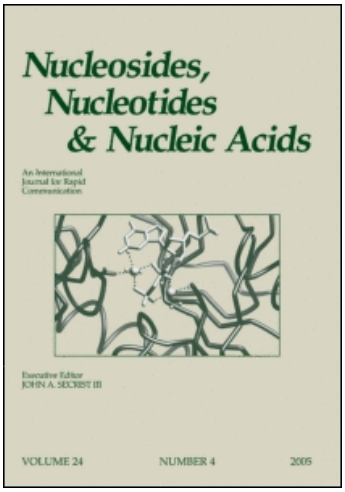


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# Regioselective 2'/3'-O-Allylation of Pyrimidine Ribonucleosides Using Phase Transfer Catalysis

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# REGIOSELECTIVE 2'/3'-O-ALLYLATION OF PYRIMIDINE RIBONUCLEOSIDES USING PHASE TRANSFER CATALYSIS

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***Abstract:*** *A short and convenient procedure for regiospecific O-allylation of uridine is reported by employing dibutyltin oxide as a mild base in conjunction with a phase transfer catalyst tetrabutylammonium bromide. The resulting isomeric 2'/3'-O-allyl uridines were separated after conversion into their corresponding 5'-O-DMT derivatives. The 2'-O-allyluridine **3** was then transformed into 2'-O-allylcytidine **7** and both were individually converted into the corresponding ß-cyanoethyl phosphoramidite monomers (**9** and **10**) and a phosphodiester monomer **11**, required for oligonucleotide assembly. The utility of **11** is demonstrated by synthesis and characterization of a 2'-O-allyl ribodinucleotide UpU.*

## INTRODUCTION

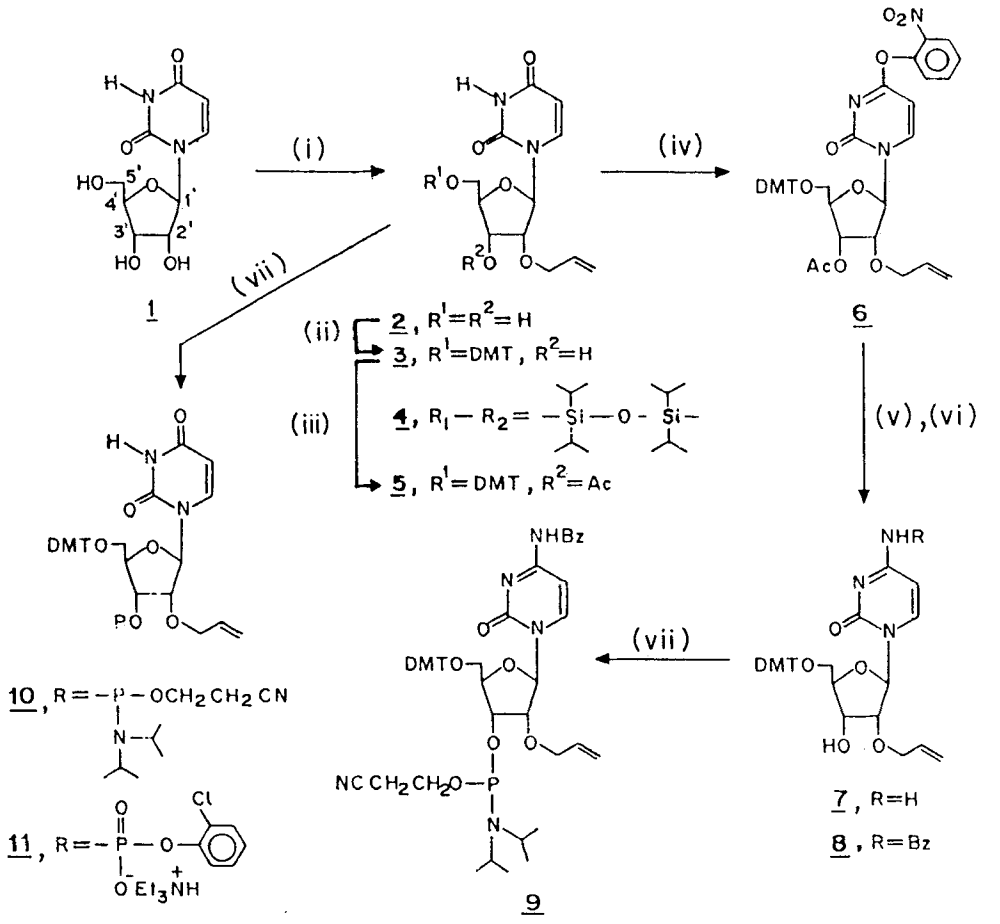
2'-O-Alkyl oligoribonucleotides have emerged recently as important antisense probes because of their hybridizing capability, nuclease resistance and better membrane penetration[1]. Among the various alkyl substituents, 2'-O-allyl derivatives have been found to be superior to 2'-O-methyl and 2'-O-dimethylallyl analogs[2]. Consequently, efficient approaches to synthesis of 2'-O-allyl ribonucleosides assume importance. A major drawback of most alkylation reactions of natural ribonucleosides is the undesirable but preferential ring N-alkylation that accompanies O-alkylation[3]. N-allylations of purines were avoided by reacting appropriate 3',5'-O-(tetraisopropyl disiloxane-1,3-diyl)-6-O-(2,6-dichlorophenyl) purine ribonucleosides either with allyl bromide and a hindered base[4], or under Pd(0) catalysis[5], to obtain 2'-O-allyl derivatives of adenosine and guanosine. Recently[5], it has been pointed out that the latter approach can be extended to pyrimidine nucleosides as well to obtain 2'-O-allyluridine and 2'-O-

