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One-step Synthesis of C-2 Dialkylamino-substituted 2',3'-O-Anhydro-*lyxo*-uridines: First Report on the Opening of 2,2'-O-Anhydro-bridge of 2,2'-O-Anhydrouridine by Secondary Amines#.

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Abstract: *Secondary amines successfully opened the 2,2'-O-anhydro-bridge of 2,2'-O-anhydrouridines* ***8a*** *and* ***8b*** *in presence of 3'-O-mesyl group to produce compounds* ***10a-13a*** *and* ***10b-13b****, a new class of isocytidine derivatives.*

We have recently demonstrated[1] that 3',5'-di-O-mesylthymidine on reaction with secondary amines undergoes "one-pot-two-step" transformation to produce 2,3'-O-anhydro-5'-deoxy-5'-alkylaminothymidines. In an attempt to broaden the scope of such reactions we decided to react various sulphonylated derivatives of the other pyrimidine nucleoside, uridine with secondary amines.

Attempted reactions between 2',3',5'-tri-O-mesyluridine[2] and neat piperidine at ambient temperature produced an inseparable mixture of compounds. Reaction with morpholine, however, produced 4-(1-oxo-3-(morpholinyl)-2-propenyl)-morpholine **1** after 24h. Although the product could not be obtained in pure form, its structure was established by comparing the spectra of the crude material with the reported[3,4] values. The additional confirmation of structure came from the mass spectral analysis of the compound. 2',3'-Di-O-mesyl-5'-O-trityluridine **7a** and 2',3'-di-O-mesyluridine **7b** also produced the same compound **1** under identical conditions. As under basic conditions 2,2'-O-anhydro-ring formation is much faster than 2,3'-O-anhydro- and 2,5'-O-anhydro- ring formation[5], it may be concluded that at least one pathway of the reactions between 2',3',5'-tri-O-mesyluridine and neat piperidine or morpholine must have been the 2,2'-O-anhydro- ring formation. The additional complications may have arisen from the direct displacement of the 5'-O-mesyl- group by piperidine in a fashion similar to that described[1] for 3',5'-di-O-mesylthymidine. In order to reduce the number of pathways involved and simplify the product distribution, we decided to study the reactions of 2',3'-di-O-mesyl-5'-O-trityluridine **7a** with secondary amines; the absence of the 5'-O-mesyl- group would remove the pathway generated from the displacement reaction.

It has been reported[6] that 2,2'-O-anhydrouridine **2**, on reaction with primary amines produced C-2 amino substituted *ara*uridine derivatives **3** (*iso*cytidines, R= alkyl, benzyl etc.) but *remained unaffected by secondary amines* due to the "steric hindrance". Attack on the C-2 positions of 2,5'-O-anhydro-2'-O-tosyluridine **4** (ref. 7), 2,3'-O-anhydro-5'-O-tosylthymidine **5** (ref. 8), 2,5'-O-anhydro-3'-O-mesylthymidine **6** (ref. 9) and 2,2'-O-anhydro-3'-O-mesyluridine **8b** (ref. 10) by *primary amines* are well documented. 8,2'-O-Anhydro purine nucleosides, however, reacted[11,12] with both primary and secondary amines to furnish C-8 amino substituted *ara*-derivatives.

2',3'-Di-O-mesyl-5'-O-trityluridine **7a** (ref. 13) was treated with piperidine either neat or in DMSO solution. In both cases single product was obtained and the structure of the product was established as 1-(2,3-O-anhydro-5-O-trityl-β-D-*lyxo*furanosyl)-2-piperidino-4-pyrimidone **10a**, an *iso*cytidine derivative. The same product was obtained within 1h when 2,2'-O-anhydro-3'-O-mesyl-5'-O-trityluridine **8a** (ref. 14) was treated with neat piperidine. As far as our knowledge goes in the literature *this is the first report on the opening of 2,2'-O-anhydro bridge by a secondary amine.*

