Supporting Information

Synthesis and evaluation of a tag-free photoactive phospho-ceramide analogue-1 (PCERA-1) probe to study immunomodulation in macrophages

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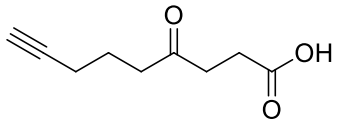
General methods

Reactions were performed using oven-dried glassware apparatus under an atmosphere of nitrogen with anhydrous, freshly distilled solvents unless otherwise stated. All other reagents were used as obtained from commercial sources. Room temperature refers to ambient temperature. Temperatures of 0 ˚C were maintained using an ice-water bath. Thin-layer chromatography was performed using silica gel 60 with F254 indicator on glass plates (Merck). Flash chromatography was performed using Merck 40-63 μm silica gel. Solvent ratios for the purification of compounds by flash chromatography are reported as percent volume (v/v). NMR spectra were recorded using a Bruker Avance DPX400 (400 MHz) or Bruker Avance DMX500 (500 MHz) spectrometer. Spectra were calibrated on residual solvent signal. All MS analyses were performed on a Thermo Scientific LCQ Fleet mass spectrometer with an ESI source. Preparative HPLC purifications were done on a Thermo Scientific / Dionex Ultimate 3000 systen equipped with a phenomenex Luna® 10μm C18(2) 100Å, LC column 250 x 21.2 mm preparative column.

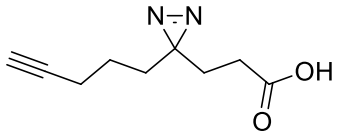
Synthetic procedures

4–oxonon-8–ynoic acid (**2**)



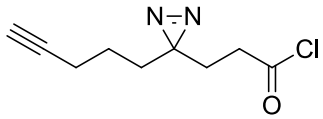
4–Oxonon-8–ynoic acid (**2)** was prepared by a known procedure[1] via lithiation of 2,3-dihydrofuran and alkylation with (5-iodopent-1-yn-1-yl)trimethylsilane, **1** followed by direct oxidation of the crude hydroxynonynone using Jones' reagent[1]. Spectral data were found to be identical to literature values.[1]

3-(3-(pent-4-ynyl)-3*H*-diazirin-3-yl)propanoic acid (**3**)



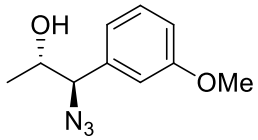
3-(3-(pent-4-ynyl)-3*H*-diazirin-3-yl)propanoic acid (**3**) was prepared following procedures described by previously published protocols.[2] Anhydrous ammonia (3.5 mL) was condensed into a round bottomed flask containing 4–Oxonon-8–ynoic acid (0. 50g, 2.9 mmol) at dry ice temperature. The mixture was stirred at -35-40 °C for 5 h. The solution was cooled with dry ice, and a solution of hydroxylamine-*O*-sulfonic acid (0.37 g, 3.3 mmol) in anhydrous methanol (1.4 mL) was added over a period of 30 minutes. The dry ice bath was removed, and the mixture was refluxed with stirring at -35 °C for 1 h. The ammonia was then allowed to evaporate overnight. The resulting slurry was filtered and the filter cake washed with several portions of methanol. The combined solution was rotary evaporated. The residue of the diaziridine derivative was dissolved in dichloromethane (1 mL) and treated with triethylamine (0.5 mL). A solution of iodine (0.5 g, 3.9 mmol) in dichloromethane (1.7 mL) was slowly added under stirring until the appearance of a persistent orange-brown coloration. The mixture was chromatographed on a column of silica gel (EtOAc: DCM 20:80) to yield (0.13 g, 25%) **3** as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.18-2.11 (m, 4H), 1.93 (t, J = 2.66 Hz, 1H), 1.76-1.72 (m, 2H), 1.55-1.49 (m, 2H), 1.36-1.27 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.33, 83.11, 68.99, 31.43, 28.03, 27.84, 27.54, 22.50, 17.76. MS (ESI) *m/z*: [M+1] 181.1 (20%), 153.0 (100%).

3-(3-(pent-4-yn-1-yl)-3*H*-diazirin-3-yl)propanoyl chloride (**4**)



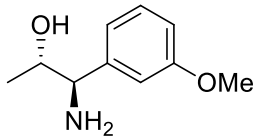
To a solution of 3-(3-(pent-4-ynyl)-3*H*-diazirin-3-yl)propanoic acid (0.23 g, 1.27 mmol) in dichloromethane (10 mL) was added oxalyl chloride (0.486 g, 3.83 mmol) and a drop of DMF. The reaction was stirred at ambient temperature for 2 h. The volatiles were evaporated, and the acid chloride was used for next step.

(1*R*,2*S*)-1-azido-1-(3-methoxyphenyl)propan-2-ol (5)[3]



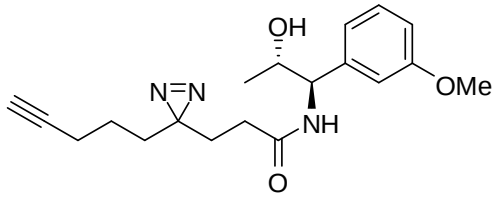
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.33 (m, 1H), 6.99 – 6.90 (m, 3H), 4.47 (d, *J* = 5.8 Hz, 1H), 4.04 – 3.95 (m, 1H), 3.86 (s, 3H), 1.79 (bs, 1H), 1.23 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.93, 137.82, 129.92, 120.08, 113.97, 113.47, 71.44, 70.53, 55.31, 18.66. MS (ESI) *m/z*: [M+1] 208.0 (100%).

(1*R*,2*S*)-1-amino-1-(3-methoxyphenyl)propan-2-ol (6)



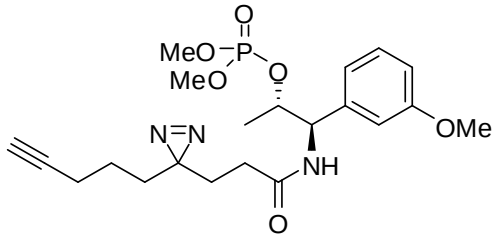
(1*R*,2*S*)-1-azido-1-(3-methoxyphenyl)propan-2-ol (**5**) (2.412g, 11.64 mmol, 1 eq) and Ph_3P (6.11 g, 23.28 mmol, 2 eq) were dissolved in 39 mL of THF dry under argon. Water (2 mL, 111.64 mmol, 10 eq) was added to the reaction mixture and stirring was continued over night at 50 ºC. THF was evaporated and the crude mixture was purified by flash chromatography (DCM: MeOH; 3:1) to yield **6** as an oil (1.897 g, 89%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (t, *J* = 8.1 Hz, 1H), 6.89-6.86 (m, 2H), 6.82–6.75 (m, 1H), 3.93–3.86 (m, 1H), 3.82 (d, *J* = 4.6 Hz, 1H), 3.78 (s, 3H), 2.14 (bs, 2H), 1.04 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.59, 143.78, 129.33, 119.73, 113.13, 112.55, 70.97, 61.07, 55.19, 18.49. MS (ESI) *m/z*: [M+1] 182.0 (100%).

