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Supporting information for article:

Influence of the fluorine substitution on the molecular conformation of 3′-deoxy-3′-fluoro-5-methyluridine

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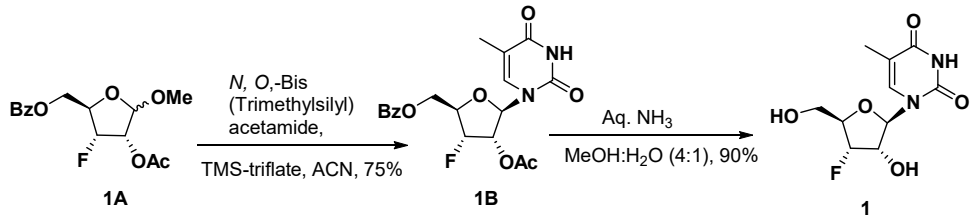
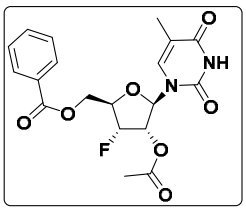
Synthesis of $^{R}T^{F}$

Coupling of 3′-deoxy-3′-fluoro-1-*O*-methyl-5′-*O*-benzoyl-2′-*O*-acetyl-D-ribofuranose **1A** with silylated base thymine by Vorbrüggen glycosylation in the presence of TMS-triflate, gave selectively β-nucleoside derivatives **1B** (75%). Compound **1B** then subjected to ammonolysis to give 3′-deoxy-3′-fluoro ribothymidine **1** $^{R}T^{F}$ (90%) (Scheme1).



Scheme 1: Synthesis of $^{R}T^{F}$

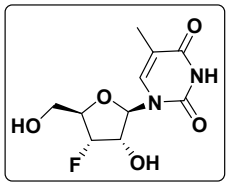
2′-*O*-acetyl-5'-*O*-benzoyl-3'-deoxy-3'-fluoro-thymidine (1B)



Under N_2 atmosphere *N,O*-Bis(trimethylsilylacetamide) (0.63mL, 0.52g, 2.54mmol) was added to a stirred solution of compound **1A** (0.5g, 1.79mmol) and Thymine (0.35g, 2.67mmol) in dry ACN (6mL). The reaction mixture was refluxed for 1h to give a clear solution and then cooled to rt. TMS-triflate (0.78mL, 0.95g, 4.27mmol) was added to the reaction mixture and the resulting mixture was again refluxed for 3h. The reaction mixture was cooled and then concentrated to dryness under reduced pressure and redissolved in DCM (100mL), washed successively with saturated aq. $NaHCO_3$ (3 X 100mL) and H_2O (100mL), dried over Na_2SO_4 and concentrated to dryness *in vacuo*. The residue obtained was purified by column chromatography using EtOAc/Pet ether (6:4) as a solvent system. The pure compound was collected as a white foam. Yield 0.44g, 75%

Mol. Formula	**:**	$C_{19}H_{19}FN_2O_7$
Mol. Weight	**:**	406.37
ESI-Ms m/z	**:**	429.56 ($M+Na^+$)
^{1}H NMR (200MHz, $CDCl_3$)	**:**	**δH**(ppm) 1.57 (s, 3H), 2.18 (s, 1H), 4.48-4.77 (m, 3H), 5.26-5.53 (m, 2H), 6.23-6.27 (d, 1H, $J_{1',2'}$= 7.33), 7.04 (s, 1H), 7.46-7.67 (m, 3H), 8.05-8.09 (m, 2H), 9.30 (s, 1H)

3′-deoxy-3′-fluoro-2′-hydroxy-thymidine (1)



The aqueous ammonia (5mL) was added to a solution of compound **1B** (0.5g) in MeOH (10mL). The reaction mixture was stirred at rt for 3h. The solvent was removed under reduced pressure. The crude product purified by column chromatography using DCM/MeOH (9:1) and the

pure compound **1** was collected as a white solid. The obtained compound **1** recrystallizes using MeOH as a solvent. Yield 0.33g, 90%.

