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Supporting Information for

A phenotypic approach to probing cellular outcomes using heterobivalent constructs

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1 General

Cell culture. HeLa ATCC and U2OS ATCC cells were cultured in complete medium [Dulbecco's Modified Eagle Medium (Sigma–Aldrich, D5796) supplemented with 10 vol% Fetal Bovine Serum (Sigma–Aldrich, F9665) and 1 vol% penicillin–streptomycin solution (Gibco), which was filtered through CA membrane (Corning, pore size 0.22 μm)] and trypsinized with 0.25% trypsin–0.02% EDTA 1× solution (Sigma–Aldrich, 59428C). For imaging, cells were fixed with 4% formaldehyde solution in PBS buffer (20 min at room temperature (RT)), bathed in AbDil–Tx buffer (TBS–Tx supplemented with 2% BSA and 0.05% sodium azide) for at least 40 min and stained with TRITC-phalloidin (Sigma–Aldrich, P1951; 1:500 dilution; 20 min) in TBS–Tx (TBS buffer with 0.1% Triton X-100) for F-actin; mouse FITC-α-tubulin DM1A (Sigma–Aldrich, F2168; 1:200 dilution; 1 h) in AbDil–Tx for tubulin and Hoechst 33342 (Sigma–Aldrich, D2261; 1:1000 dilution; 5 min) in TBS–Tx for the nucleus. Samples were mounted using antifade ProLong® Gold reagent (Molecular Probes). Rabbit p-MLC2 (S19) antibody was obtained from Cell Signaling (#3671; 1:200 dilution; 1 h) and was used along with goat anti-rabbit AlexaFluor-488 secondary antibody (Invitrogen, A31628; 1:100 dilution; 1 h).

Quantification of effects on organization of F-actin and microtubules (Figures 3C and 4C). Cell counting experiments were performed in triplicate. A total number of 500 cells were randomly selected and counted in each experiment.

Imaging (Figures 3A, 3B, and 4B). Images (Z-stacks) were recorded on Leica TSC SP8 STED 3X CW 3D (HC PL APO 93×/1.30 motCORR STED WHITE (glycerol)) or Zeiss LSM 510 Meta (PL APO 63×/1.4 (oil)) and were processed using LAS X or ImageJ (maximum intensity projection). Blue fluorescence (Hoechst, λ_{ex}= 405 nm, λ_{em} = 435–478 nm), green fluorescence (FITC, λ_{ex}= 488 nm, λ_{em} = 498–551 nm), red fluorescence (TRITC, λ_{ex}= 561 nm, λ_{em} = 569–622 nm).

Quantification of cellular uptake of DMACA constructs (Figure 5B). U2OS cells were grown for 16 h in 24-well ibidi® plates (#82406; 30k cells per well; total volume 500 μL). Cells were then treated with compounds DMACA–benzyl (**6a;** 30 μM), DMACA–C16:0 (**6c;** 10 μM, 30 μM), DMACA–DCA (**6d;** 30 μM, 50 μM) and DMACA–CDCA (**6e;** 30 μM, 50 μM) for 1 h. Live cell images were recorded after medium exchange (DMEM without phenol red; D1145, Sigma–Aldrich) on Zeiss LSM 510 Meta (PL APO 20×/0.8 DIC II) using DIC and λ_{ex}= 405 nm, λ_{em}= 435–478 nm. Experiments were done in triplicate and images were processed using ImageJ (sum slices):
mean cellular fluorescence = total fluorescence intensity / number of cells.

Small molecules. Y-27632 and GSK269962A were purchased from Cayman Chemical. Bile acids were purchased from Alfa Aesar (DCA, CDCA, LCA) and Acros (UDCA). HA-100, and ML-7 as free bases were prepared in-house. All stock solutions were 50 mM in DMSO (Sigma–Aldrich, D2650) and were diluted to the final concentration in complete medium. All small molecule experiments were repeated for at least three times (Figures 3, 4 and 5).

Synthetic chemistry. All chemicals were used as supplied. $B(OCH_2CF_3)_3$ was prepared as described.[1] Chromatographic separations were performed on ThoMar OHG silica gel 60Å (40–63 μm). Thin-layer chromatography was performed on Merck TLC Silica gel 60 F_{254} and visualised by UV (365/254 nm), $KMnO_4$ and/or phosphomolybdic acid. ^1H and ^{13}C NMR spectra were recorded on Bruker Avance 400 spectrometer. Residual solvent peaks were used as internal standards.[2] Chemical shifts are quoted in ppm using the following abbreviations: *s* singlet; *d* doublet; *t* triplet; *q* quartet; *qn* quintet; *sx* sextet; *non* nonet, *m* multiplet; *br* broad; or a combination thereof. The coupling constants *J* are measured in Hz. High resolution mass spectra (HRMS) were recorded on Agilent HPLC/Q-TOF G6540A mass spectrometer.

Rho-associated kinase activity assay. Rho kinase inhibition activity was determined using ROCK activity assay kit (Cat No. CSA001, Merck). Assay dilution buffer (10 μL), compounds (1 μL solution in DMSO), MQ water (9 μL), $MgCl_2$ solution (10 μL), ATP solution (10 μL), and active ROCK2 solution (10 μL) were added onto MYPT1 pre-coated plate. The control wells were exposed to 1 μL of DMSO. The plate was incubated at 30 °C for 30 min with medium agitation. Reaction was stopped by flicking the plate and washed with washing buffer 3 times followed by incubation with 100 μL of anti-phospho-MYPT (Thr696) primary antibody solution at 23 °C for 1 h with medium agitation. Primary antibody incubation was stopped by flicking the plate and washed with washing buffer 3 times followed by incubation with 100 μL of goat anti-rabbit IgG HRP secondary antibody solution at 23 °C for 1 h with medium agitation. Secondary antibody incubation was stopped by flicking the plate and was washed with washing buffer (3×) and TBS (2×). 100 μL of TMB/E solution was then added, it was developed in the dark for 90 sec and stopped by addition of 100 μL of the stop solution. Absorbance (450 nm) was recorded using TECAN plate reader. Rho kinase activity was expressed as percentage inhibition of control (DMSO). The Rho kinase activity was defined using the equation: $Rho\ kinase\ activity = (OD_{control} - OD_{compound})/OD_{control}$. One-way ANOVA followed by Bonferroni post-hoc test was done using SPSS. $^{***}p < 0.001$ *vs.* control to show significant difference.

Cell viability/cytotoxicity (MTT assay). MTT colorimetric assay was conducted in triplicate to determine cell viability. U2OS cells were grown for 16 h in 96-well plates (30k cells per well; total volume 200 μL). The test compounds were then added to the wells (in DMSO; less than 1% v/v final concentration in a well). The control cells were exposed to DMSO (2 μL). The cells were incubated for 3 h, then MTT (20 μL; 5 mg/mL solution in PBS) was added, and the cells were incubated for additional 2 h. The medium was then removed, DMSO (200 μL) was added, the plate was agitated and absorbance (570 nm) was recorded using TECAN plate reader. Cell viability is expressed as a percentage of control, using the equation: $cell\ viability = (OD_{compound} - OD_{blank})/(OD_{control} - OD_{blank})$. The cytotoxicity of compounds is expressed as concentration required to reduce the mean cell viability to 50% (CC_{50}). Dose–response curves were generated by non-linear regression analysis and CC_{50} values were determined using GraphPad Prism.

Figure S1.
Cytotoxicity of selected heterobivalent constructs.

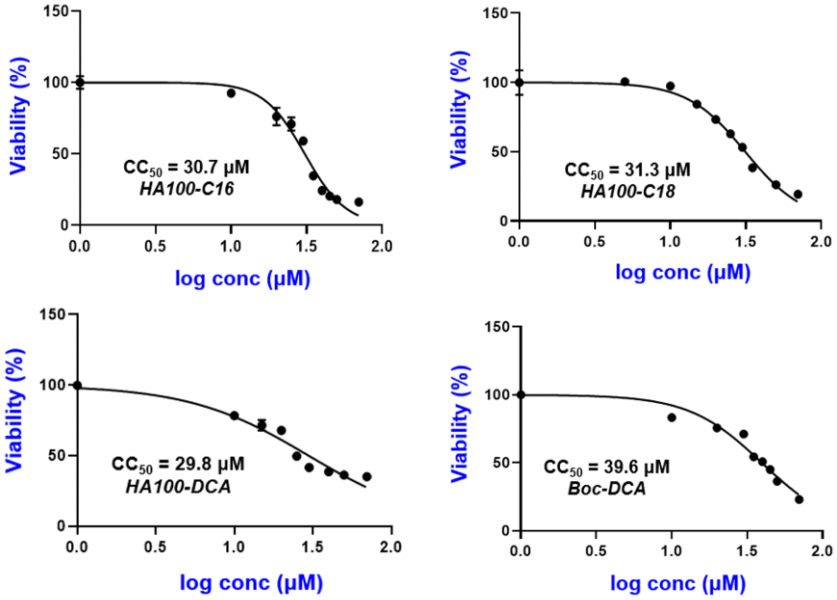


Table S1.
Cell viability of heterobivalent constructs used at 30 μM.

	#	compound	conc (μM)	viability (%)
controls		DMSO[a]	–	100.00 ± 3.57
		Y-27632	30	92.0 ± 3.46
		GSK 269962A	30	89.1 ± 4.72
	1	HA-100	30	93.6 ± 8.44
		Boc–C16:0	30	75.0 ± 6.57
		Boc–DCA	30	76.7 ± 0.93
		Boc–CDCA	30	74.5 ± 5.90
HA-100 constructs	2b	HA-100-Boc	30	88.7 ± 7.11
	2c	HA-100–C11:0	30	81.4 ± 2.44
	2d	HA-100–C15:0	30	69.0 ± 6.03
	2e	HA-100–C16:0	30	59.4± 2.49
	2f	HA-100–C18:0	30	49.4 ± 2.63
	2i	HA-100–DCA	30	37.7 ± 1.56
	2j	HA-100–CDCA	30	85.8 ± 3.22
ML-7 constructs	4	ML-7	30	63.8 ± 6.05
	5a	ML-7–Boc	30	85.4 ± 9.48
	5b	ML-7–C16:0	30	82.0 ± 2.92
	5c	ML-7–DCA	30	26.4 ± 0.84
	5d	ML-7–CDCA	30	55.2 ± 6.98

[a] DMSO (2 μL) was added as control.

Tabulated data from the table above.

compounds at 30 μM	warheads		
	Boc	HA-100	ML-7
parent compound (W)	n.a.	93.6 ± 8.44	63.8 ± 6.05
W–Boc	n.a	88.7 ± 7.11	85.4 ± 9.48
W–C16:0	75.0 ± 6.57	59.4 ± 2.49	82.0 ±2.92
W–DCA	76.7 ± 0.93	37.7 ± 1.56	26.4 ± 0.84
W–CDCA	74.5 ± 5.90	85.8 ± 3.22	55.2 ±6.98

Table S2.
Cell viability of heterobivalent constructs used at specific concentrations.

	#	*compound*	*conc (μM)*	*viability (%)*
		DMSO[a]	–	100.00 ± 3.57
controls	***1***	HA-100	70	76.1 ± 3.48
		Boc–DCA	70	30.4 ± 0.72
		Boc–CDCA	70	56.1 ± 3.11
		Boc–C16:0	70	63.4 ± 3.36
HA-100 constructs	***2c***	HA-100–C11:0	70	35.1 ± 0.31
	2d	HA-100–C15:0	70	15.1 ± 0.40
	2e	HA-100–C16:0	50	23.8 ± 0.88
	2f	HA-100–C18:0	50	30.7 ± 2.83
	2i	HA-100–DCA	50	36.3 ± 2.35
	2k	HA-100–LCA	100	150.7 ± 9.4
	2k	HA-100–LCA	200	138.1 ± 12.3
	2l	HA-100–UDCA	150	101.0 ± 2.17
	2g	HA-100–lipoic	150	93.0 ± 0.73
	2g	HA-100–lipoic	200	82.8 ± 3.38
	2h	HA-100–biotin	200	63.9 ± 2.81
ML-7 constructs	***4***	ML-7	40	36.6 ± 5.36
	5a	ML-7–Boc	100	77.5 ± 4.87
	5b	ML-7–C16:0	70	48.9 ± 3.60

[a] DMSO (2 μL) was added as control.

Figure S2.

ML-7 derivatives do not inhibit Rho kinase *in vitro.*

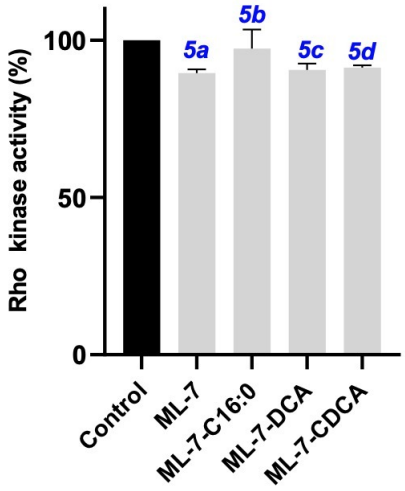


Figure S3.

HA-100 (ROCK) and bile acid Boc-PEG-linked controls show no interference. Stained for F-actin, α-tubulin and the nucleus. 5 h treatments. Scale bars, 20 μm.

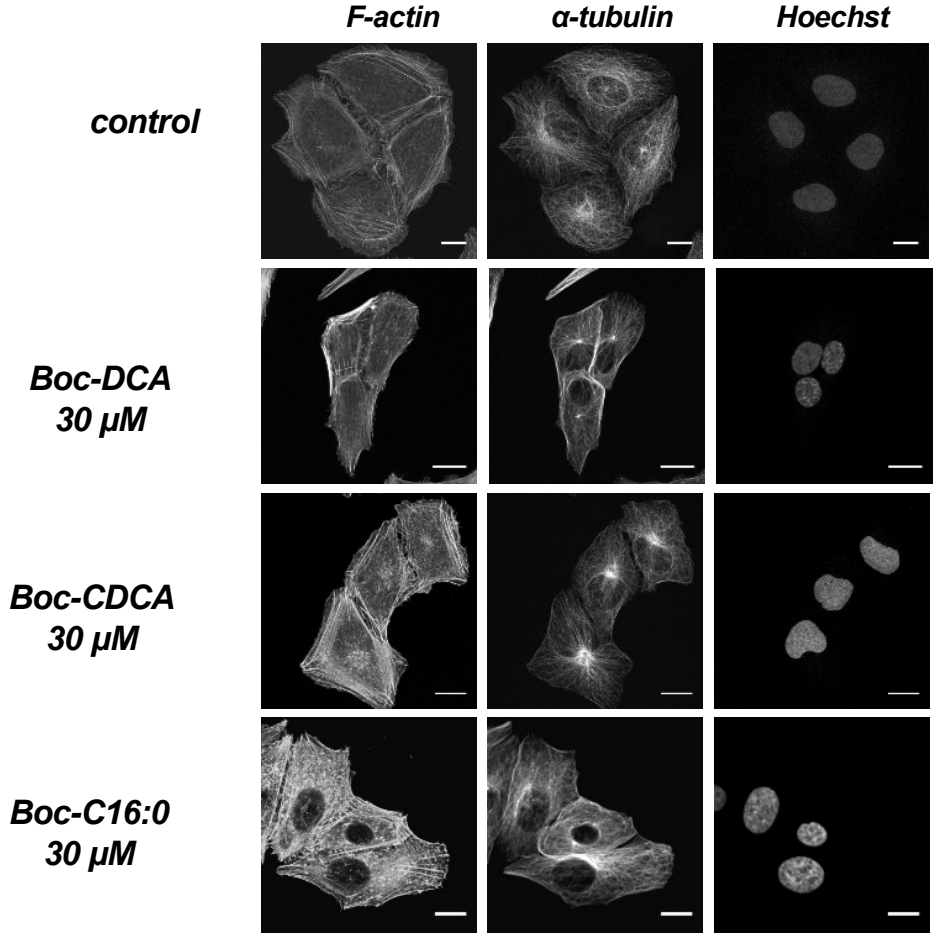
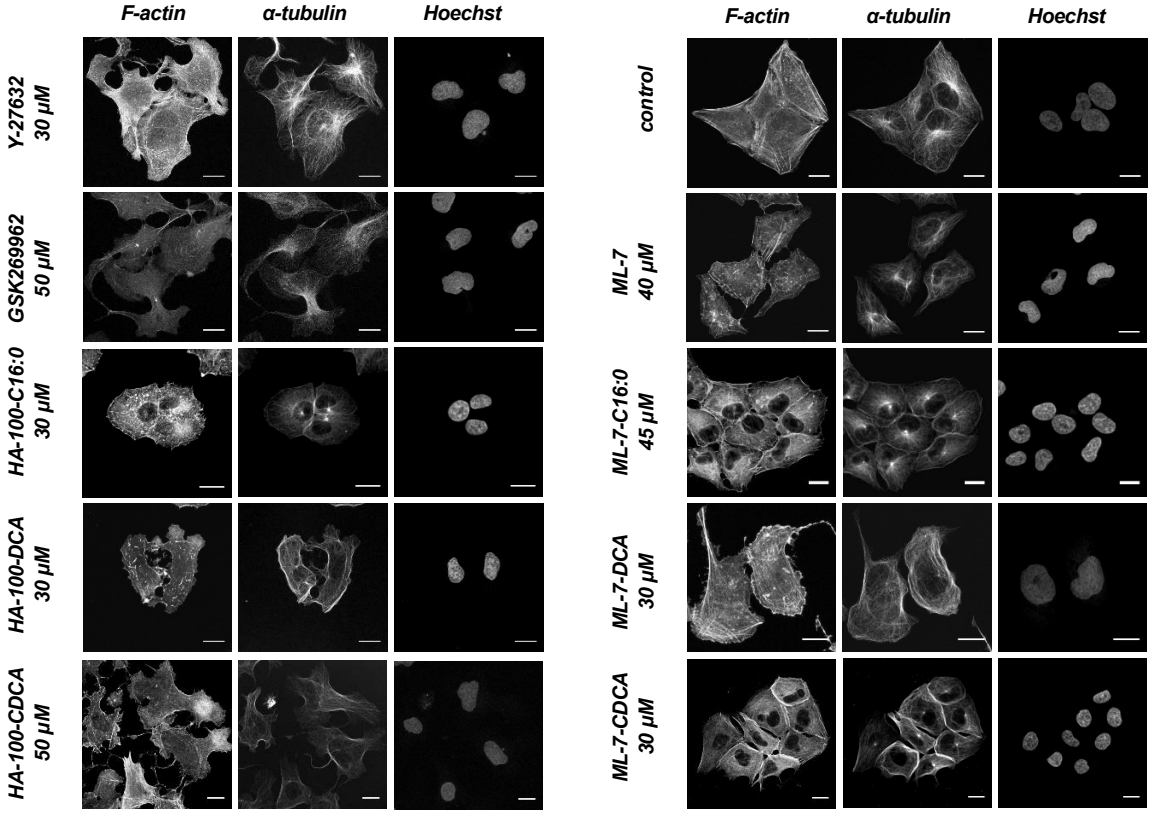


Figure S4.

Microtubule meshwork after treatment (5 h) with ROCK (Y-27632 and GSK269962) and MLCK (ML-7) inhibitors, and related C16:0, DCA, and CDCA constructs. Stained for F-actin, α-tubulin and the nucleus. 5 h treatments. Scale bars, 20 μm.

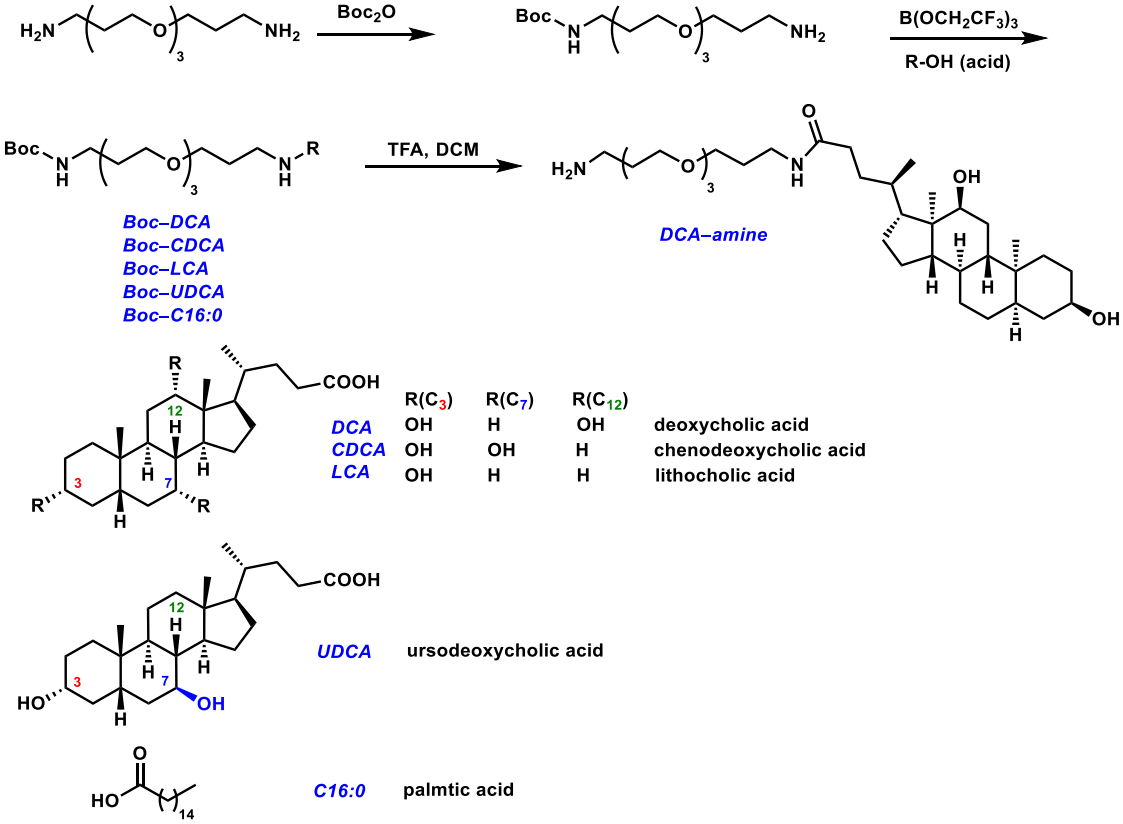


2 Synthetic Procedures

2.1 Boc-protected linker-extended bile acid constructs

Figure S5.

Boc-protected linker-extended bile acid constructs.



***tert*-Butyl (3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)carbamate**[3]

A solution of Boc anhydride (5.61 g, 25.7 mmol, 1 equiv) in DCM (15 mL) was added dropwise to a solution of 4,7,10-trioxa-1,13-tridecanediamine (5.668 g, 25.7 mmol, 1 equiv) in DCM (15 mL) at 0 °C and left to stir gruadlly warming up to room temperature. After 3 h, the reaction mixture was concentrated under reduced pressure and purified by flash chromatography (EtOAc/DCM 1:1 with 1→2% NH_3/MeOH) to give the desired compound as a colorless oil (2.41 g, 7.52 mmol, 29%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.10 (br s, 1H), 3.65–3.51 (m, 12H), 3.21 (q, 2H, *J* = 5.7), 2.79 (t, 2H, *J* = 6.7), 1.78–1.69 (m, 4H), 1.61 (br s, 2H), 1.42 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.2, 79.0, 70.7, 70.4, 70.3, 69.69, 69.65, 39.8, 38.6, 33.3, 29.8, 28.6, one carbon is not observed due to overlapping.

***tert*-Butyl ((*R*)-18-((3*R*,5*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,12-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-15-oxo-4,7,10-trioxa-14-azanonadecyl)carbamate [Boc–DCA]**

A solution of *tert*-butyl (3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)carbamate (98 mg, 0.305 mmol, 1 equiv), deoxycholic acid (121 mg, 0.305 mmol, 1 equiv) and $B(OCH_2CF_3)_3$ (198 µL, 0.915 mmol, 3 equiv) in MeCN (1.5 mL) was heated at 80 °C. After 12 h, DCM was added and the mixture washed with 1 M HCl and sat $NaHCO_3$ solutions. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the desired compound as a pale yellow oil (58 mg, 0.081 mmol, 27%).

^{1}H NMR (CD_3OD, 400 MHz) δ 3.95 (s, 1H), 3.65–3.49 (m, 13H), 3.24 (t, 2H, *J* = 6.6), 3.12 (t, 2H, *J* = 6.7), 2.27–2.20 (m, 1H), 2.13–2.06 (m, 1H), 1.93–1.66 (m, 12h), 1.61–1.46 (m, 8H), 1.43 (s, 9H), 1.37–1.20 (m, 6H), 1.18–1.07 (m, 2H), 1.02 (d, 3H, *J* = 6.3), 0.93 (s, 3H), 0.70 (s, 3H).
^{13}C NMR (CD_3OD, 100 MHz) δ 176.8, 158.4, 79.8, 74.0, 72.5, 71.6, 71.2, 69.9, 48.1, 47.6, 43.6, 38.7, 37.8, 37.4, 37.2, 36.8, 36.4, 35.3, 34.8, 34.2, 33.4, 31.1, 30.9, 30.4, 29.9, 28.7, 28.4, 27.5, 24.9, 23.7, 17.7, 13.2, five carbons are not observed due to overlapping.
HRMS for $C_{39}H_{71}N_2O_8$ $[M+H]^+$ found 695.5226, calc. 695.5205.

***tert*-Butyl (15-oxo-4,7,10-trioxa-14-azatriacontyl)carbamate [Boc–C16:0]**
A solution of *tert*-butyl (3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)carbamate (247 mg, 0.771 mmol, 1.0 equiv), palmitic acid (217 mg, 0.848 mmol, 1.0 equiv), $B(OCH_2CF_3)_3$ (498 µL, 1.542 mmol, 3.0 equiv) and TEA (247 µL, 2.313 mmol, 2.0 equiv) in MeCN (5 mL) was left to stir at 90 °C. After 12 h, DCM was added and the mixture was washed with 1 M HCl and sat K_2CO_3 solutions. The organic layer was dried over Na_2SO_4, filtered and concentrated to give the desired compound as a pale yellow oil (392 mg, 0.701 mmol, 91%).
^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.26 (br s, 1H), 4.98 (br s, 1H), 3.50–3.48 (m, 12H), 3.32–3.31 (m, 2H), 3.18–3.17 (m, 2H), 2.10 (t, 2H, *J* = 7.4), 1.75–1.72 (m, 4H), 1.56 (m, 2H), 1.39 (s, 9H), 1.26 (m, 24H), 0.83 (t, 3H, *J* = 6.2)
^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.2, 156.1, 78.9, 70.6, 70.56, 70.3, 70.2, 69.6, 38.6, 37.9, 36.9, 32.0, 29.73, 29.70, 29.6, 29.5, 29.43, 29.40, 29.1, 28.5, 25.9, 22.7, 14.2, six carbon not observed due to overlapping.
HRMS for $C_{31}H_{63}N_2O_6$ $[M+H]^+$ found 559.4684, calc. 559.4681.

***tert*-Butyl ((*R*)-18-((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3,7-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-15-oxo-4,7,10-trioxa-14-azanonadecyl)carbamate [Boc–CDCA]**
A solution of *tert*-butyl (3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)carbamate (102.8 mg, 0.321 mmol, 1.0 equiv), chenodeoxycholic acid (126 mg, 0.321 mmol, 1.0 equiv) and $B(OCH_2CF_3)_3$ (207 µL, 0.963 mmol, 3.0 equiv) in MeCN (1.5 mL) was heated at 80 °C. After 12 h, DCM was added and the mixture was washed with 1 M HCl and sat $NaHCO_3$ solutions. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the desired compound as a pale yellow oil (75 mg, 0.108 mmol, 34%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.18 (br s,1H), 4.98 (br s, 1H), 3.83 (s, 1H), 3.65–3.40 (m, 14H), 3.34 (q, 2H, *J* = 6.0), 3.20 (q, 2H, *J* = 6.2), 2.21–2.16 (m, 2H),2.07–1.90 (m, 4H),

1.82–1.73 (m, 8H), 1.69–1.58 (m, 3H), 1.52–1.47 (m, 2H), 1.43 (s, 9H), 1.37–1.24 (m, 6H), 1.15–1.10 (m, 4H), 0.92 (d, 2H, *J* = 6.5), 0.89 (s, 3H), 0.65 (s, 3H).
^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.7, 156.2, 79.1, 72.0, 70.63, 70.60, 70.3, 70.2, 69.7, 68.5, 56.0, 50.6, 42.8, 41.6, 40.0, 39.8, 39.5, 38.6, 38.0, 35.6, 35.4, 35.1, 34.7, 33.6, 32.9, 31.9, 30.7, 29.8, 29.1, 28.6, 28.3, 23.8, 22.9, 20.7, 18.5, 11.9, one carbon is not observed due to overlapping.
HRMS for $C_{39}H_{71}N_2O_8$ $[M+H]^+$ found 695.5225, calc. 695.5205.

***tert*-Butyl ((*R*)-18-((3*R*,5*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3-hydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-15-oxo-4,7,10-trioxa-14-azanonadecyl)carbamate [Boc–LCA]**
A solution of *tert*-butyl (3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)carbamate (106.8 mg, 0.333, mmol, 1 equiv), lithocholic acid (125 mg, 0.332 mmol, 1.0 equiv) and $B(OCH_2CF_3)_3$ (215 µL, 0.999 mmol, 3.0 equiv) in MeCN (1.5 mL) was heated at 80 °C. After 12 h, DCM was added and the mixture was washed with 1 M HCl and sat $NaHCO_3$ solutions. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the desired compound as a pale yellow oil (81 mg, 0.119 mmol, 36%).
^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.21 (br s, 1H), 4.99 (br s, 1H), 3.64–3.50 (m, 14H), 3.32 (q, 2H, *J* = 6.0), 3.19 (q, 2H, *J* = 6.0), 2.22–2.15 (m, 3H), 2.05–1.92(m, 2H), 1.84–1.72 (m, 8H), 1.65–1.62 (m, 1H), 1.55–1.47 (m, 2H), 1.41 (s, 9H), 1.37–1.21 (m, 10H), 1.14 –0.94 (m, 5H), 0.89 (t, 6H, *J* = 3.2), 0.61 (s, 3H)
^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.7, 156.2, 79.1, 71.8, 70.64, 70.61, 70.6, 70.3, 70.2, 69.7, 56.6, 56.1, 42.8, 42.2, 40.5, 40.3, 38.6, 37.9, 36.5, 35.9, 35.6, 35.5, 34.7, 33.7, 31.9, 30.6, 29.8, 29.1, 28.6, 28.3, 27.3, 26.5, 24.3, 23.5, 20.9, 18.5, 12.2.
HRMS for $C_{39}H_{71}N_2O_7$ $[M+H]^+$ found 679.5263, calc. 679.5256.

***tert*-Butyl ((*R*)-18-((3*R*,5*S*,7*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3,7-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-15-oxo-4,7,10-trioxa-14-azanonadecyl)carbamate [Boc–UDCA]**
A solution of *tert*-butyl (3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)carbamate (148 mg, 0.461 mmol, 1 equiv), ursodeoxycholic acid (181 mg, 0.461 mmol, 1.0 equiv) and $B(OCH_2CF_3)_3$ (199 µL, 0.922 mmol, 2.0 equiv) in MeCN (1.5 mL) was heated at 80 °C. After 12 h, DCM was added and the mixture was washed with 1 M HCl and sat $NaHCO_3$ solutions. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the desired compound as a pale yellow oil (110 mg, 0.158 mmol, 34%).
^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.29 (br s, 1H), 5.01 (br s, 1H), 3.62–3.48 (m, 14H), 3.31 (q, 2H, *J* = 6.0), 3.17, (q, 2H, *J* = 5.9), 2.22-2.14 (m, 2H), 2.04–1.95 (m, 4H), 1.82–1.71 (m, 8H), 1.62–1.46 (m, 7H), 1.40 (s, 9H), 1.30–1.21 (m, 6H), 1.14–0.98 (m, 3H), 0.91 (s, 6H), 0.63 (s, 3H).
^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.6, 156.2, 79.0, 71.3, 71.3, 70.59, 70.56, 70.3, 70.2, 70.1, 69.6, 55.9, 55.1, 43.80, 43.76, 42.5, 40.3, 39.3, 38.5, 37.9, 37.4, 37.1, 35.5, 35.0, 34.1, 33.7, 31.9, 30.4, 29.7, 29.1, 28.8, 28.5, 27.0, 23.5, 21.2, 18.6, 12.2.
HRMS for $C_{39}H_{70}N_2O_8Na$ $[M+Na]^+$ found 717.5029, calc. 717.5024.

(*R*)-*N*-(3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)-4-((3*R*,5*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,12-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanamide [DCA–amine]

A solution of *tert*-butyl ((*R*)-18-((3*R*,5*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,12-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-15-oxo-4,7,10-trioxa-14-azanonadecyl)carbamate (560 mg, 0.806 mmol, 1.0 equiv) in 4 M HCl solution in 1,4-dioxane (4 mL) was left to stir at RT. After 2 h, the mixture was concentrated under reduced pressure, redissolve in aq. K_2CO_3 solution, extracted with DCM, dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the desired product as a yellow brown oil (460 mg, 0.773 mmol, 96%).

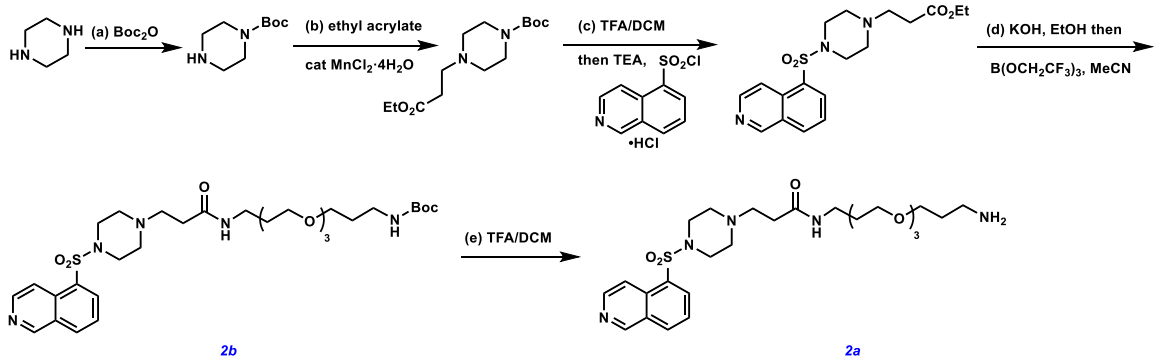
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.57 (t, 1H, *J* = 5.2), 3.95 (s, 1H), 3.65–3.63 (m, 4H), 3.61–3.55 (m, 10H), 3.34 (q, 2H, *J* = 9.0), 2.83 (br s, 2H), 2.24–2.16 (m, 4H), 2.10–2.02 (m, 1H), 1.86–1.64 (m, 11H), 1.60–1.47 (m, 5H), 1.44–1.34 (m, 6H), 1.31–1.23 (m, 2H), 1.13–1.06 (m, 2H), 0.98 (d, 3H, *J* = 6.3), 0.90 (s, 3H), 0.66 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 73.1, 71.8, 70.7, 70.6, 70.3, 70.2, 70.19, 69.8, 48.4, 47.1, 46.6, 42.2, 39.8, 37.9, 36.6, 36.2, 35.4, 35.3, 34.3, 33.8, 33.4, 32.7, 31.8, 30.7, 29.0, 28.8, 27.6, 27.3, 26.3, 23.8, 23.3, 17.6, 12.9.

HRMS for $C_{34}H_{63}N_2O_6$ $[M+H]^+$ found 595.4684, calc. 595.4681.

2.2 HA-100 constructs

Figure S6.
Preparation of the free amine HA–100 based construct.



***tert*-Butyl piperazine-1-carboxylate**[4]
A solution of Boc_2O (2.53 g, 11.6 mmol, 0.5 equiv) in DCM (10 mL) was added dropwise to a solution of piperazine (2.01 g, 23.3 mmol, 1.0 equiv) in DCM (15 mL) at 0 °C and allowed to warm up to RT. After 5 h, the reaction mixture was concentrated under reduced pressure, dissolved in Et_2O and extracted with 1 M citric acid (2×30 mL). The aqueous layer was washed with EtOAc (2×30 mL), basified by adding solid K_2CO_3 and back-extracted with EtOAc (3×30 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure to give the desired compound as a colourless solid (715 mg, 3.83 mmol, 33%).
^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.36 (t, 4H, *J* = 5.1), 2.79 (t, 4H, *J* = 5.1), 1.59 (s, 1H), 1.44 (s, 9H).
^{13}C NMR ($CDCl_3$, 100 MHz) δ 155.0, 79.7, 47.4, 46.0, 28.5.

5-(Piperazin-1-ylsulfonyl)isoquinoline [HA-100]
5-(Chlorosulfonyl)isoquinolin-2-ium chloride (191 mg, 0.725 mmol, 1.0 equiv) was added to a solution of *tert*-butyl piperazine-1-carboxylate (135 mg, 0.725 mmol, 1.0 equiv) and TEA (202 µL, 1.45 mmol, 2.0 equiv) in DCM (4 mL) and was left to stir at RT. After 2 h, aq sat $NaHCO_3$ solution was added and the reaction mixture was extracted with DCM (2×), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was treated with a 1:1 TFA/DCM solution (4 mL) for 1 h at RT, diluted with 1 M HCl and washed with DCM. The aqueous layer was basified with solid K_2CO_3, extracted with DCM, dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the desired compound as a colourless solid (112 mg, 0.404 mmol, 56%).
^{1}H NMR (400 MHz, DMSO-d_6) δ 9.51 (s, 1H), 8.72 (d, 1H, *J* = 6.1), 8.53 (d, 1H, *J* = 8.2), 8.47 (d, 1H, *J* = 6.2), 8.36 (dd, 1H, *J* = 7.4, 1.2), 7.91 (t, 1H, *J* = 7.7), 2.95 (t, 4H, *J* = 4.9), 2.68 (t, 4H, *J* = 4.9).
^{13}C NMR (100 MHz, DMSO-d_6) δ 153.5, 144.9, 134.3, 131.1, 130.9, 128.7, 126.5, 117.2, 46.3, 44.8.
HRMS for $C_{13}H_{16}N_3O_2S$ $[M+H]^+$ found 278.0962, calc. 278.0958.

***tert*-Butyl 4-(3-ethoxy-3-oxopropyl)piperazine-1-carboxylate**

A solution of *tert*-butyl piperazine-1-carboxylate (315 mg, 1.69 mmol, 1.0 equiv), ethyl acrylate (0.183 mL, 1.69 mmol, 1.0 equiv) and $MnCl_2 \cdot 4H_2O$ (33 mg, 0.166 mmol, 10 mol%) in MeOH/H_2O (1:1, 5 mL) was stirred for 4 h at RT. After removal of methanol under reduced pressure, EtOAc was added and the mixture was filtered extracted with EtOAc, dried over Na_2SO_4 filtered through silica gel pad to give the desired compound as a colorless oil (405 mg, 1.41 mmol, 84%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.14 (q, 2H, *J* = 7.1), 3.41 (br s, 4H), 2.70 (t, 2H, *J* = 7.1), 2.49 (t, 2H, *J* = 7.1), 2.45–2.35 (m, 4H), 1.45 (s, 9H), 1.25 (t, 3H, *J* = 7.2).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 154.9, 79.8, 60.6, 53.7, 52.8, 43.7, 32.4, 28.6, 14.4.

HRMS for $C_{14}H_{27}N_2O_4$ $[M+H]^+$ found 287.1972, calc. 287.1965.

Ethyl 3-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)propanoate

A solution of *tert*-butyl 4-(3-ethoxy-3-oxopropyl)piperazine-1-carboxylate (102 mg, 0.356 mmol, 1.0 equiv) in TFA/DCM (1:1 ratio, 3 mL) was left to stir at RT. After 1 h, toluene was added and the mixture was concentrated under reduced pressure (2×). 5-(Chlorosulfonyl)isoquinolin-2-ium chloride (94 mg, 0.356 mmol, 1.0 equiv) was added to a solution of the residue and Et_3N (148 μL, 1.06 mmol, 3.0 equiv) in DCM (5 mL) and the mixture was left to stir at RT. After 2 h, the mixture was basified with K_2CO_3 solution, extracted with DCM (2×20 mL), dried over Na_2SO_4, filtered, concentrated under reduced pressure and purified by flash chromatography (EtOAc/DCM 1:5→1:3) to give the desired compound as a yellow oil (98 mg, 0.259 mmol, 74%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.26 (s, 1H), 8.59 (d, 1H, *J* = 6.2), 8.45 (d, 1H, *J* = 6.2,), 8.27 (dd, 1H, *J* = 7.4, 1.1), 8.14 (d, 1H, *J* = 8.2), 7.64 (t, 1H, *J* =7.8), 3.98 (q, 2H, *J* = 7.1), 3.08 (t, 4H, *J* = 4.3), 2.57 (t, 2H, *J* = 7.1), 2.42 (t, 4H, *J* = 4.9), 2.31 (t, 2H, *J* = 7.1), 1.10 (t, 3H, *J* = 7.1).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.0, 153.3, 145.1, 134.2, 133.9, 132.0, 131.8, 129.0, 125.9, 117.7, 60.4, 53.0, 52.0, 45.6, 32.2, 14.1.

HRMS for $C_{18}H_{24}N_3O_4S$ $[M+H]^+$ found 387.1489, calc. 378.1482.

***tert*-Butyl (17-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)carbamate [HA-100–Boc]**

A solution of ethyl 3-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)propanoate (185 mg, 0.490 mmol, 1.0 equiv) and KOH (27.5 mg, 0.490 mmol, 1.0 equiv) in anhydrous ethanol was stirred at RT. After 2 h, the mixture was concentrated under reduced pressure, redissolved in acetonitrile (5 mL), charged with *tert*-butyl (3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)carbamate (157 mg, 0.490 mmol, 1.0 equiv) and $B(OCH_2CF_3)_3$ (211 μL,0.490, mmol, 2.0 equiv) and left to stir at 80 °C. After 12 h, the mixture was diluted with DCM, washed with sat. $NaHCO_3$ solution, dried over Na_2SO_4, filtered, concentrated under reduced pressure and purified by flash chromatography (DCM with 3%→10% MeOH) to give the desired compound (202 mg, 0.310 mmol, 63%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.22 (s, 1H), 8.54 (d, 1H, *J* = 6.2), 8.35 (d, 1H, *J* = 6.2), 8.23 (dd, 1H, *J* = 7.4, 1.2), 8.10 (d, 1H, *J* = 8.2), 7.59 (t, 1H, *J* = 7.7), 6.86 (s, 1H), 4.88 (s, 1H), 3.46–3.35 (m, 10H), 3.31 (t, 2H, *J* = 5.8), 3.12 (q, 2H, *J* = 6.3), 3.07 (s, 4H), 2.52 (t, 2H, *J* = 6.6), 2.39 (s, 4H), 2.16 (t, 4H, *J* = 6.6), 1.59 (qn, 2H, *J* = 6.3), 1.52 (qn, 2H, *J* = 6.2), 1.28 (s, 9H).

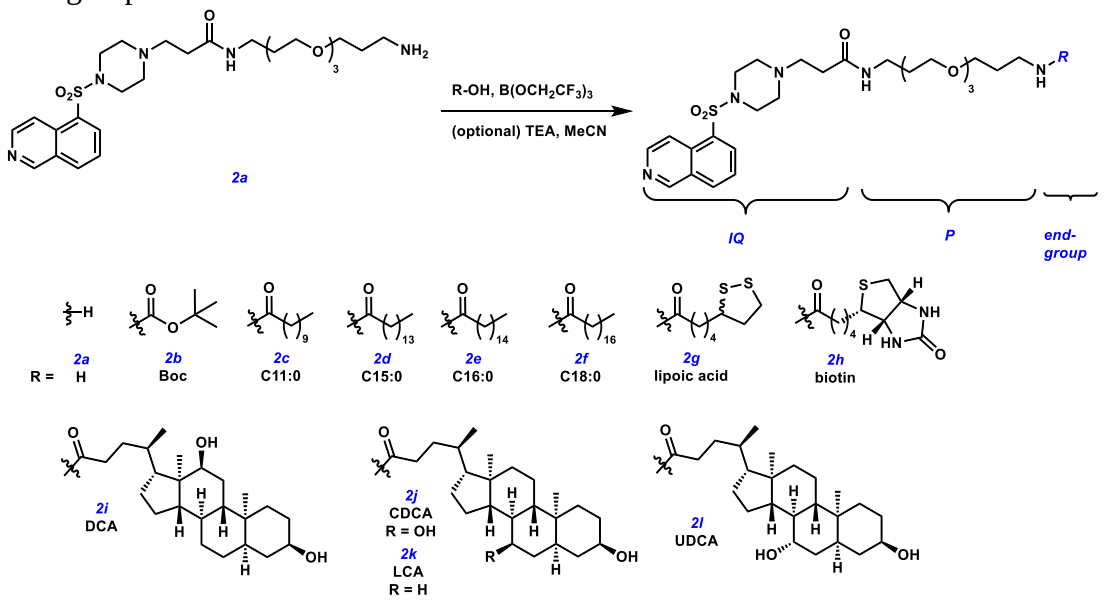
^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.4, 156.2, 153.4, 145.3, 134.4, 134.2, 132.1, 132.0, 129.2, 126.0, 117.7, 79.1, 70.6, 70.3, 70.2, 69.8, 69.6, 53.8, 52.1, 45.5, 38.6, 37.5, 33.1, 29.8, 29.2, 28.6, one carbon is not observed due to overlapping.
HRMS for $C_{31}H_{49}N_5O_8SNa$ $[M+Na]^+$ found 652.3303, calc. 652.3300.

***N*-(3-(2-(2-(3-Aminopropoxy)ethoxy)ethoxy)propyl)-3-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)propanamide**

tert-Butyl (17-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)carbamate (202 mg, 0.310 mmol, 1.0 equiv) was treated with TFA/DCM 1:1 (2 mL) and left to sitr at RT. After 1 h, the mixture was diluted with 1 M HCl and washed DCM, the aqueous layer was basified with K_2CO_3 solution, back-extracted with DCM, dried over Na_2SO_4 and concentrated under reduced pressure to give the desired compound (150 mg, 0.272 mmol, 88%).
^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.35 (s, 1H), 8.67 (d, 1H, *J* = 6.2), 8.50 (d, 1H, *J* = 6.2), 8.27 (dd, 1H, *J* = 1.2, 7.4), 8.23 (d, 1H, *J* = 8.2), 7.72 (t, 1H, *J* = 7.8), 7.28 (s, 1H), 7.11 (s, 1H), 3.61–3.50 (m, 8H), 3.44 (t, 2H, *J* = 5.8), 3.25 (q, 2H, *J* = 6.3), 3.18 (s, 4H), 2.84 (t, 2H, *J* = 6.5), 2.62 (t, 2H, *J* = 6.7), 2.51 (t, 4H, *J* = 4.8), 2.28 (t, 4H, *J* = 6.7), 1.7 (qn, 2H, *J* = 6.3), 1.66 (qn, 2H, *J* = 6.2).
^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.8, 153.4, 145.3, 134.5, 134.1, 132.2, 132.0, 129.2, 126.0, 117.8, 70.6, 70.5, 70.2, 70.1, 69.8, 69.5, 53.9, 52.1, 45.7, 39.9, 37.2, 33.2, 32.2, 29.2.
HRMS for $C_{26}H_{42}N_5O_6S$ $[M+H]^+$ found 552.2847, calc. 552.2850.

Figure S7.

End-group extension of the HA-100 free amine construct.



***N*-(17-(4-(Isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)undecanamide [HA-100–C11:0]**

A solution of *N*-(3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)-3-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)propanamide (30 mg, 0.0543 mmol, 1.0 equiv), undecanoic acid (10.3 mg, 0.0553 mmol, 1.0 equiv) and $B(OCH_2CF_3)_3$ (30 µL, 0.139 mmol, 2.5 equiv) in MeCN (2 mL) was left to stir at 100 °C. After 12 h, the mixture was diluted with DCM (5 mL), washed sat. $NaHCO_3$ solution, dried over Na_2SO_4, filtered, concentrated under reduced pressure and purified by flash chromatography (DCM with 2→5% MeOH and 1% TEA) to give the desired compound as a pale yellow oil (18 mg, 0.0250 mmol, 46%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.31 (s, 1H), 8.63 (d, 1H, *J* = 4.1), 8.46 (d, 1H, H = 5.5), 8.33 (d, 1H, *J* = 7.2), 8.20 (d, 1H, *J* = 8.0), 7.69 (t, 1H, *J* = 7.7), 7.04 (s, 1H,), 6.27 (s, 1H), 3.55-3.47 (m, 10H), 3.39 (t, 2H, *J* = 5.4), 3.28 (q, 2H, *J* = 6.2), 3.20 (q, 2H, *J* = 6.4), 3.14 (s, 4H), 2.58 (t, 2H, *J* = 6.1), 2.46 (s, 4H), 2.23 (t, 2H, *J* = 6.0), 2.10 (t, 2H , *J* = 7.4), 1.71 (qn, 2H, *J* = 6.3), 1.61 (qn, 2H, *J* = 6.3), 1.54 (t, 2H, *J* = 7.5), 1.19 (br S, 14H), 0.82 (t, 3H, *J* = 6.1).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.2, 171.3, 153.3, 145.1, 134.3, 134.1, 131.9, 131.8, 129.3, 126.0, 117.7, 70.42, 70.40, 70.05, 70.03, 69.9, 69.5, 53.7, 51.9, 45.5, 37.6, 37.2, 36.8, 33.0, 31.8, 29.5, 29.48, 29.4, 29.3, 29.27, 29.2, 29.17, 25.8, 22.6, 14.1

HRMS for $C_{37}H_{62}N_5O_7S$ $[M+H]^+$ found 720.4378, calc. 720.4364.

