Supporting Information for the Paper

Catalytic Antioxidants – Regenerable Tellurium Analogues of Vitamin E

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Experimental Section

(+)-δ-Tocopherol ≥ 90% was purchased and used as received. ^{1}H and ^{13}C NMR spectra were recorded on 300 MHz (^{1}H: 300 MHz; ^{13}C: 75 MHz) and 400 MHz (^{1}H: 399.97 MHz; ^{13}C: 100.58 MHz) spectrometers, using the residual solvent peaks of $CDCl_3$ (^{1}H: δ 7.26; ^{13}C: δ 77.0) as an indirect reference to TMS. ^{125}Te NMR spectra were recorded on 400 MHz (^{125}Te: 126.2 MHz) using Ph_2Te_2 as an external standard. Flash column chromatography was performed using silica gel (0.04-0.06 mm). The high resolution mass spectra (HRMS) were obtained using a time of flight instrument equipped with electrospray ionization. Tetrahydrofuran was dried in a solvent purification system by passing it through an activated alumina column before use. Di-*n*-octyl ditelluride[1] was prepared according to literature methods.

5-Bromo-δ-tocopherol (5a). To a solution of δ-Tocopherol (3.50 g, 8.69 mmol) in dichloromethane (50 mL) was added dropwise Bu_4NBr_3 (4.19 g, 8.69 mmol) in dichloromethane (10 mL). After stirring for 1 h, the solution was evaporated and the residue was purified by column chromatography (pentane/diethyl ether = 98:2) to give the title compound as a light red, dense liquid (4.10 g, 98%). ^{1}H and ^{13}C NMR data were in accord with reported data in the literature.[2]

THP-protected 5-bromo-δ-tocopherol (5b). To a solution of 5-bromo-δ-tocopherol (4.0 g, 8.31 mmol) and 3,4-dihydro-2*H*-pyran (3.03 mL, 33.2 mmol) was added 1 drop of conc. HCl at room temperature. After stirring for two days, the solution was quenched with a saturated sodium hydrogen carbonate solution (10 mL) and extracted

with dichloromethane (10 mL x 3). The organic phase was dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by column chromatography (pentane/ethyl acetate = 99:1) to give the title compound as a yellow oil. Yield: 4.35 g (93%). ^{1}H NMR ($CDCl_3$): δ 6.88 (s, 1H), 5.33 (quartet, *J* = 4.0 Hz, 1H), 4.01 (m, 1H), 3.61 (d, *J* = 11.3 Hz, 1H), 2.72 (t, *J* = 7.0 Hz, 2H), 2.12 (s, 3H), 0.85-1.99 (several peaks, 44H). ^{13}C NMR ($CDCl_3$): δ 147.9, 147.8, 146.1 (2C) 125.8, 121.3, 117.8 (2C), 113.0 (2C), 97.9, 97.8, 75.5, 61.9 (2C), 39.7, 39.6, 39.4, 37.4 (2C), 32.8, 32.7 (2C), 31.4, 31.3, 30.4, 28.0, 25.4, 24.8, 24.4, 24.2, 23.8, 23.7, 22.7, 22.6, 21.0, 19.7, 19.6, 18.6, 16.2. HRMS (TOF MS ES$^+$) *m/z* calcd for $C_{32}H_{53}O_3Br$ $[M+Na]^+$: 587.3076. Found: 587.3105.

THP-protected 5-(*n*-octyltelluro)-δ-tocopherol (6a). To a solution of THP-protected 5-bromo-δ-tocopherol **5b** (2.50 g, 4.41 mmol) in anhydrous THF (30 mL) was added *tert*-BuLi ((1.7 M, 5.20 mL, 8.82 mmol)) under nitrogen at -78 °C. The solution was stirred for 1.5 h at -78 °C before the addition of dioctyl ditelluride (3.19 g, 6.62 mmol). After stirring at ambient temperature for overnight, the solution was quenched with a saturated ammonium chloride solution (40 mL) and extracted with ether (50 mL x 3). The organic layer was dried over magnesium sulfate, filtered and evaporated under reduced pressure. The residue was purified by column chromatography using pentane/diethyl ether = 98:2 as eluent to the give the title compound as a light brown viscous oil (1.60 g, 50%). ^{1}H NMR ($CDCl_3$): δ 6.84 (s, 1H), 5.34 (quintet, *J* = 3.2 Hz, 1H), 4.00 (t, *J* = 10.2 Hz, 1H), 3.61 (m, 1H), 2.80-2.91 (several peaks, 5H), 2.17 (s, 3H), 1.03-2.11 (several peaks, 43H), 0.84-0.90 (several peaks, 15H). ^{13}C NMR ($CDCl_3$): 151.8, 151.7, 147.2, 147.1, 127.9, 126.5, 115.5,

115.4, 104.9, 104.8, 97.6, 97.5, 75.2, 61.9, 40.0, 39.8, 39.4, 37.5, 37.4, 37.3, 32.8, 32.7, 32.4 (2C), 31.9, 31.8, 30.8, 29.7, 29.2, 28.9, 27.9, 25.4, 24.8, 24.4, 24.0, 23.9, 22.7, 22.6, 21.0, 19.7, 19.6, 19.0, 16.5, 14.1, 7.8. ^{125}Te NMR ($CDCl_3$) δ 201.0, 201.4. HRMS (TOF MS ES$^+$) *m/z* calcd for $C_{40}H_{70}O_3Te$ $[M+Na]^+$: 751.4285. Found: 751.4322.

5-(*n*-Octyltelluro)-δ-tocopherol) (6b). To a solution of compound **6a** (0.80 g, 1.10 mmol) in dichloromethane (25 mL) was added trifluoroacetic acid (0.063 g, 0.042 mL, 0.55 mmol) at room temperature. After stirring for 2.5 h, the solution was quenched with a saturated $NaHCO_3$ solution (10 mL) and extracted with dichloromethane (10 mL x 3). The organic layer was dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by column chromatography (pentane/diethyl ether = 99.7: 0.3) to give the title compound as a pale yellow liquid (0.450 g, 64%). $[\alpha]_D^{21}$ = +15.5^o (*c* = 0.04, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 6.82 (s, 1H), 6.10 (s, 1H), 2.85 (sextet, *J* = 3.6 Hz, 2H), 2.59 (t, *J* = 7.2 Hz, 2H), 2.18 (s, 3H), 1.75-1.83 (several peaks, 2H), 1.66 (quintet, *J* = 6.8 Hz, 2H), 0.84-1.57 (several peaks, 49H). ^{13}C NMR ($CDCl_3$): δ 150.9, 145.6, 130.6, 125.9, 112.9, 102.5, 75.1, 39.7, 39.4, 37.5 (2C), 37.4, 37.3, 32.8, 32.7, 32.5, 31.8 (2C), 31.7, 29.8, 29.1, 28.8, 28.0, 24.8, 24.5, 23.9, 22.7, 22.6, 21.0, 19.7, 19.6, 16.4, 14.1, 9.0. ^{125}Te NMR ($CDCl_3$) δ -5.9. HRMS (TOF MS ES$^+$) *m/z* calcd for $C_{35}H_{62}O_2Te$ $[M-H]^+$: 643.3734; found: 643.3697.

THP-protected β-Tocopherol. THP-protected 5-bromo-δ-tocopherol **5b** (3.40 g, 6.00 mmol) in THF (60 mL) was lithiated with *tert*-BuLi (1.7 M, 7.0 mL, 12.00 mmol) following the procedure for **6a**. Then, instead of dioctyl ditelluride, methyl iodide

(0.56 g, 9.00 mmol) was added. After stirring and workup as described for **6a**, the mixture was purified by column chromatography (pentane/ethyl acetate = 98.5:1.5) to give the title compound as a pale yellow oil (2.71 g, 90%). ^{1}H NMR ($CDCl_3$): δ 6.79 (s, 1H), 5.23 (m, 1H), 3.98 (m, 1H), 3.60 (m, 1H), 2.61 (t, *J* = 6.0 Hz, 2H), 1.05-2.14 (several peaks, 38H), 0.84-0.92 (several peaks, 12H). ^{13}C NMR ($CDCl_3$): δ. 147.4, 146.9, 123.4, 123.2, 120.1, 116.2, 116.1, 97.7 (2C), 74.5, 62.2, 39.9, 39.8, 39.4, 37.4, 37.3, 32.8, 32.7, 31.8, 28.0, 25.4, 24.8, 24.4, 24.0, 23.9, 22.7, 22.6, 22.3, 21.0, 20.8, 19.7, 19.6, 19.2, 16.2, 14.0, 11.3.

