Supporting Information

Palladium-catalyzed C–H Olefination of Uridine, Deoxyuridine, Uridine Monophosphate and Uridine Analogues

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Table of Contents

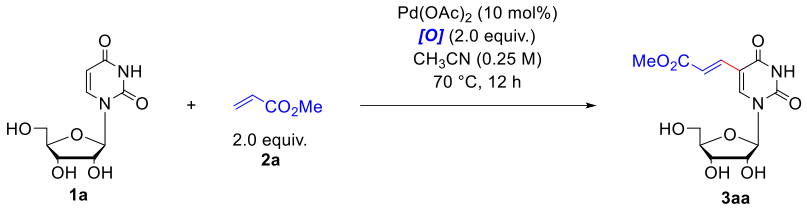
1. General information

All the chemicals were purchased commercially and used without further purification. General reagents were obtained from Adamas, Leyan, Innochem, Laajoo and Bidepharm. Anhydrous solvents were obtained from J&K. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. Visualization was carried out with UV light and Vogel's permanganate. ^{1}H NMR spectra were recorded on Bruker-400 MHz and Bruker-500 MHz instruments. When the ^{1}H NMR solvent was DMSO-*d*-6, chemical shifts were quoted in parts per million (ppm) referenced to 2.50 ppm for solvent DMSO-*d*-6. When the ^{1}H NMR solvent was Methanol-*d*-4, chemical shifts were quoted in parts per million (ppm) referenced to 3.31 ppm for solvent Methanol-*d*-4. When the ^{1}H NMR solvent was D_2O, chemical shifts were quoted in parts per million (ppm) referenced to 4.79 ppm for solvent D_2O. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiple, dd = double doublet, dt = double triplet. Coupling constants, *J*, were reported in Hertz unit (Hz). ^{13}C NMR spectra were recorded on Bruker-400 instrument (101 MHz) and Bruker-500 instrument (126 MHz), and were fully decoupled by broad band proton decoupling. When the ^{13}C NMR solvent was DMSO-*d*-6, chemical shifts were quoted in parts per million (ppm) referenced to 39.52 ppm for solvent DMSO-*d*-6. When the ^{13}C NMR solvent was Methanol-*d*-4, chemical shifts were quoted in parts per million (ppm) referenced to 49.00 ppm for solvent Methanol-*d*-4. Reverse-phase column chromatography was performed on SepaBean® machine T from Santai Technologies in Changzhou, China, using ODS 45-60 mm C18 Spherical silica. The high-resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI-TOF (electrospray ionization-time of flight). Optical rotations were measured on an Anton Paar MCP100 automatic polarimeter using a 100 mm path-length cell at 589 nm. Melting points were measured with microscope WRX-4 (Shanghai Yice).

2. Details for the direct C–H olefinations

2.1 Optimization of C–H olefinations

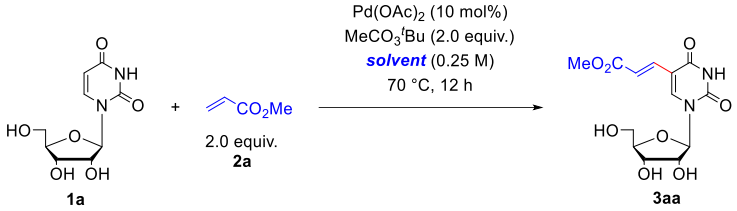
Table S1. Oxidant screening



Entry[a]	[O]	Yield[b] of 3aa	Recovery[b] of 1a
1	$PhCO_3{}^tBu$	24%	31%
2	$MeCO_3{}^tBu$	37%	60%
3	DTBP	13%	85%
4	TBHP	20%	73%
5	$PhI(OAc)_2$	14%	43%
6	Oxone	9%	78%
7	DLP	1%	93%
8	Benzoquinone	1%	23%
9	*m*-CPBA	0%	23%
10	$(NH_4)_2S_2O_8$	9%	5%
11	H_2O_2	8%	91%
12	$Cu(OAc)_2$	0%	100%
13	CaOTf	0%	97%
14	AgOAc	2%	97%

[a] Conditions: uridine **1a** (0.1 mmol), methyl acrylate **2a** (0.2 mmol), $Pd(OAc)_2$ (0.01 mmol), oxidant (0.2 mmol), CH_3CN (0.4 mL) under air at 70 ℃ for 12 hours. [b] Yields and recovery were determined by LC-MS.

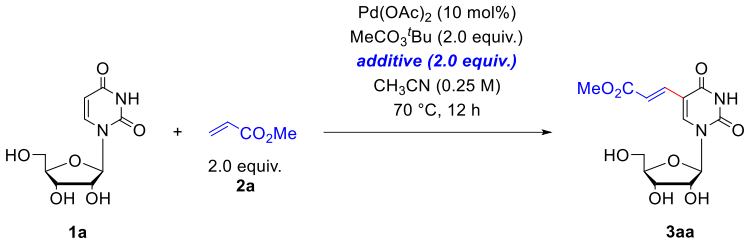
Table S2. Solvent screening



Entry[a]	Solvent	Yield[b] of 3aa	Recovery[b] of 1a
1	CH_3CN	37%	60%
2	Benzonitrile	2%	42%
3	H_2O	2%	98%
4	MeOH	< 1%	82%
5	CH_3CH_2OH	0%	83%
6	*t*-BuOH	6%	61%
7	*t*-AmlyOH	6%	69%
8	Glycol	0%	98%
9	Pyridine	0%	100%
10	DMSO	7%	91%
11	DMA	18%	77%
12	HFIP	17%	72%
13	CF_3CH_2OH	2%	76%
14	CH_3COOH	59%	24%
15	HCl	27%	0%
16	THF	2%	47%
17	Dioxane	16%	75%
18	Toluene	0%	44%
19	Cyclohexane	0%	100%
20	DCE	0%	99%

[a] Conditions: uridine **1a** (0.1 mmol), methyl acrylate **2a** (0.2 mmol), $Pd(OAc)_2$ (0.01 mmol), $MeCO_3{}^tBu$ (0.2 mmol), solvent (0.4 mL) under air at 70 ℃ for 12 hours. [b] Yields and recovery were determined by LC-MS.

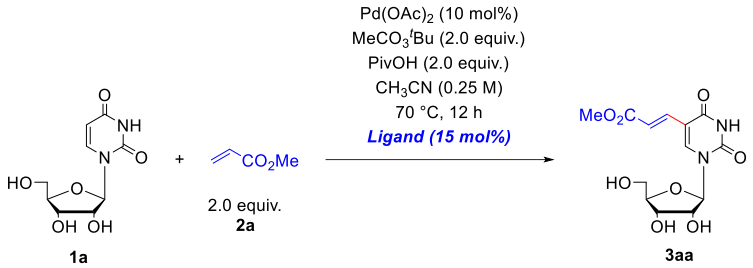
Table S3. Additive screening



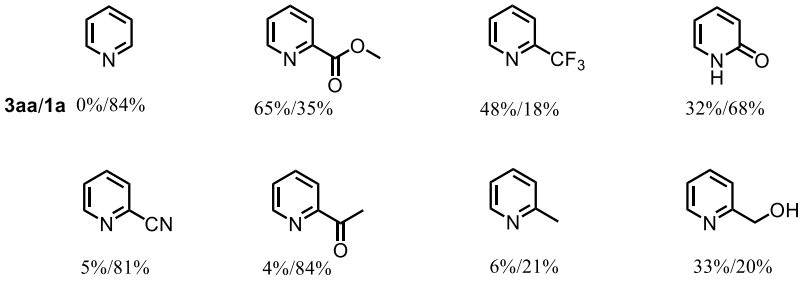
Entry[a]	Additive	Yield[b] of 3aa	Recovery[b] of 1a
1	AcOH	62%	26%
2	$CH_3CH_2C(CH_3)_2COOH$	76%	13%
3	$(CH_3)_2CHCOOH$	75%	22%
4	*p*-$CF_3(C_6H_4)CH_2COOH$	42%	35%
5	PivOH	82%	16%
6	TFA	2%	80%
7	HFIP	28%	69%
8	HCl	8%	60%
9	K_2CO_3	1%	99%
10	Li_2CO_3	0%	100%
11	Cs_2CO_3	0%	100%
12	KH_2PO_4	14%	83%
13	K_2HPO_4	13%	61%
14	$NaHCO_3$	1%	99%
15	NaH_2PO_4	17%	80%
16	LiF	0%	98%
17	CsF	0%	100%
18	$MgCl_2$	0%	100%

[a] Conditions: uridine **1a** (0.1 mmol), methyl acrylate **2a** (0.2 mmol), $Pd(OAc)_2$ (0.01 mmol), $MeCO_3{}^tBu$ (0.2 mmol), additive (0.2 mmol), CH_3CN (0.4 mL) under air at 70 ℃ for 12 hours. [b] Yields and recovery were determined by LC-MS.

Table S4. Amino acid and pyridine ligand screening

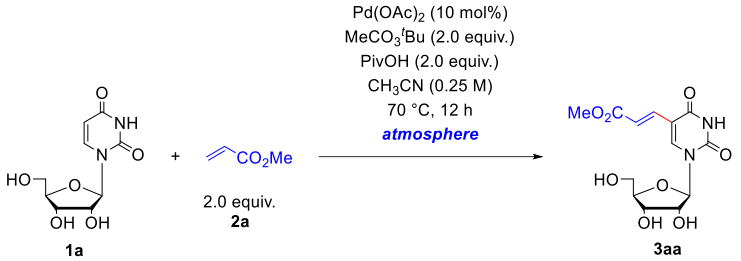


Entry[a]	ligand	Yield[b] of 3aa	Recovery[b] of 1a
1	-	79%	18%
2	Ac-Leu-OH	51%	10%
3	Ac-Gly-OH	67%	22%
4	Ac-Val-OH	78%	14%
5	Ac-Pro-OH	70%	24%
6	Ac-Phe-OH	60%	27%
7	Ac-Cys-OH	5%	93%
8	Z-Phe-OH	28%	72%
9	Z-Ala-OH	64%	25%
10	Z-Gly-OH	63%	27%
11	Boc-Gly-OH	64%	26%
12	Boc-Phe-OH	35%	61%
13	Boc-Leu-OH	74%	14%



[a] Conditions: uridine **1a** (0.1 mmol), methyl acrylate **2a** (0.2 mmol), $Pd(OAc)_2$ (0.01 mmol), $MeCO_3{}^tBu$ (0.2 mmol), PivOH (0.2 mmol), CH_3CN (0.4 mL), Ligand (0.015 mmol) under air at 70 ℃ for 12 hours.

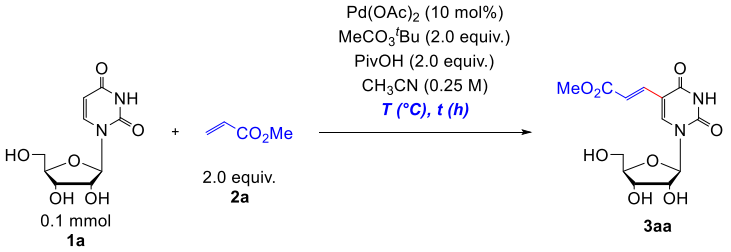
Table S5. Atmosphere screening



Entry[a]	Atmosphere	Yield[d] of 3aa	Recovery[d] of 1a
1	air	82%	15%
2[b]	Ar	21%	79%
3[c]	O_2	83%	11%

[a] Conditions: uridine **1a** (0.1 mmol), methyl acrylate **2a** (0.2 mmol), $Pd(OAc)_2$ (0.01 mmol), $MeCO_3{}^tBu$ (0.2 mmol), PivOH (0.2 mmol), CH_3CN (0.4 mL) under air at 70 ℃ for 12 hours. [b] The reaction was carried out under an argon atmosphere. [c] The reaction was carried out under an oxygen atmosphere. [d] Yields and recovery were determined by LC-MS.

Table S6. Temperature and Time screening

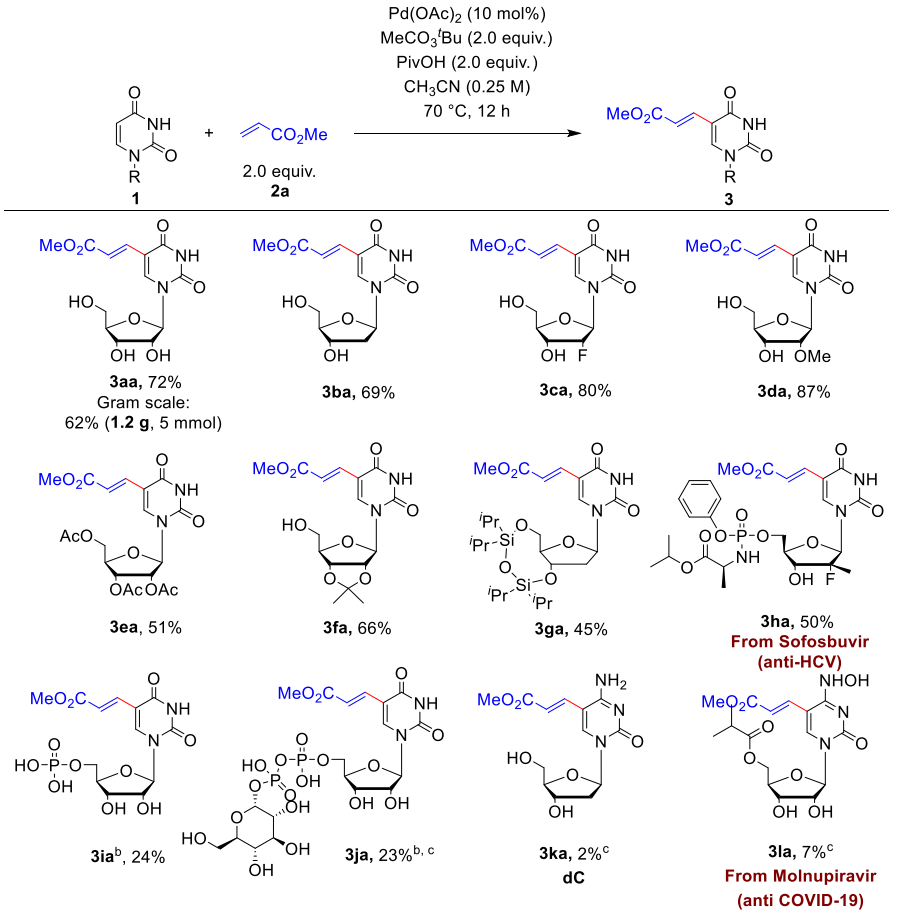


Entry[a]	T (℃)	t (h)	Yield[b] of 3aa	Recovery[b] of 1a
1	60	12	40	54
2	70	3	62	38
3	70	6	79	18
4	70	12	82	15
5	70	16	82	6
6	80	12	83	4
7	90	12	83	1

[a] Conditions: uridine **1a** (0.1 mmol), methyl acrylate **2a** (0.2 mmol), $Pd(OAc)_2$ (0.01 mmol), $MeCO_3{}^tBu$ (0.2 mmol), PivOH (0.2 mmol), CH_3CN (0.4 mL) under air. [b] Yields and recovery were determined by LC-MS.

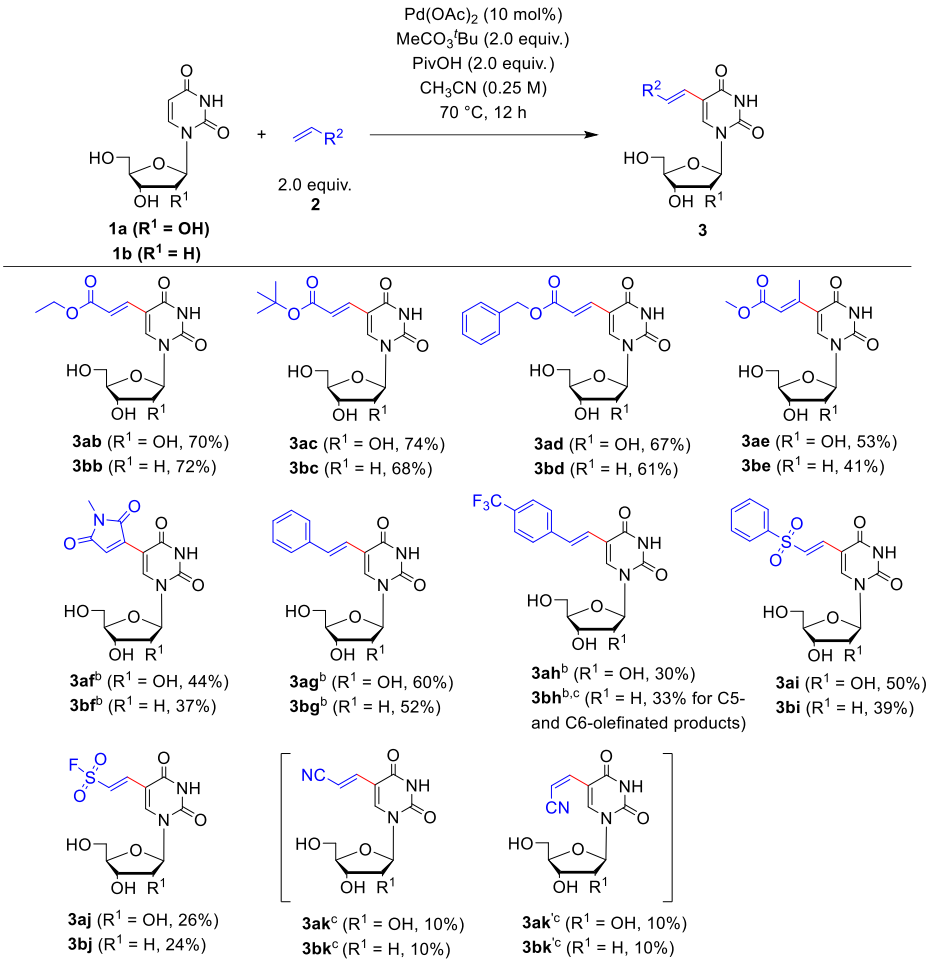
2.2. Substrate scope

Table S7. Substrate scope of the uridines



[a] Conditions: uracil-based nucleosides/nucleotides **1** (0.1 mmol), methyl acrylate **2a** (2.0 equiv.), $Pd(OAc)_2$ (10 mol%), $CH_3CO_3{}^tBu$ (2.0 equiv.), PivOH (2.0 equiv.), CH_3CN (0.4 mL) under air at 70 ℃ for 12 hours. [b] Mixed solvents of CH_3CN and H_2O (10:1, v/v) was used. [c] Yield determined by LC-MS and compound not isolated.

Table S8. Substrate scope of the alkenes



[a] Conditions: uridine **1a** or 2'-deoxyuridine **1b** (0.1 mmol), olefines **2** (2.0 equiv.), $Pd(OAc)_2$ (10 mol%), $CH_3CO_3{}^tBu$ (2.0 equiv.), PivOH (2.0 equiv.), CH_3CN (0.4 mL) under air at 70 ℃ for 12 hours. [b] The reaction was carried out under O_2 at 90 ℃ for 12 hours. [c] Yield determined by LC-MS and compound not isolated. Isolated yield.

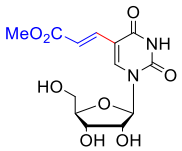
2.3 General procedure

General procedure A (0.1 mmol scale): A 10 mL reaction tube was charged with substrate **1a-1h** (0.1mmol, 1.0 equiv.), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol, 10 mol%), $CH_3CO_3{}^tBu$ (64 μL, 0.2 mmol, 2.0 equiv.) (50% solution in aromatic free mineral spirit), PivOH (20.4 mg, 0.2 mmol, 2.0 equiv.) and **2a-2j** (0.2 mmol, 2.0 equiv.), then 0.4 mL CH_3CN was added to dissolved the above mixture. The tube was sealed and the reaction mixture was then placed to a pre-heated oil bath to stir at 70 °C for 12 h. The reaction mixture was then cooled to room temperature. It was filtered through a pad of celite and washed with methanol. The filtrate was concentrated under reduced pressure and the residue was purified by PTLC (preparative TLC) (CH_2Cl_2:MeOH = 25:1 to 10:1) or reverse-phase column chromatography (C18 Spherical silica) (MeOH: H_2O = 0:1 to

1:1) to give the pure products **3aa-3ia, 3ab-3aj, 3bb-3bj**.

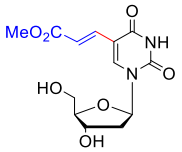
3. Characterization data for compounds 3aa-3ia, 3ab-3aj, 3bb-3bj

Methyl(*E*)-3-(1-((*2R,3R,4S,5R*)-3,4-dihydroxy-5-(hydroxy methyl) tetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)acrylate (3aa) [1]



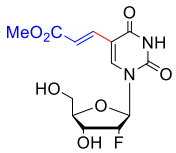
3aa was obtained following the general procedure **A** from **1a**. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (10/1) as the eluent, **3aa** was obtained as a yellow solid (23.6 mg, 72%), gram scale (5 mmol, 1.02 g, 62%). mp 180.7-182.6 °C; $[\alpha]_D^{25}$ -41.58 (c 0.670, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 11.69 (s, 1H), 8.50 (s, 1H), 7.34 (d, *J* = 16.0 Hz, 1H), 6.84 (d, *J* = 15.6 Hz, 1H), 5.76 (d, *J* = 4.0 Hz, 1H), 5.46 (d, *J* = 4.0 Hz, 1H), 5.31 (t, *J* = 5.0 Hz, 1H), 5.09 (d, *J* = 3.6 Hz, 1H), 4.10–4.04 (m, 1H), 4.04–3.97 (m, 1H), 3.90–3.84 (m, 1H), 3.76–3.69 (m, 1H), 3.68 (s, 3H), 3.63–3.56 (m, 1H). ^{13}C NMR (126 MHz, DMSO) δ 167.2, 161.8, 149.5, 144.0, 138.0, 116.2, 108.2, 88.6, 84.6, 73.9, 69.0, 60.2, 51.3. HRMS-ESI m/z calcd for $C_{13}H_{16}N_2NaO_8$ $[M+Na]^+$ 351.0799; found 351.0798.

Methyl (*E*)-3-(1-((*2R,4S,5R*)-4-hydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)acrylate (3ba) [2]



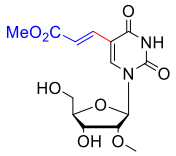
3ba was obtained following the general procedure **A** from **1b**. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (12/1) as the eluent, **3ba** was obtained as a yellow solid (19.6mg, 69%). mp 97.3-100.5 °C; $[\alpha]_D^{25}$ -1.86 (c 0.700, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 11.63 (s, 1H), 8.42 (s, 1H), 7.37 (d, *J* = 15.6 Hz, 1H), 6.85 (d, *J* = 15.6 Hz, 1H), 6.13 (t, *J* = 6.4 Hz, 1H), 5.26 (d, *J* = 4.4 Hz, 1H), 5.17 (t, *J* = 5.2 Hz, 1H), 4.28–4.23 (m, 1H), 3.83–3.77 (m, 1H), 3.68 (s, 3H), 3.67–3.62 (m, 1H), 3.61–3.54 (m, 1H), 2.24–2.10 (m, 2H). ^{13}C NMR (101 MHz, MeOD) δ 169.7, 163.6, 151.1, 144.8, 138.8, 118.4, 110.4, 89.2, 87.1, 71.7, 62.4, 52.0, 41.9. HRMS-ESI m/z calcd for $C_{13}H_{16}N_2NaO_7$ $[M+Na]^+$ 335.0850; found 335.0852.

Methyl(*E*)-3-(1-((*2R,3R,4R,5R*)-3-fluoro-4-hydroxy-5-(hydroxymethyl) tetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)acrylate (3ca)



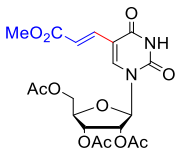
3ca was obtained following the general procedure **A** from **1c** on 0.1 mmol scale. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (15/1) as the eluent, **3ca** was obtained as a faint yellow solid (26.4 mg, 80%). mp 142.7-144.4 °C; $[\alpha]_D^{25}$ -58.49 (c 0.330, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 11.71 (s, 1H), 8.53 (s, 1H), 7.31 (d, *J* = 16.0 Hz, 1H), 6.81 (d, *J* = 16.0 Hz, 1H), 5.89 (d, *J* = 16.8 Hz, 1H), 5.64 (d, *J* = 6.4 Hz, 1H), 5.49 (t, *J* = 4.4 Hz, 1H), 5.06 (dd, *J* = 52.8, 4.0 Hz, 1H), 4.26–4.11 (m, 1H), 3.95–3.81 (m, 2H), 3.70–3.60 (m, 4H). ^{19}F NMR (376 MHz, DMSO) δ -202.05. ^{13}C NMR (101 MHz, DMSO) δ 167.2, 161.9, 149.1, 143.5, 138.0, 116.2, 108.0, 93.8 (d, *J* = 184.3 Hz), 87.6 (d, *J* = 29.9 Hz), 83.1, 66.7 (d, *J* = 16.2 Hz), 58.7, 51.4. HRMS-ESI m/z calcd for $C_{13}H_{15}FN_2NaO_7$ $[M+Na]^+$ 353.0755; found 353.0756.

Methyl(*E*)-3-(1-((*2R,3R,4R,5R*)-4-hydroxy-5-(hydroxymethyl)-3-methoxytetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)acrylate (3da) [3]



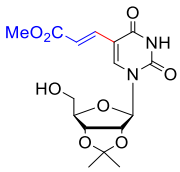
3da was obtained following the general procedure **A** from **1d** on 0.2 mmol scale. After purification by reverse-phase column chromatography (C18 Spherical silica) using MeOH/H_2O as the eluent, **3da** was obtained as a white solid (59.5 mg, 87%). mp 214.7-217.3 °C; $[\alpha]_D^{25}$ -13.524 (c 0.175, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 11.69 (s, 1H), 8.55 (s, 1H), 7.32 (d, *J* = 16.0 Hz, 1H), 6.83 (d, *J* = 16.0 Hz, 1H), 5.83 (d, *J* = 3.6 Hz, 1H), 5.42 (brs, 1H), 5.20 (d, *J* = 5.6 Hz, 1H), 4.20–4.10 (m, 1H), 3.90–3.81 (m, 2H), 3.74 (d, *J* = 12.0 Hz, 1H), 3.67 (s, 3H), 3.61 (d, *J* = 12.0 Hz, 1H), 3.39 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 167.2, 149.4, 143.7, 138.0, 116.2, 108.2, 86.8, 84.8, 83.0, 67.6, 59.7, 57.7, 51.3. HRMS-ESI m/z calcd for $C_{14}H_{18}N_2NaO_8$ $[M+Na]^+$ 365.0955; found 365.0956.

(*2R,3R,4R,5R*)-2-(acetoxymethyl)-5-(5-((*E*)-3-methoxy-3-oxoprop-1-en-1-yl)-2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)tetrahydrofuran-3,4-diyl diacetate (3ea)



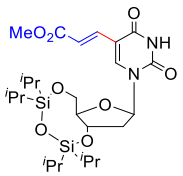
3ea was obtained following the general procedure **A** from **1e** on 0.2 mmol scale. After purification by PTLC (preparative TLC) using petroleum ether/ethyl acetate (2/3) as the eluent, **3ea** was obtained as a beige solid (46.5 mg, 51%). mp 104.2-106.6 °C; $[\alpha]_D^{25}$ -41.80 (c 0.500, MeOH); ^{1}H NMR (400 MHz, MeOD) δ 8.03 (s, 1H), 7.38 (d, *J* = 16.0 Hz, 1H), 6.94 (d, *J* = 16.0 Hz, 1H), 5.94 (d, *J* = 4.4 Hz, 1H), 5.56–5.49 (m, 1H), 5.43 (t, *J* = 5.8 Hz, 1H), 4.45–4.33 (m, 3H), 3.75 (s, 3H), 2.13–2.08 (m, 9H). ^{13}C NMR (101 MHz, MeOD) δ 172.2, 171.4, 171.3, 169.5, 163.3, 150.8, 145.1, 138.4, 119.4, 111.0, 91.0, 81.4, 74.5, 71.4, 64.0, 52.1, 20.8, 20.4, 20.3. HRMS-ESI m/z calcd for $C_{19}H_{22}N_2NaO_{11}$ $[M+Na]^+$ 477.1116; found 477.1113.

Methyl(*E*)-3-(1-((3a*R*,4*R*,6*R*,6a*R*)-6-(hydroxymethyl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)acrylate (3fa)



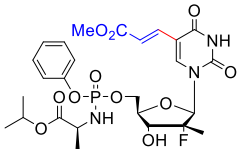
3fa was obtained following the general procedure **A** from **1f** on 0.1 mmol scale. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (22/1) as the eluent, **3fa** was obtained as a white solid (24.2 mg, 66%). mp 179.8-183.4 °C; $[\alpha]_D^{25}$ -40.36 (c 0.280, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 11.74 (s, 1H), 8.35 (s, 1H), 7.34 (d, *J* = 16.0 Hz, 1H), 6.85 (d, *J* = 16.0 Hz, 1H), 5.85 (d, *J* = 2.4 Hz, 1H), 5.24 (t, *J* = 5.2 Hz, 1H), 4.95 (dd, *J* = 6.4, 2.4 Hz, 1H), 4.77 (dd, *J* = 6.4, 3.6 Hz, 1H), 4.15–4.11 (m, 1H), 3.68 (s, 3H), 3.67–3.61 (m, 1H), 3.60–3.53 (m, 1H), 1.49 (s, 3H), 1.29 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 167.1, 161.8, 149.2, 145.0, 137.9, 116.4, 112.9, 108.2, 91.4, 87.1, 84.1, 80.2, 61.1, 51.3, 27.0, 25.2. HRMS-ESI m/z calcd for $C_{16}H_{20}N_2NaO_8$ $[M+Na]^+$ 391.1112; found 391.1114.

