SUPPORTING INFORMATION

Synthesis and evaluation of α-thymidine analogues as novel antimalarials

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Supporting Information

Biology

Enzyme purification and enzyme assays

*Pf*TMPK purification and enzyme assays were performed as described previously.[1] The K_m of *Pf*TMPK for TMP is 11 μM. Catalytic activity was determined in 50 mM Tris-HCl, pH 7.4, 50 mM KCl, 5 mM $MgCl_2$, 0.2 mM NADH, 1 mM DTT, 1 mM phosphoenolpyruvate, 4 U pyruvate kinase, 4 U lactate dehydrogenase, 50 μM TMP, 1 mM ATP and 1 μg of purified recombinant *Pf*TMPK. In this coupled assay, TMP is first phosphorylated to TDP and the resulting ADP is phosphorylated to ATP using phosphoenolpyruvate as a phosphate donor in a reaction catalysed by pyruvate kinase. The pyruvate is then converted to lactate in a reaction catalyzed by lactate dehydrogenase which uses NADH to give NAD. This latter reaction is followed spectrophotometrically at 340 nm. Some of the active inhibitors were tested for inhibition of pyruvate kinase and lactate dehydrogenase. This assay was performed as above with ADP replacing TMP and with various concentrations of inhibitors. Inhibition constants for *Pf*TMPK were obtained using TMP as substrate and variable inhibitor concentrations. For each inhibitor five to ten concentrations (ranging from 0-200 μM) were tested in duplicate to obtain IC_{50} values using SigmaPlot hyperbolic or sigmoidal dose-response curves. The resulting values are the average of two independent experiments. The inhibition K_i values were obtained according to the equation. $K_i=IC_{50}/(1+[S]/K_m)$, which relates the concentration of competitive inhibitor which inhibits activity by 50% (IC_{50}) with the K_i value, where K_m is the Michaelis constant for inosine. If the IC_{50} is not covered in the tested concentrations, then the K_i was calculated following the equation to get an average K_i constant. $K_{i(av)}=([I]/i-[I])/(1+[S]/K_m)$, $i=1-v_i/v_0$, where [I] is the inhibitor concentration, [S] is the substrate concentration, v_i is the steady state reaction rate with inhibitors and v_0 is the steady state reaction rate without inhibitor.

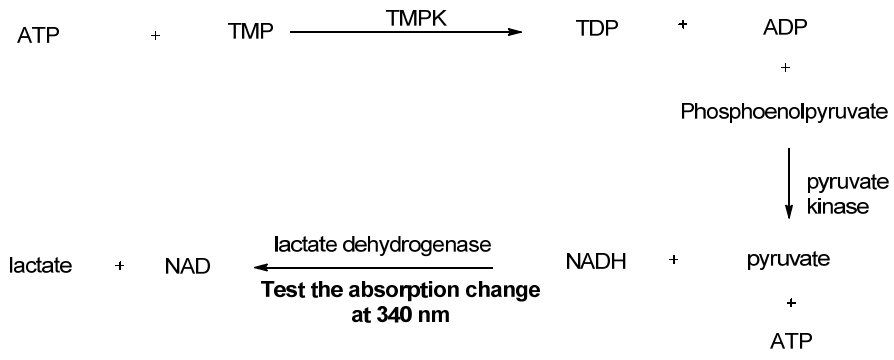

Figure S1: The coupled TMPK assay**.**

Cell based assay

In vitro activity against the erythrocytic stages of *Plasmodium falciparum* was determined by using a SYBR-green assay.[2] The parasite *P. falciparum* 3D7 was cultured using standard methods, and synchronized using 5% sorbitol as previously described.[3] Compounds were dissolved in DMSO at 100 mM and added to 48 h post-synchronization parasite cultures incubated in RPMI 1640 medium with hypoxanthine (150 μM), $NaHCO_3$ (0.2%), gentamycin (12.5 μg/mL), Albumax (0.5%), human serum (2%) and washed human red cells O^+ at 5% haematocrit (0.3% parasitaemia). Chloroquine was used as standard drug. Experiments were carried out at least twice independently and the different concentrations were tested in duplicate. After 48 h of growth, 100 μl of SYBR-green I (Molecular Probes) in lysis buffer (20 mM Tris-HCl pH 7.5, 5 mM EDTA, 0.008 % saponin, 0.08 % triton X-100 containing 0.2 μl of SYBR-green/ml of lysis buffer) was added to each well, and mixed and after 1 h of incubation in the dark at RT, fluorescence was measured with excitation and emission wavelength bands centred at 485 and 530 nm. The percentage inhibition of each compound at each concentration was determined. EC_{50} values were calculated from hyperbolic or sigmoidal dose-response curves using Sigmaplot 10.0. The EC_{50} values are the means of two independent assays. For the cell viability assay, MRC5 cells were seeded at 2000 cells per well in a volume of 200 μl of DMEM containing 10% FCS and allowed to adhere for 24 h prior to use. The MRC5 cells assay was performed as described.[4] EC_{50} values represent the concentration of compounds reducing *P. falciparum* growth by 50%. CC_{50} values stand for the concentration of compounds reducing MRC5 cells growth by 50%.

Crystallography

Crystallisation, data collection and data processing

Crystals of three different inhibitor complexes of *Pf*TMPK were obtained using hanging drop (**53**) and sitting drop (**28** and **30**) vapour diffusion with a 1:1 mixture of protein solution and reservoir solution in the drop (Table S1). The dimensions of the crystals of the complex with **53** were about 100 × 100 × 150 μm^3, while those with **28** and **30** had a brick-like shape with dimensions about 50 × 50 × 150 μm^3 and 100 × 100 × 300 μm^3, respectively. Prior to data collection, the crystals were vitrified at 120 K in a cryoprotectant solution. X-ray data sets for the three complexes were collected at the ESRF in Grenoble and processed with *MOSFLM*.[5] Other computations were made with the CCP4 suite unless otherwise stated.[6] The data collection and refinement parameters are summarised in Table S2.

Table S1. Crystallisation conditions for the three *Pf*TMPK inhibitor complexes.

Complex	**53**	**30**	**28**
Protein solution at 10 mg ml^{-1}	50 mM Tris pH 8.5, 0.2 M NaCl, 2 mM compound **53** (5% DMSO)	50 mM Tris pH 8.5, 0.1 M NaCl, 2 mM compound **30** (5% DMSO)	50 mM Tris pH 8.5, 0.1 M NaCl, 2 mM compound **31** (5% DMSO)
Reservoir solution	Optimisation of Index H4: 0.2 M tri-Ammonium Citrate pH 7.0, 25% PEG3350	Index D7: 0.1 M Bis-Tris pH 6.5, 25% PEG3350	Pact C9: 0.1 M Hepes pH 7.0, 0.2 M LiCl, 20% PEG6000
Cryo-protectant solution	50 mM Tris pH 8.5, 0.1 M NaCl, 1 mM compound **53**, 0.2 M tri-Ammonium Citrate pH 7.0, 30% PEG3350	50 mM Tris pH 8.5, 0.1 M NaCl, 0.8 mM compound **30**, 0.1 M Bis-Tris pH 6.5, 30% PEG3350	50 mM Tris pH 8.5, 0.1 M NaCl, 0.4 mM compound **30**, 0.1 M Hepes pH 7.0, 0.2 M LiCl, 28% PEG6000

Table S2. Data processing and refinement statistics for the three complexes.

Protein complex	**53**	**30**	**28**
PDB Code	2YOF	2YOH	2YOG
ESRF beamline	ID23-1	ID14-2	ID14-2
Wavelength	0.9760	0.9330	0.9330
Resolution limits (Å) [a]	51.29 – 1.82 (1.92 – 1.82)	25.09 – 1.60 (1.69 – 1.60)	23.37 – 1.50 (1.58 – 1.50)
Space Group	$P3_121$	$P2_1$	$P2_1$
Cell dimensions (Å)	*a* = 109.64 *c* = 121.89	*a* = 49.26 *b* = 58.43 *c* = 71.83 β = 96.11	*a* = 49.06 b = 58.79 *c* = 71.71 β = 95.78
No. unique reflections [a]	76207 (10991)	53617 (7803)	64980 (9435)
Completeness [a]	100.0 (100.0)	100.0 (100.0)	99.9 (100.0)
Multiplicity [a]	10.6 (10.0)	3.7 (3.7)	3.5 (3.5)
R-merge [a]	0.115 (0.977)	0.071 (0.712)	0.077 (0.803)
I / σ(I) [a]	12.9 (2.2)	11.7 (1.7)	9.2 (1.4)
R-factor / R-free	0.189 / 0.231	0.162 / 0.219	0.182 / 0.233
Rmsd bond lengths (Å)	0.020	0.021	0.016
Rmsd angles (º)	1.400	1.428	1.465
Rmsd chiral volumes ($Å^3$)	0.099	0.105	0.102
Ramachandran outliers (%)	0.86	1.10	1.16
$B_{average}$ protein atoms ($Å^2$)	28.0	21.9	20.8
$B_{average}$ ligand atoms ($Å^2$)	33.4	21.6	22.5
$B_{average}$ water molecules ($Å^2$) [b]	37.5 (645)	33.2 (439)	33.5 (434)

[a] Highest resolution shell statistics given in parentheses;
[b] Number of molecules in parentheses.

Structure solution and refinement

The structures of *Pf*TMPK complexed with **30** and **53** were solved by molecular replacement with *MOLREP* using unliganded *Pf*TMPK (PDB code 2WWF) as a search model. For **53** the space group was $P3_121$ with three molecules in the asymmetric unit, while for **30** the space group was $P2_1$ with two independent molecules. The complex of **28** was isomorphous to that of **30** which was

therefore used as a starting model. Refinement was carried out using *REFMAC*.[7] 5% of the data were excluded for R-free calculations. Manual rebuilding was carried using *COOT*[8] and the inhibitor molecules were added to the model (Table S3). Dictionaries for all of the nucleotide ligands were made using *PRODRG*.[9]

Table S3. Ligand binding in the structures of the three complexes. The quality of the density for each ligand, and the degree of order in the N-terminal and active site loops of the enzymes are summarised.

Ligand	Protein Chain	Active site	N-terminal loop	Active site loop
53	**A**	The ligand has two alternative conformations and is positioned where the active site loop is in chain C.	Ordered and closely packed against the ligand.	141-149 disordered
	B	The best density for this ligand in the three chains. **53** is positioned where the active site loop is in chain C.	Present. Close distance to ligand.	143-149 disordered
	C	The ligand has two alternative conformations. There is no density for the aromatic ring, which appears to point in the opposite direction to that seen in chains in A & B. This is related to the ordering of the active site loop e.	Folded differently than in A & B, due to the presence of the active site loop	Present
30	**A**	The ligand is most highly ordered in this chain and interacts with the N-terminal loop. There is only low density for the NO_2 moiety	Present	142-149 disordered
	B	Two alternative conformations, with no density for the ring in either. The N-terminal loop interacts with one of the two conformations, as in chain A. The NO_2 is stabilised by an interaction with Lys5 from a symmetry related molecule.	Present (Arg18 with low density)	143-150 disordered
28	**A**	The ligand has well defined density.	Present (Arg18 with low density)	141-151 disordered
	B	Very well defined ligand density. There is a clear interaction of the CF_3 group with Arg47.	Residues 17-20 disordered	142-152 disordered

The rmsd in Cα positions is 0.52 (199), 0.48 (197) and 0.63 Å (195) when superposing the structures of Chains A of the **28**, **30** and **53** complexes respectively on that of the TMP-ADP complex (Figures S2 and S3). The numbers in brackets are the number of residues in equivalent positions, and vary slightly with the loop disorder.

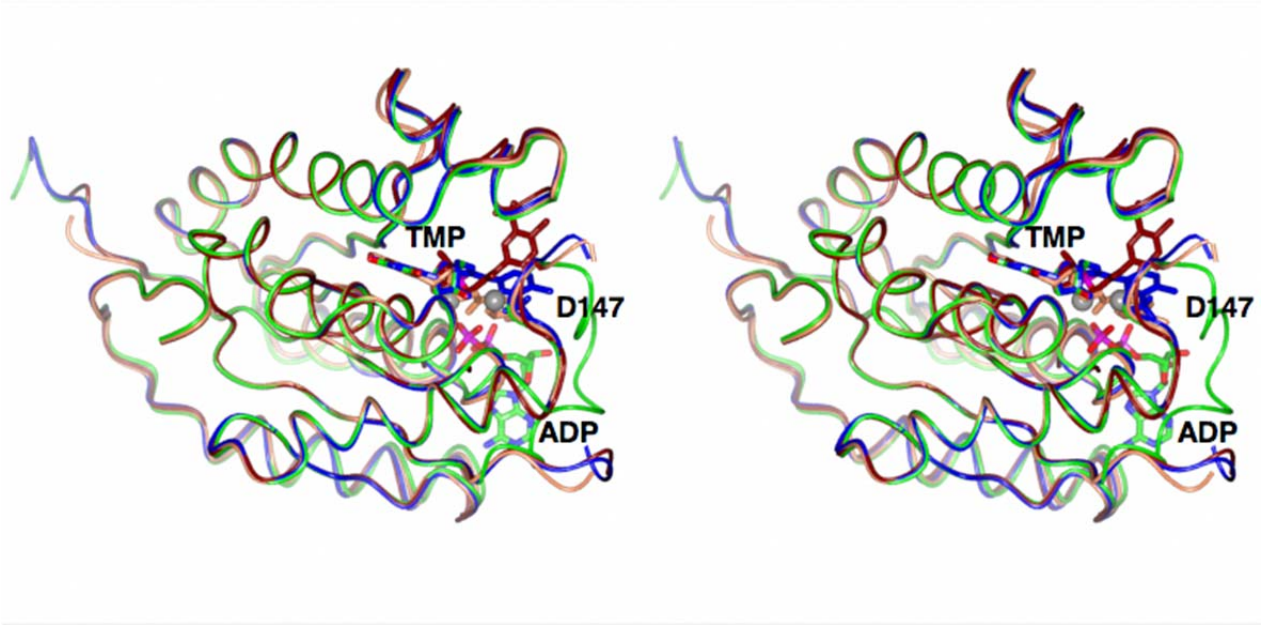

Figure S1. Stereo view of the superposition of three ligand complexes **53** (Chain B, blue), **30** (Chain A, coral) and **28** (Chain B, tan) on that of the TMP-ADP complex (green) determined previously (pdb: 1wwf). For the complexes the chain was selected in which the ligand was best ordered. The ADP and TMP are coloured by atom, the three ligands as for the parent chains. The two sodium atoms in the TMP-ADP complex are shown as spheres.

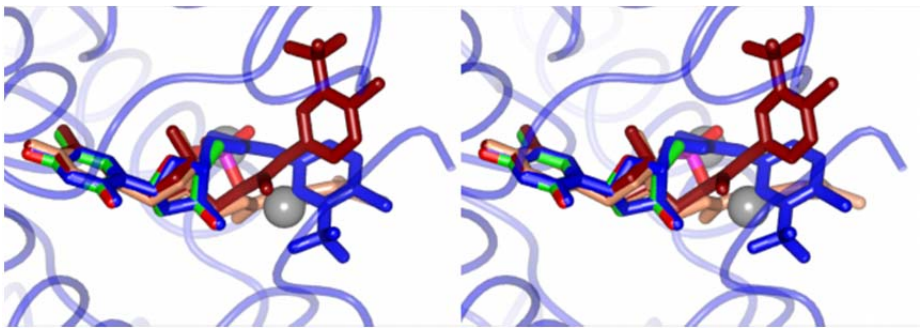

Figure S2: Close up of the superposition shown in Figure S1. This corresponds to the mono view in Figure 3A of the main text.

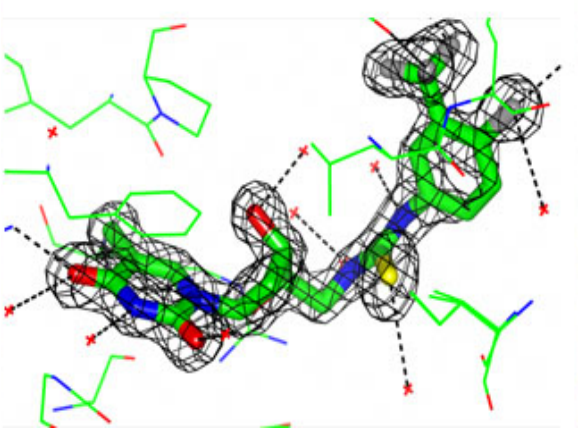

Figure S3: The electron density in the maximum likelihood weighted map around **28**. There is excellent density for essentially all the ligand, though at a lower level for the edge of the aromatic ring. The fluorine atoms are well defined. The side chains of the residues that contact the ligand are shown.

In vitro DMPK

Intrinsic clearance (C_{Li}) experiments

Test compound (0.5 μM) was incubated with female CD1 mouse liver microsomes (Xenotech LLC™; 0.5 mg/ml 50 mM potassium phosphate buffer, pH7.4) and the reaction started with addition of excess NADPH (8 mg/ml 50 mM potassium phosphate buffer, pH7.4). Immediately, at time zero, then at 3, 6, 9, 15 and 30 minutes an aliquot (50 μl) of the incubation mixture was removed and mixed with acetonitrile (100 μl) to stop the reaction. Internal standard was added to all samples, the samples centrifuged to sediment precipitated protein and the plates then sealed prior to UPLCMSMS analysis using a Quattro Premier XE (Waters Corporation, USA).

XLfit (IDBS, UK) was used to calculate the exponential decay and consequently the rate constant (k) from the ratio of peak area of test compound to internal standard at each timepoint. The rate of intrinsic clearance (C_{Li}) of each test compound was then calculated using the following calculation:

$$C_{Li}\ (\text{ml/min/g liver}) = k \times V \times \text{Microsomal protein yield}$$

Where V (mL/mg protein) is the incubation volume/mg protein added and microsomal protein yield is taken as 52.5 mg protein/ g liver. Verapamil (0.5 μM) was used as a positive control to confirm acceptable assay performance.

Plasma protein binding experiments

In brief, a 96-well equilibrium dialysis apparatus was used to determine the free fraction in plasma for each compound (HT Dialysis LLC, Gales Ferry, CT). Membranes (12-14 kDa cut-off) were conditioned in deionised water for 60 min, followed by conditioning in 80:20 deionised water:ethanol for 20 min, and then rinsed in isotonic buffer before use. Female CD1 mouse plasma was removed from the freezer and allowed to thaw on the day of experiment. Thawed plasma was then centrifuged (Allegra X12-R, Beckman Coulter, USA), spiked with test compound (10 μg/g), and 150 μl aliquots (n = 6 replicate determinations) loaded into the 96-well equilibrium dialysis plate. Dialysis vs isotonic buffer (150 μl) was carried out for 5 h in a temperature controlled incubator at *ca.* 37ºC (Barworld Scientific Ltd, UK) using an orbital microplate shaker at 125 revolutions/minute (Barworld Scientific Ltd, UK). At the end of the incubation period, aliquots of plasma or buffer were transferred to micronic tubes (Micronic B.V., The Netherlands) and the

composition in each tube balanced with control fluid, such that the volume of buffer to plasma is the same. Sample extraction was performed by the addition of 400 µl of acetonitrile containing an appropriate internal standard. Samples were allowed to mix for 1 minute and then centrifuged at 3000 rpm in 96-well blocks for 15 min (Allegra X12-R, Beckman Coulter, USA). All samples were analysed by means of UPLC-MS/MS on a Quattro Premier XE Mass Spectrometer (Waters Corporation, USA). The unbound fraction was determined as the ratio of the peak area in buffer to that in plasma.

