Supporting Information for

Synthesis and Evaluation of Photo-activatable β-Diarylsydnone-L-alanines for Fluorogenic Photo-click Cyclization of Peptides

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Supplemental Figures and Tables

General Information

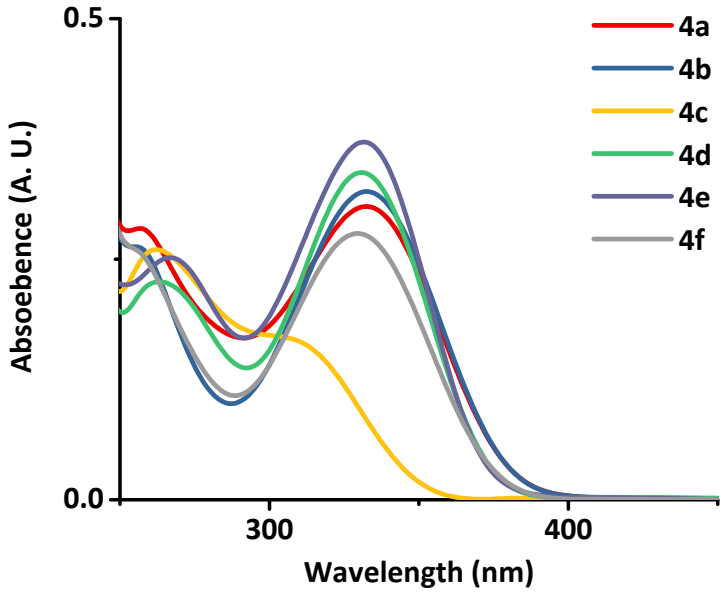
Solvents and starting materials were purchased from commercial sources and used directly without further purification. TCO[S1] (equatorial-TCO, single diastereomer was used) was synthesized according to literature procedures. Commercially available chemicals were obtained from Adamas, Acros Organics, Aldrich Chemical Co, Alfa Aesar and TCI. NMR spectra were recorded in a Brüker Advance NMR spectrometer for ^{1}H NMR at 400 MHz, ^{13}C at 101 or 151 MHz and ^{19}F at 376 MHz. Chemical shifts (δ) for ^{1}H and ^{13}C NMR spectra are given in ppm relative to TMS. The residual solvent signals were used as references for ^{1}H and ^{13}C NMR spectra and the chemical shifts converted to the TMS scale ($CDCl_3$, 7.26 ppm for ^{1}H NMR and 77.16 ppm for ^{13}C NMR; DMSO-d_6, 2.50 ppm for ^{1}H NMR and 39.52 ppm for ^{13}C NMR; methanol-d_4 3.31 ppm for ^{1}H NMR and 49.05 ppm for ^{13}C NMR;). Shifts Multiplicity was reported as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Chemical shifts (δ) for ^{19}F NMR spectra are given in ppm relative to $PhCF_3$ (artificially added $PhCF_3$, -62.72 ppm). Exact ESI mass spectra were recorded on a SHIMADZU LCMS-IT-TOF. ESI-MS were obtained on a Thermo LTQ-XL mass spectrometer.

UV-Vis absorption spectra were recorded using 1 cm quartz cuvettes on a Thermo NANODROP 2000C Spectrophotometer. Fluorescence spectra were recorded using 1 cm quartz cuvettes on a HORIBA Fluoromax-4 Spectrofluorometer at 25 ºC.

Cell imaging experiments were carried out on an Olympus IX83 live cell fluorescence microscope. Cells were stained with commercially available DIO (3,3'-dioctadecyloxacarbocyanine) dyes for cell membrane imaging and identification.

UV–Vis absorption of sydnone amino acids 4a-f.

a)

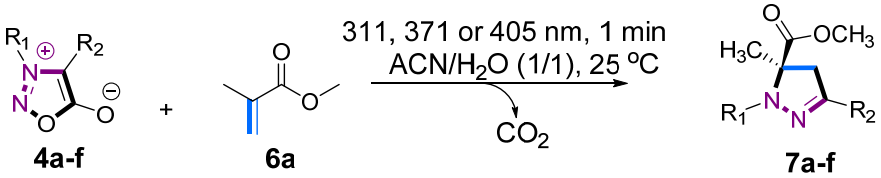


b)

Sydnone amino acids	**4a**	**4b**	**4c**	**4d**	**4e**	**4f**
λ_{max} (nm)	332	333	305	331	332	330

Figure S1. (a) UV–Vis absorption of sydnone amino acids **4a-f**; (b) Maximum absorption wavelength of sydnone amino acids **4a-f**. The final concentrations of the compounds are 30 μM in ACN/H_2O (1/1, v/v).

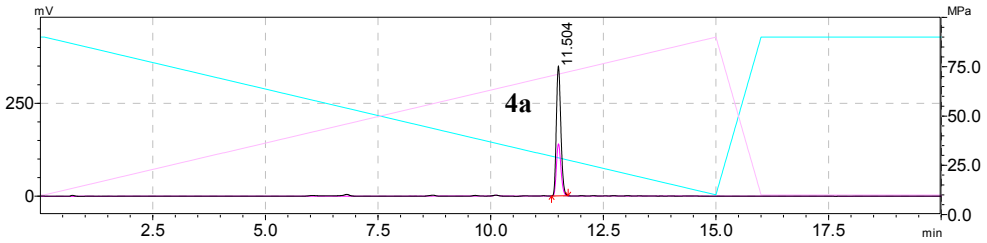
1,3-dipolar cycloaddition of SAAs 4a-f with methyl methacrylate (MMA) under photo-activation



4a/7a: R_1 = *p*-MeOPh; R_2 = Boc-L-Phe-Ome
4b/7b: R_1 = *p*-FPh; R_2 = Boc-L-Phe-Ome
4c/7c: R_1 = Boc-L-Phe-Ome; R_2 = H
4d/7d: R_1 = Boc-L-Phe-Ome; R_2 = *p*-CF_3Ph
4e/7e: R_1 = Boc-L-Phe-Ome; R_2 = *m*-2CF_3Ph
4f/7f : R_1 = Boc-L-Phe-Ome; R_2 = Ph

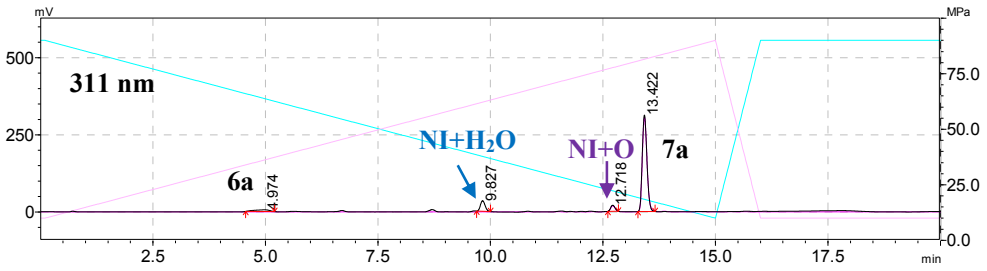
Figure S2. Photo-activated conversion of 50 µM sydnone amino acids (**4a-f**) to pyrazolines with 0.5 mM MMA (**6a**) in ACN/H_2O (1/1) using HPLC-MS. (a) HPLC trace of sydnone amino acids; (b) HPLC trace of the reaction mixture after 1 min photo-irradiation with 311, 371 or 405 nm lamp. The conversion was calculated based on the absorbance at 254 nm. HPLC peak assignments based on mass-to-charge ratio in mass spectrum: [NI] = corresponding nitrile imine or active intermediate with the same mass-to-charge ratio; [NI+H_2O] = hydrolysis product of corresponding NI; [NI+ACN] = cycloadducts of corresponding NI with acetonitrile (from solvent); [NI+O] = corresponding NI with an oxgen atom.

a)



Peak No.	Time	Area	Height	%Area
1	11.504	2417937	347774	100.000

b)



Peak No.	Time	Area	Height	%Area
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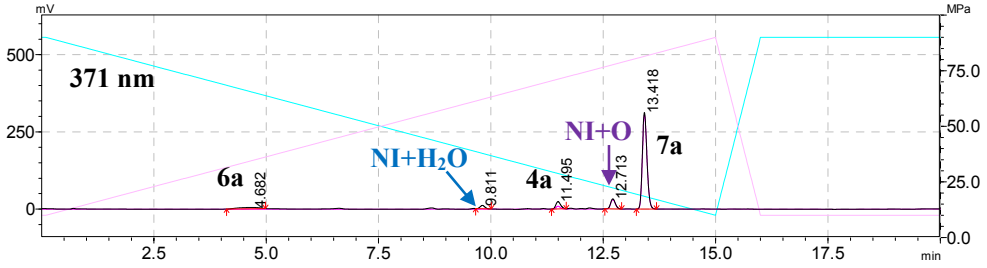
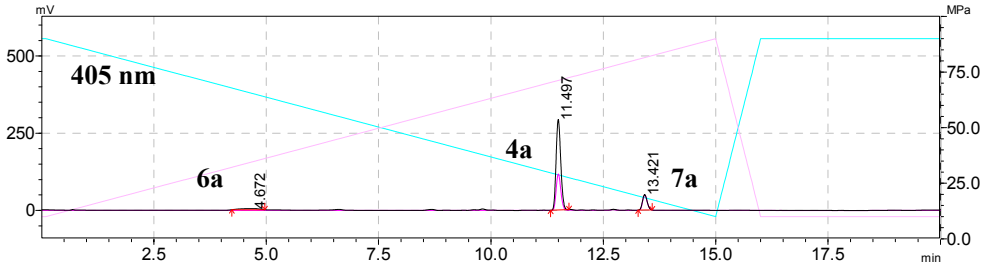


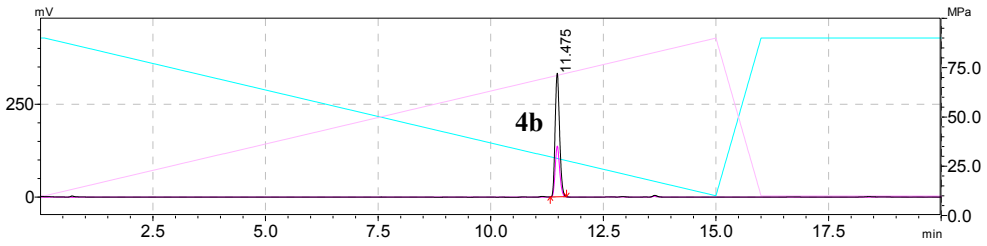
Peak No.	Time	Area	Height	%Area
1	11.495	179383	23809	7.420
2	13.418	2280112	311112	92.580



Peak No.	Time	Area	Height	%Area
1	11.497	2105460	292307	87.080
2	13.421	359318	49719	12.920

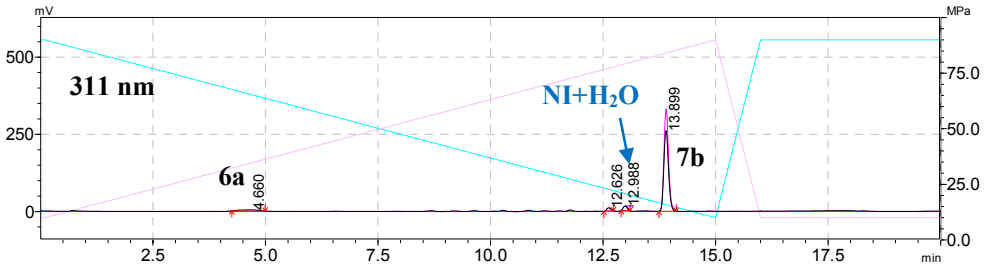
Figure S2a. The identity of Pyis **7a** was confirmed by LC-MS: MS (ESI) calcd. for **7a** $C_{28}H_{36}N_3O_7^+$ 526.25 [M+H$^+$], found 526.02.

a)



Peak No.	Time	Area	Height	%Area
1	11.475	2352482	332213	100.000

b)



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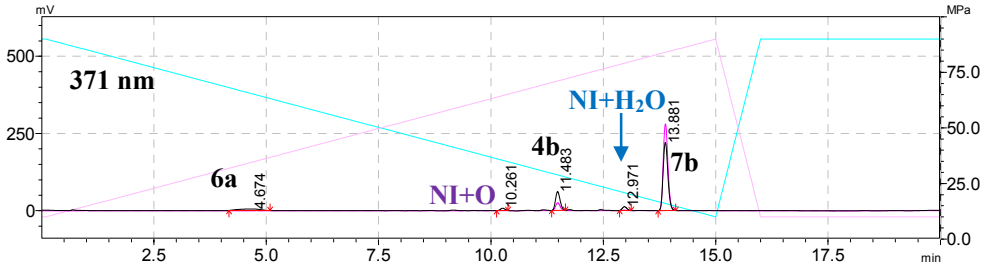
1	13.899	1881077	260656	100.000



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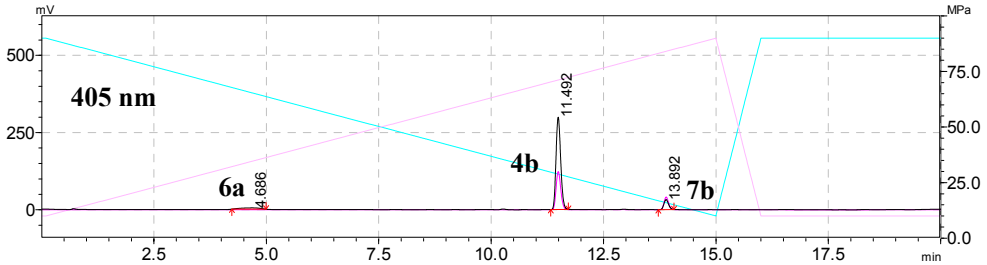
1	11.483	434655	61192	18.480
2	13.881	1614579	220583	81.520

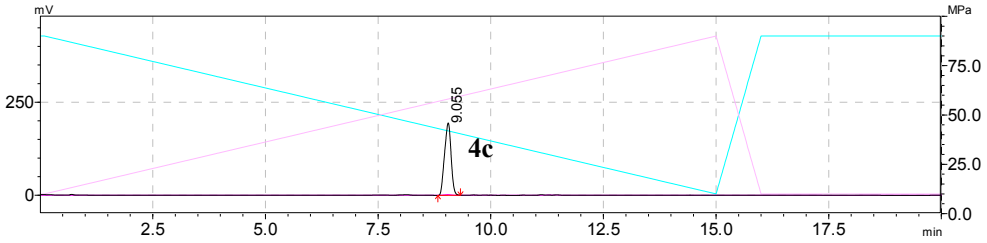


Peak No.	Time	Area	Height	%Area

1	11.492	2162570	298752	91.930
2	13.892	235667	32645	8.070

Figure S2b. The identity of Pyis **7b** was confirmed by LC-MS: MS (ESI) calcd. for **7b** $C_{27}H_{33}FN_3O_6^+$ 514.23 [M+H$^+$], found 513.99.

a)



Peak No.	Time	Area	Height	%Area
1	9.055	1953043	194404	100.000

b)

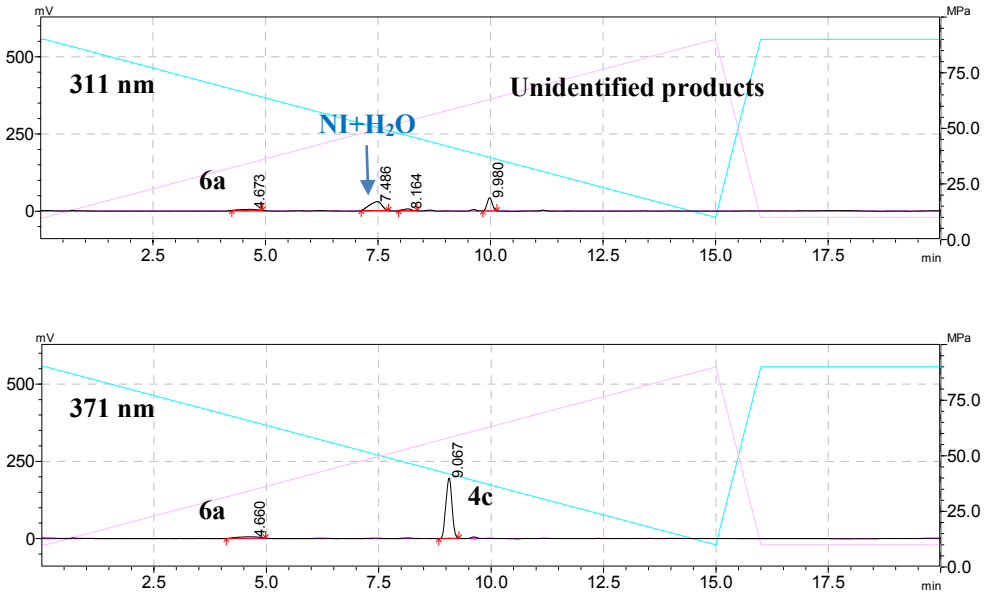
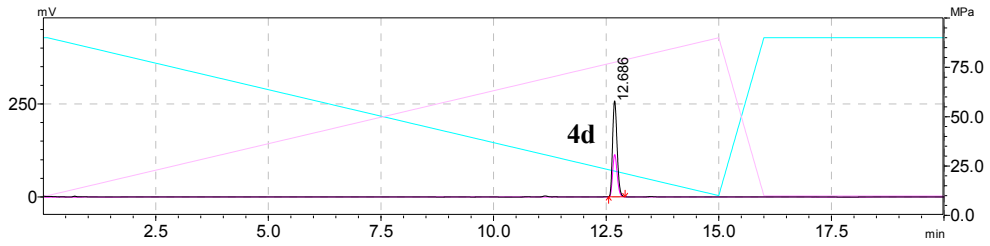


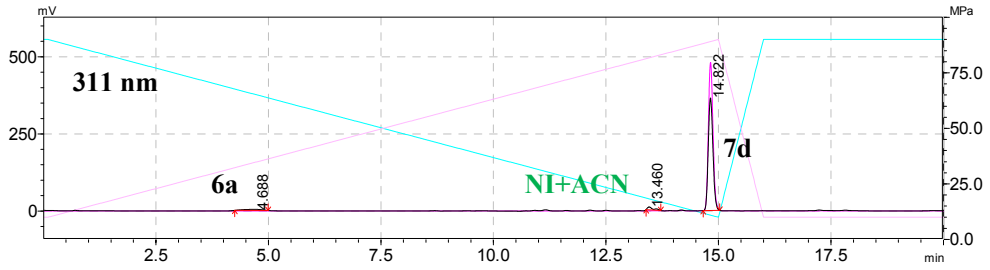
Figure S2c. The identity of Pyis **7c** was confirmed by LC-MS: MS (ESI) calcd. for **7c** $C_{21}H_{30}N_3O_6^+$ 420.21 [M+H$^+$], found N. D.

a)



Peak No.	Time	Area	Height	%Area
1	12.686	1790584	256607	100.000

b)



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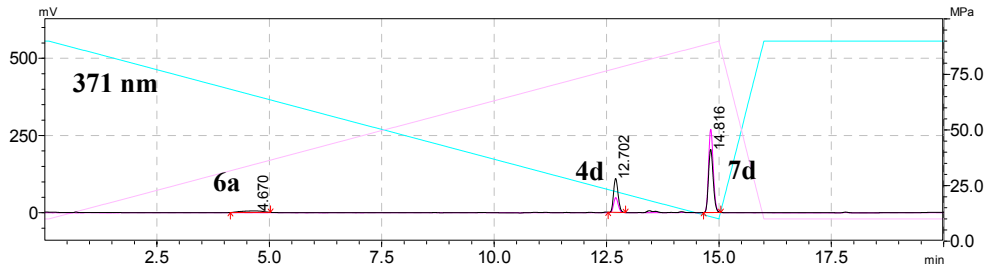
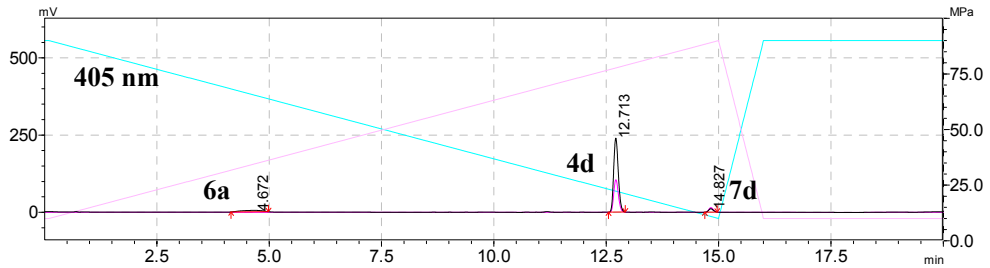


Peak No.	Time	Area	Height	%Area
1	12.702	773710	109385	43.210
2	14.816	1484194	204000	56.790

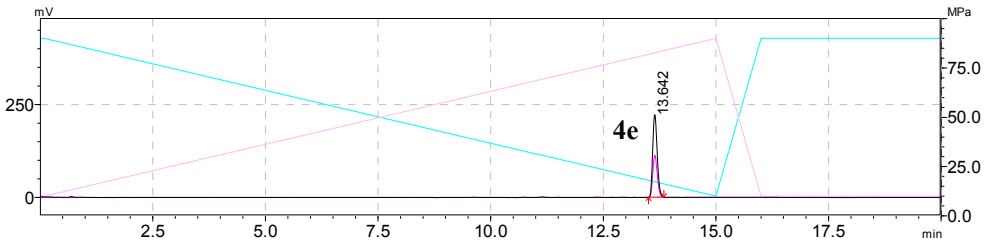


Peak No.	Time	Area	Height	%Area

1	12.713	1707779	238835	95.380
2	14.827	76769	10941	4.620

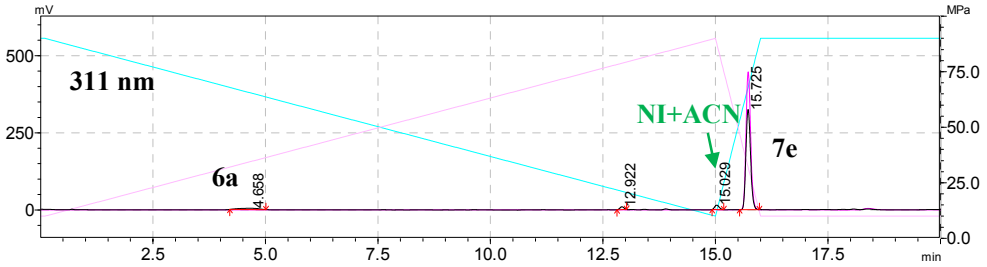
Figure S2d. The identity of Pyis **7d** was confirmed by LC-MS: MS (ESI) calcd. for **7d** $C_{28}H_{33}F_3N_3O_6^+$ 564.23 [M+H$^+$], found 564.07.

a)



Peak No.	Time	Area	Height	%Area
1	13.642	1537586	221730	100.000

b)



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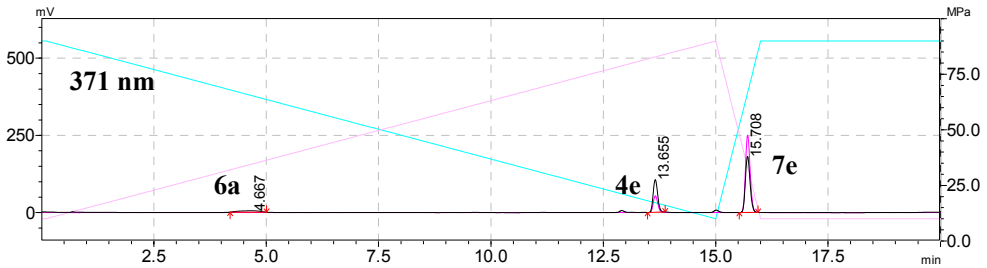
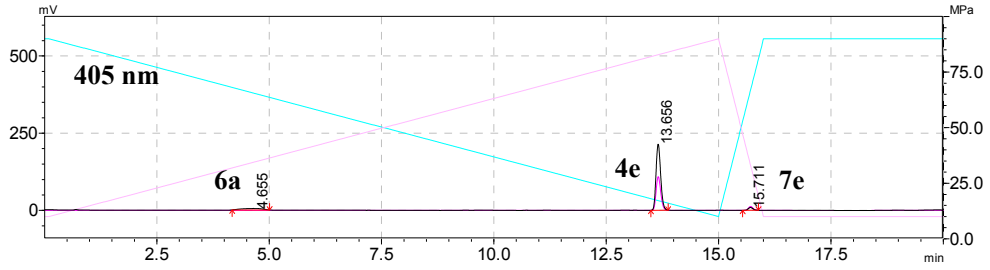
1	15.725	2333601	324275	100.000



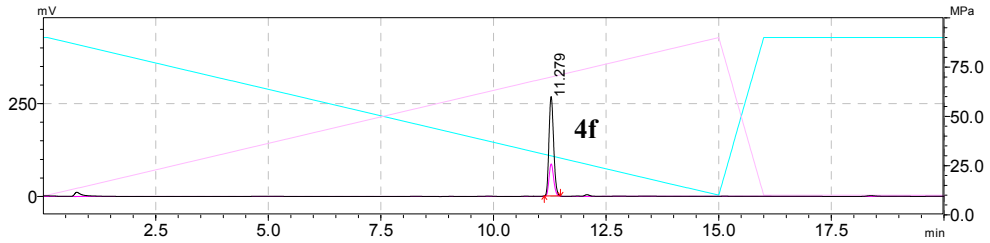
Peak No.	Time	Area	Height	%Area
1	13.655	738816	105298	48.050
2	15.708	1317371	181439	51.950



Peak No.	Time	Area	Height	%Area
1	13.656	1531472	213668	99.600
2	15.711	52833	8051	0.400

Figure S2e. The identity of Pyis **7e** was confirmed by LC-MS: MS (ESI) calcd. for **7e** $C_{29}H_{32}F_6N_3O_6^+$ 632.22 [M+H$^+$], found 632.18.

a)



Peak No.	Time	Area	Height	%Area
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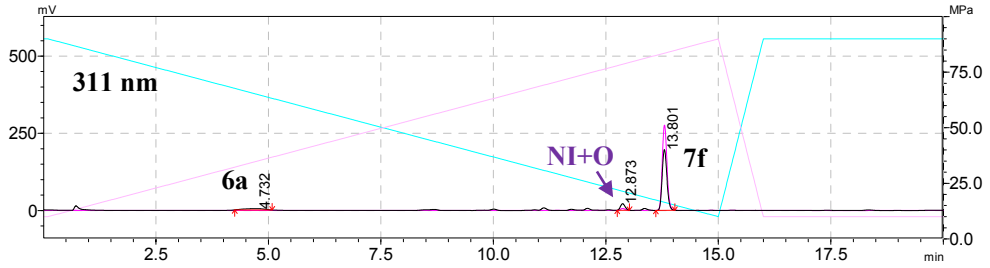
b)



Peak No.	Time	Area	Height	%Area
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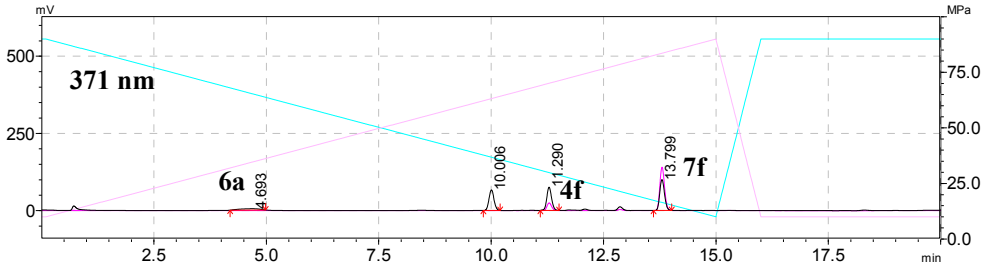
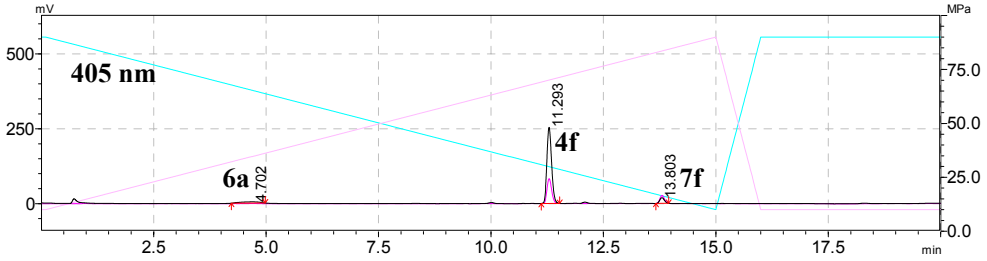


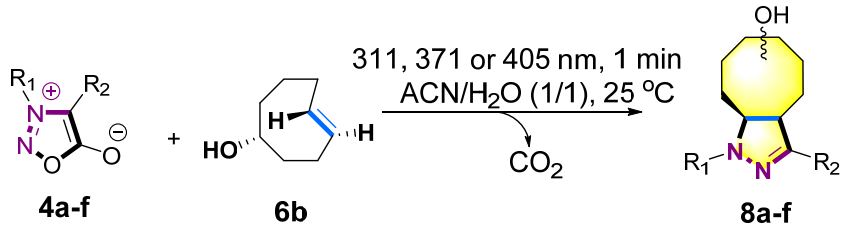
Peak No.	Time	Area	Height	%Area
1	11.290	559143	75472	29.090
2	13.799	738197	100012	70.910



Peak No.	Time	Area	Height	%Area
1	11.293	1851749	253352	96.340
2	13.803	134369	18757	3.660

Figure S2f. The identity of Pyis **7f** was confirmed by LC-MS: MS (ESI) calcd. for **7f** $C_{27}H_{34}N_3O_6^+$ 496.24 [M+H$^+$], found 496.09.

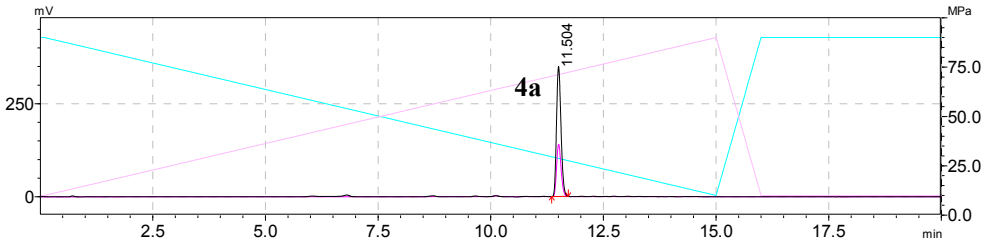
1,3-dipolar cycloaddition of SAAs 4a-f with equatorial isomer (TCO) under photo-activation



4a/8a: R_1 = *p*-MeOPh; R_2 = Boc-L-Phe-Ome
4b/8b: R_1 = *p*-FPh; R_2 = Boc-L-Phe-Ome
4c/8c: R_1 = Boc-L-Phe-Ome; R_2 = H
4d/8d: R_1 = Boc-L-Phe-Ome; R_2 = *p*-CF_3Ph
4e/8e: R_1 = Boc-L-Phe-Ome; R_2 = *m*-2CF_3Ph
4f/8f : R_1 = Boc-L-Phe-Ome; R_2 = Ph

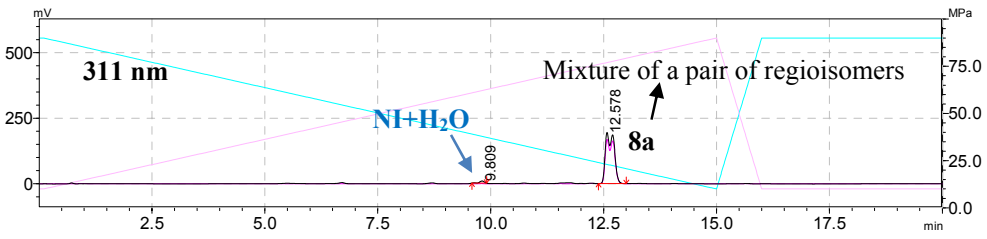
Figure S3. Photo-activated conversion of 50 µM sydnone amino acids (**4a-f**) to pyrazolines with 0.5 mM TCO (**6b**) in ACN/H_2O (1/1) using HPLC-MS. (a) HPLC trace of sydnone amino acids; (b) HPLC trace of the reaction mixture after 1 min photo-irradiation with 311, 371 or 405 nm lamp. The conversion was calculated based on the absorbance at 254 nm.

a)



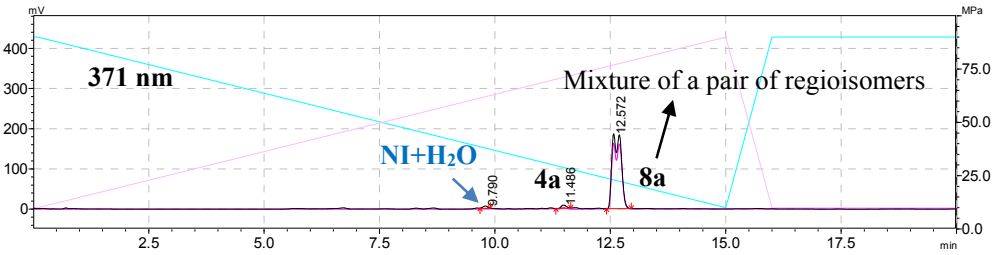
Peak No.	Time	Area	Height	%Area
1	11.504	2417937	347774	100.000

b)

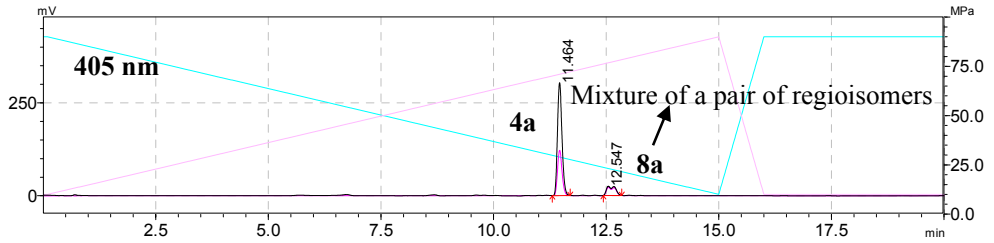


Peak No.	Time	Area	Height	%Area

1	12.578	2623425	193456	100.000



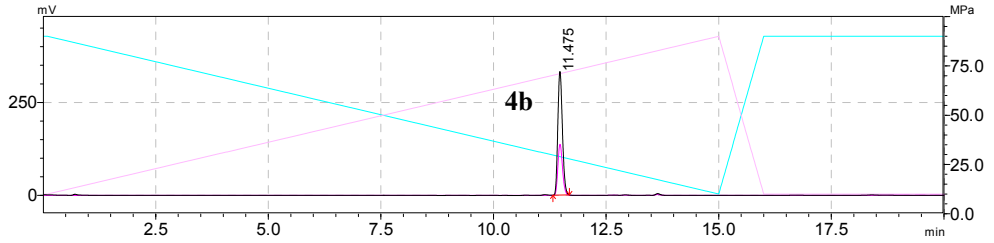
Peak No.	Time	Area	Height	%Area
1	11.486	56853	7879	2.350
2	12.572	2587900	185788	97.650



Peak No.	Time	Area	Height	%Area
1	11.464	2118962	299851	87.630
2	12.547	357046	25780	12.370

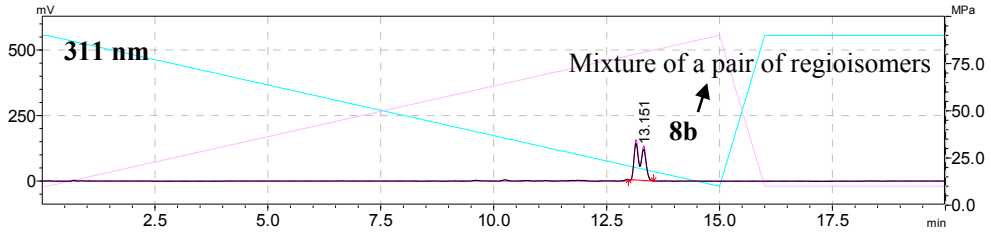
Figure S3a. The identity of Pyis **8a** was confirmed by LC-MS: MS (ESI) calcd. for **8a** $C_{31}H_{42}N_3O_6^+$ 552.31 [M+H$^+$], found 552.68.

a)



Peak No.	Time	Area	Height	%Area
1	11.475	2352482	332213	100.000

b)



Peak No.	Time	Area	Height	%Area
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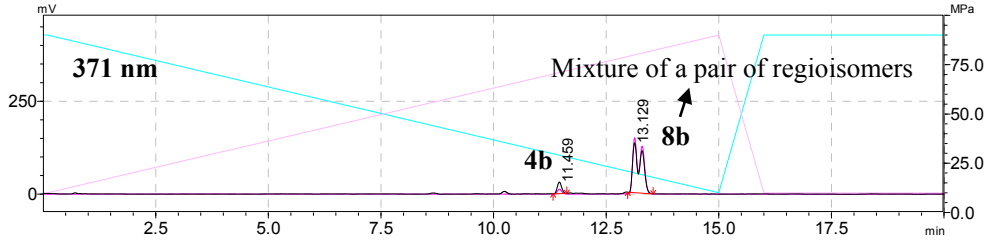
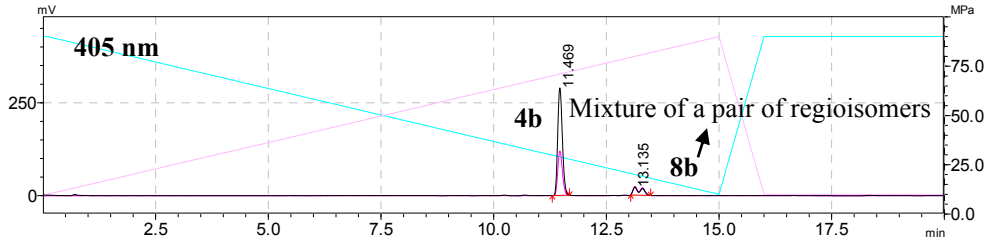


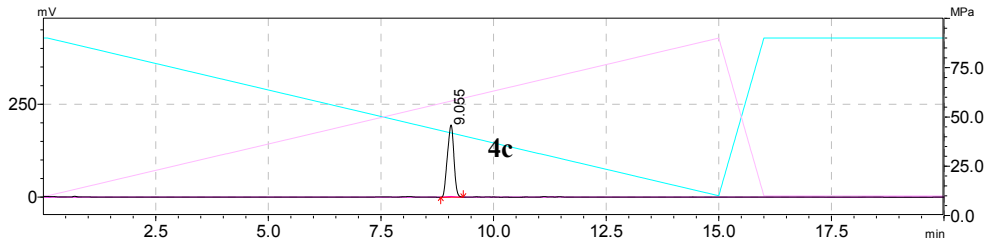
Peak No.	Time	Area	Height	%Area
1	11.459	217950	31095	9.260
2	13.129	1775559	133881	90.740



Peak No.	Time	Area	Height	%Area
1	11.469	2071712	287917	88.060
2	13.135	271774	20842	11.940

Figure S3b. The identity of Pyis **8b** was confirmed by LC-MS: MS (ESI) calcd. for **8b** $C_{30}H_{39}FN_3O_5^+$ 540.29 [M+H$^+$], found 540.90.

a)



Peak No.	Time	Area	Height	%Area
1	9.055	1953043	194404	100.000

b)

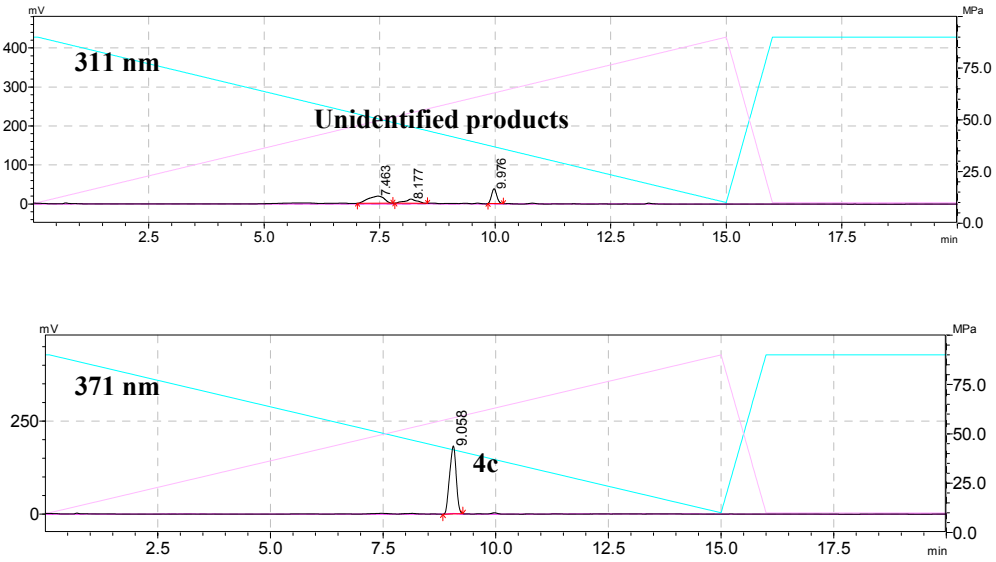
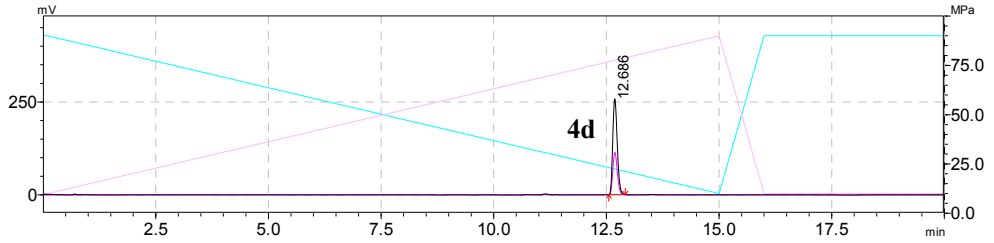


Figure S3c. The identity of Pyis **8c** was confirmed by LC-MS: MS (ESI) calcd. for **8c** $C_{24}H_{36}N_3O_5^+$ 446.26 [M+H$^+$], found N. D.

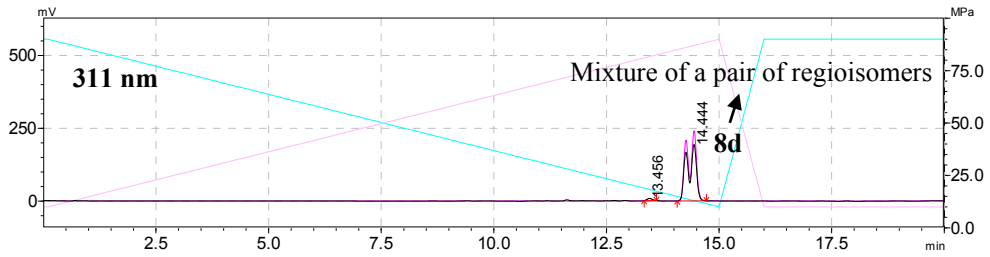
a)



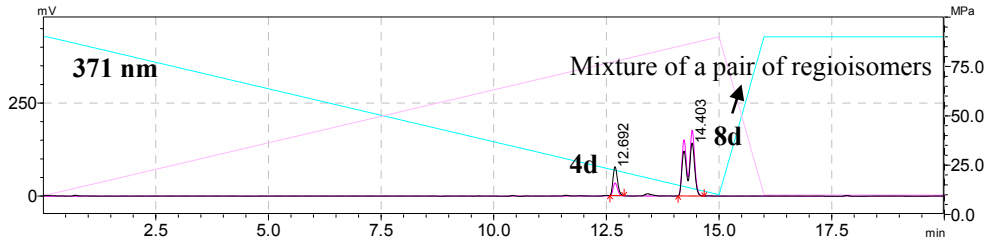
Peak No.	Time	Area	Height	%Area

1	12.686	1790584	256607	100.000

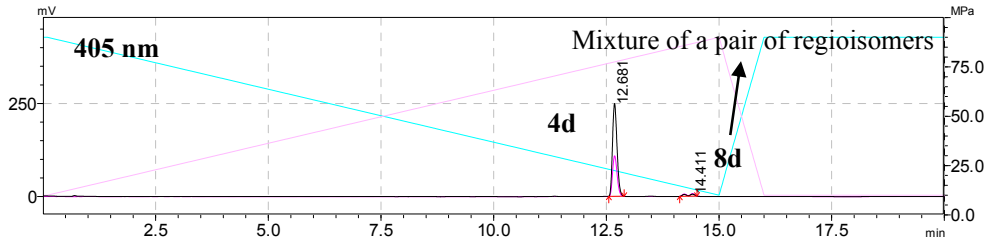
b)



Peak No.	Time	Area	Height	%Area
1	14.444	2677289	192483	100.000



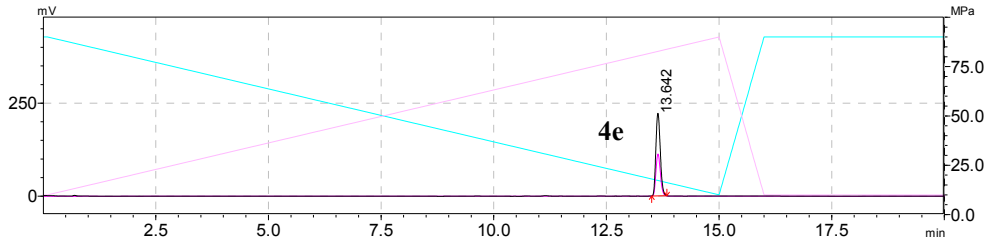
Peak No.	Time	Area	Height	%Area
1	12.692	534795	77149	29.870
2	14.403	1888657	141616	70.130



Peak No.	Time	Area	Height	%Area
1	12.681	1675397	245063	93.570
2	14.411	83795	6198	6.430

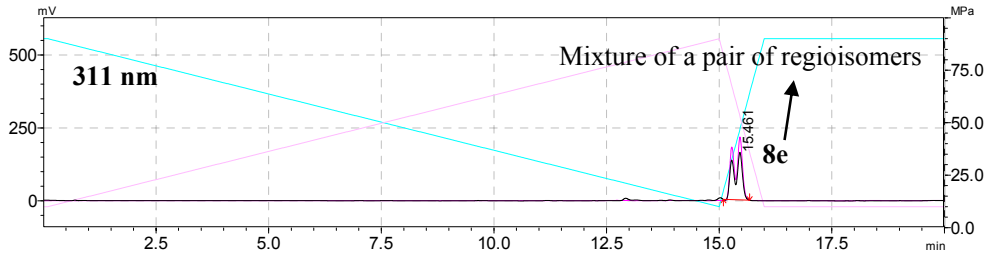
Figure S3d. The identity of Pyis **8d** was confirmed by LC-MS: MS (ESI) calcd. for **8d** $C_{31}H_{39}F_3N_3O_5^+$ 590.28 [M+H$^+$], found 589.94.

a)

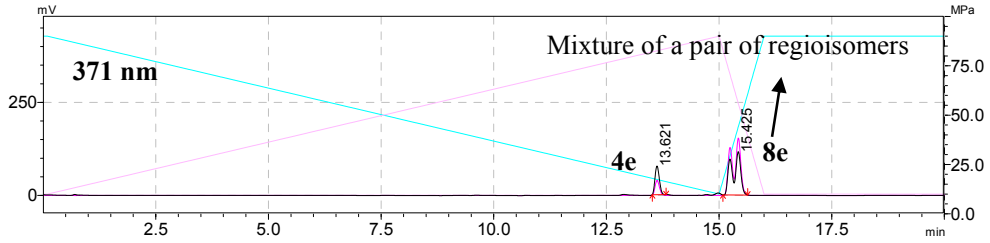


Peak No.	Time	Area	Height	%Area
1	13.642	1537586	221730	100.000

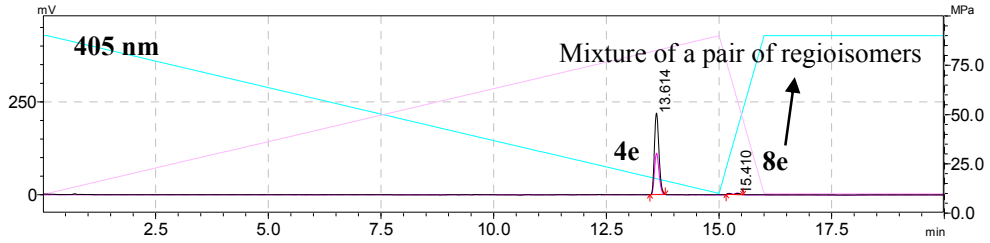
b)



Peak No.	Time	Area	Height	%Area
1	15.461	2188337	162623	100.000



Peak No.	Time	Area	Height	%Area
1	13.621	518969	76854	33.750
2	15.425	1540506	115813	66.250

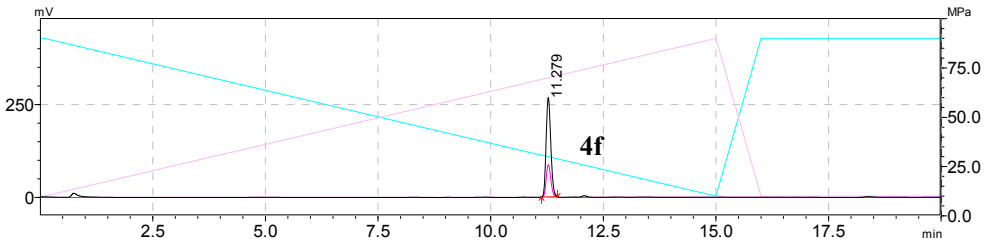


Peak No.	Time	Area	Height	%Area

1	13.614	1530646	218836	99.550
2	15.410	33188	3094	0.450

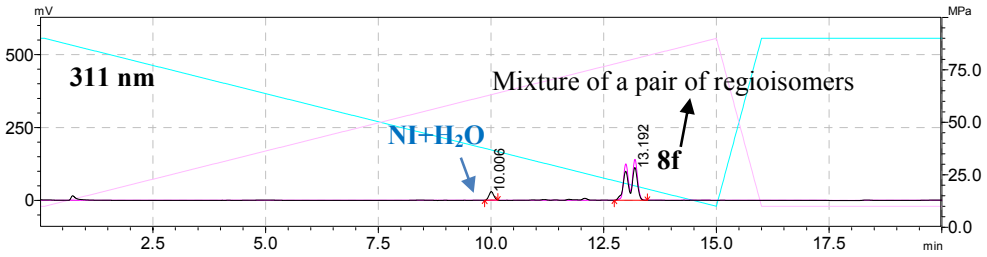
Figure S3e. The identity of Pyis **8e** was confirmed by LC-MS: MS (ESI) calcd. for **8e** $C_{32}H_{38}F_6N_3O_5^+$ 658.27 [M+H$^+$], found 658.92.

a)

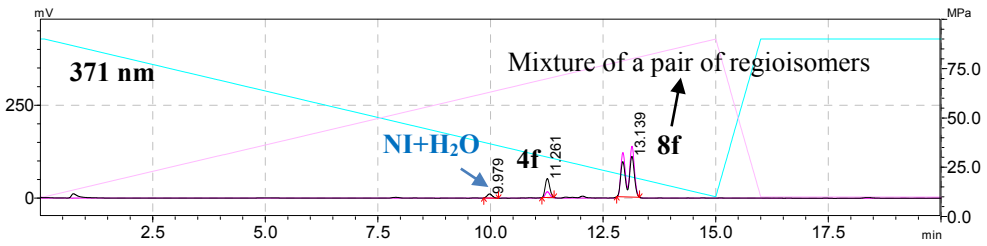


Peak No.	Time	Area	Height	%Area
1	11.279	1922011	266827	100.000

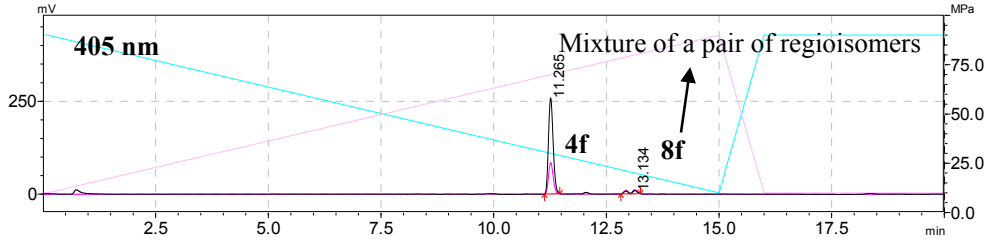
b)



Peak No.	Time	Area	Height	%Area
1	13.192	1667241	112197	100.000



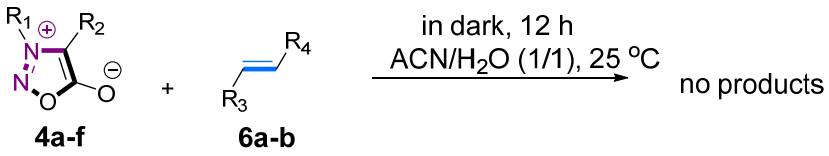
Peak No.	Time	Area	Height	%Area
1	11.261	353836	50668	18.410
2	13.139	1459225	109179	81.590



Peak No.	Time	Area	Height	%Area
1	11.265	1781574	253711	92.700
2	13.134	125937	9223	7.300

Figure S3f. The identity of Pyis **8f** was confirmed by LC-MS: MS (ESI) calcd. for **8f** $C_{30}H_{40}N_3O_5^+$ 522.30 [M+H$^+$], found 522.72.