***N*-((1*R*,2*S*)-2-hydroxy-1-(3-methoxyphenyl)propyl)-3-(3-(pent-4-ynyl)-3*H*-diazirin-3-yl)propanamide (7)**



To a solution of (1*R*,2*S*)-1-amino-1-(3-methoxyphenyl)propan-2-ol (**6**) (50 mg, 0.27 mmol) in CH_2Cl_2 (1 mL) was added triethylamine (120 µL, 0.83 mmol). The mixture was cooled to 0-5 °C followed by the addition of 3-(3-(pent-4-ynyl)-3*H*-diazirin-3-yl)propanoic acid chloride **4** (64 mg, 0.32 mmol) and stirred overnight at room temperature. Then, the reaction mixture diluted with DCM (15 mL) and washed with saturated aqueous $NaHCO_3$ (10 mL), and brine (10 mL). The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The mixture was chromatographed on a column of silica gel (EtOAc: DCM 20:80) to yield **7** (74 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (t, *J* = 7.8 Hz, 1H), 6.91-6.84 (m, 3H), 6.74-6.69 (m, 1H), 4.85 (dd, *J* = 8.0, 3.8 Hz, 1H), 4.16–4.05 (m, 1H), 3.78 (s, 3H), 2.56 (bs, 1H), 2.11 (td, *J* = 6.9, 2.4 Hz, 2H), 1.96–1.92 (m, 3H), 1.75 (t, *J* = 7.5 Hz, 2H), 1.50–1.45 (m, 2H), 1.32–1.24 (m, 2H), 1.06 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.86, 159.68, 139.23, 129.59, 120.21, 114.05, 112.88, 83.36, 69.90, 69.03, 58.74, 55.24, 31.76, 30.44, 28.46, 28.08, 22.65, 19.92, 17.85. MS (ESI) *m/z*: [M+1] 344.0 (100%).

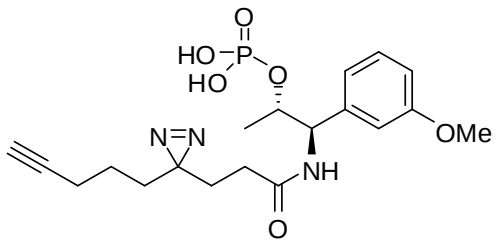
(1*R*,2*S*)-1-(3-methoxyphenyl)-1-(3-(3-(pent-4-ynyl)-3*H*-diazirin-3 yl)propanamido)propan-2-yl dimethyl phosphate (8)



N-((1*R*,2*S*)-2-hydroxy-1-(3-methoxyphenyl)propyl)-3-(3-(pent-4-ynyl)-3*H*-diazirin-3-yl)propanamide (**7**) (26 mg, 0.076 mmol) in DCM (700 µL) was cooled to 0-5 °C and *N*-methyl imidazole (12 µL, 0.15 mmol, 2 eq), dimethyl phosphorochloridate (16.2 µL, 0.15 mmol, 2 eq) was added at same temperature. After the reaction mixture was stirred at room temperature for 12 h, the reaction mixture was poured into aqueous $NaHCO_3$

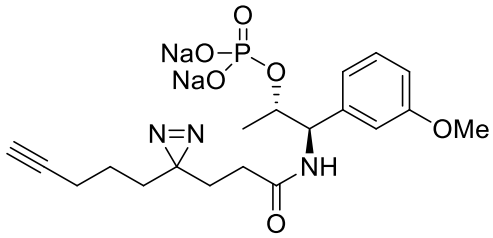
solution (10 mL) and extracted with DCM (2 x 10 mL). The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The mixture was chromatographed on a column of silica gel (EtOAc: DCM 20:80) to yield **8** (31.8 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.3 Hz, 1H), 7.27 (t, *J* = 8.1 Hz, 1H), 6.94 (d, *J* = 7.7 Hz, 1H), 6.90 (t, *J* = 2.0 Hz, 1H), 6.86-6.83 (m, 1H), 4.99 (dd, *J* = 8.3, 3.5 Hz, 1H), 4.83-4.75 (m, 1H), 3.80 (d, *J* = 11.6 Hz, 6H), 3.70 (d, *J* = 11.2 Hz, 3H), 2.13 (td, *J* = 7.0, 2.6 Hz, 2H), 2.05-2.00 (m, 2H), 1.96 (t, *J* = 2.9 Hz, 1H), 1.80-1.75 (m, 2H), 1.52-1.47 (m, 2H), 1.34-1.29 (m, 2H), 1.28 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.67, 159.51, 138.41, 129.32, 120.81, 114.46, 113.10, 83.38, 77.23, 77.17, 68.97, 57.44, 57.39, 55.22, 54.64, 31.66, 30.34, 28.43, 22.67, 19.10, 17.85. MS (ESI) *m/z*: [M+1] 452.0 (100%).

(1*R*,2*S*)-1-(3-methoxyphenyl)-1-(3-(3-(pent-4-ynyl)-3*H*-diazirin-3-yl)propanamido)propan-2-yl dihydrogen phosphate (9)



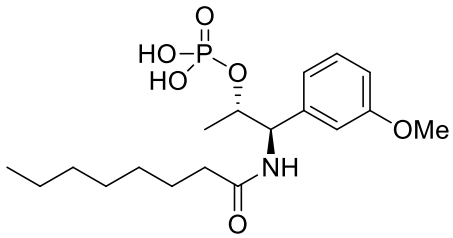
(1*R*,2*S*)-1-(3-methoxyphenyl)-1-(3-(3-(pent-4-ynyl)-3*H*-diazirin-3-yl)propanamido) propan-2-yl dimethyl phosphate (**8**) (17 mg, 0.038 mmol) in acetonitrile (700 µL) was cooled to 0-5 ^{o}C, trimethyl silyl iodide (11 µL, 0.076 mmol) was added to the reaction mixture and stirred at room temperature for 2 h. The crude reaction mixture was purified by HPLC to yield **9** (9.6 mg, 60%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (bs, 1H), 7.22 (t, *J* = 8.0 Hz, 1H), 7.05 (bs, 2H), 6.95-6.92 (m, 2H), 6.83-6.80 (m, 1H), 5.07 (d, *J* = 5.0 Hz, 1H), 4.85-4.80 (m, 1H), 3.75 (s, 3H), 2.18-2.12 (m, 1H), 2.07 – 1.97 (m, 3H), 1.90 (t, *J* = 2.1 Hz, 1H)), 1.78-1.64 (m, 2H), 1.42 (td, *J* = 8.0, 3.1 Hz, 2H), 1.23-1.18 (m, 2H), 1.14 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.22, 159.50, 137.66, 129.62, 120.79, 114.51, 113.03, 83.45, 75.51, 69.09, 57.55, 55.25, 31.47, 30.17, 28.57, 28.15, 22.62, 17.77. MS (ESI) *m/z*: [M+1] 423.9 (100%). HRMS *m/z* calculated for $C_{19}H_{26}N_3O_6PH^+$ $(M+H)^+$ 424.16320; *m/z* found $(M+H)^+$ 424.16333.

sodium (1*R*,2*S*)-1-(3-methoxyphenyl)-1-(3-(3-(pent-4-yn-1-yl)-3*H*-diazirin-3-yl) propanamido)propan-2-yl phosphate (10)



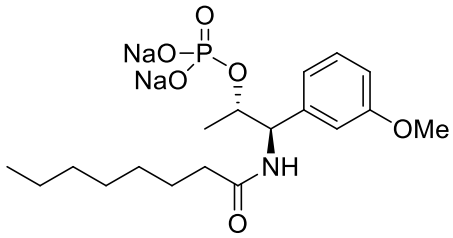
Compound **9** (6 mg, 0.014 mmol) was dissolved in ethanol (0.3 mL) and the resulting mixture was cooled to 0 °C. 1M NaOH (28 µL, 0.028 mmol) was added to reaction and stirring continued for 5 mins. Ethanol was removed under vacuum and lyophilization gave **10** as a white solid (6.3 mg, 95%). ^{1}H NMR (400 MHz, D_2O) δ 7.27 (t, *J* = 7.6 Hz, 1H), 7.01–6.94 (m, 2H), 6.89–6.83 (dd, *J* = 7.9, 1.8 Hz, 1H), 4.62 (d, *J* = 2.8 Hz, 1H), 4.49–4.41 (m, 1H), 3.77 (s, 3H), 2.22 (t, *J* = 2.0 Hz, 1H), 2.11-2.07 (m, 2H), 1.99 (td, *J* = 7.0, 2.3 Hz, 2H), 1.69–1.53 (m, 2H), 1.37–1.31 (m, 2H), 1.18–1.09 (m, 2H), 1.01 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 172.34, 159.05, 140.44, 128.04, 121.55, 114.50, 112.18, 82.98, 71.05, 71.01, 68.67, 59.06, 54.44, 31.01, 29.79, 28.71, 22.59, 18.55, 17.08.

