

Supporting Information for

Design of the new closo-dodecarborate-containing gemcitabine analogue for the albumin-based theranostics composition.

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Spectral data for new compounds

4-*N*-benzoyl-2'-deoxy-2',2'-difluorocytidine (2)

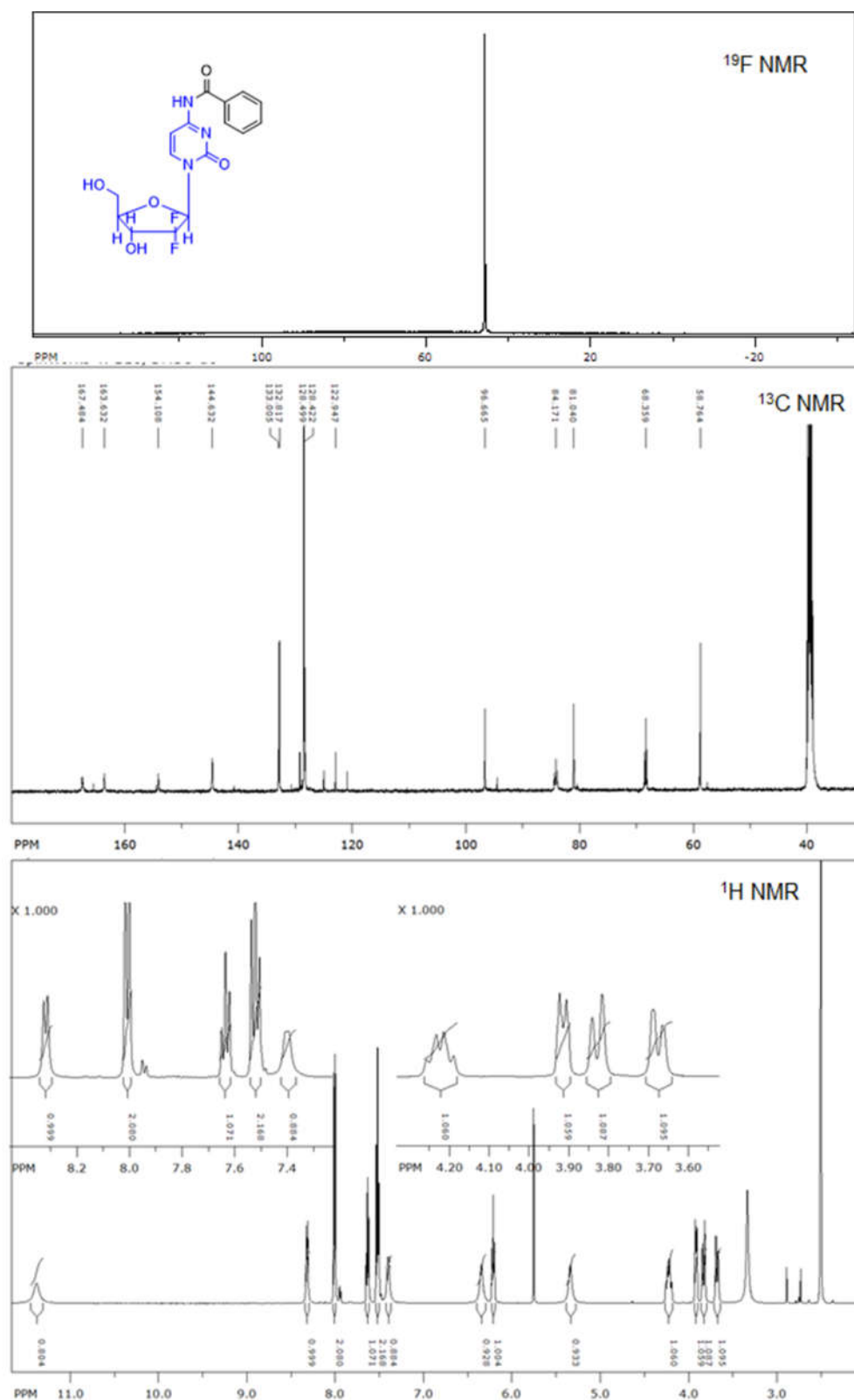


Figure S1. Characteristics of the 4-*N*-benzoyl-2'-deoxy-2',2'-difluorocytidine.