Mol. Formula	**:**	$C_{10}H_{13}FN_2O_5$
Mol. Weight	**:**	260.22
ESI-Ms m/z	**:**	282.97 ($M+Na^+$)
Melting Point	**:**	439 K
^{1}H NMR (400MHz, D_2O)	**:**	**δ_H** (ppm) 1.85 (s, 3H, CH_3), 3.75-3.79 (m, 2H, H5', H5''), 4.36-4.50 (m, 2H, H2', H4'), 4.99-5.14 (dd, *J*=4.27 & 54.32 Hz, 2H, H3'), 6.02 (d, 1H, H1' , *J*=7.32 Hz), 7.60 (s, 1H, H6')
^{13}C NMR (100MHz, CD_3OD)	**:**	**δ_C**(ppm) 12.4, 62.3-62.4 (d), 74.3-74.5 (d), 84.8-85.0 (d), 88.2, 93.0-94.8 (d), 112.1, 137.9, 152.9, 166.2
^{13}C-DEPT (100MHz, CD_3OD)	**:**	**δ_C**(ppm) Positive peaks: 12.4, 74.3-74.5 (d), 84.8-85.0 (d), 88.2, 92.9-94.8 (d), 137.9 Negative peaks: 62.3-62.4 (d)

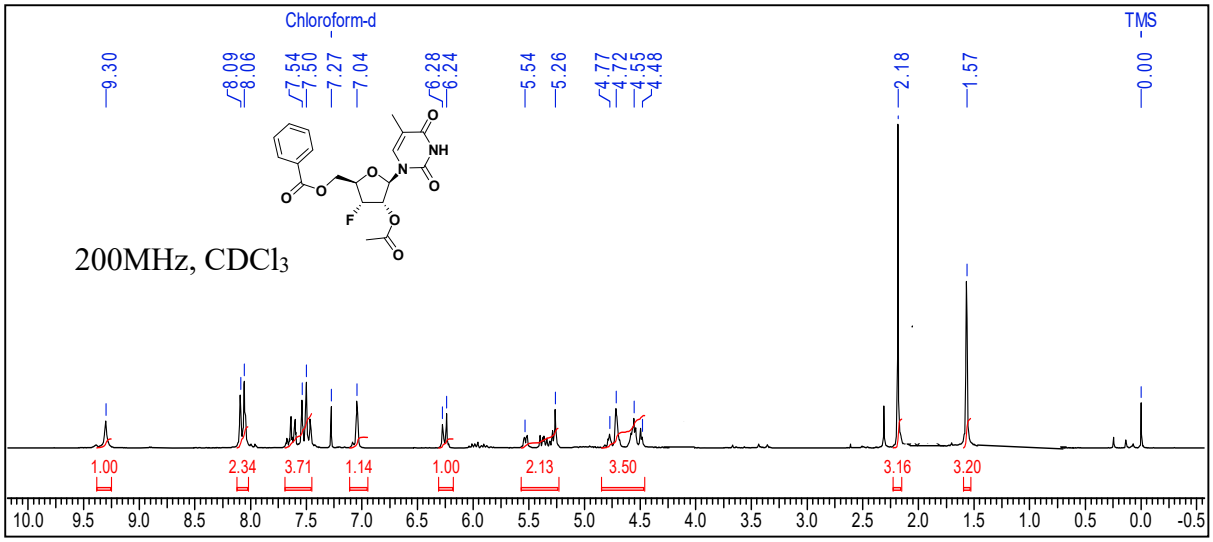


Figure S1. ^{1}H NMR spectrum of compound **1B** in $CDCl_3$.