Chemistry

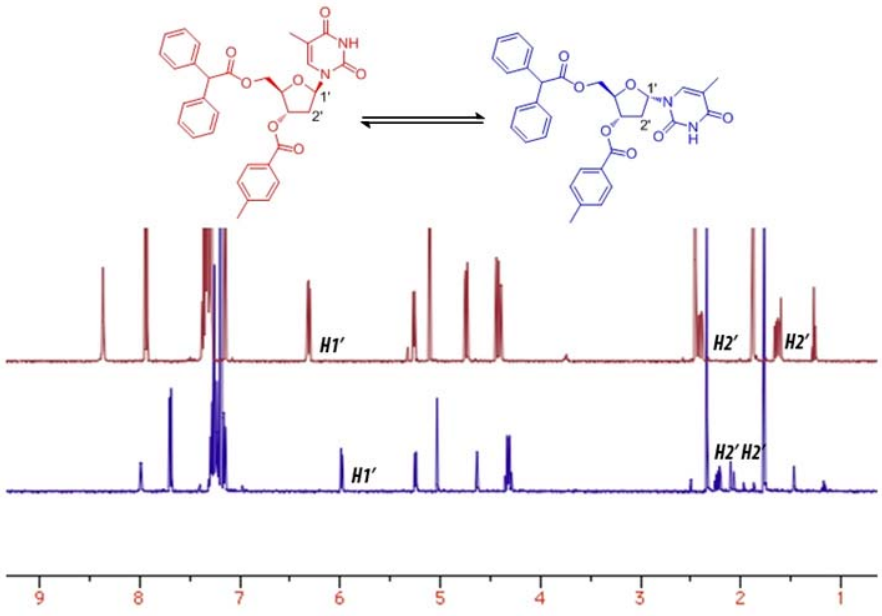

Figure S4: NMR spectra of compounds 3 and 4. The diagram shows the chemical shifts of H1' and H2'.

5'-*O*-diphenylacetyl-β-thymidine (2): To a solution of β-thymidine (1g, 4.38 mmol) in dry pyridine (32 ml) under Ar at 0°C, was added dropwise to a solution of 2, 2-diphenylacetyl chloride (1g, 4.38 mmol) dissolved in 3 ml DCM. The mixture was left under stirring for 1.5 h and the reaction was allowed to warm to room temperature. After that, water (50 ml) was added then extracted with DCM (2 × 50 ml). The organic phase was washed with 3N HCl (50 ml, 50 ml) and with a saturated solution of $NaHCO_3$ (2 × 50 ml) to neutralize. The organic layer was then dried with $MgSO_4$ and the solvent was evaporated. The residue was purified by chromatography using 2% MeOH/DCM to yield compound **2** 886 mg (50%) as a solid. ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.22-7.30 (m, 10H, *H*-Ph), 7.11 (s, 1H, *H6*), 6.15 (t, J = 5.96 Hz, 1H, *H1'*), 5.02 (s, 1H, C*H*-Ph), 4.47 (dd, J_1 = 12.21 Hz, J_2 = 4.84 Hz, 1H, *H5'*), 4.30 (dd, J_1 = 12.20 Hz, J_2 = 3.10 Hz, 1H, *H5'*), 4.12-4.17 (m, 2H, *H3'* and *H4'*), 2.20 (m, 1H, *H2'*), 1.82 (s, 3H, *H7*), 1.68 (m, 1H, *H2'*); ^{13}C-NMR (125MHz, $CDCl_3$): δ 176.3 (*C6'*), 168.1 (*C4*), 154.4 (*C2*), 141.9 (*C*-Ph), 139.1 (*C6*), 132.7, 132.6, 132.4, 131.5, 131.4 (*C*-Ph), 114.9 (*C5*), 89.0 (*C1'*), 88.3 (*C4'*), 75.1 (*C3'*), 68.5 (*C5'*), 61.1 (*C*-C-

Ph), 43.9 (*C2'*), 16.3 (*C7*); LCMS (ES^+): m/z (%) 437 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{24}H_{25}N_2O_6$ $[M+H]^+$ 437.1707 *m*/*z*, found 437.1711 *m*/*z* (-0.91 ppm).

3'-*O*-*p*-toluoyl-5'-*O*-diphenylacetyl-β-thymidine (3): To a solution of **2** (1.143 g, 2.6 mmol) in dry pyridine/DCM (18 ml / 3 ml), was added dropwise a solution of *p*-toluoyl chloride (616 mg, 4 mmol) liquid. The mixture was left under Ar and stirring for 3 h. After this, water (50 ml) was added, then extracted with DCM (2×50 ml). The organic phase was washed with 3N HCl (2×50 ml), and then washed with saturated solution of $NaHCO_3$ (2×50 ml). The organic phase was then dried with $MgSO_4$ and the solvent was evaporated. The residue was purified by chromatography. The final product **3** was 0.8 g (55.6 %) as a solid. ^{1}H-NMR (500MHz, $CDCl_3$): δ 8.36 (s, 1H, NH), 7.39 (d, J = 8.28 Hz, 2H, *H*-Ph), 7.27-7.37 (m, 10H, *H*-Ph), 7.14 (s, 1H, *H6*), 6.32 (dd, J_1 = 9.25 Hz, J_2 = 5.28Hz, 1H, *H1'*), 5.26 (d, J = 6.64 Hz, *H3'*), 5.11 (s, 1H, C*H*-Ph), 4.74 (dd, J =12.13 Hz, J = 4.01 Hz, 1H, *H4'*), 4.39-4.43 (m, 2H, *H5'*), 2.45 (s, 3H, CH_3), 2.40 (dd, J_1 =14.28 Hz, J_2 =6.47 Hz, 1H, *H2'*), 1.88 (s, 3H, *H7*), 1.64 (m, 1H, *H2'*); ^{13}C-NMR (125MHz, $CDCl_3$): δ 171.9 (*C*O), 166.1 (*C*O), 163.0 (*C4*), 149.9 (*C2*), 144.7, 138.1, 129.8, 129.3, 128.9, 128.8, 128.5, 128.5, 127.7, 127.6, 126.3 (*C*-Ph), 134.6 (*C6*), 111.3 (*C5*), 84.8 (*C1'*), 82.5 (*C4'*), 74.7 (*C3'*), 64.5 (*C5'*), 57.4 (*C*-C-Ph), 37.2 (*C2'*), 21.7 (*C*H_3), 12.6 (*C7*); LCMS (ES^+): m/z (%) 555 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{32}H_{31}N_2O_7$ $[M+H]^+$ 555.2126 *m*/*z*, found 555.2104 *m*/*z* (4.00 ppm).

3'-*O*-*p*-toluoyl-5'-*O*-diphenylacetyl-α-thymidine (4): To a solution of **3** (440 mg, 0.8 mmol) in 2 ml dry CH_3CN was added the freshly prepared solution containing H_2SO_4 (1.66 mmol, 0.088 ml) and acetic anhydride (5.5 mmol, 0.519 ml) in 2 ml dry CH_3CN. After 1.5-2 h, the mixture was quenched with saturated $NaHCO_3$ solution, and extracted with EtOAC for three times. The alpha-anomer was can be easily crystallized from the ethanol solution of the mixture, giving at least compound **4** α-anomer 160 mg (51%) as a solid. ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.99 (s, 1H, N*H*), 7.69 (d, J = 8.21 Hz, 2H, *H*-Ph), 7.14-7.30 (m, 8H, *H*-Ph and *H6*), 5.99 (dd, J_1 = 7.21 Hz, J_2 = 1.89 Hz, 1H, *H1'*), 5.25 (d, J = 6.48 Hz, 1H, *H3'*), 5.03 (s, 1H, C*H*-Ph), 4.63 (t, J = 3.60, 1H, *H4'*), 4.32 (m, 2H, *H5'*), 2.34 (s, 3H, CH_3), 2.23 (m, 1H, *H2'*); 2.09 (d, J = 15.45 Hz, 1H, *H2'*), 1.77 (s, 3H, CH_3); ^{13}C-NMR (125MHz, $CDCl_3$): δ 171.9 (*C*O), 166.1 (*C*O), 163.5 (*C4*), 150.2 (*C2*), 144.6, 138.04, 138.02, 129.8, 129.3, 129.0, 128.8, 128.54, 128.5, 127.8, 127.6, 126.2 (*C*-Ph), 134.6 (*C6*), 111.4 (*C5*), 84.7 (*C1'*), 82.5 (*C4'*), 74.8 (*C3'*), 64.6 (*C5'*), 57.4 (*C*-C-Ph), 37.1 (*C2'*), 21.8 (*C*H_3), 12.7 (*C*H_3); LCMS (ES^+): m/z (%) 555 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{32}H_{31}N_2O_7$ $[M+H]^+$ 555.2126 *m*/*z*, found 555.2112 *m*/*z* (2.41 ppm).

α-Thymidine (5): Compound **4** (2mmol) was dissolved in a solution of 0.2 M NaOMe in 40 ml Methanol. The reaction was stirred at room temperature until the disappearance of the starting material (around 3 h) was observed by TLC. The solution was neutralized by Dowex ion exchanged resin (washed by methanol before use) to be pH 6.0. The resin was filtered and washed twice with methanol, water and some DCM too. The methanol and DCM was evaporated and the precipitation was formed and filtered to get rid of them. The water was evaporated to get the pure final product **5** 436 mg (90%) as a solid. ^{1}H-NMR (500MHz, D_2O): δ 8.32 (s, 1H, N*H*), 7.62 (s, 1H, *H6*), 6.04 (s, 1H, *H1'*), 4.26, 4.30 (s, 2H, *H3'* and *H4'*), 3.58 (d, *J* = 12.35 Hz, *H5'*), 3.49 (d, *J* = 11.73 Hz, *H5'*), 2.59 (m, 1H, *H2'*), 2.04 (d, *J* = 14.82 Hz, *H2'*), 1.77 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, D_2O): δ 170.9 (*C4*), 166.7 (*C2*), 151.5 (*C6*), 138.0 (*C5*), 110.5 (*C1'*), 88.5 (*C4'*), 70.5 (*C3'*), 61.4 (*C5'*), 39.4 (*C2'*), 11.5 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 243 (100) [M+H]$^+$, 485 (52) [2M+H]$^+$; HRMS (ES$^+$): calcd for $C_{10}H_{15}N_2O_5$ [M+H]$^+$ 243.0975 *m*/*z*, found 243.0982 *m*/*z* (-2.77 ppm).

5'-*O*-methanesulfonyl-α-thymidine (6): To a solution of α-thymidine (484 mg, 2 mmol) in pyridine (8 ml) and DCM (1 ml) at -38 °C (dry ice in ethanol), methanesulfonyl chloride (154 µl, 2 mmol) in 1 ml dry DCM was added drop by drop. The reaction mixture was stirred 1 h at -38 °C, then stirred another 2 h at 0 °C. The reaction was quenched by adding 10 ml H_2O. The product was transferred to a flask to evaporate the water, DCM and pyridine. Toluene was added to co-evaporate to remove pyridine. The residue was purified by column chromatography to get a pure product **6** 272.2 mg (42.5%) as a solid. ^{1}H-NMR (500MHz, MeOD): δ 7.75 (s, 1H, *H6*), 6.19 (m, 1H, *H1'*), 4.45 (m, 1H, *H4'*), 4.35 (m, 1H, *H5*'), 4.26 (m, 1H, *H5'*), 4.19 (m, 1H, *H3'*), 3.27 (s, 3H, C*H*$_3$), 2.67 (m, 1H, *H2'*), 2.06 (m, 1H, *H2'*), 1.86 (s, 3H, CH_3); ^{13}C-NMR (125MHz, MeOD): δ 162.8 (*C4*), 152.4 (*C2*), 138.7 (*C6*), 111.1 (*C5*), 72.5 (*C1'*), 72.2 (*C4'*), 70.7 (*C3'*), 64.4 (*C5'*), 41.1 (*C2'*), 37.3 (*C*H$_3$), 12.6 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 321 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{11}H_{17}N_2O_7S_1$ [M+H]$^+$ 321.0751 *m*/*z*, found 321.0766 *m*/*z* (-4.55 ppm).

5'- azido-5'-deoxy-α-thymidine (7): A solution of compound **6** (3 mmol) and NaN_3 (6 mmol) in 30 ml dry DMF was heated to 60 °C overnight. The reaction mixture was evaporated *in vacuum* and can co-evaporate with ethanol and toluene (temperature not above 60 °C). Then the solution was cooled and get rid of the insoluble, this is the waste need to neutralize with 20% $NaNO_2$ solution to pH 6. Then the soluble solution was co-evaporated with ethanol and toluene again. The solution was put to high vacuum to evaporate the left DMF overnight. The crude product was purified by column chromatography to yield compound **7** 344 mg (43.1 %) as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.30 (s, 1H, N*H*), 7.76 (s, 1H, *H6*), 6.16 (m, 1H, *H1'*), 5.53 (d, *J* = 3.07 Hz, 1H, O*H*),

4.28 (m, 1H, *H4'*), 4.17 (m, 1H, *H3'*), 3.40 (m, 2H, *H5'*), 2.61 (m, 1H, *H2'*), 1.96 (m, 1H, *H2'*), 1.79 (s, 1H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 150.5 (*C2*), 136.8 (*C6*), 109.0 (*C5*), 85.9 (*C1'*), 84.7 (*C4'*), 70.7 (*C3'*), 51.5 (*C5'*), 39.1 (*C2'*), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 268 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{10}H_{14}N_5O_4$ [M+H]$^+$ 268.1040 *m/z*, found 268.1029 *m/z* (3.99 ppm).

5'-amino-5'-deoxy-α-thymidine (8): A solution of azide **7** (515 mg, 2 mmol) in 50ml methanol was hydrogenated under atmospheric pressure for 3 h in the presence of 10% Pd/C (100 mg, 5%mol). After 3 h, TLC checked the disappearance of compound **7**. Then the catalyst was removed by filtration through celite and the filtrate was evaporated to yield pure compound **8** 457 mg (94.8 %) as a solid. ^{1}H-NMR (500MHz, DMSO): δ 7.74 (s, 1H, *H6*), 6.09 (m, 1H, *H1'*), 5.31 (s, 1H, O*H*), 4.19 (m, 1H, *H4'*), 4.07 (m, 1H, *H3'*), 3.35 (m, 1H, *H5'*), 3.17 (s, 1H, *H5'*), 2.54 (m, 1H, *H2'*), 1.90 (m, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); LCMS (ES$^+$): m/z (%) 242 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{10}H_{16}N_3O_4$ [M+H]$^+$ 242.1135 *m/z*, found 242.1132 *m/z* (1.09 ppm).

General Procedure for compounds 9 - 30

For the synthesis of compounds **9 - 30**, compound of amine **8** (1eq.) was dissolved in DMF at 0 °C. The coupling reagents (1.1 eq.) were added and the reaction mixture was allowed to stir at room temperature for 3 h. After the completion of the reaction, the reaction mixture was evaporated to dry (ethanol and toluene were used to co-evaporate) and the residue was purified by column chromatography to yield the compounds **9 - 30** as a solid with the yields ranging from 45 % to 89 %.

5'-(4-nitrophenyl)sulfonamido-5'-deoxy-α-thymidine (9): 4-Nitrobenzolsulfonyl chloride reacted with amine **8** to yield compound **9** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.23 (s, 1H, N*H*), 8.41 (d, *J* = 8.7 Hz, 2H, *H*-Ph), 8.31 (s, 1H, N*H*), 8.05 (d, *J* = 8.7 Hz, 2H, *H*-Ph), 7.66 (s, 1H, *H6*), 5.97 (qt, *J* = 3.81 Hz, 1H, *H1'*), 5.47 (s, 1H, O*H*), 4.08-4.14 (m, 2H, *H3'* and *H4'*), 2.99 (qt, *J* = 6.16 Hz, 1H, *H5'*), 2.88 (qt, *J* = 6.76 Hz, 1H, *H5'*), 2.54 (d, *J* = 6.15 Hz, 1H, *H2'*), 1.85-1.89 (m, 1H, *H2'*), 1.76 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 150.4, 149.5 (*C*-Ph), 146.3 (*C2*), 136.7 (*C6*), 128.0, 124.5 (*C*-Ph), 108.9 (*C5*), 85.9 (*C1'*), 84.5 (*C4'*), 70.6 (*C3'*), 44.4 (*C5'*), 39.0 (*C2'*), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 449 (100) [M+Na]$^+$; HRMS (ES$^+$): calcd for $C_{16}H_{19}N_4O_8S_1$ [M+H]$^+$ 427.0918 *m/z*, found 427.0923 *m/z* (-1.17 ppm).

5'-(2-naphthyl)sulfonamido-5'-deoxy-α-thymidine (10): 2-Naphthalenesulfonyl chloride reacted with amine **8** to yield compound **10** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.23 (s, 1H, N*H*),

8.44 (s, 1H, N*H*), 8.13-8.17 (m, 2H, *H*-Ph), 8.04 (d, *J* = 7.85 Hz, 2H, *H*-Ph), 7.84 (qt, *J* = 3.40 Hz, 1H, *H*-Ph), 7.66-7.72 (m, 3H, *H6*, *H*-Ph and *H*-Ph), 6.07 (qt, *J* = 3.17 Hz, 1H, *H1'*), 5.45 (s, 1H, O*H*), 4.12-4.17 (m, 2H, *H3'* and *H4'*), 2.91 (qt, *J* = 6.23 Hz, 1H, *H5'*), 2.83 (qt, *J* = 6,61 Hz, 1H, *H5'*), 2.53-2.56 (m, 1H, *H2'*), 1.85-1.89 (m, 1H, *H2'*), 1.78 (s, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 150.4 (*C2*), 137.5 (*C6*), 136.8, 134.1, 131.7, 129.3, 129.1, 128.7, 127.8, 127.5, 127.3, 122.2 (*C*-Ph), 108.8 (*C5*), 86.3 (*C1'*), 84.7 (*C4'*), 70.7 (*C3'*), 44.5 (*C5'*), 39.0 (*C2'*), 12.3 (*C*H_3); LCMS (ES$^+$): m/z (%) 432 (74) $[M+H]^+$, 306 (100) $[M+C_{10}H_7]^+$; HRMS (ES$^+$): calcd for $C_{20}H_{22}N_3O_6S_1$ $[M+H]^+$ 432.1224 *m/z*, found 432.1227 *m/z* (-0.83 ppm).

5'-(2-naphthyl)amido-5'-deoxy-α-thymidine (11): 2-Naphthoyl chloride reacted with amine **8** to yield compound **11** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.28 (s, 1H, N*H*), 8.82 (t, *J* = 5.80 Hz, 1H, N*H*), 7.94-8.04 (m, 5H, *H*-Ph), 7.79 (s, 1H, *H6*), 7.58-7.65 (m, 2H, *H*-Ph), 6.22 (qt, *J* = 3.55 Hz, 1H, *H1'*), 5.49 (s, 1H, O*H*), 4.36 (t, *J* = 6.35 Hz, 1H, *H3'*), 4.30 (d, *J* = 5.75 Hz, 1H, *H4'*), 3.41 (m, 2H, *H5'*), 2.60-2.66 (m, 1H, *H2'*), 1.90-1.96 (m, 1H, *H2'*), 1.77 (s, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): δ 166.5 (*C*O), 163.8 (*C4*), 150.9 (*C2*), 137.0 (*C6*), 134.1, 132.1, 131.5, 129.2, 128.8, 127.9, 127.6, 127.5, 126.7, 124.1 (*C*-Ph), 108.6 (*C5*), 86.6 (*C1'*), 84.8 (*C4'*), 71.0 (*C3'*), 41.4 (*C5'*), 39.0 (*C2'*), 12.4 (*C*H_3); LCMS (ES$^+$): m/z (%) 396 (100) $[M+H]^+$; HRMS (ES$^+$): calcd for $C_{21}H_{22}N_3O_5$ $[M+H]^+$ 396.1554 *m/z*, found 396.1552 *m/z* (0.37 ppm).

