Supporting Information

Regioselective S_NAr Reaction of the Phenoxathiin-Based Thiacalixarene as a Route to Novel Macrocyclic Skeleton

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Table of Content

1. General information

All chemicals were purchased from commercial sources and used without further purification. Acetone was dried and distilled using conventional methods, THF, CH_3CN and ethanol were dried using column solvent purification system PureSolv MD7 (Inert). All samples were dried in the desiccator over P_2O_5 under vacuum (1 Torr) for at least 8 hours. Melting points were measured on Heiztisch Mikroskop Polytherm A (Wagner & Munz) and they are not corrected. ^1H, ^{13}C, COSY, HMQC, HMBC, NOE and VT spectra were measured on Bruker Avance^{III} 600 operating at 600.13 MHz for ^1H and 150.92 MHz for ^{13}C, ^1H spectrum with chiral shifting agent was measured on Agilent 400-MR DDR2 operating at 400 MHz for ^1H. Chemical shifts are given in δ-units (ppm) and are referenced to TMS or solvent signal. IR spectra were measured on FTIR spectrometer Nicolet 6700 (Thermo-Nicolet) connected with diamond ATR attachment GladiATR (PIKE) and DTGS detector. The measurement parameters were: spectral range 4000 – 400 cm^{-1}, resolution 4 cm^{-1}, 64 spectral accumulations and Happ-Genzel apodization. ESI HRMS spectra were measured on Q-TOF (Micromass) spectrometer. Substance purities and courses of the reactions were monitored by thin layer chromatography (TLC) using silica gel 60 F_{254} on aluminium-backed sheets (Merck) and analysed at 254 and 365 nm. Radial chromatography was carried out on Chromatotron (Harrison Research) connected with Lab Pump RHSY2 (Fluid Metering). Self-prepared glass discs were covered by silica gel 60 PF_{254} containing $CaSO_4$ (Merck).

2. Experimental procedures and characterization

Compound 2, compound 5 and compound 6
All the starting compounds were prepared based on the previously published procedures.[S1, S2]

Compound 7a
Macrocycle **8a** (50 mg, 0.054 mmol) was dissolved in dry acetone (5 mL) and stirred at room temperature. Iodomethane (0.08 mL, 1.30 mmol) and Cs_2CO_3 (354 mg, 1.09 mmol) were added and the mixture was heated to reflux (56 °C). After the entire starting compound disappeared (monitored by TLC, 30 min), the solvent was removed from the reaction mixture under reduced pressure. Subsequently, 1M HCl (30 mL) was added to the residue and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over $MgSO_4$. Then the solvent was removed under reduced pressure to yield pure compound **7a** as a white solid (52 mg, 100 %).

(S1) Morohashi, N.; Kojima, M.; Suzuki, A.; Ohba, Y. *Heterocycl. Commun.* **2005**, *11*, 249.
(S2) Landovsky, T.; Dvorakova, H.; Eigner, V.; Babor, M.; Krupicka, M.; Kohout, M.; Lhotak, P. *New J. Chem.* **2018**, *42*, 20074.

M.p. > 350 °C (CH_2Cl_2/methanol, decomposes).
^{1}H NMR (600 MHz, $CDCl_3$, 298 K) δ (ppm): 8.51 (d, J = 2.6 Hz, 1H, *C3*), 8.47 (d, J = 2.6 Hz, 1H, *C5*), 8.46 (d, J = 2.6 Hz, 1H, *B3*), 8.45 (d, J = 2.6 Hz, 1H, *B5*), 8.36 (d, J = 2.5 Hz, 1H, *D5*), 8.31 (d, J = 2.5 Hz, 1H, *D3*), 7.96 (s, 1H, *A3*), 3.90 (s, 3H, *D*-CH_3), 3.87 (s, 6H, *B*-CH_3), 3.78 (s, 6H, *C*-CH_3), 3.59 (s, 6H, *A*-CH_3-*6*), 2.43 (s, 3H, *A*-CH_3-*1*), 1.60 (s, 9H, *A*-tBu), 1.46 (s, 9H, *B*-tBu), 1.45 (s, 9H, *C*-tBu), 1.42 (s, 9H, *D*-tBu).
^{13}C NMR (150 MHz, $CDCl_3$, 298 K) δ (ppm): 153.6 (Cq, *C1*), 153.3 (Cq, *B1*), 152.7 (Cq, *D1*), 152.1 (Cq, *A6*), 148.7 (Cq, *B4*), 148.6 (Cq, *A1*), 147.6 (Cq, *A4*), 147.3 (Cq, *C4*), 146.1 (Cq, *D4*), 143.0 (Cq, *A*), 138.7 (Cq, *D*), 137.2 (Cq, *C*), 137.1 (Cq, *C*), 136.9 (Cq, *B*), 136.8 (Cq, *B*), 136.4 (Cq, *D*), 136.2 (Cq, *A*), 135.5 (CH, *D5*), 133.9 (CH, *B3*), 133.8 (CH, *C5*), 132.0 (CH, *C3*), 130.2 (CH, *B5*), 129.4 (CH, *D3*), 122.8 (CH, *A3*), 66.0 (*C*-CH_3), 65.6 (*D*-CH_3), 65.5 (*B*-CH_3), 61.6 (*A*-CH_3-*6*), 58.6 (*A*-CH_3-*1*), 37.8 (Cq, *A*-tBu), 35.5, 35.2 and 35.1 (Cq, *B*-tBu, *C* and *D*), 32.4 (*A*-tBu), 31.2, 31.1 and 31.0 (*B*-tBu, *C*, *D*).
IR (ATR) *v* (cm^{-1}): 3071, 2960, 2870, 1549.
HRMS (ESI^+) ($C_{45}H_{58}O_{13}S_4$) *m/z* calc: 957.26525 $[M + Na]^+$; found: 957.26582 $[M + Na]^+$.

Compound 7b
Macrocycle **8b** (50 mg, 0.054 mmol) was dissolved in dry CH_3CN (5 mL) and stirred at room temperature. Iodoethane (0.10 mL, 1.30 mmol) and Cs_2CO_3 (354 mg, 1.09 mmol) were added and the mixture was heated to reflux (82 °C). After the entire starting compound disappeared (monitored by TLC, 30 min), the solvent was removed from the reaction mixture under reduced pressure. Subsequently, 1M HCl (30 mL) was added to the residue and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over $MgSO_4$. Then the solvent was removed under reduced pressure to yield pure compound **7b** as a white solid (50 mg, 97 %).

major conformer (NMR; aprox. 10:1 mixture)
M.p. > 350 °C (CH_2Cl_2/methanol, decomposes).
^{1}H NMR (600 MHz, $CDCl_3$, 298 K) δ (ppm): 8.52 (d, J = 2.6 Hz, 1H, *C5*), 8.48 – 8.45 (m, 2H, *B3* and *B5*), 8.45 (d, J = 2.6 Hz, 1H, *C3*), 8.36 (d, J = 2.5 Hz, 1H, *D5*), 8.34 (d, J = 2.5 Hz, 1H, *D3*), 7.95 (s, 1H, *A3*), 3.97 – 3.89 (m, 1H, CH_2), 3.88 (s, 3H, *B*-CH_3), 3.86 – 3.80 (m, 1H, CH_2), 3.77 (s, 6H, *C*-CH_3 and *D*-CH_3), 2.45 (s, 3H, *A*-CH_3), 1.60 (s, 9H, *A*-tBu), 1.47 (s, 9H, *B*-tBu), 1.45 (s, 9H, *C*-tBu), 1.42 (s, 9H, *D*-tBu), 1.31 (t, J = 7.1 Hz, 3H, CH_3).
^{13}C NMR (150 MHz, $CDCl_3$, 298 K) δ (ppm): 153.6 (Cq, *C1*), 153.4 (Cq, *B1*), 152.4 (Cq, *D1*), 151.8 (Cq, *A6*), 148.8 and 148.8 (2xCq, *A1* and *B4*), 147.9 (Cq, *A4*), 147.4 (Cq, *C4*), 146.3 (Cq, *D4*), 137.9 (Cq, *A*), 139.2 (Cq, *D*), 137.2 (Cq, *C*), 137.1 and 137.1 (Cq, *D* and Cq, *B*), 136.7 (Cq, *C*), 136.4 (Cq, *B*), 136.2 (Cq, *A*), 134.4 (CH, *D5*), 133.9 (CH, *B3*), 133.6 (CH, *C3*), 132.0 (CH, *C5*), 130.3 (CH, *B5*), 129.6 (CH, *D3*), 122.6 (CH, *A3*), 72.6 (CH_2), 65.9, 65.5 and 65.3 (*D*-CH_3, *C*-CH_3 and *B*-CH_3), 58.8 (*A*-CH_3), 38.0 (Cq, *A*-tBu), 34.5, 35.2 and 35.2 (Cq, *B*-tBu, *C* and *D*), 32.4 (*A*-tBu), 31.2, 31.1 and 31.0 (*B*-tBu, *C*, *D*), 15.6 (CH_3).
IR (ATR) *v* (cm^{-1}): 3075, 2958, 2870, 1547.
HRMS (ESI^+) ($C_{46}H_{60}O_{13}S_4$) *m/z* calc: 971.28090 $[M + Na]^+$; found: 971.28137 $[M + Na]^+$.

Compound 7c
Macrocycle **8c** (50 mg, 0.054 mmol) was dissolved in dry acetone (5 mL) and stirred at room temperature. Iodomethane (0.08 mL, 1.28 mmol) and Cs_2CO_3 (349 mg, 1.07 mmol) were added and the mixture was heated to reflux (56 °C). After the entire starting compound disappeared (monitored by TLC, 30 min), the solvent was removed from the reaction mixture under reduced pressure. Subsequently, 1M HCl (30 mL) was added to the residue and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over $MgSO_4$. Then the solvent was removed under reduced pressure to yield pure compound **7c** as a white solid (51 mg, 100 %).

M.p. > 350 °C (CH_2Cl_2/methanol, decomposes).

The assignment of ^{1}H NMR and ^{13}C NMR spectra was not possible due to broad resonances caused by chemical exchange between several conformers (see VT NMR spectra in the range of 213 K – 403 K).
IR (ATR) *v* (cm^{-1}): 3075, 2957, 2870, 1704, 1549.
HRMS (ESI^+) ($C_{46}H_{60}O_{13}S_4$) *m/z* calc: 971.28090 $[M + Na]^+$, 987.25483 $[M + K]^+$; found: 971.28094 $[M + Na]^+$, 987.25470 $[M + K]^+$.

Compound 8a
Macrocycle **6** (300 mg, 0.34 mmol) was dissolved in dry THF (30 mL), sodium methoxide (109 mg, 2.03 mmol) was added and the solution was stirred and heated to reflux (67 °C). After the entire starting compound disappeared (monitored by TLC, 2 h), the solvent was removed from the reaction mixture under reduced pressure. Subsequently, 1M HCl (30 mL) was added to the residue and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over $MgSO_4$. Then the solvent was removed under reduced pressure to yield a crude mixture. Compound **8a** was isolated using radial chromatography (silica gel, eluent CH_2Cl_2:isopropanol 60:1 v/v) as a white solid (230 mg, 74 %).

M.p. 262.7-266.5 °C (CH_2Cl_2/isopropanol, decomposes).
^{1}H NMR (600 MHz, THF-d_8, 300 K) δ (ppm): 8.99 (s, 1H, OH), 8.54 and 8.52 (2xbrs, 2x1H, *B3* and *B5*), 8.48 – 8.46 (m, 2H, *D* and *C*), 8.44 (d, J = 2.6 Hz, 1H, *D*), 8.37 (d, J = 2.6 Hz, 1H, *C*), 7.75 (s, 1H, *A3*), 3.92 (s, 3H, *D*-CH_3), 3.85 (s, 3H, *C*-CH_3), 3.29 (s, 3H, *A*-CH_3), 3.18 (s, 3H, *B*-CH_3), 1.61 (s, 9H, *A*-tBu), 1.48 (s, 9H, *B*-tBu), 1.47 (s, 9H, *D*-tBu), 1.44 (s, 9H, *C*-tBu).
^{13}C NMR (150 MHz, THF-d_8, 300 K) δ (ppm): 154.2 (Cq, *B1*), 153.3 (Cq, *D1*), 152.5 (Cq, *C1*), 150.2 (Cq, *A1*), 147.8 (Cq, *A6*), 147.6 (Cq, *A4*), 146.8 and 146.4 (2xCq, *B4* and *D4*), 144.2 (Cq, *C4*), 137.9, 137.9, 137.2, 136.9, 136.8 and 136.0 (6xCq, *B2*, *B6*, *C2*, *C6*, *D2* and *D6*), 135.8 (2xCq, *A2* or *A5*), *A2* or *A5* are overlapped; 135.4 (CH, *C*), 134.0 (CH, *D*), 133.9 (CH, *B*), 132.3 (CH, *B*), 133.0 (CH, *D*), 129.0 (CH, *C*), 118.2 (CH, *A3*), 65.1 (*D*-CH_3), 65.0 (*C*-CH_3), 64.2 (*B*-CH_3), 65.1 (*A*-CH_3), 37.7 (Cq, *A*-tBu), 34.9, 34.8 and 34.8 (Cq, *B*-tBu, *C* and *D*), 32.0 (*A*-tBu), 30.3, 30.2 and 30.2 (*B*-tBu, C, D).
IR (ATR) *v* (cm^{-1}): 3337, 2959, 2872, 1550.
HRMS (ESI^+) ($C_{44}H_{56}O_{13}S_4$) *m/z* calc: 943.24960 $[M + Na]^+$, 959.22353 $[M + K]^+$; found: 943.24978 $[M + Na]^+$, 959.22317 $[M + K]^+$.
HRMS (ESI^-) ($C_{44}H_{56}O_{13}S_4$) *m/z* calc: 919.25310 $[M - H]^-$; found: 919.25414 $[M - H]^-$.

Compound 8b
Macrocycle **6** (200 mg, 0.23 mmol) was dissolved in dry THF (20 mL), dry ethanol (0.08 mL, 1.35 mmol) and sodium hydride (60% suspension in oil; 54 mg, ca 1.35 mmol) were added and the solution was stirred and heated to reflux (67 °C). After the entire starting compound disappeared (monitored by TLC, 2 h), the solvent was removed from the reaction mixture under reduced pressure. Subsequently, 1M HCl (30 mL) was added to the residue and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over $MgSO_4$. Then the solvent was removed under reduced pressure and the crude compound **8b** was obtained using radial chromatography (silica gel, eluent CH_2Cl_2:isopropanol 90:1 v/v). After trituration with *n*-hexane (3x 20 mL), the crude product was suspended in another 10 mL of *n*-hexane and the pure compound **8b** was finally filtered off as a white solid (142 mg, 67 %).

M.p. 186.6-190.6 °C (*n*-hexane).
The assignment of ^{1}H NMR and ^{13}C NMR spectra was not possible due to broad resonances caused by chemical exchange between several conformers (see VT NMR spectra in the range of 203 K – 403 K).
IR (ATR) *v* (cm^{-1}): 3234, 3145, 3076, 2960, 1548.
HRMS (ESI^+) ($C_{45}H_{58}O_{13}S_4$) *m/z* calc: 957.26525 $[M + Na]^+$; found: 957.26530 $[M + Na]^+$.
HRMS (ESI^-) ($C_{45}H_{58}O_{13}S_4$) *m/z* calc: 933.26875 $[M - H]^-$; found: 933.27759 $[M - H]^-$.

Compound 8c

Macrocycle **6** (100 mg, 0.11 mmol) was dissolved in dry THF (10 mL), *n*-propanol (0.051 mL, 0.68 mmol) and sodium hydride (60% suspension in oil; 27 mg, ca 0.68 mmol) were added and the solution was stirred and heated to reflux (67 °C). After the entire starting compound disappeared (monitored by TLC, 45 min), the solvent was removed from the reaction mixture under reduced pressure. Subsequently, 1M HCl (30 mL) was added to the residue and the mixture was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried over $MgSO_4$. Then the solvent was removed under reduced pressure to yield a crude mixture. Compound **8c** was isolated using radial chromatography (silica gel, eluent cyclohexane:ethyl acetate 3:1 v/v) as a white solid (66 mg, 62 %).

1,3-alternate

M.p. 244.8-249.5 °C (CH_2Cl_2/CH_3NO_2, decomposes).

^{1}H NMR (600 MHz, CD_3CN, 298 K) δ (ppm): 8.50 (brs, 1H, *C*), 8.48 (d, J = 2.2 Hz, 1H, *D*), 8.43 – 8.41 (m, 3H, *B, C* and *D*), 8.39 (d, J = 2.6 Hz, 1H, *B*), 7.74 (s, 1H, *A3*), 4.31 – 4.23 (m, 1H, OCH_2), 3.95 – 3.87 (m, 1H, OCH_2), 3.80 (s, 3H, *D*-CH_3), 3.48 (s, 6H, *C*-CH_3), 2.40 (brs, 3H, *A*-CH_3), 1.59 (s, 9H, *A*-tBu), 1.46 (s, 9H, *D*-tBu), 1.44 (s, 9H, *B*-tBu), 1.43 (s, 9H, *C*-tBu), 1.35 – 1.25 (m, 1H, CH_2), 1.15 – 1.05 (m, 1H, CH_2), 0.73 (t, J = 7.1 Hz, 3H, CH_3).

^{13}C NMR (150 MHz, CD_3CN, 298 K) δ (ppm): 153.7, 152.8, 150.1, 149.4, 148.8, 148.7, 147.5, 147.4, 142.7, 137.9, 137.7, 136.6, 136.3, 136.2, 136.0, 134.3 (16xCq, 1xCq is overlapped), 135.0, 134.7, 132.7, 132.6, 130.3, 129.5 and 118.1 (7xCH arom.), 79.1 (OCH_2), 65.5 (*D*-CH_3), 62.0 and 62.0 (*C*-CH_3 and *A*-CH_3), 38.3 (Cq, *A*-tBu), 35.0, 34.9 and 34.9 (Cq, *B*-tBu, *C* and *D*), 31.9 (*A*-tBu), 30.1, 30.1 and 30.0 (*B*-tBu, *C*, *D*), 21.4 (CH_2), 8.3 (CH_3).

IR (ATR) *v* (cm^{-1}): 3657, 3563, 3350, 3077, 2961, 2873, 1734, 1597, 1550.

HRMS (ESI^+) ($C_{46}H_{60}O_{13}S_4$) *m/z* calc: 971.28090 $[M + Na]^+$, 987.25483 $[M + K]^+$; found: 971.28114 $[M + Na]^+$, 987.25454 $[M + K]^+$.

HRMS (ESI^-) ($C_{46}H_{60}O_{13}S_4$) *m/z* calc: 947.28440 $[M - H]^-$; found: 947.28467 $[M - H]^-$.

partial cone D (in a mixture with *1,3-alternate*)

^{1}H NMR (600 MHz, $C_2D_2Cl_4$, 373 K) δ (ppm): 8.58 (d, J = 2.5 Hz, 1H, *B5*), 8.53 and 8.48 (2xd, 2x1H, J = 2.5 Hz, J = 2.5 Hz, *D3* and *D5*), 8.40 (d, 1H, J = 2.4 Hz, *D3*), 8.27 (brs, 1H, *C5*), 7.65 (s, 1H, *A3*), 7.54 (brs, 1H, *C3*), 4.15, 4.13 and 3.96 (3xbrs, 9H, *A*-CH_3, *C*-CH_3, *D*-CH_3), 4.16 – 4.03 (overlapped m, 2H, OCH_2), 1.55 (s, 9H, *D*-tBu), 1.49 (s, 9H, *B*-tBu), 1.29 (s, 9H, *C*-tBu), 1.00 – 0.90 (overlapped m, 2H, CH_2), 1.22 (s, 9H, *A*-tBu).

^{13}C NMR (150 MHz, $C_2D_2Cl_4$, 373 K) δ (ppm): 156.5, 155.0, 154.3, 153.6, 148.3, 148.1, 147.2, 146.2, 145.1, 139.7, 137.7, 137.3, 137.0, 136.9, 136.6, 136.3 and 135.4 (17xCq), 134.2 (CH, *D*), 133.7 (CH, *B*), 133.5 (CH, *C*), 133.2 (CH, *C*), 132.8 (CH, *A3*), 132.7 (CH, *D*), 131.3 (CH, *B*), 82.9 (OCH_2), 67.6, 67.1 and 61.9 (3x OCH_3), 38.8, 38.4, 38.3 and 37.2 (4xCq, tBu), 32.9 (*A*-tBu), 31.1, 31.1 and 31.1 (*B*-tBu, *C*, *D*), 29.7 (CH_2), 9.0 (CH_3).

HRMS (ESI^+) ($C_{46}H_{60}O_{13}S_4$) *m/z* calc: 971.28090 $[M + Na]^+$, 987.25483 $[M + K]^+$; found: 971.28139 $[M + Na]^+$, 987.25510 $[M + K]^+$.

HRMS (ESI^-) ($C_{46}H_{60}O_{13}S_4$) *m/z* calc: 947.28440 $[M - H]^-$; found: 947.28385 $[M - H]^-$.