(1*R*,2*S*)-1-(3-methoxyphenyl)-1-octanamidopropan-2-yl dihydrogen phosphate (PCERA-1)[4]



^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (t, *J* = 7.9 Hz, 1H), 6.96-6.93 (m, 2H), 6.88–6.78 (m, 3H), 5.06 (d, *J* = 4.9 Hz, 1H), 4.79 (bs, 1H), 3.75 (s, 3H), 2.37–2.17 (m, 2H), 1.61-1.48 (m, 2H), 1.26–1.16 (m, 8H), 1.10 (d, *J* = 6.2 Hz, 3H), 0.84 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.91, 159.45, 138.25, 129.38, 120.77, 114.42, 112.89, 75.15, 57.34, 55.13, 36.28, 31.67, 29.15, 29.03, 25.75, 22.57, 17.89, 14.04. MS (ESI) *m/z*: [M+1] 387.9 (100%).

sodium (1*R*,2*S*)-1-(3-methoxyphenyl)-1-octanamidopropan-2-yl phosphate (11)[4]



^{1}H NMR (400 MHz, D_2O) δ 7.25 (t, *J* = 7.8 Hz, 1H), 6.96-6.93 (m, 2H), 6.87–6.82 (m, 1H), 4.08–3.98 (m, 1H), 3.82 (s, 3H), 2.28 (t, *J* = 7.4 Hz, 2H), 1.68–1.56 (m, 2H), 1.33-1.27 (m, 8H), 1.17 (d, *J* = 6.4 Hz, 3H), 0.90 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 174.50, 159.60, 141.25, 128.80, 120.03, 113.36, 112.32, 69.15, 59.02, 54.33, 35.72, 31.46, 28.76, 28.70, 25.72, 22.20, 18.66, 13.03.

Biological evaluations

Reagents - Lipopolysaccharide (LPS; *Escherichia coli* serotype 055:B5) was purchased from Sigma-Aldrich (St Louis, MO). PCERA-1 was dissolved in phosphate-buffered saline (PBS) and freshly diluted in culture media. The PCERA-1 probe was dissolved in DMSO and freshly diluted in culture media. C16:0 C1P, purchased from Matreya (Pleasant Gap, PA), was prepared as a 2.62 mM stock in ultrapure water by sonication on ice using a probe sonicator until a clear dispersion was observed. L-glutamine, penicillin-streptomycin-nystatin was purchased from Biological Industries (Beit Haemek, Israel). Dulbecco's modified Eagle's minimum essential medium (DMEM) and fetal bovine serum (FBS) were purchased from Gibco (Carlsbad, CA). The enzyme-linked immunosorbent assay (ELISA) reagent sets for IL-10 and TNFα were purchased from R&D Systems (Minneapolis, MN).

Cell culture - Mouse RAW264.7 macrophage cells, obtained from the American Type Culture Collection (ATCC, Rockville, MD), were grown to 80–90% confluence in DMEM supplemented with 8 mM L-glutamine, 100 U/ml penicillin, 100 μg/ml streptomycin and 1250 U/ml nystatin (hereafter culture medium) with 10% FBS. The cells were grown and maintained at 37°C in a humidified incubator with 5% CO_2.

Cytokine expression measurement - RAW264.7 macrophages were seeded in 96-well plates at 1.5×10^5 cells per well and maintained for 48 hr in culture medium supplemented with 5% FBS. The culture medium was replaced 2 hr before treatment to avoid the artifact of medium replacement on signaling. The cells were stimulated with LPS (100 ng/ml), alone or together with either PCERA-1, PCERA-1 probe or C1P, at

37 °C for 2 hr (for IL-10 analysis) or 5 hr (for TNFα analysis). Cytokine secretion into the medium was measured with commercially available ELISA reagents sets, according to the manufacturer's instructions, using a microplate reader (Bio-Tek, Winooski, Vermont).

Labeling experiments in vitro with PCERA-1 probe 9 - RAW264.7 macrophage lysate was prepared by harvesting cells using a cell scraper, washing twice with PBS, adding RIPA buffer (approx. 10 million cells/ml), shaking at 4 °C for 20 min. The lysate was aliquoted and stored at -20 °C. The day of the experiment, lysate aliquots were defrosted in a bath sonicator filled with ice water for 10 min., then centrifuged (20,817 g, 4 °C) for 20 min. The protein concentration of the lysate was measured using a DC™ (detergent compatible) micro assay (Bio-Rad Laboratories, Inc., Hercules, CA, USA) and normalized by dilution with PBS to approx. 1 mg/ml. For each sample, 3 µL of stock solutions of the probe, PCERA-1, or DMSO were added to 47 µL of lysate to yield a final concentration of 100 µM of the probe with varying concentrations (0, 100, 250, or 500 µM) of the parent molecule PCERA-1. The samples were prepared in a clear 96-well plate and incubated for 30 min. at room temp. on a shaker. Then, the plate was placed on a UV table and irradiated at 365 nm for 10 min.

CuAAC chemistry for in-gel visualization- CuAAC chemistry was performed based on protocols from the Cravatt lab.[5] For each sample, 45 µL of labeled proteome was transferred to 1.5 ml tubes and the following reagents added from a master mix prepared directly before the reaction: rhodamine azide (1 µL of 5 mM in DMSO, final conc. 100 µM); sodium ascorbate (1 µL of 50 mM in PBS, prepared fresh, final conc. 1 mM); TBTA (3 µL of 1.7 mM in 1:4 DMSO:t-butanol, final conc. 100 µM); $CuSO_4$ (2 µL of 50 mM in DDW, final conc. 2 mM). The mixture was allowed to react for 2 h at room temp. on a shaker, and the reaction quenched with the addition of 10 µL of x5 gel loading buffer. Lastly, the samples were analyzed by SDS-PAGE gel (30 µL of each sample loaded on a 10.5% Tris-HCl gel), and the gel visualized using an ImageQuant LAS 4000 Imager (Fujifilm, Tokyo, Japan) set in Cy3 fluorescence mode (Ex/Em = 520 nm/575 nm). Bands were quantified using LI-COR Image Studio Lite (Table S1). As a loading control, gels were subsequently stained using Coomassie and visually examined (Fig. S1).

Table S1. Quantification values.

Name	*Signal*	*Total*	*Area*	*Bkgnd.*	*Normalized to Lane 1*
Lane 1, upper band	29400	77000	1830	26	1.00
Lane 2, upper band	24100	71700	1830	26	0.82
Lane 3, upper band	16200	54700	1830	21	0.55
Lane 4, upper band	14200	52700	1830	21	0.48
Lane 1, lower band	29200	81300	1830	28.5	1.00
Lane 2, lower band	21100	74100	1830	29	0.72
Lane 3, lower band	15400	57500	1830	23	0.53
Lane 4, lower band	12900	55000	1830	23	0.44

