Highly Enantioselective Asymmetric Transfer Hydrogenation （ATH）of α-Phthalimide Ketone†

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Supporting Information

Contents

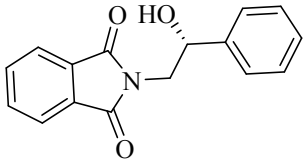
1. General information

Unless stated otherwise, all reactions were carried out under an atmosphere of Ar using standard Schlenk techniques. All solvents and reagents were obtained from commercial sources and were used without further purificaiton. ^{1}H NMR spectra were recorded on a Varian Mercury 300 MHz or Varian Mercury 400 MHz or Agilent Mercury 400 MHz spectrometer in chloroform-d. All signals were reported in ppm with the internal TMS signal at 0.0 ppm or chloroform signal at 7.26 ppm as a standard. Data for ^{1}H NMR were recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, coupling constant(s) in Hz, integration). ^{13}C NMR spectra were recorded on a Varian Mercury 75 MHz or Agilent Mercury 100 MHz spectrometer in chloroform-d. All signals are reported in ppm with the internal chloroform signal at 77.0 ppm as a standard. Enantiomeric excesses (ee) were determined by chiral high-performance liquid chromatography (chiral HPLC) using Chiralpak IC or OJ-H column. Infrared spectra were recorded on a Perkin-Elmer Spectrum One FT-IR spectrometer. Chromatography: Flash chromatography was performed on silica gel (Merck Silica Gel 60, 300-400 mesh). TLC was performed on aluminium backed silica plates (60F254, 0.2 mm) which were developed using standard visualising agents. High resolution mass spectra was determined by a micrOTOF-II HRMS/MS instrument (Bruker). Optical rotation values were measured with instruments operating at λ = 589 nm, corresponding to the sodium D line at the temperatures indicated.

2. Typical Procedure for the asymmetric transfer hydrogenation reaction.

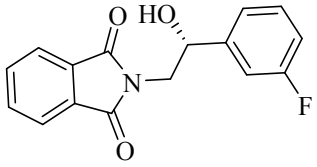
A solution of $[Ru(cymene)Cl_2]_2$ (7.6 mg, 0.0125 mmol) and Ts-DPEN (9.2 mg, 0.0250 mmol) in DMF/MeOH (4 ml, *v*/*v* 4/1) was stirred at r.t. for 3 h, then substrate (**1a**, 0.25 mmol) was added followed by HCO_2H/Et_3N (*v*/*v*, 5/2, 0.4 mL) and the mixture was stirred at 40 °C for 20 h. The reaction was then diluted with CH_2Cl_2 (15 mL) and washed with a solution of Na_2CO_3 (0.5 M, 10 mL).The aqueous layer was extracted with CH_2Cl_2 (2 x 15 mL), the combined organic layer was dried and concentrated, and the residue was purified by flash chromatography to afford **2a** (70.4 mg) as a white solid, 92% yield with 99 % *ee* (Daicel Chirapak IC, ^{i}PrOH/hexanes = 20/80, 1.0 mL/min^{-1}, λ = 254 nm: t_R (major) = 12.2 min, t_R (minor) = 13.3 min); $[a]_D^{20}$ = -28.8° (*c* = 0.60, $CHCl_3$); The absolute configuration of the major enantiomer is (*R*) by the comparison of the reported data.[1-4]

(R)-2-(2-hydroxy-2-phenylethyl)isoindoline-1,3-dione 2a[1-4]



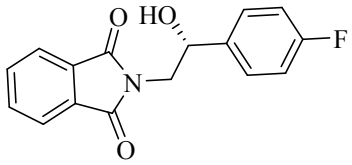
92% yield with >99 % *ee* (Daicel Chirapak IC, ^{i}PrOH/hexanes = 20/80, 1.0 mL/min^{-1}, λ = 254 nm: t_R (major) = 12.2 min, t_R (minor) = 13.3 min); $[a]_D^{20}$ = -28.8° (*c* = 0.60, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89-7.84 (m, 2H), 7.76-7.72 (m, 2H), 7.48-7.30 (m, 5H), 5.10-5.05 (m, 1H), 4.07-3.92 (m, 2H), 2.84 (d, *J* = 5.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 141.0, 134.1, 131.8, 128.5, 128.0, 125.8, 123.4, 72.5, 45.7; IR (Film) *v*: 3481, 1697, 1406, 1055 cm^{-1}; HRMS (ESI$^-$) calcd for $[C_{16}H_{12}NO_3]^-$: 266.0812. Found: 266.0810.

(R)-2-(2-(3-fluorophenyl)-2-hydroxyethyl)isoindoline-1,3-dione 2b



95% yield with 94 % *ee* (Daicel Chirapak IC, ^{i}PrOH/hexanes = 30/70, 1.0 mL/min^{-1}, λ = 254 nm: t_R (major) = 7.7 min, t_R (minor) = 7.2 min); $[\alpha]_D^{25}$ = -29.1° (*c* = 0.61, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88-7.84 (m, 2H), 7.77-7.73 (m, 2H), 7.37-7.30 (m, 1H), 7.23-7.18 (m, 2H), 7.02-6.96 (m, 1H), 5.10-5.04 (m, 1H), 4.06-3.93 (m, 2H), 3.05 (d, *J* = 5.1 Hz, 1H); ^{13}C NMR (75 MHz, d_6-acetone) δ 168.5, 134.8, 132.8, 130.7 (d, *J* = 7.9 Hz), 123.5, 122.6, 122.5(7), 114.8 (d, *J* = 21.2 Hz), 113.4, 113.2, 70.7, 46.1; IR (Film) *v*: 3466, 1697, 1139 cm^{-1}; HRMS (ESI$^-$) calcd for $[C_{16}H_{11}FNO_3]^-$: 284.0717. Found: 284.0719.

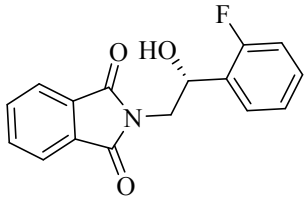
(R)-2-(2-(4-fluorophenyl)-2-hydroxyethyl)isoindoline-1,3-dione 2c[1, 3-4]



87% yield with 93 % *ee* (Daicel Chirapak OJ-H, ^{i}PrOH/hexanes = 20/80, 1.0 mL/min^{-1}, λ = 254 nm: t_R (major) = 12.0 min, t_R (minor) = 17.8 min); $[\alpha]_D^{25}$ = -34.2° (*c* = 0.59,

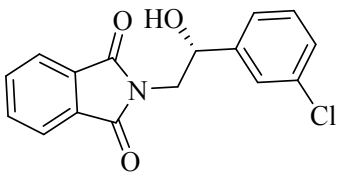
$CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.87-7.85 (m, 2H), 7.75-7.73 (m, 2H), 7.45-7.40 (m, 2H), 7.05 (t, J = 9.7 Hz, 2H), 5.09-5.04 (m, 1H), 4.05-3.90 (m, 2H), 2.95 (d, J = 5.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 164.0, 136.8, 134.2, 131.7, 127.5 (d, J = 8.0 Hz), 123.5, 115.4 (d, J = 21.1 Hz), 71.9, 45.7; IR (Film) v: 3506, 1687, 1508 cm^{-1}; HRMS (ESI^-) calcd for $[C_{16}H_{11}FNO_3]^-$: 284.0717. Found: 284.0717.

(R)-2-(2-(2-fluorophenyl)-2-hydroxyethyl)isoindoline-1,3-dione 2d



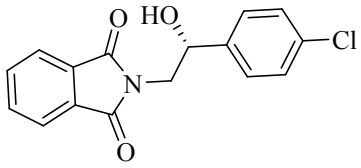
96% yield with 80 % *ee* (Daicel Chirapak IC, ^{i}PrOH/hexanes = 30/70, 1.0 mL/min^{-1}, λ = 254 nm: t_R (major) = 7.6 min, t_R (minor) = 8.8 min); $[\alpha]_D^{25}$ = -49.2° (c = 0.60, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.84-7.80 (m, 2H), 7.74-7.70 (m, 2H), 7.52 (t, J = 7.6 Hz, 1H), 7.29-7.23 (m, 1H), 7.13 (t, J = 7.4 Hz, 1H), 7.06-7.00 (m, 1H), 5.34-5.30 (m, 1H), 4.13-3.99 (m, 2H), 3.29 (d, J = 5.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.6, 159.7 (d, J = 244.6 Hz), 134.1, 131.7, 129.4 (d, J = 19.6 Hz), 134.1, 131.7, 129.4 (d, J = 8.0 Hz), 127.9 (d, J = 13.6 Hz), 127.4 (d, J = 4.1 Hz), 124.2 (d, J = 3.5 Hz), 123.4, 115.2 (d, J = 21.6 Hz), 67.2 (d, J = 2.3 Hz), 44.2 (d, J = 1.6 Hz); IR (Film) v: IR 3506, 1703, 1425, 1396 cm^{-1}; HRMS (ESI^-) calcd for $[C_{16}H_{11}FNO_3]^-$: 284.0717. Found: 284.0716.

(R)-2-(2-(3-chlorophenyl)-2-hydroxyethyl)isoindoline-1,3-dione 2e[3]



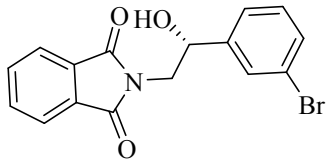
70% yield with 95 % *ee* (Daicel Chirapak OJ-H, ^{i}PrOH/hexanes = 20/80, 1.0 mL/min^{-1}, λ = 254 nm: t_R (major) = 11.9 min, t_R (minor) = 18.0 min); $[\alpha]_D^{25}$ = -28.3° (c = 0.64, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.89-7.86 (m, 2H), 7.77-7.73 (m, 2H), 7.48 (s, 1H), 7.35-7.28 (m, 3H), 5.07-5.02 (m, 1H), 4.04-3.93 (m, 2H), 3.04 (d, J = 5.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 143.1, 134.5, 134.2, 131.7, 129.8, 128.1, 126.1, 124.0, 123.5, 72.0, 45.6; IR (Film) v: 3406, 1701, 1400 cm^{-1}; HRMS (ESI^-) calcd for $[C_{16}H_{11}{}^{35}ClNO_3]^-$: 300.0422. Found: 300.0425.

(R)-2-(2-(4-chlorophenyl)-2-hydroxyethyl)isoindoline-1,3-dione 2f[1-3]



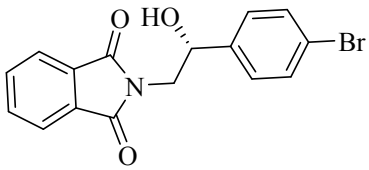
78% yield with 90 % *ee* (Daicel Chirapak OJ-H, ^{i}PrOH/hexanes = 30/70, 1.0 mL/min^{-1}, λ = 254 nm: t_R (major) = 7.9 min, t_R (minor) = 9.7 min); $[\alpha]_D^{25}$ = -26.3° (*c* = 0.63, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88-7.85 (m, 2H), 7.77-7.73 (m, 2H), 7.41-7.32 (m, 4H), 5.07-5.03 (m, 1H), 4.05-3.92 (m, 2H), 3.01 (d, *J* = 4.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 139.5, 134.2, 131.7, 128.7, 127.3, 123.5, 108.6, 72.0, 45.6; IR (Film) *v*: 3431, 1697, 1405cm^{-1}; HRMS (ESI$^-$) calcd for $[C_{16}H_{11}{}^{35}ClNO_3]^-$: 300.0422. Found: 300.0425.

(R)-2-(2-(3-bromophenyl)-2-hydroxyethyl)isoindoline-1,3-dione 2g



90% yield with 97 % *ee* (Daicel Chirapak OJ-H, ^{i}PrOH/hexanes = 20/80, 1.0 mL/min^{-1}, λ = 254 nm: t_R (major) = 12.3 min, t_R (minor) = 18.0 min); $[\alpha]_D^{25}$ = -24.6° (*c* = 0.61, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90-7.84 (m, 2H), 7.77-7.72 (m, 2H), 7.63 (s, 1H), 7.44-7.37 (m, 2H), 7.24-7.21 (m, 1H), 5.07-5.00 (m, 1H), 4.03-3.92 (m, 2H), 3.06 (d, *J* = 4.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 143.3, 134.2, 131.7, 131.1, 130.1, 129.0, 124.5, 123.5, 122.7, 71.9, 45.6; IR (Film) *v*: 3446, 1754, 1701, 1400 cm^{-1}; HRMS (ESI$^-$) calcd for $[C_{16}H_{11}{}^{79}BrNO_3]^-$: 343.9917. Found: 343.9932.

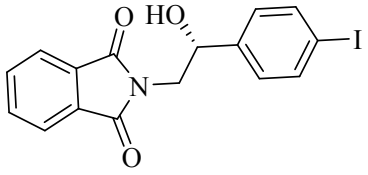
(R)-2-(2-(4-bromophenyl)-2-hydroxyethyl)isoindoline-1,3-dione 2h[1-2]



82% yield with 91 % *ee* (Daicel Chirapak OJ-H, ^{i}PrOH/hexanes = 30/70, 1.0 mL/min^{-1}, λ = 254 nm: t_R (major) = 8.3 min, t_R (minor) = 10.5 min); $[\alpha]_D^{25}$ = -32.2° (*c* = 0.41, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88-7.84 (m, 2H), 7.77-7.32 (m, 2H), 7.49 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 5.07-5.02 (m, 1H), 4.05-3.90 (m, 2H), 3.03

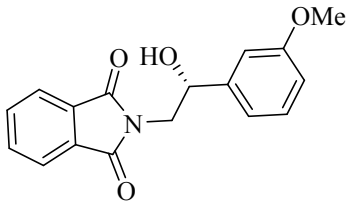
(d, J = 4.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 140.0, 134.3, 131.7, 131.6(7), 127.6, 123.5, 121.9, 72.1, 45.5; IR (Film) v: 3458, 1716, 1575 cm^{-1}; HRMS (ESI$^-$) calcd for $[C_{16}H_{11}{}^{79}BrNO_3]^-$: 343.9917. Found: 343.9922.

(R)-2-(2-hydroxy-2-(4-iodophenyl)ethyl)isoindoline-1,3-dione 2i



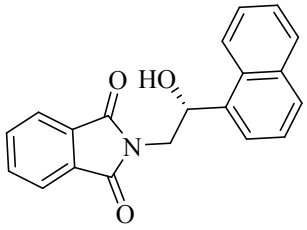
78% yield with 92 % *ee* (Daicel Chirapak OJ-H, ^{i}PrOH/hexanes = 30/70, 1.0 mL/min^{-1}, λ = 254 nm: t_R (major) = 9.3 min, t_R (minor) = 12.2 min); $[\alpha]_D^{25}$ = -23.9° (c = 0.61, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88-7.84 (m, 2H), 7.77-7.68 (m, 4H), 7.21 (d, J = 8.1 Hz, 2H), 5.06-5.02 (m, 1H), 4.04-3.89 (m, 2H), 3.02 (d, J = 5.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 140.7, 137.6, 134.3, 131.7, 127.8, 125.5, 93.6, 72.2, 45.5; IR (Film) v: 3433, 1713, 1691 cm^{-1}; HRMS (ESI$^-$) calcd for $[C_{16}H_{11}INO_3]^-$: 391.9778. Found: 391.9798.

(R)-2-(2-hydroxy-2-(3-methoxyphenyl)ethyl)isoindoline-1,3-dione 2j[1,4]



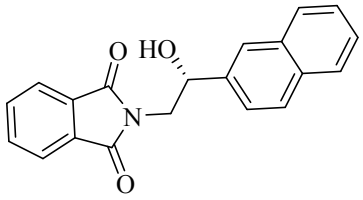
82 % yield with 96 % *ee* (Daicel Chirapak IC, ^{i}PrOH/hexanes = 30/70, 1.0 mL/min^{-1}, λ = 254 nm: t_R (major) = 15.7 min, t_R (minor) = 21.0 min); $[\alpha]_D^{25}$ = -25.5° (c = 0.42, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87-7.85 (m, 2H), 7.75-7.72 (m, 2H), 7.31-7.27 (m, 1H), 7.04-7.03 (m, 2H), 6.84 (d, J = 7.2 Hz, 1H), 5.04 (d, J = 4.8 Hz, 1H), 4.06-3.91 (m, 2H), 3.81 (s, 3H), 2.90 (s 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 159.7, 142.7, 134.1, 131.8, 129.6, 123.4, 118.1, 113.8, 111.0, 72.4, 55.2, 45.6; IR (Film) ν: 3481, 1697, 1406, 1055 cm^{-1}; HRMS (ESI) calcd for $[C_{17}H_{14}NO_4]^-$: 316.0968. Found: 316.0963.

(R)-2-(2-hydroxy-2-(naphthalen-1-yl)ethyl)isoindoline-1,3-dione 2k[2]



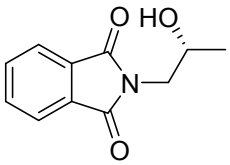
70% yield with 91 % *ee* (Daicel Chirapak IC, ^{i}PrOH/hexanes = 30/70, 1.0 mL/min^{-1}, λ = 254 nm: t_R (major) = 9.0 min, t_R (minor) = 19.9 min); $[\alpha]_D^{25}$ = -1.1° (*c* = 0.57, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.4 Hz, 1H), 7.91-7.90 (m, 3H), 7.86-7.82 (m, 2H), 7.78-7.75 (m, 2H), 7.64 (t, *J* = 7.8 Hz, 1H), 7.53 (t, J = 7.8 Hz, 2H), 5.90-5.86 (m, 1H), 4.19-4.02 (m, 2H), 2.76 (d, *J* = 4.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.9, 136.8, 133.6, 132.0, 130.2, 128.9, 128.6, 126.6, 125.8, 125.4, 123.5, 123.0, 122.9, 69.7, 45.4; IR (Film) *v*: 3506, 1697, 1319 cm^{-1}; HRMS (ESI) calcd for $[C_{20}H_{14}NO_3]^-$: 316.0968. Found: 316.0970.

(R)-2-(2-hydroxy-2-(naphthalen-2-yl)ethyl)isoindoline-1,3-dione 2l[2-4]



75% yield with 95 % *ee* (Daicel Chirapak IC, ^{i}PrOH/hexanes = 30/70, 1.0 mL/min^{-1}, λ = 254 nm: t_R (major) = 10.5 min, t_R (minor) = 11.4 min); $[\alpha]_D^{25}$ = -15.3° (*c* = 0.46, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.88-7.83 (m, 5H), 7.76-7.72 (m, 2H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.50-7.47 (m, 2H), 5.27-5.22 (m, 1H), 4.16-4.01 (m, 1H), 3.03 (d, *J* = 4.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 138.4, 134.1, 133.2, 133.1, 131.8, 128.4, 128.0, 127.7, 126.2, 126.1, 124.9, 123.7, 123.5, 72.8, 45.6;
IR (Film) *v*: 3456, 1714, 1595 cm^{-1}; HRMS (ESI) calcd for $[C_{20}H_{14}NO_3]^-$: 316.0968. Found: 316.0963.

