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Thermal Degradation of Sugar-modified Uridine *N*-Oxides: Olefination, Oxazolidination and Rearrangements[¶]

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Abstract: The degradation pattern of the *N*-oxides of various tertiary aminouridines is established. The *N*-oxide of 3'-deoxy-3'-morpholino-*ara*uridine generated double bonds in the carbohydrate moiety without much selectivity, whereas epimino uridine *N*-oxides generated only d_4U. Oxazolidine derivatives were formed from the *N*-oxides of 3'-deoxy-3'-N-pyrrolidino/morpholino-2,2'-O-anhydrouridines and 3'-deoxy-3'-N-pyrrolidino/morpholino-2'-O-mesyl*ara*uridines. 2'-Deoxy-2'-N-pyrrolidino/morpholino-2'-O-mesyl*xylo*uridines produced rearranged products 3'-O-N-pyrrolidino/morpholino-2,2'-O-anhydrouridines.

Keywords: nucleosides; *N*-oxides; elimination reactions; rearrangements

Introduction

The enzymatic oxidation of tertiary and heterocyclic aromatic nitrogen compounds to the corresponding *N*-oxides is one of the standard routes for the metabolism of such compounds in mammalian systems.[1] Tertiary amine *N*-oxides, on the other hand, under pyrolytic conditions, undergo a Cope elimination reaction[2] to generate olefins. A plethora of modified nucleosides equipped with secondary, tertiary and aromatic amino groups at the 2'- and/or 3'-sites have been synthesized[3,4] since 3'-amino-3'-deoxythymidine has been a) detected as one of the metabolites of AZT[5] and b) found to exhibit wide ranging biological activities.[6] It is expected that some of these aminonucleosides would undergo *N*-oxidation in the biological systems. Although there are quite a few reports on the synthesis and behavior of *N*-oxides derived from purine nucleobases and nucleosides,[7] to the best of our knowledge no study has been done on the synthesis and properties of *N*-oxides of the sugar modified aminonucleosides. In continuation of our interest in the area of sugar modified aminonucleosides,[4,8] we decided to study the reactivities of the tertiary amine *N*-oxides attached to the sugar moieties of pyrimidine nucleosides at ambient as well as elevated temperatures to gain information on the breakdown patterns of *N*-oxides of aminonucleosides. We also envisaged that the in-built reactivities of aminonucleosides and their derivatives, such as intramolecular participation of pyrimidine

[¶]*Dedicated to Prof. Jyoti Chattopadhyaya on occasion of his 50th birthday*

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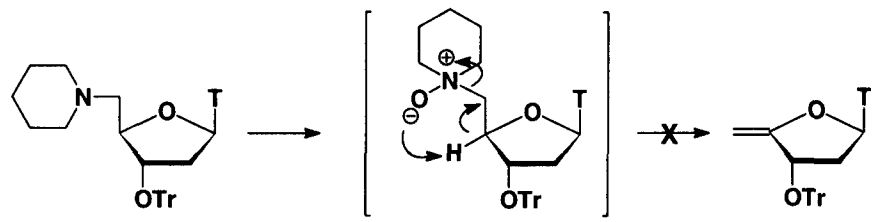
nucleobases, would lead to novel reactions other than or in addition to simple Cope elimination. These reactions would also generate new modified nucleosides. The series of sugar modified aminonucleosides, that we have synthesized by opening the known 5'-O-trityl-2',3'-O-anhydro-*lyxo*uridine **3** by amines under controlled conditions[4] were taken up as substrates for the present study. In general, aminonucleosides were converted to the corresponding *N*-oxides by reacting with m-CPBA. Crude *N*-oxides were used directly for degradation studies.

Results and Discussion

Conversion of Nucleoside N-*oxides to Olefinic Nucleosides*:[9-12] As the *N*-oxide derived from 5'-deoxy-5'-N-piperidino-3'-O-tritylthymidine **1** did not produce the desired product **2** when heated in pyridine (**Scheme 1**) [13], it was envisaged that an amine oxide connected to the 2' or 3' sites of the carbohydrate moiety