4-*N*-(2-dimethylaminoethyl)-2'-deoxy-2',2'-difluorocytidine (3)

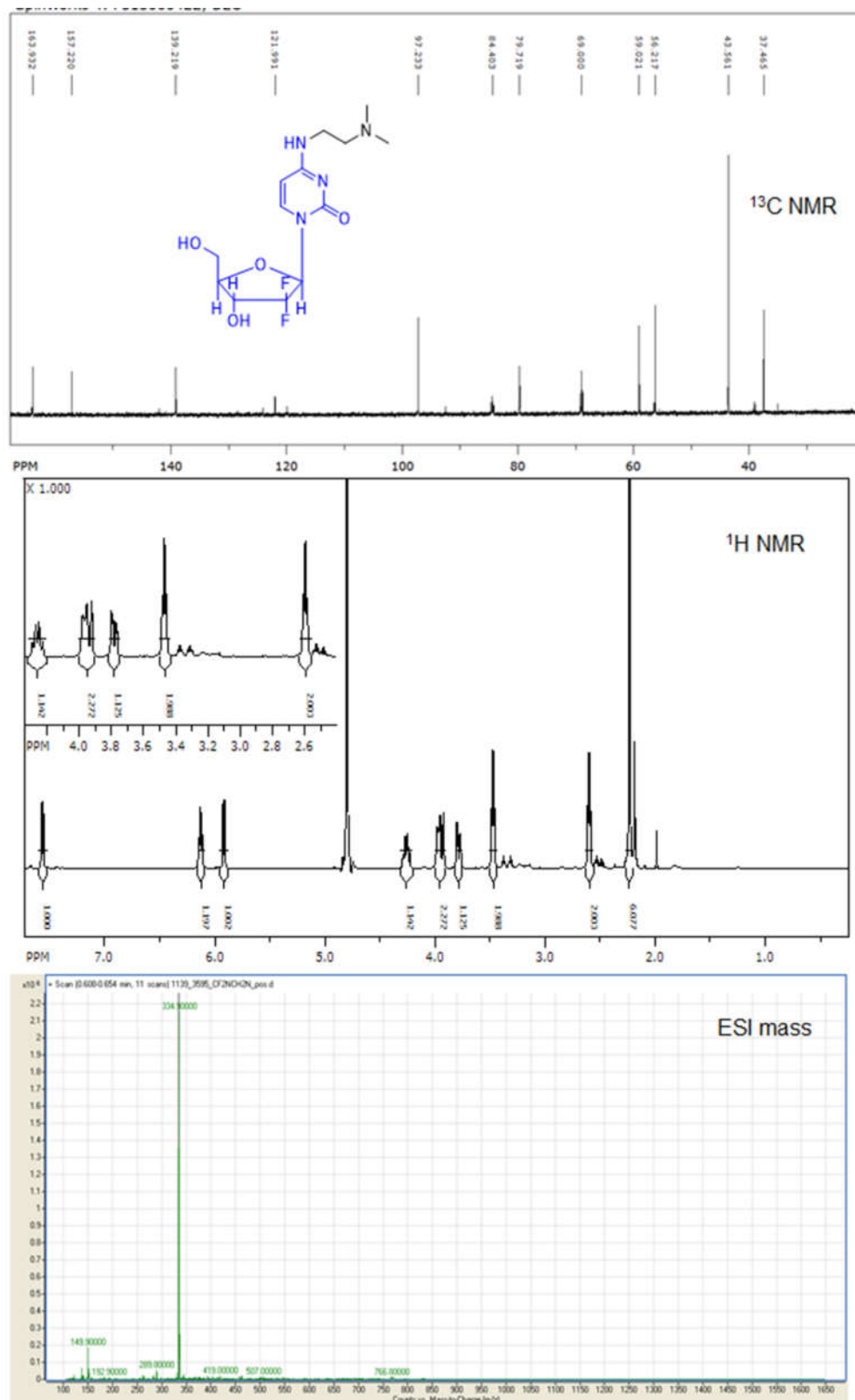


Figure S2. Characteristics of the 4-*N*-(2-dimethylaminoethyl)-2'-deoxy-2',2'-difluorocytidine

