Supplementary Information for:

Bioconjugatable, PEGylated Hydroporphyrins for Photochemistry and Photomedicine. Narrow-Band, Red-Emitting Chlorins

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1. Click Reaction Conditions

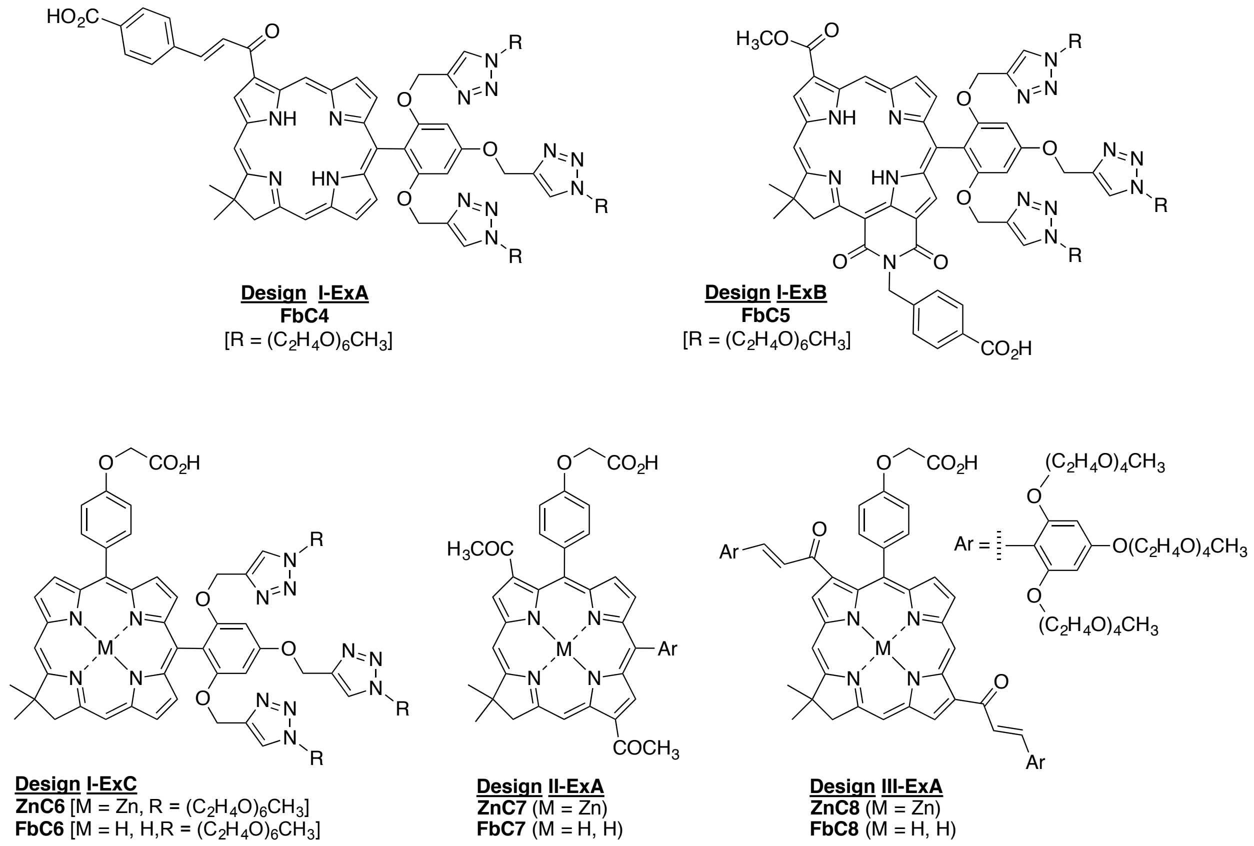
Table S1. Conditions for click reaction of chlorin **6** with PEG-azide **7** to form **ZnC1**.

Entry	Cu (I) amount	Solvent	Temp., Time	Result[a]
1	0.03 equiv	Butanol/H_2O (2:1)	RT, 16 h	**6**
2	0.03 equiv	CH_3CN/H_2O (2:1)	RT, 16 h	**6**
3	0.1 equiv	CH_3CN/H_2O (1:1)	40 °C, 36 h	mono-, di-, tri-derivatized chlorins, minor **6**
4	0.2 equiv	CH_3CN/H_2O (2:1)	40 °C, 16 h	Same as entry 3
5	1 equiv	DMSO/H_2O (4:1)	40 °C, 16 h	**ZnC1**

[a] Results are based on TLC analysis and MALDI-MS.

2. Exploratory Molecular Designs

Several targets that were pursued are shown in Chart S1. The limitations of each design with regard to syntheses, and the synthetic procedures and characterization, are provided herein. Much promising chemistry was accomplished, which potentially can be exploited in other synthetic routes. The chemistry segues naturally from that described in the body of the paper, hence the numbering system is continued without use of "S" designation as is customary for compounds in the Supplementary Information section.



Design I-ExA
FbC4
[R = $(C_2H_4O)_6CH_3$]

Design I-ExB
FbC5
[R = $(C_2H_4O)_6CH_3$]

Design I-ExC
ZnC6 [M = Zn, R = $(C_2H_4O)_6CH_3$]
FbC6 [M = H, H,R = $(C_2H_4O)_6CH_3$]

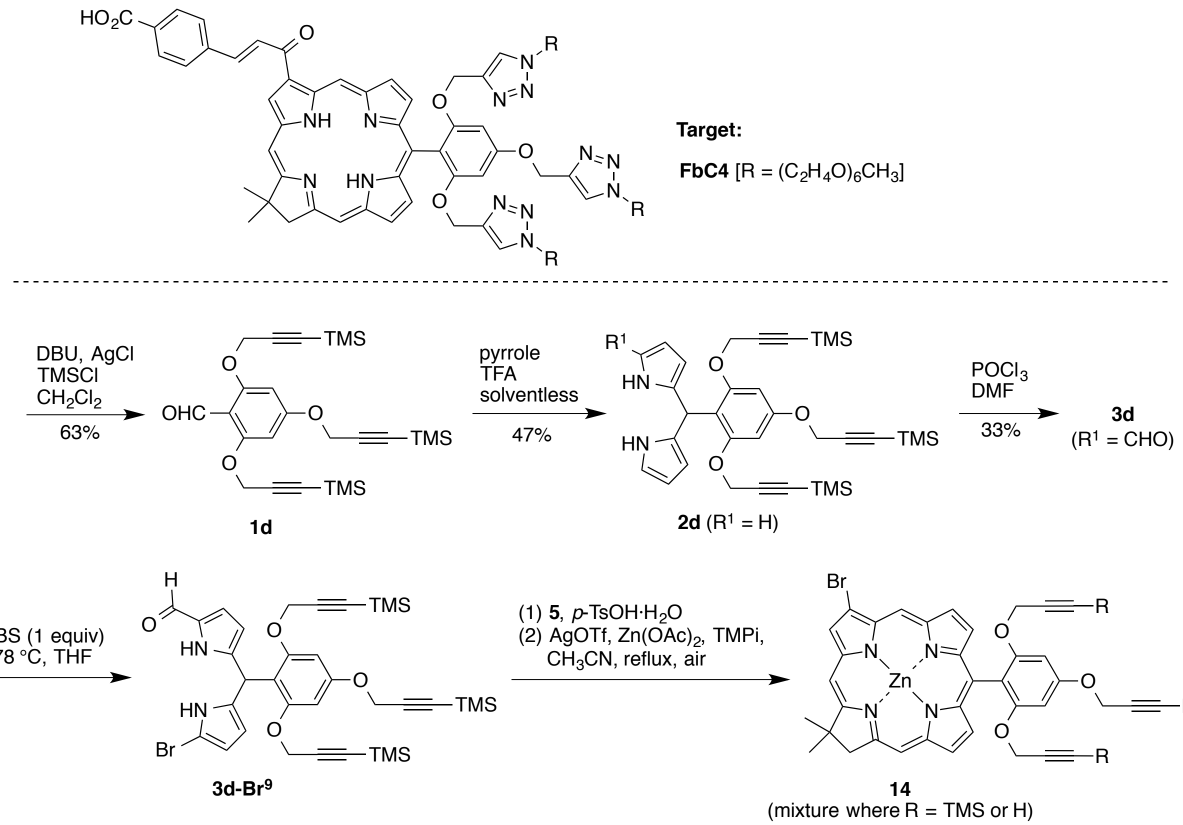
Design II-ExA
ZnC7 (M = Zn)
FbC7 (M = H, H)

Design III-ExA
ZnC8 (M = Zn)
FbC8 (M = H, H)

Chart S1. Attempted target chlorins.

Design I-ExA. In this attempted design (Scheme S1), the chalcone moieties would be incorporated at the 3-position to achieve wavelength-tunable and bioconjugatable chlorins. Here, chalcone formation entails an aldol condensation of the 3-acetylchlorin and 4-formylbenzoic acid under basic conditions. The synthesis started by protection of **1a** with TMSCl in the presence of DBU and a catalytic amount of AgCl, thereby affording the TMS-protected tris(propargyloxy)benzaldehyde **1d** in 63% yield.[S1,S2] The condensation of **1d** and pyrrole with $InCl_3$ unexpectedly gave TMS-cleaved dipyrromethane **2a** (not shown) instead of the corresponding dipyrromethane **2d**. TMS cleavage may happen when NaOH powder was added to quench the reaction; the use of NaOH addition is essential for dipyrromethane formation with $InCl_3$.[60] TFA was then used as catalyst,[S3] and 0.1 N aqueous NaOH was added to quench the reaction, which gave **2d** in 47% yield.

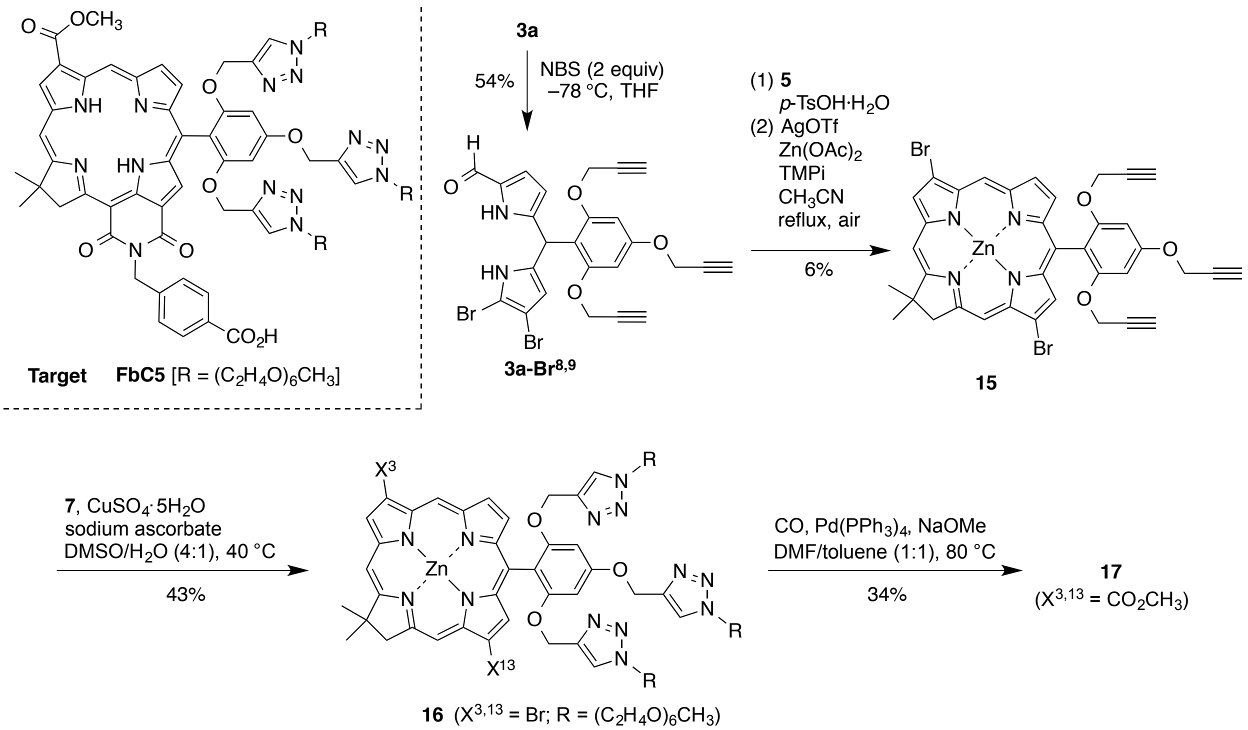
Vilsmeier formylation of TMS-protected dipyrromethane **2d** with $POCl_3$/DMF afforded 1-formyldipyrromethane **3d** in 33% yield. Bromination of **3d** with 1 equiv of NBS at –78 °C afforded **3d-Br**[9], which was used in the next step without further purification. The chlorin-forming reaction was carried out under standard conditions.[62] However, the reaction provided a mixture of zinc chlorins wherein 1–3 TMS protecting groups were cleaved, and no desired chlorin **14** was observed. The presence of the base TMPi might cause TMS deprotection during the oxidative cyclization. If successful, a Stille coupling reaction would replace the 3-bromo group with an acetyl moiety, but the synthesis was ceased here to avoid competing Sonogashira side reactions of the unprotected alkyne groups.



Scheme S1. Attempted synthesis of TMS-protected tris(propargyl)chlorin.

Design I-ExB. To avoid competing Sonogashira reaction with unprotected alkyne groups, an alternative strategy is to carry out the click reaction before Pd-catalyzed reactions. This strategy was employed to synthesize a target chlorin-imide (Scheme S2). The target chlorin-imide was expected to exhibit Q_y absorption ~705 nm, which could fill the spectral window between that of synthetic chlorins (603–687 nm) and bacteriochlorins (707–792 nm).[S4] In this design, a bioconjugatable tether would be introduced at the imide ring at the stage of ring closure, and water-solubility achieved by click reaction between the alkynes and **7**. Bromination[S5] of **3a** with 2 equiv of NBS at –78 °C afforded **3a-Br**^{8,9} in 54% yield. Note: **3a-Br**^{8,9} was unstable and decomposed quickly at room temperature; hence, the bromination was conducted immediately prior to the synthesis of the chlorin.

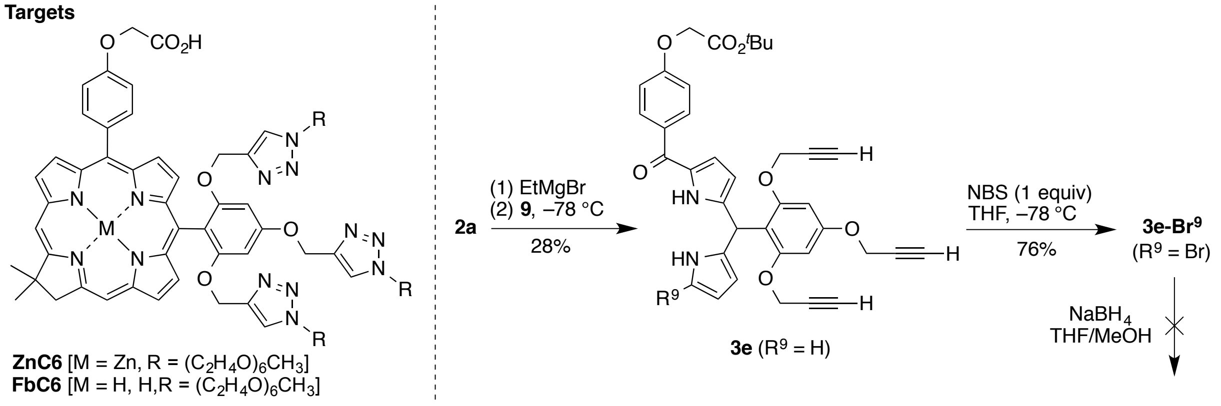
The chlorin-forming reaction was carried out under standard conditions,[62] which afforded zinc chlorin **15** in 6% yield. Treatment of **15** and **7** with a stoichiometric amount of Cu(I) in DMSO/H_2O (4:1) at 40 °C gave the zinc triazole-PEG-chlorin **16** in 43% yield. The dibromochlorin **16** was subjected to carbonylation with CO in DMF/toluene (1:1) in the presence of a stoichiometric amount of $Pd(PPh_3)_4$. Subsequent treatment of the resulting acylpalladium intermediate with NaOMe in methanol afforded chlorin–diester **17** in 34% yield.



Scheme S2. Synthesis approach toward a chlorin–imide.

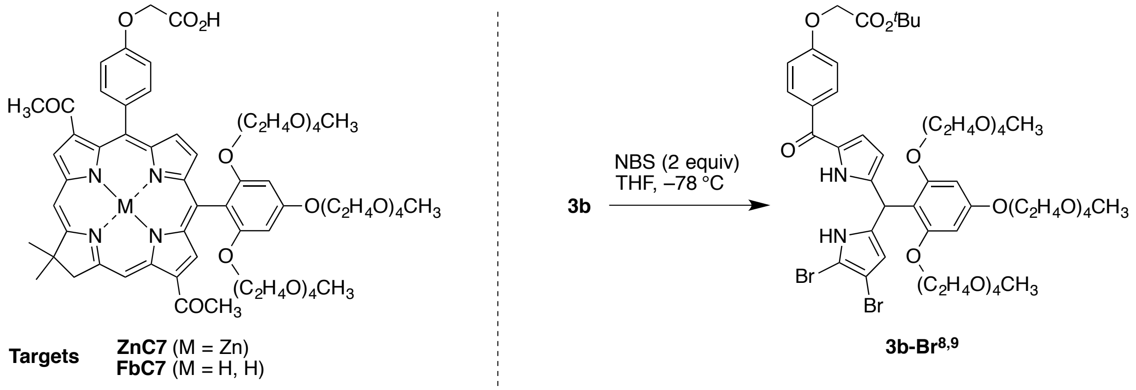
The successful formation of **17** provided an attractive methodology to synthesize water-soluble chlorins wherein only moderate derivatization is required after chlorin formation. For example, the target chlorin–chalcone **FbC4** (Scheme S1, upper panel) would be synthesized in a similar way: after preparation of the alkyne-unprotected chlorin **14**, a click reaction could be carried out first, followed by Stille coupling reaction to introduce the acetyl group. The last step would entail aldol condensation between the acetylchlorin and 4-formylbenzoic acid to incorporate a bioconjugatable tether. However, for the synthesis of the chlorin-imide, the limitation of this strategy came from the lengthy elaboration of the chlorin. Two more steps (regioselective 15-bromination, Pd-mediated carbonylation followed by ring closure to form the imide) remain to form the target chlorin-imide from **17**, but a total yield of **17** from Eastern half **3a** was less than 1%. At the same time, PEG groups were carried through all of the steps for chlorin derivatization, which complicated purification.

Design I-ExC. Target chlorins **ZnC6** and **FbC6** were pursued on the basis of the success of **ZnC1** and **FbC1**. The same PEGylation strategy was adopted with the only difference the requirement to introduce a bioconjugable tether at the 5-position. Acylation of dipyrromethane **2a** with thioester **9** afforded monoacyldipyrromethane **3e** in 28% yield along with recovery of unreacted dipyrromethane **2a** in 27% yield (Scheme S3). Acyldipyrromethane **3e** was brominated selectively at the remaining free α-position by treatment[70] with NBS in THF at –78 °C, affording **3e-Br**^{9} in 76% yield. The reduction of bromoacyldipyrromethane **3e-Br**^{9} under the standard conditions[62,66] with excess $NaBH_4$ in THF/MeOH (4:1) was inefficient, as only the starting material **3e-Br**^{9} was observed by TLC analysis, and none of the desired dipyrromethanecarbinol was detected. Unlike the analogous **3a-Br**^{9}, which was unstable, compound **3e-Br**^{9} was sufficiently stable for routine handling. The low conversion yield upon acylation of **2a** to **3e** and the failure of subsequent reduction might be attributed to the reactive terminal alkynyl groups. One workaround would entail the protection of terminal alkynyl groups and removal thereof prior to the click reaction, but this was not investigated.



Scheme S3. Synthesis of 5-substituted chlorin precursors.

Design II-ExA. Another attempted design (for **ZnC7** and **FbC7**) entailed introduction of auxochromes at the 3- and 13-positions of PEGylated chlorins, which would be synthesized via pre-installation of the PEG moieties. Bromination of **3b** with 2 equiv of NBS at –78 °C afforded the desired compound **3b-Br^{8,9}**, but a tribrominated impurity (not shown) could not be removed (Scheme S4). The inability to purify dipyrromethane **3b-Br^{8,9}** caused this approach to be discontinued.

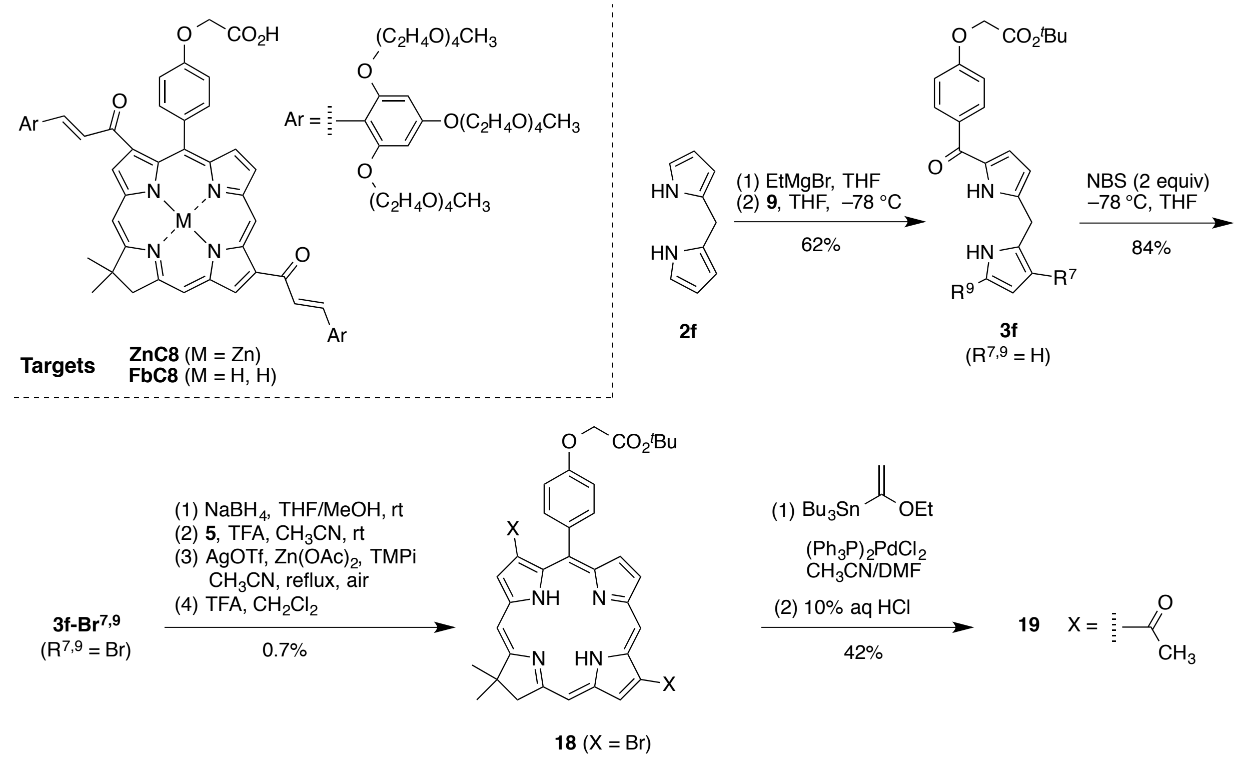


Scheme S4. Synthesis of 5-substituted chlorin precursors.

Design III-ExA. A chalcone design was employed here by derivatization of the 3,12-positions of the chlorin to achieve wavelength tunability and water solubility. The 5-position was assigned to the bioconjugatable tether. Thus, dipyrromethane[60] **2f** was acylated with thioester **9** to form monoacyldipyrromethane **3f** in 62% yield (Scheme S5). Acyldipyrromethane **3f** was brominated selectively at the 7,9-positions by treatment with 2 equiv of NBS in THF at –78 °C,[S5] affording **3f-Br^{7,9}** in 84% yield. Attempts to reduce bromoacyldipyrromethane **3f-Br^{7,9}** under the standard conditions[62] with excess $NaBH_4$ in

THF/MeOH (4:1) were unsuccessful: starting material **3f-Br^{7,9}** was observed by TLC analysis after reduction, and the yield of the chlorin-forming reaction to produce **18** was a meager 0.7%.

Stille coupling[69] of 3,12-dibromochlorin **18** with tributyl(1-ethoxyvinyl)tin and a catalytic amount of $(Ph_3P)_2PdCl_2$ in CH_3CN/DMF (3:2) followed by acidic hydrolysis gave 3,12-diacetylchlorin **19** in 42% yield. The expected Q_y band of **19** is ~690 nm in toluene, on the basis of the known 5-unsubstituted chlorins that contain 3,12- or 3,13-diacetyl groups.[70,S6] However, the Q_y band of **19** appeared at 671 nm in toluene. The failure to achieve the desired wavelength along with abysmally low yield of chlorin formation prompted us to abandon this strategy and avoid a chlorin design with a 5-substituent.



Scheme S5. Synthesis of a diacetylchlorin with a bioconjugatable tether at the 5-position.

Experimental Procedures and Characterization

2,4,6-Tris(3-trimethylsilylpropargyloxy)benzaldehyde (1d). Following a trimethylsilyl protection procedure,[S1,S2] DBU (23.80 g, 156.5 mmol) was added to a mixture of benzaldehyde **1a** (7.00 g, 26.1 mmol) and AgCl (2.20 g, 15.7 mmol) in anhydrous CH_2Cl_2 (50 mL). The reaction mixture was then heated under reflux, whereupon chlorotrimethylsilane (25.50 g, 234.9 mmol) was added dropwise. After refluxing with stirring for 36 h, the mixture was allowed to cool to room temperature. The mixture was diluted with hexanes, and then washed with aqueous $NaHCO_3$, 2 M HCl, and water. The resulting organic phase was dried (Na_2SO_4), concentrated, and chromatographed [silica, hexanes/ethyl acetate (9:1)] to afford a light yellow oil (8.0 g, 63%): ^{1}H NMR δ 0.13 (s, 18H), 0.15 (s, 9H), 4.68 (s, 2H), 4.70 (s, 4H), 6.35 (s, 2H), 10.31 (s, 1H); ^{13}C NMR δ –0.40, 56.9, 57.7, 93.6, 93.7, 94.1, 98.8, 99.15, 110.3; ESI-MS obsd 485.20011, calcd 485.19942 [$(M + H)^+$, M = $C_{25}H_{36}O_4Si_3$].

5-[2,4,6-Tris(3-trimethylsilylpropargyloxy)phenyl]dipyrromethane (2d). Following a reported procedure,[60,S7] a solution of benzaldehyde **1d** (6.00 g, 12.4 mmol) and pyrrole (33.2 g, 49.5 mmol) was degassed with a stream of argon for 10 min, and then TFA (95.0 μL, 1.24 mmol) was added. The solution was stirred for 20 min, and then diluted with CH_2Cl_2. The organic phase was washed (0.1 N aqueous NaOH, H_2O), dried (Na_2SO_4), concentrated and chromatographed [silica, hexanes/ethyl acetate (20:1)] to afford a light yellow oil (3.5 g, 47%): ^{1}H NMR δ 0.19 (s, 9H), 0.20 (s, 18H), 4.50 (s, 2H), 4.63 (s, 4H), 5.93 (s, 1H), 6.09–6.10 (m, 4H), 6.40 (s, 2H), 6.63–6.64 (m, 2H), 8.57 (s, 2H); ^{13}C NMR δ –0.12, –0.03, 32.8, 57.2, 58.6, 92.8, 93.3, 94.8, 96.3, 99.9, 100.2, 106.3, 108.0, 115.1, 116.4, 116.7,133.0, 158.2; ESI-MS obsd 601.27373, calcd 601.27325 [$(M + H)^+$, M = $C_{33}H_{44}N_2O_3Si_3$].

1-Formyl-5-[2,4,6-tris(3-trimethylsilylpropargyloxy)phenyl]dipyrromethane (3d). The Vilsmeier reagent was prepared by treatment of dry DMF (2.5 mL) with $POCl_3$ (542 μL, 5.80 mmol) at 0 °C and stirring of the resulting mixture for 10 min under argon. In a separate flask, a solution of **2d** (3.50 g, 5.80 mmol) in DMF (30 mL) was treated with the freshly prepared Vilsmeier reagent at 0 °C. The resulting mixture was stirred at 0 °C for 1.5 h. The reaction mixture was treated with saturated aqueous NaOAc (~25 mL) for 2 h. CH_2Cl_2 was added to reaction mixture, then the organic phase was washed (water, brine), dried (Na_2SO_4), concentrated, and chromatographed [silica, hexanes/ethyl acetate (9:1)] to afford an orange oil (1.2 g, 33%): ^{1}H NMR δ 0.19 (s, 18H), 0.20 (s, 9H), 4.52 (s, 2H), 4.54 (s, 2H), 4.65 (s, 2H), 5.90–5.92 (m, 1H), 6.07 (s, 1H), 6.12–6.16 (m, 2H), 6.40 (s, 2H), 6.70–6.72 (m, 1H), 6.83–6.85 (m, 1H), 8.98 (s, 1H), 9.06 (s, 1H), 9.33 (s, 1H); ^{13}C NMR δ –0.08, 33.1, 57.2, 58.2, 93.4, 93.7, 95.6, 99.58, 99.69, 108.0, 109.6, 112.6, 117.7, 122.3, 130.1, 131.6, 144.6, 157.1, 158.7, 178.1; ESI-MS obsd 629.26867, calcd 629.26816 [$(M + H)^+$, M = $C_{34}H_{44}N_2O_4Si_3$].

Zn(II)-3-Bromo-10-[2,4,6-tris(3-trimethylsilylpropargyloxy)phenyl]-18,18-dimethylchlorin (14). Following a standard procedure,[S8] a solution of **3d** (1.2 g, 1.9 mmol) in anhydrous THF (19 mL) was treated with NBS (340 mg, 1.9 mmol) under argon at –78 °C. The reaction mixture was stirred for 1 h at –78 °C, after which the ice bath was removed and the reaction mixture was allowed to warm to room temperature. Upon reaching 0 °C, hexanes and water were added. The mixture was extracted with ethyl acetate. The organic layer was dried (Na_2SO_4) and concentrated to afford 9-bromo-1-formyl-5-[2,4,6-tris(3-trimethylsilylpropargyloxy)phenyl]dipyrromethane (**3d-Br^{9}**) as a yellow oil, which was used in the next step without further purification: ^{1}H NMR δ 0.19 (s, 18H), 0.20 (s, 9H), 4.47–4.61 (m, 4H), 4.65 (s, 2H), 5.91–5.93 (m, 1H), 5.98 (s, 1H), 6.03–6.08 (m, 2H), 6.40 (s, 2H), 6.84–6.86 (m, 1H), 8.91 (s, 1H), 9.00 (s, 1H), 9.35 (s, 1H).

Following a general procedure,[62] a solution of **5** (511 mg, 1.90 mmol) and **3d-Br^{9}** (1.90 mmol) in CH_2Cl_2 (50 mL) was treated with a solution of *p*-TsOH·H_2O (1.80 g, 9.50 mmol) in methanol (12.6 mL) under argon. The reaction mixture immediately turned red. The mixture was stirred for 30 min under argon, then treated with 2,2,6,6-tetramethylpiperidine (2.40 mL, 14.0 mmol) and concentrated to dryness. The resulting brown solid was suspended in acetonitrile (190 mL) followed by the successive addition of 2,2,6,6-tetramethylpiperidine (8.10 mL, 47.5 mmol), $Zn(OAc)_2$ (5.20 g, 28.5 mmol), and AgOTf (1.40 g, 5.70 mmol). The resulting suspension was refluxed for 22 h exposed to air. The crude mixture was filtered through a silica pad with CH_2Cl_2. The crude product was a mixture of chlorins with TMS cleaved and partially cleaved.