β-Tocopherol. To a solution of THP-protected β-tocopherol (1.8 g, 3.59 mmol) in dichloromethane/methanol (40 mL, 1:1) was added *p*-toluenesulfonic acid monohydrate (112.5 mg, 0.59 mmol) at room temperature. After stirring for overnight, the solution was quenched with a saturated $NaHCO_3$ solution (40 mL) and extracted with dichloromethane (50 mL x 3). The organic layer was dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by column chromatography (pentane/ethyl acetate = 98:2) to give the title compound as a pale yellow liquid (1.29 g, 86%). As determined by ^{1}H and ^{13}C NMR, the material was identical to a sample of β-tocopherol prepared according to literature methods.[3]

7-Bromo-β-tocopherol (7a). β-Tocopherol (2.192 g, 5.26 mmol) in dichloromethane (60 mL) and Bu_4NBr_3 (2.52 g) in dichloromethane (120 mL) were reacted as described for the preparation of compound **5a**. The residue was purified by flash column chromatography (pentane/ethyl acetate = 99:1) to give the title compound as a colourless liquid (2.17 g, 83%). As determined by ^{1}H and ^{13}C NMR, the material was

identical to a sample of 7-bromo-β-tocopherol prepared according to literature methods.[2]

7-(*n*-Octyltelluro)-β–tocopherol (7b). To a solution of 7-bromo-β-tocopherol **7a** (0.74 g, 1.50 mmol) in anhydrous THF (15 mL) was added *tert*-BuLi (1.7 M, 2.64 mL, 4.5 mmol)) under nitrogen at -78 °C. The solution was stirred for 1.5 h at -78 °C before the addition of dioctyl ditelluride (1.09 g, 2.25 mmol). After stirring at ambient temperature for overnight, the solution was quenched with a saturated ammonium chloride solution (25 mL) and extracted with ether (40 mL x 3). The residue was purified by column chromatography (pentane/ethyl acetate = 99:1) to give the title compound as a yellow oil (0.29 g, 30%). $[\alpha]_D^{21}$ = -10.6° (*c* = 0.014, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 6.30 (s, 1H), 2.67 (t, *J* = 6.8 Hz, 2H), 2.61 (t, *J* = 8.0 Hz, 2H), 2.48 (s, 3H), 2.18 (s, 3H), 0.84-1.82 (several peaks, 53H). ^{13}C NMR ($CDCl_3$): δ. 148.4, 144.7, 129.6, 123.1, 117.5, 105.8, 74.9, 39.7, 39.4, 37.4, 37.3, 34.1, 32.8, 32.7, 31.8 (2C), 31.6, 31.5, 29.1, 28.8, 28.0, 24.8, 24.4, 23.8, 22.7, 22.6, 22.3, 22.2, 21.0, 20.9, 19.7, 19.6, 14.1, 12.8, 9.3. ^{125}Te NMR ($CDCl_3$) δ 27.4. Anal. Calcd for $C_{36}H_{64}O_2Te$: C, 65.86; H, 9.83. Found: C, 65.80; H, 9.80.

HPLC Peroxidation Assay. The experimental setup for recording inhibition times (T_{inh}) and inhibited rates of peroxidation (R_{inh}) during azo-initiated peroxidation of linoleic acid in a two-phase system was recently described.[4] The values reported in Table 1 for reactions performed in the presence of NAC and in the absence of NAC are means ± SD based on triplicates. We have found that R_{inh} and T_{inh} values show slight variations depending on the amount of linoleic acid hydroperoxide which is

always present in commercial samples as an impurity, and which increases upon storage. We have therefore standardized the procedure by adding small amounts of older, peroxidised linoleic acid to samples of fresh one until the final concentration of hydroperoxide is ca 175 μM at the beginning of an experiment.

Thiol Peroxidase Activity: The GPx-like activities of novel organotellurium compounds prepared were determined by UV-spectroscopy following the protocol by Tomoda[5] with slight modifications. The test mixture contained PhSH (1 mM) and catalyst (0.01 mM) at 21 ^{o}C and the reaction was initiated by addition of H_2O_2 (3.75 mM). Initial reaction rates were based on the formation of diphenyl disulfide (PhSSPh) as assessed by UV-spectroscopy at 305 nm. The initial reduction rate was determined at least 3-4 times and calculated from the first 10 seconds of reaction by using 1.24 $mM^{-1}cm^{-1}$ as the extinction coefficient for PhSSPh.

