Supporting Information for

Mechanically Triggered Release of Functionally Diverse Molecular Payloads from Masked 2-Furylcarbinol Derivatives

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I. General Experimental Details and Methods

Reagents from commercial sources were used without further purification unless otherwise stated. Methyl acrylate was passed through a short plug of basic alumina to remove inhibitor immediately prior to use. Dry THF, diethyl ether, MeCN, and DMF were obtained from a Pure Process Technology solvent purification system. All reactions were performed under a N_2 atmosphere unless specified otherwise. Column chromatography was performed on a Biotage Isolera system using SiliCycle SiliaSep HP flash cartridges.

NMR spectra were recorded using a 400 MHz Bruker Avance III HD with Prodigy Cryoprobe, a 400 MHz Bruker Avance Neo, or Varian Inova 500 MHz spectrometers. All ^{1}H NMR spectra are reported in δ units, parts per million (ppm), and were measured relative to the signals for residual chloroform (7.26 ppm), dichloromethane (5.32 ppm), methanol (3.31 ppm), acetone (2.05 ppm), or acetonitrile (1.94 ppm) in deuterated solvent. All ^{13}C NMR spectra were measured in deuterated solvents and are reported in ppm relative to the signals for chloroform (77.16 ppm). Multiplicity and qualifier abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dq = doublet of quartets, ABq = AB quartet, m = multiplet, br = broad.

High resolution mass spectra (HRMS) were analyzed by direct infusion electrospray ionization (ESI) in the positive ion mode using a Waters LCT Premier XE time-of-flight (TOF) mass spectrometer operated in the V mode. The instrument was externally calibrated with NaI clusters. Some samples were analyzed by Fast Atom Bombardment (FAB) using a JEOL JMS-60H Double-focusing high resolution magnetic sector mass spectrometer operated in the positive ion mode. The instrument was calibrated with PEG clusters over the mass range of interest. One sample was analyzed by GC-MS using an Agilent 6890N gas chromatograph interfaced to a JEOL double-focusing magnetic sector instrument using electron ionization (EI) in the positive ion mode. The instrument was calibrated with perfluorokerosene.

Analytical gel permeation chromatography (GPC) was performed using an Agilent 1260 series pump equipped with two Agilent PLgel MIXED-B columns (7.5 x 300 mm), an Agilent 1200 series diode array detector, a Wyatt 18-angle DAWN HELEOS light scattering detector, and an Optilab rEX differential refractive index detector. The mobile phase was THF at a flow rate of 1 mL/min. Molecular weights and molecular weight distributions were calculated by light scattering using a dn/dc value of 0.062 mL/g (25 °C) for poly(methyl acrylate).

Photoluminescence spectra were recorded on a Shimadzu RF-6000 spectrofluorophotometer using a quartz microcuvette (Starna Cells 18F-Q-10-GL14-C, 10 x 2 mm). Excitation and emission slit widths were 5 nm and 3 nm, respectively.

High-Performance Liquid Chromatography (HPLC) measurements were performed with an Agilent Eclipse Plus C18 column (959961-902) or a C8 column (993967-906) using a single-wavelength UV-vis detector.

Ultrasound experiments were performed using a 500 watt Vibra Cell 505 liquid processor (20 kHz) equipped with a 0.5-inch diameter solid probe (part #630-0217), sonochemical adapter (part #830-00014), and a Suslick reaction vessel made by the Caltech glass shop (analogous to vessel #830-00014 from Sonics and Materials).

LCMS measurements were performed with a Agilent 6140 Series Quadrupole LCMS Spectrometer System equipped with a Agilent Eclipse Plus C18 column using MeCN/water as the eluent.

Safety Statement

No unexpected or unusually high safety hazards were encountered.

Chemical synthesis operations were performed with the operator wearing proper PPE (including safety glasses, labcoat, and appropriate gloves) at all times and with proper engineering controls.

Triphosgene is toxic and should be handled exclusively inside of a fume hood.[1]

Care should be taken when using n-butyllithium. For example, using a luer lock syringe for transferring solutions of n-butyllithium; using a syringe with double the capacity of the volume to be transferred; and avoiding use of n-butyllithium while working alone.

Ultrasound experiments using a 20 kHz probe sonicator were performed inside of a sound abating enclosure. Personal hearing protection is recommended if ultrasonication is performed without the use of a sound abating enclosure.

II. Supplementary Figures

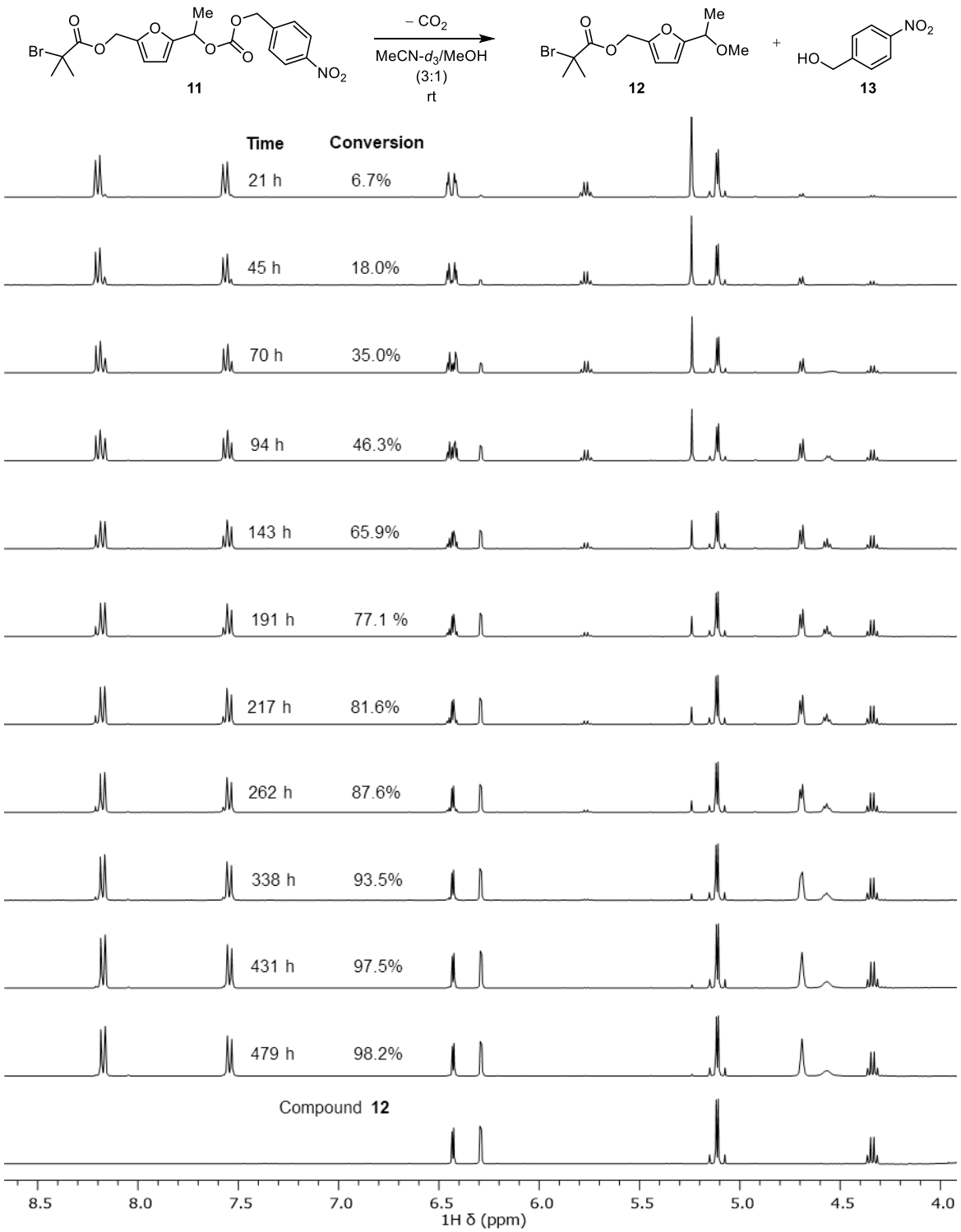


Figure S1. Partial ^{1}H NMR spectra (400 MHz) of a 42 mM solution of **11** in MeCN-d_3/MeOH (3:1) at room temperature. The starting material was cleanly converted over a period of approximately 500 h, with a new set of peaks emerging matching with the spectrum of furfuryl methyl ether **12** (bottom trace). The reaction half-life is approximately 4.1 days.

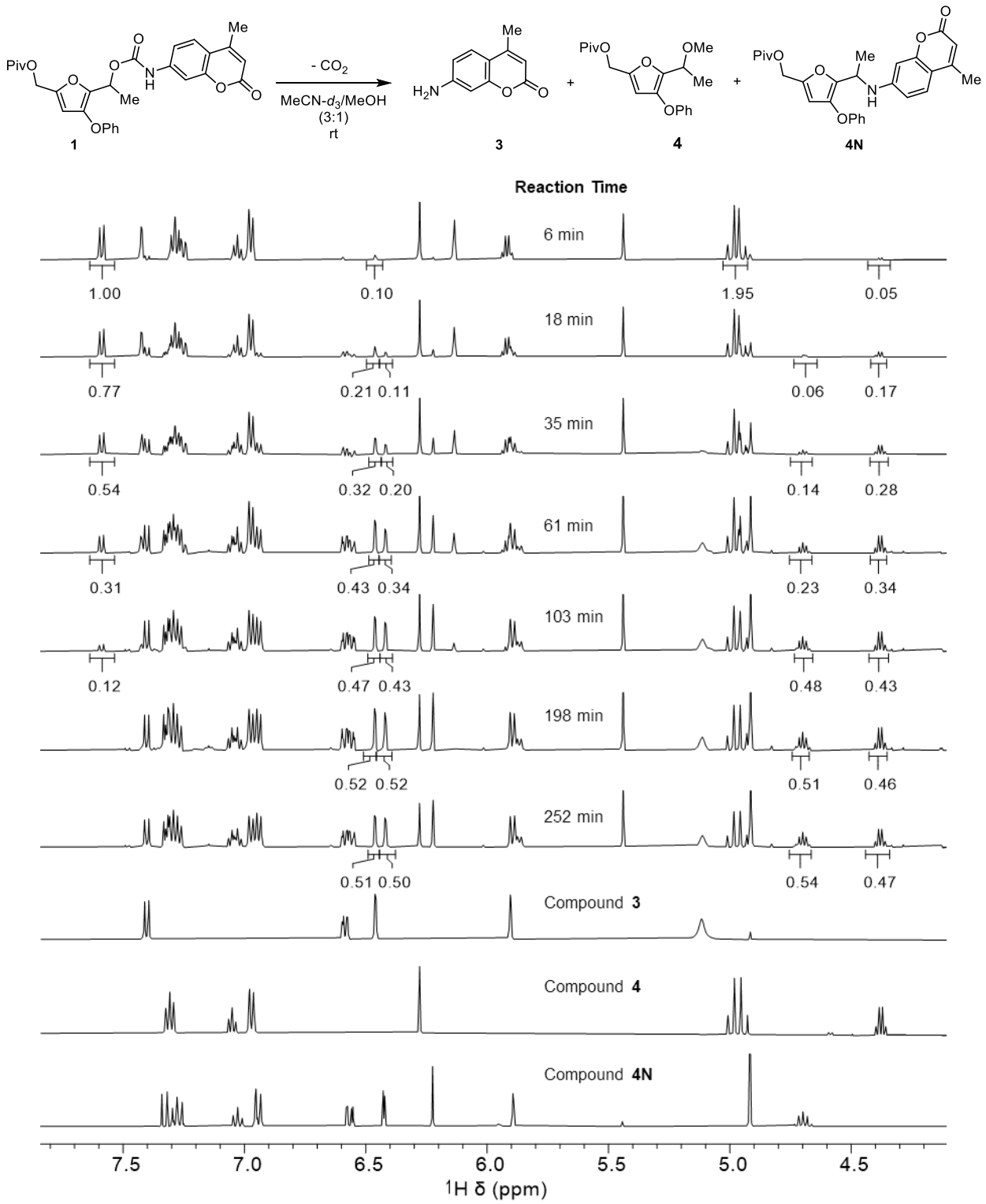


Figure S2. Partial ^{1}H NMR spectra (500 MHz) of a 14.0 mM solution of compound **1** in MeCN-d_3/MeOH (3:1) at room temperature, compared to spectra of compounds **3**, **4**, and **4N** (400 MHz) in the same solvent mixture. Decomposition of **1** at this relatively high concentration generates aminocoumarin **3** and furfuryl methyl ether **4**, as well as side product furfuryl amine **4N**.

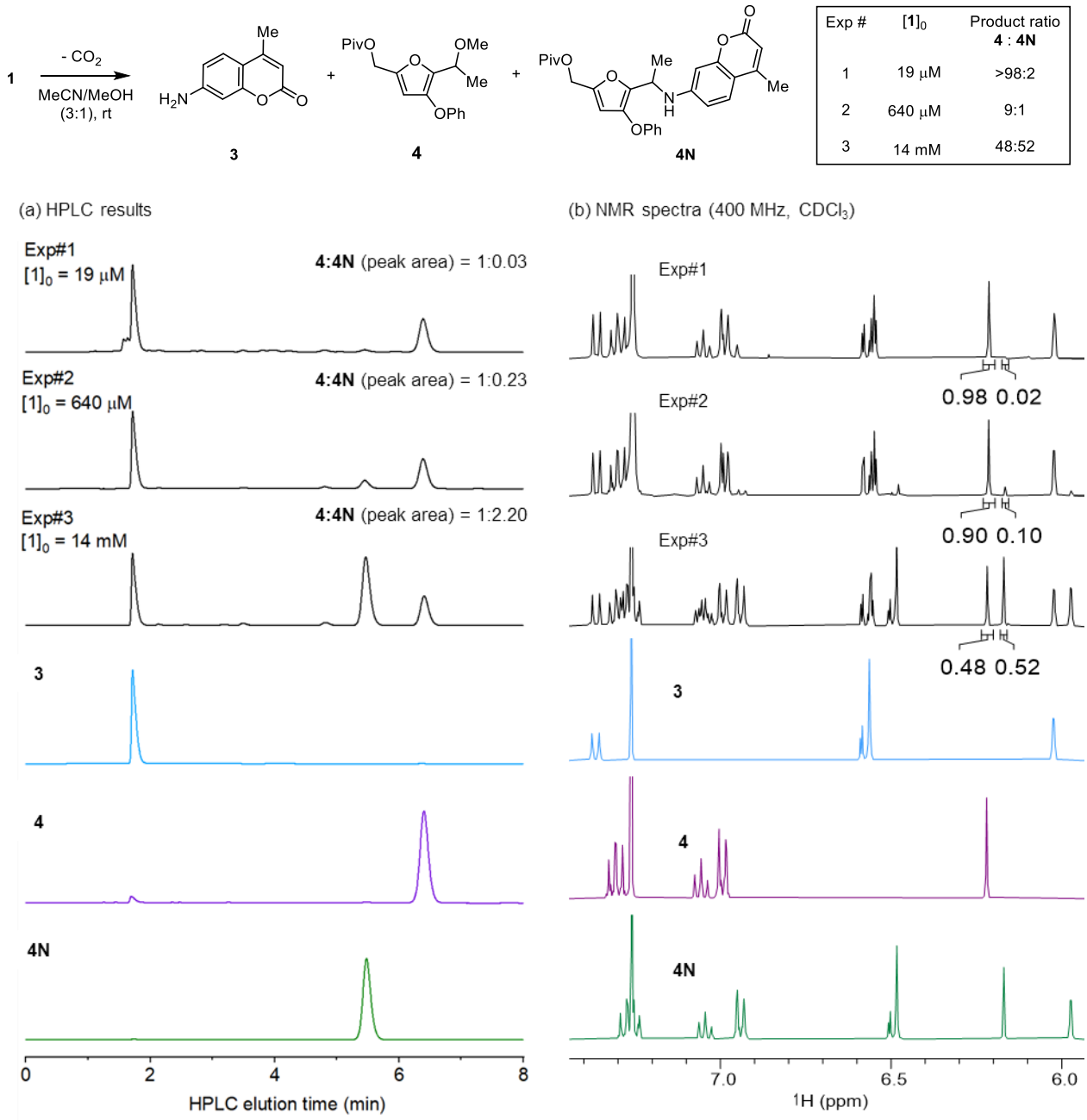


Figure S3. Quantification of products from the decomposition of model compound **1** under varying reaction concentrations by (a) HPLC and (b) ^{1}H NMR spectroscopy. Three separate experiments were performed with solutions of **1** at different initial concentrations in 3:1 MeCN/MeOH (19 μM, 640 μM, and 14 mM). Solutions were kept at room temperature for a minimum of 10 h to ensure complete conversion, then dried, dissolved in $CDCl_3$, and analyzed by HPLC equipped with a UV-vis detector (λ = 233 nm) and ^{1}H NMR spectroscopy. The reaction mixtures from each trial were compared to isolated aminocoumarin **3**, furfuryl methyl ether **4**, and furfuryl amine **4N**. HPLC conditions: MeCN/water (70:30), C8 column, 25°C, 1 mL/min.

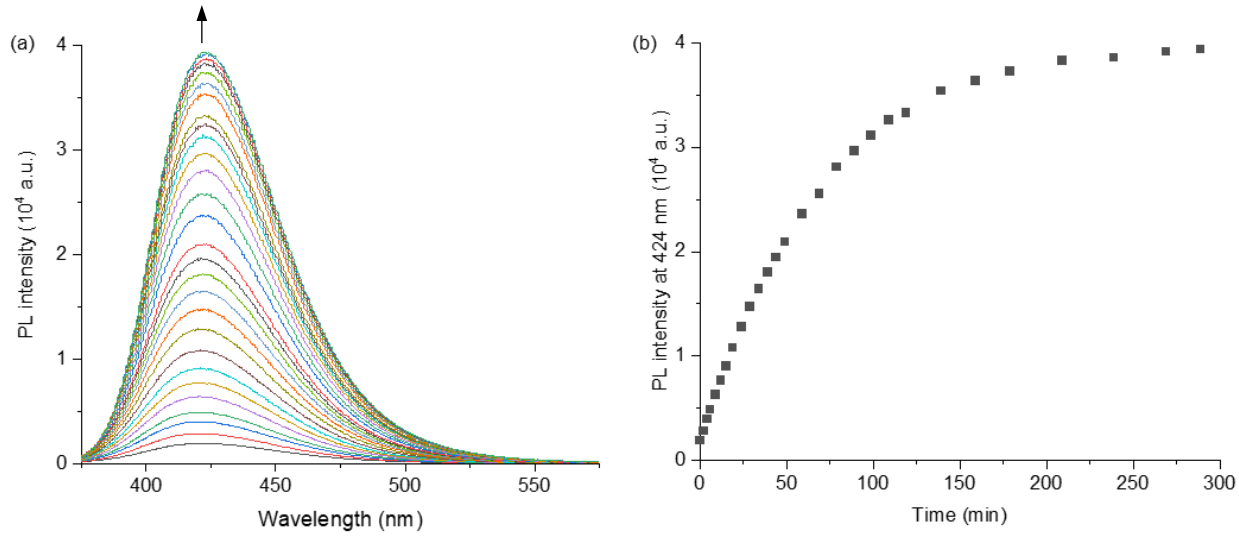


Figure S4. Photoluminescence characterization of the release of fluorogenic payload **3** from compound **1**. (a) Fluorescence emission spectra of a solution of compound **1** in 3:1 MeCN:MeOH (7.6 μM) at room temperature. (b) Fluorescence intensity at 424 nm as a function of time. The theoretical PL intensity of a 7.6 μM solution of **3** is calculated to be 4.09 x 10^4 a.u. based on the calibration curve in Figure S9. λ_{ex} = 365 nm.

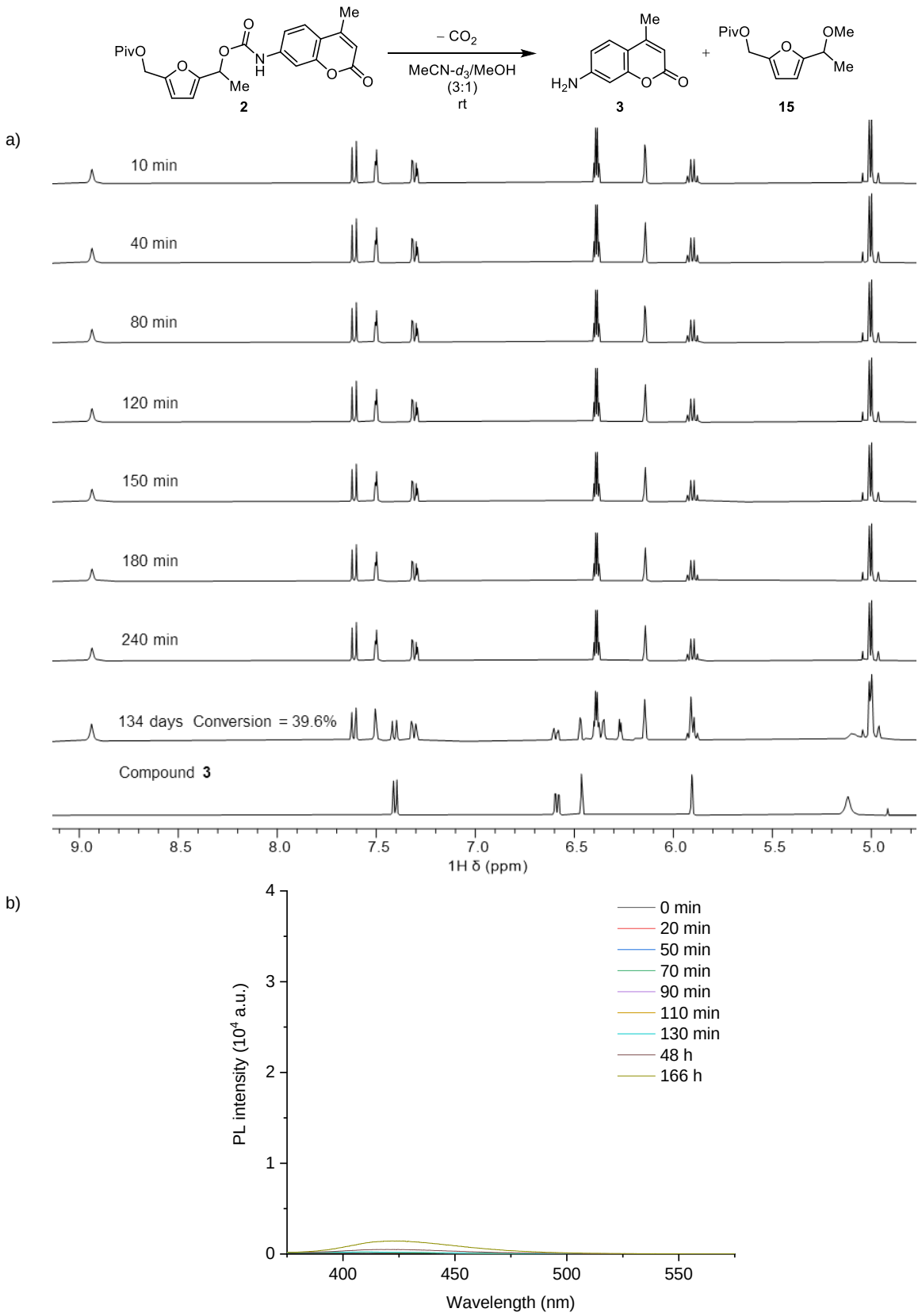
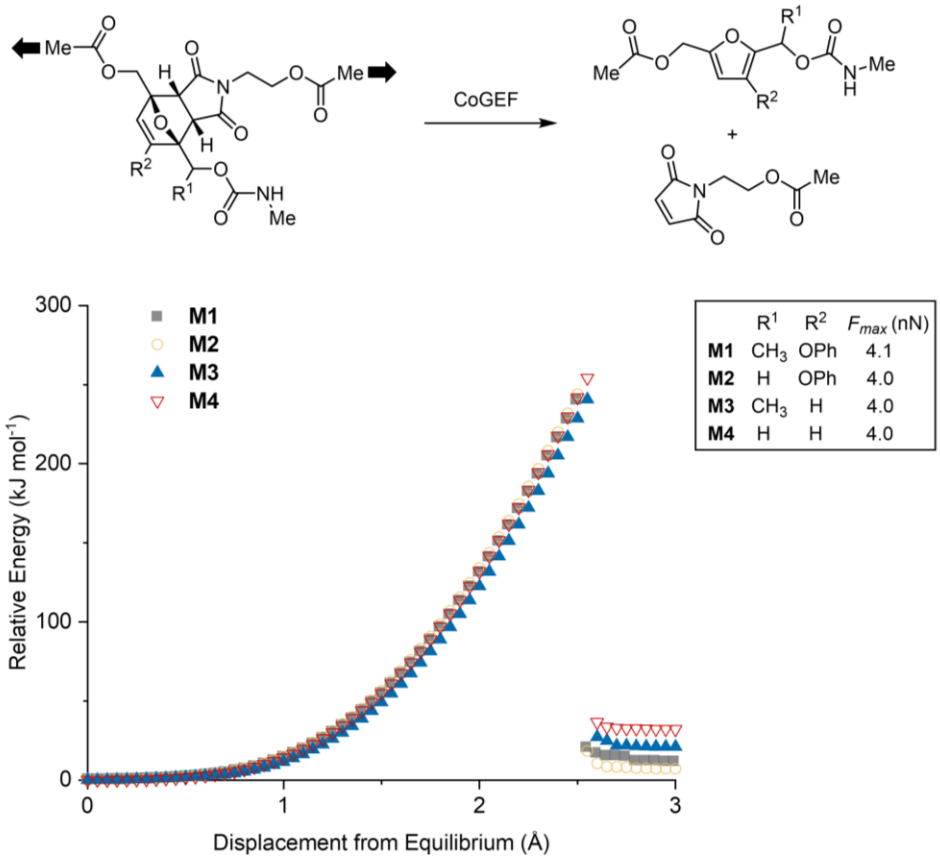


Figure S5. (a) Partial ^{1}H NMR spectra (400 MHz) of a 19.6 mM solution of compound **2** in MeCN-d_3:MeOH (3:1) at room temperature. Approximately 40% conversion is observed after 134 days. (b) Fluorescence emission spectra of a solution of compound **2** in 3:1 MeCN:MeOH (7.6 μM) at room temperature. The expected PL intensity from a 7.6 μM solution of aminocoumarin **3** is approximately 4.09 x 10^4 based on the calibration curve in Figure S9. λ_{ex} = 365 nm.



	R^1	R^2	F_{max} (nN)
M1	CH_3	OPh	4.1
M2	H	OPh	4.0
M3	CH_3	H	4.0
M4	H	H	4.0

Figure S6. Density functional theory (DFT) calculations performed on truncated furan–maleimide Diels–Alder adducts **M1–M4** using the constrained geometries simulate external force (CoGEF) method at the B3LYP/6-31G* level of theory. The energy–displacement profiles of all four adducts match closely with each other with F_{max} values calculated to be 4.0–4.1 nN. CoGEF calculations predict that all four furan–maleimide adducts generate the expected furan and maleimide products upon mechanical elongation.

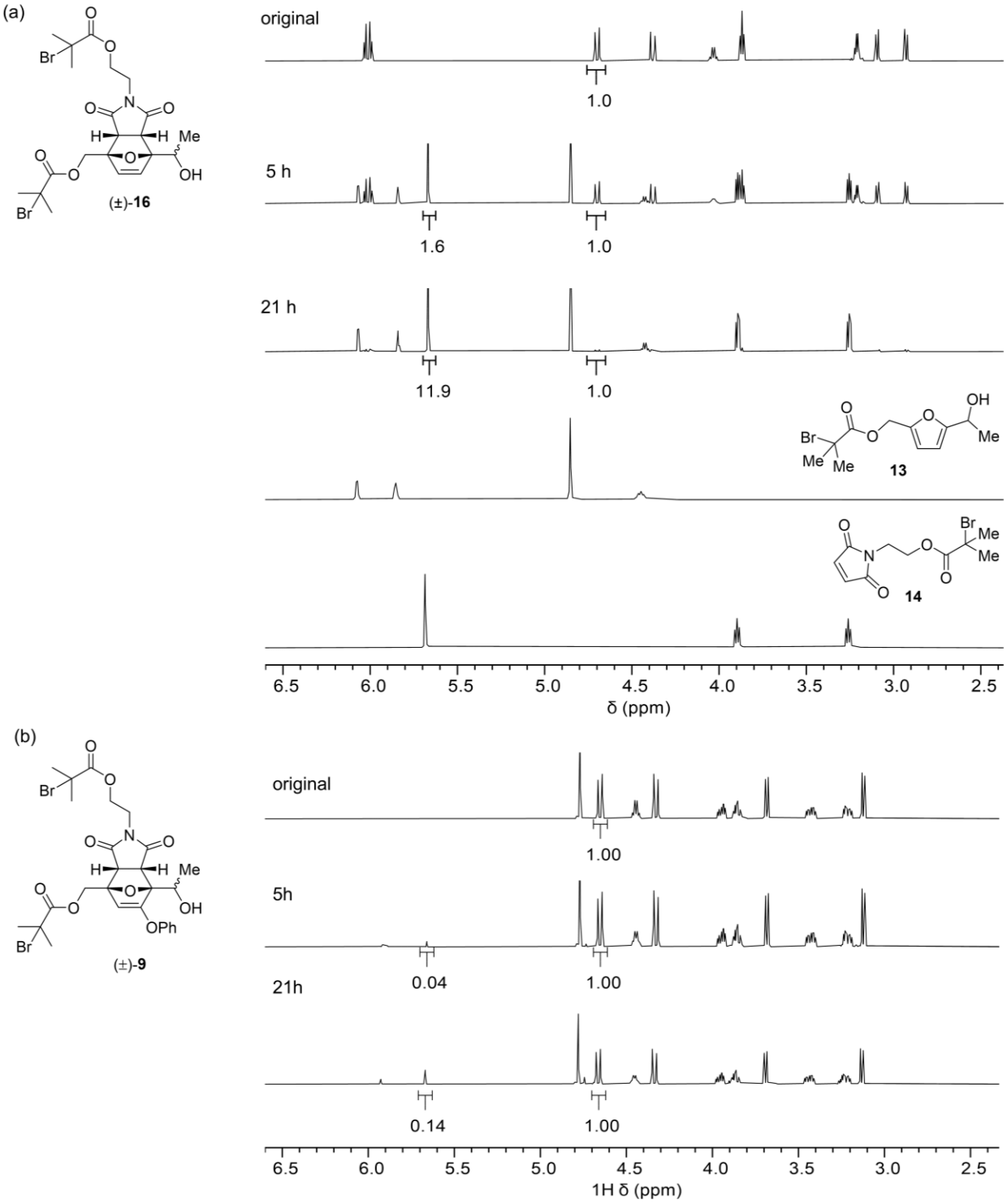


Figure S7. Partial ^{1}H NMR spectra (400 MHz) of Diels–Alder adducts (a) (±)-**16** and (b) (±)-**9** in toluene-d_8 (8.6 mM) after heating at 70 °C for the indicated amount of time. Compound (±)-**16** undergoes a retro-Diels–Alder reaction with a conversion of approximately 46% after 5 h, reaching nearly quantitative conversion after 21 h. In contrast, < 2% retro-Diels–Alder reaction is observed for compound (±)-**9** after 5 h, and < 7% after 21 h.

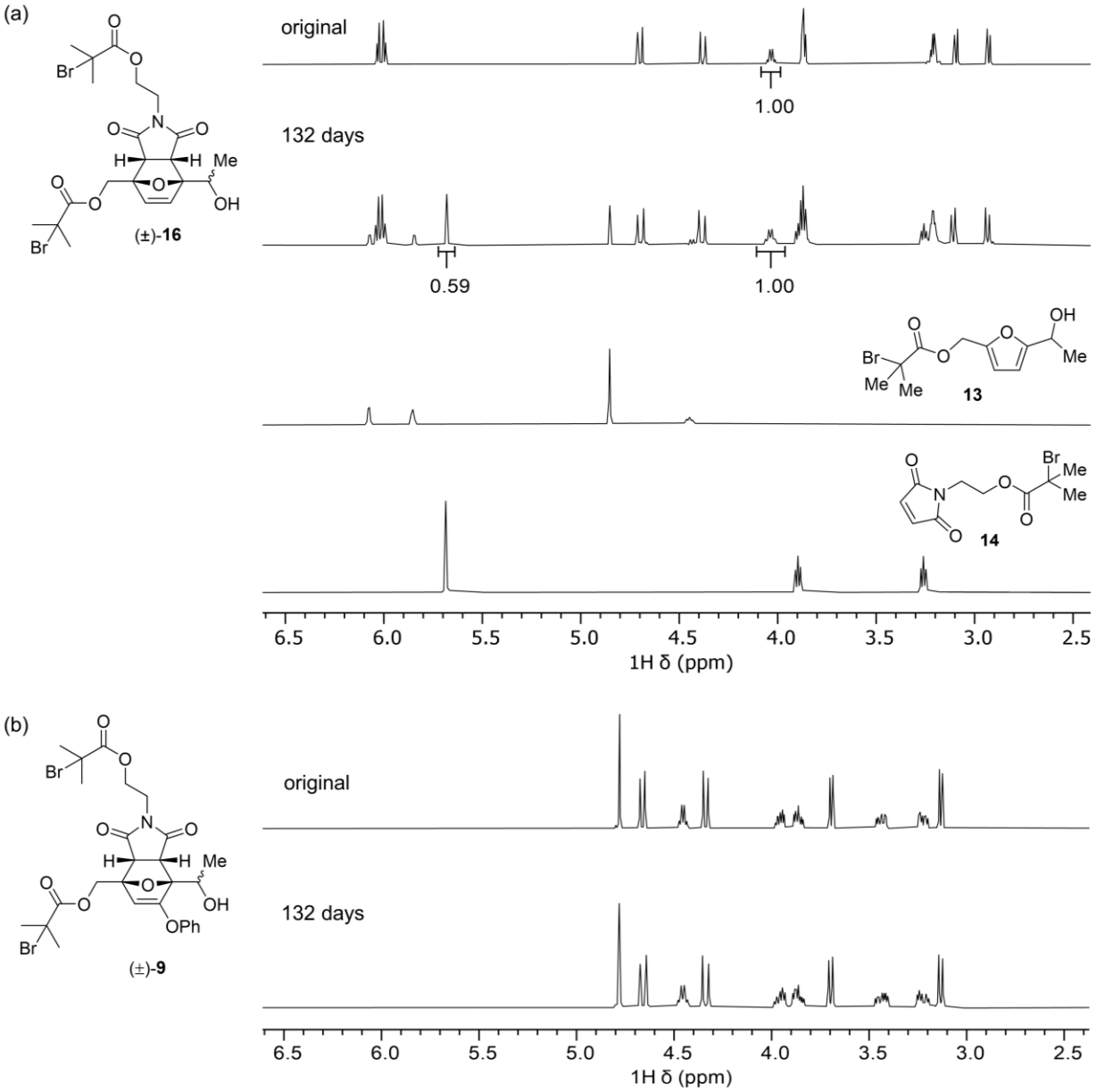


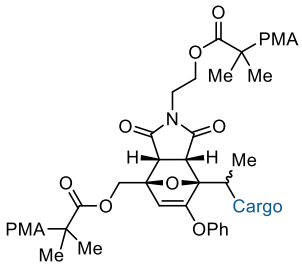
Figure S8. Partial ^{1}H NMR spectra (400 MHz) of Diels–Alder adducts (a) (±)-**16** and (b) (±)-**9** in toluene-d_8 (8.6 mM) after sitting at room temperature for the indicated amount of time. After 132 days at room temperature, approximately 23% of (±)-**16** is converted via a retro-Diels–Alder reaction, while no reaction is observed for compound (±)-**9.**

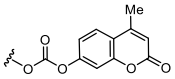
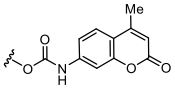
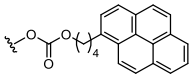
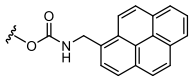
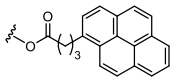
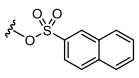
Table S1. Characterization of polymers PMA-1(O)–PMA-3(O) and PMA-1(NH)–PMA-3(NH), and release of hydroxycoumarin or aminocoumarin upon ultrasound-induced mechanochemical activation.[a]

Polymer	M_n (kg/mol)	M_p (kg/mol)	$Đ$	Half-Life	Ultimate payload release[b]
PMA-1(O)	99.8	95.4	1.04	< 5 min	34%
PMA-2(O)	102	103	1.05	< 5 min	36%
PMA-3(O)	102	95.7	1.03	46 min	38%
PMA-1(NH)	99.0	93.7	1.04	41 min	35%
PMA-2(NH)	99.6	104	1.06	6.5 days	39%
PMA-3(NH)	94.7	89.1	1.05	240 days	8%[c]

[a]Polymer solutions (2 mg/mL in 3:1 MeCN/MeOH) were sonicated for 60 min ("on" time) then warmed to room temperature. [b]Yield of payload release relative to mechanophore concentration estimated from photoluminescence measurements, reported as the average of two trials. [c]Calculated yield after 30 days post-sonication assuming a mechanophore activation of 36%.