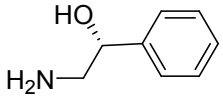
(R)-1-Phthalimide-propan-2-ol 2m[1]



89% yiled with 25% *ee* (Daicel Chirapak OD, ^{i}PrOH/hexanes = 20/80, 1.0 mL/min^{-1}, λ = 254 nm: t_R (major) = 7.6 min, t_R (minor) = 8.3 min); $[\alpha]_D^{25}$ = -4.6° (*c* = 0.80, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (d, *J* = 6.3 Hz, 3H), 2.37 (br, 1H), 3.70-3.81 (m,

2H), 4.10-4.14 (m, 1H) 7.71-7.76 (m, 2H), 7.84-7.89 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.9, 134.1, 131.9, 123.4, 66.7, 45.5, 21.0.

(R)-2-amino-1-phenylethan-1-ol 3a[5]



Known compound. $[\alpha]_D^{25}$ = -59.5° (*c* = 0.22, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H), 4.67 (dd, *J* = 7.6, 3.2 Hz, 1H), 3.02 (d, *J* = 12.0 Hz, 1H), 2.83 (m, 1H), 2.40 (bs, 3H).

4. Reference

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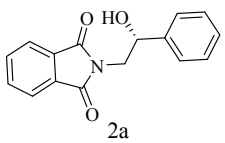
(5) G. Uccello-Barretta, A. Cuzzola, C. Balzano, R. Menicagli, A. Iuliano, P. Salvadori, *J. Org. Chem.*, 1997, **62**, 827.

5. ^1H NMR and ^{13}C NMR Spectra of Compounds



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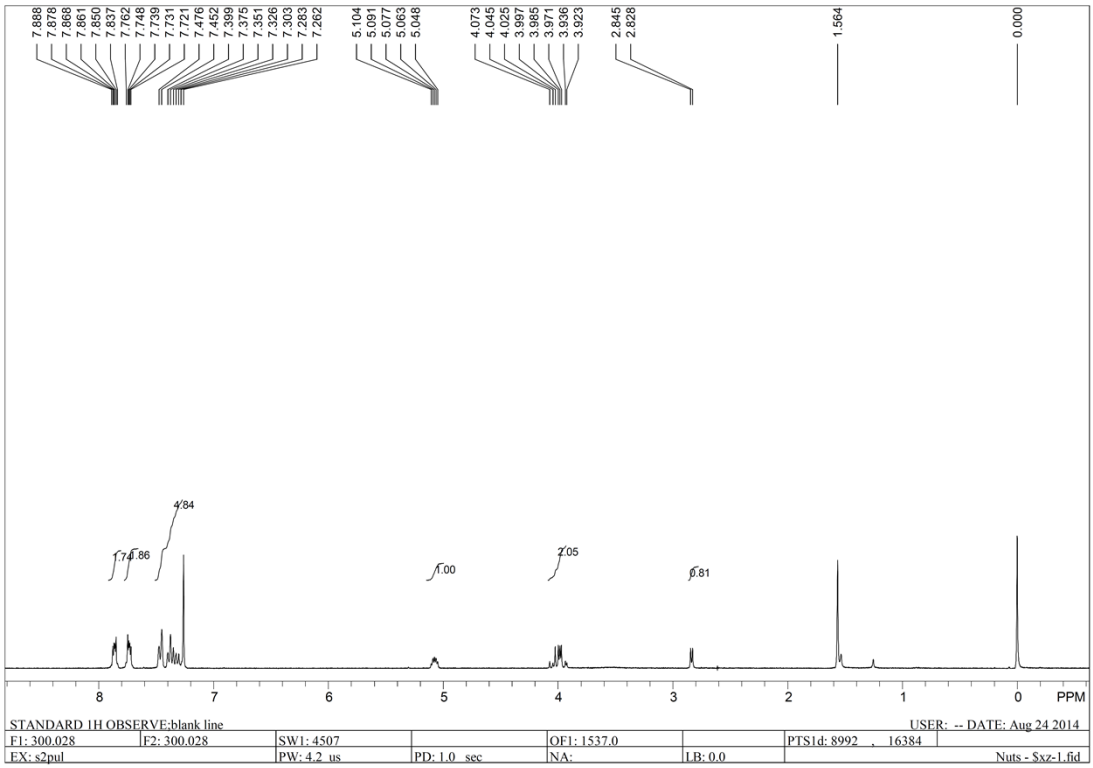
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7.731
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7.476
7.452
7.399
7.375
7.351
7.326
7.303
7.283
7.262
5.104
5.091
5.077
5.063
5.048
4.073
4.045
4.025
3.997
3.985
3.971
3.936
3.923
2.845
2.828
1.564
0.000
4.84
1.74
1.86
1.00
2.05
0.81
8
7
6
5
4
3
2
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0
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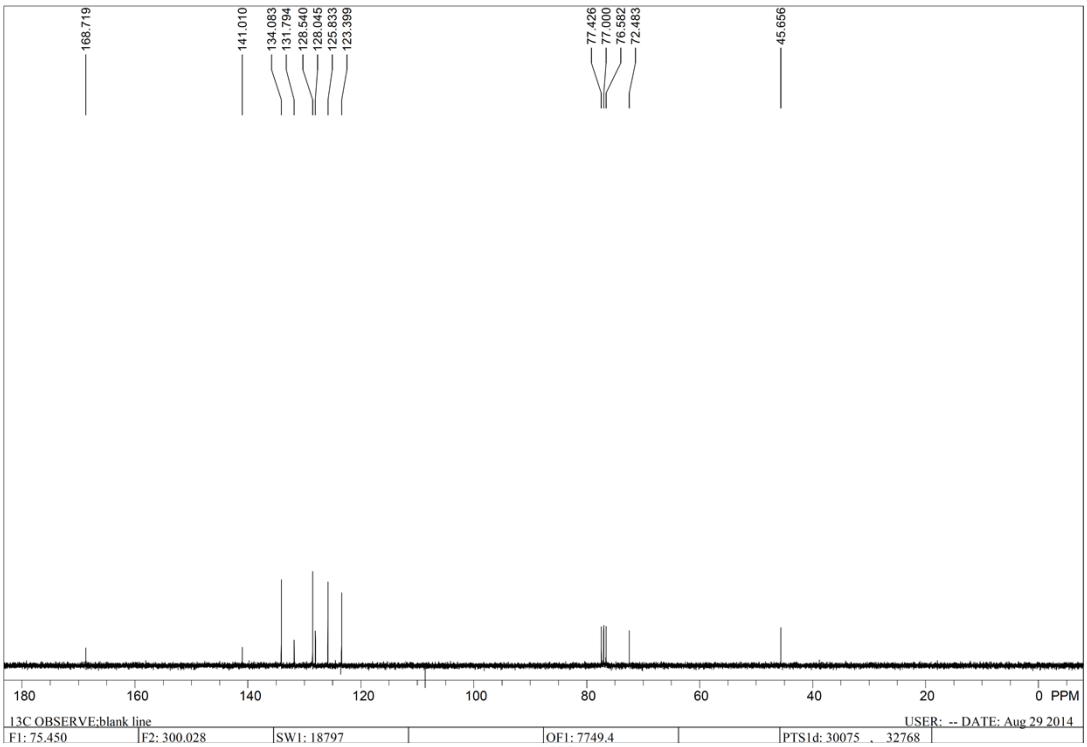
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134.083
131.794
128.540
128.045
125.833
123.399
77.426
77.000
76.582
72.483
45.656
180
160
140
120
100
80
60
40
20
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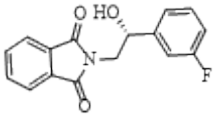
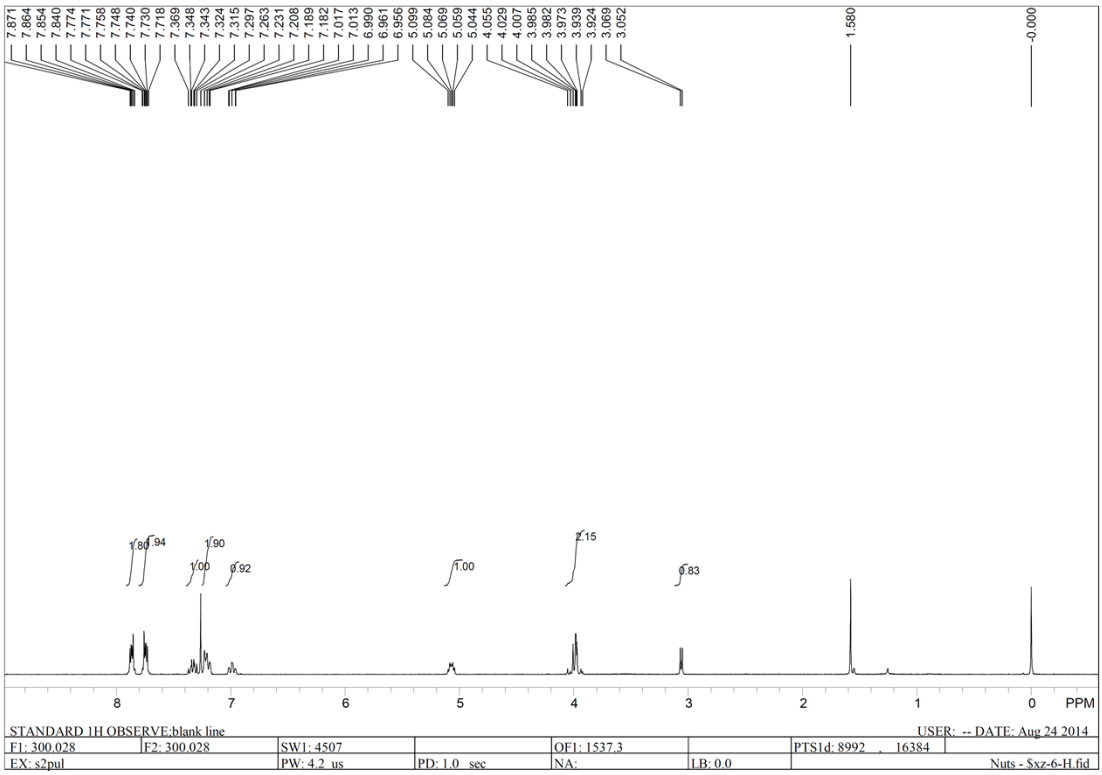
PTS1d: 30075 , 32768


O
HO
N
O
F

2b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7.348
7.343
7.324
7.315
7.297
7.263
7.231
7.208
7.189
7.182
7.017
7.013
6.990
6.961
6.956
5.099
5.084
5.069
5.059
5.044
4.055
4.029
4.007
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3.982
3.973
3.939
3.924
3.069
3.052
1.580
-0.000
1.80
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1.90
1.00
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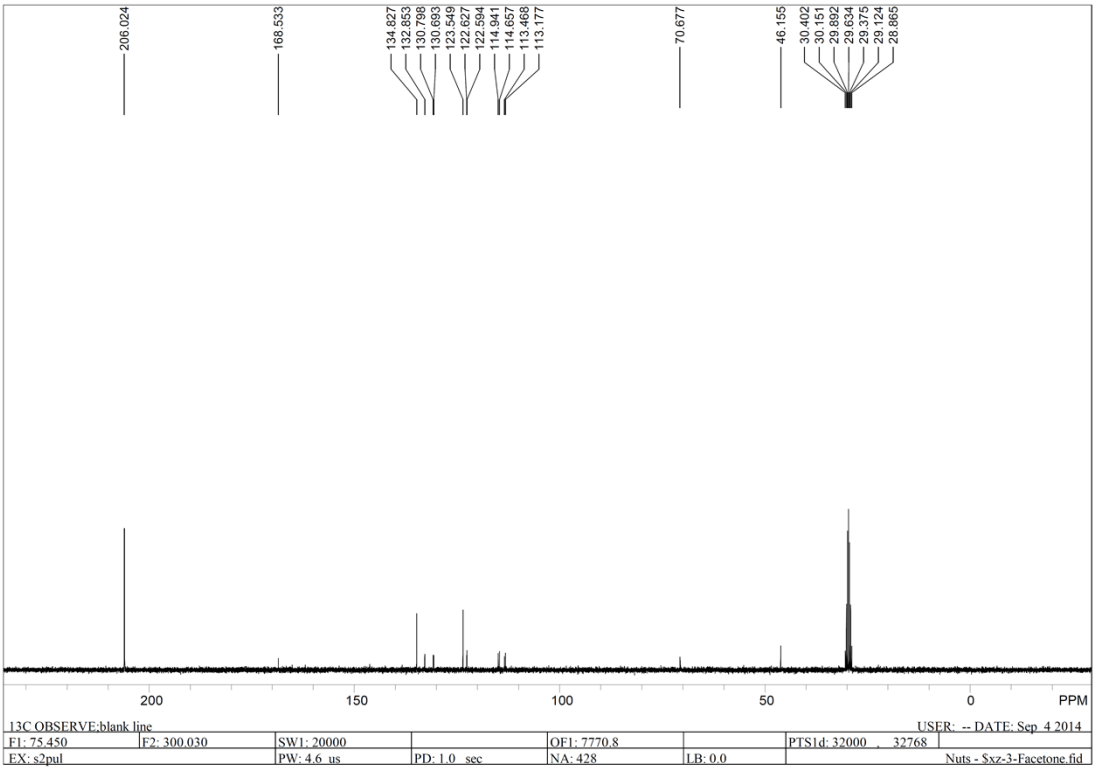
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113.177
70.677
46.155
30.402
30.151
29.892
29.634
29.375
29.124
28.865
200
150
100
50
0
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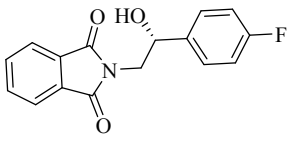
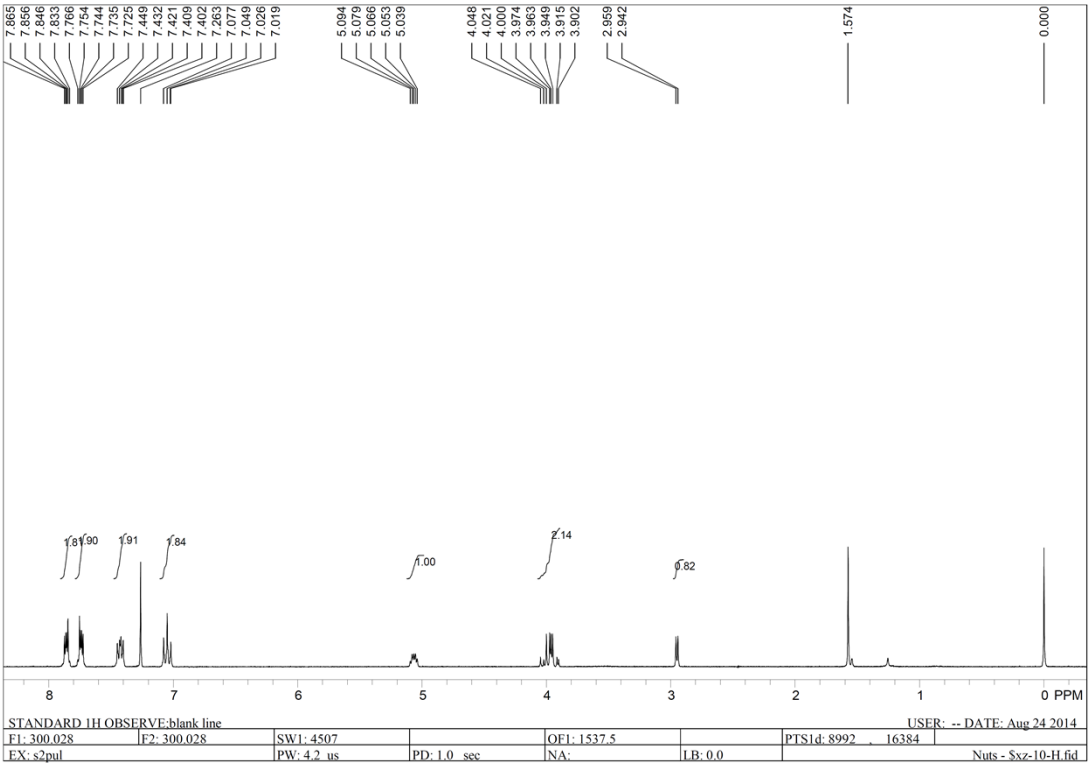

O
HO
F
N
O

2c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7.735
7.725
7.449
7.432
7.421
7.409
7.402
7.263
7.077
7.049
7.026
7.019
5.094
5.079
5.066
5.053
5.039
4.048
4.021
4.000
3.974
3.963
3.949
3.915
3.902
2.959
2.942
1.574
0.000
1.81
1.90
1.91
1.84
1.00
2.14
0.82
8
7
6
5
4
3
2
1
0 PPM
STANDARD 1H OBSERVE;blank line
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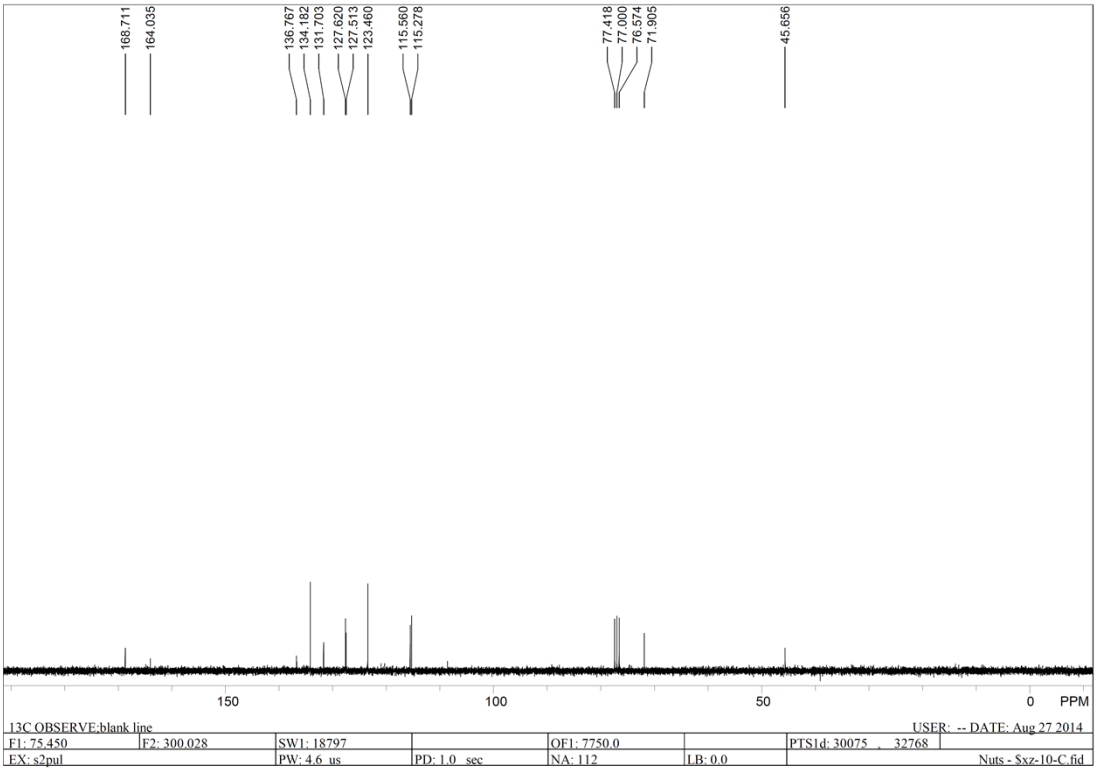
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127.620
127.513
123.460
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115.278
77.418
77.000
76.574
71.905
45.656
150
100
50
0 PPM
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F2: 300.028
SW1: 18797
OF1: 7750.0
PTS1d: 30075 , 32768
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PW: 4.6 us
PD: 1.0 sec
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LB: 0.0
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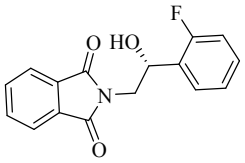
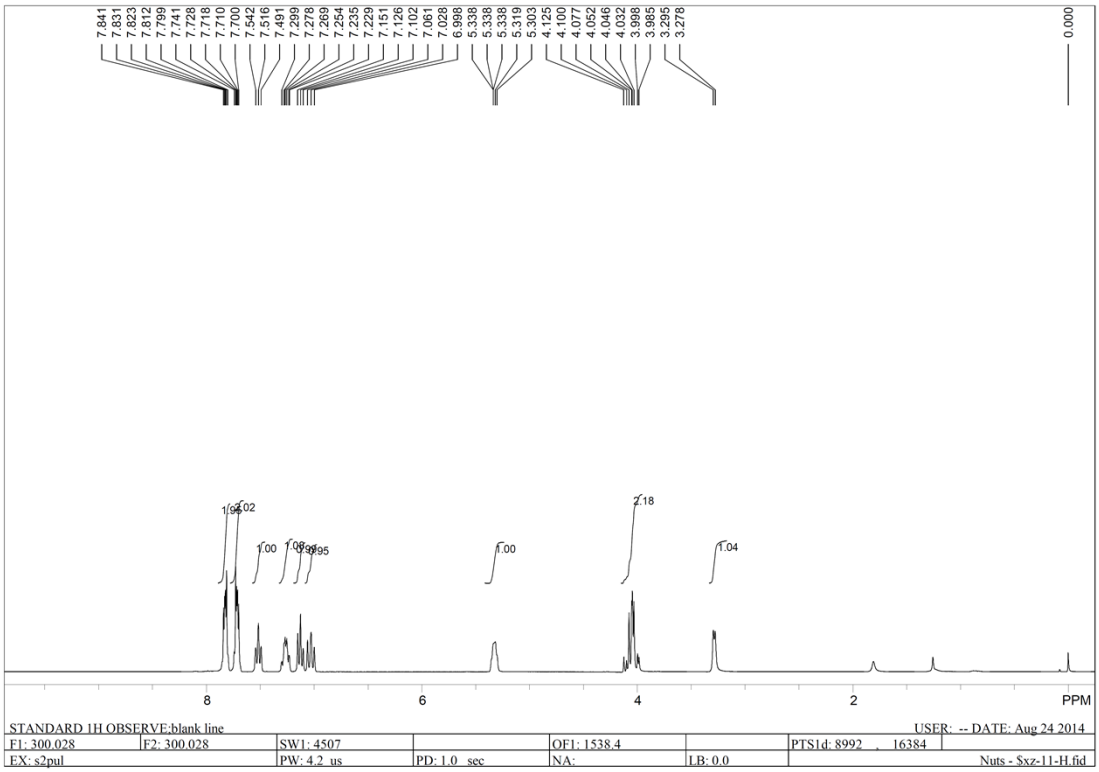