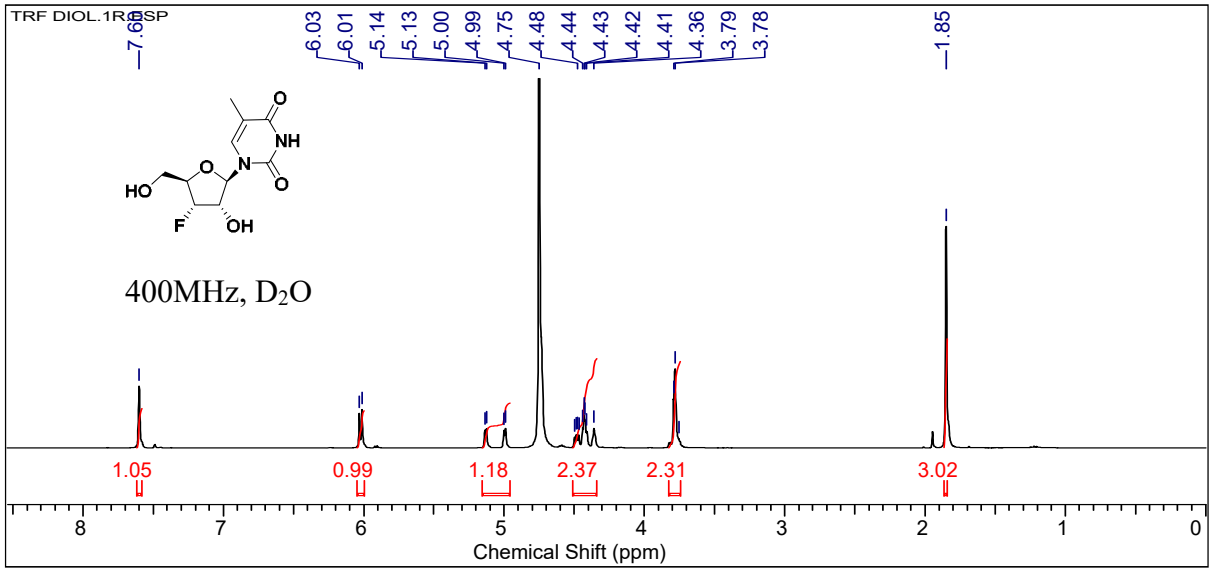


Figure S2. ^{1}H NMR spectrum of compound **1** in D_2O

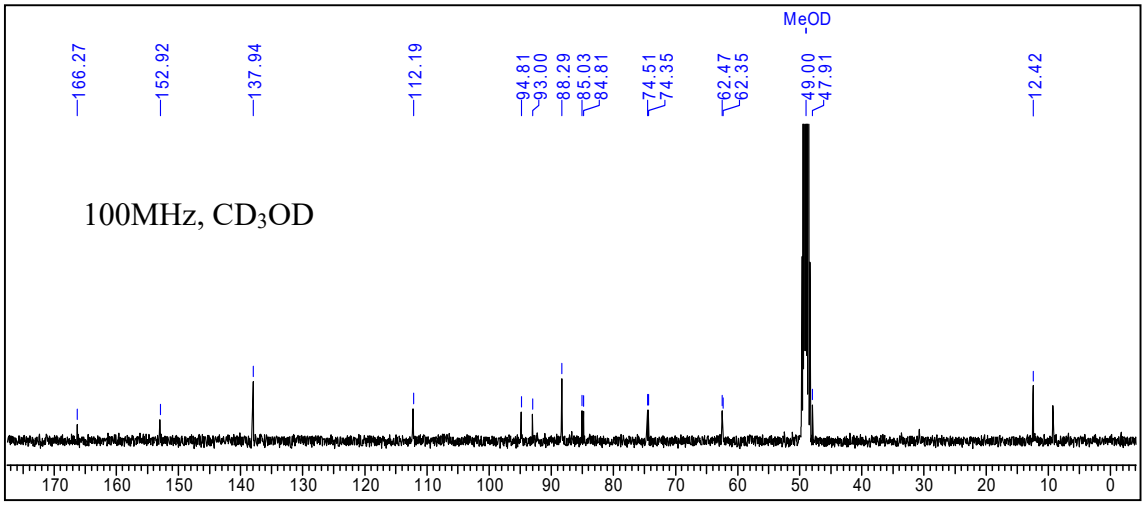


Figure S3. ^{13}C NMR spectrum of compound **1** in CD_3OD.

