An Enantioselective Chiral Brønsted Acid Catalyzed Imino-Azaenamine Reaction

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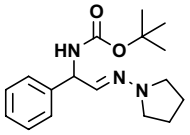
Supporting Information

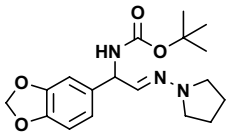
General: All reactions were performed under argon atmosphere. Unless otherwise noted, all materials were obtained from commercial suppliers and were used without further purification. Solvents for extraction and chromatography were technical grade and distilled prior to use. Solvents used in reaction were reagent grade and distilled from the indicated drying agents: CH_2Cl_2 (P_2O_5), toluene (Na), $CHCl_3$ (CaH_2). For thin-layer chromatography (TLC), silica gel coated aluminum plates (Merck, silica gel 60 F_{254}) were used and chromatograms were visualised by irradiation with UV light at 254 nm. Column chromatography was performed using silica gel Merck 60 (particle size 0.063 - 0.20 mm). Solvents mixtures are understood as volume / volume.

^{1}H-NMR and ^{13}C-NMR were recorded on a Bruker AM 250 spectrometer in $CDCl_3$. Data are reported in the following order: chemical shift (δ) in ppm; multiplicities are indicated (bs (broadened singlet), s (singlet), d (doublet), t (triplet), m (multiplet)); coupling constants (*J*) are in Hertz (Hz). High resolution mass spectra (HRMS-ESI) were conducted on Micromass/ Waters Qtof Ultima 3 instrument. IR spectra were recorded on a Jasco FT/IR-420 spectrometer and are reported in terms of frequency of absorption (cm-1). The enantiomeric excesses were determined by HPLC analysis using a chiral stationary phase column (column, Daicel Co. CHIRALCEL OD-H and AD-H; eluent: *n*-hexane / 2-propanol). The chiral HPLC method were calibrated with the corresponding racemic mixtures. Optical rotations were measured on a Perkin Elmer 241 polarimeter.

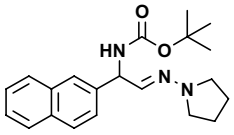
General Procedure: In a typical experiment the imine **2** (0.12 mmol, 1.2 equiv), catalyst (5 mol %), azaenamine **1** (0.10 mmol, 1 equiv) and $CHCl_3$ (0.7 mL) were added to a screw-capped test tube at rt. The resulting solution was cooled down to 0 °C and allowed to stir at the temperature for 16 h. The solvent was evaporated in vacuo, and the residue was purified by column chromatography on silica gel (hexane/ethyl acetate, 5 /1) to give the hydrazone **3**.



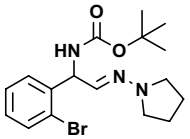
Hydrazone **3a**: colorless solid, mp: 76 °C, ^{1}H-NMR ($CDCl_3$): δ = 1.45, 1.49 (2 bs, 9H, boc rotamers), 1.85 – 1.96 (m, 4H), 3.10 – 3.25 (m, 4H), 5.30 (bs, 1H), 6.09 (bs, 1H), 6.52 (bs, 1H), 7.22 – 7.58 (m, 5H); ^{13}C-NMR ($CDCl_3$): δ = 155.1, 132.9, 128.6, 128.0, 127.3, 127.0, 125.8, 79.3; HRMS-ESI: calculated for $C_{17}H_{25}N_3O_2Na$ ($[M+Na]^+$): 326.1844, found: 326.1852; IR (neat): 3342, 2929, 1712, 1366, 700 cm^{-1}; HPLC conditions: OD-H column, hexane / 2-propanol = 98 / 2, flow rate = 0.6 mL min^{-1}, minor enantiomer: t_R = 14,71 min; major enantiomer: t_R = 16,90 min; $[\alpha]^D_{25}$ = + 33.3 (c = 1, $CHCl_3$)



Hydrazone **3b**: clear colorless oil, ^{1}H-NMR ($CDCl_3$): δ = 1.33 (bs, 9H), 1.75 – 1.85 (m, 4H), 3.06 (t, *J* = 6.5 Hz, 4H), 5.08 (bs, 1H), 5.80 – 5.90 (m, 2H), 5.97 (s, 1H), 6.35 (s, 1H), 6.61 – 6.78 (m, 3H); ^{13}C-NMR ($CDCl_3$): δ = 155.0, 147.8, 146.8, 135.5, 132.8, 120.4, 108.2, 107.4, 100.9, 89.2, 79.3, 51.3, 28.4, 23.2; HRMS-ESI: calculated for $C_{18}H_{25}N_3O_4Na$ ($[M+Na]^+$): 370.1743, found: 370.1728; IR (neat): 3413, 2975, 1717, 1486, 1246, 1168, 1039 cm^{-1}; HPLC conditions: AD-H column, hexane / 2-propanol = 90 / 10, flow rate = 0.6 mL min^{-1}, minor enantiomer: t_R = 22,87 min; major enantiomer: t_R = 24,94 min; $[\alpha]^D_{25}$ = + 54.9 (c = 1, $CHCl_3$)

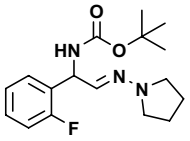


Hydrazone **3c**: clear yellowish oil, ^{1}H-NMR ($CDCl_3$): δ = 1.50 (bs, 9H), 1.76 – 2.04 (m, 4H), 3.06 – 3.32 (m, 4H), 6.10 (bs, 2H), 6.67 (bs, 1H), 7.40 – 7.69 (m, 4H), 7.82 (d, *J* = 7.5 Hz, 1H), 7.92 (dd, , *J* = 2.0 Hz, 7.5 Hz, 1H), 8.29 (d, *J* = 8.3 Hz, 1H); ^{13}C-NMR ($CDCl_3$): δ = 155.2, 134.1, 131.0, 128.8, 128.0, 126.1, 125.5, 124.3, 123.4, 79.4, 51.3, 28.4, 23.2; HRMS-ESI: calculated for $C_{21}H_{27}N_3O_2Na$ ($[M+Na]^+$): 376.2001, found: 376.2002; IR (neat): 3416, 2975, 1711, 1486, 1168, 779 cm^{-1}; HPLC conditions: AD-H column, hexane / 2-propanol = 95 / 5, flow rate = 0.6 mL min^{-1}, major enantiomer: t_R = 27,83 min; minor enantiomer: t_R = 32,93 min; $[\alpha]^D_{25}$ = + 38.7 (c = 1, $CHCl_3$)

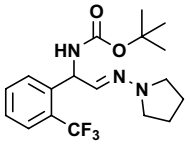


Hydrazone **3d**: white needles, mp: 115 °C, ^{1}H-NMR ($CDCl_3$): δ = 1.17, 1.36 (2 bs, 9H, boc rotamers), 1.72 – 1.88 (m, 4H), 3.05 (t, *J* = 6.5 Hz, 4H), 5.64 (bs, 1H), 6.17 (bs, 1H), 6.50 (bs, 1H), 6.95 – 7.10 (m, 1H), 7.12 – 7.34 (m, 2H), 7.45 (dd, *J* = 1.3, 6.8 Hz, 1H); ^{13}C-NMR ($CDCl_3$): δ = 154.8, 132.9, 130.7, 128.6, 127.8, 122.7, 79.5, 51.2, 28.2, 23.2; HRMS-ESI: calculated for $C_{17}H_{24}N_3O_2NaBr$ ($[M+Na]^+$) (Br-pattern) = 404.0950, found: 404.0943; IR (neat): 3413, 2933, 1717, 1483, 1467, 1390,

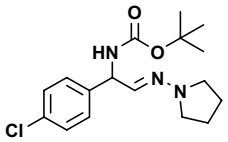
1249, 1168, 1022, 861, 725 cm^{-1}; HPLC conditions: OD-H column, hexane / 2-propanol = 99 / 1, flow rate = 0.6 mL min^{-1}, minor enantiomer: t_R = 20,47 min; major enantiomer: t_R = 22,90 min; $[\alpha]^D_{25}$ = + 53.5 (c = 1, $CHCl_3$)



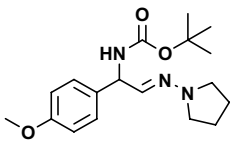
Hydrazone **3e**: clear colorless oil, ^{1}H-NMR ($CDCl_3$): δ = 1.35, 1.41 (2bs, 9H, boc rotamers), 1.71 – 1.87 (m, 4H), 3.06 (t, *J* = 6.5 Hz, 4H), 5.49 (bs, 1H), 5.99 (bs, 1H), 6.45 (bs, 1H), 6.95 – 7.06 (m, 2H), 7.08 – 7.28 (m, 2H); ^{13}C-NMR ($CDCl_3$): δ = 154.9, 138.1, 128.8, 128.6, 128.0, 124.4, 124.3, 79.5, 51.2, 28.3, 23.2; HRMS-ESI: calculated for $C_{17}H_{24}N_3O_2NaF$ ($[M+Na]^+$): 344.1750, found: 344.1756; IR (neat): 3421, 2976, 1699, 1460, 1366, 1171, 758 cm^{-1}; HPLC conditions: AD-H column, hexane / 2-propanol = 95 / 5, flow rate = 0.6 mL min^{-1}, minor enantiomer: t_R = 15,56 min; major enantiomer: t_R = 18,28 min; $[\alpha]^D_{25}$ = + 31.2 (c = 1, $CHCl_3$)



Hydrazone **3f**: clear colorless oil, ^{1}H-NMR ($CDCl_3$): δ = 1.11, 1.34 (2 bs, 9H, boc rotamers), 1.70 – 1.88 (m, 4H), 3.04 (t, *J* = 6.8 Hz, 4H), 5.60 (bs, 1H), 6.32 (d, *J* = 4.8 Hz, 2H), 7.10 – 7.34 (m, 1H), 7.38 – 7.66 (m, 3H); ^{13}C-NMR ($CDCl_3$): δ = 154.6, 132.3, 127.6, 126.9, 126.6, 122.3, 79.3, 51.2, 28.3, 23.1; HRMS-ESI: calculated for $C_{18}H_{24}N_3O_3NaF_3$ ($[M+Na]^+$): 410,1667, found: 410,1658; IR (neat): 3317, 2972, 1718, 1483, 1313, 1159, 1035 cm^{-1}; HPLC conditions: OD-H column, hexane / 2-propanol = 99 / 1, flow rate = 0.6 mL min^{-1}, major enantiomer: t_R = 15,73 min; minor enantiomer: t_R = 18,18 min; $[\alpha]^D_{25}$ = + 37.2 (c = 1, $CHCl_3$)



Hydrazone **3g**: pale yellowish solid, mp: 105 °C, ^{1}H-NMR ($CDCl_3$): δ = 1.32 (bs, 9H), 1.72 – 1.88 (m, 4H), 3.06 (t, *J* = 6.5 Hz, 4H), 5.13 (bs, 1H), 6.02 (bs, 1H), 6.33 (bs, 1H), 7.14 – 7.28 (m, 4H); ^{13}C-NMR ($CDCl_3$): δ = 155.0, 133.0, 128.7, 128.4, 128.2, 79.5, 51.2, 28.3, 23.2; HRMS-ESI: calculated for $C_{17}H_{24}N_3O2NaCl$ ($[M+Na]^+$): 360.1455, found: 360.1468; IR (neat): 3417, 2975, 1711, 1487, 1166, 829 cm^{-1}; HPLC conditions: AD-H column, hexane / 2-propanol = 95 / 5, flow rate = 0.6 mL min^{-1}, major enantiomer: t_R = 20,83 min; minor enantiomer: t_R = 24,03 min; $[\alpha]^D_{25}$ = + 54.6 (c = 1, $CHCl_3$)

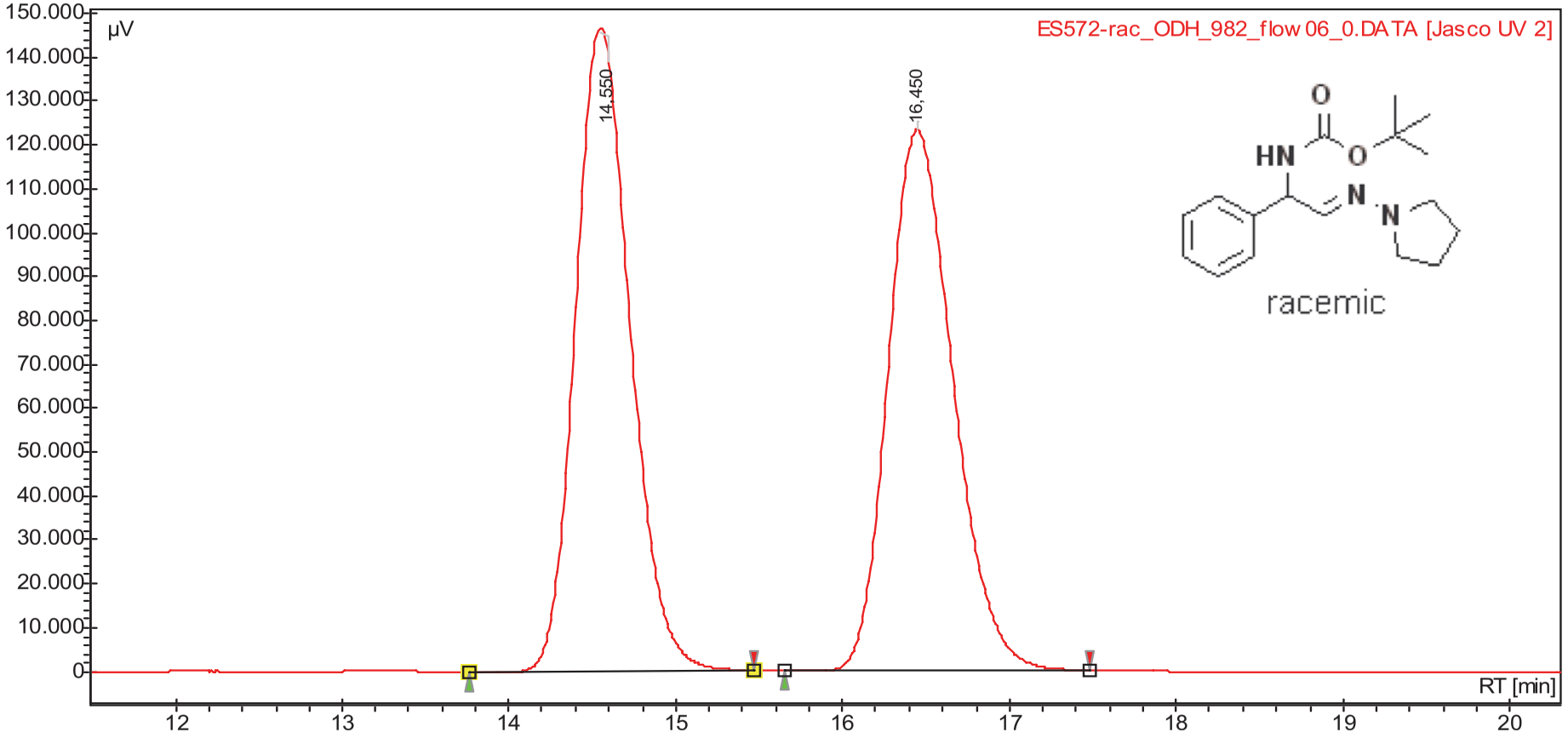


Hydrazone **3h**: clear colorless oil, ^{1}H-NMR ($CDCl_3$): δ = 1.33 (bs, 9H), 1.70 – 1.86 (m, 4H), 3.06 (t, *J* = 6.5 Hz, 4H), 3.72 (s, 3H), 5.13 (bs, 1H),

5.93 (bs, 1H), 6.39 (bs, 1H), 6.79 (d, *J* = 8.8 Hz, 2H), 7.17 (d, *J* = 8.8 Hz, 2H); ^{13}C-NMR ($CDCl_3$): δ= 158.8, 155.1, 128.3, 113.9, 79.2, 55.2, 51.3, 28.4, 23.1; HRMS-ESI: calculated for $C_{18}H_{27}N_3O_3Na$ ($[M+Na]^+$): 356.1950, found: 356.1960; IR (neat): 3415, 2974, 1713, 1511, 1248, 1169, 833 cm^{-1}; HPLC conditions: AD-H column, hexane / 2-propanol = 95 / 5, flow rate = 0.6 mL min^{-1}, minor enantiomer: t_R = 34,11 min; major enantiomer: t_R = 37,92 min; $[\alpha]^D_{25}$ = + 55,7 (c = 1, $CHCl_3$)

Chromatogram : ES572-rac_ODH_982_flow06_0

Method: ODH_982_flow06_acq30
Data file: ES572-rac_ODH_982_flow06_0.DATA
Date: 15.09.2006 16:56:58



