Electronic Supplementary Material (ESI) for Chemical Communications

Friedel-Crafts-type reactions with ureas and thioureas.

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Experimental Methods:

General. All reactions were performed using oven-dried glassware under an argon atmosphere. Trifluoromethanesulfonic acid was freshly distilled prior to use. All commercially available compounds and solvents were used as received. ^{1}H NMR and ^{13}C NMR were done either using a Brüker 300 or 500 MHz spectrometer. Low-resolution mass spectra were obtained from a gas chromatography instrument equipped with a mass-selective detector, while high-resolution mass spectra were obtained from a commercial analytical laboratory. Compounds **1**, **2**, **10-11**, **14-15**, **17**, **18**, **21, 23, 30,** and **33-34** are available from commercial suppliers or known from previous literature reports.

Urea synthesis, general procedure A: The appropriate amine (1 mmol) is added to a cooled solution (0 °C) of aryl isocyanate (1 mmol) in anhydrous THF (15 mL). The mixture is stirred for 12 hours at 25 °C, after which the products are partitioned between ethyl acetate water. The organic solution is further washed with H_2O, brine (2x) and dried over anhydrous sodium sulfate. Most urea products are formed in >95% purity and may be used in the subsequent reaction. However, further purification may be accomplished via column chromatography (hexane:ethyl acetate).

3,4-Dihydroisoquinolin-1(2*H*)-one and 3,4-dihydroisoquinolin-1(2*H*)-thione synthesis, general procedure B: Trifluoromethanesulfonic acid (1.4 mL, 16 mmol) is added to a solution of urea or thiourea (1 mmol) in anhydrous CH_2Cl_2 (2 mL). The mixture is stirred in a sealed vessel under argon for 12 hrs at 50 °C and then poured over ice. The products are extracted into $CHCl_3$ and the organic solution is washed with H_2O (2x), brine (2x) and dried over anhydrous sodium sulfate. The crude product is isolated and purified via column chromatography (hexane:ethyl acetate). Chloroform (without ethanol preservative) or 1,2-dichloroethane may also be used as solvents for the reactions.

Amide and thioamide synthesis (intermolecular), general procedure C: Trifluoromethanesulfonic acid (1.4 mL, 16 mmol) is added to a solution of urea **27** or **28** (1 mmol) in benzene (2 mL). The mixture is stirred for 12 hrs at 50 °C and then poured over ice. The products are extracted into $CHCl_3$ and the organic solution is washed with H_2O (2x), brine (2x) and dried over anhydrous sodium sulfate. The crude product is isolated and purified via column chromatography (hexane:ethyl acetate).

Procedure for the Preparation of Compound 9: 2-Nitrophenyl isocyanate (0.16 g, 1 mmol) is added to a cooled solution (0 °C) of (*S*)-2-amino-3-phenyl-1-propanol (0.15 g, 1 mmol) anhydrous THF (20 mL). The solution is stirred for 12 hrs at 25 °C, after which it is partitioned between cold water and $CHCl_3$. The organic layer is separated, washed with H_2O (2x), brine (2x) and dried over anhydrous sodium sulfate. The crude product is isolated and purification is done via column chromatography (hexane:ethyl acetate). The resulting alcohol product is dissolved in anhydrous CH_2Cl_2 (20 mL) and triethylamine (0.21 mL, 1.5 mmol) is added. To this solution, 6-chloronicotinoyl chloride (0.176 g, 1 mmol) is added and the mixture is stirred for 12 hrs at 25°C. The resulting mixture is then poured over ice/water and partition between water and $CHCl_3$. The organic solution is washed with H_2O (2x), brine (2x) and dried over anhydrous sodium sulfate. The crude product is isolated and purified via column chromatography (hexane:ethyl acetate).

1-(2-nitrophenyl)-3-phenethylurea (2): yellow solid, mp = 115-117°C. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.90 (t, 2H, *J* = 6.9 Hz), 3.57 (q, 2H, *J* = 6.9 Hz), 5.78 (s, 1H), 7.03 (t, 1H, *J* = 8.1 Hz), 7.18-7.33 (m, 5H), 7.58 (t, 1H, *J* = 8.1 Hz), 8.14 (d, 1H, *J* = 8.7 Hz), 8.63 (d, 1H, *J* = 8.7 Hz), 9.74 (s, 1H). ^{13}C NMR

($CDCl_3$, 300 MHz) δ 36.1, 41.8, 121.3, 121.6, 125.7, 126.5, 128.6, 128.8, 135.4, 135.9, 137.2, 138.8, 154.3. Low-resolution mass spectrum (EI), m/z: 285 (M+), 267, 194, 138, 91. High-resolution mass spectrum, $C_{15}H_{15}O_3N_3$ calcd, 285.11135, found 285.11054.

1-(4-methylphenethyl)-3-(4-nitrophenyl)urea (4): beige solid, mp = 153-155°C. ^{1}H NMR ($(CD_3)_2CO$, 300MHz) δ 2.28 (s, 3H), 2.80 (t, 2H, *J* = 7.2 Hz), 3.45-3.51 (m, 2H), 6.05(s, 1H), 7.12-7.16 (m, 4H), 7.70-7.73 (m, 2H), 8.12-8.15 (m, 2H), 8.67 (s, 1H). ^{13}C NMR ($(CD_3)_2CO$, 300MHz) δ 20.1, 35.5, 41.2, 117.0, 124.8, 128.6, 129.0, 135.4, 136.4, 141.4, 147.2, 154.3. High-resolution (TOF) mass spectrum, $C_{16}H_{18}O_3N_3$ (MH+) calcd, 300.1348, found 300.1350.

1-(4-ethylphenethyl)-3-(4-nitrophenyl)urea (5): yellow solid, mp = 125-127°C. ^{1}H NMR ($(CD_3)_2CO$, 300MHz) δ 1.19 (t, 3H, *J* = 7.5 Hz), 2.60(q, 2H, *J* = 7.5 Hz), 2.81 (t, 2H, *J* = 7.2 Hz), 3.45-3.52 (m, 2H), 6.08 (s, 1H), 7.14-7.15 (m, 4H), 7.70-7.73 (m, 2H), 8.12-8.15 (m, 2H), 8.67 (s, 1H). ^{13}C NMR ($(CD_3)_2CO$, 300MHz) δ 15.2, 28.1, 35.6, 41.2, 117.0, 124.8, 127.8, 128.7, 136.6, 141.3, 141.9, 147.1, 154.4. High-resolution (TOF) mass spectrum, $C_{17}H_{20}O_3N_3$ (MH+) calcd, 314.1505, found 314.1503.

1-(2-(biphenyl-4-yl)ethyl)-3-(4-nitrophenyl)urea (6): yellow solid, mp = 168-170°C. ^{1}H NMR ($(CD_3)_2CO$, 300 MHz) δ 2.88-2.94 (m, 2H), 3.56 (q, 2H, *J* = 7.5 Hz), 6.13 (s, 1H), 7.34-7.48 (m, 5H), 7.58-7.66 (m, 4H), 7.71-7.75 (m, 2H), 8.13-8.16 (m, 2H), 8.68 (s, 1H). ^{13}C NMR ($(CD_3)_2CO$, 300MHz) δ 35.58, 41.08, 117.04, 124.83, 126.65, 126.88, 127.14, 128.82, 129.34, 138.77, 138.90, 140.70, 141.33, 147.14, 154.39. High-resolution (TOF) mass spectrum, $C_{21}H_{20}O_3N_3$ (MH+) calcd, 362.1505, found 362.1504.

1-(4-nitrophenyl)-3-(2-phenylpropyl)urea (7): yellow solid, mp = 171-174°C. ^{1}H NMR ($(CD_3)_2CO$, 300MHz) δ 1.27,(d, 3H, *J* = 6.9 Hz), 2.96-3.04 (m, 1H), 3.34-3.55 (m, 2H), 7.22-7.34 (m, 5H), 7.66-7.71 (m, 2H), 8.11-8.14 (m, 2H), 8.62 (s, 1H). ^{13}C NMR ($(CD_3)_2CO$, 300MHz) δ 18.9, 40.0, 46.4, 117.0, 124.8, 126.4, 127.2, 128.5, 141.3, 144.7, 147.1, 154.4. High-resolution (TOF) mass spectrum, $C_{16}H_{18}O_3N_3$ (MH+) calcd, 300.1348, found 300.1345.

1-(1-hydroxy-3-phenylpropan-2-yl)-3-(2-nitrophenyl)urea (8): yellow solid, mp = 137-138°C. ^{1}H NMR ($(CD_3)_2CO$, 300 MHz) δ 2.83-3.03 (m, 2H), 3.61(dd, 2H, *J* = 1.8, 4.8 Hz), 4.02-4.16 (m, 2H), 7.09 (dt, 2H, *J* = 1.5, 7.2 Hz), 7.18-7.21 (m, 1H), 7.25-7.33 (m, 4H), 7.62 (dt, 1H, *J* = 1.8, 7.2 Hz), 8.11 (dd, 1H, *J* = 1.5, 8.4 Hz), 8.61 (dd, 1H, *J* = 1.5, 8.7 Hz), 9.55 (s, 1H). ^{13}C NMR ($(CD_3)_2CO$, 300MHz) δ 37.2, 53.7, 63.0, 120.8, 121.6, 125.3, 126.0, 128.2, 129.3, 135.1, 135.9, 137.1, 139.1, 154.0. High-resolution mass spectrum, $C_{16}H_{17}O_4N_3$ calcd, 315.12191, found 315.12002.

2-(3-(2-nitrophenyl)ureido)-3-phenylpropyl 6-chloronicotinate (9): yellow oily solid, ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.96-3.12 (m, 2H), 4.36-4.59 (m, 3H), 5.65 (d, 1H, *J* = 8.4 Hz), 7.05 (dt, 1H, *J* = 1.2, 7.2 Hz), 7.22-7.40 (m, 4H), 7.58 (dt, 1H, *J* = 1.5, 7.2 Hz), 8.12 (dd, 1H, *J* = 1.5, 8.4 Hz), 8.20 (dd, 1H, *J* = 2.4, 8.4 Hz), 8.55 (dd, 1H, *J* = 1.2, 8.7 Hz), 8.98 (d, 1H, *J* = 1.8 Hz), 9.72 (s, 1H). ^{13}C NMR ($CDCl_3$, 300 MHz) δ 37.9, 50.7, 66.3, 121.5, 121.6, 124.3, 124.6, 125.7, 127.0, 128.8, 129.2, 135.4, 136.0, 136.7, 136.7, 139.7, 151.8, 153.6, 155.9, 164.4. Low-resolution mass spectrum (EI), m/z: 297, 273, 199, 140, 91. High-resolution mass spectrum (CI), $C_{22}H_{20}O_5N_4Cl$ calcd, 455.1122, found 455.1120.

7-ethyl-3,4-dihydroisoquinolin-1(2H)-one (12): ^{1}H NMR ($CDCl_3$, 500MHz) δ 1.26 (t, 3H, *J* = 7.5 Hz), 2.69 (q, 2H, *J* = 7.5 Hz), 2.97 (t, 2H, J = 7), 3.57 (dt, 2H, *J* = 2, 6.5 Hz), 6.65 (s, 1H), 7.15-7.16 (m, 1H),

7.28-7.32 (m, 1H), 7.92 (m, 1H). ^{13}CNMR ($CDCl_3$, 500MHz) δ 15.5, 27.9, 28.5, 40.3, 127.2, 127.3, 128.6, 131.9, 136.1, 143.3, 166.8. Low Resolution Mass Spectra (EI); m/z: 175, 160, 146, 131, 118, 103, 91, 77, 65, 51. High-resolution mass spectrum, $C_{11}H_{13}ON$ calcd, 175.09972, found 175.10030.

