

## Supporting Information

### Photoredox-catalysed Hydroaminoalkylation of on-DNA *N*-Arylamines

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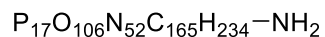
# Supporting Methods

## General Information

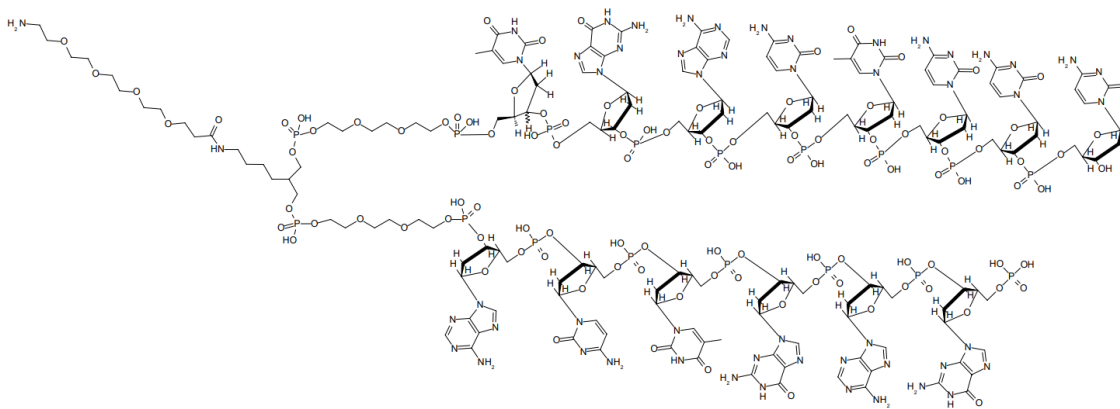
Purifications were performed by reverse-phase high-performance liquid chromatography (HPLC, Agilent 1260 Infinity II) using a C18 stationary phase (5 $\mu$ m Eclipse XDB-C18 9.4 x 250 mm). Liquid chromatography–mass spectrometry (LC–MS) analyses were performed using Agilent Infinity Lab LC/MSD system on a C18 stationary phase (HALO 400 A, ES-C18, 3.4  $\mu$ M, 2.1 x 30 mm).  $^1$ H NMR spectra were recorded at 400 MHz on a Bruker spectrometer. Processing of the spectra was performed with TopSpin software. Analytical thin-layer chromatography (TLC) was performed on aluminum plates pre-coated with silica gel 60F<sub>254</sub> as the adsorbent (Sigma-Aldrich, 1.05554). The developed plates were air-dried and exposed to UV light.

## DNA headpiece

DNA headpiece was prepared according to literature methods<sup>1</sup>.

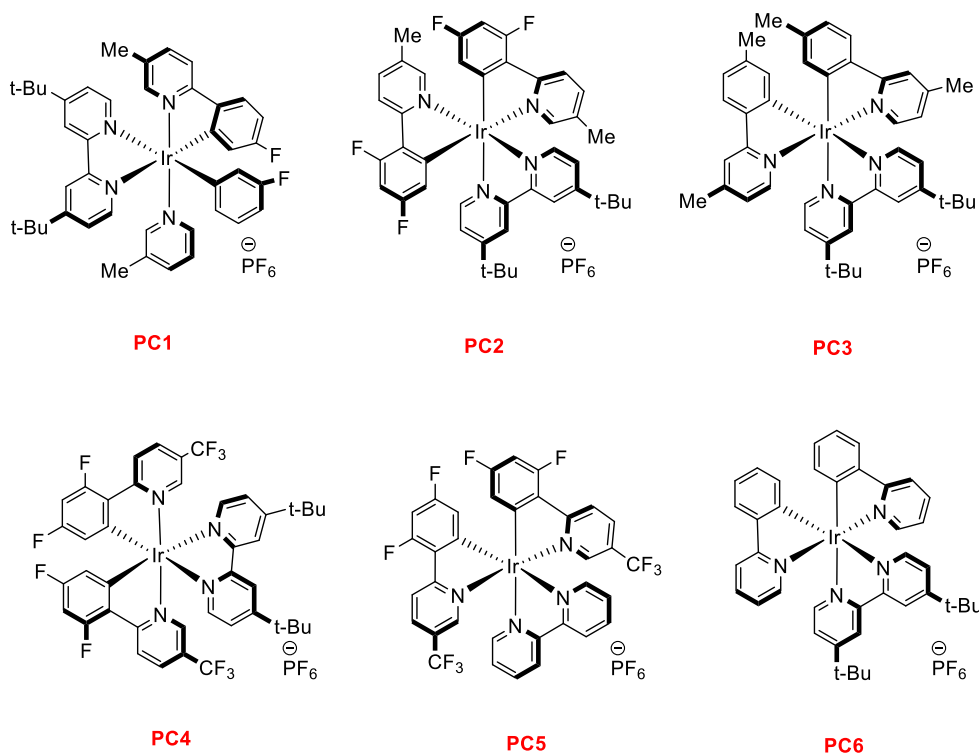


Molecular Weight: 5184 D



**Figure S1.** Structure of DNA headpiece

## Photocatalysts



**Figure S2.** Structures of photocatalysts **PC1-PC6**

**PC1** [(4,4'-di-tert-butyl-2,2'-bipyridine)-bis-(5-methyl-2-(5-fluoro-phenyl)-pyridine)-iridium(III)] hexafluorophosphate (Sigma-Aldrich, 908703)

**PC2** [4,4'-Bis(1,1-dimethylethyl)-2,2'-bipyridine-κN,κN]bis[3,5-difluoro-2-(5-methyl-2-pyridinyl)phenyl] iridium hexafluorophosphate (Strem Chemicals, 77-0330)

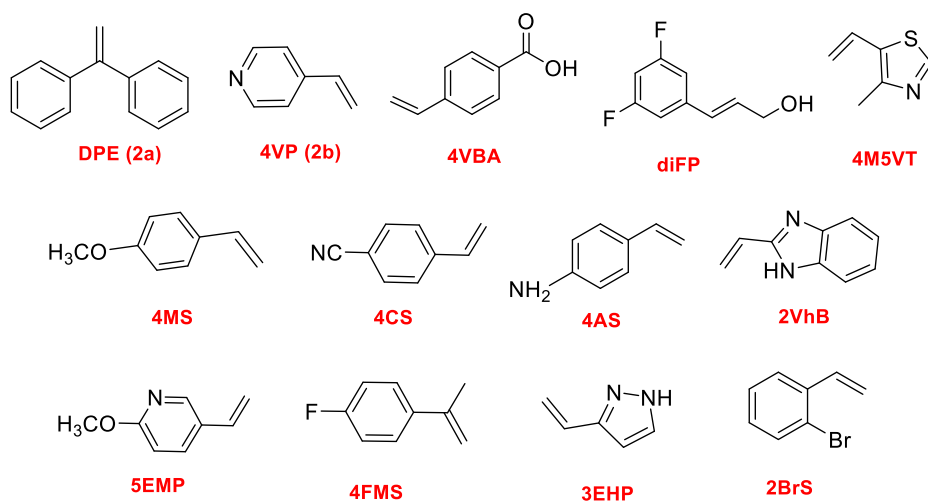
**PC3** 4,4'-Bis(t-butyl-2,2'-bipyridine]bis[5-methyl-2-(4-methyl-2-pyridinyl-κN)phenyl-κC]iridium hexafluorophosphate (Strem Chemicals, 77-0218)

**PC4** (4,4'-Di-t-butyl-2,2'-bipyridine)bis[3,5-difluoro-2-[5-(trifluoromethyl)-2-pyridinyl-κN]phenyl-κC]iridium(III) hexafluorophosphate (Strem Chemicals, 77-0425)

**PC5** (2,2'-Bipyridine)bis[3,5-difluoro-2-[5-(trifluoromethyl)-2-pyridinyl-κN]][phenyl-κC]iridium(III) hexafluorophosphate (Strem Chemicals, 77-0220)

**PC6** (4,4'-Di-t-butyl-2,2'-bipyridine)bis[2-(2-pyridinyl-κN)phenyl-κC]iridium(III) hexafluorophosphate (Strem Chemicals, 77-0410)

## Vinylarenes

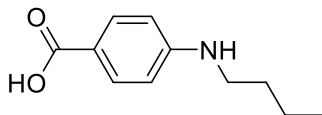


**Figure S3.** Structures of vinylarenes

<b>DPE (2a)</b>	1,1-Diphenylethylene (Sigma-Aldrich, D206806)
<b>4VP (2b)</b>	4-Vinylpyridine (Sigma-Aldrich, V3204-5ML)
<b>5EMP</b>	5-Ethenyl-2 methoxy-pyridine (Combi Blocks, QE-5274)
<b>4M5VT</b>	4-Methyl-5-vinylthiazole (Combi Blocks, OR-0987)
<b>diFP</b>	3-(3,5-Difluorophenyl)propenol (Combi Blocks, SS-9410)
<b>4MS</b>	4-Methoxystyrene (Combi Blocks, QB-0479)
<b>4AS</b>	4-Aminostyrene (Combi Blocks, 4640)
<b>4CS</b>	4-Cyanostyrene (Combi Blocks, QF-7194)
<b>2VhB</b>	2-Vinyl-1h-benzimidazole (Combi Blocks, OR-7720)
<b>2BrS</b>	2-Bromostyrene (Combi Blocks, OT-0650)
<b>4VBA</b>	4-Vinylbenzoic acid (Combi Blocks, ST-3506)
<b>3EHP</b>	3-Ethenyl-1h-pyrazole (Combi Blocks, QE-0558)
<b>4FMS</b>	4-Fluoro- $\alpha$ -methylstyrene (Combi Blocks, QC-4533)

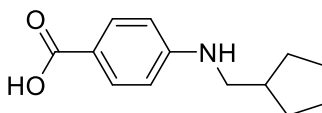
## Synthetic procedures

### 4-(N-Butylamino)benzoic acid



4-(N-Butylamino)benzoic acid was made by a procedure adapted from literature<sup>2</sup>: 4-Aminobenzoic acid (Sigma-Aldrich, A9878) (0.5 g, 3.65 mmol), butyraldehyde (Sigma-Aldrich, 8.01555.0100) (0.428 mL, 4.75 mmol, 1.3 eq) and 2-Methylpyridine borane complex (Sigma-Aldrich, 654213) (0.411 g, 3.76 mmol, 1.03 eq) were stirred at room temperature in methanol (5 mL) for 14 h. TLC showed that the reaction was complete (TLC system: 10% MeOH/DCM). The reaction mixture was then concentrated and partitioned between EtOAc (7 mL) and aqueous acid (1N HCl, 2 x 5 mL). The organic fractions were combined, dried over MgSO<sub>4</sub> (Sigma-Aldrich, MX0075-1) and concentrated to yield the product as a white powder. NMR spectrum matched literature data: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.92 (d, J = 8.8 Hz, 2H), 6.55 (d, J = 8.8 Hz, 2H), 3.18 (t, J = 7.2 Hz, 2H), 1.63 (m, 2H), 1.44 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H). HRMS Calcd for C<sub>11</sub>H<sub>16</sub>NO<sub>2</sub> (M+H): 194.1181 Found: 194.1158.

### 4-[(Cyclopentylmethyl)amino]benzoic acid



4-Aminobenzoic acid (Sigma-Aldrich, A9878) (0.25 g, 1.823 mmol), cyclopentanecarboxaldehyde 95% (Sigma-Aldrich, 526037) (0.24 mL, 2.188 mmol, 1.2 eq) and 2-Methylpyridine borane complex (Sigma-Aldrich, 654213) (0.22 g, 2 mmol, 1.1 eq) were stirred at room temperature in methanol (10 mL) for 14 hours. TLC of the top liquid showed that the reaction was complete (TLC system: 40% EtOAc/Hex). The resulting precipitate was collected, and the filtrate was acidified with 1 N hydrochloric acid to induce further precipitation. The solids were combined and dried under high vacuum to yield target material as a white powder. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.92 (d, J = 8.9 Hz, 2H), 6.56 (d, J = 8.9 Hz, 2H), 3.10 (d, J = 7.2 Hz, 2H), 2.17 (sep, J = 7.5, 1H), 1.88-1.79 (m, 2H), 1.71-1.52 (m, 4H), 1.32-1.21 (m, 2H). <sup>13</sup>C NMR (MHz, CDCl<sub>3</sub>): δ 172.08, 152.96, 132.47, 117.05, 111.44, 48.81, 39.46, 30.73, 25.38. HRMS Calcd for C<sub>13</sub>H<sub>18</sub>NO<sub>2</sub> (M+H): 220.1337 Found: 220.1326 Calcd for C<sub>13</sub>H<sub>17</sub>NaNO<sub>2</sub> (M+Na): 242.1156 Found: 242.1146

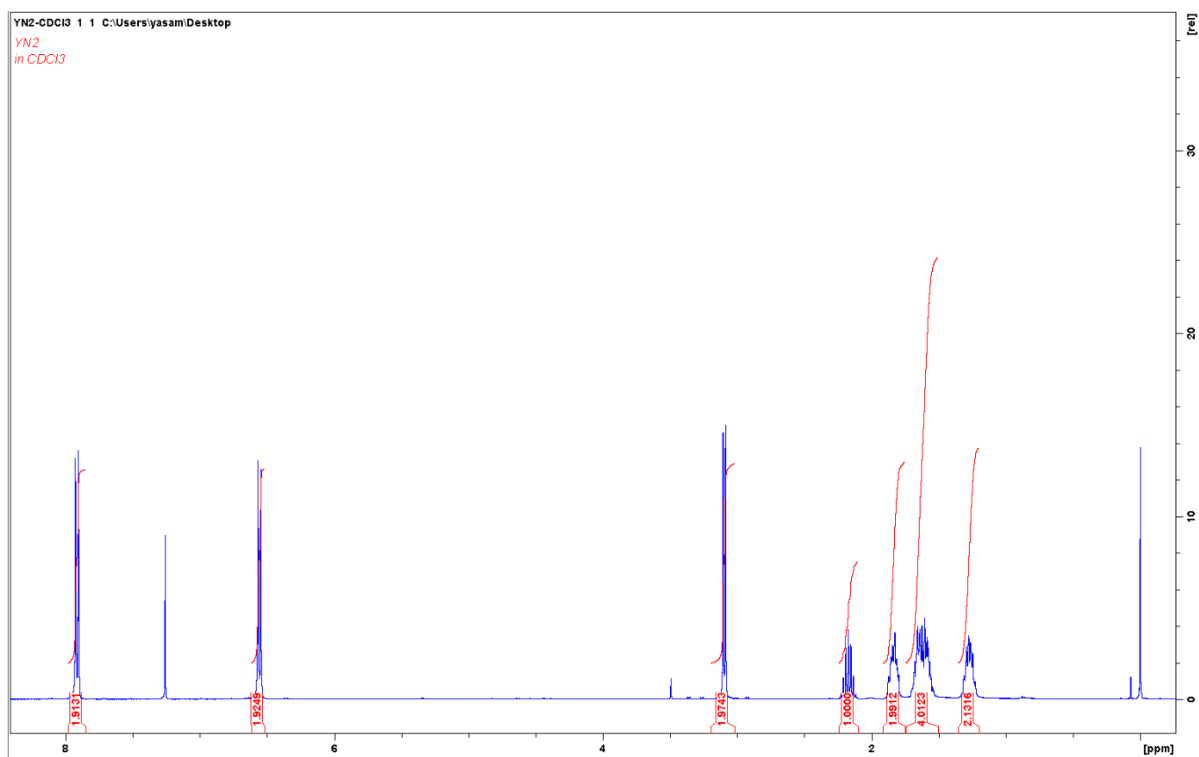


Figure S4. <sup>1</sup>H NMR spectrum of 4-[(Cyclopentylmethyl)amino]benzoic acid

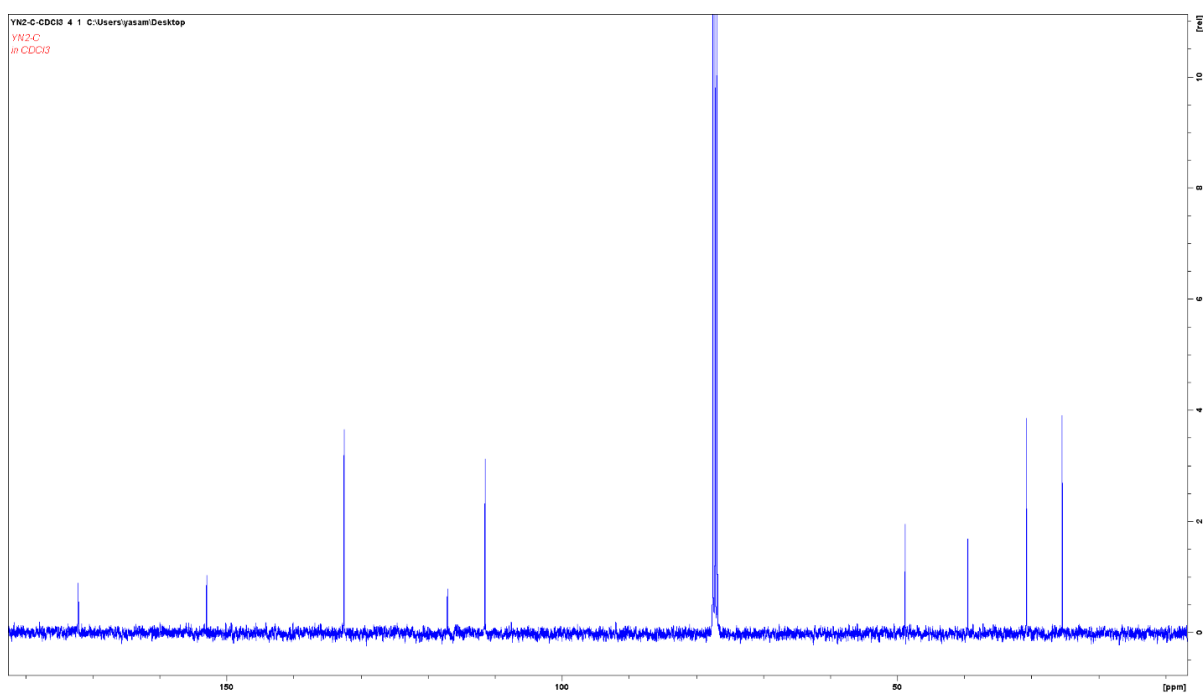
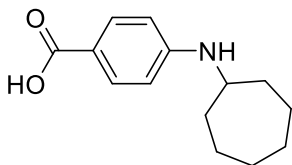


Figure S5. <sup>13</sup>C NMR spectrum of 4-[(Cyclopentylmethyl)amino]benzoic acid

#### 4-(Cycloheptylamino)benzoic acid



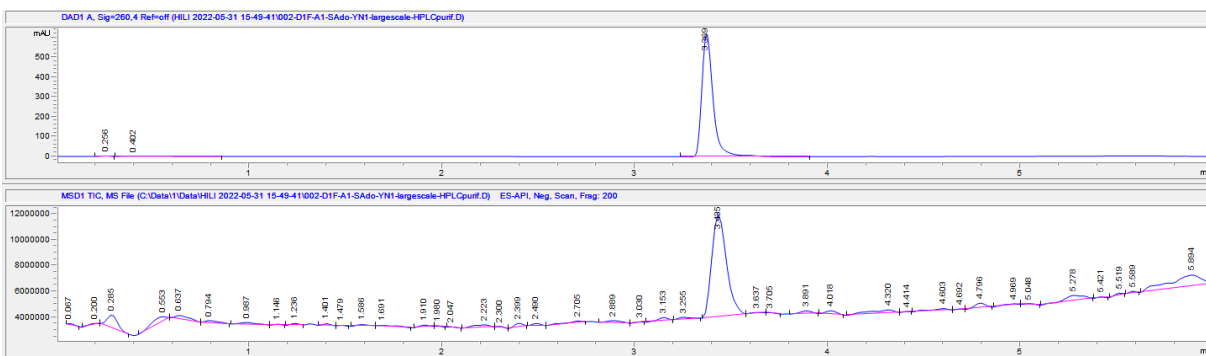
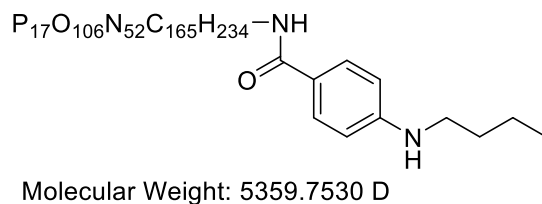
4-(Cycloheptylamino)benzoic acid was made by a procedure adapted from literature<sup>3</sup>: 4-amino benzoic acid (Sigma-Aldrich, A9878) (0.137 g, 1 mmol), cycloheptanone (Sigma-Aldrich, C99000) (236  $\mu$ L, 2 mmol), and glacial AcOH (Fisher Scientific, A38-212) (300  $\mu$ L, 5 mmol) were mixed in 1,2-dichloroethane (4.5 mL). Sodium triacetoxyborohydride (Sigma-Aldrich, 316393) (0.6 g, 2.8 mmol) was added to the above solution and the reaction mixture stirred at room temperature for 27 h. Then cycloheptanone (59  $\mu$ L, 0.5 mmol), glacial AcOH (75  $\mu$ L, 1.25 mmol), 1,2-dichloroethane (1.5 mL) and sodium triacetoxyborohydride (0.15 g, 0.7 mmol) were again added to the reaction mixture and the reaction stirred at room temperature for another 5 h after which TLC showed that the reaction was complete (TLC system: 40% Hex/EtOAc). The reaction was quenched with saturated aqueous NaHCO<sub>3</sub> (Fisher Chemical, S233-500), then the product was extracted with EtOAc (3  $\times$  7.5 mL). The EtOAc extracts were combined, dried over MgSO<sub>4</sub> (Sigma-Aldrich, MX0075-1) and concentrated to yield the crude product as a white powder. The product was triturated with ether/hexane (7:3) and the solid was filtered. The pure sample was then recrystallized from EtOAc/hexane. NMR spectrum matched literature data: <sup>1</sup>H NMR (DMSO-d<sub>6</sub>):  $\delta$  11.95 (s, 1H), 7.68 (d, J = 8.6 Hz, 2H), 6.52 (d, J = 8.6 Hz, 2H), 6.29 (d, J = 7.4 Hz, 1H), 3.45 (bs, 1H), 1.94-1.82 (m, 2H), 1.71-1.39 (m, 10H). HRMS Calcd for C<sub>14</sub>H<sub>20</sub>NO<sub>2</sub> (M+H): 234.1494 Found: 234.1494. Calcd for C<sub>14</sub>H<sub>19</sub>NaNO<sub>2</sub> (M+Na): 256.1314 Found: 256.1317

#### General procedure for the preparation of DNA conjugates

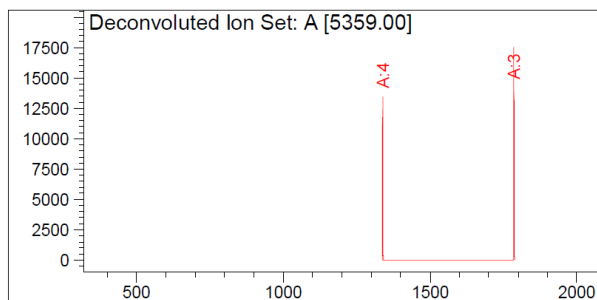
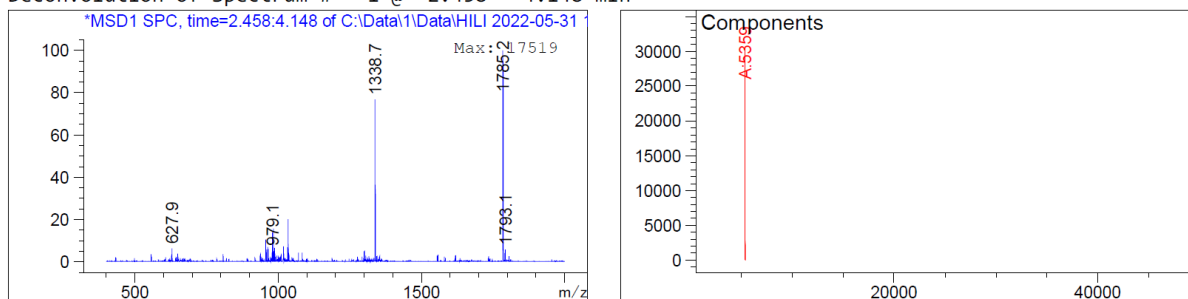
HATU (Combi Blocks, OR-0618) (400  $\mu$ L of 0.2 M in DMF), DIPEA (Alfa Aesar, A11801) (400  $\mu$ L of 0.2 M in DMF) and the respective carboxylic acid (400  $\mu$ L of 0.2 M in DMF) were mixed. The stock was cooled at 4 °C for 10 minutes then transferred to 1000  $\mu$ L of 1 mM solution of DNA headpiece in 250 mM sodium phosphate buffer (pH=9.4). The resulting solution was shaken at room temperature. After 16 h the DNA was recovered from the mixture by ethanol precipitation and then purified by HPLC.

## DNA conjugate 1a:

1a was synthesized according to the general procedure using 4-(N-Butylamino) benzoic acid.



Deconvolution of Spectrum # 1 @ 2.458 - 4.148 min



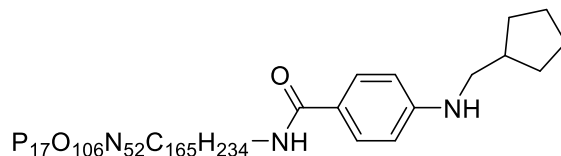
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5359.00	30540	100.00

Figure S6. Deconvoluted LCMS data for DNA conjugate 1a

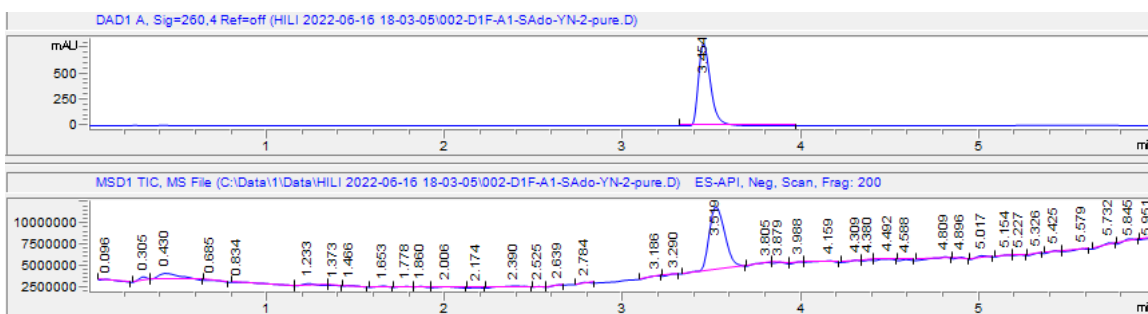


## DNA conjugate 1b:

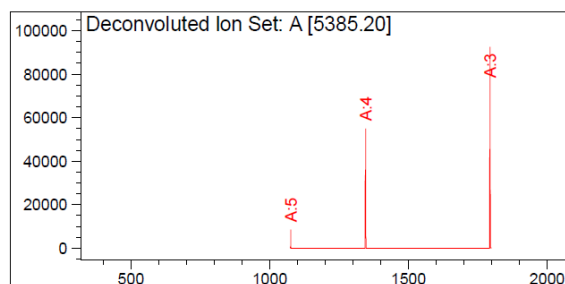
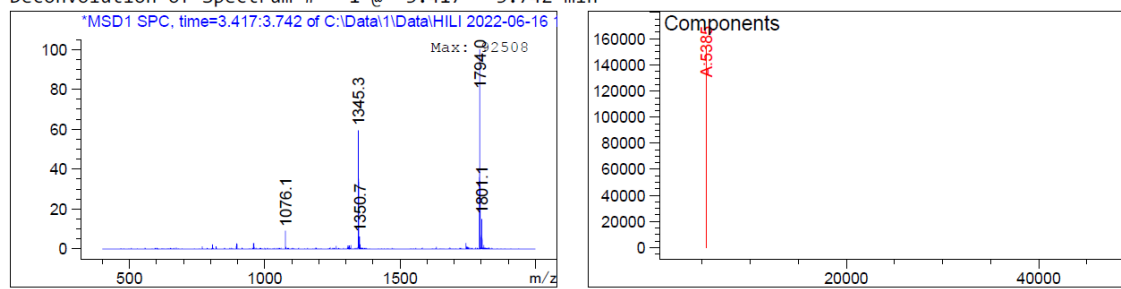
**1b** was synthesized according to the general procedure using 4-[(Cyclopentyl methyl) amino] benzoic acid.