ES572-rac_ODH_982_flow06_0.DATA [Jasco UV 2]

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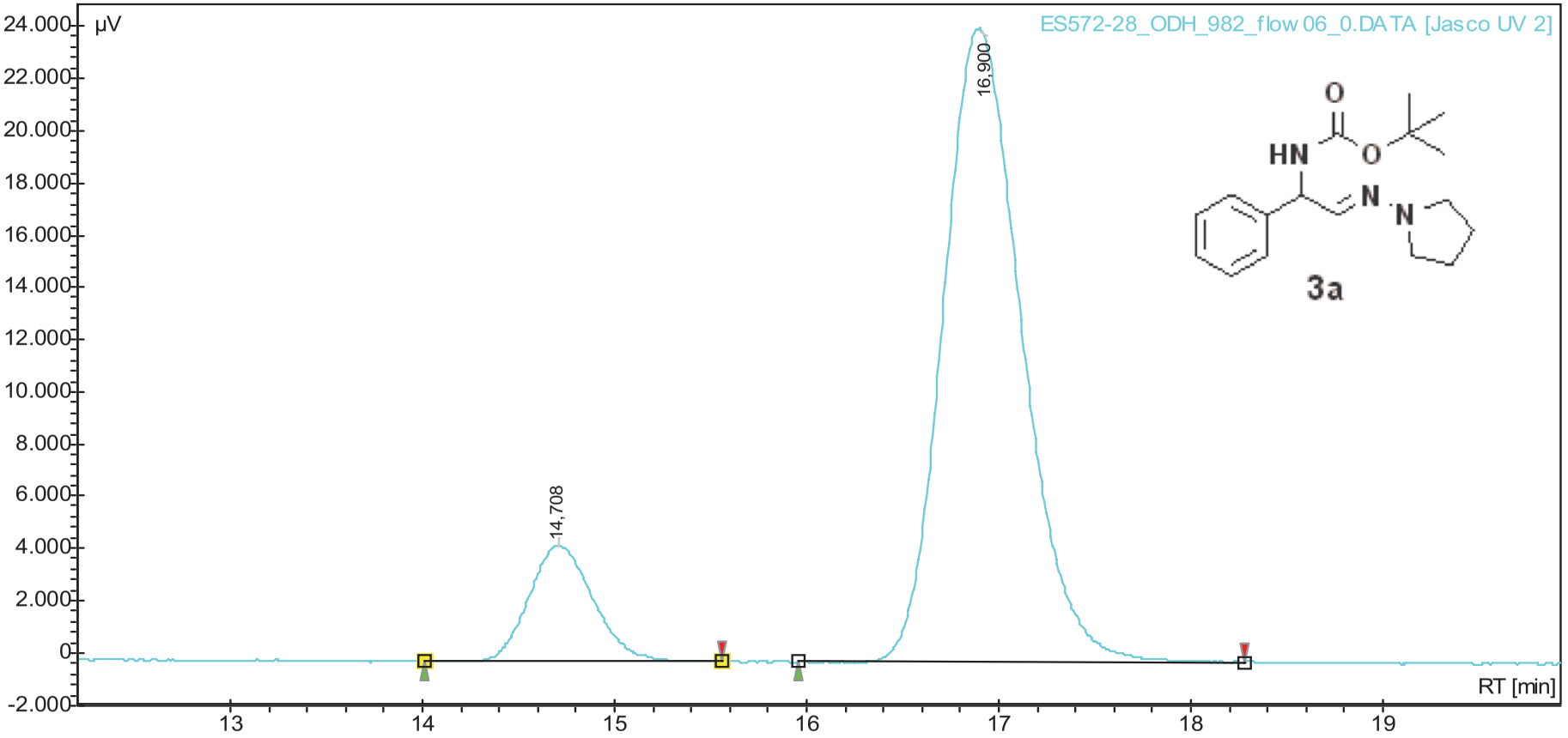
1	13,760	14,550	15,465	50,171
2	15,651	16,450	17,479	49,829
Total				100,000

Chromatogram : ES572-28_ODH_982_flow06_0

Method: ODH_982_flow06_acq30
Data file: ES572-28_ODH_982_flow06_0.DATA
Date: 21.10.2006 15:41:33



ES572-28_ODH_982_flow06_0.DATA [Jasco UV 2]

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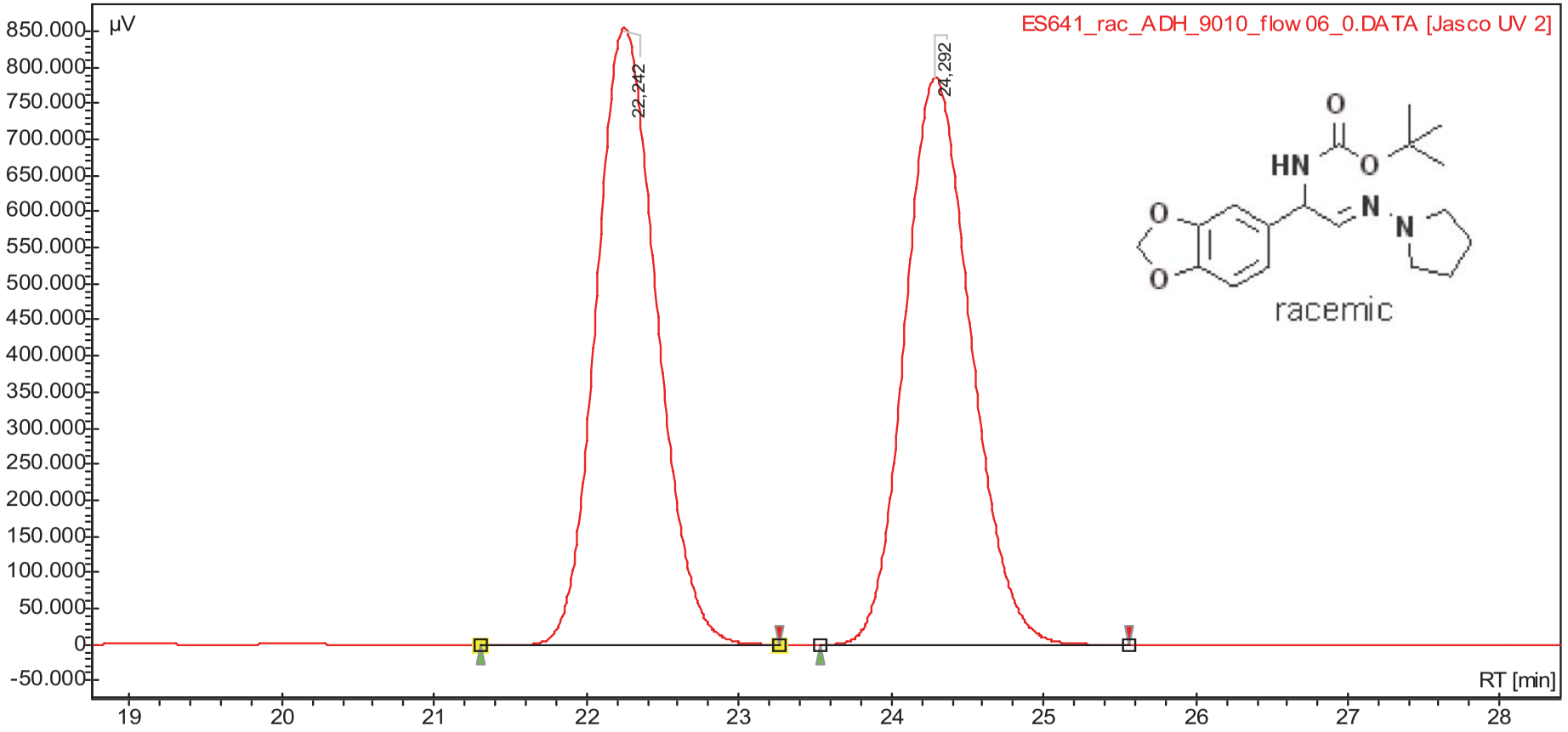
1	14,008	14,708	15,558	12,977
2	15,961	16,900	18,285	87,023
Total				100,000

Chromatogram : ES641_rac_ADH_9010_flow06_0

Method: ADH_9010_flow06_acq50
Data file: ES641_rac_ADH_9010_flow06_0.DATA
Date: 04.09.2006 17:02:44

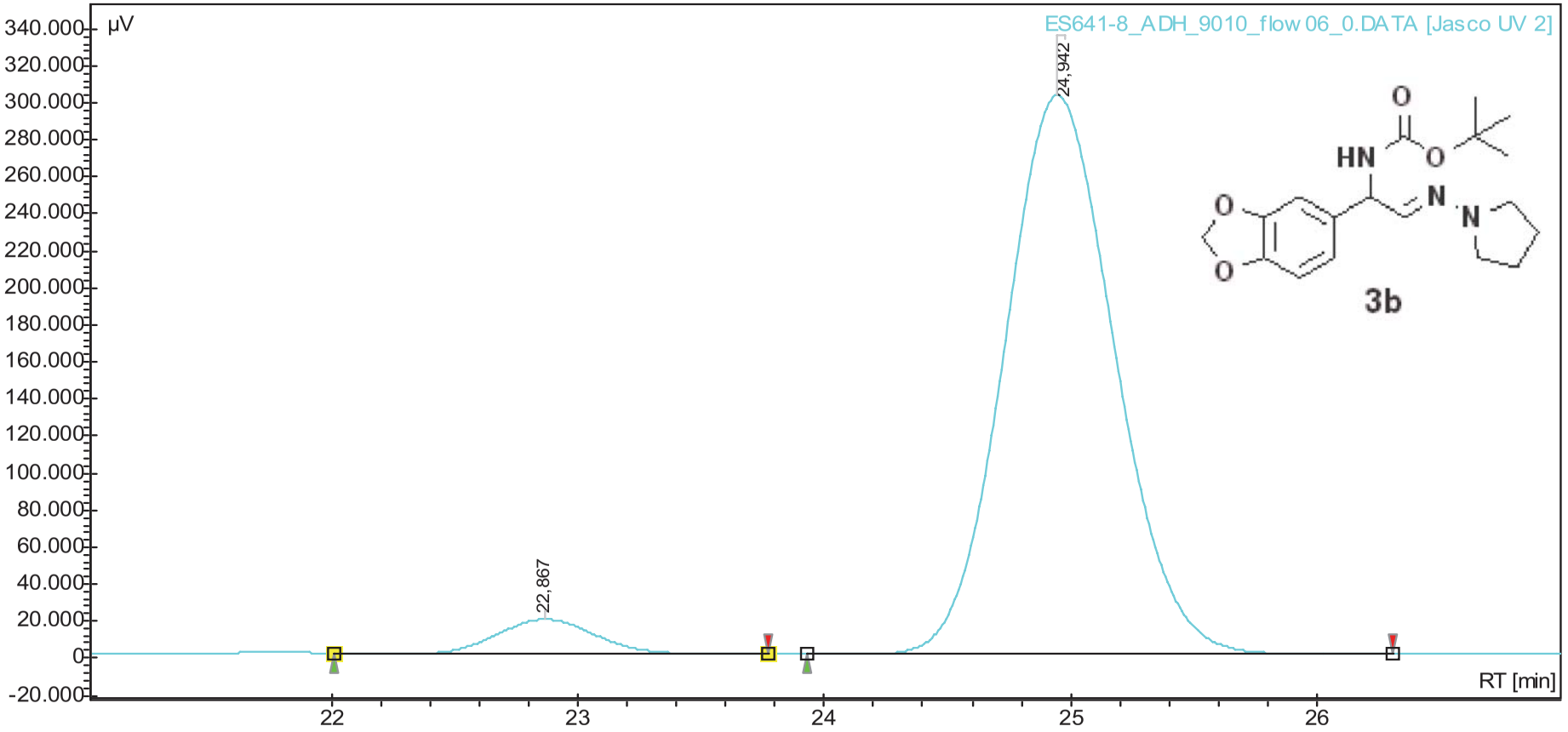


ES641_rac_ADH_9010_flow06_0.DATA [Jasco UV 2]

Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	21,309	22,242	23,259	49,912
2	23,538	24,292	25,557	50,088
Total				100,000

Chromatogram : ES641-8_ADH_9010_flow06_0

Method: ADH_9010_flow06_acq30
Data file: ES641-8_ADH_9010_flow06_0.DATA
Date: 21.10.2006 10:38:16

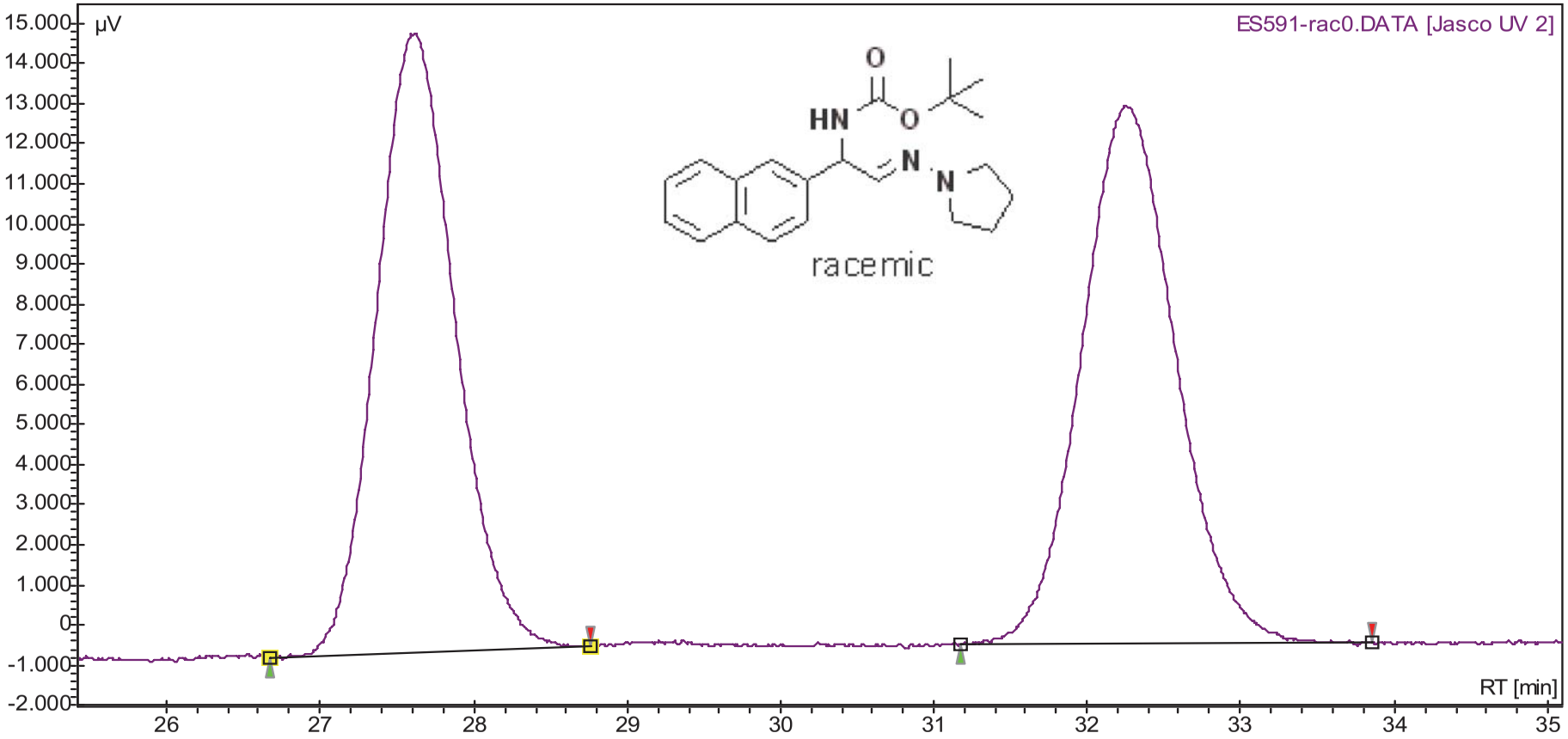


ES641-8_ADH_9010_flow06_0.DATA [Jasco UV 2]

Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	22,004	22,867	23,771	5,028
2	23,926	24,942	26,312	94,972
Total				100,000

Chromatogram : ES591-rac0

Method: HPLC1_ADH_955_flow06_acq_50
Data file: ES591-rac0.DATA
Date: 20.11.2006 12:14:08