1-{4-[2-(*tert*-Butoxy)-2-oxoethoxy]phenoxy}-5-[2,4,6-tris(propargyloxy)phenyl]dipyrromethane (3e). Following a general procedure,[67] EtMgBr (0.9 M solution in THF, 2.66 mL, 2.39 mmol) was added dropwise to a solution of **2a** (459 mg, 1.19 mmol) in THF (1.2 mL) over a 5 min period. The solution was stirred at room temperature for 10 min before cooling to –78 °C. A solution of **9** (412 mg, 1.19 mmol) in THF (1.2 mL) was added, and the mixture was stirred at –78 °C for 30 min. The cooling bath was removed and the reaction mixture was allowed to warm to room temperature for 1 h before saturated aqueous NH_4Cl was added. The aqueous layer was removed and washed with CH_2Cl_2. The combined organic extract was washed with brine, concentrated, and chromatographed [silica, hexanes/ethyl acetate (3:1)] to recover starting material **2a** (126 mg) as the first fraction followed by the title compound as a yellow oil (203 mg, 28%): ^{1}H NMR δ 1.44 (s, 9H), 2.53–2.57 (m, 3H), 4.57 (s, 2H), 4.59 (d, *J* = 2.4 Hz, 4H), 4.68 (d, *J* = 2.4 Hz, 2H), 5.92–5.95 (m, 1H), 6.10 (s, 1H), 6.12–6.13 (m, 2H), 6.43 (s, 2H), 6.70–6.72 (m, 1H), 6.73–6.76 (m, 1H), 6.93 (d, *J* = 9 Hz, 2H), 7.84 (d, *J* = 9 Hz, 2H), 8.83 (s, 1H), 9.27 (s, 1H); ^{13}C NMR δ 28.15, 33.0, 56.2, 57.2, 65.7, 76.2, 76.4, 78.1, 82.8, 95.7, 107.6, 108.0, 109.3, 114.2, 117.5, 119.9, 129.8, 130.4, 131.0, 132.3, 142.5, 156.8, 158.2, 160.7, 167.7, 182.8; ESI-MS obsd 619.24297, calcd 619.24388 $[(M + H)^+$, M = $C_{37}H_{34}N_2O_7]$.

9-Bromo-1-{4-[2-(*tert*-butoxy)-2-oxoethoxy]phenyl}-5-[2,4,6-tris(propargyloxy)-phenyl]dipyrromethane (3e-Br^9). Following a general procedure,[70] a solution of **3e** (77.0 mg, 0.124 mmol) in anhydrous THF (2.5 mL) was treated with NBS (22.1 mg, 0.124 mmol) under argon at –78 °C. The reaction mixture was stirred for 1 h at –78 °C, after which the ice bath was removed, and the reaction mixture was allowed to warm to room temperature. Upon reaching 0 °C, hexanes and water were added. The mixture was extracted with ethyl acetate. The organic layer was dried (Na_2SO_4), concentrated, and chromatographed [silica, hexanes/ethyl acetate (3:1)] to afford an orange oil (67 mg, 76%): ^{1}H NMR δ 1.48 (s, 9H), 2.56–2.57 (m, 3H), 4.56 (s, 2H), 4.62 (d, *J* = 2.4 Hz, 4H), 4.68 (d, *J* = 2.4 Hz, 2H), 5.95–5.96 (m, 1H), 6.02 (s, 1H), 6.03–6.04 (m, 2H), 6.42 (s, 2H), 6.73–6.75 (m, 1H), 6.93 (d, *J* = 9 Hz, 2H), 7.84 (d, *J* = 9 Hz, 2H), 8.80 (s, 1H), 9.38 (s, 1H); ^{13}C NMR δ 28.11, 33.2, 56.1, 57.1, 65.6, 76.3, 76.6, 77.8, 78.2, 82.8, 95.5, 96.8, 109.4, 110.0, 112.3, 114.2, 119.7, 130.0, 131.0, 132.0, 132.1, 141.4, 156.6, 158.4, 160.7, 167.6, 182.9; ESI-MS obsd 697.15421, calcd 697.15439 $[(M + H)^+$, M = $C_{37}H_{33}BrN_2O_7]$.

8,9-Dibromo-1-{4-[2-(*tert*-butoxy)-2-oxoethoxy]phenyl}-5-[2,4,6-tris(3,6,9,12-tetraoxatridecyloxy)phenyl]dipyrromethane (3b-Br^{8,9}). A solution of **3b** (1.14 g, 1.06 mmol) in anhydrous THF (10 mL) was treated with NBS (377.3 mg, 2.12 mmol) under argon at –78 °C. The reaction mixture was stirred for 1 h at –78 °C, after which the ice bath was removed and the reaction mixture was allowed to warm. Upon reaching –20 °C, hexanes (20 mL) and water (20 mL) were added. The mixture was extracted with ethyl acetate. The organic layer was dried (Na_2SO_4), concentrated, and chromatographed [silica, CH_2Cl_2/CH_3OH (97:3)] to afford the title compound mixed with tribromodipyrromethane in a ratio of 5:1 on the basis of ^{1}H NMR analysis (1000 mg, impure).

1-{4-[2-(*tert*-Butoxy)-2-oxoethoxy]phenyl}dipyrromethane (3f). Following a general procedure,[67] EtMgBr (1 M solution in THF, 6.2 mL, 6.2 mmol) was added dropwise to a solution of **2f** (0.45 g, 3.1 mmol) in THF (3.4 mL) over a 5 min period. The solution was stirred at room temperature for 10 min before cooling to –78 °C. A solution of **9** (1.07 mg, 3.10 mmol) in THF (3.4 mL) was added, and the mixture was stirred at –78 °C for 30 min. The cooling bath was removed, and the reaction mixture was allowed to warm to room temperature for 1 h before saturated aqueous NH_4Cl was added. The aqueous layer was removed and washed with CH_2Cl_2.

The combined organic layer was washed with brine, concentrated, and chromatographed [silica, hexanes/ethyl acetate (4:1)] to recover starting material **2f** as the first fraction followed by the title compound, which upon concentration gave a white solid (734 mg, 62%): mp 120–122 °C; ^{1}H NMR δ 1.52 (s, 9H), 4.09 (s, 2H), 4.59 (s, 2H), 6.066–6.069 (m, 1H), 6.12–6.15 (m, 2H), 6.62–6.64 (m, 1H), 6.80–6.82 (m, 1H), 6.95 (d, J = 8.4 Hz, 2H), 7.86 (d, J = 8.4 Hz, 2H), 8.63 (s, 1H), 10.17 (s, 1H); ^{13}C NMR δ 27.9, 49.1, 83.0, 106.3, 106.4, 108.1, 108.2, 109.6, 109.7, 114.2, 117.6, 121.5, 127.9, 130.1, 131.1, 131.9, 139.6, 160.8, 167.8, 183.8; ESI-MS obsd 381.18073, calcd 381.18008 $[(M + H)^+$, M = $C_{22}H_{24}N_2O_4]$.

Zn(II)-3,13-Dibromo-10-[2,4,6-tris(propargyloxy)phenyl]-18,18-dimethylchlorin (15). Following a standard procedure,[S8] a solution of **3a** (948 mg, 2.30 mmol) in anhydrous THF (23 mL) was treated with NBS (818 mg, 4.60 mmol) under argon at –78 °C. The reaction mixture was stirred for 1 h at –78 °C, after which the ice bath was removed. Upon reaching –20 °C, hexanes (20 mL) and water (20 mL) was added. The mixture was extracted with ethyl acetate. The organic layer was dried (Na_2SO_4), concentrated and chromatographed [silica, hexanes/ethyl acetate (4:1)] to afford 8,9-dibromo-1-formyl-5-[2,4,6-tris(propargyloxy)-phenyl]dipyrromethane (**3a-Br^{8,9}**) as a yellow oil (710 mg, 54%): ^{1}H NMR δ 2.57 (t, J = 2.4 Hz, 2H), 2.58 (t, J = 2.4 Hz, 1H), 4.63 (d, J = 2.4 Hz, 4H), 4.70 (d, J = 2.4 Hz, 2H), 5.89–5.91 (m, 1H), 6.10 (d, J = 3.0 Hz, 1H), 6.21 (s, 1H), 6.43 (s, 2H), 6.85–6.87 (m, 1H), 9.21 (s, 1H), 9.24 (s, 1H), 9.43 (s, 1H). Dibromodipyrromethane **1e** in $CDCl_3$ solution darkened and decomposed, and hence was used directly in the chlorin-forming process.

Following a general procedure,[62] a solution of **5** (161 mg, 0.600 mmol) and **3a-Br^{8,9}** (342 mg, 0.600 mmol) in CH_2Cl_2 (16 mL) was treated with a solution of p-TsOH·H_2O (570. mg, 3.00 mmol) in methanol (4 mL) under argon. The reaction mixture immediately turned red. The mixture was stirred for 30 min under argon, then treated with 2,2,6,6-tetramethylpiperidine (0.76 mL, 4.5 mmol) and concentrated to dryness. The resulting brown solid was suspended in acetonitrile (60 mL) followed by the successive addition of 2,2,6,6-tetramethylpiperidine (2.6 mL, 15.0 mmol), $Zn(OAc)_2$ (1.65 g, 9.00 mmol), and AgOTf (463 mg, 1.80 mmol). The resulting suspension was refluxed for 22 h exposed to air. The crude mixture was filtered through a silica pad with CH_2Cl_2. The crude product was chromatographed [silica, hexanes/CH_2Cl_2 (1:2)] to afford a green solid (28 mg, 6%): ESI-MS obsd 795.96584, calcd 795.96576 $[M^+$, M = $C_{37}H_{26}Br_2N_4O_3Zn]$.

Zn(II)-3,13-Dibromo-10-[2,4,6-tris(2,5,8,11,14,17-hexaoxanonadecyl-1*H*-1,2,3-triazol-4-ylmethoxy)phenyl]-18,18-dimethylchlorin (16). The Cu(I) catalyst was prepared by treatment of $CuSO_4·H_2O$ (15 mg, 0.060 mmol) and sodium ascorbate (24.0 mg, 0.120 mmol) with 600 μL of deionized H_2O under argon. The reaction mixture turned brown immediately and was stirred until homogeneous. In a separate vial, **15** (24 mg, 0.030 mmol) and **7** (87 mg, 0.27 mmol) in DMSO (1.2 mL) were treated with freshly prepared Cu (I) catalyst (300 μL) under argon. The reaction mixture was stirred at 40 °C for 16 h. Upon cooling to room temperature, H_2O was added and organic phase was extracted with CH_2Cl_2. The extract was washed (brine), dried (Na_2SO_4), concentrated, and chromatographed [silica, CH_2Cl_2 /CH_3OH (93:7)] to afford a green solid (23 mg, 43%): ESI-MS obsd 1760.54352, calcd 1760.54355 $[(M + H)^+$, M = $C_{76}H_{107}Br_2N_{13}O_{21}Zn]$.

Zn(II)-3,13-Bis(methoxycarbonyl)-10-[2,4,6-tris(2,5,8,11,14,17-hexaoxanonadecyl-1*H*-1,2,3-triazol-4-ylmethoxy)phenyl]-18,18-dimethylchlorin (17). Samples of **16** (10 mg, 0.0057 mmol) and $Pd(PPh_3)_4$ (13.2 mg, 0.0114 mmol) were dried in a Schlenk flask under high vacuum for 1 h. The solvent DMF/toluene (1:1) was purged with argon (30 min) and subsequently with CO (30 min). The reaction flask was filled with CO gas and DMF/toluene [0.6 mL, (1:1)]. CO gas was bubbled through the stirred reaction mixture for 2 h. Then excess NaOMe (6.2 mg, 0.11 mmol) in MeOH (285 μL) was added to the reaction mixture. The latter was stirred at 80 °C for 5 min before being cooled to room temperature. A saturated aqueous solution of NH_4Cl was added, and the mixture was extracted with CH_2Cl_2. The organic layer was separated, filtered through Celite (CH_2Cl_2), and concentrated. Column chromatography [silica, CH_2Cl_2/CH_3OH (7:93)] afforded a green oil (3.0 mg, 34%): MALDI-MS obsd 1742.0881, calcd 1742.7158 [$(M + Na)^+$, M = $C_{80}H_{113}N_{13}O_{25}Zn$].

3,12-Dibromo-5-[4-(carboxymethoxy)phenyl]-18,18-dimethylchlorin (18). Following a standard procedure,[S5] a solution of **3f** (734 mg, 1.93 mmol) in anhydrous THF (38 mL) was treated with NBS (686 mg, 3.86 mmol) under argon at –78 °C. The reaction mixture was stirred for 1 h at –78 °C, after which the cooling bath was removed and the reaction mixture was allowed to warm. Upon reaching –20 °C, hexanes (38 mL) and water (38 mL) were added. The mixture was extracted with ethyl acetate. The organic layer was dried (Na_2SO_4), concentrated, and chromatographed [silica, hexanes/ethyl acetate (4:1)] to afford 7,9-dibromo-1-[4-(2-(*tert*-butoxy)-2-oxoethoxy)phenyl]dipyrromethane (**3f-Br**[7,9]) as a light yellow solid (878 mg, 84%): ^1H NMR δ 1.49 (s, 9H), 4.05 (s, 2H), 4.59 (s, 2H), 6.00 (d, *J* = 3 Hz, 1H), 6.27–6.29 (m, 1H), 6.87–6.89 (m, 1H), 6.98 (d, *J* = 9 Hz, 2H), 7.87 (d, *J* = 9 Hz, 2H), 10.45 (s, 1H), 11.52 (s, 1H).

Following a general procedure,[S9] a solution of **3f-Br**[7,9] (878 mg, 1.63 mmol) in anhydrous THF (26 mL) and anhydrous methanol (6.6 mL) was treated with $NaBH_4$ (616 mg, 16.3 mmol) at room temperature for 30 min. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl, and then extracted with ethyl acetate. The combined organic phase was washed with brine, dried (Na_2SO_4), and concentrated. The resulting oil was dissolved in CH_3CN (16 mL) containing **5** (439 mg, 1.63 mmol) and TFA (125 μL, 1.63 mmol). The resulting mixture was stirred at room temperature for 30 min and then diluted with CH_3CN. Sample of 2,2,6,6-tetramethylpiperidine (4.16 mL, 24.5 mmol), $Zn(OAc)_2$ (4.49 g, 24.5 mmol) and AgOTf (1.26 g, 4.89 mmol) were added successively. The resulting suspension was refluxed for 22 h exposed to air. The crude mixture was filtered through a silica pad with ethyl acetate. The filtrate was concentrated, dissolved in anhydrous CH_2Cl_2 (100 mL), and treated dropwise with TFA (150 μL). After 10 min, saturated aqueous $NaHCO_3$ was added slowly. The organic layer was dried ($NaSO_4$), concentrated and chromatographed [silica, hexanes/CH_2Cl_2 (1:1)] to afford a green solid (8.0 mg, 0.7%): ^1H NMR δ –2.12 (br s, 1H), –1.52 (br s, 1H), 1.61 (s, 6H), 2.00 (s, 6H), 4.51 (s, 2H), 4.79 (s, 2H), 7.22 (d, *J* = 8.8 Hz, 2H), 7.84 (d, *J* = 8.8 Hz, 2H), 8.50 (d, *J* = 4.4 Hz, 1H), 8.75 (s, 1H), 8.77 (s, 1H), 8.85 (s, 1H), 8.90 (d, *J* = 4.4 Hz, 1H), 8.96 (s, 1H), 9.82 (s, 1H); ^{13}C NMR δ 28.3, 29.8, 31.3, 40.3, 46.7, 51.5, 66.2, 82.7, 94.7, 96.2, 105.6, 113.1, 116.6, 118.8, 121.8, 124.2, 128.7, 130.1, 132.1, 132.7, 133.2, 134.6, 138.6, 139.3, 151.4, 154.4, 158.4, 164.8, 168.3, 174.8; ESI-MS obsd 703.09084, calcd 703.09139 [$(M + H)^+$, M = $C_{34}H_{32}Br_2N_4O_3$]; λ_{abs} (toluene) 401, 647 nm.

3,12-Diacetyl-5-[4-(carboxymethoxy)phenyl]-18,18-dimethylchlorin (19). Following a procedure for Stille coupling of chlorins,[70] a mixture of **18** (8.0 mg, 0.011 mmol), tributyl(1-ethoxyvinyl)tin (20. μL, 0.055 mmol), and $(Ph_3P)_2PdCl_2$ (1.6 mg, 0.0022 mmol) was stirred in CH_3CN/DMF [600 μL (3:2)] under argon for 4 h at 83 °C in a Schlenk line. The reaction mixture was treated with 10% aqueous HCl (2 mL) at room temperature for 20 min.

CH_2Cl_2 was added. The organic layer was separated, washed (saturated aqueous $NaHCO_3$, water, and brine), dried (Na_2SO_4), concentrated, and chromatographed [silica, CH_2Cl_2/ethyl acetate (49:1)] to afford a brown oil (3.2 mg, 42%): ^{1}H NMR δ –1.97 (br s, 1H), –1.56 (br s, 1H), 1.61 (s, 6H), 2.04 (s, 6H), 2.17 (s, 3H), 3.27 (s, 3H), 4.57 (s, 2H), 4.79 (s, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 8.02 (d, *J* = 8.4 Hz, 2H), 8.61 (d, *J* = 4.4 Hz, 1H), 8.89 (s, 1H), 8.95 (s, 1H), 8.98 (s, 1H), 9.03 (d, *J* = 4.4 Hz, 1H), 9.27 (s, 1H), 10.81 (s, 1H); ^{13}C NMR δ 28.4, 29.9, 30.1, 31.3, 31.9, 47.0, 51.4, 66.1, 82.9, 96.6, 98.4, 109.3, 113.8, 121.2, 125.5, 126.5, 132.1, 133.1, 133.6, 135.1, 136.6, 137.0, 137.7, 143.3, 153.4, 155.5, 158.8, 163.6, 168.1, 175.4, 197.2, 201.3; ESI-MS obsd 631.29117, calcd 631.29150 [$(M + H)^+$, M = $C_{38}H_{38}N_4O_5$]; λ_{abs} (toluene) 430, 671 nm.

3. Absorption Spectra

The spectral properties of the PEGylated chlorins **ZnC1** and **FbC1** are shown in Figure S1. **ZnC1** exhibited almost unchanged spectroscopic properties over a concentration range of 1000-fold, indicating high solubility of the chlorin in water. On the other hand, at higher concentrations, **FbC1** exhibited no significant broadening in the Q_y band, but the shape of the B bands changed at concentrations ~800 μM showing some degree of aggregation.

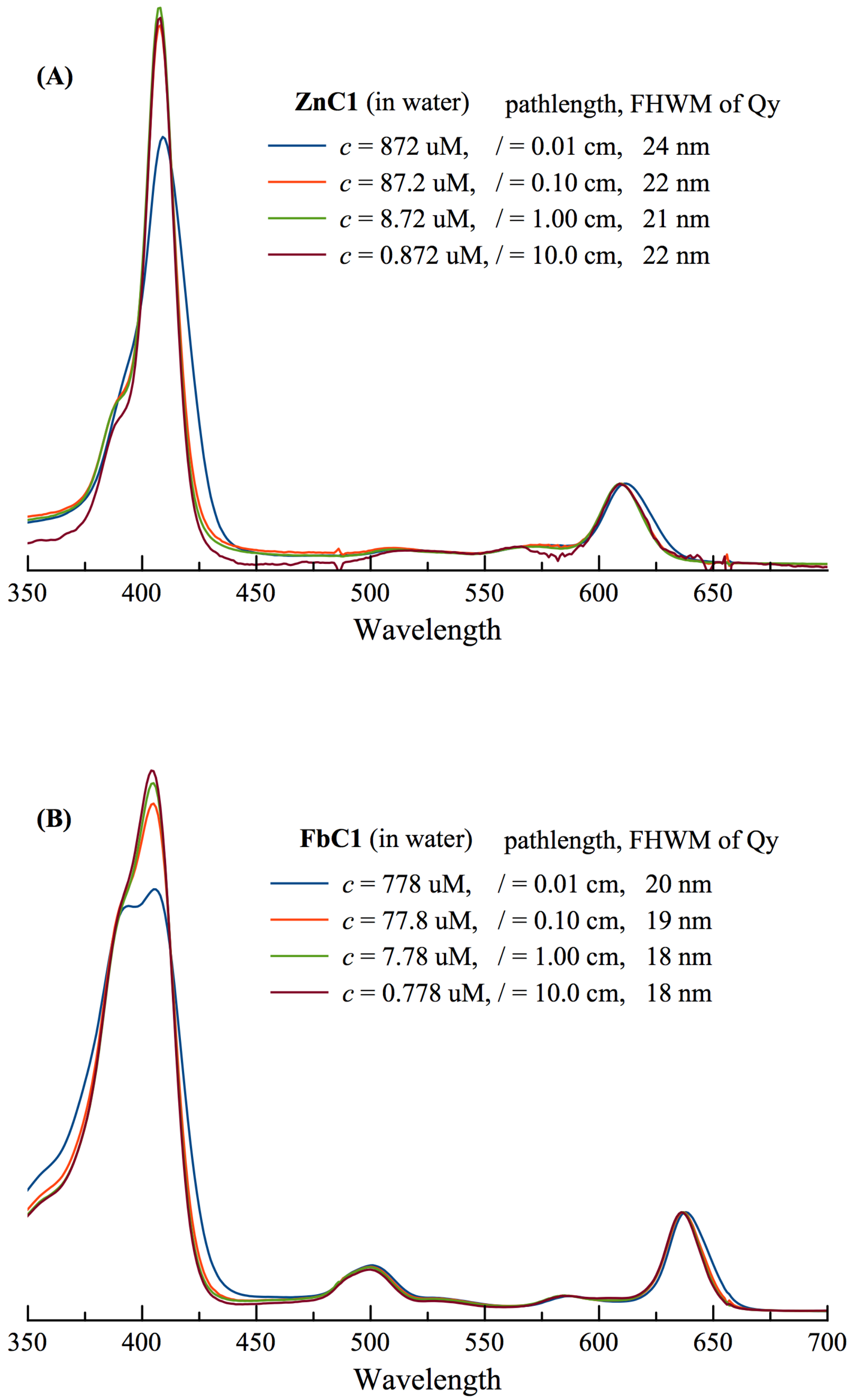


Figure S1. Absorption versus concentration of **ZnC1** and **FbC1** over a range of 1000-fold. The spectra are normalized at the Q_y band; the FWHM of the Q_y band is shown in the inset.

Absorption spectra of **ZnC3** and **FbC3** in neat water at ~5 μM are shown in Figure S2. Obvious broadening of the spectra is evident.

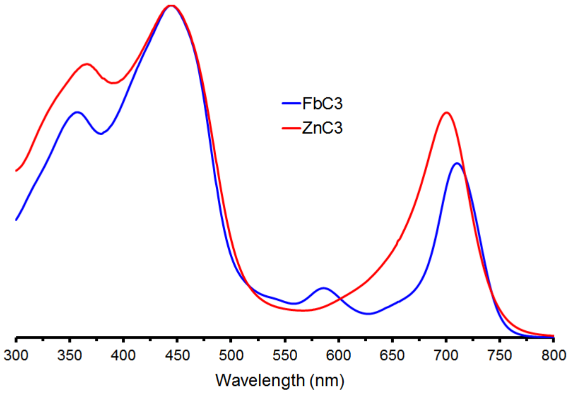


Figure S2. Absorption spectra of PEGylated chlorins in H_2O.

4. Purification of PEGylated Compounds

One essential issue arising from the pre-installation route concerns the purification process. During flash chromatography, PEGylated compounds possessing high polarity tended to bind tightly to silica gel. When the crude mixture containing the desired product was mixed with PEG-containing impurities, the resolution of the flash chromatography process was compromised. A typical flash chromatography (3 cm dia. × 15 cm) procedure entails: (1) pack the column and load the crude mixture with CH_2Cl_2 (or ethyl acetate); (2) elute with one column volume of CH_2Cl_2 (or ethyl acetate) to remove impurities while the PEGylated precursors remained bound or near the top of the column; and (3) elute with CH_2Cl_2 with a gradual increase of 0.5–5% MeOH (or EtOH with ethyl acetate[S10]) to remove PEG-containing impurities and isolate the desired product. The PEGylated precursors **1b**, **1b**′, and **2b** generally were obtained with good purity following the above procedure. For acylation of **2b**, the crude mixture often contained ~20% of unreacted starting material **2b**. Isolation of **3b** with good purity required prolonged elution (2–3 h) in step 3.

The purification of the PEGylated chlorins proceeded in the same manner as employed for separation of multiporphyrin arrays.[75] A general purification procedure for the crude PEGylated chlorin is as follows, which afforded the PEGylated chlorins **ZnC1**, **10**, and **FbC3** in good purity:

(1) Silica chromatography (2 cm dia. × 10 cm) was eluted with CH_2Cl_2 (0.5–5% MeOH).
(2) Size-exclusion chromatography (4 cm dia. × 40 cm; Bio Beads S-X3, 200–400 mesh; flow rate: ~1.5 ml/min) was eluted with toluene (HPLC grade).
(3) Flash silica chromatography (2 cm dia. × 4 cm) was eluted with CH_2Cl_2 (0.5–10% MeOH, HPLC grade).

5. 3-Dimensional Conformation

The conformation of the 2,4,6-trisubstituted aryl motif was examined by ^{1}H NMR spectroscopy. Protons on the PEG chain typically resonate at 3.4–4.6 ppm, depending on the terminal substitution groups. Indeed, the PEGylated precursors **1b**, **1b′**, **2b**, and **3b** exhibited a complicated resonance pattern in this region in the ^{1}H NMR spectra. No significant difference was found between the resonances of protons from the *ortho*- and *para*-PEG chains in the non-macrocyclic precursors. However, for the PEGylated chlorins a significant difference was observed. The protons of the *para*-PEG chain resonated similarly to that of a typical PEG-chain, while the protons of the *ortho*-PEG chains resonated at a higher frequency, ranging from 1.7–3.2 ppm. A ^{1}H NMR spectrum of PEGylated chlorins is demonstrated by **10** and shown in Figure S3. The *ortho*-PEG chains are conformationally restricted to above and below the macrocycle plane and thus are magnetically more shielded due to the aromatic ring-current effect. Although detailed analyses and assignments of PEG-protons do not relate to our main interests, the different resonance regions clearly show that the desired geometric design was achieved.

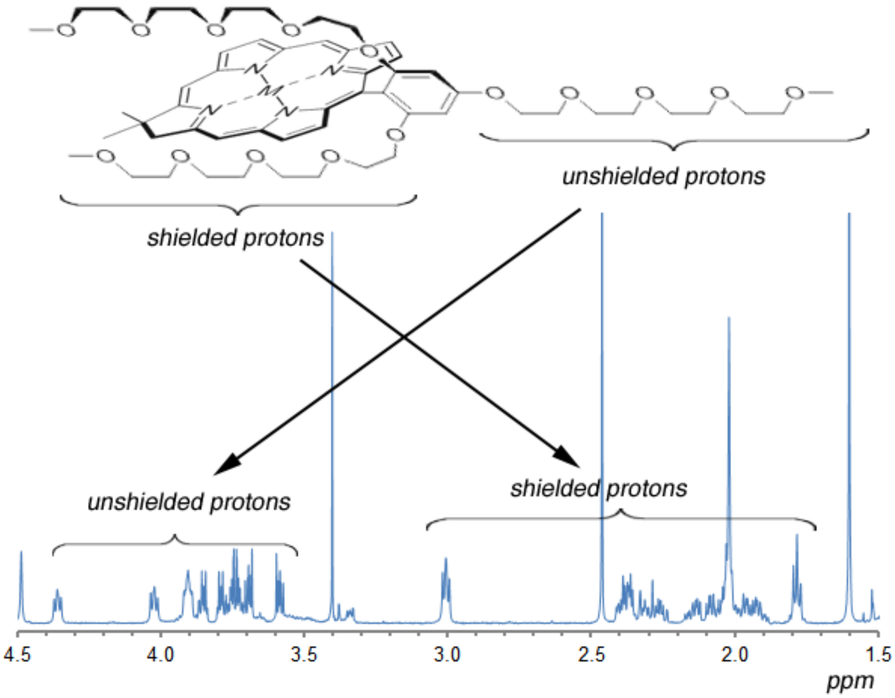


Figure S3. ^{1}H NMR spectrum (in $CDCl_3$ at room temperature) of **10** and illustrative representation of shielded and unshielded protons. Note: the scheme only represents the relative orientation of the chlorin and the PEG moiety and does not reflect the actual size and conformation.

6. Flow Cytometry Data

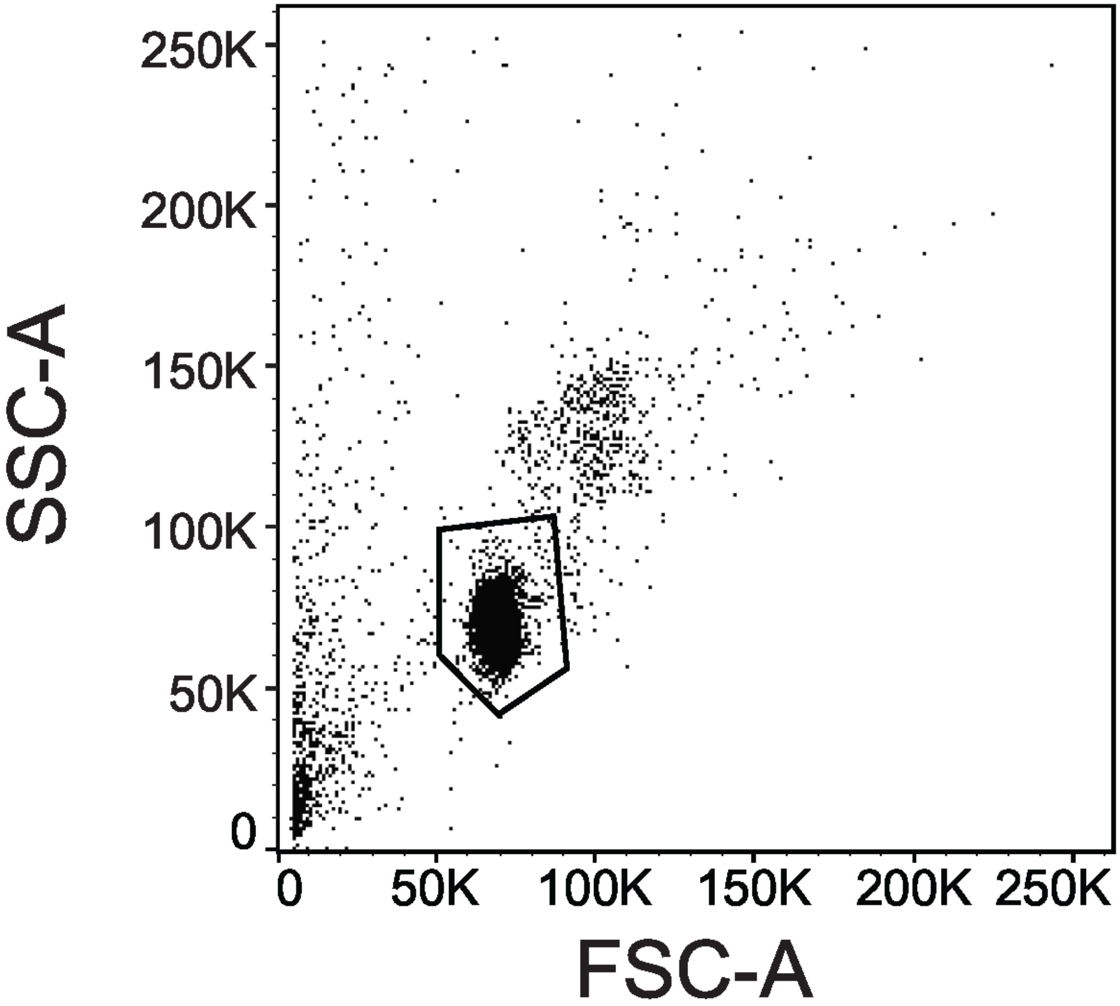


Figure S4. Dot plot of side-scattered light (SSC) versus forward-scattered light (FSC), which provide a measure of granularity and size, respectively. Selection of beads for subsequent analyses was achieved by gating around the major population of single beads, as shown.