Molecular Weight: 5385.7910 D



Deconvolution of Spectrum # 1 @ 3.417 - 3.742 min

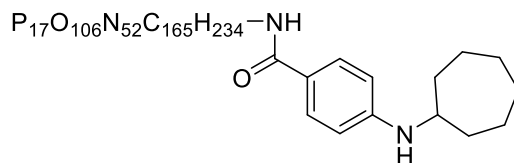


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5385.20	153884	100.00

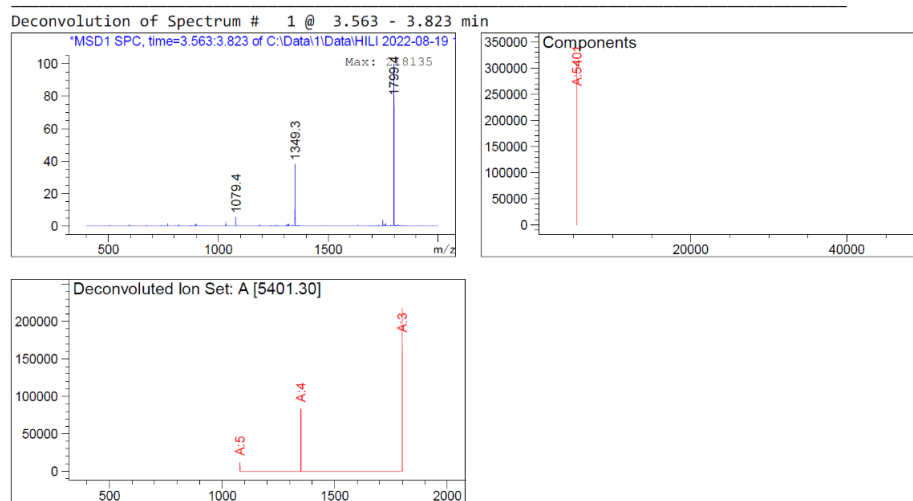
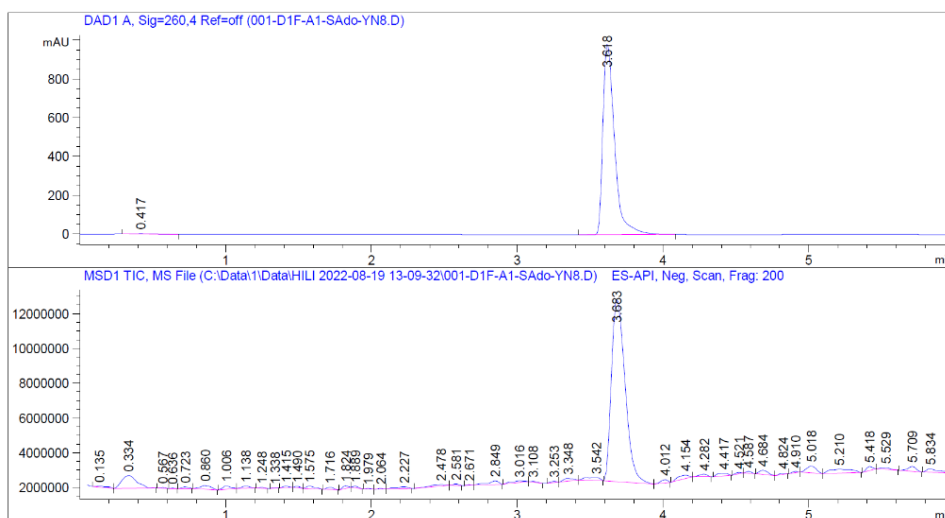
**Figure S7.** Deconvoluted LCMS data for DNA conjugate **1b**

## DNA conjugate 1c:

**1c** was synthesized according to the general procedure using 4-(Cycloheptylamino) benzoic acid.



Molecular Weight: 5399.8180 D

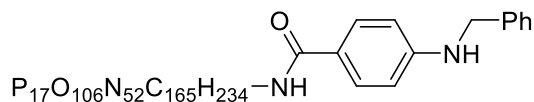


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5401.30	312393	100.00

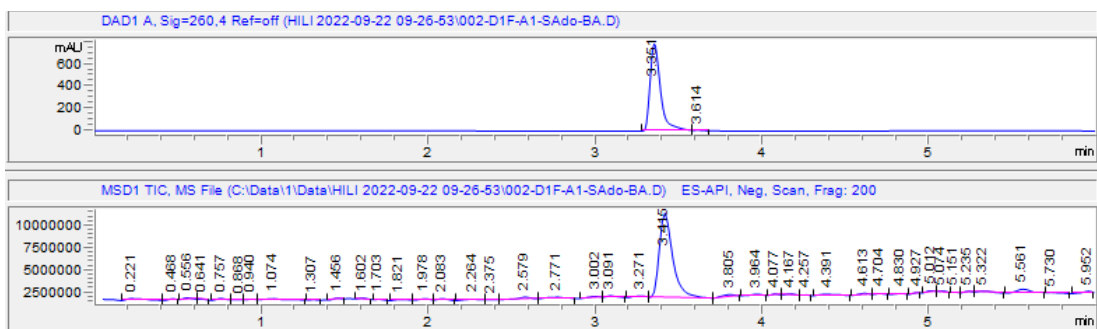
**Figure S8.** Deconvoluted LCMS data for DNA conjugate **1c**

## DNA conjugate 1d:

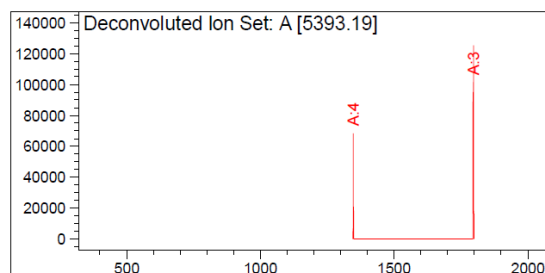
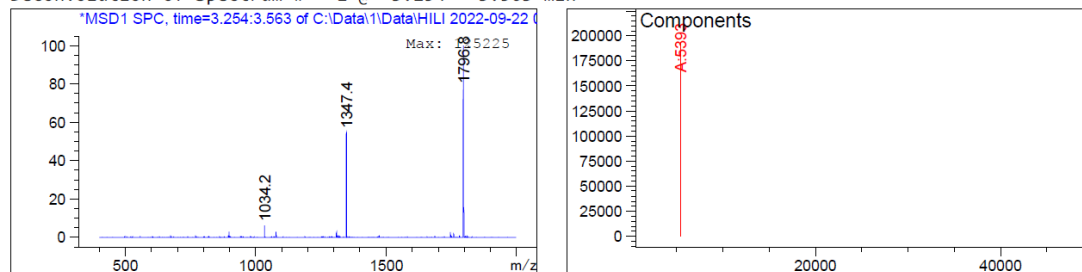
**1d** was synthesized according to the general procedure using 4-(Benzylamino) benzoic acid (Sigma Aldrich, L127728).



Molecular Weight: 5393.7700 D



Deconvolution of Spectrum # 1 @ 3.254 - 3.563 min

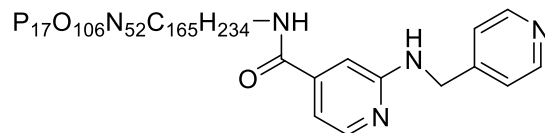


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5393.19	192952	100.00

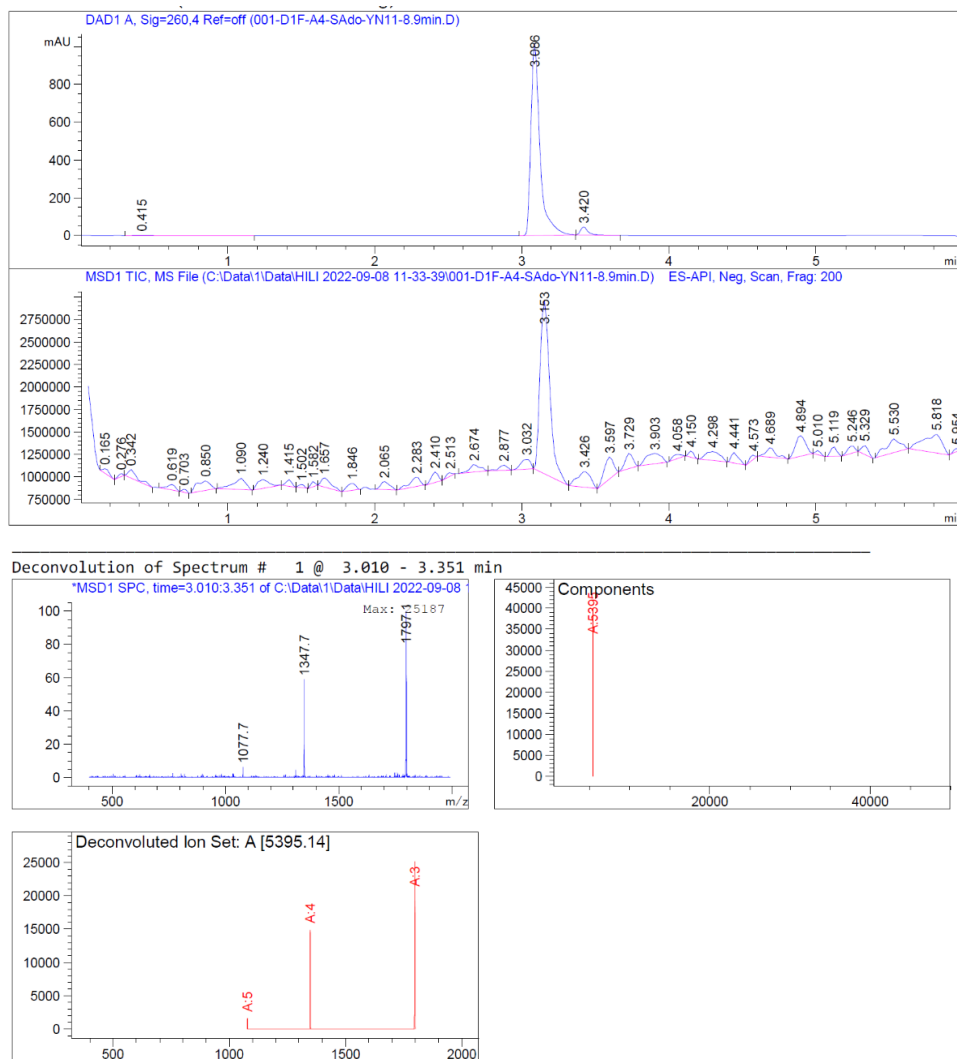
**Figure S9.** Deconvoluted LCMS data for DNA conjugate **1d**

## DNA conjugate 1e:

**1e** was synthesized according to the general procedure using 2-[(4-pyridinylmethyl) amino] isonicotinic acid (Sigma-Aldrich, CDS021130).



Molecular Weight: 5395.7460 D

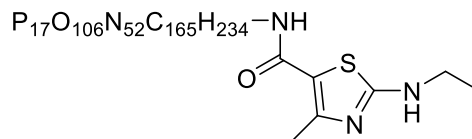


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5395.14	39883	100.00

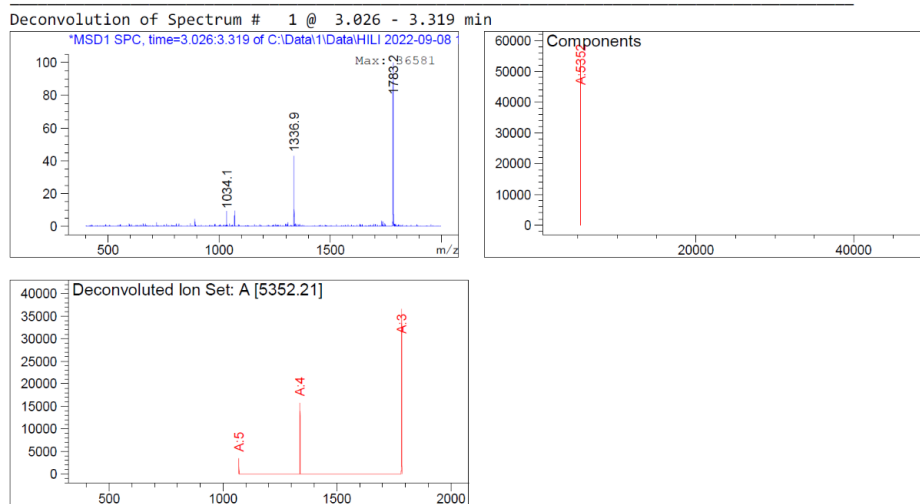
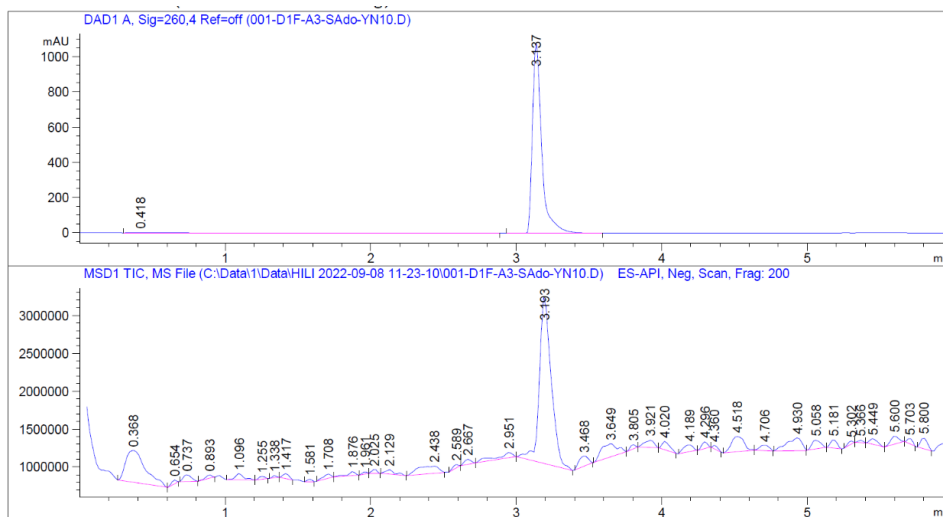
**Figure S10.** Deconvoluted LCMS data for DNA conjugate **1e**

## DNA conjugate 1f:

**1f** was synthesized according to the general procedure using 2-(Ethylamino)-4-methyl-1,3-thiazole-5-carboxylic acid (Sigma-Aldrich, CBR00568).



Molecular Weight: 5352.7360 D



Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5352.21	53606	100.00

**Figure S11.** Deconvoluted LCMS data for DNA conjugate **1f**

## HPLC purification

HPLC purifications were conducted on a 1260 Infinity II LC System from Agilent.

### HPLC method:

flow rate: 4 mL/min

Detection wavelength: 260 nm

mobile phase A: 0.1 M triethylammonium acetate (TEAA)

mobile phase B: Acetonitrile

Elapsed time (min)	%B
0	10
10	20
23	45
26	80
28	80
29	10
31	10

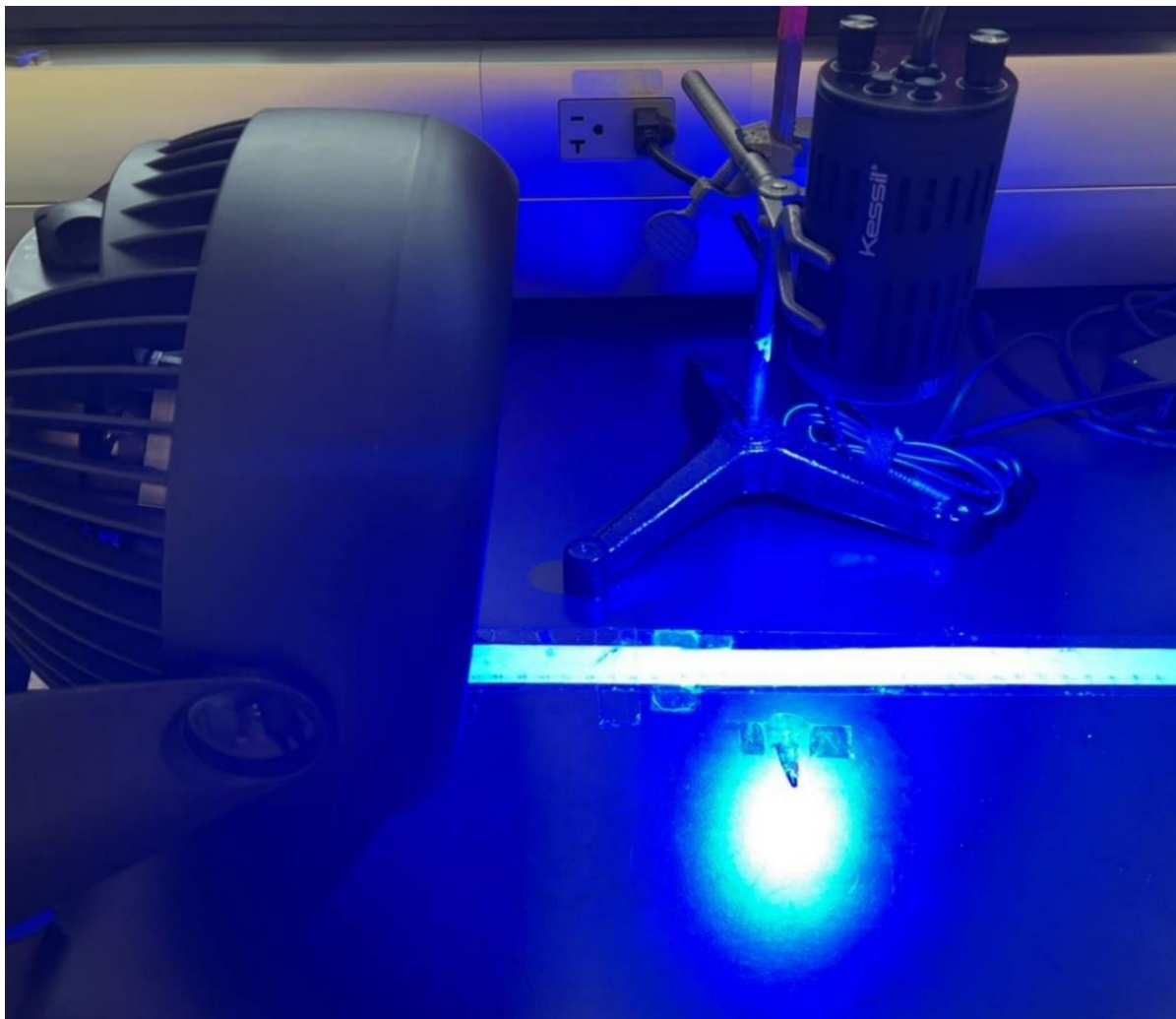
Column: Agilent 5 $\mu$ m Eclipse XDB-C18 9.4 x 250 mm

### General procedure for ethanol precipitation

To the reaction mixture containing DNA, was added 10% (V/V) 4 M NaCl and 3 times the volume ethanol. The solution was placed on dry ice for 1 hour and then centrifuged at 15000 rpm, at 4 °C for 30 minutes. the supernatant was removed, and the pellet was washed with 75% aq. ethanol and then air-dried.

## Photocatalysis reaction setup

In a PCR tube was added 10 nmol of DNA conjugate (in 10  $\mu\text{L}$   $\text{H}_2\text{O}$ ), quinuclidine (TCI America, Q0062) (10  $\mu\text{L}$  of 500 mM in DMF), alkene (10  $\mu\text{L}$  of 250 mM in DMF), and Iridium catalyst (10  $\mu\text{L}$  of 1 mM in DMF). The solution was degassed\* in glove box for 2 hours and then placed approximately 10 cm from blue light (highest intensity) with cooling. After 1.5 h, the DNA was recovered from the reaction mixture by Ethanol precipitation. Pellet was air-dried and resuspended in 100  $\mu\text{L}$  water and 5  $\mu\text{L}$  of the resulting solution was injected to LCMS.



**Reaction setup:** Sample was secured 10 cm from Kessil Tuna Blue A160WE lamp set to the highest intensity. A fan was situated directly behind the reaction vessel to dissipate heat.

\* Note that oxygen had a detrimental effect on the yield of the reaction. We observed that when the mixture was not thoroughly degassed prior to irradiation with blue light, the product was contaminated with *N*-dealkylated starting material.

## LCMS analysis

LCMS analyses were performed using Agilent Infinity Lab LC/MSD system.

### LCMS method:

Flow rate: 0.5 mL/min

Detection wavelength: 260 nm

mobile phase A: 10  $\mu$ M EDTA, 0.38% TEAA pH 7, 0.75% HFIP, in 90:10 Methanol:MilliQ water

Mobile phase B: 10  $\mu$ M EDTA, 0.38% TEAA pH 7, 0.75% HFIP, in MilliQ water

Elapsed time (min)	%B
0	90
4	10
5	90
6	90

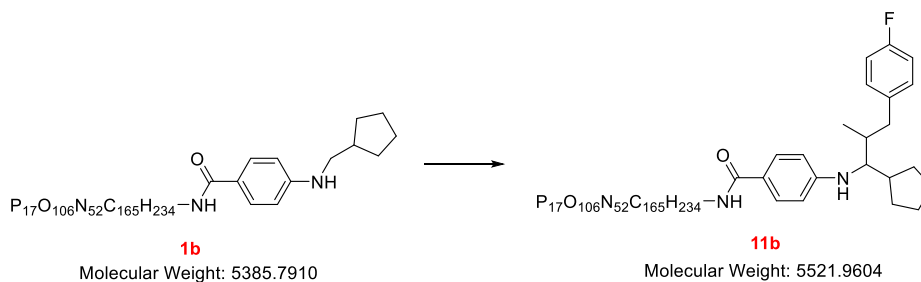
Column: HALO 400 A, ES-C18, 3.4  $\mu$ M, 2.1 x 30 mm

### Conversion calculations for on-DNA reactions through LCMS:

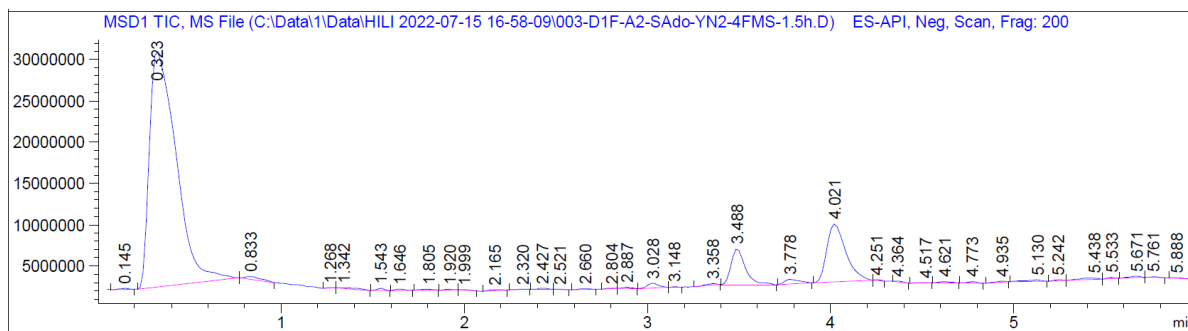
Reported % conversion as determined from LCMS analysis by comparing the abundance of all DNA-derived compounds.

$$\% \text{ Conversion} = \frac{\text{Total abundance of target material}}{\text{Total abundance of DNA material}} \times 100$$

Example of LCMS data and calculations:







Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5521.30	65013	100.00
B	5385.22	32602	50.15

A (%) = percent single addition =  $100 / (100+50.15) = 67\%$

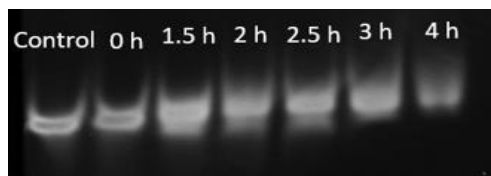
B (%) = percent starting material =  $50.15 / (100+50.15) = 33\%$

**Figure S12.** An example of conversion calculations

## ***Supporting Data***

### **Stability of DNA under photoredox conditions**

Photocatalysis reaction was performed on a model DNA conjugate with 4-vinyl pyridine for 0, 1.5, 2, 2.5, 3, 4 h and the DNA stability was assessed using non-denaturing gel analysis:



**Figure S13.** Stability of DNA under photoredox conditions

## Analysis of HAT catalyst requirement

Table S1: examination of HAT catalyst (quinuclidine) dependence on reaction

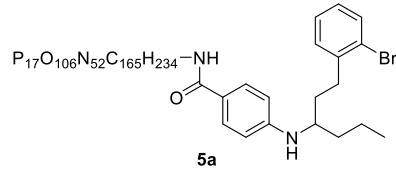
		SM	Single Addn	Double Addn	Triple Addn	Unknown	Dealkylation
1	<b>1d + 4VP</b> no quinuclidine	-	90%	-	-	-	10%
2	<b>1d + DPE</b> no quinuclidine	59%	16%	-	-	5482.31: 10%	15%
3	<b>1d + 4VP</b> with quinuclidine	-	68%	25%	7%	-	-
4	<b>1d + DPE</b> with quinuclidine	77%	23%	-	-	-	-

## LCMS spectra and deconvolution results for 1a derivatives

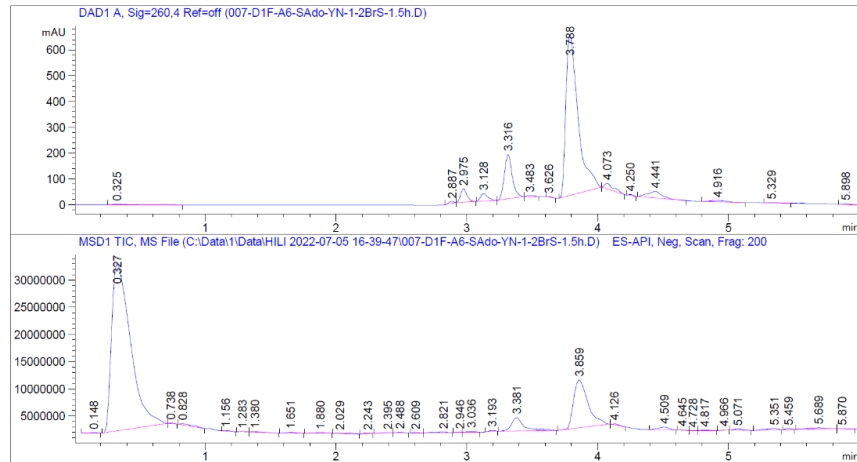
**Table S2:** Hydroaminoalkylation of various vinylarenes with DNA conjugate **1a**

	Starting Material (1a)	Single Addition	Double Addition	Triple Addition
<b>1a+4VP</b>		<b>4a:</b> 73%	27%	-
<b>1a+4CS</b>	8%	<b>7a:</b> 76%	16%	-
<b>1a+2BrS</b>	15%	<b>5a:</b> 76%	9%	-
<b>1a+2VhB</b>	15%	<b>6a:</b> 71%	14%	-
<b>1a+DPE</b>	25%	<b>3a:</b> 75%	-	-
<b>1a+diFP</b>	14%	<b>8a:</b> 86%	-	-
<b>1a+3EhP</b>	49%	<b>9a:</b> 51%	-	-
<b>1a+4M5VT</b>	51%	<b>10a:</b> 49%	-	-
<b>1a+4FMS</b>	66%	<b>11a:</b> 34%	-	-
<b>1a+5EMP</b>	68%	<b>12a:</b> 32%	-	-
<b>1a+4MS</b>	73%	<b>13a:</b> 27%	-	-
<b>1a+4VBA</b>	76%	<b>14a:</b> 24%	-	-
<b>1a+4AS</b>	100%	-	-	-

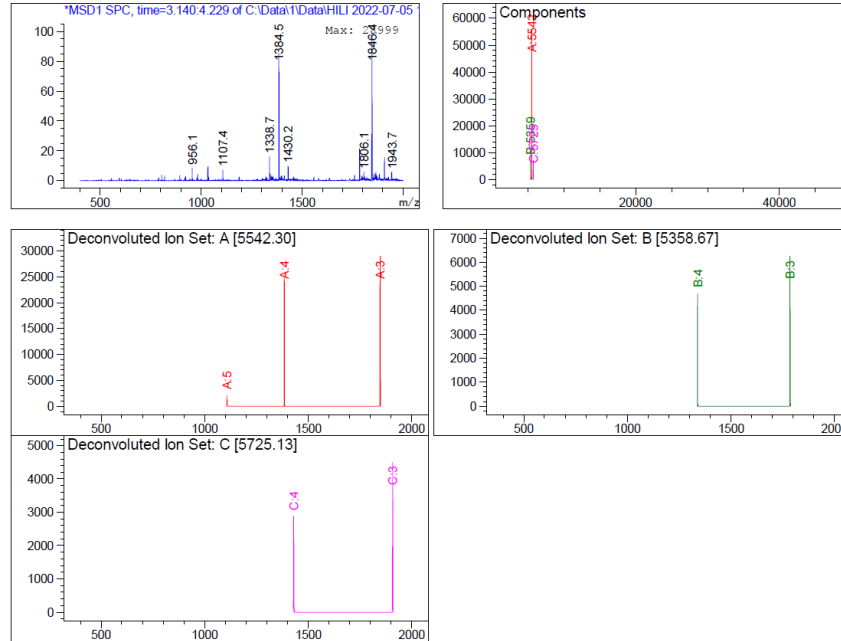




Molecular Weight: 5542.8010

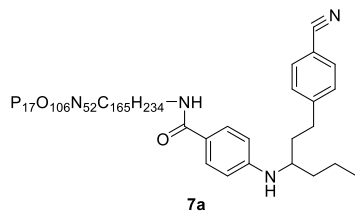


Deconvolution of Spectrum # 1 @ 3.140 - 4.229 min

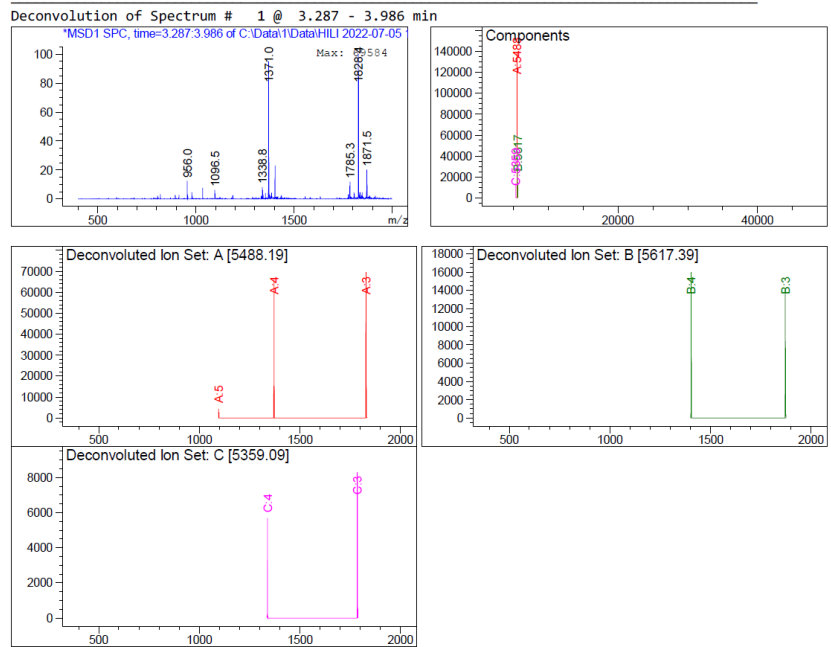
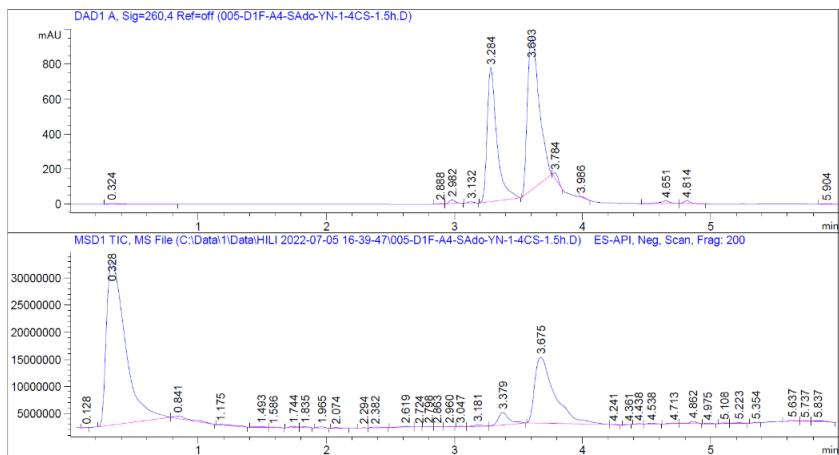


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5542.30	55761	100.00
B	5358.67	10836	19.43
C	5725.13	7163	12.85

**Figure S15.** Deconvoluted LCMS data for **5a**

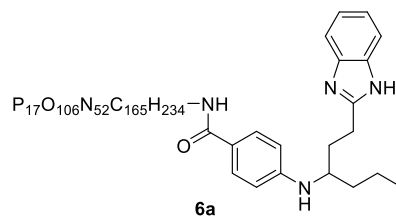


Molecular Weight: 5488.9150

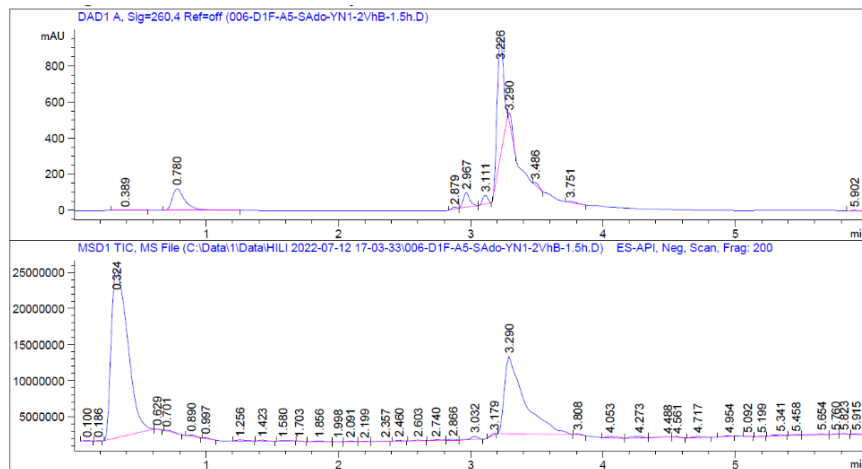


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5488.19	139142	100.00
B	5617.39	30006	21.57
C	5359.09	13902	9.99