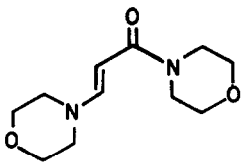
Pyrrolidine, ethyl *iso*nepicotate and N-methylpiperazine also reacted with compound **7a** in similar fashion to produce various *iso*cytidine derivative **11a**, **12a** and **13a** respectively. Morpholine produced a mixture, but one of those products certainly was the similar kind of *iso*cytidine derivatives as was evident by the ^{1}H-NMR of the mixture; the structure of the morpholino derivative was also confirmed by mass spectrum (M^+ as well as 2-morpholino-4-pyrimidone - 1 peaks). The mixture, however, after prolonged reaction time produced compound **1**. Extensive cleavage occured when **7a** was treated with diethylamine, N-methylethanolamine, N,N'-dimethylethylenediamine and N-acetylpiperizine; all these reactions, however, did produce the 2,2'-O-anhydro derivative **8a** (tlc) which eventually got cleaved.

As attempted detritylation of compounds **10a-13a** produced mixture of products, we chose to study the reactions of secondary amines with 2,2'-O-anhydro-3'-O-mesyluridine **8b** (ref. 15) which could be synthesised[5] very easily from **7b**. Thus, compound **8b** on reaction with piperidine, pyrrolidine, ethyl *iso*nepicotate and N-methylpiperazine produced compounds **10b**, **11b**, **12b** and **13b** respectively.

The structures of all new compounds were assigned unambiguously by spectroscopy. A comparison of the UV spectra of compounds **10b-13b** with that of the known epoxide **9b** (ref. 16) showed a distinct hypsochromic shift, proving thereby that the base modification must have taken place. In case of the ^{1}H-NMR, H-1' signal of compounds **10a-13a** was shielded by 0.5ppm and H-5 was deshielded by 0.3ppm when compared with the same signals of **9a** (ref. 13); the same signals of compounds **10b-13b** shifted positions in a similar fashion by 0.3ppm when compared with the same signals of **9b**. It is interesting to note that in the case of both the sets of compounds the H_5-H_6 coupling constants changed by almost 0.4 Hz. In the case of the ^{13}C-NMR, C-1', C-2/C-4 and C-5, signals of compounds **10a-13a** were deshielded by 3.5, 6-8 and 7ppm respectively when compared with the same signals of **9a**; the same signals of compounds **10b-13b** shifted positions in a similar fashion (except for compounds **10b** and **12b** where the C-4'signal shifted by 2ppm; it should be noted, however that ^{13}C-NMR of **10b** was recorded in DMSO-d_6) when compared with the same signals of **9b**. Both the proton and the carbon signals were assigned on the basis of ^{1}H-^{1}H and ^{1}H-^{13}C COSY spectra of compound **10a**. It was assumed that the proton and carbon signals of both the tritylated and non-tritylated compounds followed the same order as there was no significant change in the positions of peaks in a particular group of compounds. All tritylated derivatives **10a-13a** gave molecular ion peak in the MS but in case of the nontritylated compounds only **10b**, **11b** and **12b** gave the same. On the other hand, only **10a-10b** and **11a-11b** produced fragments corresponding to (2-piperidino-4-pyrimidone - 1) and (2-pyrrolidino-4-pyrimidone - 1).

The mechanism of formation of compounds **10a-13a** and **10b-13b** from **7a** and **7b** is believed to involve the formation of the 2,2'-O-anhydro-derivatives **8a** and **8b**. This conclusion corroborated by the fact that 2,2'-O-anhydro-3'-O-mesyl-5'-O-trityluridine **8a** on reaction with neat piperidine produced compound **10a** within 1h. The formation of compounds **10-13** from **7** or **8** was not obvious as the earlier report on the reactions of compound **2** with secondary amines, as mentioned above, ruled out the possibility of the opening of the 2,2'-O-anhydro-bridge by secondary amines because of the "steric effect". It is obvious that the presence of an electron-withdrawing and a leaving group adjacent to the C-2' position of 2,2'-O-anhydrouridine has enhanced the electrophilicity of the C-2 carbon, thereby nullifying the "steric" effect.