Methyl(*E*)-3-(2,4-dioxo-1-((6a*R*,8*R*,9a*S*)-2,2,4,4-tetraisopropyltetrahydro-6H-furo[3,2-f][1,3,5,2,4]trioxadisilocin-8-yl)-1,2,3,4-tetrahydropyrimidin-5-yl)acrylate (3ga)



3ga was obtained following the general procedure **A** from **1g** on 0.1 mmol scale. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (25/1) as the eluent, **3ga** was obtained as a white solid (25.0 mg, 45%). mp 70.1-75.8 °C; $[\alpha]_D^{25}$ -60.36 (c 0.550, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 11.70 (s, 1H), 8.06 (s, 1H), 7.31 (d, *J* = 16.0 Hz, 1H), 6.87 (d, *J* = 15.6 Hz, 1H), 6.00 (dd, *J* = 7.8, 3.4 Hz, 1H), 4.63–4.51 (m, 1H), 4.04 (dd, *J* = 12.2, 5.4 Hz, 1H), 3.95 (dd, *J* = 12.4, 3.2 Hz, 1H), 3.79–3.72 (m, 1H), 3.67 (s, 3H), 2.58–2.52 (m, 1H), 2.38–2.29 (m, 1H), 1.11–0.94 (m, 28H). ^{13}C NMR (101 MHz, DMSO) δ 167.1, 161.7, 149.0, 144.4, 138.0, 116.5, 108.1, 84.6, 84.4, 70.1, 61.8, 51.3, 17.4, 17.2(2C), 17.1, 16.9, 16.9, 16.8, 12.7, 12.5, 12.2, 11.9. HRMS-ESI m/z calcd for $C_{25}H_{42}N_2NaO_8Si_2$ $[M+Na]^+$ 577.2372; found 577.2375.

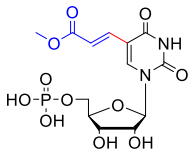
Methyl(*E*)-3-(1-((2*R*,3*R*,4*R*)-3-fluoro-4-hydroxy-5-((((*S*)-(((*S*)-1-isopropoxy-1-oxopropan-2-yl)amino)(phenoxy)phosphoryl)oxy)methyl)-3-methyltetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)acrylate (3ha)



3ha was obtained following the general procedure **A** from **1h** on 0.1 mmol scale. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (15/1) as the eluent, **3ha** was obtained as a faint yellow solid (30.7 mg, 50%). mp 95.0-98.4 °C; $[\alpha]_D^{25}$ +8.79 (c 0.633, MeOH); ^{1}H NMR (400 MHz, MeOD) δ 7.95 (s, 1H), 7.44–7.31 (m, 3H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.19 (t, *J* = 7.0 Hz, 1H), 6.98 (d, *J* = 16.0 Hz, 1H), 6.17 (d, *J* = 11.6 Hz, 1H), 4.96–4.89 (m, 2H), 4.59–4.40 (m, 2H), 4.18–4.09 (m, 1H), 4.00–3.94 (m, 1H), 3.66 (s, 3H), 1.42–1.31 (m, 6H), 1.19 (dd, *J* = 6.0, 2.0 Hz, 6H). ^{19}F NMR (376 MHz, MeOD) δ -161.9. ^{31}P NMR (162 MHz, MeOD) δ 4.0. ^{13}C NMR (101 MHz, MeOD) δ 174.4, 174.3, 169.6, 152.0, 152.0, 139.1, 130.8, 130.4, 126.3, 121.6, 121.5, 119.4, 116.2, 111.2, 102.4, 70.2, 52.0, 51.8, 25.3, 21.9, 21.9, 20.5 (d, *J* = 6.1 Hz), 17.0 (d, *J* = 25.7 Hz). HRMS-ESI m/z calcd for $C_{26}H_{33}FN_3NaO_{11}P$ $[M+Na]^+$ 636.1729; found 636.1725.

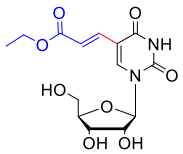
((2*R*,3*S*,4*R*,5*R*)-3,4-dihydroxy-5-(5-((*E*)-3-methoxy-3-oxoprop-1-en-1-yl)-2,4-

dioxo-3,4-dihydropyrimidin-1(2H)-yl)tetrahydrofuran-2-yl)methyl phosphate (3ia)



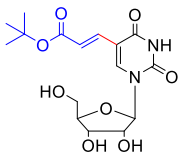
3ia was obtained following the general procedure **A** from **1i** on 0.2 mmol scale with mixed solvent of CH_3CN/H_2O (10/1, v/v). After purification by reverse-phase column chromatography (C18 Spherical silica) using $MeOH/H_2O$ as the eluent, **3ia** was obtained as a white solid (9.8 mg, 24%). mp 196.0-200.1 °C; $[\alpha]_D^{25}$ -51.652 (c 0.575, H_2O); ^1H NMR (400 MHz, D_2O) δ 8.22 (s, 1H), 7.48 (d, *J* = 15.6 Hz, 1H), 6.91 (d, *J* = 16.0 Hz, 1H), 5.98 (d, *J* = 4.8 Hz, 1H), 4.40 (t, *J* = 4.8 Hz, 1H), 4.33 (t, *J* = 4.6 Hz, 1H), 4.28 (s, 1H), 4.20–4.04 (m, 2H), 3.78 (s, 3H). ^{31}P NMR (162 MHz, D_2O) δ 0.7. ^{13}C NMR (101 MHz, D_2O) δ 170.1, 163.4, 150.6, 143.6, 137.8, 117.9, 109.9, 89.1, 83.3, 74.1, 69.5, 63.9, 52.1. HRMS-ESI m/z calcd for $C_{13}H_{17}N_2NaO_{11}P$ $[M+Na]^+$ 431.0462; found 431.0463.

Ethyl (*E*)-3-(1-((*2R,3R,4S,5R*)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)acrylate (3ab) [4]



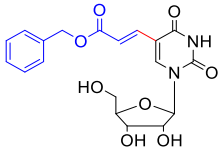
3ab was obtained following the general procedure **A** from **1a**. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (10/1) as the eluent, **3ab** was obtained as a white solid (24.0 mg, 70%). mp 198.2-200.0 °C; $[\alpha]_D^{25}$ -66.53 (c 0.473, MeOH); ^1H NMR (400 MHz, MeOD) δ 8.57 (s, 1H), 7.39 (d, *J* = 15.6 Hz, 1H), 6.88 (d, *J* = 15.6 Hz, 1H), 5.91 (d, *J* = 2.8 Hz, 1H), 4.23–4.16 (m, 4H), 4.08–4.02 (m, 1H), 3.93 (dd, *J* = 12.4, 2.4 Hz, 1H), 3.79 (dd, *J* = 12.4, 2.4 Hz, 1H), 1.29 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, MeOD) δ 169.2, 163.7, 151.3, 144.7, 138.4, 119.0, 110.4, 91.2, 86.2, 76.2, 70.6, 61.6, 61.5, 14.6. HRMS-ESI m/z calcd for $C_{14}H_{18}N_2NaO_8$ $[M+Na]^+$ 365.0955; found 365.0956.

Tert-butyl(*E*)-3-(1-((*2R,3R,4S,5R*)-3,4-dihydroxy-5-(hydroxymethyl) tetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)acrylate (3ac) [5]



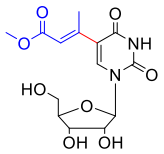
3ac was obtained following the general procedure **A** from **1a**. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (10/1) as the eluent, **3ac** was obtained as a white solid (27.4 mg, 74%). mp 165.3-167.3 °C; $[\alpha]_D^{25}$ -28.39 (c 0.830, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 11.65 (s, 1H), 8.46 (s, 1H), 7.21 (d, *J* = 15.6 Hz, 1H), 6.74 (d, *J* = 16.0 Hz, 1H), 5.76 (d, *J* = 4.4 Hz, 1H), 5.46 (d, *J* = 5.2 Hz, 1H), 5.31 (t, *J* = 5.0 Hz, 1H), 5.10 (d, *J* = 5.6 Hz, 1H), 4.08 (dd, *J* = 9.2, 4.8 Hz, 1H), 4.01 (dd, *J* = 10.2, 5.0 Hz, 1H), 3.89–3.84 (m, 1H), 3.76–3.69 (m, 1H), 3.63–3.55 (m, 1H), 1.44 (s, 9H). ^{13}C NMR (101 MHz, DMSO) δ 166.1, 161.7, 149.5, 143.6, 136.8, 118.6, 108.3, 88.6, 84.7, 79.6, 73.8, 69.0, 60.2, 27.9(3C). HRMS-ESI m/z calcd for $C_{16}H_{22}N_2NaO_8$ $[M+Na]^+$ 393.1268; found 393.1270.

Benzyl(*E*)-3-(1-((*2R,3R,4S,5R*)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)acrylate (3ad) [5]



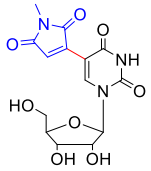
3ad was obtained following the general procedure **A** from **1a**. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (10/1) as the eluent, **3ad** was obtained as a white solid (27.0 mg, 67%). mp 179.6-183.7 °C; $[\alpha]_D^{25}$ -39.29 (c 0.330, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 11.69 (s, 1H), 8.51 (s, 1H), 7.42–7.30 (m, 6H), 6.89 (d, *J* = 16.0 Hz, 1H), 5.76 (d, *J* = 4.4 Hz, 1H), 5.45 (d, *J* = 5.2 Hz, 1H), 5.30 (t, *J* = 5.2 Hz, 1H), 5.18 (s, 2H), 5.07 (d, *J* = 5.6 Hz, 1H), 4.08 (dd, *J* = 9.6, 4.8 Hz, 1H), 4.01 (dd, *J* = 10.4, 5.2 Hz, 1H), 3.89–3.84 (m, 1H), 3.77–3.68 (m, 1H), 3.59 (ddd, *J* = 12.2, 4.8, 3.2 Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 166.5, 161.7, 149.4, 144.1, 138.3, 136.3, 128.4, 128.0, 127.9, 116.2, 108.1, 88.6, 84.6, 73.8, 68.9, 65.3, 60.1. HRMS-ESI m/z calcd for $C_{19}H_{20}N_2NaO_8$ $[M+Na]^+$ 427.1112; found 427.1118.

Methyl(*E*)-3-(1-((*2R,3R,4S,5R*)-3,4-dihydroxy-5-(hydroxy methyl)tetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)but-2-enoate (3ae)



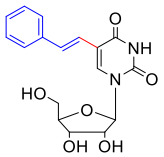
3ae was obtained following the general procedure **A** from **1a**. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (10/1) as the eluent, **3ae** was obtained as a white solid (18.1 mg, 53%). mp 163.9-168.6 °C; $[\alpha]_D^{25}$ -27.14 (c 0.280, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 11.54 (s, 1H), 8.33 (s, 1H), 6.77 (s, 1H), 5.80 (d, *J* = 4.0 Hz, 1H), 5.46 (s, 1H), 5.30 (s, 1H), 5.13 (s, 1H), 4.14–4.06 (m, 1H), 4.02 (t, *J* = 4.4 Hz, 1H), 3.92–3.86 (m, 1H), 3.73–3.55 (m, 5H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 166.9, 161.7, 149.6, 147.6, 140.6, 116.7, 113.2, 88.7, 84.7, 74.3, 69.5, 60.1, 50.9, 16.5. HRMS-ESI m/z calcd for $C_{14}H_{18}N_2NaO_8$ $[M+Na]^+$ 365.0955; found 365.0961.

1-((*2R,3R,4S,5R*)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-(1-methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)pyrimidine-2,4(1H,3H)-dione (3af)[6]



3af was obtained following the general procedure **A** from **1a** under O_2 at 90℃. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (10/1) as the eluent, **3af** was obtained as a yellow solid (15.5 mg, 44%). mp 273.9-276.5 °C; $[\alpha]_D^{25}$ -3.89 (c 0.300, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 11.89 (s, 1H), 8.92 (s, 1H), 7.13 (s, 1H), 5.86 (d, *J* = 4.4 Hz, 1H), 5.50 (d, *J* = 5.2 Hz, 1H), 5.21 (d, *J* = 5.2 Hz, 1H), 4.92 (t, *J* = 5.2 Hz, 1H), 4.07 (dd, *J* = 9.4, 4.6 Hz, 1H), 3.94–3.90 (m, 1H), 3.69–3.59 (m, 2H), 2.90 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 171.0, 170.9, 161.4, 149.2, 143.1, 135.7, 122.7, 103.6, 88.8, 85.2, 74.1, 70.3, 61.7, 23.6. HRMS-ESI m/z calcd for $C_{14}H_{15}N_3NaO_8$ $[M+Na]^+$ 376.0751; found 376.0748.

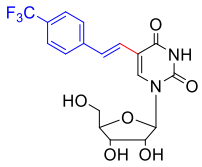
1-((*2R,3R,4S,5R*)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-((*E*)-styryl) pyrimidine-2,4(1H,3H)-dione (3ag) [7]



3ag was obtained following the general procedure **A** from **1a** under O_2 at 90℃. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (10/1) as the eluent, **3ag**

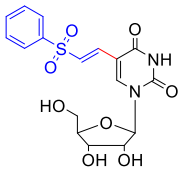
was obtained as a yellow solid (20.8 mg, 60%). mp 133.7-137.9 °C; $[\alpha]_D^{25}$ -50.11 (c 0.300, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 11.51 (s, 1H), 8.32 (s, 1H), 7.46 (d, *J* = 7.6 Hz, 2H), 7.40–7.328 (m, 3H), 7.23 (t, *J* = 7.4 Hz, 1H), 6.88 (d, *J* = 16.4 Hz, 1H), 5.81 (d, *J* = 4.4 Hz, 1H), 5.46 (d, *J* = 4.4 Hz, 1H), 5.34 (t, *J* = 4.4 Hz, 1H), 5.12 (d, *J* = 4.0 Hz, 1H), 4.14–4.07 (m, 1H), 4.07–4.01 (m, 1H), 3.91–3.87 (m, 1H), 3.78–3.73 (m, 1H), 3.65–3.60 (m, 1H). ^{13}C NMR (101 MHz, DMSO) δ 162.3, 149.8, 138.1, 137.5, 128.8(2C), 127.8, 127.5, 126.1(2C), 120.9, 110.8, 88.4, 84.7, 74.0, 69.5, 60.5. HRMS-ESI m/z calcd for $C_{17}H_{18}N_2NaO_6$ $[M+Na]^+$ 369.1057; found 369.1061.

1-((*2R,3R,4S,5R*)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-((*E*)-4-(trifluoromethyl)styryl) pyrimidine-2,4(1H,3H)-dione (3ah) [8]



3ah was obtained following the general procedure **A** from **1a** under O_2 at 90℃.. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (10/1) as the eluent, **3ah** was obtained as a beige solid (12.4 mg, 30%). mp 202.5-207.3 °C; $[\alpha]_D^{25}$ -52.27 (c 0.383, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 11.59 (s, 1H), 8.40 (s, 1H), 7.74–7.64 (m, 4H), 7.47 (d, *J* = 16.4 Hz, 1H), 7.04 (d, *J* = 16.4 Hz, 1H), 5.81 (d, *J* = 4.4 Hz, 1H), 5.48 (d, *J* = 5.2 Hz, 1H), 5.36 (t, *J* = 4.6 Hz, 1H), 5.12 (d, *J* = 5.2 Hz, 1H), 4.14–4.01 (m, 2H), 3.91–3.88 (m, 1H), 3.80–3.72 (m, 1H), 3.67–3.58 (m, 1H). ^{19}F NMR (376 MHz, DMSO) δ -60.8. ^{13}C NMR (101 MHz, DMSO) δ 162.1, 149.7, 141.6, 139.3, 127.4, 127.0, 126.5, 125.8, 125.6 (q, $J_{C\text{-}F}$ = 3.8 Hz), 124.4 (m, $J_{C\text{-}F}$ = 270.0 Hz), 124.1, 110.2, 88.4, 84.6, 73.9, 69.3, 60.3. HRMS-ESI m/z calcd for $C_{18}H_{17}F_3N_2NaO_6$ $[M+Na]^+$ 437.0931; found 437.0934.

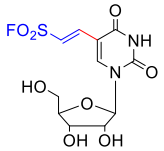
1-((*2R,3R,4S,5R*)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-((*E*)-2-(phenylsulfonyl)vinyl)pyrimidine-2,4(1H,3H)-dione (3ai)



3ai was obtained following the general procedure **A** from **1a**. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (10/1) as the eluent, **3ai** was obtained as a white solid (20.5 mg, 50%). mp 234.0-235.8 °C; $[\alpha]_D^{25}$ -52.19 (c 0.350, MeOH); ^{1}H

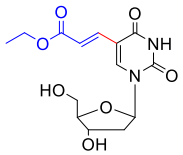
NMR (400 MHz, MeOD) δ 8.64 (s, 1H), 7.89 (d, *J* = 7.2 Hz, 2H), 7.67 (t, *J* = 7.4 Hz, 1H), 7.63-7.56 (m, 2H), 7.52 (d, *J* = 15.2 Hz, 1H), 7.35 (d, *J* = 14.8 Hz, 1H), 5.89 (d, *J* = 2.8 Hz, 1H), 4.22–4.17 (m, 1H), 4.07-4.02 (m, 1H), 3.95 (dd, *J* = 12.4, 2.4 Hz, 1H), 3.80 (dd, *J* = 12.4, 2.4 Hz, 1H). ^{13}C NMR (126 MHz, DMSO) δ 161.7, 149.7, 145.9, 141.0, 135.9, 133.5, 129.7, 127.0, 125.5, 106.5, 88.8, 84.6, 73.8, 68.8, 60.1. HRMS-ESI m/z calcd for $C_{17}H_{18}N_2NaO_8S$ $[M+Na]^+$ 433.0676; found 433.0682.

(*E*)-2-(1-((*2R,3R,4S,5R*)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)ethene-1-sulfonyl fluoride (3aj)



3aj was obtained following the general procedure **A** from **1a**. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (10/1) as the eluent, **3aj** was obtained as a yellow solid (9.2 mg, 26%). mp 162.5-166.3 °C; $[\alpha]_D^{25}$ -17.81 (c 0.640, MeOH); ^{1}H NMR (400 MHz, MeOD) δ 8.76 (s, 1H), 7.61 (dd, *J* = 15.0, 2.2 Hz, 1H), 7.51 (d, *J* = 14.8 Hz, 1H), 5.88 (d, *J* = 2.4 Hz, 1H), 4.22–4.17 (m, 2H), 4.07–4.03 (m, 1H), 3.95 (dd, *J* = 12.4, 2.4 Hz, 1H), 3.79 (dd, *J* = 12.4, 2.4 Hz, 1H). ^{19}F NMR (377 MHz, MeOD) δ 60.4 (s). ^{13}C NMR (101 MHz, MeOD) δ 163.1, 150.9, 148.9, 143.3, 117.8 (d, *J* = 27.4 Hz), 107.7, 91.6, 86.1, 76.3, 70.2, 61.3. HRMS-ESI m/z calcd for $C_{11}H_{13}FN_2NaO_8S$ $[M+Na]^+$ 375.0269; found 375.0265.

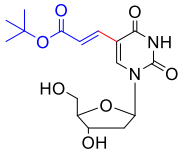
Ethyl (*E*)-3-(1-((*2R,4S,5R*)-4-hydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)acrylate (3bb) [9]



3bb was obtained following the general procedure **A** from **1b**. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (12/1) as the eluent, **3bb** was obtained as a white solid (23.4 mg, 72%). mp 167.5-169.4 °C; $[\alpha]_D^{25}$ +1.00 (c 0.400, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 11.65 (s, 1H), 8.41 (s, 1H), 7.35 (d, *J* = 16.0 Hz, 1H), 6.84 (d, *J* = 16.0 Hz, 1H), 6.13 (t, *J* = 6.4 Hz, 1H), 5.27 (d, *J* = 4.4 Hz, 1H), 5.18 (t, *J* = 5.2 Hz, 1H), 4.29–4.22 (m, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.79 (dd, *J* = 6.8, 3.6 Hz, 1H), 3.69–3.53 (m, 2H), 2.24–2.11 (m, 2H), 1.22 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, MeOD) δ 169.3, 163.7, 151.1, 144.7, 138.6, 118.9, 110.4, 89.2, 87.1, 71.7, 62.4, 61.5,

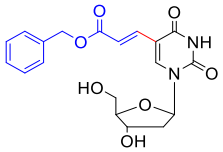
41.9, 14.6. HRMS-ESI m/z calcd for $C_{14}H_{18}N_2NaO_7$ $[M+Na]^+$ 349.1006; found 349.1004.

Tert-butyl(*E*)-3-(1-((*2R,4S,5R*)-4-hydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)acrylate (3bc) [10]



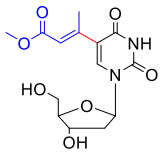
3bc was obtained following the general procedure **A** from **1b**. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (12/1) as the eluent, **3bc** was obtained as a white solid (24.2 mg, 68%). mp 105.8-107.4 °C; $[\alpha]_D^{25}$ +0.40 (c 0.420, MeOH); ^{1}H NMR (400 MHz, MeOD) δ 8.44 (s, 1H), 7.28 (d, *J* = 16.0 Hz, 1H), 6.78 (d, *J* = 16.0 Hz, 1H), 6.26 (t, *J* = 6.4 Hz, 1H), 4.45–4.40 (m, 1H), 3.95 (dd, *J* = 6.4, 3.2 Hz, 1H), 3.86 (dd, *J* = 12.0, 2.4 Hz, 1H), 3.76 (dd, *J* = 12.4, 3.2 Hz, 1H), 2.38–2.23 (m, 2H), 1.49 (s, 9H). ^{13}C NMR (101 MHz, MeOD) δ 168.7, 163.7, 151.1, 144.4, 137.5, 120.8, 110.5, 89.2, 87.0, 81.5, 71.7, 62.4, 41.9, 28.4. HRMS-ESI m/z calcd for $C_{16}H_{22}N_2NaO_7$ $[M+Na]^+$ 377.1319; found 377.1322.

Benzyl(*E*)-3-(1-((*2R,4S,5R*)-4-hydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)acrylate (3bd)



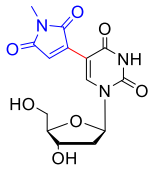
3bd was obtained following the general procedure **A** from **1b**. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (12/1) as the eluent, **3bd** was obtained as a white solid (23.7 mg, 61%). mp 89.6-90.3 °C; $[\alpha]_D^{25}$ +1.11 (c 0.330, MeOH); ^{1}H NMR (400 MHz, MeOD) δ 8.49 (s, 1H), 7.44 (d, *J* = 15.6 Hz, 1H), 7.40–7.29 (m, 4H), 6.94 (d, *J* = 16.0 Hz, 1H), 6.25 (t, *J* = 6.4 Hz, 1H), 5.20 (s, 2H), 4.42 (dt, *J* = 6.1, 4.0 Hz, 1H), 3.95 (q, *J* = 3.3 Hz, 1H), 3.85 (dd, *J* = 12.2, 3.0 Hz, 1H), 3.75 (dd, *J* = 12.2, 3.4 Hz, 1H), 2.38–2.22 (m, 2H). ^{13}C NMR (101 MHz, MeOD) δ 169.0, 163.7, 151.1, 144.9, 139.0, 137.7, 129.5(2C), 129.2(2C), 118.5, 110.4, 89.2, 87.1, 71.7, 67.2, 62.4, 41.9. HRMS-ESI m/z calcd for $C_{19}H_{20}N_2NaO_7$ $[M+Na]^+$ 411.1163; found 411.1171.

Methyl (*E*)-3-(1-((*2R,4S,5R*)-4-hydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)but-2-enoate (3be)



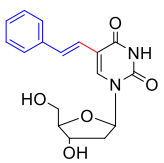
3be was obtained following the general procedure **A** from **1b**. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (12/1) as the eluent, **3be** was obtained as a white solid (13.4 mg, 41%). mp 175.4-176.7 °C; $[\alpha]_D^{25}$ +6.67 (c 0.270, MeOH); ^{1}H NMR (400 MHz, MeOD) δ 8.35 (s, 1H), 6.66 (s, 1H), 6.31 (t, *J* = 6.6 Hz, 1H), 4.46–4.40 (m, 1H), 3.96 (q, *J* = 2.9 Hz, 1H), 3.83 (dd, *J* = 12.0, 2.8 Hz, 1H), 3.75 (dd, *J* = 12.0, 2.8 Hz, 1H), 3.69 (s, 3H), 2.40 (s, 3H), 2.34–2.25 (m, 2H). ^{13}C NMR (126 MHz, MeOD) δ 169.1, 163.7, 151.4, 149.3, 141.4, 118.9, 116.1, 89.2, 87.0, 72.1, 62.5, 51.5, 41.9, 17.4. HRMS-ESI m/z calcd for $C_{14}H_{18}N_2NaO_7$ $[M+Na]^+$ 349.1006; found 349.1009.

1-((*2R,4S,5R*)-4-hydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-(1-methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)pyrimidine-2,4(1H,3H)-dione (3bf) [6]



3bf was obtained following the general procedure **A** from **1b** under O_2 at 90℃. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (12/1) as the eluent, **3bf** was obtained as a yellow solid (12.5 mg, 37%). mp >300 °C; $[\alpha]_D^{25}$ -20.42 (c 0.360, DMSO); ^{1}H NMR (400 MHz, DMSO) δ 11.84 (s, 1H), 8.99 (s, 1H), 7.12 (s, 1H), 6.15 (t, *J* = 6.4 Hz, 1H), 5.37 (d, *J* = 4.0 Hz, 1H), 4.92 (t, *J* = 5.2 Hz, 1H), 4.27-4.21 (m, 1H), 3.91-3.85 (m, 1H), 3.65–3.51 (m, 2H), 2.89 (s, 3H), 2.24-2.21 (m, 1H), 2.17–2.07 (m, 1H). ^{13}C NMR (101 MHz, DMSO) δ 171.1, 171.0, 161.6, 149.0, 143.1, 135.9, 122.2, 103.2, 88.1, 85.7, 70.7, 61.7, 23.6. HRMS-ESI m/z calcd for $C_{14}H_{15}N_3NaO_7$ $[M+Na]^+$ 360.0802; found 360.0804.

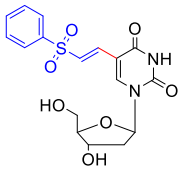
1-((*2R,4S,5R*)-4-hydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-((*E*)-styryl)pyrimidine-2,4(1H,3H)-dione (3bg) [11]



3bg was obtained following the general procedure **A** from **1b** under O_2 at 90℃. After

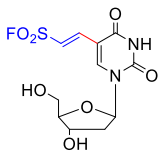
purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (12/1) as the eluent, **3bg** was obtained as a faint yellow solid (17.2 mg, 52%). mp 99.8-101.4 °C; $[\alpha]_D^{25}$ -3.49 (c 0.430, MeOH); ^{1}H NMR (400 MHz, MeOD) δ 8.32 (s, 1H), 7.45 (d, *J* = 8.0 Hz, 2H), 7.41 (d, *J* = 16.4 Hz, 1H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.20 (t, *J* = 7.2 Hz, 1H), 6.89 (d, *J* = 16.4 Hz, 1H), 6.32 (t, *J* = 6.6 Hz, 1H), 4.46 (dd, *J* = 9.2, 4.0 Hz, 1H), 3.96 (dd, *J* = 6.2, 3.0 Hz, 1H), 3.88 (dd, *J* = 12.2, 2.6 Hz, 1H), 3.79 (dd, *J* = 12.0, 3.2 Hz, 1H), 2.38–2.25 (m, 2H). ^{13}C NMR (101 MHz, MeOD) δ 164.5, 151.4, 139.1, 138.8, 130.3, 129.6(2C), 128.5, 127.3(2C), 121.0, 113.3, 89.0, 86.7, 71.9, 62.6, 41.7. HRMS-ESI m/z calcd for $C_{17}H_{18}N_2NaO_5$ $[M+Na]^+$ 353.1108; found 353.1112.