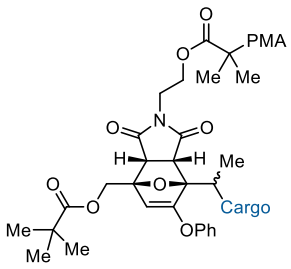
Table S2. Characterization of polymers containing functionally diverse cargo molecules and molecular release upon ultrasound-induced mechanochemical activation.[a]

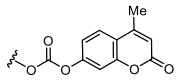
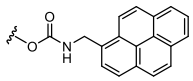
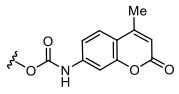
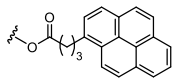
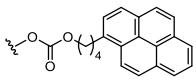
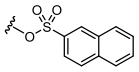


Cargo	M_n (kg/mol)	M_p (kg/mol)	$Đ$	Half-Life	Ultimate payload release[c]
	99.8	95.4	1.04	< 5 min[b]	36%
	99.0	93.7	1.04	41 min[b]	34%
	99.2	96.1	1.11	< 30 min	33%
	106	96.1	1.14	4.2 h	8%
	114	110	1.10	28 h	41%
	108	108	1.02	< 30 min	41%

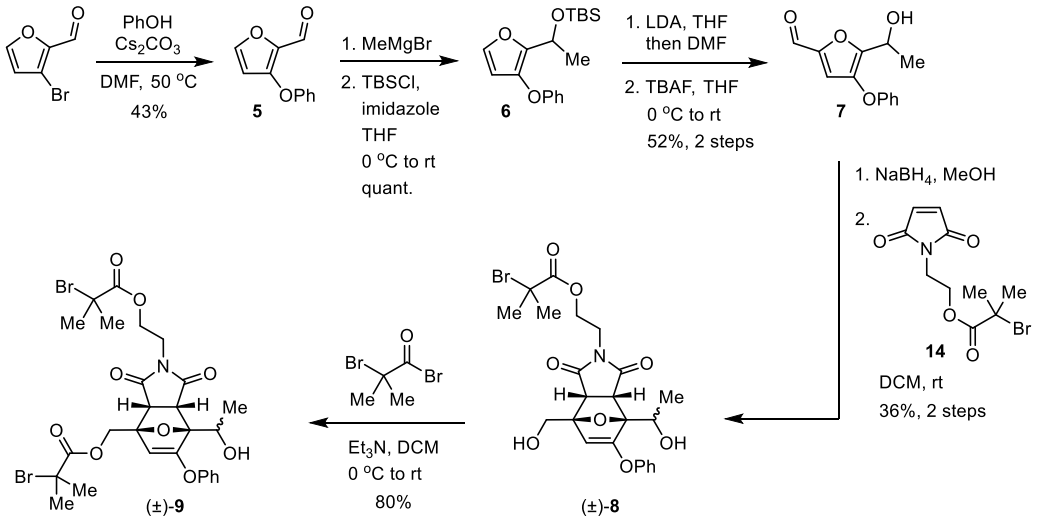
[a]Polymer solutions (2 mg/mL in 3:1 MeCN/MeOH) were sonicated for 60 min ("on" time) then warmed to room temperature and immediately monitored by photoluminescence spectroscopy or HPLC. [b]Half-lives for the release of hydroxycoumarin and aminocoumarin from photoluminescence measurements, with all others calculated using HPLC. [b]Yield of payload release relative to mechanophore concentration calculated from HPLC measurements. Half-lives and payload release are reported as the average of two trials. See Section VI for additional details.

Table S3. Characterization of chain-end functional control polymers containing functionally diverse cargo molecules.

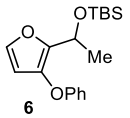


Cargo	M_n (kg/mol)	$Đ$	Cargo	M_n (kg/mol)	$Đ$
	95.6	1.16		82.7	1.19
	93.2	1.12		106	1.32
	110	1.14		87.4	1.08

III. Synthetic Details



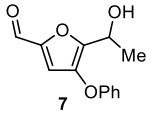
3-phenoxyfuran-2-carbaldehyde (5). A round bottom flask equipped with a stir bar was charged with phenol (16.1 g, 0.171 mol), cesium carbonate (55.7 g, 0.171 mol) and DMF (500 mL). The solution was heated to 80 °C until cesium carbonate had dissolved. The mixture was then cooled to 60 °C before adding 3-bromo-2-furfural[2] (6.30 g, 0.0360 mol), and vigorously stirred for 1 day. The reaction mixture was then cooled to room temperature before pouring into a sat. Na_2CO_3 solution (1 L), extracted with Et_2O (4 x 300 mL), and washed with copious sat. Na_2CO_3 and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (5–20% EtOAc/Hexanes) to yield the title compound as a light-yellow solid (2.90 g, 43%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 9.67 (s, 1H), 7.52 (d, J = 2.1, 1H), 7.43 – 7.37 (m, 2H), 7.25 – 7.20 (m, 1H), 7.19 – 7.13 (m, 2H), 6.22 (d, J = 2.1 Hz, 1H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 174.9, 156.1, 155.6, 147.9, 139.5, 130.3, 125.4, 119.0, 105.4 ppm. HRMS (ESI, *m/z*): calcd for $[C_{11}H_9O_3]^+$ $(M+H)^+$, 189.0546; found, 189.0568.



6

***Tert*-butyldimethyl(1-(3-phenoxyfuran-2-yl)ethoxy)silane (6).** A flame-dried round bottom flask was charged with **5** (1.50 g, 7.98 mmol) and anhydrous Et_2O (50 mL). The solution was cooled to −30 °C in an acetonitrile/dry ice bath followed by the dropwise addition of MeMgBr (3 M in Et_2O, 4.00 mL, 12.0 mmol). The solution was allowed to warm to room temperature and stirred for 1 h before being quenched with 10% NH_4Cl (50 mL) and extracted with Et_2O (2 x 50 mL). The combined organic phase was dried over Na_2SO_4, filtered, concentrated under reduced pressure to yield 1-(3-phenoxyfuran-2-yl)ethan-1-ol as a colorless oil, which was used in the next step without further purification.

A round bottom flask equipped with a stir bar was charged with 1-(3-phenoxyfuran-2-yl)ethan-1-ol (1.60 g, 7.84 mmol), imidazole (1.60 g, 23.5 mmol), and DCM (15 mL), followed by addition of tert-butylchlorodimethylsilane (2.40 g, 16.0 mmol). The reaction was allowed to stir at room temperature overnight before filtering the mixture through a cotton pad. The filtrate was concentrated under reduced pressure, and the crude product was purified by column chromatography (0–15% EtOAc/Hexanes) to yield the title compound as a light yellow oil (2.49 g, 98% over two steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.33 – 7.27 (m, 3H), 7.06 – 7.01 (m, 1H), 7.00 – 6.95 (m, 2H), 6.19 (d, *J* = 2.1 Hz, 1H), 4.93 (q, *J* = 6.6 Hz, 1H), 1.47 (d, *J* = 6.6 Hz, 3H), 0.85 (s, 9H), 0.04 (s, 3H), −0.05 (s, 3H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 158.4, 145.2, 140.7, 137.7, 129.7, 122.5, 116.2, 106.3, 61.6, 25.9, 25.8, 22.2, 18.3, -4.9, -5.0 ppm. HRMS (ESI, *m/z*): calcd for $[C_{12}H_{11}O_2]^+$ (M-OTBS)$^+$, 187.0754; found, 187.0732.

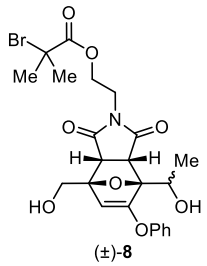


7

5-(1-hydroxyethyl)-4-phenoxyfuran-2-carbaldehyde (7). A flame-dried round bottom flask equipped with a stir bar was charged with diisopropylamine (0.80 mL, 5.7 mmol) and THF (70 mL). The solution was cooled to −78 °C in an acetone/dry ice bath before adding n-butyllithium (2.5 M in hexanes, 2.30 mL, 5.75 mmol) dropwise. After stirring the mixture for 5 min, a solution of **6** (1.06 g, 5.02 mmol) in THF (10 ml) was added to the mixture dropwise at −78 °C. The mixture was kept at −78 °C for 30 mins before adding DMF (0.52 mL, 6.7 mmol) dropwise. The mixture was then allowed to slowly warm up to room temperature for ~1 h before 10% NH_4Cl (100 mL) was added slowly to the mixture to quench the reaction. The mixture was then extracted with Et_2O (2 x 100 mL), and the organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude mixture was purified by column chromatography (0–20% EtOAc/Hexanes) to yield the crude product of 5-(1-((tert-butyldimethylsilyl)oxy)ethyl)-4-phenoxyfuran-2-carbaldehyde as a colorless oil. Approximately 10% of the crude product was identified to be the regioisomer resulting from formylation at the 4-position of the furan. The crude product was used in the next step without further purification.

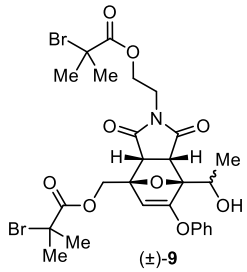
The crude product from above was dissolved in THF (25 mL) and cooled to 0 °C before adding TBAF (1 M in THF, 3.8 mL, 3.8 mmol) dropwise. The mixture was allowed to slowly warm up to room temperature and stirred for 1 h. The reaction mixture was then diluted with Et_2O (25 mL) washed with NH_4Cl (25 mL) and brine (25 mL), and the organic fraction was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (25–50% EtOAc/Hexanes) to yield compound **7** as a yellow waxy solid (602 mg, 52% over two steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.57 (s, 1H), 7.35 (dd, *J* = 8.7, 7.4 Hz, 2H),

7.19 – 7.08 (m, 1H), 7.05 – 6.96 (m, 3H), 5.04 (q, *J* = 6.7 Hz, 1H), 1.62 (d, *J* = 6.7 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 178.0, 157.4, 150.9, 149.4, 140.9, 130.1, 123.8, 116.8, 115.2, 61.9, 20.9 ppm. HRMS (ESI, *m/z*): calcd for $[C_{13}H_{13}O_4]^+$ $(M+H)^+$, 233.0808; found, 233.0808.



(±)-**8**

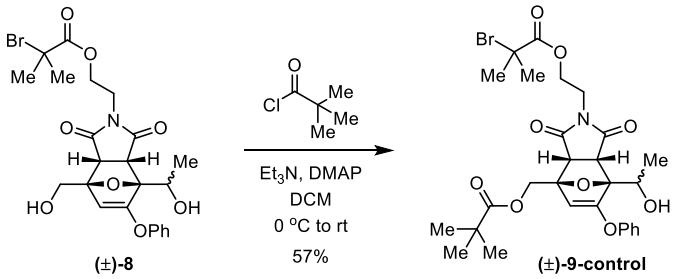
2-(-4-(1-hydroxyethyl)-7-(hydroxymethyl)-1,3-dioxo-5-phenoxy-1,3,3a,4,7,7a-hexahydro-2*H*-4,7-epoxyisoindol-2-yl)ethyl 2-bromo-2-methylpropanoate ((±)-8). A round bottom flask equipped with a stir bar was charged with **7** (350.0 mg, 1.509 mmol), THF (3 mL) and MeOH (10 mL). The solution was cooled to 0 °C in an ice bath before slowly adding $NaBH_4$ (82.0 mg, 2.17 mmol). The mixture was kept at 0 °C for 1 h before adding 10% NH_4Cl (10 mL), extracted with EtOAc (2 x 10 mL), and washed with brine (10 mL). The organic layer was dried over Na_2SO_4, and filtered. Maleimide **14**[3] (527 mg, 2.77 mmol) was then added and the solution was concentrated under reduced pressure until about 2 mL viscous solution remained. The solution was then stirred at room temperature for 4 h, and the crude mixture was purified by column chromatography (72–90% EtOAc/Hexanes). A single diastereomer of the title compound was isolated as a colorless oil (285 mg, 36% yield). ^1H NMR (400 MHz, $CDCl_3$) δ: 7.38 – 7.30 (m, 2H), 7.22-7.16 (m, 1H), 7.00 – 6.94 (m, 2H), 4.96 (s, 1H), 4.59 (s, 1H), 4.32-3.97 (m, 5H), 3.78 – 3.53 (m, 3H), 2.04 (m, 2H), 1.87 (d, *J* = 0.8 Hz, 6H), 1.54 (d, *J* = 6.6 Hz, 3H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ: 175.1, 174.1, 171.5, 163.5, 154.8, 130.2, 126.1, 119.9, 100.9, 92.3, 90.4, 65.0, 62.5, 62.4, 55.7, 50.9, 48.0, 37.5, 30.7, 30.7, 19.0 ppm. HRMS (ESI, *m/z*): calcd for $[C_{23}H_{27}BrNO_8]^+$ $(M+H)^+$, 524.0915; found, 524.0928.



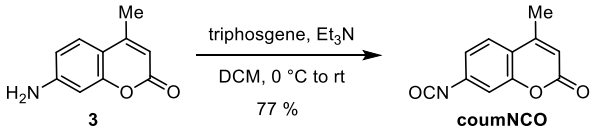
(±)-**9**

(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-7-(1-hydroxyethyl)-1,3-dioxo-6-phenoxy-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl 2-bromo-2-methylpropanoate ((±)-9). A flame-dried round bottom flask equipped with a stir bar was charged with **(±)-8** (263 mg, 0.502 mmol), Et_3N (84 µL, 0.60 mmol) and DCM (15 mL). The solution was cooled to 0 °C before adding α-bromoisobutyryl bromide (68 µL, 0.55 mmol) dropwise. The reaction was then allowed to warm to room temperature and stirred overnight until the reaction had completed, as determined by TLC. The reaction mixture was then washed with NH_4Cl (30 mL) and brine (30 mL), and the organic fraction was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (35–50% EtOAc/Hexanes) to yield the title compound as a colorless oil (270 mg, 80% yield). ^1H NMR (400 MHz, $CDCl_3$) δ: 7.39 – 7.30 (m, 2H), 7.23 – 7.15 (m, 1H), 7.01 – 6.91 (m, 2H), 4.95 (s, 1H), 4.68 (ABq, $\Delta\nu_{AB}$ = 126.4 Hz, J_{AB} = 58.0 Hz, 2H), 4.63 – 4.57 (m, 1H),

4.33-4.11 (m, 2H), 4.00 (d, *J* = 7.8 Hz, 1H), 3.79-3.52 (m, 3H), 1.96 (m, 7H), 1.86 (s, 6H), 1.52 (d, *J* = 6.6 Hz, 3H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ: 174.1, 173.7, 171.4, 171.0, 163.5, 154.6, 130.1, 126.0, 119.7, 100.8, 92.1, 88.2, 64.8, 63.5, 62.3, 55.5, 55.5, 51.1, 47.5, 37.3, 30.7, 30.6, 18.7 ppm. HRMS (ESI, *m/z*): calcd for $[C_{27}H_{32}Br_2NO_9]^+$ $(M+H)^+$, 672.0438; found, 672.0462.

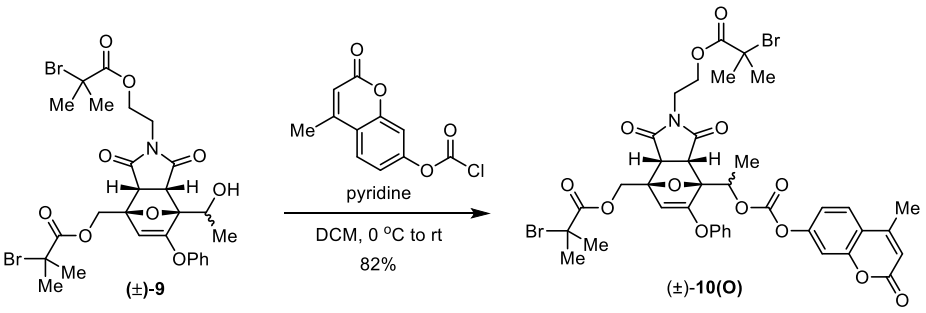


(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-7-(1-hydroxyethyl)-1,3-dioxo-6-phenoxy-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl pivalate ((±)-9-control). A flame-dried round bottom flask equipped with a stir bar was charged with (±)-**8** (137 mg, 0.261 mmol), Et_3N (52.3 µL, 0.376 mmol), DMAP (41.7 mg, 0.342 mmol) and DCM (5 mL). The solution was cooled to 0 °C before adding pivaloyl chloride (46.3 µL, 0.376 mmol) dropwise. The reaction was then allowed to warm to room temperature and stirred overnight until the reaction completed, as determined by TLC. The reaction mixture was then diluted with DCM (20 mL), washed with NH_4Cl (30 mL) and brine (30 mL), and the organic fraction was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (10–50% EtOAc/Hexanes) to yield the title compound as a white waxy solid (90 mg, 57% yield). ^1H NMR (400 MHz, $CDCl_3$) δ: 7.40 – 7.29 (m, 2H), 7.24 – 7.15 (m, 1H), 6.99 – 6.90 (m, 2H), 4.90 (s, 1H), 4.57 (ABq, $\Delta\nu_{AB}$ = 113.0 Hz, J_{AB} = 12.7 Hz, 2H), 4.55 (dt, *J* = 7.6, 6.4 Hz, 1H), 4.33-4.12 (m, 2H), 3.99 (d, *J* = 7.8 Hz, 1H), 3.79 – 3.51 (m, 3H), 1.96 (d, *J* = 7.9 Hz, 1H), 1.87 (d, *J* = 1.3 Hz, 6H), 1.52 (d, *J* = 6.6 Hz, 3H), 1.22 (s, 9H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ: 177.9, 174.3, 173.9, 171.5, 163.5, 154.8, 130.2, 126.1, 119.8, 101.1, 92.1, 88.6, 64.9, 62.5, 62.3, 55.7, 51.2, 47.7, 39.1, 37.5, 30.7, 27.3, 18.8 ppm. HRMS (ESI, *m/z*): calcd for $[C_{28}H_{35}BrNO_9]^+$ $(M+H)^+$, 608.1490; found, 608.1479.

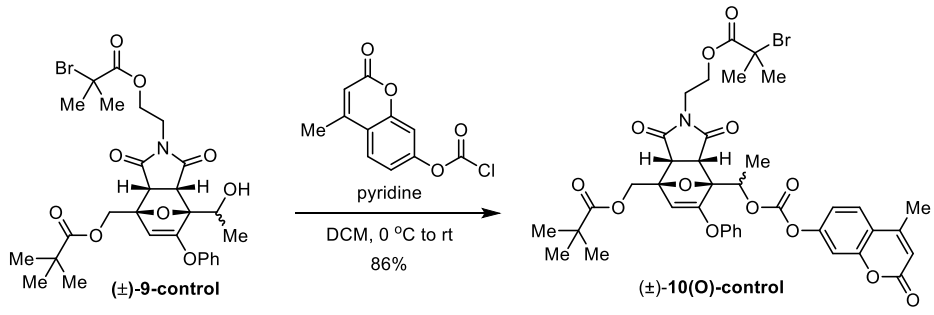


7-isocyanato-4-methyl-2H-chromen-2-one (coumNCO). A flame-dried round bottom flask equipped with a stir bar under nitrogen was charged with triphosgene (0.59 g, 2.0 mmol) and anhydrous DCM (30 mL). **CAUTION: TRIPHOSGENE IS TOXIC. ALL OPERATIONS ARE CARRIED OUT EXCLUSIVELY INSIDE A FUME HOOD.** The solution was cooled to 0 °C in an ice bath, followed by the addition of **3** (0.97 g, 5.5 mmol). Triethylamine (1.5 mL, 11 mmol) was added dropwise into the reaction. The reaction was allowed to warm to room temperature and stirred for 18 h. Hexane (30 mL) and DCM (60 mL) were added into the reaction mixture and the suspension was filtered to remove the pale yellow precipitate. The filtrate was washed with HCl (50 mL, 1 M), dried over $MgSO_4$, and filtered. The solid was discarded and the filtrate was concentrated under reduced pressure. The solid was dispersed in hexane (10 mL) and DCM (20 mL), filtered, and the filtrate was concentrated. The solid was dissolved in DCM (5 mL), and the solution was precipitated into hexane (30 mL). The fluffy white solid was collected by filtration and dried under reduced pressure to provide the title compound (0.85 g, 77%). ^1H NMR

(400 MHz, $CDCl_3$) δ: 7.54 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.09 – 6.99 (m, 2H), 6.26 (q, *J* = 1.3 Hz, 1H), 2.42 (d, *J* = 1.3 Hz, 3H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ: 160.4, 154.4, 151.8, 136.9, 125.8, 125.7, 121.3, 118.0, 114.8, 113.1, 18.8 ppm. HRMS (ESI, *m/z*): calcd for $[C_{11}H_8NO_3]^+$ $(M+H)^+$, 202.0499; found, 202.0495.

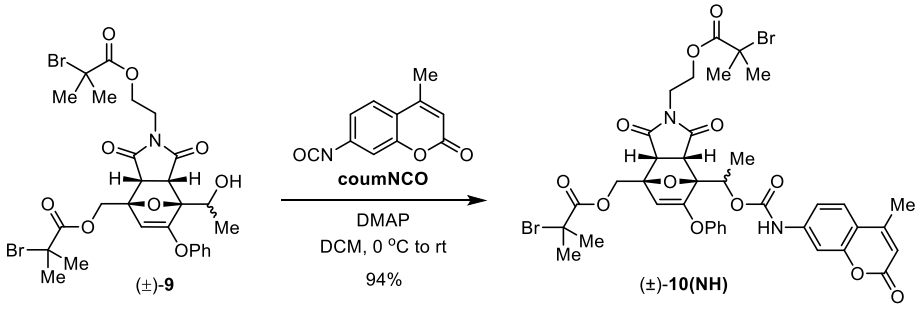


(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-7-(1-((((4-methyl-2-oxo-2H-chromen-7-yl)oxy)carbonyl)oxy)ethyl)-1,3-dioxo-6-phenoxy-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl 2-bromo-2-methylpropanoate ((±)-10(O)). A two-neck round bottom flask equipped with a stir bar was charged with (±)-**9** (20.4 mg, 0.0303 mmol)**,** dry pyridine (3.2 µL, 0.040 mmol), and DCM (0.5 mL). The solution was cooled to 0 °C in an ice bath followed by the dropwise addition of a solution of coumarin chloroformate[4] (9.4 mg, 0.039 mmol) in 0.5 mL DCM. The reaction was allowed to warm slowly to room temperature and stirred for 20 h. The reaction mixture was washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (35–55% EtOAc/Hexanes) to afford the title compound as a white foamy solid (21.7 mg, 82%). ^1H NMR (400 MHz, $CDCl_3$) δ: 7.63 (d, *J* = 8.7 Hz, 1H), 7.39 – 7.32 (m, 2H), 7.28 (d, *J* = 2.3 Hz, 1H), 7.26 – 7.17 (m, 2H), 6.29 (q, *J* = 1.3 Hz, 1H), 5.66 (q, *J* = 6.5 Hz, 1H), 5.04 (s, 1H), 4.71 (ABq, $\Delta\nu_{AB}$ = 107.6 Hz, J_{AB} = 12.6 Hz, 2H), 4.34 – 4.12 (m, 2H), 3.89 (d, *J* = 7.9 Hz, 1H), 3.77 – 3.53 (m, 3H), 2.45 (d, *J* = 1.3 Hz, 3H), 1.96 (d, *J* = 2.2 Hz, 6H), 1.86 (d, *J* = 1.4 Hz, 6H), 1.72 (d, *J* = 6.6 Hz, 3H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ: 173.7, 173.0, 171.5, 171.1, 162.5, 160.5, 154.6, 154.3, 153.3, 152.1, 151.9, 130.3, 126.3, 125.7, 119.7, 118.2, 117.5, 114.9, 110.0, 101.2, 90.3, 88.5, 72.5, 63.6, 62.4, 60.5, 55.7, 55.6, 51.4, 48.1, 37.6, 30.8, 30.7, 30.7, 21.2, 18.9, 15.8, 14.3 ppm. HRMS (ESI, *m/z*): calcd for $[C_{38}H_{37}Br_2NO_{13}]^+$ $(M)^+$, 873.0626; found, 873.0610.

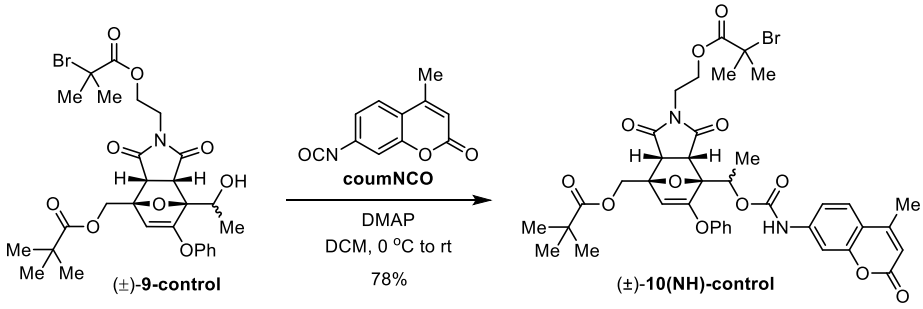


(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-7-(1-((((4-methyl-2-oxo-2H-chromen-7-yl)oxy)carbonyl)oxy)ethyl)-1,3-dioxo-6-phenoxy-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl pivalate ((±)-10(O)-control). The title compound was prepared following a similar procedure as that for compound (±)-**10(O)**, with compound (±)-**9-control** (35.0 mg, 0.0576 mmol)**,** coumarin chloroformate[4] (54.8 mg, 0.230 mmol), dry pyridine (18.6 µL, 0.230 mmol), and DCM (0.5 mL). The crude product was purified by column chromatography (35–55% EtOAc/Hexanes) to afford the title compound as a white foamy solid (43.4 mg, 86%). ^1H NMR (400 MHz, $CDCl_3$) δ: 7.63 (d, *J* = 8.7 Hz, 1H), 7.41 – 7.31 (m, 2H), 7.29 – 7.27 (m, 1H), 7.25 –

7.18 (m, 2H), 7.01 – 6.92 (m, 2H), 6.29 (d, *J* = 1.3 Hz, 1H), 5.65 (q, *J* = 6.5 Hz, 1H), 4.99 (s, 1H), 4.60 (ABq, $\Delta\nu_{AB}$ = 119.4 Hz, J_{AB} = 12.0 Hz, 2H), 4.34 – 4.24 (m, 1H), 4.23 – 4.11 (m, 1H), 3.89 (d, *J* = 7.8 Hz, 1H), 3.71 (ddd, *J* = 14.2, 6.7, 4.0 Hz, 1H), 3.66 – 3.57 (m, 2H), 2.45 (d, *J* = 1.3 Hz, 3H), 1.87 (s, 6H), 1.71 (d, *J* = 6.6 Hz, 3H), 1.23 (s, 9H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ: 177.9, 173.8, 173.1, 171.6, 162.5, 160.5, 154.7, 154.3, 153.3, 152.2, 151.9, 130.3, 126.3, 125.7, 119.7, 118.2, 117.5, 114.9, 110.0, 101.4, 90.2, 88.8, 72.5, 62.4, 62.3, 55.7, 51.4, 48.1, 39.1, 37.6, 30.7, 30.7, 27.3, 18.9, 15.7 ppm. HRMS (FAB, *m/z*): calcd for $[C_{39}H_{41}BrNO_{13}]^+$ $(M+H)^+$, 810.1756; found, 810.1764.

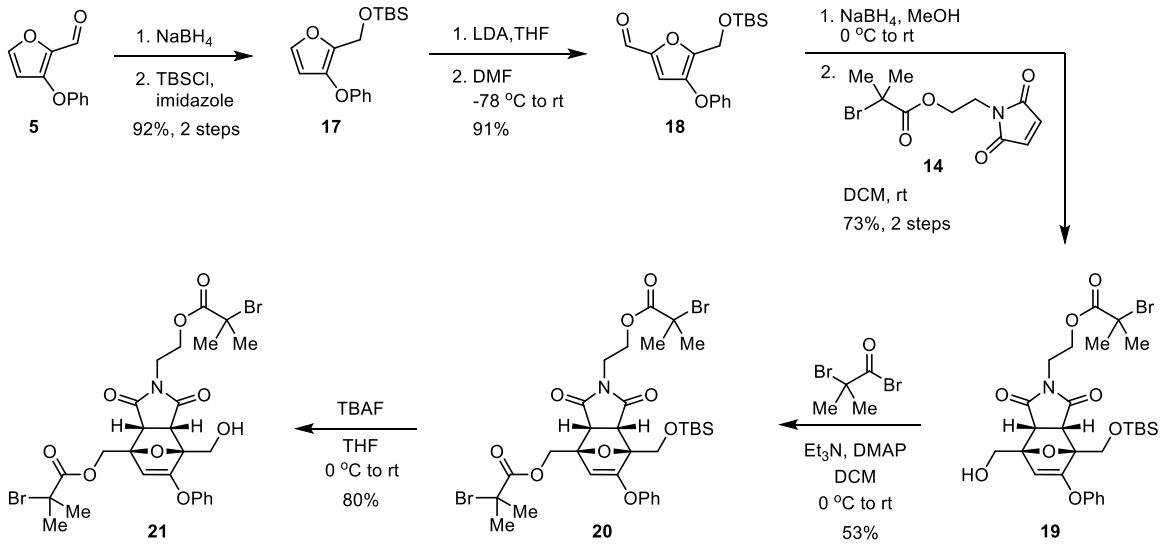


(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-7-(1-(((4-methyl-2-oxo-2H-chromen-7-yl)carbamoyl)oxy)ethyl)-1,3-dioxo-6-phenoxy-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl 2-bromo-2-methylpropanoate ((±)-10(NH)). A two-neck round bottom flask equipped with a stir bar was charged with (±)-**9** (31.5 mg, 0.0468 mmol), **coumNCO** (36.0 mg, 0.179 mmol) and DCM (3 mL). The mixture was cooled to 0 °C in ice bath before adding DMAP (21.9 mg, 0.179 mmol). The reaction was allowed to warm to room temperature and its progress was monitored by ^1H NMR spectroscopy until completion (~2 h). The mixture was then washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude produce was purified by column chromatography (35–55% EtOAc/Hexanes) to provide the title compound as a white foamy solid (38.5 mg, 94%). ^1H NMR (400 MHz, $CDCl_3$) δ: 7.57-7.50 (m, 1H), 7.48-7.41 (m, 2H), 7.39 – 7.30 (m, 2H), 7.25 – 7.17 (m, 2H), 7.01 – 6.92 (m, 2H), 6.20 (q, *J* = 1.2 Hz, 1H), 5.77 (q, *J* = 6.5 Hz, 1H), 5.02 (s, 1H), 4.70 (ABq, $\Delta\nu_{AB}$ = 99.8 Hz, J_{AB} = 12.6 Hz, 2H), 4.33-4.10 (m, 2H), 3.82 (d, *J* = 7.9 Hz, 1H), 3.76 – 3.53 (m, 3H), 2.41 (d, *J* = 1.3 Hz, 3H), 1.96 (s, 6H), 1.85 (s, 6H), 1.60 (d, *J* = 6.6 Hz, 3H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ: 173.8, 173.0, 171.6, 171.1, 162.9, 161.1, 154.7, 154.6, 152.3, 151.9, 141.3, 130.3, 126.2, 125.6, 119.6, 115.8, 114.5, 113.5, 106.1, 100.8, 90.5, 88.5, 63.6, 62.4, 55.7, 55.6, 51.3, 48.1, 37.6, 30.8, 30.7, 30.7, 18.7, 16.1 ppm. HRMS (ESI, *m/z*): calcd for $[C_{38}H_{38}Br_2N_2O_{12}]^+$ $(M)^+$, 872.0786; found, 872.0792.



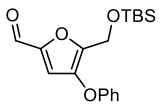
(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-7-(1-(((4-methyl-2-oxo-2H-chromen-7-yl)carbamoyl)oxy)ethyl)-1,3-dioxo-6-phenoxy-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl pivalate ((±)-10(NH)-control). The title compound was prepared following a similar procedure as that for

compound (±)-**10(NH)**, with compound (±)-**9-control** (24.4 mg, 0.0401 mmol)**, coumNCO** (16.0 mg, 0.0796 mmol), DMAP (9.8 mg, 0.080 mmol), and DCM (0.5 mL). The crude product was purified by column chromatography (35–55% EtOAc/Hexanes) to afford the title compound as a white foamy solid (25.1 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50 – 7.37 (m, 4H), 7.31 – 7.22 (m, 2H), 7.17 – 7.08 (m, 1H), 6.93 – 6.84 (m, 2H), 6.12 (s, 1H), 5.70 (q, *J* = 6.5 Hz, 1H), 4.91 (s, 1H), 4.52 (ABq, $\Delta\nu_{AB}$ = 102.8 Hz, J_{AB} = 16.0 Hz, 2H), 4.25 – 4.15 (m, 1H), 4.14 – 4.02 (m, 1H), 3.77 (d, *J* = 7.8 Hz, 1H), 3.68 – 3.44 (m, 3H), 2.34 (d, *J* = 1.3 Hz, 3H), 1.78 (d, *J* = 1.3 Hz, 7H), 1.53 (d, *J* = 6.5 Hz, 3H), 1.15 (d, *J* = 1.5 Hz, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 177.9, 173.8, 173.1, 171.5, 162.8, 161.2, 154.7, 154.5, 152.4, 152.0, 141.5, 130.2, 130.1, 126.1, 125.5, 119.6, 115.7, 114.6, 113.3, 106.4, 101.0, 90.4, 88.8, 68.1, 62.4, 62.4, 55.8, 51.3, 48.1, 39.0, 37.6, 30.7, 30.7, 27.3, 18.7, 16.1.ppm. HRMS (ESI, *m/z*): calcd for $[C_{39}H_{42}BrN_2O_{12}]^+$ $(M+H)^+$, 809.1916; found, 809.1948.



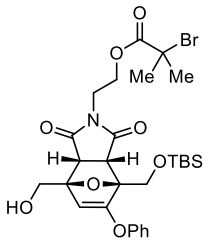
***Tert*-butyldimethyl((3-phenoxyfuran-2-yl)methoxy)silane (17).** A round bottom flask equipped with a stir bar was charged with MeOH (10 mL) and cooled to 0 °C in an ice bath before adding $NaBH_4$ (111 mg, 2.92 mmol), followed by the slow addition of **5** (303 mg, 1.61 mmol). The mixture was kept at 0 °C for 1 h before adding 10% NH_4Cl (50 mL), and extracted with EtOAc (2 x 50 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to yield (3-phenoxyfuran-2-yl)methanol as a light yellow oil (300 mg, 98%) which was used in the next step without further purification.

A round bottom flask equipped with a stir bar was charged with (3-phenoxyfuran-2-yl)methanol (300 mg, 1.58 mmol), imidazole (191 mg, 2.81 mmol), and DCM (10 mL), followed by addition of *tert*-butylchlorodimethylsilane (265 mg, 1.76 mmol). The reaction was allowed to stir at room temperature overnight before filtering the mixture through a cotton pad. The filtrate was concentrated under reduced pressure, and the crude product was purified by column chromatography (0–20% EtOAc/Hexanes) to yield the title compound as a light-yellow oil (447 mg, 92% over two steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34 – 7.26 (m, 3H), 7.08 – 6.97 (m, 3H), 6.22 (d, *J* = 2.1 Hz, 1H), 4.61 (s, 2H), 0.87 (s, 9H), 0.04 (s, 6H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 158.3, 142.4, 141.4, 139.8, 129.7, 122.6, 116.4, 106.3, 54.7, 26.0, 18.6, −5.2 ppm. HRMS (EI, *m/z*): calcd for $[C_{17}H_{23}O_3Si]^+$ $(M-H)^+$, 303.1411; found, 303.1407.