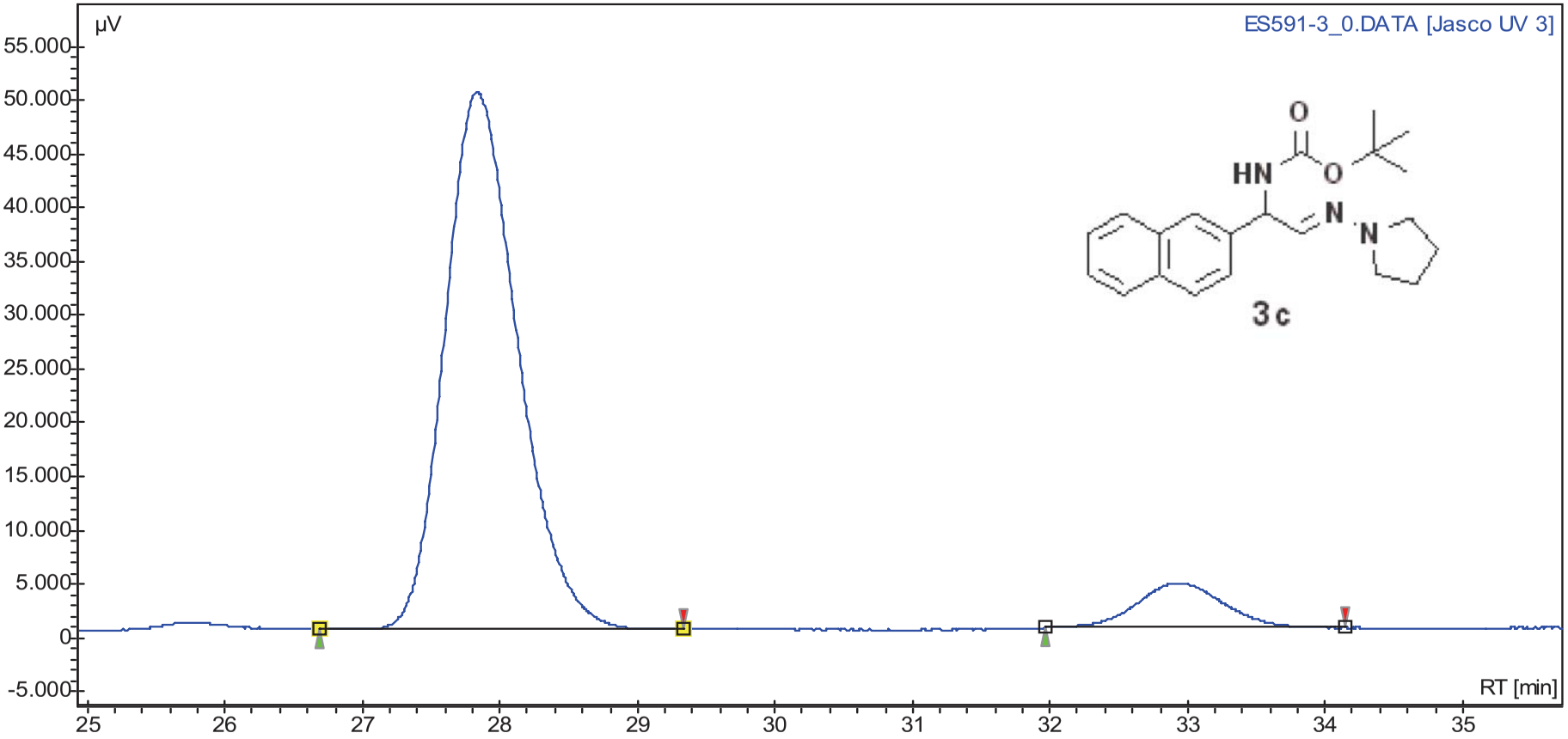


ES591-rac0.DATA [Jasco UV 2]

Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	26,678	27,625	28,765	49,110
2	31,178	32,250	33,853	50,890
Total				100,000

Chromatogram : ES591-3_0

Method: HPLC1_ADH_955_flow06_acq_50
Data file: ES591-3_0.DATA
Date: 20.11.2006 08:55:04



ES591-3_0.DATA [Jasco UV 3]

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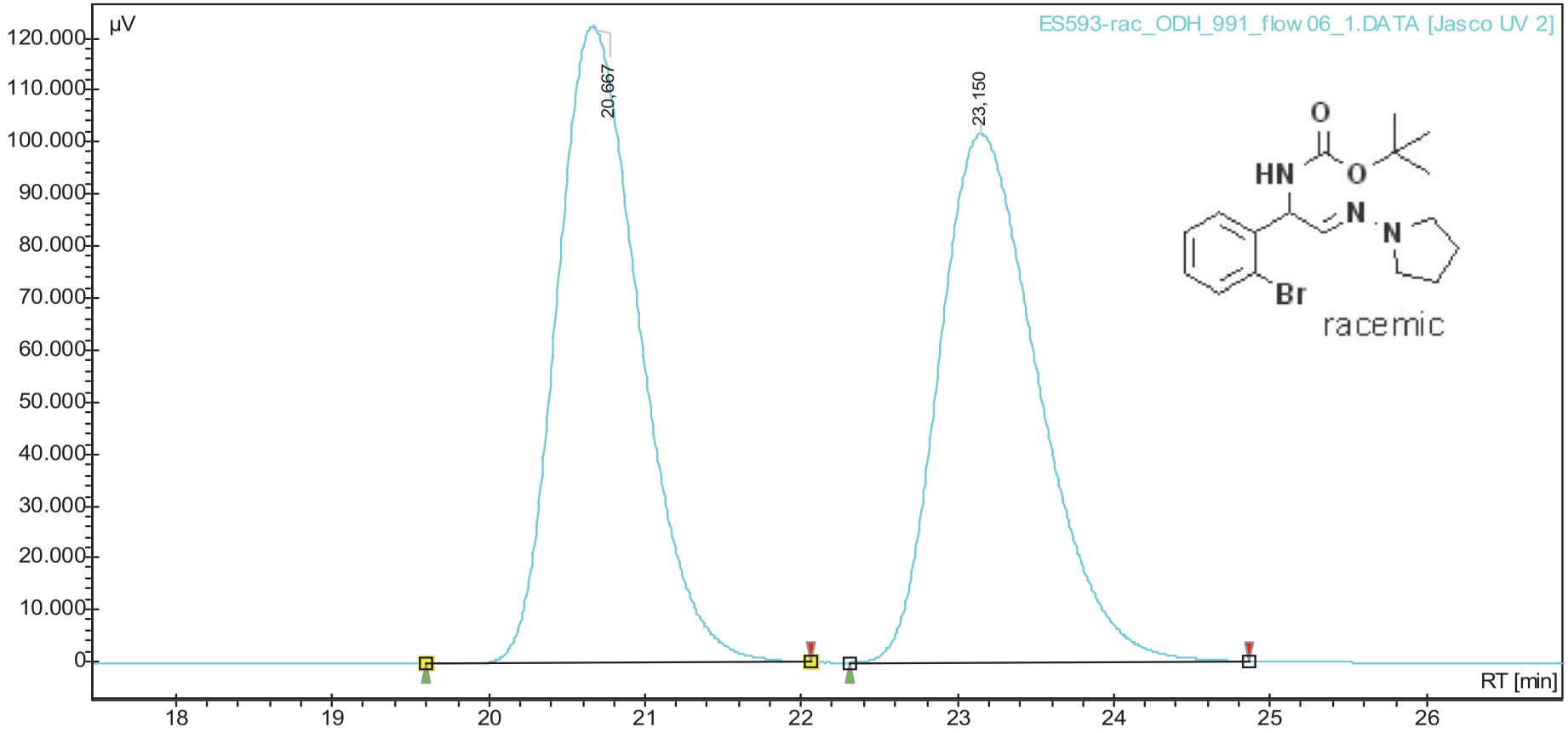
	[Min]	[Min]	[Min]	[%]
1	26,688	27,833	29,330	91,026
2	31,972	32,933	34,139	8,974
Total				100,000

Chromatogram : ES593-rac_ODH_991_flow06_1

Method: ODH_991_flow06_acq30
Data file: ES593-rac_ODH_991_flow06_1.DATA
Date: 17.09.2006 18:19:03



ES593-rac_ODH_991_flow06_1.DATA [Jasco UV 2]

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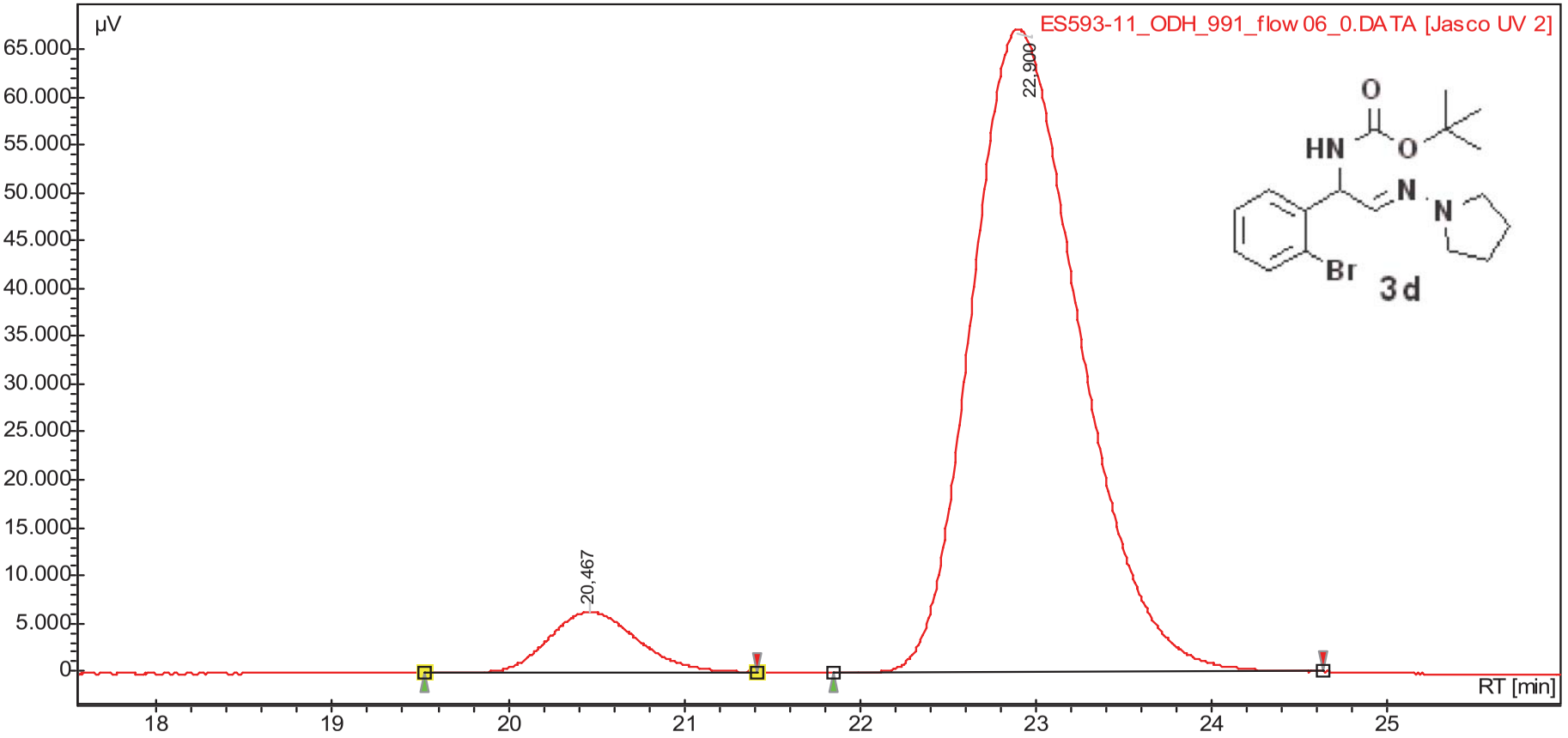
	[Min]	[Min]	[Min]	[%]
1	19,596	20,667	22,061	50,103
2	22,312	23,150	24,861	49,897
Total				100,000

Chromatogram : ES593-11_ODH_991_flow06_0

Method: ODH_991_flow06_acq30
Data file: ES593-11_ODH_991_flow06_0.DATA
Date: 17.09.2006 17:46:20

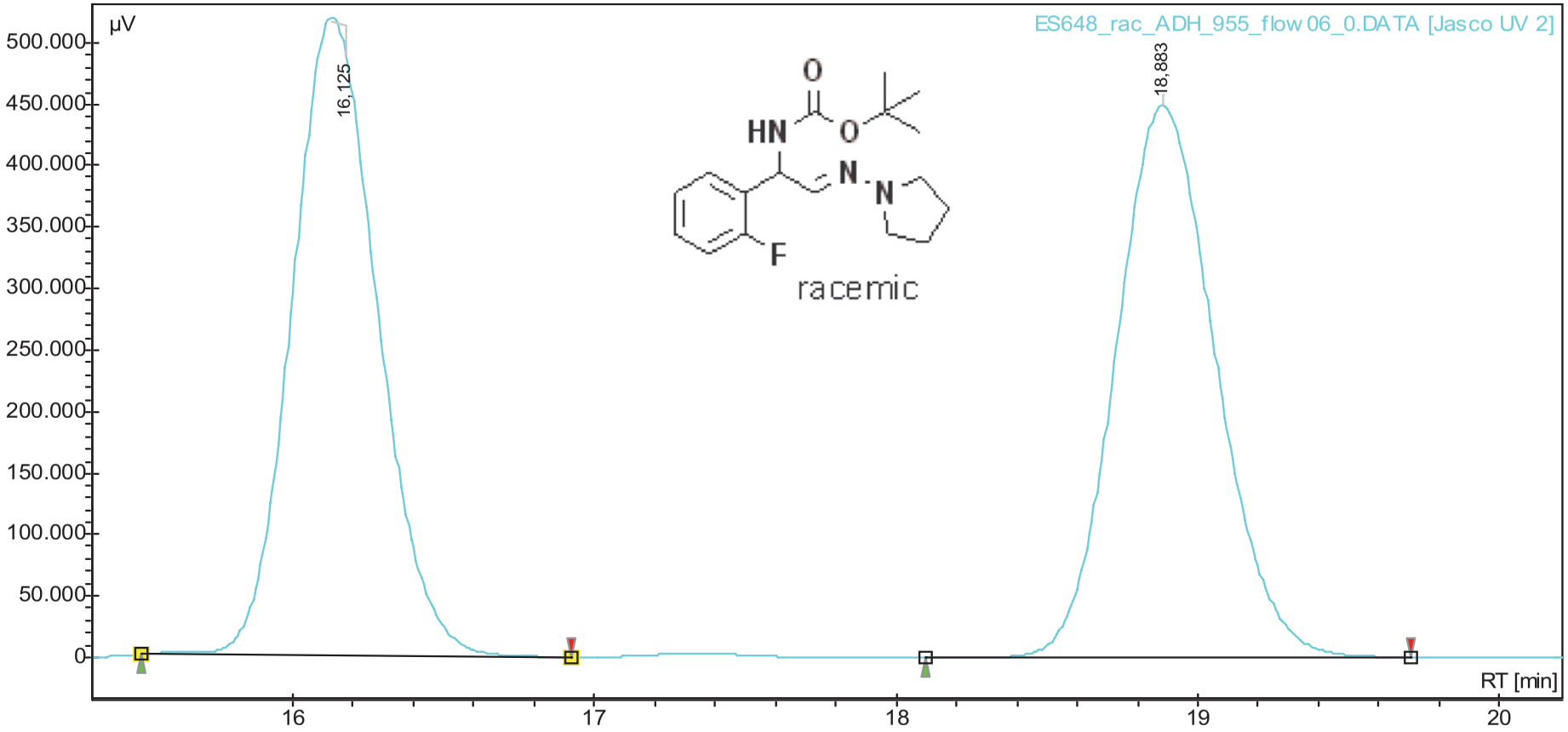


ES593-11_ODH_991_flow06_0.DATA [Jasco UV 2]

Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	19,525	20,467	21,415	7,273
2	21,849	22,900	24,638	92,727
Total				100,000

Chromatogram : ES648_rac_ADH_955_flow06_0

Method: ADH_955_flow06_acq60
Data file: ES648_rac_ADH_955_flow06_0.DATA
Date: 04.09.2006 15:27:18



ES648_rac_ADH_955_flow06_0.DATA [Jasco UV 2]