7. References

S1 J. T. Wiltshire and G. G. Qiao, *J. Polym. Sci.: Part A: Polym. Chem.*, 2009, **47**, 1485–1498.

S2 E. H. H. Wong, M. H. Stenzel, T. Junkers and C. Barner-Kowollik, *Macromolecules*, 2010, **43**, 3785–3793.

S3 C.-H. Lee and J. S. Lindsey, *Tetrahedron*, 1994, **50**, 11427–11440.

S4 M. Ptaszek, D. Lahaye, M. Krayer, C. Muthiah and J. S. Lindsey, *J. Org. Chem.*, 2010, **75**, 1659–1673.

S5 O. Mass, M. Ptaszek, M. Taniguchi, J. R. Diers, H. L. Kee, D. F. Bocian, D. Holten and J. S. Lindsey, *J. Org. Chem.*, 2009, **74**, 5276–5289.

S6 O. Mass, D. R. Pandithavidana, M. Ptaszek, K. Santiago, J. W. Springer, J. Jiao, Q. Tang, C. Kirmaier, D. F. Bocian, D. Holten and J. S. Lindsey, *New J. Chem.*, 2011, **35**, 2671–2690.

S7 B. J. Littler, M. A. Miller, C.-H. Hung, R. W. Wagner, D. F. O'Shea, P. D. Boyle and J. S. Lindsey, *J. Org. Chem.*, 1999, **64**, 1391–1396.

S8 M. Ptaszek, B. E. McDowell, M. Taniguchi, H.-J. Kim and J. S. Lindsey, *Tetrahedron*, 2007, **63**, 3826–3839.

S9 H. L. Kee, C. Kirmaier, Q. Tang, J. R. Diers, C. Muthiah, M. Taniguchi, J. K. Laha, M. Ptaszek, J. S. Lindsey, D. F. Bocian and D. Holten, *Photochem. Photobiol.*, 2007, **83**, 1110–1124.

S10 J. P. Taygerly, L. M. Miller, A. Yee and E. A. Peterson, *Green Chem.*, 2012, **14**, 3020–3025.

8. Spectra

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Ambient temperature
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Mercury-400BB "ncsumerc400"

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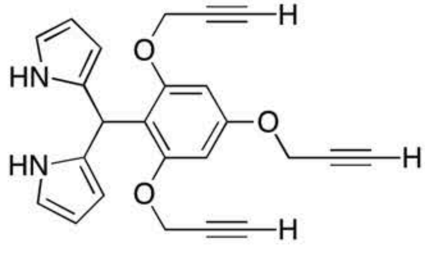
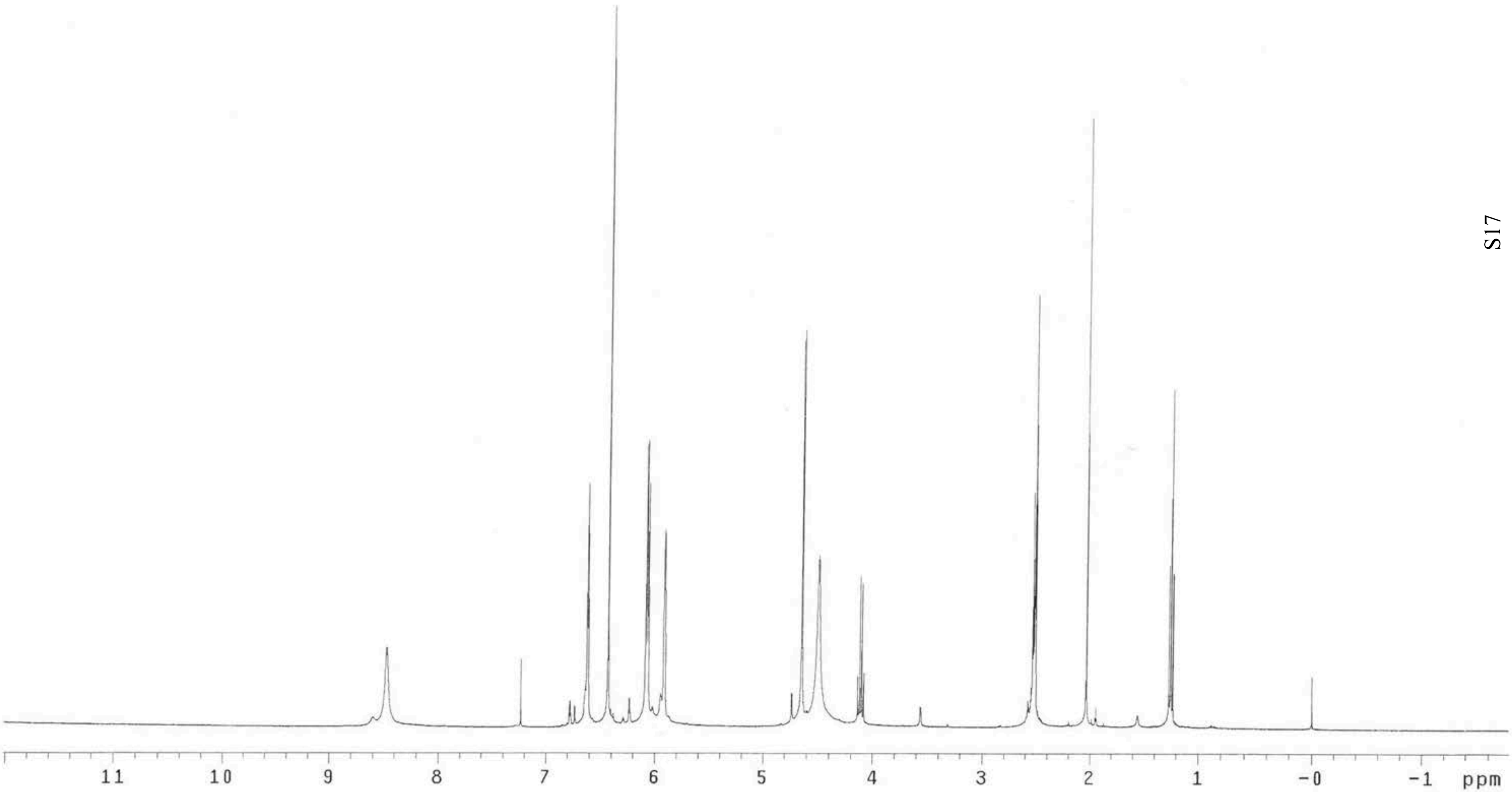


2a



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DATA PROCESSING
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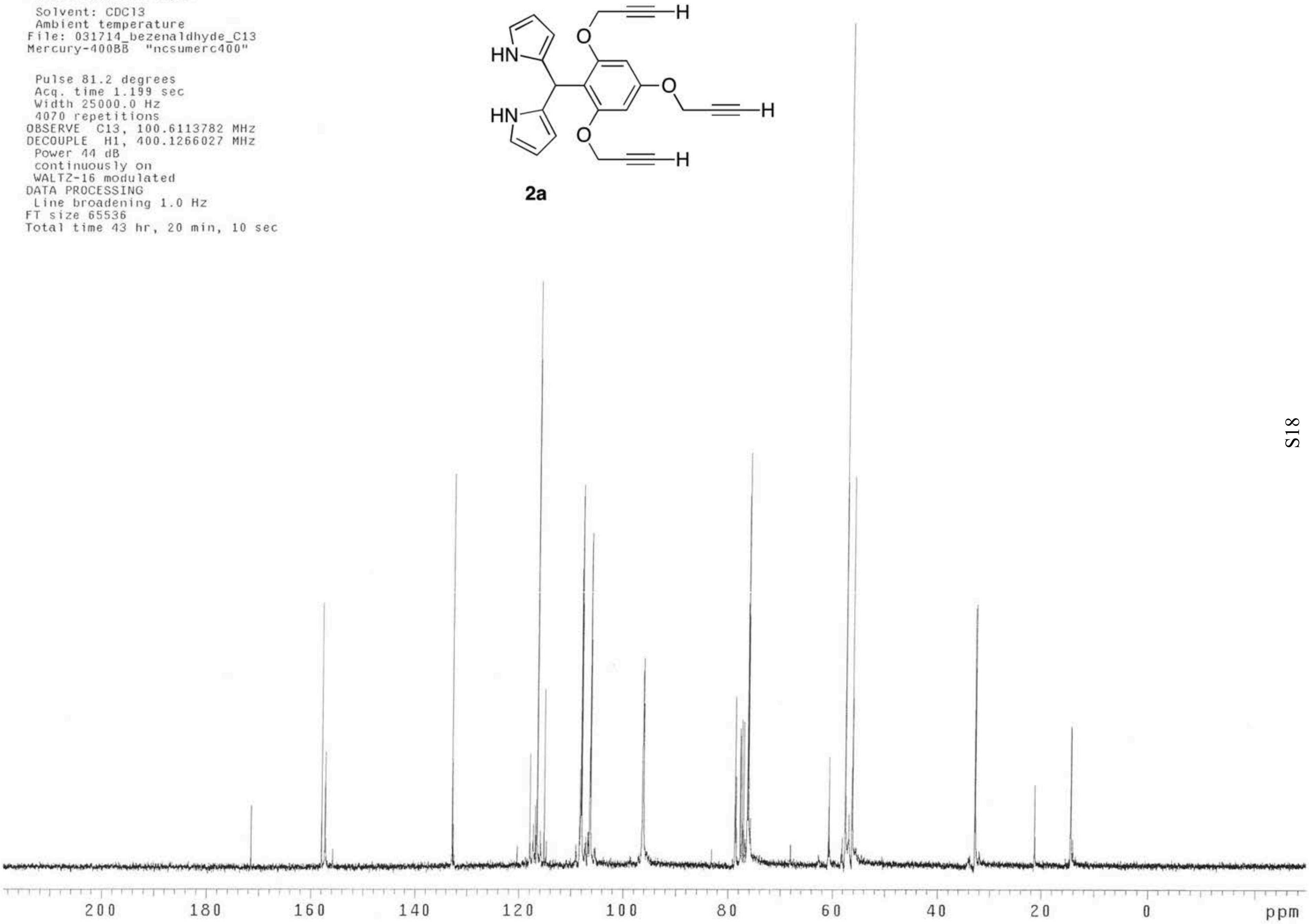

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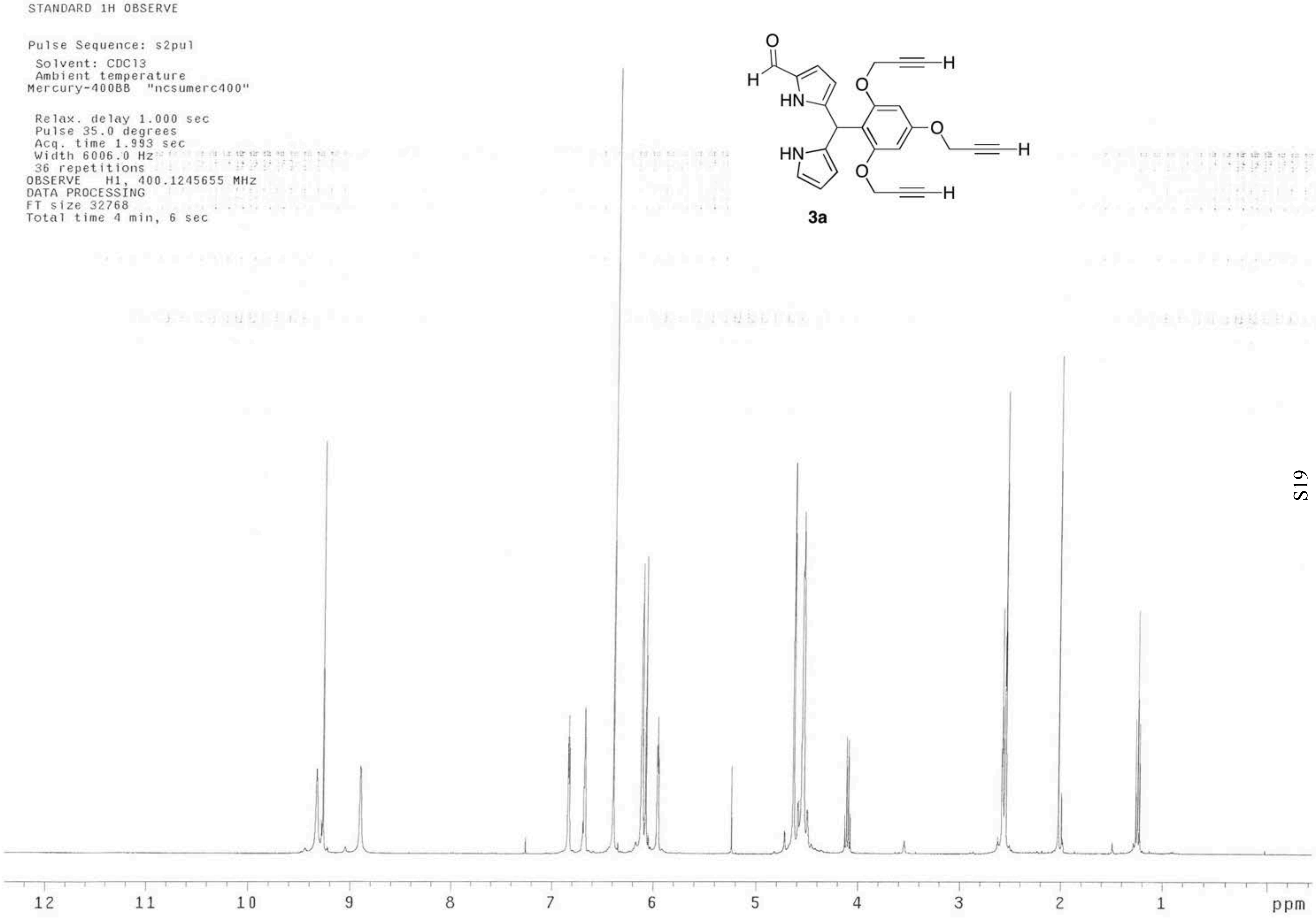

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OBSERVE   H1, 400.1245655 MHz
DATA PROCESSING
FT size 32768
Total time 4 min, 6 sec
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3a

13C OBSERVE

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Ambient temperature
Mercury-400BB "ncsumerc400"

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OBSERVE C13, 100.6114189 MHz
DECOUPLE H1, 400.1266027 MHz
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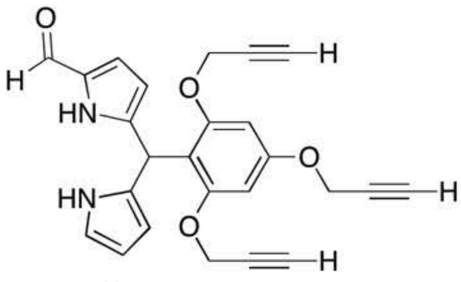
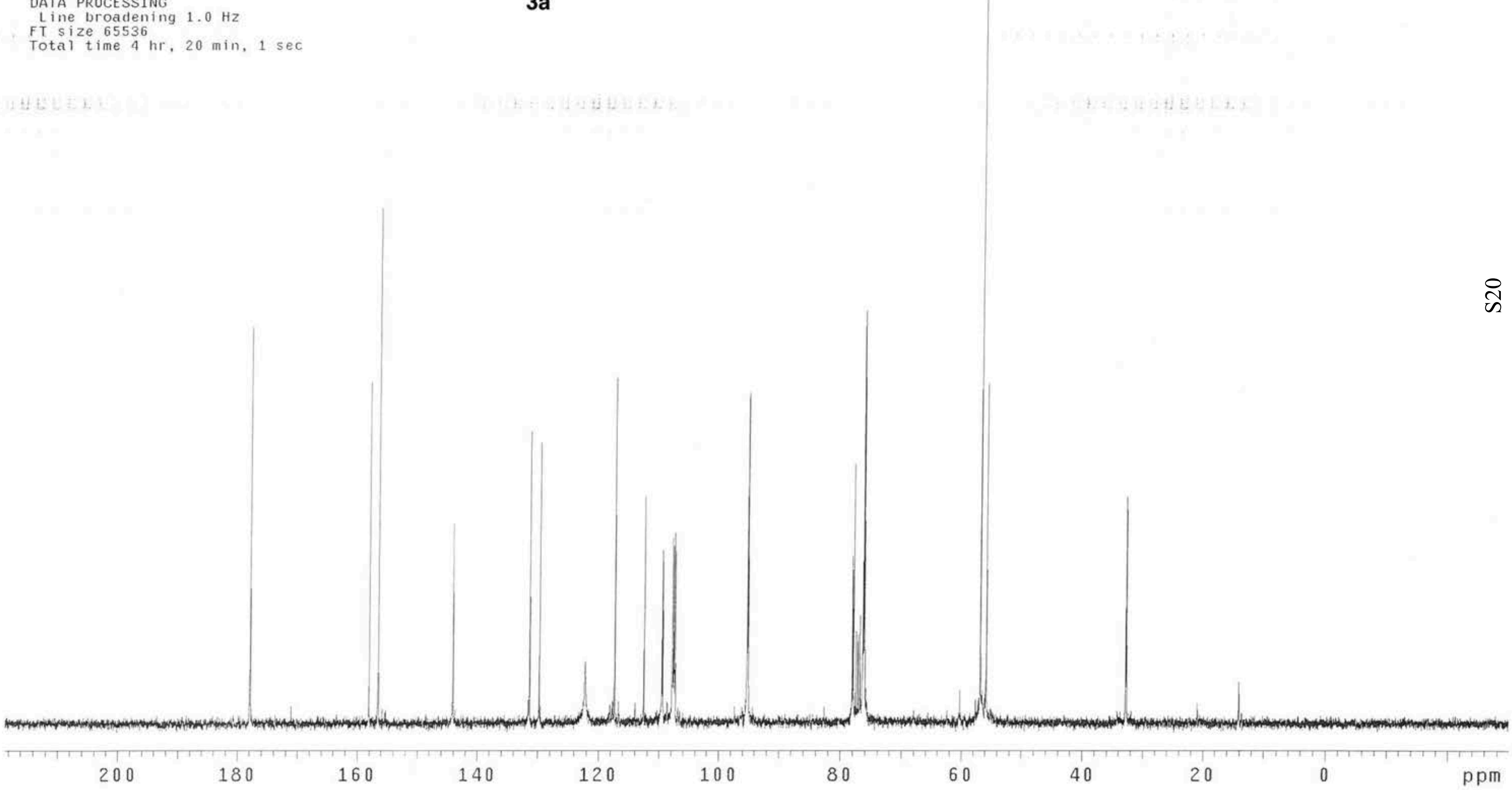


3a



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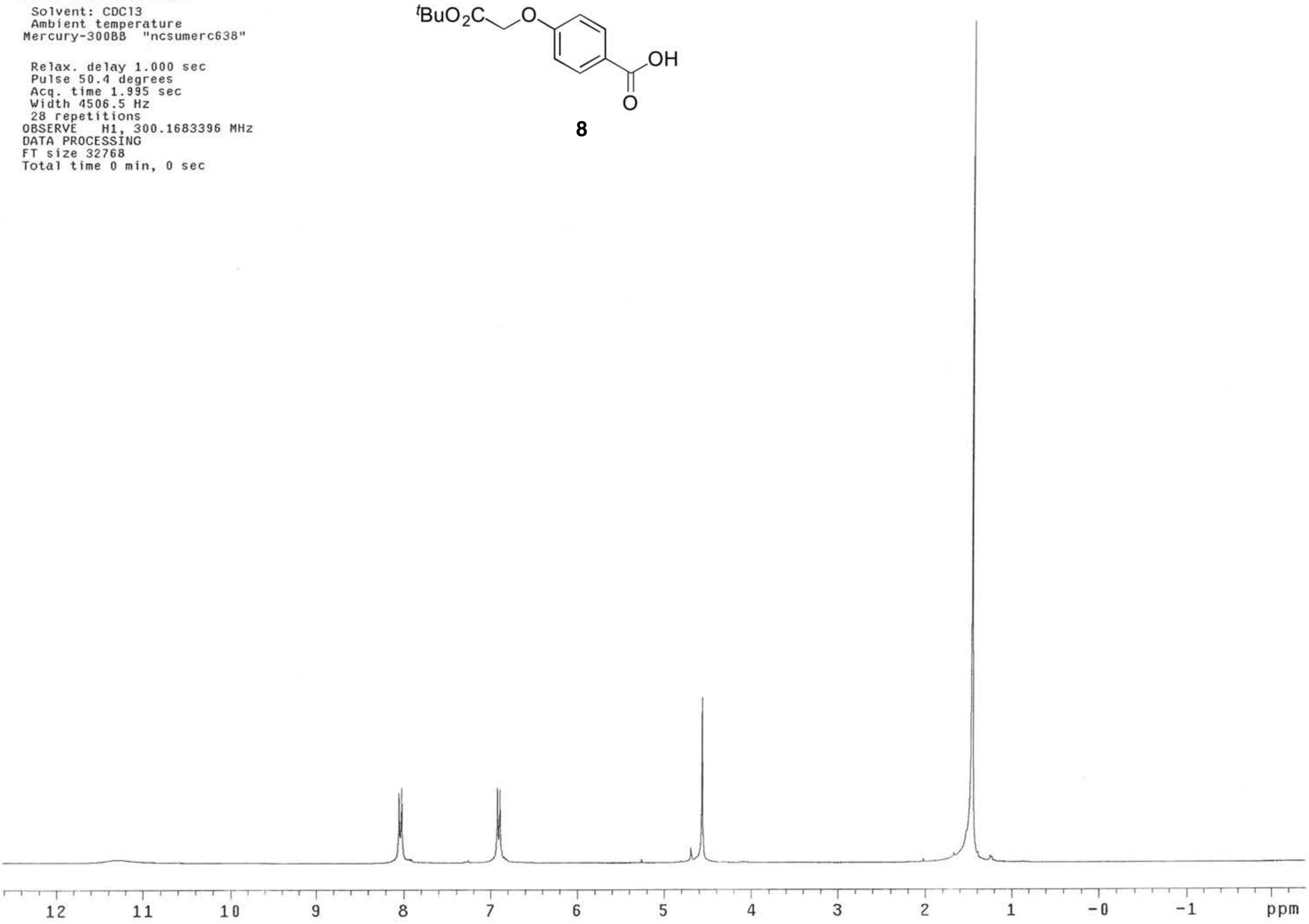

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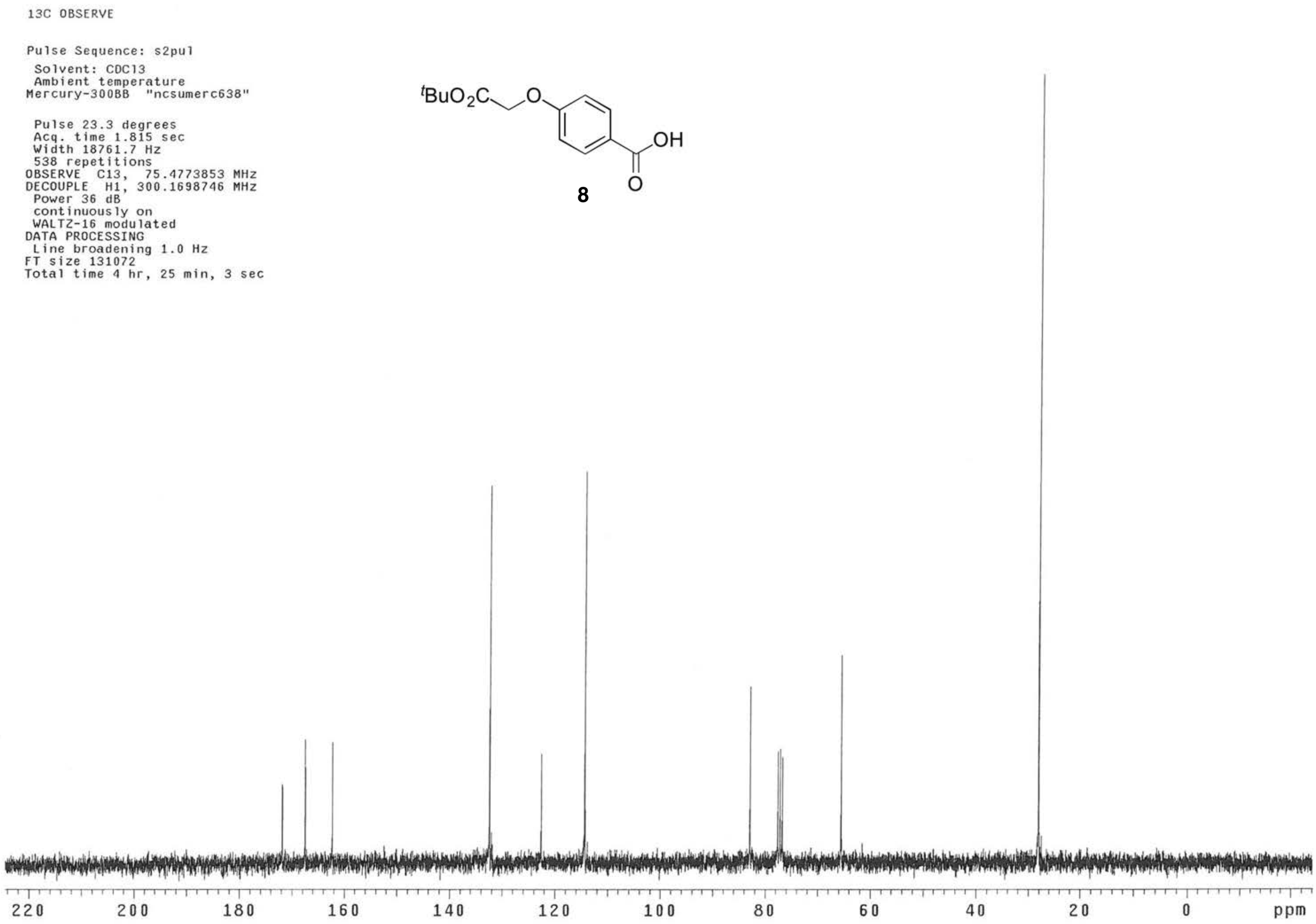

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13C OBSERVE

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DECOUPLE  H1, 300.1698746 MHz
 Power 36 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 131072
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8

STANDARD 1H OBSERVE

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Solvent: CDCl3
Ambient temperature
Mercury-400BB "ncsumerc400"

Relax. delay 1.000 sec
Pulse 35.0 degrees
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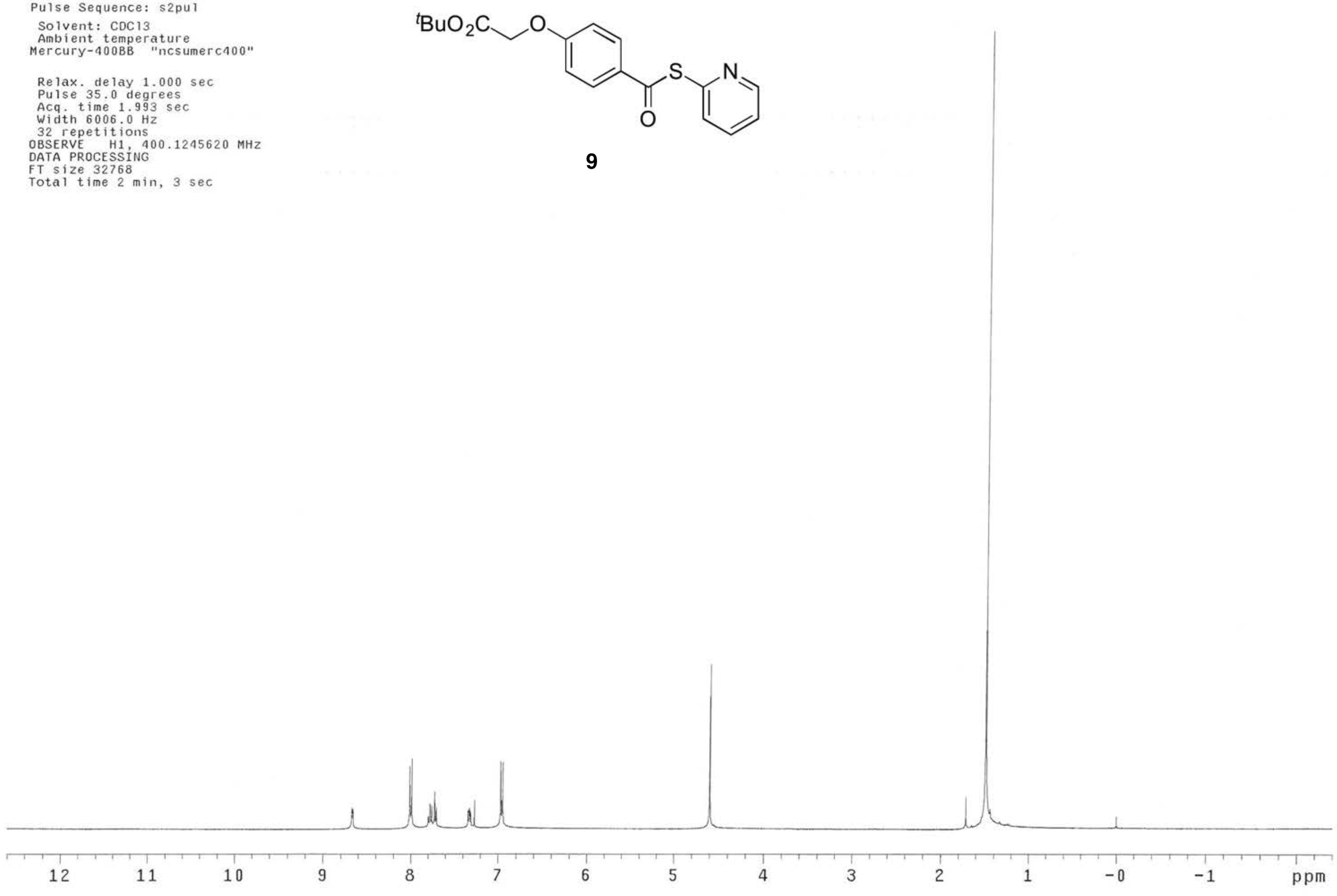
Total time 2 min, 3 sec


