Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting information for

'*E*- and *Z*-Stereoselectivity in the preparation of enamides from glycidyl sulfonamides and carbamates'

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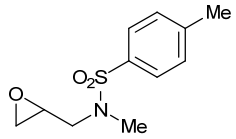
General Information

- All solvents and reagents employed in this study were standard grade except 2-MeTHF, THF, diethyl ether, toluene, diisopropylamine, 2,2,6,6-tetramethylpiperidine, diethylamine and *n*-butyl lithium which were Aldrich Sure-Seal.
- All reagents were purchased from Sigma-Aldrich, UK and Alfa Aesar, UK and used as received unless otherwise stated.
- Phosphazene bases, lithium amide, lithium bis(trimethylsilyl)amide and potassium bis(trimethylsilyl)amide were purchased as a solution from Sigma-Aldrich, UK and used as received.
- Lithium 2,2,6,6-tetramethylpiperidide, lithium diisopropylamide, lithium pyrrolidide, lithium diethylamide and lithium di-*tert*-amylamide were made *in situ via* the application of *n*-butyl lithium (2.5M in hexanes, 1eq) on the appropriate amine.
- All epoxide rearrangement reactions were carried out in oven dried glassware which was cooled to room temperature under a constant flow of nitrogen prior to charging.
- All reactions were magnetically stirred and monitored by thin layer chromatography (TLC) on pre-coated silica gel plates (254 μm). Silica plates were initially examined

under UV light and then developed using aqueous basic potassium permanganate stain.

- Flash chromatography was carried out with Fisher Chromatography Grade Silica 60A (Particle Size 35-70 micron) unless otherwise specified. Quoted yields refer to chromatographically and spectroscopically pure compounds unless otherwise stated.
- NMR spectra were recorded using a 300 MHz Varian, 400 MHz Varian or 500 MHz Bruker spectrometer (as specified). Chemical shifts (δ values) are reported in parts per million (ppm). Coupling constants are reported in Hertz (Hz), and refer to $^{3}J_{H\text{-}H}$ interactions.
- Infrared spectra were recorded on a Perkin Elmer FTIR. Absorbance values (ν_{max}) are quoted in cm^{-1}. Mass spectra were obtained on an Agilent 6890 GC with a Micromass GCT. Melting points were measured in a BÜCHI melting point B-545 apparatus and are uncorrected.

_N_,4-Dimethyl-_N_-(oxiran-2-ylmethyl)benzenesulfonamide (1a)

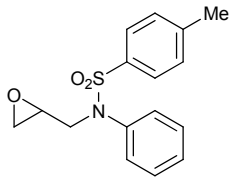


To a stirring solution of *N*,4-dimethylbenzenesulfonamide (2.00 g, 10.8 mmol) in dry THF (25 mL) was added sodium hydride (60% dispersion in mineral oil, 0.52 g, 12.95 mmol) in a portionwise manner under an atmosphere of nitrogen. Epibromohydrin (1.77 g, 12.95 mmol, 1.07 mL) was added in dropwise fashion, followed by tetrabutylammonium iodide (0.80 g, 2.16 mmol) as a single portion. The reaction mixture was left to stir for 16h, then quenched by cautious addition of aqueous saturated ammonium chloride (50 mL). The mixture was extracted with ethyl acetate (4 x 100 mL), dried ($MgSO_4$) and concentrated in *vacuo*. The crude residue was purified by flash column chromatography, eluting 50% diethyl ether in petroleum ether (bp 40-60 °C), to afford *N*,4-dimethyl-*N*-(oxiran-2-ylmethyl)benzenesulfonamide (2.41 g, 10.0 mmol, **93%**) as an oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.43 (3H, s, ArC*H*$_3$), 2.53 (1H, dd, *J* 4.8, 2.8, oxirane C*H*$_2$), 2.78 (1H, m, oxirane C*H*$_2$), 2.80 (1H, m, NC*H*$_2$), 2.84 (3H, s, NC*H*$_3$), 3.09 (1H, m, oxirane C*H*), 3.58 (1H, dd, *J* 14.4, 3.2, NC*H*$_2$), 7.32 (2H, d, *J* 8.0, Ar-*H*), 7.67 (2H, d, *J* 8.0, Ar-*H*);
^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.5, 36.0, 44.4, 50.5, 52.3, 127.4, 129.8, 134.4, 143.6;
IR (thin film) ν_{max}: 1334, 1456, 1594, 1597, 2853, 2923;

m/z (ES): 242.0828 (MH^+. $C_{11}H_{16}NO_3S$ requires 242.0851), 198 (28%).

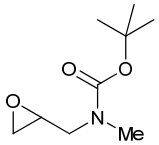
4-Methyl-*N*-(oxiran-2-ylmethyl)-*N*-phenylbenzenesulfonamide (1b)



To a stirring solution of 4-methyl-*N*-phenylbenzenesulfonamide (1.50 g, 6.07 mmol) in dry THF (25 mL) was added sodium hydride (60% dispersion in mineral oil, 0.29 g, 7.28 mmol) in a portionwise manner under an atmosphere of nitrogen. Epibromohydrin (1.00 g, 7.28 mmol, 0.60 mL) was added in dropwise fashion, followed by tetrabutylammonium iodide (0.45 g, 1.21 mmol) as a single portion and the reaction mixture was heated under reflux for 16h, then quenched by the cautious addition of aqueous saturated ammonium chloride (50 mL). The mixture was extracted with with ethyl acetate (4 x 100 mL), dried ($MgSO_4$) and concentrated in *vacuo*. The crude residue was purified by flash column chromatography, eluting 30% to 50% diethyl ether in petroleum ether (bp 40-60 °C), to give a white solid, which was recrystallised from dichloromethane-hexane to afford 4-methyl-*N*-(oxiran-2-ylmethyl)-*N*-phenylbenzenesulfonamide (1.37 g, 4.49 mmol, **74%**) as white fluffy crystals (mp 77-78 °C).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.32 (3H, s, ArC*H*$_3$), 2.35 (1H, dd, *J* 4.8, 2.4, oxirane C*H*$_2$), 2.59 (1H, app t, *J* 4.4, oxirane C*H*$_2$), 3.04 (1H, m, oxirane C*H*), 3.62 (2H, m, NC*H*$_2$), 7.02 (2H, m, Ar-*H*), 7.21 (5H, m, Ar-*H*), 7.41 (2H, d, *J* 8.4, Ar-*H*,);
^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.6, 45.8, 50.3, 53.6, 127.7, 128.2, 128.8, 129.2, 129.5, 135.4, 139.7, 143.7;
IR (solid) ν_{max}/cm^{-1} 1347, 1491, 1596, 2926, 2992, 3061;
m/z (ES) 304.0988 (MH^+. $C_{16}H_{18}NO_3S$ requires 304.1007), 149 (20%), 106 (42%).

***tert*-Butyl methyl(oxiran-2-ylmethyl)carbamate (1c)**

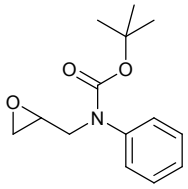


To a stirring solution of *tert*-butyl methylcarbamate (1.23 g, 9.40 mmol) in dry THF (25 mL) was added sodium hydride (60% dispersion in mineral oil, 0.45 g, 11.25 mmol) in a

portionwise manner under an atmosphere of nitrogen. Epibromohydrin (1.54 g, 11.25 mmol, 0.93 mL) was added in dropwise fashion, followed by tetrabutylammonium iodide (0.69 g, 1.88 mmol) as a single portion. The reaction mixture was left to stir for 16h, then quenched by the cautious addition of aqueous saturated ammonium chloride (50 mL). The mixture was extracted with with ethyl acetate (4 x 100 mL), dried ($MgSO_4$) and concentrated in *vacuo*. The crude residue was purified by flash column chromatography, eluting 10% Et_2O in petroleum ether (bp 40-60 °C), to afford *tert*-butyl methyl(oxiran-2-ylmethyl)carbamate (1.32 g, 7.05 mmol, **75%**) as an oil.

^{1}H NMR (400 MHz, d_6-DMSO, 90 °C) δ: 1.41 (9H, s, C(CH_3)$_3$), 2.48 (1H, m, oxirane CH_2 (obscured by solvent)), 2.70 (1H, app t, *J* 3.2, oxirane CH_2), 2.85 (3H, s, NCH_3) 3.00 (1H, m, oxirane C*H*), 3.19 (1H, dd, *J* 11.6, 4.4, NCH_2), 3.42 (1H, dd, *J* 12.0, 3.2, NCH_2);
^{13}C NMR (100 MHz, $CDCl_3$, 25 °C) δ: 28.5, 35.5, 44.7, 45.1, 50.4, 50.6, 50.8, 51.1, 79.8, 155.6, 155.9;
IR (thin film) ν_{max}/cm^{-1} 1698, 2870, 2927, 2956;
m/z (CI^+) 188.1297 (MH^+. $C_9H_{18}NO_3$ requires 188.1287), 132 (100%).

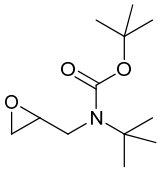
***tert*-Butyl oxiran-2-ylmethyl(phenyl)carbamate (1d)**



To a stirring solution of *tert*-butyl phenylcarbamate (3.00 g, 15.52 mmol) in dry THF (50 mL) was added sodium hydride (60% dispersion in mineral oil, 0.75 g, 18.63 mmol) in a portionwise manner under an atmosphere of nitrogen. Epibromohydrin (2.55 g, 18.63 mmol, 1.54 mL) was added in dropwise fashion, followed by tetrabutylammonium iodide (1.15 g, 3.10 mmol) as a single portion and the reaction mixture was left to stir for 16h, then quenched by the cautious addition of aqueous saturated ammonium chloride (50 mL). The mixture was extracted with with ethyl acetate (4 x 100 mL), dried ($MgSO_4$) and concentrated in *vacuo*. The crude residue was purified by flash column chromatography, eluting 20% diethyl ether in petroleum ether (bp 40-60 °C), to afford *tert*-butyl oxiran-2-ylmethyl(phenyl)carbamate (3.14 g, 12.7 mmol, **82%**) as an oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.44 (9H, s, C(CH_3)$_3$), 2.51 (1H, dd, *J* 4.8, 2.8, oxirane CH_2), 2.79 (1H, app t, *J* 4.4, oxirane CH_2), 3.24 (1H, m, oxirane C*H*), 3.63 (1H, dd, *J* 14.8, 5.6, NCH_2), 3.86 (1H, dd, *J* 14.8, 4.4, NCH_2), 7.18-7.35 (5H, m, Ar-*H*);
^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.5, 46.1, 50.6, 52.8, 80.8, 126.4, 127.1, 128.9, 142.9, 154.8;
IR (thin film) ν_{max}/cm^{-1} 1495, 1597, 1692, 2931, 2978, 3053;
m/z (ES) 250.1432 (MH^+. $C_{14}H_{20}NO_3$ requires 250.1443).

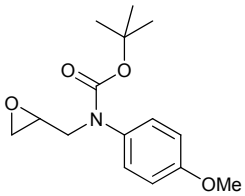
tert-Butyl methyl(oxiran-2-yl(_tert_-butyl)carbamate (1e)



To a solution of *tert*-butyl-oxiranylmethylamine (5.0 g, 38.7 mmol) in THF (50 mL) was added di-*t*-butyldicarbonate (8.45 g, 38.7 mmol) and the reaction mixture was stirred at room temp for 48 h. The reaction mixture was poured onto 0.5 M HCl (100 mL) and extracted with diethyl ether (200 mL). The organic extract was washed with brine (50 mL), dried ($MgSO_4$) and concentrated to dryness to give a yellow oil. The crude residue was purified by flash column chromatography, eluting 10% diethyl ether in *iso*-hexane, to afford *tert*-butyl methyl(oxiran-2-yl(*tert*-butyl)carbamate (5.72 g, 25.0mmol, **64%**) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.37 (9H, s, C(CH_3)$_3$), 1.45 (9H, s, C(CH_3)$_3$), 3.39 - 3.52 (2H, m), 3.48 - 3.50 (2H, m), 3.85 - 3.89 (1H, m);
^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.7, 30.0, 47.2, 49.1, 56.4, 73.7, 81.3, 151.5;
IR (thin film) ν_{max}/cm^{-1} 1156, 1390, 1647, 1675, 1698, 2975;
m/z (ES) 230.1730 (MH^+. $C_{12}H_{24}NO_3$ requires 230.1756).

tert-Butyl 4-methoxyphenyl(oxiran-2-ylmethyl)carbamate (1f)

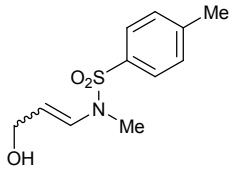


To a stirring solution of *tert*-butyl 4-methoxyphenylcarbamate (2.00 g, 8.96 mmol) in dry THF (40 mL) was added sodium hydride (60% dispersion in mineral oil, 0.43 g, 10.75 mmol)

in a portionwise manner under an atmosphere of nitrogen. Epibromohydrin (1.47 g, 10.75 mmol, 0.89 mL) was added in dropwise fashion, followed by tetrabutylammonium iodide (0.66 g, 1.79 mmol) as a single portion and the reaction mixture was left to stir for 16h, then quenched by the cautious addition of aqueous saturated ammonium chloride (50 mL). The mixture was extracted with with ethyl acetate (4 x 100 mL), dried ($MgSO_4$) and concentrated in *vacuo*. The crude residue was purified by flash column chromatography, eluting 30% to 50% diethyl ether in petroleum ether (bp 40-60 °C), to afford *tert*-butyl 4-methoxyphenyl(oxiran-2-ylmethyl)carbamate (2.24 g, 8.06 mmol, **90%**) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.43 (9H, s, C(CH_3)$_3$), 2.45 (1H, dd, *J* 5.2, 2.8, oxirane CH_2), 2.73 (1H, app t, *J* 4.8, oxirane CH_2), 3.19 (1H, m, oxirane C*H*), 3.57 (1H, dd, *J* 14.8, 5.6, NCH_2), 3.75 (3H, s, OCH_3), 3.79 (1H, dd, *J* 14.8, 3.2, NCH_2), 6.83 (2H, d, *J* 7.6, Ar-*H*), 7.15 (2H, d, *J* 7.6, Ar-*H*);
^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.0, 45.5, 50.0, 52.5, 55.0, 80.0, 113.7, 128.0, 135.4, 154.6, 157.6;
IR (thin film) ν_{max}/cm^{-1} 1511, 1585, 1609, 1690, 2933, 2976;
m/z (ES) 280.1551 (MH^+. $C_{15}H_{22}NO_4$ requires 280.1549).

_N_-(3-Hydroxyprop-1-enyl)-_N_,4-dimethylbenzenesulfonamide (2a)



To a stirring solution of diisopropylamine (0.50 g, 4.97 mmol, 0.70 mL) in dry 2-MeTHF (10 mL) was added *n*-BuLi (2.5M in hexanes, 0.32 g, 4.97 mmol, 1.99 mL) in dropwise fashion at –78 °C and the solution allowed to warm to room temperature. This solution was added in dropwise fashion to a solution of *N*,4-dimethyl-*N*-(oxiran-2-ylmethyl)benzenesulfonamide (0.50 g, 2.07 mmol) in dry 2-MeTHF (5 mL) held at –78 °C and reaction mixture stirred at -60 °C for 2h. The reaction mixture was diluted with diethyl ether (70 mL), quenched with water (100 mL), washed with ammonium chloride (3 x 100 mL), dried ($MgSO_4$) and concentrated in *vacuo*. The crude residue was purified by flash column chromatography, eluting 30% diethyl ether in petroleum ether (bp 40-60 °C), to afford *N*-(3-hydroxyprop-1-enyl)-*N*,4-dimethylbenzenesulfonamide (0.42 g, 1.74 mmol, **84%**), as a 90:10 mixture of *E*-

and *Z*- stereoisomers respectively. The crude product was recrystallised from *iso*-hexane to afford the *E*-isomer (0.11 g, 1.09 mmol, **22%**) as white fluffy needle crystals (mp 91-92 °C).

NB: data given for the *E*-stereoisomer only.

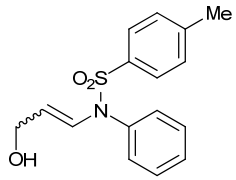
^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.23 (1H, t, O*H*, *J* 7.2), 2.43 (3H, s, ArCH_3), 2.89 (3H, s, NCH_3), 4.14 (2H, td, 3-H_2, *J* 6.0, 0.6), 4.93 (1H, dt, *J* 14.1, 6.6, 2-*H*), 7.02 (1H, dt, *J* 14.1, 0.9, 1-*H*), 7.31 (2H, d, *J* 8.1, Ar-*H*), 7.64 (2H, d, *J* 8.1, Ar-*H*);

^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.5, 32.0, 62.1, 108.6, 126.9, 129.9, 131.0, 134.8, 144.0;

IR (solid) ν_{max}/cm^{-1} 1352, 1493, 1596, 1656, 2862, 3277;

m/z (ES) 242.0852 (MH^+. $C_{11}H_{16}NO_3S$ requires 242.0851), 224 (40%).

_N_-(3-Hydroxyprop-1-enyl)-4-methyl-_N_-phenylbenzenesulfonamide (2b)



To a stirring solution of diisopropylamine (0.40 g, 3.96 mmol, 0.56 mL) in dry 2-MeTHF (10 mL) was added *n*-BuLi (2.5M in hexanes, 0.25 g, 3.96 mmol, 1.59 mL) dropwise at –78 °C and the solution allowed to warm to room temperature. This solution was added in dropwise fashion to a solution of 4-methyl-*N*-(oxiran-2-ylmethyl)-*N*-phenylbenzenesulfonamide (0.50 g, 1.65 mmol) in dry 2-MeTHF (5 mL) held at –78 °C and reaction mixture stirred at –60 °C for 2h. The reaction mixture was diluted with diethyl ether (70 mL), quenched with water (100 mL), washed with ammonium chloride (3 x 100 mL), dried ($MgSO_4$) and concentrated in *vacuo*. The crude residue was purified by flash column chromatography eluting with 40% to 60% diethyl ether in petroleum ether (bp 40-60 °C) to afford *N*-(3-hydroxyprop-1-enyl)-4-methyl-*N*-phenylbenzenesulfonamide (0.38 g, 1.25 mmol, **76%**) as a white solid as a 90:10 mixture of *E*- and *Z*- stereoisomers respectively (mp 106-108 °C).