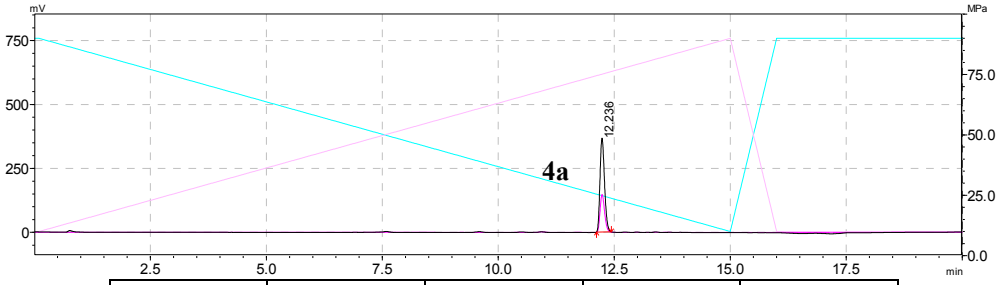
1,3-dipolar cycloaddition of SAAs 4a-f with MMA or TCO in dark



4a: R_1 = *p*-MeOPh; R_2 = Boc-L-Phe-Ome
4b: R_1 = *p*-FPh; R_2 = Boc-L-Phe-Ome
4c: R_1 = Boc-L-Phe-Ome; R_2 = H
4d: R_1 = Boc-L-Phe-Ome; R_2 = *p*-CF_3Ph
4e: R_1 = Boc-L-Phe-Ome; R_2 = *m*-2CF_3Ph
4f: R_1 = Boc-L-Phe-Ome; R_2 = Ph

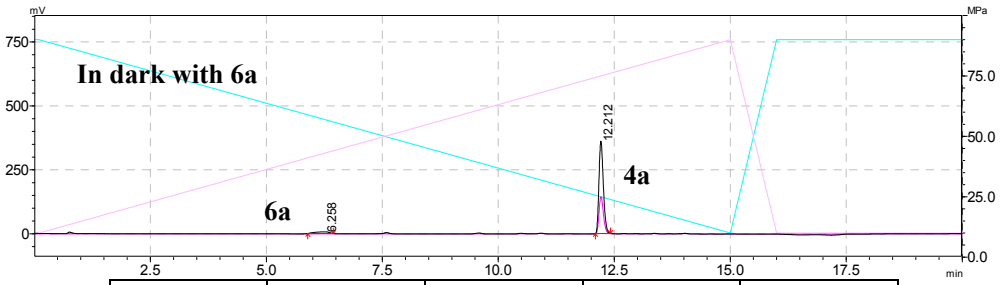
Figure S4. HPLC-MS analysis for 50 μM sydnone amino acids (**4a-f**) with 0.5 mM MMA (**6a**) or TCO (**6b**) in ACN/H_2O (1/1) after 12 h in dark. (a) HPLC trace of sydnone amino acids; (b) HPLC trace of the reaction mixture after 12 h in dark. HPLC peak assignments based on mass-to-charge ratio in mass spectrum. The HPLC instrument in our laboratory has been repaired with pipeline replacement, the retention time of DASAs **4a-f** peak in this experiments were delayed for approximate 0.7 min in comparison to the previous experiments (Figure S2-3).

a)



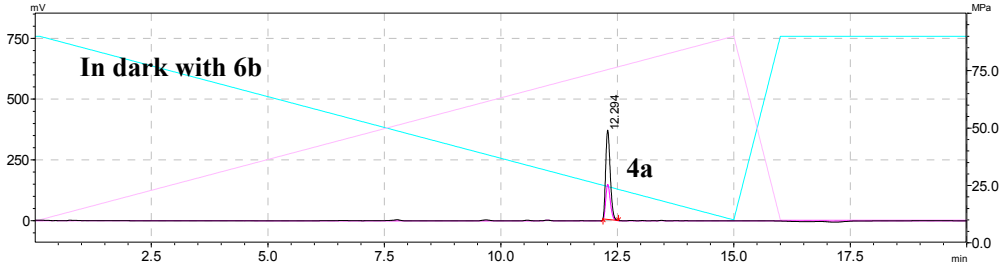
Peak No.	Time	Area	Height	%Area
1	12.236	2489713	365173	100.000

b)



Peak No.	Time	Area	Height	%Area

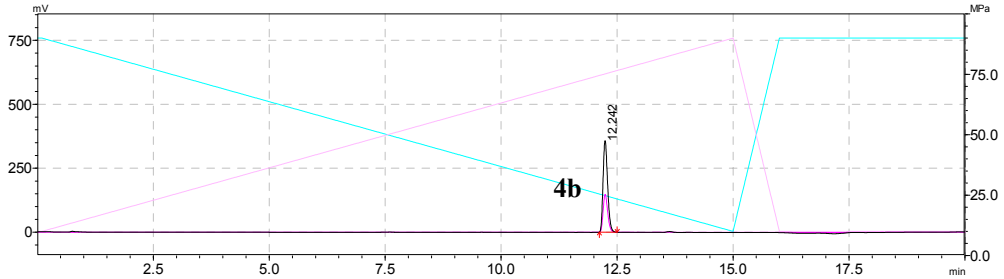
1	12.212	2402871	360476	100.000



Peak No.	Time	Area	Height	%Area
1	12.294	2496293	365423	100.000

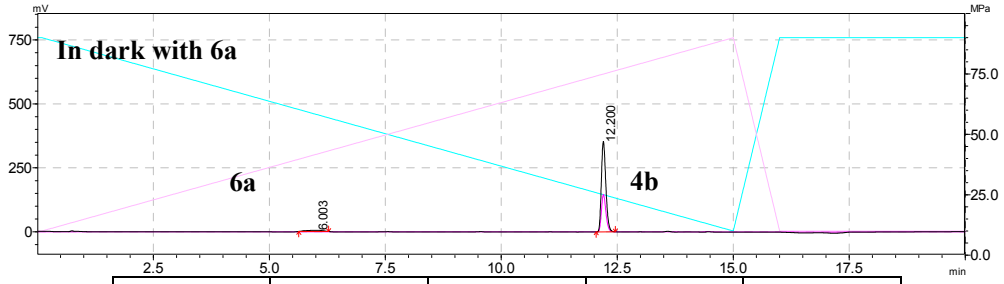
Figure S4a. The identity of **4a** was confirmed by LC-MS: MS (ESI) calcd. for **4a** $C_{24}H_{28}N_3O_7^+$ 470.19 [M+H$^+$], found 470.01.

a)

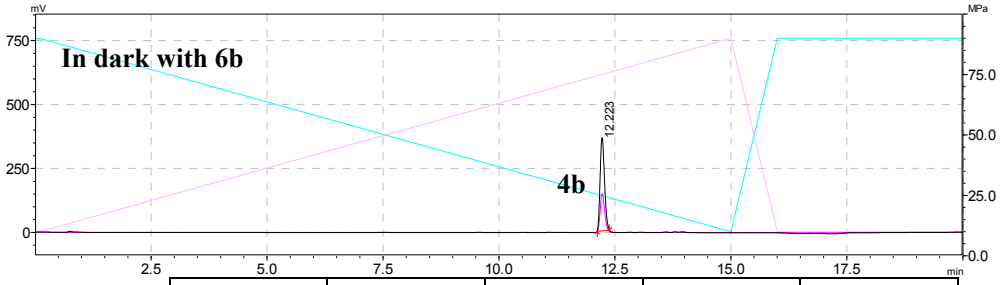


Peak No.	Time	Area	Height	%Area
1	12.242	2396938	354560	100.000

b)



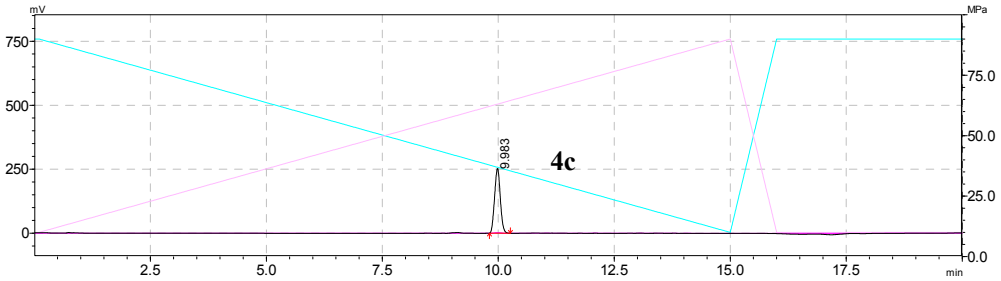
Peak No.	Time	Area	Height	%Area
1	12.200	2367300	352578	100.000



Peak No.	Time	Area	Height	%Area
1	12.223	2414545	364336	100.000

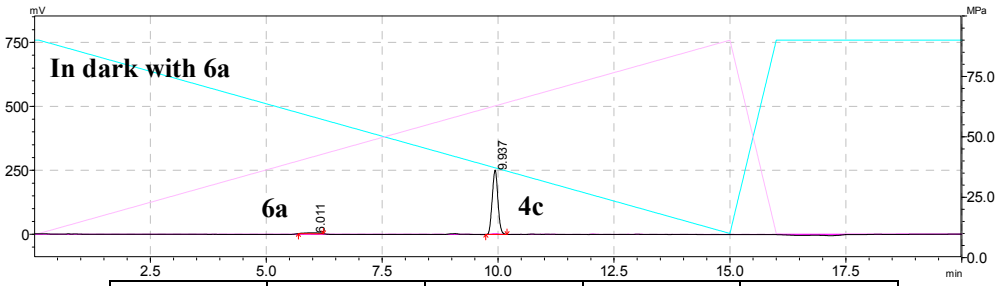
Figure S4b. The identity of **4b** was confirmed by LC-MS: MS (ESI) calcd. for **4b** $C_{23}H_{25}FN_3O_6^+$ 458.17 [M+H$^+$], found 457.94.

a)

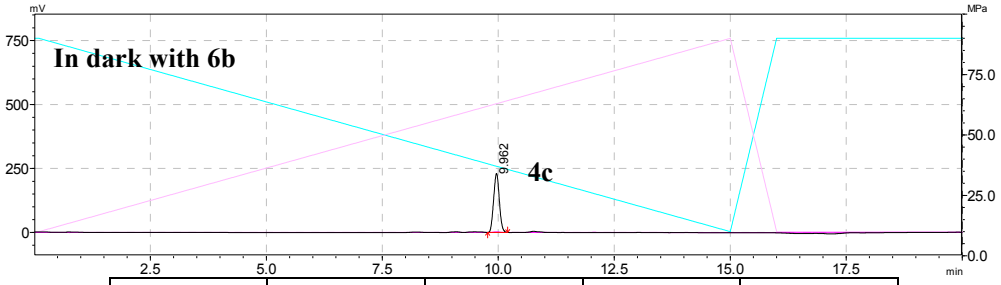


Peak No.	Time	Area	Height	%Area
1	9.983	2077714	248683	100.000

b)



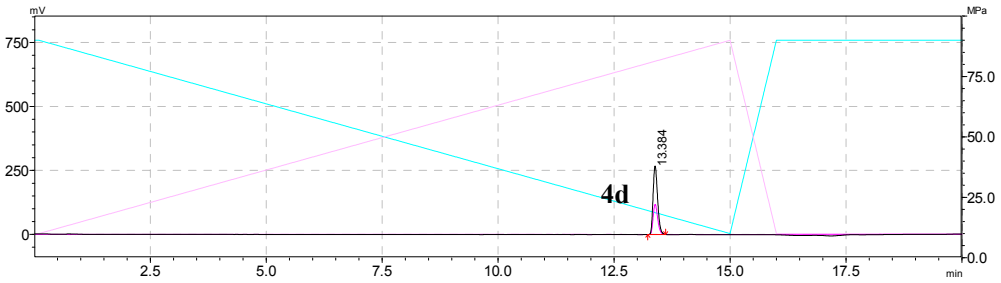
Peak No.	Time	Area	Height	%Area
1	9.937	2044562	246609	100.000



Peak No.	Time	Area	Height	%Area
1	9.962	1965120	229756	100.000

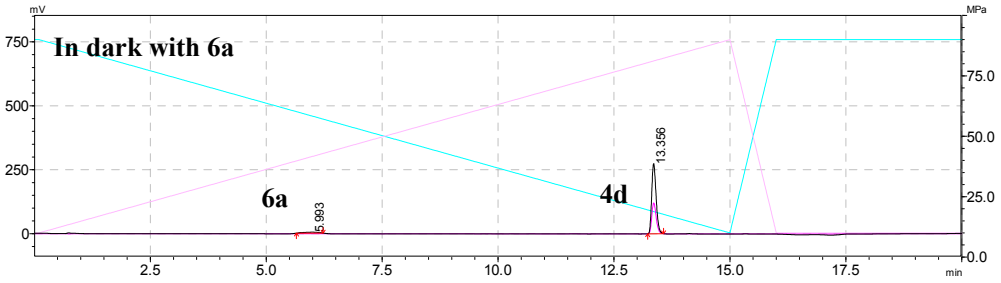
Figure S4c. The identity of **4c** was confirmed by LC-MS: MS (ESI) calcd. for **4c** $C_{17}H_{22}N_3O_6^+$ 364.15 [M+H$^+$], found 363.82.

a)

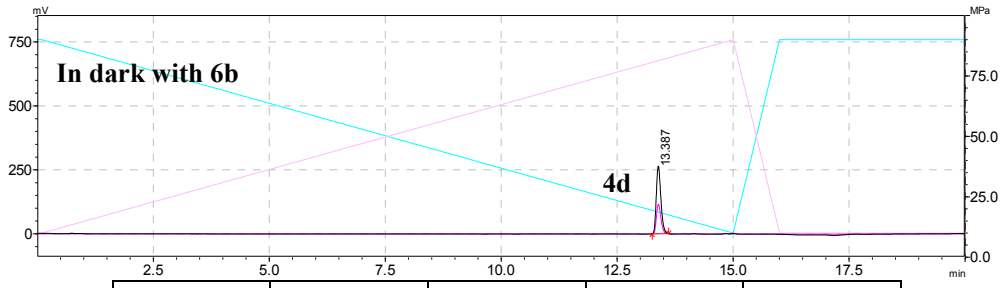


Peak No.	Time	Area	Height	%Area
1	13.384	1813259	267254	100.000

b)



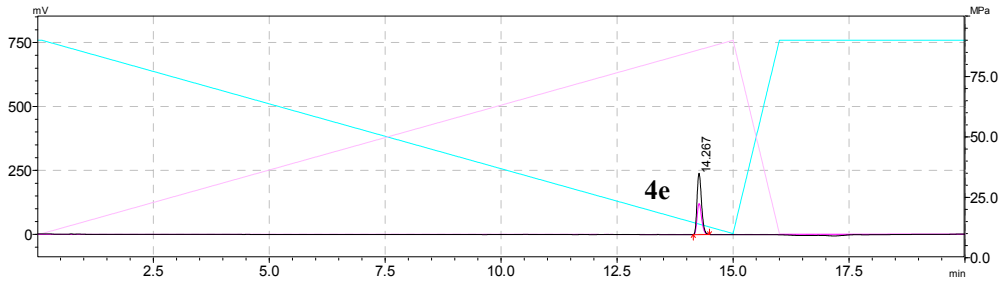
Peak No.	Time	Area	Height	%Area
1	13.356	1816118	274040	100.000



Peak No.	Time	Area	Height	%Area
1	13.387	1821122	263340	100.000

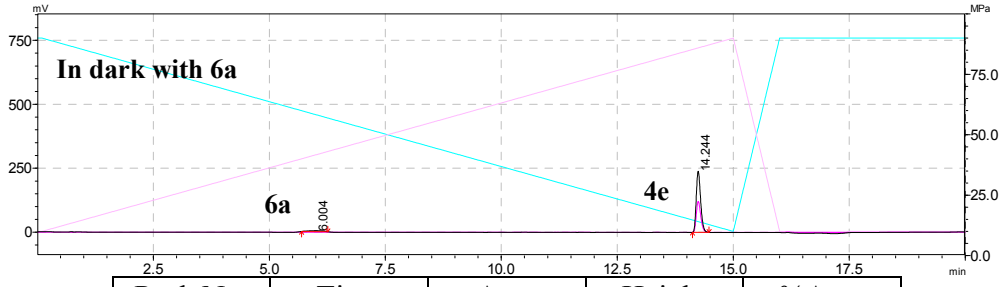
Figure S4d. The identity of **4d** was confirmed by LC-MS: MS (ESI) calcd. for **4d** $C_{24}H_{25}F_3N_3O_6^+$ 508.17 [M+H$^+$], found 507.88.

a)

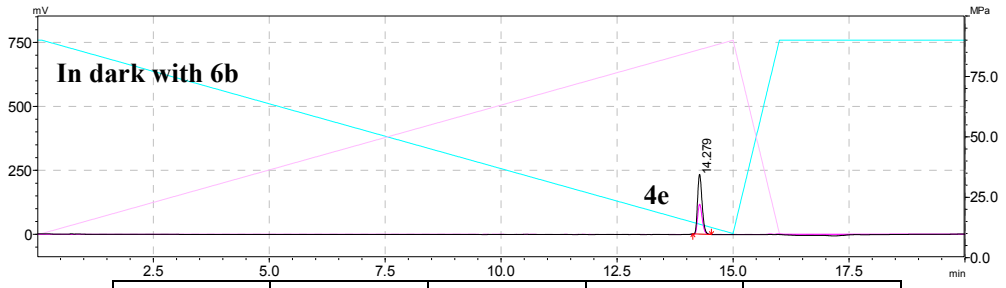


Peak No.	Time	Area	Height	%Area
1	14.267	1606744	238704	100.000

b)



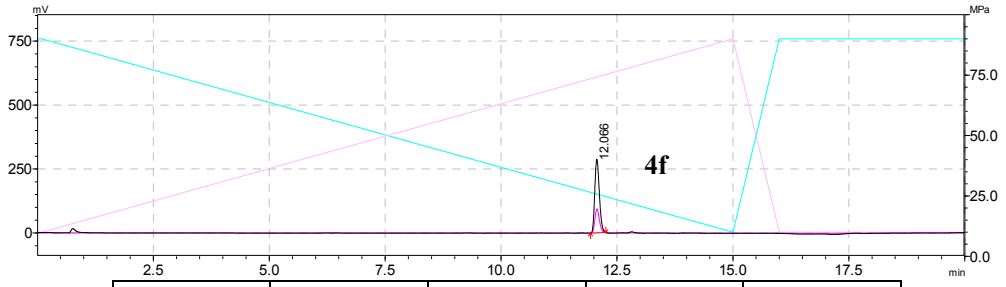
Peak No.	Time	Area	Height	%Area
1	14.244	1580592	237355	100.000



Peak No.	Time	Area	Height	%Area
1	14.279	1580779	232893	100.000

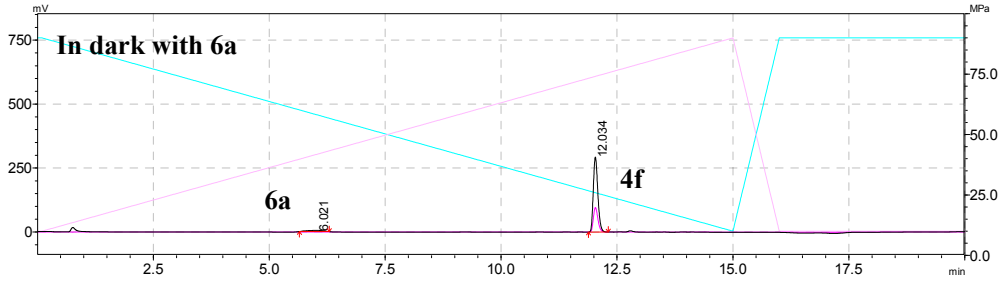
Figure S4e. The identity of **4e** was confirmed by LC-MS: MS (ESI) calcd. for **4e** $C_{25}H_{24}F_6N_3O_6^+$ 576.16 [M+H$^+$], found 576.02.

a)

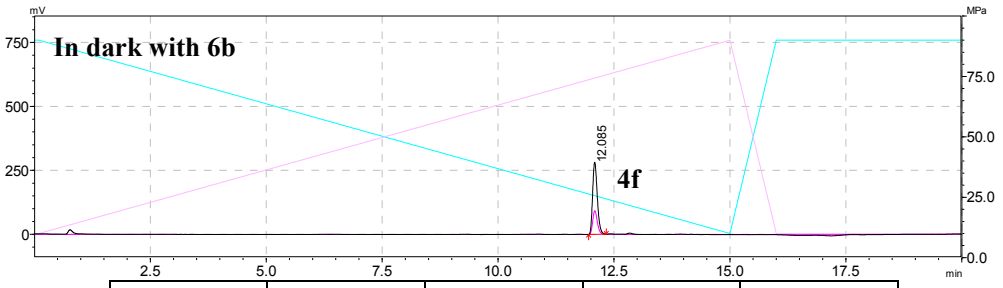


Peak No.	Time	Area	Height	%Area
1	12.066	1975017	286995	100.000

b)



Peak No.	Time	Area	Height	%Area
1	12.034	1961183	291168	100.000



Peak No.	Time	Area	Height	%Area
1	12.085	1976694	281282	100.000

Figure S4f. The identity of **4f** was confirmed by LC-MS: MS (ESI) calcd. for **4f** $C_{23}H_{26}N_3O_6^+$ 440.18 [M+H$^+$], found 439.76.

Solvent-dependent fluorescence spectra of Pyis 7b and 7d-f.

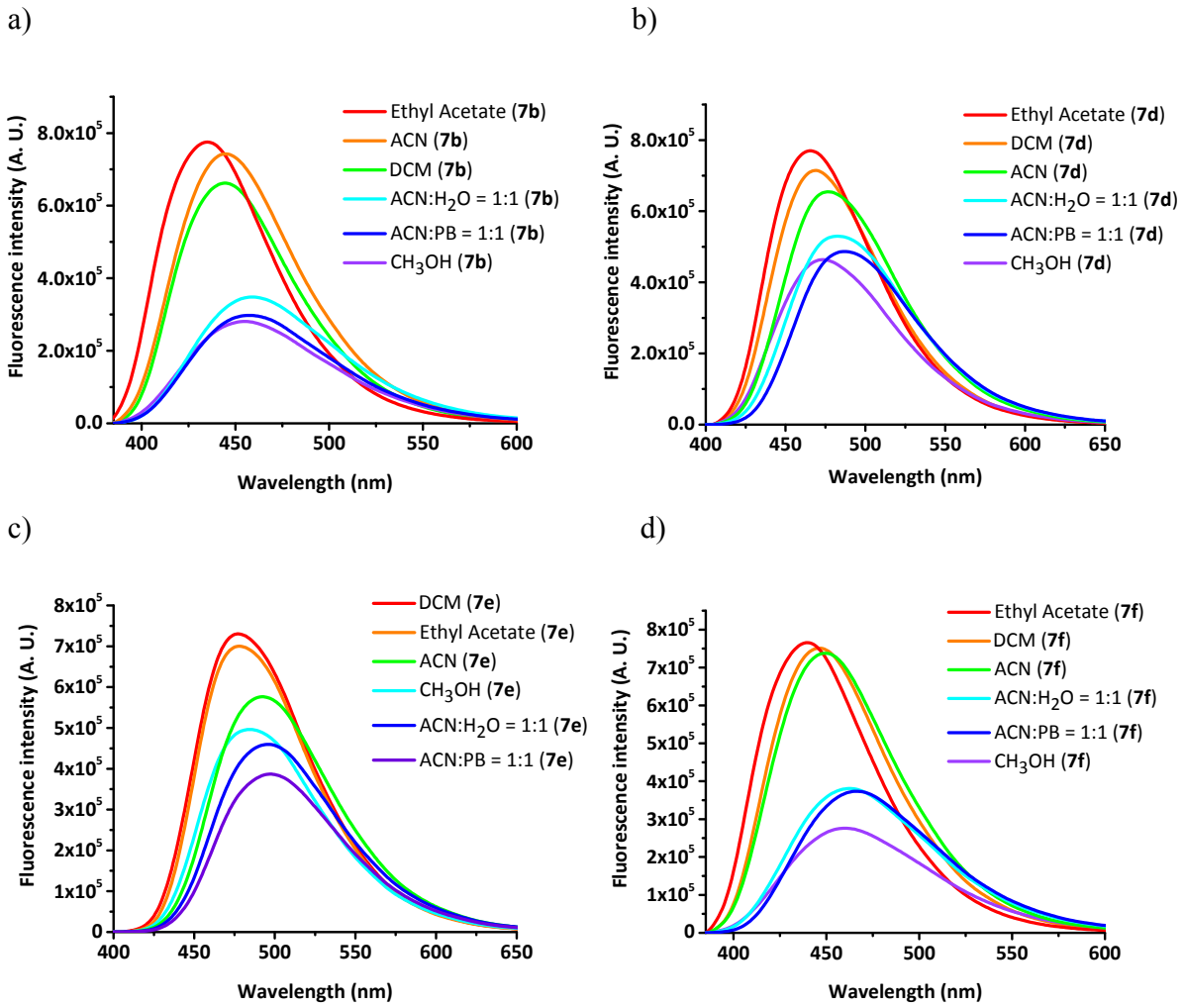
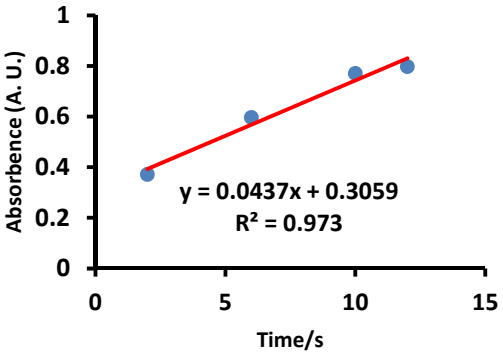


Figure S5. Solvent-dependent fluorescence spectra of Pyis **7b** and **7d-f**. The Pyis were dissolved in different solvents to derive concentrations of 30 μM, respectively. (a) **7b** and (d) **7f** were excited at 360 nm, and (b) **7d** and (c) **7e** were excited at 378 nm. Fluorescence emission were scanned in the region from 400 to 650 nm through a 1 nm slit.

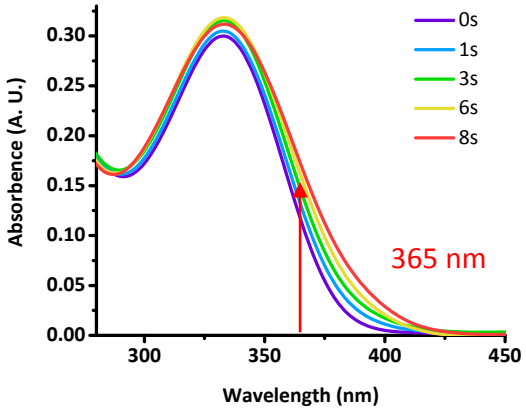
Determination of quantum yields of DASAs 4a-b and 4d-f reacted with MMA

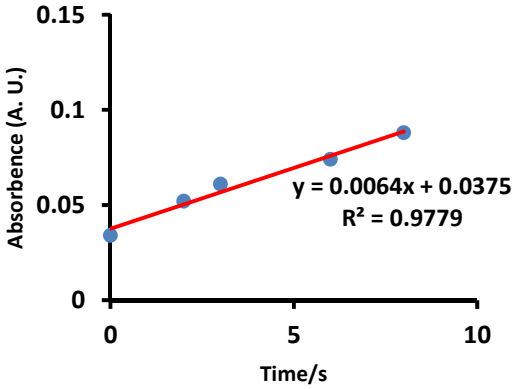
The quantum yields of DASAs **4a-b** and **4d-f** were determined using potassium ferrioxalate-based chemical actinometer.[S2] In brief, a 250 μL fresh solution of 6 mM potassium ferrioxalate in 0.1 N H_2SO_4 was irradiated with 371 nm LED in a quartz tube for specified times before quenching by addition of 4.75 mL of NaOAc/HOAc buffer (pH = 4.3) and 5 mL of 0.1% 1,10-phenanthroline solution in water. The mixture was stirred for 30 min before UV-Vis measurement. All the work were carried out in the dark and the samples were protected from light with aluminum foil during handling. The quantum yield for a test compound was calculated based on the following equation: $\Phi_t = [(\varepsilon_c/\varepsilon_t)(k_t/k_c)(c_c/c_t)]/(\varepsilon_{510}/\triangle\varepsilon_t)\,\Phi_c$,[S3] where ε_c and ε_t were extinction coefficients of the standard and DASAs **4a-b** and **4d-f** at 371 nm, respectively; k_t and k_c were slopes for the test compound and the standard (absorbance versus time), respectively; c_c and c_t were concentrations of the standard and the test compound, respectively; and ε_{510} and $\triangle\varepsilon_t$ were extinction coefficients of the Fe^{2+}-(1,10-phenanthroline)$_3$ complex at 510 nm for the actinometer and difference in extinction coefficients compared to origin of the pyrazoline products at 365 nm or 400 nm, respectively.

a)

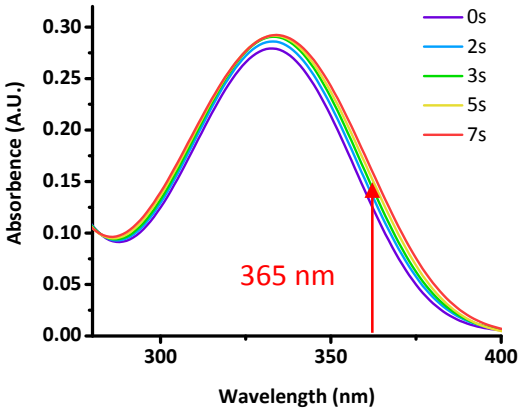


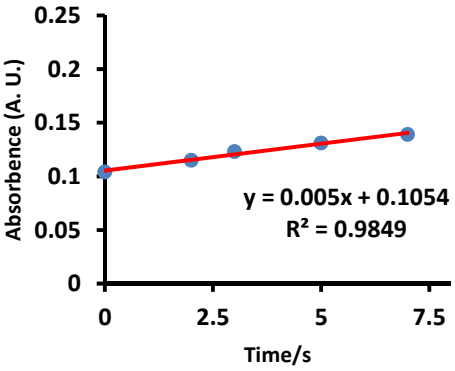
b)


0s
1s
3s
6s
8s
365 nm
Absorbence (A. U.)
Wavelength (nm)

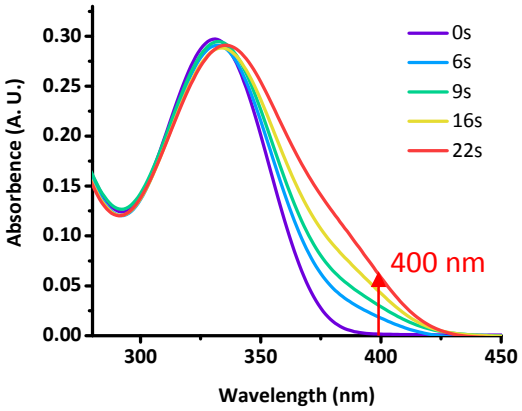

y = 0.0064x + 0.0375
R² = 0.9779
Absorbence (A. U.)
Time/s

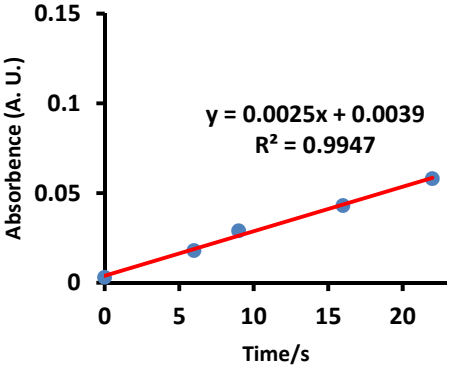
c)


0s
2s
3s
5s
7s
365 nm
Absorbence (A.U.)
Wavelength (nm)

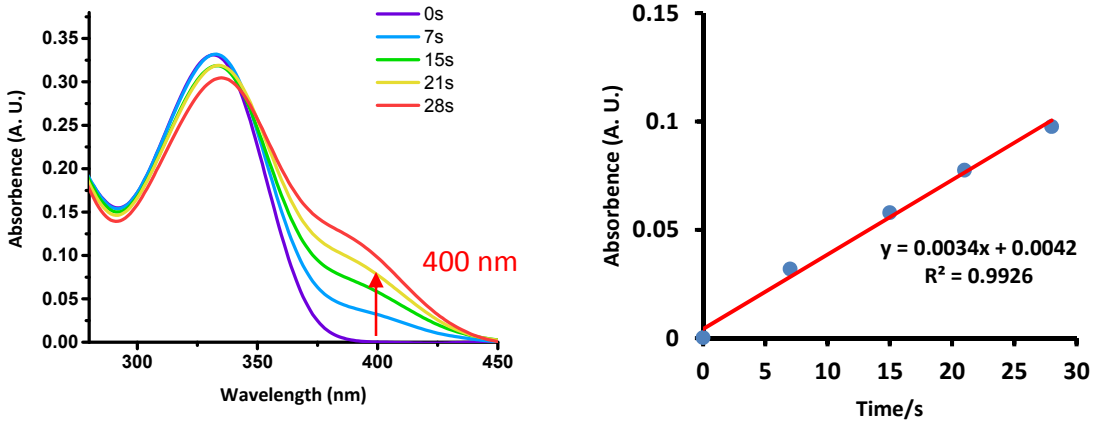

y = 0.005x + 0.1054
R² = 0.9849
Absorbence (A. U.)
Time/s

d)


0s
6s
9s
16s
22s
400 nm
Absorbence (A. U.)
Wavelength (nm)


y = 0.0025x + 0.0039
R² = 0.9947
Absorbence (A. U.)
Time/s

e)



f)

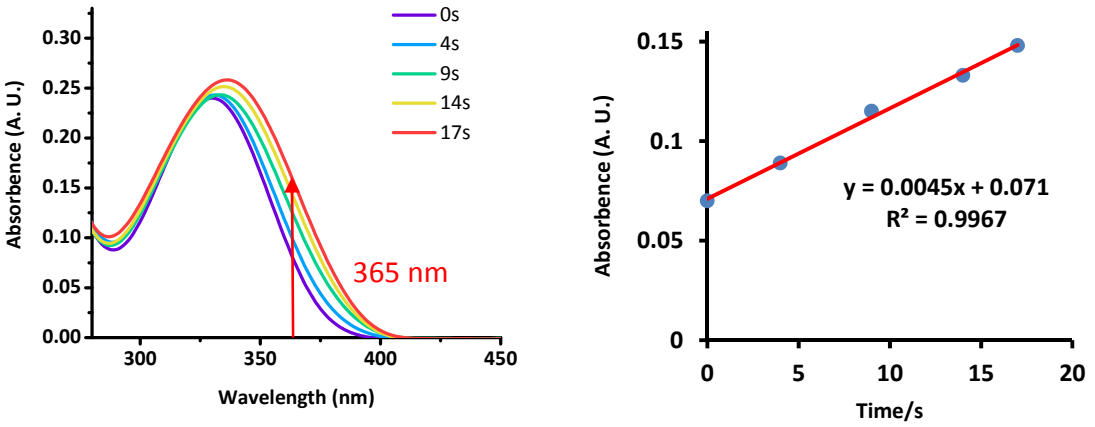


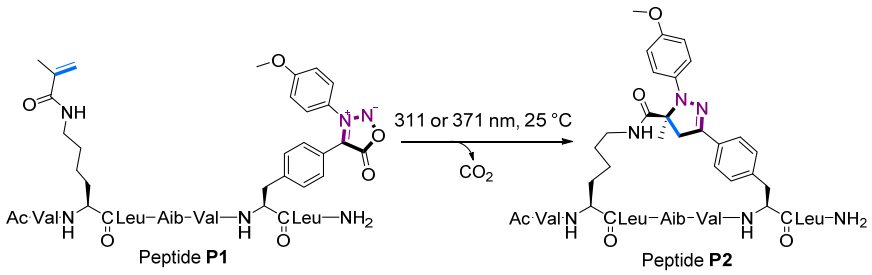
Figure S6. (a) Time-course of absorbance change of Fe^{2+}-(1,10-phenanthroline)$_3$ complex at 510 nm induced by the 371 nm LED irradiation to the actinometer with a linear fitting curve. Time-course of absorbance changes of DASAs **4a** (b), **4b** (c), **4d** (d), **4e** (e), **4f** (f) to corresponding Pyis by the same 371 nm LED irradiation with a linear fitting curve. A solution of 25 μM DASAs **4a-b** and **4d-f** and 2.5 mM MMA in ACN/PB (1/1) in quartz tubes was photo-irradiated at 371 nm for a specified time before absorbance measurement, respectively. The quantum yields of 371 nm light-induced transformation for DASAs **4a-b** and **4d-f** in ACN/PB (1/1, pH = 7.4) were determined to be 0.26, 0.32, 0.15, 0.17 and 0.29, respectively.

Fluorescence quantum yields of DASAs 4a-b and 4d-f in ACN/PB (1/1)

Sydnone amino acids	**4a**	**4b**	**4d**	**4e**	**4f**
Φ_F	<0.001	<0.001	0.002	<0.001	0.004

Figure S7. Fluorescence quantum yields (ΦF) of DASAs **4a-b** and **4d-f** in ACN/PB (1/1). ΦF of DASAs **4a-b** and **4d-f** in ACN/PB (1/1) were determined to be <0.001, <0.001, 0.002, <0.001 and 0.004, respectively.

Cyclization of linear peptide P1 under photo-irradiation in different solvents

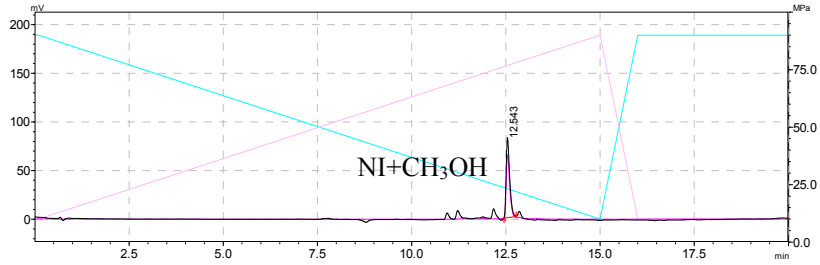


CH_3OH	CH_3OH/H_2O = 1/1	ACN	ACN/H_2O = 1/1	$ACN/NaCl_{saline}$ = 1/1	TFE	Isopropyl alcohol	EtOAc	DCM	ACN/PB = 1/1	ACN/PBS = 1/1
N. D.[a]	N. D.[a]	N. D.[a]	N. D.[a]	N. D.[a]	N. D.[a]	N. D.[a]	N. D.[a]	N. D.[a]	★	★

ACN/PB = 1/2	ACN/PB = 1/4	ACN/PB = 1/8	DMSO/PB = 1/1	PB	DMEM
★	★	★	★	★	★

Figure S8. Cyclization of peptide **P1** bearing 1,3-dipolar cycloaddition in positions i and i+4. HPLC trace of the 150 μM peptide **P1** in different solvents after photo-irradiation with 311 or 371 nm (black line = 365 nm; red line = 254 nm). [a]Not detected.

a)



b)

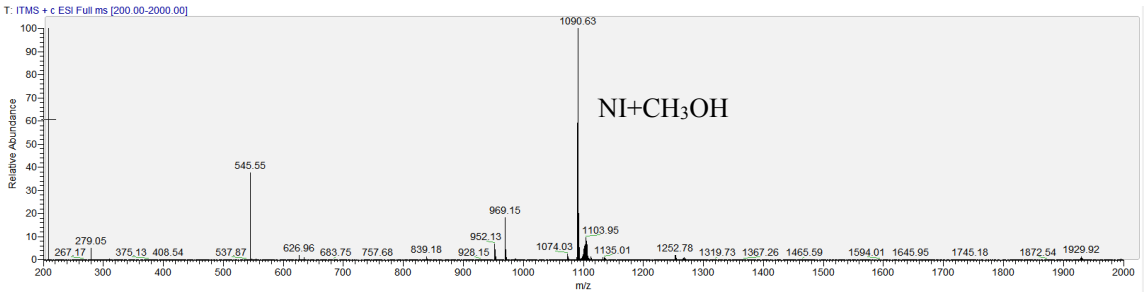
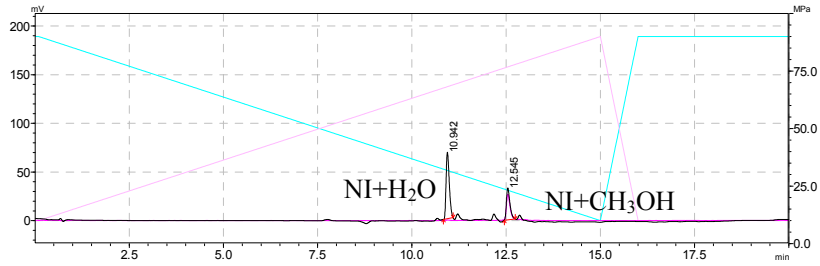
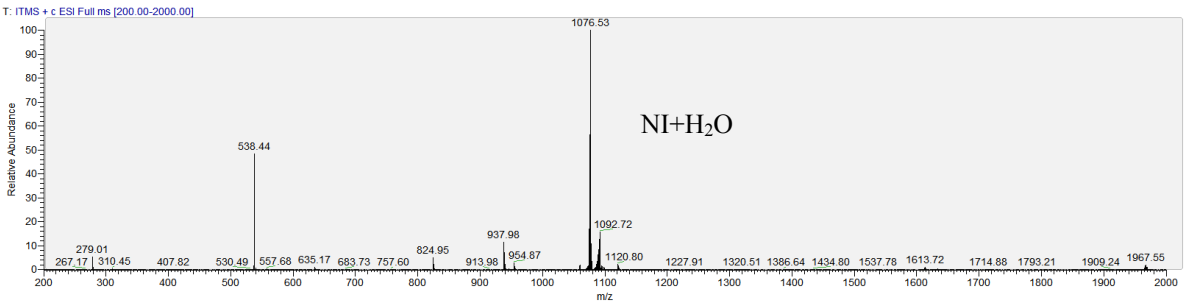


Figure S8a. Cyclization of linear peptide **P1** after 5 min photo-irradiation with 311 nm in CH_3OH. The identity of the crude mixture product was confirmed by LC-MS: MS (ESI) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^+$ 1058.64 [M+H$^+$], found 1090.63 [NI+CH_3OH].

a)



b)



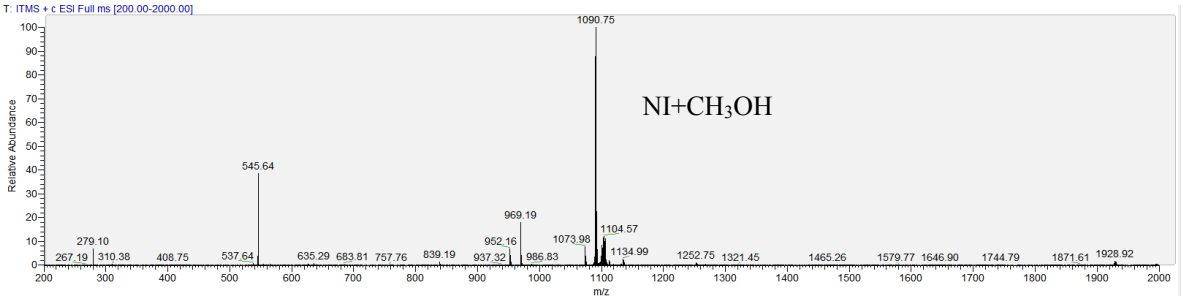
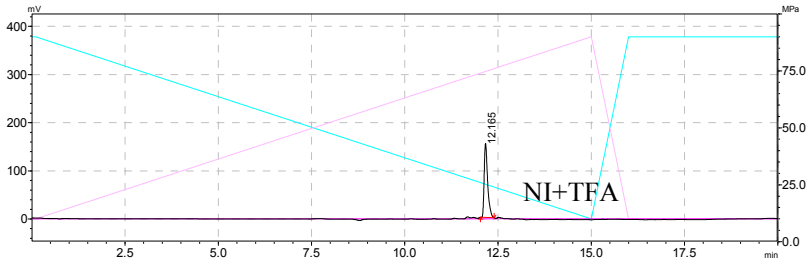


Figure S8b. Cyclization of linear peptide **P1** after 5 min photo-irradiation with 311 nm in CH_3OH/H_2O (1/1). The identity of the crude mixture product was confirmed by LC-MS: MS (ESI) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^+$ 1058.64 [$M+H^+$], found 1076.53 [$NI+H_2O$], 1090.75 [$NI+CH_3OH$].

a)



b)

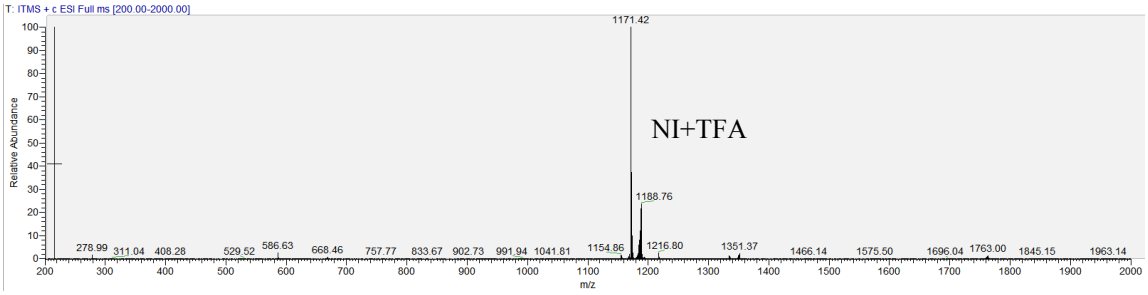
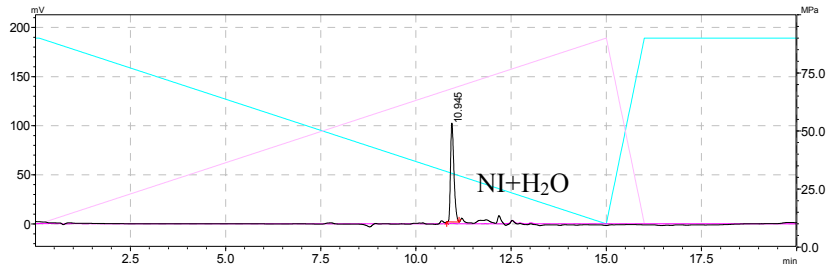