In conclusion, we have shown for the first time that some secondary amines successfully open the 2,2'-O-anhydro-bridge of 2,2'-O-anhydrouridines **8a** and **8b** containing 3'-O-mesyl group to produce compounds **10a-13a** and **10b-13b**, a new class of *iso*cytidine derivatives. It is worth mentioning that some C-2 aminosubstituted pyrimidine derivatives have interesting biological properties[17,18]. Moreover, 1-(2,3-O-anhydro-β-D-*lyxo* furanosyl)cytosine (ANLC) can be considered as active and selective anti-HIV agent[19]. Work is in progress to functionalise the compounds further by opening the epoxide ring.



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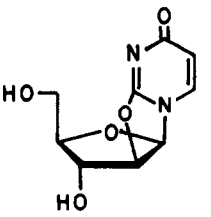

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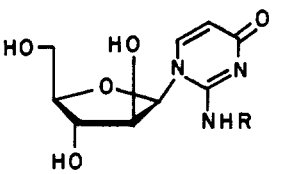

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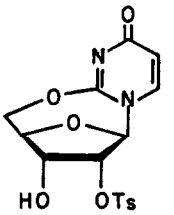

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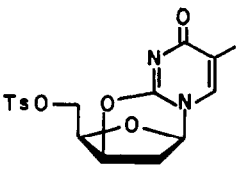

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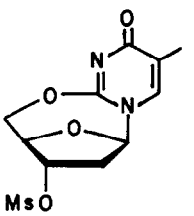

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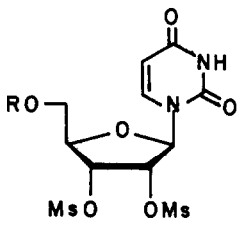
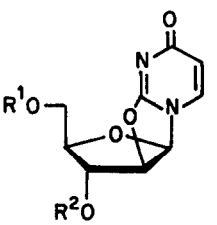
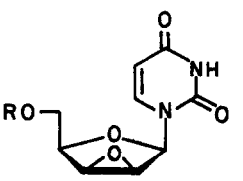


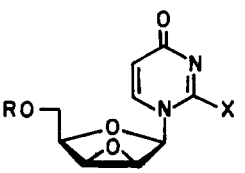
7a : R = Tr
7b : R = H



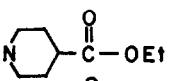
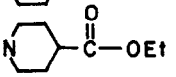
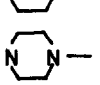
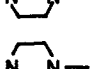
8a : R^1 = Tr ; R^2 = Ms
8b : R^1 = H ; R^2 = Ms



9a : R = Tr
9b : R = H



10a: R = Tr ; X = 
10b: R = H ; X = 
11a : R = Tr ; X = 
11b : R = H ; X = 

12a: R = Tr ; X = 
12b: R = H ; X = 
13a: R = Tr ; X = 
13b: R = H ; X = 

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Experimental:

Melting points were uncorrected. Uridine was purchased from Pharma Waldhof GmbH, Germany and used as received. Thin Layer Chromatography was performed on Merk precoated 60 F_{254} plates. Compounds were visualised on TLC plate under UV light. Column chromatographic separations were done using silica gel (Silica gel 60, 230-400 mesh, E. Merck) or basic alumina (Brockmann Grade I for Chromatography, S.D. Fine Chem. Ltd., India). ^{1}H-NMR (200 MHz) and ^{13}C-NMR (50 MHz) spectra were recorded on Bruker ACF200 NMR spectrometer (δ scale) using TMS, solvent chloroform-d or dioxane (in case of D_2O) as internal standards. UV and MS were recorded on Perkin-Elmer Lambda 15 UV-Vis Spectrometer and Finnigan MAT 1020B GC/MS respectively.

4-(1-Oxo-3-(morpholinyl)-2-propenyl)-morpholine 1 from 2',3',5'-tri-O-mesyluridine: 2',3',5'-Tri-O-mesyluridine (1mmol) was treated with neat morpholine (3ml) at ambient temperature for 24h. The amine was removed under reduced pressure and the compound was purified by column chromatography on basic alumina. ^{1}H-NMR ($CDCl_3$): δ 7.45 (d, 12.6 Hz, 1H) H-3; 4.99 (d, 12.6 Hz, 1H) H-2; 3.73-3.53 (m, 12H) and 3.19 (t, 4H) morpholine. ^{13}C-NMR ($CDCl_3$): δ 168.1, CO; 151.6, C-3; 84.9, C-2; 66.8 and 66.2, H_2C-O-CH_2; 48.7 and 44.1, H_2C-N-CH_2. MS (EI): m/z 226 (M^+, 25%); 140 (M^+ - morpholinyl, 100%).