allylcytidine. However, neither the synthetic experimental details nor the spectroscopic data for the different 2'-O-allyl pyrimidine ribonucleosides are presently available. In view of the foreseen importance of 2'-O-allyl oligoribonucleotides as antisense probes, we have presently explored an alternative method for synthesis of 2'-O-allyl pyrimidine ribonucleosides. In the present paper, we report the hitherto unknown DBTO-TBAB mediated exclusive O-allylation of uridine, followed by its transformation to the corresponding cytidine derivative, and the spectral characterization of various 2'-O-allyl pyrimidine ribonucleoside derivatives. These allyl compounds have also been used for the synthesis of protected monomers (phosphoramidite and phosphotriester), followed by synthesis and characterization of a ribodinucleotide, 2'-O-allyl UpU.

## RESULTS AND DISCUSSION

### Dibutyltin oxide mediated allylations of ribonucleosides

DBTO mediated methylation and benzylation of uridine are known[3] to be directed to 2'/3' cis-diol system without affecting either the 5'-OH or ring amide N3. This selective derivatization has been attributed to the activation of these hydroxyls by formation of the cyclic 2',3'-O-dibutylstannylidene intermediate to achieve the mono-alkylation at 2'/3'-hydroxyls of uridine. This preferential O-alkylation is restricted to uridine while with cytidine and other purines, the reaction gives preferential ring N-alkylations. We attempted allylation of pyrimidine ribonucleosides by the procedure of Wagner et al.[3], using allyl bromide as alkylation reagent. Uridine remained unaffected whereas cytidine gave $N^1$-ring allylation product. Regiospecific allylation of polyhydroxy compounds was previously reported[6] to give high yields of O-monoallyl derivatives when TBAB was used along with dibutylstannylidene derivatives. In our case, this procedure also failed to give exclusively, the required 2'/3'-O-monoallyl derivatives of ribonucleosides. We herein report a modified allylation procedure for uracil nucleosides which replaces the usual catalytic two phase system with a solid-liquid variant in which TBAB is a phase transfer catalyst, without isolating the intermediate 2',3'-O-dibutylstannylidene derivative. It was reported earlier[7] that tosylation of nucleosides under similar conditions regioselectively yields either the 2'-O- or the 3'-O- products depending upon the reaction medium and the PTC used. This might suggest the occurence of some dynamic equillibrium between the 2',3'-cis diol system of ribose sugar of the nucleoside and DBTO. The catalysis by tetrabutylammonium salt probably involves enhancement of nucleophilicity of sugar oxygen in the stannylidene complex by co-ordination of the halide ion to tin. The selectivity of 2'/3'-O derivatization may then be directed by shift in equilibrium