Figure S8c. Cyclization of linear peptide **P1** after 5 min photo-irradiation with 311 nm in ACN. The identity of the crude mixture product was confirmed by LC-MS: MS (ESI) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^+$ 1058.64 [$M+H^+$], found 1171.42 [NI+TFA].

a)



b)

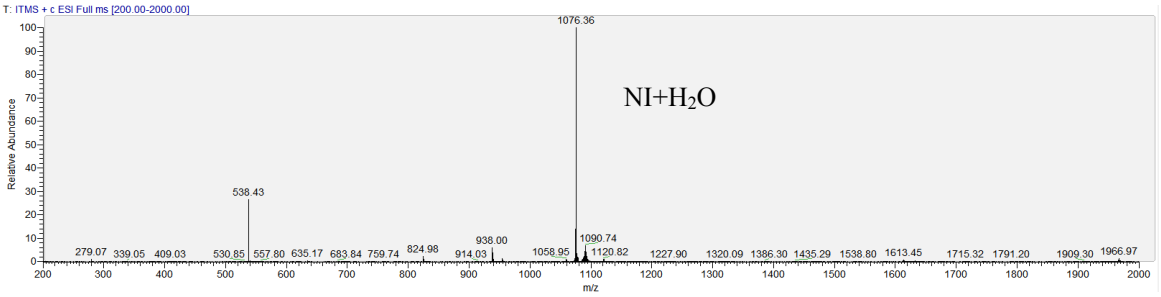
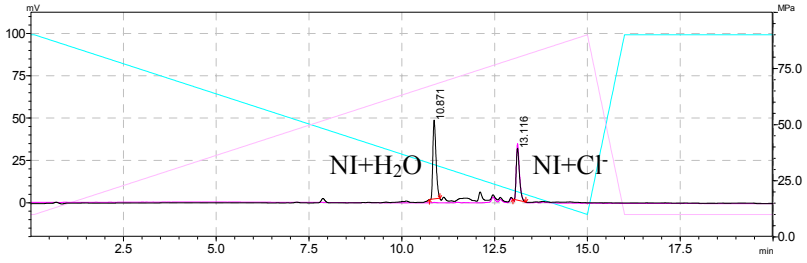


Figure S8d. Cyclization of linear peptide **P1** after 5 min photo-irradiation with 311 nm in ACN/H_2O (1/1). The identity of the crude mixture product was confirmed by LC-MS: MS (ESI) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^+$ 1058.64 [$M+H^+$], found 1076.36 [$NI+H_2O$].

a)



b)

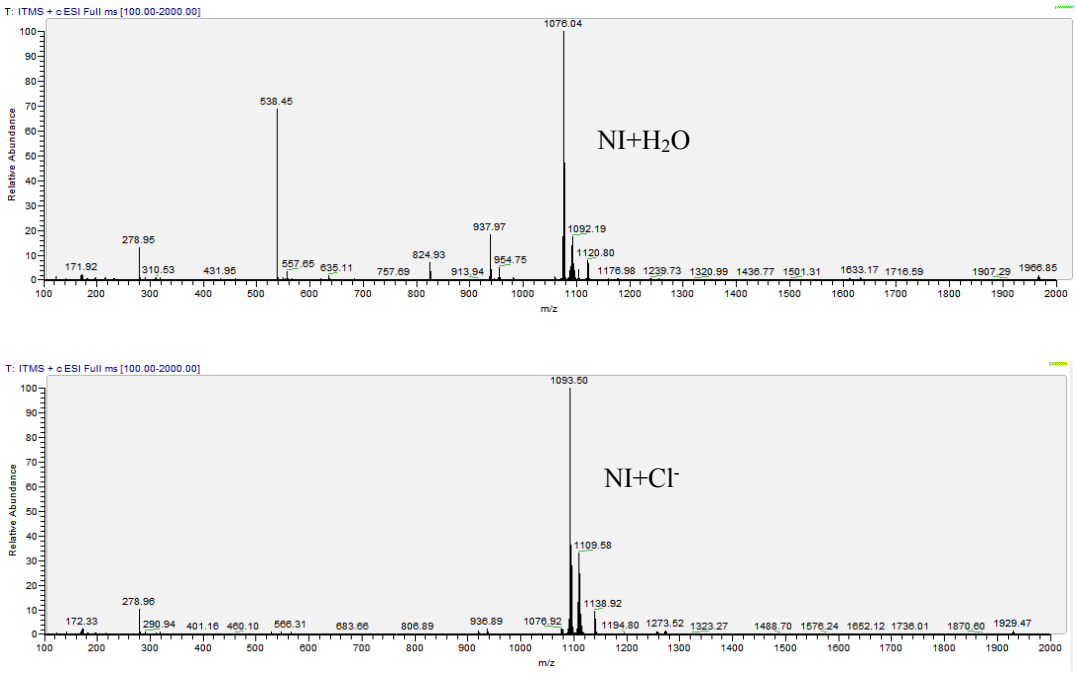
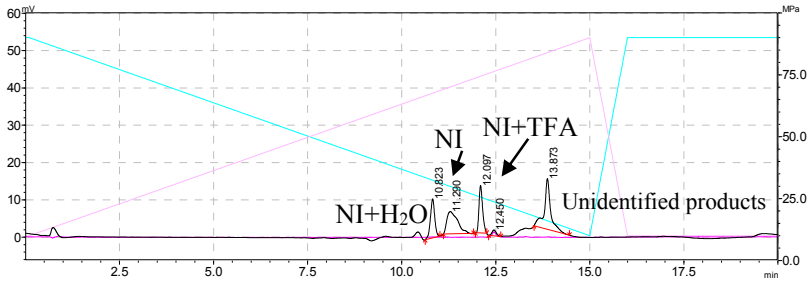


Figure S8e. Cyclization of linear peptide **P1** after 5 min photo-irradiation with 311 nm in ACN/$NaCl_{saline}$ (1/1). The identity of the crude mixture product was confirmed by LC-MS: MS (ESI) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^{+}$ 1058.64 [$M+H^{+}$], found 1076.04 [$NI+H_2O$], 1093.50 [$NI+Cl^{-}$].

a)



b)

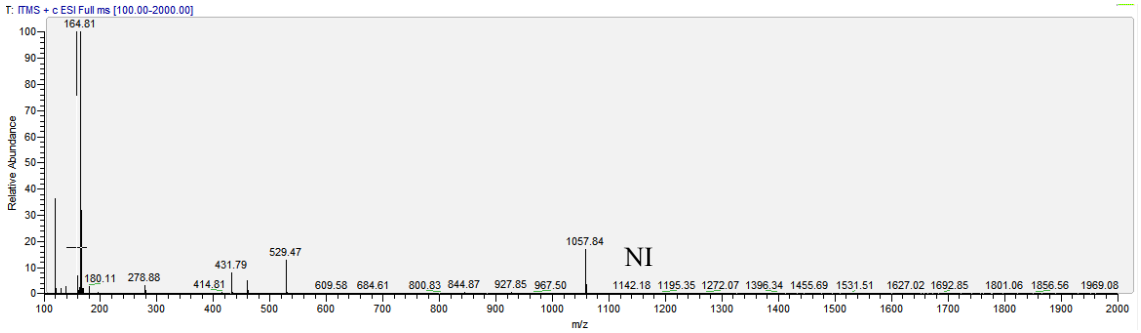
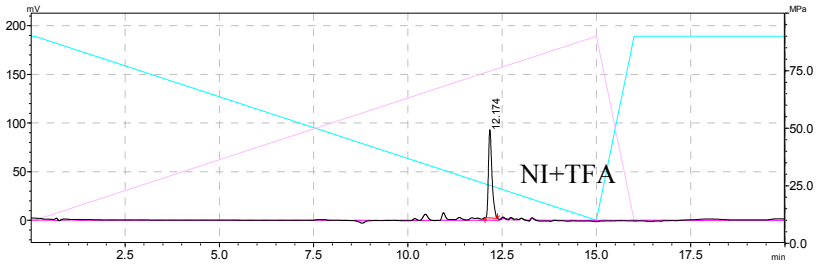


Figure S8f. Cyclization of linear peptide **P1** after 5 min photo-irradiation with 311 nm in trifluoroethanol (TFE). The identity of the crude mixture product was confirmed by LC-MS: MS (ESI) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^{+}$ 1058.64 [M+H^{+}], found 1075.62 [NI+H_2O], 1057.84 [NI], 1171.30 [NI+TFA].

a)



b)

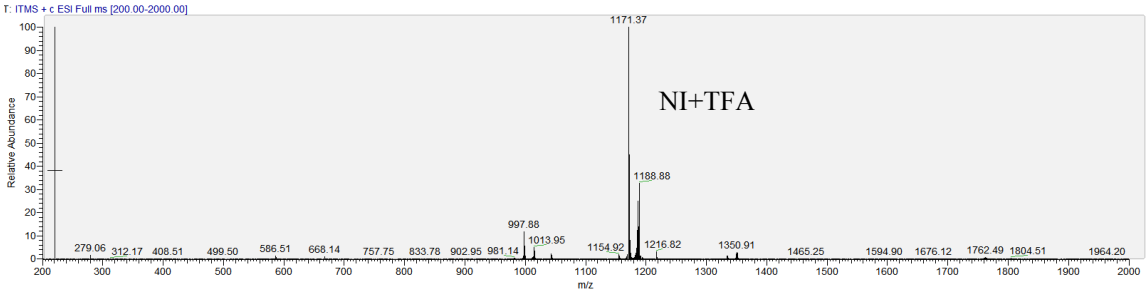
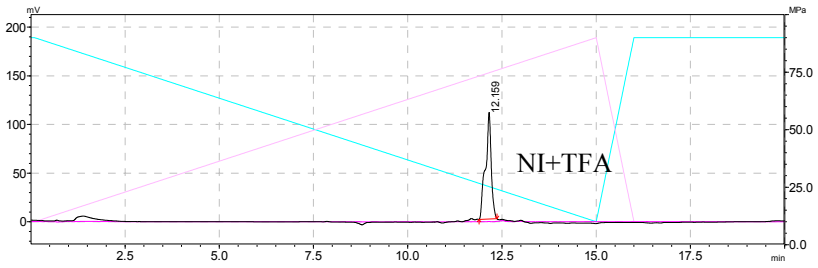


Figure S8g. Cyclization of linear peptide **P1** after 5 min photo-irradiation with 311 nm in isopropyl alcohol. The identity of the crude mixture product was confirmed by LC-MS: MS (ESI) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^{+}$ 1058.64 [M+H^{+}], found 1171.37 [NI+TFA].

a)



b)

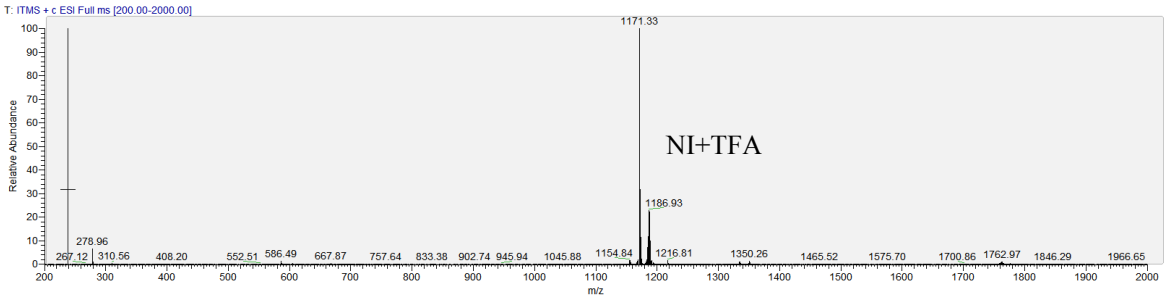
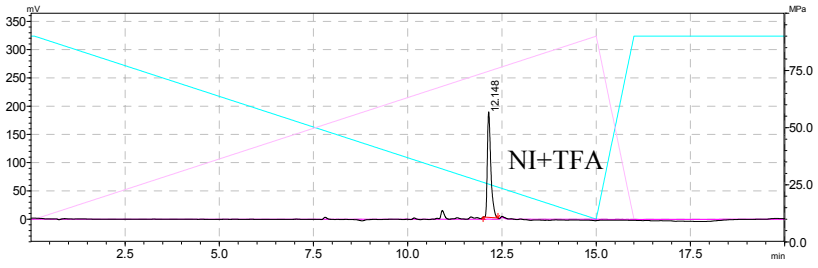


Figure S8h. Cyclization of linear peptide **P1** after 5 min photo-irradiation with 311 nm in ethyl acetate (EA). The identity of the crude mixture product was confirmed by LC-MS: MS (ESI) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^{+}$ 1058.64 [M+H^{+}], found 1171.33 [NI+TFA].

a)



b)

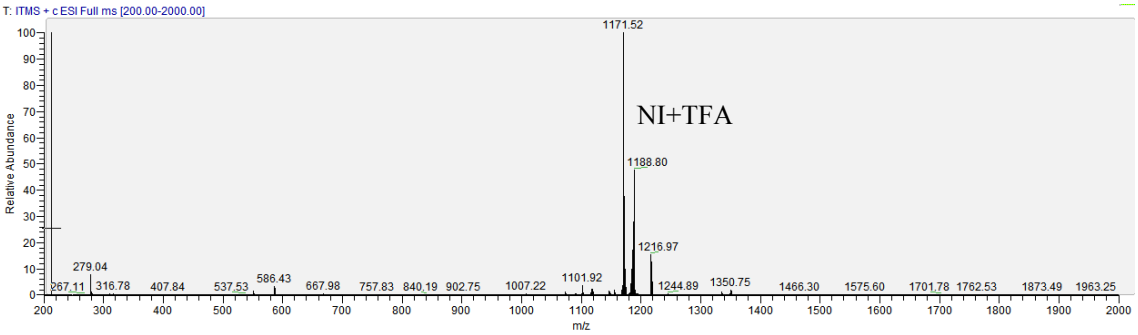
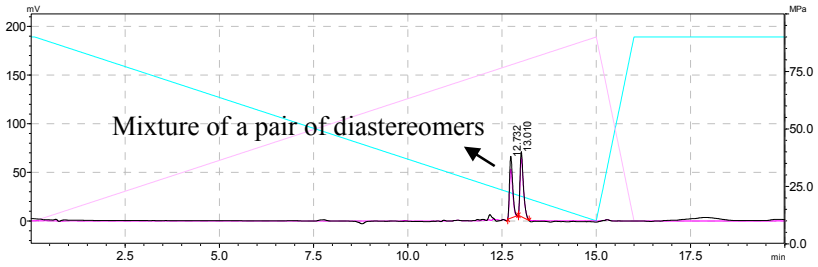


Figure S8i. Cyclization of linear peptide **P1** after 5 min photo-irradiation with 311 nm in dichloromethane (DCM). The identity of the crude mixture product was confirmed by LC-MS: MS (ESI) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^{+}$ 1058.64 [M+H^{+}], found 1171.52 [NI+TFA].

a)



b)

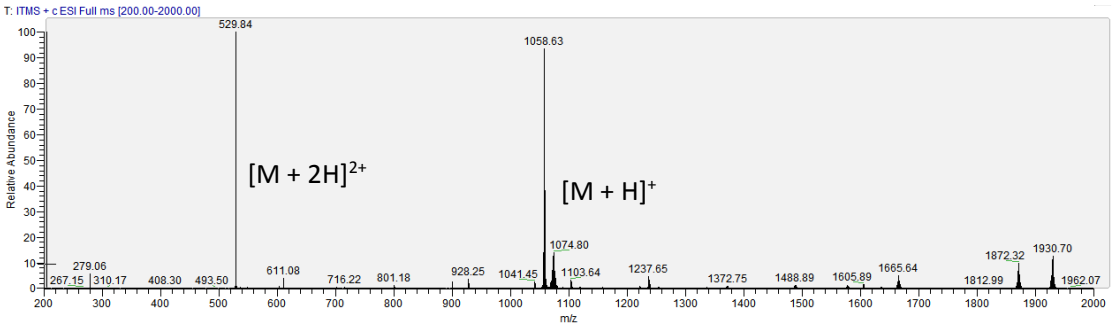
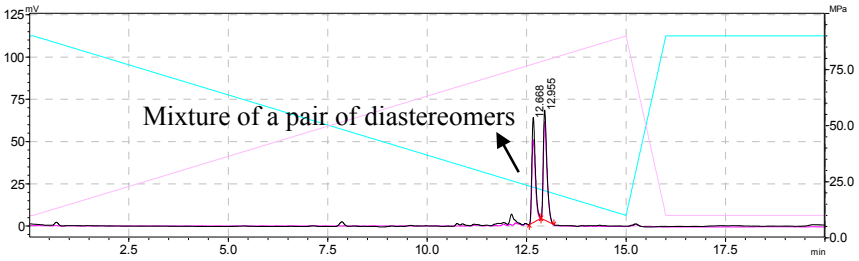


Figure S8j. Cyclization of linear peptide **P1** after 5 min photo-irradiation with 311 nm in ACN/PB (1/1). The identity of the crude mixture product was confirmed by LC-MS: MS (ESI) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^{+}$ 1058.64 [M+H^{+}], found 1058.63 [M+H^{+}].

a)



b)

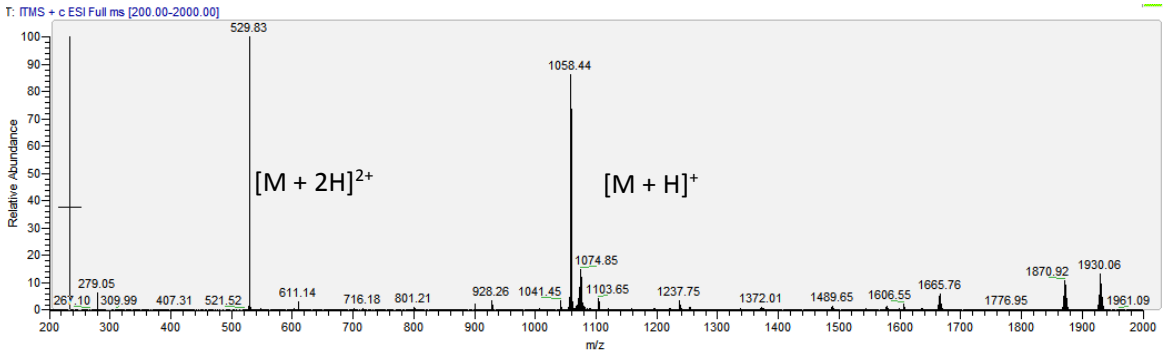
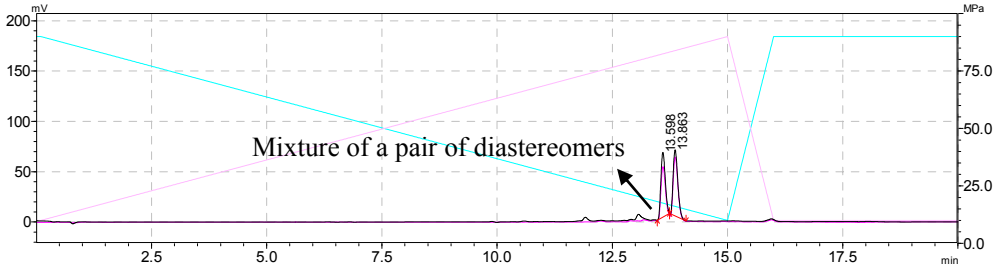


Figure S8k. Cyclization of linear peptide **P1** after 5 min photo-irradiation with 311 nm in ACN/PBS (1/1). The identity of the crude mixture product was confirmed by LC-MS: MS (ESI) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^{+}$ 1058.64 [M+H^{+}], found 1058.44 [M+H^{+}].

a)



b)

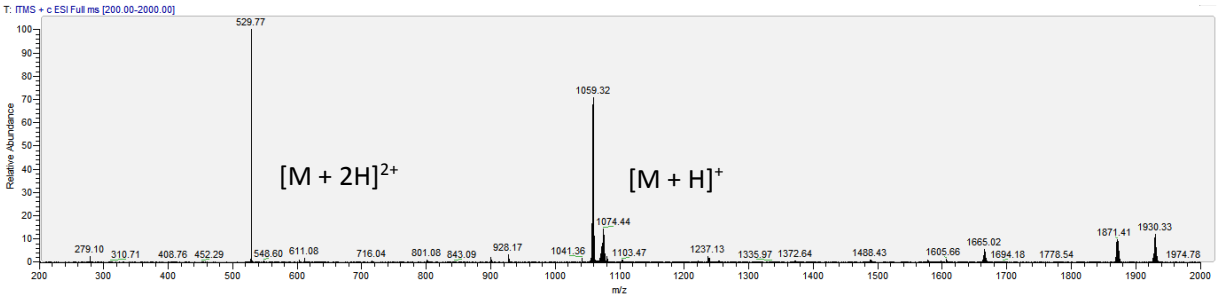
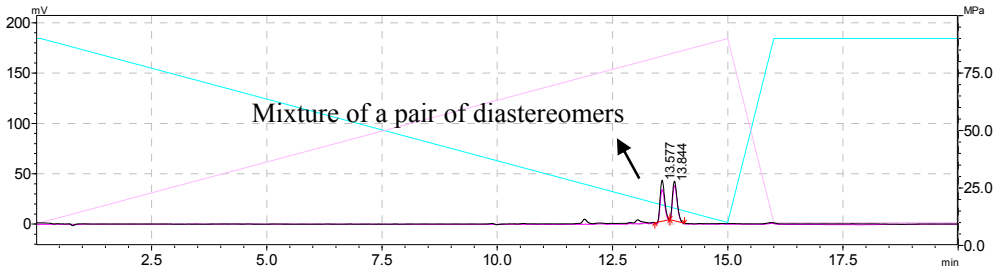


Figure S8l. Cyclization of linear peptide **P1** after 1 min photo-irradiation with 371 nm in ACN/PB (1/2). The identity of the crude mixture product was confirmed by LC-MS: MS (ESI) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^{+}$ 1058.64 [M+H^{+}], found 1059.32 [M+H^{+}].

a)



b)

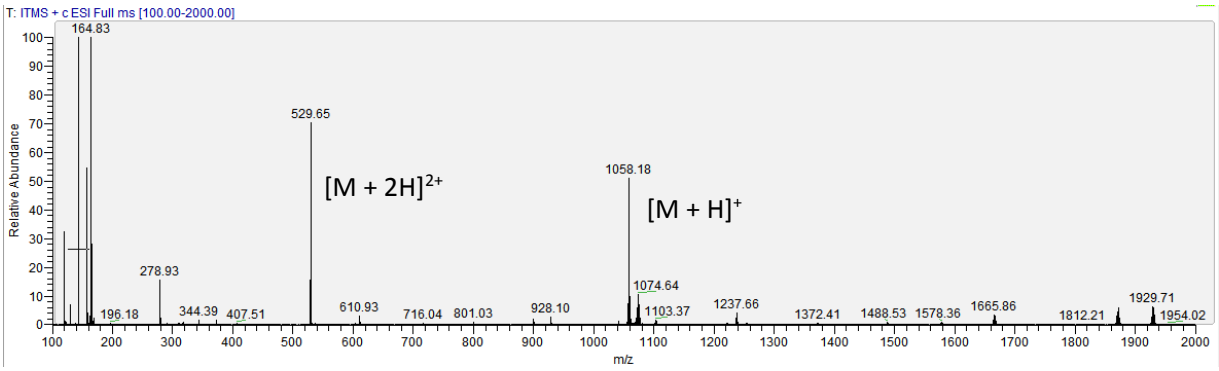
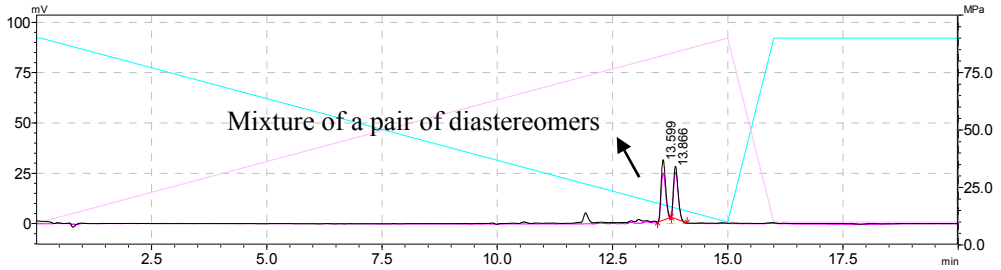


Figure S8m. Cyclization of linear peptide **P1** after 1 min photo-irradiation with 371 nm in ACN/PB (1/4). The identity of the crude mixture product was confirmed by LC-MS: MS (ESI) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^{+}$ 1058.64 [M+H^{+}], found 1058.18 [M+H^{+}].

a)



b)

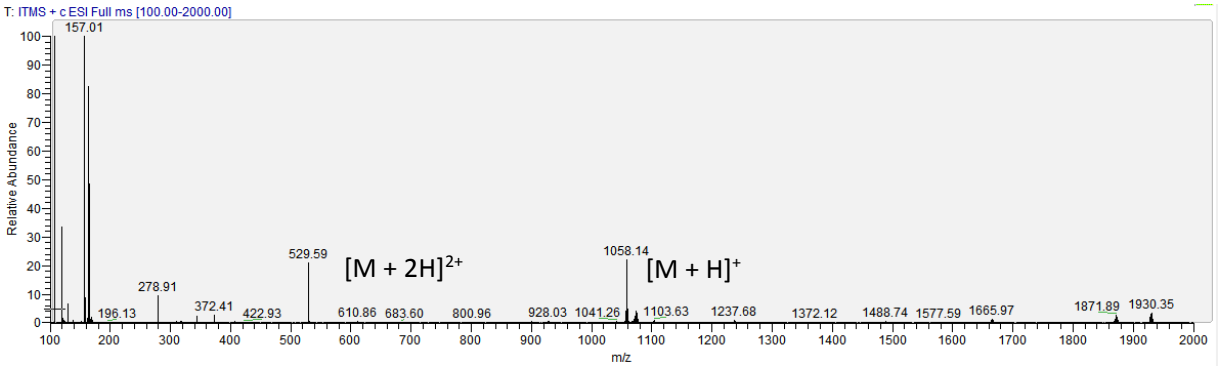
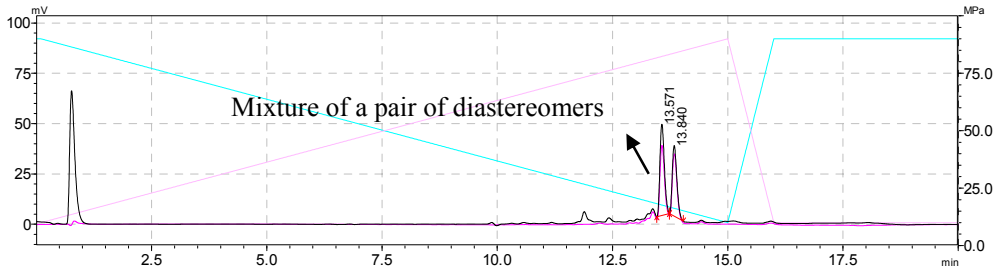


Figure S8n. Cyclization of linear peptide **P1** after 1 min photo-irradiation with 371 nm in ACN/PB (1/8). The identity of the crude mixture product was confirmed by LC-MS: MS (ESI) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^{+}$ 1058.64 [M+H^{+}], found 1058.14 [M+H^{+}].

a)



b)

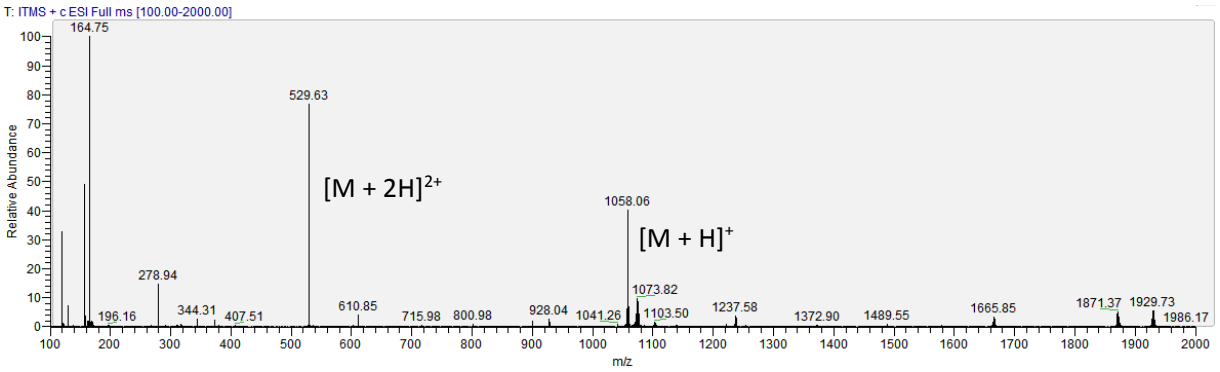
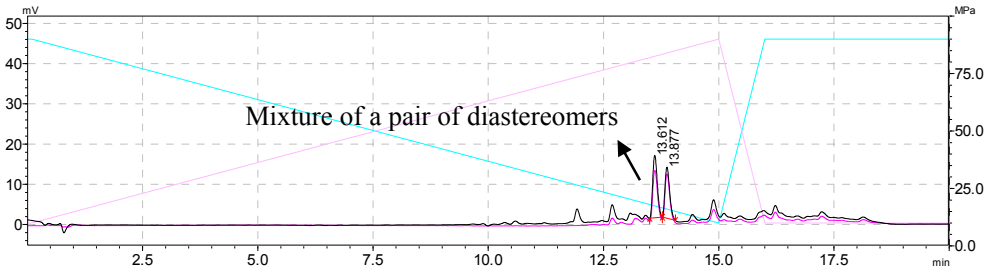


Figure S8o. Cyclization of linear peptide **P1** after 1 min photo-irradiation with 371 nm in DMSO/PB (1/1). The identity of the crude mixture product was confirmed by LC-MS: MS (ESI) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^{+}$ 1058.64 [M+H^{+}], found 1058.06 [M+H^{+}].

a)



b)

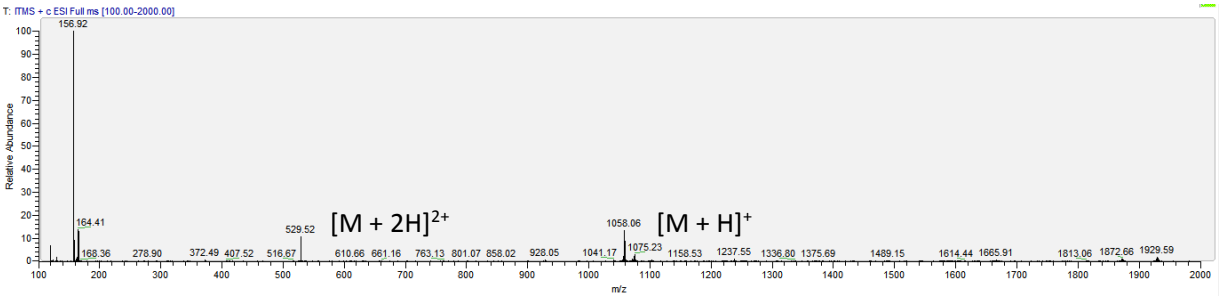
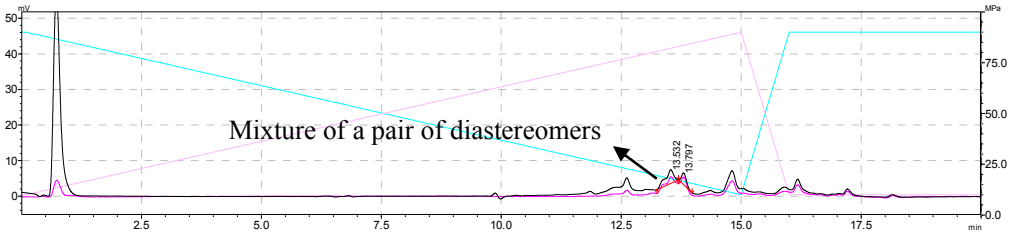


Figure S8p. Cyclization of linear peptide **P1** after 1 min photo-irradiation with 371 nm in PB. The identity of the crude mixture product was confirmed by LC-MS: MS (ESI) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^{+}$ 1058.64 [M+H^{+}], found 1058.06 [M+H^{+}].

a)



b)

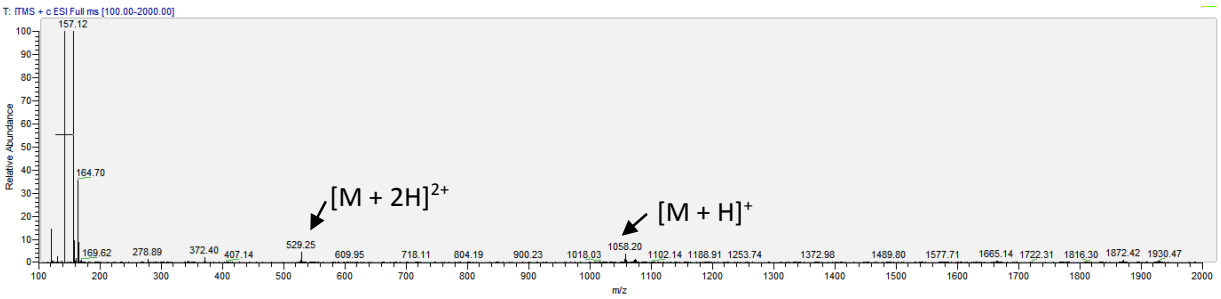


Figure S8q. Cyclization of linear peptide **P1** after 1 min photo-irradiation with 371 nm in DMEM. The identity of the crude mixture product was confirmed by LC-MS: MS (ESI) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^{+}$ 1058.64 [M+H^{+}], found 1058.20 [M+H^{+}].

MALDI-TOF mass spectra measurements of cyclic peptide P2

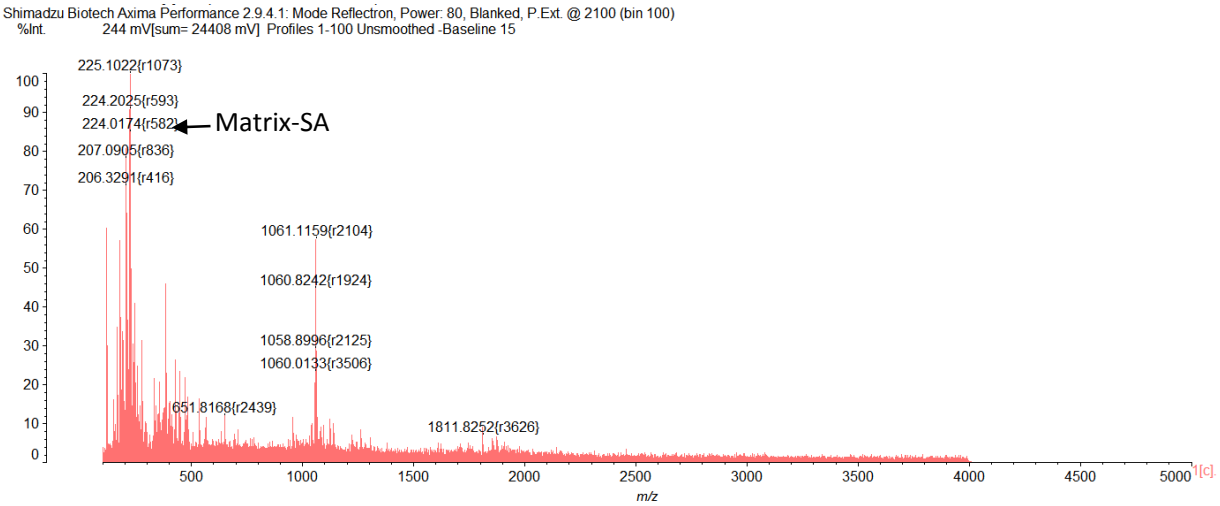
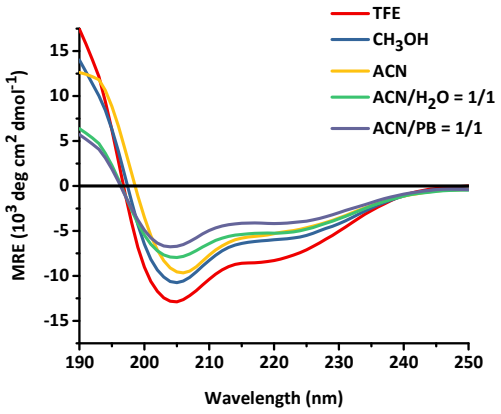


Figure S9. MALDI-TOF mass spectra measurements of cyclic peptide **P2**. After photo-irradiated linear peptide **P1** in ACN/PB (1/1), the crude cyclic peptide contain a pair of diastereomers was purified with preparative reverse-phase HPLC affording cyclic peptide **P2**. Mass measurements were performed using MALDI-TOF (SHIMADZU) calcd. for cyclic peptide $C_{55}H_{84}N_{11}O_{10}^{+}$ 1058.6397 [M+H^{+}], found 1058.8996 [M+H^{+}]. The reaction of peptide dimerization was not observed.

Circular dichroism measurements

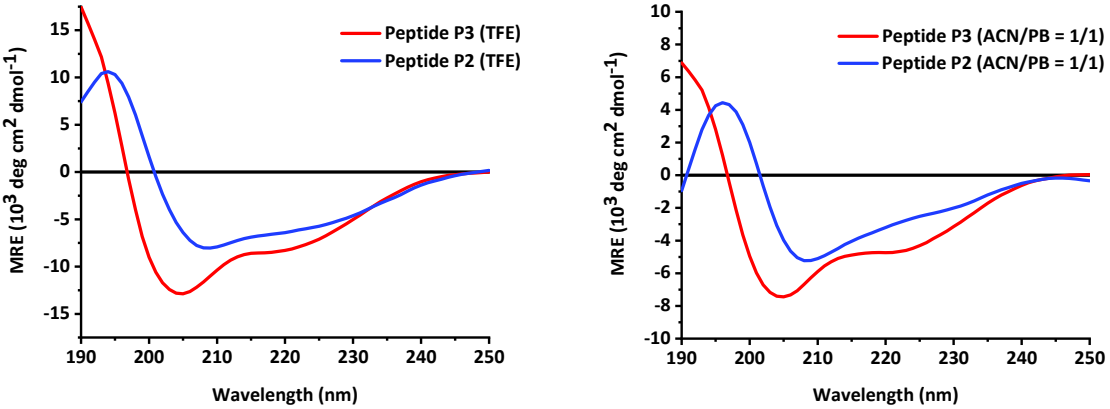
CD spectra were obtained using a 1 mm quartz cuvette at 25 ℃ on a spectropolarimeter (Chirascan) instrument. The spectra were recorded in the range of 190-250 nm and 50 nm/min of the scanning speed, 2 seconds of the response time and 1 nm of the bandwidth. The percent helicity was calculated by using the following equation: % helicity = $[[\theta]_{208\ MRE} - 4000]/-29000 \times 100$.[S4] Prediction of peptide secondary structure from circular dichroism using K2D3, a web server to estimate the α-helix and β-strand content of protein or peptide from its circular dichroism spectrum.[S5]

a)



Peptide **P1**	α-helicity (%)
TFE	53.88
CH_3OH	46.73
ACN	44.75
ACN/H_2O = 1/1	38.56
ACN/PB = 1/1	33.65

b)



Secondary structure percentages	TFE		ACN/PB = 1/1	
	Peptide **P3**	Peptide **P2**	Peptide **P3**	Peptide **P2**
α-helix (%)	22.54	13.46	7.26	2.47
β-strand (%)	12.37	28.11	14.54	25.84

Figure S10. (a) The circular dichroism measurements of 100 μM peptide **P1** in different solvents. The percent α-helicity values are listed in the table. (b) CD spectra of the cyclic peptide **P2** and peptide **P3** at 25℃. Peptides were dissolved in TFE or ACN/PB (1/1) to derive 100 μM solutions. Predicted secondary structure percentages are listed in the table.

Fluorescence images of A549 cells for *in-situ* cyclization of P1 or P3 in the medium after photo-irradiation

A549 cells were cultured in a 35-mm glass bottom microwell dish. 150 μM of linear peptide **P1** or **P3** with A549 cells were photo-irradiated with 371 nm for 1 min and then incubated in 2% DMSO serum-free DMEM medium for 3 h in a 37 ºC, 5% CO_2 incubator followed by addition of a 20 μL DIO membrane dye for 5 min. Cells were washed twice with PBS and placed into serum-free DMEM medium for fluorescent imaging acquisition.

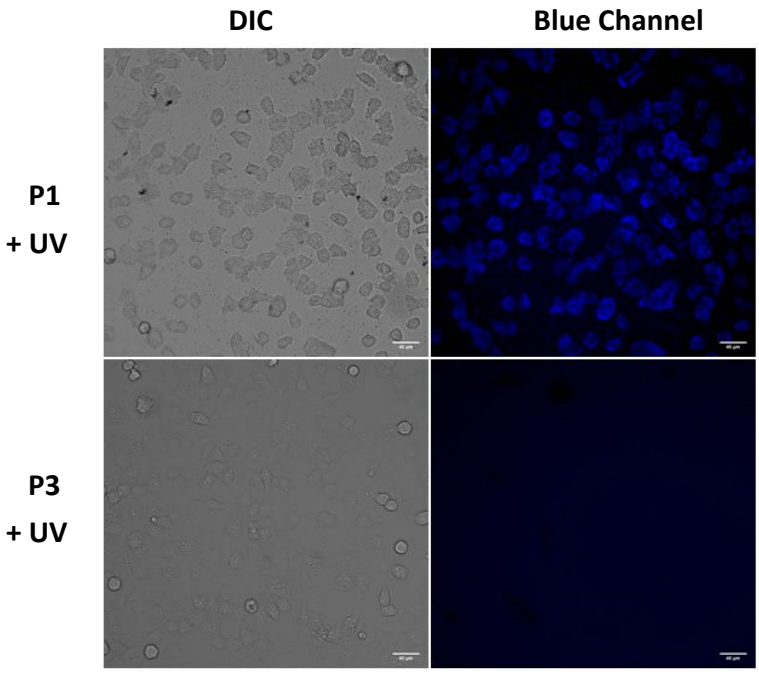


Figure S11. Fluorescence images of live A549 cells for *in-situ* cyclization of 150 μM **P1** or **P3** in the medium after 371 nm irradiation.

MTS assays

A549 cells were seeded in 96-well plates with a concentration of 6,000 cells per well. After 24 hours, peptide **P1** was added with final concentrations of 25, 50, 100 and 150 μM. Or A549 cells were subject to irradiation with the 371 nm LED array for 1, 2, 3 and 5 minutes. Or A549 cells with 150 μM peptide **P1** were subject to irradiation with the 371 nm LED array for 1 minute. Then, A549 cells were further cultured for 24 hours. MTS assay was then carried out. For each well, 20 μL MTS solution (CellTiter 96® AQ_{ueous} One Solution Cell Proliferation Assay, Promega) was added after 3 hours' incubation. The absorbance at 490 nm was then measured to indicate the cell viability.

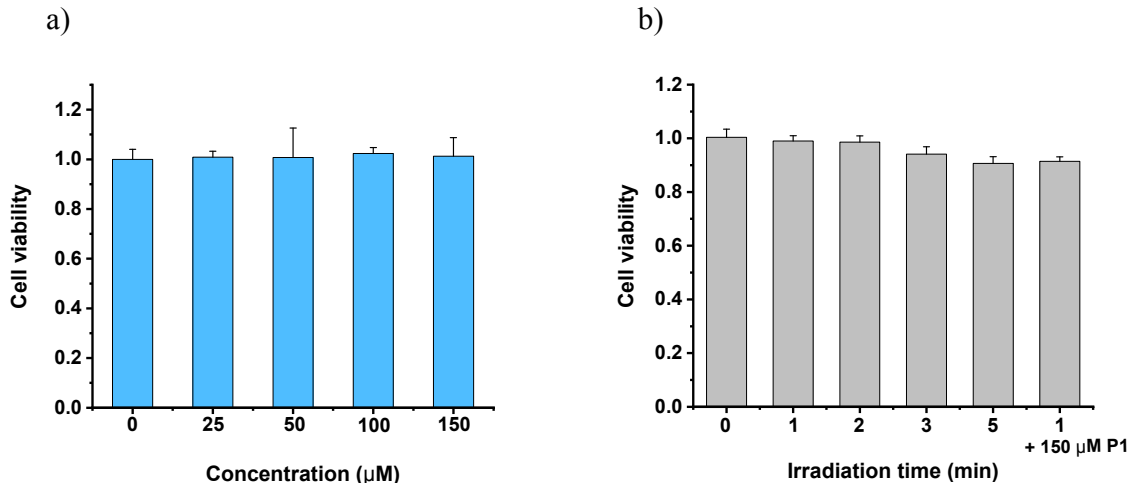


Figure S12. Cell viability of A549 cells after incubation with peptide **P1** or after irradiation with the 371 nm LED array or with both treatments. (a) A549 cells were incubated with 25-150 μM peptide **P1** for 24 hours. MTS was used to assess the cell viability. Data were shown as mean ± SEM (n=5). (b) A549 cells were irradiated for 1-5 min or A549 cells with 150 μM peptide **P1** were irradiated for 1 min and further cultured for 24 hours. MTS was used to assess the cell viability. Data are shown as mean ± SEM (n=5).

Fluorescence images of A549 cells after treatment with cyclic peptide P2 or linear peptide P4.

A549 cells were cultured in a 35-mm glass bottom microwell dish. The cells were incubated with 150 μM cyclic peptide **P2** or control peptide **P4** in 2% DMSO serum-free DMEM medium for 3 h in a 37 ºC, 5% CO_2 incubator followed by addition of a 20 μL DIO membrane dye for 5 min. Then, cells were washed twice with PBS and placed into serum-free DMEM medium for fluorescent imaging acquisition.

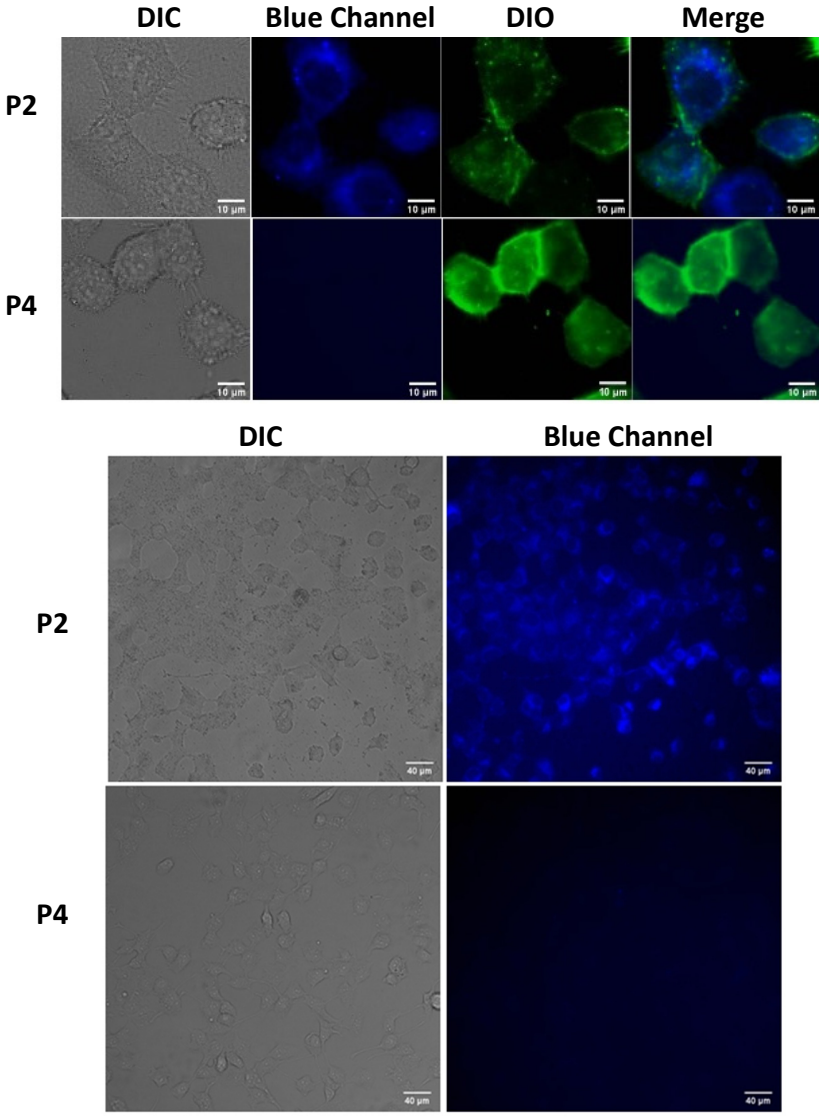
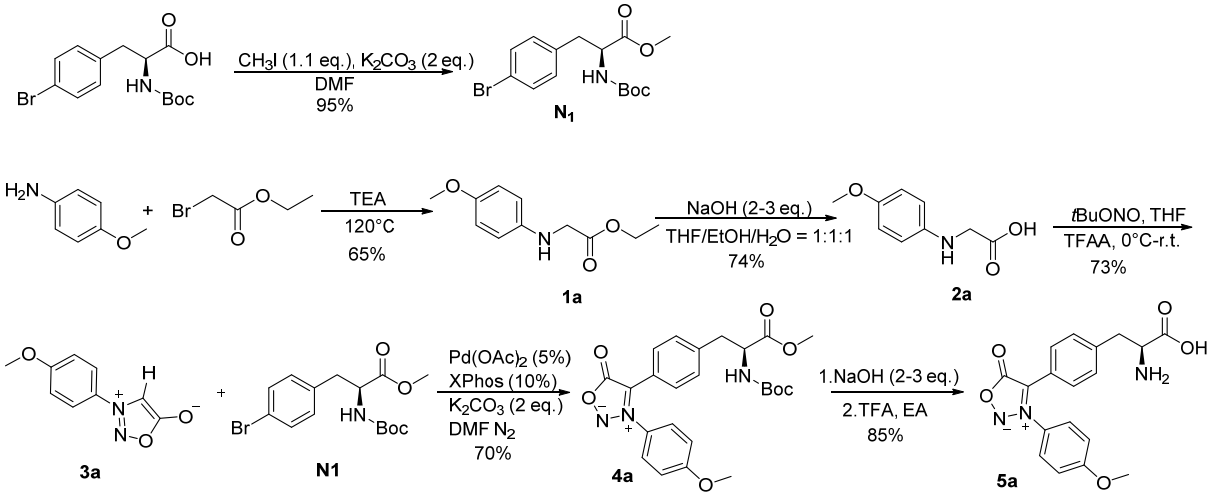
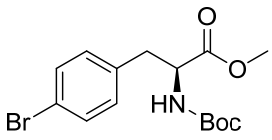


Figure S13. Fluorescence images of A549 cells after treatment with 150 μM of cyclic peptide **P2** or linear peptide **P4** for 3 h.

