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Supporting Information

Novel Borane Reduction of Ether-Protected Aromatic Lactams

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Table of contents:

General procedure	S2
¹ H NMR of 5	S5
¹ H NMR of 6a	S6
DEPT of 6a	S7
¹ H NMR of 6b	S8
DEPT of 6b	S9
¹ H NMR of 10	S10
Low Mass of 10	S11
High Mass of 10	S12

EXPERIMENTAL SECTION

IR spectra were obtained on a FT-IR spectrometer as neat. ^1H NMR spectra were recorded at 400 or 200 MHz. ^{13}C NMR spectra were recorded at 100 MHz, using CDCl_3 as a solvent. ^1H NMR chemical shifts are referenced to TMS or CDCl_3 (7.26 ppm). ^{13}C NMR was referenced to CDCl_3 (77.0 ppm). Multiplicities were determined by the DEPT sequence as s, d, t, q. Mass spectra and high resolution mass spectra (HRMS) were measured using the electron-impact (EI, 70 eV) technique by Taichung Regional Instrument Center of National Science Council at National Chung-Hsiung University. Flash chromatography was carried out on 230-400 mesh of Silica Gel.

General procedure for boranes reduction of ether protected 3,4-dihydro-2(1H)-quinolinones (4).

Reaction condition a: To a stirred solution of ether protected lactam **4a-h** (0.2 mmol) in THF (5 mL) was added 15 equiv of borane-tetrahydrofuran (3 mL, 1M in THF) under nitrogen at room temperature, then the mixture was stirred at the room temperature for 24h. The reaction mixture was poured into ice water (100 mL) and extracted four times with ethyl acetate. The combined organic phases were washed with saturated NaHCO_3 , H_2O , brine, and dried over MgSO_4 . After removal of solvent, the residue was purified by flash chromatography (hexane/ AcOEt = 50:1) to give the corresponding compounds **5**, **6a** or **6b**. The reaction yields are shown in Table 1.

Reaction condition b: To a stirred solution of ether protected lactam **4a-h** (0.2 mmol) in THF (5 mL) was added borane-dimethyl sulfide (307 μL , 10 M) under nitrogen at room temperature, then the mixture was stirred at the room temperature for

24h. The reaction mixture was poured into ice water (100 mL) and extracted four times with ethyl acetate. The combined organic phases were washed with saturated NaHCO_3 , H_2O , brine, and dried over MgSO_4 . After removal of solvent, the residue was purified by flash chromatography (hexane/ AcOEt = 50:1) to give the corresponding compounds **5**, **6a** or **6b**. The reaction yields are shown in Table 1.

1-Methyl-1,2,3,4-tetrahydroquinoline (5).¹ colorless oil; ^1H NMR (CDCl_3 , 400 MHz) δ 7.15 (td, J = 7.6, 1.4 Hz, 1H), 7.02 (dd, J = 7.2, 1.2 Hz, 1H), 6.68 (t, J = 7.6 Hz, 2H), 3.28 (t, J = 5.6 Hz, 2H), 2.95(s, J = 6.4 Hz, 3H), 2.84 (t, J = 6.4 Hz, 2H), 2.08-2.02 (m, 2H).

4-(3,4-Dihydro-2H-quinolin-1-yl)-butan-1-ol (6a). yellow oil; ^1H NMR (CDCl_3 , 400 MHz) δ 7.03 (td, J = 7.2, 2.0 Hz, 1H), 6.93 (dd, J = 7.2, 1.2 Hz, 1H), 6.57 (d, J = 8.4 Hz, 1H), 6.55 (td, J = 7.6, 0.8 Hz, 1H), 3.66 (t, J = 6.4 Hz, 2H), 3.28-3.25 (m, 4H), 2.74 (t, J = 6.4 Hz, 2H), 1.97-1.91 (m, 2H), 1.71-1.57 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 145.3 (s), 129.1 (d), 127.0 (d), 122.4 (s), 115.5 (d), 110.6 (d), 62.8 (t), 51.4 (t), 49.5 (t), 30.4 (t), 28.1 (t), 22.8 (t), 22.2 (t); IR (neat) 3367, 2947, 2837, 1596, 754 cm^{-1} ; LRMS (EI, m/z) 205 (M^+); HRMS (EI, m/z) for $\text{C}_{13}\text{H}_{19}\text{NO}$, calcd 205.1468, found 205.1474.