References

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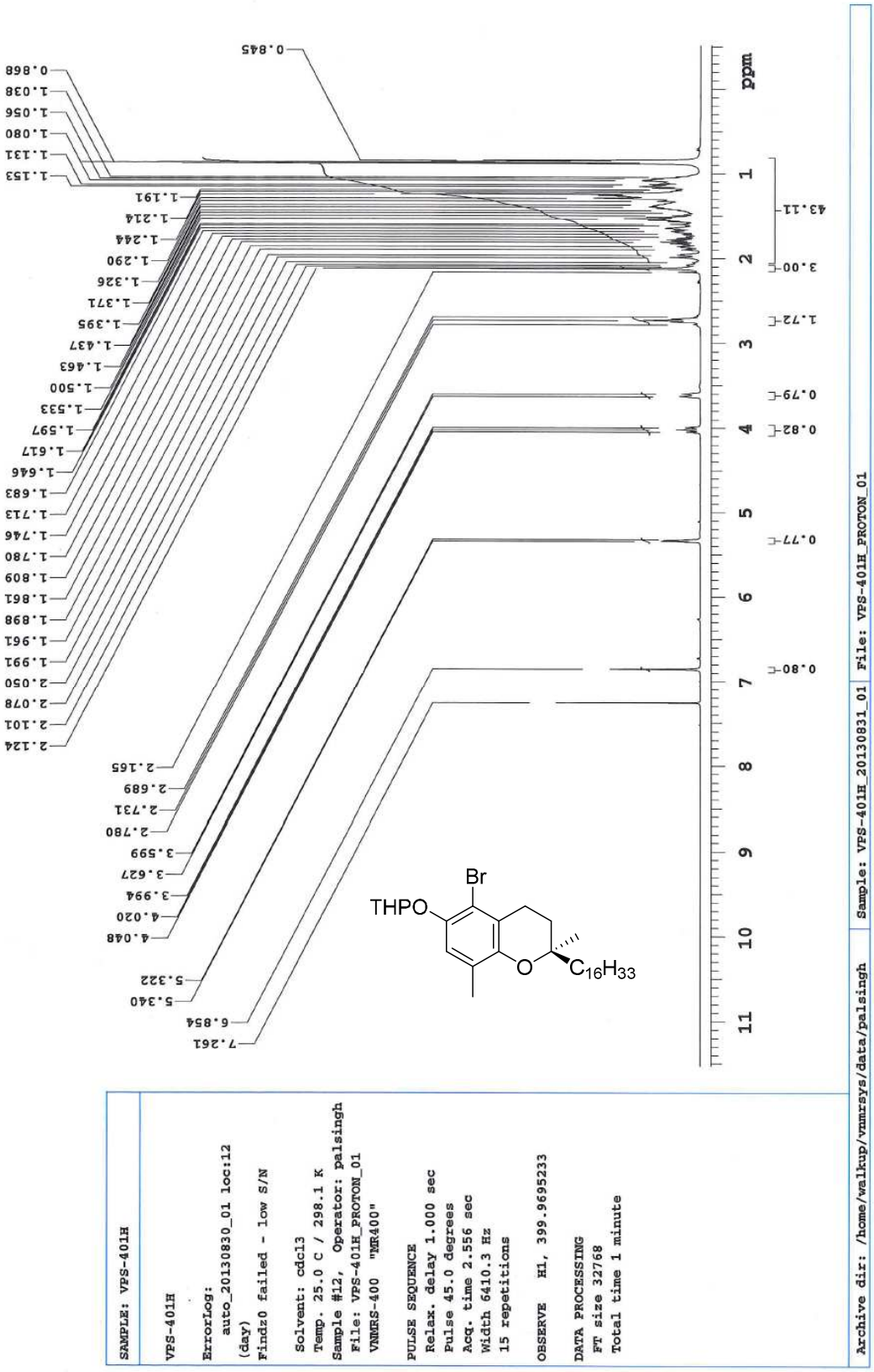
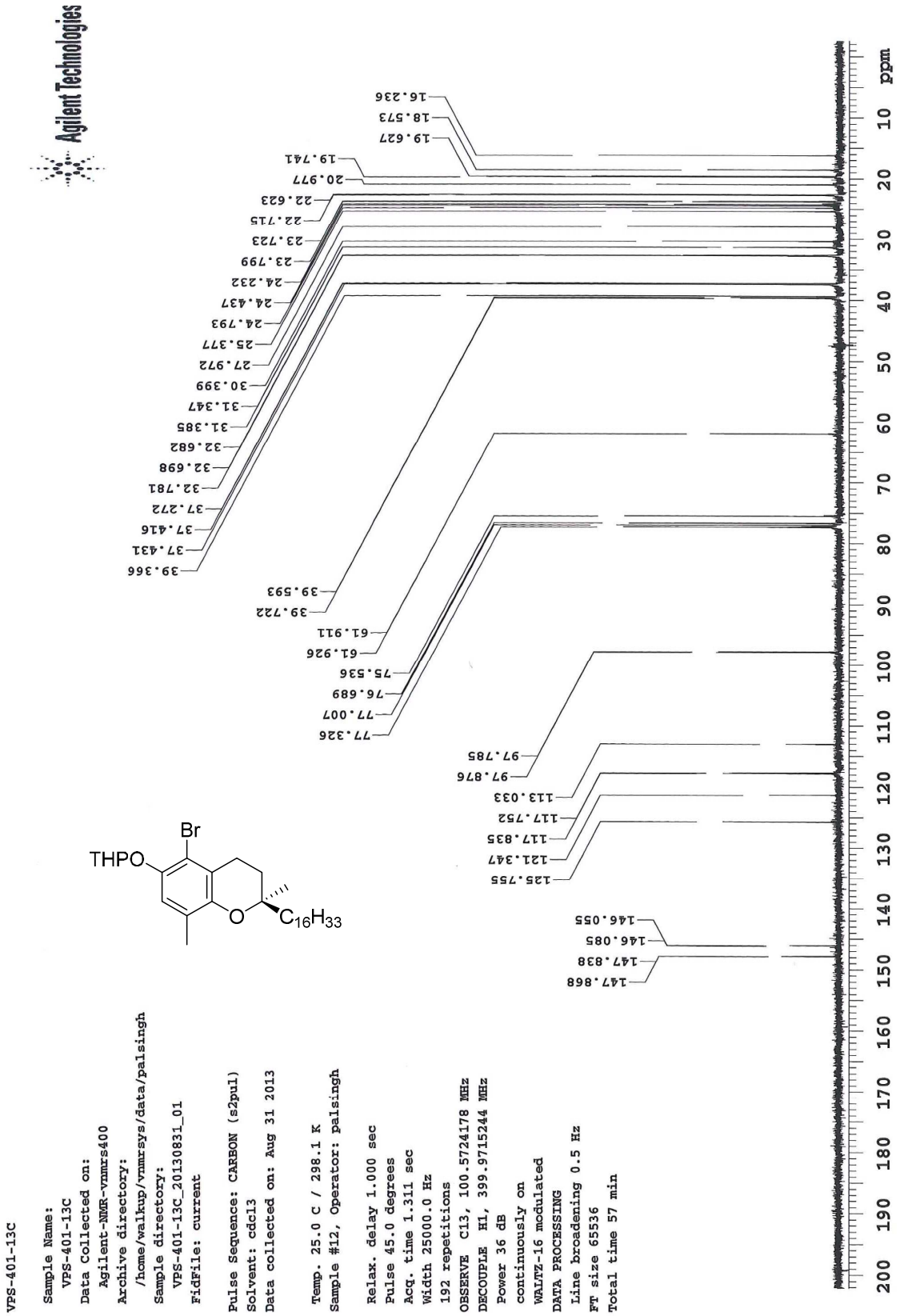
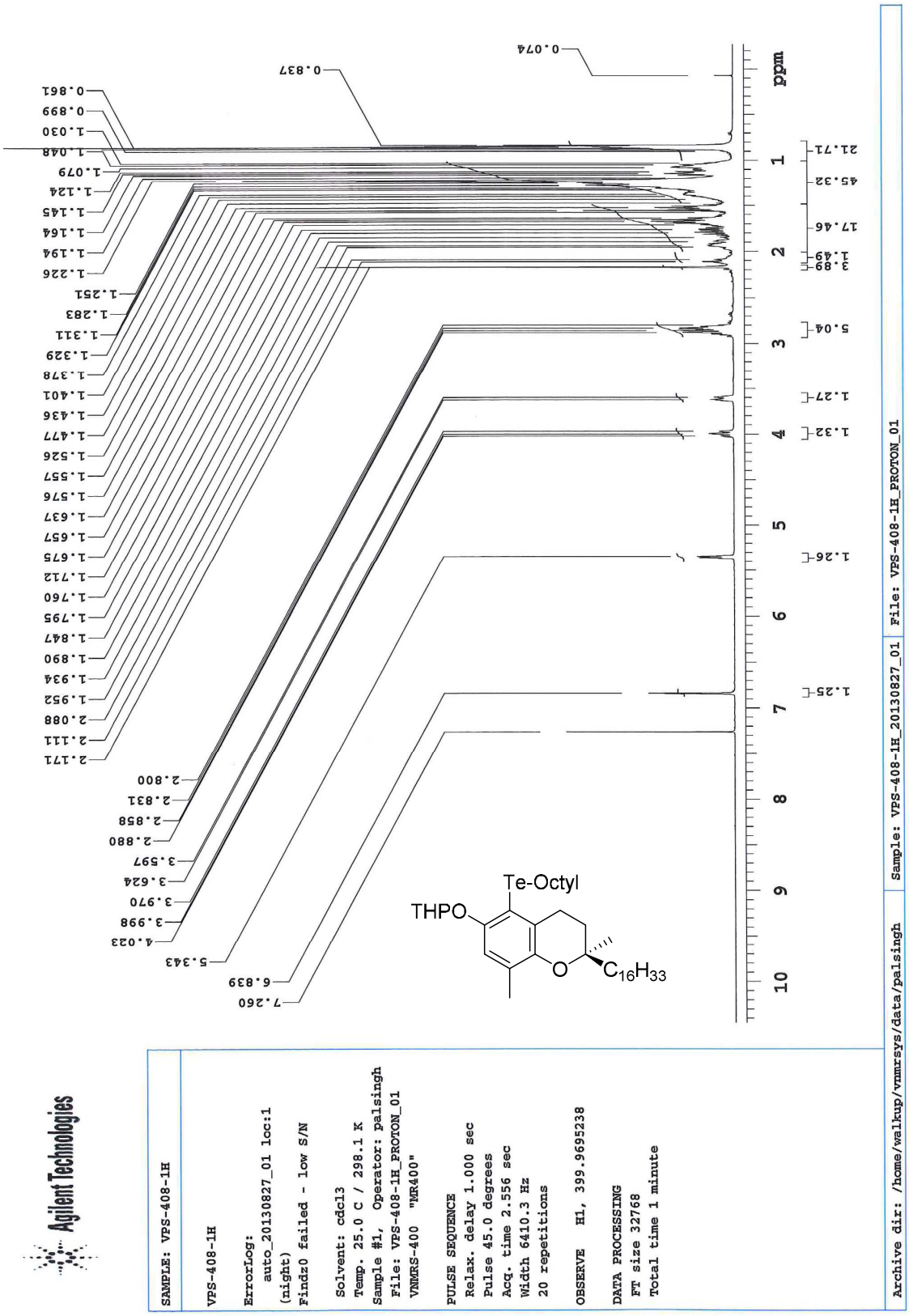
^{1}H NMR spectrum of **5b**