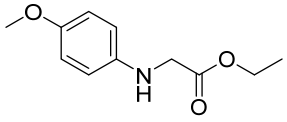
Experimental Procedures and Characterization Data for DASyd amino acids.

Scheme S1: Synthesis of DASyd amino acid **5a**. **3a** was synthesized according to a literature procedure.[S6]



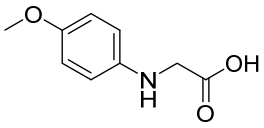


Methyl (*S*)-3-(4-bromophenyl)-2-((*tert*-butoxycarbonyl)amino) propanoate (N1): To a solution of (*S*)-3-(4-bromophenyl)-2-((*tert*-butoxycarbonyl)amino)propanoic acid (2.60 g, 7.56 mmol) and K_2CO_3 (2.10 g, 15.1 mmol) in DMF (35 mL) was added MeI (1.17 g, 8.33 mmol). Then this mixture was stirred at room temperature for 4 h. The reaction mixture was added water (50 mL) and extracted with EtOAc (50 mL x 3). The organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuum to give the desired product as a white solid (2.57 g, 95% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43-7.39 (m, 2H), 7.03-6.97 (m, 2H), 4.97 (d, J = 8.2 Hz, 1H), 4.57 (d, J = 8 Hz, 1H), 3.71 (s, 3H), 3.12-2.95 (m, 2H), 1.42 (s, 9H). HRMS (ESI) calcd. for $C_{15}H_{21}BrNO_4^+$ 358.0648 [M+H$^+$], found 358.0663.

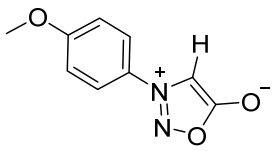


Ethyl (4-methoxyphenyl)glycinate (1a): To a solution of 4-methoxyaniline (5.00 g, 40.6 mmol) in triethylamine (100 mL) was added ethyl 2-bromoacetate (6.70 g, 40.6 mmol) under argon. The

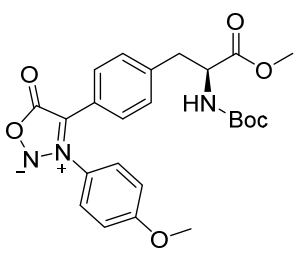
solution was stirred at 120 °C for 1 h and traced with TLC till the conversion was completed. The mixture was then evaporated to dryness in vacuum. The residue was purified through flash chromatography (pentane/EtOAc = 5/1) to give the desired product as a colorless solid (5.52 g, 65% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.84-6.75 (m, 2H), 6.63-6.54 (m, 2H), 4.23 (q, J = 8 Hz, 2H), 4.03 (s, 1H), 3.86 (s, 2H), 3.75 (s, 3H), 1.29 (t, J = 8 Hz, 3H). MS (ESI) calcd. for $C_{11}H_{16}NO_3^+$ 210.11 [M+H$^+$], found 210.32.



(4-Methoxyphenyl)glycinic acid (2a): A mixture of **1a** (4.90 g, 12.1 mmol) in THF/H_2O/EtOH = 1:1:1 (100 mL), NaOH (2.81 g, 70.3 mmol) was stirred vigorous at room temperature over 30 min and was traced with TLC till the conversion was completed. The mixture was then evaporated to remove organic solution in vacuum and was basified with 3 M aq. HCl to adjust the pH around 2 till the white solid precipitated out. The resulting mixture then was vacuum filtered to separate the white precipitate, washing with pentane/EtOAc = 5/1 then H_2O. Subsequently, dried over vacuum to give desired product as a white solid (1.61 g, yield 74%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.72-6.68 (m, 2H), 6.52-6.48 (m, 2H), 3.70 (s, 2H), 3.62 (s, 3H), 3.36 (s, 1H). MS (ESI) calcd. For $C_9H_{10}NO_3^-$ 180.07 [M-H$^-$], found 180.29.

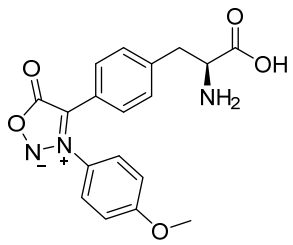


3-(4-Methoxyphenyl)-1,2,3-oxadiazol-3-ium-5-olate (3a): To a solution of **2a** (2.50 g, 13.8 mmol) was dissolved in 150 mL of anhydrous THF under argon at 0 °C and *t*butyl nitrite (2.14 g, 20.7 mmol) was added dropwise. The solution was warmed slowly to room temperature over 1 h and was traced with TLC till the conversion was completed before the introduction of TFAA (3.10 g, 15.0 mmol) and stirred at room temperature for 1 h. The reaction was quenched with EtOAc/H_2O and the aqueous layer was extracted with EtOAc. The organic layers were combined and washed with an aqueous solution of $NaCl_{sat}$ before being dried over $MgSO_4$ and evaporated. The crude was purified by column to give sydnone **3a** as a colorless solid (1.93 g, 73% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66-7.62 (m, 2H), 7.10-7.06 (m, 2H), 6.64 (s, 1H), 3.90 (s, 3H). MS (ESI) calcd. for $C_9H_9N_2O_3^+$ 193.06 [M+H$^+$], found 192.80.



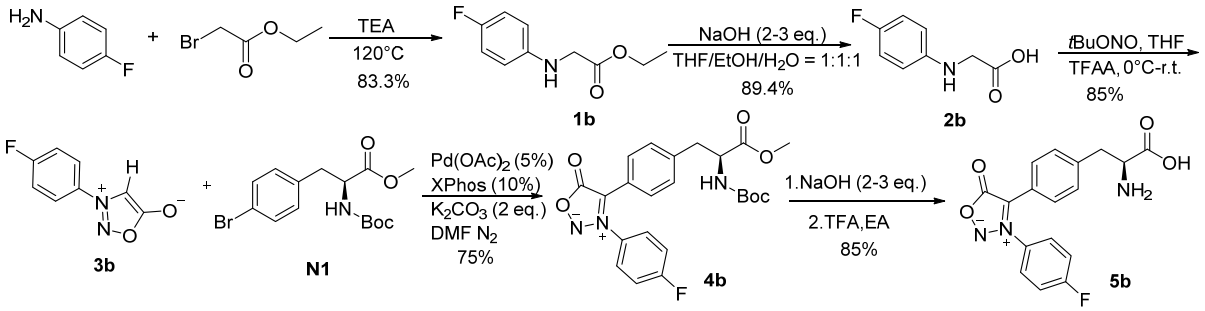
(*S*)-4-(4-(2-((*tert*-Butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) phenyl)-3-(4-methoxyphenyl)-5-oxo-5*H*-1,2,3-oxadiazol-3-ium-2-ide (4a): A flask equipped with a reflux condenser was charged with a mixture of sydnone **3a** (500 mg, 2.60 mmol), **N1** (1.11 g, 3.12 mmol), palladium acetate (29.0 mg, 0.130 mmol), XPhos (124 mg, 0.260 mmol)

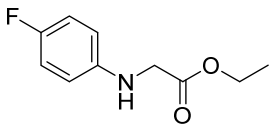
and potassium carbonate (720 mg, 5.20 mmol) in DMF (10 mL) under an atmosphere of nitrogen and heated at 120°C for 2 h.[S7] The reaction was allowed to cool to ambient temperature and water was added. The resulting mixture was extracted with EtOAc/PET = 9/1 and the combined organic layers dried over $MgSO_4$ and concentrated in vacuo. The crude was purified by silica gel column to give sydnone **4a** as a slight yellow solid (854 mg, 70% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 (d, J = 12.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.03 (dd, J = 14.7, 8.5 Hz, 4H), 4.99 (d, J = 8 Hz, 1H), 4.53 (q, J = 6.6 Hz, 1H), 3.88 (s, 3H), 3.66 (s, 3H), 3.09-2.95 (m, 2H), 1.39 (s, 9H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.1, 167.2, 162.2, 155.1, 136.9, 129.8, 127.3, 127.3, 126.3, 123.4, 115.3, 107.6, 80.1, 55.9, 54.3, 52.4, 38.1, 28.4. HRMS (ESI) calcd. for $C_{24}H_{28}N_3O_7^+$ 470.1922 [M+H$^+$], found 470.1947.



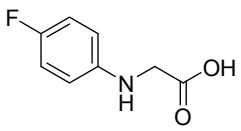
(*S*)-4-(4-(2-Amino-2-carboxyethyl)phenyl)-3-(4-methoxyphenyl)-5-oxo-5*H*-1,2,3-oxadiazol-3-ium-2-ide (5a): A mixture of **4a** (80.0 mg, 0.170 mmol) and NaOH (20.4 mg, 0.510 mmol) in THF/H_2O/MeOH = 1:1:1 (3 mL) was stirred vigorous at room temperature over 30 min and was traced with TLC till the conversion was completed. The mixture was then evaporated to remove organic solution in vacuum and immediately treated with TFA (2 mL) in EtOAc (2 mL) for 2 h. The crude mixture was poured into ice cold Et_2O. The formed precipitate was discarded and the solvent was removed in vacuum to give sydnone **5a** as a slight yellow solid (51.2 mg, 85% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.66 (dd, J = 22.6, 5.5 Hz, 2H), 7.64-7.60 (m, 2H), 7.29-7.15 (m, 6H), 4.12-4.08 (m, 1H), 3.85 (s, 3H), 3.14 (t, J = 5.7 Hz, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.2, 166.4, 161.6, 158.5, 135.7, 129.8, 127.2, 127.1, 123.6, 115.2, 107.9, 55.9, 52.9, 35.3. HRMS (ESI) calcd. for $C_{18}H_{16}N_3O_5^-$ 354.1095 [M-H$^+$], found 354.1097.

Scheme S2: Synthesis of DASyd amino acid **5b**. **3b** was synthesized according to a literature procedure.[S6]

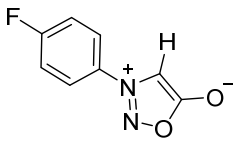




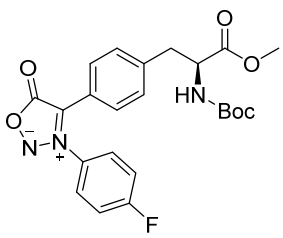
Ethyl (4-fluorophenyl)glycinate (1b): 4-fluoroaniline (4.00 g, 36.0 mmol) and ethyl 2-bromoacetate (6.02 g, 36.0 mmol) were subjected to the general condition as to afford **1a**, affording **1b** as a slight yellow solid (5.91 g, 83.3%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.93-6.88 (m, 2H), 6.57-6.53 (m, 2H), 4.24 (q, J = 8 Hz, 2H), 3.86 (s, 2H), 1.29 (t, J = 8 Hz, 3H). HRMS (ESI) calcd. for $C_{10}H_{13}FNO_2^+$ 198.0925 [M+H$^+$], found 198.0955.



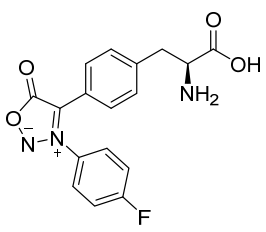
(4-Fluorophenyl)glycine (2b): A mixture of **1b** (2.50 g, 12.7 mmol) and NaOH (1.01 g, 25.4 mmol) were subjected to the general condition as to afford **2a**, affording **2b** as a yellow solid (1.92 g, 89.4% yield). ^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ 6.94-6.88 (m, 2H), 6.56-6.51 (m, 2H), 3.76 (s, 2H), 3.35 (s, 1H). HRMS (ESI) calcd. for $C_8H_7FNO_2^-$ 168.0466 [M-H$^+$], found 168.0475.



3-(4-Fluorophenyl)-1,2,3-oxadiazol-3-ium-5-olate (3b): 2b (1.81 g, 10.7 mmol)**,** *t*Butyl nitrite (1.65 g, 16.0 mmol) and TFAA (7.86 g, 37.4 mmol) were subjected to the general condition as to afford **3a**, affording **3b** as a yellow solid (1.64 g, 85.0% yield).^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (dd, J = 8.9, 4.5 Hz, 2H), 7.32 (t, J = 8.3 Hz, 2H), 6.75 (s, 1H). HRMS (ESI) calcd. for $C_8H_6FN_2O_2^+$ 181.0408 [M+H$^+$], found 181.0423.

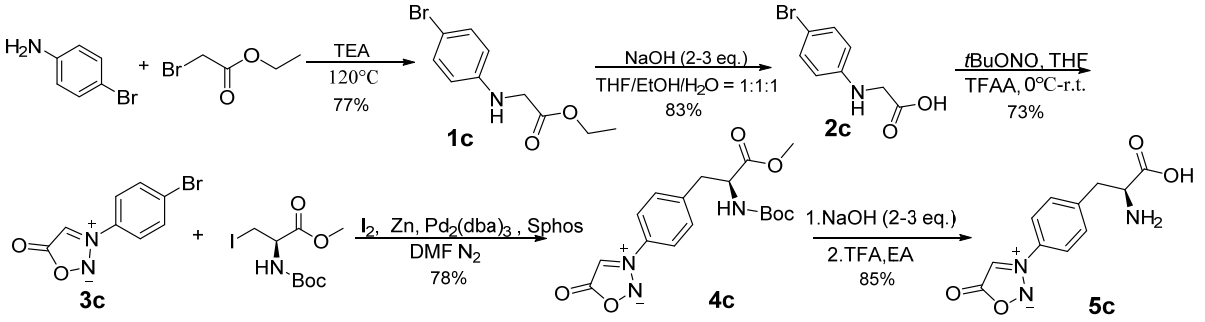


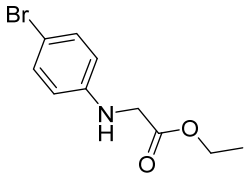
(*S*)-4-(4-(2-((*tert*-Butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) phenyl)-3-(4-fluorophenyl)-5-oxo-5*H*-1,2,3-oxadiazol-3-ium-2-ide (4b): A mixture of sydnone **3b** (500 mg, 2.78 mmol), **N1** (1.19 g, 3.33 mmol), palladium acetate (31.0 mg, 0.140 mmol), XPhos (132 mg, 0.280 mmol) and potassium carbonate (768 mg, 5.55 mmol) were subjected to the general condition as to afford **4a**, affording **4b** as a slight yellow solid (953 mg, 75%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 (dd, J = 8.9, 4.5 Hz, 2H), 7.29 (d, J = 8.2 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.09 (d, J = 8.1 Hz, 2H), 4.97 (d, J = 8.3 Hz, 1H), 4.56 (q, J = 6.6 Hz, 1H), 3.70 (s, 3H), 3.13-2.98 (m, 2H), 1.41 (s, 9H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.1, 167.1, 164.4 (d, J = 255.5 Hz), 155.1, 137.4, 130.8 (d, J = 3.0 Hz), 130.0, 127.5, 127.2 (d, J = 9.1 Hz), 123.1, 117.6 (d, J = 23.2 Hz), 108.0, 80.3, 54.3, 52.5, 38.2, 28.4; ^{19}F NMR (376 MHz, DMSO-*d*$_6$) δ -62.72, -105.62. HRMS (ESI) calcd. for $C_{23}H_{25}FN_3O_6^+$ 458.1722 [M+H$^+$], found 458.1730.



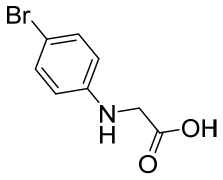
(*S*)-4-(4-(2-Amino-2-carboxyethyl)phenyl)-3-(4-fluorophenyl)-5-oxo-5*H*-1,2,3-oxadiazol-3-ium-2-ide (5b): 4b (80.0 mg, 0.170 mmol) and NaOH (20.4 mg, 0.510 mmol) were subjected to the general condition as to afford **5a**, affording **5b** as a yellow solid (49.4 mg, 85% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.55 (d, J = 5.6 Hz, 2H), 7.80 (dd, J = 8.8, 4.6 Hz, 2H), 7.52 (t, J = 8.6 Hz, 2H), 7.30-7.12 (m, 4H), 4.11 (q, J = 5.9 Hz, 1H), 3.18-3.04 (m, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.3, 163.7 (d, J = 251.5 Hz), 162.5, 136.0, 130.7 (d, J = 3 Hz), 129.9, 128.5 (d, J = 10.1 Hz), 127.5, 123.3, 117.5 (d, J = 23.2 Hz), 108.5, 53.0, 35.4; ^{19}F NMR (376 MHz, DMSO-d_6) δ -62.72, -108.93. HRMS (ESI) calcd. for $C_{17}H_{13}FN_3O_4^-$ 342.0896 [M-H$^-$], found 342.0991.

Scheme S3: Synthesis of MASyd amino acid **5c**. **3c** was synthesized according to a literature procedure.[S6]

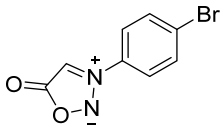




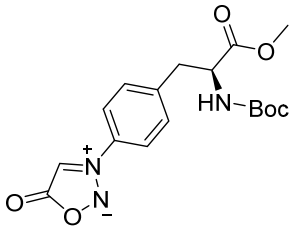
Ethyl (4-bromophenyl)glycinate (1c): 4-bromoaniline (5.00 g, 29.0 mmol) and ethyl 2-bromoacetate (4.41 g, 26.4 mmol) were subjected to the general condition as to afford **1a**, affording **1c** as a white solid (5.76 g, 77%). ^{1}H NMR (400 MHz, Chloroform-d) δ 7.29-7.26 (m, 2H), 6.50-6.47 (m, 2H), 4.25 (q, J = 7.1 Hz, 2H), 3.86 (s, 2H), 1.30 (t, J = 8 Hz, 3H). HRMS (ESI) calcd. for $C_{10}H_{13}BrNO_2^+$ 258.0124 [M+H$^+$], found 258.0131.



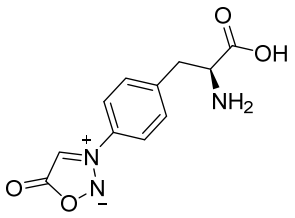
(4-Bromophenyl)glycine (2c): A mixture of **1c** (5.00 g, 19.4 mmol) and NaOH (1.17 g, 29.2 mmol) were subjected to the general condition as to afford **2a**, affording **2c** as a white solid (3.69 g, 83%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.23-7.19 (m, 2H), 6.55-6.51 (m, 2H), 3.79 (s, 2H). HRMS (ESI) calcd. for $C_8H_7BrNO_2^-$ 227.9666 [M-H$^+$], found 227.9679.



3-(4-Bromophenyl)-1,2,3-oxadiazol-3-ium-5-olate (3c): 2c (2.00 g, 8.73 mmol)**,** *t*Butyl nitrite (1.35 g, 13.1 mmol) and TFAA (6.42 g, 30.6 mmol) were subjected to the general condition as to afford **3a**, affording **3c** as a white solid (1.53 g, 73%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79-7.75 (m, 2H), 7.64-7.60 (m, 2H), 6.73 (s, 1H). HRMS (ESI) calcd. for $C_8H_6BrN_2O_2^+$ 240.9607 [M+H$^+$], found 240.9626.



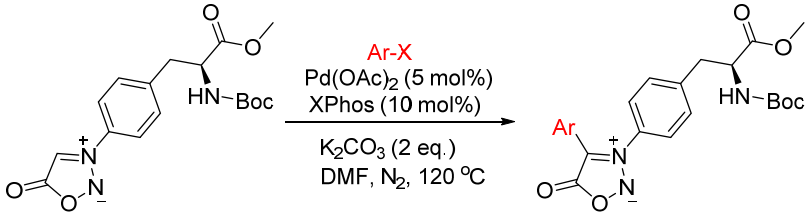
(*S*)-3-(4-(2-((*tert*-Butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) phenyl)-5-oxo-5*H*-1,2,3-oxadiazol-3-ium-2-ide (4c): Zinc dust (1.58 g, 25.0 mmol) was added to a flame-dried, nitrogen-purged side arm round-bottomed flask. Dry DMF (5 mL) was added via syringe, followed by a catalytic amount of iodine (333 mg, 1.25 mmol). A color change of the DMF was observed from colorless to yellow and back again. Protected methyl (*R*)-2-((*tert*-butoxycarbonyl)amino)-3-iodopropanoate (2.70 mg, 8.32 mmol) was added immediately, followed by a catalytic amount of iodine (333 mg, 1.25 mmol). The solution was stirred at room temperature for 5 min; $Pd_2(dba)_3$ (156 mg, 0.170 mmol), SPhos (68.2 mg,0.170 mmol) and **3c** (800 mg, 3.33 mmol) were added to the solution of organozinc reagent and the mixture was heated at 60℃ for 3 h, under a positive pressure of nitrogen.[S8] The crude was purified by silica gel column to give **4c** as a white solid (946 mg, 78% yield). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66-7.64 (m, 2H), 7.39 (d, J = 8.3 Hz, 2H), 6.71 (s, 1H), 5.10 (d, J = 8.0 Hz, 1H), 4.63 (q, J = 8 Hz, 1H), 3.75 (s, 3H), 3.19 (ddd, J = 68.8, 13.7, 6.2 Hz, 2H), 1.40 (s, 9H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.8, 169.1, 155.1, 141.8, 133.8, 131.3, 121.4, 93.7, 80.5, 54.3, 52.7, 38.4, 28.4. HRMS (ESI) calcd. for $C_{17}H_{22}N_3O_6^+$ 364.1503 [M+H$^+$], found 364.1513.



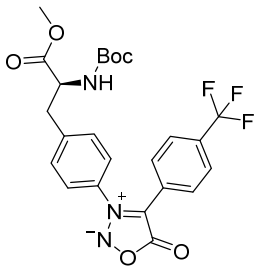
(*S*)-4-(4-(2-Amino-2-carboxyethyl)phenyl)-3-(4-fluorophenyl)-5-oxo-5*H*-1,2,3-oxadiazol-3-ium-2-ide (5c): 4c (80.0 mg, 0.220 mmol) and NaOH (26.4 mg, 0.660 mmol) were subjected to the general condition as to afford **5a**, affording **5c** as a white solid (46.4 g, 85% yield). ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.30 (d, J = 8 Hz, 2H), 7.02 (d, J = 8 Hz, 2H), 4.25-4.22 (m, 1H), 3.28-3.14 (m, 2H); ^{13}C NMR (101 MHz, Methanol-d_4) δ 171.2, 145.9, 132.4, 131.6, 129.8, 124.8, 116.4, 55.1, 36.5. HRMS (ESI) calcd. for $C_{11}H_{10}N_3O_4^-$ 248.0677 [M-H$^-$], found 248.0687.

Scheme S4: Synthesis of DASyd amino acids **5d-f**.

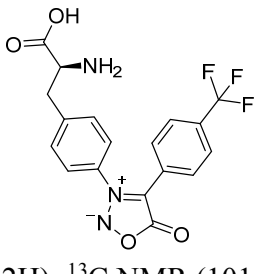
General Procedure for Palladium(II)-XPhos complex catalyzed C-H activation cross-coupling.[S7]



A flask equipped with a reflux condenser was charged with a mixture of MASyd amino acid **4c** (1.0 eq.), aryl halide (1.2 eq.), palladium acetate (5 mol%), XPhos (10 mol%) and potassium carbonate (2 eq.) in DMF (0.1-0.5 M) under an atmosphere of nitrogen and heated at 120 °C for 2 h. The reaction was allowed to cool to ambient temperature and water was added. The resulting mixture was extracted with EtOAc/PET (9/1) and the combined organic layers dried over $MgSO_4$ and concentrated in vacuo. Flash silica chromatography (eluting solvent 50% EtOAc in PET) afforded the target DASAs.

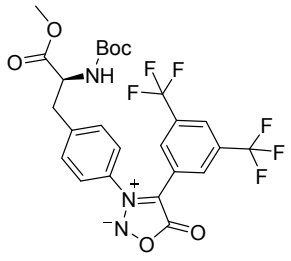


(*S*)-3-(4-(2-((*tert*-Butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) phenyl)-5-oxo-4-(4-(trifluoromethyl)phenyl)-5*H*-1,2,3-oxadiazol-3-ium -2-ide (4d): MASyd amino acid **4c** (250 mg, 0.688 mmol) and 1-bromo-4-(trifluoromethyl)benzene (186 mg, 0.826 mmol) were subjected to the general condition affording **4d** as a yellow solid (227 mg, 65%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (d, J = 8.0 Hz, 2H), 7.44-7.38 (m, 6H), 5.13 (d, J = 8.0 Hz, 1H), 4.64 (q, J = 7.0 Hz, 1H), 3.74 (s, 3H), 3.21 (ddd, J = 81.2, 13.7, 6.1 Hz, 2H), 1.41 (s, 9H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.7, 166.8, 155.1, 142.0, 133.2, 131.5, 130.3 (q, J = 33.3 Hz), 128.2, 127.1, 125.8 (q, J = 3.0 Hz), 124.9, 123.8 (q, J = 273.7 Hz), 106.5, 80.5, 54.4, 52.7, 38.7, 28.4; ^{19}FNMR (376 MHz, Chloroform-*d*) δ -62.72, -62.95. HRMS (ESI) calcd. for $C_{24}H_{25}F_3N_3O_6^+$ 508.1690 [M+H$^+$], found 508.1701.

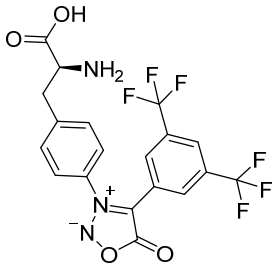


(*S*)-3-(4-(2-Amino-2-carboxyethyl)phenyl)-5-oxo-4-(4-(trifluoromethyl) phenyl)-5*H*-1,2,3-oxadiazol-3-ium-2-ide (5d): 4d (80.0 mg, 0.200 mmol) and NaOH (24.0 mg, 0.600 mmol) were subjected to the general condition as to afford **5a**, affording **5d** as a yellow solid (66.6 mg, 85% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.76 (d, J = 4 Hz, 2H), 7.71-7.63 (m, 6H), 7.43 (d, J = 8.0 Hz, 2H), 4.24 (q, J = 6.0 Hz, 1H), 3.31 (tt, J = 14.0, 7.5 Hz, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.2, 166.2, 140.2, 133.2, 131.5, 128.1 (q, J = 32.3 Hz), 127.2, 125.7, 125.5 (q, J = 4.0 Hz), 124.0 (q, J = 273.7 Hz), 123.5, 106.9, 52.9, 35.3; ^{19}F NMR

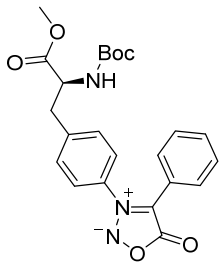
(376 MHz, Chloroform-*d*) δ -62.72, -63.00. HRMS (ESI) calcd. for $C_{18}H_{13}F_3N_3O_4^-$ 392.0864 [M-H^+], found 392.0864.



(*S*)-4-(3,5-Bis(trifluoromethyl)phenyl)-3-(4-(2-((*tert*-butoxycarbonyl)amino)-3-methoxy-3-oxopropyl)phenyl)-5-oxo-5*H*-1,2,3-oxadiazol-3-ium-2-ide (4e): MASyd amino acid **4c** (300 mg, 0.830 mmol) and 1-bromo-3,5-bis(trifluoromethyl)benzene (291 mg, 0.990 mmol) were subjected to the general condition affording **4e** as a yellow solid (282 mg, 59%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.73 (s, 3H), 7.44 (s, 4H), 5.07 (d, J = 7.8 Hz, 1H), 4.65 (t, J = 6.8 Hz, 1H), 3.75 (s, 3H), 3.26 (ddd, J = 52.0, 13.9, 6.0 Hz, 2H), 1.42 (s, 9H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.6, 166.3, 155.2, 142.6, 132.8, 132.3 (q, J = 33.3 Hz), 131.8, 126.9, 126.3 (q, J = 4.0 Hz), 124.8, 122.8 (q, J = 274.7 Hz), 121.8 (q, J = 3.5 Hz), 105.1, 80.5, 54.2, 52.7, 38.2, 28.4; ^{19}F NMR (376 MHz, Chloroform-d) δ -62.72, -63.28. HRMS (ESI) calcd. for $C_{25}H_{24}F_6N_3O_6^+$ 576.1564 [M+H^+], found 576.1567.

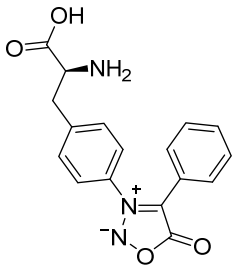


(*S*)-3-(4-(2-Amino-2-carboxyethyl)phenyl)-4-(3,5-bis(trifluoromethyl)phenyl)-5-oxo-5*H*-1,2,3-oxadiazol-3-ium-2-ide (5e): **4e** (80.0 mg, 0.140 mmol) and NaOH (16.8 mg, 0.420 mmol) were subjected to the general condition as to afford **5a** affording **5e** as a yellow solid (54.7 mg, 85% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.08 (s, 1H), 7.77 (s, 2H), 7.69-7.56 (m, 4H), 3.49 (s, 1H), 3.23 (d, J = 9.2 Hz, 1H), 3.04-2.98 (m, 1H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 169.1, 166.0, 143.2, 132.1, 131.2, 130.5 (q, J = 33.2 Hz), 127.5, 126.8 (q, J = 4.5 Hz), 125.3, 122.8 (q, J = 273.3 Hz), 121.6, 106.5, 55.1, 36.7; ^{19}F NMR (376 MHz, DMSO-d_6) δ -62.72, -63.50. HRMS (ESI) calcd. for $C_{19}H_{12}F_6N_3O_4^-$ 460.0737 [M-H^-], found 460.0765.



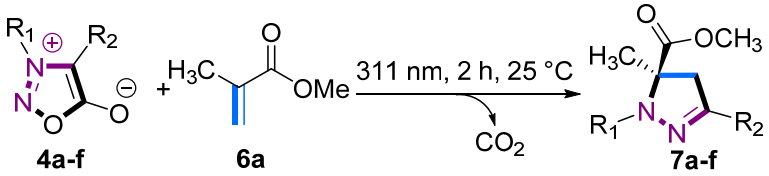
(*S*)-3-(4-(2-((*tert*-Butoxycarbonyl)amino)-3-methoxy-3-oxopropyl)phenyl)-5-oxo-4-phenyl-5*H*-1,2,3-oxadiazol-3-ium-2-ide (4f): MASyd amino acid **4c** (200 mg, 0.551 mmol) and bromobenzene (104 mg, 0.661 mmol) were subjected to the general condition affording **4f** as a yellow solid (145 mg, 60%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43-7.34 (m, 4H), 7.28 (d, J = 4 Hz, 5H), 5.13 (d, J = 8.0 Hz, 1H), 4.64 (q, J = 6.9 Hz, 1H), 3.73 (s, 3H), 3.20 (ddd, J = 63.1, 14.0, 6.1 Hz, 2H), 1.42 (s, 9H); ^{13}C NMR (101

MHz, Chloroform-*d*) δ 171.8, 167.2, 155.1, 141.4, 133.5, 131.1, 128.9, 128.8, 127.5, 124.9, 124.5, 107.9, 80.4, 54.3, 52.6, 38.5, 28.4. HRMS (ESI) calcd. for $C_{23}H_{26}N_3O_6^+$ 440.1816 [M+H$^+$], found 440.1810.



(*S*)-3-(4-(2-Amino-2-carboxyethyl)phenyl)-4-(3,5-bis(trifluoromethyl) phenyl)-5-oxo-5*H*-1,2,3-oxadiazol-3-ium-2-ide (5f): 4f (80.0 mg, 0.180 mmol) and NaOH (21.6 mg, 0.540 mmol) were subjected to the general condition as to afford **5a** affording **5f** as a yellow solid (49.6 mg, 85% yield). ^{1}H NMR (400 MHz, Methanol-*d*$_4$) δ 7.60 (s, 4H), 7.31 (d, J = 4.2 Hz, 5H), 4.36 (d, J = 6.8 Hz, 1H), 3.40 (d, J = 8.7 Hz, 2H); ^{13}C NMR (101 MHz, Methanol-*d*$_4$) δ 175.1, 169.2, 140.9, 135.2, 132.5, 130.0, 129.8, 129.0, 126.9, 125.6, 109.9, 36.9. HRMS (ESI) calcd. for $C_{17}H_{14}N_3O_4^-$ 324.0990 [M-H$^-$], found 324.1004.

Scheme S5. Photo-induced cycloaddition of DASyd amino acids with MMA.



4a/7a: R_1 = *p*-MeOPh; R_2 = Boc-L-Phe-Ome
4b/7b: R_1 = *p*-FPh; R_2 = Boc-L-Phe-Ome
4d/7d: R_1 = Boc-L-Phe-Ome; R_2 = *p*-CF_3Ph
4e/7e: R_1 = Boc-L-Phe-Ome; R_2 = *m*-2CF_3Ph
4f/7f : R_1 = Boc-L-Phe-Ome; R_2 = Ph

General Conditions: A stirred solution of DASyd amino acids and MMA (20 eq.) in EtOAc was irradiated with 311 nm UV lamp (10.8 mW/cm^2) in quartz test tubes at room temperature for 2 h. The solvent was then evaporated, and the residue was purified by silica gel flash chromatography to give the cycloaddition products.

Pyis 7a: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 7.08-7.04 (m, 2H), 6.85-6.81 (m, 2H), 5.00 (d, J = 8.0 Hz, 1H), 4.60 (q, J = 6.4 Hz, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 3.73 (s, 3H), 3.67 (dd, J = 16.0, 1.2 Hz, 1H), 3.24 (dd, J = 16.0, 1.8 Hz, 1H), 3.11 (qd, J = 13.5, 5.7 Hz, 2H), 1.54 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.3, 172.3, 155.2, 154.6, 145.1, 137.7, 136.7, 131.4, 129.6, 125.9, 117.9, 114.5, 80.1, 70.3, 55.7, 54.5, 53.0, 52.4, 47.8, 38.3, 28.4, 21.3. HRMS (ESI) calcd. for $C_{28}H_{36}N_3O_7^+$ 526.2548 [M+H$^+$], found 526.2556.

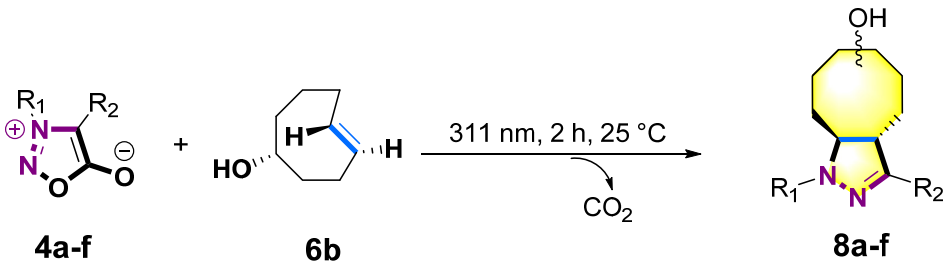
Pyis 7b: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62-7.60 (m, 2H), 7.15 (d, J = 8.0 Hz, 2H), 7.07-7.03 (m, 2H), 6.99-6.93 (m, 2H), 5.01 (d, J = 8.0 Hz, 1H), 4.60 (q, J = 7.2, 6.6 Hz, 1H), 3.76 (s, 3H), 3.72 (s, 3H), 3.71-3.66 (m, 1H), 3.27 (dd, J = 16.7, 1.9 Hz, 1H), 3.12 (qd, J = 13.7, 6.1 Hz, 2H), 1.58 (s, 3H), 1.42 (s, 9H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.1, 172.3, 158.8 (d, J = 240.4 Hz), 155.2, 145.5, 140.0 (d, J = 2 Hz), 137.0, 131.1, 129.7, 126.0, 116.8 (d, J = 8 Hz), 115.7 (d, J = 22.2 Hz), 80.2, 69.8, 54.5, 53.1, 52.5, 48.1, 38.3, 28.4, 21.3; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.72, -123.84. HRMS (ESI) calcd. for $C_{27}H_{33}FN_3O_6^+$ 514.2348 [M+H$^+$], found 514.2358.

Pyis 7d: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (d, J = 8.0 Hz, 2H), 7.63 (d, J = 8.0 Hz, 2H), 7.06-7.00 (m, 4H), 4.97 (d, J = 8.0 Hz, 1H), 4.55 (q, J = 6.6 Hz, 1H), 3.77 (s, 3H), 3.72 (s, 3H), 3.69 (d, J = 9.9 Hz, 1H), 3.29 (d, J = 16.8 Hz, 1H), 3.03 (tq, J = 13.4, 8.1, 7.4 Hz, 2H), 1.66 (s, 3H), 1.42 (s, 9H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.9, 172.6, 155.3, 143.6, 141.9, 135.8, 130.2 (q, J = 32.3 Hz), 130.2, 128.2, 125.8, 125.7 (q, J = 3.0 Hz), 124.2 (q, J = 272.7 Hz), 115.0, 80.0, 69.5, 54.6, 53.3, 52.3, 47.9, 37.6, 28.5, 21.4; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.72, -62.84. HRMS (ESI) calcd. for $C_{28}H_{33}F_3N_3O_6^+$ 564.2316 [M+H$^+$], found 564.2331.

Pyis 7e: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (d, J = 1.6 Hz, 2H), 7.79 (s, 1H), 7.07-7.02 (m, 4H), 4.98 (d, J = 8.0 Hz, 1H), 4.58-4.53 (m, 1H), 3.78 (s, 3H), 3.76 (d, J = 7.5 Hz, 1H), 3.73 (s, 3H), 3.32 (d, J = 16.7 Hz, 1H), 3.09-2.99 (m, 2H), 1.69 (s, J = 1.8 Hz, 3H), 1.43 (s, 9H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.5, 172.5, 155.3, 142.1, 141.5, 134.6, 132.2 (q, J = 33.3 Hz), 130.3, 128.7, 125.2, 123.3 (q, J = 273.7 Hz), 121.6, 115.2, 80.1, 69.8, 54.6, 53.3, 52.4, 47.6, 37.6, 28.5, 21.6; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.72, -63.02. HRMS (ESI) calcd. for $C_{29}H_{32}F_6N_3O_6^+$ 632.2190 [M+H$^+$], found 632.2196.

Pyis 7f: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70-7.68 (m, 2H), 7.42-7.35 (m, 3H), 7.05-6.99 (m, 4H), 4.97 (d, J = 8.0 Hz, 1H), 4.54 (q, J = 6.7 Hz, 1H), 3.76 (s, 3H), 3.72 (s, 3H), 3.68 (d, J = 4.9 Hz, 1H), 3.29 (d, J = 16.7 Hz, 1H), 3.02 (q, J = 5.6, 4.3 Hz, 2H), 1.63 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.3, 172.6, 155.3, 145.3, 142.4, 132.3, 130.1, 128.9, 128.7, 127.5, 125.8, 114.8, 80.0, 69.1, 54.6, 53.1, 52.3, 48.2, 37.6, 28.5, 21.2. HRMS (ESI) calcd. for $C_{27}H_{34}N_3O_6^+$ 496.2442 [M+H$^+$], found 496.2449.

Scheme S6. Photo-induced cycloaddition of DASyd amino acids with TCO



4a/8a: R_1 = *p*-MeOPh; R_2 = Boc-L-Phe-Ome
4b/8b: R_1 = *p*-FPh; R_2 = Boc-L-Phe-Ome
4d/8d: R_1 = Boc-L-Phe-Ome; R_2 = *p*-CF_3Ph
4e/8e: R_1 = Boc-L-Phe-Ome; R_2 = *m*-2CF_3Ph
4f/8f : R_1 = Boc-L-Phe-Ome; R_2 = Ph

General Condition: A stirred solution of DASyd amino acids and TCO (5.0 eq) in 50 mL EtOAc was irradiated with 311 nm UV lamp (10.8 mW/cm^2) in quartz test tubes at room temperature for 2 h. The solvent was then evaporated, and the residue was purified by silica gel flash chromatography to give the cycloaddition products. The TCO we used was the equatorial isomer, assigned as rel-(1R-4E-pR). The Pyis products contain a pair of regioisomers which couldn't be separated on TLC, therefore the NMR we collected were both the mixture of a pair of regioisomers.

Pyis 8a: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.57 (d, J = 8.0 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.11 (d, J = 8.0 Hz, 4H), 6.87 (d, J = 8.0 Hz, 2H), 5.04 (d, J = 8.0 Hz, 1H), 4.58 (dq, J = 11.4, 6.0 Hz, 1H), 4.12-3.90 (m, 2H), 3.77 (s, 3H), 3.71-3.70 (d, J = 4.0 Hz, 3H), 3.62-3.41 (m, 1H), 3.07 (dq, J = 14.9, 9.2, 7.3 Hz, 2H), 2.62-2.36 (m, 2H), 2.31-2.05 (m, 3H), 1.97-1.78 (m, 3H), 1.67 (ddd, J = 27.8, 13.8, 7.0 Hz, 3H), 1.41 (s, 9H). HRMS (ESI) calcd. for $C_{31}H_{42}N_3O_6^+$ 552.3068, found 552.3072. The ratio of the mixture of a pair of regioisomers was 0.99:1.03.

Pyis 8b: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.10 (dd, J = 16.4, 7.0 Hz, 4H), 6.98 (t, J = 8.5 Hz, 2H), 5.02 (d, J = 8.0 Hz, 1H), 4.59 (d, J = 8.0 Hz, 1H), 4.11-3.85 (m, 2H), 3.72-3.71 (d, J = 4.0 Hz, 3H), 3.65-3.43 (m, 1H), 3.09 (d, J = 18.3 Hz, 2H), 2.33 (ddd, J = 111.9, 36.8, 17.3 Hz, 3H), 2.02 (d, J = 10.5 Hz, 2H), 1.89 (s, 3H), 1.61 (d, J = 11.7 Hz, 3H), 1.41 (s, 9H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.72, -125.17, -125.27. HRMS (ESI) calcd. for $C_{30}H_{39}FN_3O_5^+$ 540.2868 [M+H$^+$], found 540.2875. The ratio of the mixture of a pair of regioisomers was 1.00:0.99.

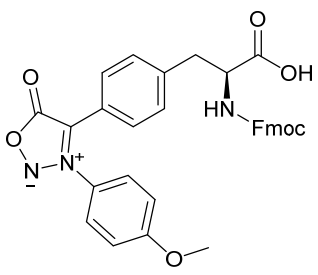
Pyis 8d: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, J = 8.1 Hz, 1H), 7.73 (d, J = 8.1 Hz, 1H), 7.61 (d, J = 8.1 Hz, 2H), 7.08 (dt, J = 16.2, 8.2 Hz, 4H), 5.00 (d, J = 8.0 Hz, 1H), 4.56 (h, J = 4.8 Hz, 1H), 4.19-3.96 (m, 2H), 3.75-3.74 (d, J = 4 Hz, 3H), 3.70-3.44 (m, 1H), 3.04 (d, J = 6.3 Hz, 2H), 2.57 (dtd, J = 55.9, 11.0, 10.6, 5.4 Hz, 2H), 2.23 (dtt, J = 28.4, 15.1, 3.9 Hz, 2H), 1.97 (ddd, J = 22.0, 7.4, 3.6 Hz, 2H), 1.80-1.58 (m, 5H), 1.43 (s, 9H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.58, -62.72, -62.86. HRMS (ESI) calcd. for $C_{31}H_{39}F_3N_3O_5^+$ 590.2836 [M+H$^+$], found 590.2845. The ratio of the mixture of a pair of regioisomers was 1.00:1.03.

Pyis 8e: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (s, 1H), 8.02 (s, 1H), 7.76 (s, 1H), 7.17-7.01 (m, 4H), 5.02 (d, J = 8.4 Hz, 1H), 4.56 (dq, J = 10.0, 5.4 Hz, 1H), 4.32-3.98 (m, 2H), 3.75-3.74 (d, J = 4 Hz, 3H), 3.71-3.46 (m, 1H), 3.06 (qt, J = 12.8, 6.9 Hz, 2H), 2.81-2.36 (m, 2H), 2.33-2.11 (m, 2H), 2.01 (dddd, J = 27.3, 14.7, 7.0, 3.6 Hz, 3H), 1.85-1.52 (m, 4H), 1.43 (s, 9H); ^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.72, -62.96 (d, J = 3.5 Hz). HRMS (ESI) calcd. for $C_{32}H_{38}F_6N_3O_5^+$ 658.2710 [M+H$^+$], found 658.2731. The ratio of the mixture of a pair of regioisomers was 0.90:1.00.

Pyis 8f: ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.66 (d, J = 6.6 Hz, 1H), 7.62 (d, J = 7.1 Hz, 1H), 7.37 (t, J = 7.7 Hz, 2H), 7.33-7.28 (m, 1H), 7.12-7.00 (m, 4H), 5.01 (d, J = 8.3 Hz, 1H), 4.54 (h, J = 5.0 Hz, 1H), 4.14-3.87 (m, 2H), 3.74-3.73 (d, J = 4 Hz, 3H), 3.71-3.42 (m, 1H), 3.03 (d, J = 5.5 Hz, 2H), 2.66-2.40 (m, 2H), 2.33-2.08 (m, 2H), 2.03-1.88 (m, 3H), 1.81-1.55 (m, 4H), 1.43 (s, 9H). HRMS (ESI) calcd. for $C_{30}H_{40}N_3O_5^+$ 522.2962 [M+H$^+$], found 522.2979. The ratio of the mixture of a pair of regioisomers was 0.98:1.00.

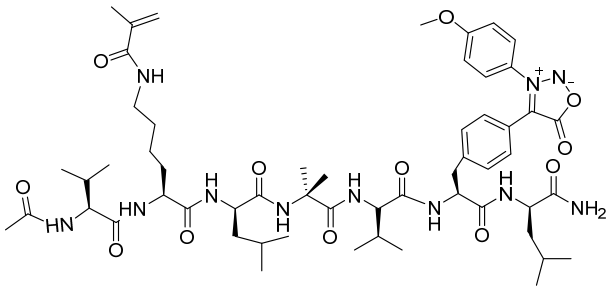
Scheme S7. Peptide Synthesis

The peptides **P1** and **P3** were synthesized by the company of GL Biochem.

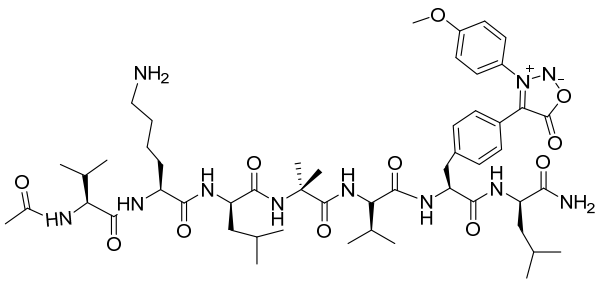


Fmoc-5a: To a solution of DASA **5a** (600 mg, 1.69 mmol) in 1,4-dioxane (5 mL) was added 9-fluorenylmethyl chloroformate (437 mg, 1.69 mmol) and K_2CO_3 (467 mg, 3.38 mmol) and stirred at room temperature. After 2 h of stirring, saturated sodium bicarbonate solution and H_2O were added and the resulting solution was washed with diethyl ether. The aqueous phase was acidified to pH 1 with 1 M HCl and extracted with diethyl ether. The organic phase was washed with 1 M HCl, H_2O, brine, dried over $MgSO_4$. The filtrate was evaporated under reduced

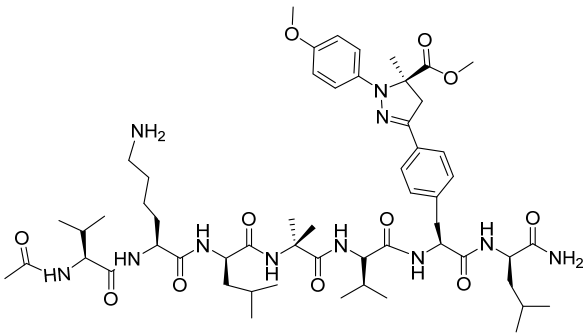
pressure to give yellow solid as crude product (829 mg, 85%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.87 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 8.0 Hz, 1H), 7.64-7.55 (m, 4H), 7.40 (t, J = 8.0 Hz, 2H), 7.31-7.09 (m, 8H), 4.22-4.12 (m, 4H), 3.80 (s, 3H), 3.07-2.82 (m, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 173.2, 166.4, 161.6, 155.9, 143.8, 143.7, 140.7, 138.6, 129.3, 127.6, 127.0, 126.9, 125.3, 125.2, 122.8, 120.1, 115.1, 107.9, 65.6, 55.8, 55.0, 46.6, 36.0. HRMS (ESI) calcd. for $C_{33}H_{26}N_3O_7^-$ 576.1776 [M+H$^+$], found 576.1780.



