Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

Three-Component Assembly of Stabilized Fluorescent Isoindoles

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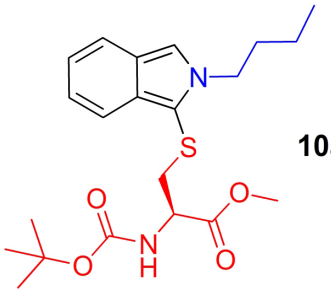
A. General Experimental Methods: Reagents were purchased from Fisher Scientific or Sigma-Aldrich unless stated otherwise. Deuterated NMR solvents were obtained from Cambridge Isotope Laboratories. Unless otherwise noted, all commercially available reagents were purchased and used without further purification. Acetonitrile (CH_3CN) was refluxed in the presence of CaH_2 and stored in the presence of molecular sieves.. All chemical reactions were conducted in glass flask or vials under N_2 atmosphere with magnetic stirring. The reaction progress was monitored by TLC analyses using anisaldehyde staining and UV light for visualization. ^1H and ^{13}C NMR spectra were recorded on Bruker Advance 400 or Bruker Advance 500 NMR spectrometers. Chemical shifts (ppm) were referenced using the corresponding solvent signals (δ_H 3.31 and δ_C 49.0 for CD_3OD, δ_H 2.05 and δ_C 29.8 for acetone-d_6). Coupling constants (J) are reported in Hertz (Hz) and coupling patterns are described by abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), p (quintet), m (multiplet). The NMR spectra were processed using Mestrenova (Mnova 14.2 Mestrelab Research). Electrospray (ESI) mass spectrometric analyses were performed using a ThermoFinnigan LCQ Deca spectrometer, and high-resolution analyses were conducted using a ThermoFinnigan MAT900XL mass spectrometer with electron impact (EI) ionization. A Thermo Scientific LTQ Orbitrap XL mass spectrometer was used for high-resolution electrospray ionization mass spectrometry analysis (HR-ESI-TOF MS positive ion mode).

B. General Procedure for Isoindole Preparation. A common procedure was used to prepare the isoindoles described in this manuscript. This began by dissolving the dialdehyde (1.0 eq) in anhydrous CH_3CN (1 mL) and cooling it to 0 °C in a foil-wrapped vial. Sequentially, thiol (1.0 eq) and amine (1.0 eq) were added. The reaction mixture was allowed to warm up to rt. The progress of each reaction was monitored by TLC analysis to determine the point in which the reaction was complete (typically 30 min). At this point, the solution was evaporated under a flow of nitrogen and the residue was purified by column chromatography (unless noted otherwise). Due to light sensitivity, especially **10a** and **12a**, care should be taken during all stages of the reaction and purification to prevent exposure to light and temperatures above rt.

C. Synthetic Methods and Characterization Data. Procedures and characterization data for **10a**, **12a**, **14a**, **16a**, **18a-d**, and **20a-f** have been provided. Copies of ^1H NMR and ^{13}C NMR spectra have also been provided at the end of this file.



10a

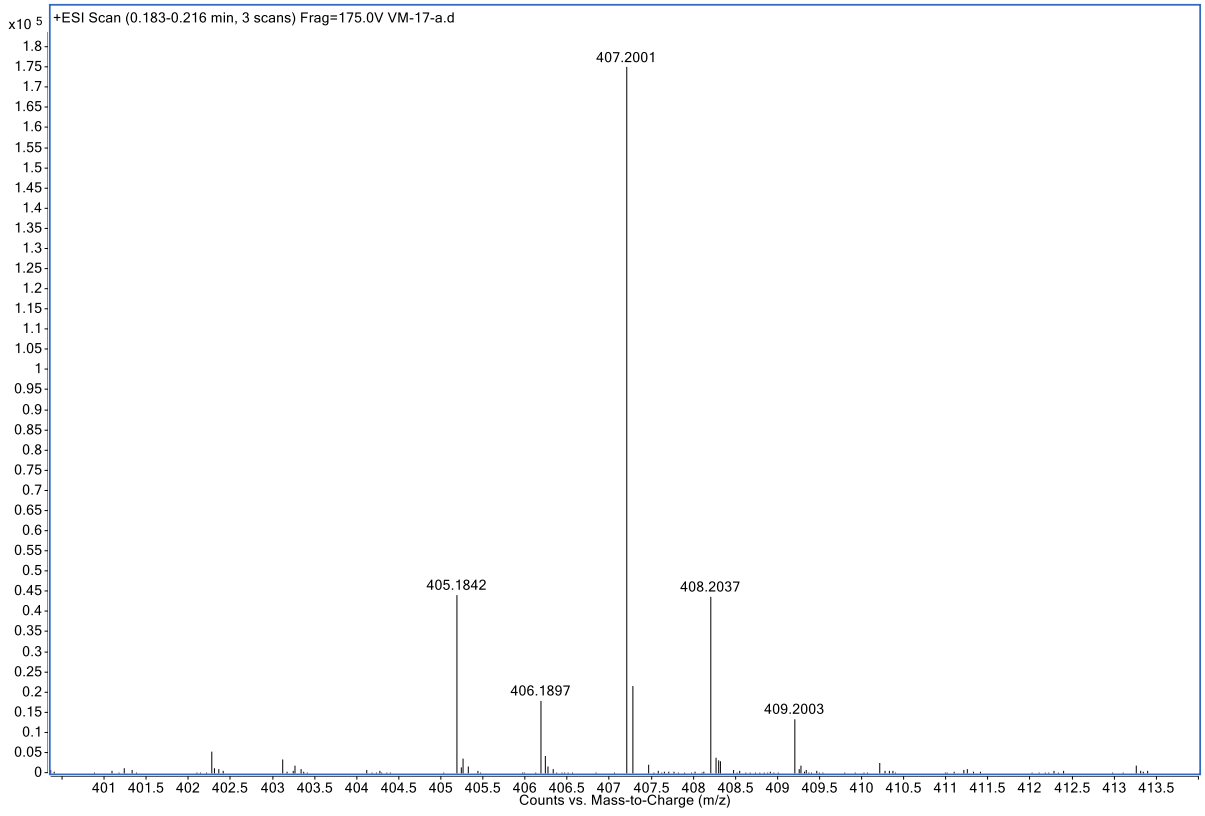
Methyl *N*-(*tert*-butoxycarbonyl)-*S*-(2-butyl-2*H*-isoindol-1-yl)-*L*-cysteinate (10a).

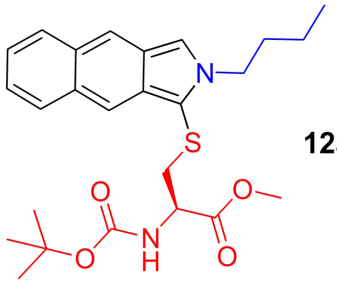
Compound **10a** was prepared from 50.0 mg (372.8 µmol) of phthalaldehyde (**7**) using the general procedure. Pure **10a** was obtained by recrystallized from acetonitrile at rt thrice to furnish a colorless solid (22.7 mg, 15% yield). Note that **10a** was not stable to chromatographic purification.

^{1}H NMR (500 MHz, CD_3OD) δ 7.59 (dd, *J* = 8.5, 1.0 Hz, 1H), 7.48 (d, *J* = 8.5 Hz, 1H), 7.44 (s, 1H), 6.97 (ddd, *J* = 8.5, 6.5, 1.0 Hz, 1H), 6.90 (ddd, *J* = 8.5, 6.5, 1.1 Hz, 1H), 4.49–4.37 (m, 2H), 4.06 (dd, *J* = 8.7, 4.4 Hz, 1H), 3.52 (s, 3H), 3.08 (dd, *J* = 13.6, 4.5 Hz, 1H), 2.87 (dd, *J* = 13.7, 8.6 Hz, 1H), 1.85 (p, *J* = 7.3 Hz, 2H), 1.43 (s, 9H), 1.37–1.30 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, CD_3OD) δ 173.0, 157.7, 131.6, 125.9, 124.0, 123.2, 122.0, 121.1, 119.9, 116.6, 80.8, 55.0, 52.7, 48.6, 39.8, 35.3, 28.7 (3C), 21.0, 14.1.

HRMS (ESI) calcd. for $C_{21}H_{31}N_2O_4S$ $[M+H]^+$: 407.1999; found: 407.2001.





12a

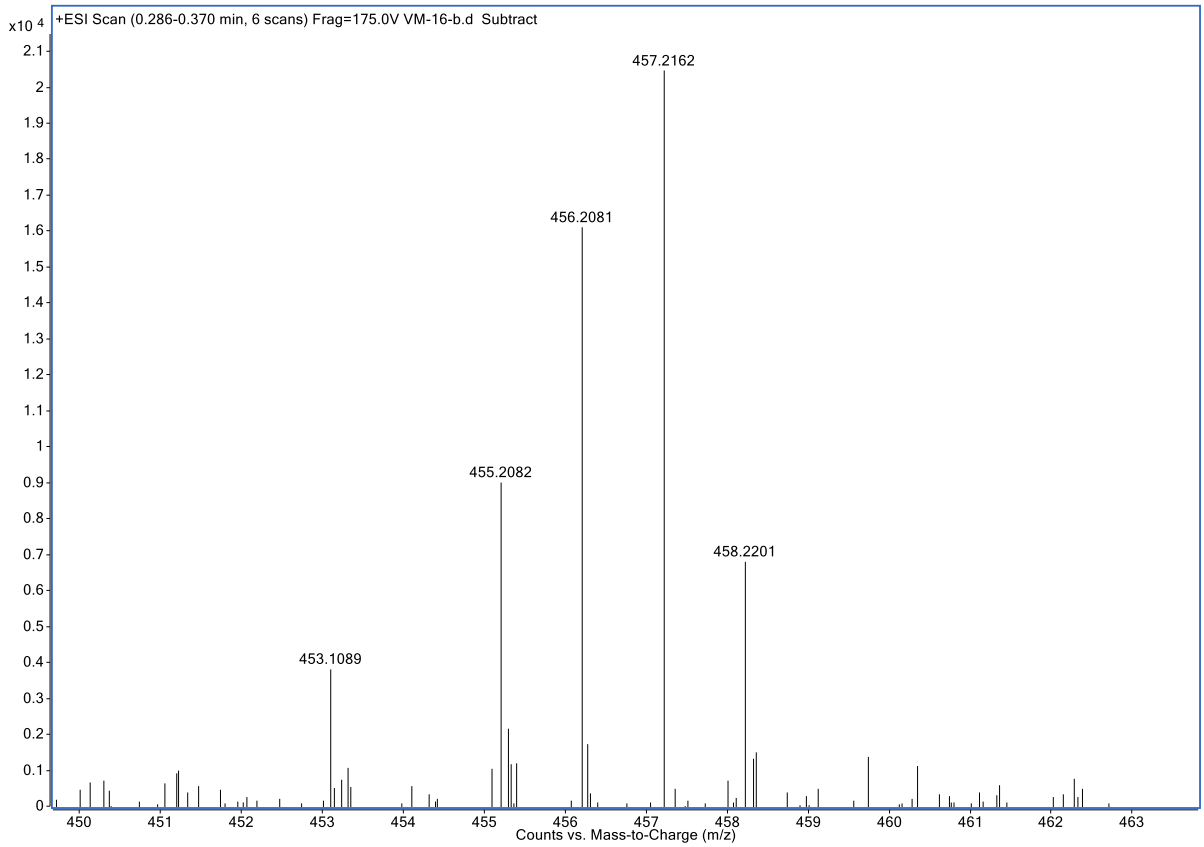
Methyl *N*-(*tert*-butoxycarbonyl)-*S*-(2-butyl-2*H*-benzo[*f*]isoindol-1-yl)-*L*-cysteinate (12a).

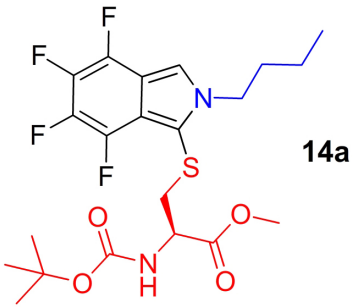
Compound **12a** was prepared from 20.0 mg (108.6 μmol) of naphthalene-2,3-dicarbaldehyde (**11**). Pure **12a** was obtained by recrystallized from acetonitrile at rt thrice to furnish a yellow solid (9.9 mg, 20% yield). Note that **12a** was not stable to chromatographic purification.

^{1}H NMR (500 MHz, CD_3OD) δ 8.17 (s, 1H), 8.11 (s, 1H), 7.77 (s, 1H), 7.77–7.68 (m, 2H), 7.13–7.04 (m, 2H), 4.67–4.53 (m, 2H), 4.10 (dd, *J* = 8.3, 4.3 Hz, 1H), 3.49 (s, 3H), 3.15 (dd, *J* = 13.6, 4.4 Hz, 1H), 2.95 (dd, *J* = 13.6, 8.6 Hz, 1H), 1.94 (p, *J* = 7.2 Hz, 2H), 1.40 (s, 9H), 1.40–1.34 (m, 2H), 0.99 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, CD_3OD) δ 173.0, 157.7, 131.8, 131.2, 129.7, 129.7, 126.4, 124.2, 123.7, 118.7 (2C), 116.8, 115.7, 105.9, 80.8, 55.1, 52.7, 49.5, 39.9, 35.4, 28.7 (3C), 21.0, 14.1.

HRMS (ESI) calcd. for $C_{25}H_{33}N_2O_4S$ $[M+H]^+$: 457.2156; found: 457.2162.





14a

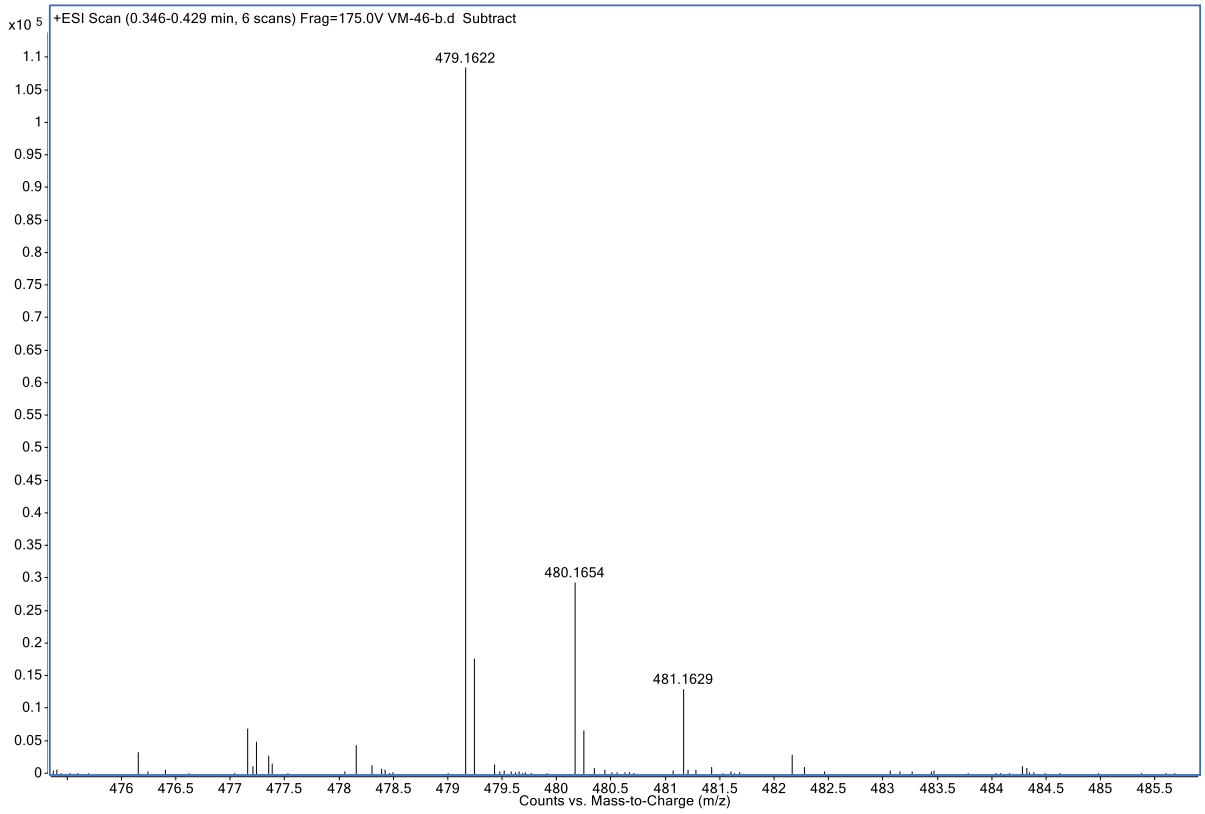
Methyl *N*-(*tert*-butoxycarbonyl)-*S*-(2-butyl-4,5,6,7-tetrafluoro-2*H*-isoindol-1-yl)-*L*-cysteinate (14a).

Compound **14a** was prepared from 10.0 mg (48.5 µmol) of dialdehyde **13**. Pure **14a** was isolated by silica gel chromatography (5/1 hexanes/acetone, R_f = 0.35), as a dark orange glass (12.1 mg, 52% yield).

^{1}H NMR (400 MHz, CD_3OD) δ 7.70 (s, 1H), 4.52–4.34 (m, 2H), 4.08 (dd, *J* = 8.4, 4.5 Hz, 1H), 3.56 (s, 3H), 3.20 (dd, *J* = 13.9, 4.4 Hz, 1H), 3.01 (dd, *J* = 13.7, 8.4 Hz, 1H), 1.85 (p, *J* = 7.4 Hz, 2H), 1.41 (s, 9H), 1.39–1.27 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, CD_3OD) δ 172.6, 157.6, 141.98–141.23 (m), 139.45–138.41 (m), 136.95–135.66 (m), 134.61–134.18 (m), 117.15–116.83 (m), 115.22 (d, *J* = 9.6 Hz), 113.06–112.75 (m), 110.97–110.73 (m), 80.9, 54.8, 52.9, 49.4, 40.2, 35.0, 28.6 (3C), 20.9, 14.0.

HRMS (ESI) calcd. for $C_{21}H_{27}F_4N_2O_4S$ $[M+H]^+$: 479.1622; found: 479.1622.



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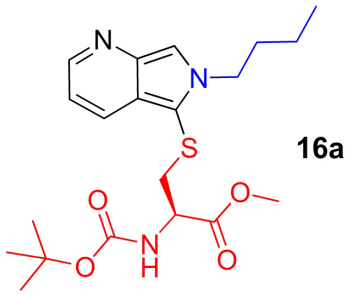


16a

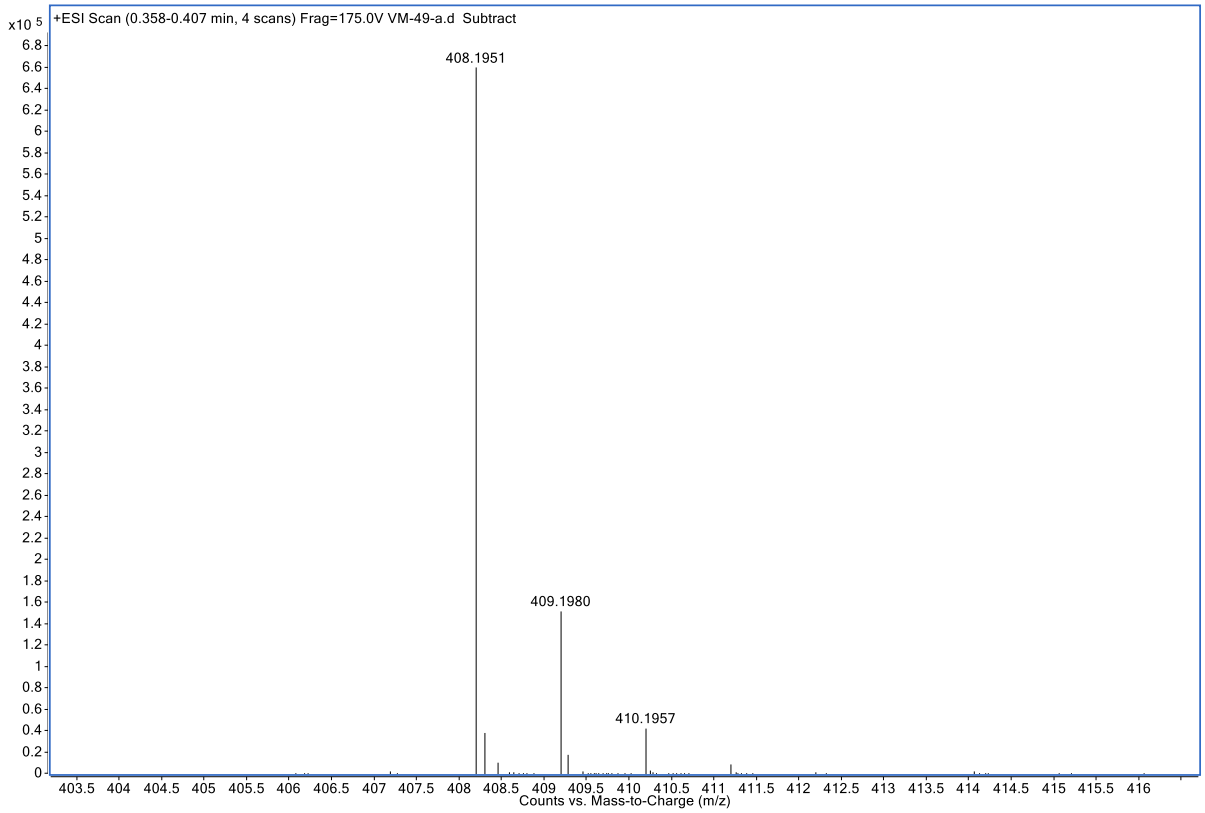
Methyl *N*-(*tert*-butoxycarbonyl)-*S*-(6-butyl-6*H*-pyrrolo[3,4-*b*]pyridin-5-yl)-*L*-cysteinate (16a).

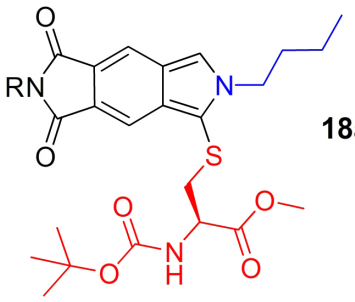
Compound **16a** was prepared from 10.0 mg (74.0 μmol) of dialdehyde **15**. Pure **16a** was isolated by silica gel chromatography (2/1 hexanes/EtOAc, R_f = 0.25), as a brown oil (18.7 mg, 62% yield).

^{1}H NMR (500 MHz, CD_3OD) δ 8.34 (dd, *J* = 4.2, 1.6 Hz, 1H), 7.96 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.48 (s, 1H), 6.90 (dd, *J* = 8.4, 4.3 Hz, 1H), 4.47–4.31 (m, 2H), 4.11 (dd, *J* = 7.0, 4.4 Hz, 1H), 3.65 (s, 3H), 3.14–3.07 (m, 1H), 2.97 (dd, *J* = 13.8, 4.5 Hz, 1H), 1.79 (p, *J* = 7.4 Hz, 2H), 1.35 (s, 9H), 1.32–1.23 (m, 2H), 0.88 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, CD_3OD) δ 173.0, 172.6, 157.8, 148.9, 131.6, 119.2, 117.8, 116.0, 109.6, 80.7, 54.6, 52.9, 52.6, 39.8, 35.1, 28.7 (3C), 20.9, 14.0.

HRMS (ESI) calcd. for $C_{20}H_{30}N_3O_4S$ $[M+H]^+$: 408.1952; found: 408.1951.