^{1}H NMR (400 MHz, $CDCl_3$, NB: * denotes the minor (*Z*) isomer) δ: 1.25 (1H, br t, *J* 5.2, O*H*), 1.58 (1H, br t, *J* 5.3, O*H**), 2.44 (3H, s, ArCH_3), 3.83 (2H, t, *J* 5.3, 3-H_2*), 4.06 (2H, t, *J* 5.4, 3-H_2), 4.55 (1H, dt, *J* 14.0, 6.8, 2-*H*), 5.38 (1H, q, *J* 5.6, 2-*H**), 6.39 (1H, d, *J* 5.6, 1-*H**),

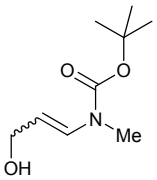
6.98 (2H, d, *J* 8.4, Ar-*H*), 7.08* (2H, d, *J* 8.4, Ar-*H*), 7.23 (1H, d, *J* 14.0, 1-*H*), 7.26-7.39 (5H, m, Ar-*H*) 7.47 (2H, d, *J* 8.4, Ar-*H**), 7.55 (2H, d, *J* 8.4, Ar-*H*);

^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.8, 62.0, 109.8, 127.7, 128.0, 129.3, 129.7, 129.8, 130.4, 132.2, 135.9, 136.3, 144.2;

IR (solid) ν_{max}/cm^{-1} 1355 s, 1490 m, 1595 m, 1653 s, 2870 w, 2927 w, 3066 w, 3377 br;

m/z (ES) 304.0979 (MH^+. $C_{16}H_{18}NO_3S$ requires 304.1007).

tert-Butyl 3-hydroxyprop-1-enyl(methyl)carbamate (2c)



To a stirring solution of diisopropylamine (0.39 g, 3.84 mmol, 0.54 mL) in dry 2-MeTHF (10 mL) was added *n*-BuLi (2.5M in hexanes, 0.24 g, 3.84 mmol, 1.54 mL) in dropwise fashion at –78 °C and the solution allowed to warm to room temperature. This solution was added in dropwise fashion to a solution of *tert*-butyl methyl(oxiran-2-ylmethyl)carbamate (0.30 g, 1.60 mmol) in dry 2-MeTHF (5 mL) held at –78 °C and reaction mixture stirred at –60 °C for 2h. The reaction mixture was diluted with diethyl ether (70 mL), quenched with water (100 mL), washed with ammonium chloride (3 x 100 mL), dried ($MgSO_4$) and concentrated in *vacuo*. The crude residue was purified by flash column chromatography eluting with 50% to 60% diethyl ether in petroleum ether (bp 40-60 °C) to afford *tert*-butyl 3-hydroxyprop-1-enyl(methyl)carbamate (0.25 g, 1.33 mmol, **83%**) as an oil as a 45:55 mixture of *E*- and *Z*-stereoisomers respectively.

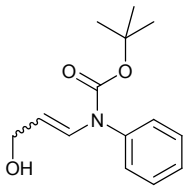
^{1}H NMR (400 MHz, d_6-DMSO, 90 °C, NB: * denotes the minor (*E*) isomer) δ: 1.42 (9H, s, $C(CH_3)_3$*), 1.44 (9H, s, $C(CH_3)_3$), 2.93 (3H, s, NCH_3*), 2.98 (3H, s, NCH_3), 3.94 (2H, dt, *J* 6.0, 0.8, 3-H_2*), 4.01 (2H, dt, *J* 1.6, 6.0, 3-H_2), 4.23 (1H, t, *J* 5.4, O*H**), 4.36 (1H, t, *J* 5.2, O*H*), 4.88-5.01 (1H, m, 2-*H* (both isomers)), 6.19 (1H, dt, 1-*H*, *J* 9.2, 1.3), 6.97 (1H, dt, *J* 14.3, 1.3, 1-*H**);

^{13}C NMR (100 MHz, d_6-DMSO, 90 °C) δ: 33.1, 33.2, 35.9, 40.7, 61.8, 65.4, 85.1, 85.7, 114.0, 123.1, 133.3, 134.6, 158.0, 158.7;

IR (thin film) ν_{max}/cm^{-1} 1654, 1702, 2931, 2977, 3404;

m/z (ES) 210.1069 (MNa^+. $C_9H_{17}NO_3Na$ requires 210.1106).

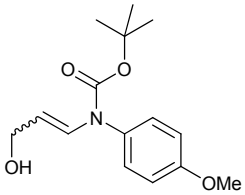
tert-Butyl 3-hydroxyprop-1-enyl(phenyl)carbamate (2d)



To a stirring solution of diisopropylamine (0.49 g, 4.81 mmol, 0.68 mL) in dry 2-MeTHF (10 mL) was added *n*-BuLi (2.5M in hexanes, 0.31 g, 4.81 mmol, 1.93 mL) in dropwise fashion at –78 °C and the solution allowed to warm to room temperature. This solution was added in dropwise fashion to a solution of *tert*-butyl oxiran-2-ylmethyl(phenyl)carbamate (0.50 g, 2.01 mmol) in dry 2-MeTHF (5 mL) held at –78 °C and reaction mixture stirred at –60 °C for 2h. The reaction mixture was diluted with diethyl ether (70 mL), quenched with water (100 mL), washed with ammonium chloride (3 x 100 mL), dried ($MgSO_4$) and concentrated in *vacuo*. The crude residue was purified by flash column chromatography eluting with 10% to 40% ethyl acetate in petroleum ether (bp 40-60 °C) to afford *tert*-butyl 3-hydroxyprop-1-enyl(phenyl)carbamate (0.41 g, 1.65 mmol, **82%**) as an oil as a 25:75 mixture of *E*- and *Z*-stereoisomers respectively.

^{1}H NMR (400 MHz, $CDCl_3$, NB: * denotes the minor (*E*) isomer) δ: 1.38 (9H, s, C(C*H*$_3$)$_3$*), 1.43 (9H, s, C(C*H*$_3$)$_3$), 2.36 (1H, br, O*H**), 2.43 (1H, br, O*H*), 3.49 (2H, dd, *J* 6.4, 1.2, 3-*H*$_2$), 3.91 (2H, d, *J* 8.0, 3-*H*$_2$*), 4.49 (1H, dt, *J* 14.4, 6.8, 2-*H**), 4.97 (1H, dt, *J* 9.2, 6.8, 2-*H*), 6.39 (1H, dt, *J* 9.2, 1.6, 1-*H*), 7.05-7.35 (6H, m, ArH + 1-*H**);
^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.3, 58.2, 62.3, 82.0, 109.3, 117.7, 126.6, 127.1, 127.8, 128.7, 128.8, 129.0, 129.4, 132.9, 141.8, 153.5;
IR (thin film) ν_{max}/cm^{-1} 1494, 1596, 1657, 1707, 2932, 2978, 3418;
m/z (ES) 272.1242 (MNa^+. $C_{14}H_{19}NO_3Na$ requires 272.1263).

tert-Butyl 3-hydroxyprop-1-enyl(4-methoxyphenyl)carbamate (2f)



To a stirring solution of diisopropylamine (0.44 g, 4.30 mmol, 0.61 mL) in dry 2-MeTHF (10 mL) was added *n*-BuLi (2.5M in hexanes, 0.28 g, 4.30 mmol, 1.73 mL) in dropwise fashion at –78 °C and the solution allowed to warm to room temperature. This solution was added in

dropwise fashion to a solution of *tert*-butyl 4-methoxyphenyl(oxiran-2-ylmethyl)carbamate (0.50 g, 1.79 mmol) in dry 2-MeTHF (5 mL) held at –78 °C and reaction mixture stirred at –60 °C for 2h. The reaction mixture was diluted with diethyl ether (70 mL), quenched with water (100 mL), washed with ammonium chloride (3 x 100 mL), dried ($MgSO_4$) and concentrated in *vacuo*. The crude residue was purified by flash column chromatography eluting with 50% to 80% diethyl ether in petroleum ether (bp 40-60 °C) to afford *tert*-butyl 3-hydroxyprop-1-enyl(4-methoxyphenyl)carbamate (0.36 g, 1.29 mmol, **72%**) as an oil as a 25:75 mixture of *E*- and *Z*- stereoisomers respectively.

^{1}H NMR (400 MHz, $CDCl_3$, NB: * denotes the minor (*E*) isomer) δ: 1.42 (9H, s, C(CH_3)$_3$*), 1.44 (9H, s, C(CH_3)$_3$), 1.85 (1H, br, O*H*), 3.60 (2H, dd, *J* 6.8, 1.6, 3-H_2), 3.80 (3H, s, OC***H***$_3$), 3.82 (3H, OCH_3*), 4.04 (2H, dd, *J* 7.2, 0.8, 3-H_2*), 4.59 (1H, dt, *J* 14.4, 7.2, 2-*H**), 4.99 (1H, dt, *J* 9.2, 6.8, 2-*H*), 6.51 (1H, dt, *J* 9.2, 1.6, 1-*H*), 6.86 (2H, d, *J* 8.8, Ar-*H*), 6.91* (2H, d, *J* 8.8, Ar-*H*), 7.04 (2H, d, *J* 8.8, Ar-*H**), 7.28 (2H, d, *J* 8.8, Ar-*H*), 7.32 (1H, br d, *J* 14.4, 1-*H**);

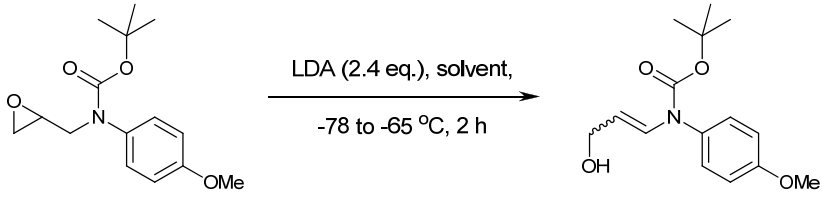
^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.1, 28.2, 55.3, 55.4, 57.8, 59.5, 81.5, 113.6, 114.0, 114.5, 116.2, 128.2, 128.4, 129.5, 130.2, 132.7, 134.1, 134.3, 153.4, 153.6, 158.0, 158.3;

IR (thin film) ν_{max}/cm^{-1} 1511, 1587, 1609, 1658, 1696, 2926, 2977, 3451;

m/z (ES) 302.1346 (MNa^+. $C_{15}H_{21}NO_4Na$ requires 302.1368), 206 (50%), 162 (100).

General procedure for solvent screen

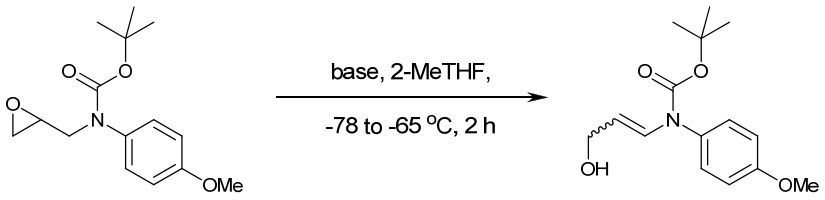
To a stirring solution of diisopropylamine (2.4 eq.) in dry solvent (10 mL) was added *n*-BuLi (2.5M in hexanes, 2.4 eq.) dropwise at –78 °C in dropwise fashion at –78 °C and the solution allowed to warm to room temperature. This solution was added in dropwise fashion to a solution of solution of *tert*-butyl 4-methoxyphenyl(oxiran-2-ylmethyl)carbamate (0.5 g, 1.79 mmol, 1 eq.) in dry solvent (5 mL) held at –78 °C and reaction mixture stirred at –60 °C for 2h.. The reaction mixture was diluted with diethyl ether (70 mL), quenched with water (100 mL), washed with ammonium chloride (3 x 100 mL), dried ($MgSO_4$) and concentrated in *vacuo*. Conversion and isomer ratio were measured by ^{1}H NMR spectroscopy.



Solvent	*E*- : *Z*- ratio	Conversion (%)
2-MeTHF	25:75	100
THF	35:65	100
Diethyl ether	60:40	100
Toluene	60:40	100

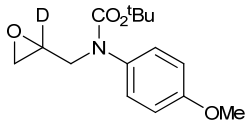
General procedure for base screen

To a stirring solution of *tert*-butyl 4-methoxyphenyl(oxiran-2-ylmethyl)carbamate (0.5 g, 1.79 mmol 1 eq) in dry 2-MeTHF (5 mL) at -78 °C was added base (variable eq) and the reaction mixture left to stir at -65 °C for 2h. The reaction mixture was diluted with diethyl ether (70 mL), quenched with water (100 mL), washed with ammonium chloride (3 x 100 mL), dried ($MgSO_4$) and concentrated in *vacuo*.



Base	*E*- : *Z*- ratio	Conversion (%)
LDA (2.4 eq.)	25:75	100
LDA (2.0 eq)	25:75	100
LDA (1.50 eq)	25:75	75
LDA (1 eq)	25:75	50
LiTMP (2.4 eq)	25: 75	100
Di-^{t}amyl lithium amide	75: 25	95
Et_2NLi (2.4 eq)	55:45	100
Li pyrrolidide (2.4 eq)	75:25	95
KHMDS (2.4 eq)	No reaction	
LHMDS (2.4 eq)	No reaction	
Phosphazene P2 (2.4 eq)	No reaction	
Phosphazene P4 (2.4 eq)	Less than 2% conversion even after warming to room temperature	

tert-Butyl 4-methoxyphenyl(2-deutero-oxiran-2-ylmethyl)carbamate _d_-1f



To a stirring solution of p-anisidine (19.7 g, 160 mmol) and diisopropylamine (41.4g, 320 mmol) in acetonitrile (160 ml) at 60 °C was added ethyl bromoacetate (26.7 g, 160 mmol) by syringe pump over 2 hr. The mixture was stirred for a further 3 hr at this temperature. The solvent was removed by evaporation under reduced pressure. Water (100 ml) was added, the product collected by filtration, washed with water, dried under vacuum. The residue was purified by chromatography on silica gel eluting 6-50% ethyl acetate – *iso*-hexane, to afford ethyl 2-(4-methoxyphenylamino)acetate (28.0 g, 134 mmol, **84 %**).

This material was dissolved in dichloromethane (200 mL). Triethylamine (17.8 g, 176 mmol) and di-*tert*-butyldicarbonate (36.0 g, 160 mmol) was added and the mixture stirred for 18 hr at r.t. The mixture was quenched with water (200 mL). The organic layer was separated, washed with 1 M aqueous hydrochloric acid (100 mL), saturated aqueous sodium choride (100 mL), dried ($MgSO_4$) and the solvent removed by evaporation under reduced pressure. The residue was purified by chromatography on silica gel, eluting 6-50% ethyl acetate – *iso*-hexane, to afford ethyl 2-(*tert*-butoxycarbonyl(4-methoxyphenyl)amino)acetate (**4**) (13.0 g, 42.0 mmol, **31%**).

^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.27 (3H, t, *J* 7.2, $CH_3CH_2O_2C$), 1.43 (9H, s, $(CH_3)_3C$), 3.80 (s, 3H, CH_3OAr), 4.19 (2H, q, *J* 7.2, $CH_3CH_2O_2C$), 4.30 (2H, s, CH_2CO_2Et), 6.85 (2H, d, *J* 8.7, Ar-*H*), 7.25 (2H, d, *J* 8.7, Ar-*H*).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.3, 14.4, 28.3, 52.3, 53.0, 55.5, 61.2, 80.7, 81.1, 113.9, 114.3, 128.0, 128.2, 135.9, 136.0, 154.7, 155.2, 158.0, 170.0, 170.3.

Lithium borodeuteride (1.1 g, 42.0 mmol) was added to a solution of **4** (13 g, 42.0 mmol) in tetrahydrofuran (260 mL) at r.t. The reaction mixture was stirred for 18 hr then quenched by addition of methanol (20 mL) and stirred for 20 min. The solvent was removed by evaporation under reduced pressure, and the residue purified by chromatography on silica gel, eluting 12 – 100 % ethyl acetate – *iso*-hexane to afford tert-butyl 2,2-dideutero-2-hydroxyethyl(4-methoxyphenyl)carbamate (5.8 g, 21.5 mmol, **51 %**) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.37 (9H, s, $(CH_3)_3C$), 3.71 (2H, s, CH_2CD_2OH), 3.77 (s, 3H, CH_3OAr), 6.83 (2H, d, *J* 8.7, Ar-*H*), 7.08 (2H, br d, *J* 8.7, Ar-*H*).

m/z (ES) 292.1482 (MNa^+. $C_{14}D_2H_{19}NO_4Na$ requires 292.1488).

To oxalyl chloride (1.56 g, 12.3 mmol) in dichloromethane (36 mL) at -78 °C was added dimethyl sulfoxide (1.91 g, 24.5 mmol) in dichloromethane (12 mL) over 15 min, keeping the temperature below -70 °C. 2,2-dideutero-2-hydroxyethyl(4-methoxyphenyl)carbamate (3.00 g, 11.1 mmol) in dichloromethane (24 mL) was added over 15 min, keeping the temperature below –70 °C and stirring continued at this temperature for 45 min. Diisopropylethylamine (7.20 g, 55.7 mmol) was added and the mixture allowed to warm to r.t. with stirring. The reaction mixture was washed with water (20 mL) and saturated aqueous citric acid (20 mL), dried ($MgSO_4$), and the solvent removed by evaporation under reduced pressure to afford *tert*-butyl 4-methoxyphenyl(2-deutero-2-oxoethyl)carbamate as a colourless oil. This material was used immediately in the following step without delay.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.40 (9H, s, $(CH_3)_3C$), 3.77 (s, 3H, CH_3OAr), 4.26 (2H, s, CH_2CDO), 6.83 (2H, d, *J* 7.9, Ar-*H*), 7.12 (2H, brs, Ar-*H*).

Trimethylsulfoxonium iodide (2.78 g, 12.3 mmol) was added to a solution of sodium hydride (0.49 g of a 60 % mineral oil suspension) in dimethyl sulfoxide (15 mL) and stirred for 5 min. This mixture was then added to a solution of tert-butyl 4-methoxyphenyl(2-deutero-2-oxoethyl)carbamate in dimethyl sulfoxide (15 mL) prepared as above. The reaction mixture was heated to 60 °C and stirred at this temperature for 30 min. Upon cooling to r.t., the reaction was quenched by addition of water (100 mL)and extracted with ether (2 x 100 mL). The combined organic extracts were washed with saturated aqueous sodium chloride solution (20 mL), dried ($MgSO_4$), and the solvent removed by evaporation under reduced pressure. The residue was purified by chromatography on silica gel, eluting 6 – 50 % ethyl acetate – *iso*-hexane to afford *tert*-Butyl 4-methoxyphenyl(2-deutero-oxiran-2-ylmethyl)carbamate (1.06 g, 3.78 mmol, **34 %**) as a colourless oil, contaminated by a residual amount of the 2-proto analogue **1f** (estimated at 5%) by ^{1}H NMR).

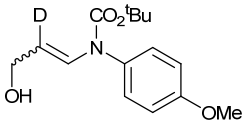
^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.40 (9H, s, $(CH_3)_3C$), 2.46 (1H, d, J 4.8, 3-CH_2), 2.75 (1H, d, J 4.8, 3-CH_2), 3.71 (2H, s, CH_2), 3.77 (s, 3H, CH_3OAr), 6.83 (2H, d, *J* 8.7, Ar-*H*), 7.08 (2H, d, *J* 8.7, Ar-*H*);

^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.3, 45.9, 50.0, 52.7, 55.4, 80.5, 114.0, 128.2, 135.6, 154.9, 157.8.