Scheme 1

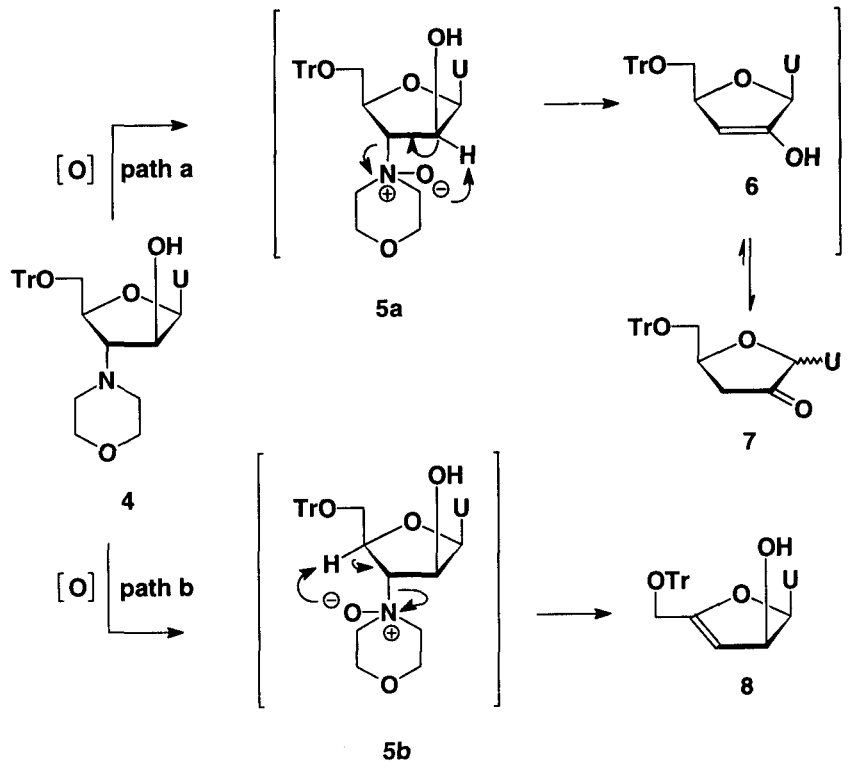


1 **2**

of nucleosides would be better suited to initiate proton abstraction from the β-position because of the conformational flexibilities of the furanose rings. The amine oxide **5** derived from the known[4] aminoalcohol **4**, when heated in pyridine, underwent elimination to produce a mixture of compounds (**Scheme 2**). Analysis of the mixture revealed the presence of three products, namely a mixture of the α- and β-anomers of the 2'-keto uridine **7**[13,14] (63%) and the 3'-deoxy-3'-ene derivative **8** (29%). Formation of **7** and **8** may be explained by invoking two different reaction pathways as depicted in **Scheme 2**. As both H-1' and H-4' were β to the amine oxide **5**, removal of either proton was possible. A mixture of 2'-keto uridines **7** would be formed if the reaction followed *path a* whereas *path b* would generate **8**. It may be assumed from the ratio of products that five membered transition state[2] formation between H-2'/ C-2'/ C-3'/ N^+-O^- was more facile than between H-4'/ C-4'/ C-3'/ N^+-O^-.

Although olefination of N-alkyl-aziridines *via N*-oxide formation has been reported in the literature,[15] the reaction, to the best of our knowledge, has never been used in case of carbohydrates in general and nucleosides in particular. 2', 3'-Dideoxy-2', 3'-(N-isobutyl)-epiminouridine[4] **11a** was easily accessible from a mixture of 2'-deoxy-2'-N-isobutylamino-*xylo*- and 3'-deoxy-3'-N-isobutylamino-*ara*uridines **9a** and **10a**