1-(2,3-O-Anhydro-5-O-trityl-β-D-*lyxo*furanosyl)-uracil 9a: Compound **9a** was synthesised using a reported procedure[13]. ^{1}H-NMR ($CDCl_3$): δ 9.18 (bs,1H) NH; 7.55 (d, 8.2 Hz, 1H) H-6; 7.49-7.22 (m, 15H) trityl; 6.2 (s, 1H) H-1'; 5.67 (d, 8.2 Hz, 1H) H-5; 4.19 (t, 5.66 and 5.77 Hz, 1H) H-4'; 3.94 (d, 2.8 Hz, 1H) H-3'; 3.89 (d, 2.8 Hz, 1H) H-2'; 3.52-3.32 (m, 2H) H-5', H-5'. ^{13}C-NMR ($CDCl_3$): δ 163.60, C-4; 150.9, C-2; 143.6, trityl; 141.5, C-6; 128.8, 128.2, 127.4, trityl; 102.6, C-5; 87.3, trityl; 81.9, C-1'; 76.9, C-4'; 62.4, C-5'; 56.4/56.2, C-2'/C-3'.

1-(2,3-O-Anhydro-5-O-trityl-β-D-*lyxo*furanosyl)-2-piperidino-4-pyrimidone 10a: Method A: Compound **7a** (1mmol) was treated with neat piperidine (3ml) at ambient temperature. After 5h, the reaction mixture was poured into petroleum ether (50ml) and the liquid was decanted off. The oily residue was purified by column chromatography on basic alumina. Yield: 50%. **Method B:** A solution of compound **7a** (1mmol) in DMSO (2ml) was treated with piperidine (15mmol) at ambient temperature. After 48h the reaction mixture was poured into water. The white precipitate was collected by filteration and dissolved in dichloromethane (25ml). The solution was dried over sodium sulphate and filtered. The filtrate was evaporated to dryness and the residue was purified as above. Yield: 55%. m.p. 102°C. ^{1}H-NMR ($CDCl_3$): δ 7.61 (d, 7.8 Hz, 1H) H-6; 7.5-7.24 (m, 15H) trityl; 6.0 (d, 7.8 Hz, 1H) H-5; 5.74 (s, 1H) H-1'; 4.16 (t, 6.1 and 6.0 Hz, 1H) H-4'; 3.95 (d, 2.9 Hz, 1H) H-3'; 3.89 (d, 2.9 Hz, 1H) H-2'; 3.53-3.18 (m, 6H) H-5', H-5'', H_2C-N-CH_2; 1.66 (bs, 6H) H_2C-CH_2-CH_2. ^{13}C-NMR ($CDCl_3$): δ 171.0, C-4; 159.3, C-2; 143.8, trityl; 140.1, C-6; 128.8, 128.2, 127.5, trityl; 110.2, C-5; 87.5, trityl; 85.8, C-1'; 76.5, C-4'; 62.3, C-5'; 56.3/55.8, C-2'/C-3'; 51.2, H_2C-N-CH_2; 25.7 and 24.4, H_2C-CH_2-CH_2. MS (EI): m/z 535 (M^+, 6%); 178 ($C_9H_{12}N_3O^+$, 100%).

Synthesis of Compound 10a from Compound 8a: Compound **8a** (1mmol) was treated with neat piperidine (3ml) at ambient temperature. After 1h, the reaction mixture was evaporated to dryness under reduced pressure. The oily residue was purified by column chromatography on basic alumina. Yield: 74%.