IR (thin film) ν_{max}/cm^{-1} 1511, 1585, 1610, 1690, 2934, 2977.

m/z (ES) 281.1601 (MH^+. $C_{15}DH_{21}NO_4$ requires 281.1601).

***tert*-Butyl 3-hydroxy-2-deutero-prop-1-enyl(4-methoxyphenyl)carbamate *d*-2f**



To a stirring solution of diisopropylamine (0.26 g, 2.56 mmol, 0.36 mL) in dry 2-MeTHF (10 mL) was added *n*-BuLi (2.5M in hexanes, 0.16 g, 2.56 mmol, 1.03 mL) dropwise at –78 °C and the solution allowed to warm to room temperature. The prepared LDA was added dropwise to a solution of *tert*-butyl 2-methoxyphenyl(oxiran-2-ylmethyl)carbamate (0.30 g, 1.07 mmol) in dry 2-MeTHF (5 mL) at –78 °C and reaction mixture left to stir at –65 °C for 2h. The reaction mixture was diluted with diethyl ether (70 mL), quenched with water (100 mL), washed with ammonium chloride (3 x 100 mL), dried ($MgSO_4$) and concentrated in *vacuo*. The crude residue was purified by flash column chromatography eluting with 50% to

60% Et_2O in petroleum ether (bp 40-60 °C) to afford *tert*-butyl 3-hydroxy-2-deuteroprop-1-enyl(2-methoxyphenyl)carbamate (0.22 g, 0.79 mmol, **73%**) as a colourless oil as a 45:55 mixture of *E*- and *Z*- stereoisomers respectively, contaminated by the corresponding 2-proto analogues ***E*-** and ***Z*-2f**. These impurities were estimated at a combined level of 5% by ^{1}H NMR, which corresponds closely to the quantity of **1f** present in the substrate ***d*-1f**. The appearance of these compounds in the product mixture may therefore be directly attributed to the presence of these impurities in the input material.

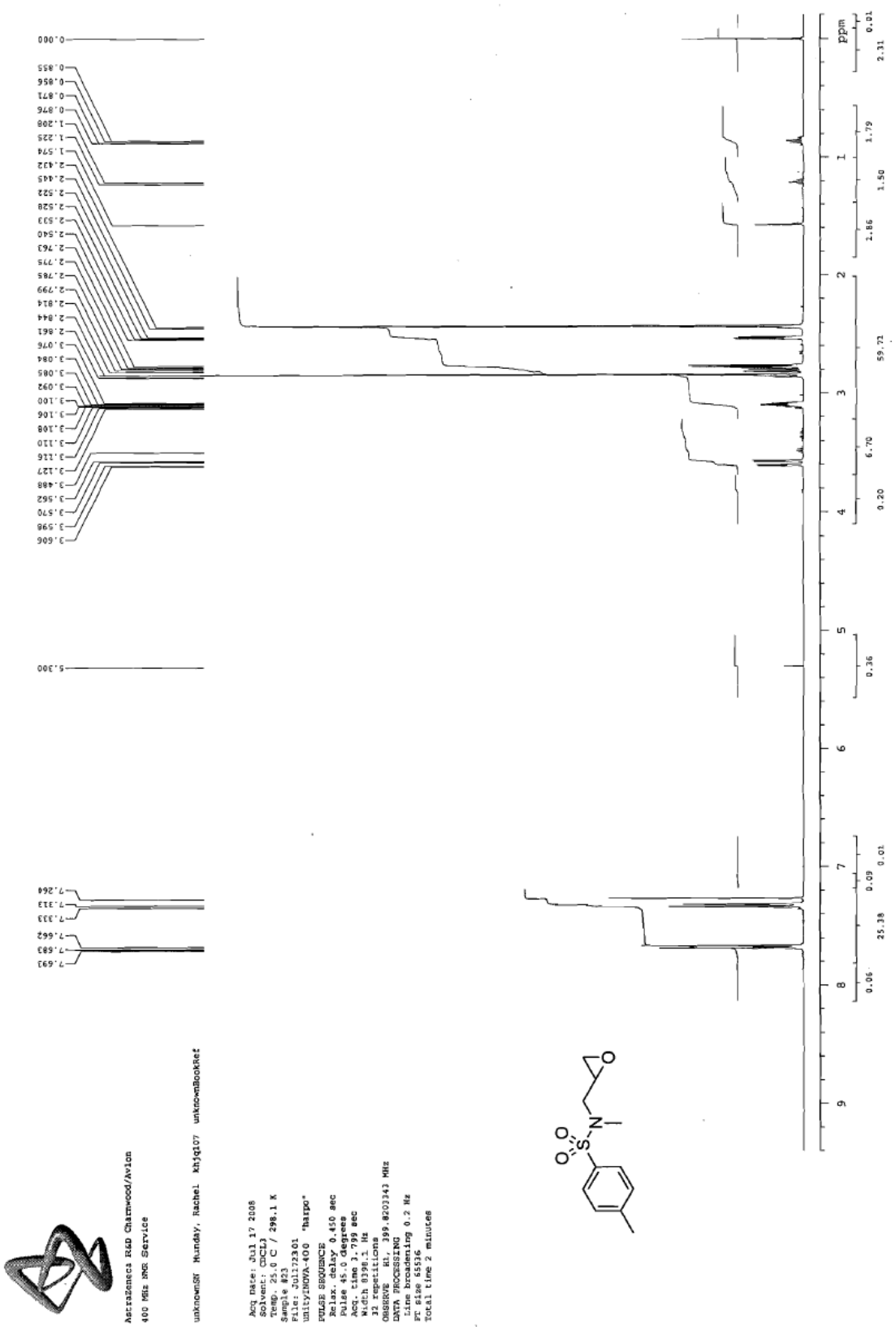
^{1}H NMR (500 MHz, $CDCl_3$, NB: * denotes the minor isomer) δ: 1.39* (9H, s, C(C***H***$_3$)$_3$), 1.41 (9H, s, C(C***H***$_3$)$_3$), 3.59 (1.5H, d, *J* 5.5, 3-*H*$_2$), 3.78 (3H, s, OC***H***$_3$), 3.80* (3H, OC***H***$_3$), 4.03* (1H, d, *J* 5.3, 3-*H*$_2$), 6.50 (1H, s, 1-*H*), 6.84 (2H, d, *J* 8.9, Ar-***H***,), 6.89* (2H, d, *J* 8.8, Ar-***H***), 7.02* (2H, d, *J* 8.4, Ar-***H***), 7.10 (2H, d, *J* 8.8, Ar-***H***), 7.30* (1H, br s, 1-*H*$_2$).

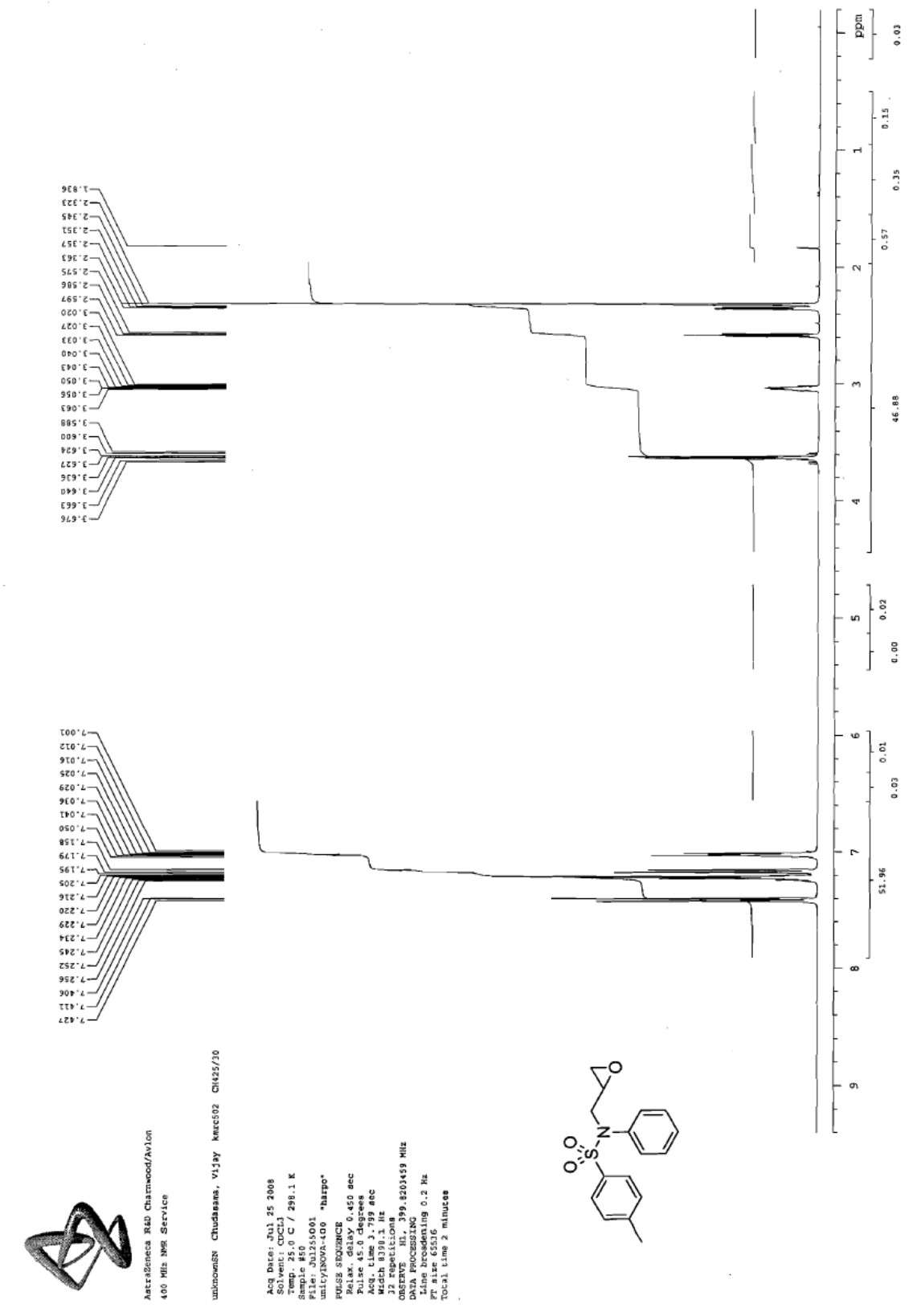
^{13}C NMR (125 MHz, $CDCl_3$) δ: 28.1, 55.4, 57.8, 62.1, 81.6, 114.1, 114.5, 128.2, 128.2, 128.6, 129.5, 130.2, 133.0, 134.3, 153.4, 153.7, 158.0, 158.8;

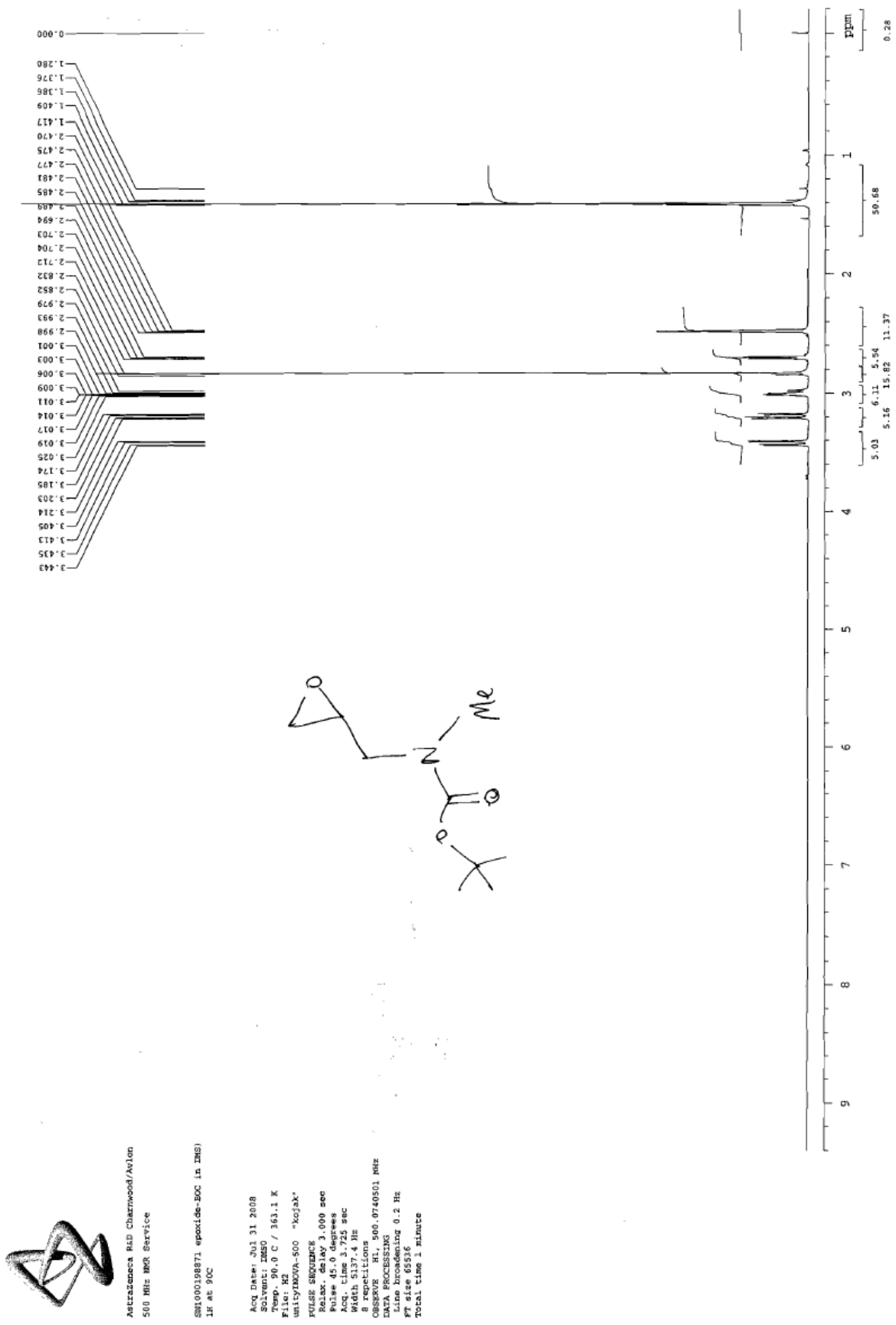
28.1, 28.2, 55.3, 55.4, 57.8, 59.5, 81.5, 113.6, 114.0, 114.5, 116.2, 128.2, 128.4, 129.5, 130.2, 132.7, 134.1, 134.3, 153.4, 153.6, 158.0, 158.3;

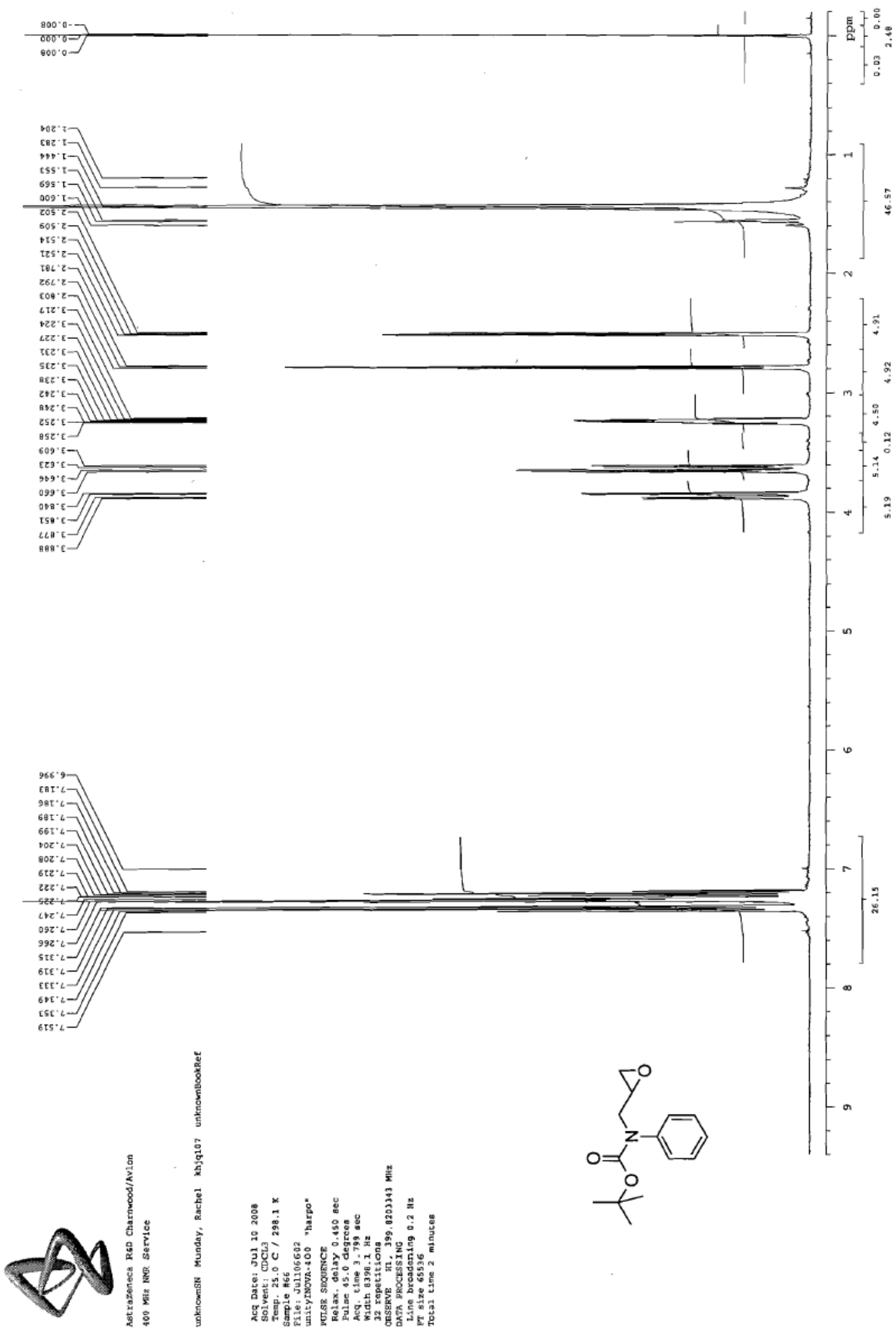
IR (thin film) ν_{max}/cm^{-1} 1510, 1645, 1704, 2935, 2977, 3418.