Index	Start	Time	End	Area %
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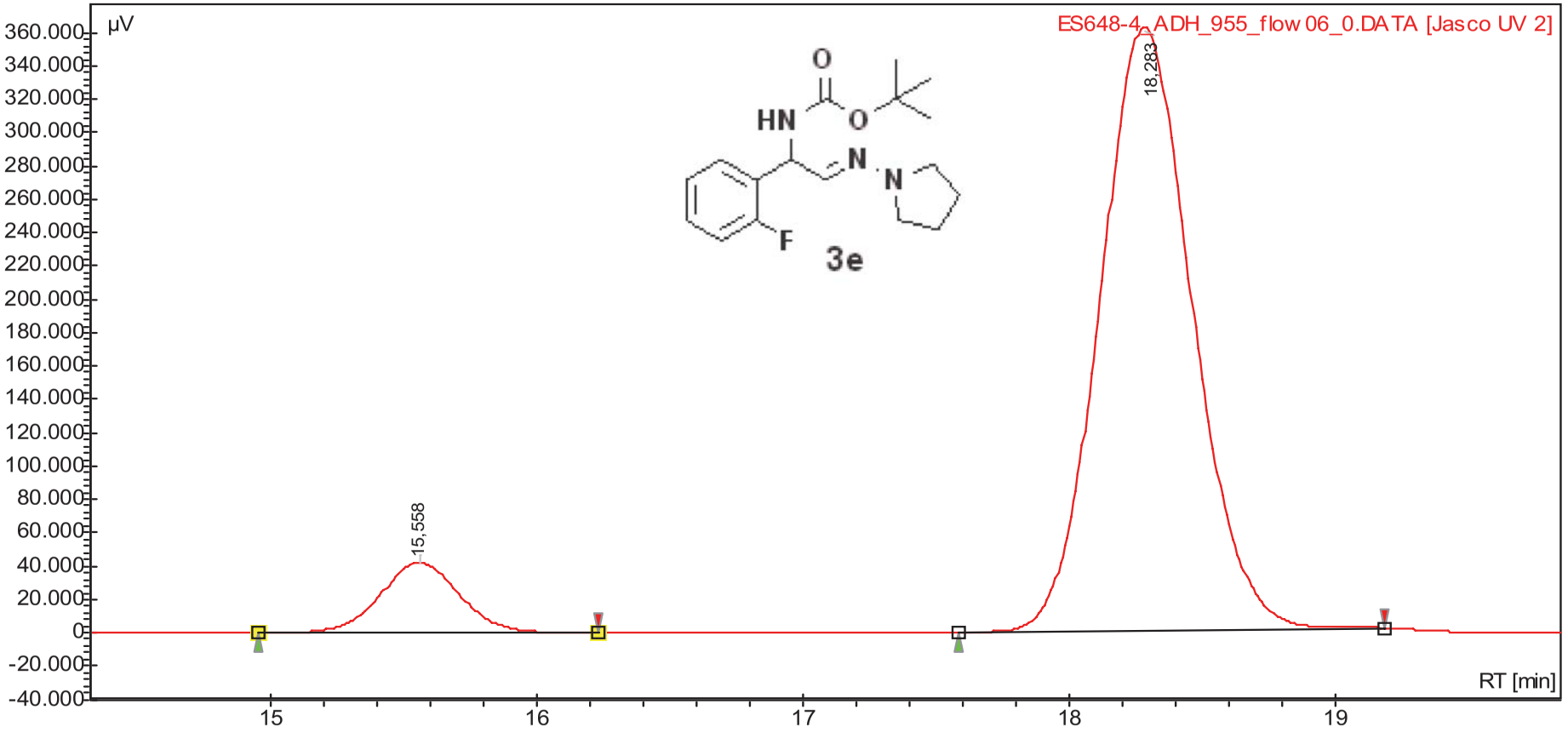
1	15,496	16,125	16,921	49,943
2	18,099	18,883	19,711	50,057
Total				100,000

Chromatogram : ES648-4_ADH_955_flow06_0

Method: ADH_955_flow06_acq30
Data file: ES648-4_ADH_955_flow06_0.DATA
Date: 12.09.2006 20:06:41



ES648-4_ADH_955_flow06_0.DATA [Jasco UV 2]

Index	Start	Time	End	Area %
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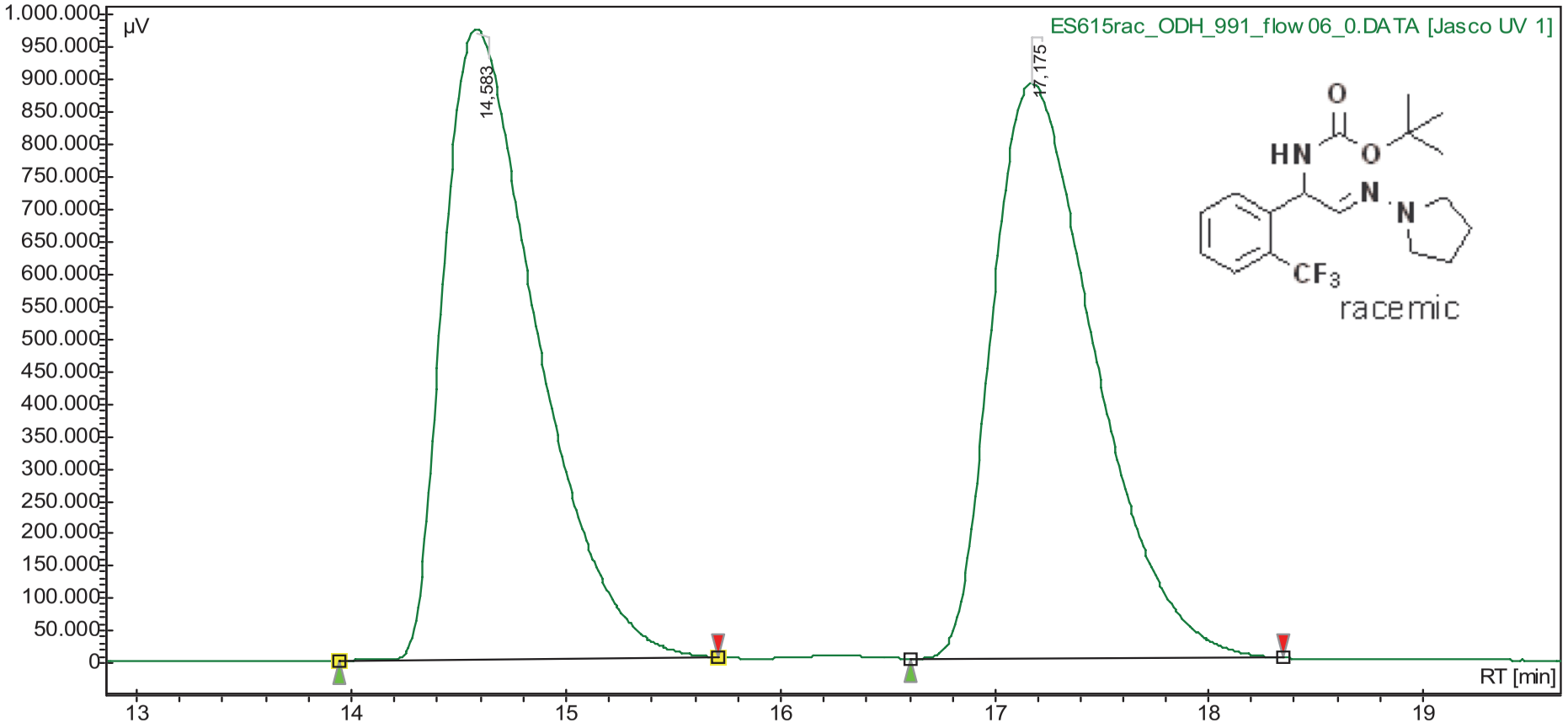
1	14,954	15,558	16,230	9,231
2	17,581	18,283	19,182	90,769
Total				100,000

Chromatogram : ES615rac_ODH_991_flow06_0

Method: ODH_991_flow06_acq30
Data file: ES615rac_ODH_991_flow06_0.DATA
Date: 03.08.2006 13:55:07



ES615rac_ODH_991_flow06_0.DATA [Jasco UV 1]

Index	Start	Time	End	Area %
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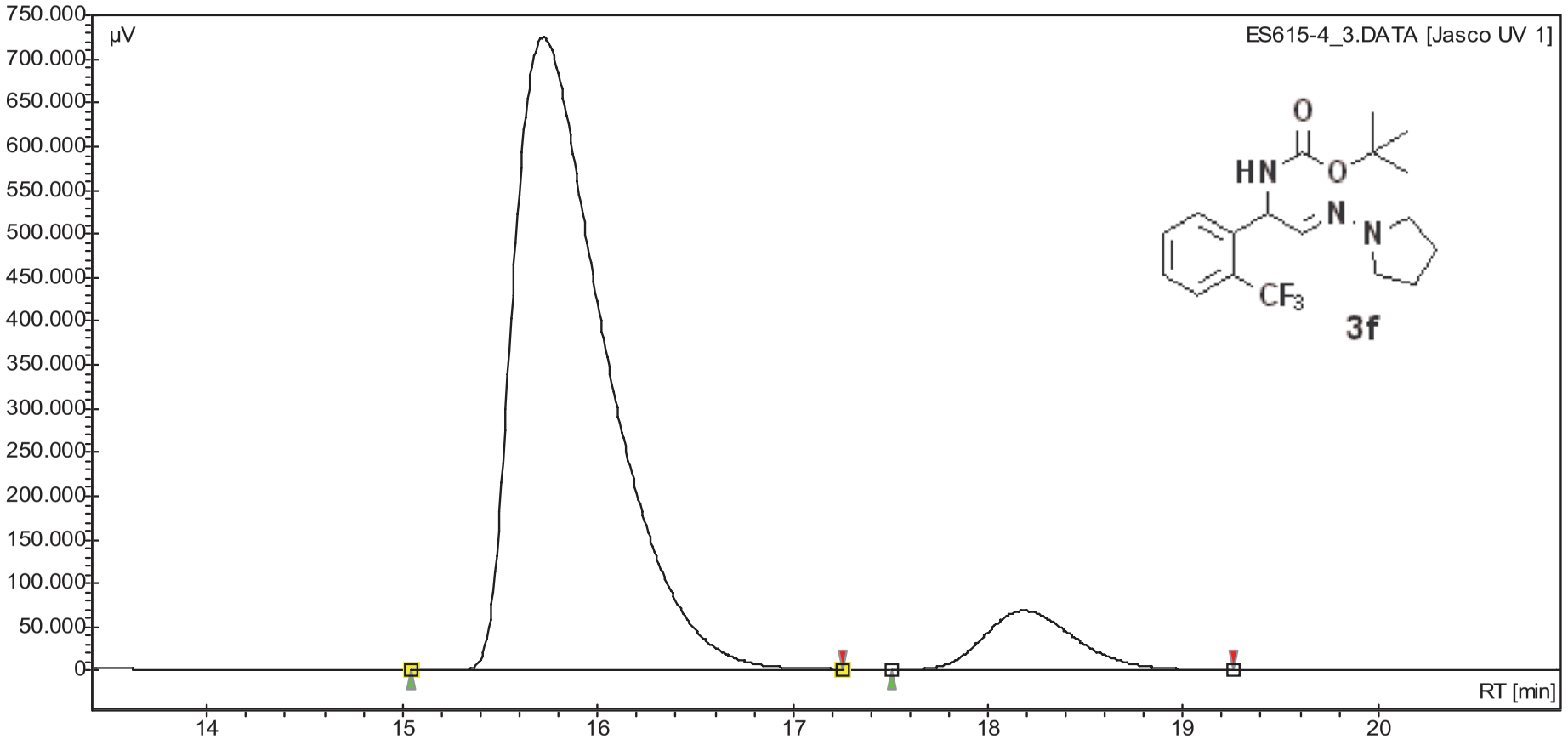
1	13,946	14,583	15,713	49,847
2	16,612	17,175	18,347	50,153
Total				100,000

Chromatogram : ES615-4_3

Method: HPLC2_ODH_991_flow06_acq30
Data file: ES615-4_3.DATA
Date: 20.11.2006 17:57:57



ES615-4_3.DATA [Jasco UV 1]

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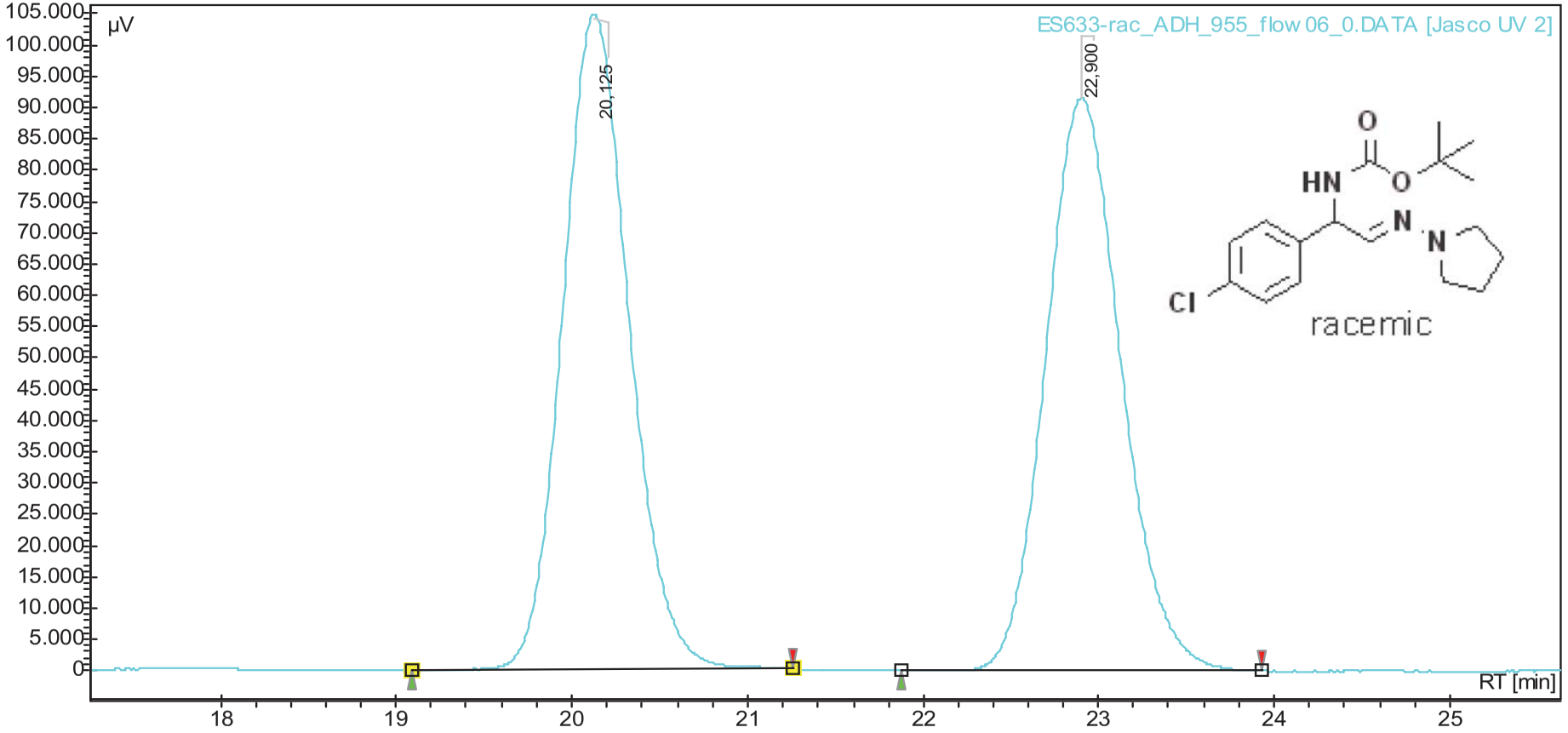
1	15,042	15,725	17,256	91,499
2	17,507	18,183	19,262	8,501
Total				100,000

Chromatogram : ES633-rac_ADH_955_flow06_0

Method: ADH_955_flow06_acq60
Data file: ES633-rac_ADH_955_flow06_0.DATA
Date: 09.09.2006 19:37:31