Scheme 2

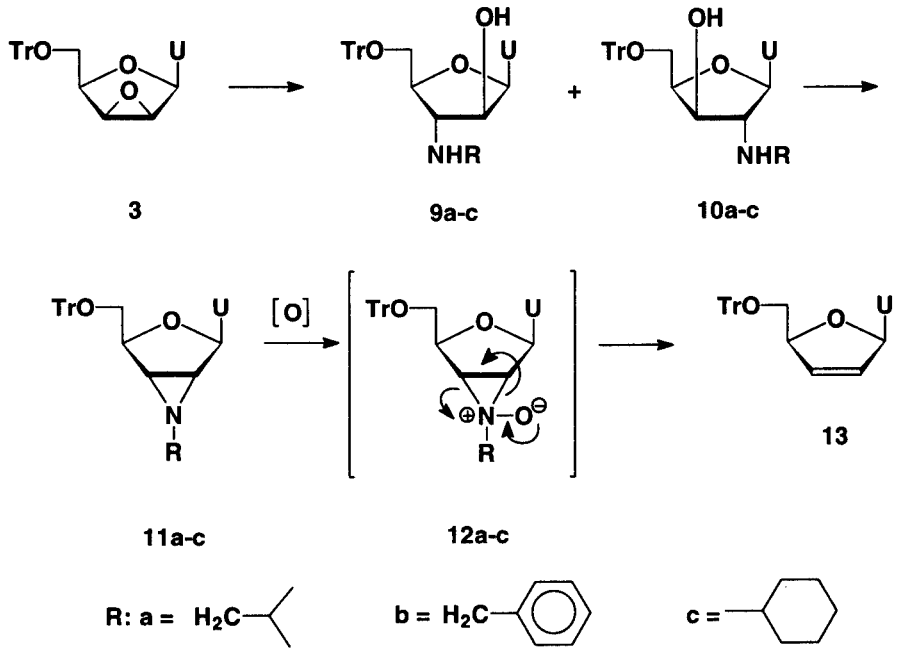


respectively. Compounds **11b** and **11c** were synthesized from the mixtures of **9b/10b**[4] and **9c/10c**,[4] respectively following the same methodology. It should be noted that except for compound **11a**,[4] **11b** and **11c** could not be obtained in pure form as they were always contaminated with triphenylphosphine oxide. Compounds **11a-c** were treated with m-CPBA in dichloromethane at ambient temperature; the only nucleoside based product that was isolated from all these reactions was 1-(2,3-dideoxy-5-O-trityl-β-D-glycero-pent-2-enofuranosyl) uracil **13**[16] in 45%, 62% and 52% yields, respectively, after two steps. The formation of an *N*-oxide of general structure **12** may be assumed which collapsed to **13** through an elimination process (**Scheme 3**). Since almost all the reactions applicable to uridine are also applicable to ribothymidine, it may be argued that the above synthetic route could be an alternative method of choice for the preparation of d_4T from ribothymidine.

Oxazolidination and Rearrangement Reactions of Nucleoside N-*oxides*: As there was no specificity of proton abstraction in case of *N*-oxides such as **5**, we decided to introduce rigidity in the molecule to see whether the lack of conformational mobility dictated the type of product formation. We have reported earlier that compounds of the type **14a** could be easily synthesized[4] from a mixture of 5'-O-trityl-2'-deoxy-2'-

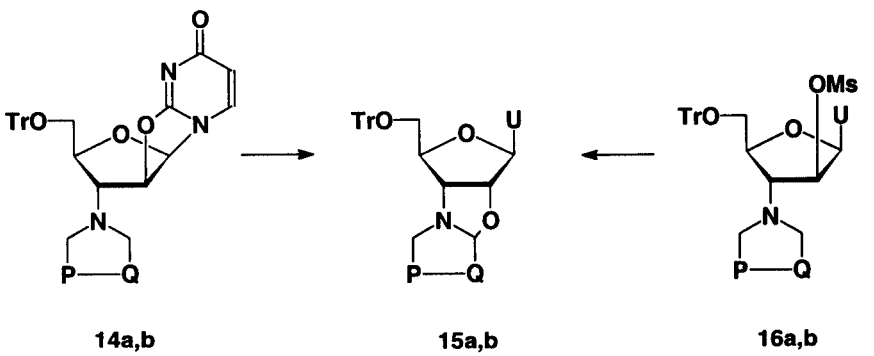
pyrrolidino-*xylo*- and 5'-O-trityl-3'-deoxy-3'-pyrrolidino-*ara*uridines. Compound **14a** was oxidized with m-CPBA and the *N*-oxide was heated in pyridine at elevated temperature. An oxazolidine derivative **15a** was

Scheme 3



isolated from the reaction mixture in 72% yield. The same product was isolated in 74% yield when **16a**[4] was oxidized and heated in pyridine. Similarly, **14b** or **16b**[8c] was converted to **15b** in 80% or 54% yield respectively (**Scheme 4**).