***N*-(17-(4-(Isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)pentadecanamide [HA-100–C15:0]**

A solution of *N*-(3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)-3-(4-(isoquinolin-5-ylsulfonyl) piperazin-1-yl)propanamide (30 mg, 0.0543 mmol, 1.0 equiv), pentadecanoic acid (13.2 mg 0.0544 mmol 1.0 equiv) and $B(OCH_2CF_3)_3$ (30 µL, 0.139 mmol, 2.5 equiv) in MeCN (2 mL) was left to stir at 100 °C. After 12 h, the mixture was diluted with DCM (5 mL), washed with sat. $NaHCO_3$ solution, dried over Na_2SO_4, filtered, concentrated under

reduced pressure and purified by flash chromatography (DCM with 2→5% MeOH and using 1% TEA) to give the desired compound as a brown yellow oil (16 mg, 0.0206 mmol, 38%).
^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.33 (s, 1H), 8.66 (d, 1H, *J* = 6.0), 8.48 (d, 1H, *J* = 6.1), 8.35 (dd, 1H, *J* = 7.4, 0.8), 8.22 (d, 1H, *J* = 8.2), 7.71 (t, 1H, *J* = 7.8), 7.03 (t, 1H, *J* = 5.0), 6.22 (t, 1H, *J* = 5.4), 3.59-3.47 (m, 10H), 3.41 (t, 2H, *J* = 5.9), 3.30 (q, 2H, *J* = 6.2), 3.22 (q, 2H, *J* = 6.3), 3.16 (s, 4H), 2.60 (t, 2H, *J* = 6.6), 2.48 (t, 4H, *J* = 4.3), 2.25 (t, 2H, *J* = 6.6), 2.10 (t, 2H , *J* = 7.6), 1.72 (qn, 2H, *J* = 6.2), 1.63 (qn, 2H, *J* = 6.3), 1.56 (t, 2H, *J* = 7.1), 1.21 (br S, 24H), 0.84 (t, 3H, *J* = 6.8).
^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.3, 171.5, 153.4, 145.2, 134.4, 134.1, 132.1, 131.9, 129.2, 126.0, 117.7, 70.51, 70.49, 70.13, 70.12, 70.0, 69.6, 53.8, 52.0, 45.6, 37.7, 37.3, 36.9, 33.1, 32.0, 29.74, 29.72, 29.70, 29.6, 29.5, 29.43, 29.41, 29.3, 29.25, 25.9, 22.7, 14.2, two carbons not observed due to overlapping.
HRMS for $C_{41}H_{70}N_5O_7S$ $[M+H]^+$ found 776.5002, calc. 776.4990.

***N*-(17-(4-(Isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)palmitamide [HA-100–C16:0]**
A solution of *N*-(3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)-3-(4-(isoquinolin-5-ylsulfonyl) piperazin-1-yl)propanamide (58 mg, 0.105 mmol, 1.0 equiv), palmitic acid (27 mg, 0.105 mmol, 1.0 equiv) and $B(OCH_2CF_3)_3$ (67 μL, 0.311 mmol, 3.0 equiv) in MeCN (1.5 mL) was left to stir at 90 °C. After 12 h, the mixture was diluted with DCM (5 mL), washed with sat. K_2CO_3 solution, dried over Na_2SO_4, filtered, concentrated under reduced pressure and purified by flash chromatography (DCM with 2→5% MeOH and 0.5→1 % ammonium hydroxide) to give the desired compound as a pale yellow oil (30 mg, 0.0380 mmol, 36%).
^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.37 (s, 1H), 8.69 (s, 1H), 8.48 (d, 1H, *J* = 4.9), 8.37 (d, 1H, *J* = 7.3), 8.24 (d, 1H, *J* = 8.1), 7.73 (t, 1H, *J* =7.8), 7.02 (s, 1H), 6.18 (s, 1H), 3.64–3.51 (m, 10H), 3.45 (t, 2H, *J* = 5.7), 3.32 (q, 2H, *J* = 6.1), 3.25 (t, 4H, *J* = 5.7), 2.69 (s, 2H), 2.58 (s, 4H), 2.33 (s, 2H), 2.12 (t, 2H, *J* = 7.6), 1.75 (qn, 2H, *J* = 6.1), 1.66 (qn, 2H, *J* = 6.1), 1.59, (t, 2H , *J* = 6.6), 1.24 (m, 26H), 0.87 (t, 3H, *J* = 6.6).
^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.2, 171.4, 153.3, 145.2, 134.4, 134.1, 132.0, 131.9, 129.1, 126.0, 117.7, 70.48, 70.47, 70.11, 70.10, 69.9, 69.6, 53.7, 52.0, 45.6, 37.7, 37.3, 36.9, 33.1, 31.9, 29.72, 29.69, 29.68, 29.6, 29.44, 29.40, 29.38, 29.3, 29.2, 25.9, 22.7, 14.2, three carbon not observed due to overlapping.
HRMS for $C_{42}H_{71}N_5O_7SNa$ $[M+Na]^+$ found 812.4970, calc. 812.4966.

***N*-(17-(4-(Isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)stearamide [HA-100–C18:0]**
A solution of *N*-(3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)-3-(4-(isoquinolin-5-ylsulfonyl) piperazin-1-yl)propanamide (63 mg, 0.114 mmol, 1.0 equiv), stearic acid (32 mg, 0.114 mmol, 1.0 equiv), $B(OCH_2CF_3)_3$ (74 μL, 0.344 mmol, 3.0 equiv) and TEA (32 μL, 0.230 mmol, 2.0 equiv) in MeCN (2 mL) was left to stir at 90 °C. After 12 h, the mixture was diluted with DCM (5 mL), washed with sat. K_2CO_3 solution, dried over Na_2SO_4, filtered, concentrated under reduced pressure and purified by flash chromatography (DCM with 2→5% MeOH and 0.5→1 % ammonium hydroxide) to give the desired compound as a pale yellow oil (38 mg, 0.0464 mmol, 41%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.36 (s, 1H), 8.68 (d, 1H, *J* = 6.0), 8.49 (d, 1H, *J* = 6.1), 8.37 (dd, 1H, *J* = 7.4, 1.1), 8.23 (d, 1H, *J* = 8.2), 7.72 (t, 1H, *J* = 7.8), 7.02 (s, 1H), 6.18 (s, 1H), 3.61–3.49 (m, 10H), 3.44 (t, 2H, *J* = 5.9), 3.32 (q, 2H, *J* = 6.3), 3.25 (q, 2H, *J* = 6.5), 3.21 (s, 4H), 2.65 (s, 2H), 2.54 (s, 4H), 2.29 (t, 2H , *J* = 6.3), 2.12 (t, 2H, *J* = 7.6), 1.75 (qn, 2H, *J* = 6.1), 1.66 (qn, 2H, *J* = 6.3), 1.58, (t, 2H, *J* = 7.2), 1.24 (m, 28H), 0.86 (t, 3H, *J* = 6.6).
^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.3, 171.4, 153.4, 145.3, 134.4, 134.2, 132.1, 132.0, 129.2, 126.0, 117.8, 70.57, 70.56, 70.2, 70.0, 69.7, 53.8, 52.1, 45.6, 37.8, 37.4, 37.0, 33.1, 32.0, 29.82, 29.79, 29.77, 29.7, 29.5, 29.49, 29.48, 29.3, 25.9, 22.8, 14.3, seven carbons are not observed due to overlapping.
HRMS for $C_{44}H_{76}N_5O_7S$ $[M+H]^+$ found 818.5469, calc. 818.5460.

5-(1,2-dithiolan-3-yl)-*N*-(17-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)pentanamide [HA-100–lipoic]
A solution of N-(3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)-3-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)propanamide (95 mg 0.172 mmol, 1.0 equiv), lipoic acid (46 mg, 0.224 mmol, 1.3 equiv) $B(OCH_2CF_3)_3$ (111 μL, 0 516 mmol, 3.0 equiv) and TEA (48 μL, 0.344 mmol, 2.0 equiv) in MeCN (2 mL) was left to stir at 90 °C. After 4 h the mixture was concentrated under reduced pressure and purified by flash chromatography (DCM with 3→5% MeOH, using 1% ammonium hydroxide) to give the desired compound as pale yellow oil (38 mg, 0.051 mmol, 30 %).
^{1}H NMR ($CDCl_3$, 400 MHz) 9.40 (s, 1H), 8.70 (s, 1H), 8.46 (d, 1H, J = 5,8), 8.35 (dd, 1H, J = 0.8, 7.4), 8.23 (d, 1H, J = 8.1), 7.71 (t, 1H, J = 7.8), 7.05 (br s, 1H), 6.35 (br s, 1H), 3.59–3.48 (m, 10H), 3.43(t, 2H, *J* = 5.9), 3.32–3.21 (m, 8H), 3.15–3.04 (m, 3H), 2.73 (br s, 2H), 2.61 (br s, 4H), 2.44–2.39 (m, 1H), 2.35 (br s, 2H), 2.12 (t, 2H, *J* = 7.5), 1.90–1.82 (m, 1H), 1.76–1.70 (m, 2H), 1.67–1.56 (m, 6H), 1.43–1.36 (m, 2H).
^{13}C NMR ($CDCl_3$, 100 MHz) δ. 172.9, 171.0, 153.3, 145.2, 134.4, 134.3, 131.9, 131.86, 129.5, 126.1, 117.8, 70.49, 70.47, 70.1, 70.0, 69.6, 56.6, 53.7, 52.0, 45.9, 45.1, 40.3, 38.5, 37.8, 37.5, 36.5, 34.7, 32.6, 29.21, 29.18, 29.0, 25.5
HRMS for $C_{34}H_{53}N_5O_7S_3$ $[M+H]^+$found 740.3167calc 740.3180.

***N*-(17-(4-(Isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)-5-((3a*S*,4*S*,6a*R*)-2-oxohexahydro-1*H*-thieno[3,4-*d*]imidazol-4-yl)pentanamide [HA-100–biotin]**
A solution of *N*-(3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)-3-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)propanamide (100 mg, 0.181 mmol, 1.0 equiv), D-biotin (50 mg, 0.223 mmol, 1.23 equiv), TEA (57 μL, 0.409 mmol, 2.26 equiv) and $B(OCH_2CF_3)_3$ (88 μL, 0.409 mmol, 2.26 equiv) in MeCN (1 mL) was left to stir at 70 °C. After 12 h, the mixture concentrated under reduced pressure and purified by flash chromatography (DCM with 5→8% MeOH and 1→2% of ammonia hydroxide) to give the desired compound as a yellow oil (13 mg, 16.7 μmol, 9%).
^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.36 (s, 1H), 8.67 (d, 1H, *J* = 6.2), 8.48 (d, 1H, *J* = 6.2), 8.37 (dd, 1H, *J* = 7.4, 1.2), 8.24 (d, 1H, *J* = 8.2), 7.73 (t, 1H, *J* =7.7), 7.23 (t, 1H, *J* = 5.3), 6.67 (t, 1H, *J* = 5.3), 6.08 (s, 1H), 5.32 (s, 1H), 4.50–4.47 (m, 1H), 4.31–4.28 (m, 1H), 3.61–3.50 (m, 10H), 3.44 (t, 2H, *J* = 6.0), 3.31 (q, 2H, *J* = 6.0), 3.27–3.22 (m, 6H), 3.15–3.10 (m, 1H), 2.88 (dd, 1H, *J* = 12.8, 4.9), 2.71 (d, 1H, *J* = 13.0), 2.67, (d, 2H, *J* = 6.6),

2.56 (s, 4H), 2.33 (t, 2H, *J* = 6.6), 2.17 (t, 2H, *J* = 7.4) 1.75 (qn, 2H, *J* = 6.2), 1.70–1.60 (m, 6H), 1.46–1.40 (m, 2H).
^{13}C NMR ($CDCl_3$, 100 MHz**)** δ 173.3, 171.6, 163.8, 153.4, 134.5, 134.2, 132.1, 132.0, 129.2, 126.1, 117.8, 70.54, 70.51, 70.1, 69.5, 61.9, 60.2, 55.7, 53.8, 52.0, 45.5, 40.7, 37.9, 37.2, 36.0, 33.0, 29.8, 29.3, 29.1, 28.2, 28.17, 25.7, one carbon is not observed due to overlapping.
HRMS $[M+Na]^+$ for $C_{36}H_{55}N_7O_8S_2Na$ found 800.3451, calc. 800.3446.

(*R*)-4-((3*R*,5*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,12-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-N-(17-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)pentanamide [HA-100–DCA]
A solution of *N*-(3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)-3-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)propanamide (213 mg, 0.386 mmol, 1.0 equiv), deoxycholic acid (152 mg, 0.387 mmol, 1.0 equiv) and $B(OCH_2CF_3)_3$ (250 μL, 1.161 mmol, 3.0 equiv) in MeCN (2 mL) was left to stir at 100 °C. After 12 h, the mixture was diluted with DCM, washed with aq. K_2CO_3 solution, dried over Na_2SO_4, filtered, concentrated under reduced and purified by flash chromatography (DCM with 5→10% MeOH and using 1% TEA) to give the desired compound as a pale yellow oil (69 mg, 74.5 μmol, 19%).
^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.36 (s, 1H), 8.68 (d, 1H, *J* = 6.2), 8.49 (d, 1H, *J* = 6.2), 8.38 (dd, 1H, *J* = 7.4, 1.1), 8.24 (d, 1H, *J* = 8.2), 7.73 (t, 1H, *J* = 7.8), 7.11 (s, 1H), 6.31 (s, 1H), 3.94 (s, 1H), 3.62–3.50 (m, 10H), 3.45 (t, 2H, *J* = 5.9), 3.33 (q, 2H, *J* = 6.1), 3.25 (q, 2H, *J* = 6.4), 3.21 (s, 4H), 3.09 (q, 1H, *J* = 7.3), 2.66 (s, 2H), 2.54 (s, 4H), 2.31 (t, 2H, *J* = 6.3), 2.24–2.16 (m, 1H), 2.09–2.01 (m, 2H), 1.77–1.71 (m, 8H), 1.69–1.63 (m, 4H), 1.53–1.47 (m, 4H), 1.42–1.37 (m, 6H), 1.25–1.22(m, 3H), 1.11–1.03 (m, 2H), 0.95 (d, 3H, *J* = 6.2), 0.89 (s, 3H), 0.65 (s, 3H).
^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.7, 171.6, 153.4, 145.2, 134.5, 134.2, 132.1, 131.9, 129.2, 126.1, 117.8, 73.1, 71.7, 70.5, 70.2, 70.12, 70.06, 69.6, 53.8, 52.0, 48.3, 47.1, 46.6, 46.1, 45.6, 42.1, 37.8, 37.3, 36.5, 36.1, 35.3, 35.25, 34.2, 33.7, 33.4, 33.1, 31.8, 30.6, 29.3, 29.2, 28.8, 27.6, 27.2, 26.3, 23.7, 23.2, 17.5, 12.8.
HRMS for $C_{50}H_{80}N_5O_9S$ $[M+H]^+$ found 926.5677, calc. 926.5671.

(*R*)-4-((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3,7-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-*N*-(17-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)pentanamide [HA-100–CDCA]
A solution of *N*-(3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)-3-(4-(isoquinolin-5-ylsulfonyl) piperazin-1-yl)propanamide (70 mg, 0.127 mmol, 1.0 equiv), chenodeoxycholic acid (50 mg, 0.127 mmol, 1.0 equiv), $B(OCH_2CF_3)_3$ (82 μL, 0.381 mmol, 3.0 equiv) and TEA (35 μL, 0.251 mmol, 2.0 equiv) in MeCN (2 mL) was left to stir at 90 °C. After 12 h, the mixture was concentrated under reduced pressure and purified by flash chromatography (DCM with 2→5% MeOH and 1→2 % ammonium hydroxide) to give the desired compound as a colourless oil (55 mg, 59.4 μmol, 47%).
^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.35 (s, 1H), 8.66 (d, 1H, *J* = 4.9), 8.47 (d, 1H, *J* = 5.4), 8.36 (d, 1H, *J* = 7.2), 8.23 (d, 1H, *J* = 8.0), 7.72 (t, 1H, *J* =7.7), 7.10 (s,1H), 6.28 (s, 1H), 3.80 (s, 1H), 3.58–3.49 (m, 10H), 3.44 (t, 2H, *J* = 5.9), 3.31 (q, 2H, *J* = 6.0), 3.26-3.22 (m,

6H), 2.66 (s, 2H), 2.54 (s, 4H), 2.30 (t, 2H, *J* = 5.8), 2.24–2.13 (m, 2H), 2.06–1.99 (m, 1H), 1.94-1.91 (m, 2H), 1.85–1.73 (m, 6H), 1.67–1.59 (m, 6H), 1.49–1.42 (m, 4H), 1.35–1.23 (m, 6H), 1.12–0.94 (m, 3H), 0.88 (d, 6H, *J* = 11.1), 0.62 (s, 3H).
^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.6, 171.3, 153.3, 145.1, 134.4, 134.1, 132.0, 131.9, 129.1, 126.0, 117.7, 71.9, 70.5, 70.4, 70.09, 70.06, 70.0, 69.6, 68.3, 55.7, 53.7, 51.9, 50.5, 45.4, 42.6, 41.5, 39.9, 39.7, 39.4, 37.8, 37.3, 35.4, 35.35, 35.1, 34.7, 33.3, 32.9, 31.8, 30.7, 29.7, 29.2, 29.1, 28.2, 23.7, 22.8, 20.6, 18.4, 11.8.
HRMS for $C_{50}H_{80}N_5O_9S$ $[M+H]^+$ found 926.5677, calc. 926.5671.

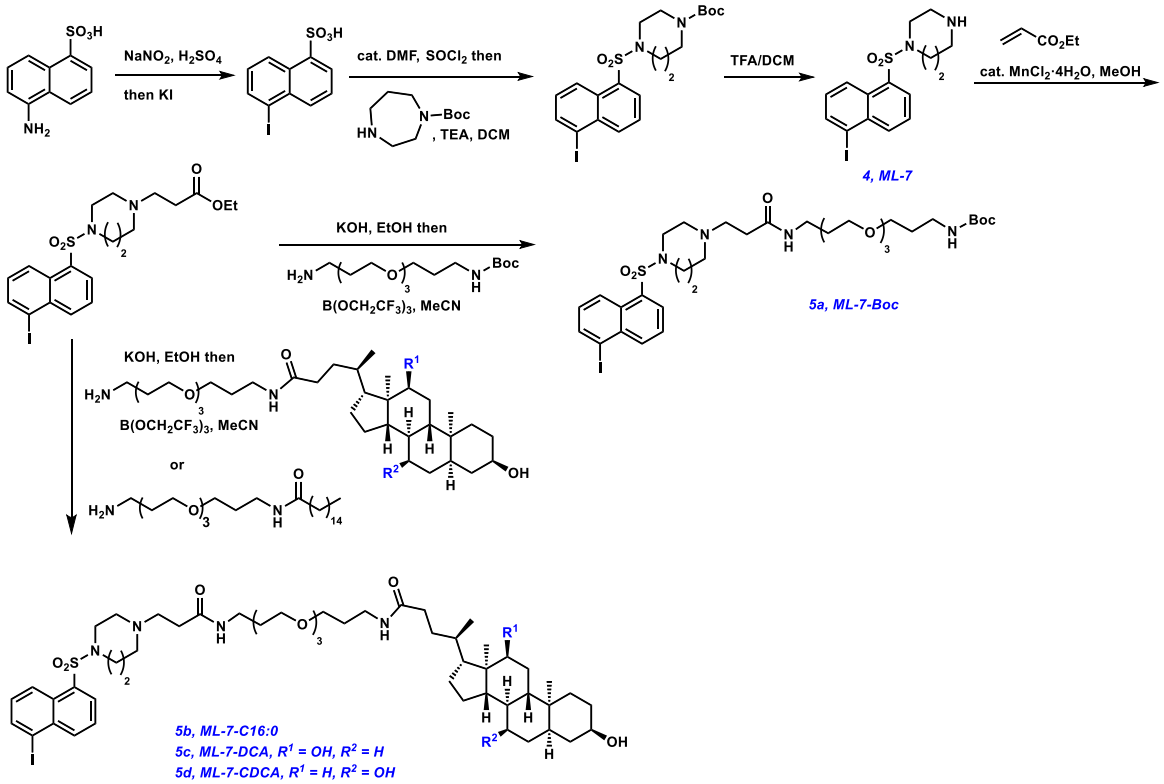
(*R*)-4-((3*R*,5*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3-hydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-*N*-(17-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)pentanamide [HA-100–LCA]
A solution of *N*-(3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)-3-(4-(isoquinolin-5-ylsulfonyl) piperazin-1-yl)propanamide (97 mg, 0.176 mmol, 1.0 equiv), lithocholic acid (66 mg, 0.175 mmol, 1.0 equiv), $B(OCH_2CF_3)_3$ (113 µL, 0.525 mmol, 3.0 equiv) and TEA (49 µL, 0.352 mmol, 2.0 equiv) in MeCN (2 mL) was left to stir at 90 °C. After 12 h, the mixture was concentrated under reduced pressure and purified by flash chromatography (DCM with 2→5% MeOH and 1→2 % ammonium hydroxide) to give the desired compound as a pale yellow oil (70 mg, 76.9 µmol, 44%).
^{1}H NMR ($CDCl_3$, 400 MHz) *δ* 9.34 (s, 1H), 8.66 (d, 1H, *J* = 6.2), 8.48 (d, 1H, *J* = 6.2), 8.36 (d, 1H, *J* = 7.4), 8.23 (d, 1H, *J* = 8.2), 7.72 (t, 1H, *J* =7.8), 7.07 (t, 1H, *J* = 5.0), 6.24 (t, 1H, *J* = 5.1), 3.59–3.48 (m, 10H), 3.43 (t, 2H, *J* = 5.9), 3.30 (q, 2H, *J* = 6.2), 3.23 (q, 2H, *J* = 6.3), 3.17 (s, 4H), 2.62 (t, 2H, *J* = 6.6), 2.49 (s, 4H), 2.27 (t, 2H, *J* = 6.6), 2.19–2.14 (m, 1H), 2.05–1.99 (m, 2H), 1.93–1.90 (m, 1H), 1.82–1.72 (m, 7H), 1.66–1.62 (m, 3H), 1.53–1.47 (m, 2H), 1.40–1.31 (m, 7H), 1.28–1.21 (m, 5H), 1.11–0.93 (m, 5H), 0.88 (d, 6H, *J* = 7.4), 0.60 (s, 3H).
^{13}C NMR ($CDCl_3$, 100 MHz) *δ* 173.8, 171.6, 153.4, 145.2, 134.4, 134.2, 132.1, 132.0, 129.2, 126.1, 117.8, 71.8, 70.5, 70.2, 70.0, 69.6, 56.6, 56.1, 53.8, 52.0, 45.6, 42.8, 42.2, 40.5, 40.3, 37.8, 37.3, 36.5, 35.9, 35.6, 35.5, 34.7, 33.6, 33.1, 31.9, 30.6, 29.3, 29.26, 28.3, 27.3, 26.5, 24.3, 23.5, 20.9, 18.5, 12.2, two carbons are not observed due to overlapping.
HRMS for $C_{50}H_{79}N_5O_8S$ $[M+H]^+$ found 910.5732, calc. 910.5722.

(*R*)-4-((3R,5*S*,7*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3,7-Dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-*N*-(17-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)pentanamide [HA-100–UDCA]
A solution of *N*-(3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)-3-(4-(isoquinolin-5-ylsulfonyl) piperazin-1-yl)propanamide (101 mg, 0.183 mmol, 1.0 equiv), ursodeoxycholic acid (72 mg, 0.183 mmol, 1.0 equiv), $B(OCH_2CF_3)_3$ (118 µL, 0.548 mmol, 3.0 equiv) and TEA (51 µL, 0.366 mmol, 2.0 equiv) in MeCN (2 mL) was left to stir at 90 °C. After 12 h, the mixture was concentrated under reduced pressure and purified by flash chromatography (DCM with 2→5% MeOH and 1→2 % ammonium hydroxide) to give the desired compound as a colourless oil (95 mg, 102.6 µmol, 56%).
^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.30 (s, 1H), 8.62 (d, 1H, *J* = 6.2), 8.45 (d, 1H, *J* = 6.1), 8.32 (d, 1H, *J* = 7.2), 8.20 (d, 1H, *J* = 8.2), 7.69 (t, 1H, *J* =7.8), 7.10 (t, 1H, *J* = 5.2), 6.39 (t, 1H, *J* = 5.2), 3.63 (q, 1H, *J* = 7.0), 3.54–3.44 (m, 10H), 3.39 (t, 2H, *J* = 5.9), 3.26 (q, 2H, *J* = 6.1), 3.19 (q, 2H, *J* = 6.3), 3.13 (s, 4H), 2.57 (t, 2H, *J* = 6.6), 2.45 (s, 4H), 2.22 (t,

2H, *J* = 6.6), 2.15–2.12 (m, 1H), 2.00–1.90 (m, 2H), 1.77–1.69 (m, 7H), 1.62–1.59 (m, 3H), 1.54–1.51 (m, 2H), 1.42–1.31 (m, 6H), 1.22–1.15 (m, 6H), 1.07–0.94 (m, 3H), 0.86 (d, 6H, *J* = 9.9), 0.59 (s, 3H).
^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.7, 171.6, 153.3, 145.0, 134.4, 134.1, 132.0, 131.8, 129.1, 126.0, 117.7, 71.1, 70.4, 70.1, 69.8, 69.5, 58.1, 55.9, 55.0, 53.7, 51.9, 45.6, 43.7, 43.6, 42.5, 40.2, 39.2, 37.6, 37.3, 37.2, 37.1, 35.4, 35.0, 34.1, 33.5, 33.0, 31.9, 30.3, 29.2, 29.16, 28.7, 26.9, 23.4, 21.2, 18.5, 18.4, 12.2, one carbon is not observed due to overlapping.
HRMS for $C_{50}H_{80}N_5O_9S$ $[M+H]^+$ found 926.5669, calc. 926.5671.

2.3 ML-7 constructs

Figure S8.
Preparation of ML–7 based constructs.



5-Iodonaphthalene-1-sulfonic acid

A solution of $NaNO_2$ (340 mg, 4.93 mmol, 1.1 equiv) in water (5 mL) was added slowly to a solution of 5-aminonaphthalene-1-sulfonic acid (1.00 g, 4.48 mmol, 1.0 equiv) in 6 M HCl (15 mL) at 0 °C, and the mixture was left to stir at 0 °C. After 30 min, a solution of KI (2.23 g, 13.4 mmol, 3.0 equiv) in water (5 mL) was added at 0 °C. After 20 min, the mixture was left to stir at 90 °C. After 30 min, it was cooled to RT, extracted with EtOAc (3×30 mL), washed with sat. $Na_2S_2O_3$, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give the desired compound as a pale yellow solid (320 mg, 0.958 mmol, 21%).

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.94 (d, 1H, J = 8.6), 8.13 (d, 1H, J = 7.2), 8.04–8.01 (m, 2H), 7.56 (t, 1H, J = 7.8), 7.27 (t, 1H, J = 8.0).

^{13}C NMR (100 MHz, DMSO-d_6) δ 144.8, 137.3, 133.8, 133.0, 130.0, 128.7, 126.9, 126.6, 125.4, 99.4.

HRMS for $C_{10}H_6ISO_3$ $[M–H]^-$ found 332.9078, calc. 332.9088.

tert-Butyl 4-((5-iodonaphthalen-1-yl)sulfonyl)-1,4-diazepane-1-carboxylate

DMF (30 μL, 0.387 mmol, 0.17 equiv) was added to a solution of 5-iodonaphthalene-1-sulfonic acid (734 mg, 2.21 mmol, 1.0 equiv) in $SOCl_2$ (4 mL), and the mixture was left to stir at 80 °C. After 3 h, toluene (2 mL) was added, and the mixture was concentrated under reduced pressure to give a brown oil, which was used without further purification. It was

added to a solution of *tert*-butyl 1,4-diazepane-1-carboxylate (663 mg, 3.31 mmol, 1.5 equiv) and TEA (923 μL, 6.62 mmol, 3.0 equiv) in DCM (5 mL) at 0 °C, and the mixture was left to stir gradually warming up to RT. After 16 h, the mixture was concentrated under reduced pressure and purified by flash chromatography (EtOAc/DCM 1:10) to give the desired product as a yellow viscous oil (287 mg, 0.556 mmol, 25%).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, 1H, *J* = 8.6), 8.41 (d, 1H, *J* = 8.6), 8.22–8.14 (m, 2H), 7.60 (t, 1H, *J* = 7.9), 7.33 (t, 1H, *J* = 8.0), 3.58–3.48 (m, 4H), 3.45–3.37 (m, 4H), 1.97–1.91 (m, 2H), 1.43 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 139.0, 138.5, 135.2, 130.0, 129.7, 129.6, 129.0, 125.9, 125.8, 100.4, 80.0, 50.4, 49.5, 47.8, 46.1, 29.8, 28.5.
HRMS for $C_{20}H_{26}IN_2O_4S$ $[M+H]^+$ found 517.0648 calc. 517.0652.

1-((5-Iodonaphthalen-1-yl)sulfonyl)-1,4-diazepane [ML-7]
A solution of *tert*-butyl 4-((5-iodonaphthalen-1-yl)sulfonyl)-1,4-diazepane-1-carboxylate (287 mg, 0.556 mmol) in TFA/DCM (1:1, 4 mL) was left to stir at RT. After 3 h, the mixture was concentrated under reduced pressure, washed with K_2CO_3 solution and extracted with DCM (3×30 mL) to give the desire compound as a brown viscous oil (211 mg, 0.507 mmol, 91%).
^{1}H NMR (400 MHz, CD_3OD) δ 8.70 (d, 1H, *J* = 8.7), 8.39 (d, 1H, *J* = 8.6), 8.24–8.22 (d, *J* = 7.4, 1H), 8.15 (d, 1H, *J* = 7.5), 7.66 (t, 1H, *J* = 8.0), 7.36 (t, 1H, *J* = 8.0), 3.50–3.46 (m, 4H), 2.91–2.88 (m, 4H), 1.87–1.81 (qn, *J* = 6.0, 2H).
^{13}C NMR (100 MHz, CD_3OD) δ 140.2, 139.1, 137.2, 136.3, 130.5, 130.49, 129.8, 127.2, 127.0, 100.7, 51.4, 50.7, 48.4, 48.0, 31.7.
HRMS for $C_{15}H_{18}IN_2O_2S$ $[M+H]^+$ found 417.0129, calc. 417.0128.

Ethyl 3-(4-((5-iodonaphthalen-1-yl)sulfonyl)-1,4-diazepan-1-yl)propanoate
$MnCl_2{\cdot}4H_2O$ (4.8 mg, 0.024 mmol, 10 mol%) and ethyl acrylate (39 μL, 0.37 mmol, 1.5 equiv) were added into a solution of 1-((5-iodonaphthalen-1-yl)sulfonyl)-1,4-diazepane (102 mg, 0.244 mmol, 1.0 equiv) in MeOH/H_2O (1:1, 3 mL), and the mixture was left to stir at RT. After 2 h, the mixture was concentrated under reduced pressure, re-dissolved in EtOAc, filtered, washed with water, and dried over $MgSO_4$, evaporated, and purified by flash chromatography (EtOAc/DCM 1:1) to give the desired compound as a yellow viscous oil (70.2 mg, 0.136 mmol, 56%).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (d, 1H, *J* = 8.7), 8.39 (d, 1H, *J* = 8.6), 8.21–8.16 (m, 2H), 7.60 (t, 1H. *J* = 8.0), 7.32 (t, 1H, *J* = 8.0), 4.11 (q, 2H, *J* = 7.2), 3.51 (s, 2H), 3.45 (t, 2H, *J* = 5.9), 2.88 (s, 2H), 2.79 (s, 4H), 2.48 (s, 2H), 1.90 (s, 2H), 1.22 (t, 3H, *J* = 7.1).
^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 138.9, 138.4, 135.6, 135.1, 130.0, 129.6, 128.9, 125.94, 125.90, 100.3, 60.7, 56.4, 54.0, 53.2, 48.0, 46.8, 32.7, 29.8, 27.9, 14.3.
HRMS for $C_{20}H_{25}IN_2O_4SNa$ $[M+Na]^+$ found 539.0492, calc. 539.0472.

***tert*-Butyl (17-(4-((5-iodonaphthalen-1-yl)sulfonyl)-1,4-diazepan-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)carbamate [ML-7–Boc]**
A solution of ethyl 3-(4- ((5- iodonaphthalen-1-yl)sulfonyl)-1,4- diazepan-1-yl)propanoate (40 mg, 82.1 μmol, 1.0 equiv) and KOH (4.3 mg, 0.077 mmol, 1.0 equiv) in EtOH (5 mL) was left to stir at RT. After 2 h, the mixture was concentrated under reduced pressure to give a brown oil. It was redissolved in MeCN (2 mL) and charged with *tert*-

butyl (3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)carbamate (48 mg, 0.150 mmol, 2.0 equiv) and $B(OCH_2CF_3)_3$ (41 μL, 0.190 mmol, 2.5 equiv) , and the mixture was left to stir at 85 °C. After 5 h, the mixture was concentrated under reduced pressure and purified by flash chromatography (DCM/MeOH 10:1) to give the desired product as a brown viscous oil (19.4 mg, 24.5 μmol, 32%).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, 1H, *J* = 8.7), 8.41 (d, 1H, *J* = 8.6), 8.22–8.17 (m, 4H), 7.61 (t, 1H, *J* = 8.0), 7.38 (br s, 1H), 7.33 (t, 1H, *J* = 8.0), 4.98 (br s, 1H), 3.64–3.62 (m, 5H), 3.58–3.57 (m, 6H), 3.54-3.50 (m, 5H), 3.49–3.45 (m, 2H), 3.32 (dd, 2H, *J* = 12.4, 6.5), 3.23–3.18 (m, 2H), 2.88 (s, 4H), 2.41 (s, 2H), 1.98 (s, 2H), 1.79–1.71 (m, 4H), 1.42 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 156.2, 139.0, 135.4, 135.2, 130.1, 129.5, 129.0, 125.9, 125.8, 100.4, 79.1, 70.7, 70.34, 70.28, 69.8, 69.7, 56.4, 53.8, 53.7, 46.7, 38.7, 37.4, 33.3, 29.8, 29.4, 28.6, five carbons are not observed.
HRMS for $C_{33}H_{52}IN_4O_8S$ $[M+H]^+$ found 791.2565, calc. 791.2545.

_N_-(17-(4-((5-Iodonaphthalen-1-yl)sulfonyl)-1,4-diazepan-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)palmitamide [ML-7–C16:0]
A solution of potassium ethyl 3-(4-((5-iodonaphthalen-1-yl)sulfonyl)-1,4-diazepan-1-yl)propanoate (55 mg, 0.104 mmol, 1.0 equiv), *N*-(3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)palmitamide (53 mg, 0.114 mmol, 1.1 equiv), $B(OCH_2CF_3)_3$ (67 μL, 0.312 mmol, 3 equiv) and TEA (29 μL, 0.208 mmol, 2 equiv) in MeCN (2 ml) was left to stir at 85 °C. After 5 h the mixture was concentrated under reduced pressure and purified by flash chromatography (DCM with 3→5% MeOH) to give the desired compound as pale yellow oil (50 mg, 0.054 mmol, 52 %).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, 1H, *J* = 8.6), 8.39 (d, 1H, *J* = 8.5), 8.18 (t, 2H, *J* = 8.1), 7.59 (t, 1H, *J* = 7.9), 7.53 (br s, 1H), 7.31 (t, 1H, *J* = 8.0), 6.23 (br s, 1H), 3.61–3.60 (m, 4H), 3.56–3.51 (m, 6H), 3.49–3.42 (m, 6H), 3.41–3.27 (m, 4H), 2.77–2.73 (m, 6H), 2.30 (t, 2H, *J* = 6.1), 2.11 (t, 2H, *J* = 7.6), 1.88–1.84 (m, 2H), 1.75–1.73 (m, 4H), 1.59–1.56 (m, 2H), 1.22 (m, 24H), 0.86 (t, 3H, *J* = 6.5).
^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 172.1, 138.9, 138.4, 135.5, 135.1, 130.0, 129.5, 128.9, 125.9, 125.8, 100.3, 70.6, 70.2, 70.18, 70.1, 69.6, 56.0, 53.7, 53.5, 47.9, 47.0, 37.8, 37.1, 36.9, 33.6, 32.0, 29.78, 29.75, 29.73, 29.6, 29.54, 29.50, 29.46, 29.44, 29.2, 28.5, 25.9, 22.8, 14.2, four carbon not observed due to overlapping.
HRMS for $C_{44}H_{74}IN_4O_7S$ $[M+H]^+$ found 929.4322, calc. 929.4317.

(*R*)-4-((3*R*,5*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,12-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-*N*-(17-(4-((5-iodonaphthalen-1-yl)sulfonyl)-1,4-diazepan-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)pentanamide [ML-7–DCA]
KOH (3.3 mg, 58.8 μmol, 1.0 equiv) was added to a stirred solution of ethyl 3-(4-((5-iodonaphthalen-1-yl)sulfonyl)-1,4-diazepan-1-yl)propanoate (30 mg, 58.1 μmol, 1.0 equiv) in EtOH (2 mL) and the mixture was left to stirred at RT. After 2 h, the mixture was concentrated under reduced pressure to give a brown oil. It was redissolved in MeCN (2 mL) and charged with(*R*)-*N*-(3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)-4-((3*R*,5*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,12-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanamide [DCA–amine] (35 mg, 58.8 μmol, 1.0

equiv), and $B(OCH_2CF_3)_3$ (32 μL, 0.149 mmol, 2.5 equiv) , and the mixture was left to stir at 85 °C. After 5 h, the mixture was concentrated under reduced pressure and purified by flash chromatography to give the desired product as a brown viscous oil (18.2 mg, 17.1 μmol, 29%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, 1H, *J* = 8.7), 8.41 (d, 1H, *J* = 8.5), 8.22–8.17 (m, 2H), 7.61 (t, 1H, *J* = 8.0), 7.59–7.56 (m, 1H), 7.33 (t, 1H, *J* = 8.0), 6.35 (br s, 1H), 3.93 (s, 1H), 3.64–3.62 (m, 5H), 3.59–3.56 (m, 6H), 3.54–3.50 (m, 5H), 3.47–3.44 (m, 2H), 3.35–3.29 (m, 4H), 2.84 (s, 4H), 2.38 (s, 2H), 2.20–2.16 (m, 1H), 2.08–2.05 (m, 2H), 1.95–1.93 (m, 2H), 1.85–1.62 (m, 12H), 1.57–1.46 (m, 6H), 1.40–1.34 (m, 6H), 1.30–1.23 (m, 3H), 1.11–1.03 (m, 2H), 0.95 (t, 3H, *J* = 5.9), 0.89 (s, 3H), 0.65 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 171.8, 139.0, 138.6, 135.4, 135.1, 130.1, 129.5, 129.0, 125.9, 125.8, 100.4, 73.2, 71.8, 70.6, 70.3, 70.2, 69.6, 56.2, 53.7, 53.65, 48.4, 47.1, 46.9, 46.6, 42.2, 38.0, 37.2, 36.6, 36.1, 35.4, 35.3, 34.2, 33.7, 33.4, 33.36, 31.8, 30.6, 29.5, 29.1, 28.8, 27.6, 27.2, 26.3, 23.8, 23.3, 17.6, 12.9, four carbons not observed due to overlapping.

HRMS for $C_{52}H_{81}IN_4O_9SNa$ $[M+Na]^+$ found 1087.4685, calc. 1087.4661.

(4R)-4-((3R,7R,8R,9S,10S,13R,14S,17R)-3,7-dihydroxy-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)-N-(17-(4-((5-iodonaphthalen-1-yl)sulfonyl)-1,4-diazepan-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)pentanamide [ML-7–CDCA]

KOH (10.0 mg, 0.178 mmol, 1.0 equiv) was added to a stirred solution of ethyl 3-(4-((5iodonaphthalen-1-yl)sulfonyl)-1,4-diazepan-1-yl)propanoate (87 mg, 0.178 mmol, 1.0 equiv) in EtOH (4 mL) and the mixture was left to stirred at RT. After 2 h, the mixture was concentrated under reduced pressure to give a brown oil. It was redissolved in MeCN (2 mL) and charged with(*R*)- (4*R*)-*N*-(3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)-4-((3*R*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3,7-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanamide [CDCA–amine] (108 mg, 0.196 mmol, 1.1 equiv), $B(OCH_2CF_3)_3$ (106 μL, 0.534 mmol, 3 equiv) and TEA (46 μL, 356 mmol, 2 equiv), the mixture was left to stir at 85 °C. After 5 h, the mixture was concentrated under reduced pressure and purified by flash chromatography (DCM with 2→4% MeOH, using 1% ammonium hydroxide) to give the desired product as a brown viscous oil (58 mg, 0.054 μmol, 31%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, 1H, *J* = 8.7), 8.38 (d, 1H, *J* = 8.5), 8.18 (dd, 2H, *J* = 10.2, 7.5), 7.59 (t, 1H, *J* = 8.0), 7.56 (br s, 1H), 7.31 (t, 1H, *J* = 8.0), 6.29 (t, 1H, *J* = 5.2), 3.80 (s, 1H), 3.62–3.60 (m, 4H), 3.57–3.54 (m, 4H), 3.52–3.48 (m, 4H), 3.45–3.42 (m, 6H), 3.33–3.27 (m, 4H), 2.76–2.71 (m, 6H), 2.29 (t, 2H, *J* = 6.2), 2.21–2.14 (m, 2H), 2.03–2.00 (m, 1H), 1.94–1.85 (m, 4H), 1.80–1.72 (m, 8H), 1.66–1.59 (m, 2H), 1.49–1.41 (m, 3H), 1.38–1.23 (m, 7H), 1.12–1.06 (m, 3H), 0.98–0.94 (m, 1H), 0.91–0.88 (m, 3H), 0.87 (s, 3H), 0.61 (s, 3H)

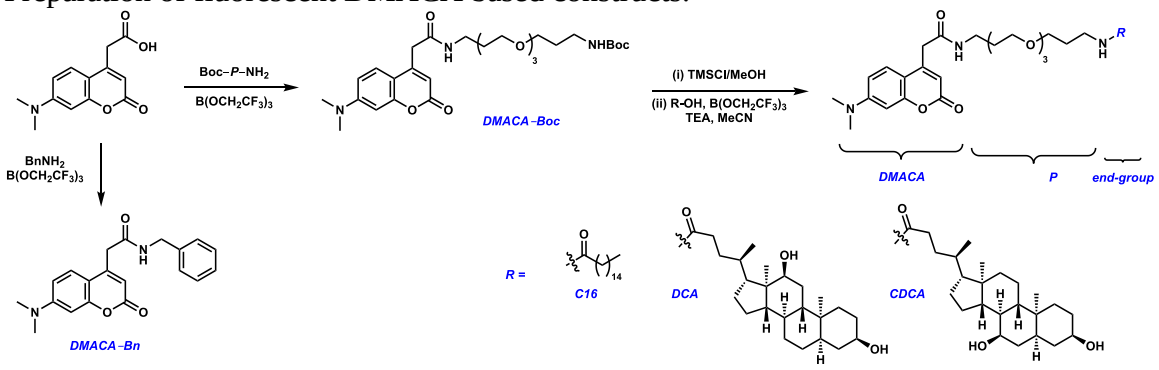
^{13}C NMR (100 MHz, $CDCl_3$) δ. 173.7, 172.2, 138.9, 138.4, 135.5, 135.1, 130.0, 129.5, 128.9, 125.9, 125.8, 100.3, 72.0, 70.6, 70.19, 70.18, 70.1, 69.5, 68.4, 55.93, 55.85, 53.7, 53.5, 50.5, 48.0, 47.0, 42.7, 41.6, 40.0, 39.7, 39.5, 37.9, 37.0, 35.5, 35.4, 35.1, 34.7, 33.6, 33.5, 32.9, 31.9, 30.7, 29.5, 29.2, 28.5, 28.3, 23.8, 22.9, 20.7, 18.5, 11.9.(one carbon not observed due to overlapping.)

HRMS for $C_{52}H_{81}IN_4O_9S$ $[M+H]^+$ found 1065.4836, calc. 1065.4842.

2.4 DMACA constructs

Figure S9.

Preparation of fluorescent DMACA based constructs.



***N*-Benzyl-2-(7-(dimethylamino)-2-oxo-2*H*-chromen-3-yl)acetamide [DMACA–Bn]**

A solution of 2-(7-(dimethylamino)-2-oxo-2*H*-chromen-4-yl)acetic acid (99 mg, 0.400 mmol, 1.0 equiv), benzylamine (44 µL, 0.400 mmol, 1.0 equiv), $B(OCH_2CF_3)_3$ (172 µL, 0.800 mmol, 2.0 equiv) and TEA (56 µL, 0.400 mmol, 1.0 equiv) in MeCN (5 mL) was left to stir at 80 °C. After 12 h, the mixture was concentrated under reduced pressure and purified by flash chromatography (EtOAc/DCM 1:8→1:4 with 0.5→1 % MeOH) to give the desired compound as a yellow oil (69 mg, 0.205 mmol, 51%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.75 (d, 1H, *J* = 8.9), 7.28–7.22 (m, 3H), 7.22–7.17 (m, 2H, ArH), 6.60 (dd, 1H, *J* = 2.2, 8.9), 6.45 (d, 1H, *J* = 2.1), 6.38 (br s, 1H), 6.01 (s, 1H), 4.41 (d, 2H, *J* = 5.7), 3.65 (s, 2H), 3.06 (s, 6H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.0, 161.9, 156.1, 153.2, 149.8, 137.9, 128.8, 127.8, 127.6, 125.9, 110.4, 109.3, 108.4, 98.3, 43.9, 40.8, 40.2.

HRMS for $C_{20}H_{21}N_2O_3$ $[M+H]^+$ found 337.1557, calc. 337.1547.

***tert*-Butyl (1-(7-(dimethylamino)-2-oxo-2*H*-chromen-3-yl)-2-oxo-7,10,13-trioxa-3-azahexadecan-16-yl)carbamate [DMACA–Boc]**

A solution of *tert*-butyl (3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)carbamate (158 mg, 0.493 mmol, 1.2 equiv), 2-(7-(dimethylamino)-2-oxo-2*H*-chromen-4-yl)acetic acid (102 mg, 0.412 mmol, 1.0 equiv) and $B(OCH_2CF_3)_3$ (177 µL, 0.824 mmol, 2.0 equiv) in MeCN (2 mL) was left to stir at 80 °C. After 12 h, the reaction mixture was concentrated under reduced pressure and purified by flash chromatography (EtOAc/DCM 1:5→1:2 with 2→3 % MeOH) to give the desired compound as a yellow oil (82 mg, 0.149 mmol, 36%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.46 (d, 1H, *J* = 9.0), 6.81 (br s, 1H), 6.55 (dd, 1H, *J* = 9.0, 2.6), 6.12 (d, 1H, *J* = 2.6), 6.01 (s, 1H), 5.00 (s, 1H), 3.57–3.44 (m, 14H), 3.30 (q, 2H, *J* = 6.0), 3.14 (q, 2H, *J* = 6.1), 3.00 (s, 6H), 1.72–1.65 (m, 4H), 1.38 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.2, 168.1, 161.9, 156.0, 153.0, 150.3, 125.9, 110.2, 109.2, 108.6, 98.1, 79.0, 70.4, 70.1, 70.04, 69.95, 69.4, 40.5, 40.1, 38.4, 29.7, 28.7, 28.5, 25.4, one carbon is not observed due to overlapping.

HRMS for $C_{28}H_{44}N_3O_8$ $[M+H]^+$ found 550.3122, calc. 550.3123.

_N_-(1-(7-(dimethylamino)-2-oxo-2_H_-chromen-4-yl)-2-oxo-7,10,13-trioxa-3-azahexadecan-16-yl)palmitamide [DMACA–C16:0]

A solution of *tert*-butyl (1-(7-(dimethylamino)-2-oxo-2*H*-chromen-4-yl)-2-oxo-7,10,13-trioxa-3-azahexadecan-16-yl)carbamate (85 mg, 0.155 mmol, 1.0 equiv) in MeOH/TMSCl 1:2 (3 mL) was left to stir at 20 °C. After 2 h, the mixture was concentrated under reduced pressure and used for next step without purification. The residue was redissolved in acetonitrile (5 mL), palmitic acid (40 mg, 0.156 mmol, 1.0 equiv), $B(OCH_2CF_3)_3$ (100 µL, 0.462 mmol, 3.0 equiv) and TEA (65 µL, 0.466 mmol, 3.0 equiv) were added and the mixture was left to stir at 80 °C. After 12 h, the mixture was concentrated under reduced pressure and purified by flash chromatography (EtOAc/DCM 1:3 with 3→5 % MeOH) to give the desired compound as a yellow oil (47 mg, 68.3 µmol, 44%)

^{1}H NMR (CD_3OD, 400 MHz) δ 7.49 (d, 1H, *J* = 9.0), 6.67 (dd, 1H, *J* = 9.0, 2.6), 6.47 (d, 1H, *J* = 2.5), 5.98 (s, 1H), 3.60 (s, 2H), 3.53–3.47 (m, 12H), 3.42 (t, 2H, *J* = 6.2), 3.25–3.21 (m, 2H), 3.16 (t, 2H, *J* = 6.9), 2.99 (s, 6H), 2.08 (t, 2H, *J* = 7.5), 1.72–1.63 (m, 4H), 1.50 (t, 2H, *J* = 6.9), 1.20 (m, 24H), 0.82 (t, 3H, *J* = 6.9).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.4, 168.0, 161.9, 156.1, 153.1, 150.4, 126.0, 110.2, 109.2, 108.6, 98.2, 70.5, 70.4, 70.2, 70.14, 70.11, 69.9, 40.8, 40.2, 38.6, 37.7, 36.9, 32.0, 29.8, 29.7, 29.6, 29.5, 29.45, 29.43, 29.3, 28.8, 25.9, 22.8, 14.2, four carbons are not observed due to overlapping.

HRMS for $C_{39}H_{65}N_3O_7Na$ $[M+Na]^+$ found 710.4714, calc. 710.4715.