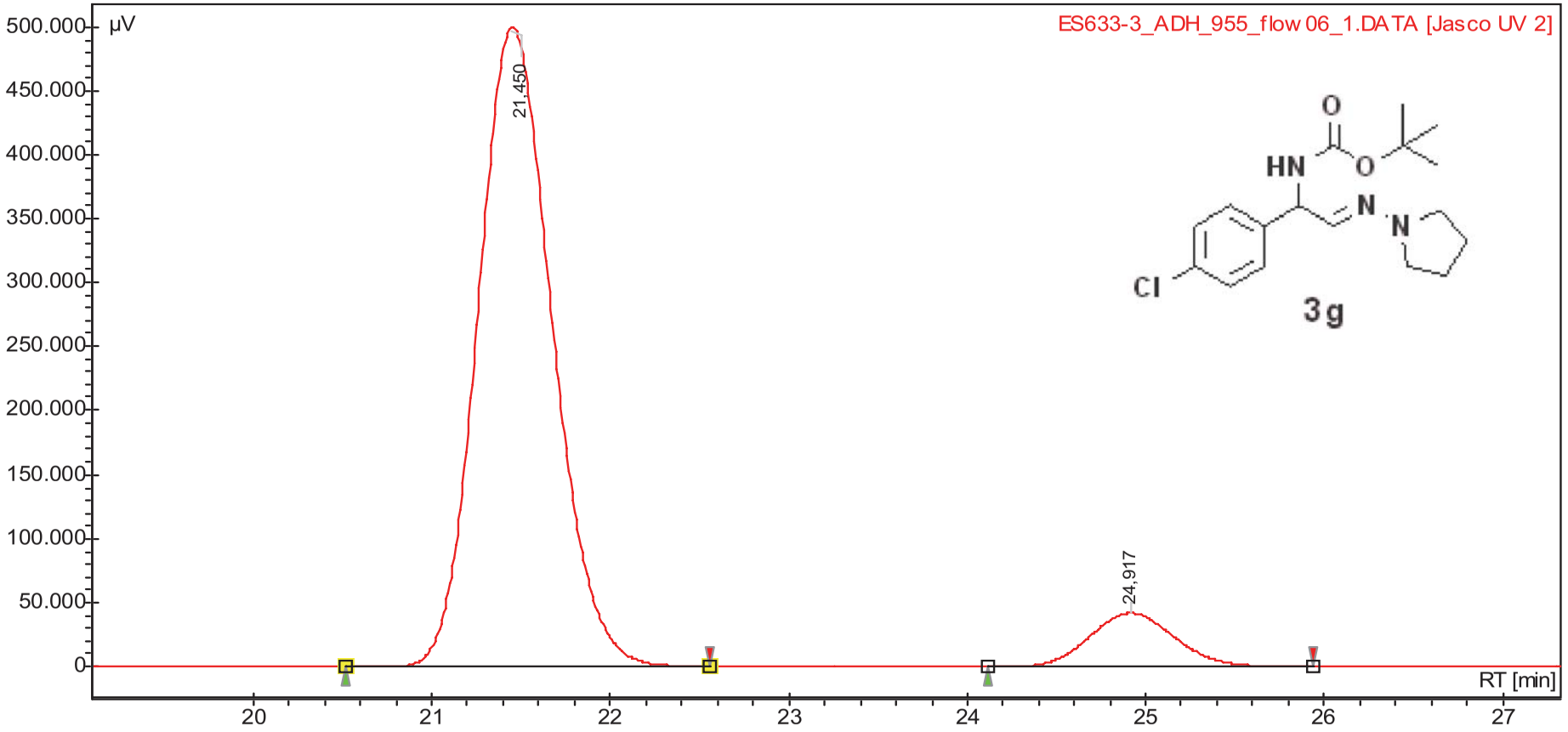


ES633-rac_ADH_955_flow06_0.DATA [Jasco UV 2]

Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	19,091	20,125	21,260	50,317
2	21,880	22,900	23,926	49,683
Total				100,000

Chromatogram : ES33-3_ADH_955_flow06_1

Method: ADH_955_flow06_acq30
Data file: ES33-3_ADH_955_flow06_1.DATA
Date: 11.09.2006 08:37:26

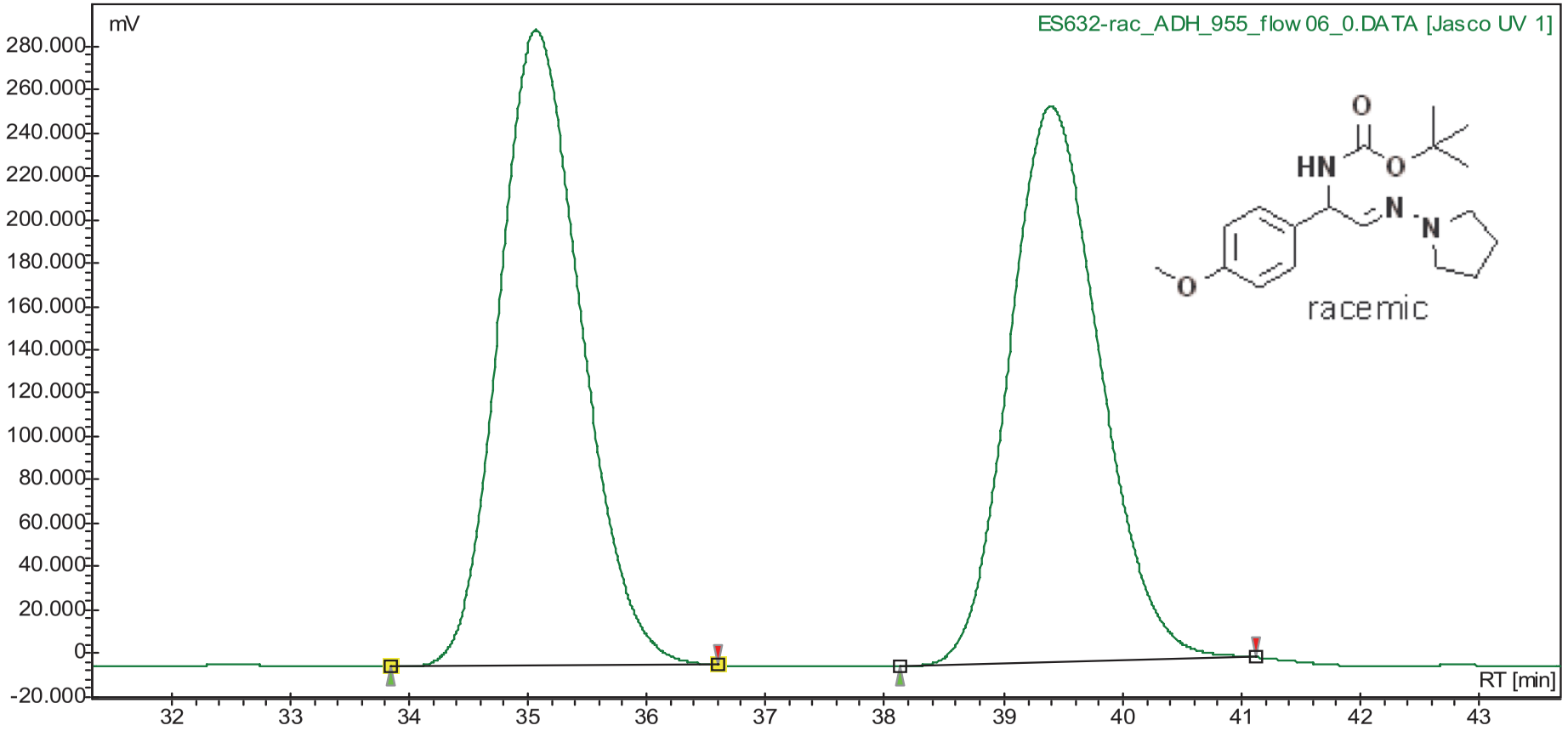


ES633-3_ADH_955_flow06_1.DATA [Jasco UV 2]

Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	20,517	21,450	22,562	91,127
2	24,112	24,917	25,940	8,873
Total				100,000

Chromatogram : ES632-rac_ADH_955_flow06_0

Method: HPLC2_ADH_955_flow06_acq45
Data file: ES632-rac_ADH_955_flow06_0.DATA
Date: 29.11.2006 12:37:24

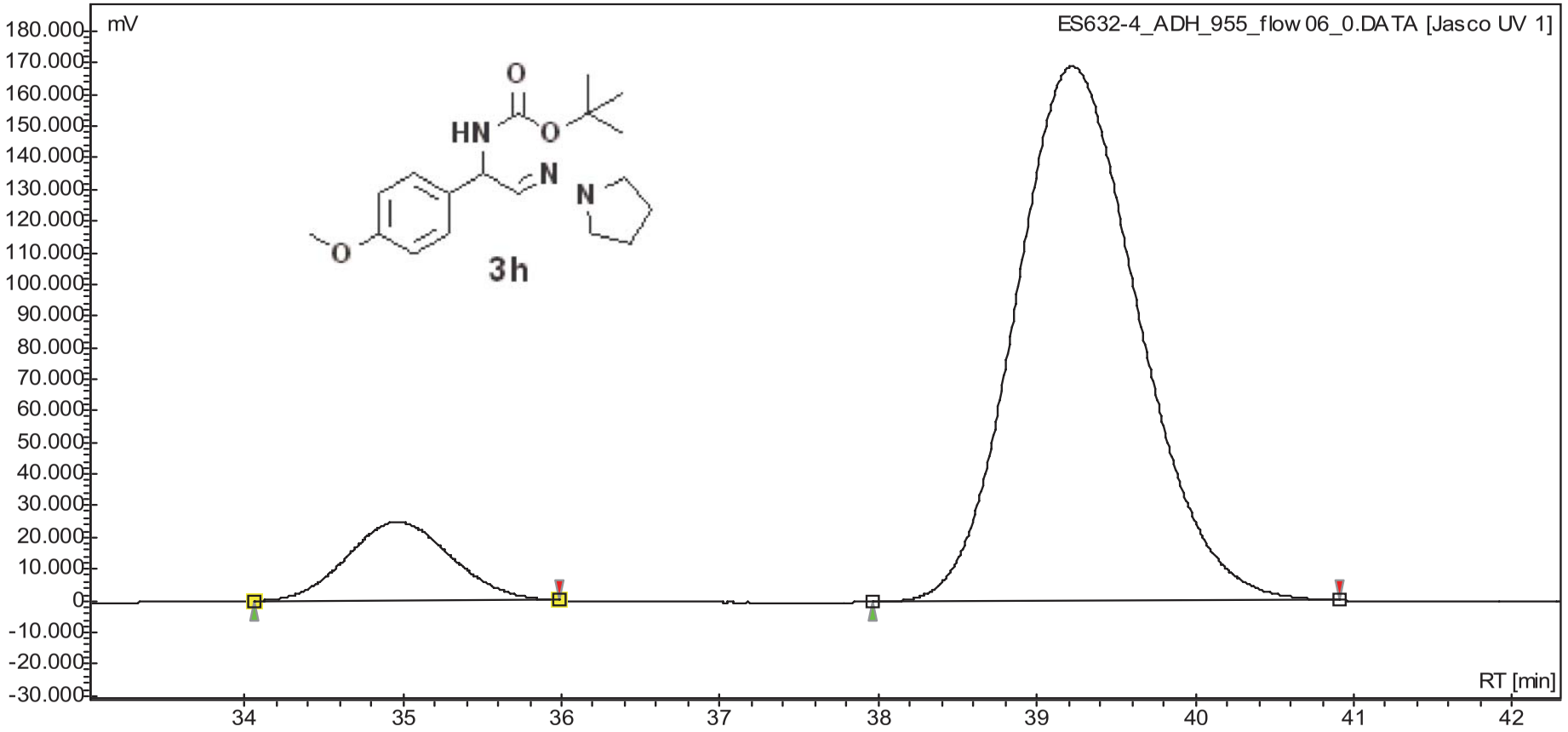


ES632-rac_ADH_955_flow06_0.DATA [Jasco UV 1]

Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	33,843	35,067	36,605	50,969
2	38,121	39,400	41,129	49,031
Total				100,000

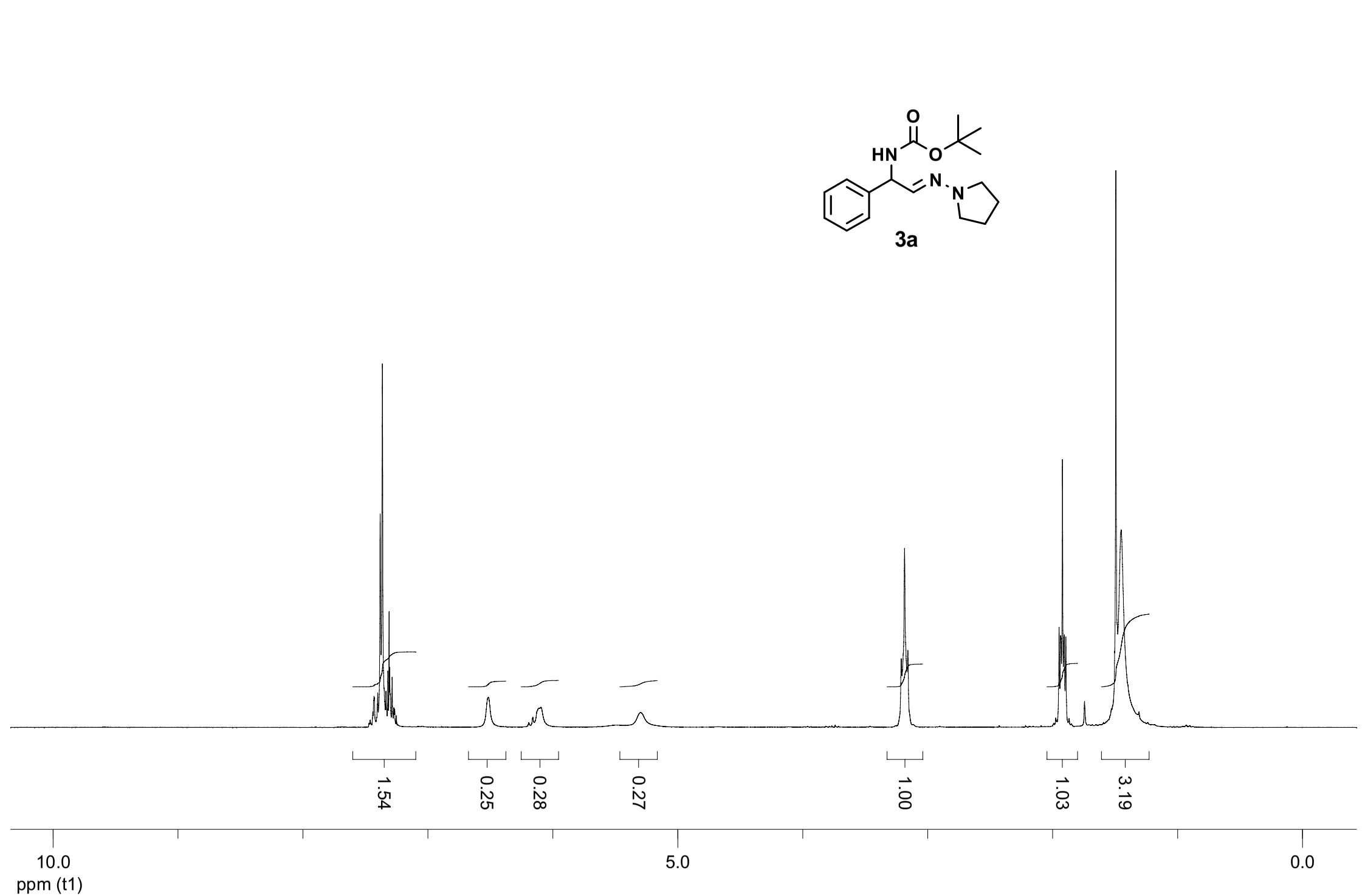
Chromatogram : ES632-4_ADH_955_flow06_0

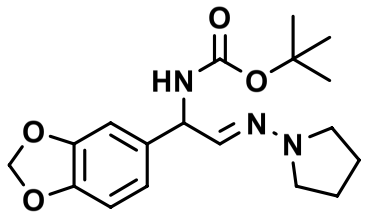
Method: HPLC2_ADH_955_flow06_acq45
Data file: ES632-4_ADH_955_flow06_0.DATA
Date: 29.11.2006 13:25:05