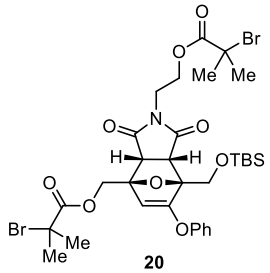
18

5-(((tert-butyldimethylsilyl)oxy)methyl)-4-phenoxyfuran-2-carbaldehyde (18). A flame-dried round bottom flask equipped with a stir bar was charged with diisopropylamine (0.30 mL, 2.1 mmol) and THF (10 mL). The solution was cooled to −78 °C in an acetone/dry ice bath before adding n-butyllithium (0.70 mL, 1.8 mmol, 2.5 M in hexanes) dropwise. After stirring the mixture for 5 mins, a solution of **17** (354 mg, 1.16 mmol) in THF (10 ml) was added dropwise at −78 °C. The mixture was kept at −78 °C for 30 mins before adding DMF (1.0 mL, 13 mmol) dropwise. The mixture was then allowed to slowly warm up to room temperature over an hour before 10% NH_4Cl (50 mL) was added slowly to quench the reaction. The mixture was extracted with Et_2O (2 x 50 mL), and the organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (0–10% EtOAc/Hexanes) to yield the title compound as a light-yellow oil (351 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.59 (s, 1H), 7.39 – 7.29 (m, 2H), 7.15 – 7.06 (m, 1H), 7.05 – 6.97 (m, 3H), 4.70 (s, 2H), 0.88 (s, 9H), 0.07 (s, 6H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 178.2, 157.3, 149.8, 148.3, 142.0, 129.8, 123.5, 116.7, 114.2, 54.9, 25.8, 18.4, -5.4 ppm. HRMS (ESI, *m/z*): calcd for $[C_{18}H_{25}O_4Si]^+$ $(M+H)^+$, 333.1517; found, 333.1543.



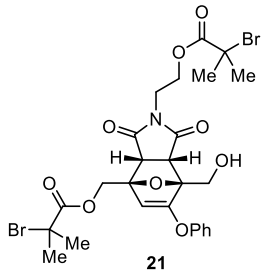
19

2-(4-(((tert-butyldimethylsilyl)oxy)methyl)-7-(hydroxymethyl)-1,3-dioxo-5-phenoxy-1,3,3a,4,7,7a-hexahydro-2H-4,7-epoxyisoindol-2-yl)ethyl 2-bromo-2-methylpropanoate (19). A round bottom flask equipped with a stir bar was charged with **18** (350 mg, 1.05 mmol), THF (4 mL), and MeOH (1 mL). The solution was cooled to 0 °C in an ice bath before slowly adding $NaBH_4$ (52.0 mg, 1.38 mmol). The mixture was kept at 0 °C for 1 h before adding 10% NH_4Cl (10 mL) and extracting with DCM (2 x 10 mL). The organic layer was dried over Na_2SO_4 and filtered. Maleimide **14**[2] was added to the solution, and then the mixture was concentrated under reduced pressure until about 2 mL viscous solution remaining. The mixture was then stirred at room temperature for 2 h to allow the Diels–Alder reaction to run to completion, and the crude mixture was purified by column chromatography (10–30% EtOAc/Hexanes). A single *endo* isomer of the title compound was isolated as a colorless oil (478 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37 – 7.28 (m, 2H), 7.23 – 7.14 (m, 1H), 7.00 – 6.93 (m, 2H), 4.95 (s, 1H), 4.35 (ABq, $\Delta\nu_{AB}$ = 5.3 Hz, J_{AB} = 12.5 Hz, 2H), 4.30 – 3.98 (m, 4H), 3.86 (d, *J* = 7.8 Hz, 1H), 3.74 (m, 1H), 3.65 – 3.49 (m, 2H), 2.02 (t, *J* = 6.5 Hz, 1H), 1.87 (d, *J* = 2.4 Hz, 6H), 0.94 (s, 9H), 0.16 (d, *J* = 7.2 Hz, 6H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 175.2, 174.0, 171.5, 163.3, 154.9, 130.1, 125.9, 119.9, 100.6, 90.6, 90.5, 62.6, 62.5, 59.7, 55.7, 50.8, 47.4, 37.4, 30.7, 30.7, 26.1, 18.7, -5.1, -5.2 ppm. HRMS (ESI, *m/z*): calcd for $[C_{28}H_{39}NO_8Si]^+$ $(M+H)^+$, 624.1623; found, 624.1642.



20

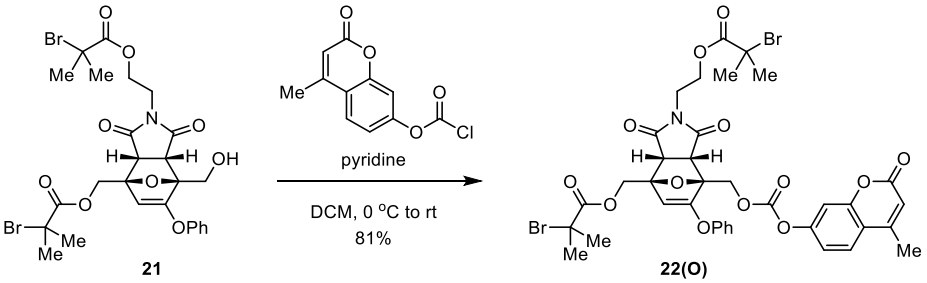
(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-7-(((tert-butyldimethylsilyl)oxy)methyl)-1,3-dioxo-6-phenoxy-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl 2-bromo-2-methylpropanoate (20). A flame-dried round bottom flask equipped with a stir bar was charged with **19** (237 mg, 0.380 mmol), Et_3N (132 µL, 0.950 mmol) and DCM (10 mL). The solution was cooled to 0 °C before adding α-bromoisobutyryl bromide (0.11 mL mg, 0.89 mmol) dropwise. The reaction was then allowed to slowly warm to room temperature and stirred overnight until the reaction had completed, as determined by TLC. The reaction mixture was then diluted with DCM (10 mL), washed with NH_4Cl (25 mL) and brine (20 mL), and the organic fraction was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (10–30% EtOAc/hexanes) to yield the title compound as a viscus colorless oil (155 mg, 53% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.36 – 7.29 (m, 2H), 7.21 – 7.15 (m, 1H), 6.99 – 6.92 (m, 2H), 4.92 (s, 1H), 4.67 (ABq, $\Delta\nu_{AB}$ = 124.7Hz, J_{AB} = 12.5 Hz, 2H), 4.34 (ABq, $\Delta\nu_{AB}$ = 11.9 Hz, J_{AB} = 12.4 Hz, 2H), 4.30-4.10 (m, , 2H), 3.85 (d, *J* = 7.8 Hz, 1H), 3.78-3.68 (m, 1H), 3.63 (d, *J* = 7.8 Hz, 1H), 3.60-3.52 (m, 1H), 1.95 (d, *J* = 4.0 Hz, 6H), 1.87 (d, *J* = 1.9 Hz, 6H), 0.93 (s, 9H), 0.14 (d, *J* = 9.4 Hz, 6H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 174.4, 173.8, 171.5, 171.2, 163.5, 154.9, 130.1, 126.0, 119.8, 100.4, 90.5, 88.3, 63.8, 62.6, 59.6, 55.7, 55.6, 50.9, 47.1, 37.4, 30.9, 30.8, 30.7, 30.7, 26.0, 18.6, -5.1, -5.2 ppm. HRMS (ESI, *m/z*): calcd for $[C_{32}H_{44}Br_2NO_9Si]^+$ $(M+H)^+$, 772.1147; found, 772.1168.



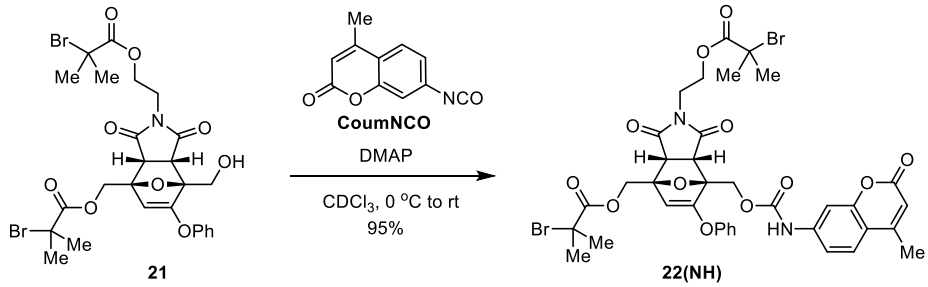
21

(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-7-(hydroxymethyl)-1,3-dioxo-6-phenoxy-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl 2-bromo-2-methylpropanoate (21). A flame-dried round bottom flask equipped with a stir bar was charged with **20** (155 mg, 0.200 mmol) and THF (3 mL). The solution was cooled to 0 °C before adding TBAF (1 M in THF, 0.26 mL, 0.26 mmol) dropwise. The mixture was allowed to slowly warm up room temperature and stirred for 1 h. The reaction mixture was washed with NH_4Cl (10 mL), extracted with EtOAc (10 mL), washed with brine (10 mL), and the organic fraction was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (40–65% EtOAc/hexanes) to yield the title compound as a white foamy solid (105 mg, 80% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.38 – 7.30 (m, 2H), 7.23 – 7.14 (m, 1H), 7.01 – 6.94 (m, 2H), 4.97 (s, 1H), 4.69 (ABq, $\Delta\nu_{AB}$ = 113.7 Hz, J_{AB} = 12.6 Hz, 2H), 4.44 (d, *J* = 13.1 Hz, 1H), 4.35 – 4.22 (m, 2H), 4.2-4.12 (m, 1H), 3.81 – 3.63 (m, 3H), 3.57 (m, 1H), 1.96 (d, *J* = 4.2 Hz, 6H), 1.86 (s, 6H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 174.0, 173.4, 171.4, 171.1,

163.1, 154.7, 130.0, 126.0, 119.7, 100.6, 90.0, 88.6, 63.4, 62.3, 59.6, 55.5, 55.5, 50.7, 47.8, 37.4, 30.7, 30.6 ppm. HRMS (ESI, *m/z*): calcd for $[C_{26}H_{30}Br_2NO_9]^+$ $(M+H)^+$, 658.0281; found, 658.0287.

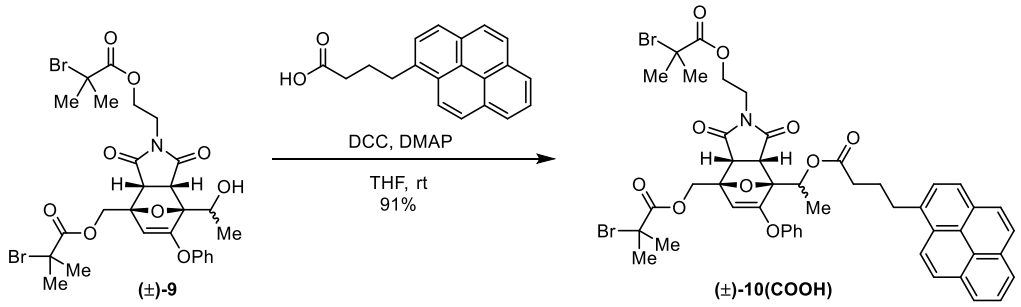


(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-7-(((((4-methyl-2-oxo-2H-chromen-7-yl)oxy)carbonyl)oxy)methyl)-1,3-dioxo-6-phenoxy-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl 2-bromo-2-methylpropanoate (22(O)). The title compound was prepared following the same procedure as that for compound (±)-**10(O)**, with compound **21** (20 mg, 0.030 mmol), dry pyridine (3.2 µL, 0.040 mmol), coumarin chloroformate[4] (9.4 mg, 0.039 mmol) and DCM (5 mL). The crude product was purified by column chromatography (20–50% EtOAc/hexanes) to provide the title compound as a white foamy solid (21 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62 (d, *J* = 8.7 Hz, 1H), 7.36 (dd, *J* = 8.4, 7.4 Hz, 2H), 7.25 – 7.16 (m, 3H), 7.04 – 6.95 (m, 2H), 6.3-6.26 (m, 1H), 5.04 (s, 1H), 5.01 (ABq, $\Delta\nu_{AB}$ = 75.3 Hz, J_{AB} = 12.6 Hz, 2H), 4.71 (ABq, $\Delta\nu_{AB}$ = 110.7 Hz, J_{AB} = 12.7 Hz, 2H), 4.35-4.25 (m, 1H), 4.23-4.11 (m, 1H), 3.86 – 3.68 (m, 3H), 3.66-3.55 (m, 1H), 2.43 (d, *J* = 1.2 Hz, 3H), 1.96 (d, *J* = 3.8 Hz, 6H), 1.87 (d, *J* = 1.2 Hz, 6H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 173.7, 172.9, 171.5, 171.2, 162.2, 160.5, 154.7, 154.3, 153.2, 152.5, 151.9, 130.3, 126.3, 125.7, 119.7, 118.3, 117.5, 114.9, 110.1, 100.8, 89.1, 87.2, 64.5, 63.4, 62.4, 55.7, 55.5, 50.7, 48.5, 37.6, 30.8, 30.7, 18.9 ppm. HRMS (ESI, *m/z*): calcd for $[C_{37}H_{36}Br_2NO_{13}]^+$ $(M+H)^+$, 860.0548; found, 860.0553.

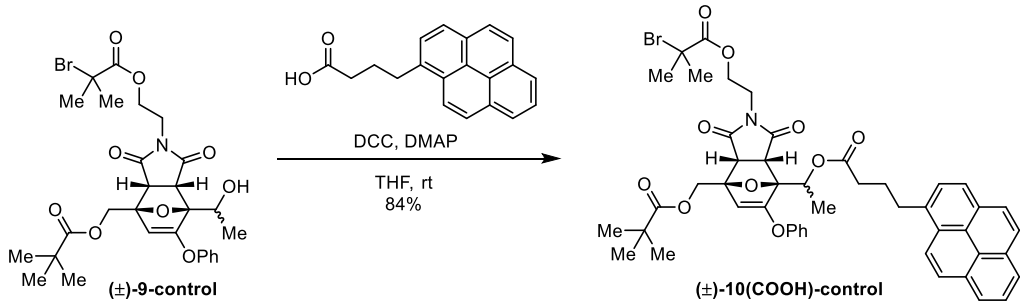


(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-7-((((4-methyl-2-oxo-2H-chromen-7-yl)carbamoyl)oxy)methyl)-1,3-dioxo-6-phenoxy-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl 2-bromo-2-methylpropanoate (22(NH)). The title compound was prepared following the same procedure as that for compound (±)-**10(NH)**, with compound **21** (40 mg, 0.061 mmol), DMAP (1.0 mg, 0.0082 mmol), **coumNCO** (18 mg, 0.089 mmol) and $CDCl_3$ (3 mL). The crude produce was purified by column chromatography (20–40% Et_2O in 1:1 Hexanes/DCM) to provide the title compound as a white foamy solid (50 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.53 (d, *J* = 8.6 Hz, 1H), 7.50 – 7.38 (m, 2H), 7.38 – 7.30 (m, 2H), 7.23 – 7.17 (m, 1H), 7.14 (s, 1H), 7.03-6.95 (m, 2H), 6.22-6.16 (m, 1H), 5.03 (s, 1H), 4.95 (ABq, $\Delta\nu_{AB}$ = 59.3 Hz, J_{AB} = 12.7 Hz, 2H), 4.70 (ABq, $\Delta\nu_{AB}$ = 108.0 Hz, J_{AB} = 12.7 Hz, 2H), 4.34-4.11 (m, 2H), 3.80 – 3.67 (m, 3H), 3.64-3.54 (m, 1H), 2.41 (d, *J* = 1.3 Hz, 3H), 1.95 (d, *J* = 3.6 Hz, 6H), 1.86 (d, *J* = 0.8 Hz, 6H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 173.8, 172.9, 171.6, 171.2, 162.5, 161.1, 154.7, 154.6, 152.3, 152.2, 141.1, 130.2, 126.2, 125.6, 119.6, 115.9, 114.6, 113.5,

106.3, 100.7, 88.9, 87.7, 63.5, 62.4, 61.5, 55.7, 55.6, 50.7, 48.9, 37.6, 30.8, 30.7, 18.7 ppm. HRMS (ESI, *m/z*): calcd for $[C_{37}H_{37}Br_2N_2O_{12}]^+$ $(M+H)^+$, 859.0708; found, 859.0704.

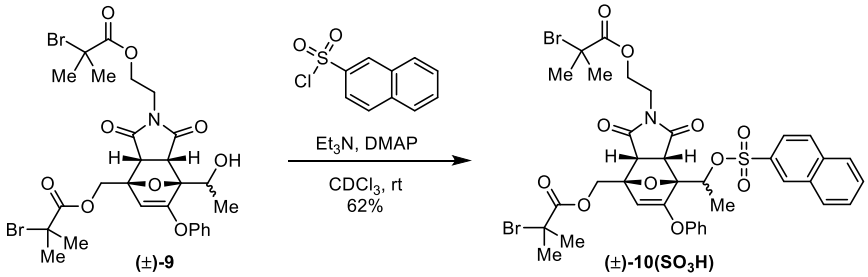


1-(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-7-(((2-bromo-2-methylpropanoyl)oxy)methyl)-1,3-dioxo-5-phenoxy-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)ethyl 4-(pyren-4-yl)butanoate ((±)-10(COOH)). A 2 dram vial equipped with a stir bar was charged with (±)-**9** (34.0 mg, 0.0505 mmol), DMAP (1.5 mg, 0.012 mmol), 1-pyrenebutanoic acid (16 mg, 0.056 mmol) and THF (0.5 mL). N,N′-Dicyclohexylcarbodiimide (11.5 mg, 0.0558 mmol) was then added to the reaction mixture slowly. The reaction was stirred at room temperature overnight until the reaction completed, as determined by ^{1}H NMR spectroscopy. The reaction mixture was filtered and then diluted with Et_2O (15 mL), washed with NH_4Cl (15 mL) and brine (15 mL), and the organic fraction was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (20–40% EtOAc/hexanes) to yield the title compound as a white foamy solid (43.6 mg, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.35 – 8.28 (m, 1H), 8.21 – 8.14 (m, 2H), 8.14 – 8.08 (m, 2H), 8.05 – 8.02 (m, 2H), 8.02 – 7.97 (m, 1H), 7.91 – 7.85 (m, 1H), 7.35 – 7.28 (m, 2H), 7.20 – 7.14 (m, 1H), 6.97 – 6.91 (m, 2H), 5.77 (q, J = 6.5 Hz, 1H), 4.98 (s, 1H), 4.66 (ABq, $\Delta\nu_{AB}$ = 119.3 Hz, J_{AB} = 12.6 Hz, 2H), 4.28-4.07 (m, 2H), 3.73 – 3.62 (m, 2H), 3.62 – 3.50 (m, 2H), 3.44 (t, J = 7.7 Hz, 2H), 2.56 (t, J = 7.3 Hz, 2H), 2.32 – 2.20 (m, 2H), 1.90 (d, J = 4.2 Hz, 6H), 1.79 (d, J = 4.0 Hz, 6H), 1.55 (d, J = 6.6 Hz, 3H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 173.8, 172.9, 172.4, 171.5, 171.1, 162.9, 154.7, 135.7, 131.5, 131.0, 130.2, 130.2, 128.9, 127.6, 127.6, 126.9, 126.1, 126.0, 125.2, 125.1, 125.1, 125.0, 124.9, 123.5, 119.7, 100.9, 90.8, 88.3, 66.8, 63.7, 62.4, 55.7, 55.6, 51.4, 47.9, 37.5, 34.1, 32.9, 30.8, 30.7, 30.6, 27.0, 16.0 ppm. HRMS (ESI, *m/z*): calcd for $[C_{47}H_{46}Br_2NO_{10}]^+$ $(M+H)^+$, 942.1483; found, 942.1509.

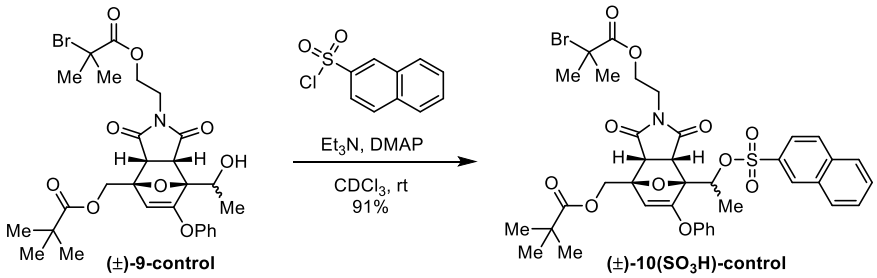


1-(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-1,3-dioxo-5-phenoxy-7-((pivaloyloxy)methyl)-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)ethyl 4-(pyren-1-yl)butanoate ((±)-10(COOH)-control). The title compound was prepared following a similar procedure as that for compound (±)-**10(COOH)**, with compound (±)-**9-control** (23.0 mg, 0.0378 mmol)**,** 1-pyrenebutanoic acid (21.8 mg, 0.0757 mmol), N,N′-dicyclohexylcarbodiimide (15.6 mg, 0.0757 mmol), DMAP (2.3 mg, 0.019 mmol), and THF (0.5 mL). Column chromatography (10–25% EtOAc/Hexanes) followed by preparative thin layer chromatography (4:1

toluene/acetone) afforded the title compound as a white foamy solid (28 mg, 84%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.34 – 8.29 (m, 1H), 8.19 – 8.14 (m, 2H), 8.14 – 8.08 (m, 2H), 8.06 – 8.02 (m, 2H), 8.02 – 7.96 (m, 1H), 7.89 – 7.86 (m, 1H), 7.35 – 7.28 (m, 2H), 7.21 – 7.14 (m, 1H), 6.95 – 6.90 (m, 2H), 5.78 (q, *J* = 6.5 Hz, 1H), 4.93 (s, 1H), 4.57 (ABq, $\Delta\nu_{AB}$ = 166.4 Hz, J_{AB} = 12.7 Hz, 2H), 4.28-4.10 (m, 2H), 3.74 – 3.61 (m, 2H), 3.61 – 3.47 (m, 2H), 3.44 (t, *J* = 7.7 Hz, 2H), 2.57 (t, *J* = 7.3 Hz, 2H), 2.32 – 2.20 (m, 2H), 1.80 (d, *J* = 6.0 Hz, 6H), 1.56 (d, *J* = 6.6 Hz, 3H), 1.18 (s, 9H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 177.8, 173.9, 172.9, 172.4, 171.5, 162.8, 154.7, 135.7, 131.5, 131.0, 130.2, 130.1, 128.9, 127.6, 127.6, 126.9, 126.1, 126.0, 126.0, 125.2, 125.1, 125.1, 125.0, 124.9, 123.5, 119.7, 119.6, 101.1, 90.7, 88.6, 66.8, 62.5, 62.4, 55.7, 51.4, 48.0, 39.0, 37.4, 34.1, 32.9, 30.6, 30.6, 27.3, 27.2, 27.0, 16.0 ppm. HRMS (ESI, *m/z*): calcd for $[C_{48}H_{49}BrNO_{10}]^+$ $(M+H)^+$, 878.2534; found, 878.2541.

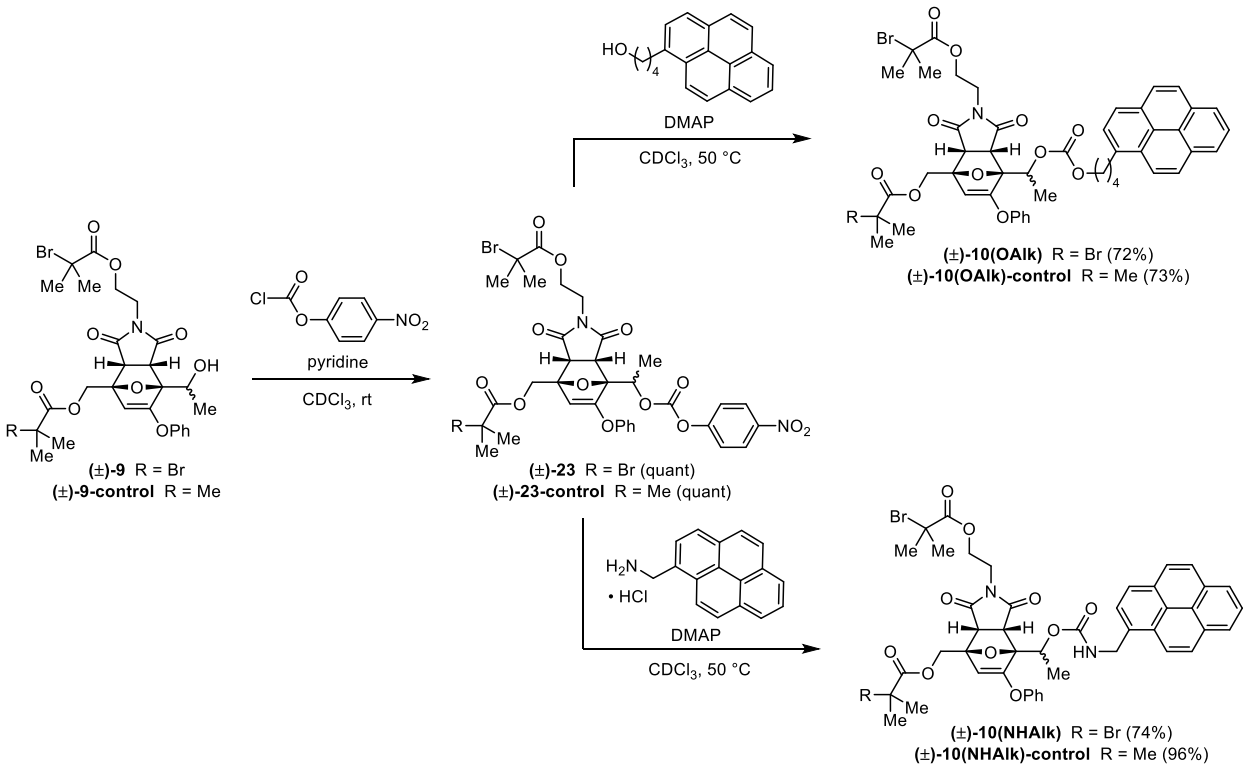


(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-7-(1-((naphthalen-2-ylsulfonyl)oxy)ethyl)-1,3-dioxo-6-phenoxy-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl 2-bromo-2-methylpropanoate ((±)-10(SO_3H)). A 2 dram vial equipped with a stir bar was charged with (±)-**9** (22 mg, 0.033 mmol), DMAP (4.2 mg, 0.035 mmol) and $CDCl_3$ (0.3 mL). Naphthalene-2-sulfonyl chloride (7.8 mg, 0.034 mmol) dissolved in $CDCl_3$ (0.2 mL) was then added to the reaction mixture slowly. The solution was then stirred at room temperature until the reaction completed, as determined by ^{1}H NMR spectroscopy (~2 h). The reaction mixture was then diluted with DCM (10 mL), washed with NH_4Cl (15 mL) and brine (15 mL), and the organic fraction was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (20–40% EtOAc/hexanes) to yield the title compound as a white foamy solid (17.6 mg, 62% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.62 (d, *J* = 1.8 Hz, 1H), 8.07 – 7.99 (m, 2H), 7.99 – 7.92 (m, 2H), 7.60-7.73 (m, 2H), 7.38 – 7.29 (m, 2H), 7.22 – 7.15 (m, 1H), 6.96 – 6.89 (m, 2H), 5.55 (q, *J* = 6.6 Hz, 1H), 4.94 (s, 1H), 4.60 (ABq, $\Delta\nu_{AB}$ = 107.3 Hz, J_{AB} = 12.6 Hz, 2H), 4.21 – 4.04 (m, 2H), 3.75 (d, *J* = 7.9 Hz, 1H), 3.68 – 3.49 (m, 3H), 1.92 (d, *J* = 4.6 Hz, 6H), 1.84 (d, *J* = 1.6 Hz, 6H), 1.57 (d, *J* = 6.6 Hz, 3H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 173.6, 172.7, 171.4, 171.1, 162.4, 154.5, 135.5, 133.8, 132.1, 130.2, 130.0, 129.9, 129.6, 129.6, 128.2, 128.0, 126.3, 122.7, 119.6, 101.1, 90.4, 88.4, 75.2, 63.5, 62.3, 55.7, 55.5, 51.3, 47.9, 37.4, 30.8, 30.7, 30.7, 17.2 ppm. HRMS (ESI, *m/z*): calcd for $[C_{37}H_{38}Br_2NO_{11}S]^+$ $(M+H)^+$, 862.0527; found, 862.0546.



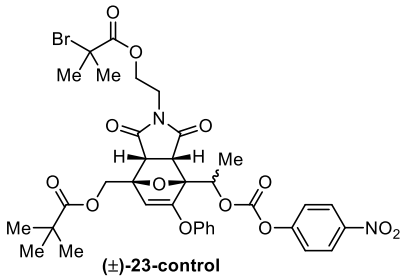
(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-7-(1-((naphthalen-2-ylsulfonyl)oxy)ethyl)-1,3-dioxo-6-phenoxy-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl pivalate ((±)-10(SO_3H)-control). The

title compound was prepared following the same procedure as that for compound (±)-**10(SO$_3$H)**, with compound (±)-**9-control** (20 mg, 0.033 mmol), DMAP (6.3 mg, 0.052 mmol), naphthalene-2-sulfonyl chloride (11.7 mg, 0.052 mmol, and $CDCl_3$ (0.5 mL). Column chromatography (25–45% EtOAc/Hexanes) afforded the title compound as a white foamy solid (24 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.62 (d, *J* = 1.8 Hz, 1H), 8.05 –7.91 (m, 4H), 7.72 – 7.61 (m, 2H), 7.38 – 7.28 (m, 2H), 7.23 – 7.16 (m, 1H), 6.95 – 6.88 (m, 2H), 5.56 (q, *J* = 6.5 Hz, 1H), 4.89 (s, 1H), 4.50 (ABq, $\Delta\nu_{AB}$ = 122.8 Hz, J_{AB} = 12.7 Hz, 2H), 4.22 – 4.06 (m, 2H), 3.75 (d, *J* = 7.9 Hz, 1H), 3.68 – 3.46 (m, 3H), 1.85 (s, 6H), 1.63 – 1.52 (m, 3H), 1.19 (s, 9H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 177.8, 173.7, 172.8, 171.4, 162.4, 154.6, 135.5, 133.8, 132.1, 130.2, 130.0, 129.8, 129.6, 129. 6, 128.1, 127.9, 126.2, 122.7, 119.6, 101.2, 90.3, 88.7, 75.2, 62.3, 62.2, 55.7, 51.2, 48.0, 39.0, 37.4, 30.7, 30.6, 27.3, 27.2, 17.2 ppm. HRMS (ESI, *m/z*): calcd for $[C_{38}H_{40}BrNO_{11}SNa]^+$ (M+Na)$^+$, 820.1398; found, 820.1392.



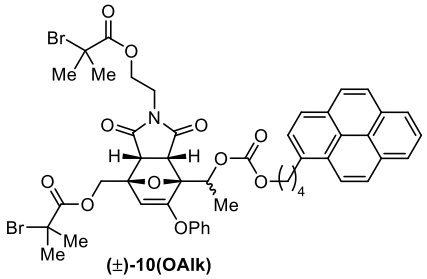
(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-7-(1-(((4-nitrophenoxy)carbonyl)oxy)ethyl)-1,3-dioxo-6-phenoxy-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl 2-bromo-2-methylpropanoate ((±)-23). A 2 dram vial equipped with a stir bar was charged with (±)-**9** (101 mg, 0.150 mmol), pyridine (14.6 µL, 0.181 mmol) and $CDCl_3$ (1 mL). 4-nitrophenyl chloroformate (33.3 mg, 0.166 mmol) dissolved in $CDCl_3$ was then added to the reaction mixture slowly. The reaction was then stirred at room temperature until the reaction had completed, as determined by ^{1}H NMR spectroscopy (~2 h). The reaction mixture was then diluted with DCM (20 mL), washed with NH_4Cl (25 mL) and brine (25 mL), and the organic fraction was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (20–45% EtOAc/Hexanes) to yield the title compound as a white foamy solid (125 mg, quant). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.34 – 8.26 (m, 2H), 7.49 – 7.41 (m, 2H), 7.36 (dd, *J* = 8.5, 7.3 Hz, 2H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.01 – 6.94 (m, 2H), 5.66 (q, *J* = 6.5 Hz, 1H), 5.03 (s, 1H), 4.71 (ABq, $\Delta\nu_{AB}$ = 106.7 Hz, J_{AB} = 12.6 Hz, 2H), 4.34 – 4.12 (m, 2H), 3.87 (d, *J* = 7.8 Hz, 1H), 3.78 – 3.54 (m, 3H), 1.96 (d, *J* = 2.0 Hz, 6H), 1.86 (d, *J* = 1.2 Hz, 6H), 1.72 (d, *J* = 6.5 Hz, 3H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 173.7, 172.9, 171.5, 171.1, 162.5, 155.6, 154.6, 151.8, 145.6,

130.3, 126.3, 125.5, 121.9, 119.7, 101.2, 90.3, 88.5, 72.9, 63.5, 62.4, 55.7, 55.5, 51.4, 48.1, 37.6, 30.8, 30.7, 30.7, 15.7 ppm. HRMS (ESI, *m/z*): calcd for $[C_{34}H_{34}Br_2N_2O_{13}Na]^+$ $(M+Na)^+$, 859.0320; found, 859.0325.



(±)-23-control

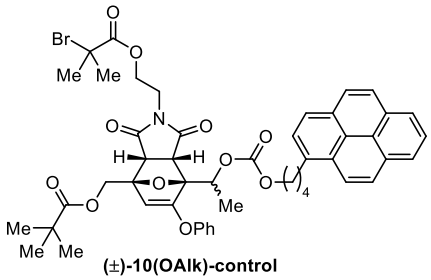
(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-7-(1-(((4-nitrophenoxy)carbonyl)oxy)ethyl)-1,3-dioxo-6-phenoxy-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl pivalate ((±)-23-control). The title compound was prepared following a similar procedure as that for compound (±)-**23**, with compound (±)-**9-control** (75.0 mg, 0.123 mmol)**,** pyridine (12.0 µL, 0.149 mmol), 4-nitrophenyl chloroformate (27.3 mg, 0.136 mmol), and $CDCl_3$ (0.7 mL). Column chromatography (20–45% EtOAc/hexanes) afforded the title compound as a white foamy solid (94.5 mg, quant). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.33 – 8.27 (m, 2H), 7.48 – 7.42 (m, 2H), 7.40 – 7.32 (m, 2H), 7.25 – 7.18 (m, 1H), 6.99 – 6.93 (m, 2H), 5.66 (q, *J* = 6.5 Hz, 1H), 4.99 (s, 1H), 4.61 (ABq, $\Delta\nu_{AB}$ = 151.1 Hz, J_{AB} = 12.8 Hz, 2H), 4.34 – 4.14 (m, 2H), 3.87 (d, *J* = 7.9 Hz, 1H), 3.75 – 3.58 (m, 3H), 1.87 (s, 6H), 1.72 (d, *J* = 6.5 Hz, 3H), 1.23 (s, 9H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 177.8, 173.7, 173.0, 171.6, 162.5, 155.6, 154.7, 151.9, 145.6, 130.3, 126.3, 125.5, 121.9, 119.7, 101.4, 90.1, 88.8, 72.8, 62.4, 62.2, 55.7, 51.4, 48.2, 39.1, 37.6, 30.7, 27.3, 15.7 ppm. HRMS (ESI, *m/z*): calcd for $[C_{35}H_{37}BrN_2O_{13}Na]^+$ $(M+Na)^+$, 795.1371; found, 795.1377.



(±)-10(OAlk)

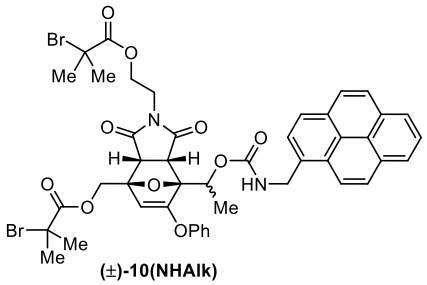
(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-1,3-dioxo-6-phenoxy-7-(1-(((4-(pyren-1-yl)butoxy)carbonyl)oxy)ethyl)-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl 2-bromo-2-methylpropanoate ((±)-10(OAlk)). A 2 dram vial equipped with a stir bar was charged with (±)-**23** (21.7 mg, 0.0259 mmol), DMAP (3.5 mg, 0.029 mmol) and $CDCl_3$ (0.5 mL), followed by the addition of 1-pyrenebutanol (7.8 mg, 0.028 mmol) dissolved in $CDCl_3$ (0.2 mL). The reaction was stirred at 50 °C overnight until the reaction had completed, as determined by ^{1}H NMR spectroscopy. The reaction mixture was then diluted with DCM (15 mL), washed with NH_4Cl (15 mL) and brine (15 mL), and the organic fraction was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (35–50% EtOAc/hexanes) to yield the title compound as a white foamy solid (18 mg, 72% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.30 – 7.85 (m, 9H), 7.39 – 7.29 (m, 2H), 7.21 – 7.13 (m, 1H), 7.01 – 6.91 (m, 2H), 5.57 (q, *J* = 6.5 Hz, 1H), 4.99 (s, 1H), 4.66 (ABq, $\Delta\nu_{AB}$ =109.8 Hz, J_{AB} = 12.6 Hz, 2H), 4.36 – 4.17 (m, 3H), 4.16 – 4.08 (m, 1H), 3.81 (d, *J* = 7.9 Hz, 1H), 3.70 – 3.51 (m, 3H), 3.40 (t, *J* = 7.5 Hz, 2H), 2.13 – 1.85 (m, 10H), 1.82 (s, 6H), 1.58 (d, J = 6.5, 3H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 173.7, 172.9, 171.4, 171.0, 162.5, 154.6, 154.5, 136.2, 131.4, 130.9, 130.1, 129.9, 128.6, 127.5, 127.4, 127.3, 126.7, 126.0, 125.9, 125.1, 125.0, 124.9, 124.8, 124.8, 123.3, 119.5,

101.0, 90.5, 88.2, 70.3, 68.3, 63.6, 62.3, 55.5, 55.5, 51.3, 47.7, 37.3, 33.0, 30.7, 30.6, 30.5, 28.7, 27.9, 15.8 ppm. HRMS (ESI, *m/z*): calcd for $[C_{48}H_{48}Br_2NO_{11}]^+$ $(M+H)^+$, 972.1589; found, 972.1597.