7-phenyl-3,4-dihydroisoquinolin-1(2H)-one (13): ^{1}H NMR ($CDCl_3$, 500MHz) δ 3.06 (t, 2H, *J* = 6.5 Hz), 3.62 (dt, 2H, *J* = 2.5, 6.5 Hz), 6.46 (s, 1H), 7.28-7.39 (m, 2H), 7.45-7.48 (m, 2H), 7.65-7.67 (m, 2H), 7.72 (dd, 1H, *J* = 2.0, 8.0 Hz), 8.35 (d, 1H, *J* = 2.0 Hz). ^{13}C NMR ($CDCl_3$, 500 MHz) δ 28.0, 40.3, 126.5, 127.0, 127.6, 127.8, 128.8, 129.2, 130.7, 137.7, 140.0, 140.2, 166.4. Low Resolution Mass Spectra (EI); m/z: 223, 204, 194, 178, 166, 152, 139, 115, 97, 82, 63. High-resolution mass spectrum, $C_{15}H_{13}ON$ calcd, 223.09972, found 223.09951.

(1-oxo-1,2,3,4-tetrahydroisoquinolin-3-yl)methyl 6-chloronicotinate (16): yellow oily solid, ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.96-3.01 (m, 1H), 3.19-3.23 (m, 1H), 4.17-4.19 (m, 1H), 4.41-4.44 (m, 1H), 4.51-4.55 (m, 1H), 7.23-7.24 (m, 1H), 7.32-7.37 (m, 2H), 7.48 (dt, 1H, *J* = 1.0, 7.5 Hz), 7.73 (s, 1H), 7.95 (dd, 1H, *J* = 1.5, 8.0 Hz), 8.18 (dd, 1H, *J* = 2.5, 8.5 Hz), 8.95 (d, 1H, *J* = 2.0 Hz). ^{13}C NMR ($CDCl_3$, 500 MHz) δ 30.2, 49.8, 67.2, 124.1, 124.4, 127.3, 127.6, 127.9, 128.2, 132.6, 136.5, 136.7, 151.3, 156.0, 164.2, 166.2. High-resolution mass spectrum (CI), $C_{16}H_{14}O_3N_2Cl$ calcd, 317.0693, found 317.0691.

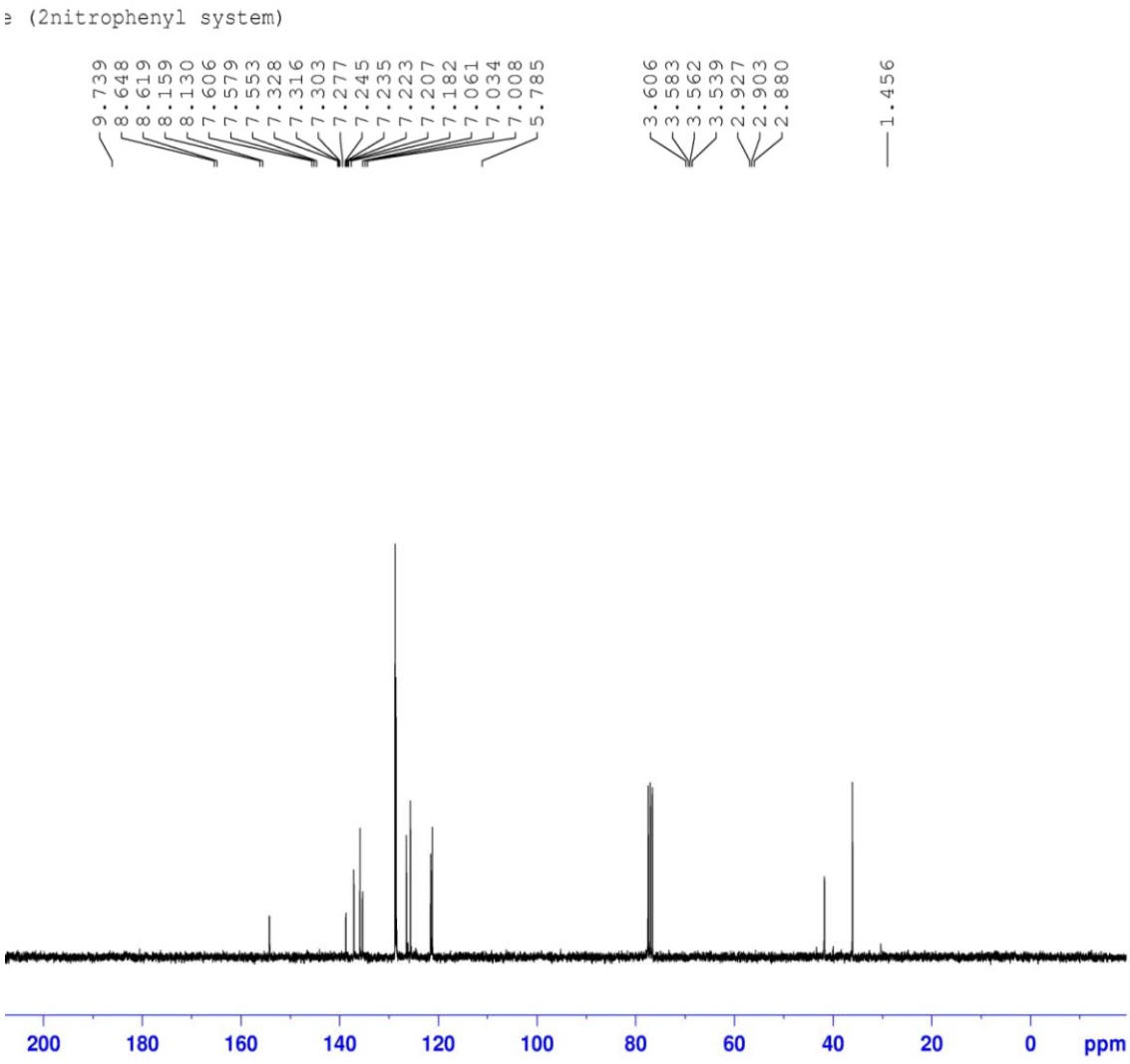
1-(4-methylphenethyl)-3-(4-nitrophenyl)thiourea (19): oily yellow solid. ^{1}H NMR ($(CD_3)_2CO$, 300 MHz) δ 2.30 (s, 3H), 2.95 (t, 2H, *J* = 7.5 Hz), 3.85-3.91 (m, 2H), 7.11-7.19 (m, 4H), 7.68 (s, 1H), 7.82-7.86 (m, 2H), 8.14-8.17 (m, 2H), 9.43 (s, 1H). ^{13}C NMR ($(CD_3)_2CO$, 300MHz) δ 20.2, 33.9, 45.8, 121.0, 124.3, 128.7, 129.1, 135.6, 136.1, 142.8, 146.0, 180.8. High-resolution (TOF) mass spectrum, $C_{16}H_{18}N_3O_2S$ (MH+) calcd, 316.1120, found 316.1116.

1-(4-chlorophenethyl)-3-(4-nitrophenyl)thiourea (20): yellow solid. ^{1}H NMR ($(CD_3)_2CO$, 500 MHz) δ 2.99 (t, 2H, *J* = 7.5 Hz), 3.88 (t, 2H, *J* = 7.5 Hz), 7.28-7.33 (m, 3H), 7.77-7.87 (m, 3H), 8.13-8.15 (m, 1H), 9.48 (s, 1H). ^{13}C NMR ($(CD_3)_2CO$, 500MHz) δ 33.7, 45.4, 120.9, 124.3, 128.5, 130.5, 131.6, 138.2, 142.9, 145.9, 180.8. High-resolution (TOF) mass spectrum, $C_{15}H_{15}N_3O_2ClS$ (MH+) calcd, 336.0574, found 336.0567.

7-methyl-3,4-dihydroisoquinoline-1(2H)-thione (22): oily yellow solid. ^{1}H NMR ($(CD_3)_2CO$, 300MHz) δ 2.88 (s, 3H), 2.96 (t, 2H, *J* = 6.9 Hz), 3.50-3.56 (m, 2H), 7.06-7.31 (m, 2H), 8.28-8.36 (m, 1H), 9.47 (s, 1H). ^{13}C NMR ($(CD_3)_2CO$, 300MHz) two isomers δ 20.2, 20.5, 27.2, 27.5, 41.4, 41.5, 127.1, 127.4, 127.6, 130.5, 131.6, 131.7, 132.6, 132.7, 134.5, 136.1, 142.6, 193.1, 193.4. High-resolution mass spectrum, $C_{10}H_{11}NS$ calcd, 177.06122, found 177.06087.

N-(2-nitrophenyl)piperidine-1-carboxamide (25): ^{1}H NMR ($CDCl_3$, 300MHz) δ 1.64 (s, 6H), 3.51-3.53 (m, 4H), 6.99 (dt, 1H, *J* = 1.2, 7.2 Hz), 7.54 (dt, 1H, *J* = 1.5, 7.2 Hz), 8.13 (dd, 1H, *J* = 1.5, 8.7 Hz), 8.57(dd, 1H, *J* = 1.2, 8.57 Hz), 10.15 (s, 1H). ^{13}C NMR ($CDCl_3$, 300MHz) δ 24.3, 25.7, 45.2, 121.1, 121.4, 125.6, 135.4, 135.9, 137.6, 153.4. High-resolution mass spectrum, $C_{12}H_{15}O_3N_3$ calcd, 249.11135, found 249.11220.

2 ($CDCl_3$)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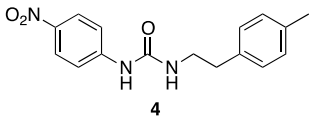

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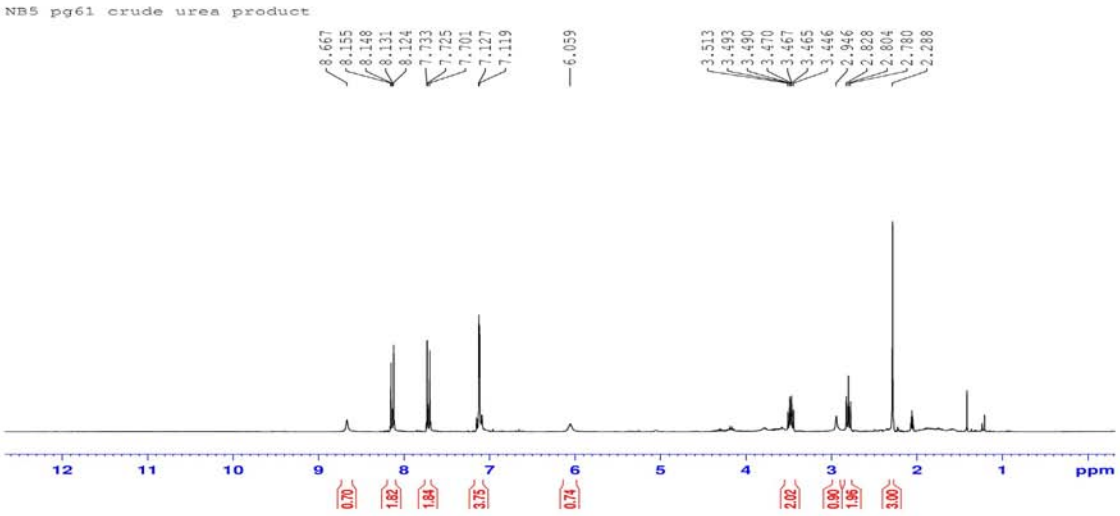
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3.470
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2.288
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10
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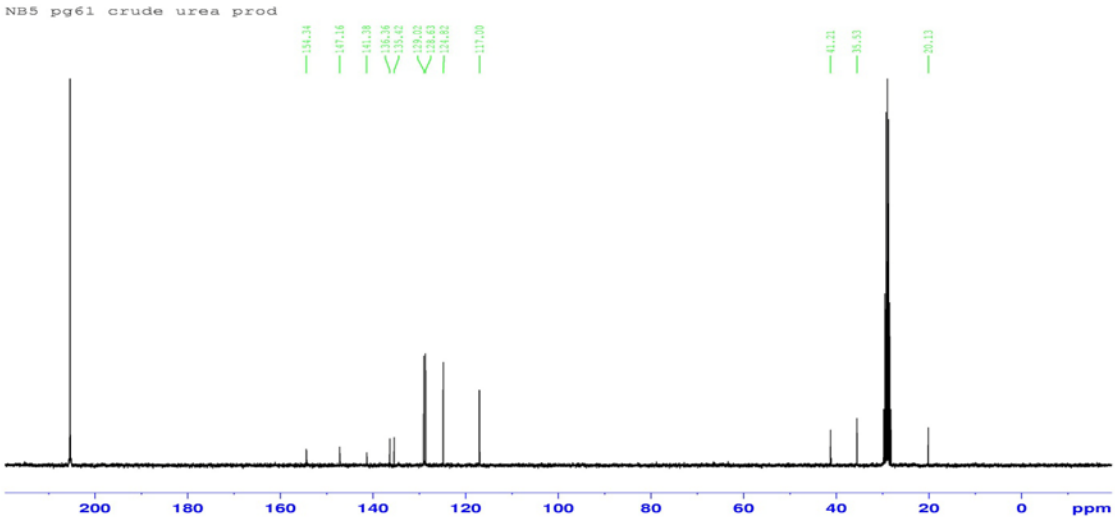
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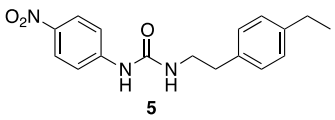

