Supporting Information

Selective Amine Recognition: Development of a Chemosensor for Dopamine and Norepinephrine

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Spectroscopic Analysis:

Fluorescence spectra were recorded on a Shimadzu RF-5301 PC spectrofluorimeter at 37 ºC. Excitation wavelengths were 446, 484 and 495 nm with excitation and emission slit widths of 5 nm each. Absorption spectra were recorded on a Cary 1E spectrophotometer at 37 ºC. Solutions of compound **2** were prepared at 10 μM in buffered water (100 mM $Na_2S_2O_3$, 50 mM HEPES, 20 mM NaCl, pH = 7.0). Sodium thiosulfate was used to prevent oxidation of the catechol guests. All guest solutions were prepared as above and contained 10 μM **2** to prevent dilution.

Titrations were fit by recording fluorescence intensity at 505 nm (for λ_{ex} = 446 and 484 nm) and 515 (for λ_{ex} = 495 nm) as a function of added analyte and fitting the data to a one-site binding isotherm using Graphpad Prism software. A 1:1 binding model was assumed and the data fit this model well for all analytes tested. The fluorescence intensity at saturation (I_{sat}) was taken from the theoretical fit to the data.

Synthetic Procedures:

General Methods. All reactions were carried out in dried glassware under N_2 atmosphere. Tetrahydrofuran (THF) and diethyl ether were distilled from sodium benzophenone ketyl under N_2 before use. Methylene chloride (CH_2Cl_2) and triethylamine (Et_3N) were distilled from CaH_2 under N_2 before use. Flash chromatography was performed with 32-63 μm silica gel. All melting points are uncorrected. NMR spectra were recorded on Bruker ARX 250, DRX 300, or DRX 500 instruments as noted below in the solvents recorded. IR spectra were recorded on a Nexus 670 FT-IR E.S.P. spectrometer.

Compound **5**: A solution of TBS-protected 5-iodopentanol (2.35 g, 7.15 mmol) and Et_2O (70 mL) in a flame-dried, N_2-flushed flask was cooled to -78 °C. tBuLi (10.0 mL, 1.5 M, 15.0 mmol) was added, and the mixture was stirred at -78 °C for 5 min., then at ambient temperature for 1 h. The solution was cooled to 0 °C, and CuI (681 mg, 3.58 mmol) was added. The mixture was stirred at 0 °C for 10 min.; the mixture turned dark purple. The reaction mixture was cooled to -78 °C, and THF (35 mL) was added. Coumarin chloroaldehyde **3** (1.00 g, 3.58 mmol) in THF (35 mL) was added via cannula. The reaction was stirred under N_2 at -78 °C for 30 min. then quenched with saturated NH_4Cl (75 mL). The mixture was extracted with CH_2Cl_2 (3 x 150 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed *in vacuo*. The resulting solid was purified via flash chromatography (EtOAc/hex, 10:90 to 15:85), and compound **5** was isolated as a yellow solid (1.01 g, 63%, mp = 103-105°C). ^{1}H NMR (250 MHz, $CDCl_3$) δ 10.36 (s, 1H), 7.61 (d, *J* = 9.3 Hz, 1H), dd (6.65, *J* = 2.6, 9.3 Hz, 1H), 6.46 (d, *J* = 2.6 Hz, 1H), 3.63 (t, *J* = 5.9 Hz, 2H), 3.46 (q, *J* = 7.1 Hz, 4H), 3.26 (t, *J* = 7.9 Hz, 2H), 1.57-1.62 (m, 6H), 1.25 (t, *J* = 7.1 Hz, 6H), 0.88 (s, 9H), 0.045 (s, 6H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 190.2, 163.5, 162.7, 157.2, 152.4, 128.3, 111.1, 109.7, 108.1, 96.9, 62.6, 44.8, 32.2, 30.0, 27.4, 26.0, 25.7, 18.0, 12.2, -5.6. FTIR (neat) 2933, 2860, 1716, 1679, 1615, 1560, 1509, 1450, 1356, 1258, 1148 cm^{-1}. HRMS: Calcd for $C_{25}H_{39}LiNO_4Si$ $(M+Li)^+$: 452.2808. Found: 452.2806.