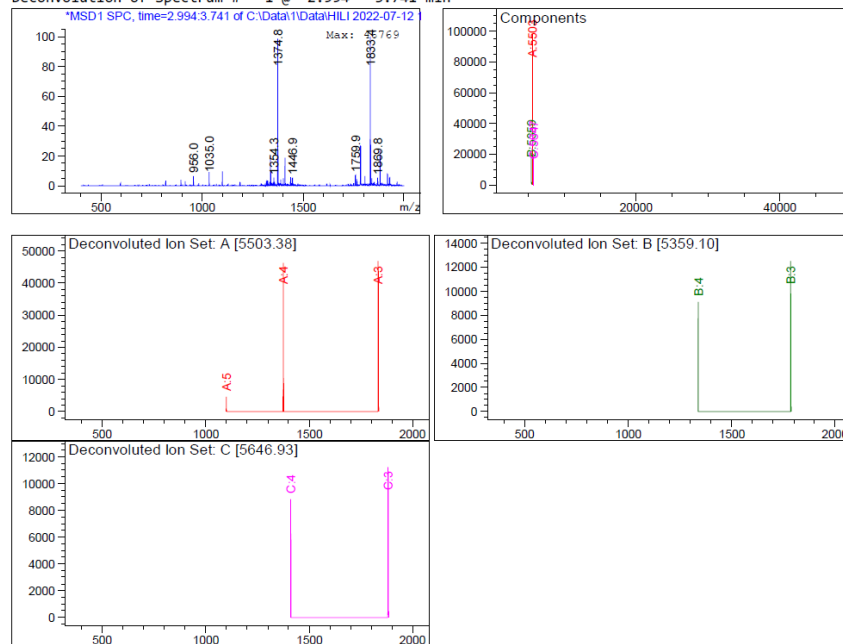
**Figure S16.** Deconvoluted LCMS data for **7a**



Molecular Weight: 5503.9300



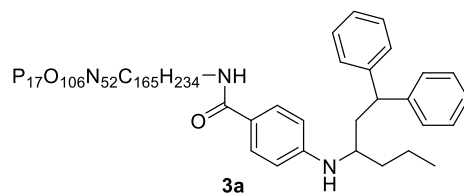
Deconvolution of Spectrum # 1 @ 2.994 - 3.741 min



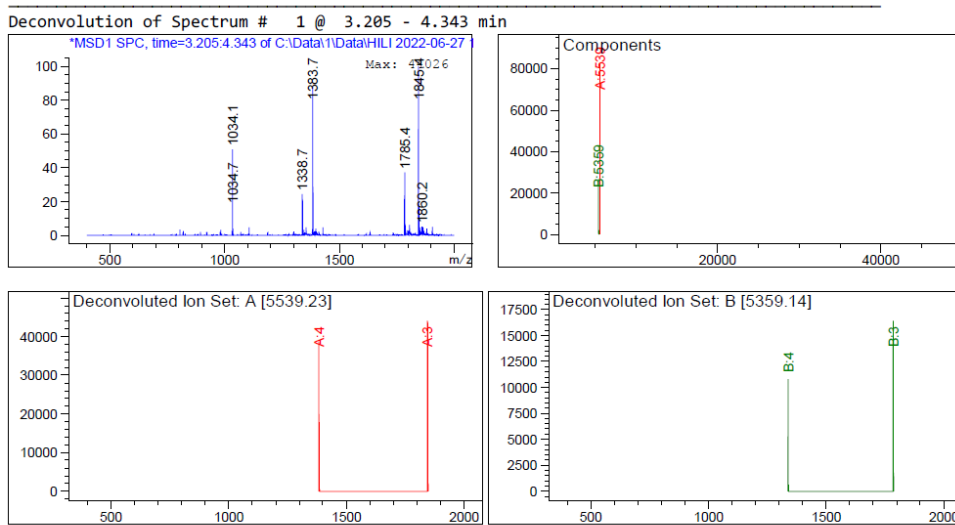
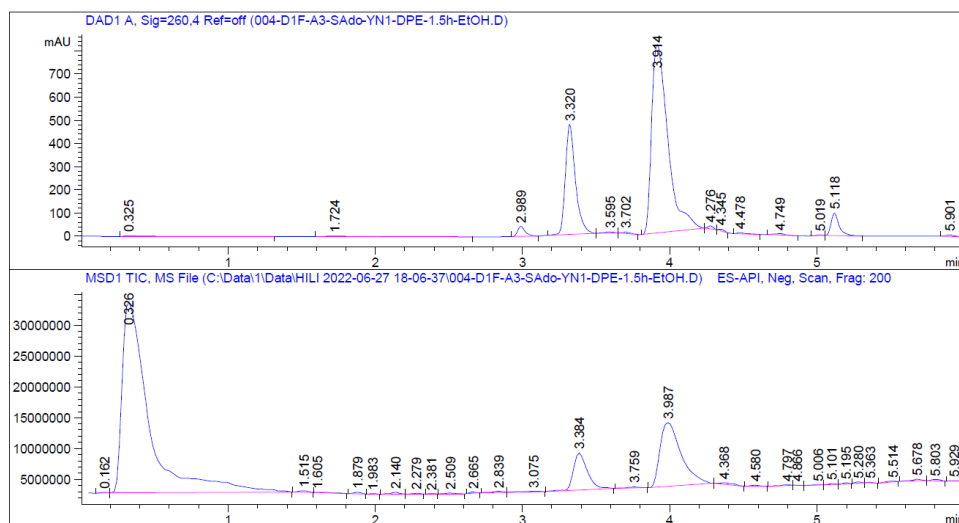
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5503.38	97490	100.00
B	5359.10	21018	21.56
C	5646.93	19824	20.33

**Figure S17.** Deconvoluted LCMS data for **6a**





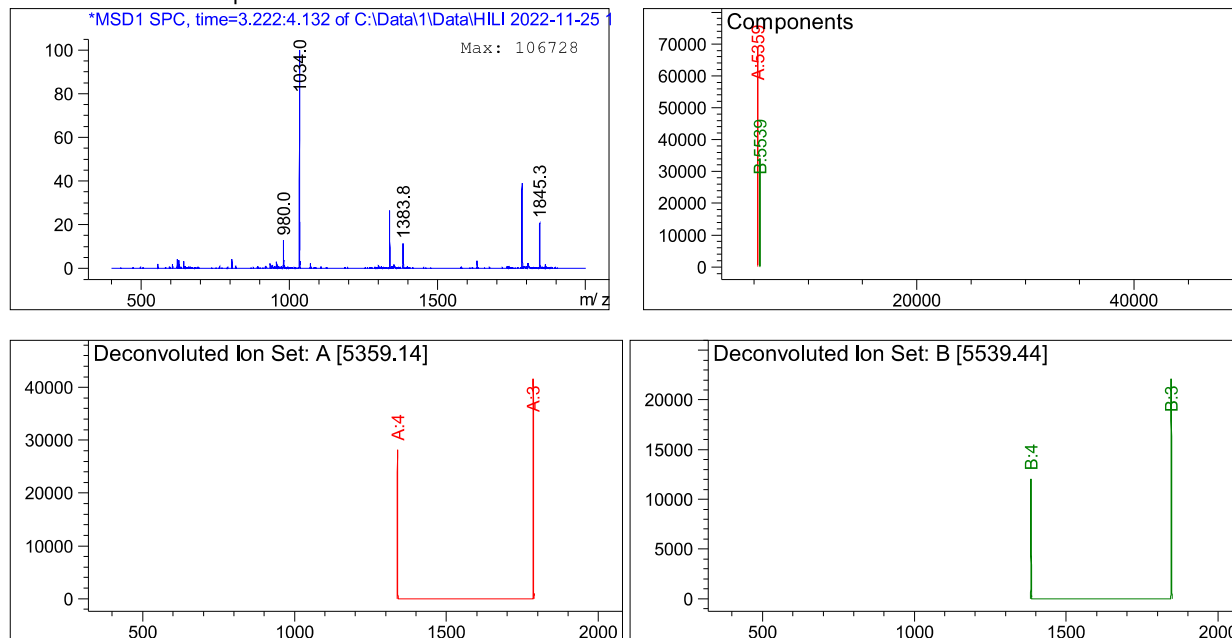
Molecular Weight: 5540.0030



Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5539.23	82233	100.00
B	5359.14	26802	32.59

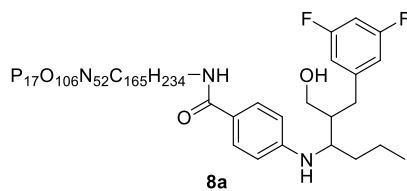
**Figure S18. Deconvoluted LCMS data for 3a (10 nmol)**

Deconvolution of Spectrum # 1 @ 3.222 - 4.132 min

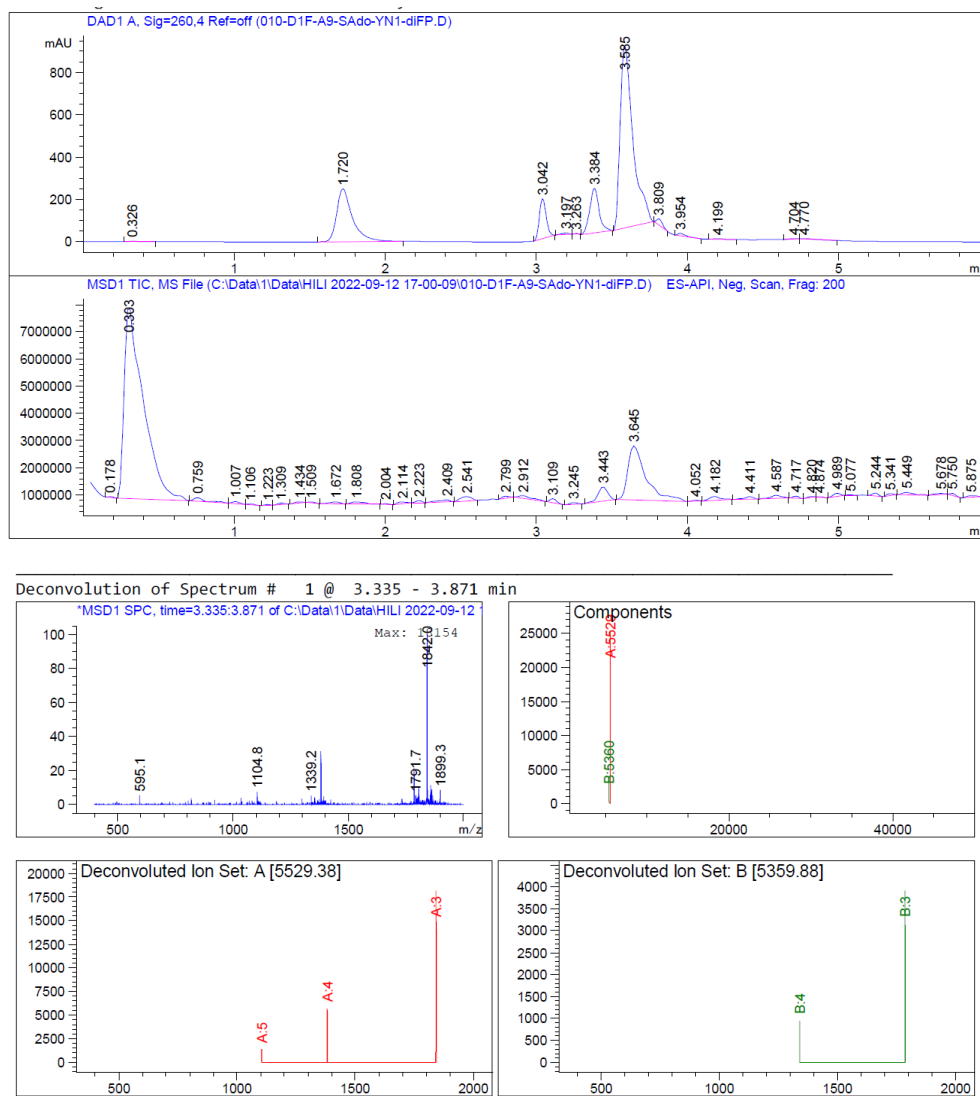


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5359.14	69043	100.00
B	5539.44	34104	49.40

Figure S19. Deconvoluted LCMS data for 3a (100 nmol)

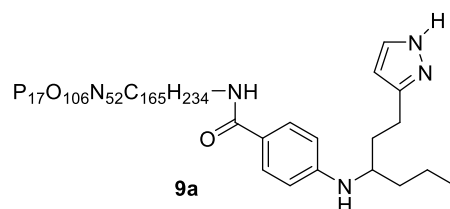


Molecular Weight: 5529.9118

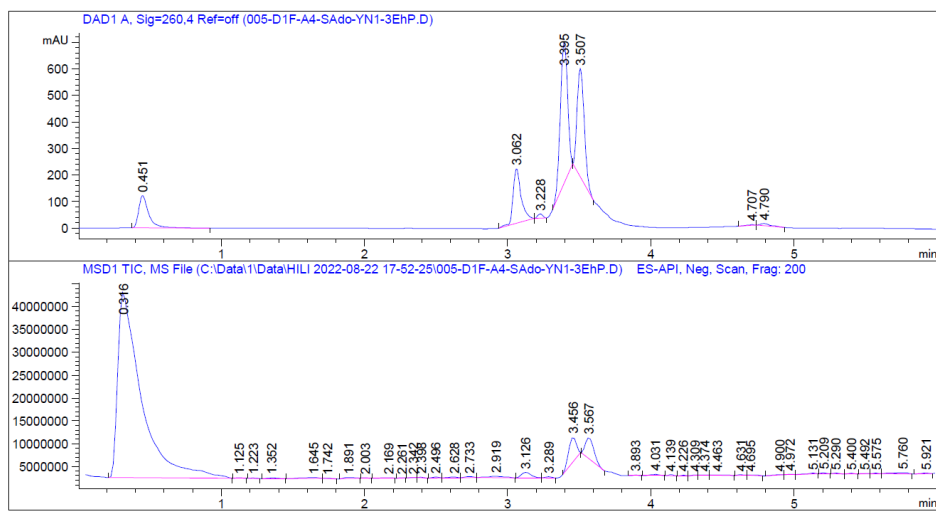


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5529.38	25190	100.00
B	5359.88	4027	15.99

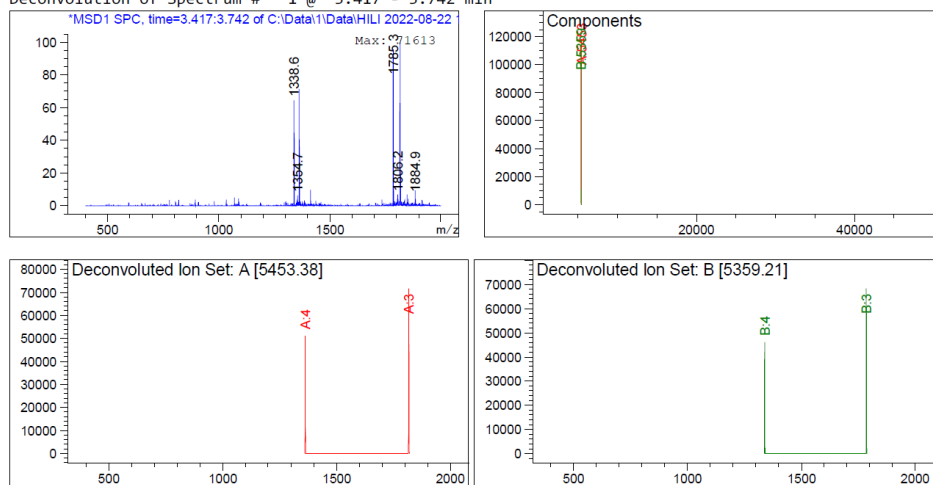
**Figure S20. Deconvoluted LCMS data for 8a**



Molecular Weight: 5453.8700

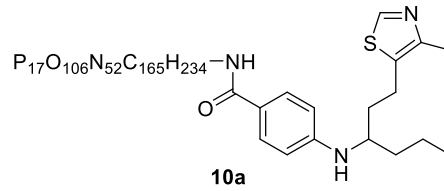


Deconvolution of Spectrum # 1 @ 3.417 - 3.742 min

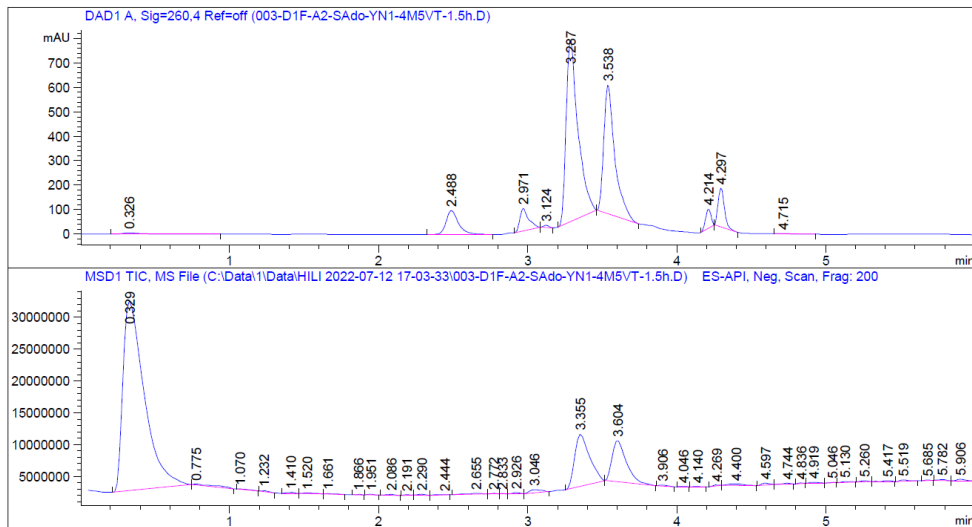


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5453.38	117571	100.00
B	5359.21	112927	96.05

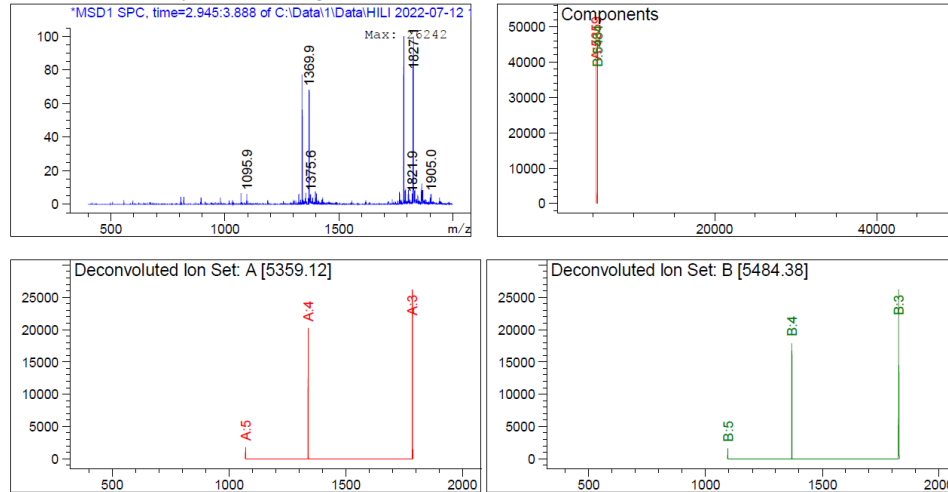
**Figure S21.** Deconvoluted LCMS data for **9a**



Molecular Weight: 5484.9420

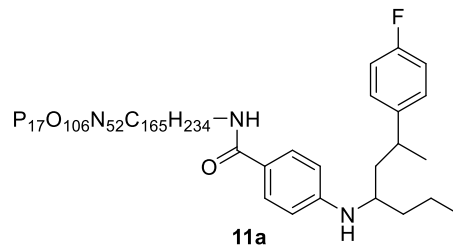


Deconvolution of Spectrum # 1 @ 2.945 - 3.888 min

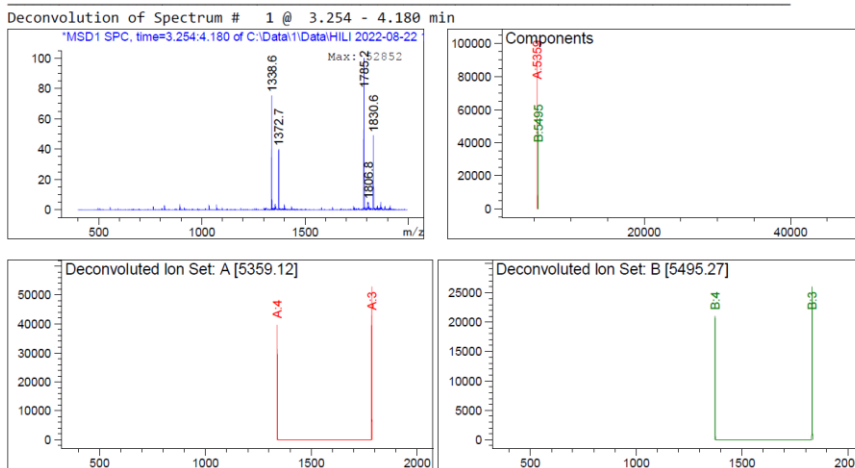
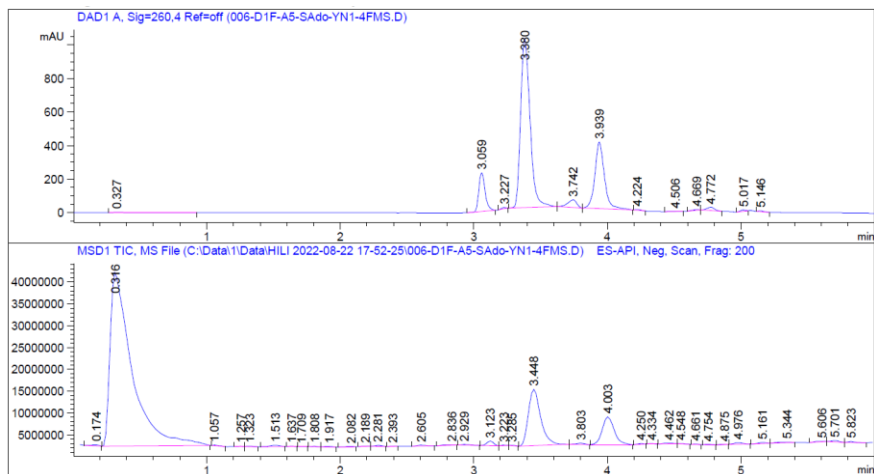


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5359.12	47998	100.00
B	5484.38	45285	94.35

**Figure S22.** Deconvoluted LCMS data for **10a**

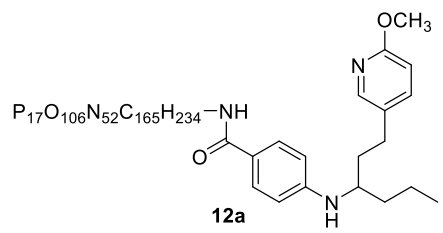


Molecular Weight: 5495.9224

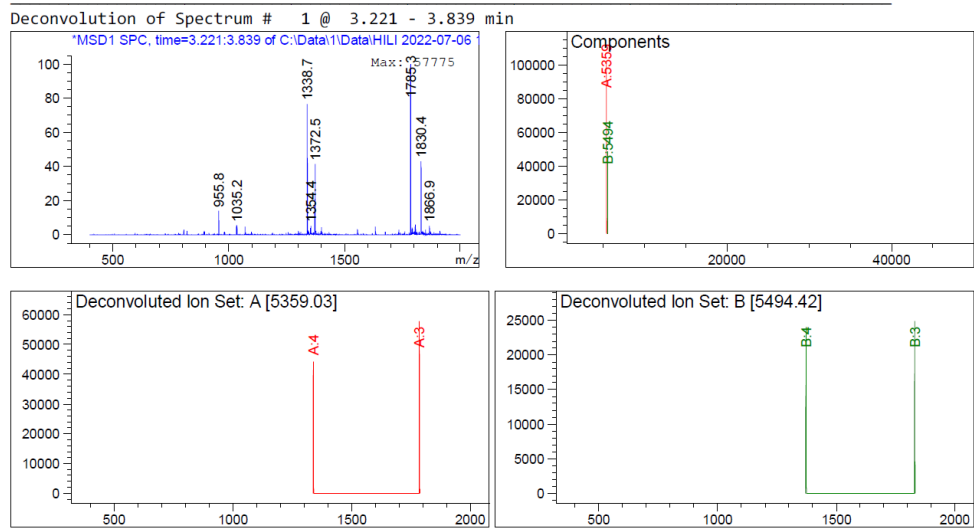
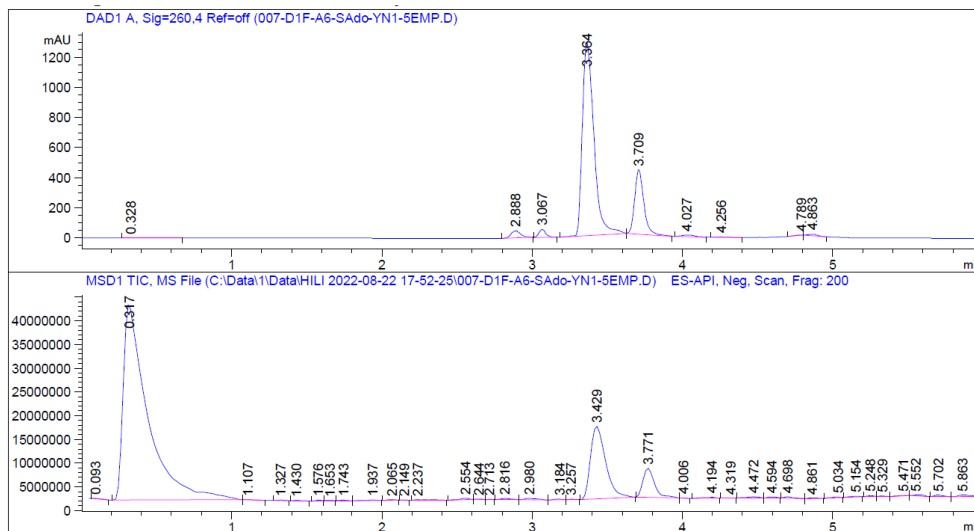


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5359.12	92400	100.00
B	5495.27	47097	50.97

**Figure S23.** Deconvoluted LCMS data for **11a**

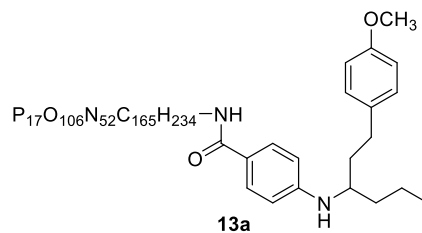


Molecular Weight: 5494.9190

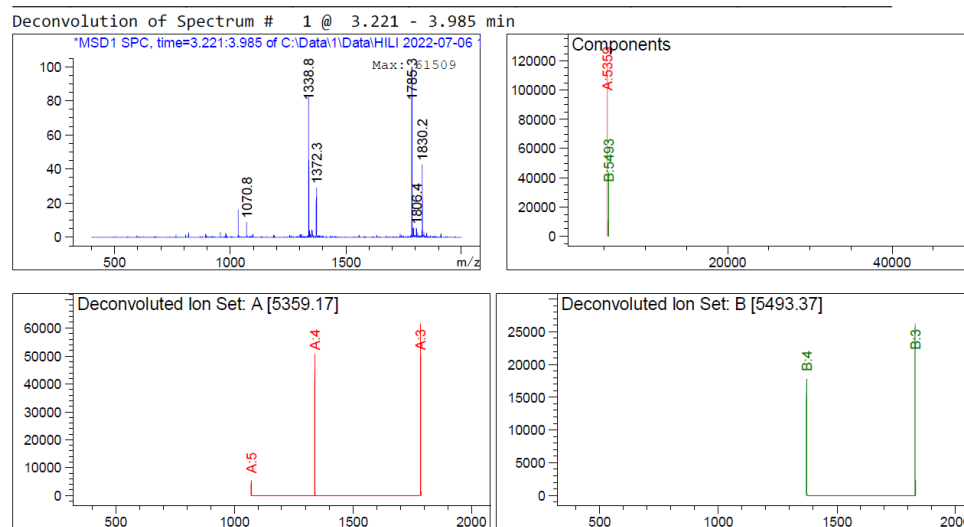
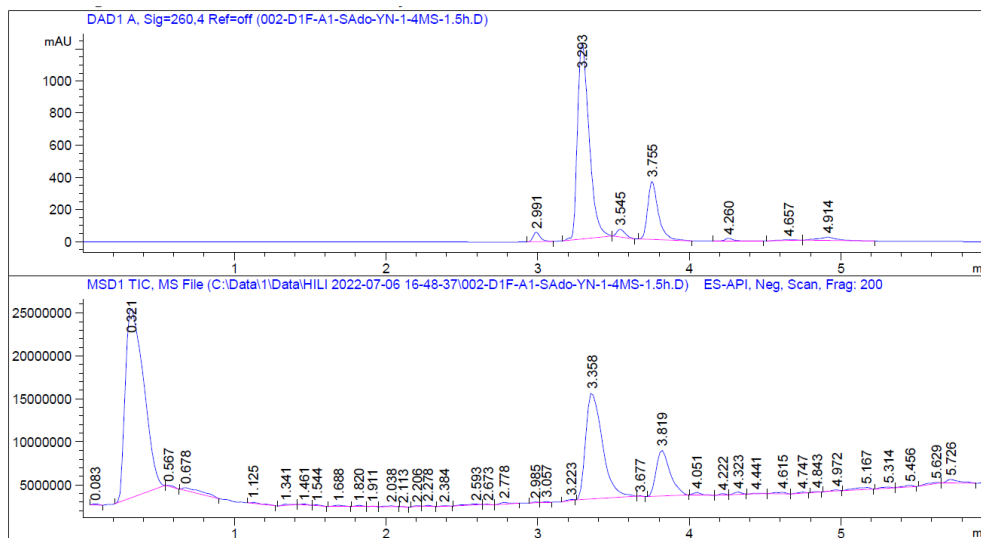


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5359.03	101842	100.00
B	5494.42	48620	47.74