1-((*2R,4S,5R*)-4-hydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-5-((*E*)-2-(phenylsulfonyl)vinyl)pyrimidine-2,4(1H,3H)-dione (3bi)



3bi was obtained following the general procedure **A** from **1b**. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (12/1) as the eluent, **3bi** was obtained as a yellow solid (15.4 mg, 39%). mp >300 °C; $[\alpha]_D^{25}$ +0.71 (c 0.380, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 11.73 (s, 1H), 8.48 (s, 1H), 7.91–7.82 (m, 2H), 7.75–7.68 (m, 1H), 7.68–7.61 (m, 2H), 7.46 (d, *J* = 15.2 Hz, 1H), 7.39 (d, *J* = 14.8 Hz, 1H), 6.10 (t, *J* = 6.4 Hz, 1H), 5.29 (d, *J* = 4.4 Hz, 1H), 5.19 (t, *J* = 5.2 Hz, 1H), 4.29–4.21 (m, 1H), 3.80 (q, *J* = 3.7 Hz, 1H), 3.71–3.52 (m, 2H), 2.21–2.13 (m, 2H). ^{13}C NMR (101 MHz, MeOD) δ 163.4, 150.9, 146.9, 142.6, 136.9, 134.5, 130.5(2C), 128.4(2C), 127.8, 108.6, 89.2, 87.2, 71.5, 62.3, 41.9. HRMS-ESI m/z calcd for $C_{17}H_{18}N_2NaO_7S$ $[M+Na]^+$ 417.0727; found 417.0727.

(*E*)-2-(1-((*2R,4S,5R*)-4-hydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)ethene-1-sulfonyl fluoride (3bj)

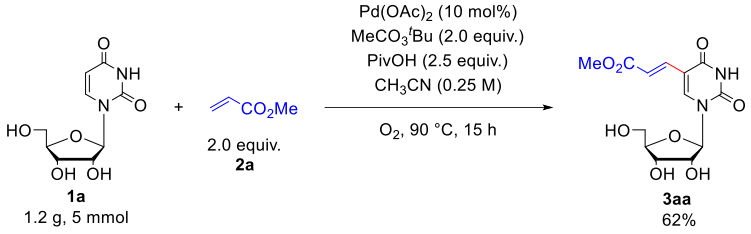


3bj was obtained following the general procedure **A** from **1b**. After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (12/1) as the eluent, **3bj** was obtained as a white solid (8.1 mg, 24%). mp 193.3-194.2 °C; $[\alpha]_D^{25}$ +5.68 (c 0.370, MeOH); ^{1}H

NMR (400 MHz, MeOD) δ 8.66 (s, 1H), 7.62 (dd, J = 14.8, 2.4 Hz, 1H), 7.55 (dd, J = 15.2, 0.8 Hz, 1H), 6.22 (t, J = 6.2 Hz, 1H), 4.41 (dt, J = 6.4, 4.0 Hz, 1H), 3.96 (dd, J = 6.8, 3.2 Hz, 1H), 3.87 (dd, J = 12.0, 2.8 Hz, 1H), 3.76 (dd, J = 12.2, 3.4 Hz, 1H), 2.42-2.34 (m, 1H), 2.30–2.20 (m, 1H). ^{19}F NMR (377 MHz, MeOD) δ 60.4 (s). ^{13}C NMR (101 MHz, MeOD) δ 163.1, 150.7, 149.0, 143.4, 117.7 (d, J = 27.6 Hz), 107.6, 89.3, 87.6, 71.4, 62.2, 42.1. HRMS-ESI m/z calcd for $C_{11}H_{13}FN_2NaO_7S$ $[M+Na]^+$ 359.0320; found 359.0315.

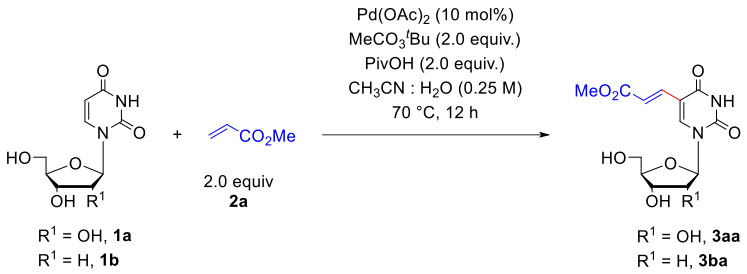
3.1 Applications of the methodology

a) Gram scale preparation of 3aa



General procedure B (gram scale): A 250 mL reaction tube was charged with substrate **1a** (1.2 g, 5 mmol, 1.0 equiv.), $Pd(OAc)_2$ (0.5 mmol, 10 mol%), $CH_3CO_3{}^tBu$ (10 mmol, 2.0 equiv.) (50% solution in aromatic free mineral spirit), PivOH (12.5 mmol, 2.5 equiv.) and **2a** (10 mmol, 2.0 equiv.), then 20 mL CH_3CN were added to dissolved the mixture. The reaction solution was bubbled with O_2 for 30 min. The tube was sealed with a Teflon-lined cap and the reaction mixture was then placed to a pre-heated oil bath to stir at 90 °C for 15 h (*Caution: The tube was carefully capped and covered with safety shield.*). The reaction mixture was then cooled to room temperature. It was filtered through a pad of celite, and then washed with methanol. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel using CH_2Cl_2/MeOH (50/1 to 25/1) as the eluent to give the pure product **3aa**.

b) On-water reaction [a]

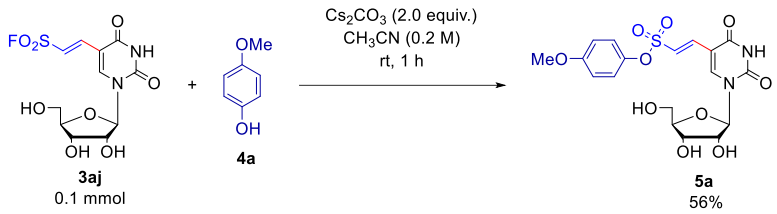


Entry	$CH_3CN:H_2O$	Yield[b] of 3		Recovery[b] of 1	
		3aa	3ba	1a	1b
1	10:1	61%	61%	32%	23%
2	7:1	48%[c]	52%	48%	35%
3	5:1	39%	38%	60%	55%
4	3:1	23%	26%	58%	65%
5	1:1	5%	9%	95%	90%
6	1:3	2%	2%	98%	98%
7	H_2O	2%	2%	98%	94%
8	CH_3CN	79%	73%	13%	8%

[a] Conditions: uridine **1a** or **1b** (0.1 mmol), methyl acrylate **2a** (0.2 mmol), $Pd(OAc)_2$ (0.01 mmol), $MeCO_3{}^tBu$ (0.2 mmol), PivOH (0.2 mmol), CH_3CN : H_2O (v/v, 0.4 mL) under air at 70 ℃ for 12 hours. [b] Yields and recovery were determined by LC-MS. [c] Isolated yield.

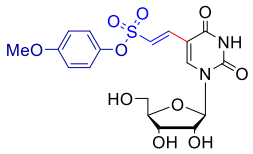
General procedure C (0.1 mmol scale): A 10 mL reaction tube was charged with substrate **1a** (0.1mmol, 1.0 equiv.), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol, 10 mol%), $CH_3CO_3{}^tBu$ (64 µL, 0.2 mmol, 2.0 equiv.) (50% solution in aromatic free mineral spirit), PivOH (20.4 mg, 0.2 mmol, 2.0 equiv.) and **2a** (18µL, 0.2 mmol, 2.0 equiv.), then 0.35 mL CH_3CN and 0.05 mL H_2O were added to dissolve the above mixture. The tube was sealed and the reaction mixture was then placed to a pre-heated oil bath to stir at 70 °C for 12 h. The reaction mixture was then cooled to room temperature. It was filtered through a pad of celite and washed with methanol. The filtrate was concentrated under reduced pressure and the residue was purified by PTLC (preparative TLC) (CH_2Cl_2:MeOH = 10:1) to give the pure product **3aa**.

c) Derivative of 3aj [12, 13]



A 10 mL sample vial was charged with **3aj** (35 mg, 0.10 mmol, 1.0 equiv.), *p*-methoxyphenol (13.6 mg, 0.11 mmol, 1.1 equiv.) and Cs_2CO_3 (65.2 mg, 0.20 mmol, 2.0 equiv.), and then CH_3CN (0.5 mL) was added to dissolve the above mixture. The reaction was stirred at ambient temperature for 1 h. Then it was filtered through a pad of celite and washed with methanol. The filtrate was concentrated under reduced pressure and the residue was purified by PTLC (preparative TLC) (CH_2Cl_2:MeOH = 10:1) to give the pure product **5a** as a white solid (26.8 mg , 56% yield).

4-methoxyphenyl (*E*)-2-(1-((2*R*,3*R*,4*S*,5*R*)-3,4-dihydroxy-5-(hydroxymethyl) tetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl) ethene-1-sulfonate (5a)



After purification by PTLC (preparative TLC) using CH_2Cl_2/MeOH (10/1) as the eluent, **5a** was obtained as a white solid (26.8 mg, 56%). mp 180.5-184.6 °C; $[\alpha]_D^{25}$ -17.36 (c 0.457, MeOH); ^{1}H NMR (400 MHz, DMSO) δ 11.84 (s, 1H), 8.54 (s, 1H), 7.46 (d, *J* = 15.2 Hz, 1H), 7.26 – 7.12 (m, 3H), 6.97 (d, *J* = 8.8 Hz, 2H), 5.73 (d, *J* = 4.0 Hz, 1H), 5.49 (d, *J* = 5.2 Hz, 1H), 5.27 (t, *J* = 5.2 Hz, 1H), 5.11 (d, *J* = 5.6 Hz, 1H), 4.06 (dd, *J* = 9.2, 4.4 Hz, 1H), 3.98 (dd, *J* = 10.4, 5.2 Hz, 1H), 3.89–3.82 (m, 1H), 3.75 (s, 3H), 3.72–3.65 (m, 1H), 3.61–3.53 (m, 1H). ^{13}C NMR (101 MHz, DMSO) δ 161.6, 157.9, 149.3, 146.6, 142.5, 139.5, 123.5, 118.4, 114.9, 106.1, 88.9, 84.6, 73.8, 68.8, 60.1, 55.5. HRMS-ESI m/z calcd for $C_{18}H_{20}N_2NaO_{10}S$ $[M+Na]^+$ 479.0731; found 479.0740.

4. References

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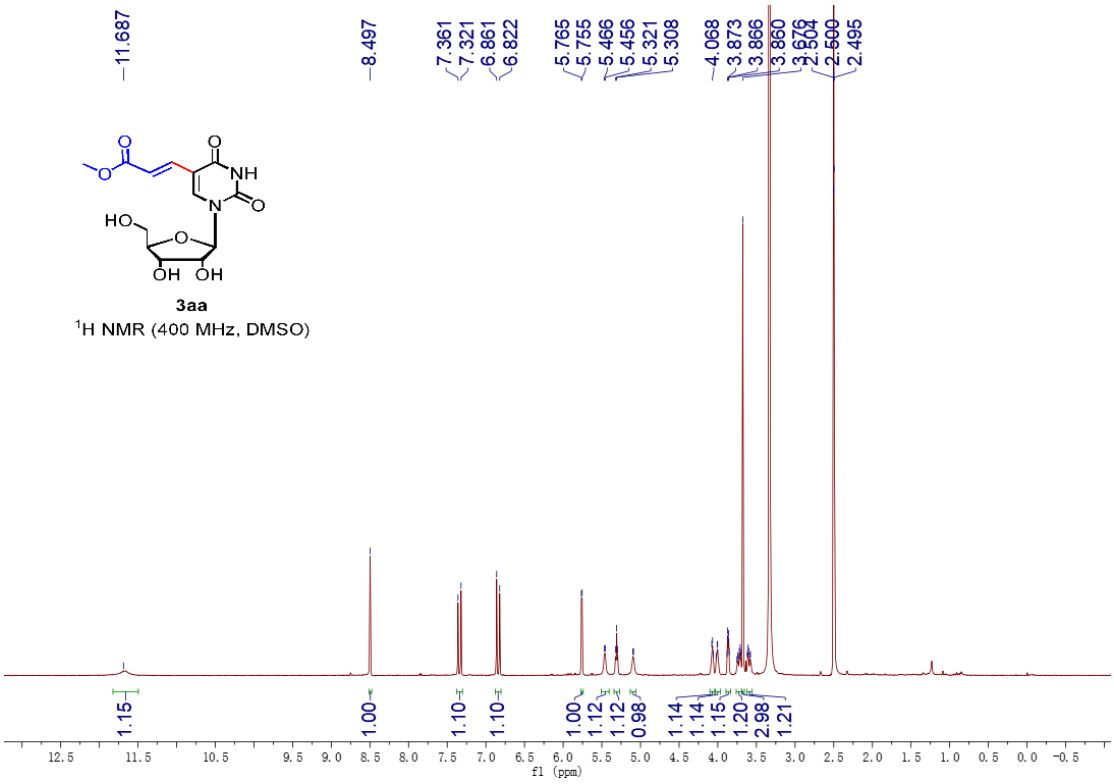
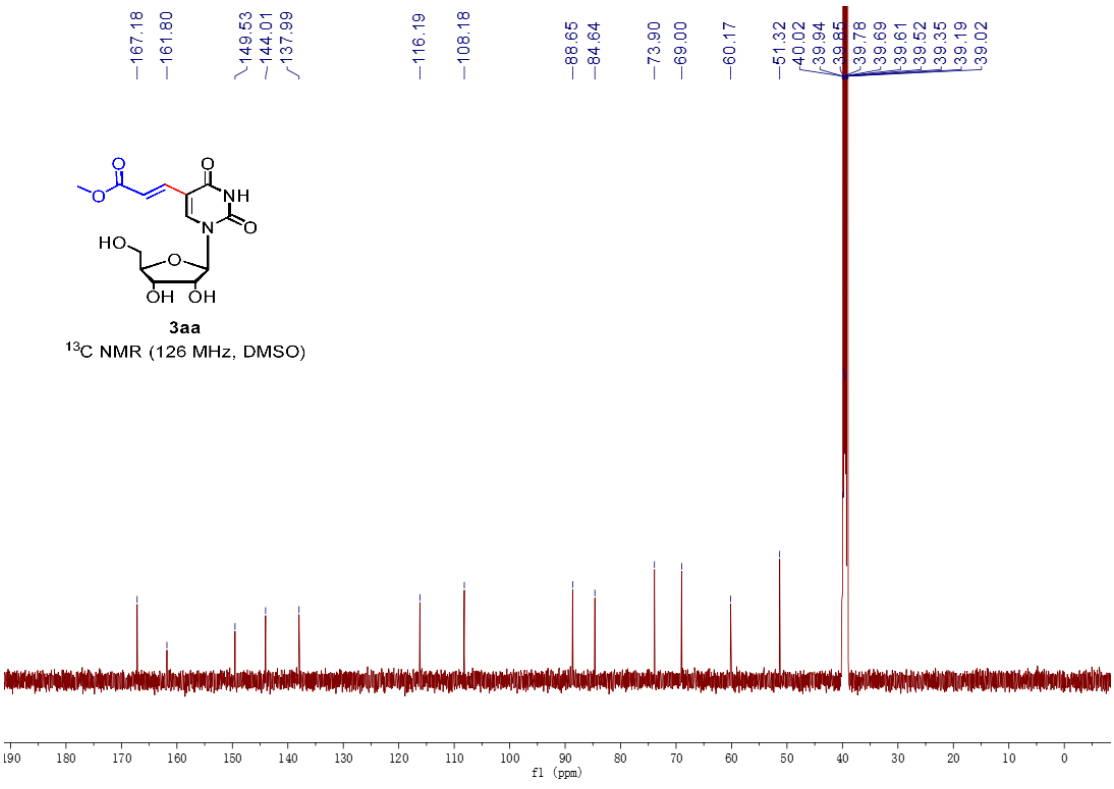
5. NMR Spectra



3aa

^{1}H NMR (400 MHz, DMSO)



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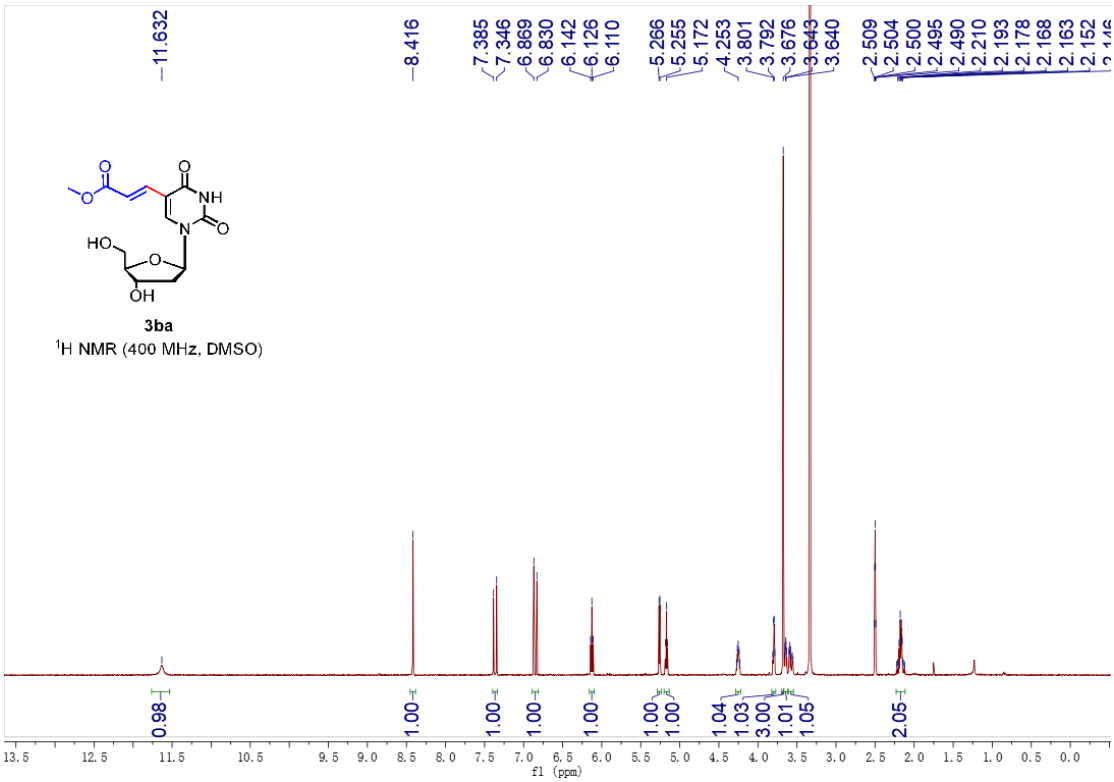
^{13}C NMR (126 MHz, DMSO)



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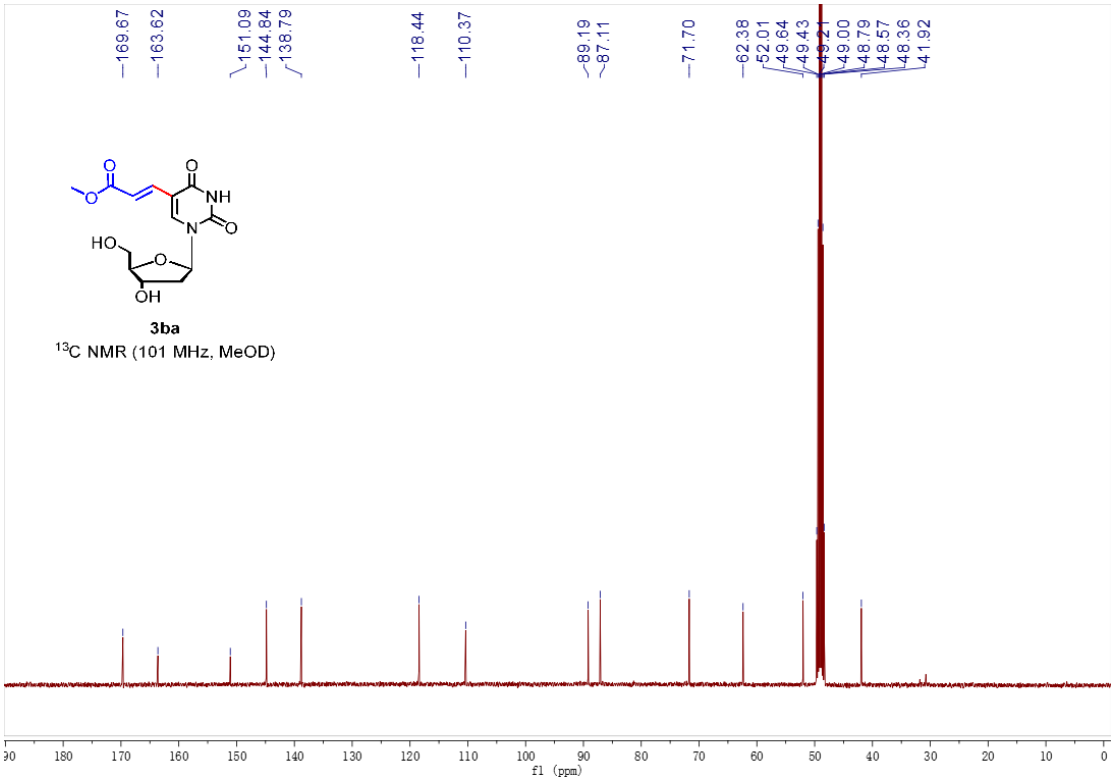
^{1}H NMR (400 MHz, DMSO)



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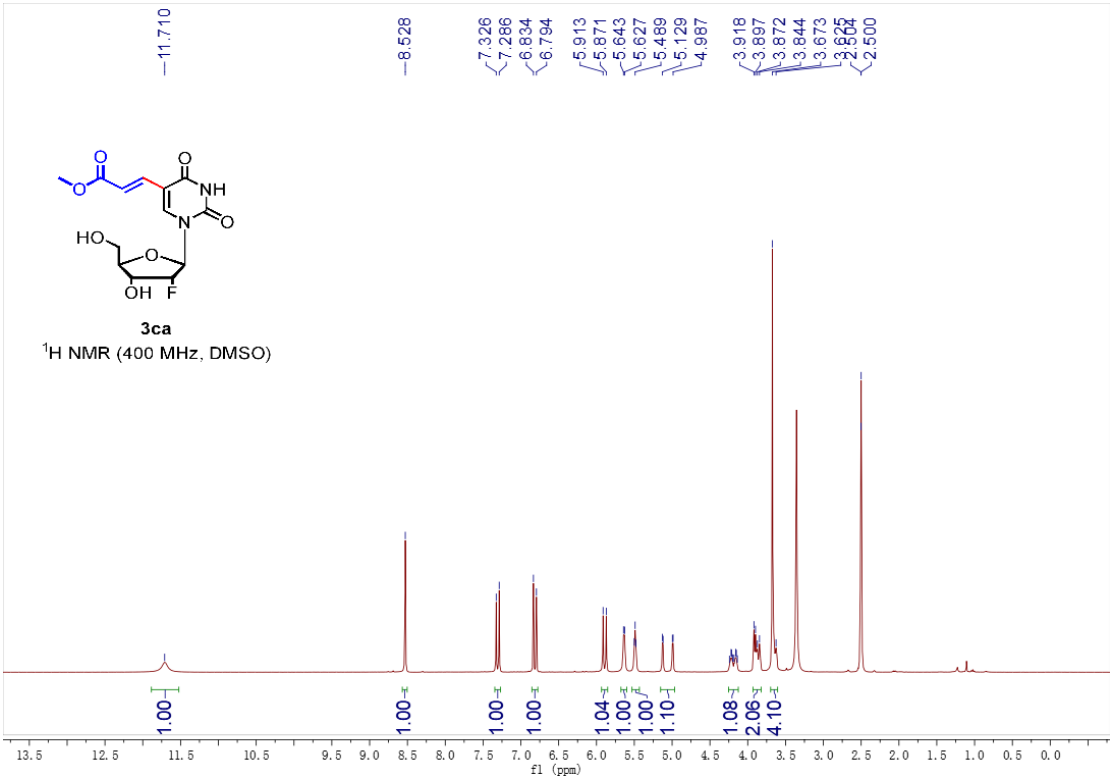
^{13}C NMR (101 MHz, MeOD)



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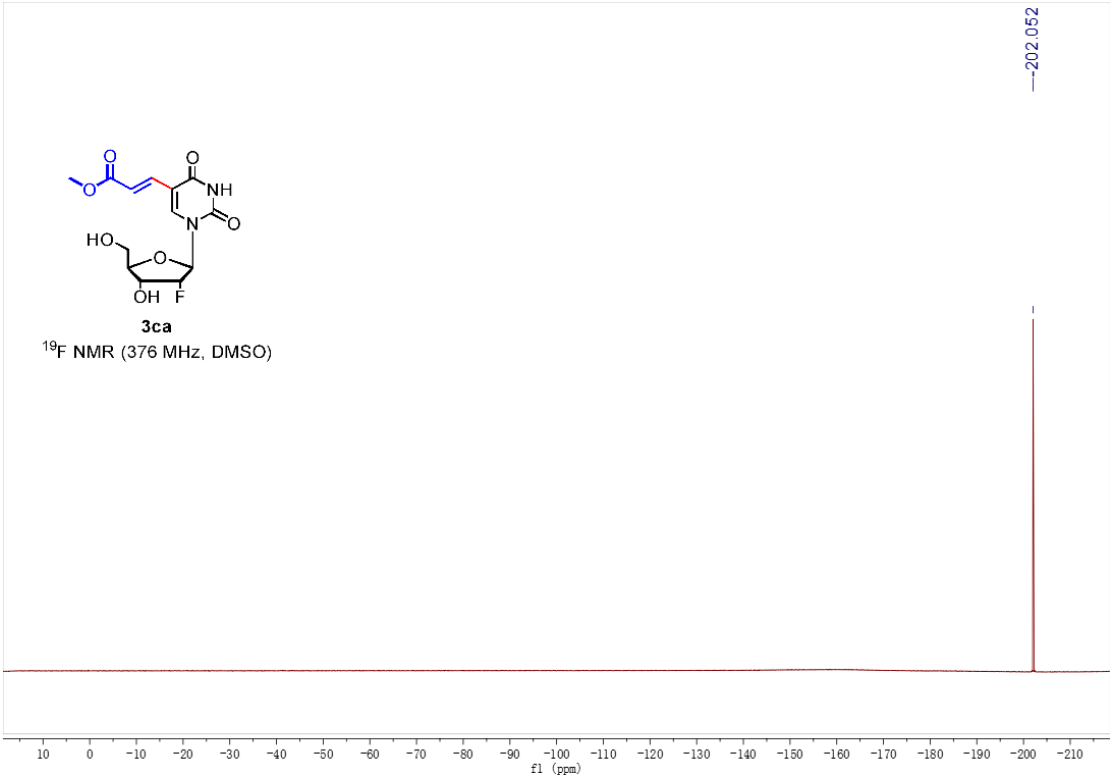
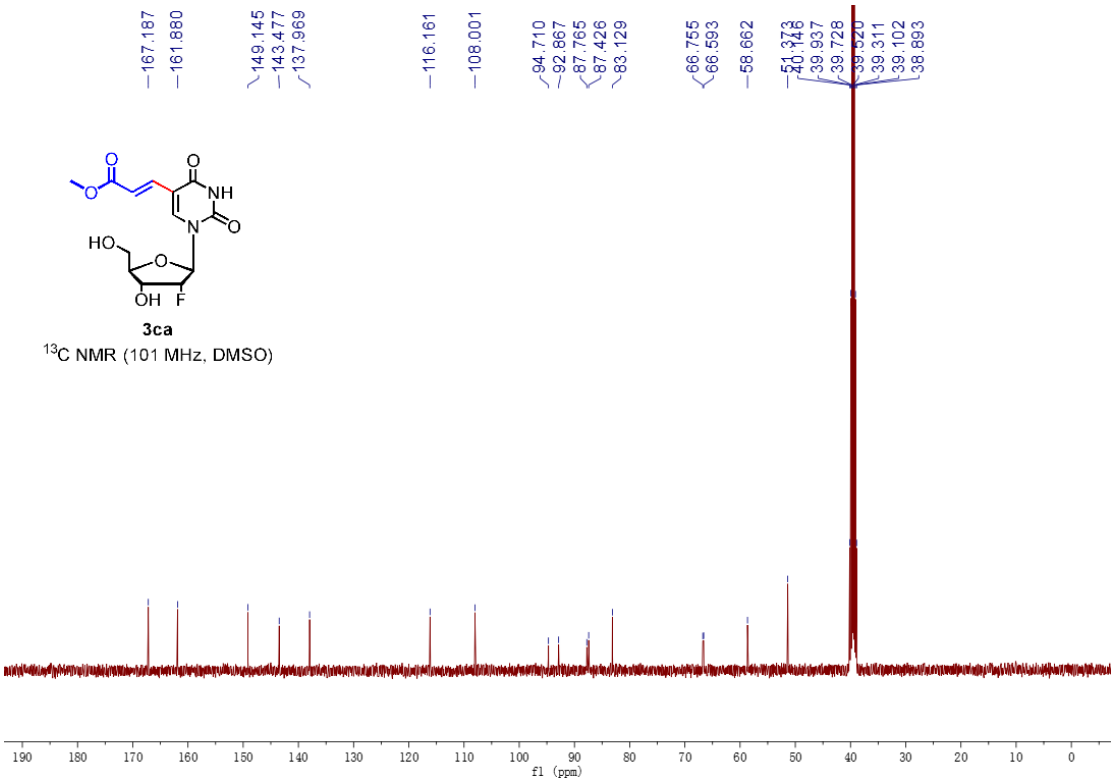