(_R_)-4-((3_R_,5_R_,8_R_,9_S_,10_S_,12_S_,13_R_,14_S_,17_R_)-3,12-Dihydroxy-10,13-dimethylhexadecahydro-1_H_-cyclopenta[_a_]phenanthren-17-yl)-_N_-(1-(7-(dimethylamino)-2-oxo-2_H_-chromen-4-yl)-2-oxo-7,10,13-trioxa-3-azahexadecan-16-yl)pentanamide [DMACA–DCA]

A solution of *tert*-butyl (1-(7-(dimethylamino)-2-oxo-2*H*-chromen-4-yl)-2-oxo-7,10,13-trioxa-3-azahexadecan-16-yl)carbamate (135 mg, 0.246 mmol, 1.0 equiv) in TFA/DCM 1:1 (2 mL) was left to stir at 20 °C. After 2 h, the reaction mixture was concentrated under reduced pressure and used for the next step without further purification. The residue was redissolved in acetonitrile (5 mL), deoxycholic acid (113 mg, 0.288 mmol, 1.2 equiv), $B(OCH_2CF_3)_3$ (103 µL, 0.478 mmol, 1.9 equiv) and TEA (67 µL, 0.481 mmol, 2.0 equiv) were added and the mixture was left to stir at 80 °C. After 12 h, the mixture was concentrated under reduced pressure and purified by flash chromatography (EtOAc/DCM 1:2→DCM with 3→5 % MeOH) to give the desired compound as a yellow oil (87 mg, 0.106 mmol, 43%)

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.50 (d, 1H, *J* = 9.0), 6.88 (s, 1H), 6.59 (dd, 1H, *J* = 2.0, 8.9), 6.46 (d, 1H, *J* = 1.9), 6.40 (s, 1H), 6.05 (s, 1H), 3.92 (s, 1H), 3.59–3.46 (m, 15H), 3.34–3.28 (m, 4H), 3.03 (s, 6H), 2.27–2.16 (m, 2H), 2.08–1.99 (m, 2H), 1.80–1.62 (m, 11H), 1.54–1.45 (m, 4H), 1.37–1.35 (m, 6H), 1.23–1.20 (m, 3H), 1.09–1.00 (m, 2H), 0.94 (d, 3H, *J* = 5.9), 0.87 (s, 3H), 0.63 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.9, 168.2, 162.1, 156.0, 153.1, 150.5, 126.0, 110.2, 109.3, 108.7, 98.2, 73.1, 71.8, 70.5, 70.4, 70.12, 70.08, 70.06, 69.9, 48.3, 47.0, 46.6, 42.2, 40.6, 40.2, 38.5, 37.7, 36.5, 36.1, 35.4, 35.3, 34.2, 33.7, 33.4, 31.8, 30.6, 29.8, 29.2, 28.8, 28.7, 27.6, 27.2, 26.3, 23.8, 23.2, 17.5, 12.8.

HRMS for $C_{47}H_{74}N_3O_9$ $[M+H]^+$ found 824.5413, calc. 824.5420.

***(4R)*-4-((3*R*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3,7-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-*N*-(1-(7-(dimethylamino)-2-oxo-2*H*-chromen-4-yl)-2-oxo-7,10,13-trioxa-3-azahexadecan-16-yl)pentanamide [DMACA–CDCA]**

A solution of *N*-(3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)-2-(7-(dimethylamino)-2-oxo-2*H*-chromen-4-yl)acetamide (80 mg, 0.178 mmol, 1.0 equiv), chenodeoxycholic acid (84 mg, 0.214 mmol, 1.2 equiv), TEA (50 μL, 0.356 mmol, 2.0 equiv) and $B(OCH_2CF_3)_3$ (115 μL, 0.534 mmol, 3.0 equiv) in MeCN (2 mL) was left to stir at 90 °C. After 14 h, the mixture was concentrated under reduced pressure and purified by flash chromatography (DCM with 2→5% MeOH) to give the desired compound as a pale yellow oil (45 mg, 0.055 mmol, 31%).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.51(d, 1H, *J* = 9.0), 6.82 (t, 1H, *J* = 5.0), 6.59 (dd, 1H, *J* = 9.0, 2.4), 6.46 (d, 1H, *J* = 2.4), 6.30 (t, 1H, *J* = 5.2), 6.05 (s, 1H), 3.80 (s, 1H), 3.61–3.42 (m, 14H), 3.34–3.28 (m, 4H), 3.03(s, 6H), 2.25–2.14 (m, 2H), 2.04–1.91 (m, 3H), 1.81–1.59 (m, 11H), 1.50–1.41 (m, 4H), 1.37–1.23 (m, 8H), 1.12–1.05 (m, 3H), 0.90–0.87 (m, 6H), 0.61 (s, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.8, 168.1, 162.0, 156.1, 153.1, 150.5, 126.0, 110.2, 109.3, 108.6, 98.2, 72.0, 70.5, 70.4, 70.14, 70.11, 70.0, 68.4, 55.8, 50.5, 42.7, 41.6, 40.7, 40.2, 40.0, 39.8, 39.5, 38.5, 37.8, 35.5, 35.4, 35.1, 34.7, 33.4, 32.9, 31.9, 30.8, 29.8, 29.8, 29.2, 28.8, 28.3, 23.8, 22.9, 20.7, 18.5, 11.9.

HRMS for $C_{47}H_{74}N_3O_9$ $[M+H]^+$ found 824.5439, calc. 824.5420

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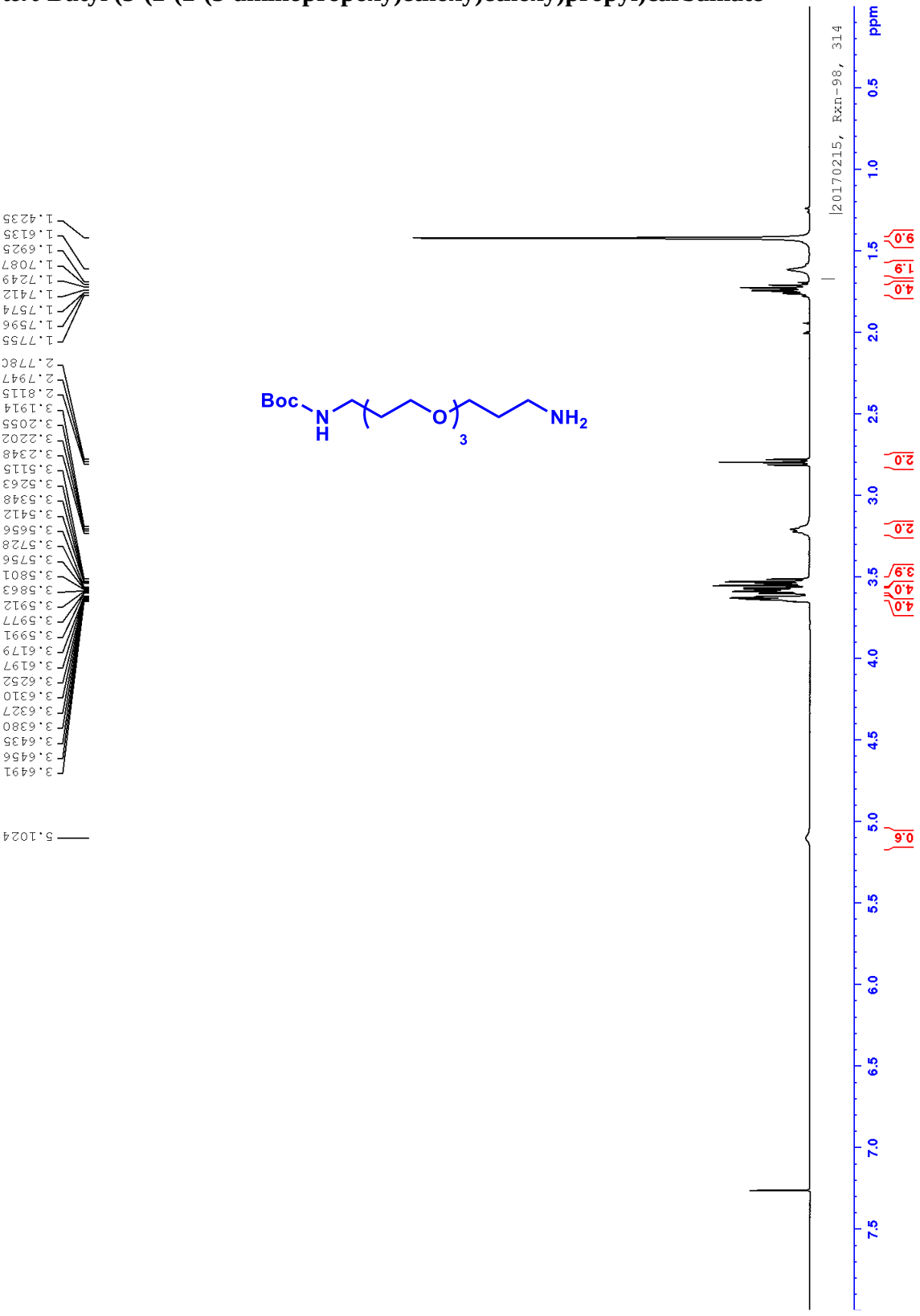
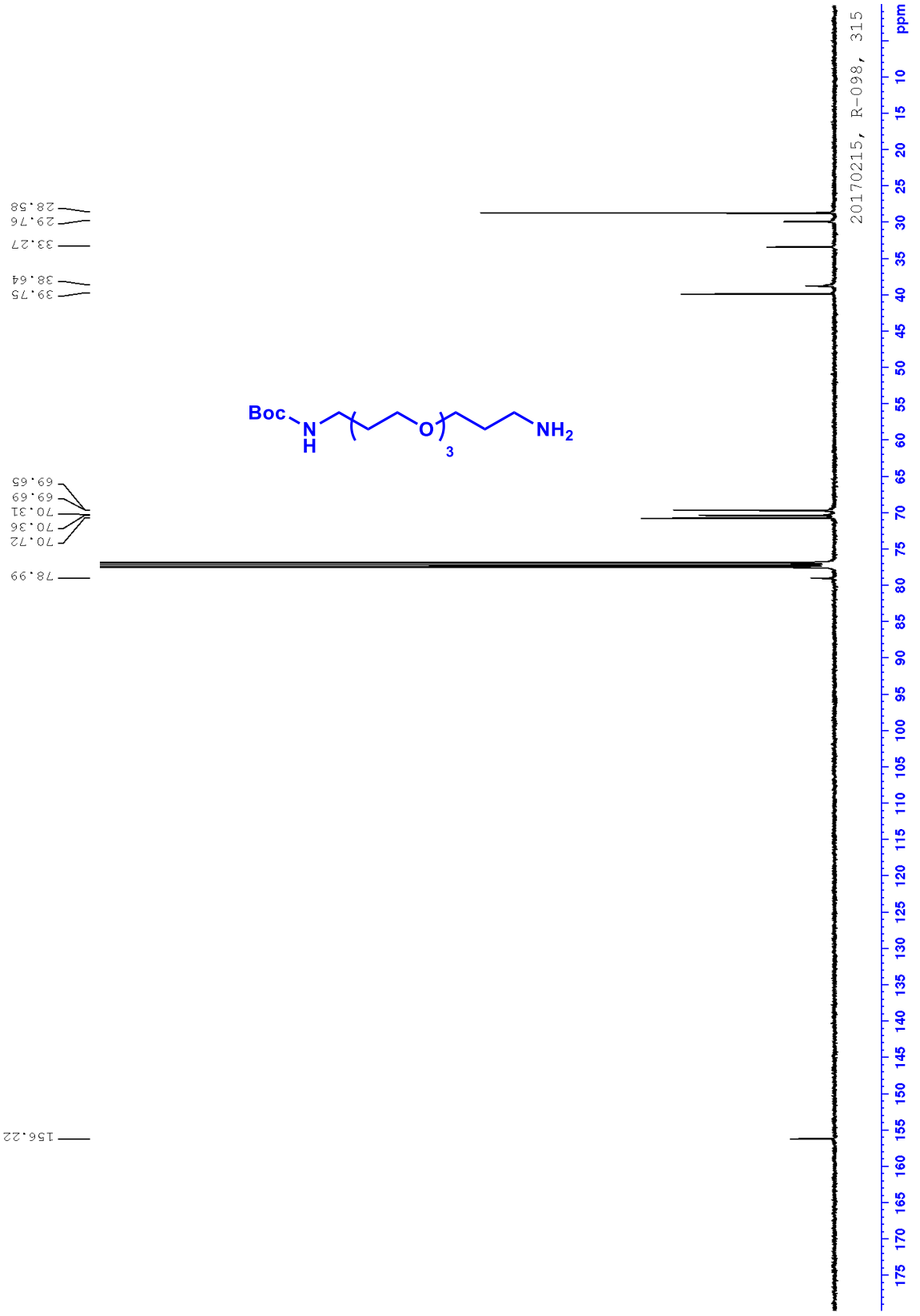
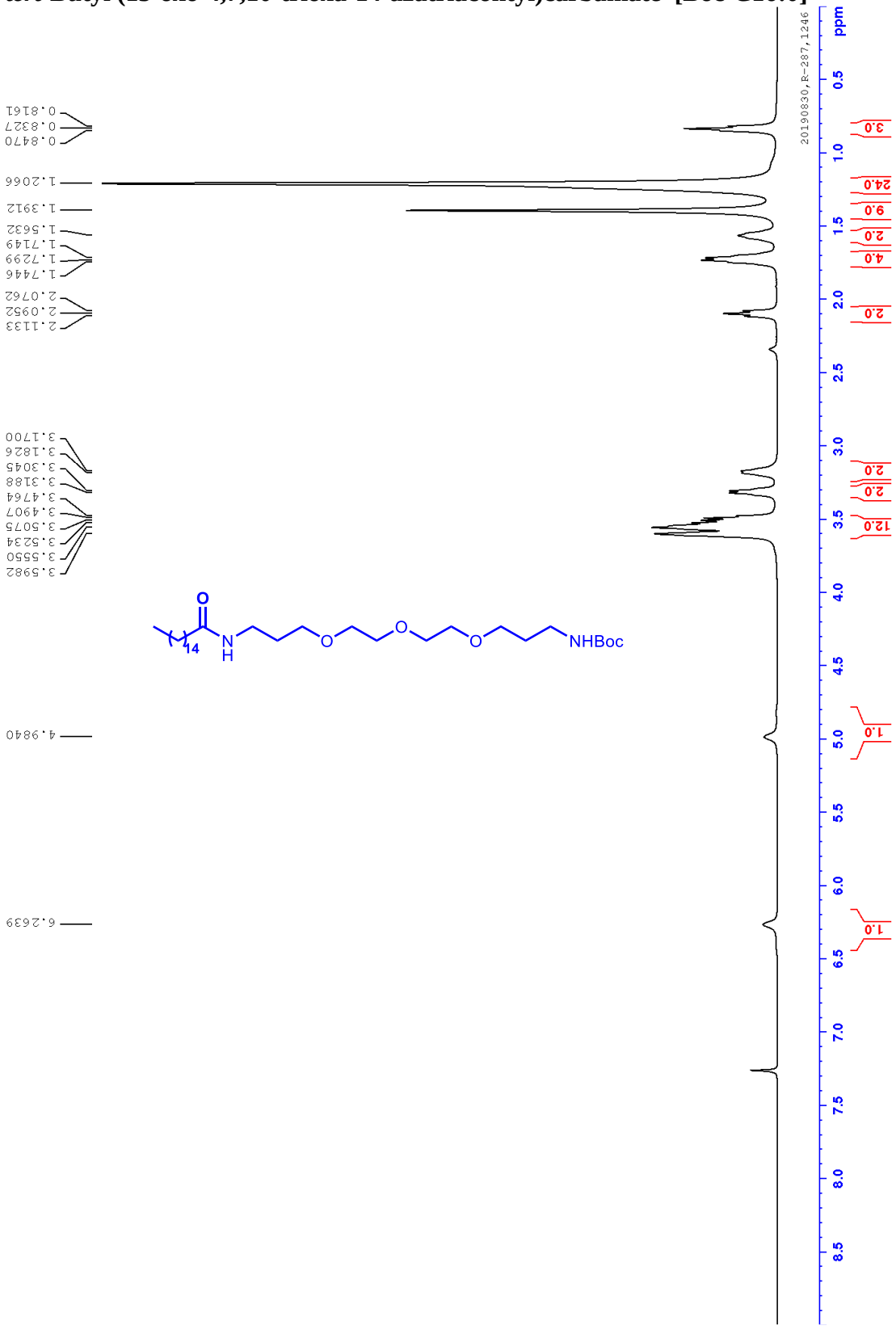
NMR Spectra

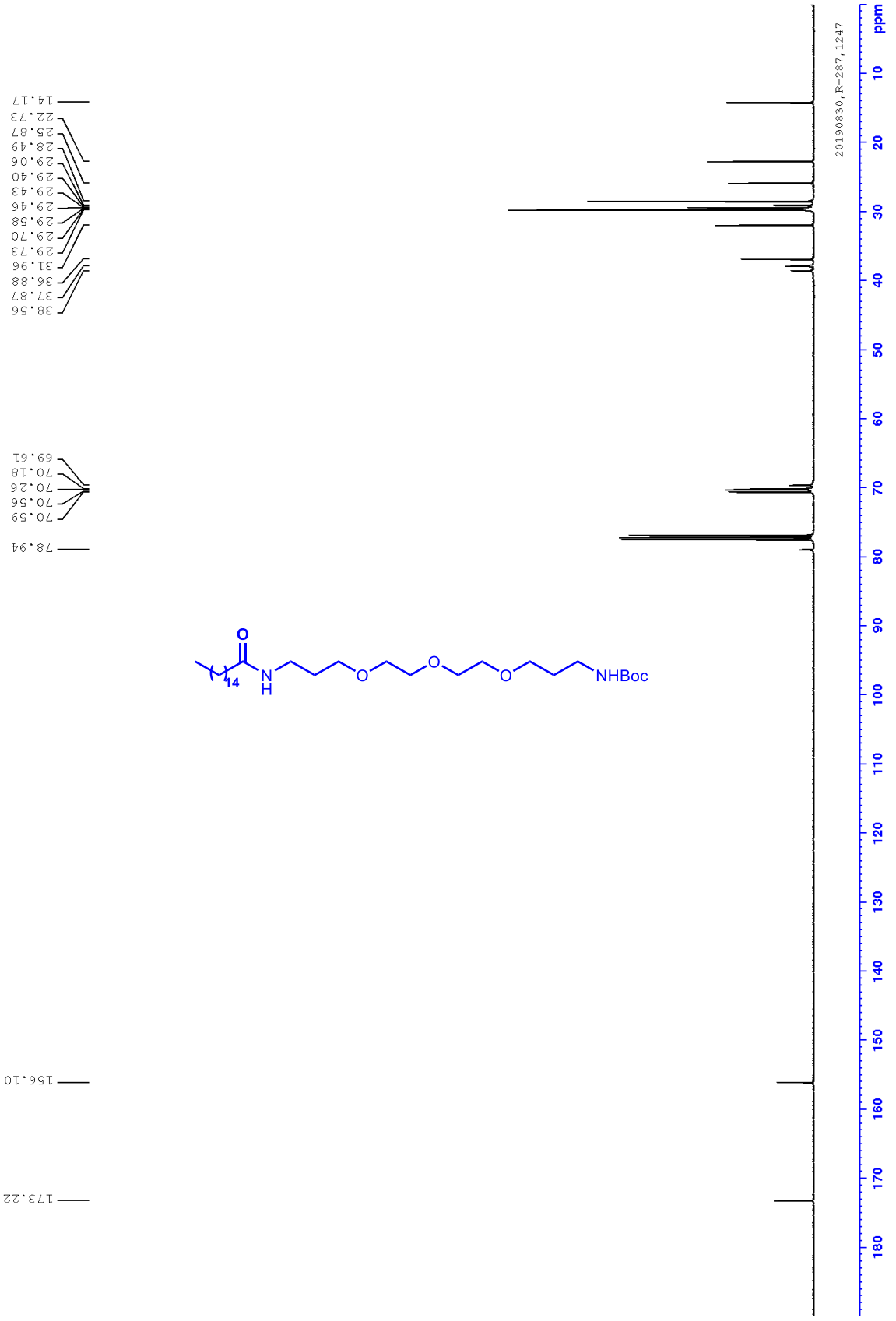
***tert*-Butyl (3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)carbamate**



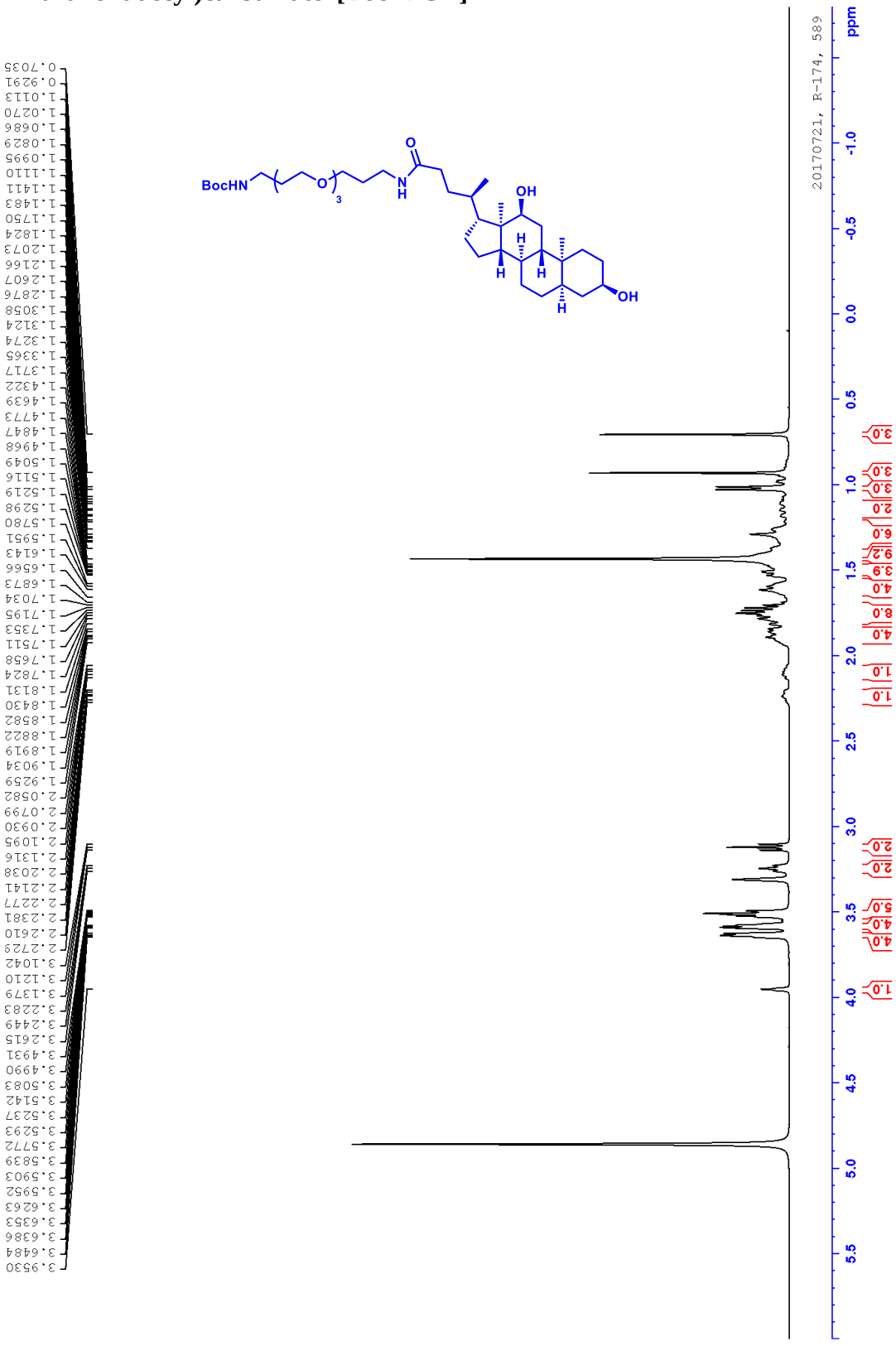

20170215, R-098, 315
ppm
Boc
N
H
O
3
NH2
28.58
29.76
33.27
38.64
39.75
69.65
69.69
70.31
70.36
70.72
78.99
156.22

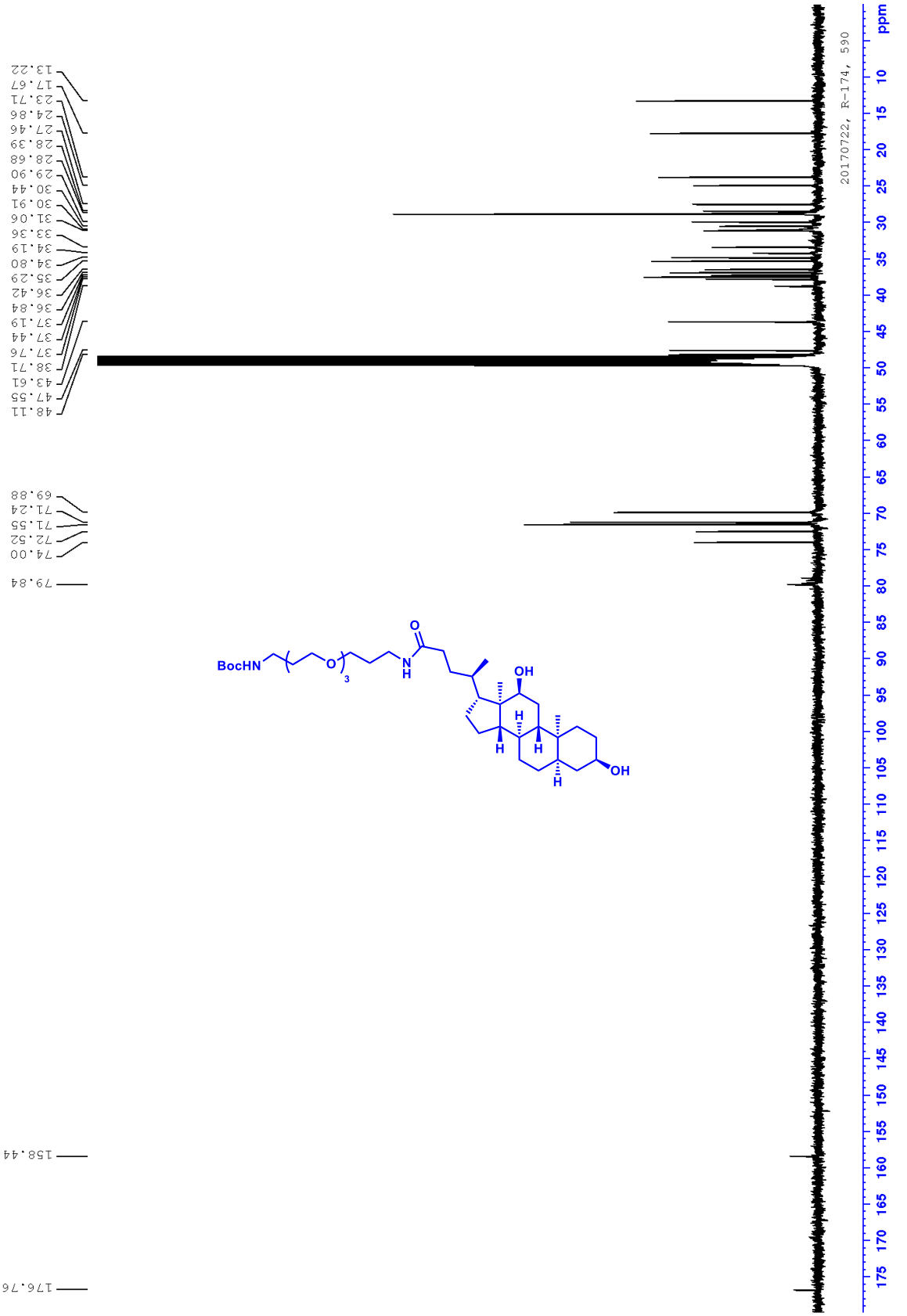
tert-Butyl (15-oxo-4,7,10-trioxa-14-azatriacontyl)carbamate [Boc-C16:0]



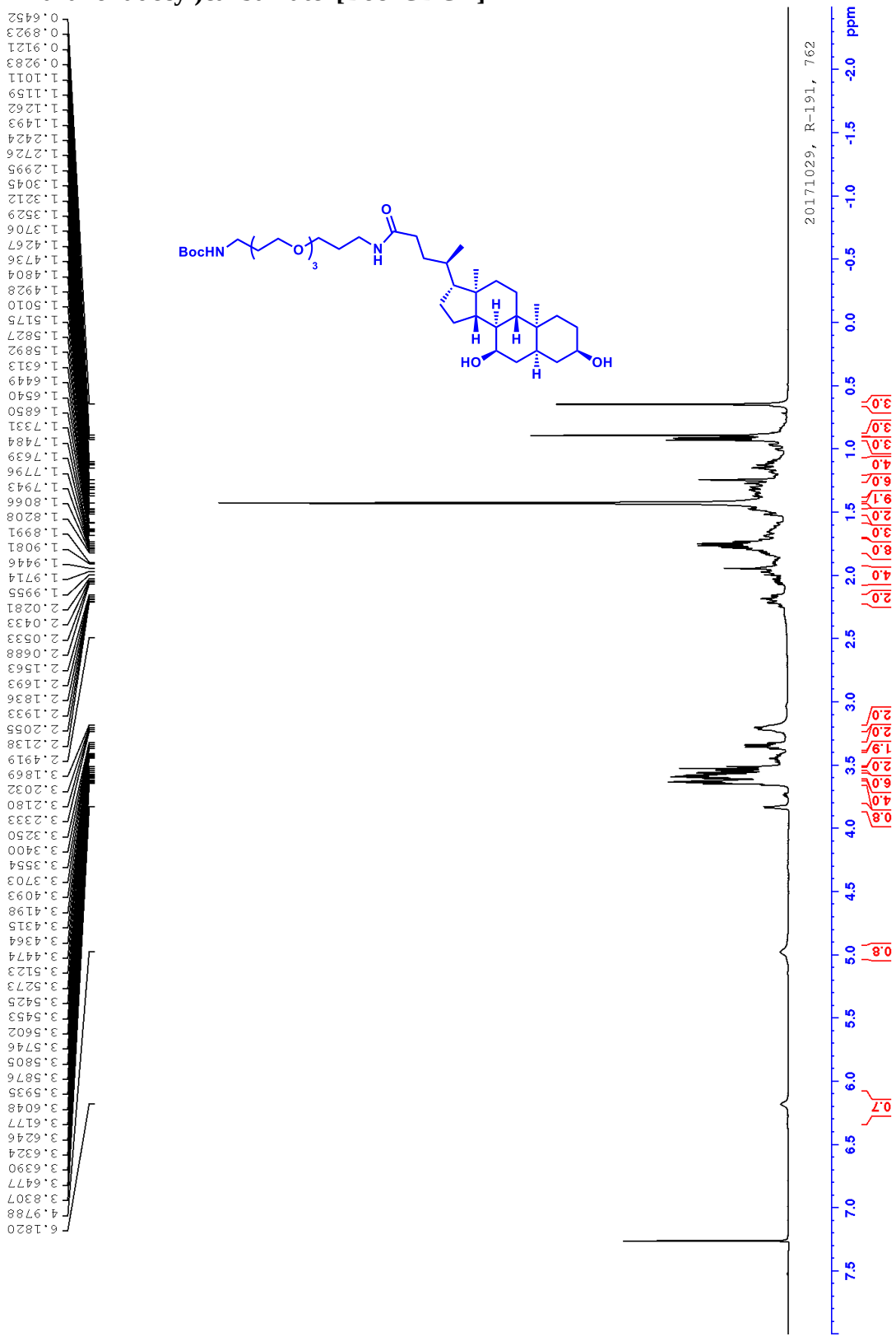

20190830,R-287,1247
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
14.17
22.73
25.87
28.49
29.06
29.40
29.43
29.46
29.58
29.70
29.73
31.96
36.88
37.87
38.56
69.61
70.18
70.26
70.56
70.59
78.94
156.10
173.22
O
14
N
H
O
O
O
NHBoc

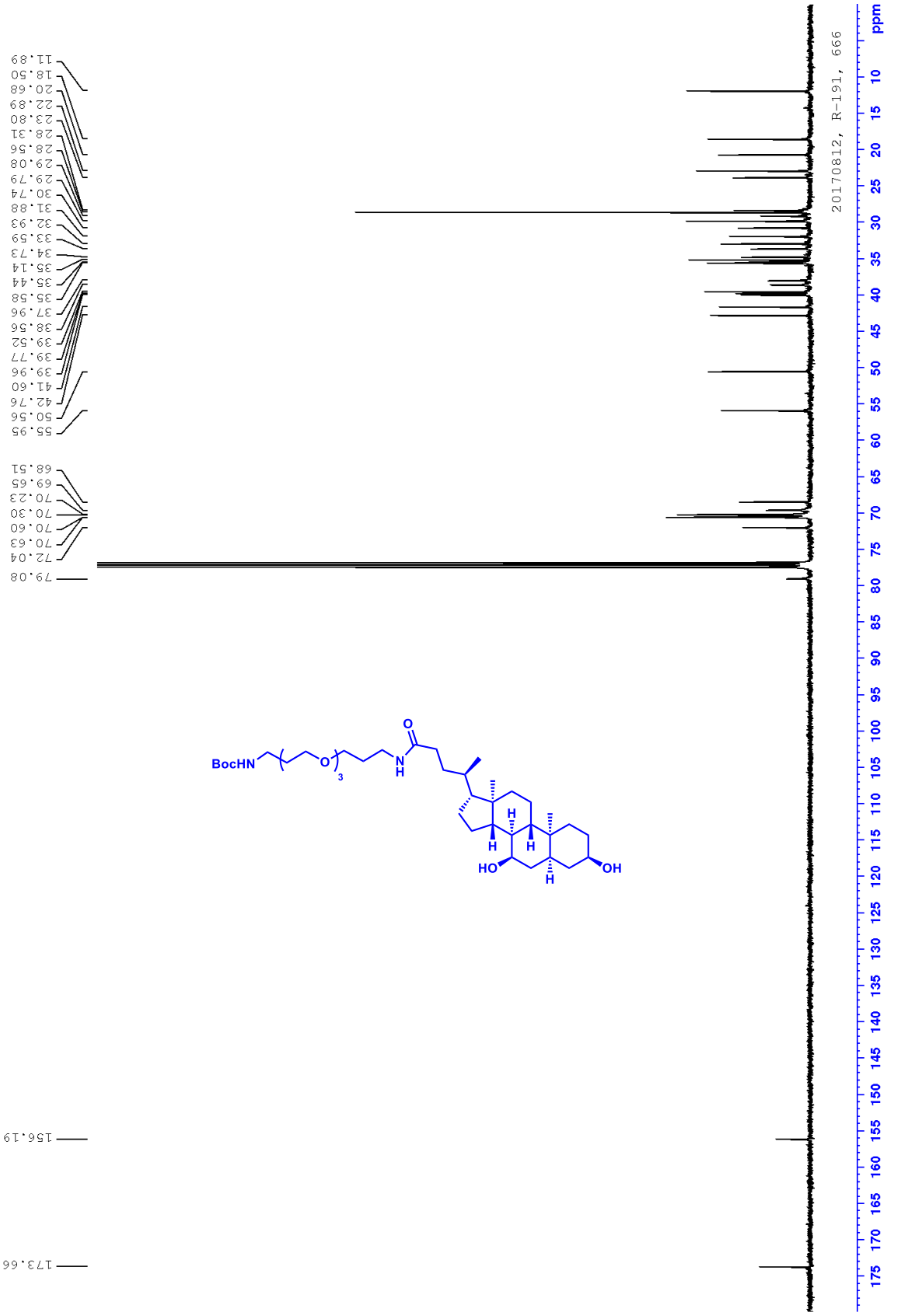
***tert*-Butyl ((*R*)-18-((3*R*,5*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,12-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-15-oxo-4,7,10-trioxa-14-azanonadecyl)carbamate [Boc–DCA]**



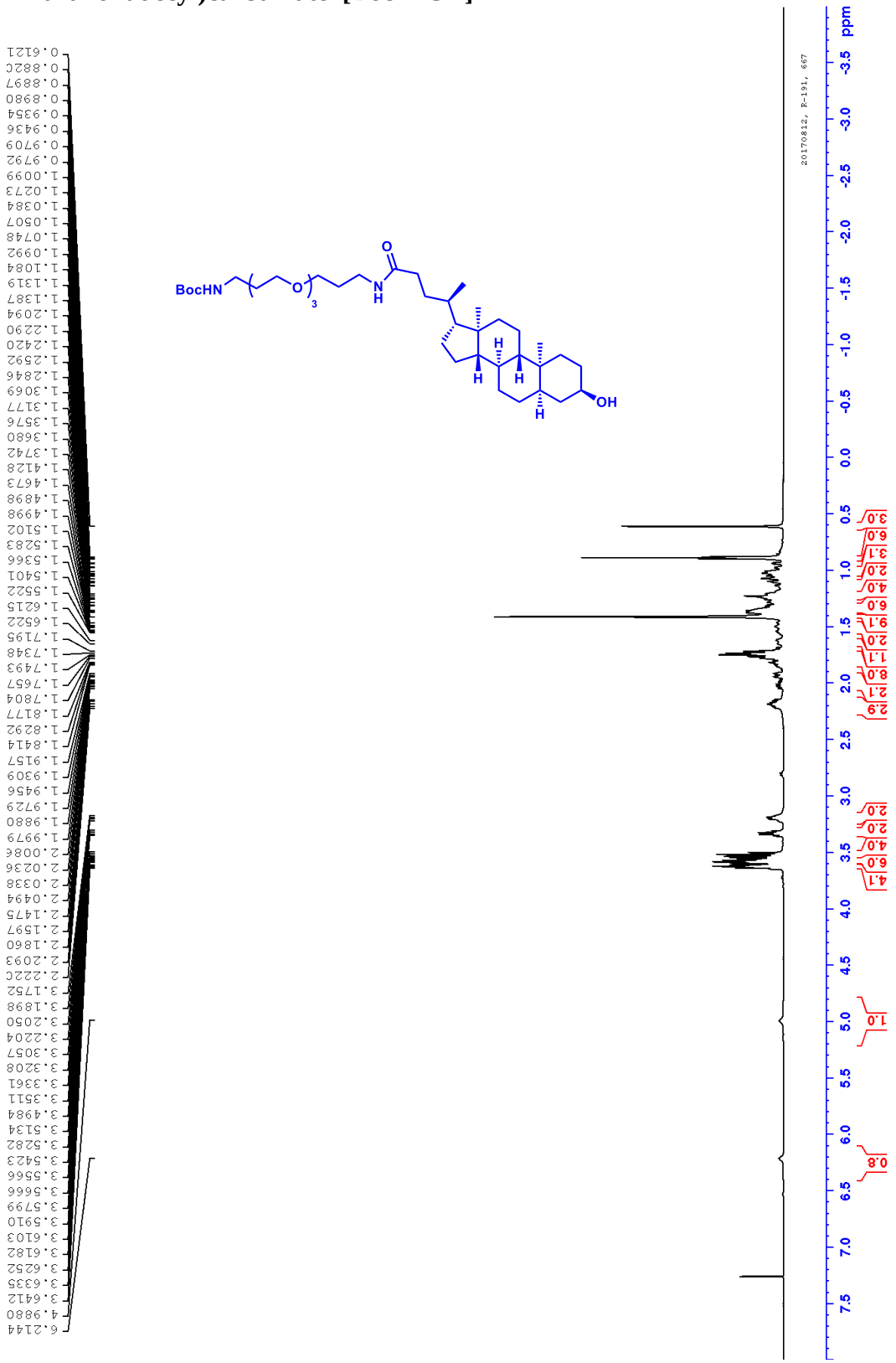

13.22
17.67
23.71
24.86
27.46
28.39
28.68
29.90
30.44
30.91
31.06
33.36
34.19
34.80
35.29
36.42
36.84
37.19
37.44
37.76
38.71
43.61
47.55
48.11
69.88
71.24
71.55
72.52
74.00
79.84
158.44
176.76
20170722, R-174, 590
ppm
BocHN
O
N
H
OH
OH
H
H
H
H

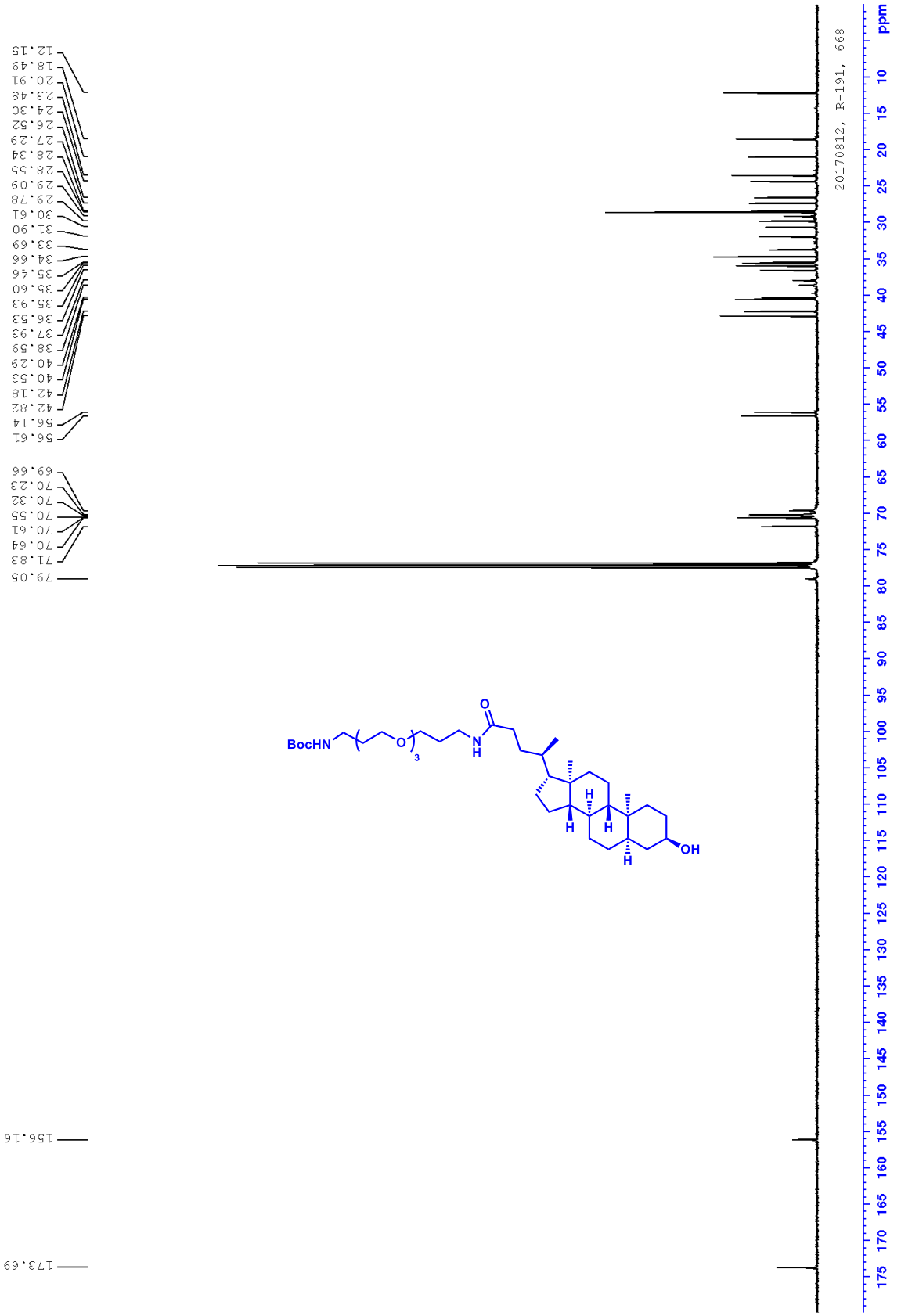
***tert*-Butyl ((*R*)-18-((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3,7-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-15-oxo-4,7,10-trioxa-14-azanonadecyl)carbamate [Boc–CDCA]**



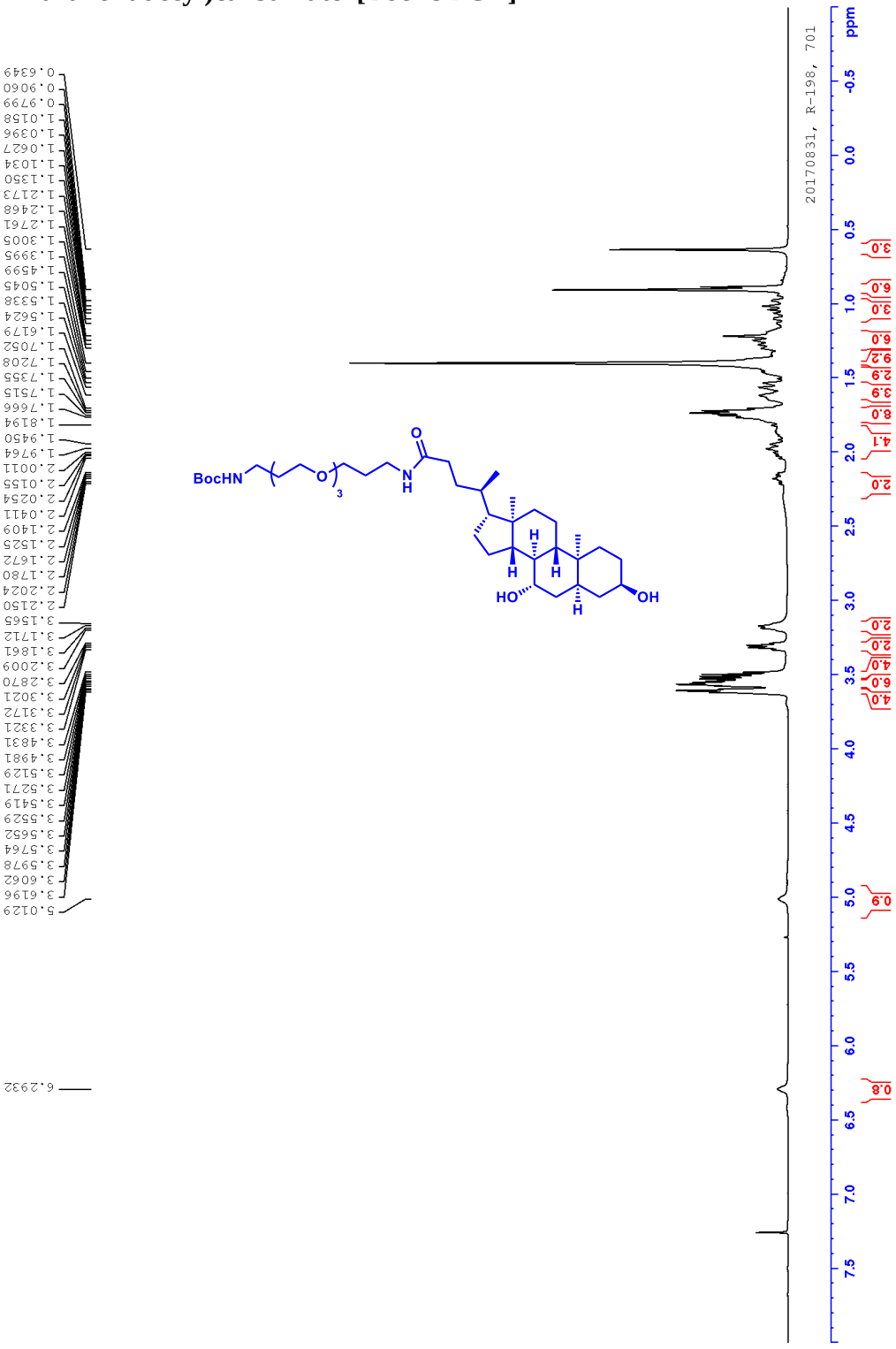

20170812, R-191, 666
ppm
11.89
18.50
20.68
22.89
23.80
28.31
28.56
29.08
29.79
30.74
31.88
32.93
33.59
34.73
35.14
35.44
35.58
37.96
38.56
39.52
39.77
39.96
41.60
42.76
50.56
55.95
68.51
69.65
70.23
70.30
70.60
70.63
72.04
79.08
156.19
173.66
BocHN
O
N
H
3
HO
OH
H
H
H
H

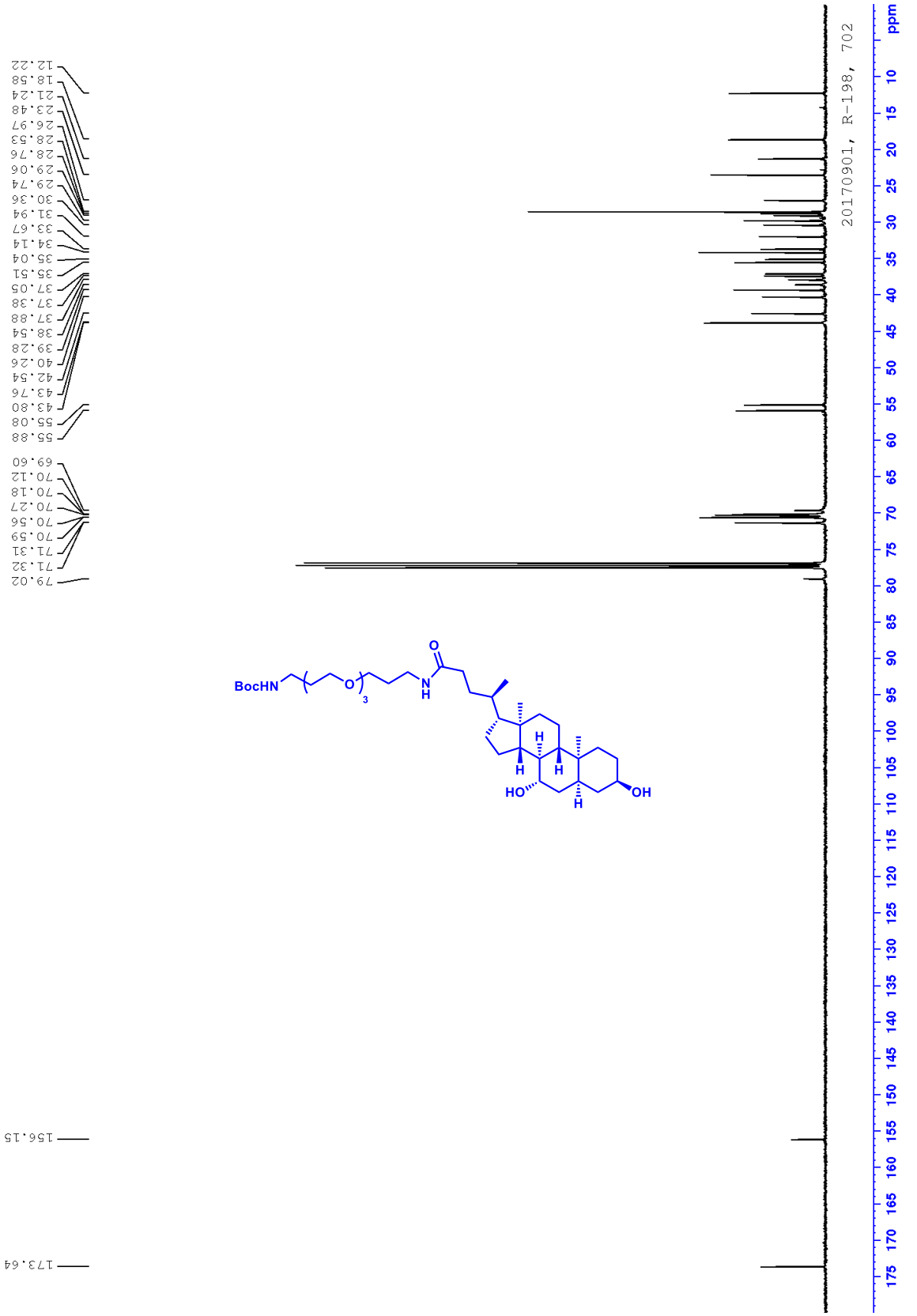
***tert*-Butyl ((*R*)-18-((3*R*,5*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3-hydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-15-oxo-4,7,10-trioxa-14-azanonadecyl)carbamate [Boc–LCA]**