5'-(4-nitrophenyl)amido-5'-deoxy-α-thymidine (12): 4-Nitrobenzoyl chloride reacted with amine **8** to yield compound **12** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.28 (s, 1H, N*H*), 8.99 (t, *J* = 5.77 Hz, 1H, N*H*), 8.33 (d, *J* = 8.70 Hz, 2H, *H*-Ph), 8.09 (d, *J* = 8.70 Hz, 2H, *H*-Ph), 7.77 (s, 1H, *H6*), 6.19 (qt, *J* = 3.58 Hz, 1H, *H1'*), 5.48 (d, *J* = 3.00 Hz, 1H, O*H*), 4.32 (t, *J* = 6.25 Hz, 1H, *H3'*), 4.25 (d, *J* = 2.6 Hz, 1H, *H4'*), 3.35 (m, 2H, *H5'*), 2.58-2.63 (m, 1H, *H2'*), 1.93 (d, *J* = 14.45Hz, 1H, *H2'*), 1.77 (s, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): δ 164.9 (*C*O), 163.8 (*C4*), 150.5 (*C2*), 149.6, 149.0, 139.8 (*C*-Ph), 137.0 (*C6*), 128.8, 123.5 (*C*-Ph), 108.7 (*C5*), 86.7 (*C1'*), 84.7 (*C4'*), 71.0 (*C3'*), 41.5 (*C5'*), 39.0 (*C2'*), 12.4 (*C*H_3); LCMS (ES$^+$): m/z (%) 391 (100) $[M+H]^+$; HRMS (ES$^+$): calcd for $C_{17}H_{19}N_4O_7$ $[M+H]^+$ 391.1248 *m/z*, found 391.1255 *m/z* (-1.71 ppm).

5'-(4-nitrobenzyl)amino-5'-deoxy-α-thymidine (13): 4-Nitrobenzyl chloride reacted with amine **8** to yield compound **13** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.27 (s, 1H, N*H*), 8.19 (d, *J* = 8.60 Hz, 2H, *H*-Ph), 7.74 (s, 1H, *H6*), 7.62 (d, *J* = 8.55 Hz, 2H, *H*-Ph), 6.10 (qt, *J* = 3.63 Hz, 1H, *H1'*), 5.35 (d, *J* = 2.95 Hz, 1H, O*H*), 4.18-4.22 (m, 1H, *H3'*), 4.12-4.13 (m, 1H, *H4'*), 3.85 (s, 2H, CH_2), 2.54-2.58 (m, 3H, *H5'*, *H5'* and *H2'*), 1.88-1.92 (m, 1H, *H2'*), 1.78 (s, 3H, CH_3); ^{13}C-NMR

(125MHz, DMSO): *δ* 163.9 (*C4*), 150.5 (*C2*), 146.3, 128.8, 123.3 (*C*-Ph), 136.9 (*C6*), 108.6 (*C5*), 87.3 (*C1'*), 84.8 (*C4'*), 71.3 (*C3'*), 52.1 (*C5'*), 50.4 (CH_2), 39.0 (*C2'*), 12.4 (CH_3); LCMS (ES^+): m/z (%) 377 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{17}H_{21}N_4O_6$ $[M+H]^+$ 377.1456 *m/z*, found 377.1469 *m/z* (-3.64 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(carboethoxyethyl)urea (14):** Ethyl 3-isocyanatopropanoate reacted with amine **8** to yield compound **14** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.22 (s, 1H, N*H*), 7.75 (d, *J* = 0.95 Hz, 1H, *H6*), 6.13 (qt, *J* = 3.66 Hz, 1H, *H1'*), 6.07 (t, *J* = 5.87 Hz, 1H, N*H*), 6.03 (t, *J* = 5.85 Hz, 1H, N*H*), 5.36 (s, 1H, O*H*), 4.11-4.13 (m, 2H, *H4'* and *H3'*), 4.04-4.08 (m, 2H, CH_2), 3.23 (qt, *J* = 6.3 Hz, 2H, CH_2), 3.01-3.14 (m, 2H, *H5'*), 2.50-2.53 (m, 3H, CH_2 and *H2'*), 2.41 (t, *J* = 6.5 Hz, 2H, CH_2), 1.88-1.91 (m, 1H, *H2'*), 1.78 (s, 1H, CH_3), 1.19 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): δ 171.7 (*C*O), 163.8 (*C4*), 157.8 (*C*O), 150.5 (*C2*), 136.9 (*C6*), 108.7 (*C5*), 87.4 (*C1'*), 84.8 (*C4'*), 70.8 (*C3'*), 59.8 (*C5'*), 41.3 (CH_2), 39.0 (*C2'*), 35.3 (CH_2), 34.9 (CH_2), 14.1 (CH_3), 12.3 (CH_3); LCMS (ES^+): m/z (%) 385 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{16}H_{25}N_4O_7$ $[M+H]^+$ 385.1718 *m/z*, found 385.1723 *m/z* (-1.31 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-benzylurea (15):** Benzyl isocyanate reacted with amine **8** to yield compound **15** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.27 (s, 1H, N*H*), 7.76 (d, *J* = 1.15 Hz, 1H, *H6*), 7.29-7.32, 7.20-7.25 (m, 5H, *H*-Ph), 6.44 (t, *J* = 6.00 Hz, 1H, N*H*), 6.15 (qt, *J* =3.68 Hz, 1H, *H1'*), 6.09 (t, *J* = 5.95 Hz, 1H, N*H*), 5.41 (d, *J* = 2.90 Hz, 1H, O*H*), 4.21 (d, *J* = 6.00 Hz, 2H, *H3'* and *H4'*), 4.11-4.16 (m, 2H, CH_2), 3.14-3.19, 3.05-3.10 (m, 2H, *H5'*), 2.52-2.56 (m, 1H, *H2'*), 1.89-1.93 (m, 1H, *H2'*), 1.78 (s, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): *δ* 163.8 (*C4*), 158.0 (*C*O), 150.5 (*C2*), 137.0 (*C6*), 140.8, 128.2, 127.0, 126.5 (*C*-Ph), 108.7 (*C5*), 87.4 (*C1'*), 84.7 (*C4'*), 70.8 (*C3'*), 42.9 (CH_2), 41.4 (*C5'*), 39.0 (*C2'*), 12.4 (CH_3); LCMS (ES^+): m/z (%) 375 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{18}H_{23}N_4O_5$ $[M+H]^+$ 375.1663 *m/z*, found 375.1654 *m/z* (2.26 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(3-pyridyl)urea (16):** Pyridine 3-isocyanate reacted with amine **8** to yield compound **16** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.24 (s, 1H, N*H*), 8.75 (s, 1H, N*H*), 8.53 (d, *J* = 2.4 Hz, 1H, *H*-Ph), 8.12 (d, *J* = 5.6 Hz, 1H, *H*-Ph), 7.87-7.89 (m, 1H, *H*-Ph), 7.77 (s, 2H, *H*-Ph), 7.25 (qt, *J* = 4.3 Hz, 1H, *H6*), 6.42 (t, *J* = 5.75 Hz, 1H, N*H*), 6.18 (qt, *J* = 3.71 Hz, 1H, *H1'*), 5.43 (d, *J* = 3.2 Hz, 1H, O*H*), 4.17-4.22 (m, 2H, *H3'* and *H4'*), 3.24-3.29 (m, 1H, *H5'*), 3.11-3.18 (m, 1H, *H5'*), 2.56-2.61 (m, 1H, *H2'*), 1.92-1.97 (m, 1H, *H2'*), 1.78 (s, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): *δ* 163.8 (*C4*), 155.1 (*C*O), 150.5 (*C2*), 142.2 (*C*O), 139.5, 173.0, 136.9,

124.4, 123.8 (*C*-Ph), 108.8 (*C5*), 86.7 (*C1'*), 84.7 (*C4'*), 70.9 (*C3'*), 41.1 (*C5'*), 39.0 (*C2'*), 12.3 (*C*H_3); LCMS (ES^+): m/z (%) 362 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{16}H_{20}N_5O_5$ $[M+H]^+$ 362.1459 *m*/*z*, found 362.1460 *m*/*z* (-0.34 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-phenylurea (17):** Phenyl isocyanate reacted with amine **8** to yield compound **17** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.24 (s, 1H, N*H*), 8.52 (s, 1H, N*H*), 7.77 (d, *J* = 1.20 Hz, 1H, *H6*), 7.37-7.39 (m, 2H, *H*-Ph), 7.20-7.24 (m, 2H, *H*-Ph), 6.88-6.91 (m, 1H, *H*-Ph), 6.25 (t, *J* = 5.85 Hz, 1H, N*H*), 6.19 (qt, *J* = 3.75 Hz, 1H, *H1'*), 5.43 (d, *J* = 3.25 Hz, 1H, O*H*), 4.17-4.21 (m, 2H, *H3'* and *H4'*), 3.24-3.29, 3.10-3.15 (m, 2H, *H5'*), 2.57-2.61 (m, 1H, *H2'*), 1.92-1.96 (m, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125 MHz, DMSO): *δ* 163.8 (*C4*), 155.2 (*C*O), 150.5 (*C2*), 136.9 (*C6*), 140.3, 128.6, 121.1, 117.6 (*C*-Ph), 108.8 (*C5'*), 86.9 (*C1'*), 84.7 (*C4'*), 70.9 (*C3'*), 56.0 (*C5'*), 41.0 (*C2'*), 12.3 (*C*H_3); LCMS (ES^+): m/z (%) 361 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{17}H_{21}N_4O_5$ $[M+H]^+$ 361.1506 *m*/*z*, found 361.1496 *m*/*z* (2.85 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(2-chlorophenyl)urea (18):** 2-Chlorophenyl isocyanate reacted with amine **8** to yield compound **18** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.29 (s, 1H, N*H*), 8.16 (s, 1H, N*H*), 7.79 (d, *J* = 1.2 Hz, *H6*), 7.39 (qt, *J* = 3.16 Hz, 1H, *H*-Ph), 7.17-7.26 (m, 2H, *H*-Ph), 6.94-6.97 (m, 1H, *H*-Ph), 6.20 (qt, *J* = 3.78 Hz, 1H, *H1'*), 5.48 (d, *J* = 3.30 Hz, 1H, O*H*), 4.15-4.21 (m, 2H, *H3'* and *H4'*), 3.28-3.33 (m, 1H, *H5'*), 3.12-3.17 (m, 1H, *H5'*), 2.56-2.62 (m, 1H, *H2'*), 1.93-1.97 (m, 1H, *H2'*), 1.79 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): *δ* 163.8 (*C4*), 154.8 (*C*O), 150.5 (*C2*), 136.6 (*C6*), 136.9, 129.1, 127.4, 122.5, 121.1, 120.8 (*C*-Ph), 108.9 (*C5*), 86.7 (*C1'*), 84.6 (*C4'*), 70.9 (*C3'*), 41.1 (*C5'*), 39.0 (*C2'*), 12.3 (*C*H_3); LCMS (ES^+): m/z (%) 395 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{17}H_{20}Cl_1N_4O_5$ $[M+H]^+$ 395.1117 *m*/*z*, found 395.1112 *m*/*z* (1.13 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(3-chlorophenyl)urea (19):** 3-Chlorophenyl isocyanate reacted with amine **8** to yield compound **19** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.25 (s, 1H, N*H*), 8.77 (s, 1H, N*H*), 7.77 (d, *J* = 1.00 Hz, 1H, *H6*), 7.67 (t, *J* = 2.00 Hz, 1H, *H*-Ph), 7.16-7.26 (m, 2H, *H*-Ph), 6.93-6.95 (m, 1H, *H*-Ph), 6.35 (t, *J* = 5.77 Hz, 1H, N*H*), 6.18 (qt, *J* = 3.75 Hz, 1H, *H1'*), 5.43 (d, *J* = 3.25 Hz, 1H, O*H*), 4.16-4.21 (m, 2H, *H3'* and *H4'*), 3.23-3.28 (m, 1H, *H5'*), 3.09-3.15 (m, 1H, *H5'*), 2.55-2.61 (m, 1H, *H2'*), 1.92-1.96 (m, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): *δ* 163.8 (*C4*), 154.9 (*C*O), 150.5 (*C2*), 136.9 (*C6*), 141.9, 133.1, 130.2, 120.7, 116.9, 116.0 (*C*-Ph), 108.8 (*C5*), 86.7 (*C1'*), 84.6 (*C4'*), 70.9 (C*3'*), 41.0 (*C5'*), 39.0 (*C2'*), 12.3

(*C*H$_3$); LCMS (ES$^+$): m/z (%) 395 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{17}H_{20}Cl_1N_4O_5$ [M+H]$^+$ 395.1117 *m*/*z*, found 395.1108 *m*/*z* (2.21 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-chlorophenyl)urea (20)[10]:** 4-Chlorophenyl isocyanate reacted with amine **8** to yield compound **20** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.28 (s, 1H, N*H*), 8.71 (s, 1H, N*H*), 7.77 (d, *J* = 1.10 Hz, 1H, *H6*), 7.40-7.43 (m, 2H, *H*-Ph), 7.25-7.28 (m, 2H, *H*-Ph), 6.31 (t, *J* = 5.82 Hz, 1H, N*H*), 6.18 (qt, *J* = 3.75 Hz, 1H, *H1'*), 5.45 (d, *J* = 3.25 Hz, 1H, O*H*), 4.15-4.21 (m, 2H, *H3'* and *H4'*), 3.23-3.28 (m, 1H, *H5'*), 3.08-3.14 (m, 1H, *H5'*), 2.55-2.60 (m, 1H, *H2'*), 1.92-1.96 (m, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 155.0 (*C*O), 150.5 (*C2*), 139.3 (*C*-Ph), 136.9 (*C6*), 128.5, 124.5, 119.0 (*C*-Ph), 108.8 (*C5*), 86.7 (*C1'*), 84.6 (*C4'*), 70.8 (*C3'*), 48.6 (*C5'*), 41.0 (*C2'*), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 395 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{17}H_{20}Cl_1N_4O_5$ [M+H]$^+$ 395.1117 *m*/*z*, found 395.1115 *m*/*z* (0.47 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-chlorophenyl)thiourea (21):** 4-Chlorophenyl isothiocyanate reacted with amine **8** to yield compound **21** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.26 (s, 1H, N*H*), 9.71 (s, 1H, N*H*), 7.86 (s, 1H, N*H*), 7.79 (d, *J* = 1.20 Hz, 1H, *H6*), 7.48-7.51, 7.35-7.38 (m, 4H, *H*-Ph), 6.21 (qt, *J* = 3.73 Hz, 1H, *H1'*), 5.48 (d, *J* = 3.35 Hz, 1H, O*H*), 4.34-4.37 (m, 1H, *H3'*), 4.22-4.25 (m, 1H, *H4'*), 3.67-3.69, 3.48-3.53 (m, 2H, *H5'*), 2.57-2.63 (m, 1H, *H2'*), 1.92-1.96 (m, 1H, *H2'*), 1.79 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 180.8 (*C*S), 163.8 (*C4*), 150.5 (*C2*), 136.9 (*C6*), 128.4, 124.6 (*C*-Ph), 108.8 (*C5*), 85.7 (*C1'*), 84.6 (*C4'*), 70.9 (*C3'*), 45.5 (*C5'*), 39.0 (*C2'*), 12.2 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 411 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{17}H_{20}Cl_1N_4O_4S_1$ [M+H]$^+$ 411.0888 *m*/*z*, found 411.0883 *m*/*z* (1.23 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-bromophenyl)urea (22):** 4-Bromophenyl isocyanate reacted with amine **8** to yield compound **22** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.25 (s, 1H, N*H*), 8.69 (s, 1H, N*H*), 7.77 (d, *J* = 1.15 Hz, 1H, *H6*), 7.36-7.41 (m, 4H, *H*-Ph), 6.30 (t, *J* = 5.82 Hz, 1H, N*H*), 6.18 (qt, *J* = 3.75 Hz, 1H, *H1'*), 5.43 (d, *J* = 3.35 Hz, 1H, O*H*), 4.15-4.21 (m, 2H, *H3'* and *H4'*), 3.23-3.28, 3.09-3.14 (m, 2H, *H5'*), 2.55-2.60 (m, 1H, *H2'*), 1.92-1.96 (m, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 155.0 (*C*O), 150.5 (*C2*), 136.9 (*C6*), 139.8, 131.4, 119.5, 112.4 (*C*-Ph), 108.8 (*C5*), 86.7 (*C1'*), 84.6 (*C4'*), 70.9 (*C3'*), 41.0 (*C5'*), 39.0 (*C2'*), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 439 (100) and 441 (100).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-bromophenyl)thiourea (23)**: 4-Bromophenyl isocyanate reacted with amine **8** to yield compound **23** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.26 (s, 1H, N*H*), 9.71 (s, 1H, N*H*), 7.88 (s, 1H, N*H*), 7.79 (d, *J* = 1.20 Hz, 1H, *H6*), 7.44-7.50 (m, 4H, *H*-Ph), 6.21 (qt, *J* = 3.73 Hz, 1H, *H1'*), 5.48 (d, *J* = 3.35 Hz, 1H, O*H*), 4.34-4.37 (m, 1H, *H3'*), 4.22-4.25 (m, 1H, *H4'*), 3.67-3.69, 3.48-3.53 (m, 2H, *H5'*), 2.57-2.63 (m, 1H, *H2'*), 1.93-1.96 (m, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 180.7 (*C*S), 163.8 (*C4*), 150.5 (*C2*), 136.9 (*C6*), 138.7, 131.3, 124.8 (*C*-Ph), 108.8 (*C5*), 85.7 (*C1'*), 84.6 (*C4'*), 79.2 (*C3'*), 70.9 (*C5'*), 45.5 (*C2'*), 12.2 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 455 (100) and 457 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{17}H_{20}Br_1N_4O_4S_1$ [M+H]$^+$ 455.0383 *m/z*, found 455.0373 *m/z* (2.33 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(2-methoxyphenyl)urea (24):** 2-Methoxyphenyl isocyanate reacted with amine **8** to yield compound **24** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.29 (s, 1H, N*H*), 8.07-8.09 (m, 1H, N*H* and N*H*), 7.78 (s, 1H, *H6*), 6.82-7.02 (m, 4H, *H*-Ph), 6.19 (qt, *J* = 3.66 Hz, 1H, *H1'*), 5.46 (s, 1H, O*H*), 4.12-4.18 (m, 2H, *H3'* and *H4'*), 3.83 (s, 3H, C*H*$_3$), 3.23-3.27, 3.11-3.17 (m, 2H, *H5'*), 2.55-2.60 (m, 1H, *H2'*), 1.94 (d, *J* = 14.20 Hz, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 155.2 (*C*O), 150.5 (*C2*), 136.9 (*C6*), 147.3, 129.3, 121.0, 120.4, 118.0, 110.5 (*C*-Ph), 108.8 (*C5*), 87.0 (*C1'*), 84.7 (*C4'*), 70.8 (*C3'*), 55.6 (*C*H$_3$), 41.0 (*C5'*), 39.0 (*C2'*), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 391 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{18}H_{23}N_4O_6$ [M+H]$^+$ 391.1612 *m/z*, found 391.1615 *m/z* (-0.61 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(3-methoxyphenyl)urea (25):** 3-Methoxyphenyl isocyanate reacted with amine **8** to yield compound **25** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.24 (s, 1H, N*H*), 8.54 (s, 1H, N*H*), 7.77 (d, *J* = 1.05 Hz, 1H, *H6*), 7.10-7.14 (m, 2H, *H*-Ph), 6.85 (qt, *J* = 3.05 Hz, 1H, *H*-Ph), 6.48 (qt, *J* = 3.36 Hz, 1H, *H*-Ph), 6.24 (t, *J* = 5.77 Hz, 1H, N*H*), 6.18 (qt, *J* = 3.71 Hz, 1H, *H1'*), 5.43 (d, *J* = 3.25 Hz, 1H, O*H*), 4.16-4.21 (m, 2H, *H3'* and *H4'*), 3.71 (s, 3H, C*H*$_3$), 3.23-3.28, 3.09-3.18 (m, 2H, *H5'*), 2.55-2.61, 1.92-1.96 (m, 2H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 159.6 (*C*O), 155.1 (*C2*), 136.9 (*C6*), 150.5, 141.6, 129.4, 109.0, 106.5, 103.4 (*C*-Ph), 110.0 (*C5*), 86.8 (*C1'*), 84.7 (*C4'*), 70.9 (*C3'*), 54.8 (*C*H$_3$), 41.0 (*C5'*), 39.0 (*C2'*), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 391 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{18}H_{23}N_4O_6$ [M+H]$^+$ 391.1612 *m/z*, found 391.1629 *m/z* (-4.33 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-methoxyphenyl)urea (26):** 4-Methoxyphenyl isocyanate reacted with amine **8** to yield compound **26** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.28 (s, 1H, N*H*), 8.34 (s, 1H, N*H*), 7.78 (s, 1H, *H6*), 7.28 (d, *J* = 8.75 Hz, 2H, *H*-Ph), 6.81 (d, *J* = 8.75 Hz, 2H,