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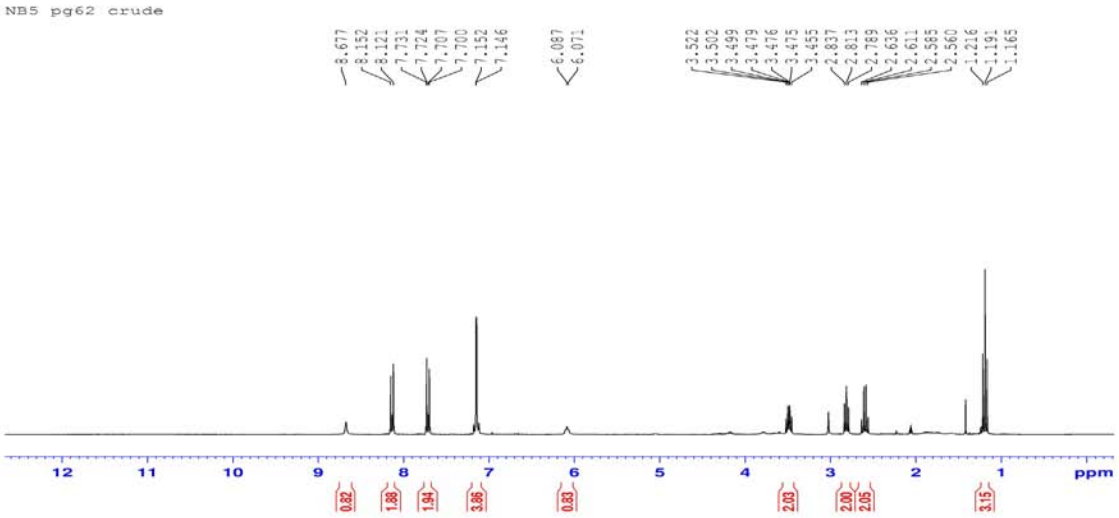
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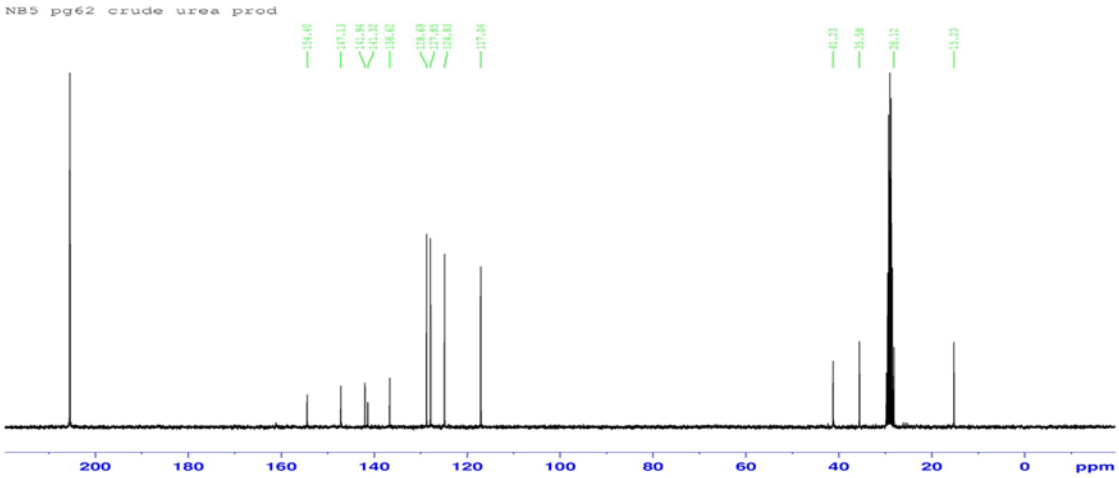
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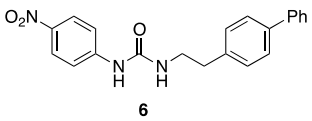
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Ph

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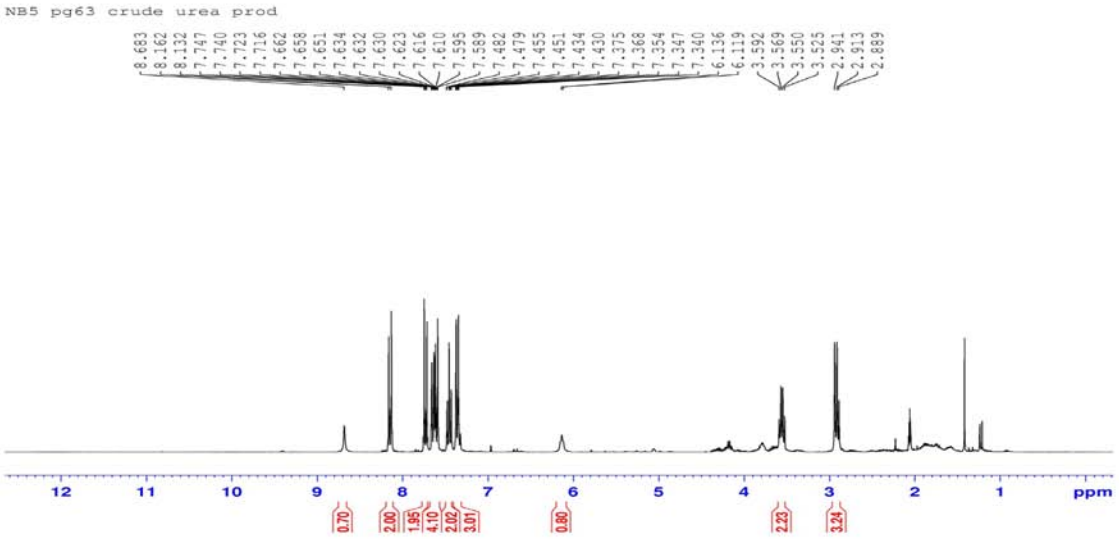
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7.479
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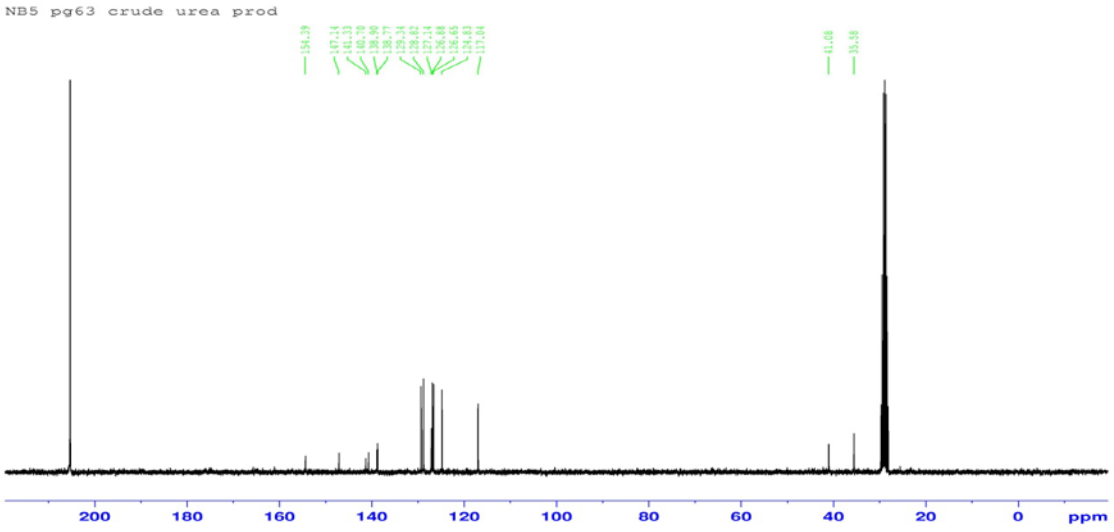
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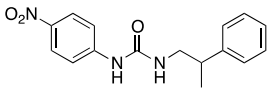
ppm