$H^+[Conjugate\ 5]$

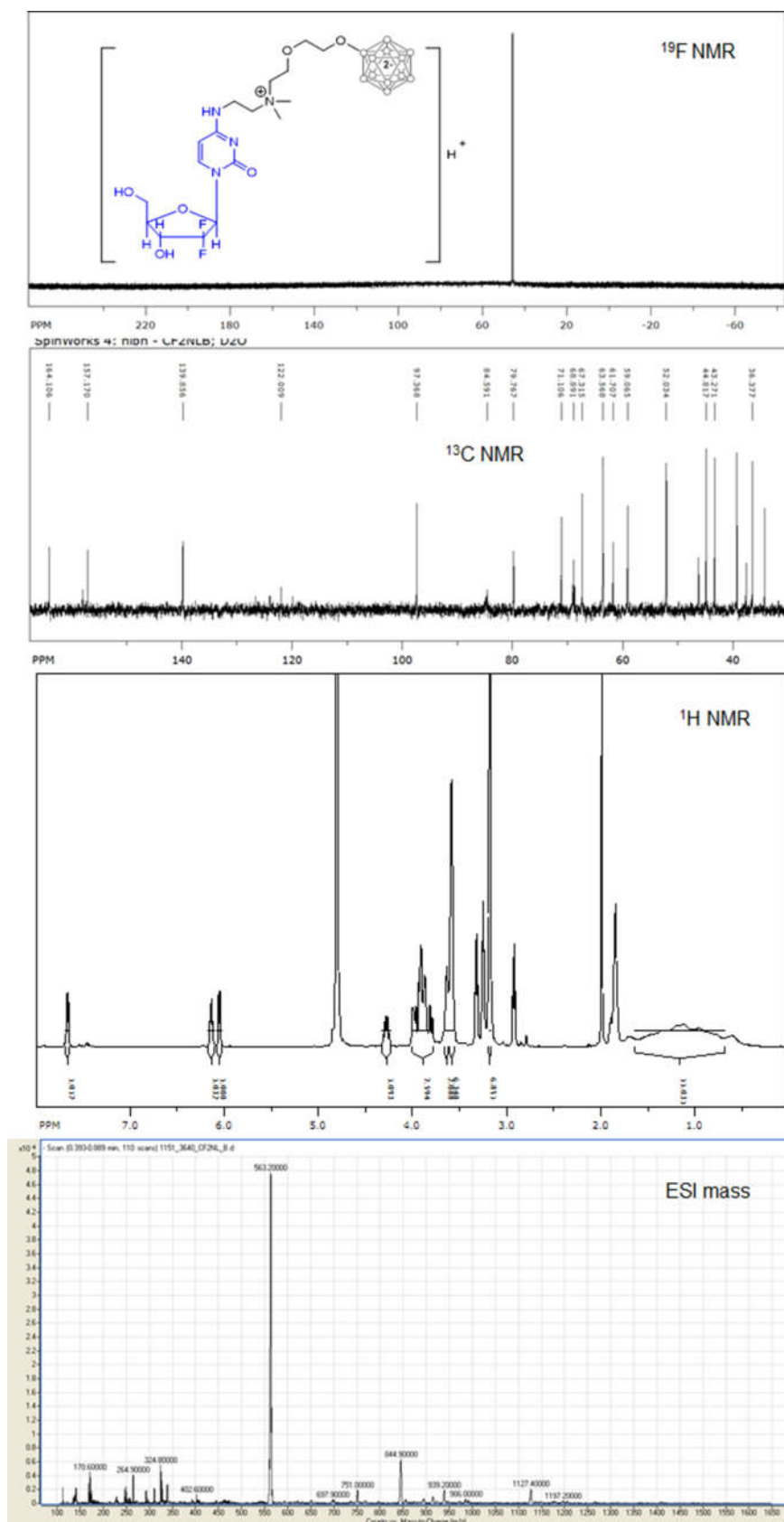


Figure S3. Characteristics of the $H^+[Compound\ 5]$.

Chemical Structure of Compound 1: A pyrimidine ring substituted with a 2-deoxy-2-(phosphonomethyl)ribose moiety at the 4-position and a 2-(dimethylamino)ethoxy group at the 5-position. The pyrimidine ring is also substituted with a 2-(dimethylamino)ethoxy group at the 2-position.

