

Synthesis of 4-Methylene-4*H*-benzo[*d*][1,3]thiazines via a Tandem Reaction of 1-(2-Alkynylphenyl)ketoximes with Lawesson's Reagent

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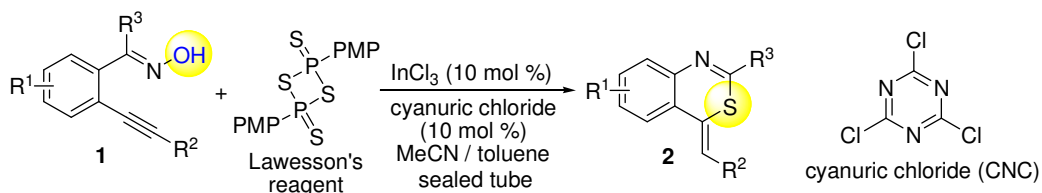
Supporting information

1. General procedure for the synthesis of compounds **2** (S1)
2. Characterization data of compounds **2** (S2-S6).
3. ¹H and ¹³C NMR spectra of compounds **2** (S7-S30)
4. X-ray ORTEP illustration of compound **2j** (S31)

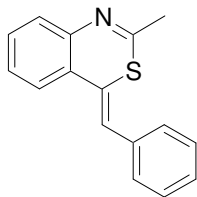
General Methods:

All reactions were performed in reaction tubes under nitrogen atmosphere. Flash column chromatography was performed using silica gel (60-Å pore size, 32–63 μm, standard grade). Analytical thin-layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light. Organic solutions were concentrated on rotary evaporators at ~20 Torr (house vacuum) at 25–35 °C. Commercial reagents and solvents were used as received. Nuclear magnetic resonance (NMR) spectra are recorded in parts per million from internal tetramethylsilane on the δ scale.

General procedure for the synthesis of 4-methylene-4H-benzo[d][1,3]thiazines via a tandem reaction of 1-(2-alkynylphenyl)ketoxime with Lawesson's reagent

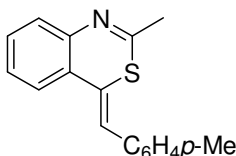


Cyanuric chloride (10 mol %) and InCl₃ (10 mol %) were added to a solution of 1-(2-alkynylphenyl)ketoxime **1** (0.2 mmol) in MeCN (0.5 mL). The mixture was stirred at 80 °C under N₂. After consumption of 1-(2-alkynylphenyl)ketoxime **1**, Lawesson's reagent (0.8 equiv) and toluene (2.0 mL) were then added. The reaction was stirred overnight at 120 °C. After completion of reaction as indicated by TLC, the mixture was cooled to room temperature and separated directly by flash chromatography column on silica gel to afford the corresponding product **2**.



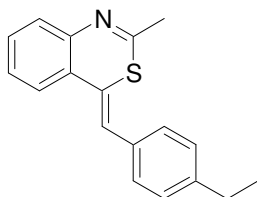
4-Benzylidene-2-methyl-4*H*-benzo[*d*][1,3]thiazine (**2a**)

^1H NMR (400 MHz, CDCl_3) δ 2.35 (s, 3H), 7.02 (s, 1H), 7.37-7.43 (m, 8H), 7.61 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 27.3, 121.2, 124.1, 124.6, 126.3, 127.4, 128.2, 128.3, 128.6, 129.1, 129.7, 135.6, 142.1, 158.6; HRMS Calcd for $\text{C}_{16}\text{H}_{13}\text{NS}$ (ESI, $\text{M}^+\text{+H}$): 252.0847; Found: 252.0850.



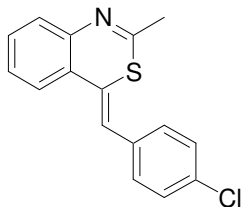
2-Methyl-4-(4-methyl-benzylidene)-4*H*-benzo[*d*][1,3]thiazine (**2b**)

^1H NMR (400 MHz, CDCl_3) δ 2.33 (s, 3H), 2.37 (s, 3H), 6.97 (s, 1H), 7.19-7.36 (m, 7H), 7.60 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.5, 27.6, 121.8, 124.3, 124.8, 125.4, 128.3, 128.7, 129.1, 129.2, 129.6, 133.0, 137.6, 142.2, 158.9; HRMS Calcd for $\text{C}_{17}\text{H}_{15}\text{NS}$ (ESI, $\text{M}^+\text{+H}$): 266.1003; Found: 266.1009.



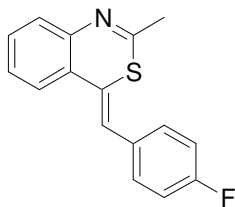
4-(4-Ethylbenzylidene)-2-methyl-4*H*-benzo[*d*][1,3]thiazine (**2c**)

^1H NMR (400 MHz, CDCl_3) δ 1.26 (t, $J = 8.0$ Hz, 3H), 2.35 (s, 3H), 2.65-2.71 (m, 2H), 6.99 (s, 1H), 7.24 (d, $J = 8.0$ Hz, 2H), 7.32-7.37 (m, 5H), 7.58 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 15.4, 27.5, 28.7, 121.5, 124.2, 124.8, 125.2, 127.8, 128.2, 128.6, 129.2, 129.6, 133.1, 142.1, 143.8, 158.9; HRMS Calcd for $\text{C}_{18}\text{H}_{17}\text{NS}$ (ESI, $\text{M}^+\text{+H}$): 280.1160; Found: 280.1163.