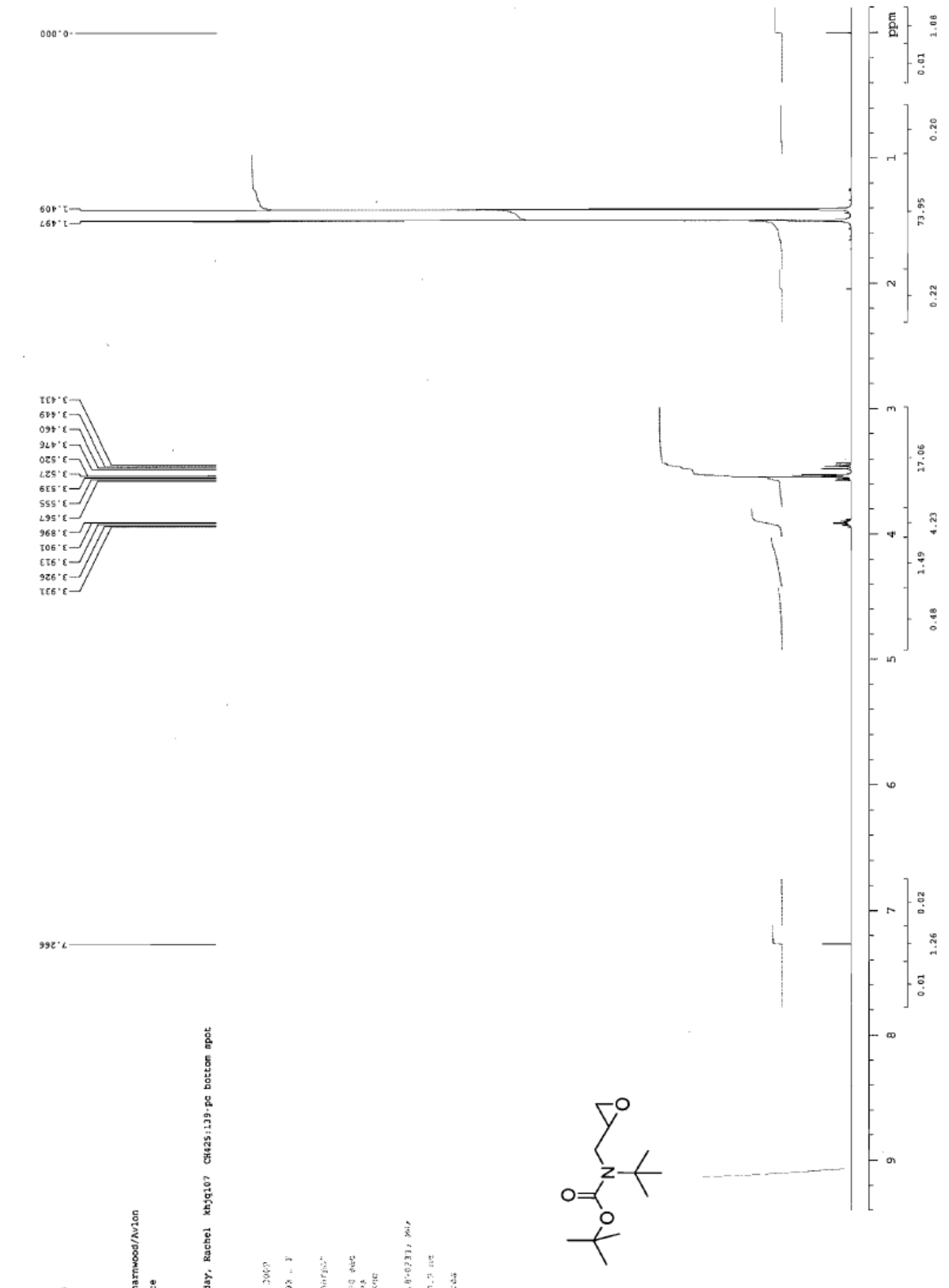
m/z (ES) 303.1436 (MNa^+. $C_{15}DH_{20}NO_4Na$ requires 303.1426).

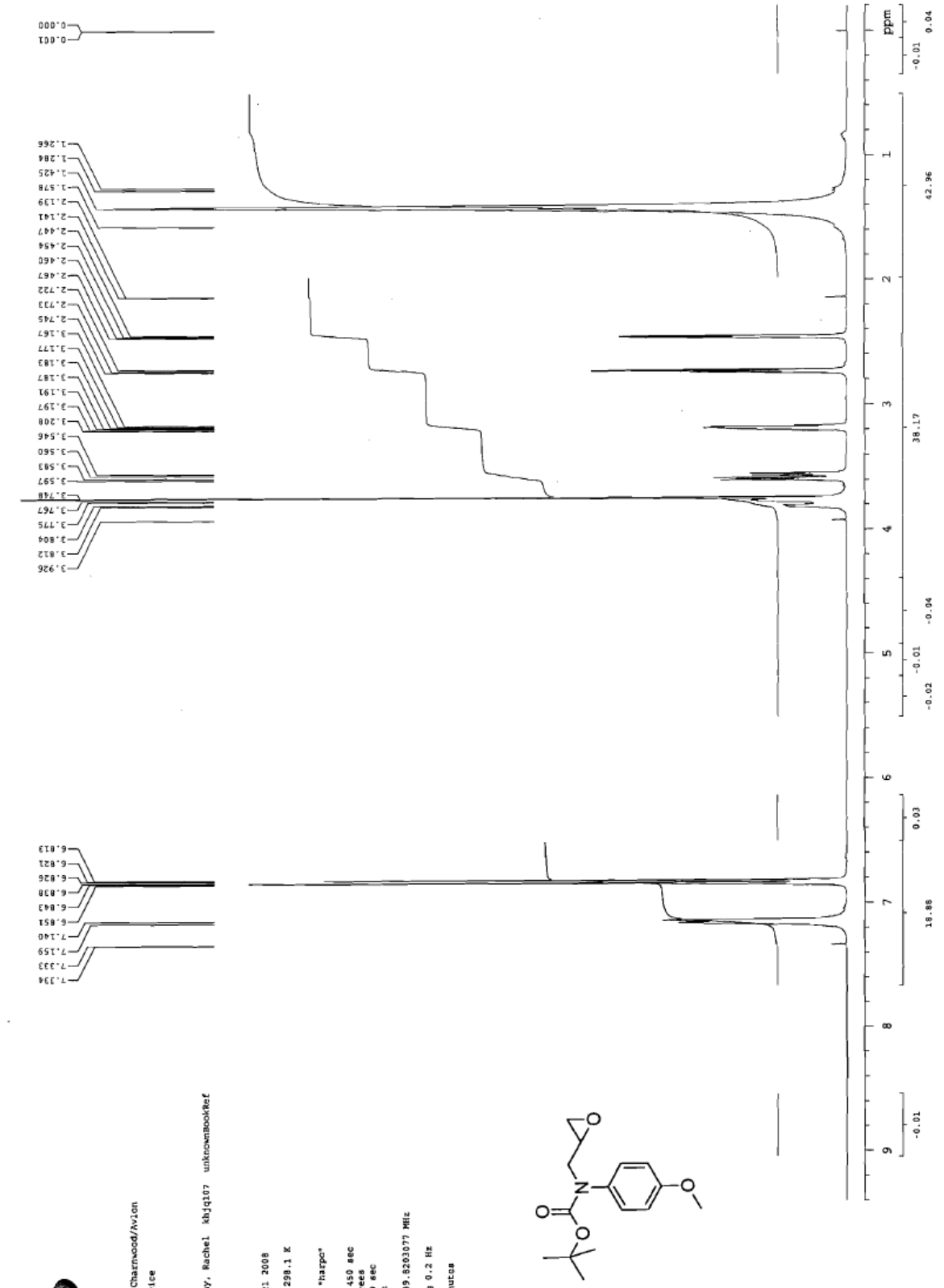








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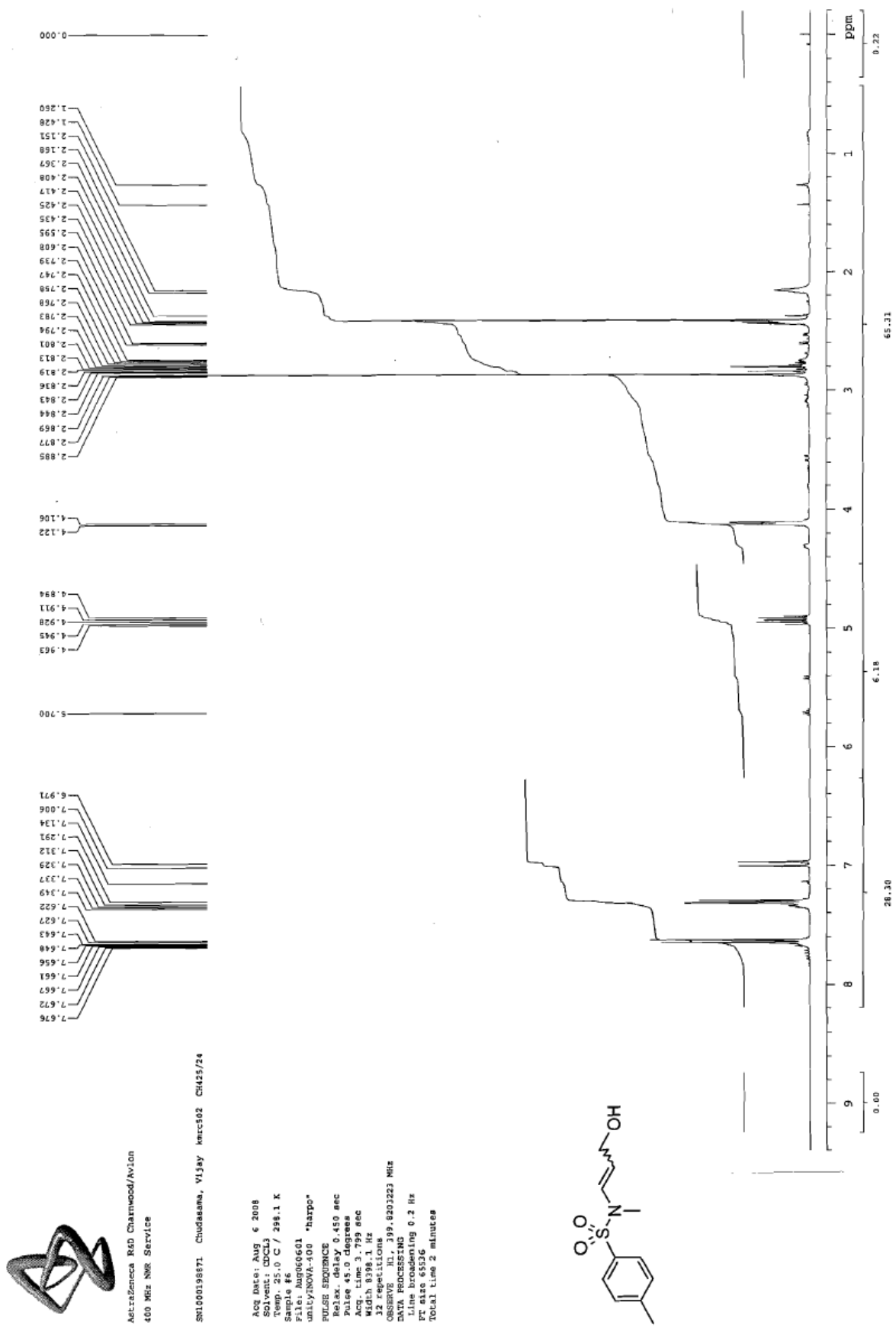