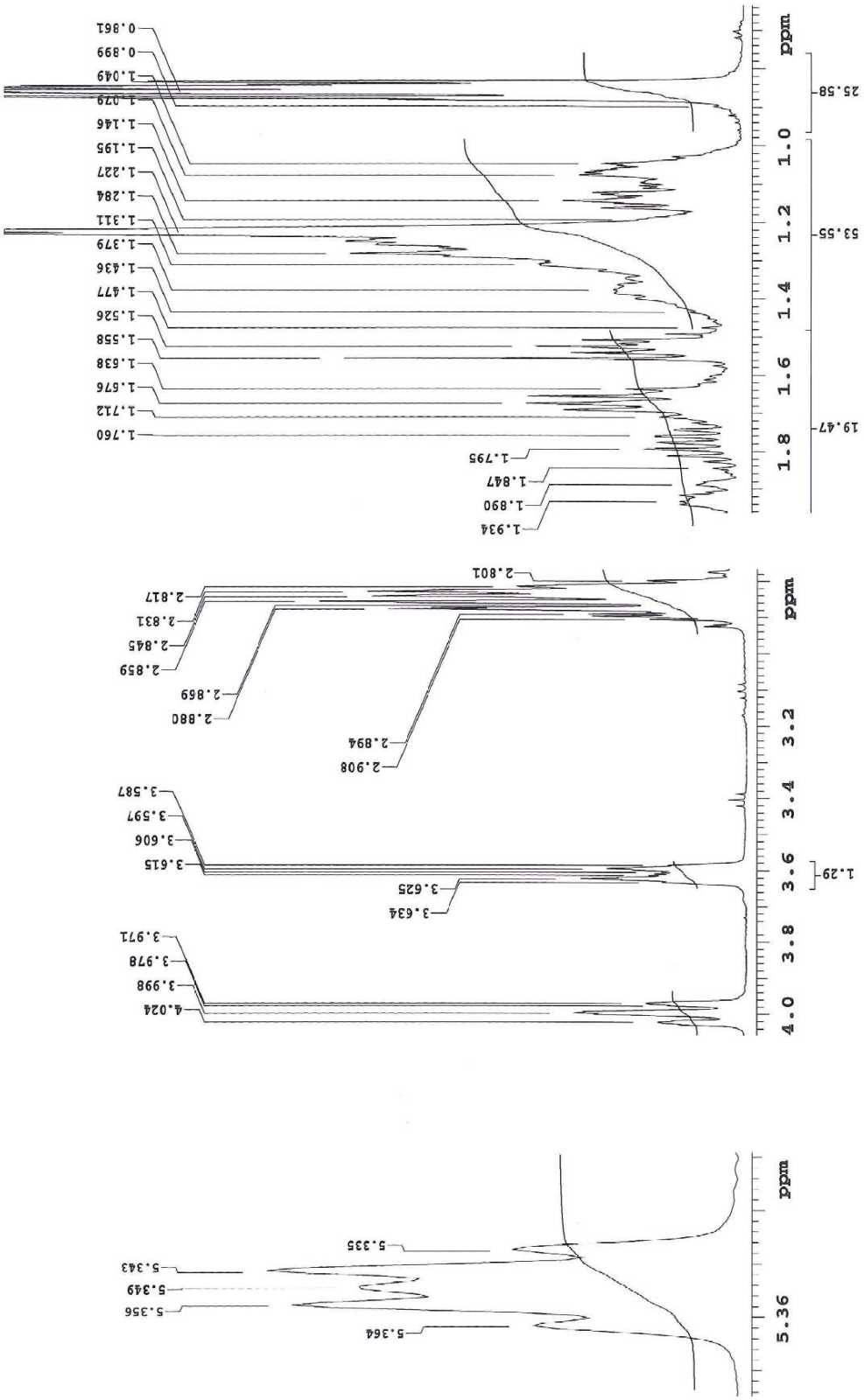
^{13}C NMR spectrum of **5b**



^{1}H NMR spectrum of **6a**



Expanded version of ^{1}H NMR spectrum of **6a**



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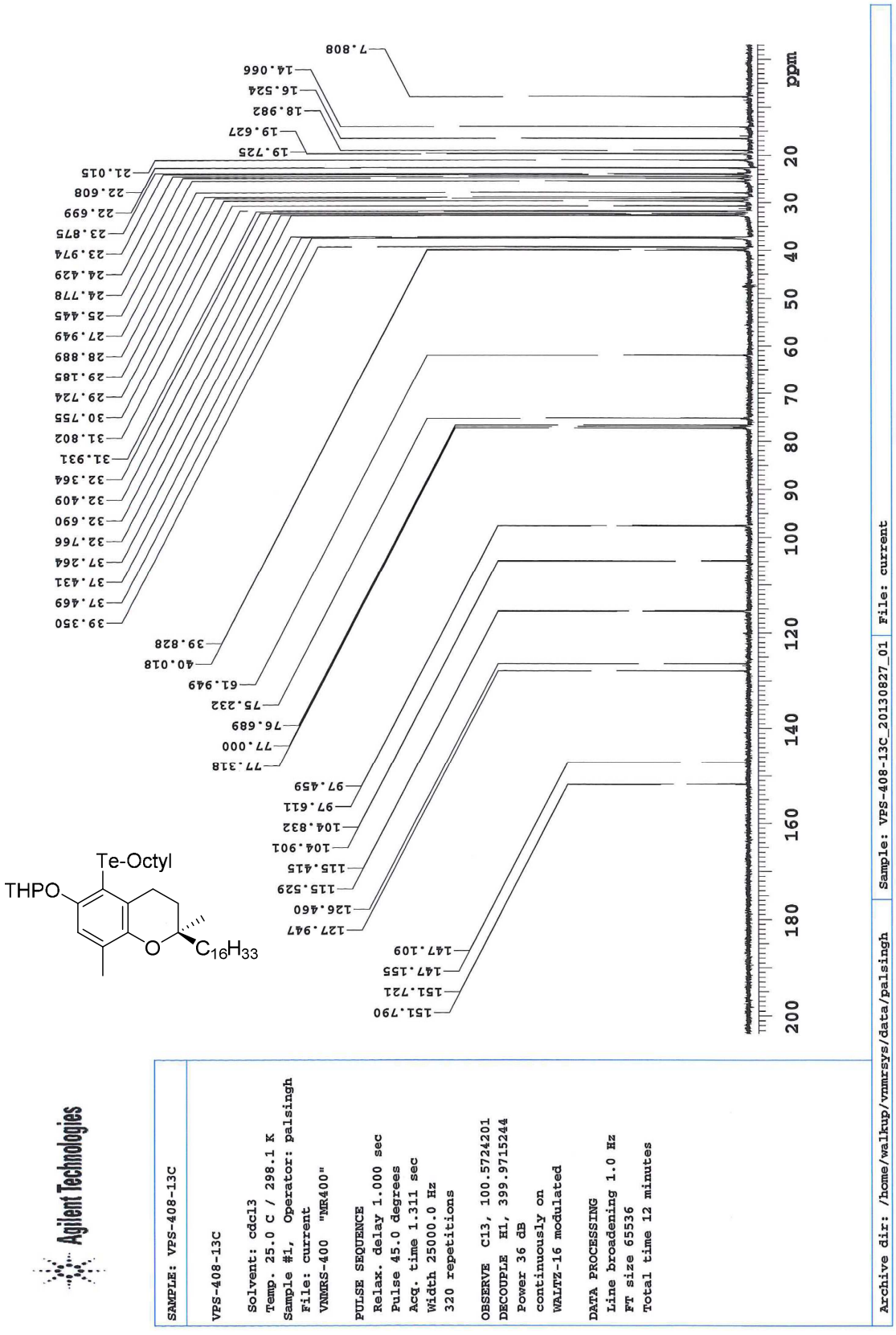
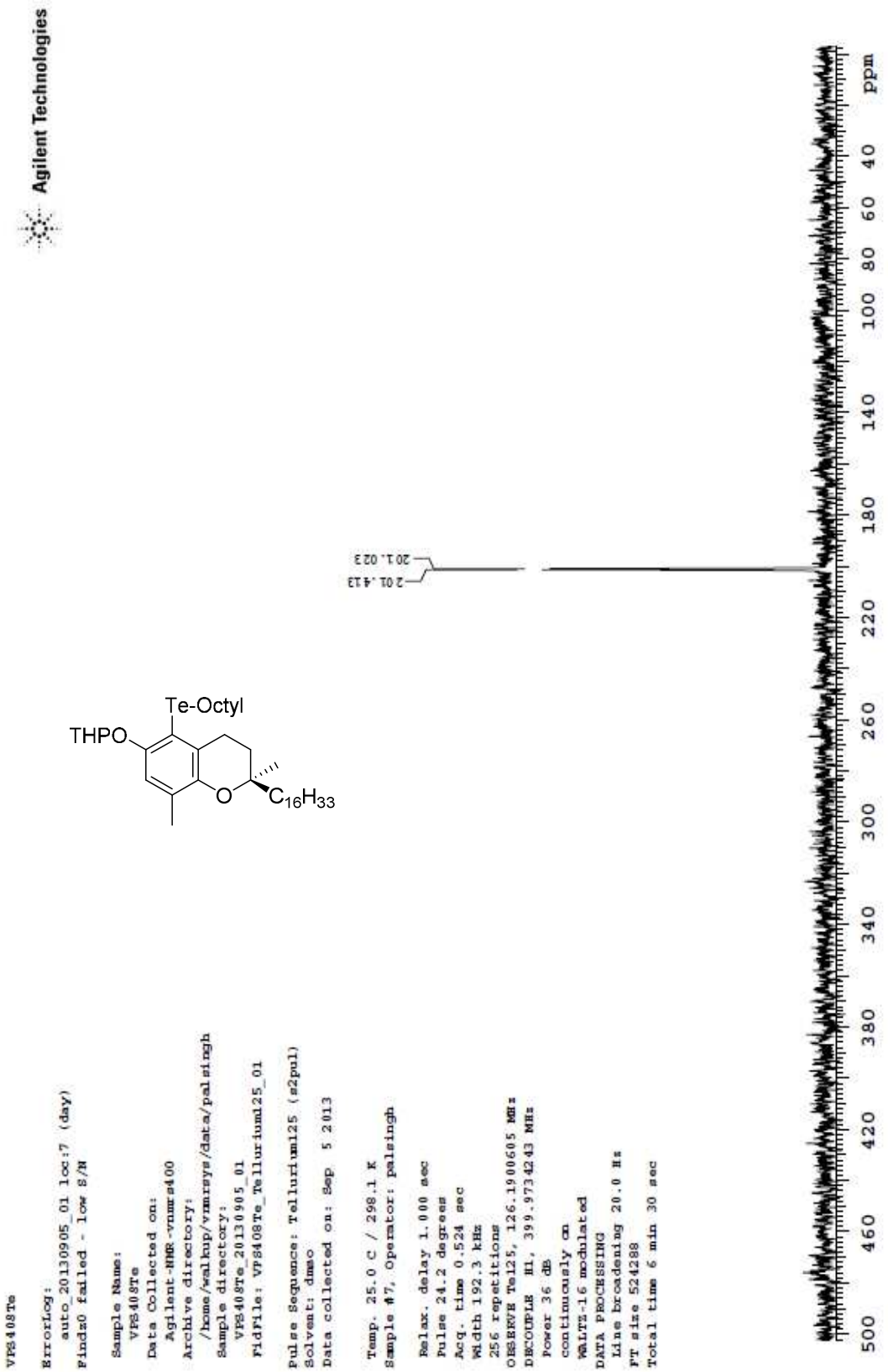