F
O
HO
N
O

2d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7.718
7.710
7.700
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7.491
7.299
7.278
7.269
7.254
7.235
7.229
7.151
7.126
7.102
7.061
7.028
6.998
5.338
5.338
5.319
5.303
4.125
4.100
4.077
4.052
4.046
4.032
3.998
3.985
3.295
3.278
0.000
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1.02
1.00
1.08
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1.00
2.18
1.04
8
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4
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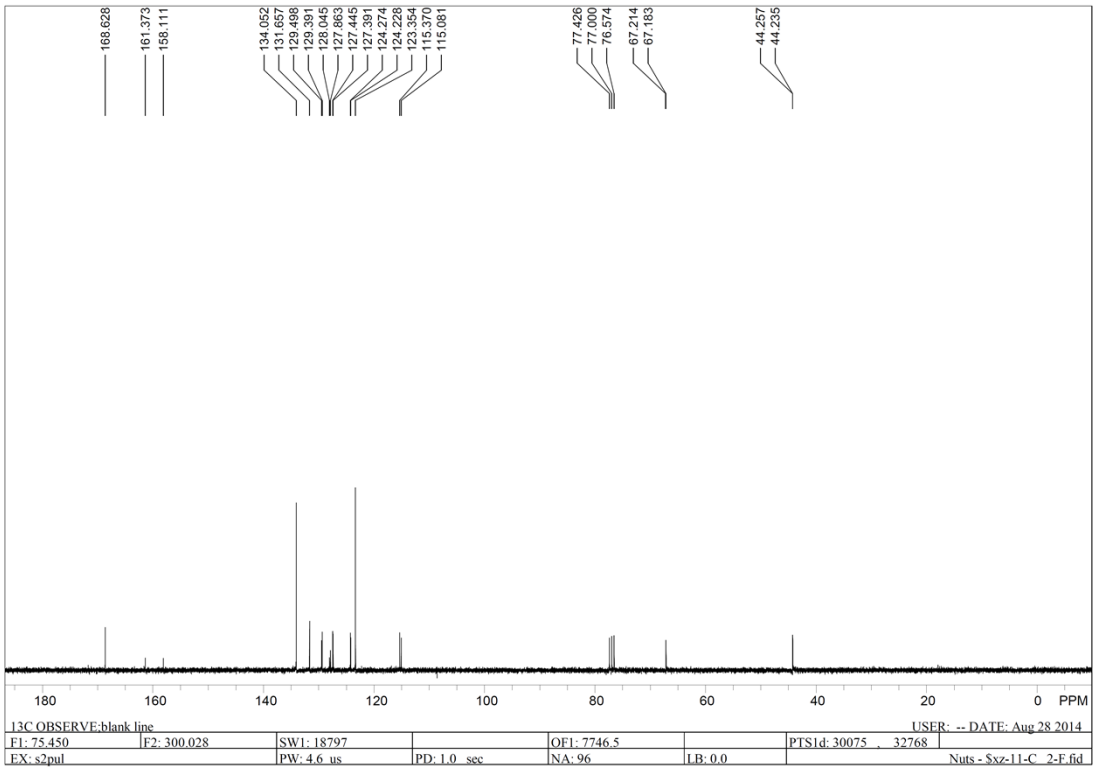
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124.228
123.354
115.370
115.081
77.426
77.000
76.574
67.214
67.183
44.257
44.235
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160
140
120
100
80
60
40
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SW1: 18797
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PTS1d: 30075 , 32768
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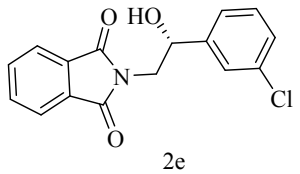
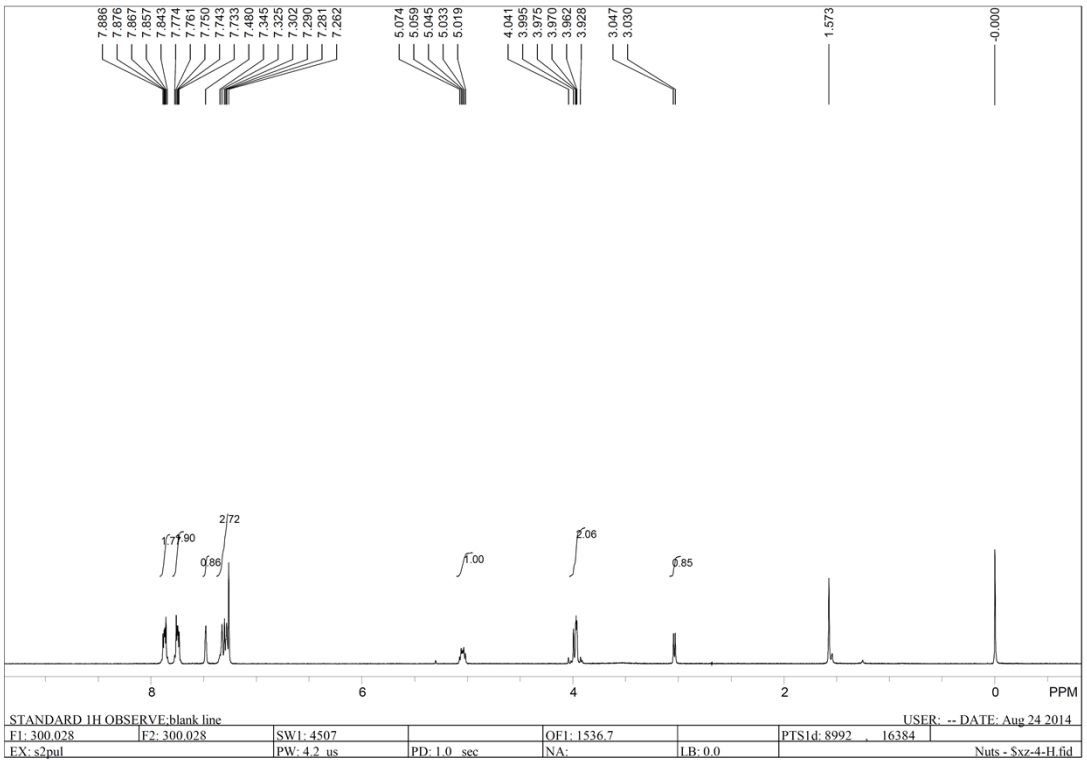

O
HO
N
Cl
O

2e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7.345
7.325
7.302
7.290
7.281
7.262
5.074
5.059
5.045
5.033
5.019
4.041
3.995
3.975
3.970
3.962
3.928
3.047
3.030
1.573
-0.000
1.77
1.90
0.86
2.72
1.00
2.06
0.85
8
6
4
2
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STANDARD 1H OBSERVE:blank line
USER: -- DATE: Aug 24 2014
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F2: 300.028
SW1: 4507
OF1: 1536.7
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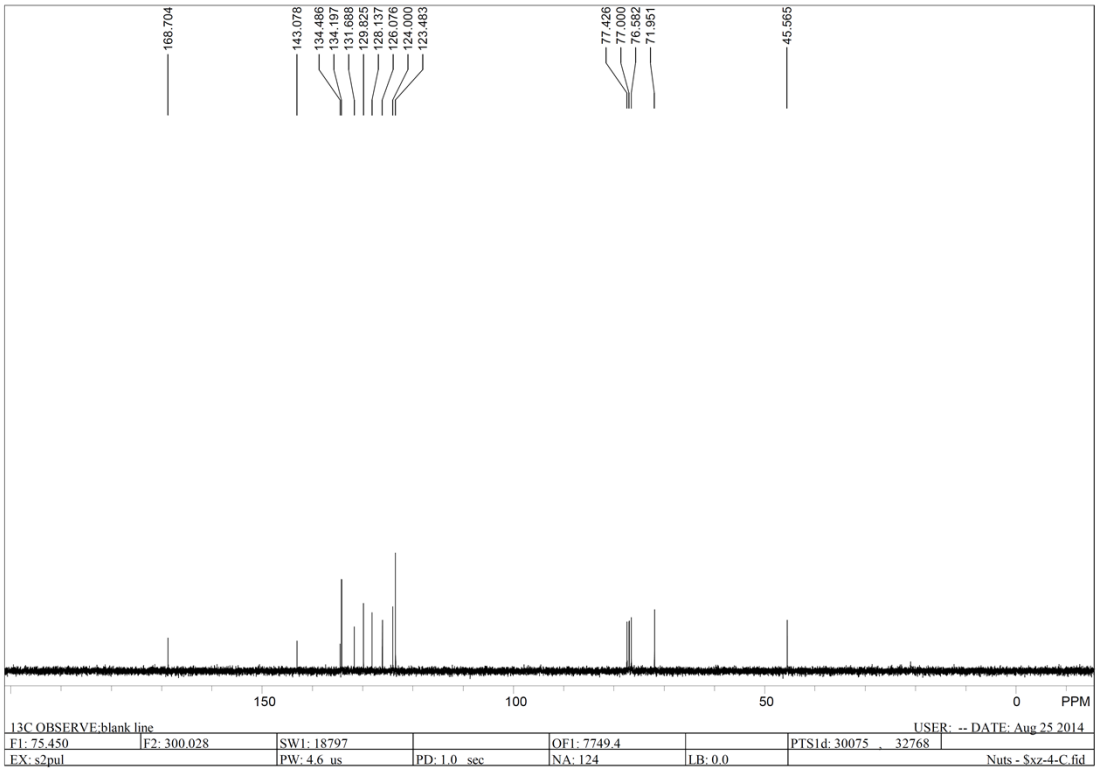
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126.076
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123.483
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77.000
76.582
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45.565
150
100
50
0
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SW1: 18797
OF1: 7749.4
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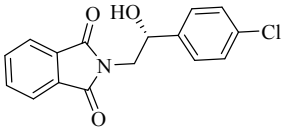
O
HO
Cl
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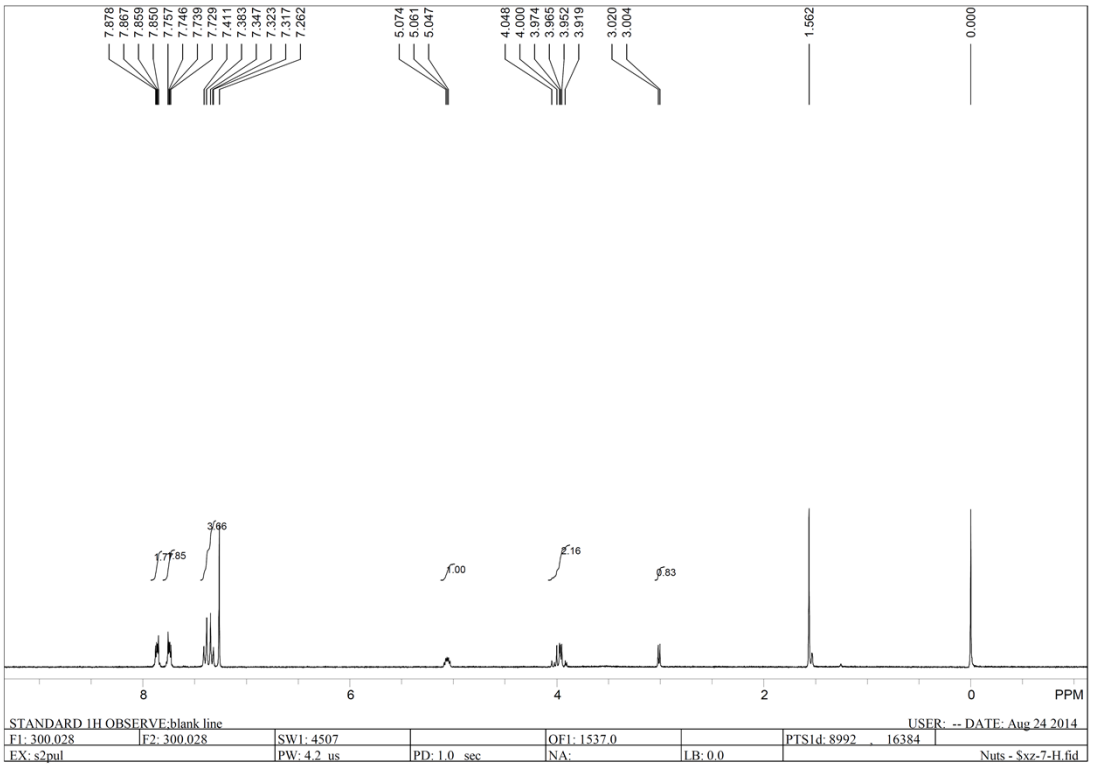
O

2f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7.729
7.411
7.383
7.347
7.323
7.317
7.262
5.074
5.061
5.047
4.048
4.000
3.974
3.965
3.952
3.919
3.020
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8
6
4
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USER: -- DATE: Aug 24 2014
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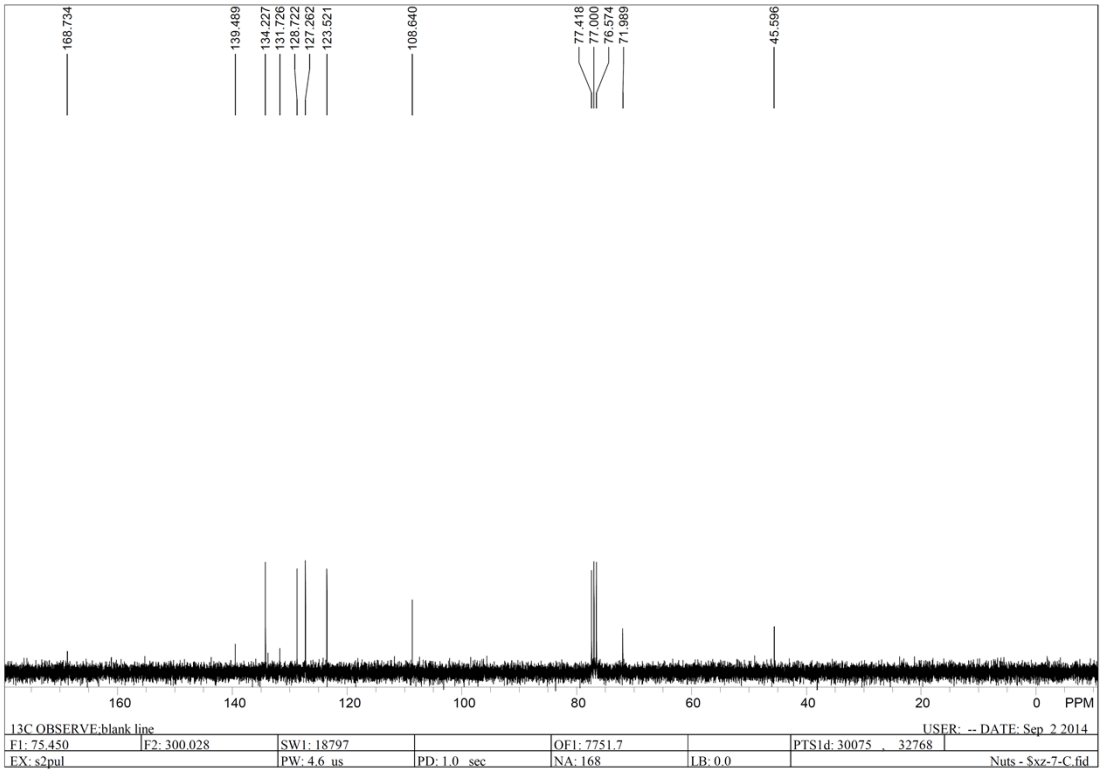
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127.262
123.521
108.640
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77.000
76.574
71.989
45.596
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140
120
100
80
60
40
20
0
PPM
13C OBSERVE;blank line
USER: -- DATE: Sep 2 2014
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F2: 300.028
SW1: 18797
OF1: 7751.7
PTS1d: 30075 , 32768
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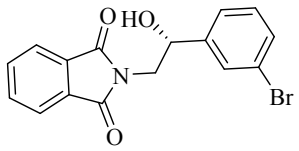
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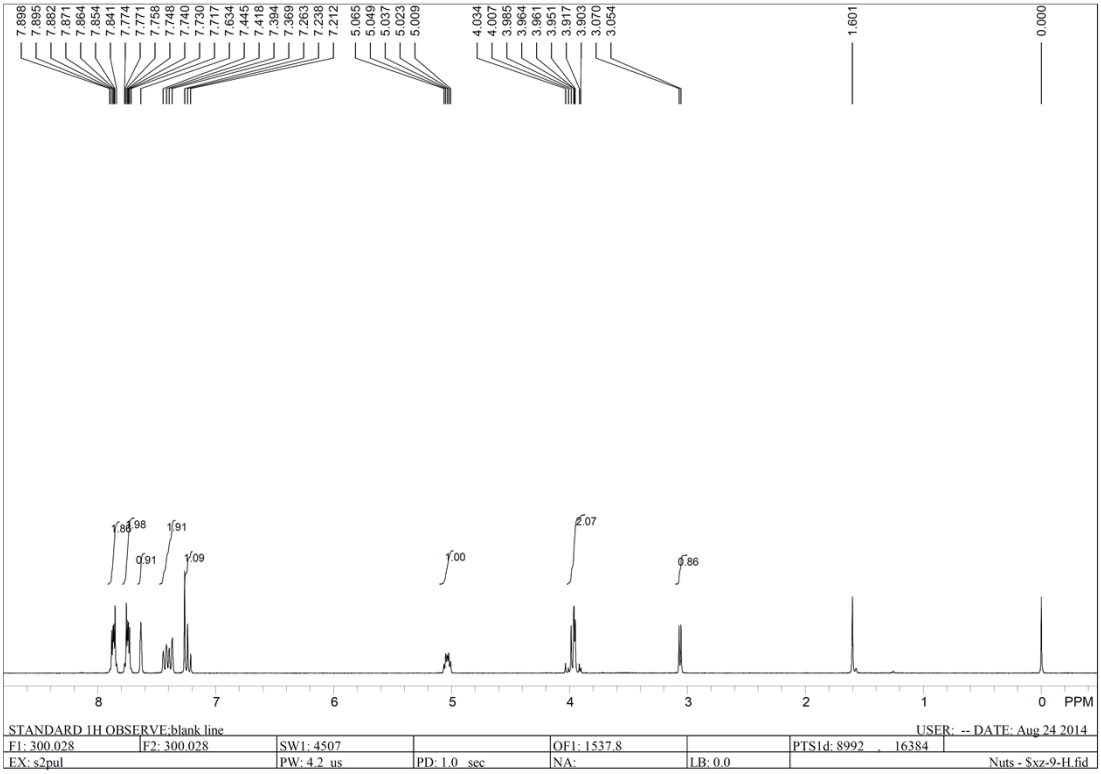
O