9

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 696 repetitions
OBSERVE  C13, 100.6113899 MHz
DECOUPLE  H1, 400.1266027 MHz
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 continuously on
 WALTZ-16 modulated
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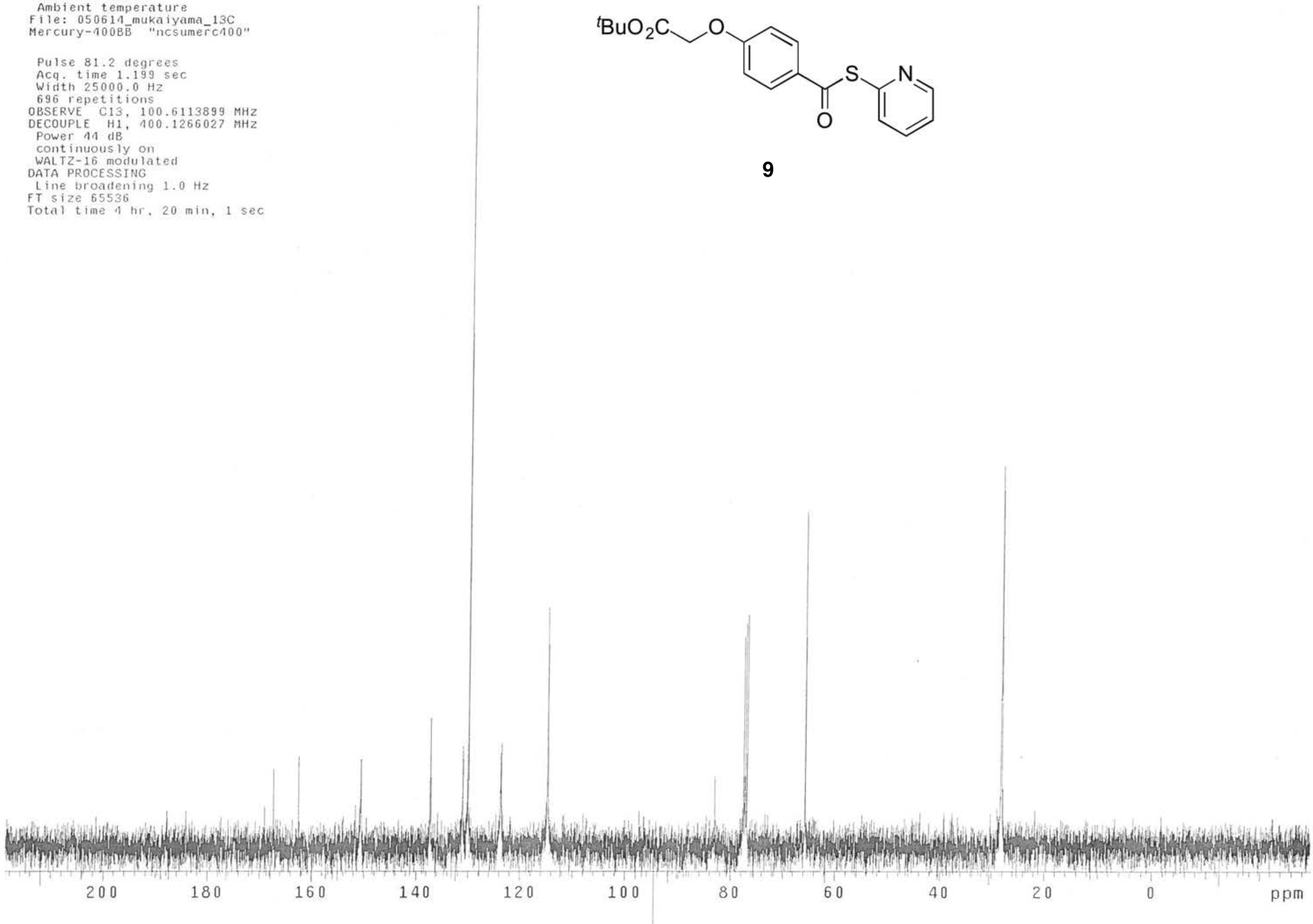

9

STANDARD 1H OBSERVE

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128 repetitions
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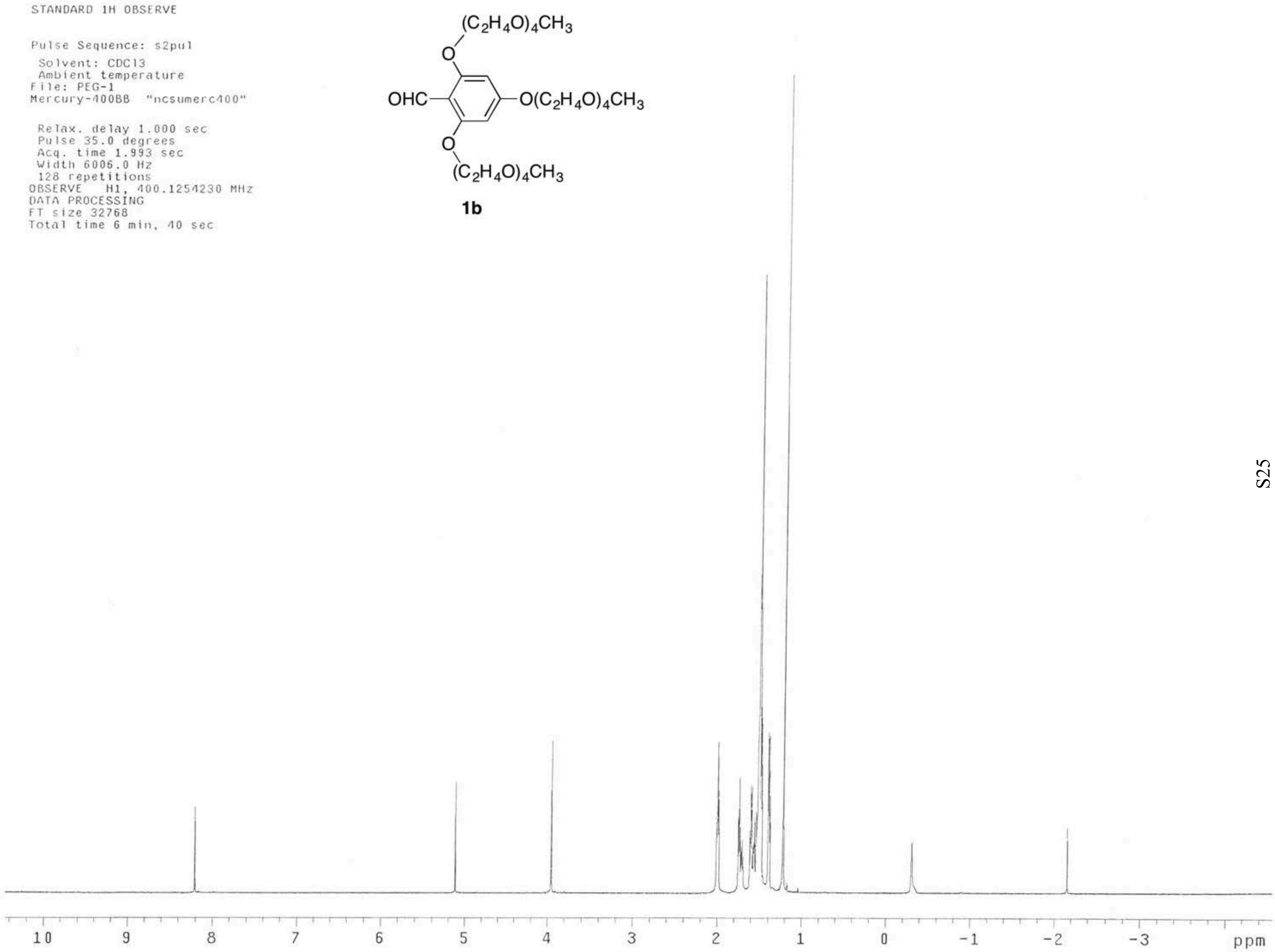
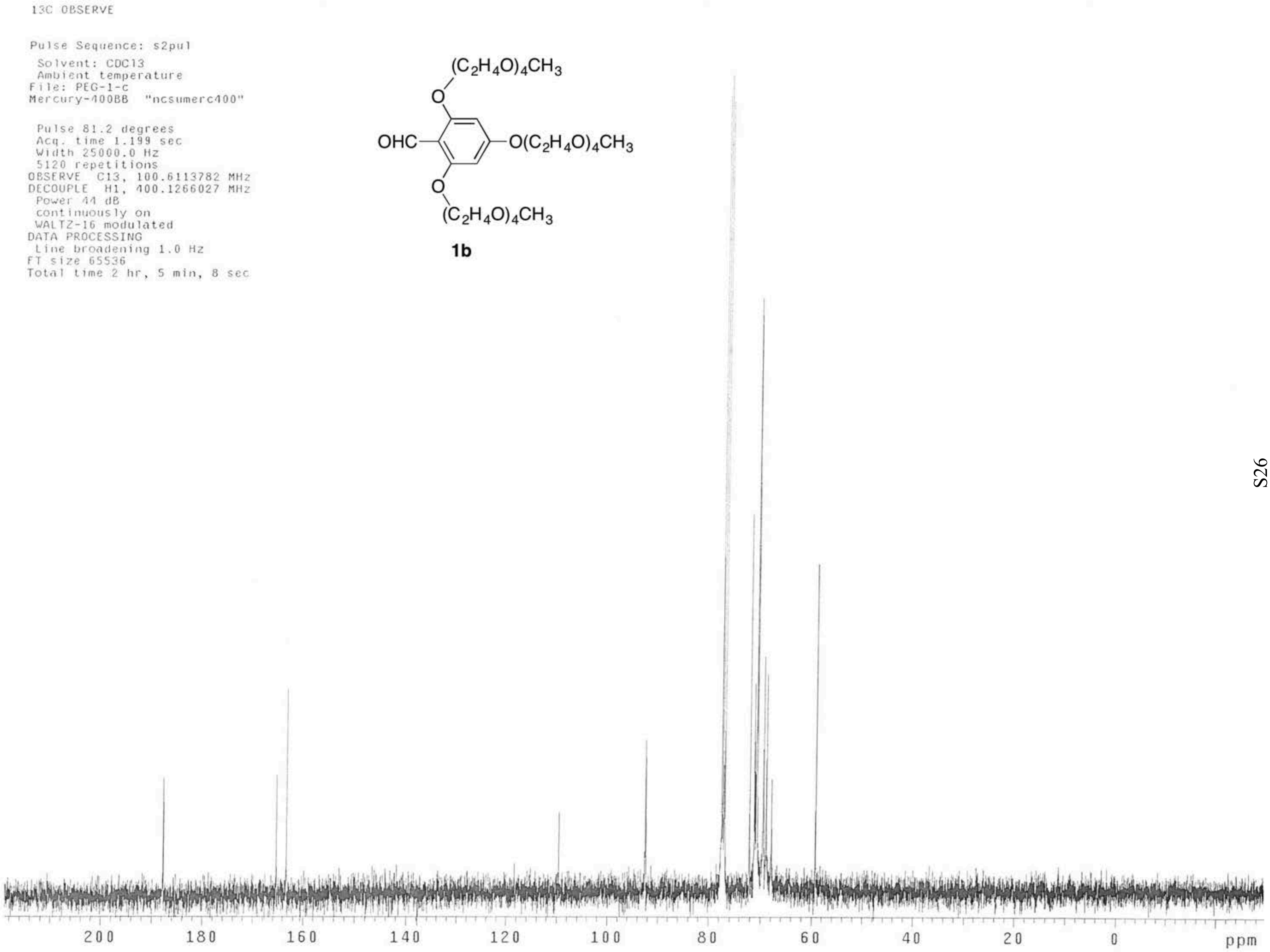
DATA PROCESSING
FT size 32768
Total time 6 min, 40 sec



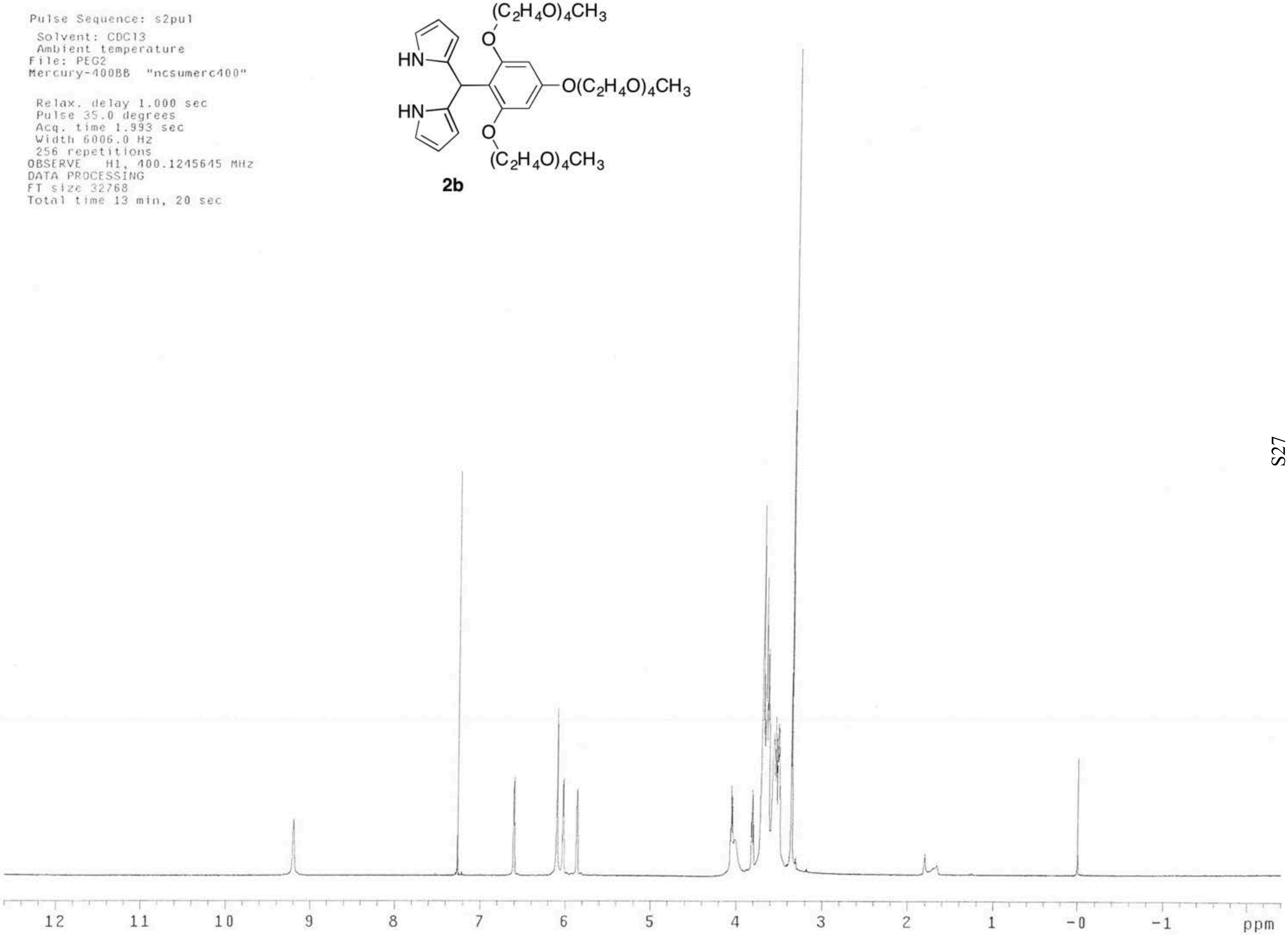
1b



```
13C OBSERVE

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
File: PEG-1-c
Mercury-400BB  "ncsumerc400"

 Pulse 81.2 degrees
 Acq. time 1.199 sec
 Width 25000.0 Hz
 5120 repetitions
OBSERVE  C13, 100.6113782 MHz
DECOUPLE  H1, 400.1266027 MHz
 Power 44 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 2 hr, 5 min, 8 sec
```

1b

```
STANDARD 1H OBSERVE

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
File: PEG2
Mercury-400BB  "ncsumerc400"

 Relax. delay 1.000 sec
 Pulse 35.0 degrees
 Acq. time 1.993 sec
 Width 6006.0 Hz
 256 repetitions
OBSERVE   H1, 400.1245645 MHz
DATA PROCESSING
FT size 32768
Total time 13 min, 20 sec
```

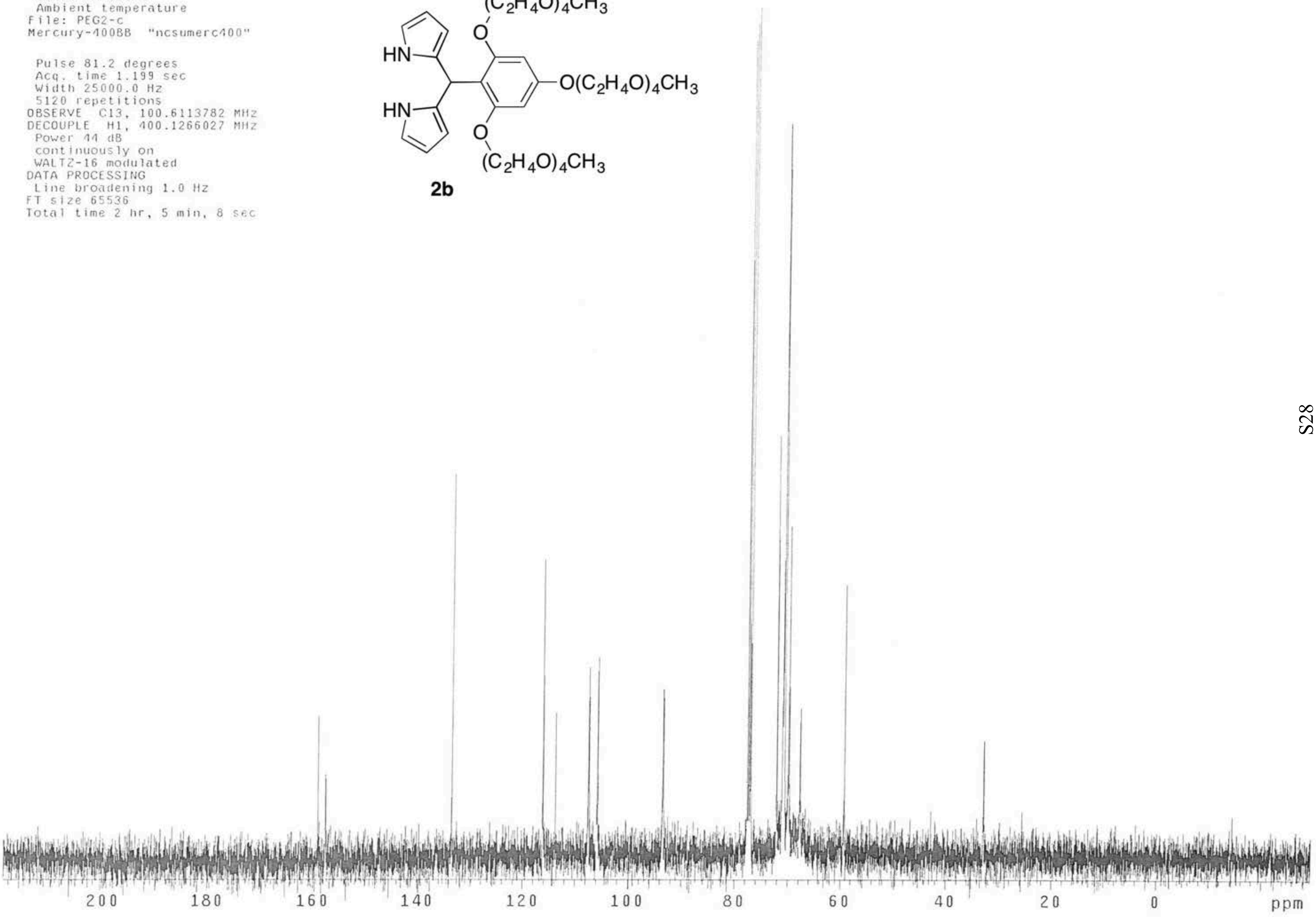


2b

13C OBSERVE

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: PEG2-c
Mercury-400BB "ncsumerc400"

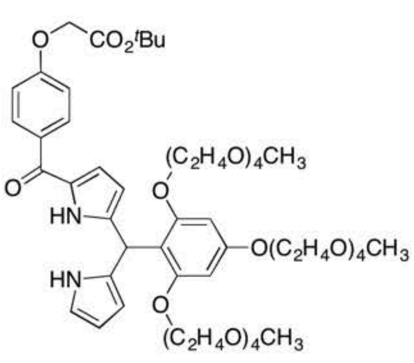
Pulse 81.2 degrees
Acq. time 1.199 sec
Width 25000.0 Hz
5120 repetitions
OBSERVE C13, 100.6113782 MHz
DECOUPLE H1, 400.1266027 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 2 hr, 5 min, 8 sec


2b

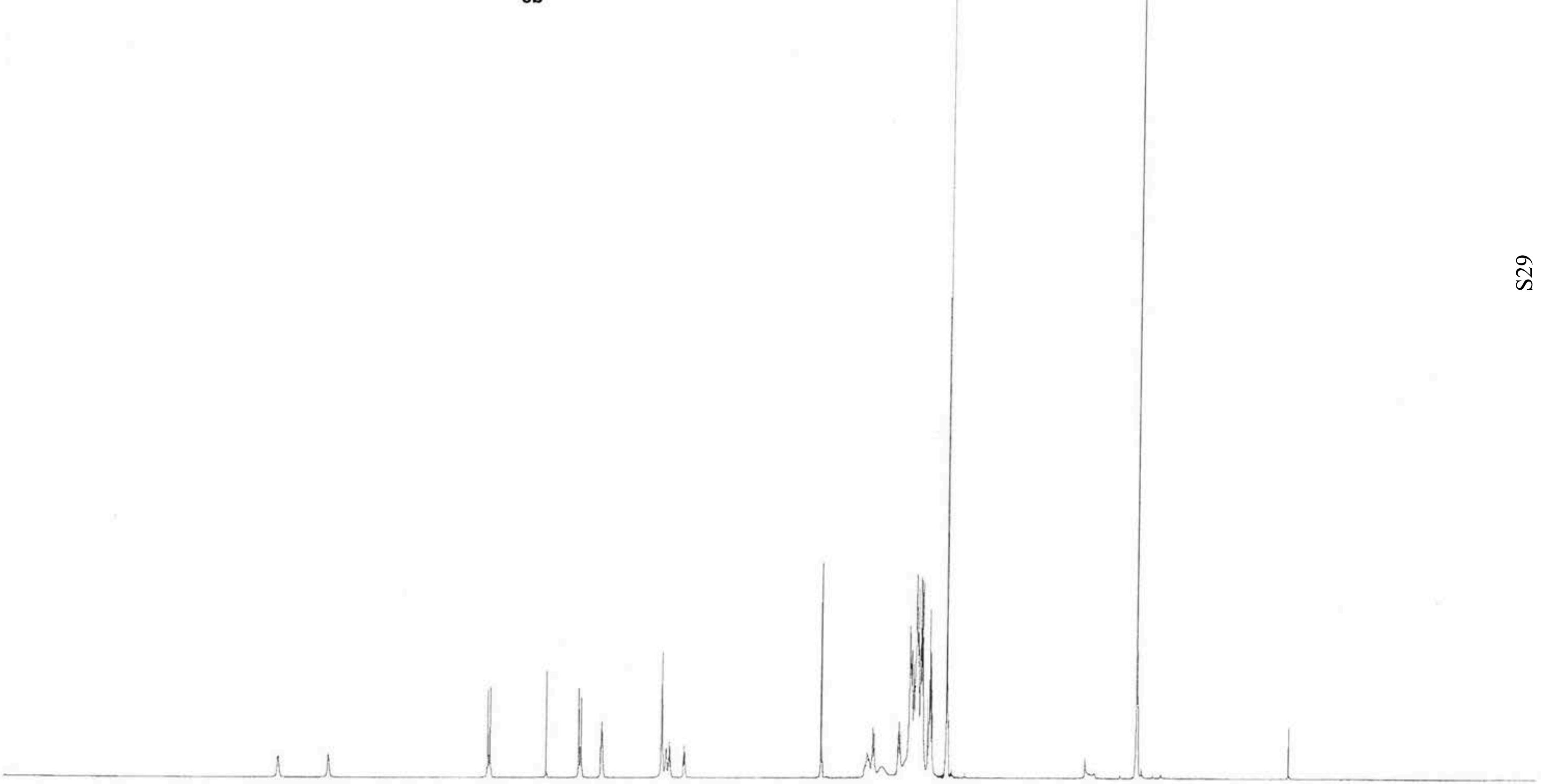
STANDARD 1H OBSERVE

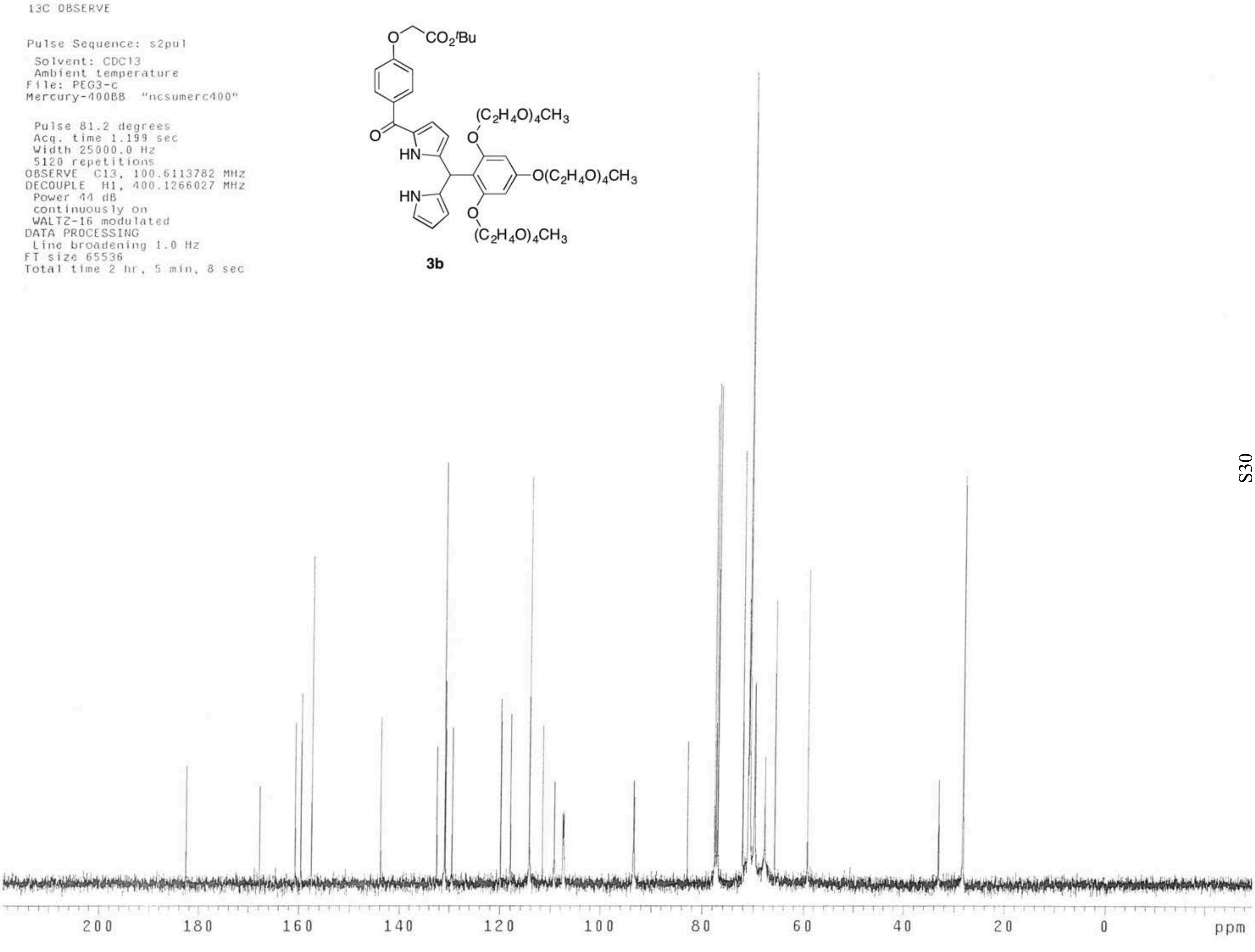
Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: PEG3
Mercury-400BB "ncsumerc400"

Relax. delay 1.000 sec
Pulse 35.0 degrees
Acq. time 1.993 sec
Width 6006.0 Hz
128 repetitions
OBSERVE H1, 400.1245609 MHz
DATA PROCESSING
FT size 32768
Total time 6 min, 40 sec



3b

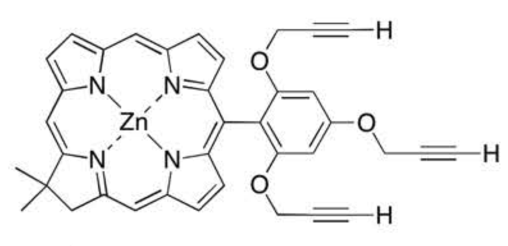




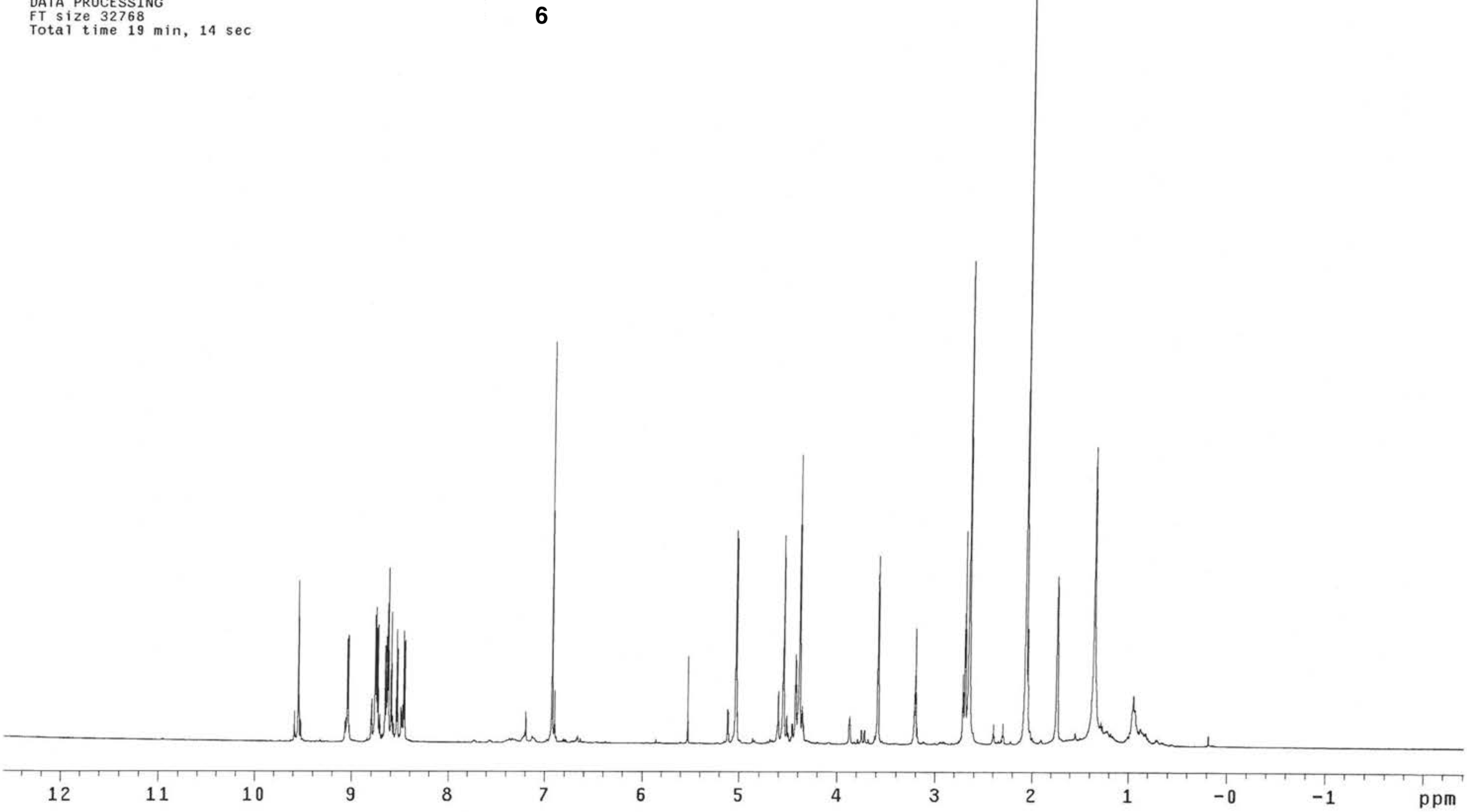
3b

```
13C OBSERVE

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
File: PEG3-c
Mercury-400BB  "ncsumerc400"

 Pulse 81.2 degrees
 Acq. time 1.199 sec
 Width 25000.0 Hz
 5120 repetitions
OBSERVE  C13, 100.6113782 MHz
DECOUPLE  H1, 400.1266027 MHz
 Power 44 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 2 hr, 5 min, 8 sec
```