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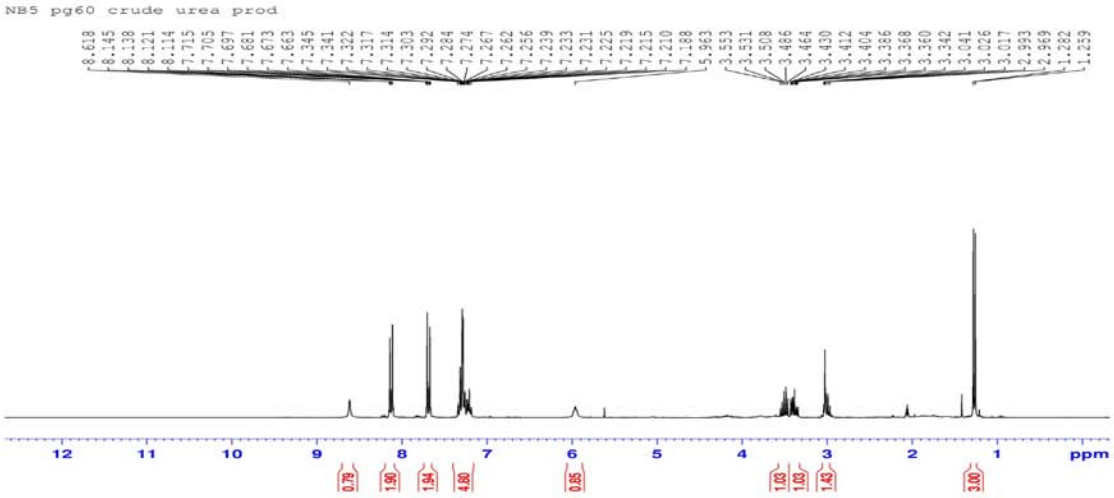
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3.017
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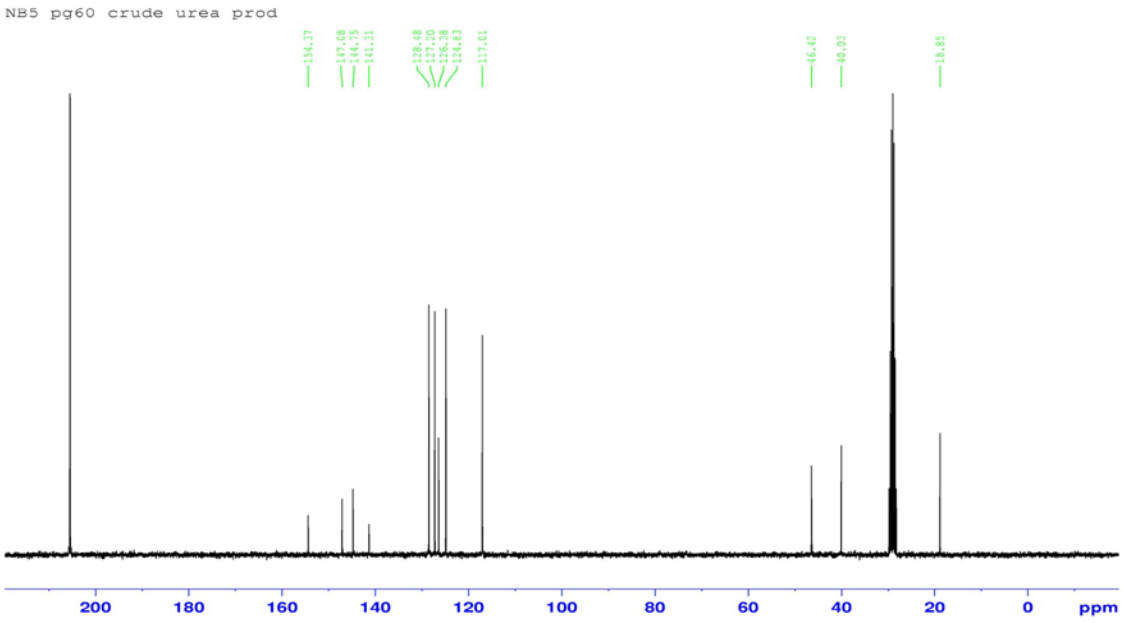
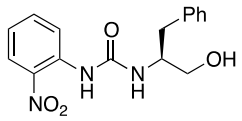
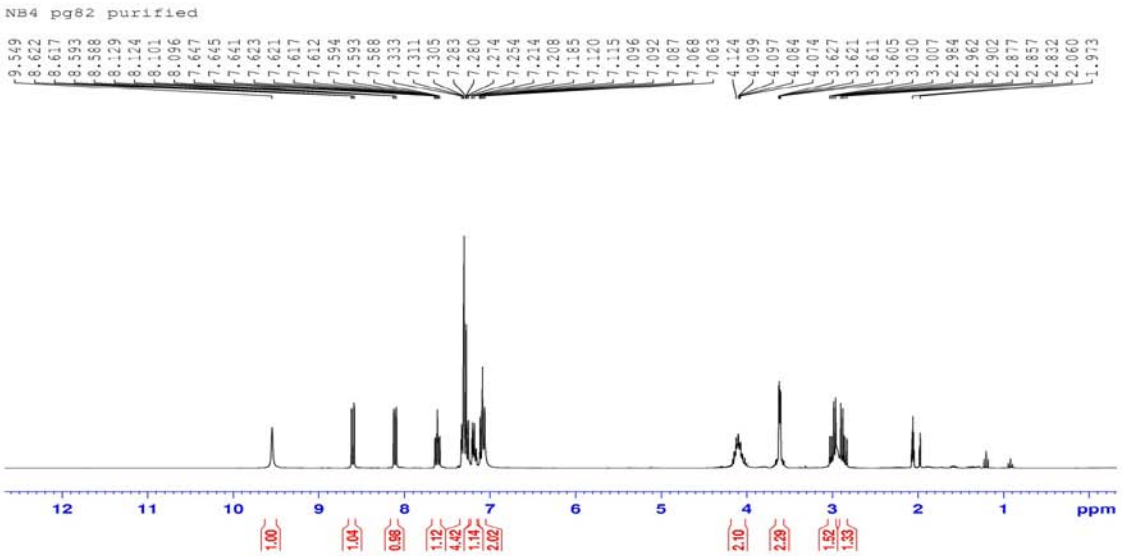
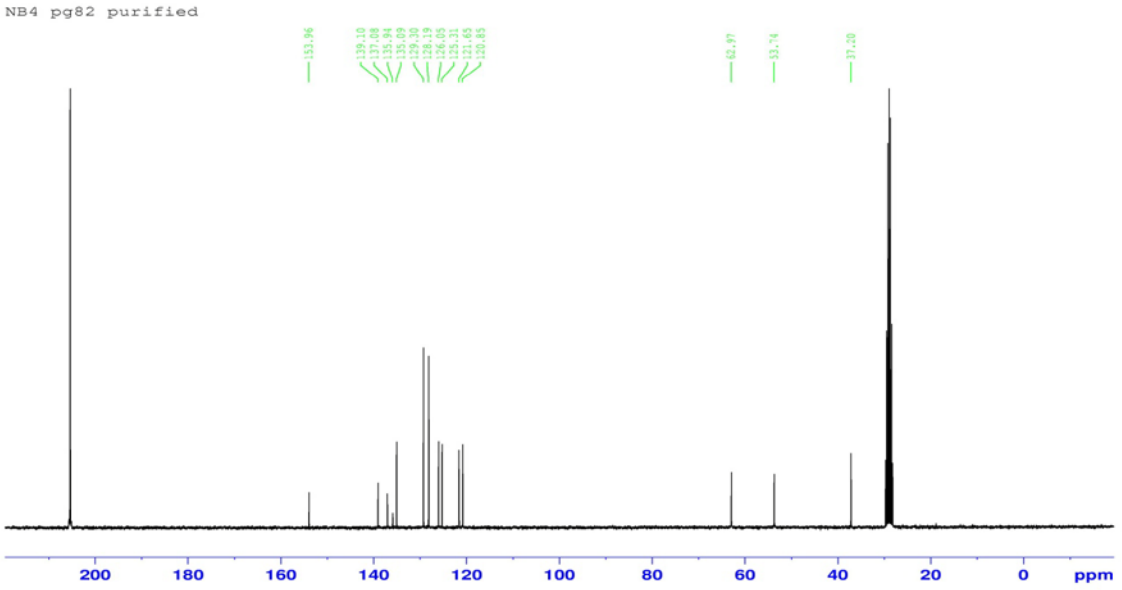
2.969
1.282
1.259
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.79
1.90
1.94
4.60
0.85
1.03
1.03
1.43
3.00

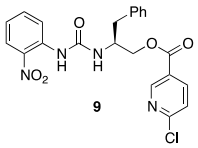

NB5 pg60 crude urea prod
154.37
147.68
144.75
141.31
128.48
127.20
126.38
124.83
117.01
46.42
40.03
18.85
200
180
160
140
120
100
80
60
40
20
0
ppm


Ph
O
OH
N
H
N
H
NO2

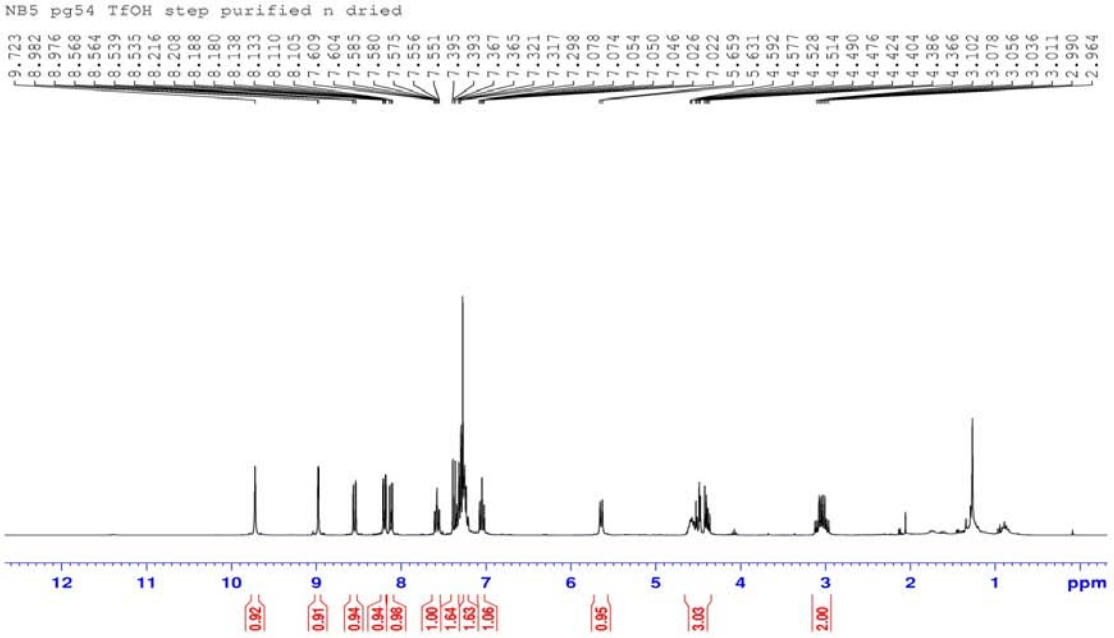
8

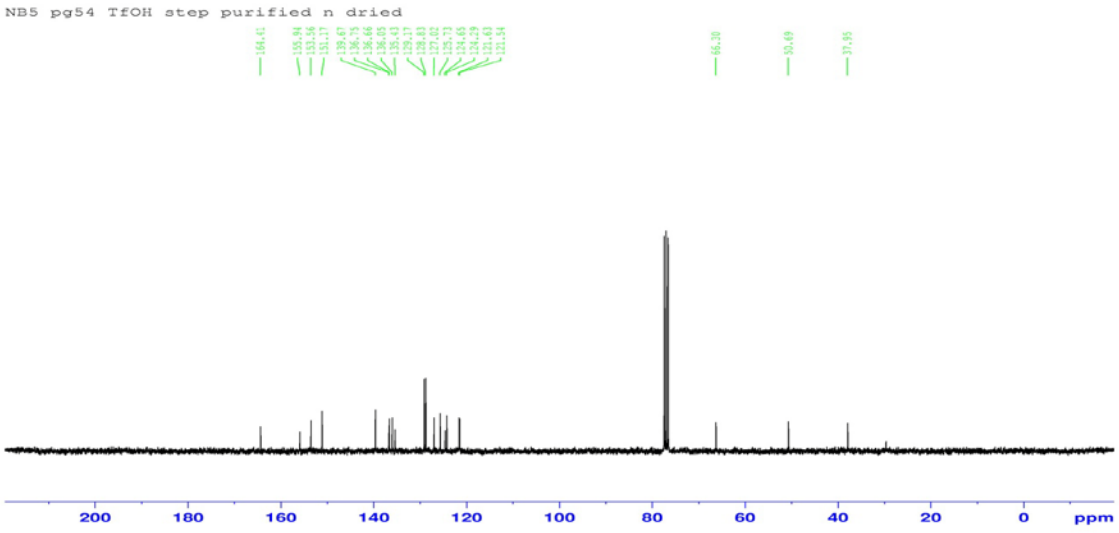

NB4 pg82 purified
9.549
8.622
8.617
8.593
8.588
8.129
8.124
8.101
8.096
7.647
7.645
7.641
7.623
7.621
7.617
7.612
7.594
7.593
7.588
7.333
7.311
7.305
7.283
7.280
7.274
7.254
7.214
7.208
7.185
7.120
7.115
7.096
7.092
7.087
7.068
7.063
4.124
4.099
4.097
4.084
4.074
3.627
3.621
3.611
3.605
3.030
3.007
2.984
2.962
2.902
2.877
2.857
2.832
2.060
1.973
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.04
0.58
1.12
4.42
1.14
2.02
2.10
2.29
1.52
1.33

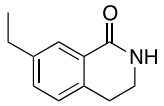

NB4 pg82 purified
153.96
139.10
137.08
135.94
135.09
129.30
128.19
126.05
125.31
121.65
120.85
62.97
53.74
37.20
200
180
160
140
120
100
80
60
40
20
0
ppm