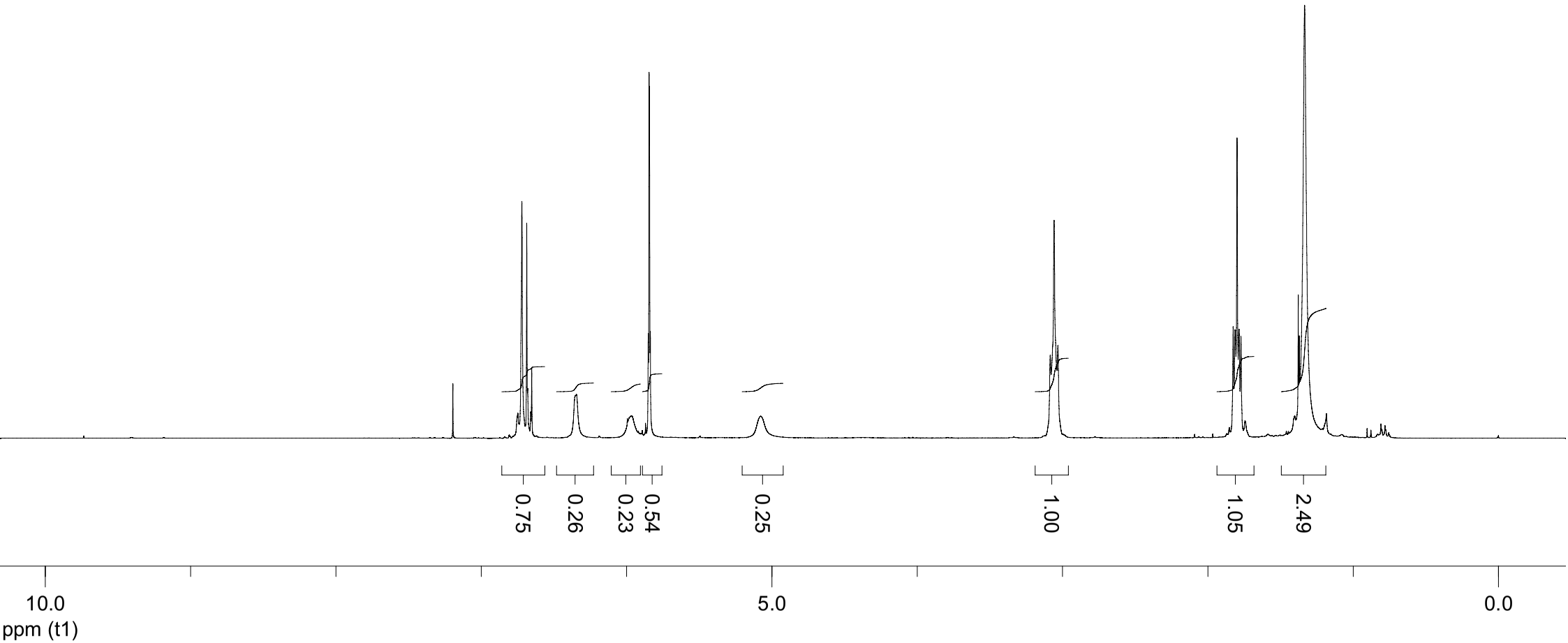
ES632-4_ADH_955_flow06_0.DATA [Jasco UV 1]

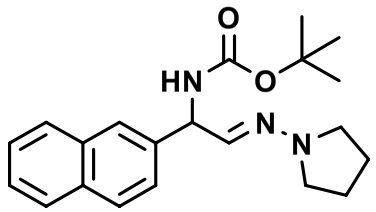
Index	Start	Time	End	Area %
	[Min]	[Min]	[Min]	[%]
1	34,061	34,967	35,984	11,143
2	37,962	39,225	40,907	88,857
Total				100,000


O
HN
O
N
N
3a
1.54
0.25
0.28
0.27
1.00
1.03
3.19
10.0
ppm (t1)
5.0
0.0

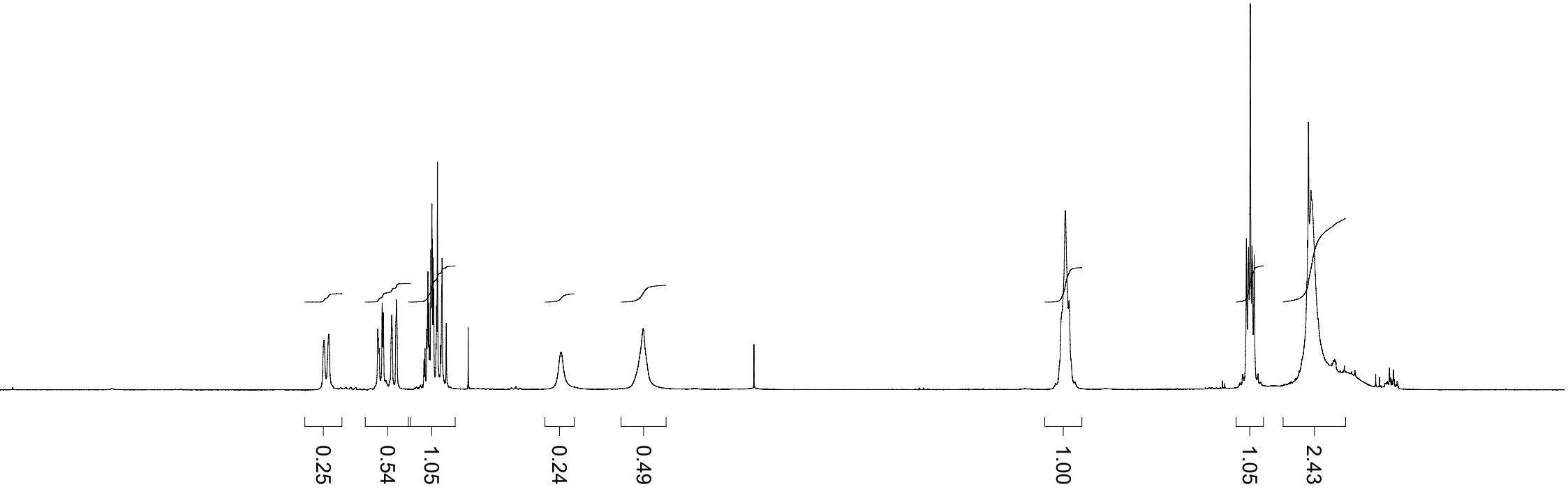


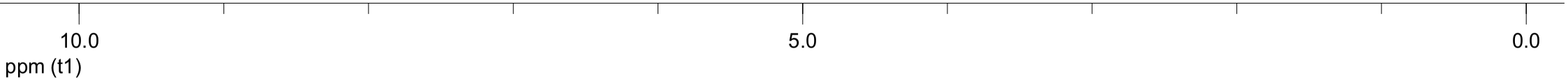
3b

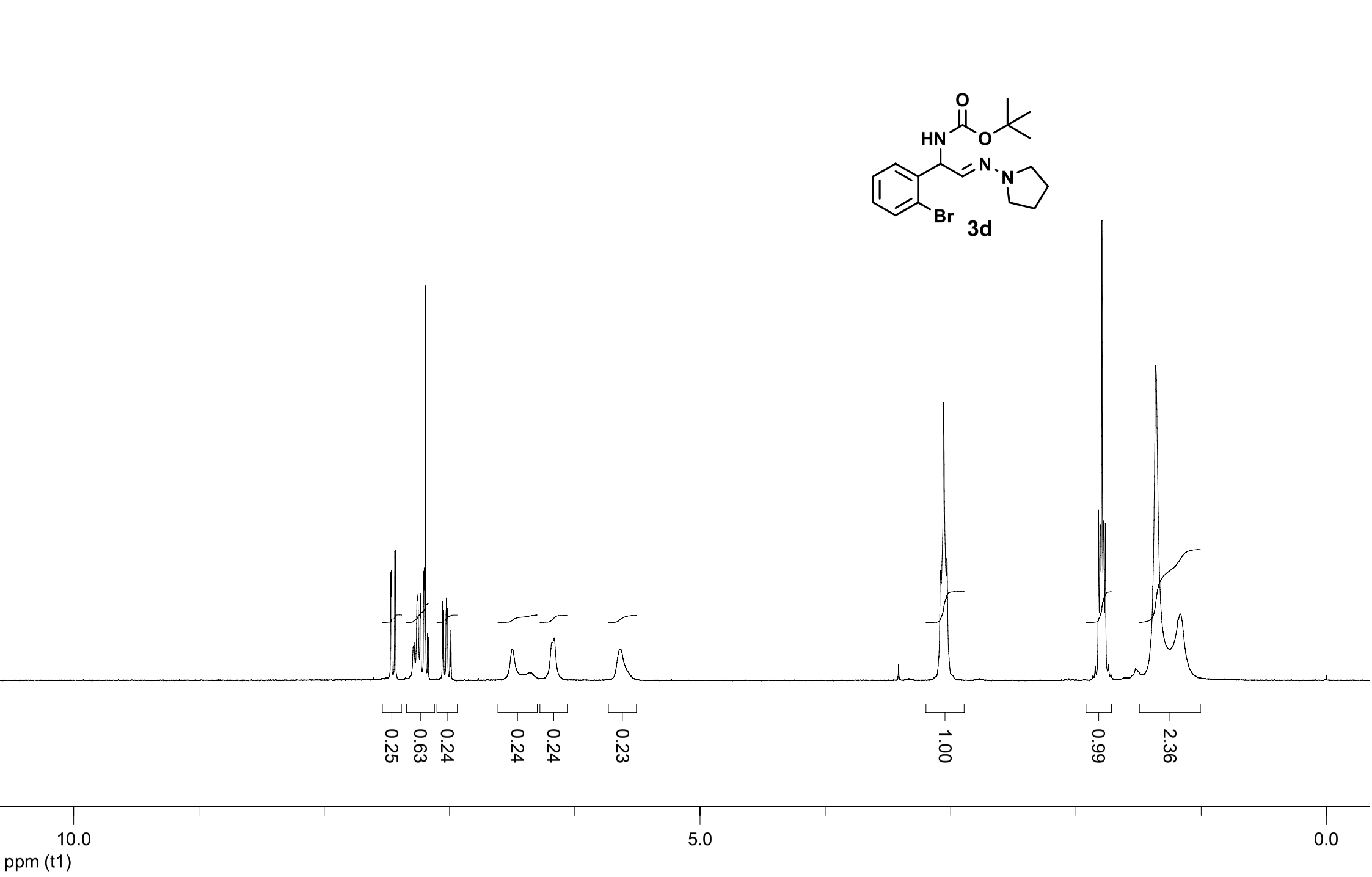


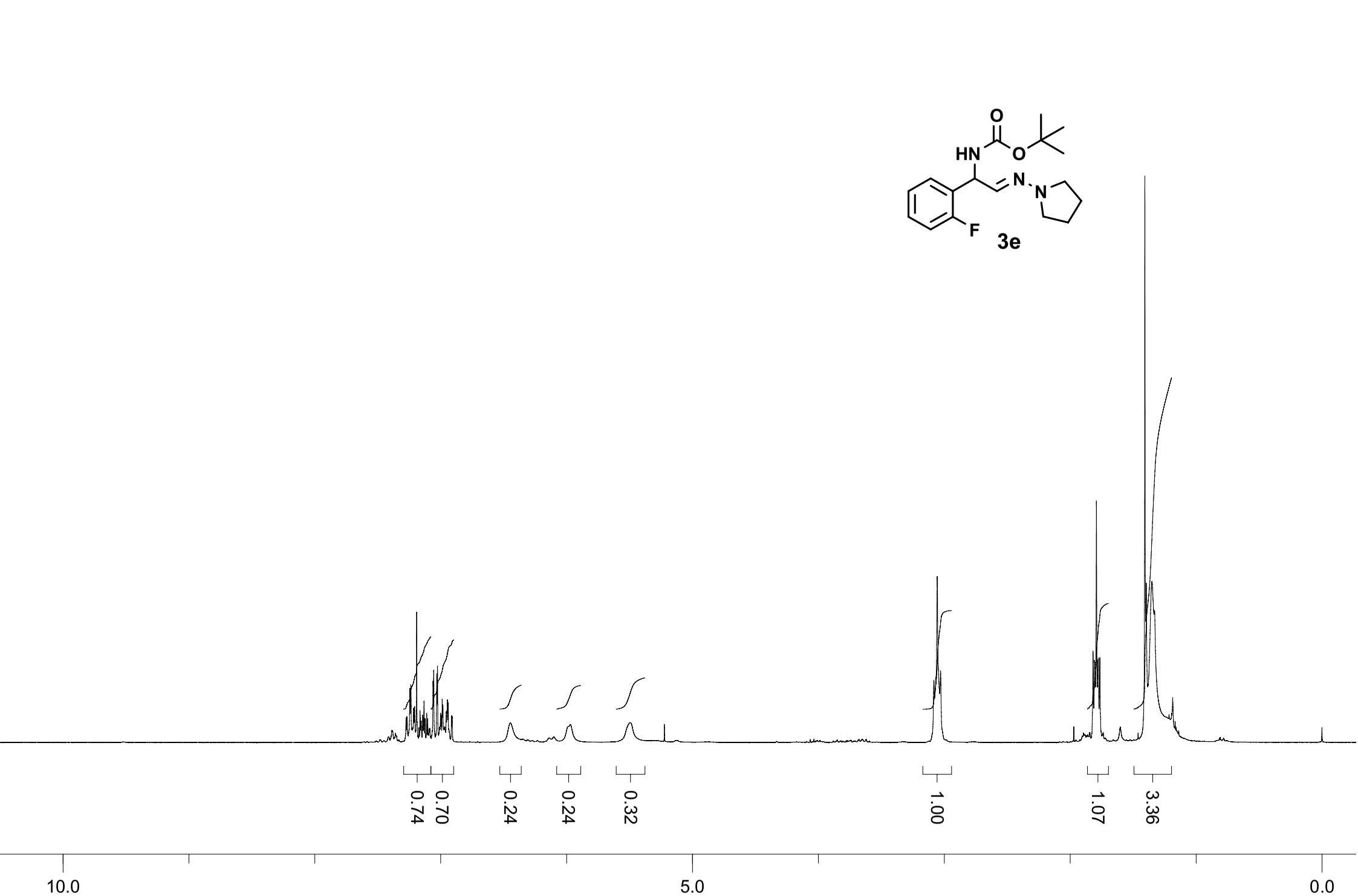


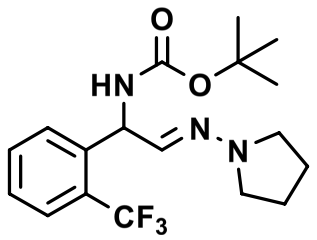
3c



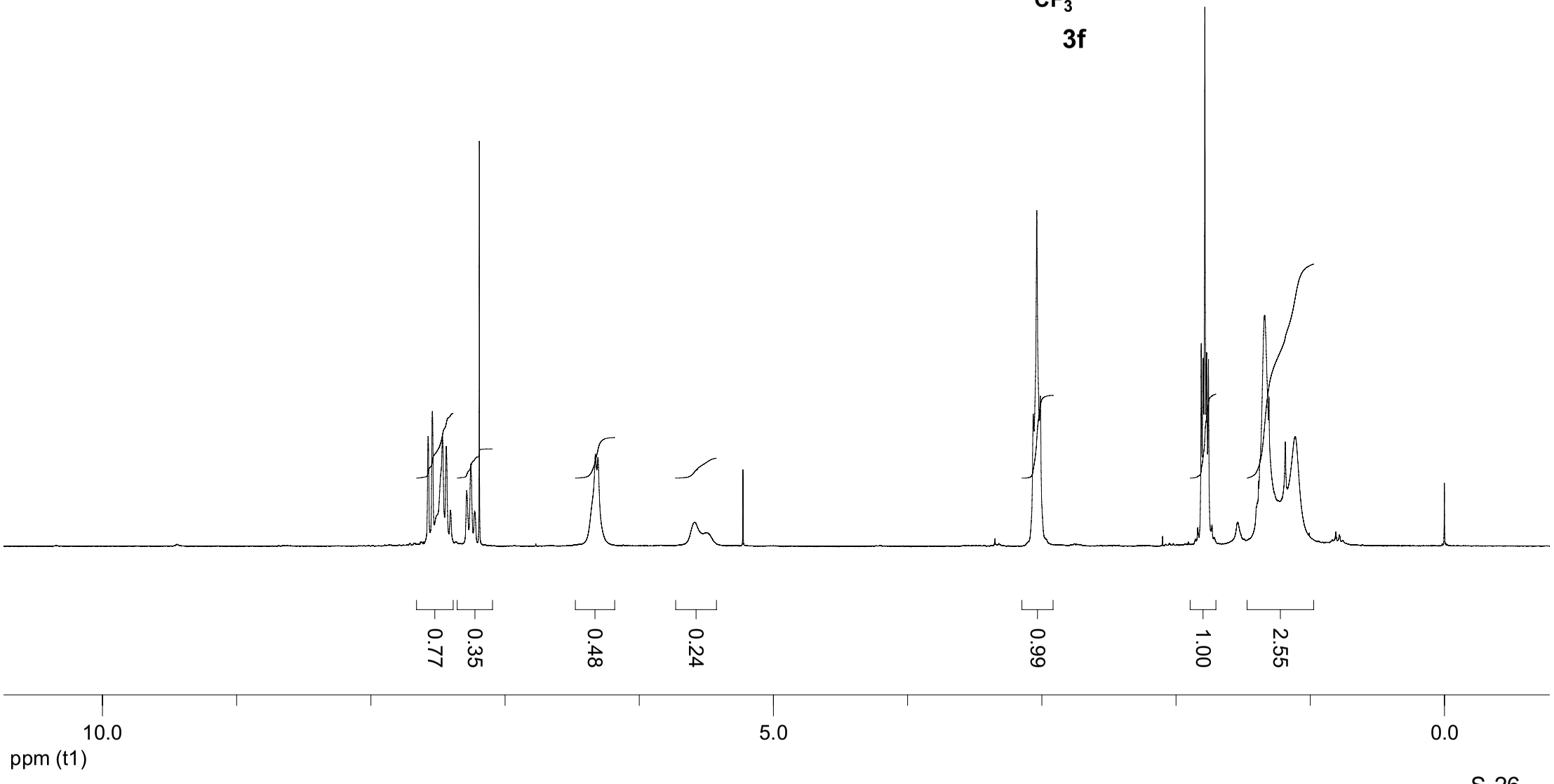


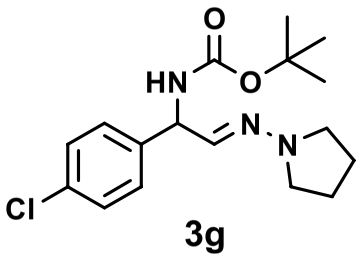

O
HN
O
N
N
Br
3d
0.25
0.63
0.24
0.24
0.24
0.23
1.00
0.99
2.36
10.0
5.0
0.0
ppm (t1)