Peptide P1: ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.22 (d, J = 5.8 Hz, 1H), 8.00 (s, 1H), 7.85 (dd, J = 17.3, 7.7 Hz, 2H), 7.75 (d, J = 6.0 Hz, 1H), 7.48 (d, J = 8.7 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 8.6 Hz, 2H), 5.67 (s, 1H), 5.34 (s, 1H), 4.42-4.36 (m, 2H), 4.18-4.12 (m, 2H), 3.95 (d, J = 6.6 Hz, 1H), 3.89 (s, 3H), 3.76 (t, J = 5.9 Hz, 1H), 3.23 (dt, J = 9.9, 5.6 Hz, 4H), 3.06 (dd, J = 14.0, 10.6 Hz, 2H), 2.07 (s, 3H), 1.92 (s, 3H), 1.78-1.54 (m, 12H), 1.47 (d, J = 15.5 Hz, 6H), 1.04-0.87 (m, 21H), 0.76 (d, J = 6.8 Hz, 3H). HRMS (ESI) calcd. for $C_{56}H_{84}N_{11}O_{12}^+$ 1102.6295 [M+H$^+$], found 1102.6301.

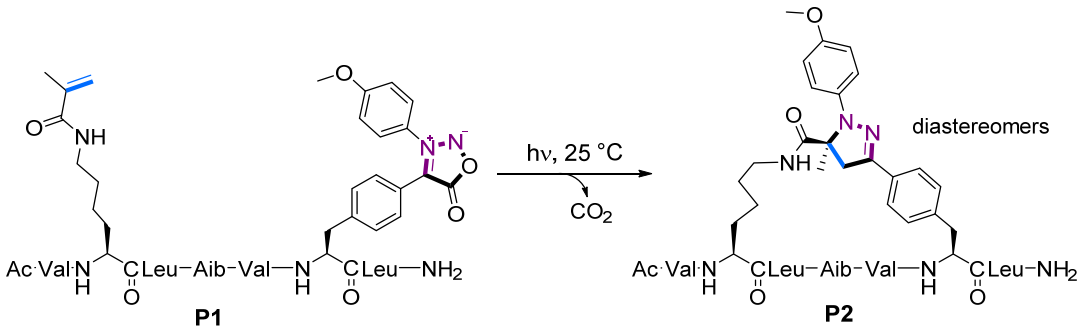


Peptide P3: ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.35 (d, J = 6.4 Hz, 1H), 8.30 (d, J = 5.4 Hz, 1H), 8.14 (s, 1H), 7.93 (d, J = 7.2 Hz, 1H), 7.85 (dd, J = 12.2, 7.2 Hz, 2H), 7.50-7.47 (m, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.28-7.20 (m, 2H), 7.16-7.09 (m, 2H), 4.49-4.17 (m, 4H), 3.93 (d, J = 6.6 Hz, 1H), 3.90 (d, J = 1.1 Hz, 3H), 3.81 (t, J = 5.7 Hz, 1H), 3.22 (dd, J = 14.0, 4.5 Hz, 1H), 3.13-2.85 (m, 3H), 2.66 (d, J = 1.1 Hz, 2H), 2.06 (s, 5H), 1.95-1.53 (m, 12H), 1.46 (d, J = 21.6 Hz, 6H), 1.04-0.85 (m, 21H), 0.75 (d, J = 6.7 Hz, 3H). HRMS (ESI) calcd. for $C_{52}H_{80}N_{11}O_{11}^+$ 1034.6033 [M+H$^+$], found 1034.6041.



Peptide P4: A stirred solution of 5.00 mg of peptide **P3** (150 μM) and MMA (50 eq.) in ACN was irradiated with 311 nm UV lamp (10.8 mW/cm^2) in quartz test tubes at room temperature for 1 h under argon. After purification, a white solid was obtained in 35% yield. ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.33 (s, 2H), 7.64 (d, J = 8.1 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.08-6.99 (m, 2H), 6.89-6.82 (m, 2H), 4.54 (dd, J = 10.6, 4.5 Hz, 1H), 4.40 (dd, J = 10.6, 4.1 Hz, 1H), 4.35-4.22 (m, 2H), 3.95 (dd, J = 7.3, 2.7 Hz, 1H), 3.86 (dd, J = 6.5, 4.9 Hz, 1H), 3.76 (d, J = 4.4 Hz, 6H), 3.68 (d, J = 16.9 Hz, 1H), 3.36 (d, J = 2.4 Hz, 1H), 3.27 (s, 1H), 3.09 (t, J = 12.8 Hz, 1H), 2.89 (td, J = 7.5, 4.6 Hz, 2H), 2.03 (s, 5H), 1.87-1.61 (m, 10H), 1.52-1.41 (m, 11H), 1.02-0.76 (m, 24H). HRMS (ESI) calcd. for $C_{56}H_{88}N_{11}O_{11}^+$ 1090.6659 [M+H$^+$], found 1090.6674.

Scheme S8. Cyclization of peptide



A stirred solution of 5 mg of peptide **P1** (150 μM) in ACN/PB (1/1) was irradiated with 311 nm UV lamp (10.8 mW/cm^2) in quartz test tubes at room temperature for 2 h under argon. The cyclic peptide contain a pair of diastereomers which could be separated. The crude peptide was purified with preparative reverse-phase HPLC affording cyclic peptide as a white powder in 66% yield, and the identity of peptide was confirmed by LC-MS: MS (ESI) calcd. $C_{55}H_{84}N_{11}O_{10}^+$ 1058.64 [M+H$^+$], found 1058.63.

Peptide P2-1: ^{1}H NMR (400 MHz, Methanol-d_4) δ 7.66-7.61 (m, 2H), 7.56 (dd, J = 7.9, 3.6 Hz, 1H), 7.26 (d, J = 8.2 Hz, 2H), 7.08-7.02 (m, 2H), 6.89-6.85 (m, 2H), 4.79-4.68 (m, 1H), 4.62 (s,

1H), 4.46-4.40 (m, 1H), 3.90 (t, J = 6.7 Hz, 1H), 3.83 (d, J = 6.3 Hz, 2H), 3.76 (s, 3H), 3.74-3.65 (m, 1H), 3.59-3.51 (m, 2H), 3.44 (dd, J = 16.2, 3.7 Hz, 1H), 3.37 (d, J = 17.7 Hz, 1H), 3.19 (dd, J = 16.2, 12.8 Hz, 1H), 3.04-2.94 (m, 1H), 2.21-2.11 (m, 1H), 2.03 (s, 4H), 1.86-1.55 (m, 8H), 1.47 (dd, J = 8.2, 5.7 Hz, 2H), 1.41 (d, J = 14.3 Hz, 9H), 1.05-0.92 (m, 21H), 0.88 (d, J = 6.4 Hz, 3H). HRMS (ESI) calcd. for $C_{55}H_{84}N_{11}O_{10}^+$ 1058.6397 [M+H$^+$], found 1058.6403.

Peptide P2-2: ^{1}H NMR (400 MHz, Methanol-d_4) δ 8.32 (dd, J = 7.3, 4.6 Hz, 1H), 7.67 (d, J = 8.1 Hz, 2H), 7.46 (d, J = 8.1 Hz, 2H), 7.07-7.03 (m, 2H), 6.87-6.83 (m, 2H), 4.67-4.60 (m, 2H), 4.47 -4.41 (m, 1H), 4.24 (dd, J = 10.4, 4.8 Hz, 1H), 3.86 (dd, J = 9.5, 4.8 Hz, 1H), 3.80 (d, J = 6.2 Hz, 1H), 3.76 (s, 4H), 3.68 (dd, J = 5.2, 3.3 Hz, 1H), 3.57-3.50 (m, 1H), 3.47-3.35 (m, 2H), 3.02-2.86 (m, 2H), 2.10 (s, 3H), 2.07-2.00 (m, 1H), 1.92-1.62 (m, 10H), 1.52 (s, 1H), 1.45 (d, J = 5.5 Hz, 6H), 1.32 (s, 3H), 1.08-0.92 (m, 18H), 0.70 (dd, J = 6.9, 3.1 Hz, 6H). HRMS (ESI) calcd. for $C_{55}H_{84}N_{11}O_{10}^+$ 1058.6397 [M+H$^+$], found 1058.6411.

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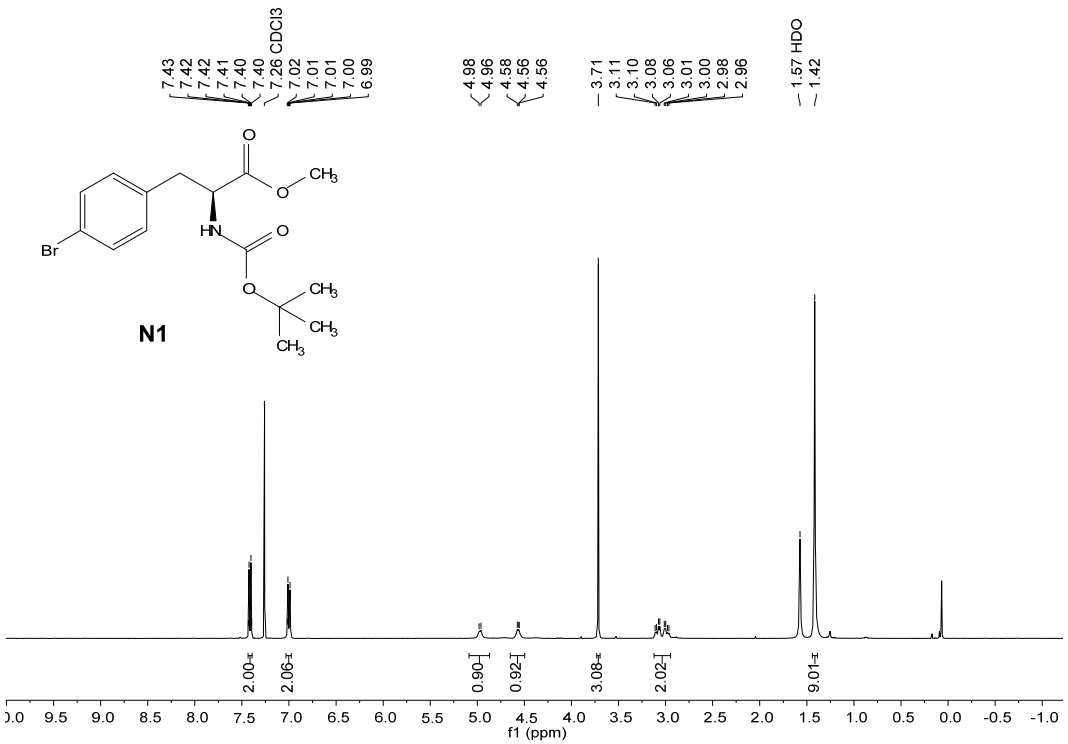
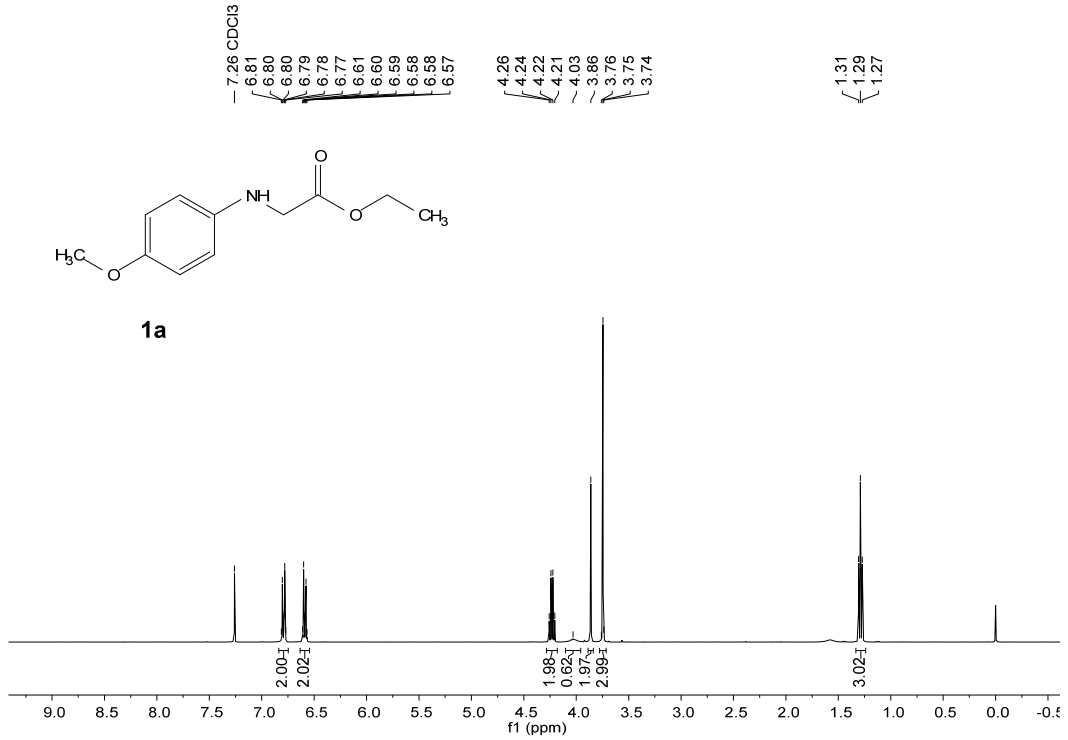
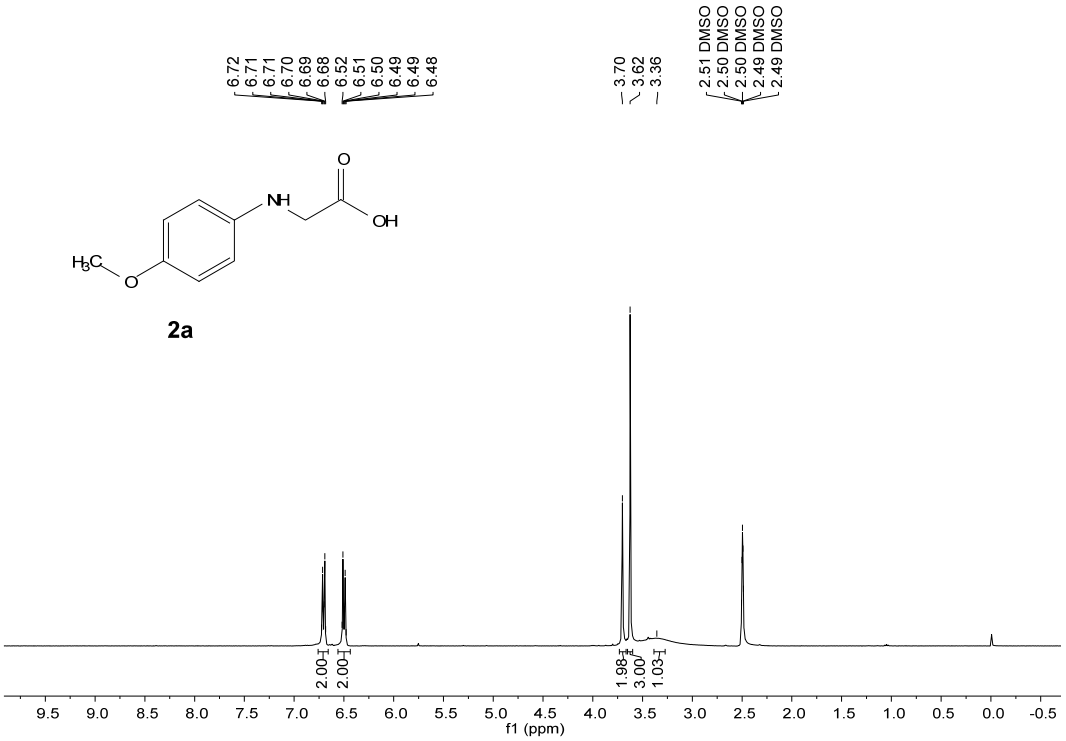
^{1}H, ^{19}F and ^{13}C NMR Spectra



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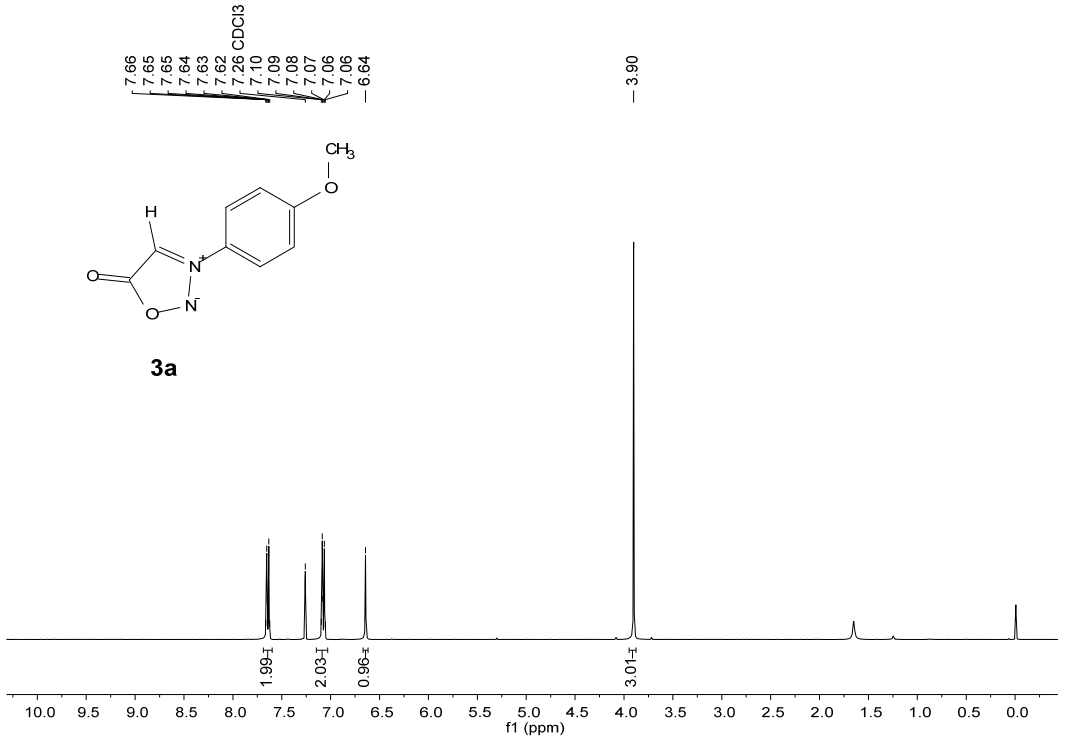
f1 (ppm)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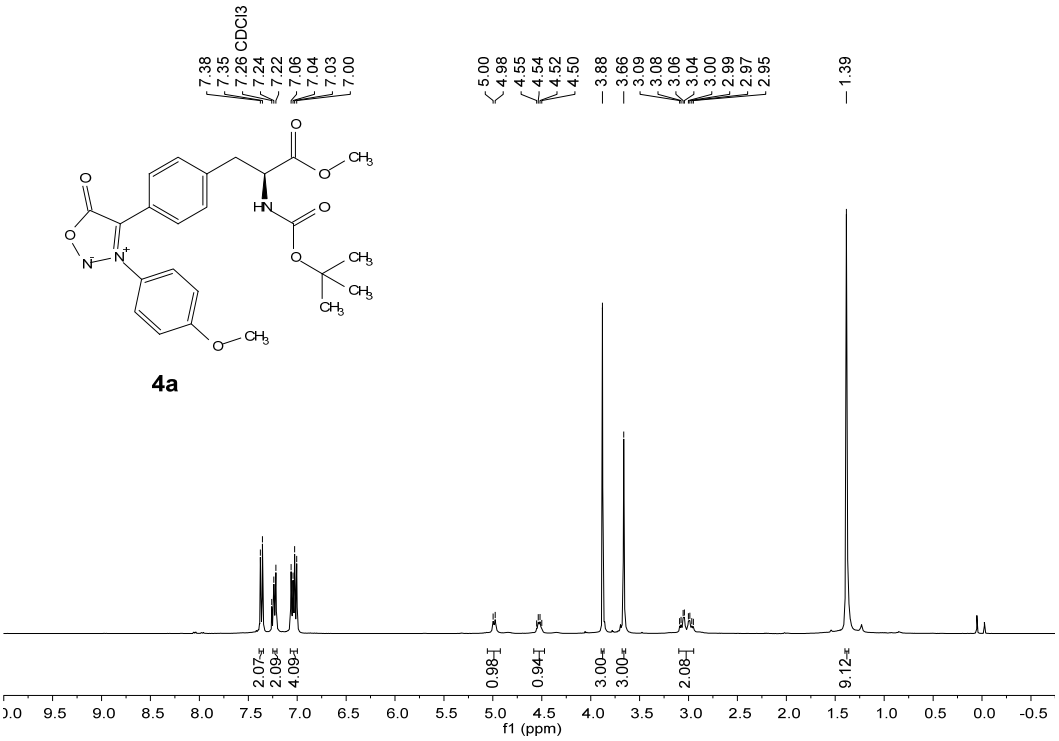
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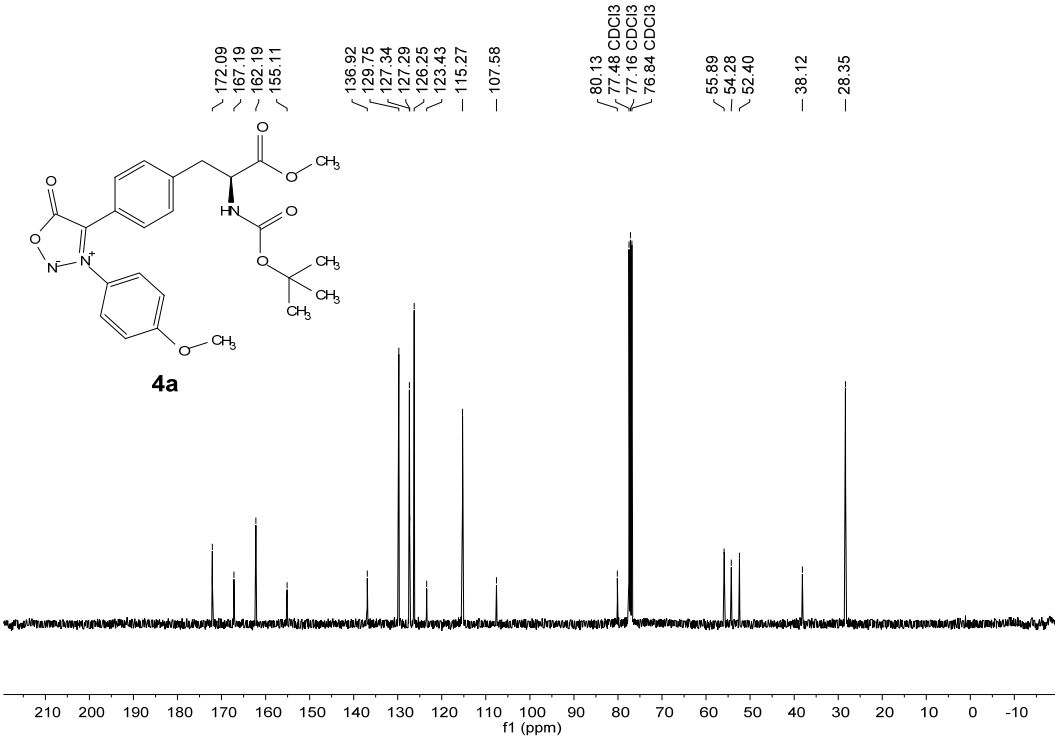
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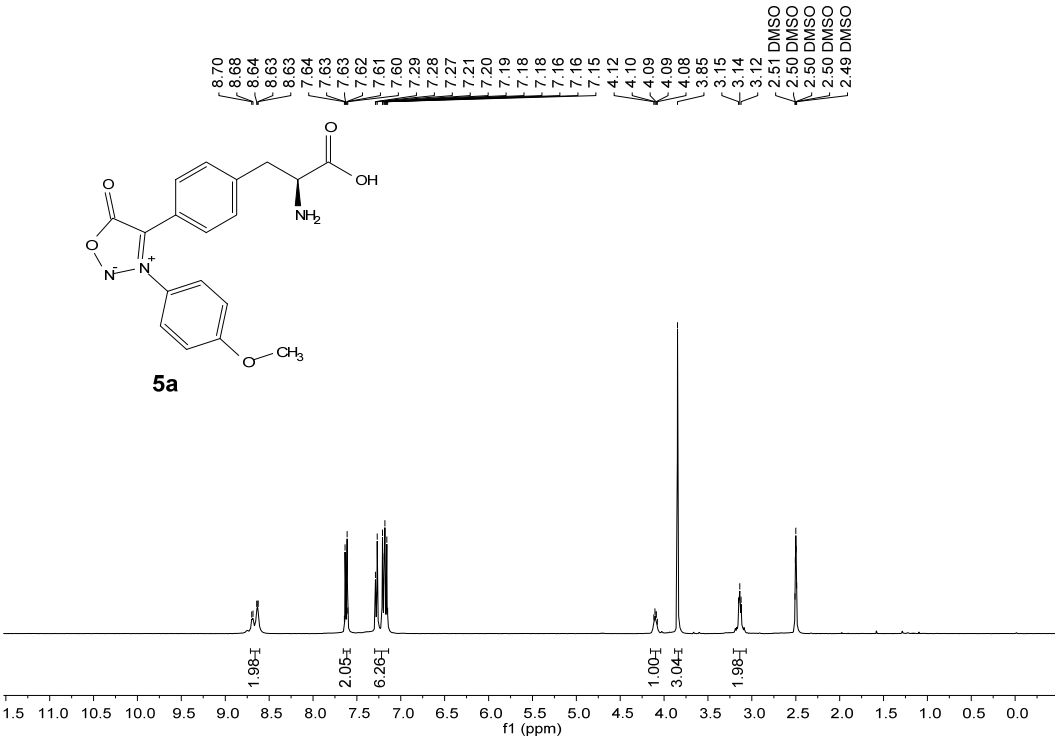
4a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N+
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CH3
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2.05
6.26
1.00
3.04
1.98
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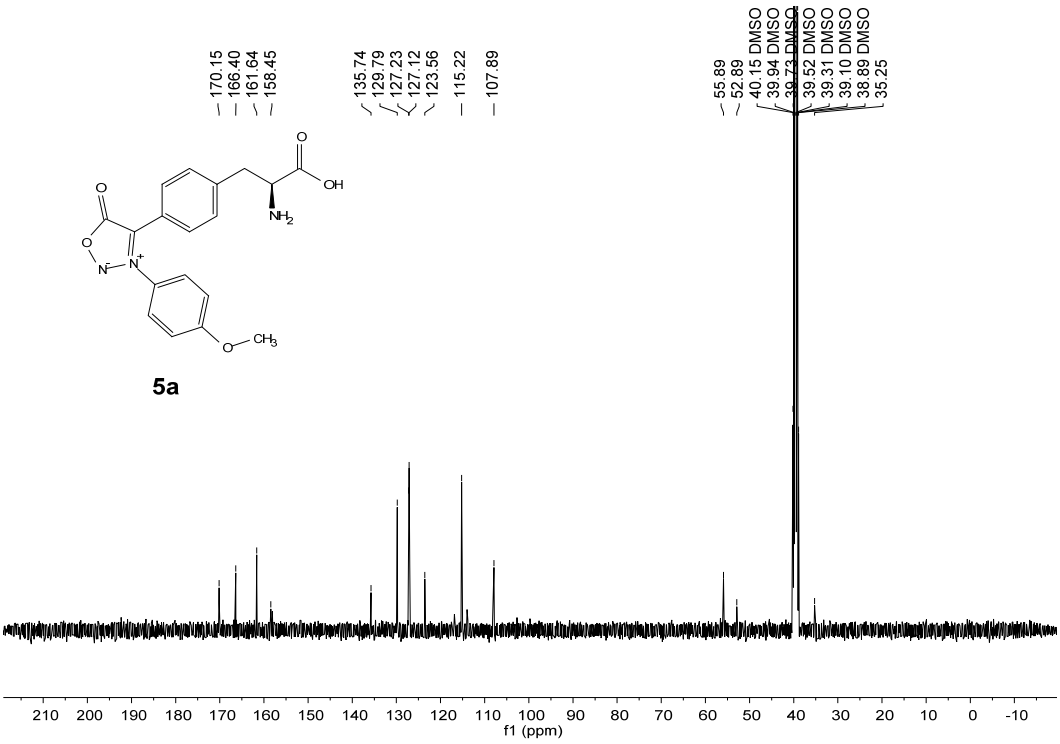
f1 (ppm)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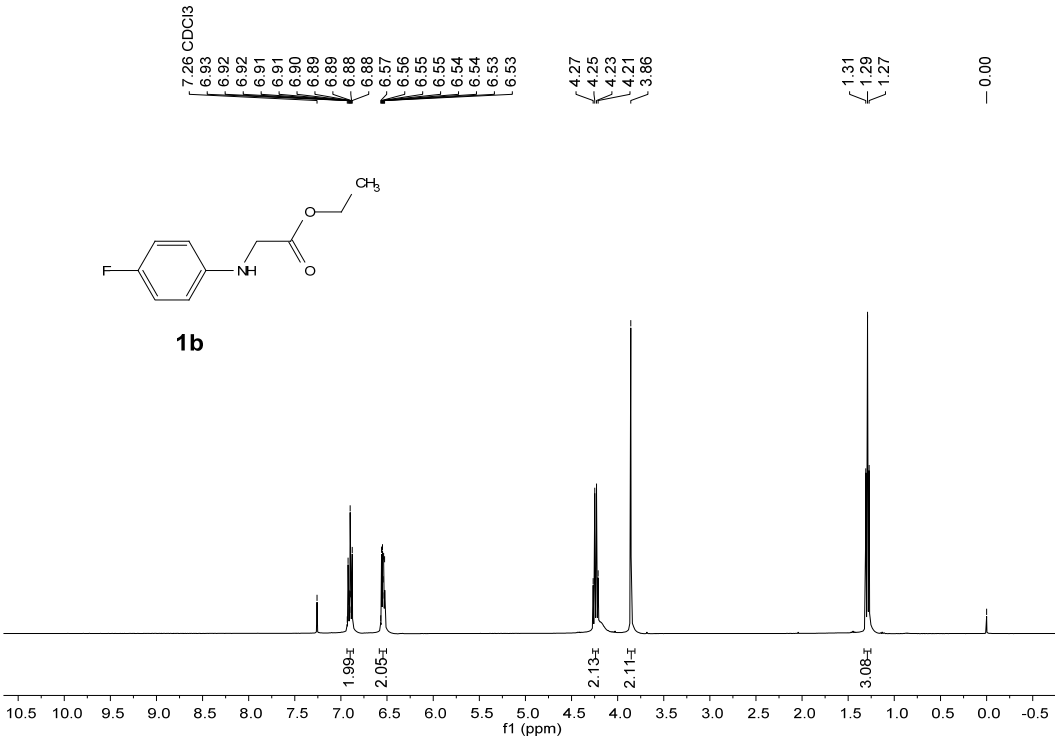
f1 (ppm)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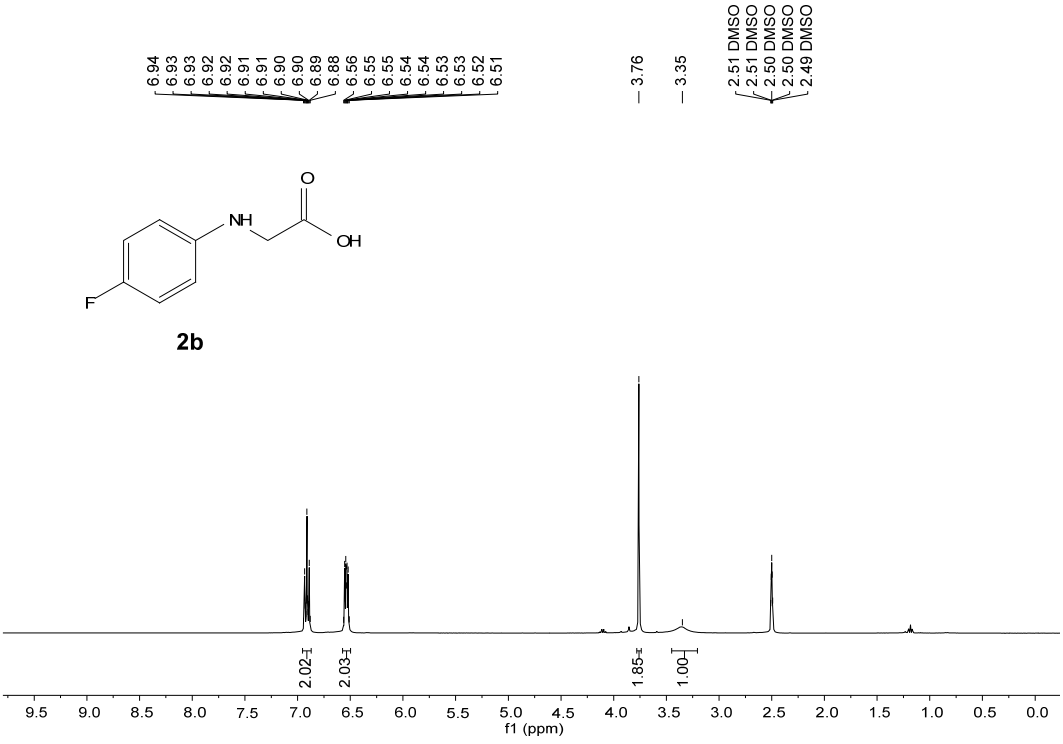
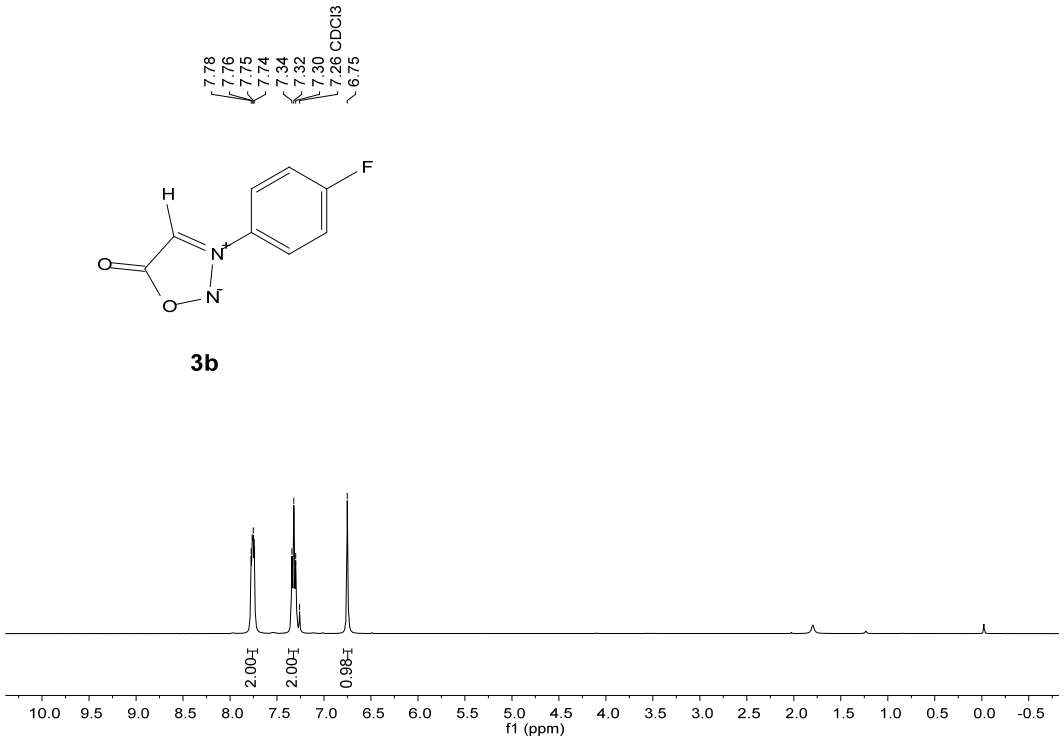
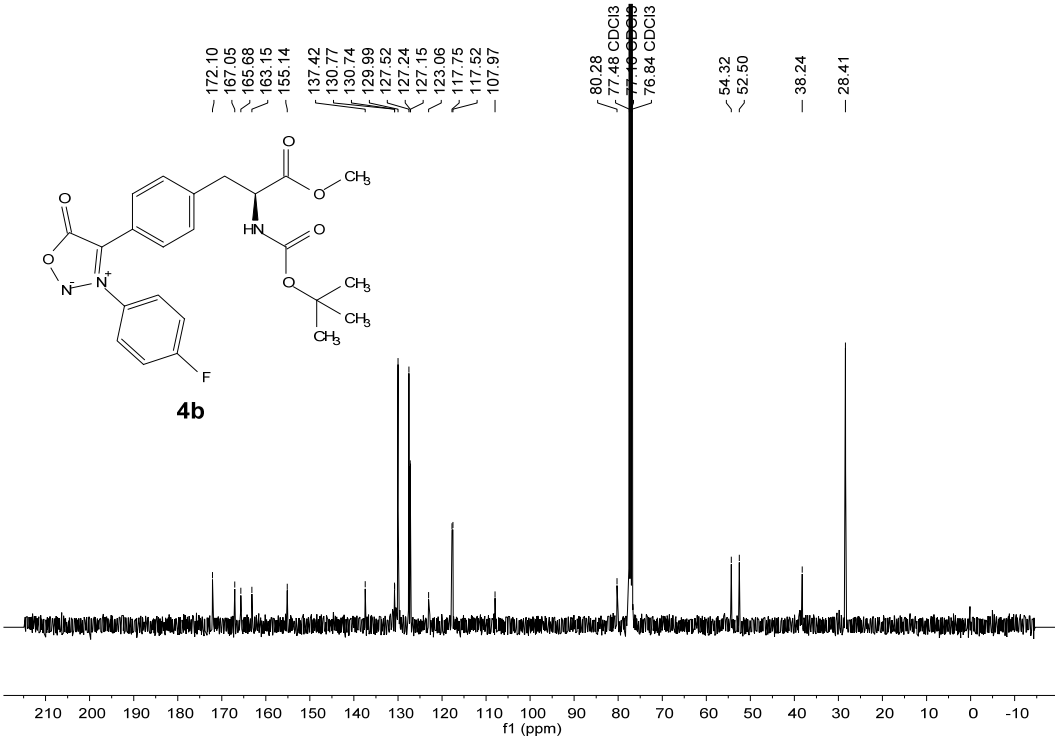
6.54
6.53
6.53
4.27
4.25
4.23
4.21
3.86
1.31
1.29
1.27
0.00
CH3
O
O
F
NH
O
1b
1.99
2.05
2.13
2.11
3.08
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

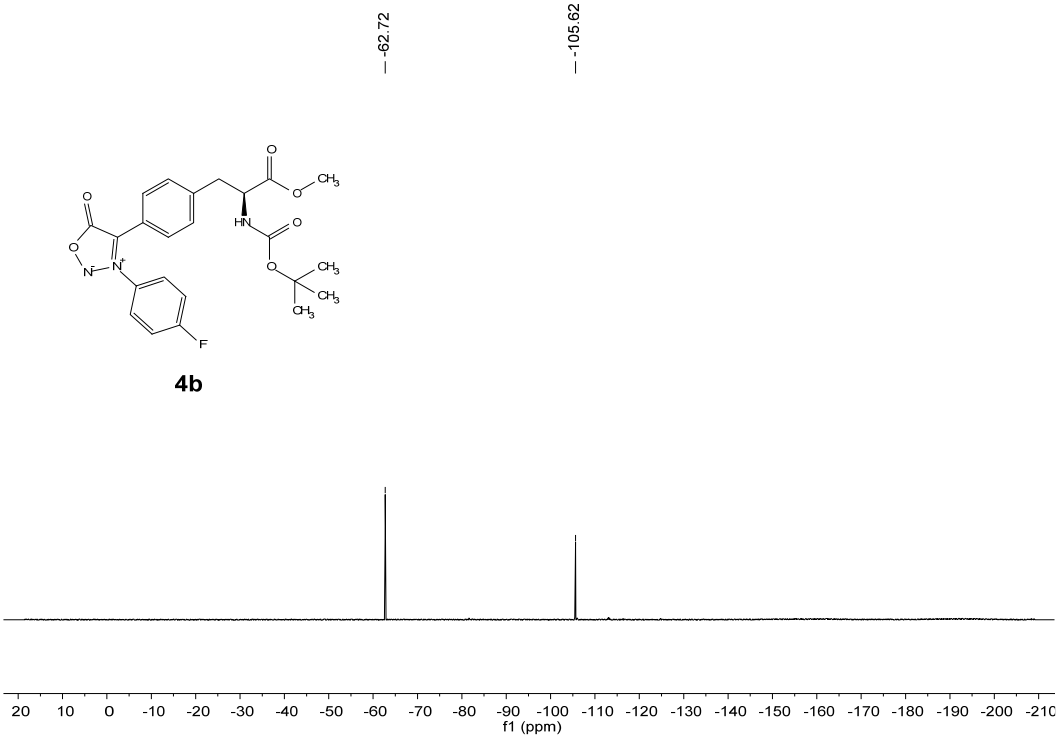

6.94
6.93
6.93
6.92
6.92
6.91
6.91
6.90
6.90
6.89
6.88
6.56
6.55
6.55
6.54
6.54
6.53
6.53
6.52
6.51
3.76
3.35
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.50 DMSO
2.49 DMSO
O
NH
OH
F
2b
2.02
2.03
1.85
1.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

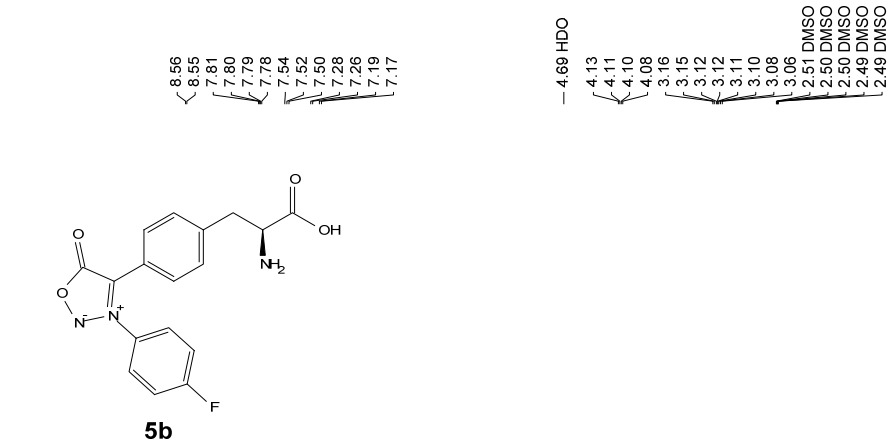

7.78
7.76
7.75
7.74
7.34
7.32
7.30
7.26 CDCl3
6.75
F
H
O
N+
O
N-
2.00
2.00
0.98
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
7.52
7.51
7.49
7.48
7.30
7.28
7.27
7.26 CDCl3
7.24
7.22
7.10
7.08
4.98
4.96
4.58
4.57
4.55
4.53
3.70
3.13
3.12
3.10
3.08
3.03
3.01
2.99
2.98
1.41
-0.00
O
O
O
CH3
HN
O
O
CH3
CH3
CH3
O
N-
N+
F
2.04
4.25
1.93
0.79
0.83
3.00
2.00
9.16
0.5 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 -0.5 -1.0
f1 (ppm)

3b

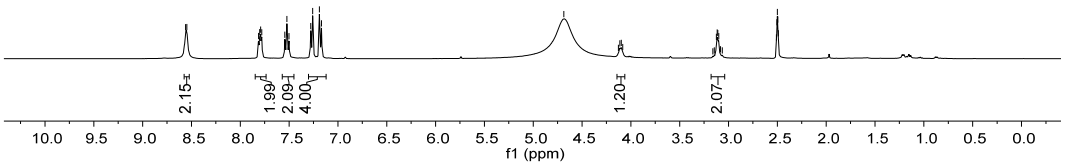
4b

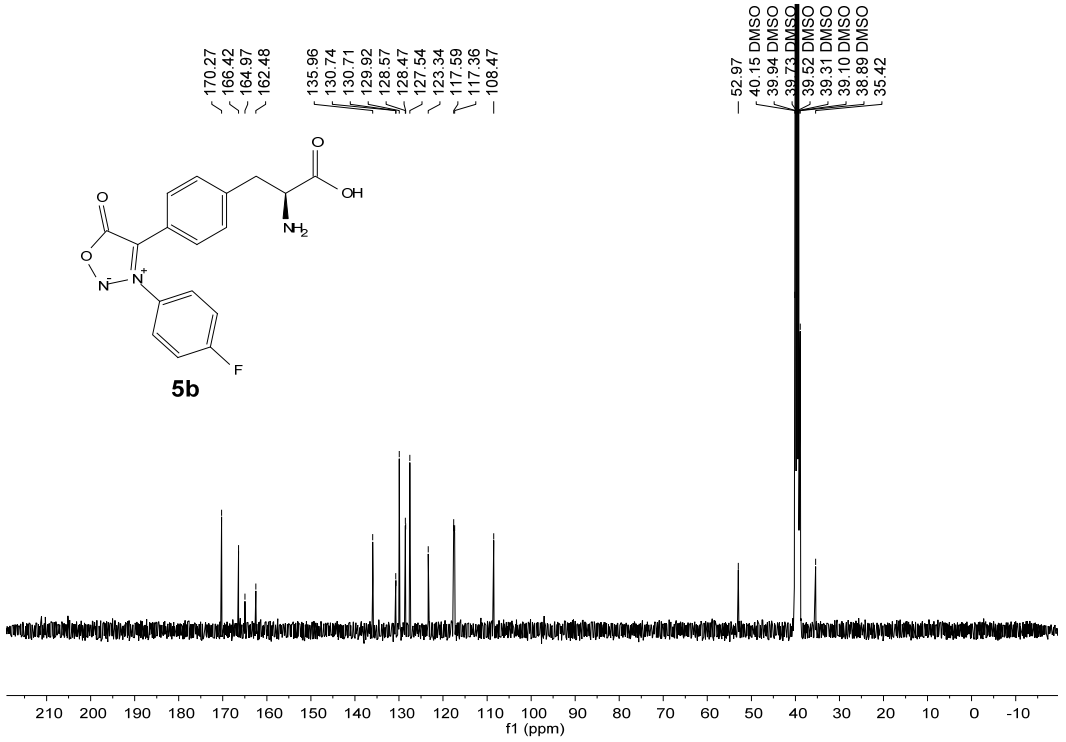

172.10
167.05
165.68
163.15
155.14
137.42
130.77
130.74
129.99
127.52
127.24
127.15
123.06
117.75
117.52
107.97
80.28
77.48 CDCl3
76.84 CDCl3
54.32
52.50
38.24
28.41
4b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-62.72
-105.62
4b
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

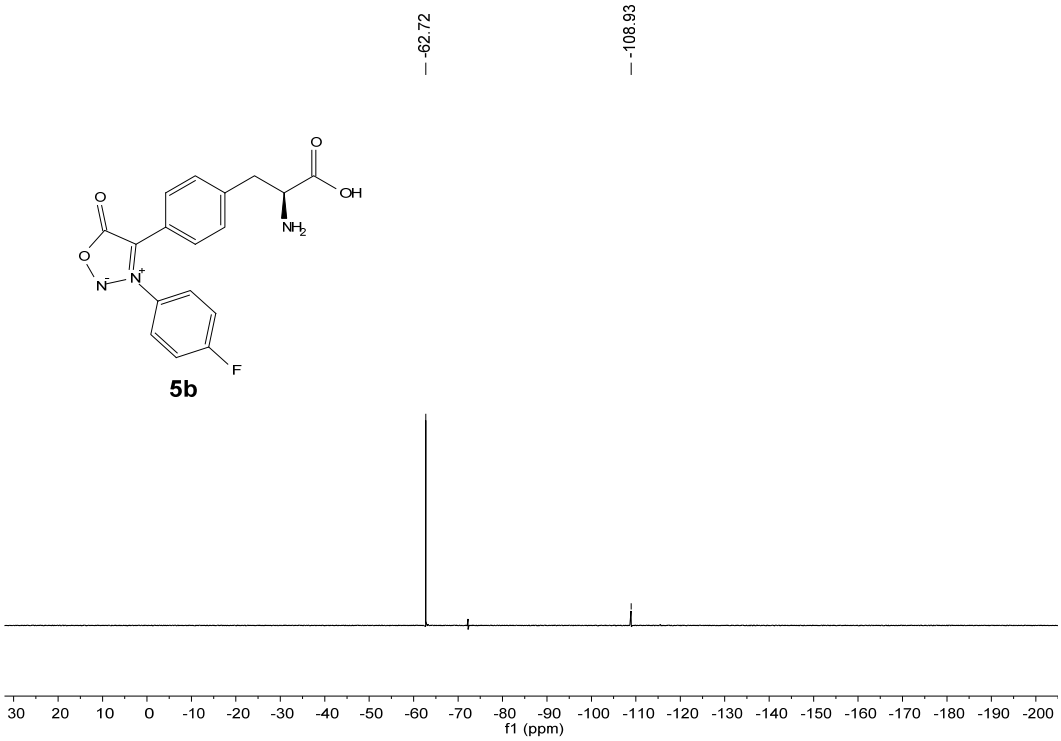

8.56
8.55
7.81
7.80
7.79
7.78
7.54
7.52
7.50
7.28
7.26
7.19
7.17
4.69 HDO
4.13
4.11
4.10
4.08
3.16
3.15
3.12
3.12
3.11
3.10
3.08
3.06
2.51 DMSO
2.50 DMSO
2.50 DMSO
2.49 DMSO
2.49 DMSO
O
OH
NH2
O
O
N
N
F