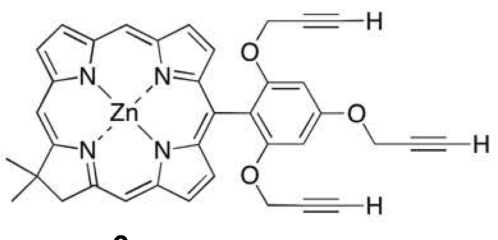
```
STANDARD 1H OBSERVE

Pulse Sequence: s2pul
 Solvent: THF
 Ambient temperature
Mercury-400BB  "ncsumerc400"

 Relax. delay 1.000 sec
 Pulse 35.0 degrees
 Acq. time 1.993 sec
 Width 6006.0 Hz
 172 repetitions
OBSERVE   H1, 400.1260306 MHz
DATA PROCESSING
FT size 32768
Total time 19 min, 14 sec
```



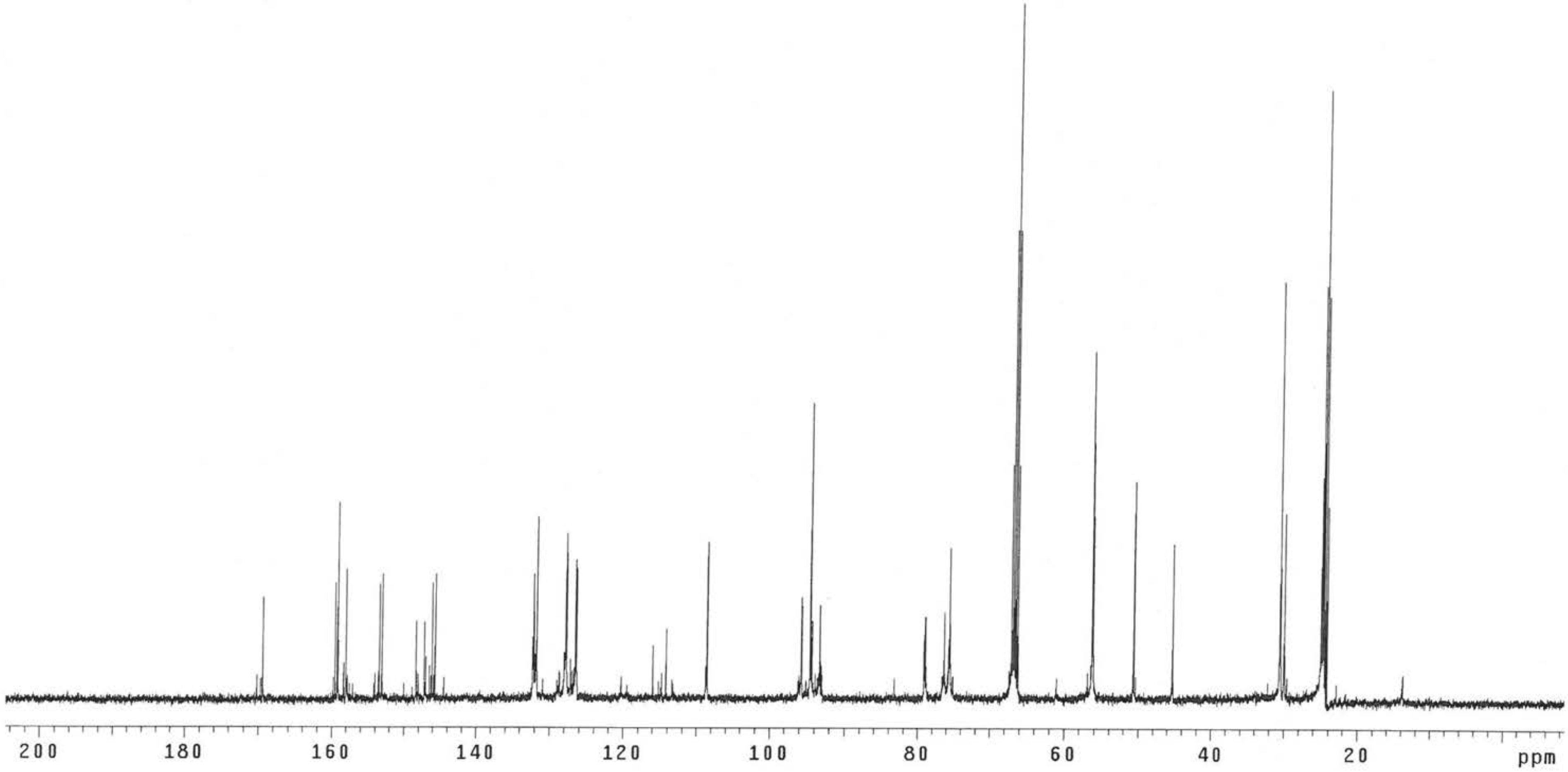
6



```
13C OBSERVE

Pulse Sequence: s2pul
 Solvent: thf
 Ambient temperature
Mercury-400BB  "ncsumerc400"

 Pulse 81.2 degrees
 Acq. time 1.199 sec
 Width 25000.0 Hz
 5696 repetitions
OBSERVE  C13, 100.6117464 MHz
DECOUPLE  H1, 400.1280672 MHz
 Power 44 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 43 hr, 20 min, 10 sec
```

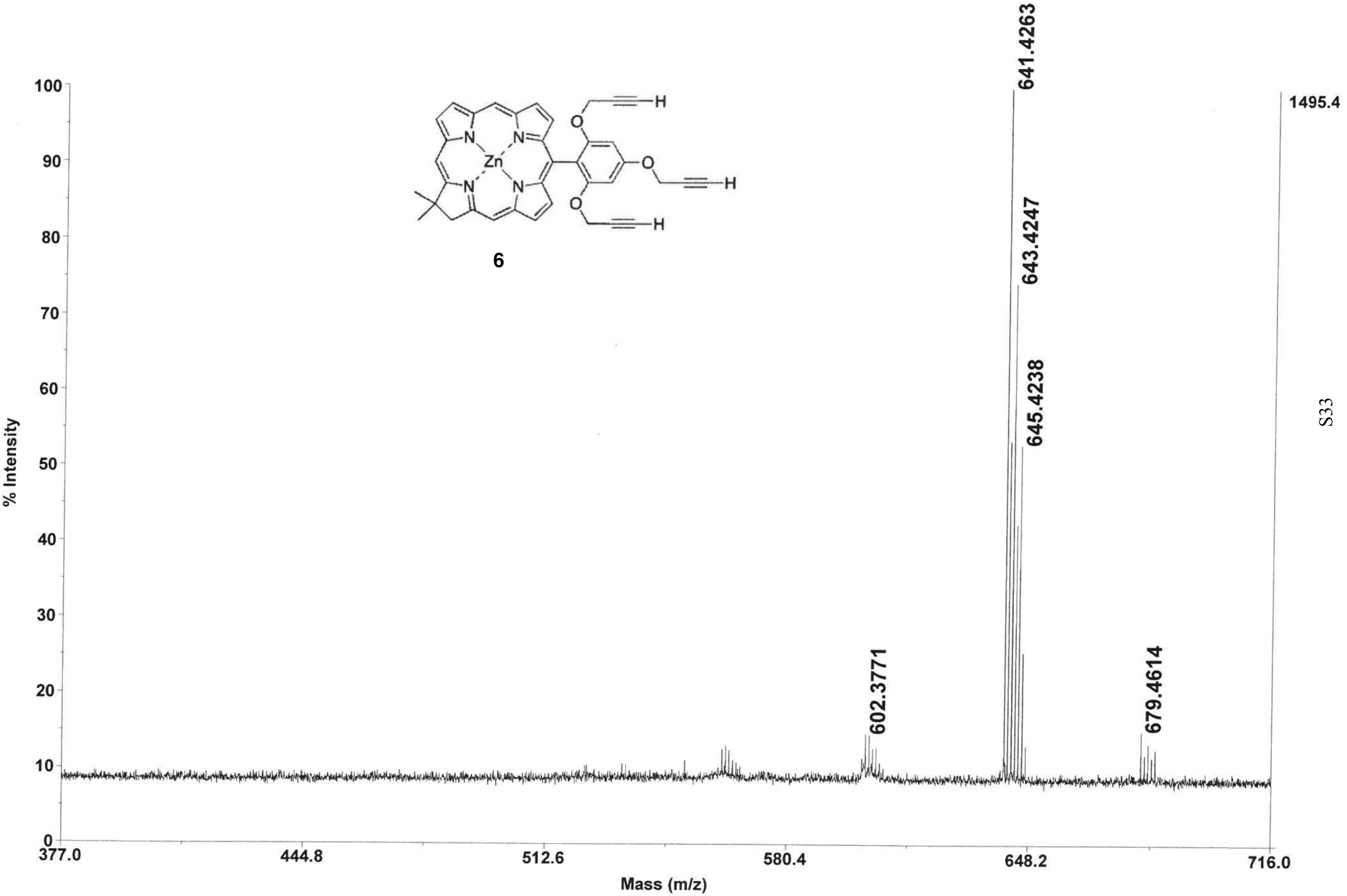


6



AB Sciex TOF/TOF™ Series Explorer™ 72098

TOF/TOF™ Reflector Spec #1 MC[BP = 641.4, 1495]



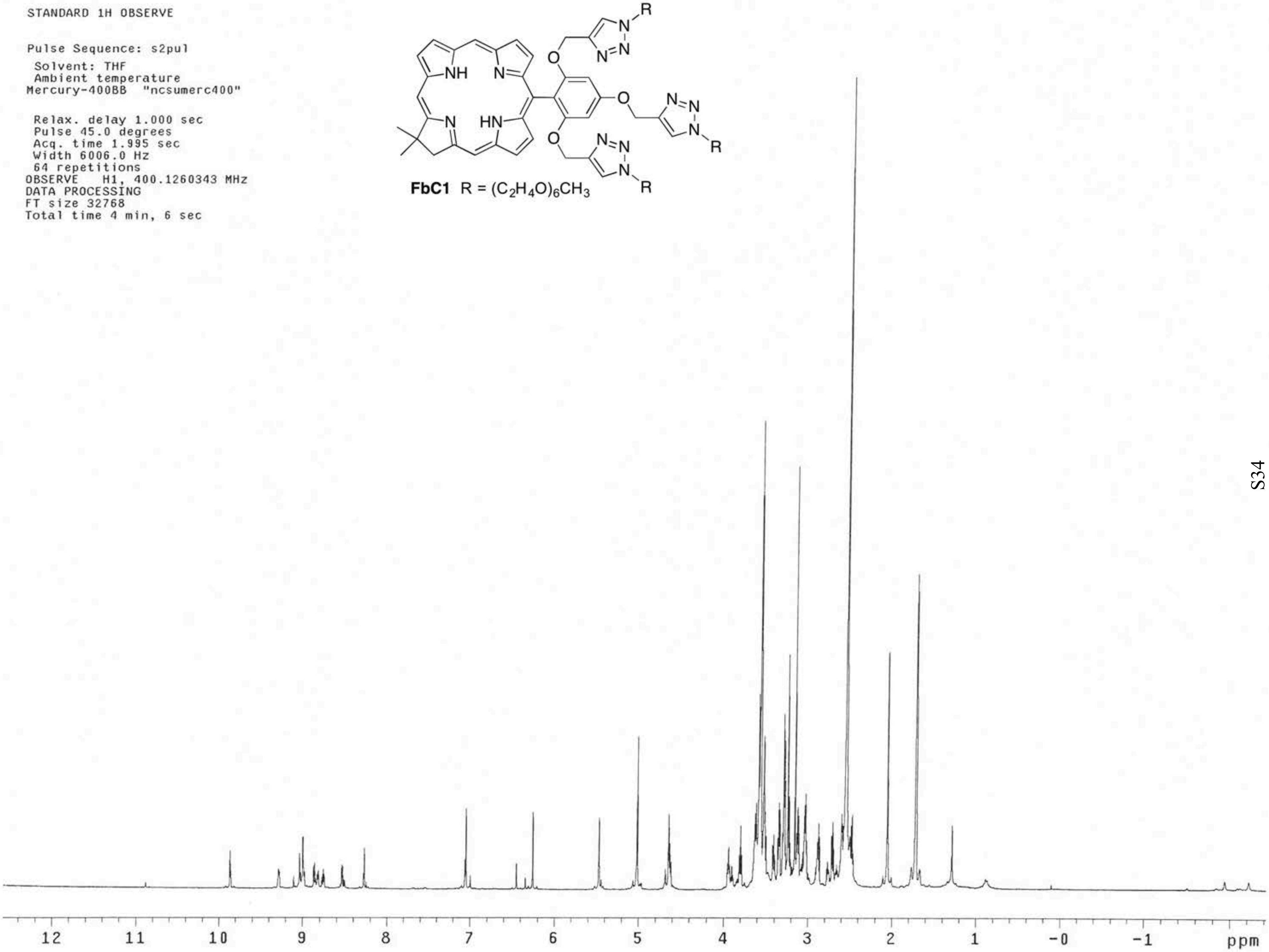
C:\AB SCIEX\TOFTOF Data\ExportT2D\User Project 1\Lindsey\Mengran\041216\B1_MS.t2d

Printed: 18:46, April 12, 2016

STANDARD 1H OBSERVE

Pulse Sequence: s2pul
Solvent: THF
Ambient temperature
Mercury-400BB "ncsumerc400"

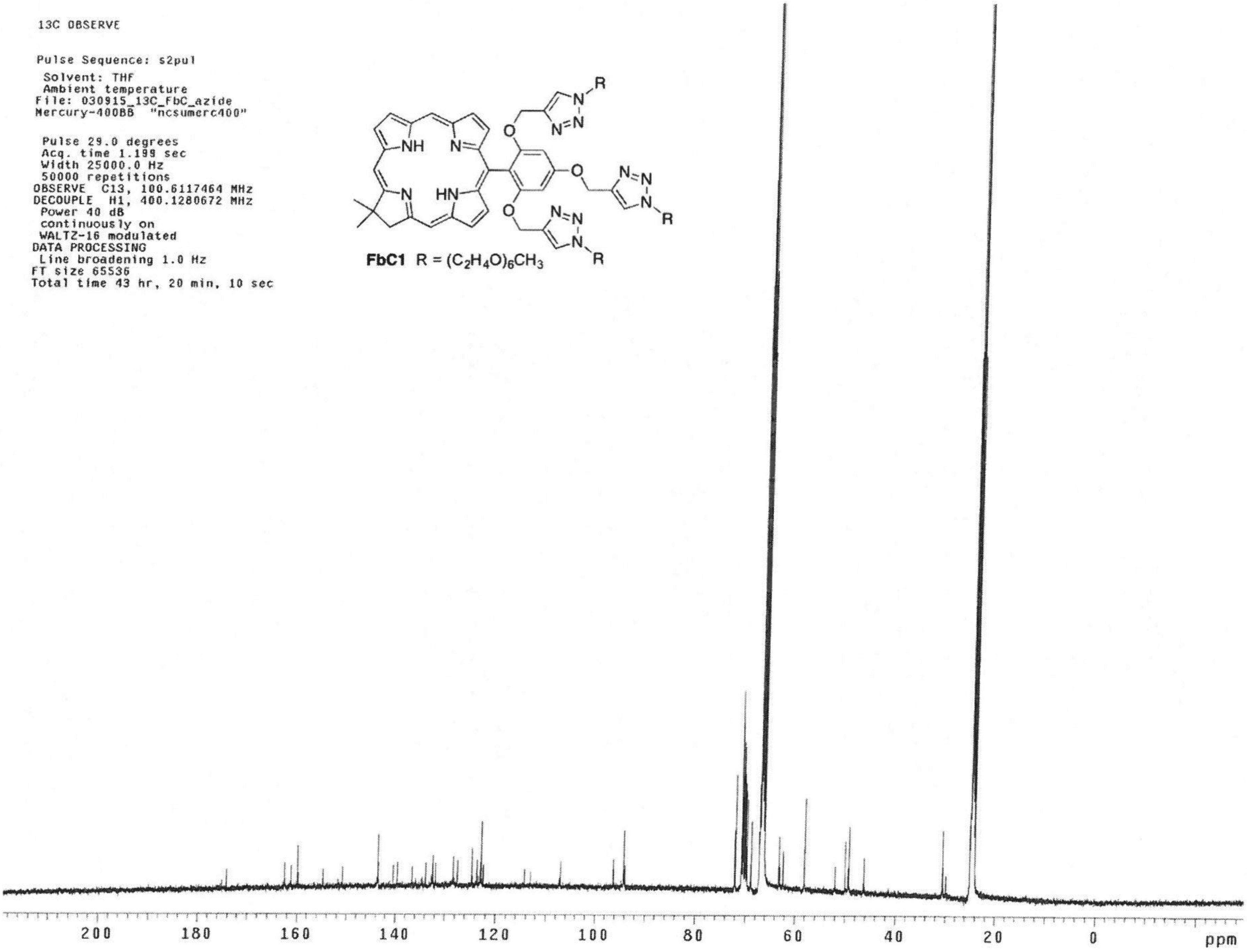
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.995 sec
Width 6006.0 Hz
64 repetitions
OBSERVE H1, 400.1260343 MHz
DATA PROCESSING
FT size 32768
Total time 4 min, 6 sec



FbC1 R = $(C_2H_4O)_6CH_3$

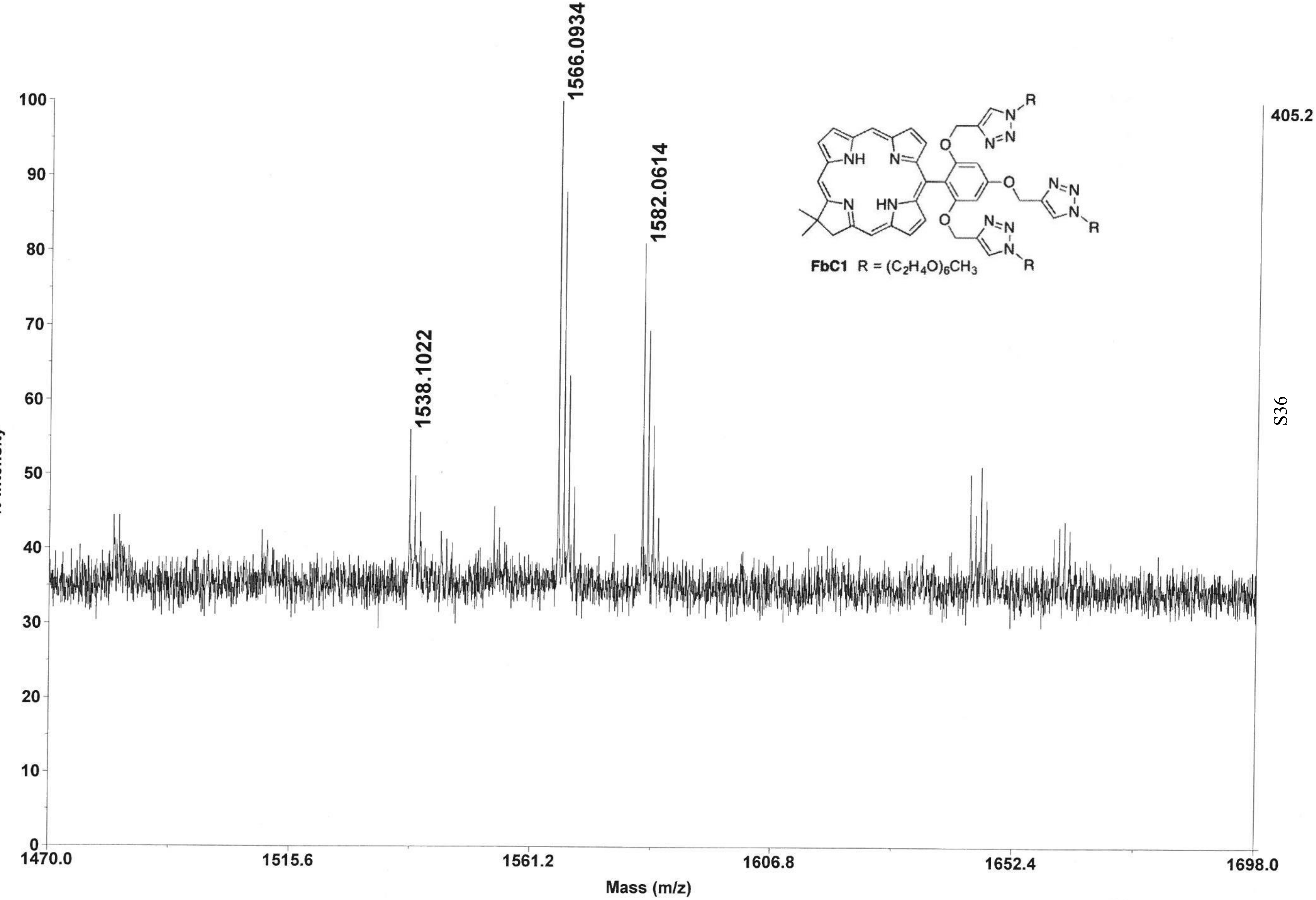
```
13C OBSERVE

Pulse Sequence: s2pul
 Solvent: THF
 Ambient temperature
File: 030915_13C_FbC_azide
Mercury-400BB  "ncsumerc400"

 Pulse 29.0 degrees
 Acq. time 1.199 sec
 Width 25000.0 Hz
 50000 repetitions
OBSERVE  C13, 100.6117464 MHz
DECOUPLE  H1, 400.1280672 MHz
 Power 40 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 43 hr, 20 min, 10 sec
```

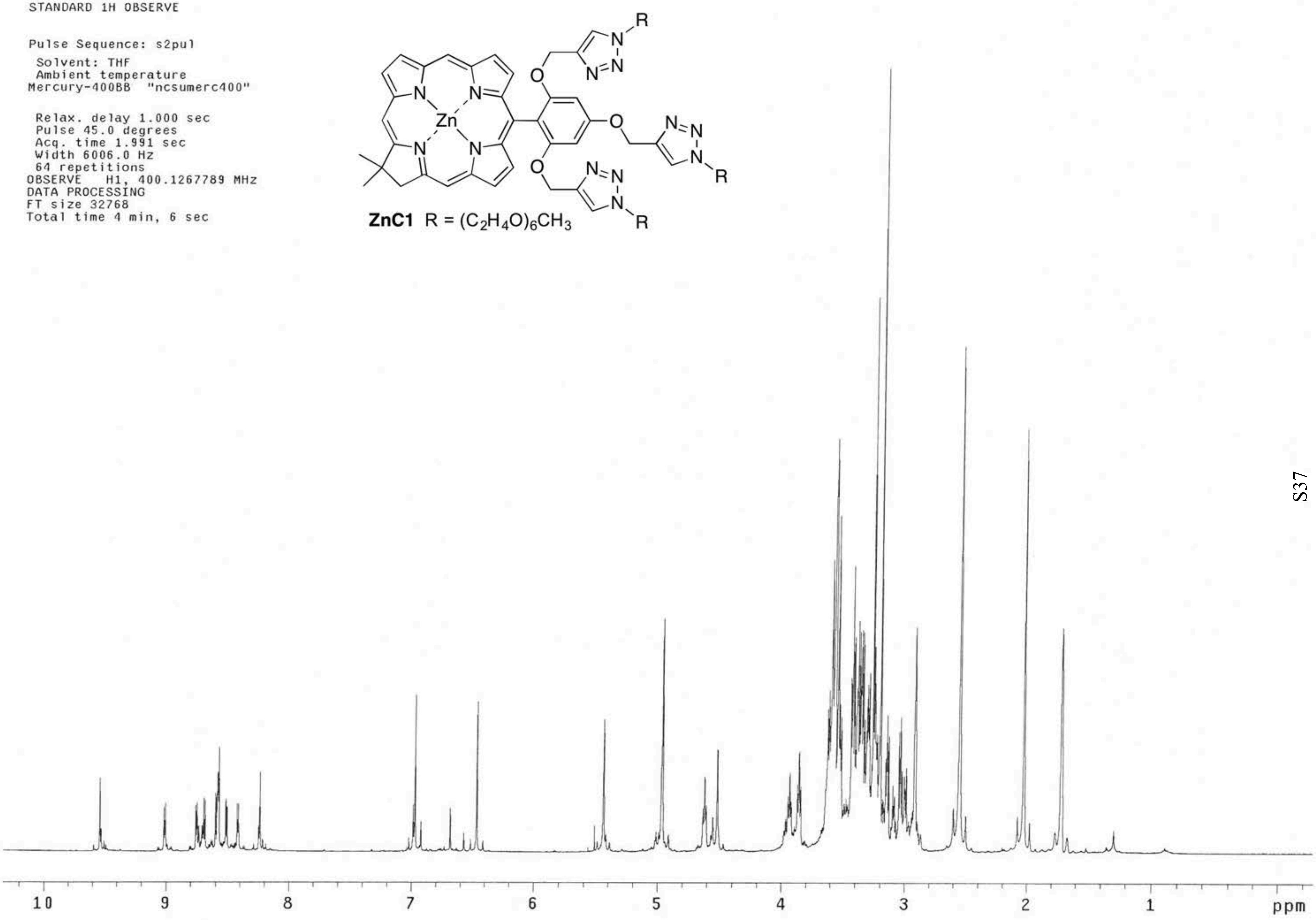
FbC1 R = $(C_2H_4O)_6CH_3$



AB Sciex TOF/TOF™ Series Explorer™ 72098

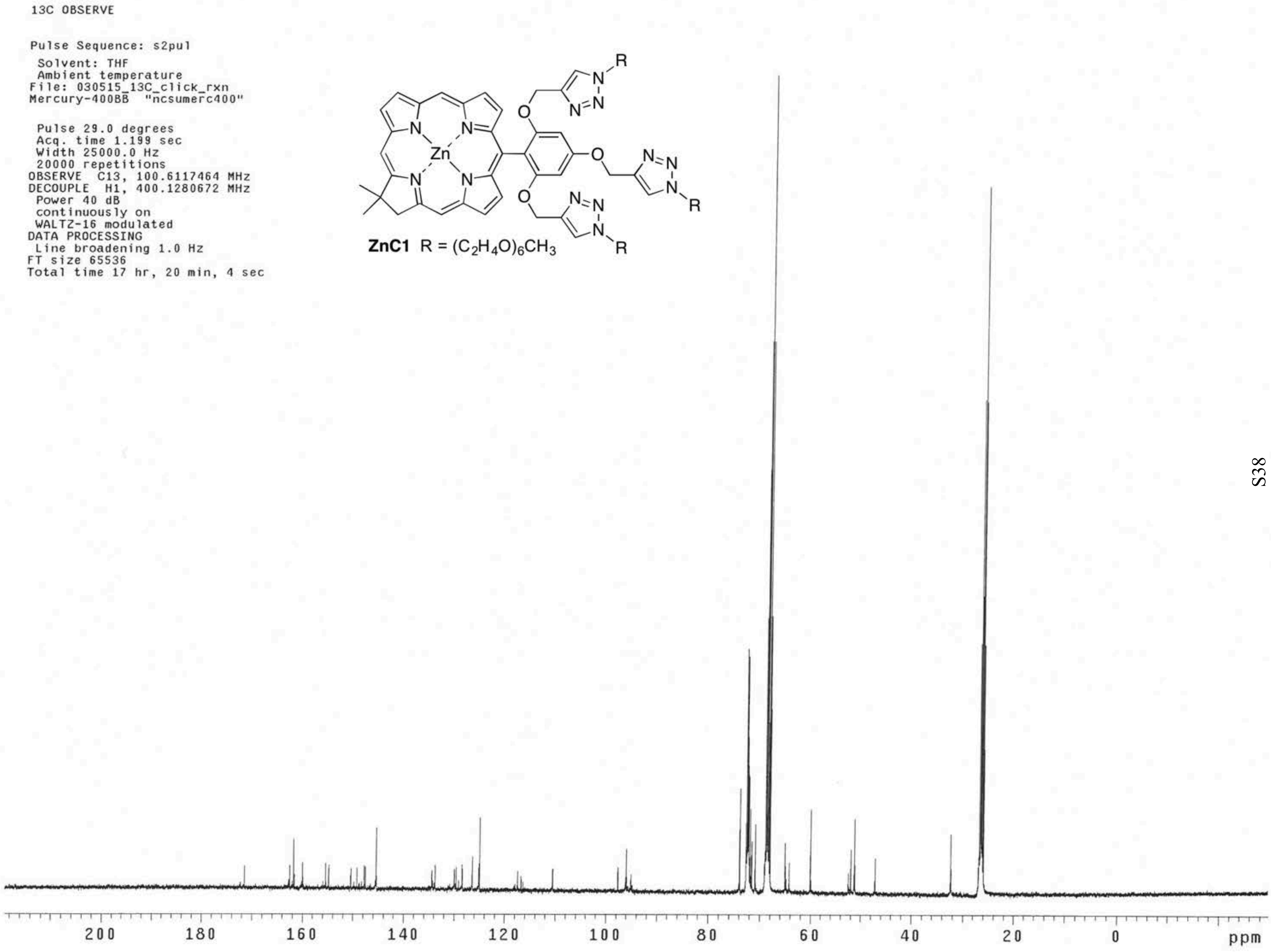
TOF/TOF™ Reflector Spec #1 MC[BP = 819.7, 7062]





```
STANDARD 1H OBSERVE

Pulse Sequence: s2pul
 Solvent: THF
 Ambient temperature
Mercury-400BB  "ncsumerc400"

 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.991 sec
 Width 6006.0 Hz
 64 repetitions
OBSERVE   H1, 400.1267789 MHz
DATA PROCESSING
FT size 32768
Total time 4 min, 6 sec
```