^{125}Te NMR spectrum of **6a**



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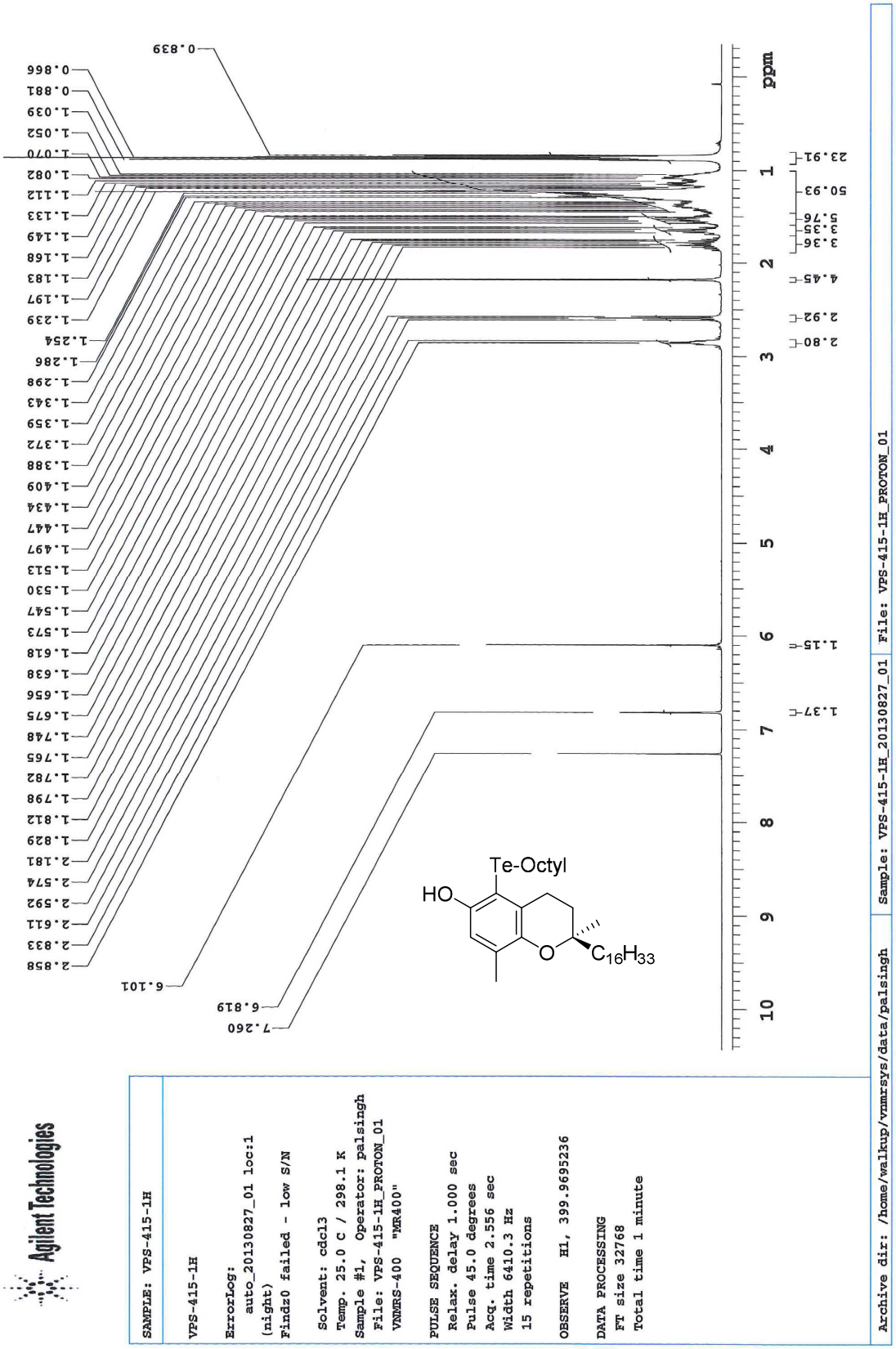