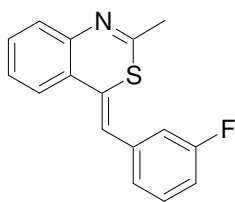
4-(4-Chlorobenzylidene)-2-methyl-4*H*-benzo[*d*][1,3]thiazine (**2d**)

^1H NMR (400 MHz, CDCl_3) δ 2.36 (s, 3H), 6.94 (s, 1H), 7.25-7.41 (m, 7H), 7.59 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 27.4, 120.9, 123.1, 124.0, 127.1, 128.3, 128.4, 128.6, 128.8, 129.9, 130.3, 133.0, 134.1, 142.1, 158.1; HRMS Calcd for $\text{C}_{16}\text{H}_{12}\text{ClNS}$ (ESI, $\text{M}^+\text{+H}$): 286.0457; Found: 286.0463.



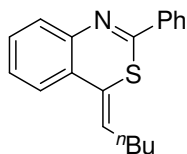
4-(4-Fluorobenzylidene)-2-methyl-4*H*-benzo[*d*][1,3]thiazine (**2e**)

^1H NMR (400 MHz, CDCl_3) δ 2.37 (s, 3H), 6.97 (s, 1H), 7.26-7.42 (m, 7H), 7.59 (d, $J = 7.6$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 27.4, 115.2 (d, $^2J_{\text{CF}} = 21$ Hz), 121.1, 123.4, 124.0, 126.1, 128.3, 128.6, 129.8, 130.8 (d, $^3J_{\text{CF}} = 8.0$ Hz), 131.8 (d, $^4J_{\text{CF}} = 3.0$ Hz), 142.0, 158.4, 161.7 (d, $^1J_{\text{CF}} = 247$ Hz); HRMS Calcd for $\text{C}_{16}\text{H}_{12}\text{FNS}$ (ESI, $\text{M}^+\text{+H}$): 270.0753; Found: 270.0740.



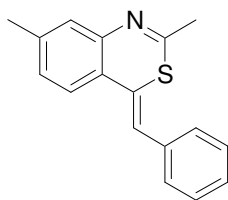
4-(3-Fluoro-benzylidene)-2-methyl-4*H*-benzo[*d*][1,3]thiazine (**2f**)

^1H NMR (400 MHz, CDCl_3) δ 2.38 (s, 3H), 6.97 (s, 1H), 7.21 (d, $J = 8.4$ Hz, 2H), 7.34-7.43 (m, 5H), 7.61 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 27.5, 114.3 (d, $^2J_{\text{CF}} = 21$ Hz), 115.6 (d, $^2J_{\text{CF}} = 22$ Hz), 120.7, 123.0, 124.0, 125.0 (d, $^4J_{\text{CF}} = 3.0$ Hz), 127.8, 128.4, 128.8, 129.4, 129.7 (d, $^3J_{\text{CF}} = 8.0$ Hz), 130.0, 137.8 (d, $^3J_{\text{CF}} = 8.0$ Hz), 142.0, 158.3, 162.5 (d, $^1J_{\text{CF}} = 244$ Hz); HRMS Calcd for $\text{C}_{16}\text{H}_{12}\text{FNS}$ (ESI, $\text{M}^+\text{+H}$): 270.0753; Found: 270.0737.



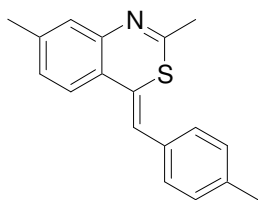
4-Pentylidene-2-phenyl-4*H*-benzo[*d*][1,3]thiazine (**2g**)

^1H NMR (400 MHz, CDCl_3) δ 0.90 (t, $J = 7.6$ Hz, 3H), 1.34-1.40 (m, 2H), 1.43-1.50 (m, 2H), 2.25-2.31 (m, 2H), 6.45 (t, $J = 7.6$ Hz, 1H), 7.12-7.25 (m, 3H), 7.39-7.45 (m, 3H), 7.49-7.53 (m, 1H), 7.72 (d, $J = 8.0$ Hz, 1H), 8.10 (d, $J = 7.6$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 13.9, 22.4, 31.1, 31.5, 120.4, 120.4, 123.3, 123.4, 124.8, 128.4, 129.3, 131.3, 134.5, 137.4, 141.2, 152.0, 164.3; HRMS Calcd for $\text{C}_{19}\text{H}_{19}\text{NS}$ (ESI, $\text{M}^+\text{+H}$): 294.1316; Found:



(*Z*)-4-Benzylidene-2,7-dimethyl-4*H*-benzo[*d*][1,3]thiazine (**2h**)

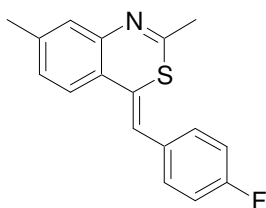
^1H NMR (400 MHz, CDCl_3) δ 2.32 (s, 3H), 2.37 (s, 3H), 6.96 (s, 1H), 7.12 (d, $J = 8.0$ Hz, 1H), 7.18 (s, 1H), 7.27 (d, $J = 7.0$ Hz, 1H), 7.36-7.48 (m, 4H), 7.49 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.0, 27.4, 118.4, 123.3, 123.9, 126.4, 127.3, 128.2, 128.6, 129.0, 129.1, 135.8, 139.9, 141.9, 158.5; HRMS Calcd for $\text{C}_{17}\text{H}_{15}\text{NS}$ (ESI, $\text{M}^+\text{+H}$): 266.1003; Found: 266.1021.