O
HN
O
N
N
F
3e
0.74
0.70
0.24
0.24
0.32
1.00
1.07
3.36
10.0
5.0
0.0
ppm (t1)

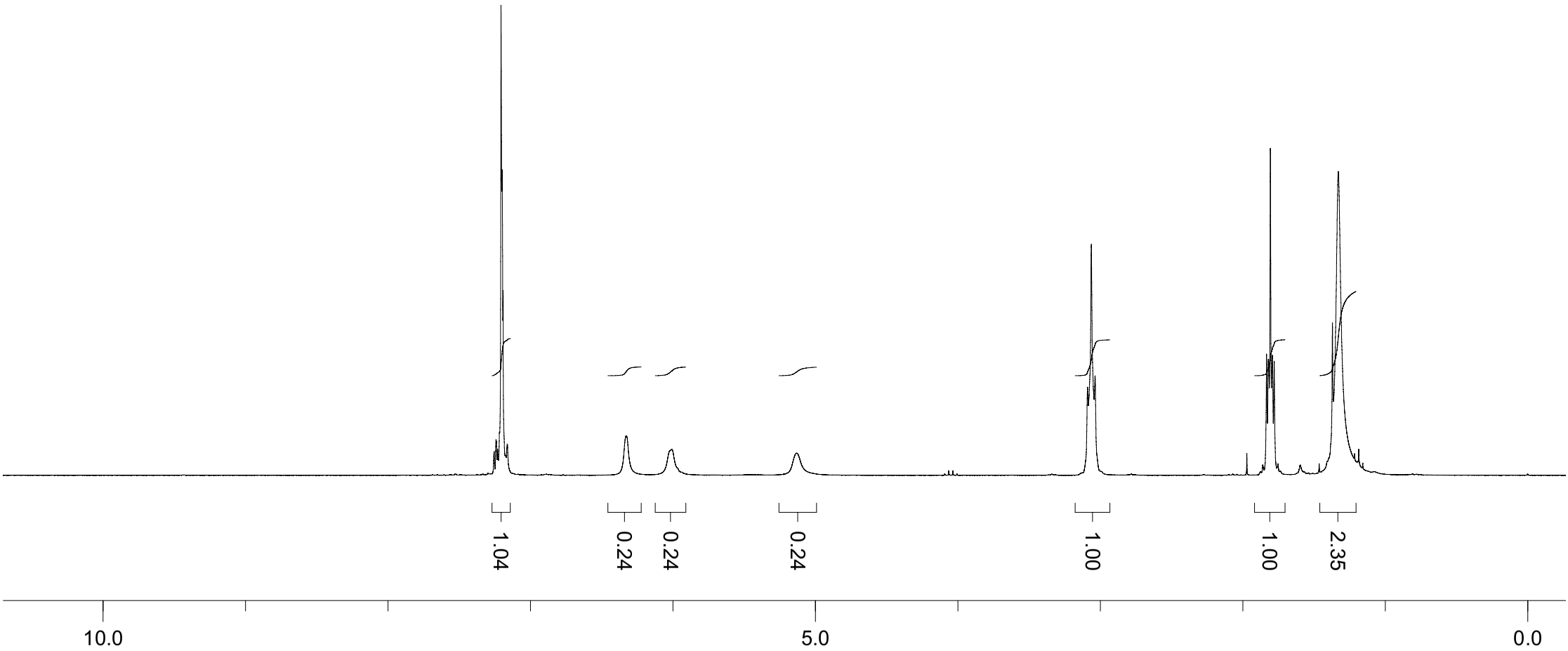


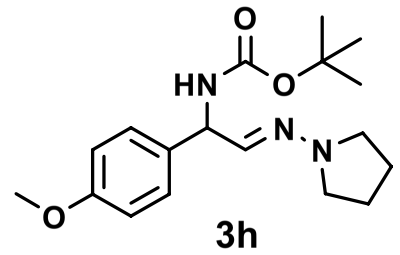
3f



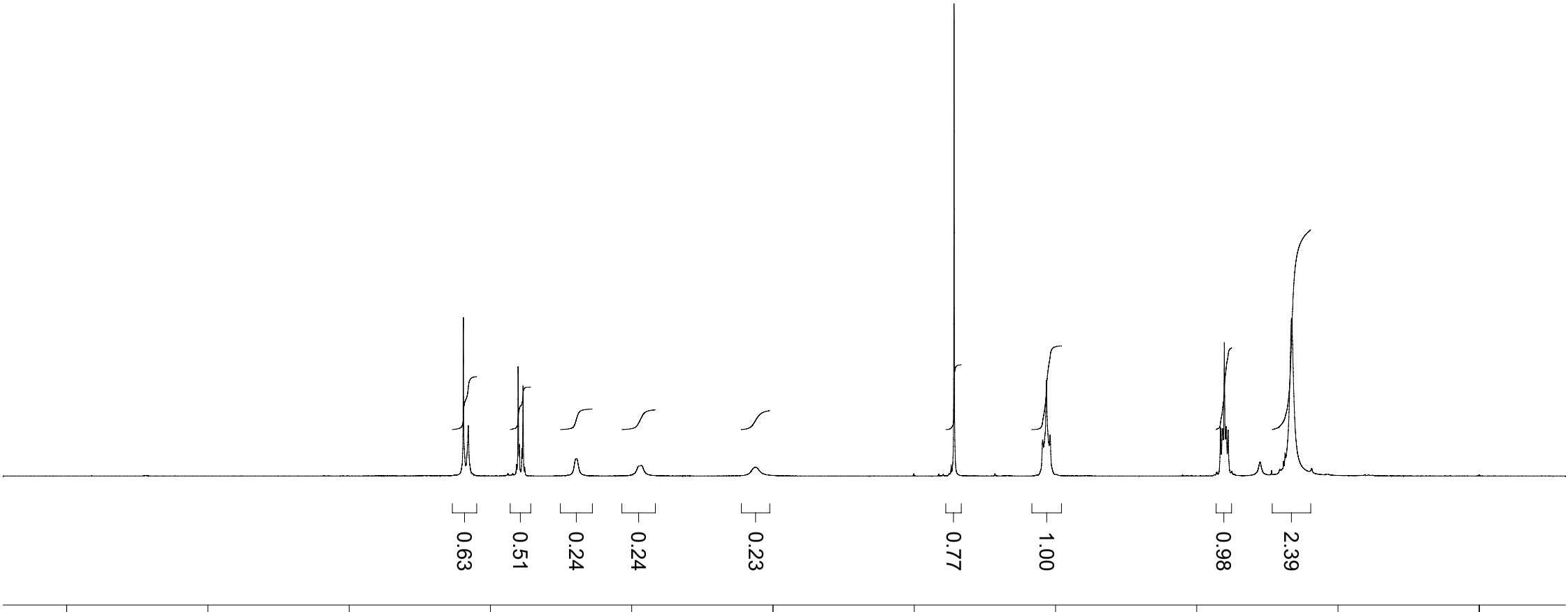


3g





3h



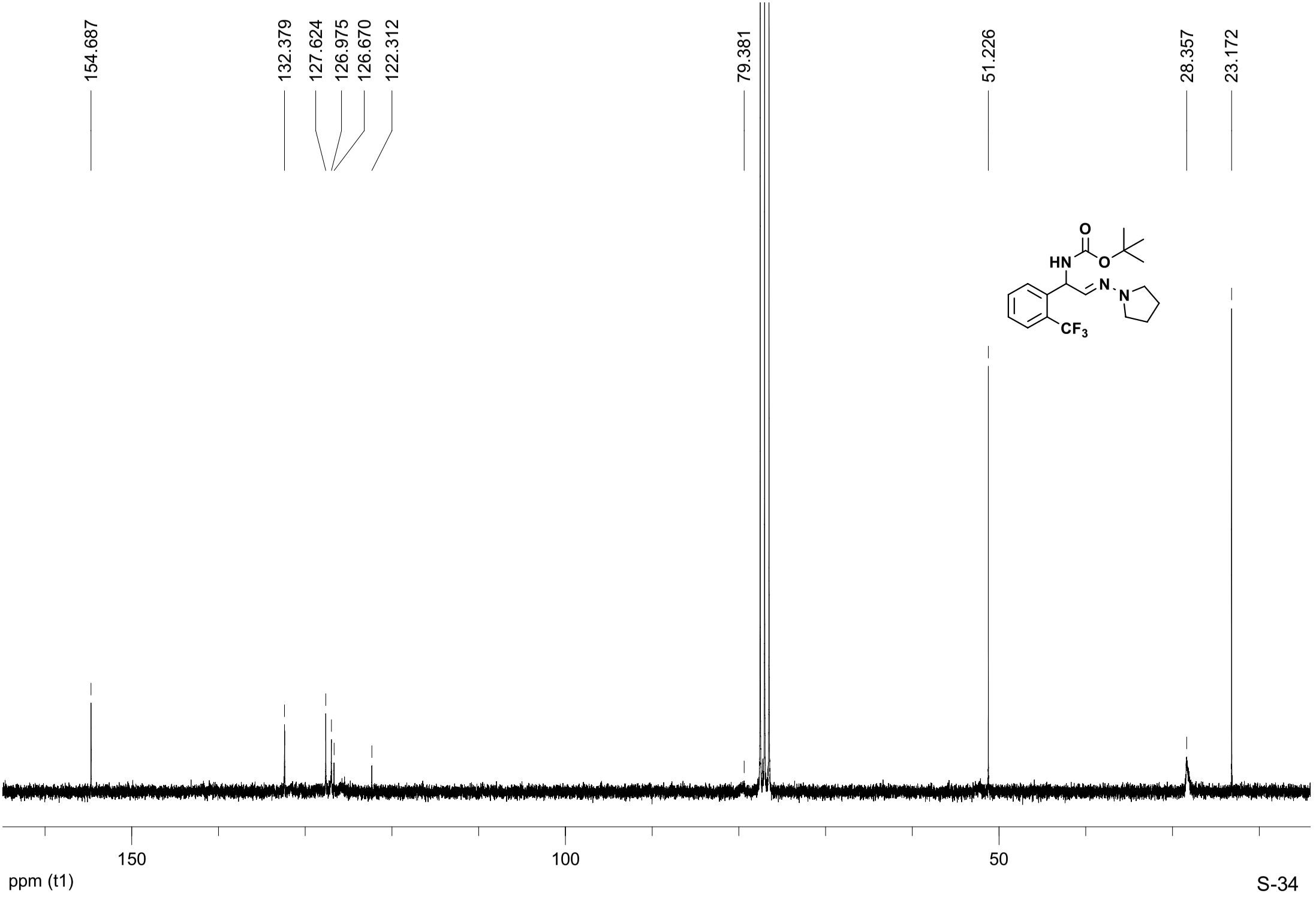
155.1
132.9
128.6
128.0
127.3
127.1
125.8
79.4
51.3
28.4
23.2
150
100
50
ppm (t1)

155.1
147.9
146.8
135.5
132.9
120.5
108.3
107.4
101.0
89.2
79.4
51.3
28.4
23.2
150
100
50
ppm (t1)

155.2
134.1
131.0
128.9
128.1
126.2
125.6
124.4
123.4
79.5
51.3
28.4
23.2
150
100
50
ppm (t1)

154.9
133.0
130.7
128.6
127.9
122.8
79.5
51.3
28.3
23.2
150
100
50
ppm (t1)
Br
NH
O
O
N
N

154.9
138.2
128.8
128.7
128.0
124.4
124.4
79.5
51.2
28.3
23.2
150
100
50
ppm (t1)
S-33

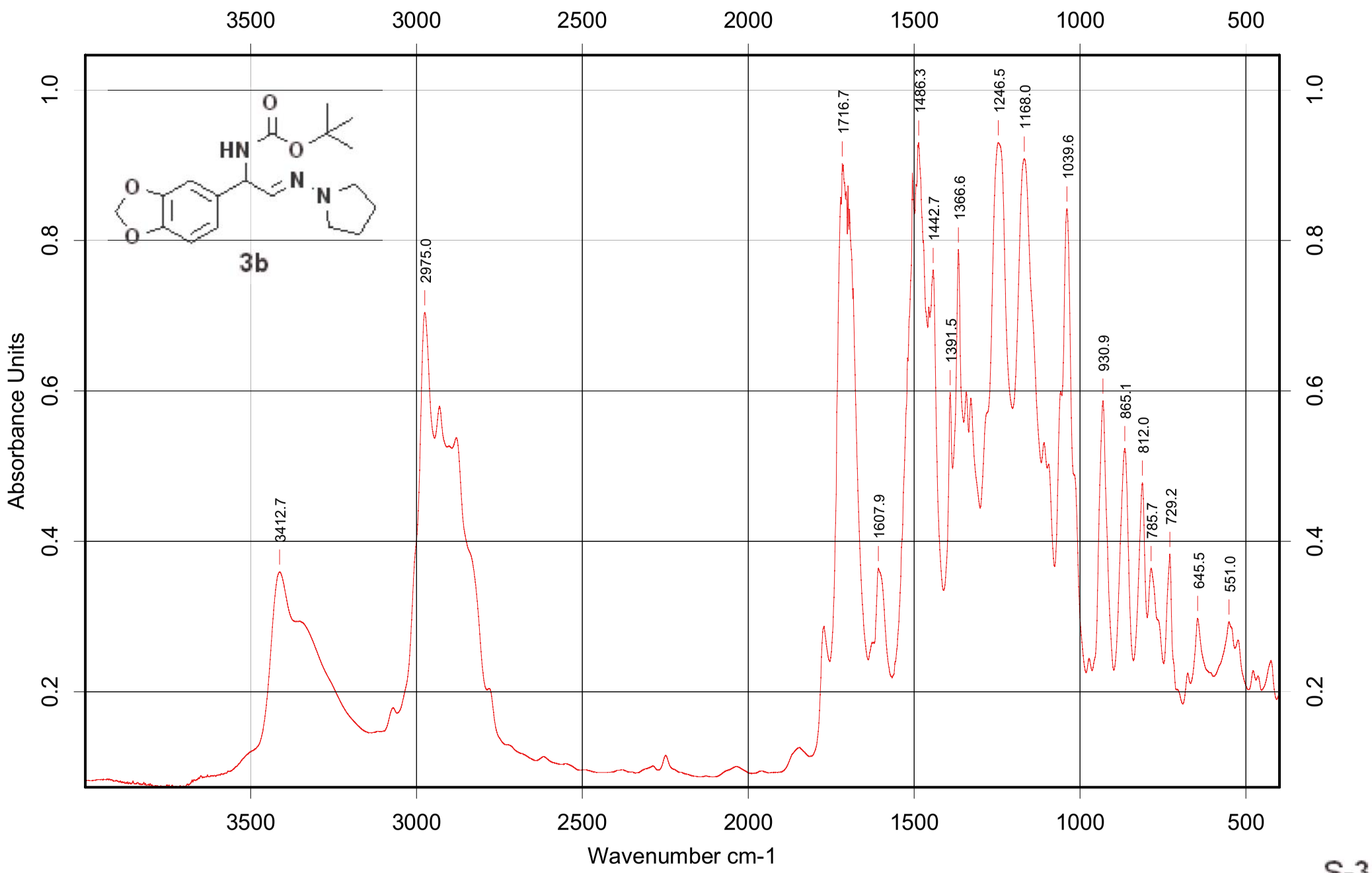

154.687
132.379
127.624
126.975
126.670
122.312
79.381
51.226
28.357
23.172
O
HN
O
N
N
CF3
150
100
50
ppm (t1)