Ph
O
N
H
N
H
O
O
NO2
N
Cl

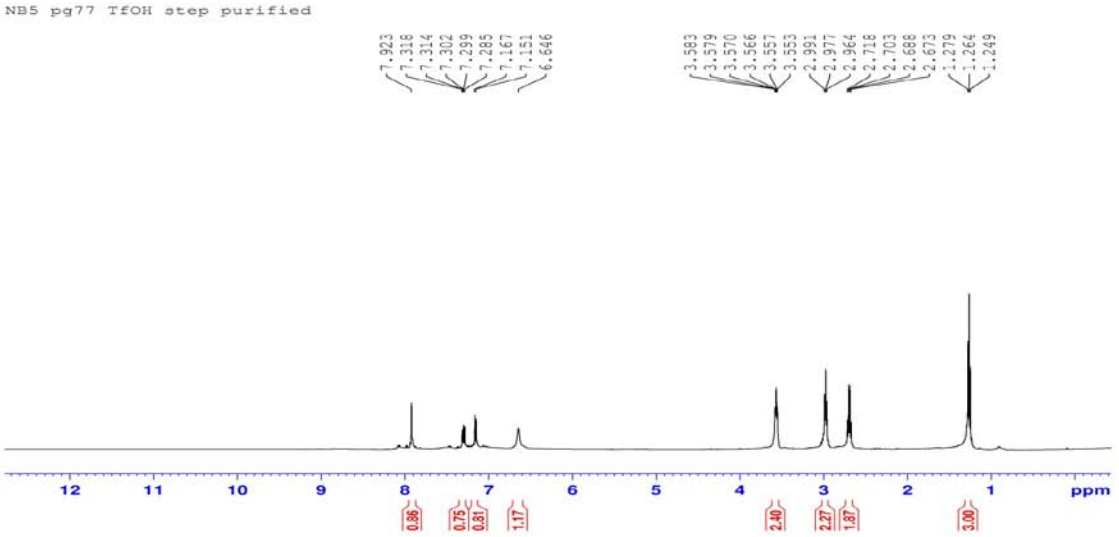
9

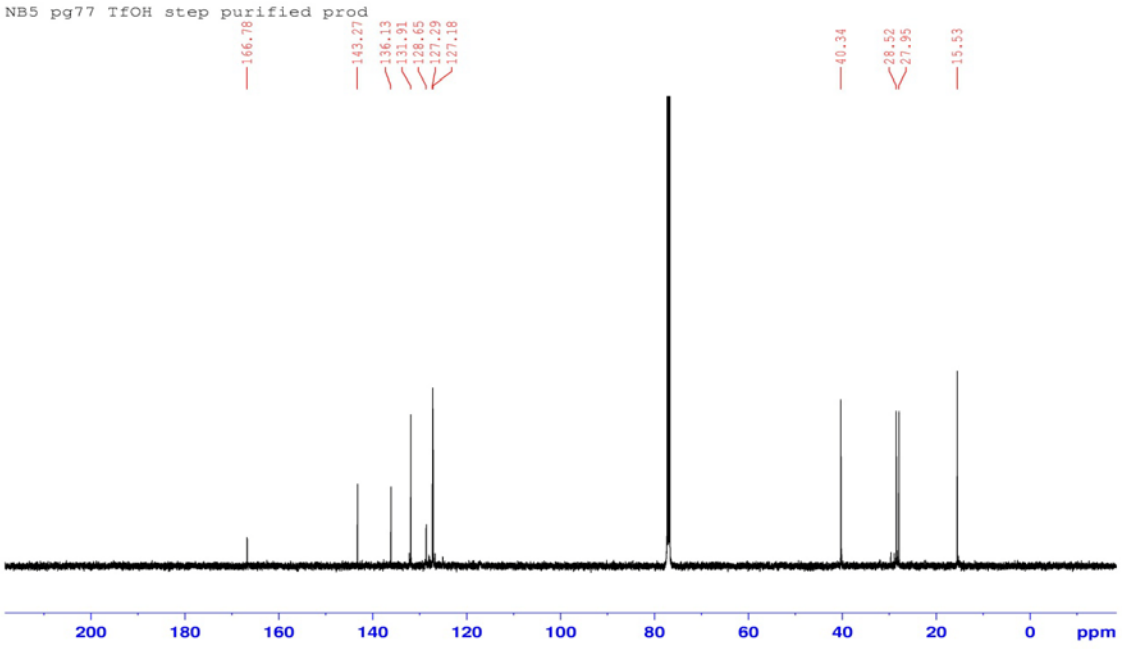

NB5 pg54 TfOH step purified n dried
9.723
8.982
8.976
8.568
8.564
8.539
8.535
8.216
8.208
8.188
8.180
8.138
8.133
8.110
8.105
7.609
7.604
7.585
7.580
7.575
7.556
7.551
7.395
7.393
7.367
7.365
7.321
7.317
7.298
7.078
7.074
7.054
7.050
7.046
7.026
7.022
5.659
5.631
4.592
4.577
4.528
4.514
4.490
4.476
4.424
4.404
4.386
4.366
3.102
3.078
3.056
3.036
3.011
2.990
2.964
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.92
0.91
0.94
0.94
0.98
1.00
1.64
1.63
1.06
0.95
3.03
2.00

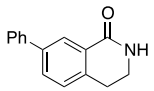

NB5 pg54 TfOH step purified n dried
164.41
155.94
153.56
151.17
139.67
136.75
136.46
136.05
135.43
129.17
128.83
127.02
125.73
124.65
124.29
121.63
121.34
66.30
50.69
37.95
200
180
160
140
120
100
80
60
40
20
0
ppm


O
NH

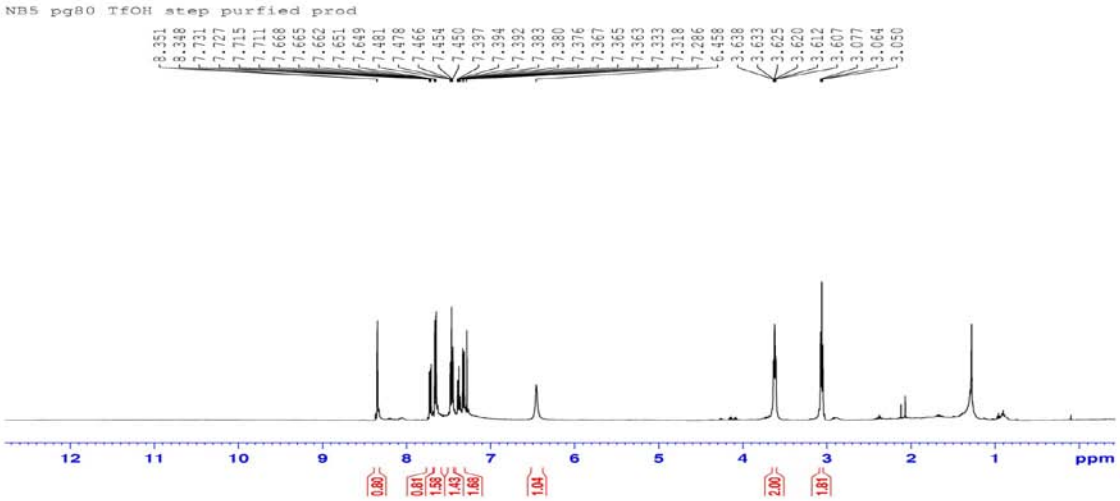
12

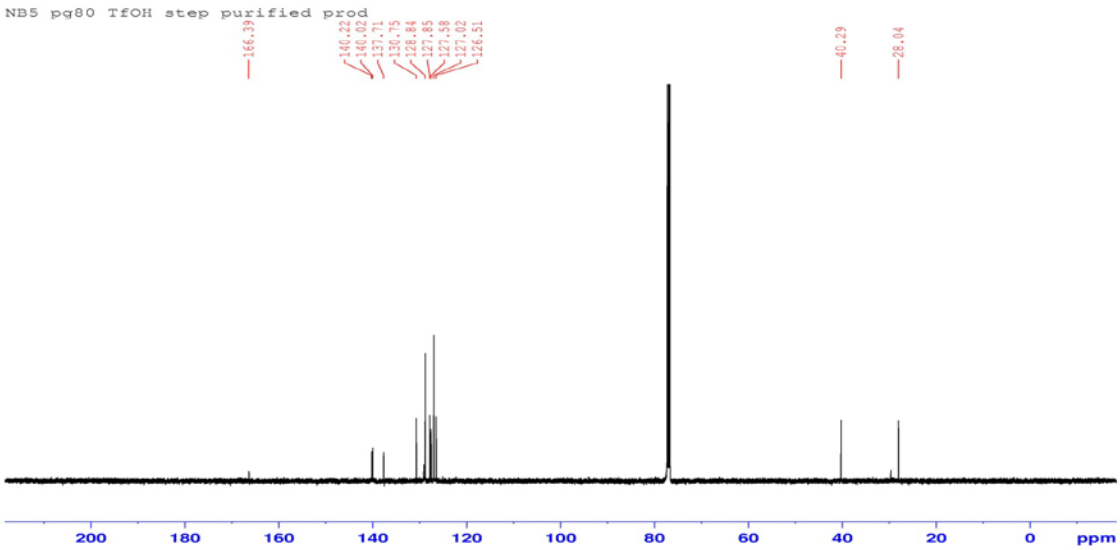

NB5 pg77 TfOH step purified
7.923
7.318
7.314
7.302
7.299
7.285
7.167
7.151
6.646
3.583
3.579
3.570
3.566
3.557
3.553
2.991
2.977
2.964
2.718
2.703
2.688
2.673
1.279
1.264
1.249
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.86
0.75
0.81
1.17
2.40
2.27
1.87
3.00


NB5 pg77 TfOH step purified prod
166.78
143.27
136.13
131.91
128.65
127.29
127.18
40.34
28.52
27.95
15.53
200
180
160
140
120
100
80
60
40
20
0
ppm

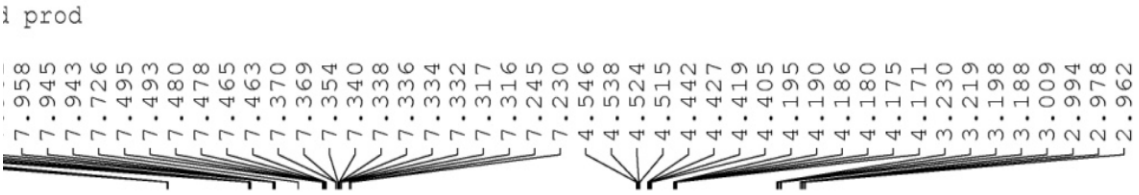

O
Ph
NH

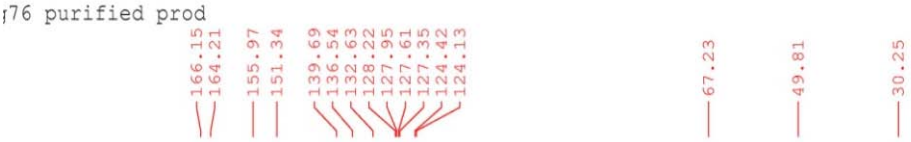
13

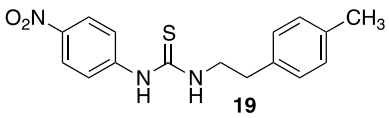

NB5 pg80 TfOH step purified prod
8.351
8.348
7.731
7.727
7.715
7.711
7.668
7.665
7.662
7.651
7.649
7.481
7.478
7.466
7.454
7.450
7.397
7.394
7.392
7.383
7.380
7.376
7.367
7.365
7.363
7.333
7.318
7.286
6.458
3.638
3.633
3.625
3.620
3.612
3.607
3.077
3.064
3.050
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.00
0.81
1.58
1.43
1.68
1.04
2.00
1.81


NB5 pg80 TfOH step purified prod
166.39
140.22
140.02
137.71
130.75
128.84
127.85
127.58
127.02
126.51
40.29
28.04
200
180
160
140
120
100
80
60
40
20
0
ppm

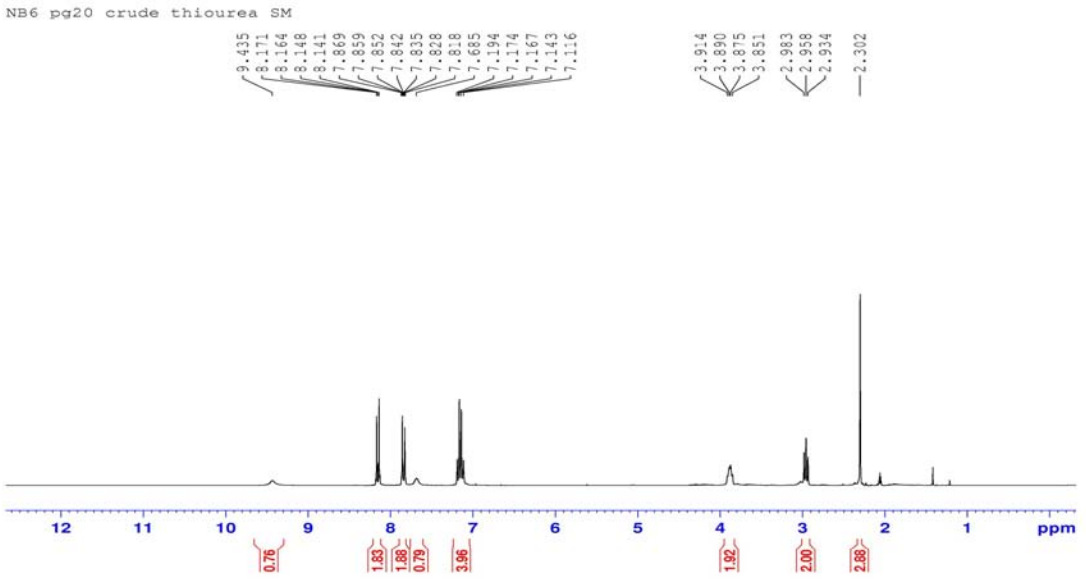
16 ($CDCl_3$)