ZnC1 R = $(C_2H_4O)_6CH_3$

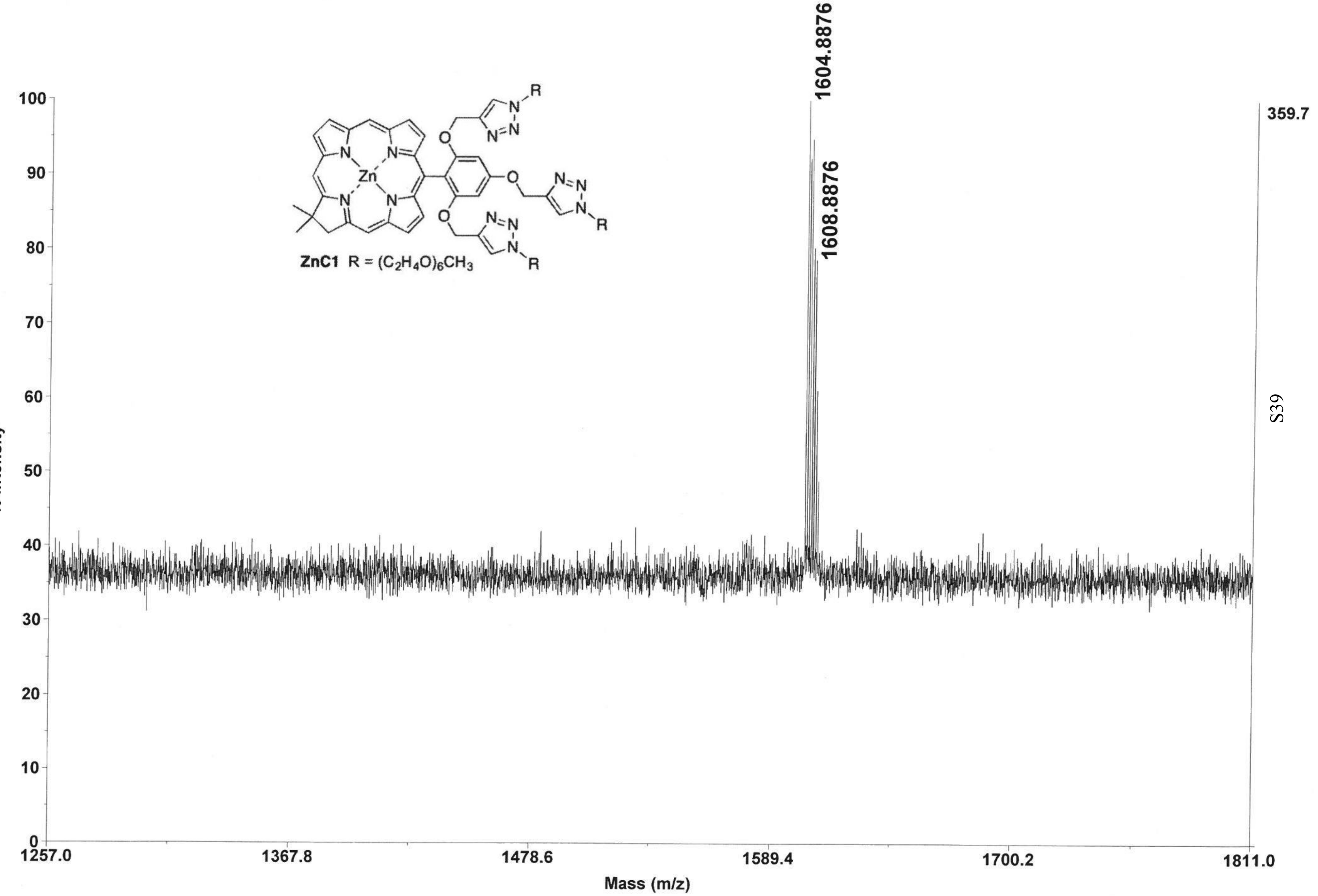


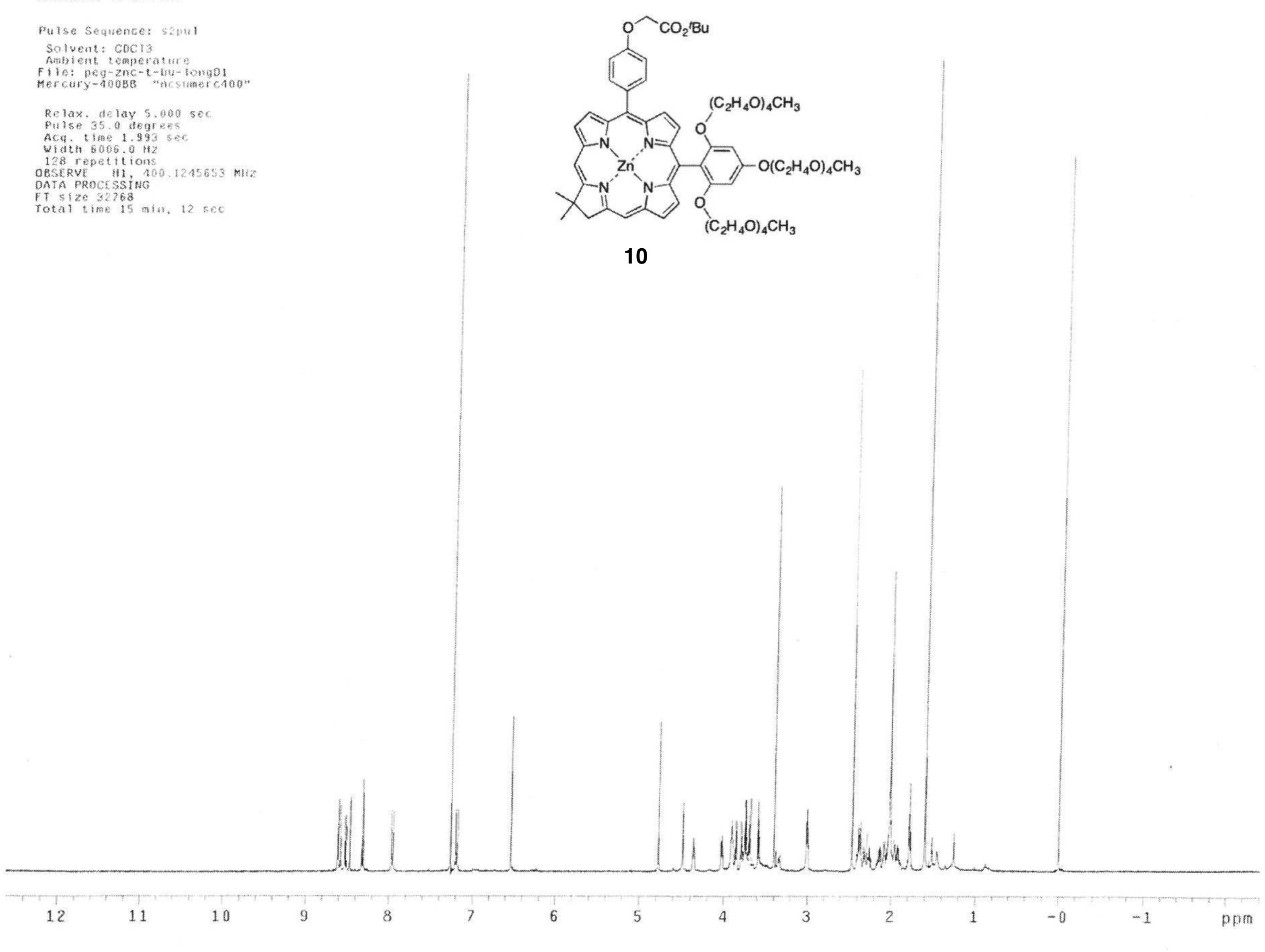
```
13C OBSERVE

Pulse Sequence: s2pul
 Solvent: THF
 Ambient temperature
File: 030515_13C_click_rxn
Mercury-400BB  "ncsumerc400"

 Pulse 29.0 degrees
 Acq. time 1.199 sec
 Width 25000.0 Hz
 20000 repetitions
OBSERVE  C13, 100.6117464 MHz
DECOUPLE  H1, 400.1280672 MHz
 Power 40 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 17 hr, 20 min, 4 sec
```

ZnC1 R = $(C_2H_4O)_6CH_3$

AB Sciex TOF/TOF™ Series Explorer™ 72098

TOF/TOF™ Reflector Spec #1 MC[BP = 1604.9, 360]

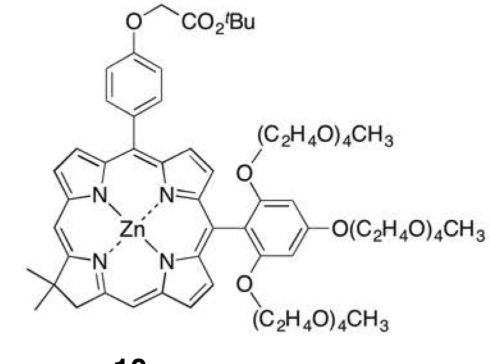




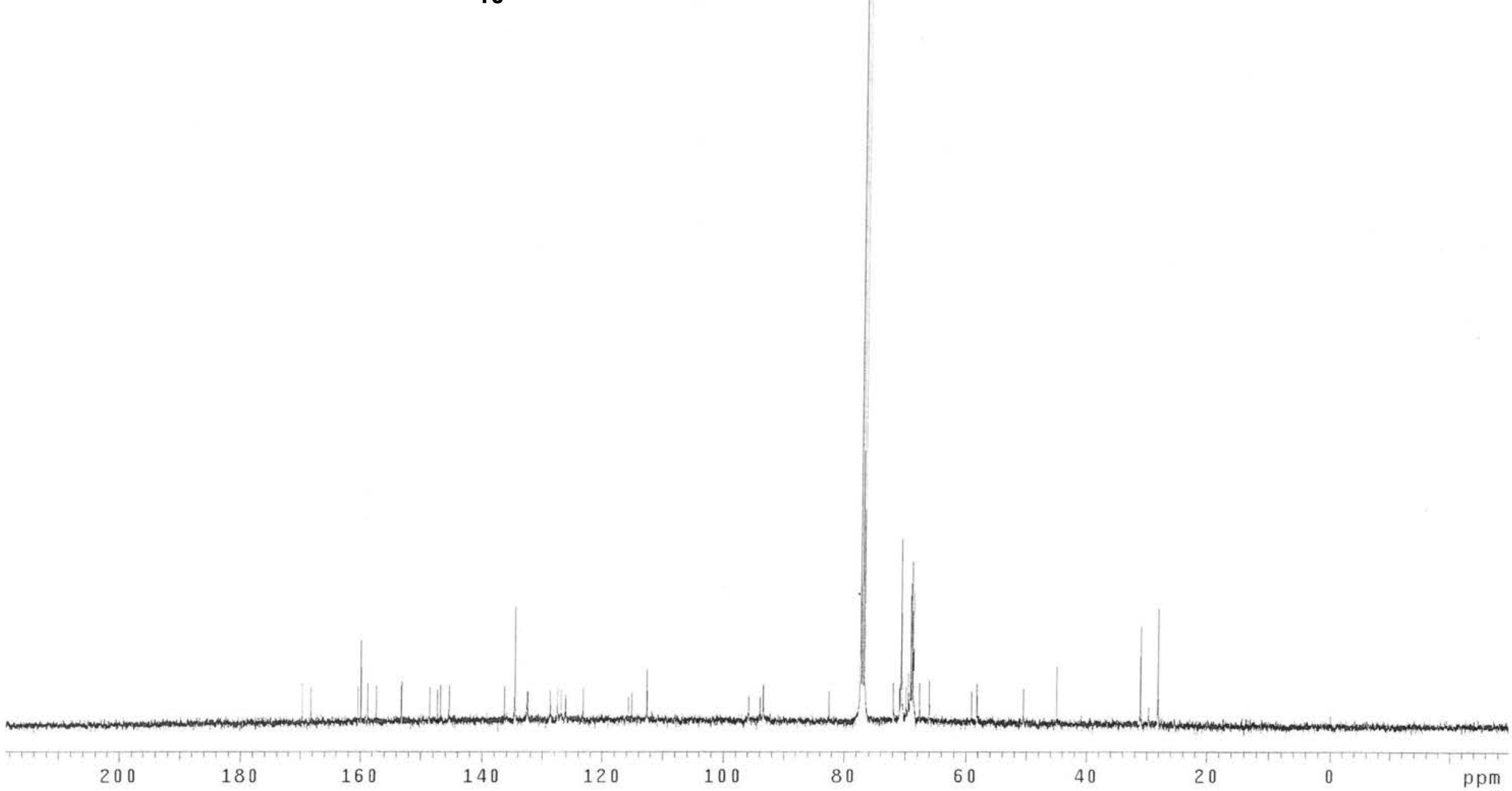
```
STANDARD 1H OBSERVE

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
File: peg-znc-t-bu-longD1
Mercury-400BB  "ncsumerc400"

 Relax. delay 5.000 sec
 Pulse 35.0 degrees
 Acq. time 1.993 sec
 Width 6006.0 Hz
 128 repetitions
OBSERVE   H1, 400.1245653 MHz
DATA PROCESSING
FT size 32768
Total time 15 min, 12 sec
```

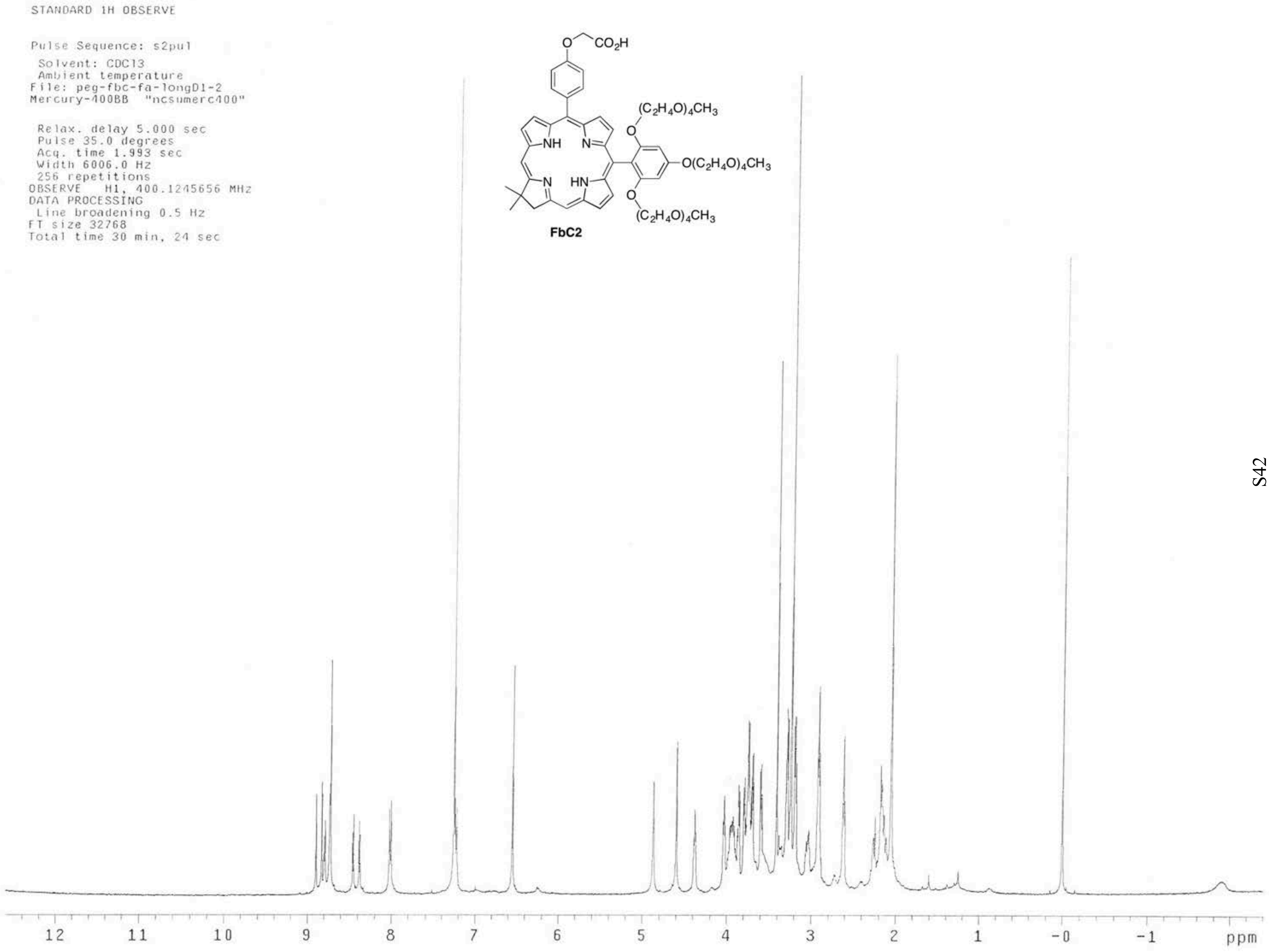
10

```
13C OBSERVE

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
File: peg-znc-t-bu-13c
Mercury-400BB  "ncsumerc400"

 Pulse 81.2 degrees
 Acq. time 1.199 sec
 Width 25000.0 Hz
 40960 repetitions
OBSERVE  C13, 100.6114037 MHz
DECOUPLE  H1, 400.1266027 MHz
 Power 44 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 16 hr, 41 min, 6 sec
```



10





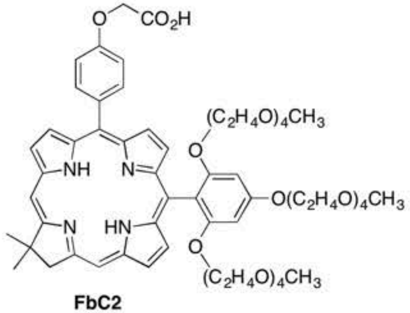
STANDARD 1H OBSERVE

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: peg-fbc-fa-longD1-2
Mercury-400BB "ncsumerc400"

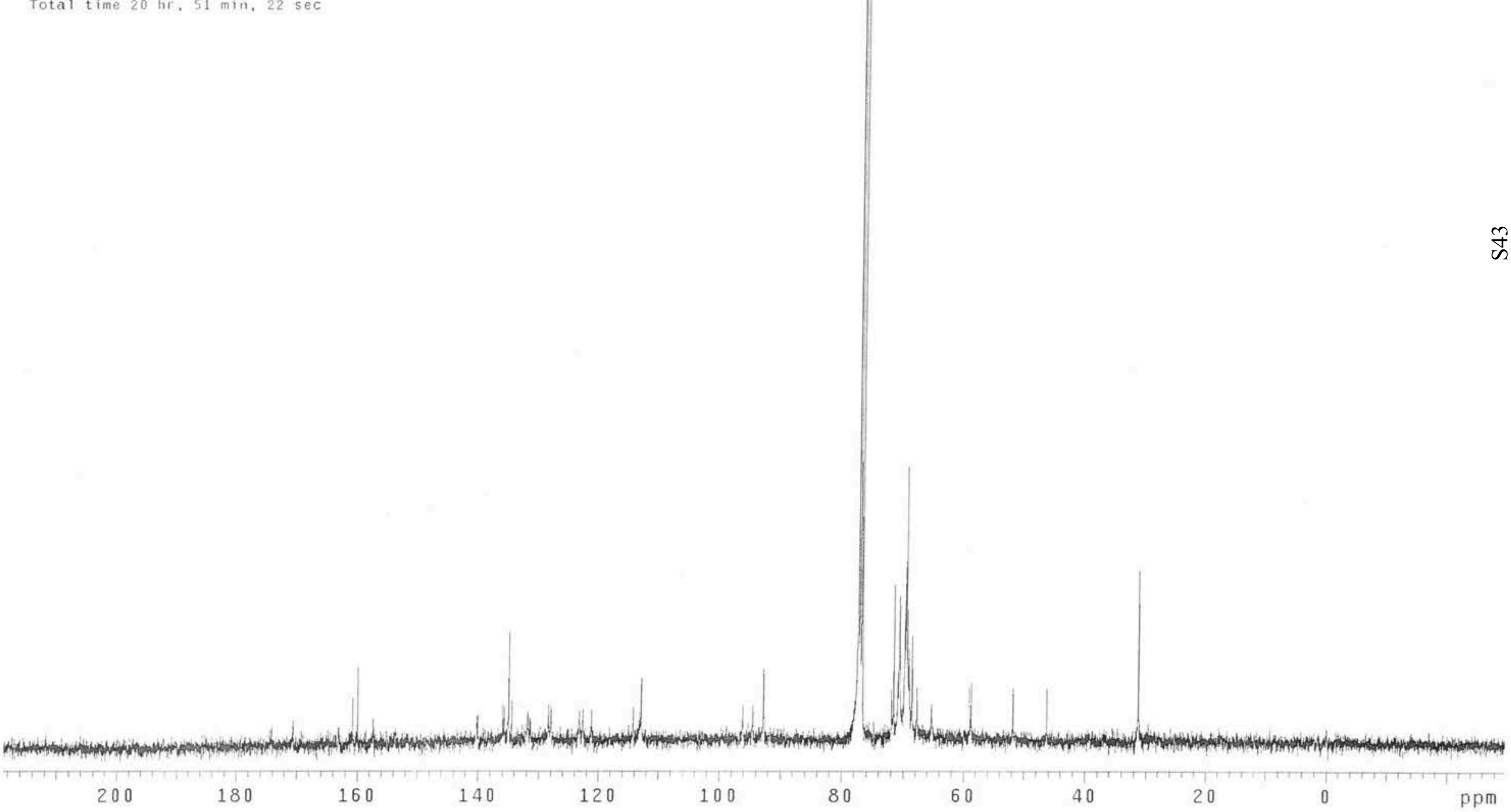
Relax. delay 5.000 sec
Pulse 35.0 degrees
Acq. time 1.993 sec
Width 6006.0 Hz
256 repetitions
OBSERVE H1, 400.1245656 MHz
DATA PROCESSING
Line broadening 0.5 Hz
FT size 32768
Total time 30 min, 24 sec

FbC2

```
13C OBSERVE

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
File: peg-fbc-fa-13C-2
Mercury-400BB  "ncsumerc400"

 Pulse 81.2 degrees
 Acq. time 1.199 sec
 Width 25000.0 Hz
 51200 repetitions
OBSERVE  C13, 100.6114037 MHz
DECOUPLE  H1, 400.1266027 MHz
 Power 44 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 20 hr, 51 min, 22 sec
```

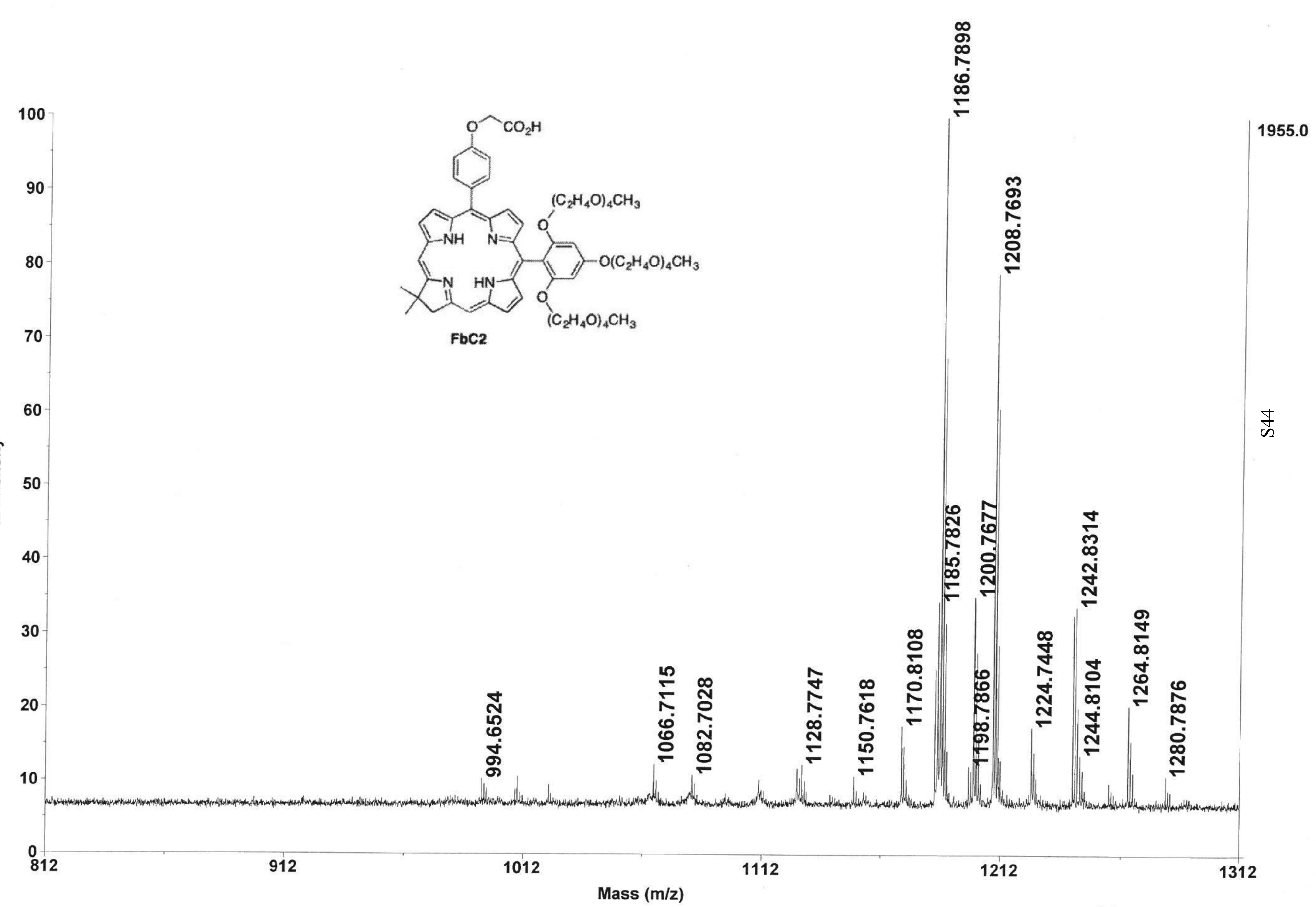


FbC2



AB Sciex TOF/TOF™ Series Explorer™ 72098

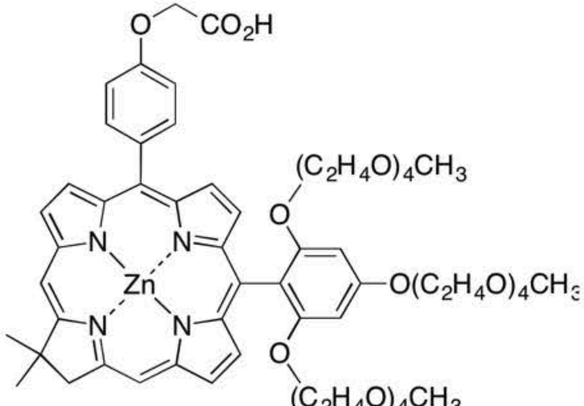
TOF/TOF™ Reflector Spec #1 MC[BP = 1186.8, 1955]



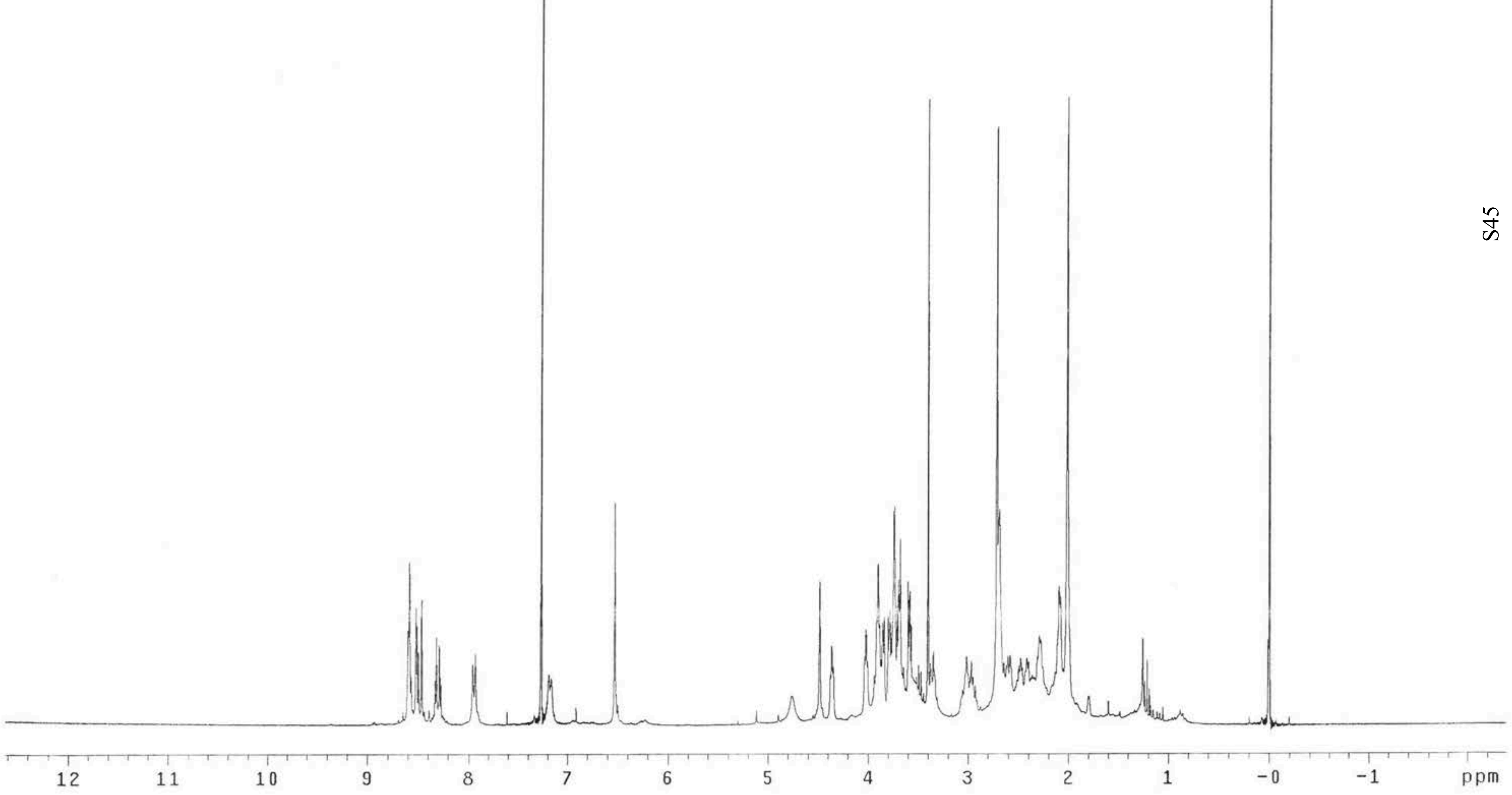
STANDARD 1H OBSERVE

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
File: peg-znc-fa-longD1
Mercury-300BB "ncsumerc638"

Relax. delay 5.000 sec
Pulse 86.4 degrees
Acq. time 1.995 sec
Width 4506.5 Hz
256 repetitions
OBSERVE H1, 300.1683379 MHz
DATA PROCESSING
FT size 32768
Total time 0 min, 0 sec



ZnC2

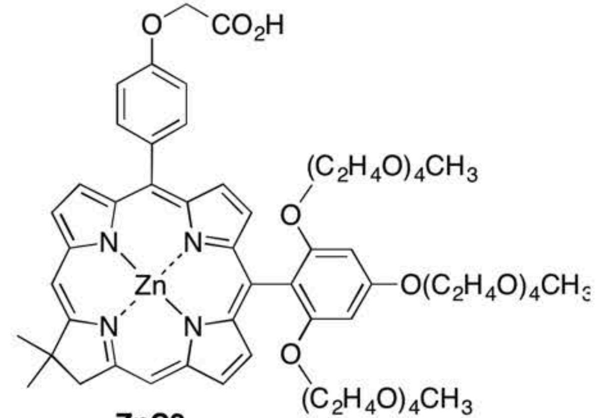


13C OBSERVE

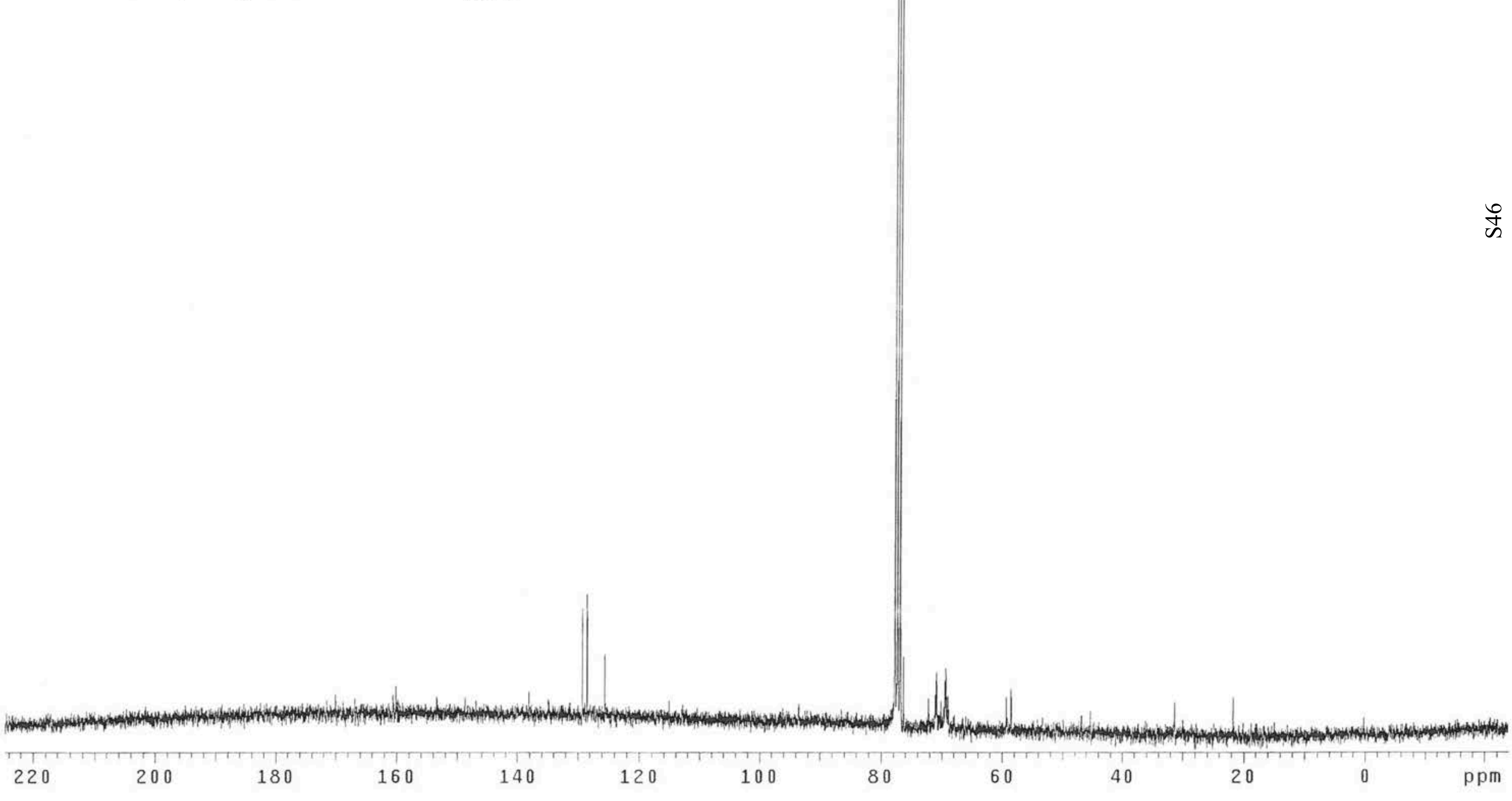
Pulse Sequence: s2pul

Solvent: CDCl3
Ambient temperature
File: peg-znc-fa-c
Mercury-300BB "ncsumerc638"

