tuning File   : C:\LabSolutions\Tuning\Tuning-ESI-pos-neg01072015a.lct
Processed by   : Admin
Modified Date   : 3/5/2019 3:48:58 PM

Medicinal Chemistry
Vrije Universiteit Amsterdam

vrije Universiteit

Chromatogram
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1 PDA Multi 1 / 254nm 4nm
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.381	4206090	100.000

MS Chromatogram
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TIC@1* 1.00

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.430-4.450(Scan#:444-446)
Mass Peaks:8   Base Peak:369.05(3233991) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.300<->4.850(431<->486)
Mass Peaks:8   Base Peak:369.05(3233991) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	333.00	54730	1.69				5	372.05	229595	7.10			
2	369.05	3233991	100.00				6	410.05	313094	9.68			
3	370.05	673836	20.84				7	411.10	58022	1.79			
4	371.05	1129791	34.93				8	412.05	100478	3.11			

Figure S102 LCMS spectrum of compound NPD-1205

103

YAZH-107/3

¹H NMR (500 MHz, DMSO-*d*₆) δ 10.37 (s, 1H), 8.68 (s, 1H), 8.46 (d, *J* = 5.3 Hz, 1H), 7.74 – 7.68 (m, 2H), 7.64 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.40 – 7.08 (m, 2H), 3.99 (d, *J* = 7.0 Hz, 2H), 1.28 (dddt, *J* = 11.6, 7.2, 4.7, 2.6 Hz, 1H), 0.62 – 0.57 (m, 2H), 0.40 – 0.35 (m, 2H).

J (s)
10.37

I (s)
8.68

H (d)
8.46

F (m)
7.70

E (m)
7.28

G (dd)
7.64

D (d)
3.99

C (dddt)
1.28

B (m)
0.60

A (m)
0.38
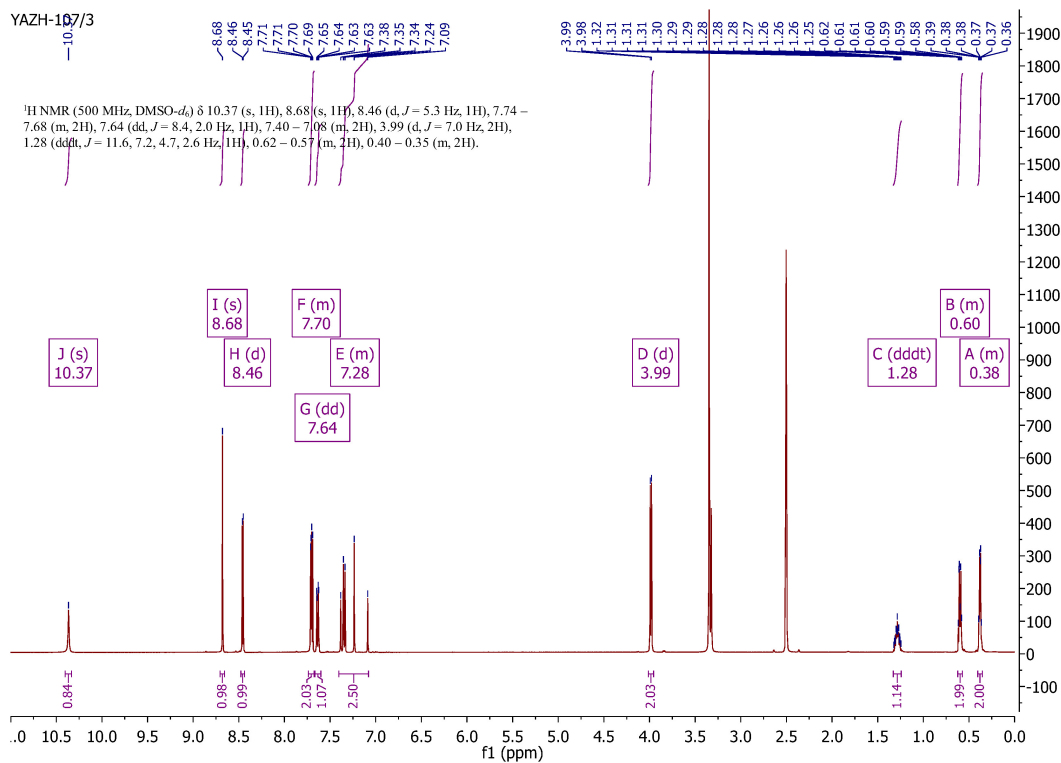
Figure S103 ¹H NMR spectrum of compound NPD-1205

YAZH-107.6.fig

¹³C NMR (126 MHz, DMSO-*d*₆) δ 164.7, 149.6, 149,6 (confirmed by HMBC), 148.2, 142.7 (t, *J* = 3.1 Hz), 140.0, 132.2, 131.2, 124.8, 120.7, 120.3, 116.5 (t, *J* = 258.3 Hz), 113.6, 73.3, 10.0, 3.1.
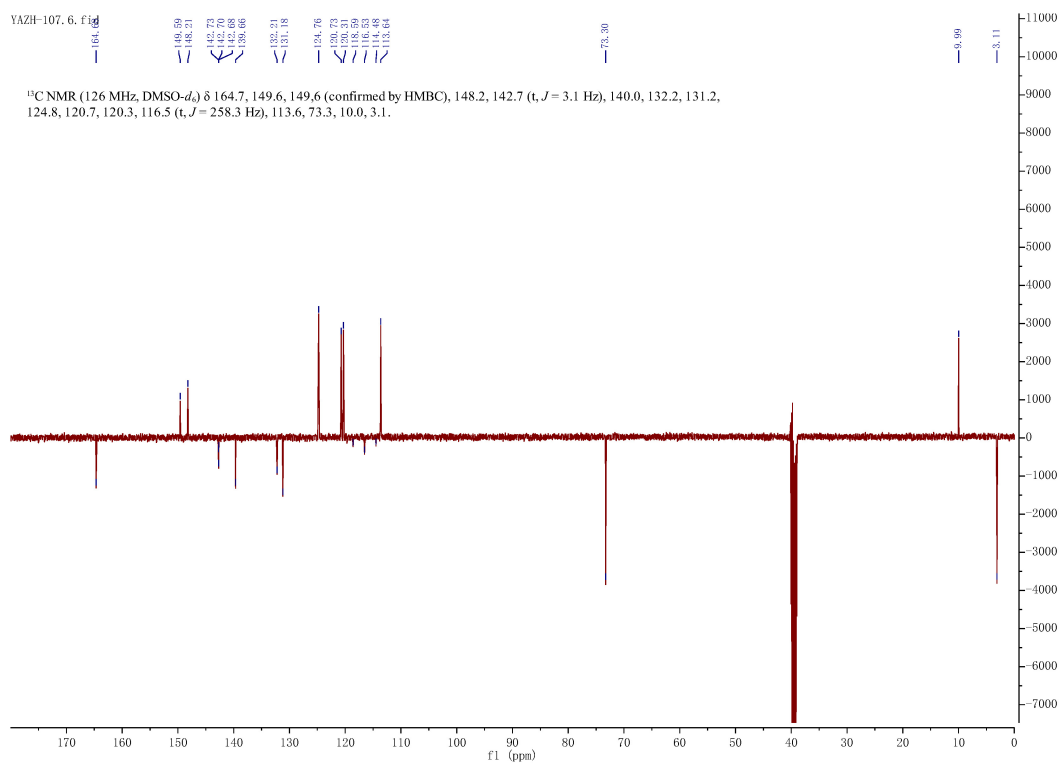
Figure S104 ¹³C NMR spectrum of compound NPD-1205

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.243	38819	1.185
2		5.218	3237832	98.815

MS Spectrum Graph

#:1 Ret.Time:Averaged 5.320-5.370(Scan#:532-537)
Mass Peaks:11   Base Peak:372.99(1220376) Polarity:Pos Segment1 - Event1
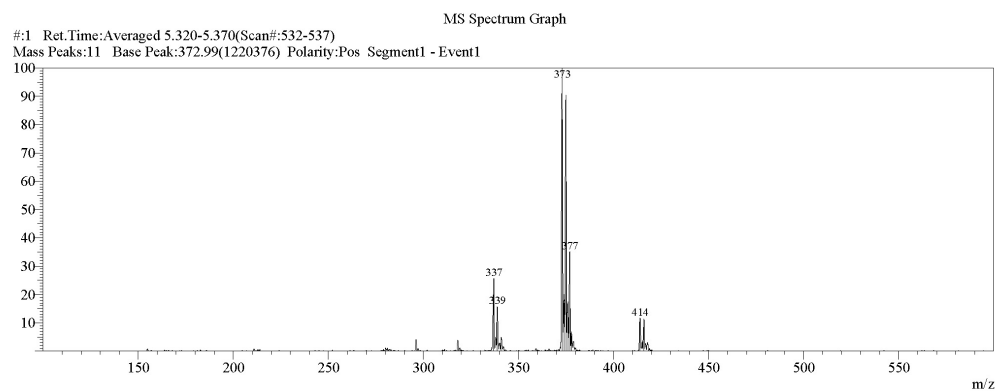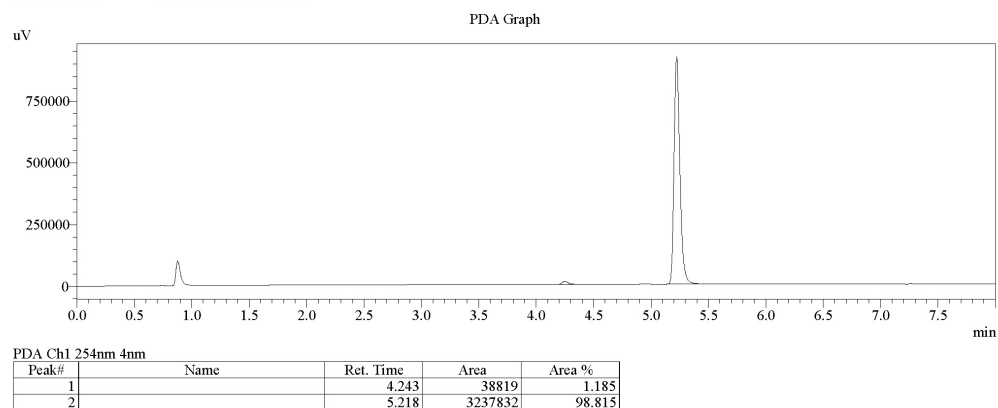
MS Spectrum Table

#:1 Ret.Time:
BG Mode:None
Mass Peaks:11   Base Peak:372.99(996605) Polarity:Pos Segment1 - Event

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	337.05	259467	26.04				7	375.99	178375	17.90			
2	338.91	157288	15.78				8	376.99	322428	32.35			
3	340.97	58254	5.85				9	377.92	67191	6.74			
4	372.99	996605	100.00				10	414.00	129525	13.00			
5	374.06	205801	20.65				11	416.06	110035	11.04			
6	374.99	921759	92.49										

Figure S105 LCMS spectrum of compound NPD-1206

105

¹H NMR (500 MHz, Chloroform-*d*) δ 8.59 – 8.50 (m, 3H), 8.46 (dd, *J* = 5.7, 3.0 Hz, 1H), 7.51 – 7.45 (m, 2H), 7.32 – 7.26 (m, 1H), 3.89 – 3.83 (m, 2H), 2.25 – 2.10 (m, 1H), 1.09 – 1.04 (m, 6H).

| B (dd) 8.46 | D (m) 7.29 |
| A (m) 8.54 | C (m) 7.48 | E (m) 3.86 | F (m) 2.17 | G (m) 1.06 |
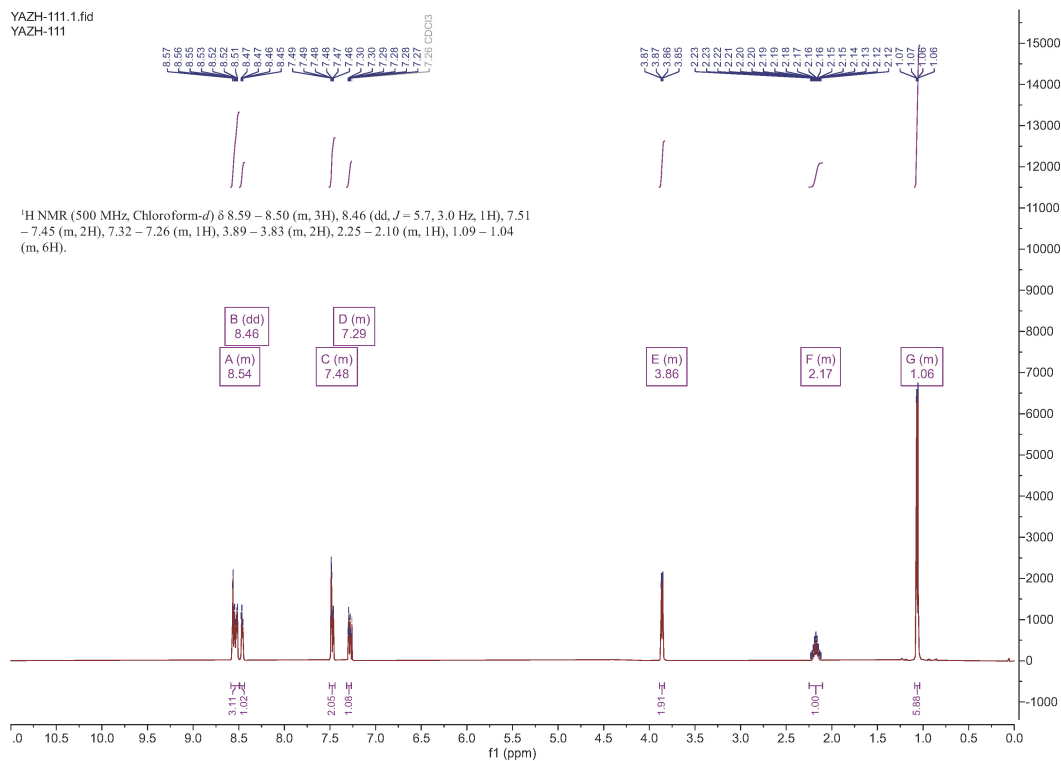
Figure S106 ¹H NMR spectrum of compound NPD-1206

¹³C NMR (126 MHz, CDCl₃) δ 166.2, 157.7, 150.7, 142.0, 134.4, 132.7, 131.1, 130.7, 121.7, 115.0, 77.9, 30.6, 21.5.
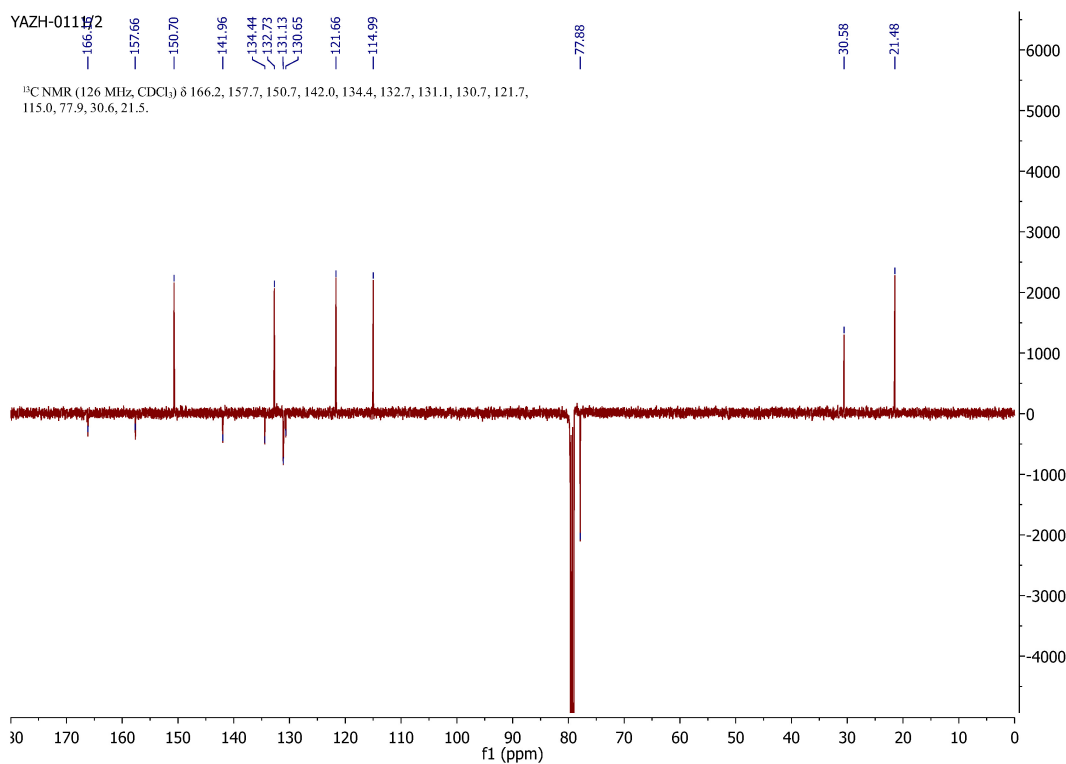
Figure S107 ¹³C NMR spectrum of compound NPD-1206

PDA Graph

uV

PDA Ch1 254nm 4nm
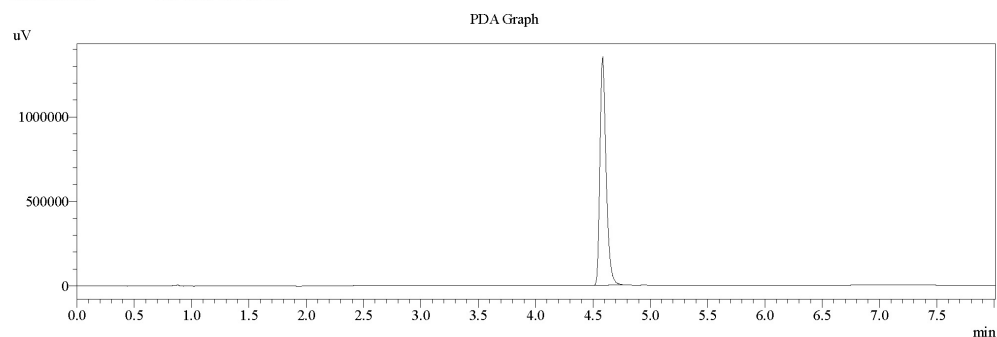
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1		4.579	5081780	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.650-4.670(Scan#:466-468)
Mass Peaks:10   Base Peak:327.95(881302) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.540<−>4.990(455<−>500)
Mass Peaks:10 Base Peak:327.95(881302) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	165.95	29510	3.35				6	332.00	89644	10.17			
2	327.95	881302	100.00				7	333.00	13321	1.51			
3	329.00	139315	15.81				8	368.95	50560	5.74			
4	329.95	589330	66.87				9	370.00	10710	1.22			
5	331.00	82638	9.38				10	371.00	33942	3.85			

Figure S108 LCMS spectrum of compound NPD-1472

YAZH-145.1.fid

¹H NMR (500 MHz, DMSO-d_6) δ 9.97 (s, 1H), 8.73 (s, 2H), 8.21 (d, J = 8.3 Hz, 1H), 6.57 (d, J = 8.3 Hz, 1H), 4.08 (s, 3H), 3.97 (s, 3H).

9.97
8.73
8.22
8.20
6.58
6.56
4.08
3.97
—2.50 DMSO-d6

F (d)
8.21

B (s)
3.97

D (s)
9.97

E (s)
8.73

C (d)
6.57

A (s)
4.08

1.03
1.89
1.04
1.04
3.03
3.00

13.5 12.5 11.5 10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5
f1 (ppm)
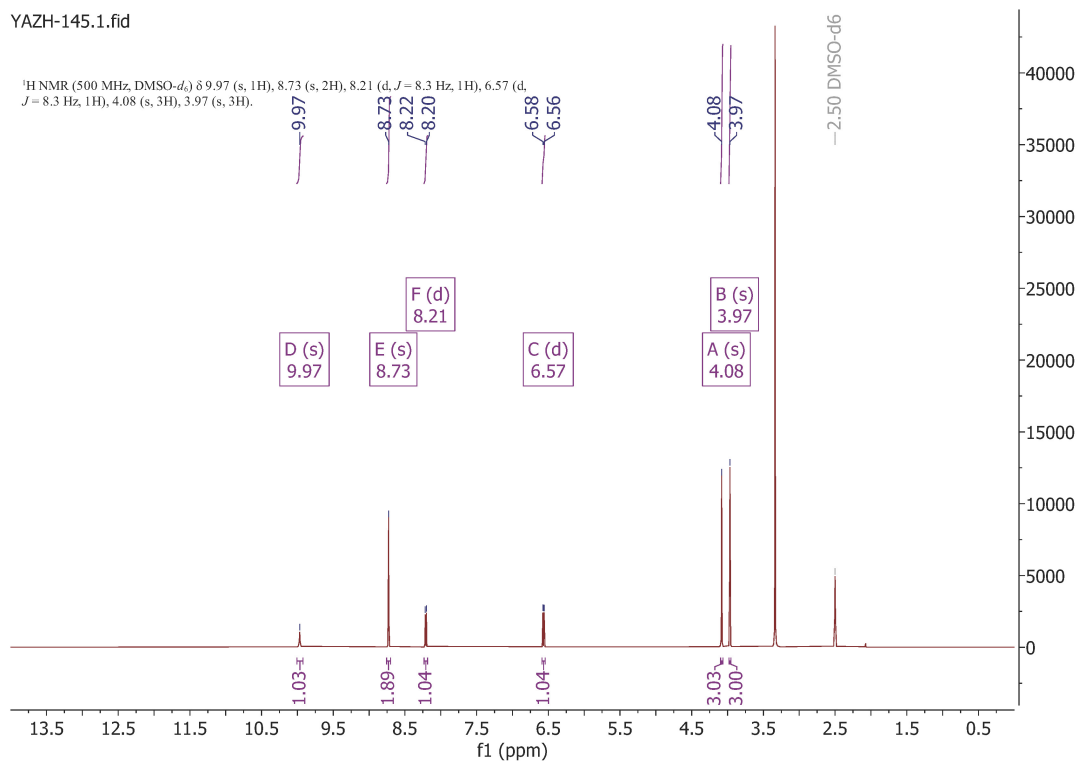
Figure S109 ¹H NMR spectrum of compound NPD-1472

YAZH-145.2.fid
group far
YAZH-145-APT

164.83
161.46
160.36
148.09
143.90
141.51
130.67
106.65
102.69
54.25
54.06
—39.52 DMSO-d6

¹³C NMR (126 MHz, DMSO) δ 164.8, 161.5, 160.4, 148.1, 143.9, 141.5, 130.7, 106.6, 102.7, 54.2, 54.1.

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
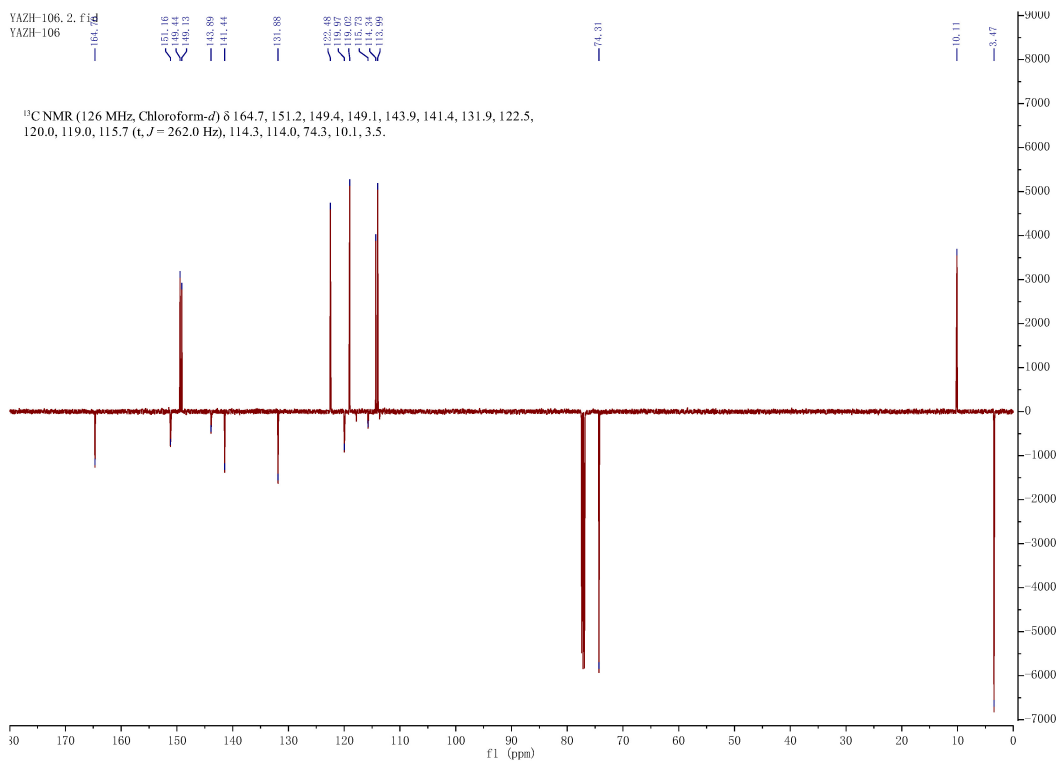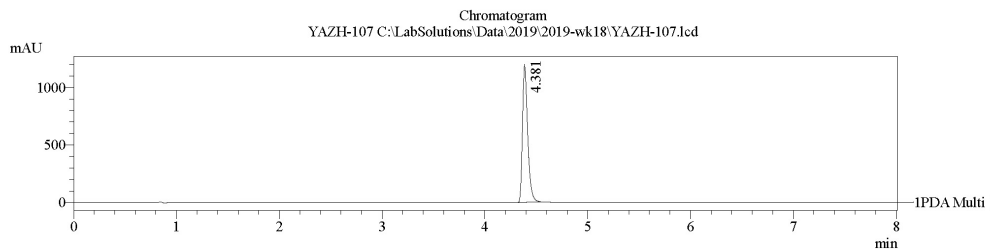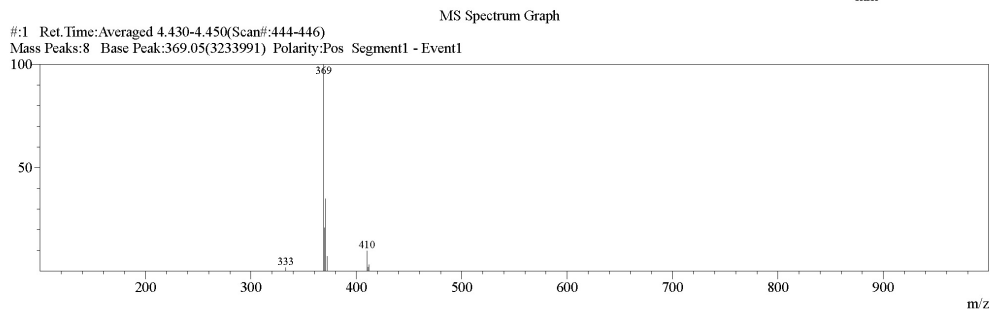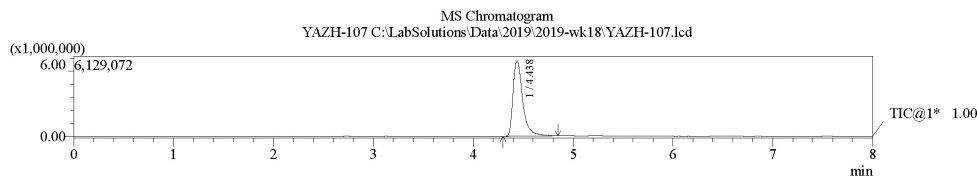f1 (ppm)

Figure S110 ¹³C NMR spectrum of compound NPD-1472

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Sample ID :
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Report Format : DefaultLCMS.lcr
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Processed by : Admin
Modified Date : 10/5/2019 4:21:59 PM

PDA Graph

mAU

PeakTable

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.281	21243	0.502
2		3.808	4200066	99.252
3		4.153	10397	0.246

MS Chromatogram
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(x1,000,000)
1,446,837 TIC@1

MS Spectrum Graph

#:1 Ret.Time:Averaged 3.860-3.880(Scan#:387-389)
BG Mode:Calc 3.730<->4.130(374<->414)
Mass Peaks:9 Base Peak:341.00(627181) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.730<->4.130(374<->414)
Mass Peaks:9 Base Peak:341.00(627181) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	179.00	23933	3.82				6	345.05	66619	10.62			
2	341.00	627181	100.00				7	346.05	11028	1.76			
3	342.05	105030	16.75				8	382.00	40100	6.39			
4	343.00	394560	62.91				9	384.05	27033	4.31			
5	344.05	65299	10.41										

Figure S111 LCMS spectrum of compound NPD-2976

YAZH01-018.1.fid

^{1}H NMR (600 MHz, DMSO-d_6) δ 10.42 (s, 1H), 8.74 (s, 2H), 7.67 (dd, J = 8.5, 2.1 Hz, 1H), 7.56 (d, J = 2.1 Hz, 1H), 7.12 (d, J = 8.4 Hz, 1H), 4.09 (q, J = 7.0 Hz, 2H), 3.85 (s, 3H), 1.36 (t, J = 6.9 Hz, 3H).

A (s) 10.42

B (s) 8.74

C (dd) 7.67

D (d) 7.56

E (d) 7.12

F (q) 4.09

G (s) 3.85

H (t) 1.36

Figure S112 ^{1}H NMR spectrum of compound NPD-2976

YAZH01-018/4

^{13}C NMR (151 MHz, DMSO) δ 164.2, 152.4, 148.2, 147.7, 141.7 (confirmed by HMBC), 130.7, 124.8, 121.6, 112.0, 111.2, 63.9, 55.7, 14.7.

Figure S113 ^{13}C NMR spectrum of compound NPD-2976

110

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		2.853	9126	1.816
2		4.007	493479	98.184

MS Spectrum Graph

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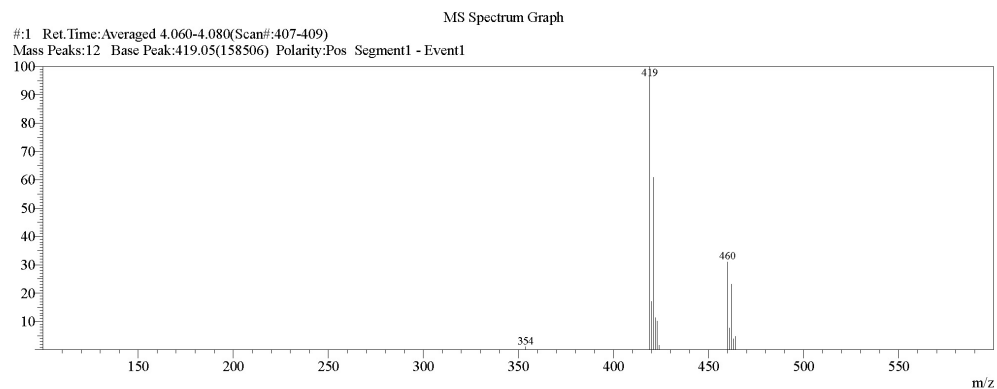
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.960<->4.240(397<->425)
Mass Peaks:12 Base Peak:419.05(158506) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	353.70	1674	1.06				7	424.10	2631	1.66			
2	419.05	158506	100.00				8	460.10	49139	31.00			
3	420.15	27037	17.06				9	461.15	12270	7.74			
4	421.10	96492	60.88				10	462.15	36868	23.26			
5	422.10	17895	11.29				11	463.10	6115	3.86			
6	423.00	16159	10.19				12	464.15	7568	4.77			

Figure S114 LCMS spectrum of compound NPD-2980

YAZH01-025.1.fid

¹H NMR (600 MHz, Chloroform-*d*) δ 8.25 (s, 2H), 7.82 (s, 1H), 7.58 (s, 1H), 7.46 (d, *J* = 8.3 Hz, 1H), 7.28 (d, *J* = 8.2 Hz, 1H), 6.74 (t, *J* = 74.8 Hz, 1H), 3.96 (d, *J* = 6.9 Hz, 2H), 1.36 – 1.27 (m, 1H), 0.70 – 0.65 (m, 2H), 0.40 – 0.36 (m, 2H).

| F (d) |
| 7.46 |

| B (m) |
| 0.68 |

| I (s) | H (s) | E (d) | D (t) | | C (d) | | J (m) | A (m) |
| 8.25 | 7.82 | 7.28 | 6.74 | | 3.96 | | 1.32 | 0.38 |

| G (s) |
| 7.58 |
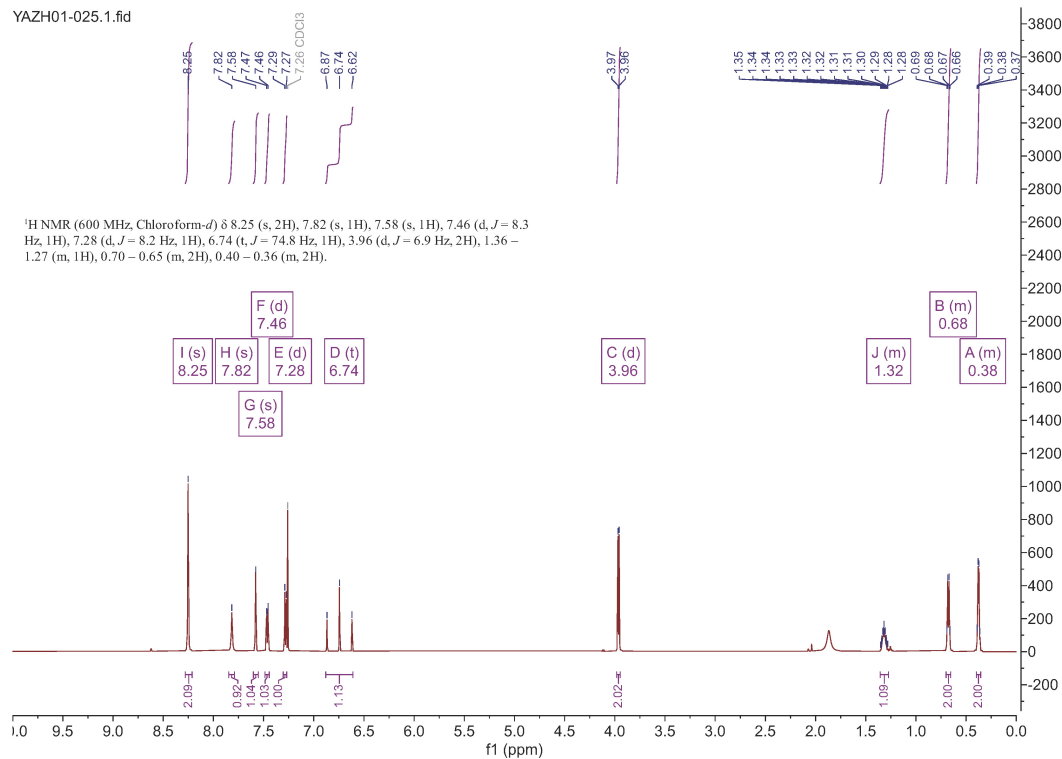
Figure S115 ¹H NMR spectrum of compound NPD-2980

YAZH01-025.4.fid

¹³C NMR (151 MHz, Chloroform-*d*) δ 164.4, 151.1, 144.1, 138.5, 131.8, 131.4, 130.6, 122.5, 119.9, 115.8 (t, *J* = 264.3 Hz), 114.3, 74.4, 10.1, 3.4.
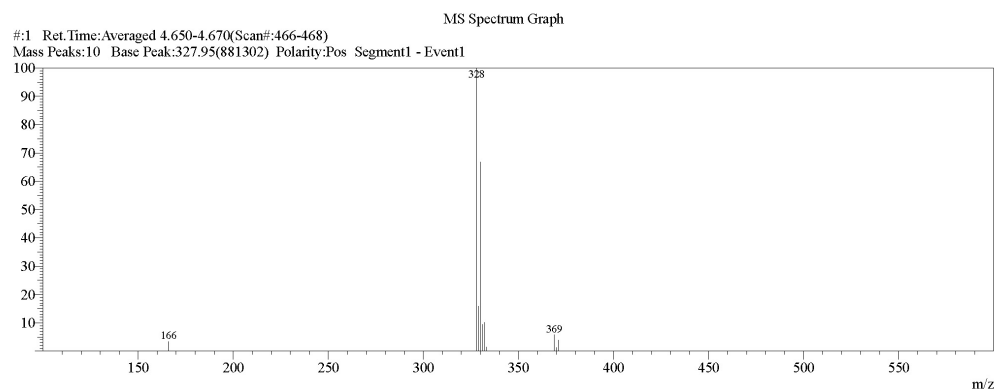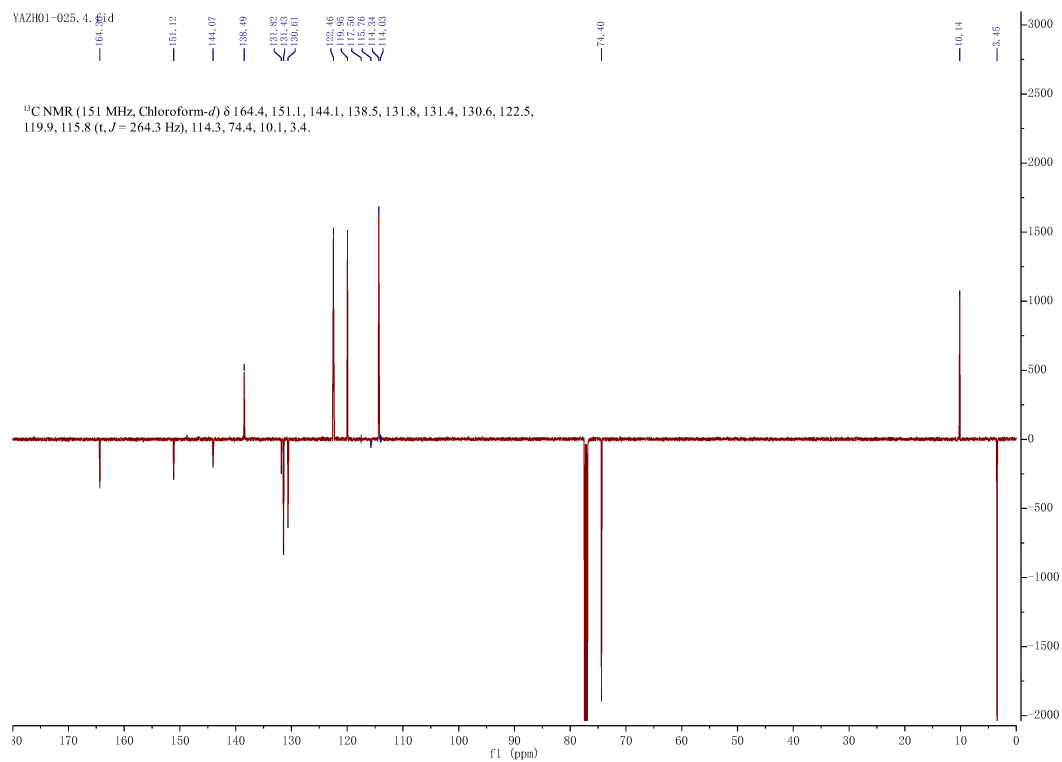

Figure S116 ¹³C NMR spectrum of compound NPD-2980

112

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Vial# : 2
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PDA Graph

mAU

PeakTable
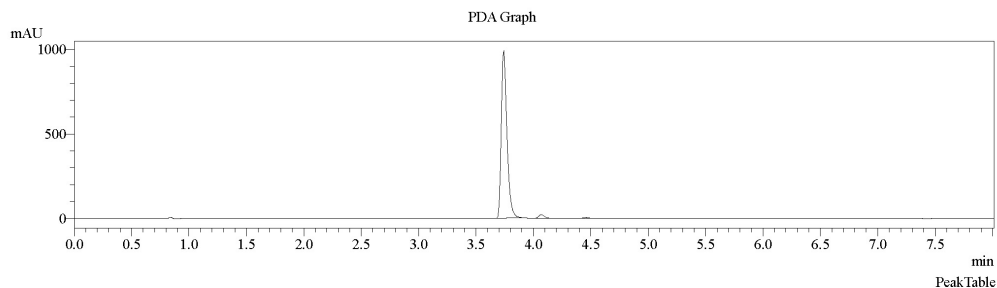
PDA Ch1 254nm 4nm

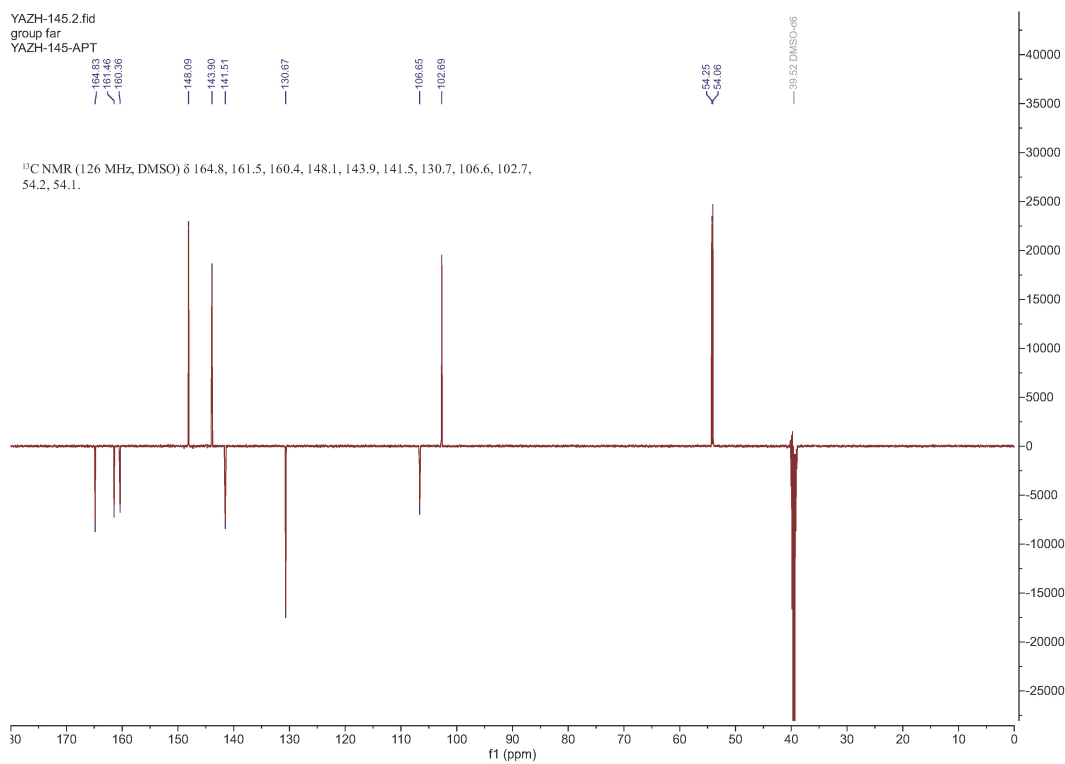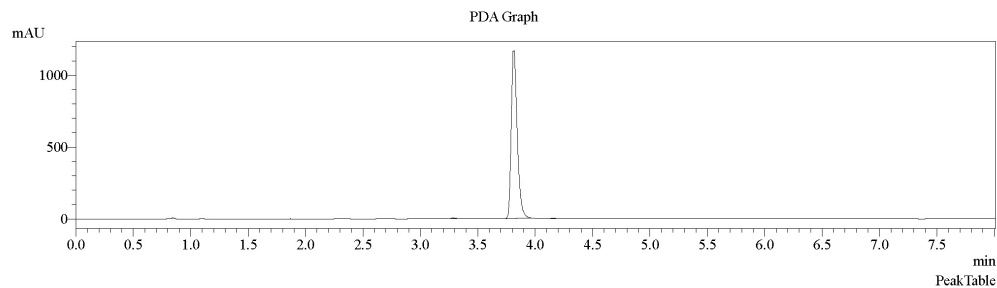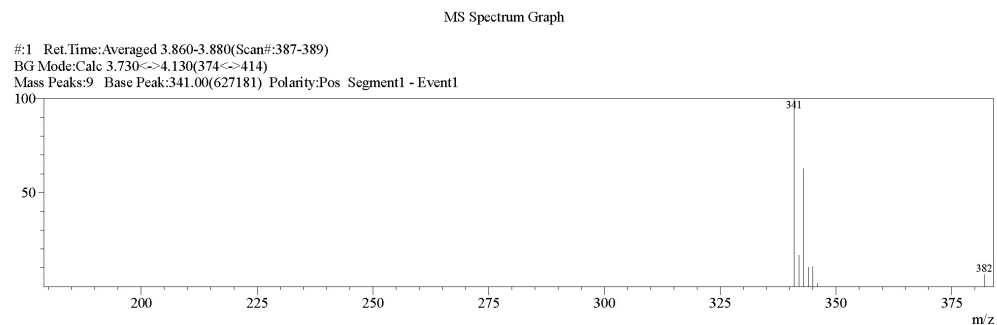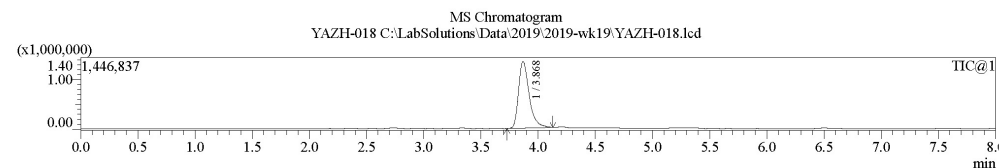| Peak#	Name	Ret. Time	Area	Area %
1		3.232	7898	0.224
2		3.735	3426277	97.259
3		4.061	64224	1.823
4		4.449	17567	0.499
5		4.648	2364	0.067
6		4.853	4499	0.128
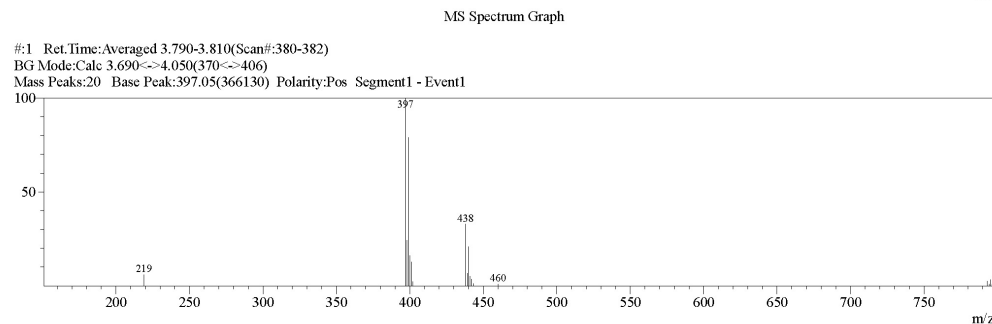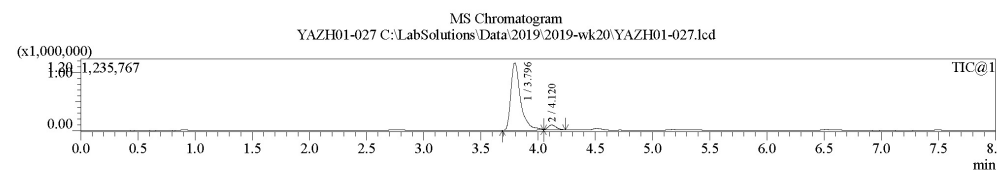
MS Chromatogram
YAZH01-027 C:\LabSolutions\Data\2019\2019-wk20\YAZH01-027.lcd

(x1,000,000)
1.235,767
TIC@1

MS Spectrum Graph

#:1 Ret.Time:Averaged 3.790-3.810(Scan#:380-382)
BG Mode:Calc 3.690<->4.050(370<->406)
Mass Peaks:20 Base Peak:397.05(366130) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.690<->4.050(370<->406)
Mass Peaks:20 Base Peak:397.05(366130) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	150.95	16336	4.46				10	439.15	24040	6.57			
2	219.10	21867	5.97				11	440.15	75756	20.69			
3	397.05	366130	100.00				12	441.15	18221	4.98			
4	398.10	88607	24.20				13	442.15	12605	3.44			
5	399.10	288995	78.93				14	443.20	4145	1.13			
6	400.10	58695	16.03				15	460.15	3774	1.03			
7	401.10	46866	12.80				16	793.10	8735	2.39			
8	402.10	8046	2.20				17	794.30	3937	1.08			
9	438.10	120100	32.80				18	795.30	12281	3.35			

Figure S117 LCMS spectrum of compound NPD-2981

YAZH01-027.3.fid
group far

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.28 (s, 2H), 7.74 (s, 1H), 7.59 − 7.43 (m, 2H), 6.93 (d, *J* = 7.8 Hz, 1H), 4.87 (s, 1H), 3.93 (s, 3H), 2.07 − 1.78 (m, 6H), 1.63 (s, 2H).