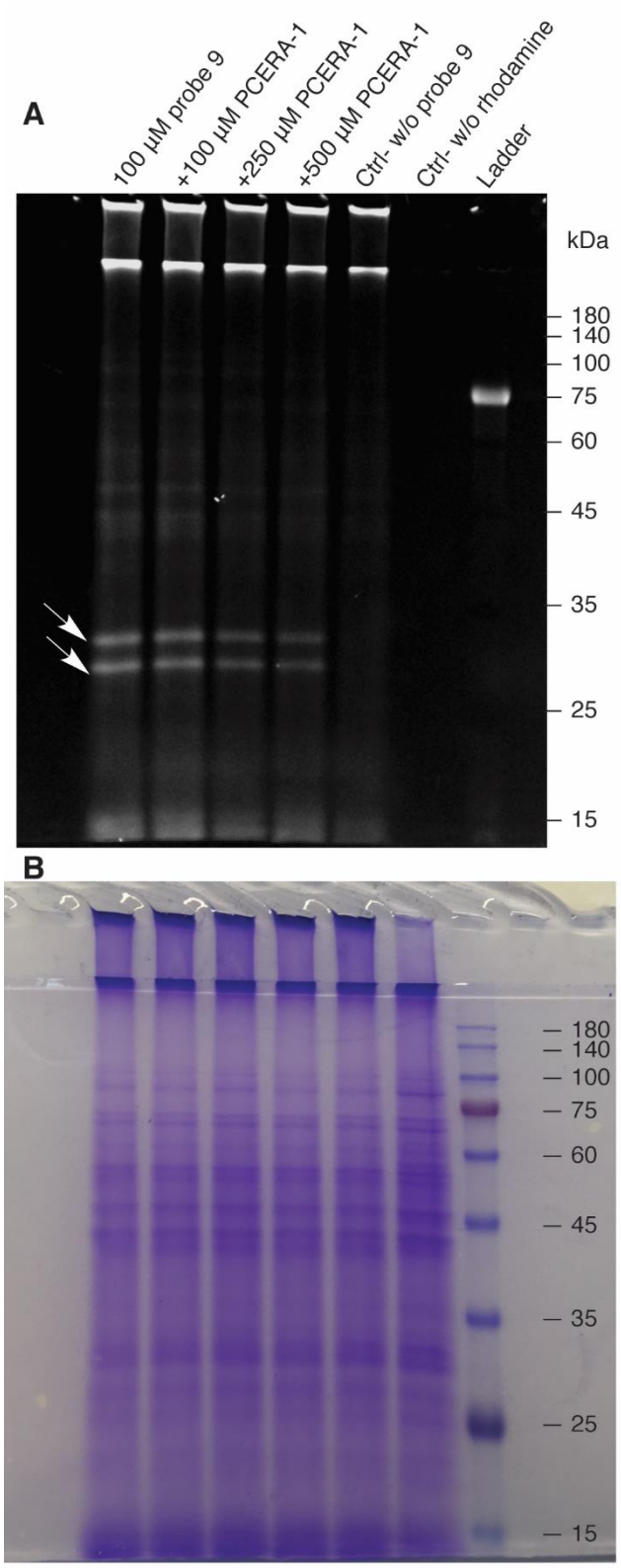


Figure S1: Fluorescent image of gel from Fig. 1 (A) as compared to the Coomassie stain (B). Note that some insoluble protein accumulates at the top and does not enter the resolving region of the gel. In the samples containing click reagents (lanes 1-5) this effect is intensified, and the insoluble bands are strongly labeled with rhodamine azide.

Since this occurs even in the absence of the PCERA-1 probe (lane 5), this appears to be an unspecific interaction between the dye and the aggregate.

Labeling experiments in vitro with PCERA-1 probe - RAW264.7 macrophage lysate was prepared by harvesting cells using a cell scraper, washing twice with PBS, adding RIPA buffer (approx. 10 million cells/ml), shaking at 4 °C for 20 min. The lysate was aliquoted and stored at -20 °C. The day of the experiment, lysate aliquots were defrosted in a bath sonicator filled with ice water for 10 min., then centrifuged (20,817 g, 4 °C) for 20 min. The protein concentration of the lysate was measured using a DC™ (detergent compatible) microassay (Bio-Rad Laboratories, Inc., Hercules, CA, USA) and normalized by dilution with PBS to approx. 1 mg/ml. For each sample, 3 µl of stock solutions of the probe, PCERA-1, and/or vehicle control (DMSO) were added to 47 µl of lysate to yield a final concentration of 100 µM of the probe with varying concentrations (0, 100, 250, or 500 µM) of the parent molecule PCERA-1, and a total of 6% DMSO per sample. The samples were prepared in a clear 96-well plate and incubated for 30 min. at room temp. on a shaker. Then, the plate was placed on a UV table and irradiated at 365 nm for 10 min.

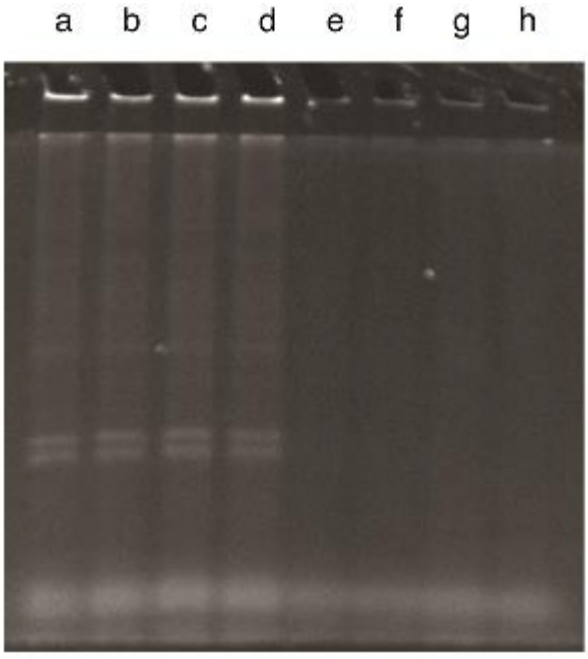


Figure S2: Fluorescent image of labeling experiment in presence of C1P. In order to examine the effect of C1P on the labeling of the PCERA probe on macrophage lysates, a labeling experiment was set up as described above. For competition samples, a stock

solution of 2.2 mM of C1P was prepared by sonication in order to form vesicles, and added to the lysate to a final concentration of 50 μM. Samples which contained only probe (a, b) showed a similar labeling pattern to samples containing the probe and C1P (c, d). No labeling was observed in samples containing only C1P and vehicle control (e, f), or vehicle control alone (g, h), other than the low molecular weight smear observed in all samples containing rhodamine, as described above.