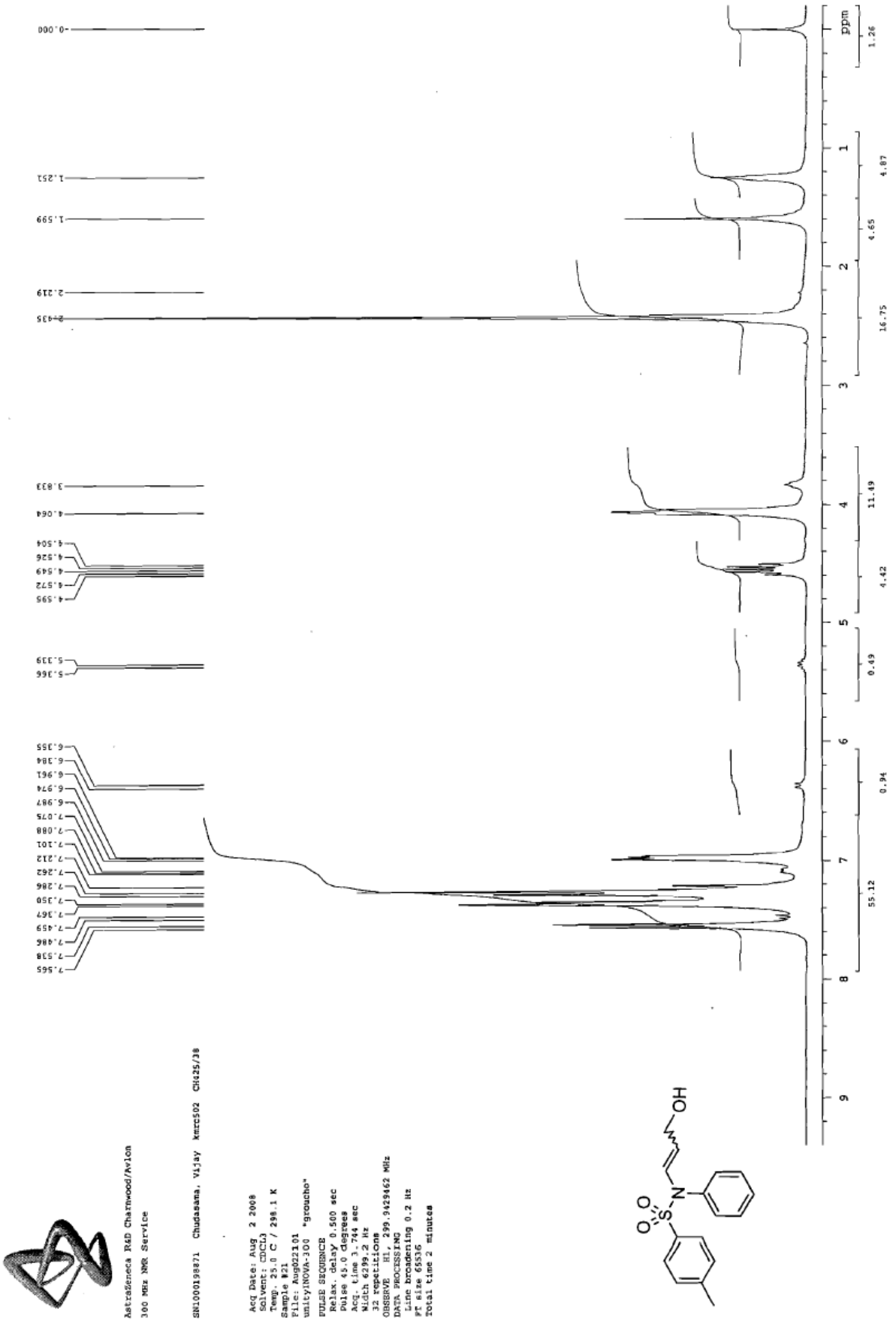

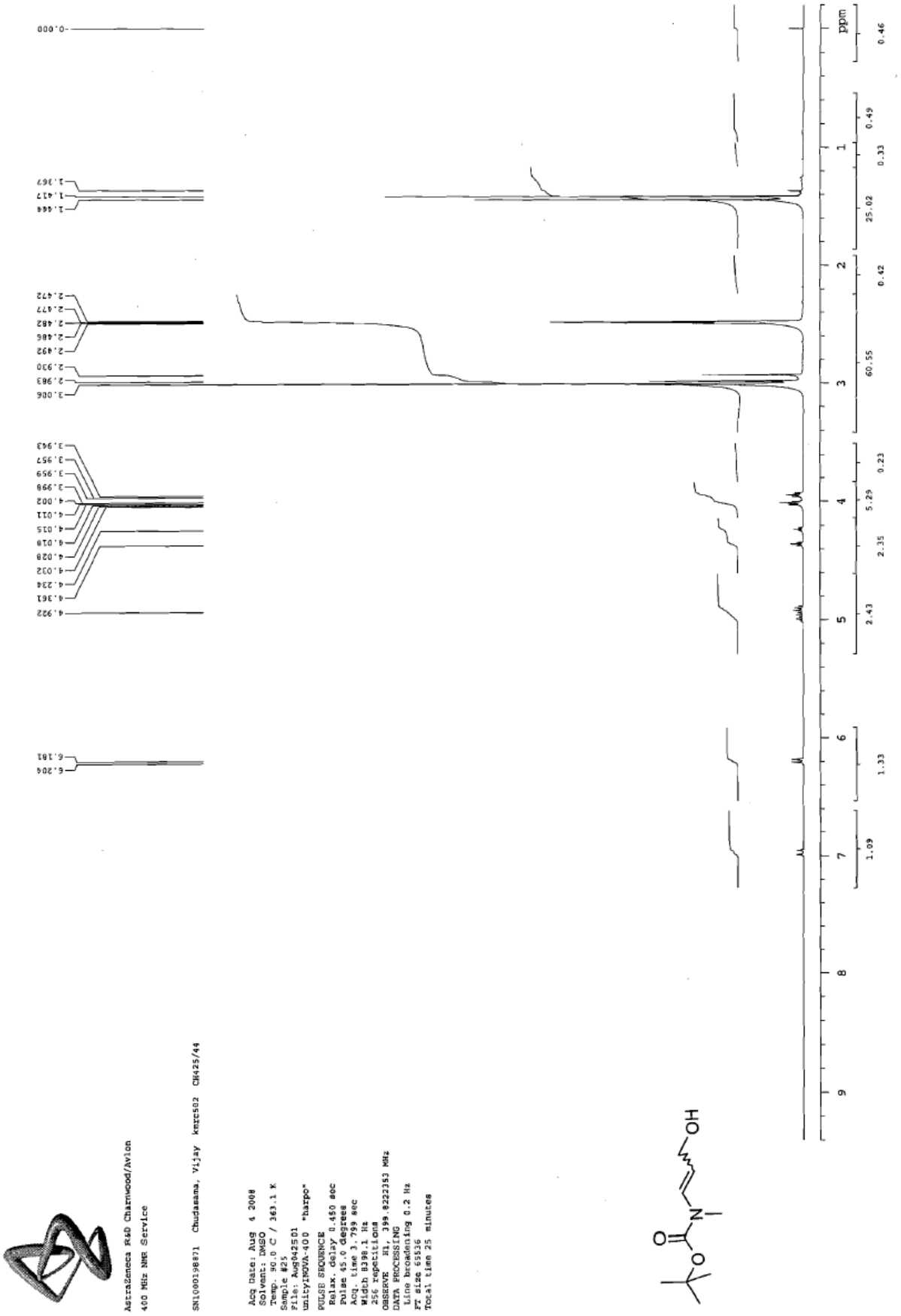

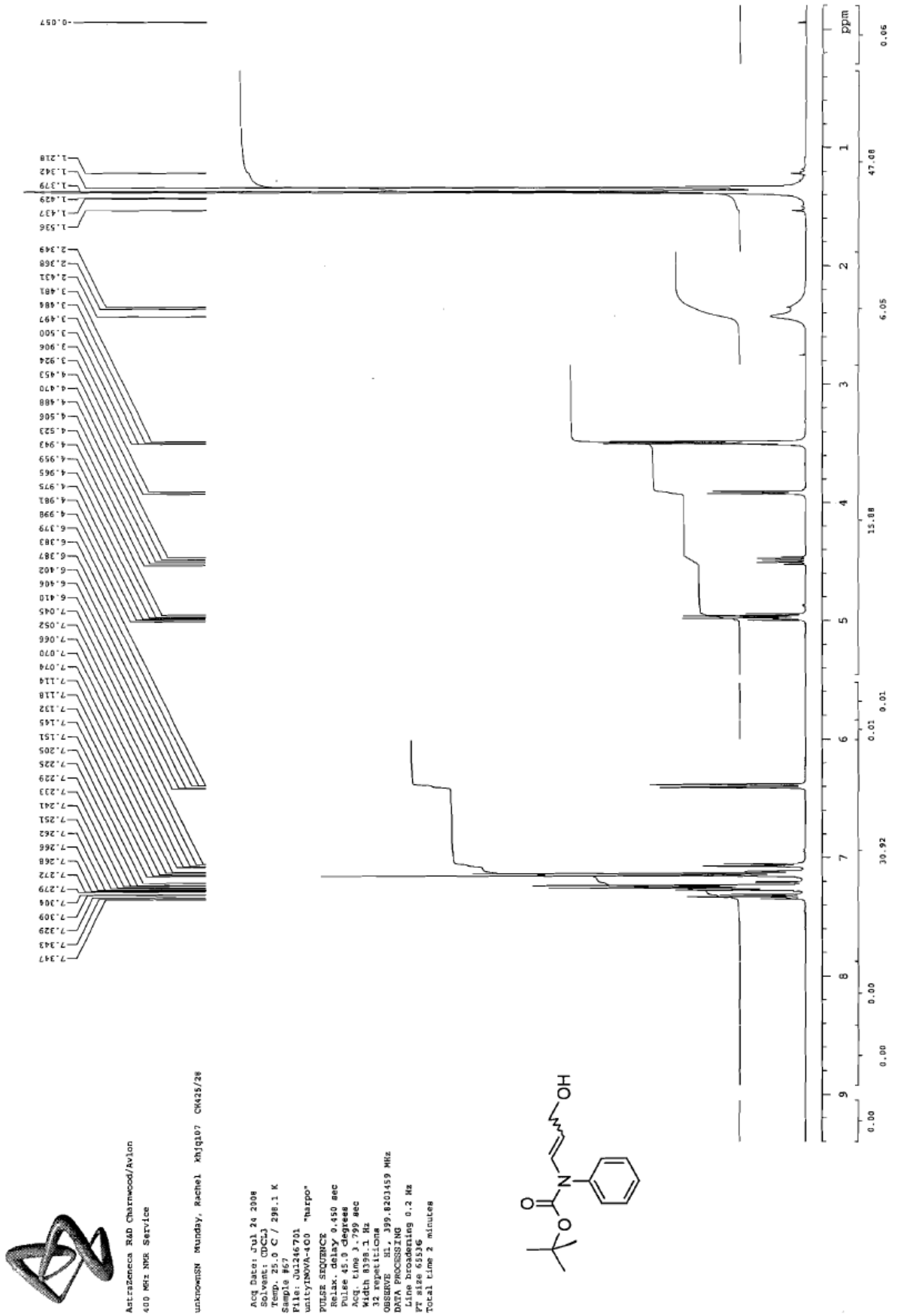

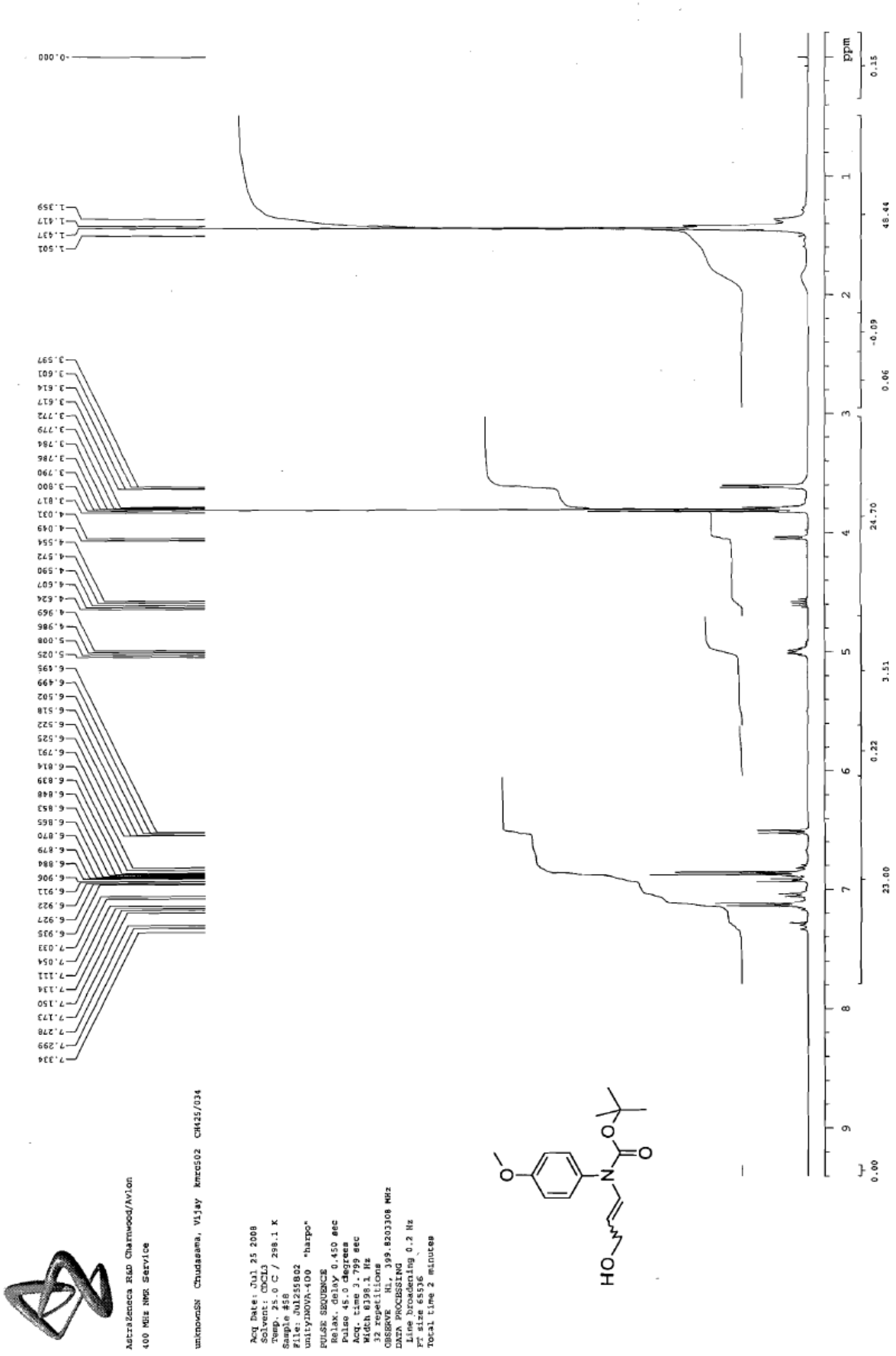

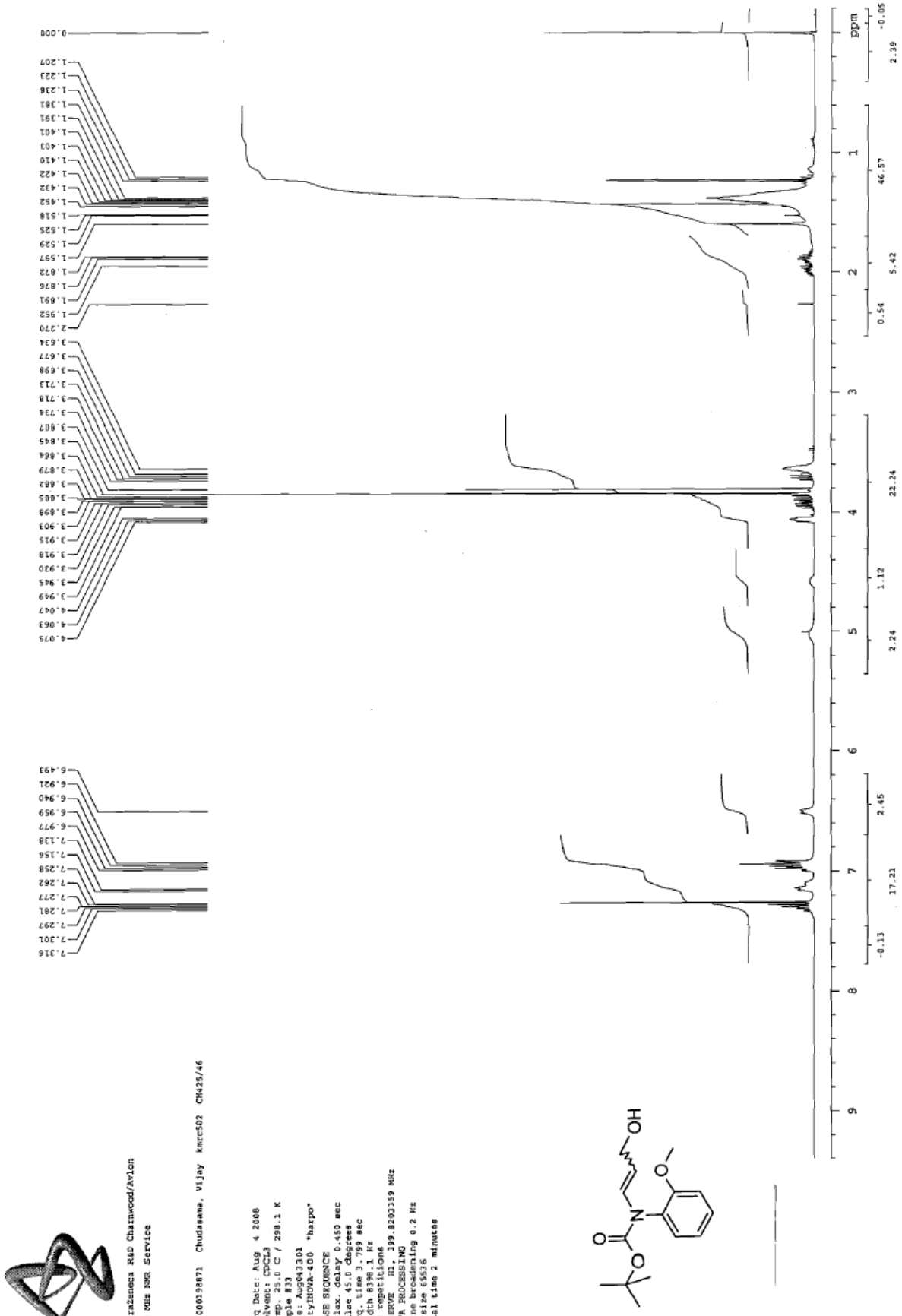

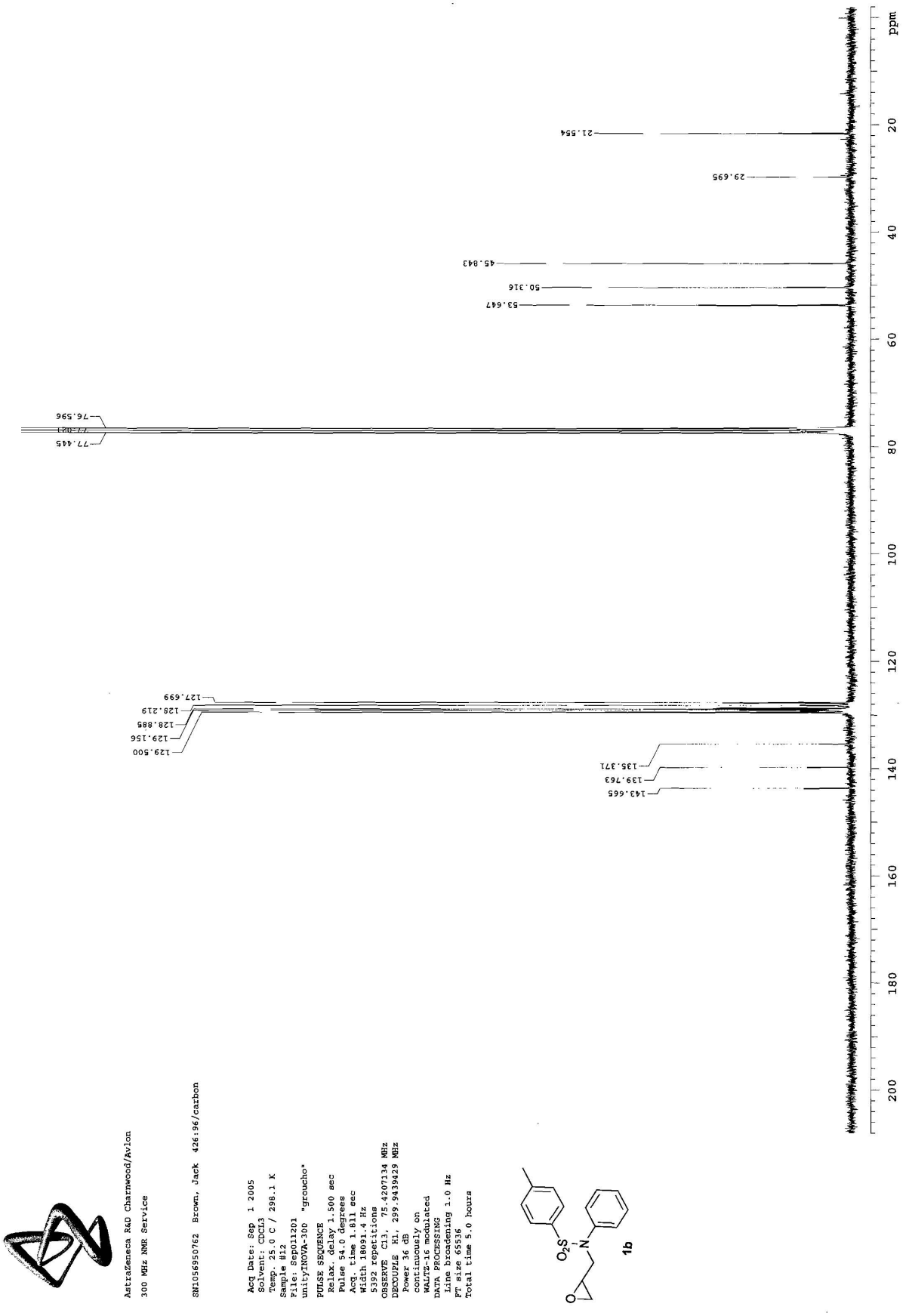

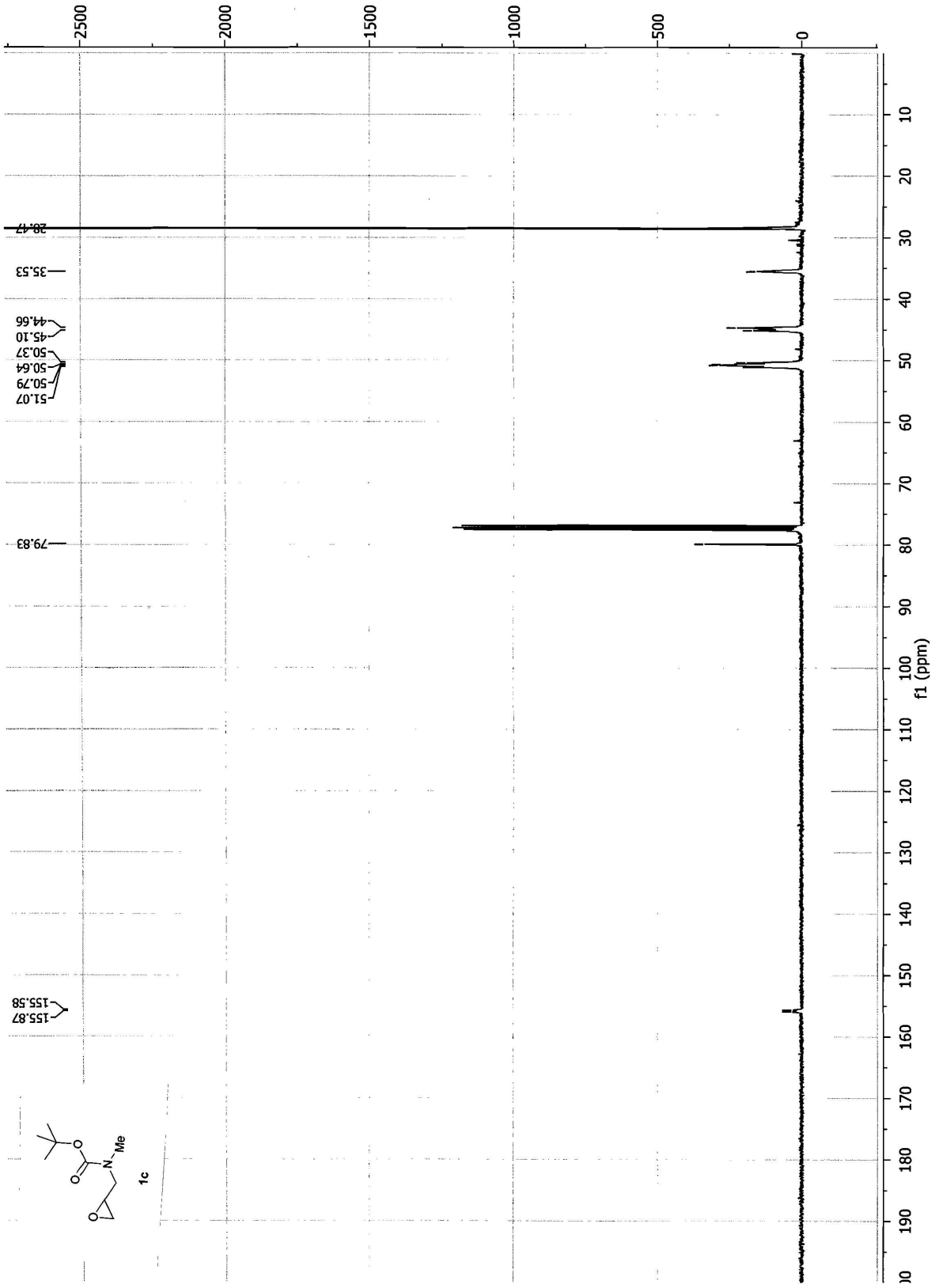

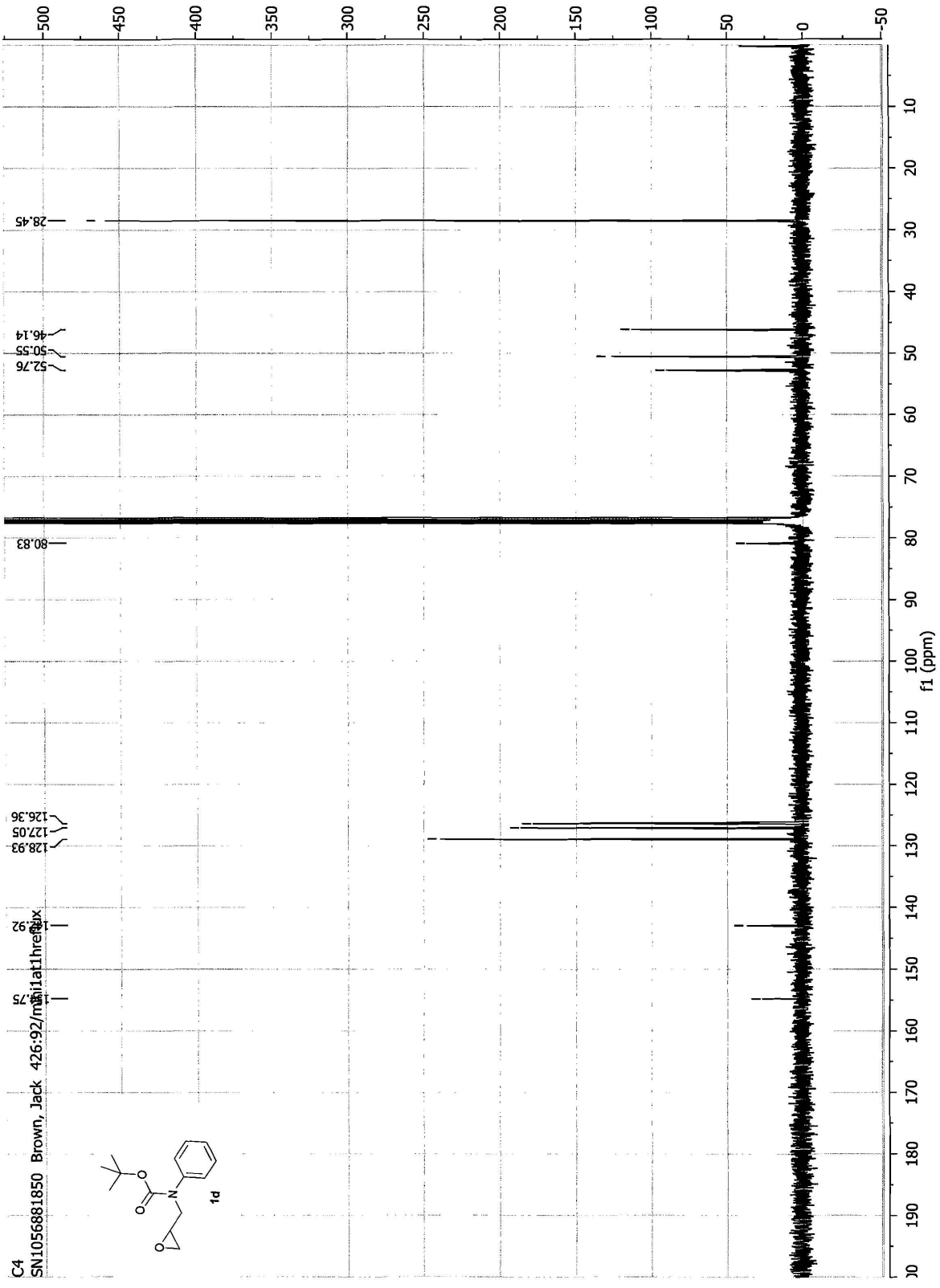

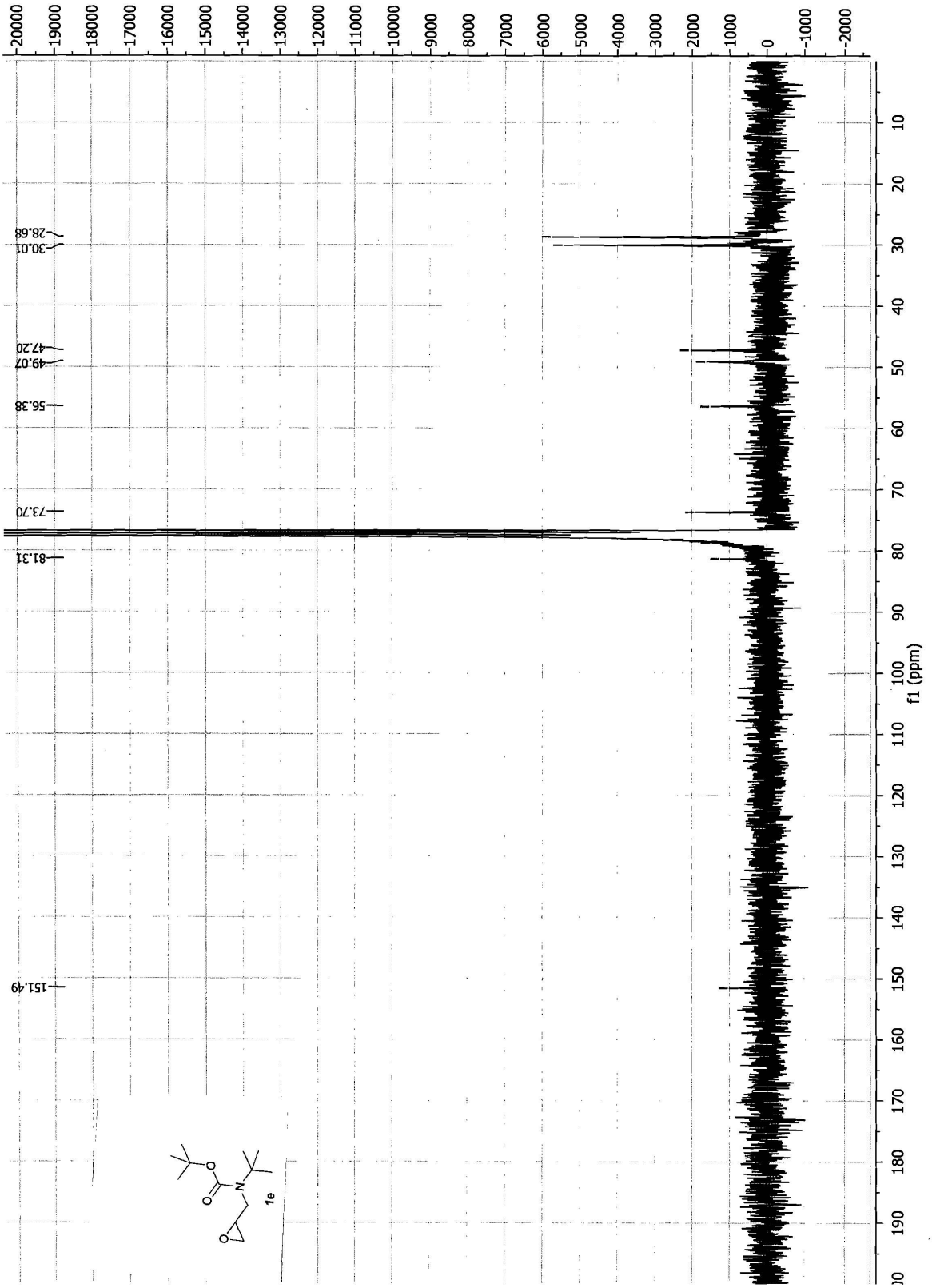