**Figure S24.** Deconvoluted LCMS data for **12a**



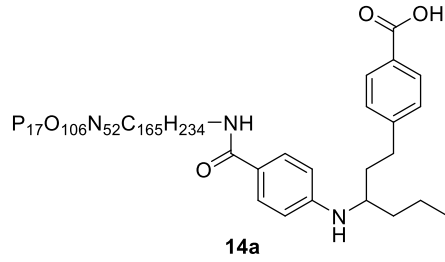
Molecular Weight: 5493.9310



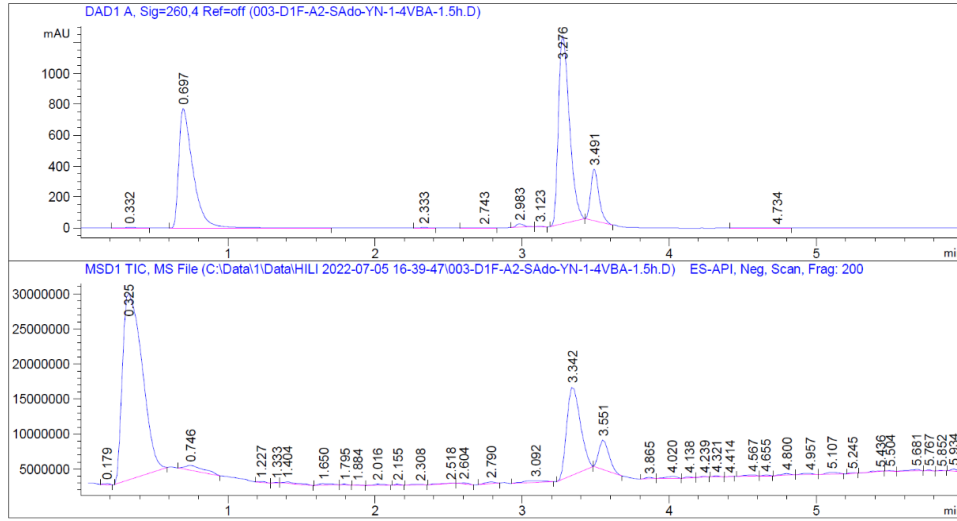
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5359.17	117613	100.00
B	5493.37	43497	36.98

**Figure S25.** Deconvoluted LCMS data for **13a**

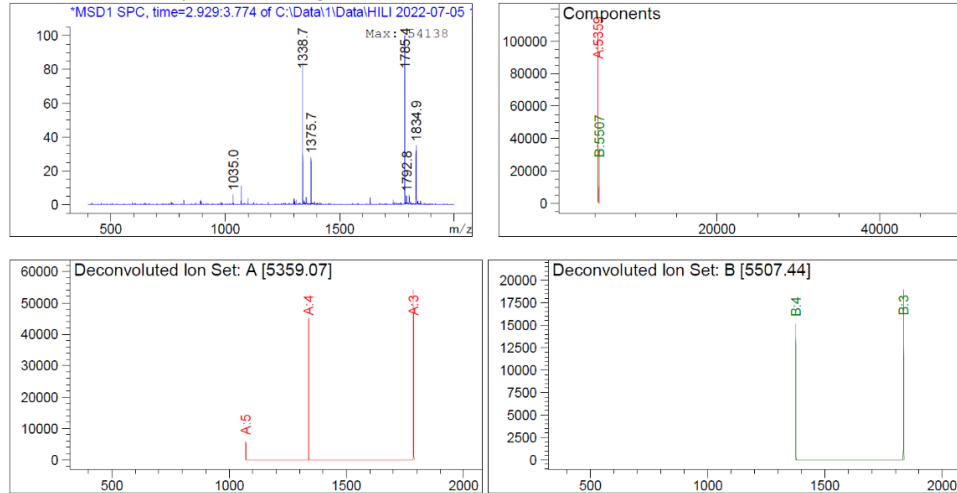




Molecular Weight: 5507.9140



Deconvolution of Spectrum # 1 @ 2.929 - 3.774 min



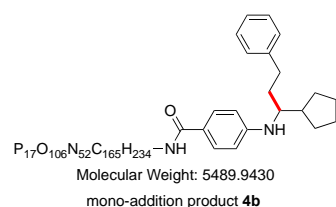
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5359.07	104935	100.00
B	5507.44	33538	31.96

**Figure S26. Deconvoluted LCMS data for 14a**

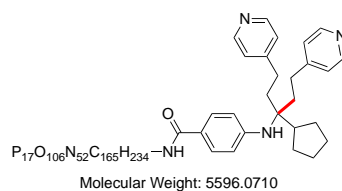
## LCMS spectra and deconvolution results for 1b derivatives

**Table S3:** Hydroaminoalkylation of various vinylarenes with DNA conjugate **1b**

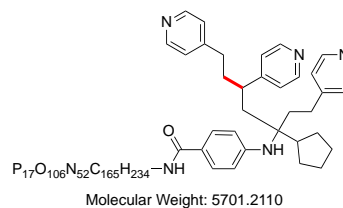
	Starting Material ( <b>1b</b> )	Single Addition	Double Addition	Triple Addition
<b>1b</b> +4VP	-	<b>4b</b> : 58%	31%	11%
<b>1b</b> +4CS	-	<b>7b</b> : 72%	28%	-
<b>1b</b> +2BrS	-	<b>5b</b> : 79%	21%	-
<b>1b</b> +2VhB	-	<b>6b</b> : 79%	21%	-
<b>1b</b> +DPE	-	<b>3b</b> : 86%	14%	-
<b>1b</b> +diFP	-	<b>8b</b> : 83%	17%	-
<b>1b</b> +4M5VT	27%	<b>10b</b> : 67%	6%	-
<b>1b</b> +4FMS	33%	<b>11b</b> : 67%	-	-
<b>1b</b> +3EhP	39%	<b>9b</b> : 61%	-	-
<b>1b</b> +5EMP	47%	<b>12b</b> : 53%	-	-
<b>1b</b> +4MS	48%	<b>13b</b> : 52%	-	-
<b>1b</b> +4VBA	67%	<b>14b</b> : 33%	-	-
<b>1b</b> +4AS	100%	-	-	-

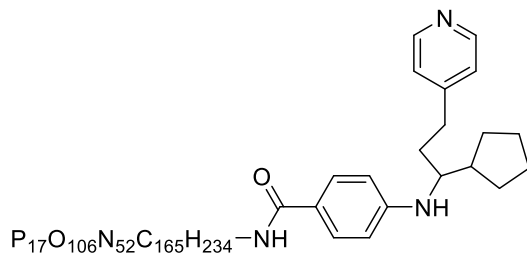


possible double-addition byproduct



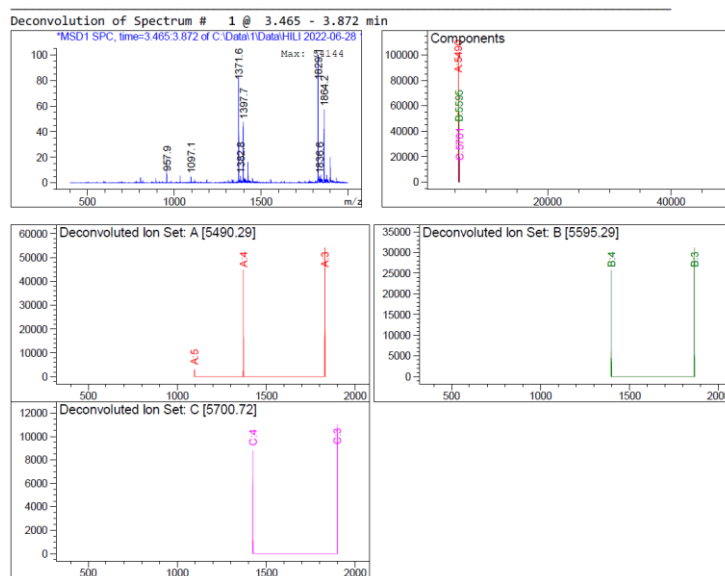
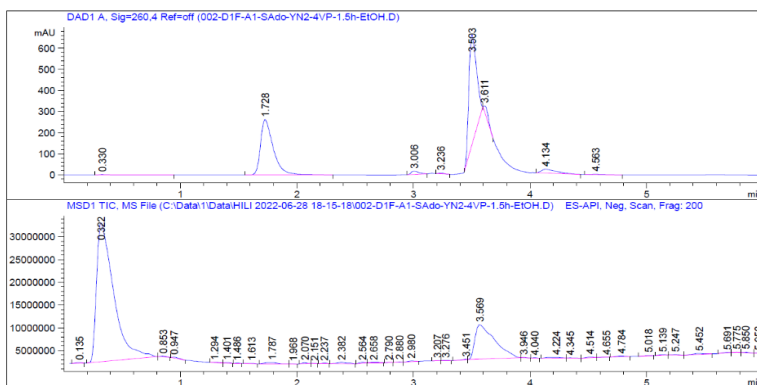
possible triple-addition byproduct





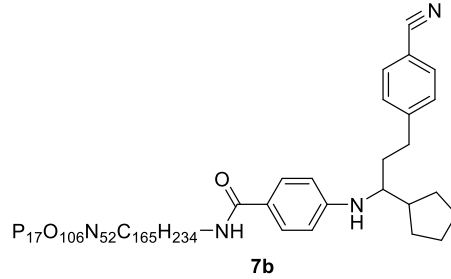
**4b**

Molecular Weight: 5490.9310

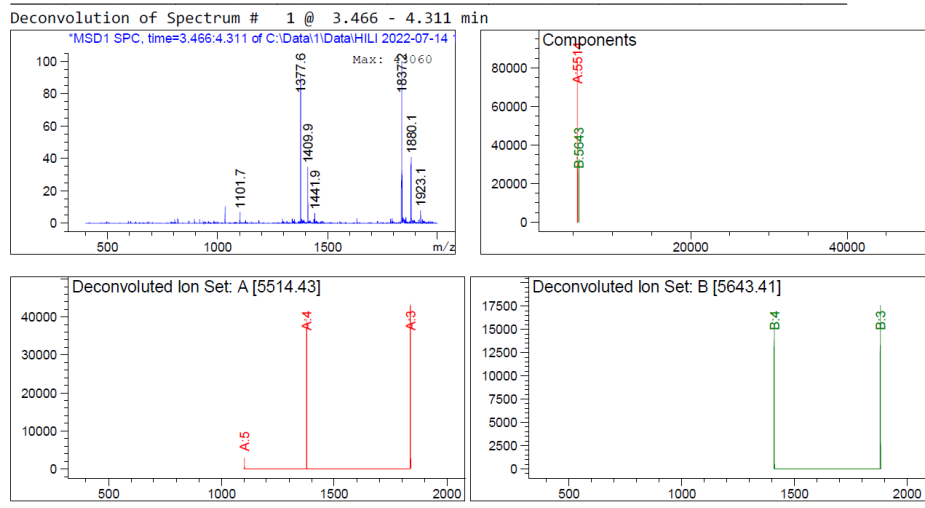
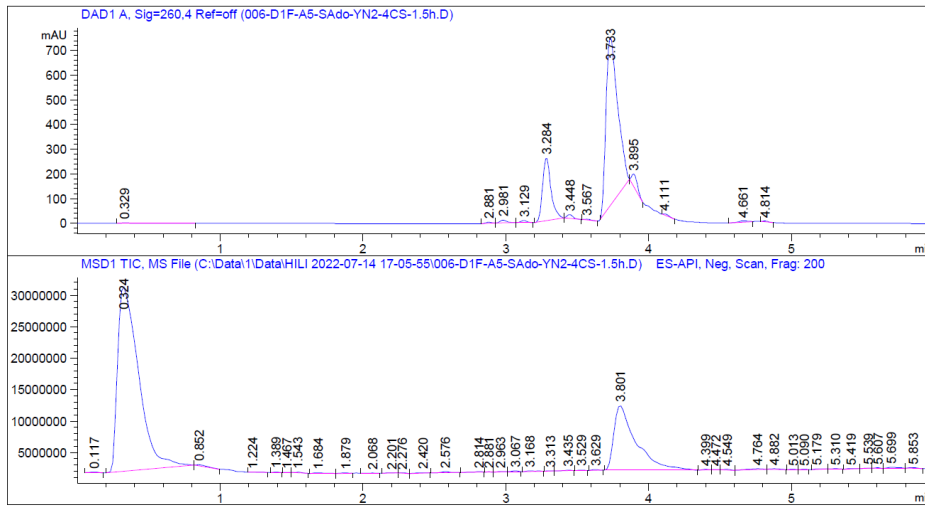


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5490.29	101564	100.00
B	5595.29	55558	54.70
C	5700.72	19660	19.36

**Figure S27.** Deconvoluted LCMS data for **4b**

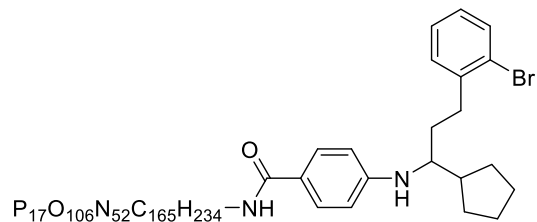


Molecular Weight: 5514.9530



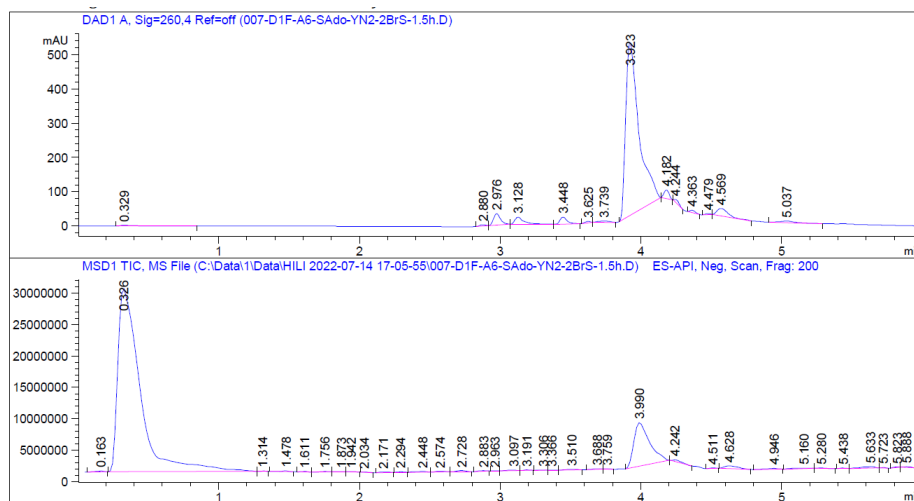
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5514.43	84625	100.00
B	5643.41	32524	38.43

**Figure S28.** Deconvoluted LCMS data for **7b**

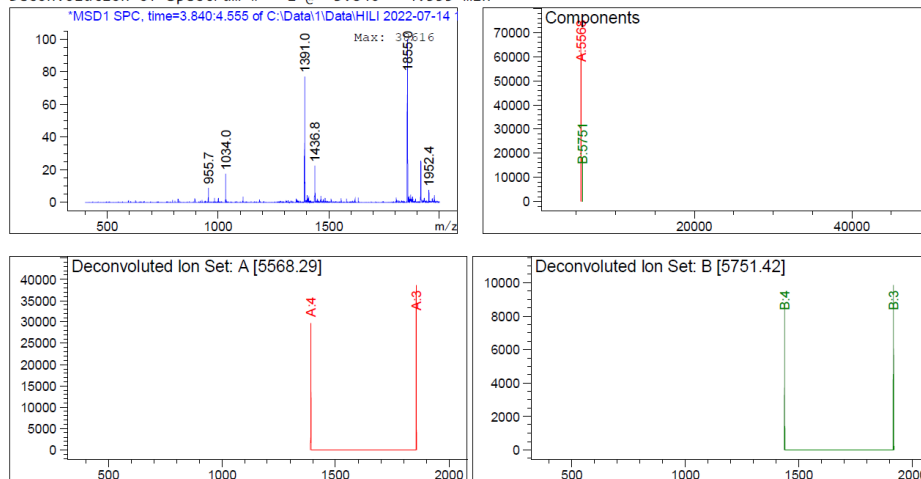


**5b**

Molecular Weight: 5568.8390

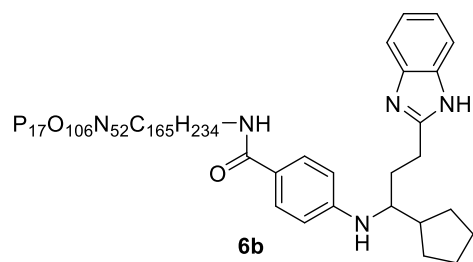


Deconvolution of Spectrum # 1 @ 3.840 - 4.555 min

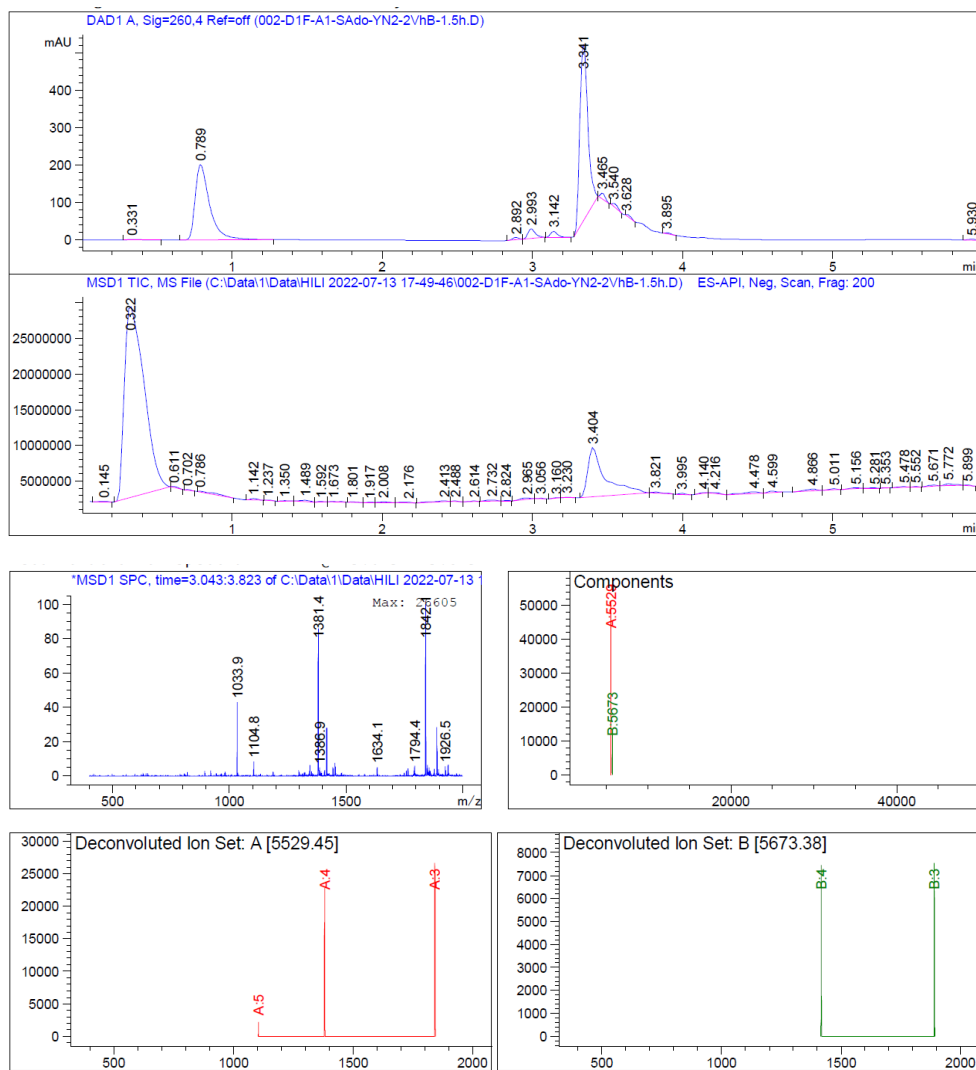


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5568.29	68333	100.00
B	5751.42	18060	26.43

**Figure S29.** Deconvoluted LCMS data for **5b**

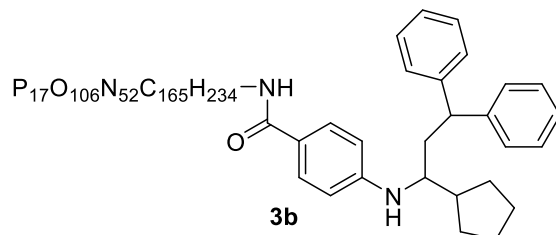


Molecular Weight: 5529.9680

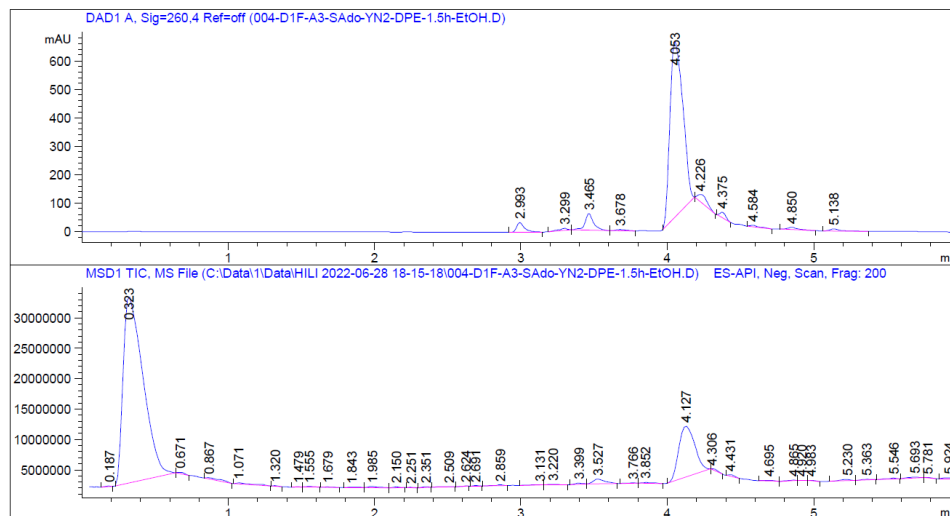


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5529.45	51037	100.00
B	5673.38	13581	26.61

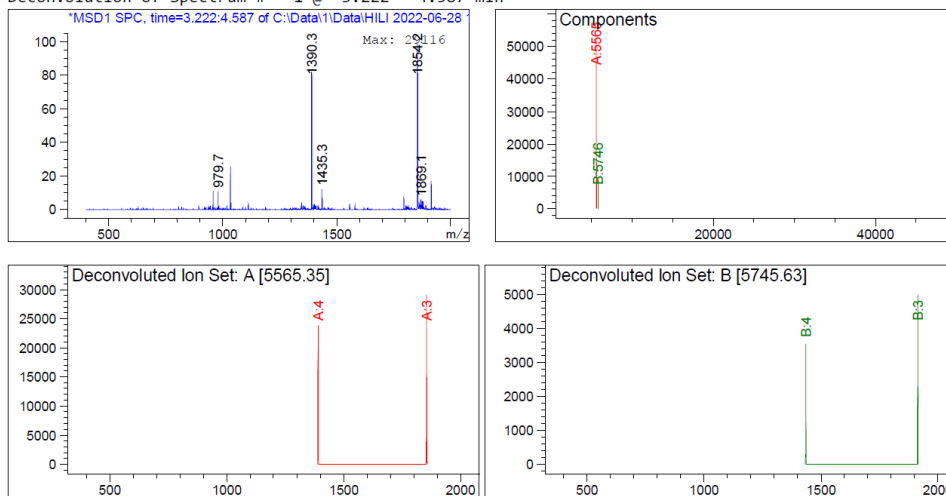
**Figure S30.** Deconvoluted LCMS data for **6b**



Molecular Weight: 5566.0410

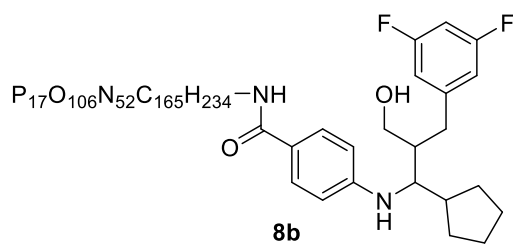


Deconvolution of Spectrum # 1 @ 3.222 - 4.587 min



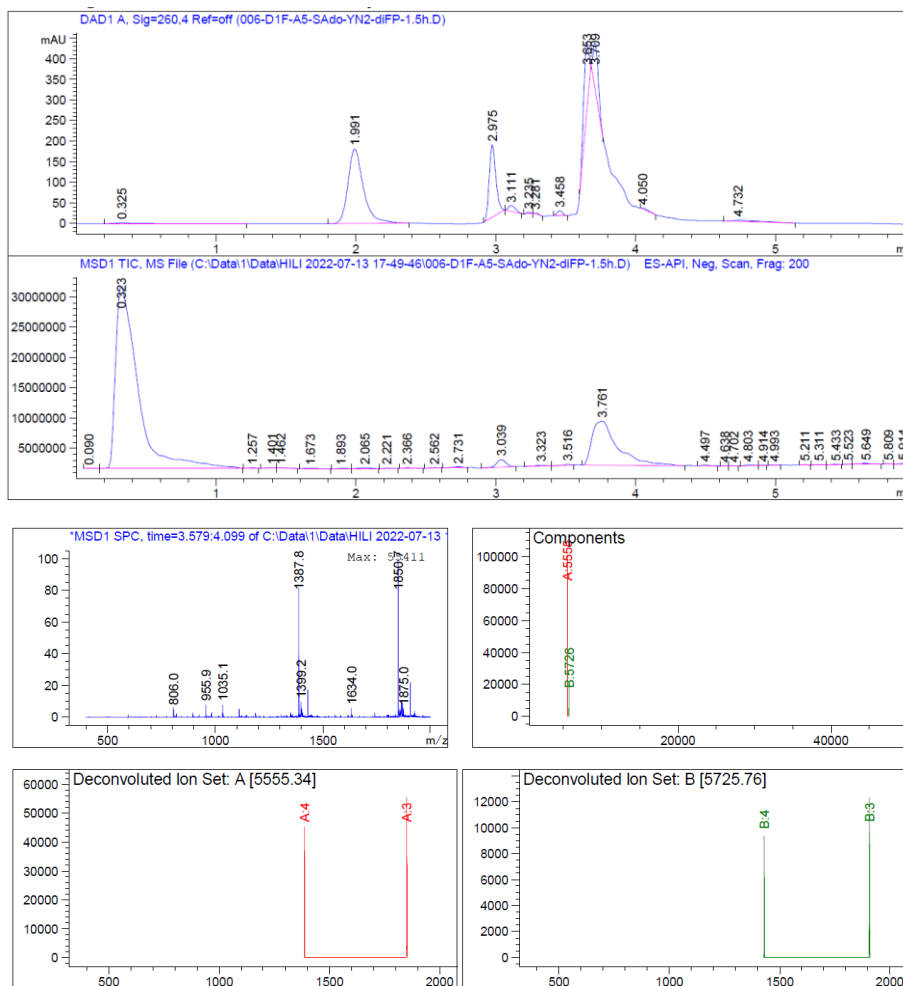
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5565.35	52284	100.00
B	5745.63	8516	16.29

**Figure S31.** Deconvoluted LCMS data for **3b**



**8b**

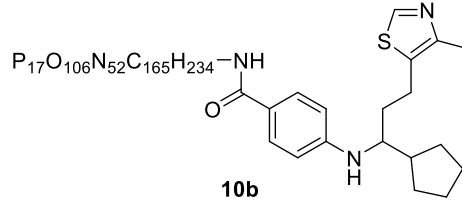
Molecular Weight: 5555.9498



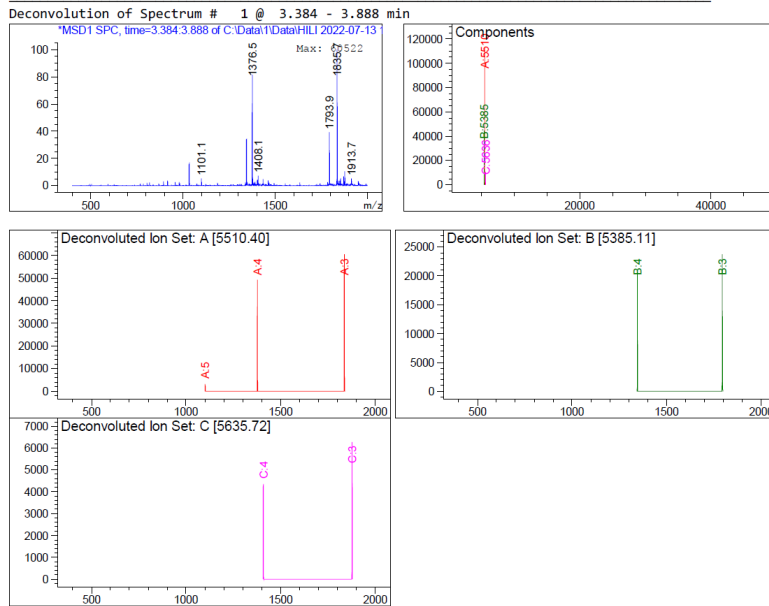
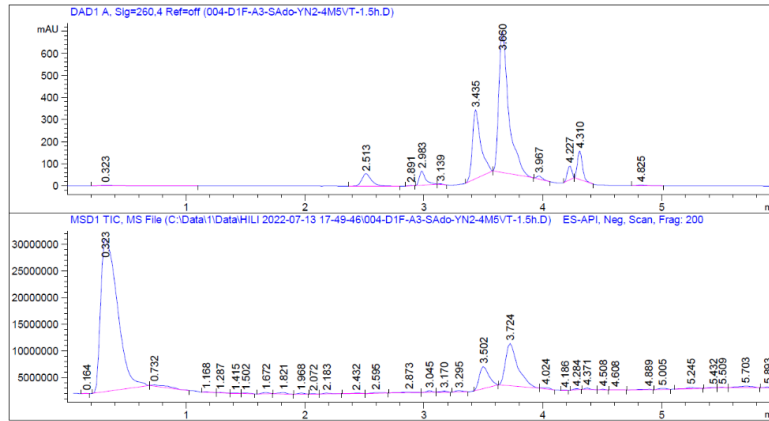
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5555.34	100210	100.00
B	5725.76	20673	20.63