3ca

^{19}F NMR (376 MHz, DMSO)



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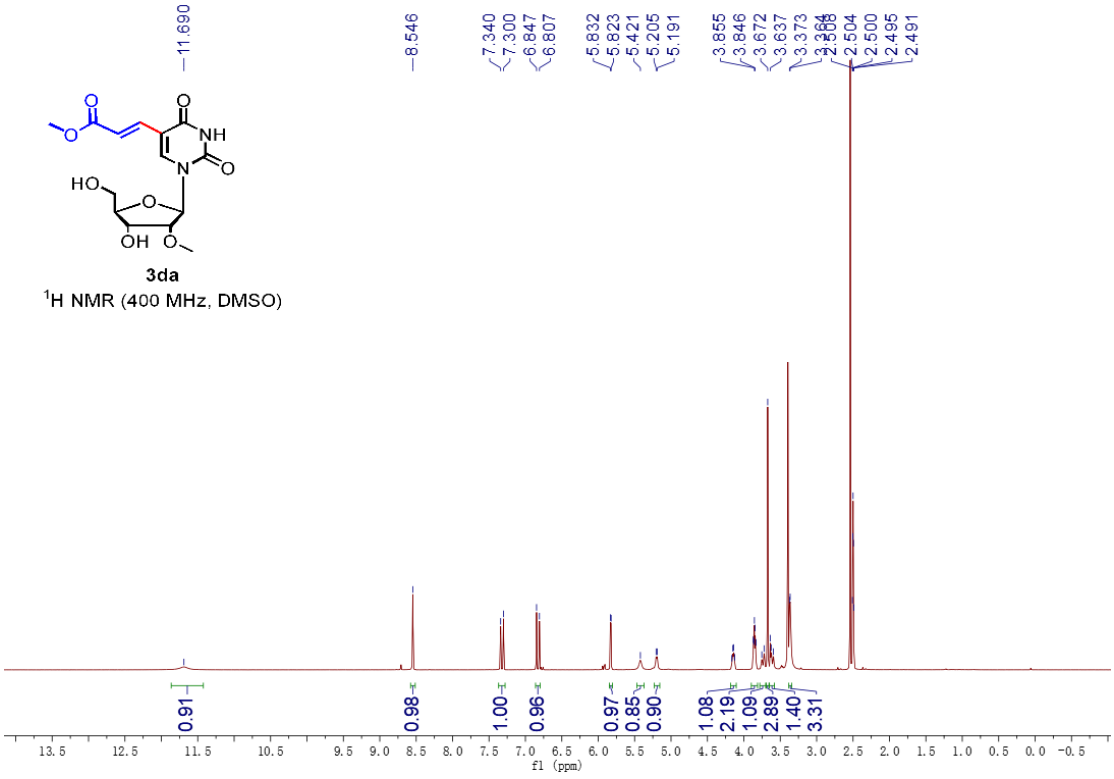
^{13}C NMR (101 MHz, DMSO)



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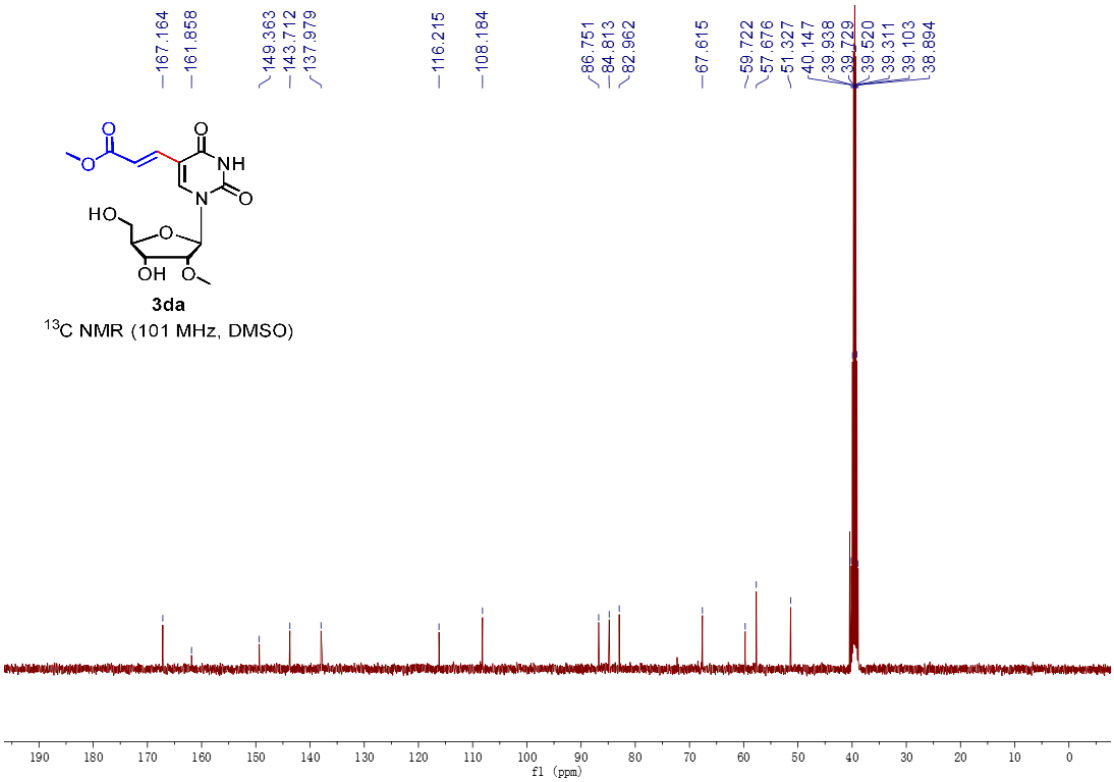
^{1}H NMR (400 MHz, DMSO)



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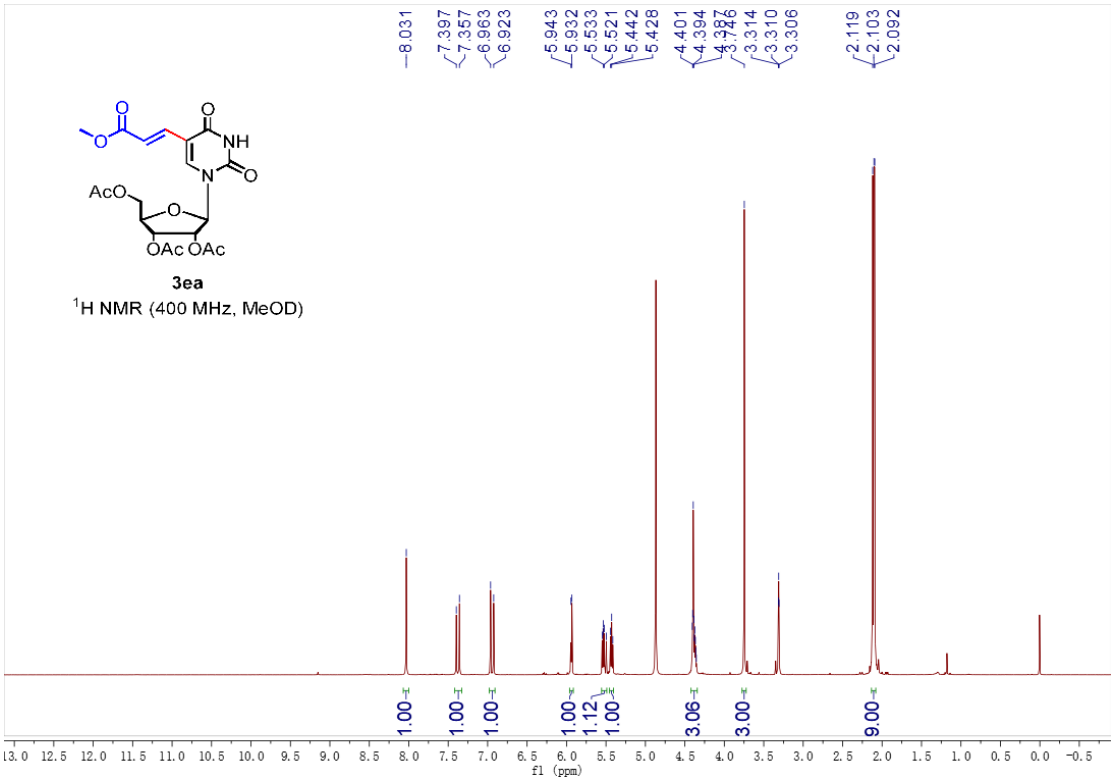

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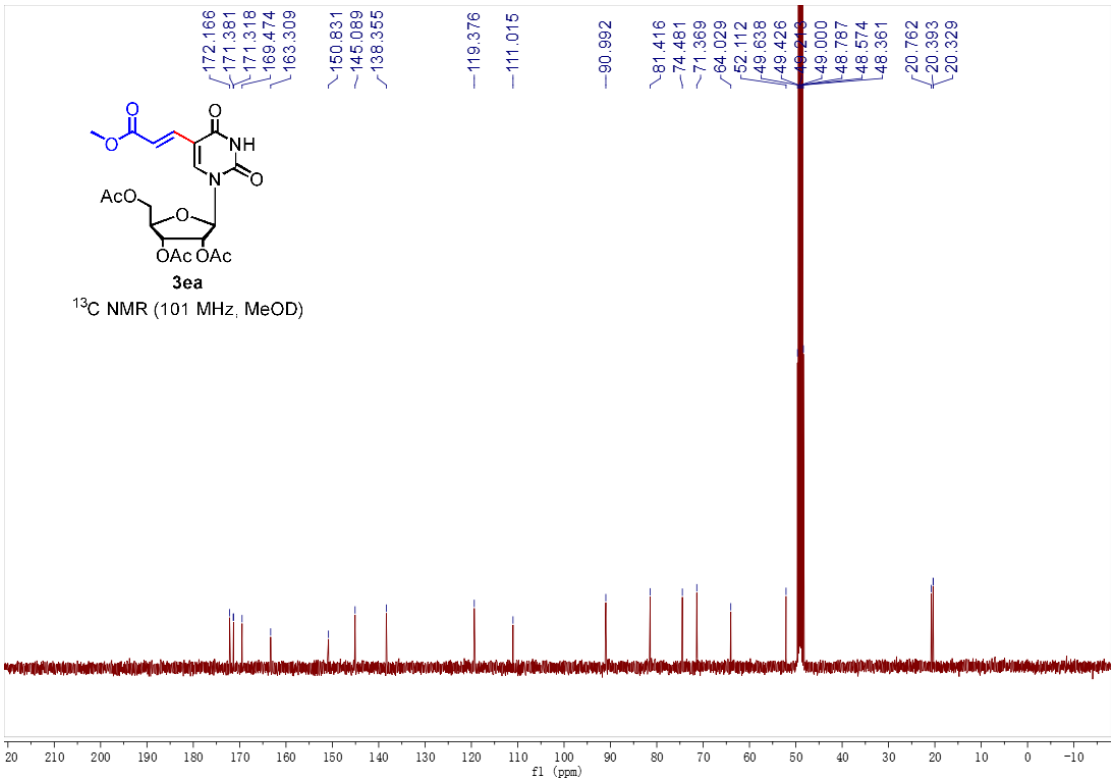
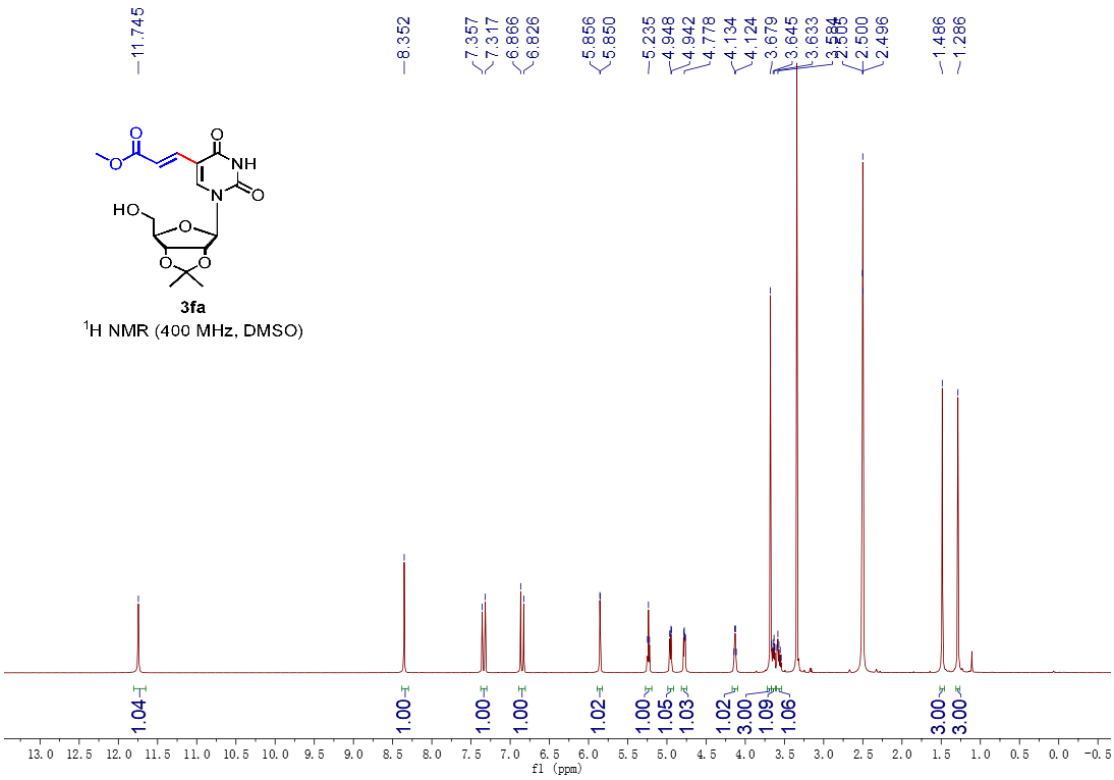
^{1}H NMR (400 MHz, MeOD)



3ea

^{13}C NMR (101 MHz, MeOD)



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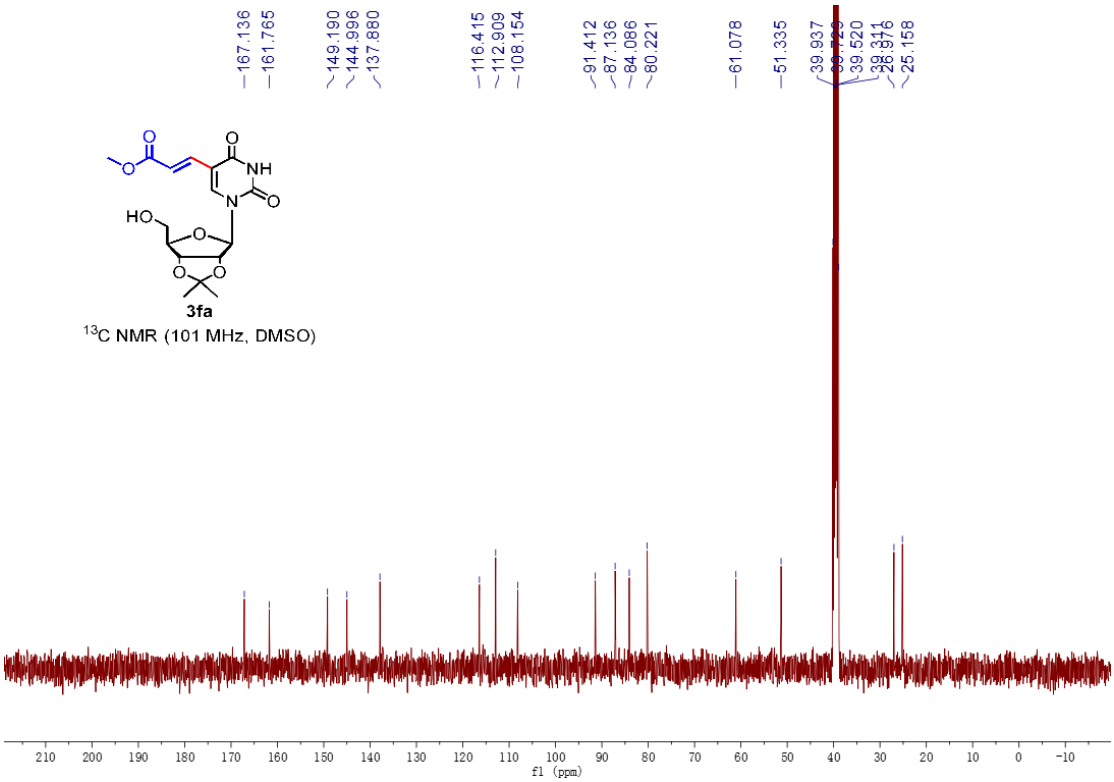
^{1}H NMR (400 MHz, DMSO)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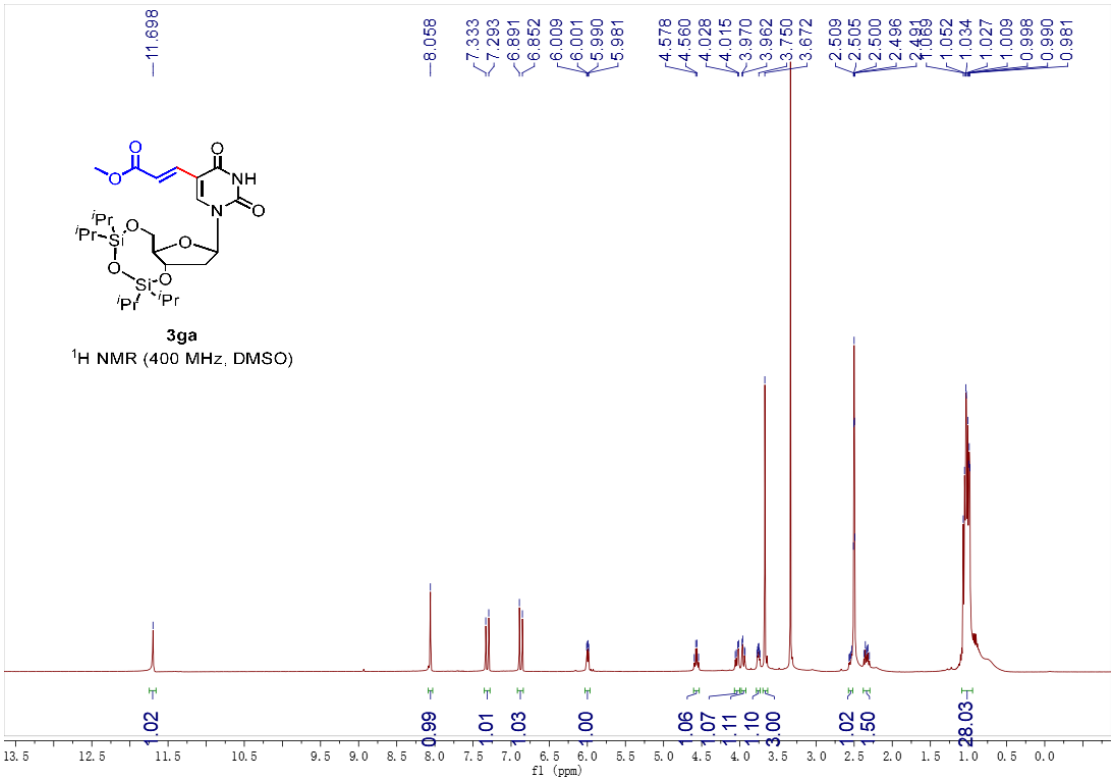
116.415
112.909
108.154
91.412
87.136
84.086
80.221
61.078
51.335
39.937
39.729
39.520
39.311
26.976
25.158
3fa
13C NMR (101 MHz, DMSO)
f1 (ppm)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8.058
7.333
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6.891
6.852
6.009
6.001
5.990
5.981
4.578
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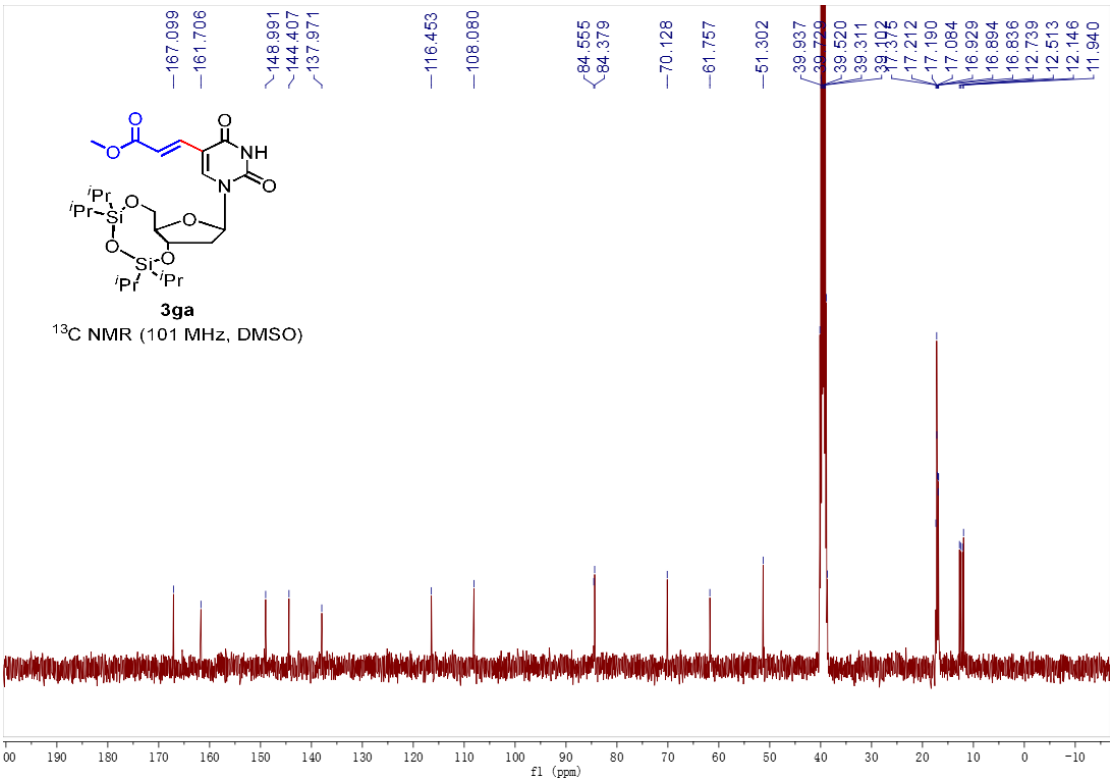
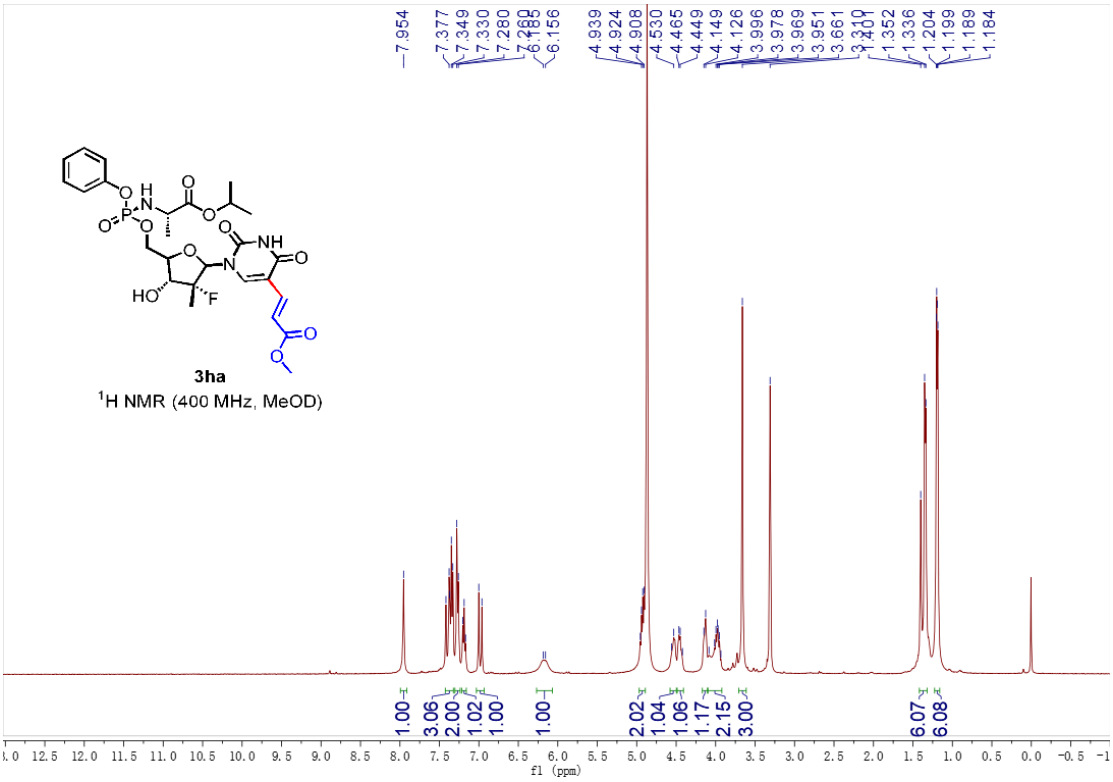
4.028
4.015
3.970
3.962
3.750
3.672
2.509
2.505
2.500
2.496
1.069
1.052
1.034
1.027
1.009
0.998
0.990
0.981
1.02
0.99
1.01
1.03
1.00
1.06
1.07
1.11
1.10
3.00
1.02
1.50
28.03
3ga
1H NMR (400 MHz, DMSO)
f1 (ppm)



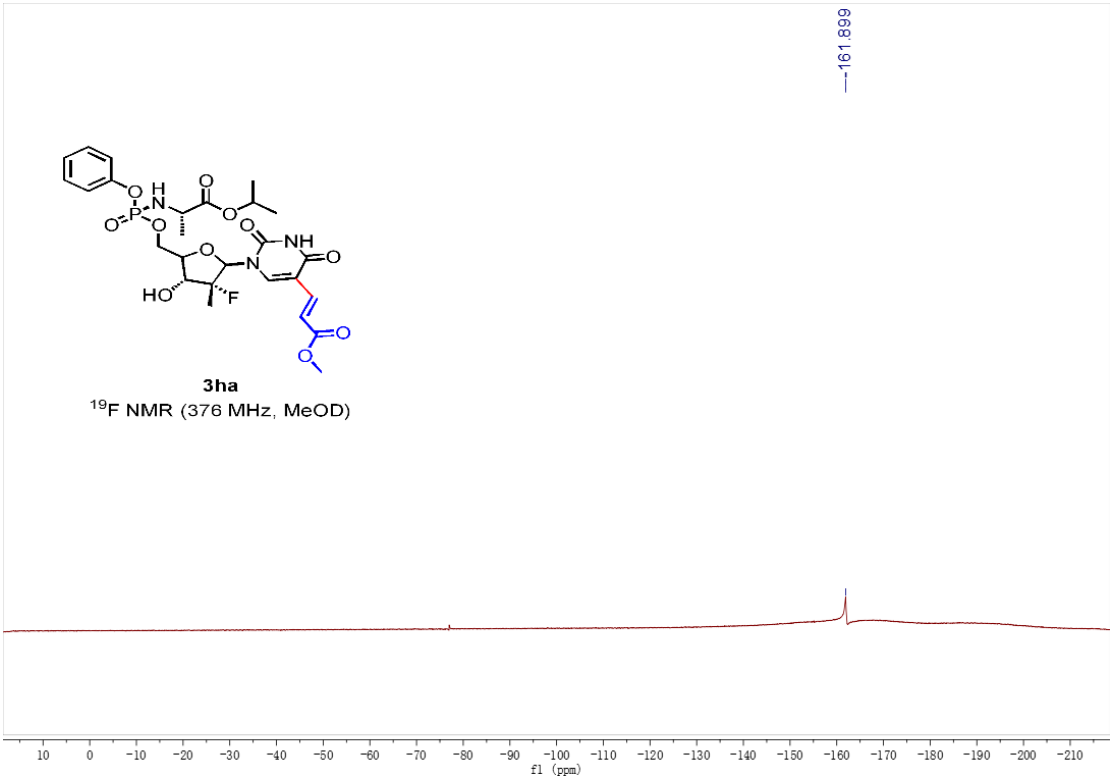
3ga

^{13}C NMR (101 MHz, DMSO)