18a R = *n*-Bu

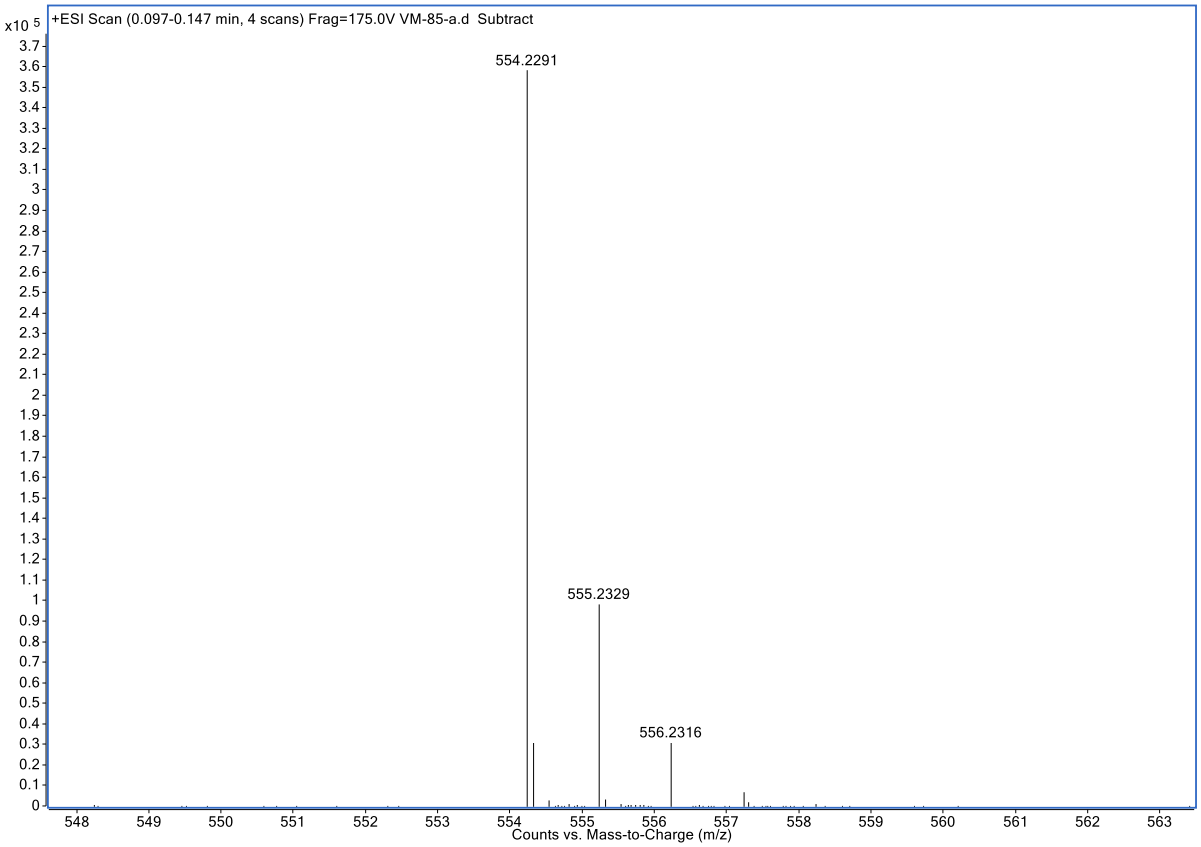
Methyl *N*-(*tert*-butoxycarbonyl)-*S*-(2,6-dibutyl-5,7-dioxo-2,5,6,7-tetrahydropyrrolo[3,4-*f*]isoindol-1-yl)-*L*-cysteinate (18a).

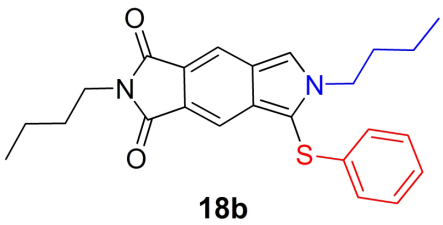
Compound **18a** was prepared from 10.0 mg (38.6 µmol) of dialdehyde **17**. Pure **18a** was isolated by silica gel chromatography (3/1 hexanes/EtOAc, R_f = 0.36), as a yellow oil (13.3 mg, 65% yield).

^{1}H NMR (500 MHz, acetone-d_6) δ 8.14 (s, 1H), 8.08 (s, 1H), 7.97 (s, 1H), 6.46 (d, *J* = 8.1 Hz, 1H), 4.67–4.46 (m, 2H), 4.29–4.14 (m, 1H), 3.65 (t, *J* = 7.2 Hz, 2H), 3.57 (s, 3H), 3.29 (dd, *J* = 13.6, 4.6 Hz, 1H), 3.15 (dd, *J* = 13.5, 8.5 Hz, 1H), 1.94 (p, *J* = 7.4 Hz, 2H), 1.71–1.56 (m, 2H), 1.44–1.32 (m, 4H), 1.39 (s, 9H), 0.97 (t, *J* = 7.4 Hz, 3H), 0.93 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, acetone-d_6) δ 170.9, 167.9, 167.9, 155.2, 130.4, 124.8, 124.7, 123.9, 120.7, 118.0, 116.9, 114.7, 78.8, 53.8, 51.6, 48.2, 38.9, 37.1, 33.7, 30.5, 27.6 (3C), 19.8, 19.7, 13.1, 13.0.

HRMS (ESI) calcd. for $C_{27}H_{37}N_3O_6SNa$ $[M+Na]^+$: 554.2295; found: 554.2291.





18b

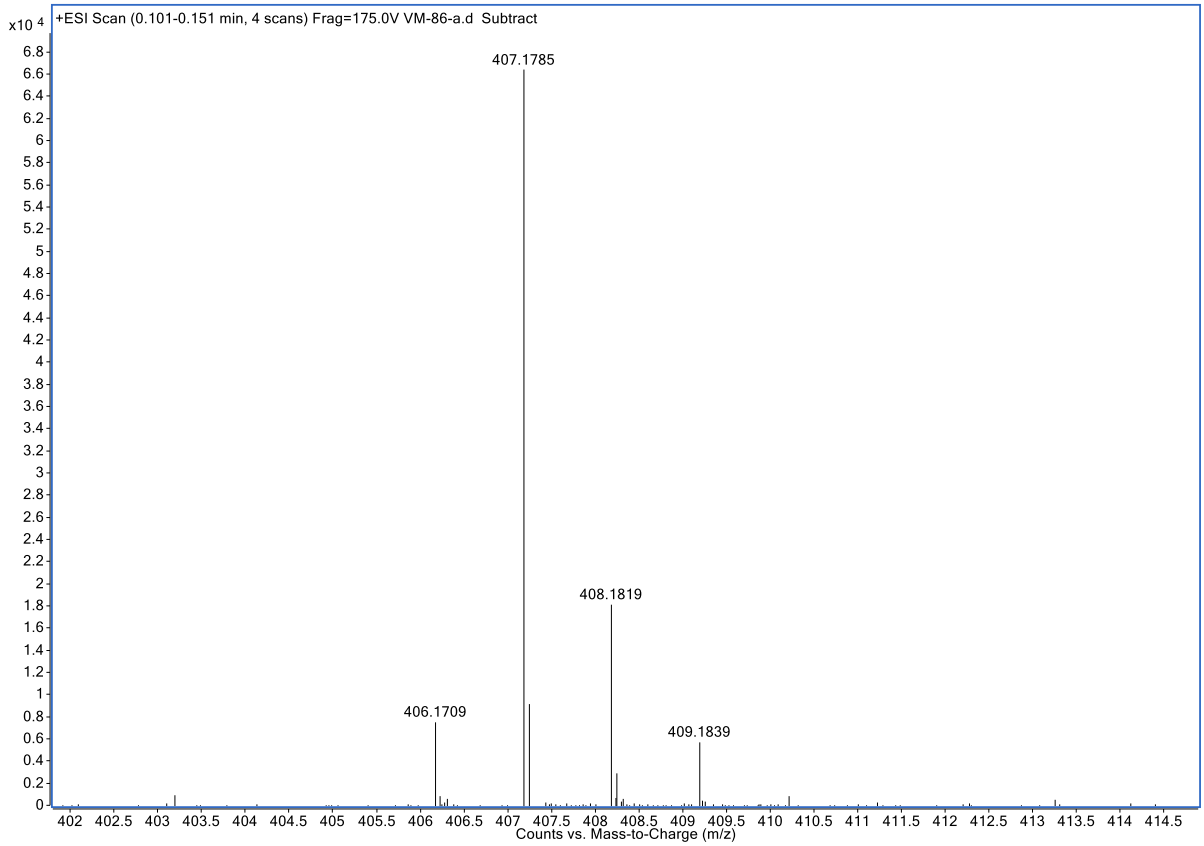
2,6-Dibutyl-5-(phenylthio)pyrrolo[3,4-*f*]isoindole-1,3(2*H*,6*H*)-dione (18b).

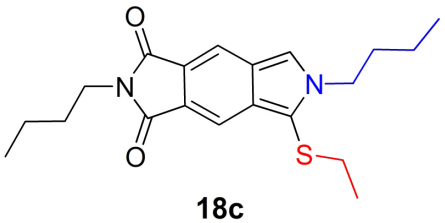
Compound **18b** was prepared from 10,0 mg (38.6 µmol) of dialdehyde **17**. Pure **18b** was isolated by silica gel chromatography (4/1 hexanes/EtOAc, R_f = 0.30), as a brown oil (7.5 mg, 48% yield).

^{1}H NMR (500 MHz, acetone-d_6) δ 8.16 (s, 1H), 8.09 (s, 1H), 8.03 (s, 1H), 7.29–7.22 (m, 2H), 7.20–7.13 (m, 1H), 7.03–6.98 (m, 2H), 4.48 (t, *J* = 7.4 Hz, 2H), 3.65 (t, *J* = 7.1 Hz, 2H), 1.85–1.76 (m, 2H), 1.71–1.60 (m, 2H), 1.41–1.29 (m, 4H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.85 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, acetone-d_6) δ 168.7, 168.7, 138.6, 132.2, 130.2 (2C), 127.1 (3C), 126.4, 125.8, 125.1, 122.6, 119.2, 116.9, 113.1, 49.4, 38.1, 34.2, 31.3, 20.7, 20.4, 13.9, 13.8.

HRMS (ESI) calcd. for $C_{24}H_{27}N_2O_2S$ $[M+H]^+$: 407.1788; found: 407.1785.





18c

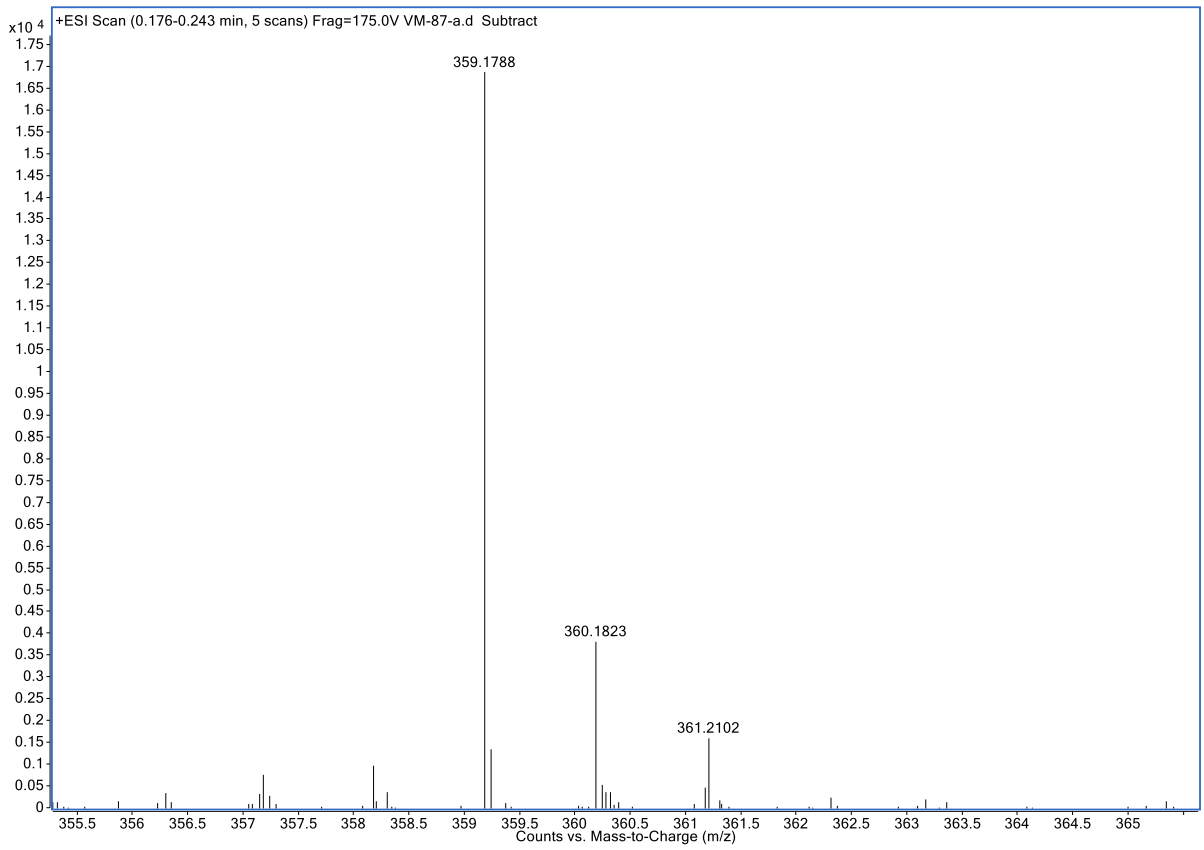
2,6-Dibutyl-5-(ethylthio)pyrrolo[3,4-*f*]isoindole-1,3(2*H*,6*H*)-dione (18c).

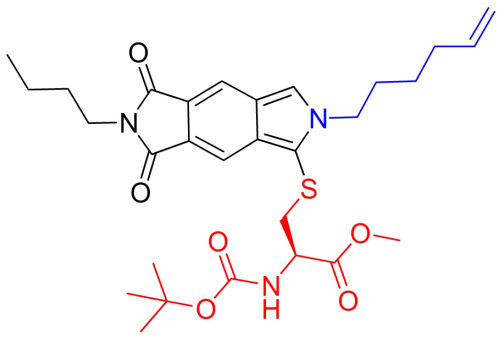
Compound **18c** was prepared from 10.0 mg (38.6 μmol) of dialdehyde **17**. Pure **18c** was isolated by silica gel chromatography (4/1 hexanes/EtOAc, R_f = 0.32), as a yellow oil (9.1 mg, 66% yield).

^{1}H NMR (500 MHz, acetone-d_6) δ 8.09 (s, 1H), 8.07 (s, 1H), 7.95 (s, 1H), 4.56 (t, *J* = 7.4 Hz, 2H), 3.65 (t, *J* = 7.1 Hz, 2H), 2.79–2.75 (m, 2H), 1.98–1.86 (m, 2H), 1.65 (p, *J* = 7.6 Hz, 2H), 1.46–1.30 (m, 4H), 1.16 (t, *J* = 7.3 Hz, 3H), 0.97 (t, *J* = 7.4 Hz, 3H), 0.94 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, acetone-d_6) δ 168.8, 168.8, 131.4, 125.5, 125.4, 124.7, 121.1, 118.9, 117.7, 116.9, 49.0, 38.0, 34.5, 32.6, 31.4, 20.7, 20.5, 15.4, 14.0, 13.9.

HRMS (ESI) calcd. for $C_{20}H_{27}N_2O_2S$ $[M+H]^+$: 359.1788; found: 359.1788.





18d

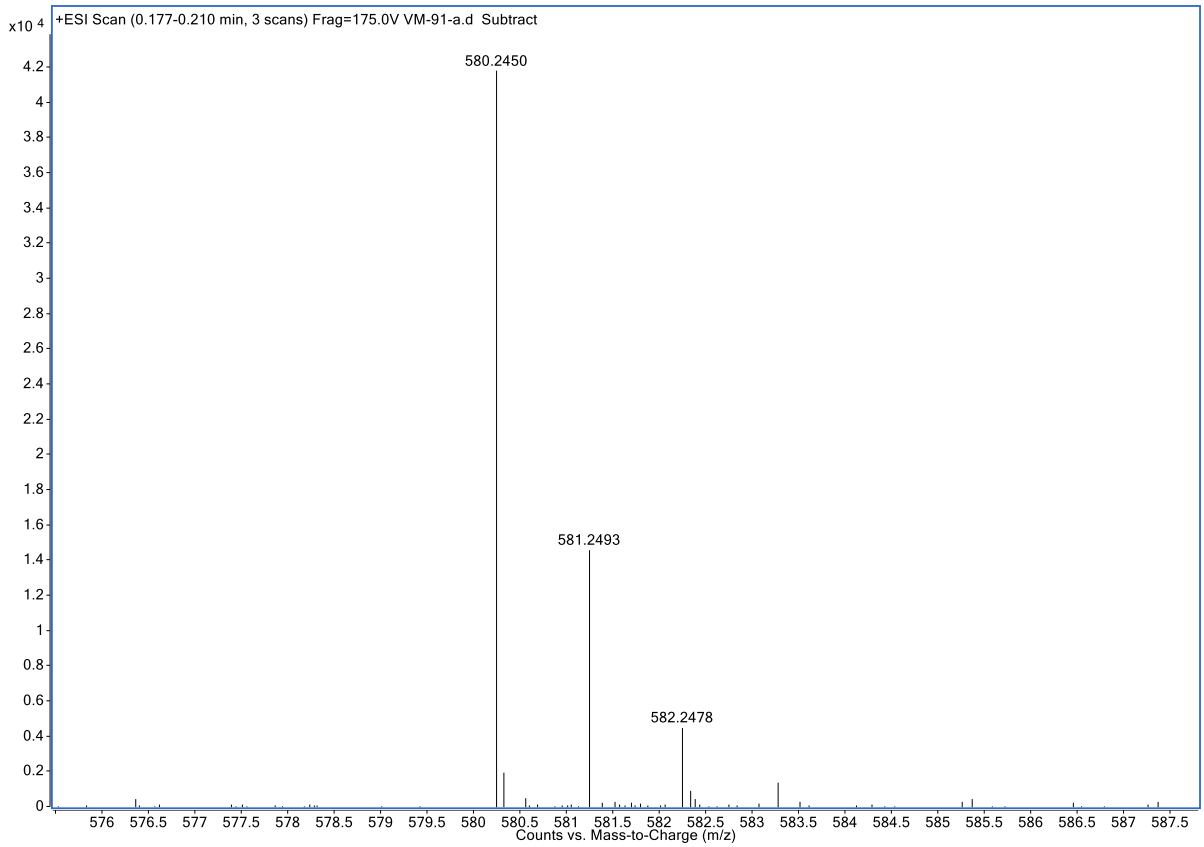
Methyl *N*-(*tert*-butoxycarbonyl)-*S*-(6-butyl-2-(hex-5-en-1-yl)-5,7-dioxo-2,5,6,7-tetrahydropyrrolo[3,4-*f*]isoindol-1-yl)-*L*-cysteinate (18d).

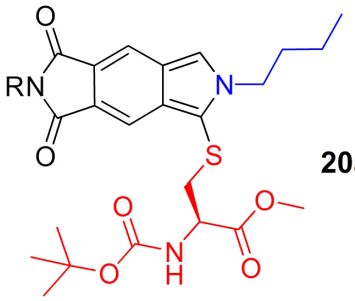
Compound **18d** was prepared from 10.0 mg (38.6 µmol) of dialdehyde **17**. Pure **18d** was isolated by silica gel chromatography (4/1 hexanes/EtOAc, R_f = 0.32), as a brown oil (11.8 mg, 55% yield).

^{1}H NMR (400 MHz, acetone-d_6) δ 8.15 (s, 1H), 8.08 (s, 1H), 7.97 (s, 1H), 6.47 (br. d, *J* = 8.3 Hz, 1H), 5.90–5.71 (m, 1H), 4.98 (m, 2H), 4.58 (dt, *J* = 13.2, 6.9 Hz, 2H), 4.30–4.15 (m, 1H), 3.65 (t, *J* = 7.1 Hz, 2H), 3.57 (s, 3H), 3.35–3.22 (m, 1H), 3.22–3.10 (m, 1H), 2.18–2.10 (m, 2H), 2.00–1.93 (m, 2H), 1.71–1.60 (m, 2H), 1.51–1.44 (m, 2H), 1.39 (s, 9H), 1.44–1.32 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, acetone-d_6) δ 171.8, 168.8 (2C), 156.2, 139.1, 131.3, 125.7, 125.6, 124.9, 121.6, 118.9, 117.8, 115.6, 115.4, 79.7, 54.7, 52.5, 49.2, 39.8, 38.0, 33.9, 31.9, 31.4, 28.5 (3C), 26.6, 20.7, 14.0.

HRMS (ESI) calcd. for $C_{29}H_{39}N_3O_6SNa$ $[M+Na]^+$: 580.2452; found: 580.2450.





20a R = octyl

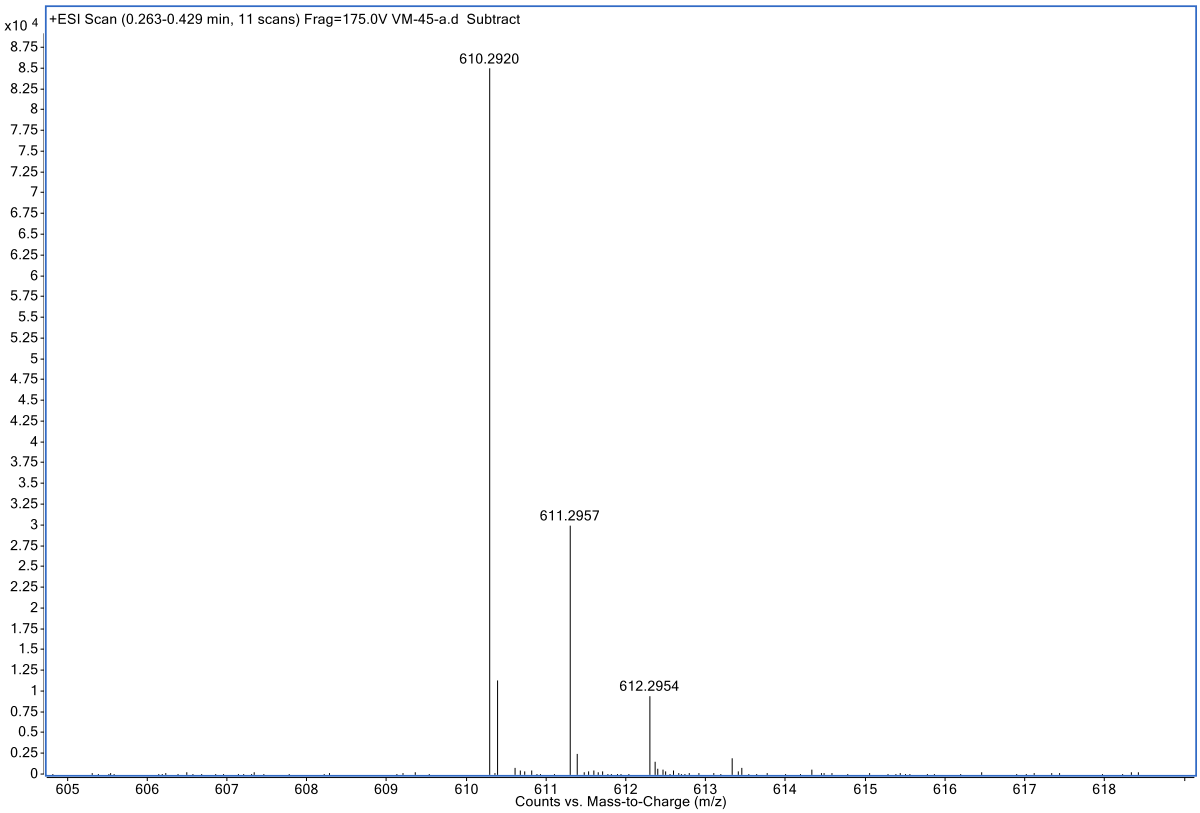
Methyl *N*-(*tert*-butoxycarbonyl)-*S*-(2-butyl-6-octyl-5,7-dioxo-2,5,6,7-tetrahydropyrrolo[3,4-*f*]isoindol-1-yl)-*L*-cysteinate (20a).