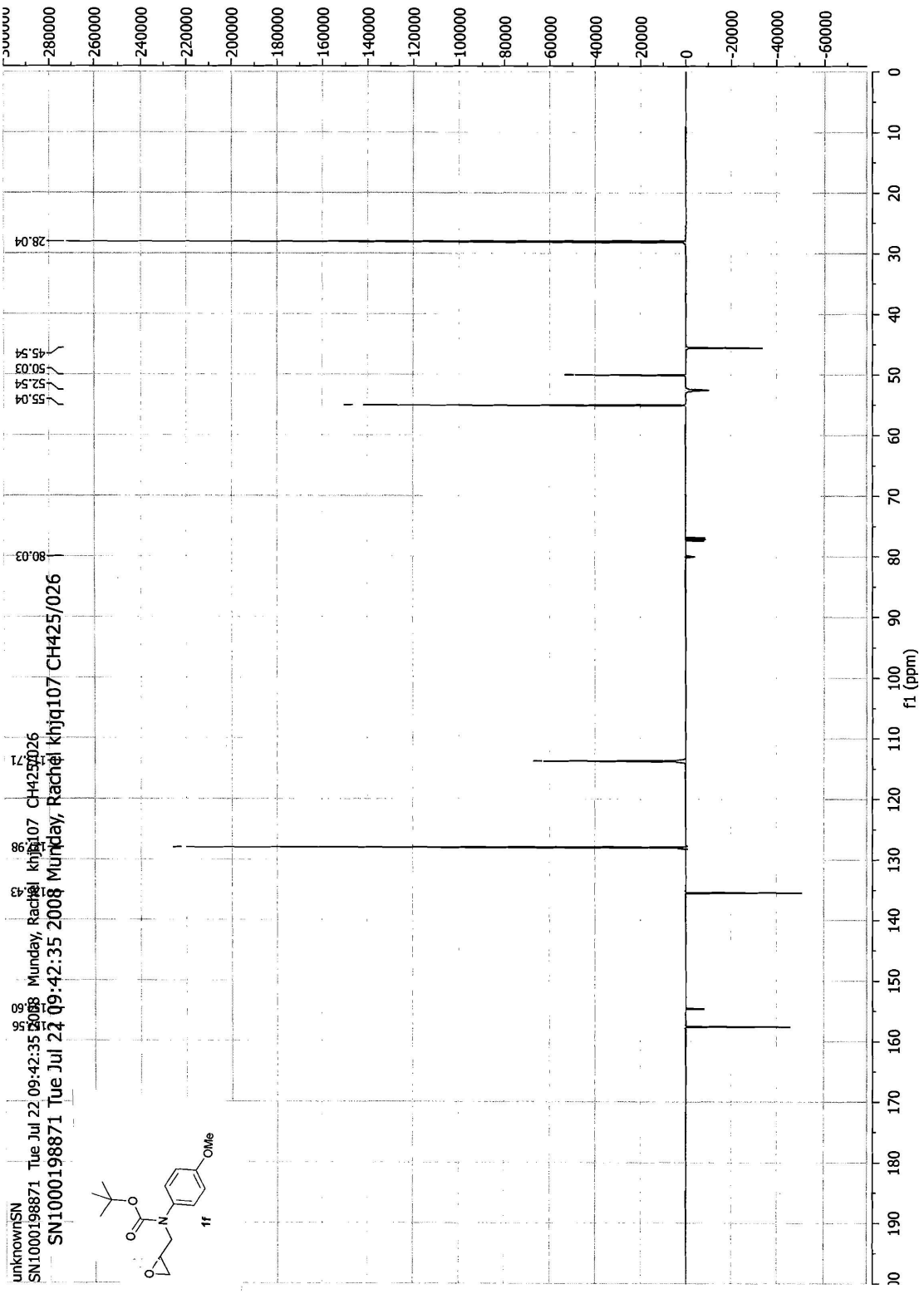

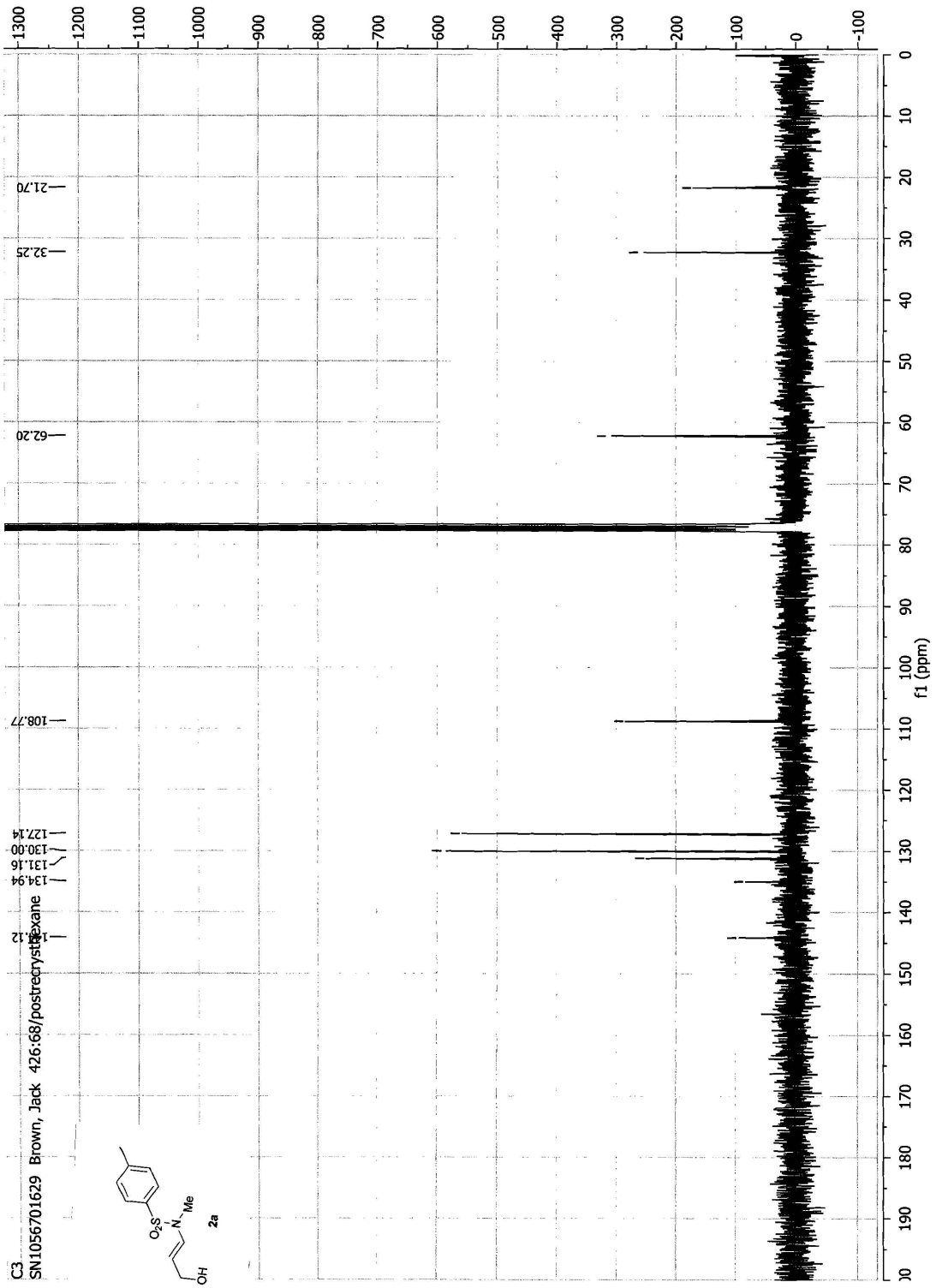

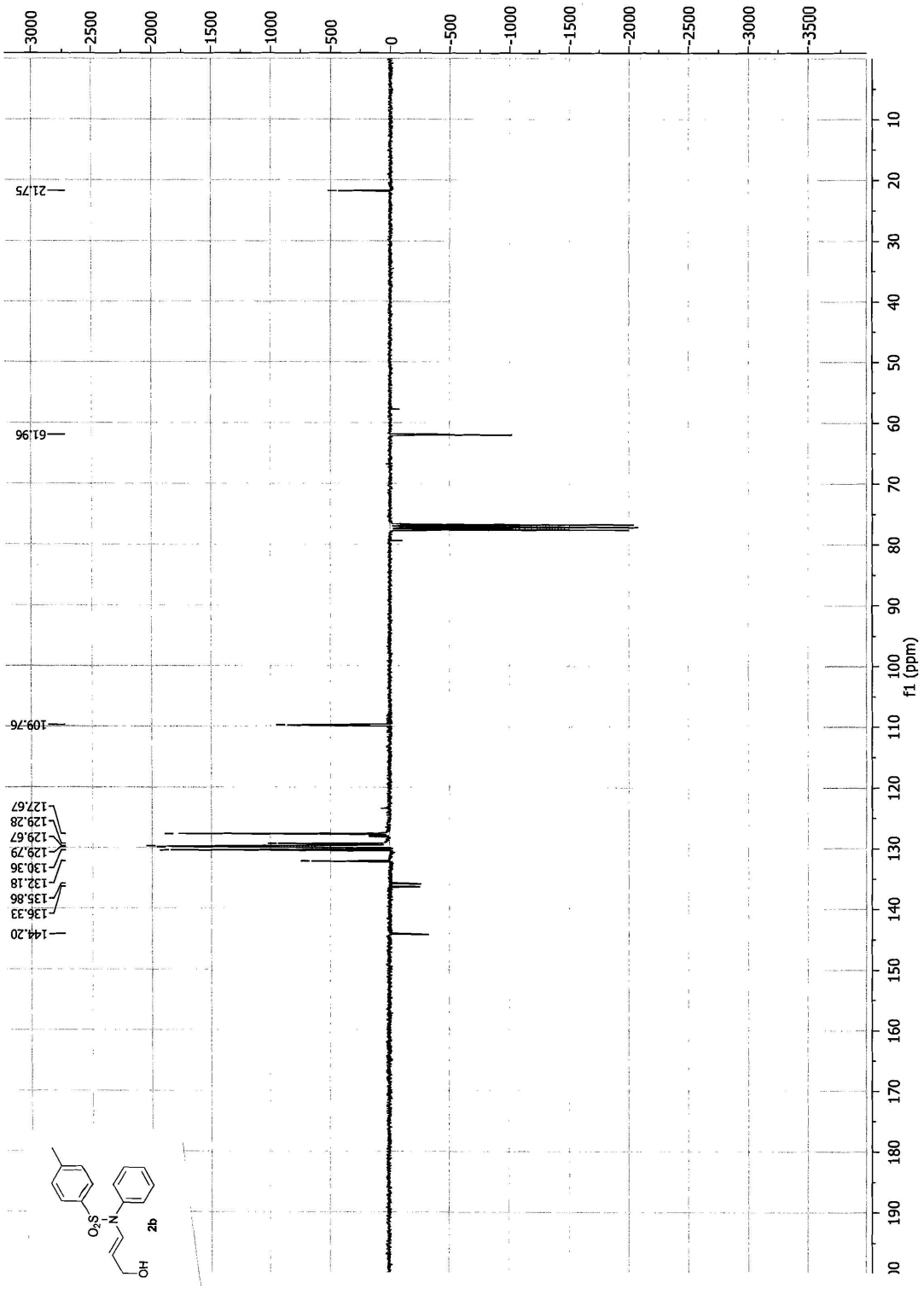

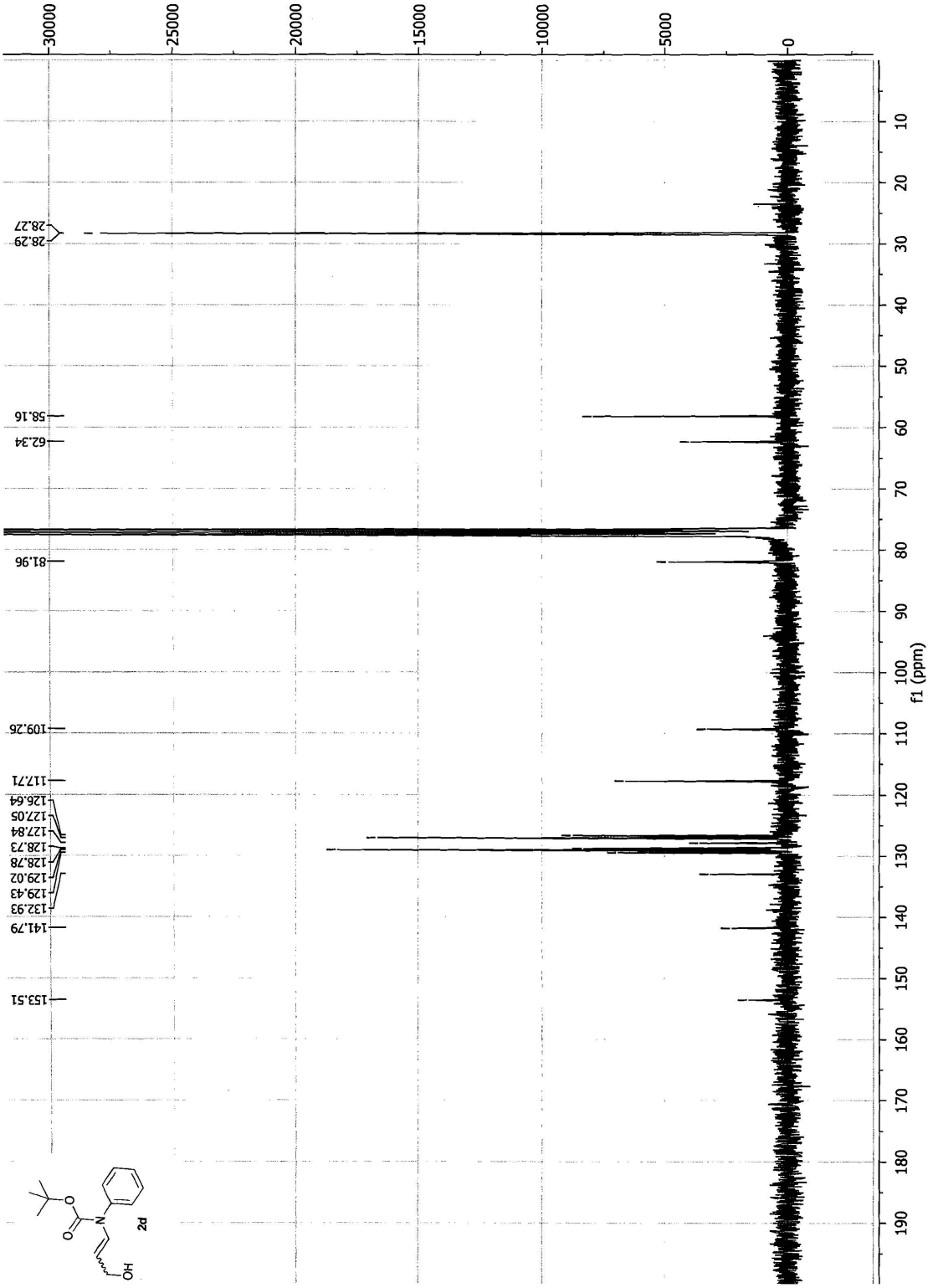

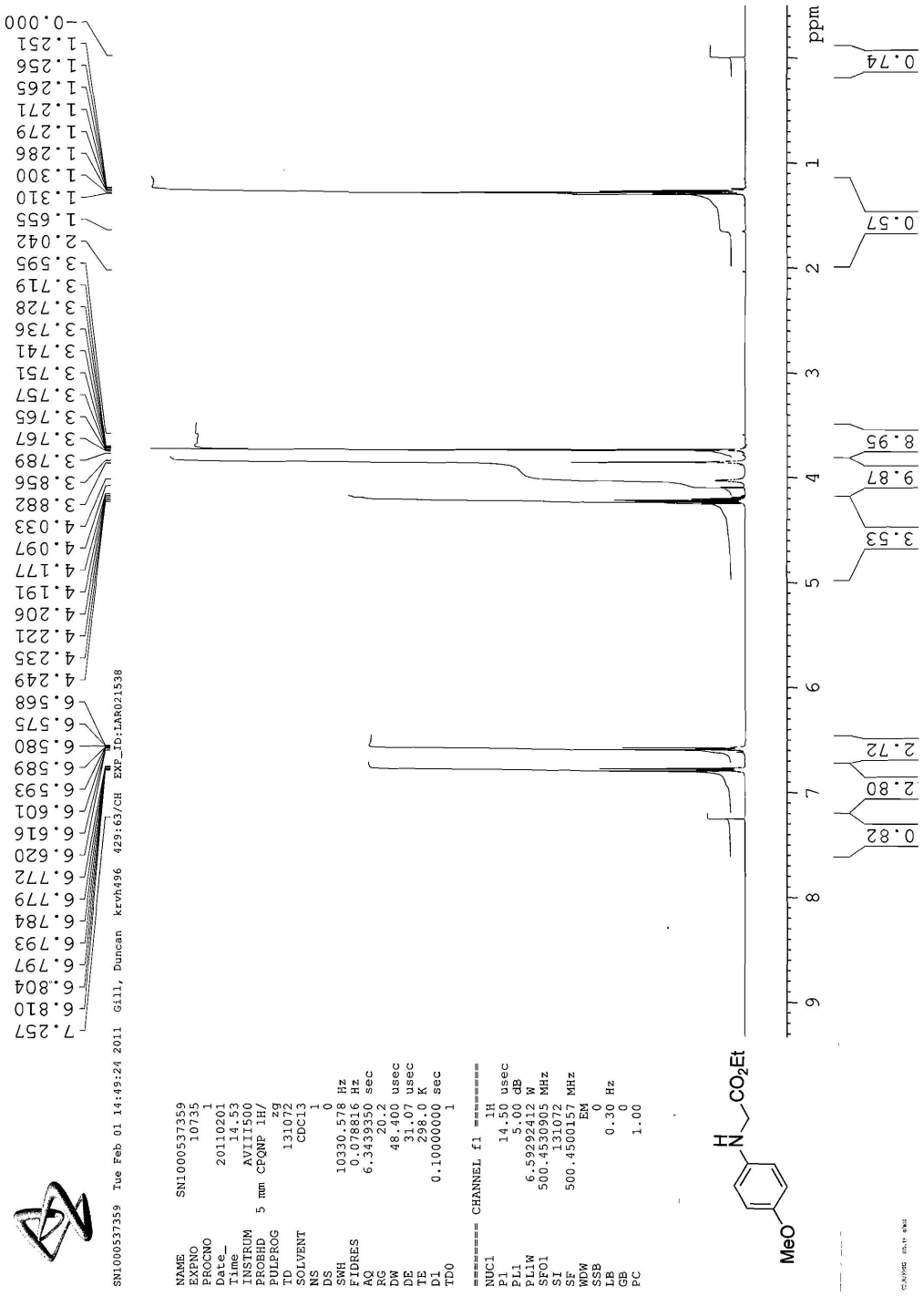
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Time 14.53
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SOLVENT CDCl3
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FIDRES 0.078816 Hz