**Figure S32.** Deconvoluted LCMS data for **8b**



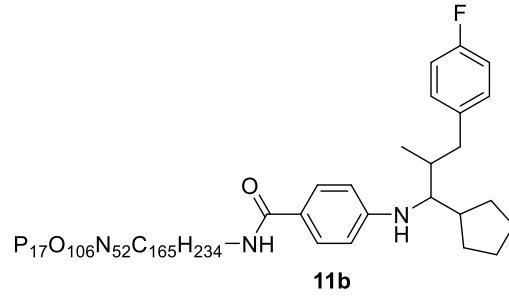


Molecular Weight: 5510.9800

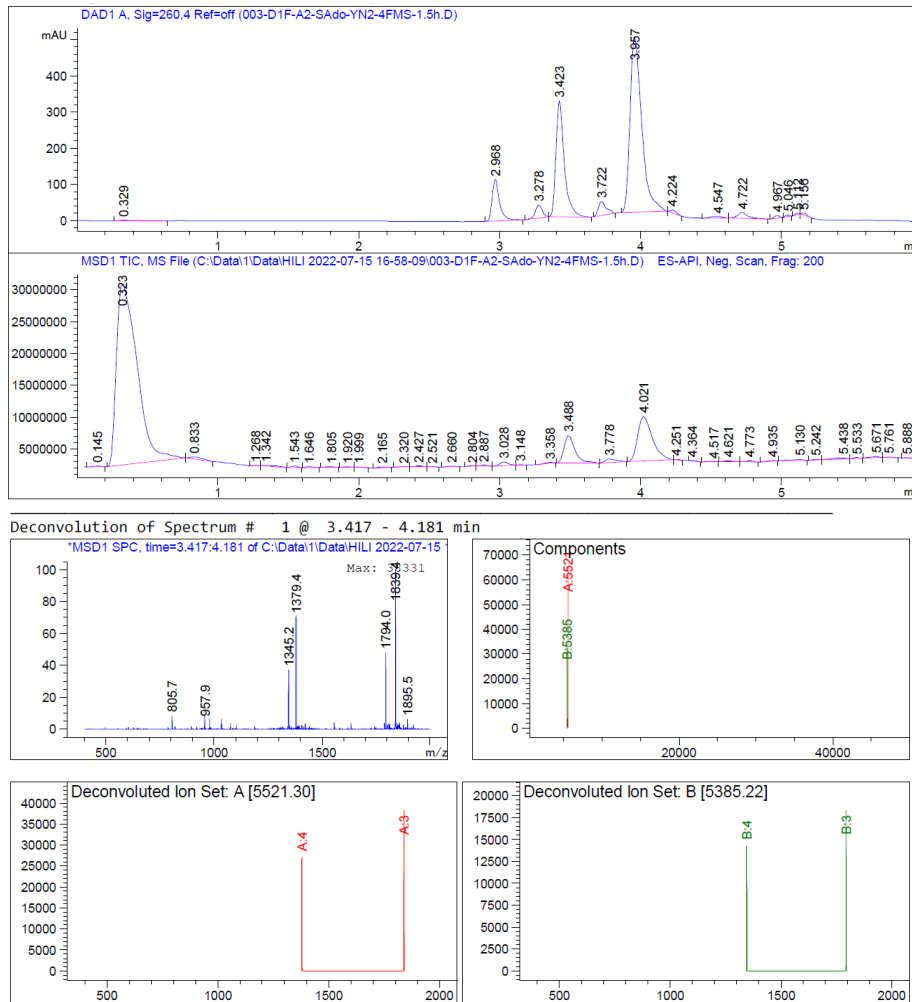


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5510.40	112765	100.00
B	5385.11	44314	39.30
C	5635.72	9991	8.86

**Figure S33.** Deconvoluted LCMS data for **10b**

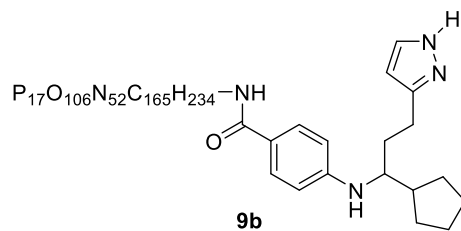


Molecular Weight: 5521.9604

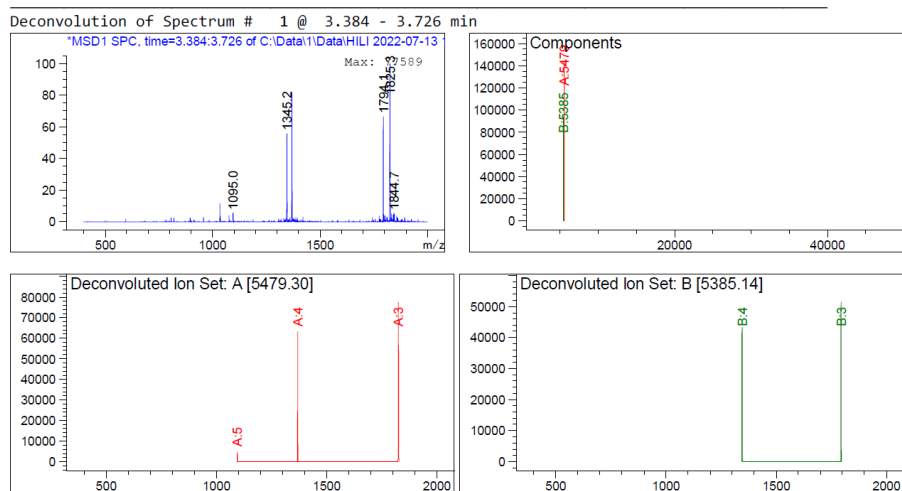
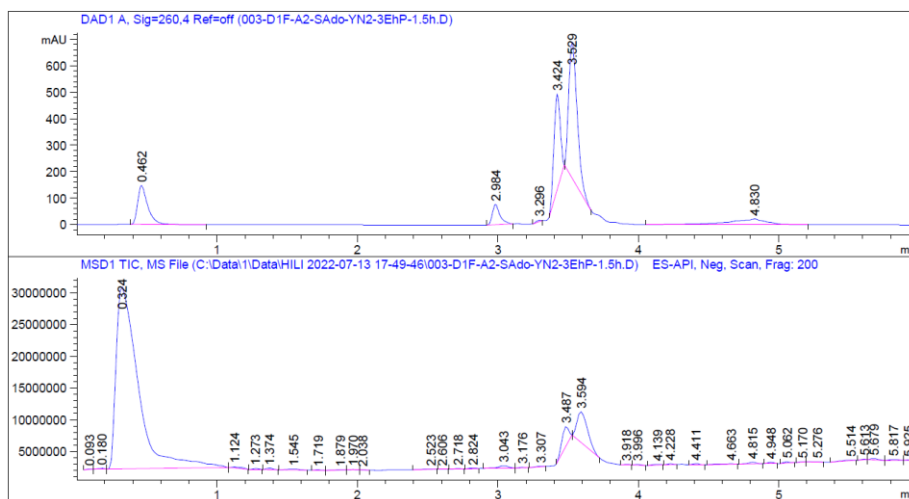


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5521.30	65013	100.00
B	5385.22	32602	50.15

**Figure S34. Deconvoluted LCMS data for 11b**

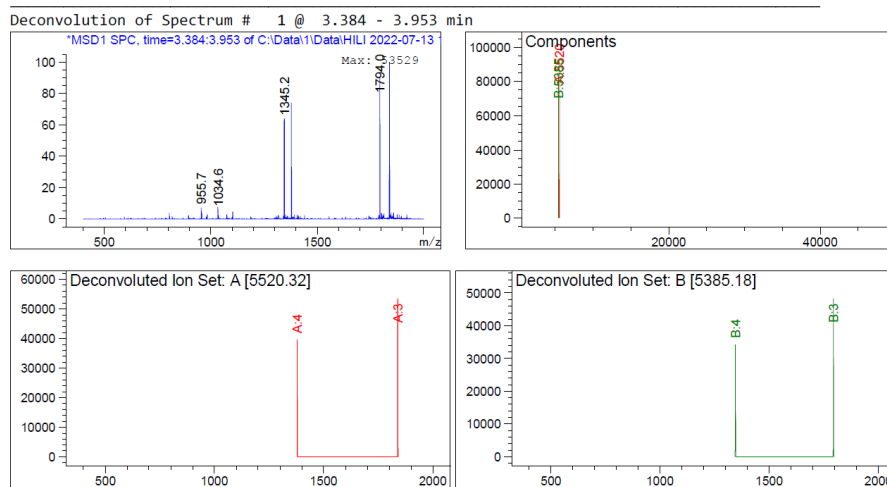
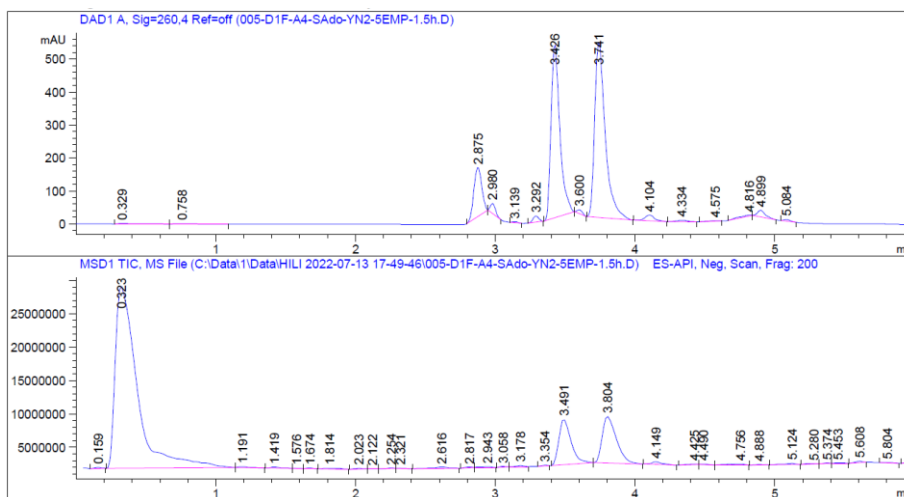
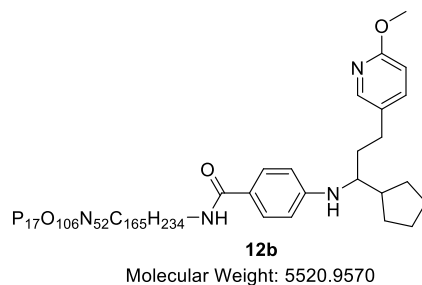


Molecular Weight: 5479.9080



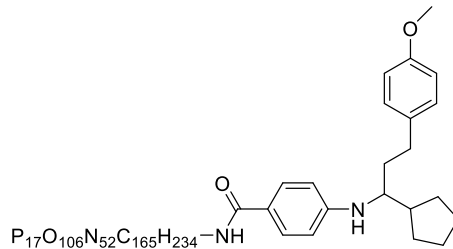
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5479.30	143998	100.00
B	5385.14	93740	65.10

**Figure S35. Deconvoluted LCMS data for 9b**



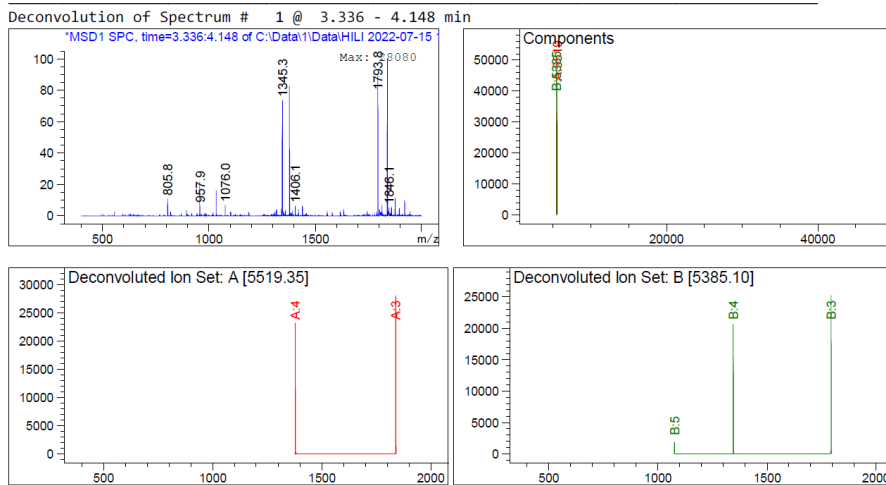
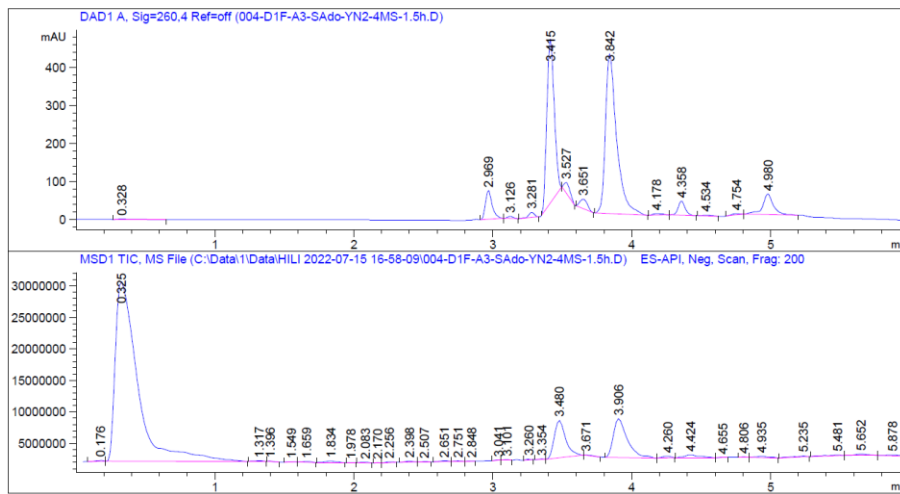
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5520.32	92687	100.00
B	5385.18	82469	88.98

**Figure S36. Deconvoluted LCMS data for 12b**



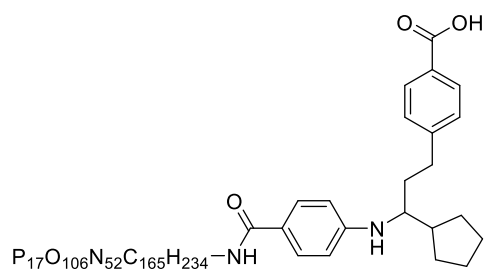
**13b**

Molecular Weight: 5519.9690



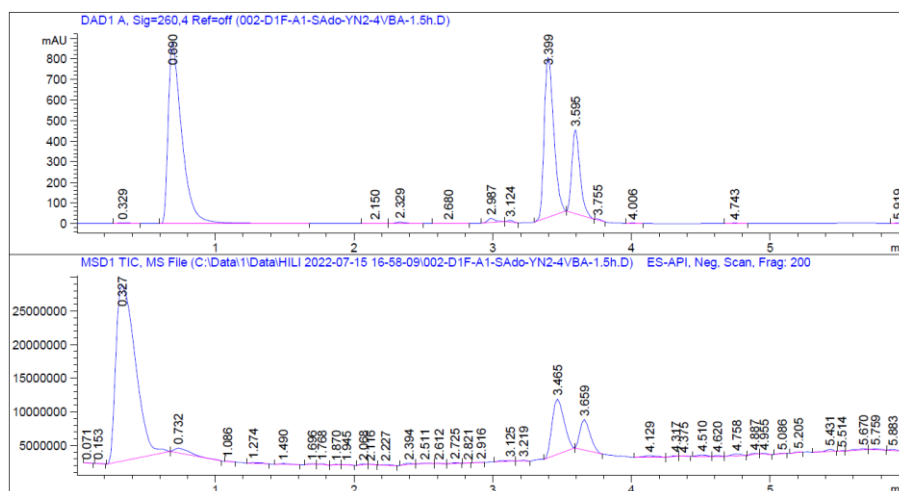
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5519.35	51096	100.00
B	5385.10	47038	92.06

**Figure S37. Deconvoluted LCMS data for 13b**

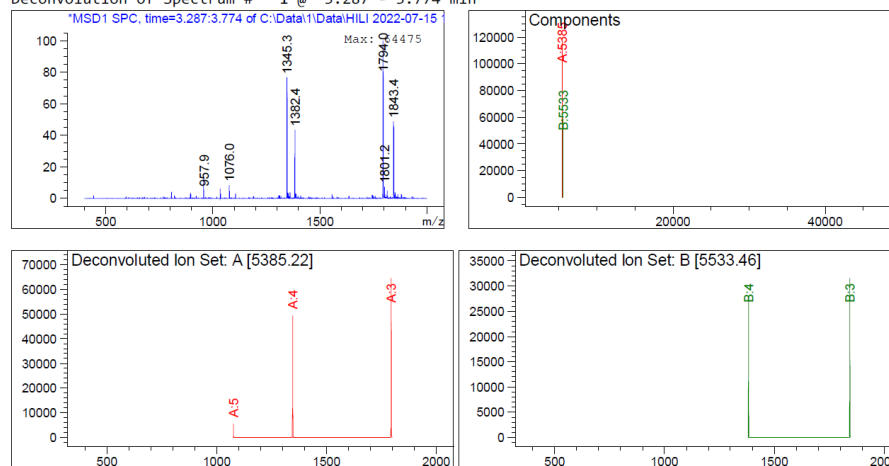


**14b**

Molecular Weight: 5533.9520



Deconvolution of Spectrum # 1 @ 3.287 - 3.774 min



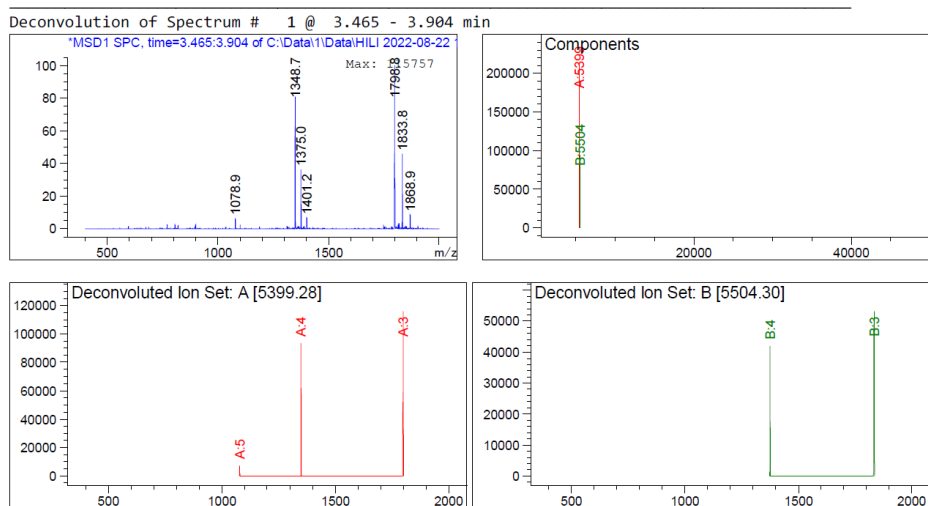
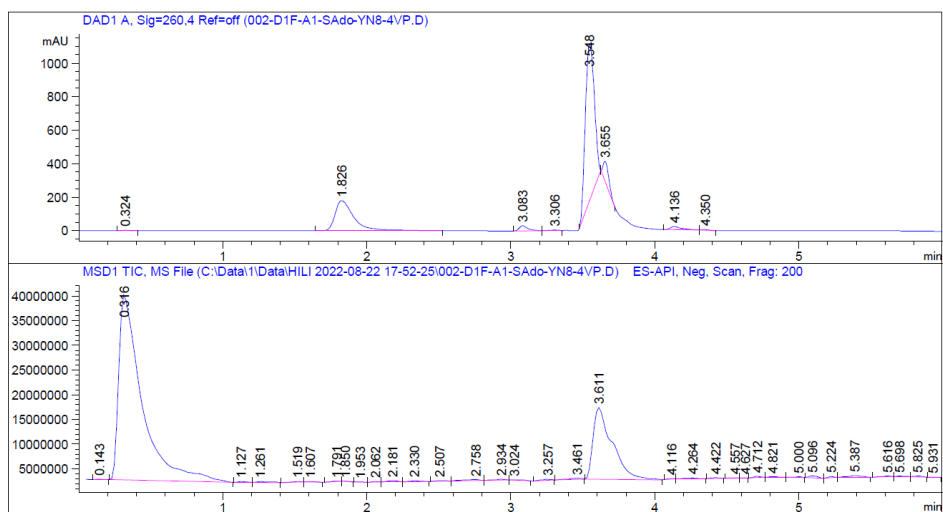
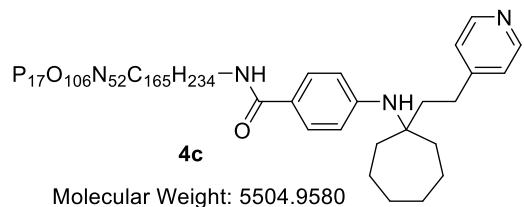
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5385.22	118981	100.00
B	5533.46	59173	49.73

**Figure S38. Deconvoluted LCMS data for 14b**

## LCMS spectra and deconvolution results for 1c derivatives

**Table S4:** Hydroaminoalkylation of various vinylarenes with DNA conjugate **1c**

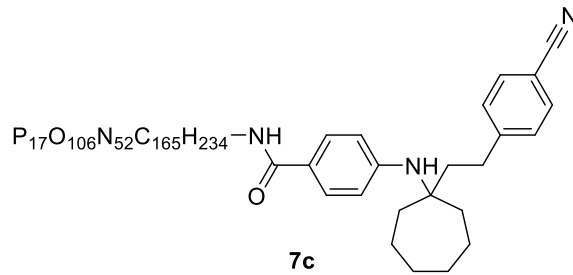
	Starting Material ( <b>1c</b> )	Single Addition	Double Addition	Triple Addition
<b>1c+4VP</b>	69%	<b>4c:</b> 31%	-	-
<b>1c+4CS</b>	83%	<b>7c:</b> 17%	-	-
<b>1c+2VhB</b>	86%	<b>6c:</b> 14%	-	-
<b>1c+2BrS</b>	88%	<b>5c:</b> 12%	-	-
<b>1c+diFP</b>	89%	<b>8c:</b> 11%	-	-
<b>1c+4M5VT</b>	93%	<b>10c:</b> 7%	-	-
<b>1c+DPE</b>	100%	<b>3c:</b> 0%	-	-
<b>1c+4FMS</b>	100%	<b>11c:</b> 0%	-	-
<b>1c+3EhP</b>	100%	<b>9c:</b> 0%	-	-
<b>1c+5EMP</b>	100%	<b>12c:</b> 0%	-	-
<b>1c+4MS</b>	100%	<b>13c:</b> 0%	-	-
<b>1c+4VBA</b>	100%	<b>14c:</b> 0%	-	-
<b>1c+4AS</b>	100%	-	-	-



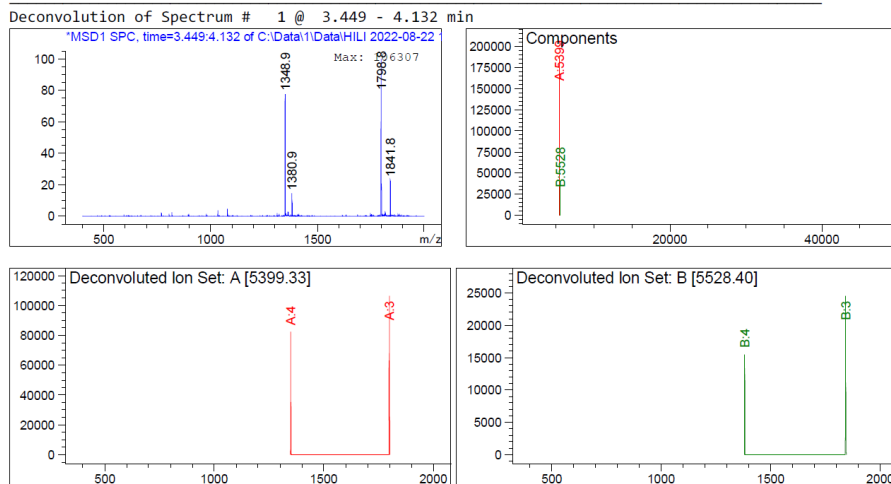
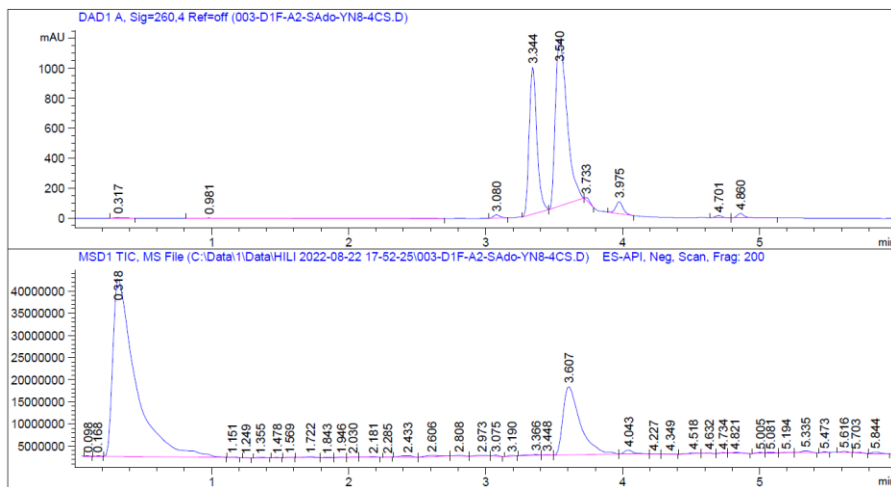
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5399.28	212905	100.00
B	5504.30	94072	44.18

**Figure S39.** Deconvoluted LCMS data for **4c**



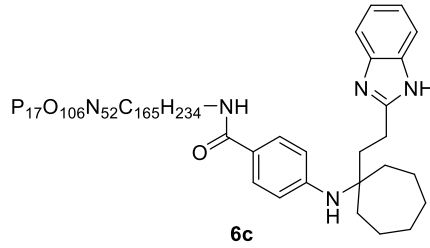


Molecular Weight: 5528.9800

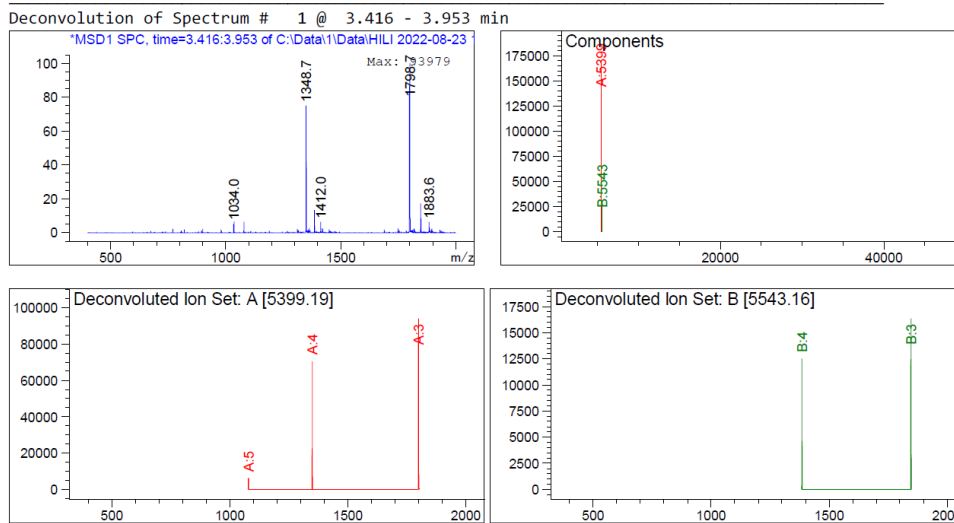
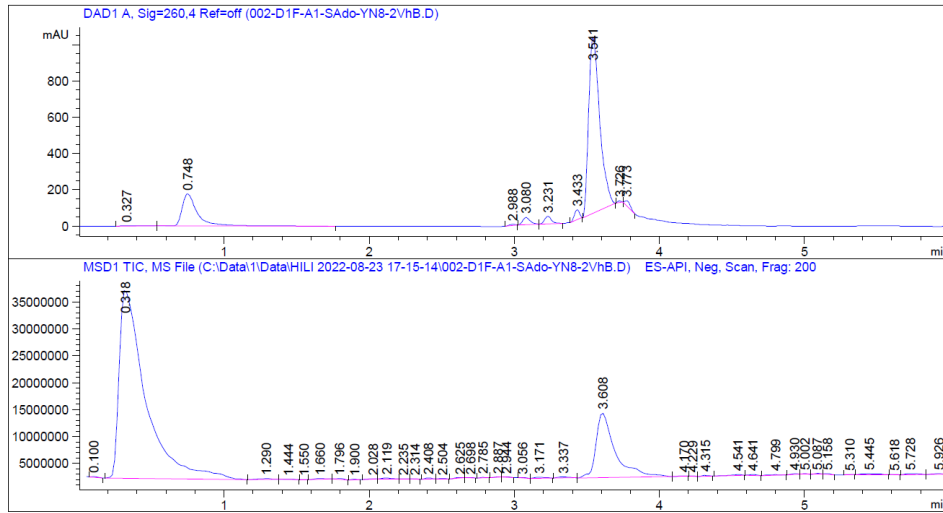


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5399.33	187971	100.00
B	5528.40	39590	21.06

**Figure S40.** Deconvoluted LCMS data for **7c**

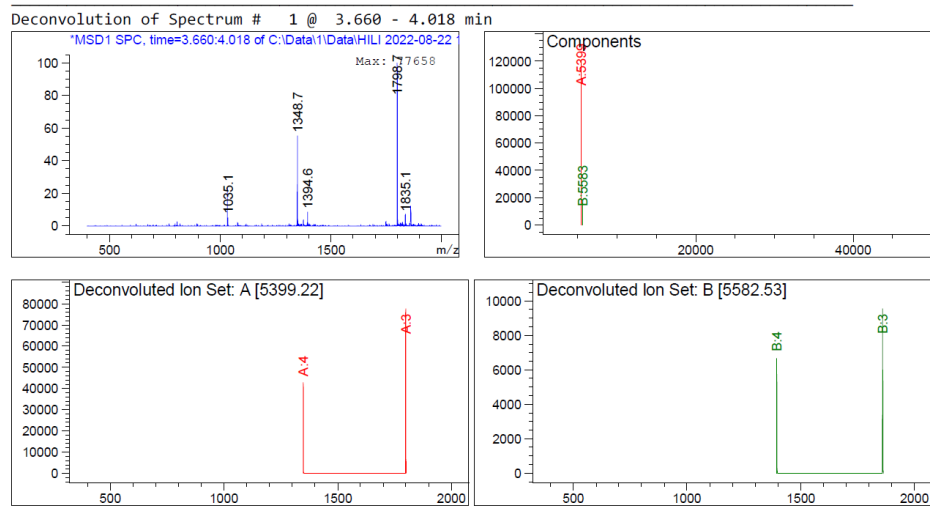
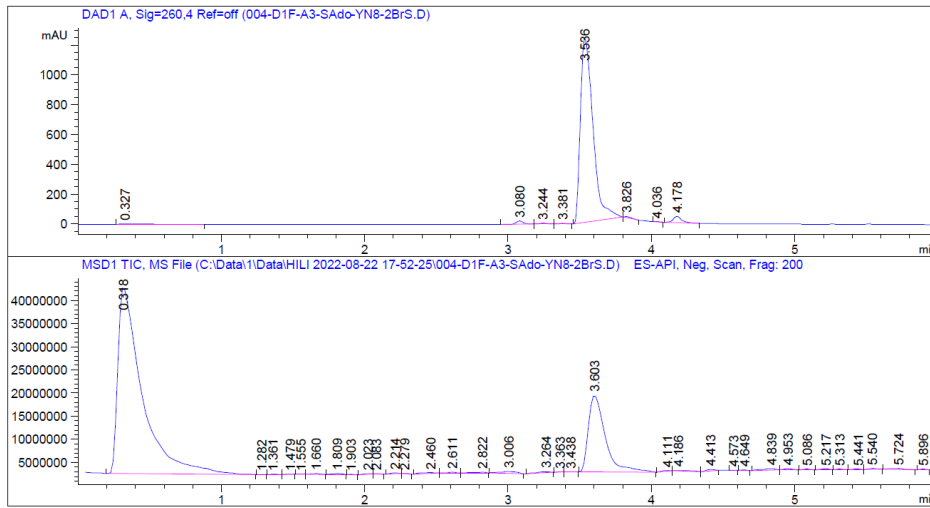
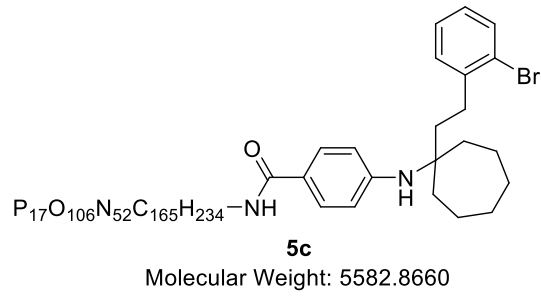