2,7-Dimethyl-4-(4-methylbenzylidene)-4*H*-benzo[*d*][1,3]thiazine (**2i**)

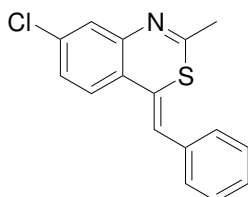
^1H NMR (400 MHz, CDCl_3) δ 2.33 (s, 3H), 2.37 (s, 3H), 2.38 (s, 3H), 6.93 (s, 1H), 7.12 (d, $J = 7.6$ Hz, 1H), 7.18-7.21 (m, 3H), 7.32 (d, $J = 7.6$ Hz, 2H), 7.48 (d, $J = 7.6$ Hz, 1H), ^{13}C NMR (100 MHz, CDCl_3) δ 21.0, 21.3, 27.4, 118.6, 123.4, 123.9, 125.4, 128.9, 129.0, 129.1, 133.0, 137.2, 139.7, 141.9, 158.7; HRMS Calcd for $\text{C}_{18}\text{H}_{17}\text{NS}$

(ESI, M^+H): 280.1160; Found: 280.1163.



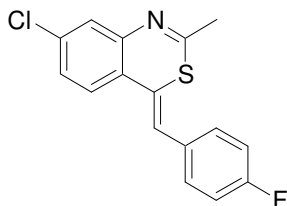
4-(3-Fluoro-benzylidene)-2,7-dimethyl-4H-benzo[d][1,3]thiazine (**2j**)

1H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3H), 2.38 (s, 3H), 6.91 (s, 1H), 7.02-7.14 (m, 3H), 7.18 (s, 1H), 7.37-7.41 (m, 2H), 7.50 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 27.5, 115.3 (d, $^2J_{CF} = 21$ Hz), 118.2, 122.0, 123.8, 126.4, 129.2 (d, $^4J_{CF} = 4.0$ Hz), 130.7 (d, $^3J_{CF} = 8.0$ Hz), 132.0, 140.0, 141.9, 158.1, 161.7 (d, $^1J_{CF} = 247$ Hz); HRMS Calcd for $C_{17}H_{14}FNS$ (ESI, M^+H): 284.0909; Found: 284.0922.



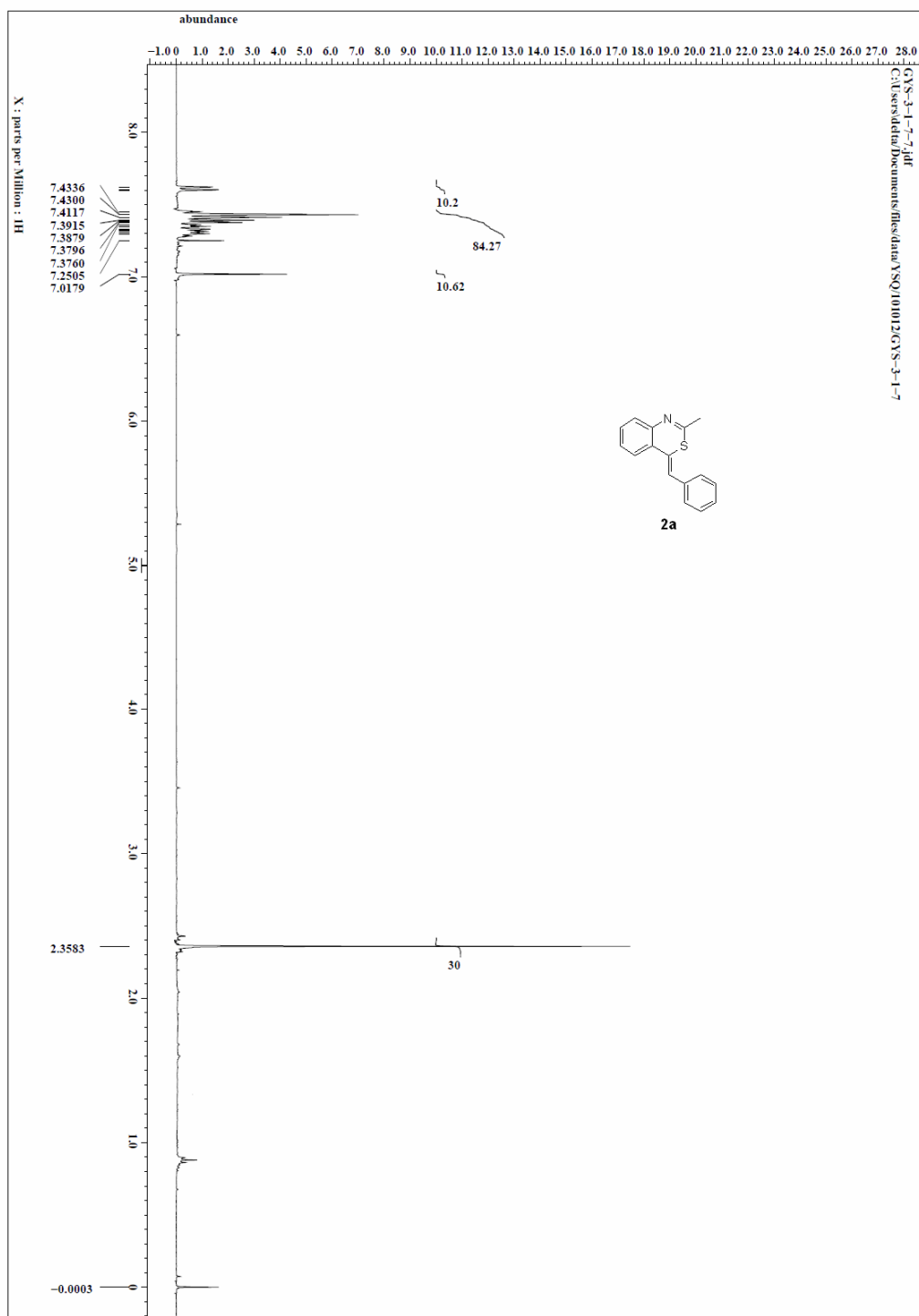
4-Benzylidene-7-chloro-2-methyl-4H-benzo[d][1,3]thiazine (**2k**)