References

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2. (a) L. Dubinsky, A. Delago, N. Amara, P. Krief, J. Rayo, T. Zor, V. V. Kravchenko, M. M. Meijler, *Chem. Commun.*, 2013, ***49***, 5826-5828. (b) Y. Xie, J. Ge, H. Lei, B. Peng, H. Zhang, D. Wang, S. Pan, G. Chen, L. Chen, Y. Wang, Q. Hao, S. Q. Yao, H. Sun, *J. Am. Chem. Soc.* 2016, **138**, 15596−15604. (c) K. Zhang, W. Sun, L. Huang, K. Zhu, F. Pei, L. Zhu, Q. Wang, Y. Lu, H. Zhang, H. Jin, L. Zhang, L. Zhang, J. Yue, *J. Am. Chem. Soc*. 2017, **139**, 156−170.
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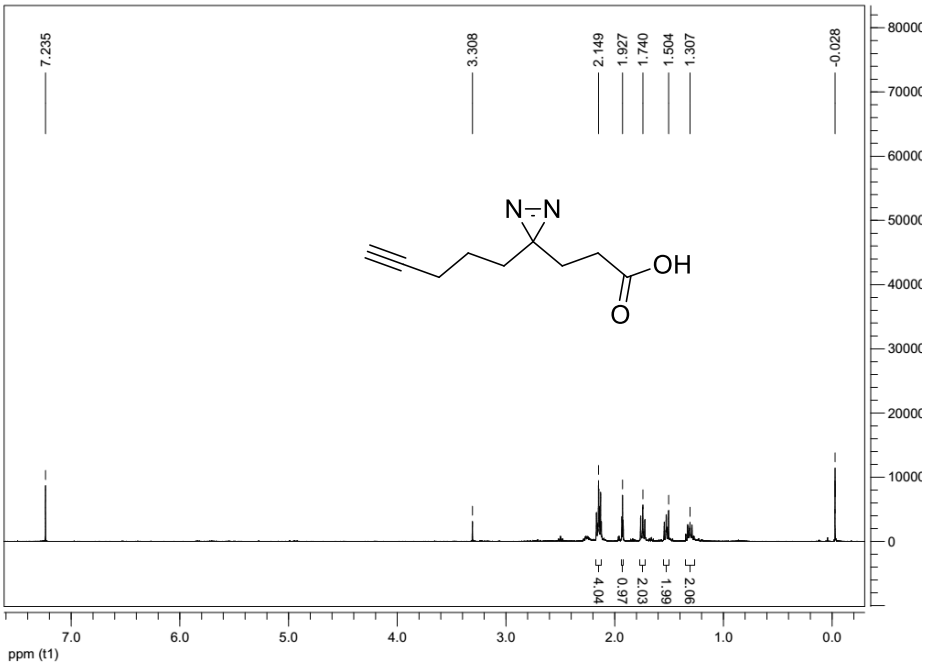
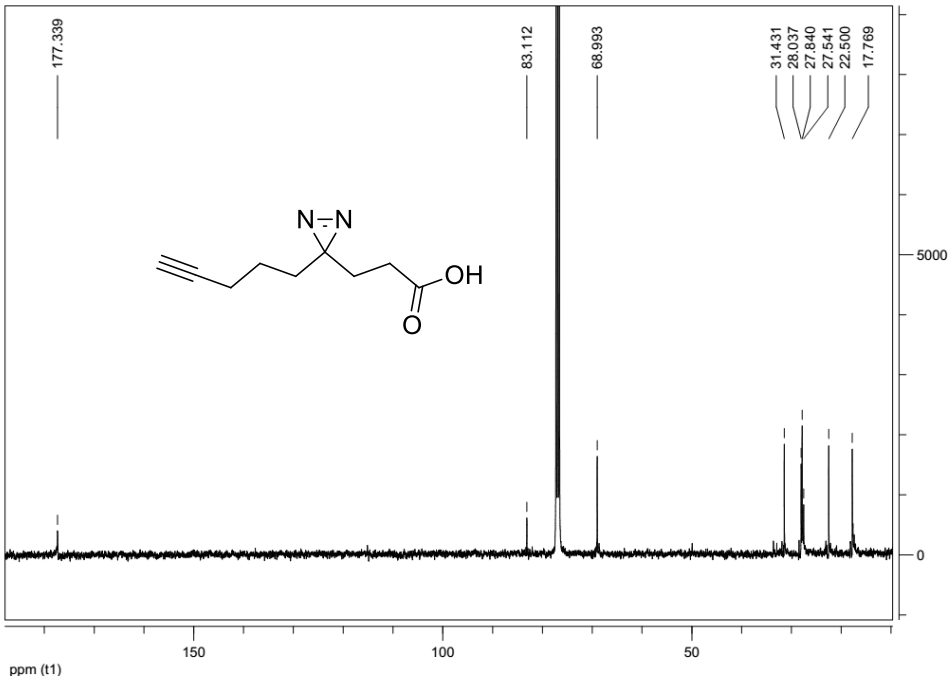
5. A. E. Speers, B. F. Cravatt, *Curr. Protoc Chem Biol.*, 2009, ***1***, 29-41.

NMR-spectra

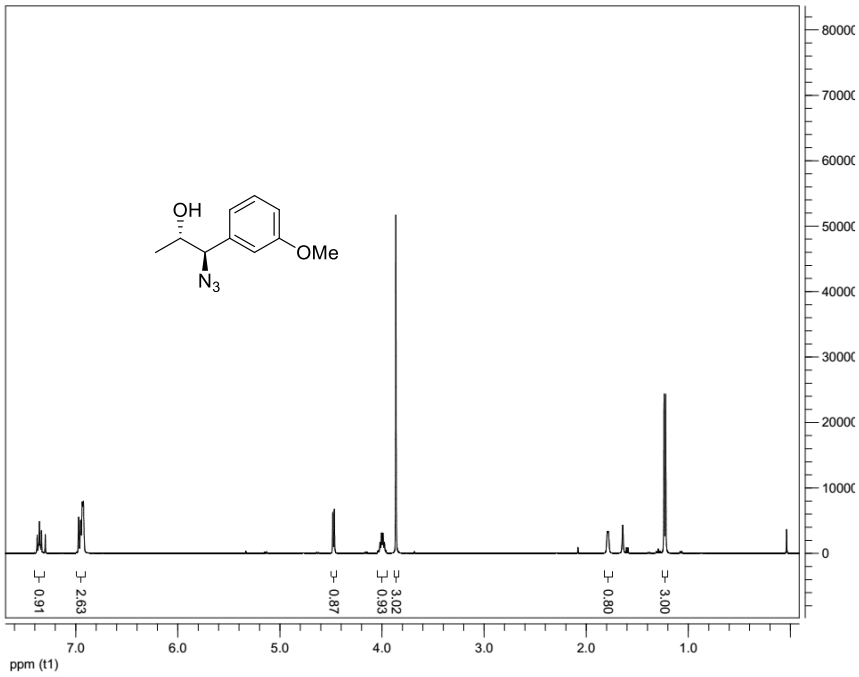
^{1}H NMR for compound **3**:



^{13}C NMR for compound **3**:



^{1}H NMR for compound **5**:



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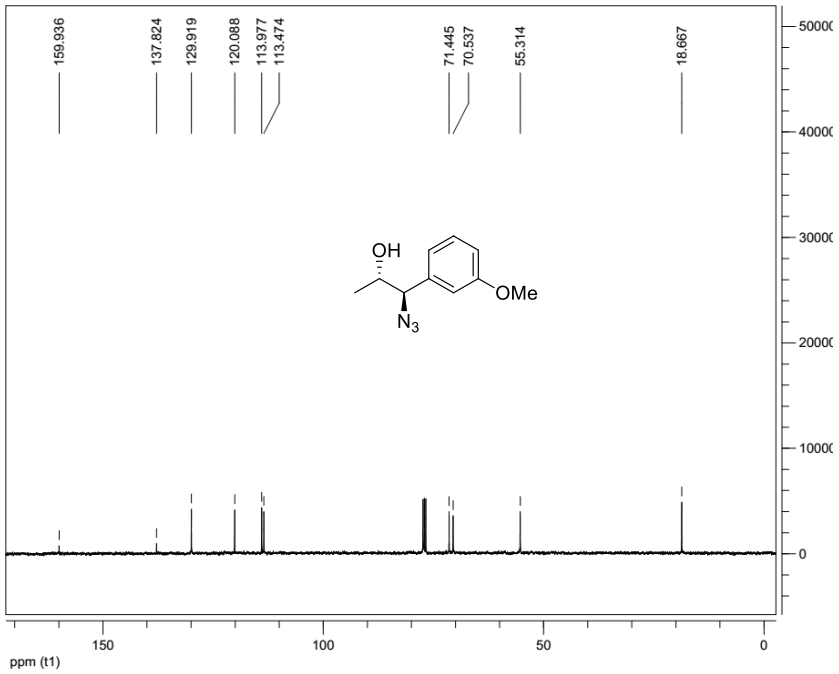

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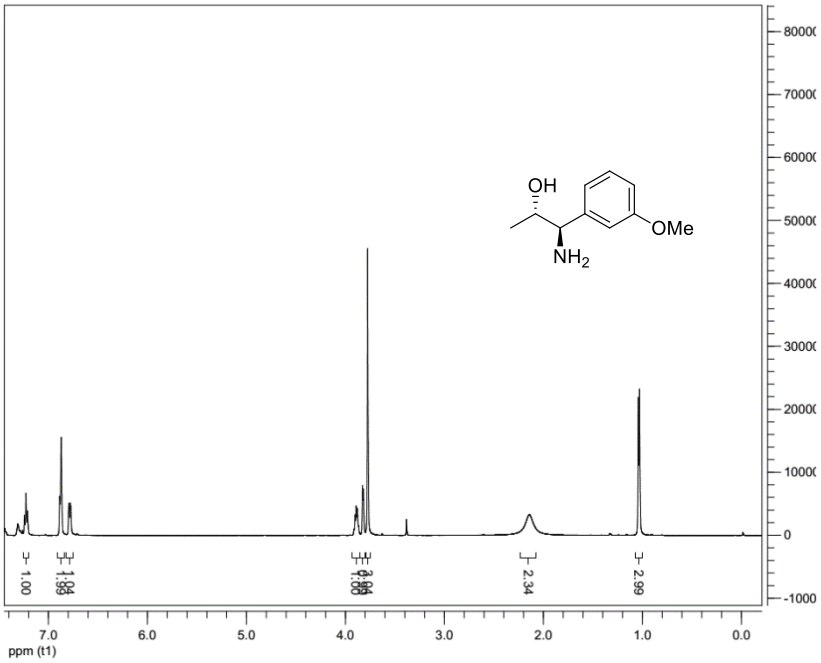