3. Spectral characterization of compounds

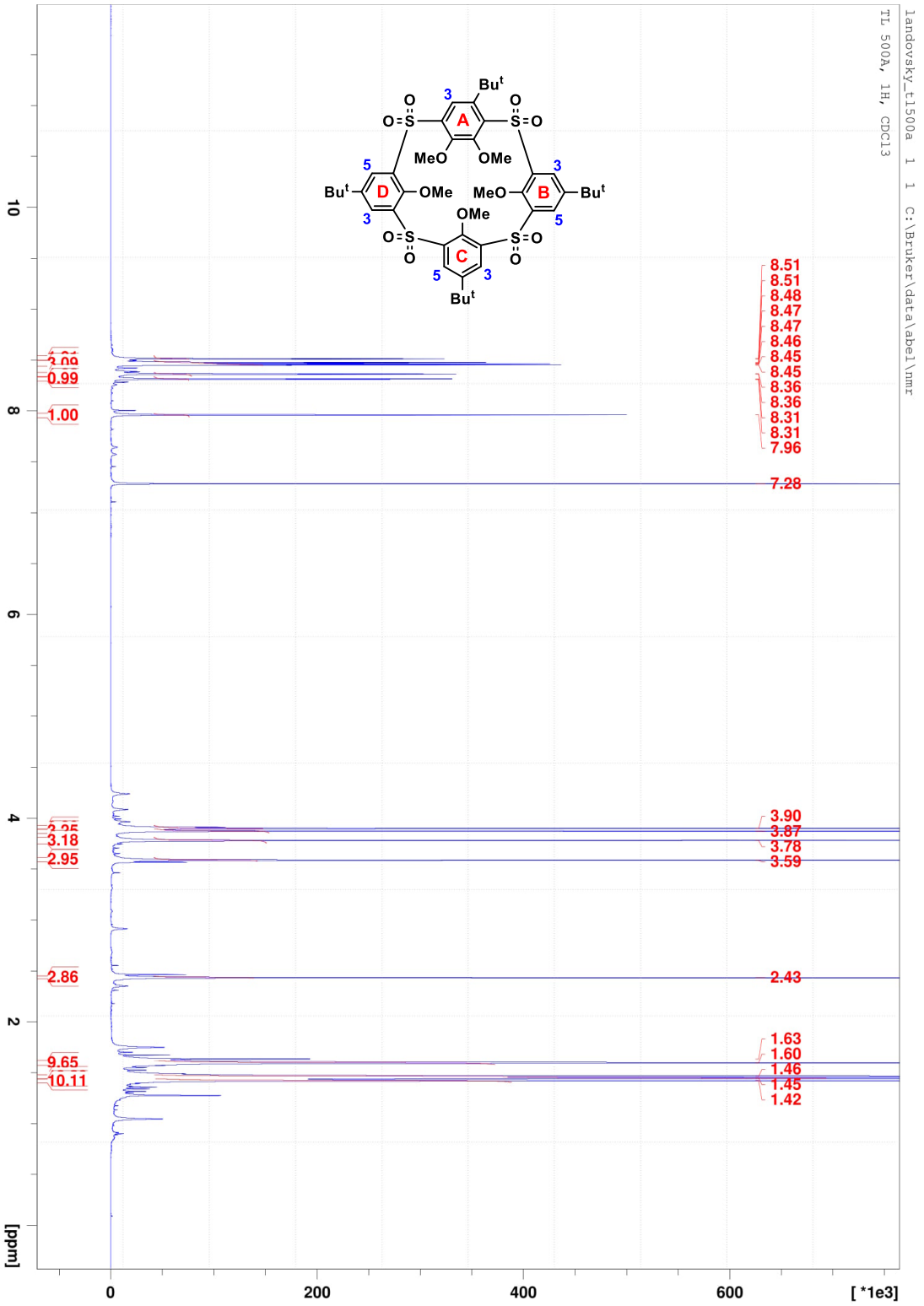


Figure S1: ^{1}H NMR spectrum of compound **7a**

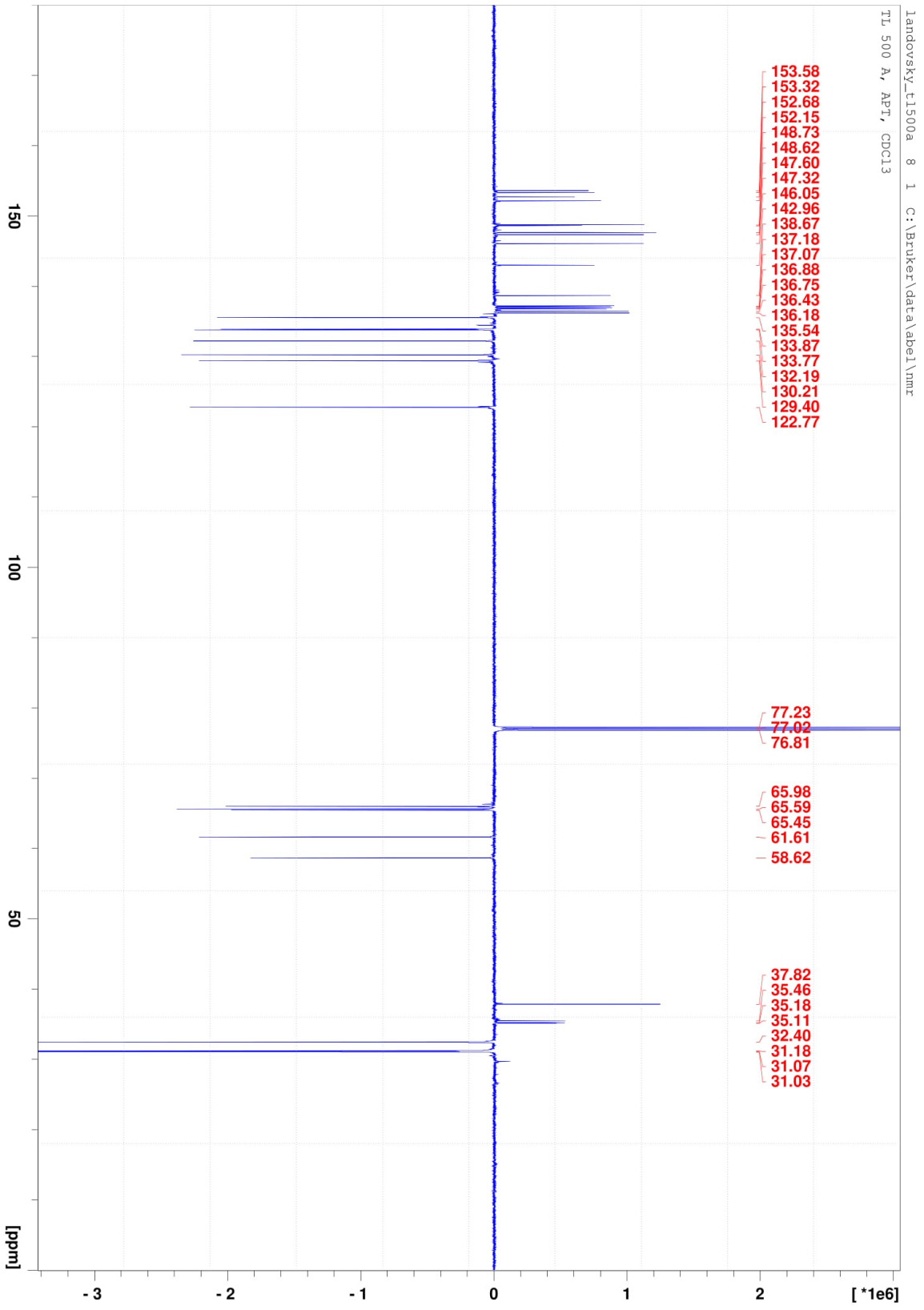


Figure S2: ^{13}C NMR (APT) spectrum of compound **7a**

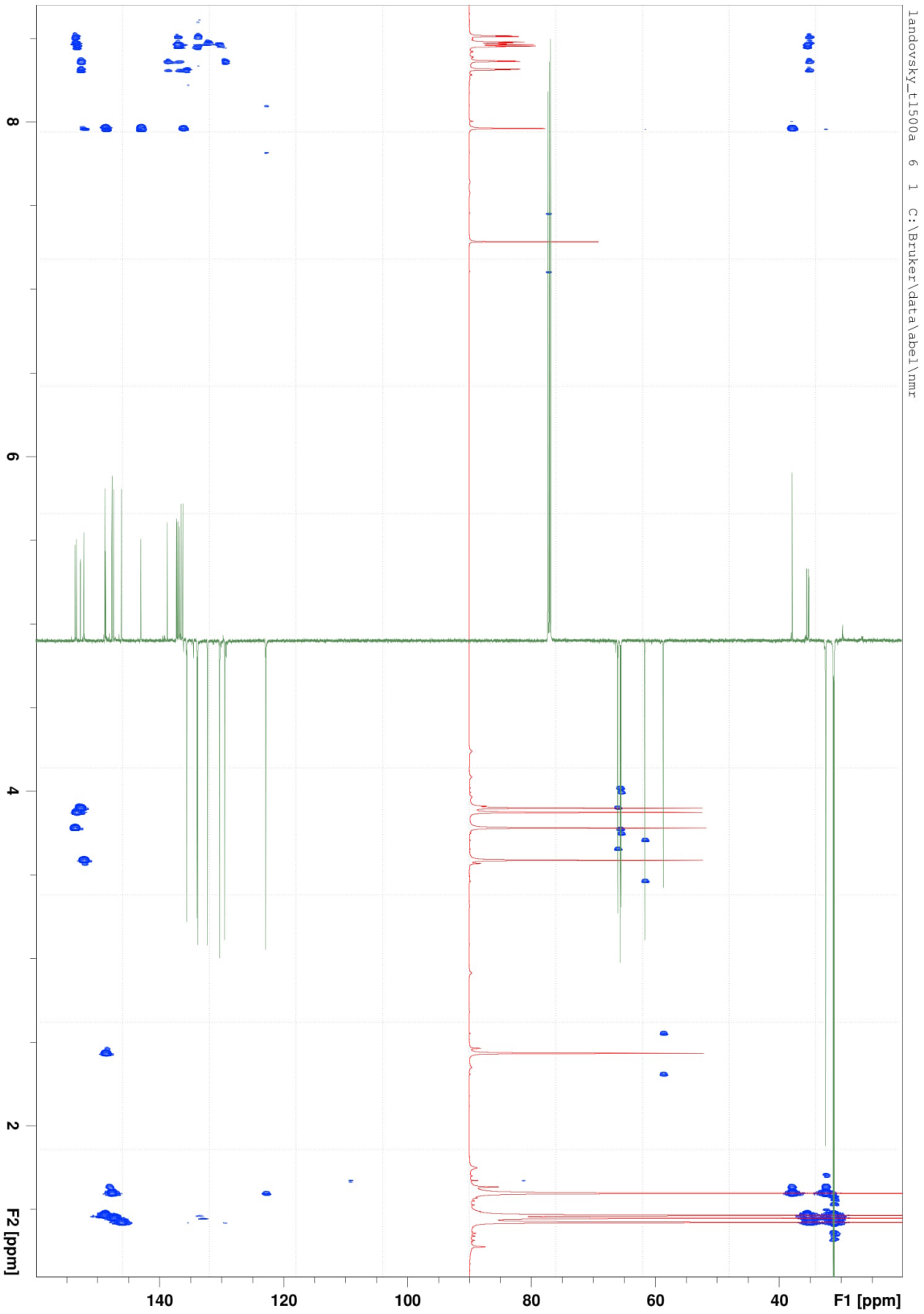


Figure S3: HMBC spectrum of compound **7a**

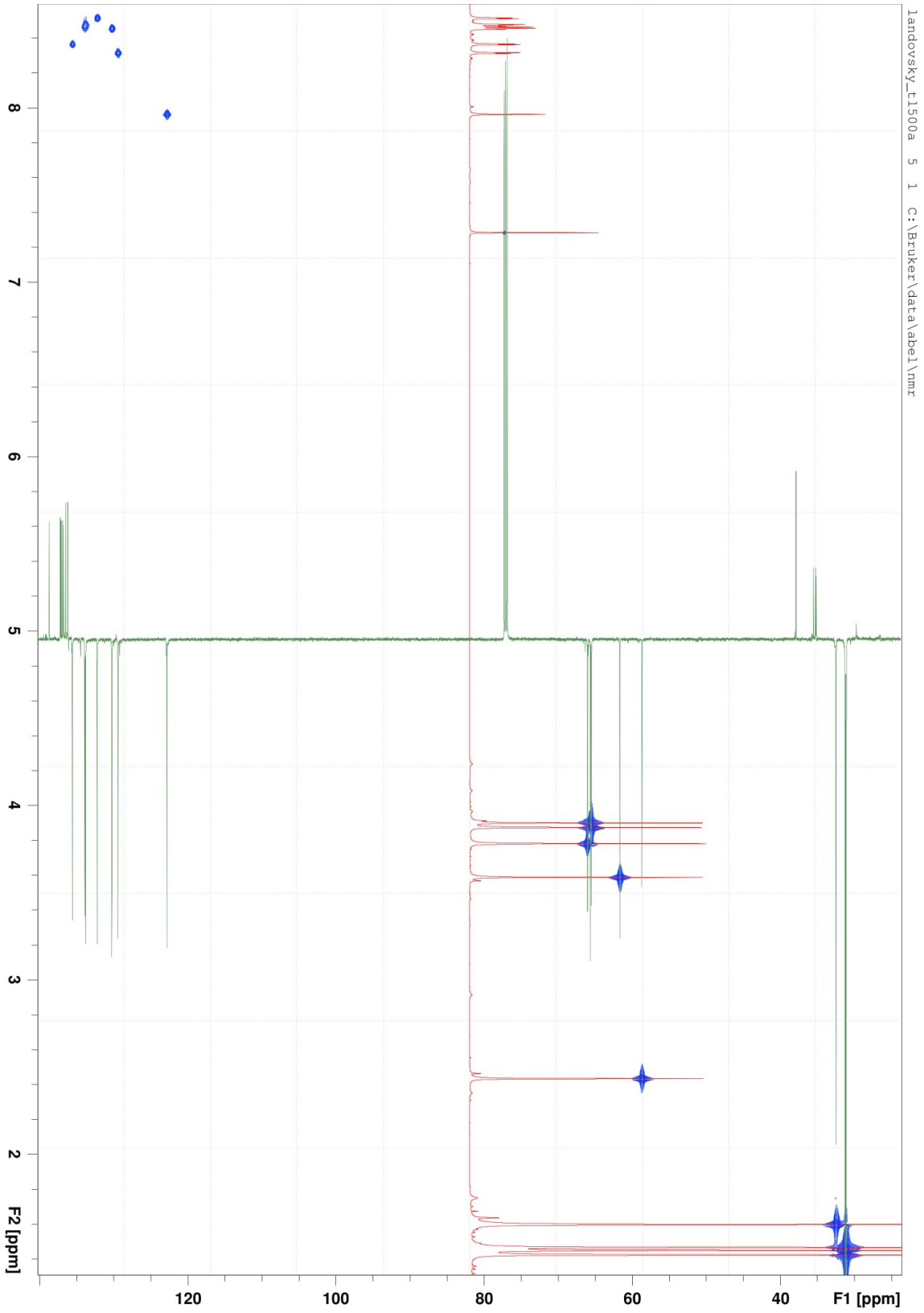


Figure S4: HMQC spectrum of compound **7a**

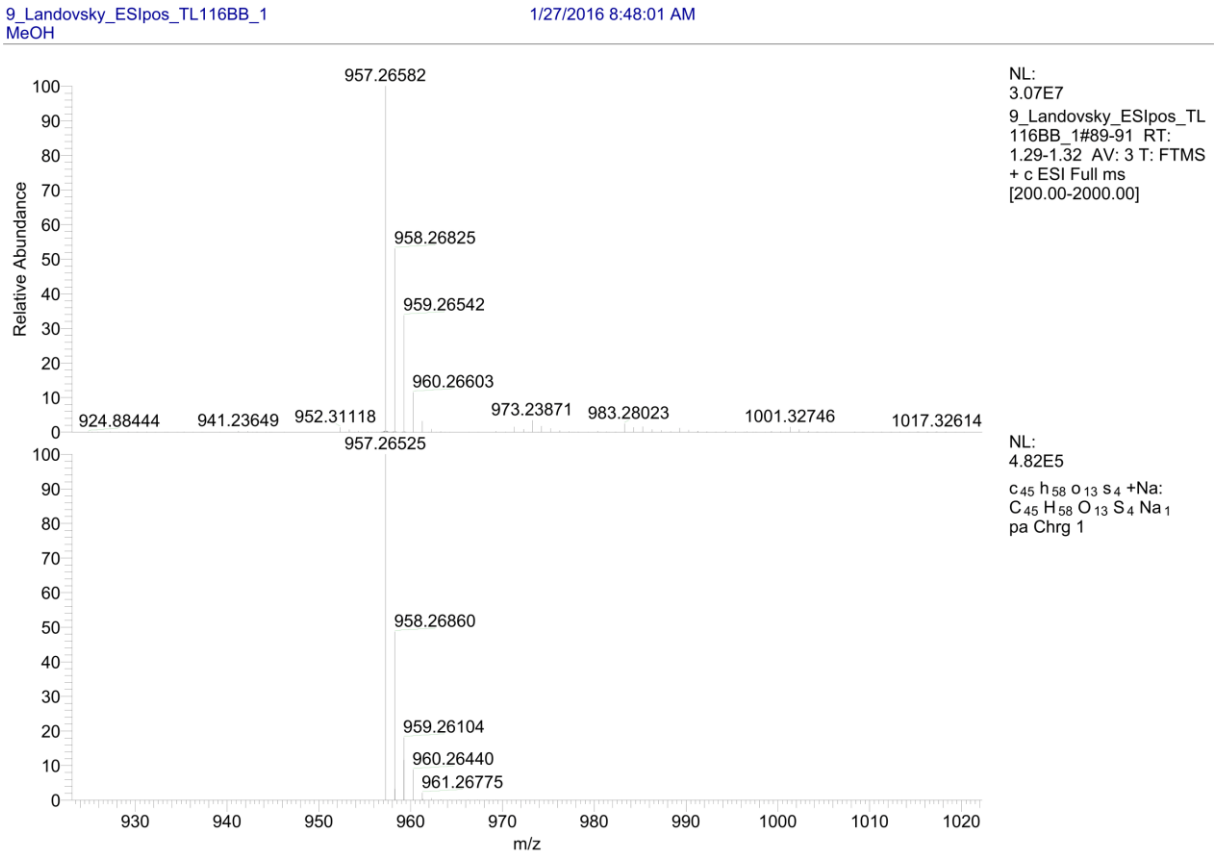


Figure S5: HRMS spectrum of compound **7a** (ESI^+)

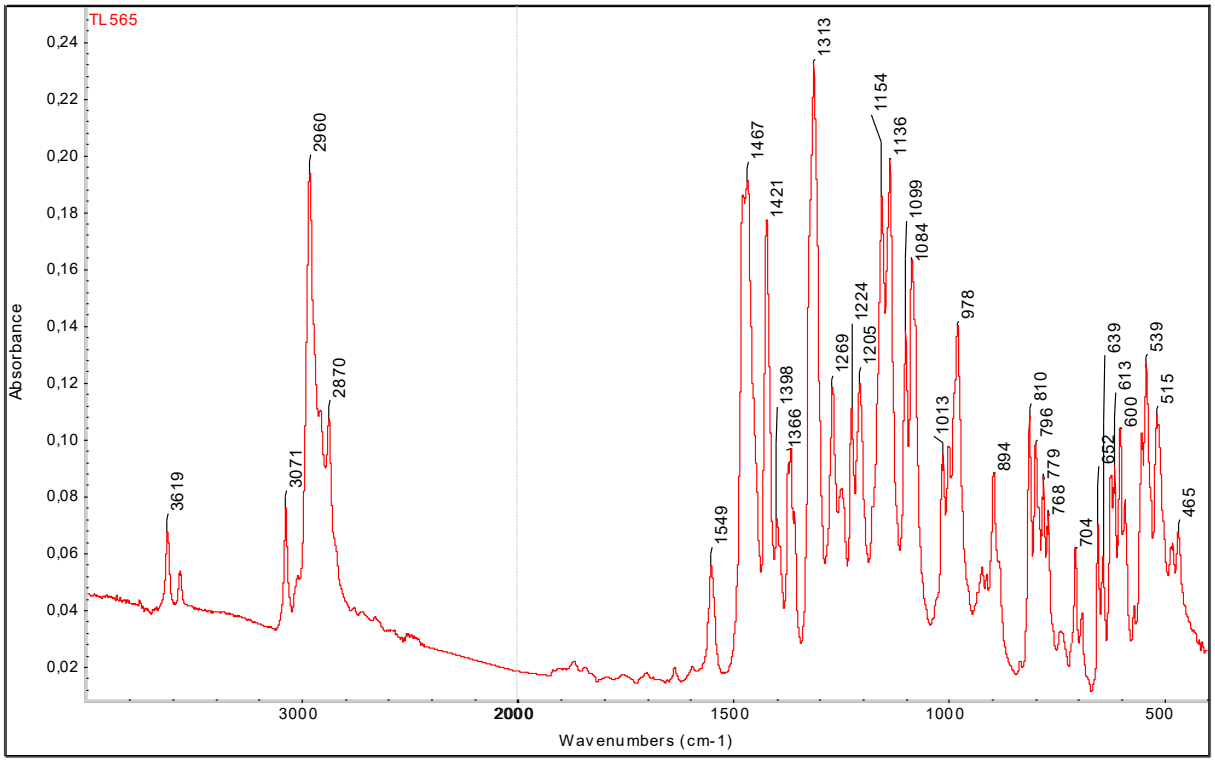


Figure S6: IR spectrum of compound **7a** (ATR)

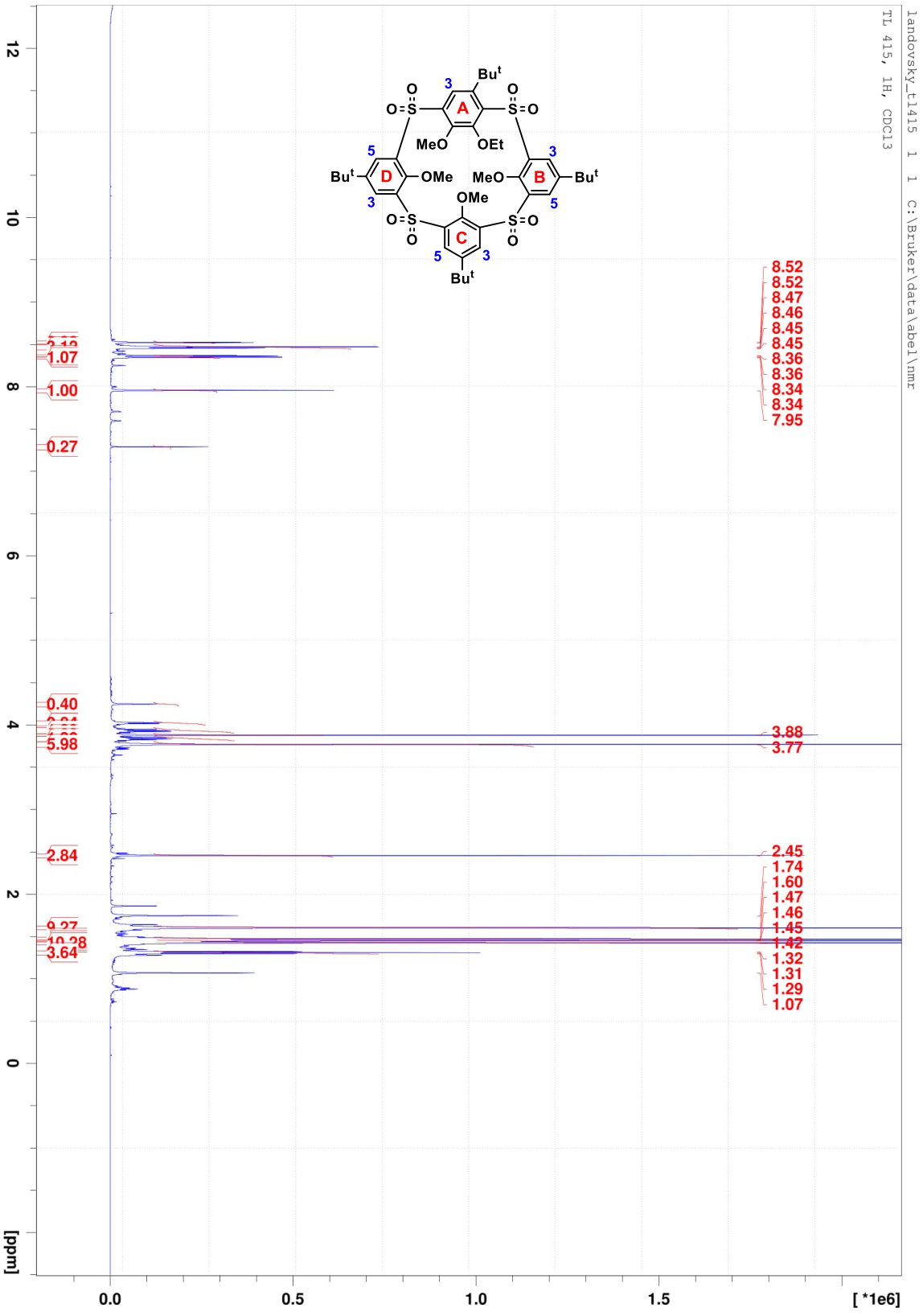


Figure S7: ^{1}H NMR spectrum of compound **7b**

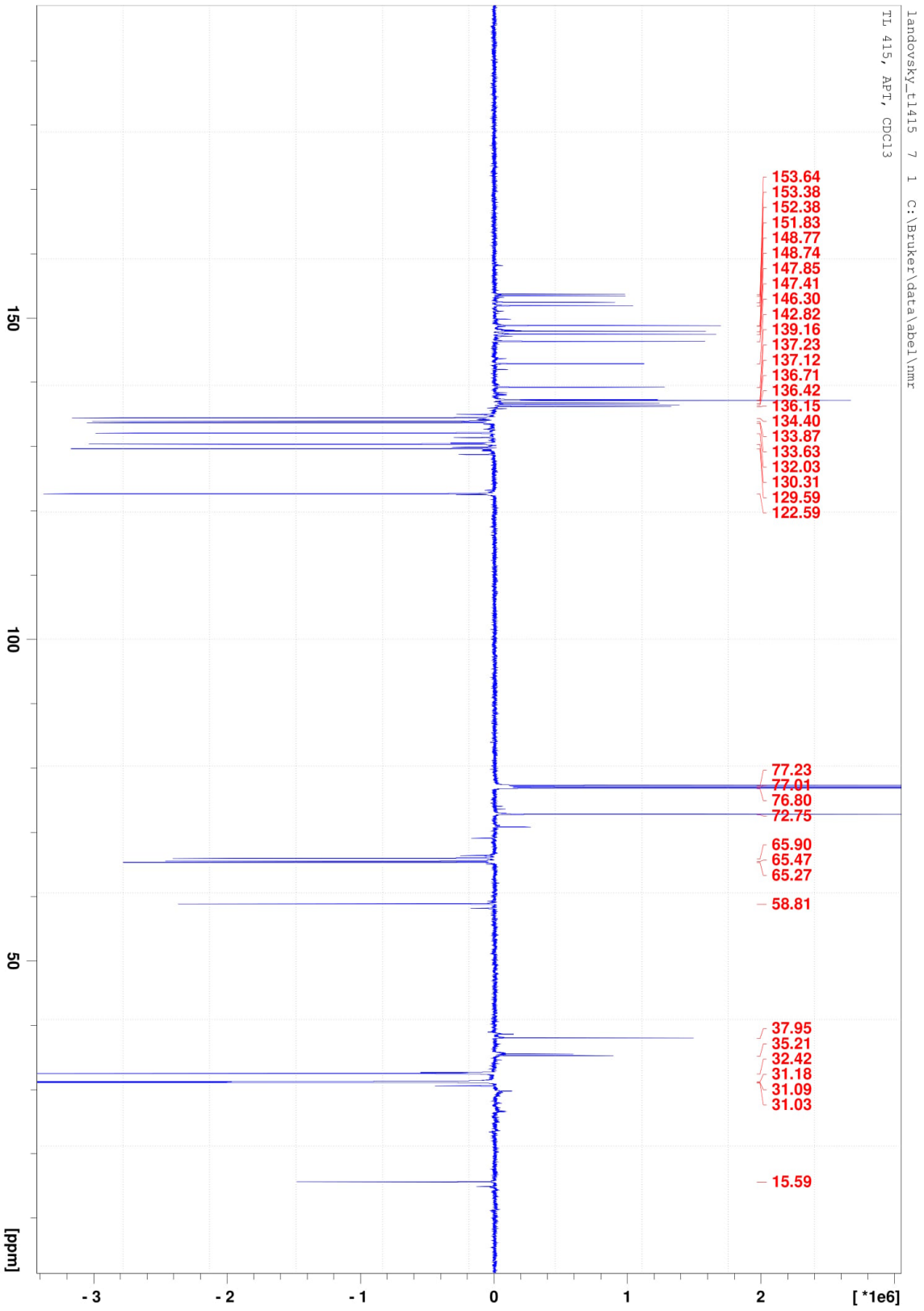


Figure S8: ^{13}C NMR (APT) spectrum of compound **7b**

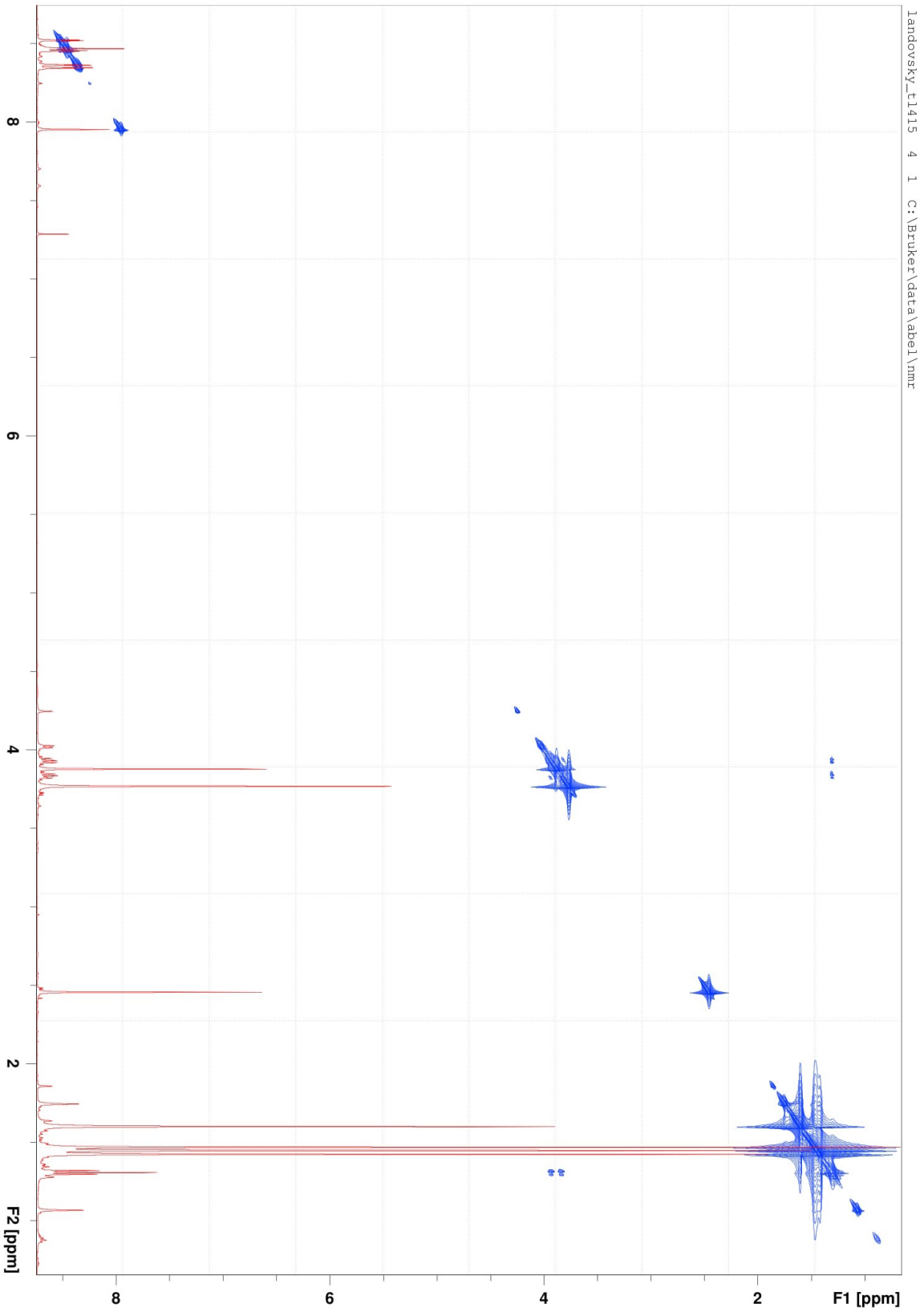


Figure S9: COSY spectrum of compound **7b**

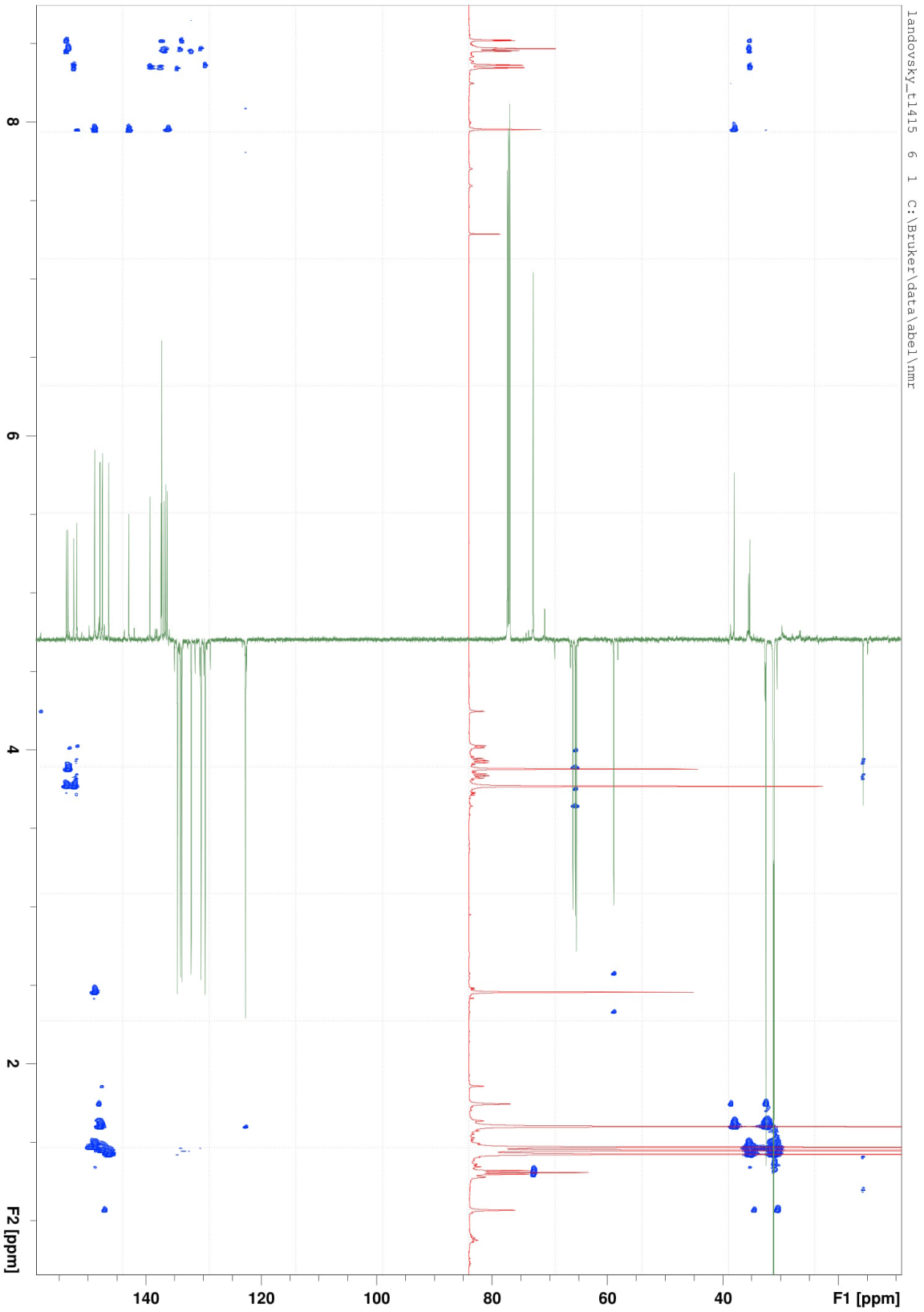


Figure S10: HMBC spectrum of compound **7b**

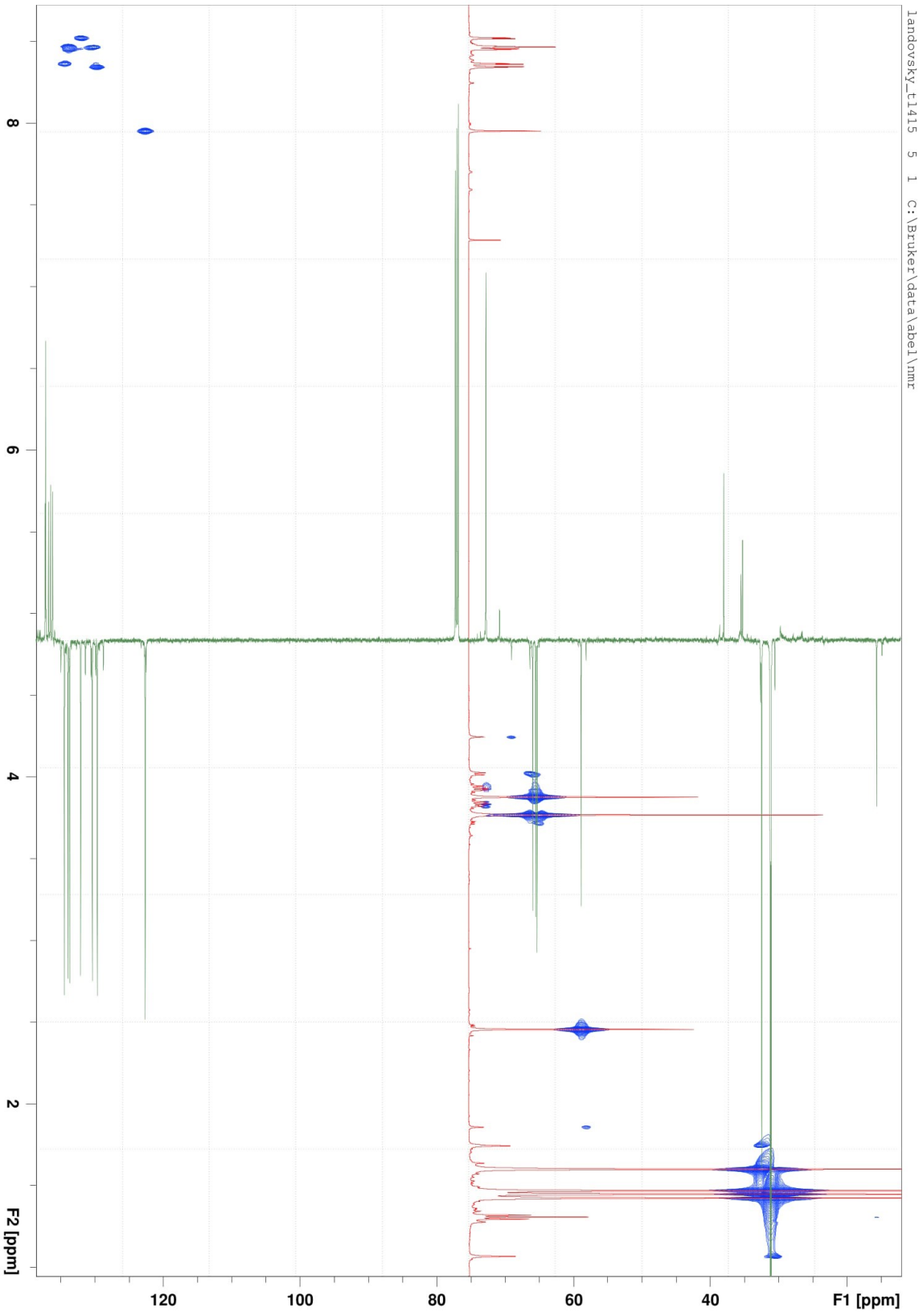


Figure S11: HMQC spectrum of compound **7b**

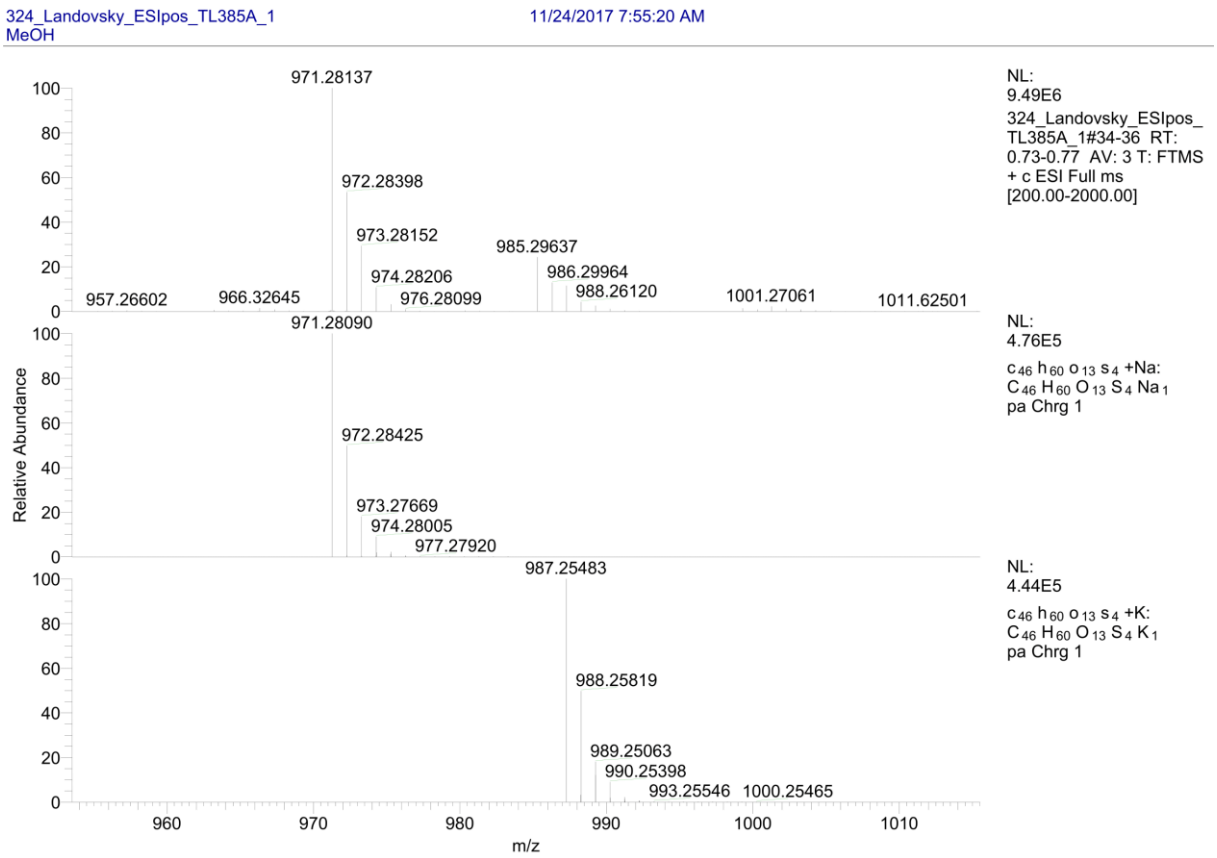


Figure S12: HRMS spectrum of compound **7b** (ESI^+)