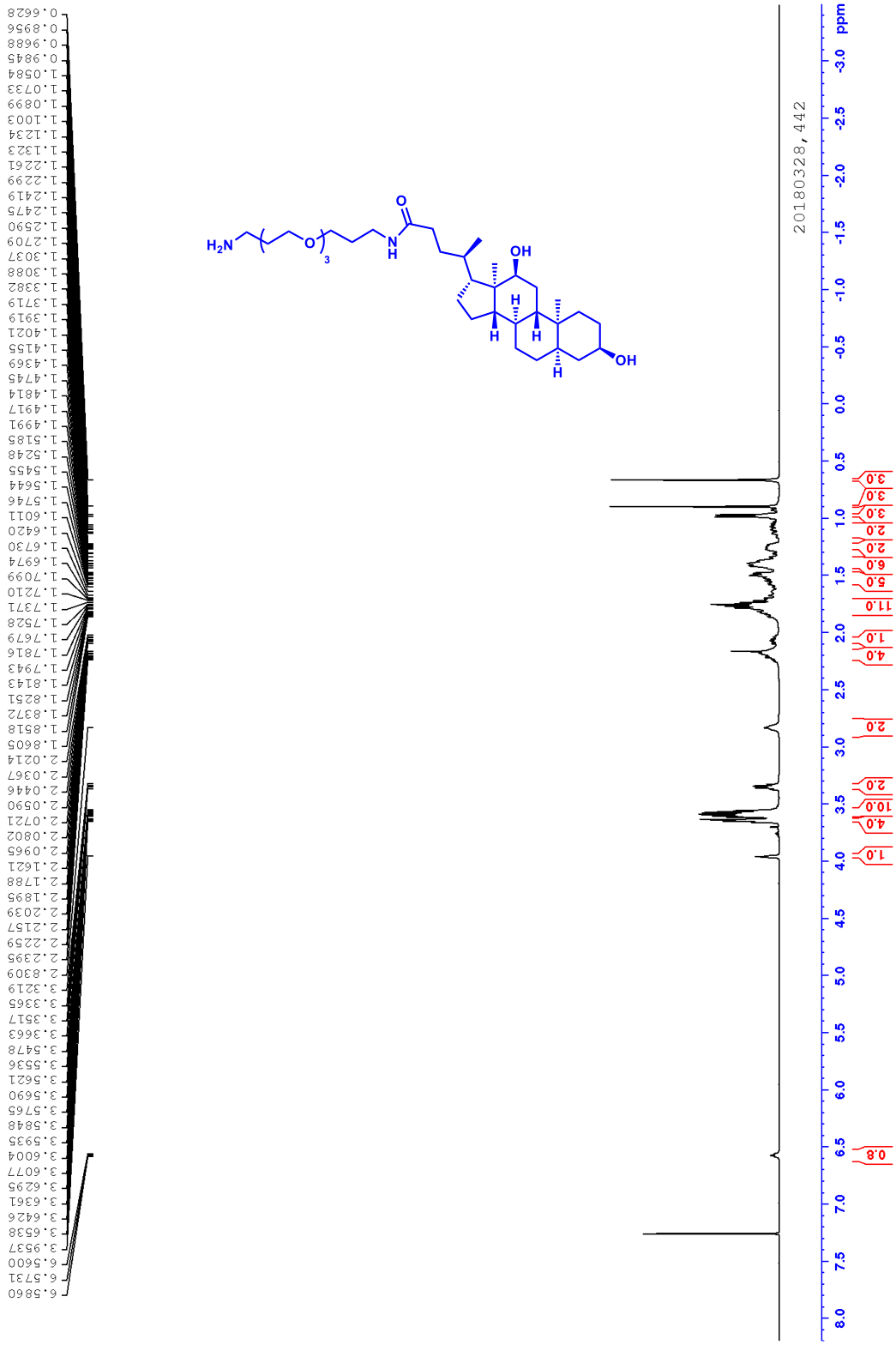

20170812, R-191, 668
ppm
BocHN
O
N
H
OH
12.15
18.49
20.91
23.48
24.30
26.52
27.29
28.34
28.55
29.09
29.78
30.61
31.90
33.69
34.66
35.46
35.60
35.93
36.53
37.93
38.59
40.29
40.53
42.18
42.82
56.14
56.61
69.66
70.23
70.32
70.55
70.61
70.64
71.83
79.05
156.16
173.69

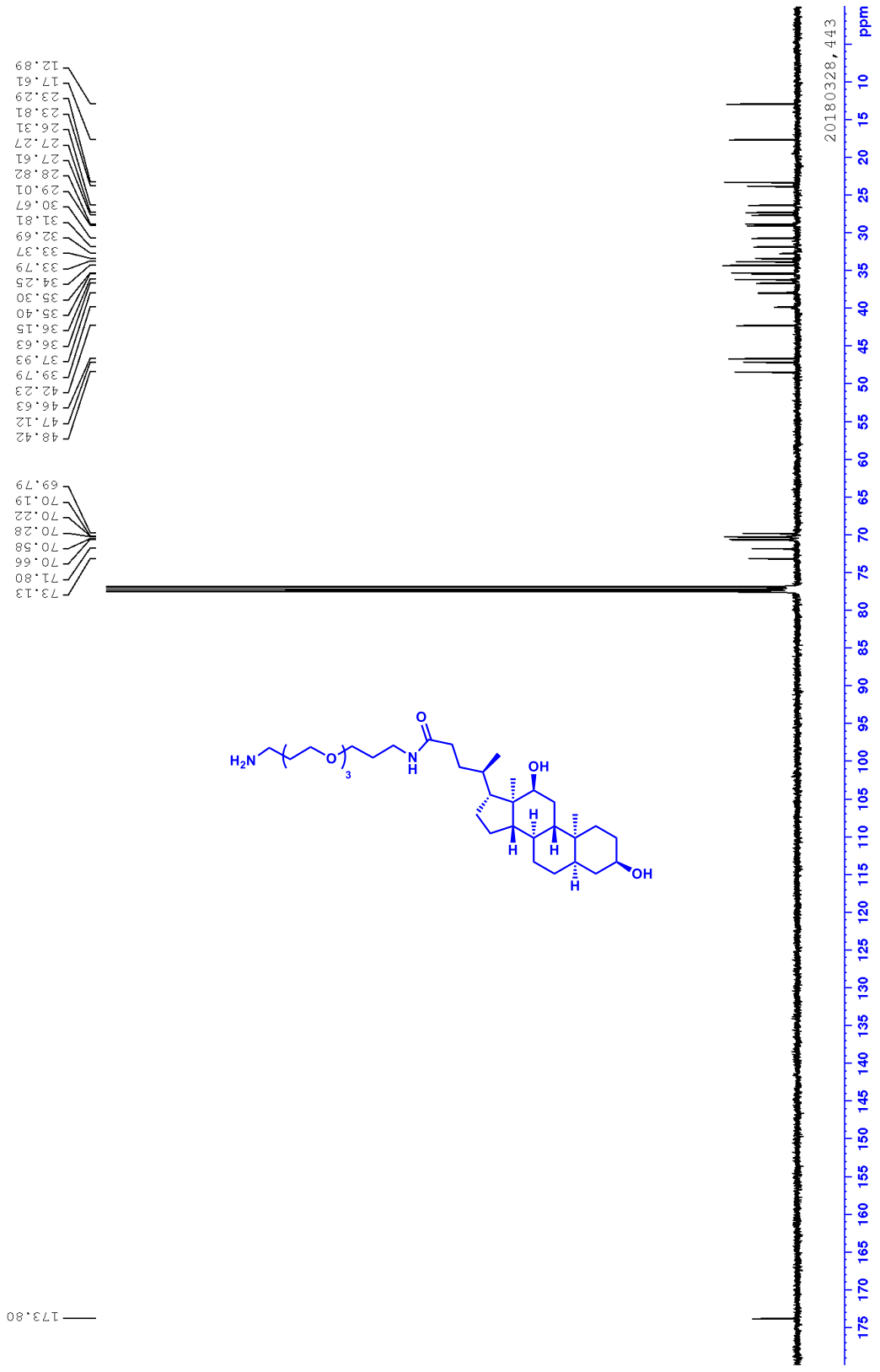
***tert*-Butyl ((*R*)-18-((3*R*,5*S*,7*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3,7-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-15-oxo-4,7,10-trioxa-14-azanonadecyl)carbamate [Boc–UDCA]**



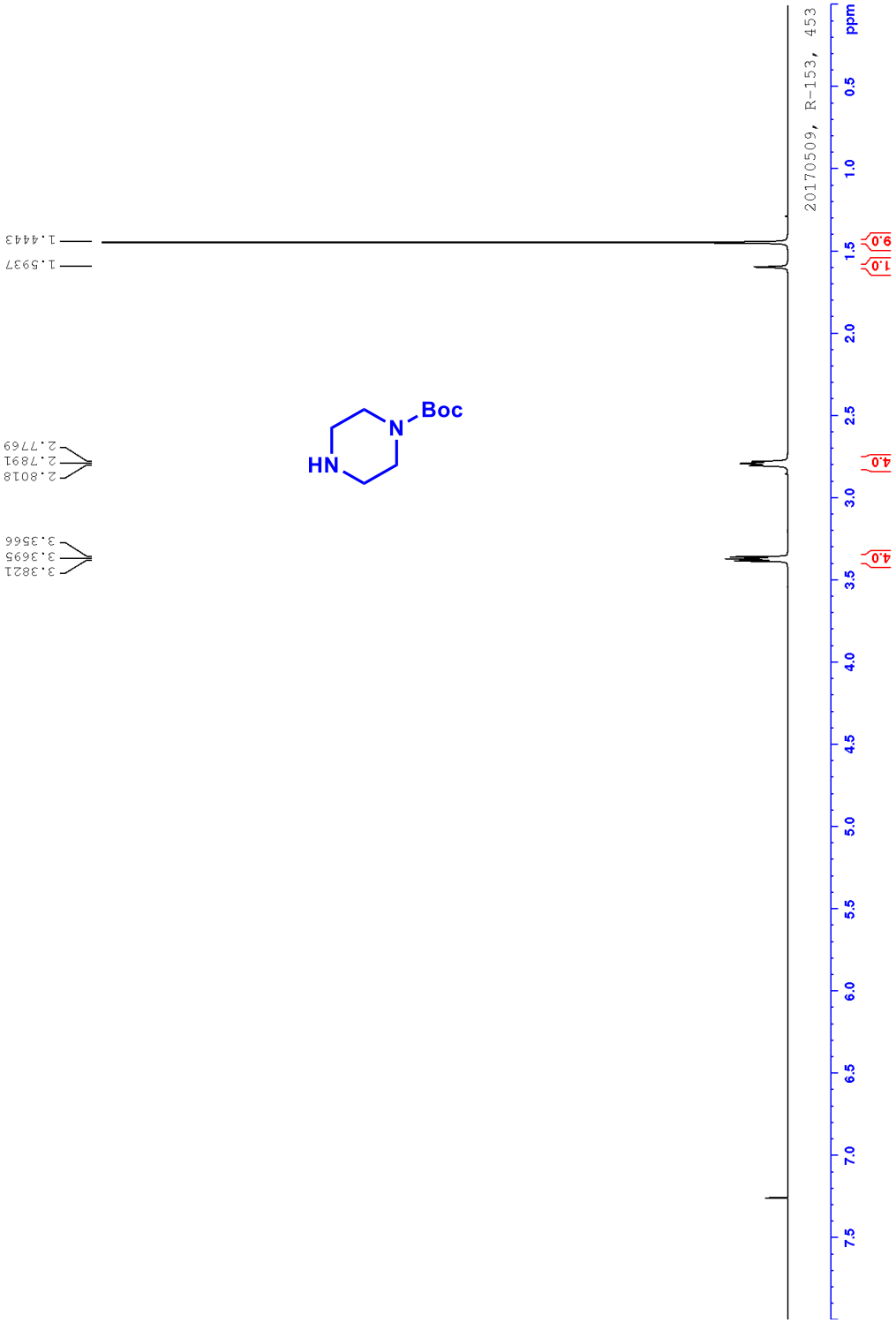

20170901, R-198, 702
ppm
BocHN
O
N
H
O
3
HO
OH
H
H
H
12.22
18.58
21.24
23.48
26.97
28.53
28.76
29.06
29.74
30.36
31.94
33.67
34.14
35.04
35.51
37.05
37.38
37.88
38.54
39.28
40.26
42.54
43.76
43.80
55.08
55.88
69.60
70.12
70.18
70.27
70.56
70.59
71.31
71.32
79.02
156.15
173.64

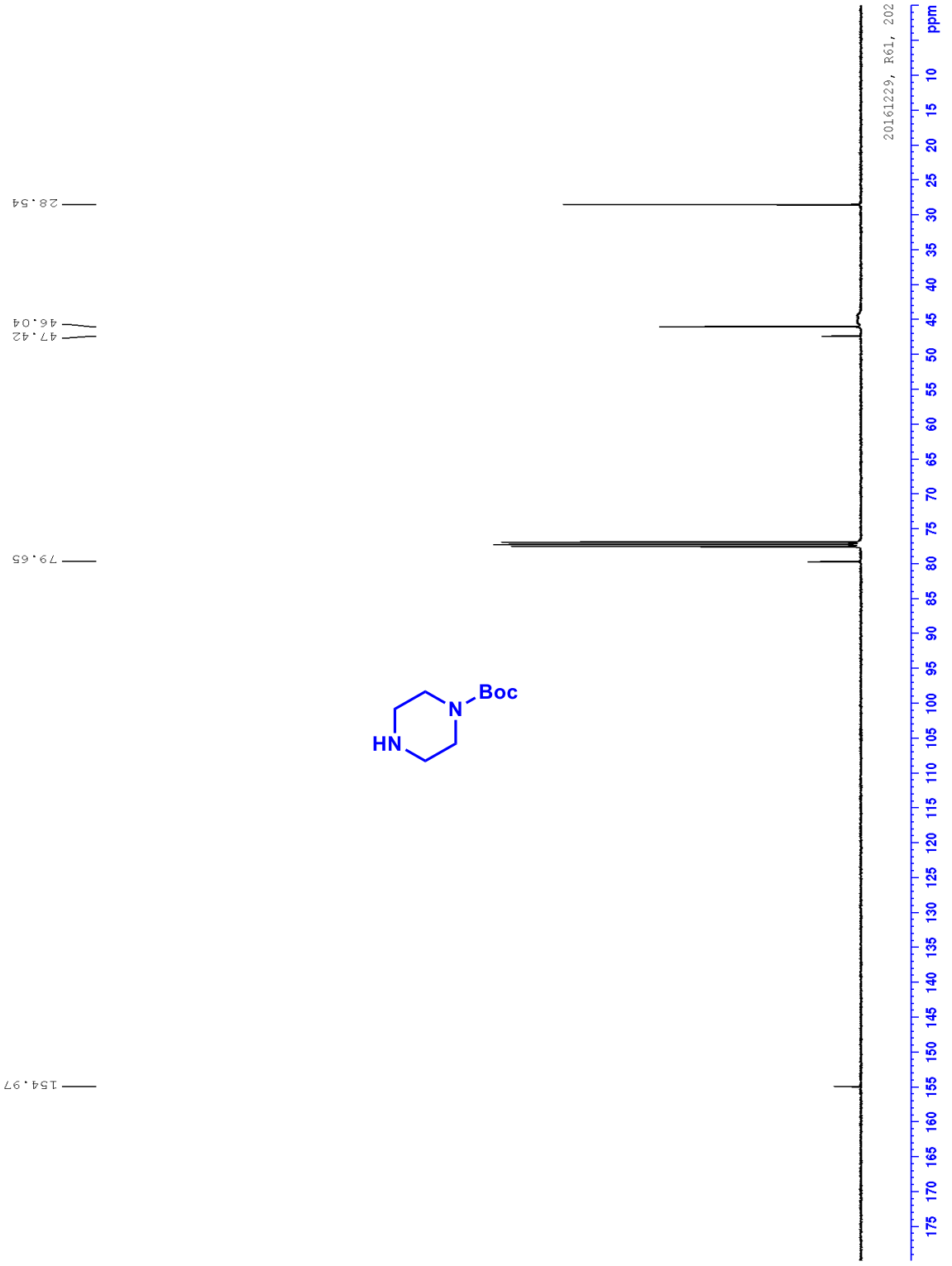
(*R*)-*N*-(3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)-4-((3*R*,5*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,12-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanamide [DCA–amine]



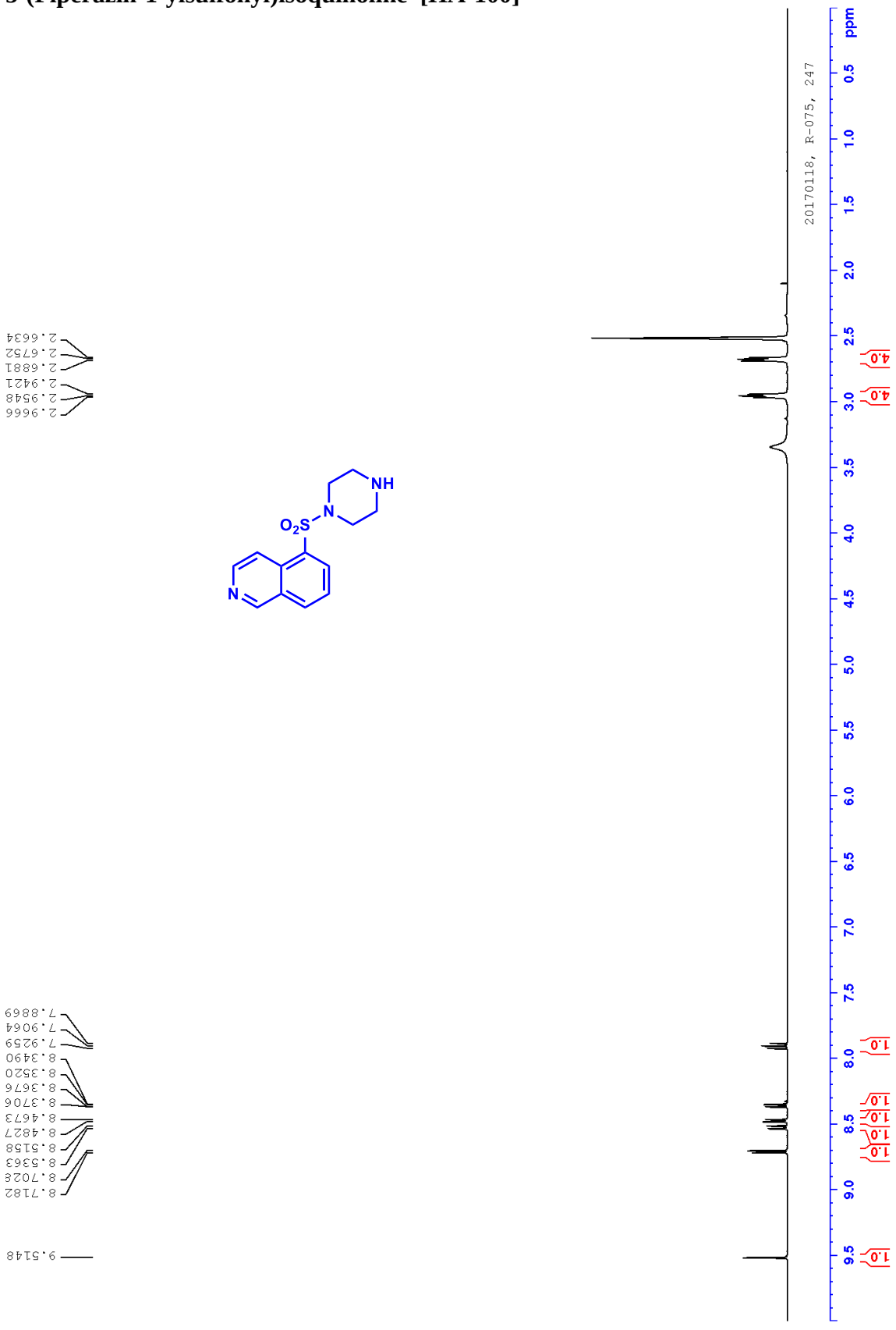

12.89
17.61
23.29
23.81
26.31
27.27
27.61
28.82
29.01
30.67
31.81
32.69
33.37
33.79
34.25
35.30
35.40
36.15
36.63
37.93
39.79
42.23
46.63
47.12
48.42
69.79
70.19
70.22
70.28
70.58
70.66
71.80
73.13
173.80
20180328,443
ppm
O
N
H
OH
H
H
H
OH
H2N
O
3

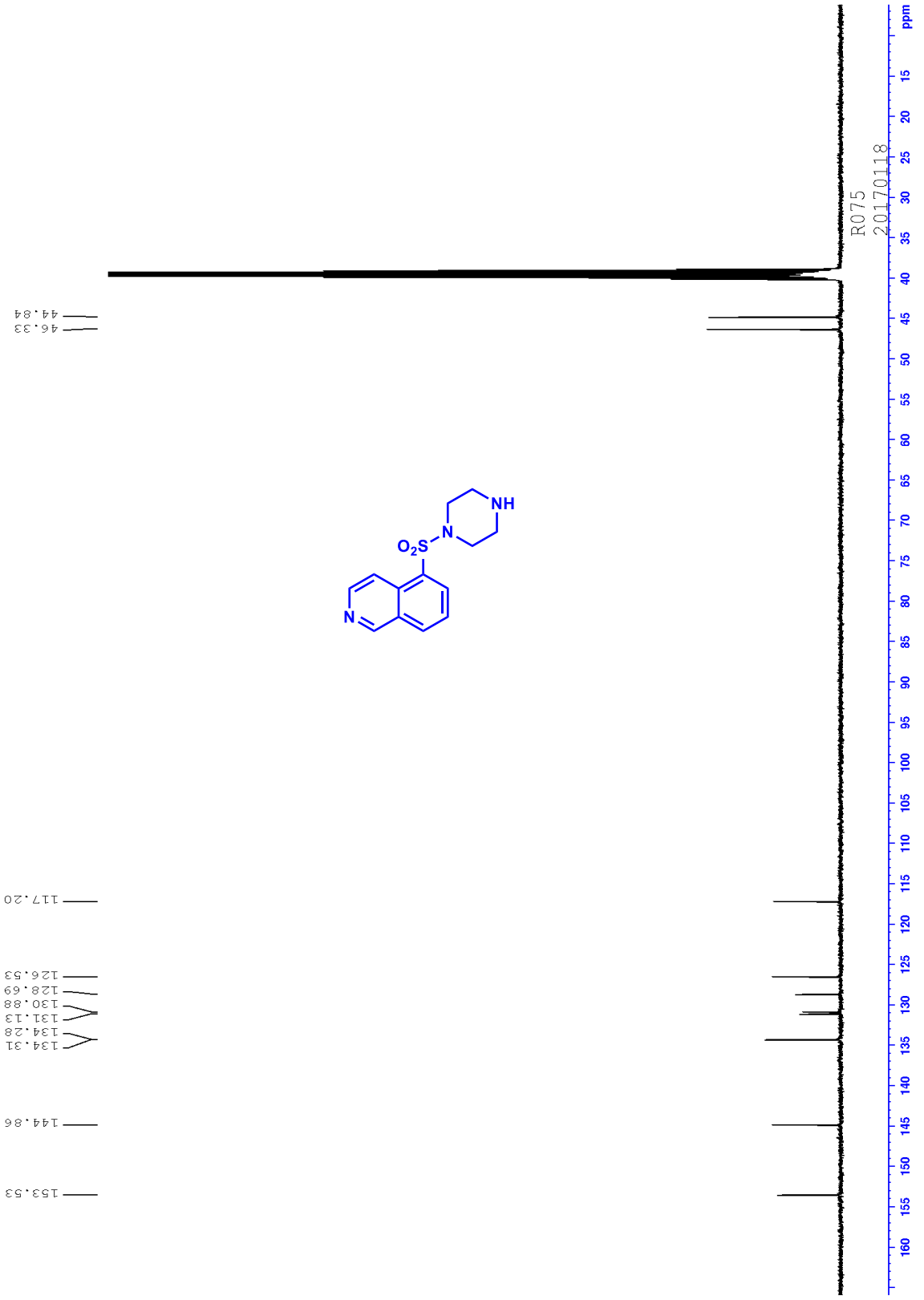
***tert*-Butyl piperazine-1-carboxylate**



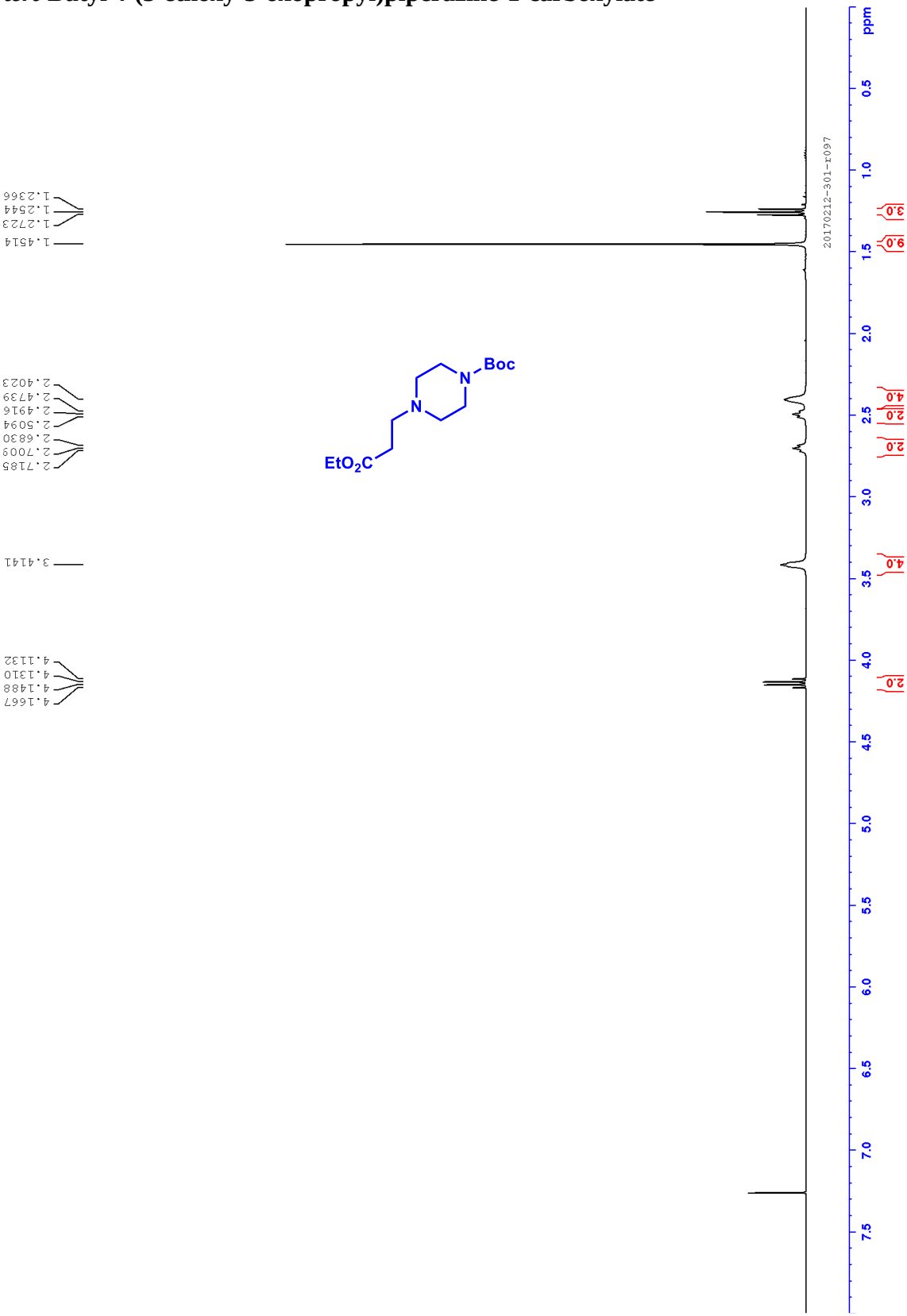

20161229, R61, 202
ppm
28.54
46.04
47.42
79.65
154.97
Boc
N
HN

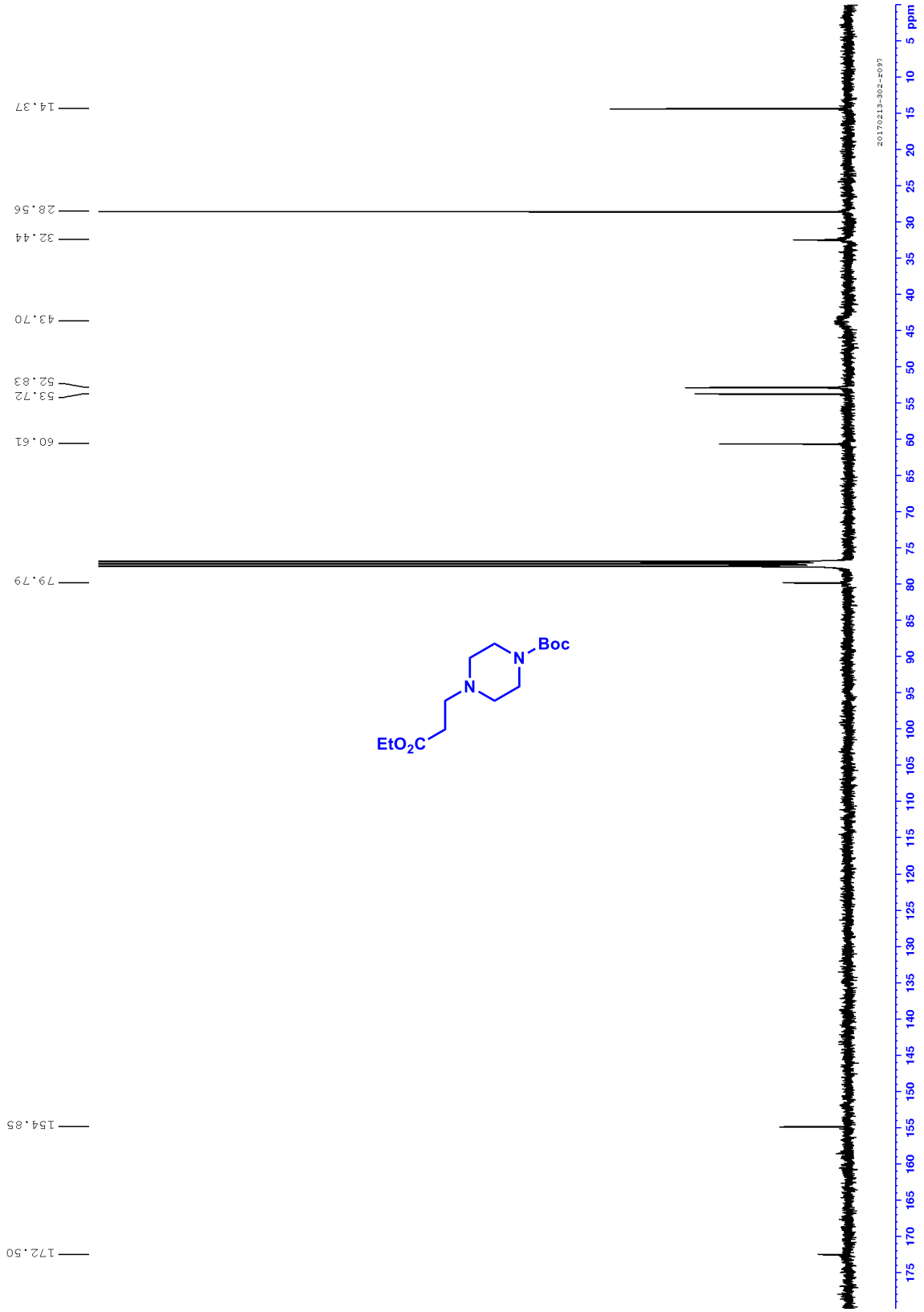
5-(Piperazin-1-ylsulfonyl)isoquinoline [HA-100]



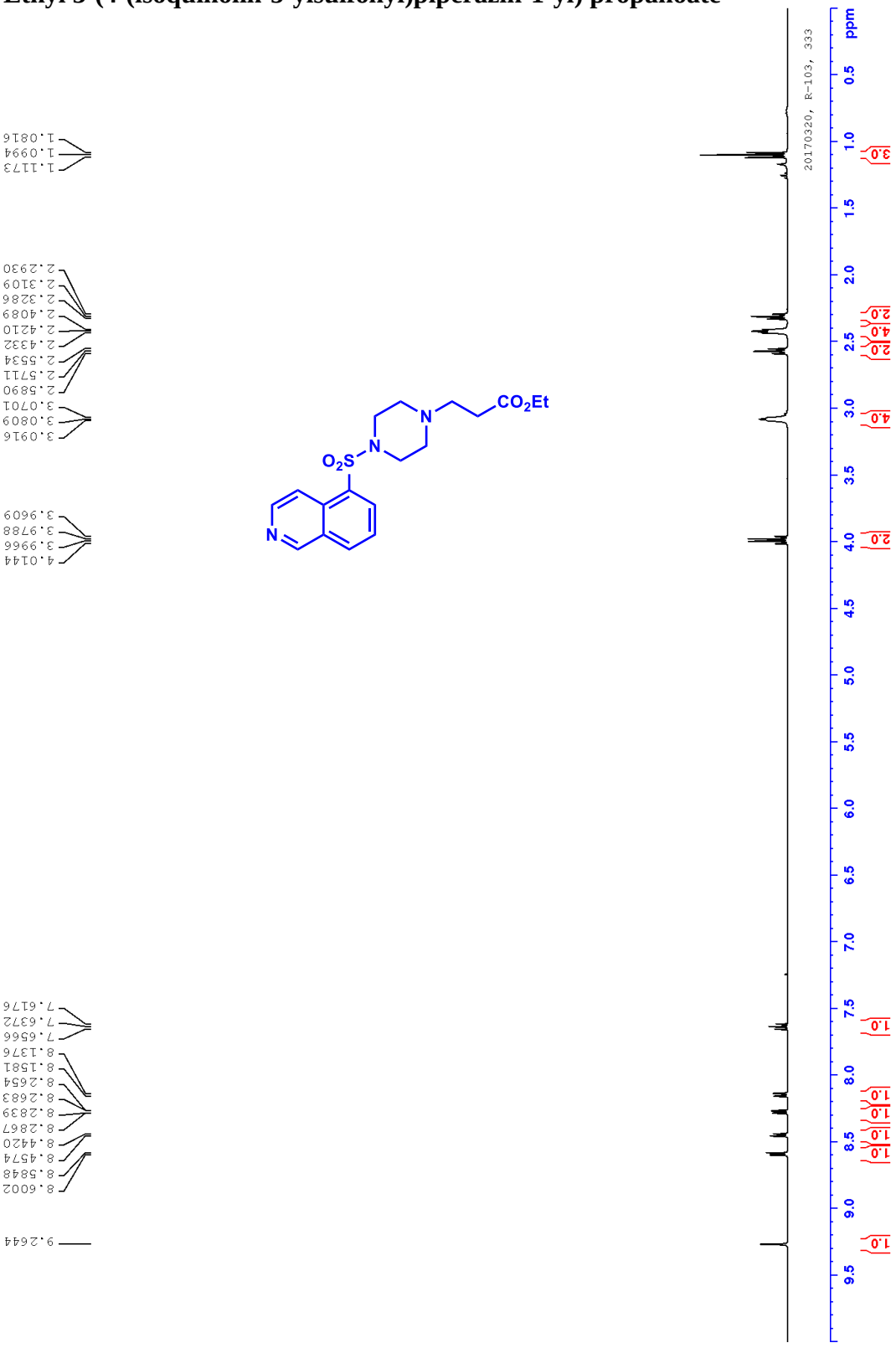

R075
20170118
ppm
44.84
46.33
117.20
126.53
128.69
130.88
131.13
134.28
134.31
144.86
153.53
NH
N
O2S
N

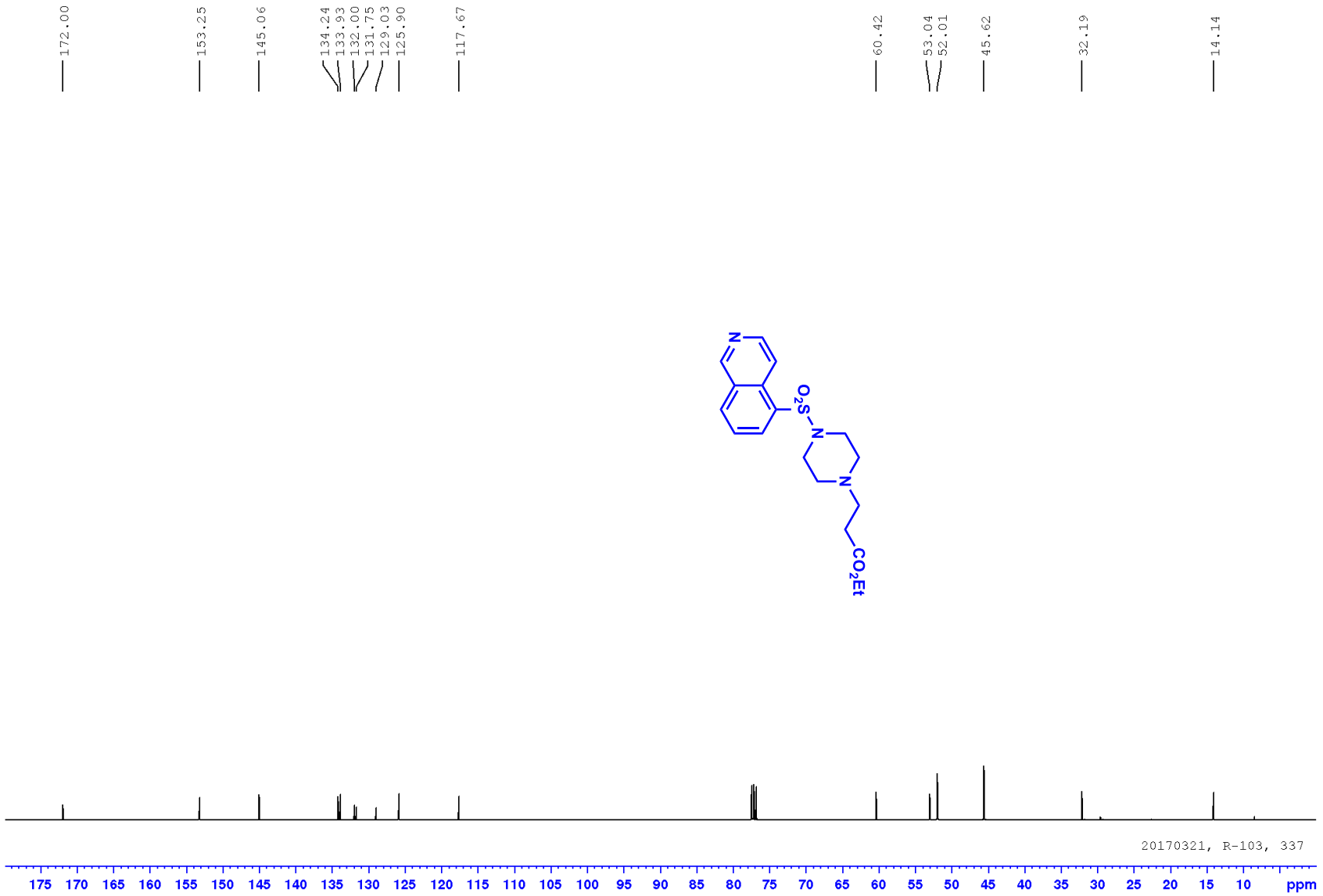
tert-Butyl 4-(3-ethoxy-3-oxopropyl)piperazine-1-carboxylate



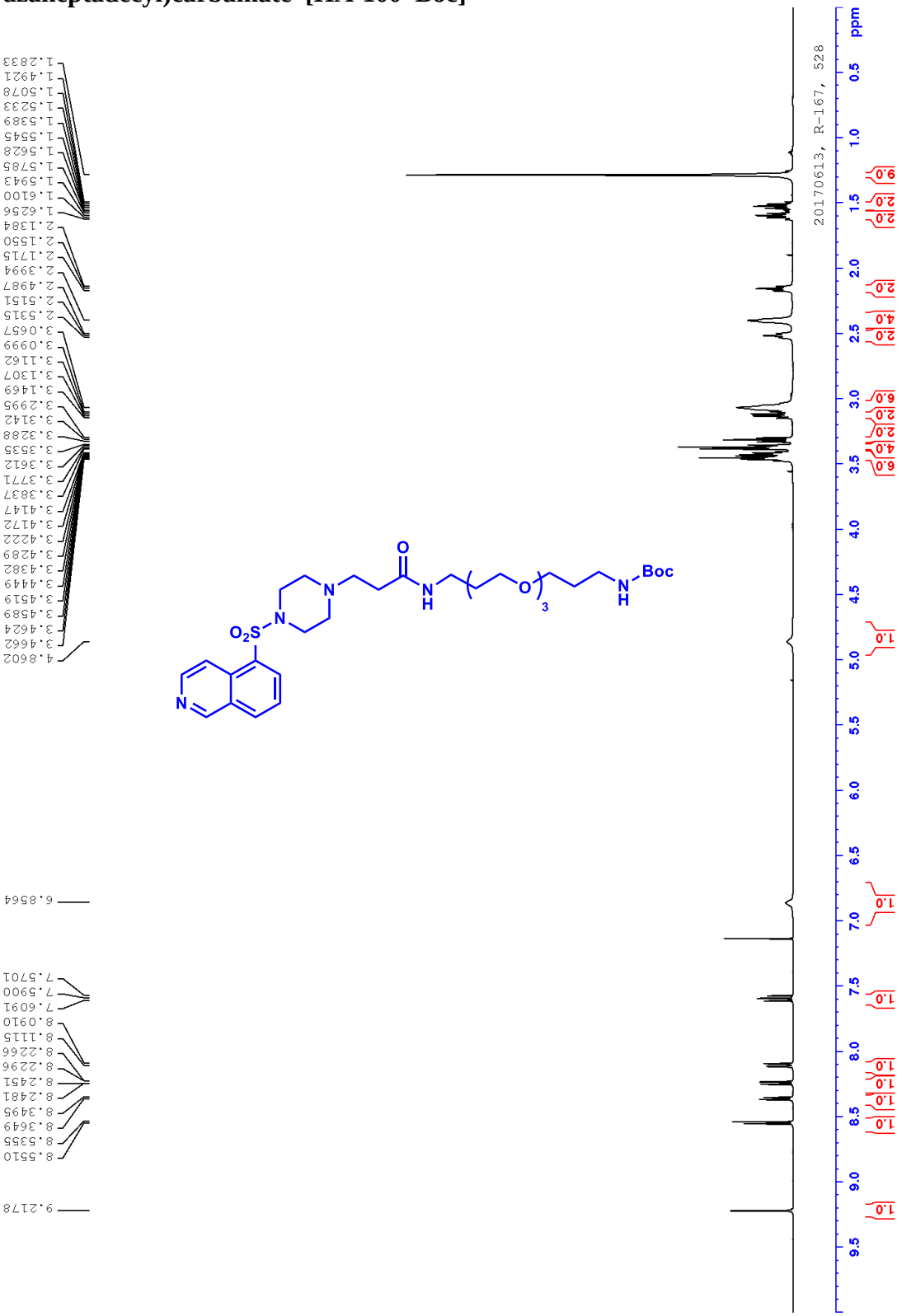

14.37
28.56
32.44
43.70
52.83
53.72
60.61
79.79
154.85
172.50
Boc
N
N
EtO2C
20170213-302-p97
ppm

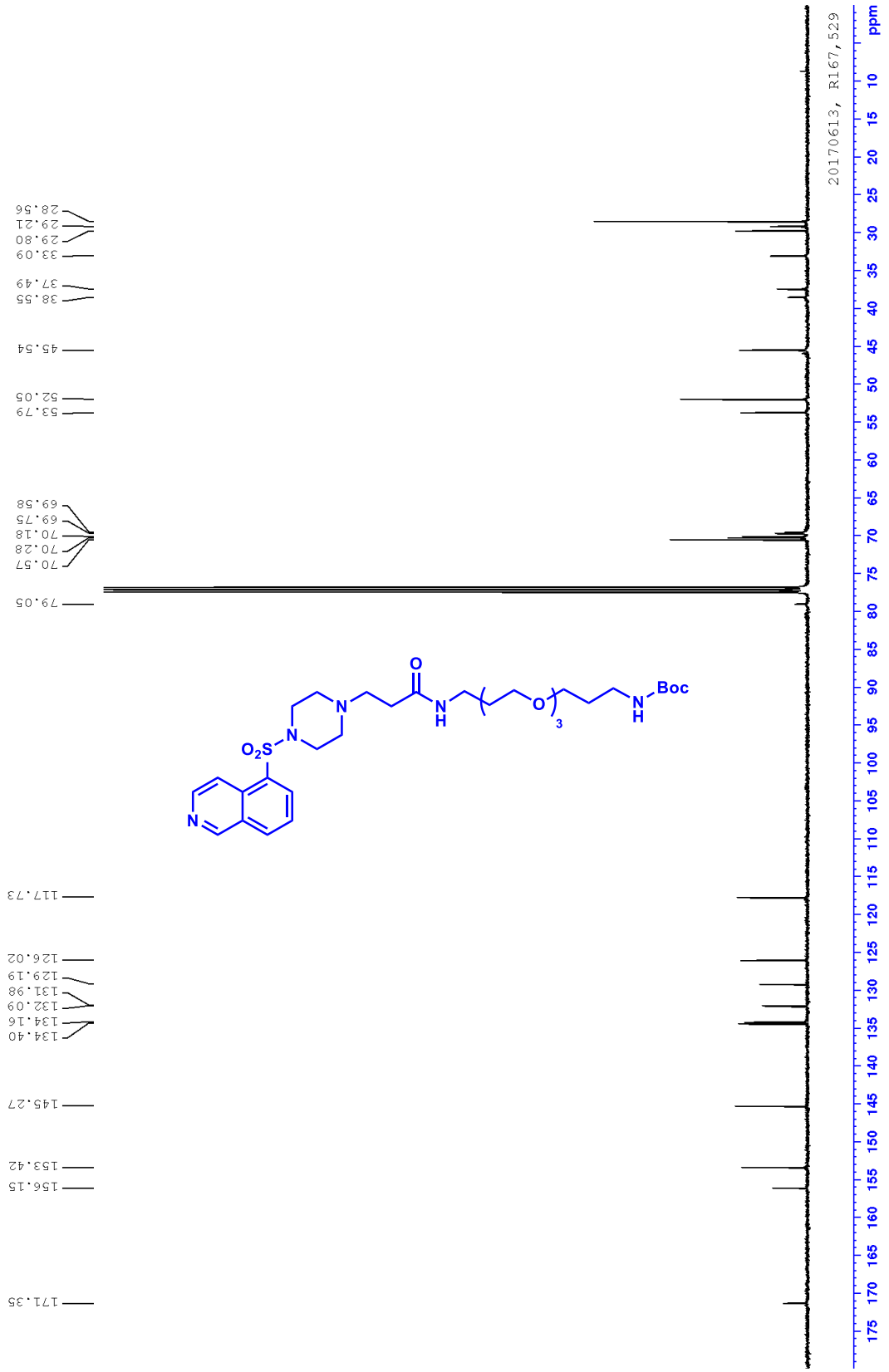
Ethyl 3-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl) propanoate