AQ 6.3439350 sec
RG 20.2
DW 48.400 usec
DE 31.07 usec
TE 298.0 K
D1 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.50 usec
PL1 5.00 dB
PL1W 6.59292412 W
SFO1 500.4530905 MHz
SI 131072
SF 500.4500157 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
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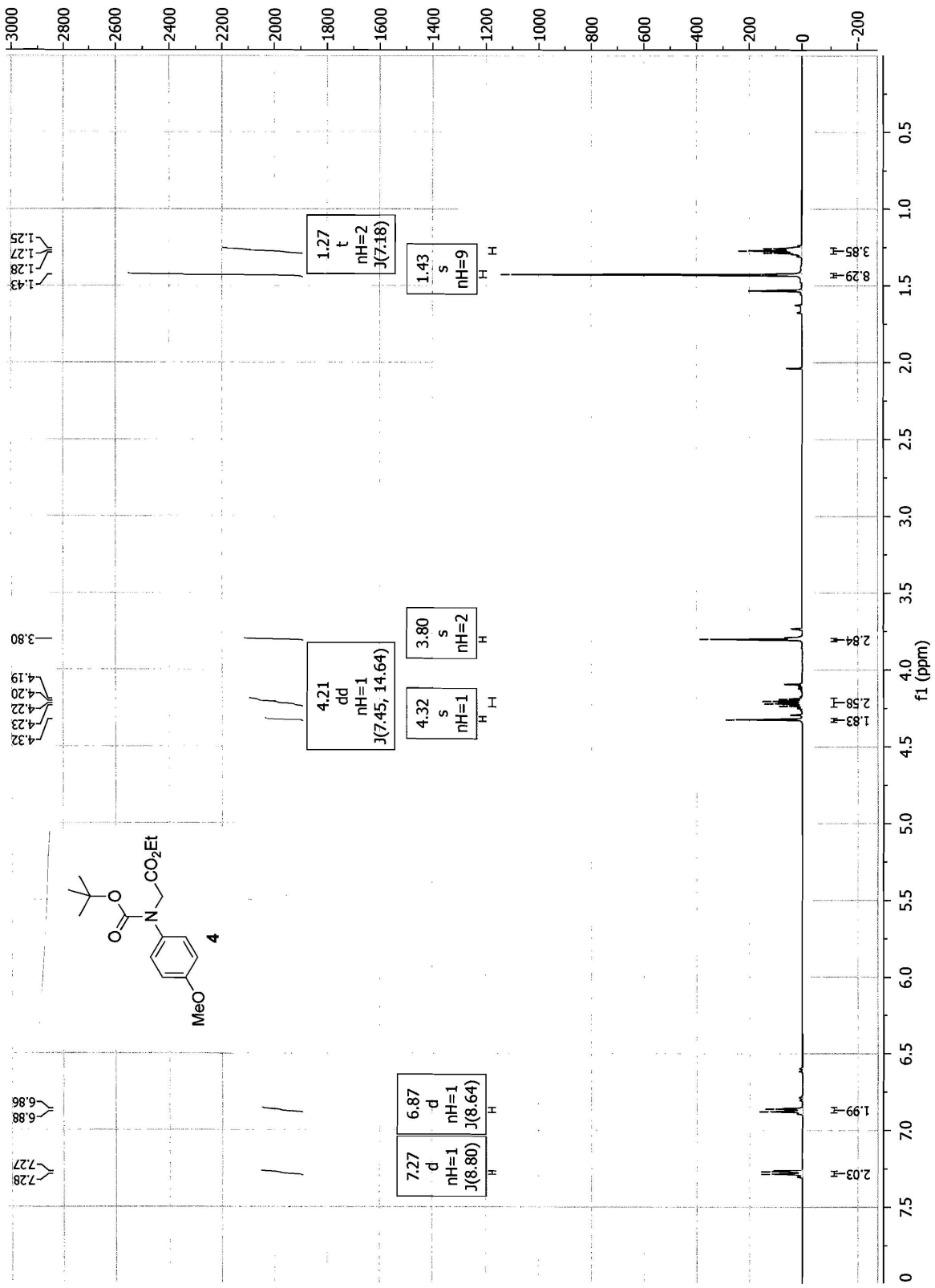