Compound **6**: H_2O (22 mL) and AcOH (66 mL) were added to a solution of compound **5**, (1.00 g, 2.24 mmol) in THF (22 mL). The mixture was stirred at ambient temperature for 2 h. The reaction mixture was quenched with solid K_2CO_3 to pH = 8, extracted with CH_2Cl_2 (3 x 150 mL), dried on $MgSO_4$, and the solvent was removed *in vacuo*. The resulting solid was purified via flash chromatography (EtOAc/hex, 20:80 to 80:20), and the product alcohol was isolated as a yellow solid (622 mg, 84%, mp = 122-123°C). ^{1}H NMR (250 MHz, $CDCl_3$) δ 10.3 (s, 1H), 7.62 (d, *J* = 9.4 Hz, 1H), 6.66 (dd, *J* = 2.5, 9.3 Hz, 1H), 6.44 (d, *J* = 2.5 Hz, 1H), 3.68 (t, *J* = 5.6 Hz, 2H), 3.47 (q, *J* = 7.1 Hz, 4H), 3.25 (t, *J* = 6.8 Hz, 2H), 2.10 (s, 1H), 1.62-1.69 (m, 6H), 1.25 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 190.7, 163.8, 163.1, 157.4, 152.6, 128.5, 111.3, 109.9, 108.3, 97.1, 62.5, 45.0, 32.2, 30.1, 27.6, 26.2, 12.4. FTIR (neat) 2932, 1709, 1675, 1612, 1556, 1505, 1447, 1354, 1268, 1203, 1147 cm^{-1}. HRMS: Calcd for $C_{19}H_{25}LiNO_4$ $(M+Li)^+$: 338.1944. Found: 338.1946.

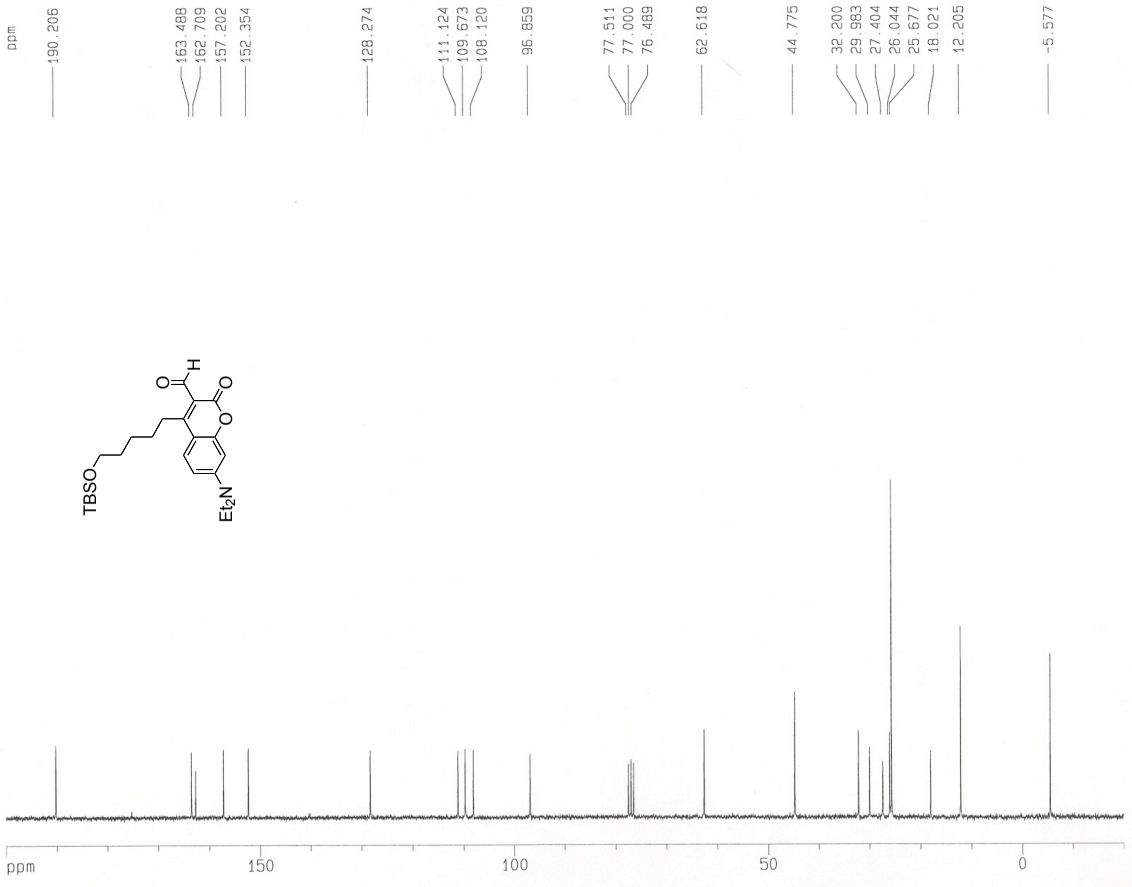
A solution of the above prepared alcohol (622 mg, 1.88 mmol), CH_2Cl_2 (30 mL), and NEt_3 (800 μL, 5.69 mmol) was placed in a flame-dried, N_2-filled flask and cooled to 0 °C. MsCl (300 μL, 3.88 mmol) was added. The reaction was stirred under N_2 at 0 °C for 20 min. The solvent was removed *in vacuo*. The resulting solid was purified via flash chromatography (EtOAc:hex, 40:60 to 50:50), and the product mesylate was isolated as a yellow solid (768 mg, 100%, mp = 96-97°C). ^{1}H NMR (250 MHz, $CDCl_3$) δ 10.30 (s, 1H), 7.61 (d, *J* = 9.3 Hz, 1H), 6.69 (dd, *J* = 2.5, 9.3 Hz, 1H), 6.43 (d, *J* = 2.5 Hz, 1H), 4.29 (t, *J* = 6.4 Hz, 2H), 3.48 (q, *J* = 7.1 Hz, 4H), 3.23 (t, *J* = 7.2 Hz, 2H), 3.06 (s, 3H), 1.87 (p, *J* = 6.4 Hz, 2H), 1.63-1.66 (m, 4H), 1.26 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 190.3, 163.0, 162.7, 157.2, 152.5, 128.2, 111.0, 109.9, 108.0, 96.9, 69.8, 44.8, 36.9, 29.3, 28.3, 27.1, 25.4, 12.2. FTIR (neat) 2935, 2361, 1708, 1674, 1613, 1557, 1506, 1449, 1351, 1267, 1203, 1171, 1115 cm^{-1}. HRMS: Calcd for $C_{20}H_{27}LiNO_6S$ $(M+Li^+)$: 416.1719. Found: 416.1700.