¹³C NMR Spectrum: Shows peaks at 166.0, 164.0, 157.0, 156.0, 139.6, 132.1, 97.3, 86.4, 78.5, 62.0, 58.2, 51.9, 46.3, 34.2, 27.9, and 16.9 ppm.

¹H NMR Spectrum: Shows peaks at 7.0, 6.0, 5.0, 4.0, 3.0, 2.0, 1.0, and 0.0 ppm. Integration values are provided for several peaks: 1.000, 1.025, 1.004, 1.075, 1.037, 3.270, 2.156, 2.112, 6.045, 2.112, 1.037, 3.270, 2.112, 5.918, 6.074, and 1.000.

³¹P NMR Spectrum: Shows a single peak at 0 ppm.

¹⁹F NMR Spectrum: Shows a single peak at 0 ppm.

ESI mass Spectrum: Shows peaks at 160.0, 212.0, 412.0, 563.0, 643.0, 698.0, 878.0, 924.0, 1016.0, 1132.0, and 1432.0 m/z.

Figure S4. Characteristics of the [Compound 6](TEA)₃.

[illegible]

6

¹³C NMR

Chemical structure of compound 10 is shown above the spectra.

¹H NMR

¹⁹F NMR

³¹P NMR

ESI mass

7

Compound 9

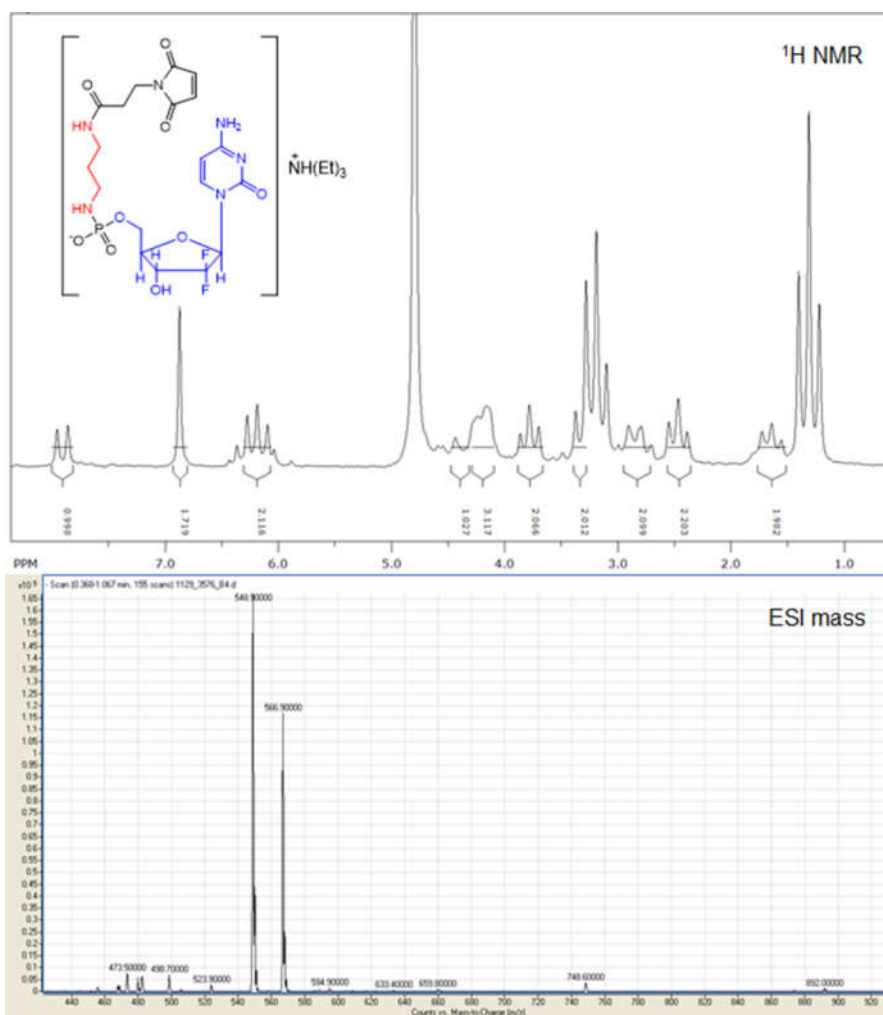


Figure S7. Characteristics of the [Compound 9](TEA).

^1H NMR (D_2O): 7.91 (1H, d, J 7.6, H6), 6.88 (2H, s, CH=CH), 6.31-6.07 (2H, m, H1', H5), 4.47-4.31 (1H, m, H3'), 4.30-4.09 (3H, m, H4', H5'), 3.78 (2H, t, J 6.5, CH₂N), 3.39-3.28 (2H, m, CH₂NHCO), 2.95-2.71 (2H, m, CH₂CO), 2.46 (2H, t, J 6.5, CH₂NHP), 1.64 (2H, t, J 6.8, CH₂). $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{19}\text{H}_{24}\text{F}_2\text{N}_6\text{O}_9\text{P}^-$ 549.13; found 548.90.

^1H NMR

Chemical structure of the compound is shown, including the $\text{NH}(\text{Et})_3^+$ counterion. The structure features a nucleoside core with a phosphate group, an amine, and a carboxylic acid moiety.

The ^1H NMR spectrum (ppm) shows peaks corresponding to the structure, with integration values provided below the baseline:

- 8.000
- 6.666
- 4.998
- 3.998
- 3.000
- 1.998
- 2.000
- 1.998
- 1.998

ESI mass

Scan (0.701-1.798 sec, 225 scans) 1217_2015_04_neg.d

The ESI mass spectrum shows peaks corresponding to the compound, with labeled m/z values:

- 524.0000
- 555.7000
- 566.0000
- 570.0000
- 590.0000
- 602.0000
- 662.0000
- 670.0000
- 702.0000

¹H NMR (D₂O): 7.92 (1H, d, *J* 7.6, H6), 6.46-5.98 (4H, m, CH=CH, H5, H1'), 4.52-4.34 (1H, m, H3'), 4.30-4.10 (3H, m, H4', H5'), 3.48 (2H, t, *J* 6.7, CH₂NH), 3.38-3.25 (2H, m, CH₂NHCO), 2.96-2.71 (2H, m, CH₂CO), 2.45 (2H, t, *J* 6.7, CH₂NHP), 1.68 (2H, t, *J* 6.8, CH₂). [M-H]⁻ calcd. for C₁₉H₂₆F₂N₆O₁₀P⁻ 567.14; found 566.90.

Compound 10

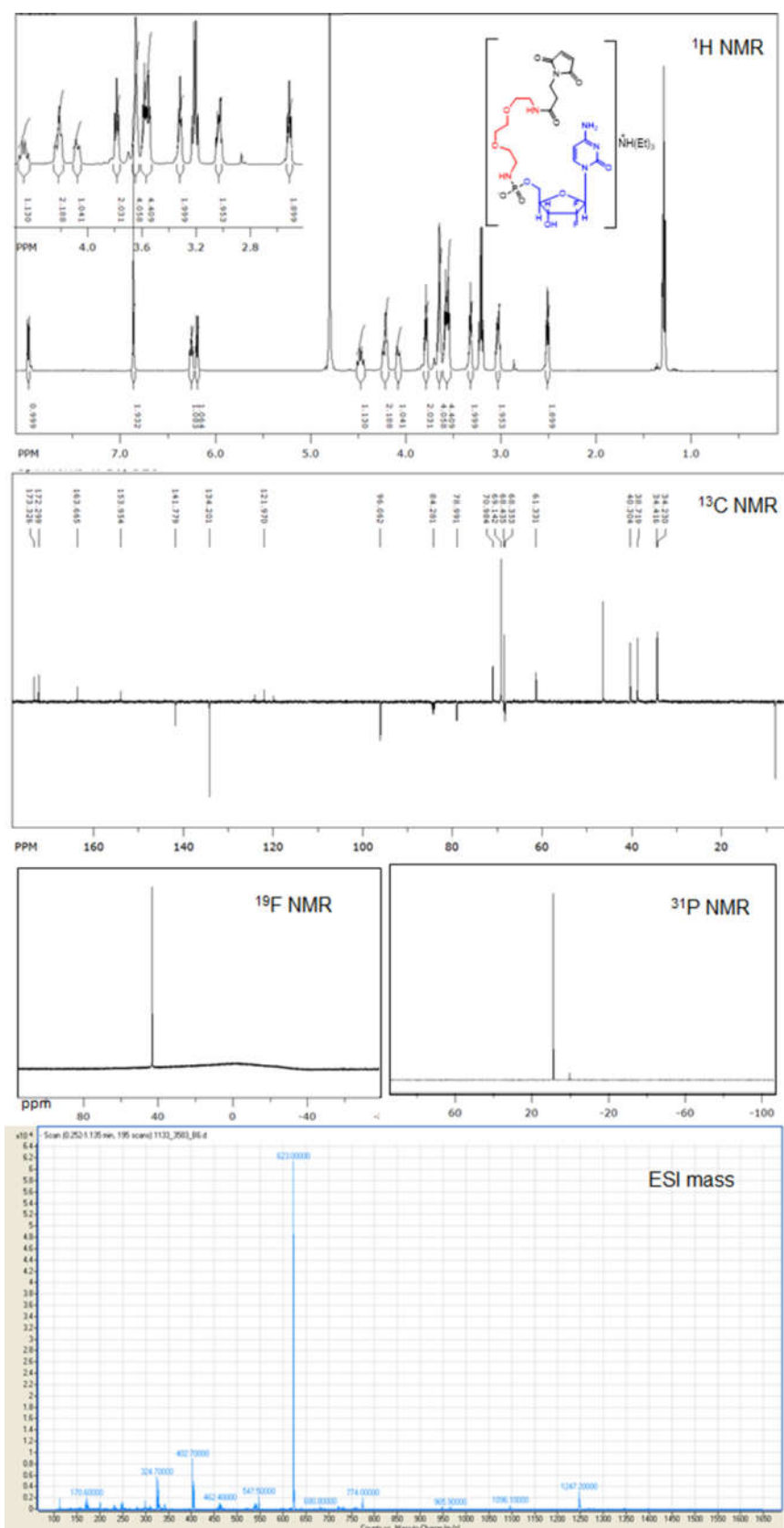


Figure S9. Characteristics of the [Compound 10](TEA).

^1H NMR (D_2O): 7.97 (1H, d, J 7.7, H6), 6.86 (2H, s, CH=CH), 6.26 (1H, t, J 7.1, H1'), 6.20 (1H, d, J 7.7, H5), 4.52-4.43 (1H, m, H3'), 4.26-4.18 (2H, m, H5'), 4.11-4.05 (1H, m, H4'), 3.79 (2H, t, J 6.3, CH_2N), 3.67-3.62 (4H, m, CH_2O), 3.58 (2H, t, J 5.5, $\text{OCH}_2\text{CH}_2\text{O}$), 3.55 (2H, t, J 5.5, $\text{OCH}_2\text{CH}_2\text{O}$), 3.32 (2H, br t, J 5.3, CH_2NHCO), 3.05-3.01 (2H, m, CH_2NHP), 2.51 (2H, t, J 6.4, CH_2CONH). ^{13}C NMR (D_2O): 173.33, 172.30, 163.67, 153.95, 141.78, 134.20, 121.97 (t, J_{CF} 259), 96.06, 84.28 (t, J_{CF} 23), 78.99, 70.98, 69.14, 68.44, 68.35 (t, J_{CF} 23), 61.33, 40.30, 38.72, 34.42, 34.23. ^{19}F NMR (D_2O): 43.14 (br s, CF_2). ^{31}P NMR: 8.67 (s). $[\text{M}-\text{H}]^-$ calcd. for $\text{C}_{22}\text{H}_{30}\text{F}_2\text{N}_6\text{O}_{11}\text{P}^-$ 623.17; found 623.00.

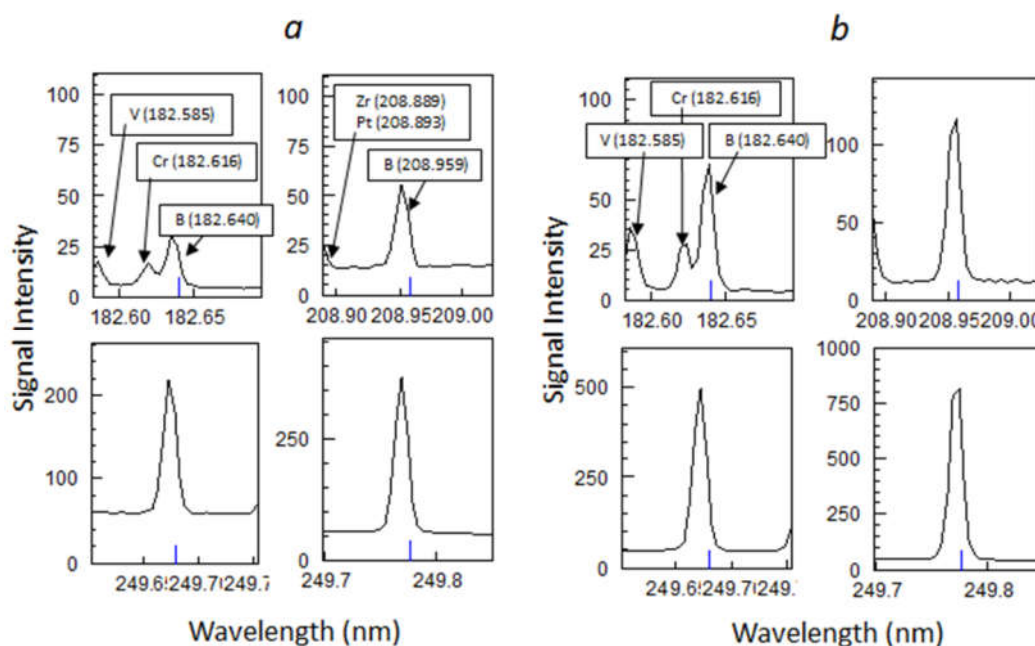


Figure S10. Inductively coupled plasma atomic emission spectrometry (ICP AES) for HSA-Cy5-HcyTFAc-GCB₁₂H₁₁ (a) and HSA-Cy7-HcyTFAc-GCB₁₂H₁₁ (b). Boron spectral lines 182.640, 208.959, 249.678 and 249.773 nm.

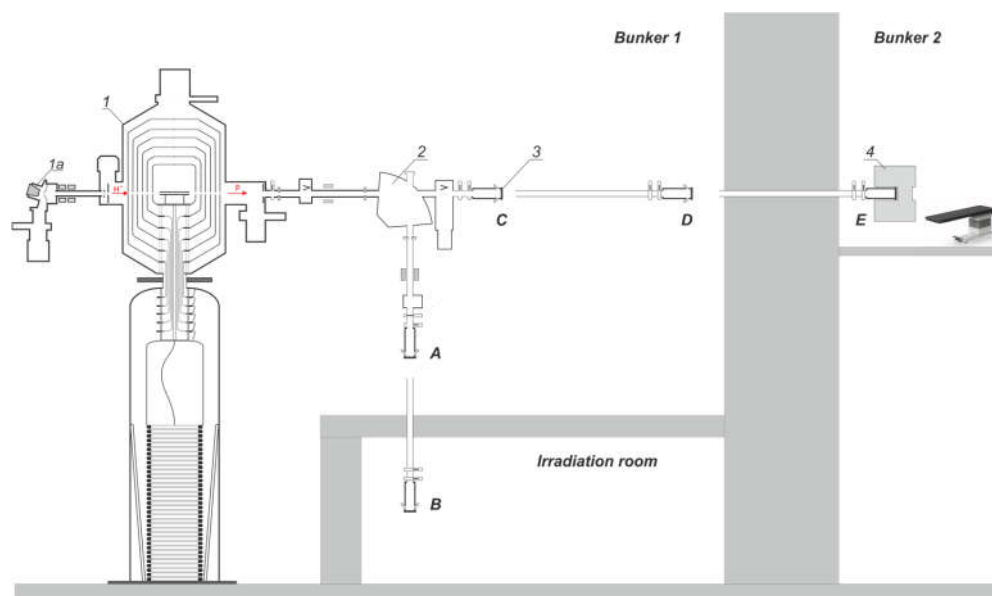


Figure S11. Layout of the experimental facility: 1 – vacuum insulated tandem accelerator, 2 – bending magnet, 3 – lithium target, 4 – beam shaping assembly. A, B, C, D, E – lithium target placement positions.