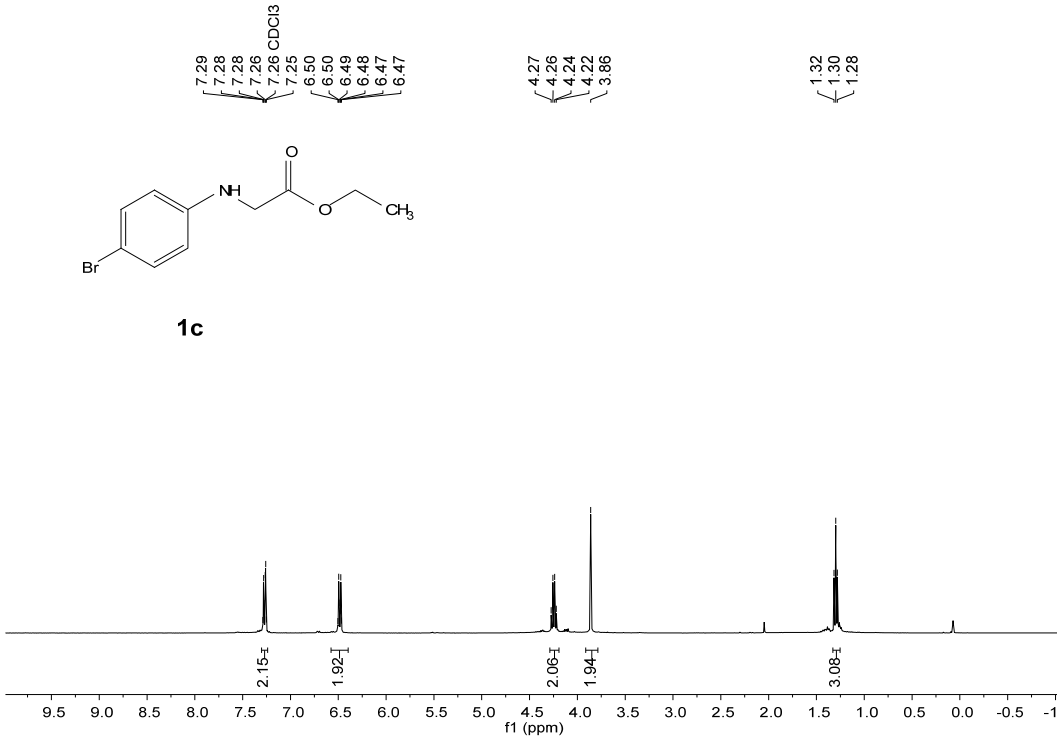
5b

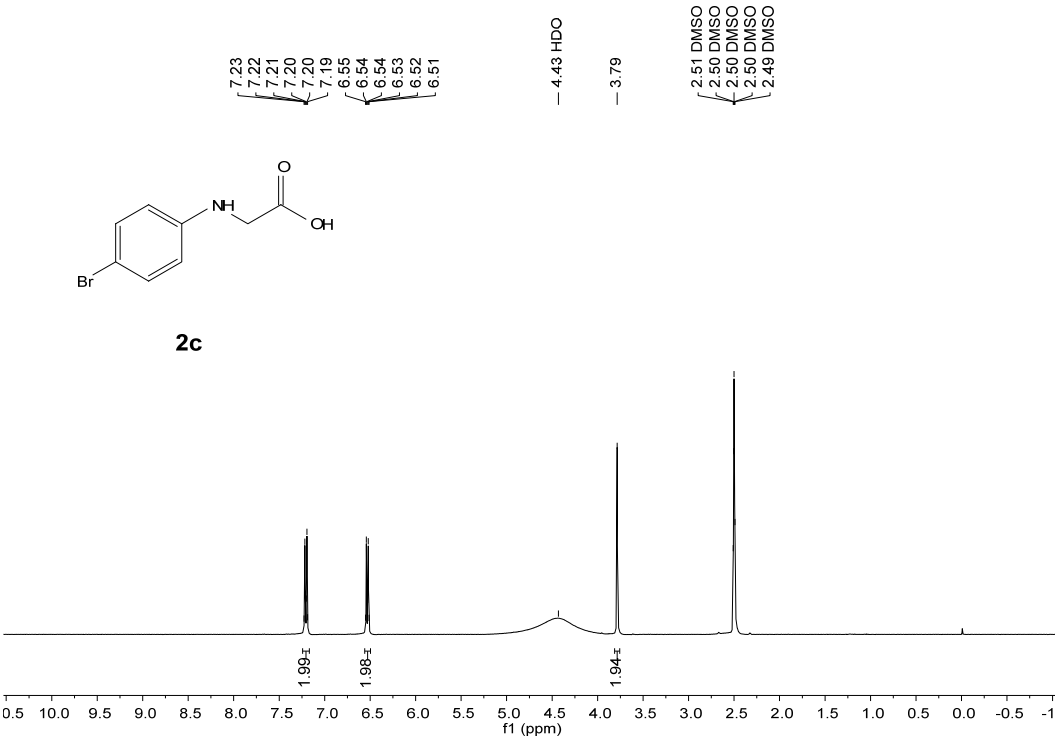

2.15
1.99
2.09
4.00
1.20
2.07
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


170.27
166.42
164.97
162.48
135.96
130.74
130.71
129.92
128.57
128.47
127.54
123.34
117.59
117.36
108.47
52.97
40.15 DMSO
39.94 DMSO
39.73 DMSO
39.52 DMSO
39.31 DMSO
39.10 DMSO
38.89 DMSO
35.42
O
OH
NH2
O
O
N
N
F
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

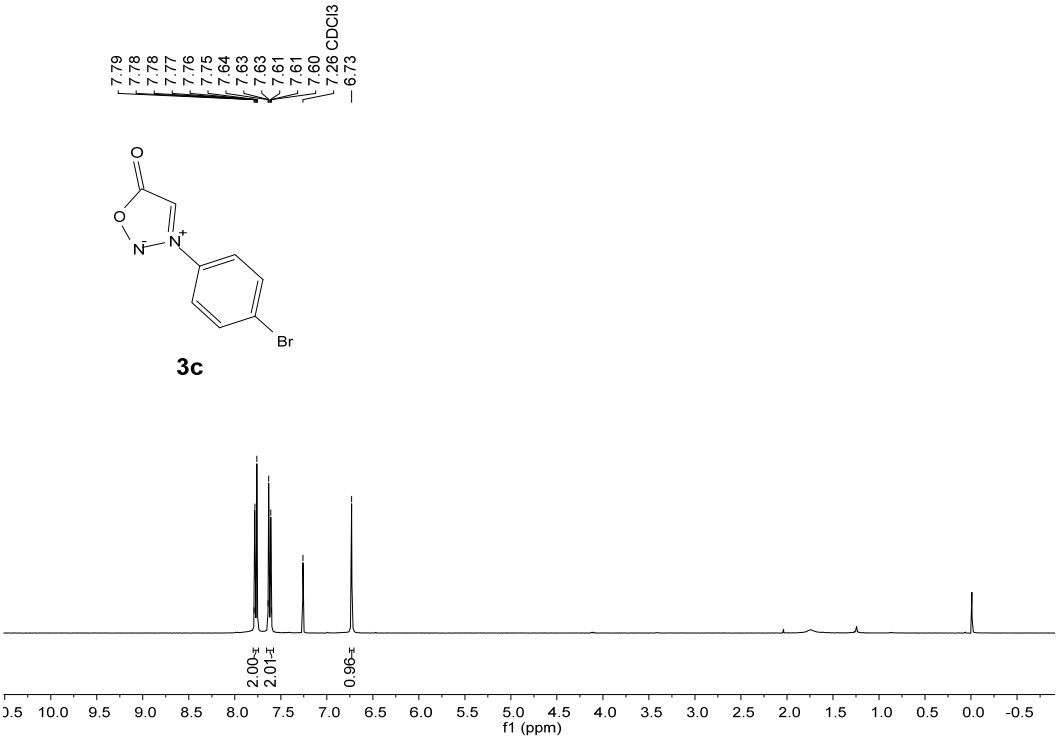
5b


-62.72
-108.93
O
OH
NH2
O
O
N
N+
F
5b
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

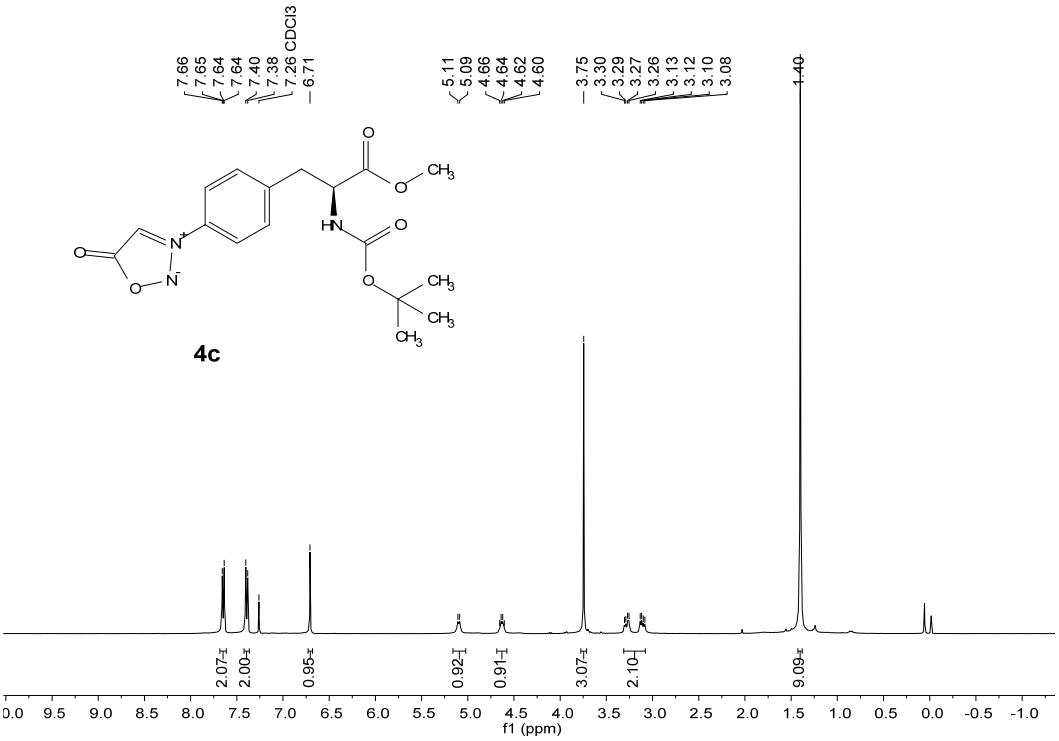

7.29
7.28
7.28
7.26
7.26 CDCl3
7.25
6.50
6.49
6.48
6.47
6.47
4.27
4.26
4.24
4.22
3.86
1.32
1.30
1.28
O
NH
O
CH3
Br
1c
2.15
1.92
2.06
1.94
3.08
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

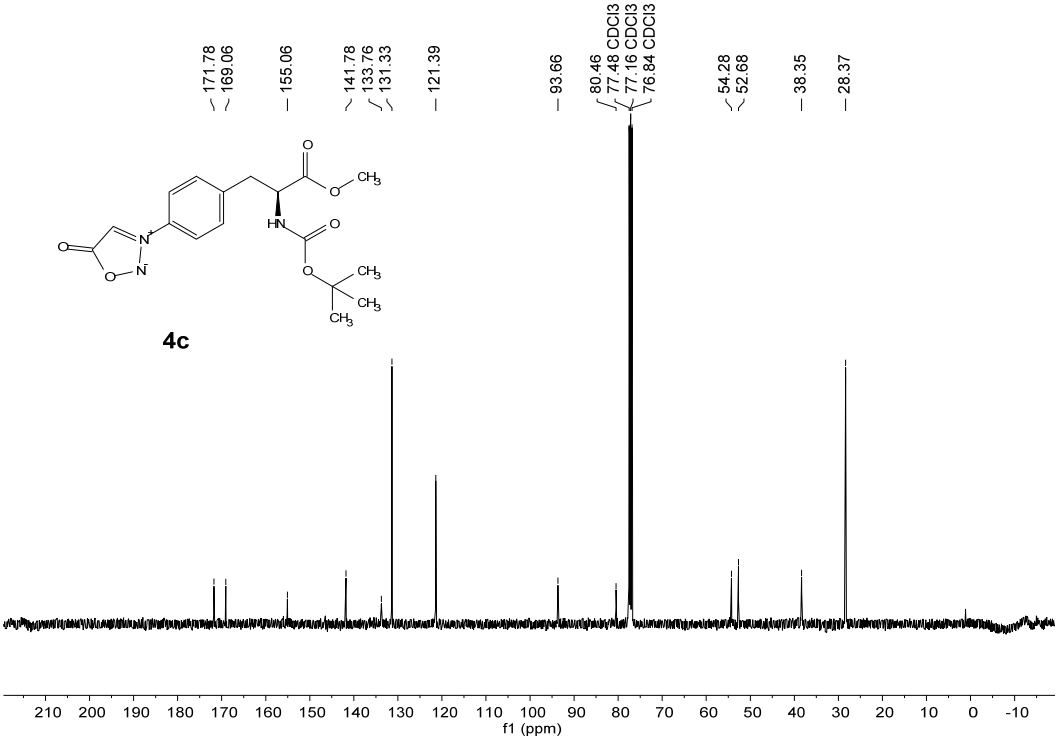

7.23
7.22
7.21
7.20
7.20
7.19
6.55
6.54
6.54
6.53
6.52
6.51
4.43 HDO
3.79
2.51 DMSO
2.50 DMSO
2.50 DMSO
2.50 DMSO
2.49 DMSO
O
NH
OH
Br
1.99
1.98
1.94
f1 (ppm)

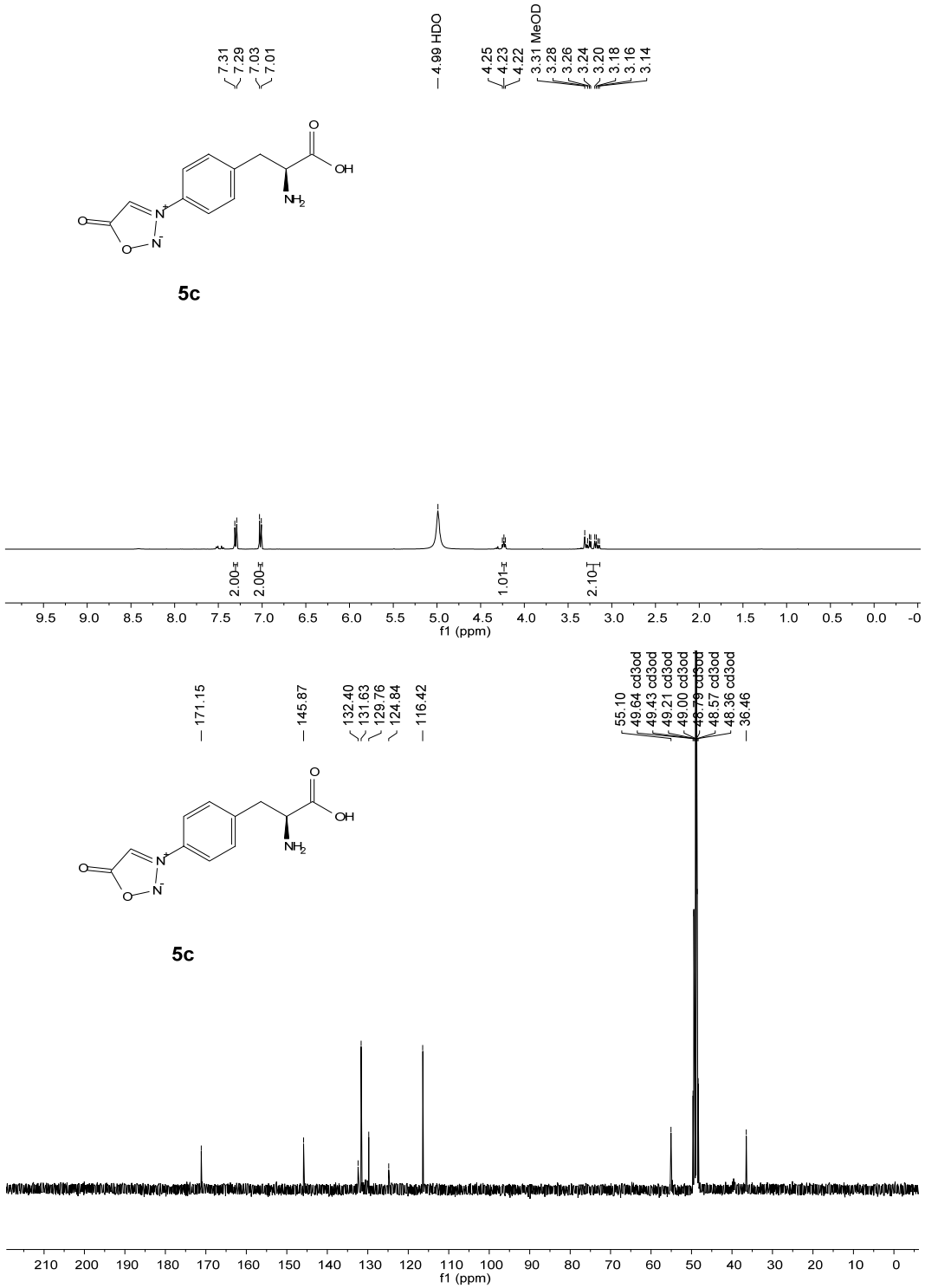
2c

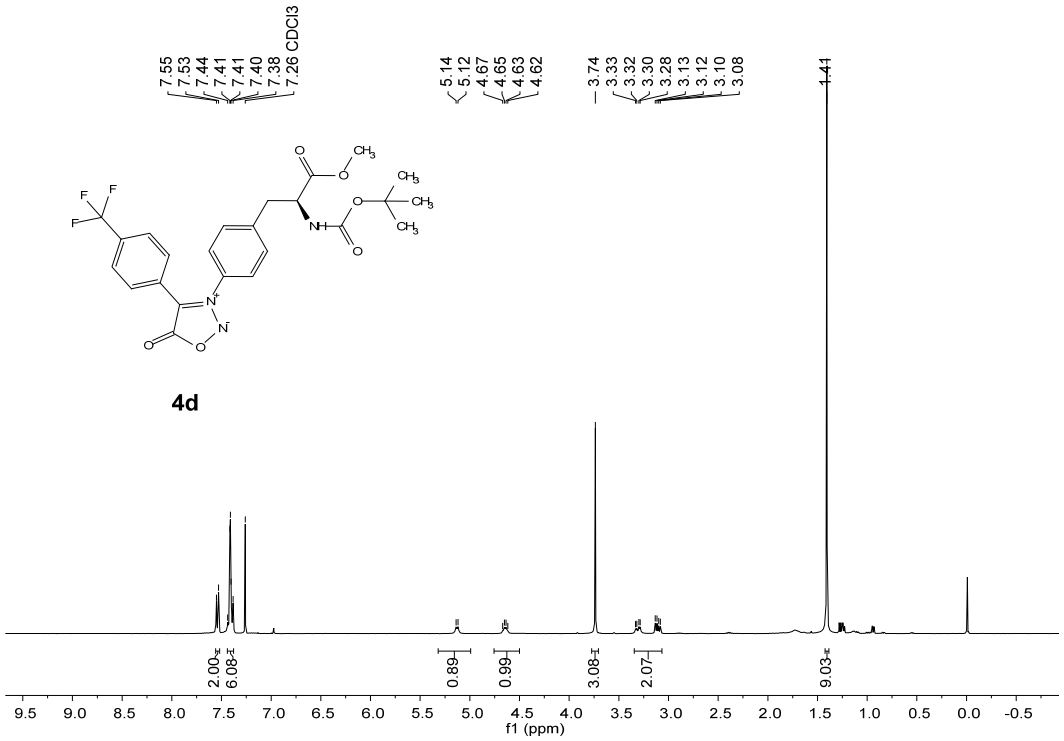

7.79
7.78
7.78
7.77
7.76
7.75
7.64
7.63
7.63
7.61
7.61
7.60
7.26 CDCl3
6.73
O
O
N
N
Br
2.00
2.01
0.96
f1 (ppm)

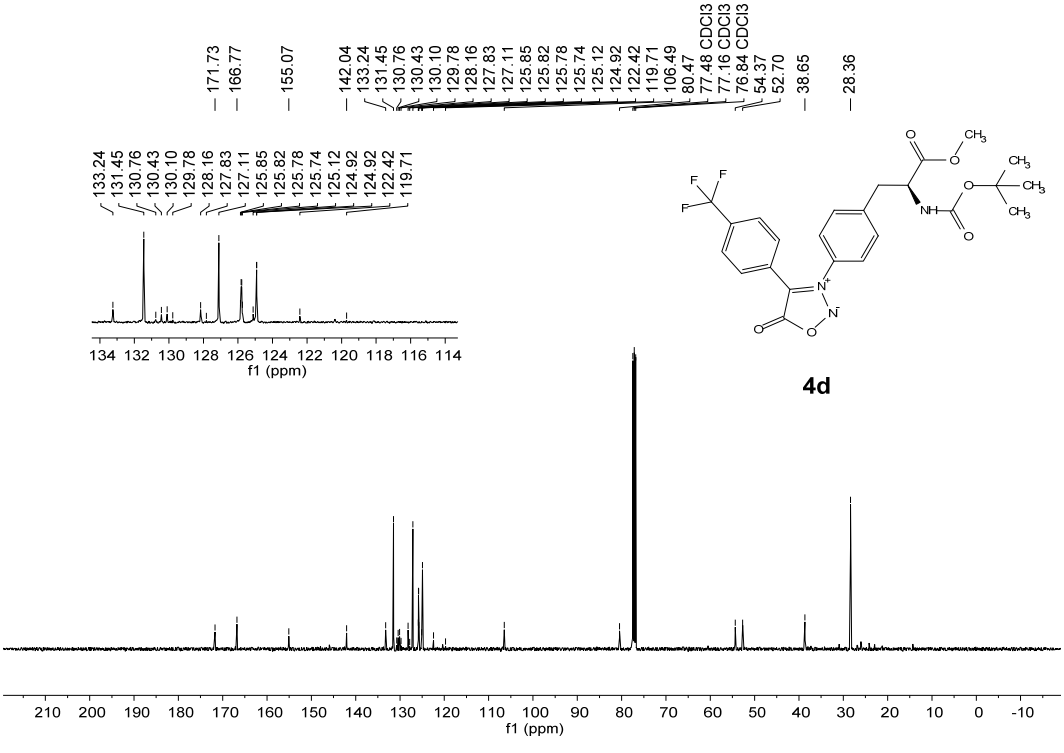
3c

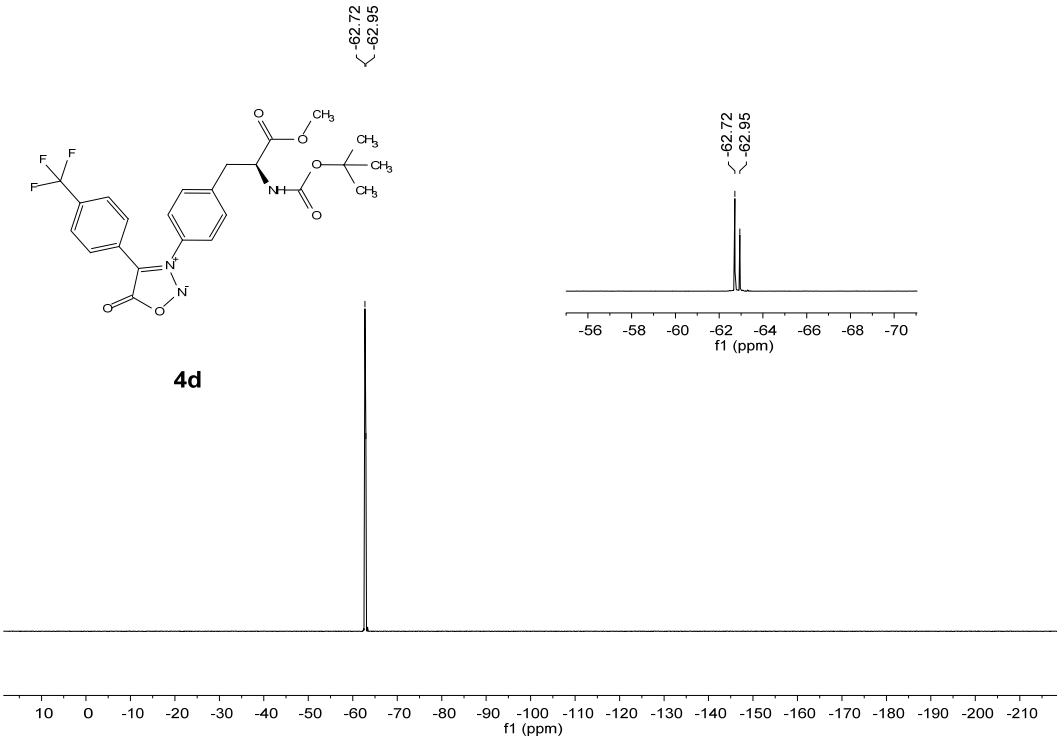

7.66
7.65
7.64
7.64
7.40
7.38
7.26 CDCl3
6.71
5.11
5.09
4.66
4.64
4.62
4.60
3.75
3.30
3.29
3.27
3.26
3.13
3.12
3.10
3.08
1.40
4c
2.07
2.00
0.95
0.92
0.91
3.07
2.10
9.09
f1 (ppm)

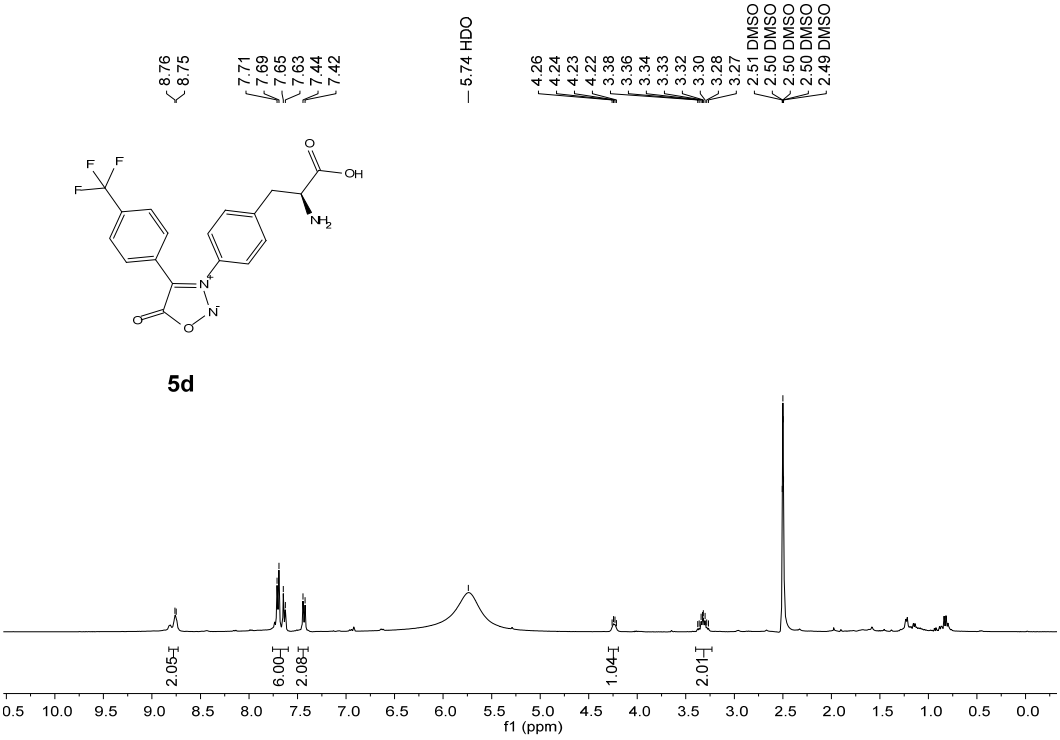

171.78
169.06
155.06
141.78
133.76
131.33
121.39
93.66
80.46
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
54.28
52.68
38.35
28.37
4c
f1 (ppm)

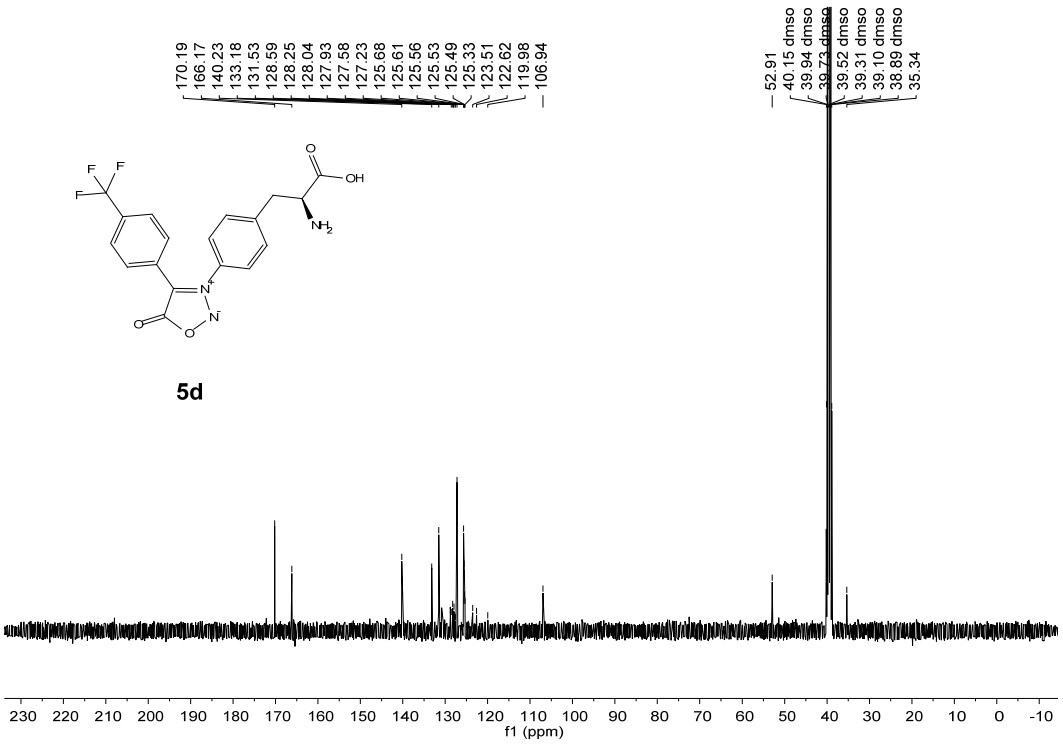

7.31
7.29
7.03
7.01
4.99 HDO
4.25
4.23
4.22
3.31 MeOD
3.28
3.26
3.24
3.20
3.18
3.16
3.14
O
OH
NH2
N+
N-
O
O
5c
2.00
2.00
1.01
2.10
f1 (ppm)
171.15
145.87
132.40
131.63
129.76
124.84
116.42
55.10
49.64 cd3od
49.43 cd3od
49.21 cd3od
49.00 cd3od
48.79 cd3od
48.57 cd3od
48.36 cd3od
36.46
f1 (ppm)

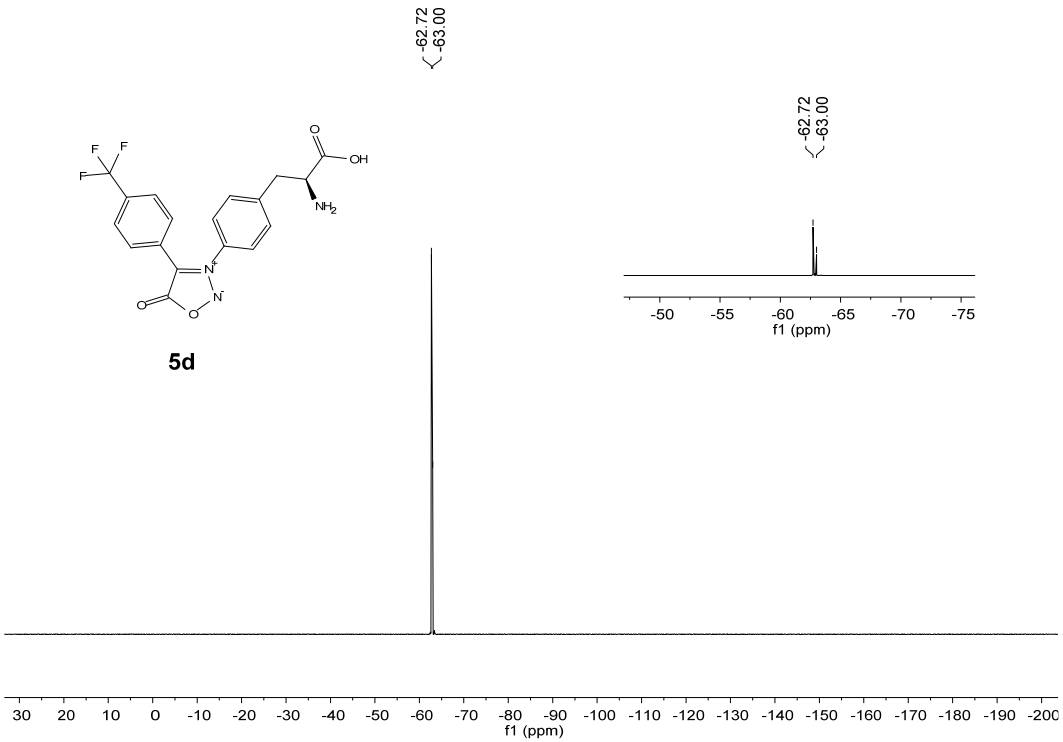

7.55
7.53
7.44
7.41
7.41
7.40
7.38
7.26 CDCl3
5.14
5.12
4.67
4.65
4.63
4.62
3.74
3.33
3.32
3.30
3.28
3.13
3.12
3.10
3.08
1.41
4d
2.00
6.08
0.89
0.99
3.08
2.07
9.03
f1 (ppm)

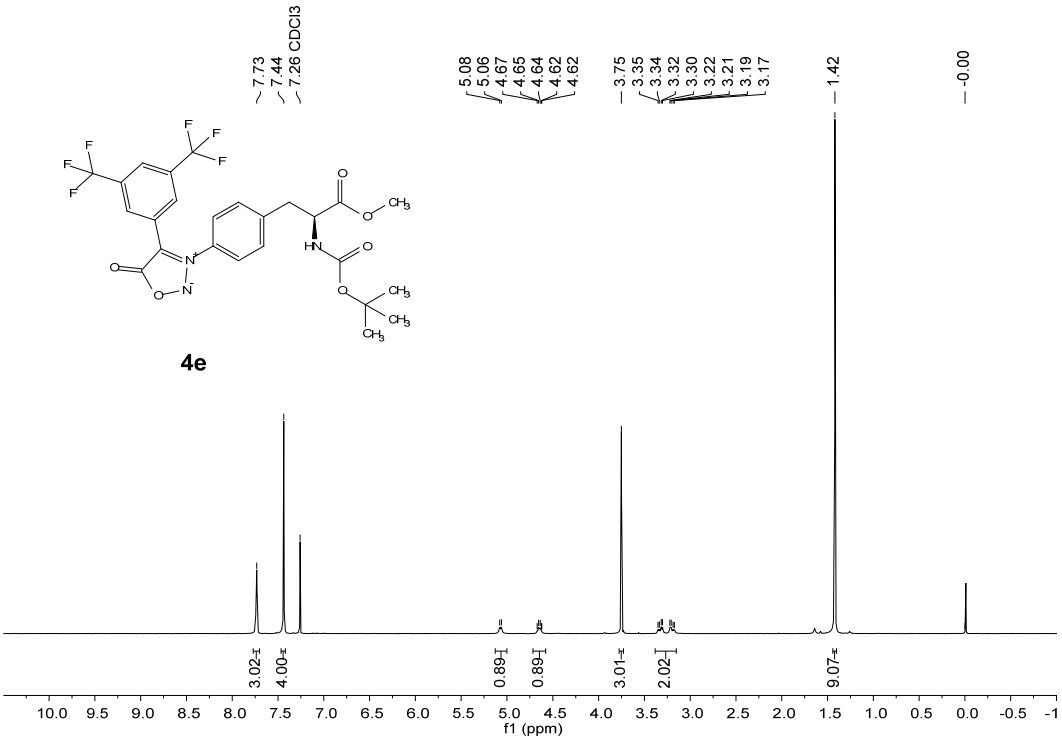

171.73
166.77
155.07
142.04
133.24
131.45
130.76
130.43
130.10
129.78
128.16
127.83
127.11
125.85
125.82
125.78
125.74
125.12
124.92
122.42
119.71
106.49
80.47
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
54.37
52.70
38.65
28.36
4d
f1 (ppm)

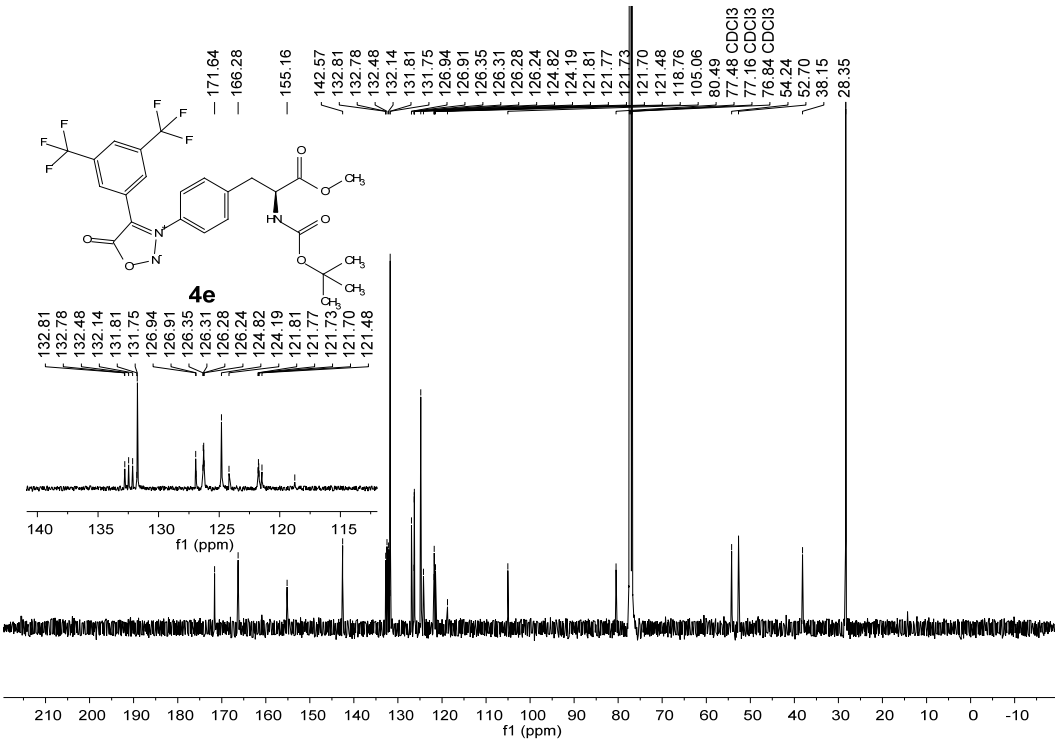

-62.72
-62.95
4d
f1 (ppm)


8.76
8.75
7.71
7.69
7.65
7.63
7.44
7.42
5.74 HDO
4.26
4.24
4.23
4.22
3.38
3.36
3.34
3.33
3.32
3.30
3.28
3.27
2.51 DMSO
2.50 DMSO
2.50 DMSO
2.50 DMSO
2.49 DMSO
5d
2.05
6.00
2.08
1.04
2.01
f1 (ppm)


170.19
166.17
140.23
133.18
131.53
128.59
128.25
128.04
127.93
127.58
127.23
125.68
125.61
125.56
125.53
125.49
125.33
123.51
122.62
119.98
106.94
52.91
40.15 dmso
39.94 dmso
39.73 dmso
39.52 dmso
39.31 dmso
39.10 dmso
38.89 dmso
35.34
5d
f1 (ppm)


-62.72
-63.00
5d
f1 (ppm)


7.73
7.44
7.26 CDCl3
5.08
5.06
4.67
4.65
4.64
4.62
4.62
3.75
3.35
3.34
3.32
3.30
3.22
3.21
3.19
3.17
1.42
-0.00
4e
3.02
4.00
0.89
0.89
3.01
2.02
9.07
f1 (ppm)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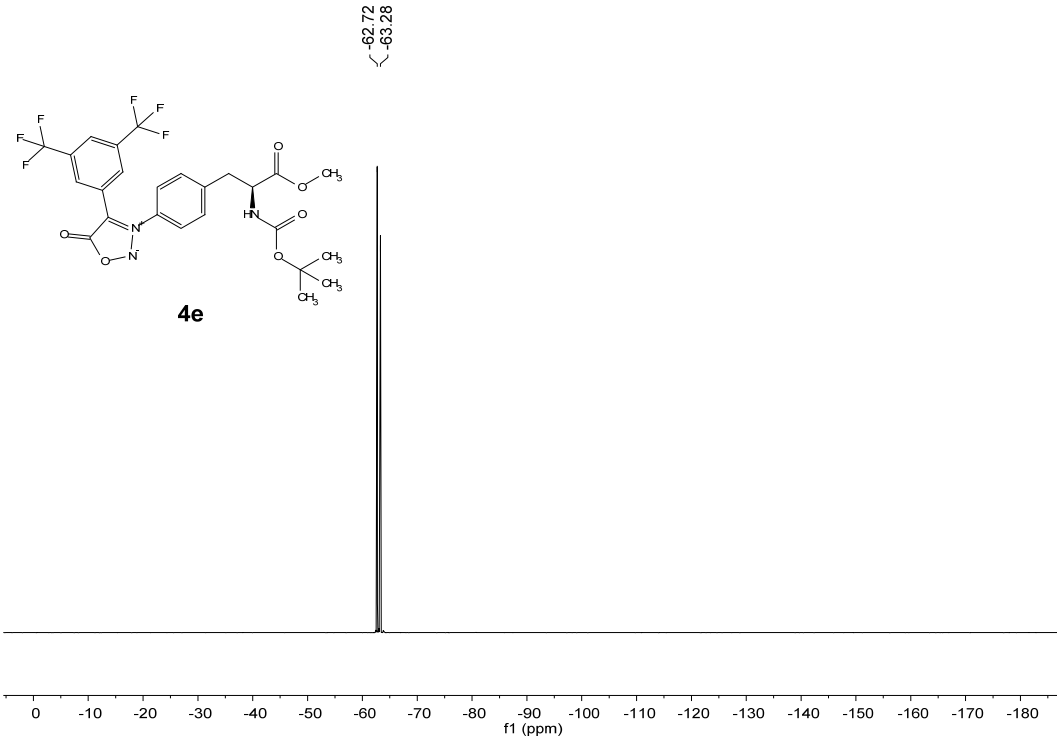
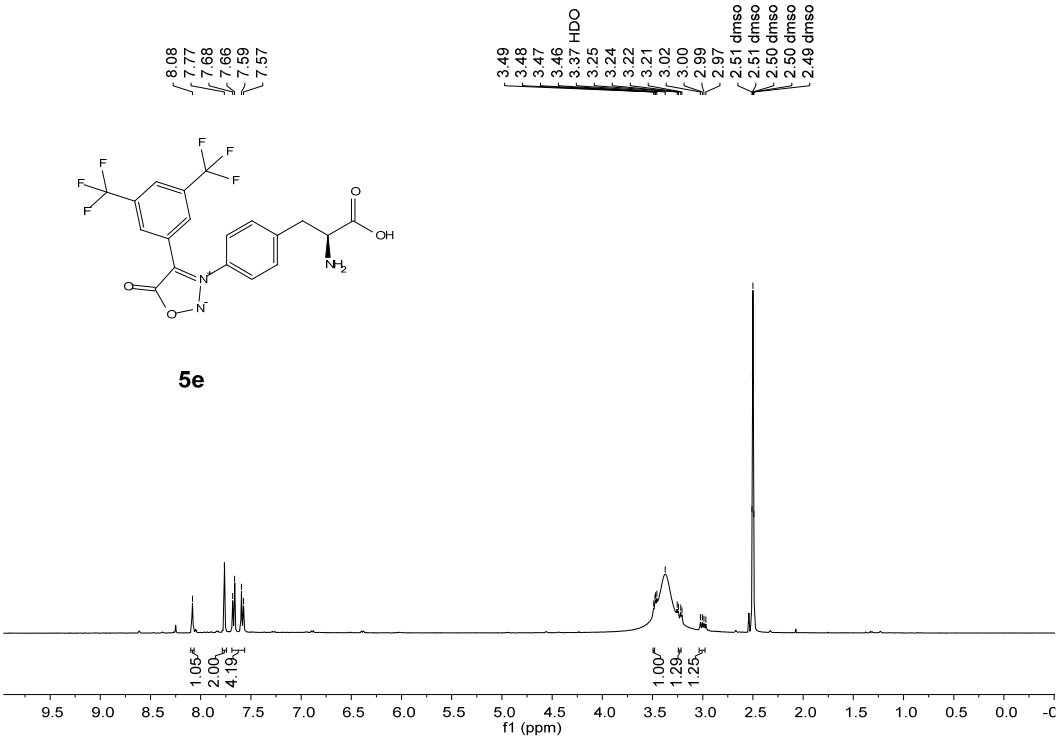
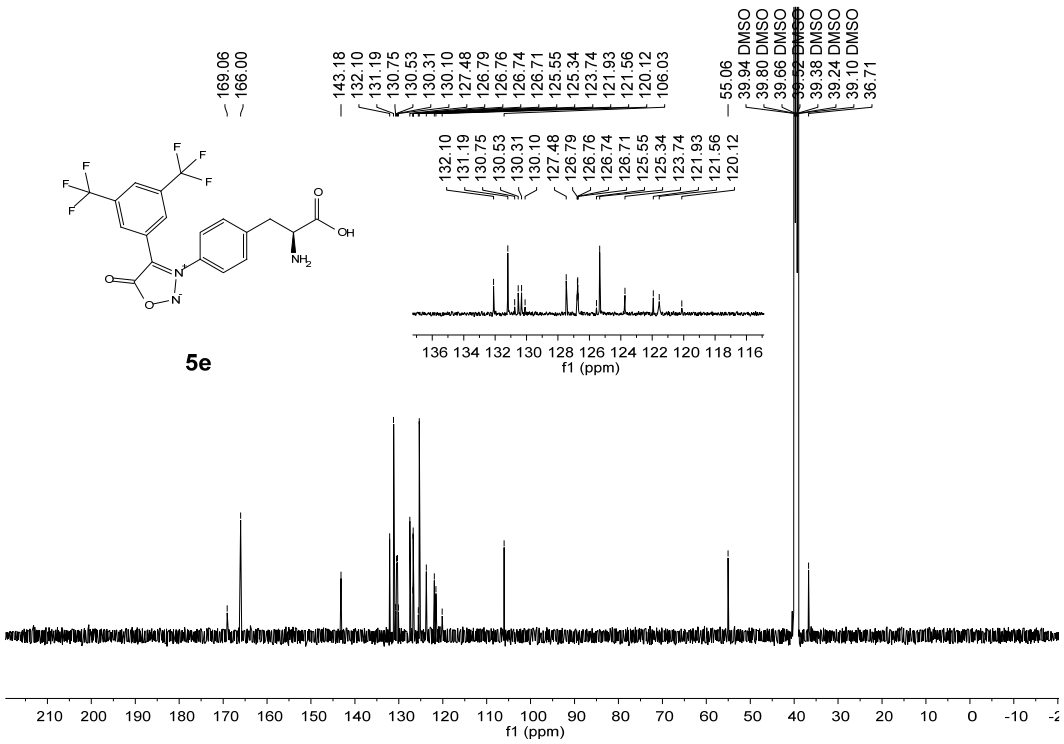
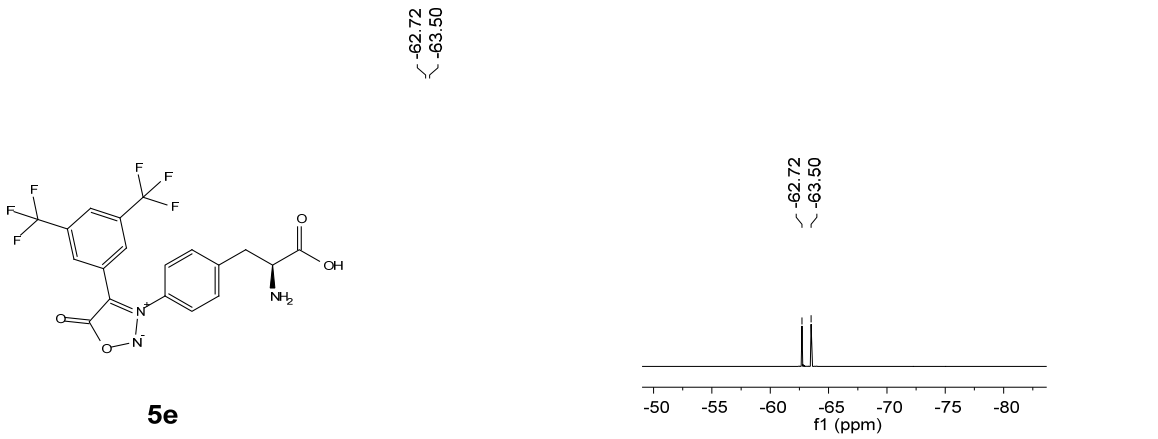
142.57
132.81
132.78
132.48
132.14
131.81
131.75
126.94
126.91
126.35
126.31
126.28
126.24
124.82
124.19
121.81
121.77
121.73
121.70
121.48
118.76
105.06
80.49
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
54.24
52.70
38.15
28.35
4e
f1 (ppm)
f1 (ppm)


-62.72
-63.28
4e
f1 (ppm)