**Reagents**: (i) DBTO, TBAB, Allyl bromide in DMF (ii) DMTCl/Pyridine (iii) $Ac_2O$/Pyridine (iv) MsCl (2.5 eq), triethylamine (3 eq), DMAP (0.2 eq) in $CH_2Cl_2$; o-nitrophenol (7 eq), TEA (10 eq), DABCO (0.5 eq) (v) Aq.$NH_3$ (vi)TMSCl/Pyridine /Benzoyl chloride (vii) Bis-N,N-diisopropyl-ß-cynoethyl phosphoramidite.

depending on solvent as well as the substrate. DMF proved to be a good solvent for this reaction, whereas in other solvents like benzene, $CH_2Cl_2$ and acetonitrile, the allylation reaction was very slow.

Uridine **1**, was treated with stoichiometric amounts of allyl bromide (1 eq) along with DBTO (1.2 eq) and TBAB (1.1 eq) in DMF (Scheme 1) to obtain (in 75% yield) a mixture of the 2'-O-monoallyl **2** and 3'-O-monoallyl **3** derivatives in relative ratios of 65:35. No N3 or 5'-O-allylation was observed even with excess of allylating reagent.

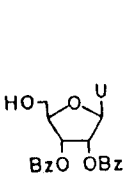
In the absence of either DBTO or TBAB no reaction was seen. In contrast to uridine, corresponding reaction of cytidine gave an inseparable mixture of N3-mono allyl, N3,2'-O- and N3,3'-O-diallyl derivatives. The cytidine ring N3-allylation could not be avoided even with either 1 eq. of allylating reagent or the absence of DBTO or TBAB.

The product mixture of 2'-O- and 3'-O-allyluridines could not be efficiently resolved directly by column chromatography since these have very close $R_f$ values. The separation into individual components was achieved in two ways. The mixture was converted into the 5'-O-DMT derivatives which were then resolved by silica gel chromatography. This short synthesis of 5'-O-DMT-2'-O-allyluridine **3** has the following advantages: (i) it is obtained in two steps as compared to the recently reported[5] six steps and (ii) higher overall yield: 45% of 5'-O-DMT-2'-O-allyl **3** from uridine as compared to 28% overall yields of 2'-O-allyl uridine[5]. Alternatively, the mixture of 2'-O- and 3'-O-allyl isomers was treated with Markiewiez disiloxane reagent[8] and only **2** reacted to give the cyclic derivative **4** which could be easily separated by chromatography. Treatment of **4** with TBAF/THF followed by dimethoxytritylation gave **3** in an overall isolated yield of 42% from uridine.

Synthesis of the desired 2'-O-allylcytidine **7** was achieved starting from the uridine derivative **3**. Its 3'-O-acetate **5** was converted to the corresponding O4-sulphonyl derivative followed by displacement with o-nitrophenyl group[9] to obtain **6**. This on treatment with aq. ammonia gave the desired 5'-O-DMT-2'-O-monoallylcytidine in an overall yield of 35% from uridine **1**. The cyclic silyl derivative **4** was also transformed into **7** in 32% overall yield by the sulphonylation displacement method followed by treatment with TBAF/THF and 5'-O-dimethoxytritylation. All products were characterized by a combination of UV, $^1H$ and $^{13}C$ NMR spectroscopy. Absence of allylation of ring nitrogens in **2** and **7** was confirmed by the lack of $N\text{-}CH_2$ signal around 42-45 ppm. The assignments of 2'/3'-O-allyl isomers were based on $^{13}C$ chemical shifts of C2' and C3'. It is known[14] that in free nucleosides C3' is shifted downfield compared to C2' by about 5 ppm. C2'-O-alkylation leads to shifts of 10-12 ppm downfield for C2', accompanied by 4-6 ppm upfield shifts for C3'. The observed $^{13}C$ NMR data of various allyl derivatives largely complied with these facts. Further, we noticed that in case of C3'-O-allylation the shifts are 5 ppm downfield for both C3' and C2'. The individual assignments were substantiated by a DEPT experiment in which the methylene carbons showed an inverted $^{13}C$ signal.