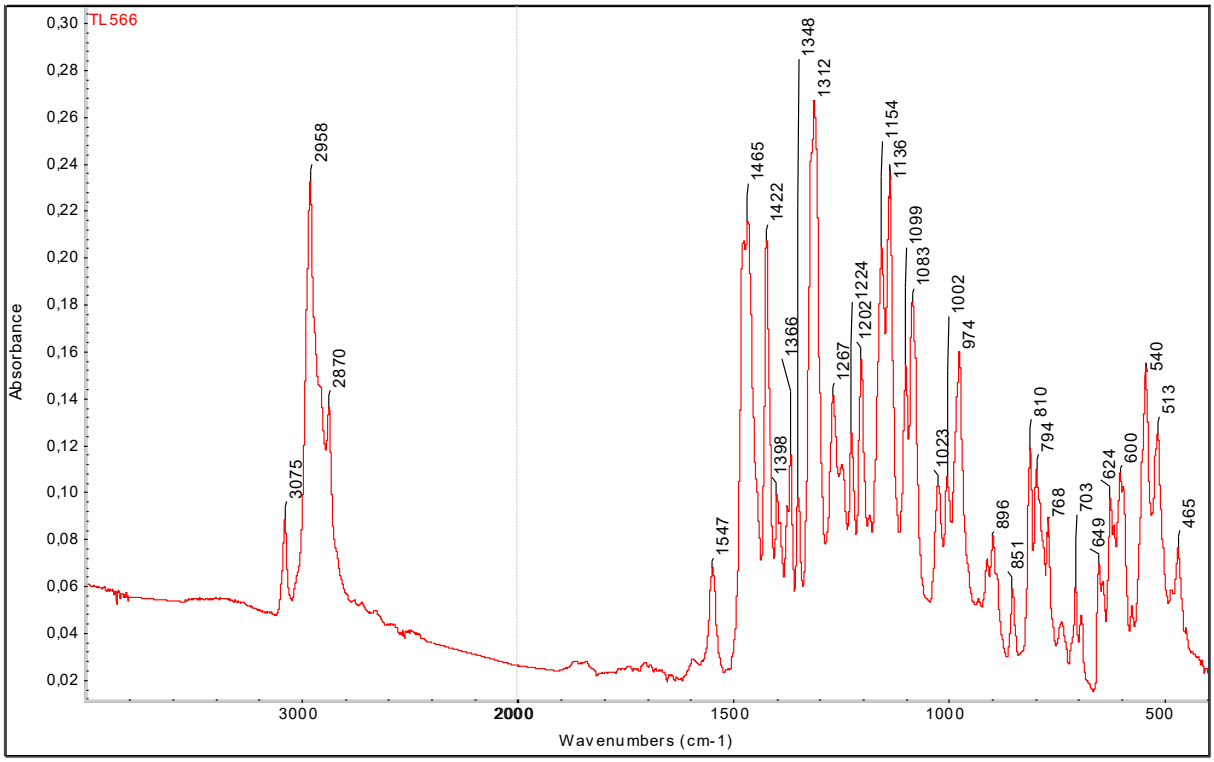


Figure S13: IR spectrum of compound **7b** (ATR)

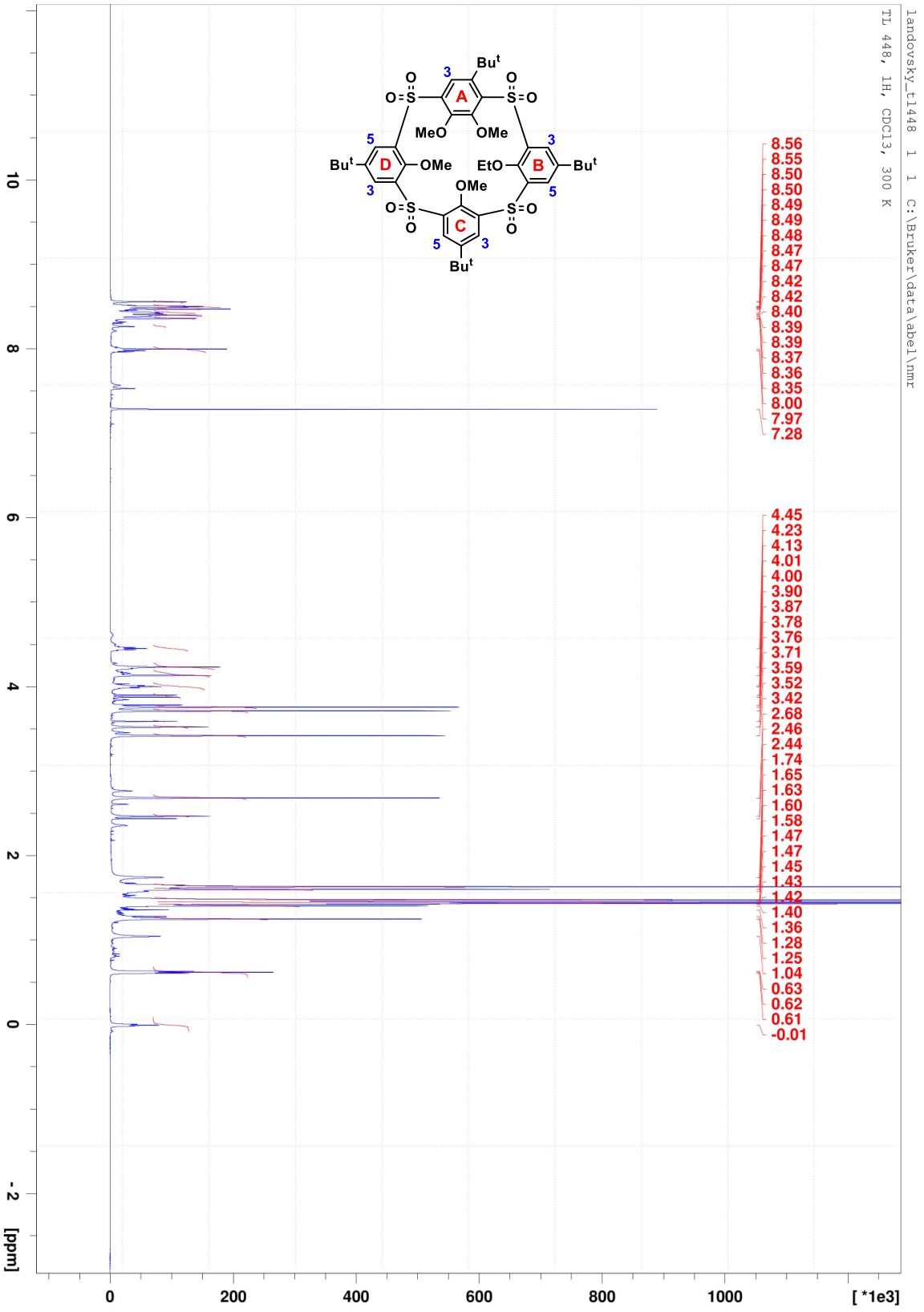


Figure S14: ^{1}H NMR spectrum of compound **7c**

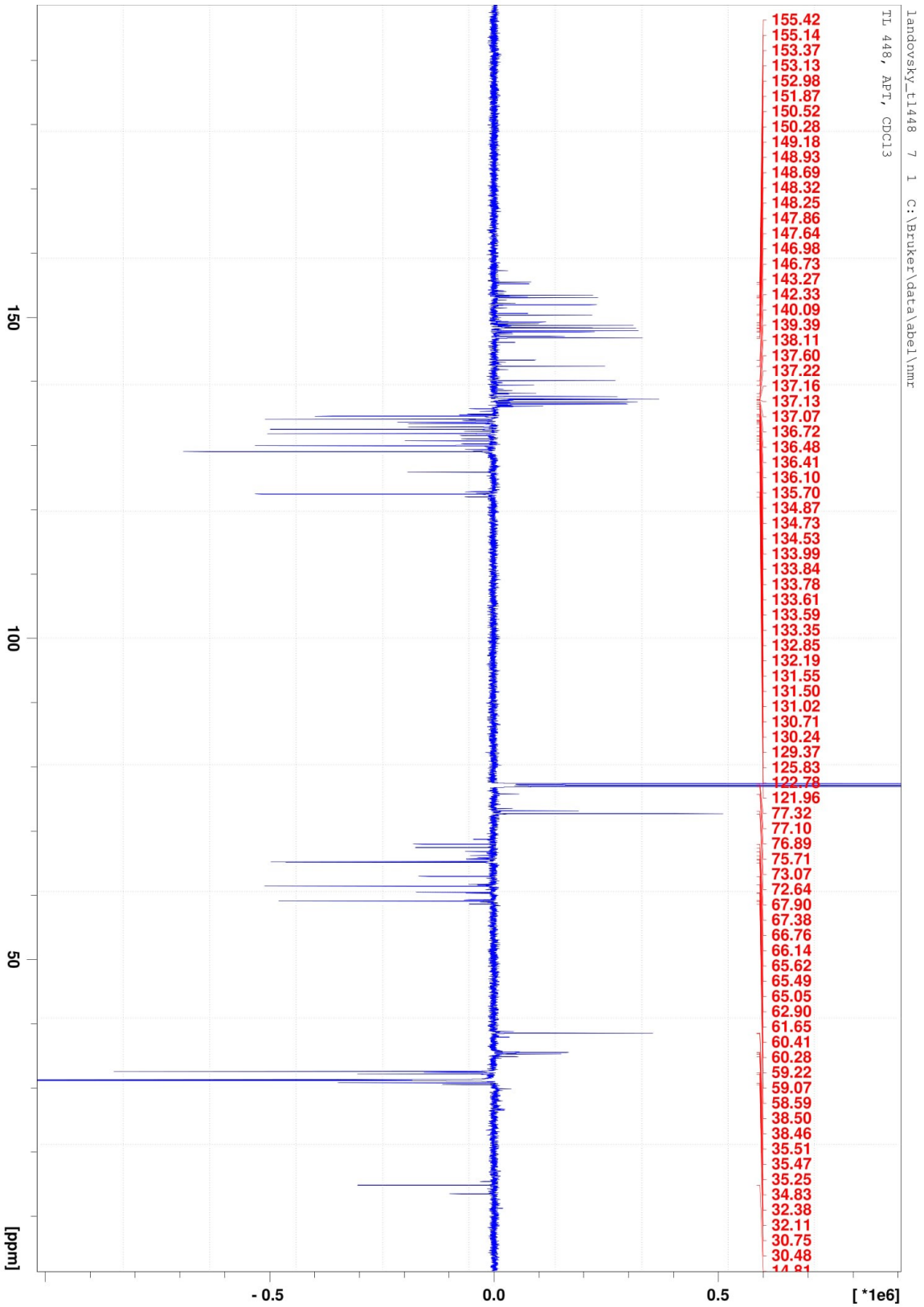


Figure S15: ^{13}C NMR (APT) spectrum of compound **7c**

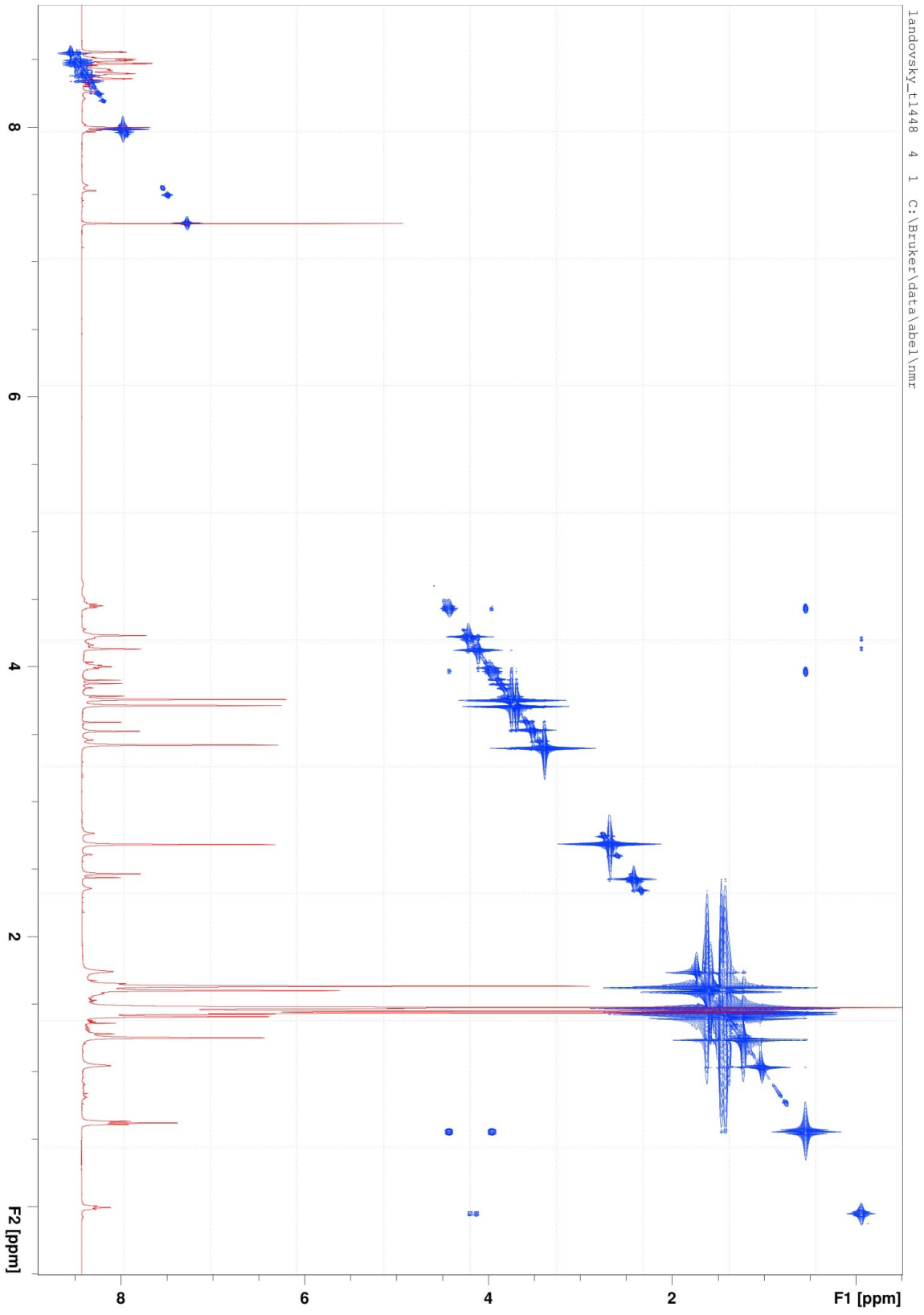


Figure S16: COSY spectrum of compound **7c**

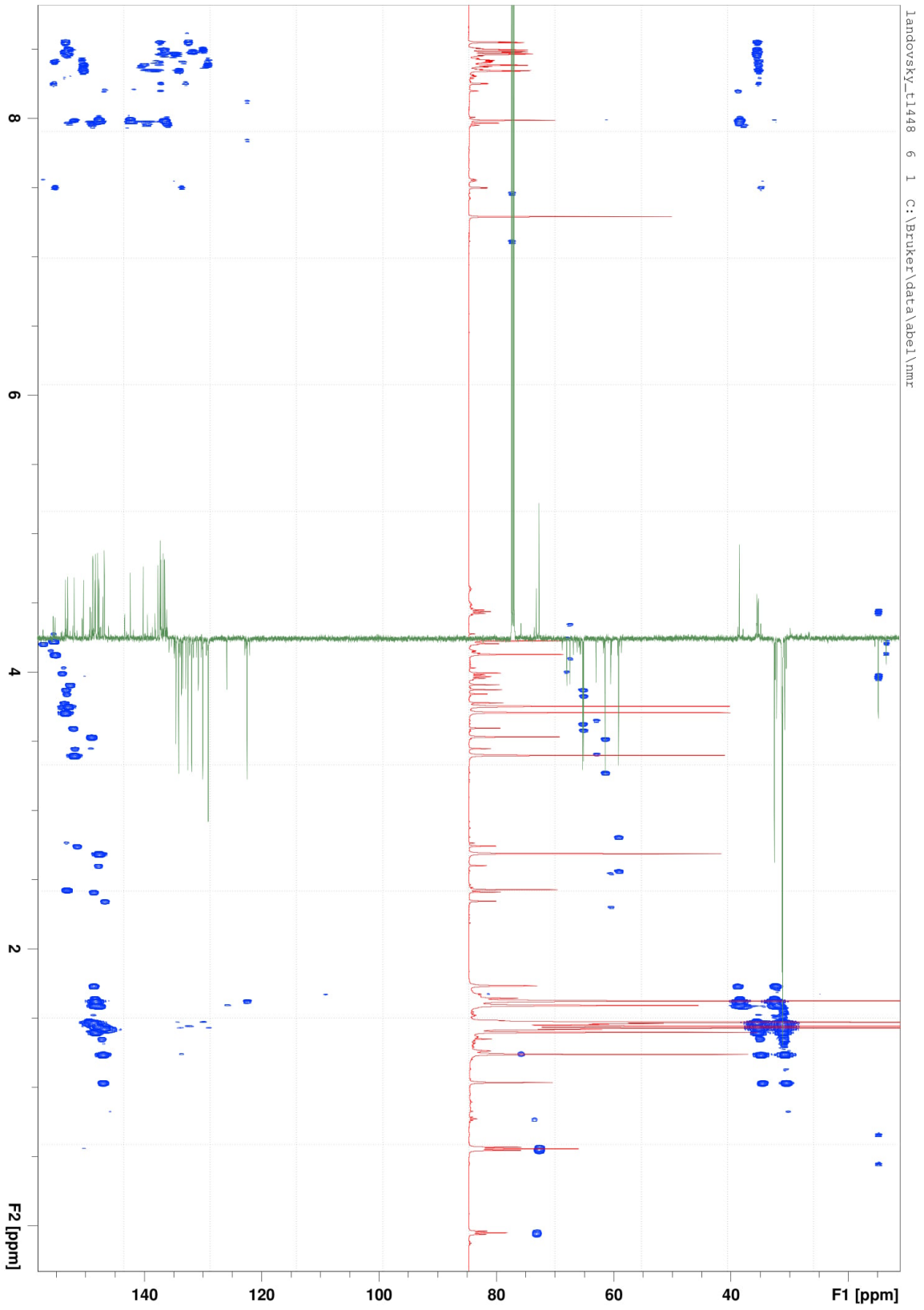


Figure S17: HMBC spectrum of compound **7c**

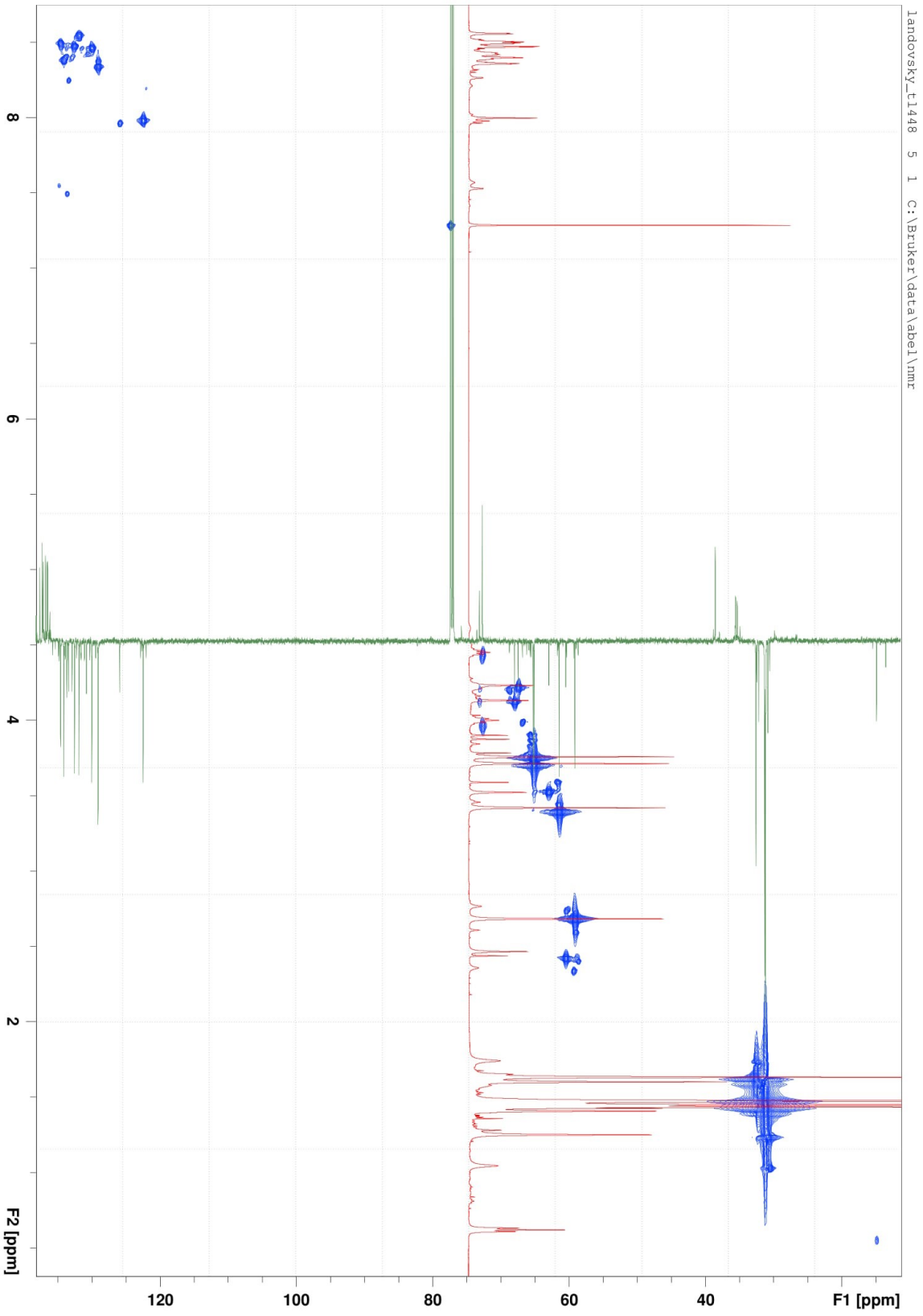


Figure S18: HMQC spectrum of compound **7c**

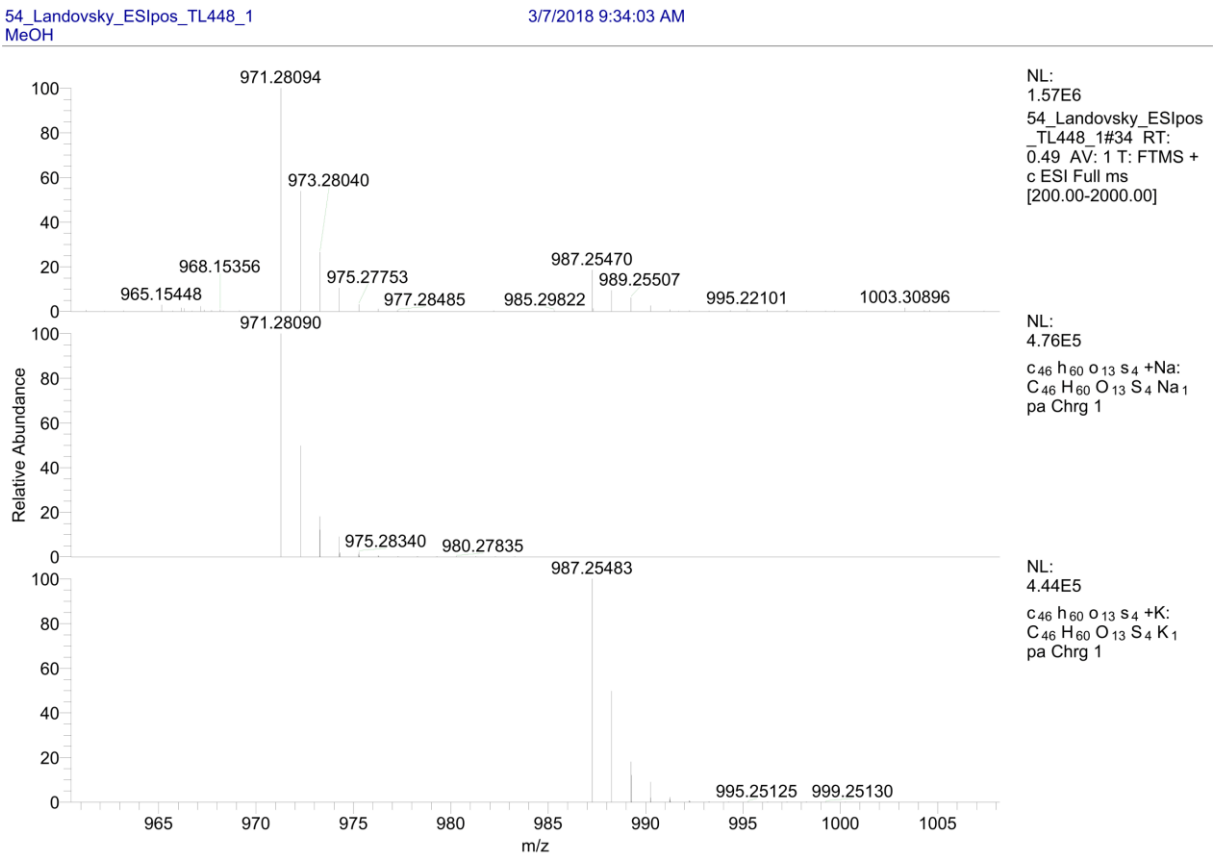


Figure S19: HRMS spectrum of compound **7c** (ESI^+)

