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NEW SYNTHESES OF 2′,3′-DIDEOXY-2′,3′-DI-SUBSTITUTED & -2′-MONO-SUBSTITUTED URIDINES & ADENOSINES BY MICHAEL ADDITION REACTIONS

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Abstract: *Michael addition reactions of the 3′-enesulfones* **5, 6** *and* **18** *with ammonia, primary amines (methylamine, benzylamine, glycine methyl ester), secondary amines (dimethylamine, pyrrolidine, piperidine, morpholine) and carbon-nucleophiles (sodium methylmalonate, conjugate base of nitromethane and pyrrolidin-1-cyclohexene) have been used as means to synthesize new 2′, 3′-dideoxy-2′,3′-disubstituted- or 2′-substituted nucleosides. Most of these nucleophilic addition reactions have given exclusively trans-adducts [***7c-j, 19d-g** *&* **20***] owing to the regiospecific protonation of the intermediary chiral α-sulfonyl cabanion at C-3′; a few of the above reactions have however produced a mixture of cis- and trans-adducts, although the latter is overwhelmingly a major product, depending upon the nature of the 2′-substituent and the type of the 3′-enesulfone [***5, 6** *or* **18***]. The Michael adducts [***7, 9, 19, 24***] have been deprotected at the 5′-end to produce 2′,3′-disubstituted-2′,3′-dideoxy-β-D-nucleosides [***8a-k, 10a,b,k** *&* **21a-g, 22j, 25a-c***]. Some of the Michael adducts have been C-3′ desulfonated to produce 5′-protected-2′,3′-dideoxy-2′-substituted nucleosides [***11a-g, 26a,f,g***] which are not easily accessible through any other routes. Finally these compounds have been also deprotected to give nucleosides [***12a-g** *&* **33***] in good yields. Compounds described herein, with free 5′-hydroxyl function, are potential inhibitors of the HIV-reverse transcriptase promoted c-DNA synthesis.*

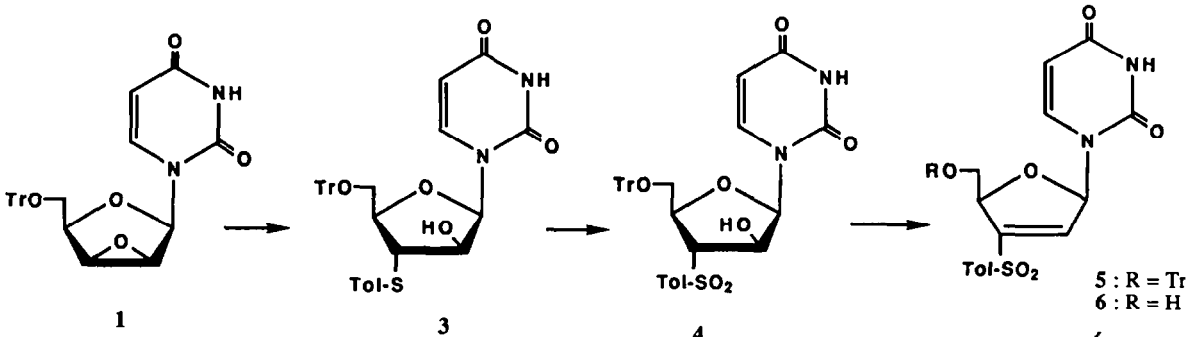
Human Immunodeficiency Virus (HIV) targets itself to the host's immunological system causing the acquired immune deficiency syndrome (AIDS). As a result, several AIDS-related complex including several opportunistic infections are initiated in HIV-infected patients causing death. Our efforts to design inhibitors against AIDS virus are based upon the possibilities of targeting suitable synthetic derivatives of nucleosides to the HIV-specific enzymes. These compounds are intended either to interfere specifically with an early event during the HIV replication (*e.g.* reverse transcriptase) or/and a late event in its life cycle (*e.g.* protease)[1-9]. Most of the compounds which have turned out to be active against the reverse transcriptase of HIV are 2′,3′-dideoxynucleosides and a few 2′,3′-dideoxy-3′-substituted (F, N_3) nucleoside analogues[4-9]. Synthetic procedures to prepare these compounds and other 2′- or 3′-substituted nucleosides involve one of the following procedures: (i) direct nucleophilic (S_N2) displacement of a leaving group[10-17], (ii) nucleophilic ring-opening reactions of 2′,3′-O-*ribo*- or *lyxo*-anhydro purine nucleosides or 2′,3′-O-*lyxo*-anhydro pyrimidine nucleosides[18-32], (iii) ring-opening reactions of 2,2′-O- or 2,3′-O-anhydro pyrimidine nucleosides or 8,2′-O- or 8,3′-O-anhydro purine nucleosides[33-35], (iv) substitution through the displacement of 2′,3′-carboxonium ion[36,37], and (v) nuclephilc addition to appropriately protected 2′- or 3′-keto nucleosides[38-47], or other procedures involving addition[54] and/or rearrangements[48-56]. The synthesis of the corresponding 2′,3′-dideoxy-3′-substituted or 2′-substituted nucleosides with an amino substituents [-NHMe, -NMe_2, -NHPh, -$NHCH_2Ph$, -N^{α}-aminoacyl, -N^{α}-oligopeptides and other N-substituted cyclic amino derivatives such as piperidino, morpholino, pyrrolidino etc.] can not be prepared by any of the above synthetic procedures[6-56] without a series of lengthy and labourious transformations. The C-3′ amino[29] and C-3′ amido[19] substituted nucleosides have been however prepared directly from 2′,3′-O-*lyxo*-anhydro pyrimidine nucleosides. Herein we report that appropriately protected 3′-enesulfones of both pyrimidine and purine nucleosides, such as **5, 6** and **18**, conveniently undergo Michael addition reactions with ammonia, primary and secondary amines and with other carbon-nucleophiles to give a variety of 2′, 3′-dideoxy-3′-sulfonyl-2′-substituted nucleosides [**5** → **7a-k + 9a,b,k**; **6** → **8a-d + 10a,b**; **18** → **19a-g + 24a-c** & **20**]. These derivatives can be easily deprotected at the 5′-end to give corresponding 5′-hydroxy derivatives (**8, 10, 21, 22** & **25**) which by virtue of their lack of 2′ and 3′-hydroxyl functions have the potential to block the HIV-specific reverse transcriptase promoted cDNA synthesis[1-3].