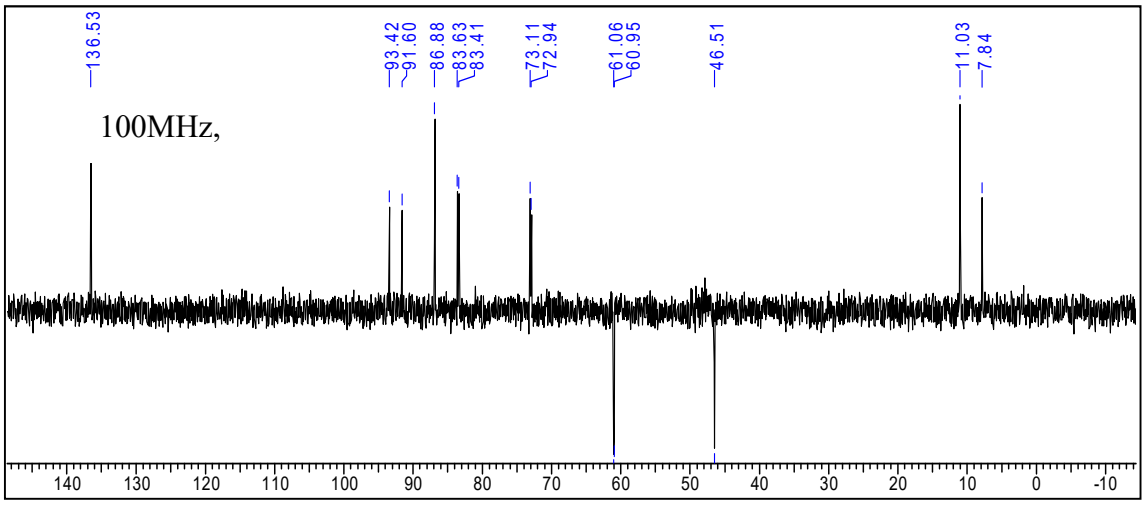


Figure S4. ^{13}C-DEPT spectrum of compound **1** in CD_3OD.

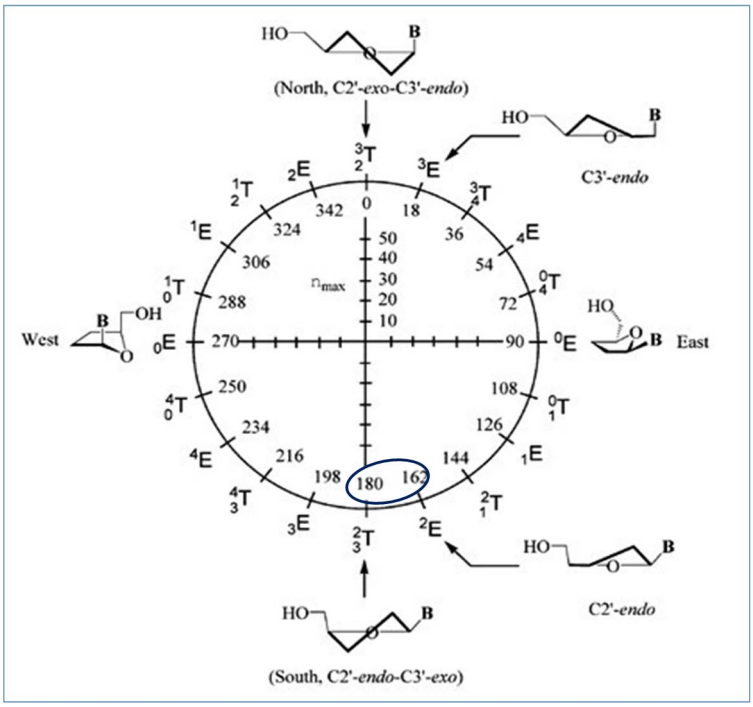


Figure S5: Pseudorotational cycle for nucleosides showing the characteristic North, South, East and West conformations. The radius of the cycle corresponds to ν_{max}. The units of P and ν_{max} values are in degrees. Envelope (E) and twist (T) forms alternate every 18°. The figure has been cited from the reference, Mathé, C. & Périgaud, C. (2008). *Eur. J. Org. Chem.* 1489-1505.