**Synthesis of 2'-O-allyl protected monomers, 9-11 and 2'-O-allyl UpU, 12**

Compound **7**, was converted by transient protection[10] method to its N4-benzoyl derivative **8**. The 2'-O-allyl pyrimidine nucleosides **3** and **8** were treated individually



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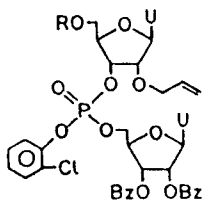
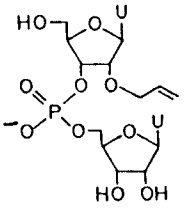


13a R = DMT
13b, R = H



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with bis-(N,N-diisopropylamino)-ß-cyanoethyl phosphoramidite reagent under standard conditions[11] to obtain the corresponding 3'-O-phosphoramidite monomers **9** and **10** in 80% isolated yields. The purity and integrity of these were confirmed by both $^{1}H$ and $^{31}P$ NMR (Figure 1a,b). Alternatively, **3** was transformed into the phosphodiester monomer **11**, useful for solution phase oligonucleotide synthesis. This was achieved by treatment with o-chlorophenyl dichlorophosphate in pyridine and stoichiometric amounts of water[12] followed by purification over silica gel and characterization by $^{1}H$ and $^{31}P$ NMR (Figure 1c). No O4-modification was noticeable. The monomer **11** was condensed with 2',3'-O-dibenzoyl uridine, **12**, in presence of 2-mesitylene sulphonyl-3-nitrotriazole and N-methylimidazole to obtain the 5'-O-DMT-UpU, **13a**, in 90% yield. The reaction of **13** with 3% DCA in $CH_2Cl_2$ and subsequent column purification afforded the detritylated product **13b**, which was then treated with sat. MeOH-$NH_3$[13] to obtain 2'-O-allyl-UpU, **14**. This was purified by ion-exchange chromatography on DEAE Sephadex and its structure established by $^{1}H$ and $^{31}P$ NMR (Figure 1d).

## CONCLUSIONS

The present procedure of allylation using DBTO-TBAB, permits the synthesis 5'-O-DMT-2'-O-allyluridine in 2 steps without prior protection of ring nitrogen (N3/O[4]) or 5'-OH groups. It also allows access to the previously unknown 3'-O-allyl isomer. The O-allyluridine derivatives can be transformed into their corresponding cytidine analogs in 3 steps. The 5'-O-DMT-2'-O-allyl pyrimidine nucleosides were converted into the desired nucleotide monomers (phosphoramidite and phosphodiester) followed by preparation of a ribodinucleotide 2'-O-allyl UpU. This short synthesis of 2'-O-allyl pyrimidine nucleosides may enable a facile and routine access to 2'-O-allyl oligoribonucleotides required for potential applications as antisense probes, for biophysical studies of hybridization and membrane penetrability.