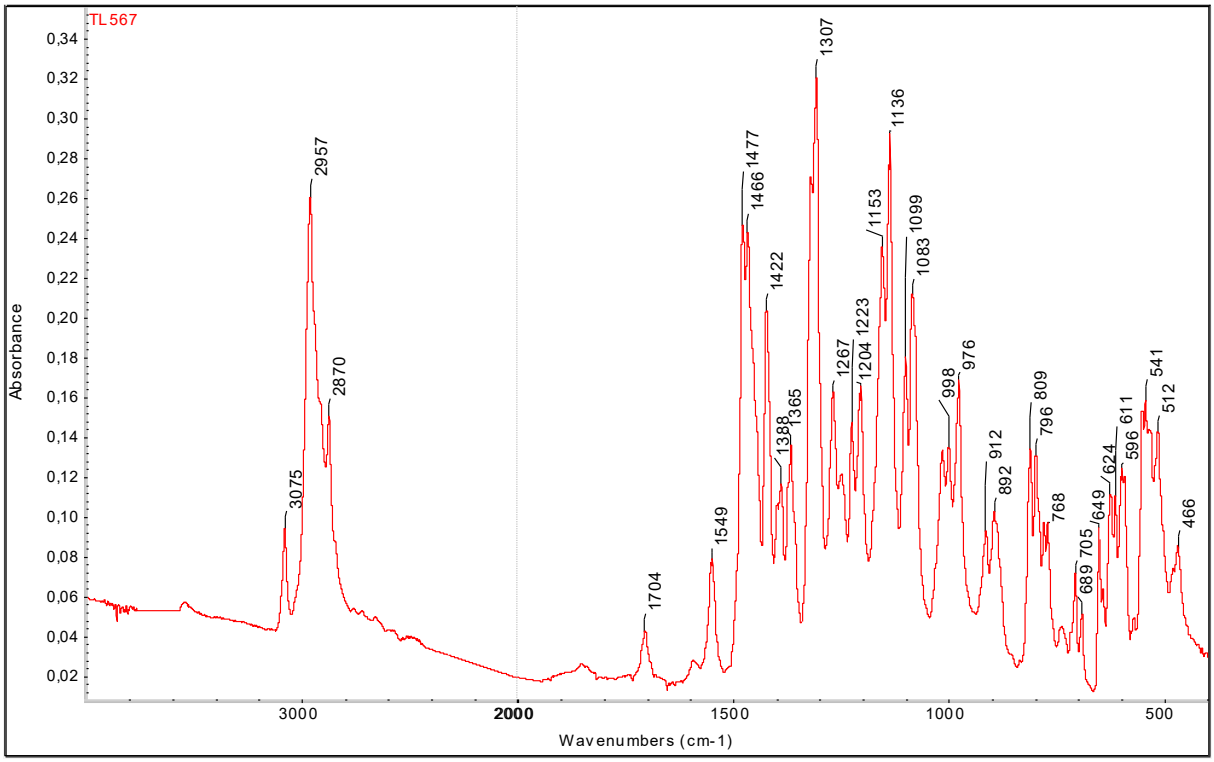


Figure S20: IR spectrum of compound **7c** (ATR)

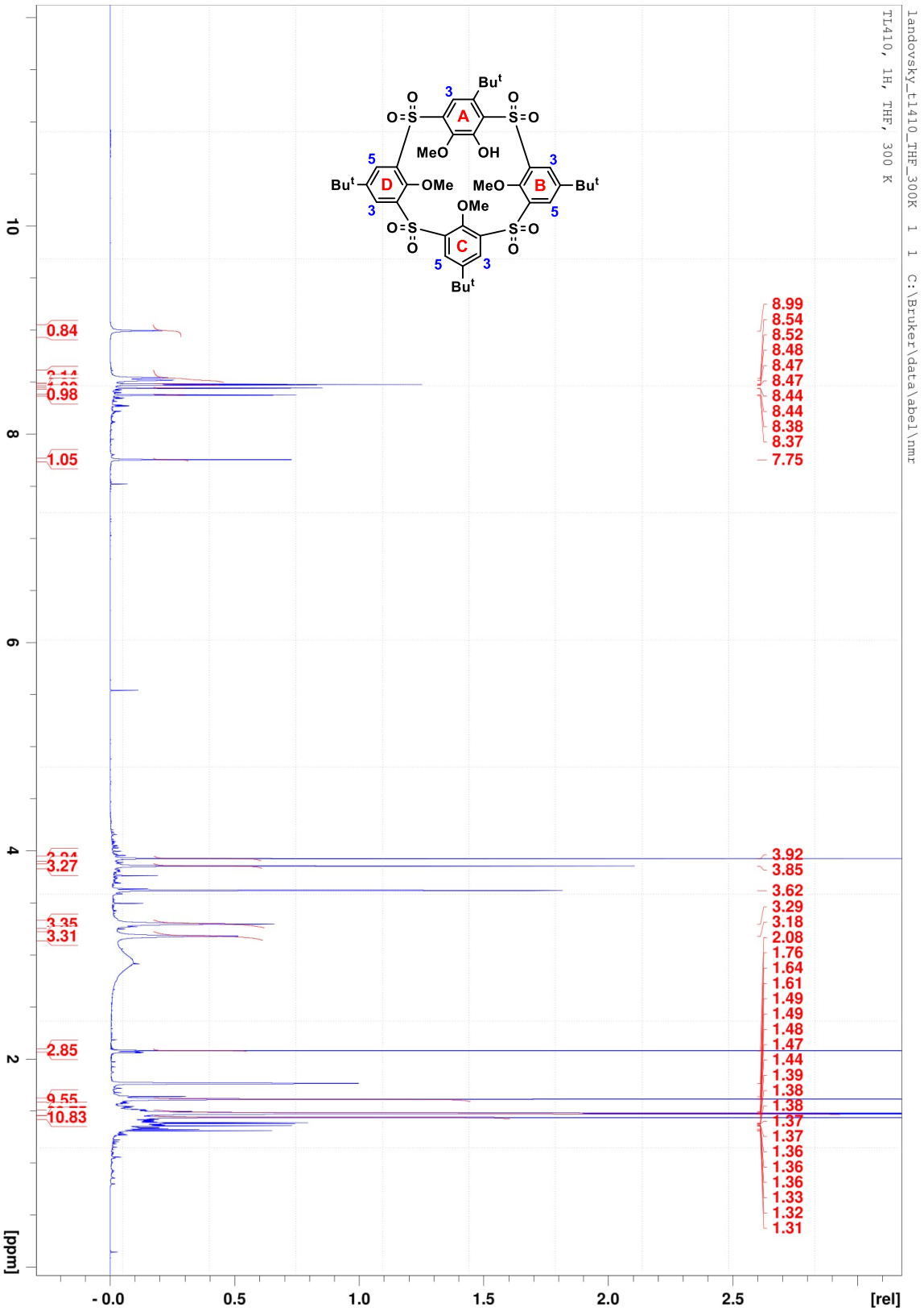


Figure S21: ^{1}H NMR spectrum of compound **8a**

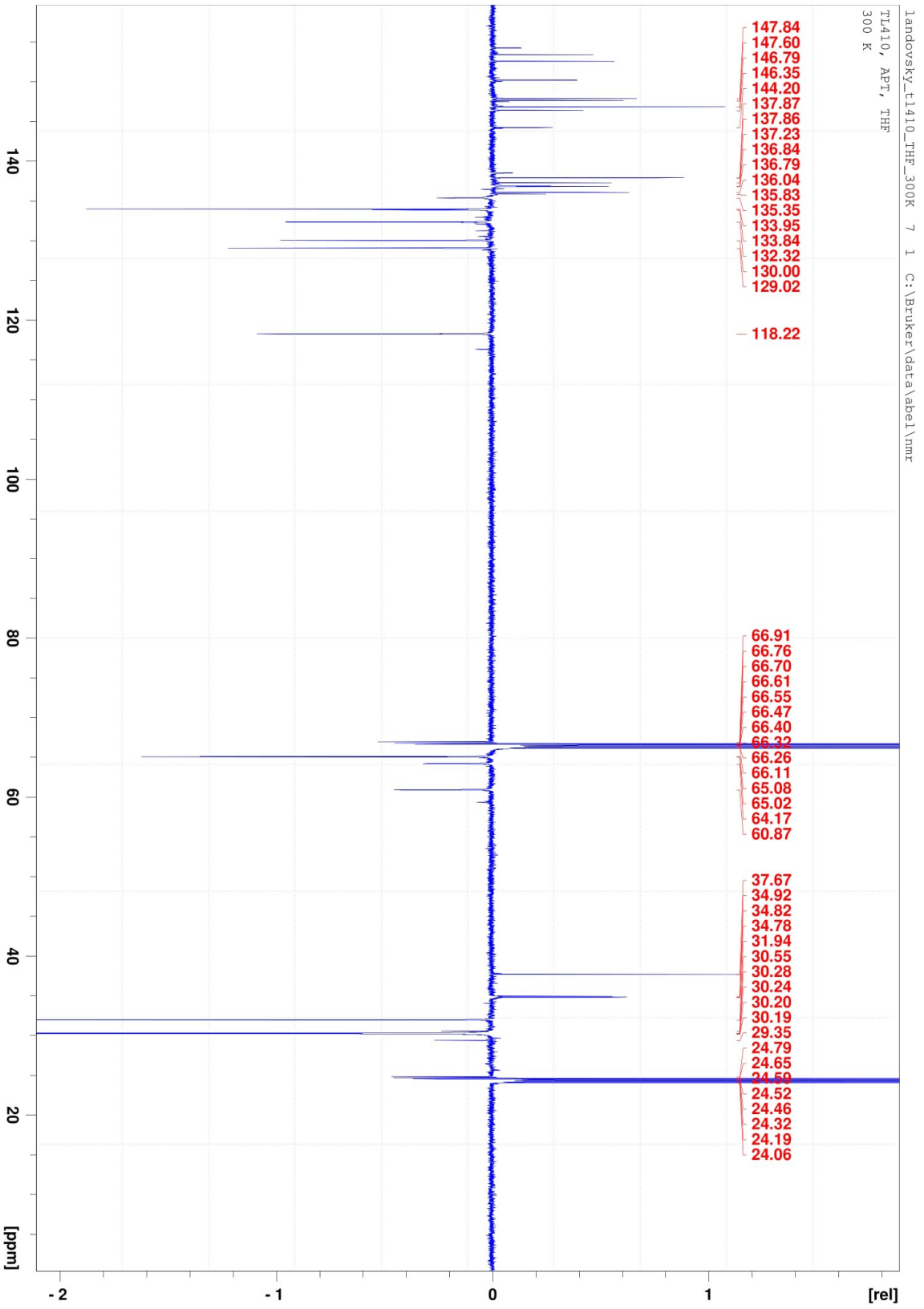


Figure S22: ^{13}C NMR (APT) spectrum of compound **8a**

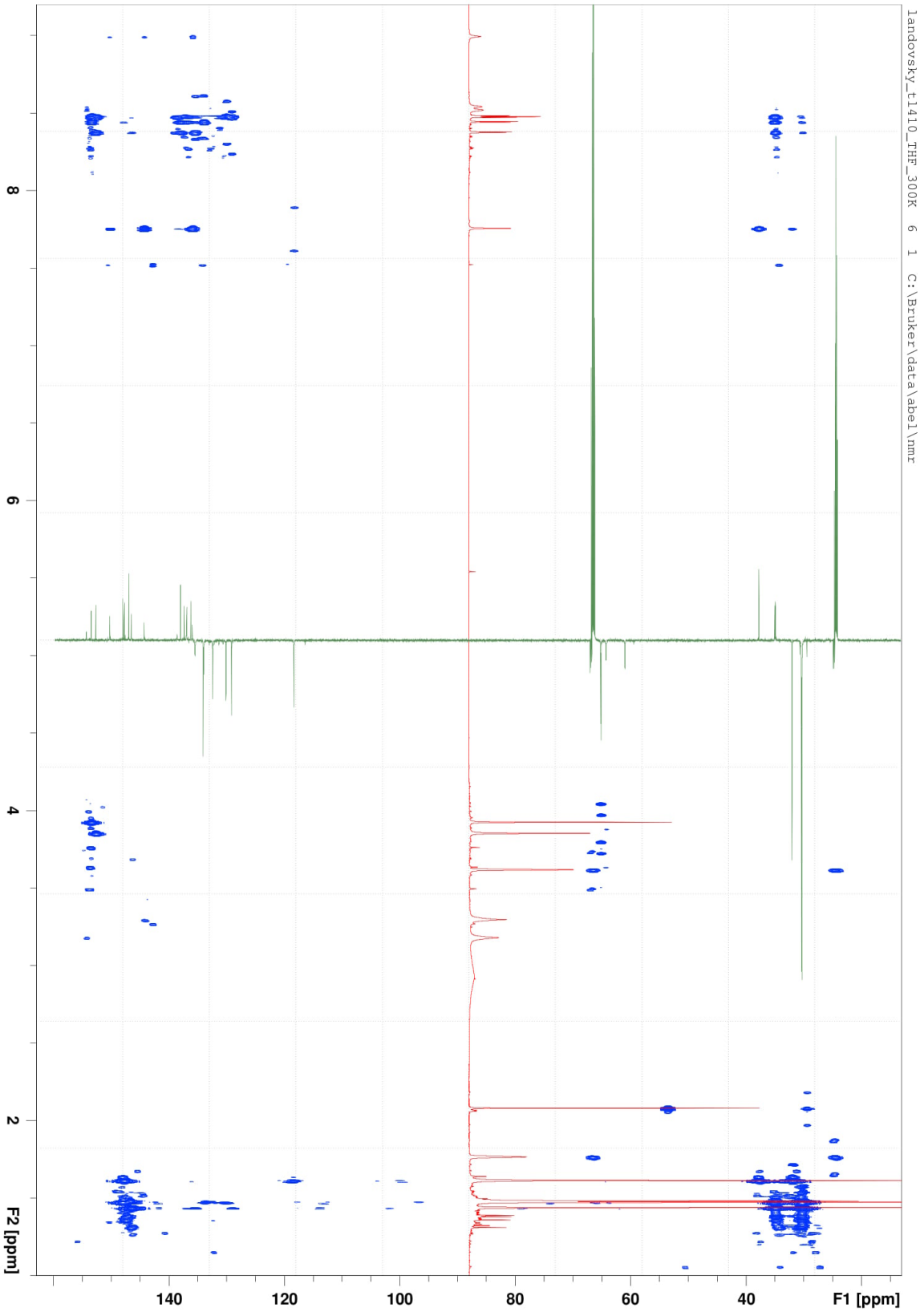


Figure S23: HMBC spectrum of compound **8a**

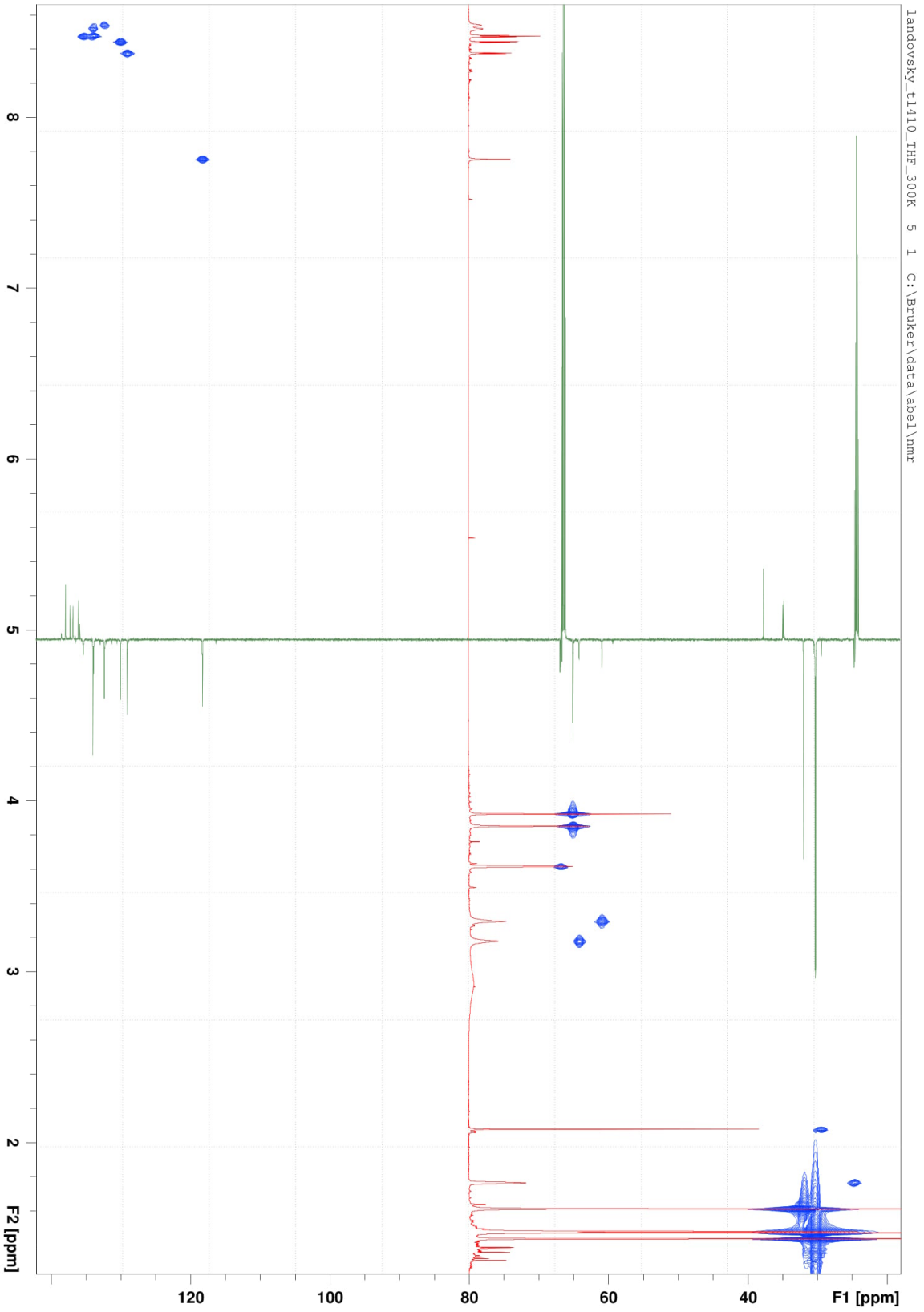


Figure S24: HMQC spectrum of compound **8a**

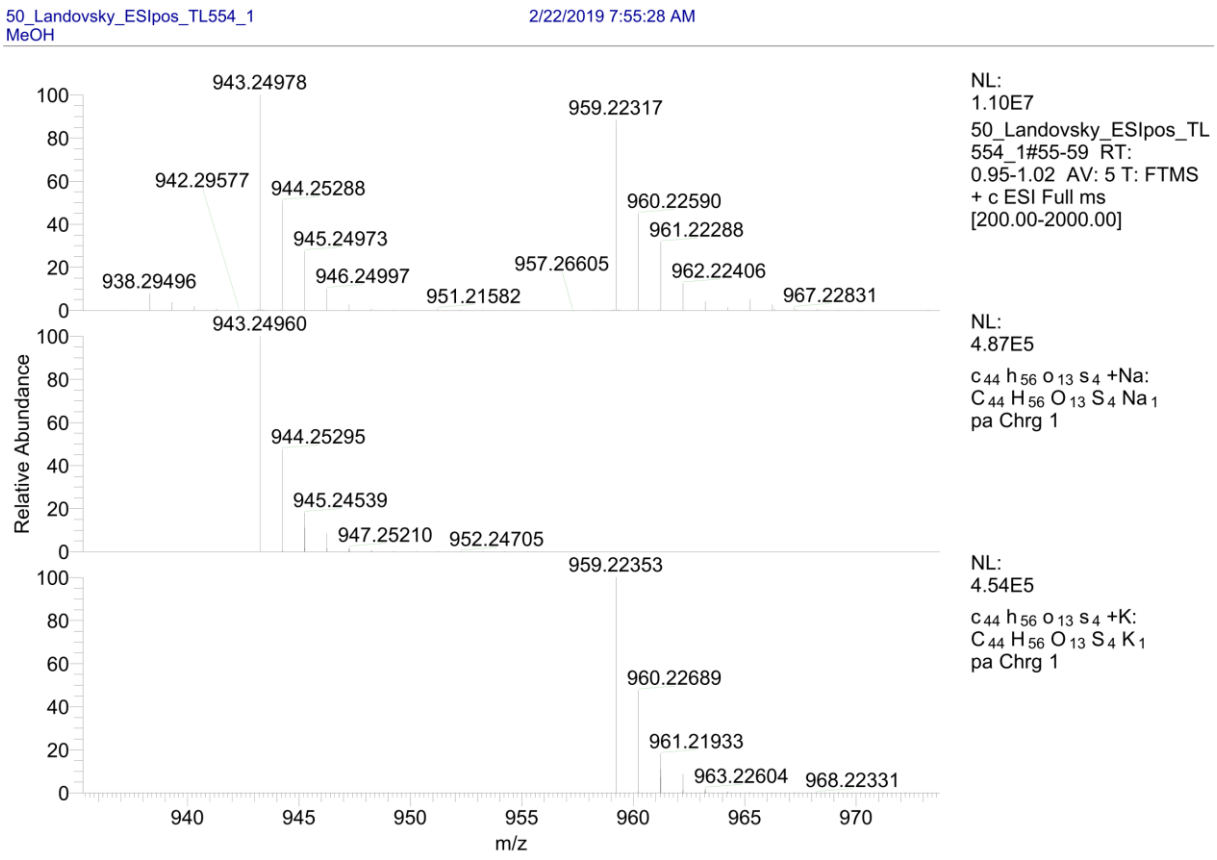


Figure S25: HRMS spectrum of compound **8a** (ESI^+)

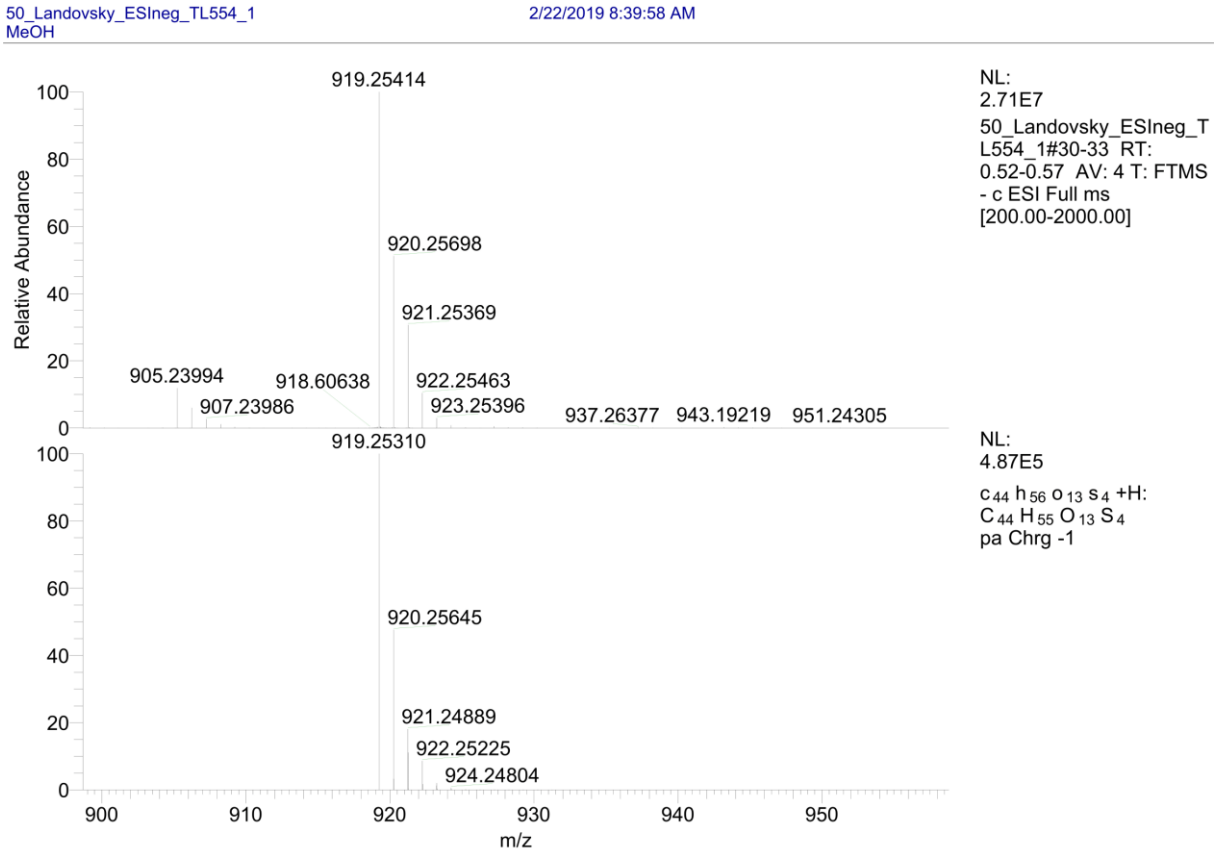


Figure S26: HRMS spectrum of compound **8a** (ESI^-)

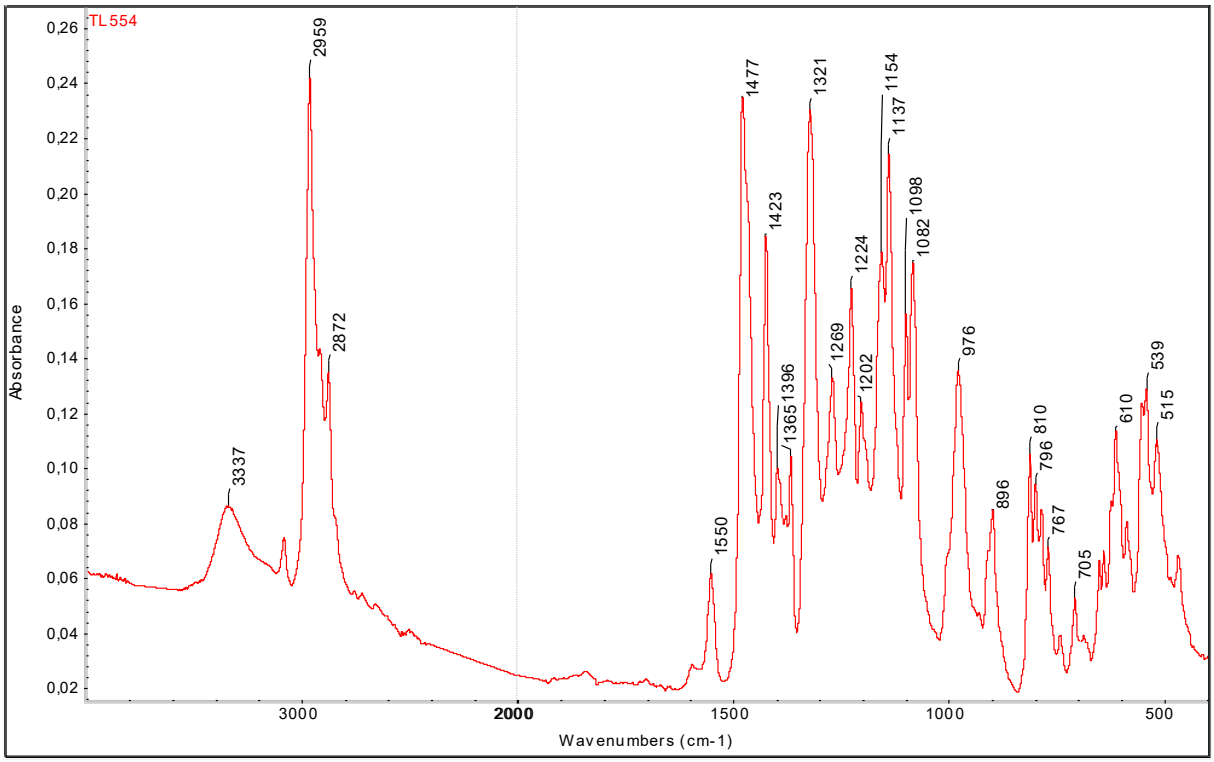


Figure S27: IR spectrum of compound **8a** (ATR)