H-Ph), 6.14-6.18 (m, 2H, *H1'* and N*H*), 5.44 (d, *J* = 2.45 Hz, 1H, O*H*), 4.18 (d, *J* = 4.50 Hz, 2H, *H3'* and *H4'*), 3.69 (s, 3H, CH_3), 3.16-3.24 (m, 1H, *H5'*), 3.07-3.12 (m, 1H, *H5'*), 2.54-2.60 (m, 1H, *H2'*), 1.93 (d, *J* = 14.20 Hz, 1H, *H2'*), 1.78 (s, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 155.4 (*C*O), 153.9, 133.7, 119.3, 113.9 (*C*-Ph), 150.5 (*C2*), 136.9 (*C6*), 108.8 (*C5*), 87.0 (*C1'*), 84.7 (*C4'*), 79.1 (*C3'*), 70.8 (*C5'*), 55.1 (*C*H_3), 41.0 (*C2'*), 12.2 (*C*H_3); LCMS (ES$^+$): m/z (%) 391 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{18}H_{23}N_4O_6$ [M+H]$^+$ 391.1612 *m*/*z*, found 391.1613 *m*/*z* (-0.27 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-*tert*-butylphenyl)urea (27):** 4-*tert*-butylphenyl isothiocyanate reacted with amine **8** to yield compound **27** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.28 (s, 1H, N*H*), 8.45 (s, 1H, N*H*), 7.78 (s, 1H, *H6*), 7.29 (d, *J* = 8.70 Hz, 2H, *H*-Ph), 7.23 (d, *J* = 8.70 Hz, 2H, *H*-Ph), 6.17-6.21 (m, 2H, *H1'* and N*H*), 5.45 (d, *J* = 3.15 Hz, 1H, O*H*), 4.16-4.20 (m, 2H, *H3'* and *H4'*), 3.22-3.27 (m, 1H, *H5'*), 3.09-3.14 (m, 1H, *H5'*), 2.54-2.60 (m, 1H, *H2'*), 1.94 (d, *J* = 7.12 Hz, 1H, *H2'*), 1.78 (s, 3H, CH_3), 1.24 (s, 9H, CH_3); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 155.2 (*C*O), 150.5 (*C2*), 143.3, 137.7 (*C*-Ph), 136.9 (*C6*), 125.2, 117.5 (*C*-Ph), 108.8 (*C5*), 86.9 (*C1'*), 84.6 (*C4'*), 79.1 (*C3'*), 70.8 (*C5'*), 41.0 (*C2'*), 33.8 (*C*$(CH_3)_3$), 31.2 (*C*H_3), 12.2 (*C*H_3); LCMS (ES$^+$): m/z (%) 417 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{21}H_{29}N_4O_5$ [M+H]$^+$ 417.2106 *m*/*z*, found 417.2120 *m*/*z* (-3.37 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(3-trifluoromethyl-4-chlorophenyl)thiourea (28)[10]:** 3-Trifluoromethyl-4-chlorophenyl isothiocyanate reacted with amine **8** to yield compound **29** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.30 (s, 1H, N*H*), 10.01 (s, 1H, N*H*), 8.15 (m, 2H, *H*-Ph and N*H*), 7.79 (s, 1H, *H6*), 7.74 (d, *J* = 9.26 Hz, 1H, *H*-Ph), 7.64 (d, *J* = 8.74 Hz, 1H, *H*-Ph), 6.22 (m, 1H, *H1'*), 5.52 (m, 1H, O*H*), 4.36 (m, 1H, *H4'*), 4.24 (m, 1H, *H3'*), 3.71 (m, 1H, *H5'*), 3.51 (m, 1H, *H5'*), 2.61 (m, 1H, *H2'*), 1.95 (m, 1H, *H2'*), 1.78 (s, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): δ 180.7 (*C*S), 163.8 (*C4*), 150.5 (*C2*), 139.1 (*C6*), 136.9, 131.6, 127.2, 124.4, 123.8 (*C*-Ph), 108.9 (*C5*), 85.5 (*C1'*), 84.6 (*C4'*), 70.9 (*C3'*), 48.6 (*C5'*), 45.5 (*C2'*), 12.3 (*C*H_3); ^{19}F-NMR (470MHz, DMSO): δ 61.47; LCMS (ES$^+$): m/z (%) 478 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{18}H_{19}Cl_1F_3N_4O_4S_1$ [M+H]$^+$ 479.0762 *m*/*z*, found 479.0781 *m*/*z* (-3.93 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(3-trifluoromethyl-4-chlorophenyl)urea (29):** 3-Trifluoromethyl-4-chlorophenyl isocyanate reacted with amine **8** to yield compound **29** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.25 (s, 1H, N*H*), 9.06 (s, 1H, N*H*), 8.06 (d, *J* = 1.60 Hz, 1H, *H*-Ph), 7.77 (d, *J* = 1.20 Hz, 1H, *H6*), 7.54-7.57 (m, 2H, *H*-Ph), 6.45 (t, *J* = 5.82 Hz, 1H, N*H*), 6.18

(qt, *J* = 3.75 Hz, 1H, *H1'*), 5.44 (d, *J* = 3.35 Hz, 1H, O*H*), 4.16-4.22 (m, 2H, *H3'* and *H4'*), 3.23-3.28, 3.11-3.18 (m, 2H, *H5'*), 2.55-2.61 (m, 1H, *H2'*), 1.92-1.96 (m, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): *δ* 163.8 (*C4*), 154.9 (*C*O), 150.5 (*C2*), 136.89 (*C6*), 140.0, 131.9, 126.5, 122.3, 121.5, 116.1 (*C*-Ph), 108.8 (*C5*), 86.6 (*C1'*), 84.6 (*C4'*), 70.8 (*C3'*), 41.1 (*C5'*), 39.0 (*C2'*), 12.2 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 463 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{18}H_{23}N_4O_5$ [M+H]$^+$ 463.0991 *m*/*z*, found 463.0989 *m*/*z* (0.35 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-nitrophenyl)urea (30):** 4-Nitrophenyl isocyanate reacted with amine **8** to yield compound **30** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.29 (s, 1H, N*H*), 9.36 (s, 1H, N*H*), 8.15 (d, *J* = 9.27 Hz, 1H, 2H, *H*-Ph), 7.78 (s, 1H, *H6*), 7.62 (d, *J* = 9.25 Hz, 2H, *H*-Ph), 6.57 (t, *J* = 5.71 Hz, 1H, N*H*), 6.19 (m, 1H, *H1'*), 5.48 (d, *J* = 3.34 Hz, 1H, O*H*), 4.17, 4.22 (m, 2H, *H3'* and *H4'*); 3.14, 3.29 (m, 2H, *H5'*), 2.59, 1.95 (m, 2H, *H2'*); 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): *δ* 163.8 (*C4*), 154.4 (*C*O), 150.5 (*C2'*), 136.9 (*C6*), 147.0, 140.4, 125.2, 116.8 (*C*-Ph), 108.9 (*C5*), 86.4 (*C1'*), 84.6 (*C4'*), 79.1 (*C3'*), 70.8 (*C5'*), 41.0 (*C2'*), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 406 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{17}H_{20}N_5O_7$ [M+H]$^+$ 406.1357 *m*/*z*, found 406.1372 *m*/*z* (-3.75 ppm).

5'-*O*-methanesulfonyl-β-thymidine (31): Thymidine (484 mg, 2 mmol) was reacted with methanesulfonyl chloride (154 μl, 2 mmol) following the procedure of compound **6** to yield compound **31** 320mg (49.8 %) as a solid. ^{1}H-NMR (500MHz, DMSO): *δ* 11.37 (s, 1H, NH), 7.49 (s, 1H, *H6*), 6.23 (t, *J* = 7.65 Hz, 1H, *H1'*), 5.51 (d, *J* = 4.00 Hz, 1H, *H4'*), 4.25-4.41 (m, 3H, *H3'* and *H5'*), 3.95-3.98 (m, 1H, O*H*), 3.23 (s, 3H, C*H*$_3$), 2.07-2.21 (m, 2H, *H2'*), 1.77 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): *δ* 163.6 (*C4*), 150.4 (*C2*), 135.8 (*C6*), 109.9 (*C5*), 83.9 (*C1'*), 83.3 (C4'), 70.1 (*C3'*), 69.6 (*C5'*), 38.3 (*C2'*), 36.7 (*C*H$_3$), 12.0 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 321 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{11}H_{17}N_2O_7S_1$ [M+H]$^+$ 321.0751 *m*/*z*, found 321.0754 *m*/*z* (-0.98 ppm).

5'- azido-5'-deoxy-β-thymidine (32): Compound **31** (3 mmol) was reacted with NaN_3 (6 mmol) following the procedure of preparation compound **7** to yield compound **32** 516 mg (64 %) as a solid. ^{1}H-NMR (500MHz, MeOD): *δ* 7.56 (s, 1H, *H6*), 6.28 (t, *J* = 6.80 Hz, 1H, *H1'*), 4.36 (m, 1H, *H4'*), 3.97 (dd, J_1 = 8.70, J_2 = 3.98, 1H, *H3'*), 3.57-3.67 (m, 2H, *H5'*), 2.25-2.35 (m, 2H, *H2'*), 1.91 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, MeOD): *δ* 166.3 (*C4*), 152.3 (*C2*), 137.8 (*C6*), 111.9 (*C5*), 86.4 (*C1'*), 86.3 (*C4'*), 72.5 (*C3'*), 53.4 (*C5'*), 40.2 (*C2'*), 12.5 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 268 (100)

$[M+H]^+$; HRMS (ES^+): calcd for $C_{10}H_{14}N_5O_4$ $[M+H]^+$ 268.1040 *m/z*, found 268.1038 *m/z* (0.88 ppm).

5'-amino-5'-deoxy-β-thymidine (33): Compound **32** (268 mg, 1 mmol) was hydrogenated to give compound **33** 237 mg (98.3 %) as a solid. ^{1}H-NMR (500MHz, MeOD): δ 7.37 (s, 1H, *H6*), 6.11 (t, *J* = 6.84 Hz, 1H, *H1'*), 4.14 (m, 1H, *H3'*), 3.17 (m, 1H, *H4'*), 3.20-3.24 (m, 2H, NH_2), 2.72-2.83 (m, 2H, *H5'*), 2.10-2.20 (m, 2H, *H2'*), 1.79 (s, 3H, CH_3); ^{13}C-NMR (125MHz, MeOD): δ 166.6 (*C4*), 152.5 (*C2*), 138.1 (*C6*), 111.9 (*C5*), 88.5 (*C1'*), 86.2 (*C4'*), 72.9 (*C3'*), 44.7 (*C5'*), 40.2 (*C2'*), 12.5 (*C*H_3); LCMS (ES^+): m/z (%) 242 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{10}H_{16}N_3O_4$ $[M+H]^+$ 242.1135 *m/z*, found 242.1131 *m/z* (1.98ppm).

General Procedure for compounds 34 - 55

For the synthesis of compounds **34** - **55**, compound of amine **33** (1 eq.) was dissolved in DMF at 0 °C. The coupling reagents (1.1 eq.) were added and the reaction mixture was allowed to stir at room temperature for 3 h. After the completion of the reaction, the reaction mixture was evaporated to dry (ethanol and toluene were used to co-evaporate) and the residue was purified by column chromatography to yield the compounds **34** - **55** as a solid with the yields ranging from 41% to 84 %.

5'-(4-nitro-phenyl)sulfoamido-5'-deoxy-β-thymidine (34): 4-Nitrobenzolsulfonyl chloride reacted with amine **33** to yield compound **34** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.31 (s, 1H, N*H*), 8.40 (d, *J* = 8.7 Hz, 2H, *H*-Ph), 8.32 (s, 1H, N*H*), 8.05 (d, *J* = 8.7 Hz, 2H, *H*-Ph), 7.48 (s, 1H, *H6*), 6.10 (t, *J* = 7.0 Hz, 1H, *H1'*), 5.34 (s, 1H, O*H*), 4.13 (d, *J* = 2.4 Hz, 1H, *H4'*), 3.68-3.71 (m, 1H, *H3'*), 3.15 (qt, *J* = 6.1 Hz, 1H, *H5'*), 3.01 (qt, *J* = 6.9 Hz, 1H, *H5'*), 2.11-2.17 (m, 1H, *H2'*), 1.99-2.04 (m, 1H, *H2'*), 1.78 (s, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 150.4, 149.4 (*C*-Ph), 146.2 (*C2*), 136.3 (*C6*), 128.0, 124.5 (*C*-Ph), 109.6 (*C5*), 84.6 (*C1'*), 83.8 (*C4'*), 70.8 (*C3'*), 44.7 (*C5'*), 38.1 (*C2'*), 12.0 (*C*H_3); LCMS (ES^+): m/z (%) 427 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{16}H_{19}N_4O_8S_1$ $[M+H]^+$ 427.0918 *m/z*, found 427.0920 *m/z* (-0.44 ppm).

5'-(2-naphthyl)sulfoamido-5'-deoxy-β-thymidine (35): 2-Naphthalenesulfonyl chloride reacted with amine **33** to yield compound **35** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.31 (s, 1H, N*H*), 8.46 (s, 1H, N*H*), 8.14 (t, *J* = 8.02 Hz, 1H, *H*-Ph), 8.04 (t, *J* =7 .57 Hz, 2H, *H*-Ph), 7.85 (qt, *J* = 3.48 Hz, 2H, *H*-Ph), 7.67-7.73 (m, 2H, *H*-Ph), 7.51 (d, *J* = 0.95 Hz, 1H, *H6*), 6.12 (qt, *J* = 4.68 Hz, 1H, *H1'*), 5.33 (d, *J* = 4.30 Hz, 1H, O*H*), 4.13-4.16 (m, 1H, *H4'*), 3.73-3.74 (m, 1H, *H3'*), 3.04-3.08 (m, 1H, *H5'*), 2.95-2.97 (m, 1H, *H5'*), 2.10-2.12 (m, 1H, *H2'*), 2.02-2.03 (m, 1H, *H2'*), 1.76 (s, 3H,

C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 150.4 (*C2*), 136.2 (*C6*), 137.5, 134.1, 131.7, 129.4, 129.1, 128.7, 127.8, 127.6, 127.3, 122.2 (*C*-Ph), 109.6 (*C5*), 84.7 (*C1'*), 83.8 (*C4'*), 70.8 (*C3'*), 44.7 (*C5'*), 38.2 (*C2'*), 12.0 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 432 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{20}H_{22}N_3O_6S_1$ [M+H]$^+$ 432.1224 *m*/*z*, found 432.1223 *m*/*z* (0.15 ppm).

5'-(2-naphthyl)amido-5'-deoxy-β-thymidine (36): 2-Naphthoyl chloride reacted with amine **33** to yield compound **37** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.33 (s, 1H, N*H*), 8.84 (t, *J* = 5.72 Hz, 1H, N*H*), 7.95-8.04 (m, 4H, *H*-Ph), 7.56-7.67 (m, 4H, *H*-Ph), 6.17 (qt, *J* = 4.66 Hz, 1H, *H1'*), 5.38 (s, 1H, O*H*), 4.30 (t, *J* = 2.80 Hz, 1H, *H3'*), 3.94-3.97 (m, 1H, *H4'*), 3.59 (t, *J* = 5.92 Hz, 2H, *H5'*), 2.07-2.19 (m, 2H, *H2'*), 1.76 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 166.5 (*C4*), 163.7 (*C*O), 150.4 (*C2*), 134.1 (*C6*), 131.6, 129.2, 128.8, 127.9, 127.6, 127.5, 126.7, 124.2 (*C*-Ph), 109.6 (*C5*), 84.9 (*C1'*), 83.9 (*C4'*), 71.3 (*C3'*), 41.7 (*C5'*), 38.4 (*C2'*), 12.0 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 396 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{21}H_{22}N_3O_5$ [M+H]$^+$ 396.1554 *m*/*z*, found 396.1565 *m*/*z* (-2.90 ppm).

5'-(4-nitro-phenyl)amido-5'-deoxy-thymidine (37): 4-Nitrobenzoyl chloride reacted with amine **33** to yield compound **36** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.36 (s, 1H, N*H*), 9.01 (s, 1H, N*H*), 8.33 (d, *J* = 8.70 Hz, 2H, *H*-Ph), 8.09 (d, *J* = 8.70 Hz, 2H, *H*-Ph), 7.53 (s, 1H, *H6*), 6.15 (t, *J* = 8.7 Hz, 1H, *H1'*), 5.40 (s, 1H, O*H*), 4.27 (m, 1H, *H3'*), 3.89-3.93 (m, 1H, *H4'*), 3.53-3.58 (m, 2H, *H5'*), 2.06-2.22 (m, 2H, *H2'*), 1.77 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 164.9 (*C*O), 163.7 (*C4*), 151.0 (*C*-Ph), 140.7 (*C*-Ph), 137.1 (*C6*), 128.8, 123.6 (*C*-Ph), 109.7 (*C5*), 84.6 (*C1'*), 84.1 (*C4'*), 71.3 (*C3'*), 57.1 (*C5'*), 38.3 (*C2'*), 12.0 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 391 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{17}H_{19}N_4O_7$ [M+H]$^+$ 391.1248 *m*/*z*, found 391.1246 *m*/*z* (0.66 ppm).