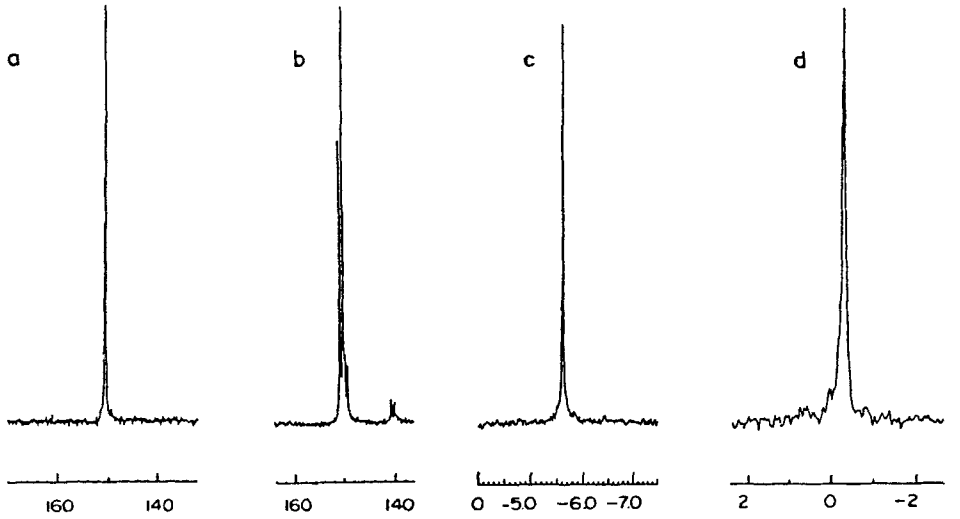


**Figure 1:** $^{31}P$ NMR of (a) **10** (b) **9** (c) **11** in $CDCl_3$ and (d) **14** in $D_2O$.

## EXPERIMENTAL

$^1H$, $^{13}C$ and $^{31}P$ NMR spectra were recorded in Ù scale using a Bruker MSL 300 NMR spectrometer fitted with an ASPECT 3000 computer at 75.7 MHz for $^{13}C$ and 121.5 MHz for $^{31}P$. TMS was used as an internal standard for $^1H$ NMR, $CDCl_3$ (77.14 ppm) as reference for $^{13}C$ and 85% $H_3PO_4$ as external standard for $^{31}P$ NMR. TLC was carried out using E. Merck precoated silica gel $60F_{254}$ plates (Cat. No. 5554) with the solvent systems, **A**: $CH_2Cl_2$:MeOH (85:15), **B**: $CH_2Cl_2$:MeOH (90:10) and **C**: $CH_2Cl_2$:MeOH (95:5). Column chromatographic separations were done using flash grade silica gel (E. Merck, Cat. No. 7729).

**2'/3'-O-allyluridine**: Uridine, **1** (1.22 g, 5 mmol) was treated with allyl bromide (2.1 mL, 20 mmol) in presence of DBTO (1.4 g, 6 mmol) and TBAB (1.2 g, 5.5 mmol) in DMF (10 mL) at 60°C for 5-6 hr. The resulting solution was evaporated to dryness at reduced pressure, the residue was directly loaded onto a silica gel column and eluted with $CH_2Cl_2$ containing increasing amounts of MeOH to obtain a mixture of 2'-O, **2** and 3'-O-allyluridine (total 0.95g, 75%) in the ratio 65:35 as estimated from $^1H$ NMR. $R_f$, system A=0.4;λmax (MeOH), 261 nm.

**2'-O-allyl-5'-O-DMT uridine, 3 and 3'-O-allyl-5'-O-DMT uridine:** The above product mixture (0.9 g, 3.5 mmol) was coevaporated with dry pyridine (1x5 mL) and redissolved in dry pyridine (7 mL) and kept at 0°C, DMTCl (1.57 g, 4.5 mmol) was added in portions during a period of 2 h. MeOH (5 mL) was added and the mixture was concentrated under reduced pressure. Aq. $NaHCO_3$ solution (5%, 10 mL) was then added and the resultant was extracted with $CH_2Cl_2$ (2 x 30 mL). The $CH_2Cl_2$ layer was washed with water (1x5 mL), dried over $Na_2SO_4$ and evaporated to a foam. This was then chromatographed on silica gel (30 g) on a column, (i.d. 3 cm) using $CH_2Cl_2$ containing increasing amounts of MeOH as eluent. Elution with $CH_2Cl_2$:MeOH (96:4) gave **3** (1.2 g, 65%). $R_f$ (system **B**) = 0.6; $^1H$ NMR ($CDCl_3$) $\delta$ : 3.55 (ddd, 2H, J=6.0 and 12.0 Hz, H5'5''), 3.79 (s, 6H, 2x$OCH_3$), 4.05 (ddd, 2H, J=5.3, 7.6 and 14.0 Hz, $OCH_2$), 4.25 (ddd, 1H, J = 1.5, 6.0 and 12.0 Hz, H4'), 4.42 (dd, 1H, J = 1.5 and 5.2 Hz, H3'), 4.47 (dd, 1H, J = 1.4 and 5.2 Hz, H2'), 5.25 (d, 1H, J= 8.5 Hz, H5), 5.26 and 5.34 (2xdd, 1H each, J = 1.5, 10.1 and 14.2 Hz, $=CH_2$), 5.8 (m, 1H, =CH), 5.97 (d, 1H, J = 1.4 Hz, H1'), 8.03 (d, 1H, J=8.5 Hz, H6). $^{13}C$ NMR ($CDCl_3$) $\delta$ : 55.15 ($OCH_3$), 61.3 (C5'), 68.5 (C3'), 71.3 ($OCH_2$), 81.2 (C2'), 83.4 (C4'), 87.5 (C1'), 102.0 (C5), 118.4 ($=CH_2$), 133.2 (=CH).