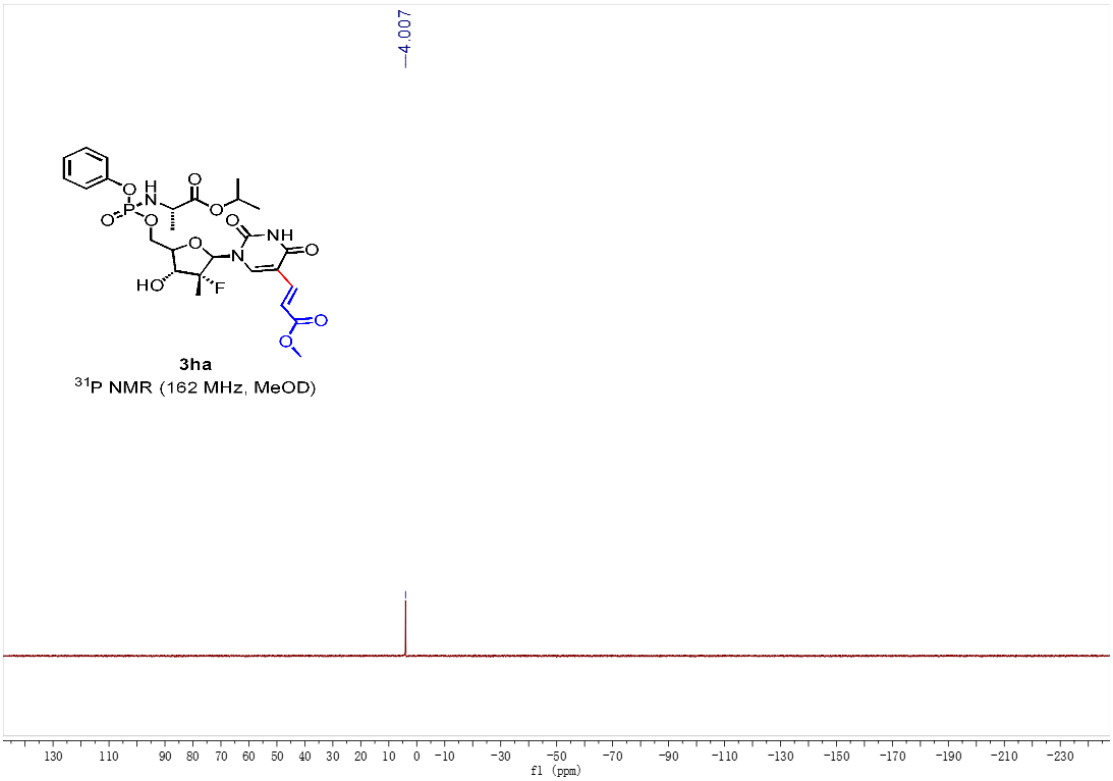
3ha

^{1}H NMR (400 MHz, MeOD)



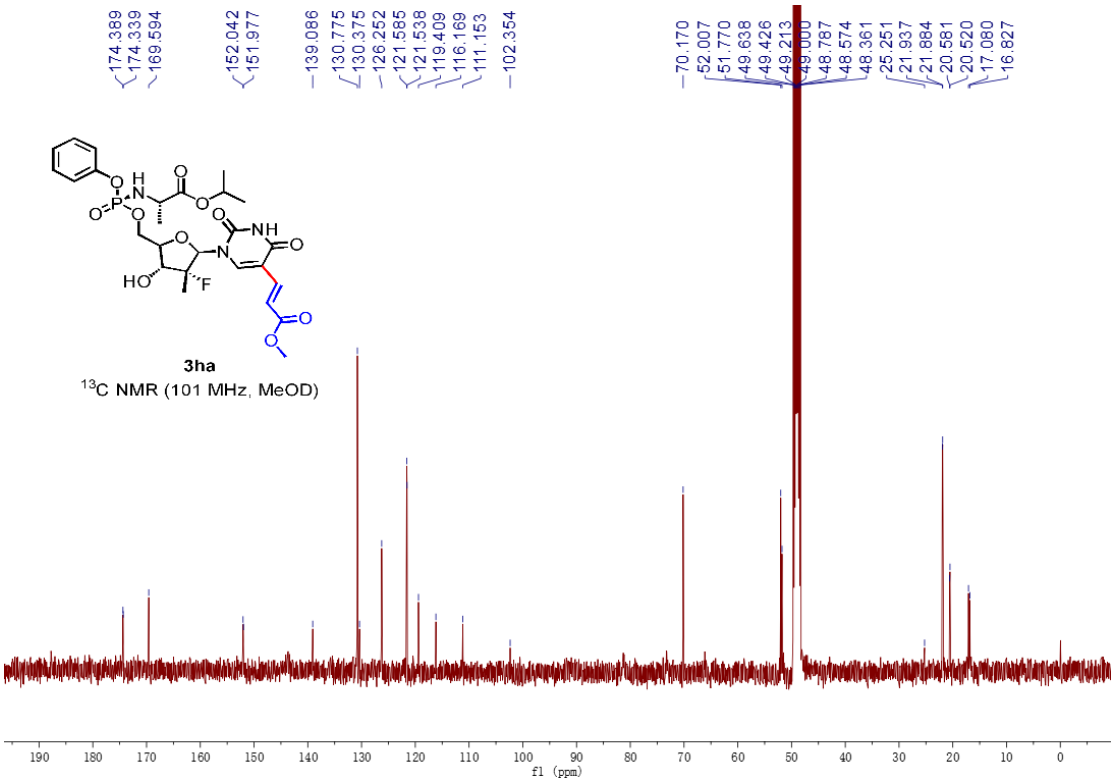
3ha

^{19}F NMR (376 MHz, MeOD)



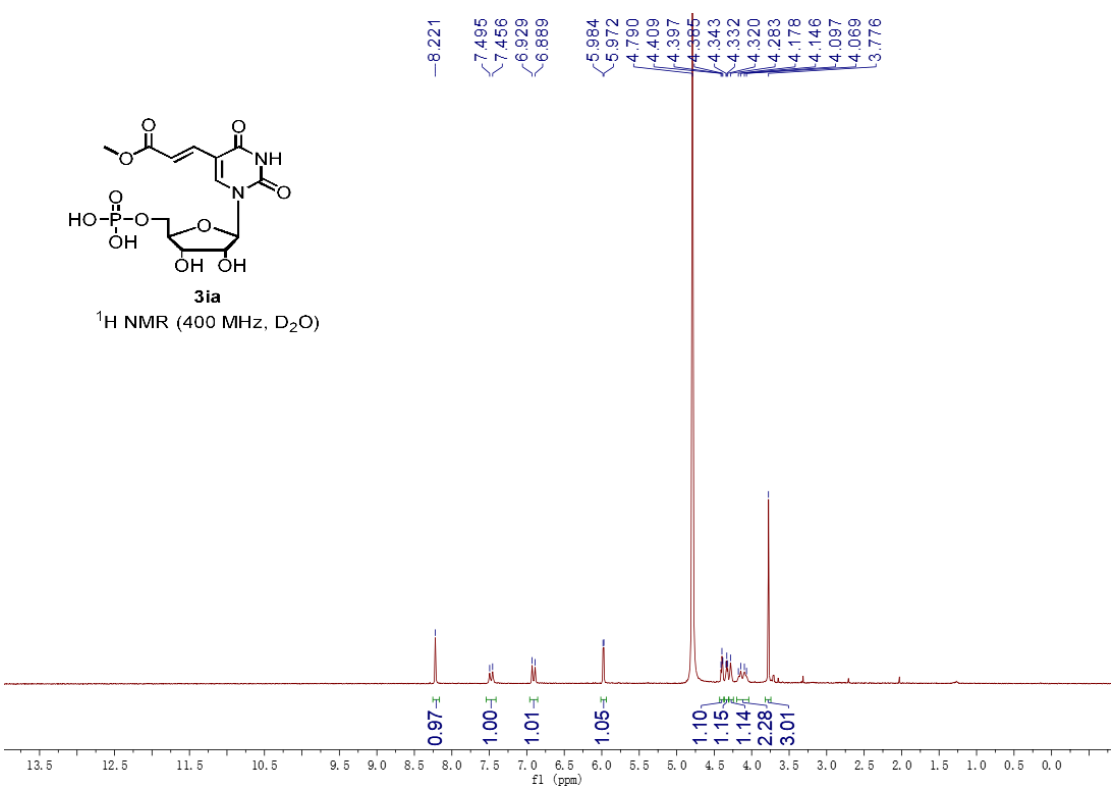
3ha

^{31}P NMR (162 MHz, MeOD)



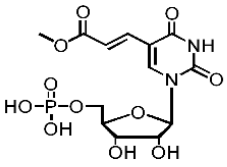
3ha

^{13}C NMR (101 MHz, MeOD)



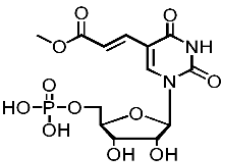
3ia

^{1}H NMR (400 MHz, D_2O)



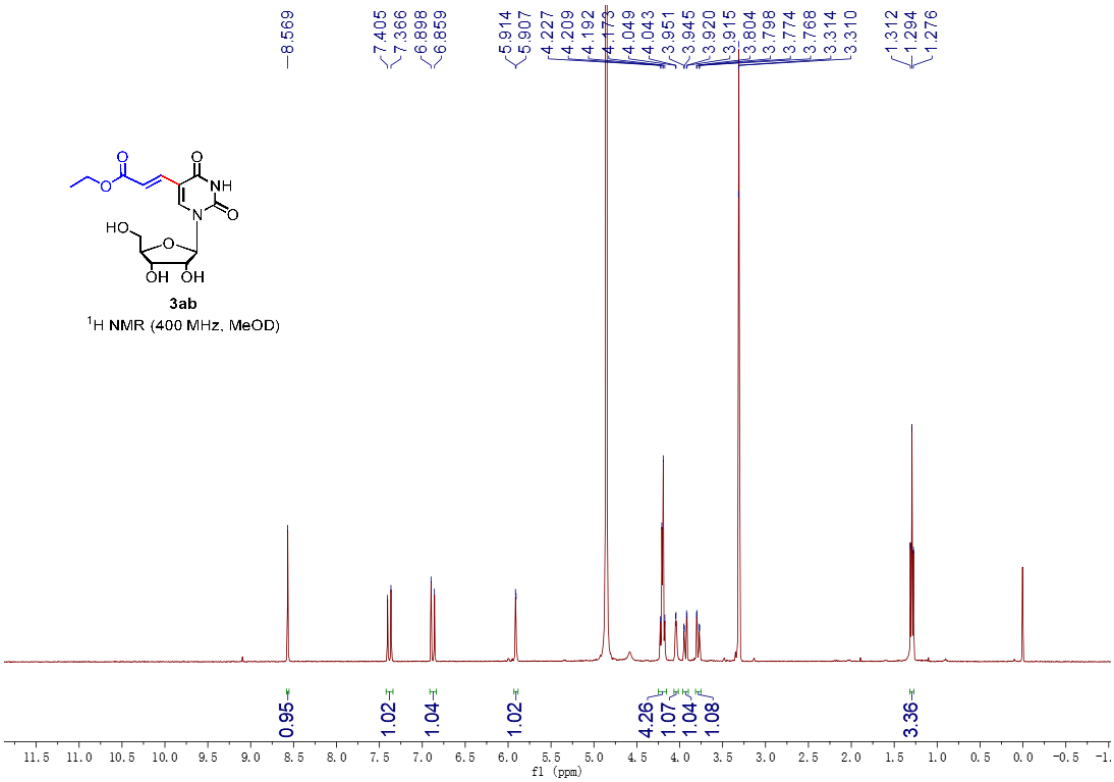
3ia

^{31}P NMR (162 MHz, D_2O)



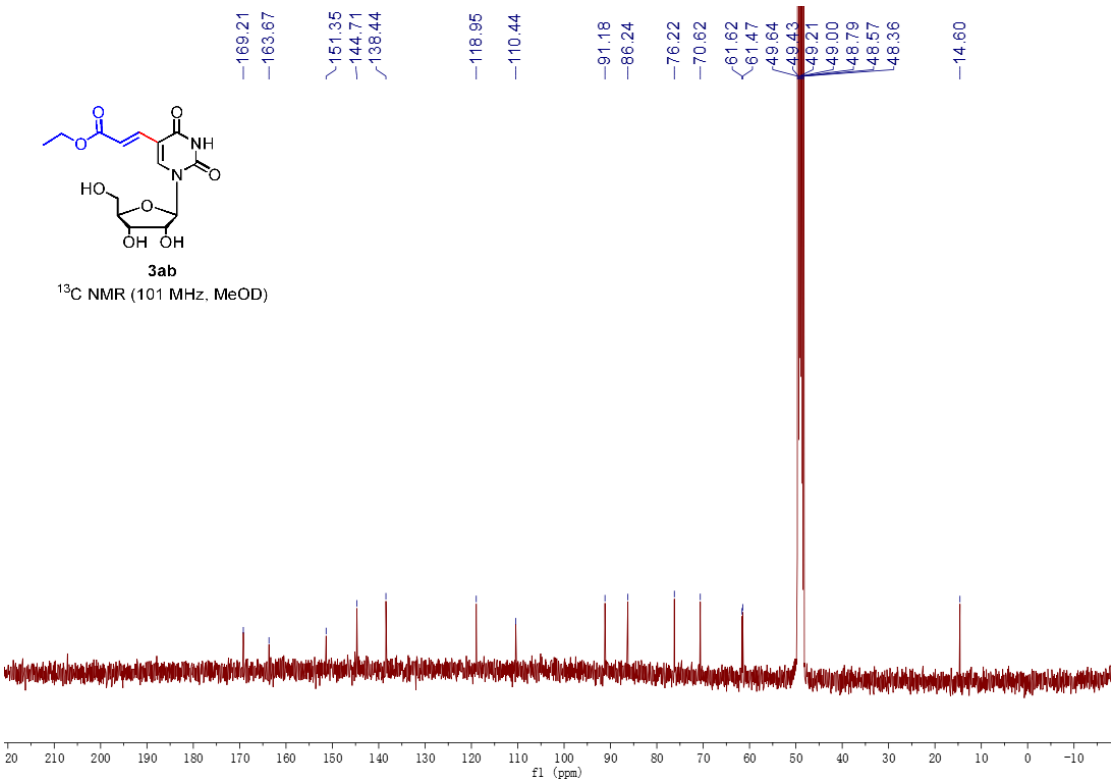
3ia

^{13}C NMR (101 MHz, D_2O)



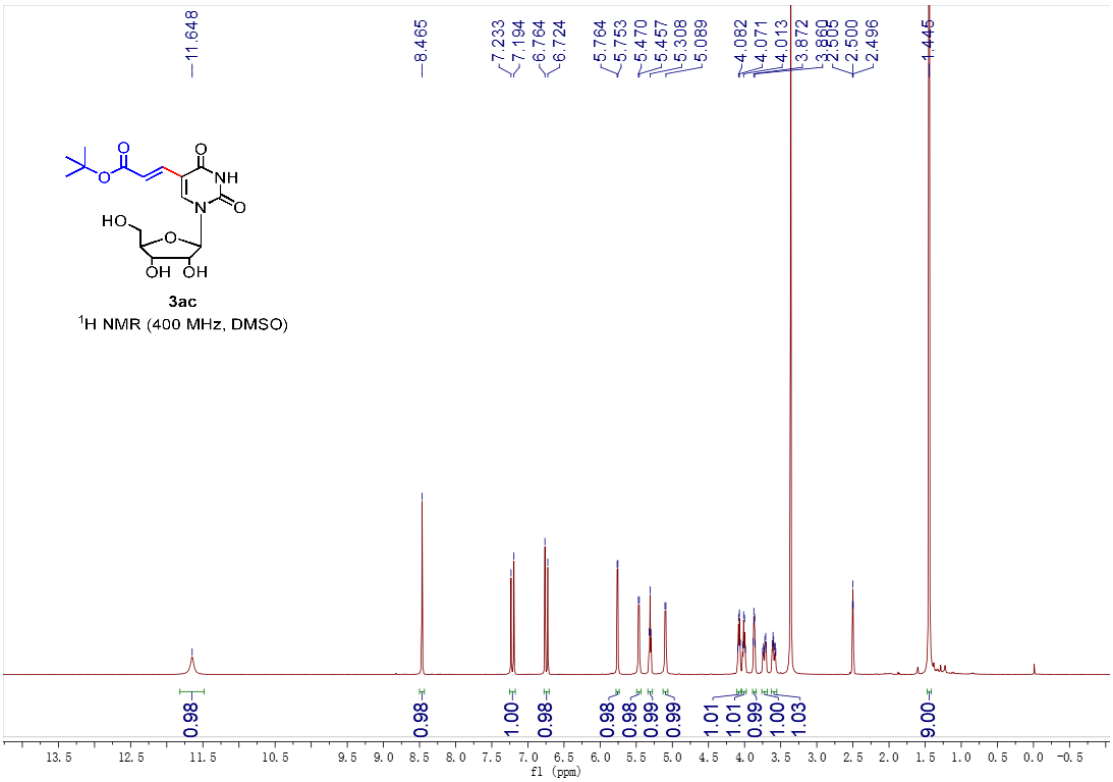
3ab

^{1}H NMR (400 MHz, MeOD)



3ab

^{13}C NMR (101 MHz, MeOD)



3ac

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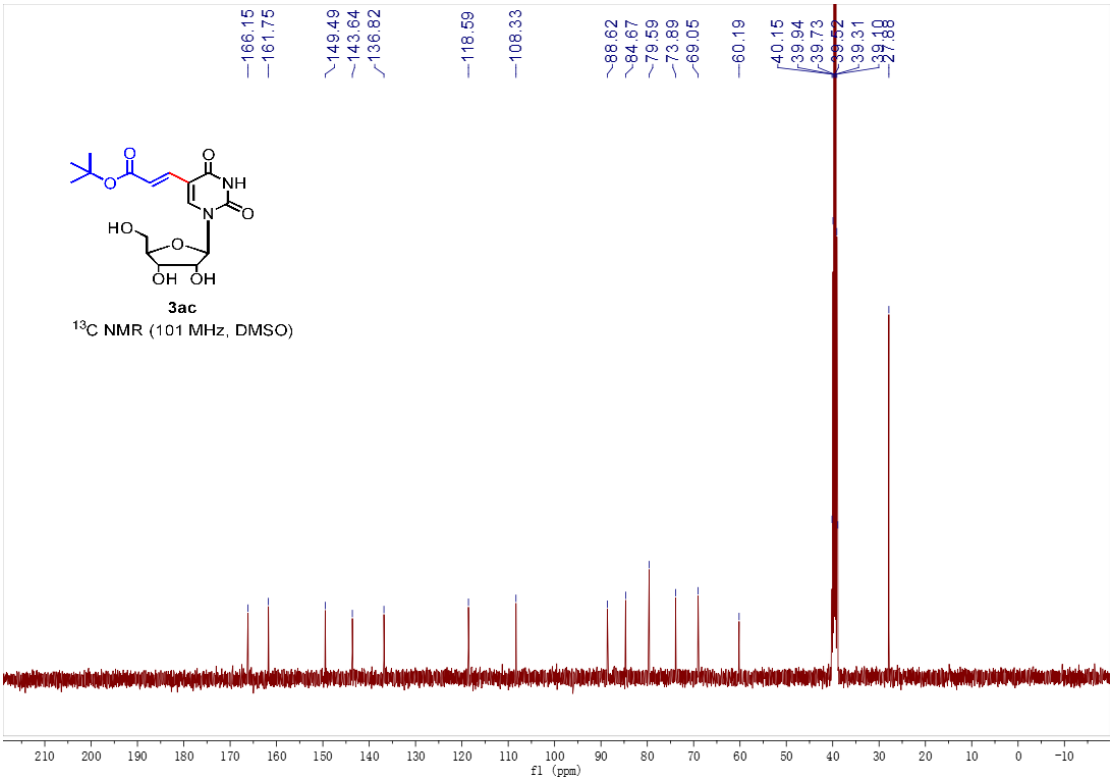
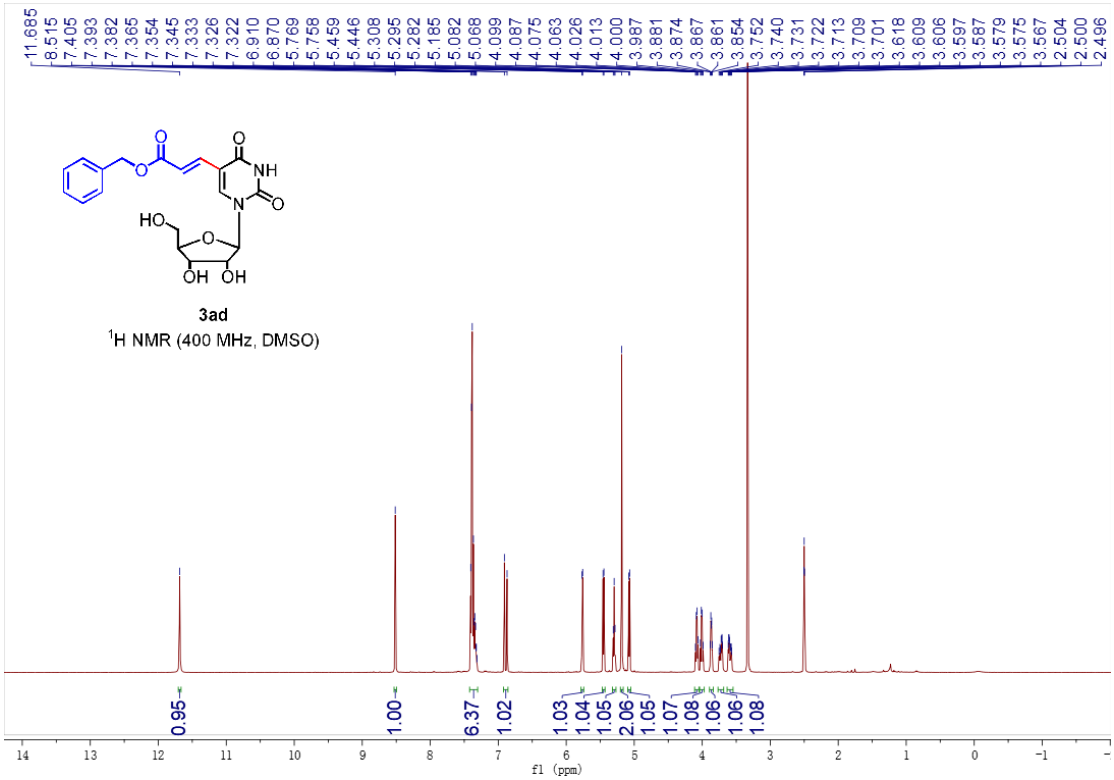


3ac

^{13}C NMR (101 MHz, DMSO)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7.382
7.365
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7.345
7.333
7.326
7.322
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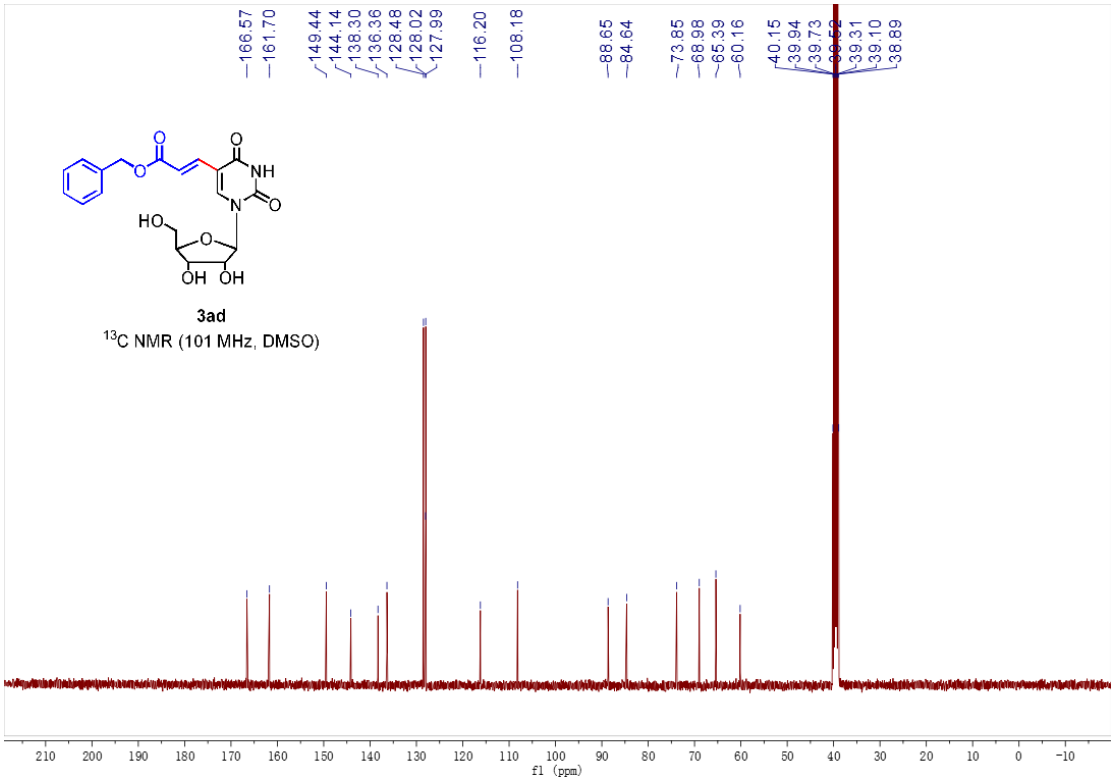
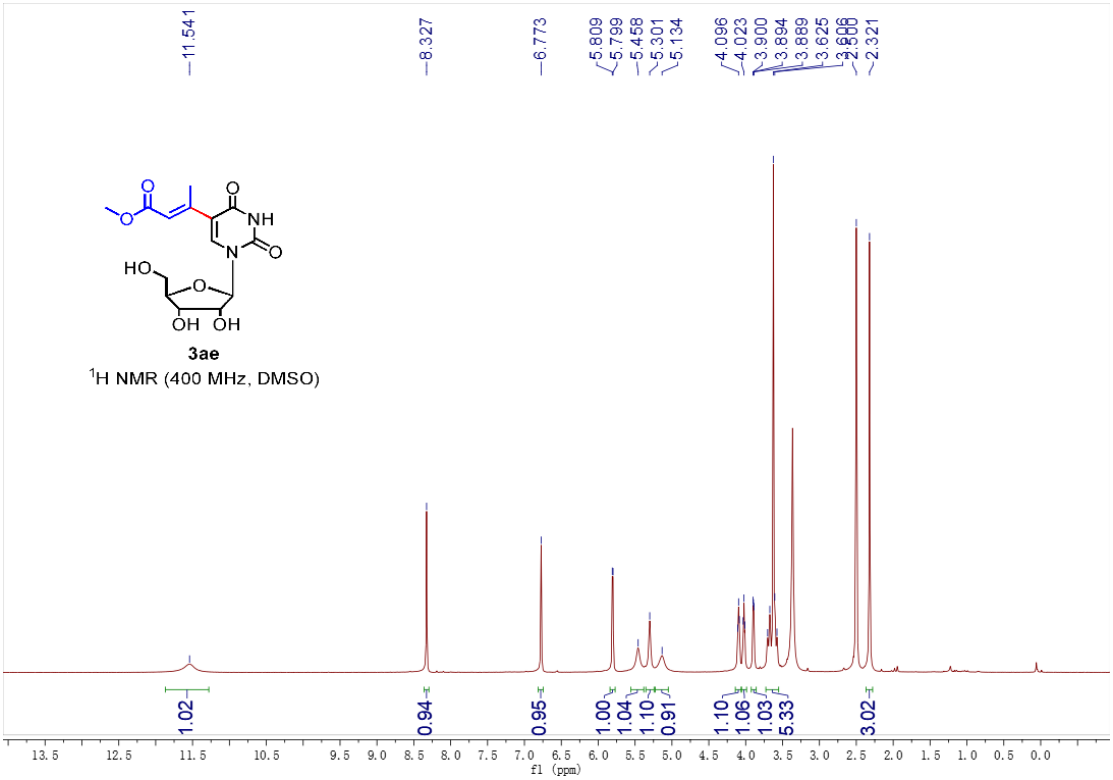
6.870
5.769
5.758
5.459
5.446
5.308
5.295
5.282
5.185
5.082
5.068
4.099
4.087
4.075
4.063
4.026
4.013
4.000
3.987
3.881
3.874
3.867
3.861
3.854
3.752
3.740
3.731
3.722
3.713
3.709
3.701
3.618
3.609
3.606
3.597
3.587
3.579
3.575
3.567
2.504
2.500
2.496
NH
O
N
HO
O
OH OH
3ad
1H NMR (400 MHz, DMSO)
0.95
1.00
6.37
1.02
1.03
1.04
1.05
2.06
1.05
1.07
1.08
1.06
1.06
1.08
f1 (ppm)


166.57
161.70
149.44
144.14
138.30
136.36
128.48
128.02
127.99
116.20
108.18
88.65
84.64
73.85
68.98
65.39
60.16
40.15
39.94
39.73
39.52
39.31
39.10
38.89
NH
O
N
HO
O
OH OH
3ad
13C NMR (101 MHz, DMSO)
f1 (ppm)