(±)-10(OAlk)-control

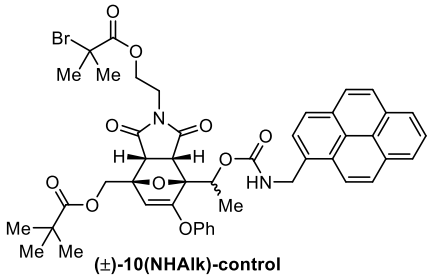
(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-1,3-dioxo-6-phenoxy-7-(1-(((4-(pyren-1-yl)butoxy)carbonyl)oxy)ethyl)-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl pivalate ((±)-10(OAlk)-control). The title compound was prepared following a similar procedure as that for compound (±)-**10(OAlk)**, with compound (±)-**23-control** (30.0 mg, 0.0388 mmol)**,** DMAP (9.5 mg, 0.078 mmol), 1-pyrenebutanol (21.3 mg, 0.777 mmol), and $CDCl_3$ (0.5 mL). Column chromatography (20–50% EtOAc/Hexanes) afforded the title compound as a white foamy solid (25.9 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.30 – 7.85 (m, 9H), 7.37 – 7.29 (m, 2H), 7.22 – 7.15 (m, 1H), 7.00 – 6.91 (m, 2H), 5.56 (q, *J* = 6.5 Hz, 1H), 4.94 (s, 1H), 4.56 (ABq, $\Delta\nu_{AB}$ = 123.5 Hz, J_{AB} = 12.7 Hz, 2H), 4.34 – 4.19 (m, 3H), 4.17 – 4.08 (m, 1H), 3.80 (d, *J* = 7.9 Hz, 1H), 3.70 – 3.49 (m, 3H), 3.40 (t, *J* = 7.5 Hz, 2H), 2.15 – 1.73 (m, 10H), 1.58 (d, *J* = 6.5 Hz, 3H), 1.20 (s, 9H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ: 177.9, 173.9, 173.1, 171.5, 162.6, 154.7, 136.3, 131.6, 131.0, 130.2, 130.0, 128.8, 127.6, 127.5, 127.4, 126.8, 126.1, 126.0, 125.2, 125.1, 125.1, 125.0, 124.9, 123.4, 119.7, 101.2, 90.5, 88.7, 70.5, 68.4, 62.4, 55.7, 51.4, 47.8, 39.0, 37.4, 33.2, 30.7, 28.8, 28.0, 27.2, 27.2, 15.9 ppm. HRMS (ESI, *m/z*): calcd for $[C_{49}H_{51}BrNO_{11}]^+$ $(M+H)^+$, 908.2640; found, 908.2626.



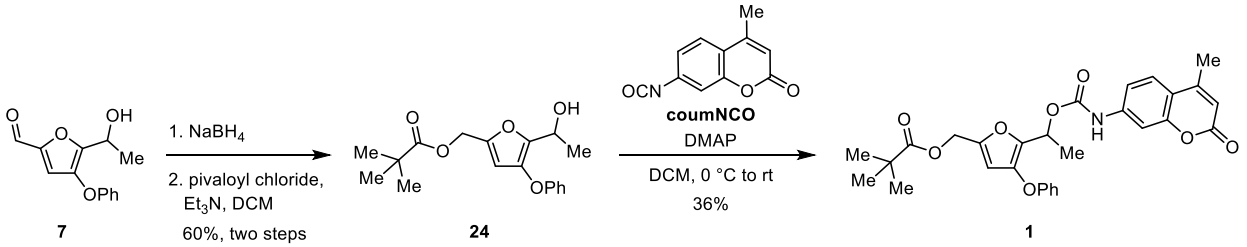
(±)-10(NHAlk)

(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-1,3-dioxo-6-phenoxy-7-(1-(((pyren-1-ylmethyl)carbamoyl)oxy)ethyl)-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl 2-bromo-2-methylpropanoate ((±)-10(NHAlk)). A 2 dram vial equipped with a stir bar was charged with (±)-**23** (24.1 mg, 0.0289 mmol), DMAP (8.4 mg, 0.069 mmol) and $CDCl_3$ (0.5 mL). Pyren-1-ylmethanamine hydrochloride (8.5 mg, 0.032 mmol) dissolved in $CDCl_3$ (0.5 mL) was then added to the reaction mixture. The reaction was stirred at 50 °C overnight until the reaction had completed, as determined by ^{1}H NMR spectroscopy. The reaction mixture was then diluted with DCM (10 mL), washed with NH_4Cl (15 mL) and brine (15 mL), and the organic fraction was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (20–60% EtOAc/hexanes) to yield the title compound as a white foamy solid (20 mg, 74% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.34 – 7.97 (m, 9H), 7.32 -7.26 (m, 2H), 7.19 – 7.13 (m, 1H), 6.93 (d, *J* = 7.9 Hz, 2H), 5.77 (q, *J* = 6.5 Hz, 1H), 5.38 – 5.30 (m, 1H), 5.16 (d, *J* = 5.6 Hz, 2H), 4.96 (s, 1H), 4.63 (ABq, $\Delta\nu_{AB}$ = 137.0 Hz, J_{AB} = 12.6 Hz, 2H), 4.34 – 4.19 (m, 1H), 4.18 – 4.08 (m, 1H), 3.77 (d, *J* = 7.9 Hz, 1H), 3.71 – 3.41 (m, 3H),

1.91 (d, *J* = 3.7 Hz, 6H), 1.82 (s, 6H), 1.57 (d, *J* = 6.5 Hz, 3H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ: 173.9, 172.9, 171.5, 171.1, 163.1, 155.3, 154.7, 131.4, 131.2, 130.9, 130.1, 129.1, 128.4, 127.7, 127.5, 127.0, 126.3, 126.0, 125.6, 125.5, 125.2, 125.0, 124.9, 122.9, 119.7, 100.7, 90.9, 88.3, 67.3, 63.7, 62.5, 55.7, 55.6, 51.3, 47.8, 43.7, 37.5, 30.8, 30.7, 30.7, 16.3 ppm. HRMS (ESI, *m/z*): calcd for $[C_{45}H_{43}Br_2N_2O_{10}]^+$ $(M+H)^+$, 929.1279; found, 929.1268.

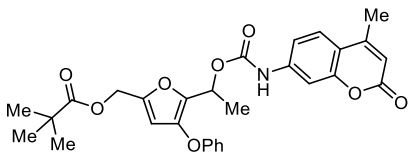


(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-1,3-dioxo-6-phenoxy-7-(1-(((pyren-1-ylmethyl)carbamoyl)oxy)ethyl)-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl pivalate ((±)-10(NHAlk)-control). The title compound was prepared following a similar procedure as that for compound (±)-**10(NHAlk)**, with compound (±)-**23-control** (38.0 mg, 0.0491 mmol)**,** DMAP (13.2 mg, 0.108 mmol), pyren-1-ylmethanamine hydrochloride (14.5 mg, 0.0542 mmol), and $CDCl_3$ (0.5 mL). Column chromatography (20–40% EtOAc/hexanes) afforded the title compound as a white foamy solid (41 mg, 96%). ^1H NMR (400 MHz, $CDCl_3$) δ: 8.35 – 7.92 (m, 9H) 7.29 (t, *J* = 7.7 Hz, 2H), 7.16 (t, *J* = 7.4 Hz, 1H), 6.92 (d, *J* = 7.9 Hz, 2H), 5.77 (q, *J* = 6.4 Hz, 1H), 5.34 (t, *J* = 5.6 Hz, 1H), 5.15 (d, *J* = 5.5 Hz, 2H), 4.91 (s, 1H), 4.53 (ABq, $\Delta\nu_{AB}$ = 124.2 Hz, J_{AB} = 12.7 Hz, 2H), 4.30 – 4.19 (m, 1H), 4.20 – 4.08 (m, 1H), 3.76 (d, *J* = 7.9 Hz, 1H), 3.72 – 3.50 (m, 2H), 3.46 (d, *J* = 7.9 Hz, 1H), 1.82 (d, *J* = 0.9 Hz, 6H), 1.56 (d, *J* = 6.5 Hz, 3H), 1.17 (s, 9H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ: 177.8, 173.9, 173.0, 171.5, 163.0, 155.3, 154.8, 131.4, 131.2, 130.9, 130.1, 129.0, 128.4, 127.7, 127.5, 127.0, 126.2, 126.0, 125.6, 125.5, 125.1, 124.9, 124.8, 122.9, 119.6, 100.8, 90.8, 88.6, 67.4, 62.5, 62.4, 55.7, 51.3, 47.9, 43.7, 39.0, 37.4, 30.7, 30.7, 27.2, 16.3 ppm. HRMS (ESI, *m/z*): calcd for $[C_{46}H_{46}BrN_2O_{10}]^+$ $(M+H)^+$, 865.2330; found, 865.2338.



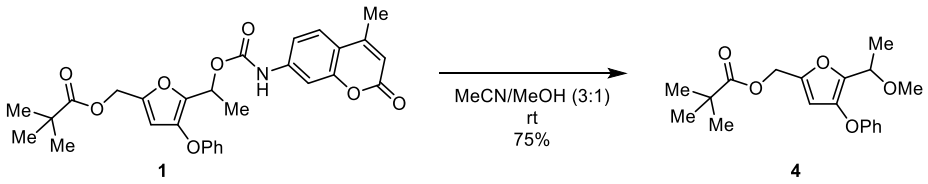
(5-(1-hydroxyethyl)-4-phenoxyfuran-2-yl)methyl pivalate (24). A round bottom flask equipped with a stir bar was charged with **7** (0.916 g, 3.95 mmol) and methanol (10 mL). The solution was cooled to 0 °C in an ice bath followed by the slow addition of $NaBH_4$ (0.246 g, 6.47 mmol). The reaction mixture was allowed to slowly warm to room temperature and stirred for 1 h. The mixture was then washed with 10% NH_4Cl (20 mL) and extracted with DCM (2 x 20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to yield 1-(5-(hydroxymethyl)-3-phenoxyfuran-2-yl)ethan-1-ol as a colorless oil, which was used in the next step without further purification. The intermediate diol is stable for approximately one month when stored at −20°C.

A flame-dried round bottom flask equipped with a stir bar was charged with 1-(5-(hydroxymethyl)-3-phenoxyfuran-2-yl)ethan-1-ol (365.2 mg, 1.559 mmol), Et_3N (228µL, 1.64 mmol) and DCM (10 mL). The solution was cooled to 0 °C before adding pivaloyl chloride (202 µL, 1.64 mmol) dropwise. The reaction was then allowed to slowly warm to room temperature and stirred for approximately 4 h. The reaction mixture was then washed with NH_4Cl (10 mL) and brine (10 mL), and the organic fraction was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography using 3:1 hexanes/EtOAc to yield the title compound as a colorless oil (315 mg, 60% yield over two steps). A small amount of pivalic anhydride coeluted with the product. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.33 – 7.24 (m, 2H), 7.07 – 7.01 (m, 1H), 7.02 – 6.93 (m, 2H), 6.19 (s, 1H), 4.97 (ABq, $\Delta\nu_{AB}$ = 8.19 Hz, J_{AB} = 14.2 Hz, 2H), 4.92 (q, *J* = 6.7 Hz, 1H), 2.36 (s, 1H), 1.53 (d, *J* = 6.8 Hz, 3H), 1.20 (s, 9H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ: 178.2, 158.0, 147.9, 145.1, 138.8, 129.7, 122.8, 116.2, 106.5, 61.3, 58.6, 38.9, 27.2, 20.7 ppm. HRMS (ESI, *m/z*): calcd for $[C_{18}H_{21}O_4]^+$ $(M-OH)^+$, 301.1434; found, 301.1455.

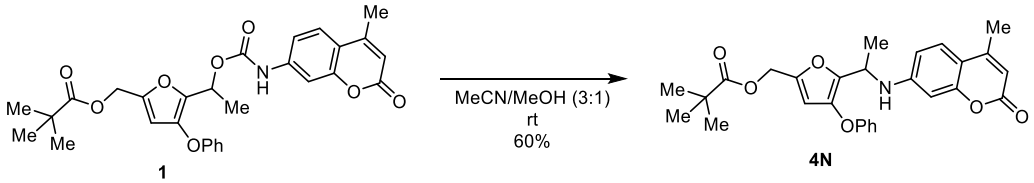


1

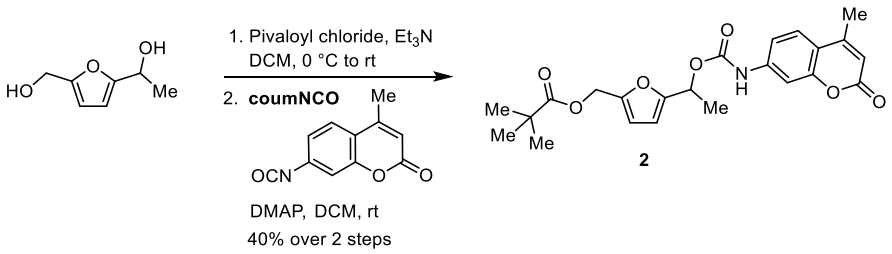
(5-(1-(((4-methyl-2-oxo-2H-chromen-7-yl)carbamoyl)oxy)ethyl)-4-phenoxyfuran-2-yl)methyl pivalate (1). A flamed-dried two-neck round bottom flask equipped with a stir bar was charged with **24** (77.2 mg, 0.243 mmol), **coumNCO** (81.8 mg, 0.407 mmol), and DCM (8 mL). DMAP (8.1 mg, 0.066 mmol) was then added into the stirred mixture at 0°C, and the reaction was allowed to warm to room temperature. After 3 h, the reaction was quenched by adding a solution of glucose (35.0 mg, 0.194 mmol) in 3 mL DMF. The mixture was stirred at room temperature for 2 h to consume the excess **coumNCO** completely, then diluted with diethyl ether (20 mL) and hexane (5 mL). A precipitate appeared immediately and the suspension was filtered to remove the excess glucose and any other insoluble products. The filtrate was washed with aqueous $NaHCO_3$ solution and brine, dried over Na_2SO_4, then concentrated. The crude material was again dispersed into a mixture of diethyl ether (5 mL) and hexane (10 mL), and then filtered to remove insoluble 7-amino-4-methylcoumarin. The filtrate was concentrated, dissolved in a small amount of DCM (0.3 mL), and then added into a mixture of diethyl ether (3 mL) and hexane (7 mL). The mixture was slowly concentrated to around half of its original volume using a rotary evaporator causing a white precipitate to form. The white solid was collected carefully by removing the solution using a pipet, then washed with hexane, and finally dried under high vacuum to yield metastable compound **1** as a fluffy white solid (45.5 mg, 36%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.49 (d, *J* = 8.6 Hz, 1H), 7.36 – 7.27 (m, 4H), 7.05 (t, *J* = 7.4 Hz, 1H), 7.00 (d, *J* = 8.1 Hz, 2H), 6.73 (s, 1H), 6.23 (s, 1H), 6.18 (d, *J* = 1.3 Hz, 1H), 6.02 (q, *J* = 6.7 Hz, 1H), 5.00 (ABq, $\Delta\nu_{AB}$ = 17.7 Hz, J_{AB} = 13.5 Hz, 2H), 2.41 (d, *J* = 1.2 Hz, 3H), 1.67 (d, *J* = 6.7 Hz, 3H), 1.22 (s, 9H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ: 178.2, 161.2, 157.9, 154.6, 152.3, 152.0, 148.9, 141.4, 141.0, 140.9, 129.8, 125.5, 123.1, 116.6, 115.7, 114.4, 113.3, 106.5, 106.0, 65.0, 58.6, 39.0, 27.2, 18.7, 18.2 ppm. HRMS (FAB, *m/z*): calcd for $[C_{29}H_{30}NO_8]^+$ $(M+H)^+$, 520.1966; found, 520.1950.



(5-(1-methoxyethyl)-4-phenoxyfuran-2-yl)methyl pivalate (4). Compound **1** (6.2 mg, 0.012 mmol) was dissolved in a mixture of MeOH (155 mL) and MeCN (465 mL) and stirred at room temperature. After 16 h, the reaction mixture was concentrated under reduced pressure and the crude product was purified by flash chromatography (0–20% EtOAc/hexanes) to provide the title compound as a colorless oil (3.0 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39 – 7.27 (m, 2H), 7.08 – 7.03 (m, 1H), 7.02 – 6.96 (m, 2H), 6.22 (d, *J* = 0.6 Hz, 1H), 5.00 (ABq, $\Delta\nu_{AB}$ = 11.6 Hz, J_{AB} = 13.4 Hz, 2H), 4.44 (q, *J* = 6.7 Hz, 1H), 3.24 (s, 3H), 1.51 (d, *J* = 6.7 Hz, 3H), 1.20 (s, 9H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 178.2, 158.1, 148.5, 142.8, 141.0, 129.8, 122.9, 116.4, 106.0, 69.2, 58.7, 56.3, 39.0, 27.2, 18.8 ppm. HRMS (FAB, *m/z*): calcd for $[C_{19}H_{24}O_5]^+$ $(M)^+$, 332.1624; found, 332.1645.

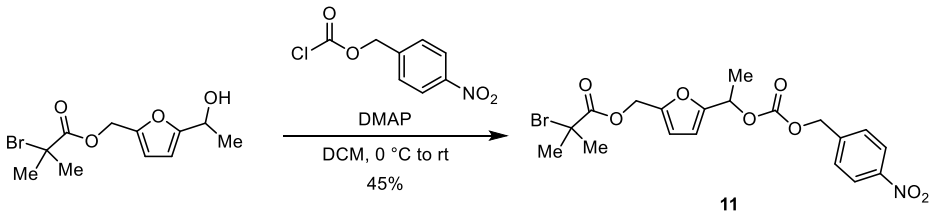


(5-(1-((4-methyl-2-oxo-2H-chromen-7-yl)amino)ethyl)-4-phenoxyfuran-2-yl)methyl pivalate (4N). Compound **1** (22 mg, 0.066 mmol) was dissolved in a mixture of MeOH (0.15 mL) and MeCN (0.45 mL) and kept at room temperature. After 16 h, the reaction mixture was concentrated under reduced pressure and the crude product was purified by flash chromatography (0–50% EtOAc/hexanes) to provide the title compound as a white solid (19 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.30 – 7.27 (m, 2H), 7.26 – 7.22 (m, 1H), 7.09 – 7.00 (m, 1H), 6.98 – 6.90 (m, 2H), 6.53 – 6.46 (m, 2H), 6.17 (s, 1H), 5.97 (q, *J* = 1.2 Hz, 1H), 4.94 (ABq, $\Delta\nu_{AB}$ = 6.6 Hz, J_{AB} = 13.2 Hz, 2H), 4.74 (dq, *J* = 8.3, 6.8 Hz, 1H), 4.45 (d, *J* = 8.2 Hz, 1H), 2.30 (d, *J* = 1.2 Hz, 3H), 1.58 (d, *J* = 6.8 Hz, 3H), 1.16 (s, 9H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 178.1, 162.0, 157.9, 155.8, 152.9, 150.1, 147.9, 143.4, 139.0, 129.8, 125.5, 123.0, 116.3, 111.2, 110.7, 110.0, 106.5, 99.5, 58.5, 44.6, 38.9, 27.2, 20.2, 18.6 ppm. HRMS (ESI, *m/z*): calcd for $[C_{28}H_{29}NO_6Na]^+$ $(M+Na)^+$, 498.1887; found, 498.1893.

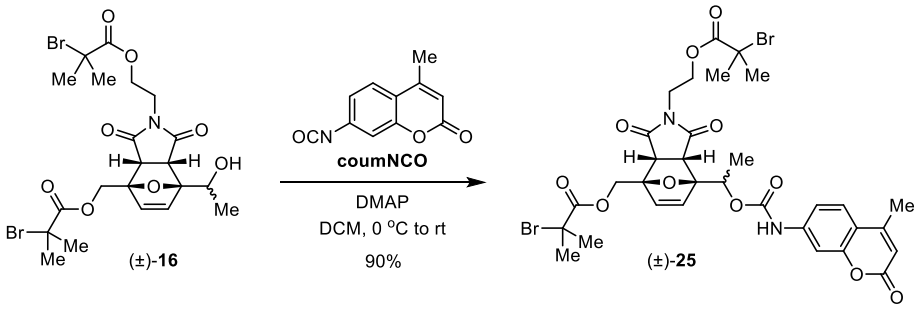


(5-(1-(((4-methyl-2-oxo-2H-chromen-7-yl)carbamoyl)oxy)ethyl)furan-2-yl)methyl pivalate (2). A flame-dried round bottom flask equipped with a stir bar was charged with 1-(5-(hydroxymethyl)furan-2-yl)ethan-1-ol[3] (1.00 g, 7.04 mmol), Et_3N (1.30 mL, 9.44 mmol) and DCM (10 mL). The solution was cooled to 0 °C before adding pivaloyl chloride (1.0 mL, 8.13 mmol) dropwise. The reaction was then allowed to slowly warm to room temperature and stirred overnight until the reaction completed, as determind by ^{1}H NMR spectroscopy. The reaction mixture was then washed with NH_4Cl (10 mL) and brine (10 mL), and the organic fraction was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford (5-(1-hydroxyethyl)furan-2-yl)methyl pivalate as a light-yellow oil (0.79 g) which was used in the next step without further purification.

A flame-dried two-neck round bottom flask equipped with a stir bar was charged with (5-(1-hydroxyethyl)furan-2-yl)methyl pivalate (195.8 mg, 0.865 mol), **coumNCO** (233.0 mg, 1.159 mol), DCM (10 mL), and then DMAP (11.2 mg, 0.0918 mmol). The reaction was kept at room temperature for 3 h. The mixture was then washed with 10% NH_4Cl, brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude produce was purified by column chromatography (25–45% EtOAc/hexanes) to provide the title compound as a white solid (296 mg, 40% yield over two steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.51 (d, *J* = 8.6 Hz, 1H), 7.42 (d, *J* = 2.3 Hz, 1H), 7.35 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.87 (broad, 1H), 6.36 – 6.32 (m, 2H), 6.19 (q, *J* = 1.3 Hz, 1H), 5.96 (q, *J* = 6.7 Hz, 1H), 5.05 (ABq, $\Delta\nu_{AB}$ = 12.6 Hz, J_{AB} = 13.3 Hz, 2H), 2.40 (d, *J* = 1.2 Hz, 3H), 1.66 (d, *J* = 6.7 Hz, 3H), 1.19 (s, 9H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 178.3, 161.2, 154.6, 153.5, 152.3, 152.3, 150.3, 141.5, 125.5, 115.7, 114.5, 113.3, 110.7, 109.2, 106.1, 66.7, 58.3, 39.0, 27.2, 18.7, 18.5 ppm. HRMS (FAB, *m/z*): calcd for $[C_{23}H_{26}NO_7]^+$ $(M+H)^+$, 428.1704; found, 428.1723.



(5-(1-((((4-nitrobenzyl)oxy)carbonyl)oxy)ethyl)furan-2-yl)methyl 2-bromo-2-methylpropanoate (11). A 20 mL septum-capped vial equipped with a stir bar was charged with (5-(1-hydroxyethyl)furan-2-yl)methyl 2-bromo-2-methylpropanoate[4] (59.5 mg, 0.204 mmol), DMAP (24.9 mg, 0.204 mmol), and DCM (2 mL). The solution was cooled to 0 °C in an ice bath followed by the dropwise addition of a solution of 4-nitrobenzyl chloroformate (45.4 mg, 0.210 mmol) in DCM (1 mL). The reaction mixture was allowed to warm to room temperature and stirred for 5 h. A saturated solution of NH_4Cl (3 mL) was added and the mixture was extracted with DCM (3 x 10 mL). The combined organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (10–40% EtOAc/hexanes) to provide the title compound as a colorless oil (43.4 mg, 45% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.25 – 8.19 (m, 2H), 7.56 – 7.50 (m, 2H), 6.40 (d, *J* = 3.3 Hz, 1H), 6.36 (d, *J* = 3.3 Hz, 1H), 5.80 (q, *J* = 6.7 Hz, 1H), 5.25 (ABq, $\Delta\nu_{AB}$ = 10.2 Hz, J_{AB} = 13.3 Hz, 2H), 5.13 (ABq, $\Delta\nu_{AB}$ = 6.4 Hz, J_{AB} = 13.0 Hz, 2H), 1.92 (s, 6H), 1.66 (d, *J* = 6.7 Hz, 3H) ppm. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ: 171.4, 154.3, 153.1, 149.4, 148.0, 142.5, 128.5, 124.0, 111.6, 109.7, 69.9, 68.1, 59.6, 55.7, 30.8, 18.3 ppm. HRMS (FAB, *m/z*): calcd for $[C_{11}H_{14}BrO_3]^+$ $(M-OCO_2CH_2C_6H_4NO_2)^+$, 273.0121; found, 273.0151. LCMS (ESI, *m/z*): calcd for $[C_{19}H_{20}BrNO_8Na]^+$ $(M+Na)^+$, 492.0; found, 492.0.



(2-(2-((2-bromo-2-methylpropanoyl)oxy)ethyl)-7-(1-(((4-methyl-2-oxo-2H-chromen-7-yl)carbamoyl)oxy)ethyl)-1,3-dioxo-1,2,3,3a,7,7a-hexahydro-4H-4,7-epoxyisoindol-4-yl)methyl 2-bromo-2-methylpropanoate ((±)-25). The title compound was prepared following a similar procedure as that for

compound (±)-**10(NH)**, with compound (±)-**16**[4] (46.1 mg, 79.3 μmol)**,** DMAP (1.0 mg, 8.2 μmol), **coumNCO** (31.8 mg, 158.1 μmol) and DCM (1 mL). Column chromatography (20–40% Et_2O in 1:1 Hexanes/DCM) afforded the title compound as a white foamy solid (55.6 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.53 (d, *J* = 8.7 Hz, 1H), 7.47 – 7.36 (m, 2H), 7.10 (s, 1H), 6.53 – 6.40 (m, 2H), 6.19 (q, *J* = 1.3 Hz, 1H), 5.57 (q, *J* = 6.6 Hz, 1H), 4.80(ABq, $\Delta\nu_{AB}$ = 86.5 Hz, J_{AB} = 12.6 Hz, 2H), 4.22 (t, *J* = 5.1 Hz, 2H), 3.80 – 3.61 (m, 3H), 3.56 (d, *J* = 7.8 Hz, 1H), 2.41 (d, *J* = 1.3 Hz, 3H), 1.93 (d, *J* = 6.8 Hz, 6H), 1.90 (s, 6H), 1.53 (d, *J* = 6.6 Hz, 3H) ppm. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ: 173.7, 173.6, 171.5, 171.2, 161.1, 154.6, 152.3, 152.0, 141.2, 135.7, 135.3, 125.6, 115.8, 114.5, 113.5, 106.1, 92.8, 89.4, 69.6, 63.2, 62.6, 55.7, 55.5, 49.4, 48.1, 37.7, 30.8, 30.8, 18.7, 16.2 ppm. HRMS (ESI, *m/z*): calcd for $[C_{32}H_{34}Br_2N_2O_{11}Na]^+$ $(M+Na)^+$, 803.0422; found, 803.0427.

General Polymerization Procedures. Polymers were synthesized following the procedure reported previously.[4] A 10 mL Schlenk flask equipped with a stir bar was charged with the initiator (1 equiv), methyl acrylate (~1,500 equiv), Me_6TREN (2 equiv), and DMSO (equal volume to methyl acrylate). The flask was sealed, the solution was deoxygenated with three freeze-pump-thaw cycles, and then backfilled with nitrogen. The flask was opened briefly under a flow of N_2, and freshly cut copper wire (1.0 cm length, 20 gauge) was added on top of the frozen mixture. The flask was resealed, evacuated for an additional 15 min, warmed to room temperature, and then backfilled with nitrogen. The mixture was stirred at room temperature until the solution became sufficiently viscous, indicating that the desired monomer conversion was reached (1–6 h). The flask was then opened to air and the solution was diluted with DCM. The polymer was precipitated into cold methanol (2x) and the isolated polymer was thoroughly dried under vacuum.

IV. General Procedure for Ultrasonication Experiments

An oven-dried sonication vessel was fitted with rubber septa, placed onto the sonication probe, and allowed to cool under a stream of dry argon. The vessel was charged with a solution of the polymer in anhydrous acetonitrile/methanol (3:1 v/v, 2.0 mg/mL, 20 mL) and submerged in an ice bath. The solution was sparged continuously with argon beginning 20 min prior to sonication and for the duration of the sonication experiment. Pulsed ultrasound (1 s on/1 s off, 20% amplitude, 20 kHz, 8.2 W/cm^2) was then applied to the system for 60 min (sonication "on" time). The solution temperature during sonication was measured to be 8–10 °C. Then the sonicated solution was filtered through a 0.45 μm syringe filter prior to analysis. Ultrasonic intensity was calibrated using the method described by Berkowski *et al*.[5]

V. Characterization of Molecular Release Using Photoluminescence Spectroscopy

Aliquots from the sonication experiments were added to a quartz microcuvette . The samples were then monitored with fluorescence spectroscopy at room temperature. Emission spectra were recorded using an excitation wavelength of 330 nm for **PMA-1(O)**–**PMA-3(O)** (hydroxycoumarin), and 365 nm for **PMA-1(NH)**–**PMA-3(NH)** (aminocoumarin).

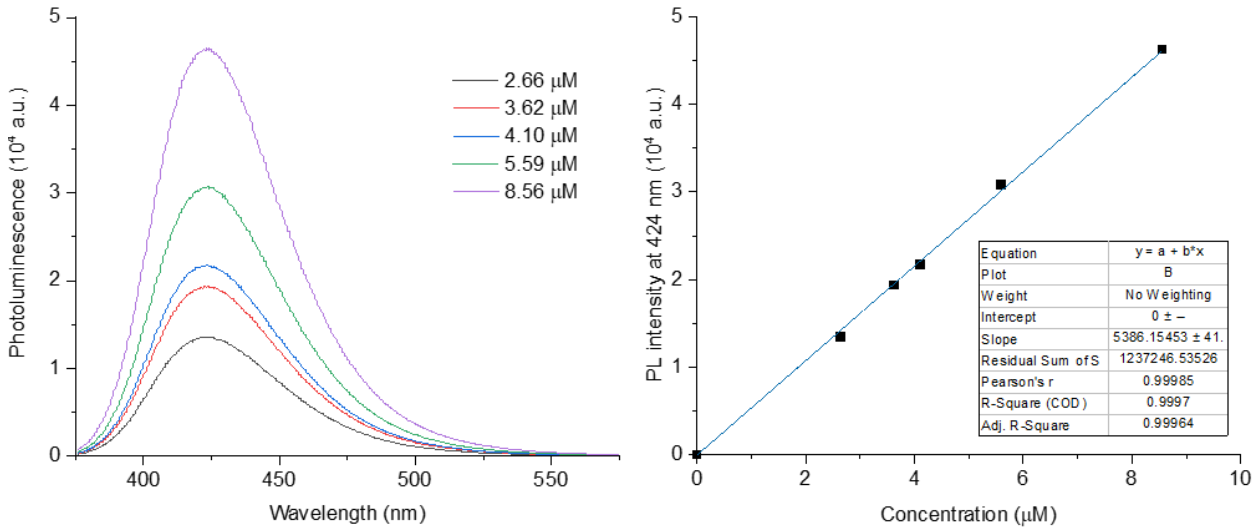


Figure S9. Construction of a calibration curve for experimental determination of the concentration of aminocoumarin **3**. (a) Fluorescence emission spectra (λ_{ex} = 365 nm) and (b) intensity at 424 nm for solutions of aminocoumarin **3** in MeCN/MeOH (3:1 v/v) as a function of concentration. A linear regression of the data in (b) gives the calibration function: Y = 5386X

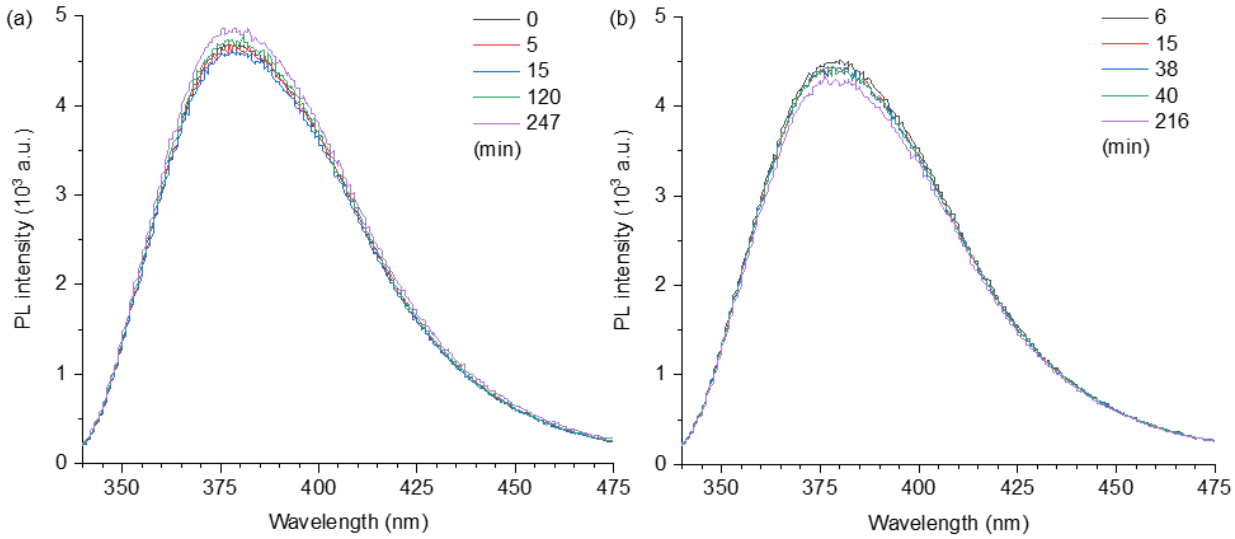


Figure S10. Fluorescence emission spectra of a 2.0 mg/ml solution of (a) **PMA-1(O)** and (b) **PMA-2(O)** in 3:1 MeCN/MeOH at room temperature monitored immediately after ultrasonication for 60 min. λ_{ex} = 330 nm.

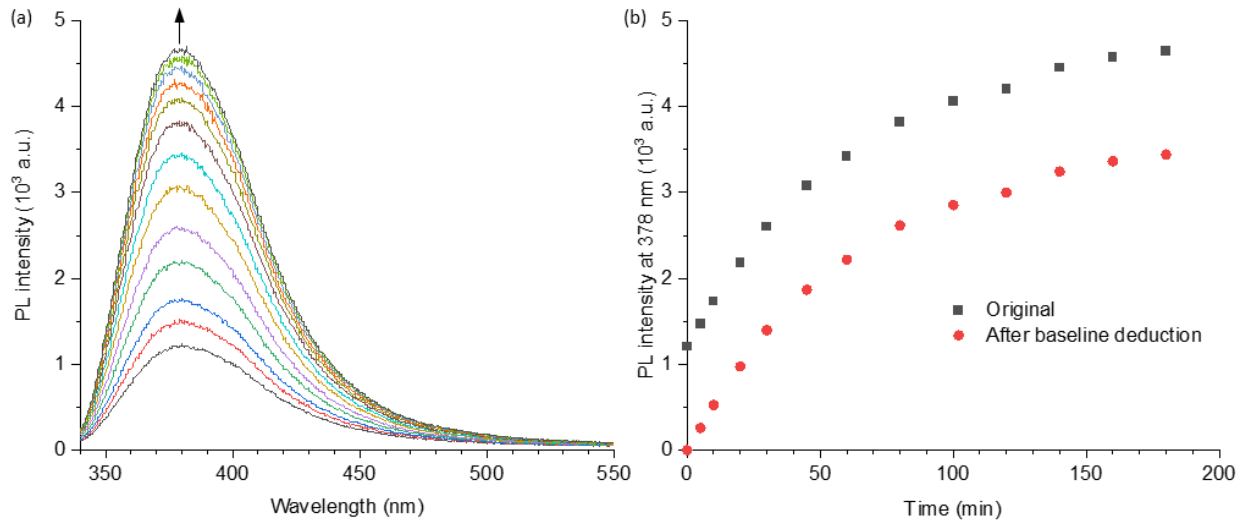


Figure S11. Characterization of hydroxycoumarin release from a 2.0 mg/ml solution of **PMA-3(O)** in 3:1 MeCN/MeOH immediately after ultrasonication for 60 min. (a) Fluorescence emission spectra of the solution acquired over time at room temperature. (b) Fluorescence intensity at 378 nm as a function of time. The background fluorescence at the start of the monitoring experiment (resulting from the release of hydroxycoumarin cargo during ultrasonication) was subtracted from each measurement. λ_{ex} = 330 nm.