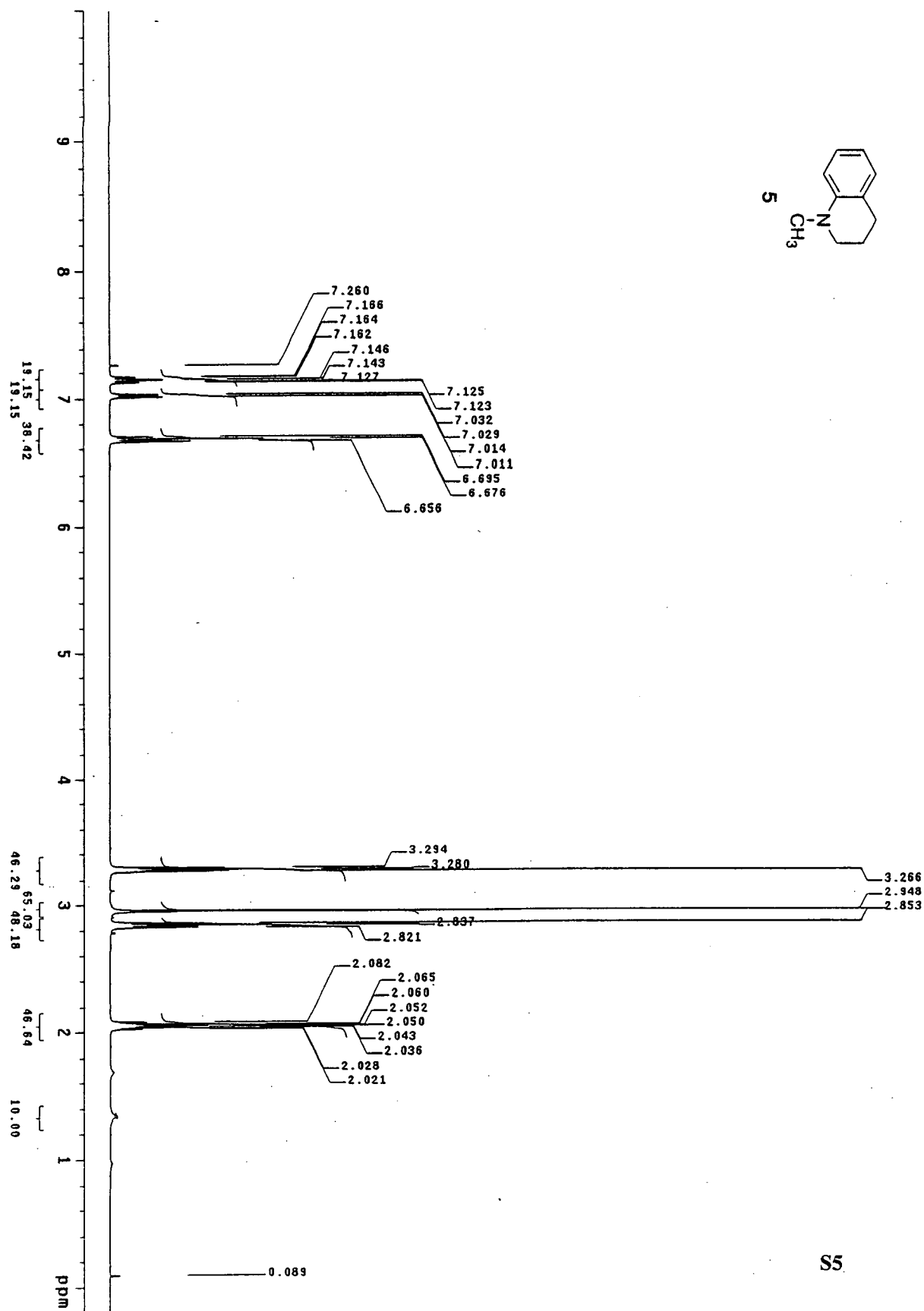
4-(3,4-Dihydro-2H-quinolin-1-yl)-butane-1-thiol (6b). yellow oil; ^1H NMR (CDCl_3 , 400 MHz) δ 7.03 (td, J = 8.0, 1.6 Hz, 1H), 6.93 (dd, J = 7.6, 0.8 Hz, 1H), 6.56-6.53 (m, 2H), 3.28-3.23 (m, 4H), 2.76-2.68 (m, 2H), 2.59-2.54 (m, 2H),