Further elution with $CH_2Cl_2$:MeOH (94:6) gave 5'-O-DMT-3'-O-allyluridine, (0.7 g, 40%). $R_f$ (system **B** ) = 0.5; $^1H$ NMR ($CDCl_3$) $\delta$ : 3.37 and 3.54 (2xdd, 1H each, J = 2.0 and 10.0 Hz, H5'5"), 3.80 (s, 6H, 2x$OCH_3$), 4.07 (d, 2H, J = 5.0 Hz, $OCH_2$), 4.15 (d, 1H, J = 5.0 Hz, H2'), 4.29 (dd, 1H, J = 4.5 and 10.5 Hz, H4'), 4.18 (dd, 1H, J = 4.5 and 5.0 Hz, H3'), 5.23 (dd, 1H, J = 1.2 and 10.3 Hz) and 5.27 (dd, 1H, J = 1.5 and 17.2 Hz) [$=CH_2$], 5.39 (dd, 1H, J = 1.7 and 8.2 Hz, H5), 5.80 (m, 1H, m, =CH), 5.94 (d, 1H, J = 4.5 Hz, H1'), 7.83 (d, 1H, J = 8.2 Hz, H6). 8.36 (s, 1H, NH). $^{13}C$ NMR ($CDCl_3$) $\delta$ : 55.15 ($OCH_3$), 62.1 (C5'), 71.3 ($OCH_2$), 73.9 (C2'), 76.3 (C3') 81.1 (C4'), 89.8 (C1'), 102.1 (C5), 117.9 ($=CH_2$), 133.6 (=CH).

**2'-O-allyl-3',5'-O-(Tetraisopropyldisiloxane-l,3-diyl) uridine 4:** The crude reaction mixture of 2'-O-allyl, **2** and 3'-O-allyl uridines (0.9 g, 3.5 mmol) was coevaporated with dry pyridine (1x5 mL) and redissolved in dry pyridine (28 mL). The solution was cooled to 0°C and TIPSC (1.44 mL, 4.96 mmol) was added dropwise. The reaction was stirred at ambient temperature for 5 h and was subsequently quenched with TEAB (lM, l0 mL). This was then concentrated in vacuo, redissolved in $CH_2Cl_2$ and washed with aq. $NaHCO_3$ (5%, l0 mL). The organic layer was dried ($Na_2SO_4$) and concentrated. Column chromatography on silica gel using $CH_2Cl_2$ as eluent gave

**4** (1.0 g, 60%), $R_f$ (system **B**) = 0.7; $^1$H NMR ($CDCl_3$) $\delta$ : 1.0 (bs, 28H, overlap with a multiplet, 2x$CH(CH_3)_2$), 3.81 (d, 1H, J = 2.5 Hz) and 3.91 (d, 1H, J = 13 Hz) [H5'5"], 4.10 (s, 1H, H3'), 4.11 (s, 1H, H2'), 4.19 (d, 1H, J = 13 Hz, H4'), 4.32 (dd, 2H, J = 1.3 and 13.5 Hz, $OCH_2$), 5.14 (qd, 1H, J = 1.3 and 10.0 Hz) and 5.30 (qd, 1H, J = 1.7 and 18.0 Hz) [$=CH_2$], 5.61 (d, 1H, J = 8.2 Hz, H5), 5.69 (s, 1H, H1'), 5.86 (m, 1H, =CH), 7.86 (d, 1H, J = 8.2 Hz, H6), 9.39 (br s, 1H, NH).