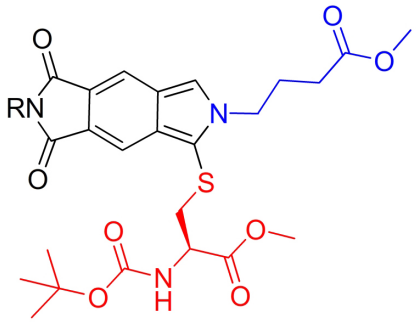
Compound **20a** was prepared from 10.0 mg (31.7 µmol) of dialdehyde **19**. Pure **20a** was isolated by silica gel chromatography (2/1 hexanes/EtOAc, R_f = 0.33), as a dark yellow oil (12.7 mg, 68% yield).

^{1}H NMR (500 MHz, CD_3OD) δ 8.15 (s, 1H), 8.07 (s, 1H), 7.87 (s, 1H), 7.10 (d, *J* = 7.9 Hz, 1H), 4.54–4.45 (m, 2H), 4.08–4.03 (m, 1H), 3.67 (t, *J* = 7.2 Hz, 2H), 3.59 (s, 3H), 3.20 (td, *J* = 13.4, 4.5 Hz, 1H), 3.00 (dd, *J* = 13.6, 8.7 Hz, 1H), 1.91 (p, *J* = 7.4 Hz, 2H), 1.74–1.63 (m, 2H), 1.39 (s, 9H), 1.37–1.27 (m, 12H), 0.99 (t, *J* = 7.4 Hz, 3H), 0.89 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, CD_3OD) δ 171.3, 168.9, 168.8, 156.3, 130.5, 124.8, 124.1, 123.3, 120.8, 118.4, 117.3, 114.8, 79.5, 53.6, 51.5, 51.5, 38.1, 37.4, 33.5, 31.5, 28.9, 28.8, 28.1, 27.3 (3C), 26.5, 22.3, 19.5, 13.0, 12.6.

HRMS (ESI) calcd. for $C_{31}H_{45}N_3O_6SNa$ $[M+Na]^+$: 610.2921; found: 610.2920.





20b R = octyl

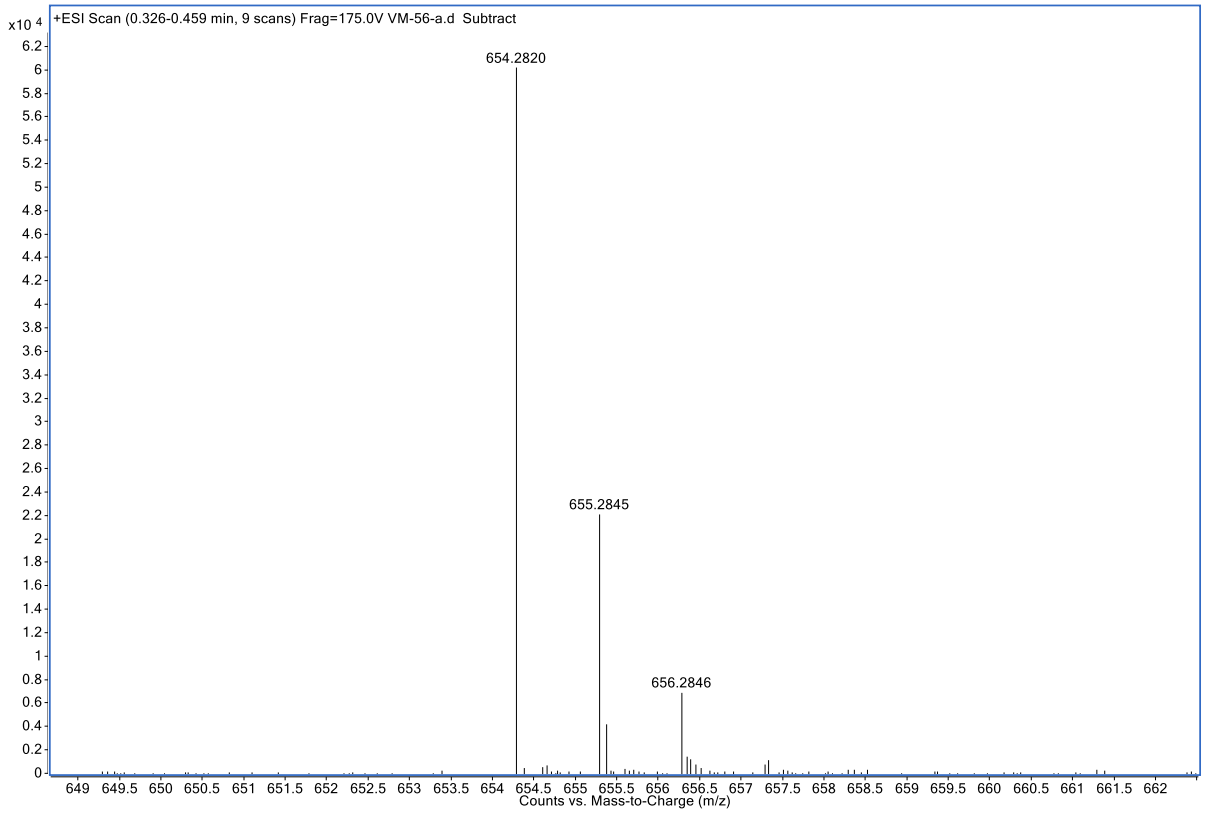
Methyl (*R*)-4-(1-((2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl)thio)-6-octyl-5,7-dioxo-6,7-dihydropyrrolo[3,4-*f*]isoindol-2(5*H*)-yl)butanoate (20b).

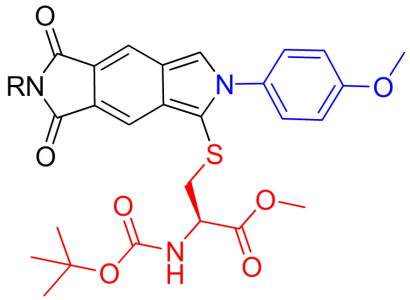
Compound **20b** was prepared from 10.0 mg (31.7 µmol) of dialdehyde **19**. Pure **20b** was isolated by silica gel chromatography (1/1 hexanes/EtOAc, R_f = 0.38), as a dark yellow oil (12.4 mg, 62% yield).

^{1}H NMR (400 MHz, CD_3OD) δ 8.16 (s, 1H), 8.08 (s, 1H), 7.88 (s, 1H), 4.65–4.45 (m, 2H), 4.06 (dd, *J* = 8.4, 4.4 Hz, 1H), 3.67 (t, *J* = 7.2 Hz, 2H), 3.64 (s, 3H), 3.59 (s, 3H), 3.23 (dd, *J* = 13.7, 4.5 Hz, 1H), 3.01 (dd, *J* = 13.7, 8.6 Hz, 1H), 2.40 (t, *J* = 7.1 Hz, 2H), 2.23 (p, *J* = 7.1 Hz, 2H), 1.76–1.61 (m, 2H), 1.39 (s, 9H), 1.42–1.21 (m, 10H), 0.89 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, CD_3OD) δ 174.7, 172.7, 170.3, 170.2, 157.7, 132.0, 126.2, 125.6, 124.8, 122.3, 119.8, 118.8, 116.4, 80.9, 55.0, 52.9, 52.2, 49.4, 39.4, 38.8, 32.9, 31.5, 30.3, 30.2, 29.5, 28.6 (3C), 28.0, 27.9, 23.7, 14.4.

HRMS (ESI) calcd. for $C_{32}H_{45}N_3O_8SNa$ $[M+Na]^+$: 654.2820; found: 654.2820.





20c R = octyl

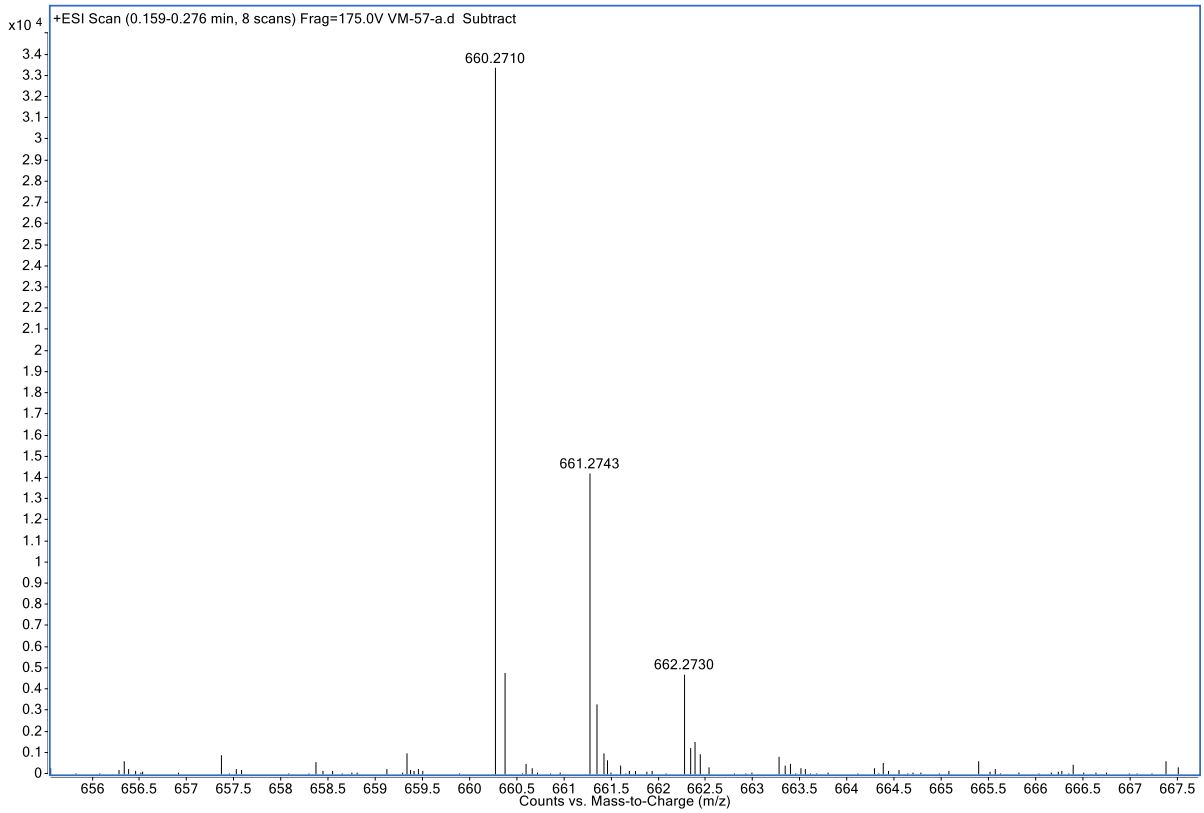
Methyl *N*-(*tert*-butoxycarbonyl)-*S*-(2-(4-methoxyphenyl)-6-octyl-5,7-dioxo-2,5,6,7-tetrahydropyrrolo[3,4-*f*]isoindol-1-yl)-*L*-cysteinate (20c).

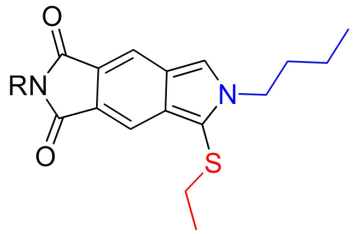
Compound **20c** was prepared from 10.0 mg (31.7 μmol) of dialdehyde **19**. Pure **20c** was isolated by silica gel chromatography (2/1 hexanes/EtOAc, R_f = 0.18), as a colorless glass (11.3 mg, 56% yield).

^{1}H NMR (500 MHz, CD_3OD) δ 8.17 (s, 1H), 8.12 (s, 1H), 7.90 (s, 1H), 7.49 (d, *J* = 8.9 Hz, 2H), 7.13 (d, *J* = 8.8 Hz, 2H), 6.76 (br. d, *J* = 7.8 Hz, 1H), 3.91 (s, 3H), 3.90–3.85 (m, 1H), 3.68 (t, *J* = 7.1 Hz, 2H), 3.48 (s, 3H), 2.81 (dd, *J* = 13.7, 4.9 Hz, 1H), 2.72 (dd, *J* = 13.7, 7.8 Hz, 1H), 1.73–1.65 (m, 2H), 1.35 (s, 9H), 1.33–1.28 (m, 10H), 0.89 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, CD_3OD) δ 172.5, 170.1, 170.0, 161.8, 157.4, 132.8, 132.4, 129.3 (2C), 126.0, 125.9, 125.2, 124.1, 120.0, 119.2, 117.5, 115.4 (2C), 80.8, 56.2, 54.6, 52.8, 38.9, 38.5, 32.9, 30.3, 30.3, 29.5, 28.6 (3C), 28.0, 23.7, 14.4.

HRMS (ESI) calcd. for $C_{34}H_{43}N_3O_7SNa$ $[M+Na]^+$: 660.2714; found: 660.2710.





20d, R = octyl

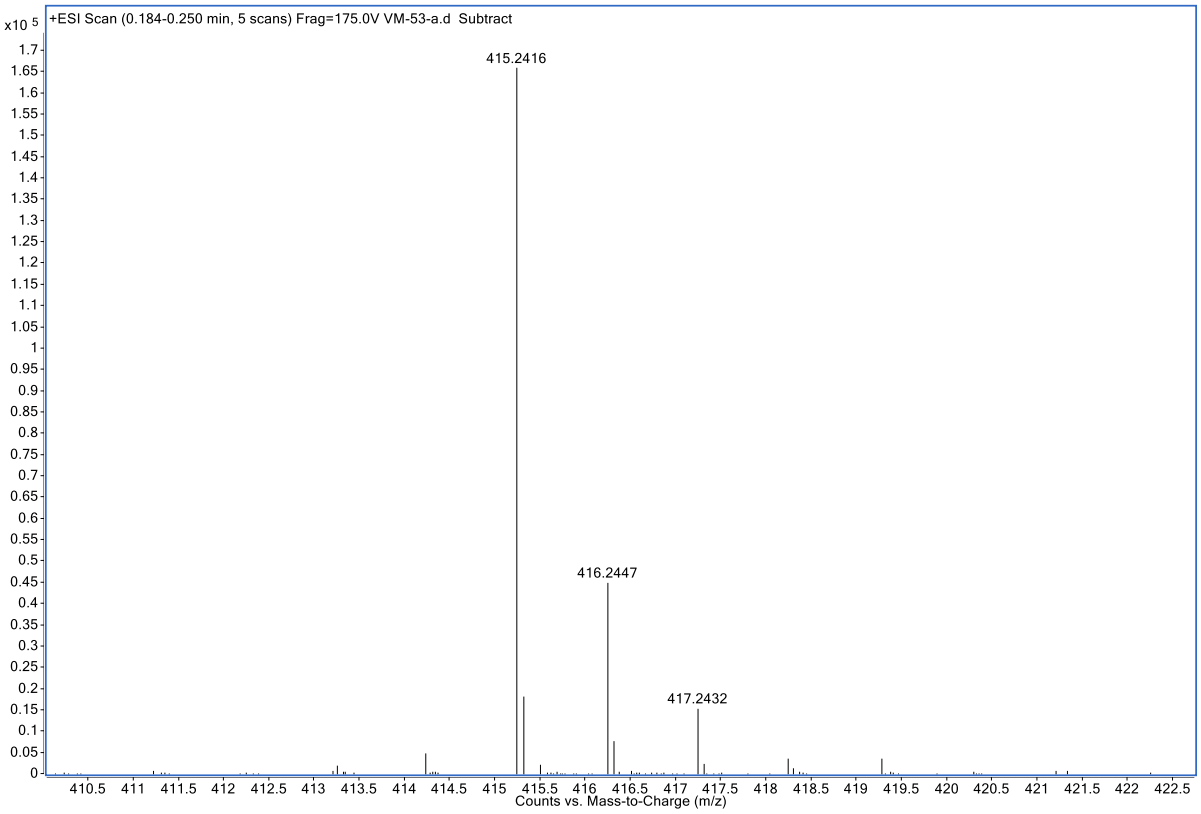
6-Butyl-5-(ethylthio)-2-octylpyrrolo[3,4-*f*]isoindole-1,3(2*H*,6*H*)-dione (20d).

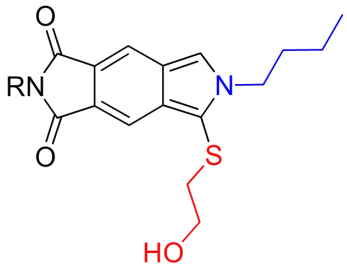
Compound **20d** was prepared from 10.0 mg (31.7 µmol) of dialdehyde **19** and an excess of ethanethiol (4.6 µL, 3.9 mg, 63.4 µmol, 2.0 eq, due to its volatility). Pure **20d** was isolated by silica gel chromatography (3/1 hexanes/EtOAc, R_f = 0.35), as a yellow oil (5.4 mg, 41% yield).

^{1}H NMR (500 MHz, CD_3OD) δ 8.13 (s, 1H), 8.07 (d, *J* = 1.0 Hz, 1H), 7.84 (s, 1H), 4.50 (t, *J* = 7.4 Hz, 2H), 3.66 (t, *J* = 7.2 Hz, 2H), 2.74 (q, *J* = 7.4 Hz, 2H), 1.91 (p, *J* = 7.5 Hz, 2H), 1.67 (p, *J* = 7.0 Hz, 2H), 1.42–1.27 (m, 12H), 1.16 (t, *J* = 7.4 Hz, 3H), 0.99 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, CD_3OD) δ 170.4, 170.4, 131.9, 126.0, 125.1, 124.5, 121.5, 119.8, 118.8, 118.1, 49.5, 38.8, 34.9, 32.9, 32.9, 30.3, 30.2, 29.5, 27.9, 23.7, 20.9, 15.4, 14.4, 14.0.

HRMS (ESI) calcd. for $C_{24}H_{35}N_2O_2S$ $[M+H]^+$: 415.2414; found: 415.2416.





20e, R = octyl

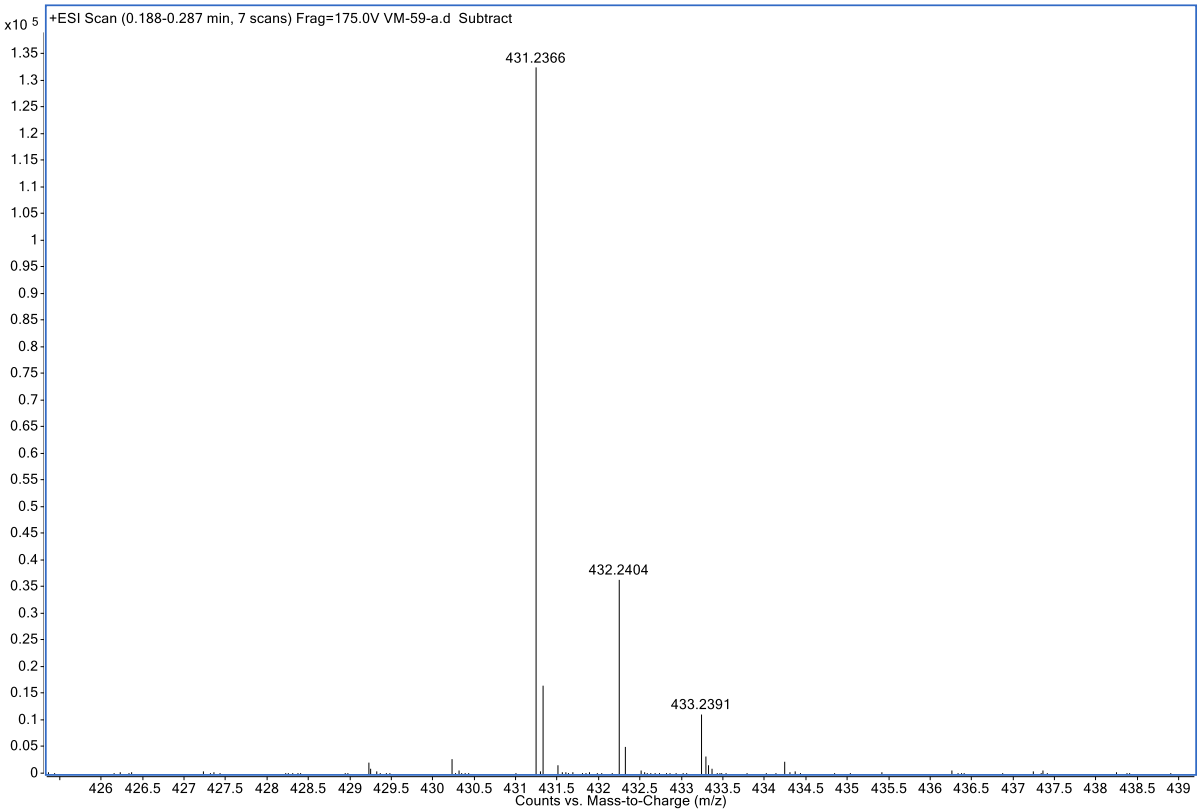
6-Butyl-5-((2-hydroxyethyl)thio)-2-octylpyrrolo[3,4-*f*]isoindole-1,3(2*H*,6*H*)-dione (20e).

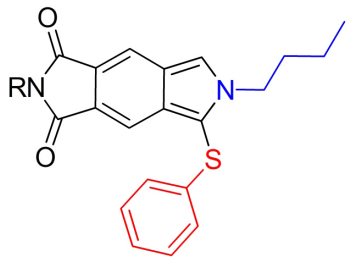
Compound **20e** was prepared from 10.0 mg (31.7 μmol) of dialdehyde **19**. Pure **20e** was isolated by silica gel chromatography (1/1 hexanes/EtOAc, R_f = 0.35), as a yellow oil (8.2 mg, 60% yield).

^{1}H NMR (500 MHz, CD_3OD) δ 8.19 (d, *J* = 0.9 Hz, 1H), 8.07 (d, *J* = 1.0 Hz, 1H), 7.84 (s, 1H), 4.53 (t, *J* = 7.3 Hz, 2H), 3.67 (t, *J* = 7.2 Hz, 2H), 3.59 (t, *J* = 6.5 Hz, 2H), 2.84 (t, *J* = 6.5 Hz, 2H), 1.91 (p, *J* = 7.6 Hz, 2H), 1.73–1.63 (m, 2H), 1.42–1.27 (m, 13H), 0.99 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, CD_3OD) δ 170.4, 170.4, 131.8, 126.0, 125.2, 124.6, 121.6, 119.8, 118.8, 117.8, 61.8, 49.4, 41.1, 38.8, 35.0, 32.9, 30.3, 30.2, 29.5, 27.9, 23.7, 20.9, 14.4, 14.0.

HRMS (ESI) calcd. for $C_{24}H_{35}N_2O_3S$ $[M+H]^+$: 431.2363; found: 431.2366.