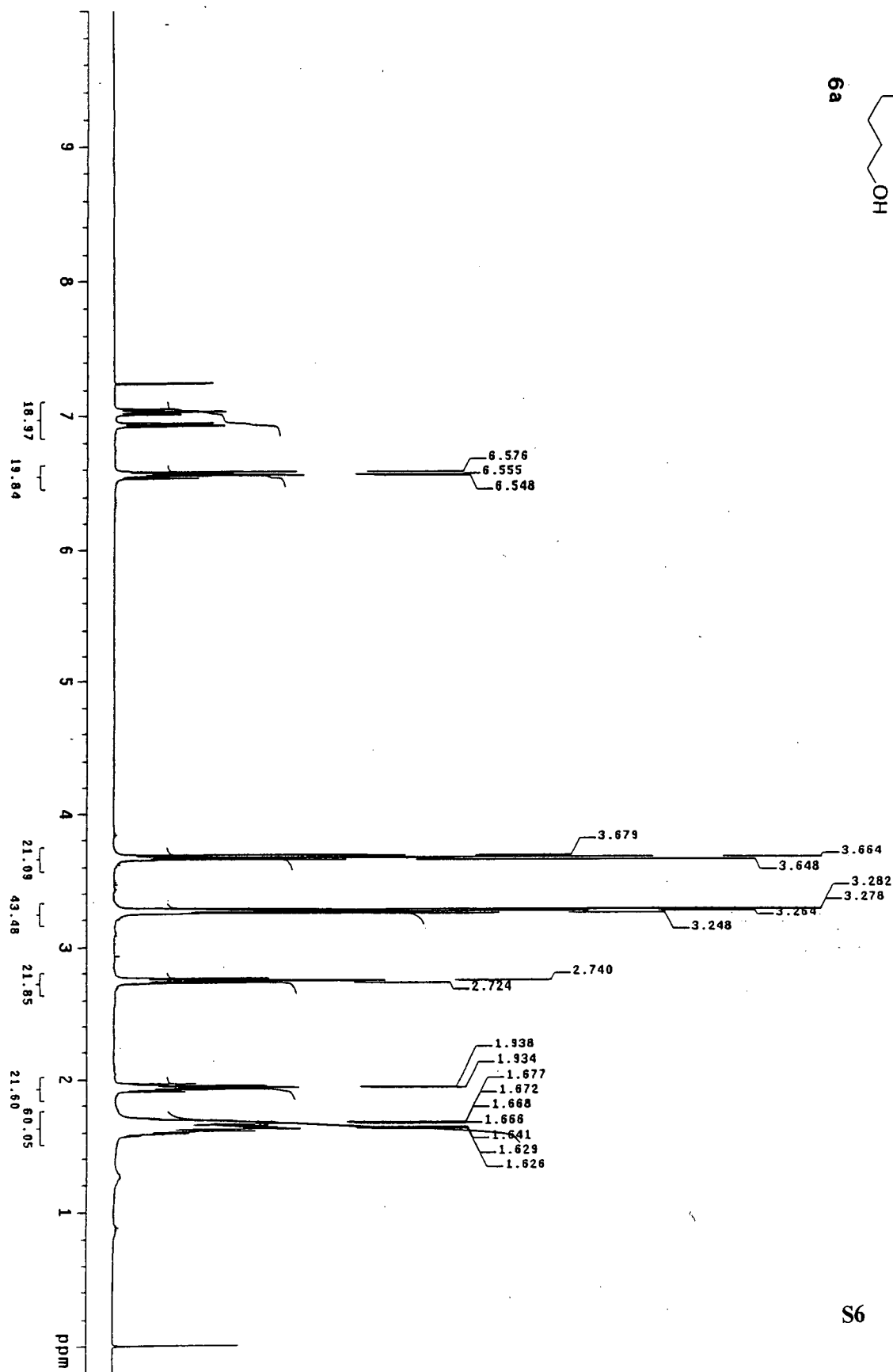
¹ Shaffer, C. L.; Morton, M. D.; Hanzilk, R. P. *J. Am. Chem. Soc.* **2001**, *123*, 8502.