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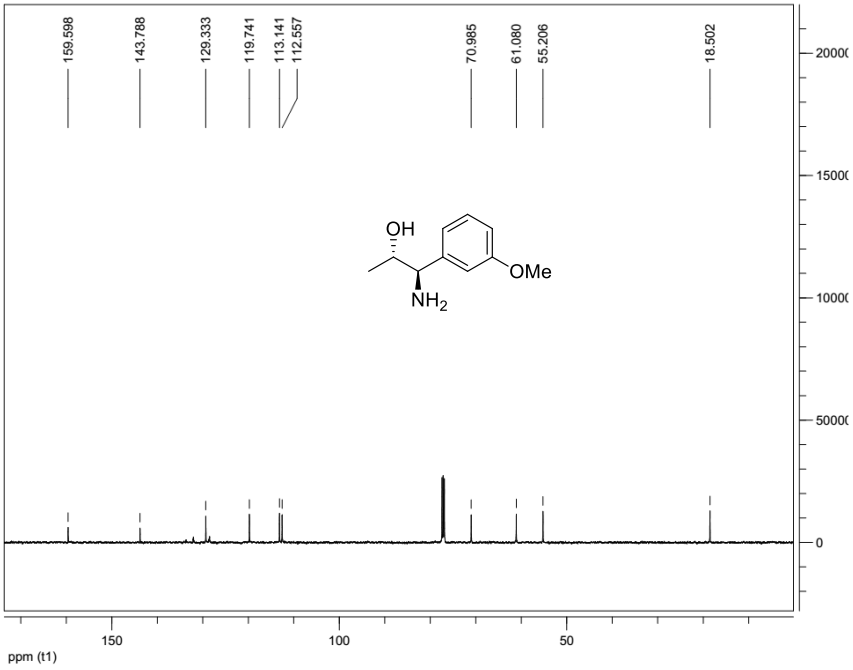

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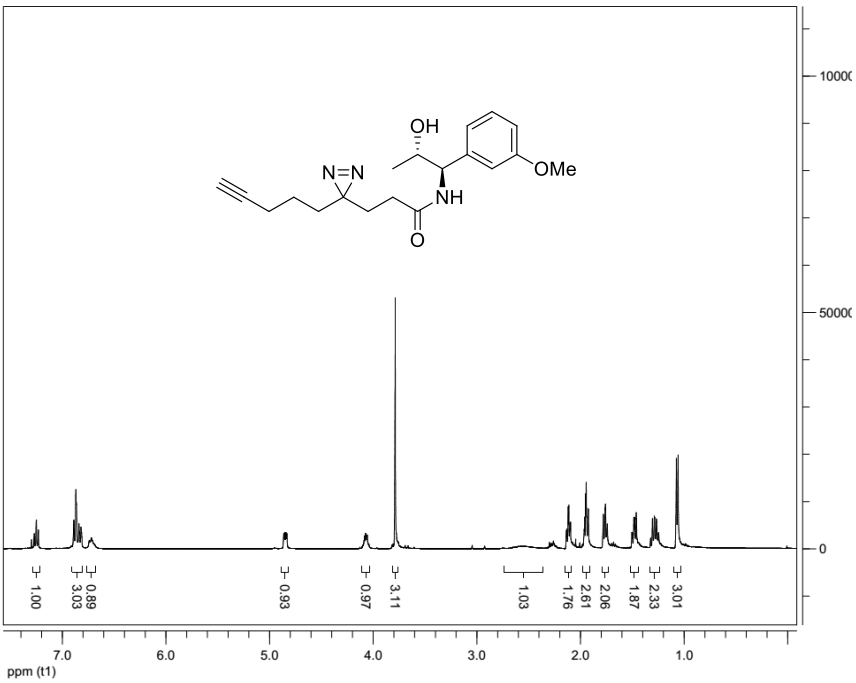

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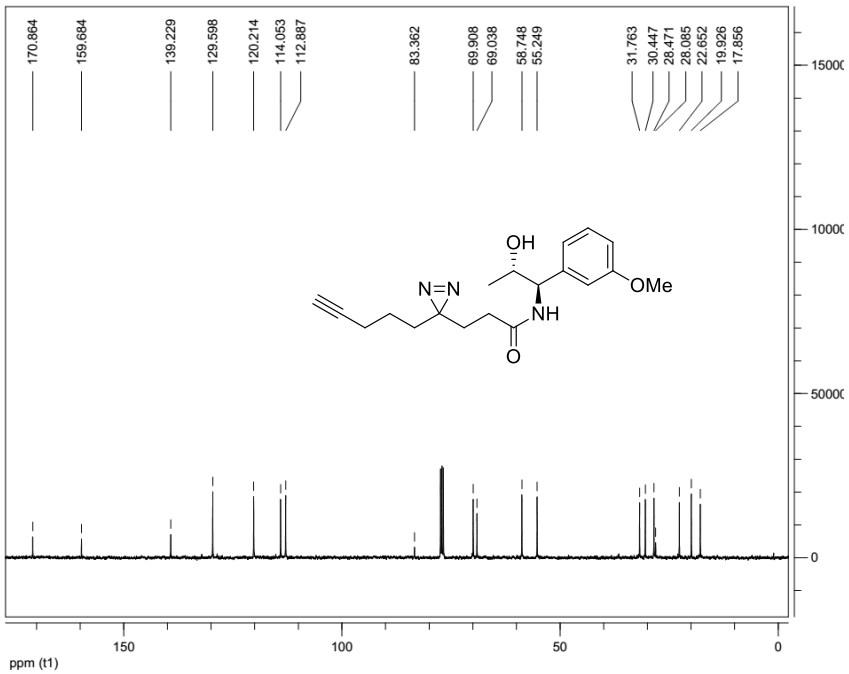
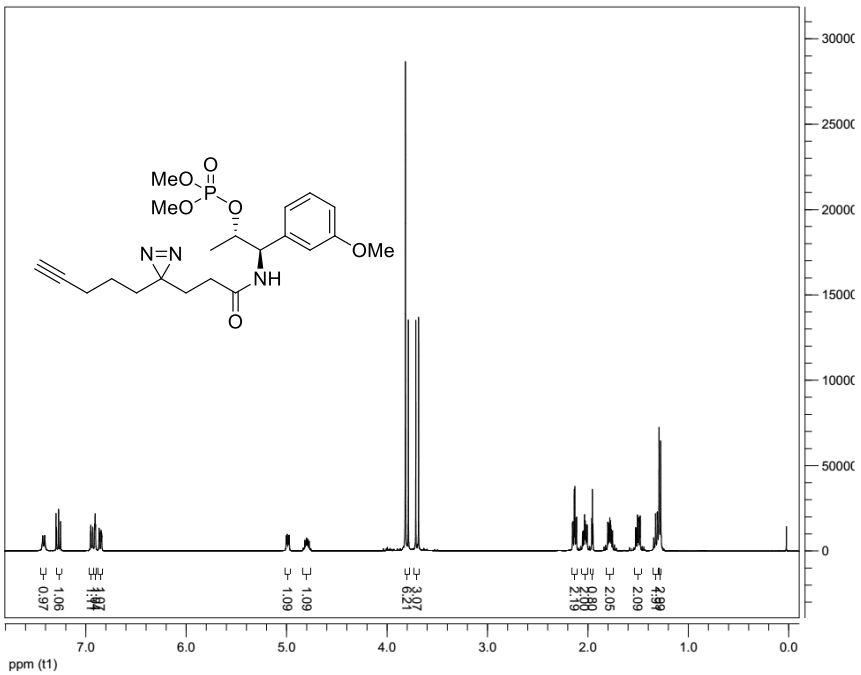