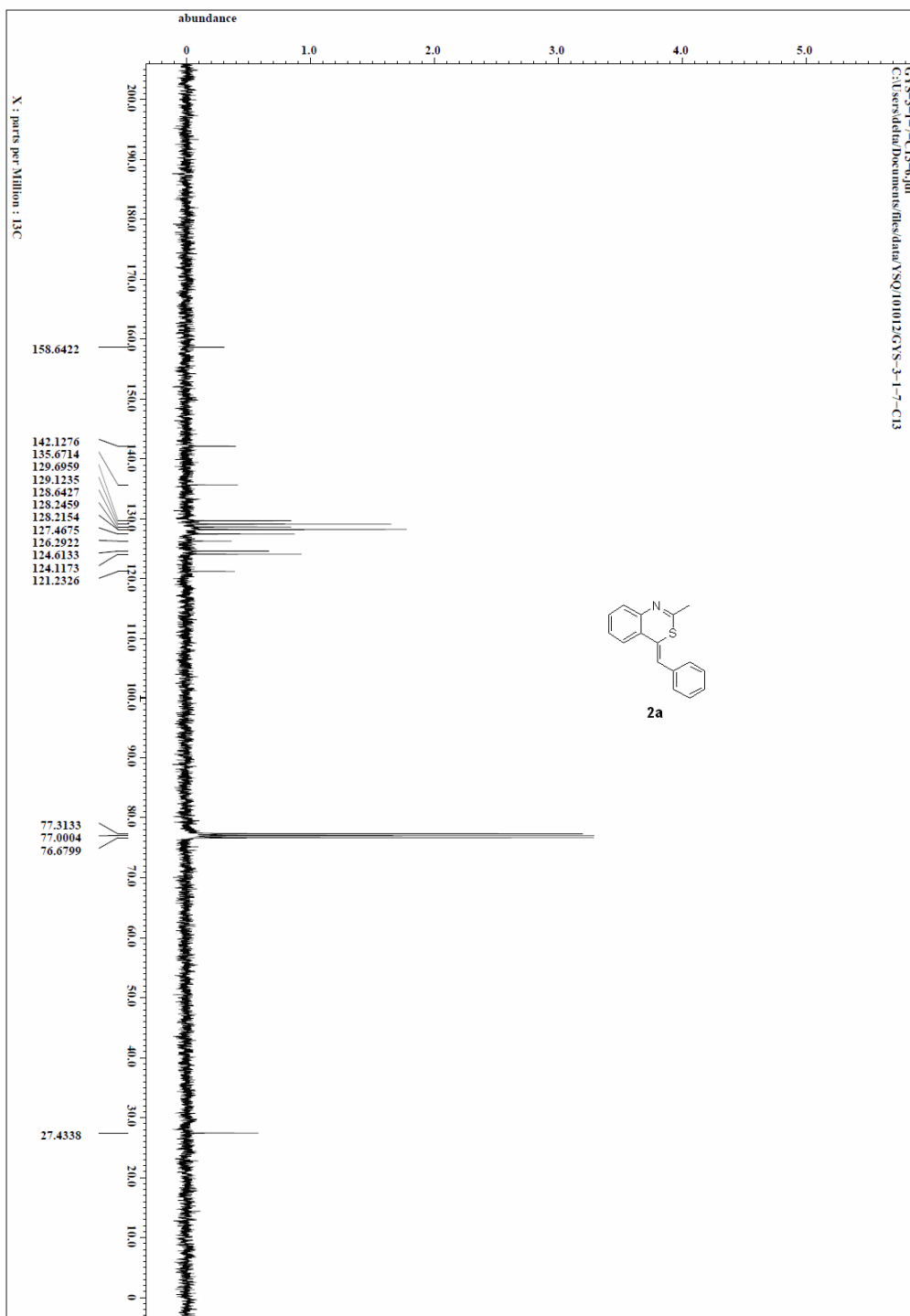
1H NMR (400 MHz, $CDCl_3$) δ 2.25 (s, 3H), 6.87 (s, 1H), 7.16-7.33 (m, 7H), 7.41 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.5, 119.9, 125.0, 125.3, 125.3, 127.7, 128.1, 128.3, 128.4, 129.1, 135.1, 135.4, 143.3, 160.5; HRMS Calcd for $C_{16}H_{12}ClNS$ (ESI, M^+H): 286.0457; Found: 286.0479.