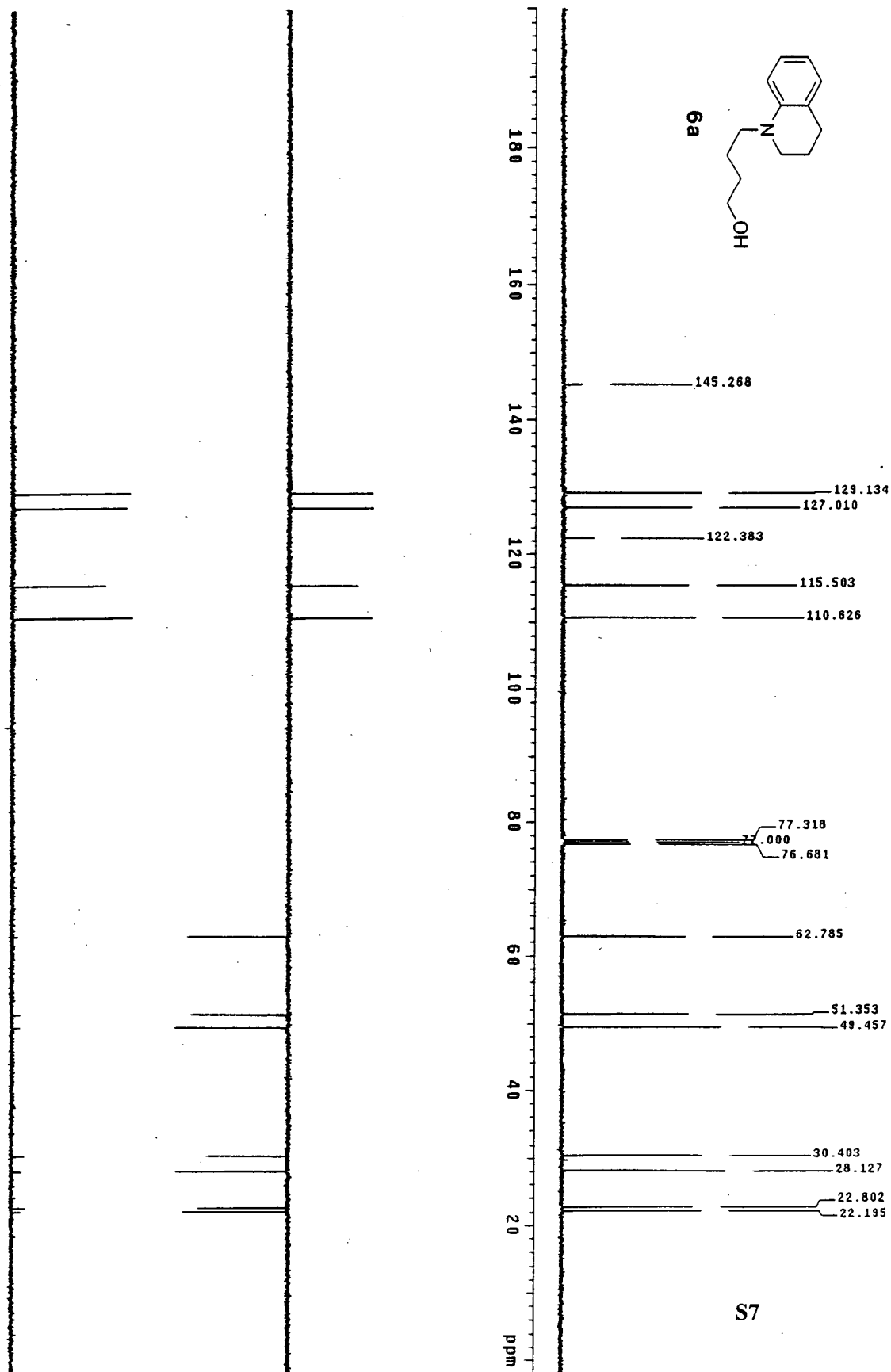
129.2 (d), 127.0 (d), 122.3 (s), 115.4 (d), 110.4 (d), 50.9 (t), 49.5 (t), 31.7 (t), 28.1 (t), 25.2 (t), 24.6 (t), 22.2 (t); IR (neat) 2930, 2857, 1604, 1507, 747 cm^{-1} ; LRMS (EI, m/z) 221(M^+); HRMS (EI, m/z) for $\text{C}_{13}\text{H}_{19}\text{NS}$, calcd 221.1240, found 221.1234.