5'-(4-nitro-benzyl)amino-5'-deoxy-β-thymidine (38): 4-Nitrobenzyl chloride reacted with amine **33** to yield compound **38** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.31 (s, 1H, N*H*), 8.19 (d, *J* = 8.65 Hz, 2H, *H*-Ph), 7.63 (d, *J* = 8.55 Hz, 2H, *H*-Ph), 7.56 (s, 1H, *H6*), 6.14 (t, *J* = 6.90 Hz, 1H, *H1'*), 5.26 (d, *J* = 4.30 Hz, 1H, O*H*), 4.20 (m, 1H, *H3'*), 3.87 (s, 2H, C*H*$_2$), 3.78-3.81 (m, 1H, *H4'*), 2.65-2.75 (m, 2H, *H5'*), 2.03-2.16 (m, 2H, *H2'*), 1.73 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 150.4 (*C2*), 149.4, 146.2 (*C*-Ph), 136.2 (*C6*), 128.8, 123.3 (*C*-Ph), 109.5 (*C5*), 85.7 (*C1'*), 83.6 (*C4'*), 71.3 (*C3'*), 52.2 (*C5'*), 50.5 (*C*H$_2$), 38.7 (*C2'*), 12.1 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 377 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{17}H_{21}N_4O_6$ [M+H]$^+$ 377.1456 *m*/*z*, found 377.1440 *m*/*z* (4.10 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(carboethoxyethyl)urea (39):** Ethyl 3-isocyanatopropanoate reacted with amine **33** to yield compound **39** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.27 (s, 1H, N*H*), 7.48 (s, 1H, *H6*), 6.11-6.16 (m, 2H, *H1'* and N*H*), 6.00 (t, *J* = 5.55 Hz, 1H, N*H*), 5.25 (d, *J* = 4.0 Hz, 1H, O*H*), 4.03 (m, 1H, *H4'*), 4.03-4.08 (m, 2H, CH_2), 3.70 (m, 1H, *H3'*), 3.21-3.24 (m, 2H, CH_2), 3.11-3.16 (m, 1H, *H5'*), 2.50 (s, 1H, *H5'*), 2.40 (t, *J* = 6.45 Hz, 2H, CH_2), 2.04-2.11 (m, 2H, CH_2), 1.80 (s, 3H, CH_3), 1.18 (t, *J* = 7.07 Hz, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): δ 171.7 (*C*O), 163.7 (*C4*), 157.9 (*C*O), 150.4 (*C2*), 136.0 (*C6*), 109.7 (*C5*), 85.6 (*C1'*), 83.7 (*C4'*), 71.1 (*C3'*), 59.8 (*C5'*), 41.6 (*C*H_2), 38.5 (*C2'*), 35.3 (*C*H_2), 34.9 (*C*H_2), 14.0 (*C*H_3), 12.0 (*C*H_3); LCMS (ES^+): m/z (%) 385 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{16}H_{25}N_4O_7$ $[M+H]^+$ 385.1718 *m/z*, found 385.1708 *m/z* (2.64 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-benzylurea (40):** Benzyl isocyanate reacted with amine **33** to yield compound **40** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.33 (s, 1H, N*H*), 7.51 (s, 1H, *H6*), 7.20-7.32 (m, 5H, *H*-Ph), 6.43 (t, *J* = 5.87 Hz, 1H, N*H*), 6.15-6.18 (m, 2H, N*H* and *H1'*), 5.32 (d, *J* = 3.92 Hz, 1H, O*H*), 4.23 (t, *J* = 5.62 Hz, 2H, CH_2), 4.15 (s, 1H, *H3'*), 3.73-3.75 (m, 1H, *H4'*), 3.37-3.41 (m, 1H, *H5'*), 3.17-3.21 (m, 1H, *H5'*), 2.03-2.13 (m, 2H, *H2'*), 1.78 (s, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): *δ* 163.7 (*C4*), 158.1 (*C*O), 150.5 (*C2*), 140.8 (*C*-Ph), 136.0 (*C6*), 128.2, 126.92, 126.5 (*C*-Ph), 109.8 (*C5*), 85.6 (C*1'*), 83.7 (*C4'*), 71.1 (*C3'*), 42.9 (*C5'*), 41.8 (*C*H_2), 38.5 (*C2'*), 12.0 (*C*H_3); LCMS (ES^+): m/z (%) 375 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{18}H_{23}N_4O_5$ $[M+H]^+$ 375.1663 *m/z*, found 375.1661 *m/z* (0.54ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(3-pyridyl)urea (41):** Pyridine 3-isocyanate reacted with amine **33** to yield compound **41** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.32 (s, 1H, N*H*), 8.72 (s, 1H, N*H*), 8.53 (d, *J* = 2.4 Hz, 1H, *H*-Ph), 8.12 (m, 1H, *H*-Ph), 7.87 (m, 1H, *H*-Ph), 7.51 (d, *J* = 0.9 Hz, 1H, *H6*), 7.25 (qt, *J* = 4.3 Hz, 1H, *H*-Ph), 6.45 (s, 1H, N*H*), 6.18 (qt, *J* = 4.6 Hz, 1H, *H1'*), 5.33 (d, *J* = 4.2 Hz, 1H, O*H*), 4.17 (d, *J* = 2.8 Hz, 1H, *H3'*), 3.79 (m, 1H, *H4'*), 3.46-3.52 (m, 1H, *H5'*), 3.24-3.30 (m, 1H, *H5'*), 2.15-2.21 (m, 1H, *H2'*), 2.05-2.11 (m, 1H, *H2'*); 1.77 (s, 1H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): *δ* 163.7 (*C4*), 155.2 (*C*O), 150.5 (*C2*), 137.0 (*C6*), 142.2, 139.5, 136.0, 124.4, 123.5 (*C*-Ph), 109.7 (*C5*), 85.2 (*C1'*), 83.8 (*C4'*), 71.1 (*C3'*), 41.5 (*C5'*), 38.4 (*C2'*); LCMS (ES^+): m/z (%) 362 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{16}H_{20}N_5O_5$ $[M+H]^+$ 362.1459 *m/z*, found 362.1454 *m/z* (1.27 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-phenylurea (42):** Phenyl isocyanate reacted with amine **33** to yield compound **42** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.33 (s, 1H, N*H*), 8.54 (s, 1H, N*H*),

7.53 (d, *J* = 0.75 Hz, 1H, *H6*), 7.38 (d, *J* = 7.65 Hz, 2H, *H*-Ph), 7.22 (t, *J* = 7.90 Hz, 2H, *H*-Ph), 6.89 (t, *J* = 7.32 Hz, 1H, *H*-Ph), 6.31 (t, *J* = 5.65 Hz, 1H, N*H*), 6.18 (qt, *J* = 4.68 Hz, 1H, *H1'*), 5.35 (d, *J* = 4.20, 1H, O*H*), 4.17 (d, *J* = 2.6 Hz, 1H, *H3'*), 3.76-3.79 (m, 1H, *H4'*), 3.44-3.49 (m, 1H, *H5'*), 3.20-3.26 (m, 1H, *H5')*, 2.14-2.19 (m, 1H, *H2'*), 2.05-2.09 (m, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): *δ* 163.7 (*C4*), 155.2 (*C*O), 150.5 (*C2*), 136.1 (*C5*), 140.4, 128.6, 121.1, 117.5 (*C*-Ph), 109.8 (*C6*), 85.3 (*C1'*), 83.7 (*C4'*), 71.1 (*C3'*), 41.4 (*C5'*), 38.4 (*C2'*), 12.0 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 361 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{17}H_{21}N_4O_5$ [M+H]$^+$ 361.1506 *m*/*z*, found 361.1513 *m*/*z* (-1.80ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(2-chloro-phenyl)urea (43):** 2-Chlorophenyl isocyanate reacted with amine **33** to yield compound **43** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.34 (s, 1H, N*H*), 8.16 (d, *J* = 8.10 Hz, 2H, N*H*), 8.12 (s, 1H, N*H*), 7.51 (s, 1H, *H6*), 7.39 (d, *J* = 7.40 Hz, 1H, *H*-Ph), 7.23 (t, *J* = 7.32 Hz, 2H, *H*-Ph), 6.95 (t, *J* = 7.17 Hz, 1H, *H*-Ph), 6.20 (t, *J* = 6.95 Hz, 1H, *H1'*), 5.38 (d, *J* = 4.15 Hz, 1H, O*H*), 4.17 (d, *J* = 2.35 Hz, 1H, *H3'*), 3.77 (t, *J* = 3.47 Hz, 1H, *H4'*), 3.50-3.55 (m, 1H, *H5'*), 3.22-3.27 (m, 1H, *H5'*), 2.16-2.22 (m, 1H, *H2'*), 2.06-2.11 (m, 1H, *H2'*), 1.77 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): *δ* 163.7 (*C4*), 154.8 (*C*O), 150.5 (*C2*), 136.6 (*C6*), 136.0, 129.0, 127.4, 122.5, 121.1, 120.7 (*C*-Ph), 109.8 (*C5*), 85.2 (*C1'*), 83.6 (*C4'*), 71.1 (*C3'*), 41.4 (*C5'*), 38.4 (*C2'*), 12.0 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 395 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{17}H_{20}Cl_1N_4O_5$ [M+H]$^+$ 395.1117 *m*/*z*, found 395.1103 *m*/*z* (3.45 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-N'-(3-chloro-phenyl)urea (44):** 3-Chlorophenyl isocyanate reacted with amine **33** to yield compound **44** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.35 (s, 1H, N*H*), 8.81 (s, 1H, N*H*), 7.71 (s, 1H, *H*-Ph), 7.56 (s, 1H, H6), 7.26 (t, *J* = 8.0 Hz, 1H, *H*-Ph), 7.18 (d, *J* = 8.2 Hz, 1H, *H*-Ph), 6.96 (d, *J* = 7.8 Hz, 1H, *H*-Ph), 6.43 (t, *J* = 5.6 Hz, 1H, N*H*), 6.21 (t, *J* = 6.97 Hz, 1H, *H1'*), 5.38 (d, *J* = 4.18 Hz, 1H, O*H*), 4.19 (m, 1H, *H3'*), 3.80 (t, *J* = 3.15 Hz, 1H, *H4'*), 3.45-3.53 (m, 1H, *H5'*), 3.24-3.29 (m, 1H, *H5'*), 2.16-2.21 (m, 1H, *H2'*), 2.07-2.11 (m, 1H, *H2'*), 1.80 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 155.0 (*C*O), 150.5 (*C2*), 141.9 (*C*-Ph), 136.1 (*C6*), 133.1, 130.3, 120.7, 116.9, 116.0 (*C*-Ph), 109.8 (*C5*), 85.2, 83.7 (*C4'*), 71.1 (*C3'*), 41.4 (*C5'*), 38.4 (*C2'*), 12.0 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 395 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{17}H_{20}Cl_1N_4O_5$ [M+H]$^+$ 395.1117 *m*/*z*, found 395.1105 *m*/*z* (2.25 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-N'-(4-chloro-phenyl)urea (45):** 4-Chlorophenyl isocyanate reacted with amine **33** to yield compound **45** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.30 (s, 1H, N*H*), 8.72 (s, 1H, N*H*), 7.51 (d, *J* = 1.05 Hz, 1H, *H6*), 7.40-7.43 (m, 2H, *H*-Ph), 7.25-7.28 (m, 2H, *H*-Ph),

6.36 (t, *J* = 5.82 Hz, 1H, N*H*), 6.18 (qt, *J* = 4.70 Hz, 1H, *H1'*), 5.33 (d, *J* = 4.25 Hz, 1H, O*H*), 4.15-4.18 (m, 1H, *H3'*), 3.76-3.78 (m, 1H, *H4'*), 3.44-3.49 (m, 1H, *H5'*), 3.21-3.26 (m, 1H, *H5'*), 2.14-2.19 (m, 1H, *H2'*), 2.05-2.09 (m, 1H, *H2'*), 1.77 (s, 3H. C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 155.1 (*C*O), 150.5 (*C2*), 139.4 (*C*-Ph), 136.1 (*C6*), 128.5, 124.5, 119.0 (*C*-Ph), 109.8 (*C5*), 85.2 (*C1'*), 83.7 (*C4'*), 71.1 (*C3'*), 41.4 (*C5'*), 38.4 (*C2'*), 12.0 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 395 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{17}H_{20}Cl_1N_4O_5$ [M+H]$^+$ 395.1117 *m*/*z*, found 395.1114 *m*/*z* (0.49 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-N′-(4-chloro-phenyl)thiourea (46):** 4-Chlorophenyl isothiocyanate reacted with amine **33** to yield compound **46** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.35 (s, 1H, N*H*), 9.70 (s, 1H, N*H*), 7.92 (s, 1H, N*H*), 7.48-7.51, 7.34-7.37 (m, 5H, *H6* and *H*-Ph), 6.19 (qt, *J* = 4.70 Hz, 1H, *H1'*), 5.39 (d, *J* = 4.40 Hz, 1H, O*H*), 4.23 (d, *J* = 2.55 Hz, 1H, *H3'*), 3.92-3.94 (m, 2H, *H4' and H5'),* 3.61-3.63 (m, 1H, *H5'*), 2.17-2.22, 2.06-2.10 (m, 2H, *H2'*), 1.79 (s, 3H, *C*H$_3$); ^{13}C-NMR (125MHz, DMSO): *δ* 180.7 (*C*S), 163.7 (*C4*), 150.5 (*C2*), 136.1 (*C6*), 138.3, 128.3, 127.8, 124.4 (*C*-Ph), 109.8 (*C5*), 84.1 (*C1'*), 83.9 (*C4'*), 71.2 (*C3'*), 46.3 (*C5'*), 38.2 (*C2'*), 12.2 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 411 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{17}H_{20}Cl_1N_4O_4S_1$ [M+H]$^+$ 411.0888 *m*/*z*, found 411.0885 *m*/*z* (0.74 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N*′-(4-bromo-phenyl)urea (47):** 4-Bromophenyl isocyanate reacted with amine **33** to yield compound **47** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.34 (s, 1H, N*H*), 8.70 (s, 1H, N*H*), 7.51 (s, 1H, *H6*), 7.35-7.41 (m, 4H, *H*-Ph), 6.37 (t, *J* = 5.03 Hz, 1H, N*H*), 6.18 (t, *J* = 7.35 Hz, 1H, *H1'*), 5.35 (d, *J* = 4.20 Hz, 1H, O*H*), 4.16 (m, 1H, *H3'*), 3.77 (m, 1H, *H4'*), 3.46 (m, 1H, *H5'*), 3.22 (m, 1H, *H5'*), 2.16 (m, 1H, *H2'*), 2.06 (m, 1H, *H2'*), 1.77 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): *δ* 163.7 (*C4*), 155.0 (*C*O), 150.5 (*C2*), 136.1 (*C6*), 139.8, 131.6, 119.5, 112.3 (*C*-Ph), 109.8 (*C5*), 85.2 (*C1'*), 83.7 (*C4'*), 71.1 (*C3'*), 41.4 (*C5'*), 38.3 (*C2'*), 12.0 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 439 and 441 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{17}H_{20}Br_1N_4O_5$ [M+H]$^+$ 439.0612*m*/*z*, found 436.0615 *m*/*z* (-0.72 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N*′-(4-bromo-phenyl)thiourea (48):** 4-Bromophenyl isothiocyanate reacted with amine **33** to yield compound **48** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.32 (s, 1H, N*H*), 9.68 (s, 1H, N*H*), 7.93 (s, 1H, N*H*), 7.44-7.51 (m, 5H, *H*-Ph), 6.19 (qt, *J* = 4.70 Hz, 1H, *H1'*), 5.36 (d, *J* = 4.35 Hz, 1H, O*H*), 4.22-4.23 (m, 1H, *H3'*), 3.92-3.94 (m, 2H, *H4'* and *H5'*), 3.61-3.64 (m, 1H, *H5'*), 2.17-2.22, 2.06-2.11 (m, 2H, *H2'*), 1.79 (s, 3H. C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): *δ* 180.7 (*C*S), 163.7 (*C4*), 150.5 (*C2*), 136.1 (*C6*), 138.8, 131.2,

124.7 (*C*-Ph), 109.8 (*C5*), 84.1 (*C1'*), 83.9 (*C4'*), 71.3 (*C3'*), 40.0 (*C5'*), 38.2 (*C2'*), 12.3 (*C*H_3); LCMS (ES^+): m/z (%) 455 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{17}H_{20}Br_1N_4O_4S_1$ $[M+H]^+$ 455.0383 *m*/*z*, found 455.0393 *m*/*z* (-2.12 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(2-methoxy-phenyl)urea (49):** 2-Methoxyphenyl isocyanate reacted with amine **33** to yield compound **49** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.33 (s, 1H, N*H*), 8.09 (qt, *J* = 3.16 Hz, 1H, N*H*), 8.03 (s, 1H, N*H*), 7.51 (d, *J* = 0.8 Hz, 1H, *H6*), 7.07 (t, *J* = 5.80 Hz, 1H, *H*-Ph), 6.89-6.96 (m, 1H, *H*-Ph), 6.81-6.89 (m, 2H, *H*-Ph), 6.19 (qt, *J* = 4.66 Hz, 1H, *H1'*), 5.35 (d, *J* = 4.30 Hz, 1H, O*H*), 4.14-4.17 (m, 1H, *H3'*), 3.74-3.77 (m, 1H, *H4'*), 3.45-3.50 (m, 1H, *H5'*), 3.36 (s, 3H, C*H*$_3$), 3.20-3.25 (m, 1H, *H5'*), 2.14-2.19 (m, 1H, *H2'*), 2.05-2.09 (m, 1H, *H2'*), 1.77 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 155.2 (*C*O), 150.5 (*C2*), 147.3 (*C*-Ph), 136.0 (*C6*), 129.3, 121.0, 120.4, 117.9, 110.5 (*C*-Ph), 109.8 (*C6*), 85.4 (*C1'*), 83.6 (*C4'*), 71.1 (*C3'*), 55.6 (*C*H_3), 41.3 (*C5'*), 38.4 (*C2'*), 12.0 (*C*H_3); LCMS (ES^+): m/z (%) 391 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{18}H_{23}N_4O_6$ $[M+H]^+$ 391.1612 *m*/*z*, found 391.1614 *m*/*z* (-0.57 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(3-methoxy-phenyl)urea (50):** 3-Methoxyphenyl isocyanate reacted with amine **33** to yield compound **50** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.33 (s, 1H, N*H*), 8.55 (s, 1H, N*H*), 7.52 (s, 1H, *H6*), 7.09-7.15 (m, 2H, *H*-Ph), 6.84 (t, *J* = 4.52 Hz, 1H, *H*-Ph), 6.47 (qt, *J* = 3.40 Hz, 1H, *H*-Ph), 6.29 (t, *J* = 5.82 Hz, 1H, N*H*), 6.18 (t, *J* = 7.0 Hz, 1H, *H1'*), 5.35 (d, *J* = 4.20 Hz, 1H, O*H*), 4.16-4.17 (m, 1H, *H3'*), 3.75-3.78 (m, 1H, *H4'*), 3.70 (s, 3H, C*H*$_3$), 3.43-3.48 (m, 1H, *H5'*), 3.20-3.25 (m, 1H, *H5')*, 2.13-2.19 (m, 1H, *H2'*), 2.04-2.09 (m, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 159.6 (*C*O), 155.1 (*C2*), 150.5, 141.6 (*C*-Ph), 136.1 (*C6*), 129.4, 109.9, 109.8, 106.5 (*C*-Ph), 103.3 (*C5*), 85.3 (*C1'*), 83.7 (*C4'*), 71.1 (*C3'*), 54.8 (*C*H_3), 41.4 (*C5'*), 38.4 (*C2'*), 12.0 (*C*H_3); LCMS (ES^+): m/z (%) 391 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{18}H_{23}N_4O_6$ $[M+H]^+$ 391.1612 *m*/*z*, found 391.1615 *m*/*z* (-0.78 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(4-methoxy-phenyl)urea (51):** 4-Methoxyphenyl isocyanate reacted with amine **33** to yield compound **51** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.33 (s, 1H, N*H*), 8.32 (s, 1H, N*H*), 7.52 (d, *J* = 1.00 Hz, 1H, *H6*), 7.28 (qt, *J* = 3.0 Hz, 2H, *H*-Ph), 6.81 (qt, *J* = 3.00 Hz, 2H, *H*-Ph), 6.17-6.20 (m, 2H, N*H* and *H1'*), 5.34 (d, *J* = 4.25 Hz, 1H, O*H*), 4.14-4.18 (m, 1H, *H3'*), 3.75-3.78 (m, 1H, *H4'*), 3.43-3.48 (m, 1H, *H5'*), 3.36 (s, 3H, C*H*$_3$), 3.19-3.24 (m, 1H, *H5'*), 2.13-2.18 (m, 1H, *H2'*), 2.05-2.09 (m, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz,