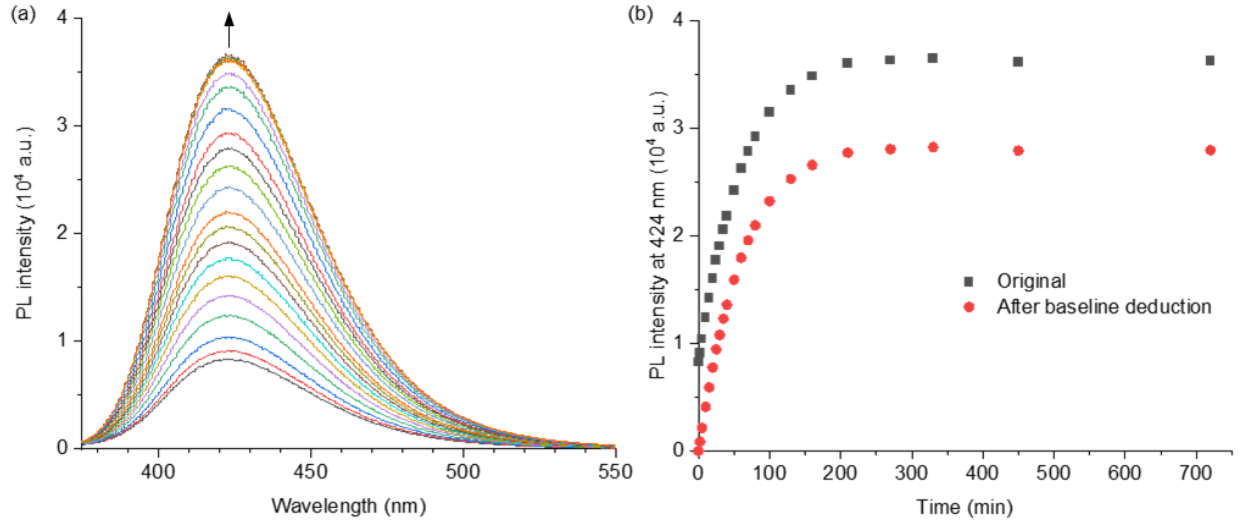


Figure S12. Characterization of aminocoumarin release from a 2.0 mg/ml solution of **PMA-1(NH)** in 3:1 MeCN/MeOH immediately after ultrasonication for 60 min. (a) Fluorescence emission spectra of the solution acquired over time at room temperature. (b) Fluorescence intensity at 424 nm as a function of time. The background fluorescence at the start of monitoring experiment (resulting from the release of aminocoumarin cargo during ultrasonication) was subtracted from each measurement. λ_{ex} = 365 nm.

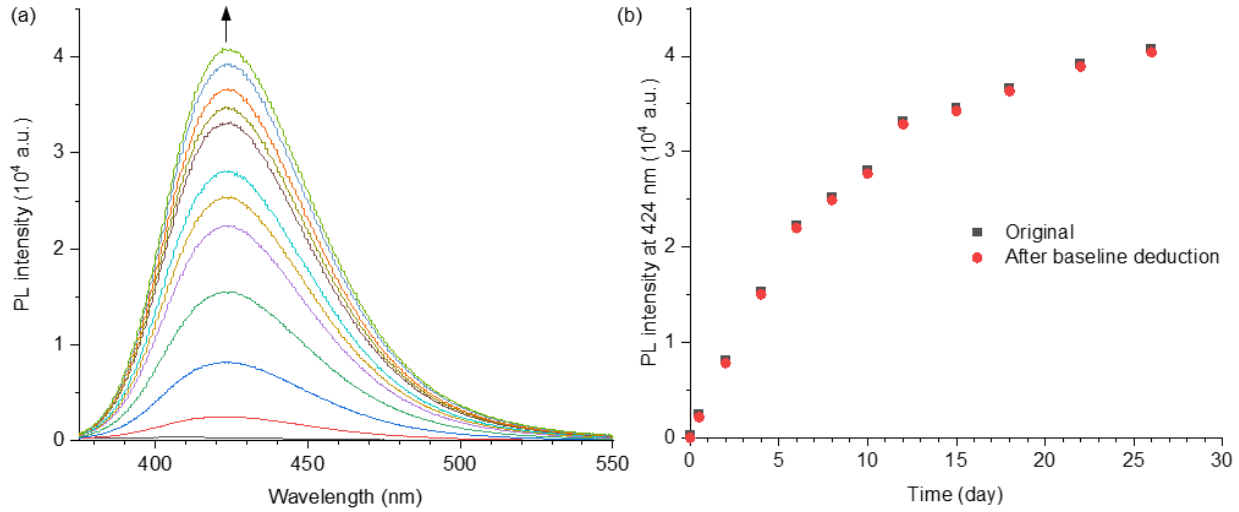


Figure S13. Characterization of aminocoumarin release from a 2.0 mg/ml solution of **PMA-2(NH)** in 3:1 MeCN/MeOH immediately after ultrasonication for 60 min. (a) Fluorescence emission spectra of the solution acquired over time at room temperature. (b) Fluorescence intensity at 424 nm as a function of time. The background fluorescence at the start of monitoring experiment (resulting from the release of aminocoumarin cargo during ultrasonication) was subtracted from each measurement. λ_{ex} = 365 nm.

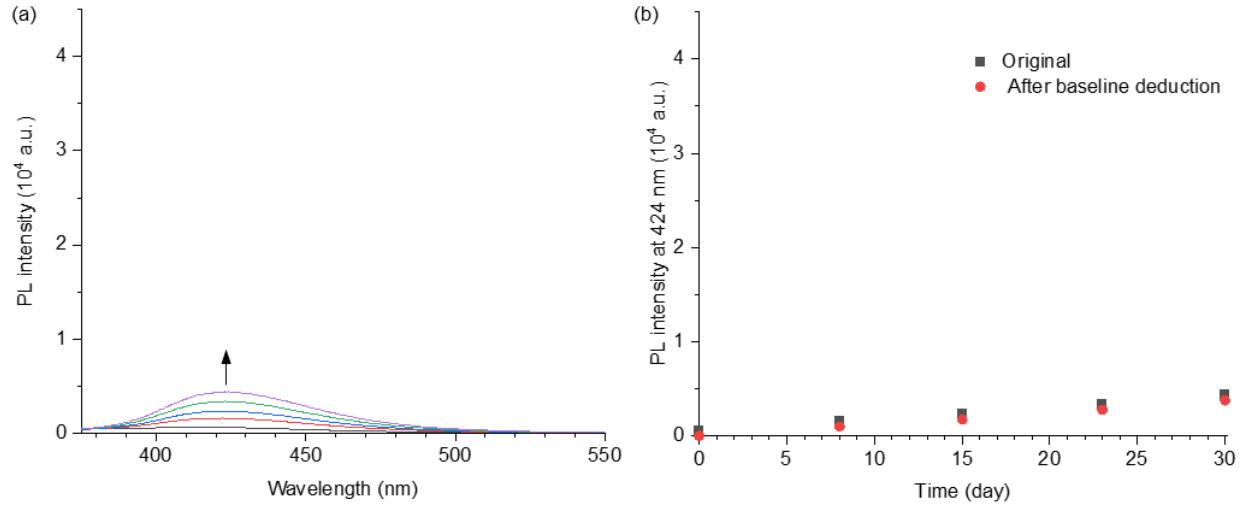


Figure S14. Characterization of aminocoumarin release from a 2.0 mg/ml solution of **PMA-3(NH)** in 3:1 MeCN/MeOH immediately after ultrasonication for 60 min. (a) Fluorescence emission spectra of the solution acquired over time at room temperature. (b) Fluorescence intensity at 424 nm as a function of time. The background fluorescence at the start of monitoring experiment (resulting from the release of aminocoumarin cargo during ultrasonication) was subtracted from each measurement. Assuming 36% mechanophore activation, the total concentration of aminocoumarin released is calculated to be 7.6 μM. The expected PL intensity from a 7.6 μM solution of aminocoumarin **3** is approximately 4.09 x 10^4 based on the calibration curve in Figure S9. λ_{ex} = 365 nm.

VI. Characterization of Molecular Release Using HPLC and LCMS

Calculation of Relative Response Factors (RRF). A standard solution with known concentrations of the internal standard (IS) molecule and the small molecule analyte was prepared and analyzed by HPLC equipped with a UV detector. The RRF is calculated from the HPLC results of the standard solution using the following equation:

$$RRF = \frac{Response\ Factor\ of\ the\ analyte}{Response\ Factor\ of\ the\ IS} = \left(\frac{Peak\ Area\ of\ the\ analyte}{Concentration\ of\ the\ analyte}\right)/\left(\frac{Peak\ Area\ of\ the\ IS}{Concentration\ of\ the\ IS}\right)$$

Table S4. Determination of relative response factors (RRF)

Entry	Payload	Internal Standard (IS)	Payload Peak Area (%)	IS Peak Area (%)	[Payload] (μM)	[IS] (μM)	RRF
1	7-Hydroxy-4-methyl-coumarin	3-Cyano-7-hydroxy-4-methylcoumarin	68.5	31.5	158	126	1.74
2	1-Pyrenebutanol	1-Pyrenebutanoic acid	43.0	57.0	59.3	79.5	1.01
3	7-Amino-4-methylcoumarin	Quinoline	45.5	54.5	100	400	3.32
4	1-Pyrenemethylamine hydrochloride	4-Methyl-7-hydroxycoumarin	69.6	30.4	67.2	112	3.82
5	1-Pyrenebutanoic acid	1-Pyrenebutanol	57.0	43.0	79.5	59.3	0.989
6	Naphthalene-2-sulfonic acid	7-hydroxy-4-methylcoumarin	59.4	40.6	600	336	0.819

Determination of the concentration of released payload molecules from polymers after ultrasound-induced mechanical activation. After 60 min of ultrasonication, a known concentration of internal standard (IS) was added into the solution of sonicated polymer. The solution was then kept at room temperature and analyzed by HPLC at various time intervals. The concentration of the released payload molecule (the analyte) in the solution was calculated using the following relationship:

$$Concentration\ of\ analyte = \frac{Peak\ area\ of\ analyte}{Peak\ area\ of\ IS} * \frac{1}{RRF} * Concentration\ of\ IS$$

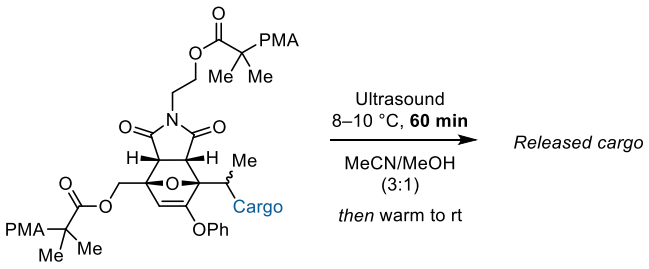
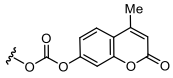
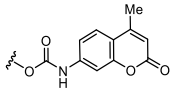
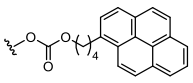
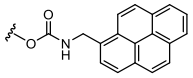
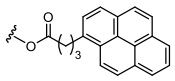
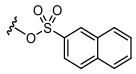


Table S5. Characterization of mechanically triggered payload release from polymers with a chain-centered second-generation mechanophore.

Cargo	M_n (kg/mol)	[Polymer] (mg/mL)	[Polymer] (μM)	Half-Life	[Released Payload][a] (μM)	Ultimate Payload Release[a]
	99.8	2.0	20	< 5 min[b]	7.26	36%
	99.0	2.0	20	41 min[b]	6.91	34%
	99.2	2.0	20	< 30 min	6.67	33%
	106	2.0	19	4.2 h	1.46	8%
	114	2.0	17	28 h	7.14	41%
	108	2.0	19	< 30 min	7.62	41%

[a]Average of two replicate experiments determined by HPLC. [b]Half-lives for the release of hydroxycoumarin and aminocoumarin are from photoluminescence measurements, with all others from HPLC measurements.

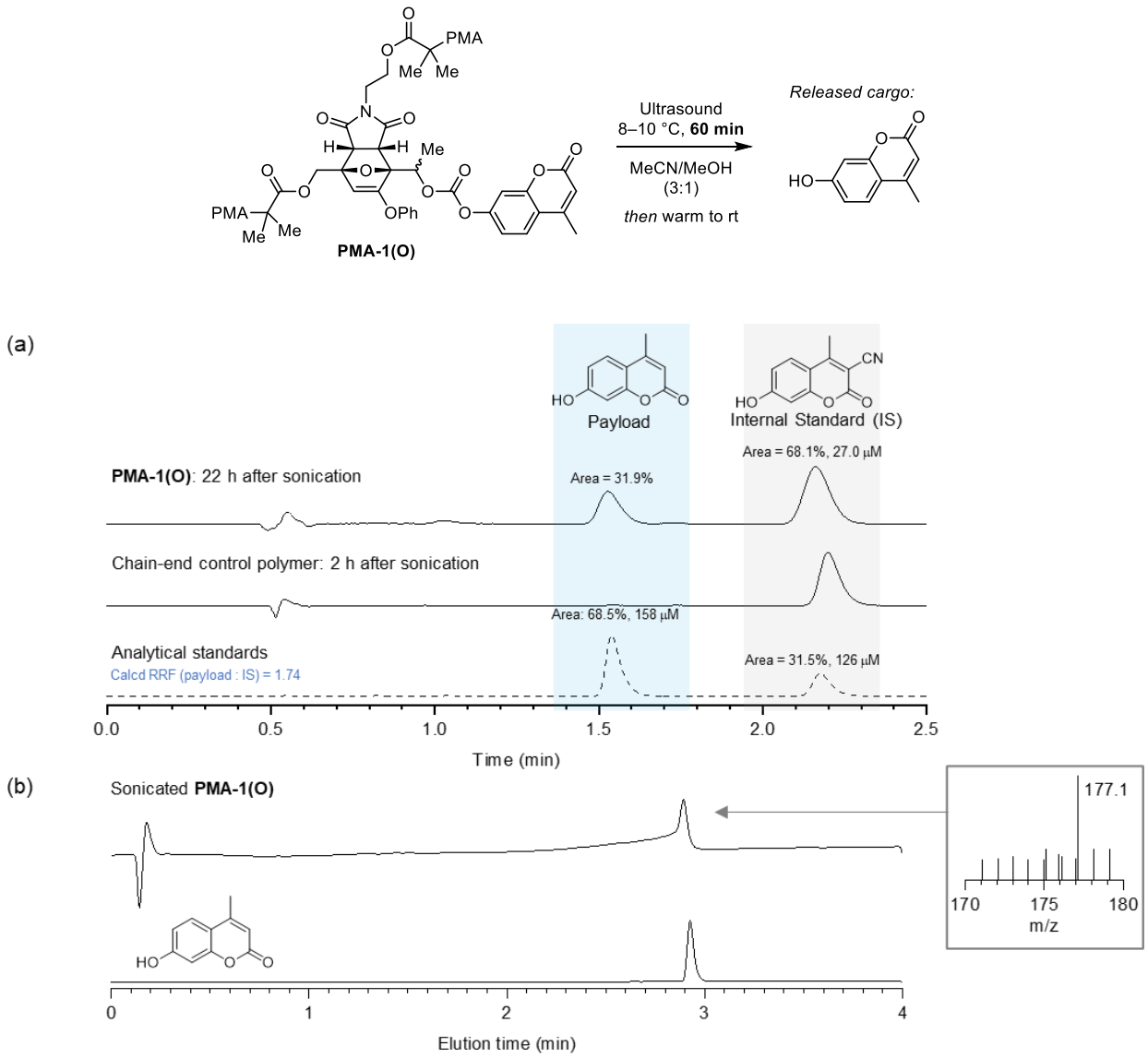


Figure S15. (a) Representative HPLC chromatograms for the analysis of mechanically triggered molecular release of hydroxycoumarin from the polymer containing a chain-centered mechanophore, and a chain-end control polymer (30:70 MeCN/water (with 0.1% acetic acid) isocratic, 2 ml/min, λ = 320 nm). (b) LCMS measurements further support the identity of the released molecule. The mass of the analyte (*m/z* = 177.1 amu) matches the calculated *m/z* for 7-hydroxy-4-methylcoumarin, $[C_{10}H_9O_3]^+$ $(M+H)^+$ (177.1). LCMS conditions: positive ion mode, 4 min (0–30% MeCN in water).

Table S6. Release of 7-hydroxy-4-methylcoumarin payload monitored by HPLC[a]

Trial 1				Trial 2			
Time Post-Sonication	Payload Peak Area (%)	IS Peak Area (%)	Released Payload, Calcd (μM)	Time Post-Sonication	Payload Peak Area (%)	IS Peak Area (%)	Released Payload, Calcd (μM)
22 h	31.9	68.1	7.27	22 h	31.9	68.2	7.25

[a]IS: 3-Cyano-7-hydroxy-4-methylcoumarin (27.0 μM). RRF = 1.74.

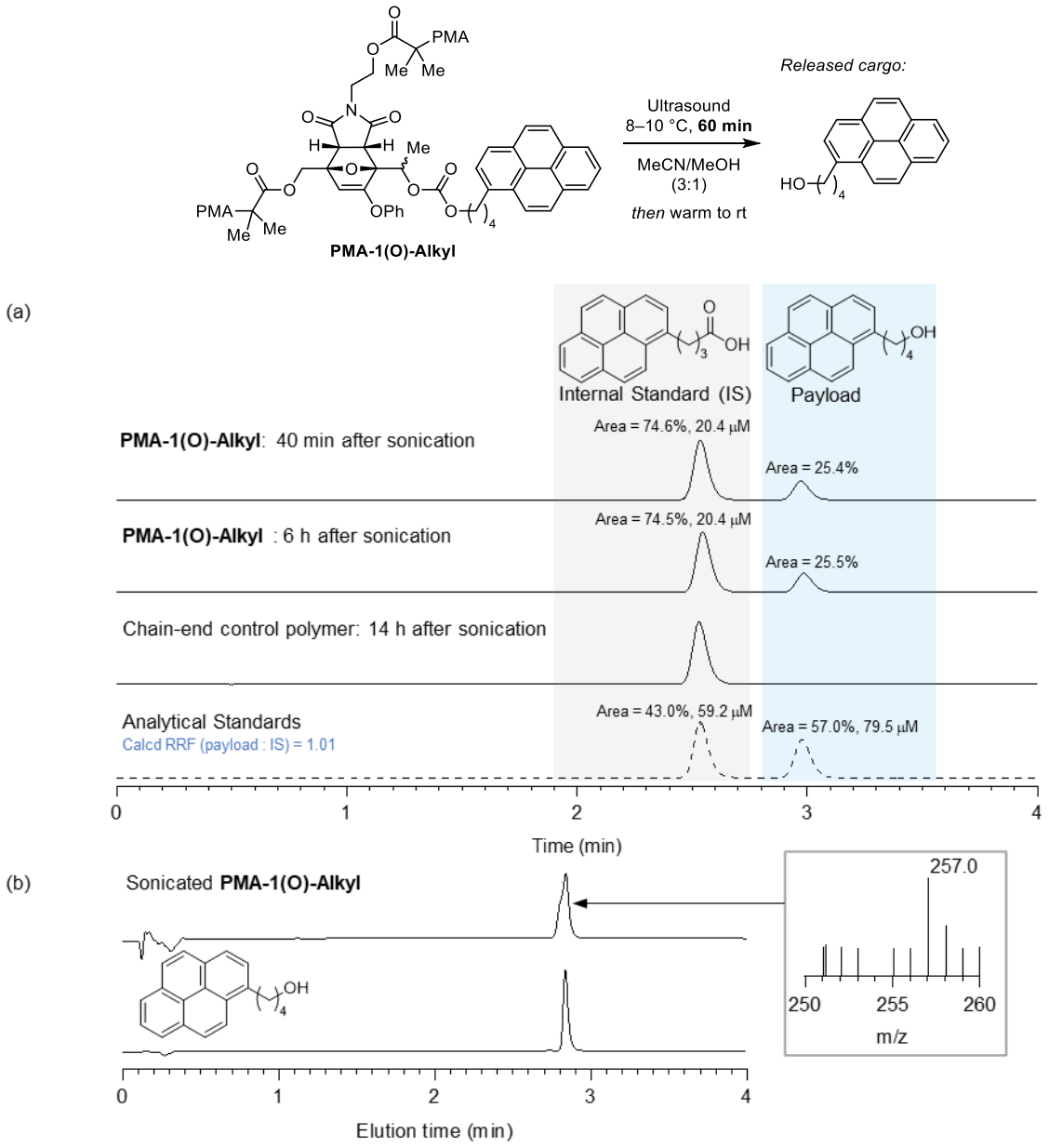


Figure S16. (a) Representative HPLC chromatograms for the analysis of mechanically triggered molecular release of 1-pyrenebutanol from the polymer containing a chain-centered mechanophore, and a chain-end control polymer (60:40 MeCN/water (with 0.1% acetic acid) isocratic, 2 ml/min, λ = 340 nm). (b) LCMS measurements further support the identity of the released molecule. The mass of the analyte (*m/z* = 257.0 amu) matches the calculated *m/z* for 1-pyrenebutanol, $[C_{20}H_{17}]^+$ $(M-OH)^+$(257.1). LCMS conditions: positive ion mode, 4 min (25–75% MeCN in water).

Table S7. Release of 1-pyrenebutanol payload monitored by HPLC [a]

Trial 1				Trial 2			
Time Post-Sonication	Payload Peak Area (%)	IS Peak Area (%)	Released Payload, Calcd (μM)	Time Post-Sonication	Payload Peak Area (%)	IS Peak Area (%)	Released Payload, Calcd (μM)
40 min	25.4	74.6	6.88	1 h	24.0	76.0	6.39
6 h	25.5	74.5	6.91	2 h	24.2	75.8	6.44

[a]IS: 1-Pyrenebutyric acid (20.4 μM). RRF = 1.01.

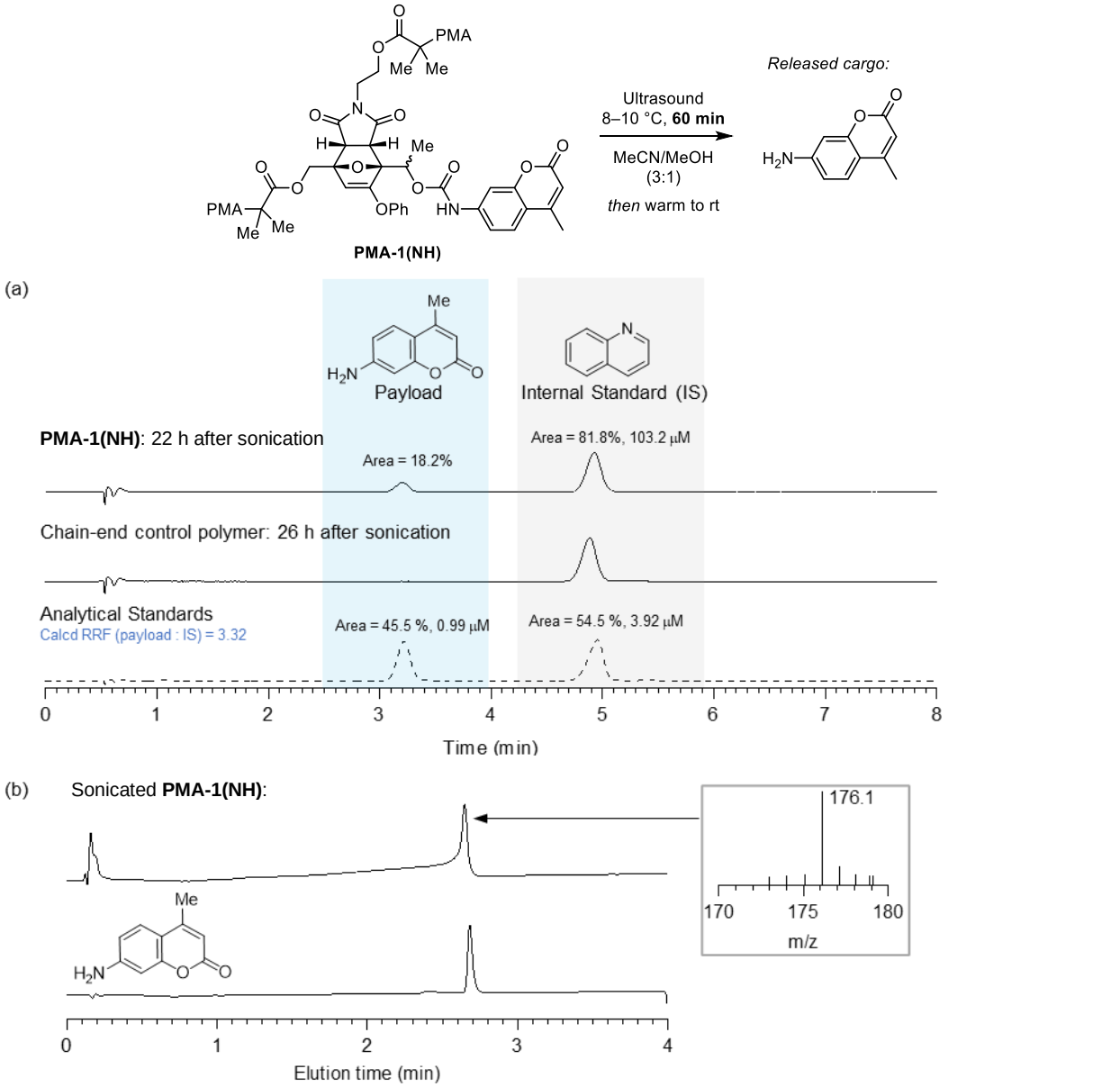


Figure S17. (a) Representative HPLC chromatograms for the analysis of mechanically triggered molecular release of aminocoumarin from the polymer containing a chain-centered mechanophore, and a chain-end control polymer (20:80 MeCN/water (with 0.1% acetic acid) isocratic, 2 ml/min, λ = 315 nm). (b) LCMS measurements further support the identity of the released molecule. The mass of the analyte (*m/z* = 176.1 amu) matches the calculated *m/z* for 7-amino-4-methylcoumarin, $[C_{10}H_{10}NO_2]^+$ $(M+H)^+$ (176.1). LCMS conditions: positive ion mode, 4 min (0–30% MeCN in water).

Table S8. Release of 7-amino-4-methylcoumarin payload monitored by HPLC [a]

Trial 1				Trial 2			
Time Post-Sonication	Payload Peak Area (%)	IS Peak Area (%)	Released Payload, Calcd (μM)	Time Post-Sonication	Payload Peak Area (%)	IS Peak Area (%)	Released Payload, Calcd (μM)
22 h	18.2	81.8	6.90	22 h	18.2	81.8	6.93

[a]IS: Quinoline (103.2 μM). RRF = 3.32.

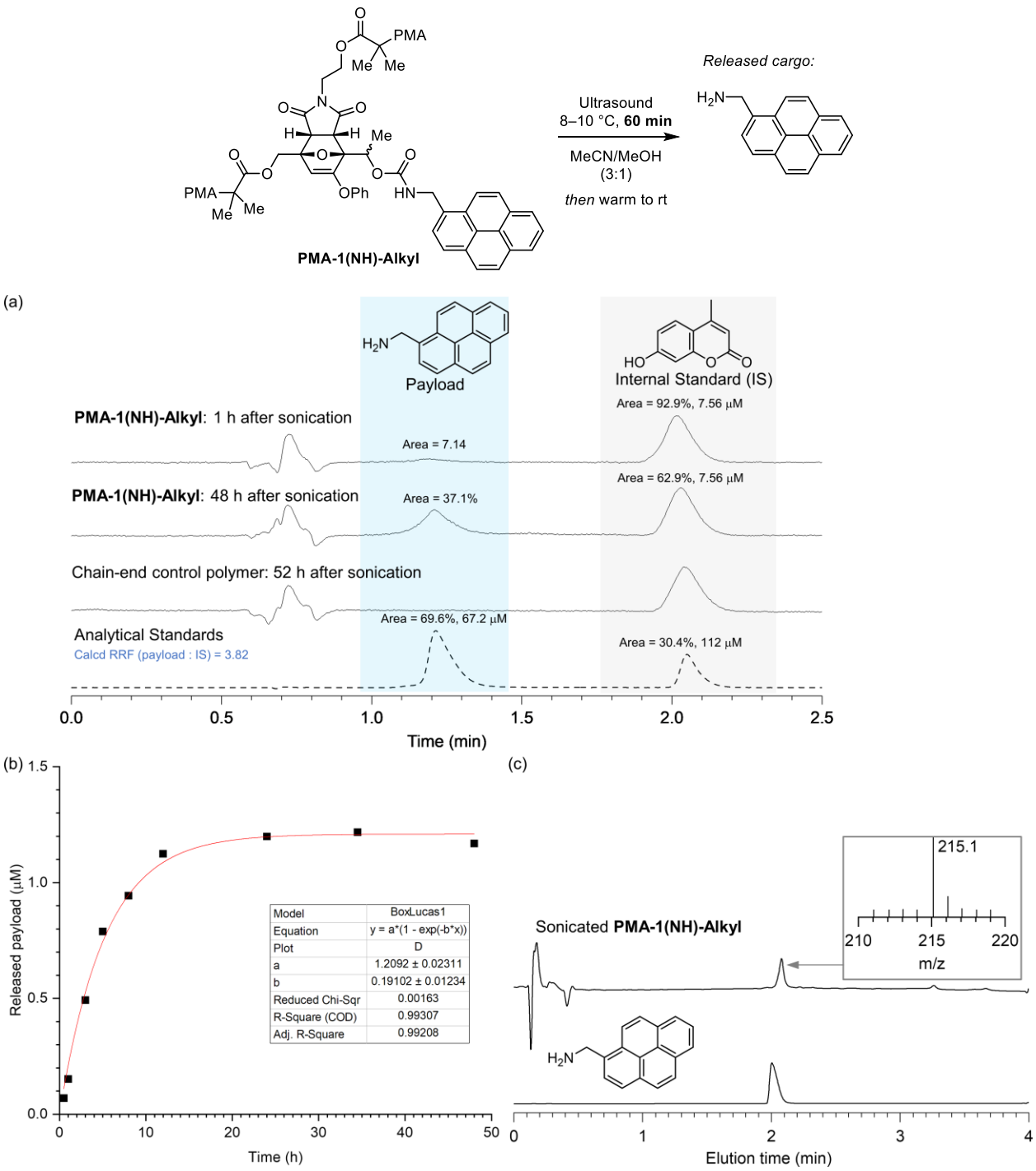


Figure S18. (a) Representative HPLC chromatograms for the analysis of mechanically triggered molecular release of 1-pyrenemethylamine from the polymer containing a chain-centered mechanophore, and a chain-end control polymer (30:70 MeCN/water (with 0.1% acetic acid) isocratic, 1.5 ml/min, λ = 340 nm). (b) Payload release from sonicated **PMA-1(NH)-Alkyl** as a function of time post-sonication. (c) LCMS measurements further support the identity of the released molecule. The mass of the analyte (*m/z* = 215.1 amu) matches the calculated *m/z* for 1-pyrenemethylamine, $[C_{17}H_{11}]^+$ $(M-NH_2)^+$ (215.1). LCMS conditions: positive ion mode, 4 min (5–50% MeCN in water).

Table S9. Release of 1-pyrenemethylamine payload monitored by HPLC [a]

Trial 1				Trial 2			
Time Post-Sonication	Payload Peak Area (%)	IS Peak Area (%)	Released Payload, Calcd (μM)	Time Post-Sonication	Payload Peak Area (%)	IS Peak Area (%)	Released Payload, Calcd (μM)
0.5	3.40	96.6	0.0697	1	7.28	92.7	0.155
1	7.14	92.9	0.152	3	17.7	82.3	0.425
3	19.9	80.1	0.492	6	31.7	68.3	0.920
5	28.5	71.5	0.788	9.5	39.3	60.7	1.28
8	32.3	67.7	0.943	21	45.1	54.9	1.63
12	36.2	63.8	1.12	31.5	46.2	53.8	1.70
24	37.7	62.3	1.20	45	45.1	54.9	1.63
34.5	38.1	61.9	1.22	Plateau value: 1.71 μM; $t_{1/2}$ = 5.4 h			
48	37.1	62.9	1.17				
Plateau value: 1.21 μM; $t_{1/2}$ = 3.6 h							

[a]IS: 4-Methyl-7-hydroxycoumarin (7.56 μM). RRF = 3.82.

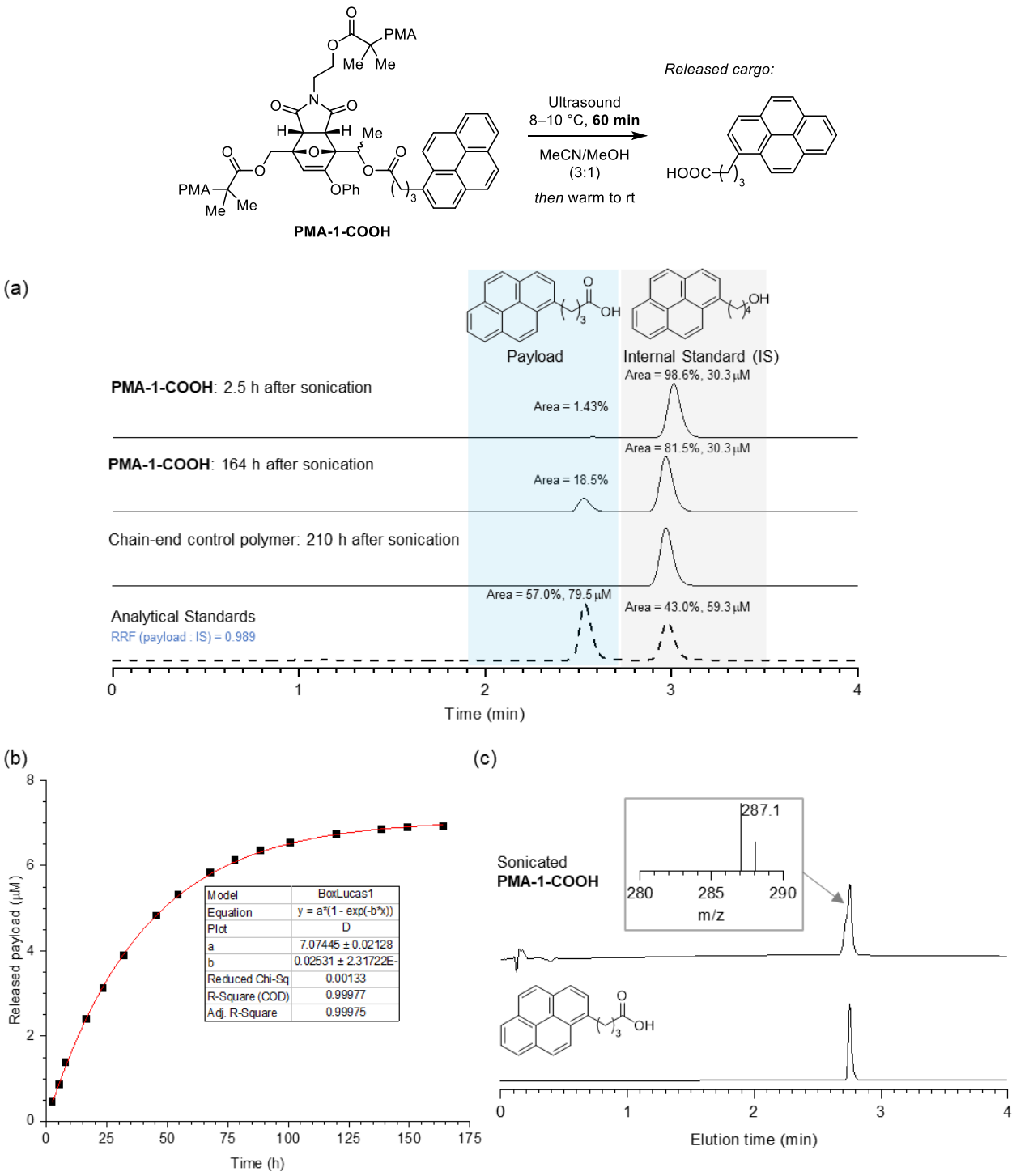


Figure S19. (a) Representative HPLC chromatograms for the analysis of mechanically triggered molecular release of 1-pyrenebutanoic acid from the polymer containing a chain-centered mechanophore, and a chain-end control polymer (60:40 MeCN/water (with 0.1% acetic acid) isocratic, 2 ml/min, λ = 340 nm). (b) Payload release from sonicated **PMA-1-COOH** as a function of time post-sonication. (c) LCMS measurements further support the identity of the released molecule. The mass of the analyte (*m/z* = 287.1 amu) matches the calculated *m/z* for 1-pyrenebutanoic acid $[C_{20}H_{15}O_2]^-$ $(M-H)^-$ (287.1). LCMS conditions: negative ion mode, 4 min (0–100% MeCN in water).