NaI (697 mg, 3.75 mmol) was added to a solution of the mesylate (768 mg, 1.88 mmol) in acetone (25 mL). The mixture was stirred at ambient temperature for 13 h. The solvent was removed *in vacuo*, and the resulting yellow solid was dissolved in CH_2Cl_2 (100 mL) and H_2O (100 mL). The layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (2 x 100 mL). The combined organic extracts were dried on $MgSO_4$, and the solvent was removed *in vacuo*. The resulting yellow solid was purified via flash chromatography (EtOAc:hex, 20:80 to 25:75), and the product, compound **6**, was isolated as a yellow solid (648 mg, 83%, mp = 104-106°C). ^{1}H NMR (250 MHz, $CDCl_3$) δ 10.35 (s, 1H), 7.60 (d, *J* = 9.3 Hz, 1H), 6.66 (dd, *J* = 2.4, 9.3 Hz, 1H), 6.46 (d, *J* = 2.3 Hz, 1H), 3.47 (q, *J* = 7.1 Hz, 4H), 3.20-3.26 (m, 4H), 1.92 (p, *J* = 6.7 Hz, 2H), 1.62-1.63 (m 4H), 1.25 (t, *J* = 7.1 Hz, 6H. ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 190.8, 163.4, 163.4, 157.6, 152.6, 128.4, 111.6, 109.9, 108.4, 97.3, 45.1, 32.9, 30.8, 29.2, 27.5, 12.5, 6.8. FTIR (neat) 1711, 1674, 1213, 1557, 1506, 1446, 1383. HRMS: Calcd for $C_{19}H_{24}ILiNO_3$ $(M+Li^+)$: 448.0961. Found: 448.0961.