**2'-O-allyl-3'-O-acetyl-5'-O-DMT-4-O-(o-nitrophenyl)-uridine, 6**: Compound **3** (1.2 g, 2 mmol) was acetylated with $Ac_2O$ (0.24 mL, 2.5 mmol) in pyridine (2 mL) to obtain compound **5** (1.25 g, 95%). This was was dissolved in $CH_2Cl_2$ (18 mL) and MSCl (1.0 g, 2.5 eq) was added followed by triethylamine (0.6 mL, 2.5 eq) and 4-N,N-dimethylaminopyridine (42 mg, 0.2 eq). After 30 min, TLC (system **B**) showed completion of reaction. o-Nitrophenol (1.8 g, 7 eq) was then added followed by more of triethylamine (1.5 mL, l0 eq) and DABCO (75 mg, 0.5 eq). The reaction mixture was stirred for a further 1-2 h, worked up in the usual way and purified on a silica gel column. Elution with $CH_2Cl_2$ (150 mL) gave **6** (1.3 g, 90%). $R_f$ (system **B**) = 0.8; $^1$H NMR ($CDCl_3$) $\delta$ : 2.1 (s, 3H, $COCH_3$), 3.45 (dd, 1H, J = 2.2 and 11.0 Hz) and 3.67 (dd, 1H, J = 2.0 and 11.0 Hz) [H5'5"], 3.82 (s, 6H, 2x$OCH_3$), 3.92 (dd, 1H, J = 6.3 and 11.0 Hz, H4'), 4.08 (d, 1H, J = 5.2 Hz) and 4.16 (d, 1H, J = 8.7 Hz) [$OCH_2$], 4.32 (dd, 1H, J = 4.5 and 8.7 Hz, H2'), 5.16 (dd, 1H, J = 1.4 and 10.4 Hz) and 5.23 (dd, 1H, J = 1.5 and 17.2 Hz) [$=CH_2$], 5.46 (dd, 1H, J = 4.5 Hz, H3'), 5.71 (m, 1H, =CH), 5.78 (d, 1H, J = 7.3 Hz, H5), 6.01 (s, 1H, H1'), 7.5 (m, ArH), 8.57 (d, 1H, J = 7.4 Hz, H6).

**2'-O-allyl-5'-O-DMT-cytidine, 7**: Compound **6** (1.0 g, 1.2 mmol) was treated with aq. ammonia (20 mL) in a sealed tube for 10 h followed by usual workup to yield **7** (0.65 g, 85%). $R_f$ (system **B**) = 0.4; $^1$H NMR ($CDCl_3$) $\delta$ : 3.30 and 3.50 (d, 1H each, J = 9.0 Hz, H5'5"), 3.75 (s, 6H, 2x$OCH_3$), 3.96 (dd, 1H, J = 6.0 and, 9.0 Hz, H4'), 4.14 (m, 2H, $OCH_2$), 4.20 (dd, 1H, J = 2.5 and 6.0 Hz, H3'), 4.32 (br d, 1H, J = 2.5 Hz, H2'), 5.13 (dd, 1H, J = 1.3 and 11.0 Hz) and 5.22 (dd, 2H, J = 1.5 and 17.0 Hz) [$=CH_2$], 5.24 (s, 1H, H1'), 5.71 (m, 1H, =CH), 6.82 (d, 1H, J = 8.0 Hz, H5), 7.99 (d, 1H, J = 8.0 Hz, H6); $^{13}$C NMR ($CDCl_3$) $\delta$: 55.1 ($OCH_3$), 61.4 (5'$CH_2$), 69.0 (C3'), 71.3 ($OCH_2$), 78.7 (C2'), 79.1 (C4'), 90.3 (C1'), 95.9 (C5), 117.2 ($=CH_2$).

**2'-O-allyl-N4-benzoyl-5'-O-DMT cytidine, 8:** To compound **7** (0.19 g, 0.32 mmol) was added, while cooling, chlorotrimethylsilane (0.14 ml, 1.12 mmol) in dry pyridine