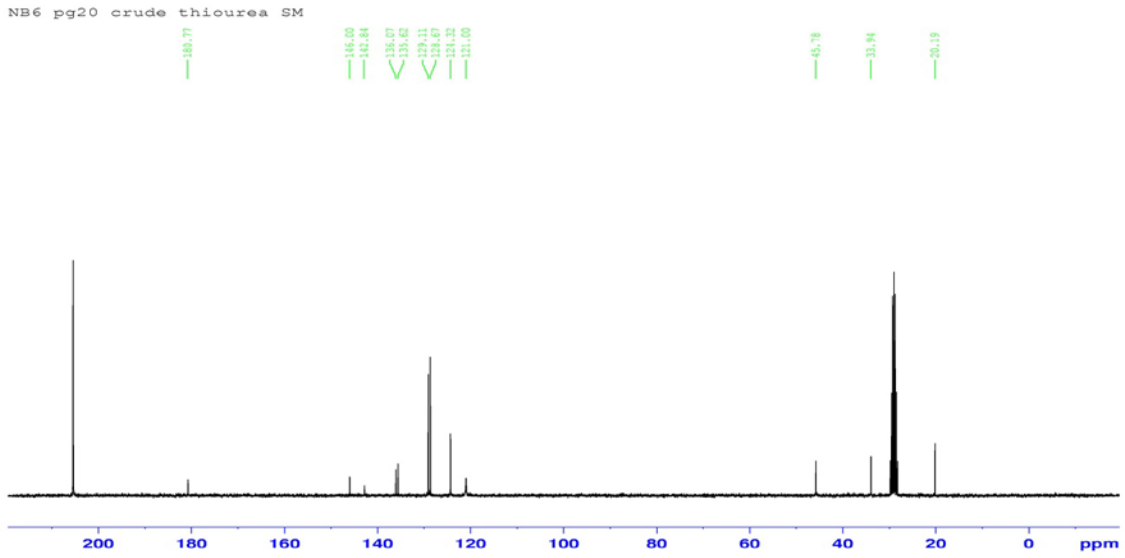

i prod
7.958
7.945
7.943
7.726
7.495
7.493
7.480
7.478
7.465
7.463
7.370
7.369
7.354
7.340
7.338
7.336
7.334
7.332
7.317
7.316
7.245
7.230
4.546
4.538
4.524
4.515
4.442
4.427
4.419
4.405
4.195
4.190
4.186
4.180
4.175
4.171
3.230
3.219
3.198
3.188
3.009
2.994
2.978
2.962

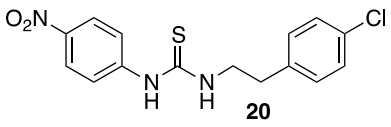

176 purified prod
166.15
164.21
155.97
151.34
139.69
136.54
132.63
128.22
127.95
127.61
127.35
124.42
124.13
67.23
49.81
30.25


O2N
S
N
H
N
H
CH3

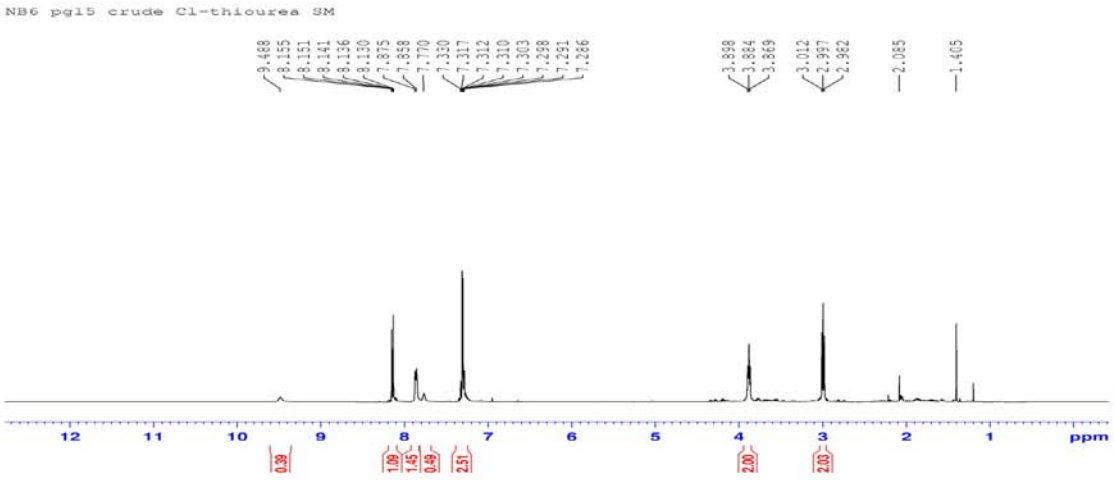
19

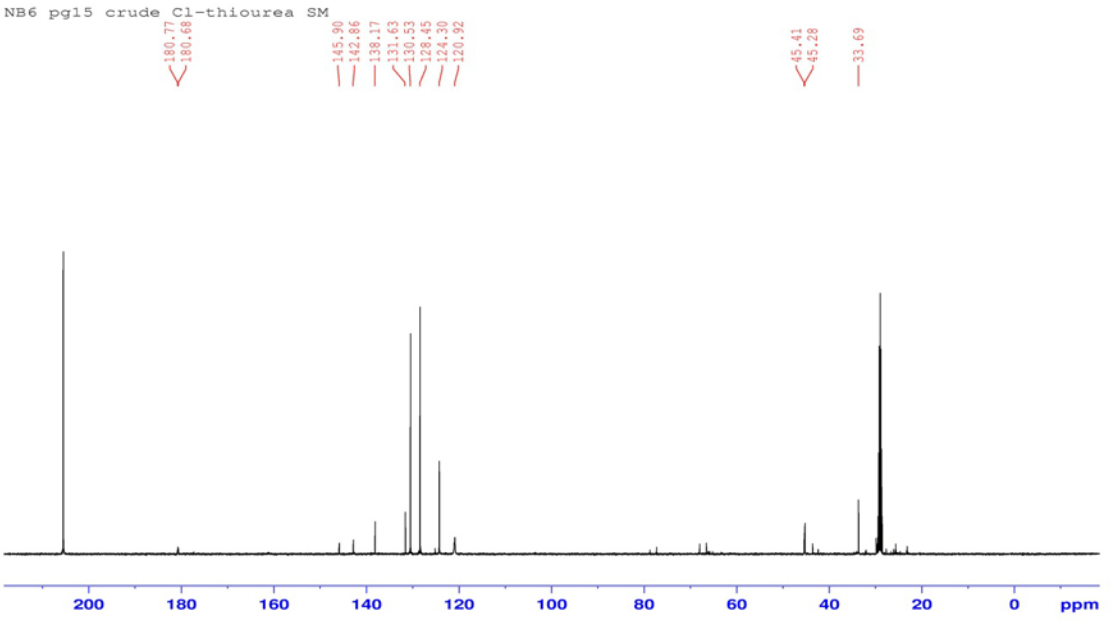

NB6 pg20 crude thiourea SM
9.435
8.171
8.164
8.148
8.141
7.869
7.859
7.852
7.842
7.835
7.828
7.818
7.685
7.194
7.174
7.167
7.143
7.116
3.914
3.890
3.875
3.851
2.983
2.958
2.934
2.302
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.76
1.83
1.88
0.79
3.96
1.92
2.00
2.88

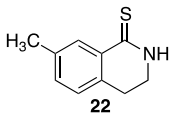

NB6 pg20 crude thiourea SM
180.77
146.00
142.84
136.07
135.62
129.11
126.67
124.32
121.00
45.78
33.84
20.19
200
180
160
140
120
100
80
60
40
20
0
ppm


O2N
S
N
H
N
H
Cl

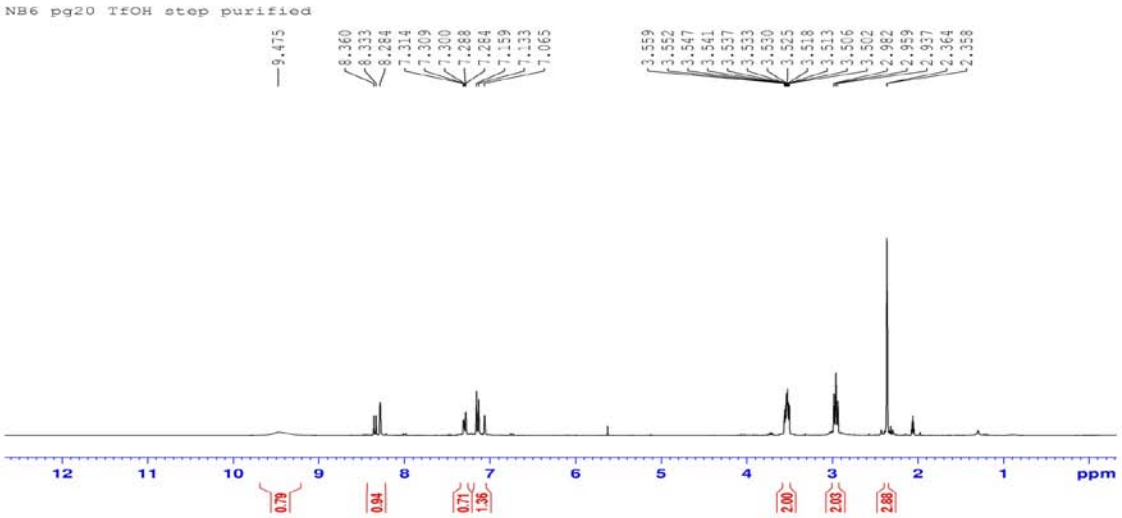
20

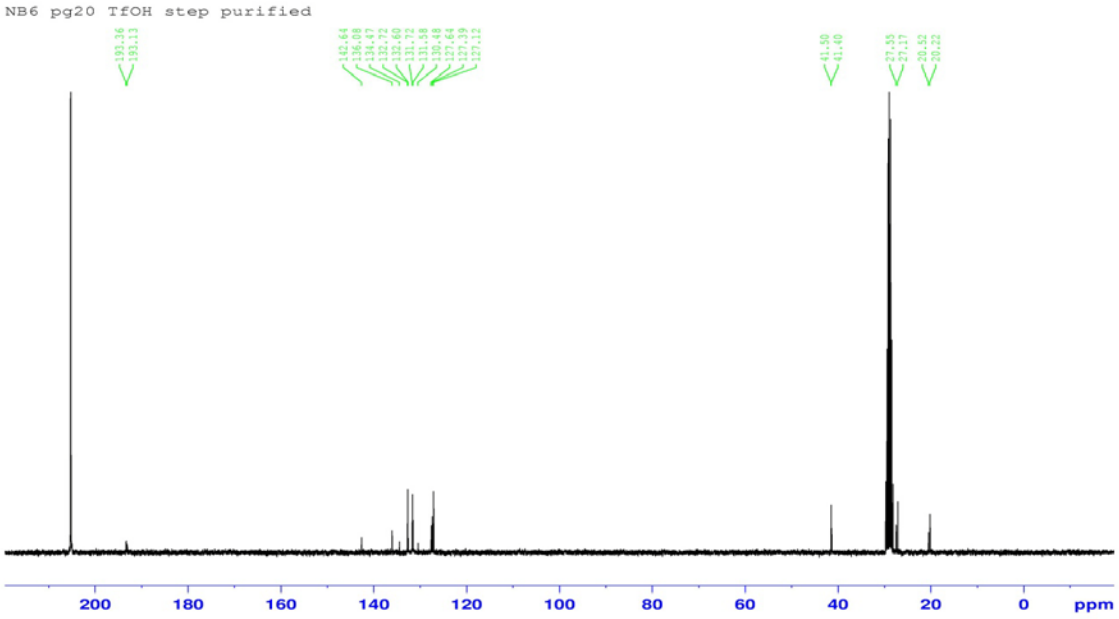

NB6 pg15 crude Cl-thiourea SM
9.468
8.155
8.151
8.141
8.136
8.130
7.875
7.858
7.770
7.330
7.317
7.312
7.310
7.303
7.298
7.291
7.286
3.898
3.884
3.869
3.012
2.997
2.982
2.085
1.405
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.39
1.09
1.45
0.49
2.51
2.00
2.03