20f, R = octyl

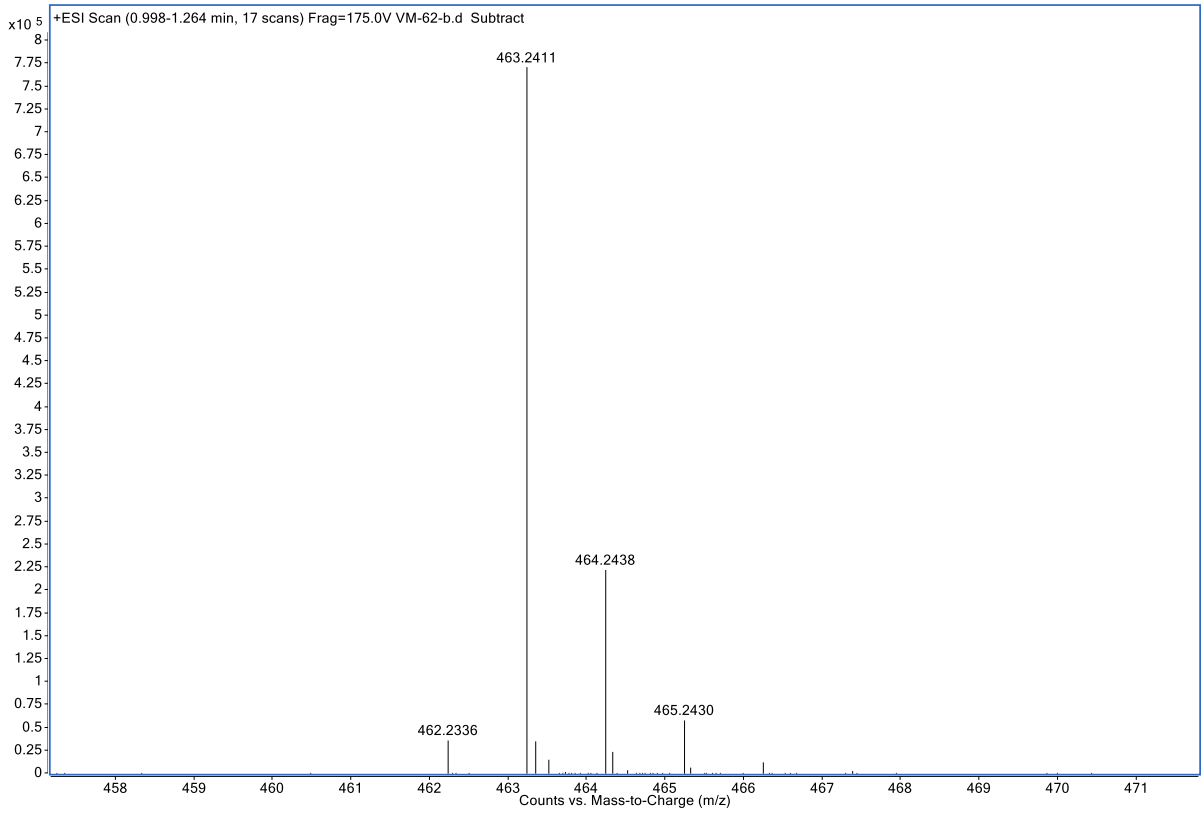
6-Butyl-2-octyl-5-(phenylthio)pyrrolo[3,4-*f*]isoindole-1,3(2*H*,6*H*)-dione (20f).

Compound **20f** was prepared from 10.0 mg (31.7 μmol) of dialdehyde **19**. Pure **20f** was isolated by silica gel chromatography (5/1 hexanes/EtOAc, R_f = 0.28), as a light-yellow glass (9.2 mg, 63% yield).

^{1}H NMR (500 MHz, CD_3OD) δ 8.13 (d, *J* = 1.1 Hz, 1H), 8.07–8.03 (m, 1H), 7.95 (s, 1H), 7.21 (tt, *J* = 8.3, 6.8 Hz, 2H), 7.16–7.11 (m, 1H), 6.96–6.92 (m, 2H), 4.39 (t, *J* = 7.4 Hz, 2H), 3.65 (t, *J* = 7.2 Hz, 2H), 1.80–1.70 (m, 2H), 1.66 (p, *J* = 6.9 Hz, 2H), 1.37–1.32 (m, 4H), 1.30–1.25 (m, 8H), 0.87 (t, *J* = 6.9 Hz, 3H), 0.85 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, CD_3OD) δ 170.2 (2C), 138.8, 132.6, 130.4 (2C), 127.4 (2C), 127.3, 126.2, 126.1, 124.9, 122.9, 119.9, 118.0, 114.4, 49.7, 38.8, 34.5, 32.9, 30.3, 30.2, 29.5, 27.9, 23.7, 20.8, 14.4, 13.8.

HRMS (ESI) calcd. for $C_{28}H_{35}N_2O_2S$ $[M+H]^+$: 463.2414; found: 463.2411.

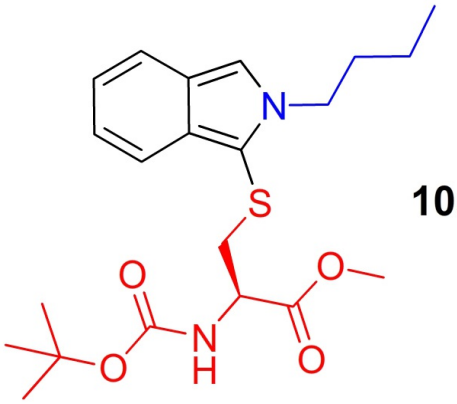


B. General Procedure for Testing Isoindole Stability. A protocol was developed to test long term storage (neat) and usage under laboratory conditions (in solution). Here, the same sample of material was passed through three consecutive steps as given by: (1) long-term storage as a neat material; (2) a solution in acetone-d_6 at 23 °C in the dark; and, (3) a solution in acetone-d_6 at 23 °C under ambient light.

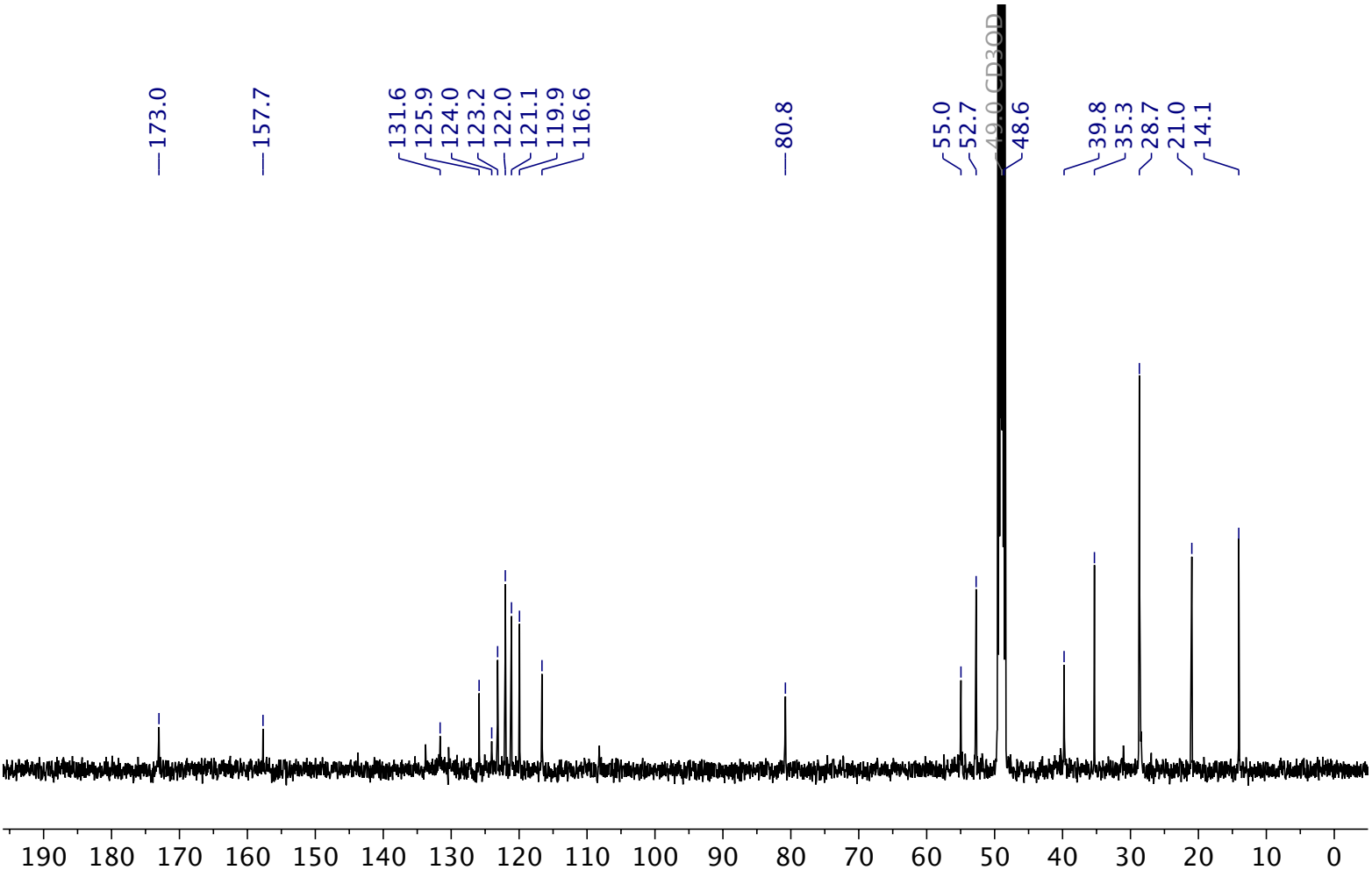
Protocol: Immediately after preparation neat samples of **18a**-**d** were stored for >30 days at -20 °C (in the dark), warmed to rt (in the dark), and stored at 23 °C (in the dark) for additional 48 h (a test of long term storage). After this period, samples of **18a**-**d** were dissolved at 1.0±0.2 mg/mL in acetone-d_6 and placed in a 3 mm NMR tube (Norell). These samples were first incubated at 23 °C in the dark. After 6 h, the samples were taken back into the laboratory and evaluated further at 23 °C under ambient light. Dark conditions were created by wrapping the vial or tube in aluminum foil and placed closed box.

Note: Based on their light sensitivity, absorption and emission spectral data was not collected or reported. As noted in the conclusion of the manuscript efforts are underway to further explore the utility of this light sensitivity as well as further develop analogues whose stability would match that commonly required for a fluorescent probe. To ensure proper stability analyses, we did not use fluorescence measurements rather turned to NMR spectroscopy.

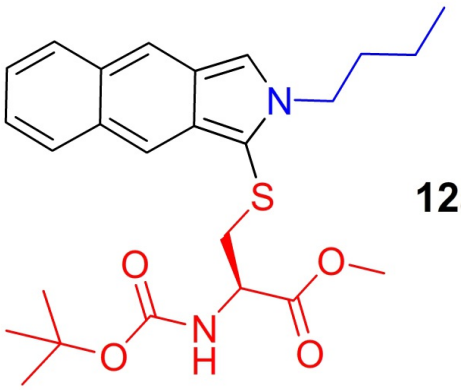
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **10a** in CD_3OD



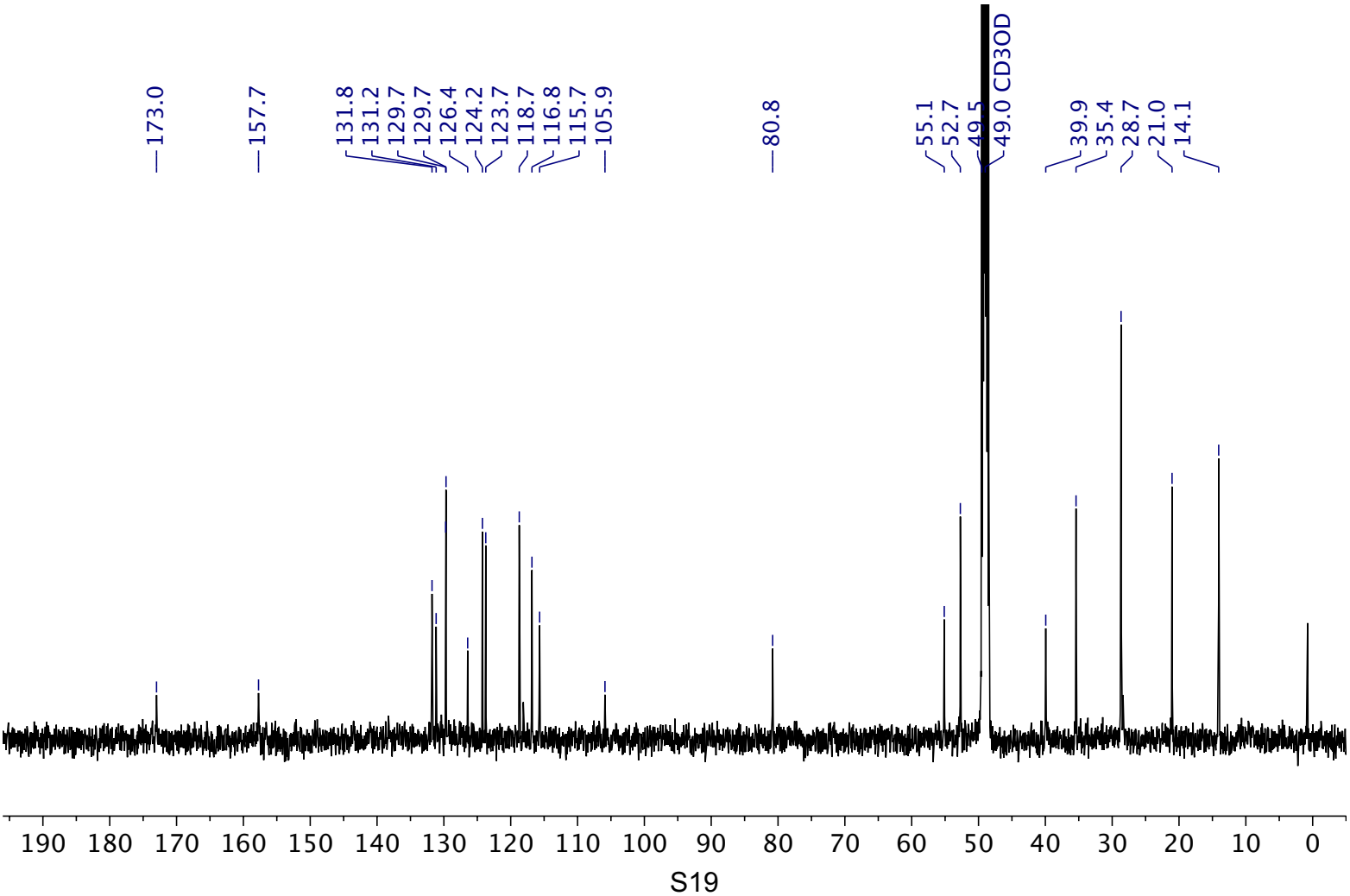
10a



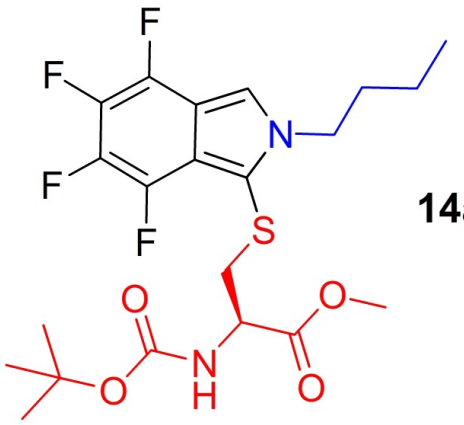
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **12a** in CD_3OD



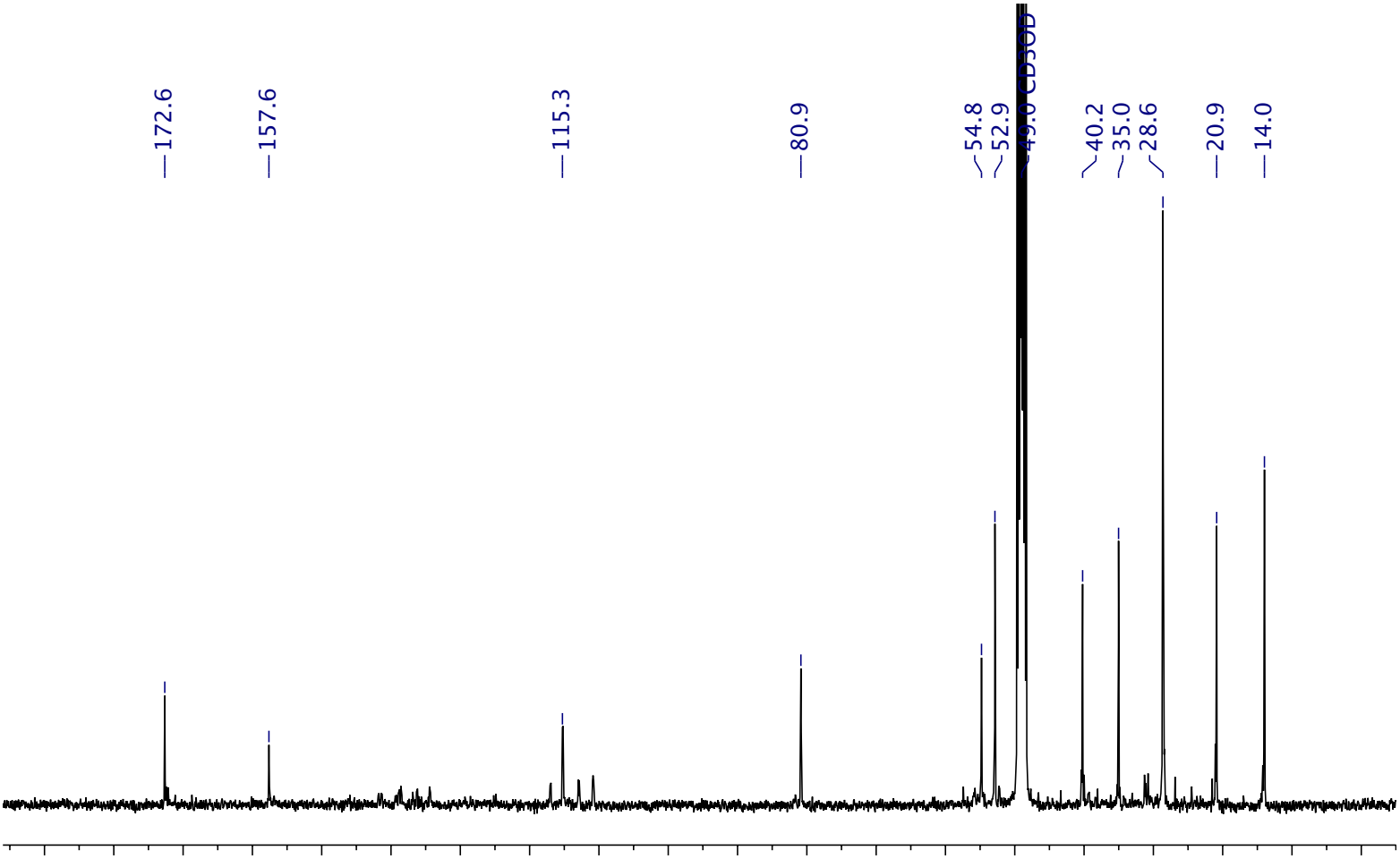
12a



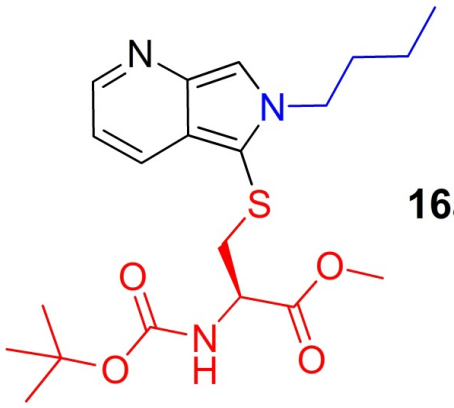
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **14a** in CD_3OD



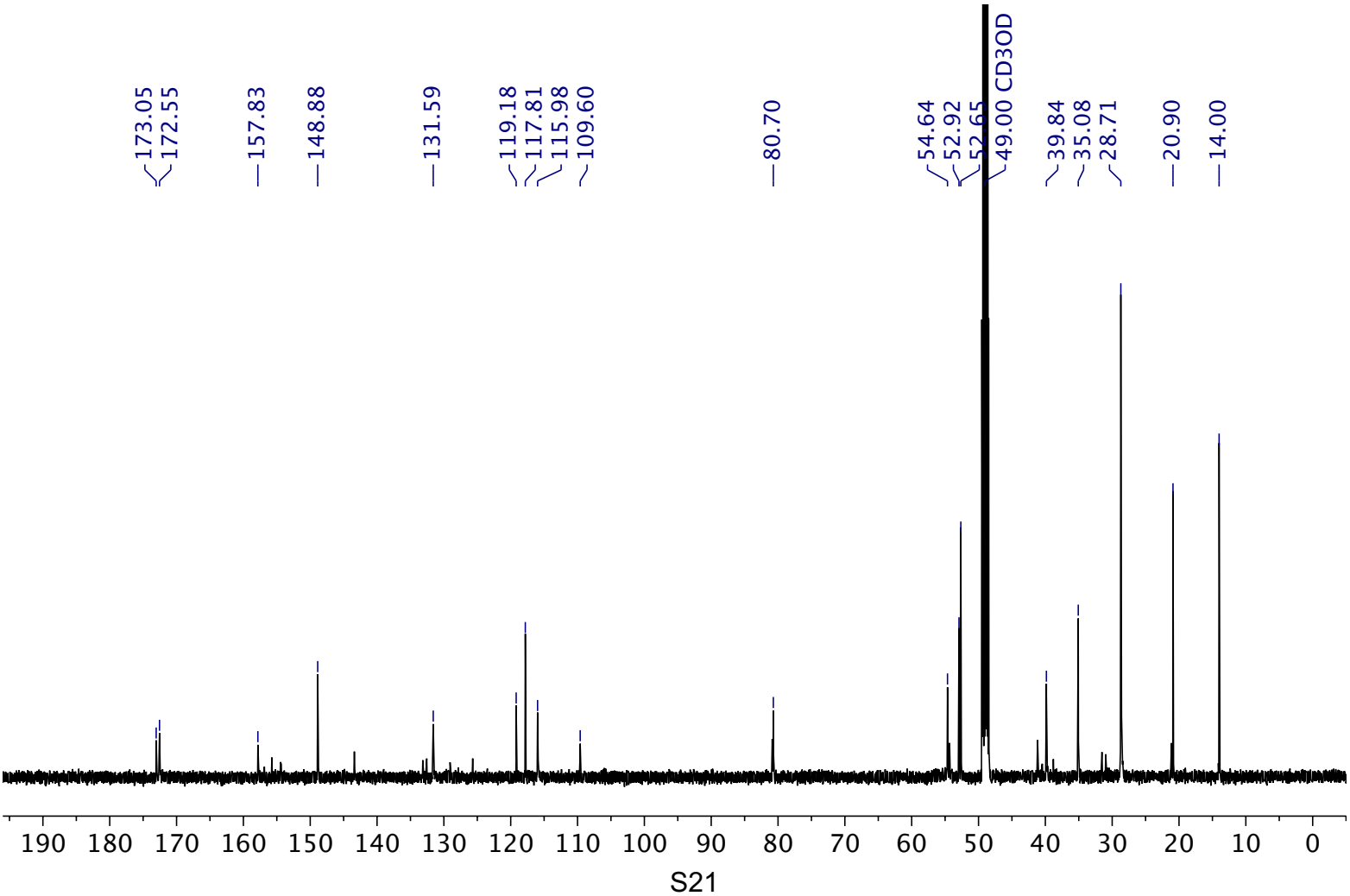
14a



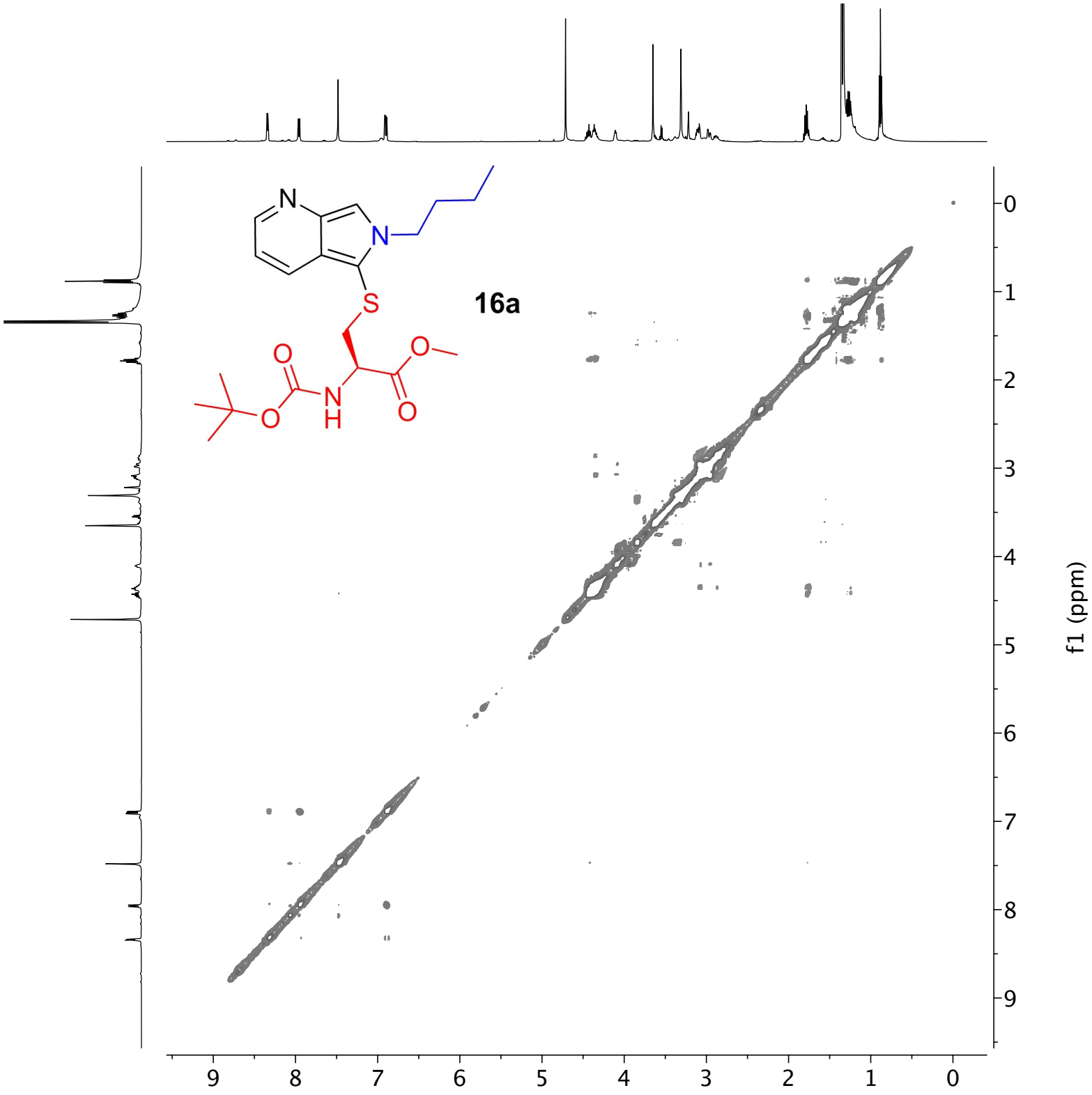
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **16a** in CD_3OD