Compound **2**. Compound **6** (85 mg, 0.194 mmol), amine **7** (47 mg, 0.285 mmol), and K_2CO_3 (134 mg, 0.968 mmol) were placed in a sealed vessel with THF (2 mL). The mixture was stirred at 48 °C for 14 h. The mixture was cooled, poured onto H_2O (10 mL), extracted with CH_2Cl_2 (3 x 10 mL), dried on $MgSO_4$, and the solvent was removed *in vacuo*. The resulting solid was purified by HPLC (Xorbax XDB-C18 column, 0.1% TFA/H_2O:0.1% TFA/MeCN, 90:10 to 0:100) to give compound **2** as a yellow solid (37.4 mg, 40%, mp = 92-94°C). ^{1}H NMR (250 MHz, MeOD) δ 10.21 (s, 1H), d (7.76, *J* = 9.4 Hz, 1H), 7.57 (d, *J* = 6.8 Hz, 1H), 7.10-7.26 (m, 3H), 6.28 (dd, *J* = 2.6, 9.4 Hz, 1H), 6.52 (d, *J* = 2.6 Hz, 1H), 4.09 (s, 2H), 3.53 (q, *J* = 7.1 Hz, 4H), 2.98 (t, *J* = 8.2 Hz, 2H), 2.57 (s, 3H), 1.78-1.85 (m, 2H), 1.59 (m, 4H), 1.23 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (125 MHz, MeOD) δ 191.7, 165.6, 165.1, 159.1, 154.8, 134.8, 133.6, 132.4, 130.2, 129.9, 128.5, 127.6, 112.0, 111.8, 109.5, 98.0, 64.1, 56.4, 46.0, 40.2, 31.1, 28.3, 28.2, 24.6, 12.8. FTIR (neat) 2361, 2336, 1704, 1673, 1610, 1555, 1503, 1444, 1351, 1263, 1201,

1140. For ESI MS, the sensor was dissolved in MeOH, generating the boronic acid dimethyl ester - HRMS: Calcd for $C_{29}H_{39}BN_2O_5Na$ ($M+Na^+$): 529.2844. Found: 529.2834.