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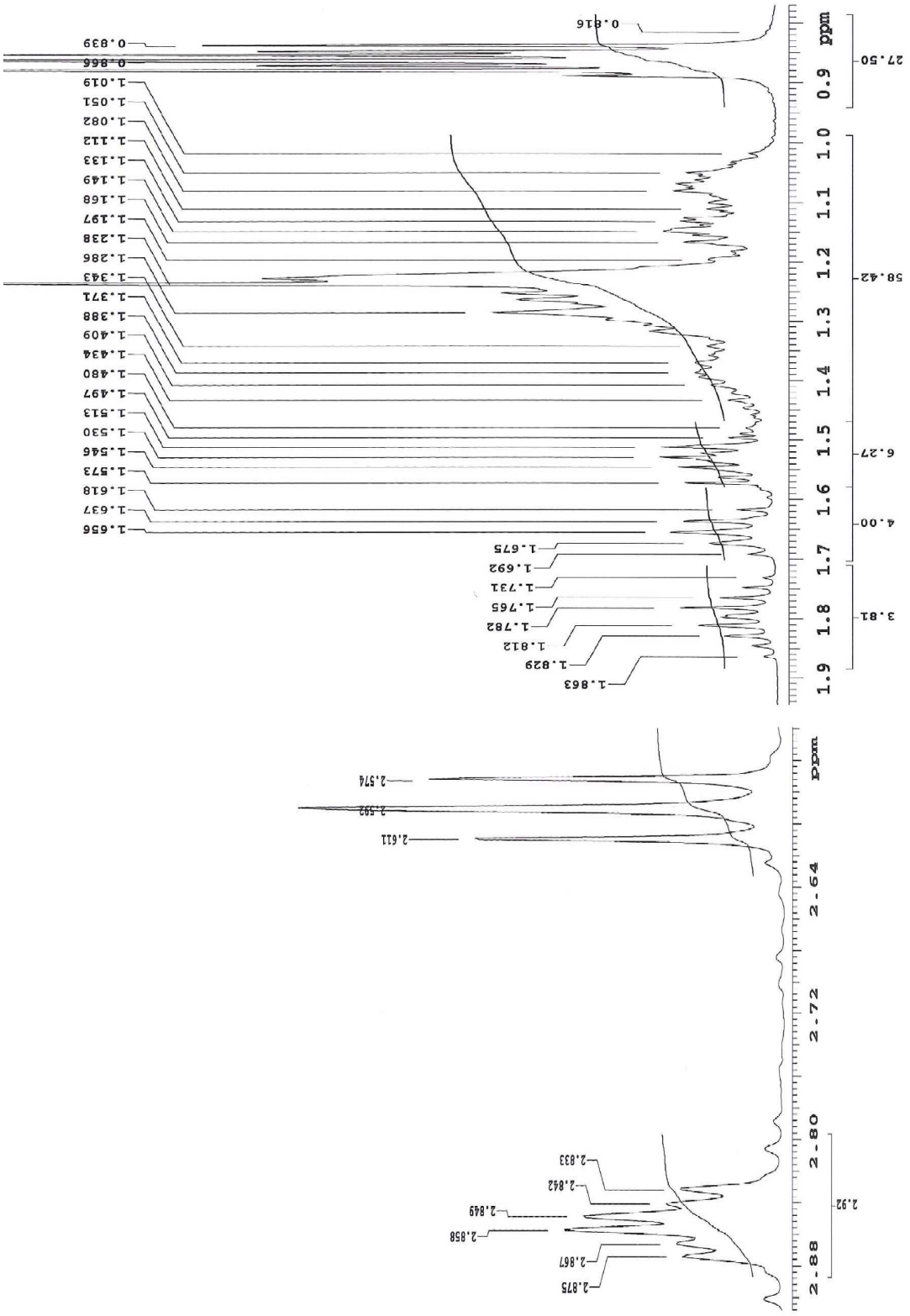

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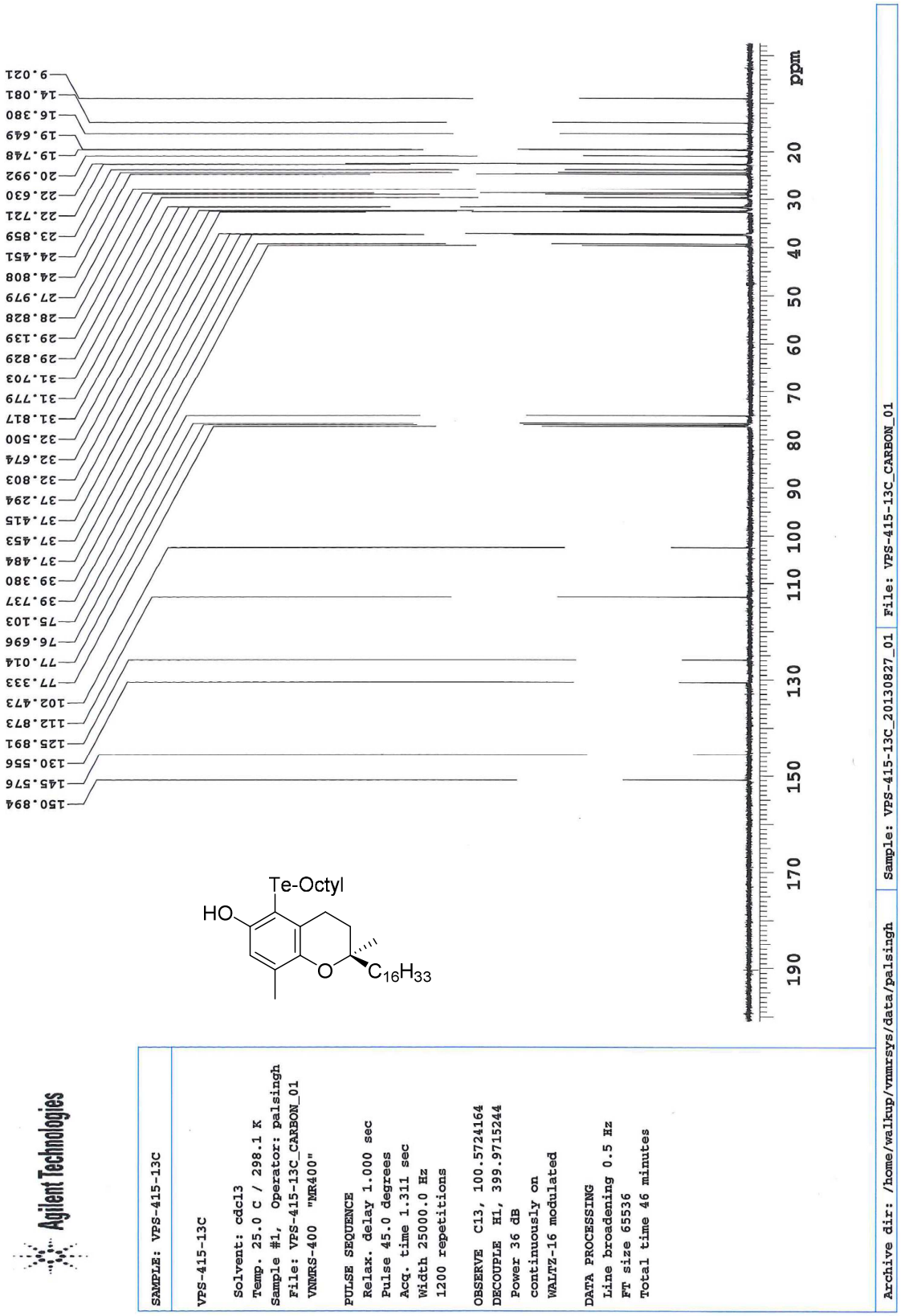