Pulse 23.3 degrees
Acq. time 1.815 sec
Width 18761.7 Hz
40960 repetitions
OBSERVE C13, 75.4773710 MHz
DECOUPLE H1, 300.1698746 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 24 hr, 1 min, 52 sec

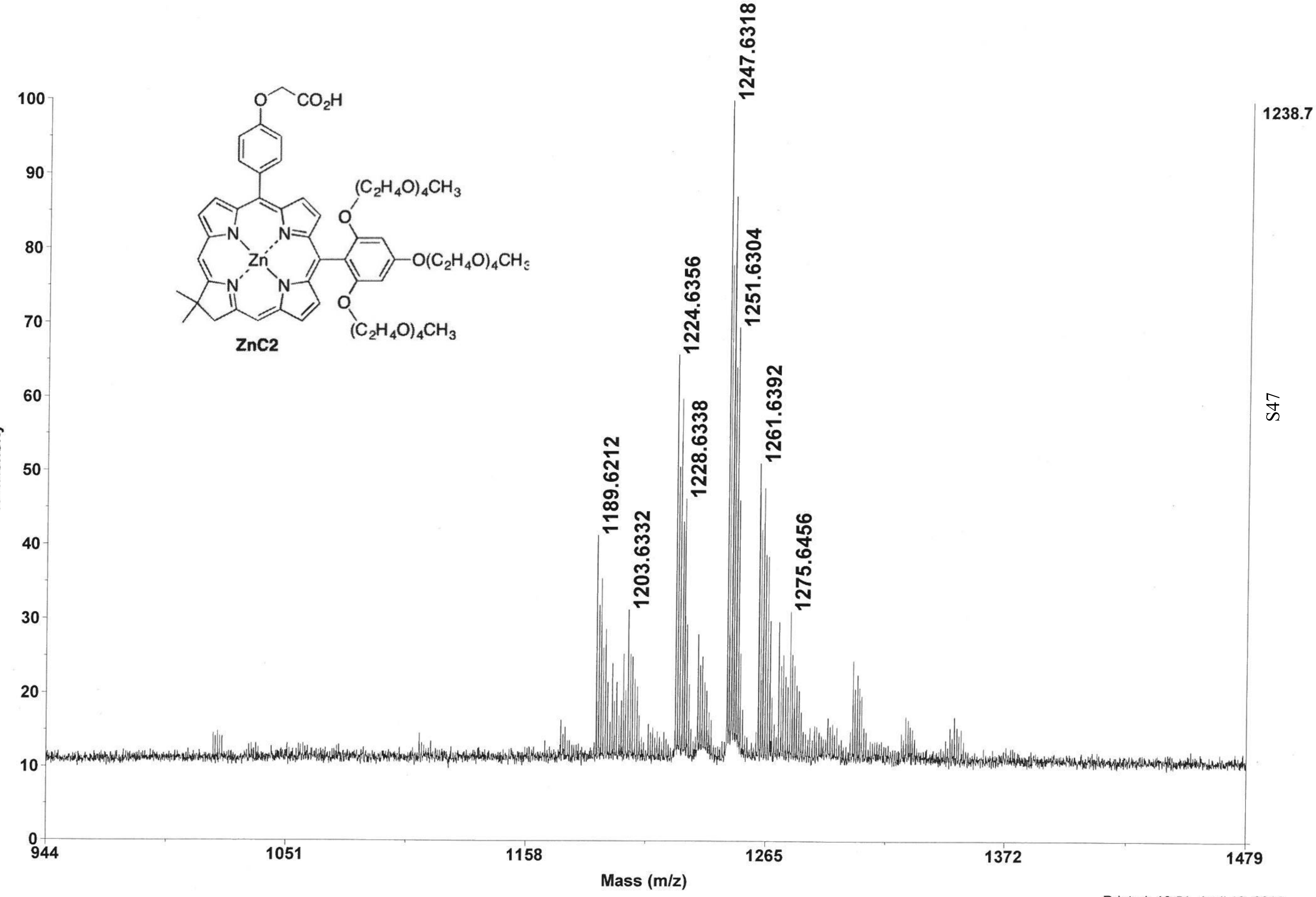


ZnC2

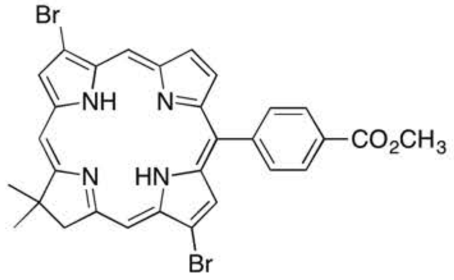


AB Sciex TOF/TOF™ Series Explorer™ 72098

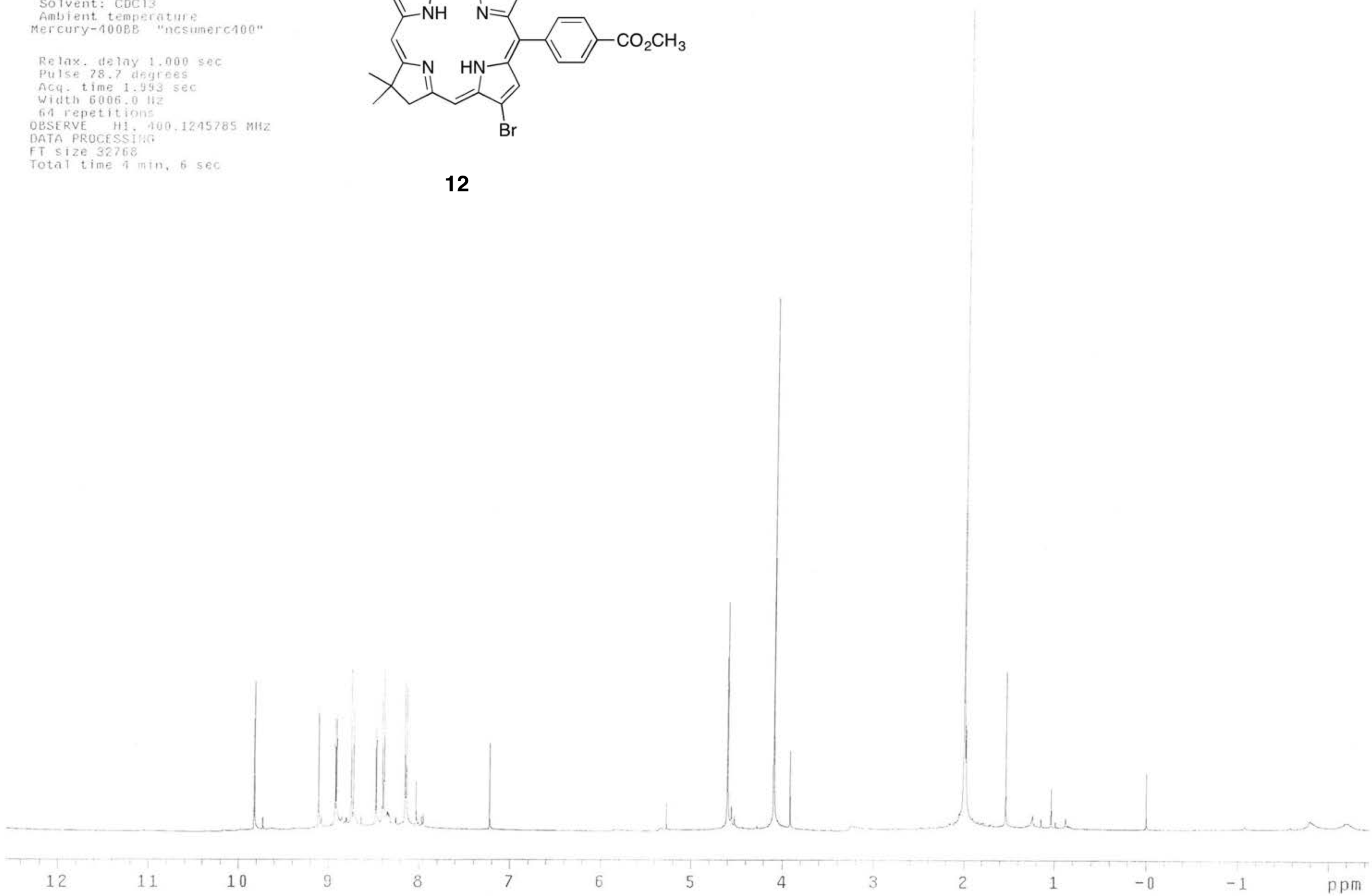
TOF/TOF™ Reflector Spec #1 MC[BP = 1247.6, 1239]



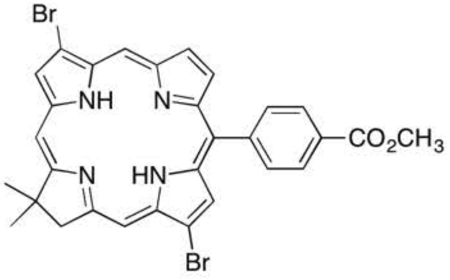
```
STANDARD 1H OBSERVE

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
Mercury-400BB  "ncsumerc400"

 Relax. delay 1.000 sec
 Pulse 78.7 degrees
 Acq. time 1.993 sec
 Width 6006.0 Hz
 64 repetitions
OBSERVE   H1, 400.1245785 MHz
DATA PROCESSING
FT size 32768
Total time 4 min, 6 sec
```



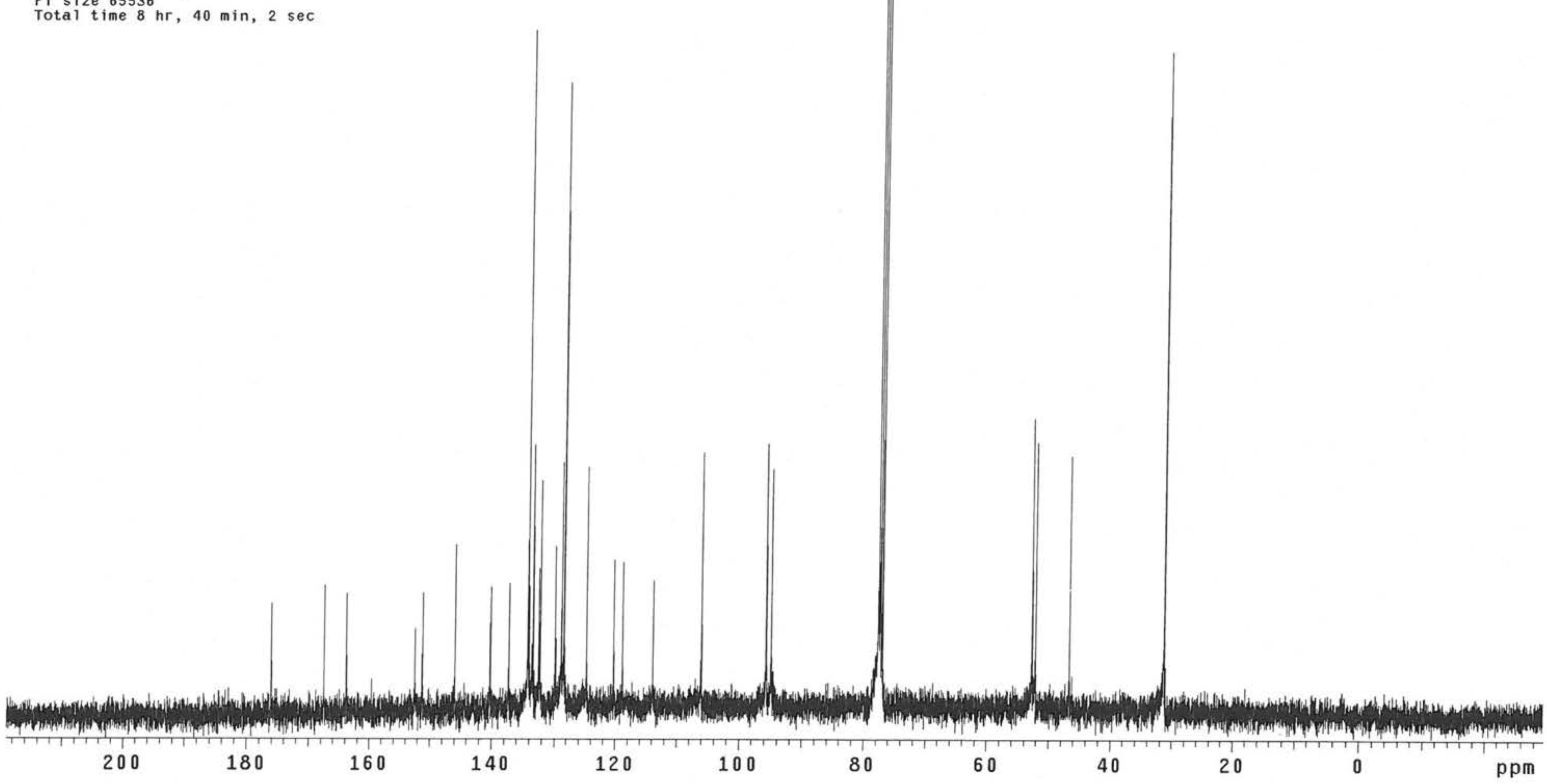
12



```
13C OBSERVE

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
Mercury-400BB  "ncsumerc400"

 Pulse 46.9 degrees
 Acq. time 1.199 sec
 Width 25000.0 Hz
 6880 repetitions
OBSERVE  C13, 100.6113806 MHz
DECOUPLE  H1, 400.1266027 MHz
 Power 39 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 8 hr, 40 min, 2 sec
```

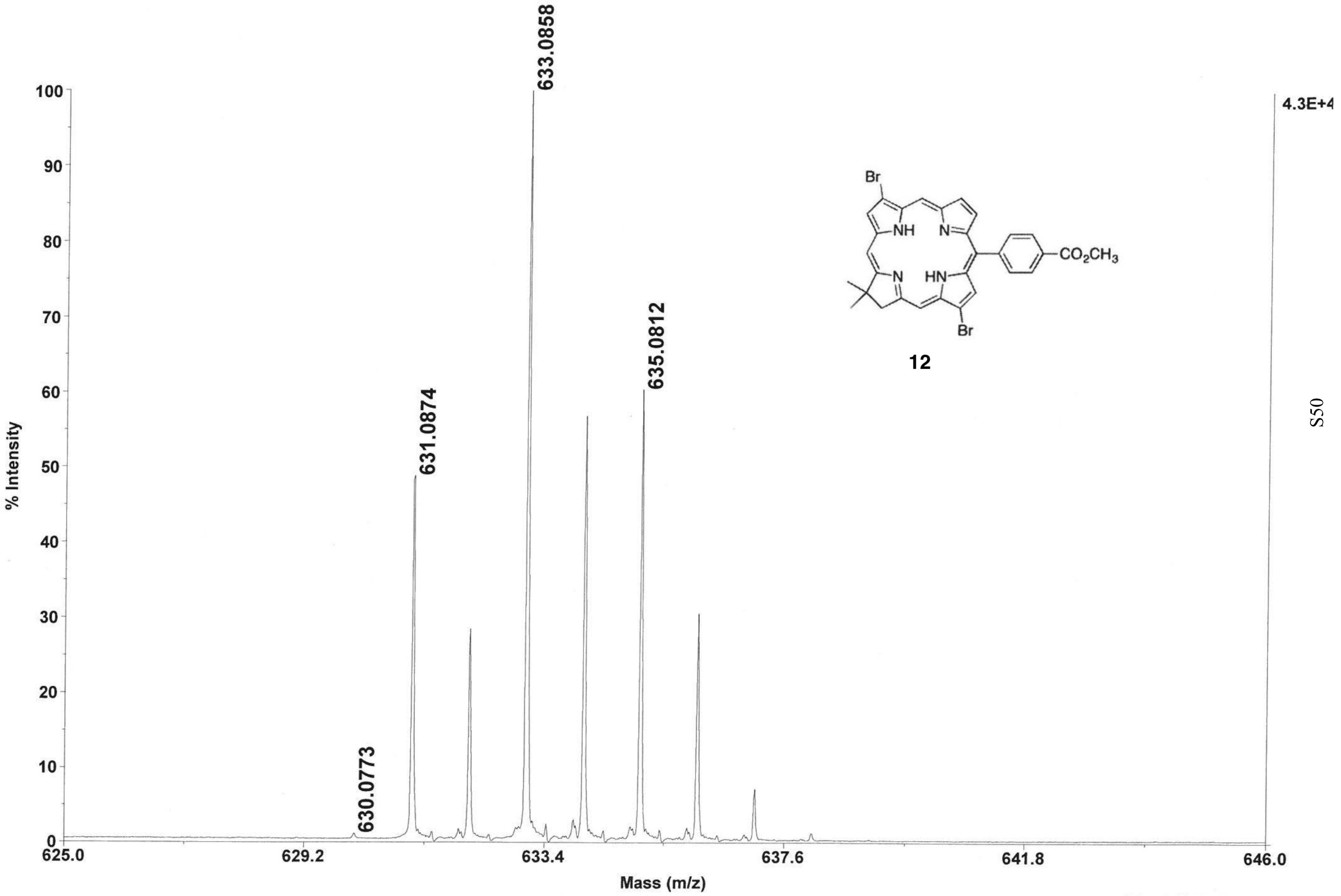


12



AB Sciex TOF/TOF™ Series Explorer™ 72098

TOF/TOF™ Reflector Spec #1 MC[BP = 633.1, 43452]



12

Printed: 20:55, April 12, 2016

C:\AB SCIEX\TOFTOF Data\ExportT2D\User Project 1\Lindsey\Mengran\041216\B6_MS.t2d

```
===============================================================================
Spectrum/Peak Report                    Date 11/4/2014 Time 11:48:52 Page  1 of 1
===============================================================================


Method file :        <method not saved>
Information :        Default Method
Data File   :        C:\CHEM32\1\DATA\MENGRAN\110414_DIBROMO_PH_COOME_TOLUENE.SD
                     Created : 11/4/14 11:39:10

Overlaid Spectra:
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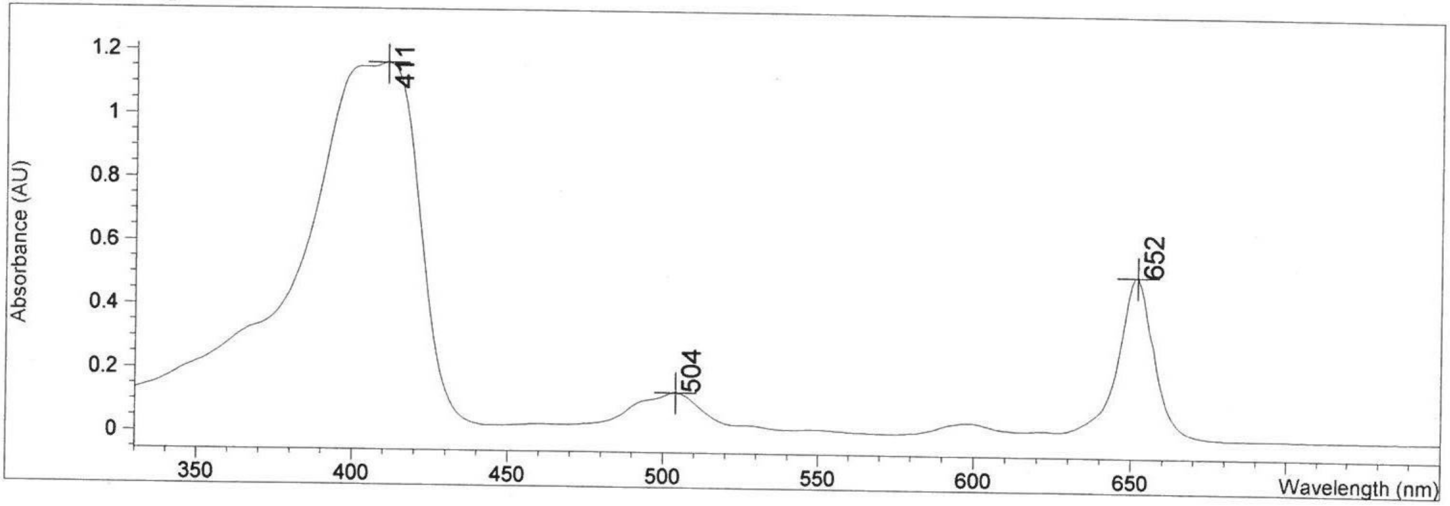

```
 #  Name                    Peaks(nm)    Abs(AU)
------------------------------------------------
 1                              411.0    1.16240
 1                              652.0    0.51388
 1                              504.0    0.13340

Report generated by : jon

--------------------------------------------------------------
                   *** End Spectrum/Peak Report ***
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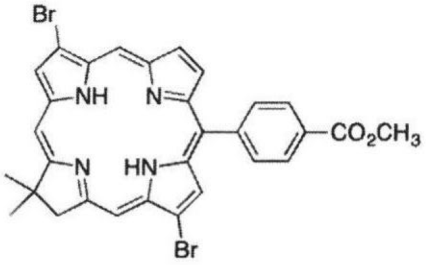
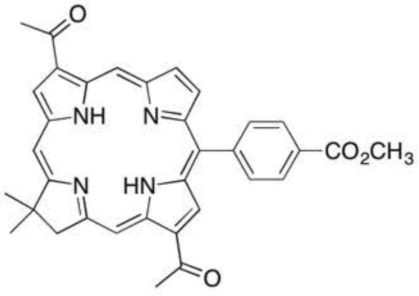
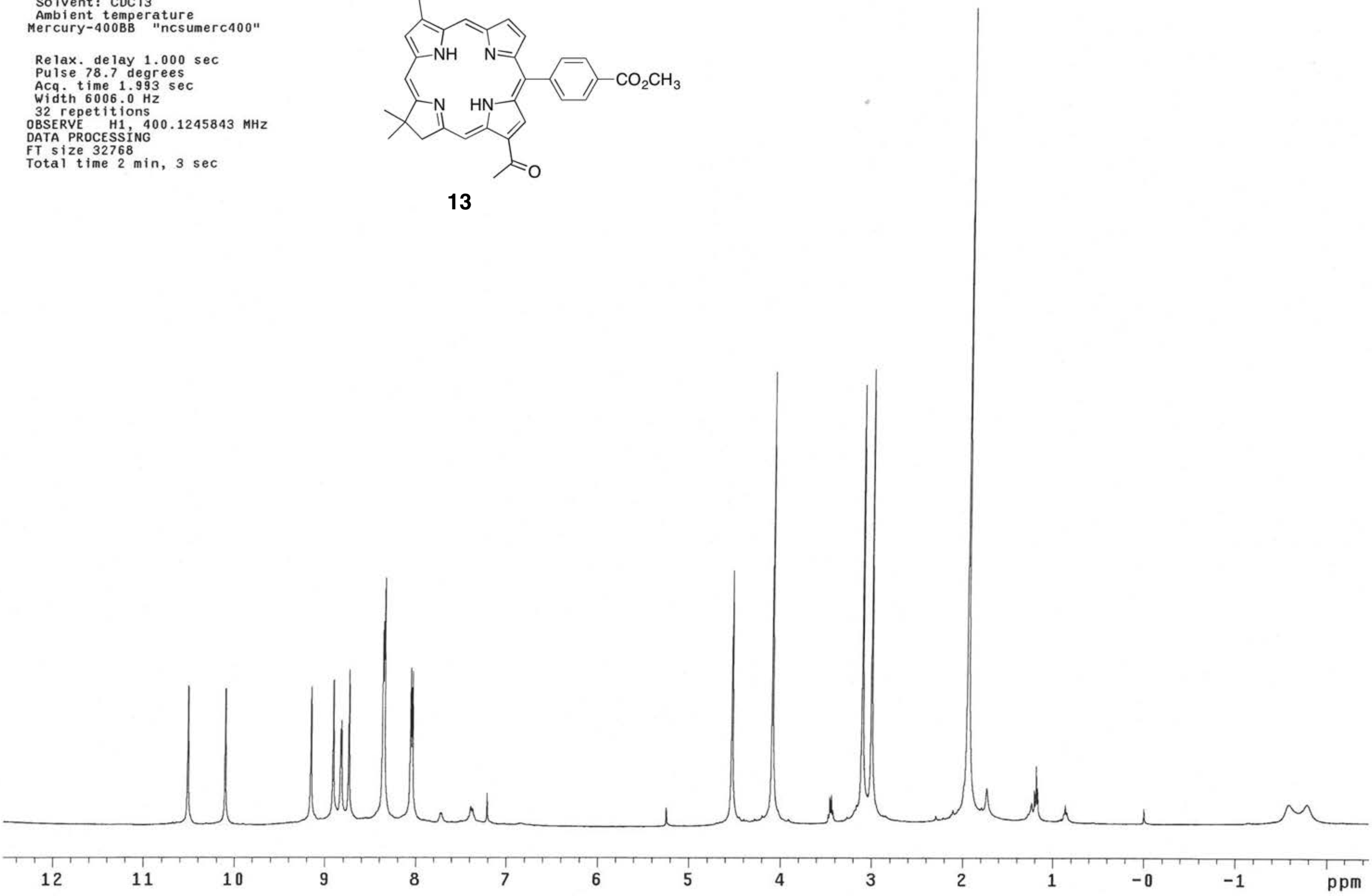


12

```
STANDARD 1H OBSERVE

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
Mercury-400BB  "ncsumerc400"

 Relax. delay 1.000 sec
 Pulse 78.7 degrees
 Acq. time 1.993 sec
 Width 6006.0 Hz
 32 repetitions
OBSERVE   H1, 400.1245843 MHz
DATA PROCESSING
FT size 32768
Total time 2 min, 3 sec
```



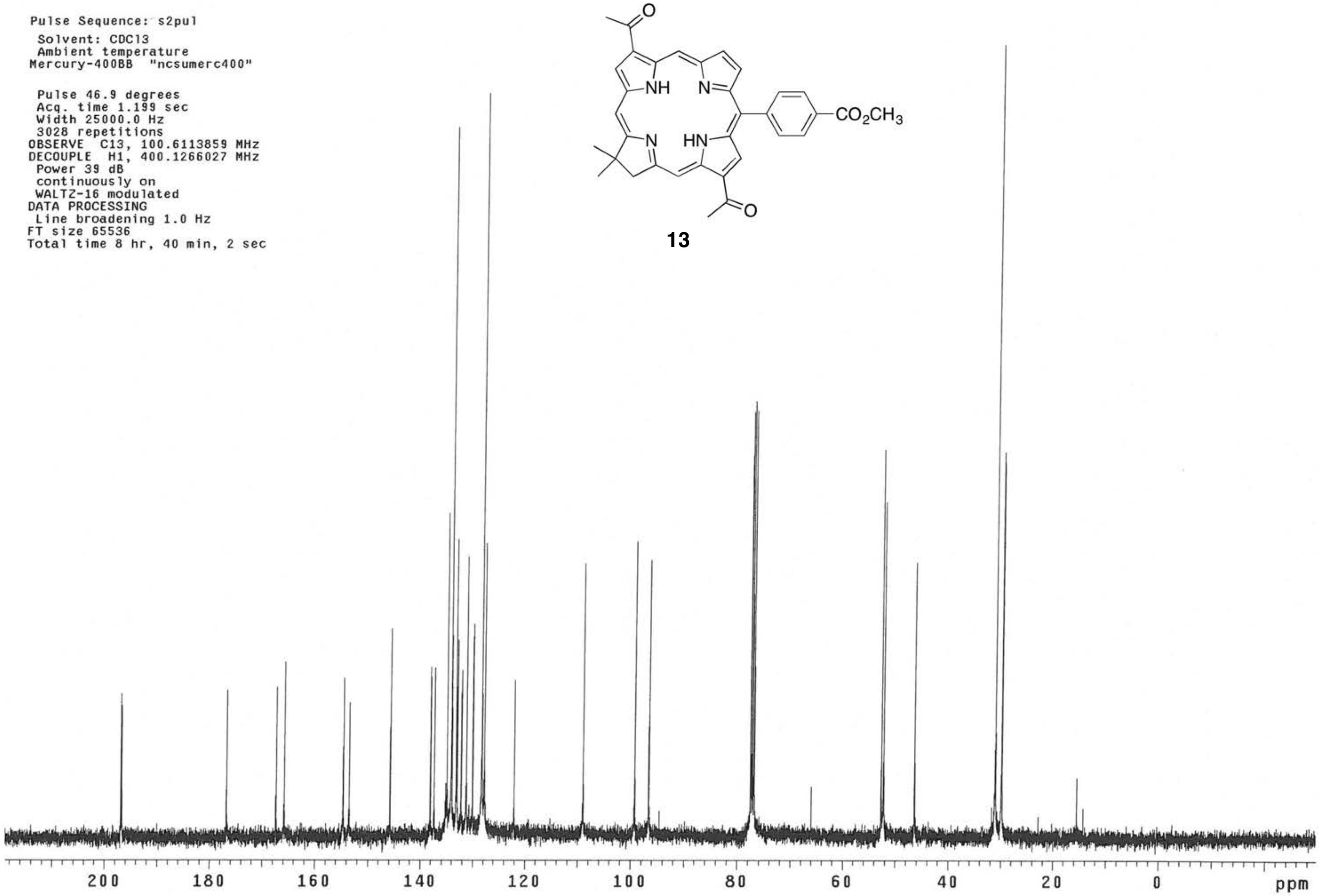
13



13C OBSERVE

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
Mercury-400BB "ncsumerc400"