TBSO-pentyl coumarin



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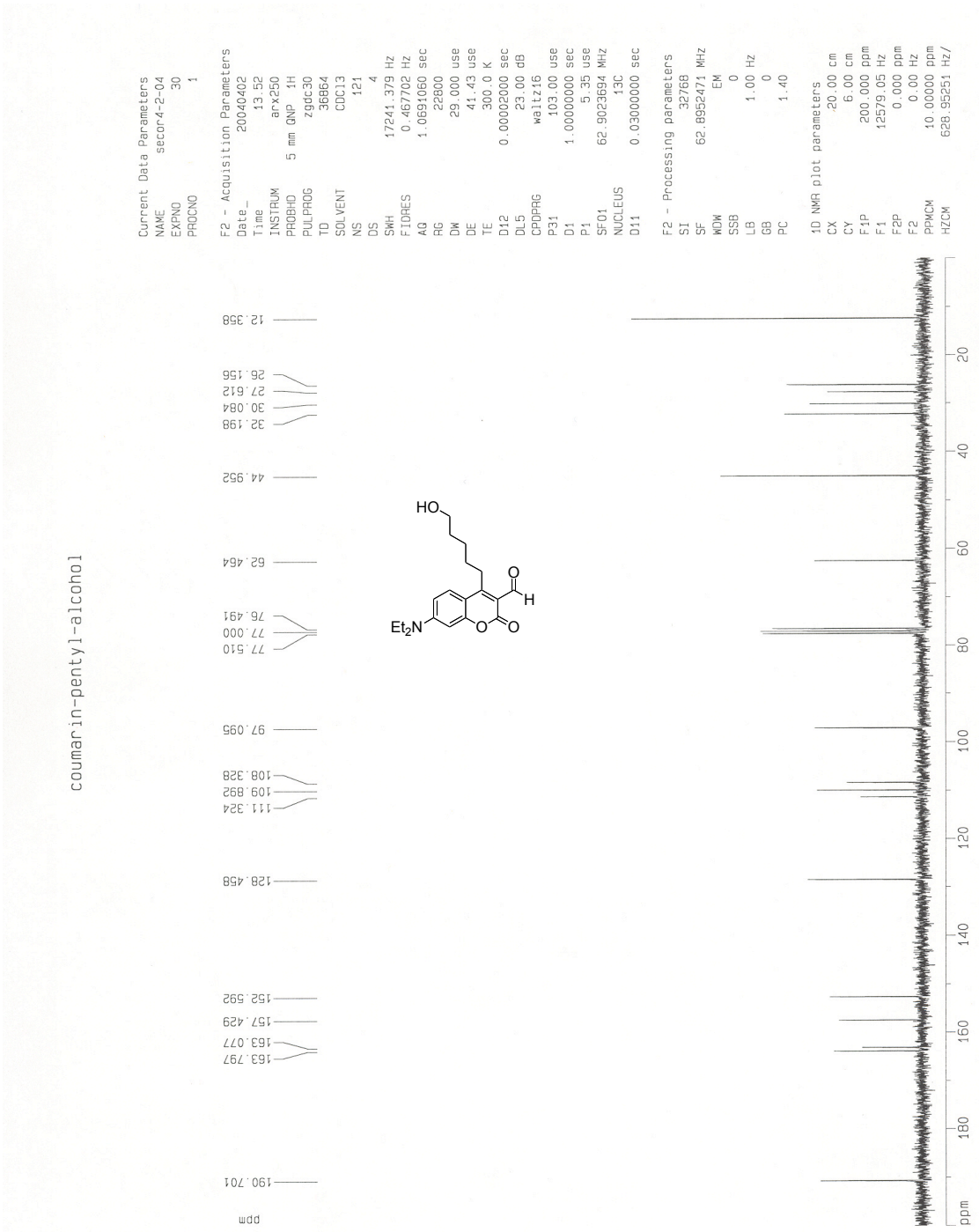
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