(1.2 mL). The reaction was stirred for 30 min. at 25°C following which benzoyl chloride (0.02 mL, 0.5 mmol) was added at 0°C. The reaction was stirred for 2 h after which it was worked up as usual to yield **8** (0.20 g, 88%). $R_f$ (system **B**) = 0.6; $^1H$ NMR ($CDCl_3$) $\delta$: 3.60 (dq, 2H, J = 2.5 and 11.0 Hz, H5'5''), 3.83 (s, 6H, 2x$OCH_3$), 4.0 (d, 1H, J = 5.2 Hz) and 4.08 (dd, 1H, J = 2.3 and 9.0 Hz) [$OCH_2$], 4.39 (dd, 1H, J = 6.0 and 13.0 Hz, H3'), 4.46 (m, 1H, H2'), 4.63 (dd, 1H, J = 6.0 and 11.5 Hz, H4'), 5.36 (dd, 1H, J = 1.3 and 10.4 Hz) and 5.42 (dd, 1H, J = 1.5 and 17.3 Hz) [$=CH_2$], 5.94 (m, 1H, =CH), 6.01 (s, 1H, H1'), 6.87 (d, 1H, J = 7.5 Hz, H5), 7.2-7.6 (m, ArH, DMT, Bz), 7.89 (d, 1H, J = 8 Hz, H6), 8.61 (d, 1H, NH).

**2'-O-allyl-5'-O-DMT-3'-O-(o-chlorophenylphosphate) uridine triethylammonium salt, 11**: 2'-O-allyl-5'-O-DMT uridine, **3** (0.58 g, 1 mmol) was coevaporated with anhydrous pyridine (15 mL) leaving a final volume of 5 mL. In a separate flask 2-chlorophenyldichlorophosphate (0.8 mL, 5 mmol) was dissolved in dry pyridine (10 ml) to which was added water (90 uL, 5 mmol) slowly, while cooling. The mixture was left at room temperature for 10 min, after which pyridine hydrochloride precipitated out. This was filtered and the filtrate added to the nucleoside solution. The mixture was concentrated to a final volume of 10 mL and kept stirred for 30 min. The reaction mixture was then cooled and quenched by the addition of TEAB solution (1M, 15 mL). It was then extracted into $CH_2Cl_2$ (100 mL) and washed with TEAB solution (0.1M, 2x50 mL). The organic phase was dried over $Na_2SO_4$ and concentrated to a foam. This was then purified on silica gel using $CH_2Cl_2$: MeOH (95:5) to yield pure **11** (0.7 g, 80%), $R_f$ (system **B**) = 0.1; $^{31}P$ NMR ($CDCl_3$) $\delta$: -5.84.

**2'-O-allyl r(UpU), 13**: 2',3'-O-dibenzoyluridine **12** (18 mg, 0.04 mmol) and **6** (41 mg, 0.05 mmol) were coevaporated twice with pyridine (0.2 mL) and redissolved in dry pyridine (0.4 mL). MSCl (46 mg, 0.21 mmol) and N-methylimidazole (0.36 mL, 0.4 mmol) were then added and the reaction mixture stirred for 20 min at 25°C. After the completion of reaction as followed by TLC, the reaction was quenched with saturated $NaHCO_3$ (0.2 mL) and extracted into $CH_2Cl_2$ (10 mL). The organic layer was washed with water (3 mL), dried over $Na_2SO_4$ and concentrated. The residue was purified by silica gel chromatography using $CH_2Cl_2$:MeOH to yield the product **13a** (41 mg, 89%). $R_f$ (system **C**) = 0.5. This was then detritylated using DCA in $CH_2Cl_2$ (2%, 5 mL) at 10°C. On completion (10 min, TLC, system **C**), the reaction mixture was quenched with saturated $NaHCO_3$ (3 mL) and extracted into $CH_2Cl_2$ (10

mL). The organic layer was washed with water (2 mL), dried over $Na_2SO_4$ and concentrated. The product was separated from tritanol by silica gel chromatography to yield **13b** (21 mg, 90%). Rf (system C) = 0.4; $^{31}P$ NMR ($H_2O$) $\delta$ : -6.21 and -7.06.

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17. Abbreviations: DBTO, dibutyltinoxide; DCA, dichloroacetic acid; DMF, dimethylformamide; DEPT, distortionless enhancement in polaraization transfer; DMAP, 4-dimethylaminopyridine; DMT, 4,4'-dimethoxytriphenyl methyl; MSCl, 2-mesitylenesulphonyl chloride; TBAB, tetrabutyl ammonium bromide; TBAF, teterabutylammonium fluoride; TMSCl, chlorotrimethylsilane.

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