3ae

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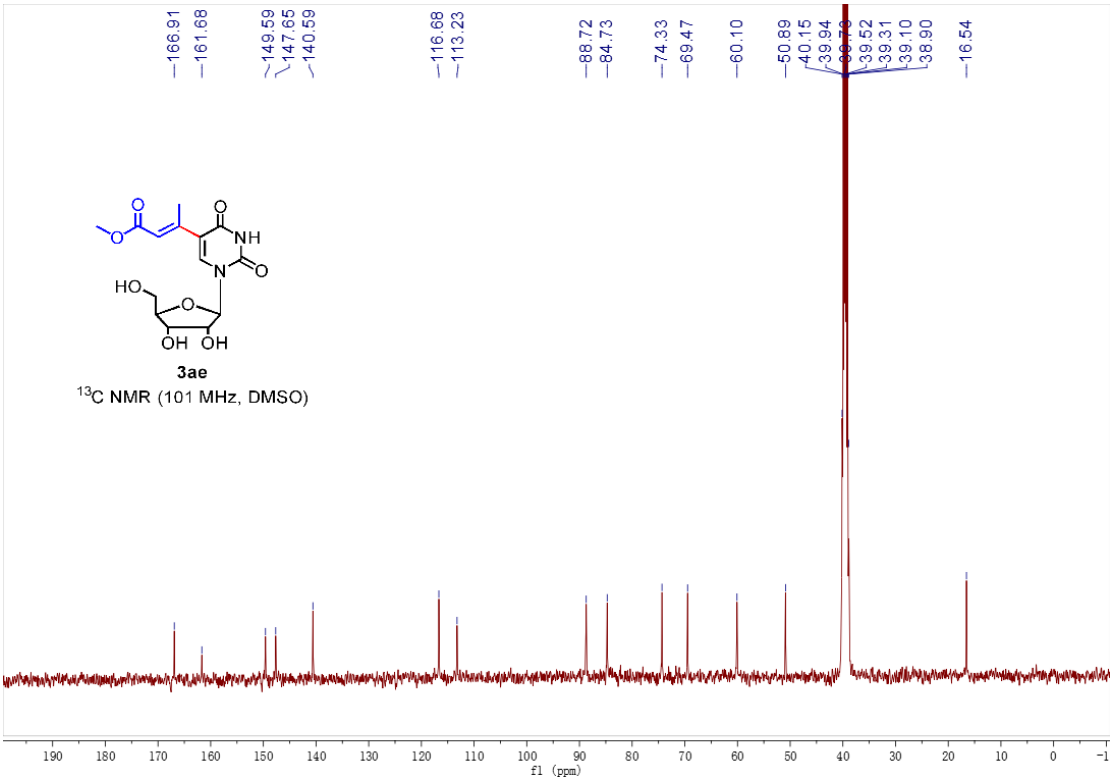

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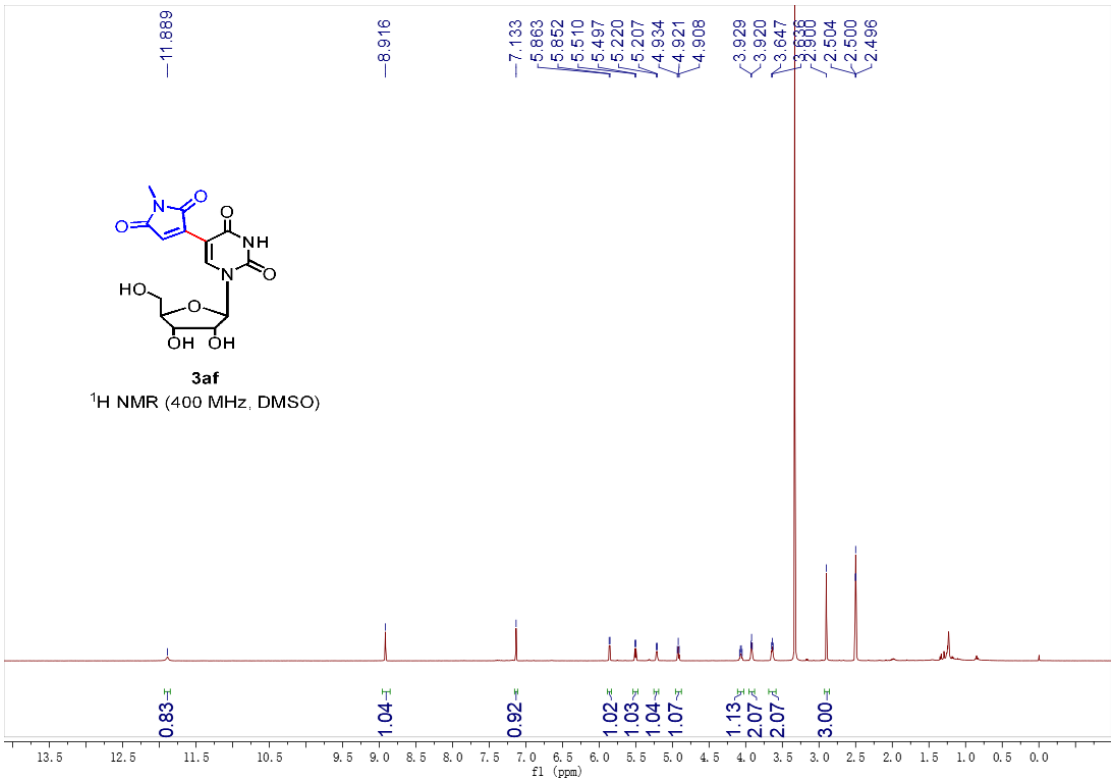

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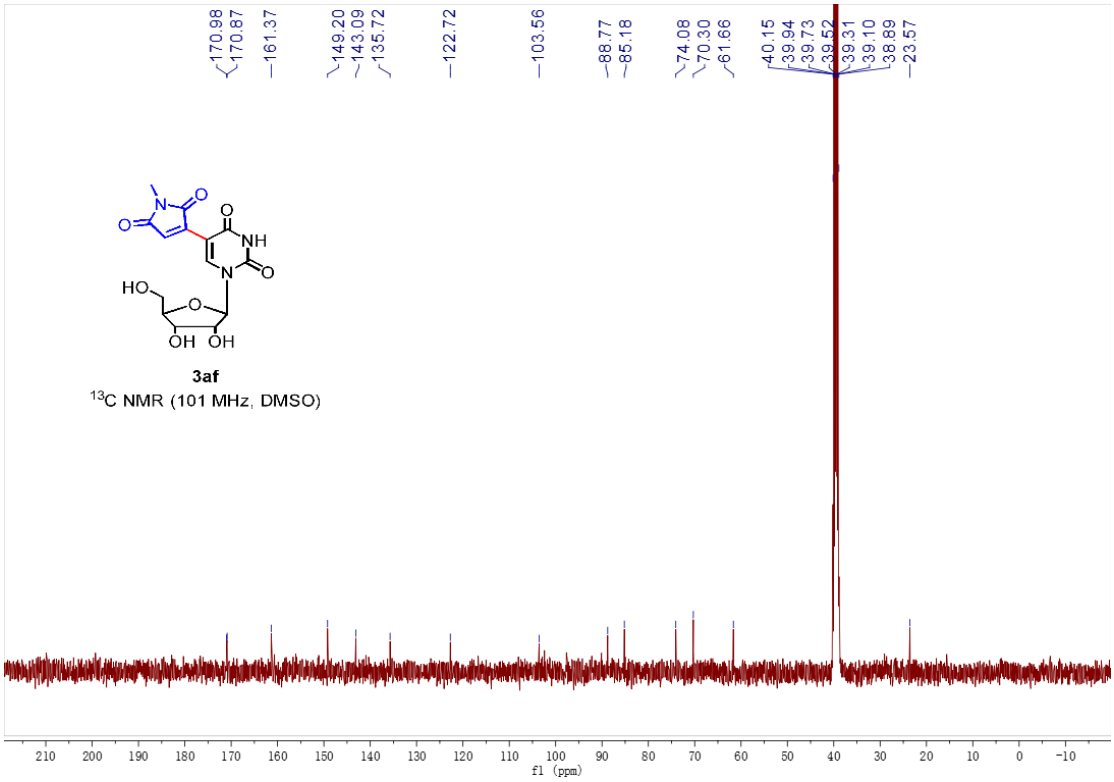

3af

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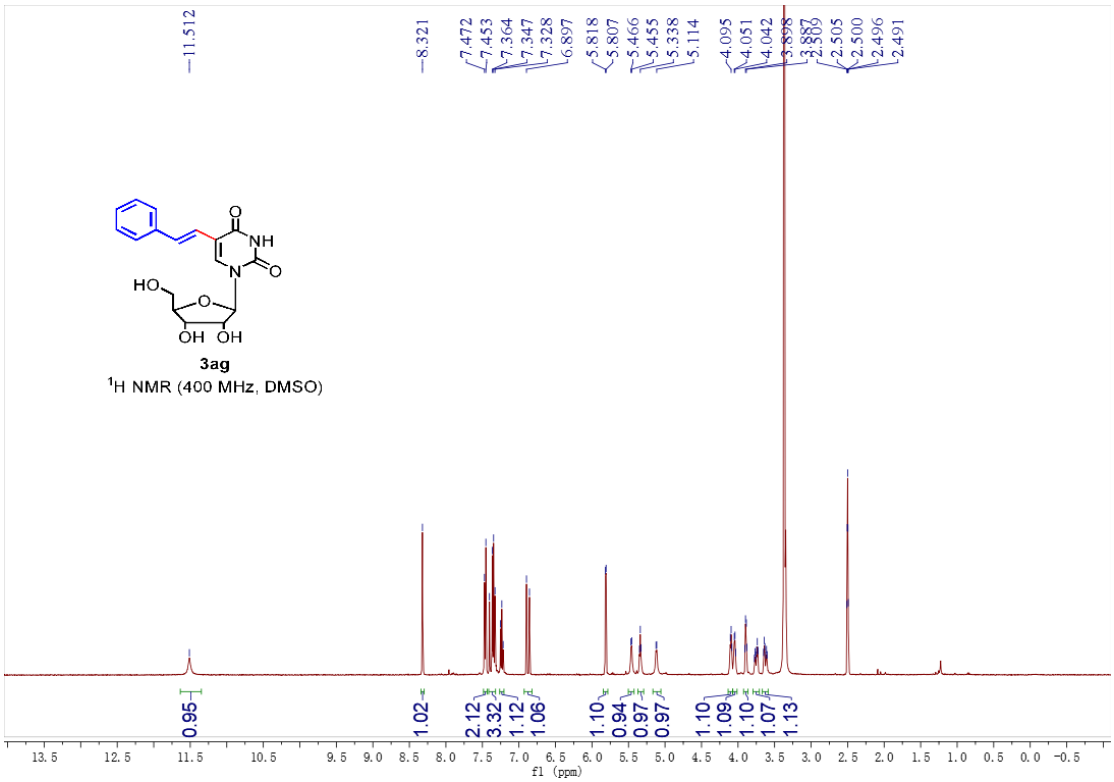

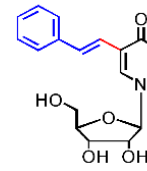

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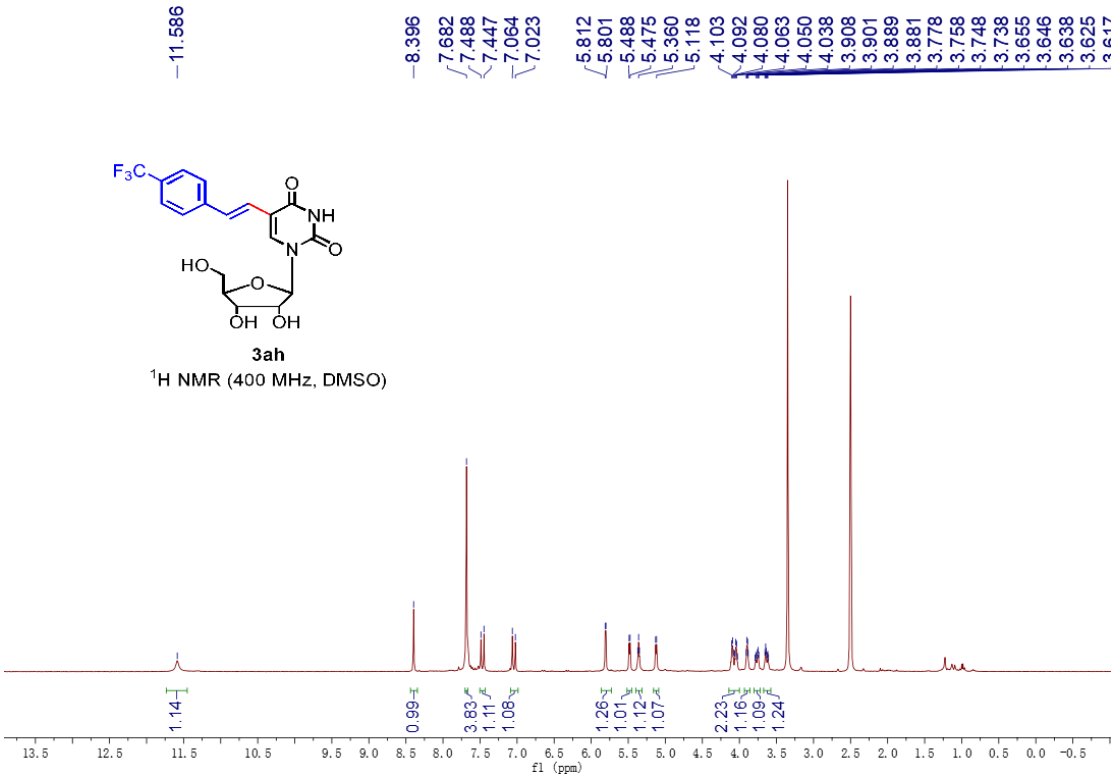
^{1}H NMR (400 MHz, DMSO)

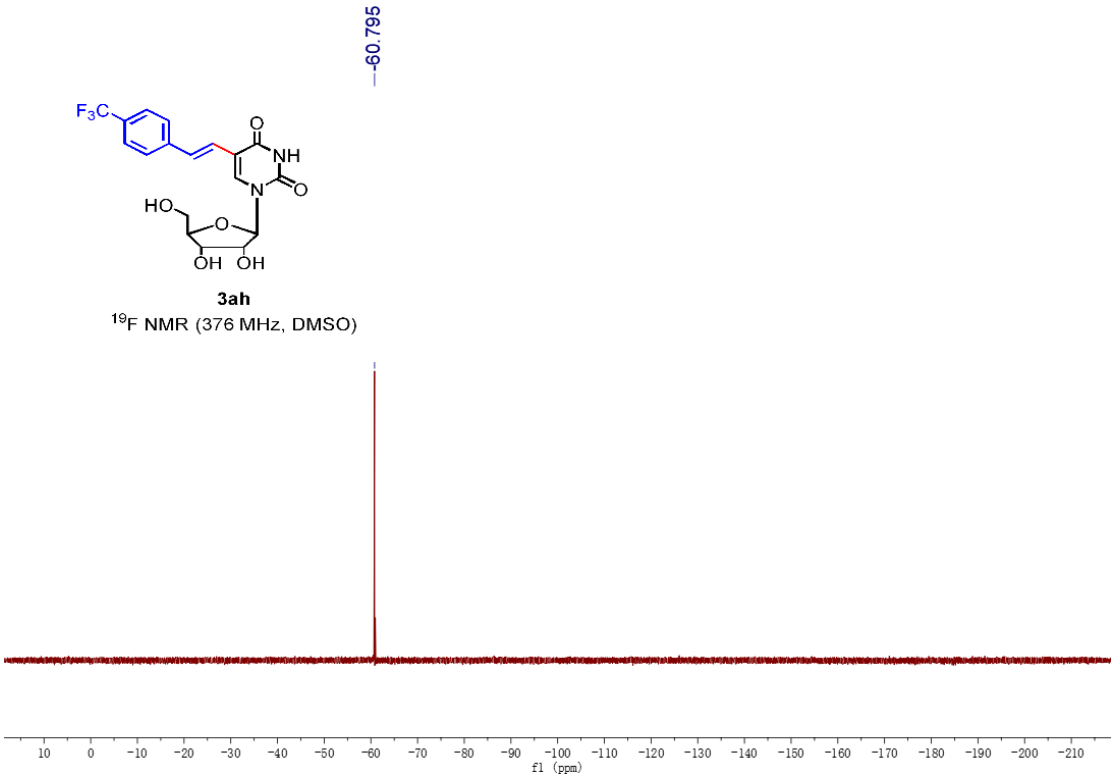
3ag

^{13}C NMR (101 MHz, DMSO)



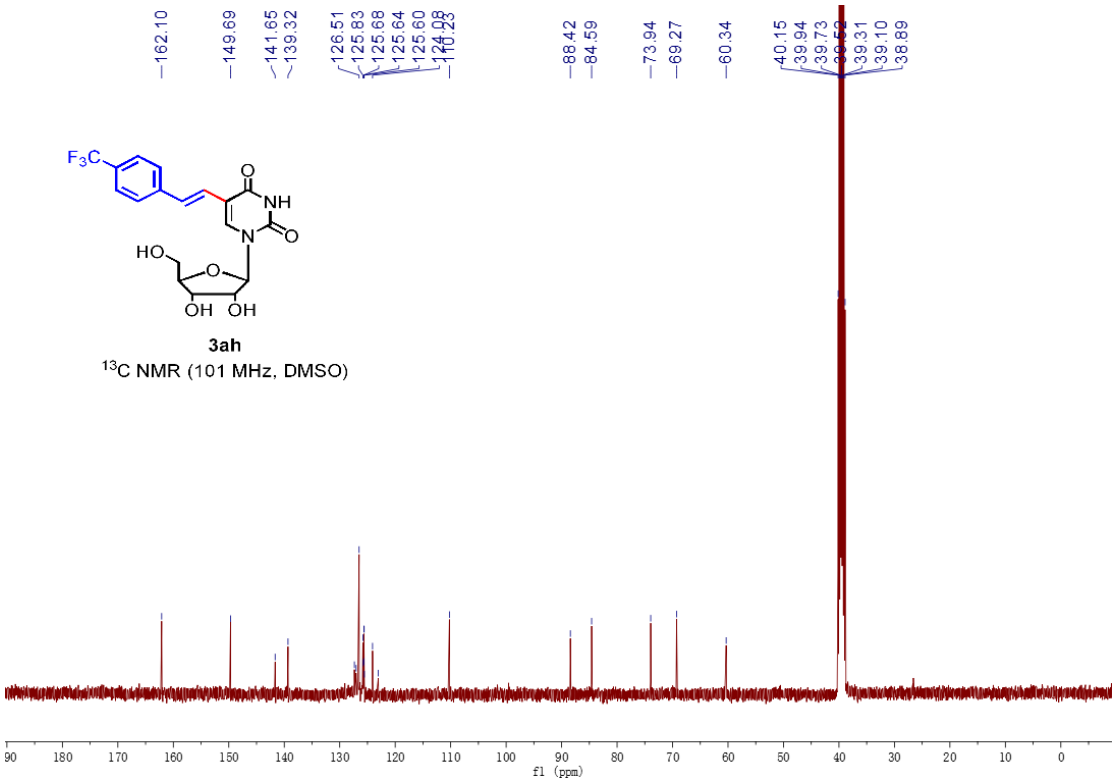
3ah

^{1}H NMR (400 MHz, DMSO)



3ah

^{19}F NMR (376 MHz, DMSO)



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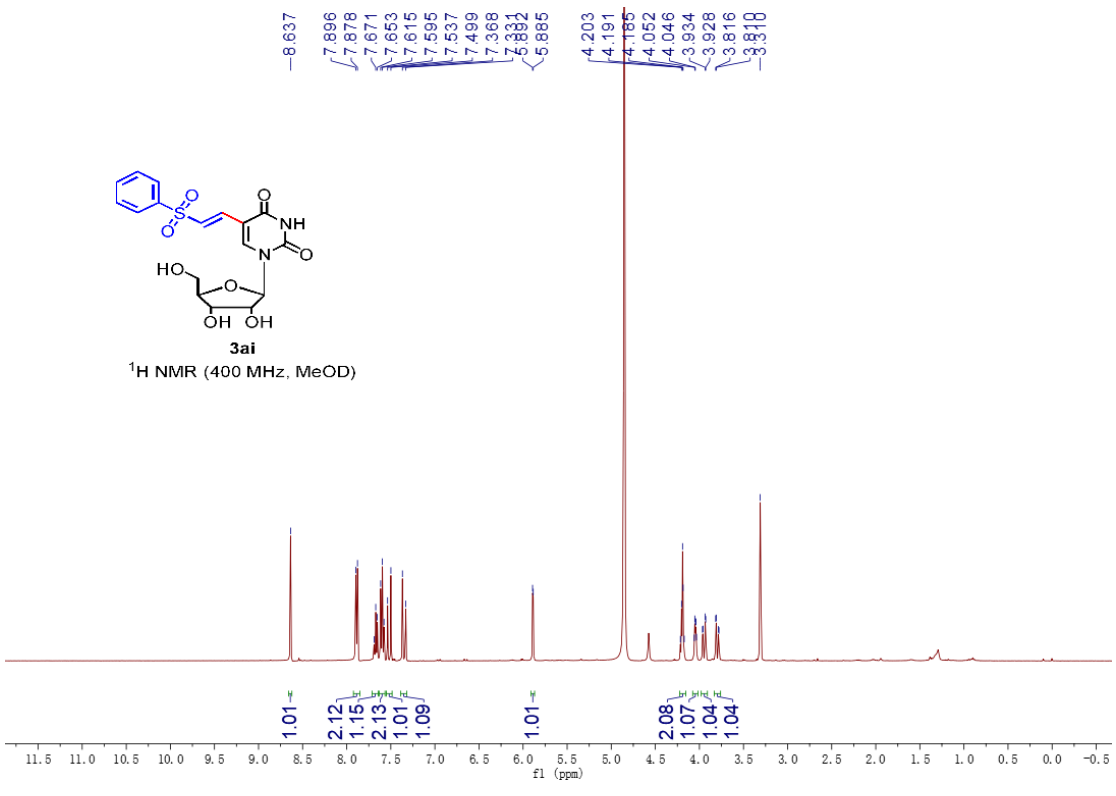
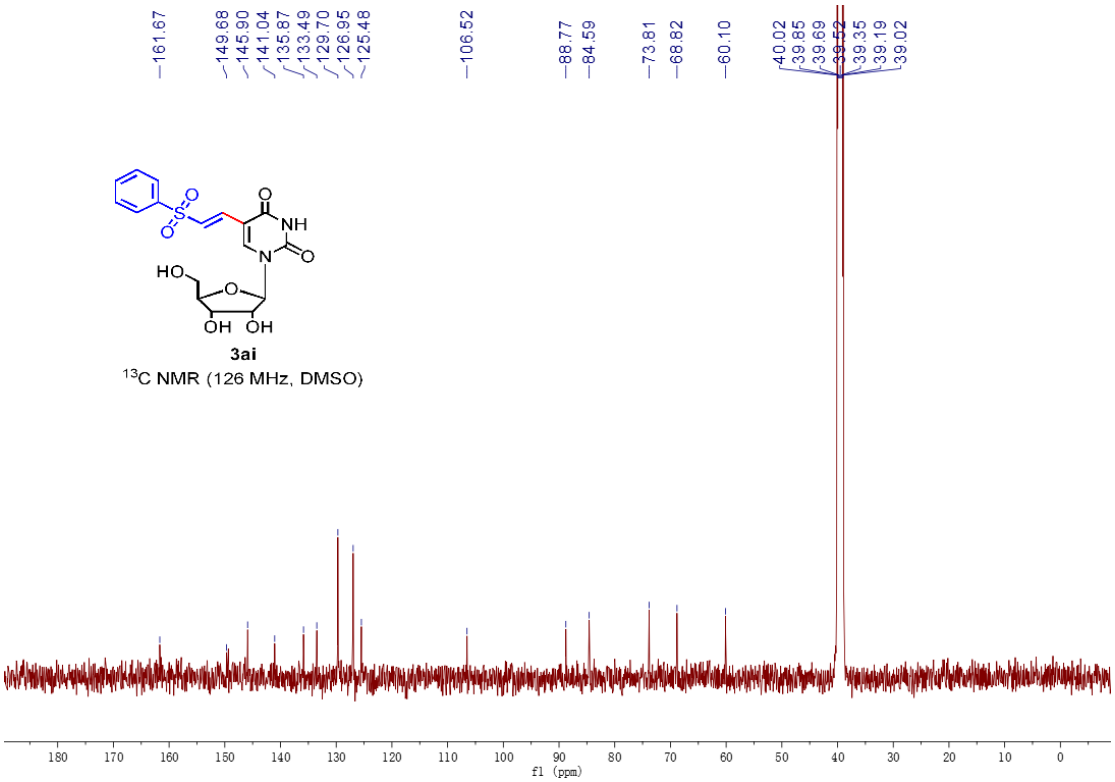


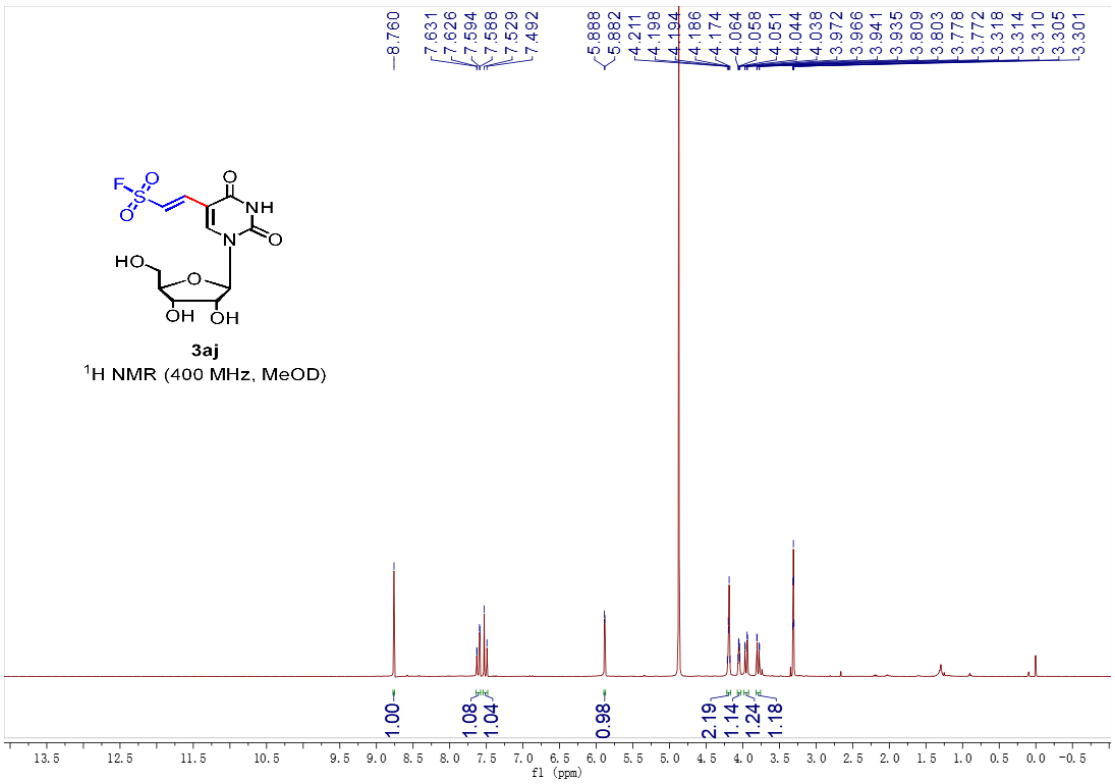
3ai

^{1}H NMR (400 MHz, MeOD)



3ai

^{13}C NMR (126 MHz, DMSO)



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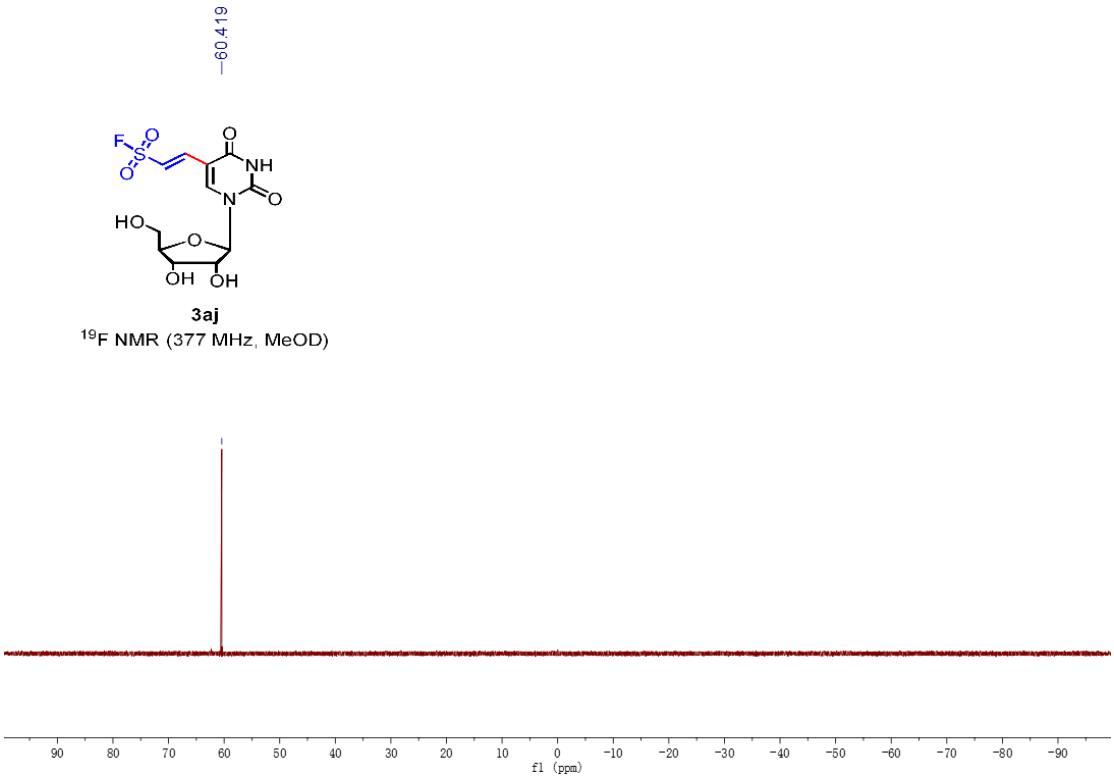