D (m)
7.49

B (s)   C (s)   F (d)   G (s)   A (s)   I (s)
8.28   7.74   6.93   4.87   3.93   1.63

H (m)
1.92
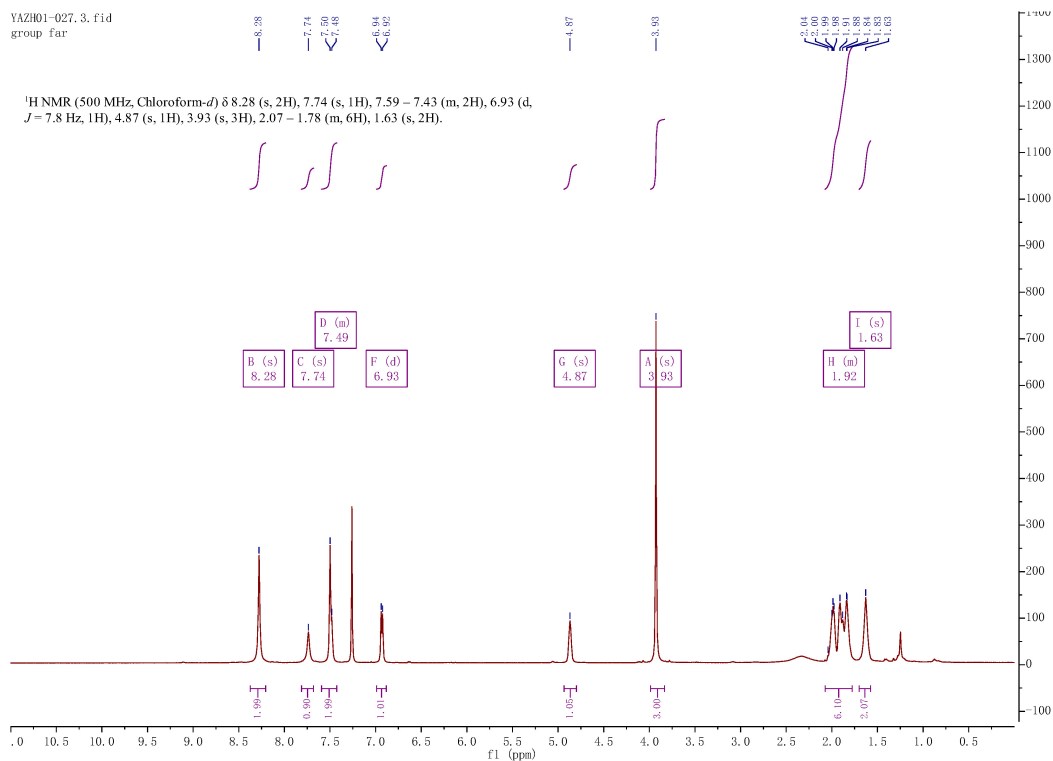
Figure S118 ^{1}H NMR spectrum of compound NPD-2981

YAZH01-27.2.fid

^{13}C NMR (126 MHz, CDCl$_3$) δ 164.6, 154.4, 148.2, 138.5, 134.4, 131.0, 124.5, 120.8, 114.3, 111.0, 80.9, 56.3, 32.9, 24.2.
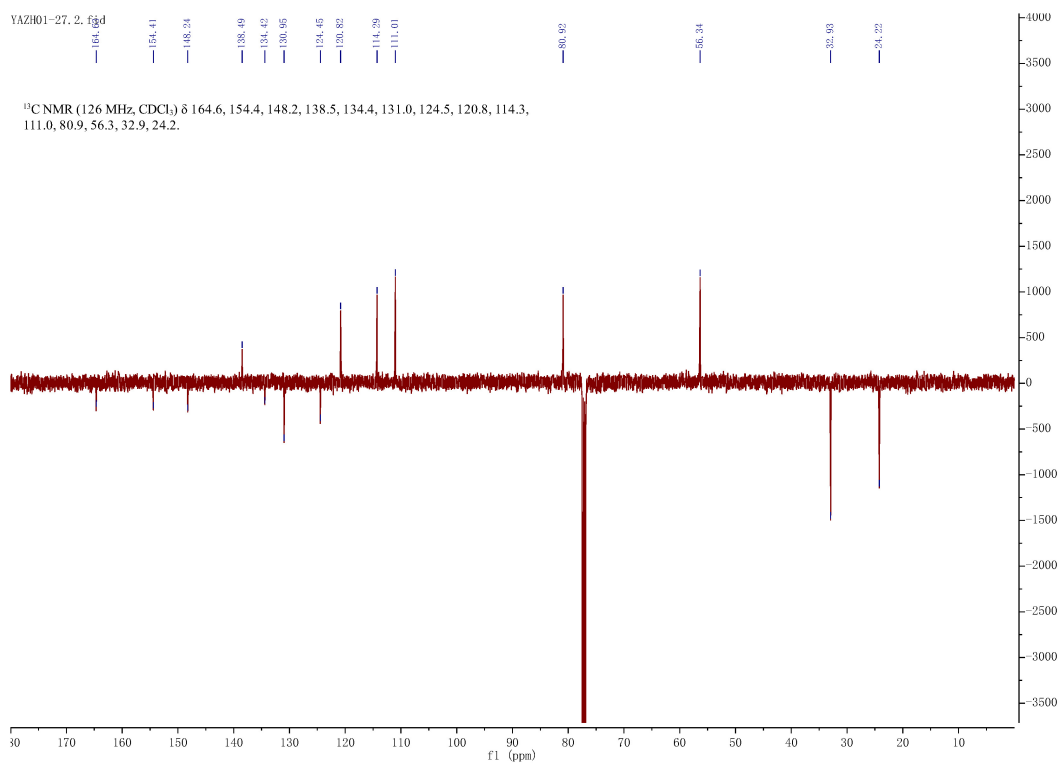
Figure S119 ^{13}C NMR spectrum of compound NPD-2981

114

PDA Graph
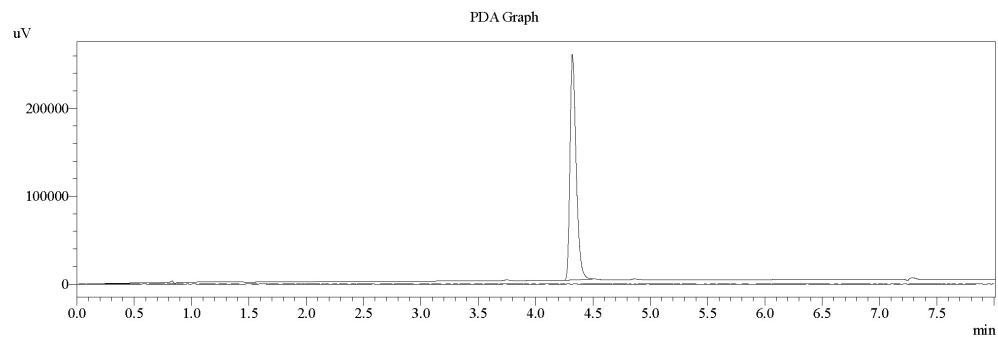
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.318	962680	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.360-4.380(Scan#:437-439)
Mass Peaks:6 Base Peak:292.05(217591) Polarity:Pos Segment1 - Event1
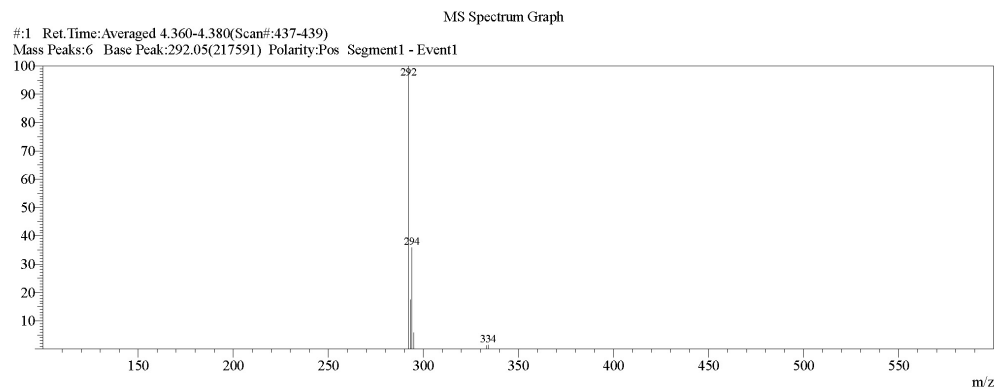
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.270<~>4.520(428<~>453)
Mass Peaks:6 Base Peak:292.05(217591) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	292.05	217591	100.00				4	295.10	12584	5.78			
2	293.05	37967	17.45				5	333.15	2847	1.31			
3	294.05	78124	35.90				6	334.20	3111	1.43			

Figure S120 LCMS spectrum of compound NPD-2991

115

PC-001.1.fid
group far

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 8.5 Hz, 2H), 7.71 – 7.65 (m, 2H), 7.50 (dd, *J* = 8.8, 2.1 Hz, 1H), 6.96 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 1H), 3.90 (s, 3H), 3.87 (s, 3H).

F (m)
7.68

D (d)
6.96

B (s)
3.87

E (dd)
7.50

C (d)
6.91

A (s)
3.90

G (d)
7.82
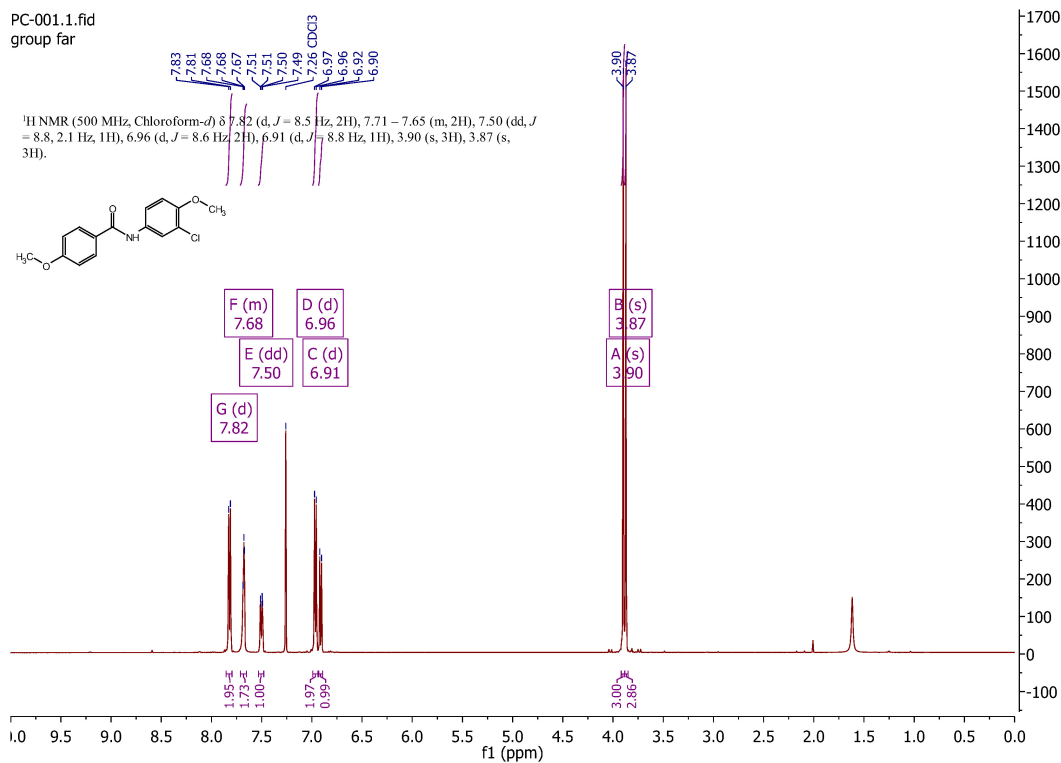
Figure S121 ^{1}H NMR spectrum of compound NPD-2991

PC-002/2
group far

^{13}C NMR (126 MHz, CDCl$_3$) δ 165.3, 162.7, 152.1, 131.7, 129.0, 126.8, 122.9, 122.6, 120.1, 114.1, 112.4, 56.5, 55.6.
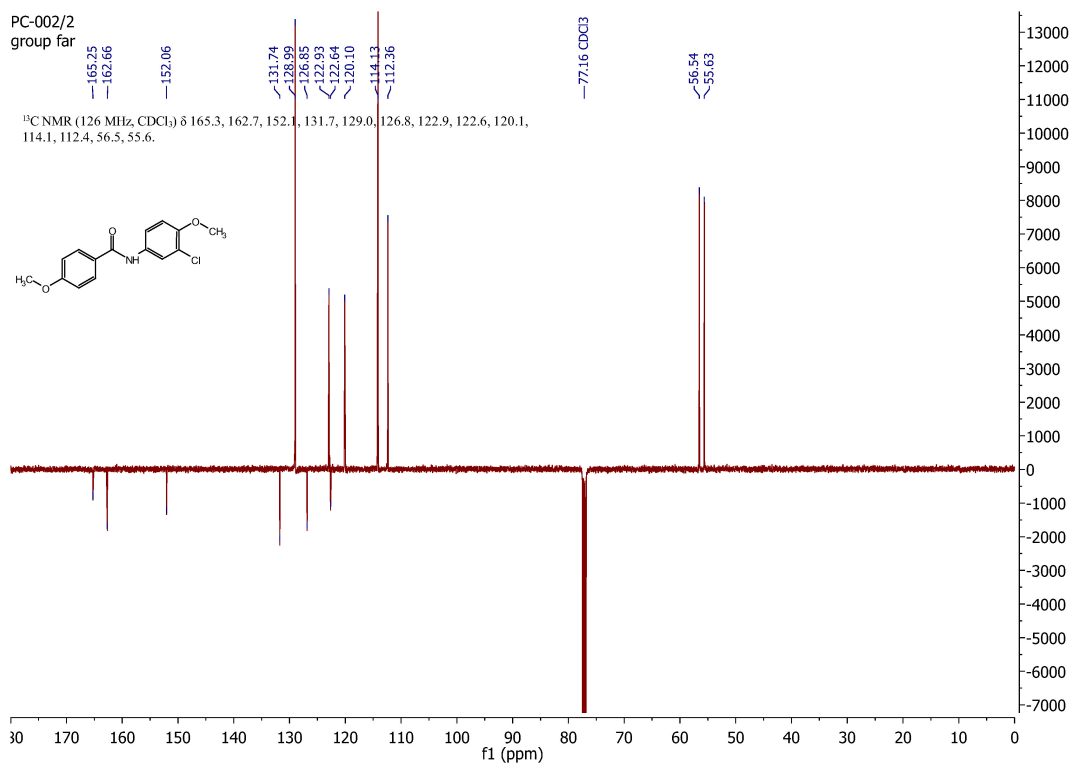
Figure S122 ^{13}C NMR spectrum of compound NPD-2991

PDA Graph

uV
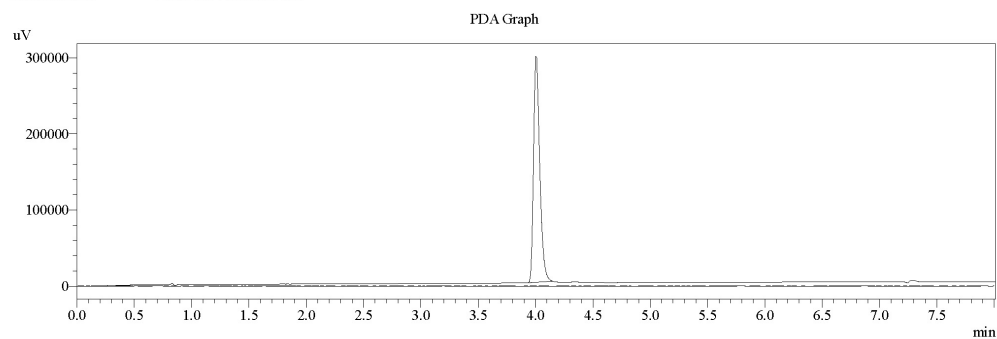
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.000	1123956	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.050-4.070(Scan#:406-408)
Mass Peaks:19 Base Peak:297.00(300798) Polarity:Pos Segment1 - Event1
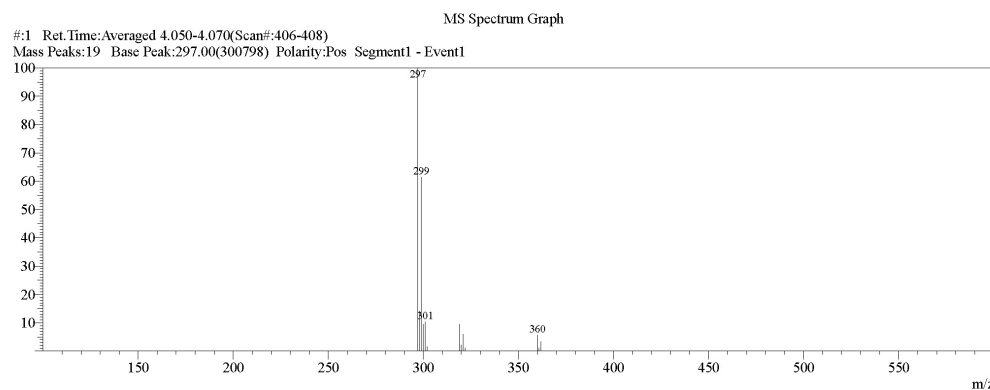
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.930<->4.310(394<->432)
Mass Peaks:19 Base Peak:297.00(300798) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	297.00	300798	100.00				10	322.00	3453	1.15			
2	298.00	42559	14.15				11	360.00	17128	5.69			
3	299.00	184817	61.44				12	360.90	3156	1.05			
4	299.95	28497	9.47				13	361.95	10308	3.43			
5	301.05	30936	10.28				14	615.05	9214	3.06			
6	301.95	4667	1.55				15	616.05	4246	1.41			
7	319.00	28681	9.53				16	617.00	16108	5.36			
8	320.00	6262	2.08				17	618.00	4738	1.58			
9	320.95	17935	5.96				18	619.05	6994	2.33			

Figure S123 LCMS spectrum of compound NPD-2992
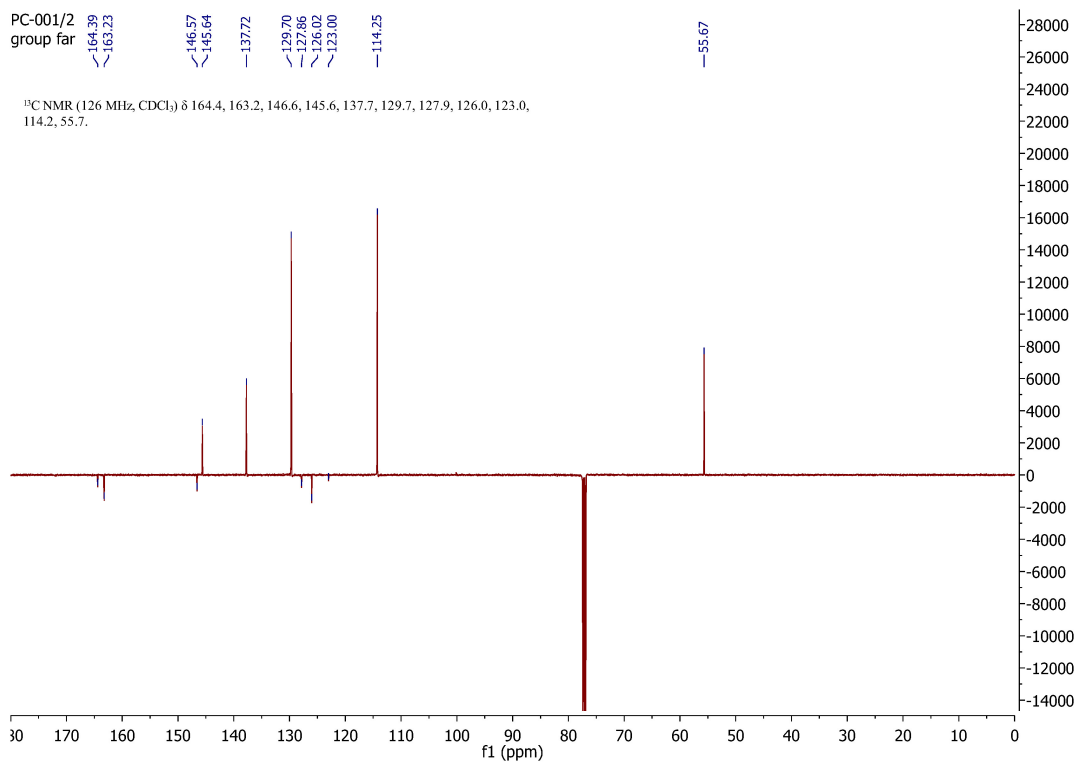
117

PC-002.1.fid
group far

¹H NMR (500 MHz, Chloroform-*d*) δ 8.38 (d, *J* = 1.7 Hz, 1H), 8.30 (s, 1H), 7.90 (d, *J* = 8.7 Hz, 2H), 7.78 (d, *J* = 2.1 Hz, 1H), 6.99 (d, *J* = 8.7 Hz, 2H), 3.88 (s, 3H).

F (d)	D (d)
8.38	7.90

E (s)	C (d)	B (d)
8.30	7.78	6.99

A (s)
3.88

Figure S124 ¹H NMR spectrum of compound NPD-2992

PC-001/2
group far

¹³C NMR (126 MHz, CDCl₃) δ 164.4, 163.2, 146.6, 145.6, 137.7, 129.7, 127.9, 126.0, 123.0, 114.2, 55.7.

Figure S125 ¹³C NMR spectrum of compound NPD-2992

118

PDA Graph

uV

PeakTable

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		2.481	6369576	100.000

MS Chromatogram
Practical Course-121-1 C:\LabSolutions\Data\2017\2017-wk08\Practical Course-121-1.lcd

(x1,000,000)

1,385,925

1 / 2.550

TIC@1* 1.00

MS Spectrum Graph

#:1 Ret.Time:Averaged 2.540-2.560(Scan#:255-257)
Mass Peaks:3 Base Peak:243.10(1122590) Polarity:Pos Segment1 - Event1
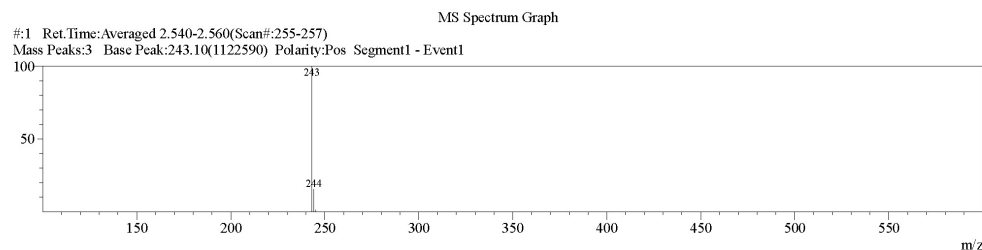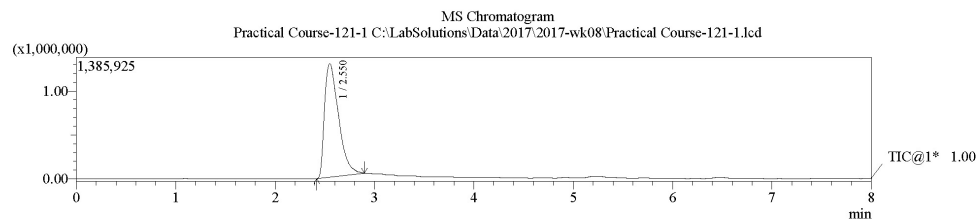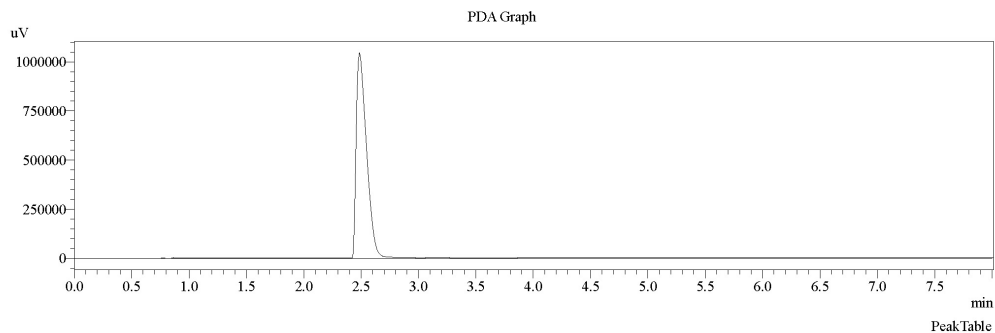
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 2.420<->2.900(243<->291)
Mass Peaks:3 Base Peak:243.10(1122590) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	243.10	1122590	100.00				3	245.10	14910	1.33			
2	244.10	172408	15.36										

Figure S126 LCMS spectrum of compound NPD-2993

119

PC-003/1
group far

8.44
8.43

7.26 CDCl3
7.14
7.13
7.11
6.97
6.95
6.92
6.89
6.88
6.87
6.84
6.82

3.71

3.51

^{1}H NMR (500 MHz, Chloroform-d) δ 8.44 (d, J = 4.6 Hz, 2H), 7.13 (t, J = 7.9 Hz, 1H), 6.96 (d, J = 6.0 Hz, 2H), 6.92 (s, 1H), 6.88 (dd, J = 8.2, 2.4 Hz, 1H), 6.83 (d, J = 7.6 Hz, 1H), 3.71 (s, 3H), 3.51 (s, 3H).

F (dd)
6.88

D (d)
6.96

B (s)
3.51

H (d)
8.44

C (t)
7.13

A (s)
3.71

E (s)
6.92

G (d)
6.83

1.94

1.01
1.97
0.98
0.98
0.98

3.00
2.97

f1 (ppm)

Figure S127 ^{1}H NMR spectrum of compound NPD-2993

PC-003/2
group far

170.66

159.45

152.22
150.56

136.28

129.43
121.12
120.20
116.84
113.92

55.41

37.51

^{13}C NMR (126 MHz, CDCl$_3$) δ 170.7, 159.5, 152.2, 150.6, 136.3, 129.4, 121.1, 120.2, 116.8, 113.9, 55.4, 37.5.

f1 (ppm)
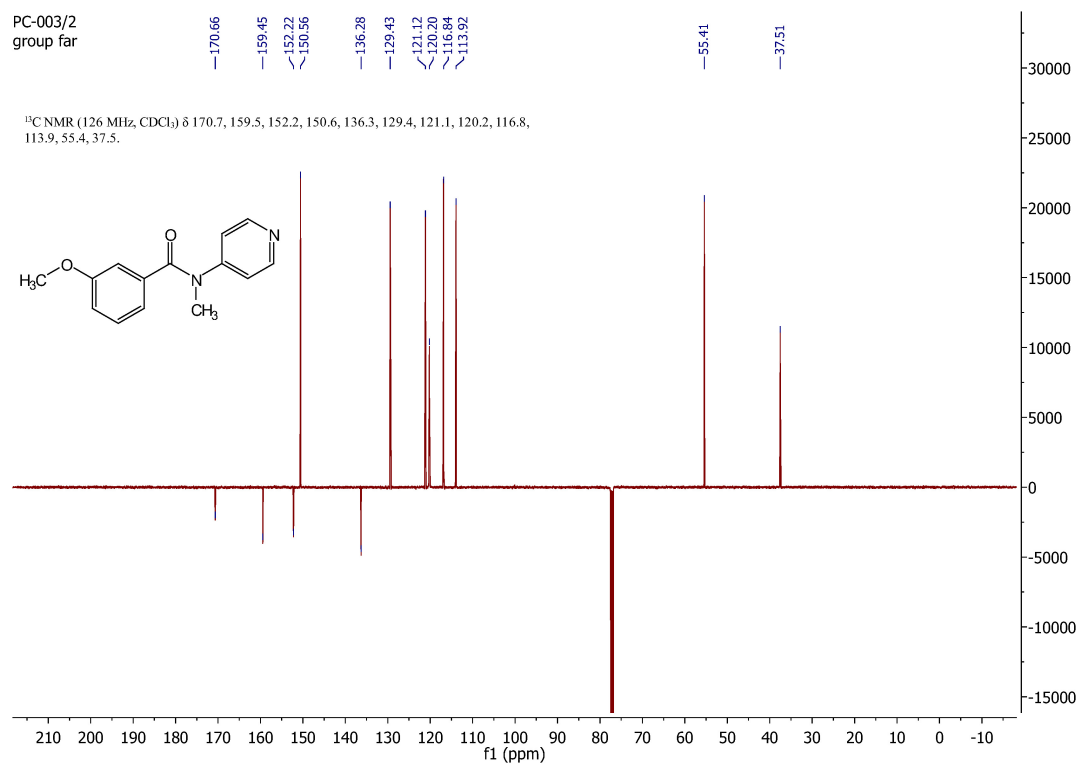
Figure S128 ^{13}C NMR spectrum of compound NPD-2993

120

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.059	2366839	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 3.110-3.130(Scan#:312-314)
Mass Peaks:6   Base Peak:230.05(380325) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.010<->3.190(302<->320)
Mass Peaks:6   Base Peak:230.05(380325) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	180.00	7033	1.85				4	232.00	5927	1.56			
2	230.05	380325	100.00				5	271.10	34608	9.10			
3	231.05	53980	14.19				6	272.10	6395	1.68			

Figure S129 LCMS spectrum of compound NPD-2994

121

PC-004/1

9.20
9.01
8.17
7.47
7.47
7.46
7.45
7.45
7.44
7.44
7.43
7.41
7.40
7.14
7.14
7.13
7.13
7.12
7.12
3.88

^{1}H NMR (600 MHz, Chloroform-*d*) δ 9.20 (s, 2H), 9.01 (s, 1H), 8.17 (s, 1H), 7.49 – 7.38 (m, 3H),
7.13 (ddd, *J* = 7.9, 2.5, 1.1 Hz, 1H), 3.88 (s, 3H).

B (s)
9.01

E (ddd)
7.13

A (s)
9.20

C (s)
8.17

D (m)
7.44

F (s)
3.88

2.00
1.01
0.91
3.02
0.94
2.94
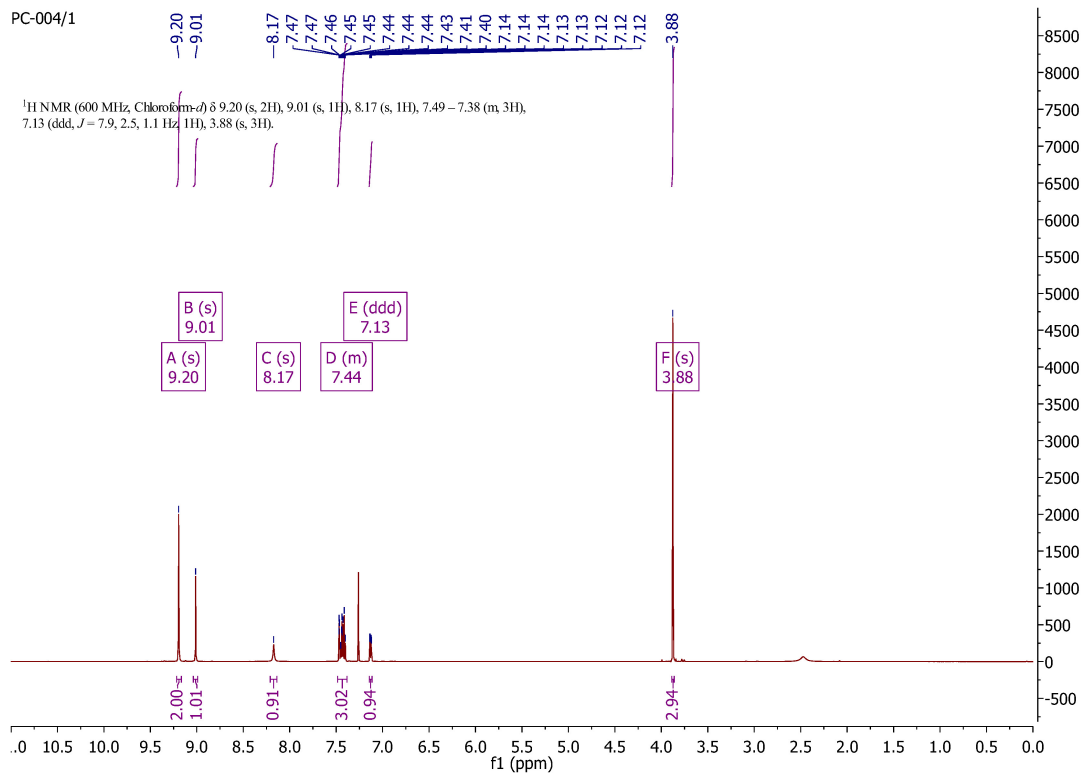
Figure S130 ^{1}H NMR spectrum of compound NPD-2994

PC-004/2

166.05
160.27
153.78
148.24
134.79
133.93
130.17
119.09
119.04
112.90
55.73

^{13}C NMR (151 MHz, CDCl₃) δ 166.0, 160.3, 153.8, 148.2, 134.8, 133.9, 130.2, 119.1, 119.0, 112.9, 55.7.
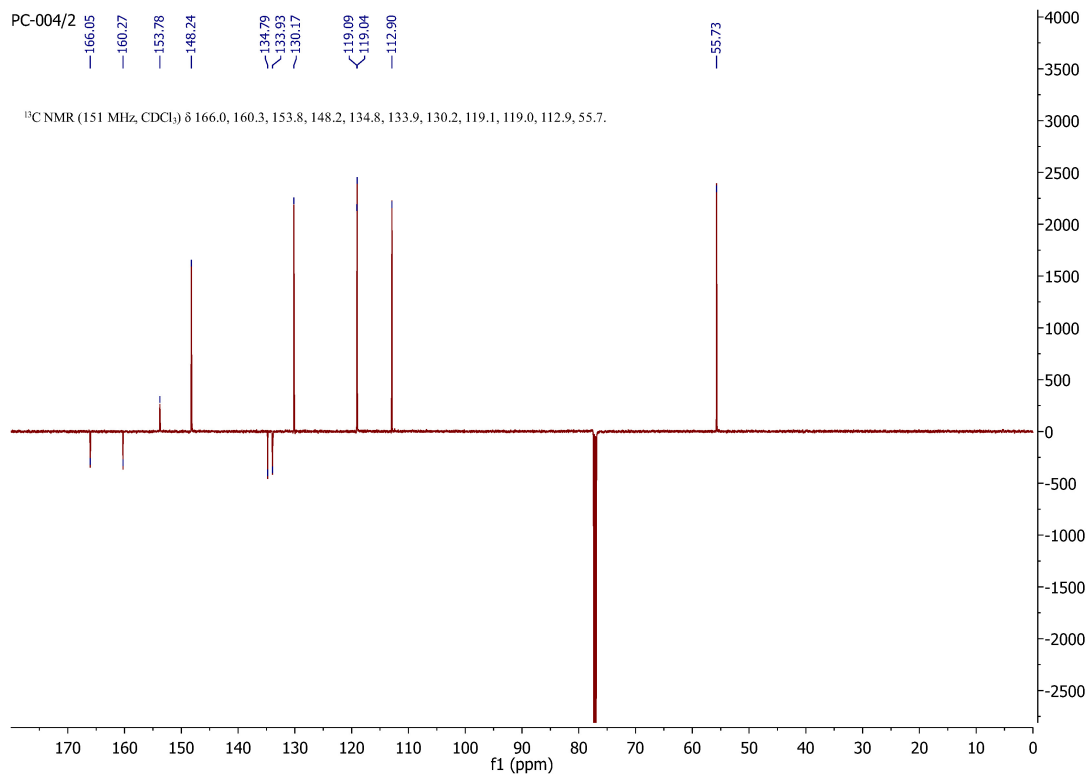
Figure S131 ^{13}C NMR spectrum of compound NPD-2994

122

PDA Graph
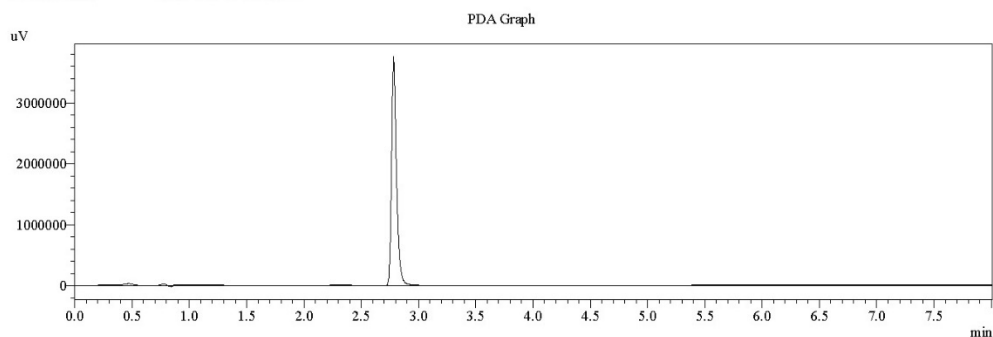
PDA Ch1 230nm 4nm

Peak#	Name	Ret. Time	Area	Area%
1		2.778	11122396	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 2.830-2.850(Scan#:284-286)
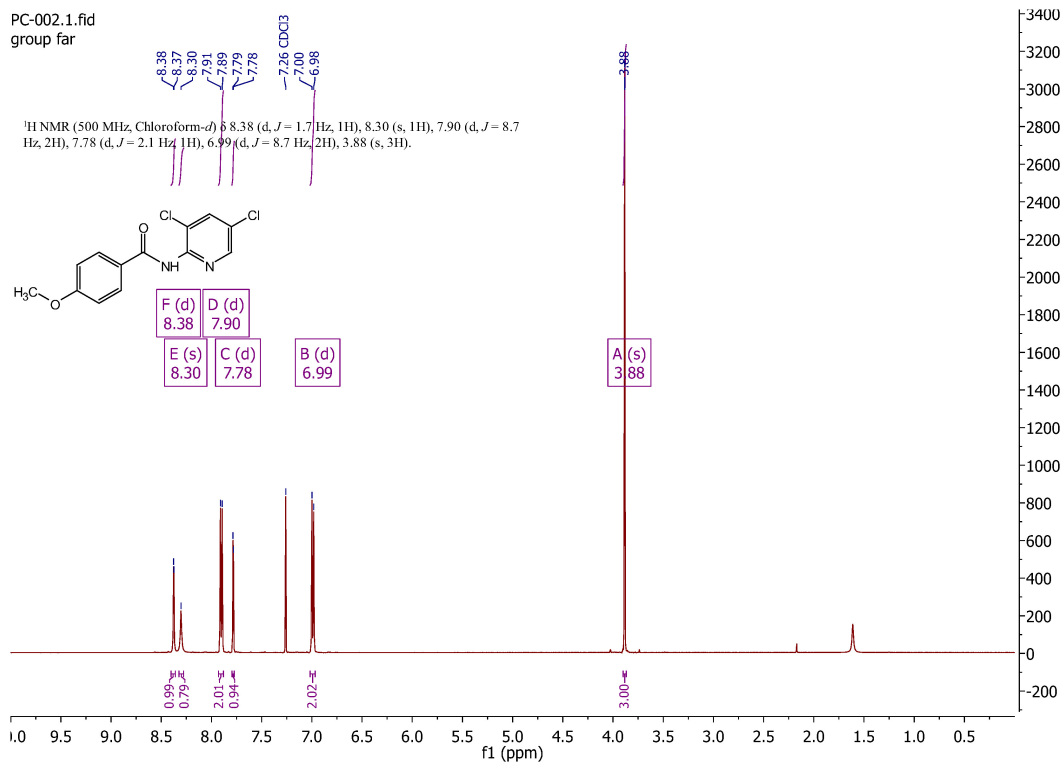Mass Peaks:5 Base Peak:274.10(981528) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 2.730<->3.100(274<->311)
Mass Peaks:5 Base Peak:274.10(981528) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	274.10	981528	100.00				4	315.10	50688	5.16			
2	275.15	173963	17.72				5	316.10	11287	1.15			
3	276.10	28897	2.94										

Figure S132 LCMS spectrum of compound NPD-2995

123

8.94
8.91

7.41
7.26 CDCl3
6.90
6.89
6.88
6.86
6.82

3.89
3.88
3.73

¹H NMR (500 MHz, Chloroform-*d*) δ 8.97 – 8.88 (m, 3H), 7.41 (s, 1H), 6.92 – 6.85 (m, 2H), 6.82 (s, 1H), 3.91 – 3.87 (m, 6H), 3.73 (s, 2H).

F (m)
8.93

D (m)
6.89

C (s)
6.82

E (s)
7.41

B (s)
3.73

A (m)
3.89

2.94
0.91
2.01
1.01
5.94
2.00

f1 (ppm)

Figure S133 ¹H NMR spectrum of compound NPD-2995

170.15

154.27
149.70
148.95
147.82

133.31

125.87
121.86

112.44
111.85

56.11
56.07

44.14

¹³C NMR (126 MHz, CDCl₃) δ 170.2, 154.3, 149.7, 149.0, 147.8, 133.3, 125.9, 121.9, 112.4, 111.9, 56.1, 56.1, 44.1.

f1 (ppm)

Figure S134 ¹³C NMR spectrum of compound NPD-2995

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		2.782	364495	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 2.830-2.850(Scan#:284-286)
Mass Peaks:9 Base Peak:275.00(135963) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 2.730<->3.000(274<->301)
Mass Peaks:9 Base Peak:275.00(135963) Polarity:Pos Segment1 - Event1

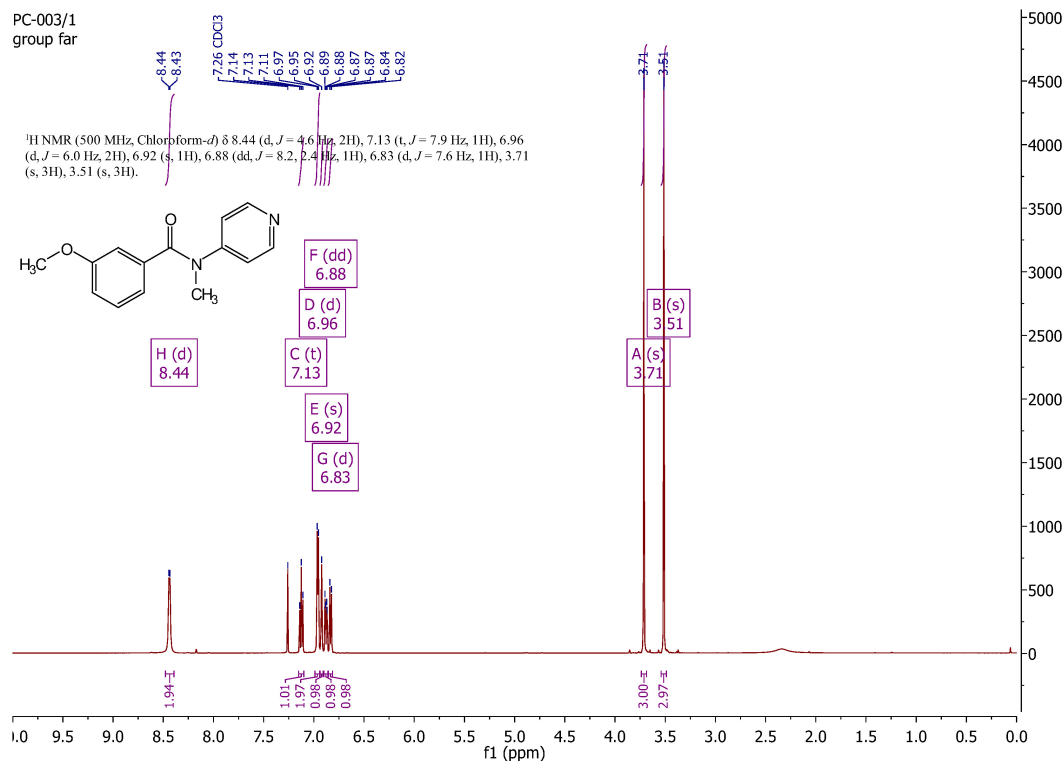| #	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	190.95	1918	1.41				6	279.00	16514	12.15			
2	275.00	135963	100.00				7	280.15	1778	1.31			
3	276.00	20916	15.38				8	316.10	4588	3.37			
4	277.00	90163	66.31				9	318.10	3465	2.55			
5	278.05	13972	10.28										

Figure S135 LCMS spectrum of compound NPD-2996

Figure S136 ¹H NMR spectrum of compound NPD-2996

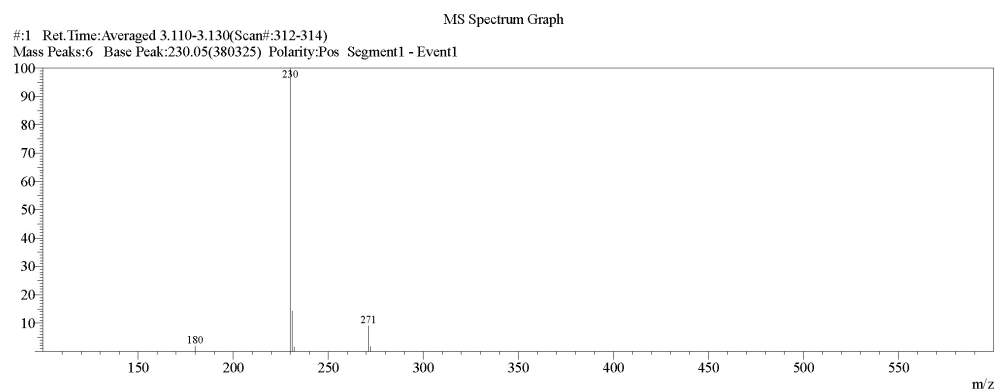¹H NMR (500 MHz, Chloroform-*d*) δ 8.52 (s, 2H), 5.80 (d, *J* = 7.3 Hz, 1H), 4.31 – 4.22 (m, 1H), 3.98 (s, 2H), 3.58 – 3.49 (m, 2H), 2.08 – 2.02 (m, 2H), 1.66 – 1.53 (m, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 161.4, 147.9, 142.2, 129.1, 66.7, 46.7, 32.9.

Figure S137 ¹³C NMR spectrum of compound NPD-2996

PDA Graph

uV

PeakTable

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.262	2880432	100.000

MS Chromatogram
PC-134 C:\LabSolutions\Data\2017\2017-wk08\PC-134.lcd

(x100,000)

TIC@1* 1.00

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.310-4.330(Scan#:432-434)
Mass Peaks:15 Base Peak:330.95(137025) Polarity:Pos Segment1 - Event1
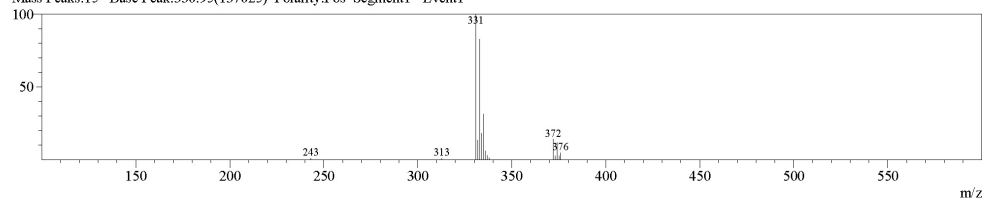
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.210<=>4.510(422<=>452)
Mass Peaks:15 Base Peak:330.95(137025) Polarity:Pos Segment1 - Event1

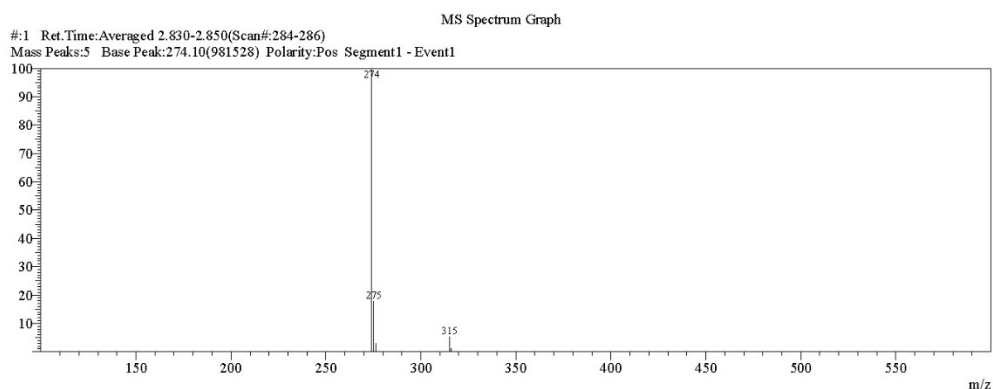| #	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	243.10	1560	1.14				9	336.90	4317	3.15			
2	312.80	1561	1.14				10	337.90	1887	1.38			
3	330.95	137025	100.00				11	372.00	19257	14.05			
4	332.00	18575	13.56				12	373.00	3712	2.71			
5	332.95	113425	82.78				13	374.00	16322	11.91			
6	334.00	25041	18.27				14	375.00	3773	2.75			
7	335.00	42988	31.37				15	376.00	6662	4.86			
8	335.90	8190	5.98										

Figure S138 LCMS spectrum of compound NPD-2997

127

PC-007.1.fid
group far

¹H NMR (500 MHz, Chloroform-*d*) δ 8.56 (s, 2H), 7.68 – 7.64 (m, 1H), 7.59 (s, 1H), 7.52 – 7.46 (m, 1H), 7.26 (s, 1H), 6.94 (d, *J* = 8.8 Hz, 1H), 3.92 (s, 3H).

E (s)
7.26

C (s)
7.59

A (s)
8.56

B (m)
7.66

F (d)
6.94

G (s)
3.92

D (m)
7.49
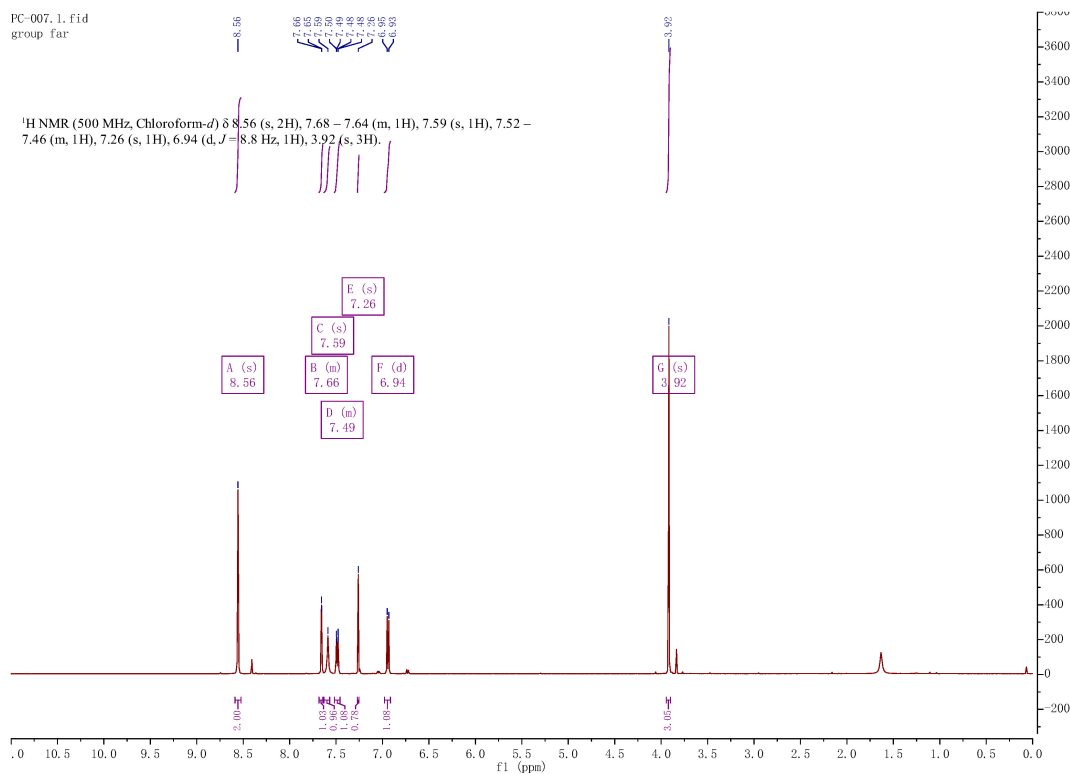
Figure S139 ¹H NMR spectrum of compound NPD-2997

PC-007/2
group far

¹³C NMR (126 MHz, CDCl₃) δ 160.1, 153.1, 148.0, 141.8, 129.9, 129.2, 123.3, 123.0, 120.5, 112.4, 56.6.
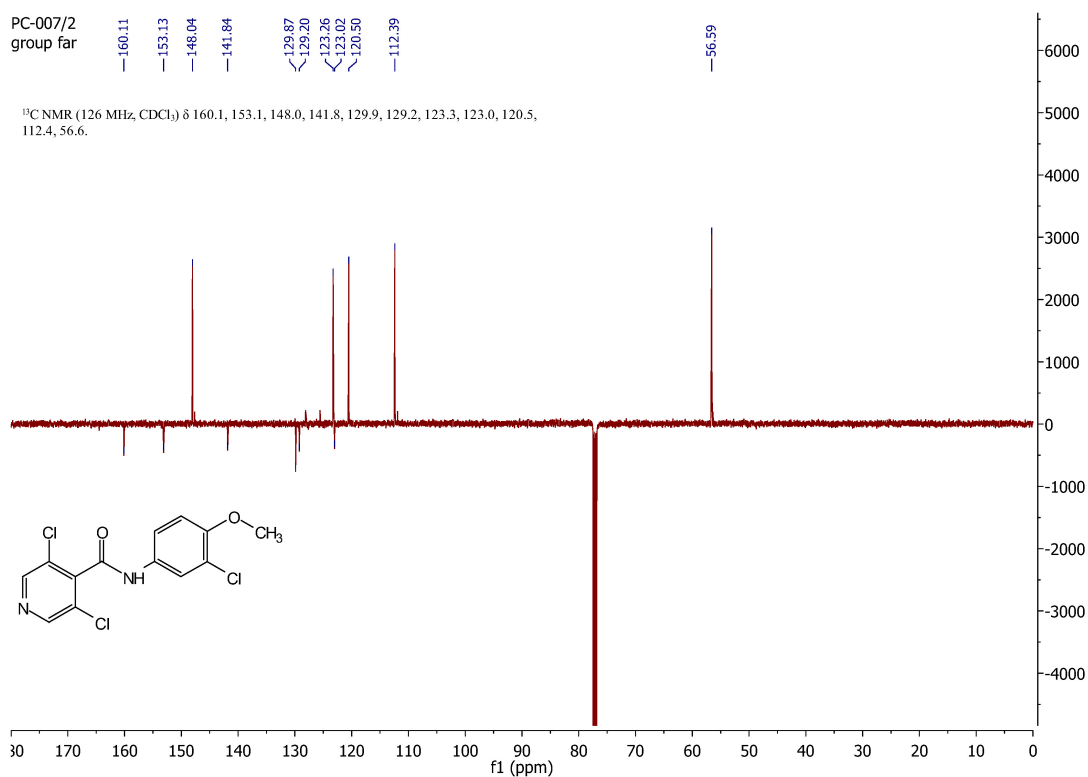
Figure S140 ¹³C NMR spectrum of compound NPD-2997

128

PDA Graph
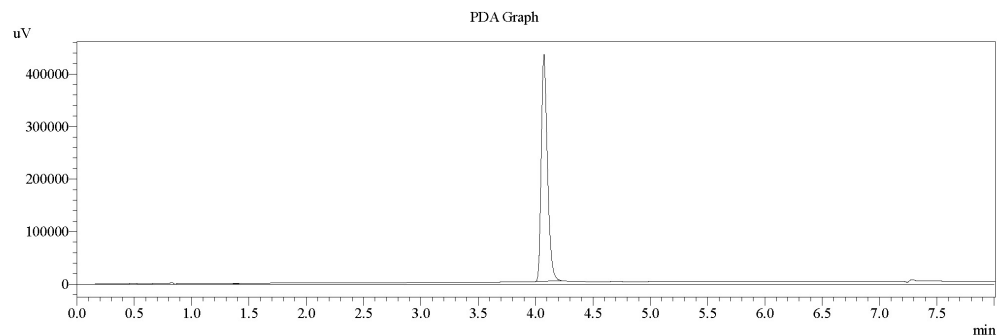
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.067	1602139	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.120-4.140(Scan#:413-415)
Mass Peaks:14   Base Peak:337.90(199602) Polarity:Pos Segment1 - Event1
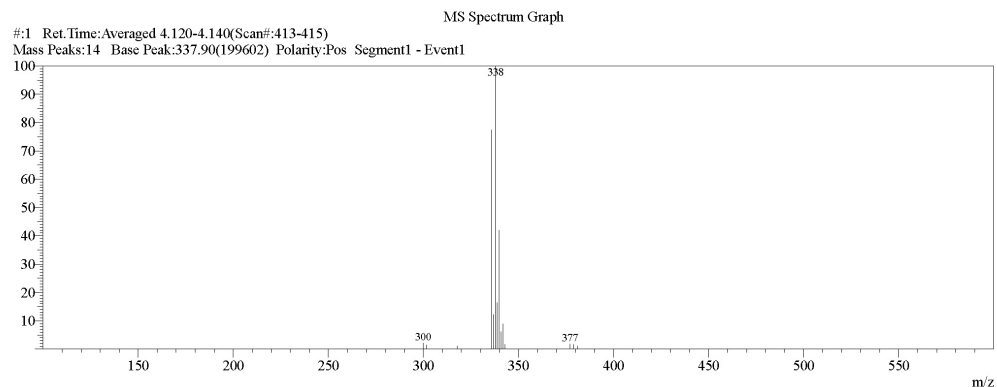
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.020<->4.320(403<->433)
Mass Peaks:14   Base Peak:337.90(199602) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	299.85	4378	2.19				8	339.85	83797	41.98			
2	301.80	3054	1.53				9	340.85	12125	6.07			
3	317.85	2056	1.03				10	341.90	17832	8.93			
4	335.90	154624	77.47				11	342.95	3371	1.69			
5	336.90	24398	12.22				12	377.00	3659	1.83			
6	337.90	199602	100.00				13	378.80	3293	1.65			
7	338.90	32867	16.47				14	380.95	2116	1.06			

Figure S141 LCMS spectrum of compound NPD-2998

8.52
8.42
7.75
7.26 CDCl3

¹H NMR (500 MHz, Chloroform-*d*) δ 8.52 (s, 2H), 8.42 (s, 1H), 7.75 (s, 2H).

C (s)
8.42

B (s)
8.52

A (s)
7.75

2.51
0.83
2.00

f1 (ppm)

Figure S142 ¹H NMR spectrum of compound NPD-2998

149.05
147.51
145.05
144.22
137.88
128.46
77.16 CDCl3

¹³C NMR (126 MHz, CDCl₃) δ 149.0, 147.5, 145.1, 144.2, 137.9, 128.5.

f1 (ppm)

Figure S143 ¹³C NMR spectrum of compound NPD-2998

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.604	1268254	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 3.650-3.670(Scan#:366-368)
Mass Peaks:4 Base Peak:349.10(2022664) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.520<->3.980(353<->399)
Mass Peaks:4 Base Peak:349.10(2022664) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	254.05	34110	1.69				3	350.10	431483	21.33			
2	349.10	2022664	100.00				4	351.10	55256	2.73			

Figure S144 LCMS spectrum of compound NPD-2999

¹H NMR (500 MHz, Chloroform-*d*) δ 8.47 (d, *J* = 5.3 Hz, 2H), 7.04 − 6.98 (m, 4H), 6.85 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.62 (t, *J* = 74.9 Hz, 1H), 3.74 (d, *J* = 7.0 Hz, 2H), 3.52 (s, 3H), 1.22 − 1.10 (m, 1H), 0.66 − 0.57 (m, 2H), 0.34 − 0.28 (m, 2H).

A (d)
8.47

C (dd)
6.85

B (m)
7.01

E (t)
6.62

I (s)
3.52

H (d)
3.74

N (m)
0.31

K (m)
1.16

L (m)
0.62

Figure S145 ¹H NMR spectrum of compound NPD-2999

¹³C NMR (126 MHz, Chloroform-*d*) δ 169.9, 152.7, 150.3, 149.8, 142.3, 132.8, 122.0, 121.9, 119.9, 115.8 (t, *J* = 260.5 Hz), 115.0, 74.1, 37.7, 10.0, 3.4.

Figure S146 ¹³C NMR spectrum of compound NPD-2999

132

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		5.001	628557	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 5.050-5.070(Scan#:506-508)
Mass Peaks:12 Base Peak:398.10(150868) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.950<->5.250(496<->526)
Mass Peaks:12 Base Peak:398.10(150868) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	398.10	150868	100.00				7	441.05	1771	1.17			
2	399.10	34813	23.08				8	623.60	3408	2.26			
3	400.10	50380	33.39				9	624.70	4133	2.74			
4	401.10	11841	7.85				10	625.75	2207	1.46			
5	402.10	1575	1.04				11	631.70	1871	1.24			
6	439.15	4307	2.85				12	823.40	1534	1.02			

Figure S147 LCMS spectrum of compound NPD-3000

133

7.70
7.68
7.53
7.50
7.49
7.32
7.30
7.26 CDCl3
7.24
7.22
6.94
6.92
6.87
6.72
6.57
3.95
3.94
3.91
1.59
1.35
1.34
1.33
1.32
1.31
1.30
1.29
1.27
0.67
0.66
0.37
0.36

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.73 – 7.66 (m, 2H), 7.53 (s, 1H), 7.49 (d, *J* = 8.6 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.23 (d, *J* = 8.2 Hz, 1H), 6.93 (d, *J* = 8.8 Hz, 1H), 6.72 (t, *J* = 75.0 Hz, 1H), 3.94 (d, *J* = 6.9 Hz, 2H), 3.91 (s, 3H), 1.59 (s, 2H), 1.31 (m, 1H), 0.67 (d, *J* = 7.6 Hz, 2H), 0.37 (d, *J* = 4.5 Hz, 2H).

F (s)
7.53

C (d)
7.31

B (t)
6.72

I (d)
3.94

K (m)
1.31

M (d)
0.37

E (d)
7.49

A (d)
6.93

H (s)
3.91

J (s)
1.59

L (d)
0.67

G (m)
7.69

D (d)
7.23
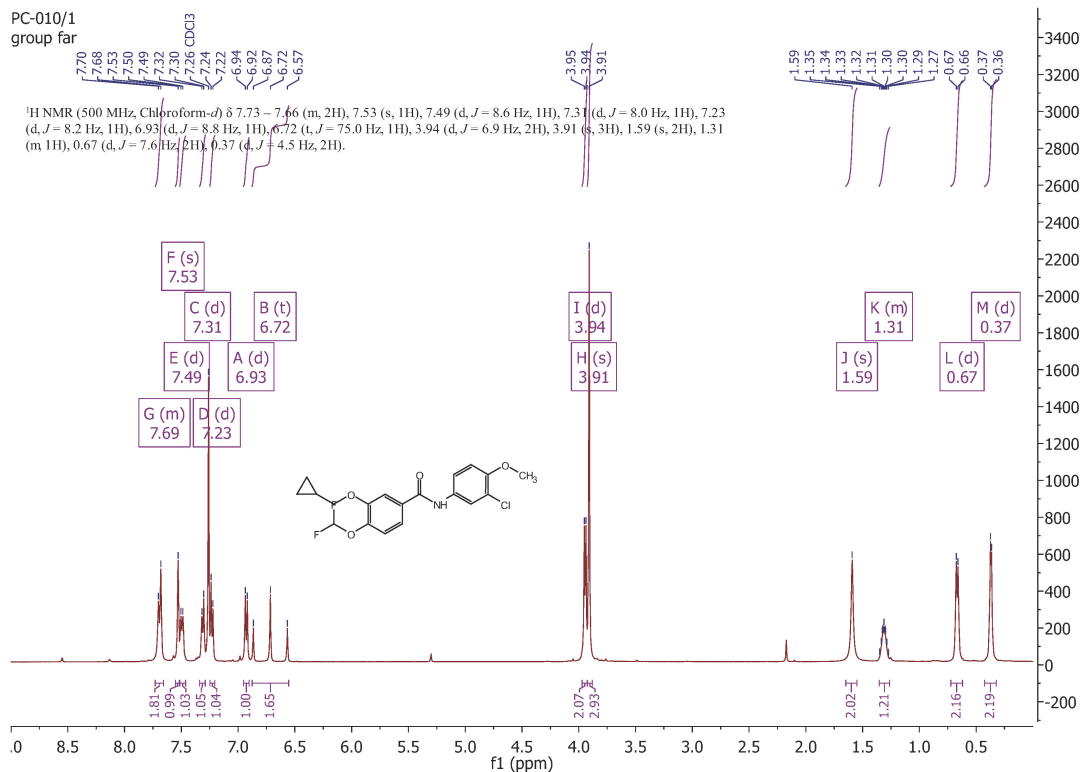
Figure S148 ^{1}H NMR spectrum of compound NPD-3000

164.72
152.36
150.96
143.15
133.04
131.27
123.02
122.75
122.34
120.17
118.80
115.89
113.89
112.36
74.27
56.54
10.15
3.43

^{13}C NMR (126 MHz, Chloroform-*d*) δ 164.7, 152.4, 151.0, 143.1, 133.0, 131.3, 123.0, 122.8, 122.3, 120.2, 118.8, 115.9 (t, *J* = 260.4 Hz), 113.9, 112.4, 74.3, 56.5, 10.2, 3.4.
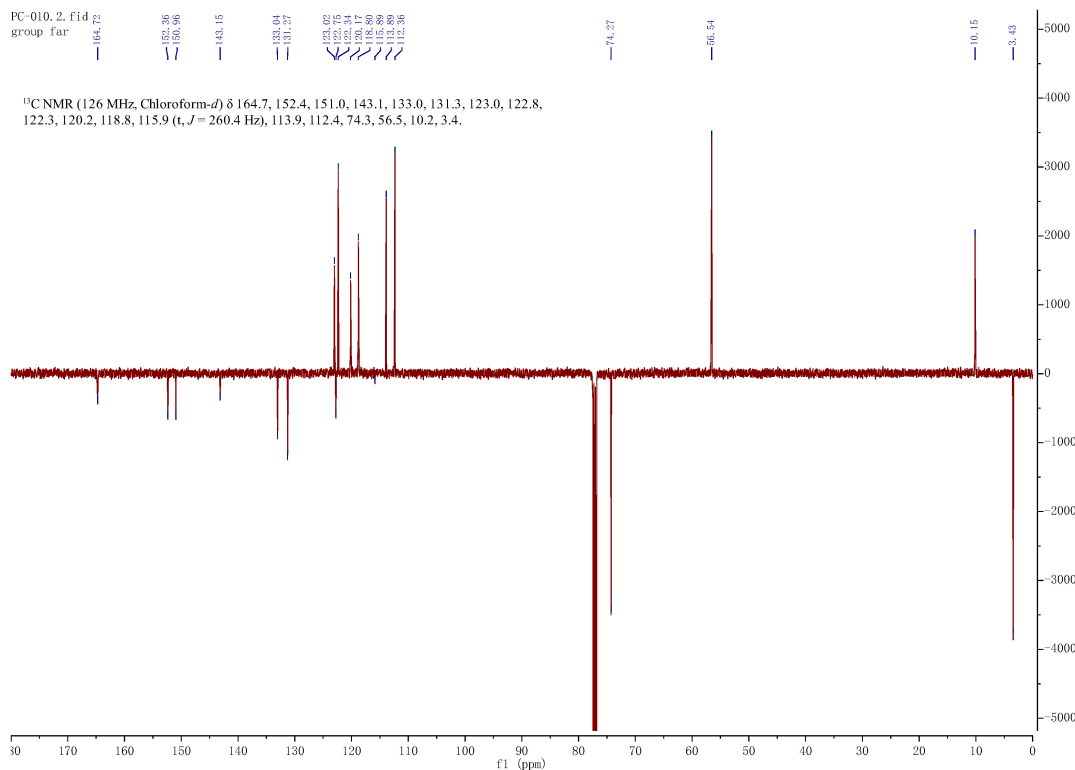
Figure S149 ^{13}C NMR spectrum of compound NPD-3000

PDA Graph

uV
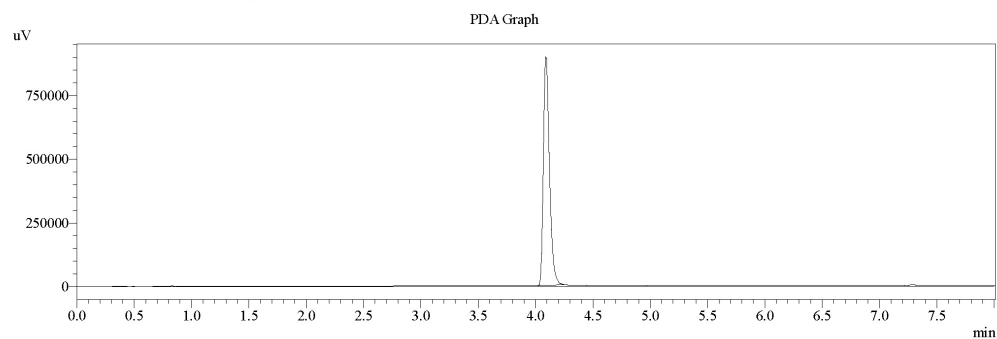
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.085	3291341	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.130-4.150(Scan#:414-416)
Mass Peaks:5   Base Peak:336.10(1142073) Polarity:Pos Segment1 - Event1
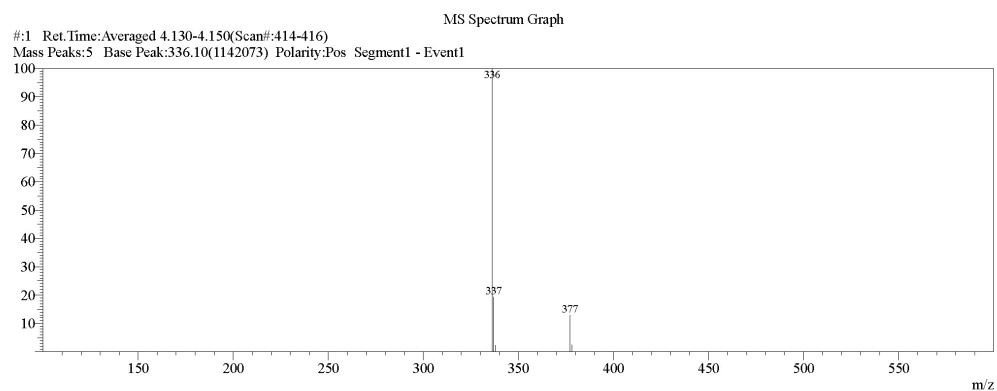
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.020<->4.420(403<->443)
Mass Peaks:5   Base Peak:336.10(1142073) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	336.10	1142073	100.00				4	377.10	147807	12.94			
2	337.10	221193	19.37				5	378.10	27991	2.45			
3	338.10	26083	2.28										

Figure S150 LCMS spectrum of compound NPD-3001

135

PC-011/1
group far

9.16
9.02

8.18

7.56
7.41
7.39
7.26 CDCl3
7.24
6.89
6.74
6.59

3.95
3.94

1.35
1.33
1.33
1.32
1.31
1.31
1.30
1.29
1.28
1.27
0.69
0.68
0.66
0.65
0.38
0.37
0.36
0.35

¹H NMR (500 MHz, Chloroform-*d*) δ 9.16 (s, 2H), 9.02 (s, 1H), 8.18 (s, 1H), 7.56 (s, 1H), 7.40 (d, *J* = 8.1 Hz, 1H), 7.24 (d, *J* = 8.1 Hz, 1H), 6.74 (t, *J* = 74.8 Hz, 1H), 3.95 (d, *J* = 6.9 Hz, 2H), 1.31 (tt, *J* = 12.7, 7.8 Hz, 1H), 0.67 (q, *J* = 7.6 Hz, 2H), 0.37 (q, *J* = 4.7 Hz, 3H).

K (s)
9.16

G (d)
7.40

D (q)
0.37

J (s)
9.02

I (s)
8.18

F (s)
7.56

E (t)
6.74

A (d)
3.95

B (tt)
1.31

C (q)
0.67

H (d)
7.24

1.90
0.97

0.88

0.97
1.01
0.45

1.30

2.00

1.02

2.30
2.56

Figure S151 ¹H NMR spectrum of compound NPD-3001

PC-011.2.fid
group far

165.18

154.62
151.08
148.36
143.71
143.68

133.53
131.63

122.33
119.17
117.84
115.76
114.00
113.68

74.36

10.11

3.44

¹³C NMR (126 MHz, Chloroform-*d*) δ 165.2, 154.6, 151.1, 148.4, 143.7 (d, *J* = 3.2 Hz), 133.5, 131.6, 122.3, 119.2, 115.8 (t, *J* = 264.2 Hz), 114.0, 74.4, 10.1, 3.4.

Figure S152 ¹³C NMR spectrum of compound NPD-3001

136

PDA Graph

uV

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.014	12268611	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 3.070-3.090(Scan#:308-310)
Mass Peaks:7   Base Peak:236.05(353179) Polarity:Pos Segment1 - Event1
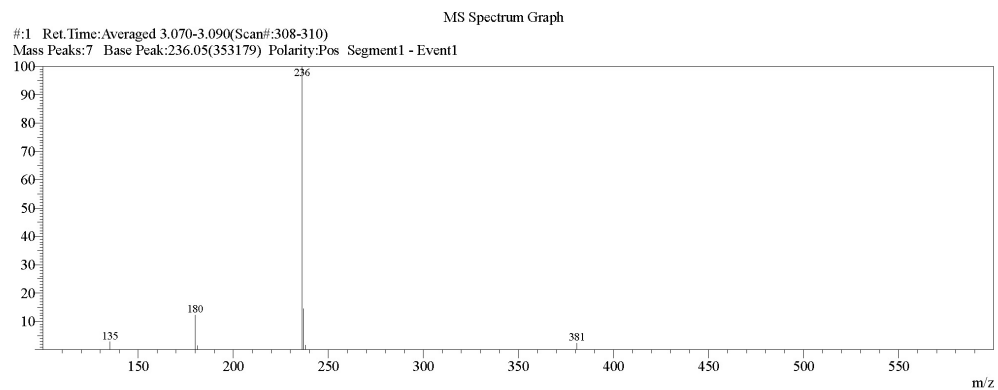
#:1 Ret.Time:
BG Mode:Calc 2.980<->3.290(299<->330)
Mass Peaks:7   Base Peak:236.05(353179) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	135.05	9777	2.77				5	237.05	50876	14.41			
2	180.05	43065	12.19				6	238.10	5796	1.64			
3	181.30	5006	1.42				7	380.70	8174	2.31			
4	236.05	353179	100.00										

Figure S153 LCMS spectrum of compound NPD-3002

137
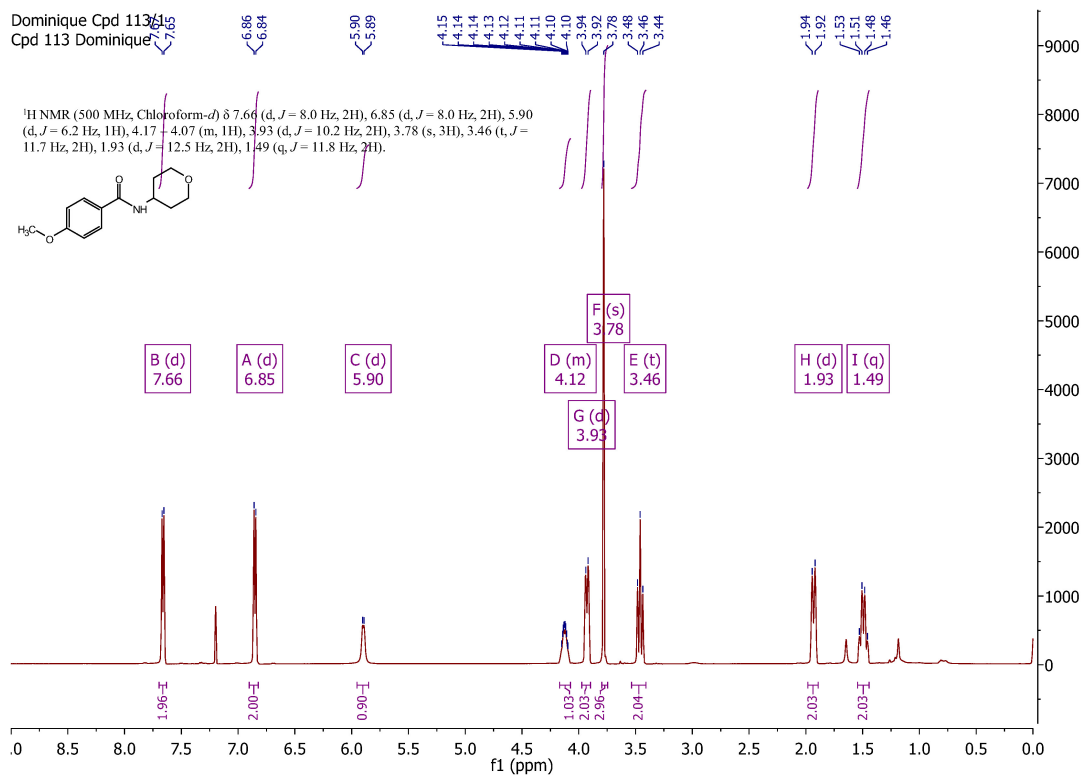
Figure S154 ¹H NMR spectrum of compound NPD-3002

¹H NMR (500 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 8.0 Hz, 2H), 5.90 (d, *J* = 6.2 Hz, 1H), 4.17 – 4.07 (m, 1H), 3.93 (d, *J* = 10.2 Hz, 2H), 3.78 (s, 3H), 3.46 (t, *J* = 11.7 Hz, 2H), 1.93 (d, *J* = 12.5 Hz, 2H), 1.49 (q, *J* = 11.8 Hz, 2H).
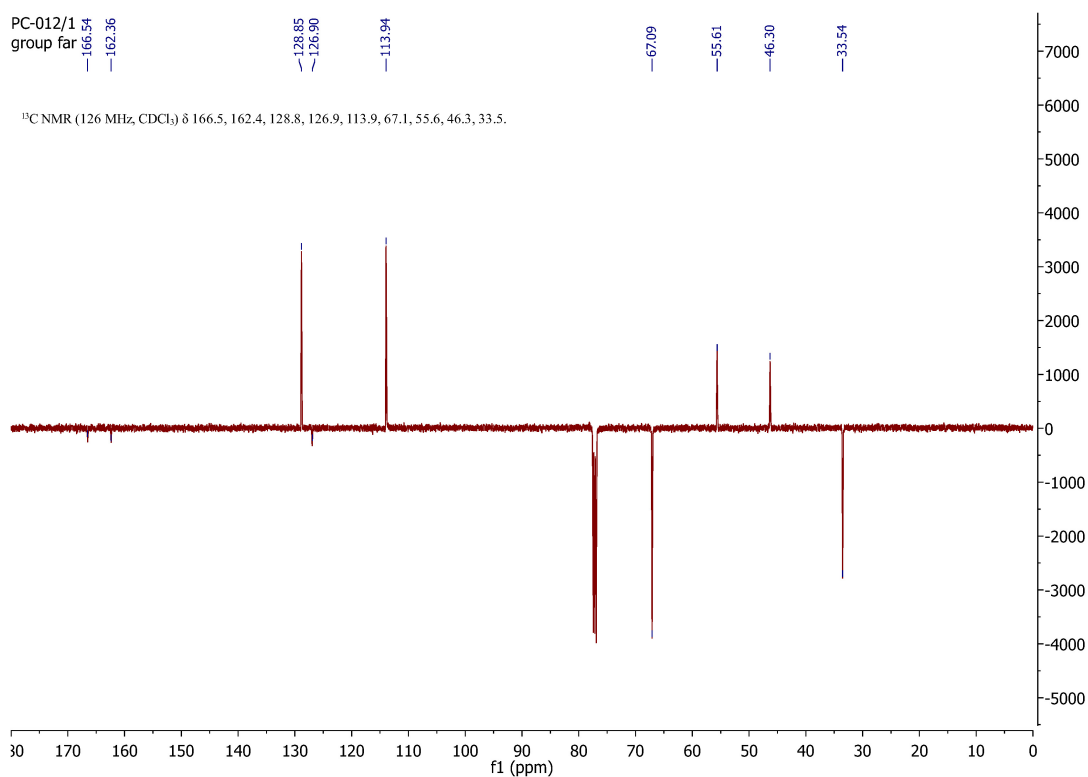
Figure S155 ¹³C NMR spectrum of compound NPD-3002

¹³C NMR (126 MHz, CDCl₃) δ 166.5, 162.4, 128.8, 126.9, 113.9, 67.1, 55.6, 46.3, 33.5.

PDA Graph
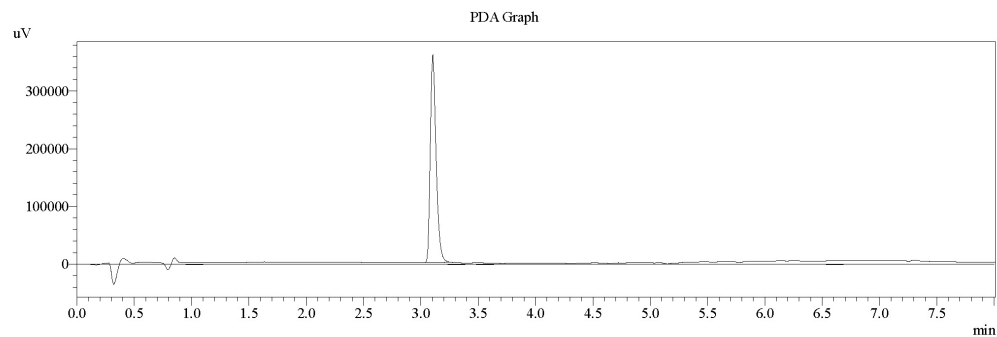
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.098	1270468	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 3.140-3.160(Scan#:315-317)
Mass Peaks:9   Base Peak:236.10(247954) Polarity:Pos Segment1 - Event1
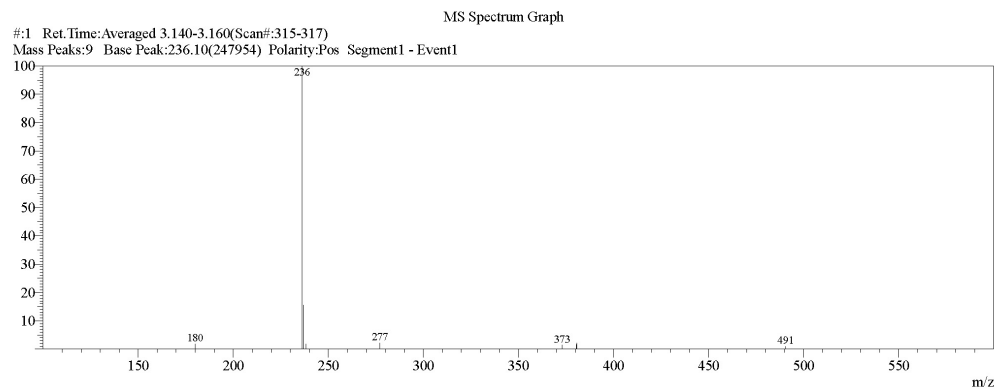
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.040<->3.350(305<->336)
Mass Peaks:9   Base Peak:236.10(247954) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	179.90	4384	1.77				6	373.00	3481	1.40			
2	236.10	247954	100.00				7	380.50	3832	1.55			
3	237.05	38579	15.56				8	380.80	5476	2.21			
4	238.15	4569	1.84				9	490.60	2505	1.01			
5	277.15	5512	2.22										

Figure S156 LCMS spectrum of compound NPD-3003
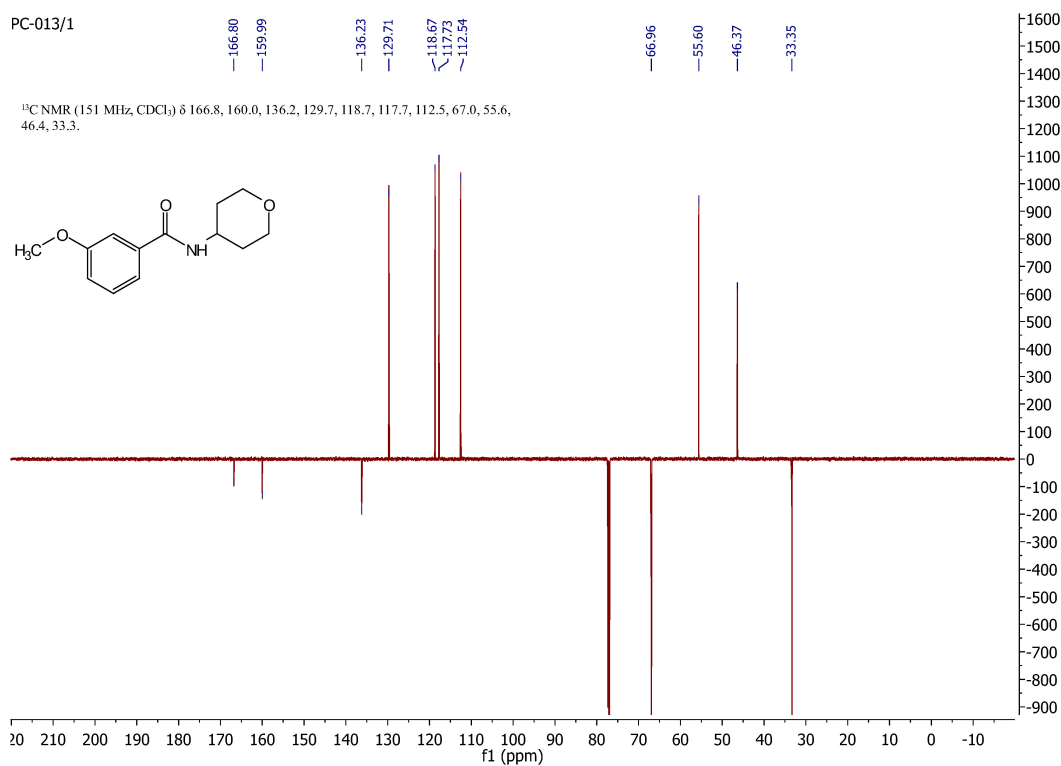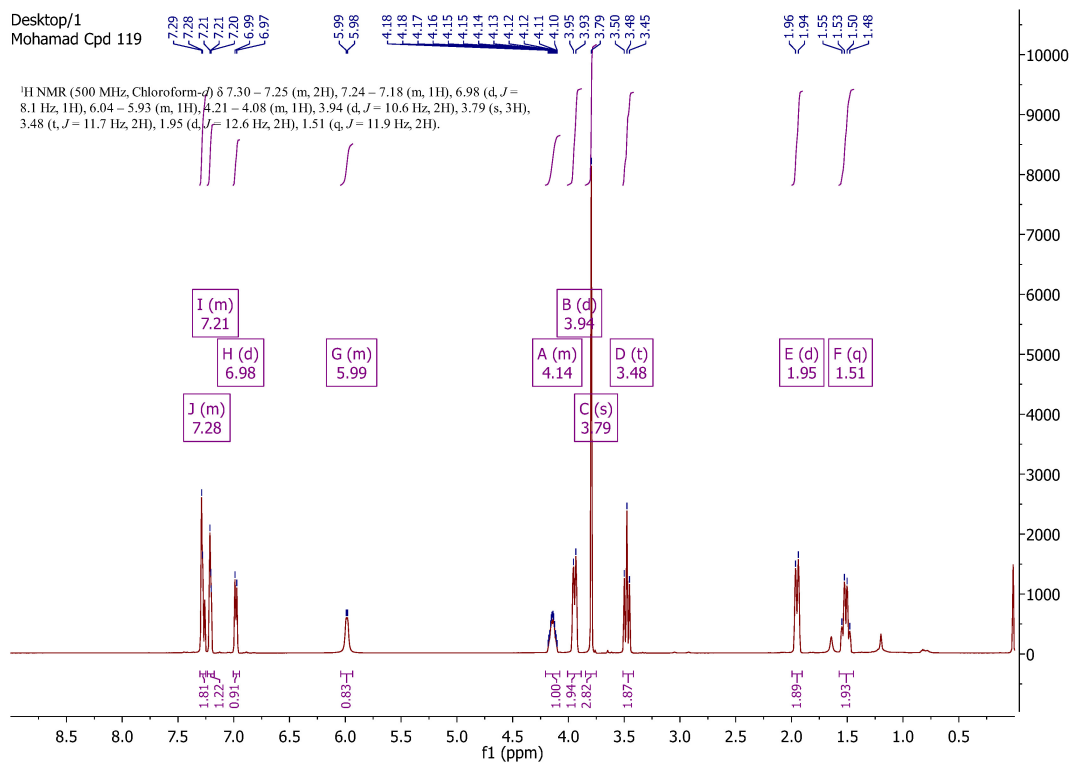
139

Desktop/1
Mohamad Cpd 119

¹H NMR (500 MHz, Chloroform-*d*) δ 7.30 − 7.25 (m, 2H), 7.24 − 7.18 (m, 1H), 6.98 (d, *J* = 8.1 Hz, 1H), 6.04 − 5.93 (m, 1H), 4.21 − 4.08 (m, 1H), 3.94 (d, *J* = 10.6 Hz, 2H), 3.79 (s, 3H), 3.48 (t, *J* = 11.7 Hz, 2H), 1.95 (d, *J* = 12.6 Hz, 2H), 1.51 (q, *J* = 11.9 Hz, 2H).

I (m) 7.21
H (d) 6.98
J (m) 7.28
G (m) 5.99
B (d) 3.94
A (m) 4.14
C (s) 3.79
D (t) 3.48
E (d) 1.95
F (q) 1.51

Figure S157 ¹H NMR spectrum of compound NPD-3003

PC-013/1

¹³C NMR (151 MHz, CDCl₃) δ 166.8, 160.0, 136.2, 129.7, 118.7, 117.7, 112.5, 67.0, 55.6, 46.4, 33.3.

Figure S158 ¹³C NMR spectrum of compound NPD-3003

140

PDA Graph

uV
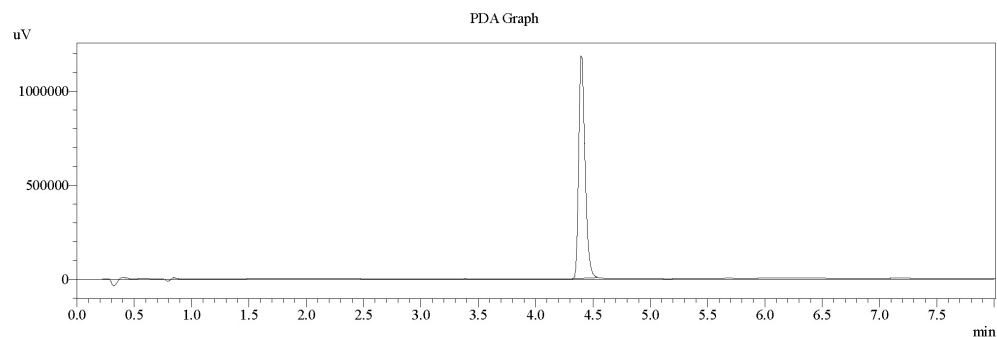
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.394	4518440	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.440-4.460(Scan#:445-447)
Mass Peaks:11   Base Peak:292.05(359384) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.330<->4.690(434<->470)
Mass Peaks:11 Base Peak:292.05(359384) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	292.05	359384	100.00				7	335.15	4939	1.37			
2	293.10	59297	16.50				8	465.55	8571	2.38			
3	294.00	111312	30.97				9	465.95	7184	2.00			
4	295.10	19875	5.53				10	610.75	3990	1.11			
5	333.10	12236	3.40				11	612.05	4036	1.12			
6	334.10	4080	1.14										

Figure S159 LCMS spectrum of compound NPD-3004

141

Maurice cpd 122/1
Maurice cpd 122

7.86
7.68
7.51
7.49
7.41
7.36
7.35
7.26 CDCl3
7.07
6.91
6.89

3.89
3.85

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.86 (s, 1H), 7.68 (s, 1H), 7.50 (d, *J* = 8.8 Hz, 1H), 7.41 (s, 1H), 7.39 – 7.32 (m, 2H), 7.07 (s, 1H), 6.90 (d, *J* = 8.8 Hz, 1H), 3.89 (s, 3H), 3.85 (s, 3H).

H (s) 7.68	
G (d) 7.50	D (s) 7.07
I (s) 7.86	E (m) 7.36	C (d) 6.90
F (s) 7.41	

B (s) 3.89
A (s) 3.85

0.86
0.95
1.00
0.99
2.00
1.00
1.02

3.00
2.97

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 0.0
f1 (ppm)

Figure S160 ^{1}H NMR spectrum of compound NPD-3004

PC-014/1
group far

165.47
159.97
152.08
136.06
131.37
129.80
122.81
122.54
119.98
118.59
118.11
112.43
112.20
56.40
55.50

^{13}C NMR (126 MHz, CDCl₃) δ 165.5, 160.0, 152.1, 136.1, 131.4, 129.8, 122.8, 122.5, 120.0, 118.6, 118.1, 112.4, 112.2, 56.4, 55.5.

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Figure S161 ^{13}C NMR spectrum of compound NPD-3004

142

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Date Acquired   : 15/5/2019 2:06:17 PM
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Sample ID   :
Tray#   : 1
Vial#   : 17
Injection Volume   : 2
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Background File   : blanco 15052019.lcd
Method File   : Method SCAN ACID standard.lcm
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Tuning File   : C:\LabSolutions\Tuning\Tuning-ESI-pos-neg01072015a.lct
Processed by   : Admin
Modified Date   : 15/5/2019 3:39:17 PM

PDA Graph

PeakTable
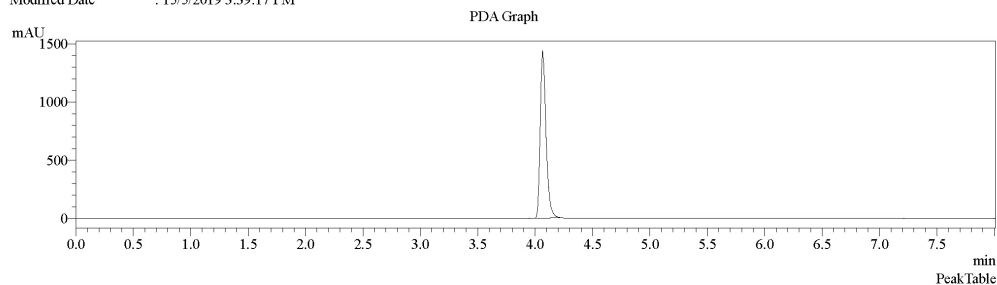
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
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2		4.708	8066	0.159
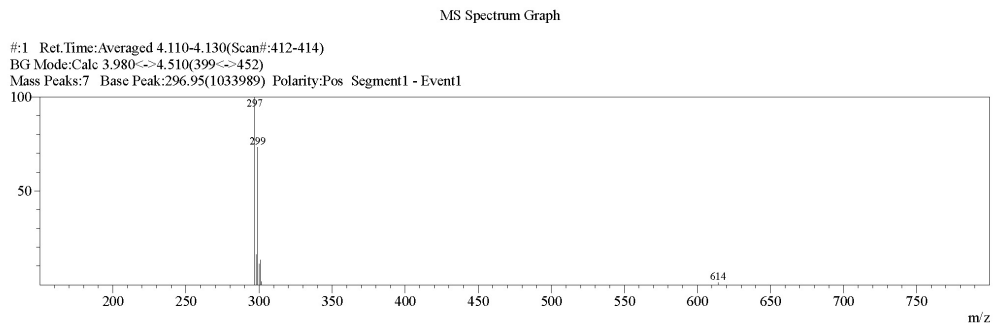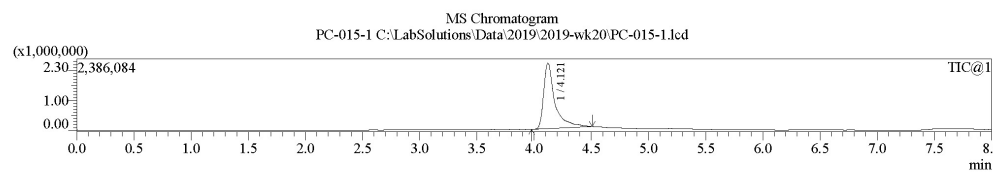
MS Chromatogram
PC-015-1 C:\LabSolutions\Data\2019\2019-wk20\PC-015-1.lcd

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.110-4.130(Scan#:412-414)
BG Mode:Calc 3.980<->4.510(399<->452)
Mass Peaks:7 Base Peak:296.95(1033989) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.980<->4.510(399<->452)
Mass Peaks:7 Base Peak:296.95(1033989) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	296.95	1033989	100.00				5	300.95	137316	13.28			
2	298.00	166920	16.14				6	301.85	17748	1.72			
3	299.00	759043	73.41				7	614.15	11671	1.13			
4	299.95	113931	11.02										

Figure S162 LCMS spectrum of compound NPD-3005

143

—8.38
—7.79
7.49
7.46
7.45
7.43
7.41
7.39
7.26 CDCl3
7.13
7.12
3.88

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.38 (s, 2H), 7.79 (s, 1H), 7.49 (s, 1H), 7.45 (d, *J* = 7.5 Hz, 1H), 7.41 (t, *J* = 7.7 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 3.88 (s, 3H).

| E (t) |
| 7.41 |

| C (s) |
| 7.49 |

| G (s) | F (s) | B (d) | A (s) |
| 8.38 | 7.79 | 7.13 | 3.88 |

| D (d) |
| 7.45 |

1.75
0.96
1.00
0.97
1.04
1.03
3.00

f1 (ppm)

Figure S163 ^{1}H NMR spectrum of compound NPD-3005

—164.78
—160.15
146.29
145.73
137.75
135.33
130.06
128.18
123.14
119.28
118.91
—113.03
—55.66

^{13}C NMR (126 MHz, CDCl$_3$) δ 164.8, 160.2, 146.3, 145.7, 137.7, 135.3, 130.1, 128.2, 123.1, 119.3, 118.9, 113.0, 55.7.

f1 (ppm)
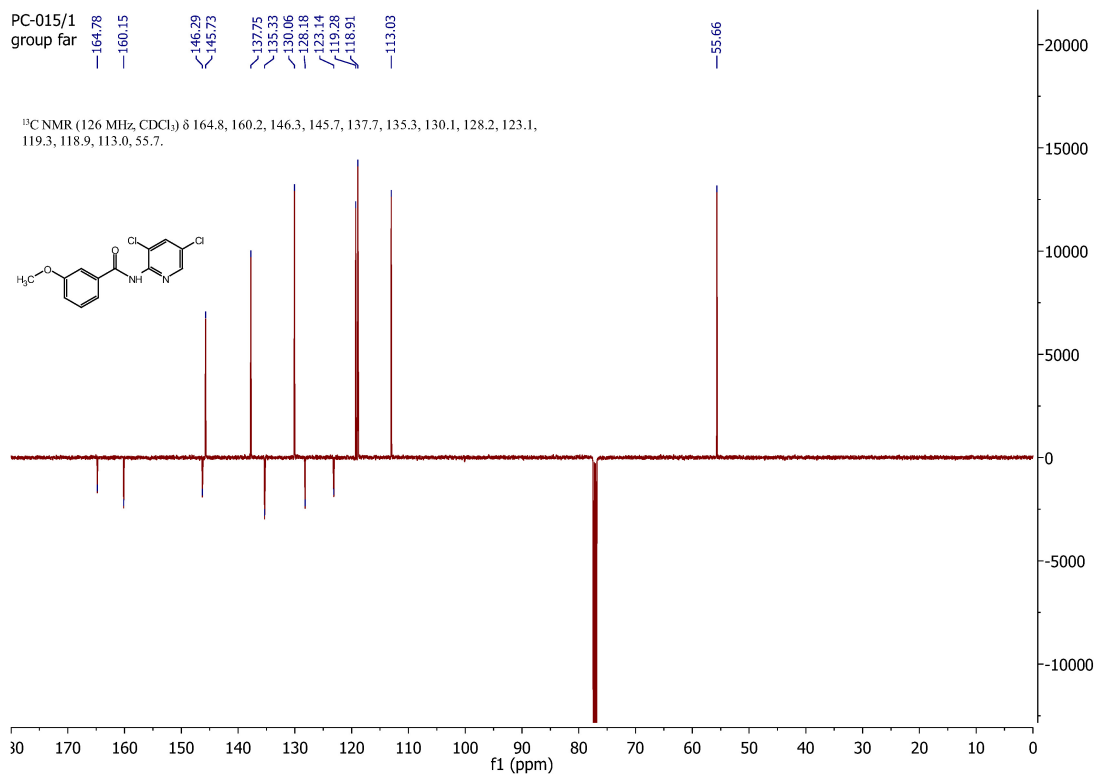
Figure S164 ^{13}C NMR spectrum of compound NPD-3005

144

Acquired by   : Admin
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Sample ID   :
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Vial#   : 7
Injection Volume   : 2
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Background File   : blanco 22052019.lcd
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Report Format   : DefaultLCMS.lcr
Tuning File   : C:\LabSolutions\Tuning\Tuning-ESI-pos-neg01072015a.lct
Processed by   : Admin
Modified Date   : 22/5/2019 12:59:26 PM

PDA Graph

mAU

PDA Ch1 254nm 4nm

PeakTable
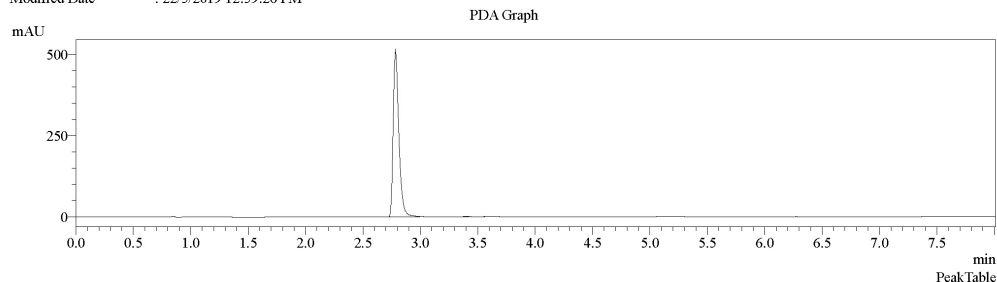
Peak#	Name	Ret. Time	Area	Area %
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2		2.778	1738088	99.543
3		3.387	1798	0.103
4		3.593	4001	0.229

MS Chromatogram
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(x1,000,000)
2.00 2,003,318   TIC@1

MS Spectrum Graph
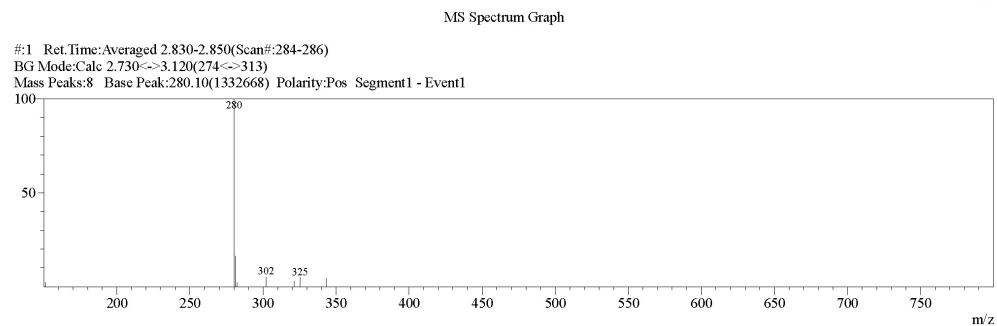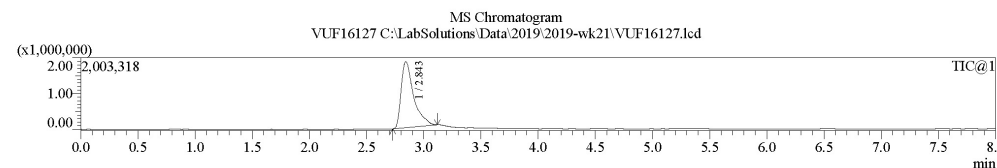
#:1 Ret.Time:Averaged 2.830-2.850(Scan#:284-286)
BG Mode:Calc 2.730<->3.120(274<->313)
Mass Peaks:8   Base Peak:280.10(1332668) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 2.730<->3.120(274<->313)
Mass Peaks:8   Base Peak:280.10(1332668) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	151.00	30849	2.31				5	302.05	66981	5.03			
2	280.10	1332668	100.00				6	321.10	39725	2.98			
3	281.10	219538	16.47				7	325.20	62900	4.72			
4	282.05	28743	2.16				8	343.15	61585	4.62			

Figure S165 LCMS spectrum of compound NPD-3006
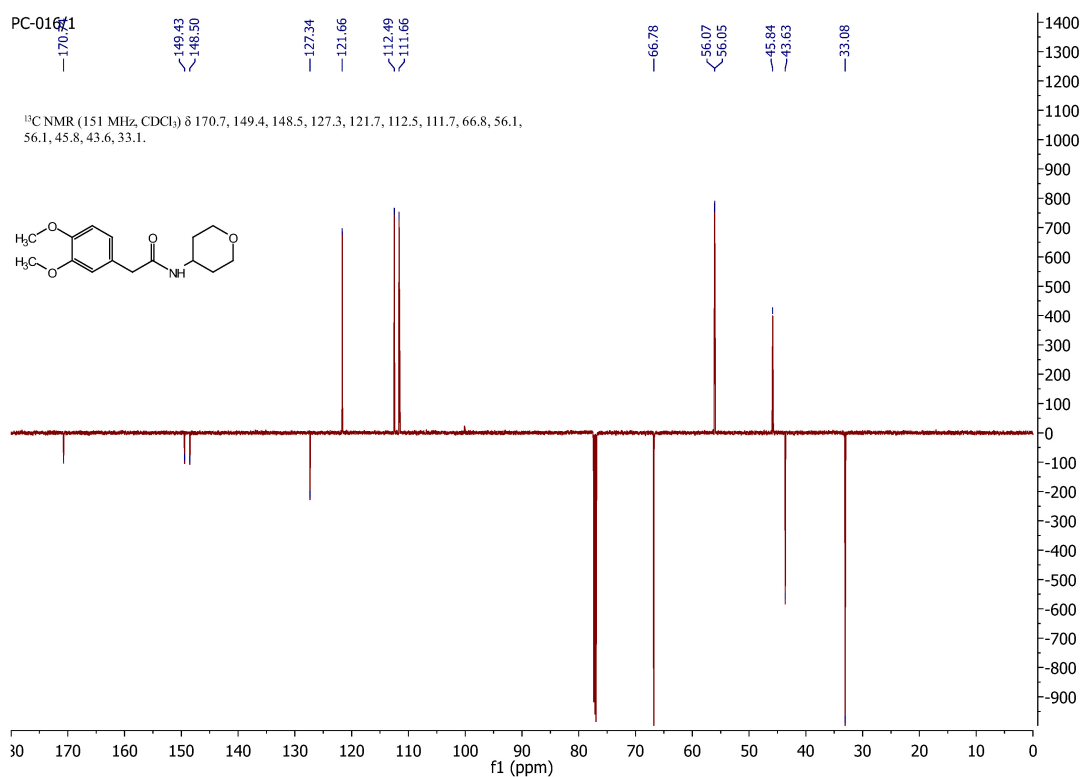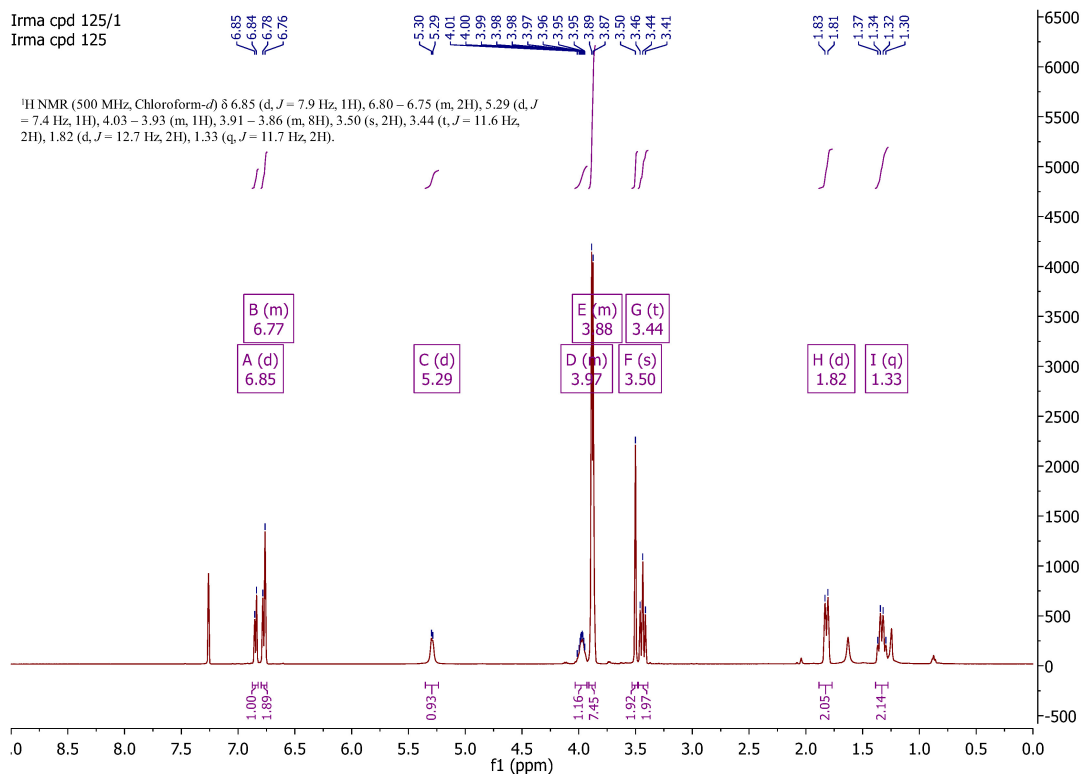
Irma cpd 125/1
Irma cpd 125

¹H NMR (500 MHz, Chloroform-*d*) δ 6.85 (d, *J* = 7.9 Hz, 1H), 6.80 – 6.75 (m, 2H), 5.29 (d, *J* = 7.4 Hz, 1H), 4.03 – 3.93 (m, 1H), 3.91 – 3.86 (m, 8H), 3.50 (s, 2H), 3.44 (t, *J* = 11.6 Hz, 2H), 1.82 (d, *J* = 12.7 Hz, 2H), 1.33 (q, *J* = 11.7 Hz, 2H).

B (m)
6.77

A (d)
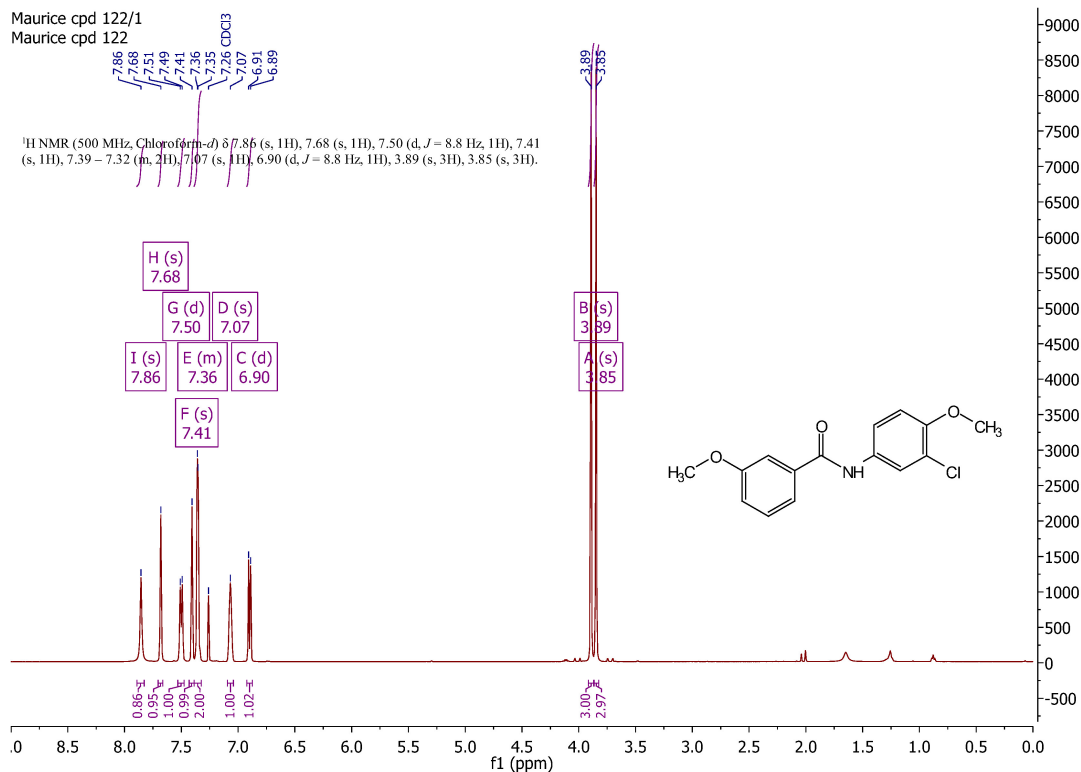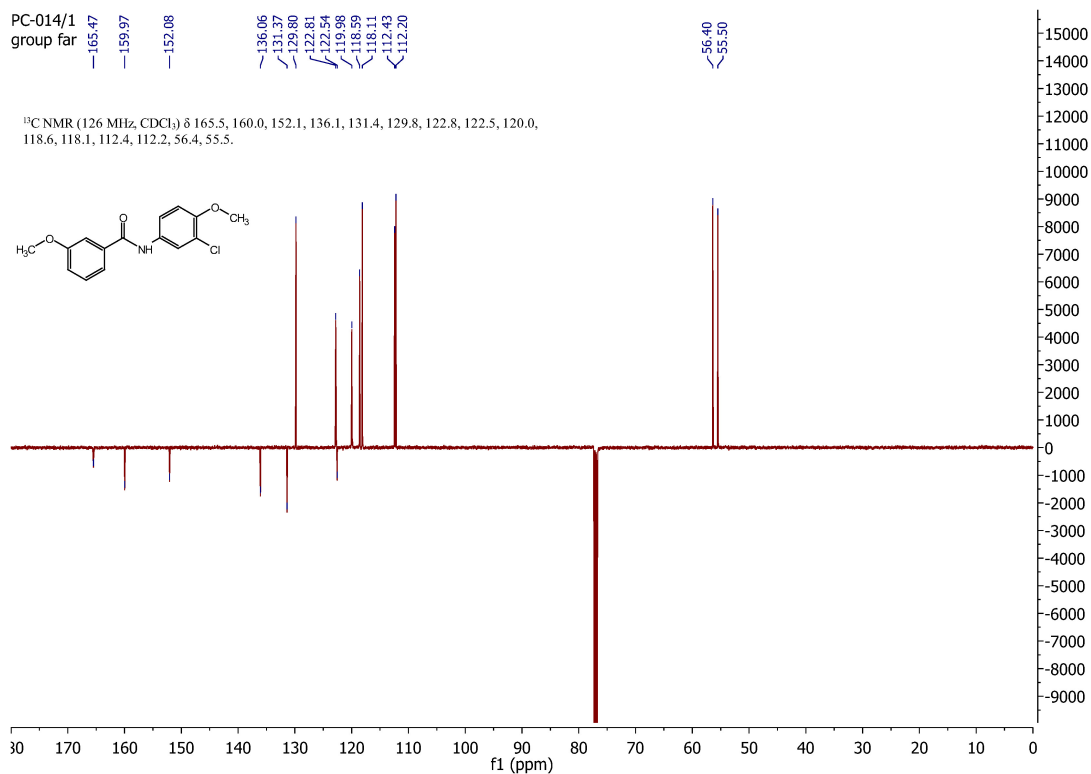6.85

C (d)
5.29

E (m)
3.88

G (t)
3.44

D (m)
3.97

F (s)
3.50

H (d)
1.82

I (q)
1.33

Figure S166 ¹H NMR spectrum of compound NPD-3006

PC-016/1

¹³C NMR (151 MHz, CDCl₃) δ 170.7, 149.4, 148.5, 127.3, 121.7, 112.5, 111.7, 66.8, 56.1, 56.1, 45.8, 43.6, 33.1.

Figure S167 ¹³C NMR spectrum of compound NPD-3006

146

PDA Graph

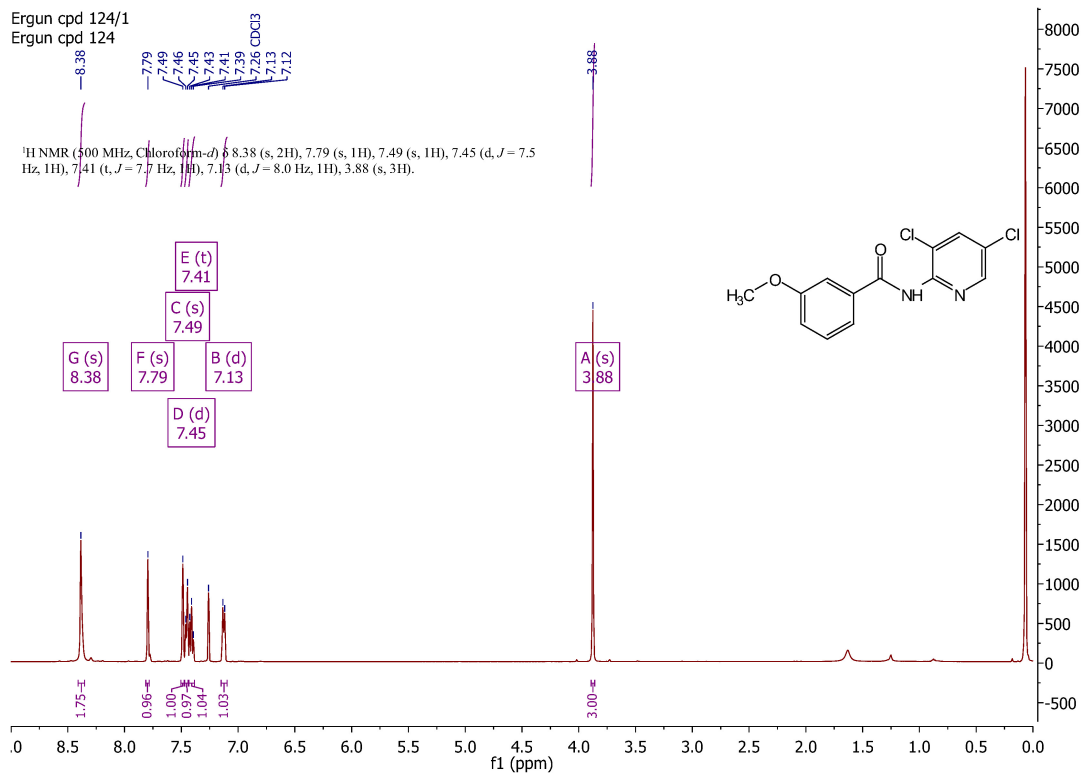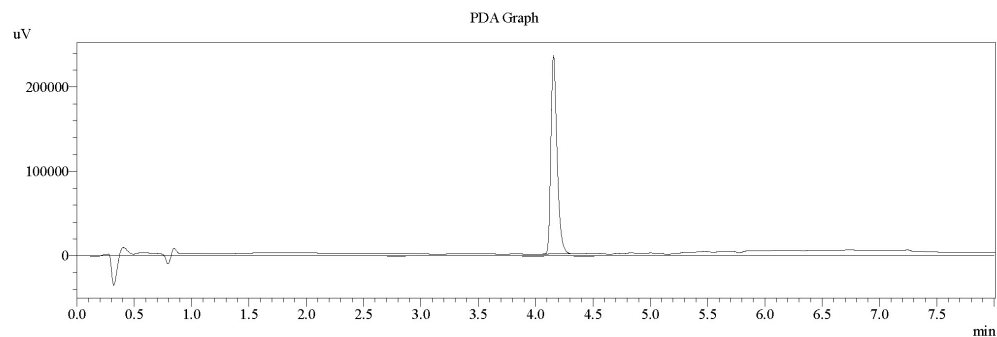PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.151	886700	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.200-4.220(Scan#:421-423)
Mass Peaks:8 Base Peak:342.10(393978) Polarity:Pos Segment1 - Event1
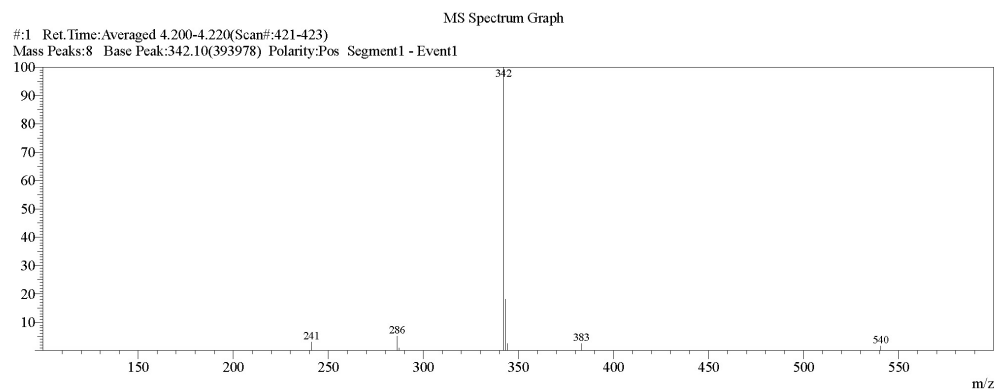
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.090<->4.390(410<->440)
Mass Peaks:8 Base Peak:342.10(393978) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	241.00	12221	3.10				5	343.15	71695	18.20			
2	286.10	20021	5.08				6	344.15	10110	2.57			
3	287.10	3949	1.00				7	383.05	9814	2.49			
4	342.10	393978	100.00				8	540.50	6261	1.59			

Figure S168 LCMS spectrum of compound NPD-3007

147

Narjisse cpd 143/1
Narjisse cpd 143

1H NMR (500 MHz, Chloroform-d) δ 7.46 (s, 1H), 7.19 (s, 2H), 6.69 (t, J = 75.1 Hz, 2H), 5.95 (d, J = 6.7 Hz, 1H), 4.23 − 4.12 (m, 1H), 4.00 (d, J = 10.8 Hz, 2H), 3.93 (d, J = 6.8 Hz, 2H), 3.53 (t, J = 11.7 Hz, 2H), 2.00 (d, J = 12.0 Hz, 2H), 1.62 − 1.54 (m, 2H), 1.30 (dt, J = 12.2, 7.0 Hz, 1H), 0.66 (d, J = 7.0 Hz, 2H), 0.36 (m 2H).

B (s) 7.19

A (s) 7.46

C (t) 6.69

D (d) 5.95

K (d) 4.00

J (m) 4.18

I (t) 3.53

L (d) 3.93

M (d) 2.00

H (dt) 1.30

G (m) 1.58

F (d) 0.66

E (d) 0.36

Figure S169 ¹H NMR spectrum of compound NPD-3007

PC-017/1

13C NMR (151 MHz, Chloroform-d) δ 165.93 , 150.82 , 142.89 (t, J = 3.1 Hz), 122.26 , 118.73 , 115.93 (t, J = 261.1 Hz), 113.91 , 74.26 , 66.94 , 46.55 , 33.34 , 10.20 , 3.39 .

Figure S170 ¹³C NMR spectrum of compound NPD-3007

148

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		5.178	460616	100.000

MS Spectrum Graph

#:1 Ret.Time:Single 5.250(Scan#:526)
Mass Peaks:18   Base Peak:368.00(22258) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:None
Mass Peaks:18   Base Peak:368.00(22258) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	278.85	1220	5.48				10	354.10	1616	7.26			
2	285.85	1285	5.77				11	359.10	1286	5.78			
3	296.20	2831	12.72				12	366.10	1123	5.05			
4	297.20	1297	5.83				13	368.00	22258	100.00			
5	318.20	3083	13.85				14	369.15	4968	22.32			
6	319.15	1303	5.85				15	370.05	7876	35.39			
7	325.15	1431	6.43				16	371.00	2806	12.61			
8	341.15	3222	14.48				17	408.95	2369	10.64			
9	342.15	1463	6.57				18	410.95	1282	5.76			

Figure S171 LCMS spectrum of compound NPD-3075

149

YAZH01-078/1
group far

¹H NMR (500 MHz, Chloroform-*d*) δ 7.80 (s, 1H), 7.76 (t, *J* = 2.0 Hz, 1H), 7.53 (d, *J* = 2.0 Hz, 1H), 7.49 – 7.45 (m, 1H), 7.34 – 7.27 (m, 2H), 7.24 (d, *J* = 8.2 Hz, 1H), 7.14 (ddd, *J* = 8.0, 1.9, 0.9 Hz, 1H), 6.72 (t, *J* = 74.9 Hz, 1H), 3.94 (d, *J* = 7.0 Hz, 2H), 1.35 – 1.27 (m, 1H), 0.69 – 0.65 (m, 2H), 0.39 – 0.35 (m, 2H).

J (s) 7.80	K (m) 7.30			B (m) 0.67
I (t) 7.76	F (ddd) 7.14			
G (m) 7.47	E (t) 6.72	D (d) 3.94	C (m) 1.31	A (m) 0.37
H (d) 7.53				
L (d) 7.24				

Figure S172 ¹H NMR spectrum of compound NPD-3075

YAZH01-078. 2.fid
group far

¹³C NMR (126 MHz, Chloroform-*d*) δ 164.8, 151.0, 143.3, 138.9, 135.0, 132.9, 130.3, 124.9, 122.4, 120.4, 118.8, 118.2, 115.9 (t, *J* = 263.6 Hz), 113.9, 74.3, 10.1, 3.4.
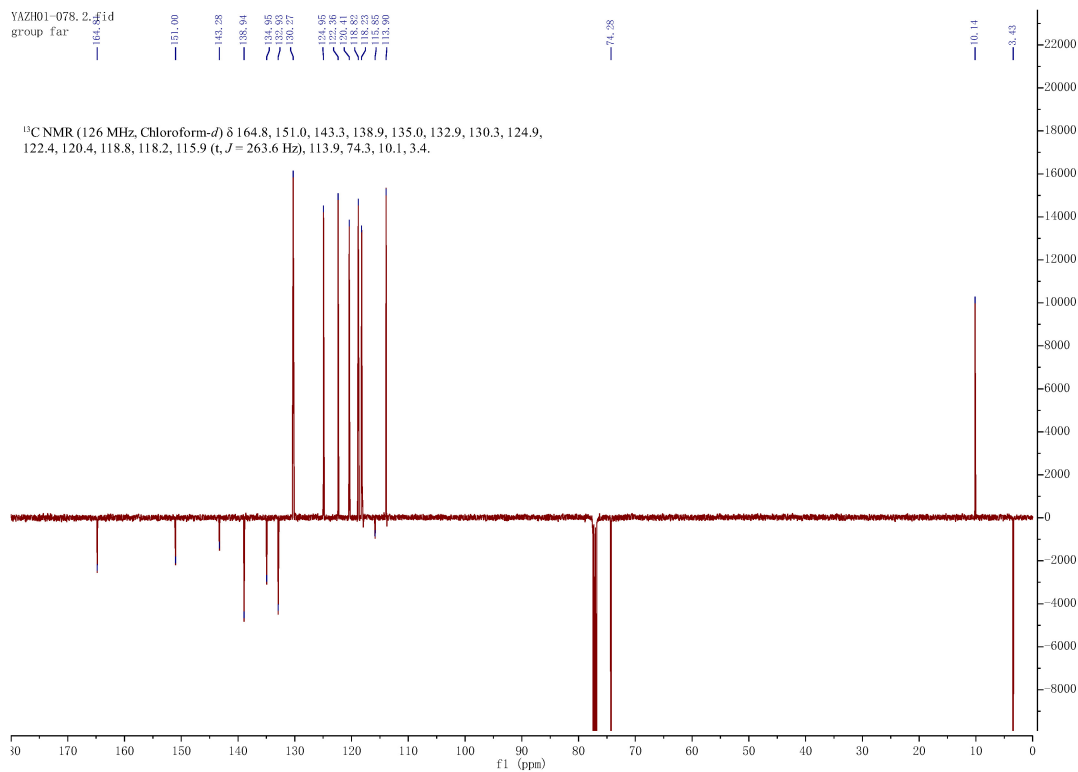
Figure S173 ¹³C NMR spectrum of compound NPD-3075

Acquired by   : Admin
Date Acquired   : 12/5/2017 11:50:26 AM
Sample Name   : YAZH01-079
Sample ID   :
Tray#   : 1
Vial#   : 22
Injection Volume   : 1
Data File   : C:\LabSolutions\Data\2017\2017-wk19\YAZH01-079.lcd
Background File   : blanco 12052017.lcd
Method File   : Method SCAN ACID standard.lcm
Report Format   : DefaultLCMS.lcr
Tuning File   : C:\LabSolutions\Tuning\Tuning-ESI-pos-neg01072015a.lct
Processed by   : Admin
Modified Date   : 14/6/2019 12:10:57 PM

PDA Graph

mAU

PDA Ch1 254nm 4nm

Peak Table
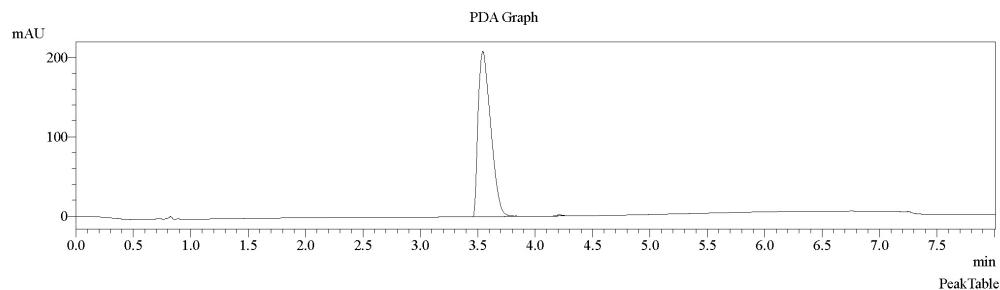
Peak#	Name	Ret. Time	Area	Area %
1		3.539	1584592	99.557
2		4.205	7059	0.443

MS Chromatogram
YAZH01-079 C:\LabSolutions\Data\2017\2017-wk11-20\2017-wk19\YAZH01-079.lcd

(x1,000,000)
1.60 1,602,943   173.598   TIC@1
1.00
0.00

MS Spectrum Graph

#:1 Ret.Time:Averaged 3.590-3.610(Scan#:360-362)
BG Mode:Calc 3.460<->3.930(347<->394)
Mass Peaks:4 Base Peak:335.15(1242993) Polarity:Pos Segment1 - Event1
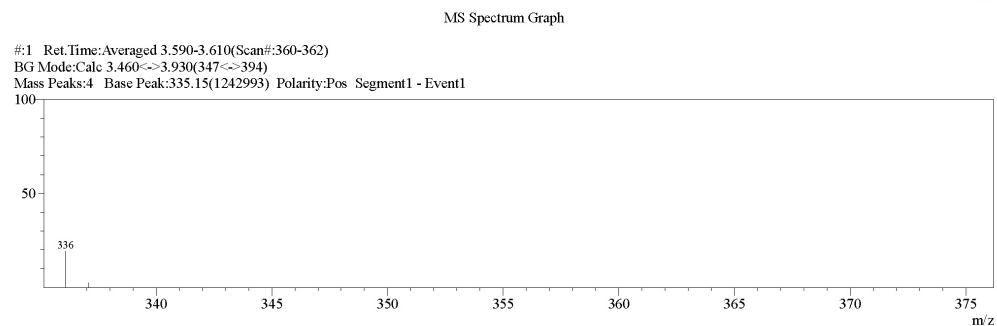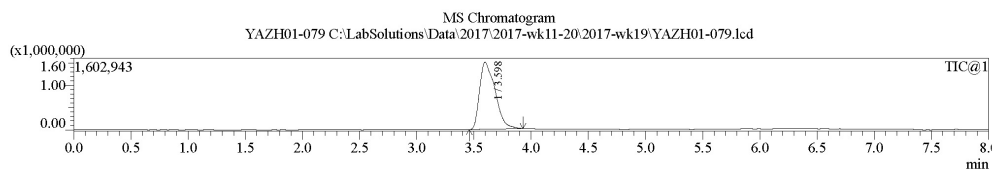
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.460<->3.930(347<->394)
Mass Peaks:4 Base Peak:335.15(1242993) Polarity:Pos Segment1 - Event1

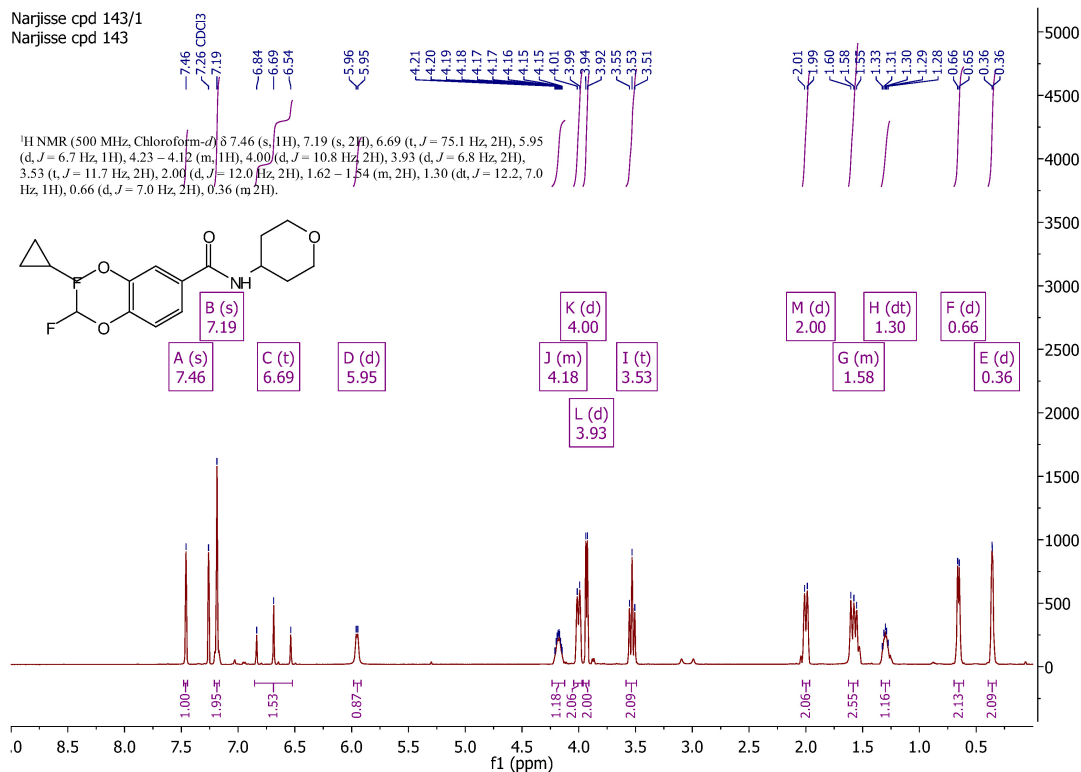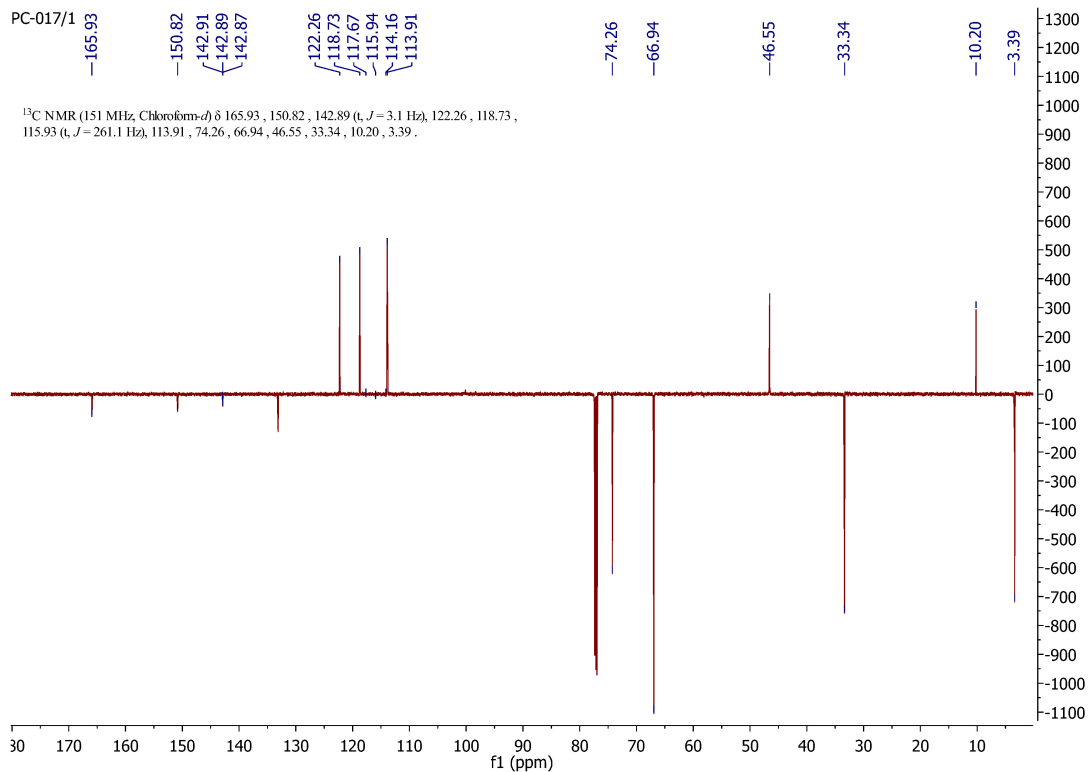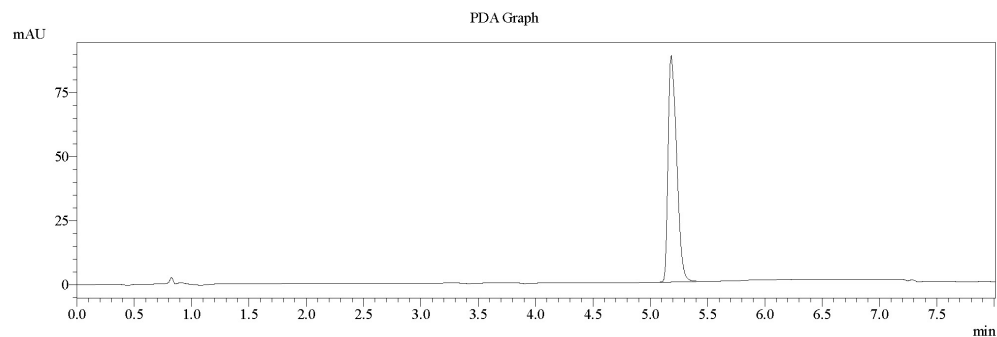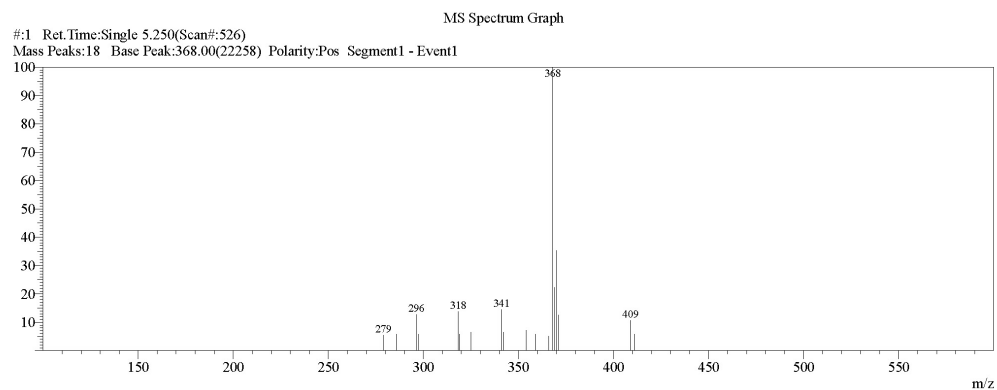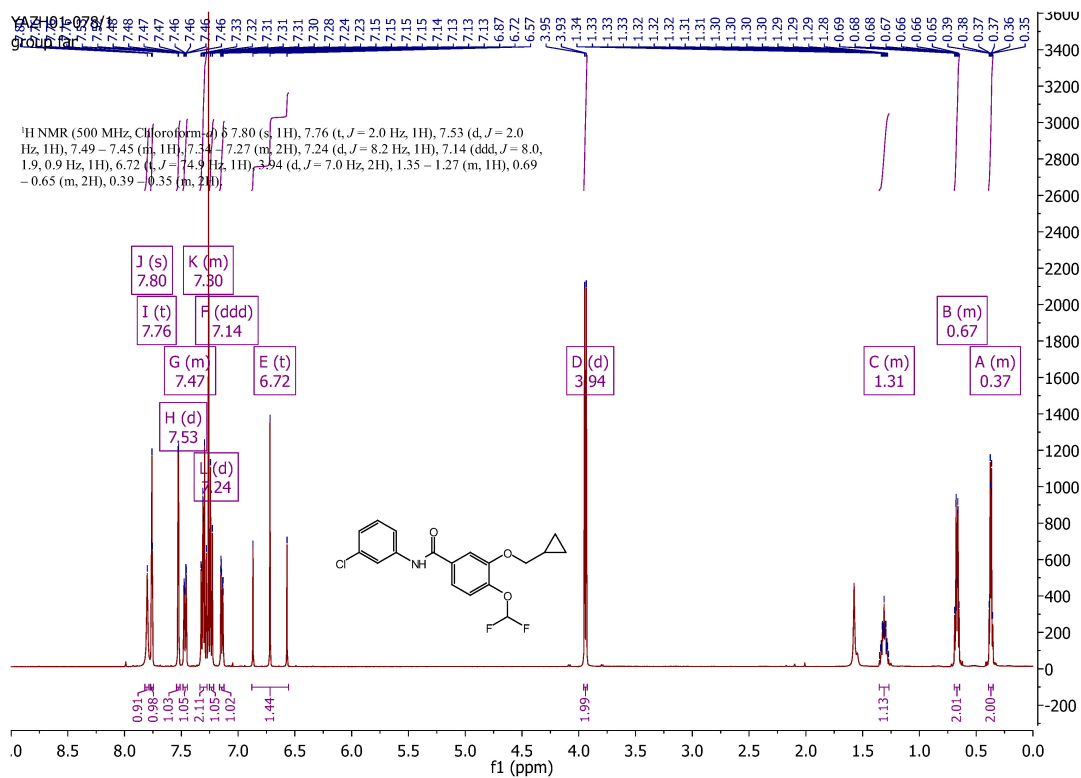| #	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	335.15	1242993	100.00				3	337.10	29418	2.37			
2	336.10	238815	19.21				4	376.20	30999	2.49			

Figure S174 LCMS spectrum of compound NPD-3076
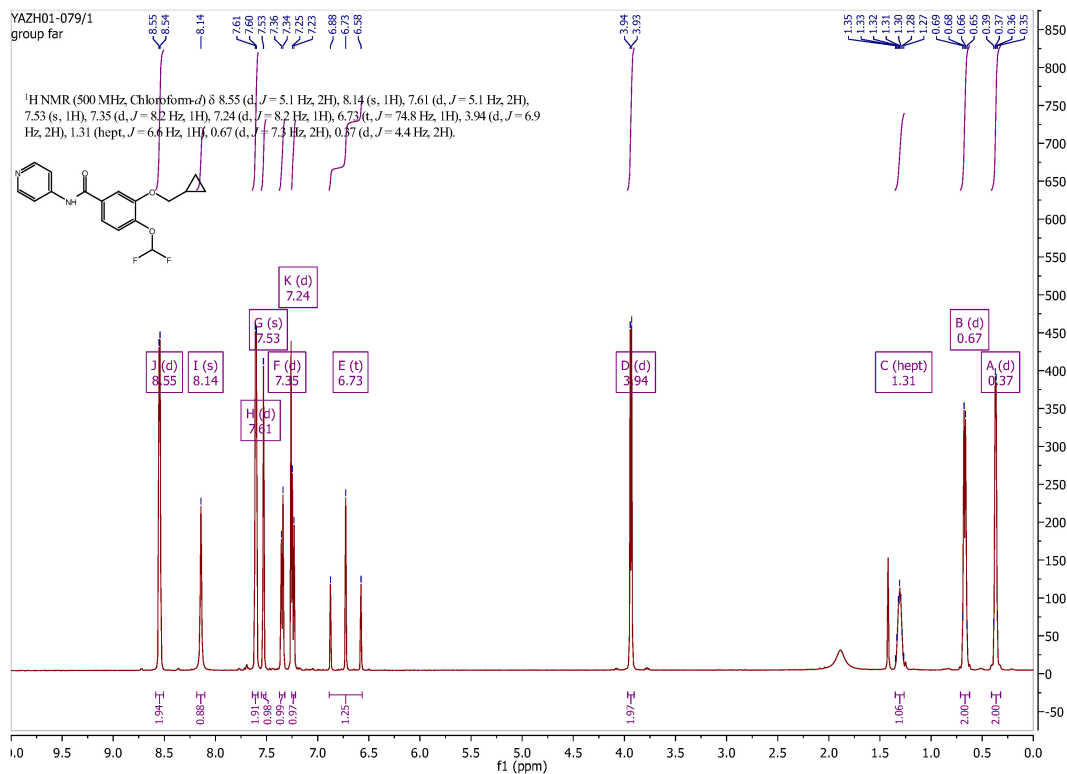
Figure S175 ¹H NMR spectrum of compound NPD-3076

¹H NMR (500 MHz, Chloroform-*d*) δ 8.55 (d, *J* = 5.1 Hz, 2H), 8.14 (s, 1H), 7.61 (d, *J* = 5.1 Hz, 2H), 7.53 (s, 1H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.24 (d, *J* = 8.2 Hz, 1H), 6.73 (t, *J* = 74.8 Hz, 1H), 3.94 (d, *J* = 6.9 Hz, 2H), 1.31 (hept, *J* = 6.6 Hz, 1H), 0.67 (d, *J* = 7.3 Hz, 2H), 0.37 (d, *J* = 4.4 Hz, 2H).

Figure S176 ¹³C NMR spectrum of compound NPD-3076

¹³C NMR (126 MHz, Chloroform-*d*) δ 165.3, 151.1, 150.9, 145.1, 143.6 (t, *J* = 3.1 Hz), 132.4, 122.3, 119.1, 115.8 (t, *J* = 264.7 Hz), 114.0, 74.3, 10.1, 3.4.

Acquired by   : Admin
Date Acquired   : 4/24/2017 10:17:07 AM
Sample Name   : YAZH01-084
Sample ID   :
Tray#   : 1
Vial#   : 15
Injection Volume   : 1
Data File   : C:\LabSolutions\Data\2017\2017-wk17\YAZH01-084.lcd
Background File   : blanco 24042017.lcd
Method File   : Method SCAN ACID standard.lcm
Report Format   : DefaultLCMS.lcr
Tuning File   : C:\LabSolutions\Tuning\Tuning-ESI-pos-neg01072015a.lct
Processed by   : Admin
Modified Date   : 4/24/2017 12:09:47 PM

Chromatogram
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1 PDA Multi 1 / 254nm 4nm
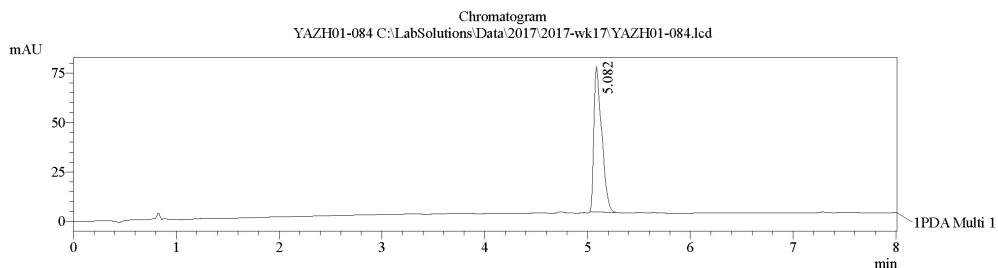
PeakTable

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		5.082	386966	100.000

MS Chromatogram
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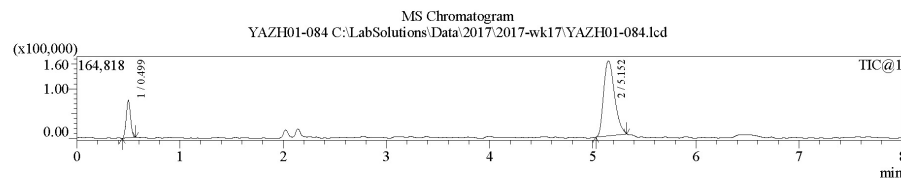
#:1 Ret.Time:Averaged 5.140-5.160(Scan#:515-517)
Mass Peaks:17 Base Peak:368.05(79748) Polarity:Pos Segment1 - Event1
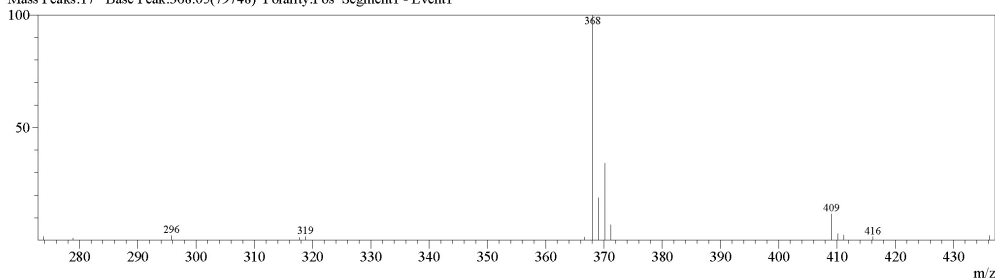
MS Spectrum Table
#:1 Ret.Time:
BG Mode:Calc 5.030<->5.330(504<->534)
Mass Peaks:17 Base Peak:368.05(79748) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	272.85	1747	2.19				9	369.05	15089	18.92			
2	273.85	1303	1.63				10	370.15	27281	34.21			
3	278.85	828	1.04				11	371.20	5504	6.90			
4	295.80	1617	2.03				12	409.05	9311	11.68			
5	317.80	932	1.17				13	410.15	2387	2.99			
6	318.75	1363	1.71				14	411.15	1756	2.20			
7	366.70	1133	1.42				15	416.15	1230	1.54			
8	368.05	79748	100.00				16	436.20	1718	2.15			

Figure S177 LCMS spectrum of compound NPD-3080
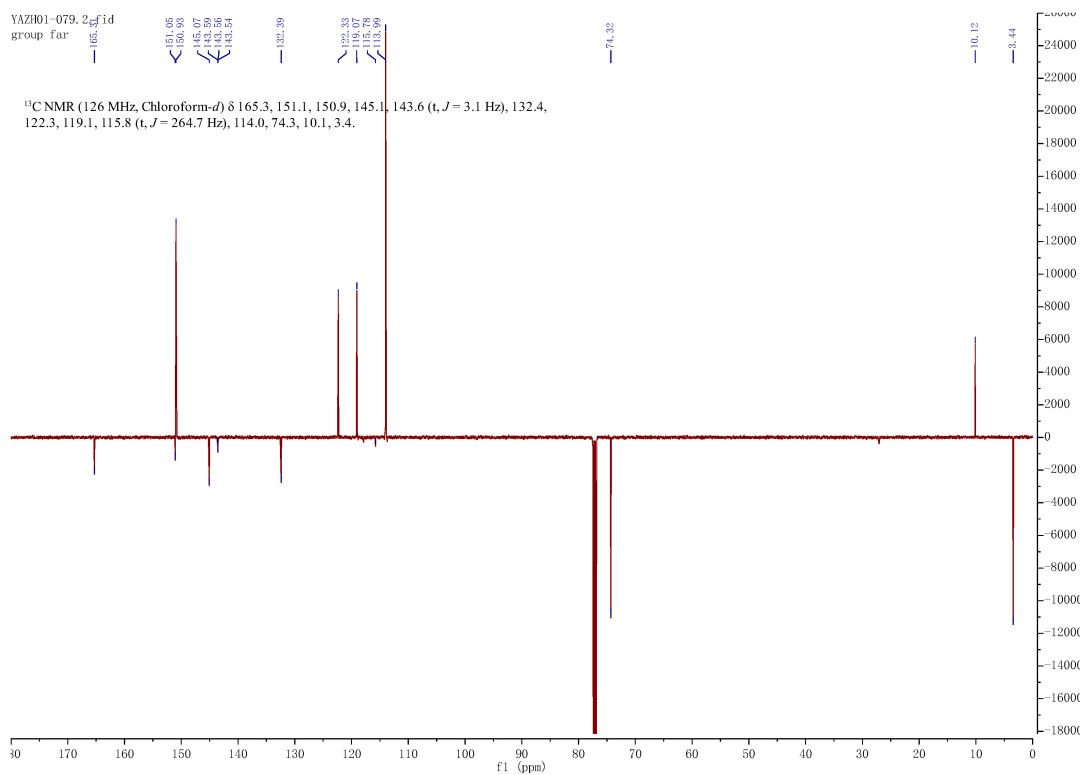
153

Figure S178 ^{1}H NMR spectrum of compound NPD-3080

^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.52 (dd, *J* = 8.3, 1.5 Hz, 1H), 8.40 (s, 1H), 7.59 (d, *J* = 2.0 Hz, 1H), 7.44 – 7.38 (m, 2H), 7.36 – 7.32 (m, 1H), 7.27 (d, *J* = 8.2 Hz, 1H), 7.10 (td, *J* = 7.8, 1.5 Hz, 1H), 6.73 (t, *J* = 74.9 Hz, 1H), 3.97 (d, *J* = 7.0 Hz, 2H), 1.37 – 1.29 (m, 1H), 0.71 – 0.65 (m, 2H), 0.42 – 0.36 (m, 2H).

Figure S179 ^{13}C NMR spectrum of compound NPD-3080

^{13}C NMR (126 MHz, Chloroform-*d*) δ 164.4, 151.0, 143.4, 134.6, 133.1, 129.2, 128.1, 125.1, 123.2, 122.5, 121.6, 118.9, 115.9 (t, *J* = 261.6 Hz), 114.0, 74.2, 10.2, 3.4.

PDA Graph

mAU

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		2.055	16150	0.935
2		2.290	30545	1.769
3		2.815	1680226	97.296

MS Spectrum Graph

#:1   Ret.Time:Averaged 2.870-2.890(Scan#:288-290)
Mass Peaks:6   Base Peak:260.05(166073) Polarity:Pos Segment1 - Event1
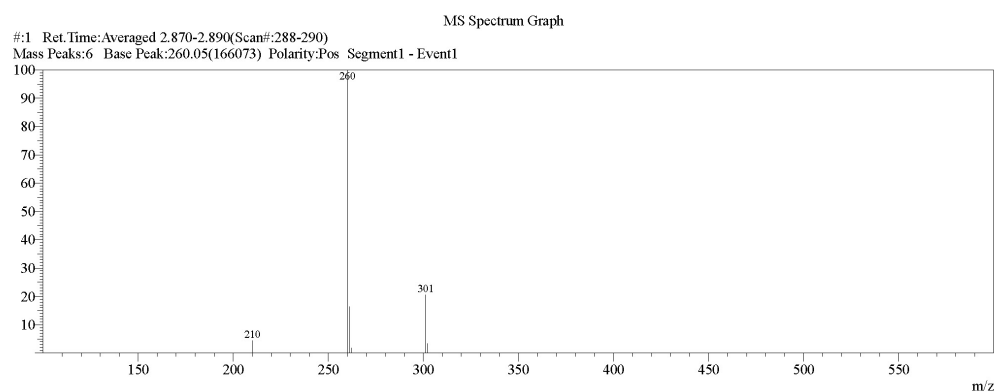
MS Spectrum Table

#:1   Ret.Time:
BG Mode:Calc 2.770<->3.100(278<->311)
Mass Peaks:6   Base Peak:260.05(166073) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	209.90	7420	4.47				4	262.15	3063	1.84			
2	260.05	166073	100.00				5	301.10	34183	20.58			
3	261.10	27240	16.40				6	302.20	5541	3.34			

Figure S180 LCMS spectrum of compound NPD-3081

155
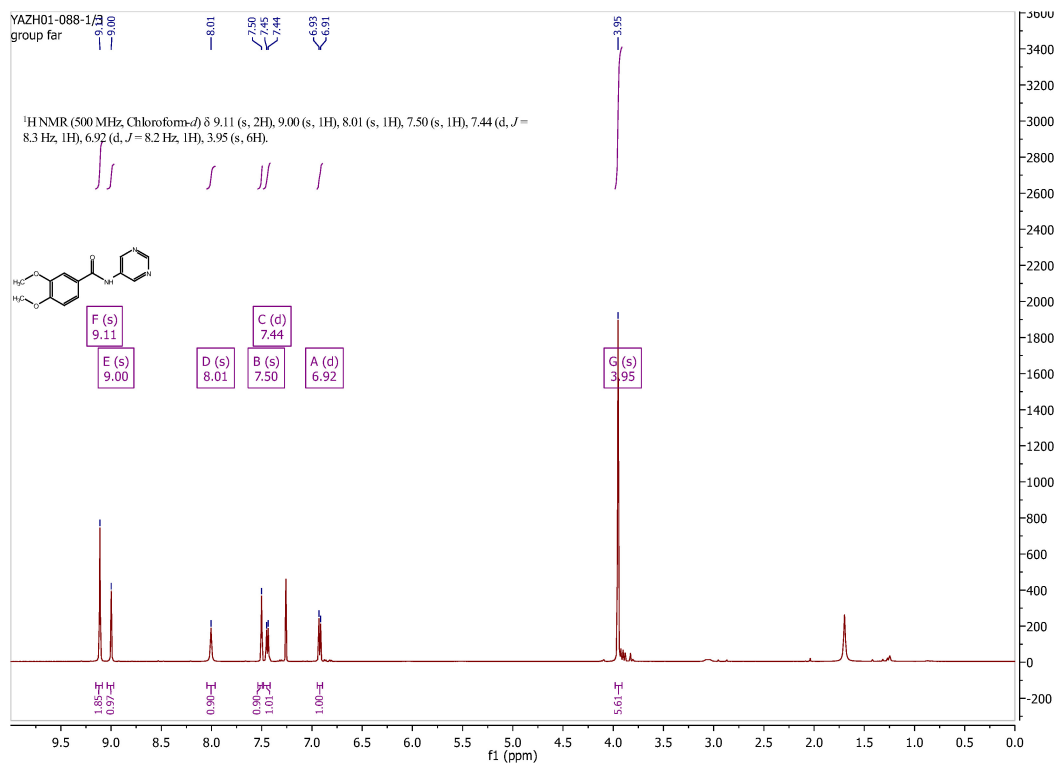
Figure S181 ¹H NMR spectrum of compound NPD-3081

¹H NMR (500 MHz, Chloroform-*d*) δ 9.11 (s, 2H), 9.00 (s, 1H), 8.01 (s, 1H), 7.50 (s, 1H), 7.44 (d, *J* = 8.3 Hz, 1H), 6.92 (d, *J* = 8.2 Hz, 1H), 3.95 (s, 6H).
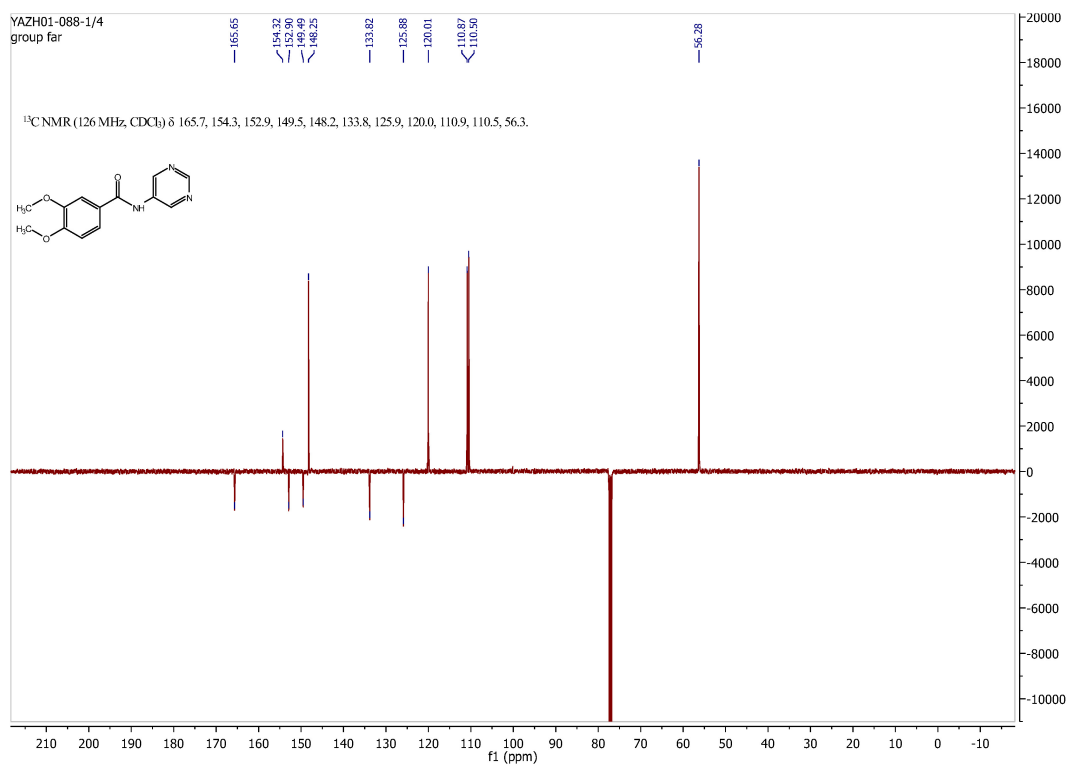
Figure S182 ¹³C NMR spectrum of compound NPD-3081

¹³C NMR (126 MHz, CDCl₃) δ 165.7, 154.3, 152.9, 149.5, 148.2, 133.8, 125.9, 120.0, 110.9, 110.5, 56.3.

Medicinal Chemistry
Vrije Universiteit Amsterdam

PDA Graph

mAU

PeakTable
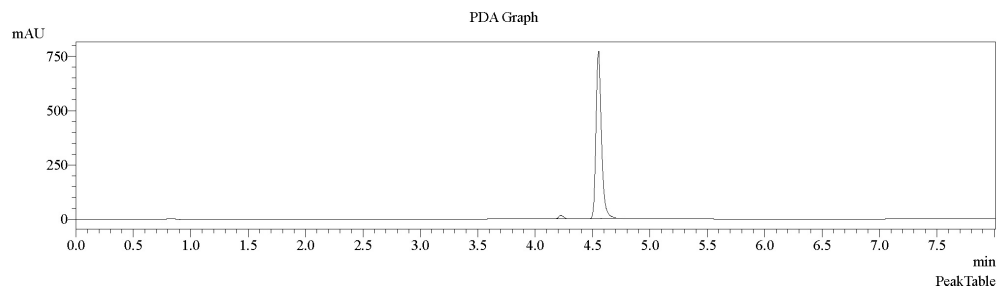
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.219	49829	1.939
2		4.546	2520313	98.061
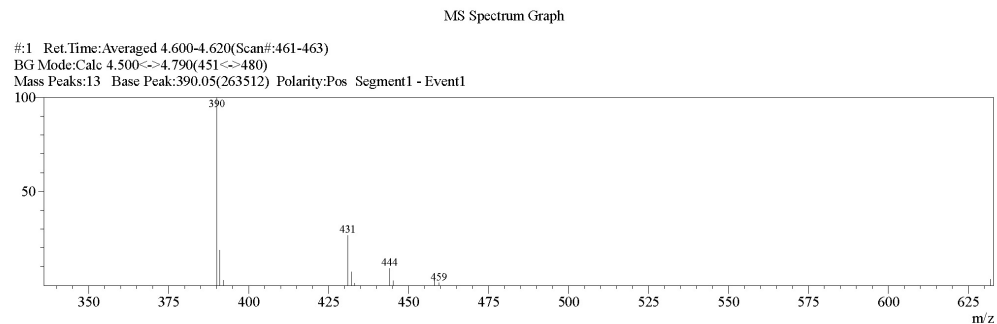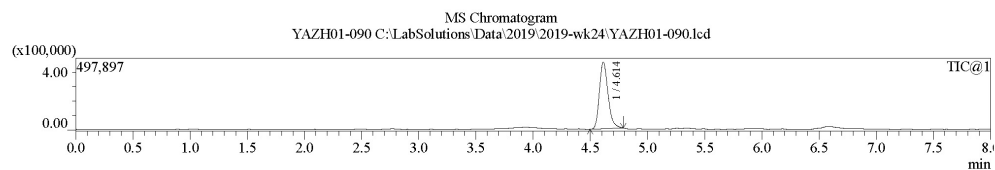
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(x100,000)
497,897   TIC@1

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.600-4.620(Scan#:461-463)
BG Mode:Calc 4.500<->4.790(451<->480)
Mass Peaks:13 Base Peak:390.05(263512) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.500<->4.790(451<->480)
Mass Peaks:13 Base Peak:390.05(263512) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	336.00	4295	1.63				8	444.15	23916	9.08			
2	390.05	263512	100.00				9	445.20	6710	2.55			
3	391.05	49449	18.77				10	458.15	8657	3.29			
4	392.15	6842	2.60				11	459.50	3424	1.30			
5	431.05	70092	26.60				12	631.95	8285	3.14			
6	432.10	18744	7.11				13	632.90	2853	1.08			
7	433.10	3133	1.19										

Figure S183 LCMS spectrum of compound NPD-3083

¹H NMR (500 MHz, Chloroform-*d*) δ 8.23 (s, 2H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.55 (s, 1H), 7.47
(d, *J* = 8.2 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.29 − 7.24 (m, 1H), 6.73 (t, *J* = 74.8 Hz, 1H),
5.32 (s, 2H), 3.96 (d, *J* = 6.9 Hz, 2H), 1.32 (tq, *J* = 12.5, 7.8 Hz, 1H), 0.68 (q, *J* = 5.4 Hz, 2H),
0.38 (q, *J* = 4.8 Hz, 2H).

Peak	Shift
A (s)	8.23
B (d)	7.87
C (s)	7.55
D (d)	7.47
E (d)	7.39
F (m)	7.26
G (t)	6.73
H (s)	5.32
I (d)	3.96
J (tq)	1.32
K (q)	0.68
L (q)	0.38
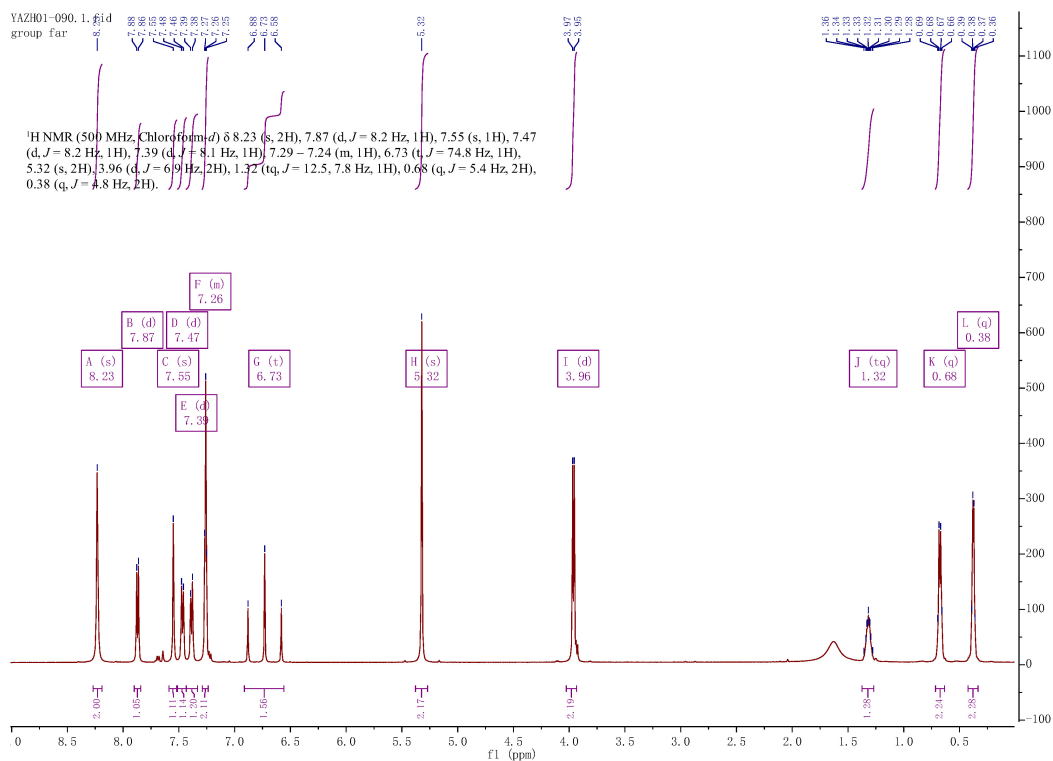
Figure S184 ¹H NMR spectrum of compound NPD-3083

¹³C NMR (126 MHz, Chloroform-*d*) δ 170.7, 165.0, 150.9, 148.6, 143.4 (t, *J* = 3.1 Hz), 143.2, 132.4, 126.7, 122.3,
121.3, 120.6, 119.0, 115.7 (t, *J* = 261.1 Hz), 113.8, 112.7, 74.2, 69.6, 10.0, 3.3.

Figure S185 ¹³C NMR spectrum of compound NPD-3083

PDA Graph

mAU

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.330	718824	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 3.380-3.400(Scan#:339-341)
Mass Peaks:8 Base Peak:263.05(235116) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 3.280<->3.540(329<->355)
Mass Peaks:8 Base Peak:263.05(235116) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	263.05	235116	100.00				5	304.05	45539	19.37			
2	264.05	34390	14.63				6	305.05	8033	3.42			
3	265.05	88056	37.45				7	306.05	17888	7.61			
4	266.00	11890	5.06				8	307.10	3432	1.46			

Figure S186 LCMS spectrum of compound NPD-3085

159

8.83
8.80
7.83
7.70
7.52
7.51
6.95
6.93
3.92

¹H NMR (500 MHz, Chloroform-*d*) δ 8.80 (d, *J* = 3.5 Hz, 2H), 7.83 (s, 1H), 7.70 (s, 3H), 7.52 (d, *J* = 8.6 Hz, 1H), 6.94 (d, *J* = 8.7 Hz, 1H), 3.92 (s, 3H).

C (s)
7.70

E (d)
8.80

B (d)
7.52

A (d)
6.94

F (s)
3.92

D (s)
7.83

Figure S187 ¹H NMR spectrum of compound NPD-3085

163.72
152.72
150.97
141.81
130.69
123.13
122.88
120.91
120.30
112.35
56.54

¹³C NMR (126 MHz, CDCl₃) δ 163.7, 152.7, 151.0, 141.8, 130.7, 123.1, 122.9, 120.9, 120.3, 112.3, 56.5.
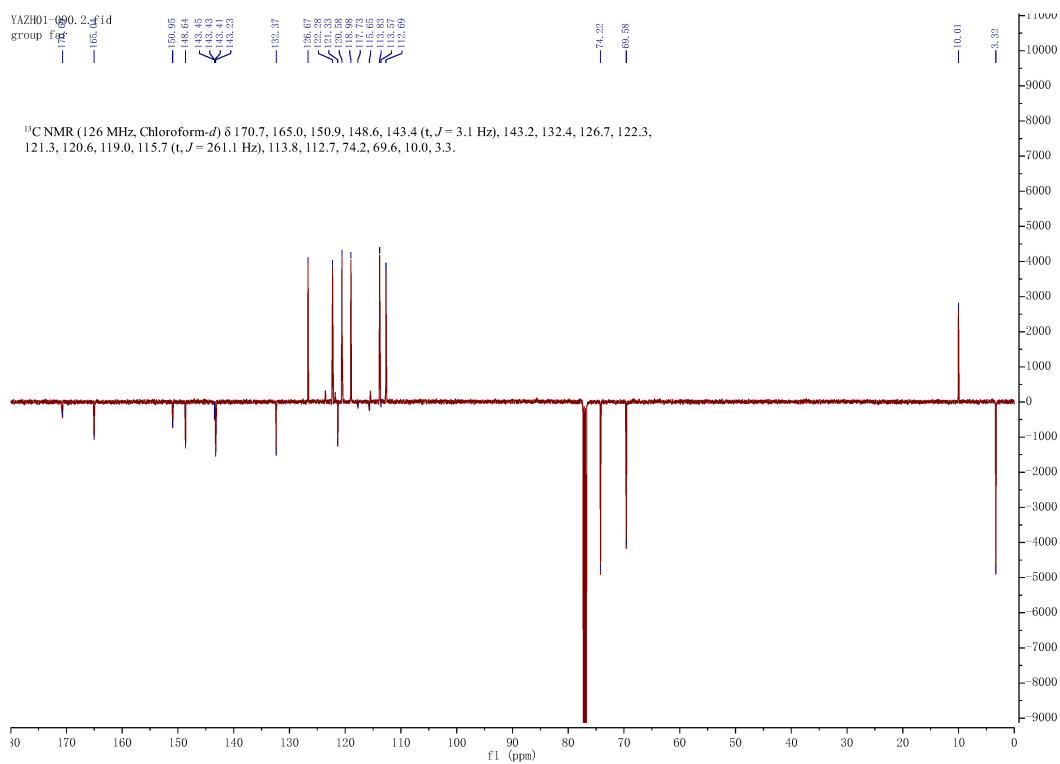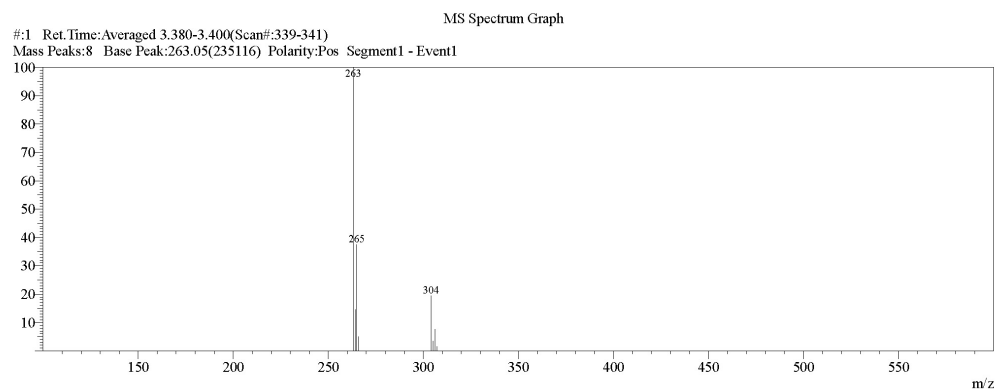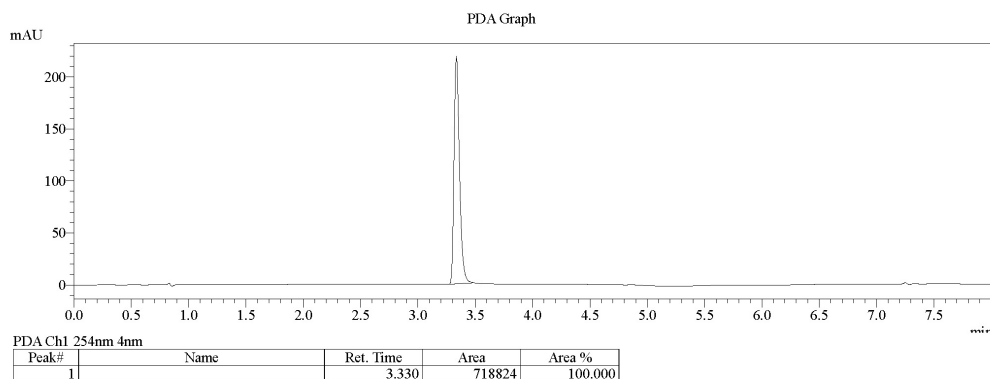
Figure S188 ¹³C NMR spectrum of compound NPD-3085

Acquired by   : Admin
Date Acquired   : 5/17/2017 9:12:22 AM
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Sample ID   :
Tray#   : 1
Vial#   : 11
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Background File   : blanco17052017.lcd
Method File   : Method SCAN ACID standard.lcm
Report Format   : DefaultLCMS.lcr
Tuning File   : C:\LabSolutions\Tuning\Tuning-ESI-pos-neg01072015a.lct
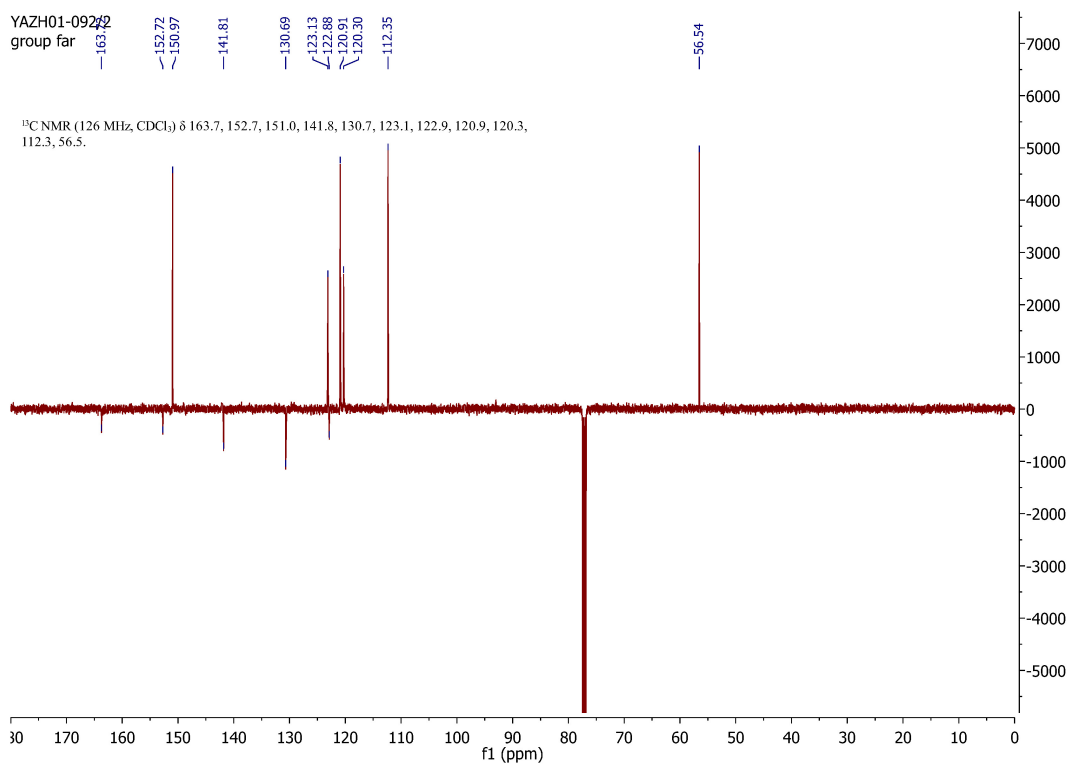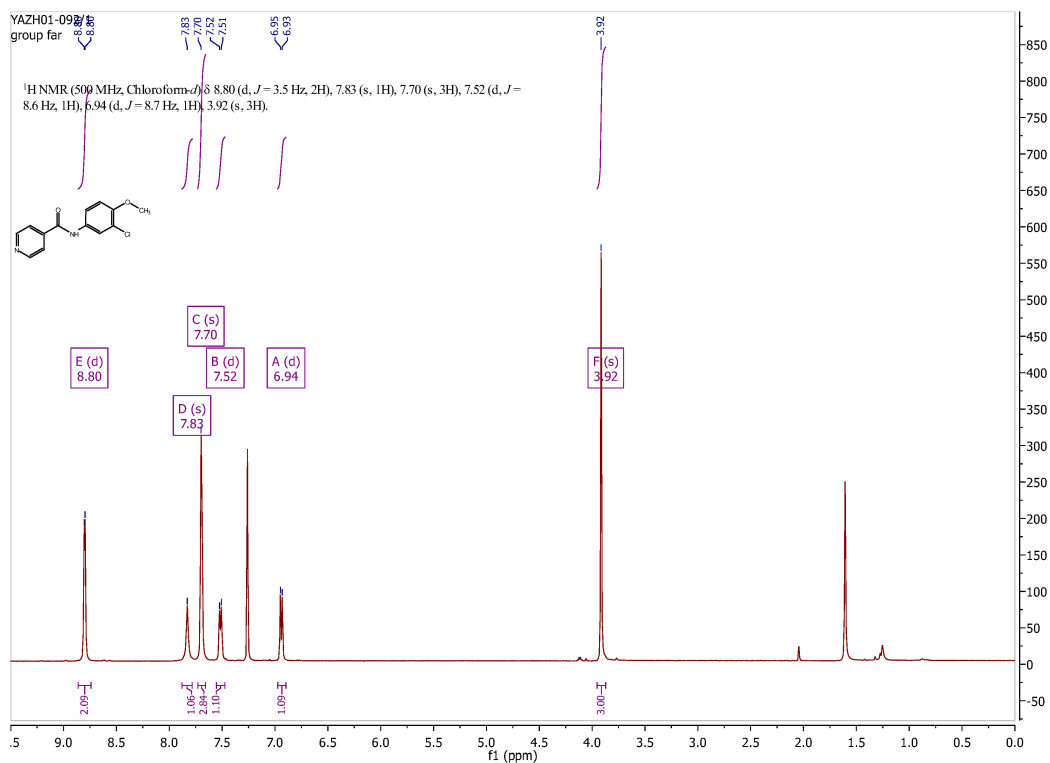Processed by   : Admin
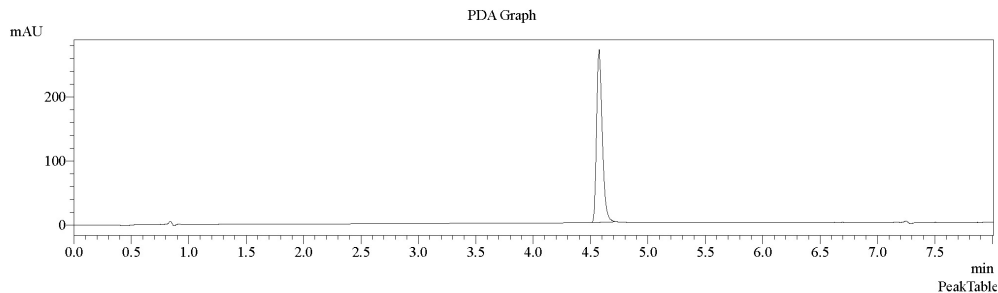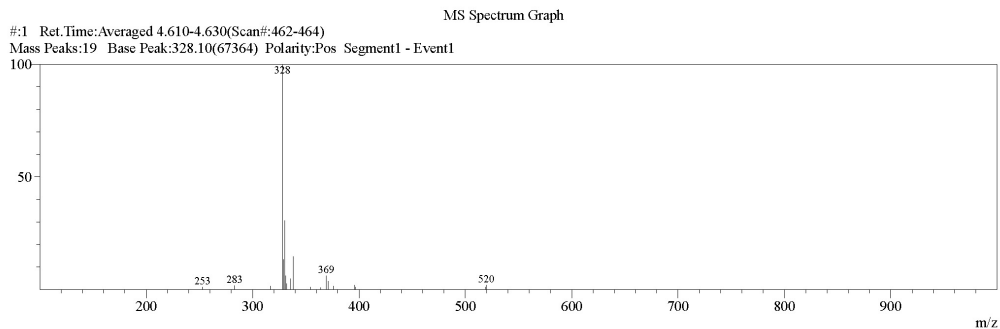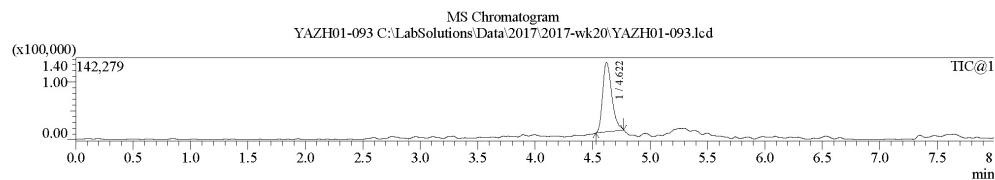Modified Date   : 5/17/2017 9:42:43 AM

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.569	921148	100.000

MS Chromatogram
YAZH01-093 C:\LabSolutions\Data\2017\2017-wk20\YAZH01-093.lcd

(x100,000)
142,279   TIC@1

MS Spectrum Graph
#:1 Ret.Time:Averaged 4.610-4.630(Scan#:462-464)
Mass Peaks:19 Base Peak:328.10(67364) Polarity:Pos Segment1 - Event1

MS Spectrum Table
#:1 Ret.Time:
BG Mode:Calc 4.530<->4.770(454<->478)
Mass Peaks:19 Base Peak:328.10(67364) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	252.85	787	1.17				10	338.25	9871	14.65			
2	282.85	1206	1.79				11	354.25	850	1.26			
3	316.80	1036	1.54				12	364.25	689	1.02			
4	328.10	67364	100.00				13	369.25	4189	6.22			
5	329.10	8988	13.34				14	371.15	2563	3.80			
6	330.10	20637	30.64				15	376.20	1150	1.71			
7	331.20	4201	6.24				16	396.20	1321	1.96			
8	332.30	1871	2.78				17	397.05	737	1.09			
9	336.00	3207	4.76				18	518.95	727	1.08			

Figure S189 LCMS spectrum of compound NPD-3086

YAZH01-093/1
group far

7.88, 7.86, 7.76, 7.67, 7.50, 7.48, 7.21, 7.19, 6.92, 6.90, 6.74, 6.59, 6.44

3.90

^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.87 (d, *J* = 7.7 Hz, 2H), 7.76 (s, 1H), 7.67 (s, 1H), 7.49 (d, *J* = 8.8 Hz, 1H), 7.20 (d, *J* = 7.8 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 1H), 6.59 (t, *J* = 73.1 Hz, 1H), 3.90 (s, 3H).

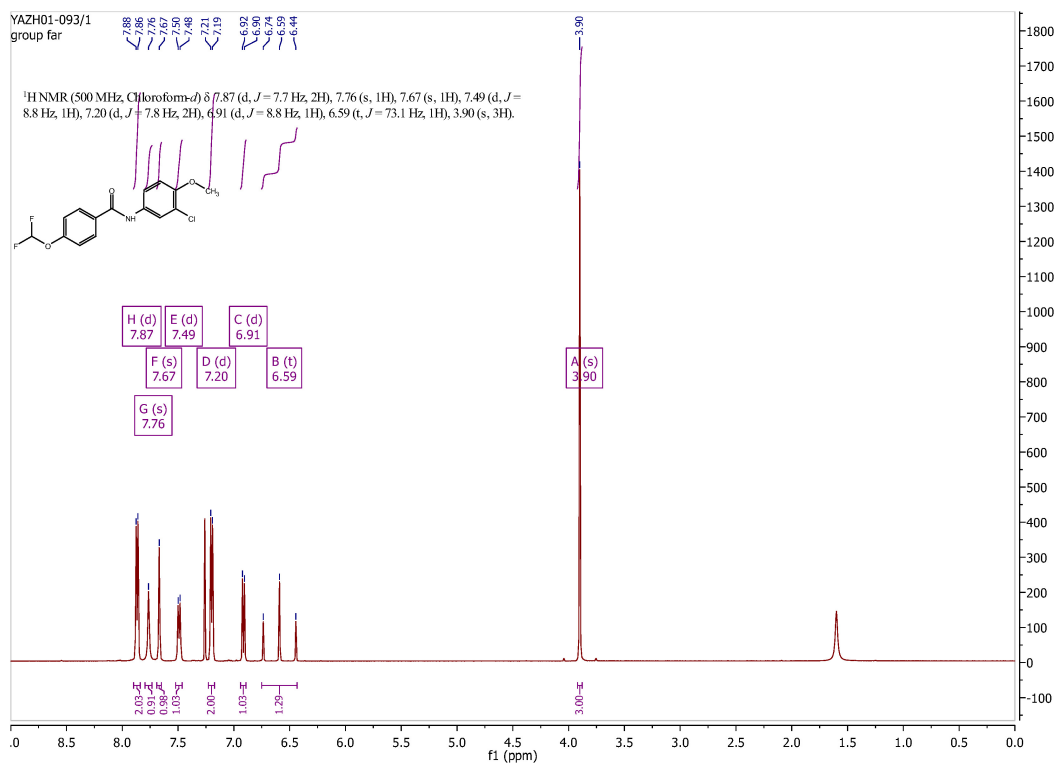| H (d) 7.87 | E (d) 7.49 | | C (d) 6.91 |
| F (s) 7.67 | D (d) 7.20 | B (t) 6.59 | A (s) 3.90 |
| G (s) 7.76 | | | |

Figure S190 ^{1}H NMR spectrum of compound NPD-3086

YAZH01-093/2
group far

164.57, 153.77, 153.75, 153.72, 152.22, 131.45, 131.15, 128.98, 122.97, 122.58, 120.15, 119.26, 117.45, 115.37, 113.29, 112.20

56.39

^{13}C NMR (126 MHz, Chloroform-*d*) δ 164.57 , 153.75 (t, *J* = 2.7 Hz), 152.22 , 131.45 , 131.15 , 128.98 , 122.97 , 122.58 , 120.15 , 119.26 , 115.37 (t, *J* = 261.5 Hz), 112.20 , 56.39 .
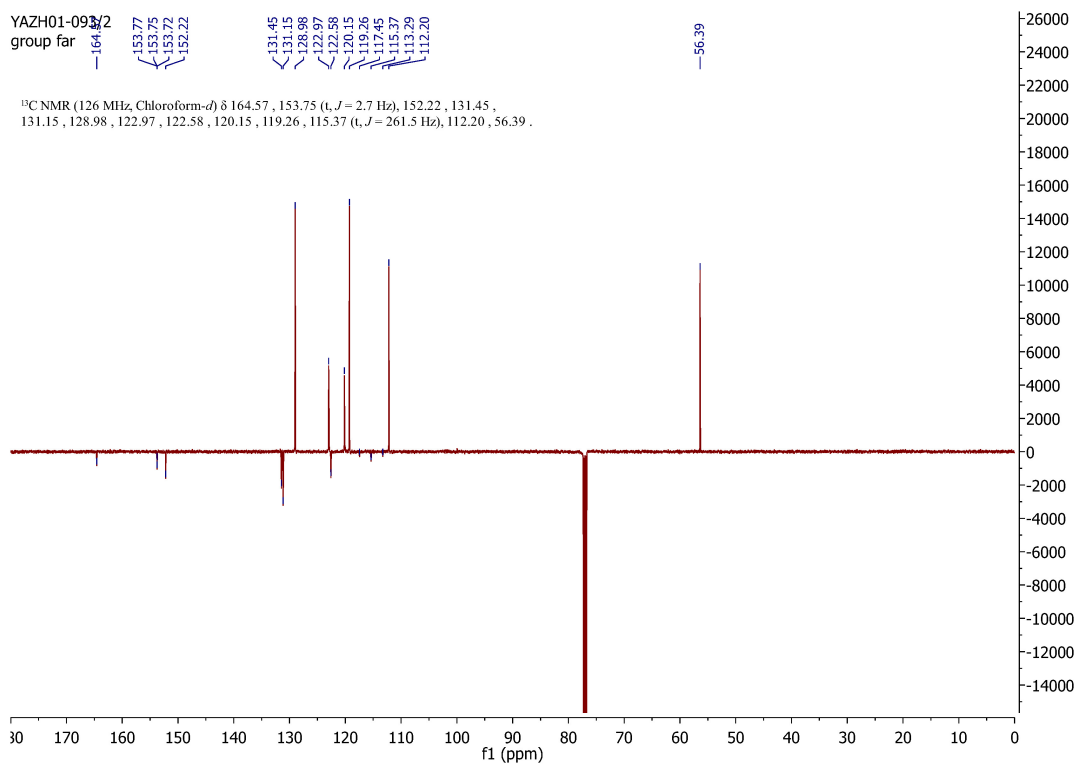
Figure S191 ^{13}C NMR spectrum of compound NPD-3086

Medicinal Chemistry
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Chromatogram
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mAU

1 PDA Multi 1

1   PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm
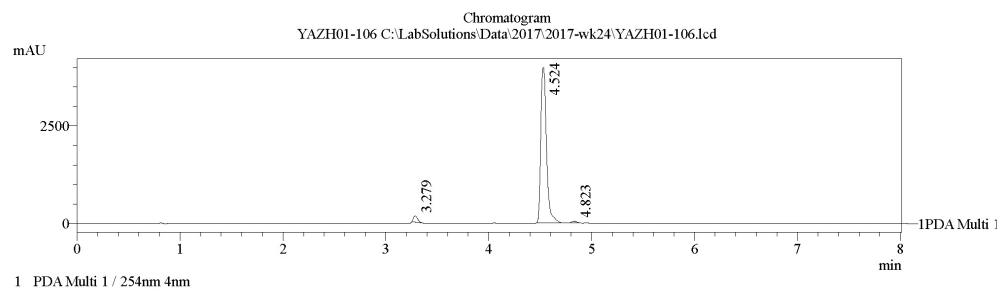
Peak#	Name	Ret. Time	Area	Area %
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2		4.524	15085442	96.406
3		4.823	147330	0.942

MS Chromatogram
YAZH01-106 C:\LabSolutions\Data\2017\2017-wk24\YAZH01-106.lcd

(x1,000,000)

TIC@1

MS Spectrum Graph

#:1   Ret.Time:Averaged 4.570-4.590(Scan#:458-460)
Mass Peaks:14   Base Peak:355.05(650409) Polarity:Pos Segment1 - Event1

#:1   Ret.Time:
BG Mode:Calc 4.470<->4.850(448<->486)
Mass Peaks:14   Base Peak:355.05(650409) Polarity:Pos Segment1 - Event1
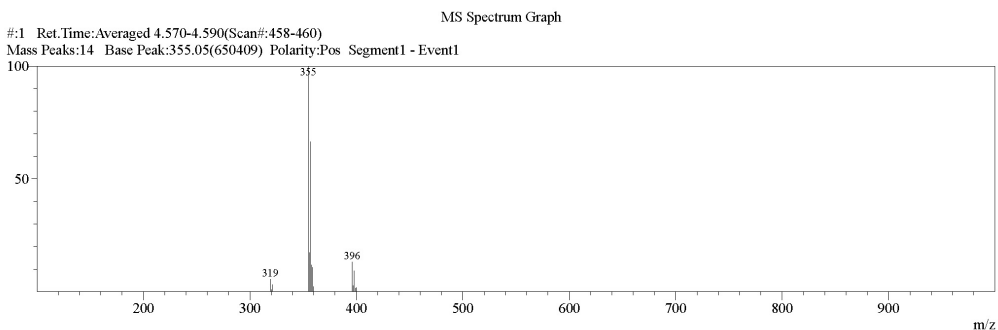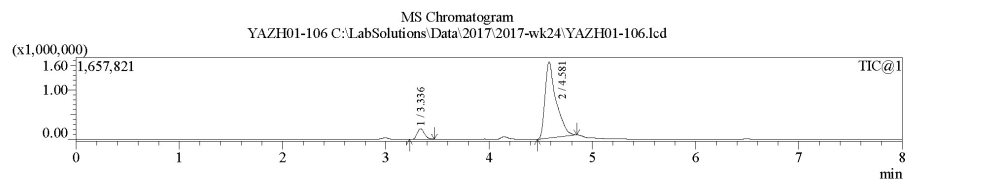
#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	319.00	36020	5.54				8	359.00	69909	10.75			
2	320.10	6725	1.03				9	360.10	14187	2.18			
3	321.10	19904	3.06				10	396.05	85324	13.12			
4	355.05	650409	100.00				11	397.05	17455	2.68			
5	356.05	112147	17.24				12	398.10	60249	9.26			
6	357.05	432794	66.54				13	399.15	10412	1.60			
7	358.05	77271	11.88				14	400.10	11893	1.83			

Figure S192 LCMS spectrum of compound NPD-3093

163

¹H NMR (500 MHz, Chloroform-*d*) δ 8.57 (s, 2H), 7.68 (s, 1H), 7.59 (dd, *J* = 8.0, 2.1 Hz, 1H), 7.46 (ddd, *J* = 8.3, 4.0, 2.2 Hz, 1H), 7.20 (dd, *J* = 10.5, 8.4 Hz, 1H), 3.96 (d, *J* = 7.0 Hz, 2H), 1.38 – 1.29 (m, 1H), 0.71 – 0.65 (m, 2H), 0.38 (q, *J* = 4.8 Hz, 2H).
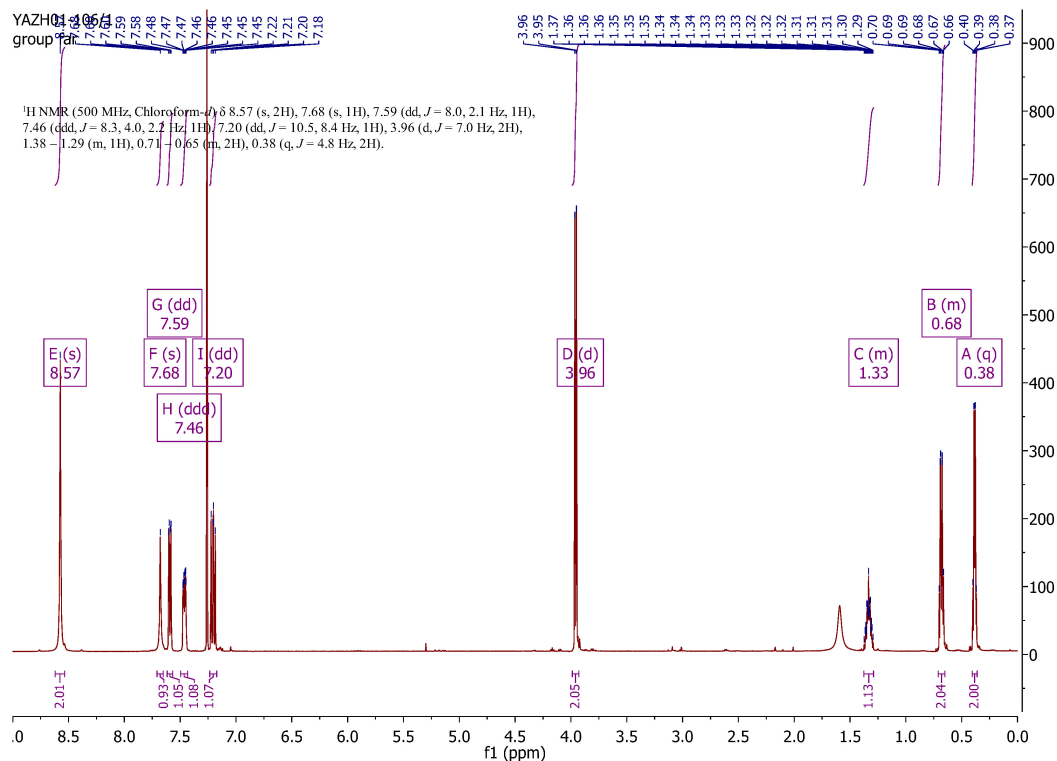
Figure S193 ¹H NMR spectrum of compound NPD-3093

¹³C NMR (126 MHz, Chloroform-*d*) δ 163.8, 155.8 (d, *J* = 254.3 Hz), 148.5, 147.9 (d, *J* = 10.9 Hz), 139.9, 129.2 (d, *J* = 3.2 Hz), 128.9, 120.3 (d, *J* = 8.2 Hz), 116.5 (d, *J* = 19.5 Hz), 115.2 (d, *J* = 3.2 Hz), 74.6, 10.2, 3.5.
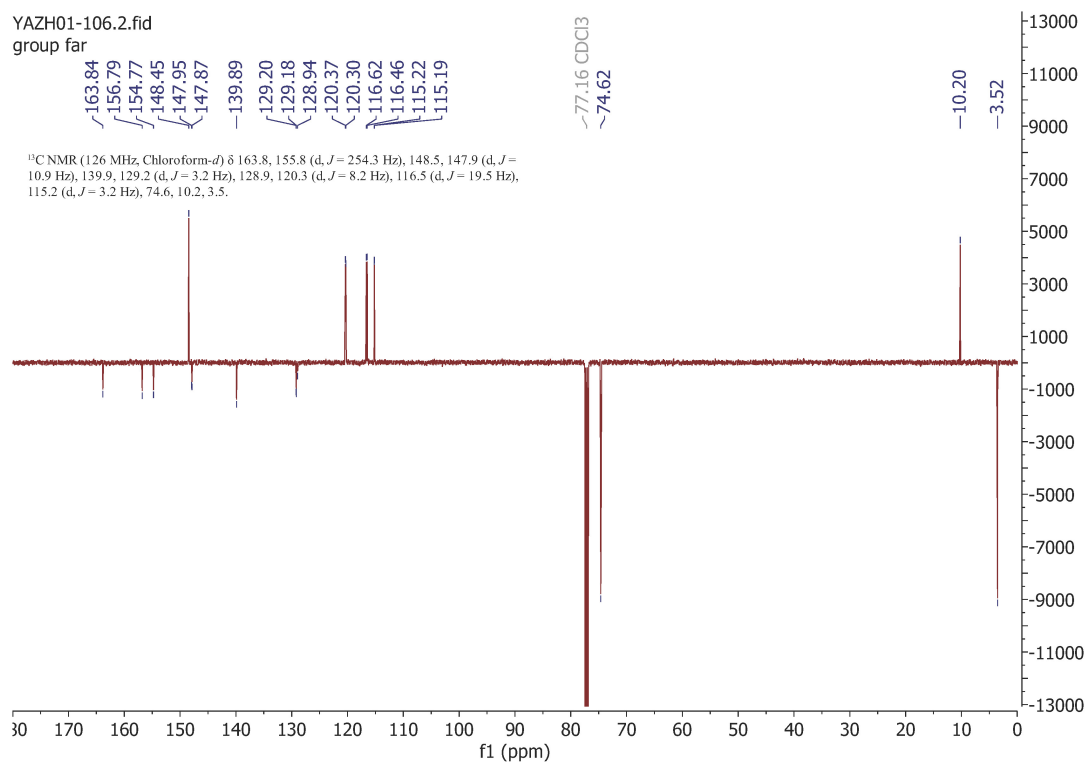
Figure S194 ¹³C NMR spectrum of compound NPD-3093

Medicinal Chemistry
Vrije Universiteit Amsterdam

Chromatogram
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1 PDA Multi 1 / 254nm 4nm

PDA Ch1 254nm 4nm
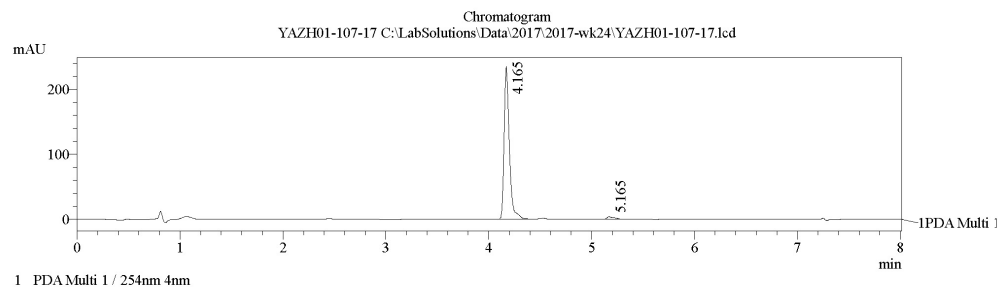
Peak Table

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MS Chromatogram
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#:1 Ret.Time:Averaged 4.210-4.230(Scan#:422-424)
Mass Peaks:17 Base Peak:367.05(201830) Polarity:Pos Segment1 - Event1

MS Spectrum Graph

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.110<->4.420(412<->443)
Mass Peaks:17 Base Peak:367.05(201830) Polarity:Pos Segment1 - Event1
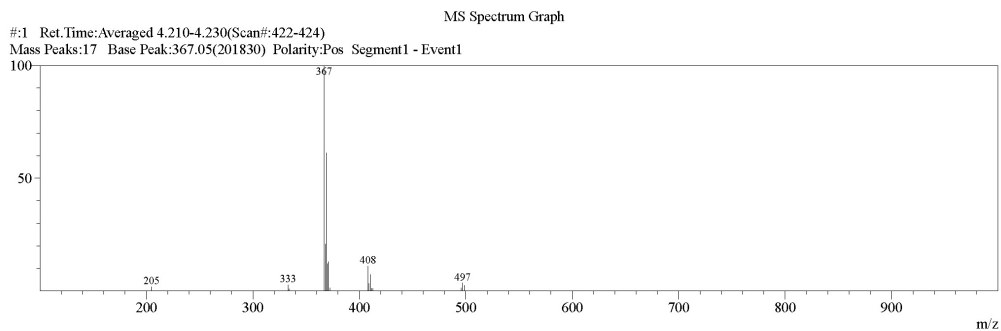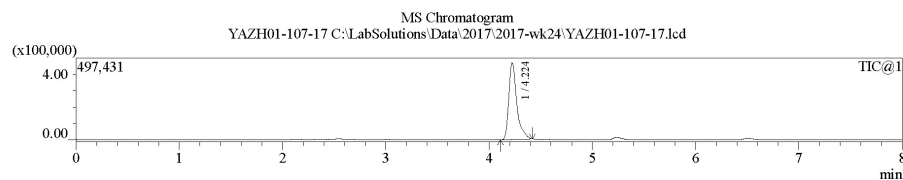
#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	204.95	3679	1.82				9	372.20	2827	1.40			
2	333.10	5364	2.66				10	408.15	22053	10.93			
3	334.10	2122	1.05				11	409.15	6829	3.38			
4	367.05	201830	100.00				12	410.25	14735	7.30			
5	368.10	42127	20.87				13	411.10	2372	1.18			
6	369.05	123618	61.25				14	412.55	2504	1.24			
7	370.05	24134	11.96				15	495.45	2906	1.44			
8	371.00	25963	12.86				16	496.95	7050	3.49			

Figure S195 LCMS spectrum of compound NPD-3094

165

YAZH01-107/2
group far

E (m)
7.53

F (s)
8.57

D (d)
6.97

C (m)
3.97

G (m)
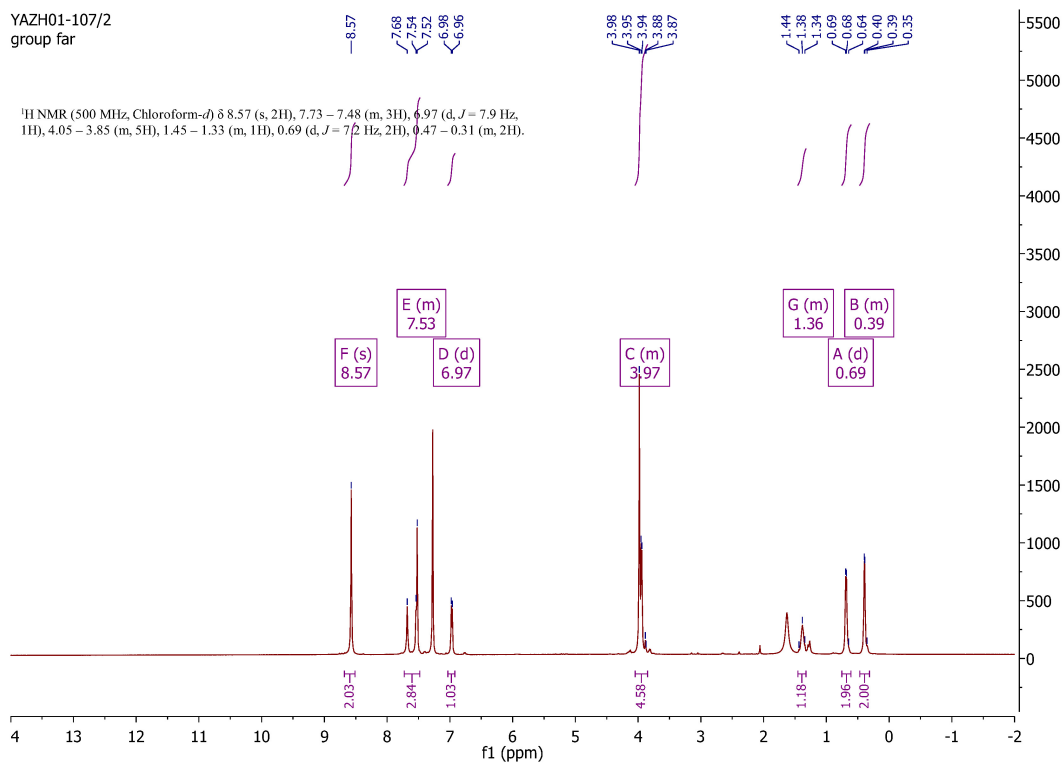1.36

B (m)
0.39

A (d)
0.69

Figure S196 ^{1}H NMR spectrum of compound NPD-3094

YAZH01-107/3
group far
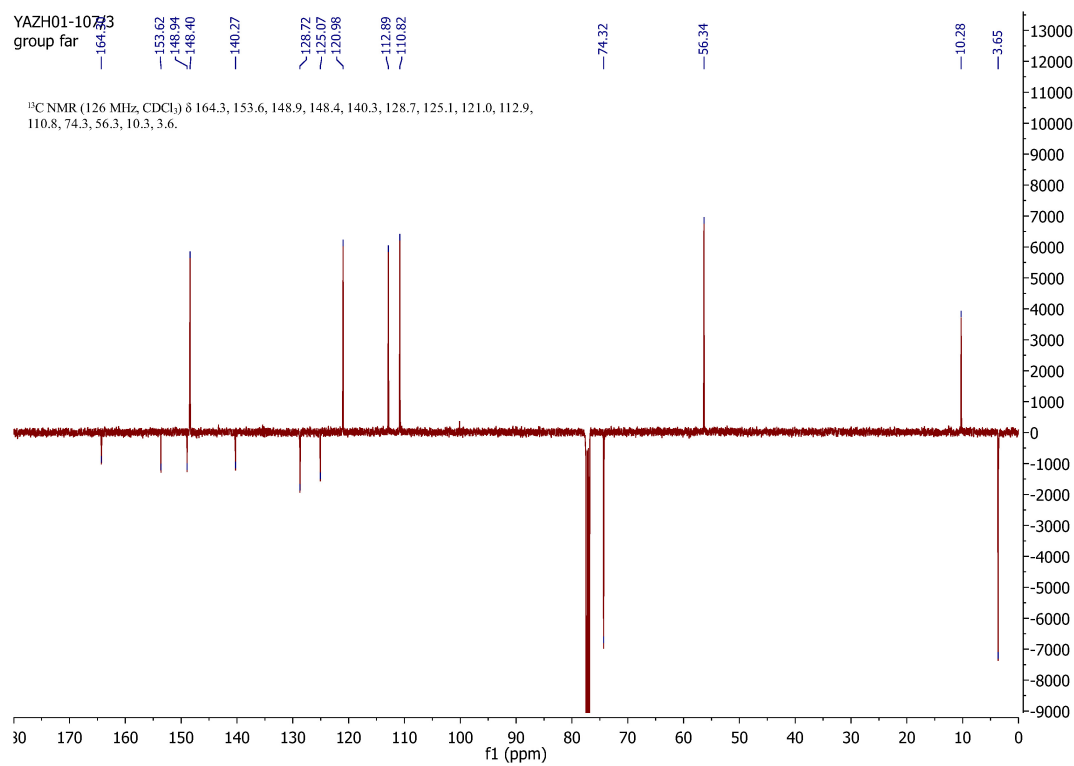
Figure S197 ^{13}C NMR spectrum of compound NPD-3094

166

PDA Graph

mAU

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.809	471773	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.860-4.880(Scan#:487-489)
Mass Peaks:23   Base Peak:371.00(61613) Polarity:Pos Segment1 - Event1
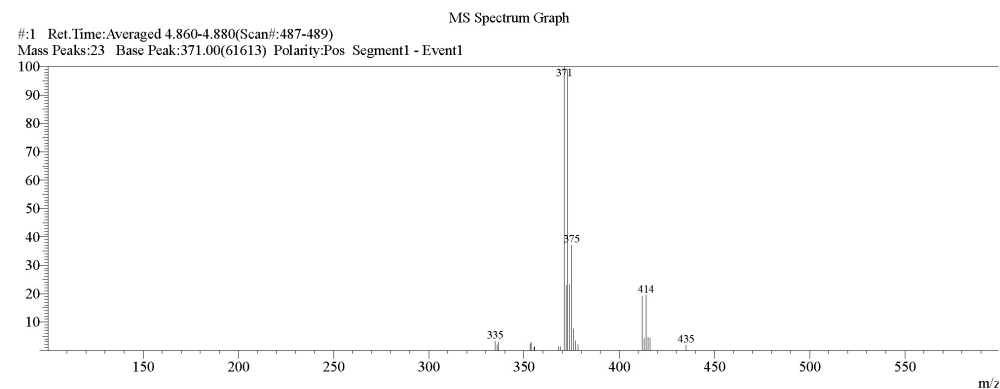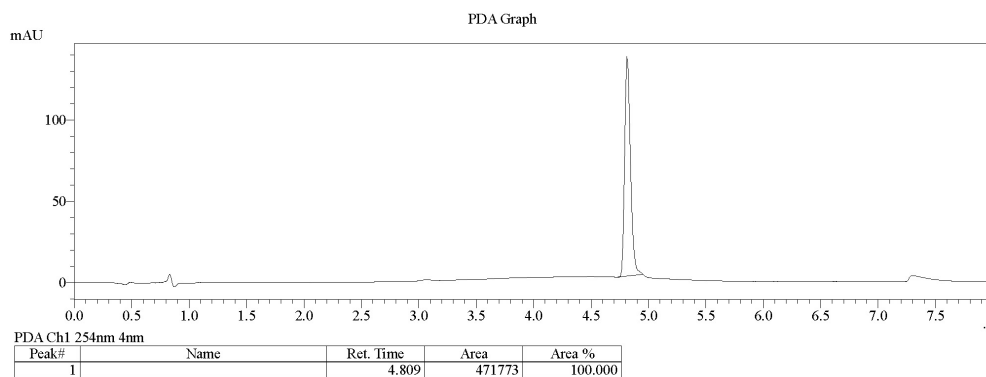
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.770<->5.050(478<->506)
Mass Peaks:23   Base Peak:371.00(61613) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	334.75	2002	3.25				13	374.00	14328	23.25			
2	335.75	1222	1.98				14	375.05	22855	37.09			
3	336.75	1765	2.86				15	376.05	4665	7.57			
4	353.15	1447	2.35				16	376.95	2130	3.46			
5	353.70	1783	2.89				17	378.20	1272	2.06			
6	355.20	672	1.09				18	411.95	11738	19.05			
7	355.70	832	1.35				19	413.15	2627	4.26			
8	368.15	815	1.32				20	413.95	12012	19.50			
9	369.10	796	1.29				21	415.10	2901	4.71			
10	371.00	61613	100.00				22	416.05	2677	4.34			
11	372.05	14081	22.85				23	435.00	1176	1.91			
12	373.00	61021	99.04										

Figure S198 LCMS spectrum of compound NPD-3096

167

¹H NMR (500 MHz, Chloroform-*d*) δ 8.58 (s, 2H), 7.69 (s, 1H), 7.56 – 7.48 (m, 2H), 7.40 (dd, *J* = 8.1, 1.6 Hz, 1H), 3.98 (q, *J* = 6.8 Hz, 2H), 1.39 – 1.30 (m, 1H), 0.68 (q, *J* = 5.5 Hz, 2H), 0.41 (q, *J* = 5.1 Hz, 2H).
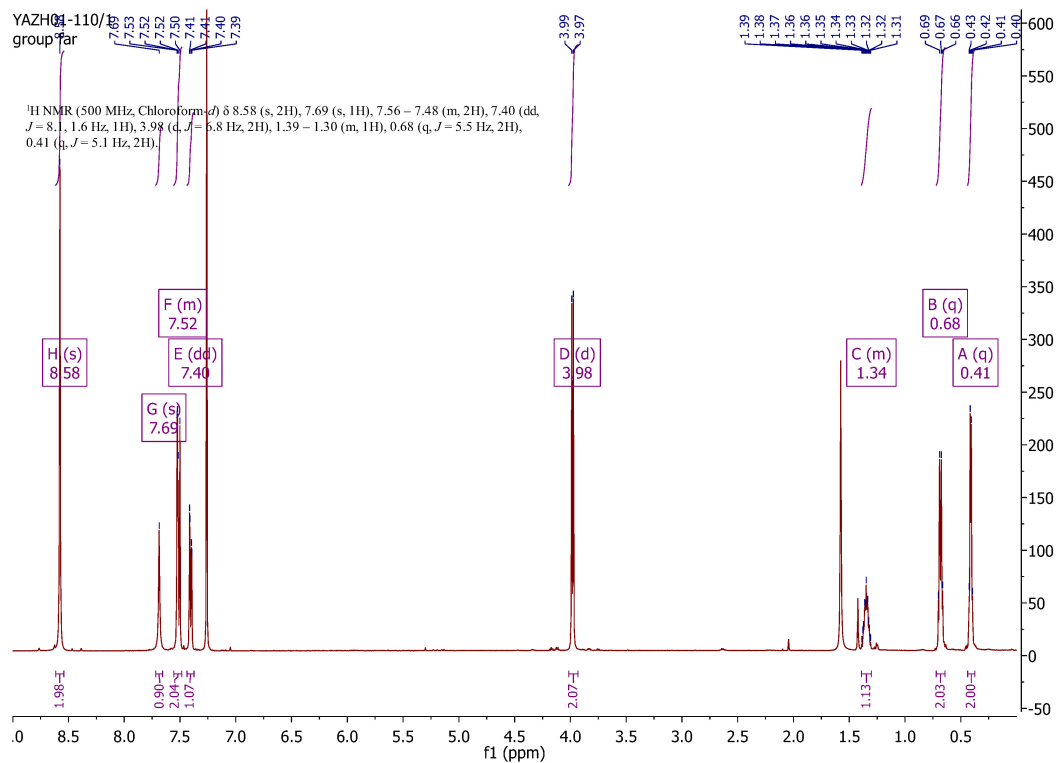
Figure S199 ¹H NMR spectrum of compound NPD-3096

¹³C NMR (126 MHz, CDCl₃) δ 163.9, 155.3, 148.5, 139.8, 132.3, 130.7, 129.0, 128.6, 119.7, 113.3, 74.3, 10.1, 3.5.

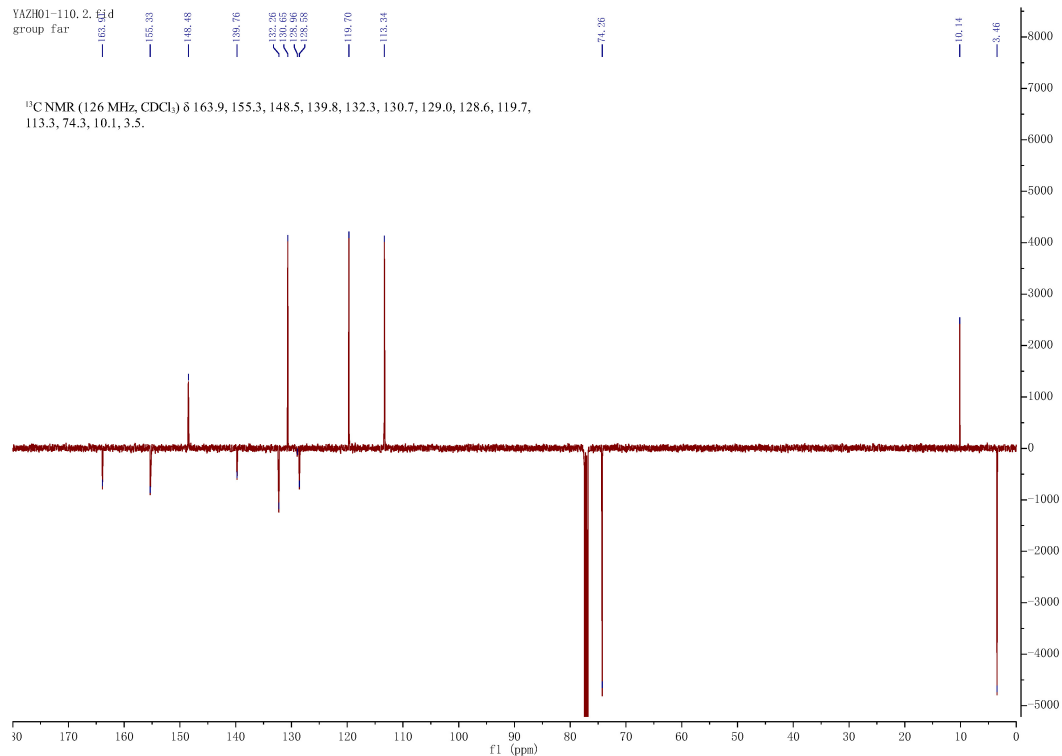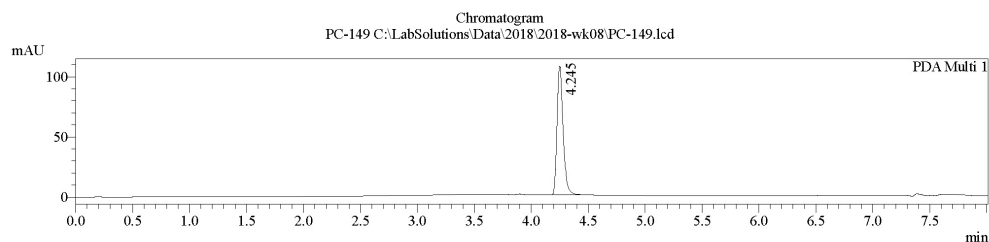**Figure S200 ¹³C NMR spectrum of compound NPD-3096**

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Sample Name   : PC-149
Sample ID   :
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Injection Volume   : 1
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Processed by   : Admin
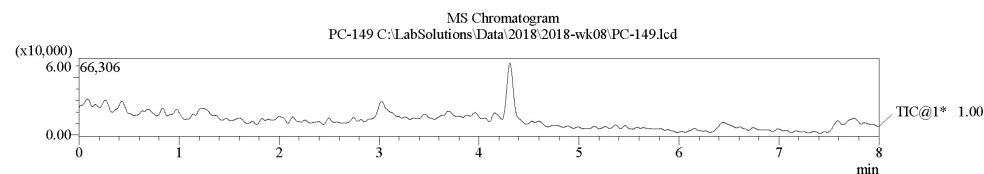Modified Date   : 19/2/2018 2:44:57 PM

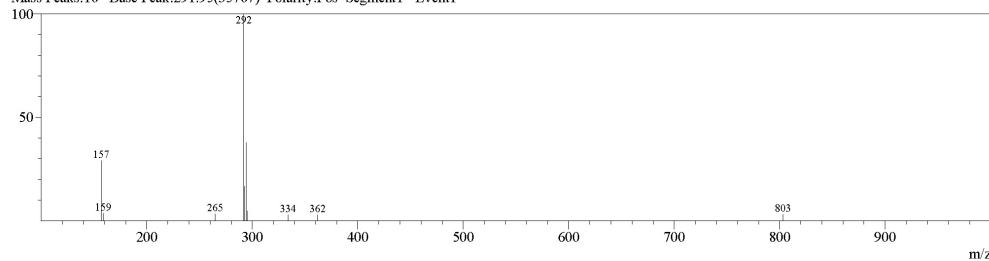**Medicinal Chemistry**
Vrije Universiteit Amsterdam

Chromatogram
PC-149 C:\LabSolutions\Data\2018\2018-wk08\PC-149.lcd

1   PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.245	396497	100.000

MS Chromatogram
PC-149 C:\LabSolutions\Data\2018\2018-wk08\PC-149.lcd

MS Spectrum Graph

#:1 Ret.Time:Single 4.310(Scan#:432)
Mass Peaks:10 Base Peak:291.95(35707) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:None
Mass Peaks:10 Base Peak:291.95(35707) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	157.05	10374	29.05				6	294.00	13482	37.76			
2	158.95	1299	3.64				7	295.15	1720	4.82			
3	264.80	1209	3.39				8	334.10	1065	2.98			
4	291.95	35707	100.00				9	362.05	1037	2.90			
5	293.00	5925	16.59				10	803.25	1159	3.25			

Figure S201 LCMS spectrum of compound NPD-3286

169

PC-046.1.fid

^{1}H NMR (600 MHz, Chloroform-d) δ 7.89 (d, J = 2.1 Hz, 1H), 7.78 (dd, J = 8.6, 2.2 Hz, 1H), 7.63 (s, 1H), 7.51 (d, J = 8.7 Hz, 2H), 6.99 (d, J = 8.5 Hz, 1H), 6.91 (d, J = 8.9 Hz, 2H), 3.97 (s, 3H), 3.82 (s, 3H).

B (dd)
7.78

F (d)
6.91

H (s)
3.82

A (d)
7.89

D (d)
7.51

E (d)
6.99

G (s)
3.97

C (s)
7.63
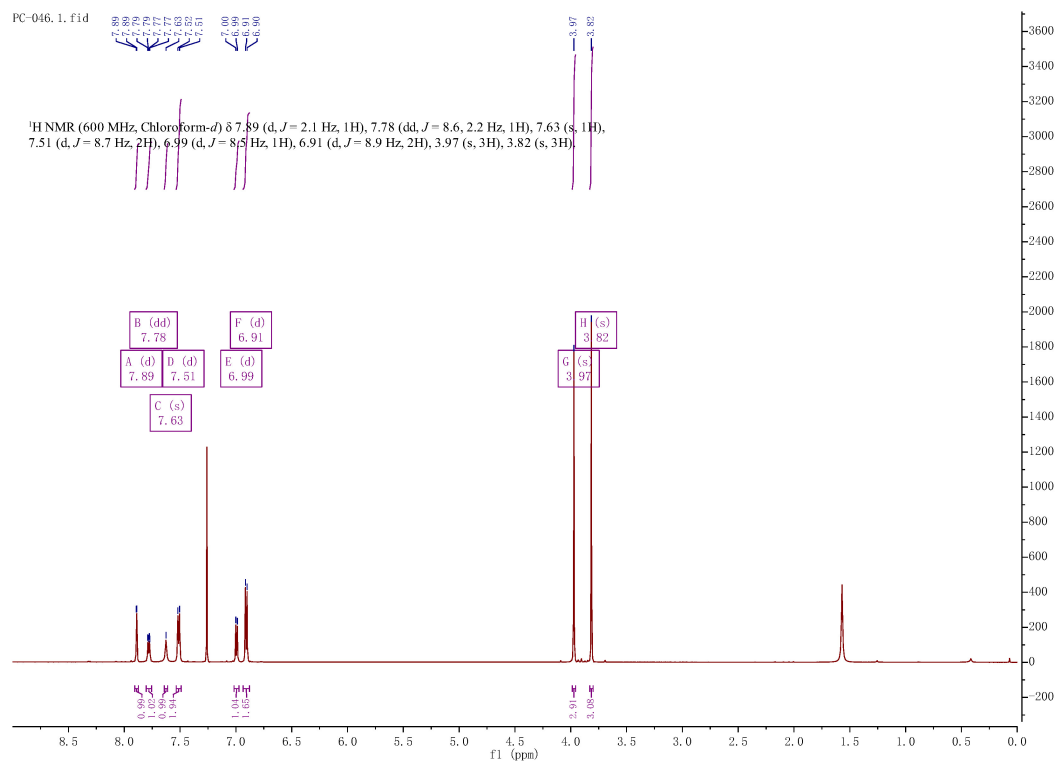
Figure S202 ^{1}H NMR spectrum of compound NPD-3286

PC-046/2

^{13}C NMR (151 MHz, CDCl$_3$) δ 164.0, 157.7, 156.7, 130.8, 129.1, 128.0, 127.2, 122.8, 122.2, 114.3, 111.6, 56.4, 55.5.
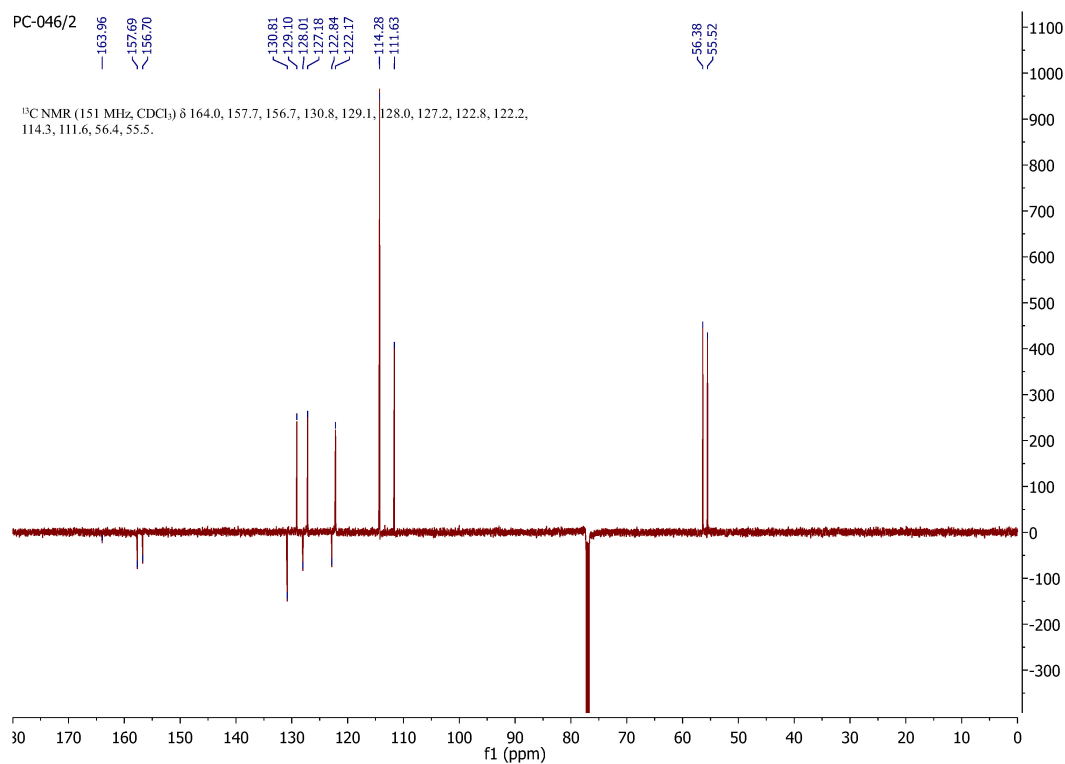
Figure S203 ^{13}C NMR spectrum of compound NPD-3286

170

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Chromatogram
PC-150 C:\LabSolutions\Data\2018\2018-wk08\PC-150.lcd

mAU

PDA Multi 1

1 PDA Multi 1 / 254nm 4nm

Peak Table

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.057	468487	99.018
2		4.250	4647	0.982

MS Chromatogram
PC-150 C:\LabSolutions\Data\2018\2018-wk08\PC-150.lcd

(x100,000)

TIC@1* 1.00

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.100-4.120(Scan#:411-413)
Mass Peaks:7 Base Peak:293.00(53322) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.030<->4.210(404<->422)
Mass Peaks:7 Base Peak:293.00(53322) Polarity:Pos Segment1 - Event1
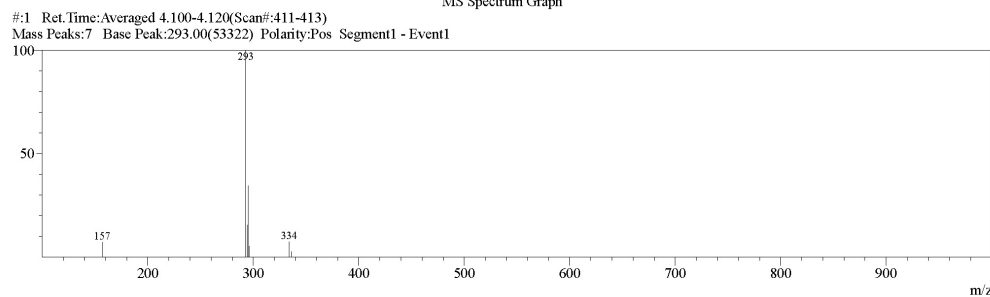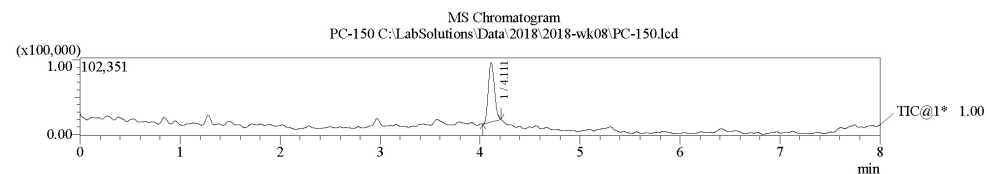
#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	157.00	3767	7.06				5	296.10	2842	5.33			
2	293.00	53322	100.00				6	333.90	3900	7.31			
3	294.05	8219	15.41				7	336.10	1452	2.72			
4	295.00	18471	34.64										

Figure S204 LCMS spectrum of compound NPD-3287

171

PC-047/1

I (s)
8.70

H (d)
8.09

F (s)
7.64

E (d)
7.51

G (s)
7.70

D (d)
6.95

C (d)
6.86

B (s)
4.03

A (s)
3.93

Figure S205 ¹H NMR spectrum of compound NPD-3287

PC-047/2

Figure S206 ¹³C NMR spectrum of compound NPD-3287

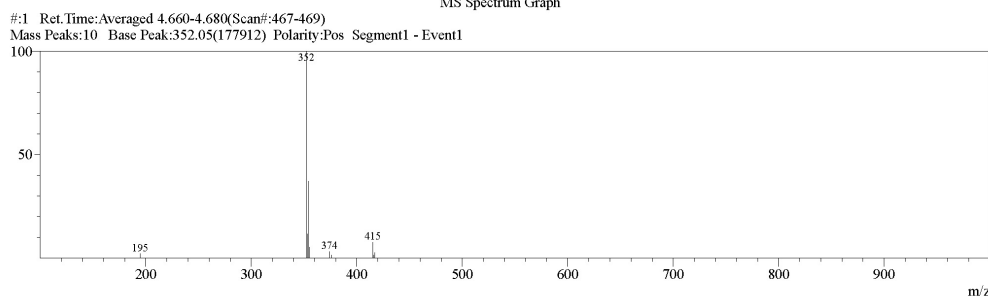172

Medicinal Chemistry
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Chromatogram
PC-151 C:\LabSolutions\Data\2018\2018-wk08\PC-151.lcd

1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.610	714742	100.000

MS Chromatogram
PC-151 C:\LabSolutions\Data\2018\2018-wk08\PC-151.lcd

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.660-4.680(Scan#:467-469)
Mass Peaks:10   Base Peak:352.05(177912) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.560<->4.840(457<->485)
Mass Peaks:10   Base Peak:352.05(177912) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	194.95	3762	2.11				6	374.00	5700	3.20			
2	352.05	177912	100.00				7	376.00	2427	1.36			
3	353.10	20562	11.56				8	415.15	13568	7.63			
4	354.05	65945	37.07				9	416.15	2698	1.52			
5	355.00	9550	5.37				10	417.05	4652	2.61			

Figure S207 LCMS spectrum of compound NPD-3288

PC-48/1

E (s)
9.87

B (d)
7.72

A (d)
7.98

C (dd)
7.58

I (d)
6.83

D (d)
6.92

G (s)
3.93

F (s)
4.07

H (m)
3.91
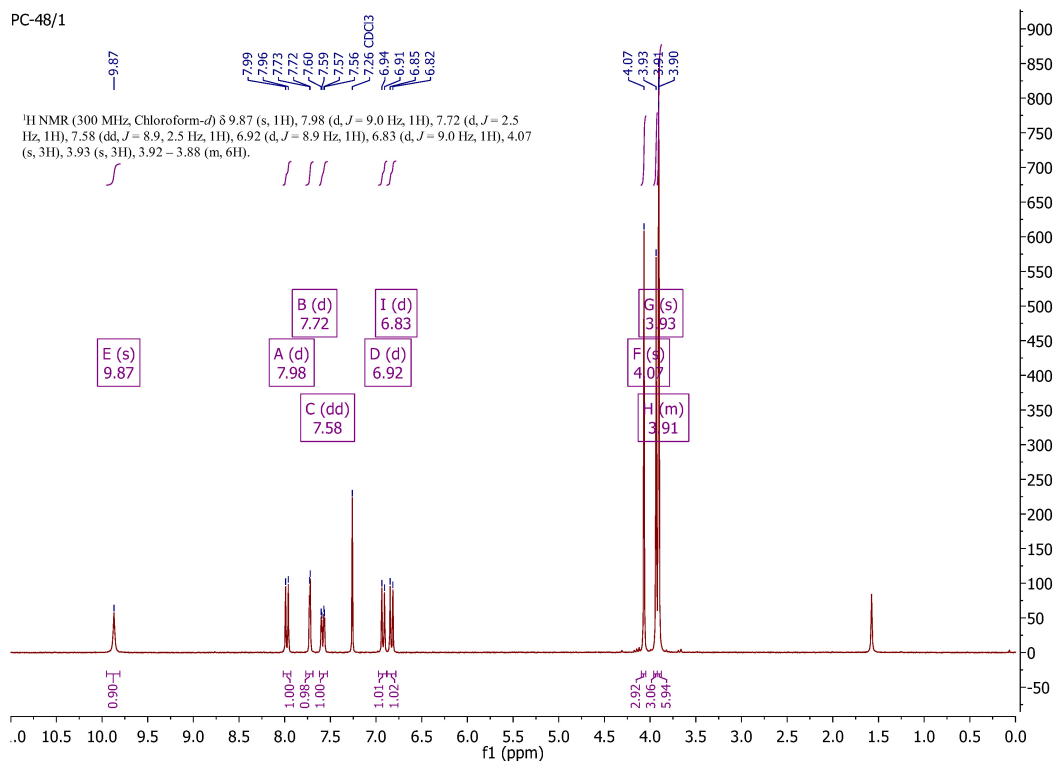
Figure S208 ¹H NMR spectrum of compound NPD-3288

PC-048/2
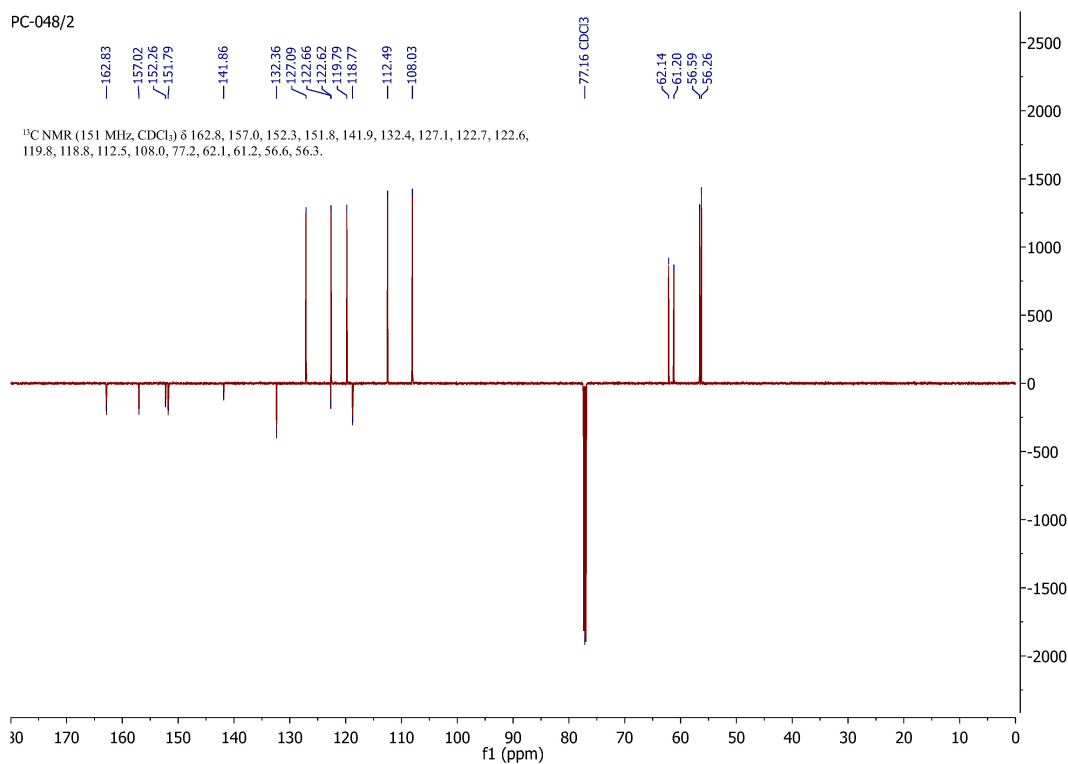
Figure S209 ¹³C NMR spectrum of compound NPD-3288

174

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vrije Universiteit

Chromatogram
PC-151-Thijs C:\LabSolutions\Data\2018\2018-wk09\PC-151-Thijs.lcd

1   PDA Multi 1 / 254nm 4nm
PDA Ch1 254nm 4nm
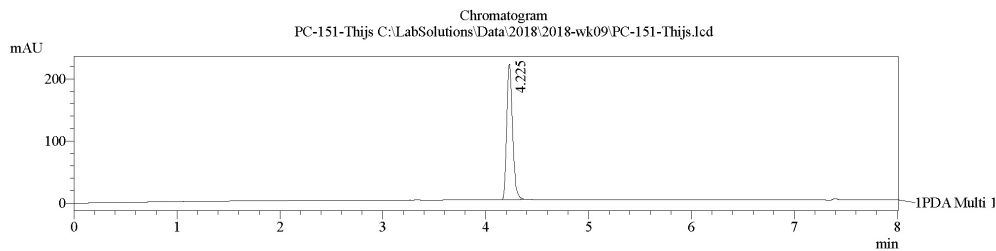
Peak#	Name	Ret. Time	Area	Area %
1		4.225	851213	100.000

MS Chromatogram
PC-151-Thijs C:\LabSolutions\Data\2018\2018-wk09\PC-151-Thijs.lcd
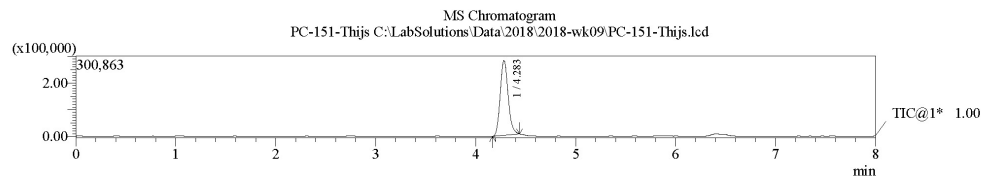
MS Spectrum Graph
#:1   Ret.Time:Averaged 4.270-4.290(Scan#:428-430)
Mass Peaks:6   Base Peak:352.10(192449)   Polarity:Pos   Segment1 - Event1
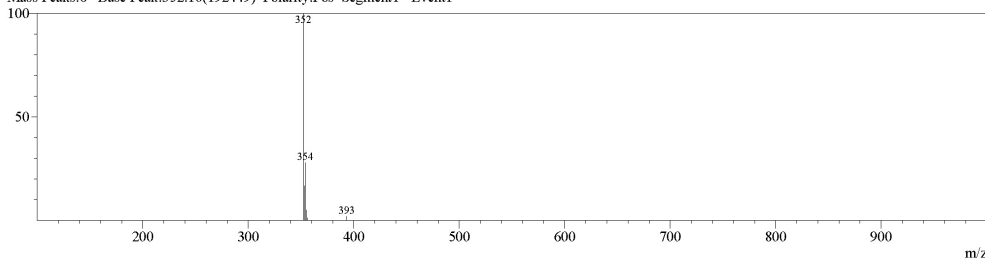
MS Spectrum Table
#:1   Ret.Time:
BG Mode:Calc 4.170<->4.440(418<->445)
Mass Peaks:6   Base Peak:352.10(192449)   Polarity:Pos   Segment1 - Event1

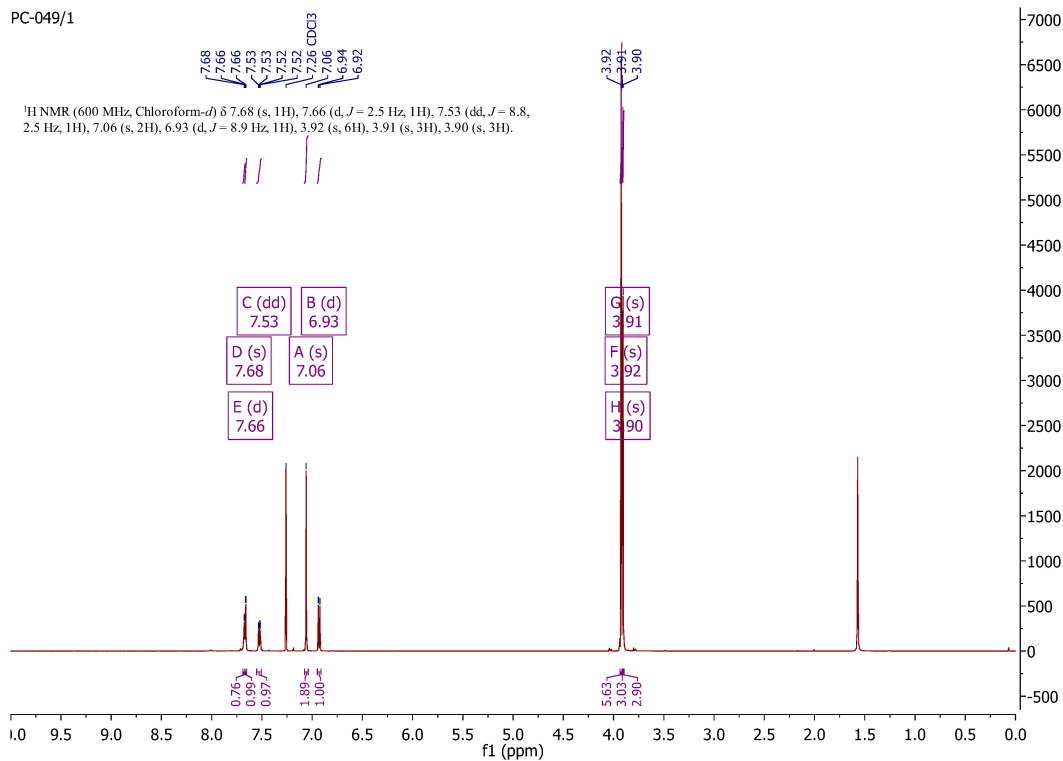| #	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	352.10	192449	100.00				4	355.10	9257	4.81			
2	353.05	31737	16.49				5	356.20	2157	1.12			
3	354.05	53672	27.89				6	393.15	3681	1.91			

Figure S210 LCMS spectrum of compound NPD-3289

PC-049/1

7.68
7.66
7.66
7.53
7.53
7.52
7.52
7.26 CDCl3
7.06
6.94
6.92

3.92
3.91
3.90

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.68 (s, 1H), 7.66 (d, *J* = 2.5 Hz, 1H), 7.53 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.06 (s, 2H), 6.93 (d, *J* = 8.9 Hz, 1H), 3.92 (s, 6H), 3.91 (s, 3H), 3.90 (s, 3H).

C (dd) 7.53	B (d) 6.93
D (s) 7.68	A (s) 7.06
E (d) 7.66	

| G (s) 3.91 |
| F (s) 3.92 |
| H (s) 3.90 |

0.76
0.99
0.97

1.89
1.00

5.63
3.03
2.90

f1 (ppm)

Figure S211 ^{1}H NMR spectrum of compound NPD-3289

PC-049/2

165.53

153.52
152.29

141.47

131.51
130.20

123.03
122.75
120.21

112.42

104.59

77.16 CDCl3

61.12

56.56

^{13}C NMR (151 MHz, CDCl$_3$) δ 165.5, 153.5, 152.3, 141.5, 131.5, 130.2, 123.0, 122.8, 120.2, 112.4, 104.6, 77.2, 61.1, 56.6.

f1 (ppm)

Figure S212 ^{13}C NMR spectrum of compound NPD-3289

Medicinal Chemistry
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Chromatogram
PC-152 C:\LabSolutions\Data\2018\2018-wk08\PC-152.lcd

1   PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		3.828	365000	97.265
2		4.603	10263	2.735

MS Chromatogram
PC-152 C:\LabSolutions\Data\2018\2018-wk08\PC-152.lcd

MS Spectrum Graph

#:1 Ret.Time:Single 3.900(Scan#:391)
Mass Peaks:5 Base Peak:157.05(7910) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:None
Mass Peaks:5 Base Peak:157.05(7910) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	157.05	7910	100.00				4	341.80	1854	23.44			
2	339.90	5759	72.81				5	947.70	3011	38.07			
3	340.80	2284	28.87										

Figure S213 LCMS spectrum of compound NPD-3290

177

PC-50.1.fid

8.16
8.13
7.98
7.95
7.84
7.83
7.59
7.59

6.91
6.88

3.82

3.07

10.16

¹H NMR (300 MHz, Chloroform-*d*) δ 10.16 (s, 1H), 8.14 (d, *J* = 8.4 Hz, 2H), 7.96 (d, *J* = 8.4 Hz, 2H), 7.83 (d, *J* = 2.4 Hz, 1H), 7.62 − 7.57 (m, 1H), 6.89 (d, *J* = 8.9 Hz, 1H), 3.82 (s, 3H), 3.07 (s, 3H).

| D (s) | | F (d) | | | | | | B (s) | A (s) |
| 10.16 | | 7.96 | | | | | | 3.82 | 3.07 |

E (d) H (m) C (d)
8.14   7.59   6.89

G (d)
7.83

0.85

1.93
1.94
0.98
0.85

1.00

3.10

3.00

10.5 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
f1 (ppm)
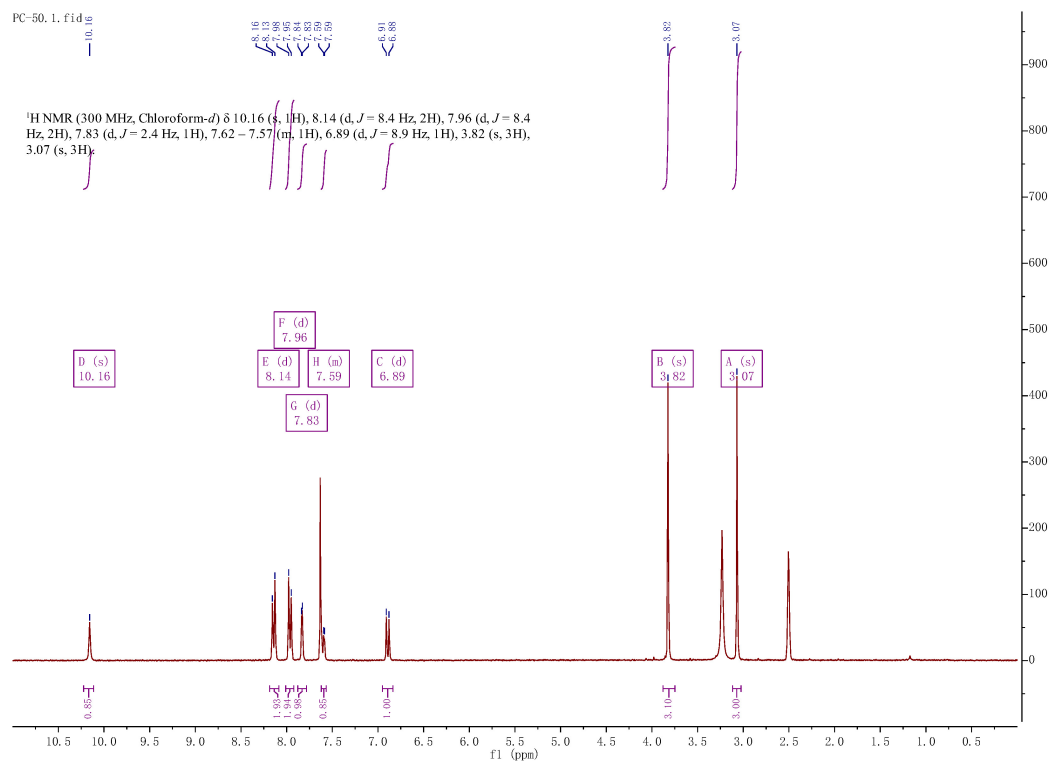
Figure S214 ¹H NMR spectrum of compound NPD-3290

PC-050/2

163.16

150.65

141.95
138.83

131.45
127.90
126.27
122.01
120.69
119.51

111.16

77.16 CDCl3

55.35

43.26

¹³C NMR (151 MHz, CDCl₃) δ 163.2, 150.6, 142.0, 138.8, 131.4, 127.9, 126.3, 122.0, 120.7, 119.5, 111.2, 77.2, 55.3, 43.3.

30 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)
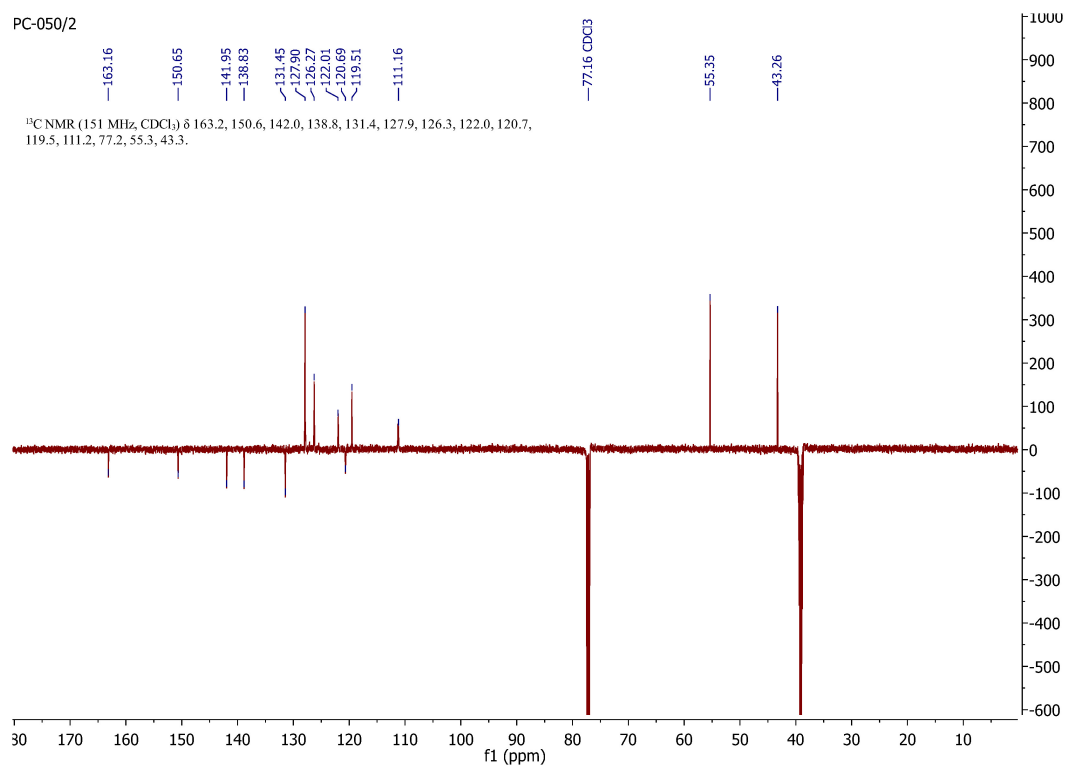
Figure S215 ¹³C NMR spectrum of compound NPD-3290

178

Chromatogram
PC-155-1 C:\LabSolutions\Data\2018\2018-wk08\PC-155-1.lcd

1 PDA Multi 1 / 254nm 4nm
PDA Ch1 254nm 4nm
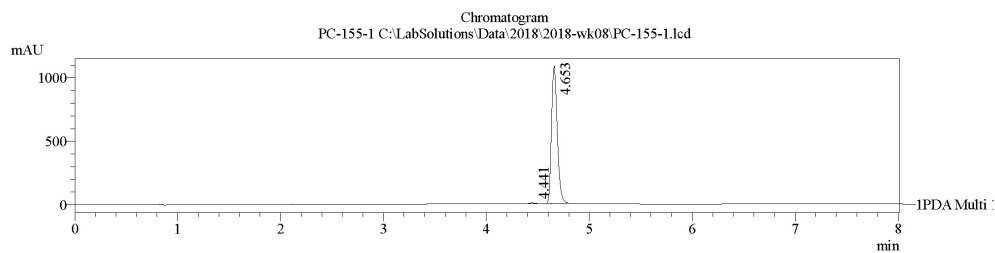
Peak#	Name	Ret. Time	Area	Area %
1		4.441	26653	0.633
2		4.653	4183901	99.367
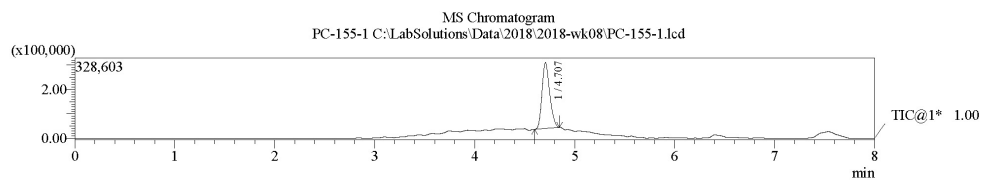
MS Chromatogram
PC-155-1 C:\LabSolutions\Data\2018\2018-wk08\PC-155-1.lcd

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.700-4.720(Scan#:471-473)
Mass Peaks:5 Base Peak:292.00(187969) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.600<->4.850(461<->486)
Mass Peaks:5 Base Peak:292.00(187969) Polarity:Pos Segment1 - Event1
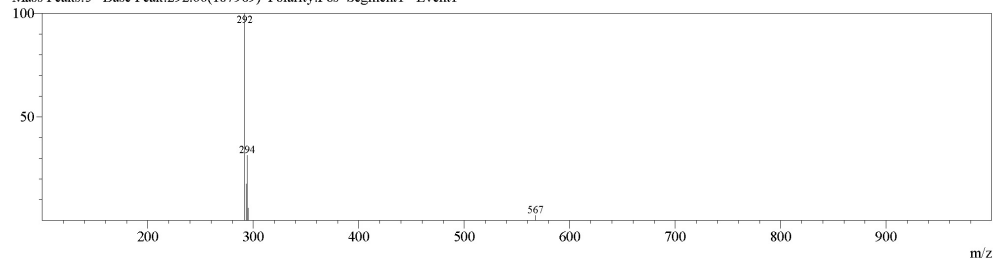
#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	292.00	187969	100.00				4	294.95	10936	5.82			
2	293.05	32956	17.53				5	567.45	4178	2.22			
3	294.05	58856	31.31										

Figure S216 LCMS spectrum of compound NPD-3291

PC-51/1

8.48
8.45
8.43
8.43
8.41
7.88
7.85
7.26 CDCl3
7.11
7.10
7.09
7.02
6.99
3.95
3.89

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.48 (s, 1H), 8.43 (dd, *J* = 5.8, 4.0 Hz, 1H), 7.86 (d, *J* = 8.8 Hz, 2H), 7.11 (s, 1H), 7.10 (d, *J* = 1.9 Hz, 1H), 7.01 (d, *J* = 8.8 Hz, 2H), 3.95 (s, 3H), 3.89 (s, 3H).

G (dd) 8.43		F (s) 7.11		B (s) 3.89
C (s) 8.48	D (d) 7.86	E (d) 7.01		A (s) 3.95
		H (d) 7.10		

0.83
1.02
1.99
0.92
0.86
1.96
3.03
3.00

f1 (ppm)

Figure S217 ^{1}H NMR spectrum of compound NPD-3291

PC-051/2

164.98
162.86
145.19
133.54
129.08
127.00
126.93
125.50
124.96
118.99
114.29
77.16 CDCl3
61.08
55.66

^{13}C NMR (151 MHz, CDCl3) δ 165.0, 162.9, 145.2, 133.5, 129.1, 127.0, 126.9, 125.5, 125.0, 119.0, 114.3, 77.2, 61.1, 55.7.

f1 (ppm)

Figure S218 ^{13}C NMR spectrum of compound NPD-3291

Medicinal Chemistry
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Chromatogram
PC-156 C:\LabSolutions\Data\2018\2018-wk08\PC-156.lcd

1 PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.460	1487845	100.000

MS Chromatogram
PC-156 C:\LabSolutions\Data\2018\2018-wk08\PC-156.lcd

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.510-4.530(Scan#:452-454)
Mass Peaks:7 Base Peak:322.05(186972) Polarity:Pos Segment1 - Event1
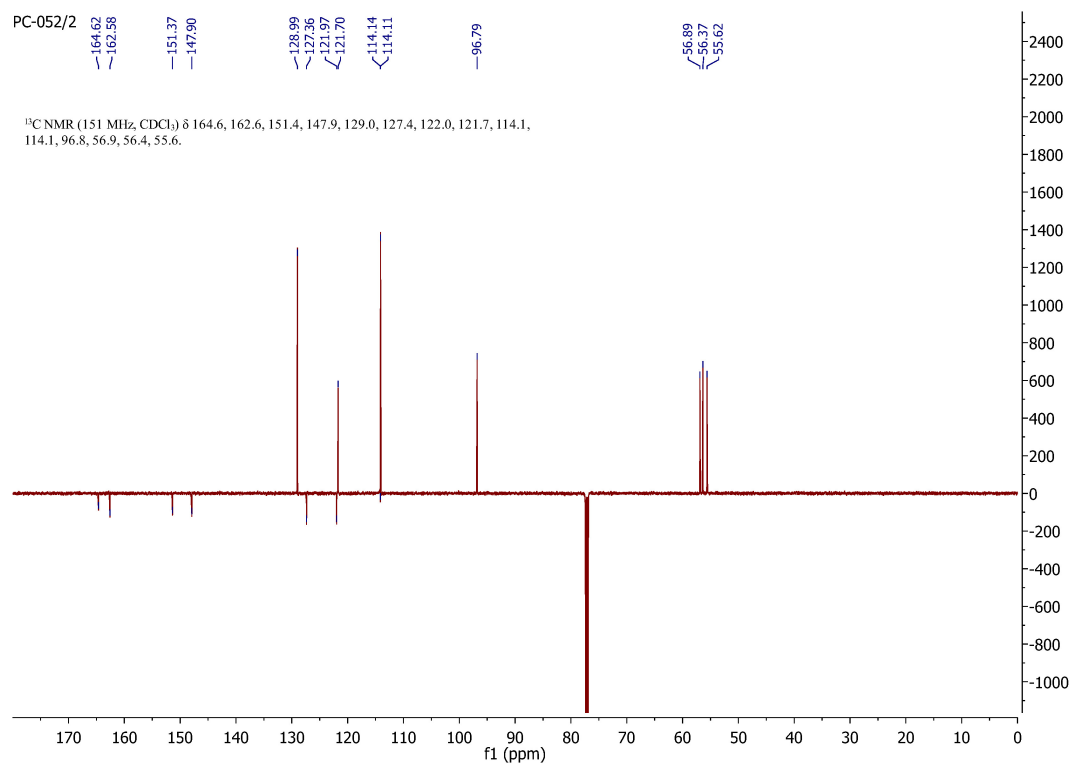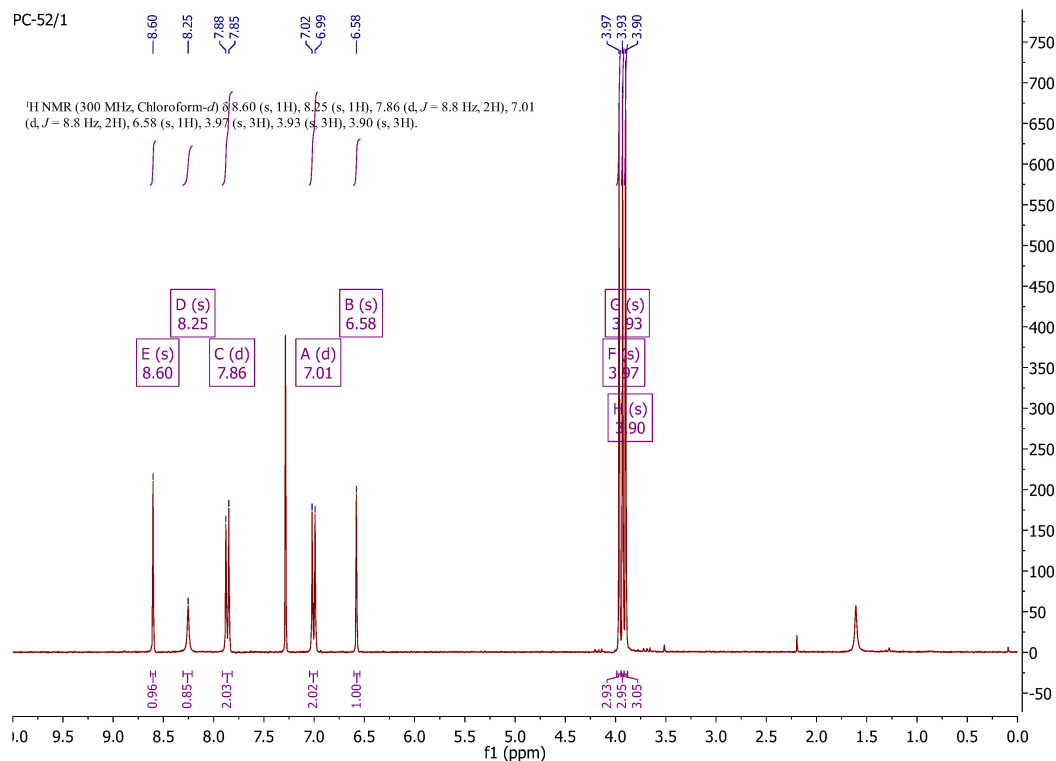

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.410<->4.690(442<->470)
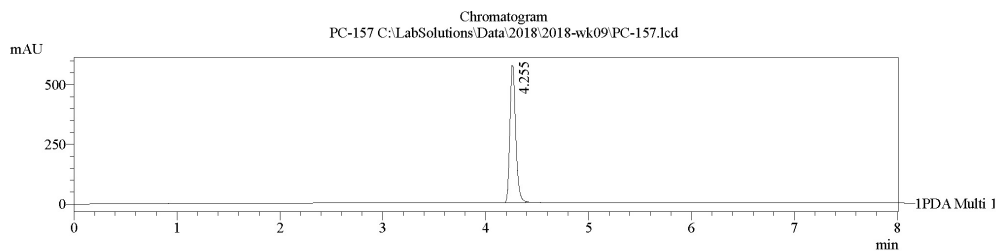Mass Peaks:7 Base Peak:322.05(186972) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	322.05	186972	100.00				5	326.10	1909	1.02			
2	323.10	40864	21.86				6	343.95	2512	1.34			
3	324.05	59111	31.61				7	385.05	4520	2.42			
4	325.05	11728	6.27										

Figure S219 LCMS spectrum of compound NPD-3292

PC-52/1

8.60 8.25 7.88 7.85 7.02 6.99 6.58   3.97 3.93 3.90

^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.60 (s, 1H), 8.25 (s, 1H), 7.86 (d, *J* = 8.8 Hz, 2H), 7.01 (d, *J* = 8.8 Hz, 2H), 6.58 (s, 1H), 3.97 (s, 3H), 3.93 (s, 3H), 3.90 (s, 3H).

D (s)
8.25

B (s)
6.58

E (s)
8.60

C (d)
7.86

A (d)
7.01

G (s)
3.93

F (s)
3.97

H (s)
3.90

Figure S220 ^{1}H NMR spectrum of compound NPD-3292

PC-052/2

164.62 162.58   151.37 147.90   128.99 127.36 121.97 121.70 114.14 114.11   96.79   56.89 56.37 55.62

^{13}C NMR (151 MHz, CDCl$_3$) δ 164.6, 162.6, 151.4, 147.9, 129.0, 127.4, 122.0, 121.7, 114.1, 114.1, 96.8, 56.9, 56.4, 55.6.

Figure S221 ^{13}C NMR spectrum of compound NPD-3292

Medicinal Chemistry
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Chromatogram
PC-157 C:\LabSolutions\Data\2018\2018-wk09\PC-157.lcd

1 PDA Multi 1 / 254nm 4nm
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.255	2260471	100.000

MS Chromatogram
PC-157 C:\LabSolutions\Data\2018\2018-wk09\PC-157.lcd
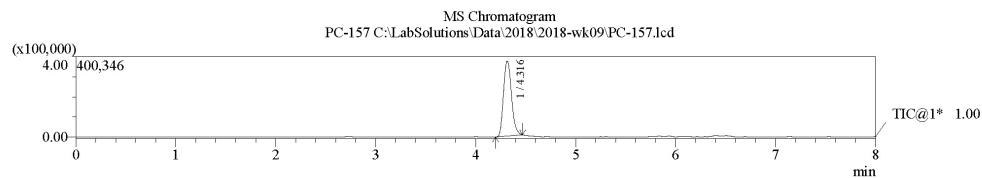
#:1 Ret.Time:Averaged 4.310-4.330(Scan#:432-434)
Mass Peaks:5 Base Peak:292.05(246719) Polarity:Pos Segment1 - Event1
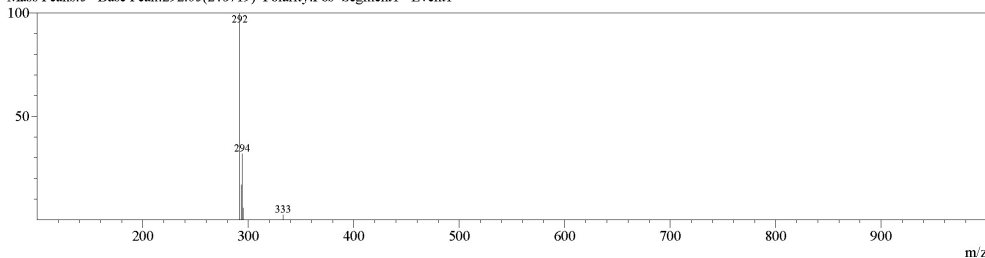
MS Spectrum Table
#:1 Ret.Time:
BG Mode:Calc 4.200<->4.470(421<->448)
Mass Peaks:5 Base Peak:292.05(246719) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	292.05	246719	100.00				4	295.00	13930	5.65			
2	293.05	41250	16.72				5	333.05	5381	2.18			
3	294.05	78405	31.78										

Figure S222 LCMS spectrum of compound NPD-3293

PC-53/1

^{1}H NMR (300 MHz, Chloroform-d) δ 8.38 (d, J = 9.1 Hz, 1H), 8.14 (s, 1H), 7.88 (d, J = 8.8 Hz, 2H), 7.04 – 6.94 (m, 3H), 6.88 (dd, J = 9.1, 2.8 Hz, 1H), 3.88 (s, 3H), 3.81 (s, 3H).

D (s)
8.14

B (m)
6.99

G (s)
3.81

E (d)
8.38

C (d)
7.88

A (dd)
6.88

F (s)
3.88
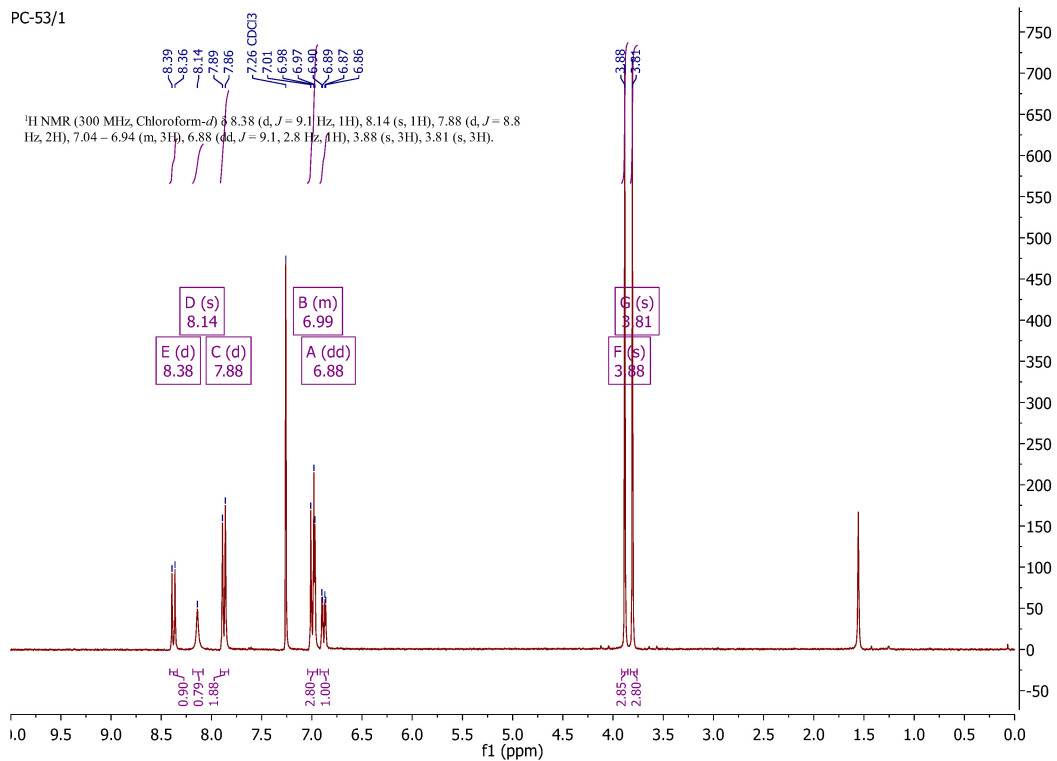
Figure S223 ^{1}H NMR spectrum of compound NPD-3293

PC-053/2

^{13}C NMR (151 MHz, CDCl$_3$) δ 164.8, 162.8, 156.3, 129.1, 128.4, 127.1, 124.3, 123.0, 114.7, 114.2, 113.4, 55.9, 55.6.
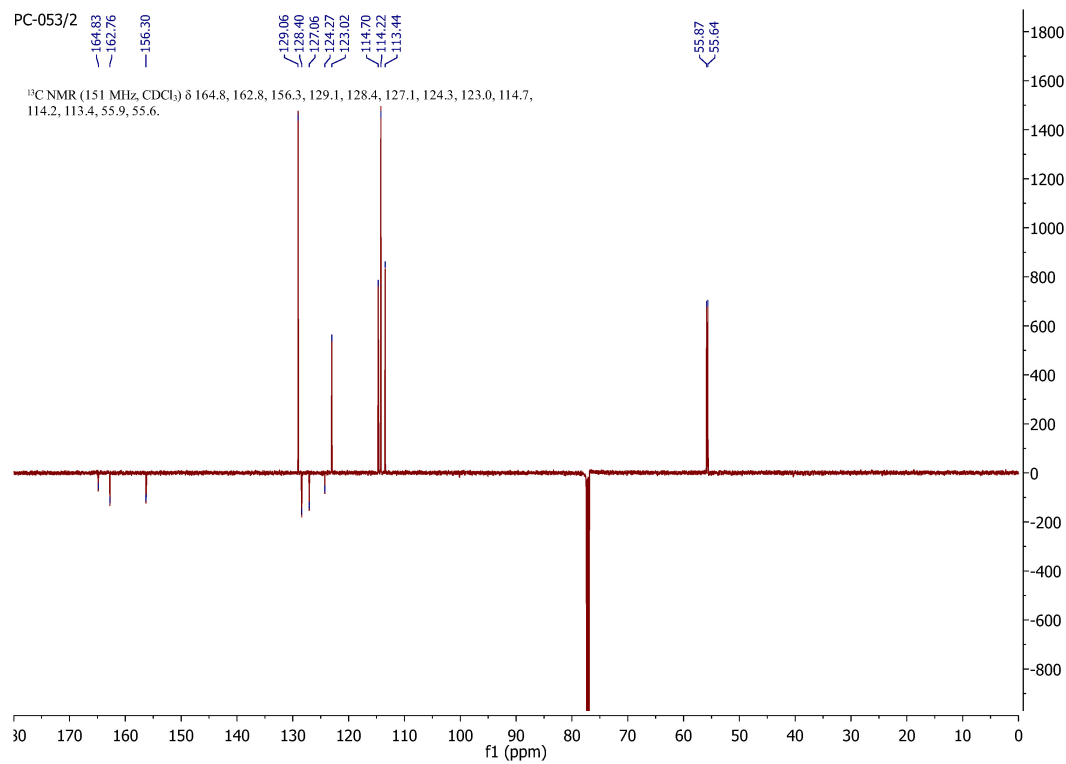
Figure S224 ^{13}C NMR spectrum of compound NPD-3293

184

PDA Graph

mAU
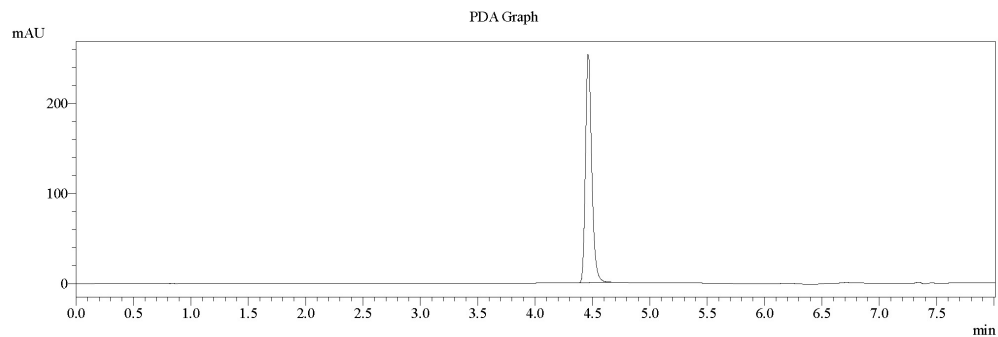
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.458	971595	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.510-4.530(Scan#:452-454)
Mass Peaks:11 Base Peak:292.00(80593) Polarity:Pos Segment1 - Event1
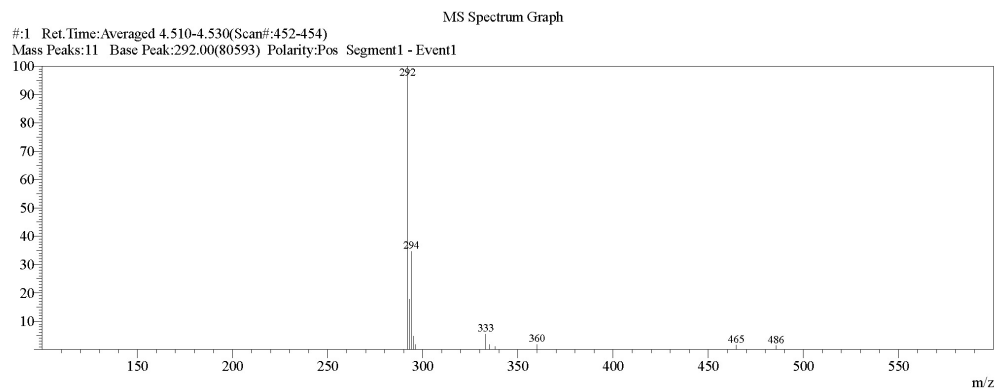
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.420<->4.650(443<->466)
Mass Peaks:11 Base Peak:292.00(80593) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	292.00	80593	100.00				7	335.10	1402	1.74			
2	293.00	14279	17.72				8	338.00	903	1.12			
3	294.00	27976	34.71				9	359.95	1511	1.87			
4	295.10	3835	4.76				10	464.80	1265	1.57			
5	296.10	1420	1.76				11	485.80	1108	1.37			
6	333.00	4410	5.47										

Figure S225 LCMS spectrum of compound NPD-3294

185

PC-54/1

¹H NMR (300 MHz, Chloroform-*d*) δ 7.81 (s, 1H), 7.72 (d, *J* = 2.2 Hz, 1H), 7.43 (s, 1H), 7.39 (d, *J* = 7.2 Hz, 2H), 7.32 (d, *J* = 8.5 Hz, 1H), 7.10 (dt, *J* = 7.2, 2.3 Hz, 1H), 6.90 (dd, *J* = 8.5, 2.3 Hz, 1H), 3.95 (s, 3H), 3.88 (s, 3H).

E (d)
7.39

F (d)
7.72

B (dt)
7.10

I (s)
3.88

D (s)
7.43

A (dd)
6.90

H (s)
3.95

G (s)
7.81

C (d)
7.32

0.82
1.00
1.09
1.78
1.00
1.00
1.00

2.94
3.13

f1 (ppm)
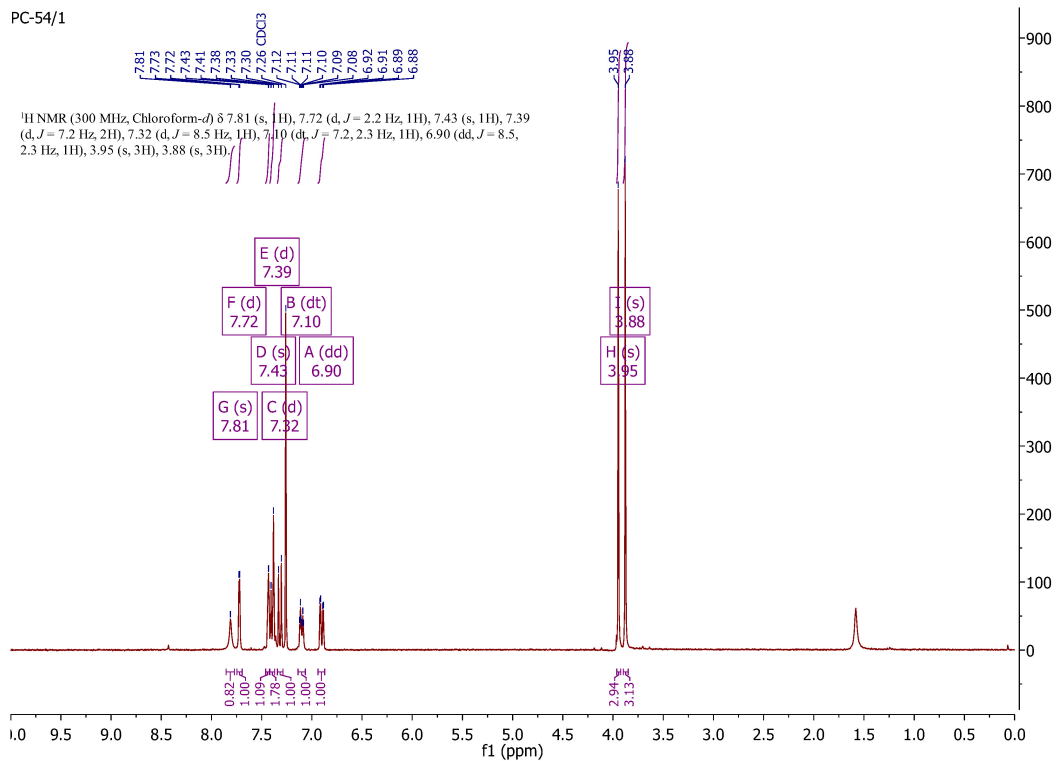
Figure S226 ¹H NMR spectrum of compound NPD-3294

PC-054/2

¹³C NMR (151 MHz, CDCl₃) δ 165.7, 160.2, 155.5, 137.9, 136.2, 130.2, 130.0, 118.7, 118.4, 117.9, 112.6, 112.3, 104.7, 56.4, 55.7.

f1 (ppm)
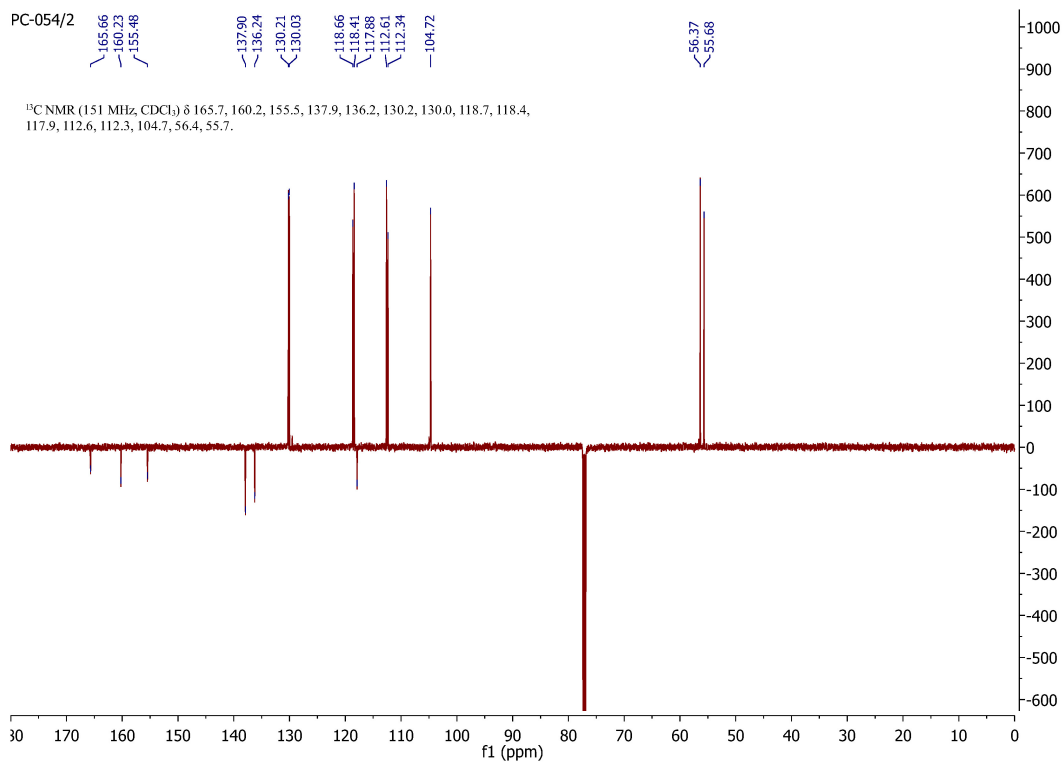
Figure S227 ¹³C NMR spectrum of compound NPD-3294

186

Medicinal Chemistry
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Chromatogram
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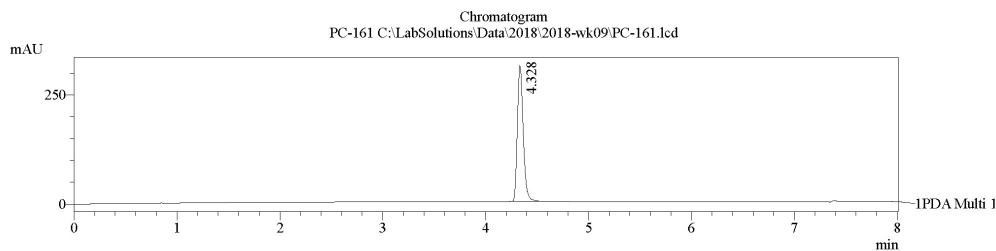
1 PDA Multi 1 / 254nm 4nm
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.328	1216400	100.000

MS Chromatogram
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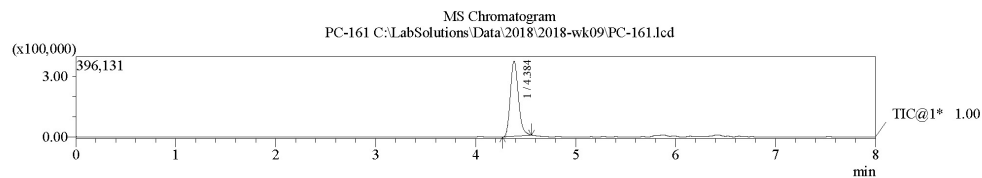
#:1 Ret.Time:Averaged 4.370-4.390(Scan#:438-440)
Mass Peaks:7 Base Peak:292.00(245124) Polarity:Pos Segment1 - Event1
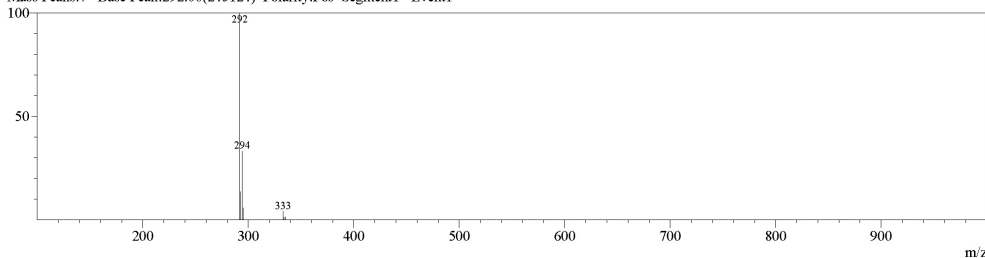
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.270<->4.560(428<->457)
Mass Peaks:7 Base Peak:292.00(245124) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	292.00	245124	100.00				5	333.10	9442	3.85			
2	293.00	33269	13.57				6	334.00	2712	1.11			
3	294.00	80877	32.99				7	335.10	3083	1.26			
4	295.00	14030	5.72										

Figure S228 LCMS spectrum of compound NPD-3295

PC-55/1

¹H NMR (300 MHz, Chloroform-*d*) δ 8.38 (d, *J* = 9.1 Hz, 1H), 8.21 (s, 1H), 7.51 – 7.45 (m, 1H), 7.42 (d, *J* = 6.6 Hz, 2H), 7.10 (dt, *J* = 6.5, 2.5 Hz, 1H), 6.98 (d, *J* = 2.8 Hz, 1H), 6.89 (dd, *J* = 9.1, 2.8 Hz, 1H), 3.89 (s, 3H), 3.81 (s, 3H).

I (d) 8.38	G (m) 7.47	D (d) 6.98	B (s) 3.89
H (s) 8.21	F (d) 7.42	C (dd) 6.89	A (s) 3.81
		E (dt) 7.10	
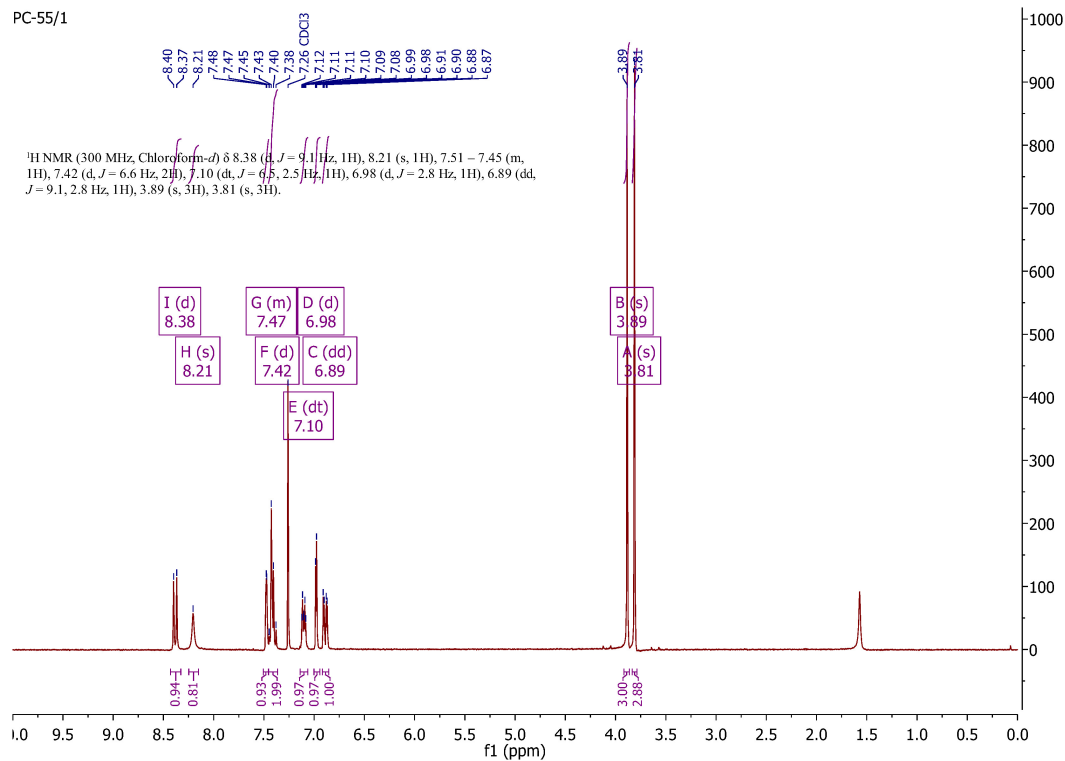
Figure S229 ¹H NMR spectrum of compound NPD-3295

PC-055/2

¹³C NMR (151 MHz, CDCl₃) δ 165.2, 160.2, 156.5, 136.4, 130.0, 128.2, 124.4, 123.1, 118.8, 118.3, 114.7, 113.5, 112.7, 55.9, 55.6.

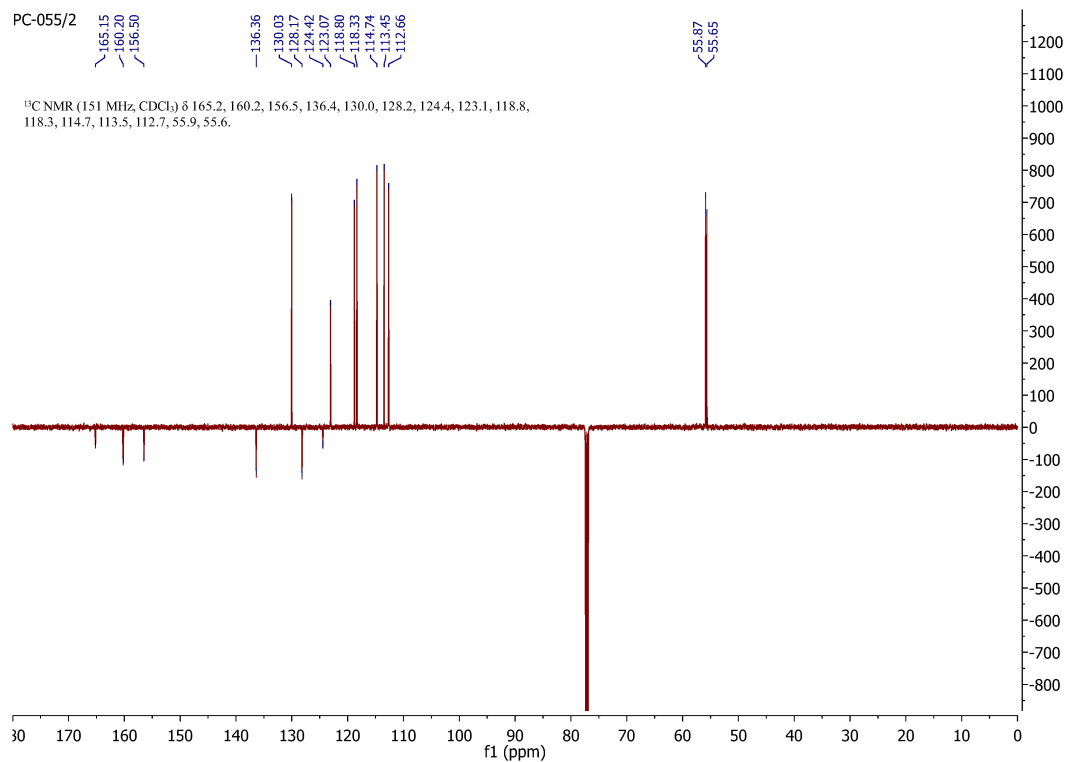**Figure S230 ¹³C NMR spectrum of compound NPD-3295**

188

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Date Acquired : 26/2/2018 10:28:00 AM
Sample Name : PC-162
Sample ID :
Tray# : 1
Vial# : 4
Injection Volume : 1
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Background File : Blanco_26022018.lcd
Method File : Method SCAN ACID standard.lcm
Report Format : DefaultLCMS.lcr
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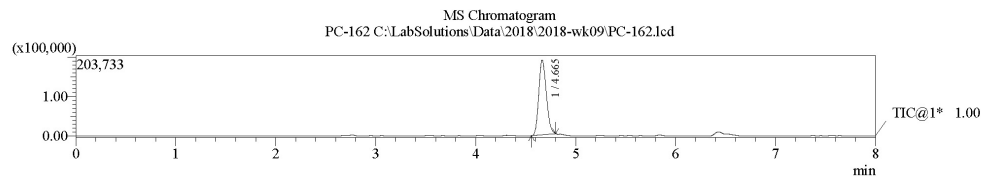Processed by : Admin
Modified Date : 26/2/2018 10:43:14 AM

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Chromatogram
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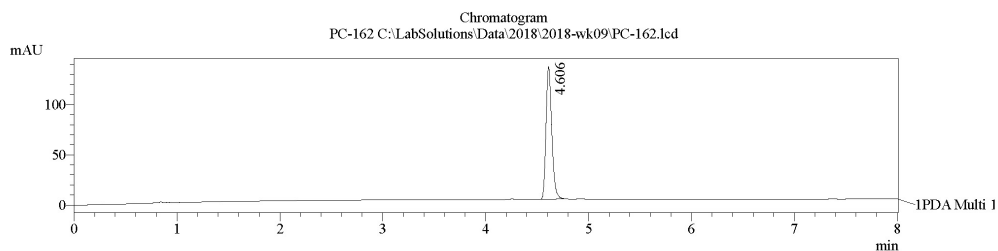
1 PDA Multi 1 / 254nm 4nm
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.606	514067	100.000

MS Chromatogram
PC-162 C:\LabSolutions\Data\2018\2018-wk09\PC-162.lcd

#:1 Ret.Time:Averaged 4.660-4.680(Scan#:467-469)
Mass Peaks:8   Base Peak:306.05(112146) Polarity:Pos Segment1 - Event1

MS Spectrum Graph
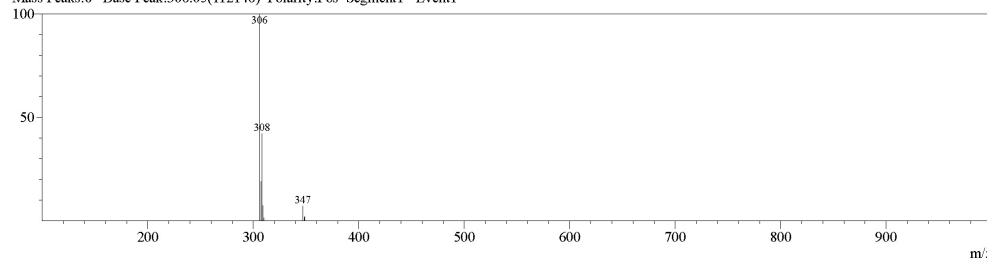
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.560<->4.800(457<->481)
Mass Peaks:8   Base Peak:306.05(112146) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	306.05	112146	100.00				5	310.05	1551	1.38			
2	307.05	21393	19.08				6	347.15	8050	7.18			
3	308.05	47234	42.12				7	348.20	1764	1.57			
4	309.05	8193	7.31				8	349.00	2376	2.12			

Figure S231 LCMS spectrum of compound NPD-3296

189

PC-056/1

¹H NMR (300 MHz, Chloroform-*d*) δ 7.71 (s, 1H), 7.68 (d, *J* = 2.6 Hz, 1H), 7.49 (dd, *J* = 8.9, 2.6 Hz, 1H), 7.44 – 7.40 (m, 1H), 7.40 – 7.33 (m, 2H), 7.08 (dt, *J* = 7.0, 2.5 Hz, 1H), 6.92 (d, *J* = 8.9 Hz, 1H), 4.11 (q, *J* = 7.0 Hz, 2H), 3.87 (s, 3H), 1.47 (t, *J* = 7.0 Hz, 3H).

E (m) 7.37
F (s) 7.71
B (dt) 7.08
I (s) 3.87
C (dd) 7.49
A (d) 6.92
H (q) 4.11
J (t) 1.47
D (m) 7.42
G (d) 7.68
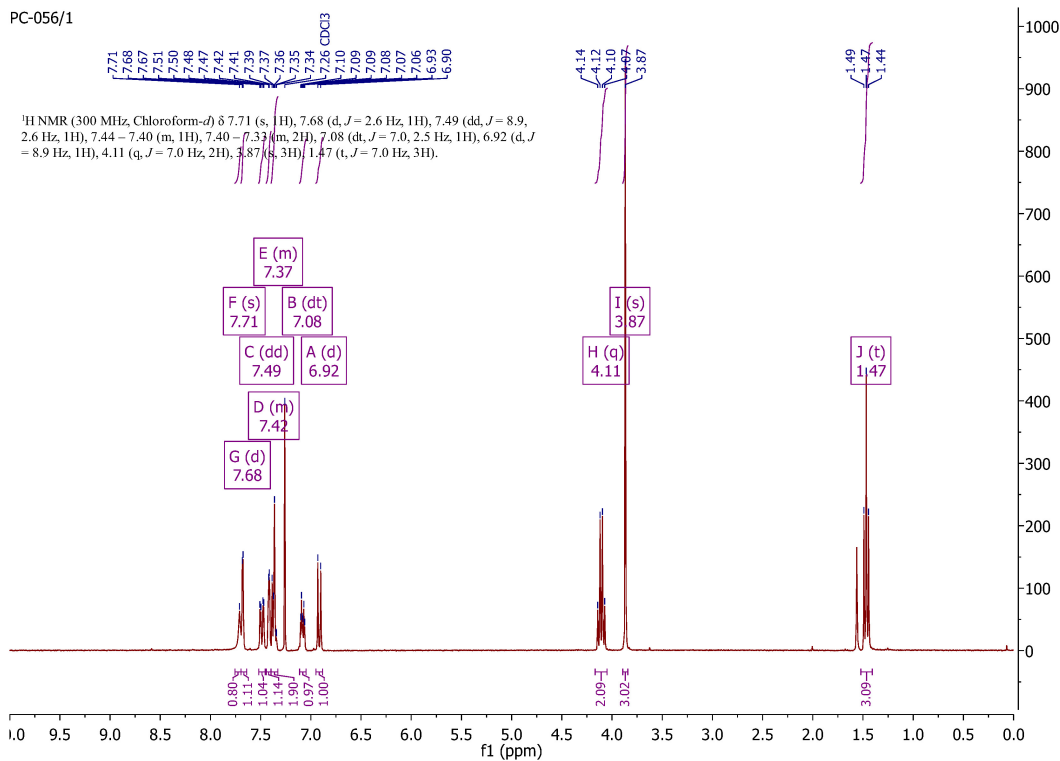
Figure S232 ¹H NMR spectrum of compound NPD-3296

PC-056/2

¹³C NMR (151 MHz, CDCl₃) δ 165.6, 160.1, 151.7, 136.3, 131.5, 129.9, 123.3, 122.9, 120.1, 118.7, 118.2, 113.9, 112.6, 65.3, 55.6, 14.9.
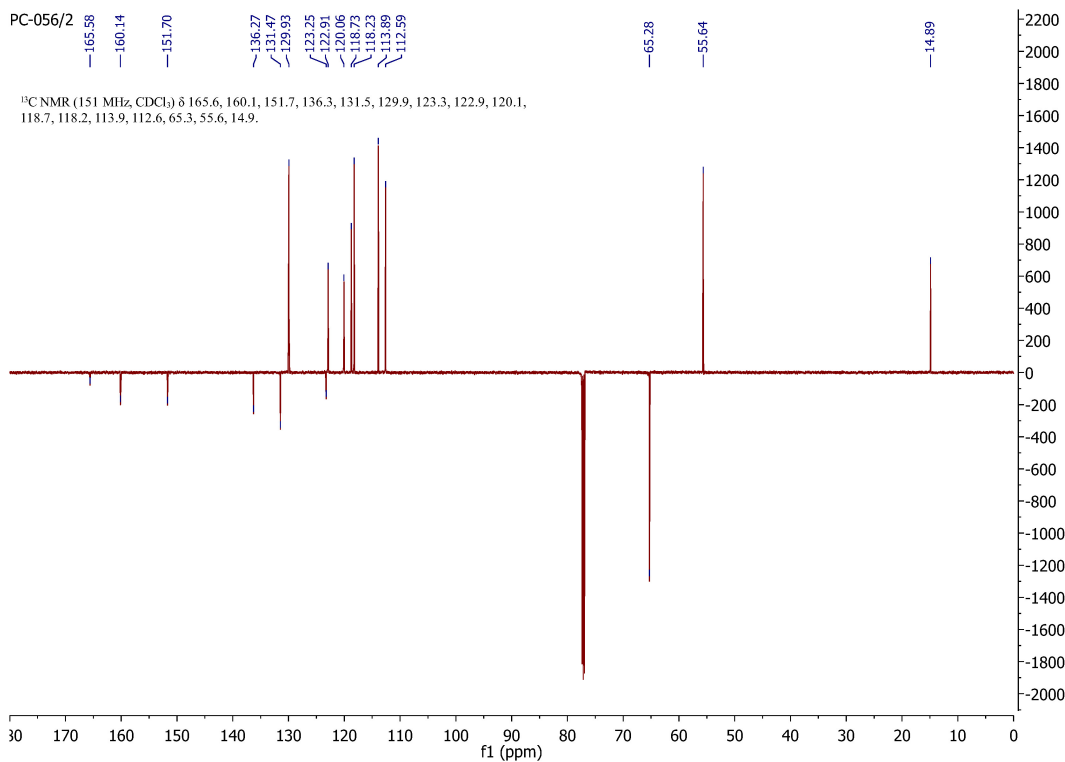
Figure S233 ¹³C NMR spectrum of compound NPD-3296

190

PDA Graph
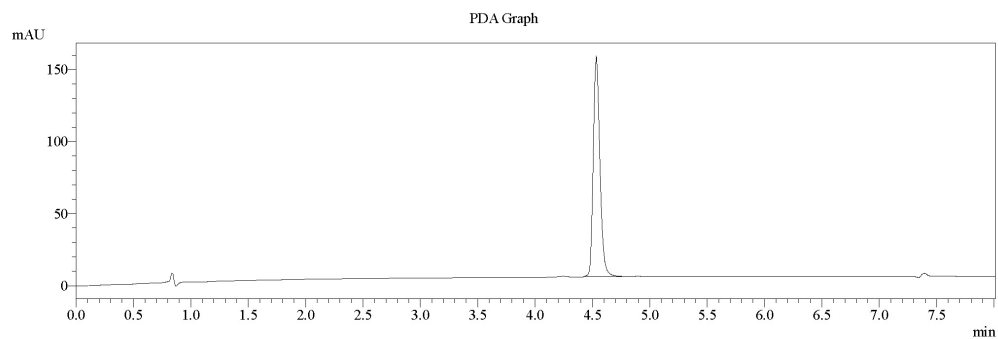
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.528	608948	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.570-4.590(Scan#:458-460)
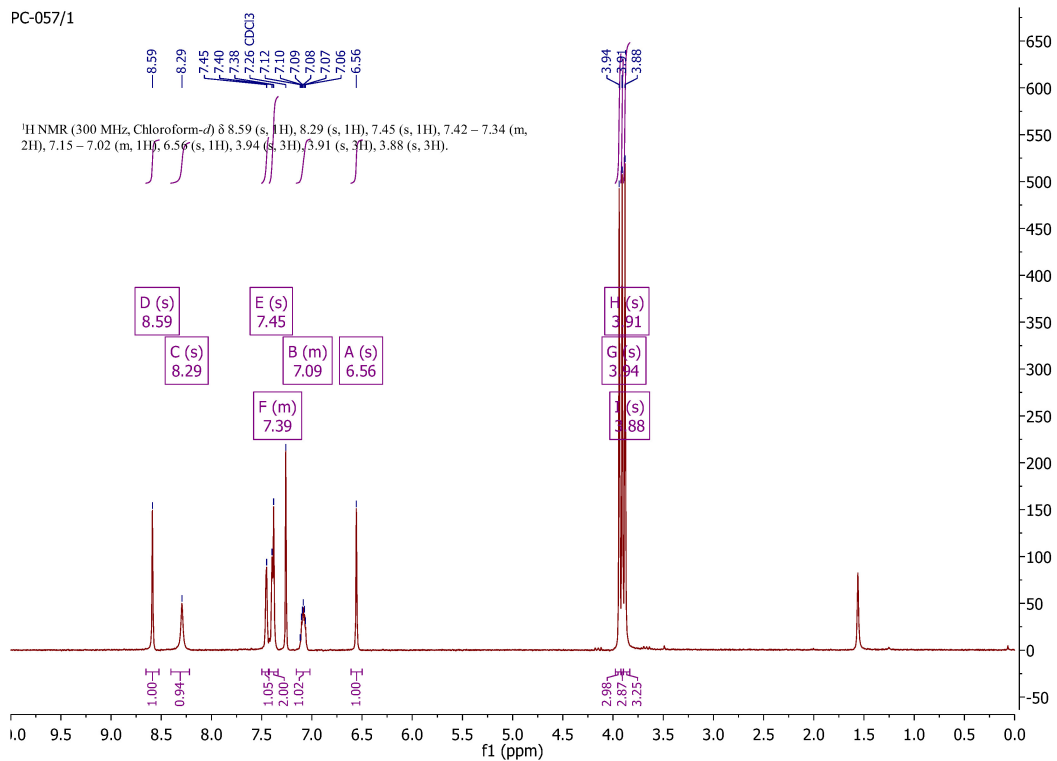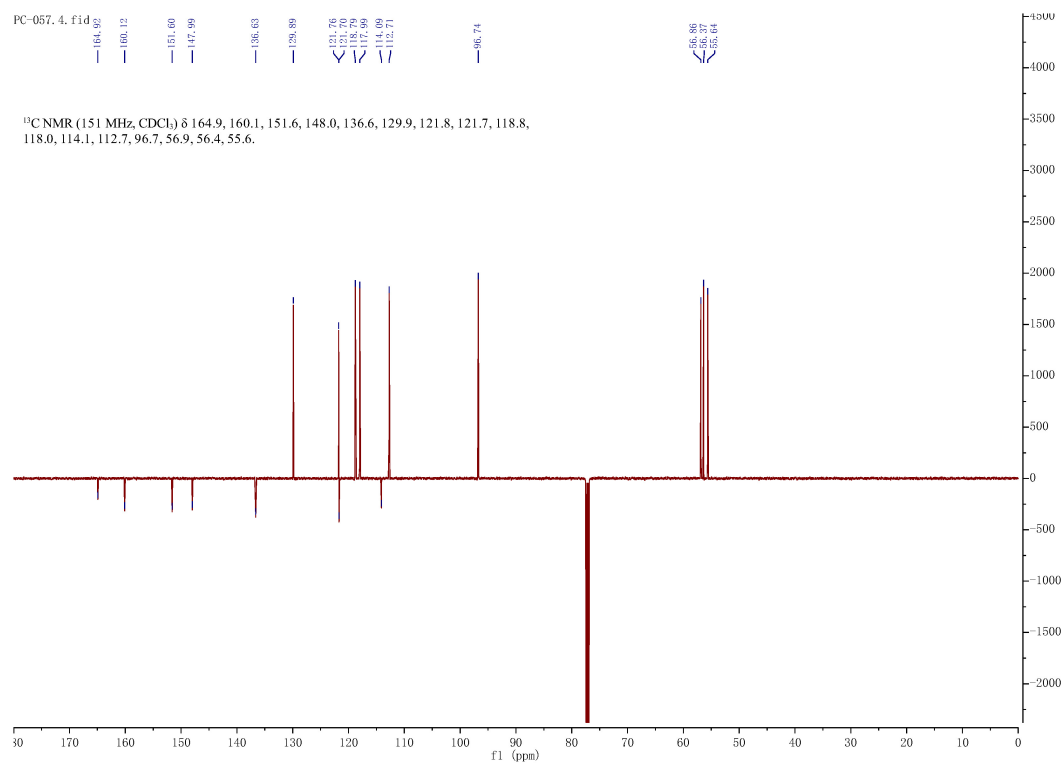Mass Peaks:5 Base Peak:322.00(238263) Polarity:Pos Segment1 - Event1
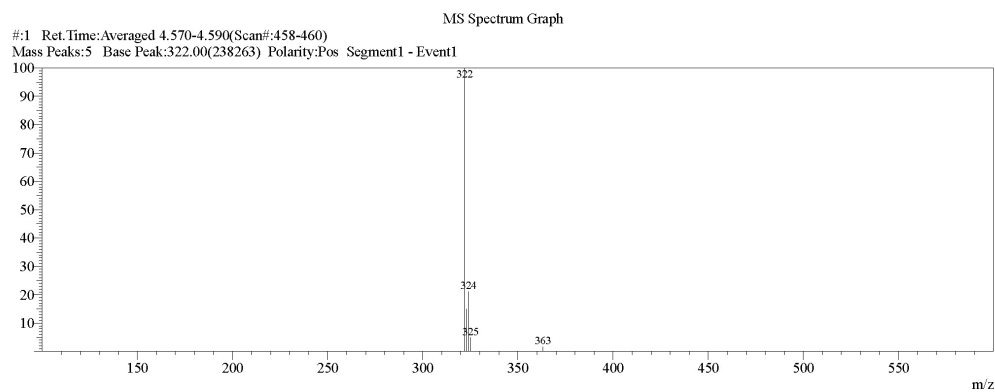
MS Spectrum Table

#:1   Ret.Time:
BG Mode:Calc 4.470<->4.740(448<->475)
Mass Peaks:5 Base Peak:322.00(238263) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	322.00	238263	100.00				4	325.05	11620	4.88			
2	323.10	35687	14.98				5	363.05	4028	1.69			
3	324.05	50159	21.05										

Figure S234 LCMS spectrum of compound NPD-3297

191

PC-057/1

D (s)
8.59

E (s)
7.45

H (s)
3.91

C (s)
8.29

B (m)
7.09

A (s)
6.56

G (s)
3.94

F (m)
7.39

I (s)
3.88

Figure S235 ^{1}H NMR spectrum of compound NPD-3297

PC-057.4.fid

Figure S236 ^{13}C NMR spectrum of compound NPD-3297

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.735	787463	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.790-4.810(Scan#:480-482)
Mass Peaks:12   Base Peak:290.00(138269) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.690<->4.930(470<->494)
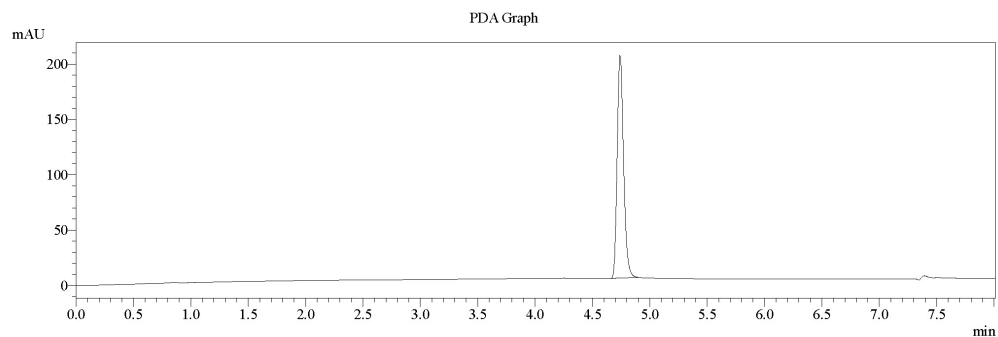Mass Peaks:12   Base Peak:290.00(138269) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	290.00	138269	100.00				7	333.15	2105	1.52			
2	291.05	29704	21.48				8	567.40	3766	2.72			
3	292.10	46657	33.74				9	568.50	2826	2.04			
4	293.10	8236	5.96				10	569.45	1539	1.11			
5	331.00	6970	5.04				11	688.20	1420	1.03			
6	332.00	1636	1.18				12	690.25	2169	1.57			

Figure S237 LCMS spectrum of compound NPD-3298

193

PC-058/1

H (d) 7.77	F (d) 7.31
B (dd) 7.52	A (d) 6.92
G (d) 7.69	

E (s) 3.90

C (q) 2.72

D (t) 1.27
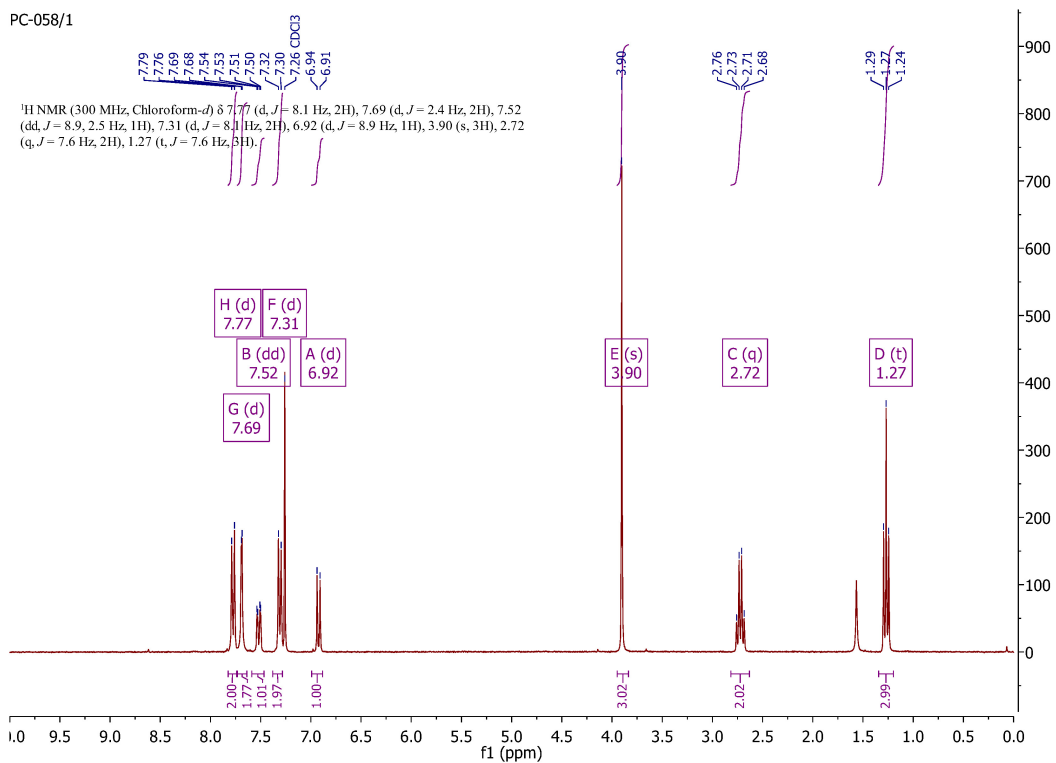
Figure S238 ¹H NMR spectrum of compound NPD-3298

PC-058/2

Figure S239 ¹³C NMR spectrum of compound NPD-3298

PDA Graph
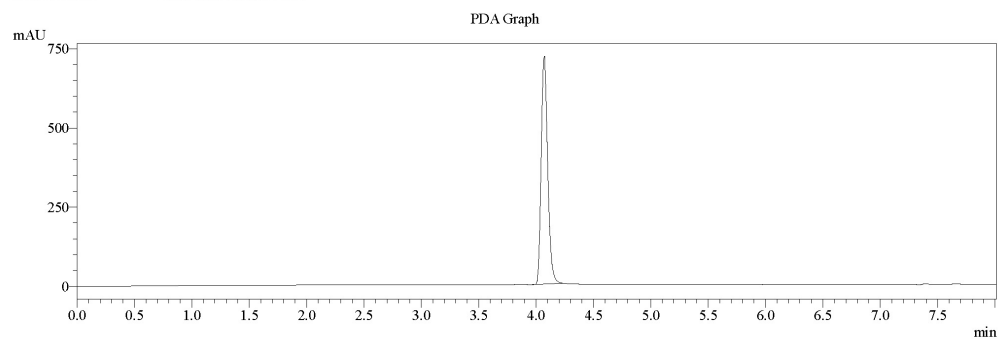
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.065	2796959	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.120-4.140(Scan#:413-415)
Mass Peaks:6 Base Peak:322.05(298138) Polarity:Pos Segment1 - Event1
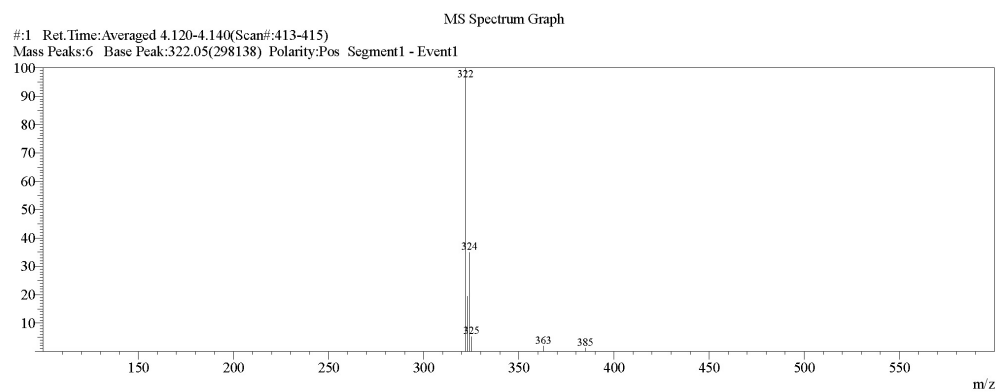
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.020<->4.310(403<->432)
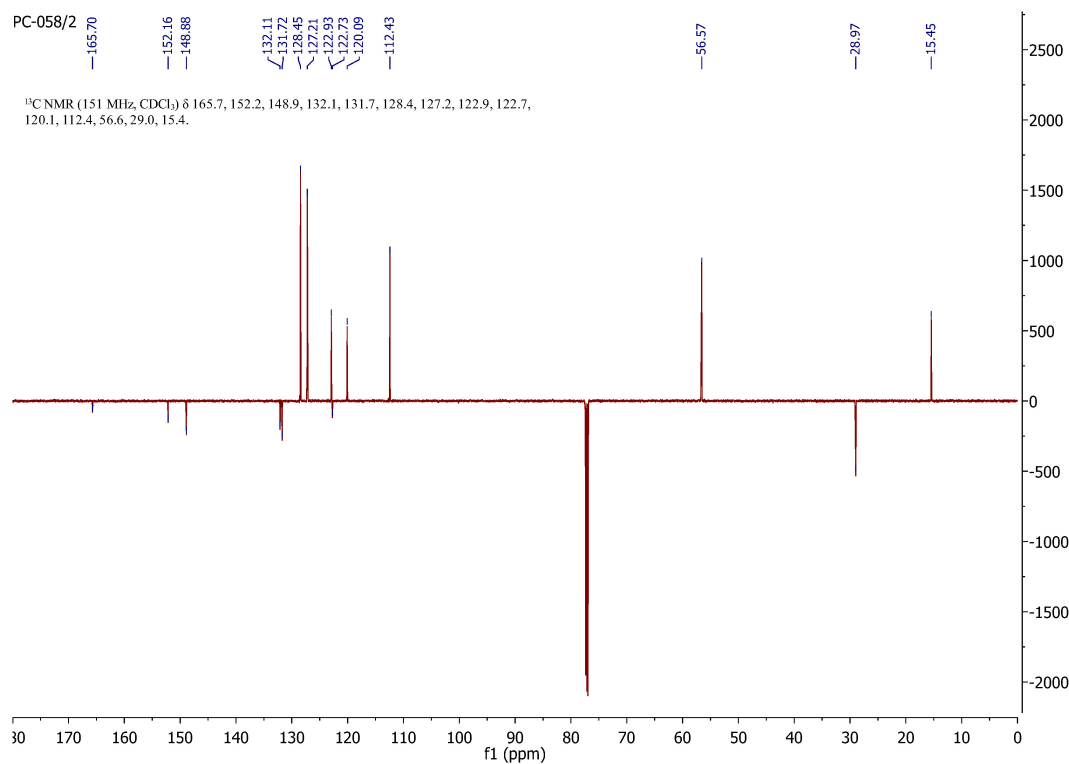Mass Peaks:6 Base Peak:322.05(298138) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	322.05	298138	100.00				4	325.05	15475	5.19			
2	323.05	57859	19.41				5	363.05	5473	1.84			
3	324.05	104210	34.95				6	384.95	3319	1.11			

Figure S240 LCMS spectrum of compound NPD-3299

PC-059/1

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.70 (s, 1H), 7.67 (d, *J* = 2.6 Hz, 1H), 7.52 (dd, *J* = 8.8, 2.6 Hz, 1H), 7.48 (d, *J* = 2.0 Hz, 1H), 7.37 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.95 – 6.87 (m, 2H), 3.95 (s, 6H), 3.90 (s, 3H).

G (s)
7.70

D (dd)
7.37

E (dd)
7.52

C (m)
6.91

F (d)
7.48

H (d)
7.67

B (s)
3.90

A (s)
3.95

Figure S241 ^{1}H NMR spectrum of compound NPD-3299

PC-059/2

^{13}C NMR (151 MHz, CDCl$_3$) δ 165.3, 152.3, 152.1, 149.4, 131.7, 127.3, 123.0, 122.7, 120.1, 119.5, 112.4, 110.8, 110.5, 56.6, 56.2.

Figure S242 ^{13}C NMR spectrum of compound NPD-3299

PDA Graph

mAU

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.515	752916	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.570-4.590(Scan#:458-460)
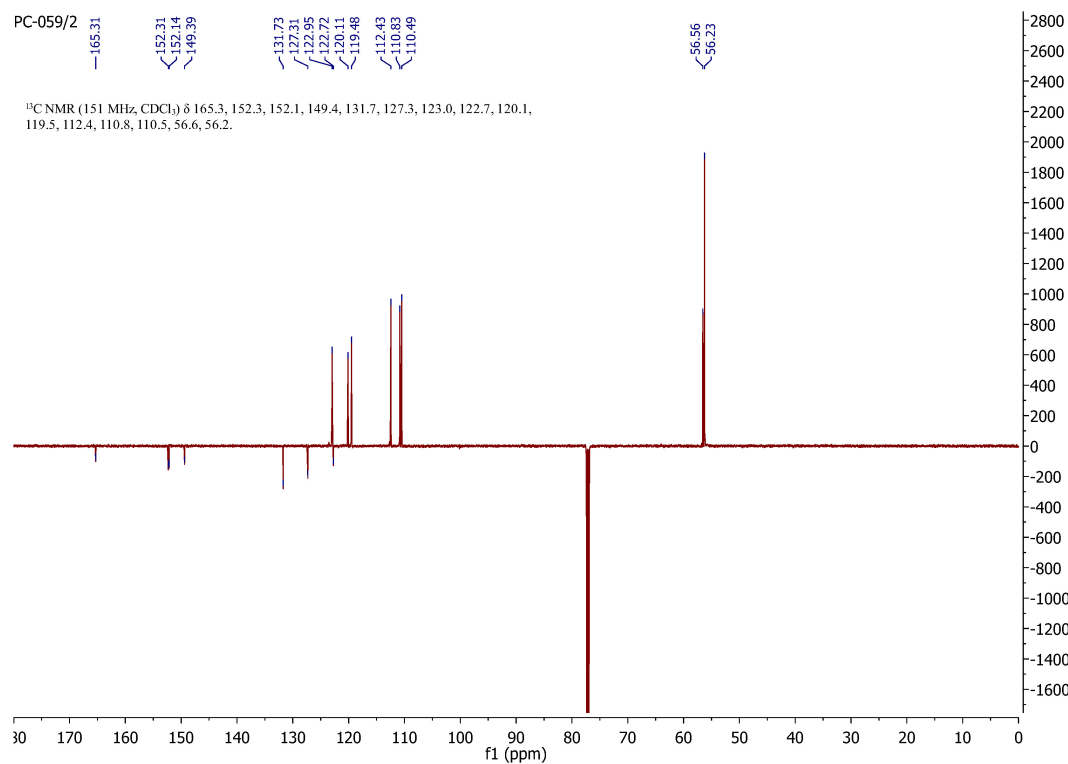Mass Peaks:5   Base Peak:306.00(133343) Polarity:Pos Segment1 - Event1
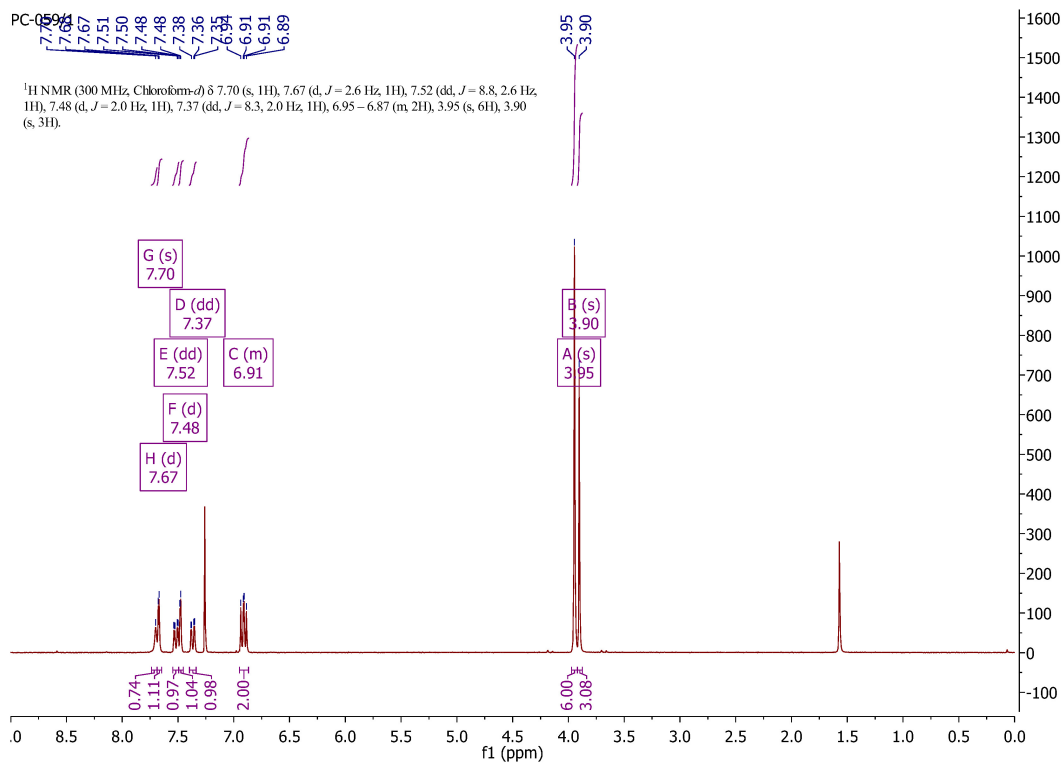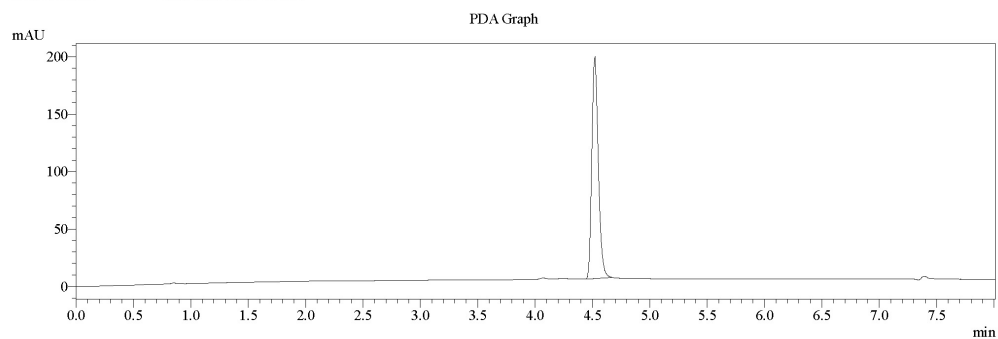
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.470<->4.710(448<->472)
Mass Peaks:5   Base Peak:306.00(133343) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	306.00	133343	100.00				4	309.05	7035	5.28			
2	307.05	23782	17.84				5	310.05	1413	1.06			
3	308.05	43538	32.65										

Figure S243 LCMS spectrum of compound NPD-3300

197

PC-060/1

F (m)
7.67

E (dd)
7.50

D (m)
6.93

C (s)
3.90

B (q)
4.10

A (t)
1.45

G (d)
7.81
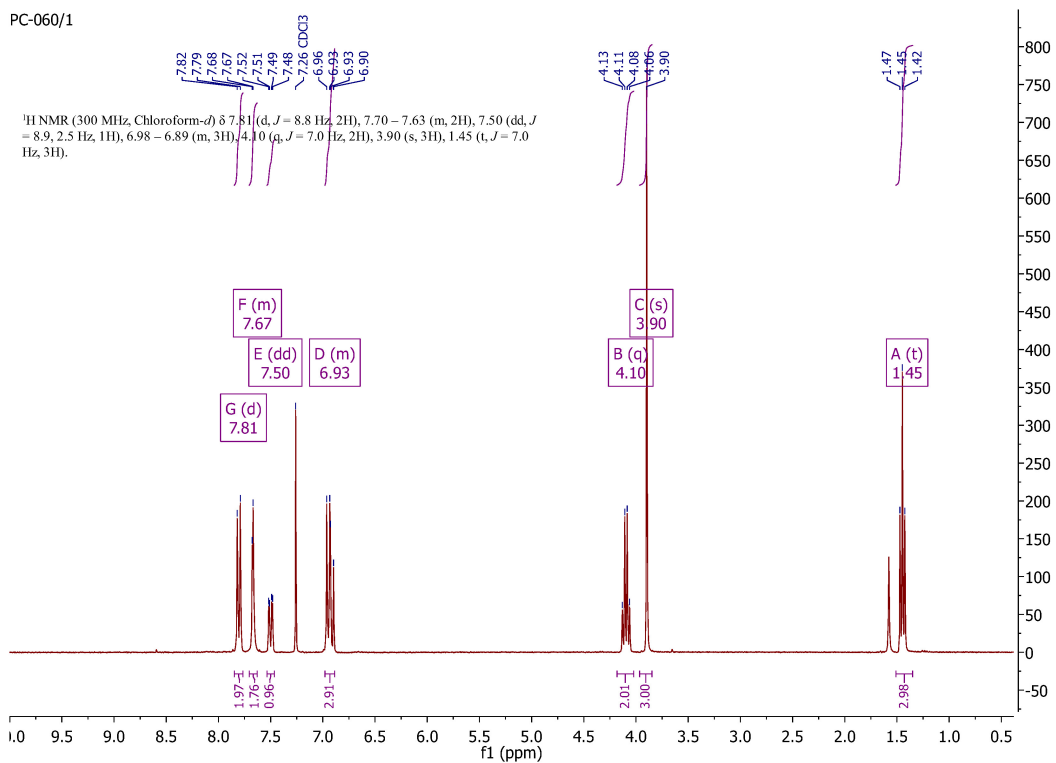
Figure S244 ¹H NMR spectrum of compound NPD-3300

PC-060/2
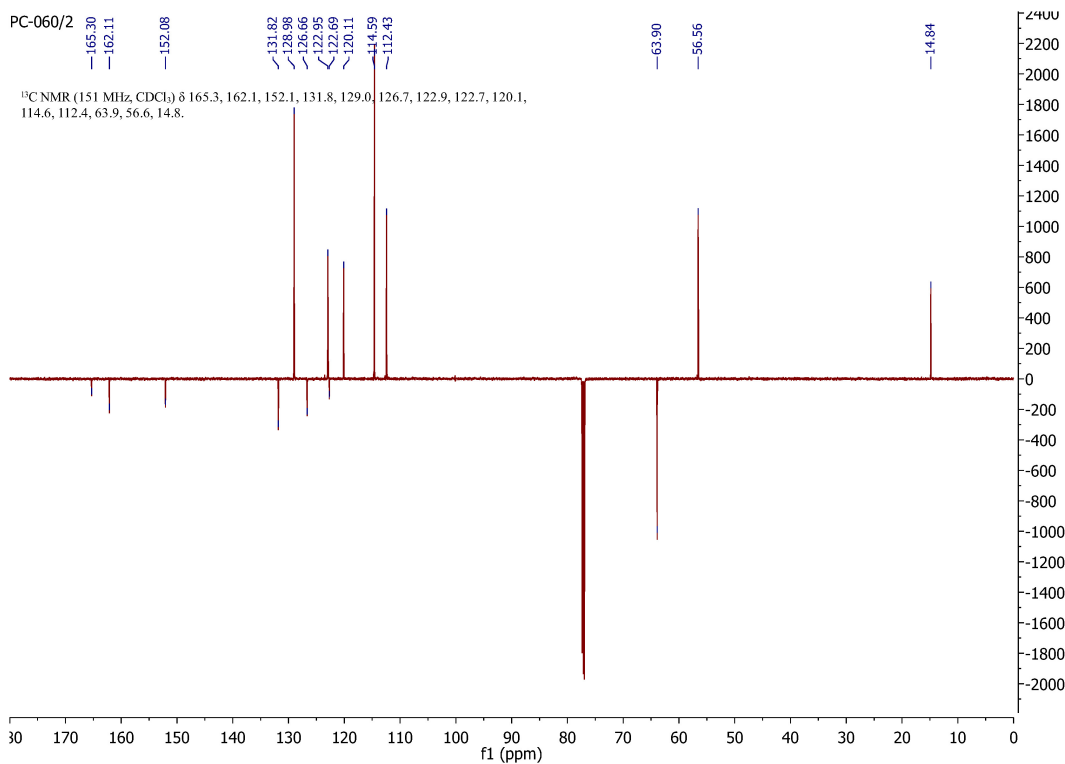
Figure S245 ¹³C NMR spectrum of compound NPD-3300

198

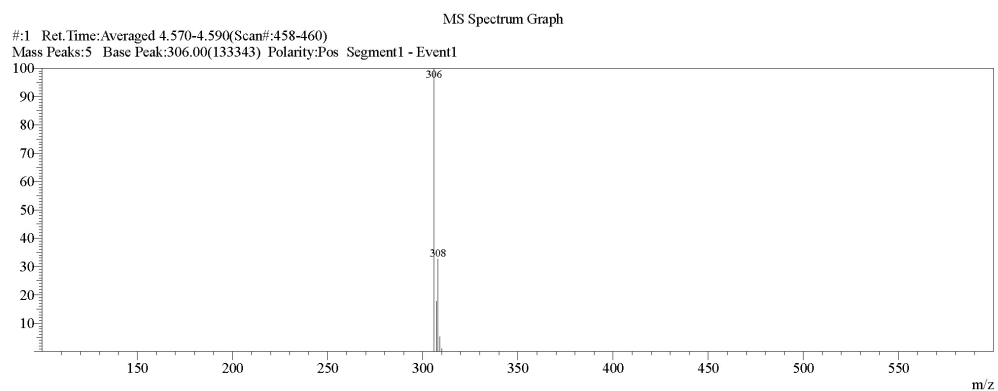Acquired by   : Admin
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Method File   : Method SCAN ACID standard.lcm
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PDA Graph
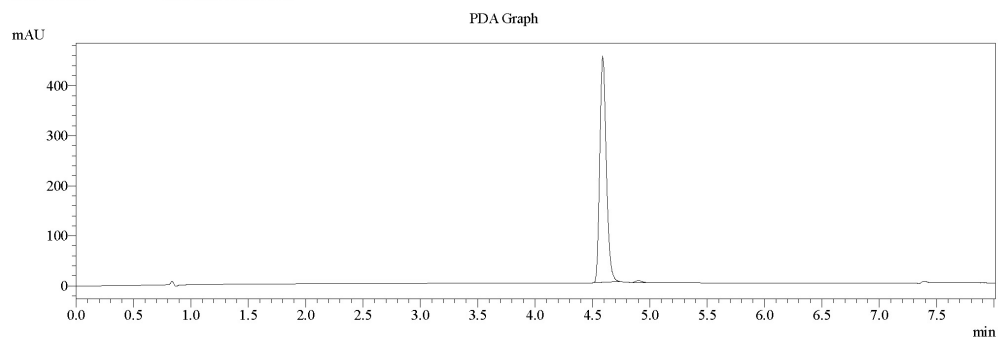
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.585	1795958	99.263
2		4.895	13330	0.737

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.630-4.650(Scan#:464-466)
Mass Peaks:9 Base Peak:322.05(295796) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.530<->4.810(454<->482)
Mass Peaks:9 Base Peak:322.05(295796) Polarity:Pos Segment1 - Event1

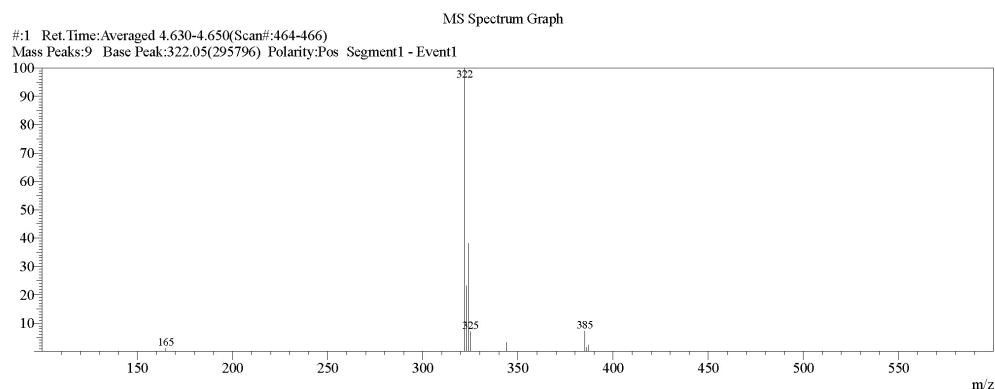| #	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	164.95	3424	1.16				6	344.05	9240	3.12			
2	322.05	295796	100.00				7	385.05	21226	7.18			
3	323.00	68808	23.26				8	386.15	4237	1.43			
4	323.95	112837	38.15				9	387.15	6883	2.33			
5	325.05	20903	7.07										

Figure S246 LCMS spectrum of compound NPD-3301

199

PC-061/1

9.59

8.26
8.23

7.67
7.66
7.61
7.60
7.26 CDCl3
6.92
6.89
6.67
6.66
6.64
6.63
6.54
6.53

4.03
3.90
3.88

^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.59 (s, 1H), 8.24 (d, *J* = 8.8 Hz, 1H), 7.67 (d, *J* = 2.5 Hz, 1H), 7.60 (d, *J* = 2.4 Hz, 1H), 6.91 (d, 1H), 6.65 (dd, *J* = 8.8, 2.3 Hz, 1H), 6.53 (d, *J* = 2.1 Hz, 1H), 4.03 (s, 3H), 3.90 (s, 3H), 3.88 (s, 3H).

| G (s) | | A (d) | B (d) | C (d) | D (d) | E (dd) | F (d) | H (s) | I (s) | J (s) |
| 9.59 | | 8.24 | 7.67 | 7.60 | 6.91 | 6.65 | 6.53 | 4.03 | 3.90 | 3.88 |

0.91

1.00

0.97
1.01

1.02
0.99
0.98

2.86
2.86
3.04

f1 (ppm)
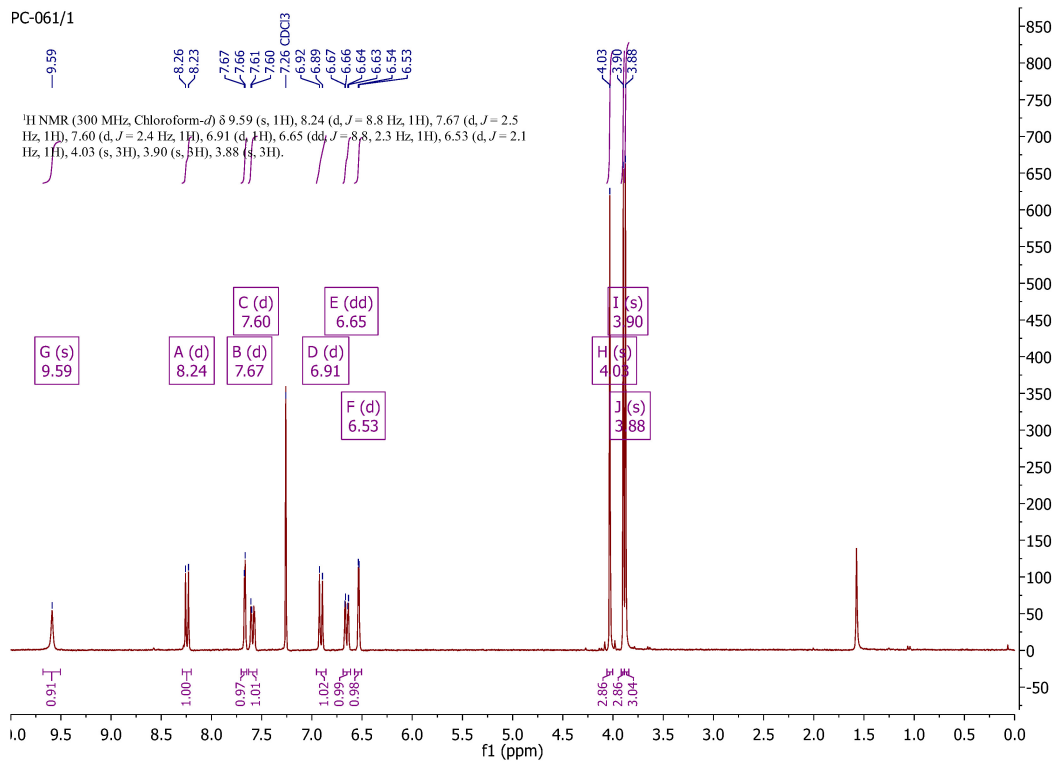
Figure S247 ^{1}H NMR spectrum of compound NPD-3301

PC-061/2

^{13}C NMR (75 MHz, CDCl₃) δ 164.0, 158.5, 132.4, 122.9, 122.5, 120.1, 114.6, 112.4, 105.9, 98.9, 56.6, 56.4, 55.8

56.58
56.38
55.75

f1 (ppm)
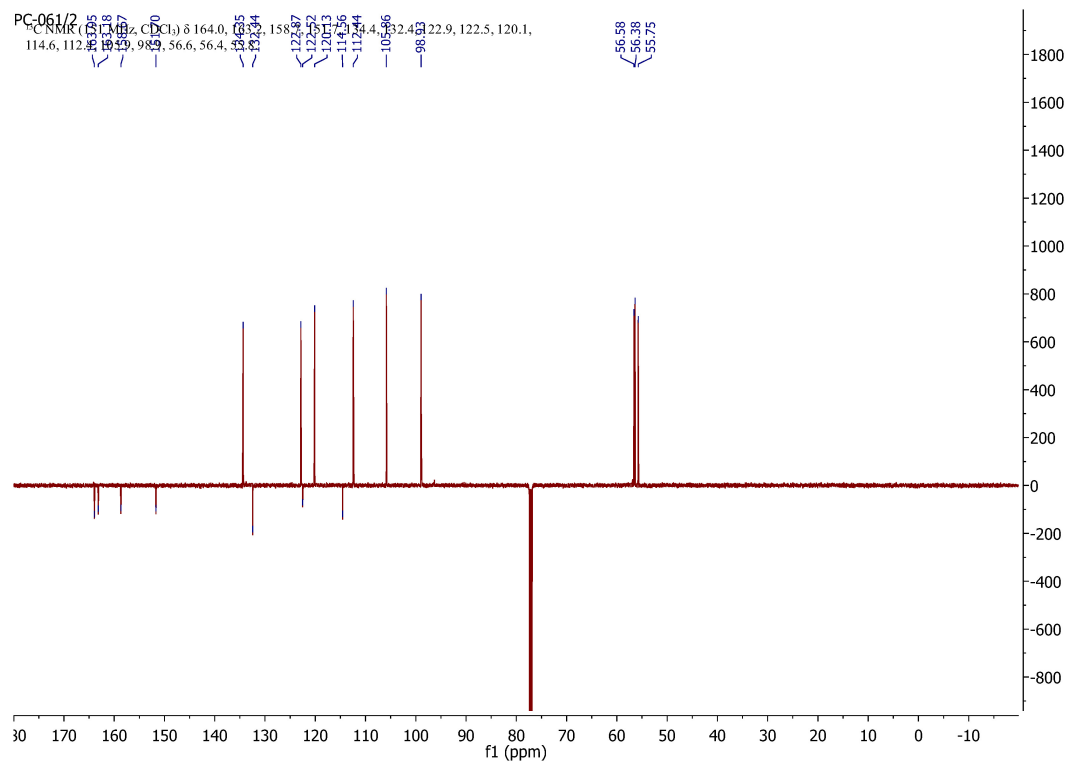
Figure S248 ^{13}C NMR spectrum of compound NPD-3301

PDA Graph

PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.860	1917737	100.000

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.910-4.930(Scan#:492-494)
Mass Peaks:8 Base Peak:346.00(57689) Polarity:Pos Segment1 - Event1
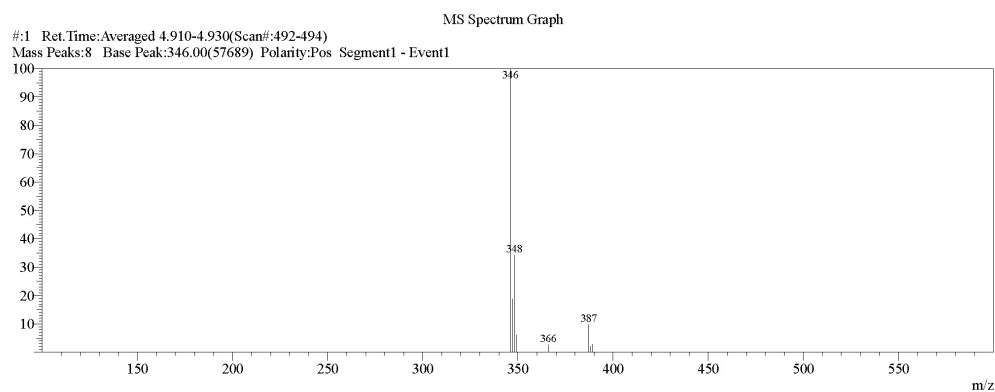
MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.810<->5.090(482<->510)
Mass Peaks:8 Base Peak:346.00(57689) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	346.00	57689	100.00				5	366.05	1538	2.67			
2	347.05	10904	18.90				6	387.10	5665	9.82			
3	348.00	19782	34.29				7	388.00	1231	2.13			
4	349.05	3498	6.06				8	389.15	1638	2.84			

Figure S249 LCMS spectrum of compound NPD-3302

201

PC-062/1

7.91
7.88
7.74
7.67
7.66
7.51
7.50
7.48
7.47
7.32
7.30
7.26 CDCl3
6.93
6.90

3.90

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 8.7 Hz, 2H), 7.74 (s, 1H), 7.67 (d, *J* = 2.4 Hz, 1H), 7.49 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 8.9 Hz, 1H), 3.90 (s, 3H).

| E (s) |
| 7.74 |

| F (d) | | B (d) |
| 7.89 | | 7.31 |

| | C (dd) | | A (d) | | G (s) |
| | 7.49 | | 6.92 | | 3.90 |

| D (d) |
| 7.67 |

2.02
0.88
0.99
1.00
1.99
1.00

3.05

f1 (ppm)
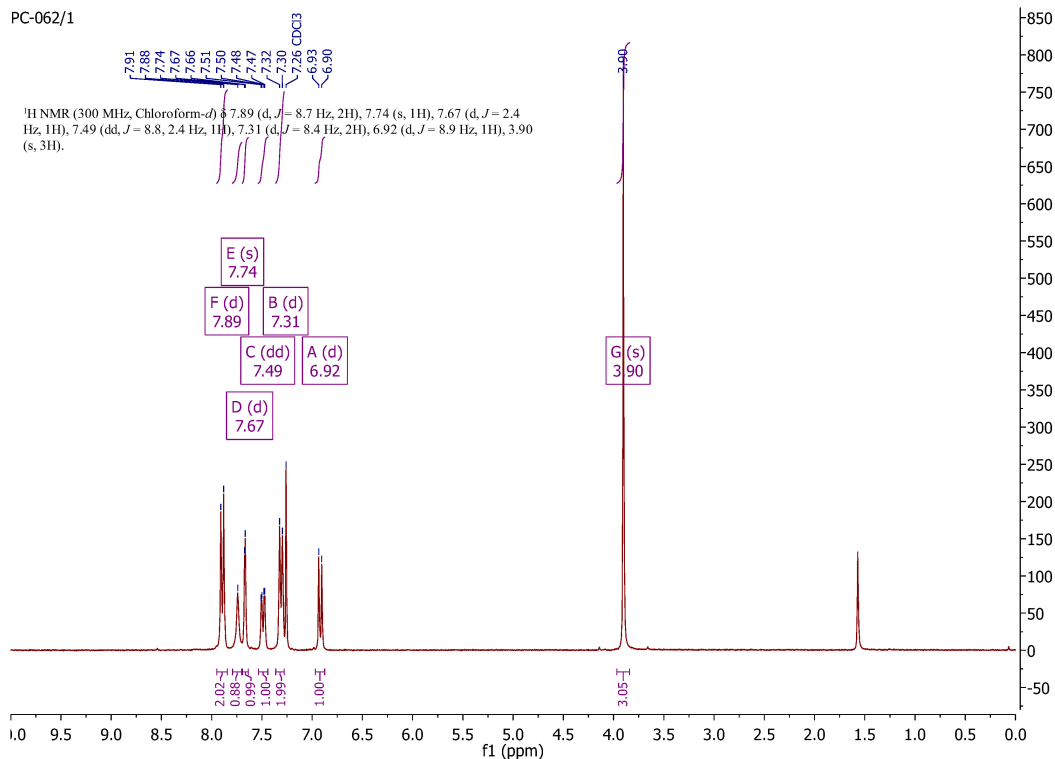
Figure S250 ^{1}H NMR spectrum of compound NPD-3302

PC-062/7

164.29
152.36
151.79
133.05
131.06
128.92
122.96
122.73
121.17
120.87
120.11
119.46
112.29
56.43

^{13}C NMR (151 MHz, Chloroform-*d*) δ 164.3 , 152.4 , 151.8 , 133.1 , 131.1 , 128.9 , 123.0 , 122.7 , 120.9 , 120.1 , 119.5 (q, *J* = 260.4 Hz), 112.3 , 56.4 .

f1 (ppm)
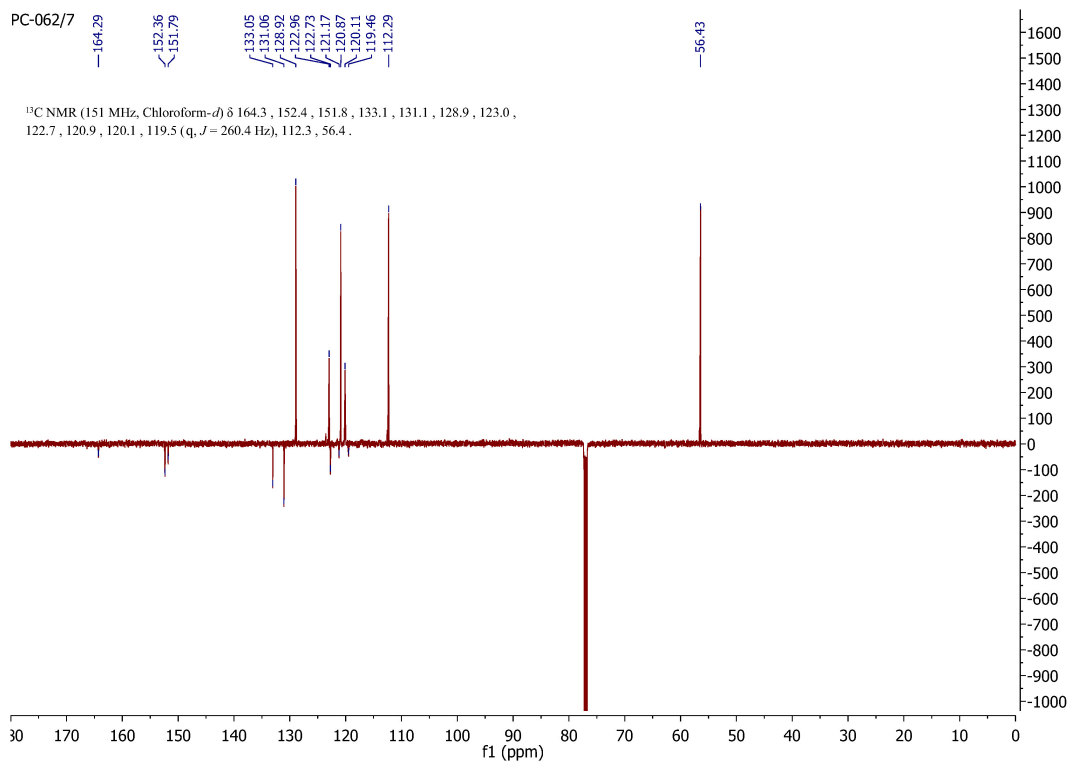
Figure S251 ^{13}C NMR spectrum of compound NPD-3302

202

Medicinal Chemistry
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Chromatogram
PC-170-3 C:\LabSolutions\Data\2018\2018-wk09\PC-170-3.lcd

1   PDA Multi 1 / 254nm 4nm

PeakTable

PDA Ch1 254nm 4nm
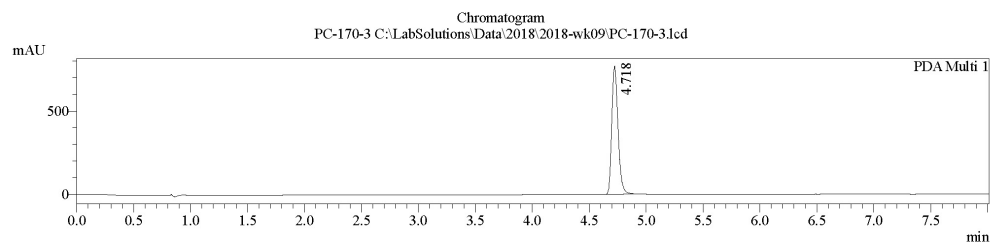
Peak#	Name	Ret. Time	Area	Area %
1		4.718	2912045	100.000

MS Chromatogram
PC-170-3 C:\LabSolutions\Data\2018\2018-wk09\PC-170-3.lcd

MS Spectrum Graph

#:1 Ret.Time:Averaged 4.780-4.800(Scan#:479-481)
Mass Peaks:6   Base Peak:320.05(355884) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:Calc 4.670<->4.990(468<->500)
Mass Peaks:6   Base Peak:320.05(355884) Polarity:Pos Segment1 - Event1
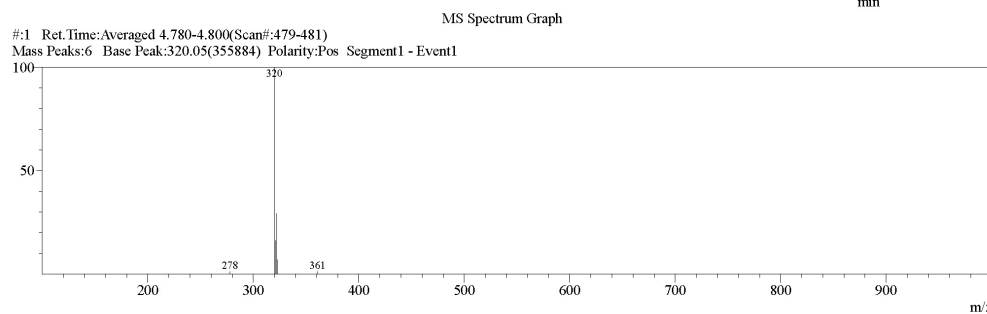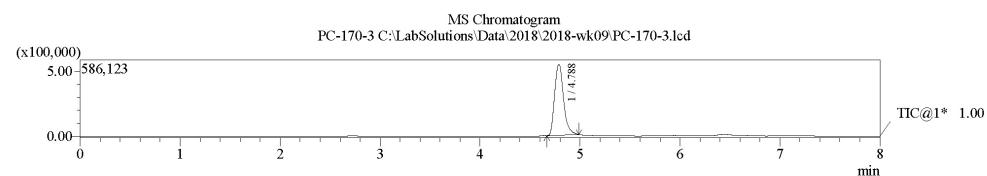
#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	278.00	4713	1.32				4	322.05	104423	29.34			
2	320.05	355884	100.00				5	323.05	24296	6.83			
3	321.05	57697	16.21				6	361.15	4157	1.17			

Figure S252 LCMS spectrum of compound NPD-3303

203

PC-063/1

7.81
7.78
7.68
7.67
7.63
7.52
7.51
7.49
7.48
CDCl3
7.26
6.96
6.93
6.90
4.70
4.68
4.66
4.64
4.62
4.60
4.58
3.90
1.38
1.36

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.80 (d, *J* = 8.8 Hz, 2H), 7.68 (d, *J* = 2.5 Hz, 1H), 7.63 (s, 1H), 7.50 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.98 – 6.89 (m, 3H), 4.64 (hept, *J* = 6.1 Hz, 1H), 3.90 (s, 3H), 1.37 (d, *J* = 6.1 Hz, 6H).

H (d)
7.80

F (s)
7.63

E (dd)
7.50

D (m)
6.93

A (hept)
4.64

B (s)
3.90

C (d)
1.37

G (d)
7.68

1.91
0.94
0.80
0.94
2.90
1.00
2.96
5.80

f1 (ppm)
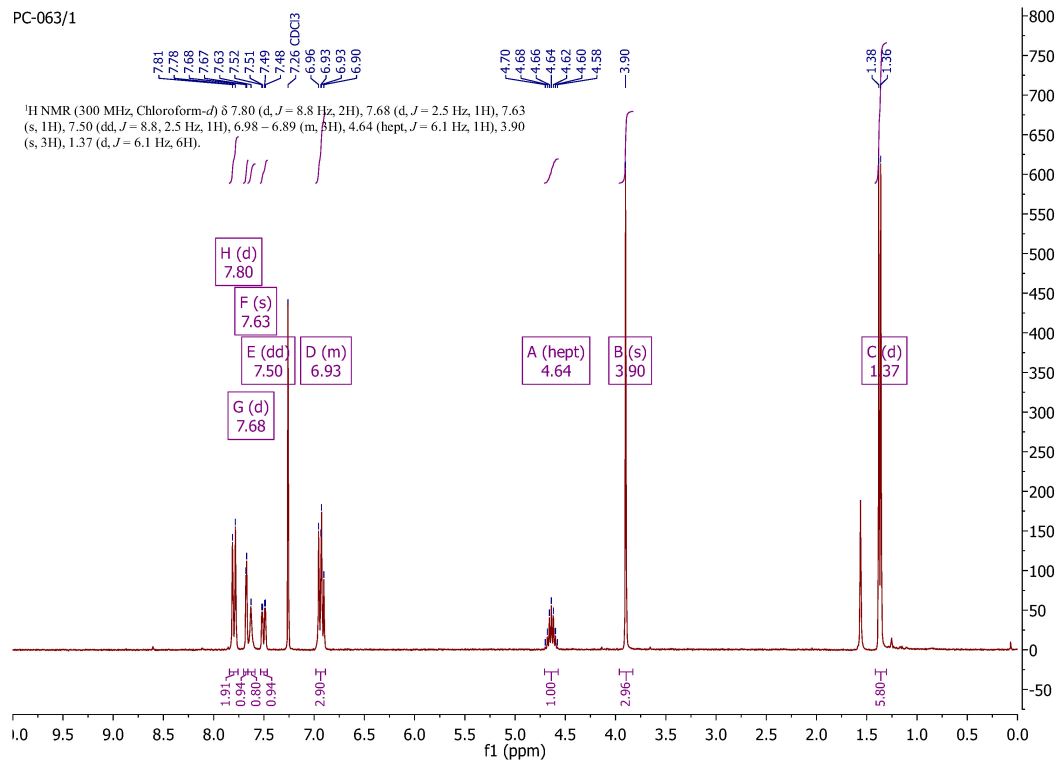
Figure S253 ^{1}H NMR spectrum of compound NPD-3303

PC-063/2

165.28
161.17
152.07
131.84
129.00
126.44
122.92
122.72
120.07
115.64
112.45
70.28
56.57
22.06

^{13}C NMR (151 MHz, CDCl₃) δ 165.3, 161.2, 152.1, 131.8, 129.0, 126.4, 122.9, 122.7, 120.1, 115.6, 112.4, 70.3, 56.6, 22.1.

f1 (ppm)
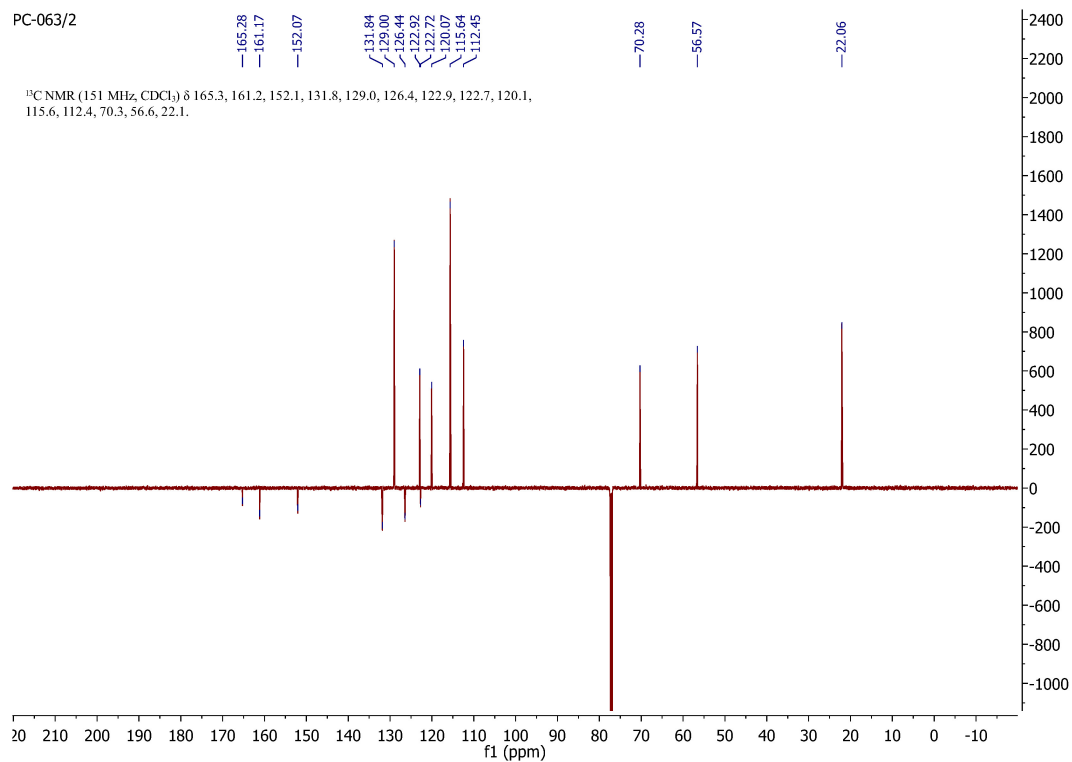
Figure S254 ^{13}C NMR spectrum of compound NPD-3303

PDA Graph

mAU
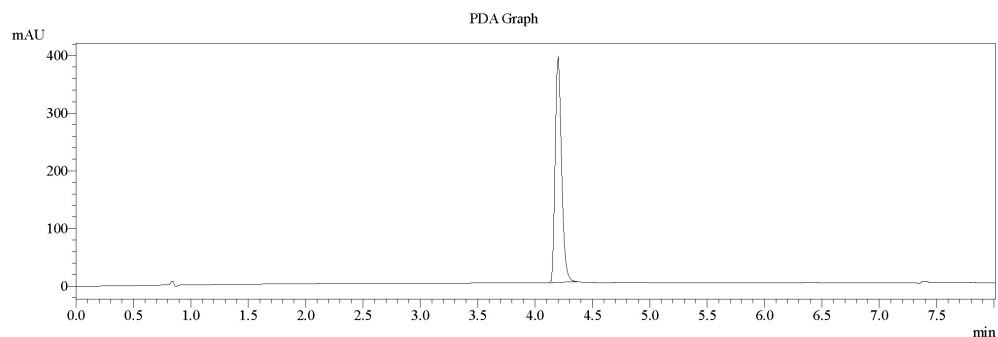
PDA Ch1 254nm 4nm

Peak#	Name	Ret. Time	Area	Area %
1		4.195	1506868	100.000
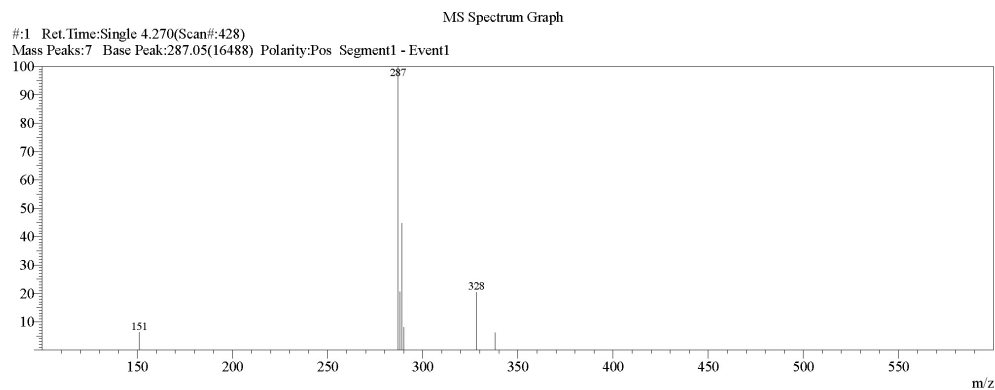
MS Spectrum Graph

#:1 Ret.Time:Single 4.270(Scan#:428)
Mass Peaks:7 Base Peak:287.05(16488) Polarity:Pos Segment1 - Event1

MS Spectrum Table

#:1 Ret.Time:
BG Mode:None
Mass Peaks:7 Base Peak:287.05(16488) Polarity:Pos Segment1 - Event1

#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic	#	m/z	Abs.Inten.	Rel.Inten.	Charge	Polarity	Monoisotopic
1	151.00	1034	6.27				5	290.00	1334	8.09			
2	287.05	16488	100.00				6	328.15	3365	20.41			
3	288.00	3385	20.53				7	338.00	1021	6.19			
4	289.15	7381	44.77										

Figure S255 LCMS spectrum of compound NPD-3304

205

PC-064/1

F (d)
7.79

D (d)
7.68

C (dd)
7.50

B (d)
6.94

A (s)
3.91

E (s)
7.75

G (d)
7.96

Figure S256 ¹H NMR spectrum of compound NPD-3304

VUF16524/2

Figure S257 ¹³C NMR spectrum of compound NPD-3304

Reference:
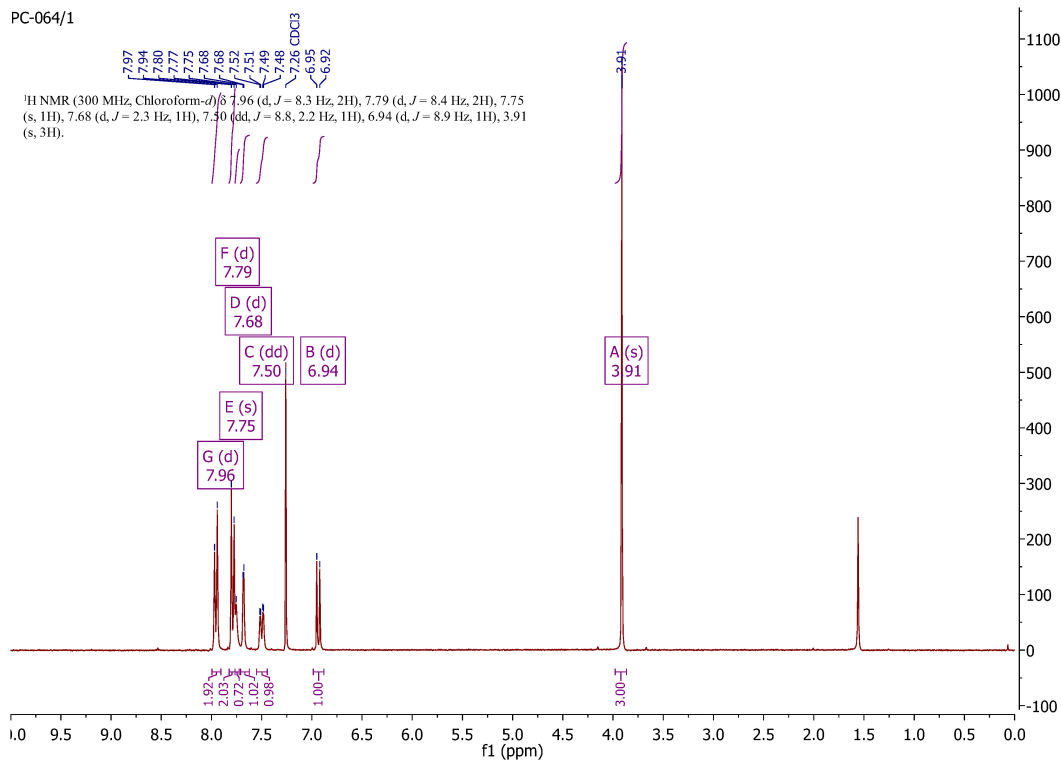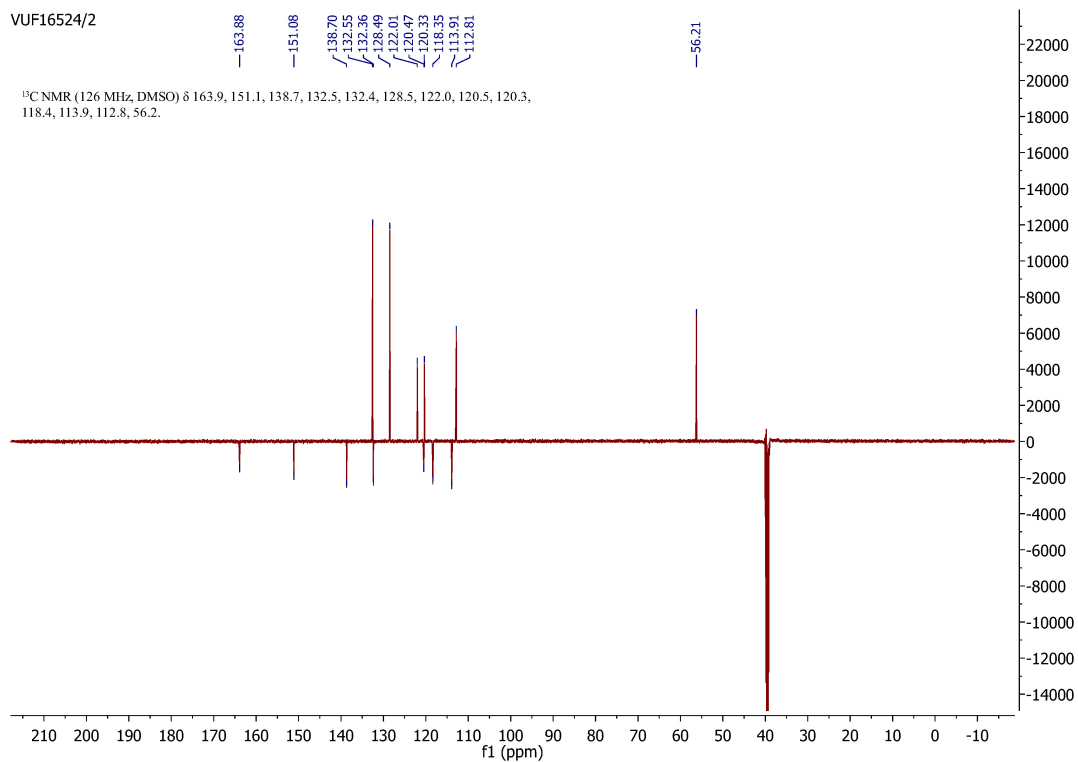
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