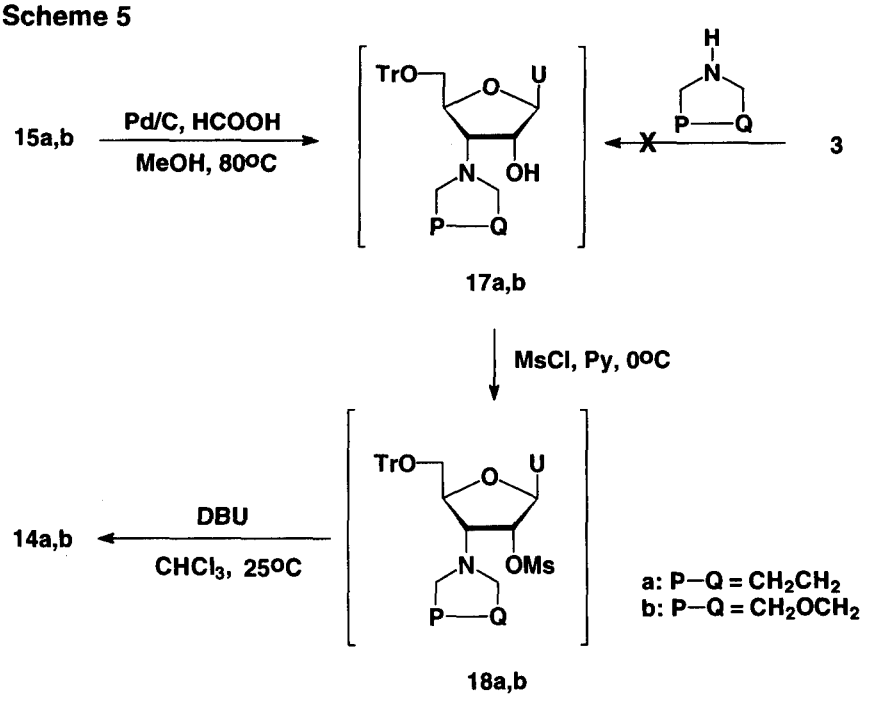
Scheme 4



a: P–Q = CH_2CH_2; b: P–Q = CH_2OCH_2

Attempted acetylation (pyridine/acetic anhydride) of **15b** failed, therefore indicating the absence of any free amino- or hydroxyl groups in **15b**. However, the following experiments were performed to establish the structures of the oxazolidine derivatives unambiguously. We expected that under catalytic hydrogenation/hydrogenolysis the C-O bonds of compounds **15a,b** would cleave to generate 3'-deoxy-3'-N-alkylaminouridines. Therefore, we subjected **15a** to catalytic transfer hydrogenation using 4% formic acid as the hydrogen source. The product which was formed following the C-O bond scission was *not* similar to the *ara*- and *xylo*- derivatives obtained by the ring opening of **3** by morpholine.[4] This product, on mesylation followed by DBU treatment at room temperature produced the known[4] 2,2'-O-anhydro derivative **14a**. The product was, therefore, 3'-deoxy-3'-pyrrolidino-5'-O-trityluridine **17a**. Similarly, **15b** was converted to **14b** via **17b** and **18b** (**Scheme 5**) to establish its structure.

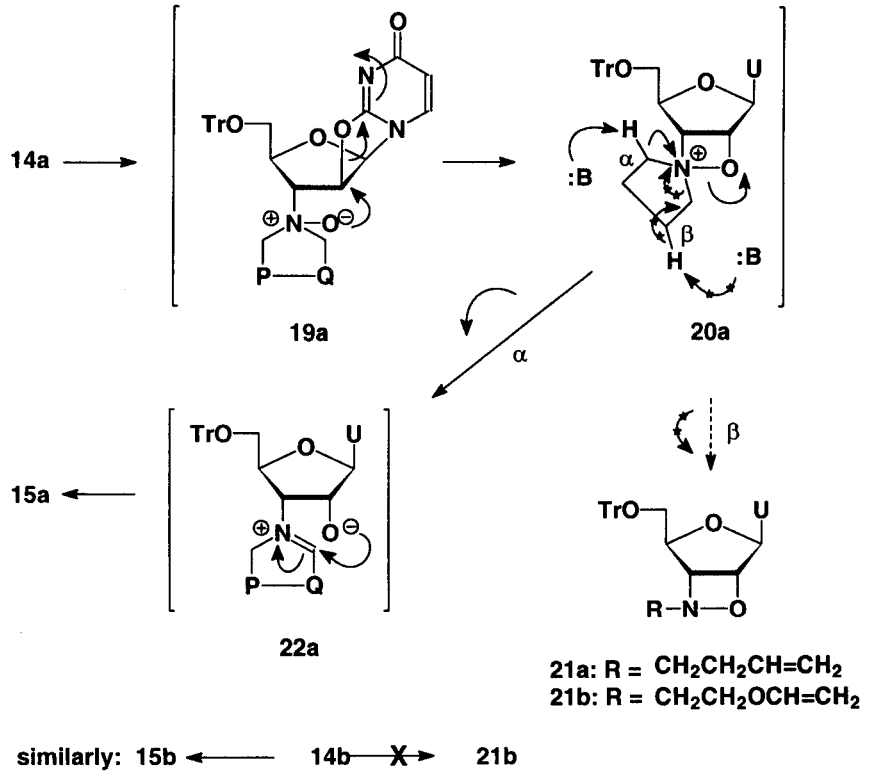
Scheme 5



The first step of the above conversion of **14a** to **15a** is the intramolecular nucleophilic attack (instead of Cope elimination into the furanose ring) at C-2' (intermediate **19a, Scheme 6**) resulting in the formation of the oxazetidinium ion **20a**. It may be argued that in the presence of a leaving group at the β-position (in this case, C-2'), an attack by the nucleophilic O^- of *N*-oxide is preferred to Cope elimination. Formation of **15a** from **16a** also supports this view (**Scheme 4**). There were two possible pathways for the neutralization of the positive charge on the nitrogen atom of the intermediate **20a**; the abstraction of a) an α-hydrogen to generate an iminium intermediate **22a** or b) a β-hydrogen to produce the oxazetidine derivative **21a**. Formation of

compound **21a**, having the same molecular formula as that of the actual product **15a**, was ruled out by the absence of any olefinic carbons in the ^{13}C NMR spectra. For example, all four carbon signals arising from the methylene groups of **15a** appeared at 63.6, 54.0, 31.0 and 23.9 ppm. Those of **15b** appeared at 65.6, 65.1, 64.3 and 48.8 ppm. The terminal methylene carbons of **21a,b**, had those been the products, would have had appeared above 100 ppm.[17] Conversions of **15a,b** to **17a,b** (**Scheme 5**) also ruled out structure **21a,b**. The abstraction of an α-hydrogen was, therefore, the preferred route. The iminium ion intermediate **22a** underwent intramolecular attack to produce the oxazolidine derivatives **15a**. Similarly, **14b** was converted to **15b** and not to **21b** (**Scheme 6**).