3aj

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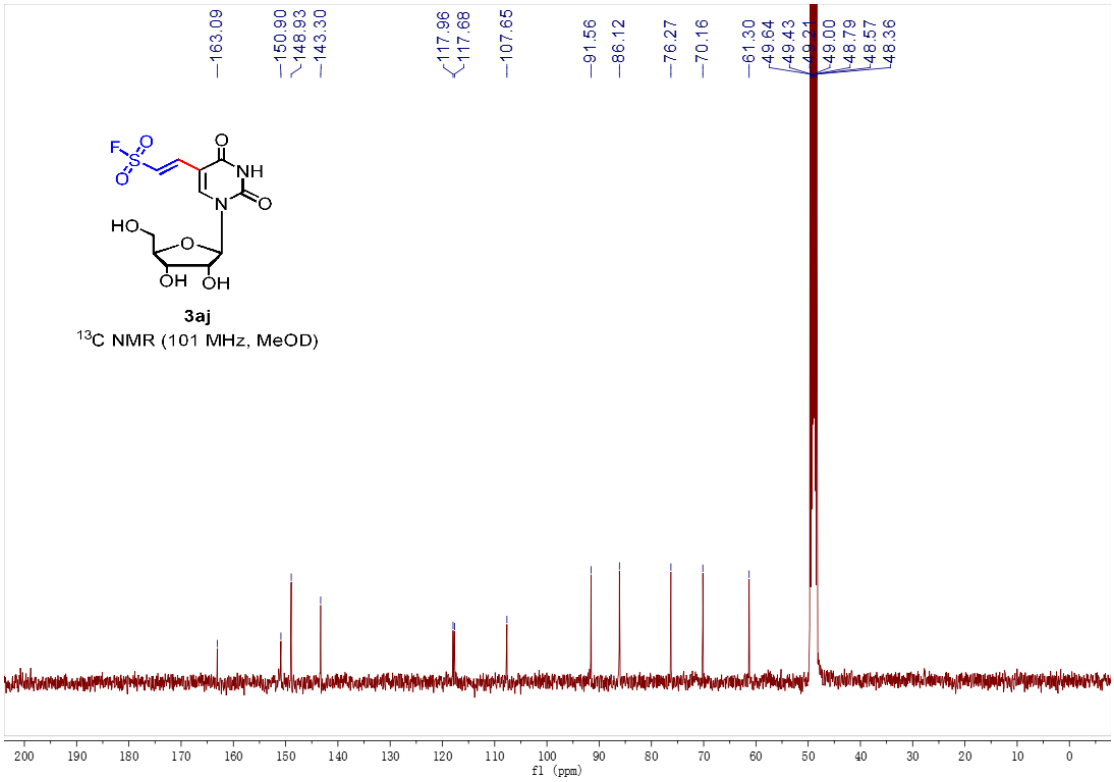
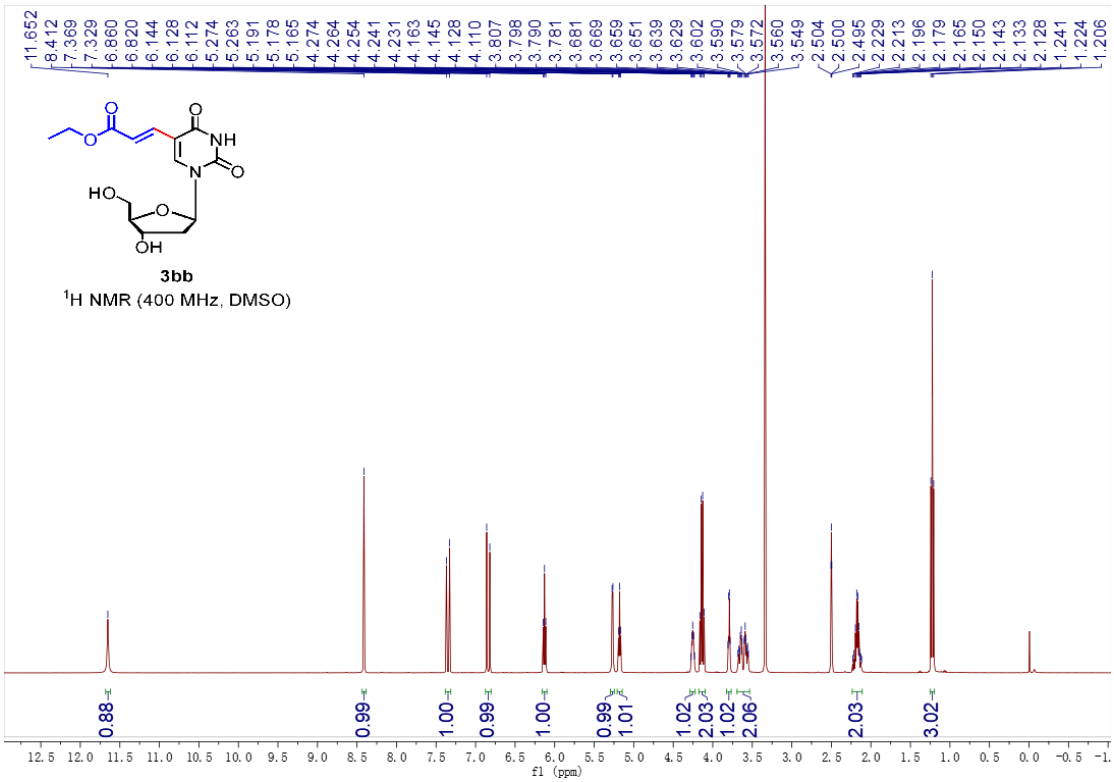


3aj

^{13}C NMR (101 MHz, MeOD)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7.329
6.860
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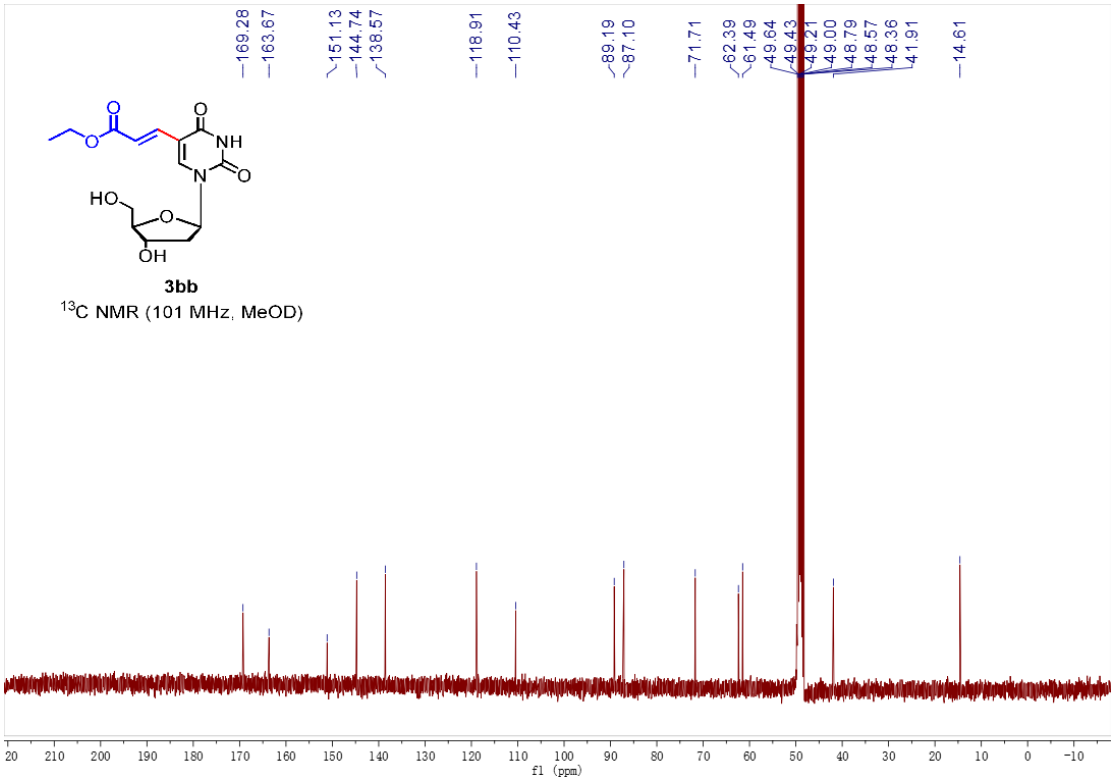
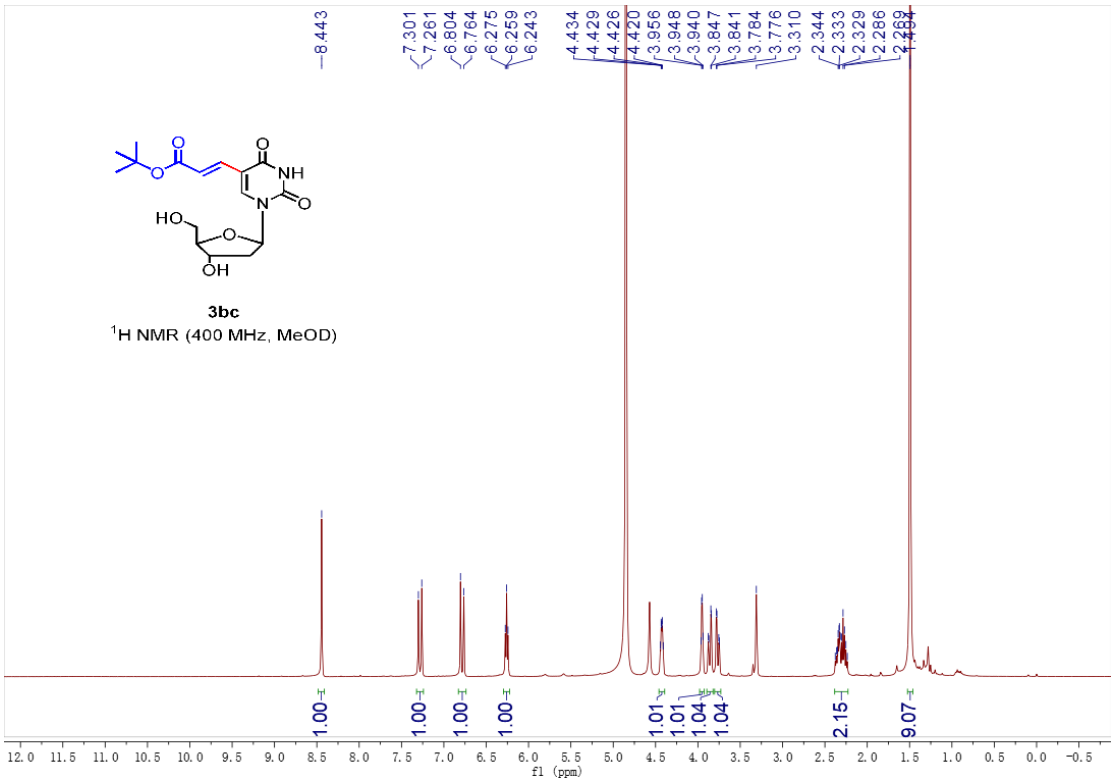
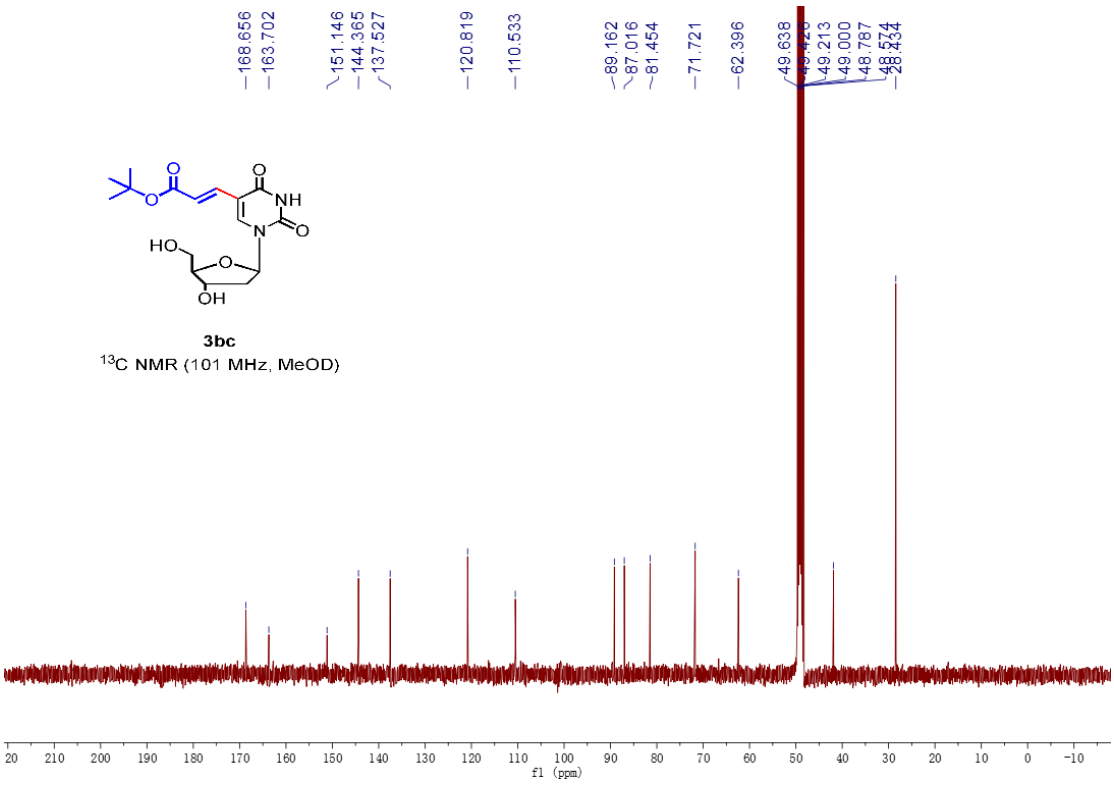
6.144
6.128
6.112
5.274
5.263
5.191
5.178
5.165
4.274
4.264
4.254
4.241
4.231
4.163
4.145
4.128
4.110
3.807
3.798
3.790
3.781
3.681
3.669
3.659
3.651
3.639
3.629
3.602
3.590
3.579
3.572
3.560
3.549
2.504
2.500
2.495
2.229
2.213
2.196
2.179
2.165
2.150
2.143
2.133
2.128
1.241
1.224
1.206
NH
O
N
HO
OH
3bb
1H NMR (400 MHz, DMSO)
0.88
0.99
1.00
0.99
1.00
0.99
1.01
1.02
2.03
1.02
2.06
2.03
3.02
f1 (ppm)


169.28
163.67
151.13
144.74
138.57
118.91
110.43
89.19
87.10
71.71
62.39
61.49
49.64
49.43
49.21
49.00
48.79
48.57
48.36
41.91
14.61
NH
O
N
HO
OH
3bb
13C NMR (101 MHz, MeOD)
f1 (ppm)



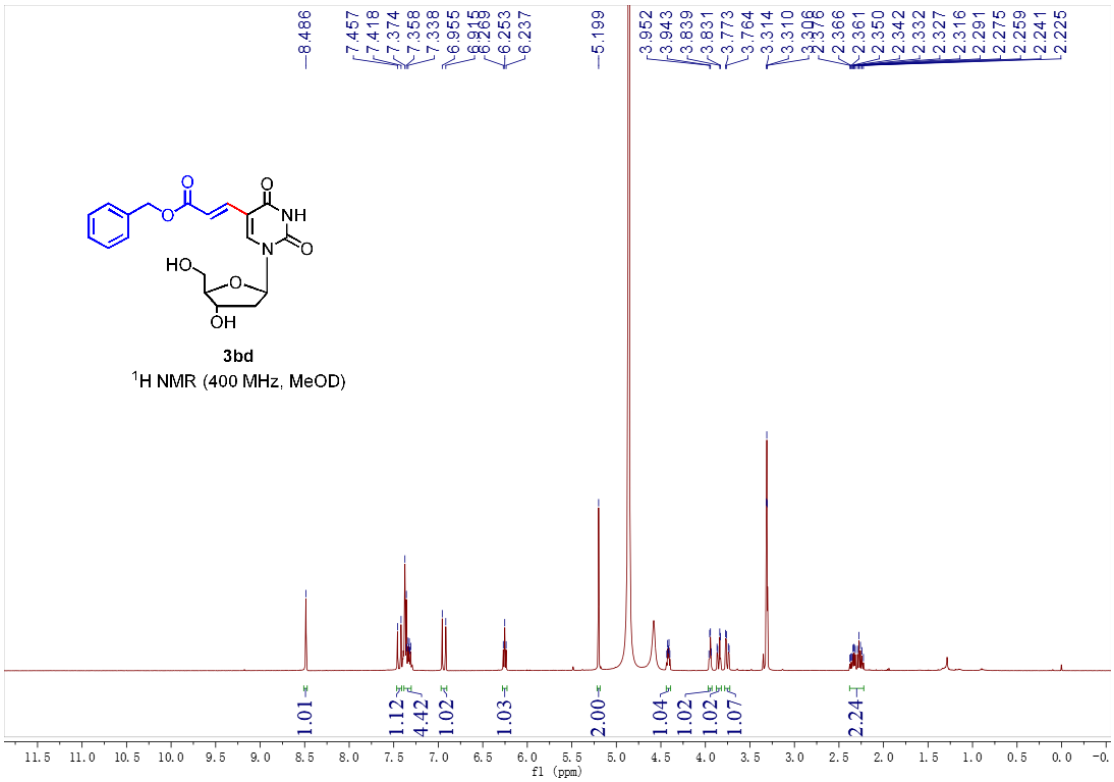
3bc

^{1}H NMR (400 MHz, MeOD)



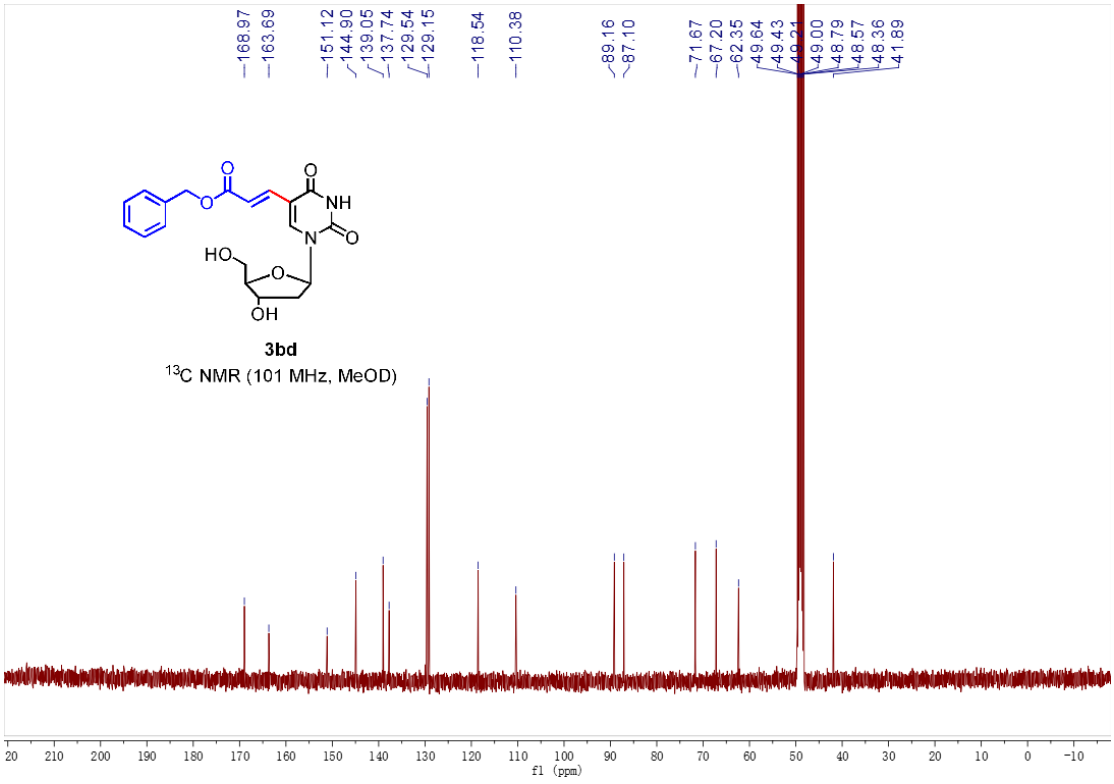
3bc

^{13}C NMR (101 MHz, MeOD)



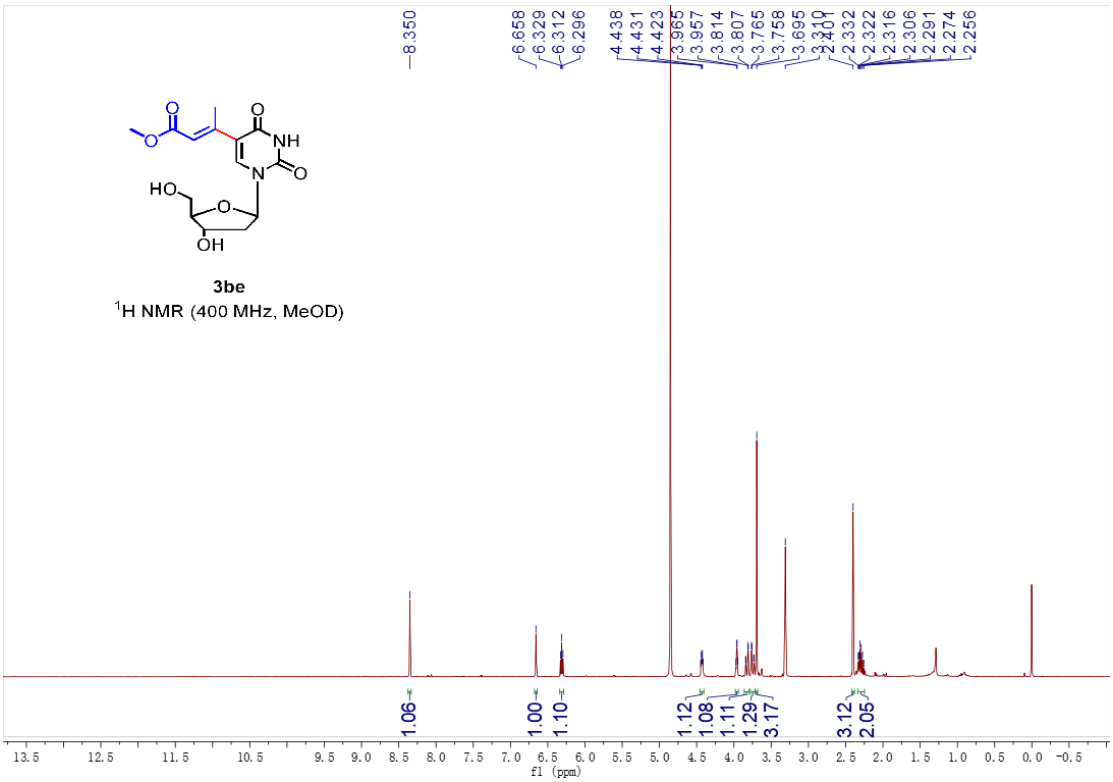
3bd

^{1}H NMR (400 MHz, MeOD)



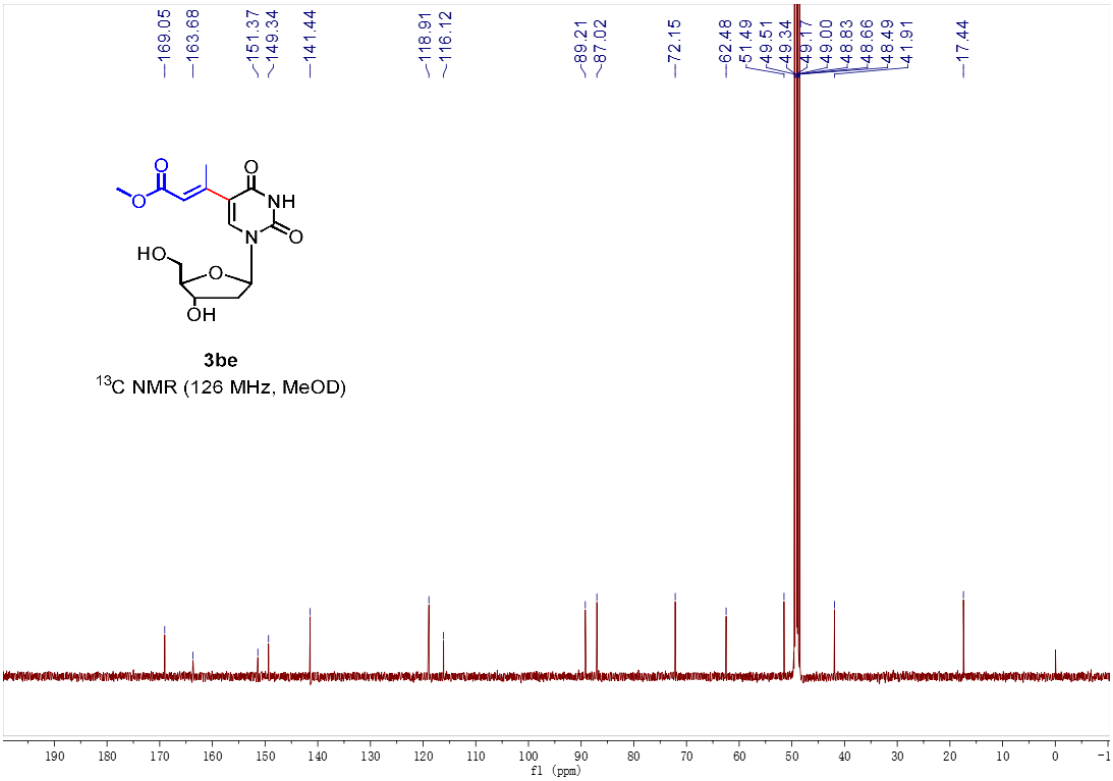
3bd

^{13}C NMR (101 MHz, MeOD)



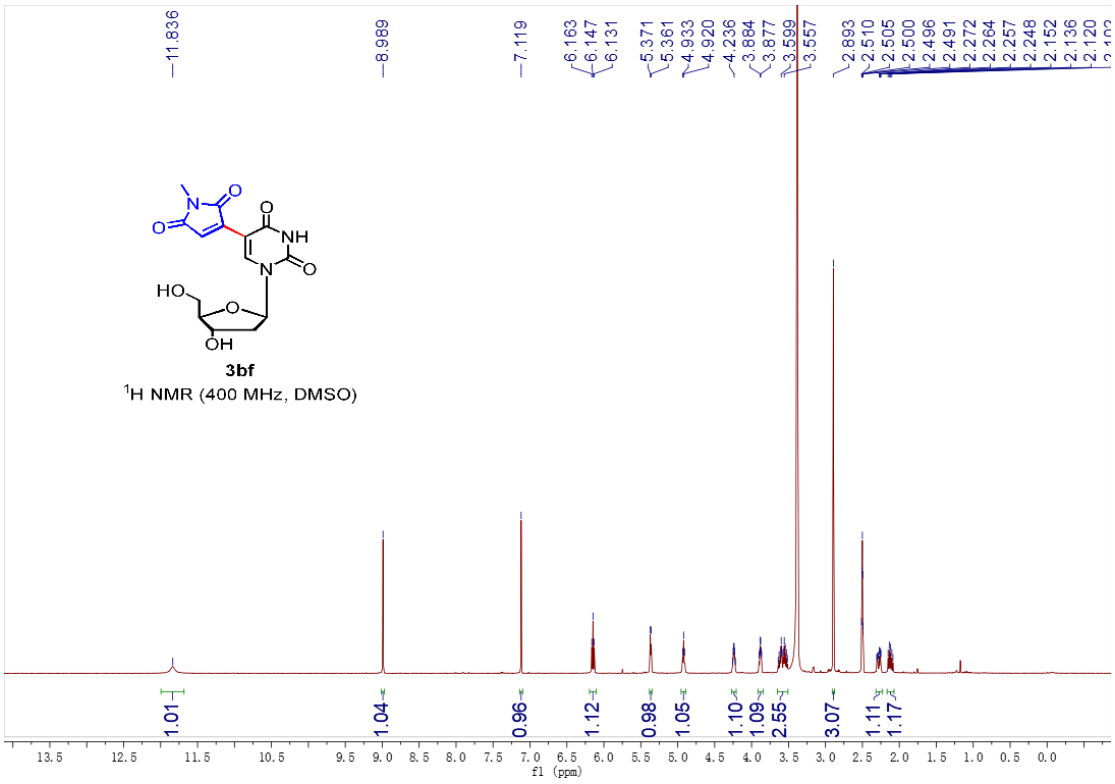
3be

^{1}H NMR (400 MHz, MeOD)