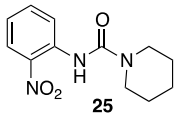

NB6 pg15 crude Cl-thiourea SM
180.77
180.68
145.90
142.86
138.17
131.63
130.53
128.45
124.30
120.92
45.41
45.28
33.69
200
180
160
140
120
100
80
60
40
20
0
ppm


S
H3C
NH

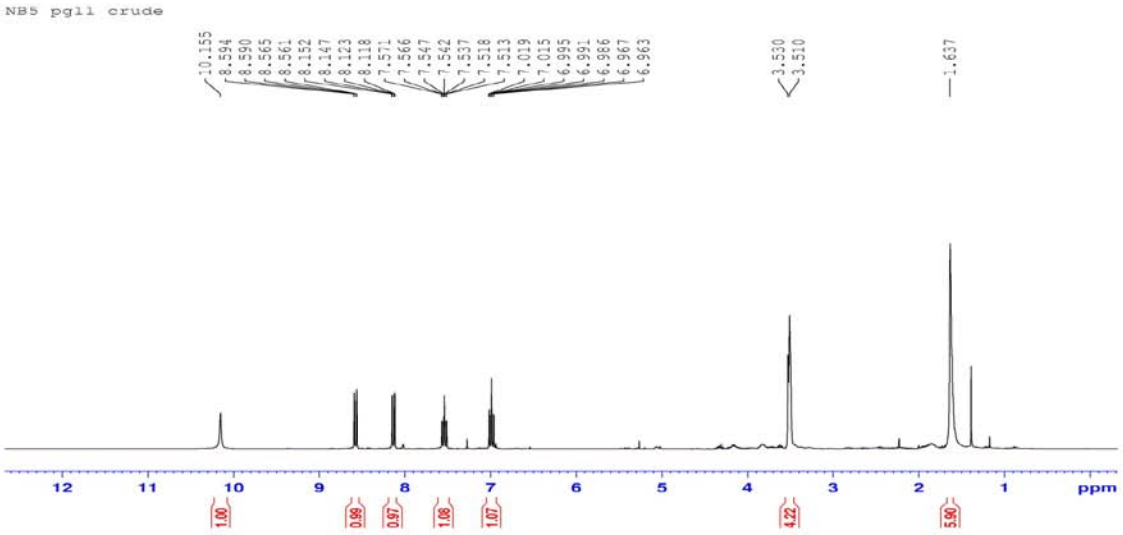
22

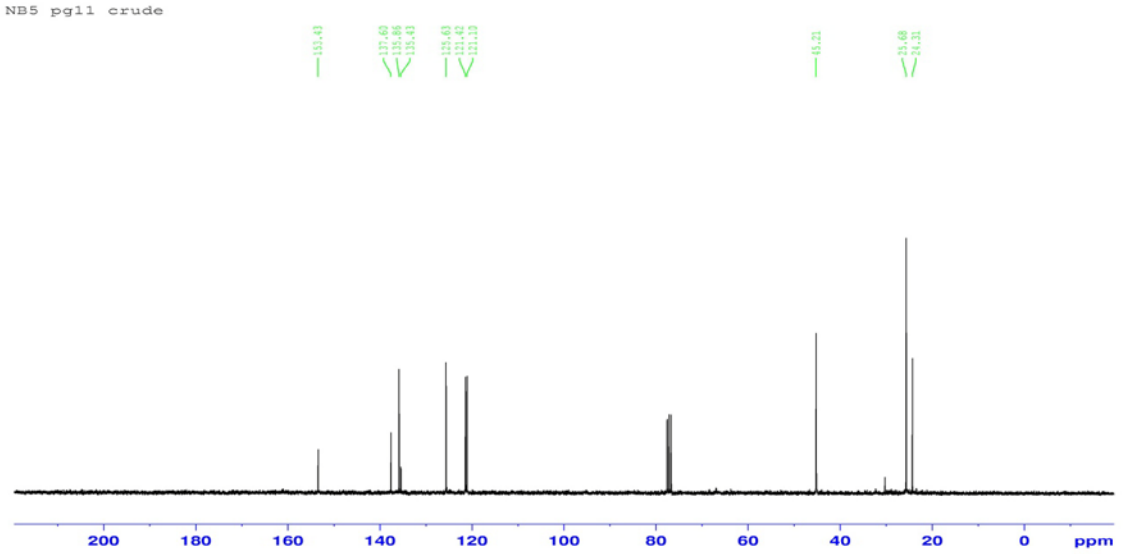

NB6 pg20 TfOH step purified
9.475
8.360
8.333
8.284
7.314
7.309
7.300
7.288
7.284
7.159
7.133
7.065
3.559
3.552
3.547
3.541
3.537
3.533
3.530
3.525
3.518
3.513
3.506
3.502
2.982
2.959
2.937
2.364
2.358
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.79
0.94
0.71
1.36
2.00
2.03
2.88


NB6 pg20 TfOH step purified
193.36
193.13
142.64
136.08
134.47
132.72
132.60
131.72
131.58
130.48
127.64
127.39
127.12
41.50
41.40
27.55
27.17
20.58
20.22
200
180
160
140
120
100
80
60
40
20
0
ppm


O
N
H
N
NO2

25


NB5 pg11 crude
10.155
8.594
8.590
8.565
8.561
8.152
8.147
8.123
8.118
7.571
7.566
7.547
7.542
7.537
7.518
7.513
7.019
7.015
6.995
6.991
6.986
6.967
6.963
3.530
3.510
1.637
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.00
0.99
0.97
1.08
1.07
4.22
5.90

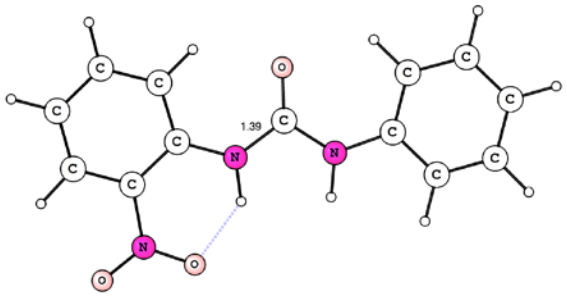

NB5 pg11 crude
153.43
137.60
135.86
135.43
125.63
121.42
121.19
45.21
25.68
24.31
200
180
160
140
120
100
80
60
40
20
0
ppm

Computational Methods:

In the mechanistic studies, intermediates and transition states were studied using density functional theory (DFT). Geometries were optimized in the gas phase at the M06/6-31G(d) level of theory[1] using Jaguar.[2] Gibbs' free energy corrections (ΔG) were calculated, and structures were verified to be minima or transition states by identifying the number of imaginary frequencies. In a second step, single-point energies were calculated using M06/cc-pVTZ(-f),[3,4] giving a basis set correction term (ΔBS). In a third step, solvent phase single point calculations were done at the M06/6-31G(d) level of theory. Using a Poisson-Boltzmann solver as implemented in Jaguar,[5] electrostatic solvation effects from the surroundings were calculated using the SCRF method with CF_3SO_3H as a solvent (dielectric constant = 77.4, probe radius = 2.5985274).[6,7] The free energy (ΔG) and basis set correction terms (ΔBS) were added to the solution phase energy to give the final energies reported in the paper.

1. Zhao, Y.; Truhlar, D. *Theor. Chem. Acc*. **2008**, *120*, 215–241.
2. Jaguar, version 7.7; Schrodinger, LLC: New York, 2010.
3. Dunning, T. H. *J. Chem. Phys.* **1989**, *90*, 1007–1023
4. Woon, D. E.; Dunning, T. H. *J. Chem. Phys.* **1993**, *98*, 1358–1371.
5. Marten, B.; Kim, K.; Cortis, C.; Friesner, R. A.; Murphy, R. B.; Ringnalda, M. N.; Sitkoff, D.; Honig, B. *J. Phys. Chem.* **1996**, *100*, 11775–11788.
6. Lira, A. L.; Zolotukhin, M.; Fomina, L.; Fomine, S. *J. Phys. Chem. A* **2007**, *111*, 13606–13610
7. Naredla, R. R.; Zheng, C.; Nilsson Lill, S. O.; and Klumpp, D. A. *J. Am. Chem. Soc.*, **2011**, *133*, 13169-13175

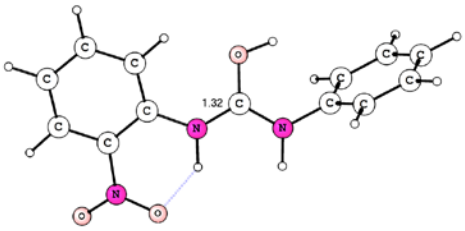
Cartesian Coordinates



Compound **24:**

E: -891.3006984

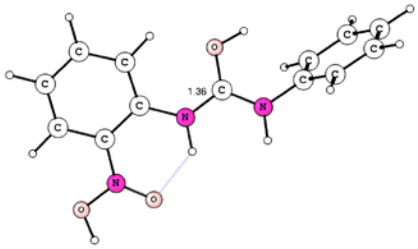
6	0.889300863	-1.844899453	0.012229363
6	1.803945578	-0.791423221	0.037642541
6	-0.455768160	-1.552634377	-0.016638566
1	2.872160383	-1.000314248	0.060449889
1	-1.206782571	-2.335530813	-0.037254100
6	1.388680183	0.525590971	0.034484376
6	-0.896286859	-0.225880996	-0.020707478
1	2.107984936	1.334939384	0.055895584
6	0.022412239	0.856350041	0.005112716
7	-0.414576769	2.166996884	-0.001899825
1	-1.428705692	2.241438740	-0.024292984
6	0.354661365	3.329577561	0.034170319
8	1.568244348	3.357509430	0.094041746
7	-0.449234729	4.446093356	-0.004088089
1	-1.447749709	4.302602861	-0.086429157
7	-2.341784266	-0.045125469	-0.053340067
8	-3.050191079	-1.035559880	-0.066888027
8	-2.808747749	1.100443804	-0.066683034
1	1.226287368	-2.878192051	0.014887079
6	-0.055360018	5.797591444	0.000774669
6	-1.074172870	6.745618528	-0.126660776
6	1.268987750	6.221133347	0.131471379
6	-0.778644673	8.099905508	-0.124781604
6	1.547531268	7.582717166	0.130016151
6	0.537772246	8.528731151	0.003265551
1	-2.108895369	6.414085689	-0.228564940
1	2.061923371	5.489111555	0.229527231
1	-1.586101373	8.822911531	-0.225283867
1	2.582746237	7.904637167	0.231774784
1	0.773526349	9.590981562	0.004278585



Compound **36**:

E: -891.65032795426

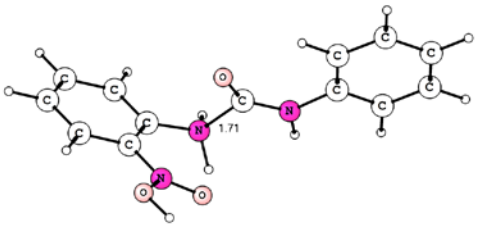
6	1.005214135	-1.700441923	-0.437542063	7	-2.143692412	-0.095382698	0.701529573
6	1.729081876	-0.617152124	-0.919272348	8	-2.613504733	-1.057677922	1.260191390
6	-0.257035442	-1.493269099	0.091900326	8	-2.752347046	0.974426040	0.562887649
1	2.715454502	-0.768331402	-1.351491889	1	1.416702685	-2.704948523	-0.481636732
1	-0.856628370	-2.316087348	0.469556953	6	-0.219043280	5.802163469	-0.050639227
6	1.207047485	0.669003874	-0.870372156	6	-0.402051402	6.691494733	-1.105736614
6	-0.788927374	-0.209992650	0.145981956	6	0.498534386	6.161814855	1.090392612
1	1.783657453	1.496861844	-1.266545178	6	0.140873757	7.966035418	-1.009571942
6	-0.054042240	0.897217498	-0.328394538	6	1.054317138	7.434375516	1.162938562
7	-0.632652259	2.188491752	-0.269908023	6	0.871005781	8.333298613	0.117732942
1	-1.643930623	2.133156996	-0.078432806	1	-0.963945953	6.385544970	-1.986521386
6	-0.053739571	3.378915728	-0.225092320	1	0.592015801	5.461156394	1.920167837
8	1.248273533	3.460313881	-0.268697704	1	-0.000919877	8.673803325	-1.822665058
7	-0.793875769	4.484968625	-0.132856945	1	1.615775169	7.727422077	2.046685823
1	-1.805461920	4.388057794	-0.142820719	1	1.297388005	9.331662139	0.183068722
				1	1.535142307	4.397915598	-0.224408988