1-(2,3-O-Anhydro-5-O-trityl-β-D-*lyxo*furanosyl)-2-pyrrolidino-4-pyrimidone 11a: Compound **7a** (1mmol) was treated with neat pyrrolidine (3ml) at ambient temperature. After 3h, the reaction mixture was evaporated to

dryness under reduced pressure. The oily residue was purified by column chromatography on basic alumina. Yield: 50%, m.p. 95°C. ^{1}H-NMR ($CDCl_3$): δ 7.62 (d, 7.7 Hz, 1H) H-6; 7.51-7.23 (m, 15H) trityl; 5.98 (d, 7.7 Hz, 1H) H-5; 5.68 (s, 1H) H-1'; 4.13 (t, 6.2 and 6.0 Hz, 1H) H-4'; 3.95 (d, 2.9 Hz, 1H) H-3'; 3.88 (d, 2.9 Hz, 1H) H-2'; 3.58-3.27 (m, 6H) H-5', H-5'', H_2C-N-CH_2; 2.0-1.92 (m, 4H) CH_2-CH_2. ^{13}C-NMR ($CDCl_3$): δ 170.6, C-4; 156.9, C-2; 143.8, trityl; 139.6, C-6; 128.9, 128.2, 127.6, trityl; 109.8, C-5; 87.5, trityl; 85.4, C-1'; 76.5, C-4'; 62.3, C-5'; 56.4/55.7, C-2'/C-3'; 50.9, H_2C-N-CH_2; 25.9, CH_2-CH_2. MS (EI): m/z 521 (M^+, 2%); 164($C_8H_{10}N_3O^+$, 100%)

1-(2,3-O-Anhydro-5-O-trityl-β-D-*lyxo*furanosyl)-2-(ethyl *iso*nipecotyl)-4-pyrimidone 12a: Compound **7a** (1mmol) was treated with neat ethyl *iso*nipecotate (2ml) at ambient temperature for 21h. The product was isolated and purified as described in Method A for the preparation of compound **10a**. Yield: 40%, m.p. 93°C. ^{1}H-NMR ($CDCl_3$): δ 7.67 (d, 7.7 Hz, 1H) H-6; 7.57-7.27 (m, 15H) trityl; 6.04 (d, 7.7 Hz, 1H) H-5; 5.75 (s, 1H) H-1'; 4.24-4.12 (m, 3H) H-4', ethyl CH_2; 3.96 (d, 2.7 Hz, 1H) H-3'; 3.88 (d, 2.7 Hz, 1H) H-2'; 3.87-3.37/3.14-2.79/2.58-2.48/2.12-1.7 (m, 11H) H-5', H-5'', H_2C-N-CH_2, H_2C-CH-CH_2; 1.3 (t, 3H) ethyl CH_3. ^{13}C-NMR ($CDCl_3$): δ 174.5, ethyl CO; 170.9, C-4; 158.9, C-2; 143.7, trityl; 140.1, C-6; 128.9, 128.2, 127.5, trityl; 110.4, C-5; 87.5, trityl; 85.7, C-1'; 76.5, C-4'; 62.2, C-5'; 60.9 ethyl CH_2; 56.2/55.8, C-2'/C-3'; 50.0 and 49.3, H_2C-N-CH_2; 40.9 nipecotyl CH; 28.0 and 27.9, nipecotyl CH_2; 14.4, ethyl CH_3. MS (EI): m/z 607 (M^+, 2%).

1-(2,3-O-Anhydro-5-O-trityl-β-D-*lyxo*furanosyl)-2-(N-methylpiperazino)-4-pyrimidone 13a: Compound **13a** (1mmol) was treated with neat N-methylpiperazine (2ml) at ambient temperature for 48h. The product was isolated and purified as described in Method B for the preparation of compound **10a**. Yield: 42%, m.p. 96°C. ^{1}H-NMR ($CDCl_3$): δ 7.65 (d, 7.7 Hz, 1H) H-6; 7.54-7.24 (m, 15H) trityl; 6.02 (d, 7.7 Hz, 1H) H-5; 5.73 (s, 1H) H-1'; 4.15 (t, 6.2 and 6.0 Hz, 1H) H-4'; 3.97 (d, 2.9 Hz, 1H) H-3'; 3.88 (d, 2.9 Hz, 1H) H-2'; 3.59-3.28 (m, 6H) H-5', H-5'', H_2C-N-CH_2; 2.64-2.43 (m, 4H) H_2C-N-CH_2; 2.35 (s, 3H) N-CH_3. ^{13}C-NMR ($CDCl_3$): δ 170.7, C-4; 158.3, C-2; 143.6, trityl; 139.9, C-6; 128.7, 128.0, 127.4, trityl; 110.2, C-5; 87.4, trityl; 85.6, C-1'; 76.4, C-4'; 62.1, C-5'; 56.1/55.6, C-2'/C-3'; 54.4 and 49.6 $(H_2C\text{-}N\text{-}CH_2)_2$; 46.0, N-$CH_3$. MS (EI): m/z 550 ($M^+$, 2%).