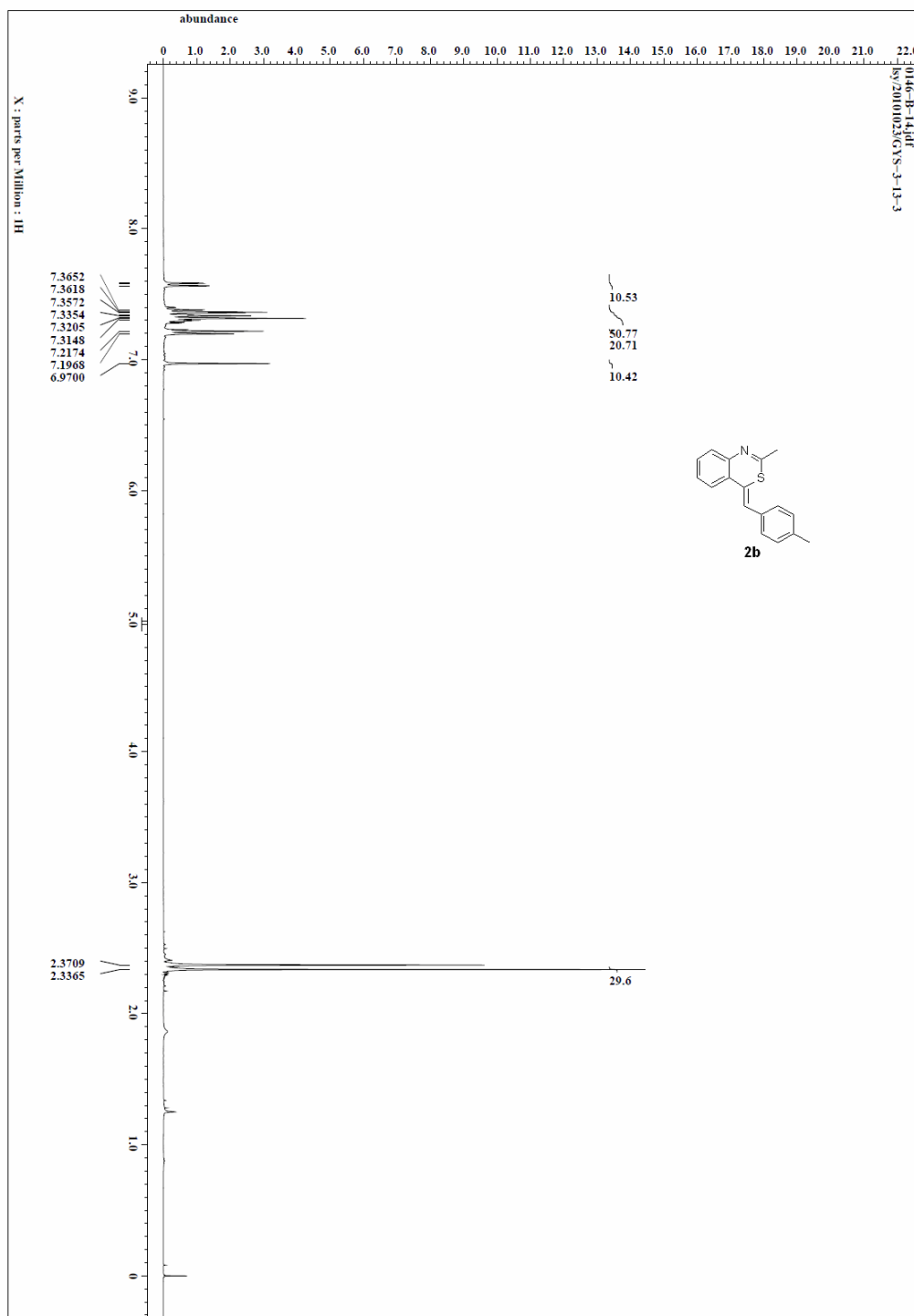


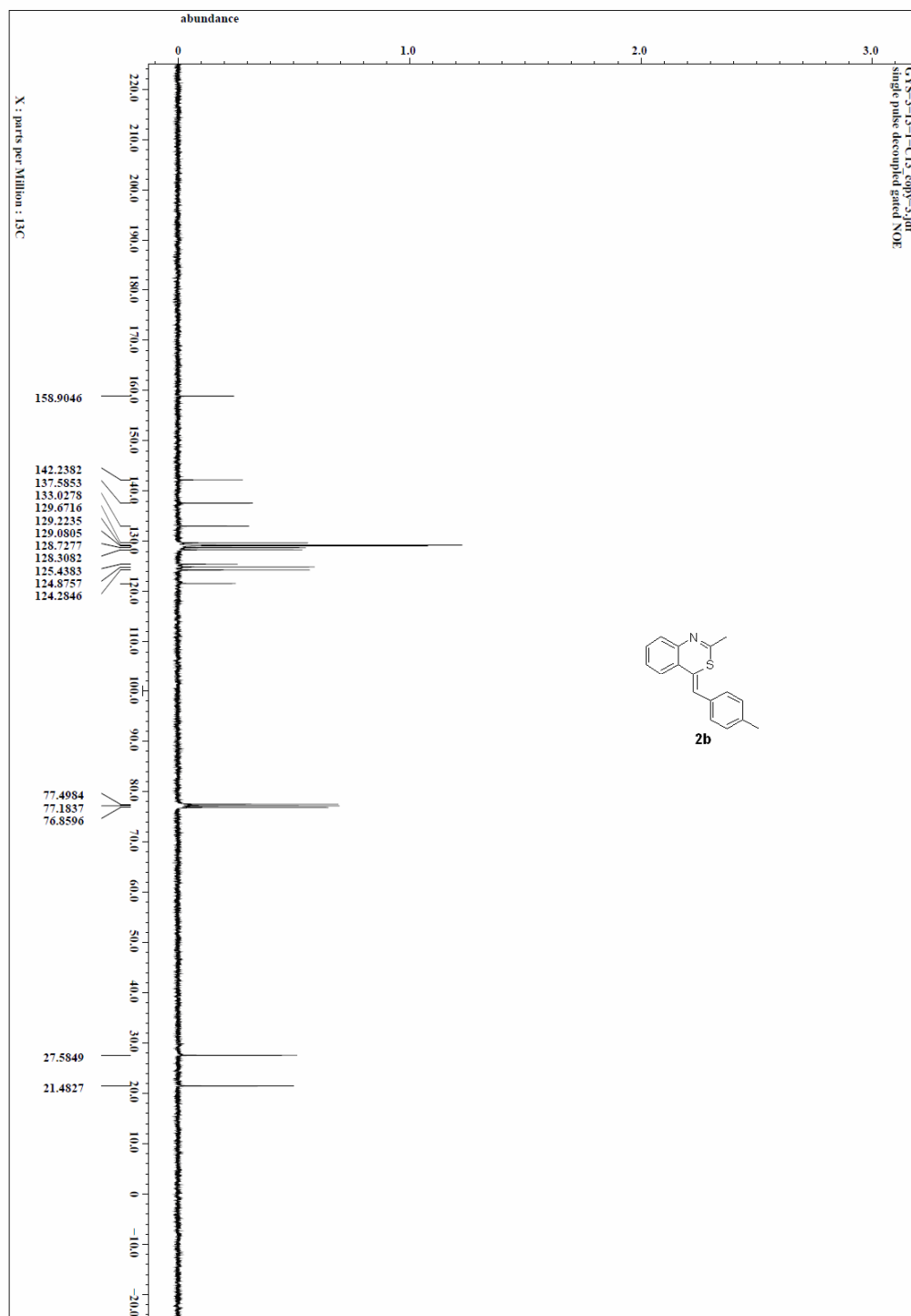
7-Chloro-4-(4-fluoro-benzylidene)-2-methyl-4H-benzo[d][1,3]thiazine (**2l**)