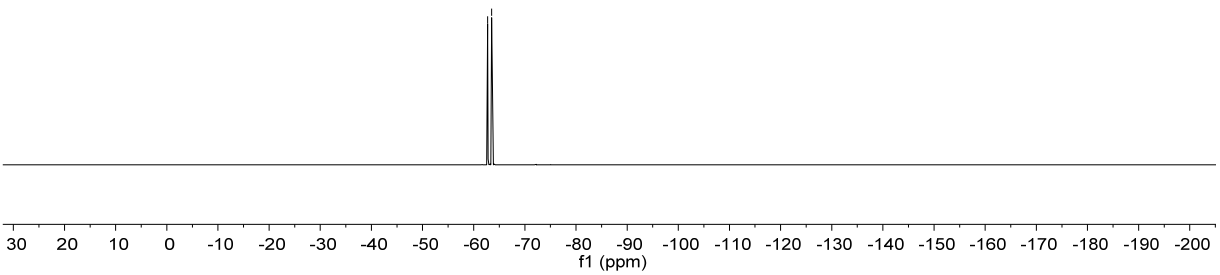

8.08
7.77
7.68
7.66
7.59
7.57
3.49
3.48
3.47
3.46
3.37 HDO
3.25
3.24
3.22
3.21
3.02
3.00
2.99
2.97
2.51 dmso
2.51 dmso
2.50 dmso
2.50 dmso
2.49 dmso
5e
1.05
2.00
4.19
1.00
1.29
1.25
f1 (ppm)

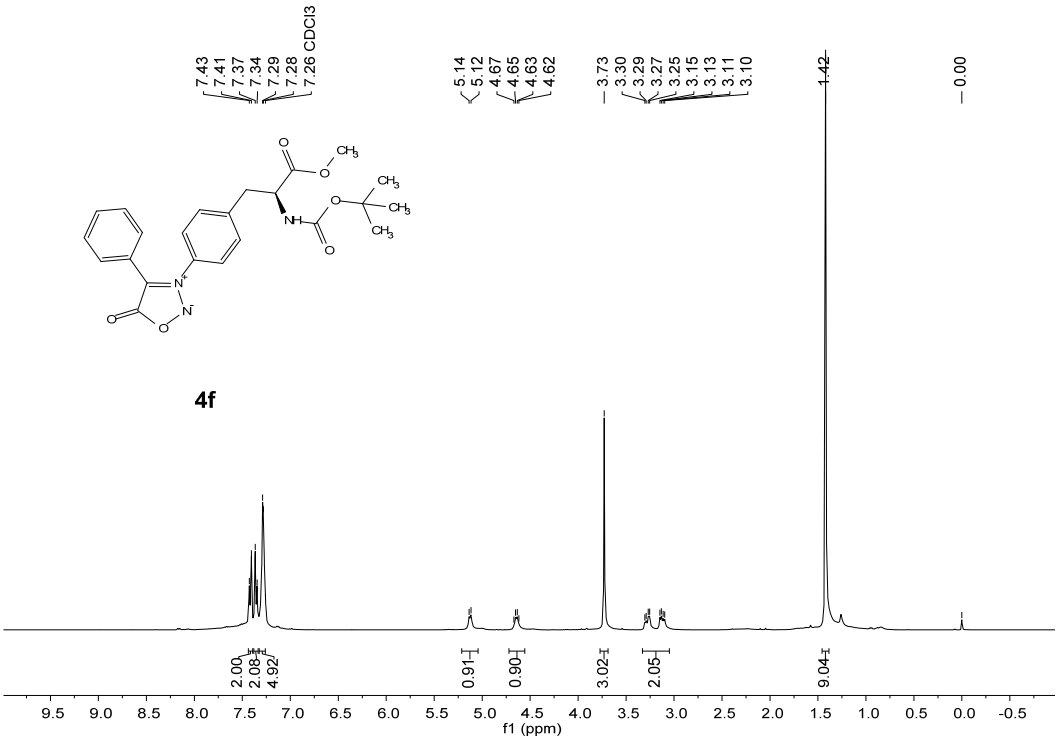

169.06
166.00
143.18
132.10
131.19
130.75
130.53
130.31
130.10
127.48
126.79
126.76
126.74
126.71
125.55
125.34
123.74
121.93
121.56
120.12
106.03
55.06
39.94 DMSO
39.80 DMSO
39.66 DMSO
39.52 DMSO
39.38 DMSO
39.24 DMSO
39.10 DMSO
36.71
f1 (ppm)

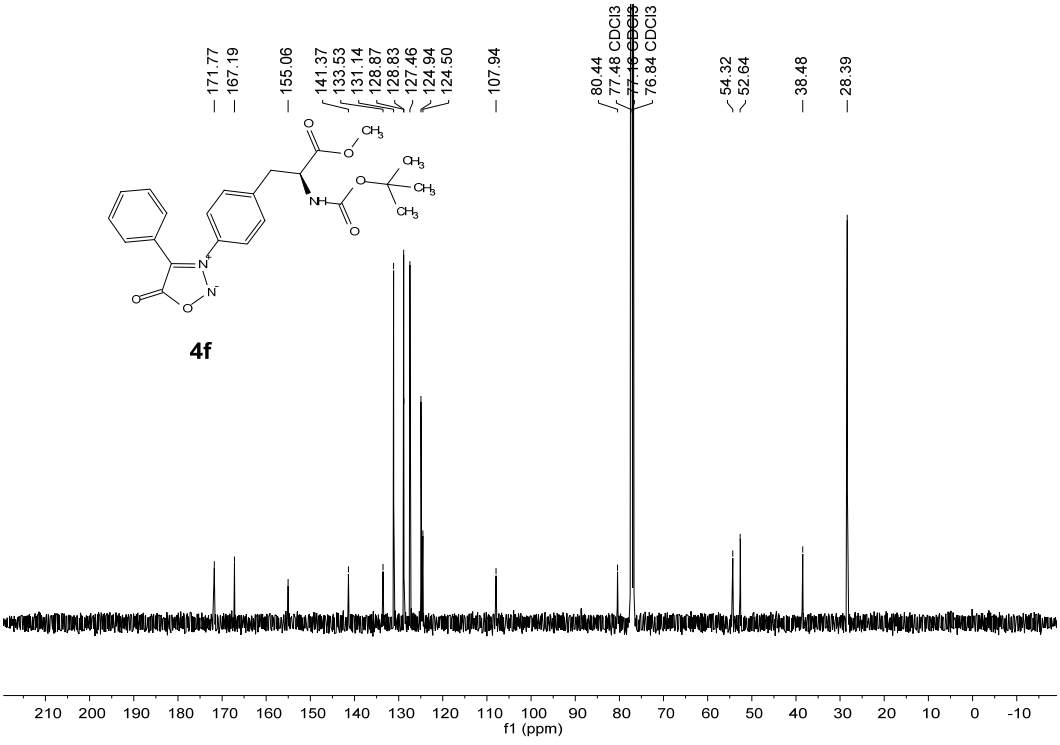
5e

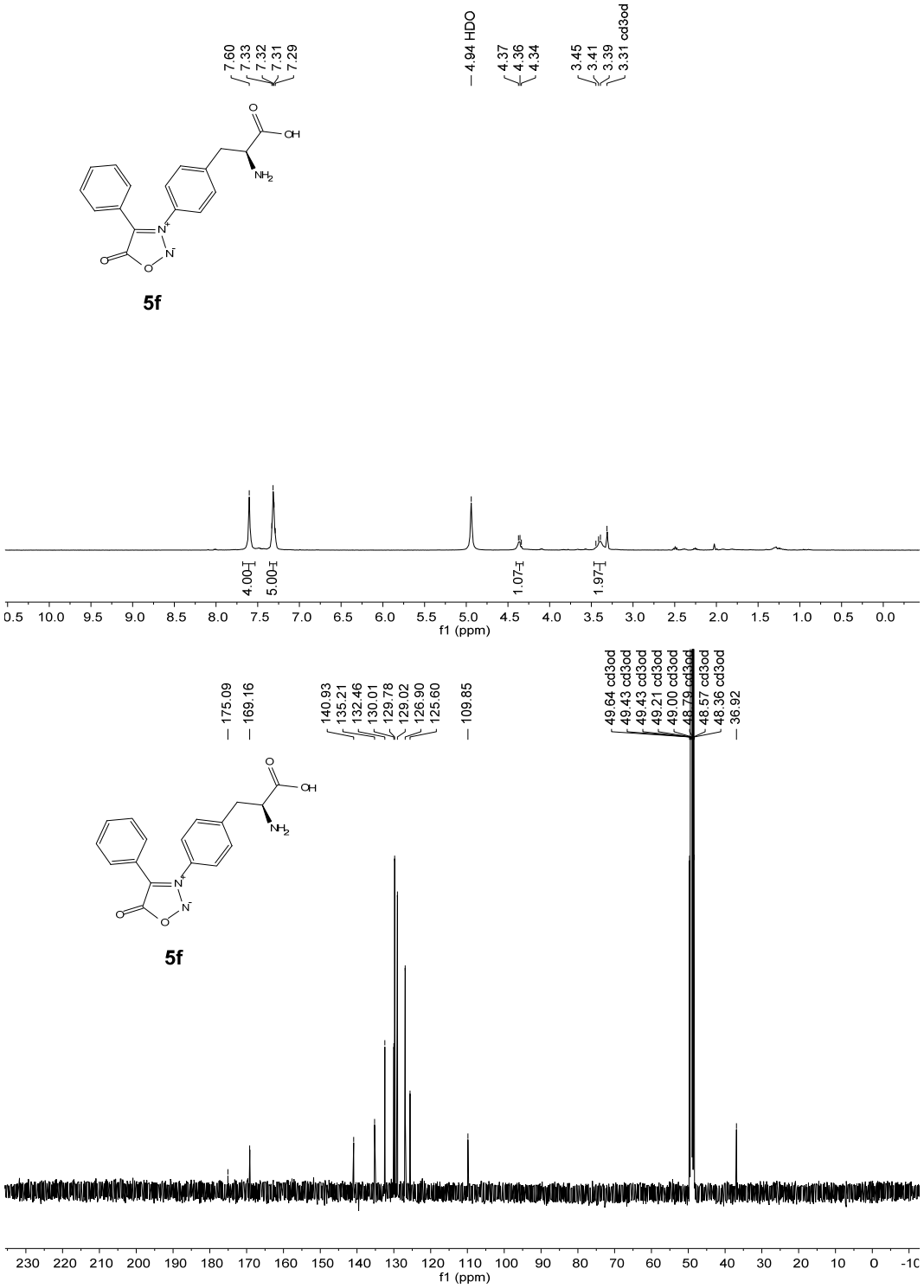

-62.72
-63.50
f1 (ppm)

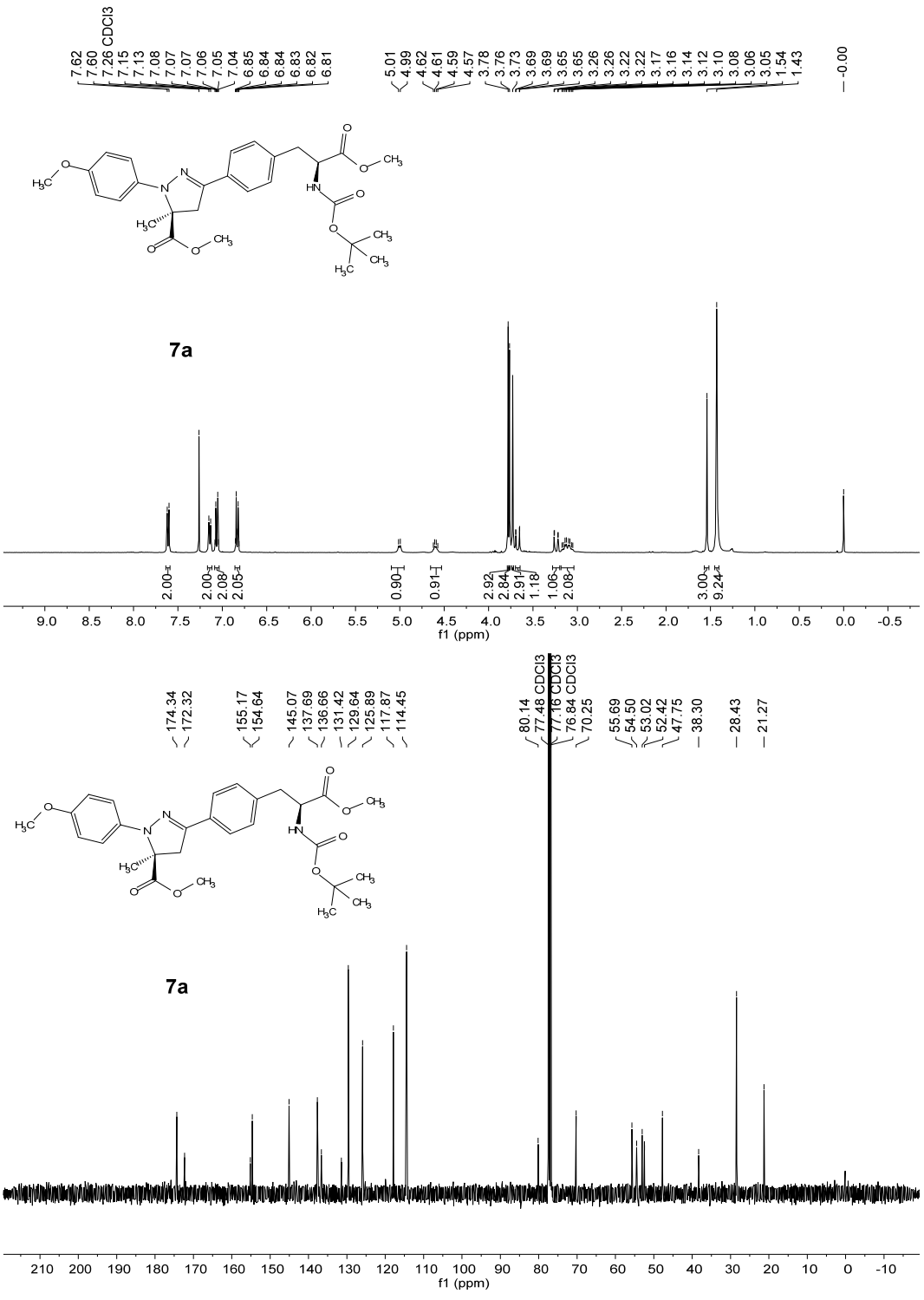
5e

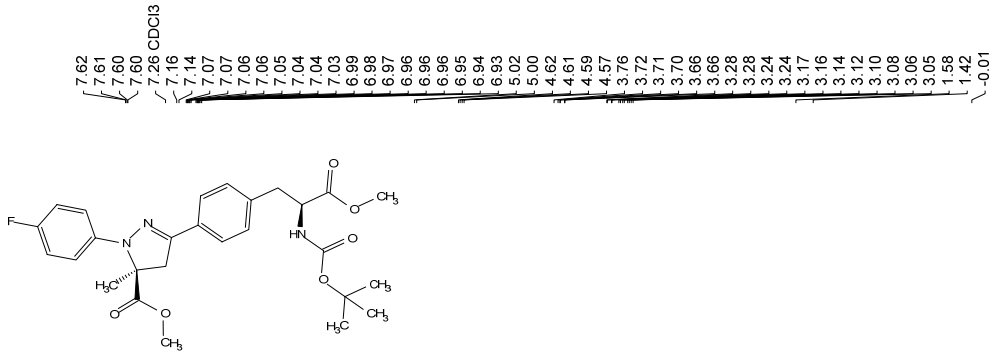

f1 (ppm)


7.43
7.41
7.37
7.34
7.29
7.28
7.26 CDCl3
5.14
5.12
4.67
4.65
4.63
4.62
3.73
3.30
3.29
3.27
3.25
3.15
3.13
3.11
3.10
1.42
0.00
4f
2.00
2.08
4.92
0.91
0.90
3.02
2.05
9.04
f1 (ppm)

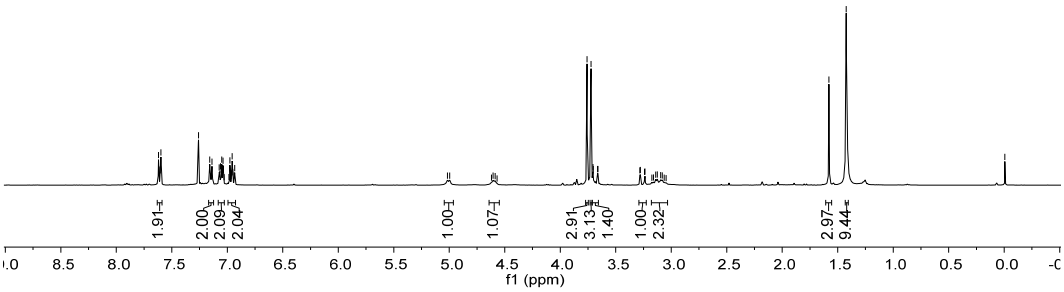

171.77
167.19
155.06
141.37
133.53
131.14
128.87
128.83
127.46
124.94
124.50
107.94
80.44
77.48 CDCl3
76.84 CDCl3
54.32
52.64
38.48
28.39
4f
f1 (ppm)

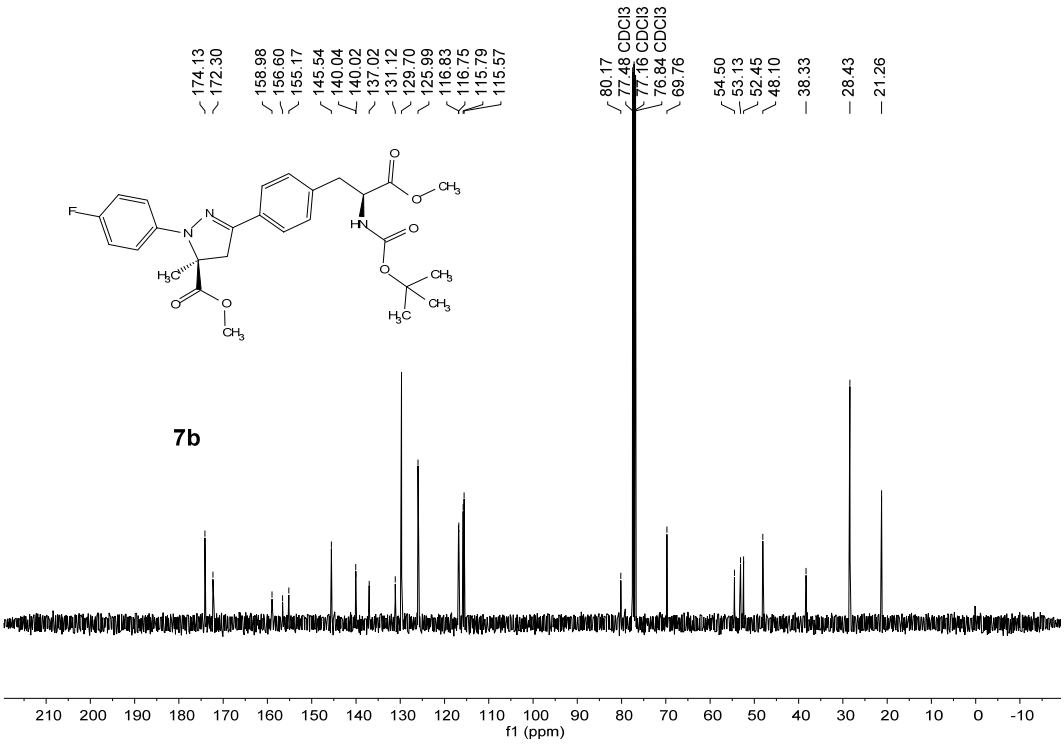

7.60
7.33
7.32
7.31
7.29
4.94 HDO
4.37
4.36
4.34
3.45
3.41
3.39
3.31 cd3od
OH
NH2
5f
4.00
5.00
1.07
1.97
f1 (ppm)
175.09
169.16
140.93
135.21
132.46
130.01
129.78
129.02
126.90
125.60
109.85
49.64 cd3od
49.43 cd3od
49.43 cd3od
49.21 cd3od
49.00 cd3od
48.79 cd3od
48.57 cd3od
48.36 cd3od
36.92
OH
NH2
5f
f1 (ppm)


7.62
7.60
CDCl3
7.26
7.15
7.13
7.08
7.07
7.07
7.06
7.05
7.04
6.85
6.84
6.84
6.83
6.82
6.81
5.01
4.99
4.62
4.61
4.59
4.57
3.78
3.76
3.73
3.69
3.69
3.65
3.65
3.26
3.26
3.22
3.22
3.17
3.16
3.14
3.12
3.10
3.08
3.06
3.05
1.54
1.43
-0.00
7a
2.00
2.00
2.08
2.05
0.90
0.91
2.92
2.84
2.91
1.18
1.06
2.08
3.00
9.24
f1 (ppm)
174.34
172.32
155.17
154.64
145.07
137.69
136.66
131.42
129.64
125.89
117.87
114.45
80.14
77.48
CDCl3
77.16
CDCl3
76.84
CDCl3
70.25
55.69
54.50
53.02
52.42
47.75
38.30
28.43
21.27
7a
f1 (ppm)

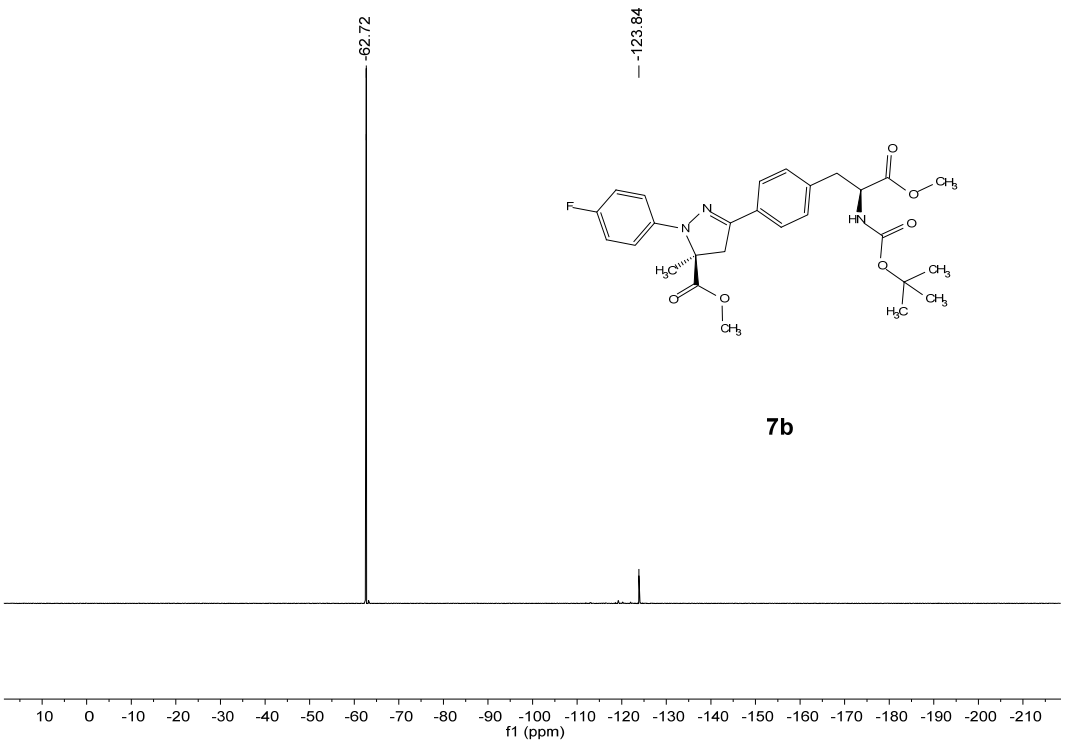

7.62
7.61
7.60
7.60
7.26 CDCl3
7.16
7.14
7.07
7.07
7.06
7.06
7.05
7.04
7.04
7.03
6.99
6.98
6.97
6.96
6.96
6.96
6.95
6.94
6.93
5.02
5.00
4.62
4.61
4.59
4.57
3.76
3.72
3.71
3.70
3.66
3.66
3.28
3.28
3.24
3.24
3.17
3.16
3.14
3.12
3.10
3.08
3.06
3.05
1.58
1.42
-0.01

7b

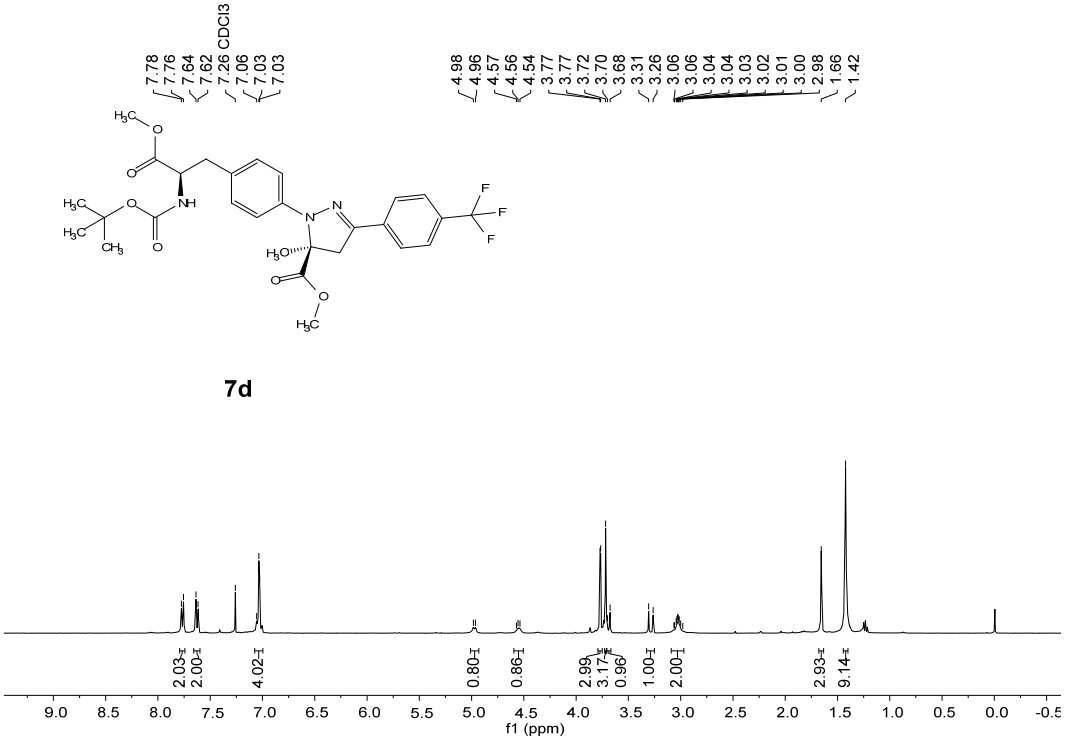

1.91
2.00
2.09
2.04
1.00
1.07
2.91
3.13
1.40
1.00
2.32
2.97
9.44
f1 (ppm)


174.13
172.30
158.98
156.60
155.17
145.54
140.04
140.02
137.02
131.12
129.70
125.99
116.83
116.75
115.79
115.57
80.17
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
69.76
54.50
53.13
52.45
48.10
38.33
28.43
21.26
f1 (ppm)

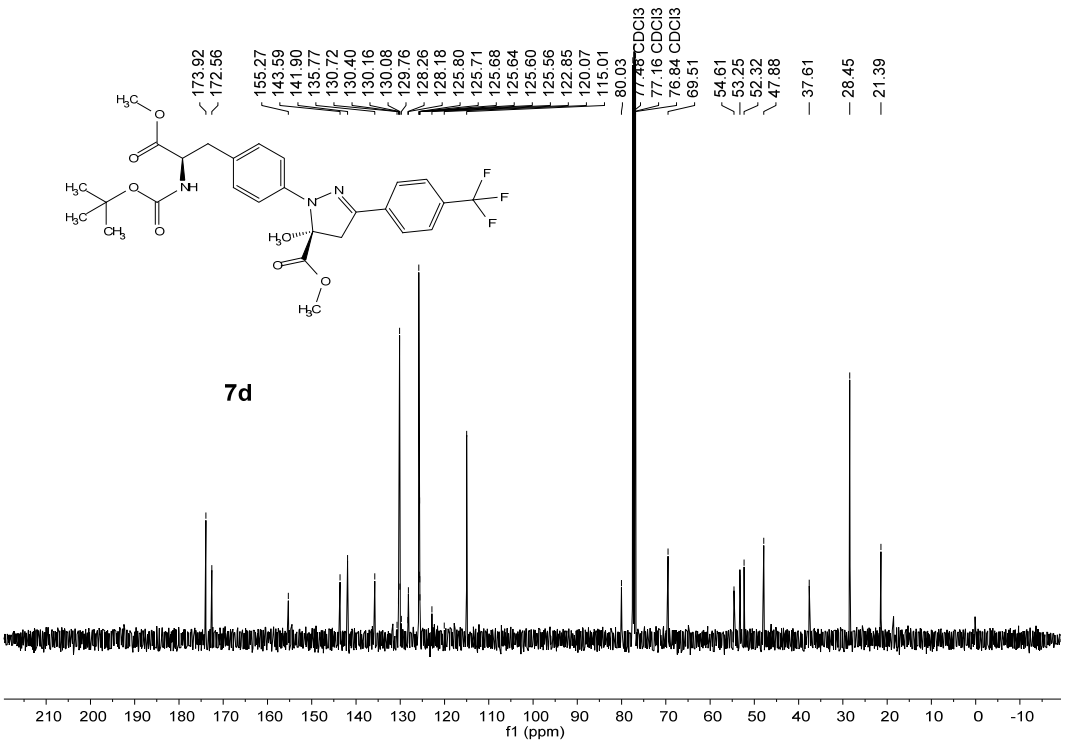
7b

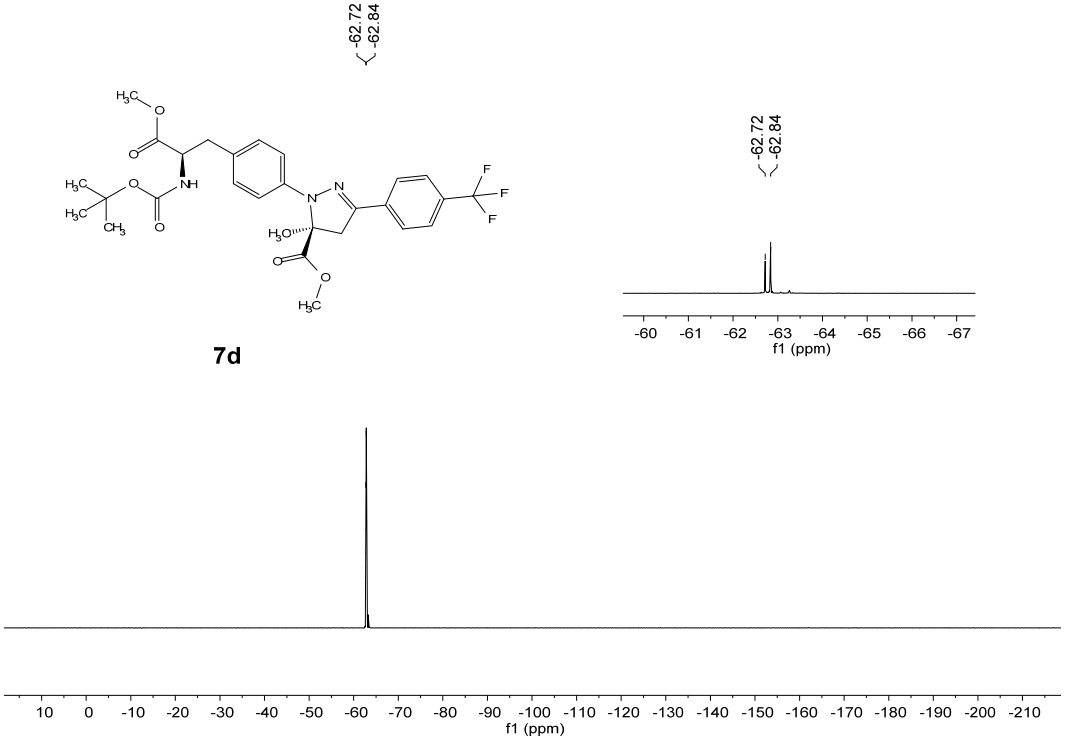

-62.72
--123.84
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

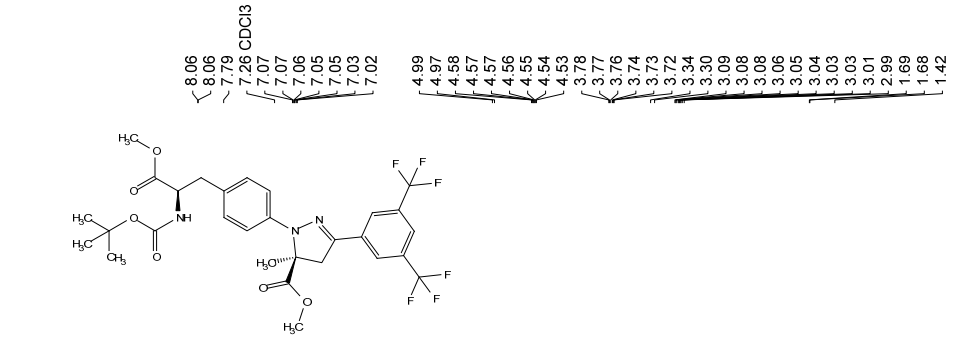
7b


7.78
7.76
7.64
7.62
7.26 CDCl3
7.06
7.03
7.03
4.98
4.96
4.57
4.56
4.54
3.77
3.77
3.72
3.70
3.68
3.31
3.26
3.06
3.06
3.04
3.04
3.03
3.02
3.01
3.00
2.98
1.66
1.42
2.03
2.00
4.02
0.80
0.86
2.99
3.17
0.96
1.00
2.00
2.93
9.14
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 -0.5
f1 (ppm)

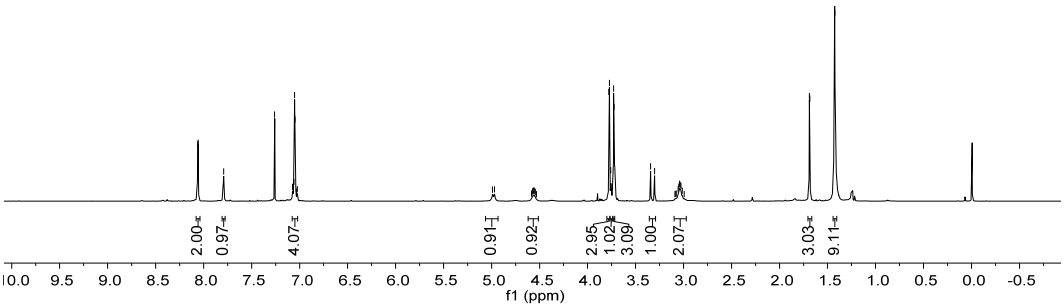
7d

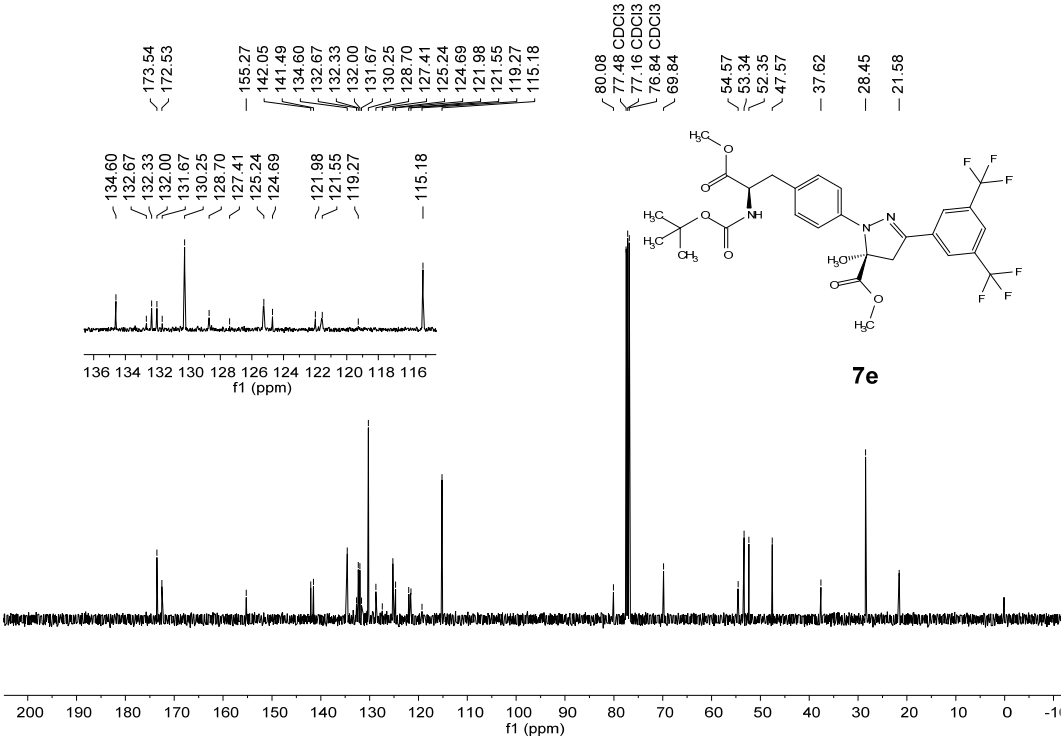

173.92
172.56
155.27
143.59
141.90
135.77
130.72
130.40
130.16
130.08
129.76
128.26
128.18
125.80
125.71
125.68
125.64
125.60
125.56
122.85
120.07
115.01
80.03
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
69.51
54.61
53.25
52.32
47.88
37.61
28.45
21.39
7d
f1 (ppm)


-62.72
-62.84
7d
f1 (ppm)


8.06
8.06
7.79
7.26 CDCl3
7.07
7.07
7.06
7.05
7.05
7.03
7.02
4.99
4.97
4.58
4.57
4.57
4.56
4.55
4.54
4.53
3.78
3.77
3.76
3.74
3.73
3.72
3.34
3.30
3.09
3.08
3.08
3.06
3.05
3.04
3.03
3.03
3.01
2.99
1.69
1.68
1.42

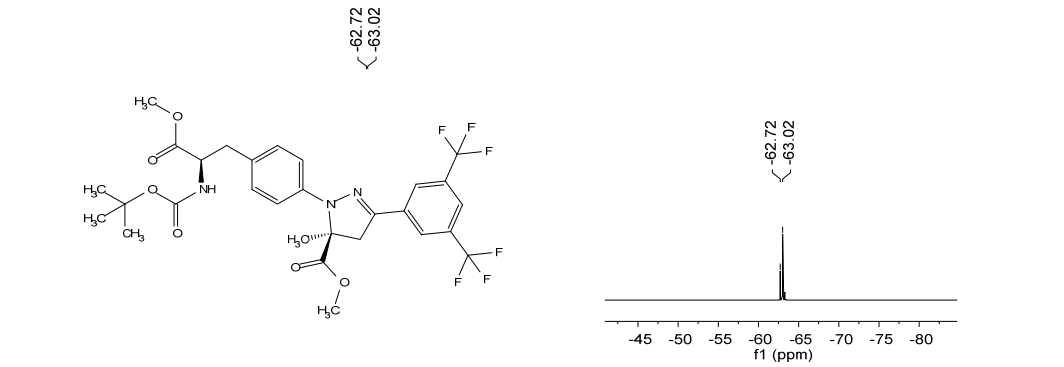
7e


2.00
0.97
4.07
0.91
0.92
2.95
1.02
3.09
1.00
2.07
3.03
9.11
f1 (ppm)

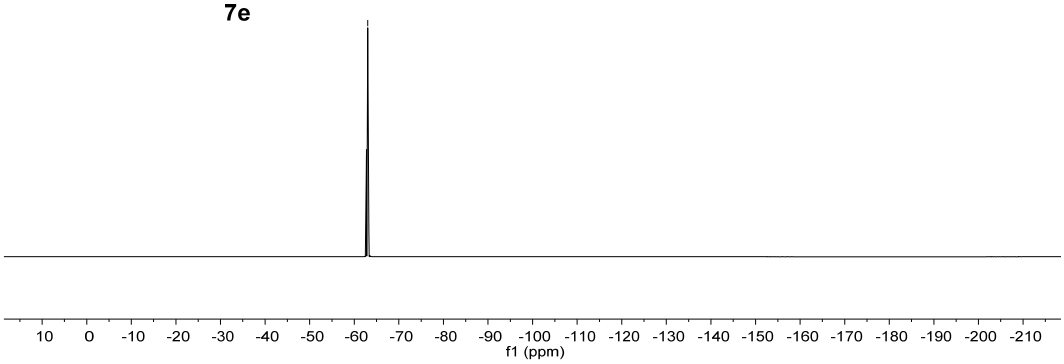

173.54
172.53
155.27
142.05
141.49
134.60
132.67
132.33
132.00
131.67
130.25
128.70
127.41
125.24
124.69
121.98
121.55
119.27
115.18
80.08
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
69.84
54.57
53.34
52.35
47.57
37.62
28.45
21.58
f1 (ppm)

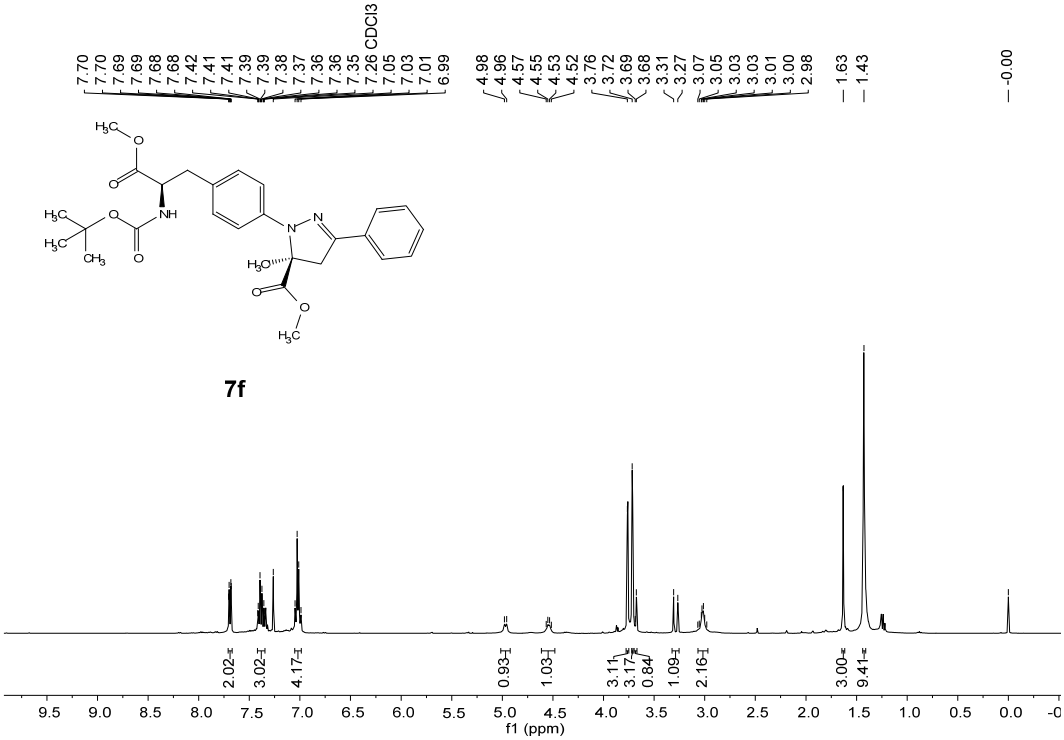
134.60
132.67
132.33
132.00
131.67
130.25
128.70
127.41
125.24
124.69
121.98
121.55
119.27
115.18
136 134 132 130 128 126 124 122 120 118 116
f1 (ppm)

7e

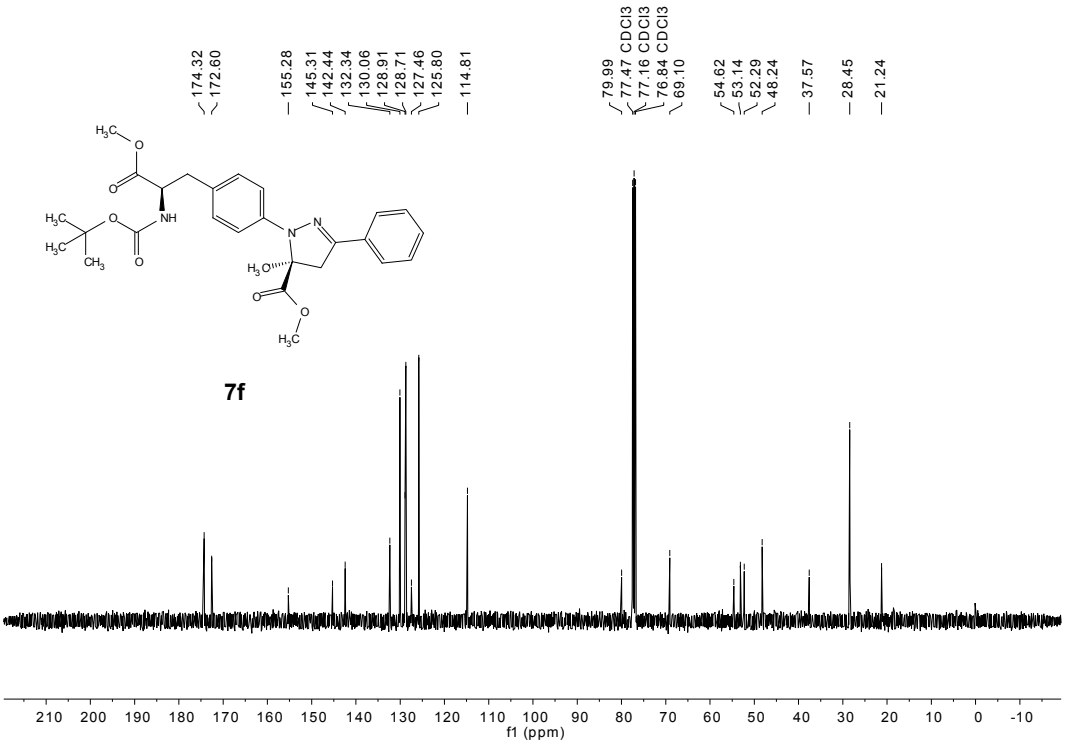

-62.72
-63.02
-62.72
-63.02
-45 -50 -55 -60 -65 -70 -75 -80
f1 (ppm)

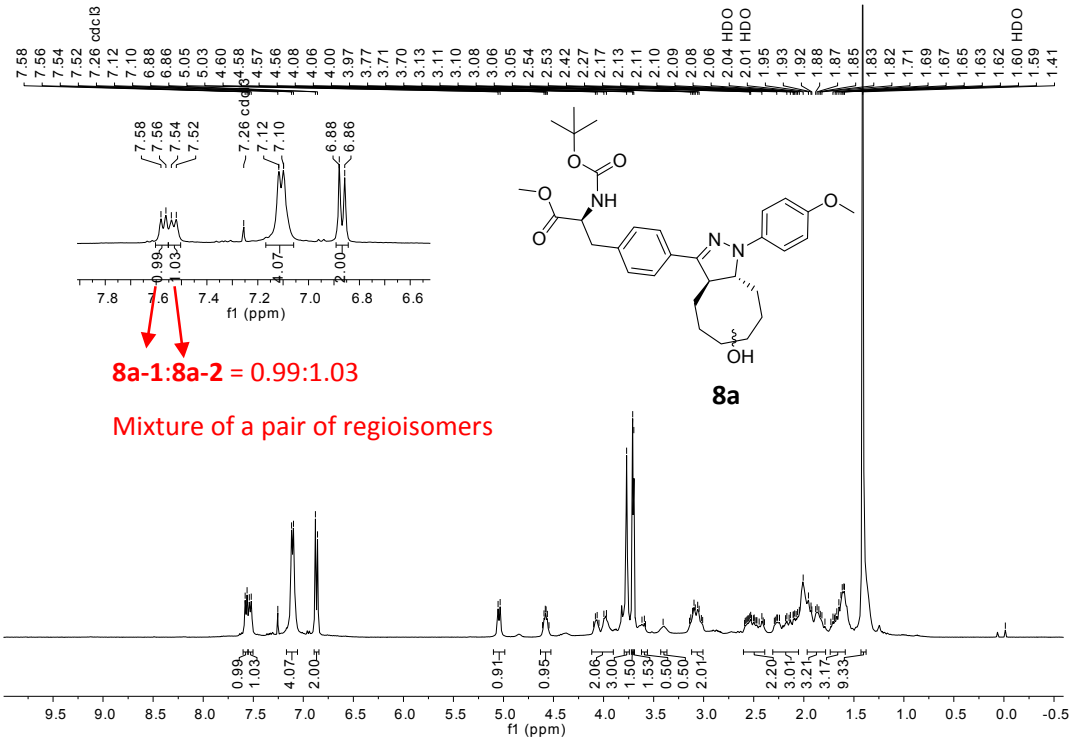
7e

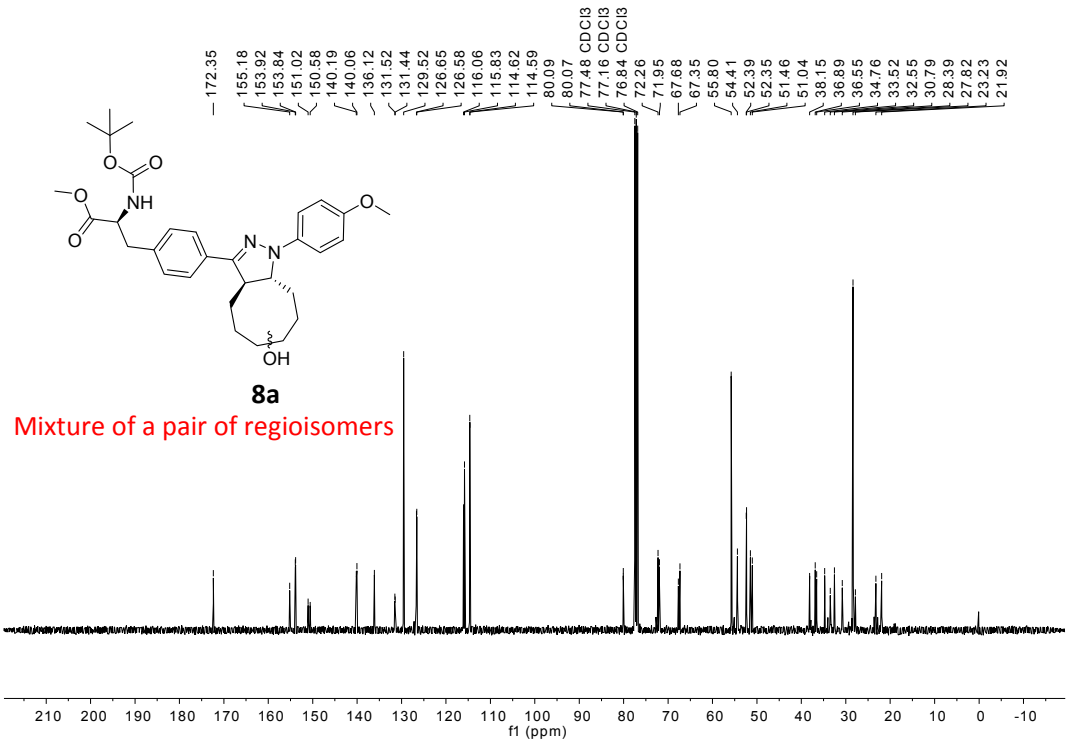

10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)