1-(2,3-O-Anhydro-β-D-*lyxo*furanosyl)-uracil 9b: Compound **9b** was synthesised using a reported procedure[16]. UV: λ_{max} (H_2O): 259.7 nm. ^{1}H-NMR (D_2O): δ 7.88 (d, 8.2 Hz, 1H) H-6;6.2 (s, 1H) H-1'; 5.87 (d, 8.2 Hz, 1H) H-5; 4.29 (t, 6.01 and 5.23 Hz, 1H) H-4'; 4.18 (d, 3.6 Hz, 1H) H-3'; 4.12 (d, 3.6 Hz, 1H) H-2'; 3.98-3.81 (m, 2H) H-5', H-5''; ^{13}C-NMR (D_2O): δ 167.2, C-4; 152.7, C-2; 143.9, C-6; 103.1, C-5; 83.2, C-1'; 78.9, C-4'; 61.1, C-5'; 57.2/57.1, C-2'/C-3'.

1-(2,3-O-Anhydro-β-D-*lyxo*furanosyl)-2-piperidino-4-pyrimidone 10b: A solution of compound **8b** (1mmol) in DMSO (2ml) was treated with piperidine (2ml) at ambient temperature. After 8h the reaction mixture was poured into ether (50ml) and the liquid was decanted off. The residue was purified by column chromatography on basic alumina. Yield: 80%, m.p. 75°C. UV: λ_{max} (H_2O): 235.2 nm. ^{1}H-NMR (D_2O): δ 8.0 (d, 7.7 Hz, 1H) H-6; 6.13 (d, 7.7 Hz, 1H) H-5; 5.89 (s, 1H) H-1'; 4.28 (t, 5.7 and 5.6 Hz, 1H) H-4'; 4.19 (d, 3.2 Hz, 1H) H-3'; 4.12 (d, 3.2 Hz, 1H) H-2'; 4.0-3.8 (m, 2H) H-5', H-5''; 3.41-3.38 (m, 4H) H_2C-N-CH_2; 1.69 (bs, 6H) H_2C-CH_2-CH_2. ^{13}C-NMR (DMSO-d_6): δ 168.9, C-4; 158.3, C-2; 139.9, C-6; 108.9, C-5; 85.2, C-1'; 77.4, C-4'; 59.4, C-5'; 55.7/55.1, C-2'/C-3'; 50.1, H_2C-N-CH_2; 24.7 and 23.5, H_2C-CH_2-CH_2. MS (EI): m/z 293 (M^+, 11%); 178 ($C_9H_{12}N_3O^+$, 100%).

1-(2,3-O-Anhydro-β-D-*lyxo*furanosyl)-2-pyrrolidino-4-pyrimidone 11b: A solution of compound **8b** (1mmol) in DMSO (2ml) was treated with pyrrolidine (2ml) for 10h at ambient temperature. The product was isolated and purified as described in case of compound **10b**. Yield: 75%, m.p. 70°C. UV: λ_{max} (H_2O): 230.3 nm. ^{1}H-NMR (D_2O): δ 7.89 (d, 7.7 Hz, 1H) H-6; 6.01 (d, 7.7 Hz, 1H) H-5; 5.95 (s, 1H) H-1'; 4.22 (t, 5.7 and 5.6 Hz, 1H) H-4'; 4.16 (d, 3.3 Hz, 1H) H-3'; 4.07 (d, 3.3 Hz, 1H) H-2'; 3.97-3.8 (m, 2H) H-5', H-5''; 3.7-3.55 (m, 4H) H_2C-N-CH_2; 2.0-1.88 (m, 4H) H_2C-CH_2. ^{13}C-NMR (D_2O): δ 174.2, C-4; 157.9, C-2; 143.3, C-6; 108.0, C-5; 86.7, C-1'; 78.7, C-4'; 61.2, C-5'; 57.3/56.7, C-2'/C-3'; 51.9, H_2C-N-CH_2; 26.3, CH_2-CH_2. MS (EI): m/z 279 (M^+, 4%); 164 ($C_8H_{10}N_3O^+$, 100%).