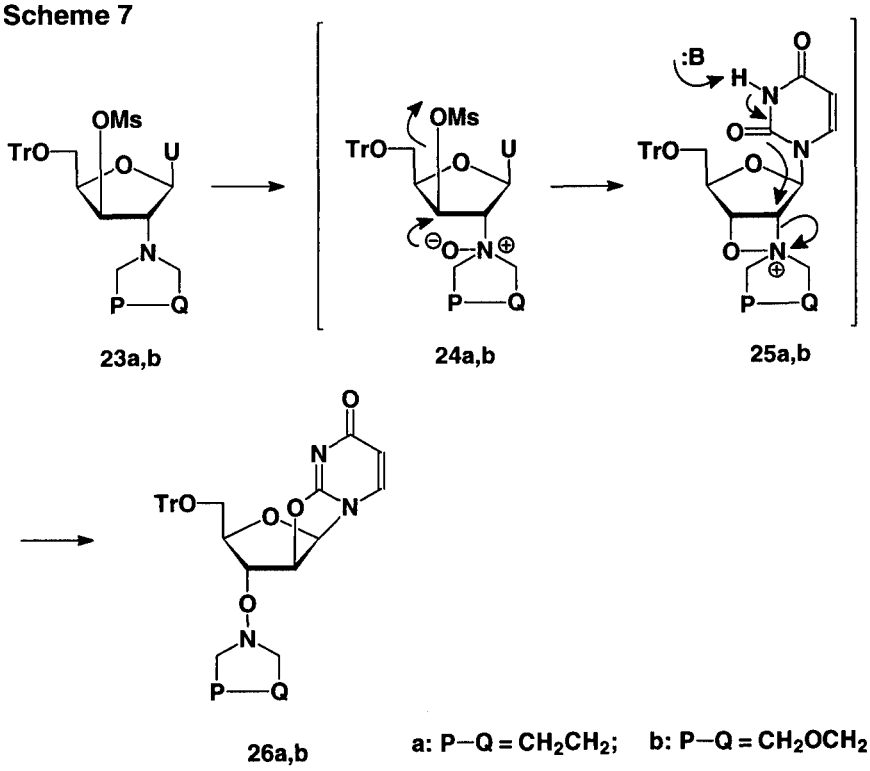
Scheme 6



The interesting conversion of **14a,b** to **15a,b** or **16a,b** to **15a,b** (**Scheme 4**) led us to study the behavior of the regioisomers of **16a,b**, namely compounds **23a,b** under the similar reaction conditions. Thus, compound **23a**[4] was oxidized and the *N*-oxide was heated in pyridine. To our surprise, we found that a product completely unrelated (^1H NMR) to compound **15a** was obtained (**Scheme 7**). The ^1H NMR and ^{13}C NMR data of product **26a** were identical to those[4] of compound **14a** except for the downward movement of the peaks arising from H-3' (δ 4.42 for **26a** ; δ 3.35 for **14a**[4]) and C-3' (δ 84.5 for **26a** ; δ 70.1 for **14a**[4]) . It may be

assumed that an oxazetidine intermediate **25a** was formed by the direct displacement of the C-3' mesylate and subsequently the C-2 oxygen attacked the C-2' position from the top as 2,2'-O-anhydro ring formation is known[18] to be a highly facile reaction in the presence of a leaving group at C-2' position; the electron deficient pyrrolidinium moiety acted as a leaving group and remained connected to the C-3' position through the oxygen atom after C2'-N(+) bond scission took place. The 2'-deoxy-2'-N-morpholino-*xylo* derivative **23b**[8c] under the same reaction conditions rearranged to **26b** in a similar fashion (**Scheme 7**).

Scheme 7



Conclusion

We have established for the first time the degradation patterns of the *N*-oxides of various aminonucleosides at ambient as well as high temperatures. Some of these *N*-oxides may be useful intermediates for generating new and structurally interesting compounds. More importantly, it has emerged from this study that proper functionalization of the pentose moiety or imposition of rigidity on the ring leads to selectivity in the reaction pattern of *N*-oxides (**Scheme 2** *vs* **Schemes 4** and **7**) although the mode of reactions turned out to be very different.