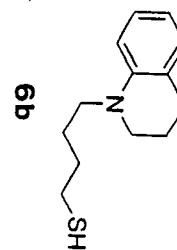
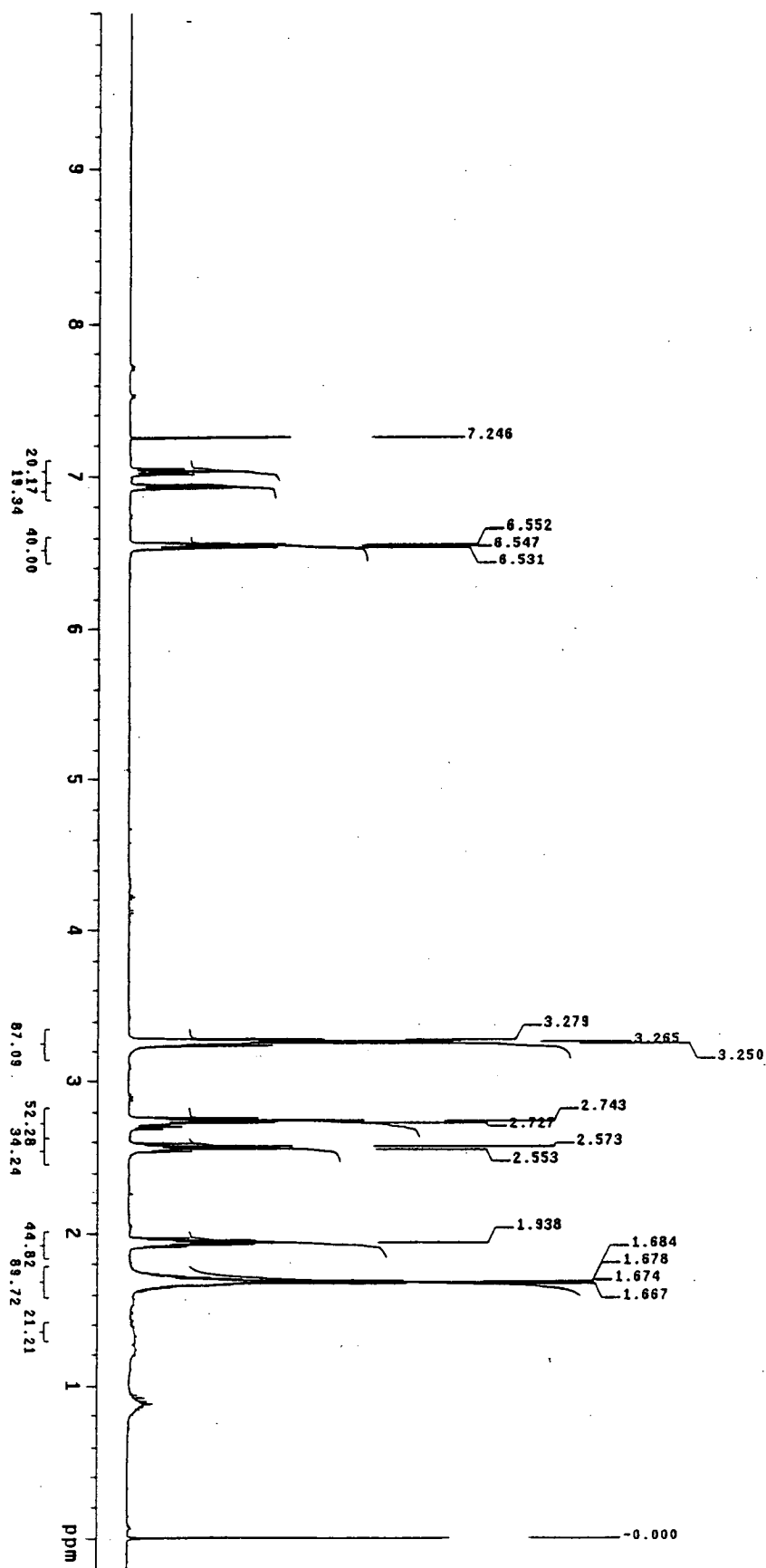
Synthesis of 1-(ethoxymethyl)-1,2,3,4-tetrahydroquinoline (10). To a stirred solution of 1,2,3,4-tetrahydroquinoline (5 g, 37.5 mmol) and sodium hydride (1.8 g, 56.25 mmol) in DMF (40 mL) was added slowly ethoxymethyl chloride (EOMCl) (5.38 mL, 56.3 mmol) at 0 $^{\circ}\text{C}$. The resulting reaction mixture was stirred at room temperature for 1.5 h and then poured into ice-water (300 mL) and extracted with ether (4 X 150 mL). The combined organic layer was dried over sodium sulfate. After removal of solvent, the residue was distilled under reduced pressure to yield **10** (63%); b.p. 100 $^{\circ}\text{C}$ (2.5 mm). ^1H NMR (CDCl_3 , 200 MHz) δ 7.15-7.00 (m, 2H), 6.91 (d, J = 8.0 Hz, 1H), 6.72 (t, J = 7.0 Hz, 1H), 4.79 (s, 2H), 3.62-3.46 (m, 4H), 2.82 (t, J = 6.4 Hz, 2H), 2.061-1.94 (m, 2H), 1.28 (t, J = 7.0 Hz, 3H); LRMS (EI, m/z) 191 (M^+); HRMS (EI, m/z) for $\text{C}_{12}\text{H}_{17}\text{NO}$, calcd 191.1311, found 191.1309.

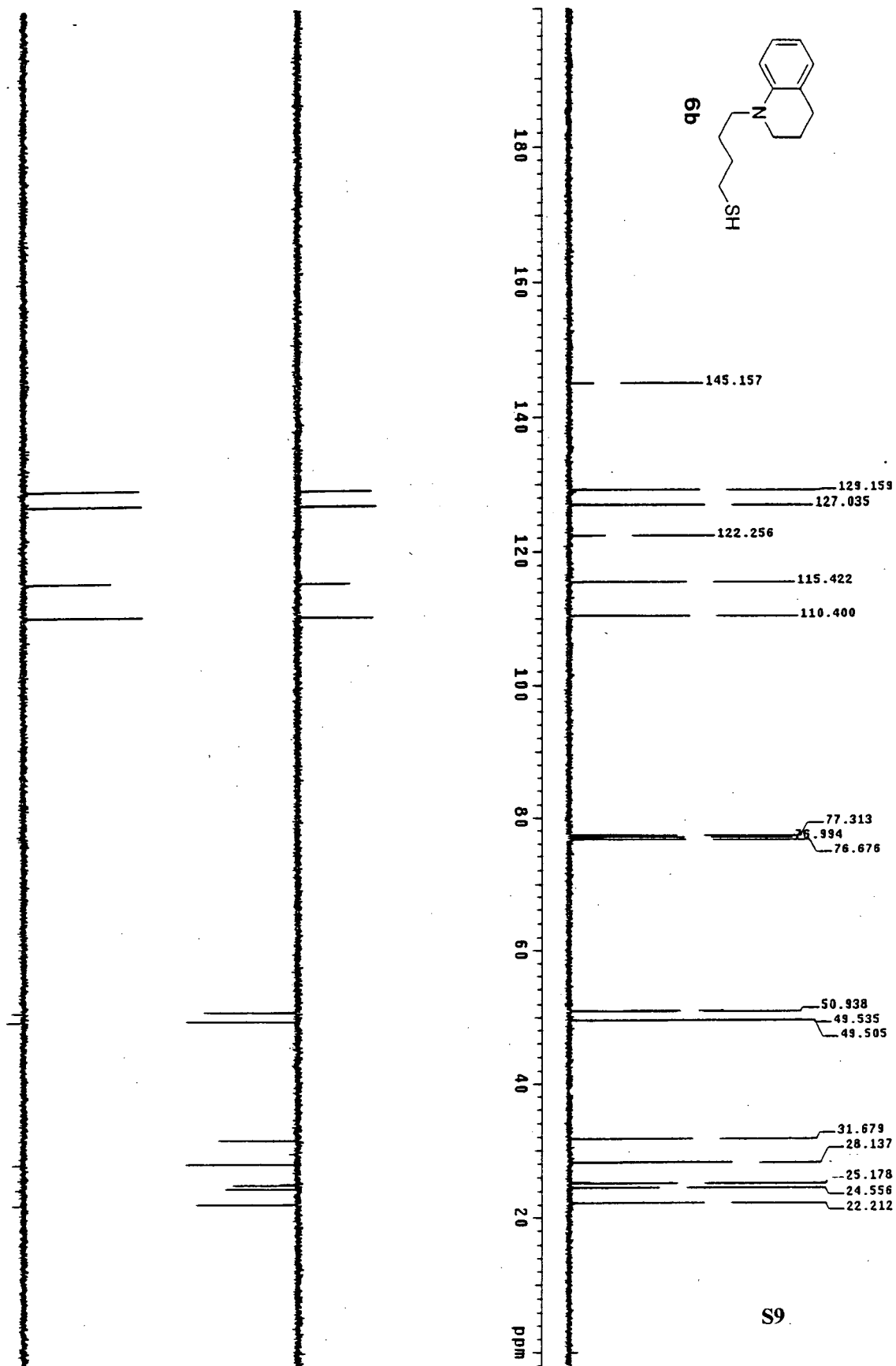
Borane reduction of 1-(ethoxymethyl)-1,2,3,4-tetrahydroquinoline (10) to 1-Methyl-1,2,3,4-tetrahydroquinoline (5). To a stirred solution of compound **10** (38 mg, 0.2 mmol) in THF (5 mL) was added 1 equiv of borane-tetrahydrofuran (200 μL , 1M in THF) under nitrogen at room temperature, then the mixture was stirred at the room temperature for 1 h. The reaction mixture was poured into ice water (100 mL) and extracted four times with ethyl acetate. The combined organic phases were washed with saturated NaHCO_3 , H_2O , brine, and dried over MgSO_4 . After removal of solvent, the residue was purified by flash chromatography (hexane/AcOEt = 50:1) to give compound **5**: yield 27 mg (98%).

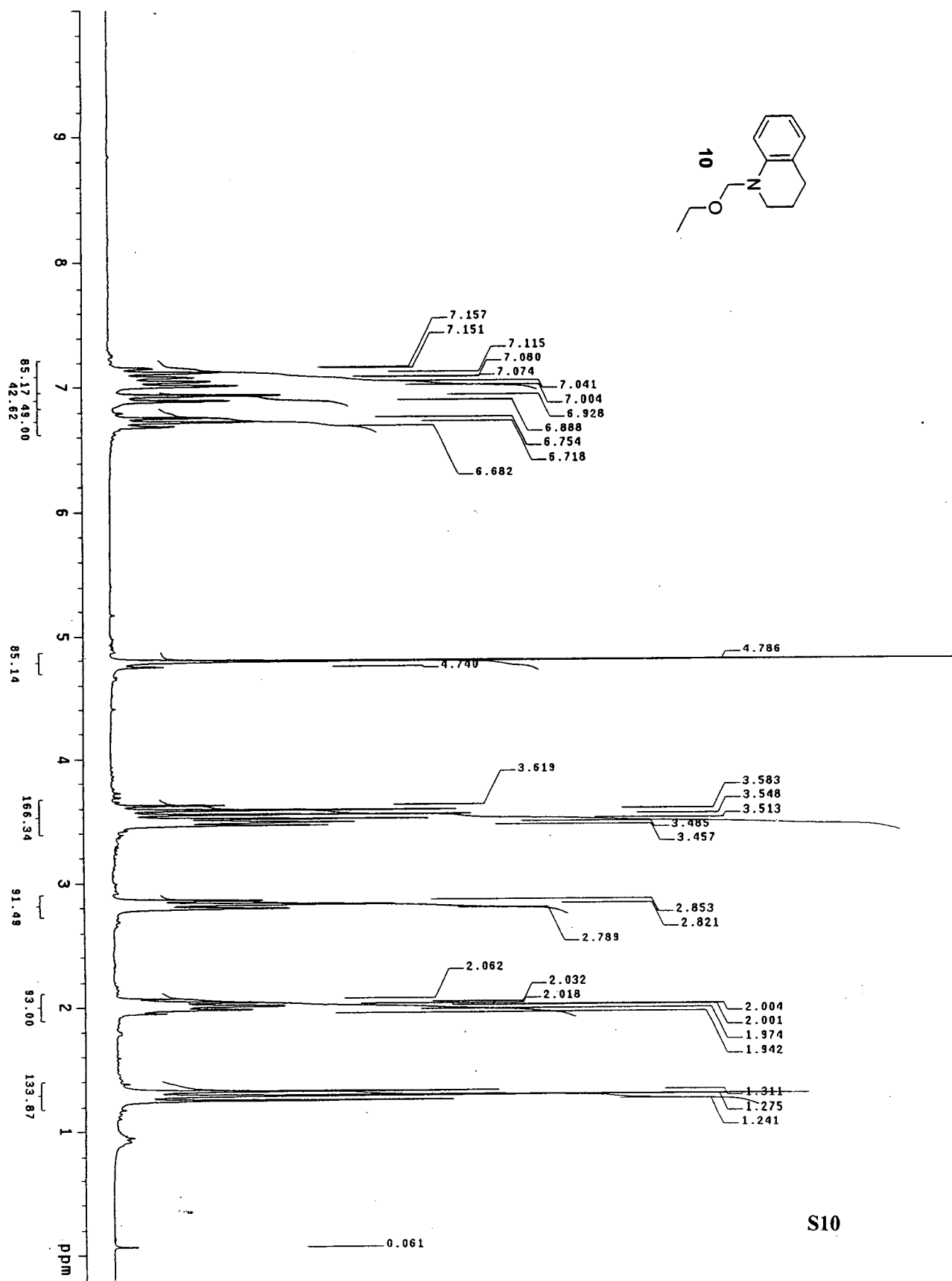










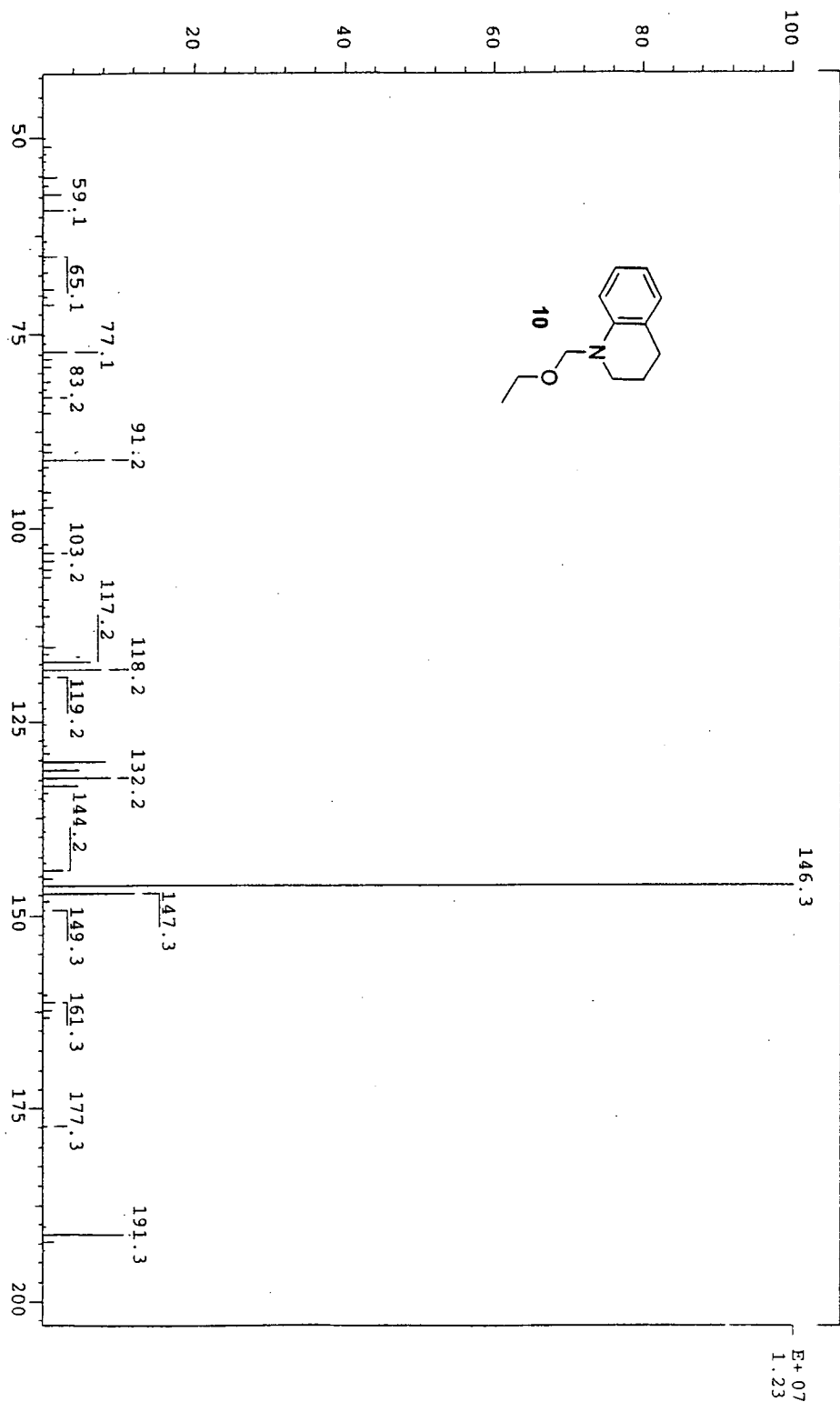


S10

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Norm: 146.3
Peak: 1000.00
Data: +/2>43

25-Feb-10
REG : 00:03.8
Start : 11:30:09
#9

Inlet :
Masses: 45 > 200
#peaks: 157



S11

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 Oper: Inlet :
 Limt: (0)
 : (541) C38.H41.O.N2
 Peak: 1000.00 mmu R+D: -2.0 > 60.0
 Data: +/259>328 (CMASS : converted; CMASS : converted |CMASS : conve

Mass	Intensity	%RA	Flags	Delta	R+D	Composition
191.1309	375010	14.68	#	0.1	5.0	C12.H17.O.N