Molecular Weight: 5543.9950



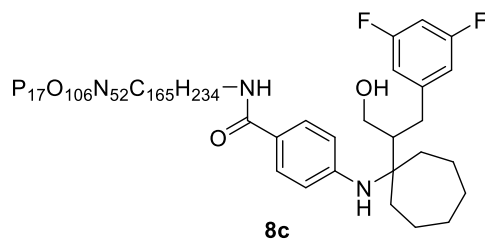
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5399.19	169927	100.00
B	5543.16	28136	16.56

**Figure S41.** Deconvoluted LCMS data for **6c**

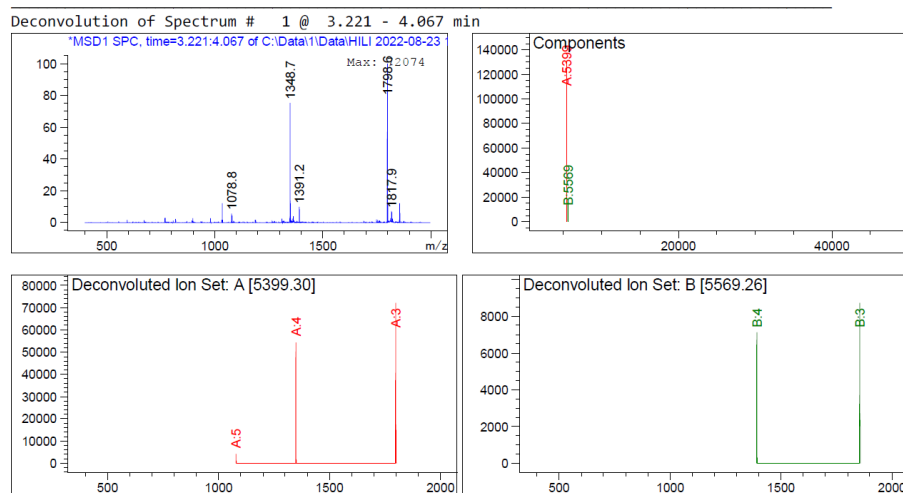
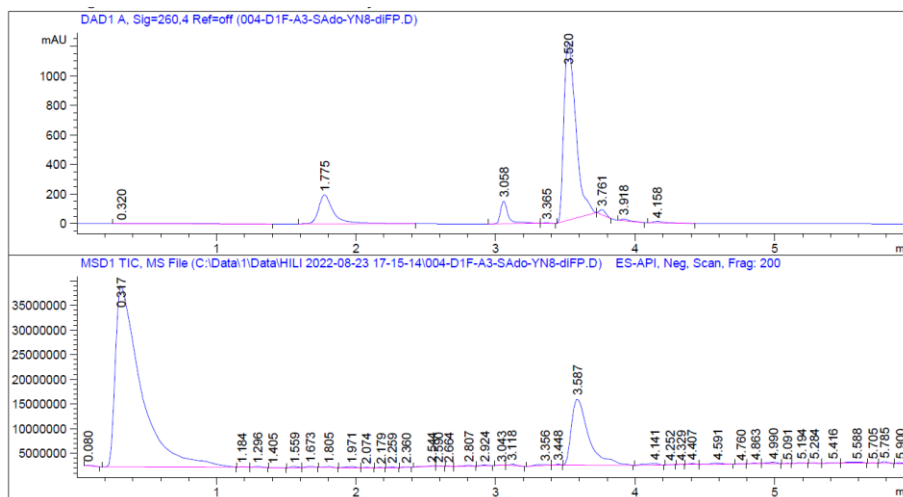


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5399.22	120466	100.00
B	5582.53	15979	13.26

**Figure S42.** Deconvoluted LCMS data for **5c**

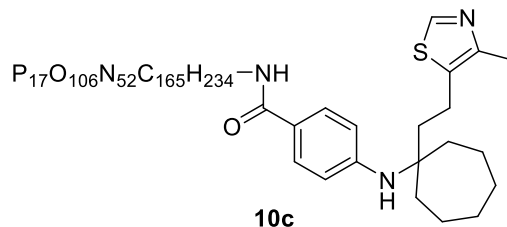


Molecular Weight: 5569.9768

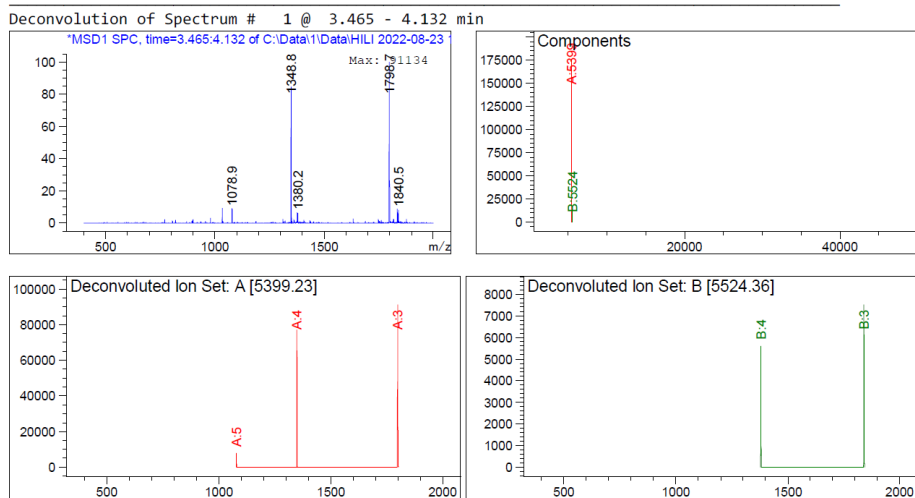
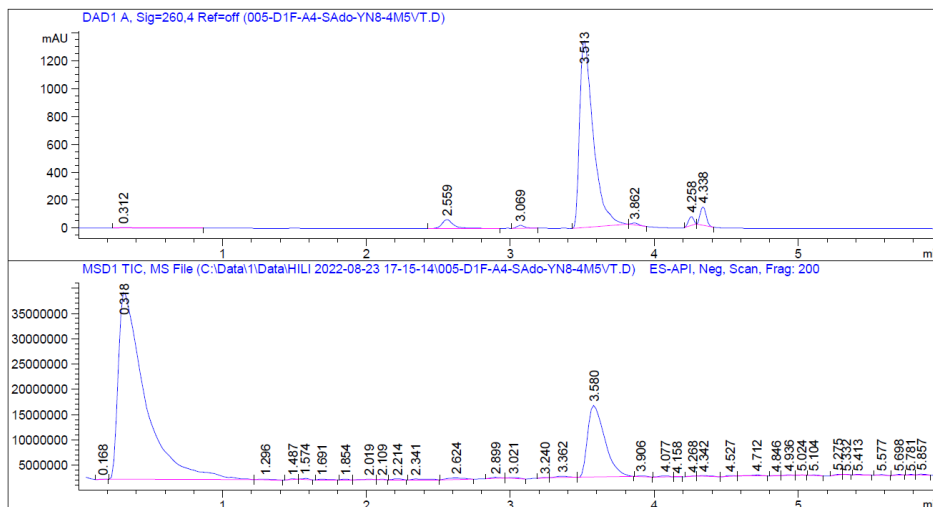


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5399.30	130458	100.00
B	5569.26	15674	12.01

**Figure S43.** Deconvoluted LCMS data for **8c**



Molecular Weight: 5525.0070



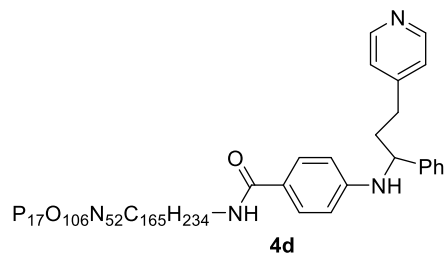
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5399.23	175435	100.00
B	5524.36	13121	7.48

**Figure S44.** Deconvoluted LCMS data for **10c**

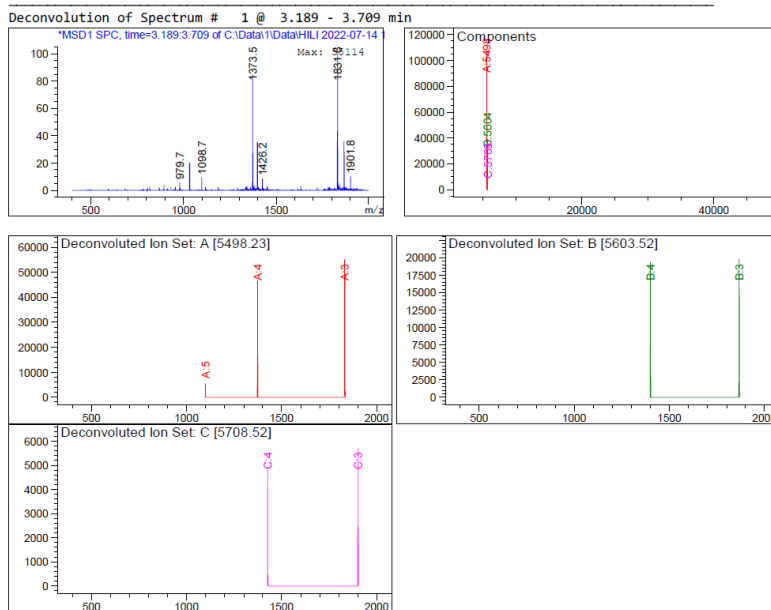
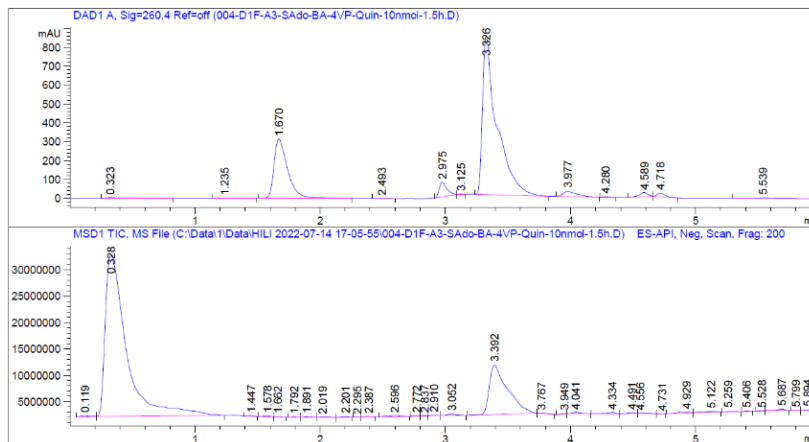
## LCMS spectra and deconvolution results for 1d derivatives

**Table S5:** Hydroaminoalkylation of various vinylarenes with DNA conjugate **1d**

	Starting Material ( <b>1d</b> )	Single Addition	Double Addition	Triple Addition	Other
<b>1d</b> +4VP	-	<b>4d</b> : 68%	25%	7%	-
<b>1d</b> +4CS	13%	<b>7d</b> : 75%	12%	-	-
<b>1d</b> +2BrS	60%	<b>5d</b> : 40%	-	-	-
<b>1d</b> +2VhB	44%	<b>6d</b> : 56%	-	-	-
<b>1d</b> +DPE	77%	<b>3d</b> : 23%	-	-	-
<b>1d</b> +4M5VT	67%	<b>10d</b> : 33%	-	-	-
<b>1d</b> +diFP	100%	<b>8d</b> : 0%	-	-	-
<b>1d</b> +4FMS	100%	<b>11d</b> : 0%	-	-	-
<b>1d</b> +3EhP	82%	<b>9d</b> : 0%	-	-	<b>9d</b> -quinuclidine adduct: 18%
<b>1d</b> +5EMP	100%	<b>12d</b> : 0%	-	-	-
<b>1d</b> +4MS	91%	<b>13d</b> : 0%	-	-	<b>13d</b> -quinuclidine adduct: 9%
<b>1d</b> +4VBA	90%	<b>14d</b> : 0%	-	-	<b>14d</b> -quinuclidine adduct: 10%
<b>1d</b> +4AS	100%	-	-	-	-

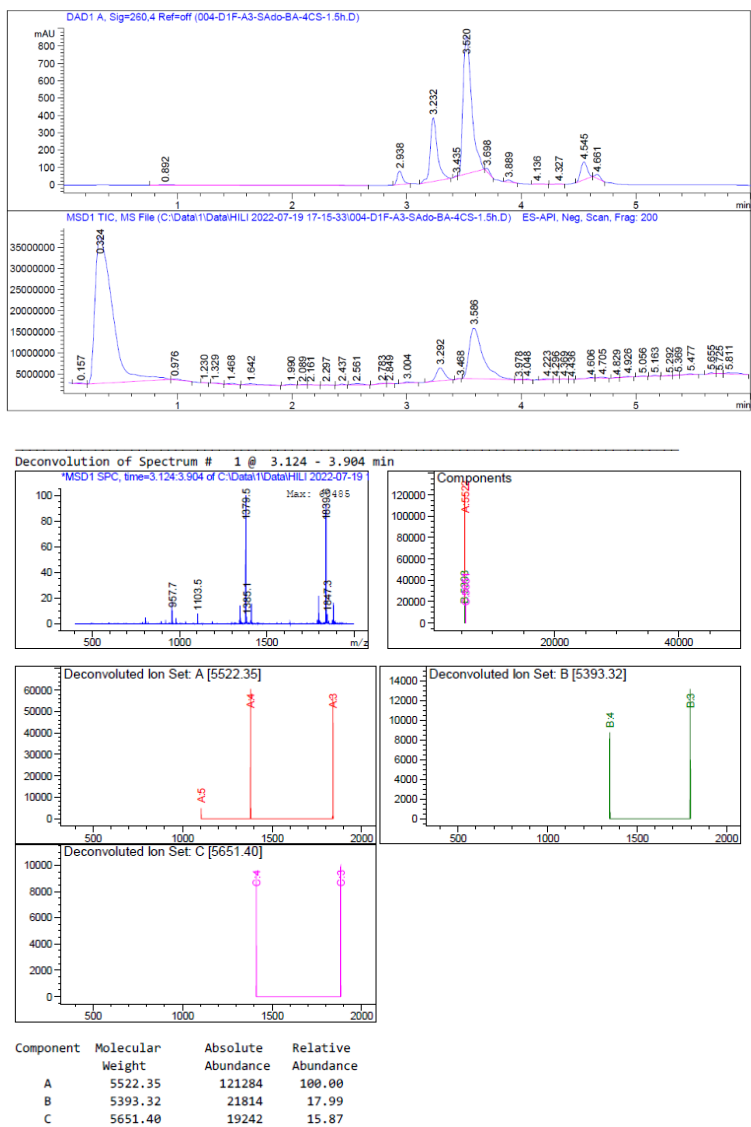
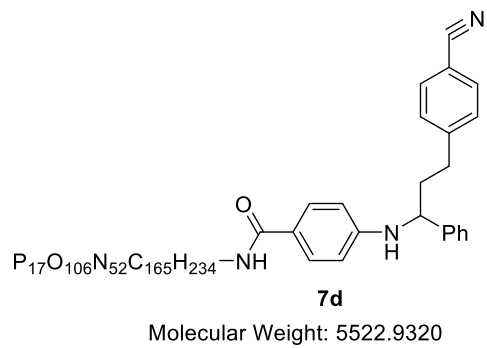


Molecular Weight: 5498.9100



Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5498.23	106623	100.00
B	5603.52	38941	36.52
C	5708.52	10481	9.83

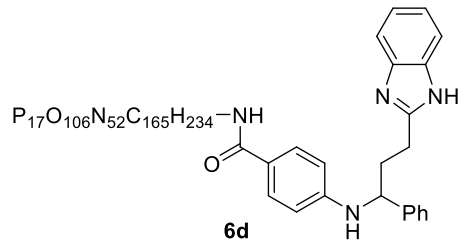
**Figure S45.** Deconvoluted LCMS data for **4d**



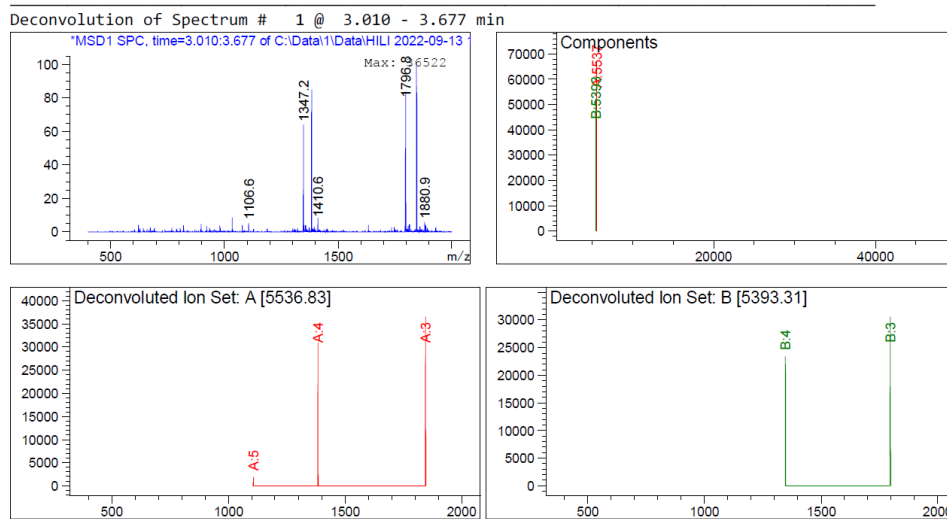
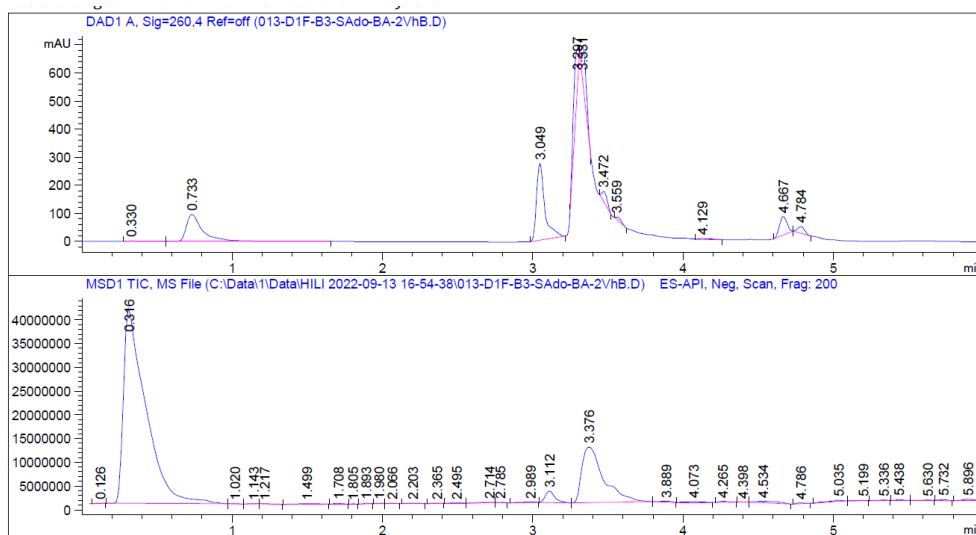
**Figure S46.** Deconvoluted LCMS data for **7d**





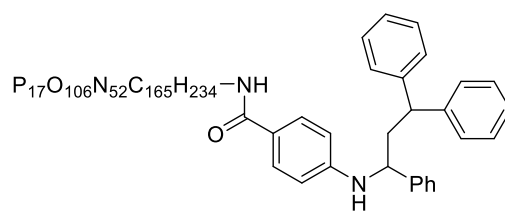


Molecular Weight: 5537.9470



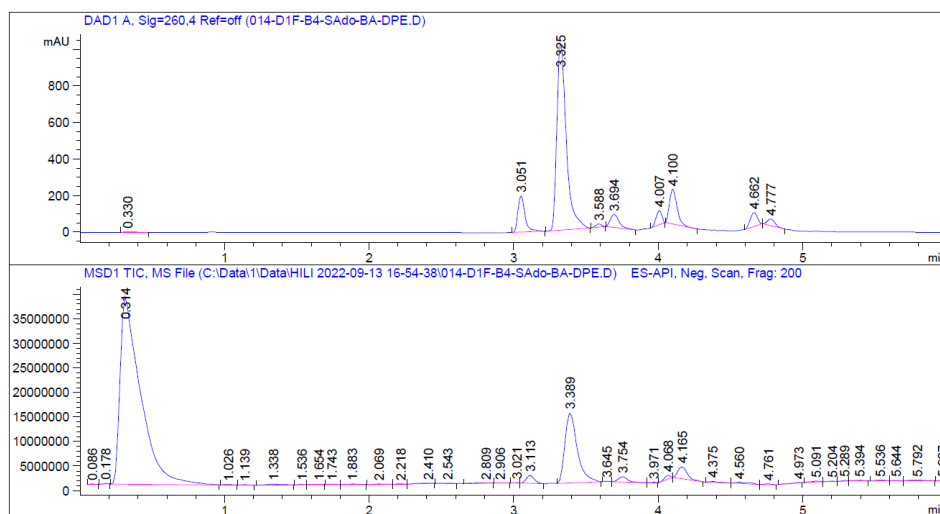
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5536.83	66853	100.00
B	5393.31	52213	78.10

**Figure S48.** Deconvoluted LCMS data for **6d**

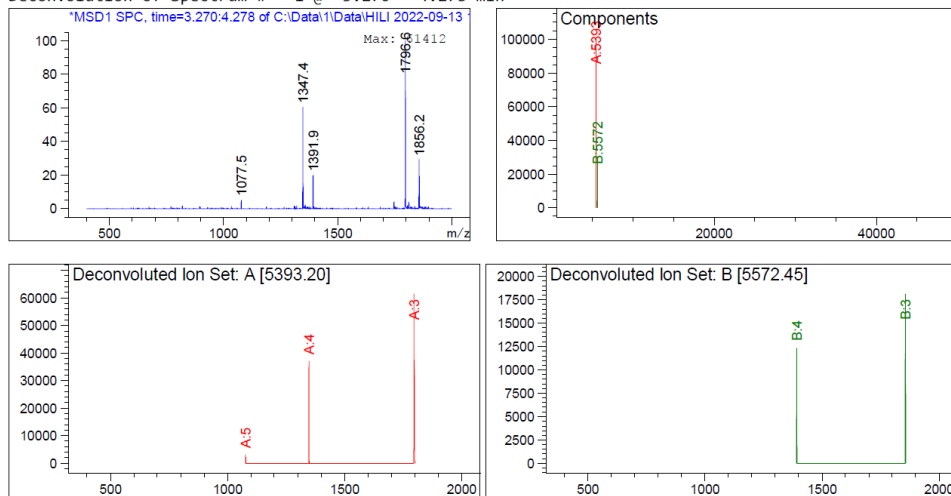


**3d**

Molecular Weight: 5574.0200

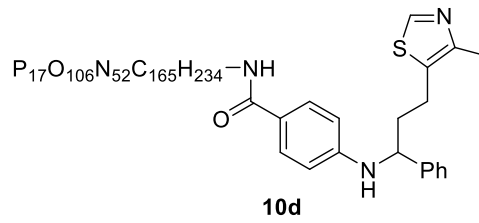


Deconvolution of Spectrum # 1 @ 3.270 - 4.278 min

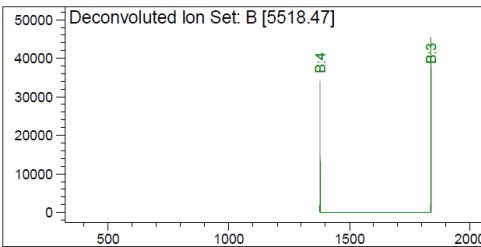
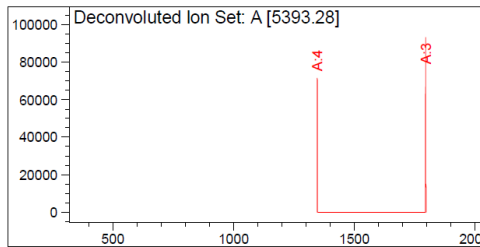
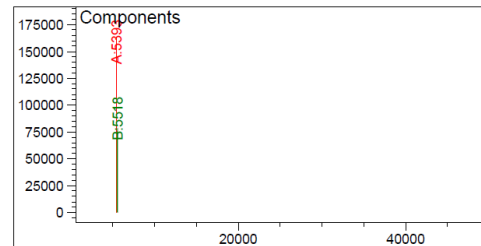
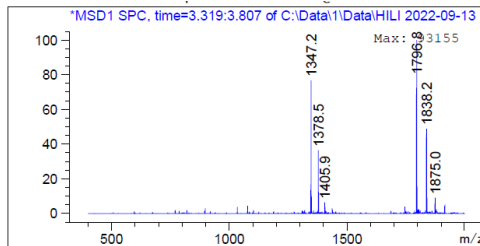
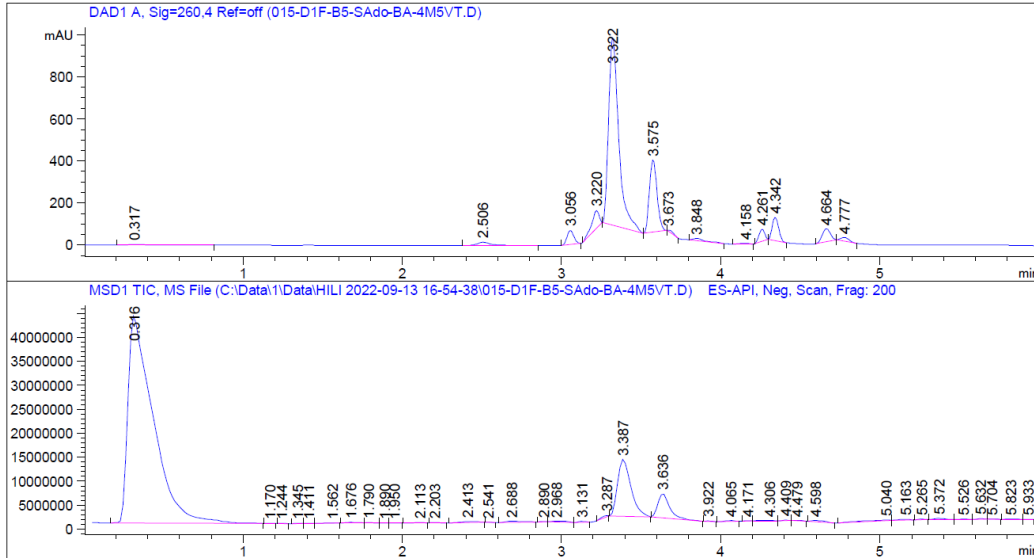


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5393.20	100616	100.00
B	5572.45	30459	30.27

**Figure S49.** Deconvoluted LCMS data for **3d**



Molecular Weight: 5518.9590



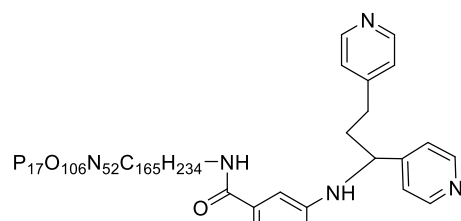
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5393.28	162858	100.00
B	5518.47	78733	48.34

Figure S50. Deconvoluted LCMS data for 10d

## LCMS spectra and deconvolution results for 1e derivatives

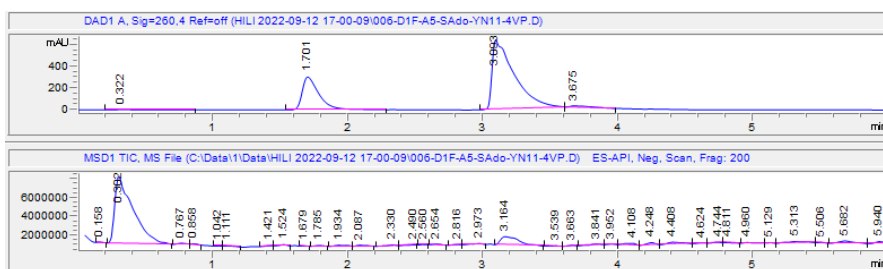
**Table S6:** Hydroaminoalkylation of various vinylarenes with DNA conjugate **1e**

	Starting Material (1e)	Single Addition	Double Addition	Triple Addition
<b>1e+4VP</b>	39%	<b>25:</b> 40%	15%	6%
<b>1e+4CS</b>	63%	<b>26:</b> 31%	6%	-
<b>1e+2BrS</b>	72%	<b>27:</b> 28%	-	-
<b>1e+2VhB</b>	78%	<b>28:</b> 22%	-	-
<b>1e+DPE</b>	86%	<b>29:</b> 14%	-	-
<b>1e+diFP</b>	72%	<b>30:</b> 28%	-	-
<b>1e+4M5VT</b>	90%	<b>31:</b> 10%	-	-
<b>1e+3EhP</b>	100%	-	-	-
<b>1e+4FMS</b>	100%	-	-	-
<b>1e+5EMP</b>	100%	-	-	-
<b>1e+4MS</b>	100%	-	-	-
<b>1e+4VBA</b>	100%	-	-	-
<b>1e+4AS</b>	100%	-	-	-