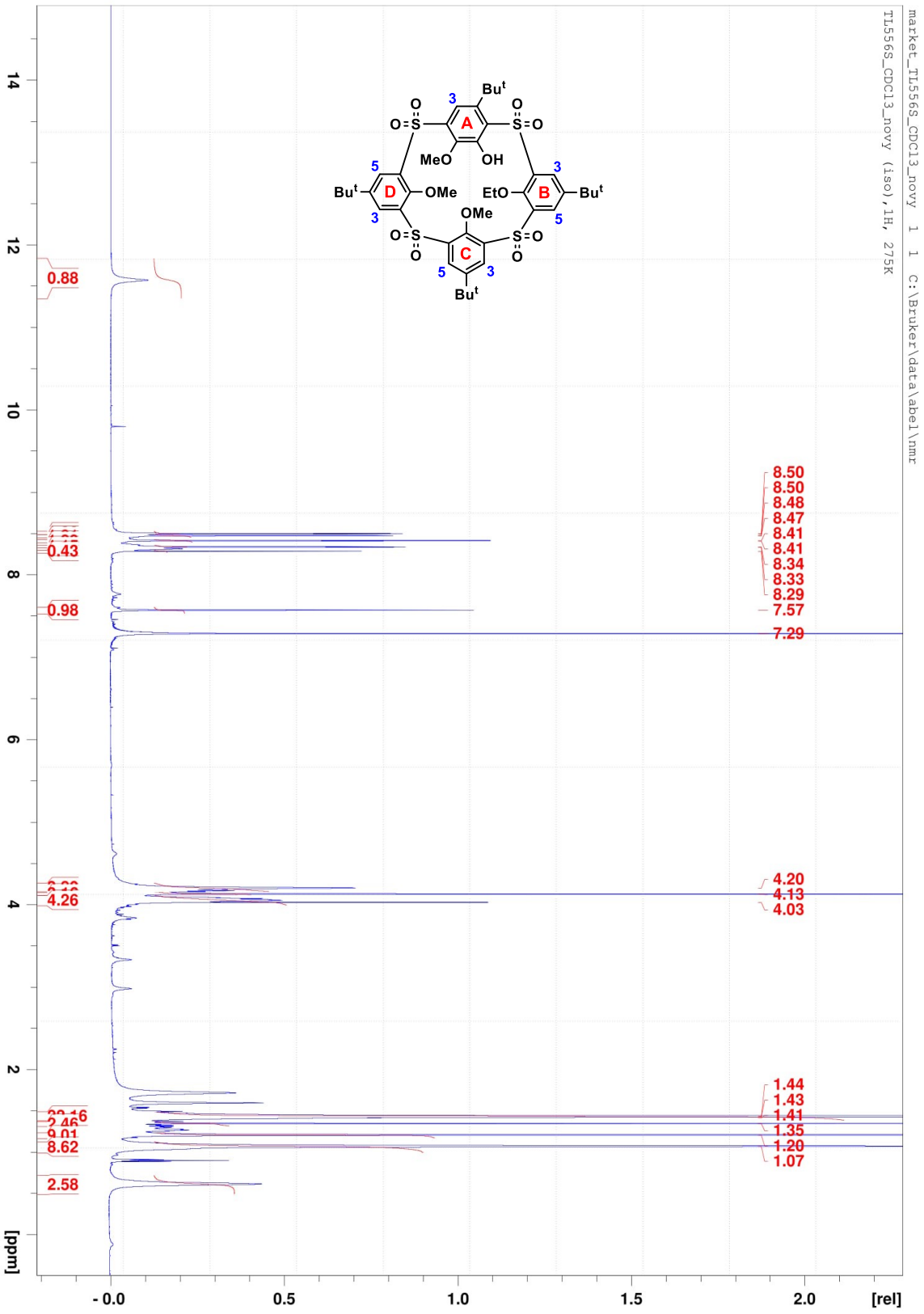


Figure S28: ^{1}H NMR spectrum of compound **8b**

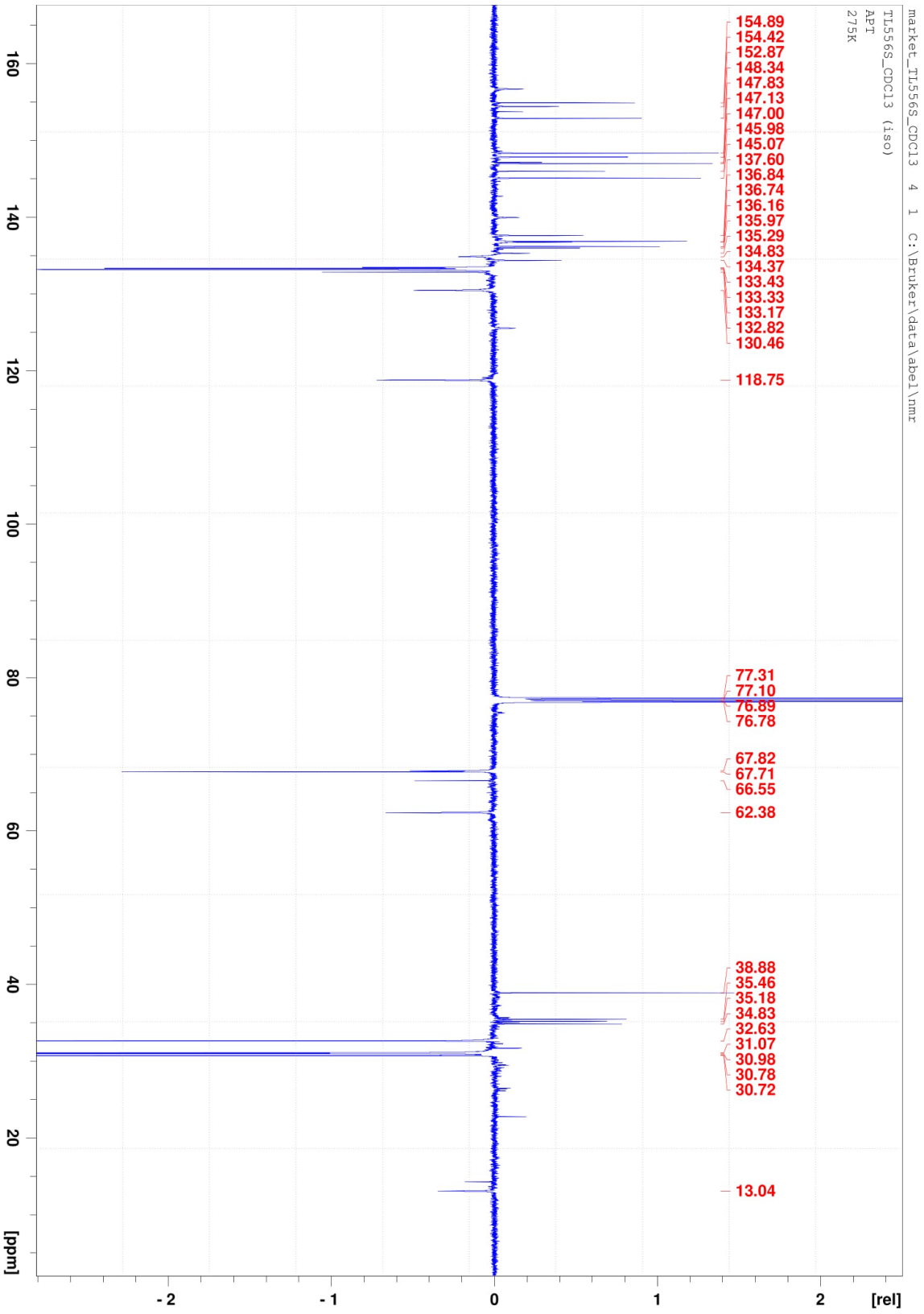


Figure S29: ^{13}C NMR (APT) spectrum of compound **8b**

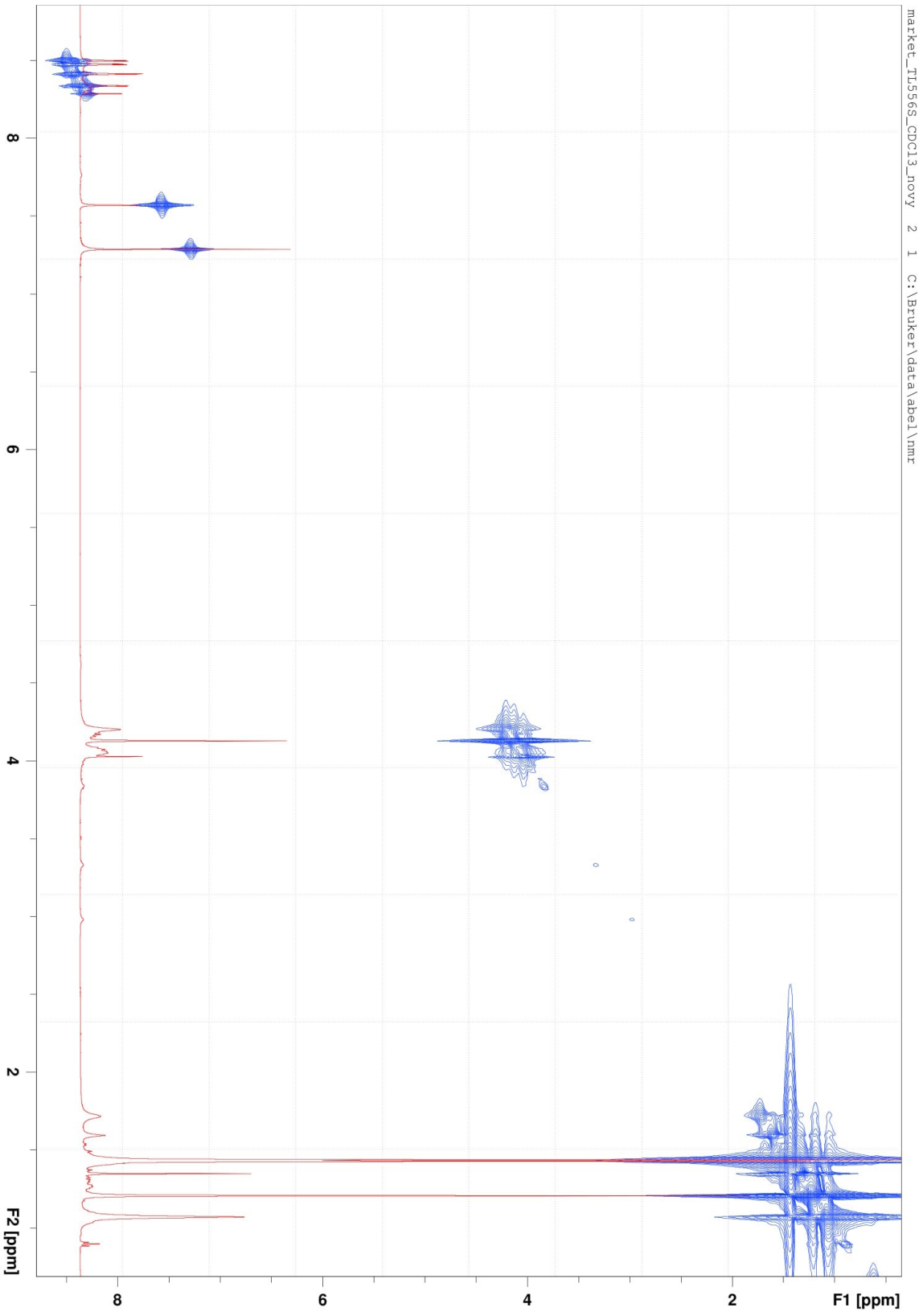


Figure S30: COSY spectrum of compound **8b**

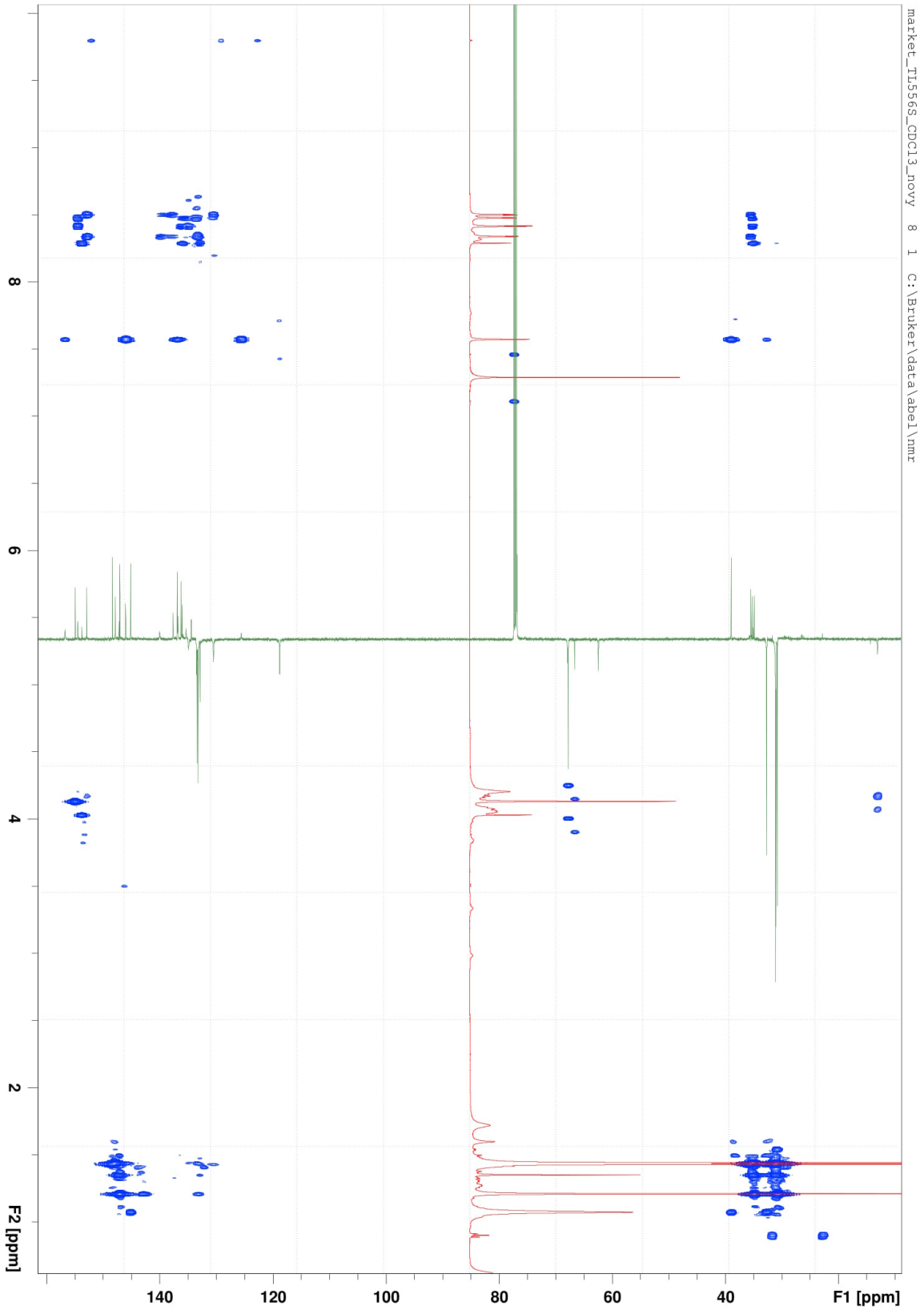


Figure S31: HMBC spectrum of compound **8b**

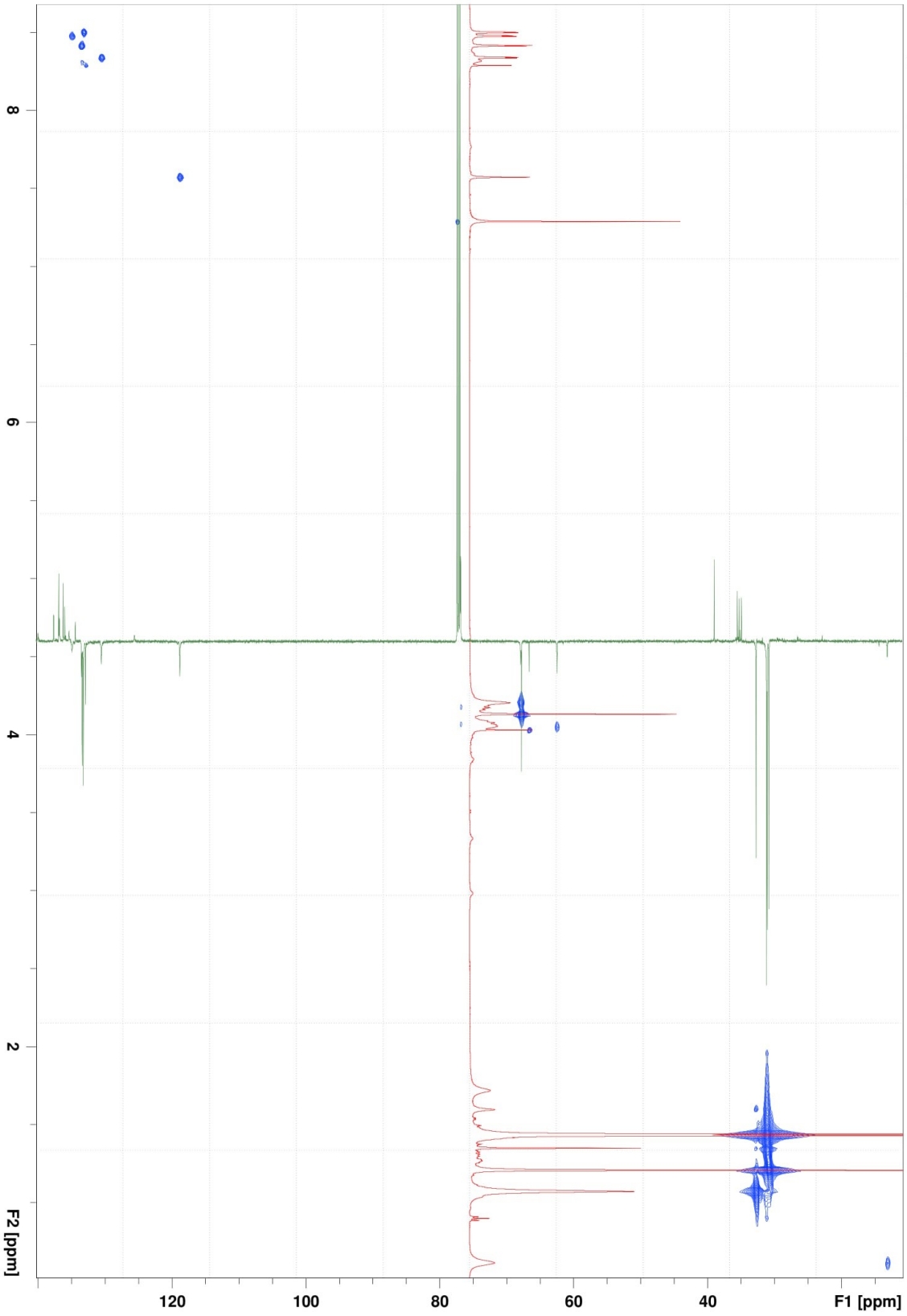


Figure S32: HMQC spectrum of compound **8b**

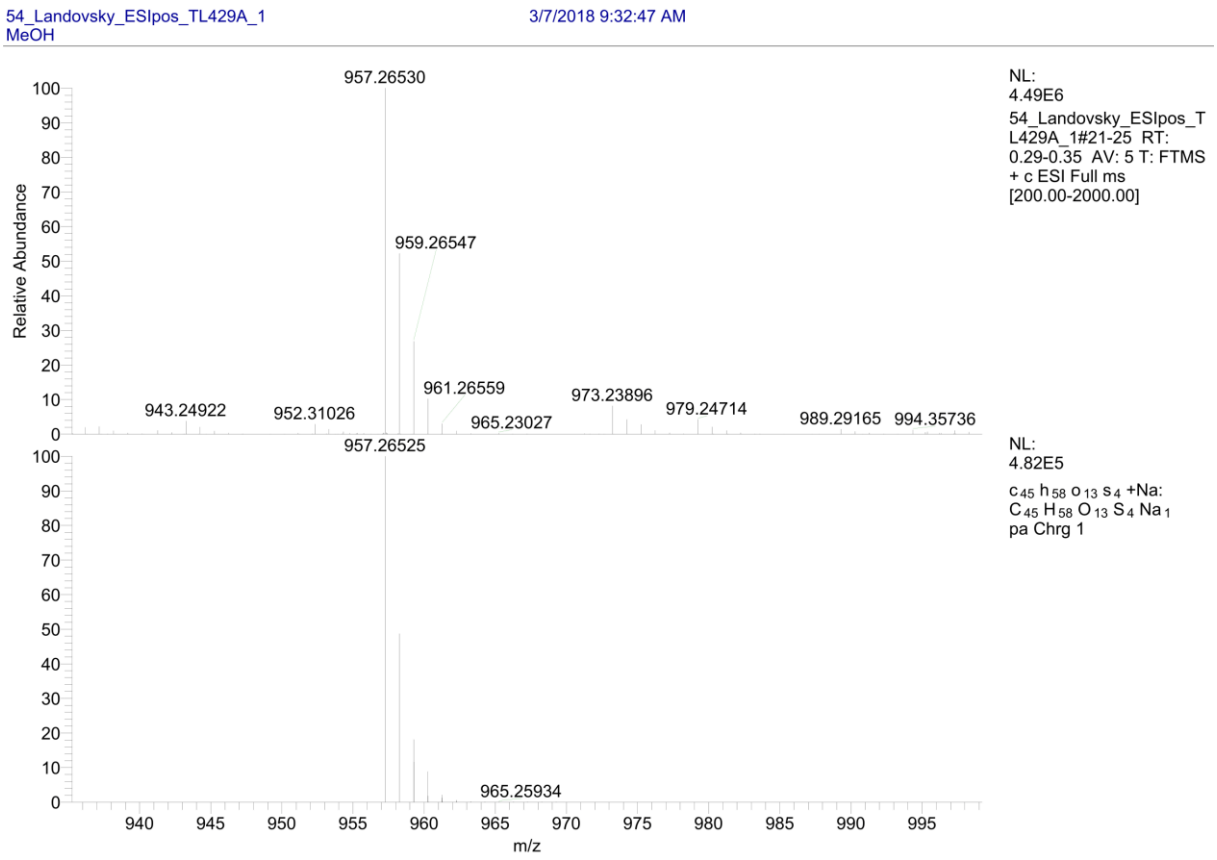


Figure S33: HRMS spectrum of compound **8b** (ESI^+)

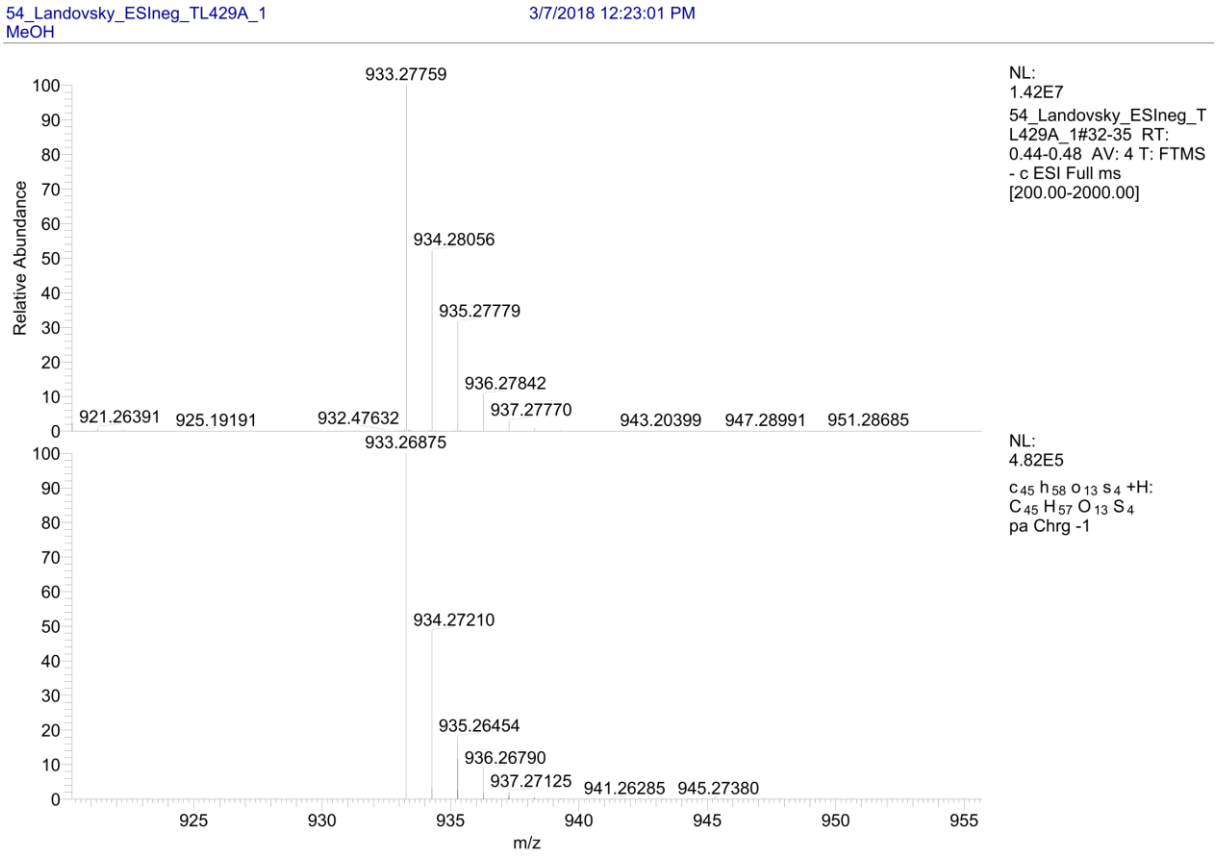


Figure S34: HRMS spectrum of compound **8b** (ESI^-)

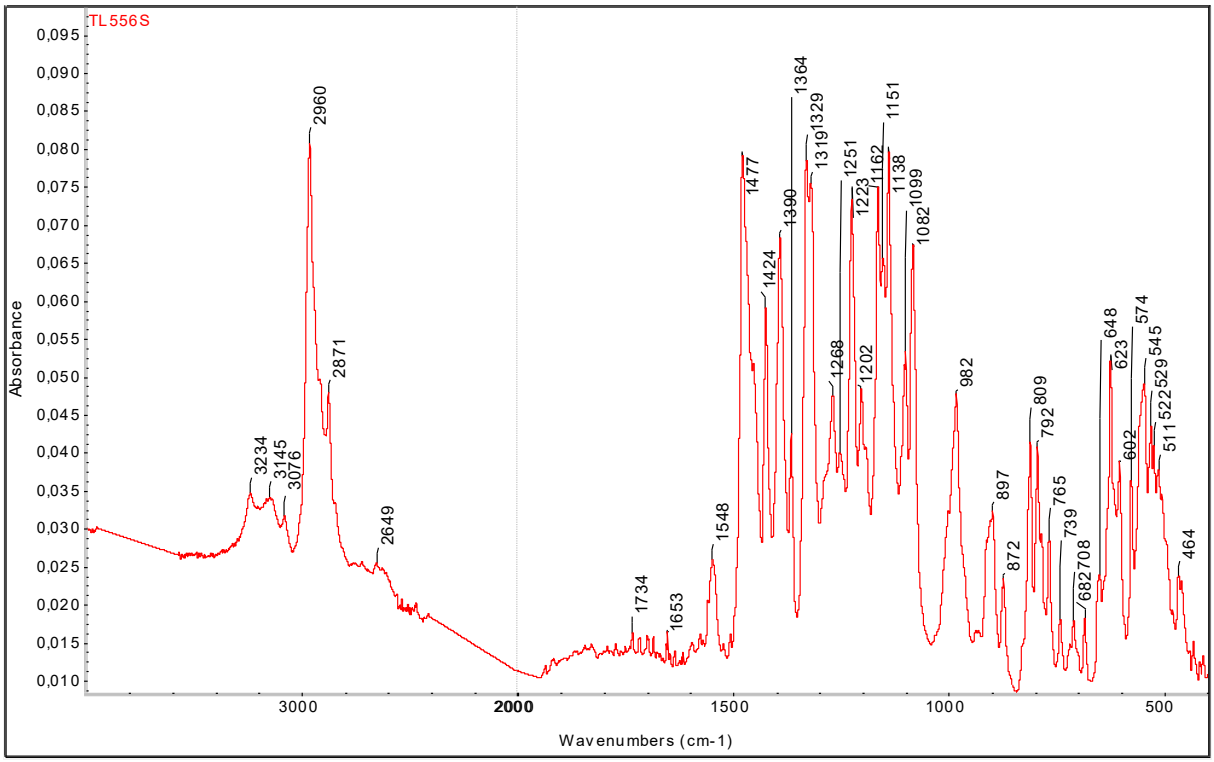


Figure S35: IR spectrum of compound **8b** (ATR)

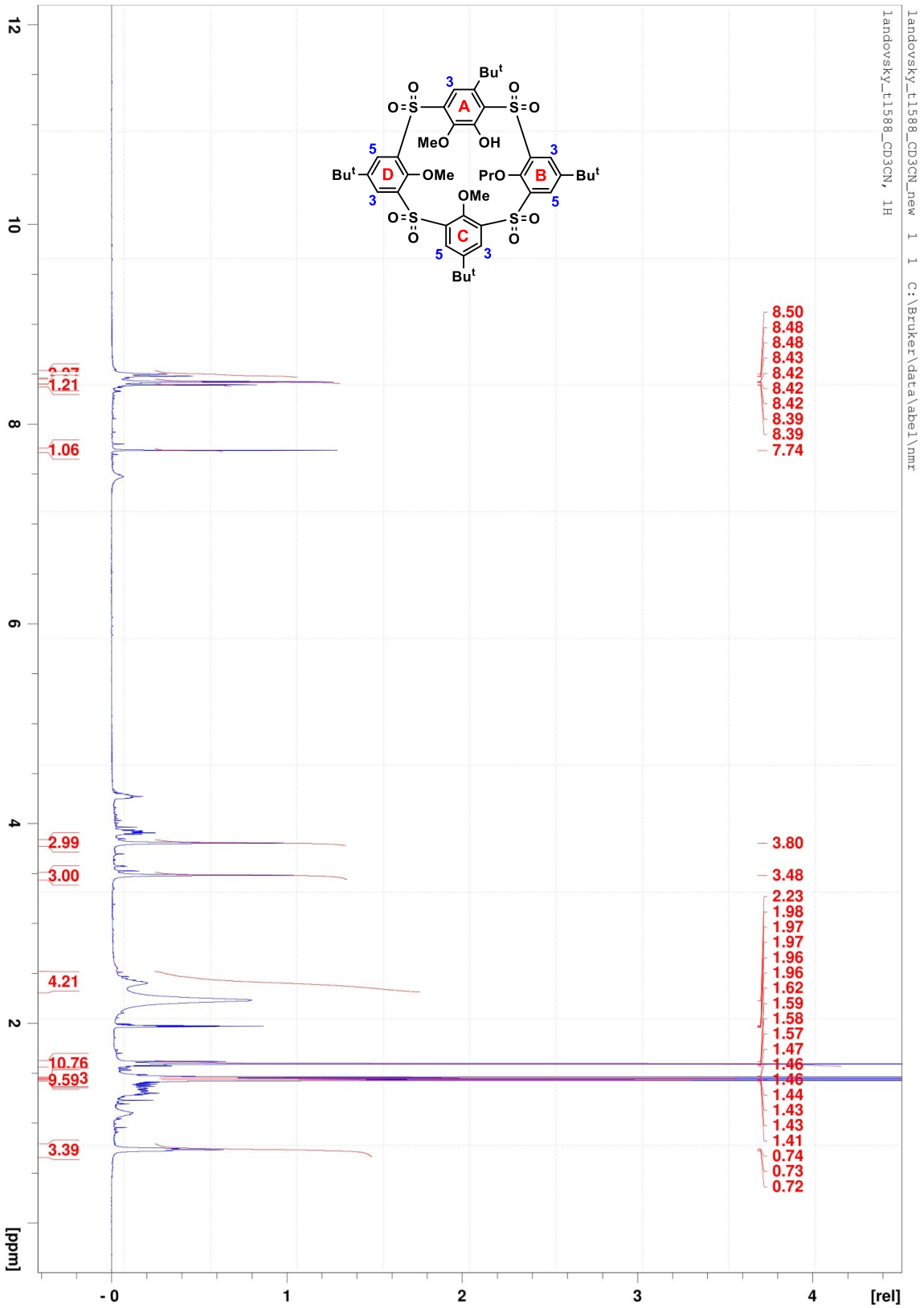


Figure S36: ^{1}H NMR spectrum of compound **8c** *1,3-alternate*

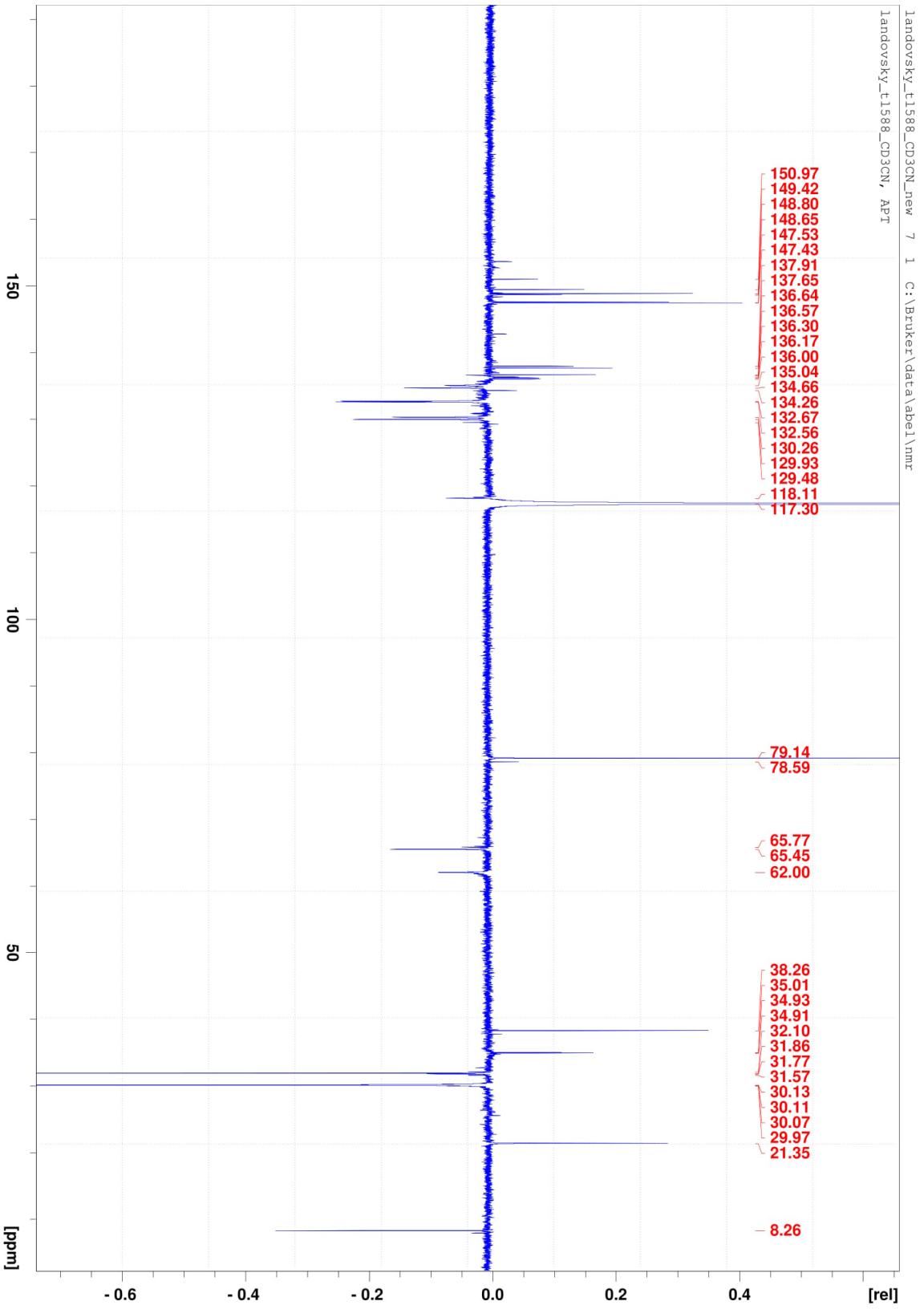


Figure S37: ^{13}C NMR (APT) spectrum of compound **8c** *1,3-alternate*

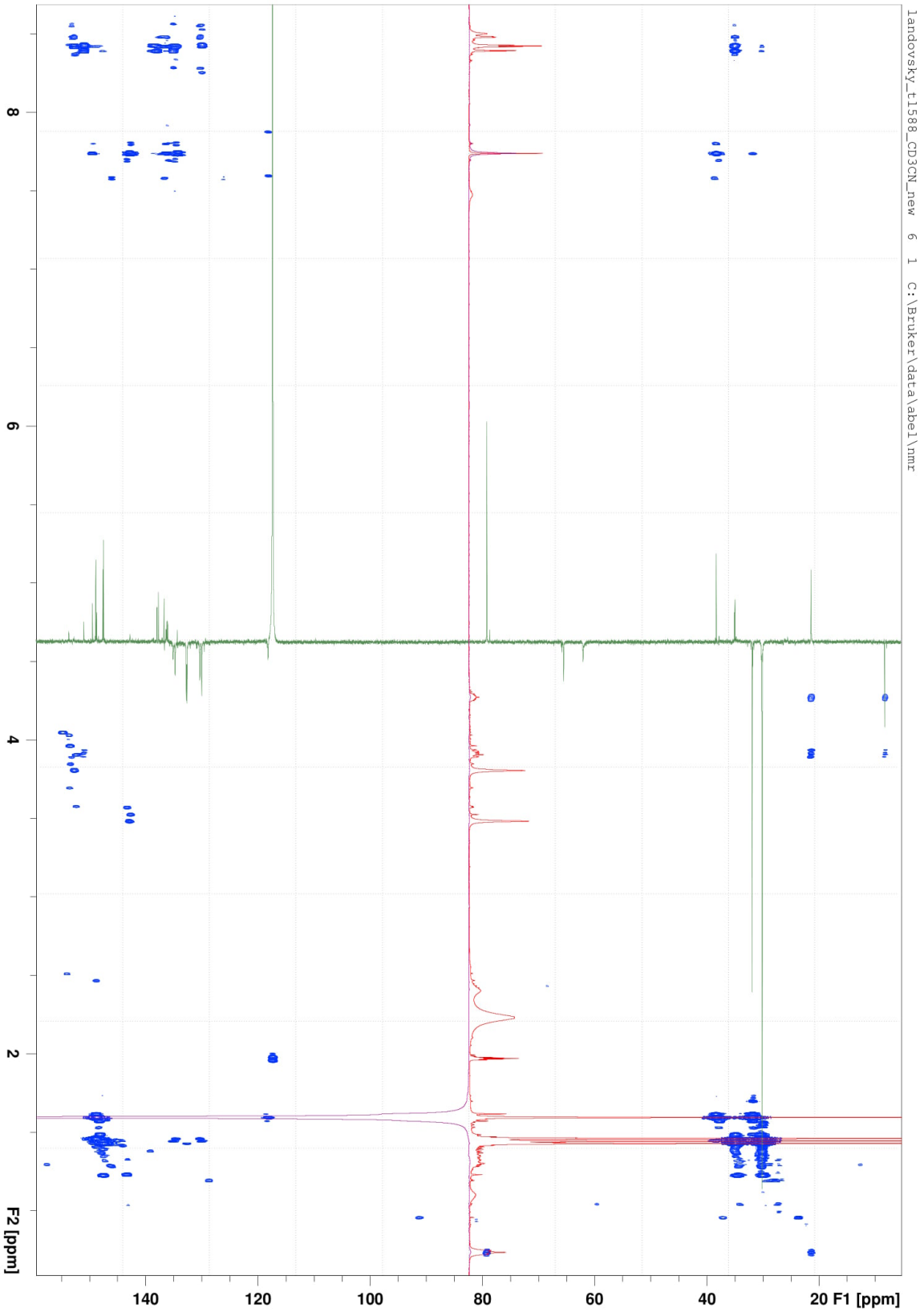


Figure S38: HMBC spectrum of compound **8c** *1,3-alternate*

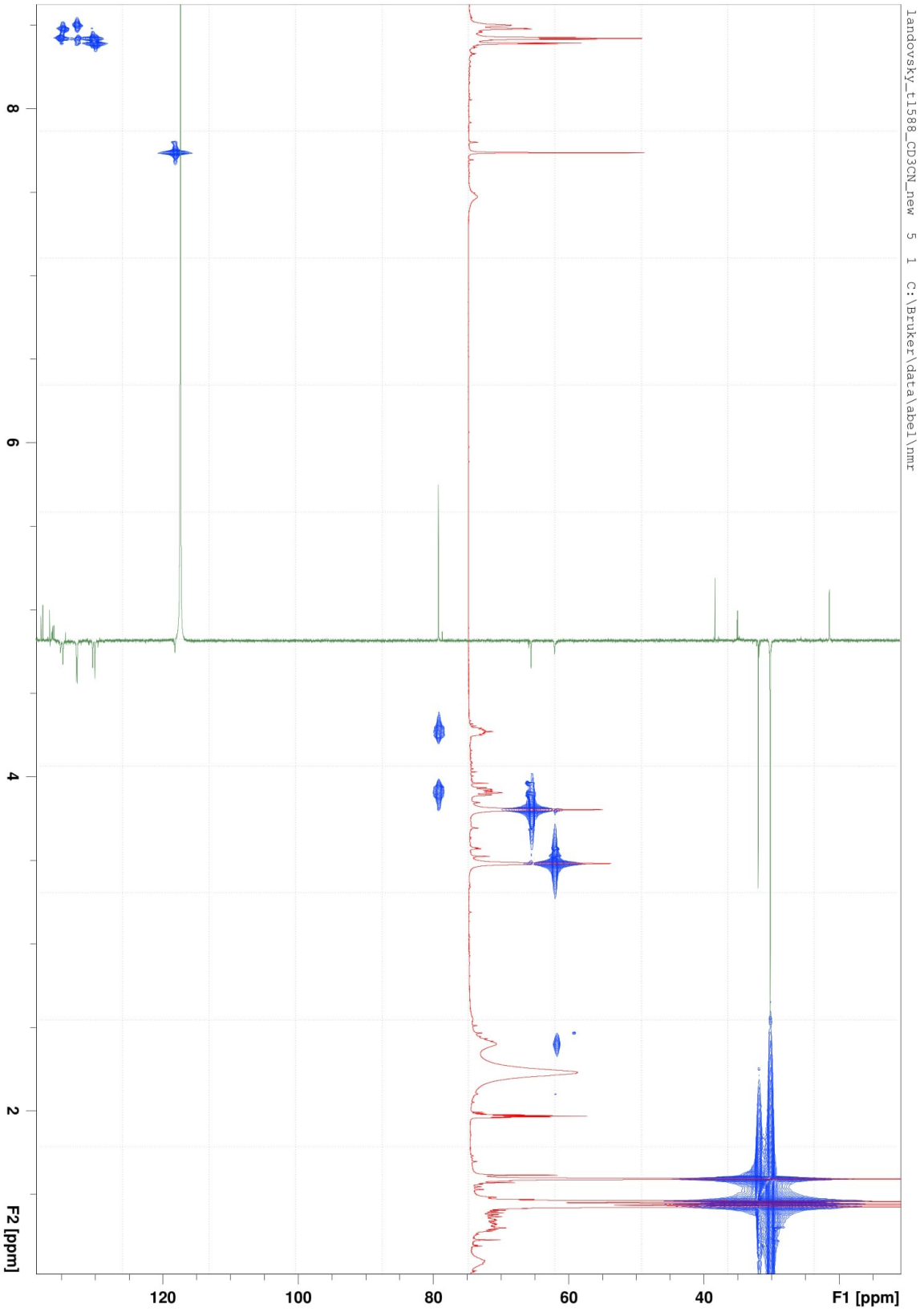


Figure S39: HMQC spectrum of compound **8c** *1,3-alternate*

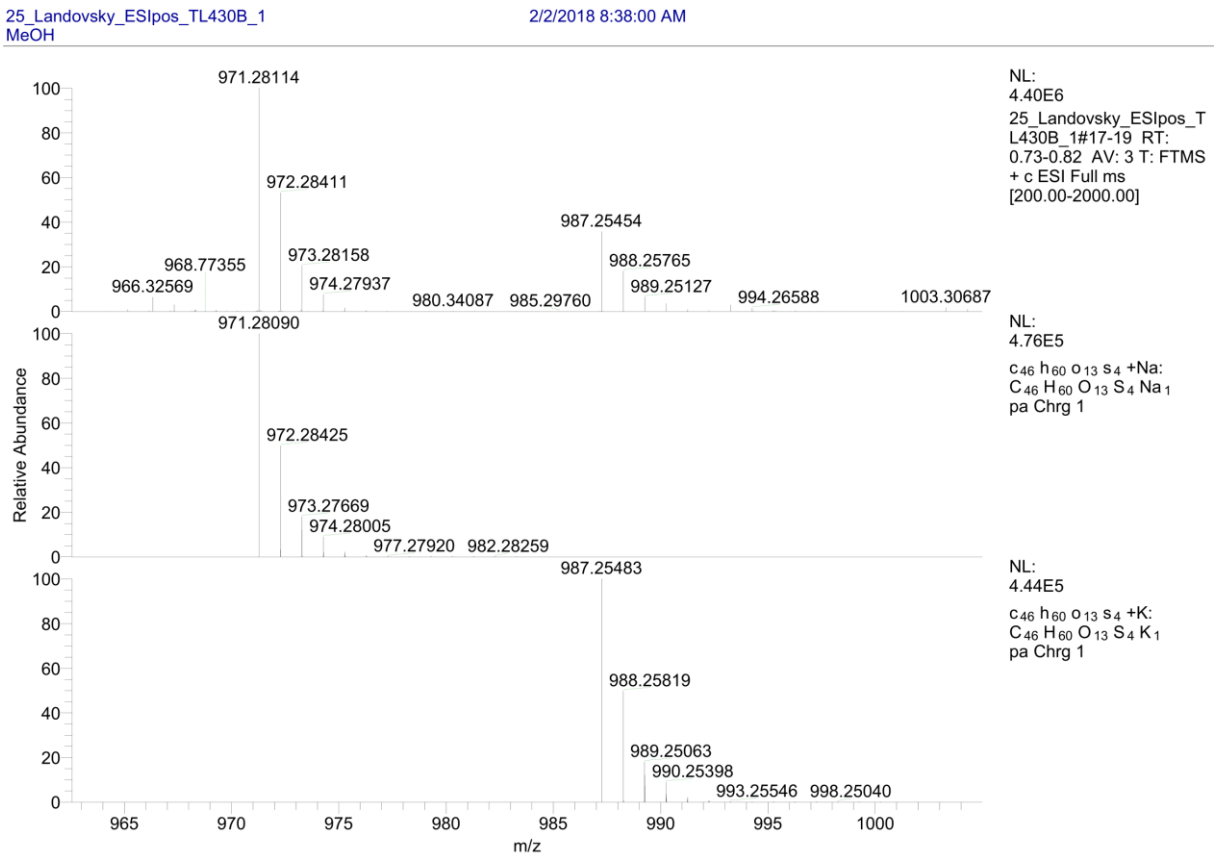


Figure S40: HRMS spectrum of compound **8c** *1,3-alternate* (ESI^+)

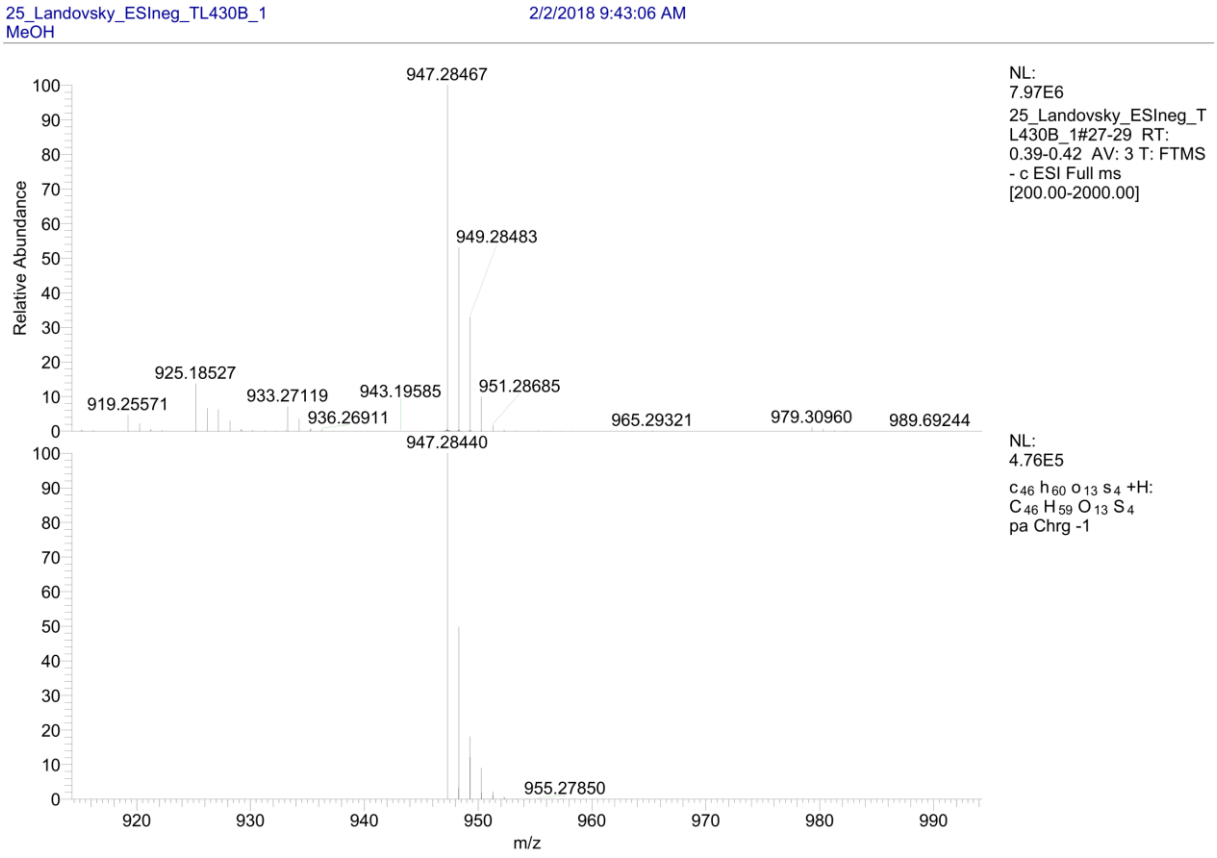


Figure S41: HRMS spectrum of compound **8c** *1,3-alternate* (ESI^-)

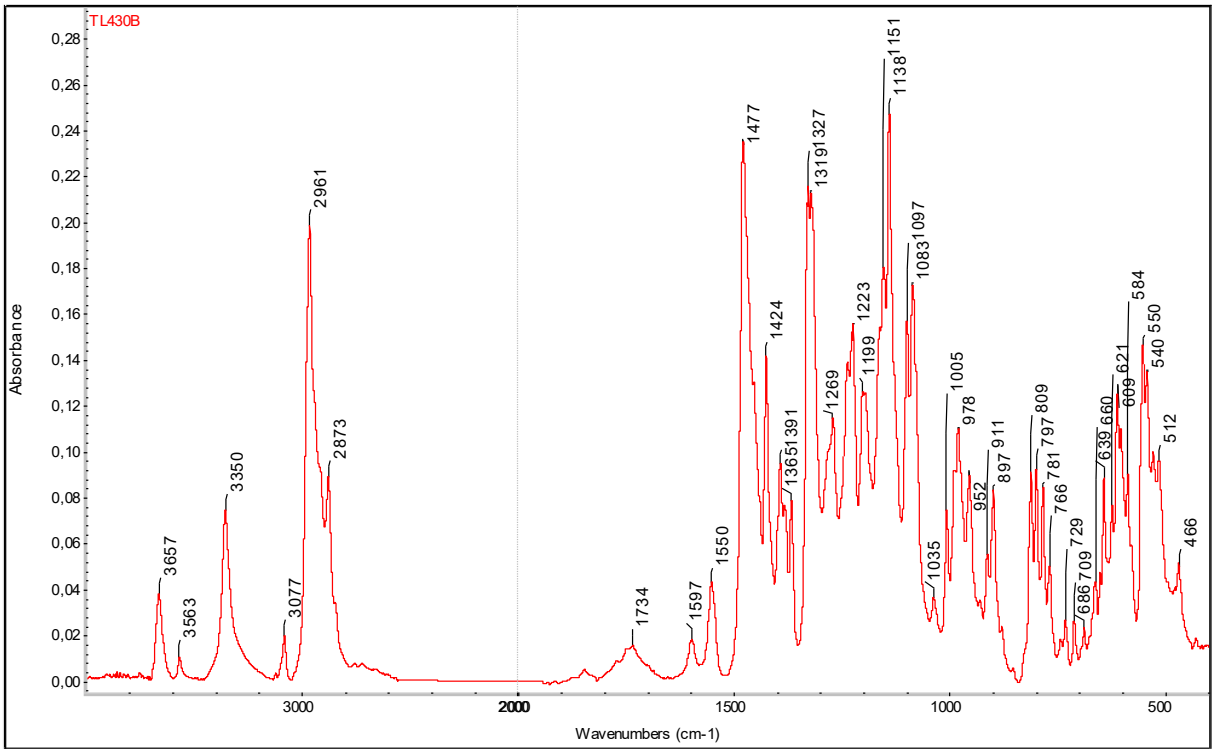


Figure S42: IR spectrum of compound **8c** *1,3-alternate* (ATR)

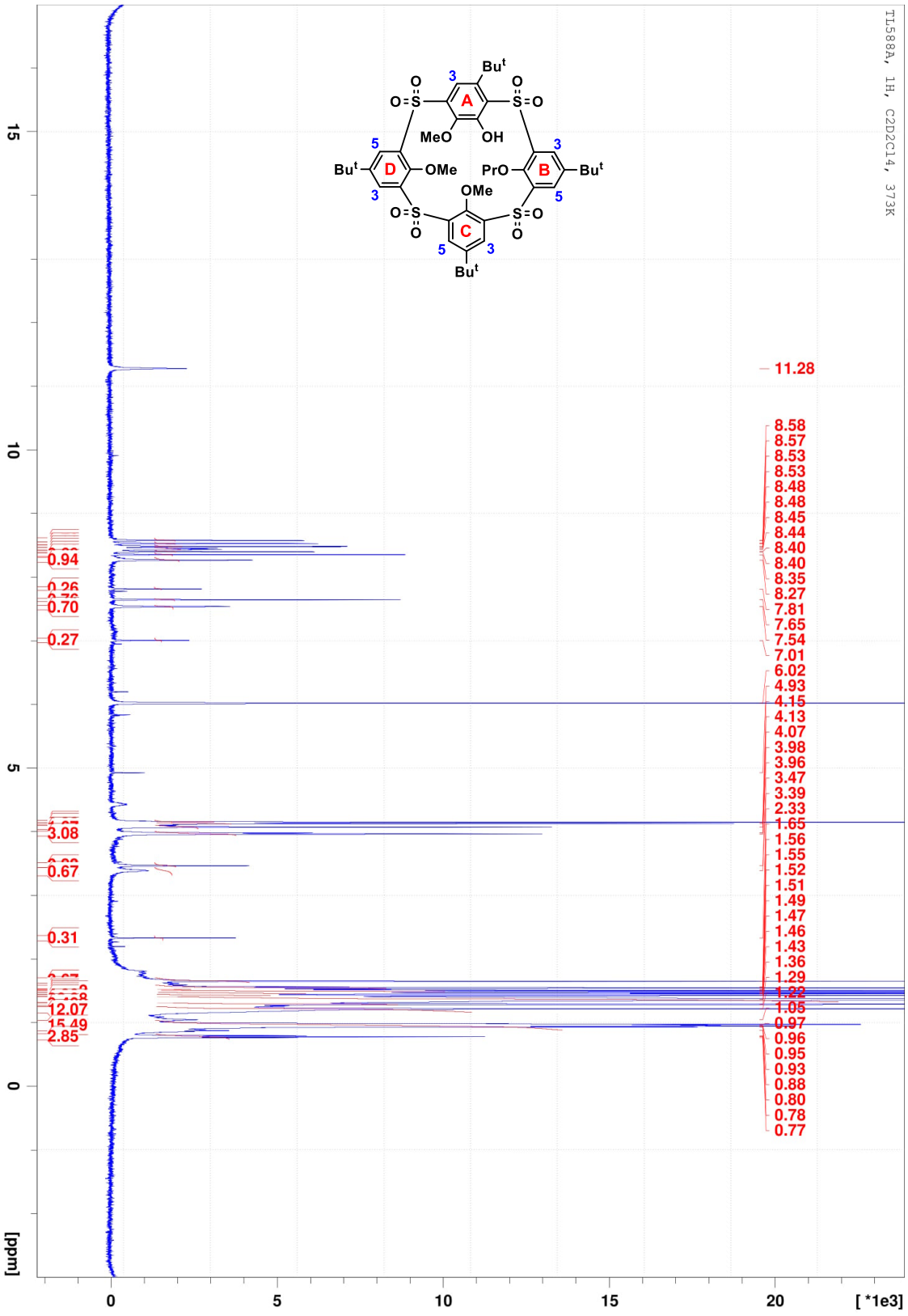


Figure S43: ^{1}H NMR spectrum of compound **8c** *partial cone D*

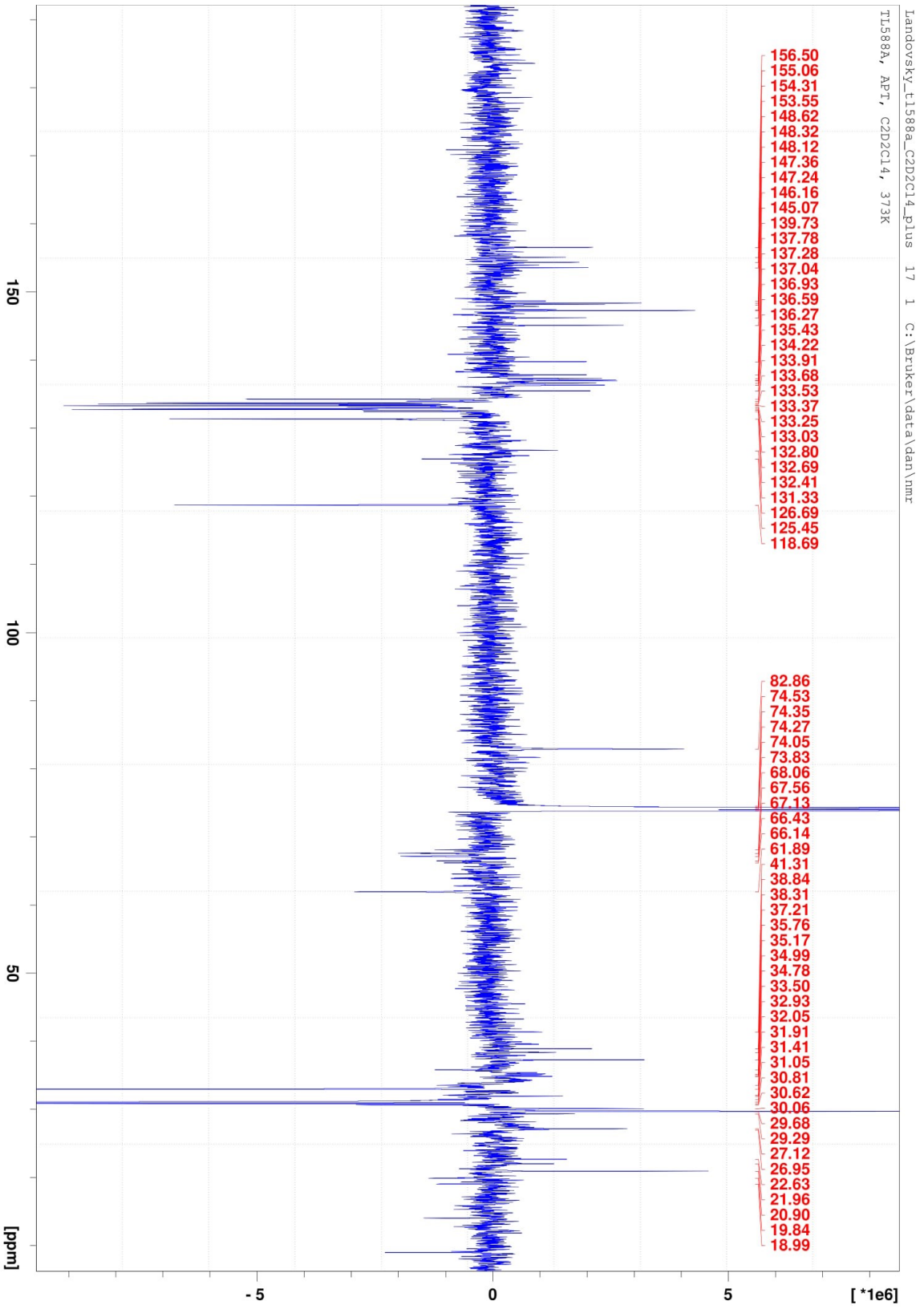


Figure S44: ^{13}C NMR (APT) spectrum of compound **8c** *partial cone D*

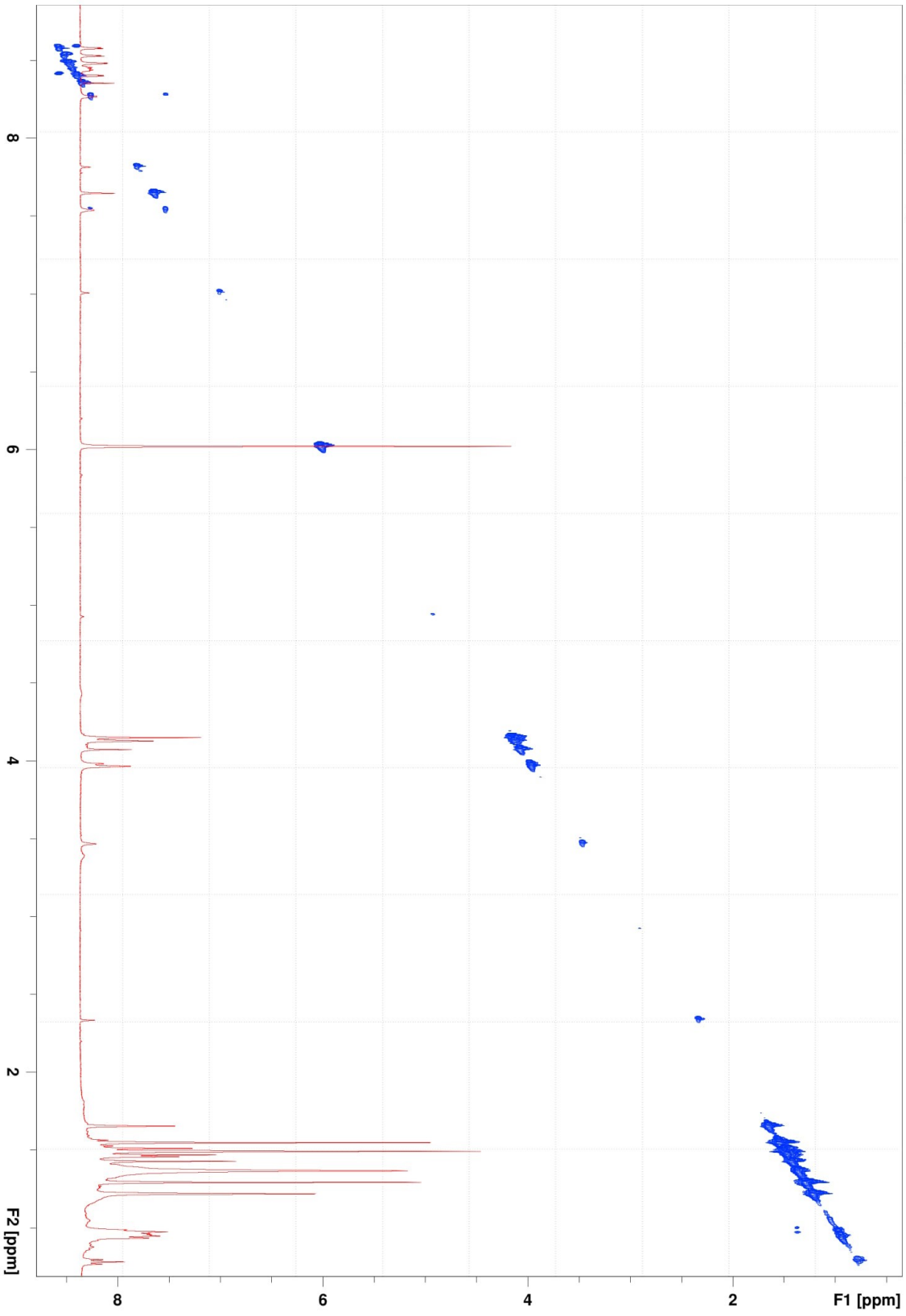


Figure S45: COSY spectrum of compound **8c** *partial cone D*

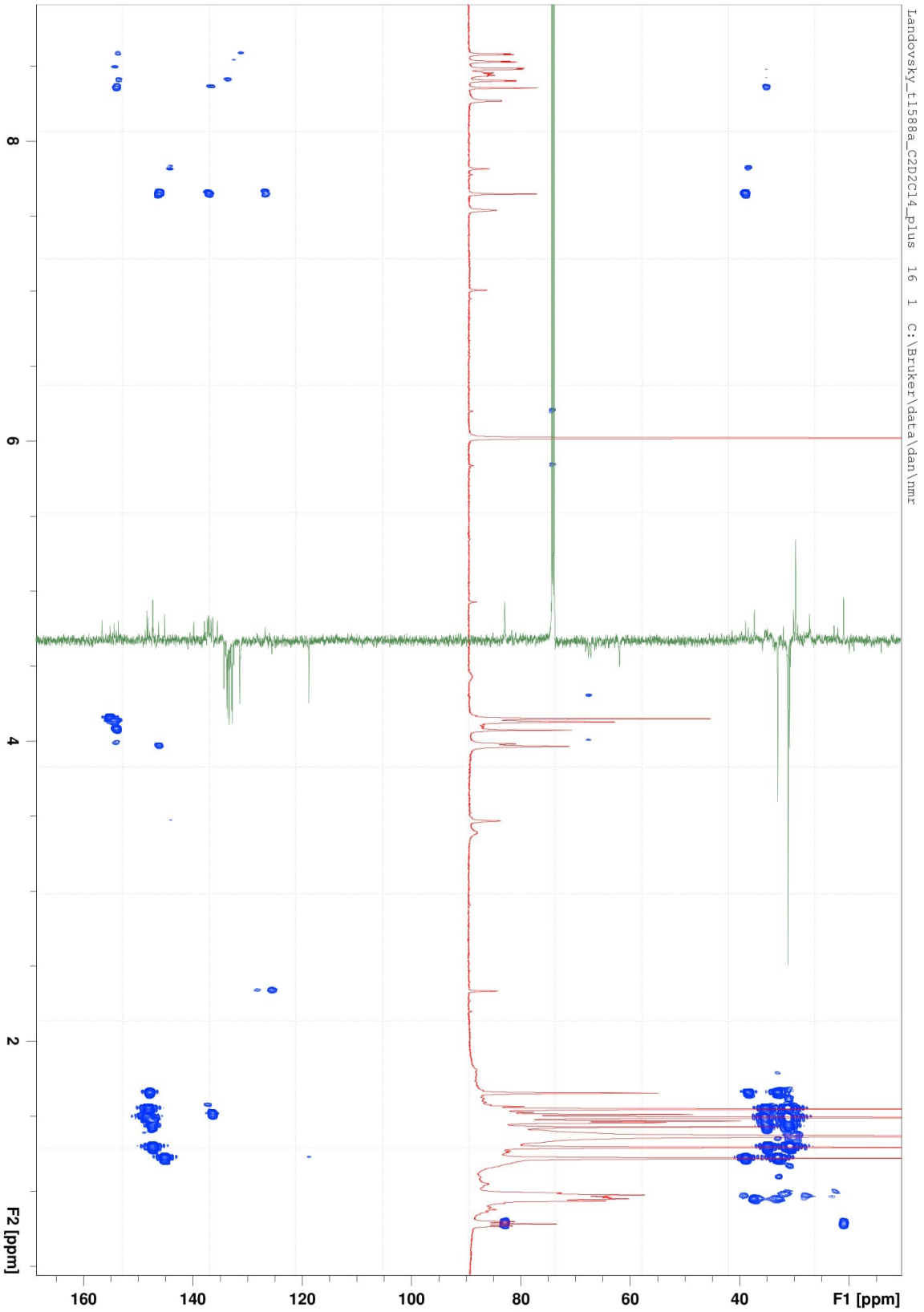


Figure S46: HMBC spectrum of compound **8c** *partial cone D*

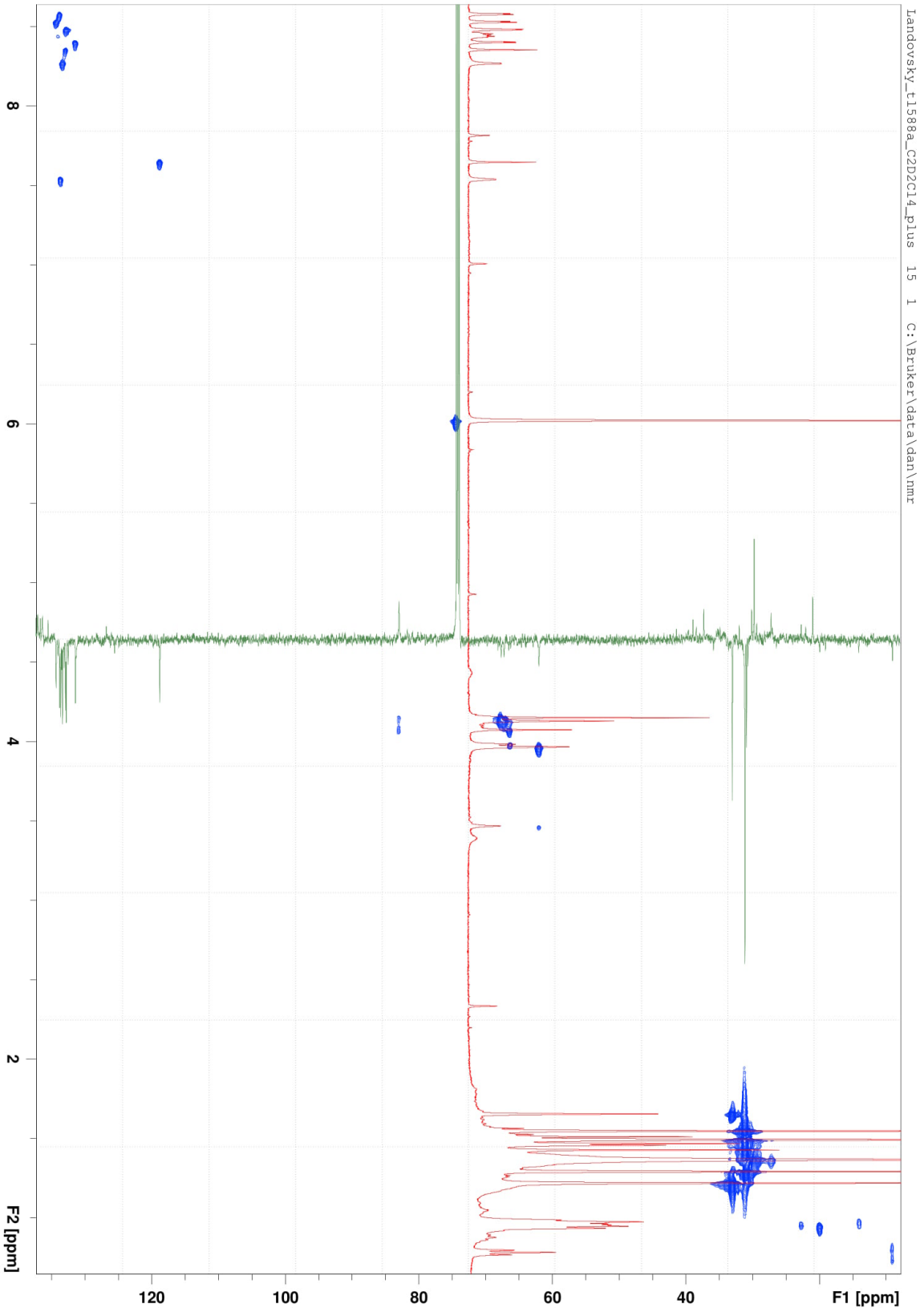


Figure S47: HMQC spectrum of compound **8c** *partial cone D*

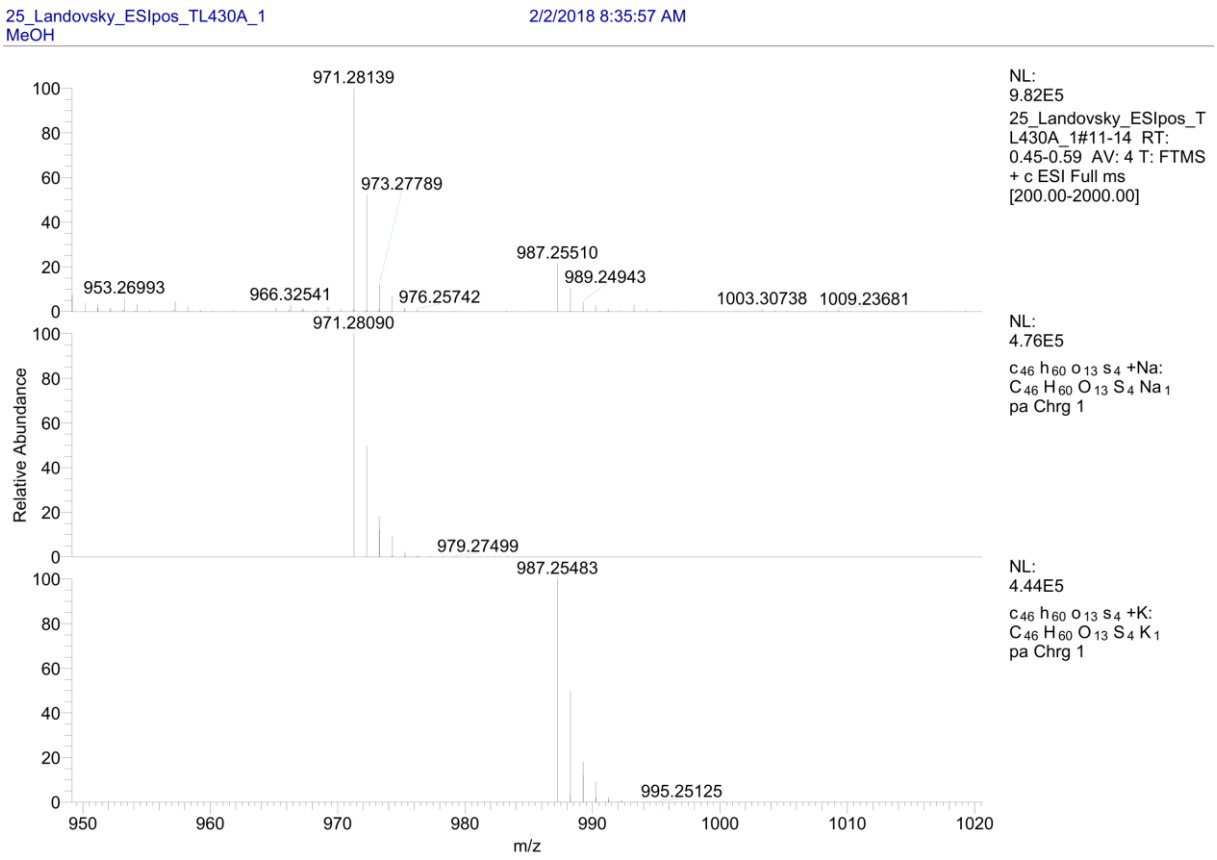


Figure S48: HRMS spectrum of compound **8c** *partial cone D* (ESI^+)

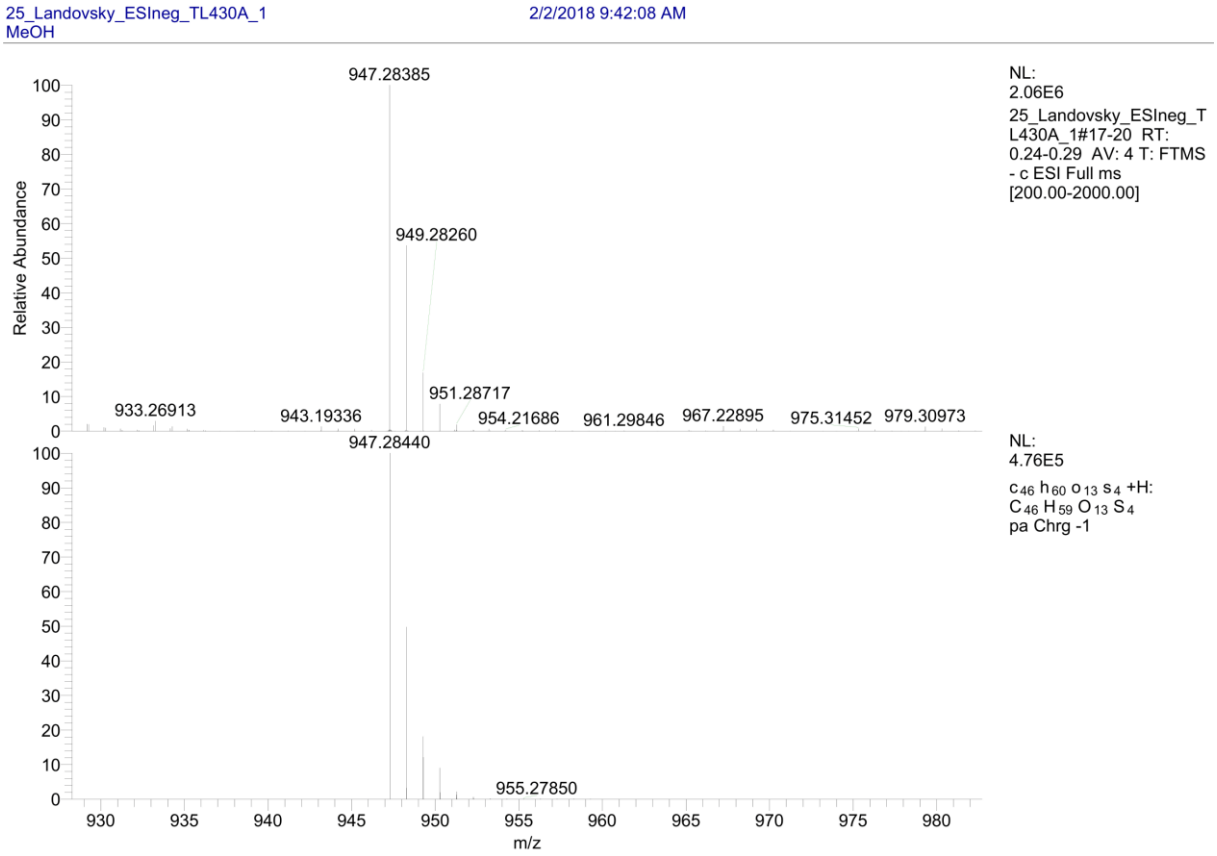


Figure S49: HRMS spectrum of compound **8c** *partial cone D* (ESI^-)

4. Crystallographic data

Crystallographic data for compound 7a

M = 936.50 g.mol^{-1}, orthorhombic system, space group *Pbcn*, a = 39.4032(8) Å, b = 10.2963(2) Å, c = 23.4609(5) Å, Z = 8, V = 9518.3(3) Å^3, D_c = 1.307 g.cm^{-3}, μ(Cu-Kα) = 2.36 mm^{-1}, crystal dimensions of 0.37 × 0.21 × 0.09 mm. Data were collected at 180 K on a D8 Venture Photon CMOS diffractometer with Incoatec microfocus sealed tube Cu-Kα radiation. The structure was solved by charge flipping methods[S3] and anisotropically refined by full matrix least squares on F squared using the CRYSTALS suite of programs[S4] to final value R = 0.046 and wR = 0.096 using 8733 independent reflections (Θ_{max} = 68.3°), 639 parameters and 88 restrains. The disordered functional group positions were found in difference electron density maps and refined with restrained geometry. The occupancy of disordered functional group was restrained to full. The hydrogen atoms present in structure model were placed in calculated positions and refined with riding constrains. Hydrogen atoms of weakly occupied water molecule could not be located in difference electron density maps; therefore, they are absent in the structure model. The MCE program[S5] was used for visualization of residual electron density maps. The structure was deposited into Cambridge Structural Database under number CCDC 1955160.

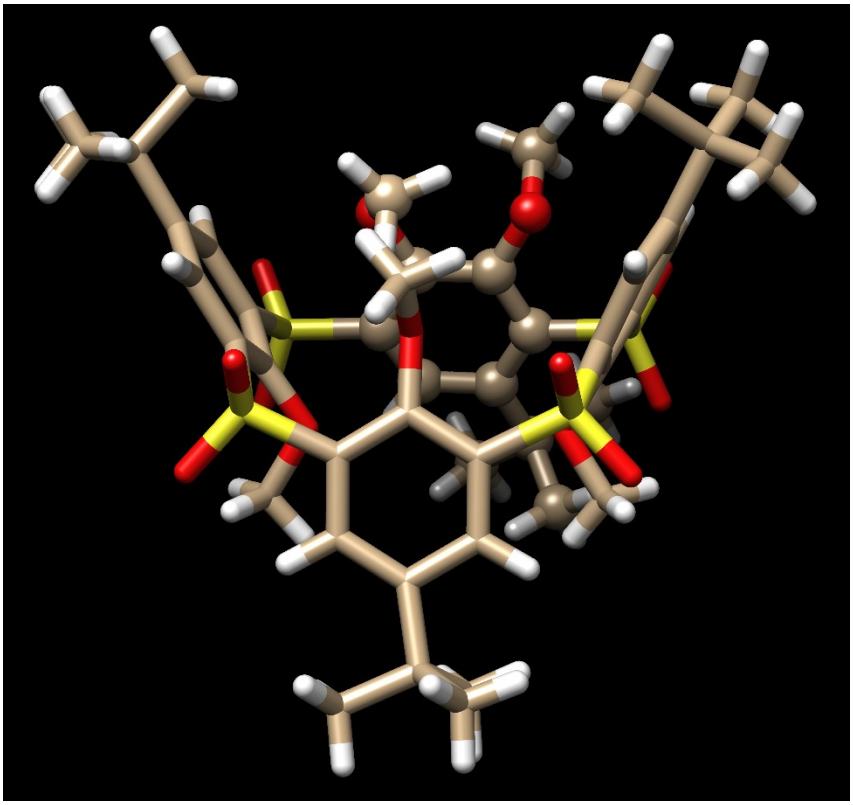
Crystallographic data for compound 8c

M = 1010.22 g.mol^{-1}, monoclinic system, space group $P2_1/c$, a = 18.5665(5) Å, b = 21.0808(6) Å, c = 13.5866(4) Å, β = 103.8797(9)°, Z = 4, V = 5162.5(3) Å^3, D_c = 1.300 g.cm^{-3}, μ(Cu-Kα) = 2.238 mm^{-1}, crystal dimensions of 0.51 × 0.36 × 0.23 mm. Data were collected at 180 K on a D8 Venture Photon CMOS diffractometer with Incoatec microfocus sealed tube Cu-Kα radiation. The structure was solved by charge flipping methods[S3] and anisotropically refined by full matrix least squares on F squared using the CRYSTALS suite of programs[S4] to final value R = 0.039 and wR = 0.0943 using 10175 independent reflections (Θ_{max} = 72.225°), 633 parameters and 46 restrains. The hydrogen atoms were placed in calculated positions and refined with riding constrains. The disordered functional group positions were found in difference electron density maps and refined with restrained geometry. The electron density maps were visualized using MCE software.[S6] The occupancy of disordered functional group was constrained to full. The structure was deposited into Cambridge Structural Database under number CCDC 1943887.

(S3) Palatinus, L.; Chapuis, G. *J. Appl. Cryst.* **2007**, *40*, 786.
(S4) Betteridge, P. W.; Carruthers, J. R.; Cooper, R. I.; Prout, K.; Watkin D. J. *J. Appl. Cryst.* **2003**, *36*, 1487.
(S5) Rohlicek, J.; Husak, M. *J. Appl. Cryst.* **2007**, *40*, 600.
(S6) Husak, M.; Kratochvil, B. *J. Appl. Cryst.* **2003**, *36*, 1104.

5. Crystal structure of the compound **7a**

a)



b)

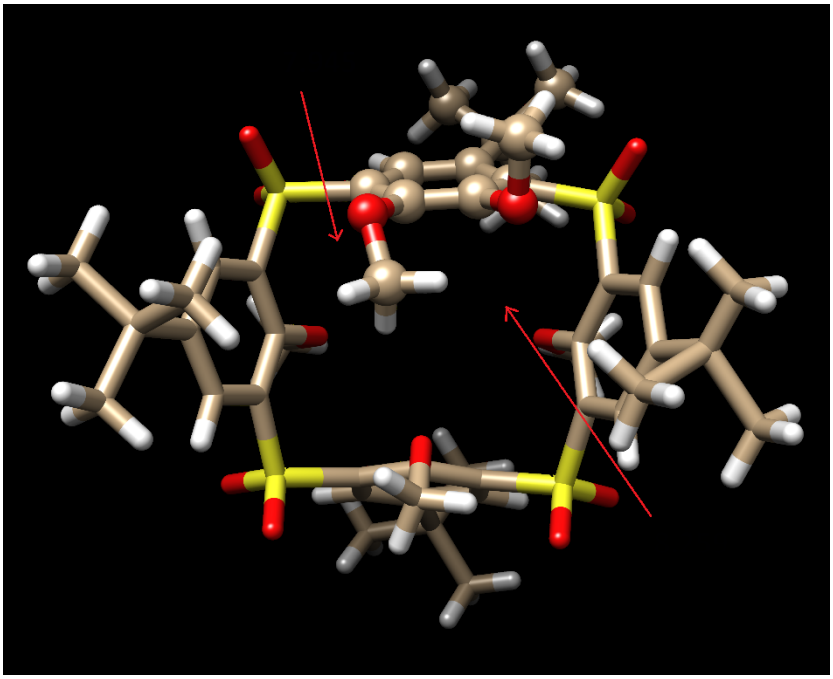


Figure S50: Single crystal X-ray structures of the compound **7a**: (a) side-view, (b) top-view (the *para*-substituted moiety shown as balls for better clarity).

6. NMR spectra of **7a, 7b** with chiral shift agent

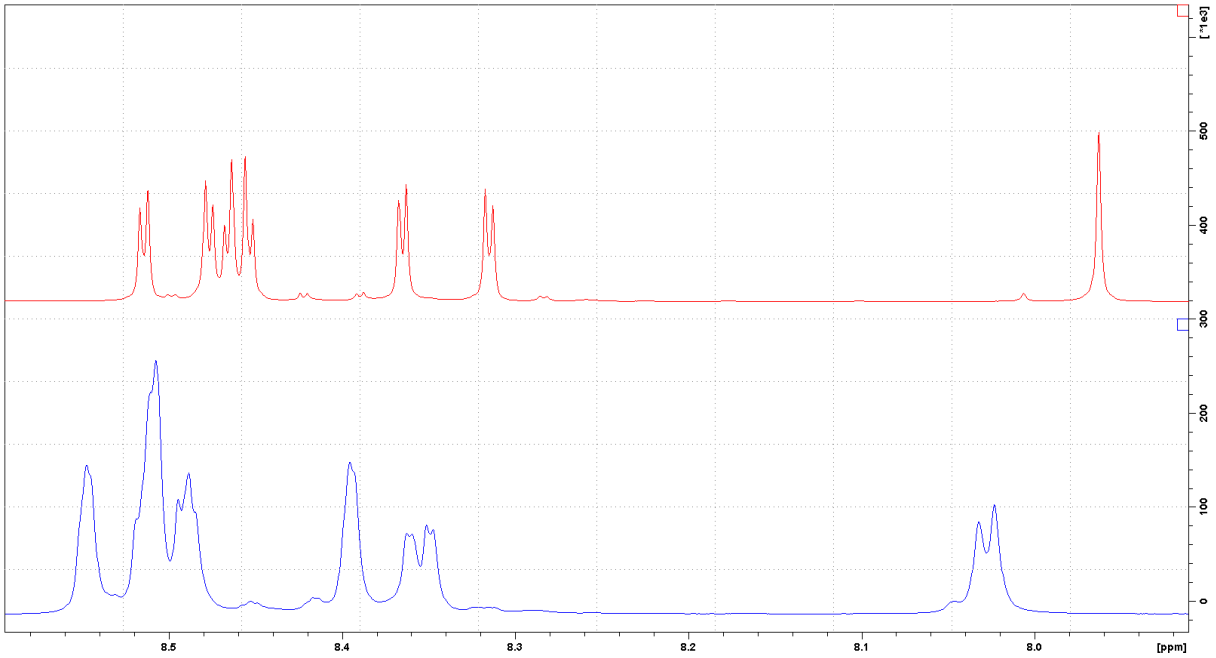


Figure S51a: ^{1}H NMR spectra (600 MHz, 298 K, $CDCl_3$) of: (a) compound **7a**, (b) **7a** with 2 molar eq. of europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate]

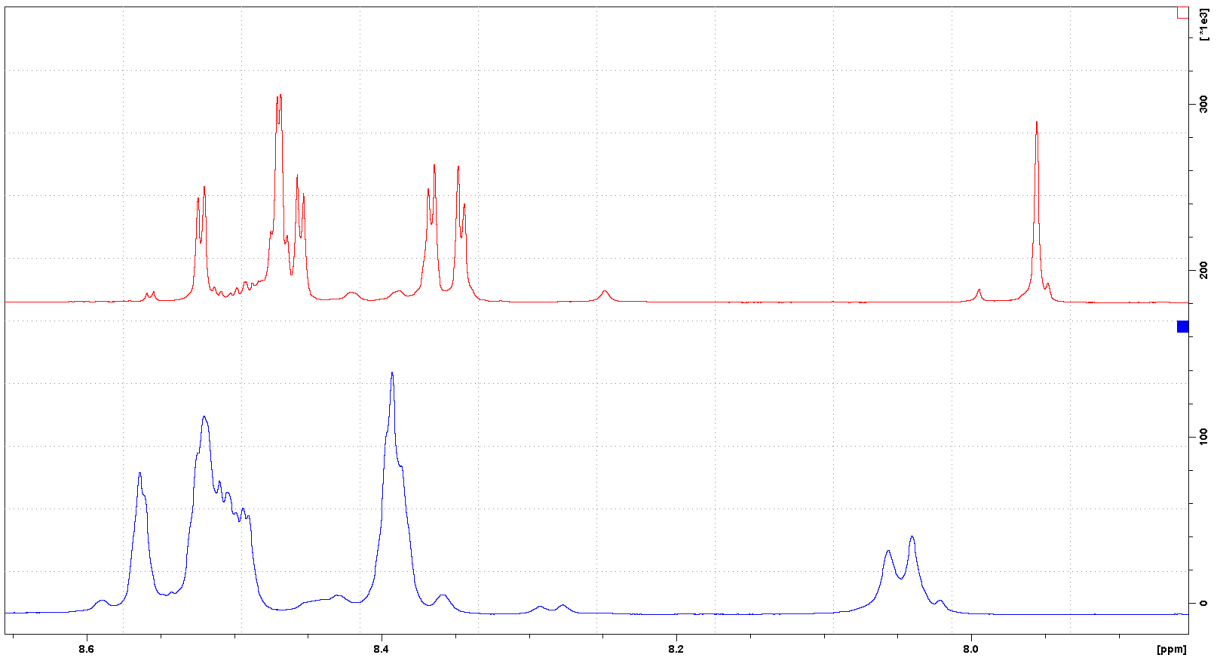


Figure S51b: ^{1}H NMR spectra (600 MHz, 298 K, $CDCl_3$) of: (a) compound **7b**, (b) **7b** with 2 molar eq. of europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate].