DMSO): *δ* 163.7 (*C4*), 155.4 (*C*O), 153.9 (*C*-Ph), 150.5 (*C2*), 136.0 (*C6*), 133.5 (*C*-Ph), 119.3, 113.8 (*C*-Ph), 109.8 (*C5*), 85.4 (*C1'*), 83.7 (*C4'*), 71.1 (*C3'*), 55.4 (*C*H_3), 41.4 (*C5'*), 38.4 (*C2'*), 12.0 (*C*H_3); LCMS (ES^+): m/z (%) 391 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{18}H_{23}N_4O_6$ $[M+H]^+$ 391.1612 *m*/*z*, found 391.1599 *m*/*z* (3.43 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(4-*tert*-butyl-phenyl)urea (52):** 4-*tert*-Butylphenyl isocyanate reacted with amine **33** to yield compound **52** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.33 (s, 1H, N*H*), 8.43 (s, 1H, N*H*), 7.52 (d, *J* = 1.1 Hz, 1H, *H6*), 7.28-7.30 (m, 2H, *H*-Ph), 7.22-7.24 (m, 2H, *H*-Ph), 6.24 (t, *J* = 5.90 Hz, 1H, N*H*), 6.18 (qt, *J* = 4.70 Hz, 1H, *H1'*), 5.34 (d, *J* = 4.25 Hz, 1H, O*H*), 4.16 (qt, *J* = 3.18 Hz, 1H, *H3'*), 3.75-3.78 (m, 1H, *H4'*), 3.43-3.49 (m, 1H, *H5'*), 3.19-3.24 (m, 1H, *H5'*), 2.13-2.19 (m, 1H, *H2'*), 2.04-2.09 (m, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 155.3 (*C*O), 150.5 (*C2*), 143.3, 173.7 (*C*-Ph), 136.1 (*C6*), 125.2, 117.4 (*C*-Ph), 109.8 (*C5*), 85.4 (*C1'*), 83.7 (*C4'*), 71.1 (*C3'*), 41.4 (*C5'*), 38.4 (*C2'*), 33.8 (*C*$(CH_3)_3$), 31.2 (*C*H_3), 12.0 (*C*H_3); LCMS (ES^+): m/z (%) 417 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{21}H_{29}N_4O_5$ $[M+H]^+$ 417.2132 *m*/*z*, found 417.2131 *m*/*z* (0.39 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(3-trifluoromethyl-4-chloro-phenyl)thiourea (53):** 3-Trifluoromethyl-4-chlorophenyl isothiocyanate reacted with amine **33** to yield compound **53** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.35 (s, 1H, N*H*), 9.99 (s, 1H, NH), 8.19 (m, 2H, N*H* and *H*-Ph), 7.72 (d, *J* = 10.80 Hz, 1H, *H*-Ph), 7.52 (s, 1H, *H6*), 6.20 (t, *J* = 6.35 Hz, 1H, *H1'*), 5.40 (d, *J* = 4.36 Hz, 1H, O*H*), 4.23 (m, 1H, *H4'*), 3.94 (m, 2H, *H5'*), 3.62 (m, 1H, *H3'*), 2.21 (m, 1H, *H2'*), 2.08 (m, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{19}F-NMR (470MHz, DMSO): *δ* 61.47; LCMS (ES^+): m/z (%) 479 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{18}H_{19}Cl_1F_3N_4O_4S_1$ $[M+H]^+$ 479.0762 *m*/*z*, found 479.0775 *m*/*z* (-2.68 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(3-trifluoromethyl-4-chlorophenyl)urea (54):** 3-Trifluoromethyl-4-chlorophenyl isocyanate reacted with amine **33** to yield compound **54** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.35 (s, 1H, N*H*), 9.05 (s, 1H, N*H*), 8.10 (d, *J* = 2.20 Hz, 1H, *H6*), 7.52-7.56 (m, 3H, *H*-Ph), 6.50 (t, *J* = 5.90 Hz, 1H, N*H*), 6.18 (qt, *J* = 4.70 Hz, 1H, *H1'*), 5.35 (d, *J* = 4.25 Hz, 1H, O*H*), 4.15-4.18 (m, 1H, *H3'*), 3.78-3.81 (m, 1H, *H4'*), 3.43-3.48 (m, 1H, *H5'*), 3.23-3.28 (m, 1H, *H5'*), 2.13-2.18, 2.04-2.09 (m, 2H, *H2'*), 1.76 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): *δ* 163.7 (*C4*), 154.9 (*C*O), 150.5 (*C2*), 136.1 (*C6*), 140.0, 131.9, 126.7, 122.3, 121.4, 116.0 (*C*-Ph), 109.7 (*C5*), 85.1 (*C1'*), 83.8 (*C4'*), 71.1 (*C3'*), 41.5 (*C5'*), 38.3 (*C2'*), 12.3 (*C*H_3); LCMS

(ES^+): m/z (%) 463 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{18}H_{19}Cl_1F_3N_4O_5$ $[M+H]^+$ 463.0991 *m*/*z*, found 463.0977 *m*/*z* (2.85 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(4-nitro-phenyl)urea (55):** 4-Nitrophenyl isocyanate reacted with amine **33** to yield compound **55** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.34 (s, 1H, N*H*), 9.34 (s, 1H, N*H*), 8.15 (d, *J* = 12.14 Hz, 2H, *H*-Ph), 7.62 (d, *J* = 11.97 Hz, 2H, *H*-Ph), 7.51 (s, 1H, *H6*), 6.61 (t, *J* = 6.00 Hz, N*H*), 6.19 (t, *J* = 7.53 Hz, *H1'*), 5.37 (d, *J* = 17.05 Hz, O*H*), 4.17 (m, 1H, *H3'*), 3.79 (m, 1H, *H4'*), 3.50 (m, 1H, *H5'*), 3.26 (m, 1H, *H5'*), 2.19 (m, 1H, *H2'*), 2.08 (m, 1H, H2'), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 154.5 (*C*O), 150.5 (*C2'*), 147.0 (*C*-Ph), 140.4 (*C*-Ph), 136.1 (*C6*), 125.2 (*C*-Ph), 116.8 (*C*-Ph), 109.8 (*C5*), 85.0 (*C1'*), 83.7 (*C4'*), 71.1 (*C3'*), 41.5 (*C5'*), 38.3 (*C2'*), 12.1 (*C*H$_3$); LCMS (ES^+): m/z (%) 406 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{17}H_{20}N_5O_7$ $[M+H]^+$ 406.1357 *m*/*z*, found 406.1374 *m*/*z* (-4.17 ppm).

General Procedure for compounds 56 – 69

For the synthesis of compounds **56** – **69**, compound of amine **8** (1eq.) was dissolved in DMF at 0 °C. The coupling reagents (1.1 eq.) were added and the reaction mixture was allowed to stir at room temperature for 3 h. After the completion of the reaction, the reaction mixture was evaporated to dry (ethanol and toluene were used to co-evaporate) and the residue was purified by column chromatography to yield the compounds **56** – **69** as a solid with the yields ranging from 41 % to 91 %.

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(2-phenylphenyl)urea (56):** 2-Phenylphenyl isocyanate reacted with amine **8** to yield compound **56** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.23 (s, 1H, N*H*), 7.88 (qt, *J* = 3.05 Hz, 1H, N*H*), 7.76 (d, *J* = 1.15 Hz, 1H, *H6*), 7.05-7.89 (m, 9H, *H*-Ph), 6.72 (t, *J* = 5.80 Hz, 1H, N*H*), 6.14 (qt, *J* = 3.73 Hz, 1H, *H1'*), 5.41 (d, *J* = 1.85 Hz, 1H, O*H*), 4.15-4.17 (m, 2H, *H3'* and *H4'*), 3.20-3.25, 3.08-3.13 (m, 2H, *H5'*), 2.52-2.57 (m, 1H, *H2'*), 1.91-1.95 (m, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 155.6 (*C*O), 150.5 (*C2*), 136.4 (*C6*), 138.7, 136.9, 132.3, 130.1, 129.1, 128.7, 127.6, 127.3, 122.6, 122.5 (*C*-Ph), 108.8 (*C5*), 87.1 (*C1'*), 84.7 (*C4'*), 70.9 (*C3'*), 41.2 (*C5'*), 39.0 (*C2'*), 12.3 (*C*H$_3$); LCMS (ES^+): m/z (%) 437 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{23}H_{25}N_4O_5$ $[M+H]^+$ 437.1819 *m*/*z*, found 437.1811 *m*/*z* (1.92 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-phenylphenyl)urea (57)**: 4-Phenylphenyl isocyanate reacted with amine **8** to yield compound **57** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.25 (s, 1H, N*H*),

8.66 (s, 1H, N*H*), 7.78 (d, *J* = 1.15 Hz, 1H, *H6*), 7.28-7.62 (m, 9H, *H*-Ph), 6.30 (t, *J* = 5.85 Hz, 1H, N*H*), 6.20 (qt, *J* = 3.75 Hz, 1H, *H1'*), 5.44 (d, *J* = 3.25 Hz, 1H, O*H*), 4.18-4.23 (m, 2H, *H3'* and *H4'*), 3.26-3.30, 3.12-3.18 (m, 2H, *H5'*), 2.57-2.62 (m, 1H, *H2'*), 1.93-1.97 (m, 1H, *H2'*), 1.79 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 155.1 (*C*O), 150.5 (*C2*), 136.9 (*C6*), 139.9, 132.8, 128.8, 126.9, 126.6, 126.0, 118.0 (*C*-Ph), 108.8 (*C5*), 86.8 (*C1'*), 84.7 (*C4'*), 70.9 (*C3'*), 41.1 (*C5'*), 39.0 (*C2'*), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 437 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{23}H_{25}N_4O_5$ [M+H]$^+$ 437.1819 *m*/*z*, found 437.1821 *m*/*z* (-0.35 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(3-(phenoxymethyl)phenyl) urea (58):** 3-(Phenoxylmethyl)phenyl isocyanate reacted with amine **8** to yield compound **58** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.29 (s, 1H, N*H*), 8.63 (s, 1H, N*H*), 7.78 (d, *J* = 1.15 Hz, 1H, *H6*), 7.49 (s, 1H, *H*-Ph), 7.22-7.35 (m, 4H, *H*-Ph), 6.92-7.00 (m, 4H, *H*-Ph), 6.27 (t, *J* = 5.87 Hz, 1H, N*H*), 6.18 (qt, *J* = 3.73 Hz, 1H, *H1'*), 5.45 (d, *J* = 3.30 Hz, 1H, O*H*), 5.04 (s, 2H, C*H*$_2$), 4.16-4.21 (m, 2H, *H3'* and *H4'*), 3.23-3.28 (m, 1H, *H5'*), 3.09-3.15 (m, 1H, *H5'*), 2.55-2.60 (m, 1H, *H2'*), 1.92-1.96 (m, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 155.1 (*C*O), 150.5 (*C2*), 158.3, 140.5, 137.7, 129.5, 128.8, 120.6, 120.27, 117.0, 116.5, 114.7 (*C*-Ph), 136.9 (*C6*), 108.8 (*C5*), 86.9 (*C1'*), 84.6 (*C4'*), 70.8 (*C3'*), 69.1 (*C*H$_2$), 41.0 (*C5'*), 39.0 (*C2'*), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 467 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{24}H_{27}N_4O_6$ [M+H]$^+$ 467.1925 *m*/*z*, found 467.1929 *m*/*z* (-0.76 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(2-(phenoxymethyl)phenyl) urea (59):** 2-(Phenoxylmethyl)phenyl isocyanate reacted with amine **8** to yield compound **59** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.28 (s, 1H, N*H*), 7.94 (s, 1H, N*H*), 7.85 (d, *J* = 7.60 Hz, 1H, N*H*), 7.79 (d, *J* = 1.15 Hz, 1H, *H6*), 7.39 (qt, *J* = 3.00 Hz, 1H, *H*-Ph), 7.25-7.32 (m, 3H, *H*-Ph), 6.88-7.03 (m, 5H, *H*-Ph), 6.19 (qt, *J* = 3.75 Hz, 1H, *H1'*), 5.47 (d, *J* = 3.20 Hz, 1H, O*H*), 5.04 (s, 2H, C*H*$_2$), 4.17-4.22 (m, 2H, *H3'* and *H4'*), 3.26-3.31 (m, 1H, *H5'*), 3.09-3.18 (m, 1H, *H5'*), 2.54-2.60 (m, 1H, *H2'*), 1.92-1.96 (m, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 155.4 (*C*O), 150.5 (*C2*), 158.3, 141.1, 138.0, 129.4, 129.3, 128.4, 126.3, 122.2, 121.6, 120.7 (*C*-Ph), 136.9 (*C6*), 108.8 (*C5*), 87.0 (*C1'*), 84.6 (*C4'*), 70.9 (*C3'*), 66.3 (*C*H$_2$), 41.2 (*C5'*), 39.0 (*C2'*), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 467 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{24}H_{27}N_4O_6$ [M+H]$^+$ 467.1925 *m*/*z*, found 467.1921 *m*/*z* (0.93 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-benzyloxyphenyl)urea (60):** 4-Benzyloxyphenyl isocyanate reacted with amine **8** to yield compound **60** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.29 (s, 1H,

N*H*), 8.37 (s, 1H, N*H*), 7.78 (s, 1H, *H6*), 7.28-7.44 (m, 7H, *H*-Ph), 6.90 (d, *J* = 9.01 Hz, 2H, *H*-Ph), 6.18 (m, 2H, *H1'* and N*H*), 5.45 (d, *J* = 3.16 Hz, 1H, O*H*), 5.03 (s, 2H, CH_2-Ph), 4.19 (m, 2H, *H3'* and *H4'*), 3.24 (m, 1H, *H5'*), 3.11 (m, 1H, H5'), 2.57 (m, 1H, *H2'*), 1.93 (m, 1H, *H2'*), 1.78 (s, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): δ 163.9 (*C4*), 155.4 (*C*O), 150.5 (*C2*), 137.3 (*C6*), 153.0, 133.7, 128.4, 127.7, 119.3, 114.9 (*C*-Ph), 108.8 (*C5*), 87.0 (*C1'*), 84.7 (*C4'*), 79.1 (*C3'*), 70.8 (*C*H_2-Ph), 69.3 (*C5'*), 41.04 (*C2'*), 12.3 (*C*H_3); LCMS (ES$^+$): m/z (%) 467 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{24}H_{27}N_4O_6$ [M+H]$^+$ 467.1925 *m*/*z*, found 467.1937 *m*/*z* (-2.53 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-benzyloxyphenyl)thiourea (61):** 4-Benzyloxyphenyl isothiocyanate reacted with amine **8** to yield compound **61** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.28 (s, 1H, N*H*), 9.47 (s, 1H, N*H*), 7.79 (d, *J* = 1.15 Hz, 1H, *H6*), 7.59 (s, 1H, N*H*), 7.25-7.46 (m, 7H, *H*-Ph), 6.97-6.99 (m, 2H, *H*-Ph), 6.19 (qt, *J* = 5.46 Hz, 1H, *H1'*), 5.48 (d, *J* = 3.15 Hz, 1H, O*H*), 4.35 (t, *J* = 5.35 Hz, 1H, *H3'*), 4.24 (t, *J* = 2.67 Hz, 1H, *H4'*), 3.58-3.62 (m, 1H, *H5'*), 3.48-3.50 (m, 1H, *H5'*), 2.56-2.61 (m, 1H, *H2'*), 1.92 (d, *J* = 14.40 Hz, 1H, *H2'*), 1.78 (s, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 155.6 (*C*O), 150.5 (*C2*), 137.0 (*C6*), 137.1, 128.4, 127.8, 127.7, 125.7, 114.8 (*C*-Ph), 108.7 (*C5*), 86.0 (*C1'*), 84.7 (*C4'*), 70.8 (*C3'*), 69.3 (*C*H_2), 46.5 (*C5'*), 39.0 (*C2'*), 12.36 (*C*H_3); LCMS (ES$^+$): m/z (%) 483 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{24}H_{27}N_4O_5S_1$ [M+H]$^+$ 483.1697 *m*/*z*, found 483.1688 *m*/*z* (1.71 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-tetrahydropyran-4-oxyphenyl)urea (62):** 4-tetrahydropyran-4-oxyphenyl isocyanate reacted with amine **8** to yield compound **62** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.27 (s, 1H, N*H*), 8.35 (s, 1H, N*H*), 7.76 (d, *J* = 1.15 Hz, 1H, *H6*), 7.24-7.27 (m, 2H, *H*-Ph), 6.83-6.86 (m, 2H, *H*-Ph), 6.14-6.17 (m, 2H, N*H* and *H1'*), 5.43 (d, *J* = 3.25 Hz, 1H, O*H*), 4.39-4.44 (m, 1H, C*H*), 4.13-4.18 (m, 2H, *H3'* and *H4')*, 3.80-3.84 (m, 2H, CH_2), 3.41-3.46 (m, 2H, CH_2), 3.19-3.24 (m, 1H, *H5'*), 3.06-3.11 (m, 1H, *H5'*), 2.53-2.58 (m, 1H, *H2'*), 1.89-1.94 (m, 3H, *H2'* and CH_2), 1.76 (s, 3H, CH_3), 1.49-1.56 (m, 2H, CH_2); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 155.3 (*C*O), 151.3 (*C2*), 136.9 (*C6*), 155.3, 133.8, 119.3, 116.4 (*C*-Ph), 108.8 (*C5*), 87.0 (*C1'*), 84.6 (*C4'*), 71.7 (*C3'*), 70.8 (*C*H), 64.5 (*C*H_2), 41.0 (*C5'*), 39.0 (*C2'*), 31.8 (*C*H_2), 12.3 (*C*H_3); LCMS (ES$^+$): m/z (%) 461 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{22}H_{29}N_4O_7$ [M+H]$^+$ 461.2031 *m*/*z*, found 461.2024 *m*/*z* (1.46 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-piperdin-1-ylphenyl)urea (63)**: 4-Piperdin-1-ylphenyl isocyanate reacted with amine **8** to yield compound **63** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.28 (s, 1H, N*H*), 8.25 (s, 1H, N*H*), 7.77 (d, *J* = 1.20 Hz, 1H, *H6*), 7.19-7.22 (m, 2H, *H*-Ph), 6.80-