Compound **37:**

E: -891.8650147

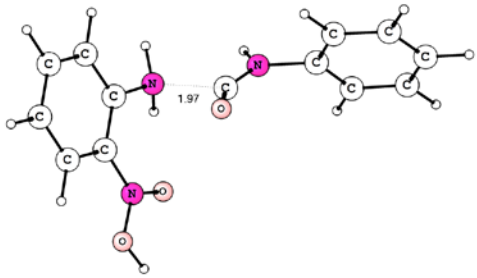
6	1.015711230	-1.680132329	-0.452792476
6	1.703818004	-0.551443197	-0.919707880
6	-0.241309430	-1.525644448	0.067739220
1	2.691163991	-0.670035164	-1.362247703
1	-0.809559610	-2.385389432	0.408914283
6	1.157081789	0.727092921	-0.853856246
6	-0.817799461	-0.230066615	0.145392741
1	1.725811392	1.562664261	-1.243181111
6	-0.104050793	0.937029124	-0.313852414
7	-0.682233987	2.205225361	-0.220535370
1	-1.688409487	2.219108679	-0.067017064
6	-0.073801531	3.418021523	-0.197310006
8	1.220855649	3.449621998	-0.164689191
7	-0.796103355	4.519699348	-0.181930734
1	-1.807889515	4.453634007	-0.279890649
7	-2.087591206	-0.118640742	0.676068945
8	-2.595731357	-1.245446590	1.168445075
8	-2.760155749	0.885978537	0.736013129
1	1.462771530	-2.667751441	-0.520430973
6	-0.199406263	5.837371278	-0.092405610
6	-0.384573663	6.728094675	-1.145447047
6	0.519306046	6.177887148	1.055109613
6	0.173332601	7.995543232	-1.042400591
6	1.084134898	7.446249993	1.130647176
6	0.908446511	8.349812396	0.086930266
1	-0.952461831	6.436669339	-2.027396744
1	0.596937270	5.482573576	1.891455625
1	0.036714057	8.709095862	-1.851087777
1	1.643760224	7.733951897	2.017153724
1	1.342488073	9.344427442	0.156706562
1	-3.505533082	-1.018689631	1.481892672
1	1.546328448	4.382049149	-0.137412058



Compound **38**:

E: -891.8227687

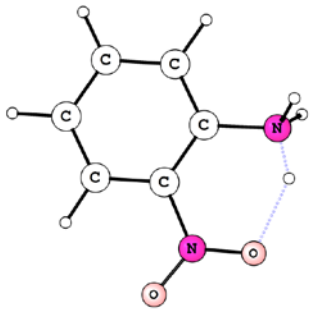
6	0.175350474	-1.403155242	1.868528662
6	0.761351719	-0.620649682	2.861400659
6	-0.777813341	-0.855195255	1.031808366
1	1.512964429	-1.050663227	3.520114395
1	-1.247916943	-1.455379783	0.257680491
6	0.403746237	0.725648084	3.024081197
6	-1.149347079	0.491861646	1.200743611
1	0.894070848	1.320016320	3.794247344
6	-0.552283454	1.292007873	2.215757514
7	-0.835242755	2.706126981	2.348089508
1	-1.845925507	2.888559834	2.411290109
6	-0.226410430	3.555416195	0.998519913
8	0.355482036	2.872294950	0.227015495
7	-0.564957507	4.822025926	1.116859242
1	-1.126727349	5.124988437	1.908036219
7	-2.125706609	1.042005964	0.375226809
8	-2.521562712	0.264695738	-0.622604323
8	-2.618386727	2.136528951	0.510551003
1	0.463152968	-2.444207614	1.748465090
6	-0.158309911	5.883736866	0.234764340
6	-0.620386643	7.156511988	0.572090394
6	0.647399800	5.659668598	-0.879834887
6	-0.275088891	8.229517228	-0.231489420
6	0.984816047	6.749453368	-1.669144013
6	0.528920104	8.028439415	-1.352307821
1	-1.248065378	7.309178200	1.450782376
1	1.011263774	4.667813116	-1.130914421
1	-0.632929324	9.225161062	0.017468769
1	1.614647910	6.597999836	-2.542069147
1	0.803896068	8.872426053	-1.980039711
1	-3.235303097	0.758660803	-1.097206760
1	-0.389936537	3.061418766	3.204408706



Compound **39**:

E: : -891.8215457

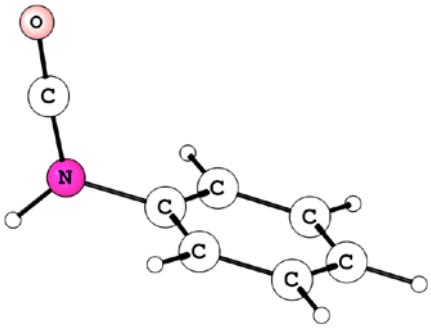
6	0.250284428	-1.321034475	1.525531509	8	-3.007656998	0.237419606	-0.210703344
6	1.021250925	-0.525233187	2.378437011	8	-2.841900240	2.159606766	0.810824342
6	-0.878196779	-0.794020411	0.941546079	1	0.535943611	-2.349925375	1.324369094
1	1.914102768	-0.938843000	2.843585876	6	0.131621558	6.041380243	0.139188336
1	-1.492482024	-1.397459933	0.279670372	6	-0.828541513	7.003548322	-0.143740614
6	0.668466626	0.799148273	2.650213977	6	1.386884045	6.021769481	-0.452003108
6	-1.241403006	0.545245626	1.214600606	6	-0.498320808	8.002318681	-1.050548440
1	1.293048649	1.392601628	3.316750847	6	1.690659818	7.020807444	-1.368248007
6	-0.463280546	1.361483748	2.094135997	6	0.752669805	8.006126445	-1.662556890
7	-0.738651014	2.734134003	2.338993521	1	-1.807257627	6.979860220	0.332276712
1	-1.735810262	2.936043630	2.456231515	1	2.115948972	5.253792715	-0.198196766
6	-0.203378772	3.758661546	0.738481932	1	-1.225045901	8.776221559	-1.284570256
8	-0.008443344	3.000025234	-0.125151943	1	2.666912652	7.033194517	-1.846084000
7	-0.205773988	4.998468671	1.114996770	1	0.999205099	8.787613062	-2.377363453
1	-0.462281632	5.261637361	2.062858319	1	-3.805592306	0.721784843	-0.538990796
7	-2.387841649	1.060576063	0.625050388	1	-0.229636868	3.051249463	3.169568426



Compound **40**:

E: -492.1410439

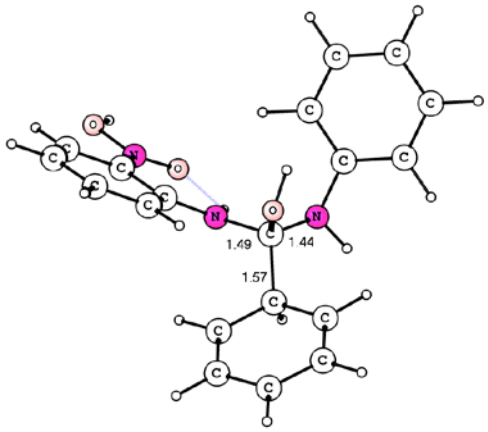
6	1.016460651	-1.594483608	-0.485404122
6	1.719245462	-0.484370504	-0.936803749
6	-0.254330228	-1.445995855	0.054324934
1	2.713935795	-0.599236013	-1.359808350
1	-0.822917057	-2.299529656	0.413283780
6	1.153663669	0.785614832	-0.850669864
6	-0.823007579	-0.183072273	0.142809870
1	1.703500537	1.657425858	-1.203634630
6	-0.110738160	0.933583050	-0.313292958
7	-2.173813102	-0.091628207	0.723833818
8	-2.694880152	1.029684832	0.807452595
8	-2.704071276	-1.107734809	1.087794449
1	1.457139283	-2.585587237	-0.552390409
7	-0.685803237	2.289082513	-0.233216907
1	-0.780448987	2.724208790	-1.159447278
1	-1.642357875	2.179123914	0.198210123
1	-0.120466148	2.914533950	0.354558677



Compound **41**:

E: -399.7660422

6	0.241661923	3.543889282	-0.396435650
8	0.609668896	2.908692083	-1.268421979
7	-0.145501054	4.300425503	0.541920830
1	-0.601717114	3.903033801	1.369377155
6	0.095222028	5.758589856	0.368956768
6	-0.901755328	6.514265064	-0.230308180
6	1.302920779	6.273888613	0.816348521
6	-0.671030600	7.877159301	-0.369062304
6	1.508121309	7.639528266	0.664579023
6	0.526580911	8.432029634	0.075033740
1	-1.830148919	6.058083619	-0.567560252
1	2.052850608	5.634596381	1.277599567
1	-1.430175215	8.504992809	-0.828303573
1	2.439399531	8.082839185	1.007469674
1	0.698555538	9.499364554	-0.042346716



Compund **42**:

E: -1123.895825

6	0.688382593	8.857576435	-4.319874680
6	-0.006522211	8.606948833	-3.113575024
6	1.317119661	7.830339584	-4.951020806
1	-0.502670447	9.433178206	-2.607555388
1	1.859409929	7.993095573	-5.876355215
6	-0.081459479	7.353456714	-2.555011614
6	1.265485901	6.517314848	-4.394600981
1	-0.598224381	7.214478867	-1.612844007
6	0.537829285	6.239083401	-3.166413733
7	0.457768889	4.990845911	-2.656935942
1	0.931930118	4.247636921	-3.164708496
6	0.087322462	4.546336626	-1.283129243
8	0.226785078	5.562857899	-0.362552369
7	0.889703210	3.378568926	-1.049043109
1	0.379501451	2.560283323	-0.735021538
7	1.959759522	5.520686714	-5.022172645
8	2.664445217	5.907458254	-6.098397554
8	2.015750764	4.348202410	-4.707064170
1	0.721304907	9.860308319	-4.735889193
6	2.127606367	3.540969267	-0.359334146
6	2.380364401	2.787274318	0.786013641
6	3.082919418	4.453708223	-0.817848835
6	3.585152183	2.933966888	1.459707590
6	4.273585616	4.616561868	-0.115977685
6	4.528908514	3.857583303	1.019612666
1	1.636498236	2.074434156	1.145474924
1	2.919808341	5.007273761	-1.743599571
1	3.782190841	2.332350155	2.343874720
1	5.013921026	5.329117399	-0.472773599
1	5.464996480	3.980127655	1.558594321
1	3.089964203	5.082893635	-6.430303299
1	1.168102370	5.626333395	-0.099287456
6	-3.020349020	4.213600773	0.690530777
6	-3.887747067	4.991707748	-0.096516975
6	-1.818068311	3.826914702	0.172320776
1	-4.838410294	5.313063044	0.329239539
1	-1.113354040	3.273444734	0.793070901
6	-3.563598565	5.385184219	-1.410314866
6	-1.430436923	4.138342542	-1.215720486
1	-4.265514800	5.987863826	-1.980765936
1	-1.472122540	3.176733424	-1.783792045
6	-2.368603995	5.004498962	-1.948404559
1	-2.113920858	5.279562668	-2.970901327
1	-3.297705387	3.953603269	1.708702074