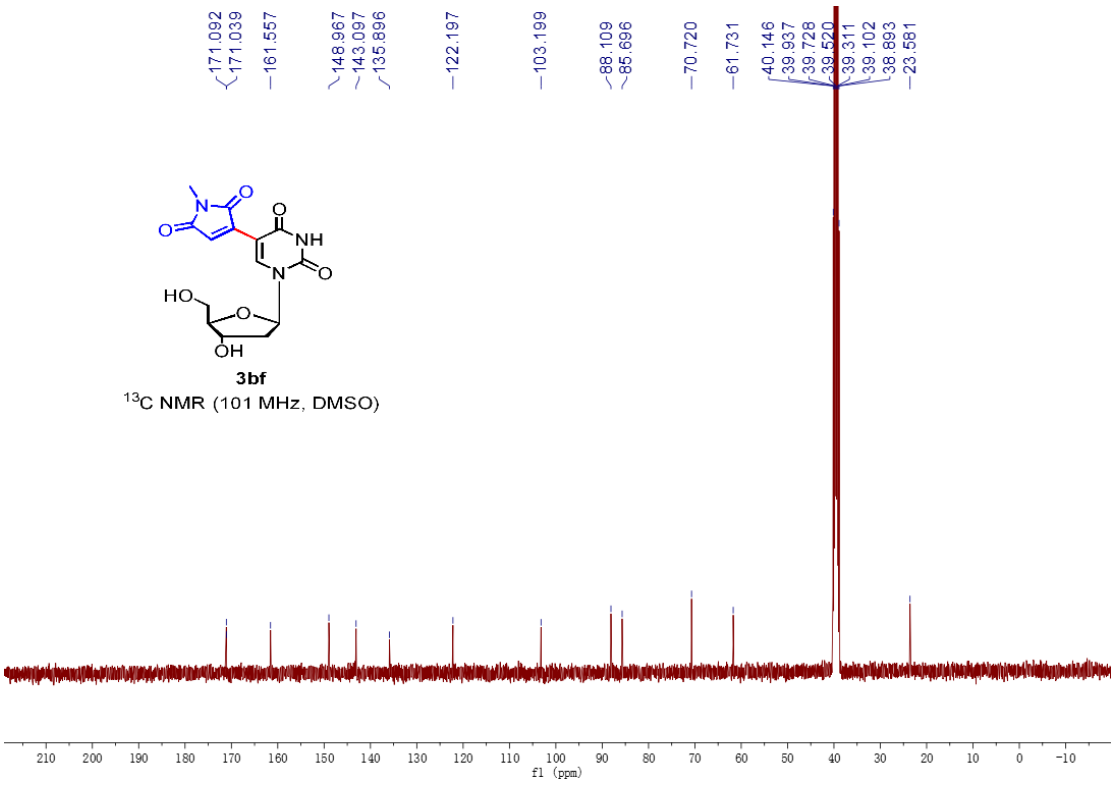
3be

^{13}C NMR (126 MHz, MeOD)



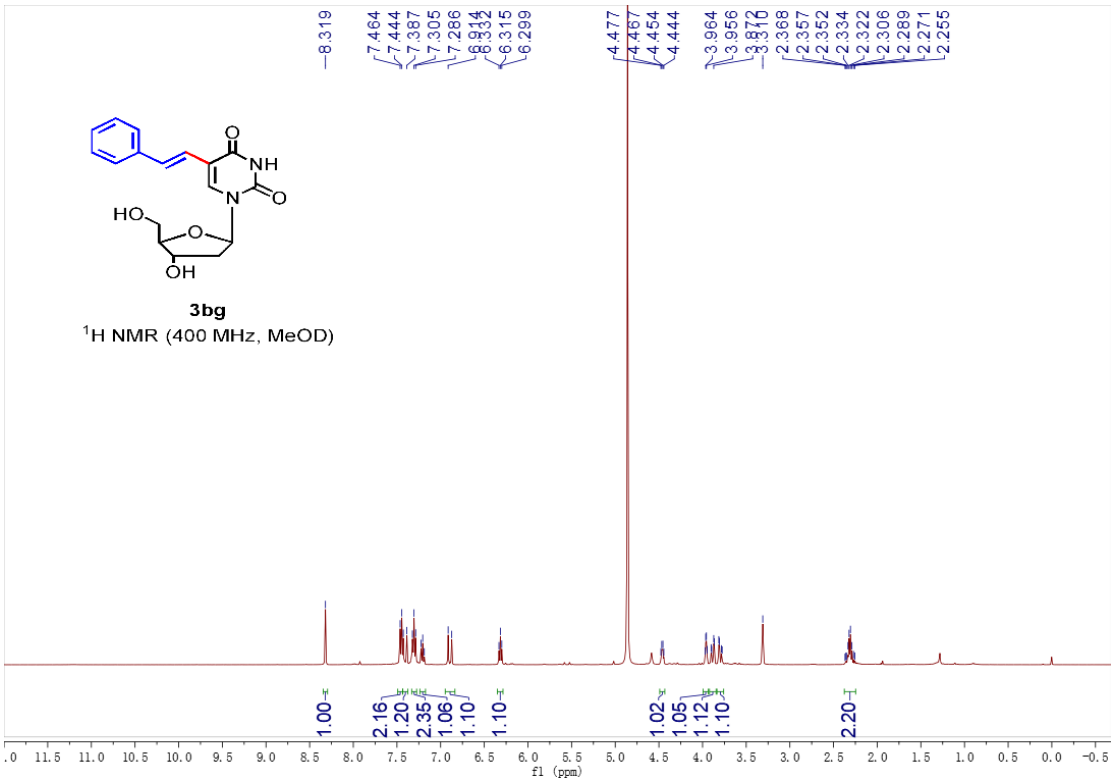
3bf

^{1}H NMR (400 MHz, DMSO)



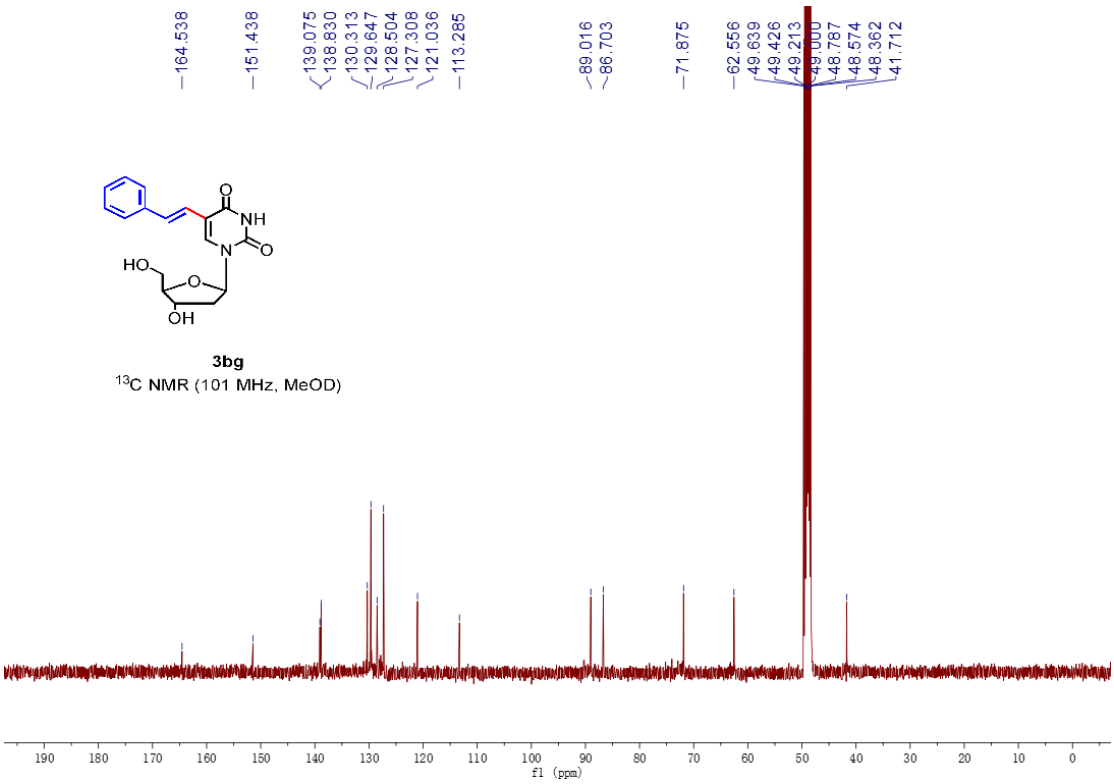
3bf

^{13}C NMR (101 MHz, DMSO)



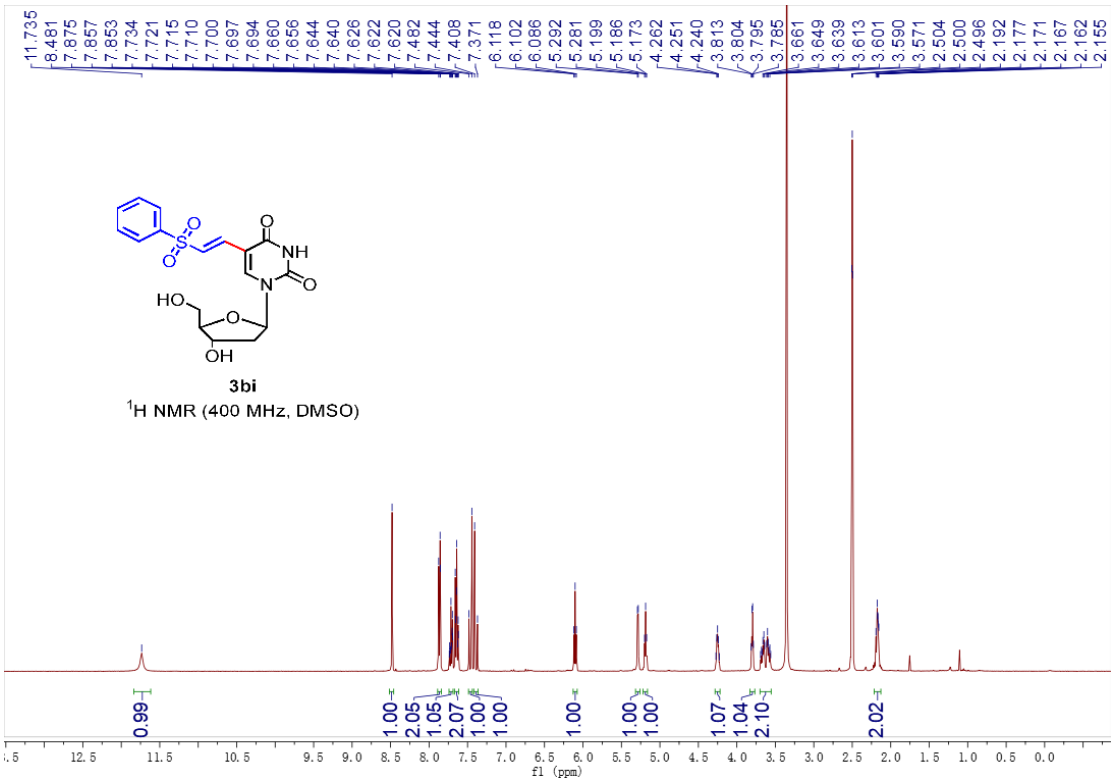
3bg

^{1}H NMR (400 MHz, MeOD)



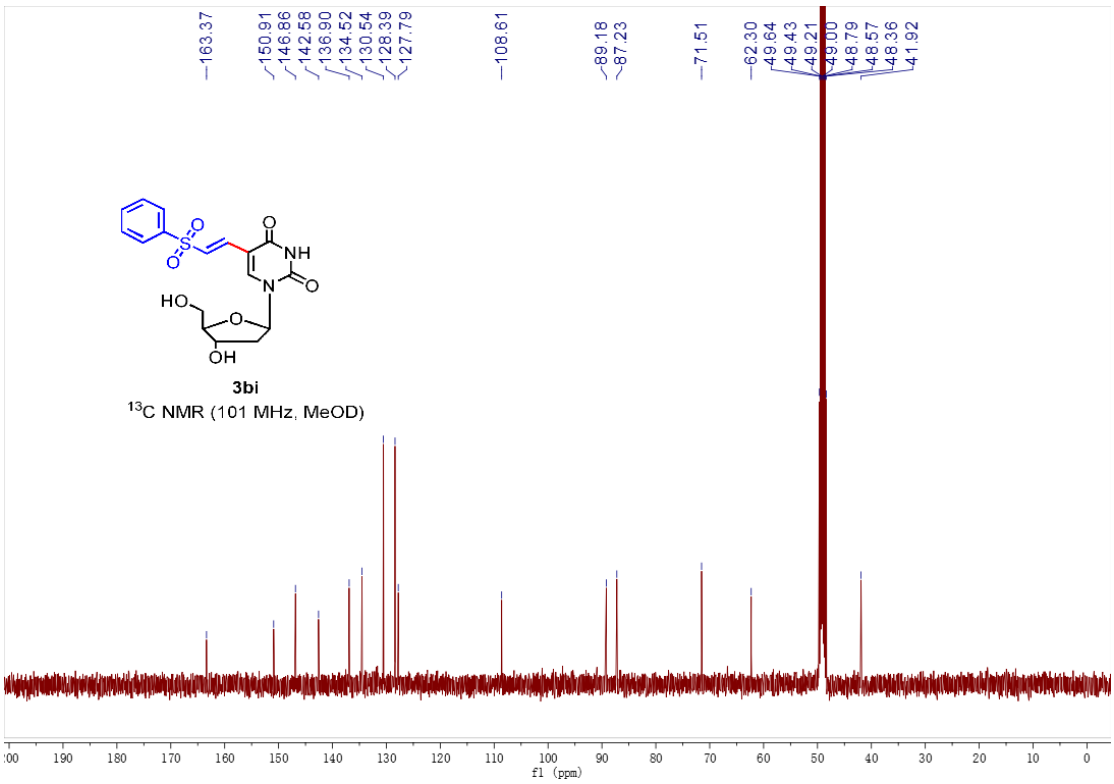
3bg

^{13}C NMR (101 MHz, MeOD)



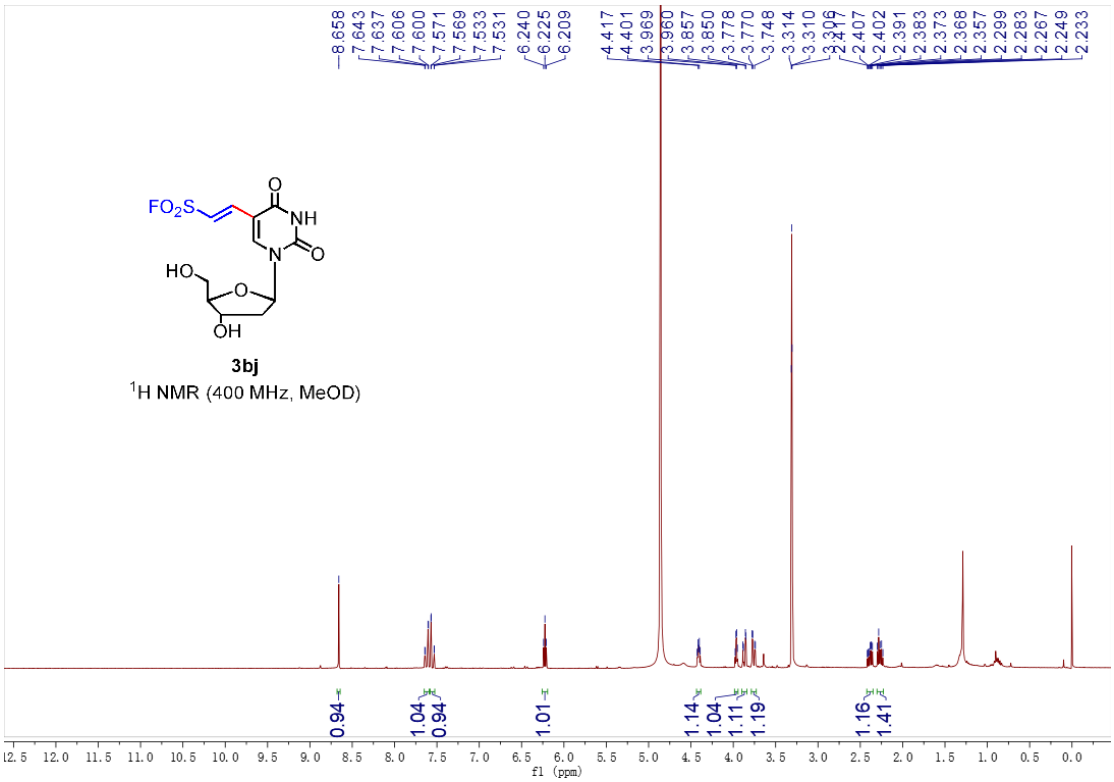
3bi

^{1}H NMR (400 MHz, DMSO)



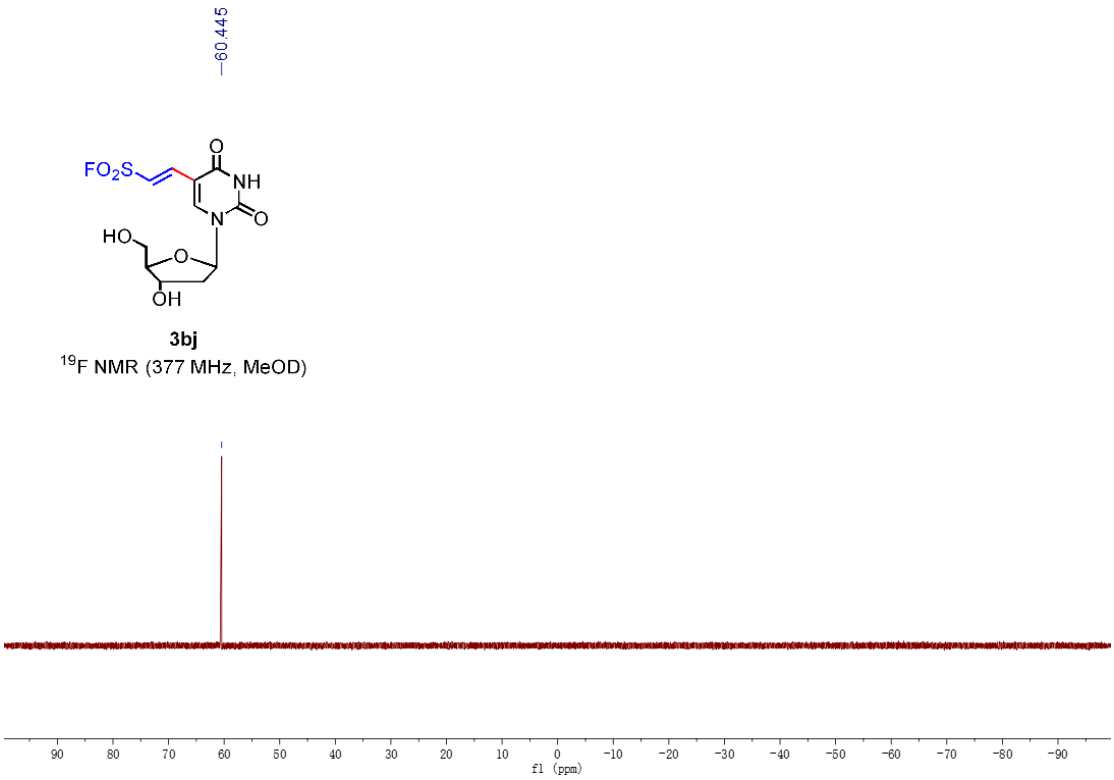
3bi

^{13}C NMR (101 MHz, MeOD)



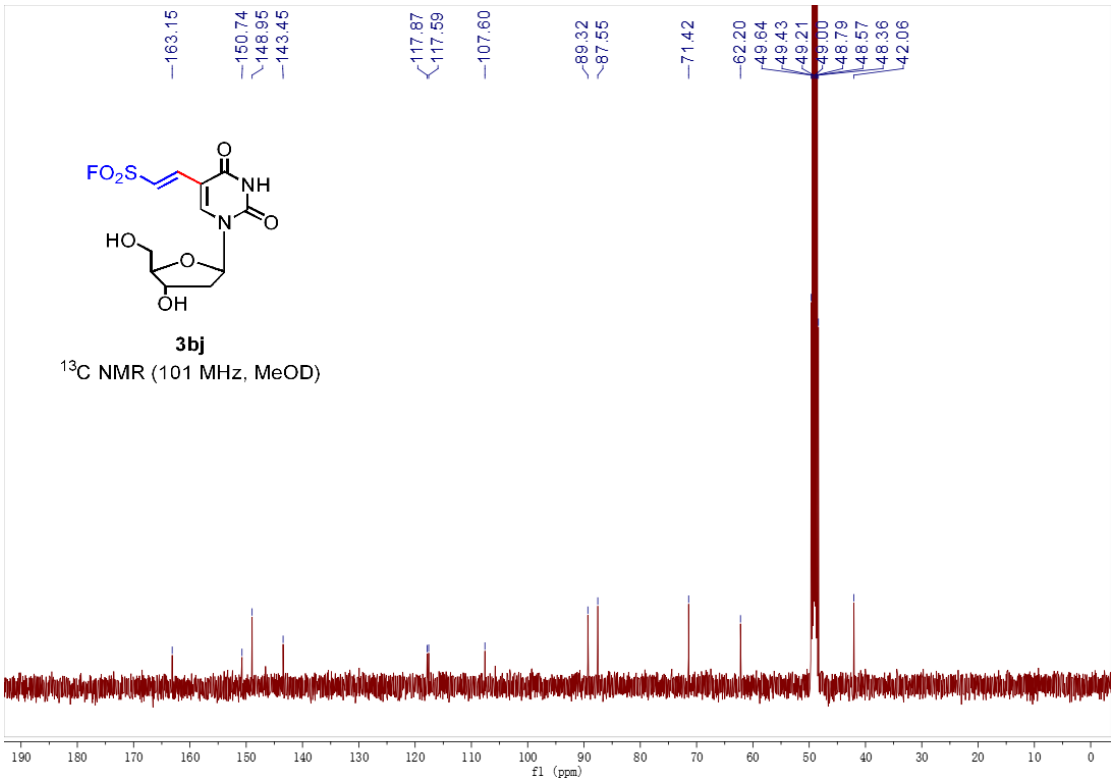
3bj

^{1}H NMR (400 MHz, MeOD)



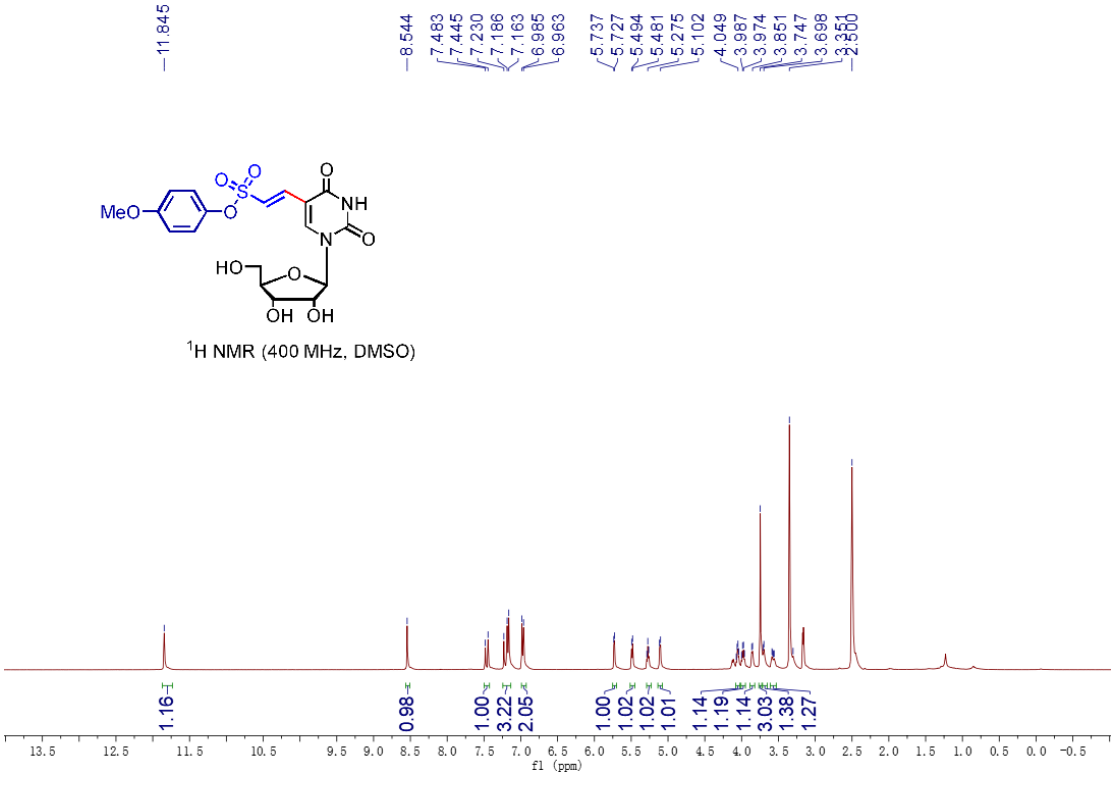
3bj

^{19}F NMR (377 MHz, MeOD)

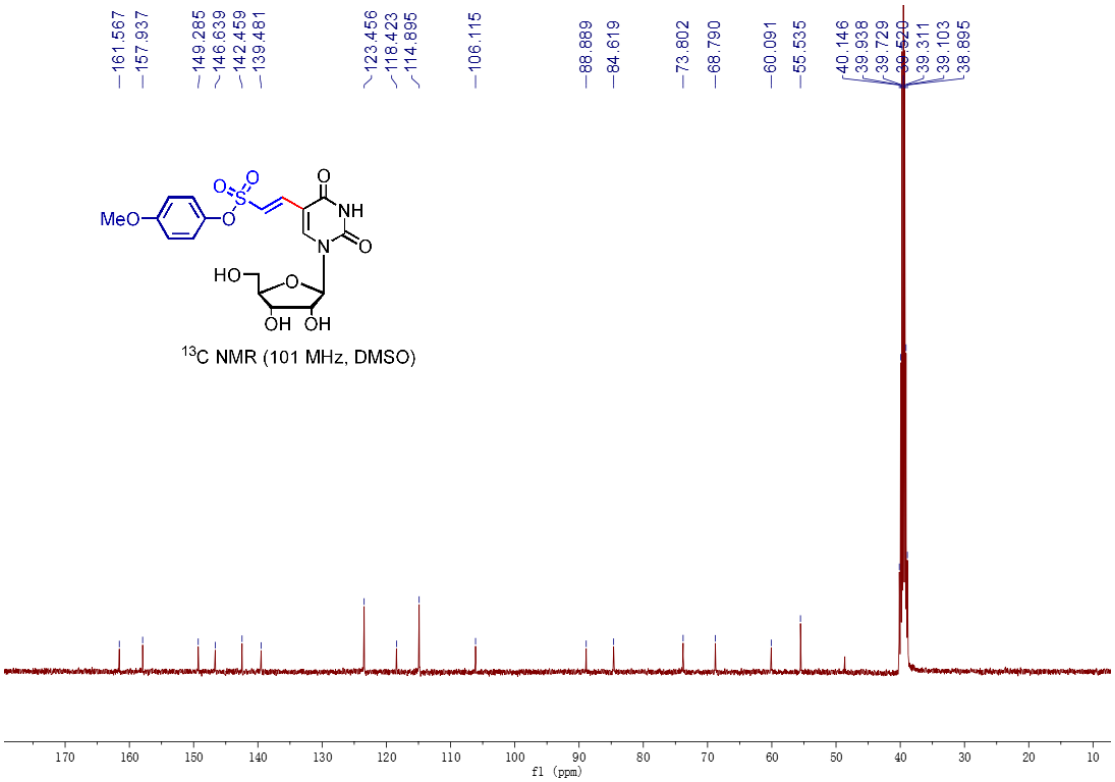


3bj

^{13}C NMR (101 MHz, MeOD)



^{1}H NMR (400 MHz, DMSO)



^{13}C NMR (101 MHz, DMSO)