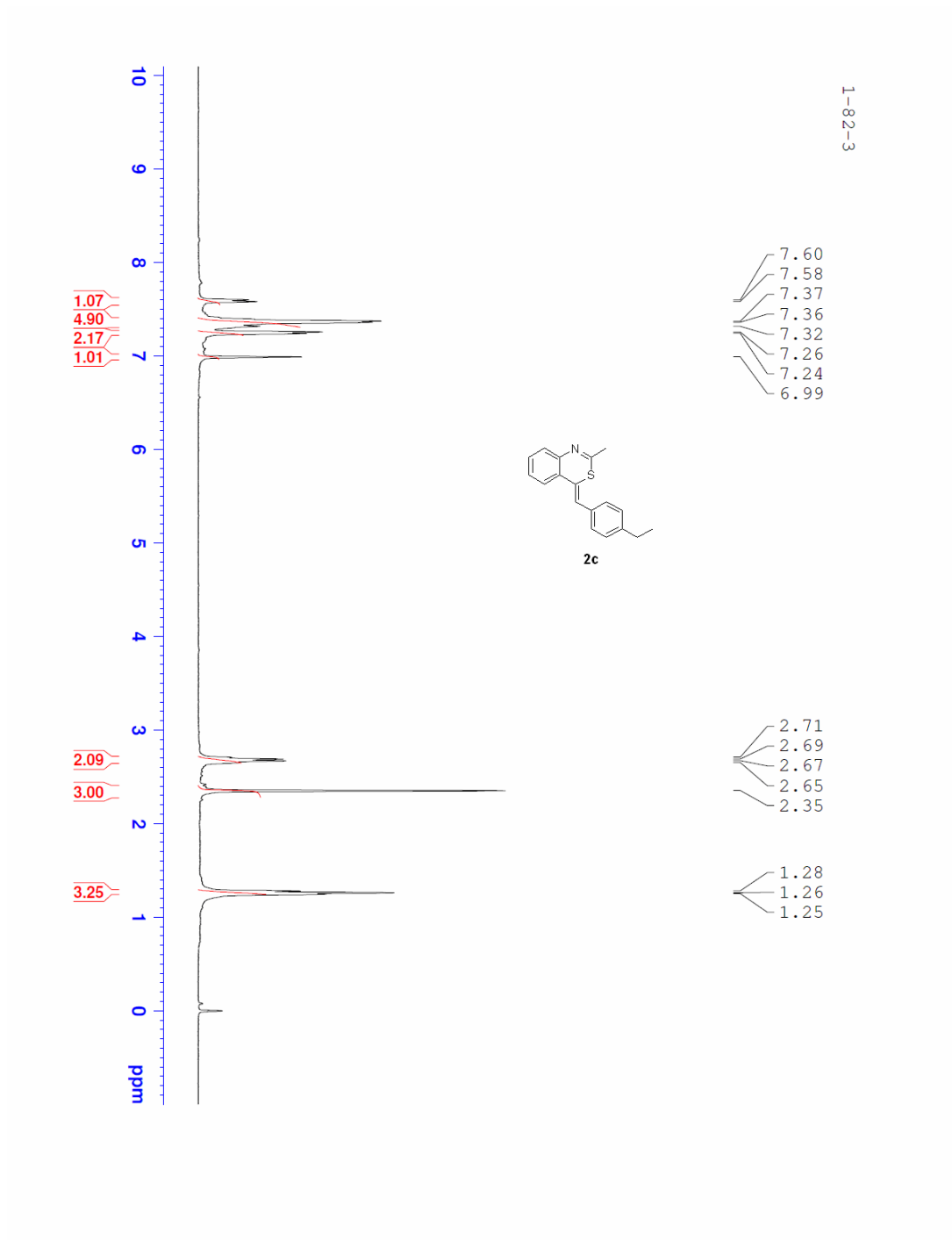
1H NMR (400 MHz, $CDCl_3$) δ 2.35 (s, 3H), 6.92 (s, 1H), 7.08-7.12 (m, 2H), 7.26-7.30 (m, 1H), 7.36-7.41 (m, 3H), 7.50 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.5, 115.3 (d, $^2J_{CF} = 22$ Hz), 119.7, 123.8, 125.2, 128.2, 128.5, 130.8 (d, $^3J_{CF} = 8.0$ Hz), 131.6, 143.3, 160.2; HRMS Calcd for $C_{16}H_{11}ClFNS$ (ESI, M^+H): 304.0363; Found: 304.0359.