155.017
133.020
128.743
128.449
128.210
79.526
51.257
28.398
23.247
150
100
50
ppm (t1)
S-35

158.9
155.1
133.5
128.3
114.0
79.2
55.3
51.3
28.4
23.2
150
100
50
ppm (t1)

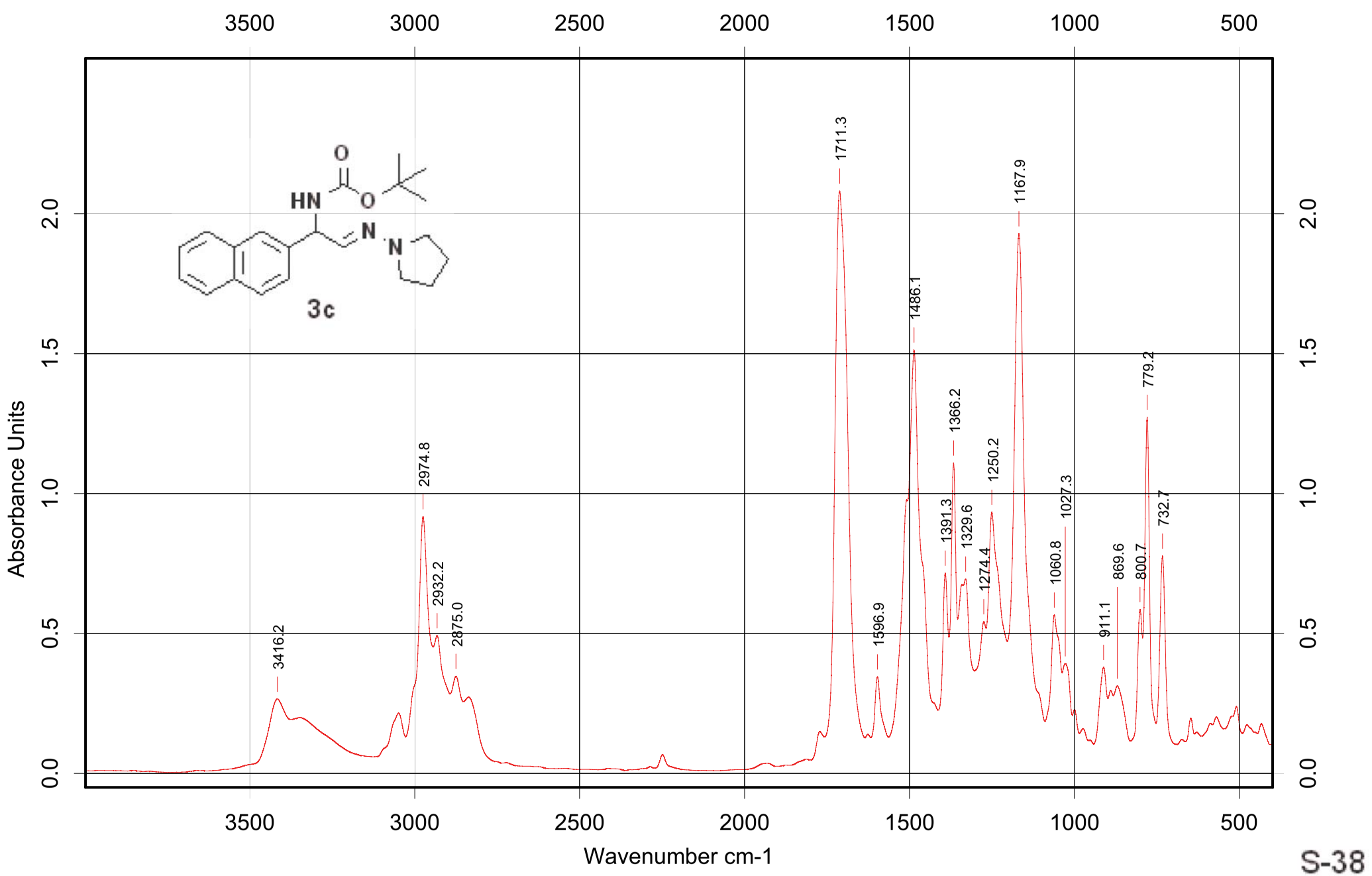
21.11.2006 11:57:00 D:\Spektren\zaac\zmij\ES641-5.0

Probenname ES641-5	Experiment DTGS CSI.XPM	Probenscans 32	Probenform rein



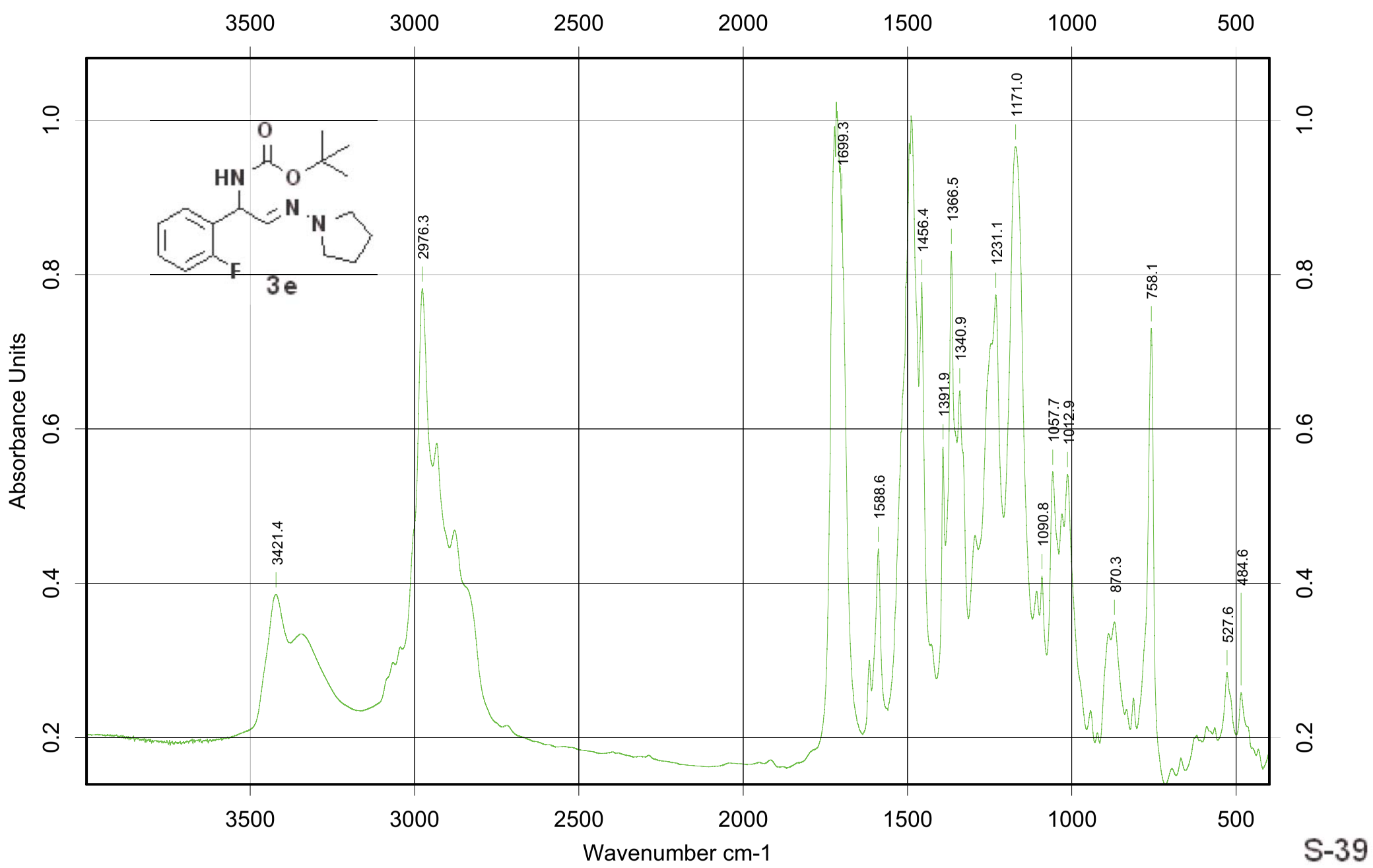
21.11.2006 11:46:11 D:\Spektren\zaac\zmij\ES591-2.0

Probenname ES491-2	Experiment DTGS CSI.XPM	Probenscans 32	Probenform rein



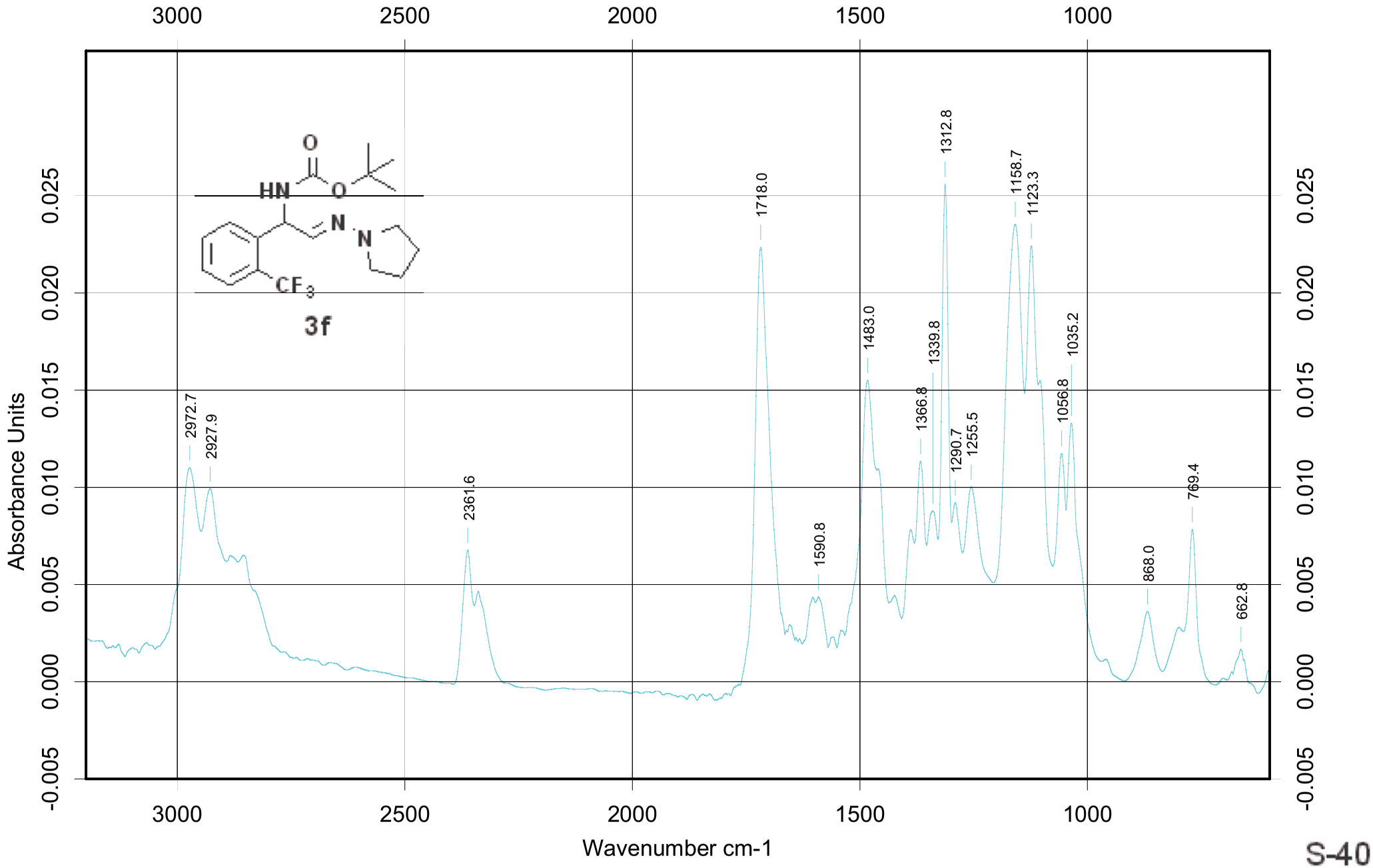
21.11.2006 12:06:38 D:\Spektren\zaac\zmij\ES648-4.0

Probenname ES648-4	Experiment DTGS CSI.XPM	Probenscans 32	Probenform rein



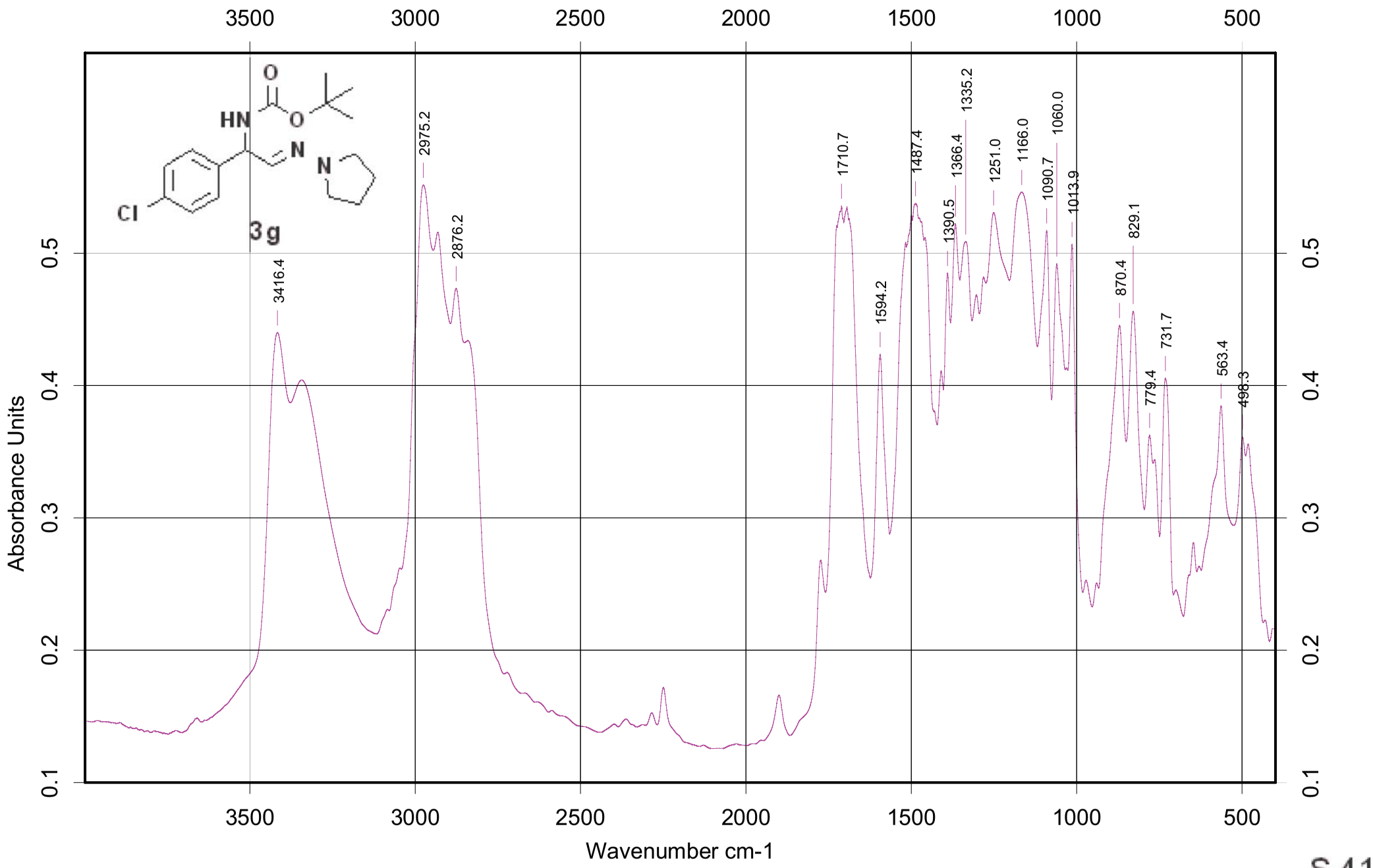
21.11.2006 12:13:04 D:\Spektren\zaac\zmij\ES615-5.0

Probenname ES615-5	Experiment DTGS CSI.XPM	Probenscans 32	Probenform rein



21.11.2006 12:03:26 D:\Spektren\zaac\zmij\ES633-4.0

Probenname ES633-4	Experiment DTGS CSI.XPM	Probenscans 32	Probenform rein



21.11.2006 12:25:45 D:\Spektren\zaac\zmij\ES632-4.0

Probenname ES632-4	Experiment DTGS CSI.XPM	Probenscans 32	Probenform rein