Table S10. Release of 1-pyrenebutanoic acid payload monitored by HPLC[a]

Trial 1				Trial 2			
Time Post-Sonication	Payload Peak Area (%)	IS Peak Area (%)	Released Payload, Calcd (μM)	Time Post-Sonication	Payload Peak Area (%)	IS Peak Area (%)	Released Payload, Calcd (μM)
2.5	1.43	98.6	0.443	2	0.739	99.3	0.228
5.5	2.75	97.3	0.866	5.5	2.58	97.4	0.811
8	4.30	95.7	1.37	14	6.09	93.9	1.99
16.5	7.27	92.7	2.40	21	8.35	91.7	2.79
23.5	9.25	90.8	3.12	27.5	10.6	89.4	3.63
32	11.3	88.7	3.89	43	13.2	86.9	4.63
45.5	13.6	86.4	4.83	52	14.4	85.6	5.17
54.5	14.8	85.2	5.32	65.5	15.9	84.1	5.77
68	16.0	84.0	5.83	75.5	16.5	83.5	6.07
78	16.7	83.3	6.13	98	17.6	82.4	6.54
88.5	17.2	82.8	6.35	117.5	18.1	81.9	6.75
101	17.6	82.4	6.53	136	18.4	81.6	6.91
120	18.0	82.0	6.74	147	18.6	81.4	6.97
138.5	18.3	81.7	6.85	Plateau value: 7.20 μM; $t_{1/2}$ = 28.6 h			
149.5	18.4	81.6	6.90				
164	18.5	81.5	6.92				
Plateau value: 7.07 μM; $t_{1/2}$ = 27.4 h							

[a]IS: 1-Pyrenebutanol (30.3 mM). RRF = 0.989.

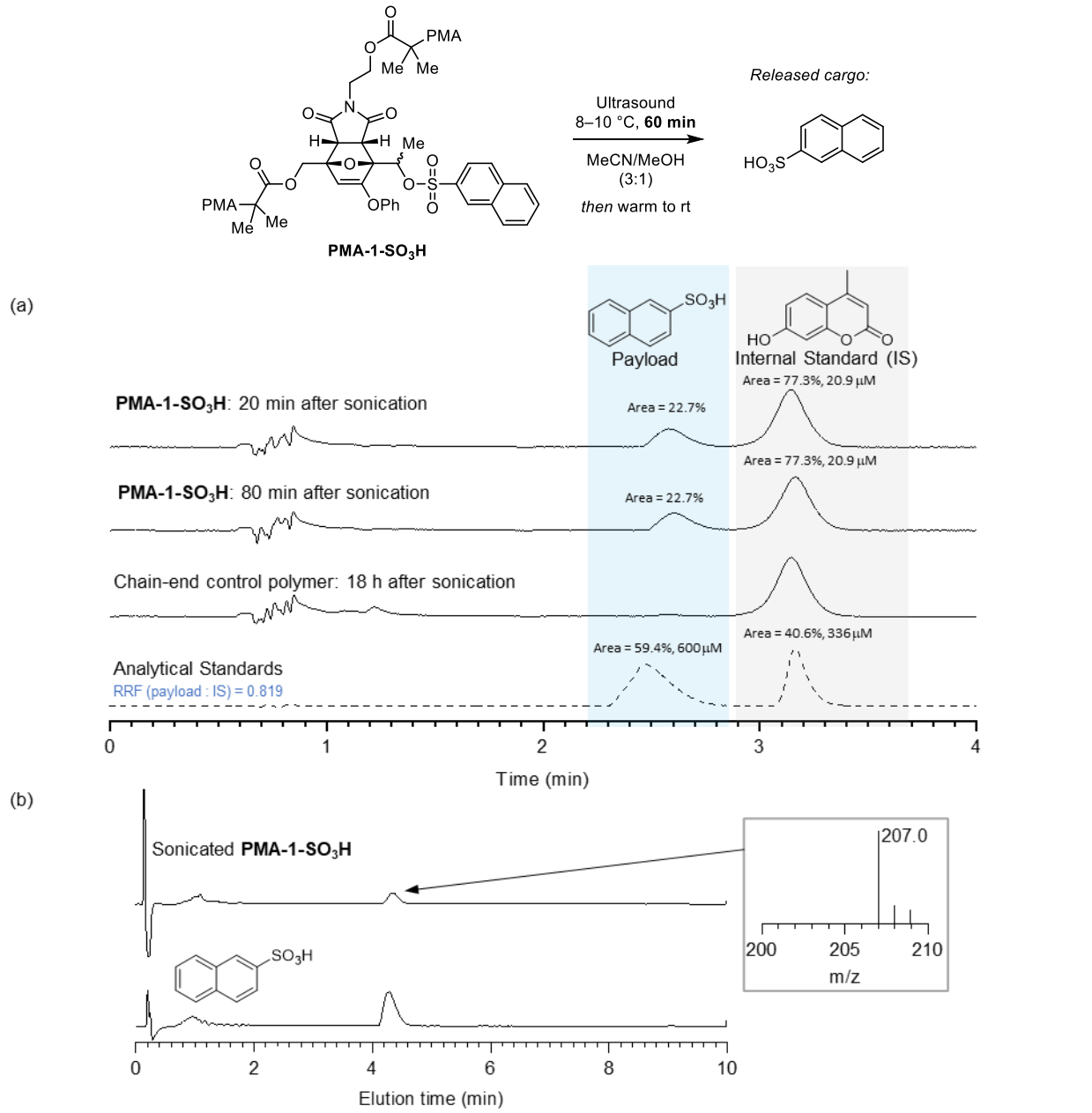


Figure S20. (a) Representative HPLC chromatograms for the analysis of mechanically triggered molecular release of 2-naphthalenesulfonic acid from the polymer containing a chain-centered mechanophore, and a chain-end control polymer (40:60 MeOH/water (with 0.1% acetic acid) isocratic, 1.5 ml/min, λ = 280 nm). (b) LCMS measurements further support the identity of the released molecule. The mass of the analyte (*m/z* = 207.0 amu) matches the calculated *m/z* for 2-naphthalenesulfonic acid, $[C_{10}H_7O_3S]^-$ $(M-H)^-$ (207.0). LCMS conditions: negative ion mode, 10 min (0–30% MeCN in water).

Table S11. Release of 2-naphthalenesulfonic acid payload monitored by HPLC[a]

Trial 1				Trial 2			
Time Post-Sonication	Payload Peak Area (%)	IS Peak Area (%)	Released Payload, Calcd (μM)	Time Post-Sonication	Payload Peak Area (%)	IS Peak Area (%)	Released Payload, Calcd (μM)
20 min	22.7	77.3	7.49	1 h	23.0	77.0	7.61
80 min	22.7	77.3	7.49	2 h	23.0	77.0	7.60

[a]IS: 7-hydroxy-4-methylcoumarin (20.9 μM). RRF = 0.818.

VII. DFT Calculations

CoGEF calculations. CoGEF calculations were performed using Spartan '18 Parallel Suite according to previously reported methods.[6,7] Ground state energies were calculated using DFT at the B3LYP/6-31G* level of theory. Starting from the equilibrium geometry of the unconstrained molecule (relative energy = 0 kJ/mol), the distance between the terminal methyl groups of the truncated structure was increased in increments of 0.05 Å and the energy was minimized at each step. The maximum force associated with the retro-Diels–Alder reaction was calculated from the slope of the curve immediately prior to bond cleavage.

Calculation of Activation Energies. Activation energies for model furfuryl carbonate and carbamate compounds were calculated using Spartan '18 Parallel Suite following our previous methods.[3] All calculations were run with a solvent dielectric constant of 37.22. Equilibrium geometries and corresponding energies of each furfuryl carbonate or carbamate reactant were calculated at the M06-2X/6-311+G** level of theory with a fine integration grid (99,590). Transition state geometries were approximated using an initial energy profile at the HF/6-31+G* level of theory by lengthening the C–O bond involved in the desired fragmentation reaction. The energy maximum from each profile was then chosen as the starting point for a transition state geometry optimization, which was conducted at the same level of theory. Subsequent geometry optimizations were performed at the M06-2X/6-311+G** level of theory and the optimized structures were subjected to a final energy and frequency calculation at the M06-2X/6-311+G** level of theory using a fine integration grid (99,590). Each structure returned a single imaginary vibrational frequency corresponding to the expected bond-breaking mode.

<u>Optimized geometry coordinates determined for reactants:</u>

FC1(O)

C	0.335401	-0.39409	-3.18552
C	0.236203	-1.56517	-2.50619
C	-0.45764	-1.24826	-1.29352
C	-0.73207	0.081323	-1.30961
O	-0.24994	0.605243	-2.47269
C	0.924145	-0.02343	-4.49668
O	-0.81573	-2.14637	-0.32556
C	0.070732	-2.38063	0.705027
C	-0.33455	-3.32886	1.642275
C	0.489448	-3.61439	2.722699
C	1.712793	-2.96042	2.871346
C	2.101916	-2.01677	1.927389
C	1.285672	-1.7161	0.837118
C	-1.39205	1.026535	-0.37406
O	-0.32675	1.863856	0.165311
C	-0.67781	3.079916	0.572979
O	0.399419	3.689141	1.0482
O	-1.78488	3.553984	0.518142

C	0.189318	5.025912	1.531968
C	-2.13177	0.349564	0.764796
H	0.60007	-2.53165	-2.81771
H	1.706726	0.727889	-4.36938
H	1.356908	-0.90725	-4.96348
H	0.160246	0.388296	-5.16009
H	-1.28884	-3.82525	1.510777
H	0.173572	-4.35114	3.45215
H	2.352992	-3.18492	3.715752
H	3.049744	-1.50156	2.032154
H	1.593831	-0.97644	0.108789
H	-2.06048	1.67908	-0.93943
H	-0.17344	5.661814	0.72544
H	1.162265	5.363654	1.87625
H	-0.52576	5.016412	2.353577
H	-1.43954	-0.22204	1.385155
H	-2.61872	1.106653	1.379598
H	-2.89146	-0.32453	0.367011

Gibbs free energy: -957.001799 hartrees

FC2(O)

C	-0.0126	-0.71797	-3.65067
C	-0.23516	-1.76005	-2.80568
C	0.367885	-1.38183	-1.56649
C	0.919415	-0.15152	-1.73336
C	0.676346	0.261869	-3.01099
C	-0.36334	-0.47148	-5.0718
C	0.412844	-2.15599	-0.44165
C	-0.08769	-1.63616	0.738727
C	0.43286	-2.17122	1.912944
C	-0.05086	-1.7253	3.137483
C	-1.0455	-0.75062	3.190608
C	-1.56017	-0.23092	2.006304
C	-1.08974	-0.67107	0.771124
C	1.632309	0.751269	-0.80947
C	0.697338	1.713465	-0.26162
C	0.743066	1.921619	1.052159
C	-0.24386	2.745936	1.374596
C	1.545264	1.453884	1.819933
C	-0.33222	3.082854	2.768416
C	-0.75353	-2.67874	-3.02983
C	-0.91895	-1.32311	-5.46196
C	-0.97904	0.425663	-5.16684
C	0.537941	-0.33235	-5.67307
C	1.209883	-2.9239	1.85101

C	0.357167	-2.13821	4.052661
C	-1.41619	-0.39977	4.146359
C	-2.33781	0.524231	2.035867
C	-1.49307	-0.26557	-0.14889
C	2.410755	1.312414	-1.32702
C	2.074309	0.17663	0.003448
C	0.574971	3.595552	3.086212
H	-1.19223	3.7408	2.851889
H	-0.48039	2.179617	3.359585

C	-0.0126	-0.71797	-3.65067
C	-0.23516	-1.76005	-2.80568
C	0.367885	-1.38183	-1.56649
C	0.919415	-0.15152	-1.73336
C	0.676346	0.261869	-3.01099
C	-0.36334	-0.47148	-5.0718
C	0.412844	-2.15599	-0.44165
C	-0.08769	-1.63616	0.738727
C	0.43286	-2.17122	1.912944
C	-0.05086	-1.7253	3.137483
C	-1.0455	-0.75062	3.190608
C	-1.56017	-0.23092	2.006304
C	-1.08974	-0.67107	0.771124
C	1.632309	0.751269	-0.80947
C	0.697338	1.713465	-0.26162
C	0.743066	1.921619	1.052159
C	-0.24386	2.745936	1.374596
C	1.545264	1.453884	1.819933
C	-0.33222	3.082854	2.768416
C	-0.75353	-2.67874	-3.02983
C	-0.91895	-1.32311	-5.46196
C	-0.97904	0.425663	-5.16684
C	0.537941	-0.33235	-5.67307
C	1.209883	-2.9239	1.85101
C	0.357167	-2.13821	4.052661
C	-1.41619	-0.39977	4.146359
C	-2.33781	0.524231	2.035867
C	-1.49307	-0.26557	-0.14889
C	2.410755	1.312414	-1.32702
C	2.074309	0.17663	0.003448
C	0.574971	3.595552	3.086212
H	-1.19223	3.7408	2.851889
H	-0.48039	2.179617	3.359585

Gibbs free energy: -917.719607 hartrees

FC3(O)

C	0.625870	0.060233	-3.079388
C	-0.637531	-0.421937	-2.982456
C	-0.958334	-0.466695	-1.578856
C	0.141027	-0.011012	-0.934275
O	1.112139	0.314046	-1.827252
C	0.489080	0.196547	0.504506
O	-0.676679	-0.235035	1.232016
C	-0.838989	0.275808	2.450477
O	-1.929208	-0.255985	2.982270
O	-0.120637	1.085376	2.979217
C	-2.251437	0.195065	4.308507
C	1.709154	-0.601630	0.937563
C	1.534882	0.347566	-4.218350
H	-1.267337	-0.711777	-3.809040
H	-1.876857	-0.792916	-1.118582
H	0.643752	1.260760	0.698978
H	-3.160018	-0.334074	4.579274
H	-2.420655	1.270945	4.304919
H	-1.442508	-0.055861	4.993306
H	1.532383	-1.666656	0.776346
H	1.923473	-0.420230	1.991323
H	2.572651	-0.292093	0.347233
H	1.031381	0.101527	-5.152617
H	1.814767	1.403443	-4.238781
H	2.449632	-0.245416	-4.146337

Gibbs free energy: -650.852643 hartrees

FC4(O)

C	0.019327	0.000000	-3.098191
C	1.307178	0.000000	-2.674464
C	1.271559	0.000000	-1.234255
C	-0.039456	0.000000	-0.899003
O	-0.814993	0.000000	-2.014158
C	-0.782857	0.000000	0.391271
O	0.204520	0.000000	1.425364
C	-0.275829	0.000000	2.667298
O	0.743286	0.000000	3.510586
O	-1.443069	0.000000	2.963487
C	0.389766	0.000000	4.903960
C	-0.627821	0.000000	-4.434814
H	2.180755	0.000000	-3.307440

H	2.105893	0.000000	-0.551557
H	-1.413977	0.887720	0.482497
H	-1.413977	-0.887720	0.482497
H	-0.186149	0.893532	5.141647
H	1.334137	0.000000	5.439979
H	-0.186149	-0.893532	5.141647
H	0.139180	0.000000	-5.208646
H	-1.255662	-0.884678	-4.563854
H	-1.255662	0.884678	-4.563854

Gibbs free energy: -611.569904 hartrees

FC1(NH)

C	2.614270	1.251867	-0.701635
C	2.020212	1.386590	0.511024
C	1.293082	0.165899	0.717100
C	1.492973	-0.621366	-0.367825
O	2.312629	0.038678	-1.238426
C	3.489648	2.139563	-1.507909
C	1.051103	-1.996703	-0.721510
O	0.148483	-1.959470	-1.851308
C	-1.137529	-1.626294	-1.595609
N	-1.849568	-1.528391	-2.729890
O	-1.584150	-1.451184	-0.475904
C	-3.268369	-1.218032	-2.699580
C	2.199808	-2.901482	-1.132083
O	0.598545	-0.206605	1.833064
C	-0.437854	0.597911	2.258001
C	-0.869046	0.391946	3.566334
C	-1.928348	1.142216	4.061818
C	-2.553796	2.096680	3.260365
C	-2.112905	2.287915	1.954772
C	-1.054876	1.539719	1.440996
H	2.081052	2.238236	1.170495
H	3.670544	3.064841	-0.962532
H	3.019756	2.380297	-2.464243
H	4.447734	1.655934	-1.710794
H	0.517762	-2.405030	0.137274
H	-1.382059	-1.693908	-3.608075
H	-3.443074	-0.238163	-2.249349
H	-3.635325	-1.208763	-3.723853
H	-3.817474	-1.970813	-2.129989
H	2.710287	-2.495218	-2.006751

H	2.914561	-2.977875	-0.311445
H	1.821299	-3.896461	-1.367949
H	-0.369580	-0.352657	4.174989
H	-2.263708	0.981404	5.079895
H	-3.376934	2.682960	3.650480
H	-2.595031	3.022586	1.320203
H	-0.724125	1.683174	0.419848

Gibbs free energy: -937.132509 hartrees

FC2(NH)

C	-1.217557	2.869436	-0.440392
C	-1.249325	2.332535	0.806319
C	-1.304644	0.913607	0.607359
C	-1.303834	0.683237	-0.727818
O	-1.258612	1.882963	-1.376630
C	-1.159268	4.265193	-0.942089
C	-1.343720	-0.556118	-1.528120
O	-0.029288	-0.776100	-2.075391
C	0.092220	-1.868366	-2.861545
N	1.337563	-1.989755	-3.346870
O	-0.827367	-2.634186	-3.092310
C	1.705631	-3.111863	-4.192937
O	-1.417788	-0.051035	1.568777
C	-0.364058	-0.212281	2.445770
C	0.915337	0.270436	2.190755
C	1.923089	0.031953	3.123990
C	1.660814	-0.680667	4.289272
C	0.373021	-1.161997	4.524130
C	-0.643290	-0.929312	3.606547
H	-1.231873	2.867410	1.743019
H	-1.134116	4.953509	-0.098347
H	-2.033507	4.491451	-1.556648
H	-0.265303	4.419260	-1.550579
H	-1.621051	-1.393204	-0.886232
H	-2.061345	-0.475712	-2.346497
H	2.031437	-1.313363	-3.066944
H	1.606006	-4.057924	-3.657047
H	2.741912	-2.981632	-4.496206
H	1.075713	-3.142466	-5.083141
H	1.126337	0.819654	1.281379
H	2.920909	0.407636	2.929109
H	2.450422	-0.860420	5.008695

H	0.156045	-1.719012	5.428180
H	-1.650512	-1.292867	3.772442

Gibbs free energy: -897.85118 hartrees

FC3(NH)

C	-0.14632	0.75383	-3.19103
C	0.149257	-0.56713	-3.11736
C	0.223819	-0.89808	-1.71705
C	-0.03889	0.250451	-1.04999
O	-0.26377	1.263924	-1.92816
C	-0.35502	1.701803	-4.31512
C	-0.12309	0.614614	0.397898
C	0.851048	1.720277	0.780174
O	0.182658	-0.59323	1.106562
C	-0.30892	-0.70176	2.362818
O	-1.03437	0.128071	2.881406
N	0.104248	-1.83601	2.947719
C	-0.31621	-2.1813	4.294644
H	0.300978	-1.22713	-3.95723
H	0.438902	-1.85623	-1.27253
H	-1.36053	2.127904	-4.28518
H	0.363756	2.523499	-4.27193
H	-0.22695	1.175205	-5.2603
H	-1.14491	0.915417	0.642597
H	1.874055	1.405112	0.564994
H	0.755819	1.950729	1.841954
H	0.629335	2.620664	0.205241
H	0.699143	-2.45925	2.423291
H	-0.01651	-1.40802	5.003086
H	0.161601	-3.11836	4.568554
H	-1.39913	-2.30502	4.344942

Gibbs free energy: -630.983099 hartrees

FC4(NH)

C	0.190223	2.435073	-1.73503
C	-0.90683	3.030603	-1.19952
C	-1.63723	1.999703	-0.51581
C	-0.92917	0.857074	-0.68616
O	0.185549	1.10827	-1.43024
C	1.331972	2.932498	-2.54445
C	-1.14436	-0.53902	-0.24425
O	-0.16014	-0.84466	0.761713
C	-0.17271	-2.11663	1.216285

N	0.785267	-2.32161	2.133624
O	-0.96796	-2.95781	0.834746
C	0.971277	-3.6271	2.743119
H	-1.16205	4.075331	-1.28316
H	-2.56325	2.094074	0.030074
H	2.278017	2.766998	-2.02376
H	1.212041	4.000585	-2.7221
H	1.379732	2.419134	-3.50758
H	-1.03062	-1.23859	-1.0745
H	-2.14548	-0.63976	0.176139
H	1.412444	-1.56292	2.353498
H	1.241321	-4.37464	1.994645
H	1.772839	-3.54908	3.474041
H	0.059113	-3.94754	3.248663

Gibbs free energy: -591.702026 hartrees

Optimized geometry coordinates determined for transition states:

FC1(O)‡

C	1.609469	0.919928	-2.17316
C	0.582814	1.520656	-1.48926
C	0.312769	0.663925	-0.39755
C	1.199656	-0.40086	-0.46659
O	1.984749	-0.22267	-1.5854
C	2.336252	1.318593	-3.40038
C	1.339531	-1.53123	0.339126
O	0.036612	-2.8206	-0.48551
C	-0.46033	-3.74259	0.246959
O	-0.03837	-3.691	1.540294
O	-1.2428	-4.61099	-0.12143
C	-0.54468	-4.70382	2.409973
O	-0.61964	0.764893	0.553868
C	-1.34774	1.957927	0.602319
C	-0.73805	3.10838	1.081743
C	-1.48991	4.277349	1.154901
C	-2.8257	4.27874	0.756578
C	-3.41589	3.109312	0.283577
C	-2.67374	1.932959	0.201412
C	2.566637	-2.37079	0.274622
H	0.097262	2.4471	-1.75028
H	1.932853	2.255217	-3.78046
H	3.399159	1.444871	-3.18217
H	2.23458	0.544243	-4.16402
H	0.79623	-1.49575	1.27569
H	-0.11243	-4.49844	3.3868

H	-1.63252	-4.65576	2.462309
H	-0.23977	-5.69201	2.064331
H	0.301542	3.081973	1.389586
H	-1.03038	5.185353	1.52768
H	-3.40669	5.19133	0.817177
H	-4.45469	3.108052	-0.0256
H	-3.10731	1.009789	-0.16514
H	2.409122	-3.31726	0.786095
H	2.874785	-2.54088	-0.75589
H	3.366586	-1.82595	0.787797

Gibbs free energy: -956.972698 hartrees

FC2(O)‡

C	1.479834	0.355767	-2.57038
C	0.816807	0.972953	-1.53791
C	1.104652	0.198095	-0.39388
C	1.927823	-0.85388	-0.79218
O	2.142784	-0.72517	-2.14981
C	1.583726	0.695847	-4.00725
C	2.439093	-1.94137	-0.10449
O	1.233276	-3.51758	-0.39017
C	0.074534	-3.45419	0.151199
O	-0.0721	-2.39408	0.98589
O	-0.84258	-4.24706	-0.02874
C	-1.33403	-2.26794	1.640038
O	0.762241	0.398889	0.877313
C	-0.31866	1.2326	1.154942
C	-0.13678	2.204044	2.126744
C	-1.21684	3.010387	2.476043
C	-2.45151	2.838972	1.855689
C	-2.6116	1.851441	0.885684
C	-1.54343	1.03388	0.530928
H	0.218448	1.8665	-1.60994
H	2.627411	0.880211	-4.27172
H	1.220408	-0.13608	-4.61462
H	0.994282	1.585183	-4.22112
H	3.244704	-2.50959	-0.54934
H	2.357451	-1.93365	0.973363
H	-1.25744	-1.37443	2.256569
H	-2.13598	-2.15026	0.910245
H	-1.53244	-3.1405	2.263187
H	0.833831	2.317593	2.594203
H	-1.08863	3.774543	3.233357
H	-3.28846	3.470032	2.12928
H	-3.57317	1.707848	0.407415

H	-1.65766	0.251005	-0.21055

Gibbs free energy: -917.685373 hartrees

FC3(O)‡

C	0.073604	-0.834324	-2.979311
C	-0.869568	-1.766528	-2.596366
C	-1.385115	-1.320899	-1.370519
C	-0.737277	-0.135217	-1.071603
O	0.160097	0.143795	-2.074375
C	-0.847487	0.729874	0.015097
O	0.581266	-0.098879	1.385189
C	0.270574	0.178566	2.584081
O	1.183177	-0.316826	3.475021
O	-0.706692	0.808274	2.988891
C	0.929207	-0.050229	4.853305
C	0.953177	-0.744765	-4.165913
C	-0.295783	2.103570	-0.005012
H	-1.136816	-2.651513	-3.151222
H	-2.143208	-1.784077	-0.755986
H	-1.637803	0.502012	0.720133
H	0.920061	1.023505	5.044726
H	1.743875	-0.518718	5.401374
H	-0.023924	-0.480650	5.162460
H	0.772576	-1.593836	-4.822418
H	0.756368	0.182168	-4.709369
H	2.000866	-0.742062	-3.856617
H	0.661026	2.146153	-0.523101
H	-0.210336	2.493176	1.006863
H	-1.011866	2.727429	-0.555329

Gibbs free energy: -650.817542 hartrees

FC4(O)‡

C	-0.089307	-0.457224	-2.978056
C	0.864223	-1.442826	-2.775394
C	1.473224	-1.149423	-1.554719
C	0.871185	0.006906	-1.068962
O	-0.094158	0.407101	-1.967838
C	1.059359	0.721824	0.094100
O	-0.324984	-0.112644	1.498072
C	-0.205194	0.480796	2.616311

O	-1.053341	-0.037013	3.555118
O	0.548098	1.407782	2.906643
C	-0.999200	0.559454	4.850452
C	-1.042407	-0.221496	-4.083352
H	1.070883	-2.259486	-3.448611
H	2.264186	-1.689069	-1.054948
H	1.897470	0.464482	0.726443
H	0.606006	1.695329	0.218330
H	-0.008085	0.440691	5.289691
H	-1.737657	0.032125	5.450652
H	-1.247966	1.620019	4.799197
H	-0.933859	-0.997994	-4.837671
H	-2.065509	-0.224375	-3.700130
H	-0.852967	0.755039	-4.535328

Gibbs free energy: -611.528848 hartrees

FC1(NH)‡

C	2.735674	1.177537	-0.135067
C	1.745311	1.396164	0.790857
C	0.903904	0.265626	0.706121
C	1.431295	-0.584801	-0.259440
O	2.563736	0.013541	-0.770791
C	3.915461	1.987091	-0.514813
C	0.964877	-1.794472	-0.759166
O	-0.367347	-1.204610	-2.239427
C	-1.348819	-2.033981	-2.362814
N	-2.332617	-1.630701	-3.241945
O	-1.468993	-3.108196	-1.750488
C	-3.351041	-2.562709	-3.692584
C	1.821254	-2.678200	-1.593035
O	-0.201059	-0.031742	1.391656
C	-0.708998	0.946392	2.251641
C	-0.635199	0.716878	3.615748
C	-1.181767	1.662502	4.480133
C	-1.783698	2.811244	3.973396
C	-1.846085	3.018084	2.596719
C	-1.308833	2.079272	1.721297
H	1.652675	2.255949	1.434379
H	3.934206	2.907640	0.065288
H	3.875997	2.229193	-1.579108
H	4.831514	1.422311	-0.327485
H	0.155171	-2.251002	-0.202878

H	-2.075959	-0.880145	-3.865392
H	-3.918573	-2.938251	-2.840942
H	-4.032994	-2.034062	-4.357387
H	-2.926642	-3.418110	-4.227931
H	2.400706	-2.104577	-2.315280
H	2.519398	-3.193257	-0.922938
H	1.210753	-3.422748	-2.098596
H	-0.160838	-0.185083	3.983486
H	-1.134365	1.498439	5.550037
H	-2.206899	3.543924	4.649994
H	-2.318685	3.908692	2.200086
H	-1.352518	2.216168	0.646670

Gibbs free energy: -937.094549 hartrees

FC2(NH)‡

C	-1.396284	2.498731	-0.222258
C	-0.820616	1.887733	0.868332
C	-0.719939	0.528123	0.518438
C	-1.257765	0.375668	-0.763760
O	-1.656194	1.625588	-1.196680
C	-1.760145	3.911765	-0.465399
C	-1.361614	-0.728626	-1.577374
O	0.405368	-0.787042	-2.686398
C	0.457660	-1.860050	-3.403903
N	1.639019	-2.027743	-4.095671
O	-0.435356	-2.718235	-3.484718
C	1.748017	-3.028987	-5.141964
O	-0.203729	-0.494247	1.192685
C	0.181392	-0.271466	2.519499
C	1.527839	-0.374095	2.827032
C	1.921029	-0.203348	4.152201
C	0.973622	0.066868	5.136014
C	-0.375300	0.162990	4.799785
C	-0.783682	-0.010764	3.480962
H	-0.516662	2.372214	1.781906
H	-1.479768	4.520036	0.392068
H	-2.836572	3.993628	-0.633089
H	-1.248071	4.278989	-1.357519
H	-1.177559	-1.702558	-1.146136
H	-1.963768	-0.682634	-2.473887
H	2.219605	-1.206099	-4.171160
H	1.552298	-4.020370	-4.733027

H	2.764189	-3.009893	-5.533706
H	1.047661	-2.851000	-5.964279
H	2.243593	-0.584230	2.041450
H	2.970020	-0.280467	4.411875
H	1.284999	0.199747	6.165109
H	-1.114629	0.367852	5.564738
H	-1.828661	0.051921	3.198832

Gibbs free energy: -897.806889 hartrees

FC3(NH)‡

C	-0.03743	0.810186	-3.14227
C	-1.1563	-0.00044	-3.18806
C	-1.62172	-0.09796	-1.87131
C	-0.76999	0.664276	-1.08602
O	0.200949	1.210956	-1.89266
C	0.884557	1.283431	-4.19788
C	-0.75597	0.911416	0.279552
C	0.069751	1.971734	0.897225
O	0.458646	-0.78851	1.038943
C	0.162158	-1.02684	2.263627
O	-0.78699	-0.52134	2.894533
N	1.013194	-1.90539	2.915029
C	0.631522	-2.4984	4.184731
H	-1.56553	-0.45242	-4.07717
H	-2.47544	-0.64743	-1.50283
H	0.874725	2.37498	-4.24077
H	1.904331	0.961238	-3.97543
H	0.57923	0.880714	-5.16157
H	-1.58741	0.510853	0.846131
H	1.03144	2.079984	0.398404
H	0.199079	1.776244	1.959317
H	-0.48234	2.914337	0.78635
H	1.598221	-2.45817	2.306327
H	0.474546	-1.71836	4.929869
H	1.442131	-3.14232	4.52412
H	-0.28536	-3.09277	4.111812

Gibbs free energy: -630.937014 hartrees

FC4(NH)‡

C	-0.02706	2.445821	-2.01952
C	-1.01645	3.026214	-1.23772
C	-1.63549	1.980985	-0.55633
C	-1.00399	0.803206	-0.95547

O	-0.01155	1.12771	-1.85683
C	0.951074	3.032152	-2.95932
C	-1.18263	-0.50671	-0.58285
O	0.198257	-0.80548	1.126963
C	0.132517	-2.028	1.516034
N	0.826577	-2.30614	2.681494
O	-0.50838	-2.93569	0.955507
C	1.091292	-3.6795	3.073071
H	-1.23667	4.080664	-1.19155
H	-2.4514	2.032958	0.149313
H	1.965456	2.766559	-2.65352
H	0.845722	4.11499	-2.97578
H	0.784219	2.633856	-3.96292
H	-0.67831	-1.30598	-1.10682
H	-2.02431	-0.75767	0.046761
H	1.510075	-1.61279	2.944765
H	1.694197	-4.21847	2.333958
H	1.624087	-3.67055	4.023726
H	0.15277	-4.21816	3.207017

Gibbs free energy: -591.648877 hartrees

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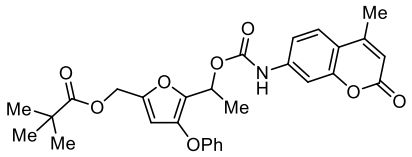

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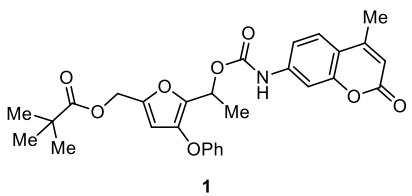
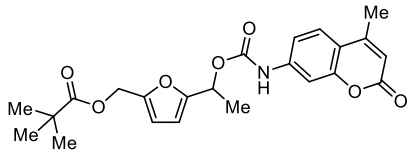
^{1}H (500 MHz, $CDCl_3$)



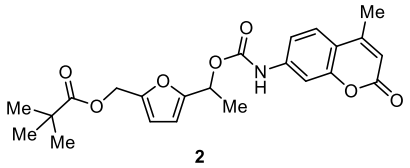
1

^{13}C (125 MHz, $CDCl_3$)



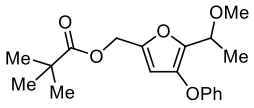
2

^{1}H (400 MHz, $CDCl_3$)



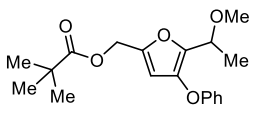
2

^{13}C (100 MHz, $CDCl_3$)



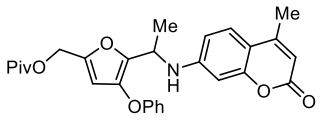
4

^{1}H (400 MHz, $CDCl_3$)



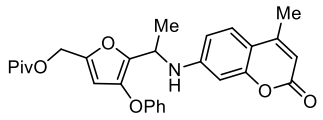
4

^{13}C (100 MHz, $CDCl_3$)



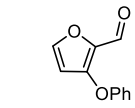
4N

^{1}H (400 MHz, $CDCl_3$)