2g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7.717
7.634
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7.418
7.394
7.369
7.263
7.238
7.212
5.065
5.049
5.037
5.023
5.009
4.034
4.007
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3.951
3.917
3.903
3.070
3.054
1.601
0.000
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1.98
1.91
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1.09
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NA:
LB: 0.0
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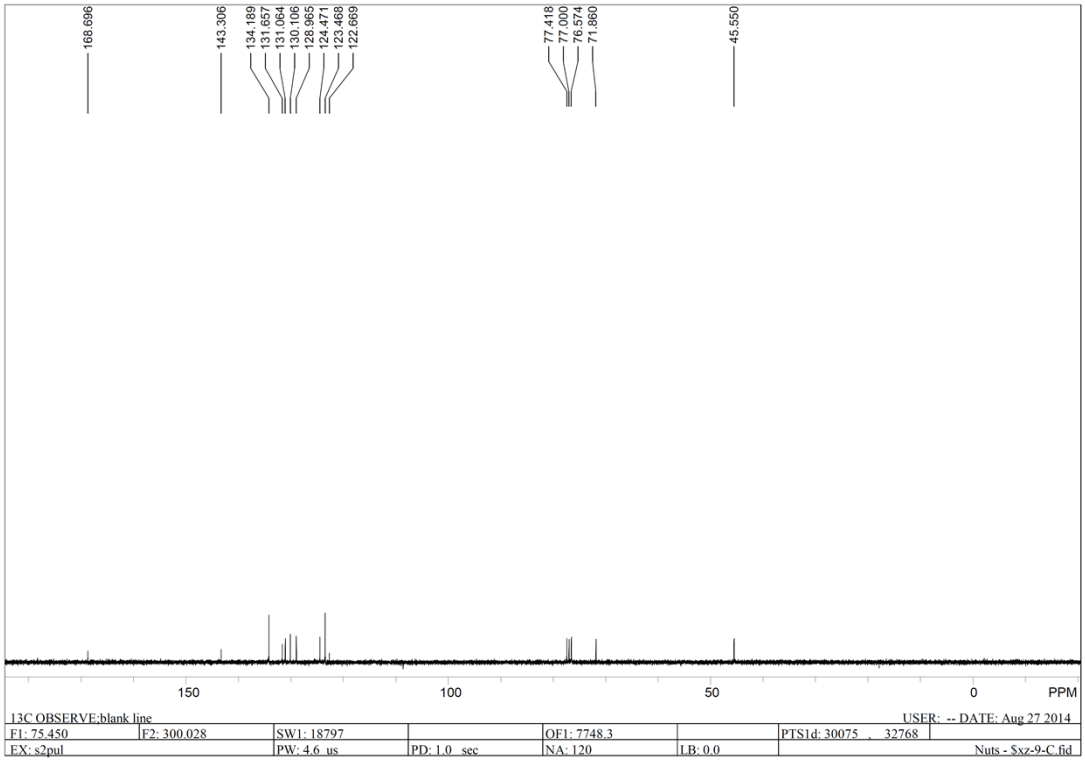
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124.471
123.468
122.669
77.418
77.000
76.574
71.860
45.550
150
100
50
0
PPM
13C OBSERVE;blank line
USER: -- DATE: Aug 27 2014
F1: 75.450
F2: 300.028
SW1: 18797
OF1: 7748.3
PTS1d: 30075 , 32768
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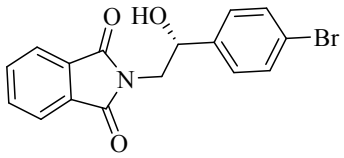
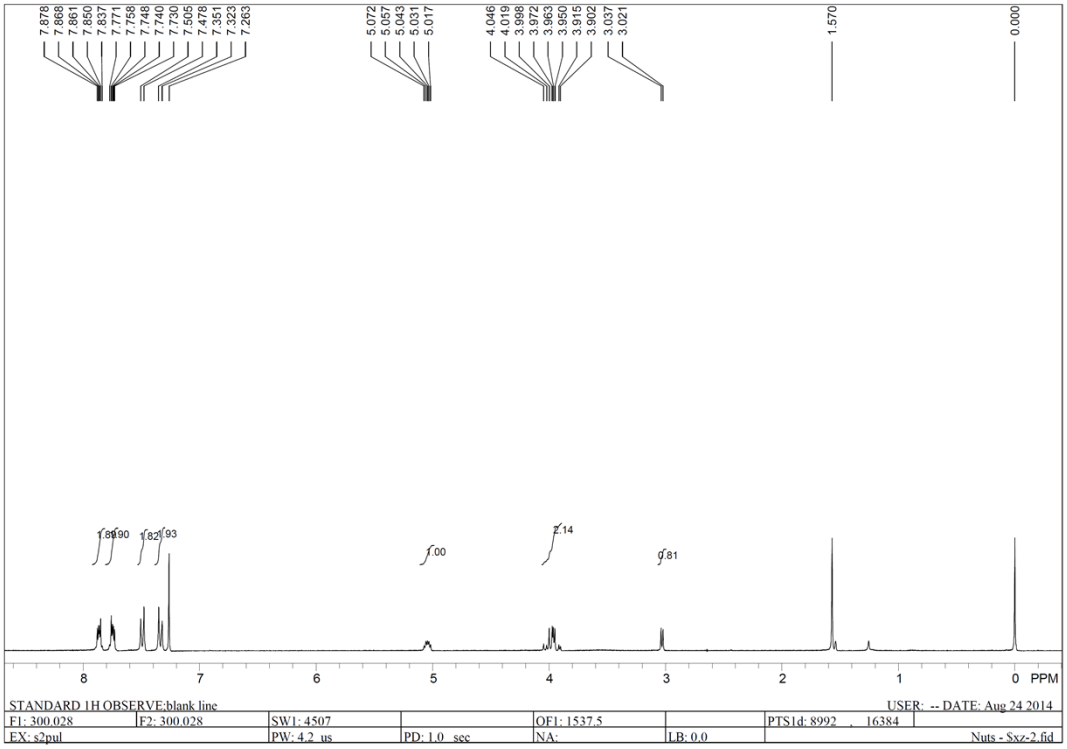

O
HO
Br
N
O

2h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7.323
7.263
5.072
5.057
5.043
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3.915
3.902
3.037
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0.000
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1.90
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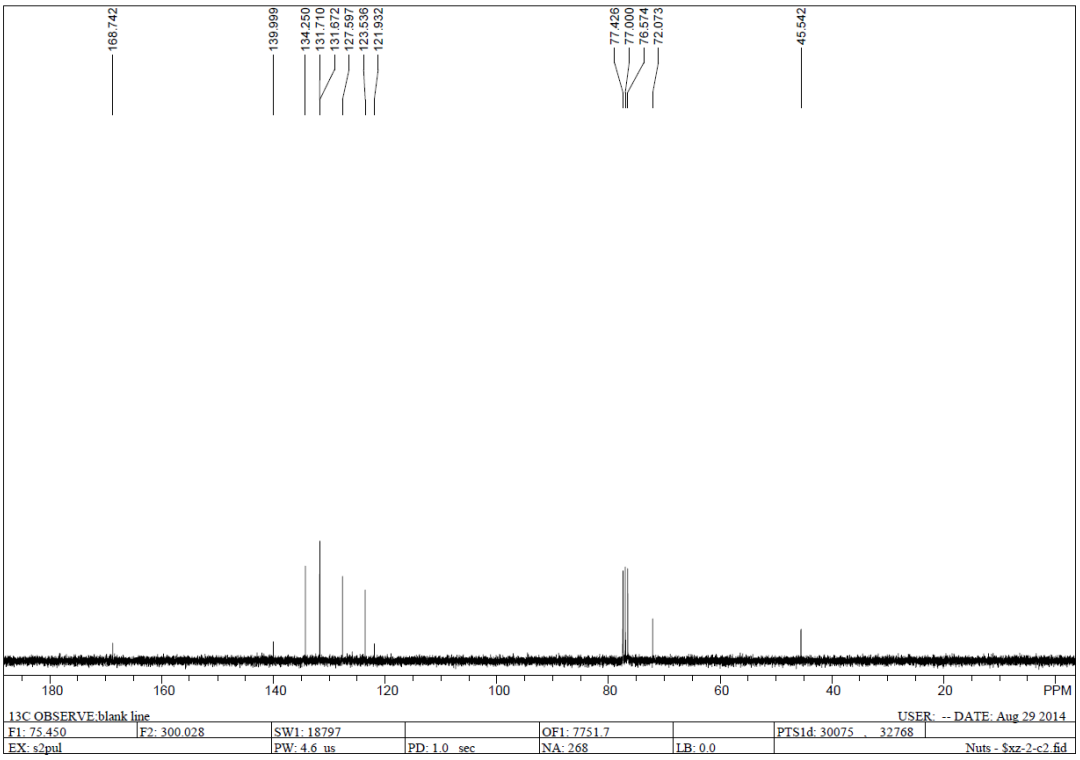
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123.536
121.932
77.426
77.000
76.574
72.073
45.542
180
160
140
120
100
80
60
40
20
PPM
13C OBSERVE:blank line
USER: -- DATE: Aug 29 2014
F1: 75.450
F2: 300.028
SW1: 18797
OF1: 7751.7
PTS1d: 30075 , 32768
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PD: 1.0 sec
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LB: 0.0
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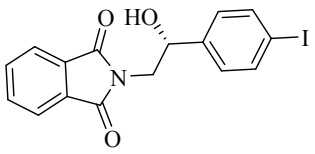
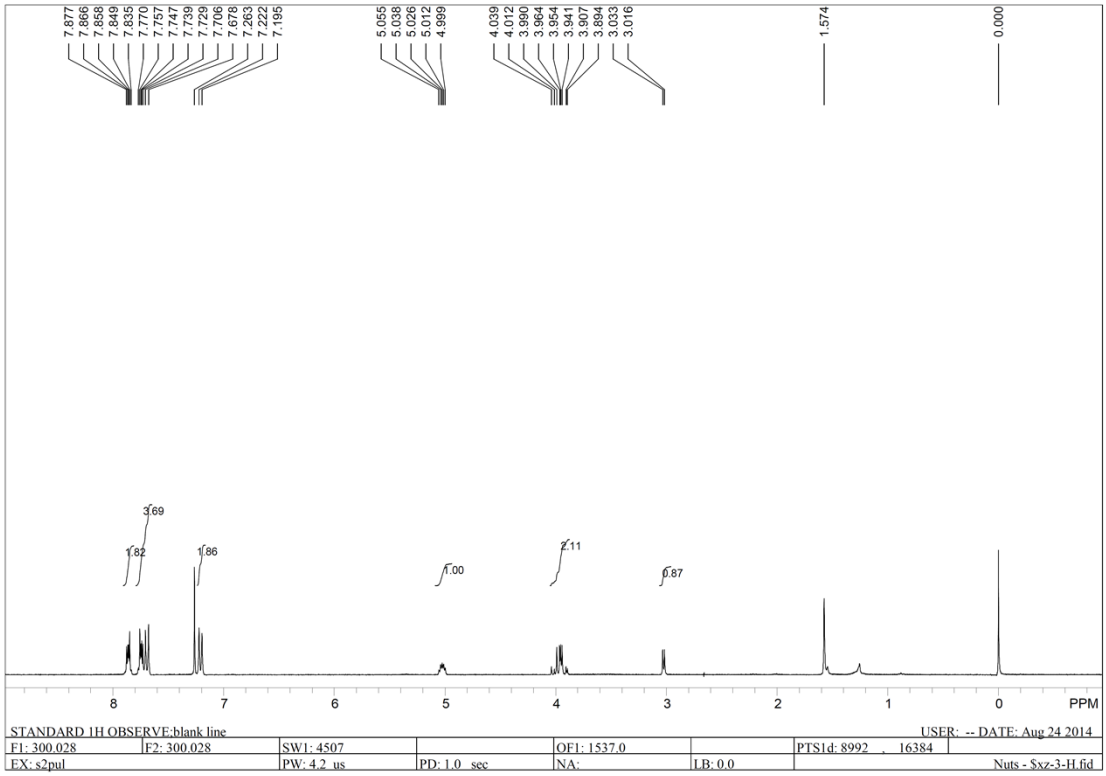