CDCl3
7.70
7.70
7.69
7.69
7.68
7.68
7.42
7.41
7.41
7.39
7.39
7.38
7.37
7.36
7.36
7.35
7.26
7.05
7.03
7.01
6.99
4.98
4.96
4.57
4.55
4.53
4.52
3.76
3.72
3.69
3.68
3.31
3.27
3.07
3.05
3.03
3.03
3.01
3.00
2.98
1.63
1.43
0.00
2.02
3.02
4.17
0.93
1.03
3.11
3.17
0.84
1.09
2.16
3.00
9.41
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
f1 (ppm)

7f

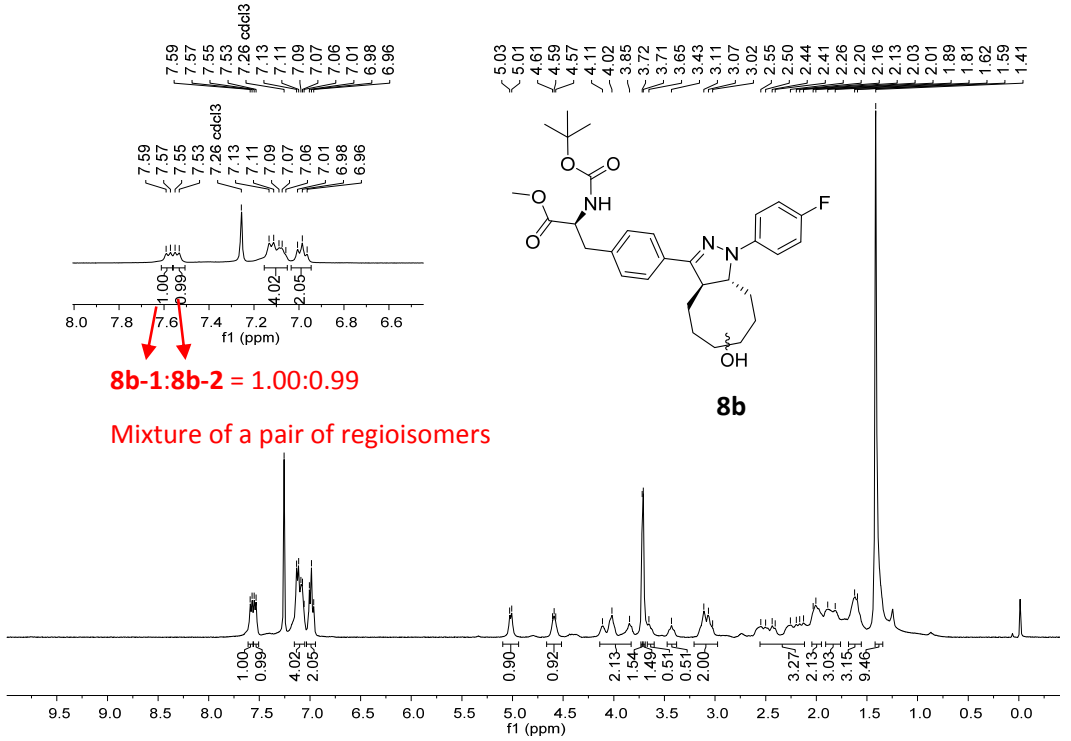

174.32
172.60
155.28
145.31
142.44
132.34
130.06
128.91
128.71
127.46
125.80
114.81
79.99
77.47 CDCl3
77.16 CDCl3
76.84 CDCl3
69.10
54.62
53.14
52.29
48.24
37.57
28.45
21.24
7f
f1 (ppm)


7.58
7.56
7.54
7.52
7.26 cdcl3
7.12
7.10
6.88
6.86
5.05
5.03
4.60
4.58
4.57
4.56
4.08
4.06
4.00
3.97
3.77
3.71
3.70
3.13
3.11
3.10
3.08
3.06
3.05
2.54
2.53
2.42
2.27
2.17
2.13
2.11
2.10
2.09
2.08
2.06
2.04 HDO
2.01 HDO
1.95
1.93
1.92
1.88
1.87
1.85
1.83
1.82
1.71
1.69
1.67
1.65
1.63
1.62
1.60 HDO
1.59
1.41
0.99
1.03
4.07
2.00
f1 (ppm)
8a
8a-1:8a-2 = 0.99:1.03
Mixture of a pair of regioisomers
0.99
1.03
4.07
2.00
0.91
0.95
2.06
3.00
1.50
1.53
0.50
0.50
2.01
2.20
3.01
3.21
3.17
9.33
f1 (ppm)



8a

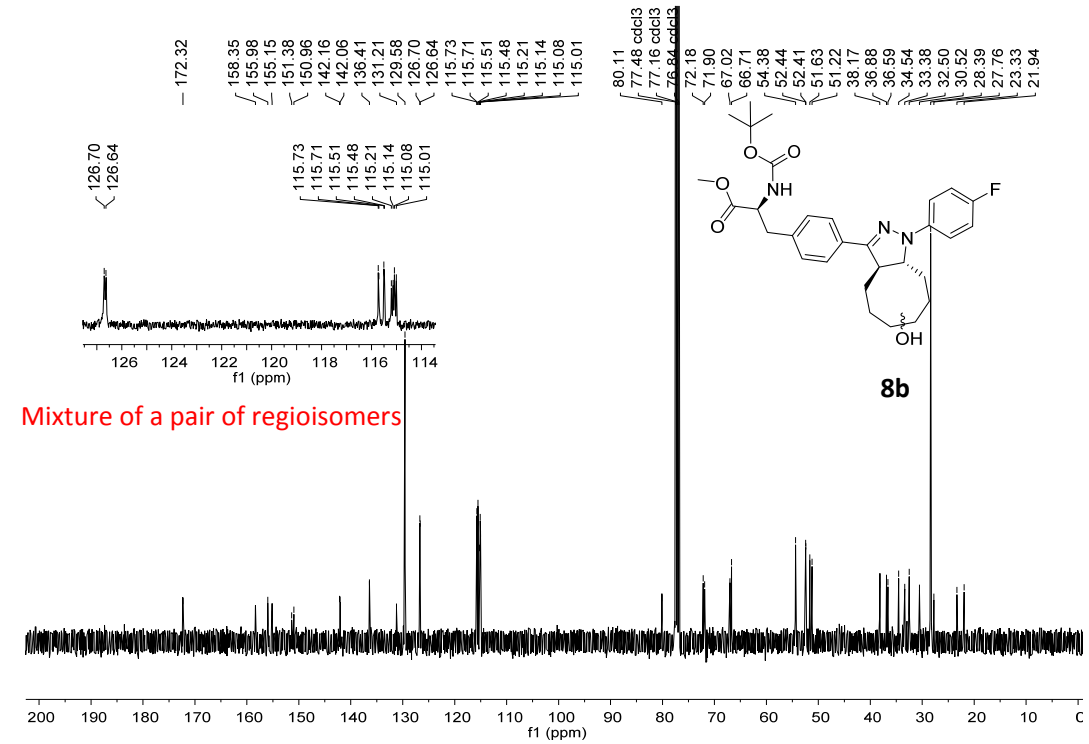
Mixture of a pair of regioisomers

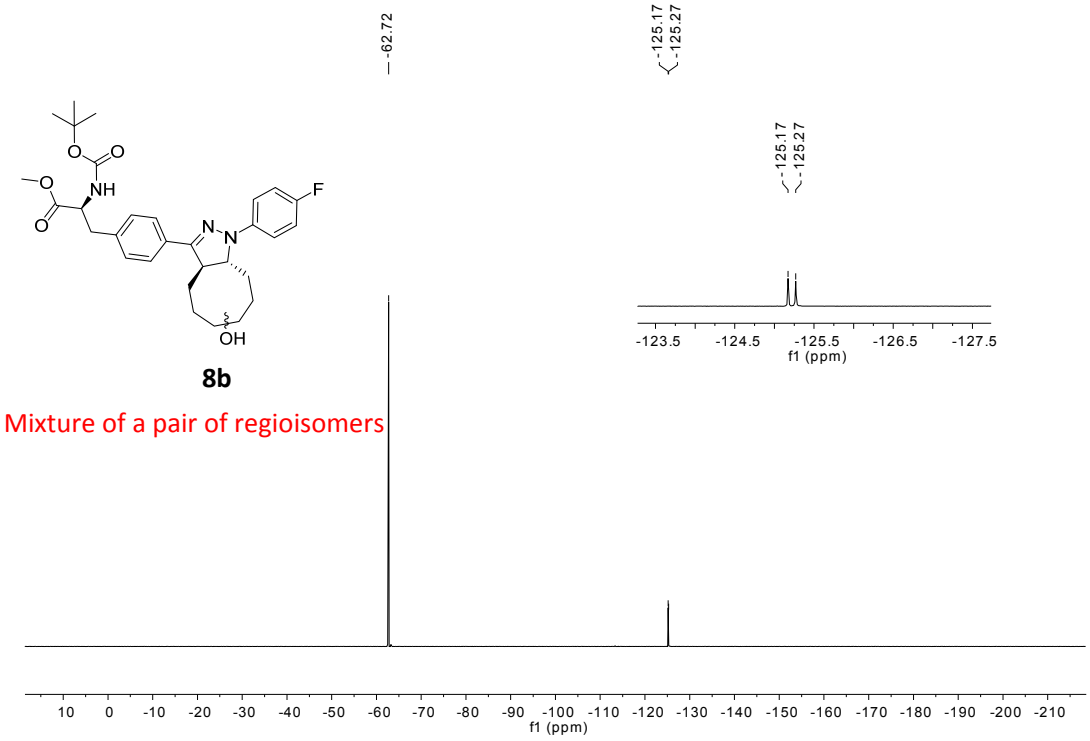


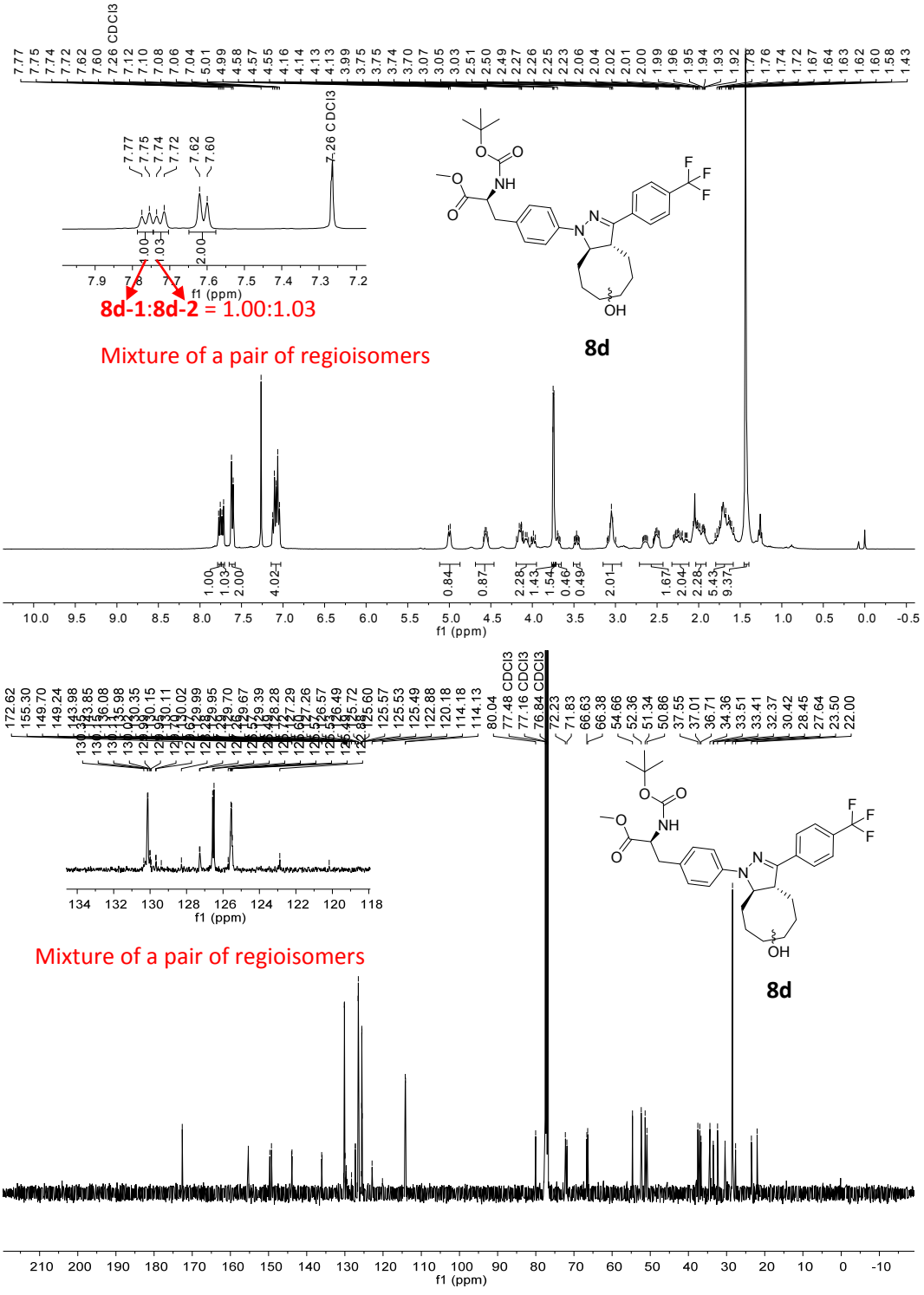
8b-1:**8b-2** = 1.00:0.99

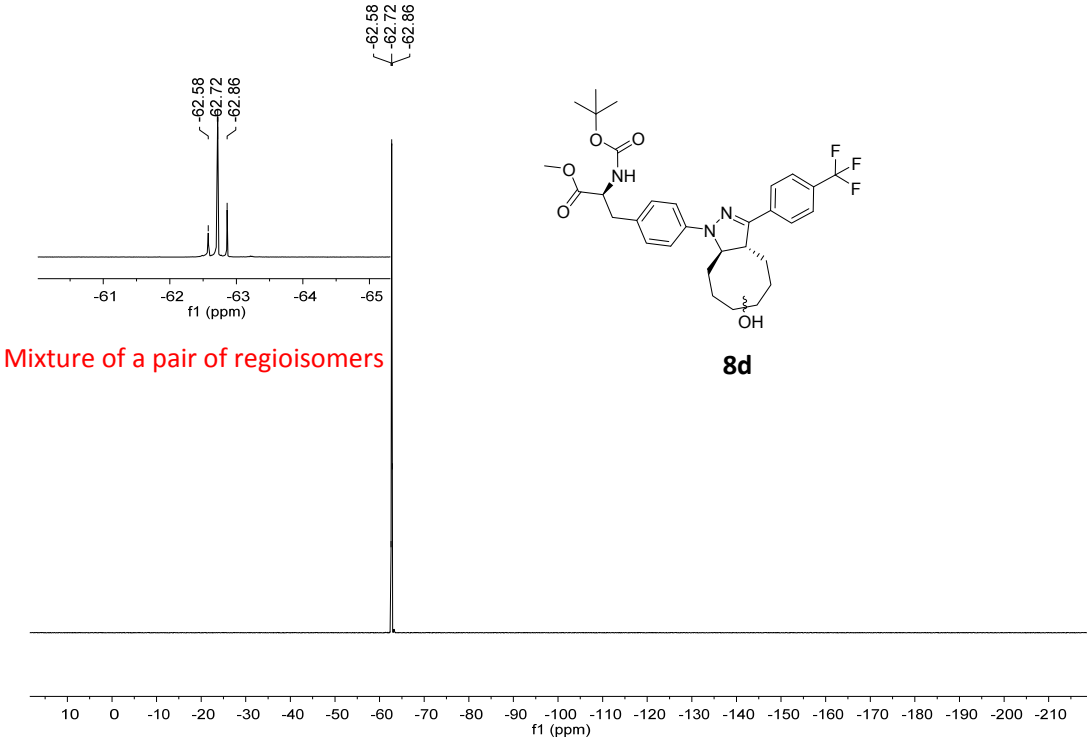
8b

Mixture of a pair of regioisomers


172.32
158.35
155.98
155.15
151.38
150.96
142.16
142.06
136.41
131.21
129.58
126.70
126.64
115.73
115.71
115.51
115.48
115.21
115.14
115.08
115.01
80.11
77.48 cdcl3
77.16 cdcl3
76.84 cdcl3
72.18
71.90
67.02
66.71
54.38
52.44
52.41
51.63
51.22
38.17
36.88
36.59
34.54
33.38
32.50
30.52
28.39
27.76
23.33
21.94
126.70
126.64
115.73
115.71
115.51
115.48
115.21
115.14
115.08
115.01
126
124
122
120
118
116
114
f1 (ppm)
Mixture of a pair of regioisomers
8b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

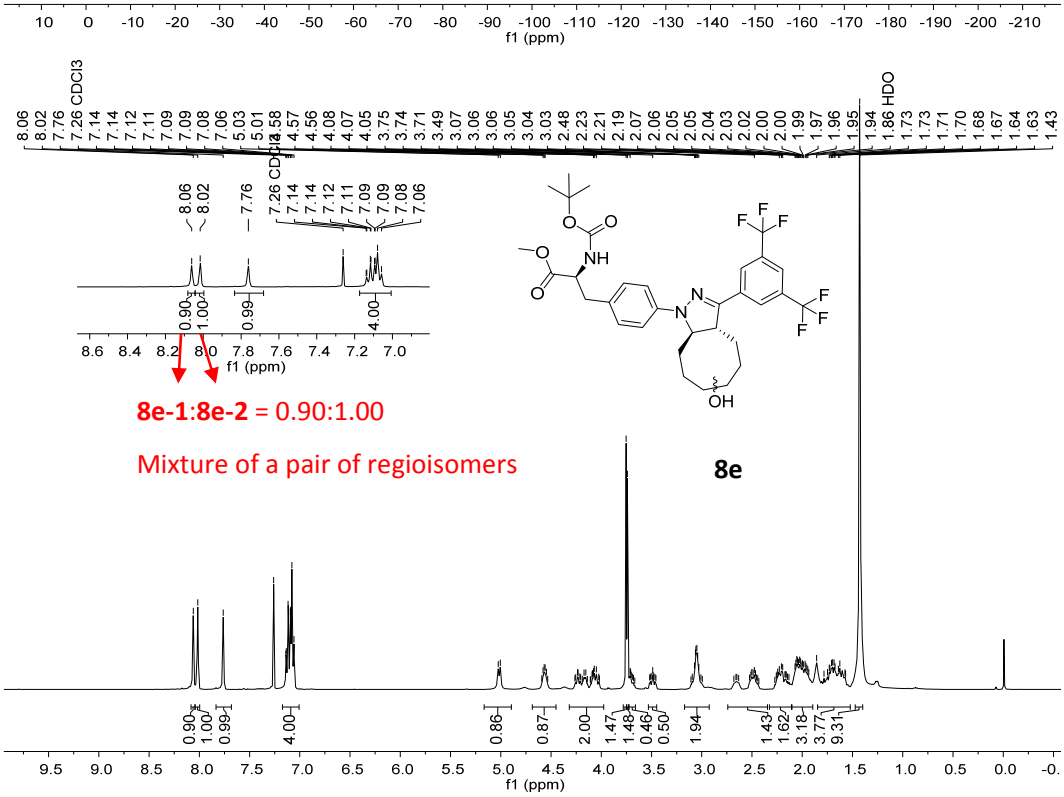

-62.72
-125.17
-125.27
-125.17
-125.27
-123.5
-124.5
-125.5
-126.5
-127.5
f1 (ppm)
8b
Mixture of a pair of regioisomers
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


8d-1:8d-2 = 1.00:1.03
Mixture of a pair of regioisomers
8d
f1 (ppm)
8d-1:8d-2 = 1.00:1.03
Mixture of a pair of regioisomers
8d
f1 (ppm)



Mixture of a pair of regioisomers

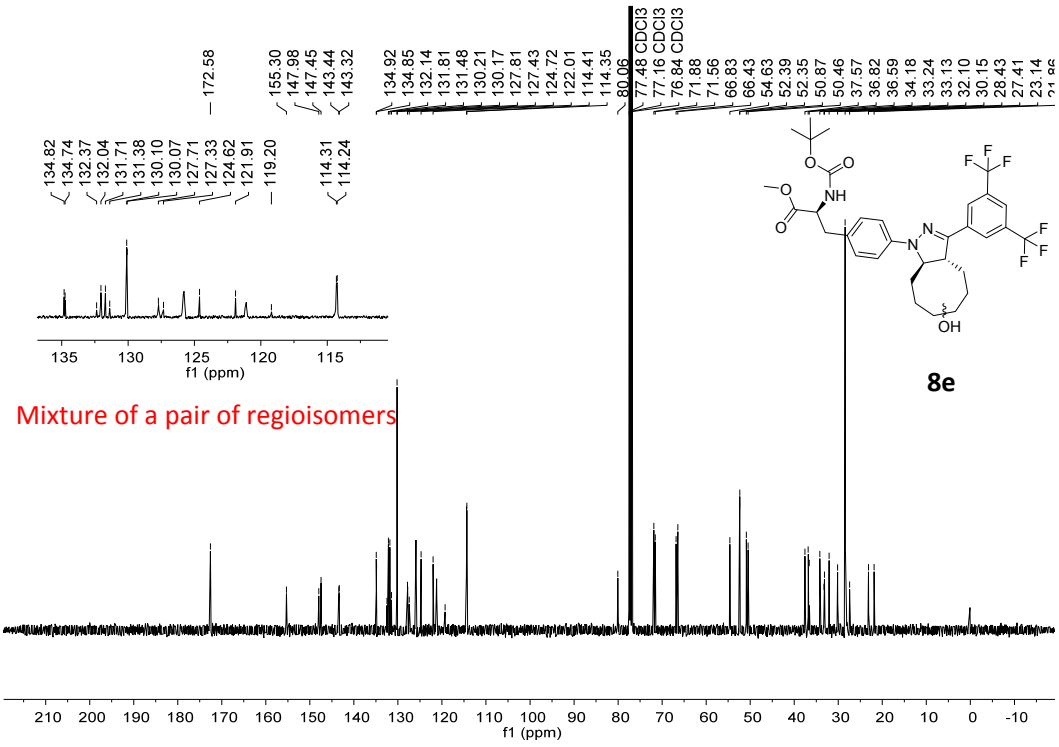
8d

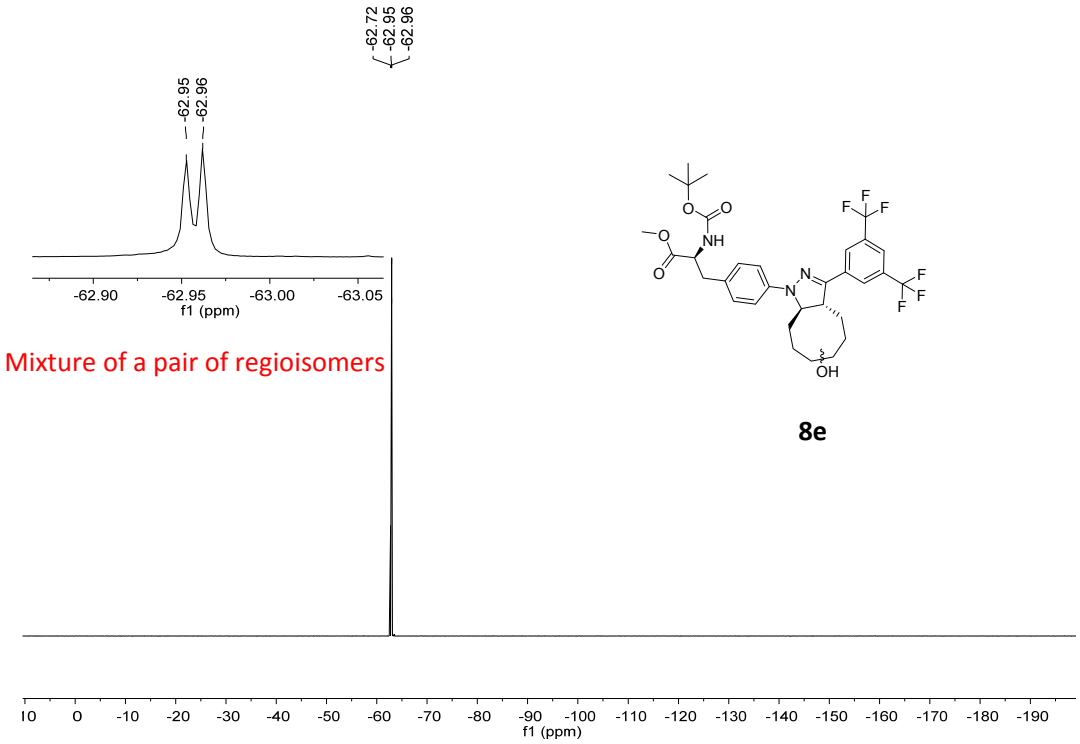


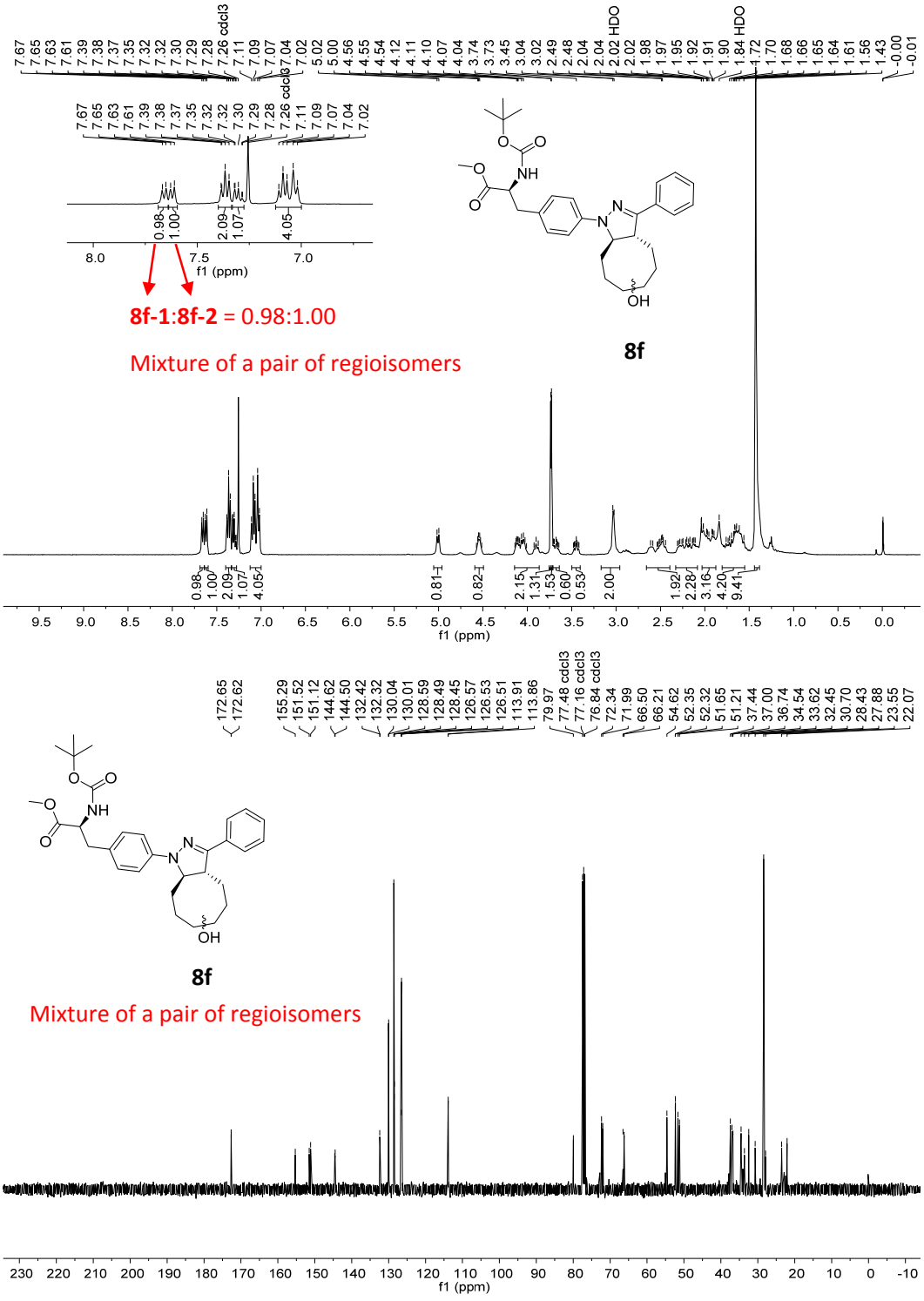
8e-1:**8e-2** = 0.90:1.00

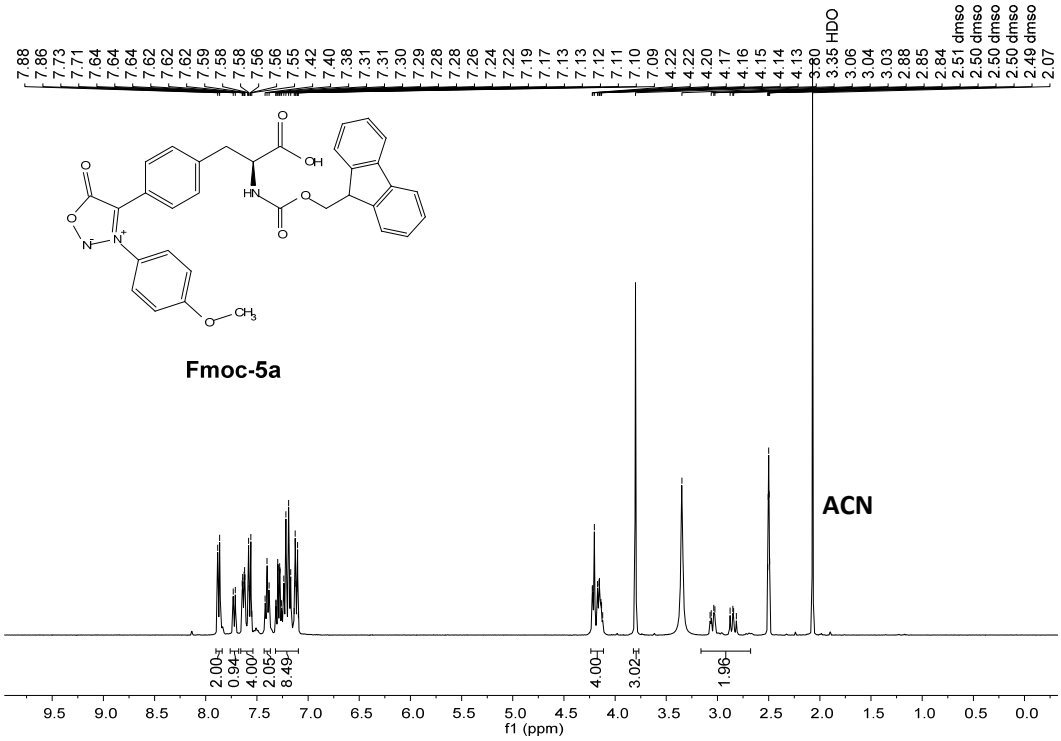
Mixture of a pair of regioisomers

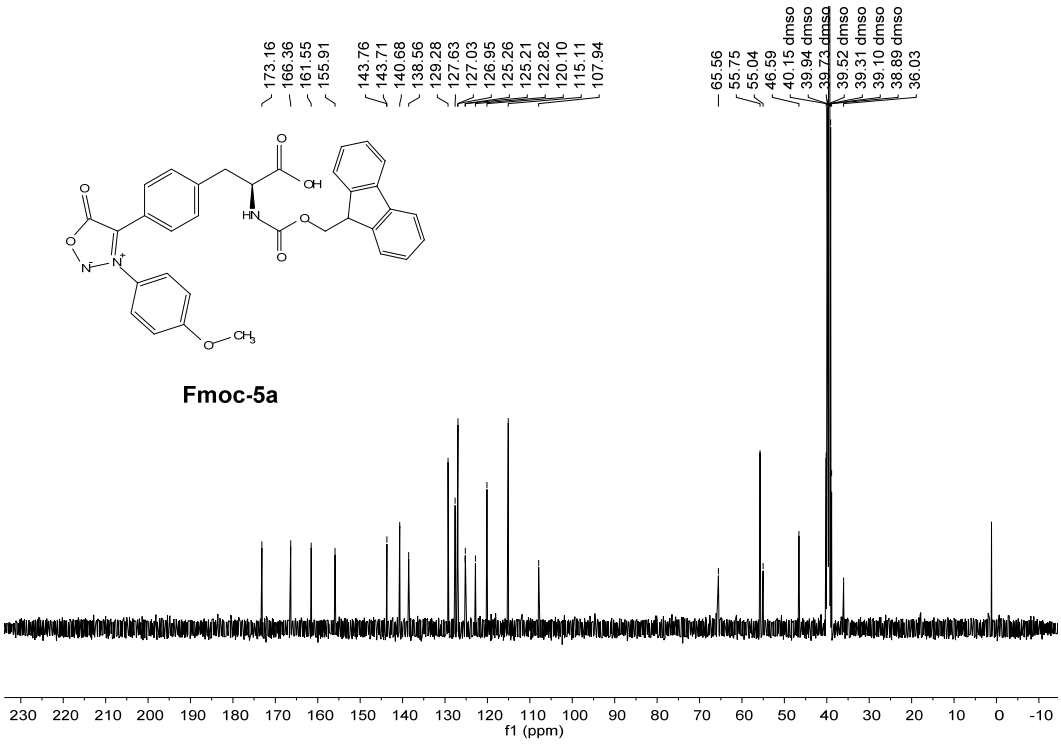
8e

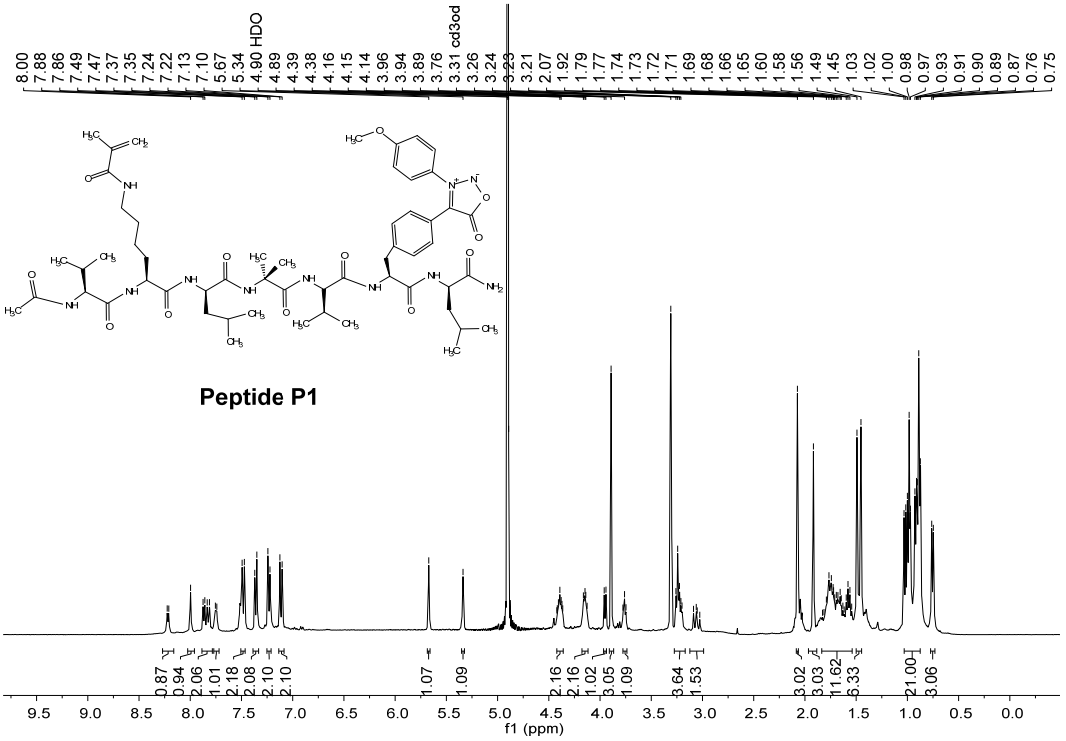

Mixture of a pair of regioisomers
8e

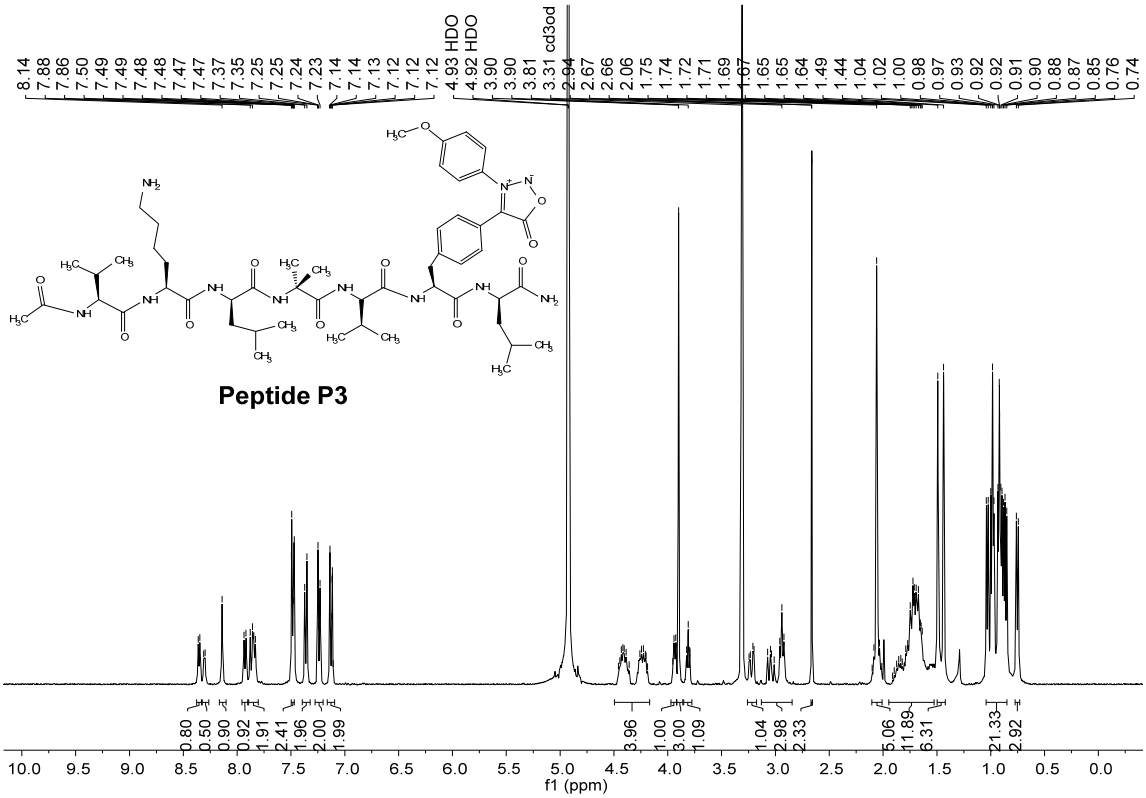

Mixture of a pair of regioisomers
8e

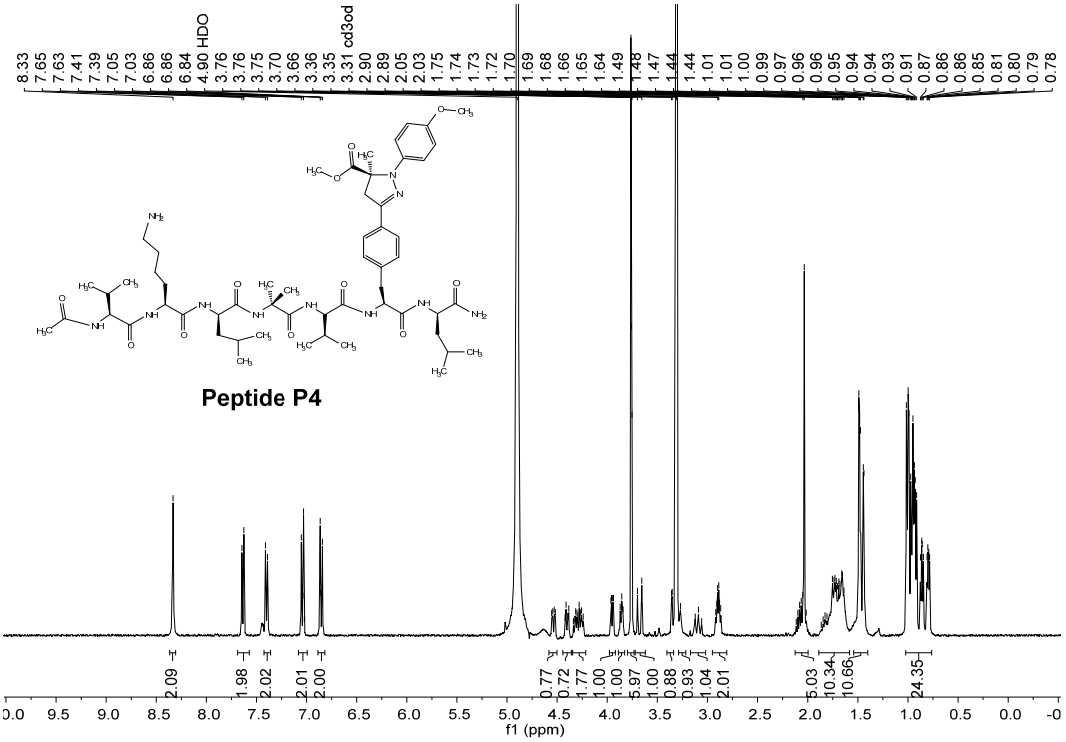

8f-1:8f-2 = 0.98:1.00
Mixture of a pair of regioisomers
8f
f1 (ppm)
8f
Mixture of a pair of regioisomers
f1 (ppm)

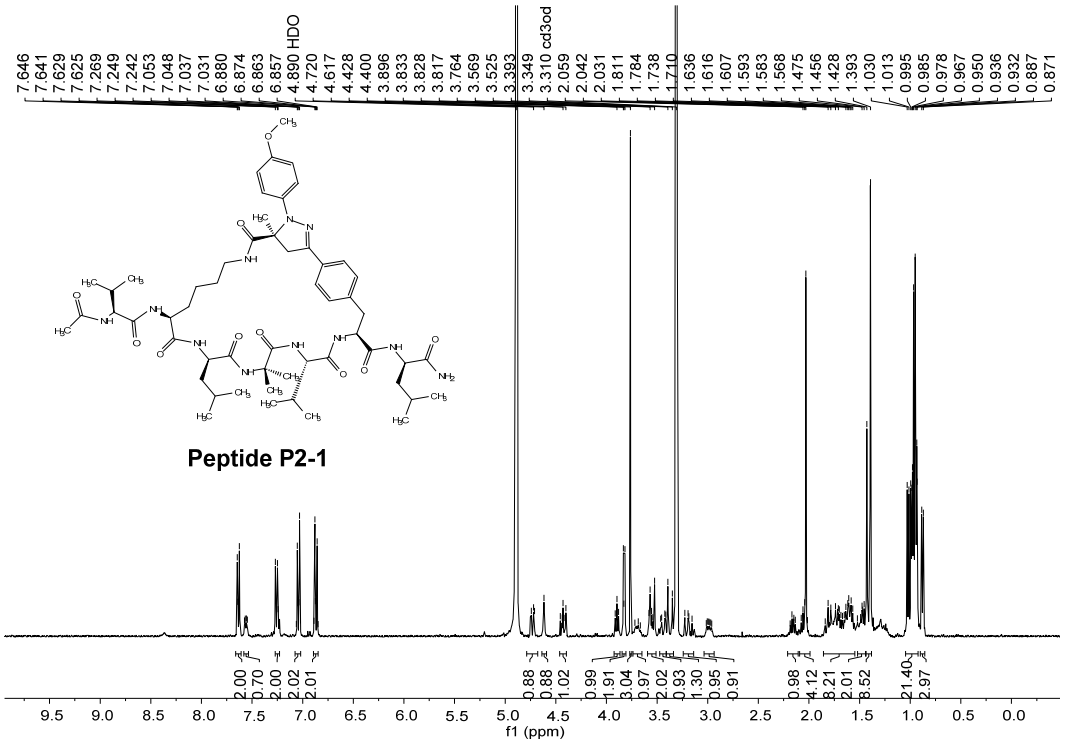

Fmoc-5a
ACN
f1 (ppm)

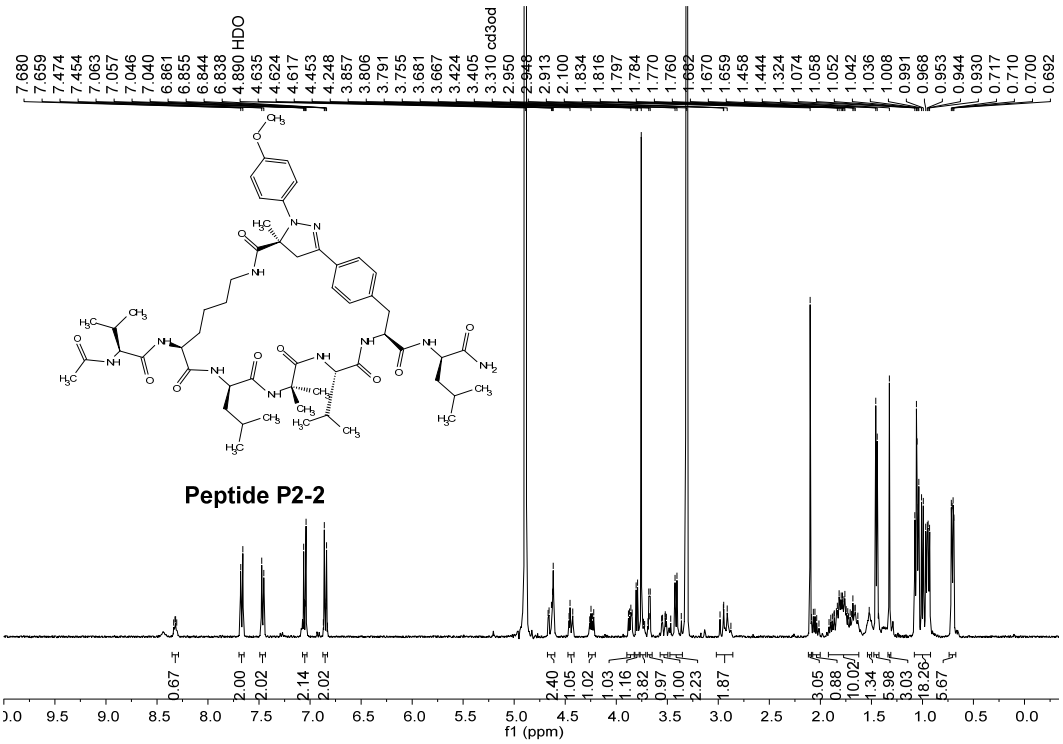

Fmoc-5a
f1 (ppm)


HDO
cd3od
Peptide P1
f1 (ppm)


HDO
HDO
cd3od
Peptide P3
f1 (ppm)


Peptide P4
f1 (ppm)


Peptide P2-1
f1 (ppm)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7.659
7.474
7.454
7.063
7.057
7.046
7.040
6.861
6.855
6.844
6.838
4.890 HDO
4.635
4.624
4.617
4.453
4.248
3.857
3.806
3.791
3.755
3.681
3.667
3.424
3.405
3.310 cd3od
2.950
2.948
2.913
2.100
1.834
1.816
1.797
1.784
1.770
1.760
1.682
1.670
1.659
1.458
1.444
1.324
1.074
1.058
1.052
1.042
1.036
1.008
0.991
0.968
0.953
0.944
0.930
0.717
0.710
0.700
0.692
Peptide P2-2
0.67
2.00
2.02
2.14
2.02
2.40
1.05
1.02
1.03
1.16
3.82
0.97
1.00
2.23
1.87
3.05
0.88
10.02
1.34
5.98
3.03
18.26
5.67
f1 (ppm)