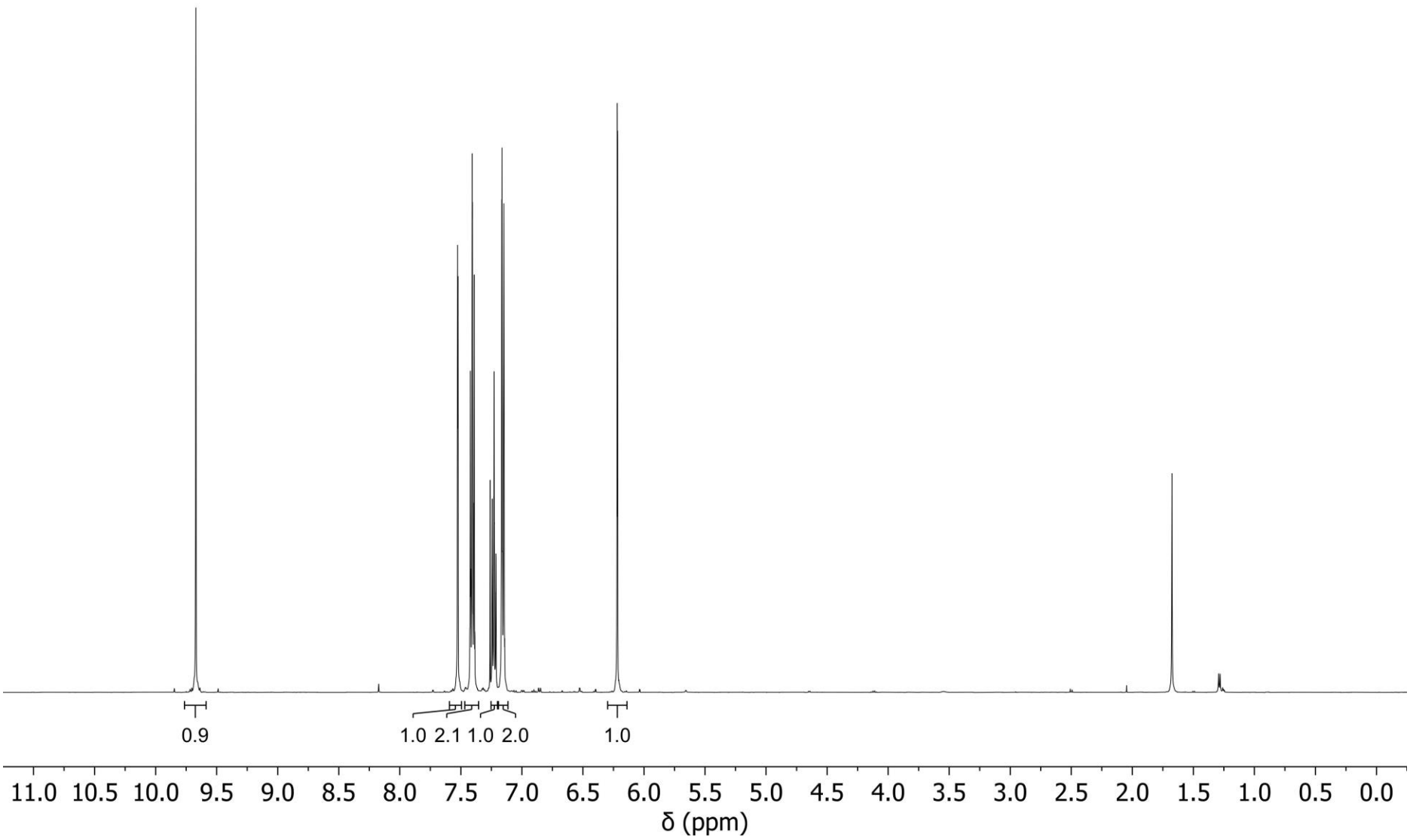
4N

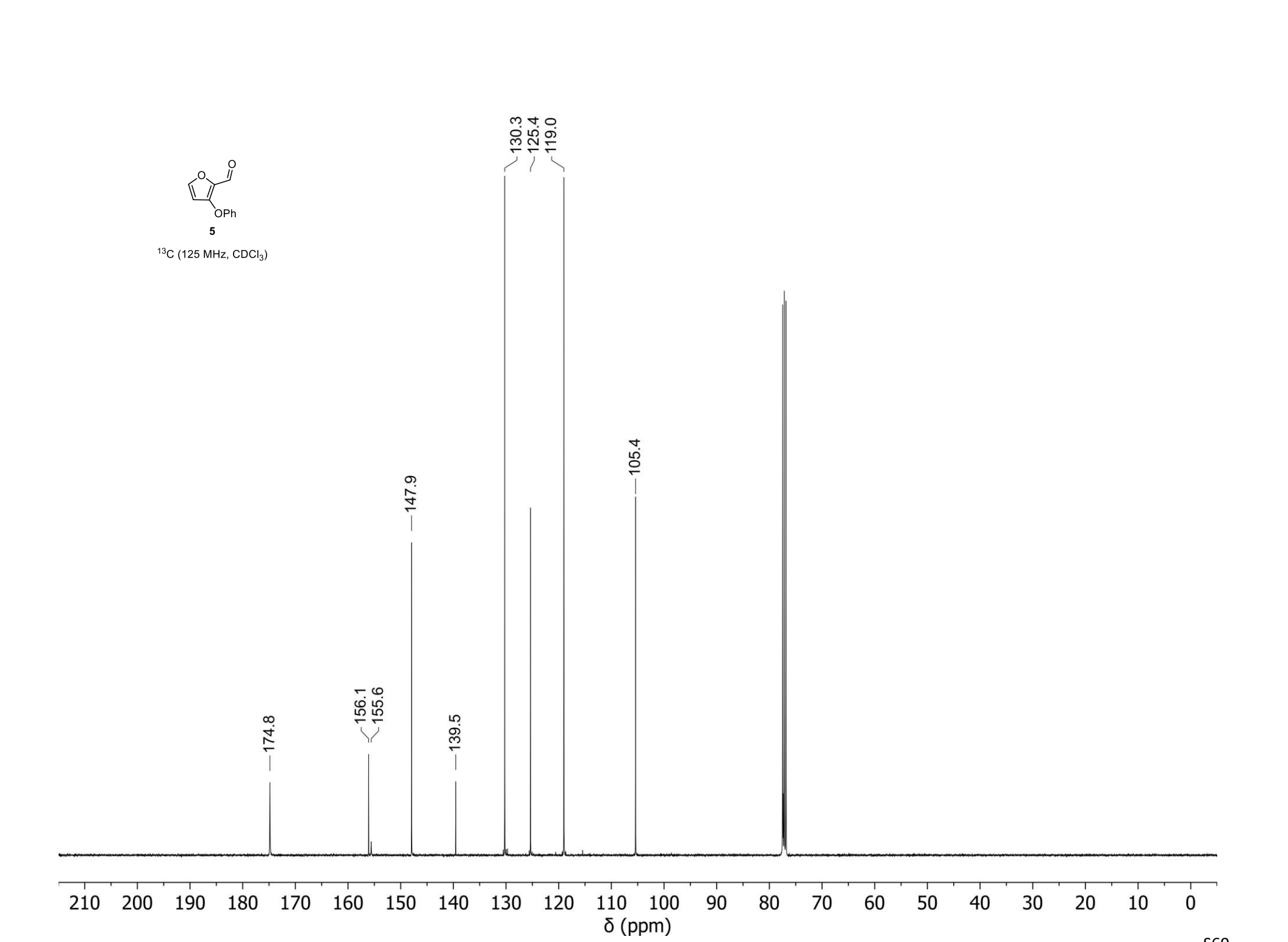
^{13}C (100 MHz, $CDCl_3$)

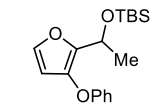


5

^{1}H (500 MHz, $CDCl_3$)

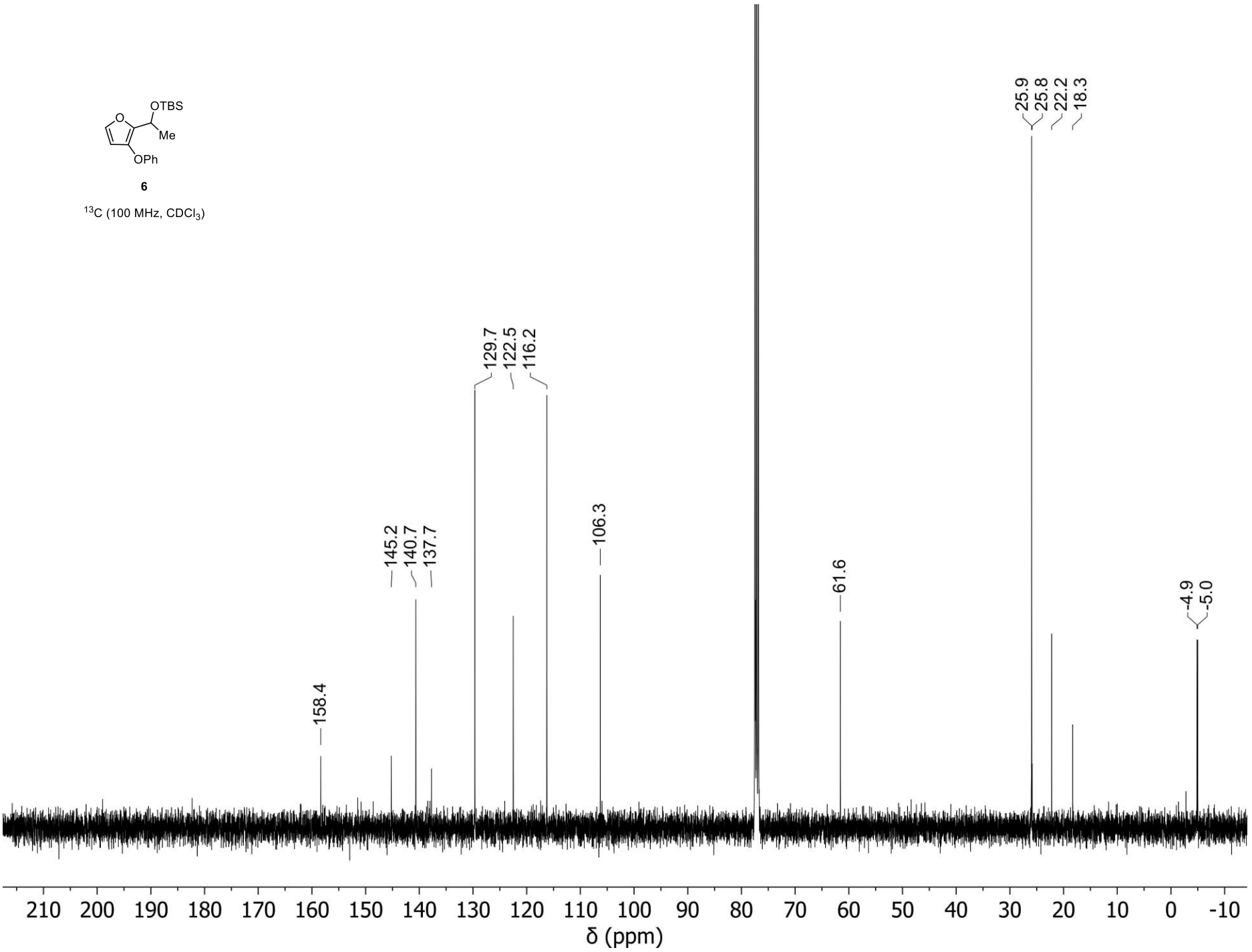


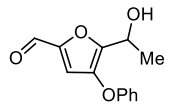

O
O
OPh
5
^{13}C (125 MHz, $CDCl_3$)
130.3
125.4
119.0
105.4
147.9
156.1
155.6
139.5
174.8
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
δ (ppm)



6

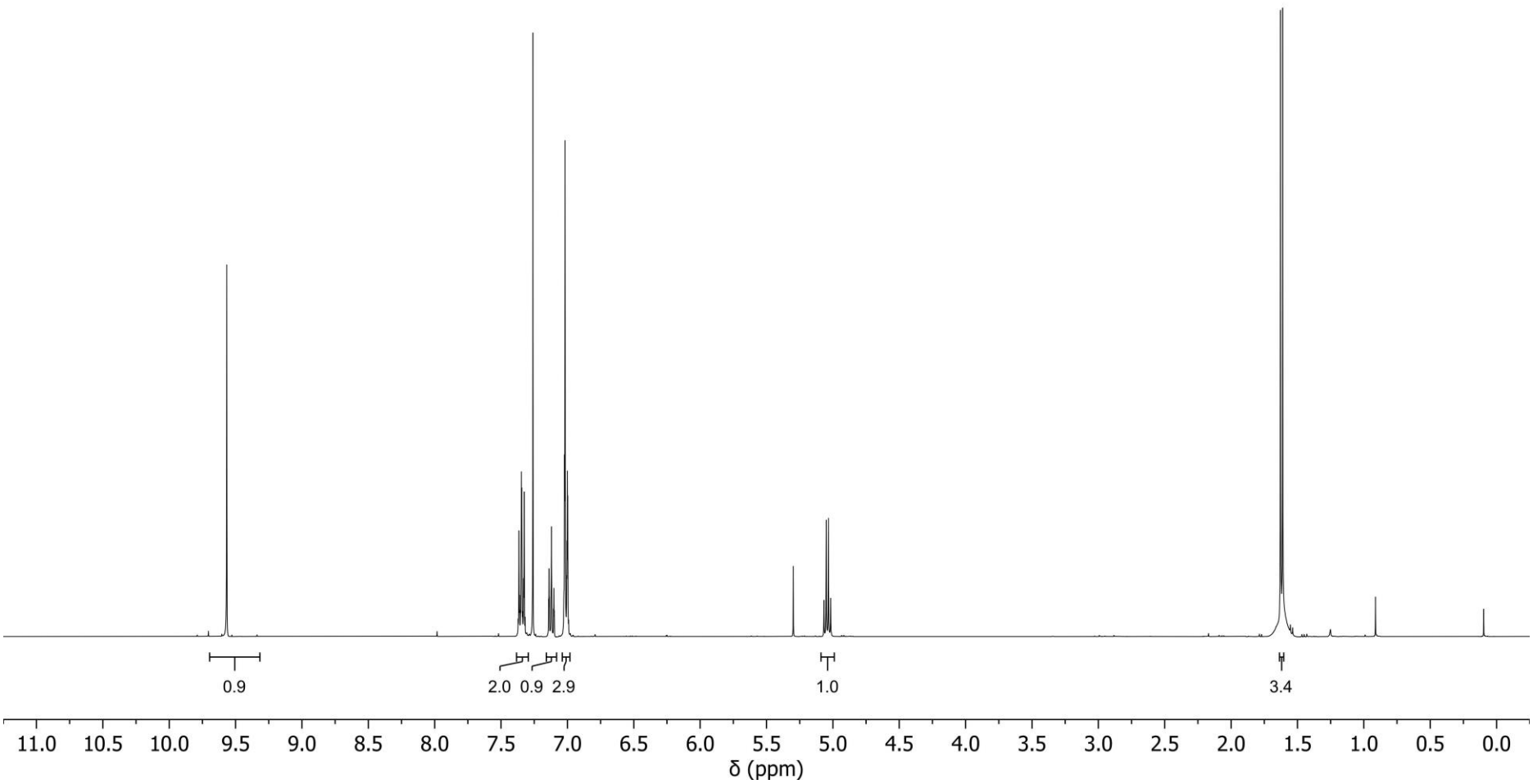
^{1}H (400 MHz, $CDCl_3$)

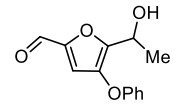

OTBS
Me
OPh
6
^{13}C (100 MHz, $CDCl_3$)
158.4
145.2
140.7
137.7
129.7
122.5
116.2
106.3
61.6
25.9
25.8
22.2
18.3
-4.9
-5.0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
δ (ppm)



7

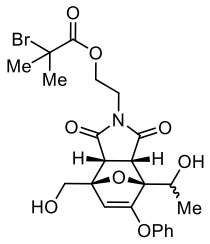
^{1}H (400 MHz, $CDCl_3$)





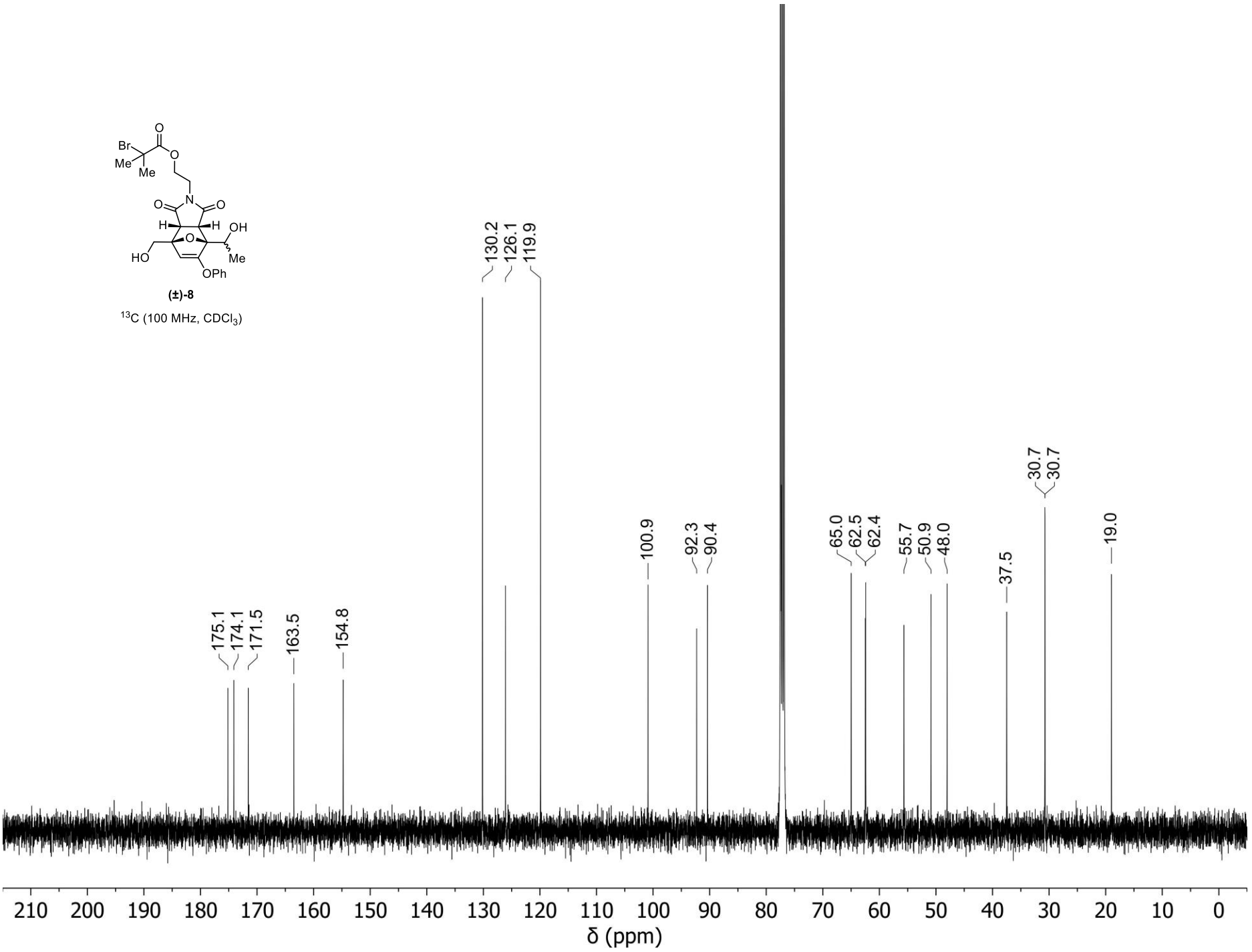
7

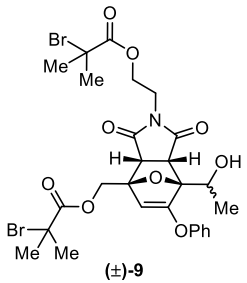
^{13}C (100 MHz, $CDCl_3$)



(±)-8

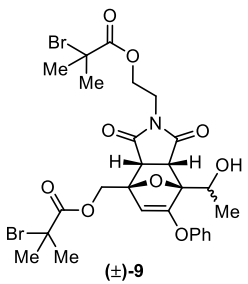
^{1}H (400 MHz, $CDCl_3$)


(±)-8
13C (100 MHz, CDCl3)
175.1
174.1
171.5
163.5
154.8
130.2
126.1
119.9
100.9
92.3
90.4
65.0
62.5
62.4
55.7
50.9
48.0
37.5
30.7
30.7
19.0
δ (ppm)



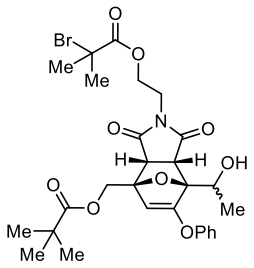
(±)-9

^{1}H (400 MHz, $CDCl_3$)



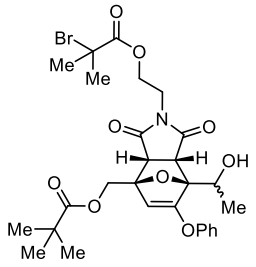
(±)-9

^{13}C (100 MHz, $CDCl_3$)



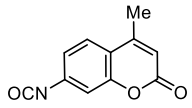
(±)-9-control

^{1}H (400 MHz, $CDCl_3$)



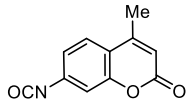
(±)-9-control

^{13}C (100 MHz, $CDCl_3$)



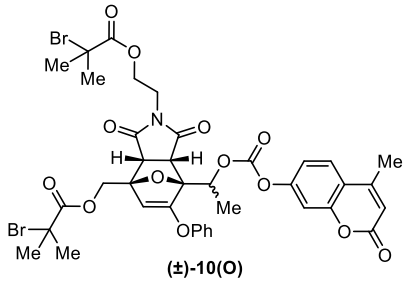
coumNCO

^{1}H (400 MHz, $CDCl_3$)



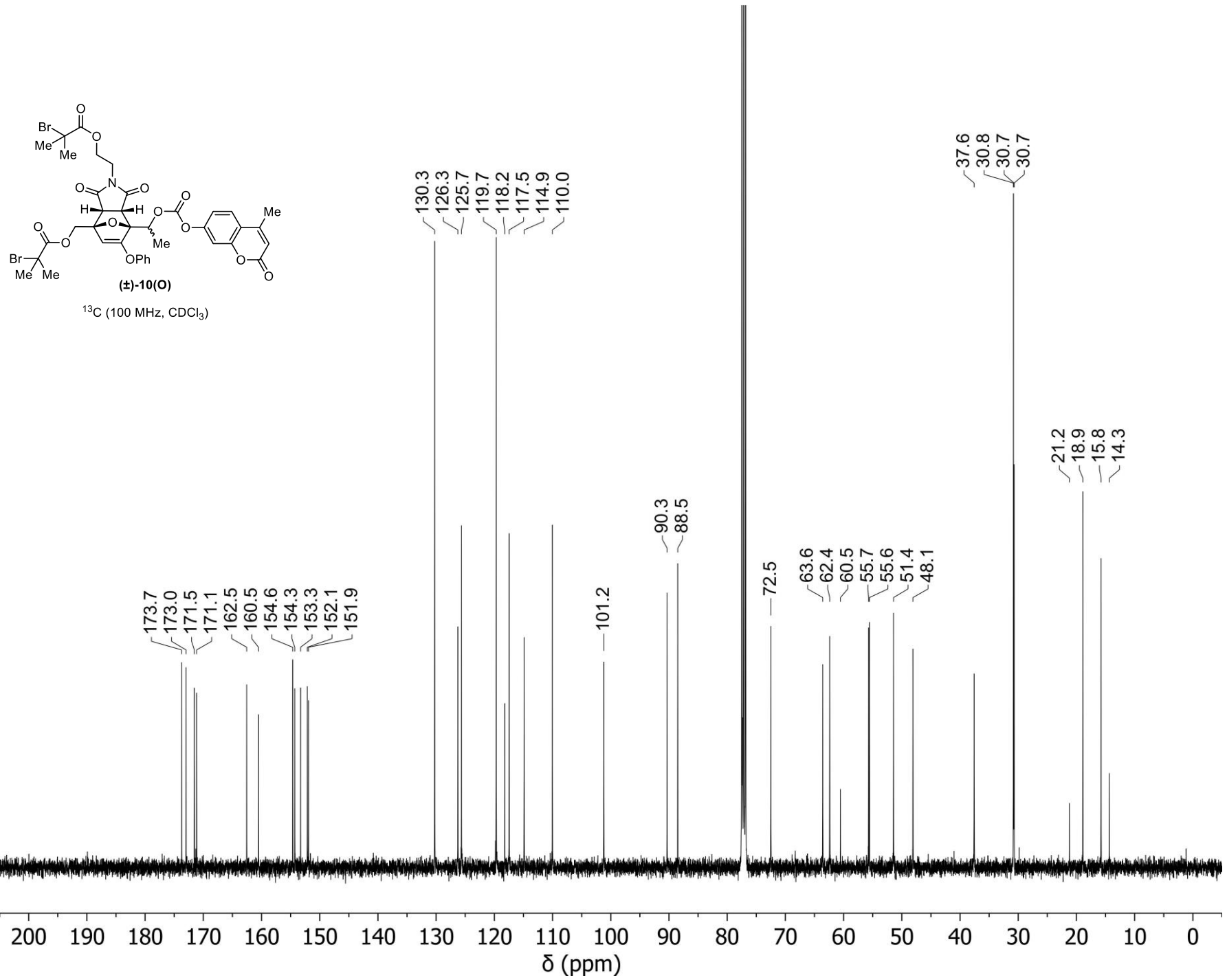
coumNCO

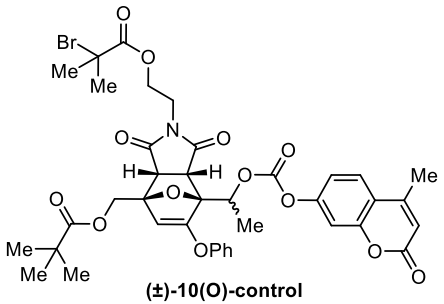
^{13}C (100 MHz, $CDCl_3$)



(±)-10(O)

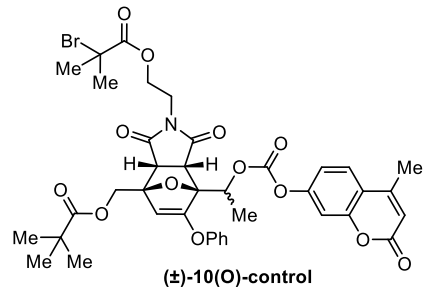
^{1}H (400 MHz, $CDCl_3$)


(±)-10(O)
^{13}C (100 MHz, $CDCl_3$)
173.7
173.0
171.5
171.1
162.5
160.5
154.6
154.3
153.3
152.1
151.9
130.3
126.3
125.7
119.7
118.2
117.5
114.9
110.0
101.2
90.3
88.5
72.5
63.6
62.4
60.5
55.7
55.6
51.4
48.1
37.6
30.8
30.7
30.7
21.2
18.9
15.8
14.3
δ (ppm)



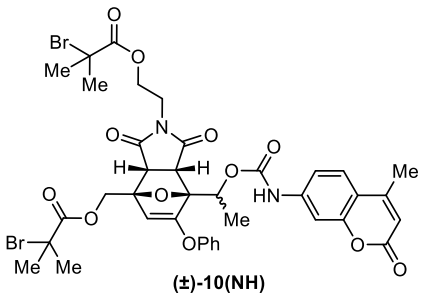
(±)-10(O)-control

^{1}H (400 MHz, $CDCl_3$)



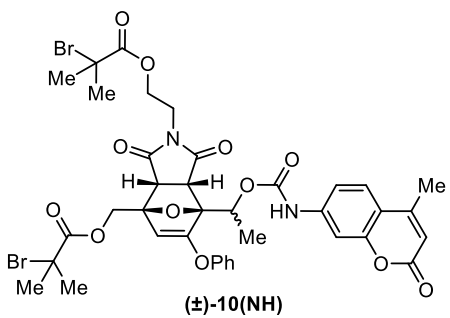
(±)-10(O)-control

^{13}C (100 MHz, $CDCl_3$)



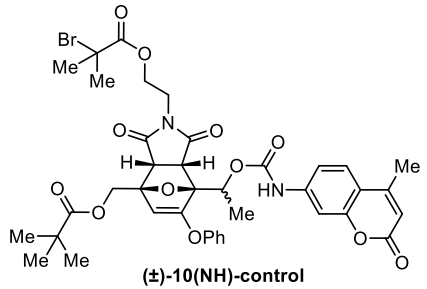
(±)-10(NH)

^{1}H (400 MHz, $CDCl_3$)



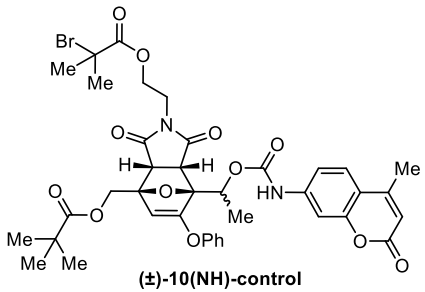
(±)-10(NH)

^{13}C (100 MHz, $CDCl_3$)



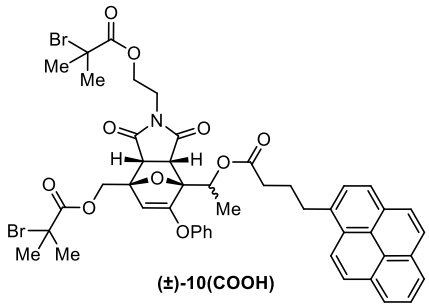
(±)-10(NH)-control

^{1}H (400 MHz, $CDCl_3$)



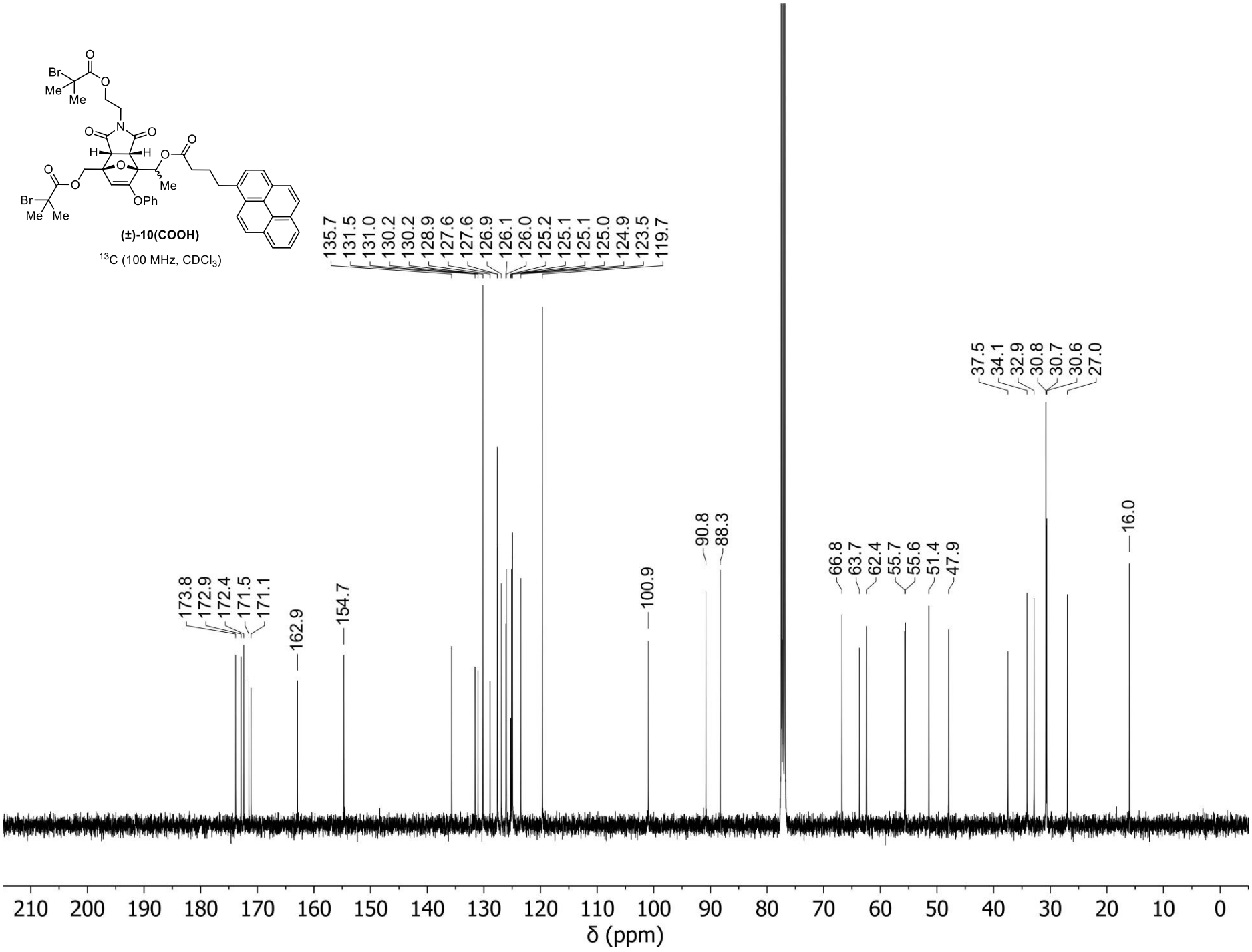
(±)-10(NH)-control

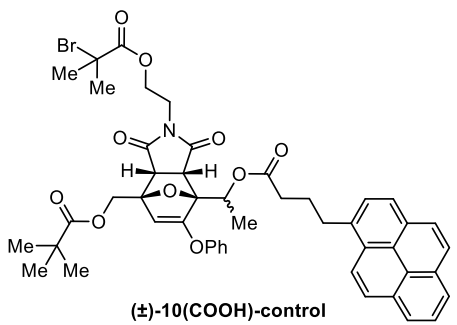
^{13}C (100 MHz, $CDCl_3$)



(±)-10(COOH)

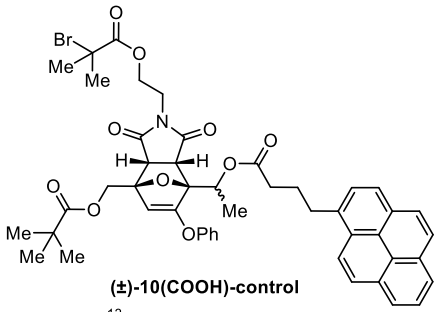
^{1}H (400 MHz, $CDCl_3$)


(±)-10(COOH)
^{13}C (100 MHz, $CDCl_3$)
135.7
131.5
131.0
130.2
130.2
128.9
127.6
127.6
126.9
126.1
126.0
125.2
125.1
125.1
125.0
124.9
123.5
119.7
173.8
172.9
172.4
171.5
171.1
162.9
154.7
100.9
90.8
88.3
66.8
63.7
62.4
55.7
55.6
51.4
47.9
37.5
34.1
32.9
30.8
30.7
30.6
27.0
16.0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
δ (ppm)



(±)-10(COOH)-control

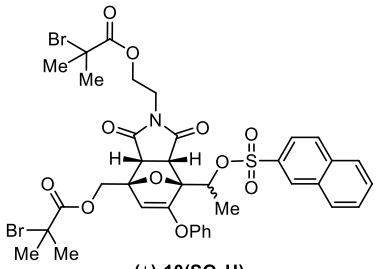
^{1}H (500 MHz, $CDCl_3$)



(±)-10(COOH)-control

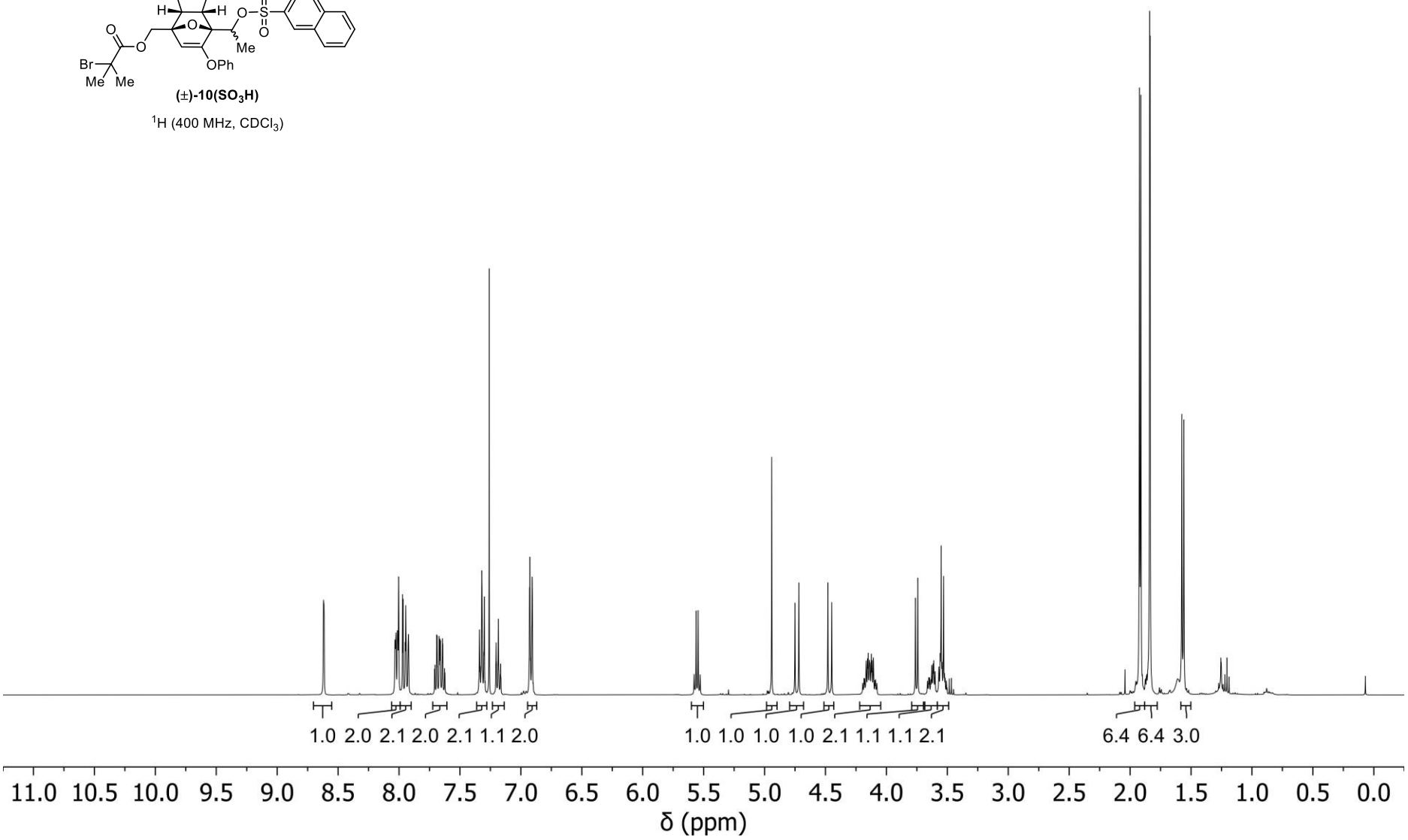
^{13}C (100 MHz, $CDCl_3$)