^{1}H NMR for compound **8**:



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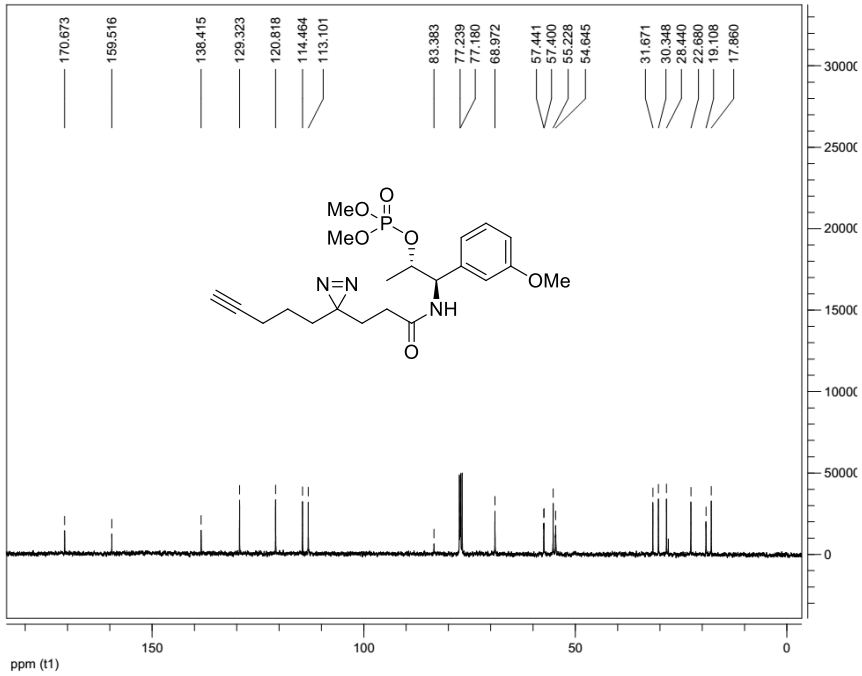

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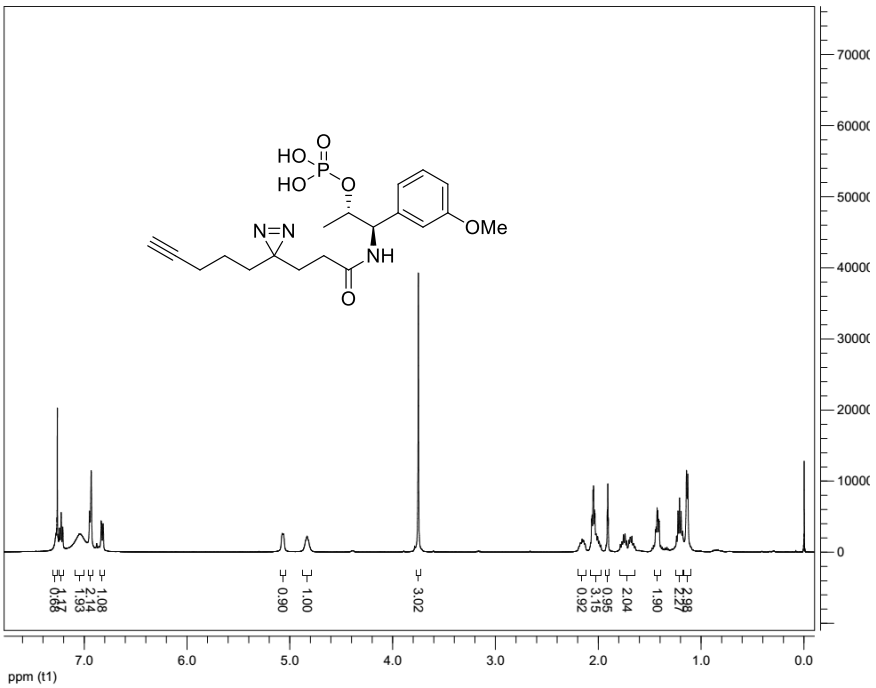

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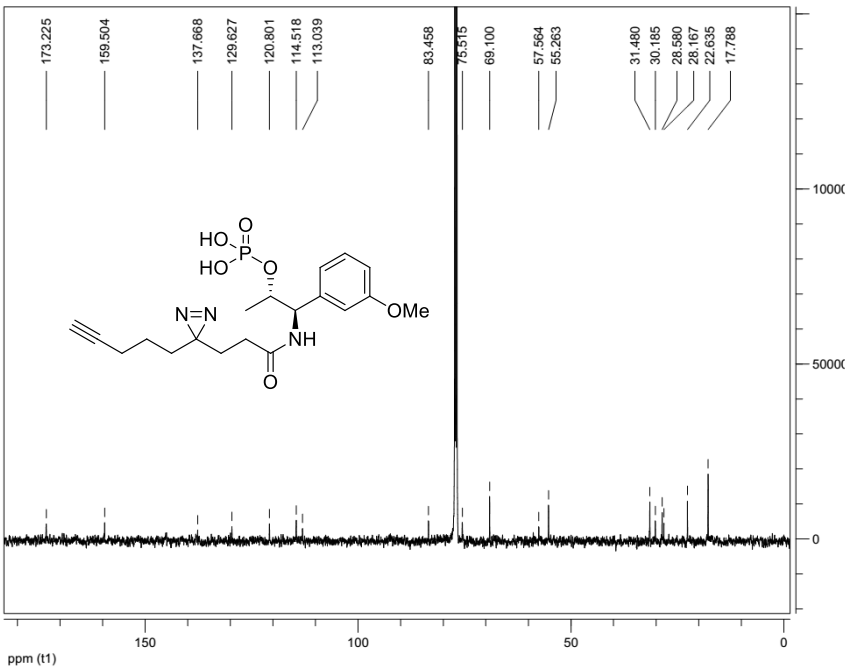

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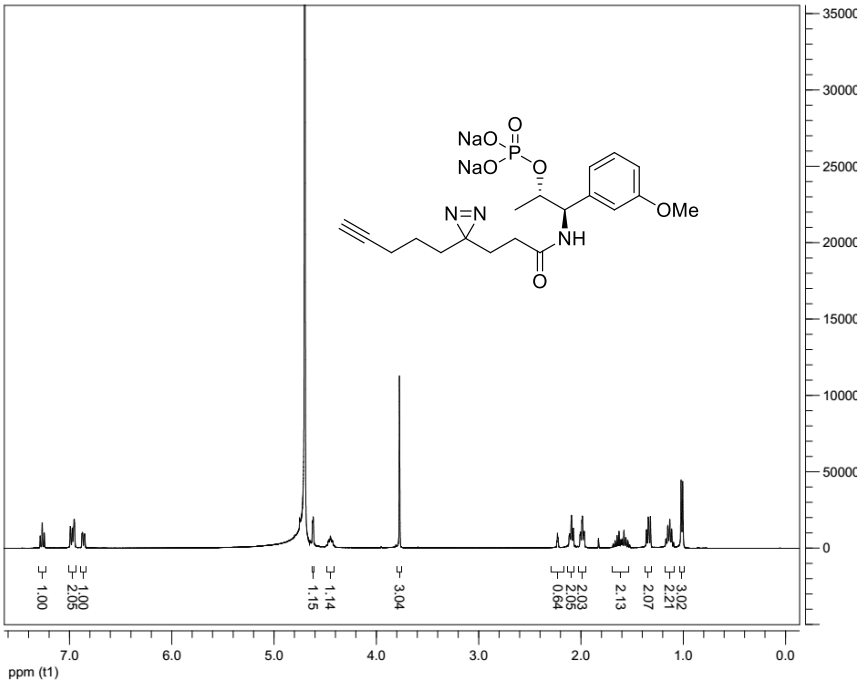