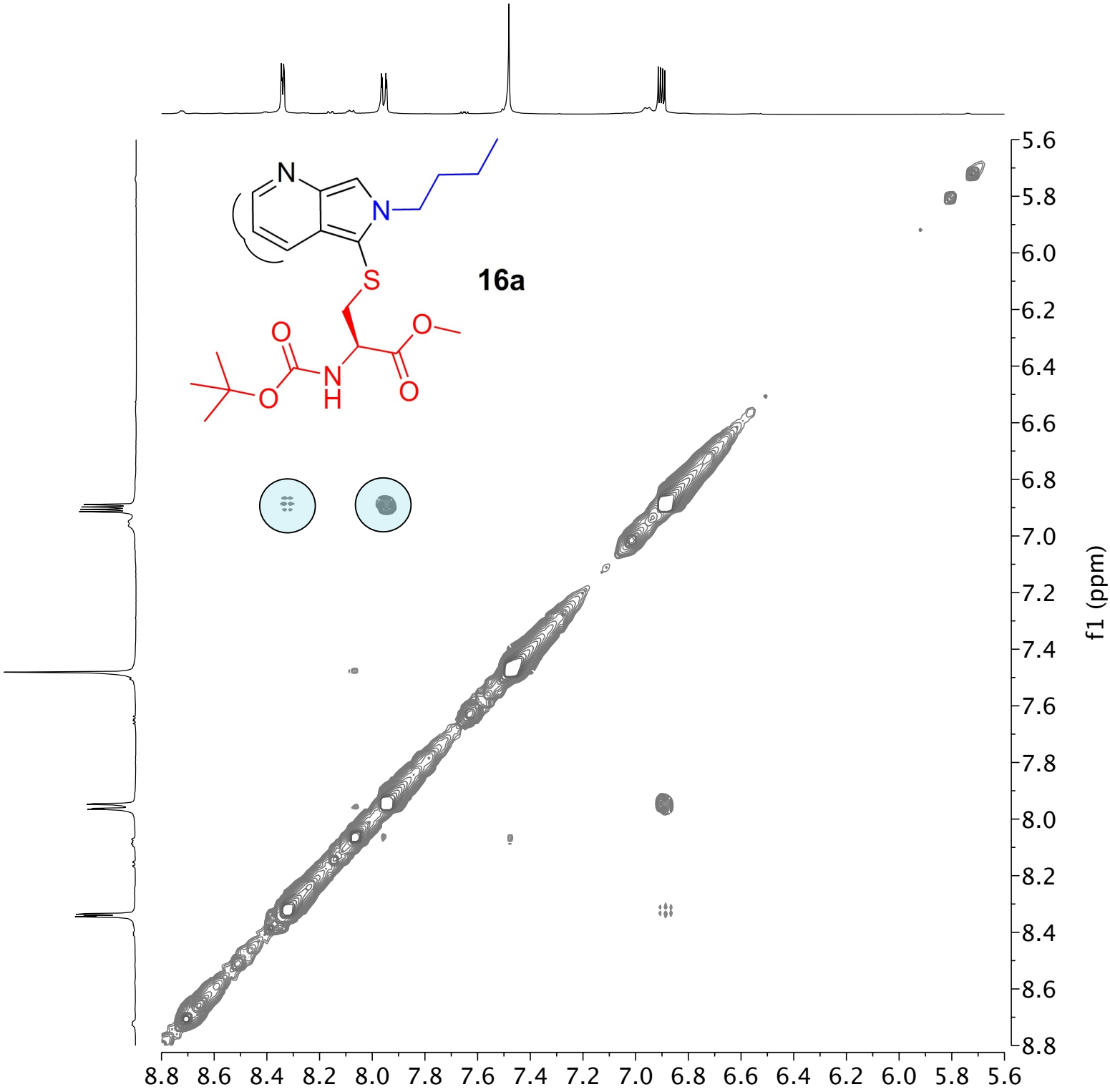
16a



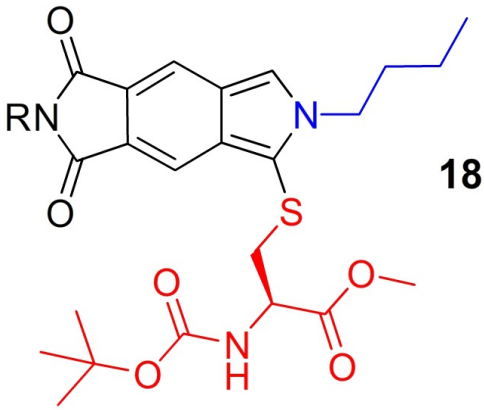
$^{1}H,^{1}H$ NOESY (500 MHz) NMR spectrum of **16a** in CD_3OD



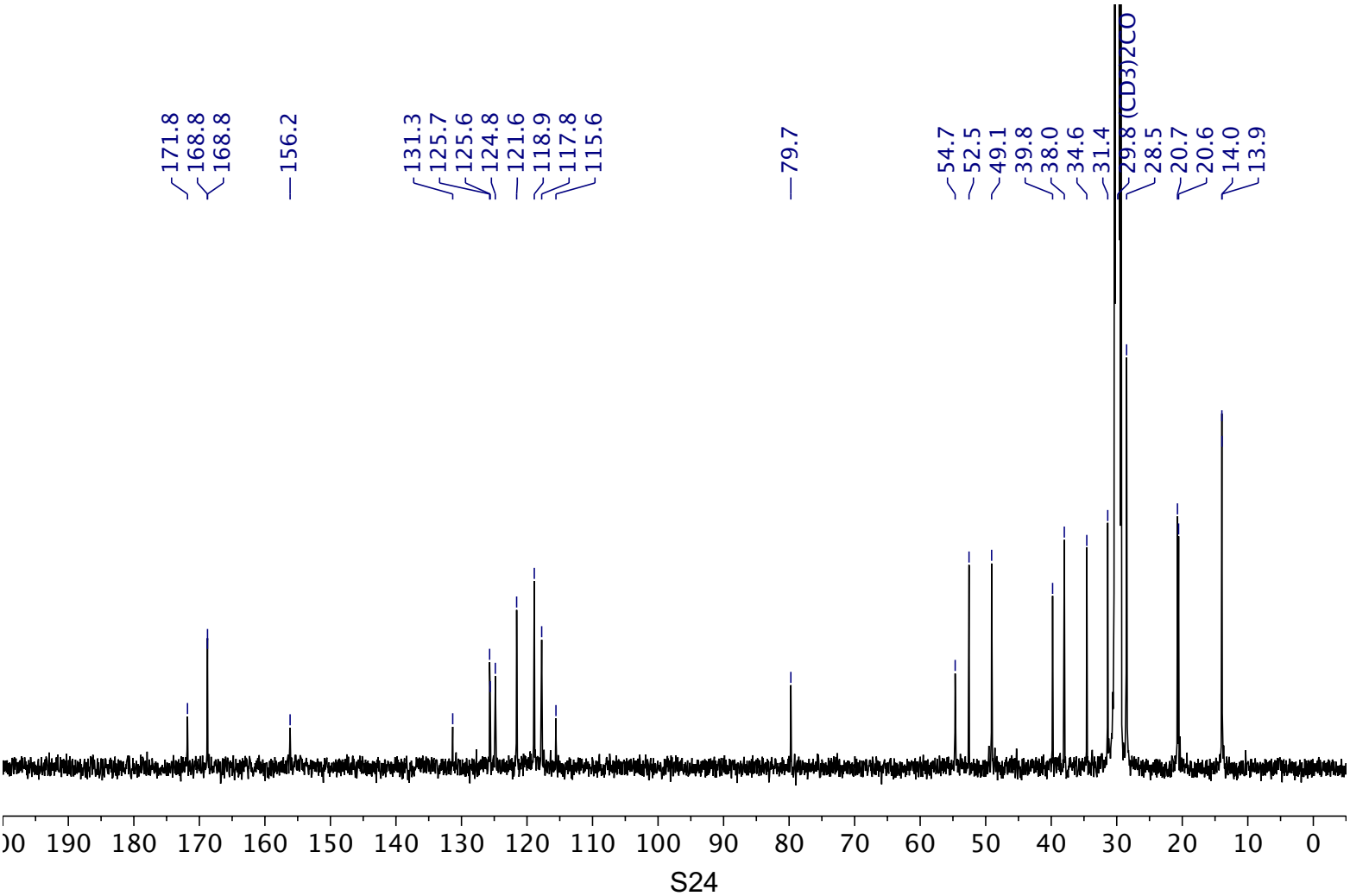
$^{1}H,^{1}H$ NOESY (500 MHz) NMR spectrum of **16a** in CD_3OD



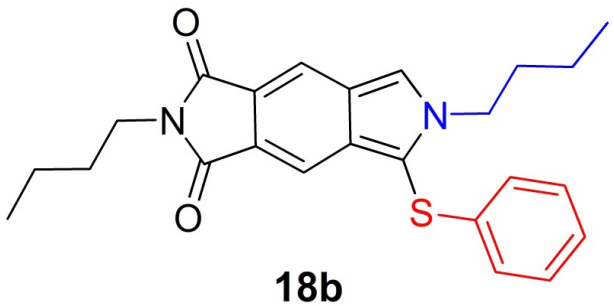
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **18a** in acetone-d_6



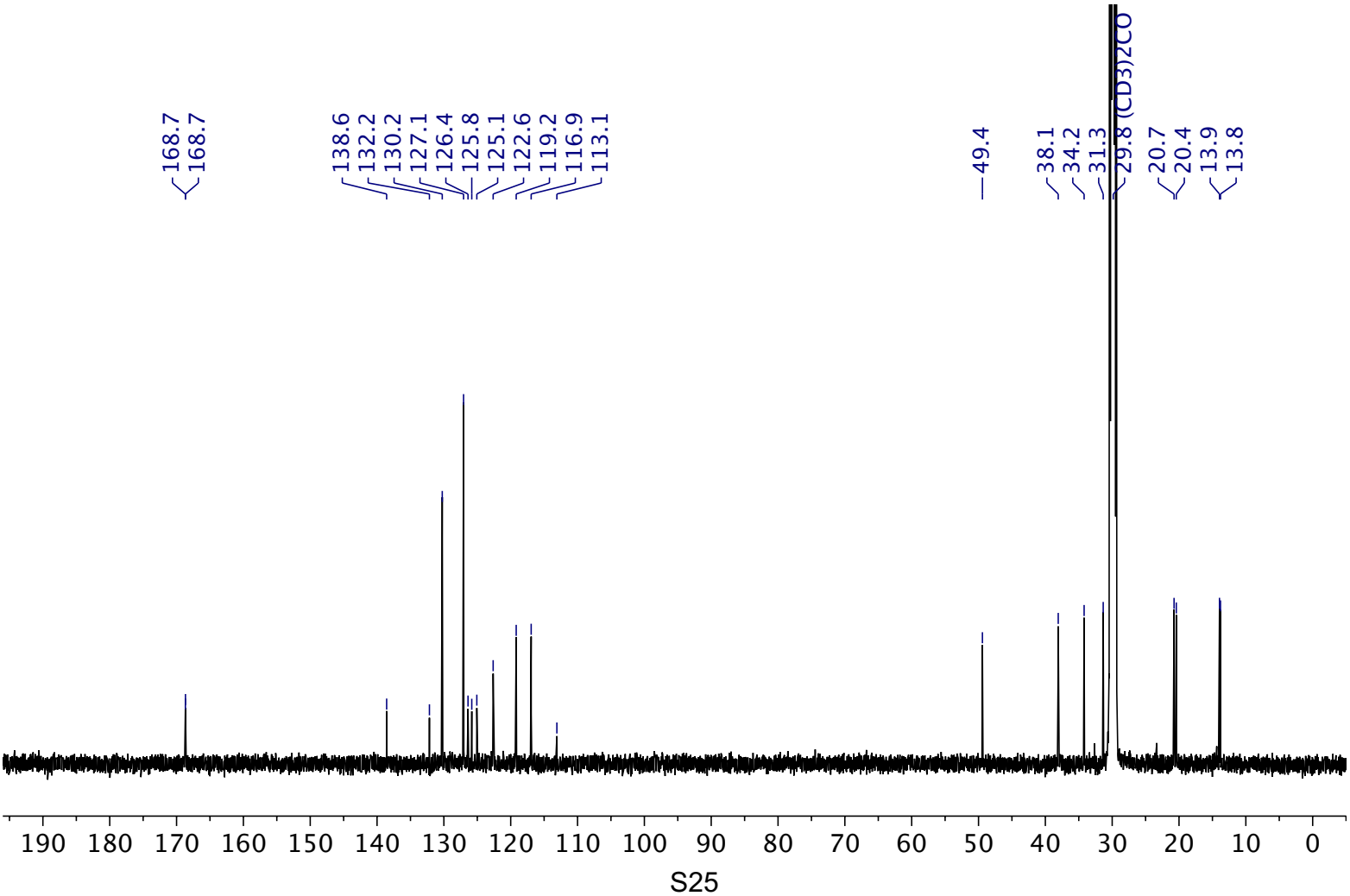
18a R = *n*-Bu



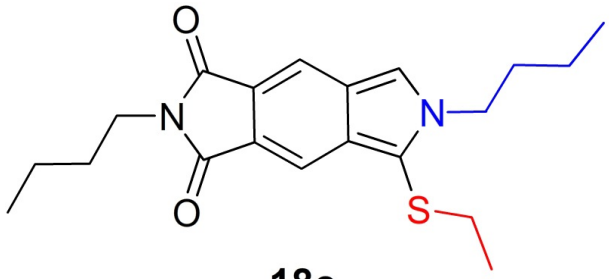
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **18b** in acetone-d_6



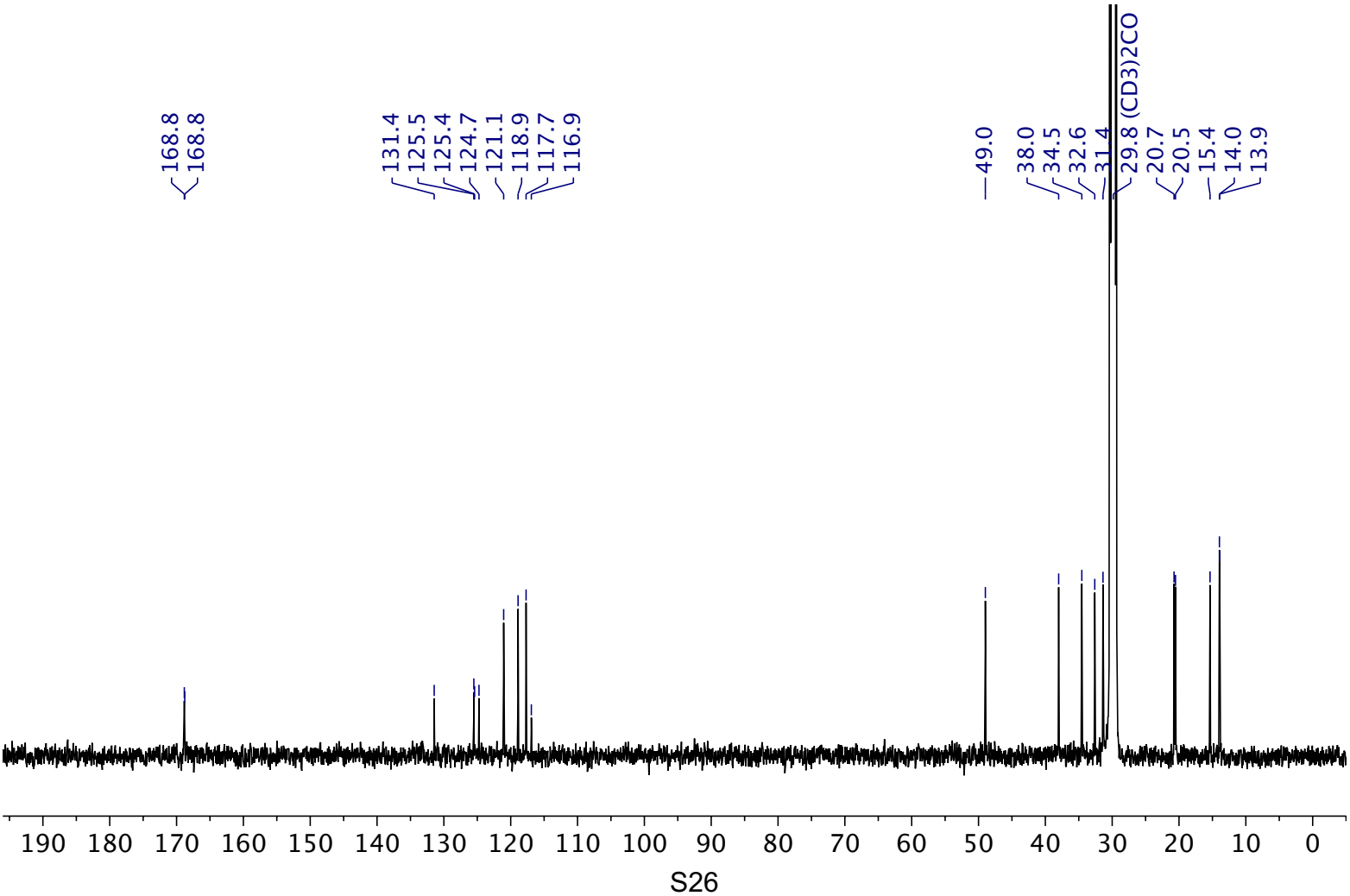
18b



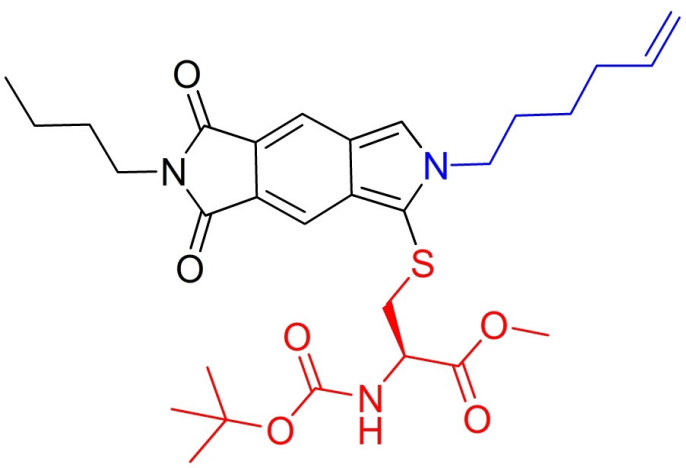
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **18c** in acetone-d_6



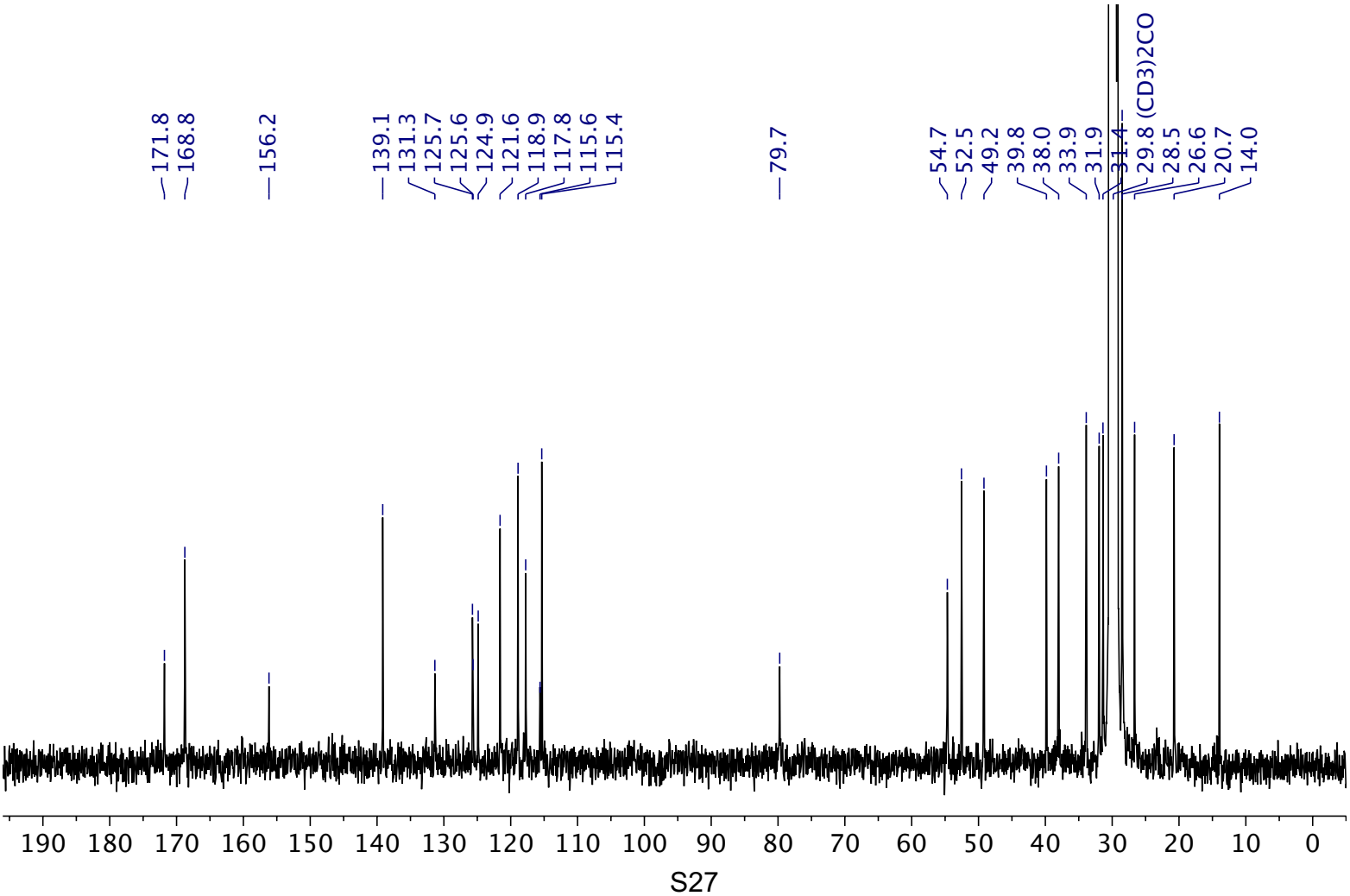
18c



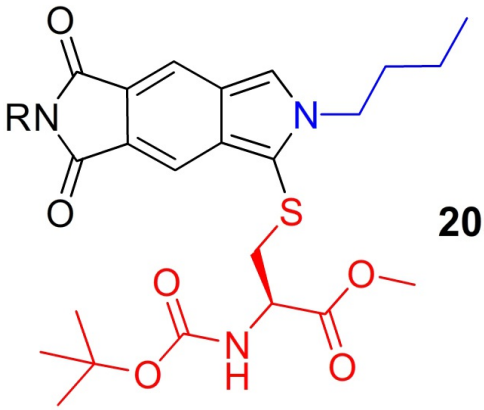
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **18d** in acetone-d_6



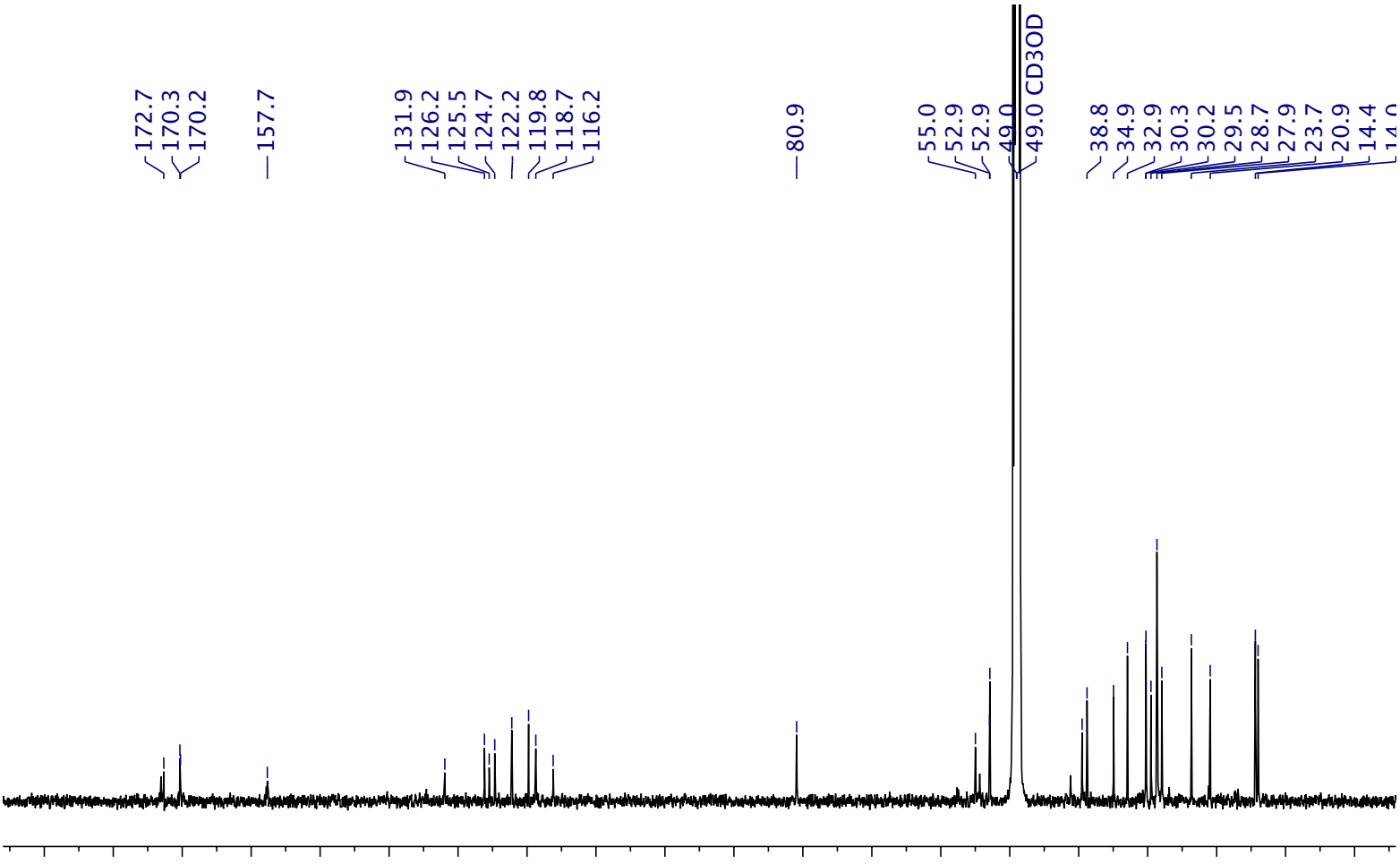
18d



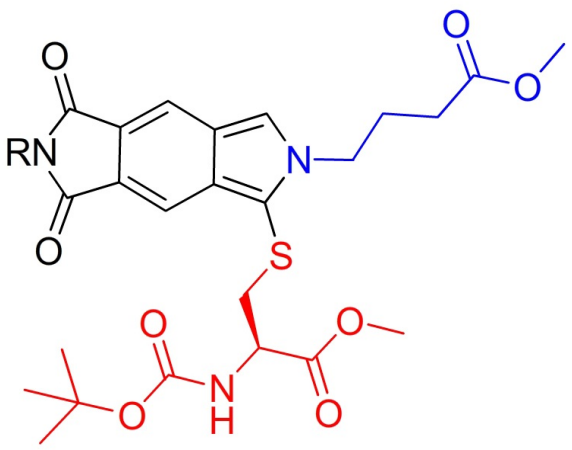
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **20a** in CD_3OD



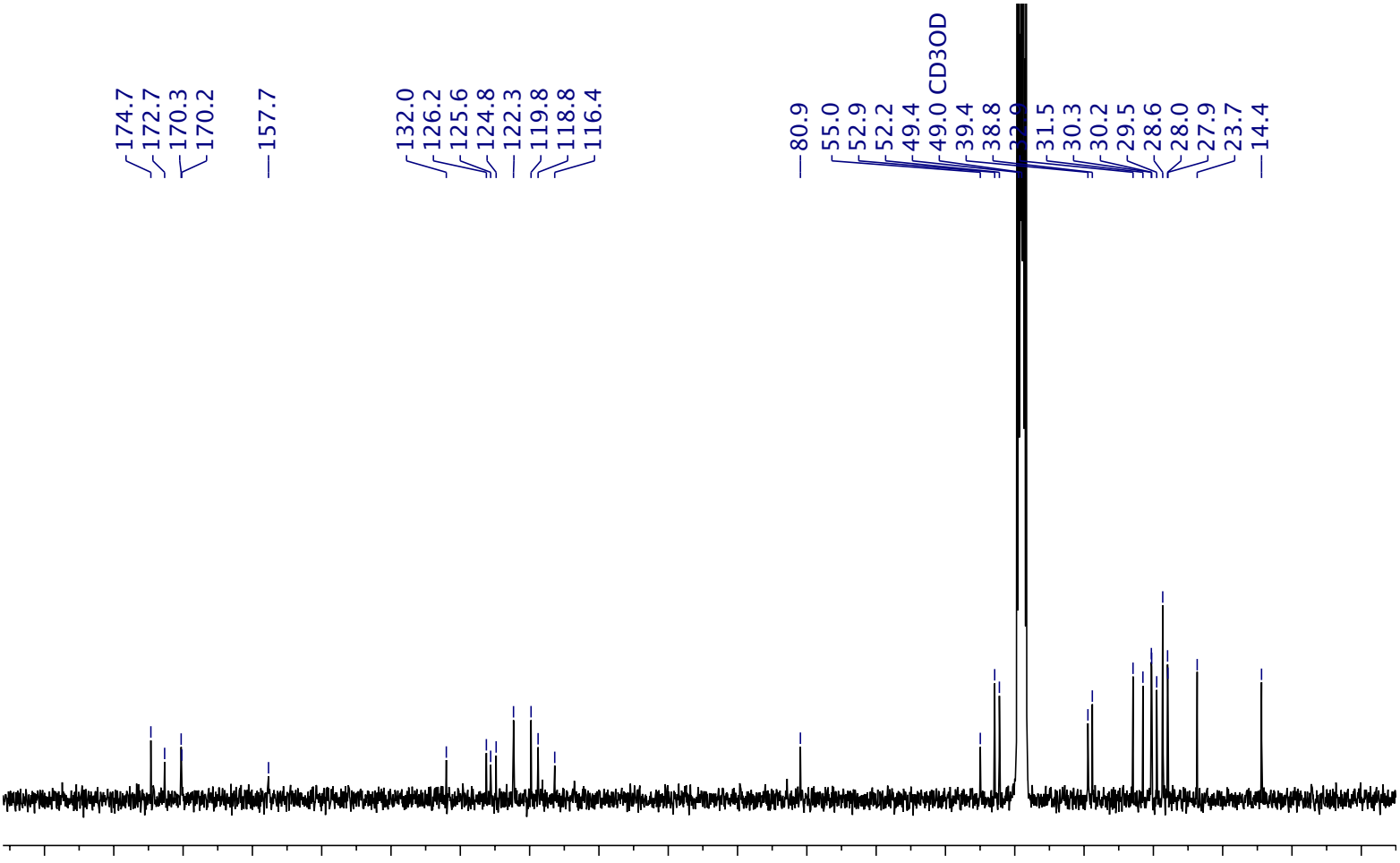
20a R = octyl



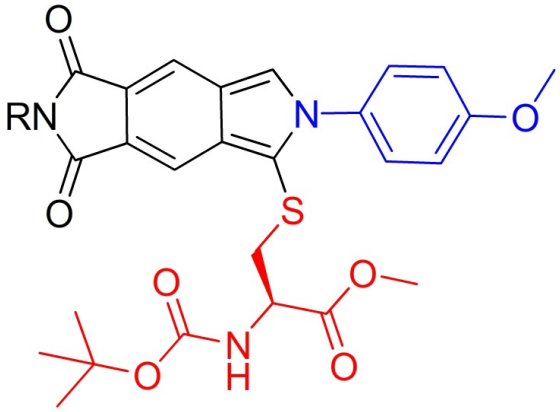
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **20b** in CD_3OD



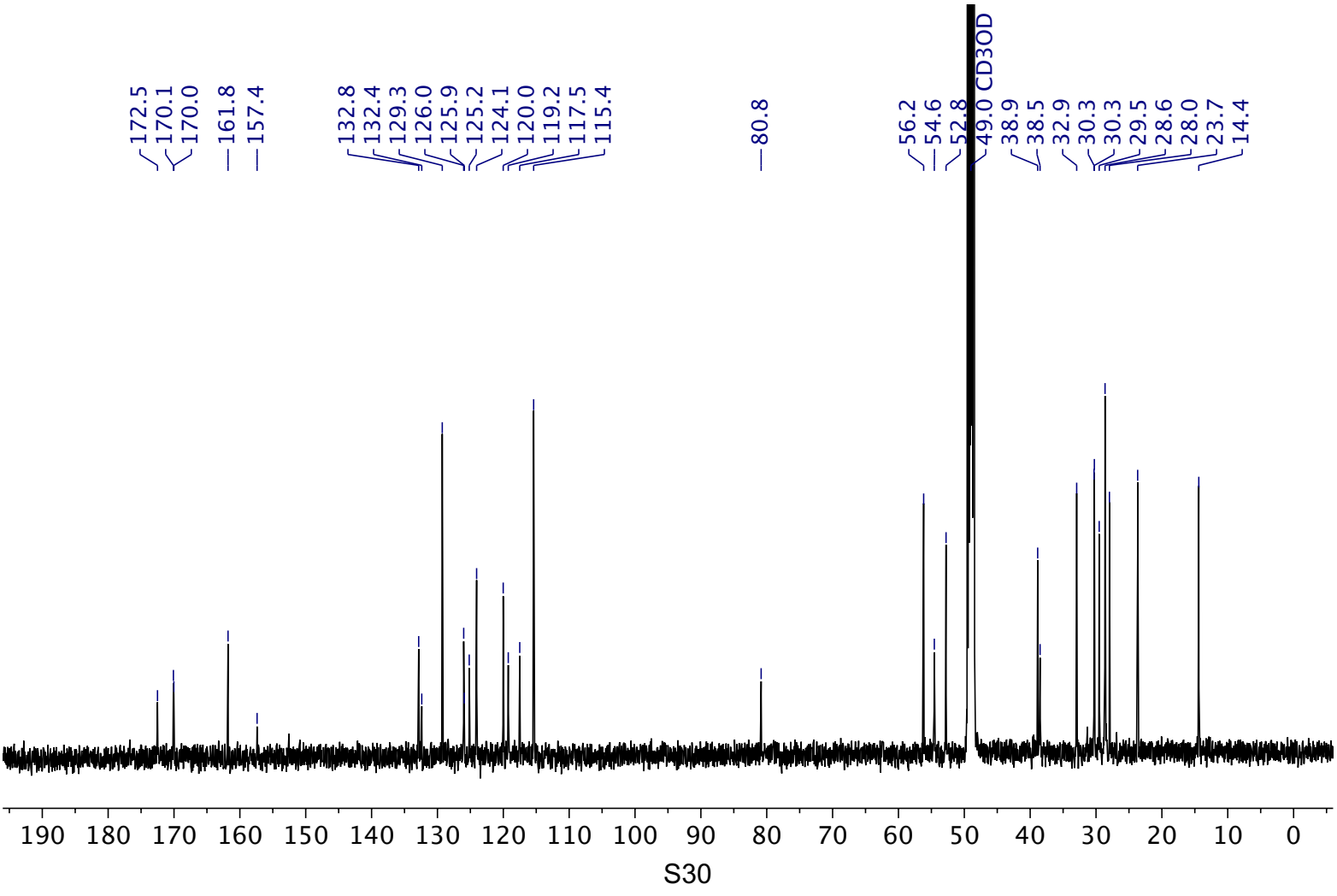
20b R = octyl



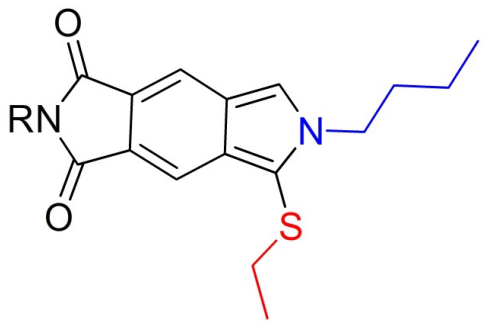
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **20c** in CD_3OD



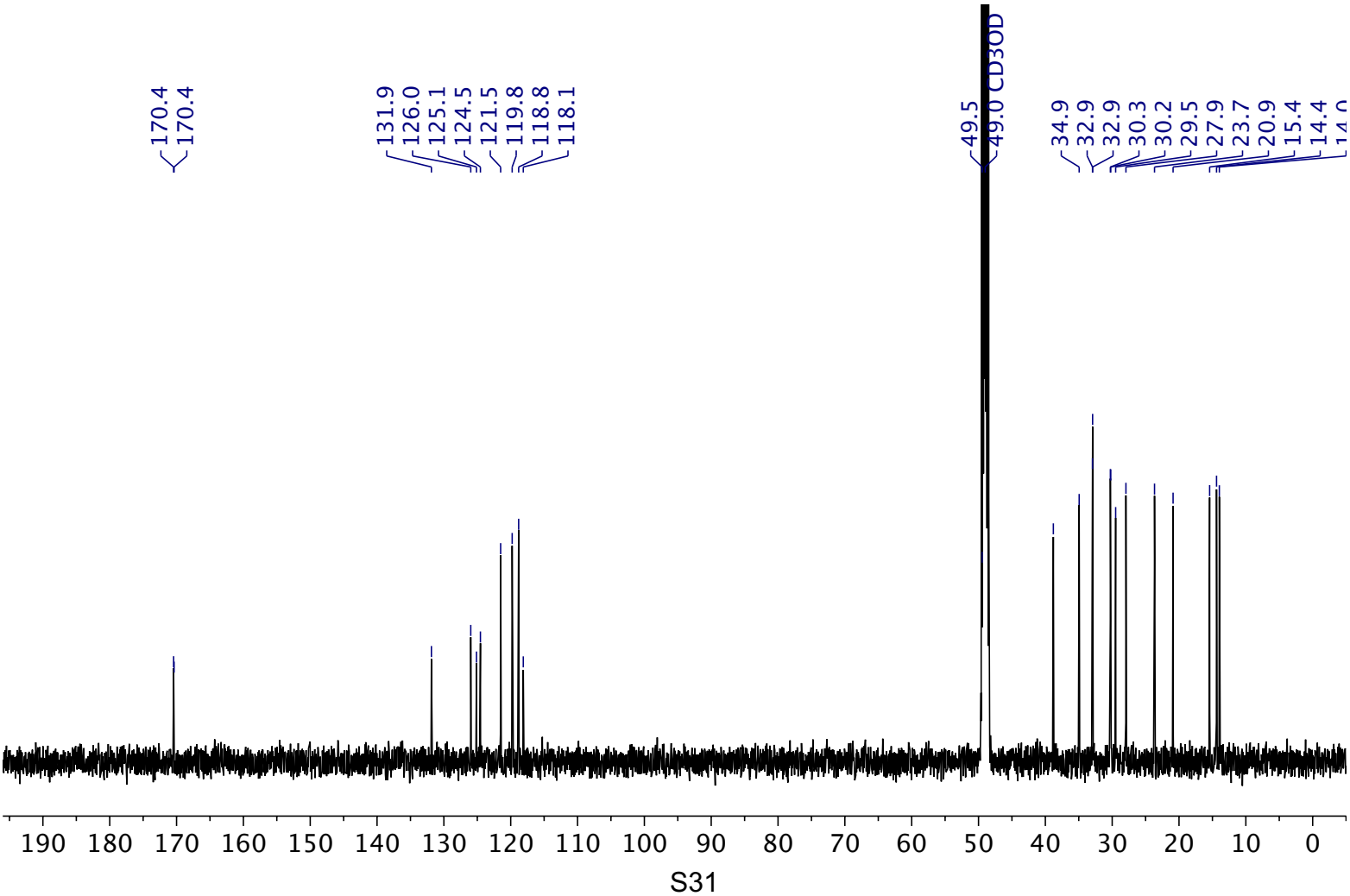
20c R = octyl



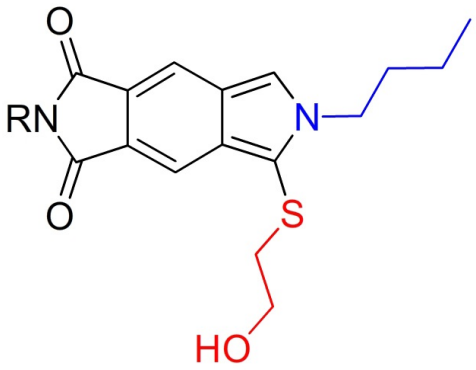
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **20d** in CD_3OD



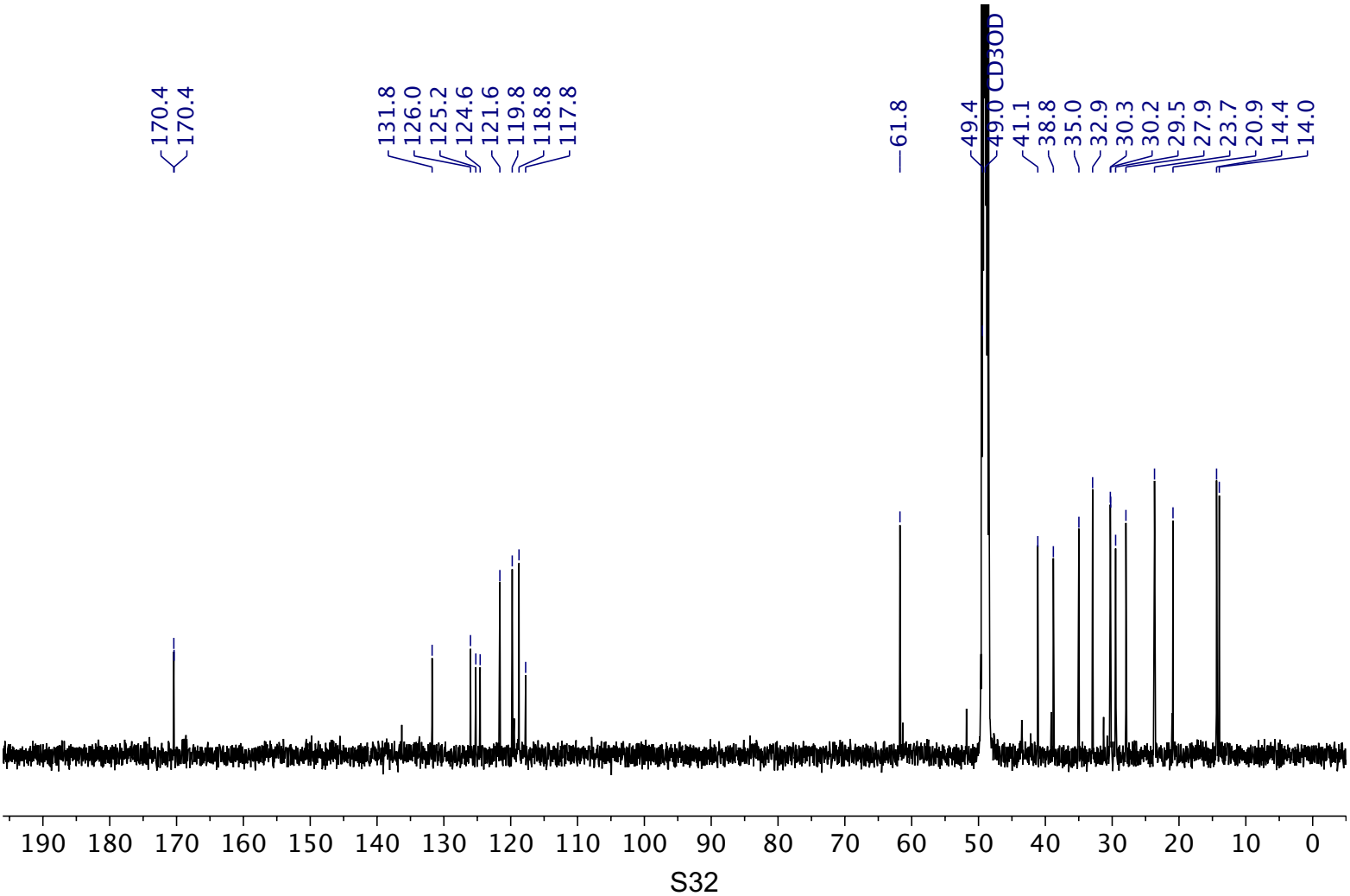
20d, R = octyl



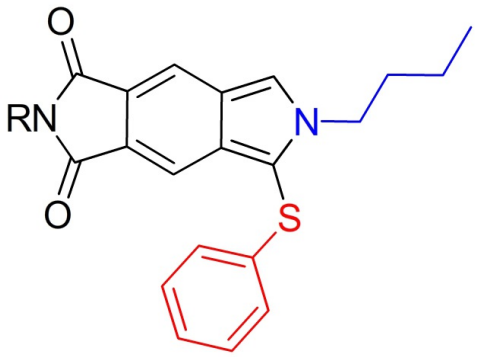
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **20e** in CD_3OD



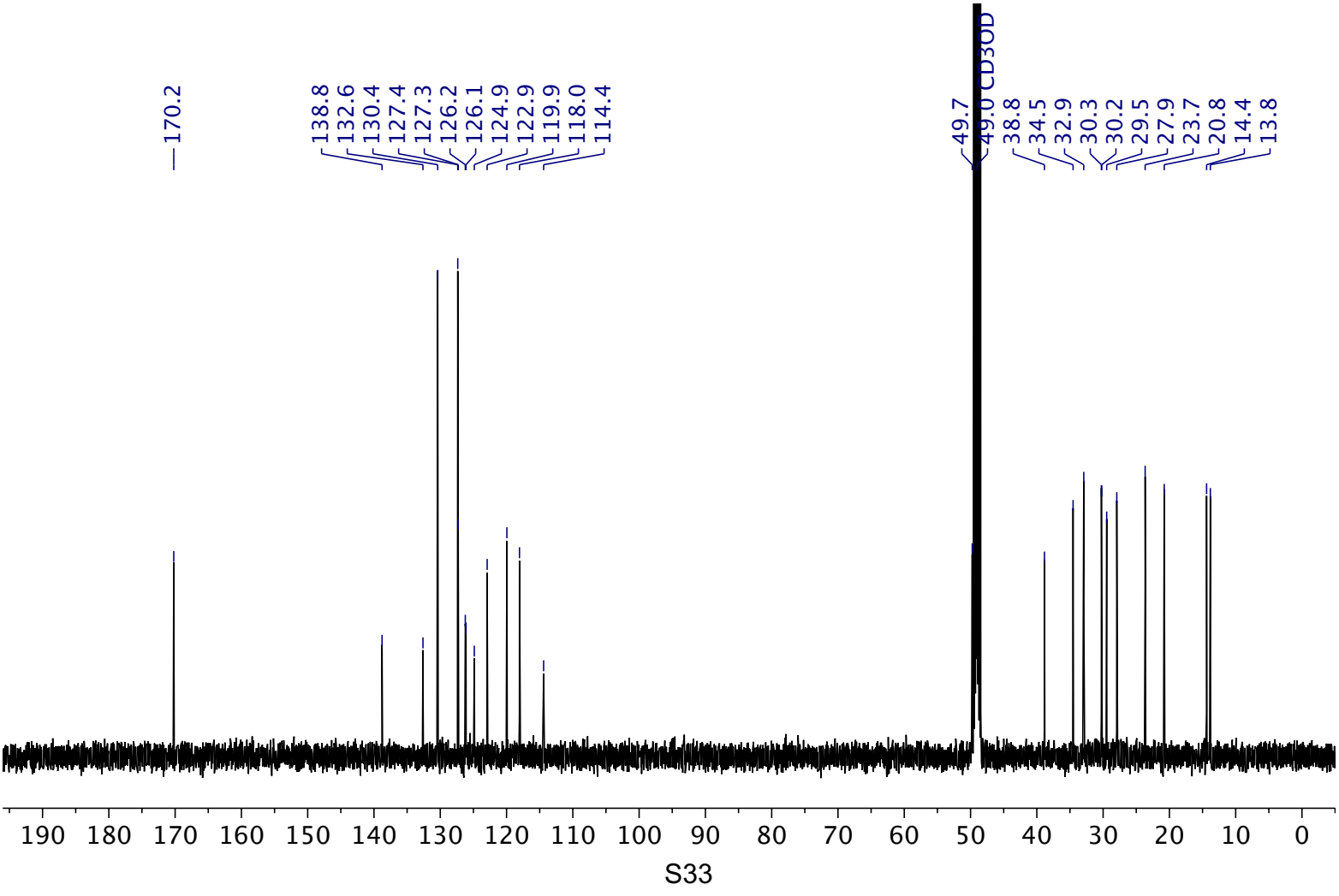
20e, R = octyl



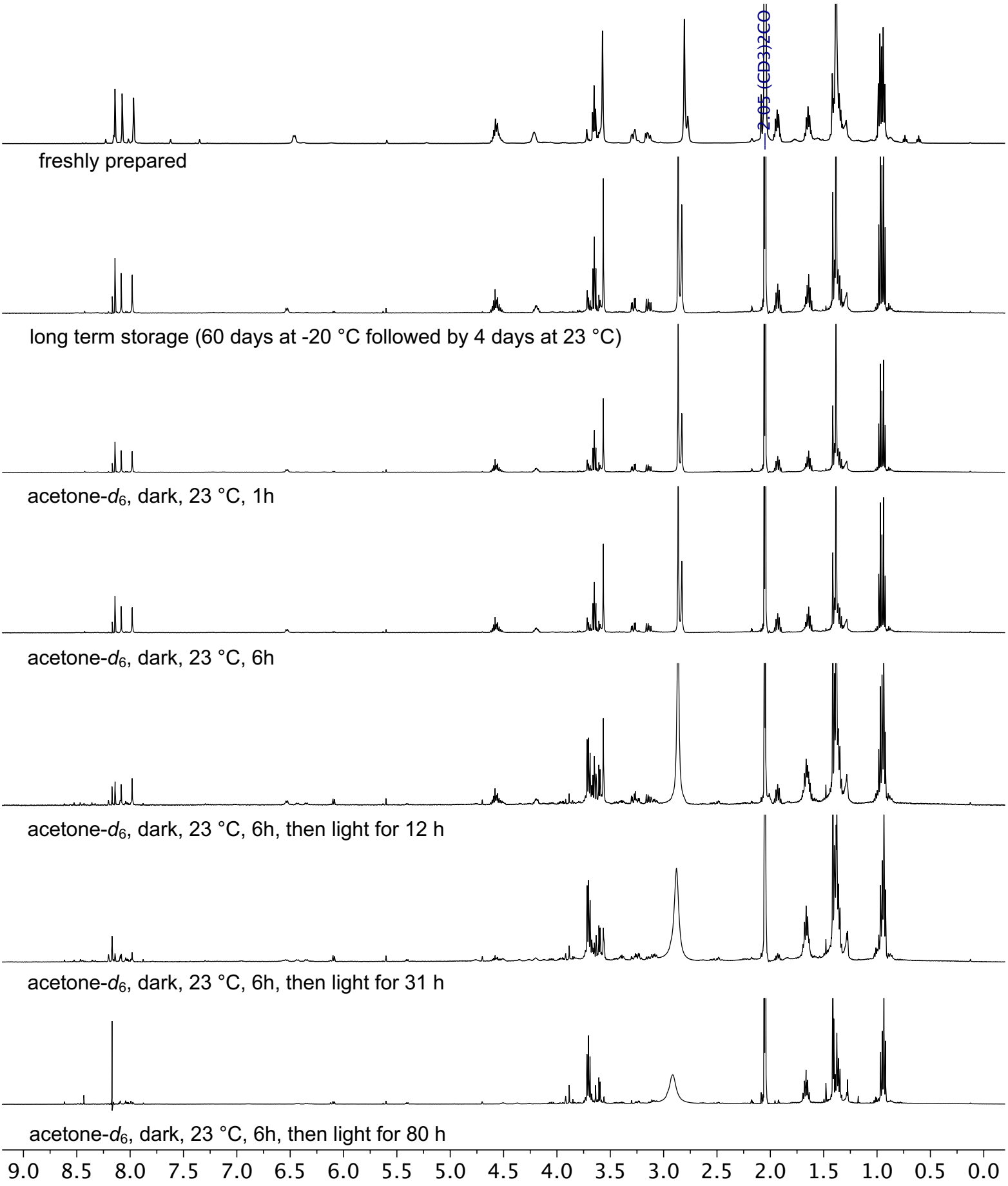
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of **20f** in CD_3OD



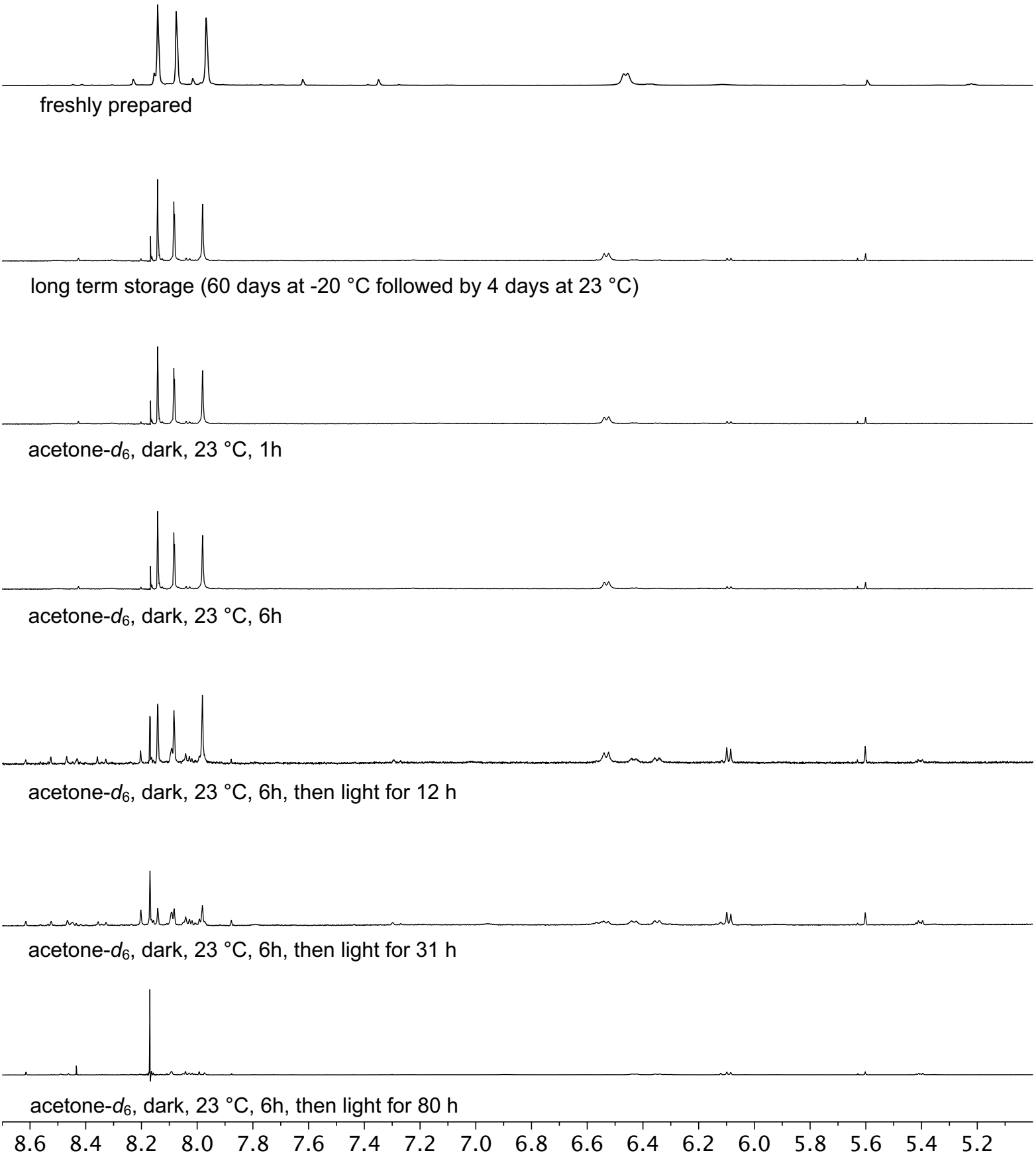
20f, R = octyl



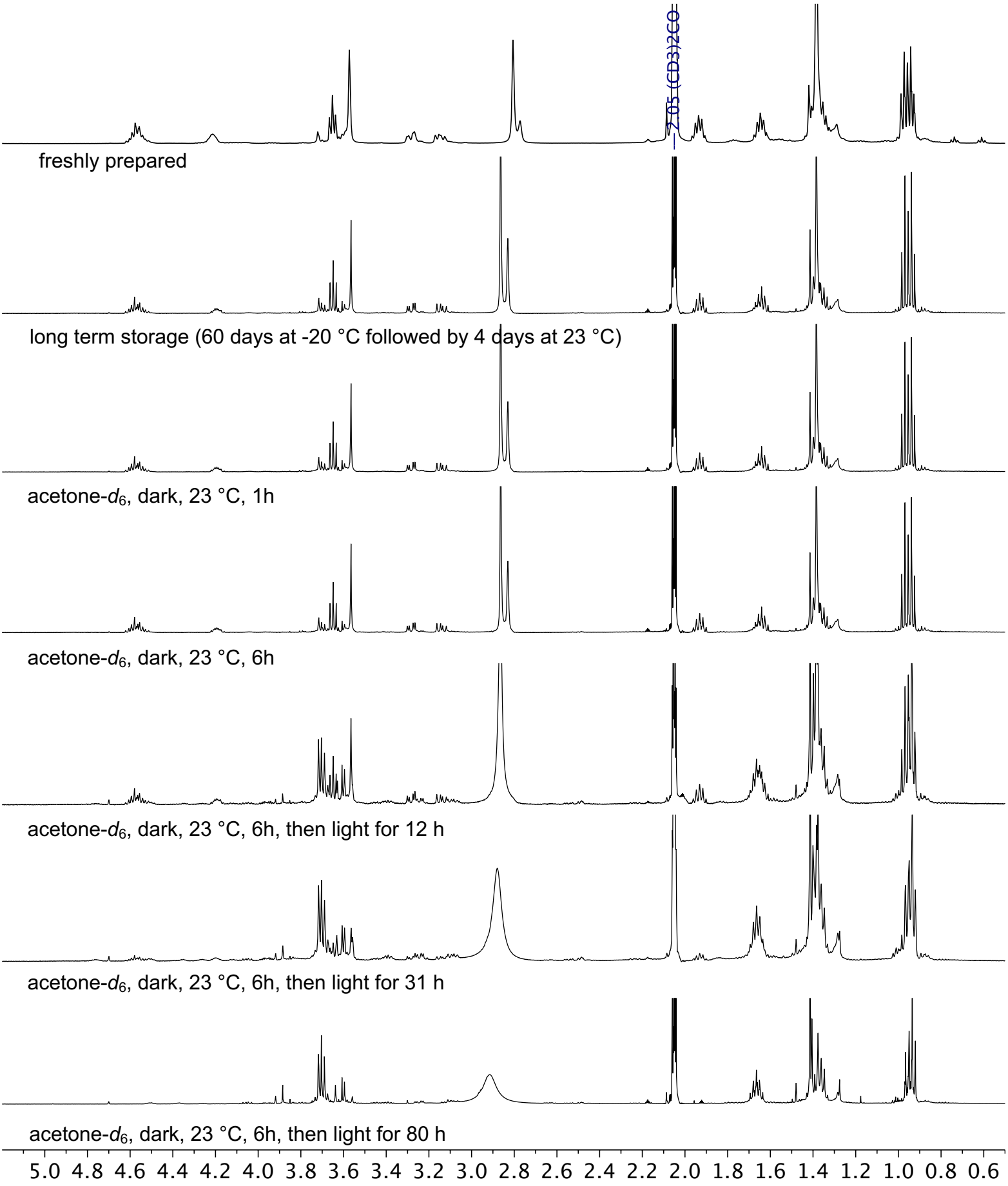
^{1}H NMR (500 MHz) spectra depicting the stability of **18a** (same sample) in acetone-d_6



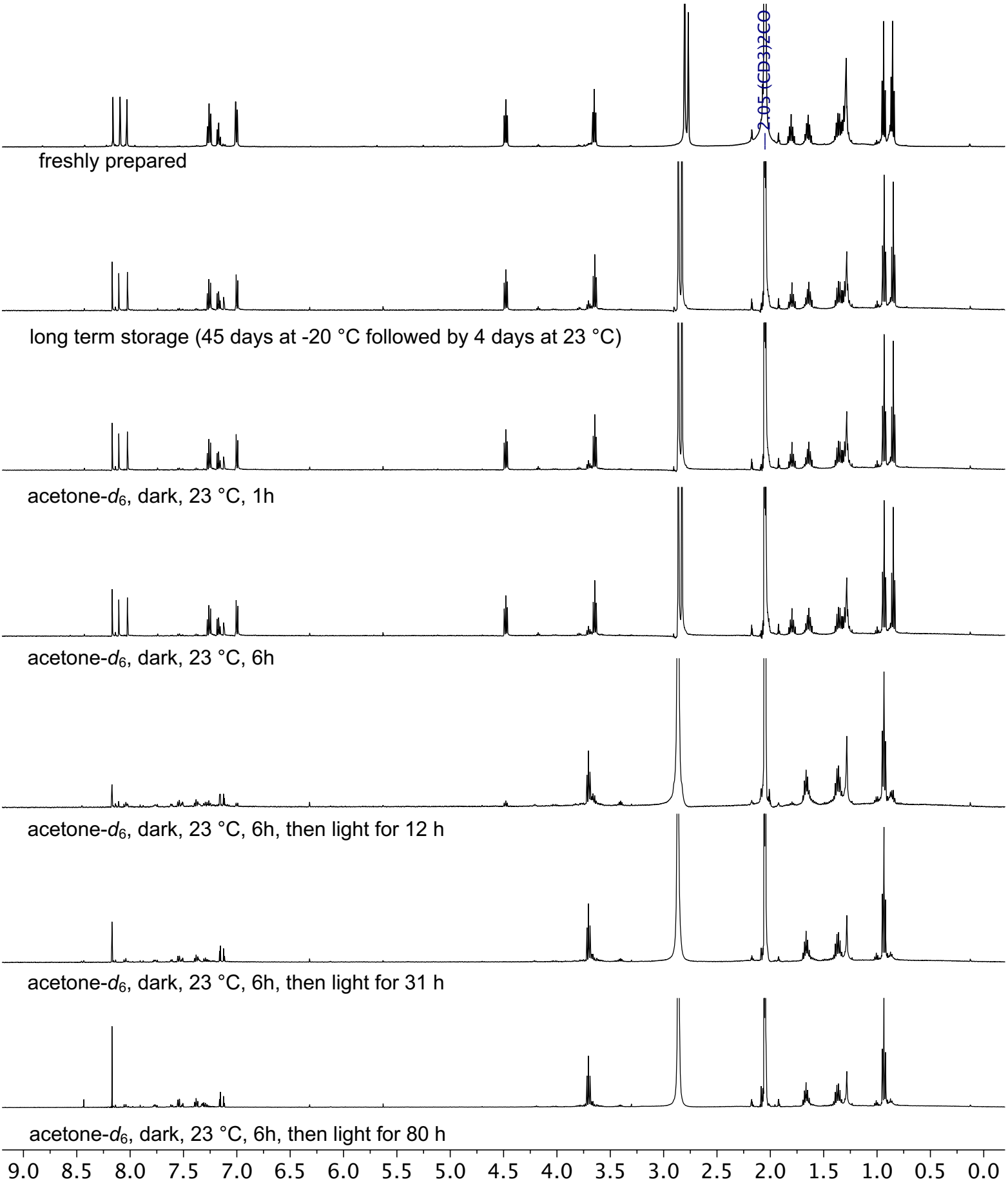
^{1}H NMR (500 MHz) spectra depicting the stability of **18a** (same sample) in acetone-d_6



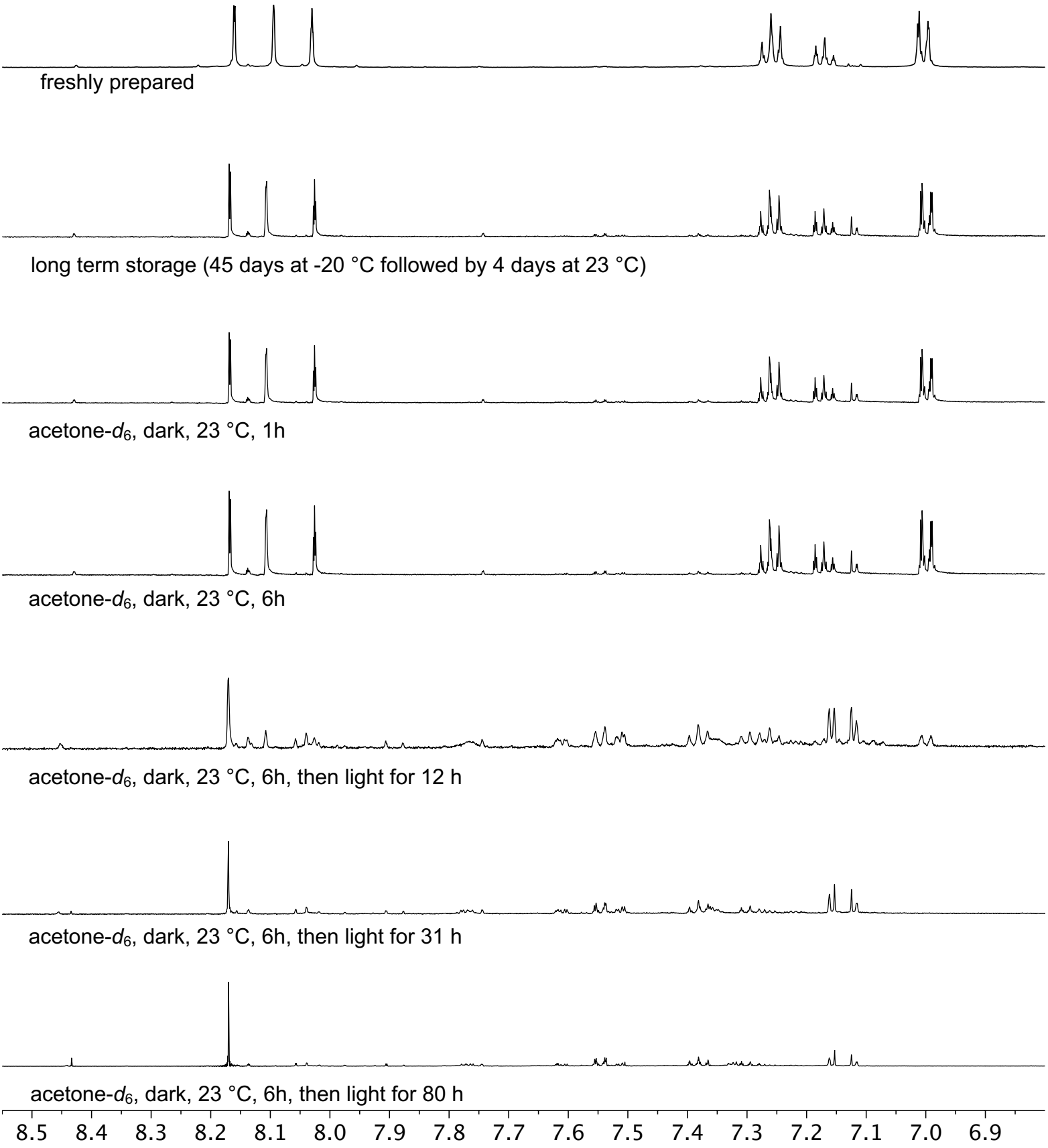
^{1}H NMR (500 MHz) spectra depicting the stability of **18a** (same sample) in acetone-d_6