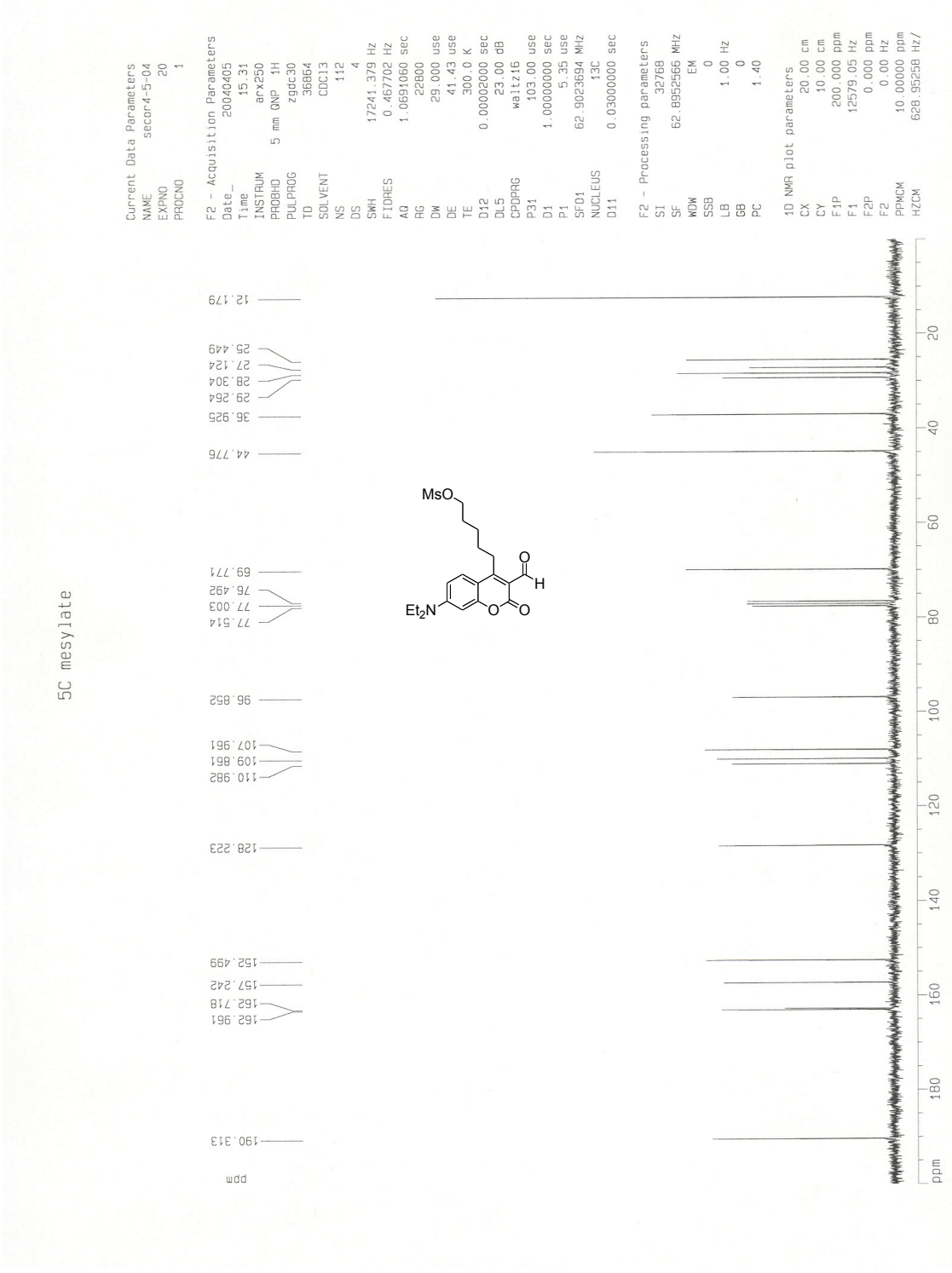
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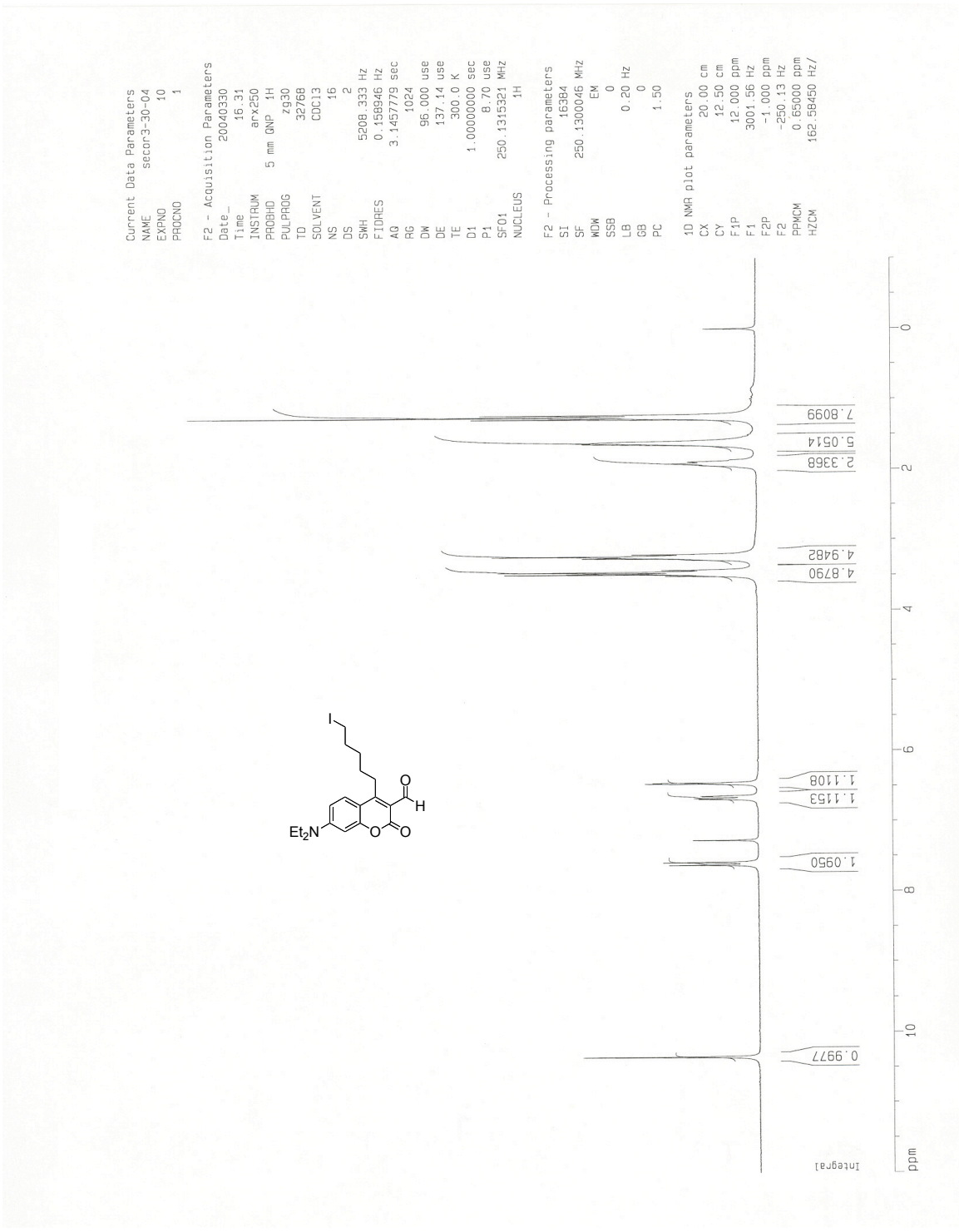