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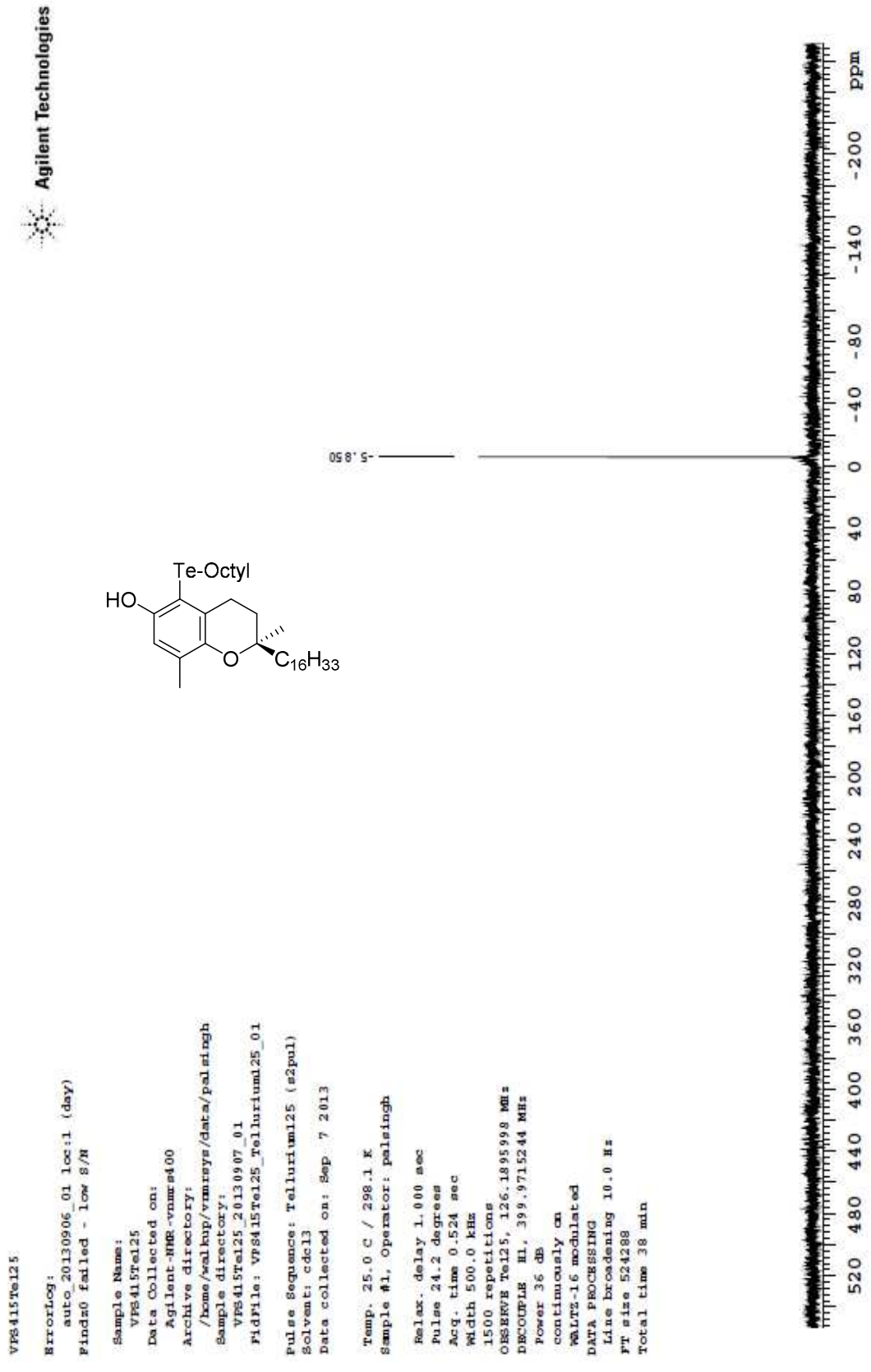
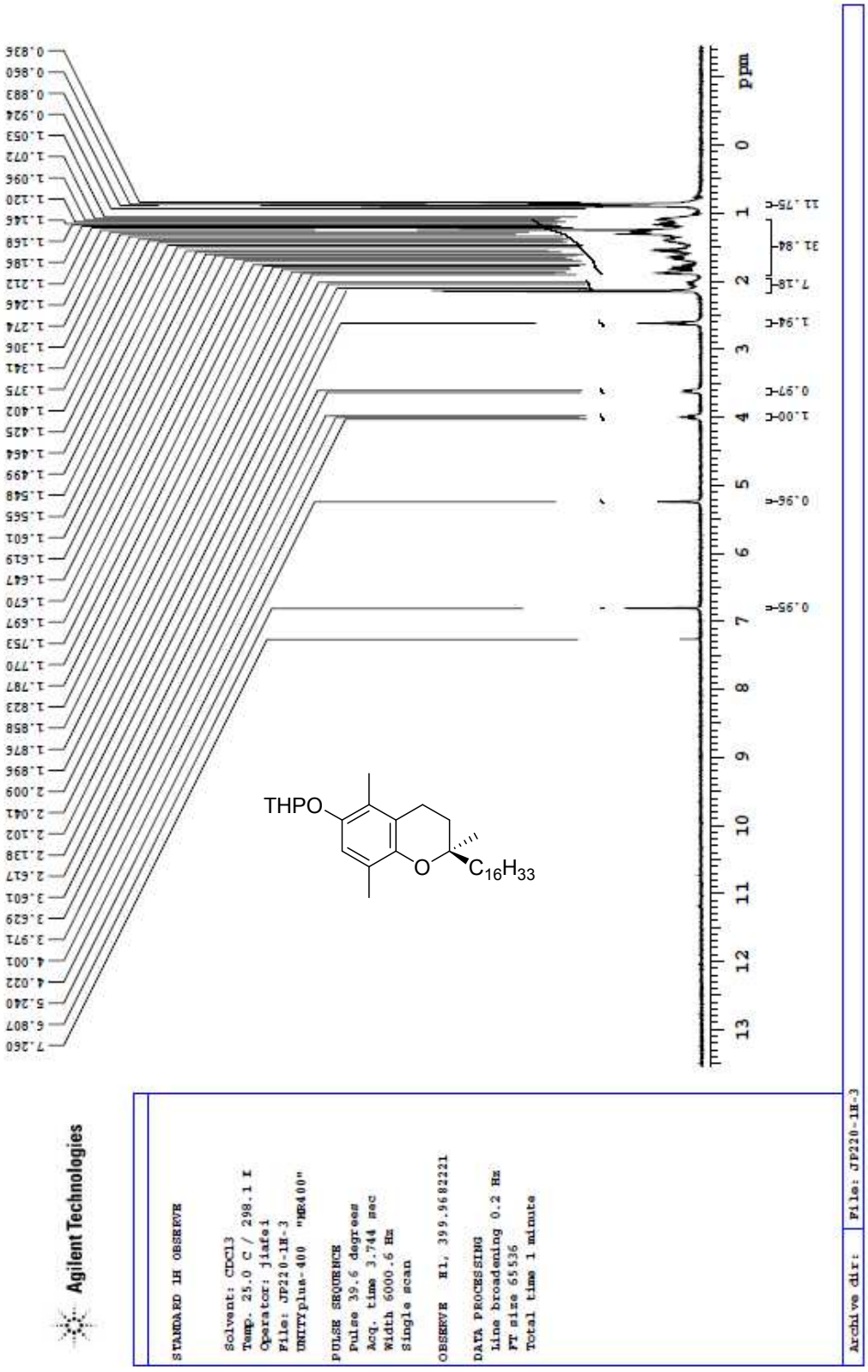


^{1}H NMR spectrum of THP-protected β-Tocopherol



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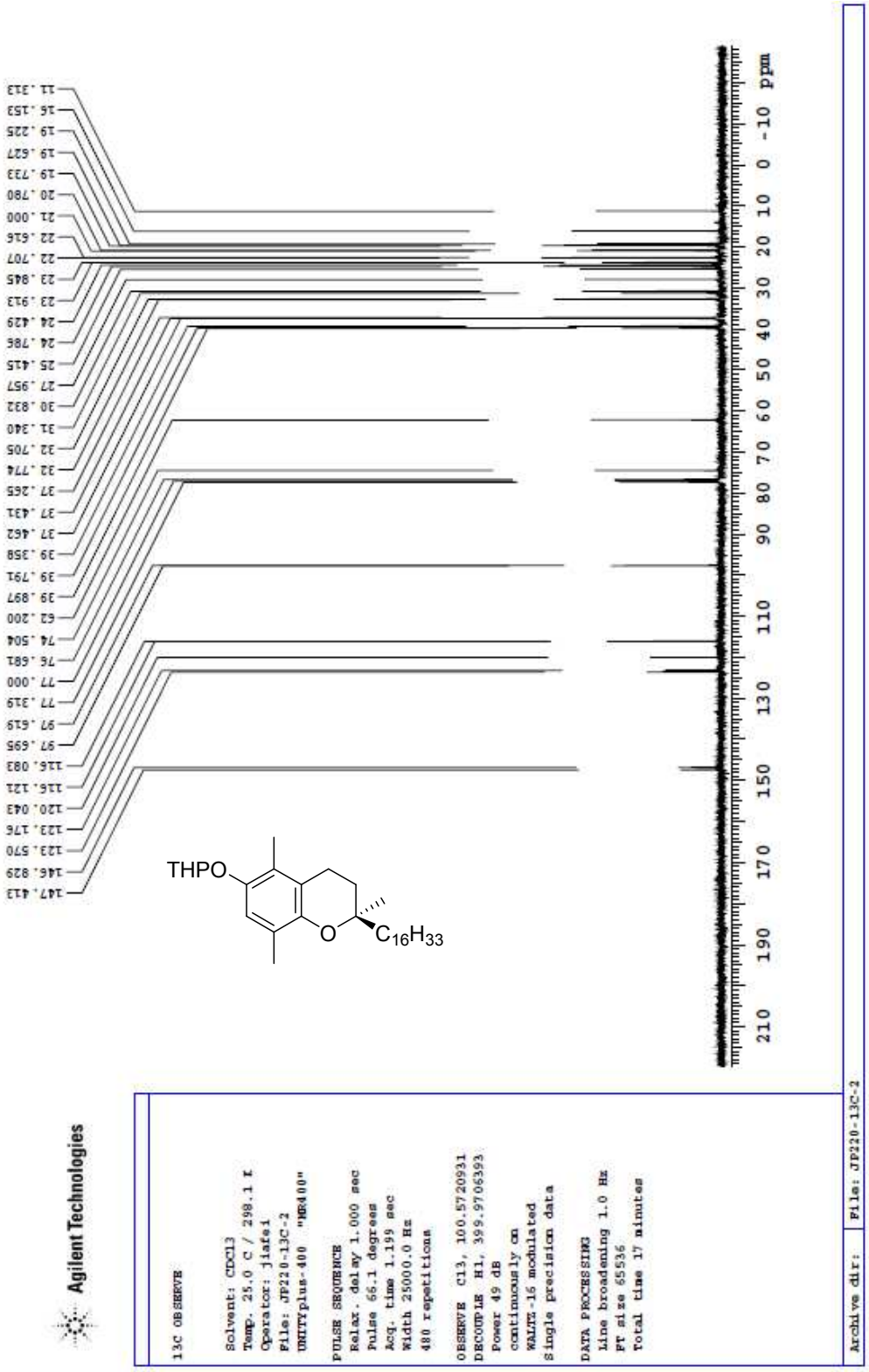