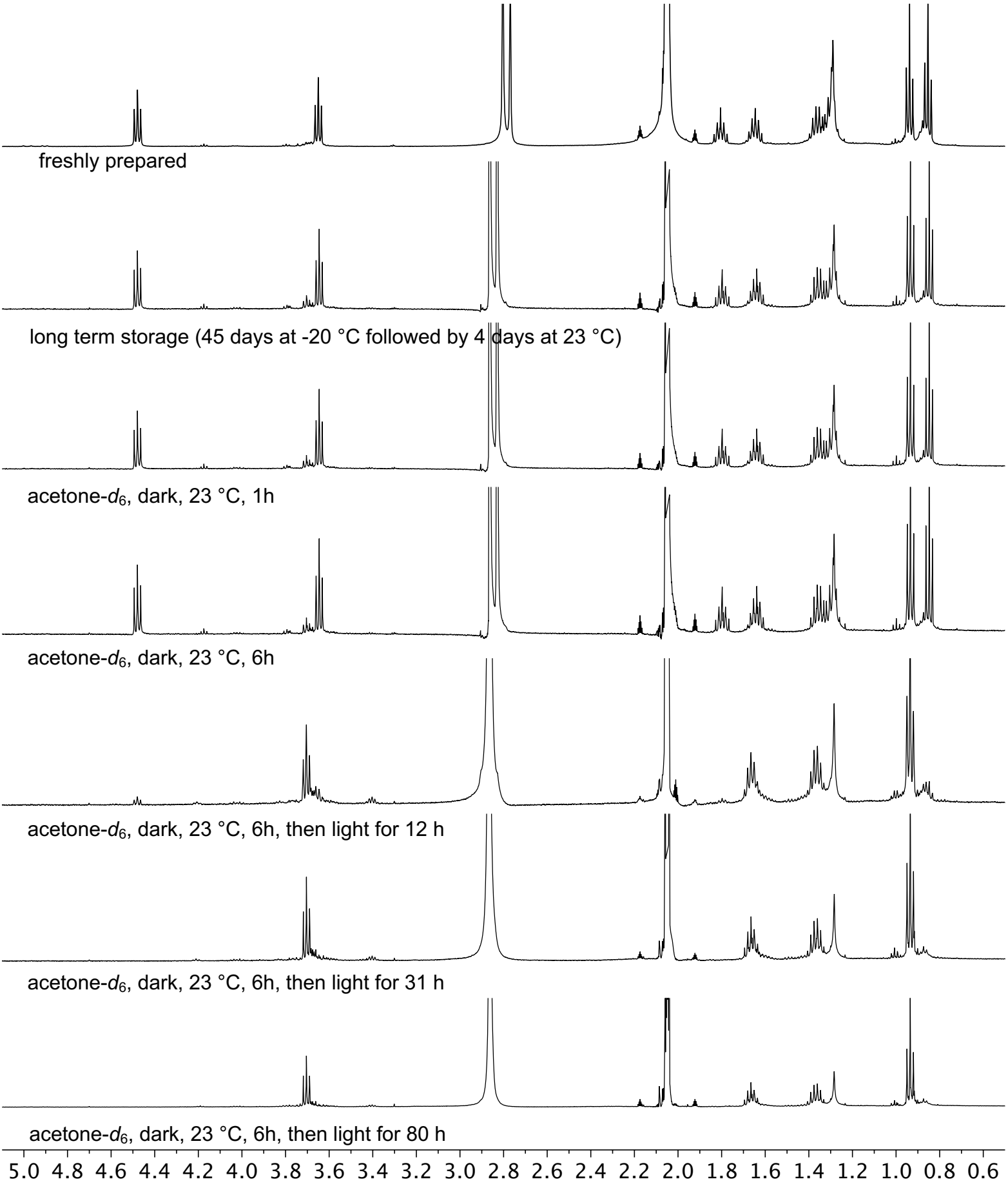
^{1}H NMR (500 Mhz) spectra depicting the stability of **18b** (same sample) in acetone-d_6



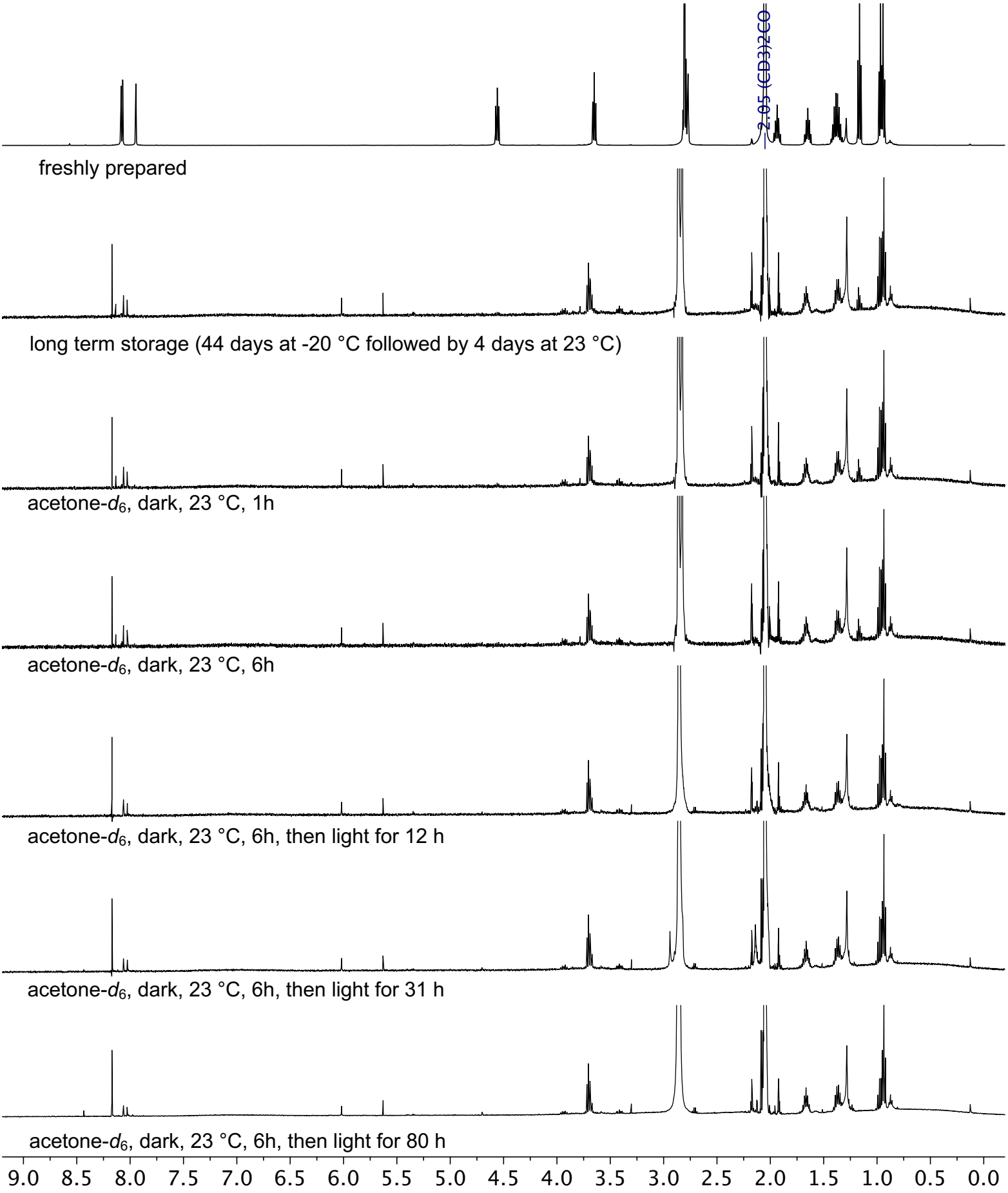
^{1}H NMR (500 Mhz) spectra depicting the stability of **18b** (same sample) in acetone-d_6



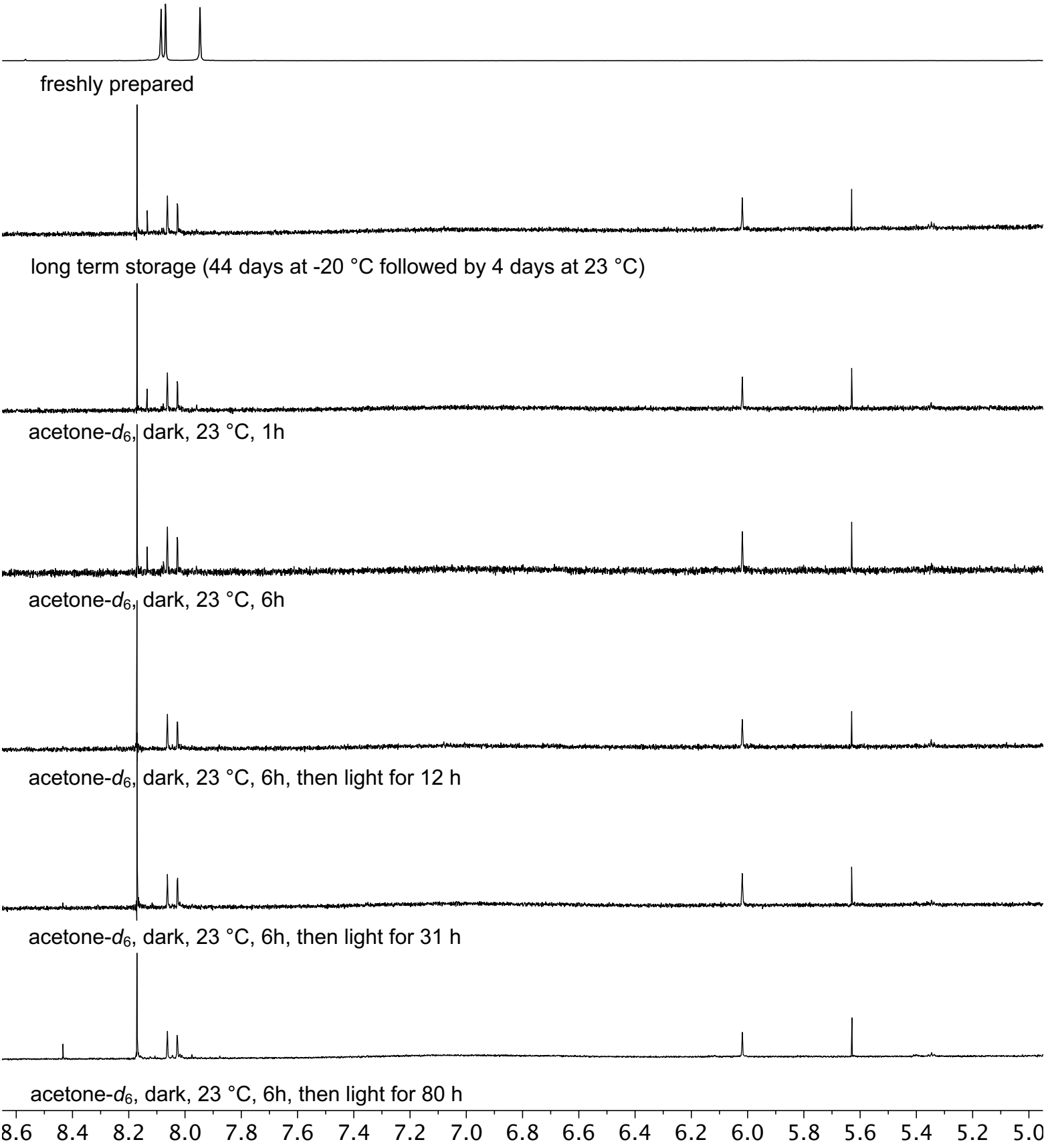
^{1}H NMR (500 Mhz) spectra depicting the stability of **18b** (same sample) in acetone-d_6



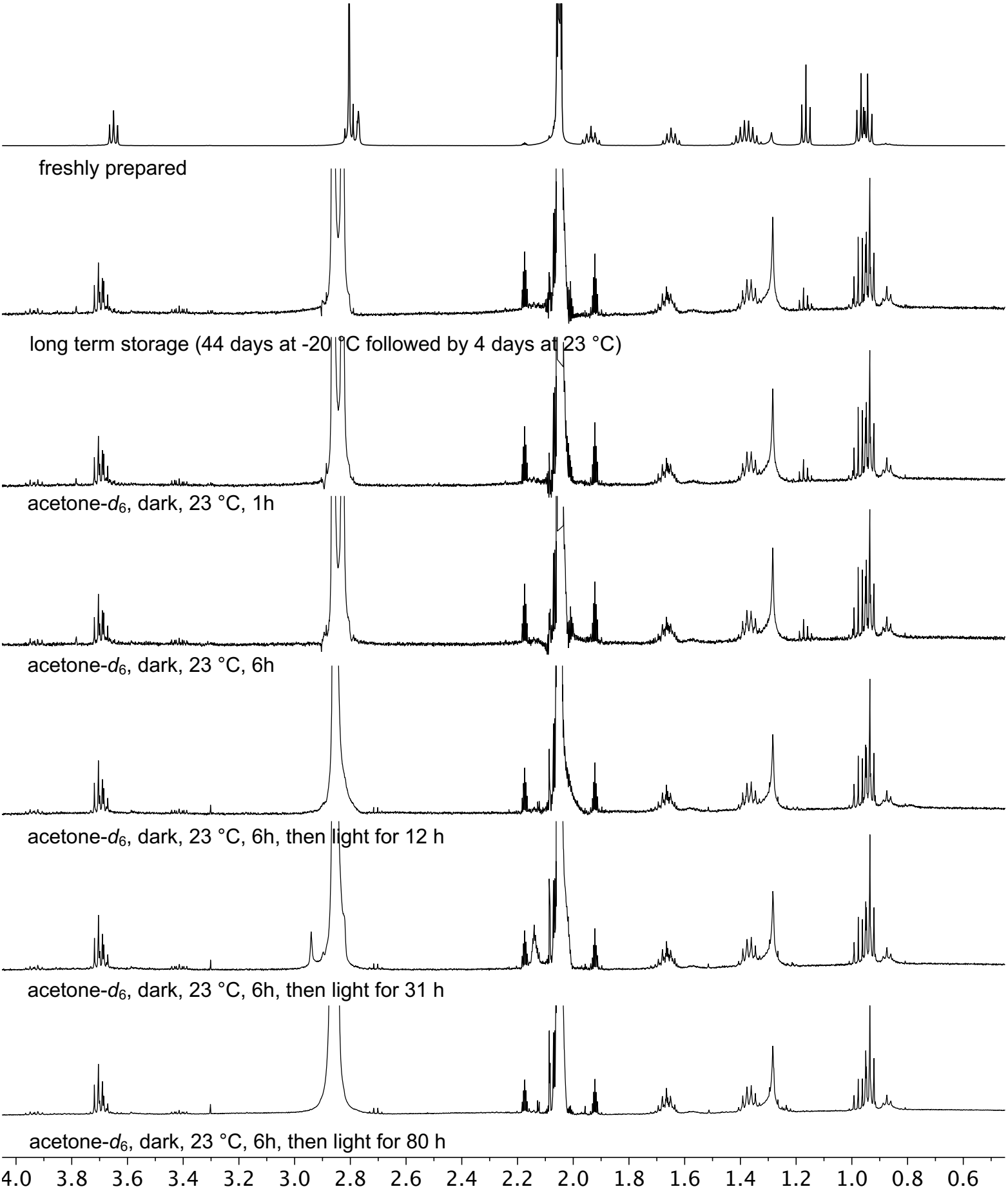
^{1}H NMR (500 MHz) spectra depicting the stability of **18c** (same sample) in acetone-d_6



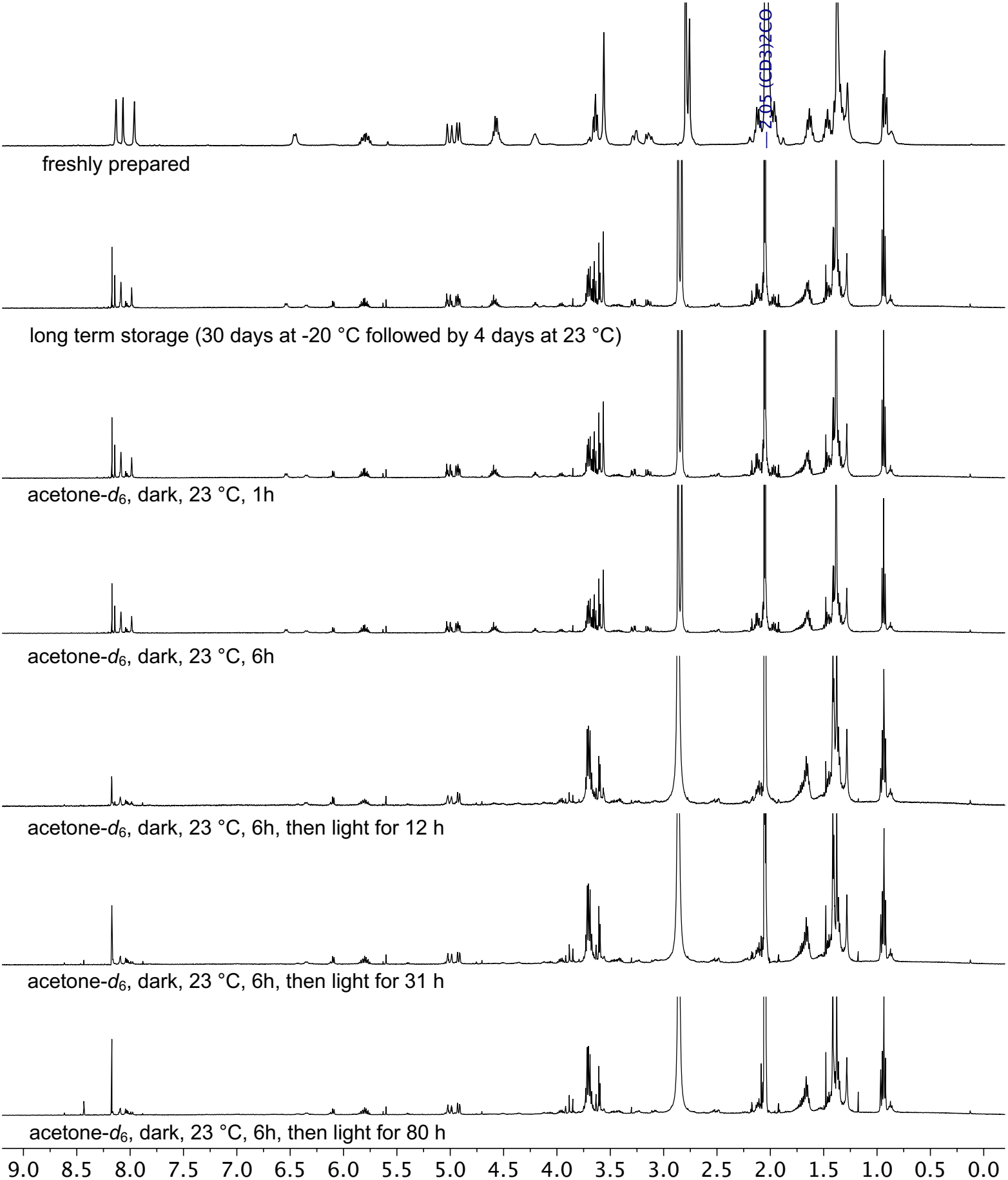
^{1}H NMR (500 MHz) spectra depicting the stability of **18c** (same sample) in acetone-d_6



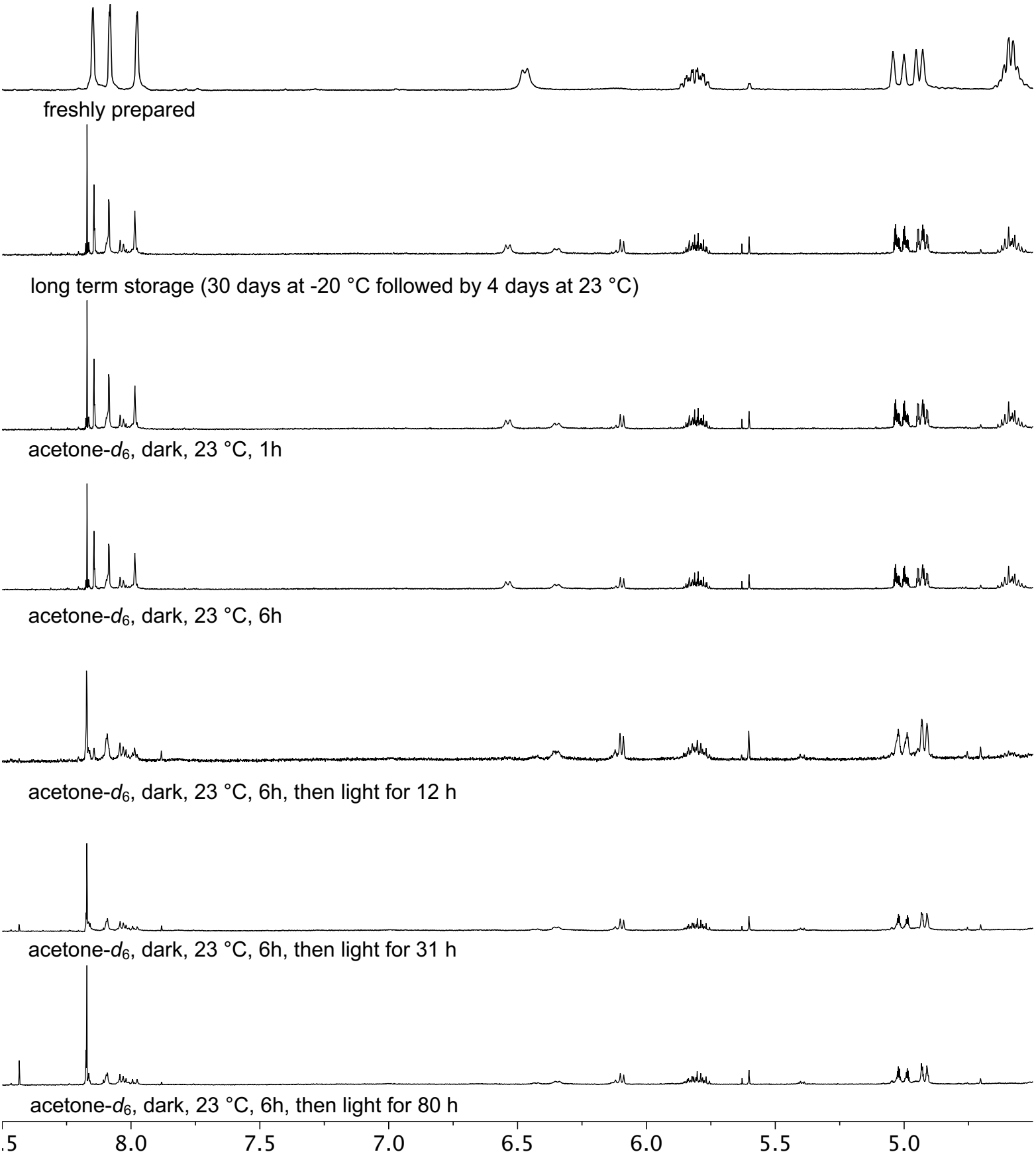
^{1}H NMR (500 MHz) spectra depicting the stability of **18c** (same sample) in acetone-d_6



^{1}H NMR (500 MHz) spectra depicting the stability of **18d** (same sample) in acetone-d_6



^{1}H NMR (500 MHz) spectra depicting the stability of **18d** (same sample) in acetone-d_6



^{1}H NMR (500 MHz) spectra depicting the stability of **18d** (same sample) in acetone-d_6