7. NOE experiments of **8c** *partial cone D*

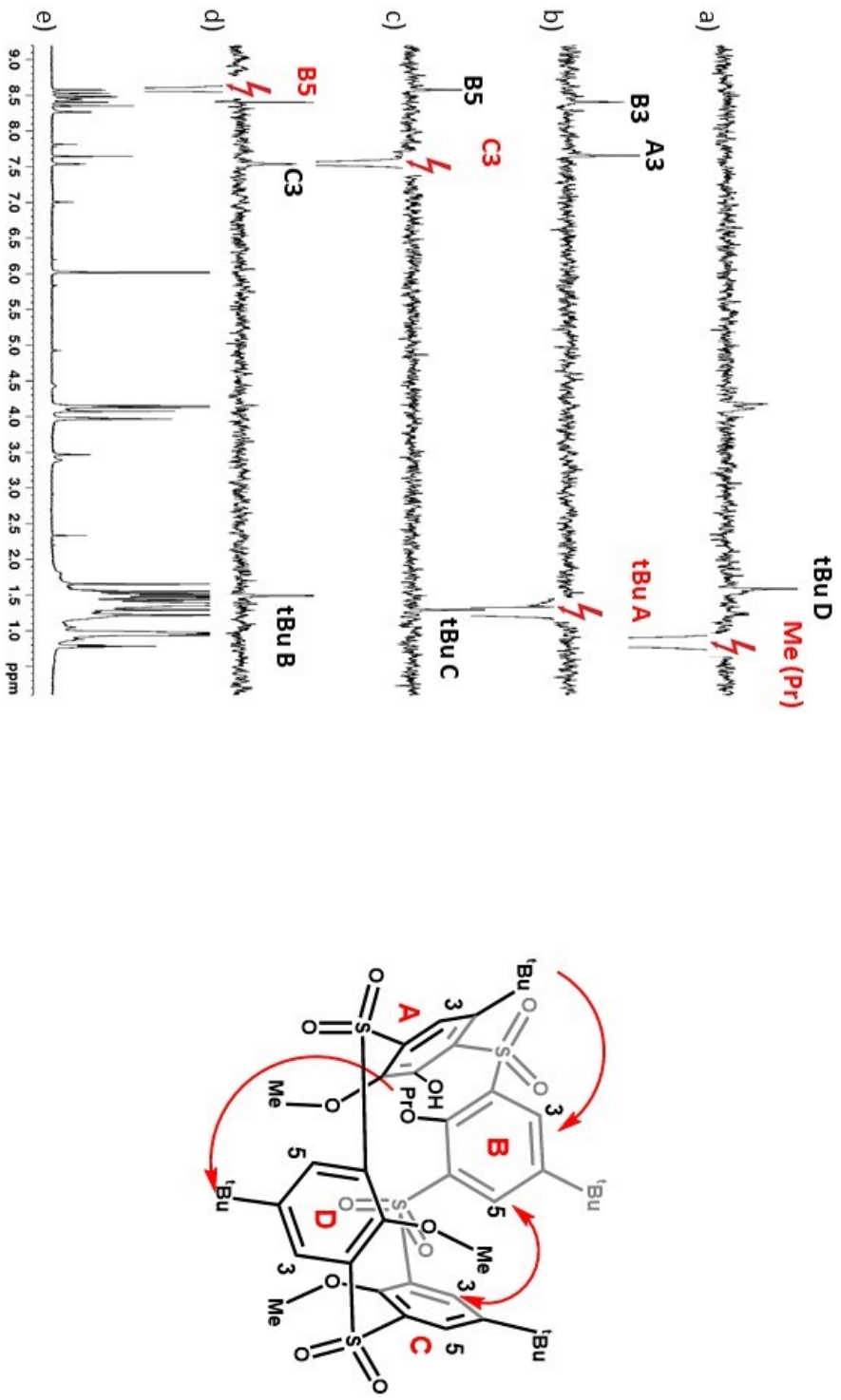


Figure S52: NOE experiment of **8c** *partial cone D* (600 MHz, $C_2D_2Cl_4$, 373 K)**:** a) NOE spectrum with Me (Pr) irradiated, b) NOE spectrum with tBu *A* irradiated, c) NOE spectrum with *C3* irradiated, d) NOE spectrum with *B5* irradiated, e) ^{1}H NMR of compound **8c** *partial cone D* in $C_2D_2Cl_4$.

8. Dissolution of **8c** *1,3-alternate* in various solvents

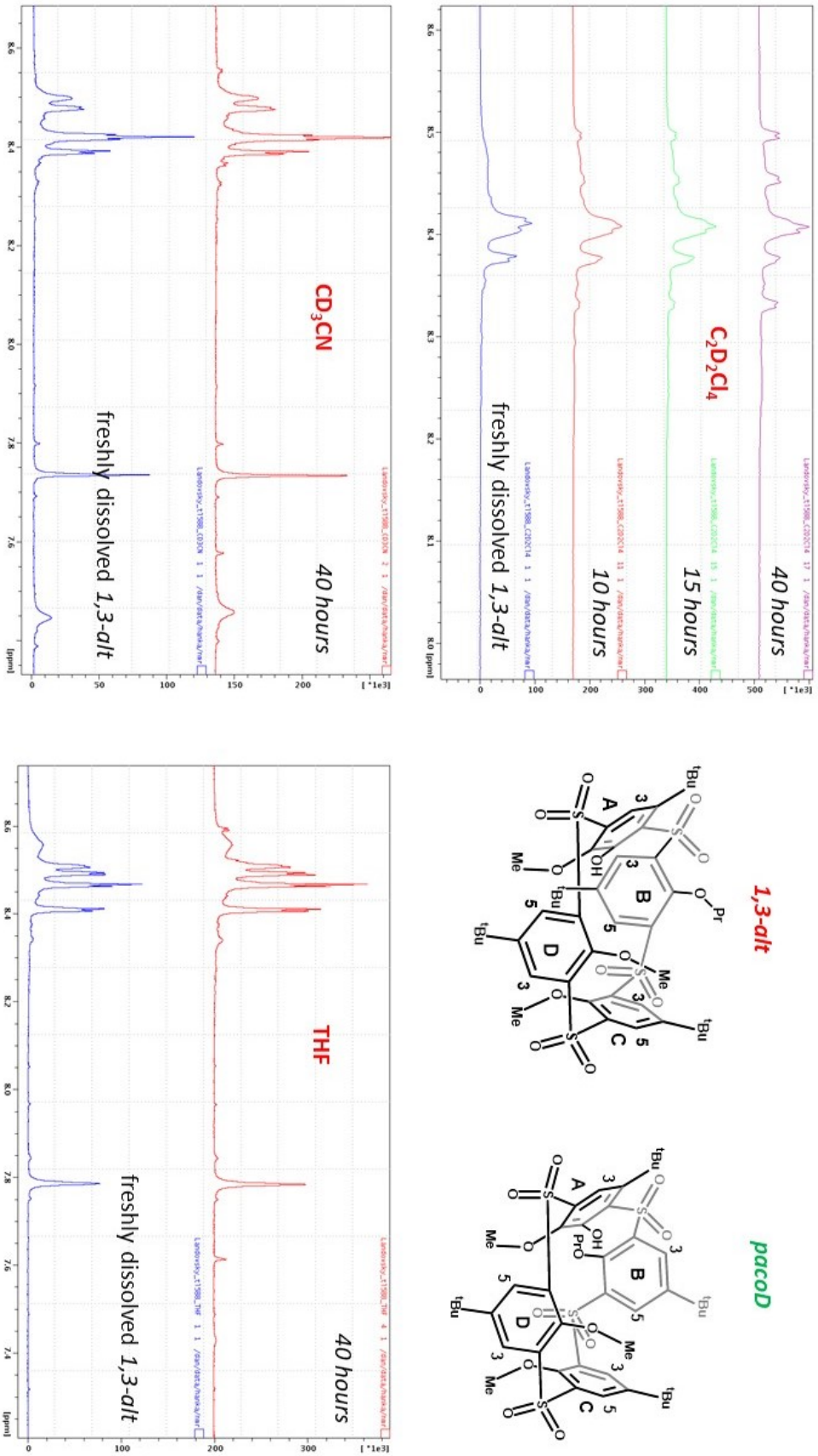


Figure S53: Standing of **8c** *1,3-alternate* solutions in various solvents (600 MHz, 298 K).

9. Variable temperature NMR spectra

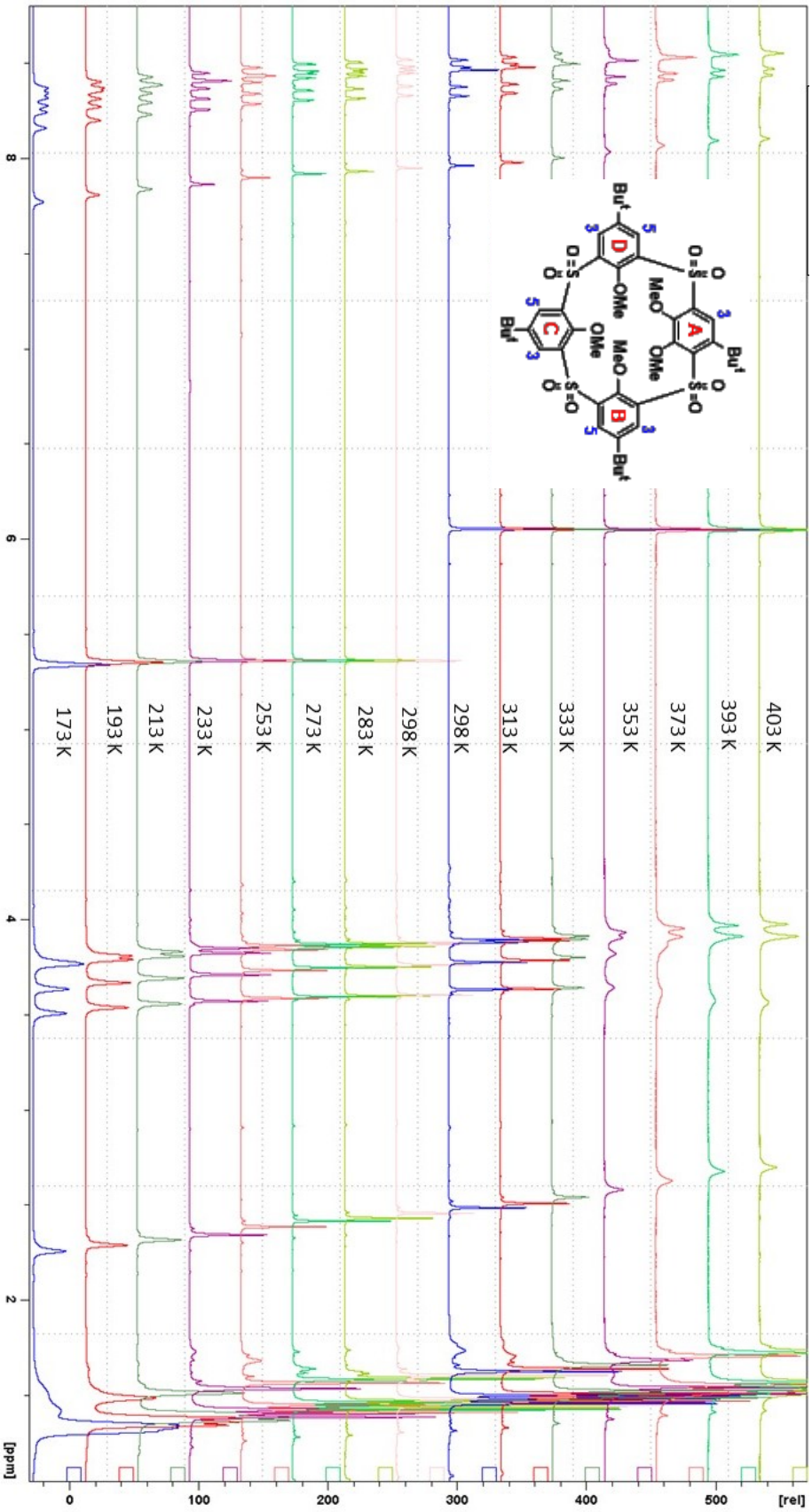


Figure S54: VT NMR spectra (600 MHz, above 298 K $C_2D_2Cl_4$, below 298 K CD_2Cl_2) of compound **7a**

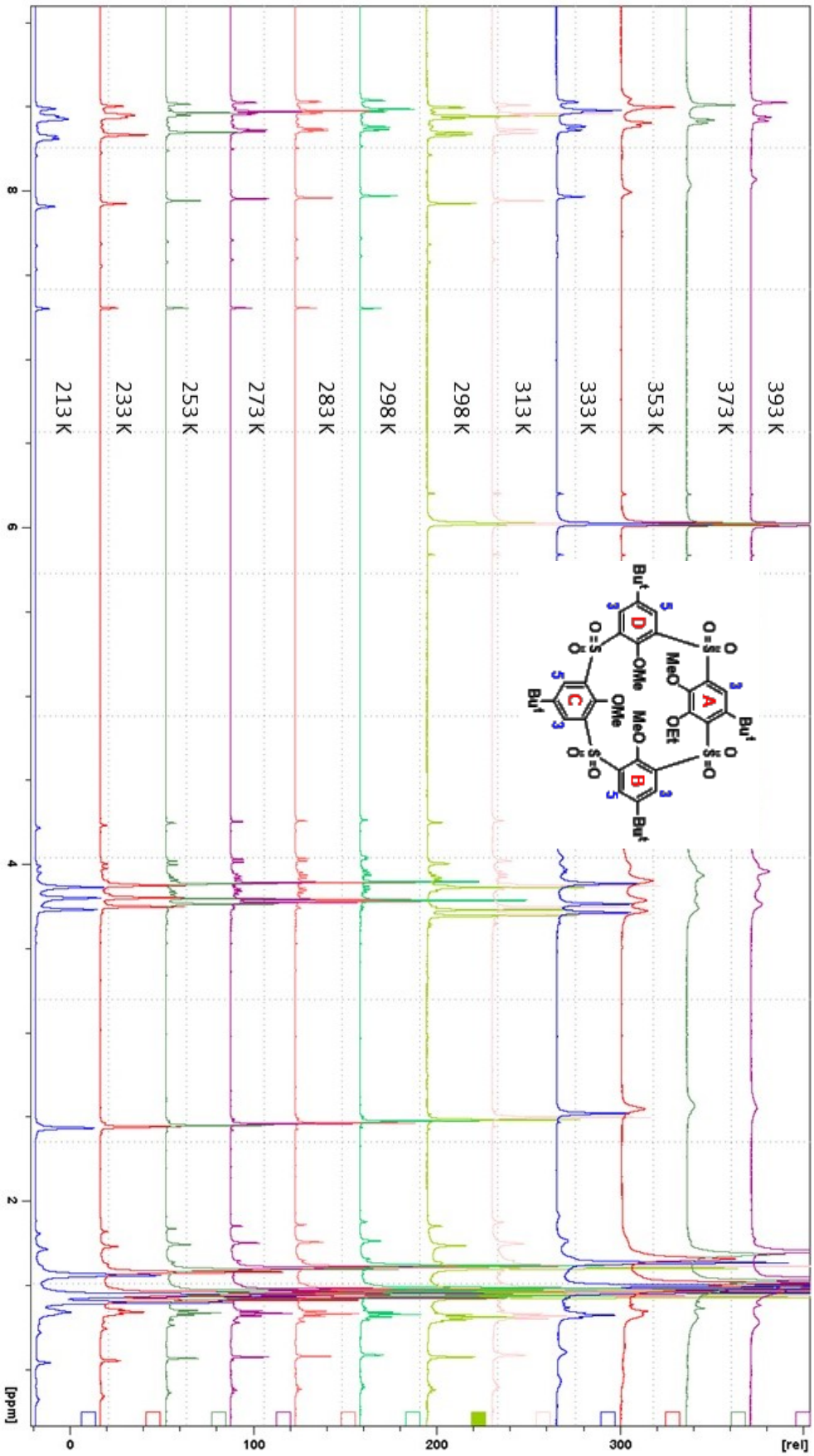


Figure S55: VT NMR spectra (600 MHz, above 298 K $C_2D_2Cl_4$, below 298 K $CDCl_3$) of compound **7b**

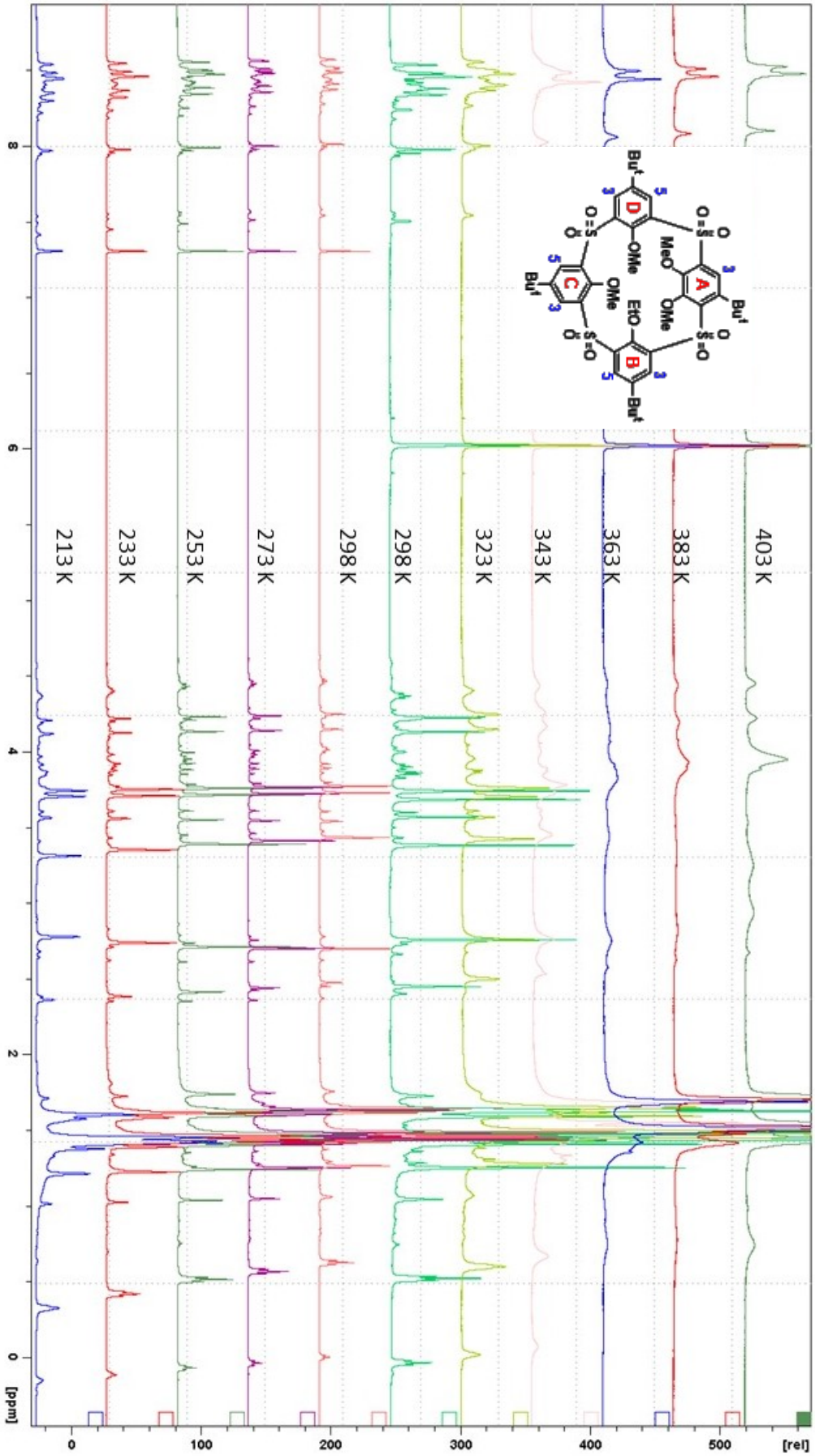


Figure S56: VT NMR spectra (600 MHz, above 298 K $C_2D_2Cl_4$, below 298 K $CDCl_3$) of compound **7c**

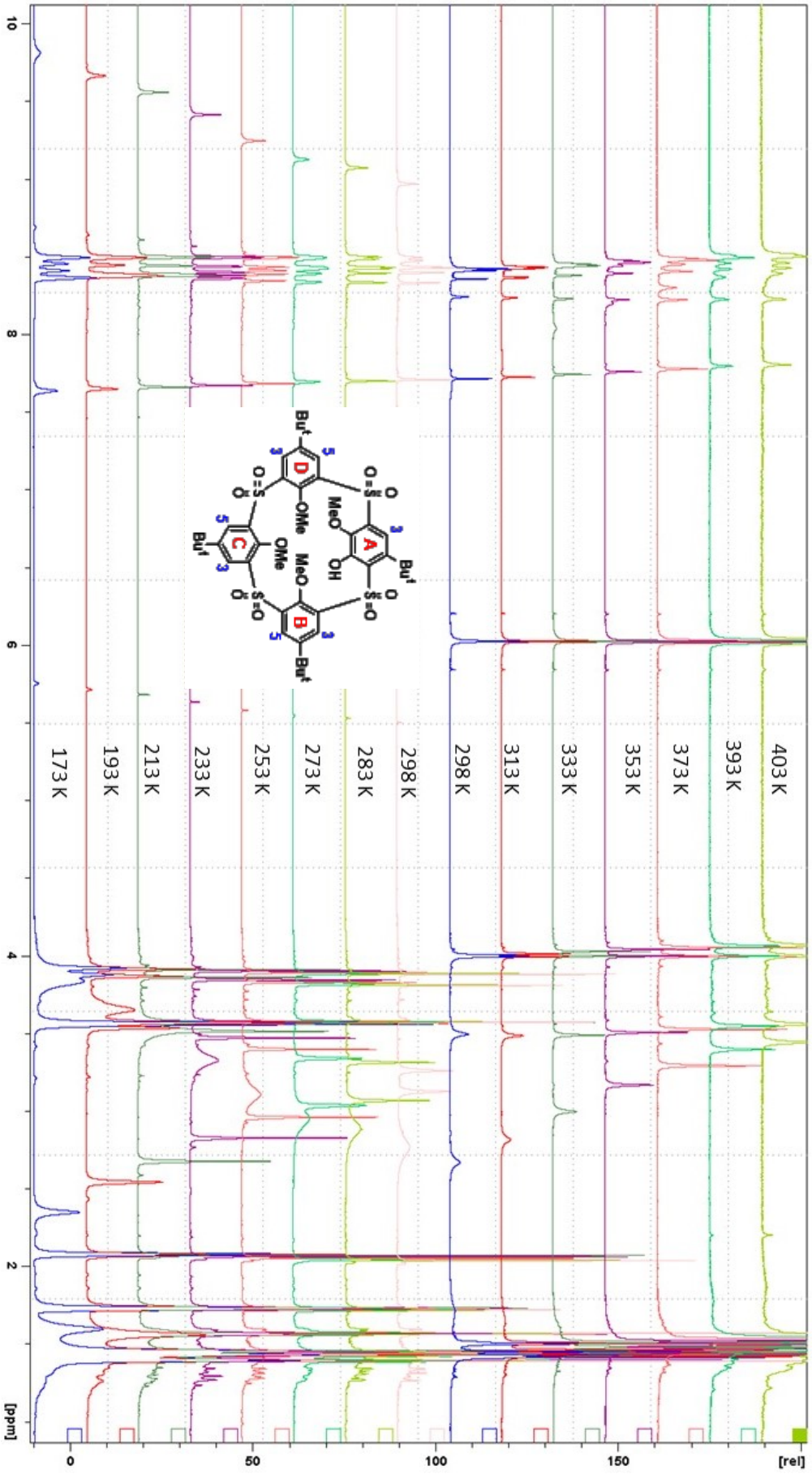


Figure S57: VT NMR spectra (600 MHz, above 298 K $C_2D_2Cl_4$, below 298 K THF-d_8) of compound **8a**

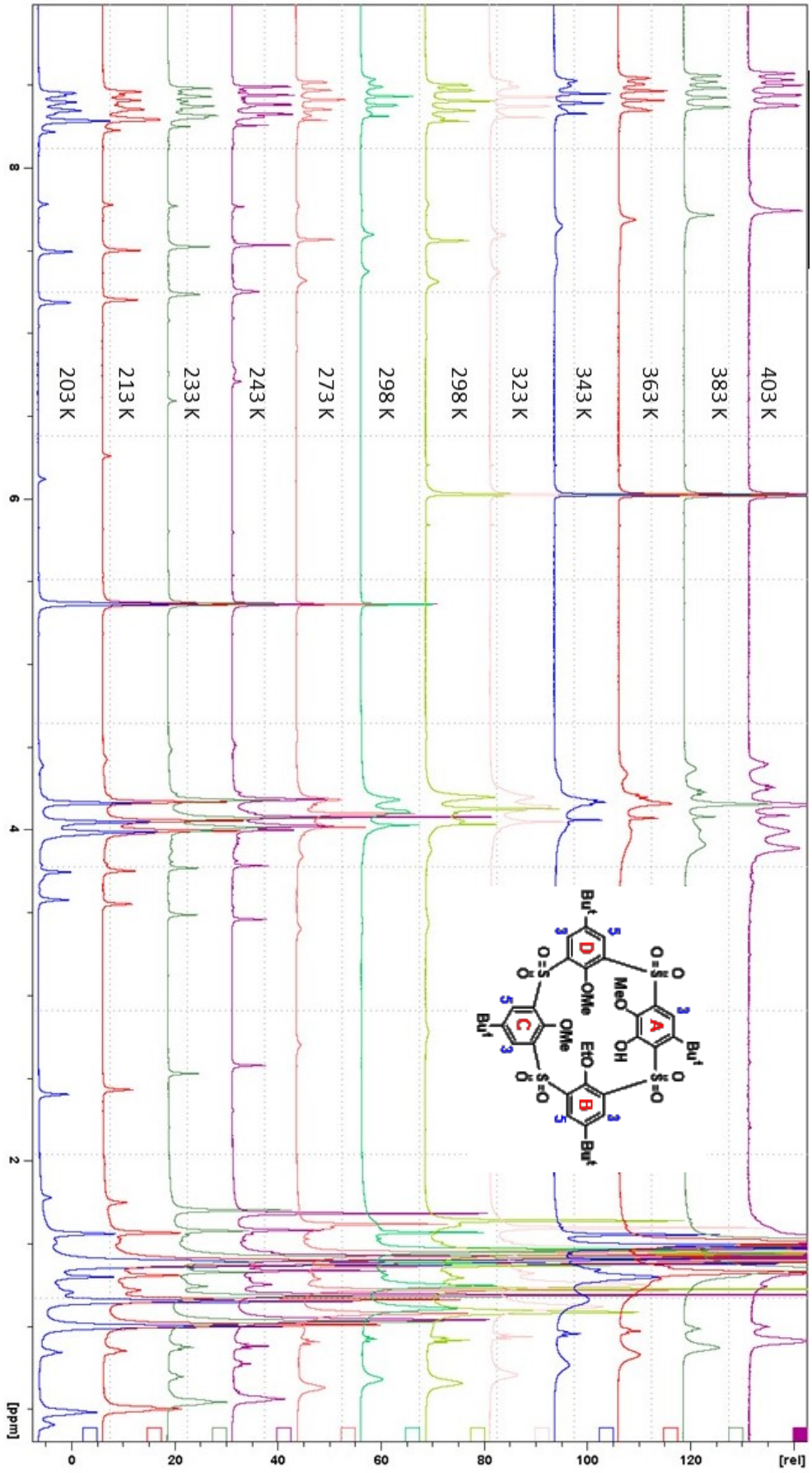


Figure S58: VT NMR spectra (600 MHz, above 298 K $C_2D_2Cl_4$, below 298 K CD_2Cl_2) of compound **8b**

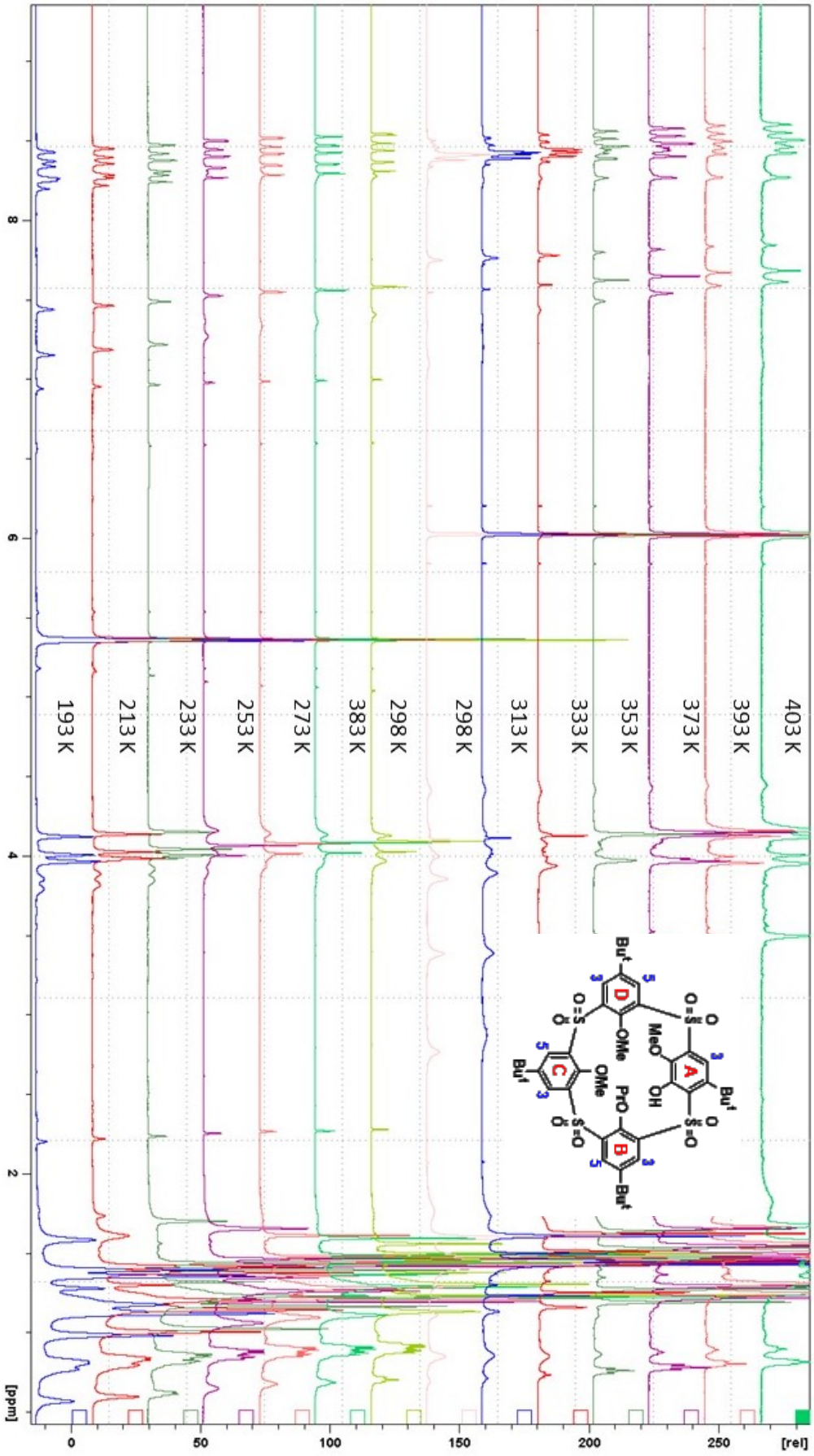


Figure S59: VT NMR spectra (600 MHz, above 298 K $C_2D_2Cl_4$, below 298 K CD_2Cl_2) of compound **8c**