Experimental

General Infornation: See refs. 4 and 8a-d. ^{1}H NMR spectra were recorded at 200 MHz and ^{13}C NMR at 50 or 75 MHz. HRMS were recorded using the LSIMS technique with cesium ion (22Kv); glycerol was used as matrix. All compounds were purified starting with a mixture of petroleum ether (60-80) and ETOAc (4:1, v/v); polarity of the solvent was increased with EtOAc until the desired product was eluted.

Oxidative degradation of 5'-O-trityl-3'-deoxy-3'-N-morpholino-*ara*-uridine 4. To a solution of **4**[4] (0.34 g, 0.61 mmol) in chloroform (20 ml), m-CPBA (0.27 g, 1.5 mmol) was added and the mixture was stirred at room temperature for 0.5h. Chloroform was removed under reduced pressure and the residue was dissolved in pyridine (20 ml). The pyridine solution was heated at 100°C for 10h. Pyridine was removed under reduced pressure and residual pyridine was coevaporated with toluene. The oily residue was dissolved in EtOAc (60 ml) and the solution was washed with saturated $NaHCO_3$ (2 x 20 ml) solution followed by water (2 x 50 ml). The organic layer was separated, dried over anhydrous Na_2SO_4 and filtered. The filtrate was evaporated to dryness and the residue was purified over silica gel to give 5'-O-trityl-3'-deoxy-2'-ketouridines **7**[13,14] (0.18 g, 63%) and 5'-O-trityl-3'-deoxy-3',4'- didehydro-*ara*-uridine **8**[13] (0.085g, 29%) as white solids. Compound **8**: mp 99-101°C; **^{1}H NMR**($CDCl_3$): δ 10.65 (s, 1H); 7.55-7.20 (m, 16H); 6.52 (d, 6.4Hz, 1H); 5.62 (d, 8.0Hz, 1H); 5.42 (s, 1H); 5.27 (d, 6.3Hz, 1H), 3.76 (s, 2H); **^{13}C NMR**($CDCl_3$): δ 165.4, 158.5, 150.8, 143.6, 143.2, 128.8, 128.2, 127.5, 101.3, 101.1, 87.6, 87.1, 71.9, 59.4; **HRMS** (FAB+, M+Na^+): for $C_{28}H_{24}N_2O_5Na$ calcd. 491.1582 obsd. 491.1569.

1-(2,3-Dideoxy-5-O-trityl-β-D-glycero-pent-2-enofuranosyl)uracil 13. *General Method*: A mixture of **3**[4]and the appropriate amine (5 eq) in DMSO (3 ml/mmol) was heated at 90-95°C. After the disappearance of the starting material (tlc) the reaction mixture was diluted with EtOAc (40 ml/mmol) and washed with water. The organic layer was dried over anhydrous Na_2SO_4 and filtered. The filtrate was evaporated to dryness and the solid residue was purified by column chromatography to furnish a mixture of **9a-c** and **10a-c**. The mixture of **9a-c** and **10a-c** and triphenylphosphine (1.5 eq) was dissolved in dichloromethane (20 ml/mmol) and the solution was cooled using an ice-bath under argon. To this ice-cold solution, diisopropyl azodicarboxylate (2 eq) was added slowly. The ice-bath was removed and the reaction mixture was stirred at ambient temperature for 6-8 h. The solution was evaporated to dryness and the mixture was purified over silica gel to produce 1-[2,3-dideoxy-2,3-(N-alkyl)-epimino-5-O-trityl-β-D-*ribo*-furanosyl]-uracil **11a-c** as white solids. Compounds **11a-c** were treated with m-CPBA (1 eq) in dichloromethane (15 ml/mmol). After 2-8 h at ambient temperature, dichloromethane was removed under reduced pressure and the residue was dissolved in EtOAc (25 ml/mmol). The EtOAc solution was washed with saturated aqueous K_2CO_3 solution (3 x 25 ml) followed by water (3 x 25 ml). The organic layer was dried over Na_2SO_4, filtered and evaporated to dryness. The colored material was purified by column chromatography to obtain **13** as white solid in 45%,

62% and 52% overall (based on **3**[4] in 3 steps) yield from **11a, 11b** and **11c** respectively. The product was identical to the reported[16] compound in every respect (mp 189-191°C, lit[16] 188-191°C).

5'-O-Trityl-3'-deoxy-3'-N-pyrrolidino-2,2'-O-anhydrouridine 14a. The compound was synthesized following the literature procedure.[4]

5'-O-Trityl-3'-deoxy-3'-N-morpholino-2,2'-O-anhydrouridine 14b. This compound was prepared following the same literature procedure[4] for the synthesis of **14a** in 61% overall yield as a pale yellow foam from **3**. mp 96-98°C; **^{1}H NMR**($CDCl_3$): δ 7.38-7.24 (m, 16H), 6.09 (d, 6.0Hz, 1H), 5.96 (d, 7.6Hz, 1H), 5.35 (dd, 1.4Hz, 5.9Hz, 1H), 4.45 (m, 1H), 3.71 (t, 4H), 3.37 (m, 1H), 3.01 (m, 2H), 2.60-2.40 (m, 4H); **^{13}C NMR**($CDCl_3$): δ 171.8, 159.5, 143.5, 134.9, 128.6, 128.0, 127.4, 110.1, 90.6, 87.3, 84.6, 81.6, 71.9, 66.8, 64.3, 50.3; **HRMS** (FAB+, $M+Na^+$): for $C_{32}H_{31}N_3O_5Na$ calcd. 560.2161 obsd. 560.2145.