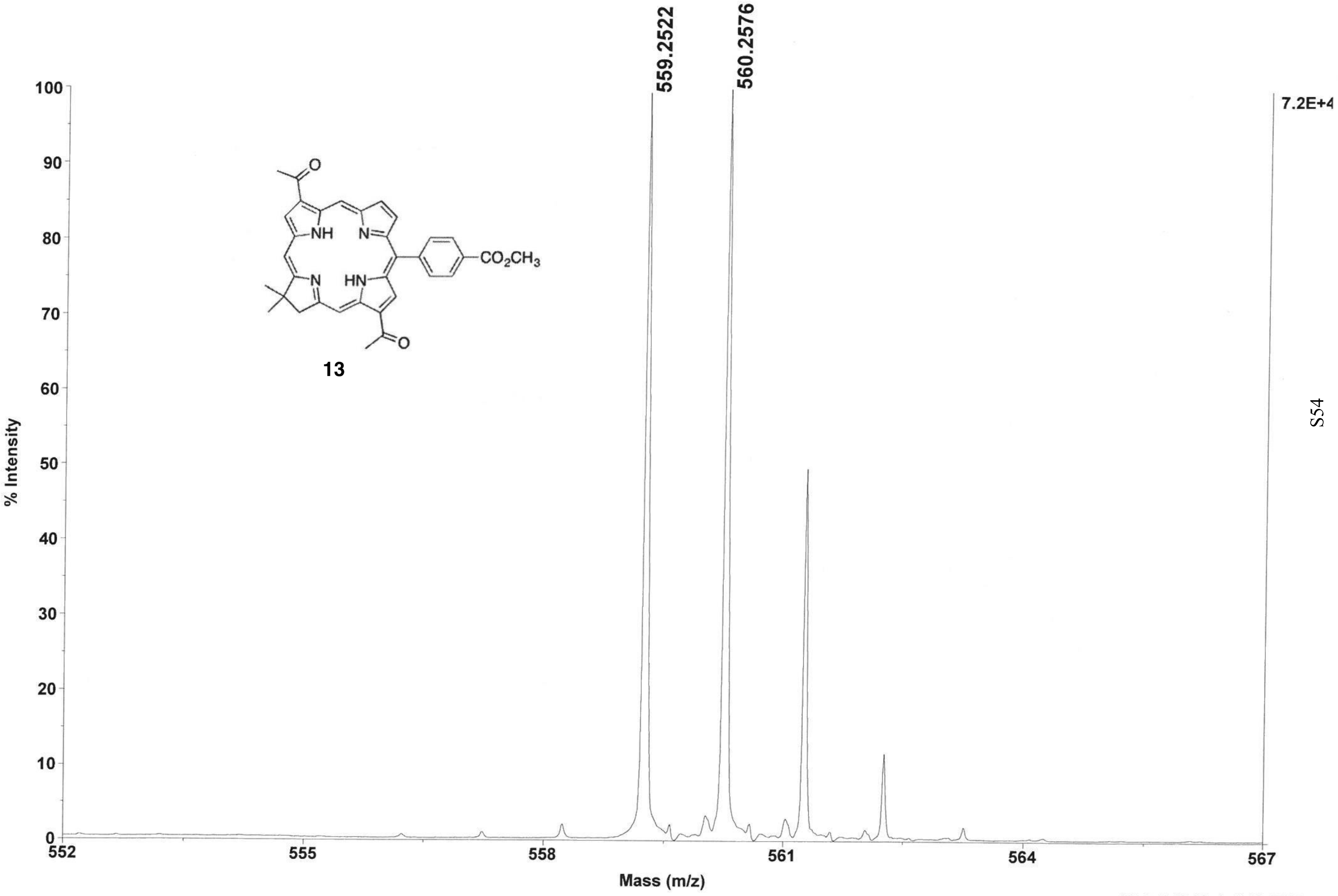
 Pulse 46.9 degrees
 Acq. time 1.199 sec
 Width 25000.0 Hz
 3028 repetitions
OBSERVE C13, 100.6113859 MHz
DECOUPLE H1, 400.1266027 MHz
 Power 39 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 8 hr, 40 min, 2 sec



13

AB Sciex TOF/TOF™ Series Explorer™ 72098

TOF/TOF™ Reflector Spec #1 MC[BP = 340.0, 89210]

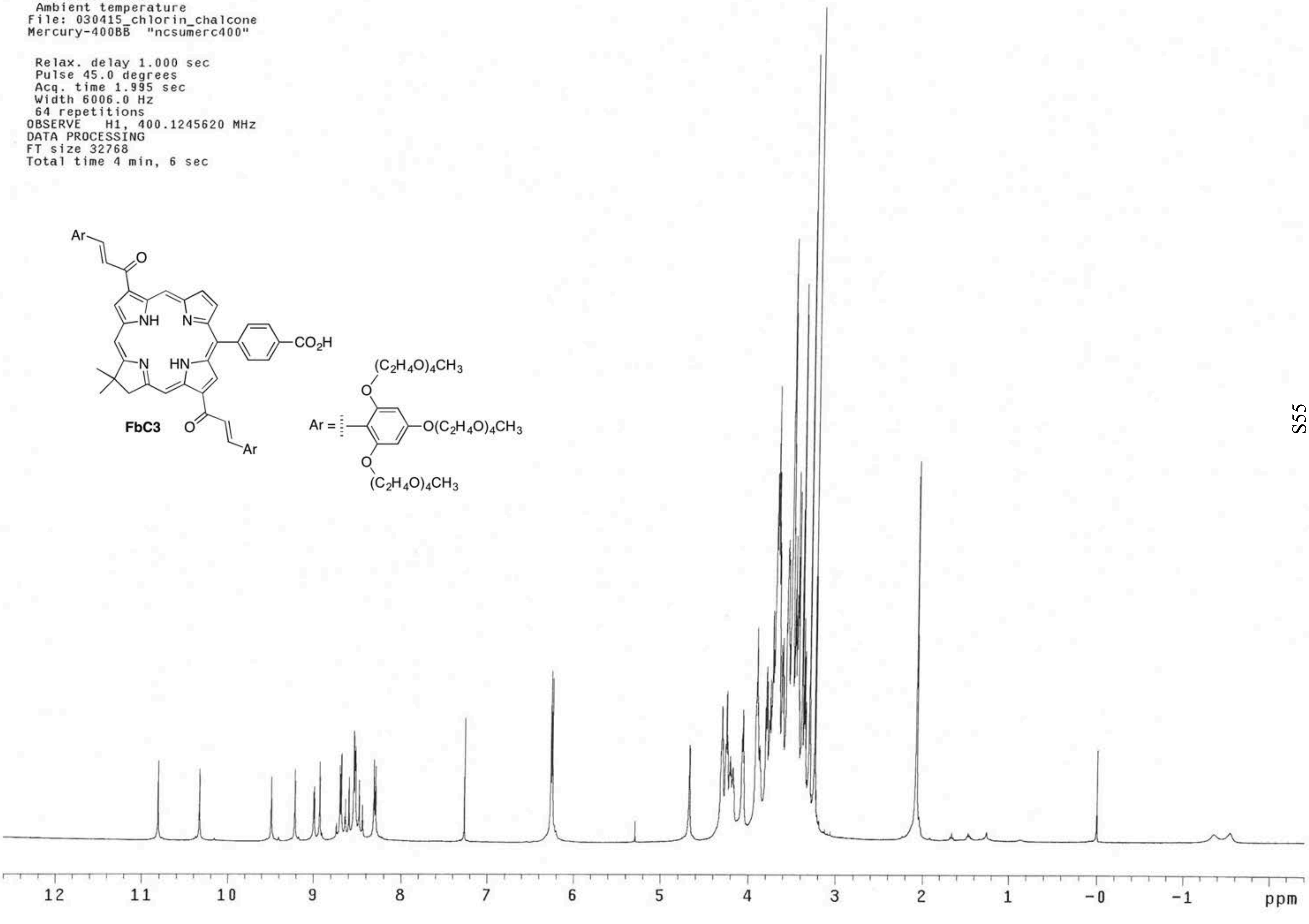


13

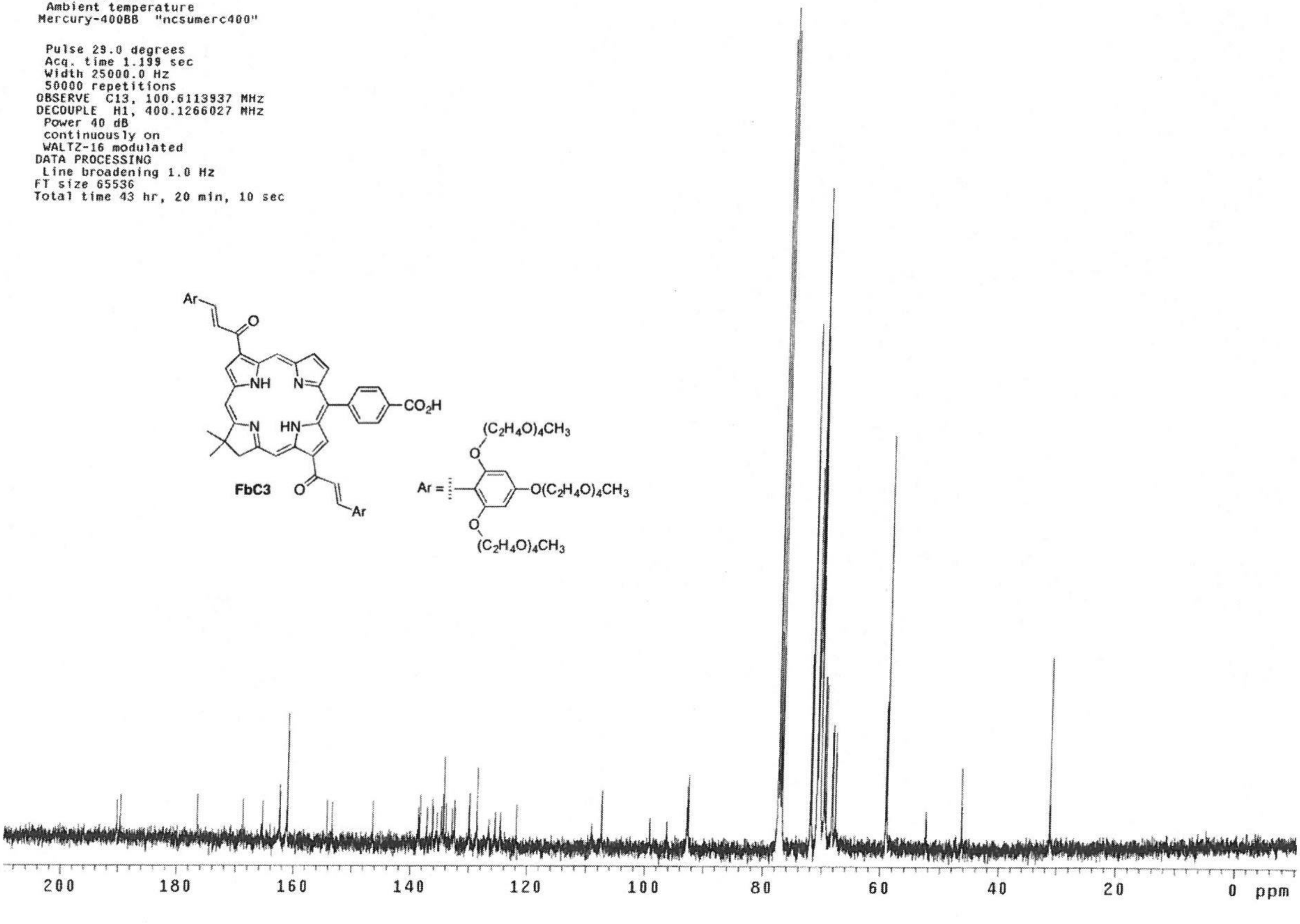
C:\AB SCIEX\TOFTOF Data\ExportT2D\User Project 1\Lindsey\Mengran\041216\B7_MS.t2d

Printed: 18:52, April 12, 2016

```
STANDARD 1H OBSERVE

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
File: 030415_chlorin_chalcone
Mercury-400BB  "ncsumerc400"

 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.995 sec
 Width 6006.0 Hz
 64 repetitions
OBSERVE   H1, 400.1245620 MHz
DATA PROCESSING
FT size 32768
Total time 4 min, 6 sec
```


FbC3

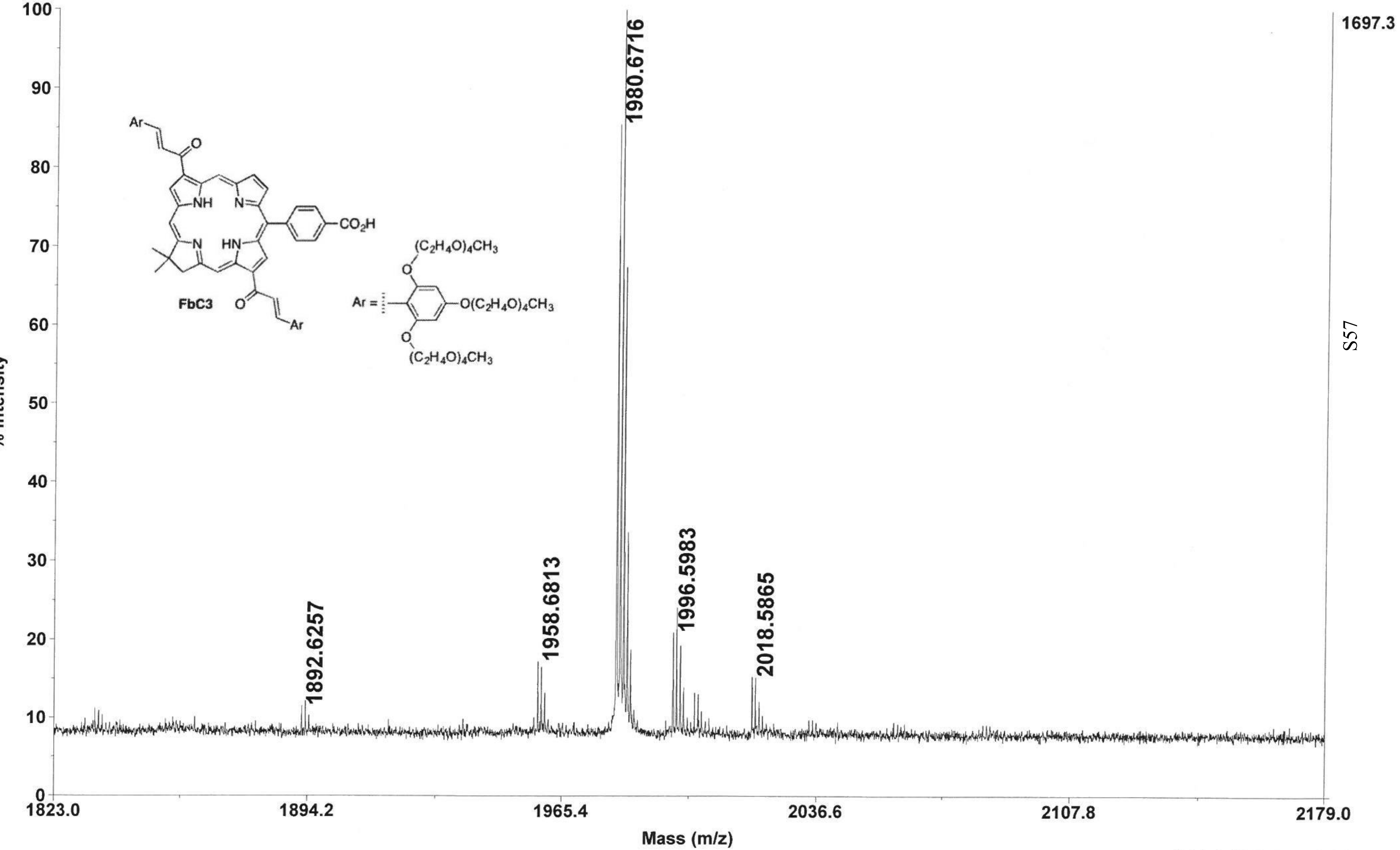
```
13C OBSERVE

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
Mercury-400BB  "ncsumerc400"

 Pulse 29.0 degrees
 Acq. time 1.199 sec
 Width 25000.0 Hz
 50000 repetitions
OBSERVE  C13, 100.6113937 MHz
DECOUPLE  H1, 400.1266027 MHz
 Power 40 dB
 continuously on
 WALTZ-16 modulated
DATA PROCESSING
 Line broadening 1.0 Hz
FT size 65536
Total time 43 hr, 20 min, 10 sec
```



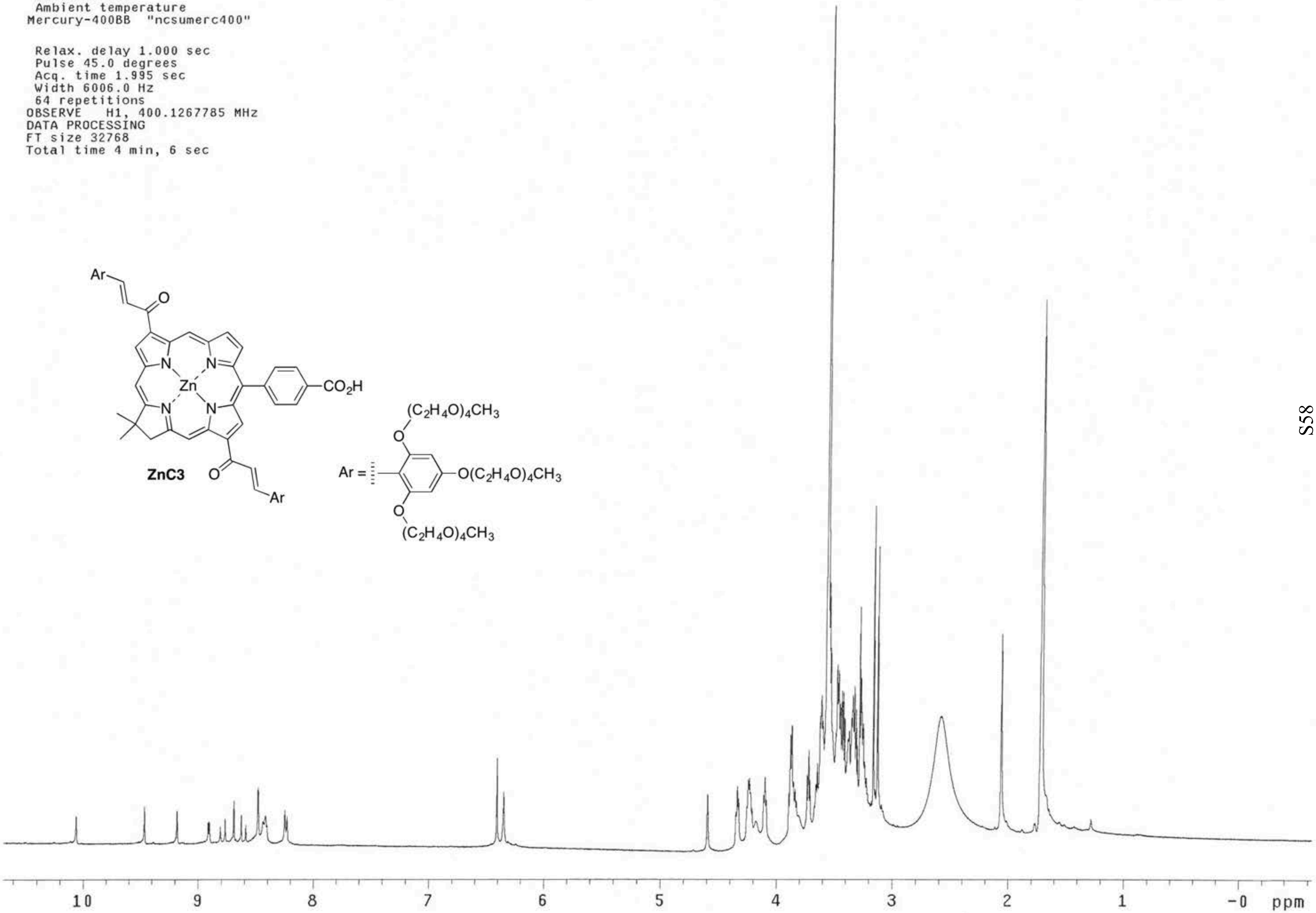
FbC3

AB Sciex TOF/TOF™ Series Explorer™ 72098

TOF/TOF™ Reflector Spec #1 MC[BP = 1981.7, 1697]

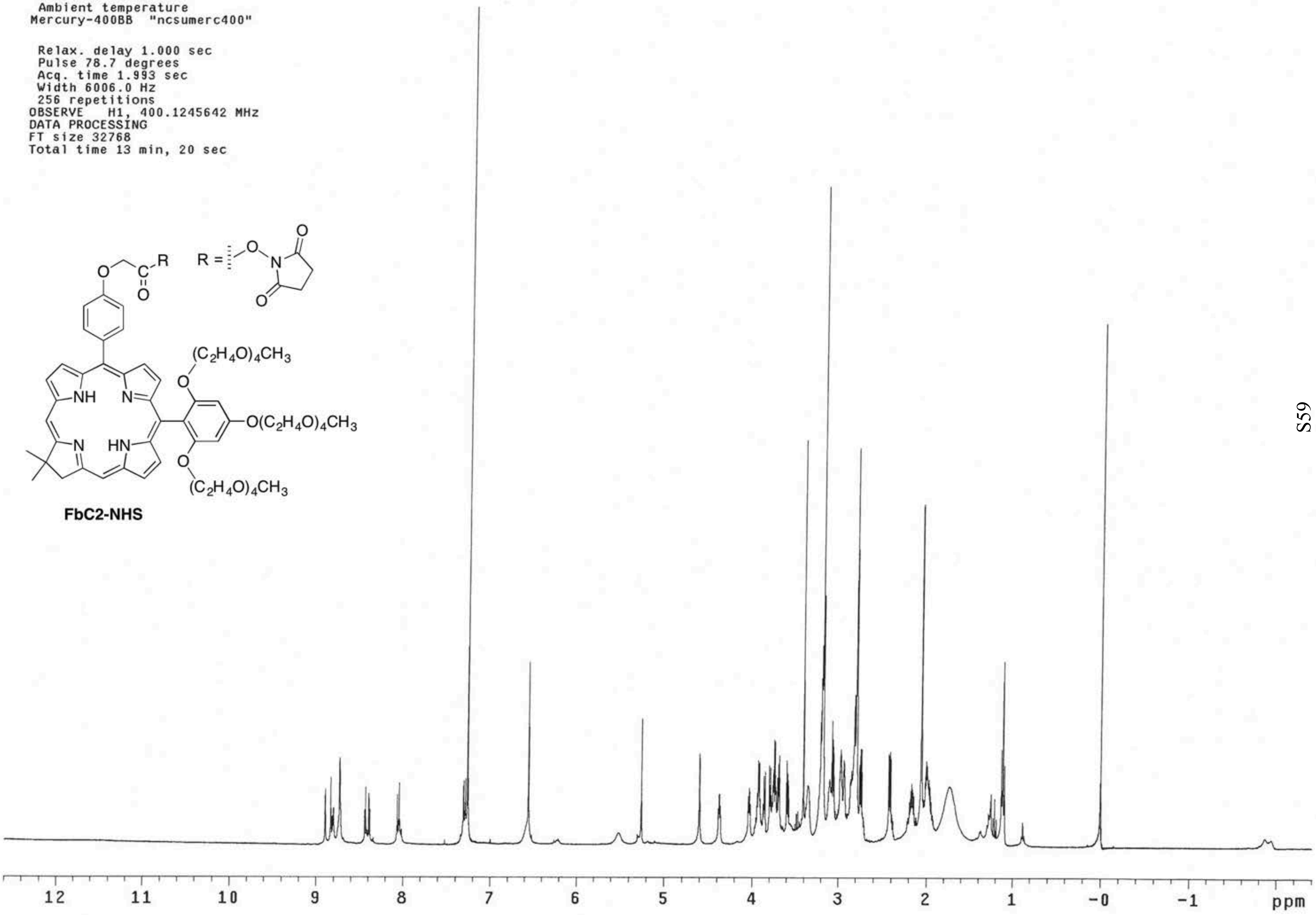


```
STANDARD 1H OBSERVE

Pulse Sequence: s2pul
 Solvent: THF
 Ambient temperature
Mercury-400BB  "ncsumerc400"

 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.995 sec
 Width 6006.0 Hz
 64 repetitions
OBSERVE   H1, 400.1267785 MHz
DATA PROCESSING
FT size 32768
Total time 4 min, 6 sec
```



ZnC3

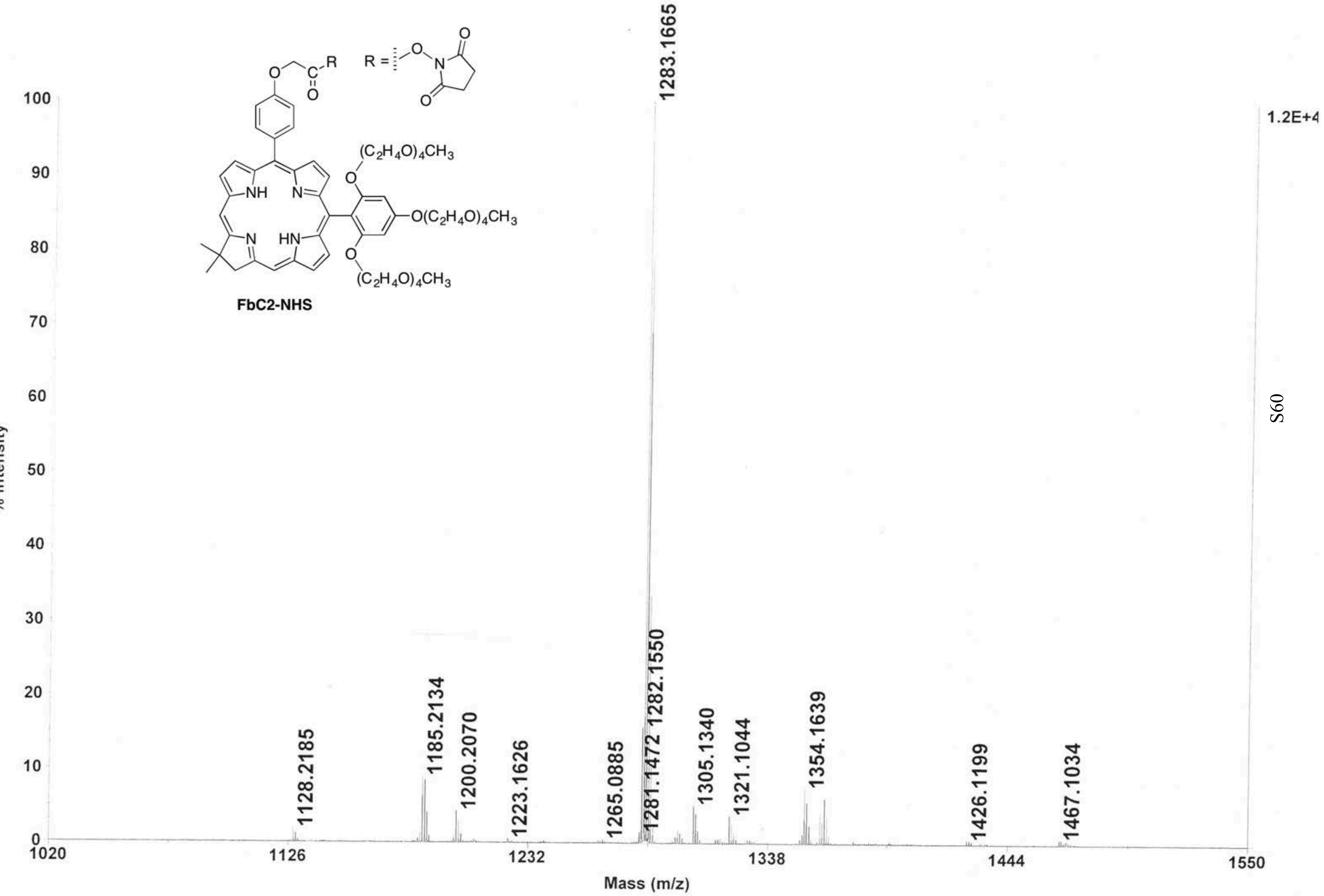
```
STANDARD 1H OBSERVE

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
Mercury-400BB  "ncsumerc400"

 Relax. delay 1.000 sec
 Pulse 78.7 degrees
 Acq. time 1.993 sec
 Width 6006.0 Hz
 256 repetitions
OBSERVE   H1, 400.1245642 MHz
DATA PROCESSING
FT size 32768
Total time 13 min, 20 sec
```

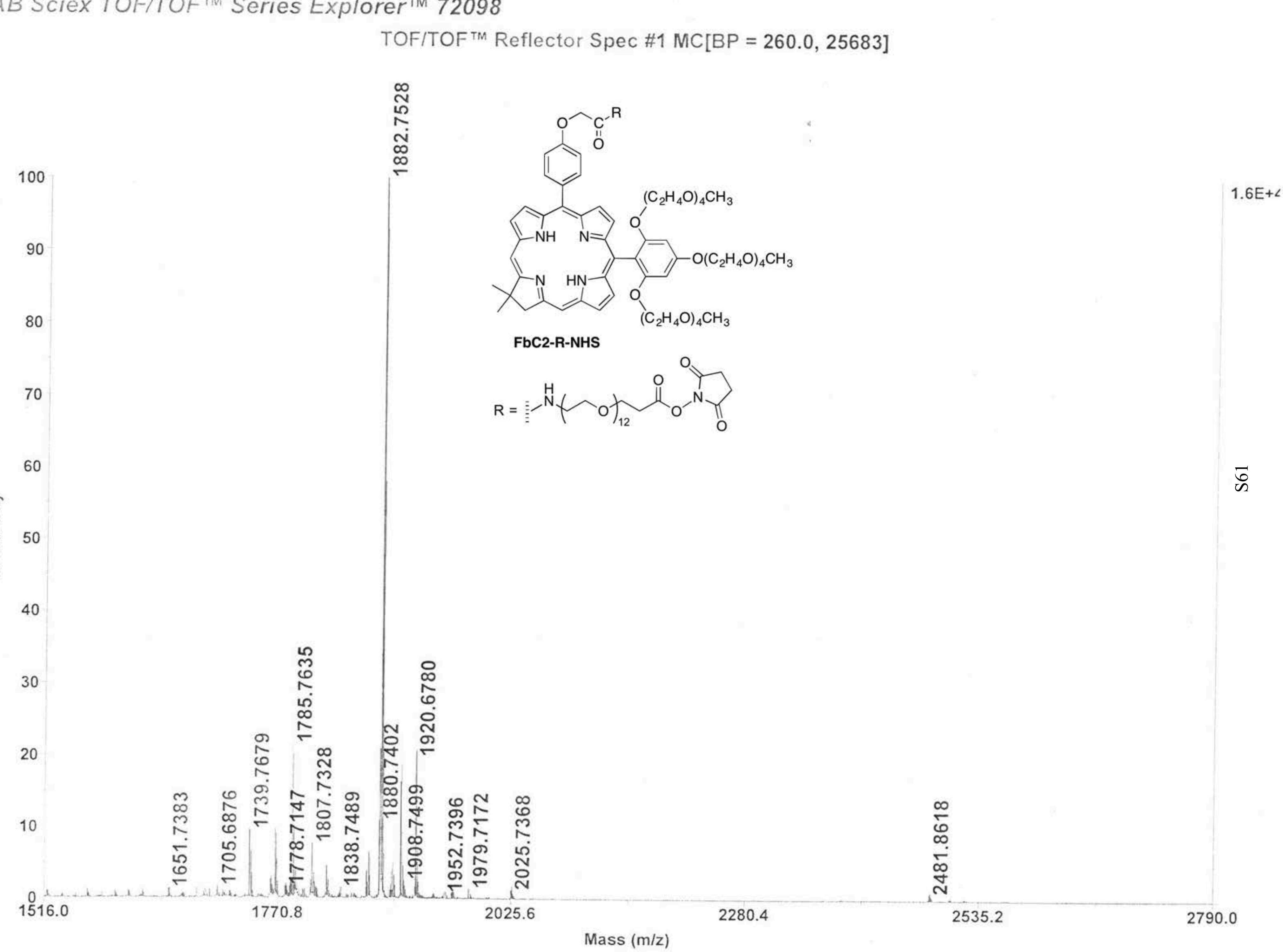


FbC2-NHS

AB Sciex TOF/TOF™ Series Explorer™ 72098

TOF/TOF™ Reflector Spec #1 MC[BP = 379.9, 21284]




AB Sciex TOF/TOF™ Series Explorer™ 72098
TOF/TOF™ Reflector Spec #1 MC[BP = 260.0, 25683]
1.6E+4
100
90
80
70
60
50
40
30
20
10
0
1516.0
1770.8
2025.6
2280.4
2535.2
2790.0
Mass (m/z)
1882.7528
1651.7383
1705.6876
1739.7679
1778.7147
1785.7635
1807.7328
1838.7489
1880.7402
1908.7499
1920.6780
1952.7396
1979.7172
2025.7368
2481.8618
FbC2-R-NHS
R =
NH
N
HN
O
R
12
$(C_2H_4O)_4CH_3$
$O(C_2H_4O)_4CH_3$