O
HO
I
N
O

2i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7.747
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7.729
7.706
7.678
7.263
7.222
7.195
5.055
5.038
5.026
5.012
4.999
4.039
4.012
3.990
3.964
3.954
3.941
3.907
3.894
3.033
3.016
1.574
0.000
3.69
1.82
1.86
1.00
2.11
0.87
8
7
6
5
4
3
2
1
0
PPM
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USER: -- DATE: Aug 24 2014
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SW1: 4507
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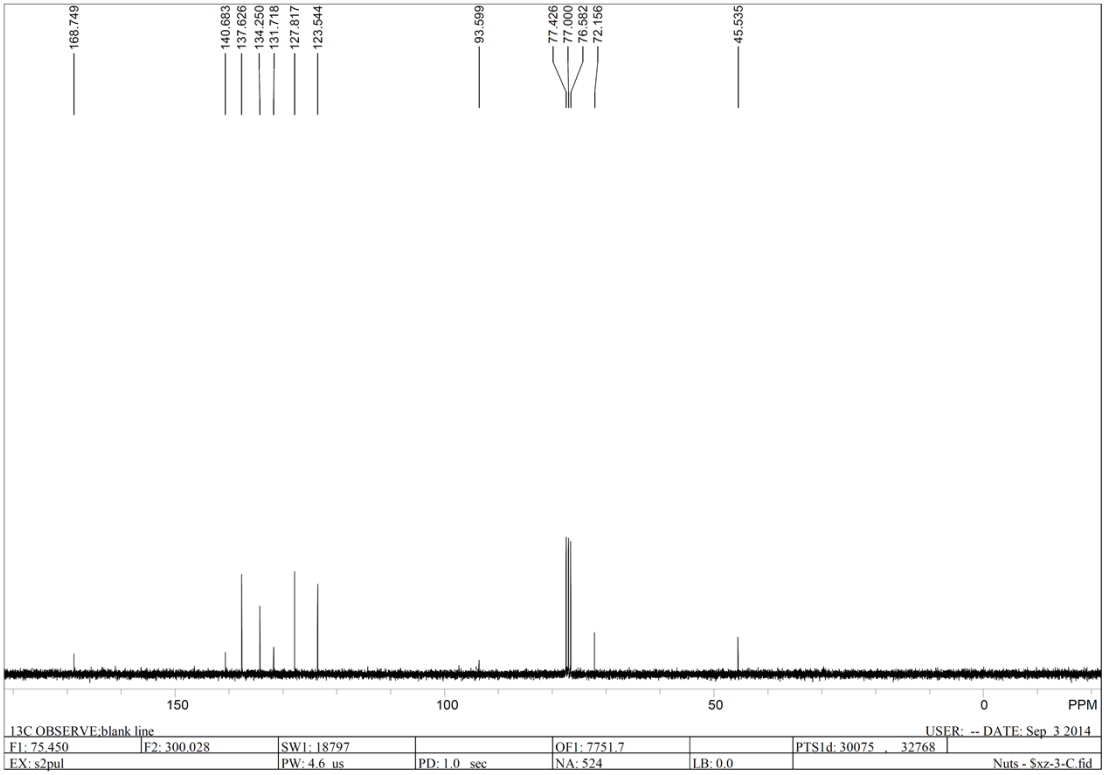
PW: 4.2 us
PD: 1.0 sec
NA:
LB: 0.0
Nuts - $xz-3-H.fid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134.250
131.718
127.817
123.544
93.599
77.426
77.000
76.582
72.156
45.535
150
100
50
0
PPM
13C OBSERVE:blank line
USER: -- DATE: Sep 3 2014
F1: 75.450
F2: 300.028
SW1: 18797
OF1: 7751.7
PTS1d: 30075 , 32768
EX: s2pul
PW: 4.6 us
PD: 1.0 sec
NA: 524
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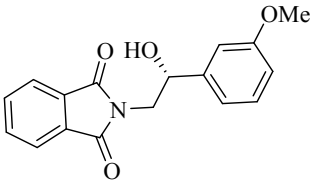
Nuts - $xz-3-C.fid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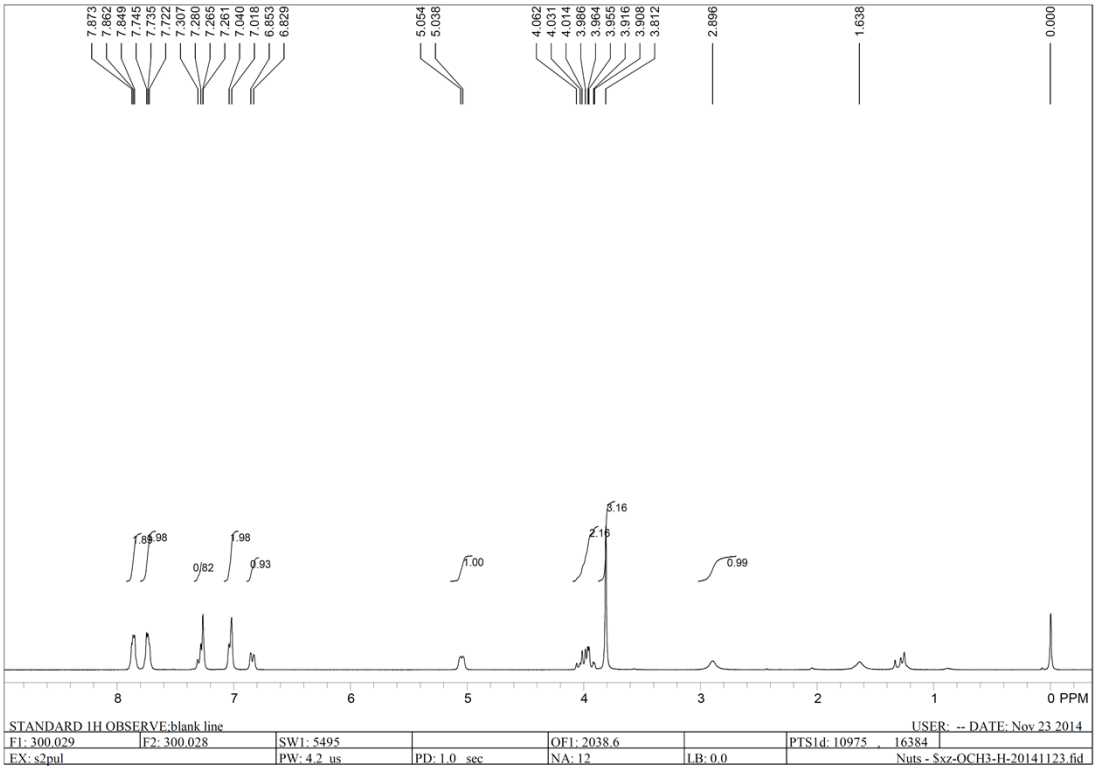
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7.261
7.040
7.018
6.853
6.829
5.054
5.038
4.062
4.031
4.014
3.986
3.964
3.955
3.916
3.908
3.812
2.896
1.638
0.000
1.98
1.98
0.82
0.93
1.00
3.16
2.16
0.99
8
7
6
5
4
3
2
1
0 PPM
STANDARD 1H OBSERVE;blank line
USER: -- DATE: Nov 23 2014
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SW1: 5495
OF1: 2038.6
PTS1d: 10975 , 16384
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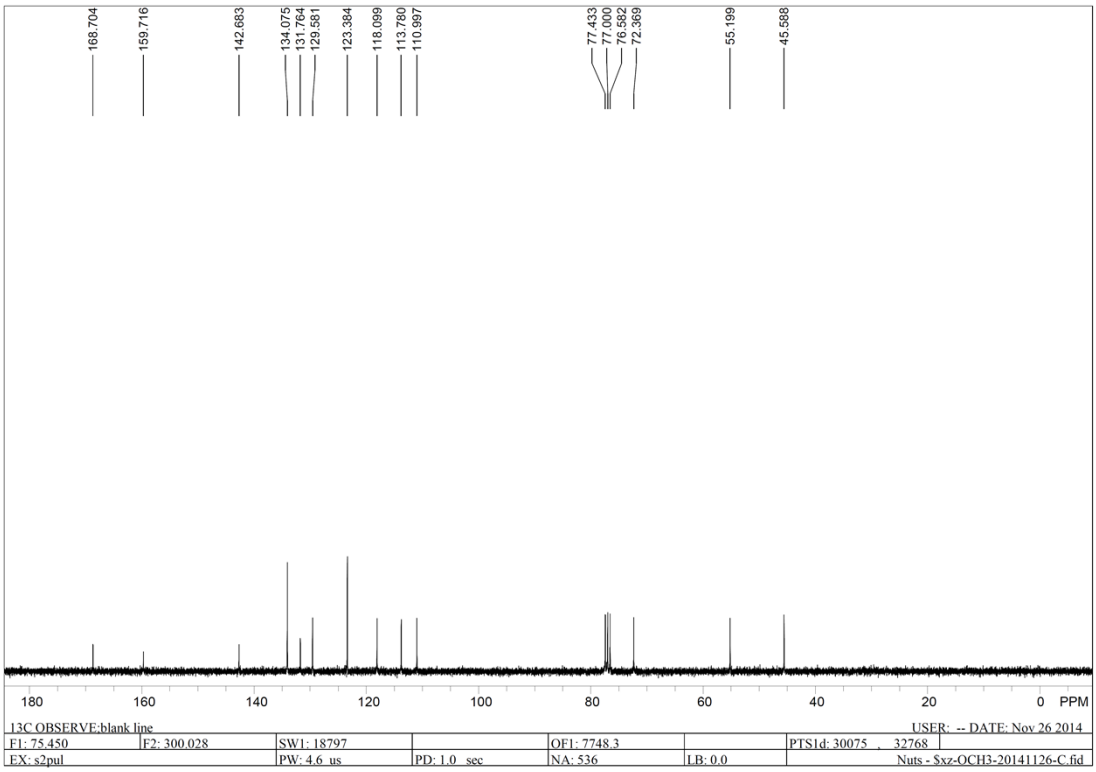
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160
140
120
100
80
60
40
20
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PTS1d: 30075 , 32768
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PW: 4.6 us
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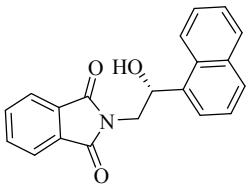
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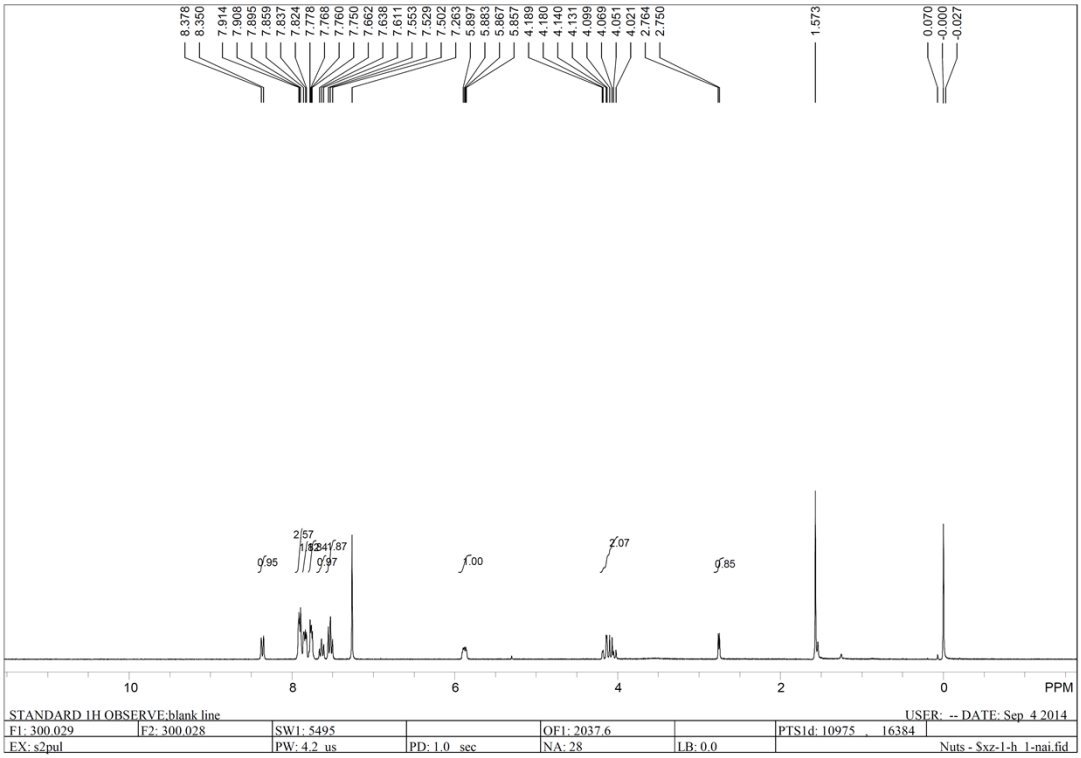
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7.768
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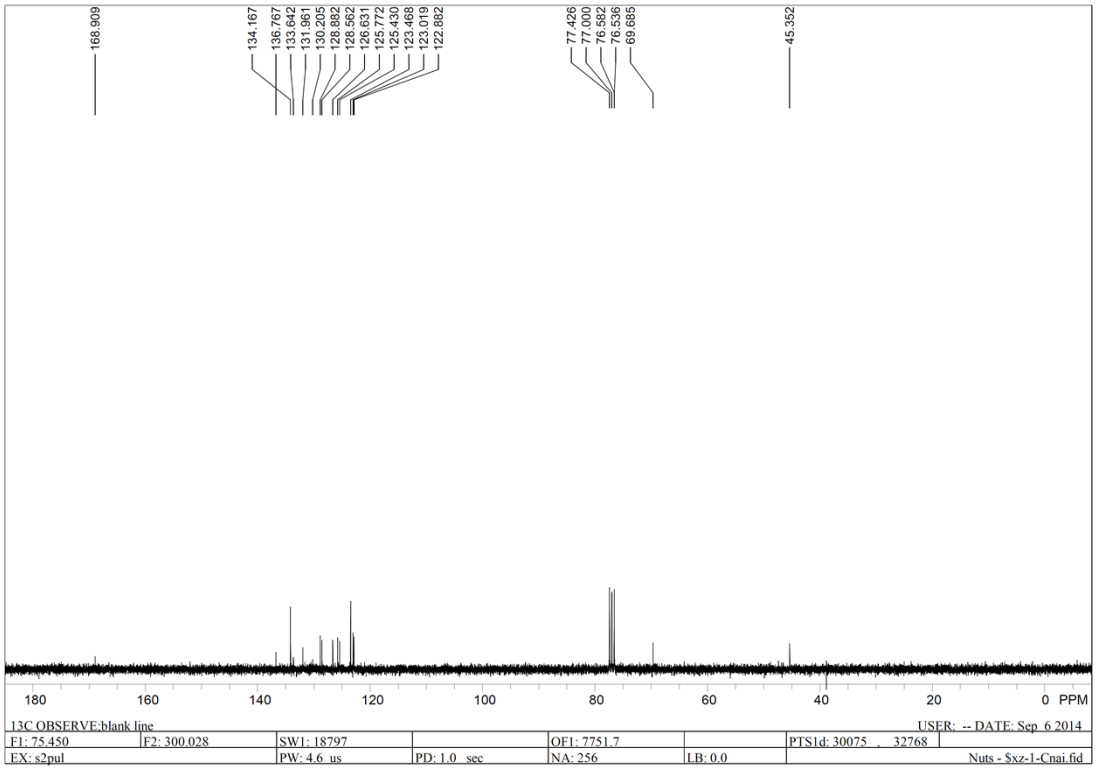
7.750
7.662
7.638
7.611
7.553
7.529
7.502
7.263
5.897
5.883
5.867
5.857
4.189
4.180
4.140
4.131
4.099
4.069
4.051
4.021
2.764
2.750
1.573
0.070
-0.000
-0.027
2.57
0.95
0.97
1.00
2.07
0.85
10
8
6
4
2
0
PPM
STANDARD 1H OBSERVE:blank line
USER: -- DATE: Sep 4 2014
F1: 300.029
F2: 300.028
SW1: 5495
OF1: 2037.6
PTS1d: 10975 , 16384
EX: s2pul
PW: 4.2 us
PD: 1.0 sec
NA: 28
LB: 0.0
Nuts - $xz-1-h 1-nai.fid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122.882
77.426
77.000
76.582
76.536
69.685
45.352
180
160
140
120
100
80
60
40
20
0 PPM
13C OBSERVE:blank line
USER: -- DATE: Sep 6 2014
F1: 75.450
F2: 300.028
SW1: 18797
OF1: 7751.7
PTS1d: 30075 , 32768
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PW: 4.6 us
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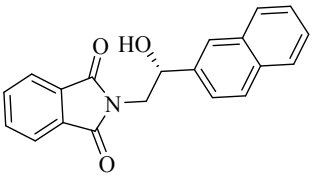
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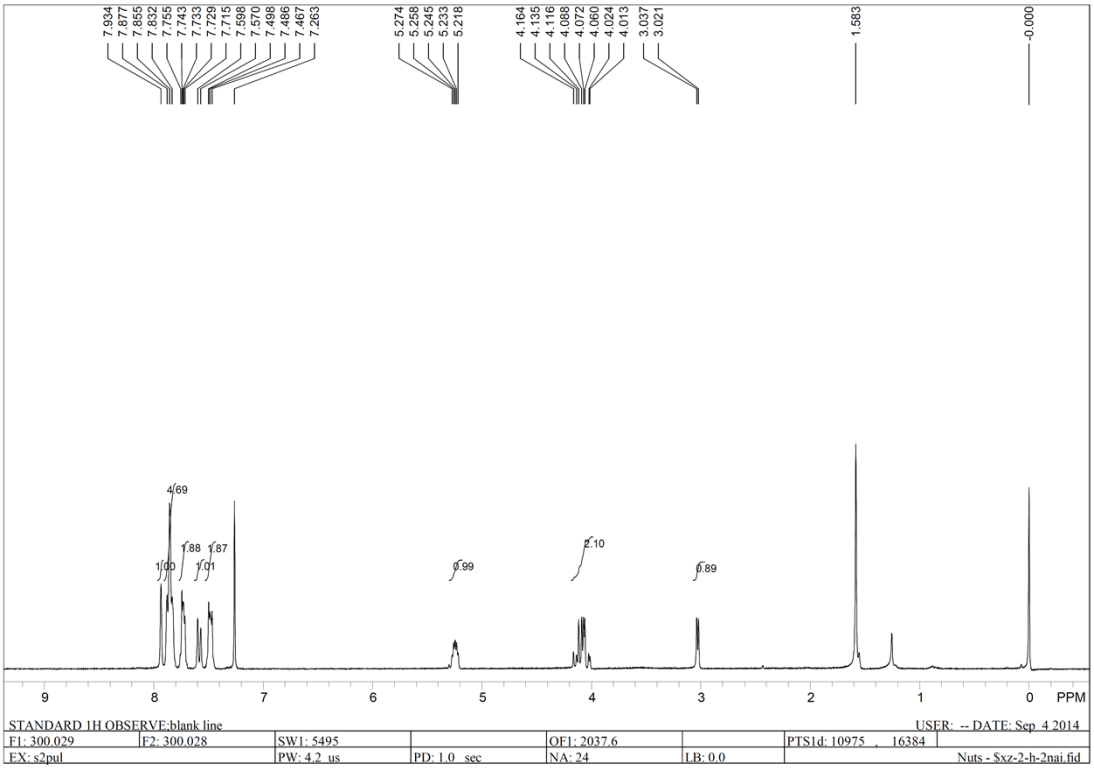
21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7.467
7.263
5.274
5.258
5.245
5.233
5.218
4.164
4.135
4.116
4.088
4.072
4.060
4.024
4.013
3.037
3.021
1.583
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4.69
1.88
1.87
1.00
1.01
0.99
2.10
0.89
9
8
7
6
5
4
3
2
1
0
PPM
STANDARD 1H OBSERVE:blank line
USER: -- DATE: Sep 4 2014
F1: 300.029
F2: 300.028
SW1: 5495
OF1: 2037.6
PTS1d: 10975 , 16384
EX: s2pul
PW: 4.2 us
PD: 1.0 sec
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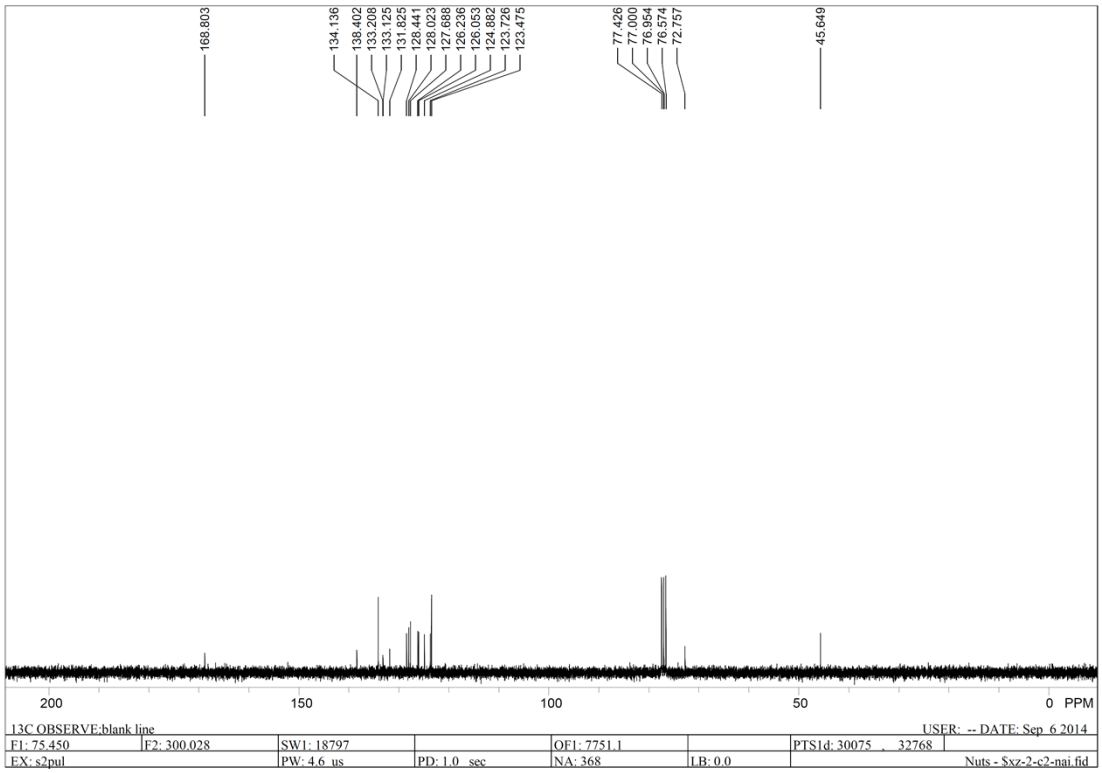
LB: 0.0
Nuts - $xz-2-h-2nai.fid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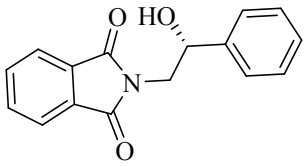
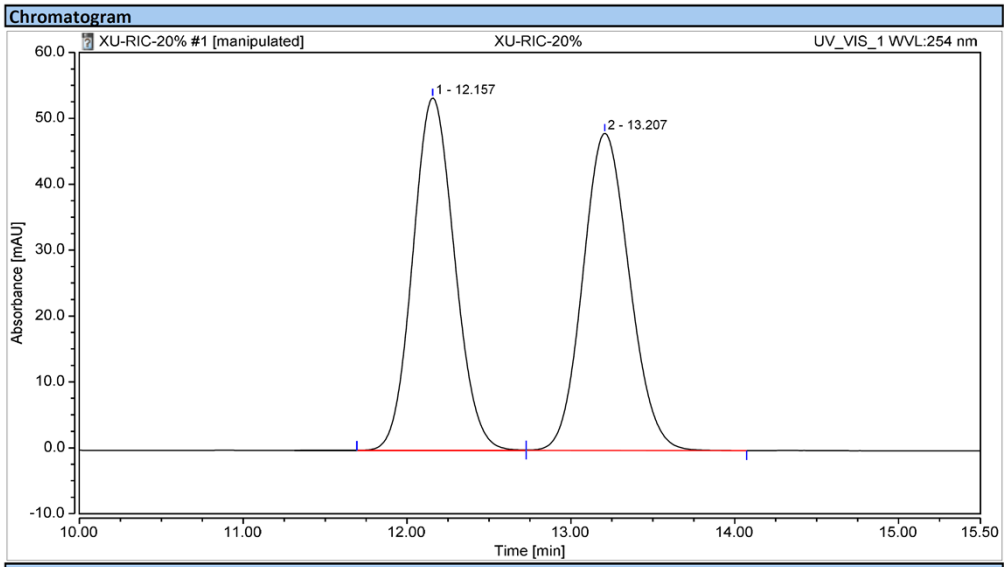
126.236
126.053
124.882
123.726
123.475
77.426
77.000
76.954
76.574
72.757
45.649
200
150
100
50
0
PPM
13C OBSERVE:blank line
USER: -- DATE: Sep 6 2014
F1: 75.450
F2: 300.028
SW1: 18797
OF1: 7751.1
PTS1d: 30075 , 32768
EX: s2pul
PW: 4.6 us
PD: 1.0 sec
NA: 368
LB: 0.0
Nuts - $xz-2-c2-nai.fid