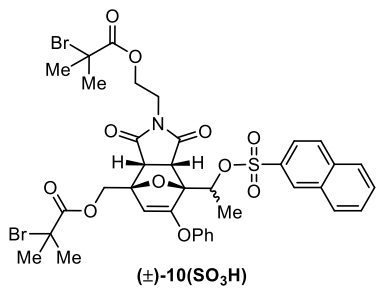
δ (ppm)



(±)-10(SO_3H)

^1H (400 MHz, $CDCl_3$)

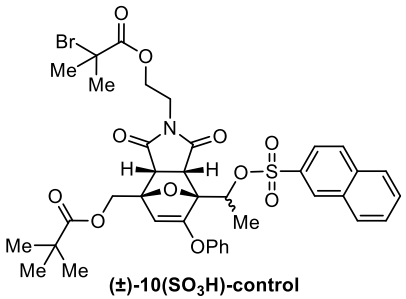




(±)-10(SO_3H)

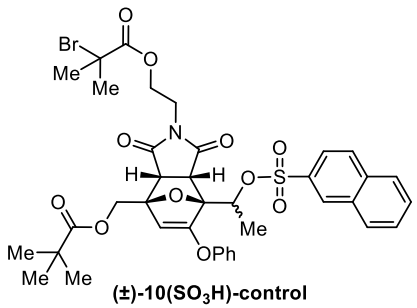
^{13}C (100 MHz, $CDCl_3$)

δ (ppm)



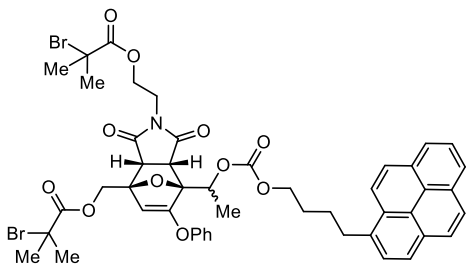
(±)-10(SO_3H)-control

^1H (400 MHz, $CDCl_3$)



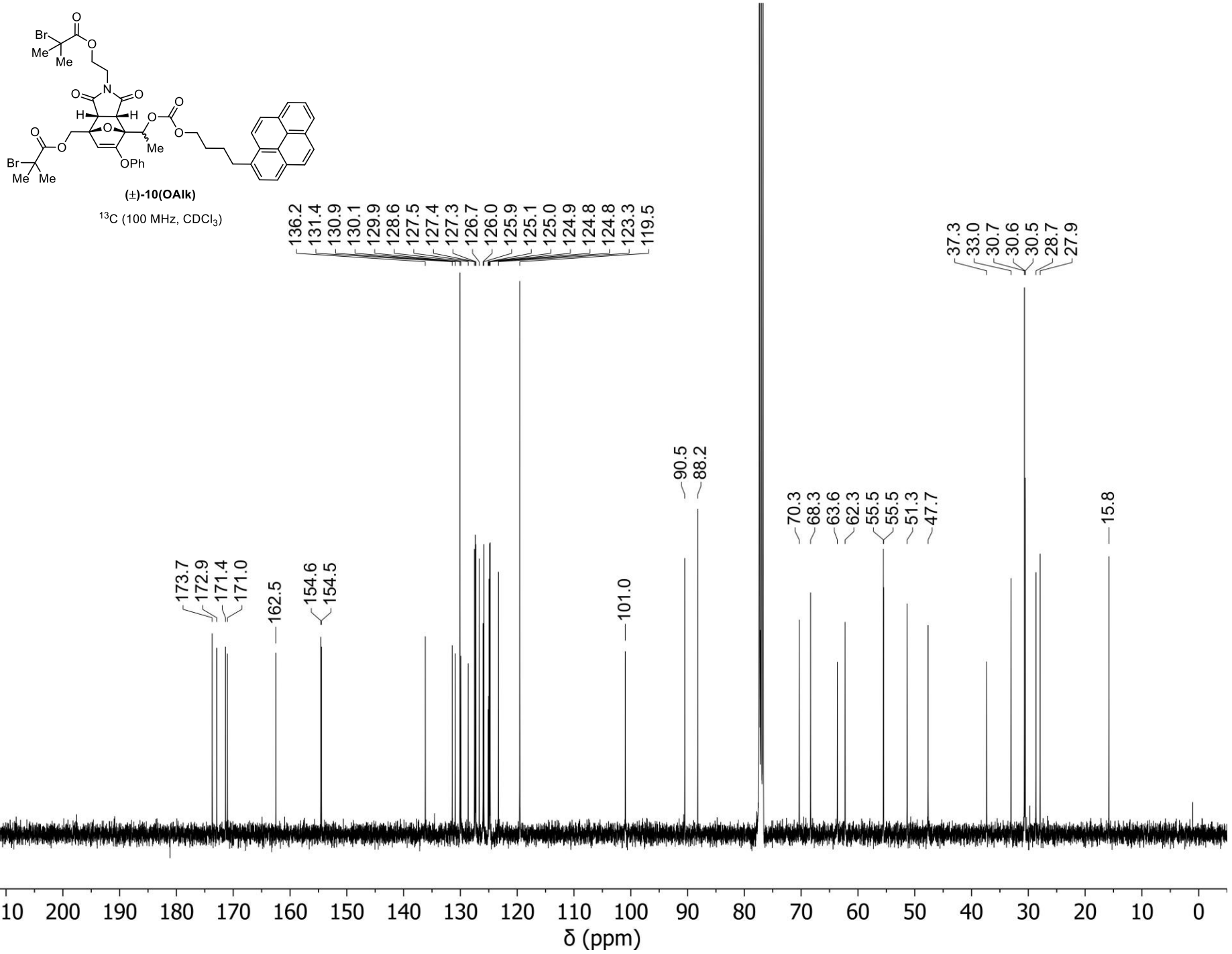
(±)-10(SO_3H)-control

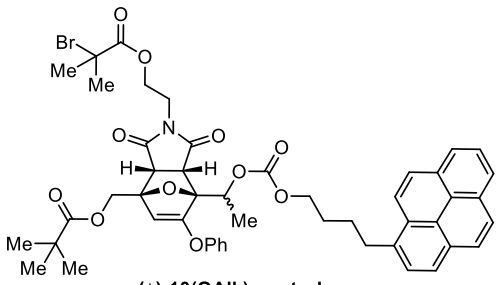
^{13}C (100 MHz, $CDCl_3$)



(±)-10(OAlk)

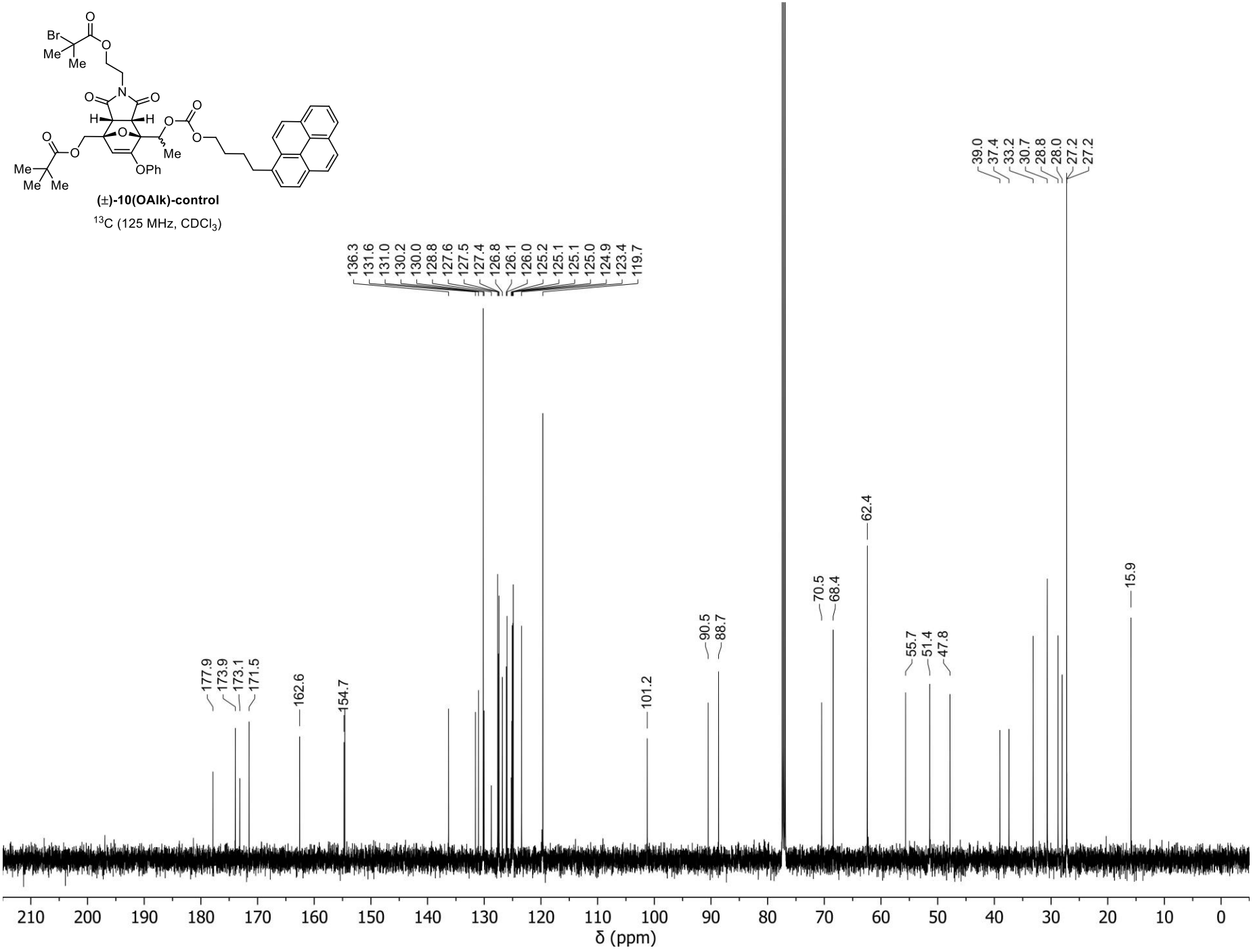
^{1}H (400 MHz, $CDCl_3$)

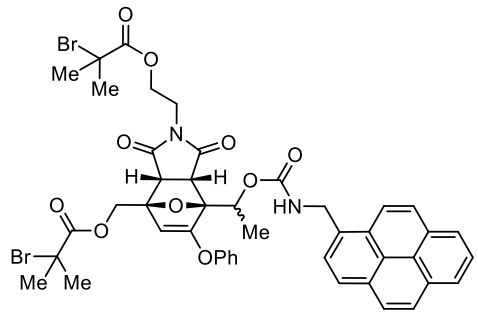

(±)-10(OAlk)
^{13}C (100 MHz, $CDCl_3$)
136.2
131.4
130.9
130.1
129.9
128.6
127.5
127.4
127.3
126.7
126.0
125.9
125.1
125.0
124.9
124.8
124.8
123.3
119.5
37.3
33.0
30.7
30.6
30.5
28.7
27.9
90.5
88.2
70.3
68.3
63.6
62.3
55.5
55.5
51.3
47.7
15.8
173.7
172.9
171.4
171.0
162.5
154.6
154.5
101.0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
δ (ppm)



(±)-10(OAlk)-control

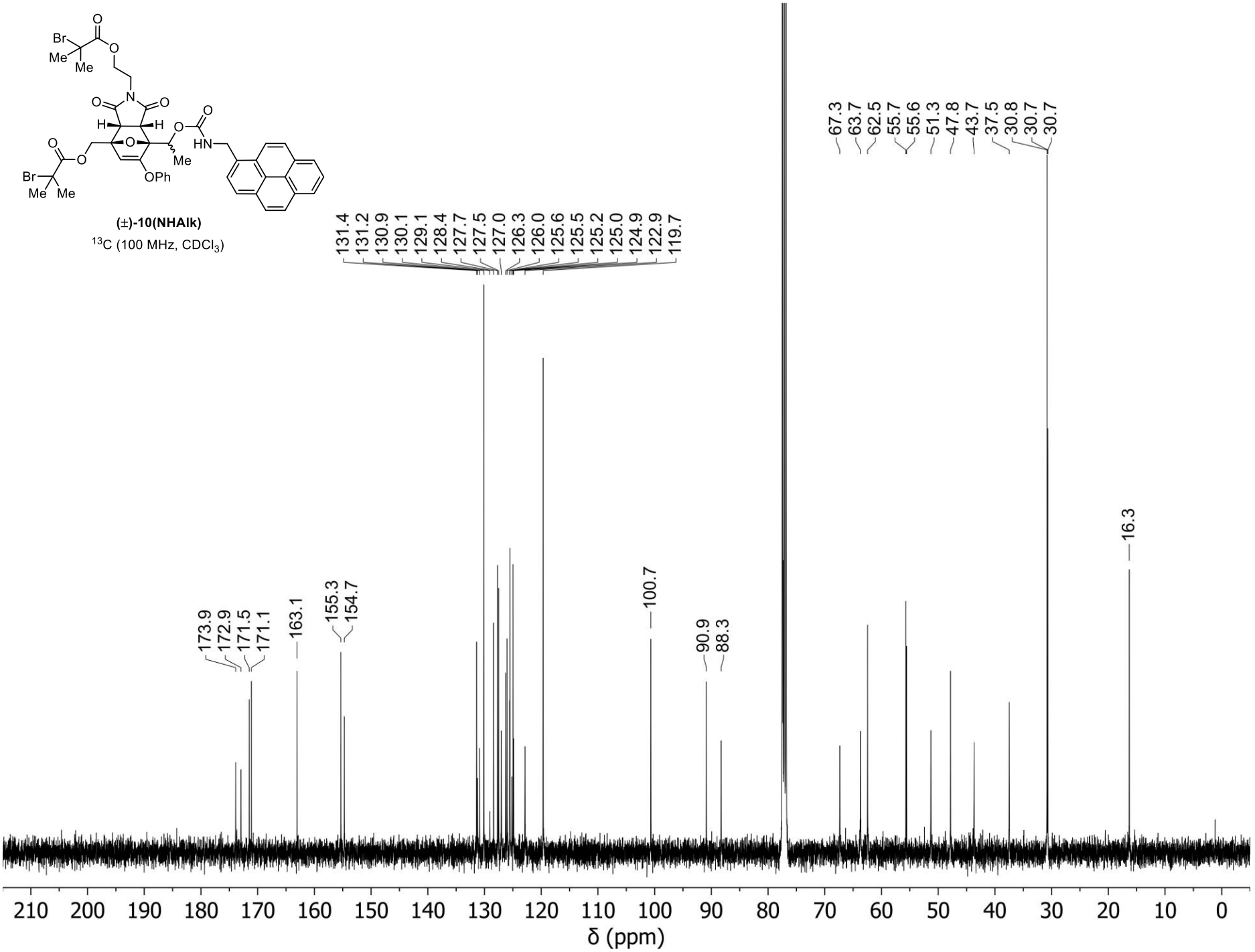
^{1}H (400 MHz, $CDCl_3$)

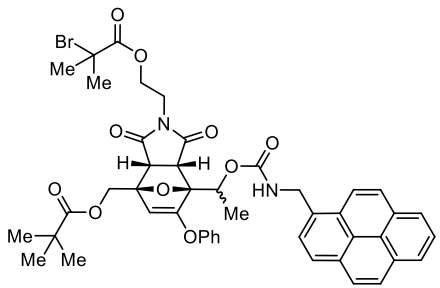

(±)-10(OAlk)-control
13C (125 MHz, CDCl3)
δ (ppm)



(±)-10(NHAlk)

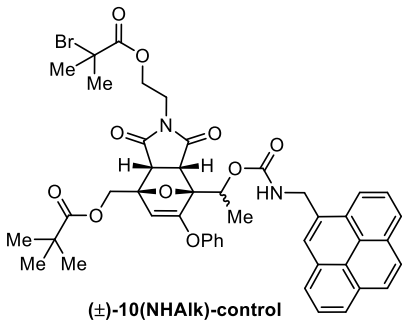
^{1}H (500 MHz, $CDCl_3$)


(±)-10(NHAlk)
13C (100 MHz, CDCl3)
δ (ppm)



(±)-10(NHAlk)-control

^{1}H (400 MHz, $CDCl_3$)



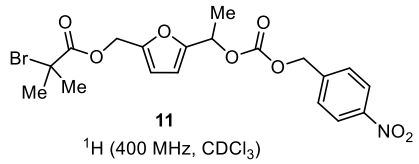
(±)-10(NHAlk)-control

^{13}C (100 MHz, $CDCl_3$)

67.4
62.5
62.4
55.7
51.3
47.9
43.7
39.0
37.4
30.7
30.7
27.2
131.4
131.2
130.9
130.1
129.0
128.4
127.7
127.5
127.0
126.2
126.0
125.6
125.5
125.1
124.9
124.8
122.8
119.6
177.8
173.9
173.0
171.5
163.0
155.3
154.8
100.8
90.8
88.6
16.3

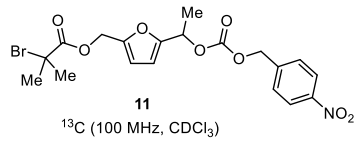
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

δ (ppm)



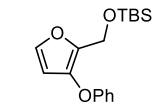
11

^{1}H (400 MHz, $CDCl_3$)



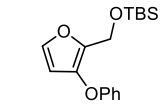
11

^{13}C (100 MHz, $CDCl_3$)



17

^{1}H (400 MHz, $CDCl_3$)



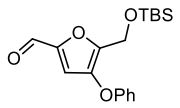
17

^{13}C (100 MHz, $CDCl_3$)

158.3
142.4
141.4
139.8
129.7
122.6
116.4
106.3
54.7
26.0
18.6
-5.2

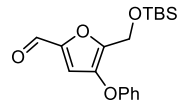
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

δ (ppm)



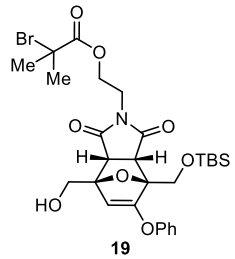
18

^{1}H (400 MHz, $CDCl_3$)



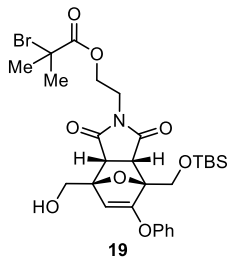
18

^{13}C (100 MHz, $CDCl_3$)



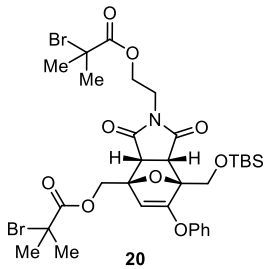
19

^{1}H (400 MHz, $CDCl_3$)



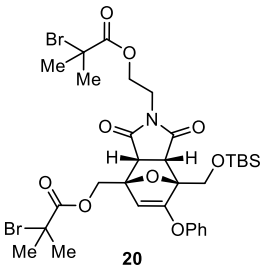
19

^{13}C (100 MHz, $CDCl_3$)



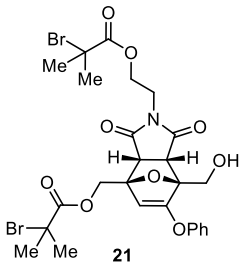
20

^{1}H (400 MHz, $CDCl_3$)



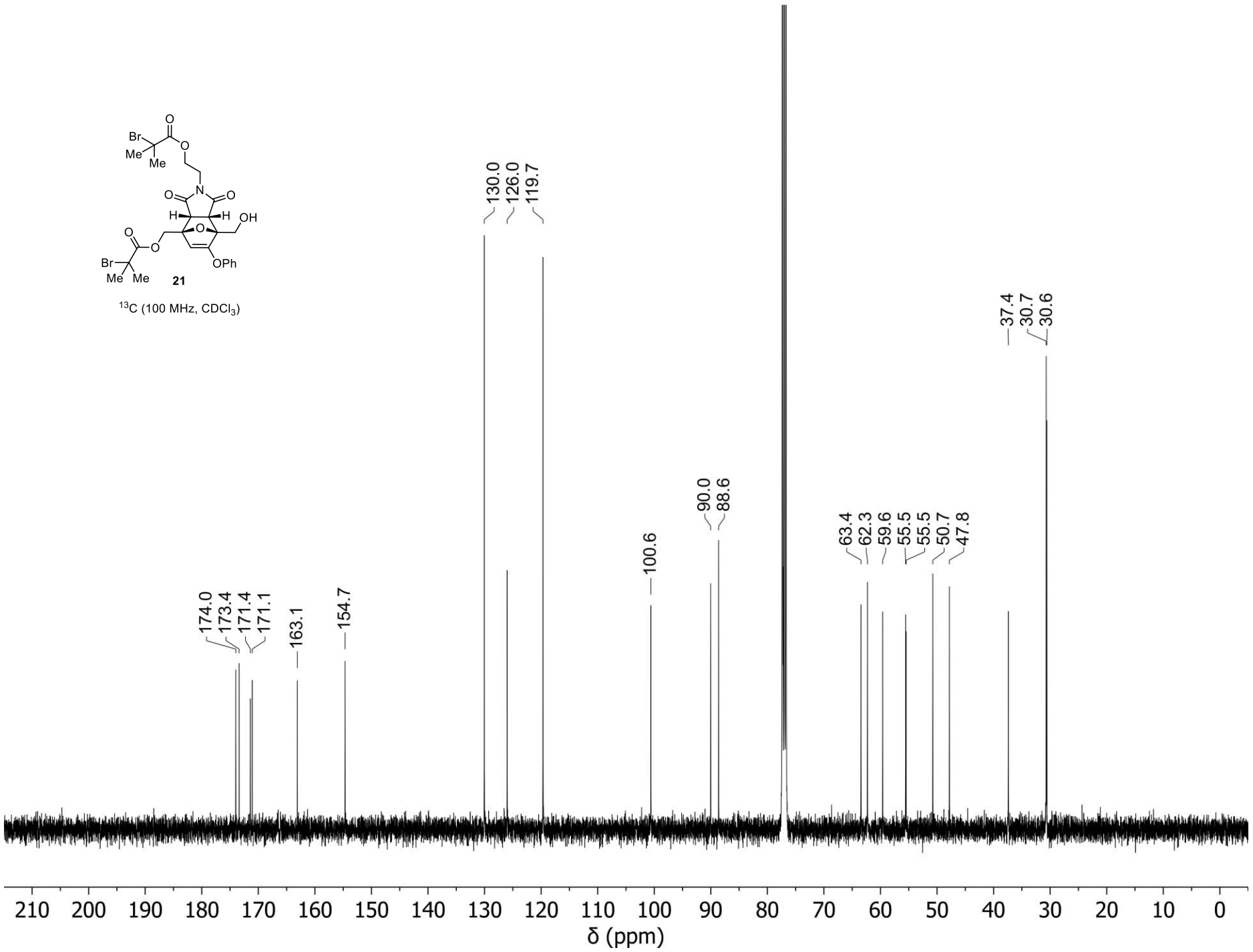
20

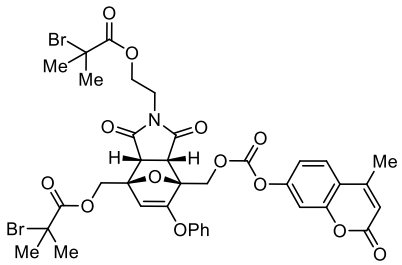
^{13}C (100 MHz, $CDCl_3$)



21

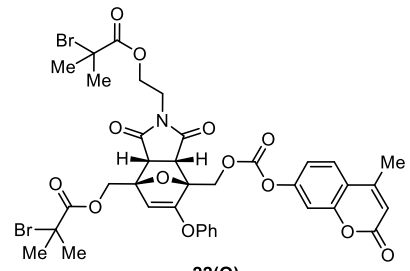
^{1}H (400 MHz, $CDCl_3$)


21
^{13}C (100 MHz, $CDCl_3$)
130.0
126.0
119.7
174.0
173.4
171.4
171.1
163.1
154.7
100.6
90.0
88.6
63.4
62.3
59.6
55.5
55.5
50.7
47.8
37.4
30.7
30.6
δ (ppm)



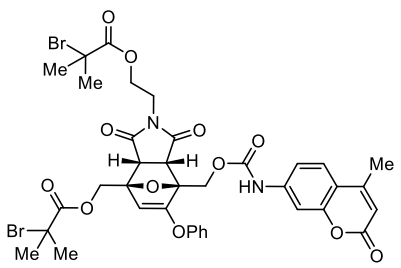
22(O)

^{1}H (400 MHz, $CDCl_3$)



22(O)

^{13}C (100 MHz, $CDCl_3$)



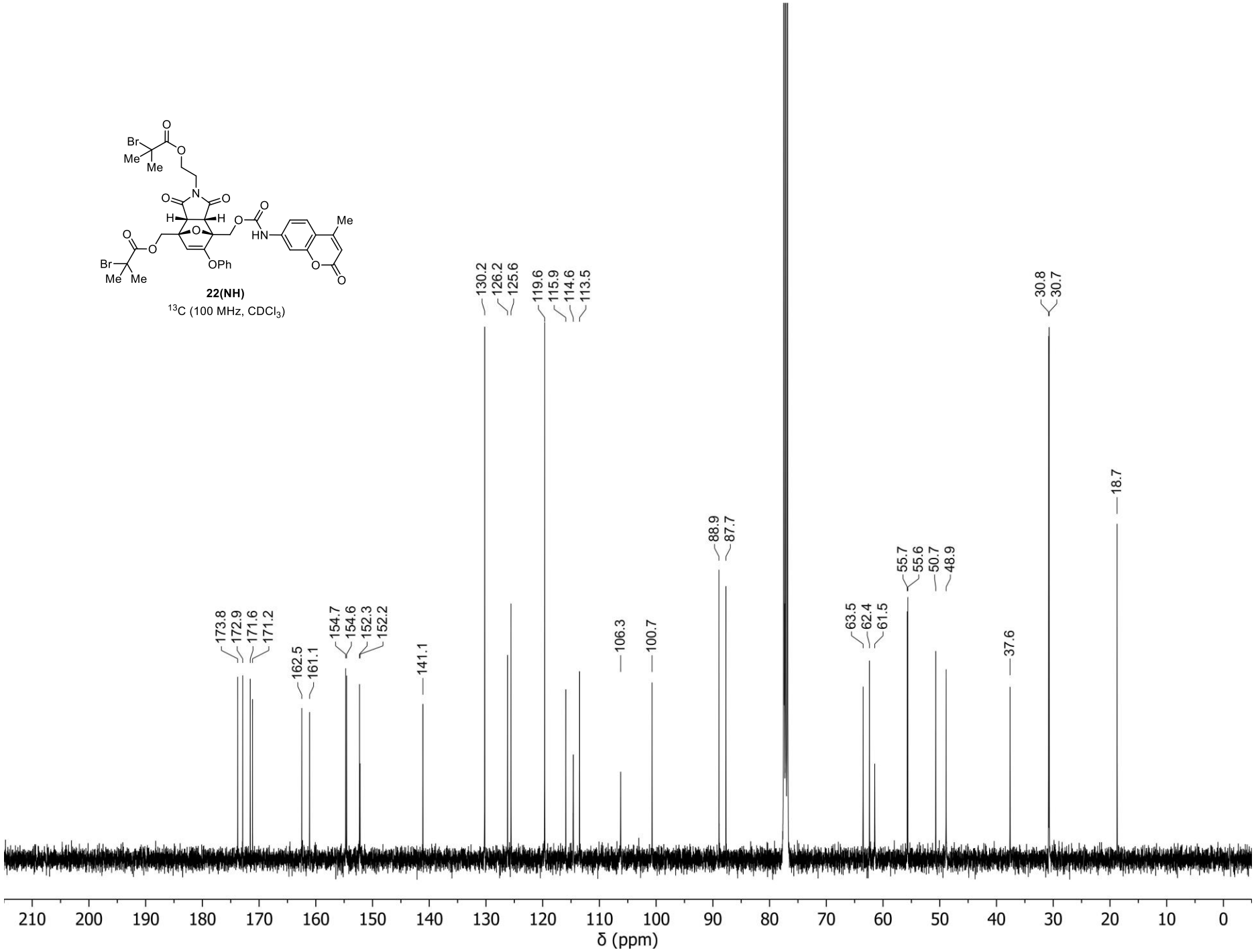
22(NH)

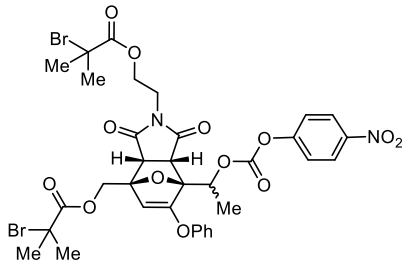
^{1}H (400 MHz, $CDCl_3$)

1.0 2.0 2.0 1.0 0.9 2.0 1.0 2.0 2.0 1.0 1.0 1.0 3.0 1.0 3.0 5.9 5.9

11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

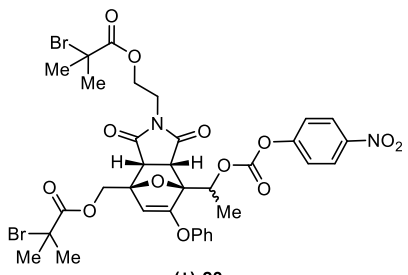
δ (ppm)


22(NH)
13C (100 MHz, CDCl3)
173.8
172.9
171.6
171.2
162.5
161.1
154.7
154.6
152.3
152.2
141.1
130.2
126.2
125.6
119.6
115.9
114.6
113.5
106.3
100.7
88.9
87.7
63.5
62.4
61.5
55.7
55.6
50.7
48.9
37.6
30.8
30.7
18.7
δ (ppm)



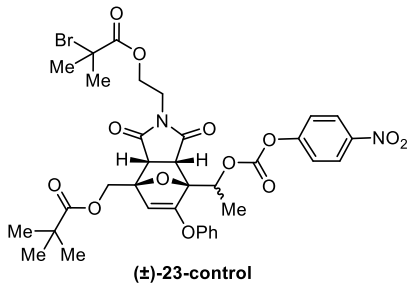
(±)-23

^{1}H (400 MHz, $CDCl_3$)



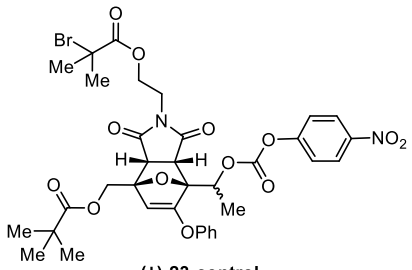
(±)-23

^{13}C (100 MHz, $CDCl_3$)



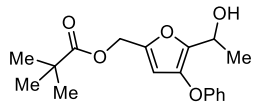
(±)-23-control

^{1}H (500 MHz, $CDCl_3$)



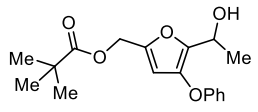
(±)-23-control

^{13}C (100 MHz, $CDCl_3$)



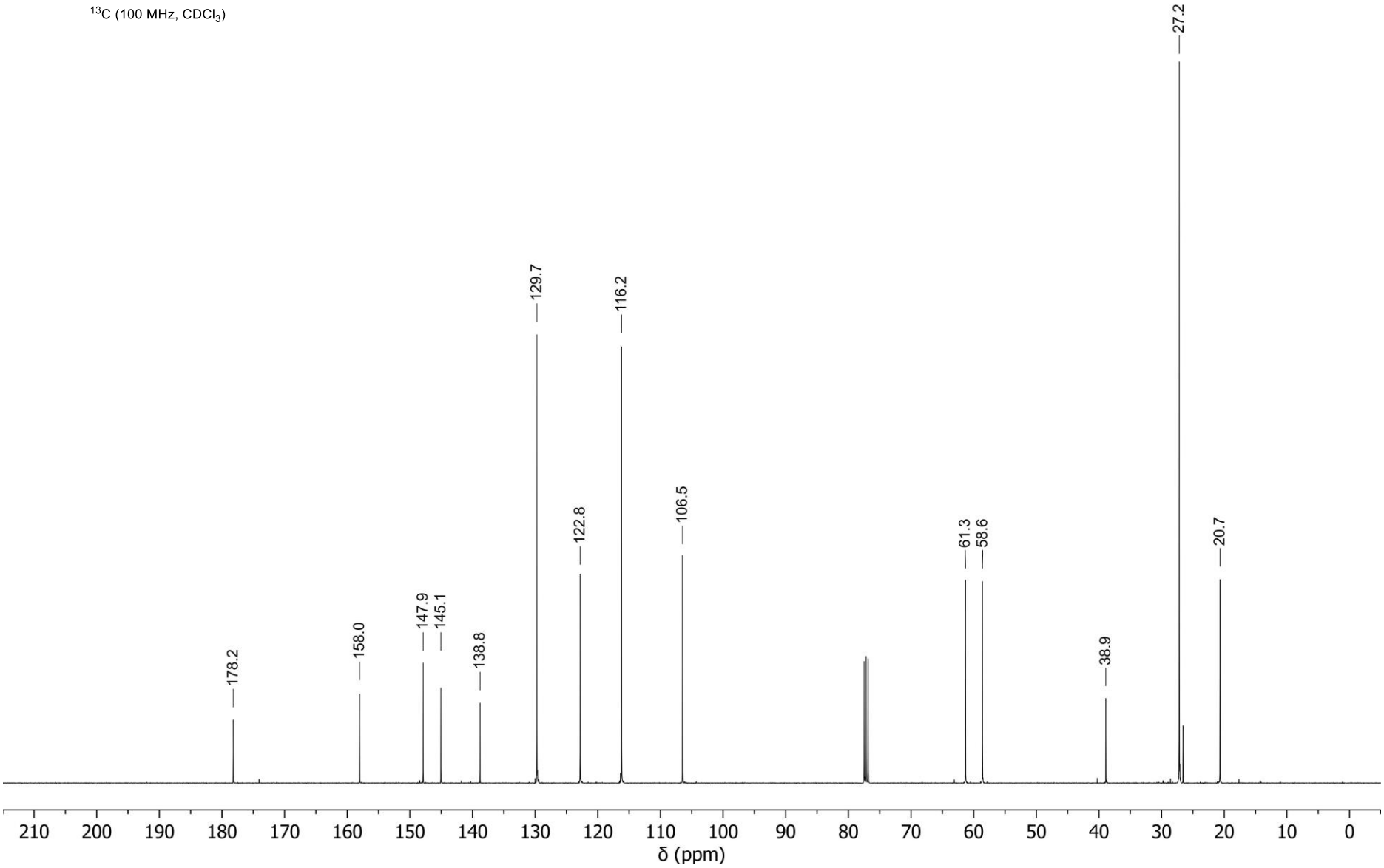
24

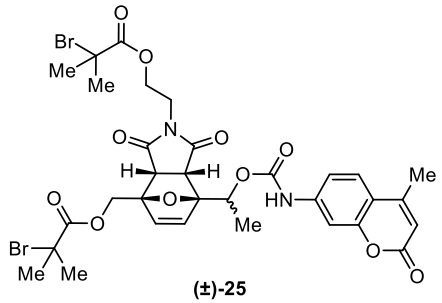
^{1}H (400 MHz, $CDCl_3$)



24

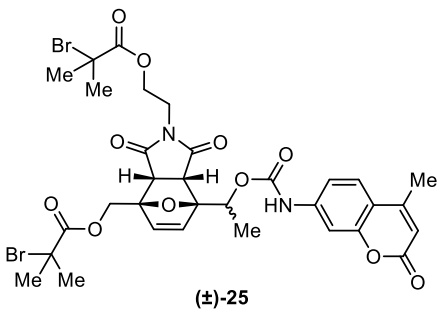
^{13}C (100 MHz, $CDCl_3$)





(±)-25

^{1}H (400 MHz, $CDCl_3$)



(±)-25

^{13}C (100 MHz, $CDCl_3$)