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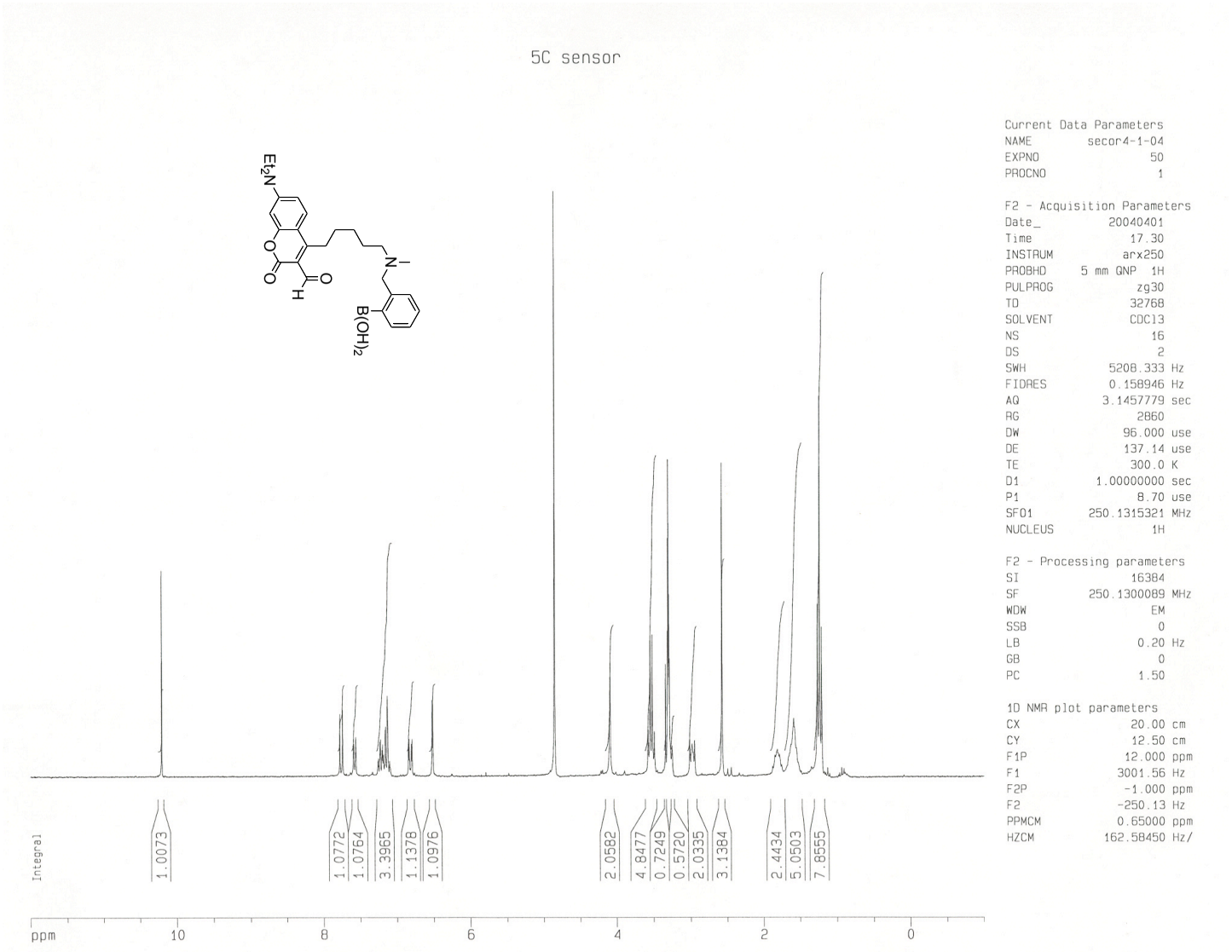

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