1-(2,3-O-Anhydro-β-D-*lyxo*furanosyl)-2-(ethyl *iso*nipecotyl)-4-pyrimidone 12b: A solution of compound **8b** (1mmol) in DMSO (2ml) was treated with pyrrolidine (2ml) for 24h at ambient temperature. The product was isolated and purified as described in case of compound **10b**.Yield: 40%, m.p.62°C. UV: λ_{max} (H_2O): 234.4 nm. ^{1}H-NMR (D_2O): δ 8.05 (d, 7.7 Hz, 1H) H-6; 6.18 (d, 7.7 Hz, 1H) H-5; 5.93 (s, 1H) H-1'; 4.34-4.14 (m, 5H) H-2', H-3', H-4', ethyl CH_2 ; 4.03-3.72 (m, 4H)/3.2-3.05 (m, 2H)/2.8-2.65 (m, 1H)/2.1-1.79 (m, 4H) H-5', H-5'', H_2C-N-CH_2, H_2C-CH-CH_2; 1.32 (t, 3H) ethyl CH_3. ^{13}C-NMR (D_2O): δ 173.9, ethyl CO; 168.9, C-4; 158.2, C-2; 140.1, C-6; 109.1, C-5; 85.2, C-1'; 77.5, C-4'; 59.8/59.4, ethyl CH_2/ C-5'; 55.8/55.2, C-2'/C-3'; 48.7 and 48.5, H_2C-N-CH_2; 39.7, nipecotyl CH; 27.2 and 27.0, nipecotyl CH_2; 14.0, ethyl CH_3. MS (EI): m/z 210 ((M^+-$C_8H_{14}NO_2$)+1, 6%).

1-(2,3-O-Anhydro-β-D-*lyxo*furanosyl)-2-(N-methylpiperazino)-4-pyrimidone 13b: A solution of compound **8b** (1mmol) in DMSO (2ml) was treated with N-methylpiperazine (2ml) at ambient temperature. After 16h the reaction mixture was loaded directly on a basic alumina column packed in petroleum ether. The column was eluted with the same solvent until all the DMSO and excess amine were removed. The polarity of the eluent was increased gradually and the product was eluted with a mixture of methanol-ethyl acetate (1:9). Yield: 65%, m.p. 65°C. UV: λ_{max} (H_2O): 232.4 nm. ^{1}H-NMR (D_2O): δ8.05 (d, 7.7 Hz, 1H) H-6; 6.19 (d, 7.7 Hz, 1H) H-5; 5.96 (s, 1H) H-1'; 4.29 (t, 6.1 and 5.2 Hz, 1H) H-4'; 4.19 (d, 3.0 Hz, 1H) H-3'; 4.13 (d, 3.5 Hz, 1H) H-2'; 4.0-3.85 (m, 2H) H-5', H-5''; 3.6-3.4 (m, 4H) H_2C-N-CH_2; 2.64 (bs, 4H) H_2C-N-CH_2; 2.34 (s, 3H) N-CH_3. ^{13}C-NMR (D_2O): δ 174.6, C-4; 160.2, C-2; 143.9, C-6; 109.4, C-5; 87.4, C-1'; 78.7, C-4'; 61.1, C-5'; 57.1/56.6, C-2'/C-3'; 54.3, H_2C-N-CH_2; 49.8, H_2C-N-CH_2; 45.6, N-CH_3. MS (EI): m/z 308 (M^+, 1%).

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NCL Communication No. 5836

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