6.83 (m, 2H, *H*-Ph), 6.17 (qt, *J* = 3.71 Hz, 1H, *H1'*), 6.12 (t, *J* = 5.90 Hz, 1H, N*H*), 5.44 (d, *J* = 3.25 Hz, 1H, O*H*), 4.15-4.20 (m, 2H, *H3'* and *H4'*), 3.20-3.24 (m, 1H, *H5'*), 3.07-3.12 (m, 1H, *H5'*), 2.99 (t, *J* = 5.42 hz, 4H, CH_2), 2.54-2.59 (m, 1H, *H2'*), 1.91-1.95 (m, 1H, *H2'*), 1.78 (s, 3H, CH_3), 1.58-1.63 (m, 4H, CH_2), 1.48-1.51 (m, 2H, CH_2); ^{13}C-NMR (125MHz, DMSO): *δ* 163.8 (*C4*), 155.4 (*C*O), 150.5 (*C2*), 136.9 (*C6*), 146.9, 132.4, 119.0, 116.8 (*C*-Ph), 108.8 (*C5*), 87.0 (*C1'*), 84.6 (*C4'*), 70.8 (*C3'*), 50.6 (*C*H_2), 41.0 (*C5'*), 39.0 (*C2'*), 25.4 (*C*H_2), 23.8 (*C*H_2), 12.3 (*C*H_3); LCMS (ES$^+$): m/z (%) 444 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{22}H_{30}N_5O_5$ [M+H]$^+$ 444.2241 *m*/*z*, found 444.2231 *m*/*z* (2.31 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-(4-methylpiperazin-1-yl)phenyl)urea (64):** 4-(4-Methylpiperazinyl)phenyl isocyanate reacted with amine **8** to yield compound **64** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.28 (s, 1H, N*H*), 8.27 (s, 1H, N*H*), 7.79 (d, *J* = 1.10 Hz, 1H, *H6*), 7.20-7.31 (m, 2H, *H*-Ph), 6.82-6.91 (m, 2H, *H*-Ph), 6.17 (qt, *J* = 3.75 Hz, 1H, *H1'*), 6.12 (t, *J* = 5.87 Hz, 1H, N*H*), 5.46 (d, *J* = 3.34 Hz, 1H, O*H*), 4.17-4.22 (m, 2H, *H3'* and *H4'*), 3.20-3.27 (m, 1H, *H5'*), 3.07-3.14 (m, 1H, *H5'*), 2.99 (m, 4H, CH_2), 2.54-2.59 (m, 1H, *H2'*), 2.42-2.51 (m, 4H, CH_2), 2.17-2.23 (s, 3H, CH_3), 1.91-1.97 (m, 1H, *H2'*), 1.78 (s, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): *δ* 163.8 (*C4*), 155.4 (*C*O), 150.5 (*C2*), 136.9 (*C6*), 146.0, 132.5, 132.0, 119.4, 119.0, 116.2, 116.1 (*C*-Ph), 108.8 (*C5*), 87.0 (*C1'*), 84.6 (*C4'*), 79.2 (*C*H_2), 70.8 (*C3'*), 54.7 (*C*H_2), 48.9, 48.9 (*C*H_2), 45.8 (*C5'*), 41.0 (*C2'*), 12.3 (*C*H_3); LCMS (ES$^+$): m/z (%) 459 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{22}H_{31}N_6O_5$ [M+H]$^+$ 459.2350 *m*/*z*, found 459.2361 *m*/*z* (-2.31 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-(6-methyl-2-benzothiazolyl)phenyl) urea (65):** 4-(6-Methyl-2-benzothiazolyl)phenyl isocyanate reacted with amine **8** to yield compound **65** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.17 (s, 1H, N*H*), 8.86 (s, 1H, N*H*), 7.81-7.83, 7.74-7.77 (m, 4H, *H*-Ph), 7.67 (d, *J* = 1.15 Hz, 1H, *H6*), 7.46 (qt, *J* = 2.93 Hz, 2H, *H*-Ph), 7.21 (qt, *J* = 3.16 Hz, 2H, *H*-Ph), 6.32 (t, *J* = 5.34 Hz, 1H, N*H*), 6.08 (qt, *J* = 3.75 Hz, 1H, *H1'*), 5.36 (d, *J* = 3.30 Hz, 1H, O*H*), 4.07-4.10 (m, 2H, *H3'* and *H4'*), 3.15-3.20 (m, 1H, *H5'*), 3.00-3.05 (m, 1H, *H3'*), 2.44-2.51 (m, 1H, *H2'*), 2.33 (s, 3H, CH_3), 1.81-1.86 (m, 1H, *H2'*), 1.66 (s, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): *δ* 163.8 (*C4*), 150.5 (*C2*), 154.8, 151.8, 143.3, 134.7, 134.2, 127.9, 125.7, 121.9, 117.6 (*C*-Ph), 136.9 (*C6*), 108.9 (*C5*), 86.7 (*C1'*), 84.6 (*C4'*), 70.8 (*C3'*), 41.0 (*C5'*), 39.0 (*C2'*), 21.0 (*C*H_3), 12.3 (*C*H_3); LCMS (ES$^+$): m/z (%) 508 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{25}H_{26}N_5O_5S_1$ [M+H]$^+$ 508.1649 *m*/*z*, found 508.1658 *m*/*z* (-1.82 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-phenyloxyphenyl) urea (66):** 4-Phenlyoxyphenyl isocyanate reacted with amine **8** to yield compound **66** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.25 (s, 1H, N*H*), 8.56 (s, 1H, N*H*), 7.78 (d, *J* = 1.15 Hz, 1H, *H6*), 7.39-7.42, 7.33-7.37 (m, 4H, *H*-Ph), 7.05-7.09 (m, 1H, *H*-Ph), 6.92-6.95 (m, 4H, *H*-Ph), 6.24 (t, *J* = 5.85 Hz, 1H, N*H*), 6.19 (qt, *J* = 3.73 Hz, 1H, *H1'*), 5.43 (d, *J* = 3.25 Hz, 1H, O*H*), 4.17-4.22 (m, 2H, *H3'* and *H4'*), 3.24-3.29, 3.10-3.18 (m, 2H, *H5'*), 2.57-2.61 (m, 1H, *H2'*), 1.92-1.97 (m, 1H, *H2'*), 1.79 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 155.2 (*C*O), 150.5 (*C2*), 136.5 (*C6*), 157.8, 150.0, 136.9, 129.8, 122.6, 119.8, 119.2, 117.4 (*C*-Ph), 108.8 (*C5*), 86.9 (*C1'*), 84.7 (*C4'*), 70.9 (*C3'*), 41.1 (*C5'*), 39.0 (*C2'*), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 453 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{23}H_{25}N_4O_6$ [M+H]$^+$ 453.1769 *m*/*z*, found 453.1756 *m*/*z* (2.76 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-morpholino-1-yl-phenyl) thiourea (67):** 4-Morpholinophenyl isothiocyanate reacted with amine **8** to yield compound **67** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.25 (s, 1H, N*H*), 9.40 (s, 1H, N*H*), 7.78 (d, *J*=1.15 Hz, 1H, *H6*), 7.50 (s, 1H, N*H*), 7.20 (d, *J* = 8.90 Hz, 2H, *H*-Ph), 6.91 (d, *J* = 9.05 Hz, 2H, *H*-Ph), 6.18 (qt, *J* = 3.61 Hz, 1H, *H1'*), 5.45 (d, *J* = 3.30 Hz, 1H, O*H*), 4.34-4.37 (m, 1H, *H3'*), 4.23-4.26 (m, 1H, *H4'*), 3.73 (t, *J* = 4.80 Hz, 4H, C*H*$_2$), 3.60-3.63, 3.47-3.52 (m, 2H, *H5'*), 3.08 (t, *J* = 4.82 Hz, 4H, C*H*$_2$), 2.56-2.61, 1.90-1.94 (m, 2H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 180.8 (*C*S), 163.8 (*C4*), 150.5 (*C2*), 137.0 (*C6*), 148.4, 125.2, 115.2 (*C*-Ph), 108.7 (*C5*), 86.0 (*C1'*), 84.7 (*C4'*), 70.8 (*C3'*), 66.1 (*C*H$_2$), 48.6 (*C*H$_2$), 45.5 (*C5'*), 39.0 (*C2'*), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 462 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{21}H_{28}N_5O_5S_1$ [M+H]$^+$ 462.1806 *m*/*z*, found 462.1794 *m*/*z* (2.48 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-benzylphenyl) urea (68) :** 4-Phenlyoxyphenyl isocyanate reacted with amine **8** to yield compound **68** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.28 (s, 1H, N*H*), 8.48 (s, 1H, N*H*), 7.07-7.30 (m, 9H, *H*-Ph), 6.22 (t, *J* = 5.82 Hz, 1H, N*H*), 6.18 (qt, *J* = 3.71 Hz, 1H, *H1'*), 5.45 (d, *J* = 3.25 Hz, 1H, O*H*), 4.15-4.20 (m, 2H, *H3'* and *H4'*), 3.84 (s, 2H, C*H*$_2$), 3.21-3.26, 3.08-3.13 (m, 2H, *H5'*), 2.54-2.59, 1.91-1.95 (m, 2H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 155.2 (*C*O), 150.5 (*C2*), 136.9 (*C6*), 141.7, 138.3, 133.9, 128.9, 128.5, 128.3, 125.8, 117.8 (*C*-Ph), 108.8 (*C5*), 86.9 (*C1'*), 84.6 (*C4'*), 70.8 (*C3'*), 41.0 (*C*H$_2$), 40.4 (*C5'*), 39.0 (*C2'*), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 451 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{24}H_{27}N_4O_5$ [M+H]$^+$ 451.1976 *m*/*z*, found 451.1965 *m*/*z* (2.35 ppm).

***N*-(5'-deoxy-α-thymidin-5'-yl)-*N'*-(4-(6-(trifluoromethyl)pyridin-3-yl)phenyl) urea (69)** : 4-(6-(Trifluoromethyl)pyridin-3-yl)phenyl isocyanate reacted with amine **8** to yield compound **69** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.28 (s, 1H, N*H*), 8.97 (t, *J* = 1.12 Hz, 1H, *H*-Ph), 8.88 (s, 1H, N*H*), 8.21 (qt, *J* = 3.51 Hz, 1H, *H*-Ph), 8.08-8.12 (m, 3H, *H*-Ph), 7.79 (t, *J* = 1.12 Hz, 1H, *H6*), 7.56 (d, *J* = 8.85 Hz, 2H, *H*-Ph), 6.40 (t, *J* = 5.70 Hz, 1H, N*H*), 6.20 (qt, *J* = 3.75 Hz, 1H, *H1'*), 5.48 (d, *J* = 3.30 Hz, 1H, O*H*), 4.18-4.23 (m, 2H, *H3'* and *H4'*), 3.26-3.31, 3.12-3.17 (m, 2H, *H5'*), 2.56-2.62, 1.93-1.97(m, 2H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.8 (*C4*), 155.9 (*C*O), 150.5 (*C2*), 136.9 (*C6*), 159.5, 129.7, 127.8, 119.2, 117.5 (*C*-Ph), 108.9 (*C5*), 86.7 (*C1'*), 84.6 (*C4'*), 70.8 (*C3'*), 41.0 (*C5'*), 39.0 (*C2'*), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 506 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{23}H_{23}F_3N_5O_5$ [M+H]$^+$ 506.1646 *m*/*z*, found 506.1636 *m*/*z* (1.91 ppm).

General Procedure for compounds 70 – 79

For the synthesis of compounds **70** – **79**, compound of amine **33** (1 eq.) was dissolved in DMF at 0 °C. The coupling reagents (1.1 eq.) were added and the reaction mixture was allowed to stir at room temperature for 3 h. After the completion of the reaction, the reaction mixture was evaporated to dry (ethanol and toluene were used to co-evaporate) and the residue was purified by column chromatography to yield the compounds **70** – **79** as a solid with the yields ranging from 43 % to 87 %.

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(2-phenylphenyl)urea (70):** 2-Phenylphenyl isocyanate reacted with amine **33** to yield compound **70** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.32 (s, 1H, N*H*), 7.90 (d, *J* = 7.90 Hz, 1H, N*H*), 7.04-7.48 (m, 10H, *H6* and *H*-Ph), 6.79 (t, *J* = 5.77 Hz, 1H, N*H*), 6.16 (t, *J* = 7.00 Hz, 1H, *H1'*), 5.33 (d, *J* = 4.25 Hz, 1H, O*H*), 4.11-4.14 (m, 1H, *H3'*), 3.70-3.73 (m, 1H, *H4'*), 3.43-3.48 (m, 1H, *H5'*), 3.15-3.20 (m, 1H, *H5'*), 2.04-2.14 (m, 2H, *H2'*), 1.73 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 155.6 (*C*O), 150.4 (*C2*), 138.6, 136.4 (*C*-Ph), 136.0 (*C6*), 136.0, 132.0, 130.2, 129.1, 128.7, 127.6, 127.3, 122.5, 122.2 (*C*-Ph), 109.8 (*C5*), 85.4 (*C1'*), 83.6 (*C4'*), 71.1 (*C3'*), 41.5 (*C5'*), 38.5 (*C2'*), 12.0 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 437 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{23}H_{25}N_4O_5$ [M+H]$^+$ 437.1819 *m*/*z*, found 437.1829 *m*/*z* (-2.16 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(4-phenylphenyl)urea (71):** 4-Phenylphenyl isocyanate reacted with amine **33** to yield compound **71** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.34 (s, 1H, N*H*), 8.66 (s, 1H, N*H*), 7.28-7.62 (m, 10H, *H6* and *H*-Ph), 6.36 (t, *J* = 5.72 Hz, 1H, N*H*), 6.20 (t, *J* = 7.00

Hz, 1H, *H1'*), 5.37 (d, *J* = 4.15 Hz, 1H, O*H*), 4.18 (d, *J* = 2.50 Hz, 1H, *H3'*), 3.79-3.81 (m, 1H, *H4'*), 3.47-3.52 (m, 1H, *H5'*), 3.22-3.28 (m, 1H, *H5'*), 2.15-2.21 (m, 1H, *H2'*), 2.06-2.10 (m, 1H, *H2'*), 1.79 (s, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): *δ* 163.7 (*C4*), 155.1 (*C*O), 150.5 (*C2*), 139.9, 139.9 (*C*-Ph), 136.1 (*C6*), 132.8, 128.8, 126.9, 126.6, 126.0, 117.9 (*C*-Ph), 109.8 (*C5*), 85.3, 83.7 (*C4'*), 71.1 (*C3'*), 41.5 (*C5'*), 38.4 (*C2'*), 12.1 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 437 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{23}H_{25}N_4O_5$ [M+H]$^+$ 437.1819 *m/z*, found 437.1823 *m/z* (-0.79 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(1-naphthyl)urea (72):** 1-Naphthyl isocyanate reacted with amine **33** to yield compound **72** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.33 (s, 1H, N*H*), 8.61 (s, 1H, N*H*), 7.41-8.09 (m, 8H, *H6* and *H*-Ph), 6.83 (t, *J* = 5.51 Hz, 1H, N*H*), 6.22 (t, *J* = 7.22 Hz, 1H, *H1'*), 5.39 (d, *J* = 4.26 Hz, 1H, O*H*), 4.20 (m, 1H, *H3'*), 3.81 (m, 1H, *H4'*), 3.58 (m, 1H, *H5'*), 3.29 (m, 1H, *H5'*), 2.21 (m, 1H, *H2'*), 2.10 (m, 1H, *H2'*), 1.75 (s, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): *δ* 163.7 (*C4*), 155.6 (*C*O), 150.5 (*C2*), 136.1 (*C6*), 135.0, 133.7, 128.3, 125.9, 125.7, 125.4, 125.3, 122.0, 121.2, 116.2 (*C*-Ph), 109.8 (*C5*), 85.3 (*C1'*), 83.6 (*C4'*), 71.1 (*C3'*), 41.6 (*C5'*), 38.4 (*C2'*), 12.0 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 411 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{21}H_{23}N_4O_5$ [M+H]$^+$ 411.1663 *m/z*, found 411.1684 *m/z* (-5.14 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(3-(phenoxymethyl)phenyl)urea (73):** 3-(Phenoxylmethyl)phenyl isocyanate reacted with amine **33** to yield compound **73** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.33 (s, 1H, N*H*), 8.60 (s, 1H, N*H*), 7.52 (d, *J* = 1.15 Hz, 1H, *H6*), 7.49, 7.21-7.34, 6.92-7.00 (m, 9H, *H*-Ph), 6.31 (t, *J* = 5.35 Hz, 1H, N*H*), 6.18 (qt, *J* = 4.68 Hz, 1H, *H1'*), 5.35 (d, *J* = 4.25 Hz, 1H, O*H*), 5.03 (s, 2H, CH_2), 4.15-4.17 (m, 1H, *H3'*), 3.76-3.79 (m, 1H, *H4'*), 3.45-3.47 (m, 1H, *H5'*), 3.23-3.25 (m, 1H, *H5'*), 2.13-2.16, 2.06-2.09 (m, 2H, *H2'*), 1.77 (s, 3H, CH_3); ^{13}C-NMR (125MHz, DMSO): *δ* 163.7 (*C4*), 155.2 (*C*O), 150.5 (*C2*), 158.3, 140.5, 137.7, 129.5, 128.7, 120.3, 116.9, 116.5, 114.7 (*C*-Ph), 136.0 (*C6*), 85.3 (*C1'*), 83.7 (*C4'*), 71.1 (*C3'*), 69.1 (*C*H$_2$), 41.4 (*C5'*), 39.4 (*C2'*), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 467 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{24}H_{27}N_4O_6$ [M+H]$^+$ 467.1925 *m/z*, found 467.1910 *m/z* (3.18 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(2-(phenoxymethyl)phenyl)urea (74):** 2-(Phenoxylmethyl)phenyl isocyanate reacted with amine **33** to yield compound **74** as a solid; ^{1}H-NMR (500MHz, DMSO): *δ* 11.29 (s, 1H, N*H*), 7.91 (s, 1H, N*H*), 7.85 (qt, *J* = 2.98 Hz, 1H, N*H*), 7.52 (d, *J* = 1.20 Hz, 1H, *H6*), 7.39 (qt, *J* = 3.01 Hz, 1H, *H*-Ph), 7.24-7.31 (m, 3H, *H*-Ph), 6.89-7.03 (m, 5H, *H*-Ph), 6.18 (qt, *J* = 4.66 Hz, 1H, *H1'*), 5.33 (d, *J* = 4.35 Hz, 1H, O*H*), 5.03 (s, 2H, CH_2),