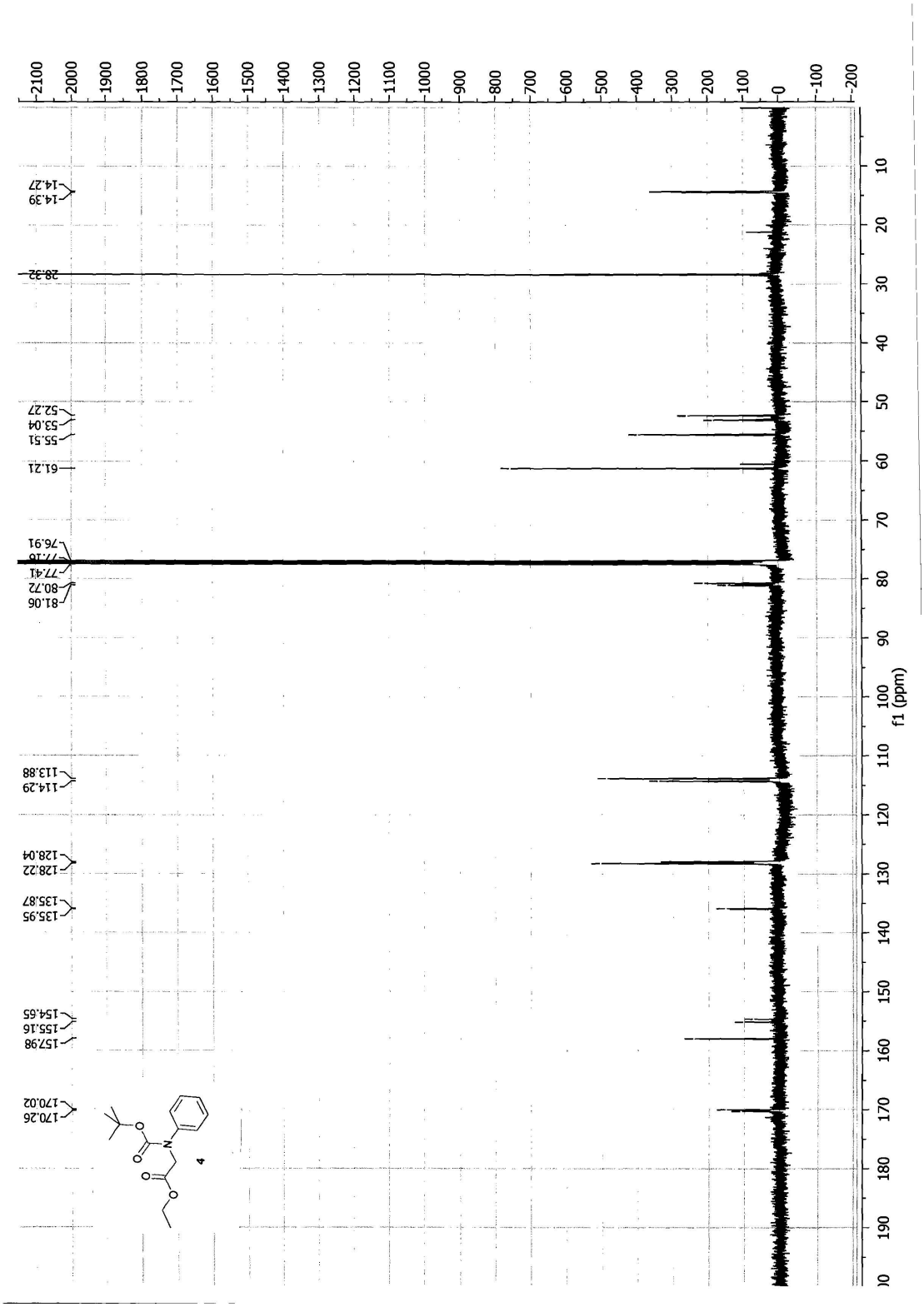

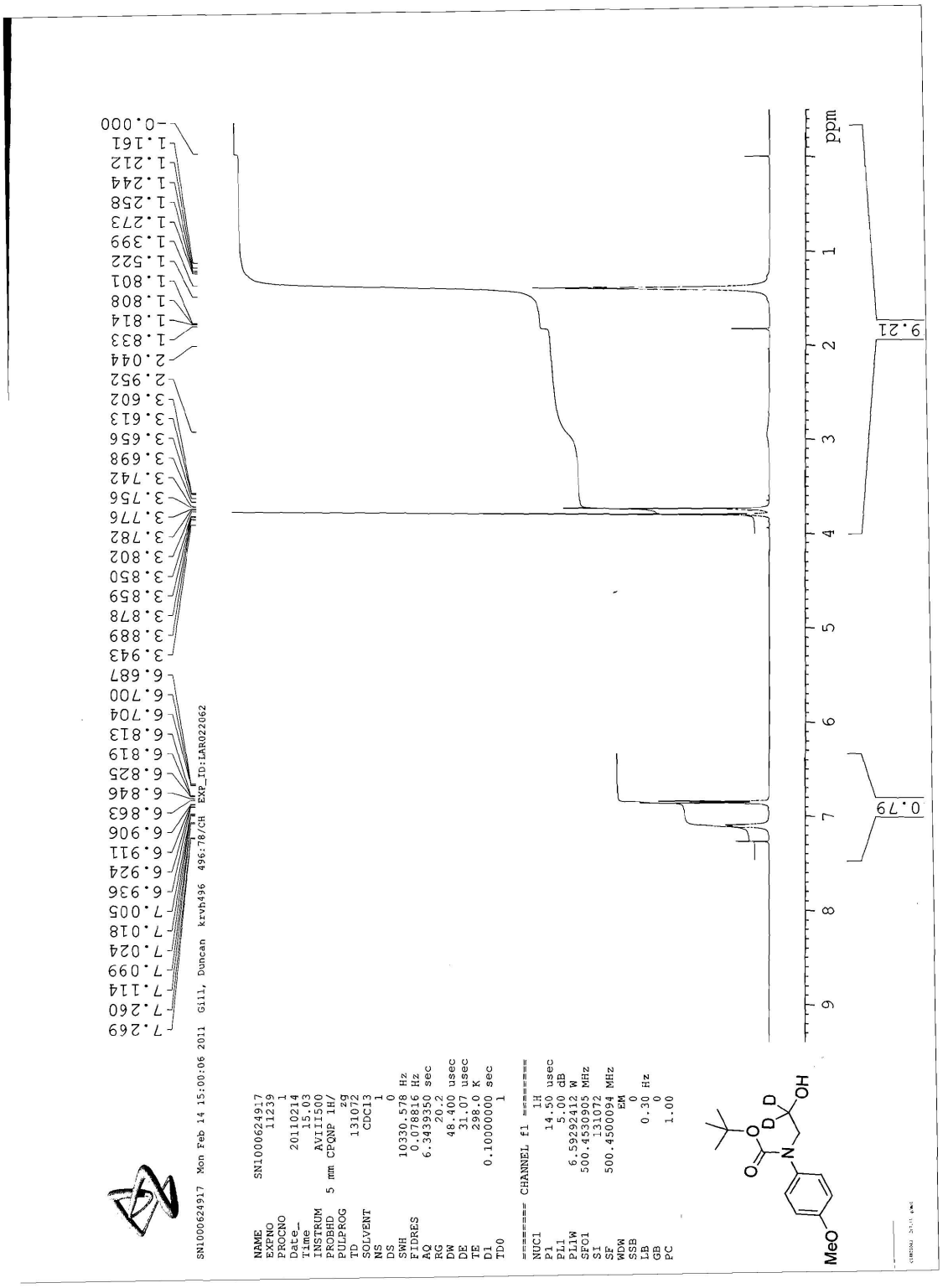

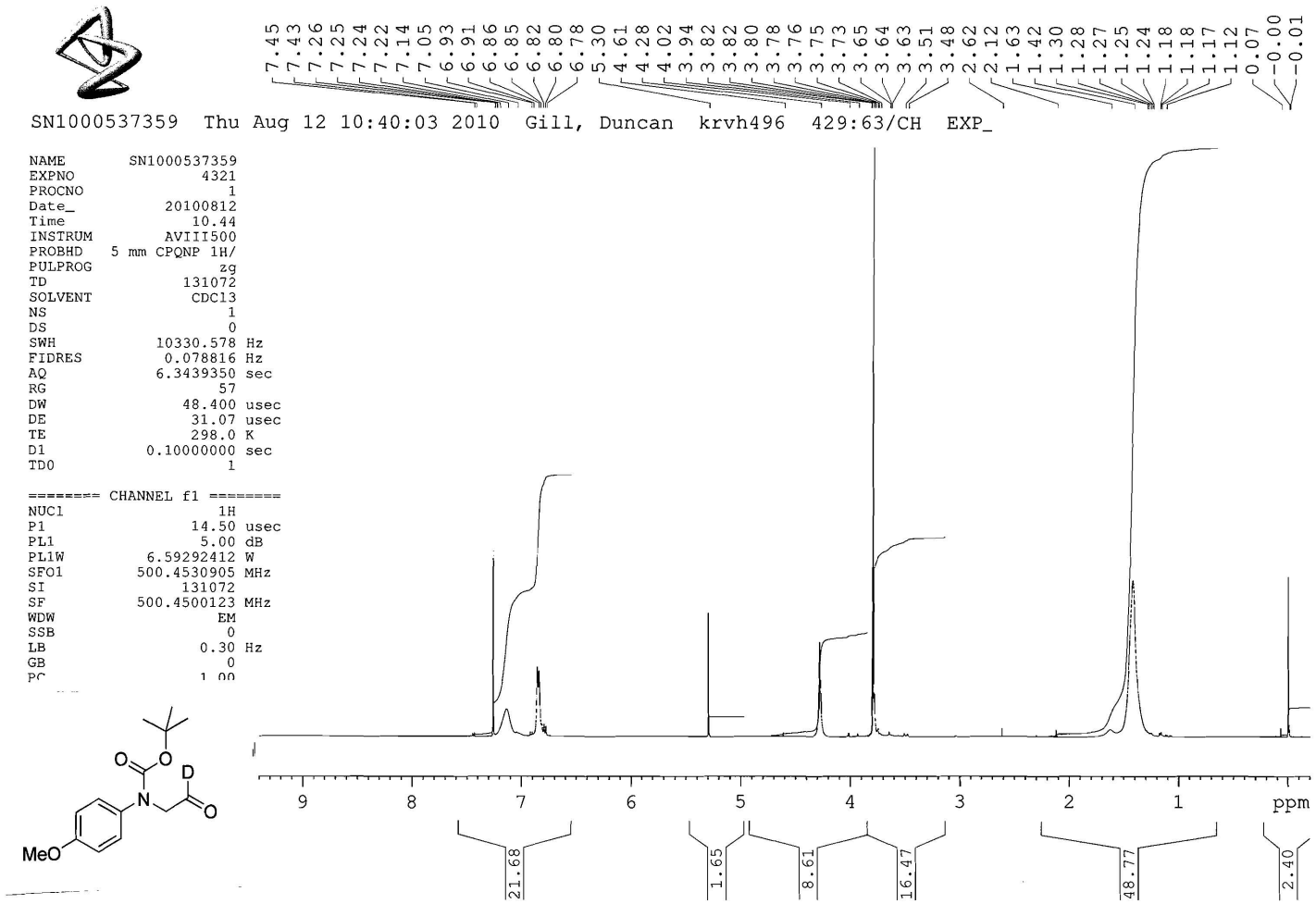

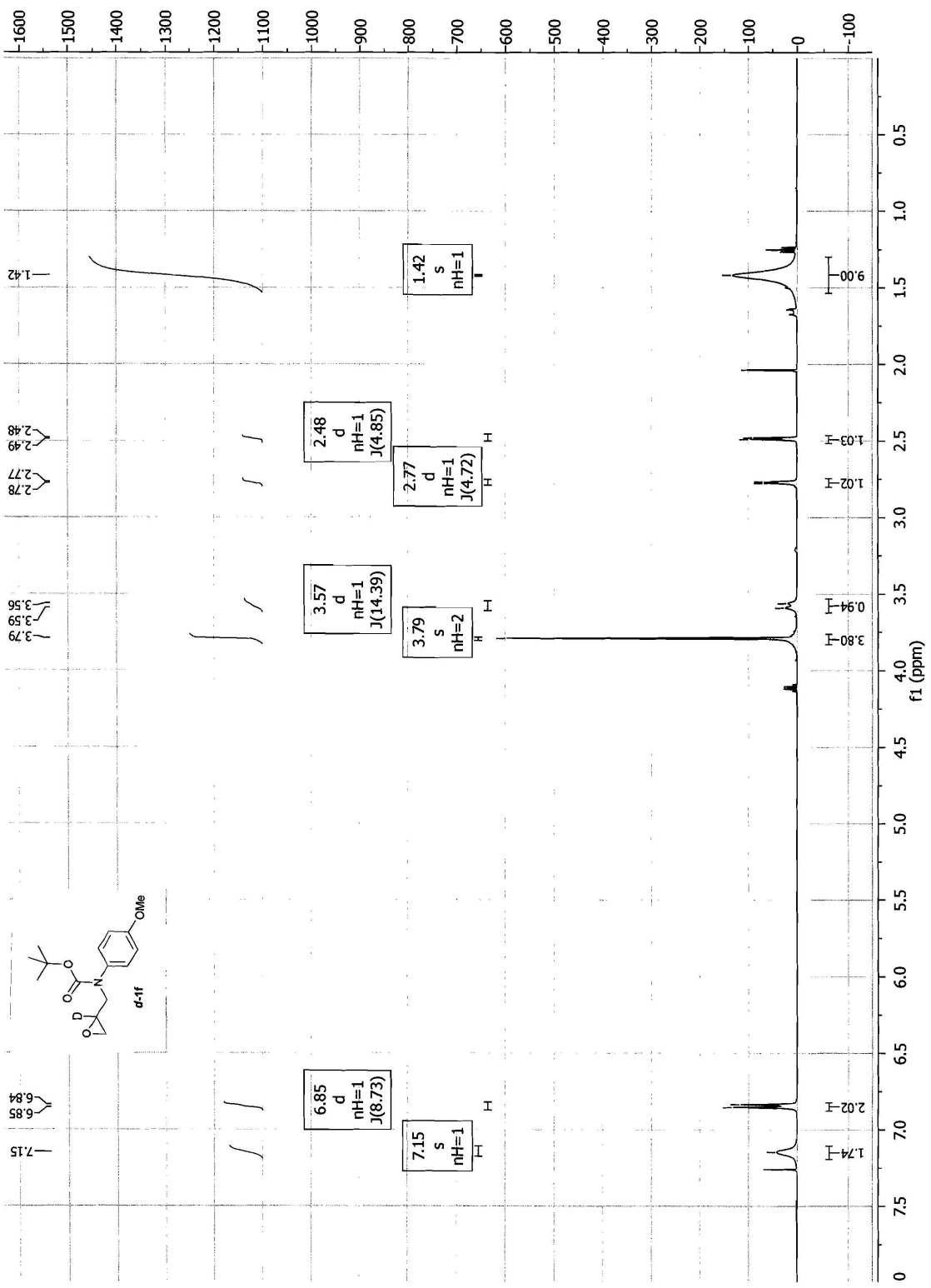

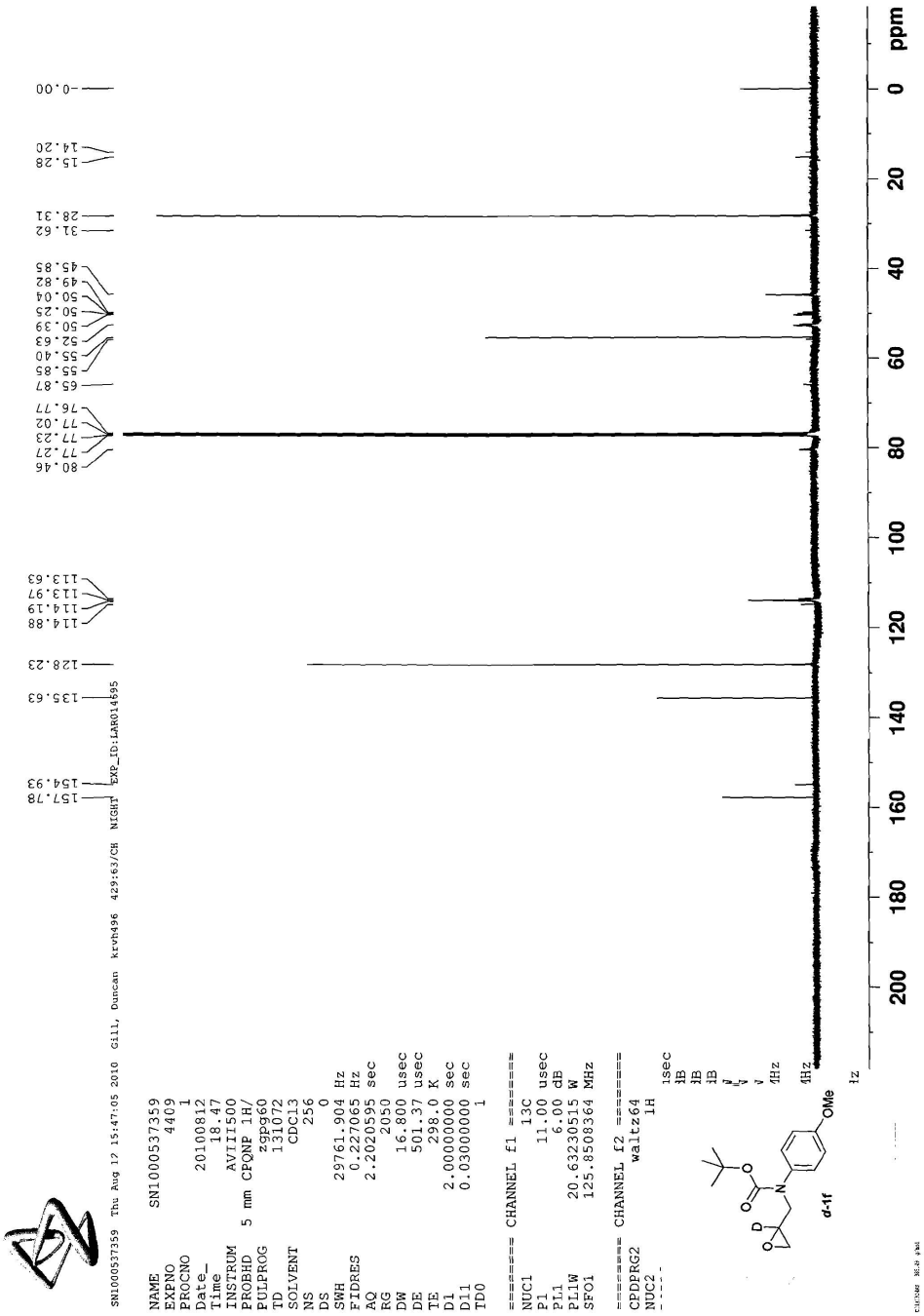
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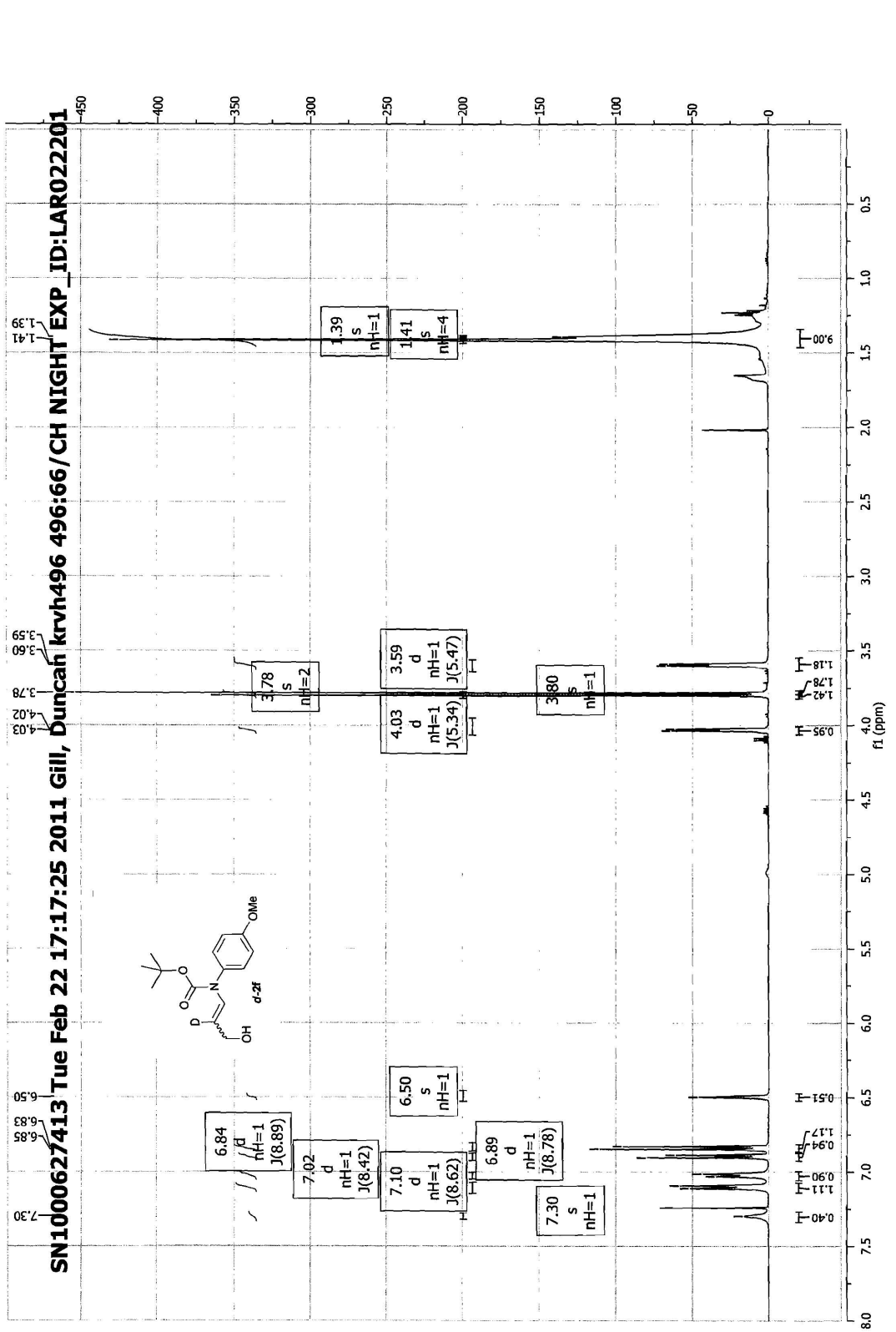

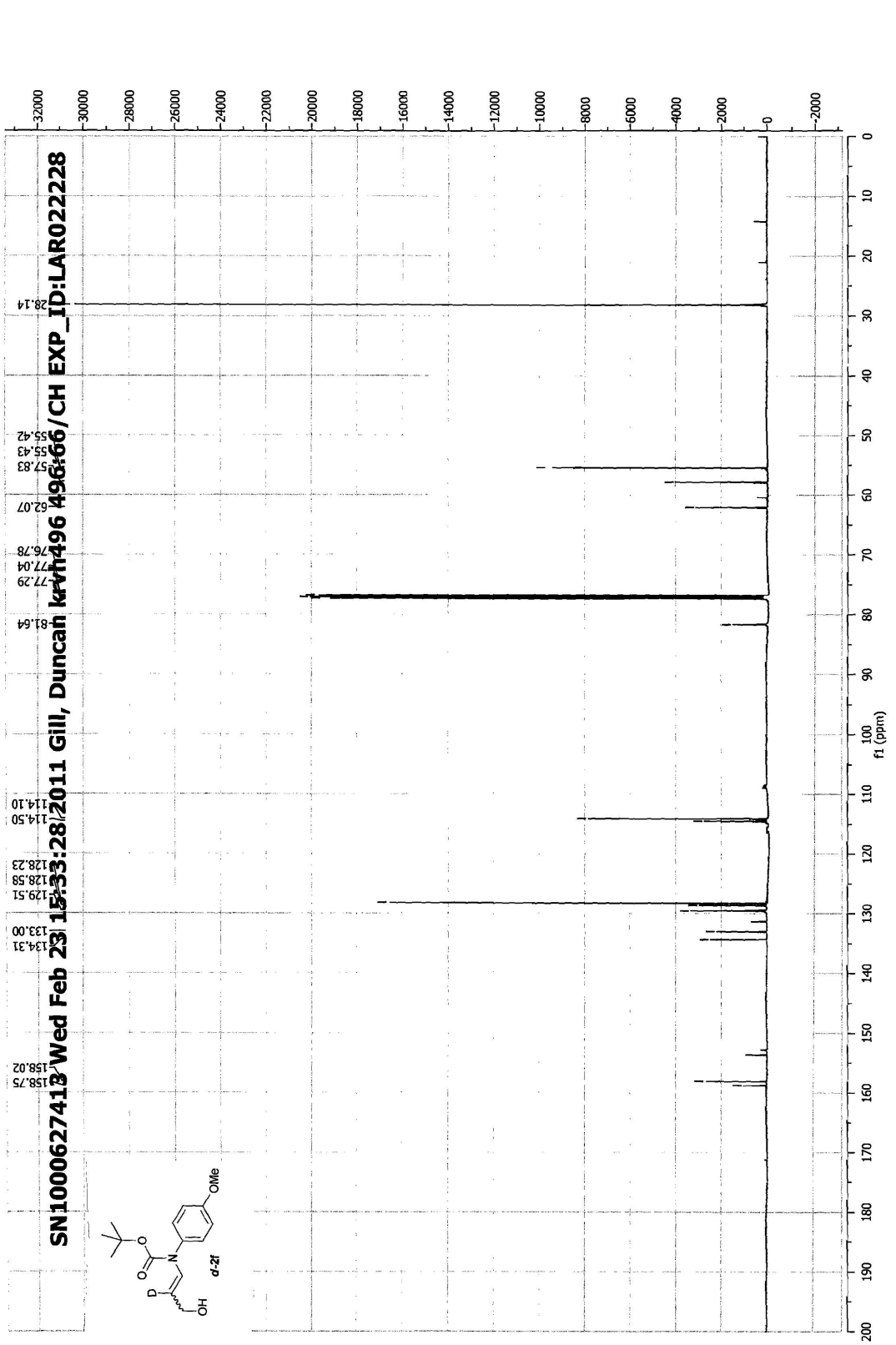
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OMe
OH
D
d-2f
f1 (ppm)