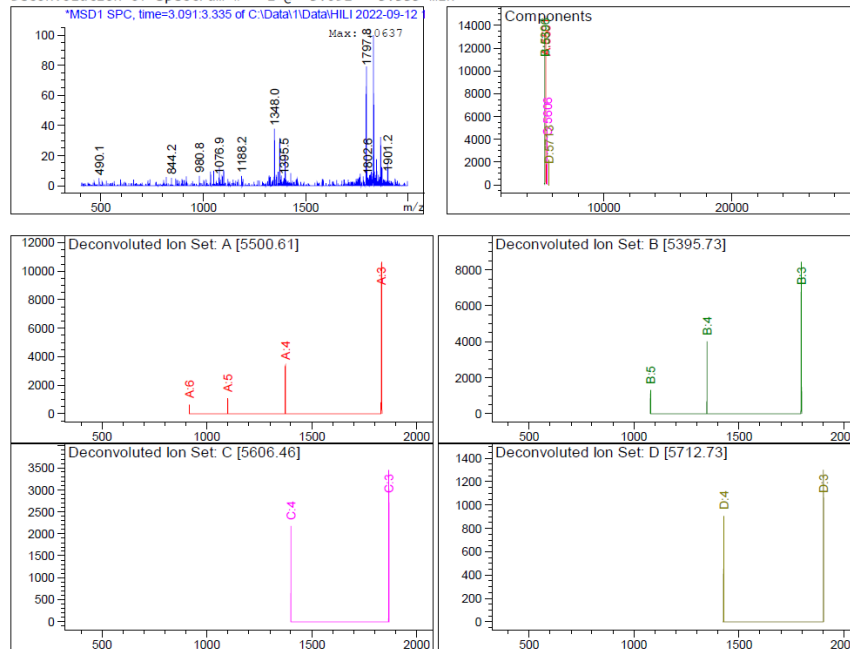


**25**

Molecular Weight: 5500.8860

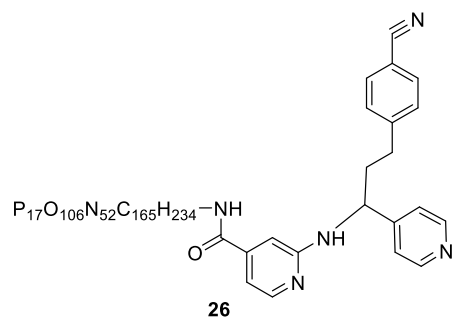


Deconvolution of Spectrum # 1 @ 3.091 - 3.335 min

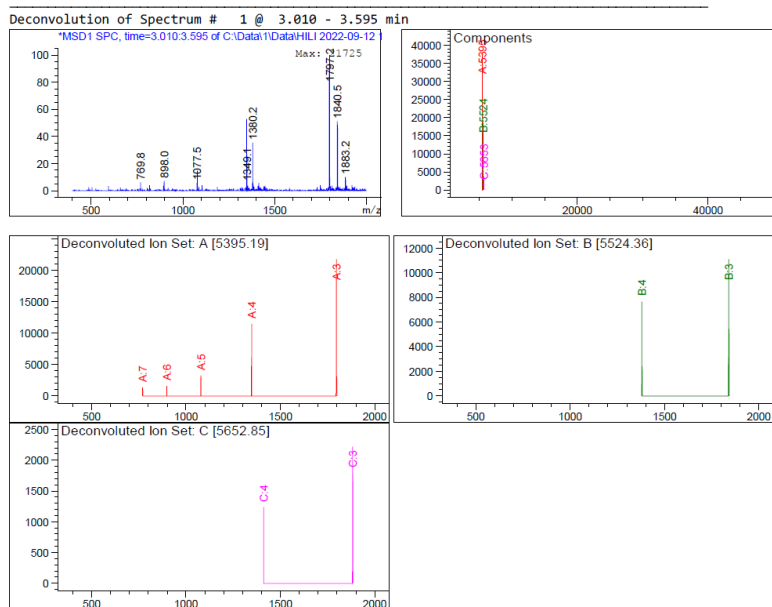
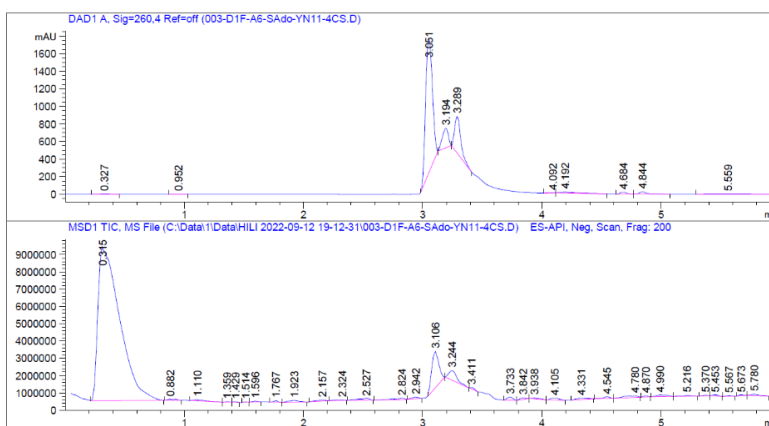


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5500.61	13318	100.00
B	5395.73	13279	99.71
C	5606.46	5036	37.81
D	5712.73	2139	16.06

**Figure S51.** Deconvoluted LCMS data for **25**

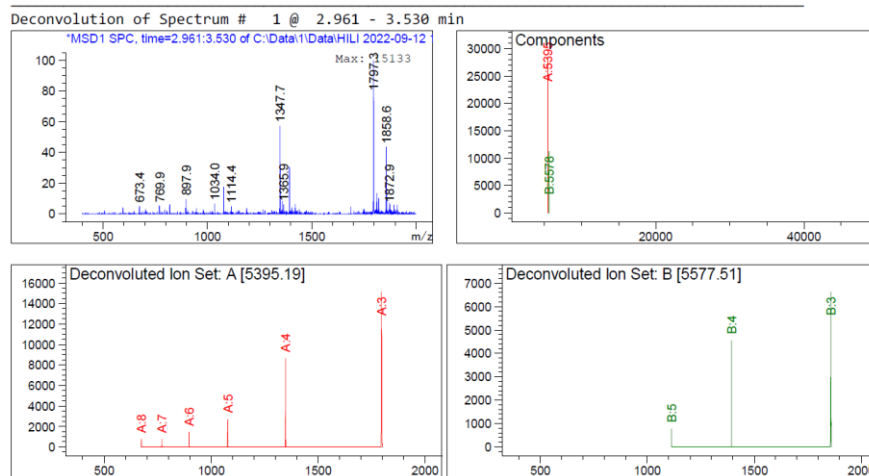
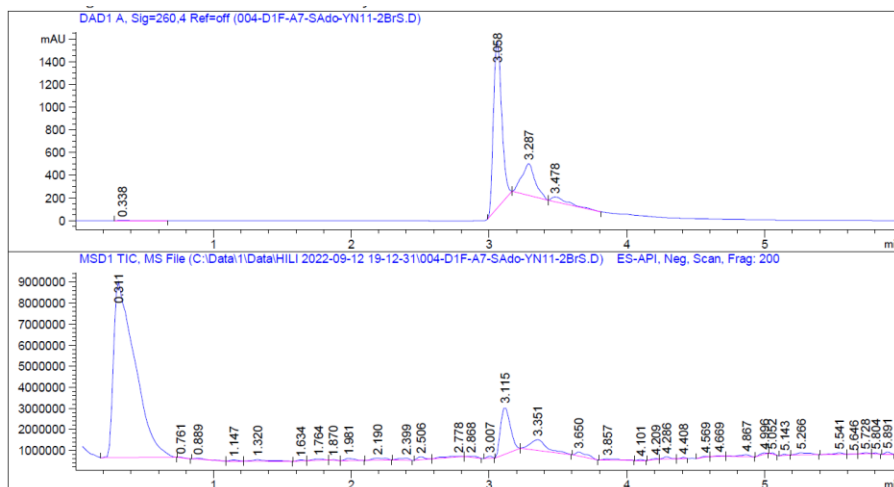
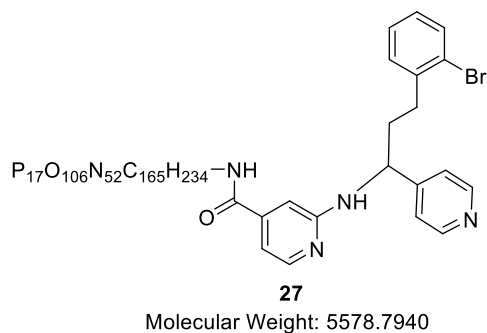


Molecular Weight: 5524.9080



Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5395.19	37767	100.00
B	5524.36	18597	49.24
C	5652.85	3453	9.14

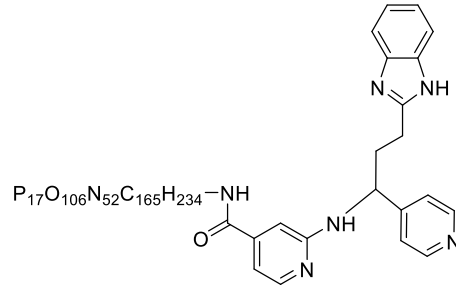
**Figure S52.** Deconvoluted LCMS data for **26**



Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5395.19	28271	100.00
B	5577.51	11176	39.53

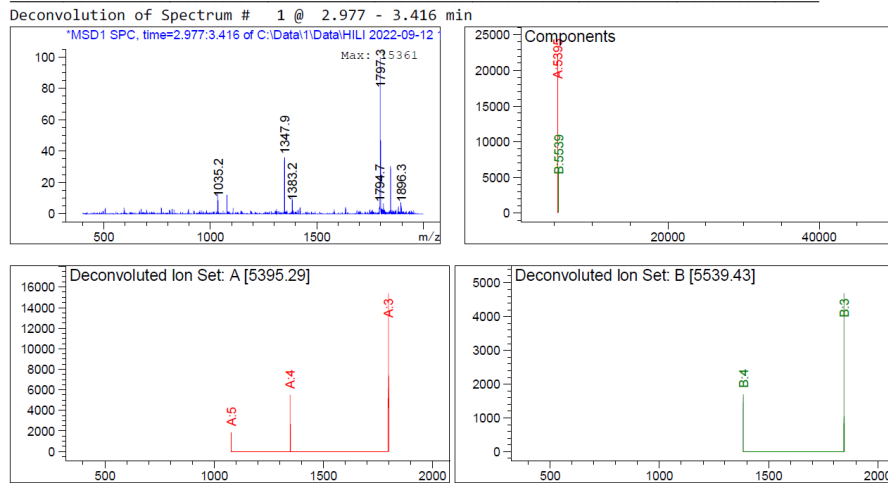
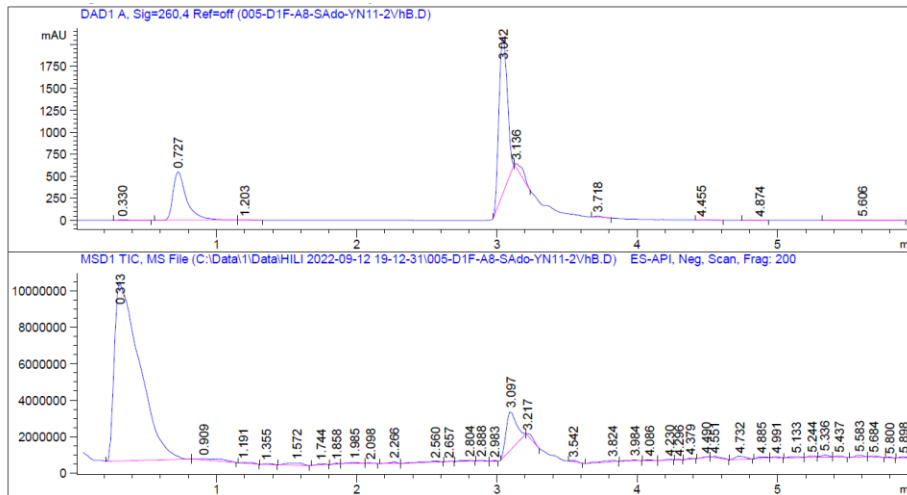
**Figure S53.** Deconvoluted LCMS data for **27**





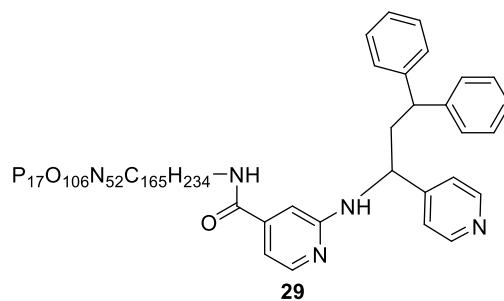
**28**

Molecular Weight: 5539.9230

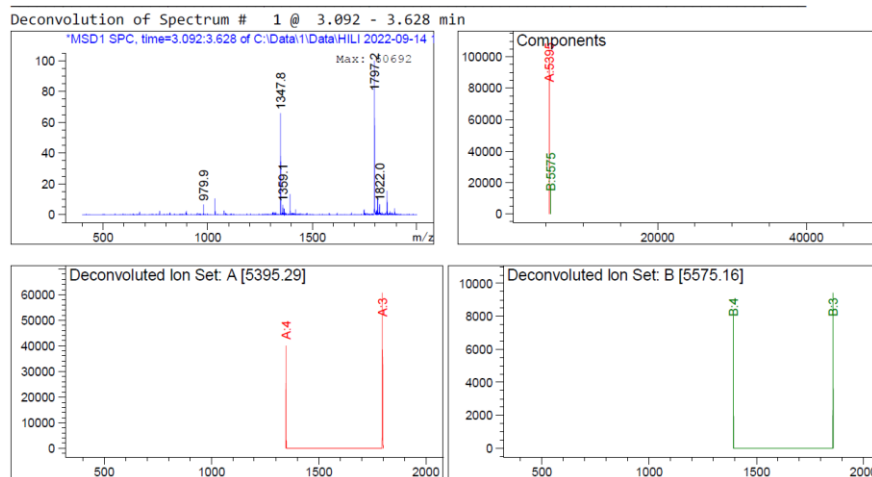
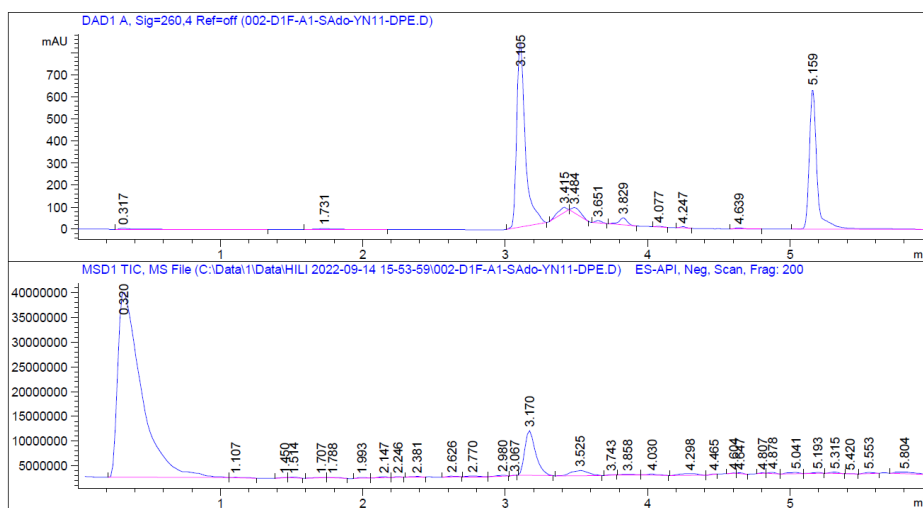


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5395.29	22199	100.00
B	5539.43	6370	28.69

**Figure S54.** Deconvoluted LCMS data for **28**

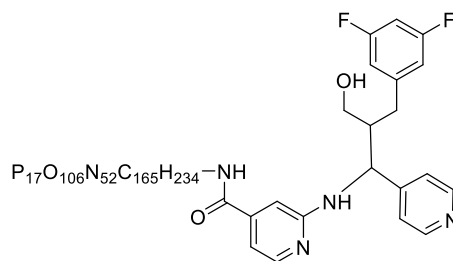


Molecular Weight: 5575.9960



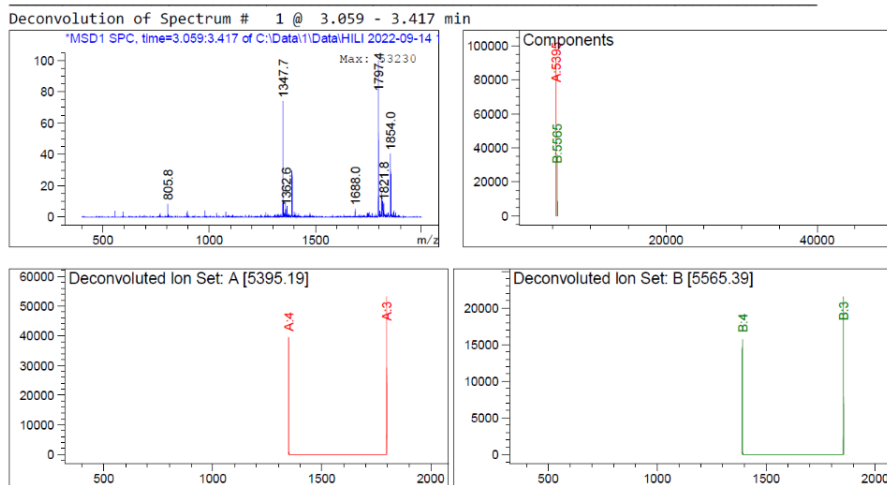
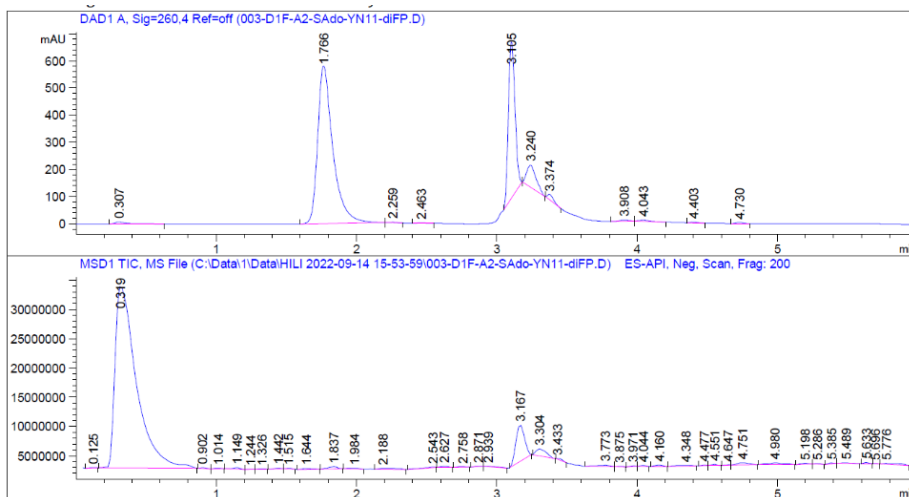
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5395.29	98910	100.00
B	5575.16	16746	16.93

**Figure S55. Deconvoluted LCMS data for 29**



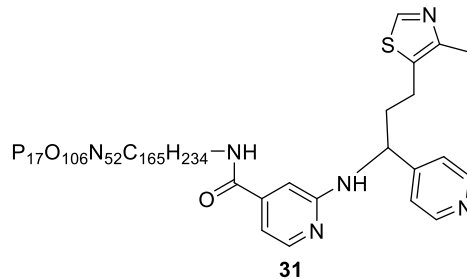
**30**

Molecular Weight: 5565.9048

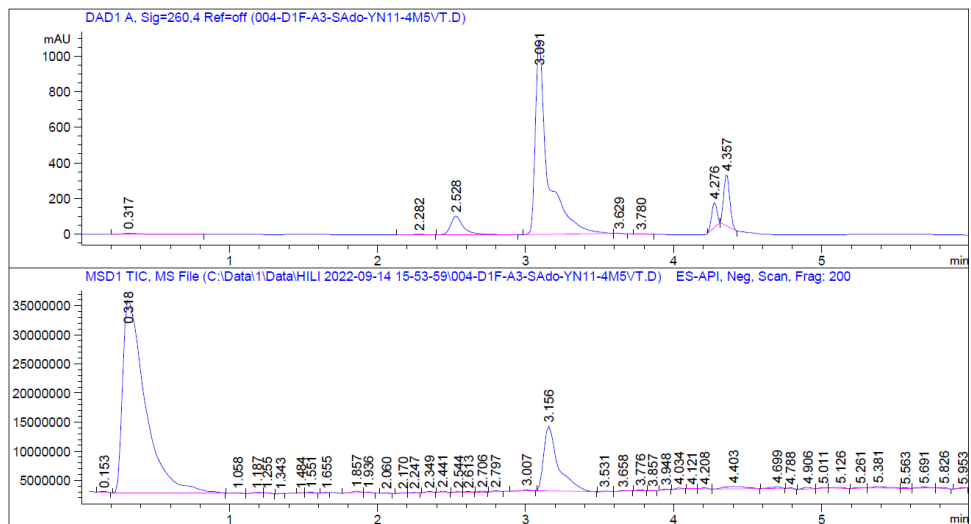


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5395.19	92618	100.00
B	5565.39	36139	39.02

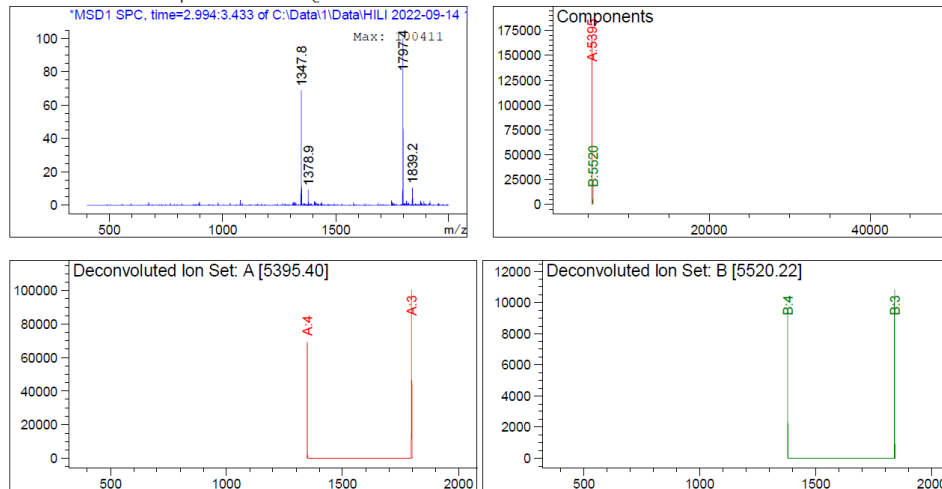
**Figure S56.** Deconvoluted LCMS data for **30**



Molecular Weight: 5520.9350



Deconvolution of Spectrum # 1 @ 2.994 - 3.433 min



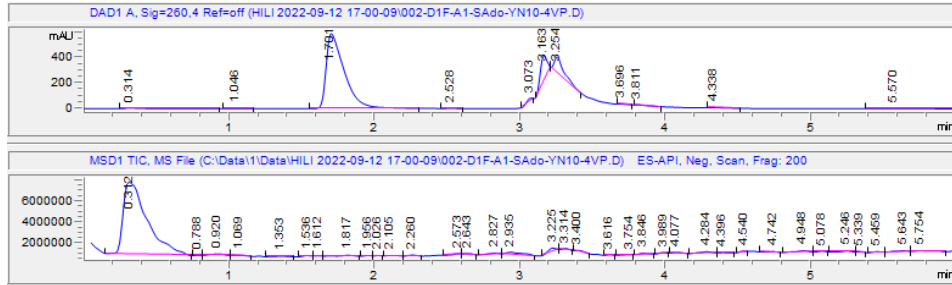
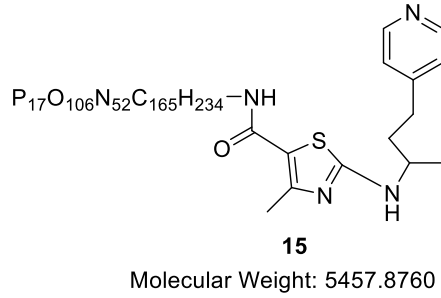
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5395.40	169561	100.00
B	5520.22	19791	11.67

**Figure S57.** Deconvoluted LCMS data for **31**

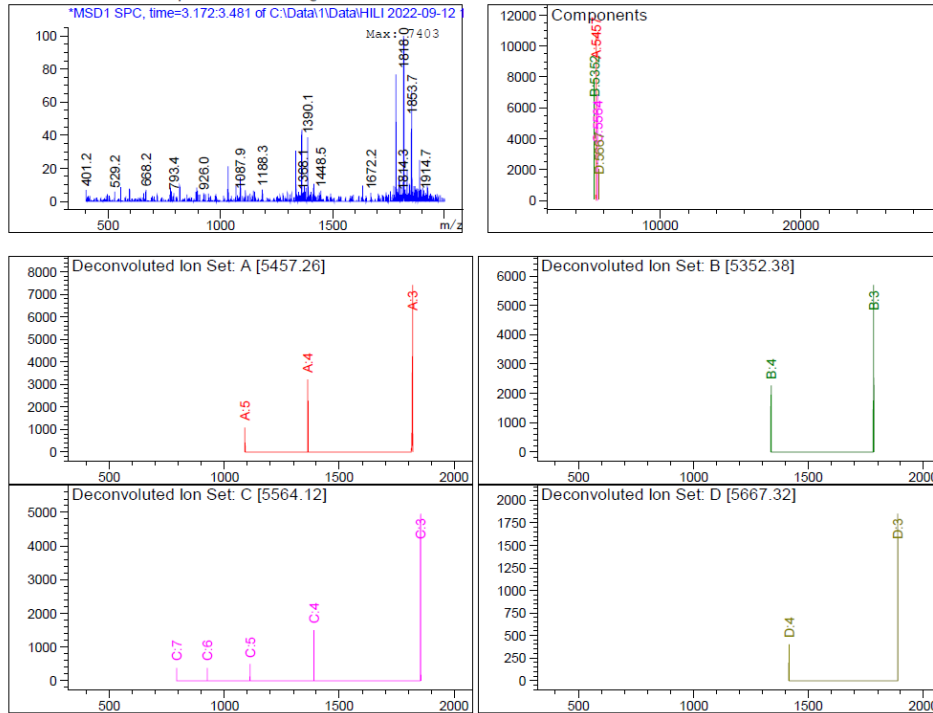
## LCMS spectra and deconvolution results for 1f derivatives

**Table S7:** Hydroaminoalkylation of various vinylarenes with DNA conjugate **1f**

	Starting Material ( <b>1f</b> )	Single Addition	Double Addition	Triple Addition	Other
<b>1f+4VP</b>	29%	<b>15:</b> 39%	25%	7%	-
<b>1f+4CS</b>	47%	<b>16:</b> 40%	13%	-	-
<b>1f+2BrS</b>	80%	<b>17:</b> 20%	-	-	-
<b>1f+2VhB</b>	72%	<b>18:</b> 28%	-	-	-
<b>1f+DPE</b>	73%	<b>19:</b> 27%	-	-	-
<b>1f+diFP</b>	57%	<b>20:</b> 23%	-	-	Dealkylated <b>1f:</b> 20%
<b>1f+3EhP</b>	91%	<b>21:</b> 9%	-	-	-
<b>1f+4M5VT</b>	87%	<b>22:</b> 13%	-	-	-
<b>1f+5EMP</b>	93%	<b>24:</b> 7%	-	-	-
<b>1f+4FMS</b>	100%	<b>23:</b> 0%	-	-	-
<b>1f+4MS</b>	100%	-	-	-	-
<b>1f+4VBA</b>	100%	-	-	-	-
<b>1f+4AS</b>	100%	-	-	-	-

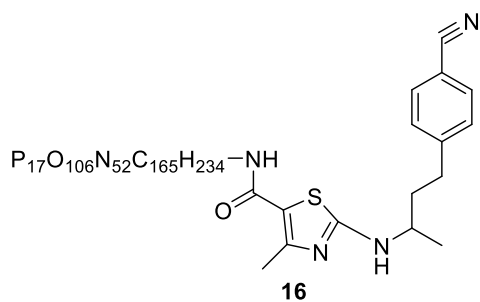


Deconvolution of Spectrum # 1 @ 3.172 - 3.481 min

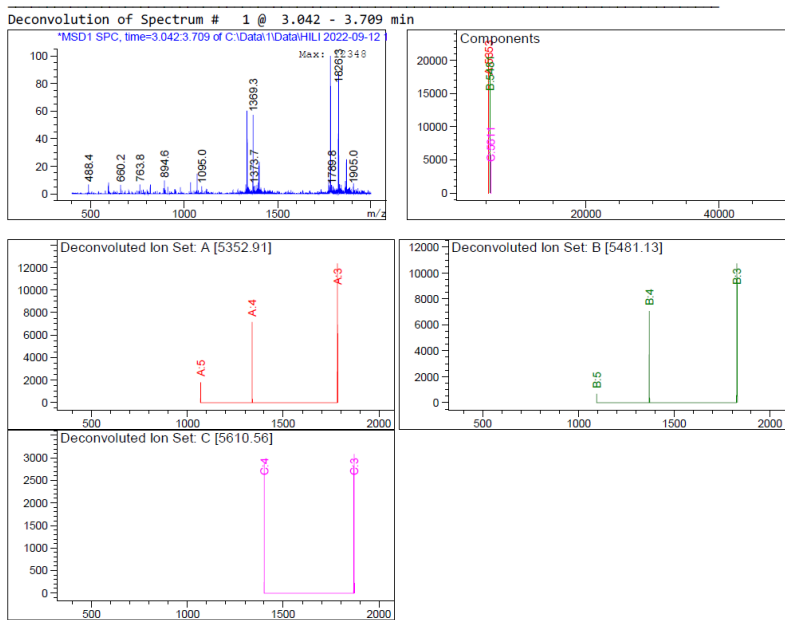
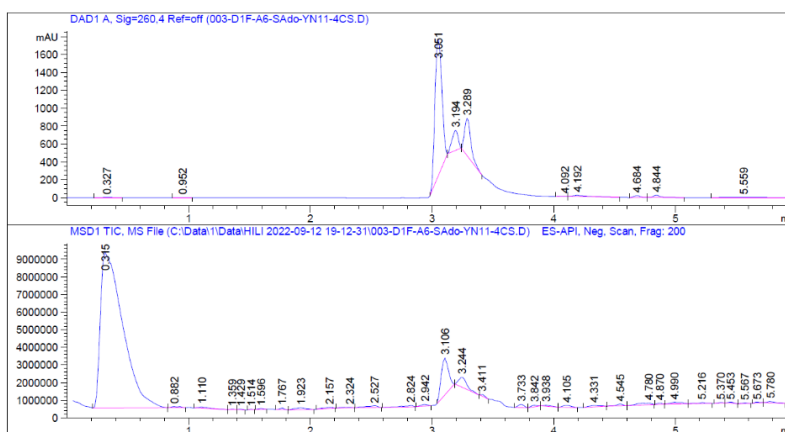


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5457.26	10806	100.00
B	5352.38	7884	72.96
C	5564.12	6808	63.00
D	5667.32	2005	18.55