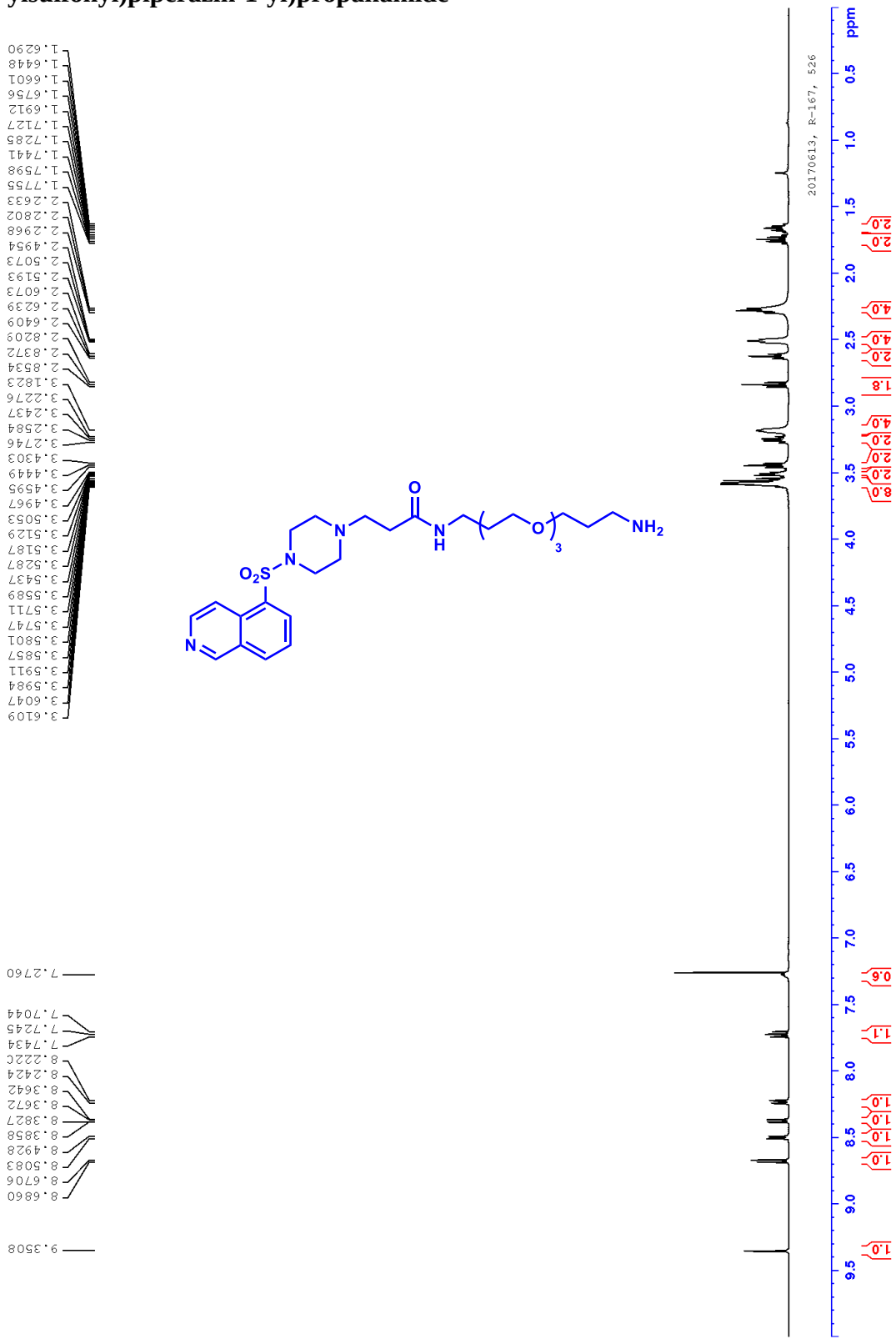

172.00
153.25
145.06
134.24
133.93
132.00
131.75
129.03
125.90
117.67
60.42
53.04
52.01
45.62
32.19
14.14
20170321, R-103, 337
175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 ppm

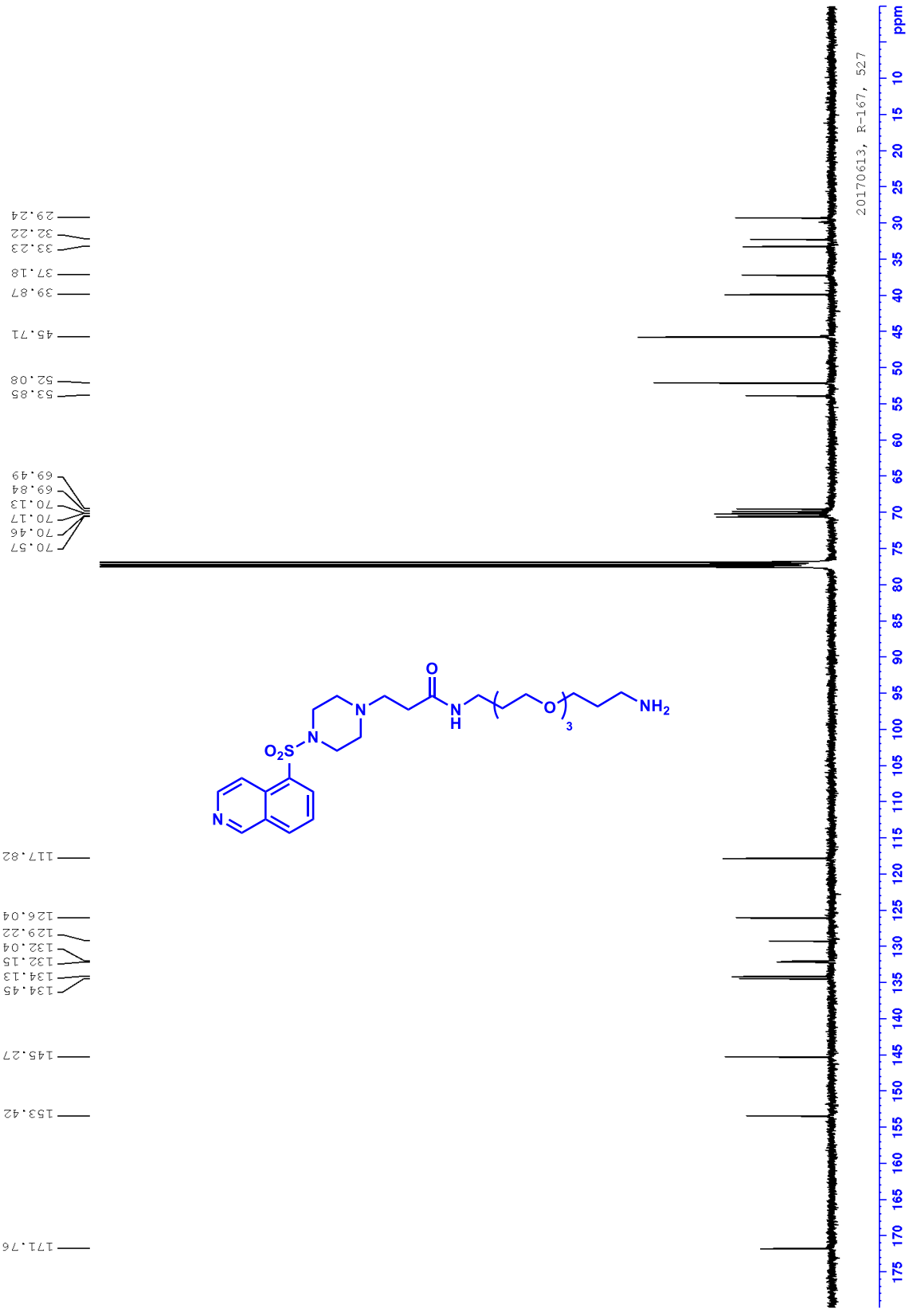
***tert*-Butyl (17-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)carbamate [HA-100–Boc]**



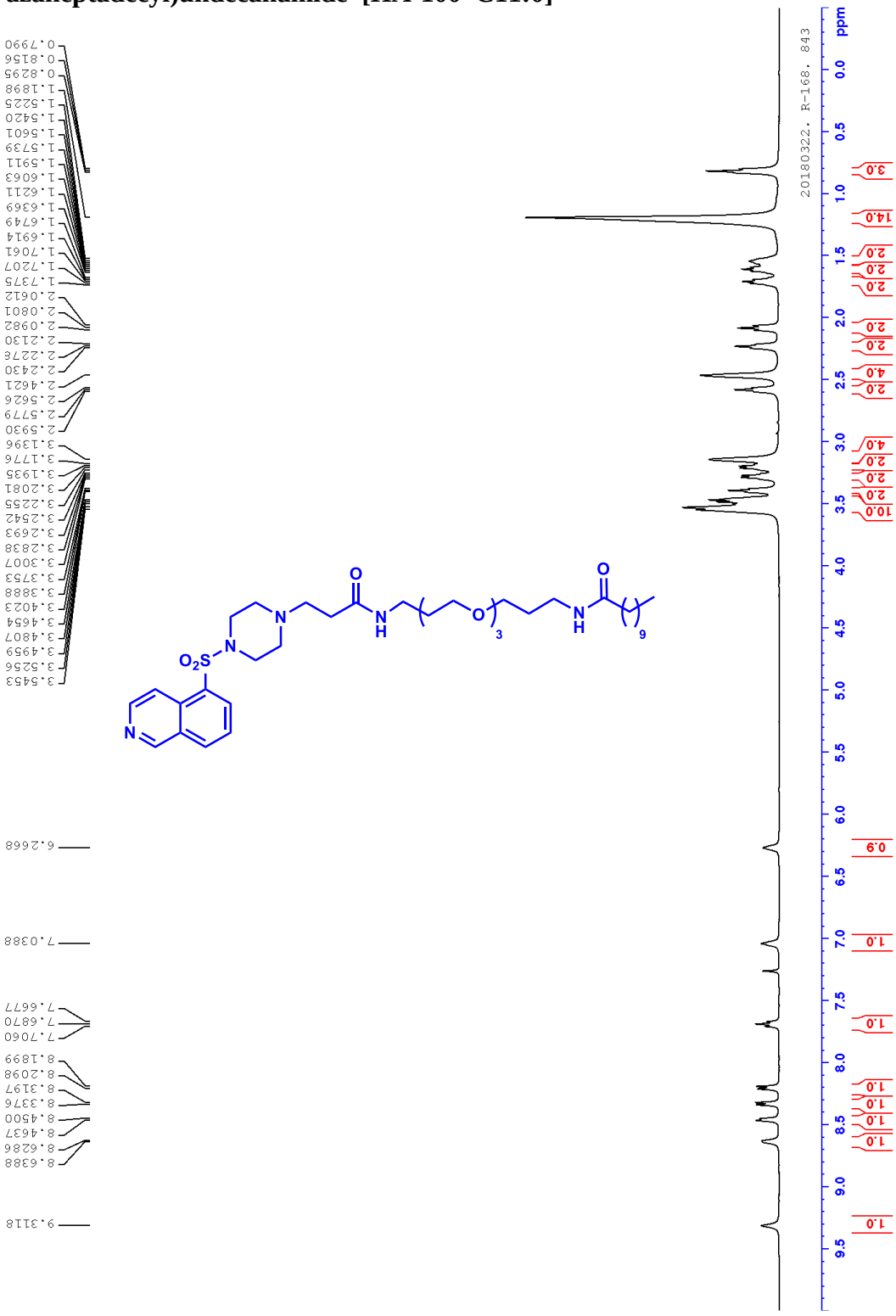

20170613, R167,529
ppm
28.56
29.21
29.80
33.09
37.49
38.55
45.54
52.05
53.79
69.58
69.75
70.18
70.28
70.57
79.05
117.73
126.02
129.19
131.98
132.09
134.16
134.40
145.27
153.42
156.15
171.35
O
N
H
O
3
N
H
Boc
O2S
N
N

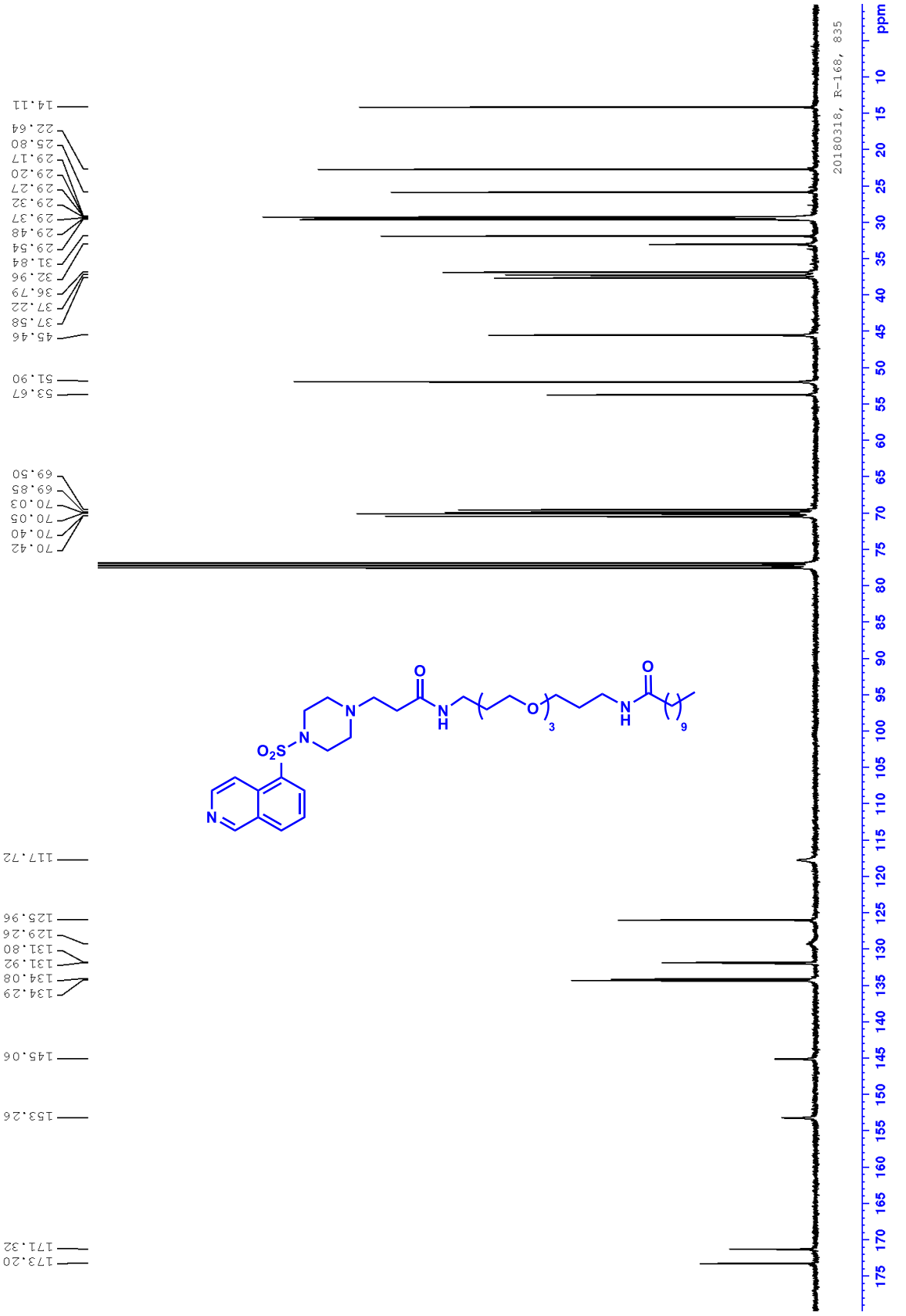
_N_-(3-(2-(2-(3-aminopropoxy)ethoxy)ethoxy)propyl)-3-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)propanamide



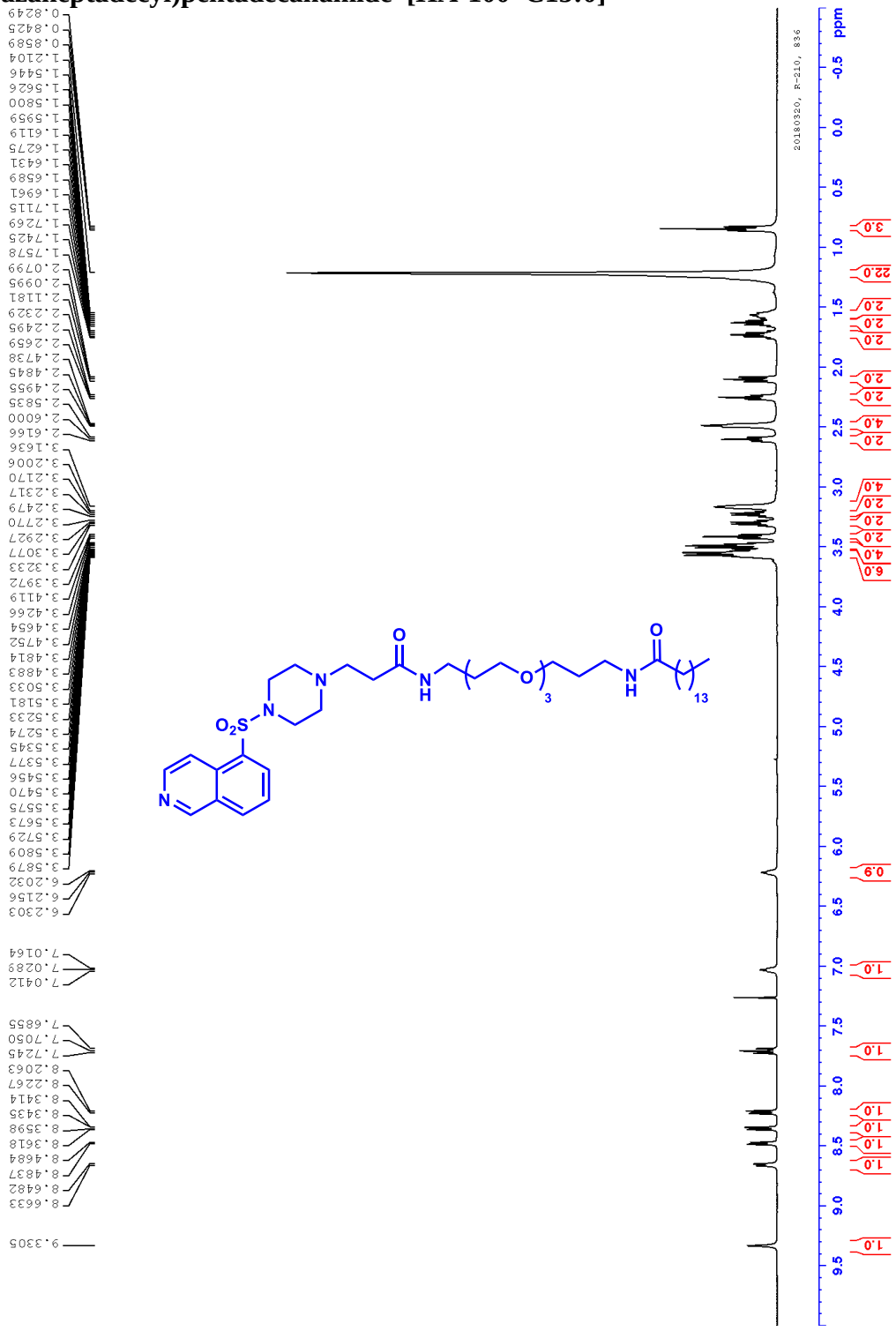

20170613, R-167, 527
ppm
29.24
32.22
33.23
37.18
39.87
45.71
52.08
53.85
69.49
69.84
70.13
70.17
70.46
70.57
117.82
126.04
129.22
132.04
132.15
134.13
134.45
145.27
153.42
171.76
O
N
N
H
O
3
NH2
O2S
N

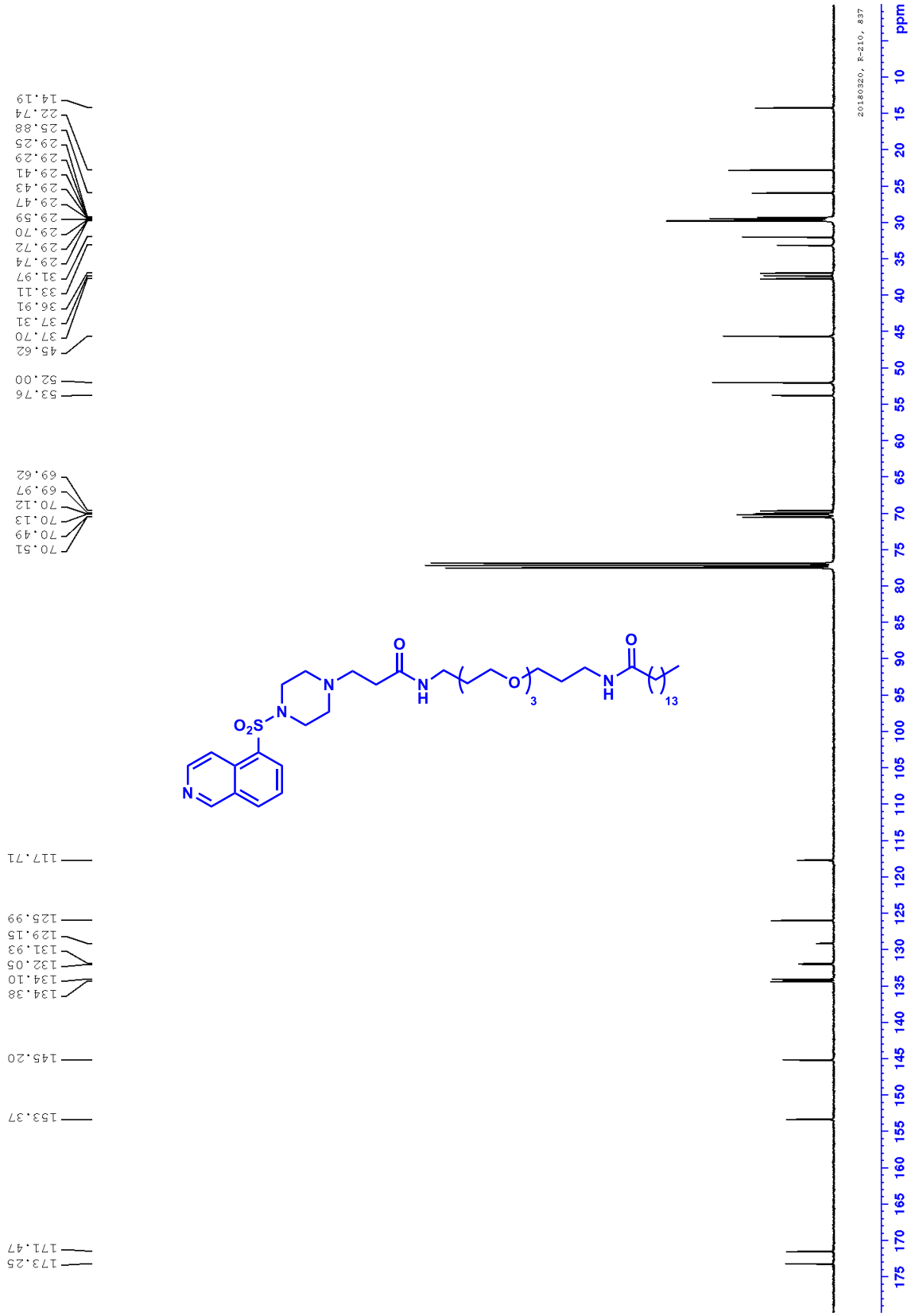
***N*-(17-(4-(Isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)undecanamide [HA-100–C11:0]**



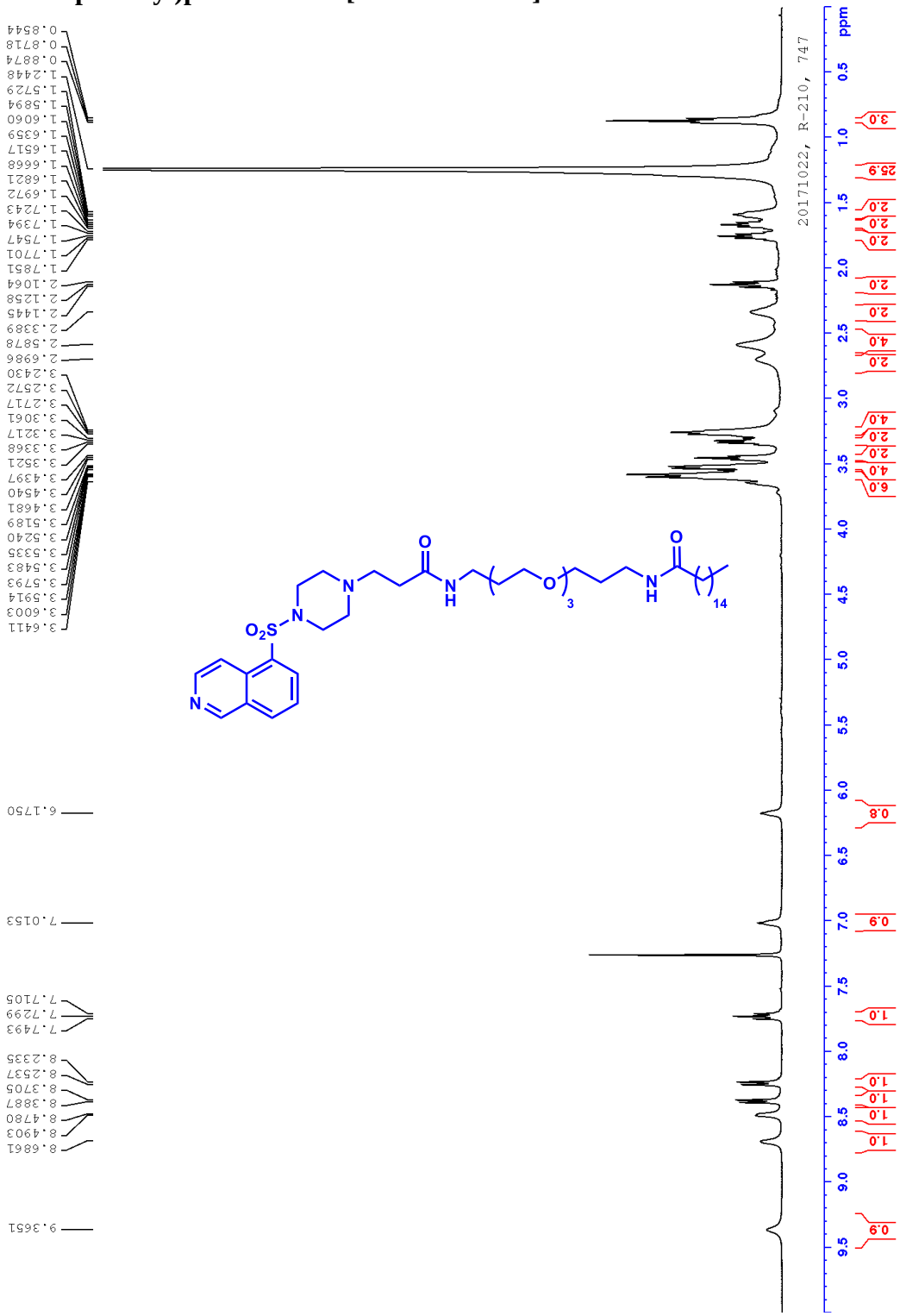

20180318, R-168, 835
ppm
14.11
22.64
25.80
29.17
29.20
29.27
29.32
29.37
29.48
29.54
31.84
32.96
36.79
37.22
37.58
45.46
51.90
53.67
69.50
69.85
70.03
70.05
70.40
70.42
117.72
125.96
129.26
131.80
131.92
134.08
134.29
145.06
153.26
171.32
173.20
O
N
H
O
3
N
H
O
9
N
N
O2S
N

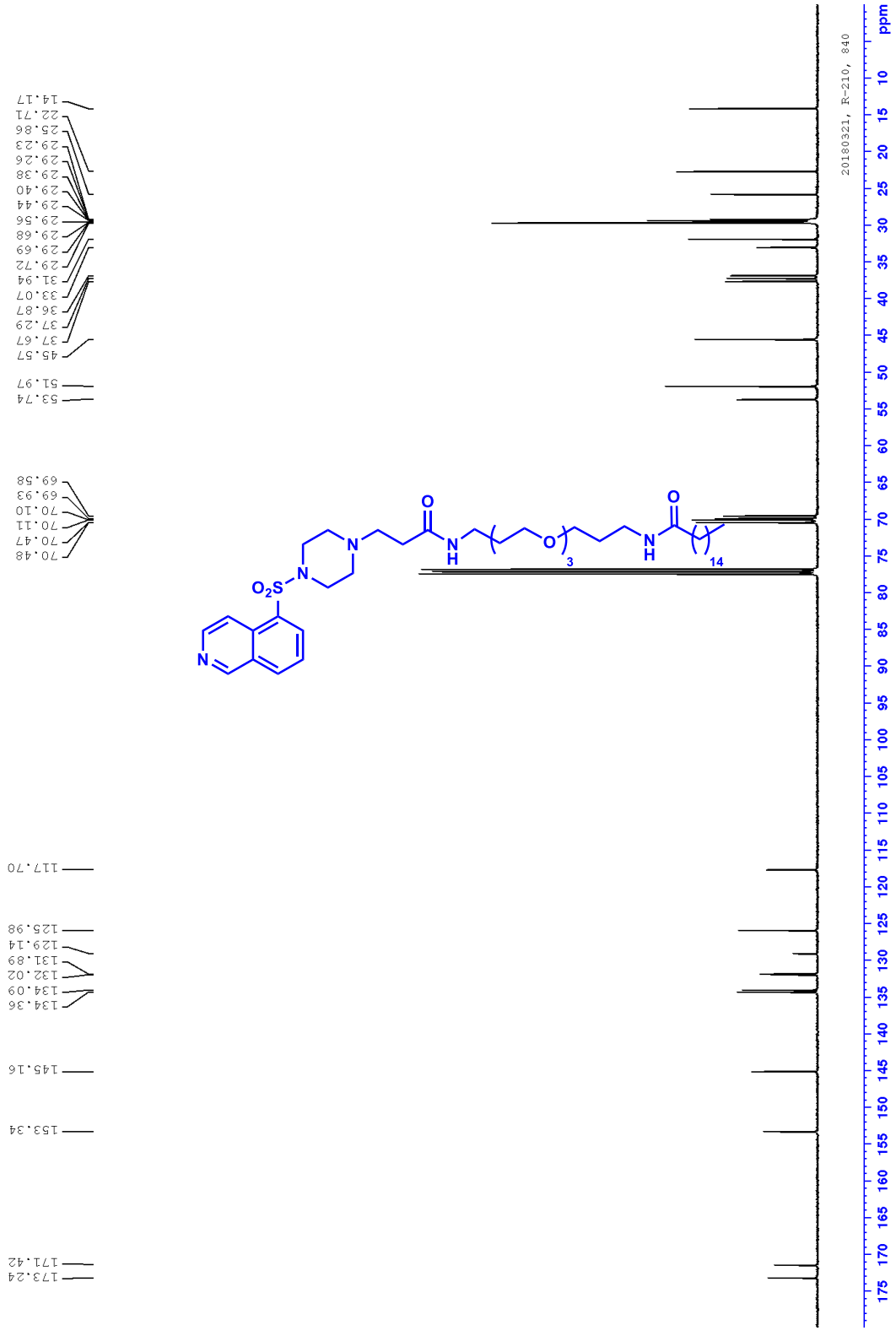
***N*-(17-(4-(Isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)pentadecanamide [HA-100–C15:0]**



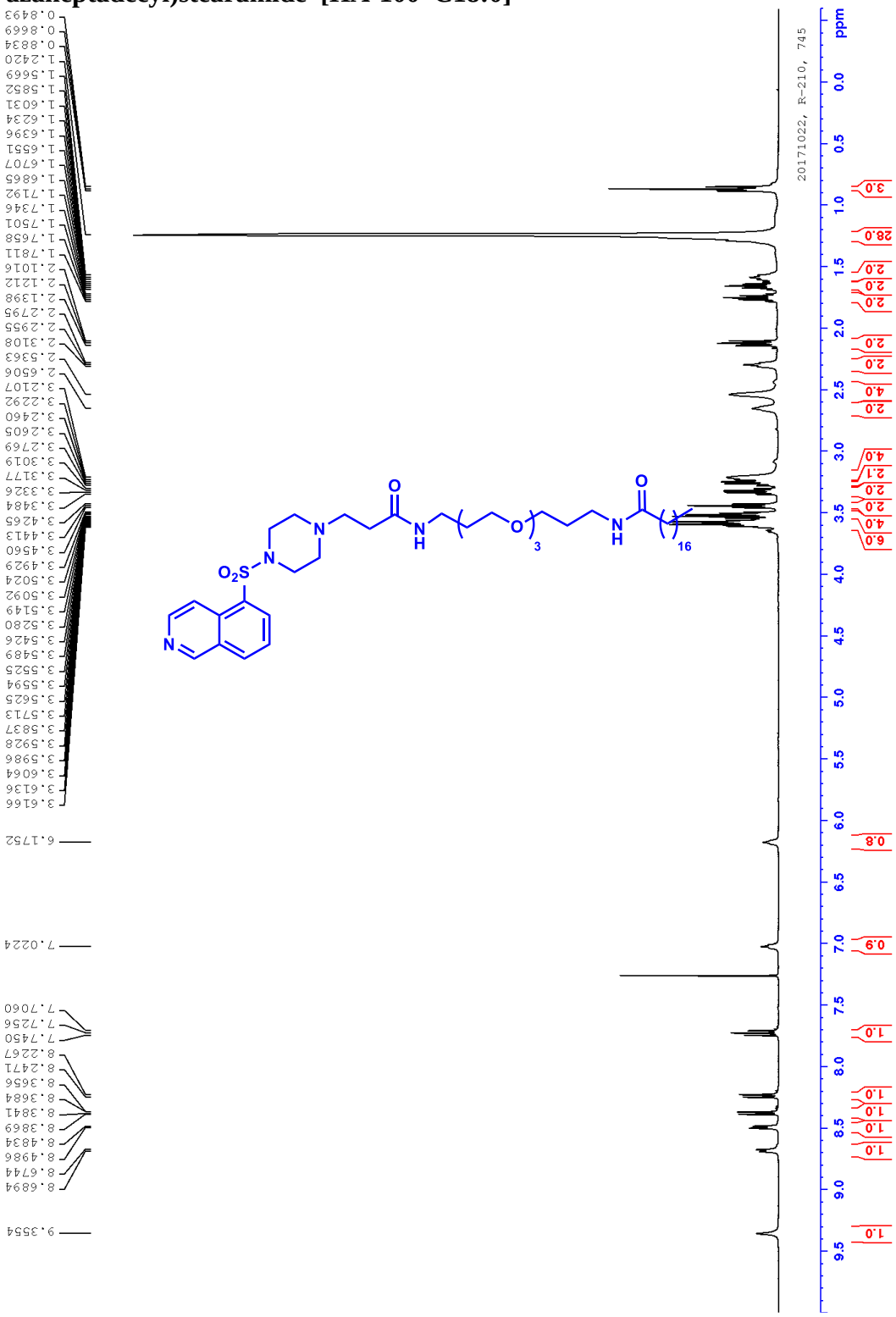

20180320, R-210, 837
ppm
14.19
22.74
25.88
29.25
29.29
29.41
29.43
29.47
29.59
29.70
29.72
29.74
31.97
33.11
36.91
37.31
37.70
45.62
52.00
53.76
69.62
69.97
70.12
70.13
70.49
70.51
117.71
125.99
129.15
131.93
132.05
134.10
134.38
145.20
153.37
171.47
173.25
O
N
H
O2S
N
3
13

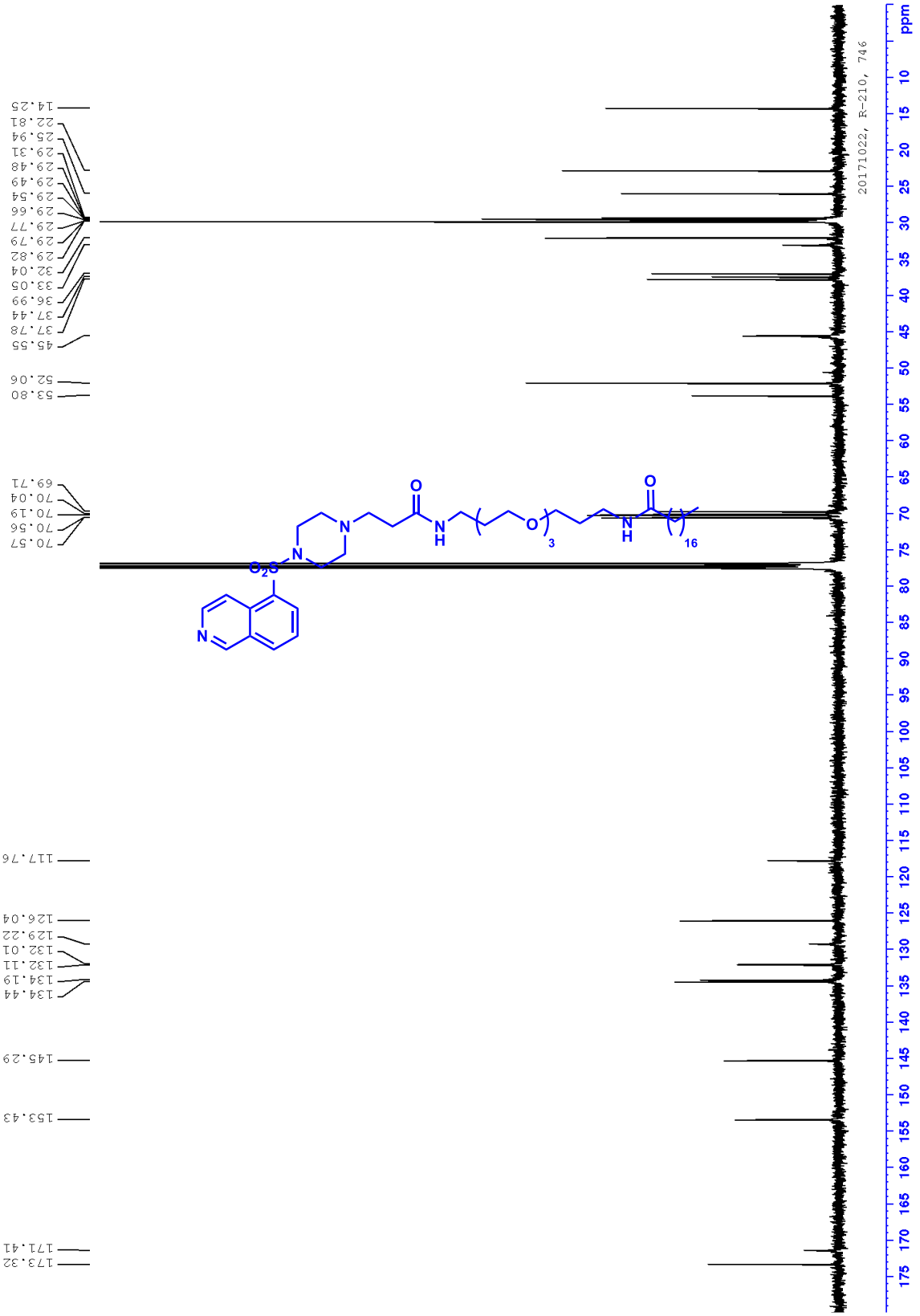
***N*-(17-(4-(Isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)palmitamide [HA-100–C16:0]**



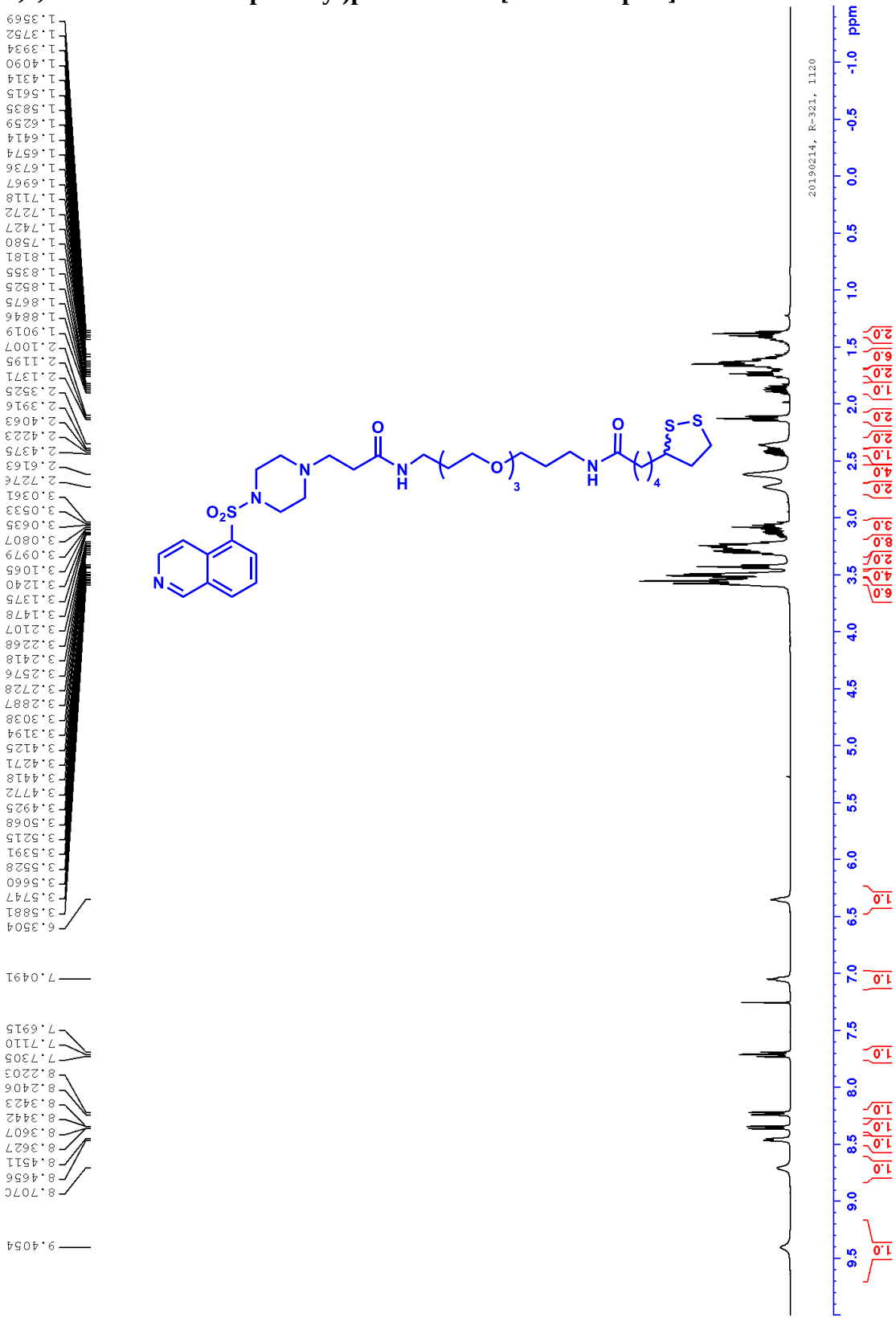

20180321, R-210, 840
ppm
14.17
22.71
25.86
29.23
29.26
29.38
29.40
29.44
29.56
29.68
29.69
29.72
31.94
33.07
36.87
37.29
37.67
45.57
51.97
53.74
69.58
69.93
70.10
70.11
70.47
70.48
117.70
125.98
129.14
131.89
132.02
134.09
134.36
145.16
153.34
171.42
173.24
O
N
H
O
3
N
H
O
14
N
N
O2S
N

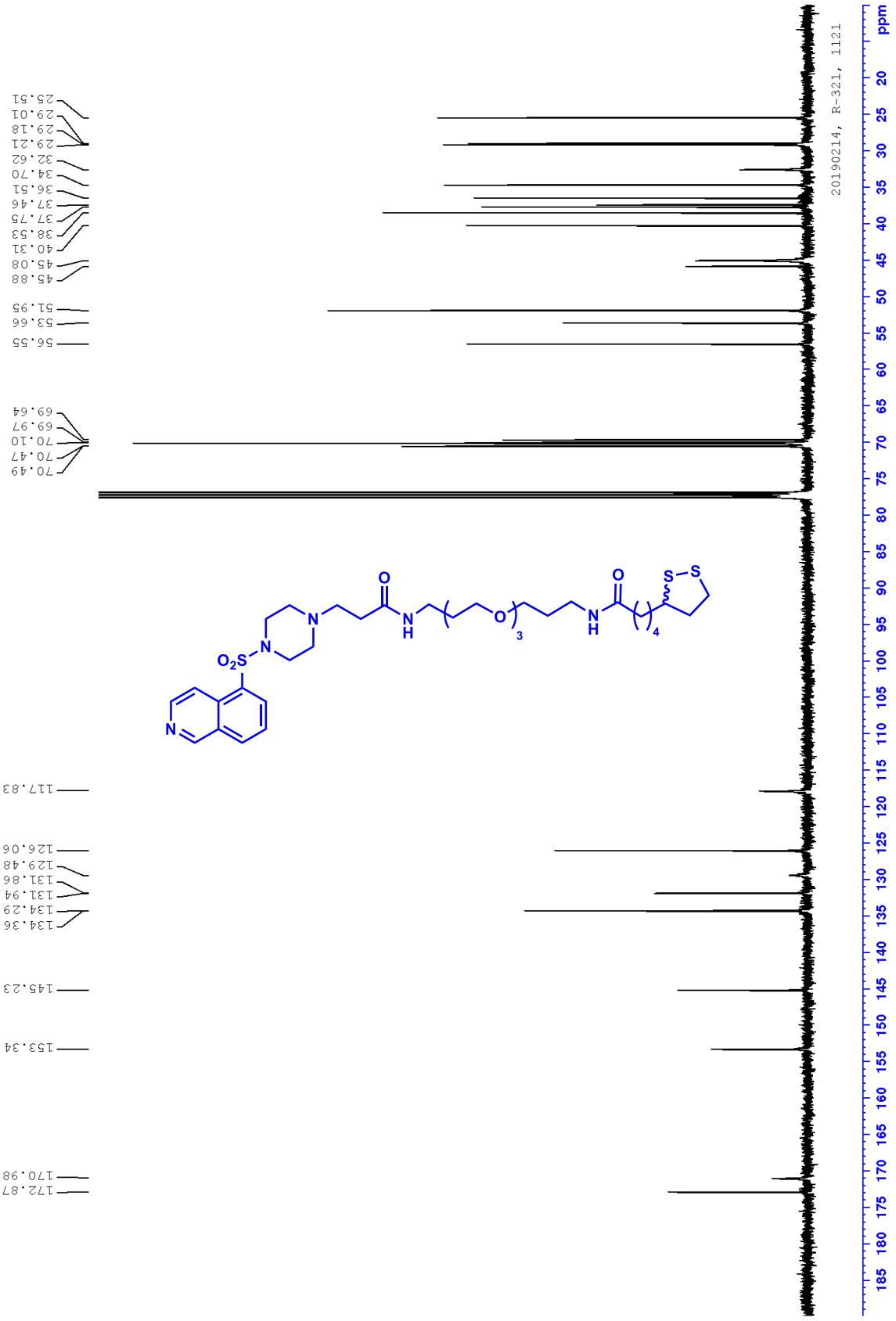
***N*-(17-(4-(Isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)stearamide [HA-100–C18:0]**



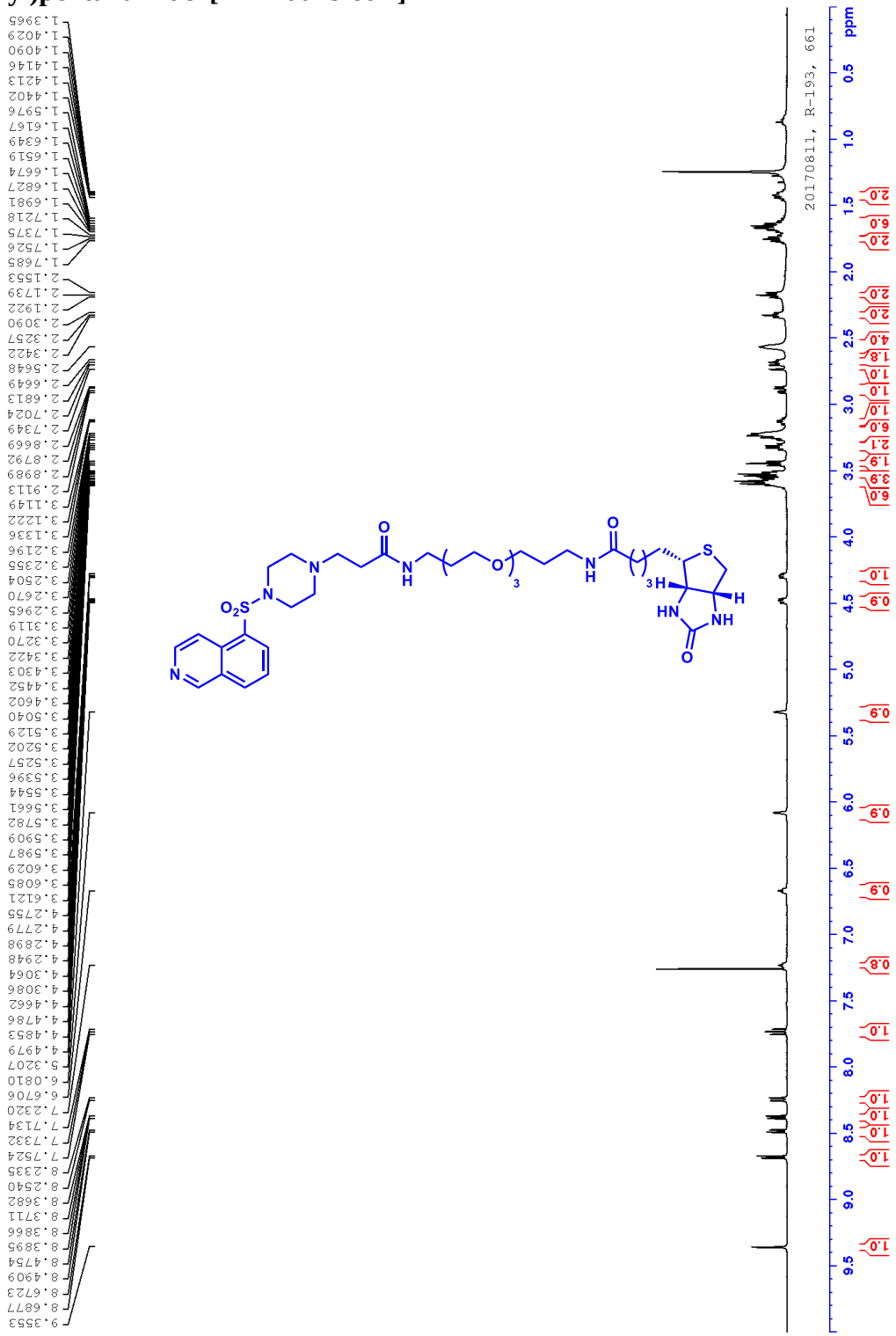

20171022, R-210, 746
ppm
14.25
22.81
25.94
29.31
29.48
29.49
29.54
29.66
29.77
29.79
29.82
32.04
33.05
36.99
37.44
37.78
45.55
52.06
53.80
69.71
70.04
70.19
70.56
70.57
117.76
126.04
129.22
132.01
132.11
134.19
134.44
145.29
153.43
171.41
173.32

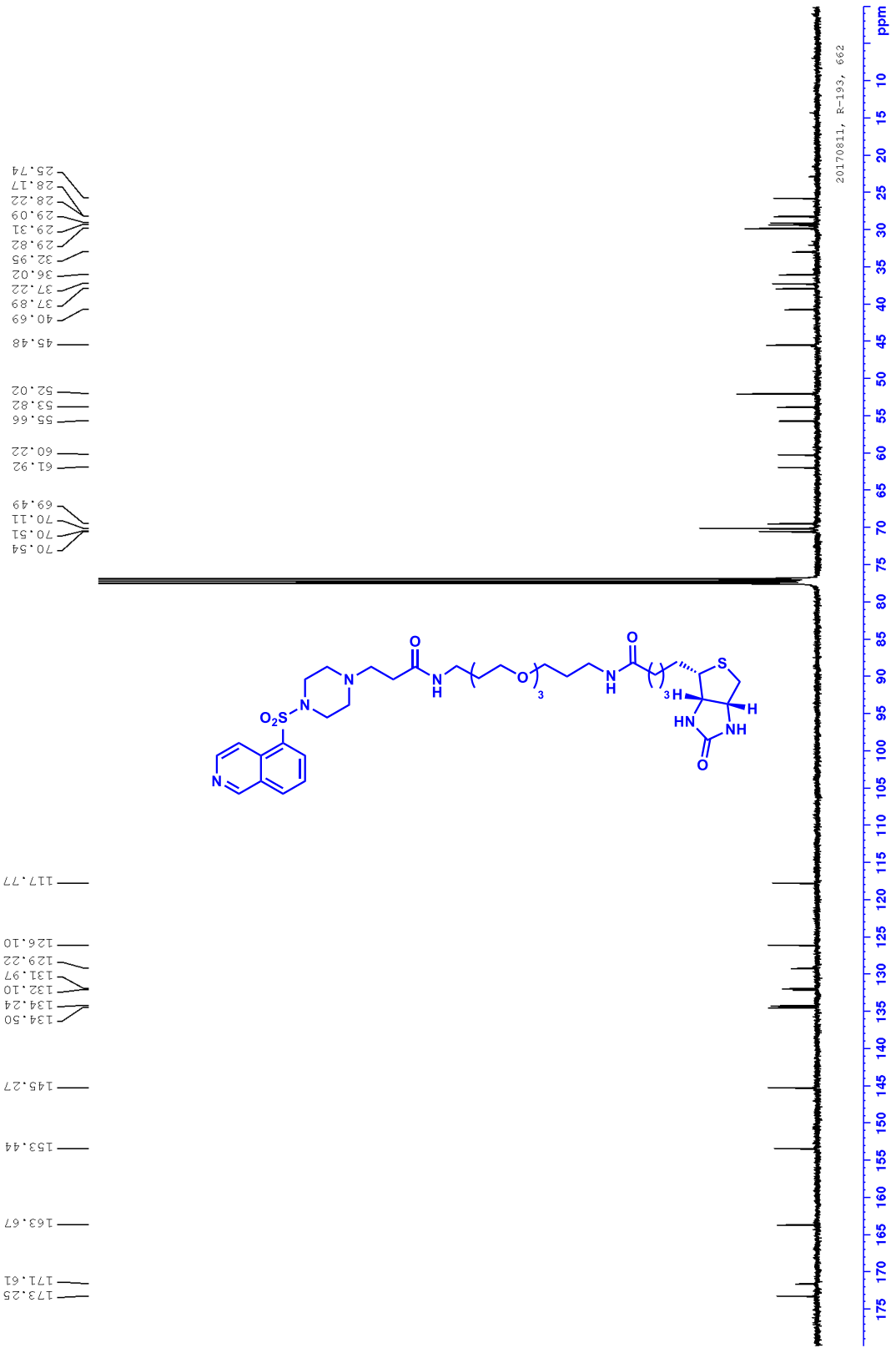
5-(1,2-dithiolan-3-yl)-*N*-(17-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)pentanamide [HA-100–lipoic]



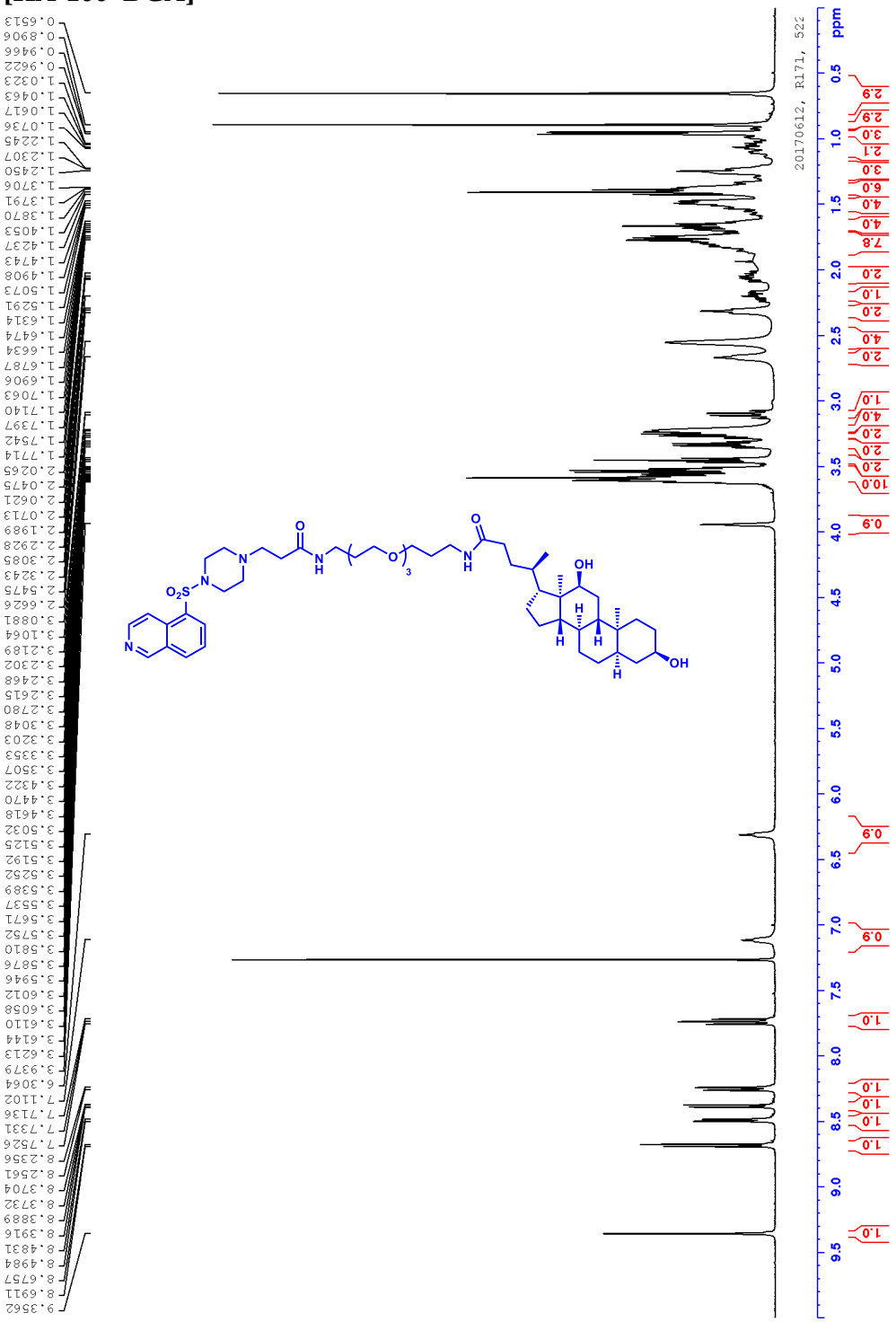

20190214, R-321, 1121
ppm
25.51
29.01
29.18
29.21
32.62
34.70
36.51
37.46
37.75
38.53
40.31
45.08
45.88
51.95
53.66
56.55
69.64
69.97
70.10
70.47
70.49
117.83
126.06
129.48
131.86
131.94
134.29
134.36
145.23
153.34
170.98
172.87

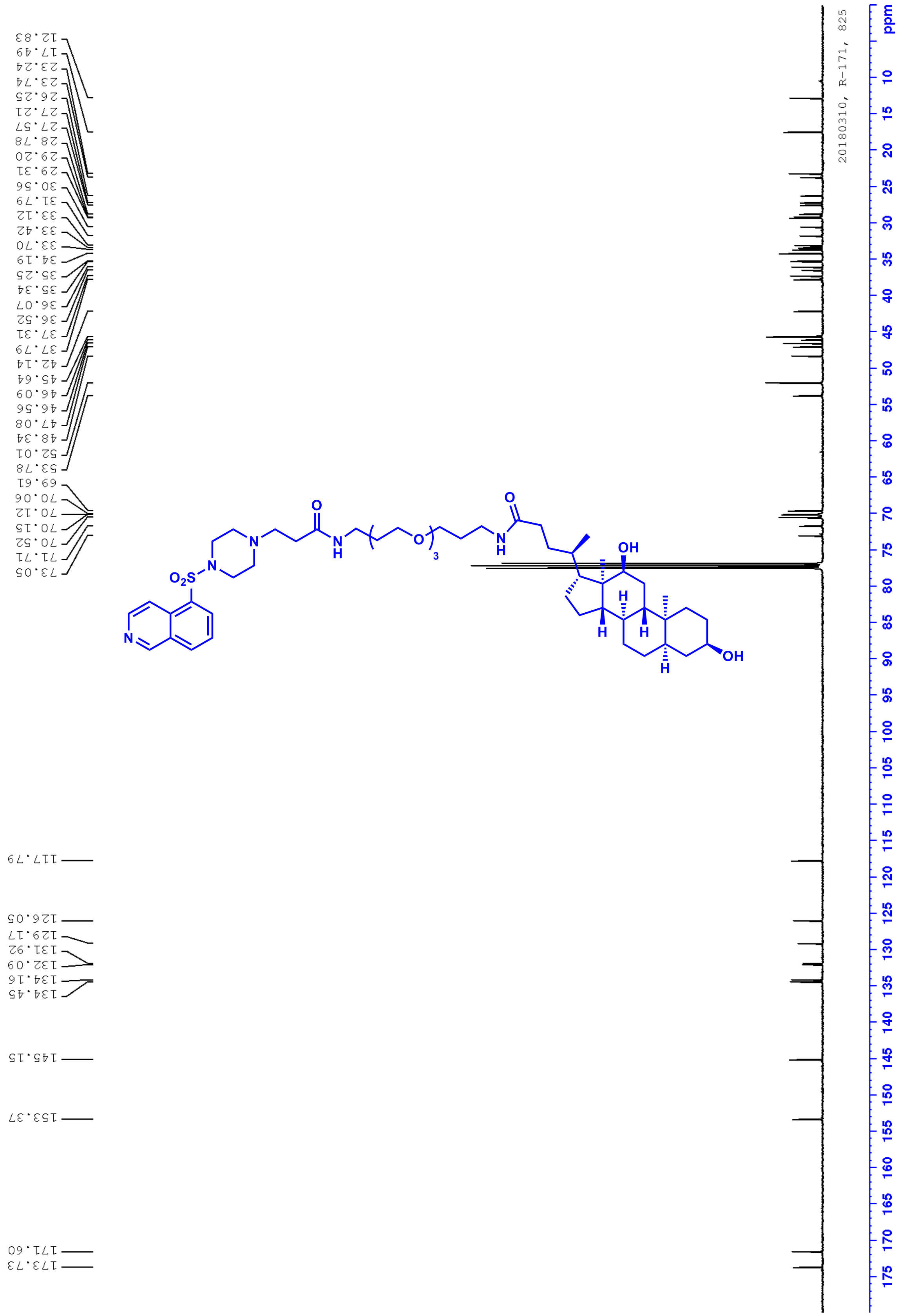
***N*-(17-(4-(Isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)-5-((3a*S*,4*S*,6a*R*)-2-oxohexahydro-1*H*-thieno[3,4-*d*]imidazol-4-yl)pentanamide [HA-100–biotin]**




20170811, R-193, 662
ppm
25.74
28.17
28.22
29.09
29.31
29.82
32.95
36.02
37.22
37.89
40.69
45.48
52.02
53.82
55.66
60.22
61.92
69.49
70.11
70.51
70.54
117.77
126.10
129.22
131.97
132.10
134.24
134.50
145.27
153.44
163.67
171.61
173.25

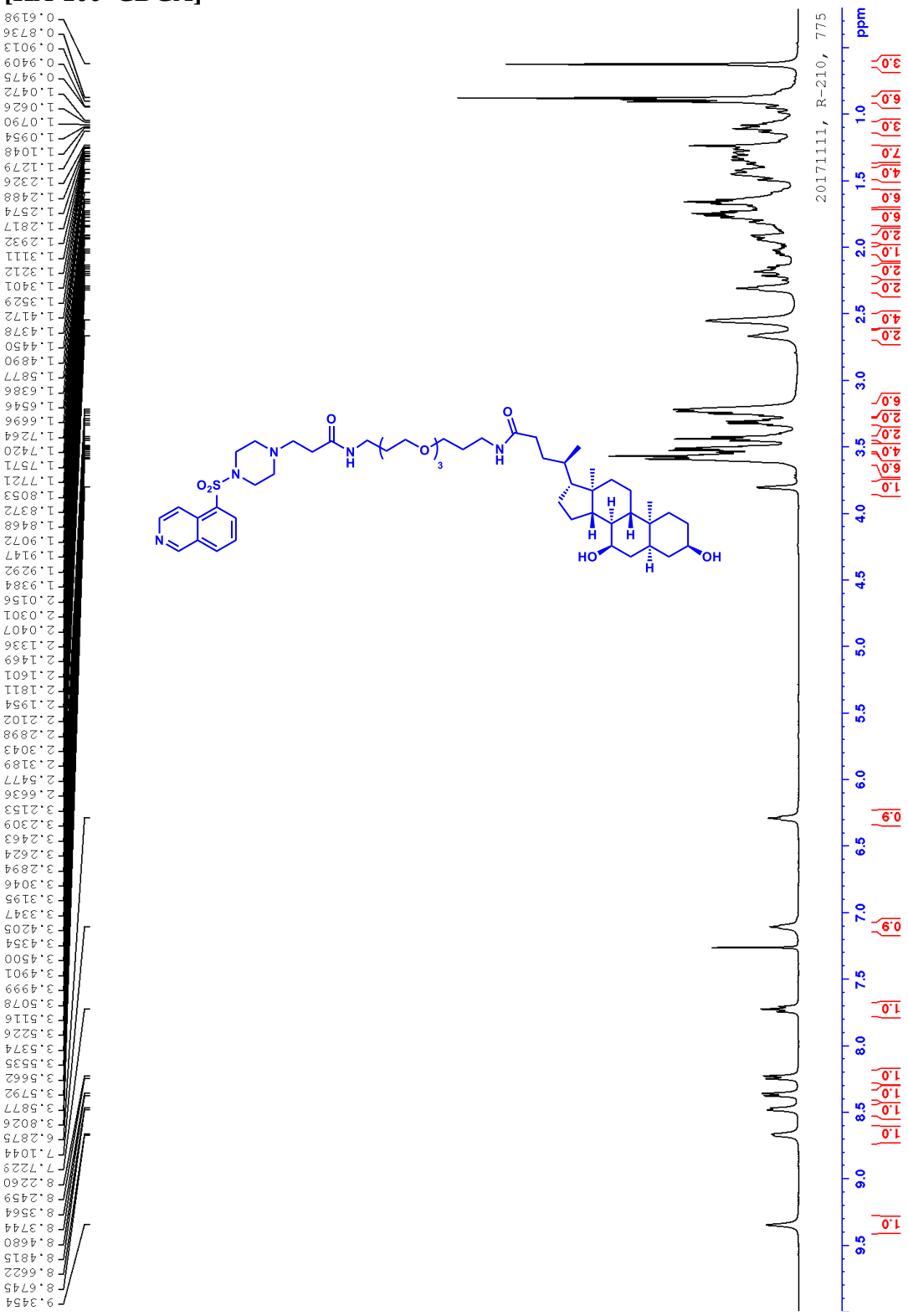
(*R*)-4-((3*R*,5*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,12-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-*N*-(17-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)pentanamide [HA-100–DCA]

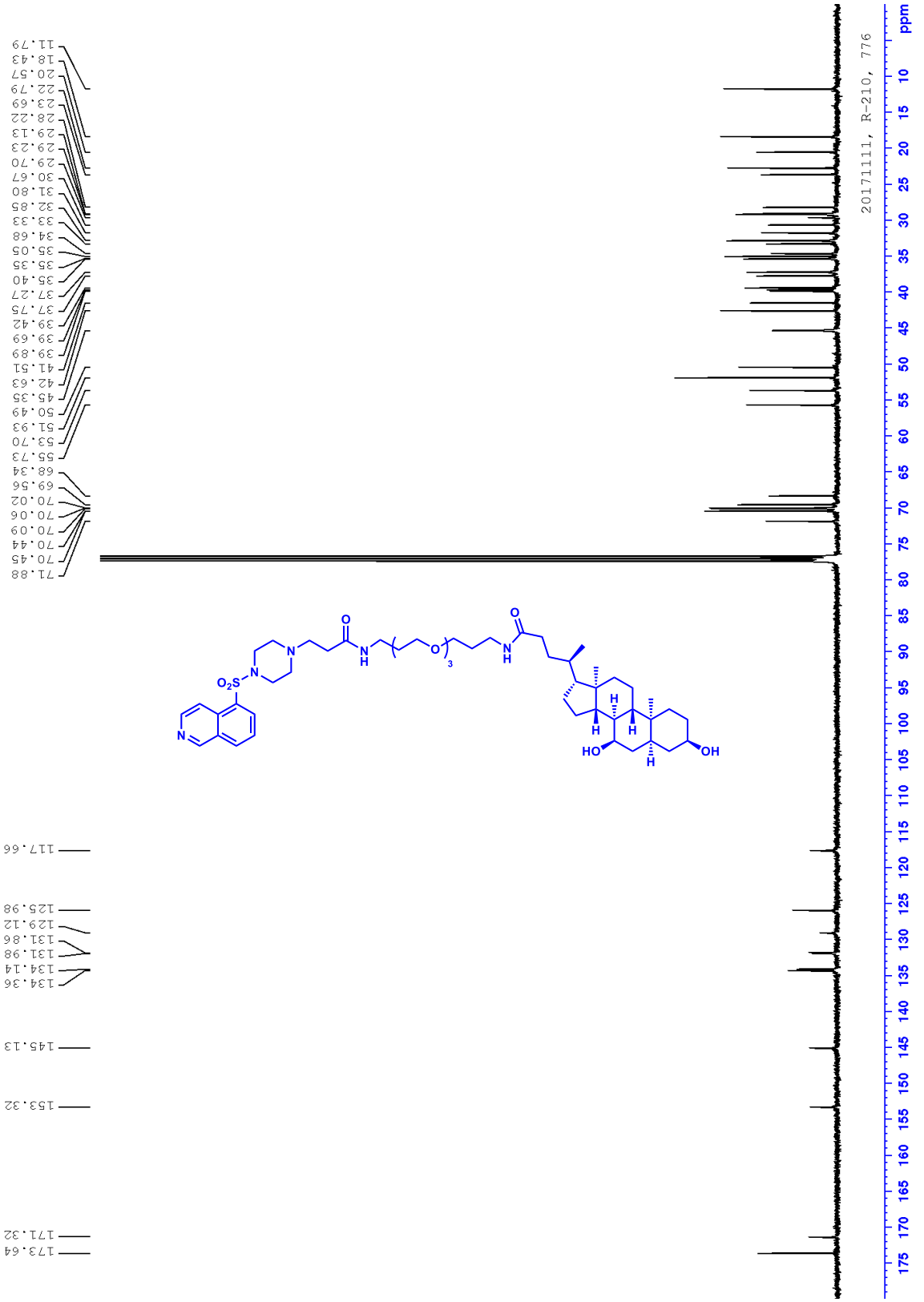




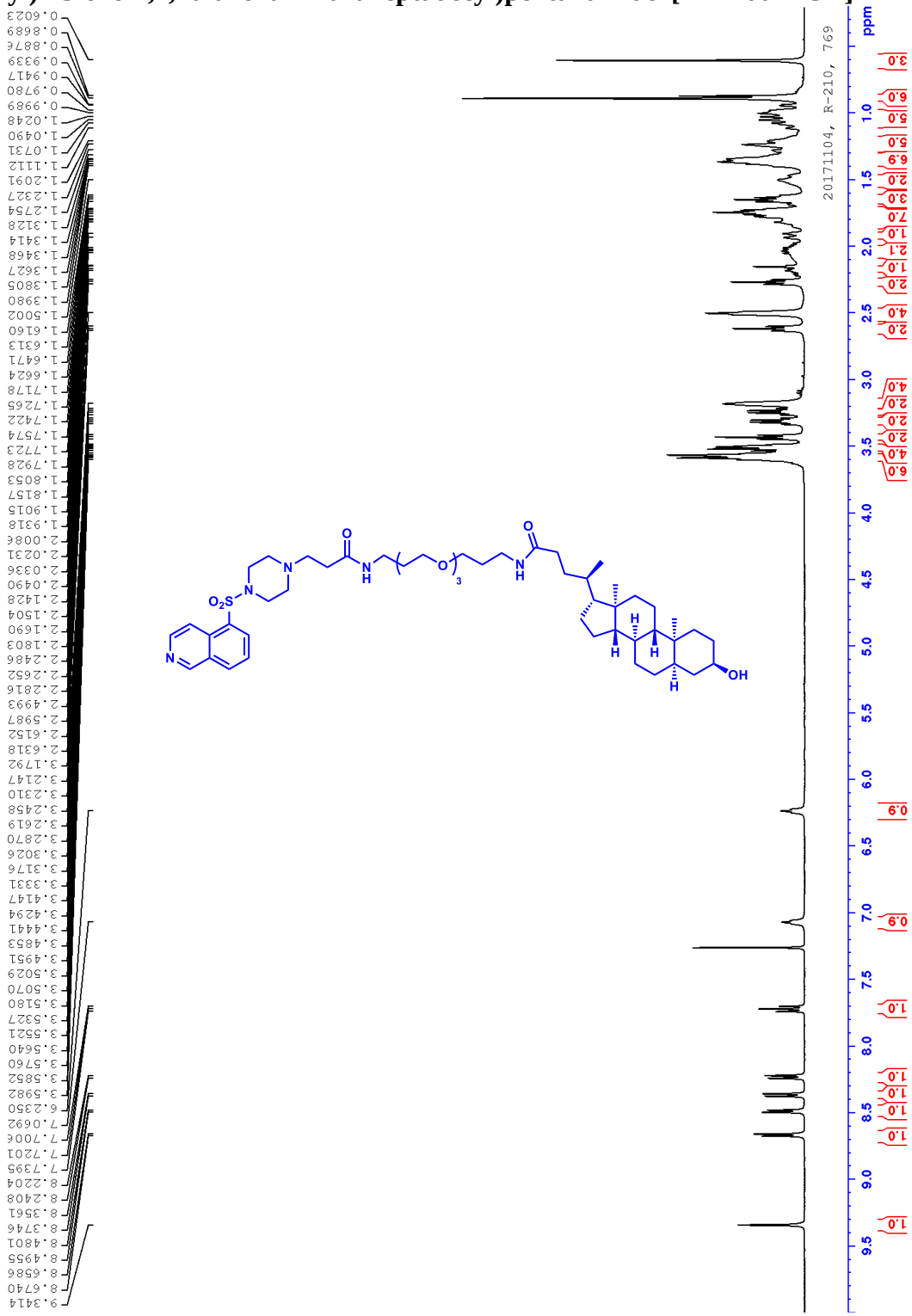
12.83
17.49
23.24
23.74
26.25
27.21
27.57
28.78
29.20
29.31
30.56
31.79
33.12
33.42
33.70
34.19
35.25
35.34
36.07
36.52
37.31
37.79
42.14
45.64
46.09
46.56
47.08
48.34
52.01
53.78
69.61
70.06
70.12
70.15
70.52
71.71
73.05
117.79
126.05
129.17
131.92
132.09
134.16
134.45
145.15
153.37
171.60
173.73
20180310, R-171, 825
ppm

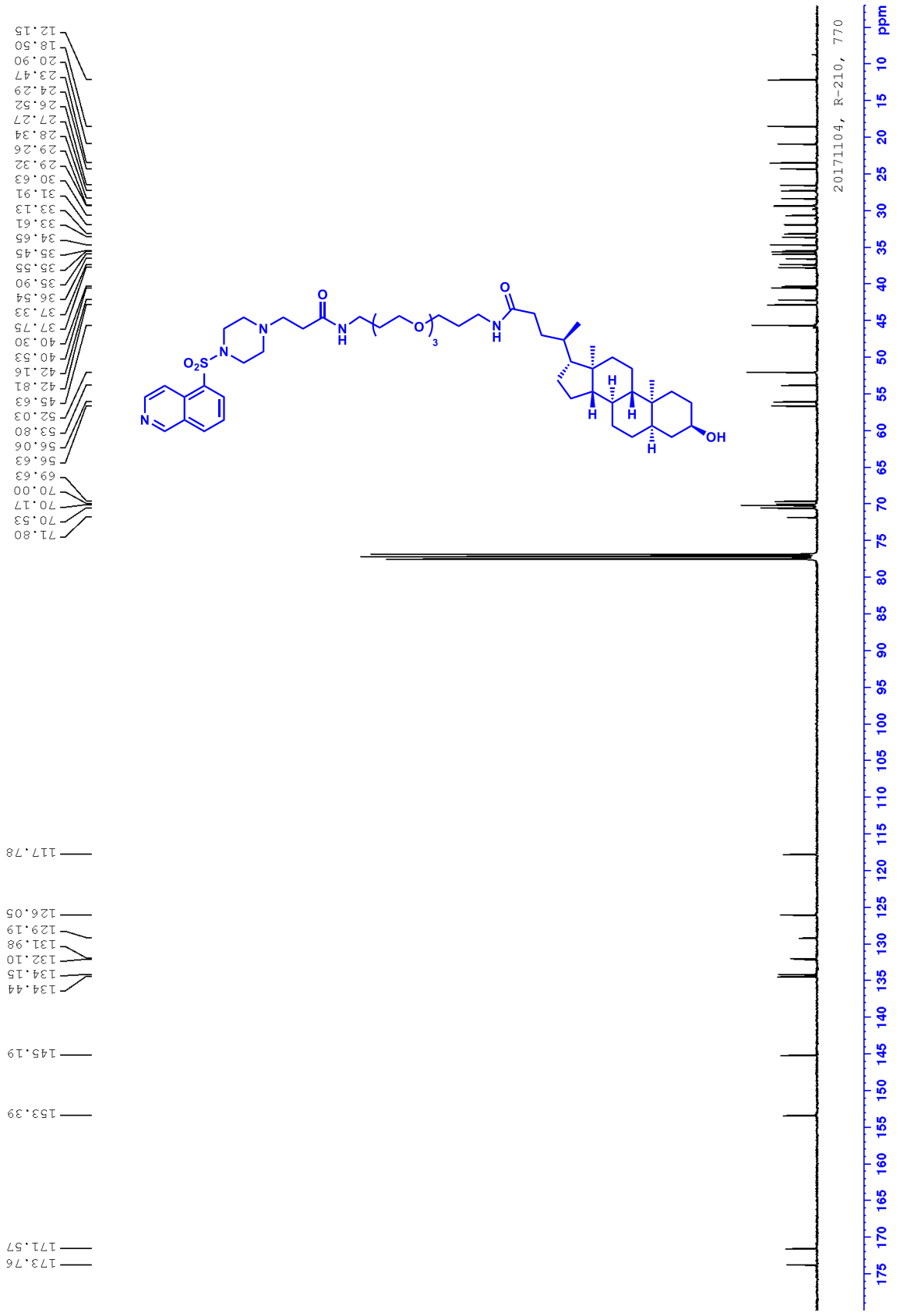
(*R*)-4-((3*R*,5*S*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3,7-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-*N*-(17-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)pentanamide [HA-100–CDCA]



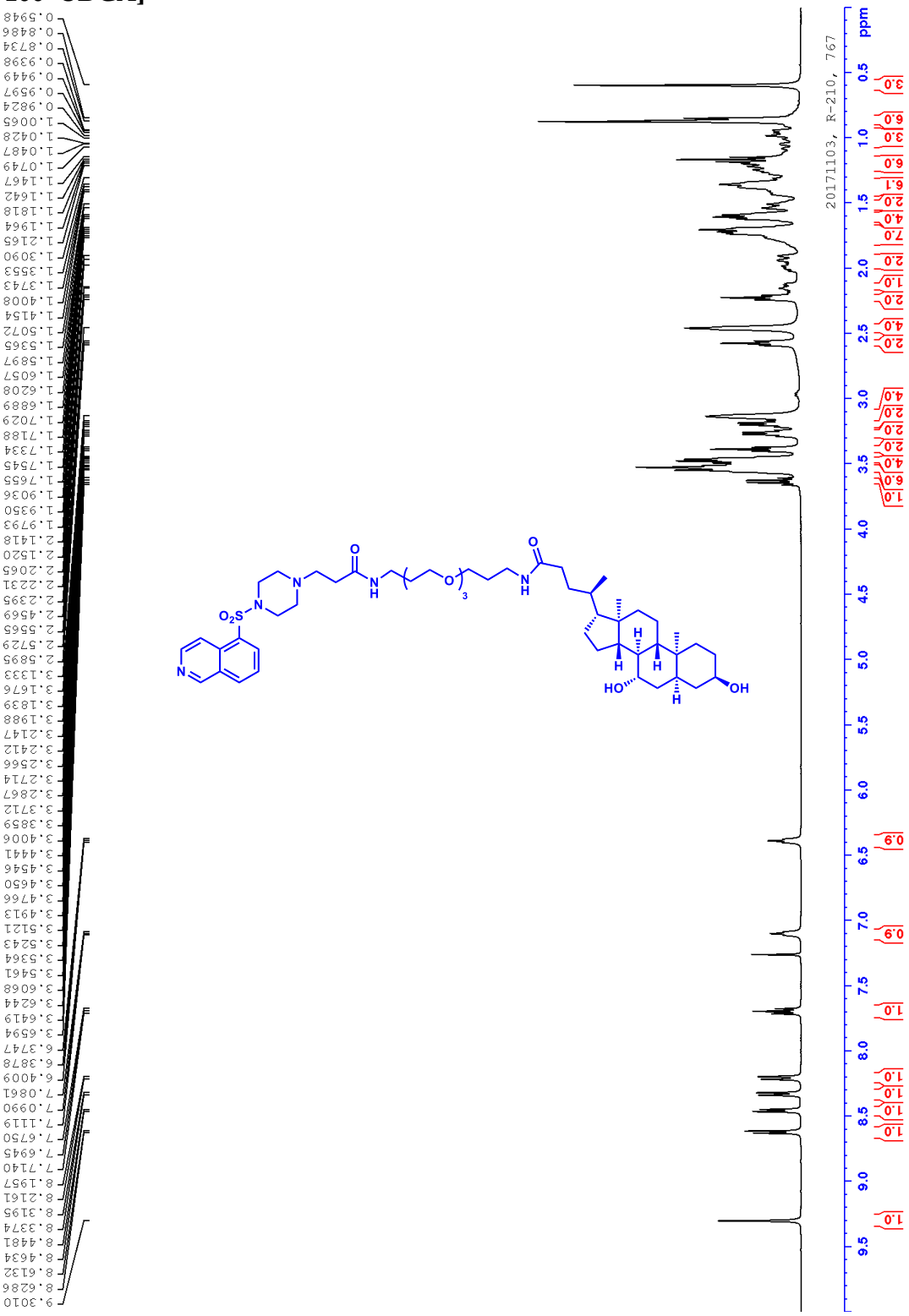

20171111, R-210, 776
ppm
11.79
18.43
20.57
22.79
23.69
28.22
29.13
29.23
29.70
30.67
31.80
32.85
33.33
34.68
35.05
35.35
35.40
37.27
37.75
39.42
39.69
39.89
41.51
42.63
45.35
50.49
51.93
53.70
55.73
68.34
69.56
70.02
70.06
70.09
70.44
70.45
71.88
117.66
125.98
129.12
131.86
131.98
134.14
134.36
145.13
153.32
171.32
173.64

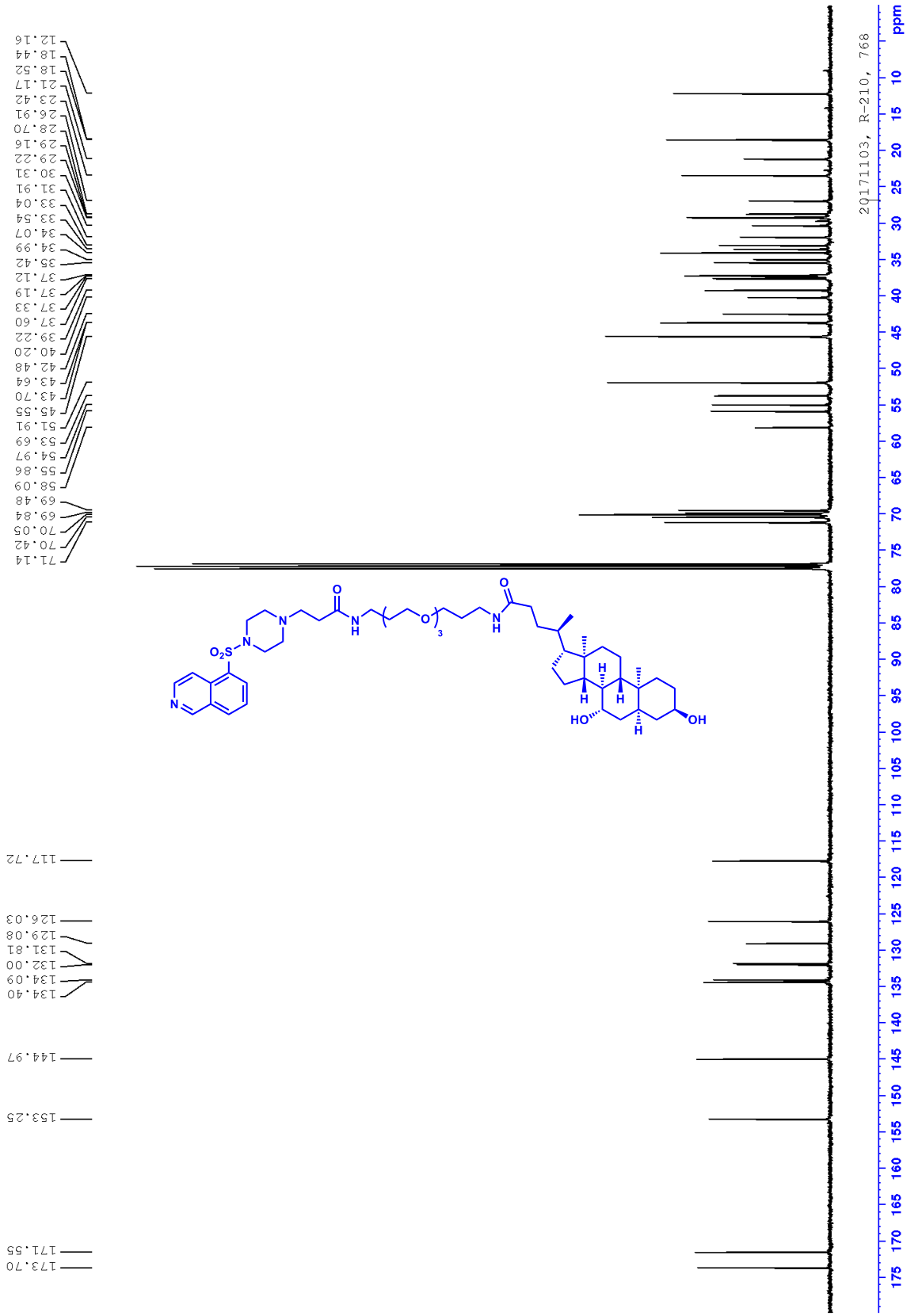
(*R*)-4-((3*R*,5*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3-hydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-*N*-(17-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)pentanamide [HA-100–LCA]



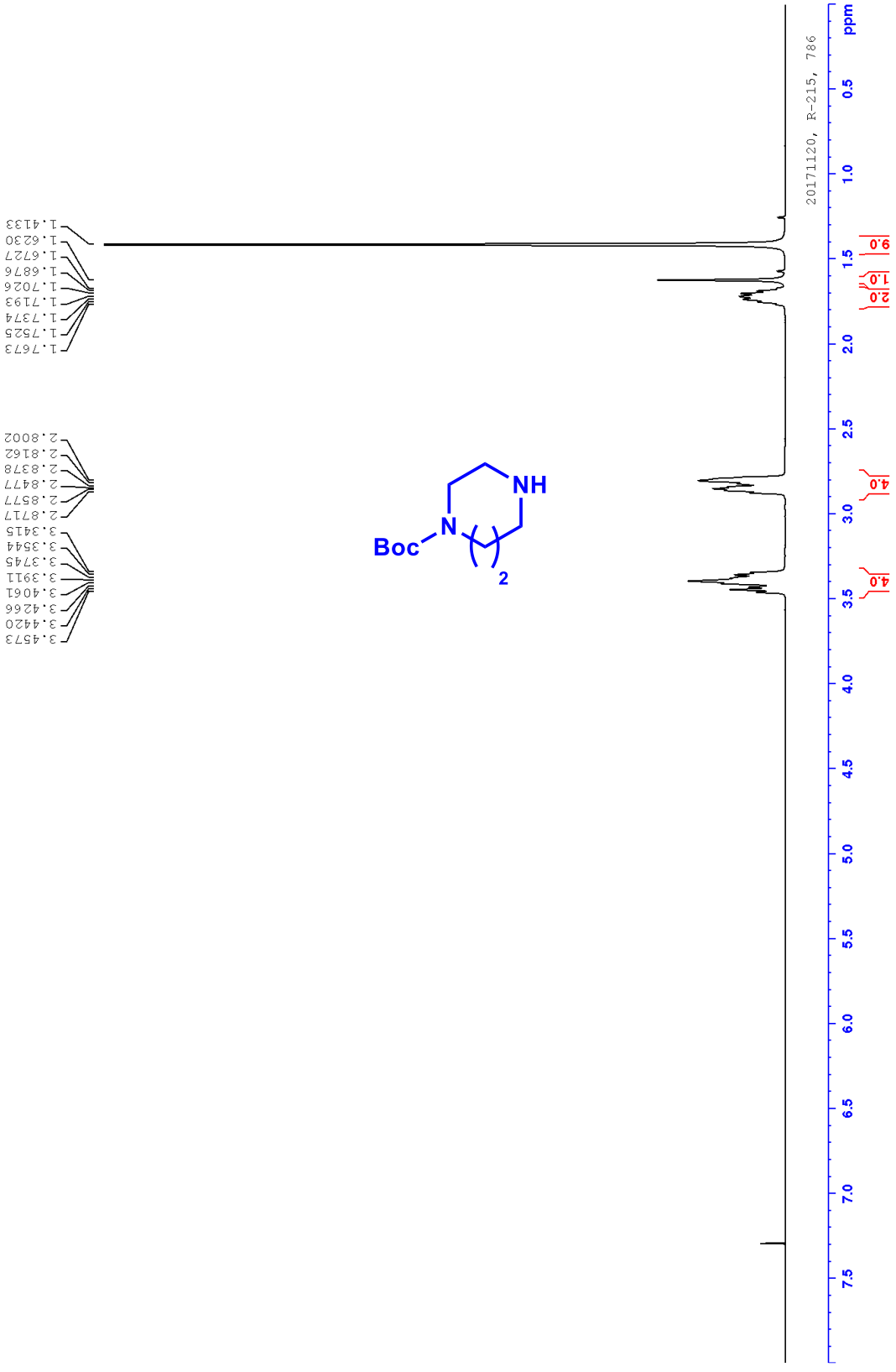

20171104, R-210, 770
ppm
12.15
18.50
20.90
23.47
24.29
26.52
27.27
28.34
29.26
29.32
30.63
31.91
33.13
33.61
34.65
35.45
35.55
35.90
36.54
37.33
37.75
40.30
40.53
42.16
42.81
45.63
52.03
53.80
56.06
56.63
69.63
70.00
70.17
70.53
71.80
117.78
126.05
129.19
131.98
132.10
134.15
134.44
145.19
153.39
171.57
173.76

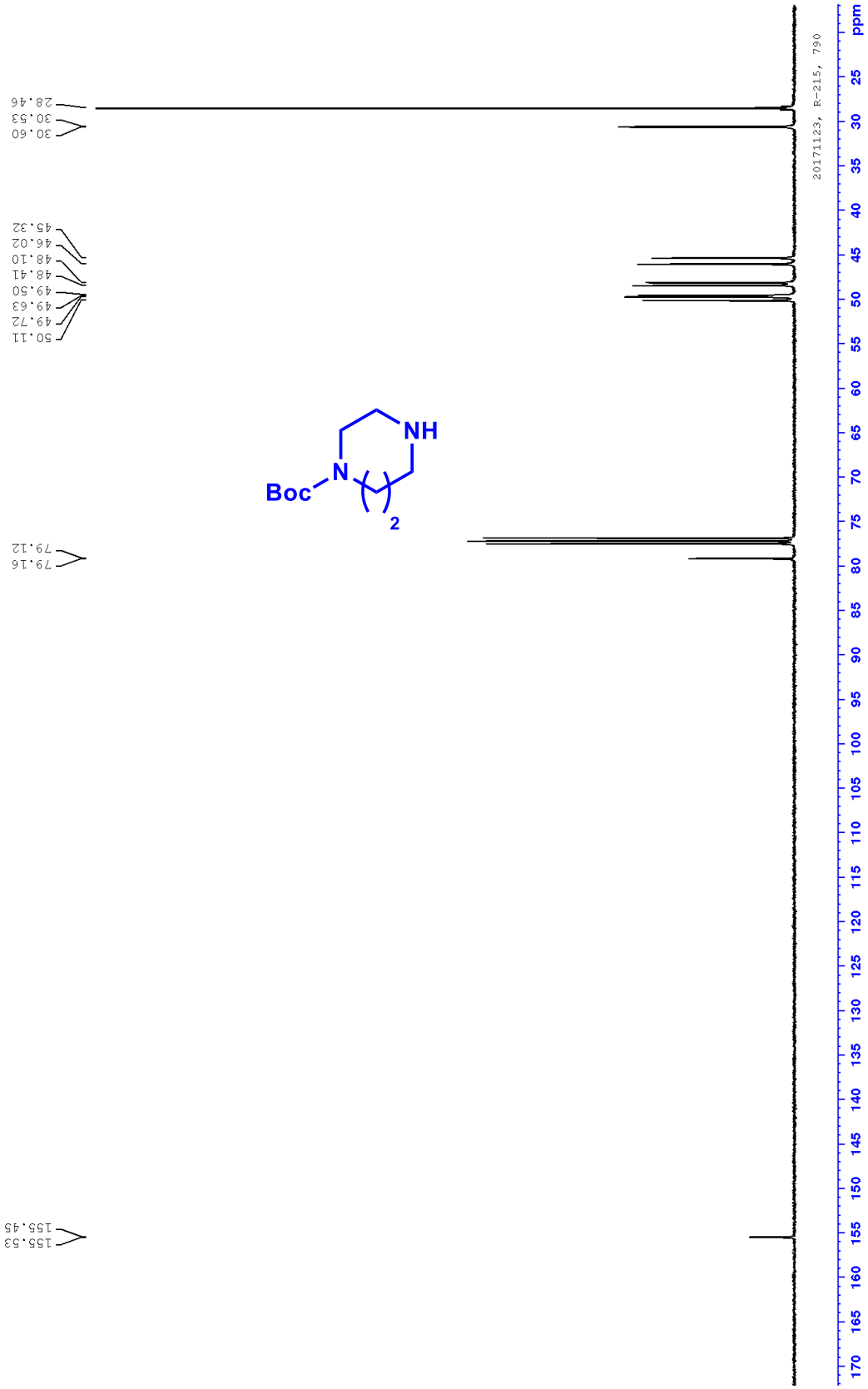
(R)-4-((3R,5S,7S,8R,9S,10S,13R,14S,17R)-3,7-Dihydroxy-10,13-dimethylhexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)-N-(17-(4-(isoquinolin-5-ylsulfonyl)piperazin-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)pentanamide **[HA-100–UDCA]**



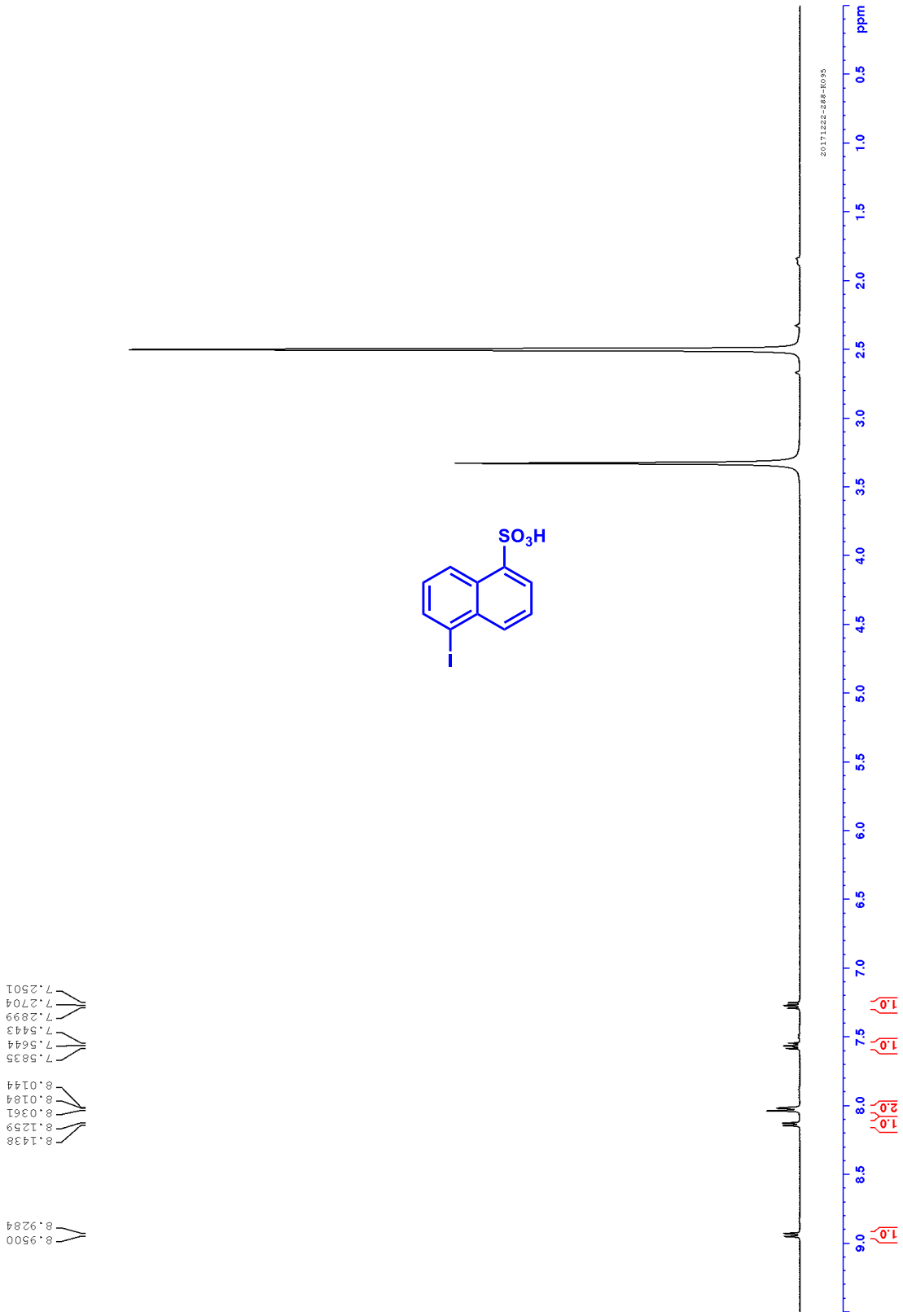

20171103, R-210, 768
ppm
12.16
18.44
18.52
21.17
23.42
26.91
28.70
29.16
29.22
30.31
31.91
33.04
33.54
34.07
34.99
35.42
37.12
37.19
37.33
37.60
39.22
40.20
42.48
43.64
43.70
45.55
51.91
53.69
54.97
55.86
58.09
69.48
69.84
70.05
70.42
71.14
117.72
126.03
129.08
131.81
132.00
134.09
134.40
144.97
153.25
171.55
173.70

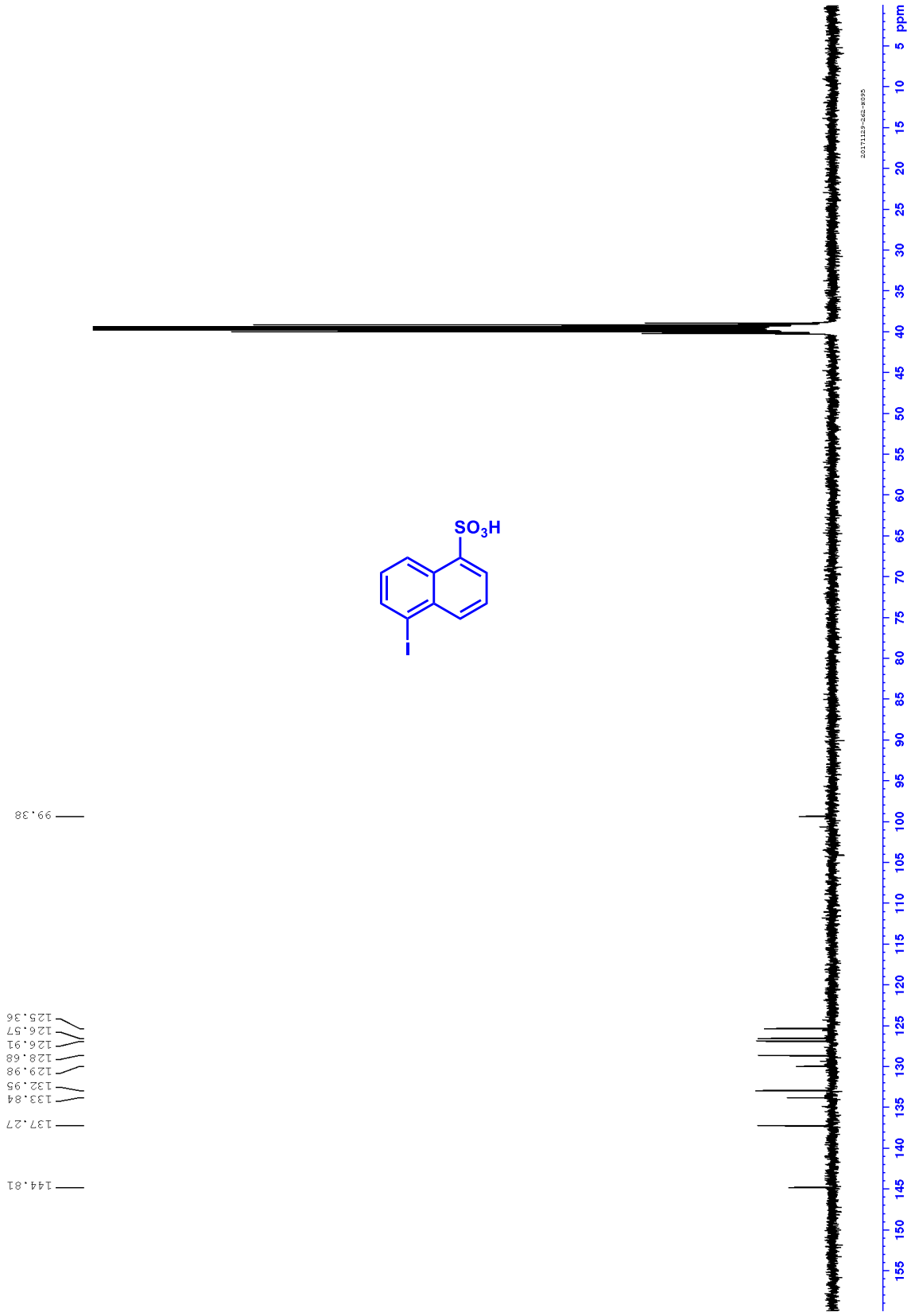
***tert*-Butyl 1,4-diazepane-1-carboxylate**



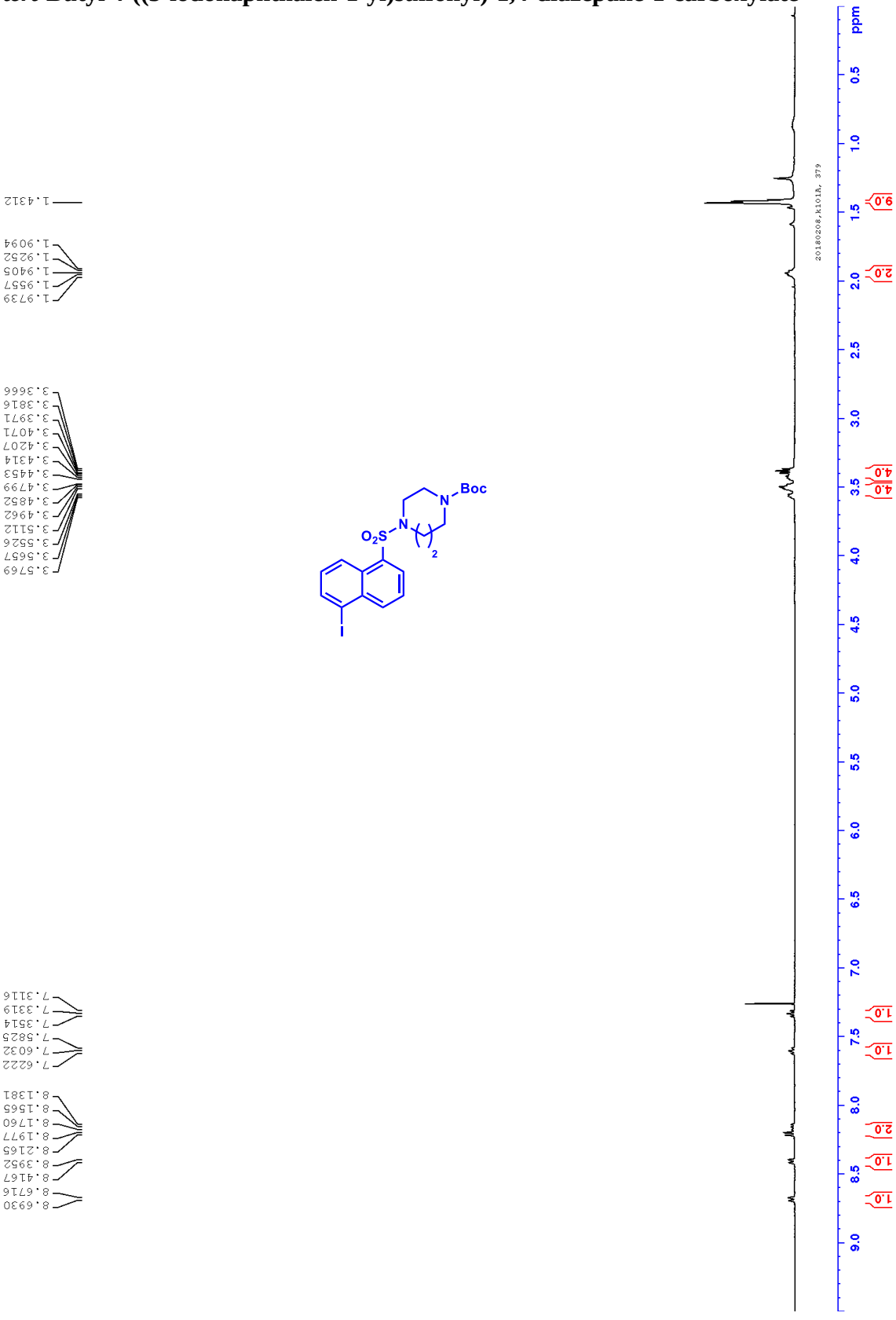

20171123, R-215, 790
ppm
28.46
30.53
30.60
45.32
46.02
48.10
48.41
49.50
49.63
49.72
50.11
79.12
79.16
155.45
155.53
NH
N
Boc
2

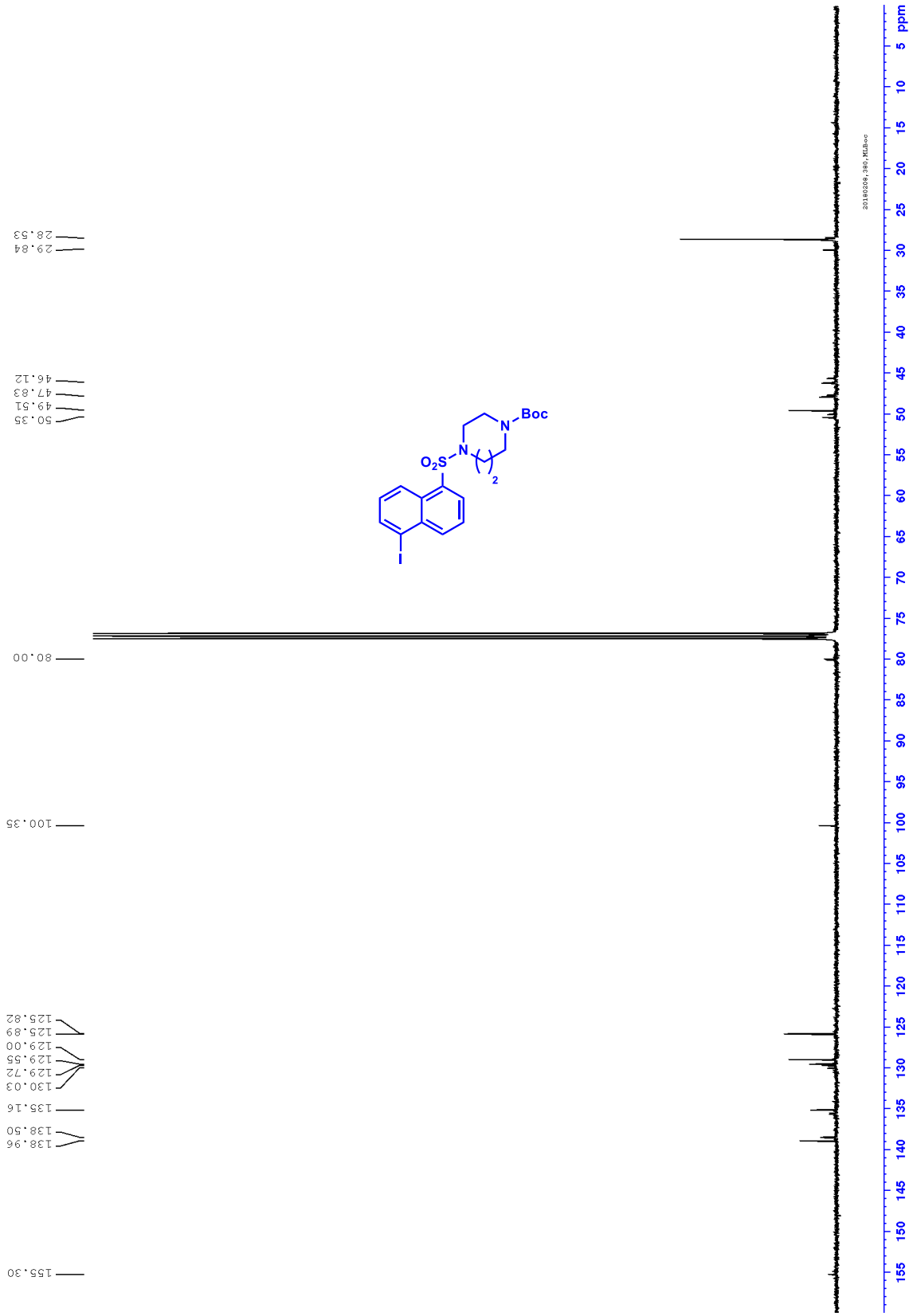
5-Iodonaphthalene-1-sulfonic acid



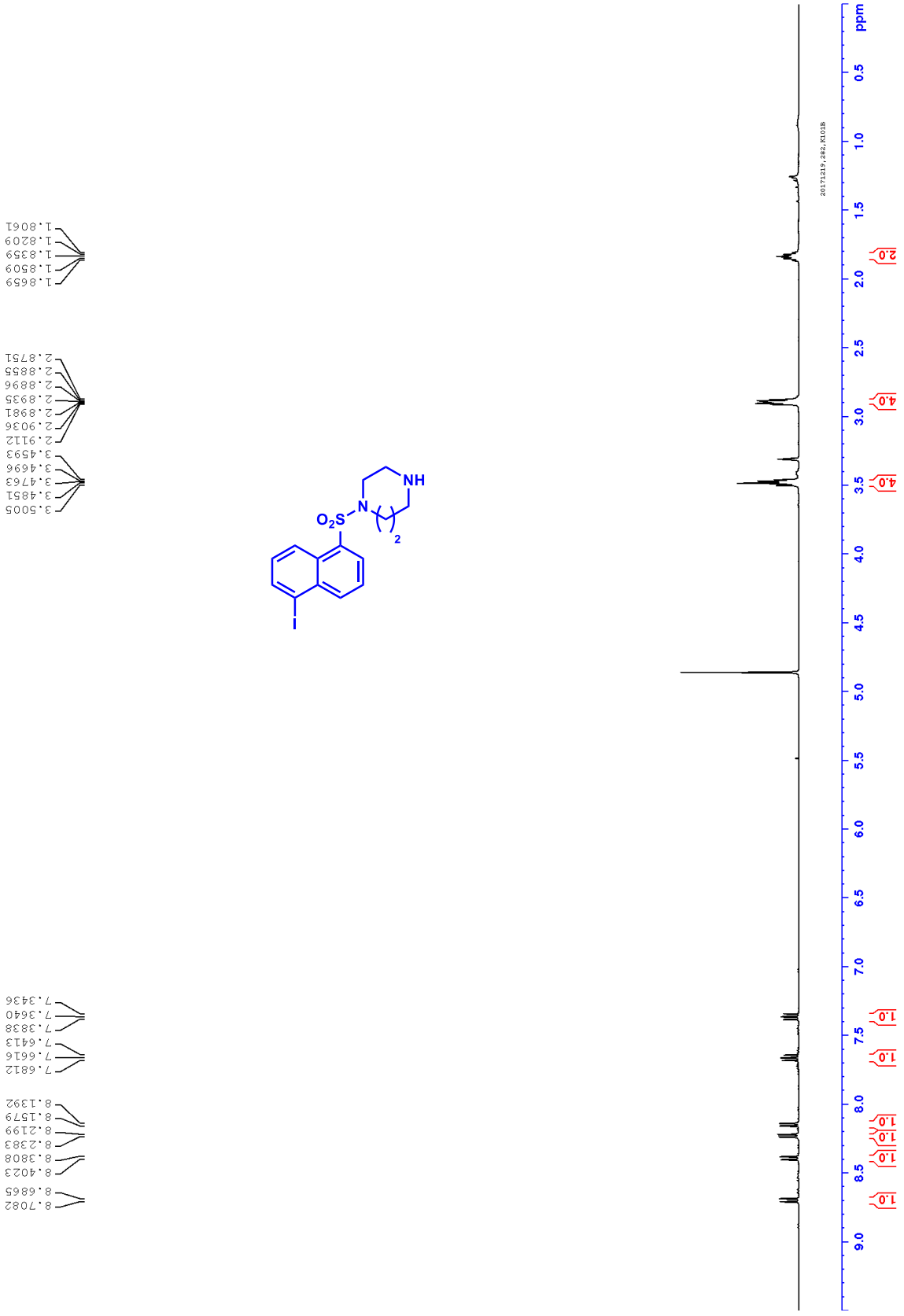

SO3H
I
99.38
125.36
126.57
126.91
128.68
129.98
132.95
133.84
137.27
144.81
20171129-2GZ-4095
ppm

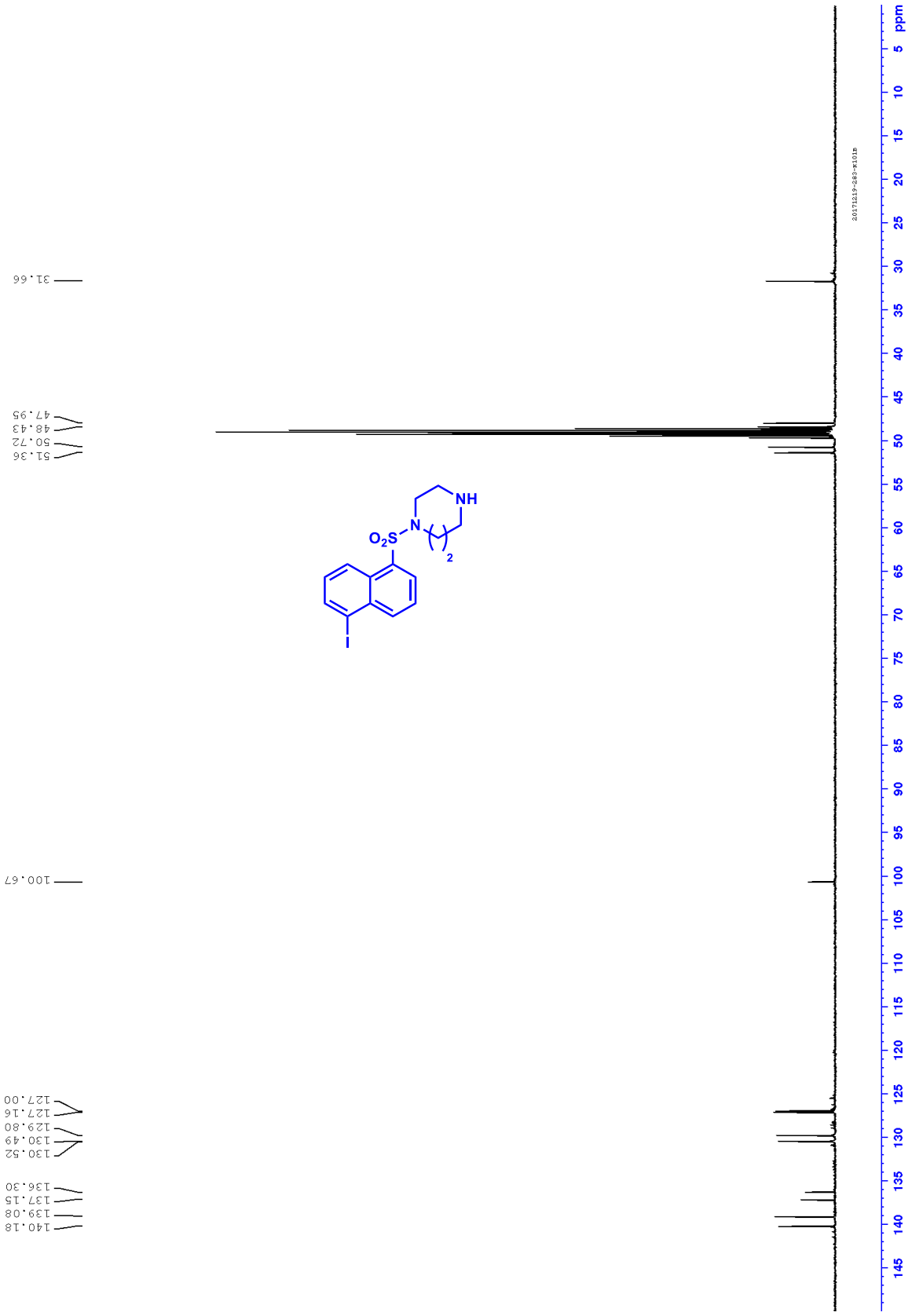
tert-Butyl 4-((5-iodonaphthalen-1-yl)sulfonyl)-1,4-diazepane-1-carboxylate



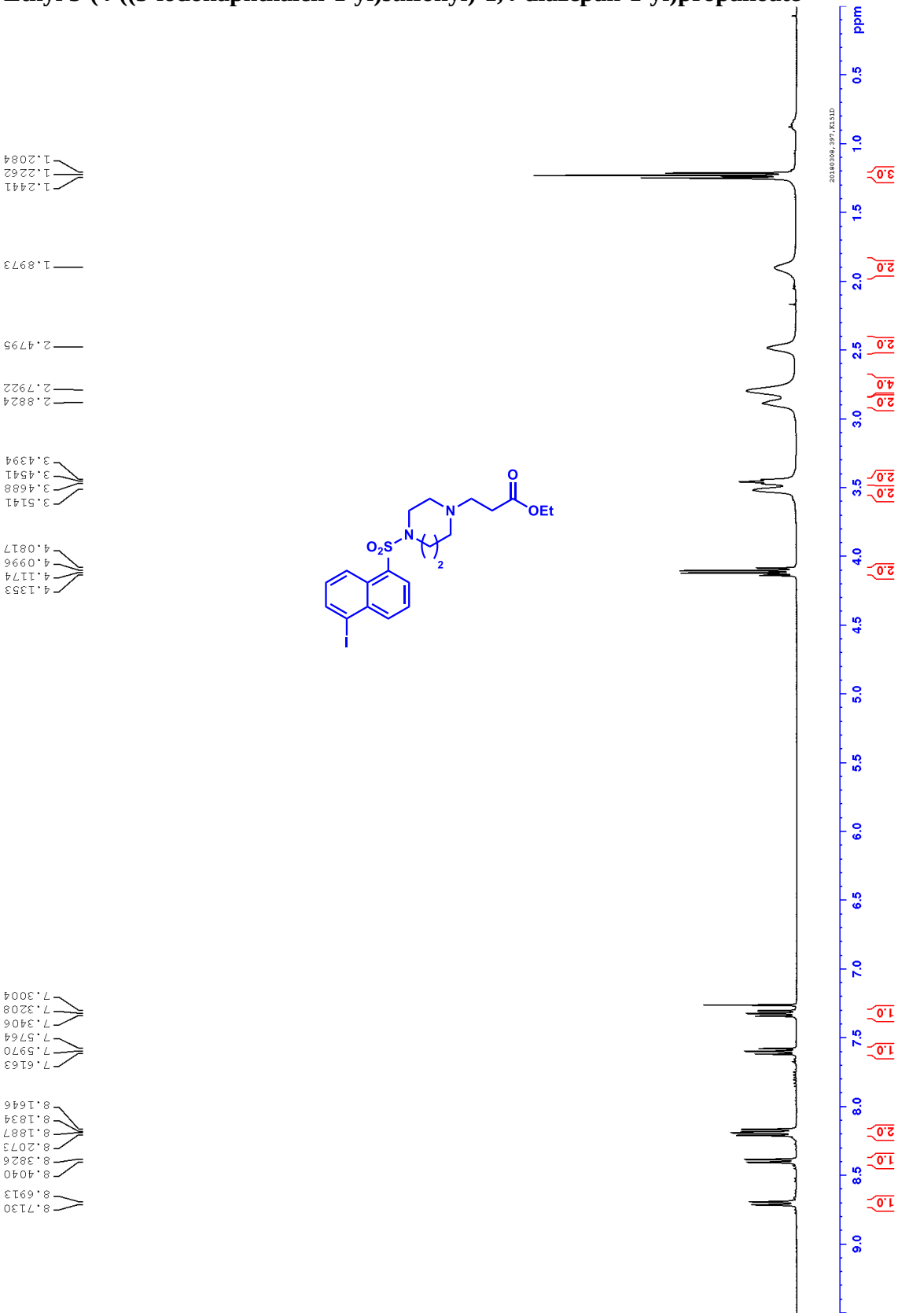

155.30
138.96
138.50
135.16
130.03
129.72
129.55
129.00
125.89
125.82
100.35
80.00
50.35
49.51
47.83
46.12
29.84
28.53
Boc
N
N
O2S
2
I
ppm

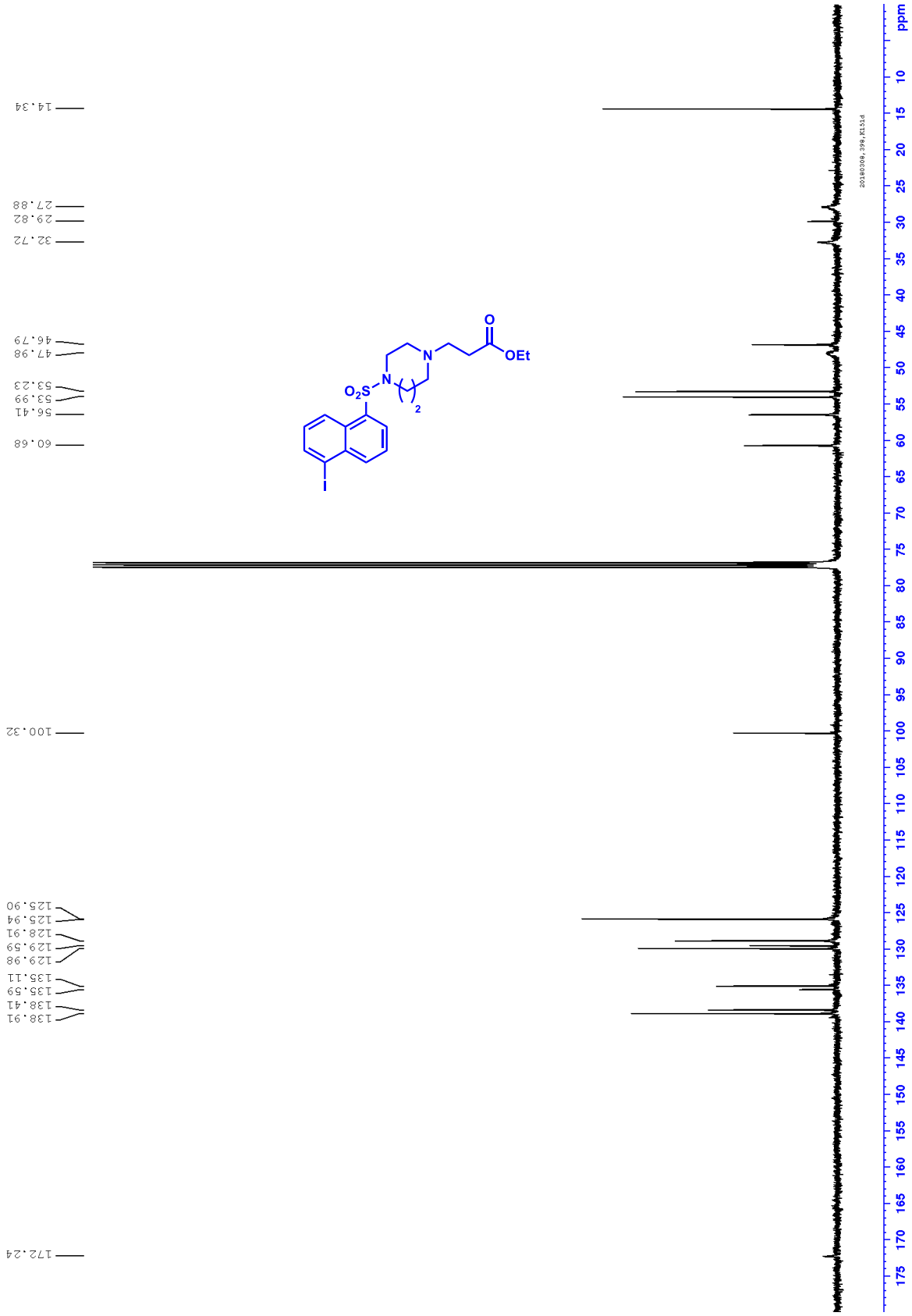
1-((5-Iodonaphthalen-1-yl)sulfonyl)-1,4-diazepane [ML-7]



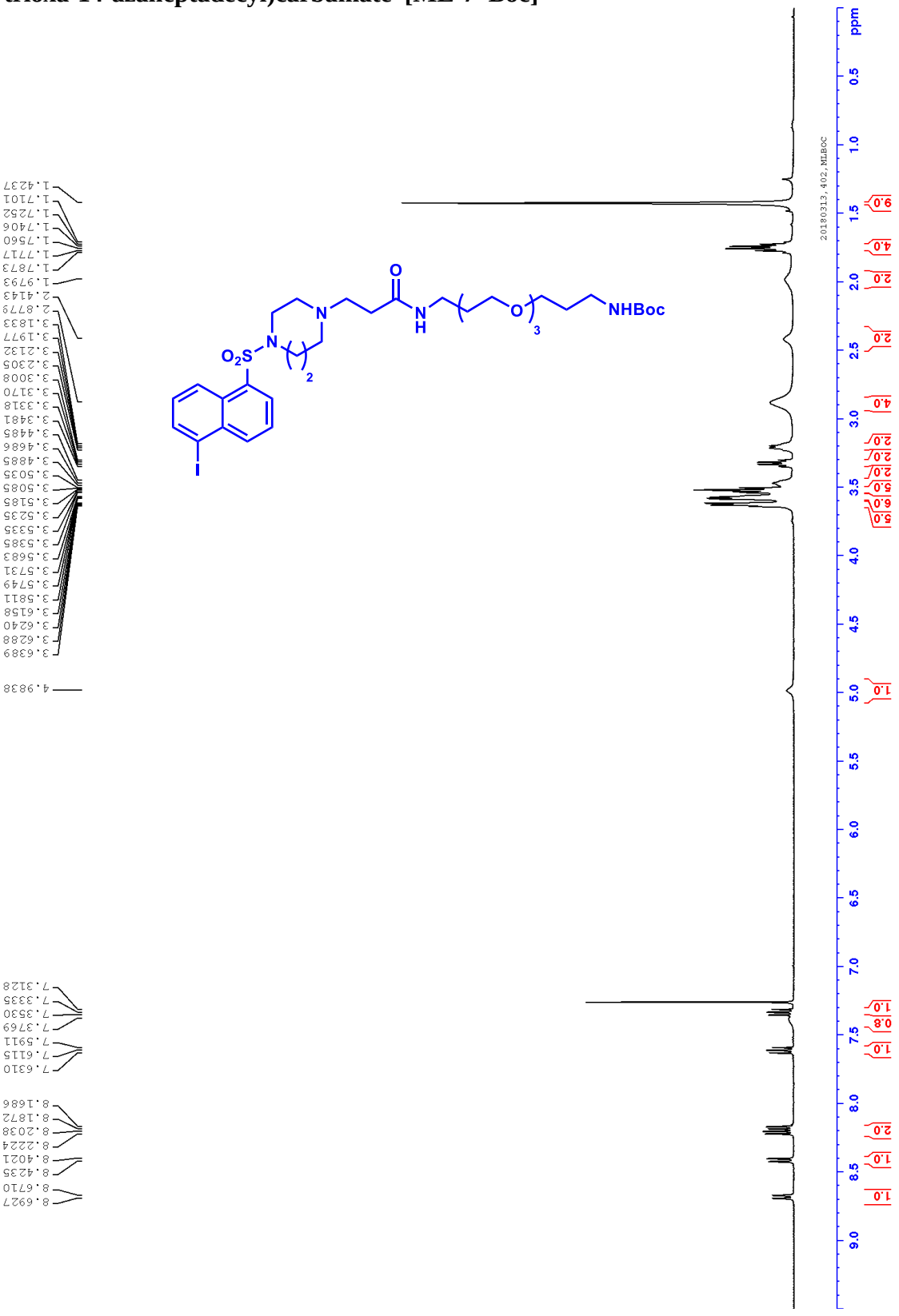

31.66
47.95
48.43
50.72
51.36
100.67
127.00
127.16
129.80
130.49
130.52
136.30
137.15
139.08
140.18
NH
N
O2S
2
I
20171219-283-H101B
ppm

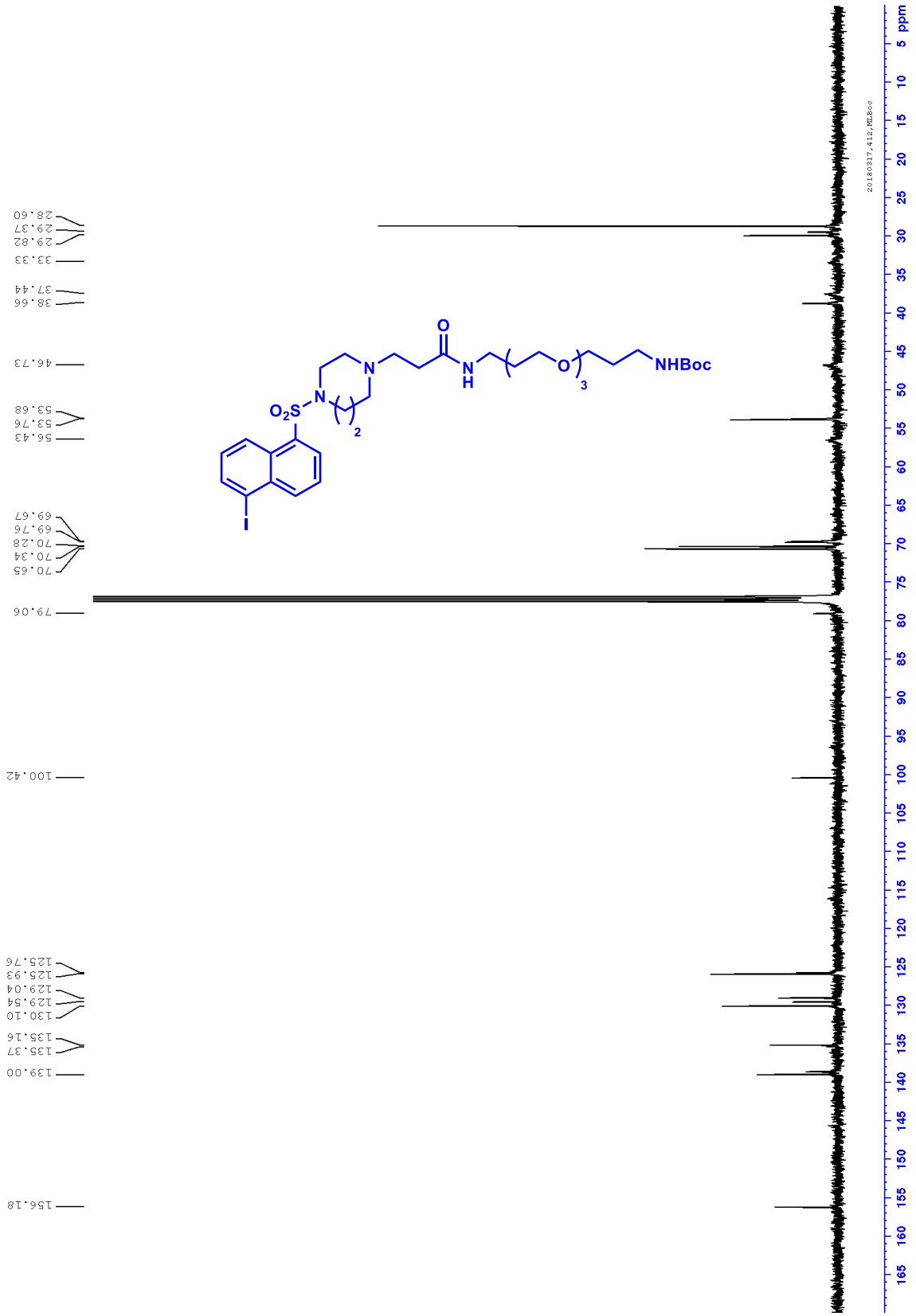
Ethyl 3-(4-((5-iodonaphthalen-1-yl)sulfonyl)-1,4-diazepan-1-yl)propanoate



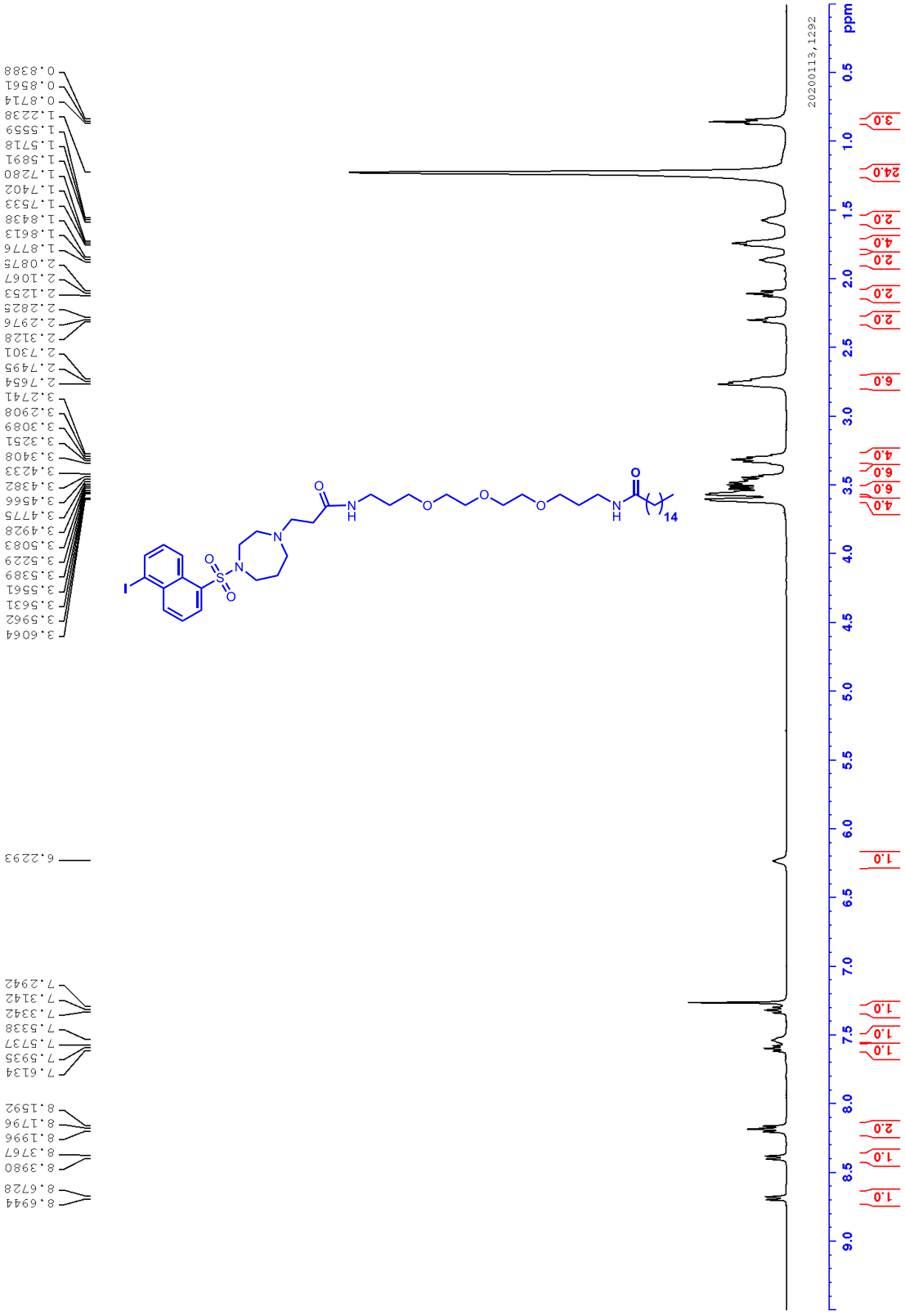

14.34
27.88
29.82
32.72
46.79
47.98
53.23
53.99
56.41
60.68
100.32
125.90
125.94
128.91
129.59
129.98
135.11
135.59
138.41
138.91
172.24
O
OEt
N
N
O2S
2
I
ppm
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
100
105
110
115
120
125
130
135
140
145
150
155
160
165
170
175

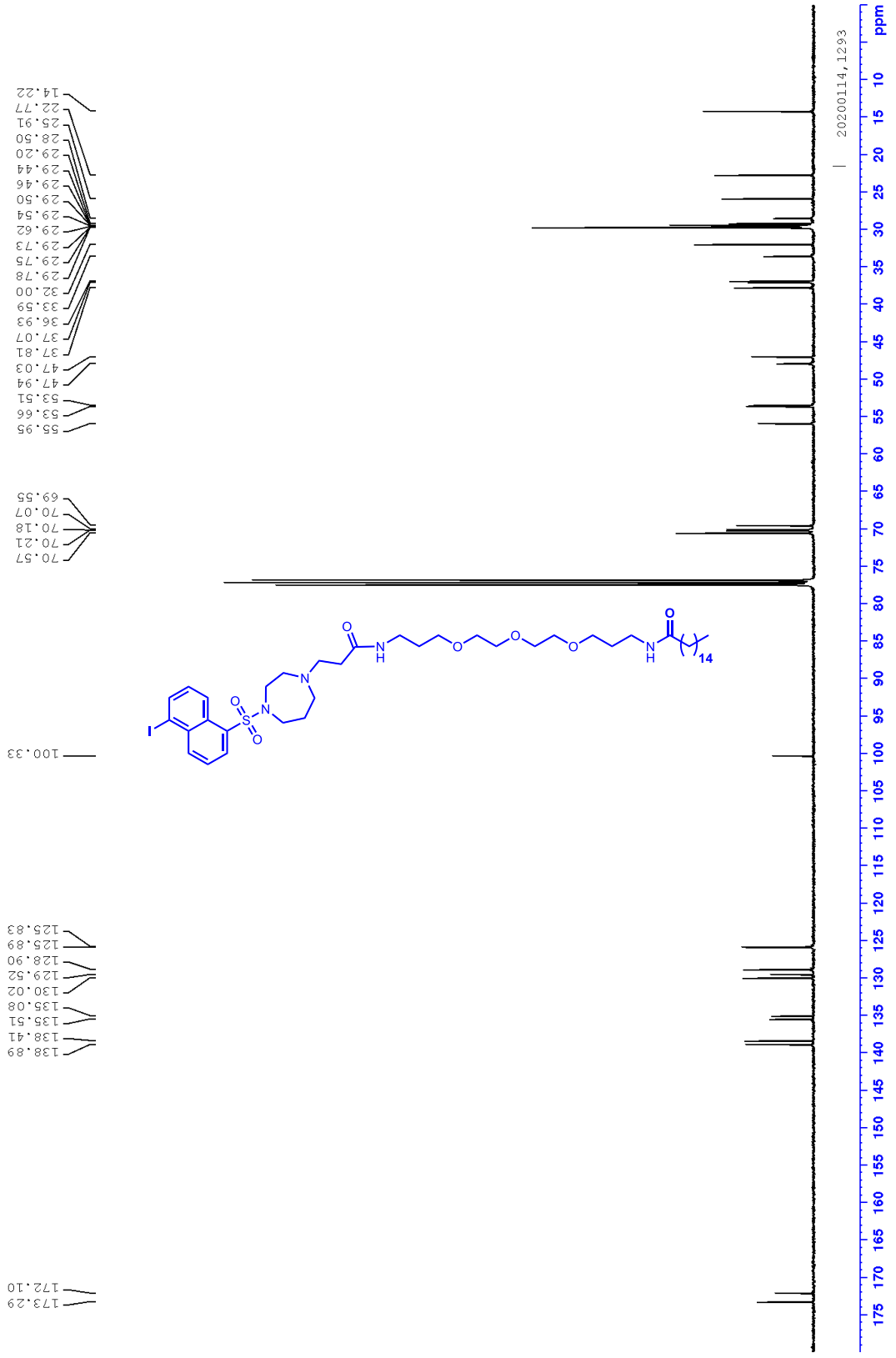
tert-Butyl (17-(4-((5-iodonaphthalen-1-yl)sulfonyl)-1,4-diazepan-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)carbamate [ML-7–Boc]



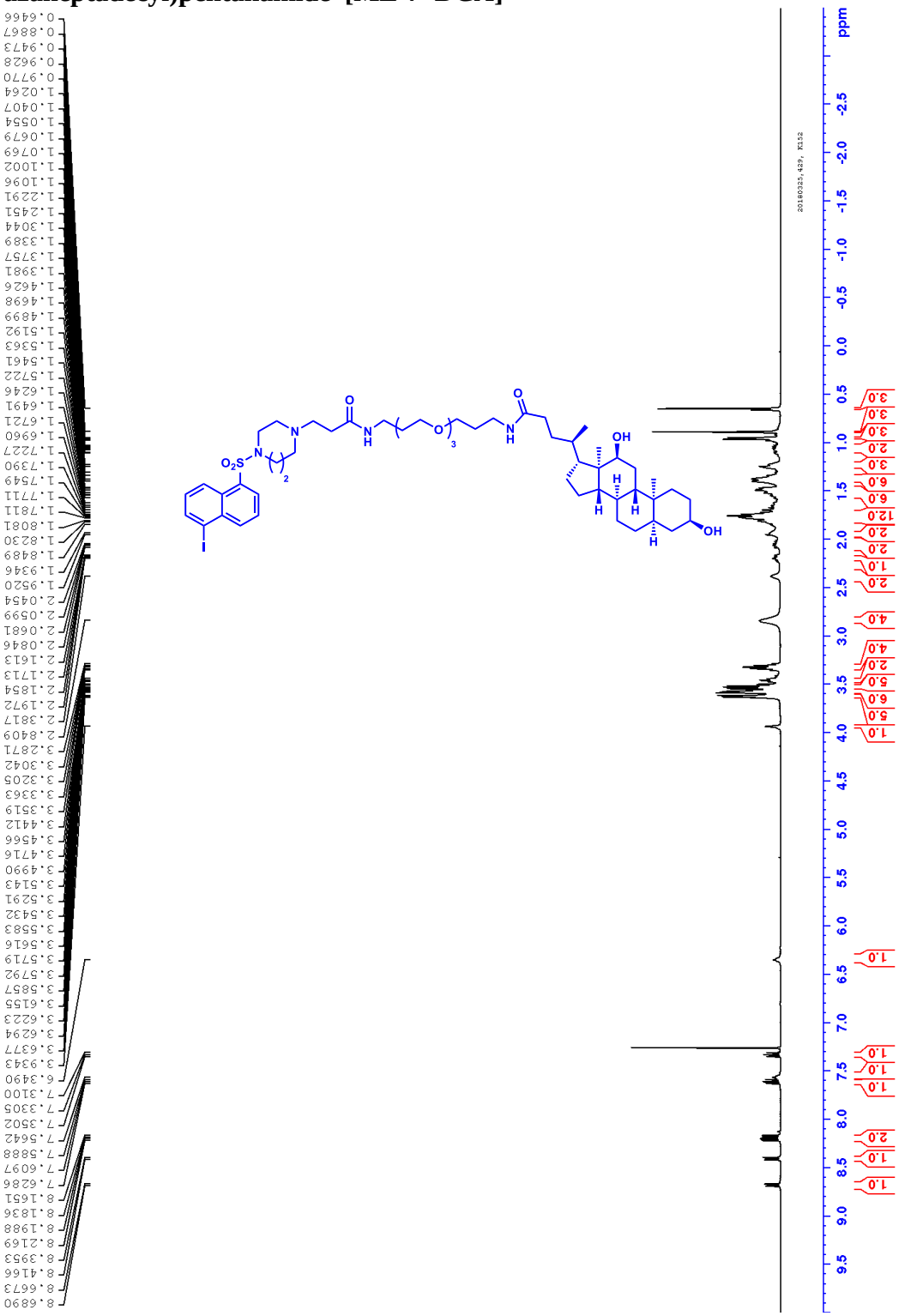

28.60
29.37
29.82
33.33
37.44
38.66
46.73
53.68
53.76
56.43
69.67
69.76
70.28
70.34
70.65
79.06
100.42
125.76
125.93
129.04
129.54
130.10
135.16
135.37
139.00
156.18
O
N
H
N
O
3
NHBoc
N
2
O2S
I
20180317,412,MLBoc
5 ppm

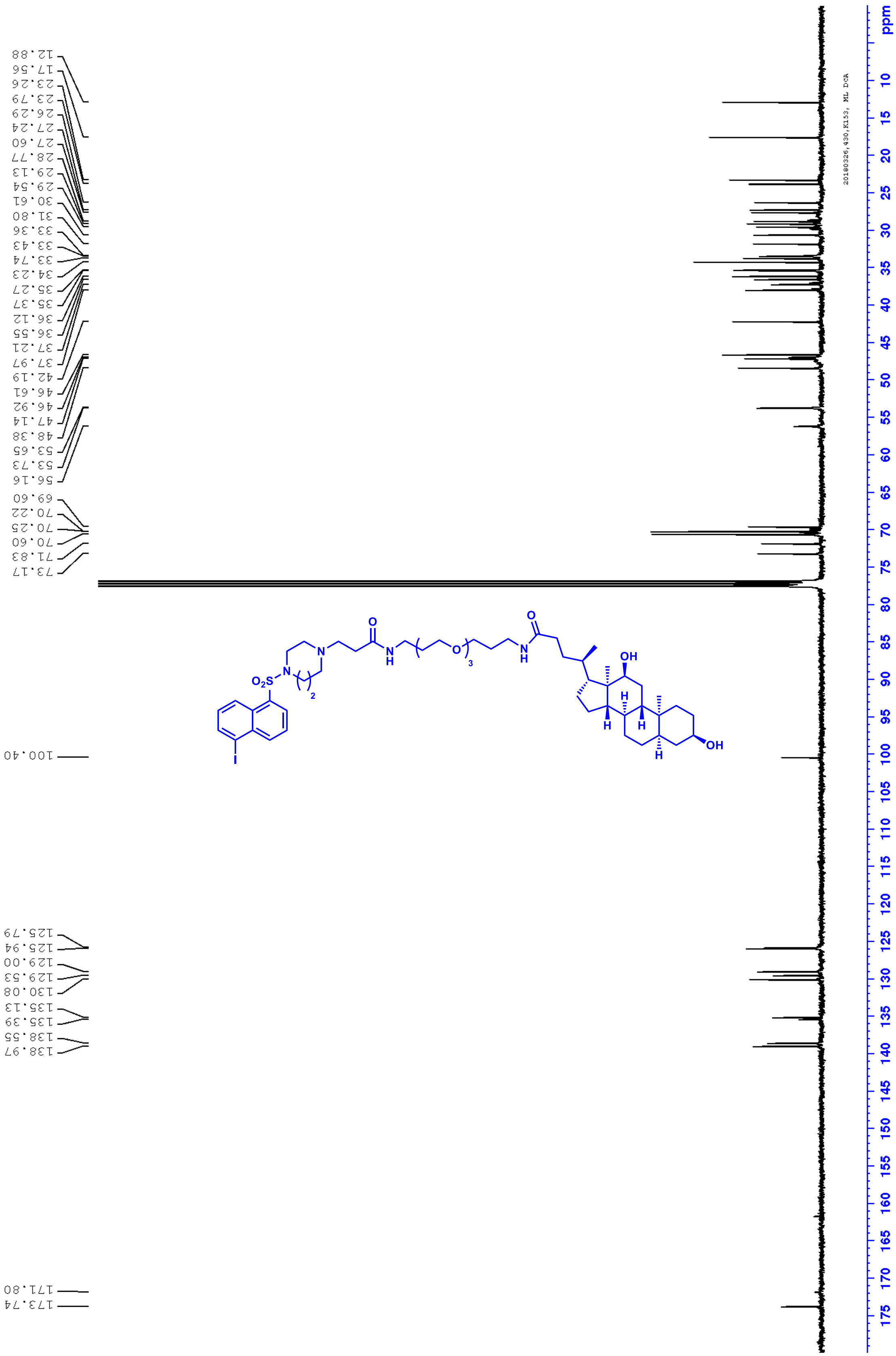
***N*-(17-(4-((5-iodonaphthalen-1-yl)sulfonyl)-1,4-diazepan-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)palmitamide [ML-7-C16:0]**



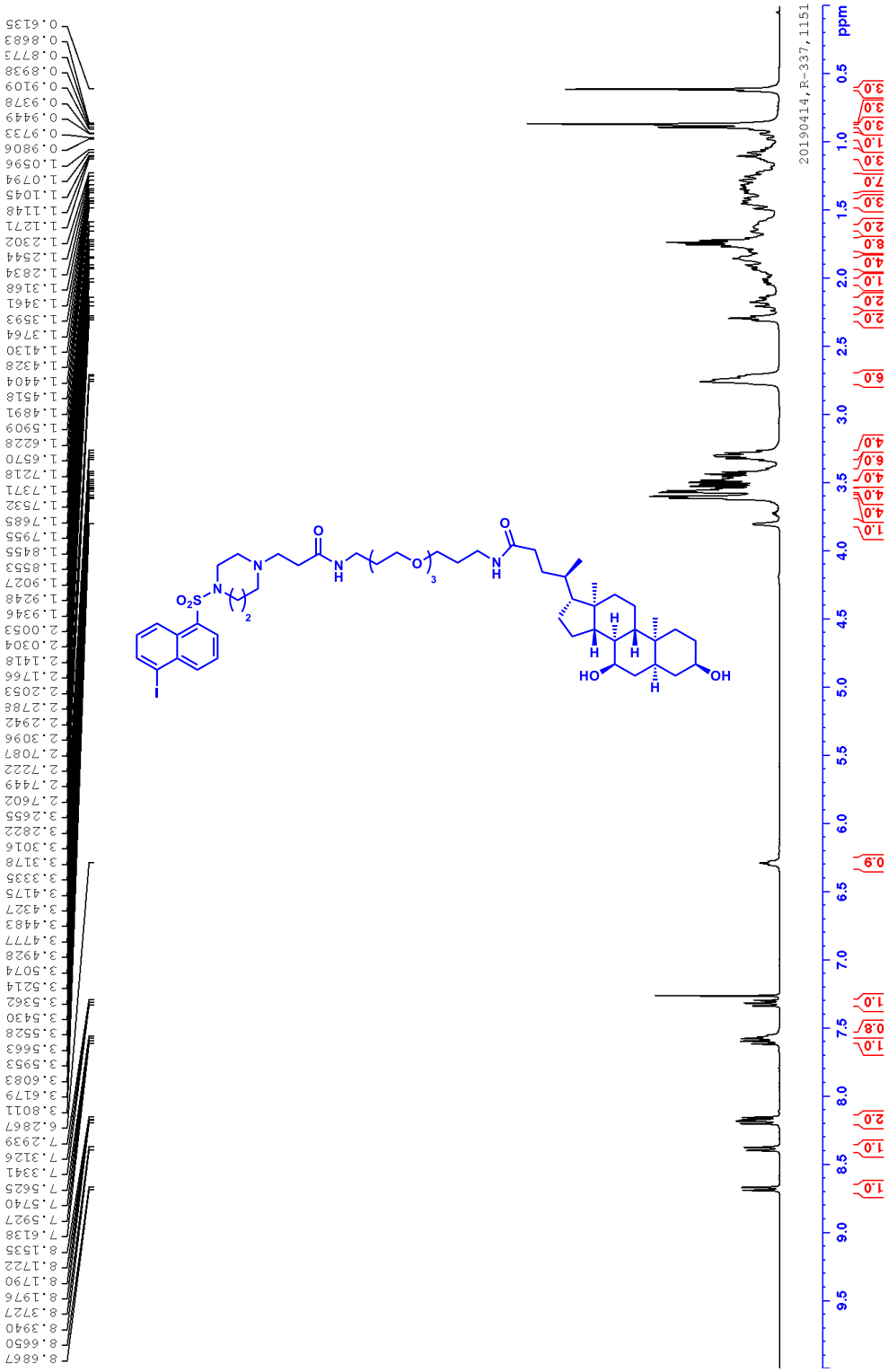

20200114,1293
ppm
14.22
22.77
25.91
28.50
29.20
29.44
29.46
29.50
29.54
29.62
29.73
29.75
29.78
32.00
33.59
36.93
37.07
37.81
47.03
47.94
53.51
53.66
55.95
69.55
70.07
70.18
70.21
70.57
100.33
125.83
125.89
128.90
129.52
130.02
135.08
135.51
138.41
138.89
172.10
173.29

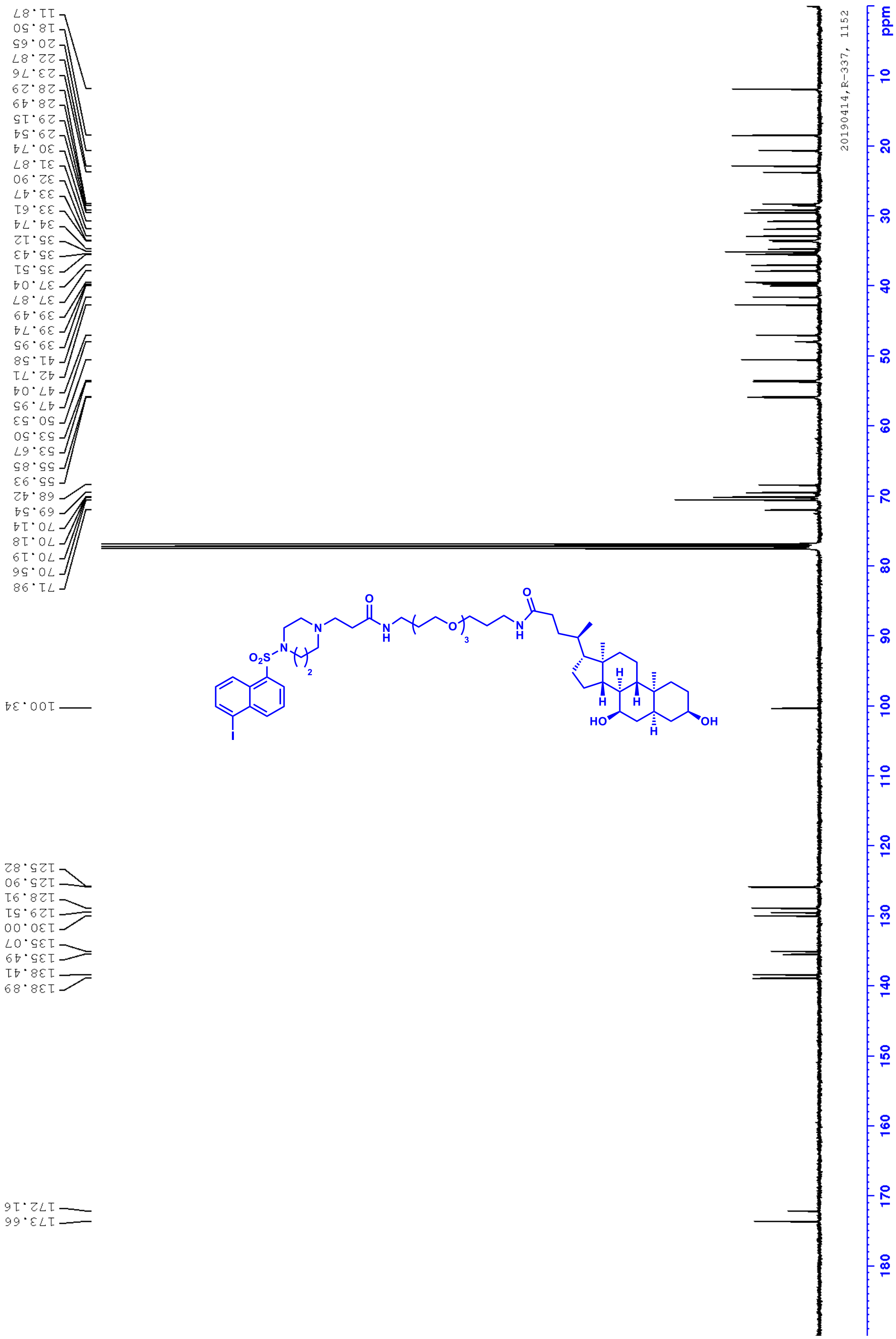
(*R*)-4-((3*R*,5*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,12-Dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-*N*-(17-(4-((5-iodonaphthalen-1-yl)sulfonyl)-1,4-diazepan-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)pentanamide [ML-7–DCA]



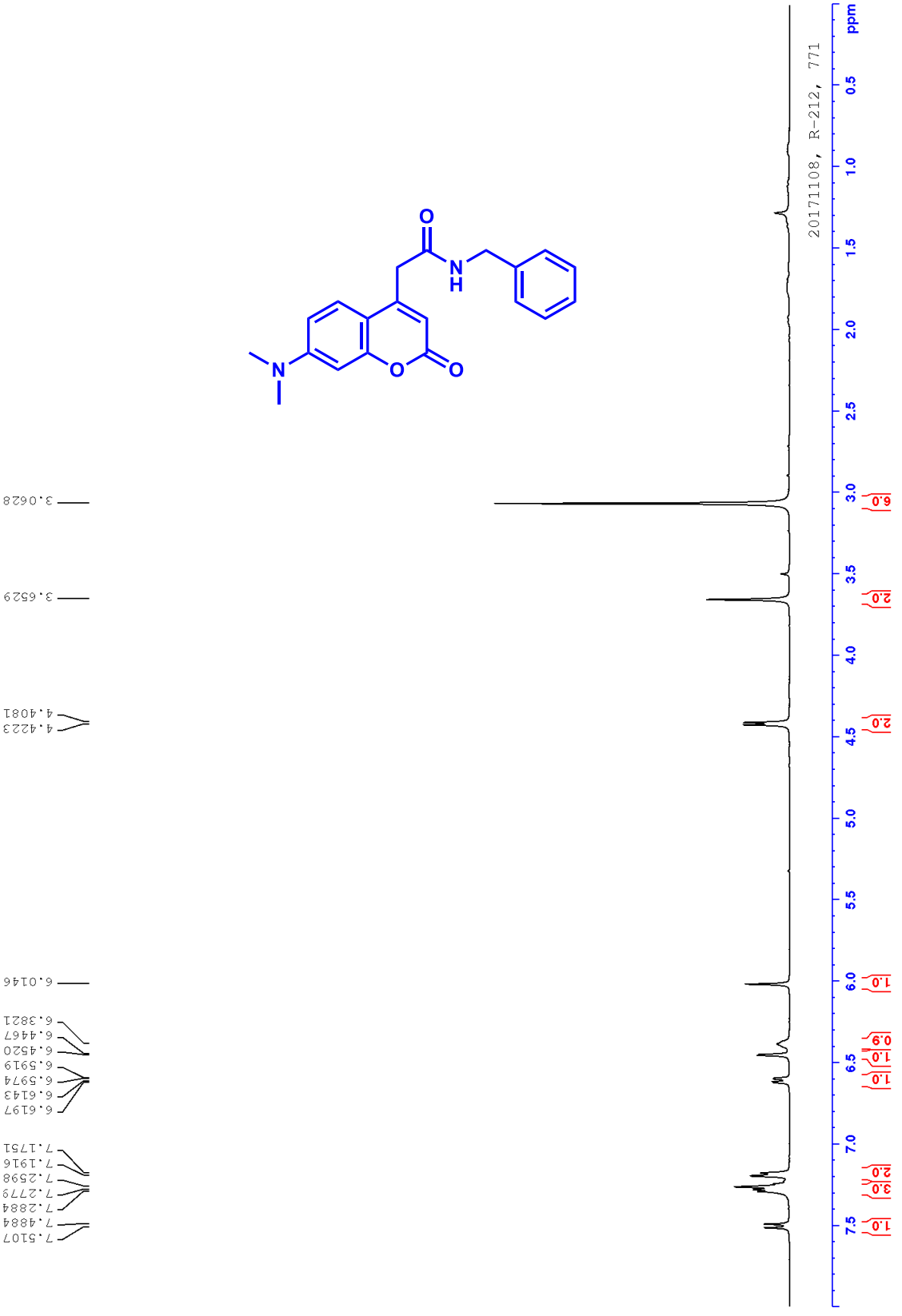

12.88
17.56
23.26
23.79
26.29
27.24
27.60
28.77
29.13
29.54
30.61
31.80
33.36
33.43
33.74
34.23
35.27
35.37
36.12
36.55
37.21
37.97
42.19
46.61
46.92
47.14
48.38
53.65
53.73
56.16
69.60
70.22
70.25
70.60
71.83
73.17
100.40
125.79
125.94
129.00
129.53
130.08
135.13
135.39
138.55
138.97
171.80
173.74
ppm

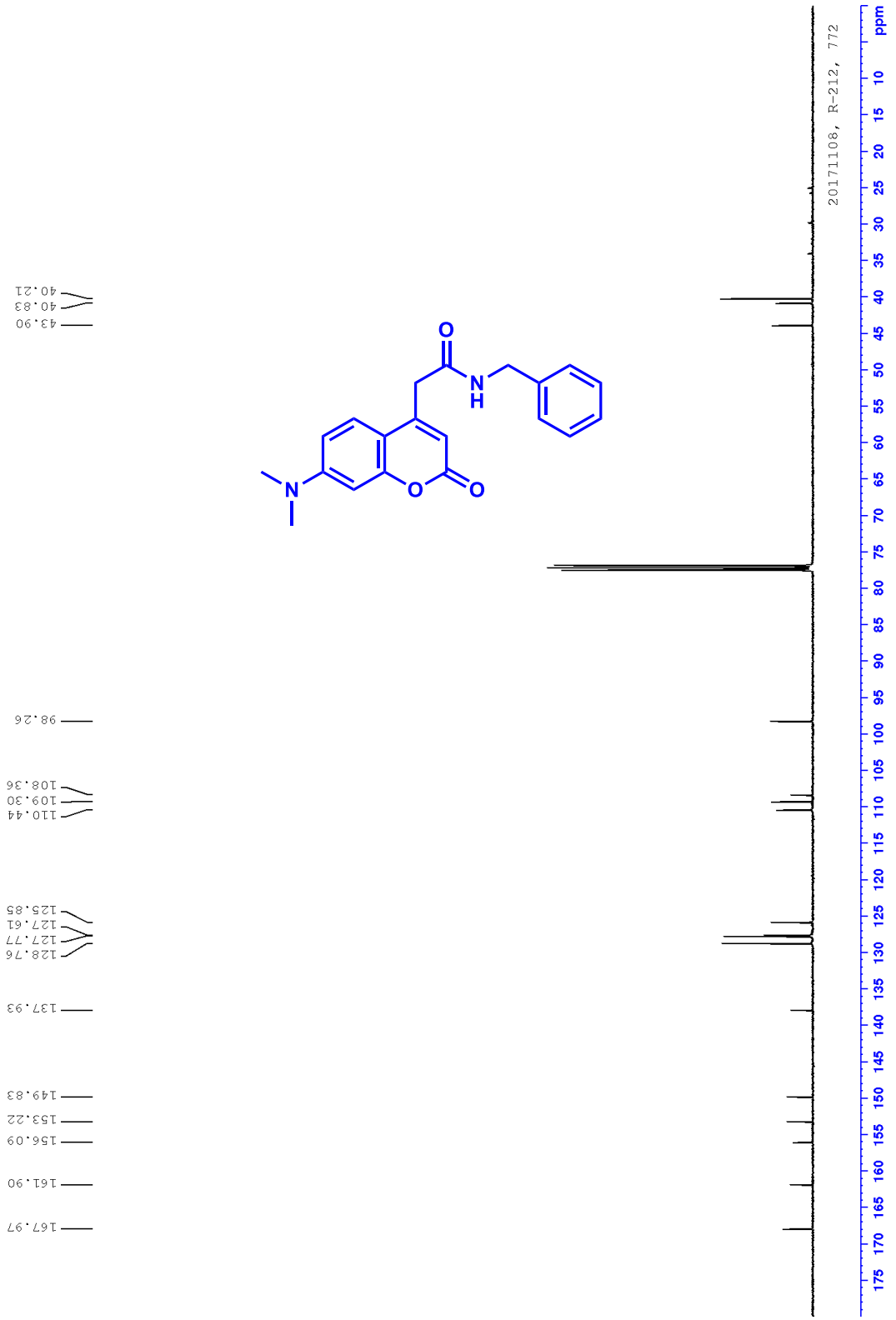
(4*R*)-4-((3*R*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3,7-dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-*N*-(17-(4-((5-iodonaphthalen-1-yl)sulfonyl)-1,4-diazepan-1-yl)-15-oxo-4,7,10-trioxa-14-azaheptadecyl)pentanamide [ML-7-CDCA]



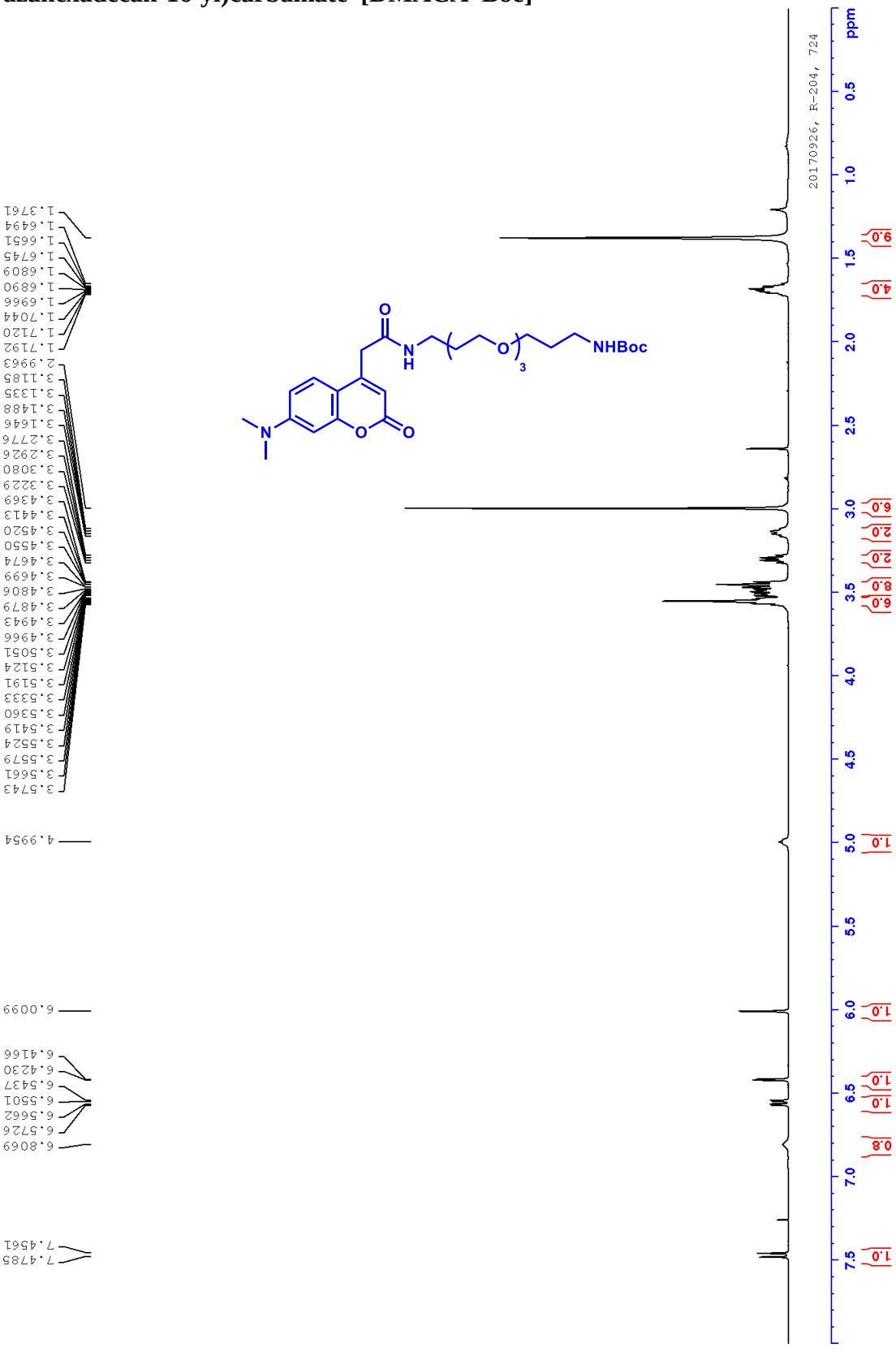

11.87
18.50
20.65
22.87
23.76
28.29
28.49
29.15
29.54
30.74
31.87
32.90
33.47
33.61
34.74
35.12
35.43
35.51
37.04
37.87
39.49
39.74
39.95
41.58
42.71
47.04
47.95
50.53
53.50
53.67
55.85
55.93
68.42
69.54
70.14
70.18
70.19
70.56
71.98
100.34
125.82
125.90
128.91
129.51
130.00
135.07
135.49
138.41
138.89
172.16
173.66
20190414,R-337, 1152
ppm

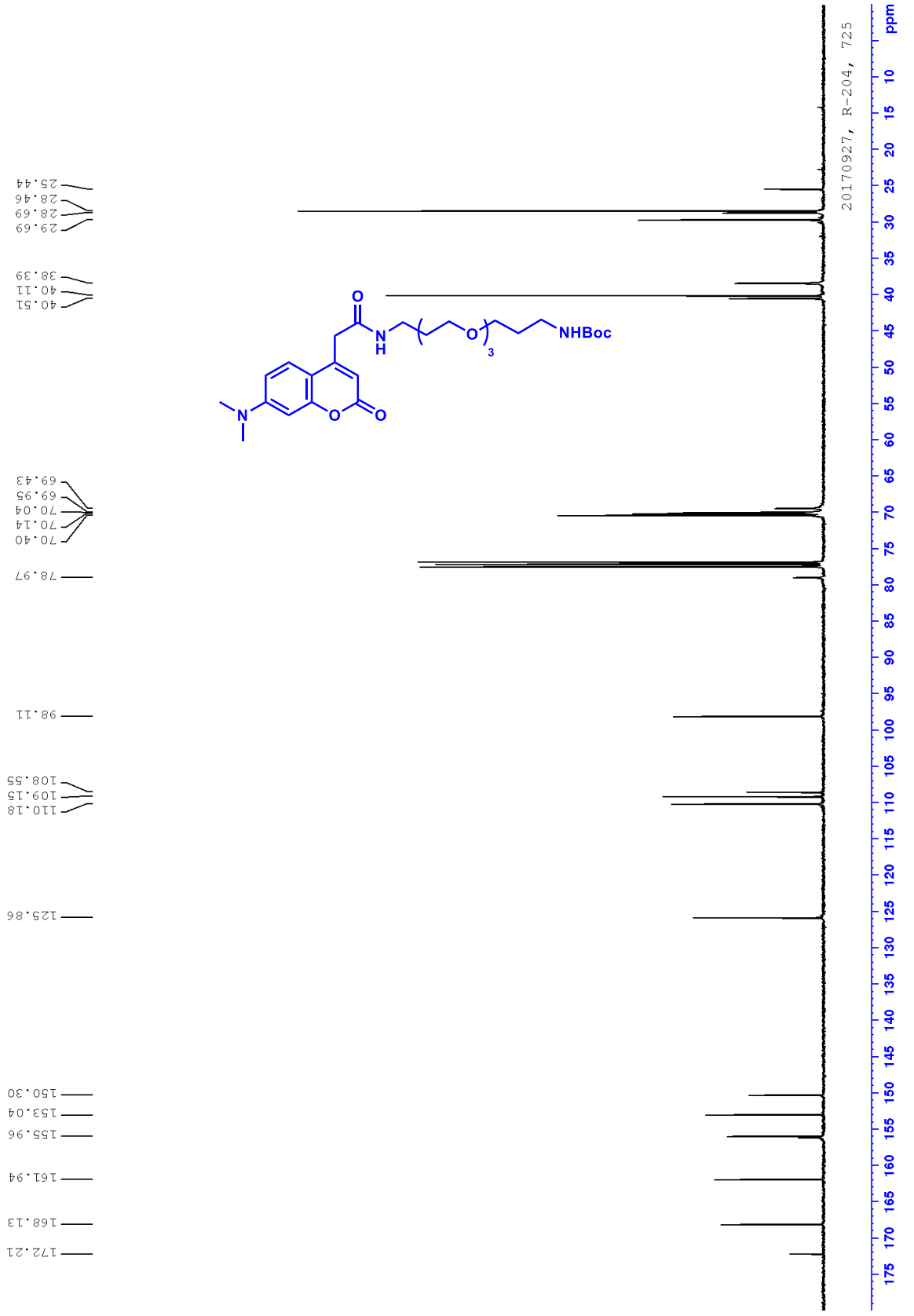
_N_-Benzyl-2-(7-(dimethylamino)-2-oxo-2_H_-chromen-4-yl)acetamide [DMACA–Bn]



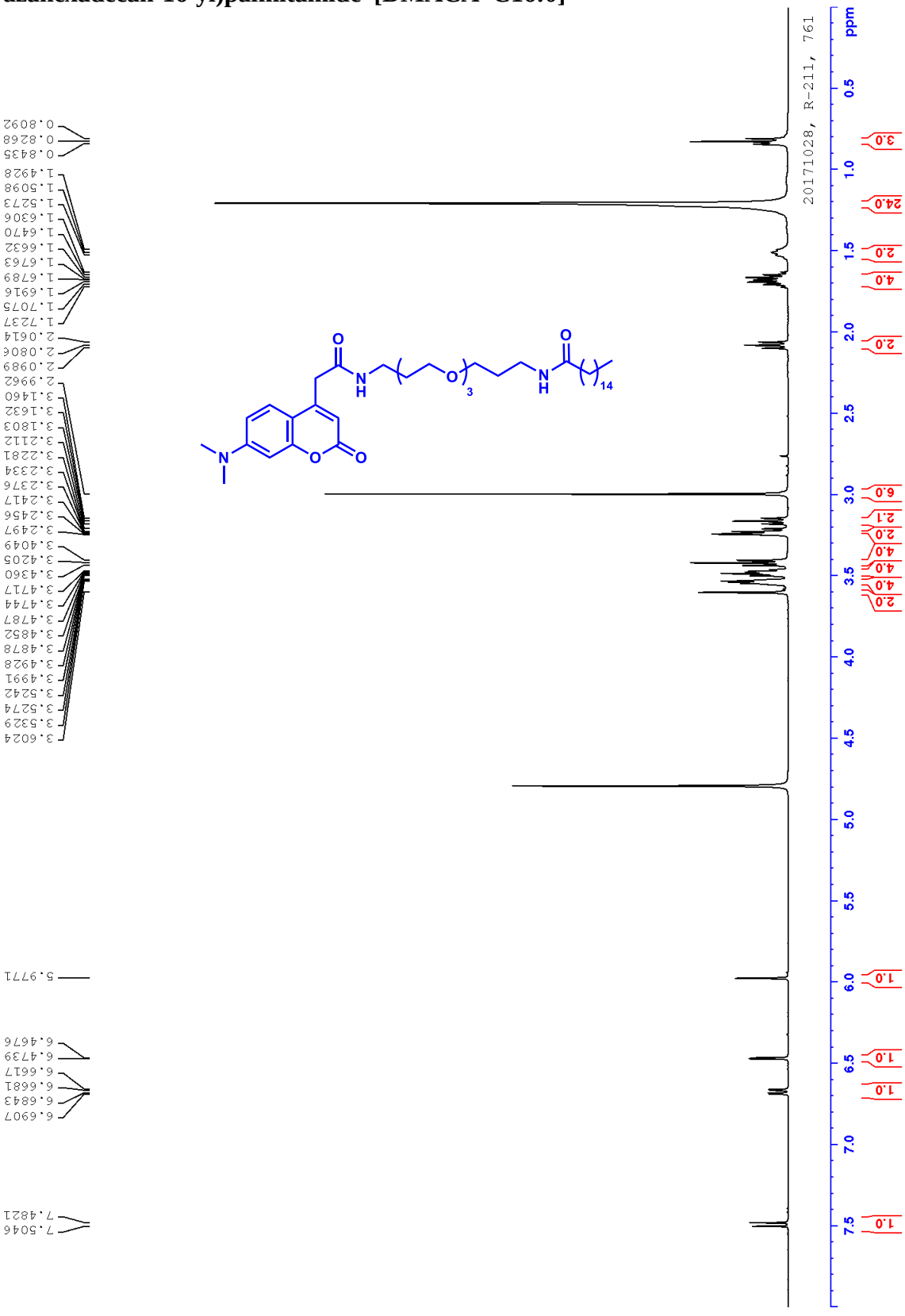

20171108, R-212, 772
ppm
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
100
105
110
115
120
125
130
135
140
145
150
155
160
165
170
175
40.21
40.83
43.90
98.26
108.36
109.30
110.44
125.85
127.61
127.77
128.76
137.93
149.83
153.22
156.09
161.90
167.97
O
N
H
N
O
O

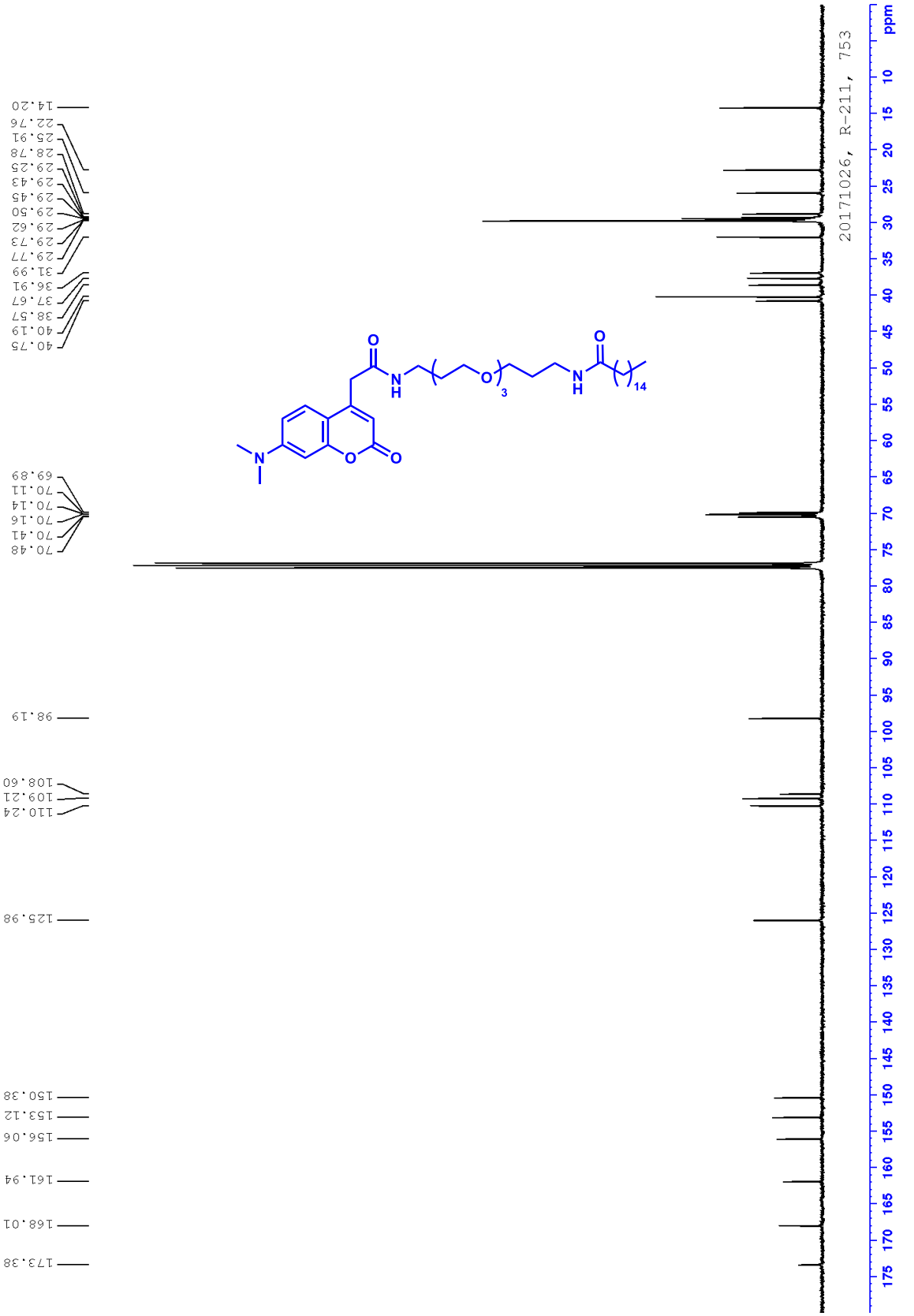
***tert*-Butyl (1-(7-(dimethylamino)-2-oxo-2*H*-chromen-4-yl)-2-oxo-7,10,13-trioxa-3-azahexadecan-16-yl)carbamate [DMACA–Boc]**



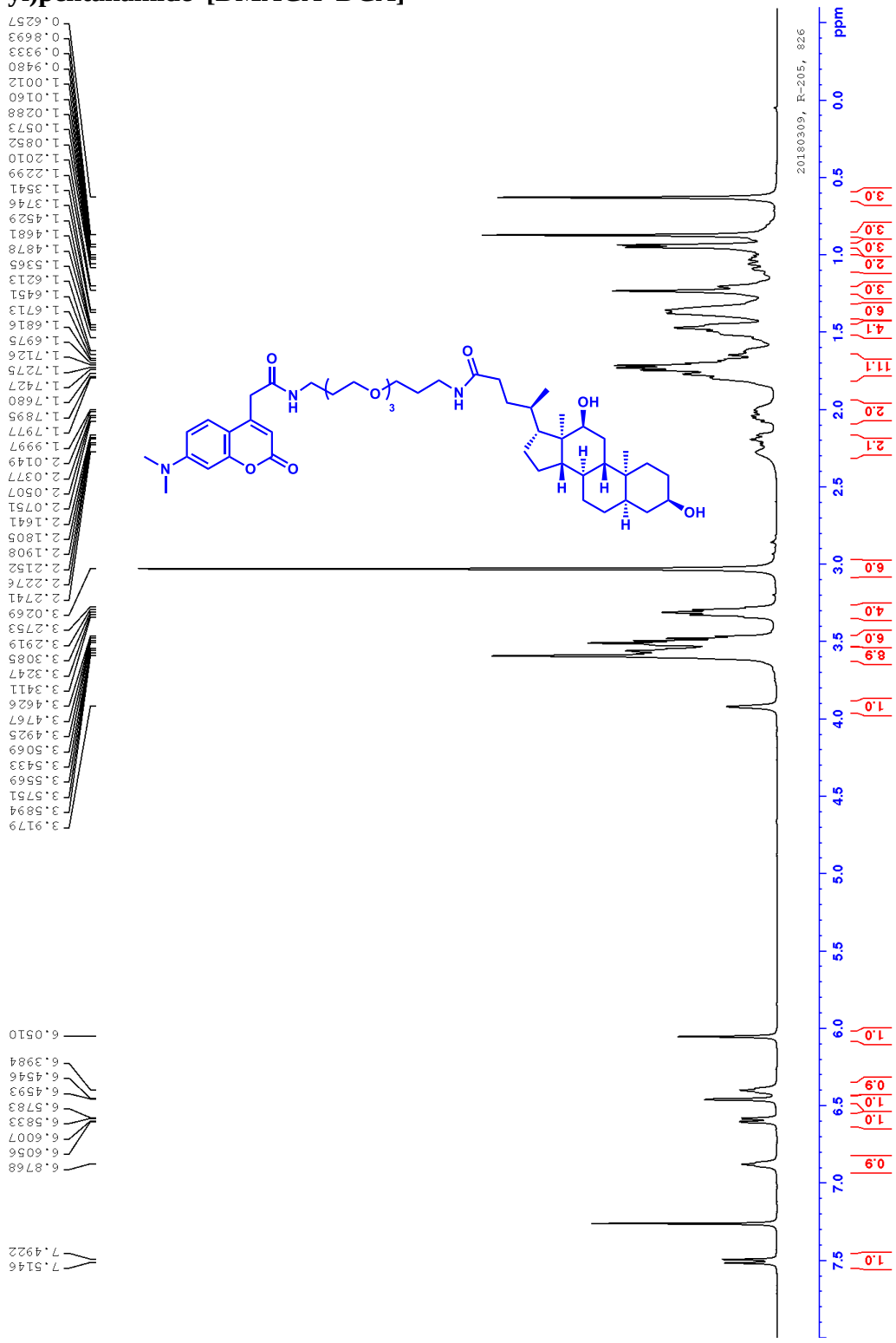

20170927, R-204, 725
ppm
NHBoc
O
N
H
O
3
N
O
O
25.44
28.46
28.69
29.69
38.39
40.11
40.51
69.43
69.95
70.04
70.14
70.40
78.97
98.11
108.55
109.15
110.18
125.86
150.30
153.04
155.96
161.94
168.13
172.21

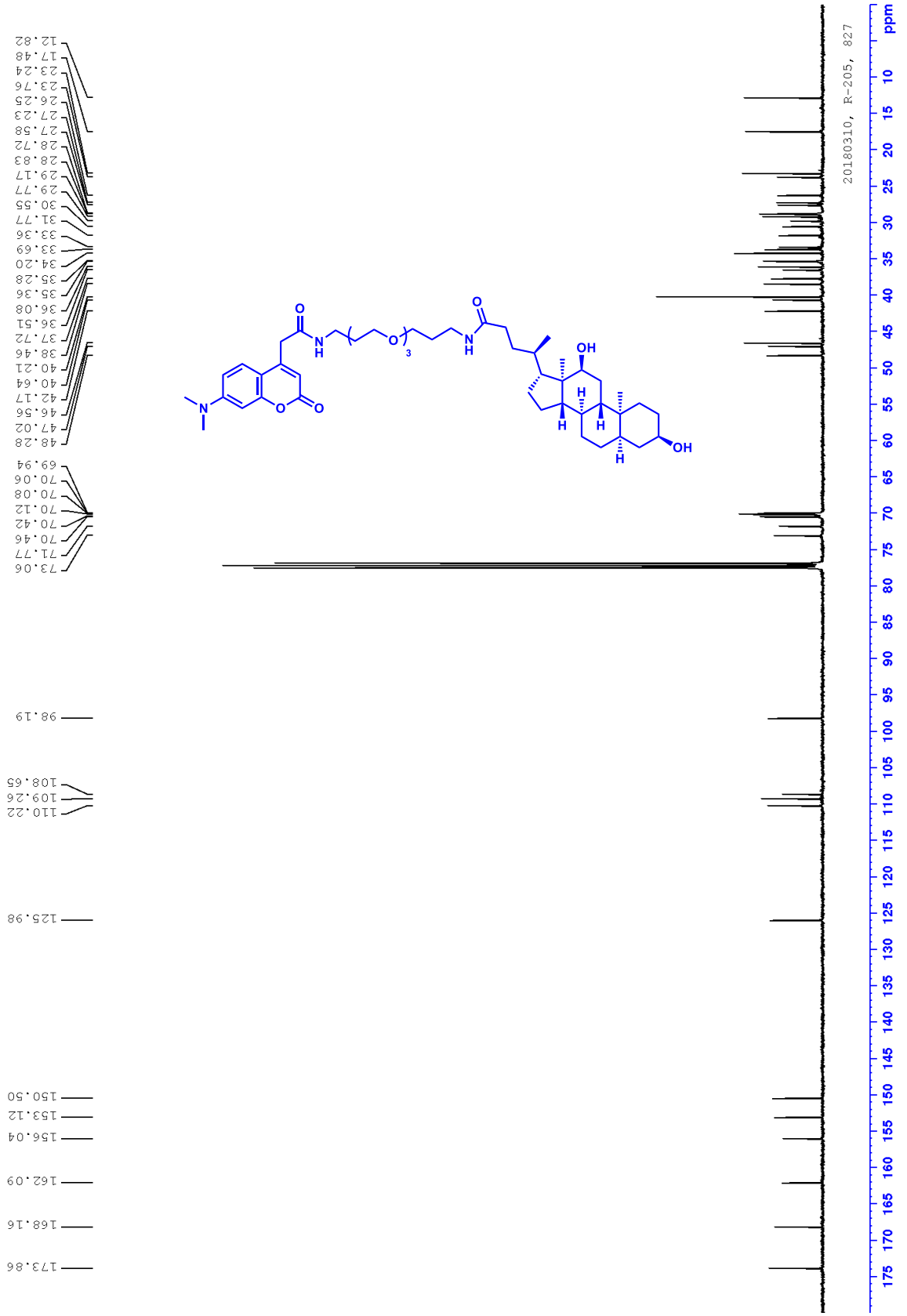
***N*-(1-(7-(Dimethylamino)-2-oxo-2*H*-chromen-4-yl)-2-oxo-7,10,13-trioxa-3-azahexadecan-16-yl)palmitamide [DMACA–C16:0]**



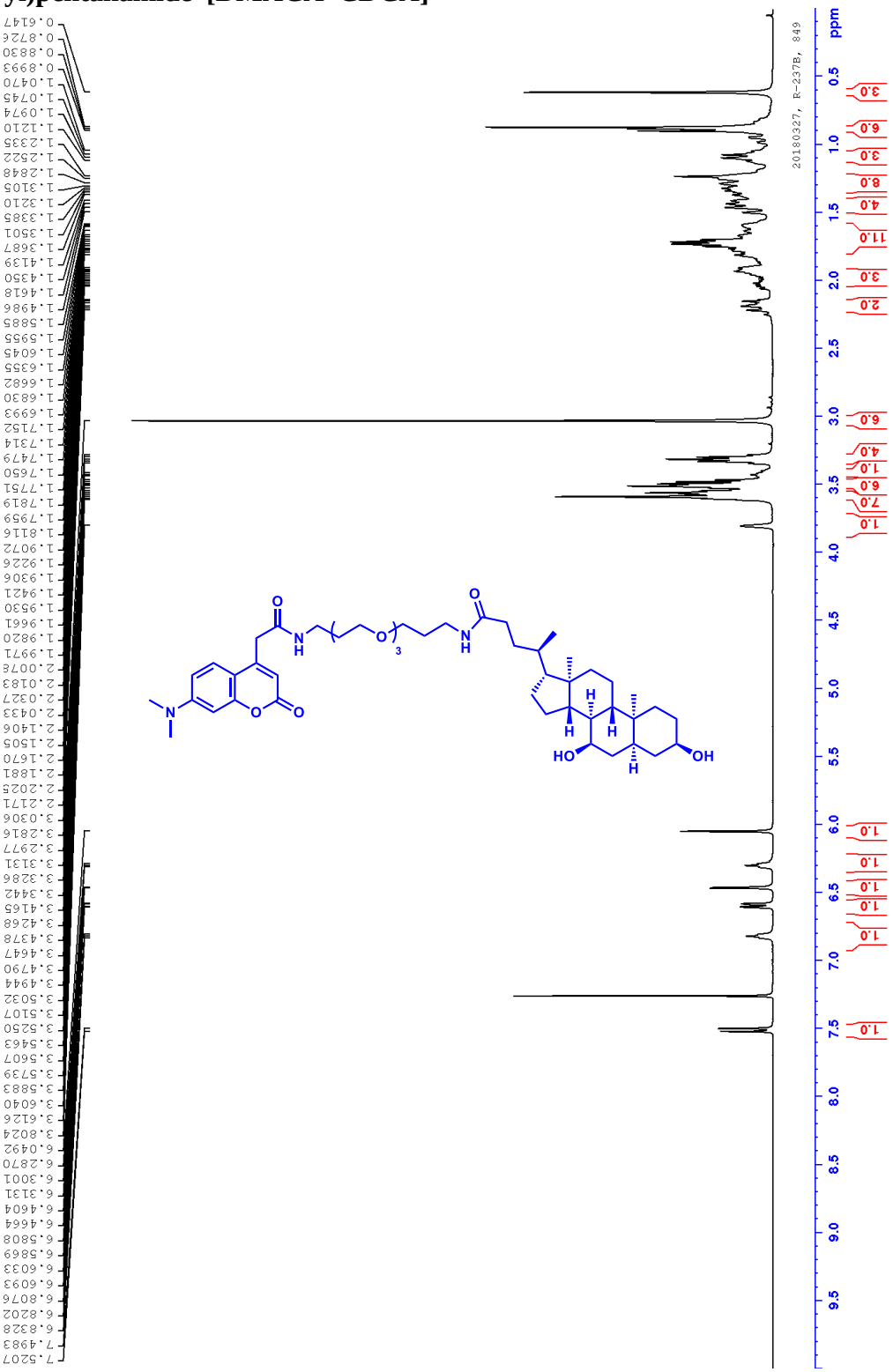

20171026, R-211, 753
ppm
14.20
22.76
25.91
28.78
29.25
29.43
29.45
29.50
29.62
29.73
29.77
31.99
36.91
37.67
38.57
40.19
40.75
69.89
70.11
70.14
70.16
70.41
70.48
98.19
108.60
109.21
110.24
125.98
150.38
153.12
156.06
161.94
168.01
173.38
O
N
H
O
3
N
H
O
14
N
O
O

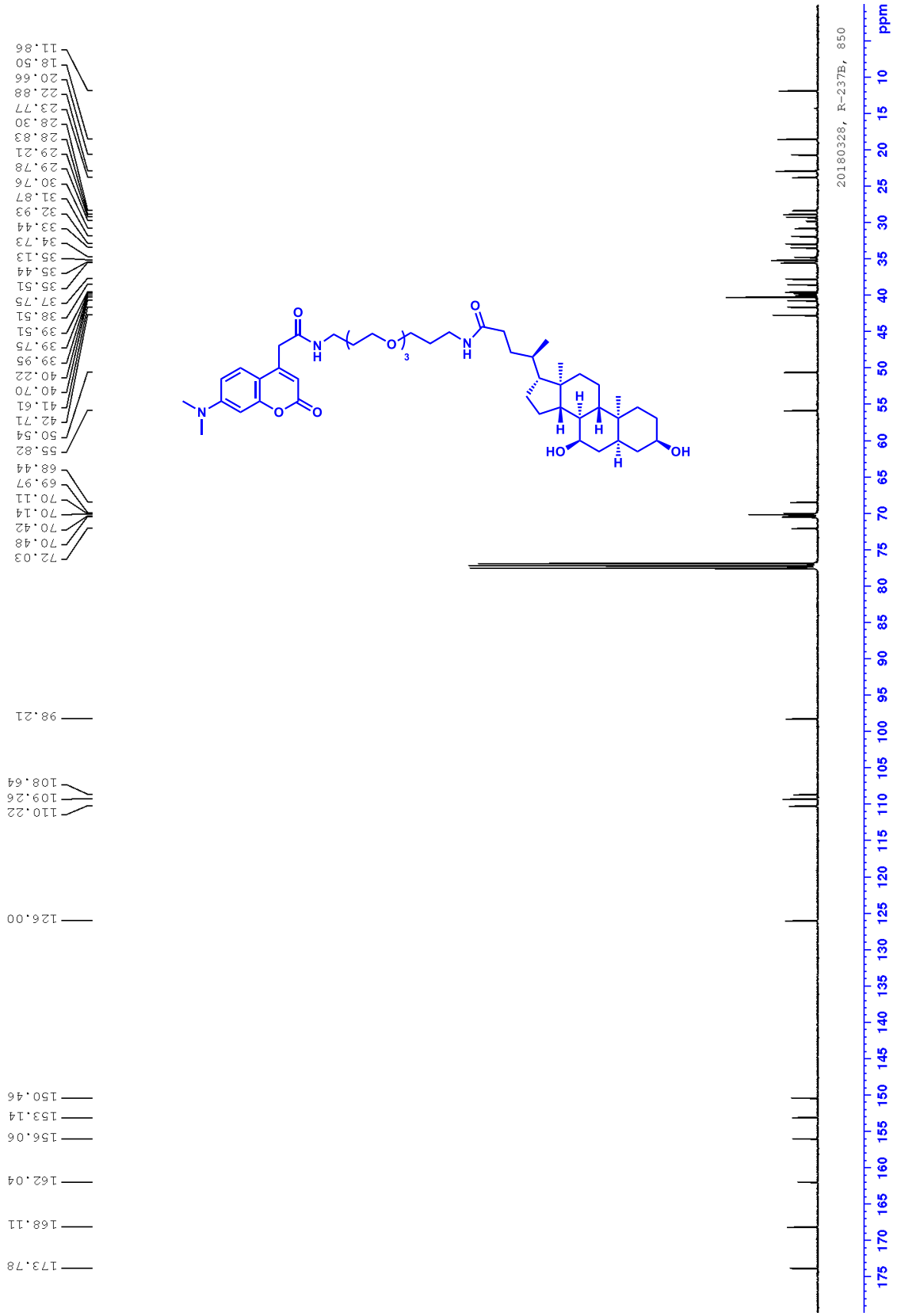
(*R*)-4-((3*R*,5*R*,8*R*,9*S*,10*S*,12*S*,13*R*,14*S*,17*R*)-3,12-Dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-*N*-(1-(7-(dimethylamino)-2-oxo-2*H*-chromen-4-yl)-2-oxo-7,10,13-trioxa-3-azahexadecan-16-yl)pentanamide [DMACA–DCA]




20180310, R-205, 827
ppm
12.82
17.48
23.24
23.76
26.25
27.23
27.58
28.72
28.83
29.17
29.77
30.55
31.77
33.36
33.69
34.20
35.28
35.36
36.08
36.51
37.72
38.46
40.21
40.64
42.17
46.56
47.02
48.28
69.94
70.06
70.08
70.12
70.42
70.46
71.77
73.06
98.19
108.65
109.26
110.22
125.98
150.50
153.12
156.04
162.09
168.16
173.86
O
N
H
O
3
N
H
O
O
N
OH
H
H
H
OH

***(4R)*-4-((3*R*,7*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3,7-Dihydroxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)-*N*-(1-(7-(dimethylamino)-2-oxo-2*H*-chromen-4-yl)-2-oxo-7,10,13-trioxa-3-azahexadecan-16-yl)pentanamide [DMACA–CDCA]**




20180328, R-237B, 850
ppm
11.86
18.50
20.66
22.88
23.77
28.30
28.83
29.21
29.78
30.76
31.87
32.93
33.44
34.73
35.13
35.44
35.51
37.75
38.51
39.51
39.75
39.95
40.22
40.70
41.61
42.71
50.54
55.82
68.44
69.97
70.11
70.14
70.42
70.48
72.03
98.21
108.64
109.26
110.22
126.00
150.46
153.14
156.06
162.04
168.11
173.78