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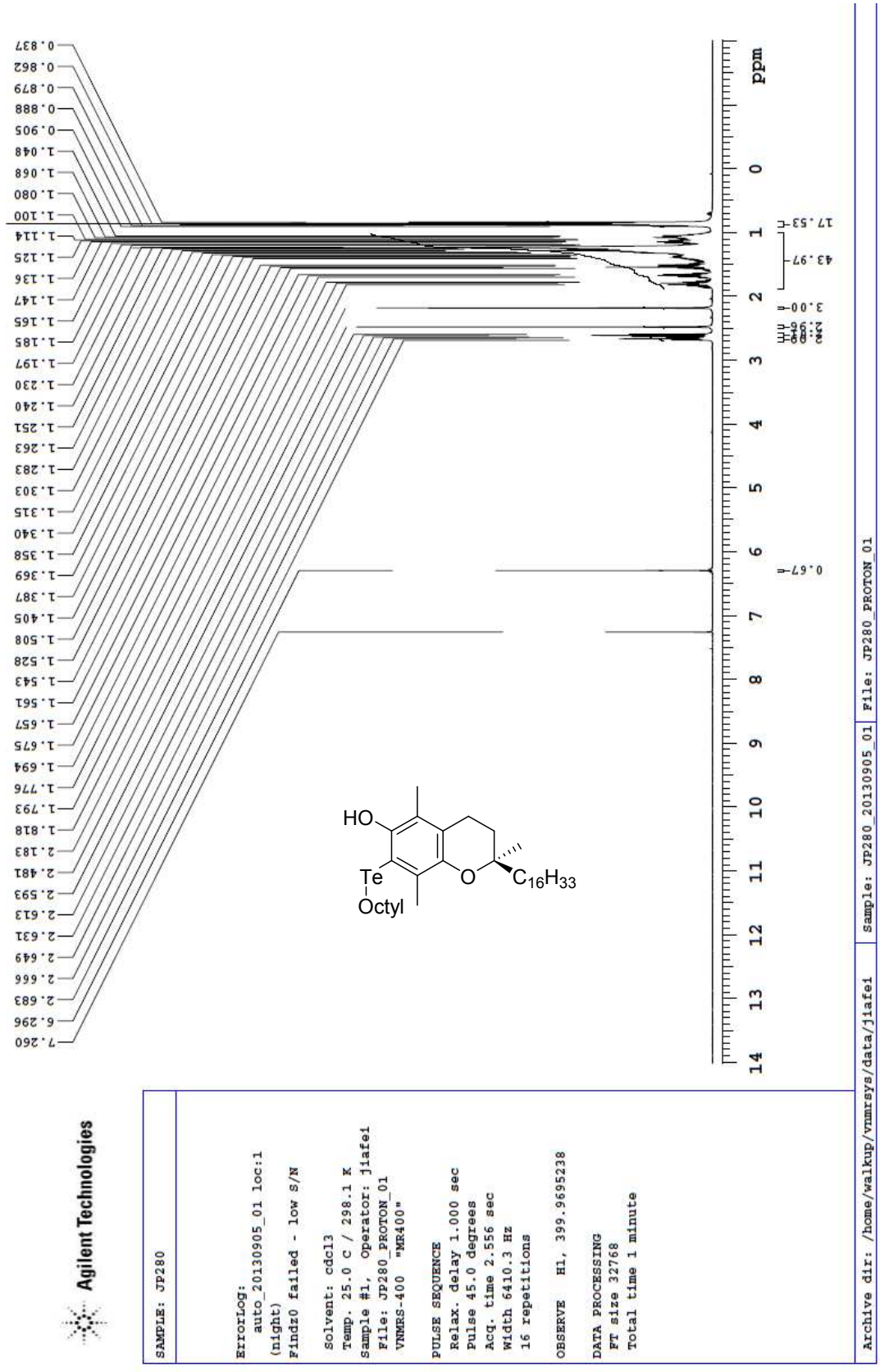

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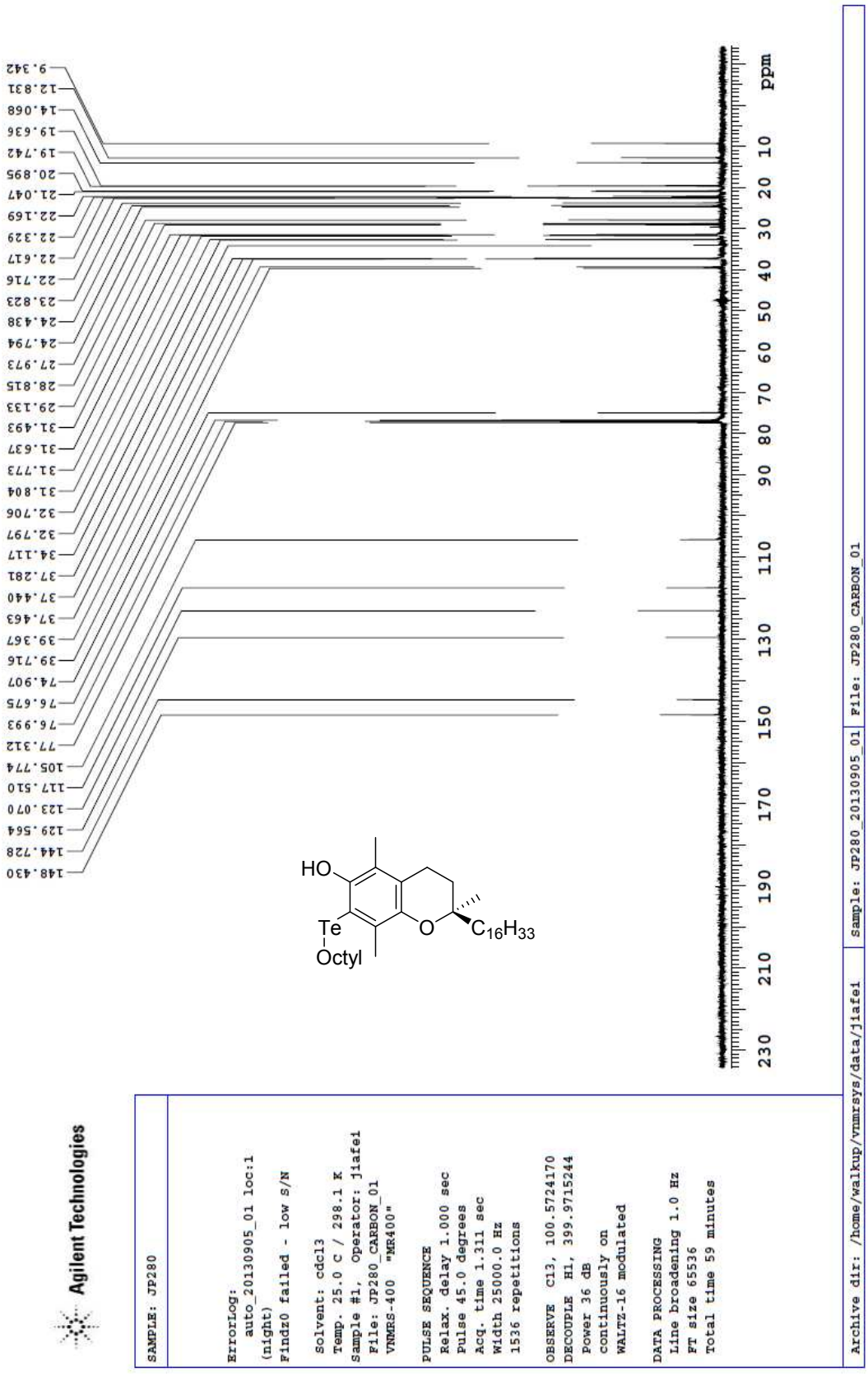

^{125}Te NMR spectrum of **7b**