4.16-4.18 (m, 1H, *H3'*), 3.75-3.78 (m, 1H, *H4'*), 3.47-3.51 (m, 1H, *H5'*), 3.22-3.27 (m, 1H, *H5'*), 2.13-2.17 (m, 1H, *H2'*), 2.06-2.09 (m, 1H, *H2'*), 1.75 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 154.5 (*C*O), 150.5 (*C2*), 158.3, 138.0, 129.4, 129.3, 128.3, 126.4, 122.3, 121.6, 120.7, 114.8 (*C*-Ph), 136.1 (*C6*), 109.8 (*C5*), 85.4 (*C1'*), 83.6 (*C4'*), 71.1 (*C3'*), 66.3 (*C*H$_2$), 41.6 (*C5'*), 38.4 (*C2'*), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 467 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{24}H_{27}N_4O_6$ [M+H]$^+$ 467.1925 *m*/*z*, found 467.1919 *m*/*z* (1.28 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(4-benzyloxyphenyl)urea (75):** 4-Benzyloxyphenyl isocyanate reacted with amine **33** to yield compound **75** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.34 (s, 1H, N*H*), 8.34 (s, 1H, N*H*), 7.52 (s, 1H, *H6*), 7.28-7.44 (m, 7H, *H*-Ph), 6.89 (d, *J* = 7.05 Hz, 2H, *H*-Ph), 6.20 (m, 2H, *H1'* and N*H*), 5.03 (s, 2H, C*H*$_2$-Ph), 4.17 (s, 1H, *H3'*), 3.77 (m, 1H, *H4'*), 3.44 (m, 1H, *H5'*), 3.22 (m, 1H, *H5'*), 2.16 (m, 1H, *H2'*), 2.07 (m, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 155.4 (*C*O), 150.5 (*C2*), 152.9, 137.3, 133.7, 128.4, 127.7, 127.6, 119.2, 114.9 (*C*-Ph), 136.1 (*C6*), 109.8 (*C5*), 85.4 (*C1'*), 83.7 (*C4'*), 71.1 (*C3'*), 69.3 (*C*H$_2$-Ph), 41.4 (*C5'*), 38.4 (*C2'*), 12.1 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 467 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{24}H_{27}N_4O_6$ [M+H]$^+$ 467.1925 *m*/*z*, found 467.1941 *m*/*z* (-3.51 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(4-tetrahydropyran-4-oxyphenyl)urea (76):** 4-tetrahydropyran-4-oxyphenyl isocyanate reacted with amine **33** to yield compound **76** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.33 (s, 1H, N*H*), 8.33 (s, 1H, N*H*), 7.52 (d, *J* = 1.15 Hz, 1H, *H6*), 7.25-7.28 (m, 2H, *H*-Ph), 6.84-6.87 (m, 2H, *H*-Ph), 6.16-6.21 (m, 2H, N*H* and *H1'*), 5.34 (d, *J* = 4.25 Hz, 1H, O*H*), 4.40-4.45 (m, 1H, C*H*), 4.14-4.17 (m, 1H, *H3'*), 3.81-3.85 (m, 2H, C*H*$_2$), 3.74-3.78 (m, 1H, *H4'*), 3.42-3.47 (m, 2H, C*H*$_2$), 3.16-3.24 (m, 1H, *H5'*), 2.12-2.18, 2.04-2.08 (m, 2H, *H2'*), 1.90-1.94 (m, 2H, C*H*$_2$), 1.77 (s, 3H, C*H*$_3$), 1.50-1.57 (m, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 155.4 (*C*O), 150.5 (*C2*), 136.0 (*C6*), 151.3, 133.8, 119.3, 116.4 (*C*-Ph), 109.8 (*C5*), 85.4 (*C1'*), 83.7 (*C4'*), 71.7 (*C3'*), 71.1 (*C*H), 64.5 (*C*H$_2$), 41.4 (*C5'*), 39.0 (*C2'*), 31.8 (*C*H$_2$), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 461 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{22}H_{29}N_4O_7$ [M+H]$^+$ 461.2031 *m*/*z*, found 461.2029 *m*/*z* (0.44 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(4-piperdin-1-ylphenyl)urea (77):** 4-Piperdin-1-ylphenyl isocyanate reacted with amine **33** to yield compound **77** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.30 (s, 1H, N*H*), 8.21 (s, 1H, N*H*), 7.52 (d, *J* = 0.8 Hz, 1H, *H6*), 7.21 (d, *J* = 8.95 Hz, 2H, *H*-Ph), 6.82 (d, *J* = 8.95 Hz, 2H, *H*-Ph), 6.14-6.19 (m, 2H, N*H* and *H1'*), 5.32 (d, *J* = 4.25 Hz, 1H, O*H*), 4.14-4.18 (m, 1H, *H3'*), 3.75-3.78 (m, 1H, *H4'*), 3.42-3.47 (m, 1H, *H5'*), 3.19-3.24 (m, 1H, *H5'*),

2.99 (t, *J* = 5.35 Hz, 4H, C*H*$_2$), 2.09-2.18, 2.05-2.09 (m, 2H, *H2'*), 1.78 (s, 3H, C*H*$_3$), 1.59-1.63 (m, 4H, C*H*$_2$), 1.47-1.52 (m, 2H, C*H*$_2$); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 155.5 (*C*O), 150.5 (*C2*), 136.0 (*C6*), 146.9, 132.4, 119.0, 116.8 (*C*-Ph), 109.8 (*C5*), 85.4 (*C1'*), 83.7 (*C4'*), 71.1 (*C3'*), 50.6 (*C*H$_2$), 41.0 (*C5'*), 38.4 (*C2'*), 25.4 (*C*H$_2$), 23.8 (*C*H$_2$), 12.3 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 444 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{22}H_{30}N_5O_5$ [M+H]$^+$ 444.2241 *m*/*z*, found 444.2232 *m*/*z* (2.11 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(4-(4-methylpiperazin-1-yl)phenyl)urea (78):** 4-(4-Methylpiperazinyl)phenyl isocyanate reacted with amine **33** to yield compound **78** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.33 (s, 1H, N*H*), 8.27, 8.24 (s, 2H, N*H*), 7.52 (d, *J* = 1.10 Hz, 1H, *H6*), 7.21-7.28 (m, 2H, *H*-Ph), 6.81-6.87 (m, 2H, *H*-Ph), 6.15-6.19 (m, 1H, *H1'*), 5.33 (d, *J* = 4.25 Hz, 1H, O*H*), 4.14-4.16 (m, 1H, *H3'*), 3.74-3.77 (m, 1H, *H4'*), 3.42-3.47 (m, 1H, *H5'*), 3.18-3.23 (m, 1H, *H5'*), 3.00-3.04 (m, 4H, C*H*$_2$), 2.42-2.45 (m, 4H, C*H*$_2$), 2.21 (s, 3H, C*H*$_3$), 2.12-2.18 (m, 1H, *H2'*), 2.04-2.08 (m, 1H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 155.4 (*C*O), 150.5 (*C2*), 136.0 (*C6*), 146.3, 146.0, 132.0, 119.4, 118.9, 116.1 (*C*-Ph), 109.8 (*C5*), 85.4 (*C1'*), 83.7 (*C4'*), 71.1 (*C3'*), 54.7 (*C*H$_2$), 48.9, 48.9 (*C*H$_2$), 45.8 (*C5'*), 38.4 (*C2'*), 12.2 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 459 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{22}H_{31}N_6O_5$ [M+H]$^+$ 459.2350 *m*/*z*, found 459.2340 *m*/*z* (2.20 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(4-(6-methyl-2-benzothiazolyl)phenyl)urea (79):** 4-(6-Methyl-2-benzothiazolyl)phenyl isocyanate reacted with amine **33** to yield compound **79** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.34 (s, 1H, N*H*), 8.95 (s, 1H, N*H*), 7.53 (d, *J* = 1.15 Hz, 1H, *H6*), 7.86-7.95, 7.57-7.59, 7.32-7.34 (m, 7H, *H*-Ph), 6.47 (t, *J* = 5.34 Hz, 1H, N*H*), 6.19 (qt, *J* = 4.70 Hz, 1H, *H1'*), 5.37 (d, *J* = 4.25 Hz, 1H, O*H*), 4.18-4.20 (m, 1H, *H3'*), 3.79-3.80 (m, 1H, *H4'*), 3.47-3.53 (m, 1H, *H5'*), 3.23-3.28 (m, 1H, *H5'*), 2.45 (s, 3H, C*H*$_3$), 2.16-2.23 (m, 1H, *H2'*), 2.06-2.10 (m, 1H, *H2'*), 1.79 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 151.8 (*C*O), 150.5 (*C2*), 136.1 (*C6*), 145.9, 143.3, 134.2, 127.9, 125.7, 121.9, 117.6 (*C*-Ph), 109.8 (*C5*), 85.2 (*C1'*), 83.7 (*C4'*), 71.1 (*C3'*), 41.5 (*C5'*), 38.3 (*C2'*), 21.0 (*C*H$_3$), 12.2 (*C*H$_3$); LCMS (ES$^+$): m/z (%) 508 (100) [M+H]$^+$; HRMS (ES$^+$): calcd for $C_{25}H_{26}N_5O_5S_1$ [M+H]$^+$ 508.1649 *m*/*z*, found 508.1634 *m*/*z* (3.05 ppm).

General Procedure for compounds 81 a-e

A suspension of 60% sodium hydride in mineral oil (2 mmol) was added to a suspension of *tert*-butyl (4-hydroxyphenyl)carbamate in 5 ml DMF under Ar and cooled with ice bath. Then

appropriate substituted benzyl bromides (**80 a-e)** were added to the mixture. The reaction was left under RT for 3 h. The reaction mixture was removed DMF and purified by chromatography by Hexane/EtOAC (7/3) to give the compounds **81 a-e**.

***N-tert*butoxycarbonyl-(4-((2-chlorobenzyl)oxy)phenyl)amine (81a):** 2-Chlorobenzyl bromide reacted with 4-((pivaloyloxy)amino)phenol to yield compound **81a** as a solid; ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.55-7.57, 7.40-7.42, 7.26-7.32, 6.93-6.96 (m, 8H, *H*-Ph), 6.35 (s, 1H, NH), 5.16 (s, 2H, CH_2), 1.53 (s, 9H, CH_3); ^{13}C-NMR (125MHz, $CDCl_3$): δ 154.6 (*C*O), 134.8, 132.6, 131.9, 129.4, 128.9, 128.8, 127.0, 115.3 (*C*-Ph), 76.8 ($C(CH_3)_3$), 67.5 (CH_2), 28.4 (CH_3); LCMS (ES^+): m/z (%) 278 (100) $[M+H]^+$.

***N- tert*butoxycarbonyl- (4-((3-chlorobenzyl)oxy)phenyl)amine (81b):** 3-Chlorobenzyl bromide reacted with 4-((pivaloyloxy)amino)phenol to yield compound **81b** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 9.17 (s, 1H, N*H*), 7.34-7.50, 6.90-6.93 (m, 8H, *H*-Ph), 5.06 (s, 2H, CH_2), 2.30 (s, 3H, CH_3), 1.46 (s, 9H, CH_3); ^{13}C-NMR (125MHz, DMSO): δ 153.2 (*C*O), 152.9, 139.9, 133.0, 133.0, 130.3, 127.6, 127.2, 119.5, 114.8 (*C*-Ph), 78.7 ($C(CH_3)_3$), 68.4 (CH_2), 28.1 (CH_3); LCMS (ES^+): m/z (%) 278 (100) $[M+H]^+$.

***N- tert*butoxycarbonyl- (4-((4-chlorobenzyl)oxy)phenyl)amine (81c):** 4-Chlorobenzyl bromide reacted with 4-((pivaloyloxy)amino)phenol to yield compound **81c** as a solid; ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.37, 7.28-7.29, 6.90-6.92 (m, 8H, *H*-Ph), 6.37 (s, 1H, NH), 5.01 (s, 2H, CH_2), 3.83 (s, 3H, CH_3), 1.53 (s, 9H, CH_3); ^{13}C-NMR (125MHz, $CDCl_3$): δ 154.5 (CO), 135.6, 133.7, 131.9, 128.8, 128.7, 120.4, 115.3 (*C*-Ph), 76.8 ($C(CH_3)_3$), 69.6 (CH_2), 28.4 (CH_3); LCMS (ES^+): m/z (%) 278 (100) $[M+H]^+$.

***N- tert*butoxycarbonyl- (4-((4-methoxybenzyl)oxy)phenyl)amine (81d):** 4-Methoxybenzyl bromide reacted with 4-((pivaloyloxy)amino)phenol to yield compound **81d** as a solid; ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.27-7.32, 7.00-7.02, 6.87-6.94 (m, 8H, *H*-Ph), 6.37 (s, 1H, NH), 5.03 (s, 2H, CH_2), 3.83 (s, 3H, CH_3), 1.53 (s, 9H, CH_3); ^{13}C-NMR (125MHz, $CDCl_3$): δ 159.8 (CO), 154.8, 138.7, 131.7, 129.6, 120.5, 119.6, 115.3, 113.5, 112.8 (*C*-Ph), 70.2 (CH_2), 55.3 (CH_3), 28.4 (CH_3); LCMS (ES^+): m/z (%) 274 (100) $[M+H]^+$.

***N- tert*butoxycarbonyl- (4-((4-tertbutylbenzyl)oxy)phenyl)amine (81e):** 4-tertbutylbenzyl bromide reacted with 4-((pivaloyloxy)amino)phenol to yield compound **81e** as a solid; ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.36-7.43, 7.27-7.28, 6.92-6.95 (m, 8H, *H*-Ph), 6.35 (s, 1H, NH), 5.01 (s, 2H,

C*H*$_2$), 1.53 (s, 9H, C*H*$_3$), 1.34 (s, 9H, C*H*$_3$); ^{13}C-NMR (125MHz, $CDCl_3$): δ 151.0 (*C*O), 134.0, 127.5, 125.8, 125.5, 115.2 (*C*-Ph), 76.8 (*C*(CH_3)$_3$), 70.2 (*C*H_2), 34.6 (*C*(CH_3)$_3$), 31.4 (*C*H_3), 28.4 (*C*H_3); LCMS (ES^+): m/z (%) 300 (100) $[M+H]^+$.

General Procedure for compounds 82a –e

The Boc group protected **81 a–e** (1.4 mmol) was dissolved in 40 ml DCM and stirred at RT for few minutes. TFA (2 ml) was added with a syringe. The solution changed from colorless to a slight yellow. After 3 h, the reaction was evaporated under reduced pressure and purified by chromatography to get a brown to grey color solid.

4-(2-Chlorobenzoxy)phenyl amine (82a): Compound **81a** was removed the Boc group to give compound **82a** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 9.37 (s, 2H, N*H*$_2$), 7.57-7.60, 7.51-7.54, 7.37-7.43, 7.19-7.34, 7.08-7.14 (m, 8H, *H*-Ph), 5.16 (s, 2H, C*H*$_2$); ^{13}C-NMR (125MHz, DMSO): δ 134.0, 132.6, 130.2, 130.0, 129.4, 127.4, 123.0, 115.8 (*C*-Ph), 67.2 (*C*H_2); LCMS (ES^+): m/z (%) 234 (100) $[M+H]^+$.

4-(3-Chlorobenzoxy)phenyl amine (82b): Compound **81b** was removed the Boc group to give compound **82b** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 9.28 (s, 1H, N*H*), 7.39-7.51, 7.17-7.19, 7.06-7.08 (m, 8H, *H*-Ph), 5.13 (s, 2H, C*H*$_2$); ^{13}C-NMR (125MHz, DMSO): δ 133.1, 130.4, 127.8, 127.3, 126.2, 115.8 (*C*-Ph), 68.5 (*C*H_2); LCMS (ES^+): m/z (%) 234 (100) $[M+H]^+$.

4-(4-Chlorobenzoxy)phenyl amine (82c): Compound **81c** was removed the Boc group to give compound **82c** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 9.49 (s, 2H, N*H*$_2$), 7.47, 7.20-7.22, 7.07-7.08 (m, 8H, *H*-Ph), 5.11 (s, 2H, C*H*$_2$); ^{13}C-NMR (125MHz, DMSO): δ 135.8, 132.5, 129.5, 128.4, 123.3, 115.8 (*C*-Ph), 68.6 (*C*H_2); LCMS (ES^+): m/z (%) 234 (100) $[M+H]^+$.

4-(4-Methoxybenzoxy)phenyl amine (82d): Compound **81d** was removed the Boc group to give compound **82d** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 9.48 (s, 2H, N*H*$_2$), 7.29-7.32, 7.19-7.22, 7.06-7.09, 7.00-7.01, 6.89-6.91 (m, 8H, *H*-Ph), 5.09 (s, 2H, C*H*$_2$), 3.76 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 159.3, 138.3, 129.6, 123.3, 119.7, 115.8, 113.2, 113.2 (*C*-Ph), 69.3 (*C*H_2), 55.0 (*C*H_3); LCMS (ES^+): m/z (%) 230 (100) $[M+H]^+$.

4-(4-*tert*butylbenzoxy)phenyl amine (82e): Compound **81e** was removed the Boc group to give compound **82e** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 9.37 (s, 2H, N*H*$_2$), 7.42-7.36, 7.25-7.27, 7.08-7.10, (m, 8H, *H*-Ph), 5.07 (s, 2H, C*H*$_2$), 1.28 (s, 9H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ

157.4, 150.4, 133.7, 127.6, 125.6, 125.4, 125.2, 123.8, 115.7 (*C*-Ph), 69.3 (*C*H_2), 34.3 (*C*$(CH_3)_3$), 31.1 (*C*H_3); LCMS (ES^+): m/z (%) 256 (100) $[M+H]^+$.

General Procedure for compounds 83a – e

Et_3N (0.5 mmol) was added to a solution of the amines **82a – e** in 10 ml EtOAC. The mixture was kept at 0 - 5 °C and trisphogene (2 mmol) was added. The reaction mixture was gradually brought to reflux at 77 °C for 2 h. The progression of the reaction was monitored by TLC. Excess solvent was removed in vacuoand the crude product was flashed by a short pad of SiO_2 to yield the isocyanates **(83a – e)**. Because the isocyanates were very active, they were directly use for the next step.

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(4-(2-chlorobenzyloxy)phenyl)urea 89:** 4-(2-Chlorobenzyloxy)phenyl isocyanate reacted with amine **33** to yield compound 8**9** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.33 (s, 1H, NH), 8.37 (s, 1H, NH), 7.57-7.59, 7.50-7.52, 7.37-7.39, 7.29-7.31, 6.90-6.92 (m, 9H, *H6* and *H*-Ph), 6.17-6.23 (m, 1H, *H1'* and N*H*), 5.35 (d, *J*=4.30 Hz, 1H, O*H*), 5.09 (s, 2H, C*H*$_2$), 4.15-4.17 (m, 1H, *H3'*), 3.75-3.77 (m, 4H, *H4'*), 3.44-3.45, 3.22-3.24 (m, 2H, *H5'*), 2.14-2.16, 2.07-2.09 (m, 2H, *H2'*), 1.78 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 155.4 (*C*O), 150.5 (*C2*), 152.8, 134.6, 134.0, 132.5, 130.00, 129.7, 129.3, 127.3, 119.2, 114.9 (*C*-Ph), 136.1 (*C6*), 109.8 (*C5*), 85.4 (*C1'*), 83.7 (*C4'*), 71.1 (*C3'*), 67.0 (*C*H_2), 41.4 (*C5'*), 38.4 (*C2'*), 12.0 (*C*H_3); LCMS (ES^+): m/z (%) 501 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{24}H_{26}Cl_1N_4O_6$ $[M+H]^+$ 501.1535 *m*/*z*, found 501.1516 *m*/*z* (3.91 ppm).

***N*-(5'-deoxy-β-thymidin-5'-yl)-*N'*-(4-(4-methoxybenzyloxy)phenyl)urea 90:** 4-(4-Methoxybenzyloxy)phenyl isocyanate reacted with amine **33** to yield compound **90** as a solid; ^{1}H-NMR (500MHz, DMSO): δ 11.32 (s, 1H, N*H*), 8.33 (s, 1H, N*H*), 7.52 (d, *J* = 1.15 Hz, 1H, *H6*), 7.72-7.79, 6.98-7.00, 6.88-6.89 (m, 8H, *H*-Ph), 6.18-6.22 (qt, *J* = 3.48 Hz, 1H, *H1'*), 5.35 (d, *J* = 3.10 Hz, 1H, O*H*), 5.01 (s, 2H, C*H*$_2$), 4.15-4.19 (m, 1H, *H3'*), 3.75-3.78 (m, 4H, *H4'* and C*H*$_3$), 3.42-3.46, 3.18-3.24 (m, 2H, *H5'*), 2.13-2.17, 2.05-2.08 (m, 2H, *H2'*), 1.77 (s, 3H, C*H*$_3$); ^{13}C-NMR (125MHz, DMSO): δ 163.7 (*C4*), 150.5 (*C2*), 155.4 (*C*O), 152.9, 137.3, 133.7, 128.4, 127.7, 127.6, 119.2, 114.9 (*C*-Ph), 136.1 (*C6*), 109.8 (*C5*), 85.37 (*C1'*), 83.7 (*C4'*), 71.1 (*C3'*), 69.3 (*C*H_2-Ph), 41.4 (*C5'*), 38.4 (*C2'*), 12.1 (*C*H_3); LCMS (ES^+): m/z (%) 497 (100) $[M+H]^+$; HRMS (ES^+): calcd for $C_{25}H_{29}N_4O_7$ $[M+H]^+$ 497.2031 *m*/*z*, found 497.2017 *m*/*z* (2.74 ppm).

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