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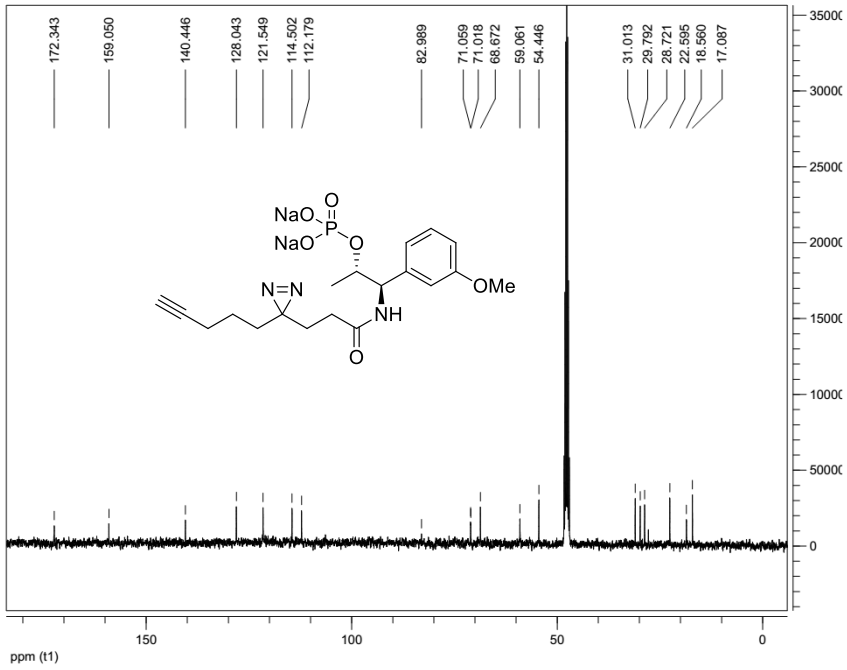

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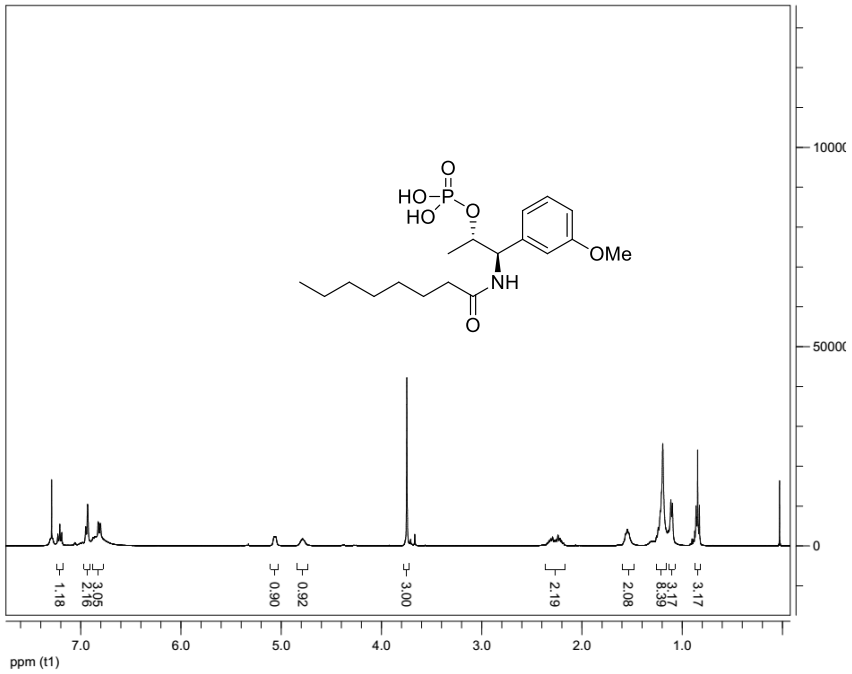

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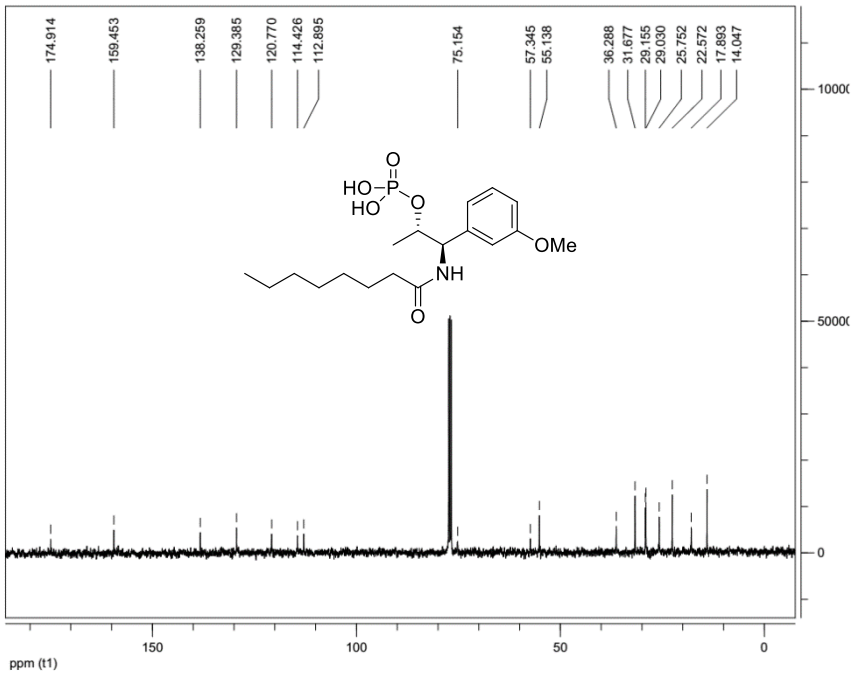
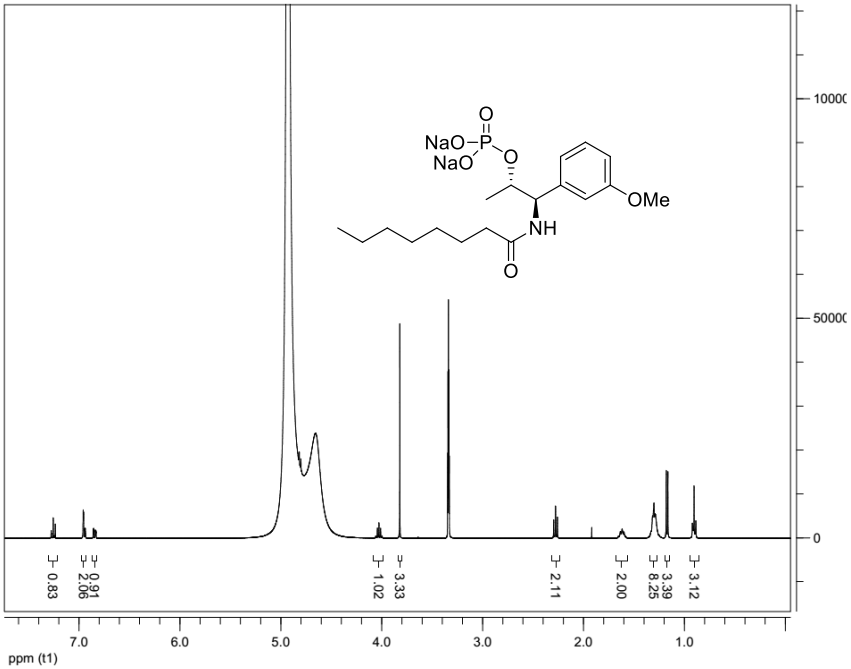


^{1}H NMR for **11**:



^{13}C NMR for **11**: