Supporting Information

Rapid Synthesis of Nucleoside Diphosphates Accelerated by Water

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General Information

Chemicals and solvents were purchased as reagent grade and used without further purification unless otherwise specified. Dry solvents were purchased from Acros Organics (Thermo Fisher scientific, USA). The reaction pure water was freshly collected from Thermo Scientific Barnstead GenPure Pro Water Purification System.

NMR spectra were recorded at ambient temperature (ca. 22 °C) on a Bruker 400 (or 600) AVANCE III spectrometers. Chemical shifts are reported in δ ppm, and multiplicities are reported by peak identity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, m = multiplet) and coupling constant (J, Hz). NMR spectra were processed and analyzed with TopSpin 3.5 and Mestrenova 14.3 software.

Semi-preparative HPLC was performed on a Shimadzu prominence HPLC system (Shimadzu Corp., Japan) with a CBM20A communication bus module, a FRC-10A fraction collector, two pumps LC-20AP, and a SPD-20A UV/VIS detector, using a Shimadzu Shim-pack GIST C18-AQ column. LC-MS measurements were performed on Thermo Scientific Q Exactive Plus Orbitrap LC-MS System, utilizing a Luna C18 column (2 mm × 100 mm, 5 μm particle size, 100 Å). External calibration using Thermo LTQ Velos ESI Positive Ion Calibration Solution and Negative Ion Calibration Solution (calibration performed daily before sample analysis to ensure mass accuracy <5 ppm). The instrument control and data processing were conducted using Thermo Scientific Xcalibur software. Conversions were quantified based on the area-under-the-curve (AUC) in the UV chromatogram or in the total-ion-chromatogram (TIC).

The following HPLC methods were used in this setup:

General Gradient A: For the separation of dinucleoside diphosphate, the following linear gradient was employed at a flow rate of 3 mL/min: from 0 to 1 minute: 5:95 v/v (MeCN: 0.05 M aqueous triethylammonium acetate (TEAA, pH 7.0)), from 1 to 30 minutes: 5:95 v/v to 30:70 v/v, back to the initial ratio of 5:95 v/v in 1 min.

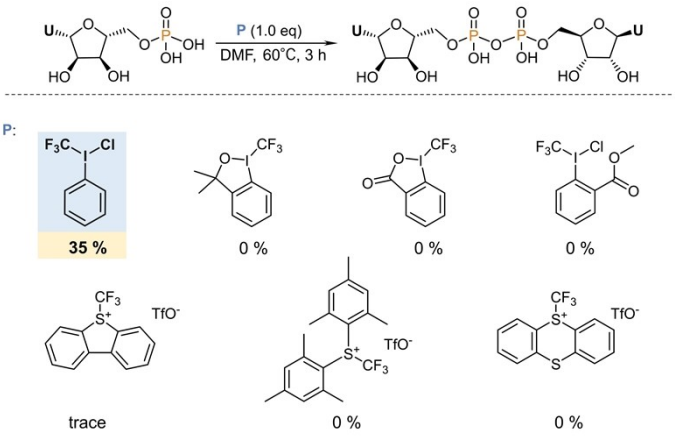


Fig. S1 Screening of trifluoromethylating reagents in this study.

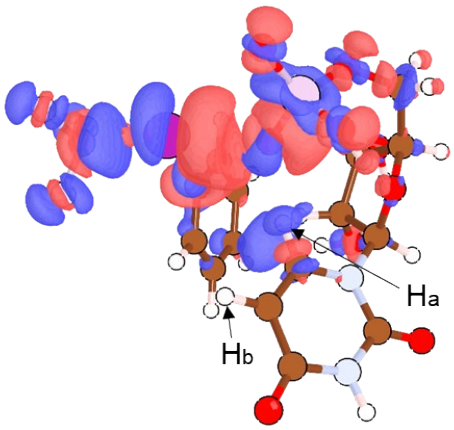


Fig. S2 Isosurface plot of the electron density difference of the $[PhICF_3]^+$-UMP complex. Blue and red iso-surfaces represent regions of electron accumulation and depletion, respectively.

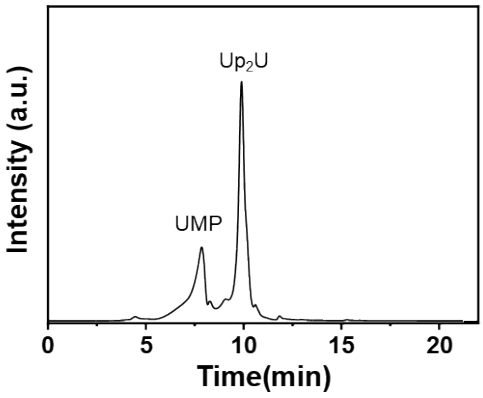


Fig. S3 HPLC chromatogram of the reaction mixture obtained under optimized conditions (*Gradient A*).

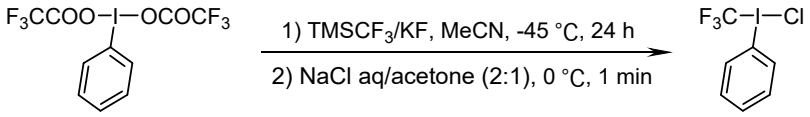


Fig. S4 $PhICF_3Cl$ was synthesized according to the reported procedure.[1]

Procedure for the preparation of nucleoside monophosphate mono-tetrabutylammonium salts: The nucleoside monophosphate (free acid form, 0.5 mmol, 1.0 equiv) was suspended in deionized water. To this mixture, a 25% aqueous solution of tetrabutylammonium hydroxide (TBAOH, 0.5 mmol, 1.0 equiv) was added dropwise. The resulting clear solution was stirred at room temperature for 30 min. Subsequently, the mixture was frozen and lyophilized to afford the desired nucleoside monophosphate mono-tetrabutylammonium salt as a white foam, which was used in the next step without further purification.

Procedure for preparation of Ap_2A and Up_2U. To a solution of adenosine 5'-monophosphate (or UMP, 0.02 mmol, 1.0 equiv) in 2 mL DMF was added $PhICF_3Cl$ (0.01 mmol, 0.5 equiv). The reaction mixture was heated to 80 °C and stirred for 5 hours under ambient atmosphere. Upon completion, the mixture was allowed to cool to room temperature and diluted with deionized water. The resulting solution was directly subjected to purification by RP-HPLC, eluting with the previously mentioned *General Gradient A*. The fractions containing the target compound were pooled and lyophilized to afford diadenosine diphosphate as the triethylammonium salt.

General procedure for other symmetrical dinucleoside diphosphates. A mixture of [TBA][NMP] (0.02 mmol, 1.0 equiv) and $PhICF_3Cl$ (0.01 mmol, 0.5 equiv) in 1.0 mL pyridine was stirred at 70 °C for 5 min. Then 100 μL H_2O was added. The mixture was cooled to room temperature and diluted with deionized water. The resulting solution was directly subjected to purification by RP-HPLC using *Gradient A*. The fractions containing the target compound were pooled and lyophilized to afford diadenosine diphosphate as the triethylammonium salt.

General procedure for asymmetric dinucleoside diphosphates. A mixture of [TBA][NMP] (0.01 mmol, 1.0 equiv) and $PhICF_3Cl$ (0.01 mmol, 1.0 equiv) in 0.5 mL pyridine was stirred at 70 °C for 5 min. Then another [TBA][N'MP] (0.01 mmol, 1.0 equiv) in 0.5 mL pyridine was added. The mixture was stirred at 70 °C for 5 min. Then 100 μL H_2O was added. The mixture was cooled to room temperature and diluted with deionized water. The resulting solution was directly subjected to purification by RP-HPLC using *Gradient A*. The fractions containing the target compound were pooled and lyophilized to afford asymmetric diadenosine diphosphate as the triethylammonium salt.

$PhICF_3Cl$: Yield = 57%. ^1H NMR (600 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 7.9 Hz, 2H), 7.71 (td, *J* = 7.5, 1.1 Hz, 1H), 7.54 (tt, *J* = 7.5, 1.1 Hz, 2H). ^{19}F NMR (565 MHz, Chloroform-*d*) δ -35.66.

Ap_2A: Obtained in 68% yield as its triethylammonium salt. ^1H NMR (400 MHz, D_2O) δ 8.01 (s, 1H), 7.87 (s, 1H), 5.79 (d, J = 5.1 Hz, 1H), 4.40 (t, J = 5.1 Hz, 1H), 4.28 (t, J = 4.6 Hz, 1H), 4.20 (d, J = 9.0 Hz, 1H), 4.09 (s, 1H). ^{31}P NMR (162 MHz, D_2O) δ -11.29. MS (ESI^-): *m/z* = 675.1068 $[M - H]^-$.

Ap_2U: Obtained in 35% yield as its triethylammonium salt. ^1H NMR (400 MHz, D_2O) δ 8.31 (s, 1H), 8.06 (s, 1H), 7.51 (d, J = 8.1 Hz, 1H), 5.94 (d, J = 5.9 Hz, 1H), 5.68 (d, J = 4.8 Hz, 1H), 5.53 (d, J = 8.1 Hz, 1H), 4.62 (t, J = 5.5 Hz, 1H), 4.38 (dd, J = 5.1, 3.5 Hz, 1H), 4.24 (s, 1H), 4.17 – 3.99 (m, 7H). ^{31}P NMR (162 MHz, D_2O) δ -11.41. MS (ESI^-): *m/z* = 652.0790 $[M - H]^-$.

Ap_2G: Obtained in 25% yield as its triethylammonium salt. ^1H NMR (400 MHz, D_2O) δ 8.16 (s, 1H), 8.04 (d, *J* = 1.2 Hz, 1H), 7.78 (s, 1H), 5.89 (d, *J* = 4.7 Hz, 1H), 5.64 (d, *J* = 5.4 Hz, 1H), 4.49 (dt, *J* = 9.4, 5.0 Hz, 2H), 4.33 (dt, *J* = 8.8, 4.7 Hz, 2H), 4.21 (d, *J* = 13.3 Hz, 3H), 4.11 (d, *J* = 9.3 Hz, 2H). ^{31}P NMR (162 MHz, D_2O) δ -11.30. MS (ESI^-): *m/z* = 691.1021 $[M - H]^-$.

Ap_2C: Obtained in 35% yield as its triethylammonium salt. ^1H NMR (400 MHz, D_2O) δ 8.32 (d, J = 2.8 Hz, 1H), 8.09 (d, J = 6.1 Hz, 1H), 7.60 (d, J = 7.7 Hz, 1H), 5.95 (dd, J = 6.0, 4.0 Hz, 1H), 5.73 (d, J = 7.7 Hz, 1H), 5.69 (dd, J = 3.9, 1.6 Hz, 1H), 4.68 – 4.59 (m, 1H), 4.38 (dt, J = 5.1, 3.5 Hz, 1H), 4.26 (d, J = 3.9 Hz, 1H), 4.23 – 3.98 (m, 6H). ^{31}P NMR (162 MHz, D_2O) δ -11.40. MS (ESI^-): *m/z* = 651.0955 $[M - H]^-$.

Up_2U: Obtained in 59% yield as its triethylammonium salt. ^1H NMR (400 MHz, D_2O) δ 7.76 (d, *J* = 8.1 Hz, 1H), 5.82 – 5.73 (m, 2H), 4.23 – 4.15 (m, 2H), 4.14 – 4.07 (m, 2H), 4.03 (q, *J* = 2.9 Hz, 1H). ^{31}P NMR (162 MHz, D_2O) δ -11.48. MS (ESI^-): *m/z* = 629.0523 $[M - H]^-$.

Up_2C: Obtained in 30% yield as its triethylammonium salt. ^1H NMR (400 MHz, D_2O) δ 7.93 – 7.88 (m, 1H), 7.82 – 7.75 (m, 1H), 6.04 (d, *J* = 7.9 Hz, 1H), 5.83 – 5.80 (m, 2H), 4.24 – 4.11 (m, 10H). ^{31}P NMR (162 MHz, D_2O) δ -11.47. MS (ESI^-): *m/z* = 628.0674 $[M - H]^-$.

Up_2G: Obtained in 20% yield as its triethylammonium salt. ^1H NMR (400 MHz, D_2O) δ 8.30 (s, 1H), 7.93 (s, 1H), 7.63 (d, *J* = 8.1 Hz, 1H), 5.73 (dd, *J* = 12.6, 5.3 Hz, 2H), 5.66 (d, *J* = 8.2 Hz, 1H), 4.37 (s, 1H), 4.18 – 4.10 (m, 4H). ^{31}P NMR (162 MHz, D_2O) δ -11.43. MS (ESI^-): *m/z* = 668.0743 $[M - H]^-$.

Cp_2C: Obtained in 42% yield as its triethylammonium salt. ^{1}H NMR (400 MHz, D_2O) δ 7.87 (dd, *J* = 7.5, 2.0 Hz, 1H), 6.00 (dd, *J* = 7.6, 1.9 Hz, 1H), 5.95 – 5.88 (m, 1H), 4.32 – 4.25 (m, 2H), 4.23 (d, *J* = 4.1 Hz, 2H), 4.15 (d, *J* = 11.7 Hz, 1H). ^{31}P NMR (162 MHz, D_2O) δ -11.42. MS (ESI^-): *m/z* = 627.0838 $[M - H]^-$.

dCp_2dC: Obtained in 38% yield as its triethylammonium salt. ^{1}H NMR (400 MHz, D_2O) δ 7.84 (d, *J* = 7.7 Hz, 1H), 6.20 (t, *J* = 6.7 Hz, 1H), 5.98 (d, *J* = 7.6 Hz, 1H), 4.46 (s, 1H), 4.11 (d, *J* = 12.7 Hz, 3H), 2.30 (dd, *J* = 8.7, 4.7 Hz, 1H), 2.16 (dt, *J* = 13.6, 6.8 Hz, 1H). ^{31}P NMR (162 MHz, D_2O) δ -11.38. MS (ESI^-): *m/z* = 595.0940 $[M - H]^-$.

dAp_2dA: Obtained in 58% yield as its triethylammonium salt. ^{1}H NMR (400 MHz, D_2O) δ 8.10 (s, 1H), 7.97 (s, 1H), 6.22 (t, *J* = 6.6 Hz, 1H), 4.54 (d, *J* = 4.1 Hz, 2H), 4.11 (d, *J* = 10.6 Hz, 3H), 2.53 (dt, *J* = 13.3, 6.5 Hz, 2H), 2.39 (dt, *J* = 13.9, 5.7 Hz, 2H). ^{31}P NMR (162 MHz, D_2O) δ -11.27. MS (ESI^-): *m/z* = 643.1169 $[M - H]^-$.

Ip_2I: Obtained in 66% yield as its triethylammonium salt. ^{1}H NMR (400 MHz, D_2O) δ 8.13 (s, 1H), 7.97 (s, 1H), 5.87 (d, J = 5.3 Hz, 1H), 4.53 (t, J = 5.2 Hz, 1H), 4.35 (t, J = 4.6 Hz, 1H), 4.22 (d, J = 3.6 Hz, 1H), 4.19 – 4.06 (m, 2H). ^{31}P NMR (162 MHz, D_2O) δ -11.33. MS (ESI^-): *m/z* = 677.0737 $[M - H]^-$.

Procedure for determination of the conversion-time profile: A mixture of [TBA][UMP] (0.02 mmol, 1.0 equiv) and $PhICF_3Cl$ (0.01 mmol, 1.0 equiv) in 1.0 mL pyridine-d5 was stirred at 70 °C. The reaction progress was monitored by withdrawing aliquots at regular time intervals for ^{31}P NMR analysis, with trimethyl phosphate serving as the internal standard.

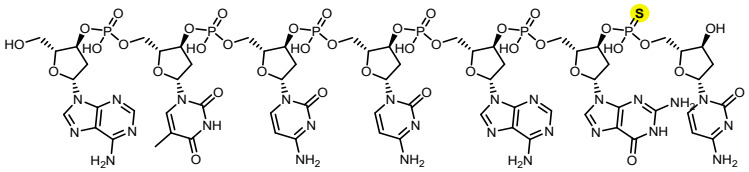
For another reaction mixture, upon heating the reaction mixture to 70 °C for 3~5min, 50 μL of water (or D_2O, $H_2{}^{18}O$) was added. The mixture was then rapidly quenched by immersion in an ice-water bath, followed by ^{31}P NMR analysis to calculate the conversion.

Table S1. The amount of added water and the final conversion.

entry	H_2O (v/v%)	conversion (%)
1	0.1	8
2	5	60
3	10	68
4	20	68

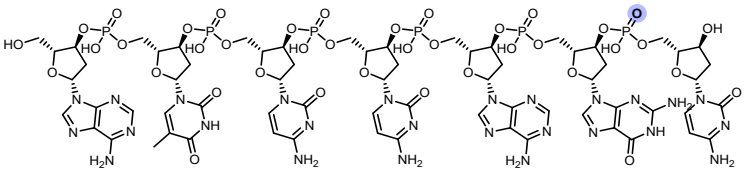
Procedure for preparation of the desulfurization of phosphorothioate oligonucleotides. A solution of the phosphorothioate oligonucleotide (sequence: 5'-d(ATCCAG*C)-3', 5 nmol) was prepared in a mixture of DMF and water (1:1 v/v, 200 μL). To this solution was added a solution of $PhICF_3Cl$ reagent in DMF (0.1 M, 10 μL).

The reaction mixture was stirred at room temperature for 3 hours. Subsequently, 1 μL of the crude mixture was diluted with 100 μL DEPC-treated water (deionized water treated with 0.1% diethyl pyrocarbonate), and subjected to mass spectrometric analysis.



Oligo-S

The initial sequence of the nucleic acid **Oligo-S**: 5'-d(ATCCAG*C)-3'. Exact mass = 2080.3743 Da.



Oligo-O

The sequence of the nucleic acid after the reaction **Oligo-O**: 5'-d(ATCCAGC)-3'. Exact mass = 2064.3971 Da.

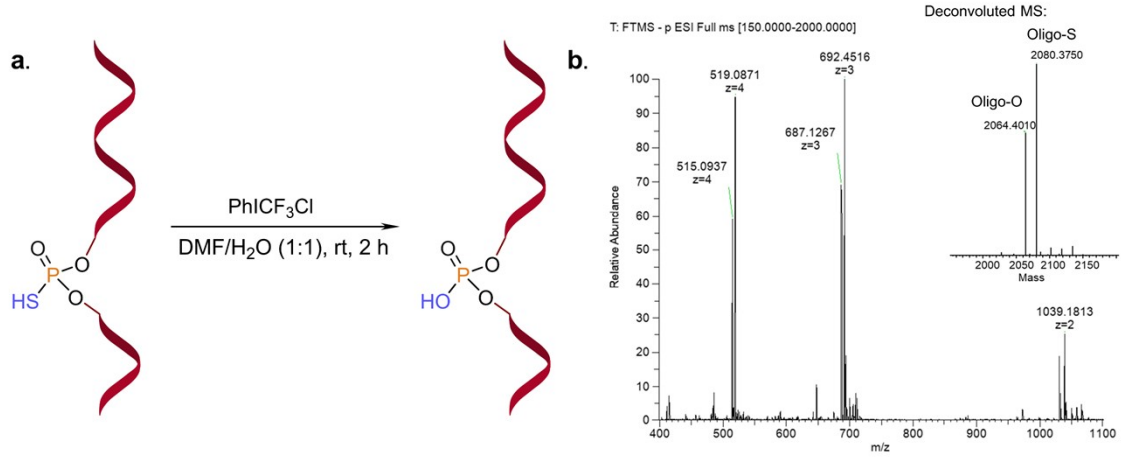


Fig. S5. **a**. Schematic representation of the desulfurization of a phosphorothioate oligonucleotide. **b**. ESI-MS spectrum of the reaction mixture. (**Oligo-S**: 5'-d(ATCCAG*C)-3', HRMS: m/z: 692.4516 $[M-3H]^{3-}$, calcd. m/z: 692.4508, **Oligo-O**: 5'-d(ATCCAGC)-3', HRMS: m/z: 687.1267 $[M-3H]^{3-}$, calcd. m/z: 687.1251)

Computational Details

All DFT calculations were carried out using the Gaussian 16 software package. The geometry optimizations were performed using the B3LYP-D3(BJ) functional with a mixed basis set of SDD for I atoms and the 6-31G(d) for the other atoms. Frequencies were computed analytically at the same level of theory to confirm whether the structures are minima (no imaginary frequencies) or transition states (only one imaginary frequency). Selected transition-state structures were confirmed to connect the correct reactants and products by intrinsic reaction coordinate (IRC) calculations. Single-point energies for the optimized geometries were recalculated using wb97xd functional, SDD for I atoms and 6-311+g(d,p) for all other atoms. 3D structures of the optimized geometries were generated using CYLview. Electron density difference (EDD) analyses were performed using the Multiwfn code.[2]

Cartesian coordinates

$[PhICF_3]^+$-UMP complex

C	-1.63287800	1.43698823	3.68775052
H	-1.35184890	1.76977827	4.68049815
C	-2.50965803	0.36143177	3.53990157
H	-2.89855251	-0.15378473	4.40952342
C	-2.89067464	-0.06488189	2.26793039
H	-3.56801782	-0.89672472	2.13659389
C	-2.36707228	0.61643964	1.18078283
C	-1.48128195	1.67778451	1.28524401
H	-1.08441489	2.16835035	0.40801471
C	-1.11701009	2.08870441	2.56751668
H	-0.42707038	2.91553222	2.68266036
C	-4.50934371	1.55413484	-0.81197645
F	-5.31304965	1.44674308	0.24758881
F	-5.23582152	1.41967672	-1.92247607
F	-3.96025670	2.77075038	-0.80169612
I	-2.92890929	-0.05062956	-0.78179165
C	1.87293238	1.06121100	-0.83574127
C	1.48566513	0.04915898	-0.03599728
C	3.60509621	-0.01264734	1.14793521
C	3.19208766	1.64087070	-0.69044772
H	1.21634936	1.44837983	-1.60070773

H	0.51597904	-0.43070689	-0.13187362
O	3.65840817	2.56150735	-1.34053192
O	4.35910394	-0.47409678	1.98275360
N	3.95671280	1.02866660	0.31718196
H	4.89548170	1.38792556	0.44837876
N	2.29982920	-0.47827146	0.94574135
P	-0.93555680	-2.92453775	-1.01267645
O	-1.04106522	-4.12130544	0.09813010
C	0.05878207	-4.60782465	0.87877185
H	0.80715935	-5.06614295	0.22584862
H	-0.36111003	-5.38614490	1.51706174
C	0.72377636	-3.58110067	1.77435936
H	1.35316867	-4.11944274	2.49330222
O	1.56993184	-2.70954309	0.98418554
C	-0.22250051	-2.64685676	2.56062468
H	-1.17639225	-2.57007367	2.04563520
C	0.50242575	-1.27019844	2.52079668
H	-0.09632402	-0.55065655	1.97347024
O	0.81537059	-0.78954992	3.82316222
H	0.14035051	-0.14583331	4.06934870
O	-0.45719115	-3.09632933	3.88060547
C	1.81644324	-1.55478943	1.78475822
H	2.60026587	-1.75889204	2.51461959
H	0.10967198	-2.54919074	4.44578423
O	0.59116666	-3.02122426	-1.55792587
H	1.20821644	-2.81024394	-0.83268474
O	-1.07502358	-1.59659285	-0.23763816
O	-1.90340188	-3.17949694	-2.11207393

INT1

C	-1.63287800	1.43698800	3.68775000
H	-1.35184900	1.76977800	4.68049800
C	-2.50965800	0.36143200	3.53990100
H	-2.89855200	-0.15378500	4.40952300

C	-2.89067400	-0.06488200	2.26793000
H	-3.56801800	-0.89672500	2.13659400
C	-2.36707200	0.61644000	1.18078200
C	-1.48128200	1.67778400	1.28524400
H	-1.08441500	2.16835000	0.40801500
C	-1.11701000	2.08870400	2.56751700
H	-0.42707000	2.91553200	2.68266000
C	-4.50934300	1.55413500	-0.81197600
F	-5.31304900	1.44674300	0.24758900
F	-5.23582100	1.41967700	-1.92247600
F	-3.96025700	2.77075000	-0.80169600
I	-2.92890900	-0.05063000	-0.78179100

INT2

P	2.02253000	-1.84217100	0.00719400
O	1.16300300	-1.49871300	1.28317400
O	3.31450500	-0.71944100	-0.11065500
C	3.73165100	-0.02423900	1.10673800
H	4.81618100	-0.09195800	1.14782800
H	3.29612400	-0.50687100	1.98203100
C	3.32356100	1.43322600	1.07795800
H	3.49123600	1.86343100	2.06550000
O	4.17190100	2.15646500	0.12385200
C	1.88707300	1.68824600	0.63545300
H	1.23673100	0.84635500	0.86677800
C	2.01478700	1.95477200	-0.87912300
H	1.93933900	1.02280000	-1.43514600
O	1.01588400	2.91153100	-1.31802800
H	0.25172000	2.47061400	-1.71667000
O	1.38033500	2.88364900	1.27908900
C	3.39136500	2.59814300	-1.01762700
H	3.28501500	3.68414600	-0.99787100
H	3.90431000	2.29644100	-1.92840000
H	0.92493400	3.40923200	0.59500800

O	2.82898500	-3.31454900	0.30280200
H	3.34823100	-3.66532100	-0.43576300
O	1.28636400	-1.87986800	-1.40898800
C	-4.51086100	2.44667700	0.87110400
H	-5.25308600	3.10508300	1.29972500
C	-3.16441100	2.62264100	1.18713800
H	-2.85722100	3.41324300	1.85623200
C	-2.20140900	1.77328700	0.64516300
H	-1.15773300	1.90049200	0.89711800
C	-2.62595900	0.75853900	-0.20722200
C	-3.95940700	0.57169600	-0.55270000
H	-4.25573800	-0.22146500	-1.22222000
C	-4.90754900	1.42807800	0.00455600
H	-5.95132500	1.29535800	-0.24098600
C	-1.61206800	-1.95414500	0.66485900
F	-1.44613400	-1.36269100	1.87417500
F	-0.91160500	-3.11025900	0.56364100
F	-2.95168600	-2.26224200	0.53944100
I	-1.11434600	-0.54087600	-0.98234200

TS

P	2.00056500	-1.80430700	-0.17753900
O	0.86402500	-1.45309900	0.93888800
O	3.12755300	-0.56309100	-0.06921300
C	3.49820800	0.08479100	1.19537300
H	4.57574300	-0.01951900	1.28885700
H	3.00352000	-0.40609900	2.03353500
C	3.12094900	1.54786200	1.15119900
H	3.28039800	1.97835400	2.14010400
O	3.99264600	2.24287500	0.19750100
C	1.69316100	1.81320900	0.68937200
H	1.03592700	0.96670700	0.88152000
C	1.84555000	2.11839500	-0.81439100
H	1.81500400	1.19888900	-1.39431500

O	0.82755100	3.04899800	-1.25591200
H	0.07197300	2.58265200	-1.64370600
O	1.17884600	2.99175100	1.35419700
C	3.20915400	2.79451300	-0.89594500
H	3.09083700	3.87248200	-0.77052500
H	3.72991200	2.58654800	-1.82719000
H	0.70463600	3.51917200	0.68438000
O	2.79050100	-3.16249700	0.43118700
H	3.47410000	-3.56221300	-0.13020100
O	1.49851200	-1.94556300	-1.66103400
C	-4.63817400	2.12512800	1.01602800
H	-5.41894500	2.69628300	1.49830500
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H	-1.25166800	1.87726700	0.90880800
C	-2.64516900	0.66283600	-0.21392700
C	-3.97315100	0.37050000	-0.50970600
H	-4.22621000	-0.41746300	-1.20303900
C	-4.97305100	1.11520300	0.11411700
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F	-1.07055400	-1.57593100	2.11586900
F	-0.44570400	-3.40144300	0.83049600
F	-2.33268300	-2.39421300	0.55502600
I	-1.09370100	-0.45672200	-1.13764900

INT3

P	-1.53338600	1.22124000	0.37453000
O	-2.43791400	0.09259800	-0.43603100
O	-0.04886100	0.88822500	0.01437300
C	0.46937300	0.74247900	-1.33423800
H	0.36773000	1.69473400	-1.85247800
H	-0.09774200	-0.02911800	-1.85642700

C	1.92251300	0.34397400	-1.23817500
H	2.26517500	0.14709300	-2.25781500
O	2.67204200	1.42315400	-0.67626000
C	2.18994400	-0.89019000	-0.37308200
H	1.28602000	-1.47996600	-0.20896000
C	2.72953100	-0.27618200	0.93115700
H	1.90025700	0.00146000	1.58187600
O	3.63498100	-1.13759400	1.59747600
H	3.15043700	-1.65617200	2.24318000
O	3.18781900	-1.68218600	-0.98960400
C	3.45102500	0.96313700	0.41789100
H	4.46257900	0.69458200	0.09370700
H	3.51137800	1.76127800	1.15602000
H	3.71696800	-2.05603500	-0.27659400
O	-1.86689800	2.48335500	-0.51795100
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C	-2.56456800	-1.20468400	-0.10393100
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F	-3.23978300	-1.37958900	1.03232400
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INT4

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H	-0.81415800	-1.56132000	1.22381500
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H	1.00900100	1.26120900	-0.88920300
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O	-2.61811700	1.49566800	-0.96234000
F	-2.03934100	0.74179700	1.39513900

References

(1) Xu, C.; Song, X.; Guo, J.; Chen, S.; Gao, J.; Jiang, J.; Gao, F.; Li, Y.; Wang, M. Synthesis of Chloro(Phenyl)Trifluoromethyliodane and Catalyst-Free Electrophilic Trifluoromethylations. *Org. Lett.* **2018**, *20*, 3933–3937.

(2) Lu, T. A Comprehensive Electron Wavefunction Analysis Toolbox for Chemists, Multiwfn. *J. Chem. Phys.* **2024**, *161*.

Mass Spectrum

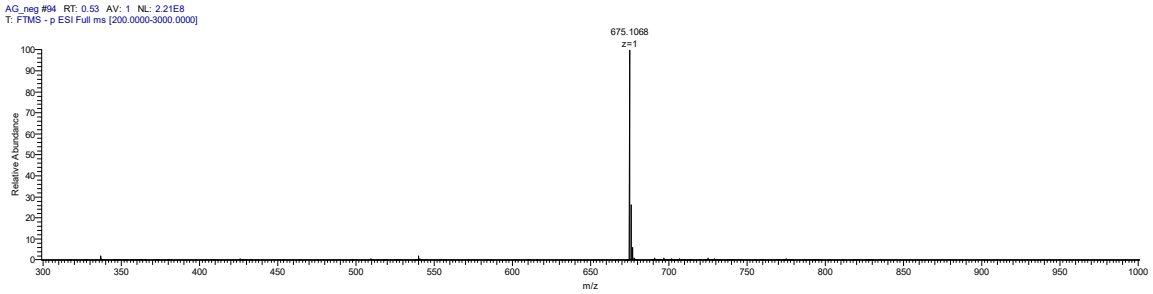

Fig. S6 HRMS spectrum of Ap_2A.

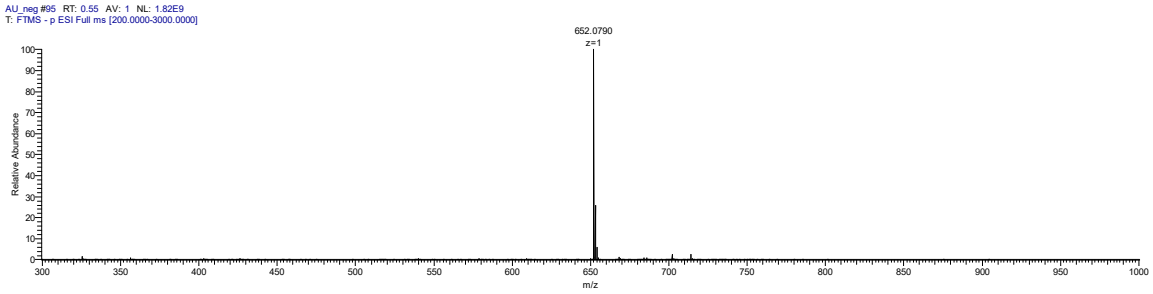

Fig. S7 HRMS spectrum of Ap_2U.

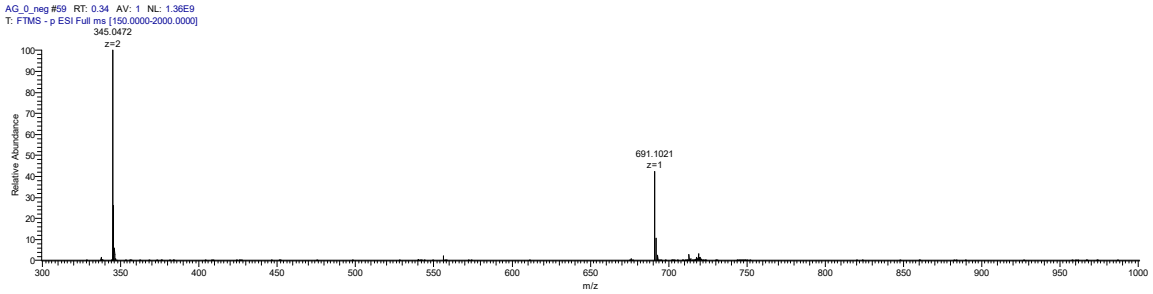

Fig. S8 HRMS spectrum of Ap_2G.

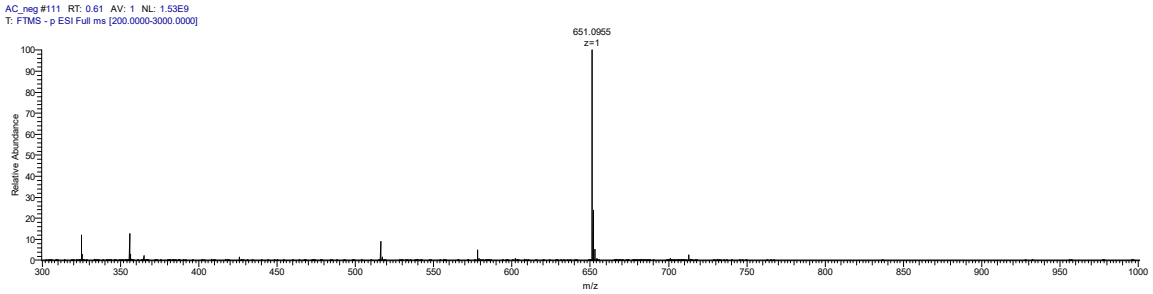

Fig. S9 HRMS spectrum of Ap_2C.

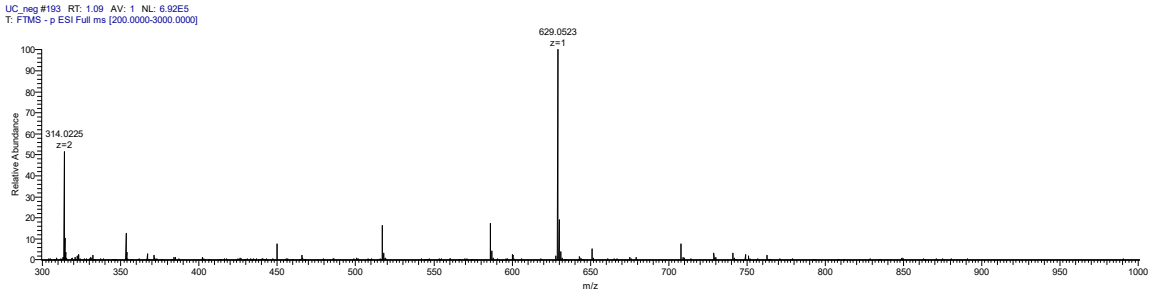

Fig. S10 HRMS spectrum of Up_2U.

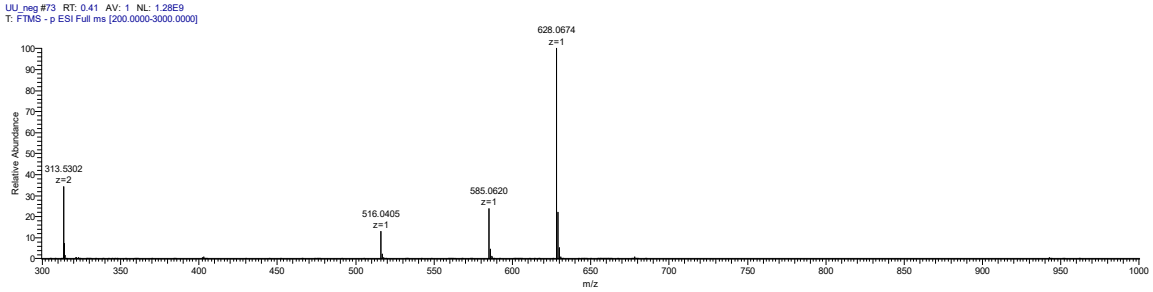

Fig. S11 HRMS spectrum of Up_2C.

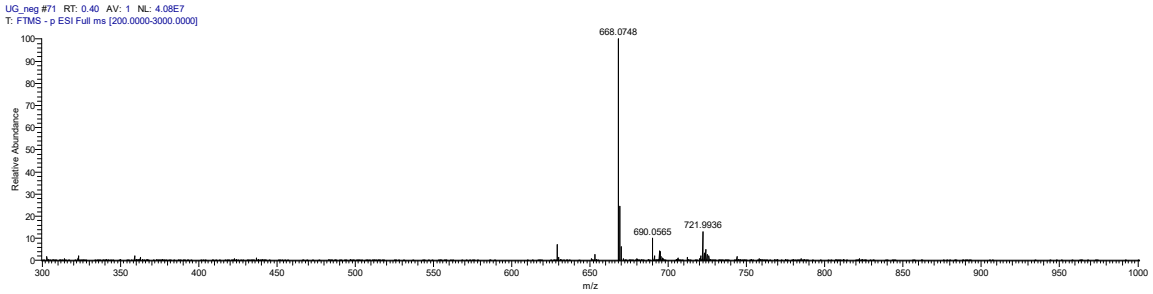

Fig. S12 HRMS spectrum of Up_2G.

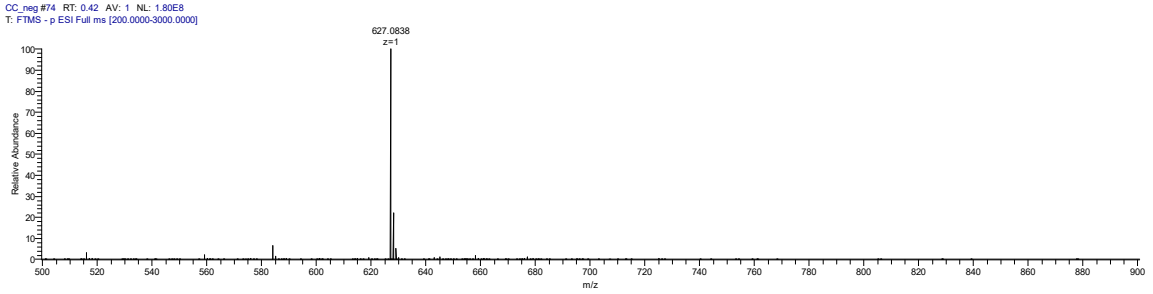

Fig. S13 HRMS spectrum of Cp_2C.

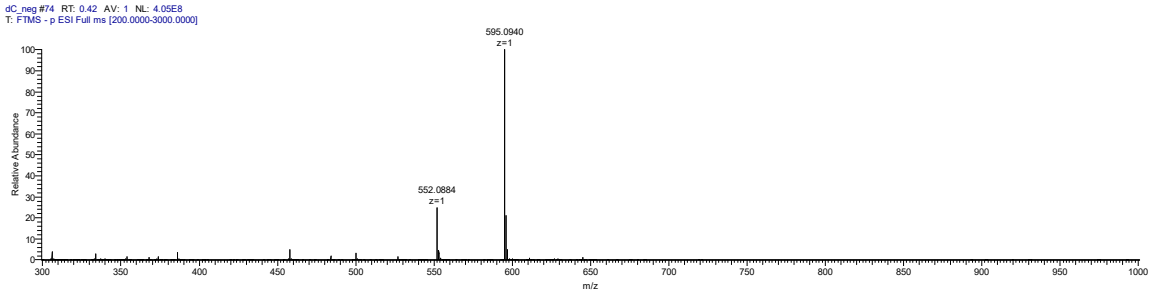

Fig. S14 HRMS spectrum of dCp_2dC.

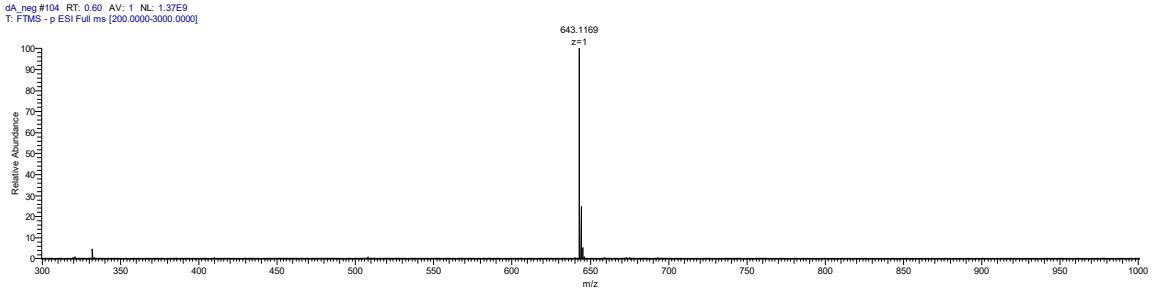

Fig. S15 HRMS spectrum of dAp_2dA.

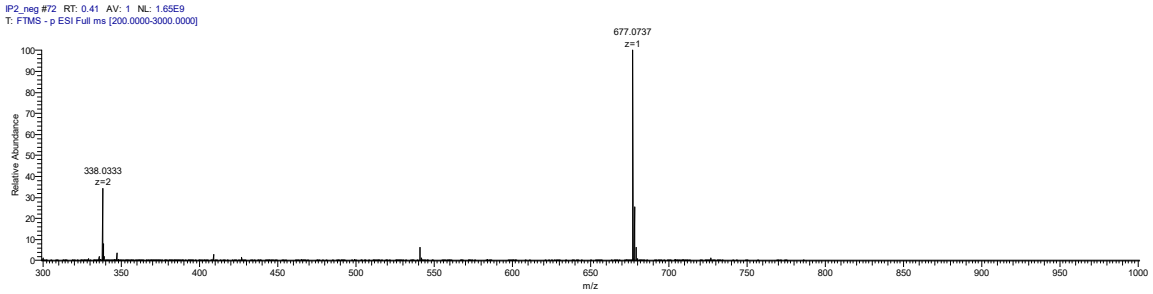

Fig. S16 HRMS spectrum of Ip_2I.

NMR spectrum

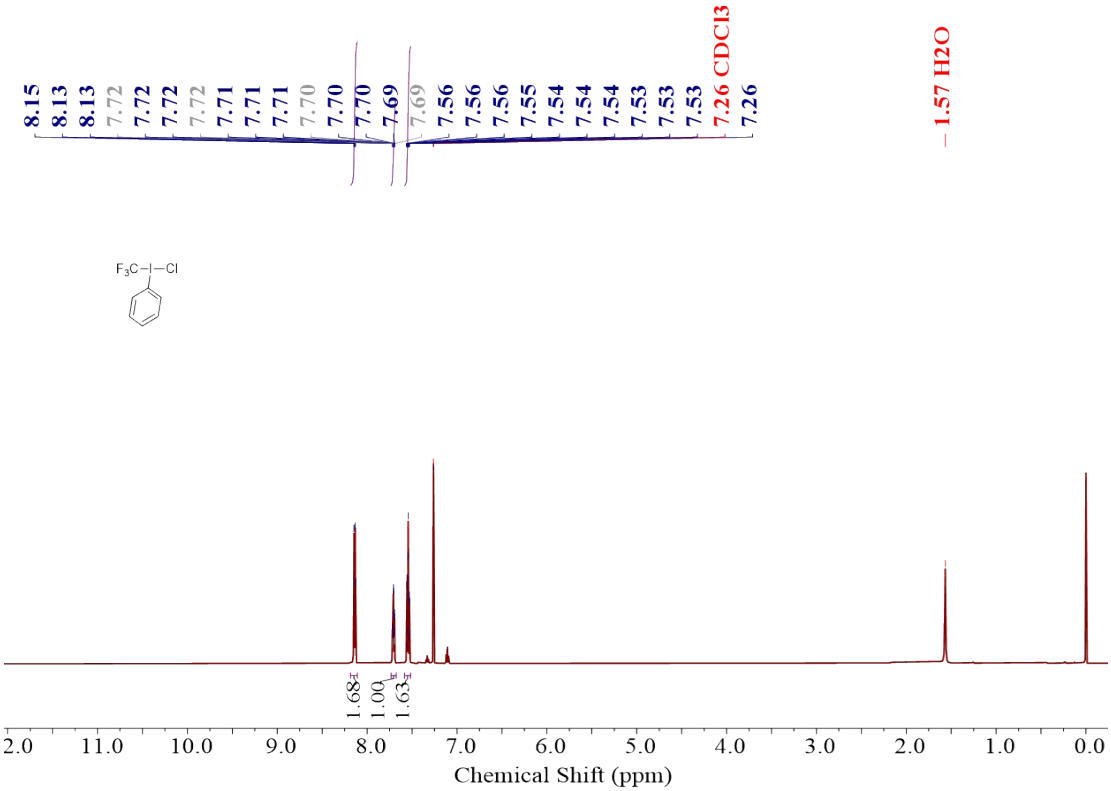

Fig. S17 ^{1}H NMR spectrum of $PhICF_3Cl$ (600 MHz, $CDCl_3$)

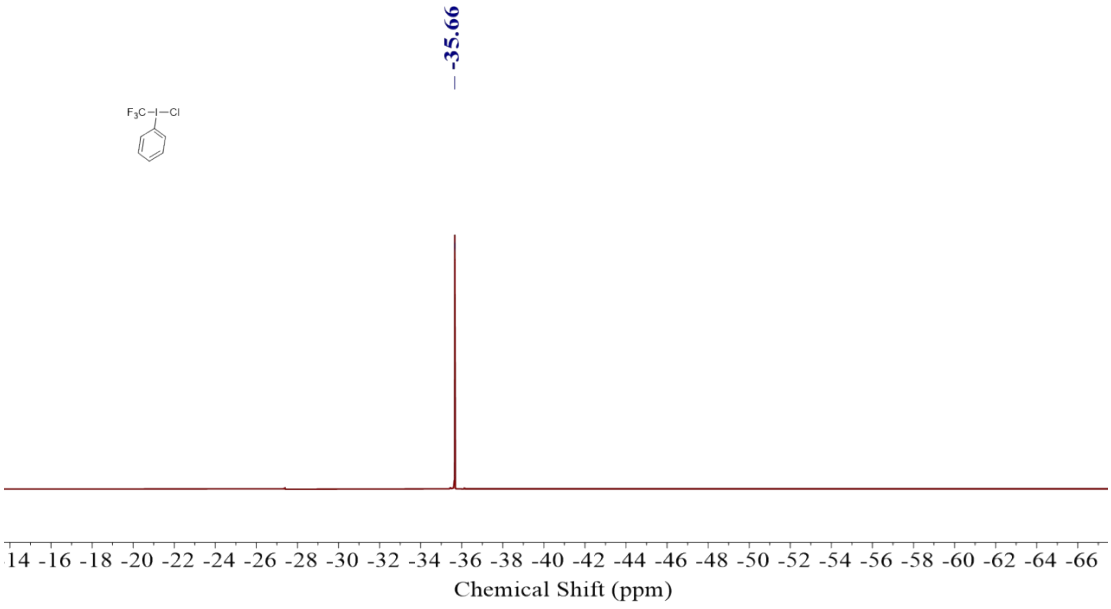

Fig. S18 ^{19}F NMR spectrum of $PhICF_3Cl$ (565 MHz, $CDCl_3$)

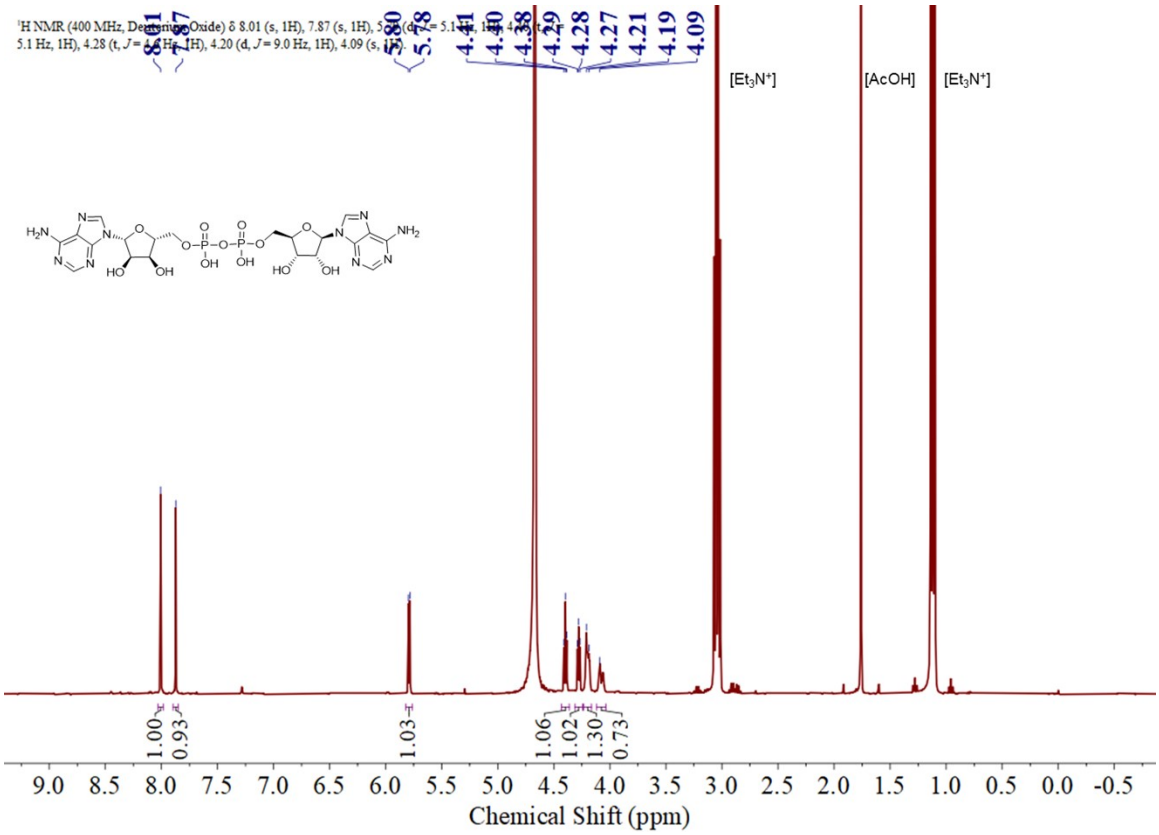

Fig. S19 ^{1}H NMR spectrum of Ap_2A (400 MHz, D_2O)

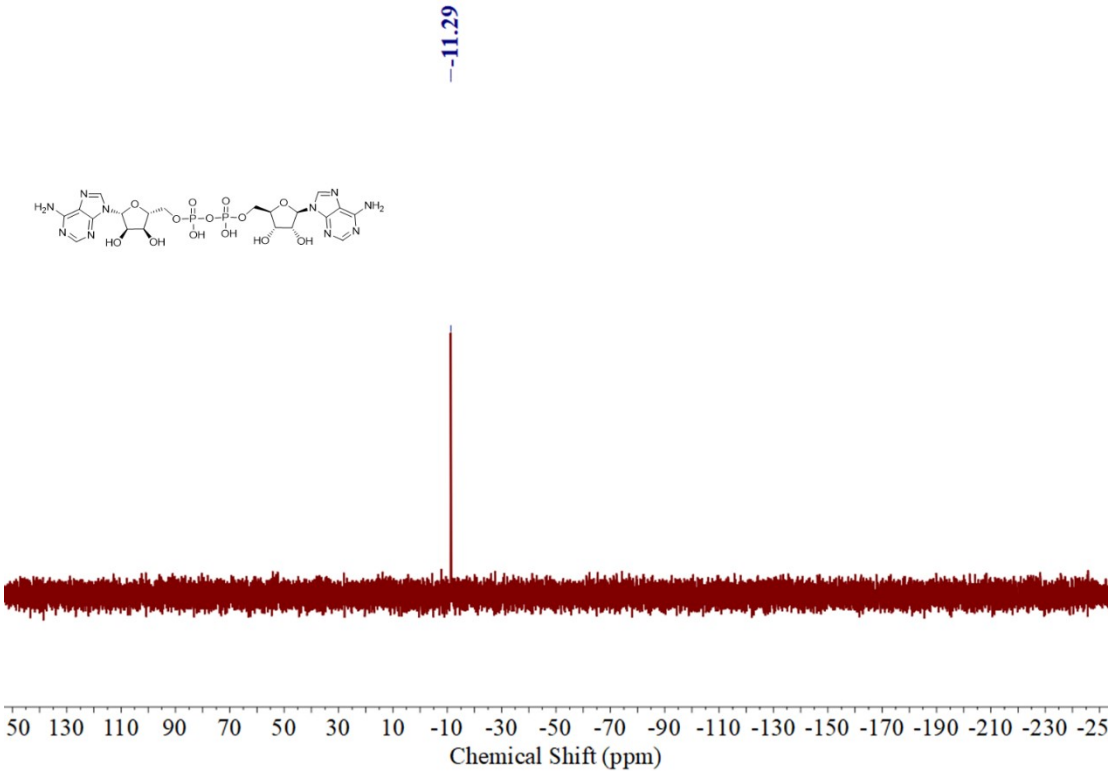

Fig. S20 ^{31}P NMR spectrum of Ap_2A (162 MHz, D_2O)

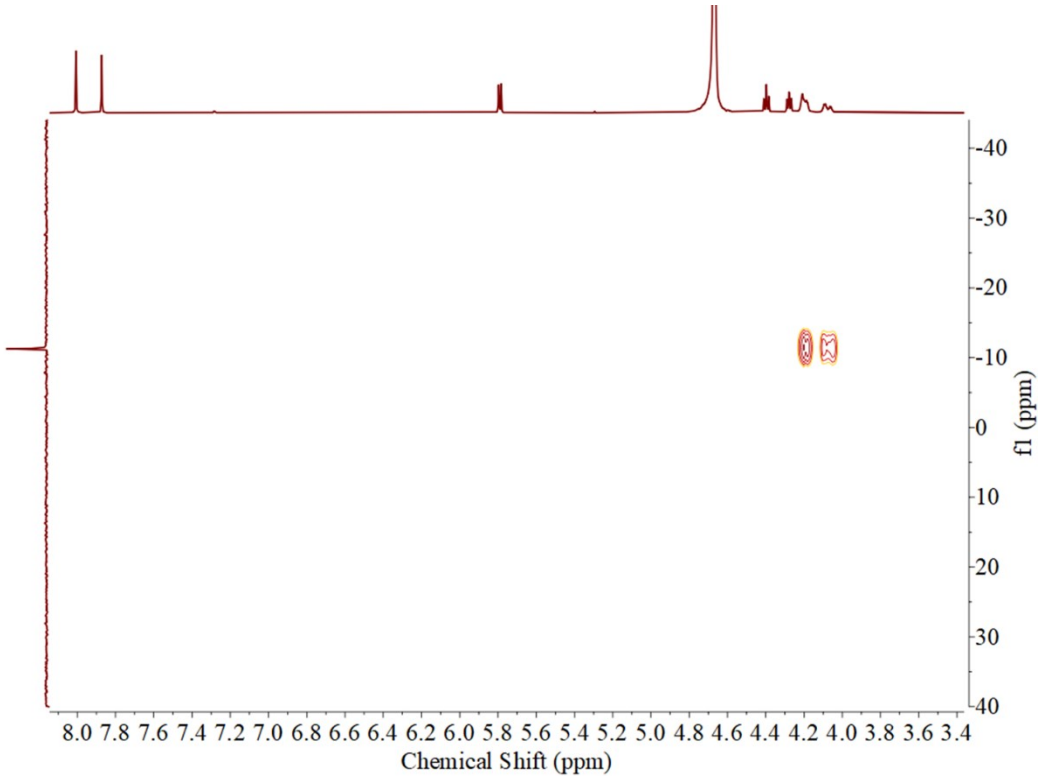

Fig. S21 ^{1}H-^{31}P-HMBC spectrum of Ap_2A (D_2O)

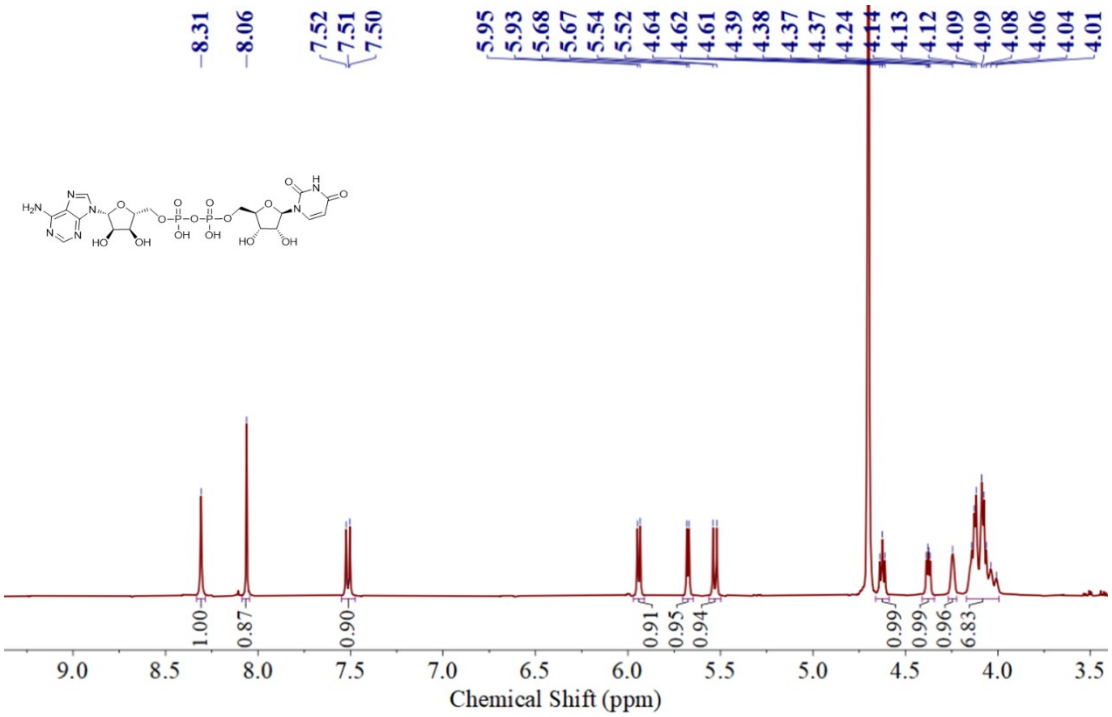

Fig. S22 ^{1}H NMR spectrum of Ap_2U (400 MHz, D_2O)

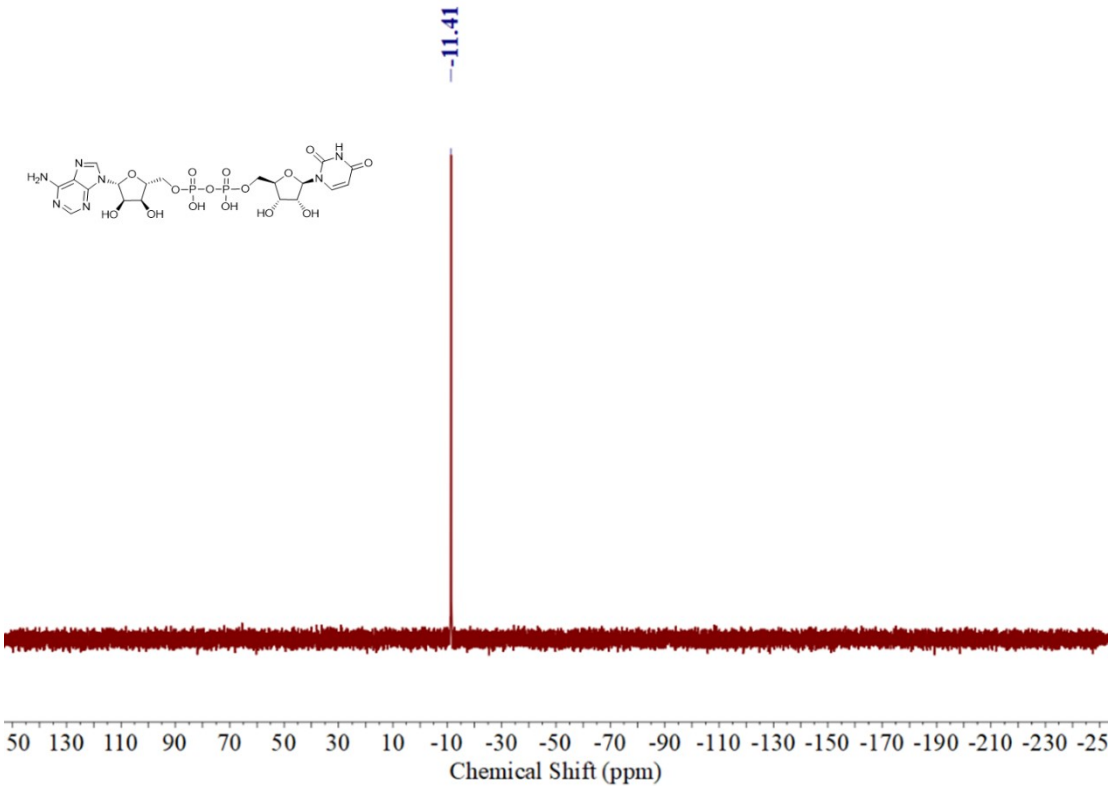

Fig. S23 ^{31}P NMR spectrum of Ap_2U (162 MHz, D_2O)

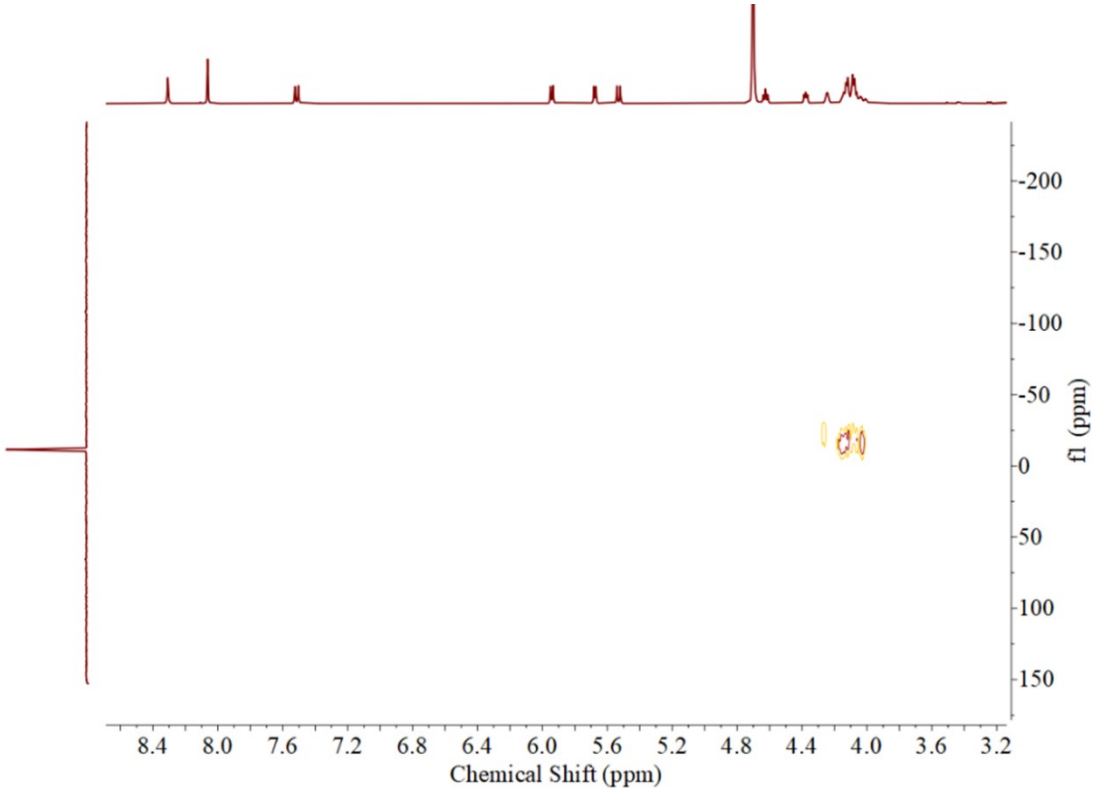

Fig. S24 ^{1}H-^{31}P-HMBC spectrum of Ap_2U (D_2O)

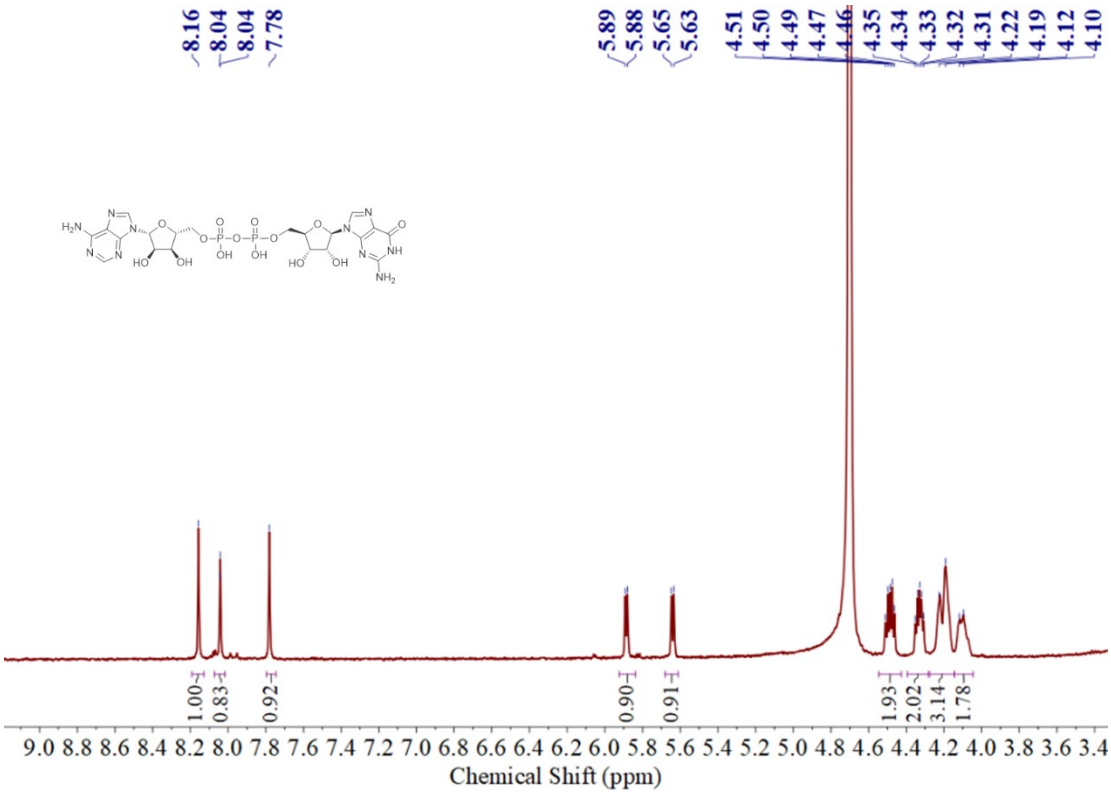

Fig. S25 ^{1}H NMR spectrum of Ap_2G (162 MHz, D_2O)

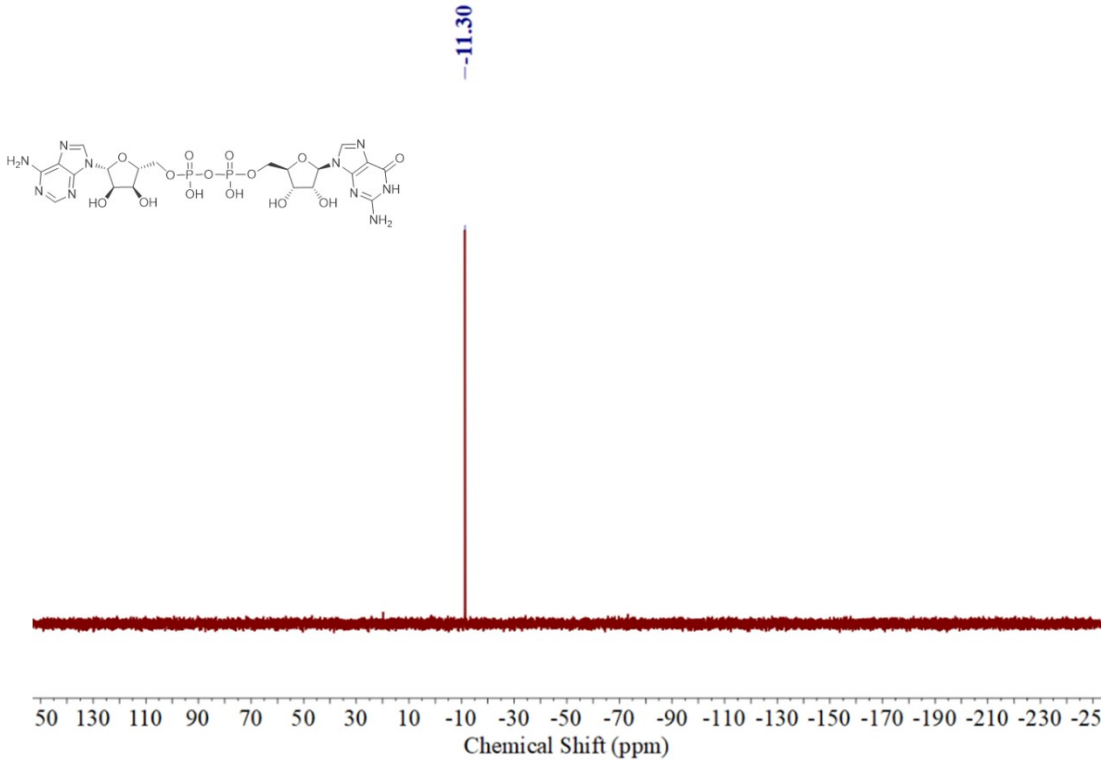

Fig. S26 ^{31}P NMR spectrum of Ap_2G (162 MHz, D_2O)

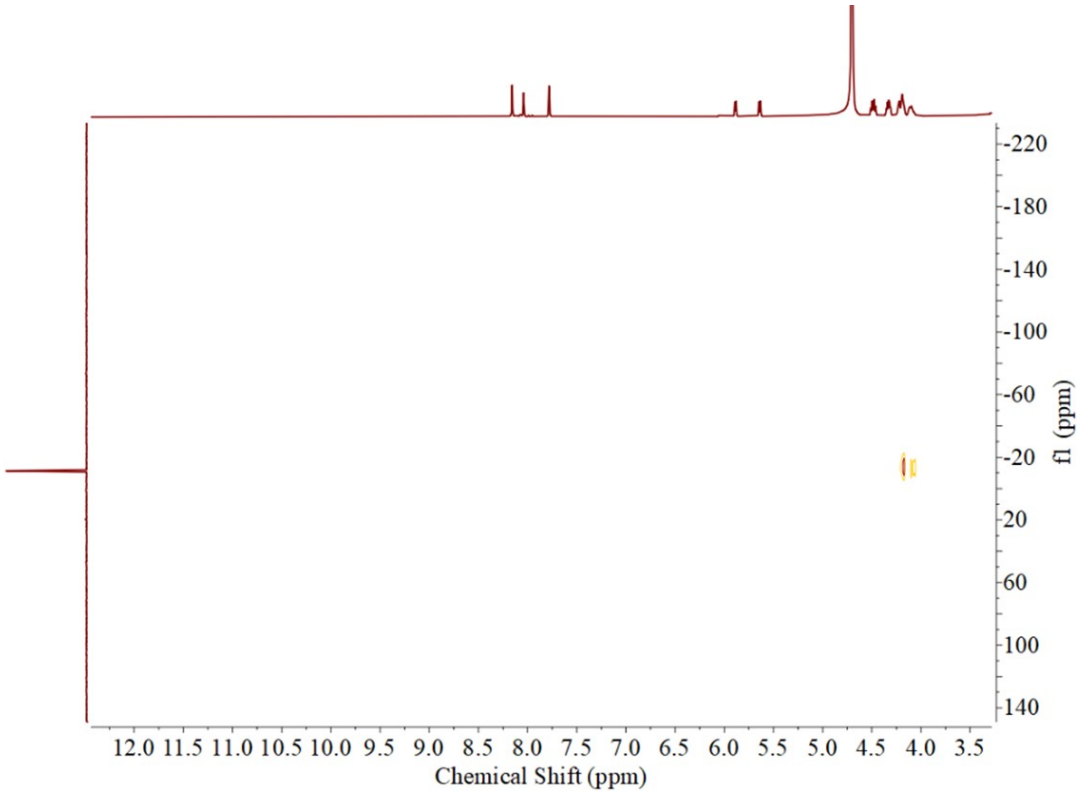

Fig. S27 ^{1}H-^{31}P-HMBC spectrum of Ap_2G (D_2O)

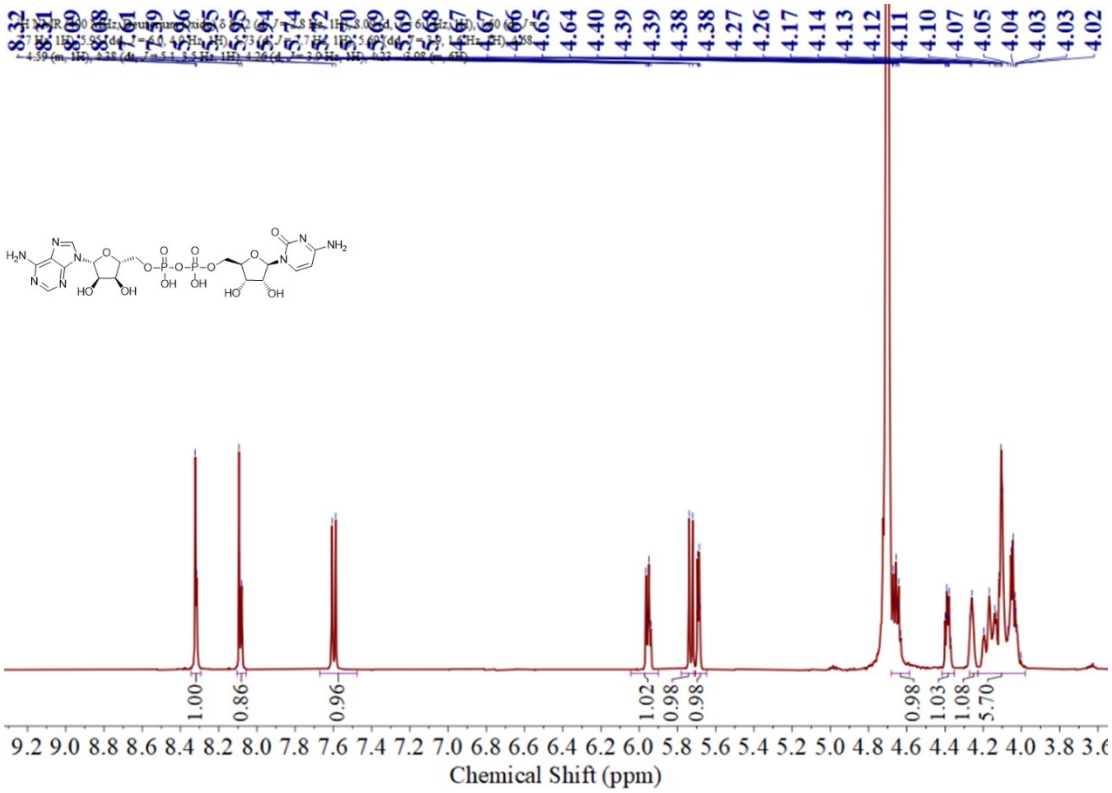

Fig. S28 ^{1}H NMR spectrum of Ap_2C (400 MHz, D_2O)

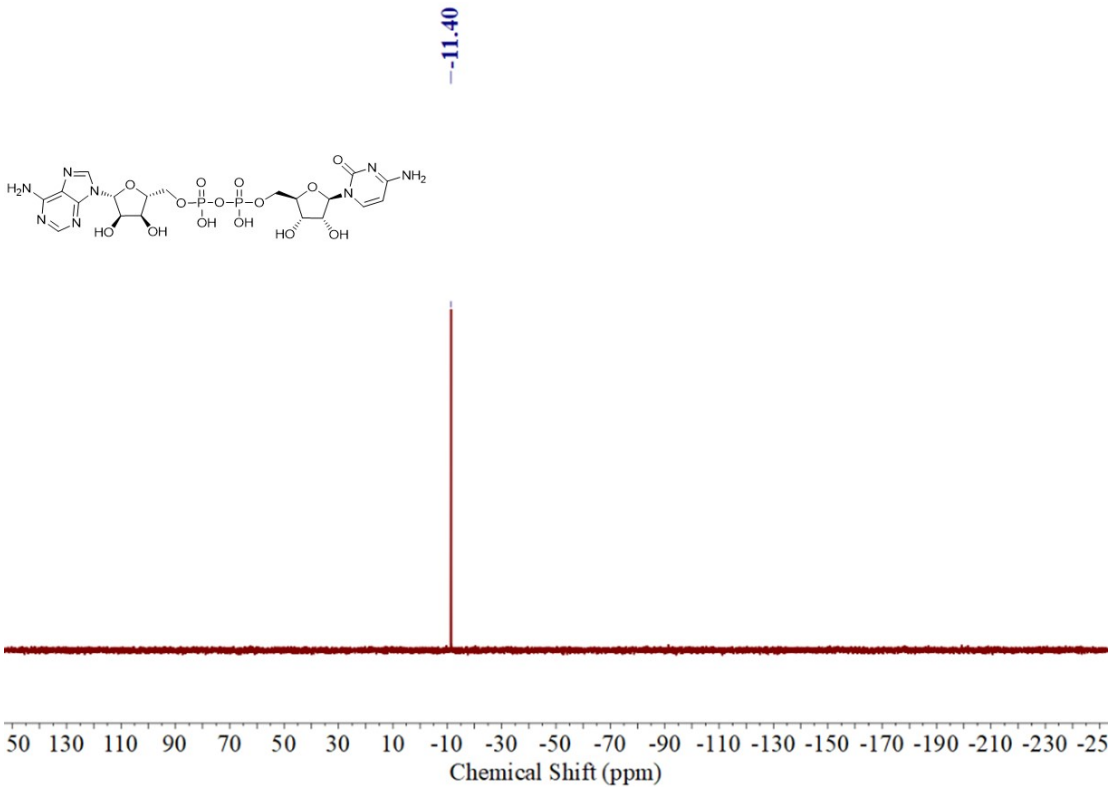

Fig. S29 ^{31}P NMR spectrum of Ap_2C (162 MHz, D_2O)

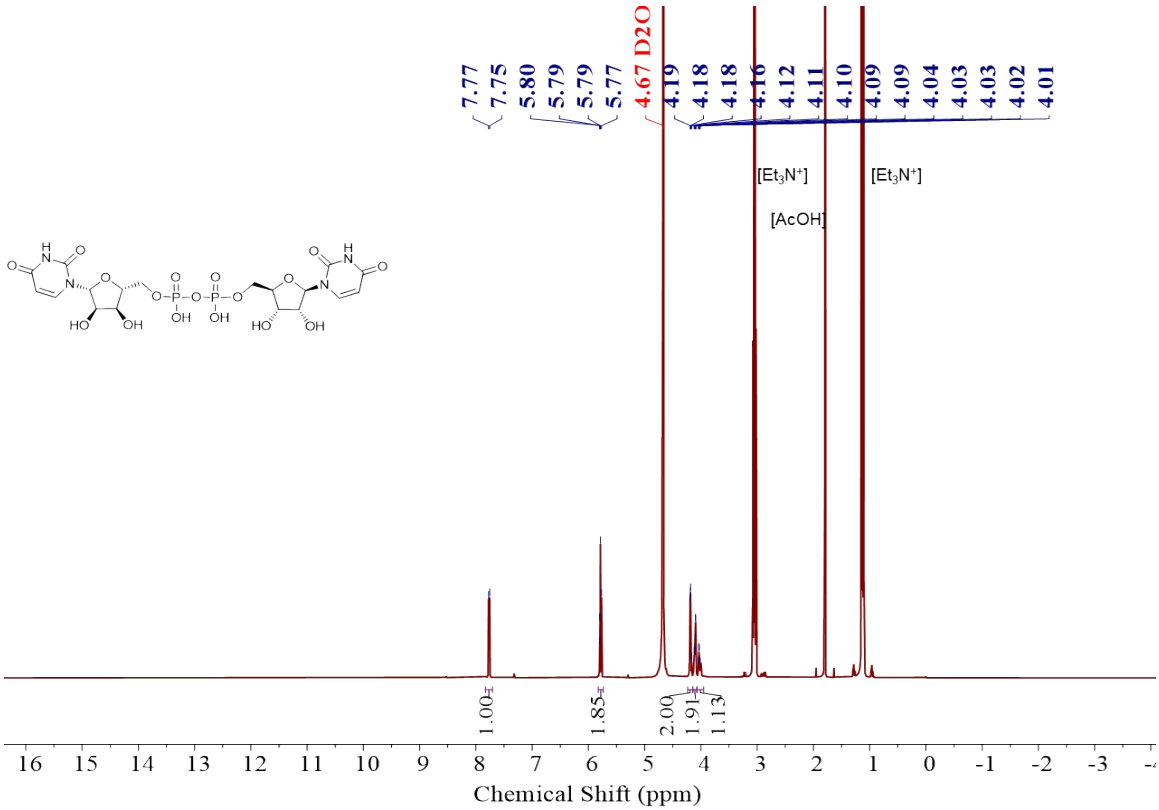

Fig. S30 ^{1}H NMR spectrum of Up_2U (400 MHz, D_2O)

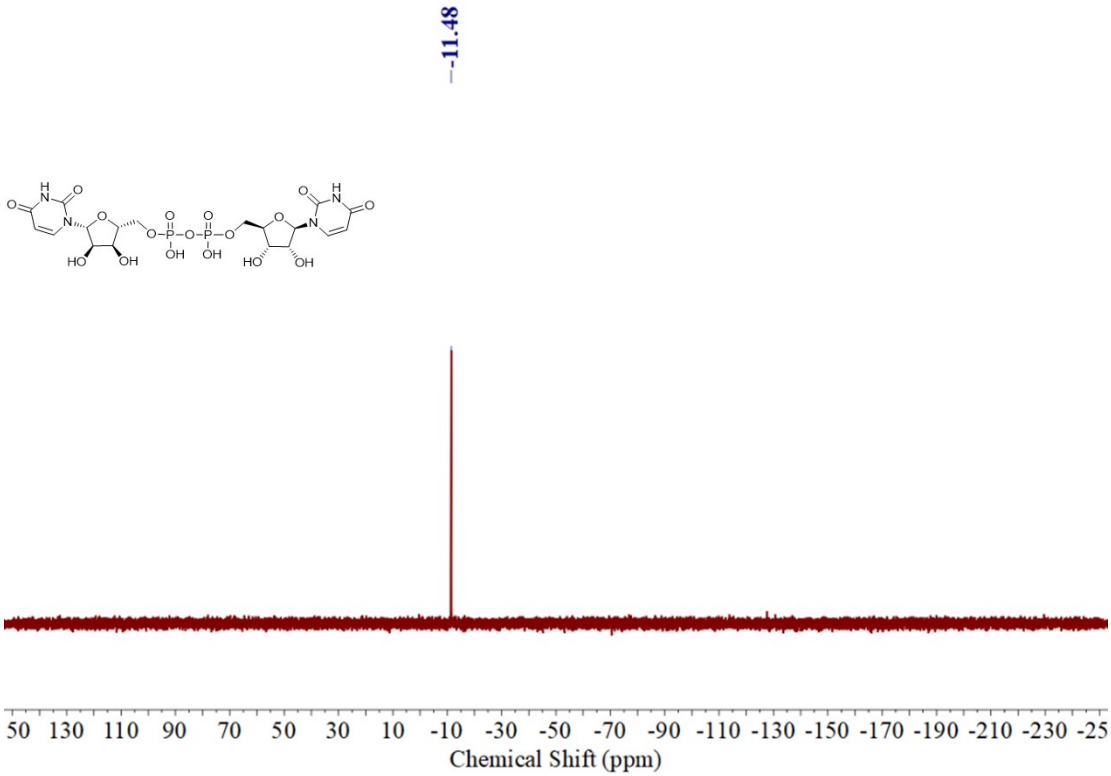

Fig. S31 ^{31}P NMR spectrum of Up_2U (162 MHz, D_2O)

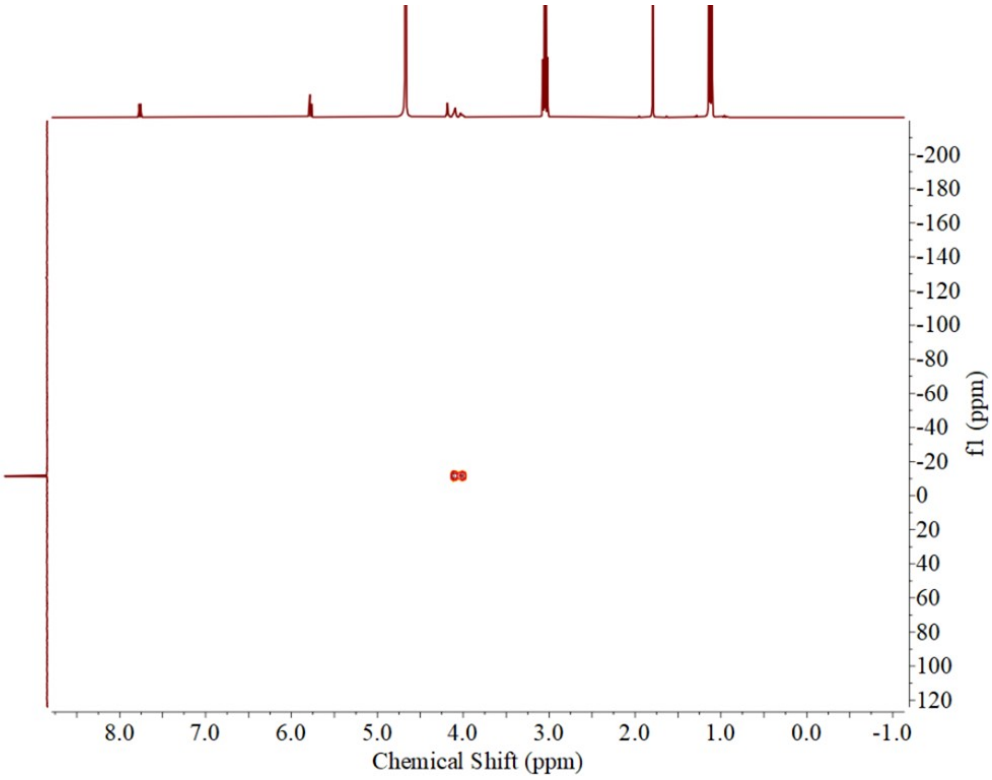

Fig. S32 ^{1}H-^{31}P-HMBC spectrum of Up_2U (D_2O)

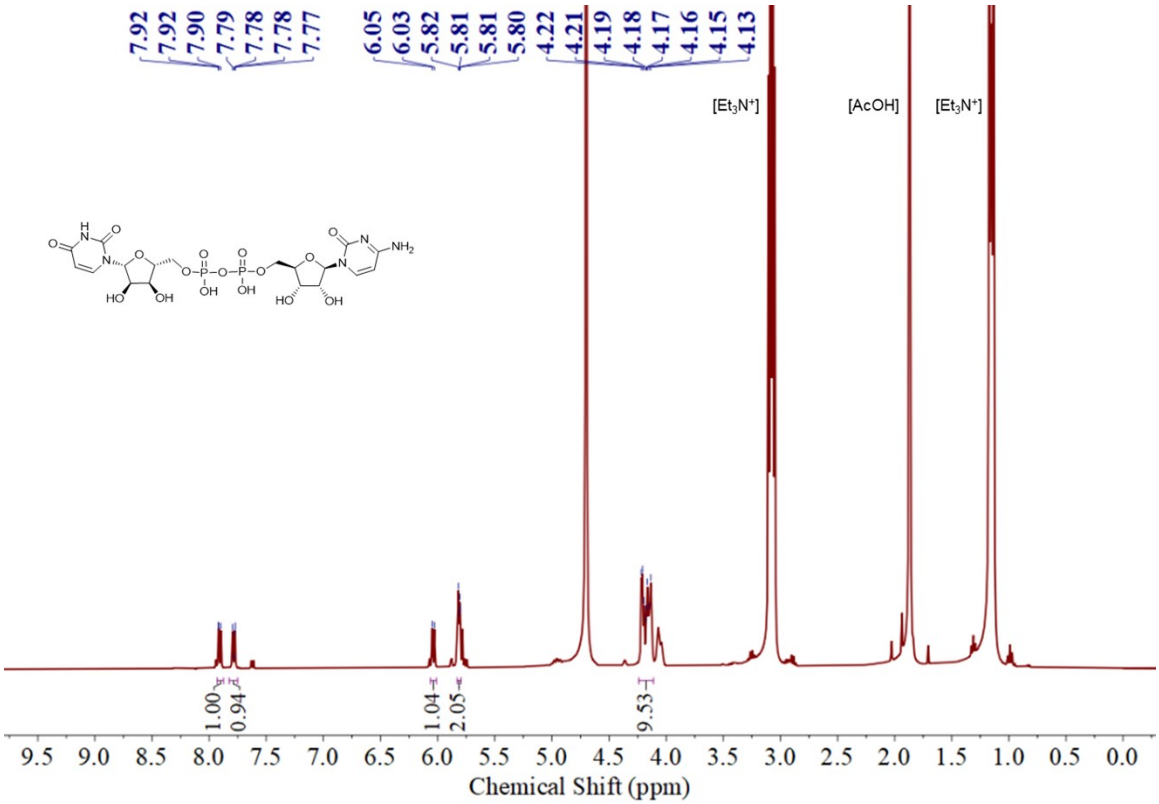

Fig. S33 ^{1}H NMR spectrum of Up_2C (400 MHz, D_2O)

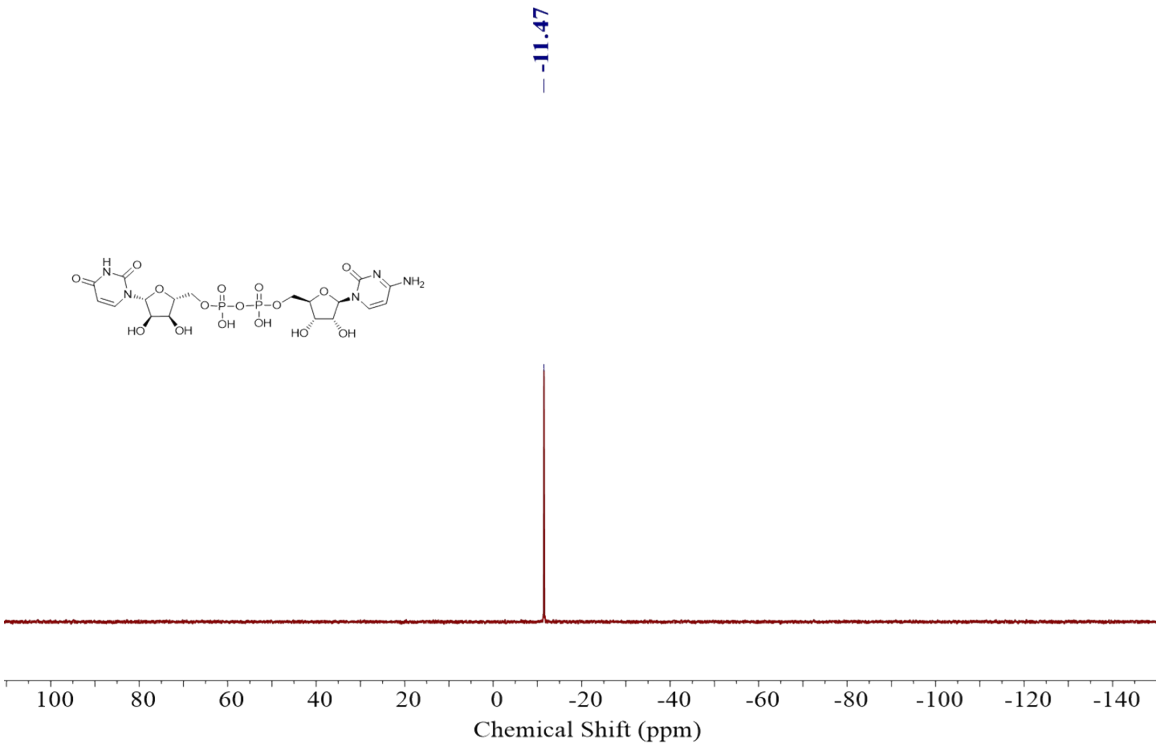

Fig. S34 ^{31}P NMR spectrum of Up_2C (162 MHz, D_2O)

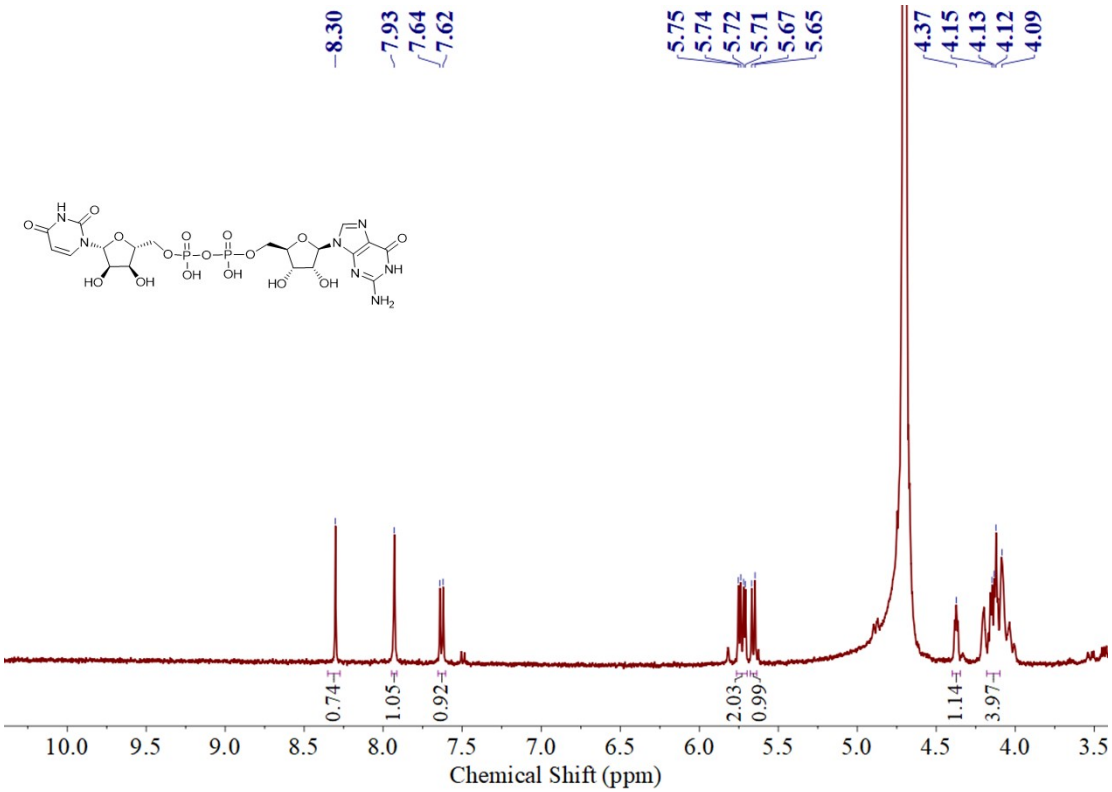

Fig. S35 ^{1}H NMR spectrum of Up_2G (400 MHz, D_2O)

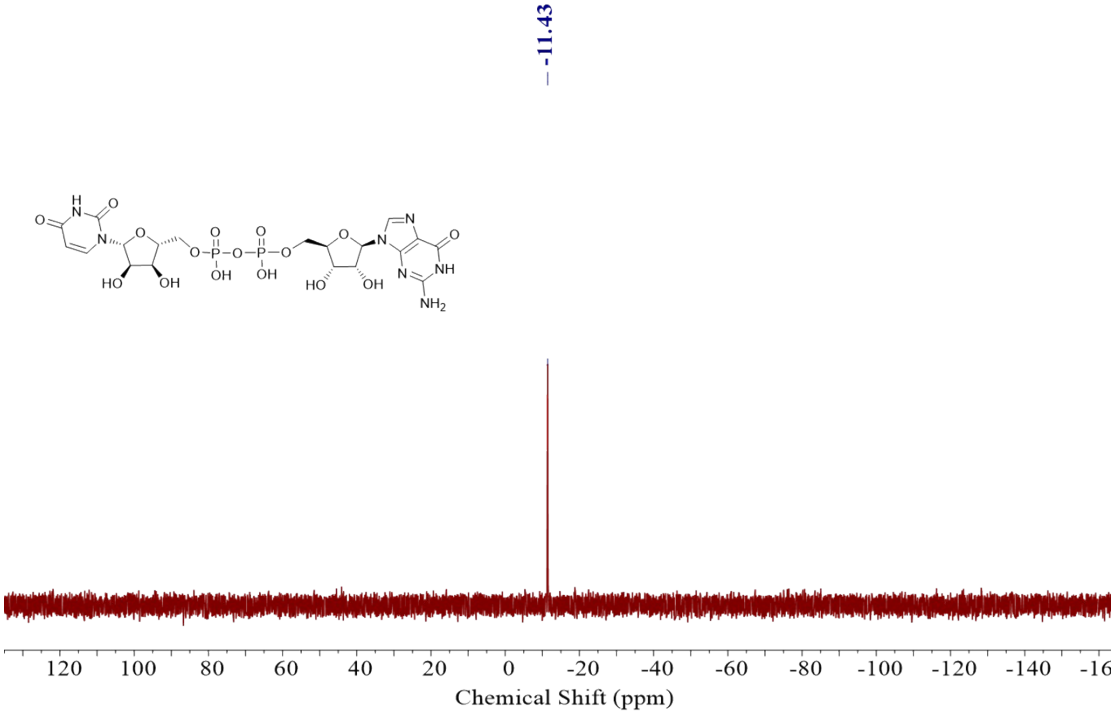

Fig. S36 ^{31}P NMR spectrum of Up_2G (162 MHz, D_2O)

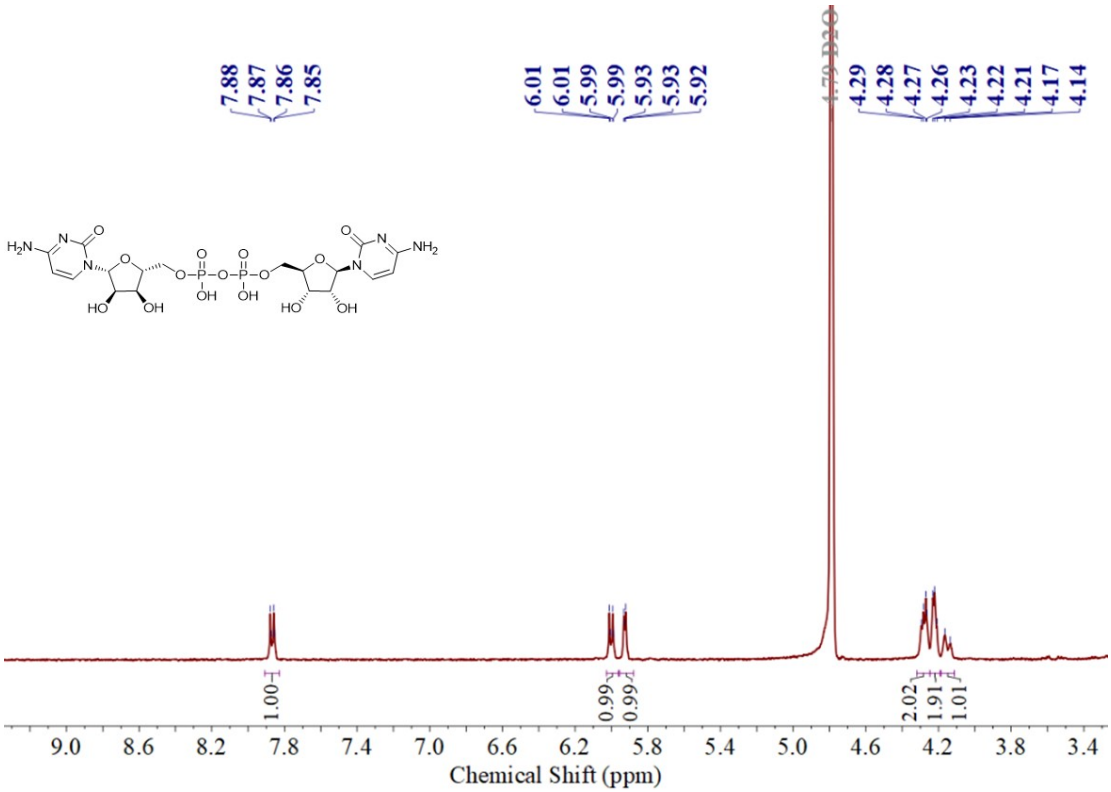

Fig. S37 ^{1}H NMR spectrum of Cp_2C (400 MHz, D_2O)

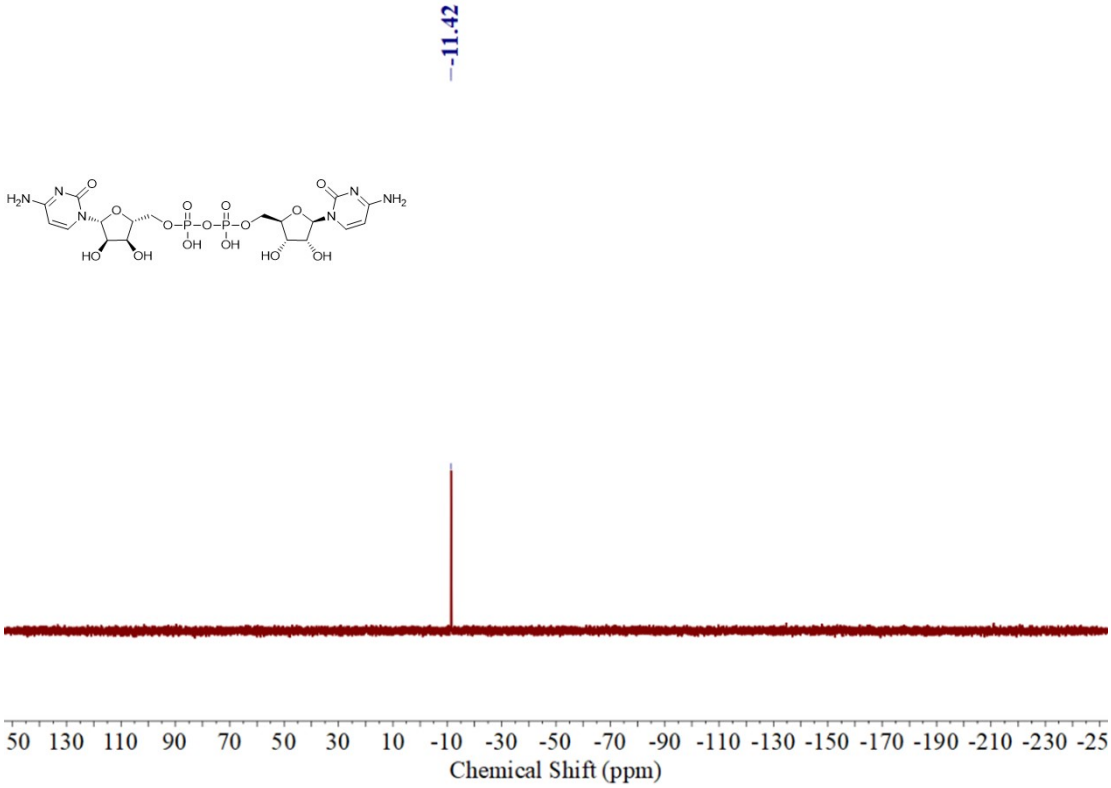

Fig. S38 ^{31}P NMR spectrum of Cp_2C (162 MHz, D_2O)

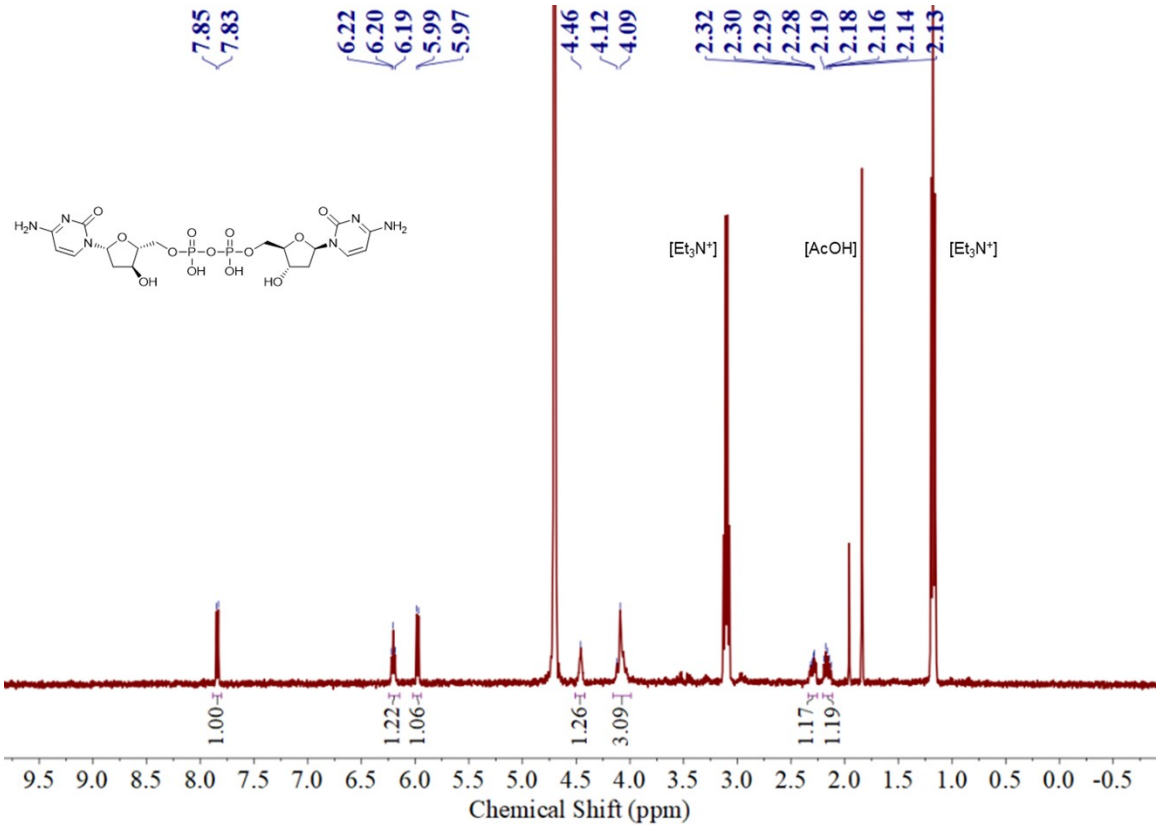

Fig. S39 ^{1}H NMR spectrum of dCp_2dC (400 MHz, D_2O)

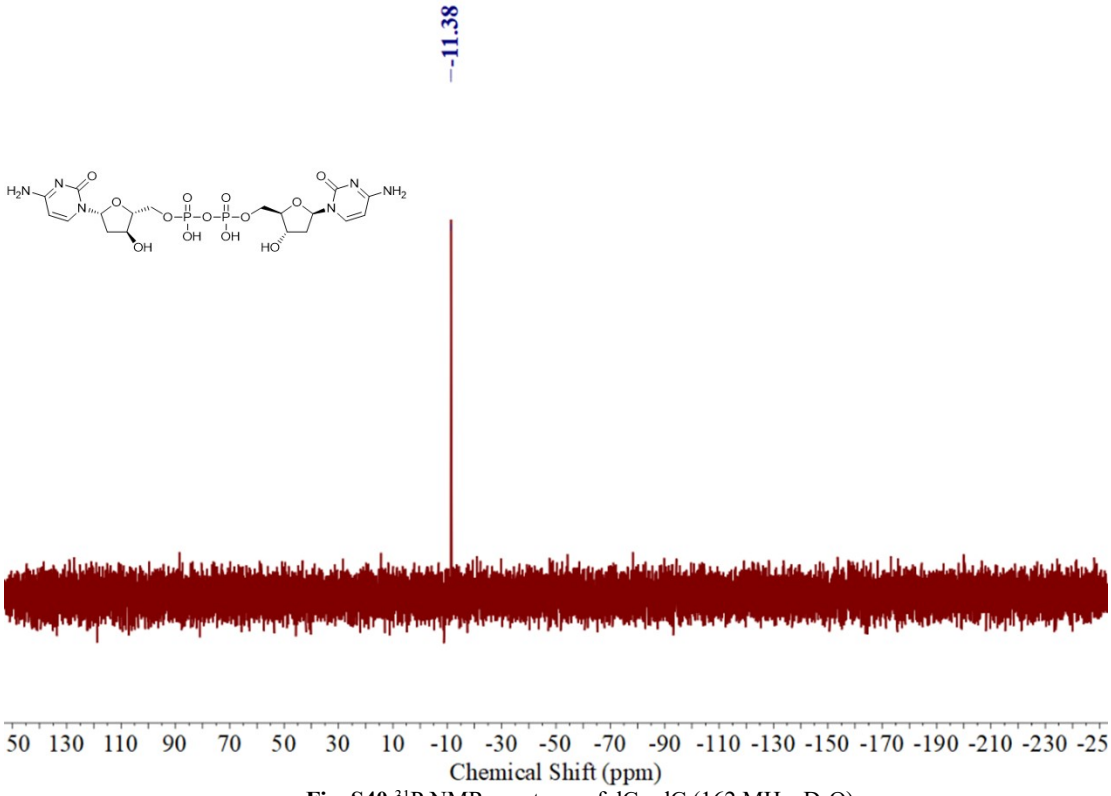

Fig. S40 ^{31}P NMR spectrum of dCp_2dC (162 MHz, D_2O)

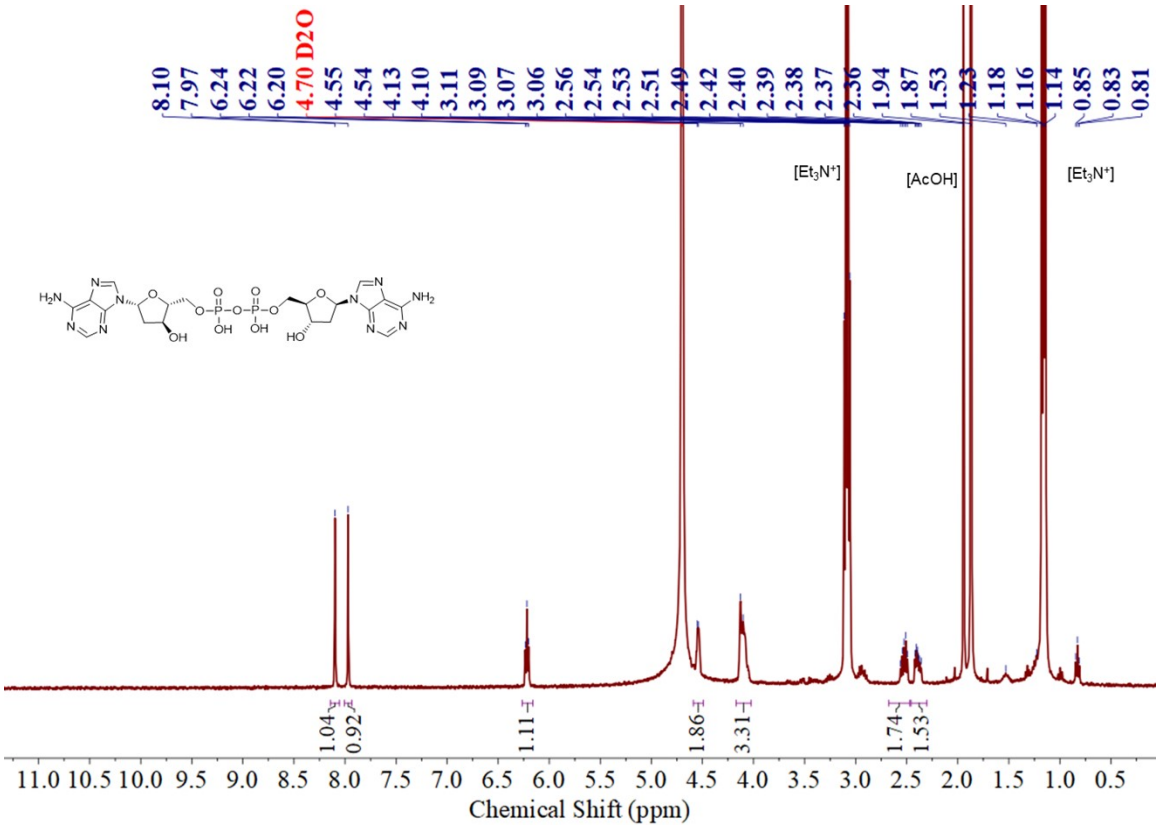

Fig. S41 ^{1}H NMR spectrum of dAp$_2$dA (400 MHz, D$_2$O)

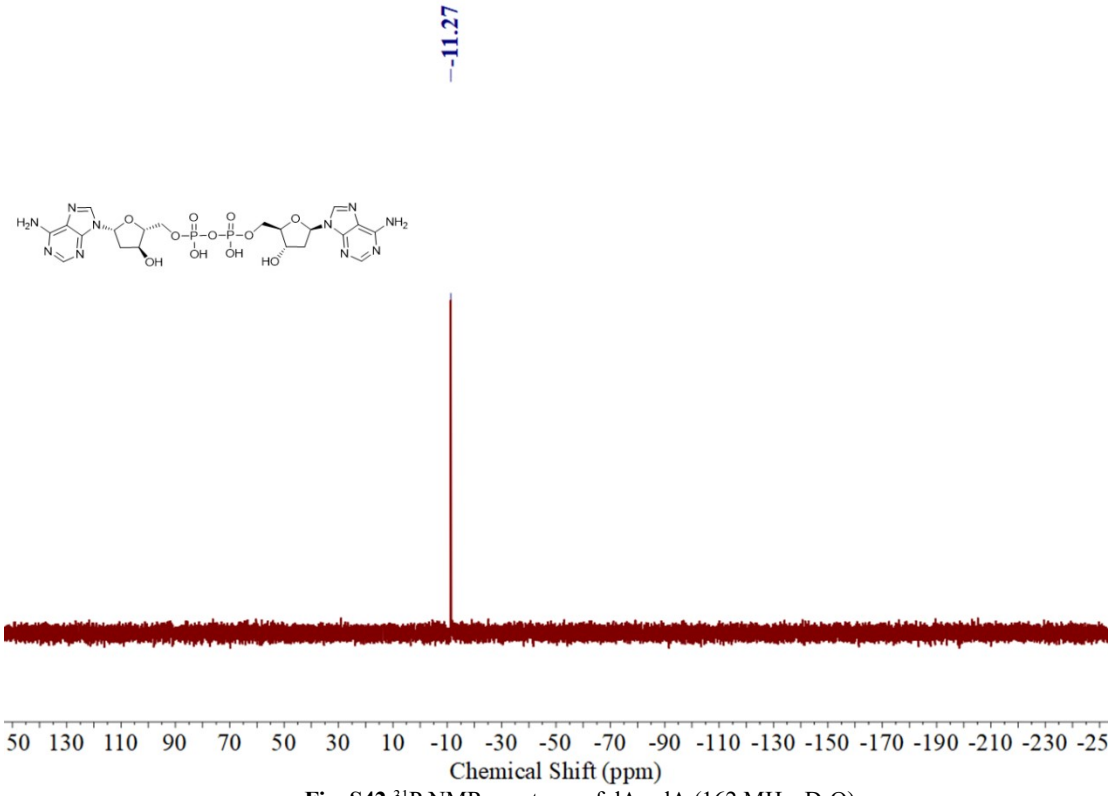

Fig. S42 ^{31}P NMR spectrum of dAp$_2$dA (162 MHz, D$_2$O)

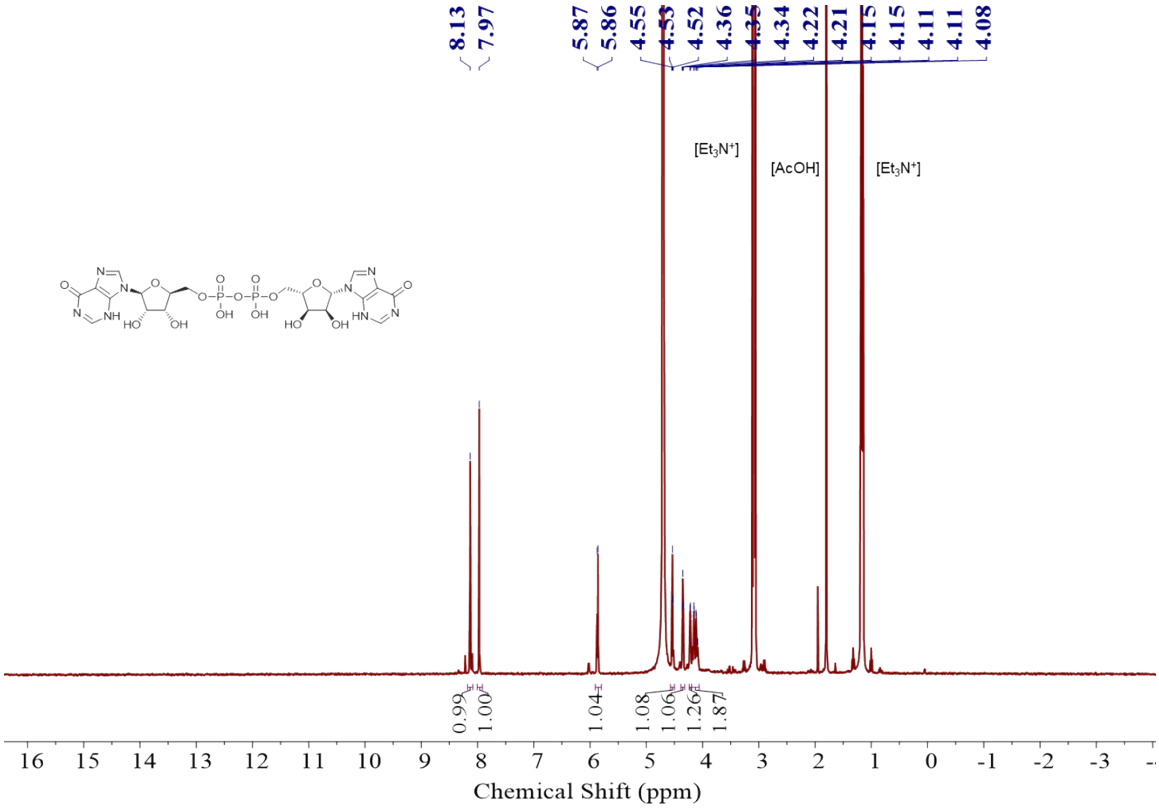

Fig. S43 ^{1}H NMR spectrum of Ip_2I (400 MHz, D_2O)

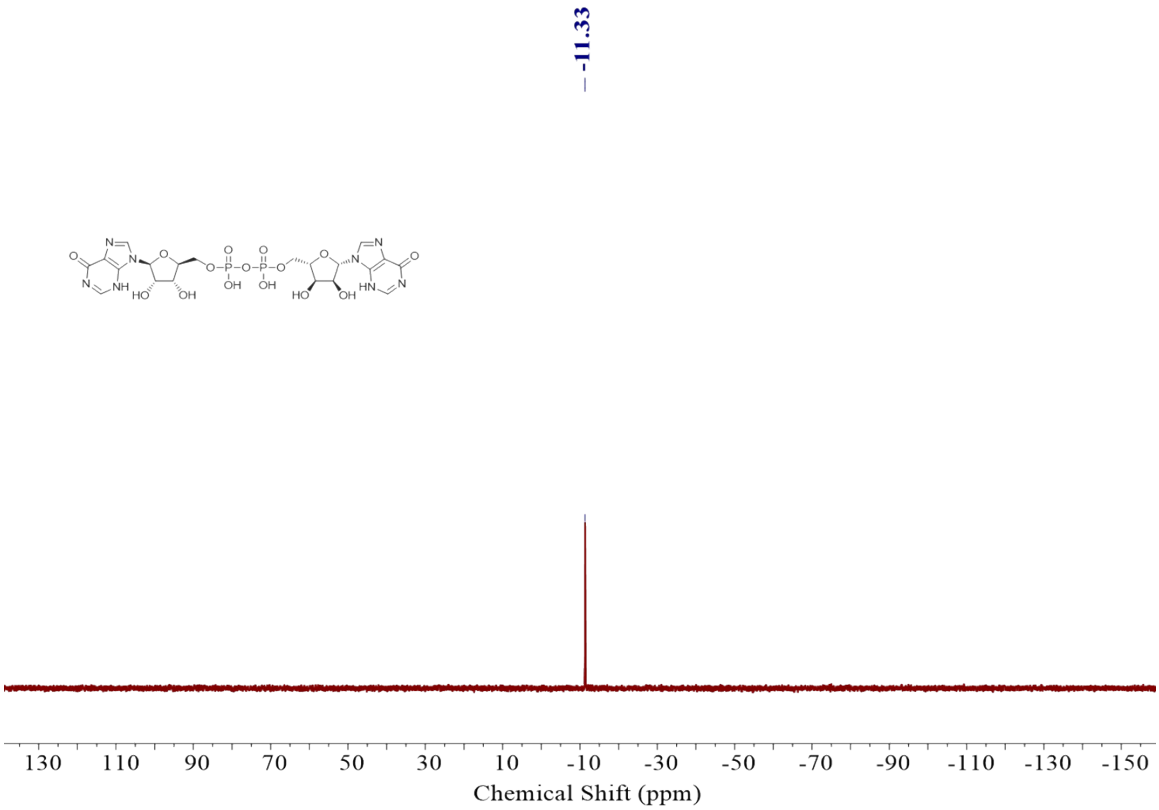

Fig. S44 ^{31}P NMR spectrum of Ip_2I (162 MHz, D_2O)