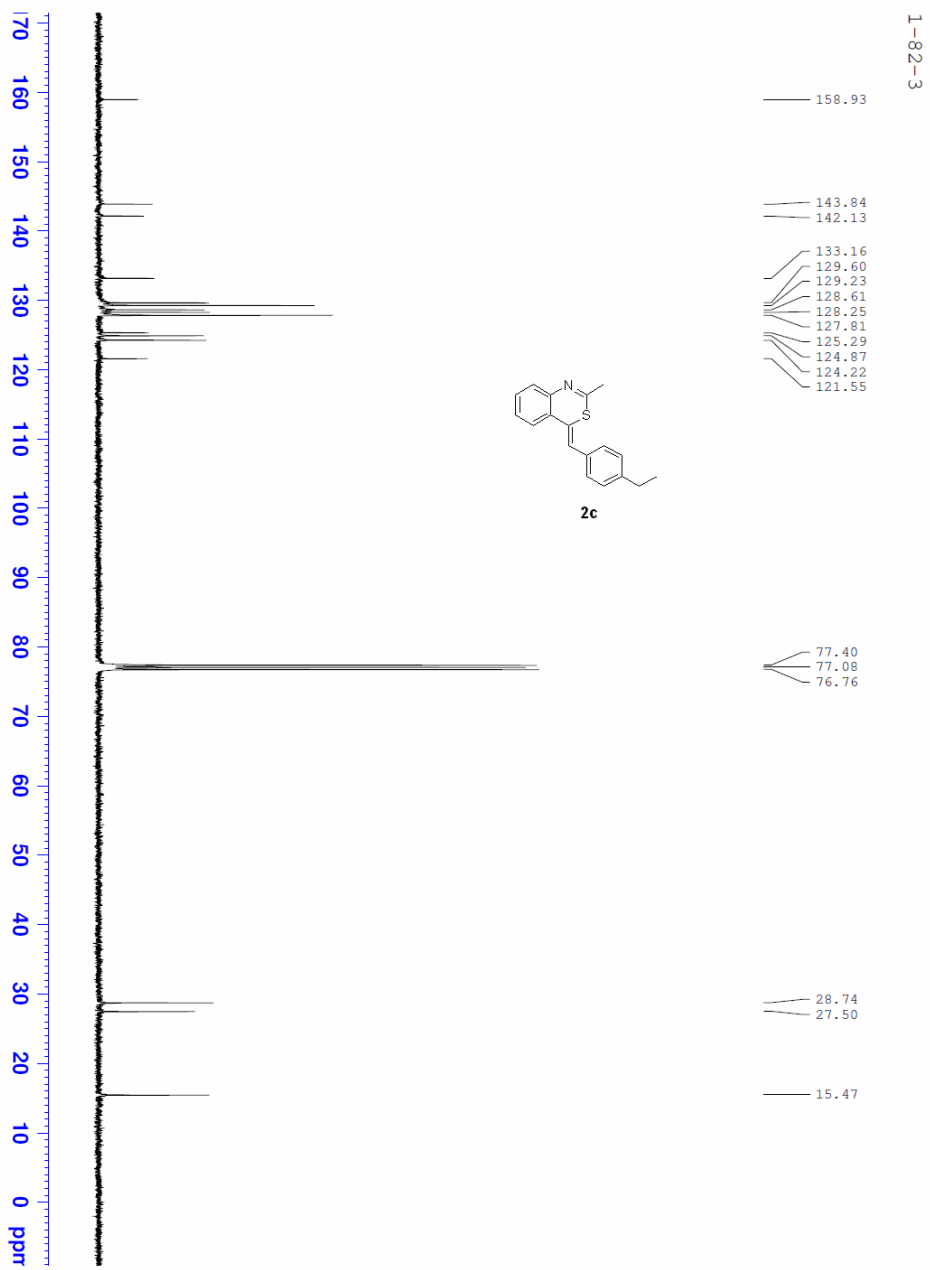


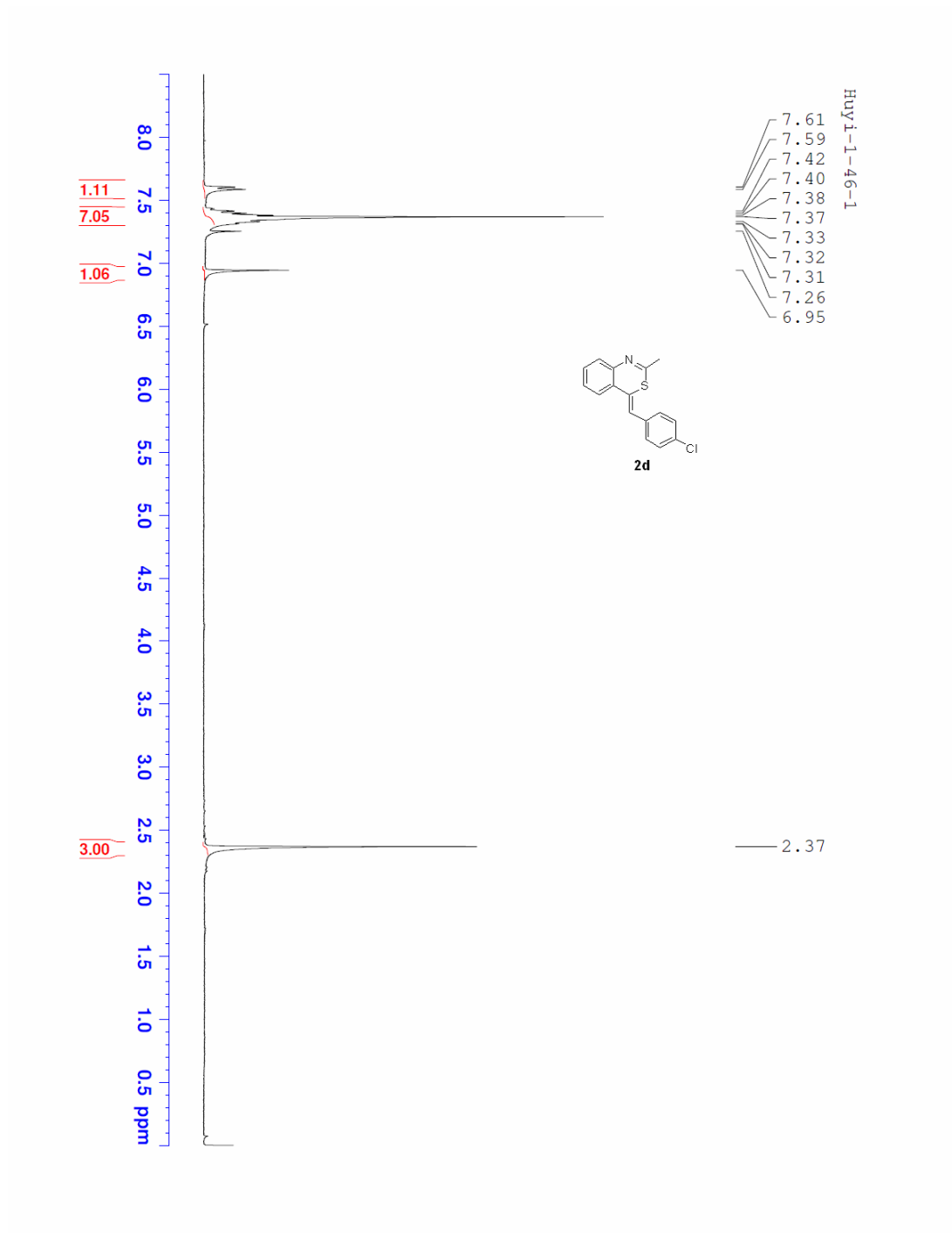




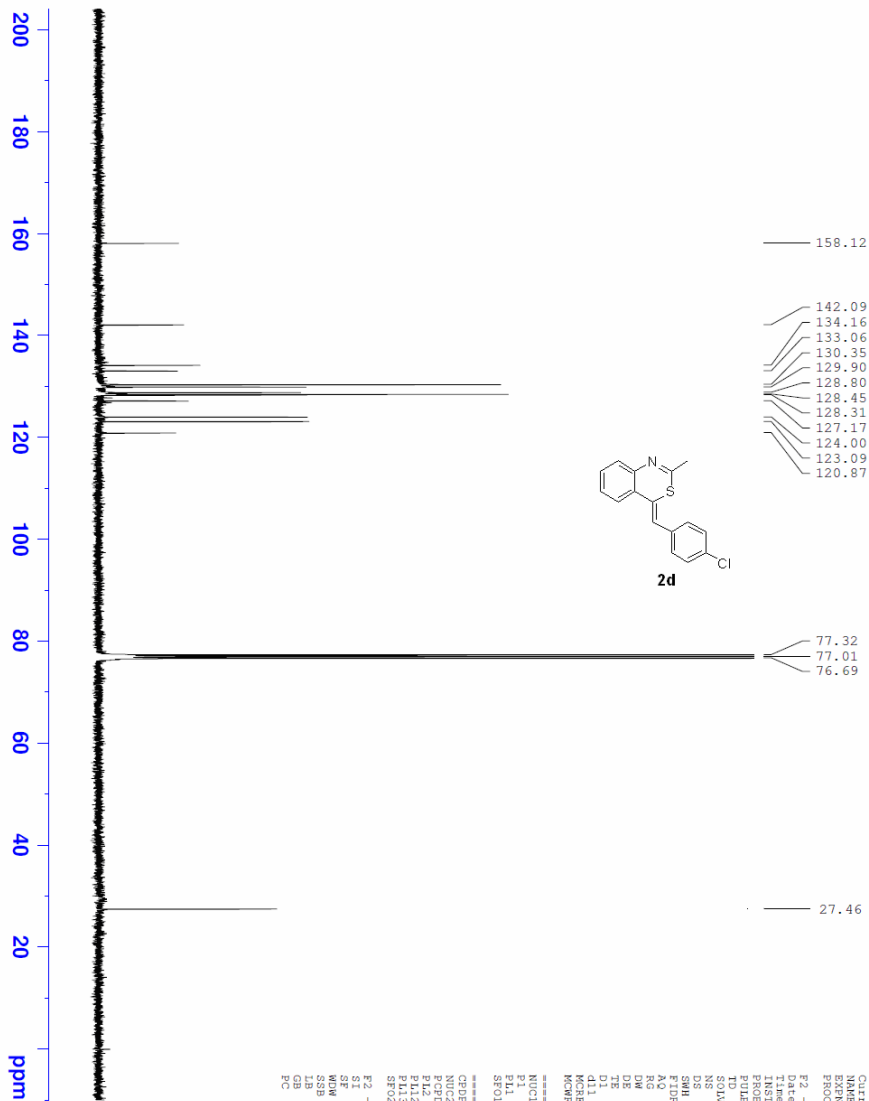








Huy1-1-46-1



Current Data Parameters

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EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

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PROBHD	5 mm BBO-H1H
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TD0	65536
TD1	65536
TD2	65536
TD3	65536
SOLVENT	CDCl3
DS	3072
SS	23980.814 Hz
SMH	0.365918 Hz
FIDRES	1.15852
RG	20.850 usec
DW	20.850 usec
DE	5.00 usec
TE	29.2
DI	2.00000000 sec
d11	0.03000000 sec
MCRESPT	0.02000000 sec
MMMR	0.02000000 sec

===== CHANNEL f1 =====

NUC1	13C
PL1	8.50 usec
PL12	-2.00 dB
SFO1	100.6282828 MHz

===== CHANNEL f2 =====

CPDPRG2	waltz16
NUC2	1H
PL2	90.1H usec
PL12	-3.00 dB
PL13	16.27 dB
PL14	16.00 dB
PL15	16.00 dB
SFO2	400.1300013 MHz

F2 - Processing parameters

SF	100.6127278 MHz
WDW	EM
SSB	0
GB	1.00 Hz
PC	1.40