**Figure S58.** Deconvoluted LCMS data for **15**

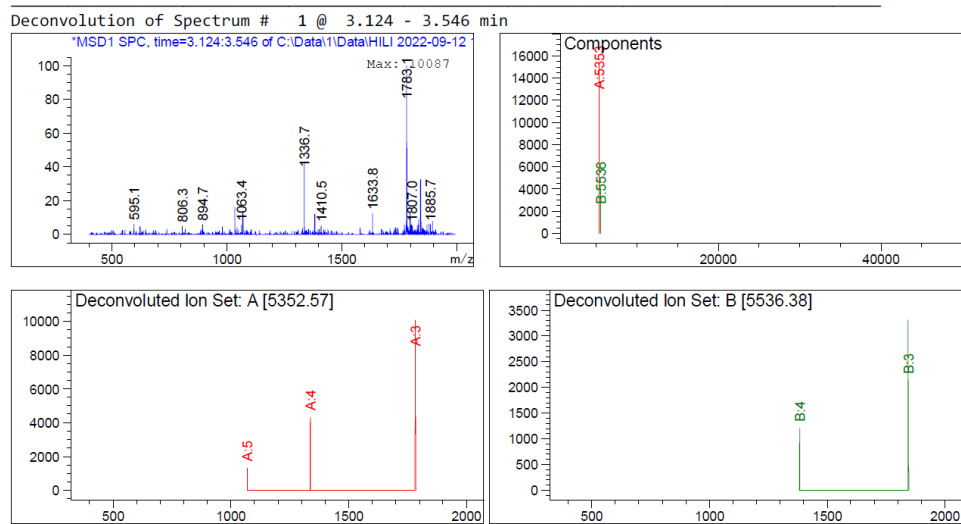
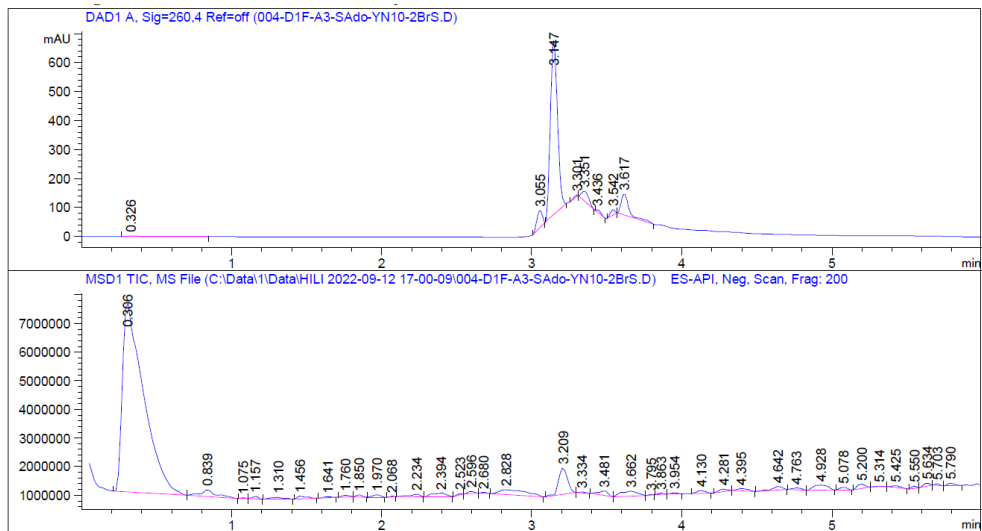
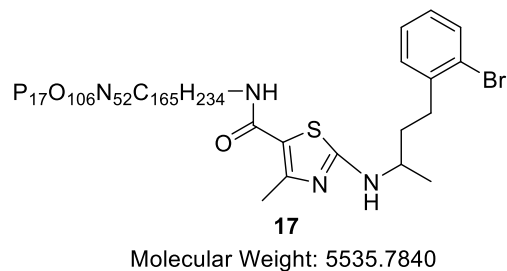


Molecular Weight: 5481.8980



Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5352.91	20957	100.00
B	5481.13	18169	86.70
C	5610.56	5687	27.14

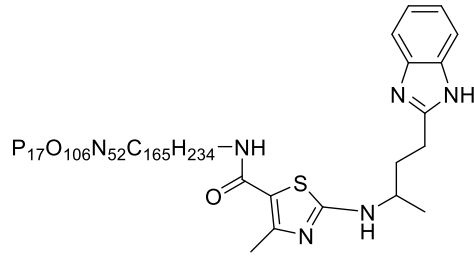
**Figure S59.** Deconvoluted LCMS data for **16**



Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5352.57	15344	100.00
B	5536.38	3823	24.92

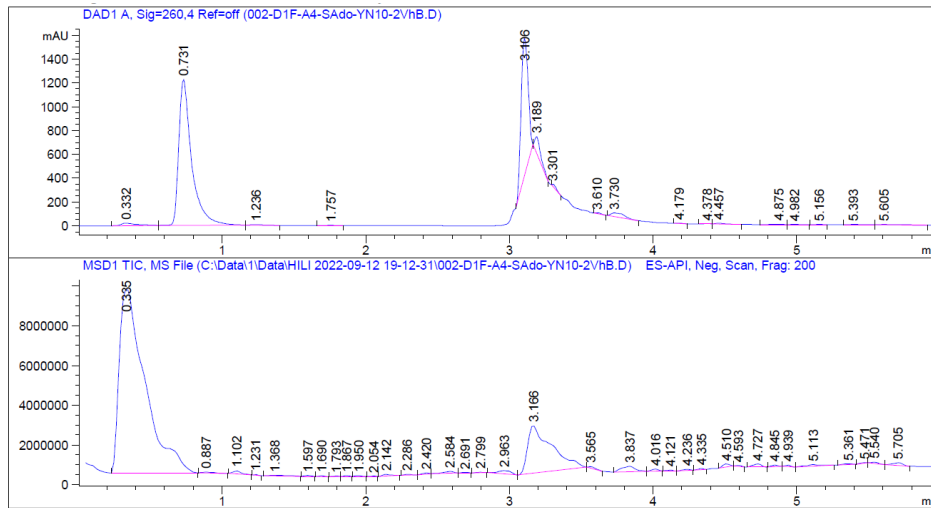
**Figure S60.** Deconvoluted LCMS data for **17**



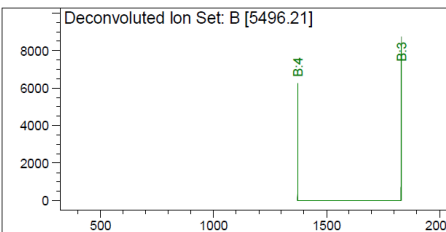
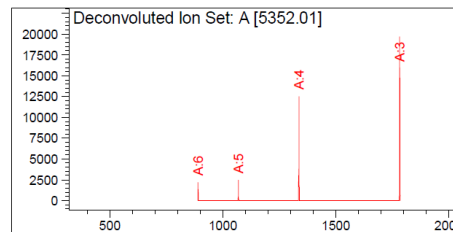
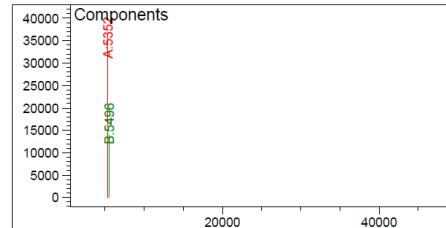
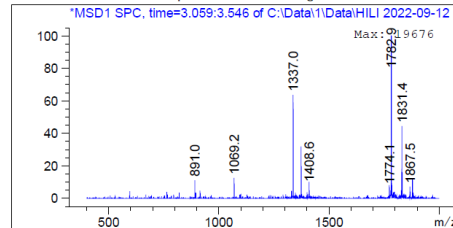


**18**

Molecular Weight: 5496.9130

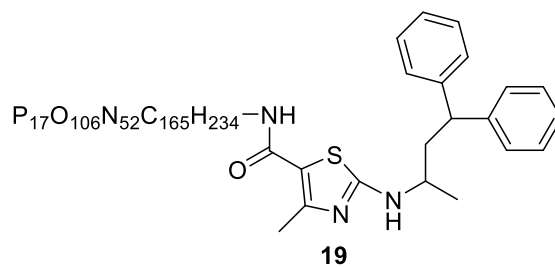


Deconvolution of Spectrum # 1 @ 3.059 - 3.546 min

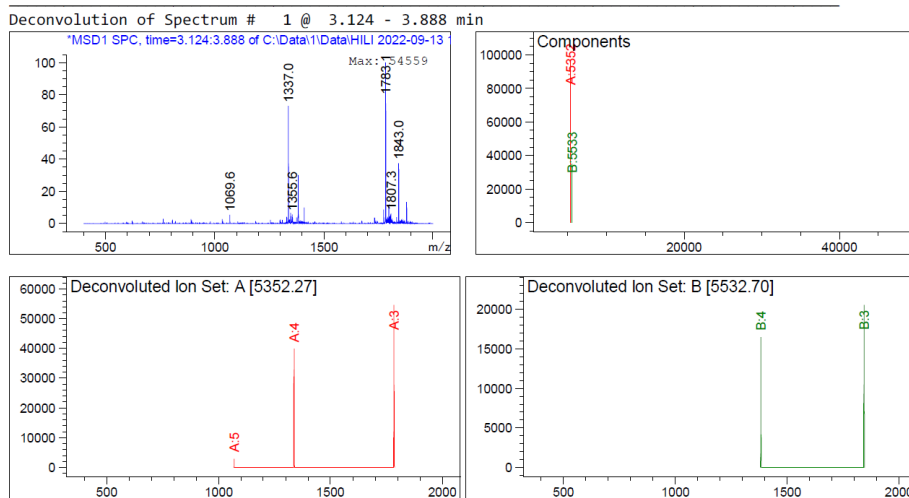
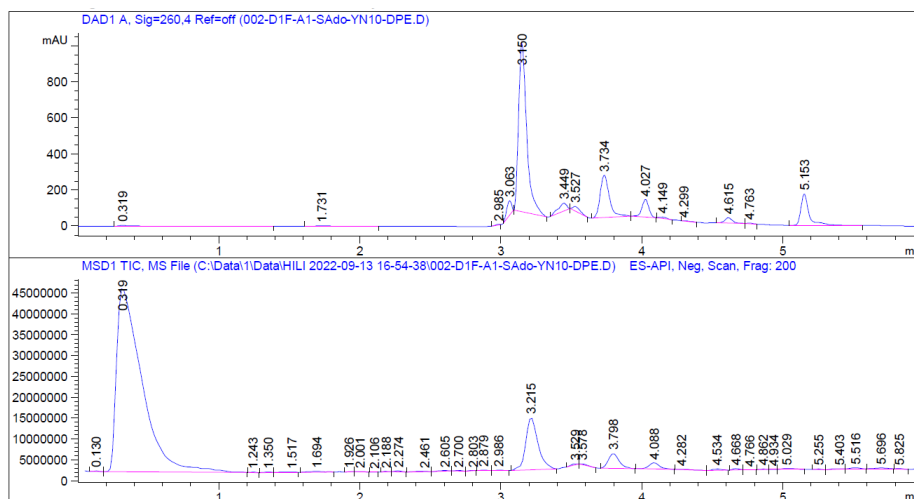


Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5352.01	36598	100.00
B	5496.21	13925	38.05

**Figure S61.** Deconvoluted LCMS data for **18**

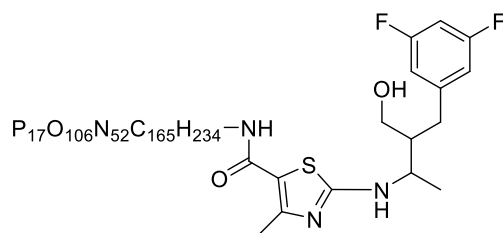


Molecular Weight: 5532.9860



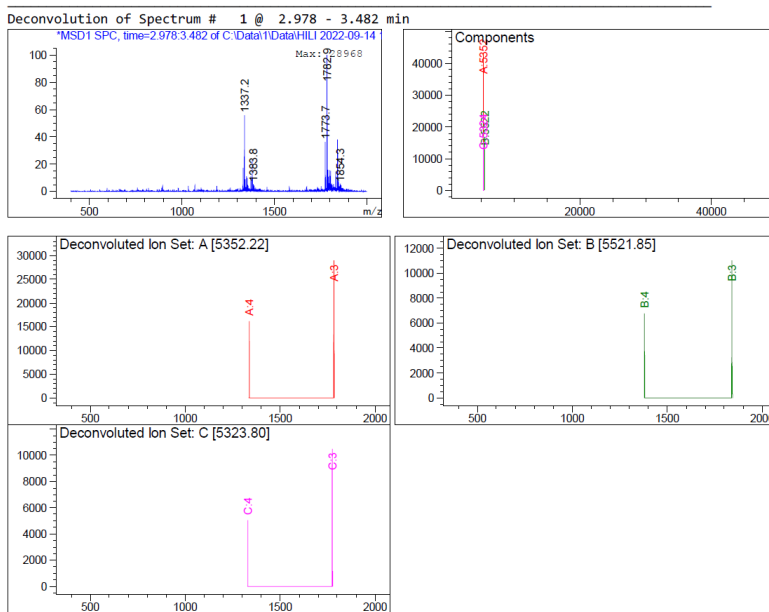
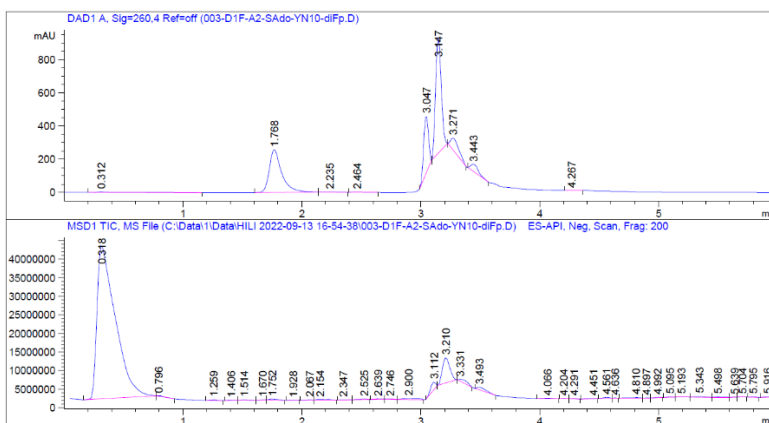
Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5352.27	96726	100.00
B	5532.70	34981	36.17

**Figure S62.** Deconvoluted LCMS data for **19**



20

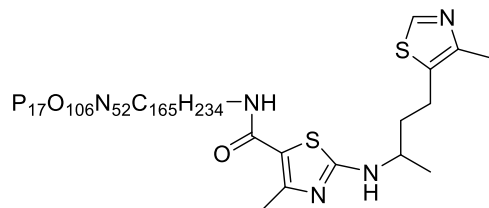
Molecular Weight: 5522.8948



Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5352.22	43189	100.00
B	5521.85	16761	38.81
C	5323.80	15220	35.24

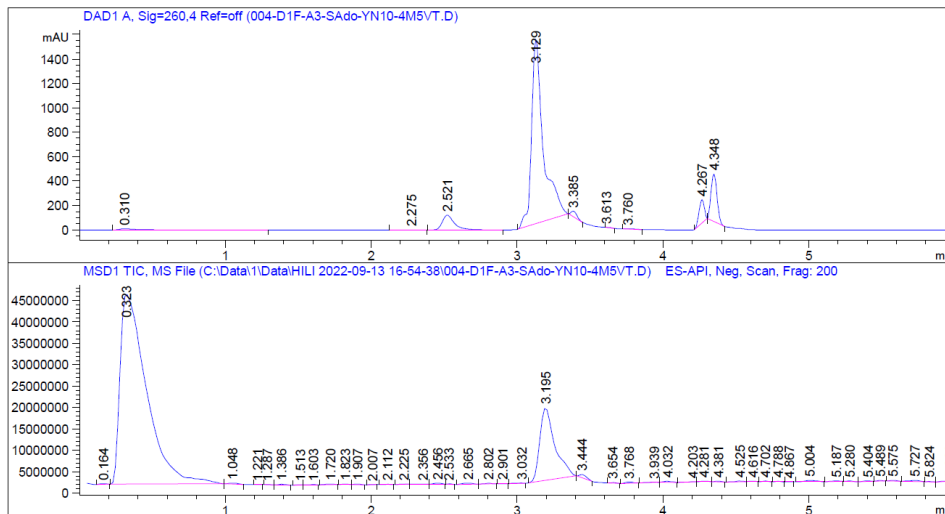
Figure S63. Deconvoluted LCMS data for 20



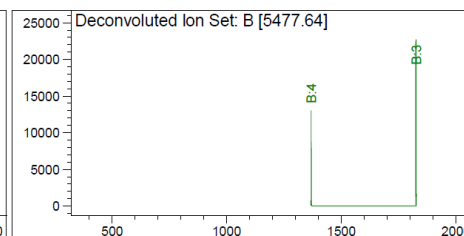
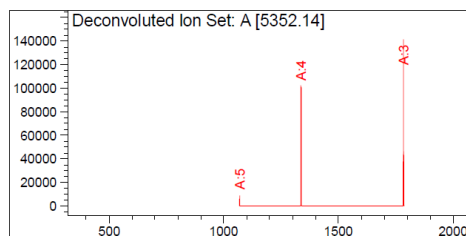
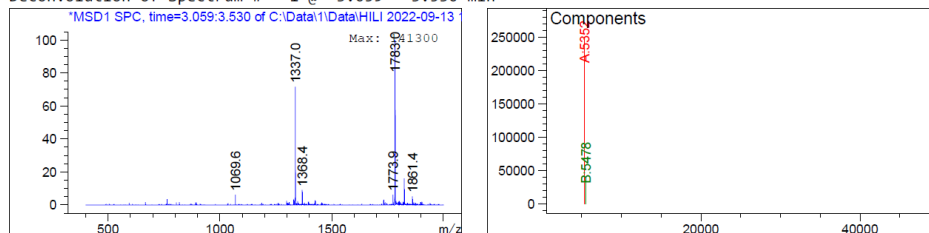


**22**

Molecular Weight: 5477.9250

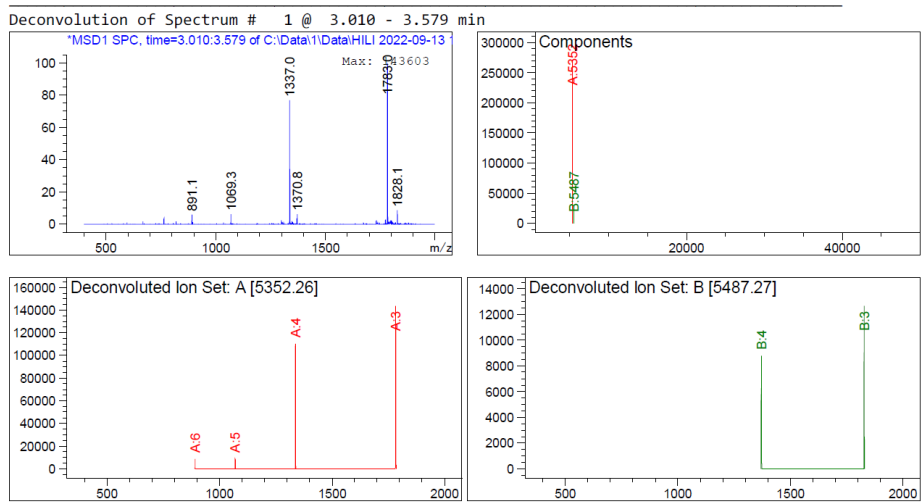
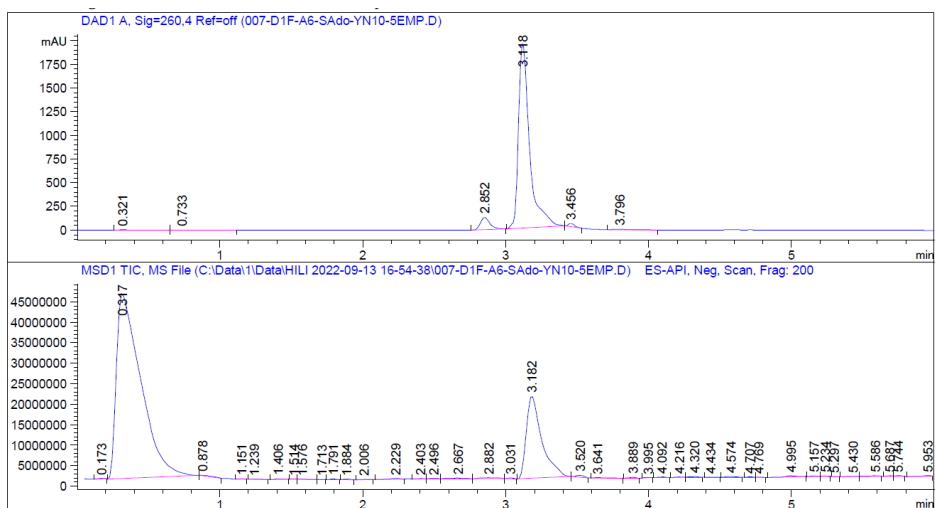
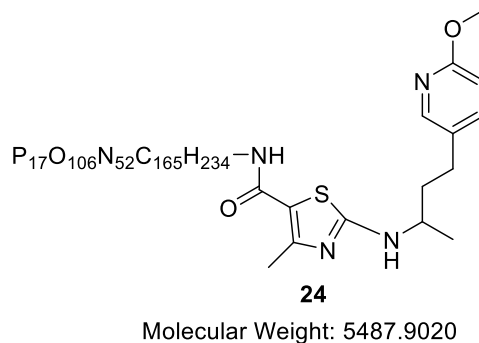


Deconvolution of Spectrum # 1 @ 3.059 - 3.530 min



Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5352.14	249573	100.00
B	5477.64	35657	14.29

**Figure S65.** Deconvoluted LCMS data for **22**



Component	Molecular Weight	Absolute Abundance	Relative Abundance
A	5352.26	270283	100.00
B	5487.27	21224	7.85

**Figure S66.** Deconvoluted LCMS data for **24**

## Analysis of post-reaction DNA integrity

### Synthesis and Purification of LongSAdo-HP-YN1



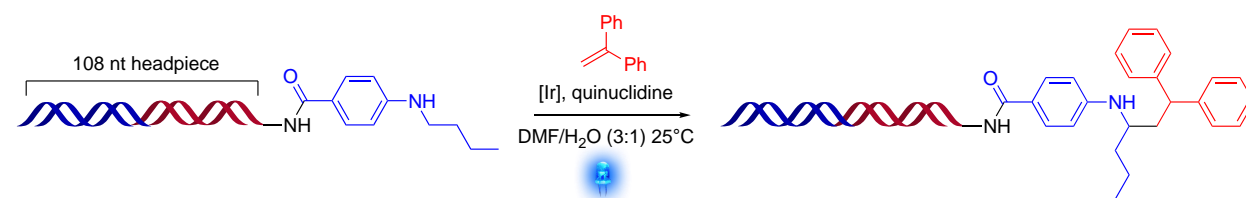
#### Elongation Duplex Sequences:

5'-/5Phos/AAA TCG ATG TGT TCC GCA AGA AGC CTG GTA AGC GGA GAA AGG TCG TT -3'

5'-/5Phos/CGA CCT TTC TCC GCT TAC CAG GCT TCT TGC GGA ACA CAT CGA TTT GG -3'

Ligation was conducted using a modified procedure.<sup>1,4</sup> The elongation duplex (IDT) were first combined by adding 100  $\mu$ L of 2 mM of each strand, in water (200  $\mu$ L total). The duplex was annealed by heating to 95  $^{\circ}$ C for 5 minutes, then cooling to rt at a ramp of -0.1  $^{\circ}$ C/s. The annealed duplex solution (1.4 equiv, 185.9  $\mu$ L, 1 mM) was added to SAdo-HP-YN1 (1 equiv, 132.8 nmol, 132.8  $\mu$ L, 1 mM), along with 150.2  $\mu$ L of water, and 53  $\mu$ L 10x T4 ligation buffer. The sample was then heated to 95  $^{\circ}$ C for 1 minute, and cooled to 16  $^{\circ}$ C over 10 minutes. T4 ligase (7.98  $\mu$ L, 400,000 cohesive end units/mL, NEB) was added, the reaction was mixed gently by pipetting up and down, and left to react overnight at 16  $^{\circ}$ C. Ethanol precipitation was completed according to the general procedure for ethanol precipitation. The product was purified using HPLC and the collected fractions were lyophilized three times, prior to the hydroaminoalkylation photoreaction.

#### Quantitative PCR analysis protocol



#### Forward and Reverse Primer Sequences:

DELPCR1: 5'-TGA CTC CCA AAT CGA TGT G-3' T<sub>m</sub> (50 mM NaCl) = 52.2  $^{\circ}$ C

DELPCR3: 5'-AAC GAC CTT TCT CCG CT -3' T<sub>m</sub> (50 mM NaCl) = 53.7  $^{\circ}$ C

Quantitative PCR was performed after the hydroaminoalkylation photoreaction on LongSAdo-HP-YN1 and compared against a no-reaction control. Data was collected using a CFX Connect instrument from Bio-Rad. A standard curve was prepared at 100 nM, 10 nM, 1 nM, 0.1 nM and 0.01 nM concentrations. The qPCR reagents were prepared with SYBR Green I as the detection dye. To 10  $\mu$ L of 1  $\mu$ M of the template sequence, was added 2.5  $\mu$ L of each primer (IDT) at 10  $\mu$ M, 5  $\mu$ L of 10x SYBR Green, 5  $\mu$ L of water, and 25  $\mu$ L of 2X Q5 Master Mix (NEB), for a total of 50  $\mu$ L. The resulting  $\Delta$ C<sub>t</sub> value was calculated using CFX manager. The qPCR cycles were as follows:

Cycle Step	Temperature, $^{\circ}$ C	Time (seconds)	Cycles
Initiation	95	30	1

Denaturation	95	10	30
Annealing	58	30	
Extension	72	30 + plate read	

### **Ligation Test on LongSAdo-HP-YN1**

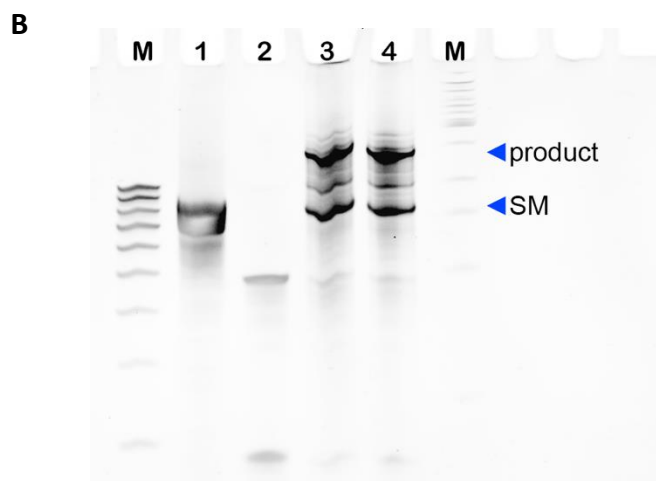
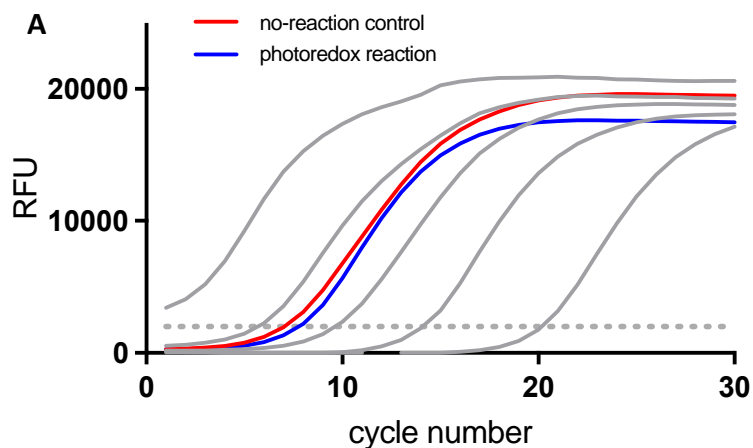
#### Closing Primer Sequences:

5'-/5Phos/ACG ATG CCC GGT CTA CNN NNN NNN NNN NCT GAT GGC GCG AGG GAG GC-3'

5'-GTA GAC CGG GCA TCG TAA-3'

Following the photoreaction on LongSAdo-HP-YN1, ligation efficacy was assessed to evaluate the integrity of the DNA code for downstream applications. Closing primers were ligated on as previously described. The 10 nmol hydroaminoalkylation reaction and no reaction control were both cleaned up by ethanol precipitation (according to the general procedure), and 30 pmols of each sample was loaded with Gel Loading Buffer II (ThermoFisher) onto a 15% denaturing gel for polyacrylamide gel electrophoresis (150 V, 70 minutes). The gel was stained with ethidium bromide and visualized using Bio-Rad Gel Doc XR+. Densitometry was performed using Rio-Rad Image Lab.





**Figure S67.** Analysis of DNA tag integrity following photoredox-catalysed hydroaminoalkylation of longSAdo-YN1 and DPE. **A)** Photoredox reactions were performed on 10 nmol scale. qPCR analysis was performed using Q5 polymerase (M0492, NEB). Grey lines indicate 10-fold dilution series. Red and blue curves indicate no-reaction control and photoredox reaction, respectively. Cycle threshold values were used to calculate concentrations. 29.9% degradation was observed for this process compared to the no-reaction control. **B)** Ligation efficiency comparison between the no-reaction control and DNA photoredox catalysed hydroaminoalkylation reaction using T4 DNA ligase (M0202, NEB). M: molecular weight ladder, 1: starting long SAdo-YN1 substrate, 2: closing duplex, 3: ligation reaction of long-SAdo-YN1 photoreacted with 1,1-dipheylethylene, 4: ligation reaction of long-SAdo-YN1 as no-reaction control, M: molecular weight ladder.

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- (1) Clark, M. A.; Acharya, R. A.; Arico-Muendel, C. C.; Belyanskaya, S. L.; Benjamin, D. R.; Carlson, N. R.; Centrella, P. A.; Chiu, C. H.; Creaser, S. P.; Cuozzo, J. W.; Davie, C. P.; Ding, Y.; Franklin, G. J.; Franzen, K. D.; Gefter, M. L.; Hale, S. P.; Hansen, N. J. V.; Israel, D. I.; Jiang, J.; Kavarana, M. J.; Kelley, M. S.; Kollmann, C. S.; Li, F.; Lind, K.; Mataruse, S.; Medeiros, P. F.; Messer, J. A.; Myers, P.; O'Keefe, H.; Oliff, M. C.; Rise, C. E.; Satz, A. L.; Skinner, S. R.; Svendsen, J. L.; Tang, L.; van Vloten, K.; Wagner, R. W.; Yao, G.; Zhao, B.; Morgan, B. A. Design, Synthesis and Selection of DNA-Encoded Small-Molecule Libraries. *Nat. Chem. Biol.* **2009**, *5* (9), 647–654. <https://doi.org/10.1038/nchembio.211>.
- (2) Andrade, A. L.; Melich, K.; Whatley, G. G.; Kirk, S. R.; Karpen, J. W. Cyclic Nucleotide-Gated Channel Block by Hydrolysis-Resistant Tetracaine Derivatives. *J. Med. Chem.* **2011**, *54* (13), 4904–4912. <https://doi.org/10.1021/jm200495g>.
- (3) Abdel-Magid, A. F.; Carson, K. G.; Harris, B. D.; Maryanoff, C. A.; Shah, R. D. Reductive Amination of Aldehydes and Ketones with Sodium Triacetoxyborohydride. Studies on Direct and Indirect Reductive Amination Procedures. *J. Org. Chem.* **1996**, *61* (11), 3849–3862. <https://doi.org/10.1021/jo960057x>.
- (4) J. P. Phelan, S. B. Lang, J. Sim, S. Berritt, A. J. Peat, K. Billings, L. Fan and G. A. Molander, *J. Am. Chem. Soc.*, 2019, **141**, 3723–3732. <https://doi.org/10.1021/jacs.9b00669>.