6. HPLC spectra of the products

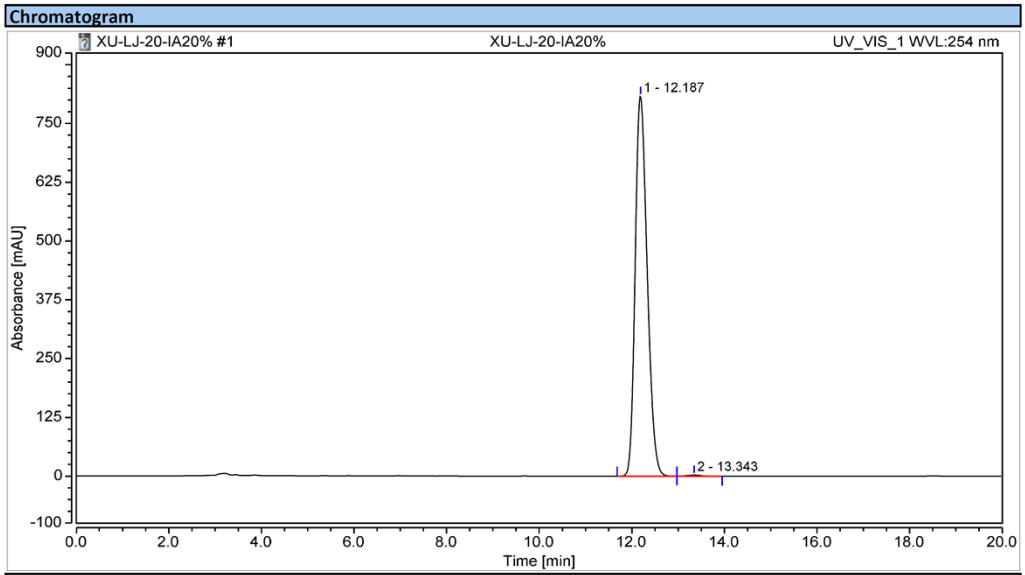


2a



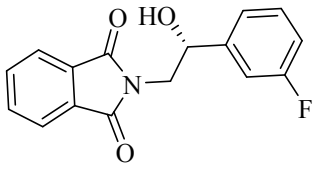
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		12.157	15.829	53.485	49.95	52.63	n.a.
2		13.207	15.857	48.134	50.05	47.37	n.a.
Total:			**31.686**	**101.619**	**100.00**	**100.00**	



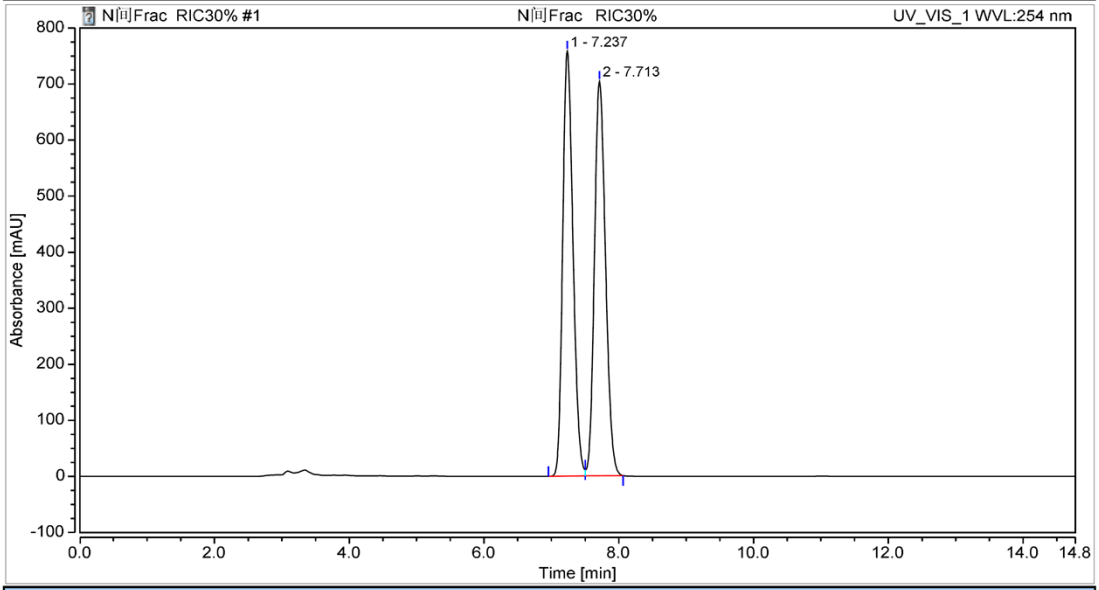
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		12.187	242.791	807.975	99.68	99.72	n.a.
2		13.343	0.786	2.300	0.32	0.28	n.a.
Total:			**243.577**	**810.275**	**100.00**	**100.00**	



2b

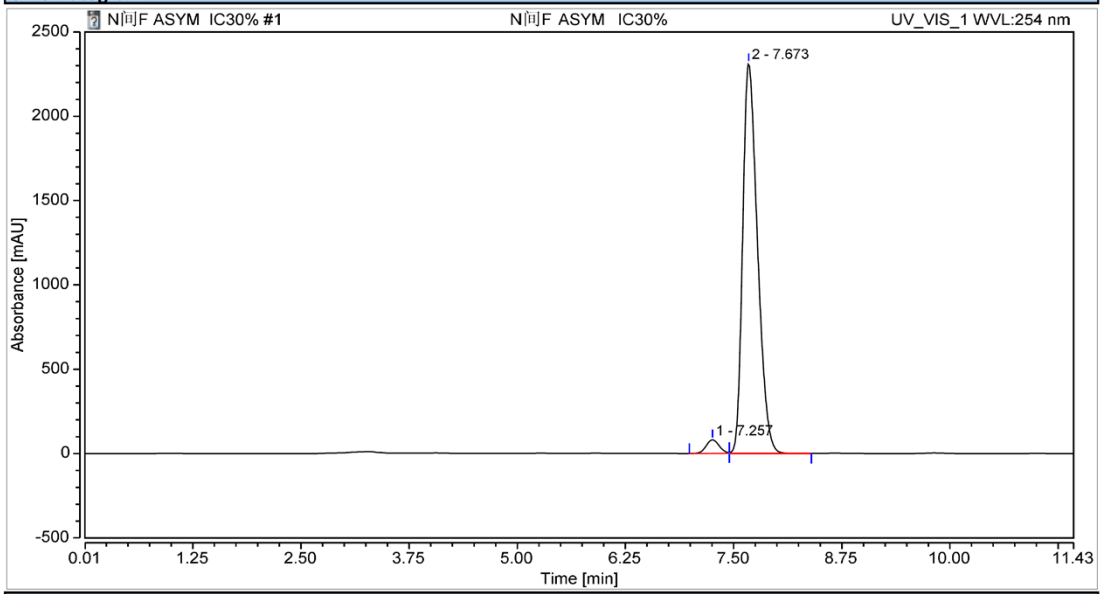
Chromatogram



Integration Results

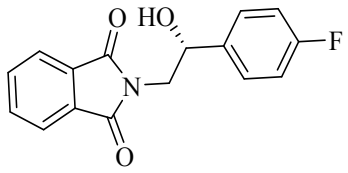
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		7.237	134.090	758.023	49.96	51.85	n.a.
2		7.713	134.298	703.858	50.04	48.15	n.a.
Total:			**268.389**	**1461.881**	**100.00**	**100.00**	

Chromatogram



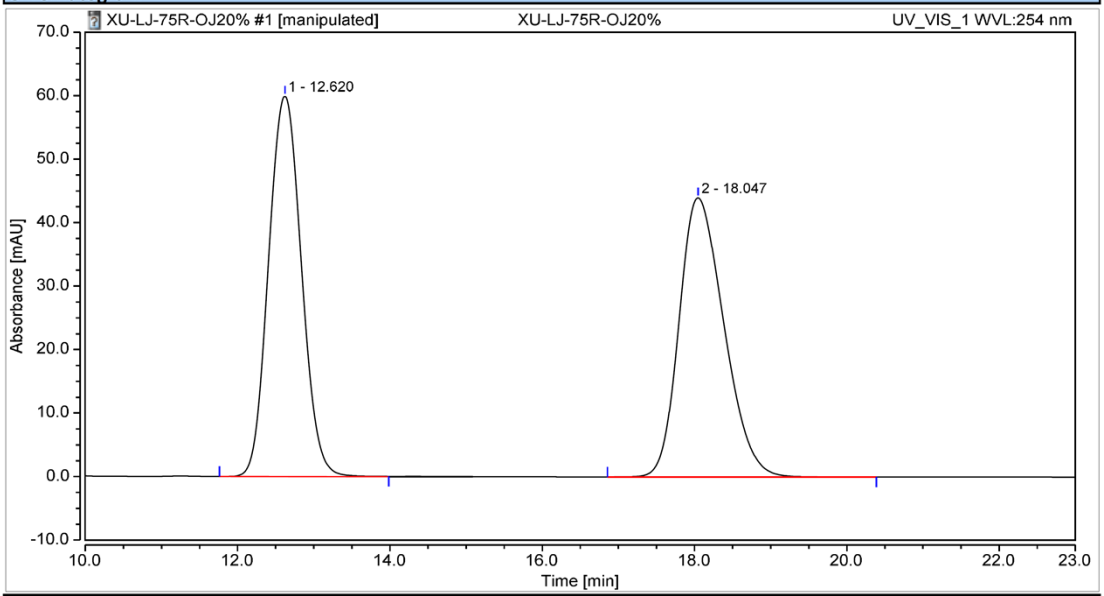
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		7.257	14.281	80.968	3.02	3.38	n.a.
2		7.673	458.656	2312.086	96.98	96.62	n.a.
Total:			**472.937**	**2393.054**	**100.00**	**100.00**	



2c

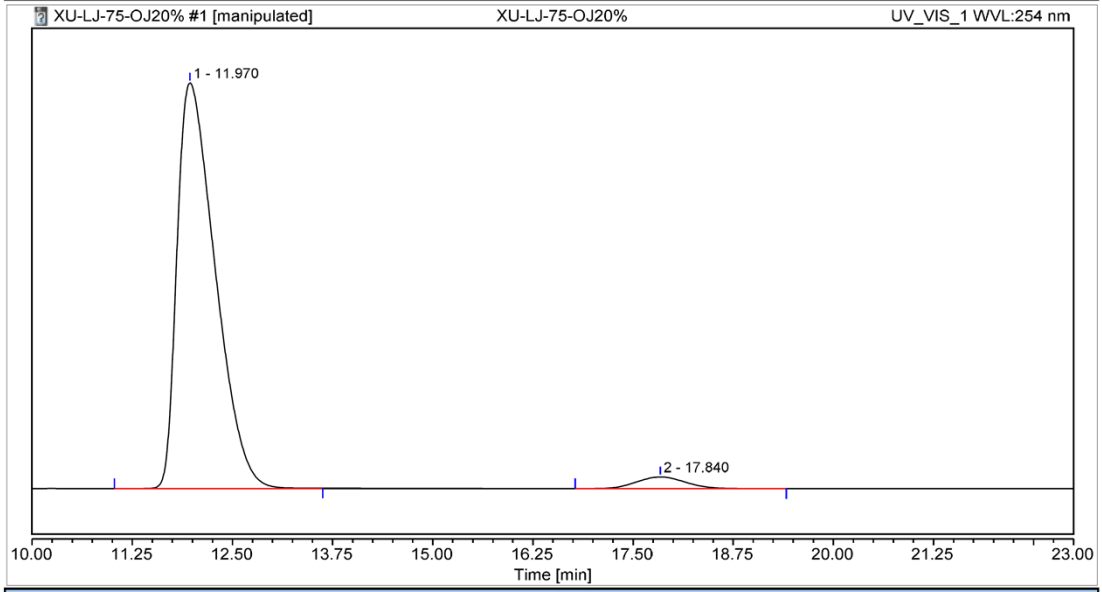
Chromatogram



Integration Results

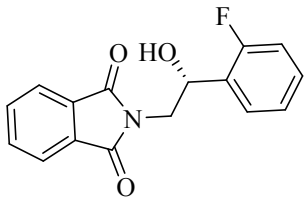
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		12.620	29.865	59.911	49.93	57.67	n.a.
2		18.047	29.944	43.969	50.07	42.33	n.a.
Total:			**59.808**	**103.880**	**100.00**	**100.00**	

Chromatogram



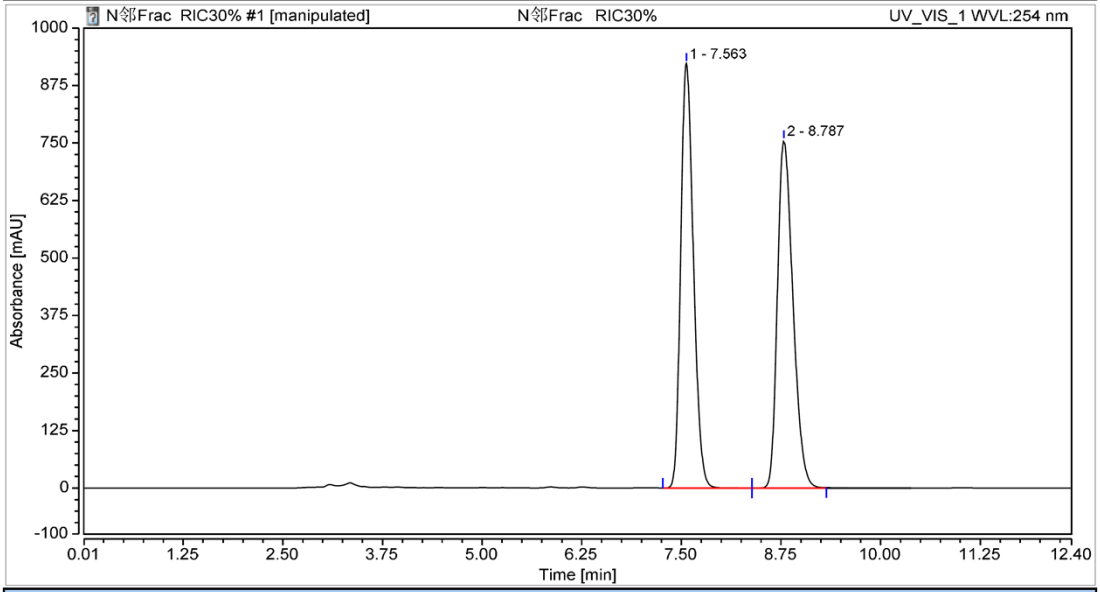
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		11.970	242.876	441.221	96.49	97.23	n.a.
2		17.840	8.847	12.592	3.51	2.77	n.a.
Total:			**251.724**	**453.813**	**100.00**	**100.00**	



2d

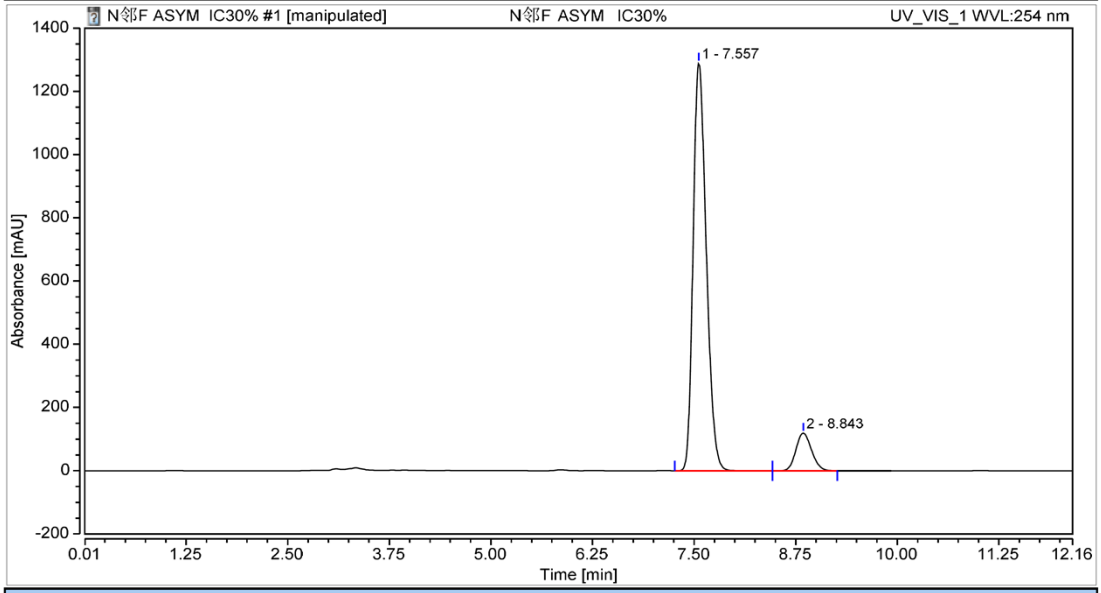
Chromatogram



Integration Results

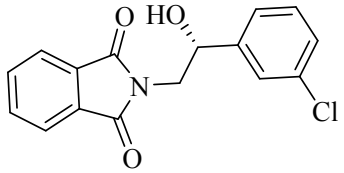
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		7.563	170.325	923.295	49.94	54.99	n.a.
2		8.787	170.744	755.734	50.06	45.01	n.a.
Total:			**341.069**	**1679.029**	**100.00**	**100.00**	

Chromatogram



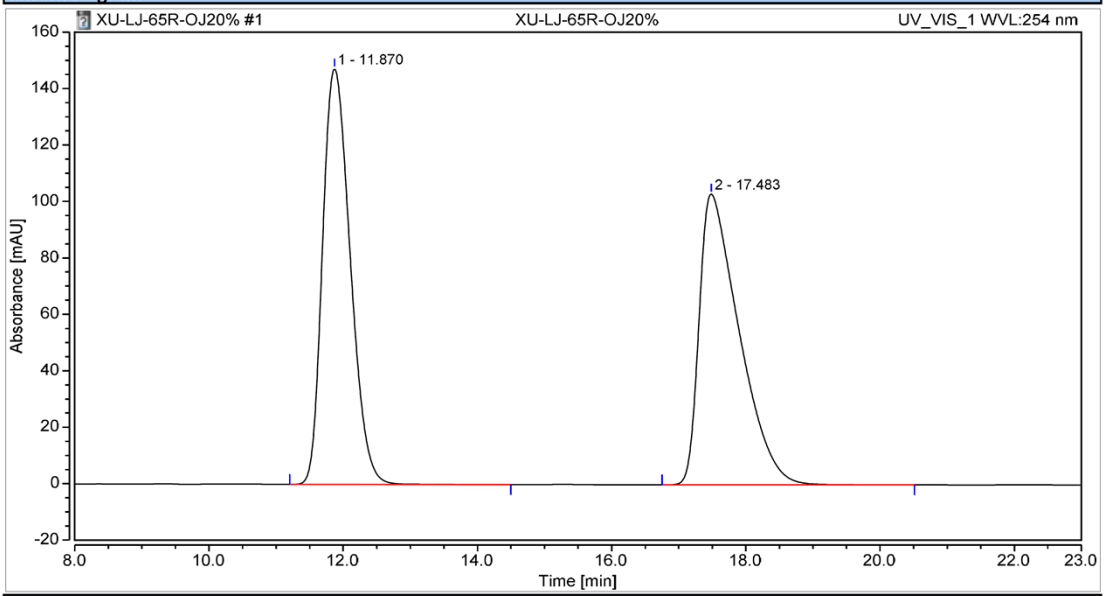
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		7.557	241.856	1290.023	90.06	91.52	n.a.
2		8.843	26.696	119.489	9.94	8.48	n.a.
Total:			**268.552**	**1409.512**	**100.00**	**100.00**	



2e

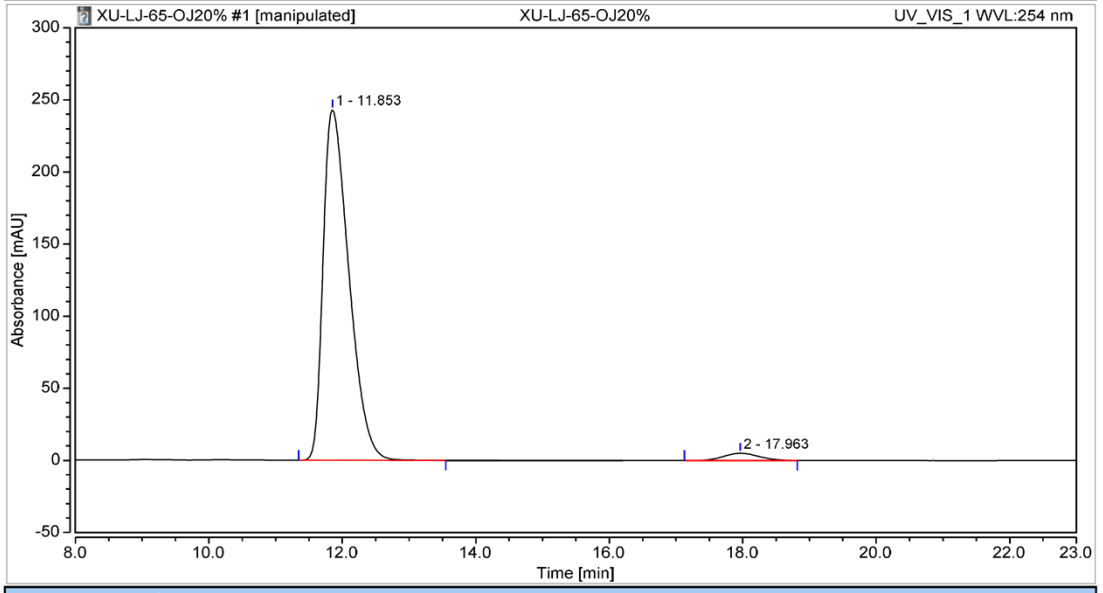
Chromatogram



Integration Results

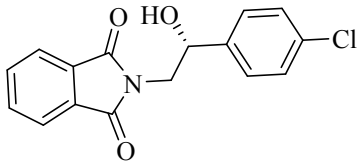
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		11.870	70.351	147.258	49.80	58.83	n.a.
2		17.483	70.908	103.039	50.20	41.17	n.a.
Total:			**141.258**	**250.298**	**100.00**	**100.00**	

Chromatogram



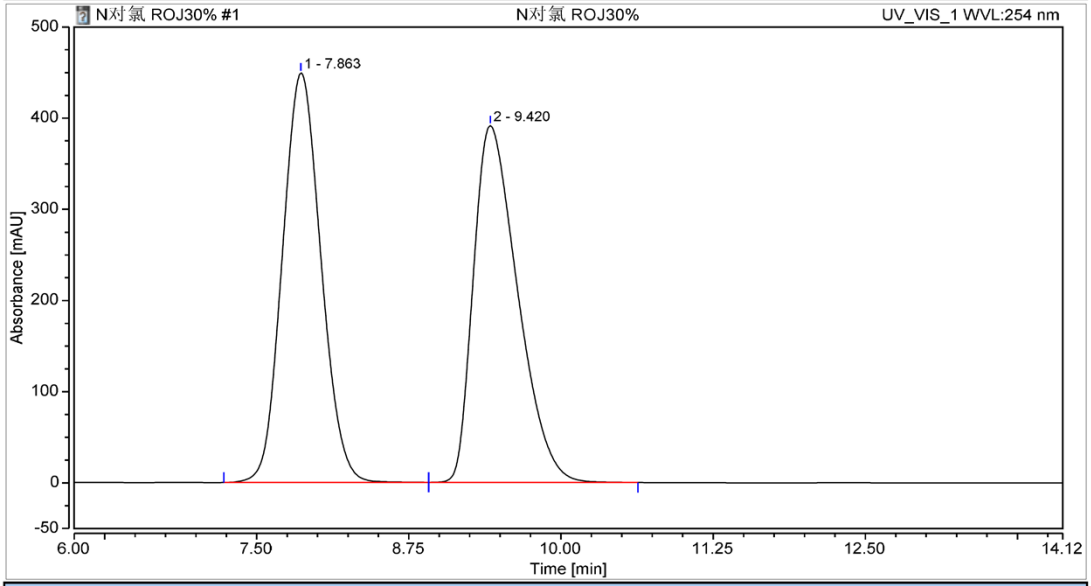
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		11.853	108.511	242.986	97.26	97.99	n.a.
2		17.963	3.058	4.985	2.74	2.01	n.a.
Total:			**111.570**	**247.970**	**100.00**	**100.00**	



2f

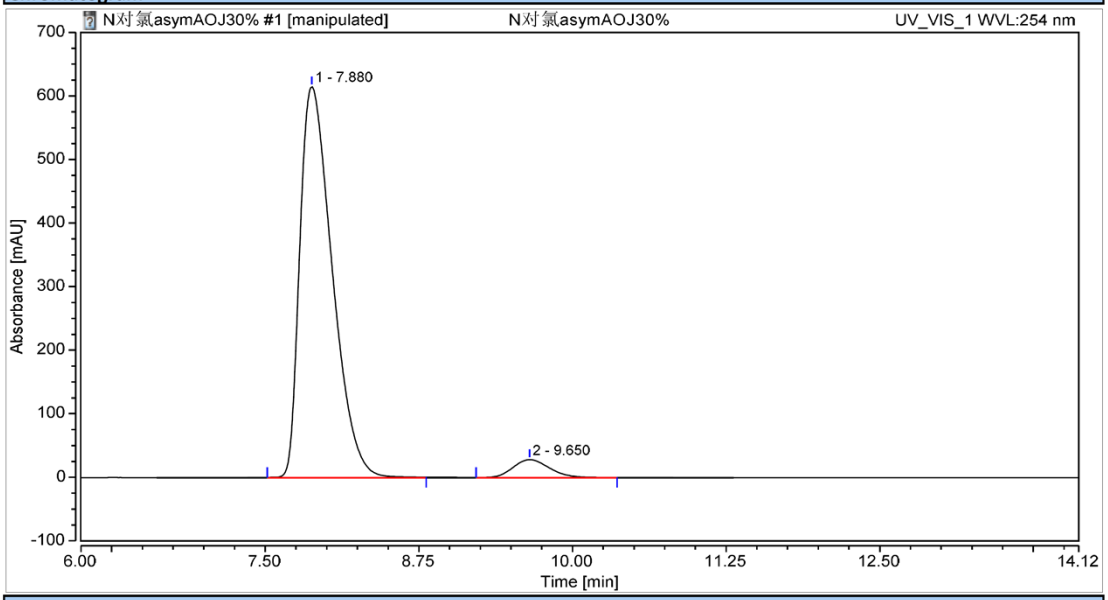
Chromatogram



Integration Results

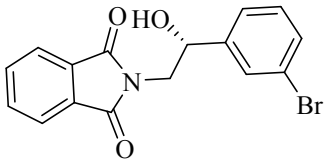
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		7.863	164.825	449.188	50.02	53.45	n.a.
2		9.420	164.677	391.262	49.98	46.55	n.a.
Total:			**329.502**	**840.450**	**100.00**	**100.00**	

Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		7.880	187.410	615.361	95.01	95.61	n.a.
2		9.650	9.842	28.277	4.99	4.39	n.a.
Total:			**197.252**	**643.638**	**100.00**	**100.00**	



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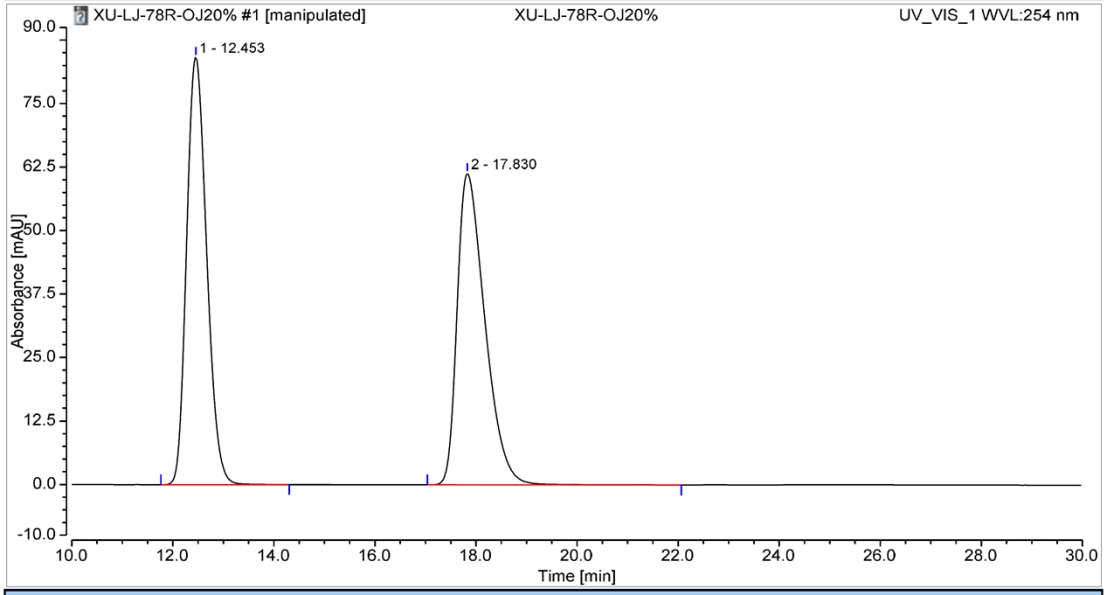
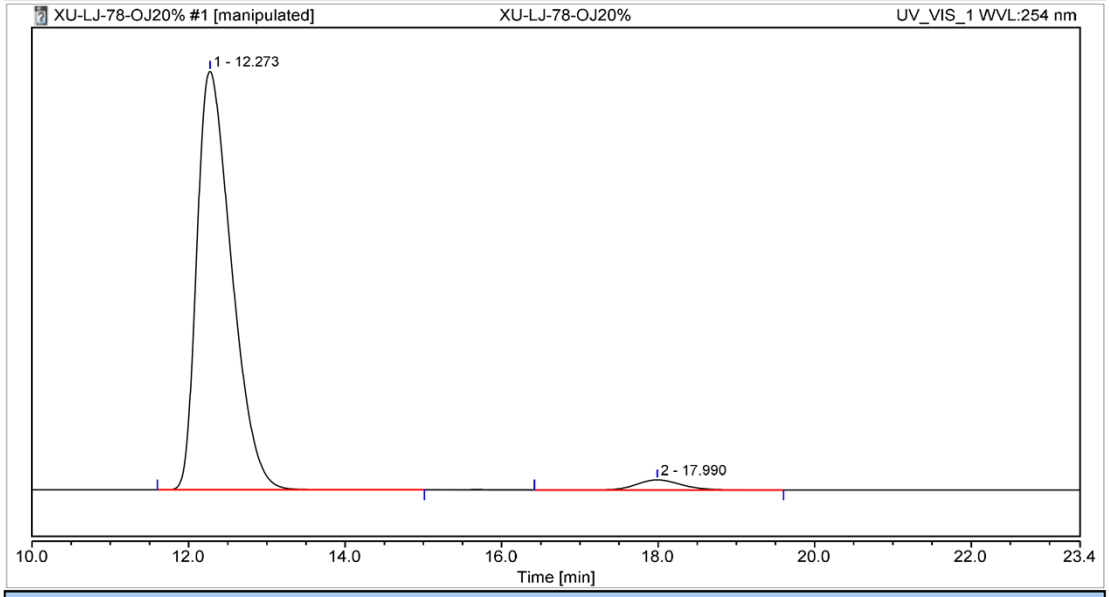
Chromatogram



Integration Results

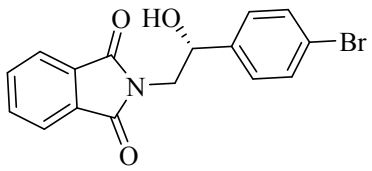
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		12.453	38.681	84.162	49.80	57.86	n.a.
2		17.830	38.986	61.288	50.20	42.14	n.a.
Total:			**77.667**	**145.451**	**100.00**	**100.00**	

Chromatogram



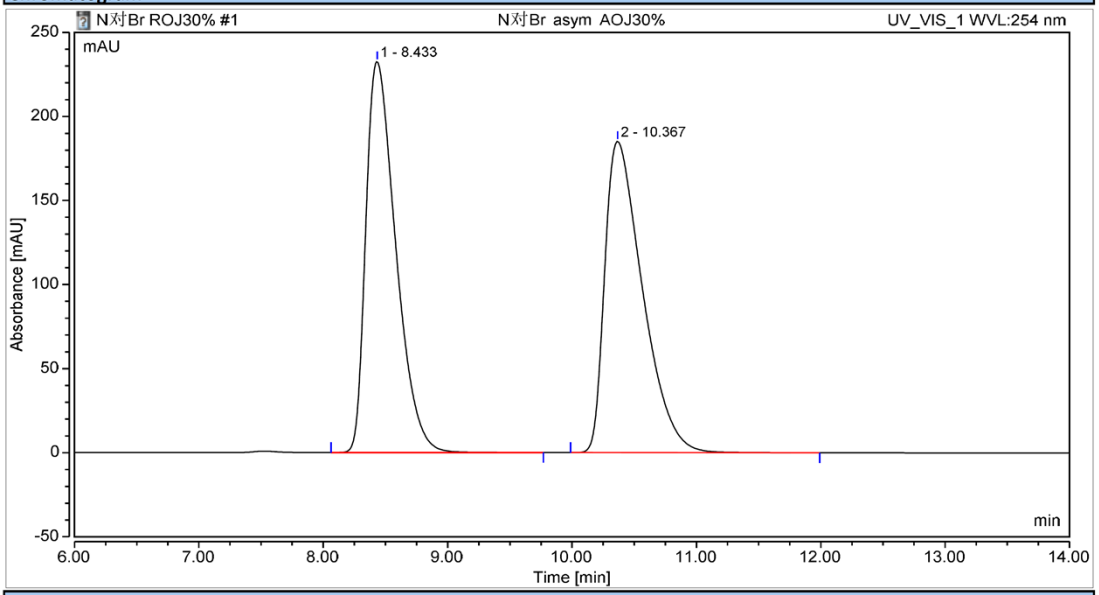
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		12.273	232.616	452.678	96.99	97.65	n.a.
2		17.990	7.226	10.909	3.01	2.35	n.a.
Total:			**239.842**	**463.587**	**100.00**	**100.00**	



2h

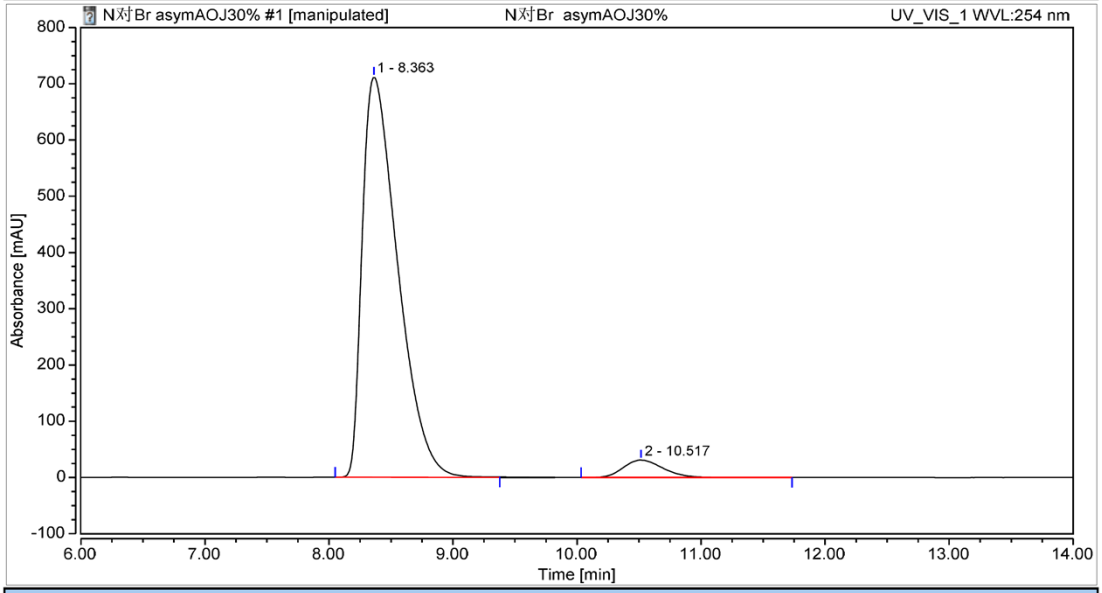
Chromatogram



Integration Results

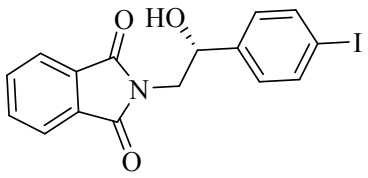
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		8.433	64.749	232.584	49.87	55.68	n.a.
2		10.367	65.082	185.122	50.13	44.32	n.a.
Total:			**129.830**	**417.707**	**100.00**	**100.00**	

Chromatogram



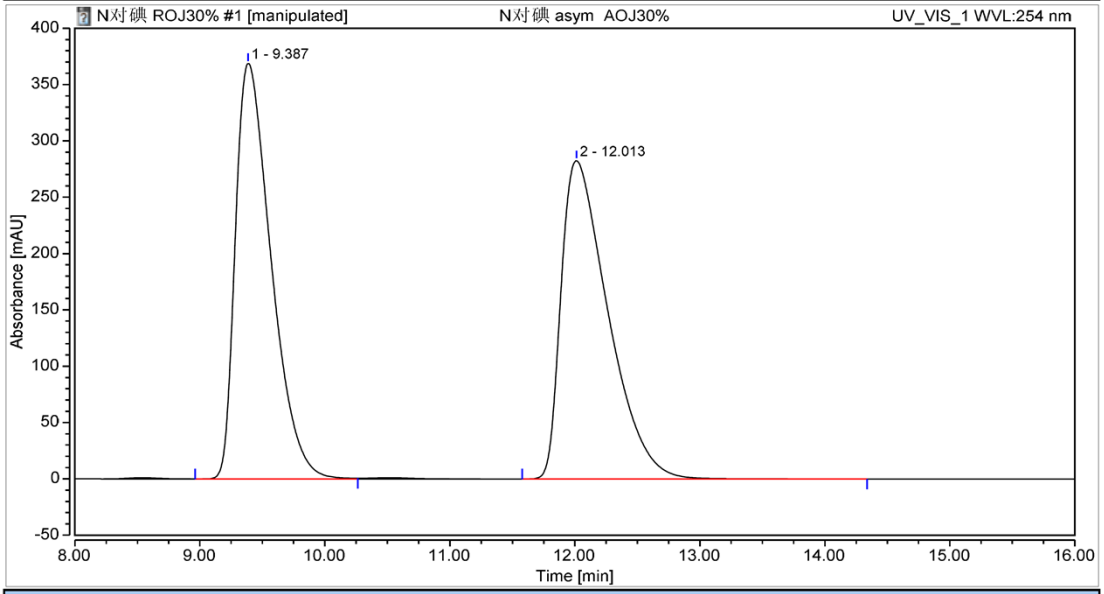
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		8.363	235.548	711.357	95.37	95.84	n.a.
2		10.517	11.436	30.897	4.63	4.16	n.a.
Total:			**246.984**	**742.253**	**100.00**	**100.00**	



2i

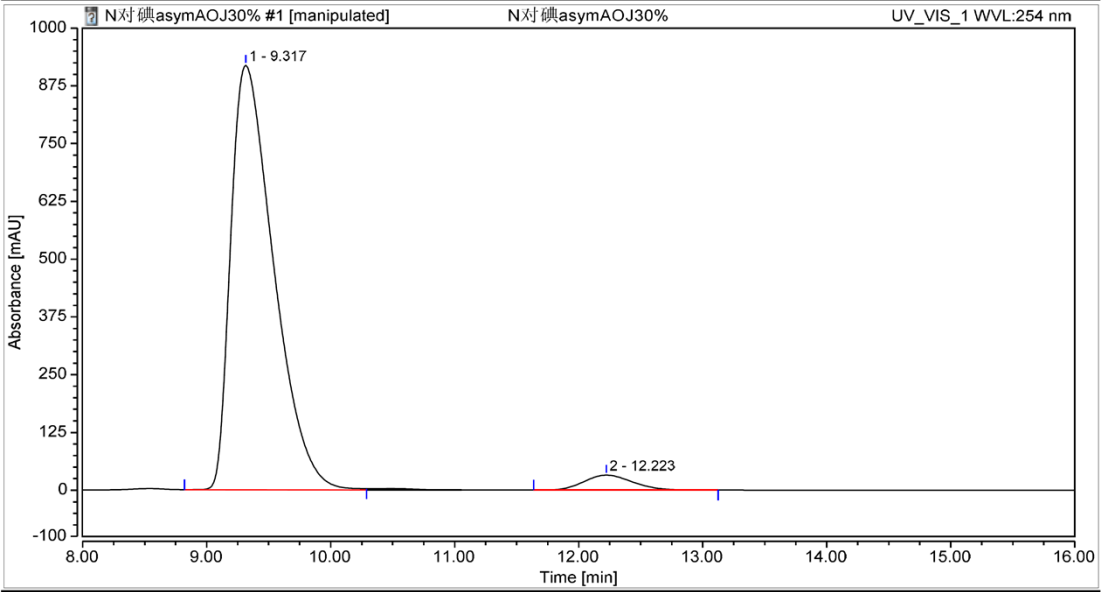
Chromatogram



Integration Results

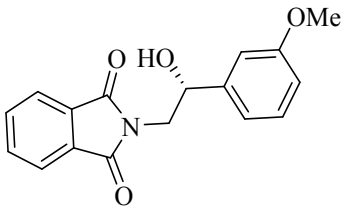
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		9.387	122.112	368.983	49.87	56.63	n.a.
2		12.013	122.752	282.603	50.13	43.37	n.a.
Total:			**244.864**	**651.586**	**100.00**	**100.00**	

Chromatogram



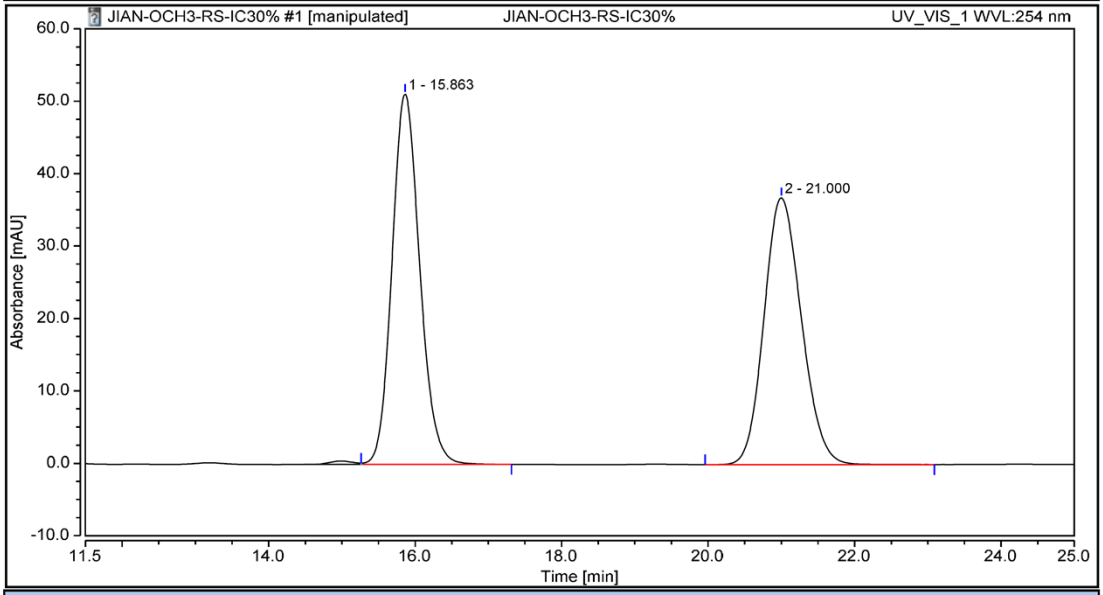
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		9.317	367.343	918.294	96.16	96.60	n.a.
2		12.223	14.685	32.279	3.84	3.40	n.a.
Total:			**382.028**	**950.572**	**100.00**	**100.00**	



2j

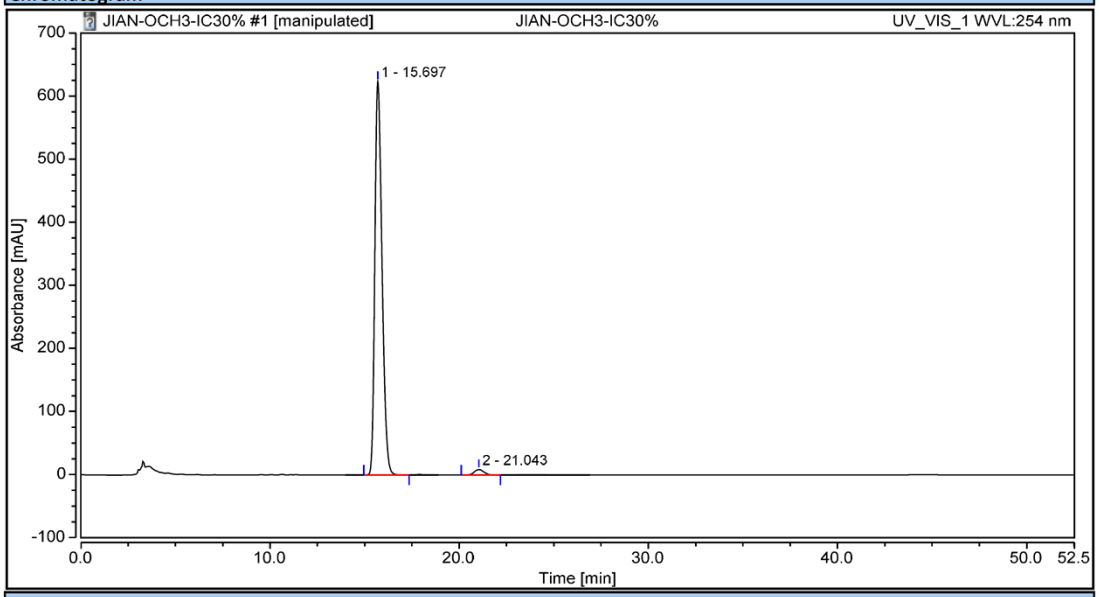
Chromatogram



Integration Results

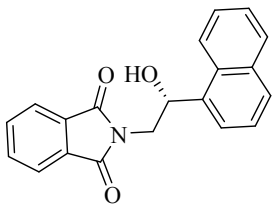
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		15.863	22.431	51.136	50.76	58.13	n.a.
2		21.000	21.758	36.835	49.24	41.87	n.a.
Total:			**44.188**	**87.971**	**100.00**	**100.00**	

Chromatogram



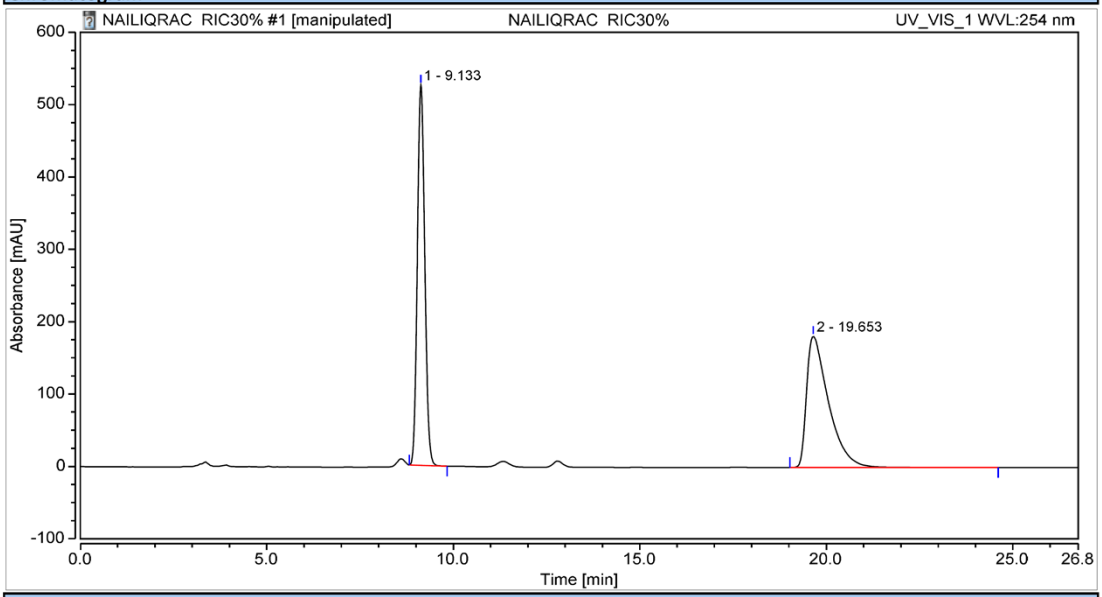
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		15.697	273.921	623.864	98.18	98.64	n.a.
2		21.043	5.090	8.604	1.82	1.36	n.a.
Total:			**279.011**	**632.468**	**100.00**	**100.00**	



2k

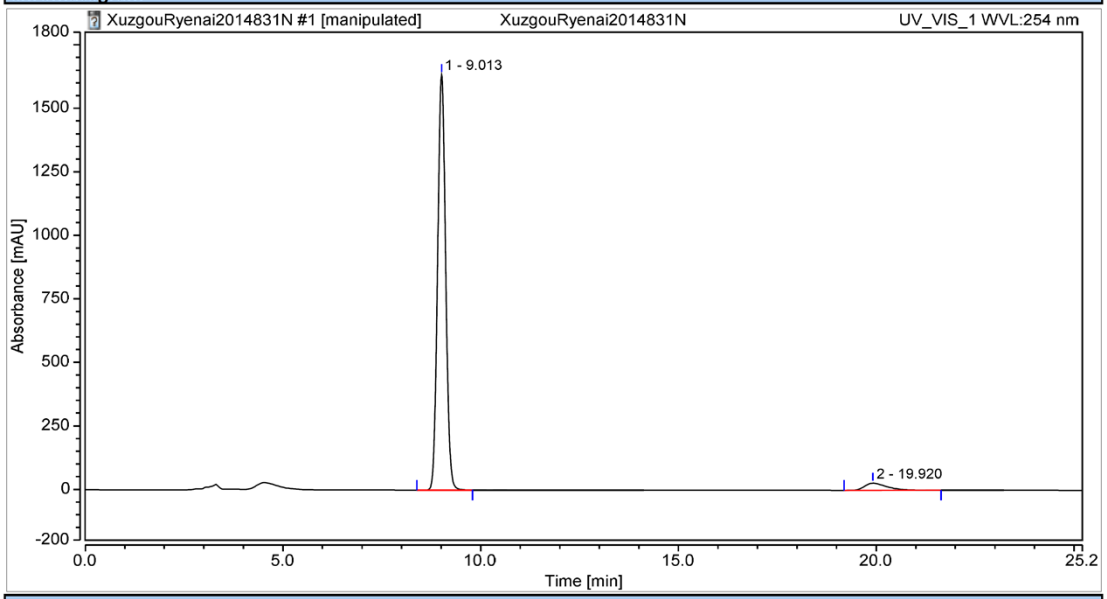
Chromatogram



Integration Results

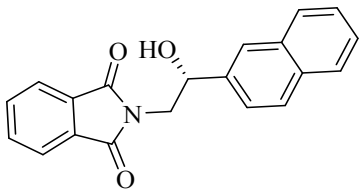
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		9.133	120.966	525.833	49.51	74.37	n.a.
2		19.653	123.367	181.197	50.49	25.63	n.a.
Total:			**244.333**	**707.030**	**100.00**	**100.00**	

Chromatogram



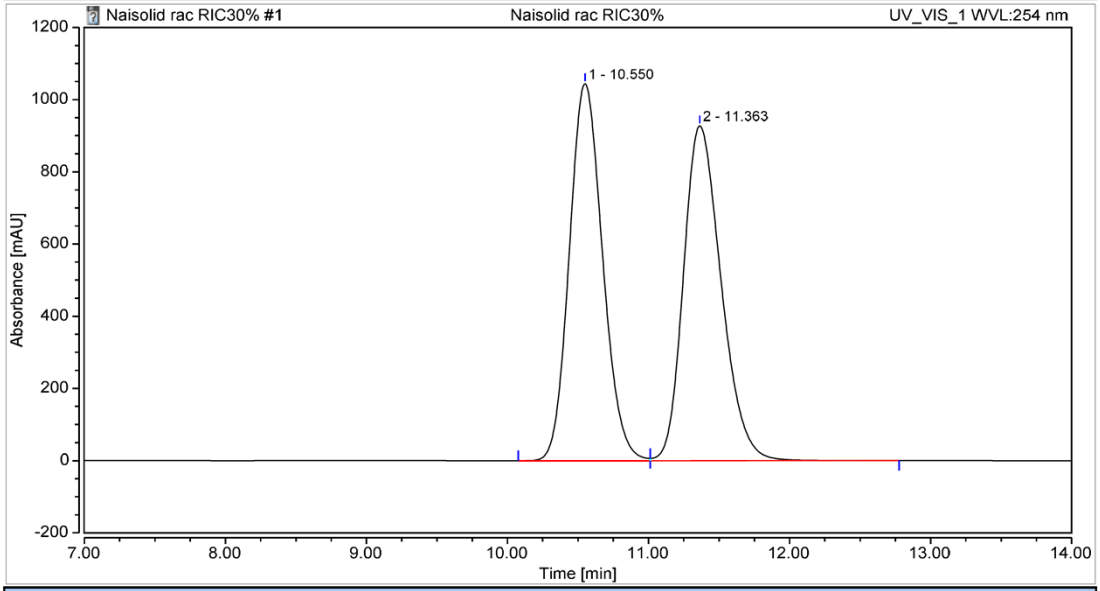
Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		9.013	386.064	1636.568	95.46	98.32	n.a.
2		19.920	18.359	27.910	4.54	1.68	n.a.
Total:			**404.422**	**1664.477**	**100.00**	**100.00**	



21

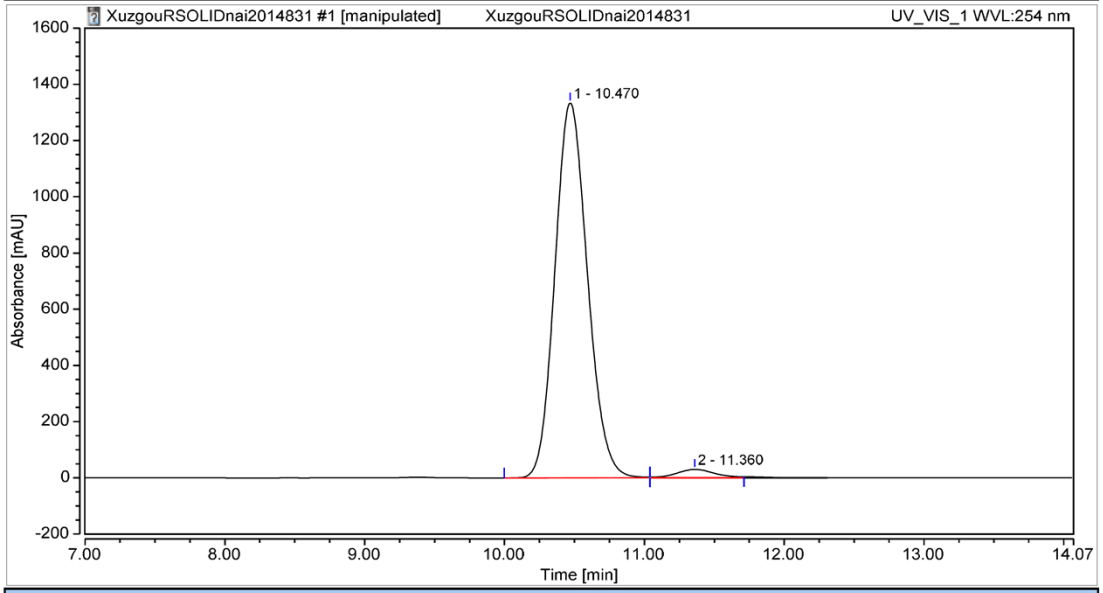
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		10.550	285.101	1044.378	49.88	52.97	n.a.
2		11.363	286.474	927.347	50.12	47.03	n.a.
Total:			**571.575**	**1971.725**	**100.00**	**100.00**	

Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		10.470	360.027	1334.645	97.38	97.80	n.a.
2		11.360	9.673	29.955	2.62	2.20	n.a.
Total:			**369.701**	**1364.600**	**100.00**	**100.00**	