Compound 15a. **Method A**: To a solution of **14a** (0.54 g, 1 mmol) in dichloromethane (20 ml), m-CPBA (0.41 g, 2.4 mmol) was added and the reaction mixture was stirred at room temperature for 1 h. Dichloromethane was removed and the residue was dissolved in pyridine (25 ml). The pyridine solution was heated at 75°C for 9h. Pyridine was removed under reduced pressure by coevaporation with toluene. The residue was dissolved in EtOAc (100 ml) and washed with saturated $NaHCO_3$ (3 x 25 ml) and water (50 ml). The EtOAc part was dried over Na_2SO_4 and evaporated to dryness. The residue was purified over silica gel to give **15a** (0.4 g, 72%). **Method B**: To a solution of 5'-O-trityl-3'-deoxy-3'-N-pyrrolidino*ara*uridine[4] (0.46 g, 0.85 mmol) in pyridine (10 ml), mesyl chloride (0.5 g, 4.2 mmol) was added dropwise at 0°C. After the addition, the reaction mixture was kept at +4°C overnight. The brown solution was poured into cold saturated $NaHCO_3$ solution. The precipitate was filtered and washed thoroughly with water. The residue was dissolved in dichloromethane, dried over Na_2SO_4 and evaporated to dryness at <30°C to generate 5'-O-trityl-3'-deoxy-3'-pyrrolidino-2'-O-mesyl*ara*uridine **16a**. Compound **16a** was dissolved in chloroform (25 ml), m-CPBA (0.35 g, 2 mmol) was added and the mixture was stirred at ambient temperature. After 1h, the solvent was evaporated and the residue was dissolved in pyridine (20 ml). The pyridine solution was heated at 75°C. After 4.5h the solution was poured into saturated $NaHCO_3$ solution. The precipitate was filtered and washed with water. The residue was dissolved in EtOAc, dried over Na_2SO_4 and evaporated to dryness. The residue was purified over silica gel to give **15a** as a white solid (0.35 g, 74% for three steps); mp 107-109°C; **^{1}H NMR**($CDCl_3$): δ 9.01 (bs, 1H), 7.60-7.23 (m, 16H), 5.89 (d, 1.7Hz, 1H), 5.53 (dd, 8.0Hz, 2.0Hz, 1H), 5.12 (d, 3.9Hz, 1H), 4.52 (dd, 6.0Hz, 1.8HZ, 1H), 4.08 (m, 2H), 3.54 (m, 2H), 3.08 (m, 1H), 2.54 (q, 1H), 2.0 (m, 4H); **^{13}C NMR**($CDCl_3$): δ 163.6, 150.2, 143.7, 141.3, 128.8, 128.0, 127.3, 102.6, 98.9, 92.5, 87.3, 83.3, 83.1, 70.0, 63.6, 54.0, 31.0, 23.9; **HRMS** (FAB+, MH^+): for $C_{32}H_{32}N_3O_5$ calcd. 538.2341 obsd. 538.2375.

Compound 15b. **Method A**: Compound **14b** (0.27 g, 0.5 mmol) was oxidized as above described for **14a** and the *N*-oxide was heated in pyridine at 75°C for 8h. After usual work-up the crude product was purified over silica gel (0.22 g, 80%). **Method B**: 5'-O-Trityl-3'-deoxy-3'-N-morpholino-2'-O-mesylarauridine **16b** was synthesized from **4** (0.41 g, 0.73 mmol) using a literature procedure[8c]. Compound **16b** was oxidized

as described for **16a** and the *N*-oxide was heated in pyridine at 75°C for 4h. After usual work-up and purification over silica gel, **15b** was obtained as a white solid (0.22 g, 54% for three steps); mp 127-130°C; **^{1}H NMR**($CDCl_3$): δ 9.20 (bs, 1H, NH); 7.47-7.21 (m, 16H, H-6), 5.80 (d, 1.6Hz, 1H), 5.58 (dd, 8.0Hz, 1.8Hz, 1H), 4.75 (d, 6.4Hz, 1H), 4.44 (s, 1H), 4.22 (d, 13.2Hz, 1H), 4.03 (m, 1H), 3.84 (m, 3H), 3.53 (m, 3H), 2.61 (m, 2H); **^{13}C NMR**($CDCl_3$): δ 163.7, 150.2, 143.6, 141.8, 128.8, 127.9, 127.3, 102.7, 94.05, 87.6, 87.1, 82.4, 82.1, 71.9, 65.6, 65.1, 64.3, 48.8; **HRMS** (FAB+, MH^+): for $C_{32}H_{32}N_3O_6$ calcd. 554.2291 obsd. 554.2293.

Compound 14a from 15a. To a solution of **15a** (0.23 g, 0.43 mmol) in 4% formic acid in methanol (25 ml), Pd/C (0.22 g, 10% Pd) was added. The suspension was heated at 80°C for 15 mins. The mixture was cooled at room temperature and filtered. Pyridine (5 ml) was added to the filtrate and solvents were evaporated to dryness under reduced pressure to obtain crude **17a**. Mesyl chloride (1 ml, 13 mmol) in pyridine (5 ml) was added to a solution of **17a** in pyridine (15 ml) at 0°C. The reaction mixture was left at +4°C overnight. The brown solution was poured into saturated $NaHCO_3$ solution. The precipitate was filtered, washed with water and dried. The residue was dissolved in EtOAc. The solution was dried over Na_2SO_4 and filtered. The filtrate was evaporated to dryness. The brown residue was purified over silica gel to obtain **18a**. To a solution of **18a** in chloroform (20 ml), DBU (0.1 g, 0.6 mmol) was added. The solution was left at room temperature for 1.75 h. The solution was washed with water, dried over Na_2SO_4 and filtered. The filtrate was evaporated to dryness under reduced pressure. The residue was purified over silica gel to give **14a** (0.14 g, 62% for three steps).

Compound 14b from 15b. To a solution of **15b** (0.25 g, 0.45 mmol) in 4% formic acid in methanol (50 ml), Pd/C (0.3 g, 10% Pd) was added. The suspension was heated at 80°C for 8 hrs. After usual work-up and purification (described for **17a**) **17b** was obtained. Compound **17b** was mesylated to **18b** as above. Compound **18b** was converted to **14b** by treatment with DBU (0.06 g, 25% for three steps).

5'-O-Trityl-3'-O-N-pyrrolidino-2,2'-O-anhydrouridine 26a. 5'-O-Trityl-2'-deoxy-2'-pyrrolidino-*xylo*uridine[4] (0.37 g, 0.68 mmol) was mesylated following the literature procedure.[8c] The crude mesylated product **23a**[13] was oxidized as above and the *N*-oxide was heated in pyridine at 75°C for 4.5h. After usual work-up and purification over silica gel, **26a** was obtained as a pale yellow solid (0.21 g, 57%); mp 89-91°C; **^{1}H NMR**($CDCl_3$): δ 7.38-7.23 (m, 16H), 6.09 (d, 5.7Hz, 1H), 5.95 (d, 7.4Hz, 1H), 5.38 (d, 5.7Hz, 1H), 4.42 (m, 2H), 2.99 (m, 6H), 1.81 (bs, 4H); **^{13}C NMR**($CDCl_3$): δ 171.8, 159.5, 143.3, 134.8, 128.5, 128.1, 127.4, 110.1, 90.4, 87.0, 86.2, 84.5, 63.2, 56.9, 21.9; **HRMS** (FAB+, MH^+): for $C_{32}H_{32}N_3O_5$ calcd. 538.2341 obsd. 538.2344.

5'-O-Trityl-3'-O-N-morpholino-2,2'-O-anhydrouridine 26b. 5'-O-Trityl-2'-deoxy-2'-morpholino-*xylo*uridine[4] (0.31 g, 0.55 mmol) was mesylated following the literature procedure.[8c] The crude mesylated product **23b**[13] was oxidized as above and the *N*-oxide was heated in pyridine at 75°C for 4.5h. After usual work-up and purification over silica gel, **26b** was obtained as a off-white solid (0.21g, 69%); mp 95-98°C; **^{1}H NMR**($CDCl_3$): δ 7.45-7.25 (m, 16H), 6.13 (d, 5.8Hz, 1H), 5.95 (d, 7.4Hz, 1H), 5.29 (d, 5.8Hz, 1H), 4.54 (m,

1H), 4.41 (m, 1H), 3.91 (d, 2H), 3.58 (t, 2H), 3.10 (m, 3H), 2.92(m, 1H), 2.72 (m, 2H); **^{13}C NMR**($CDCl_3$): δ 171.7, 159.4, 143.3, 134.8, 128.4, 128.1, 127.5, 110.2, 90.3, 87.1, 86.1, 84.5, 83.7, 66.1; 62.9; 56.8; 56.3; **HRMS** (FAB+, MH^+): for $C_{32}H_{32}N_3O_6$ calcd. 554.2291 obsd. 554.2306.

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