Alternatively, these compounds have been desulfonated at the C-3′ to give the 5′-protected 2′,3′-dideoxy-2′-substituted nucleosides (**11** & **26**) which have been subsequently deprotected at the 5′ to give the 2′, 3′-dideoxy-2′-substituted nucleosides **12** & **33** which also have unique potential to block the HIV-specific reverse transcriptase proimoted cDNA synthesis[1-3].

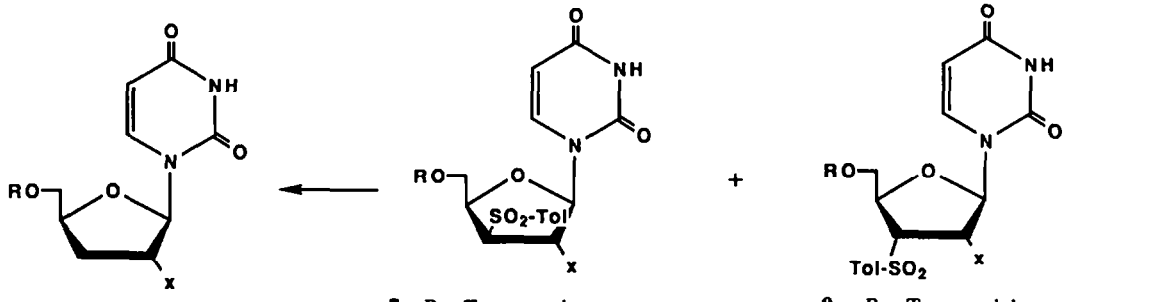
Preparation of 3′-enesulfone derivatives of uridine (5) : The key intermediate, 5′-O-trityl-2′,3′-O-anhydro-lyxofuranosyl uridine **1**[24] [Tr = trityl] was prepared in ~ 80 % yield by an alkaline treatment of 5′-O-trityl-2′,3′-O-dimesyl uridine. Compound **1** was then reacted with p-toluenethiolate to give an isomeric mixture of 1-(2′-(4-toluenethio)-β-D-xylofuranosyl)uracil **2** & 1-(3′-(4-toluenethio)-β-D-arabinofuranosyl)uracil **3** in 1:2 ratio. They were separated by standard column chromatography to give the 3′-toluenethio- derivative **3** in 55 % yield. Compound **3** was easily oxidized by m-chloroperbenzoic acid in dichloromethane at room temperature to corresponding sulfone **4** in 99 % yield. When a dry pyridine solution of **4** was treated overnight with an excess of methanesulfonyl (= mesyl = Ms) chloride at 20 °C and then at 50 °C for 1 h in presence of water gave a product, which was isolated upon usual work up and chromatography and characterized as the 3′-enesulfone **5**. The 5′-O-trityl group from **5** could be easily deprotected in boiling 80% aqueous acetic acid for 10 min to provide the 5′-hydroxy-3′-enesulfone **6** in ca. 90% yield upon an usual column chromatographic purification step.

Preparation of N^6,N^6-dibenzoyl-5′-O-(4-methoxytrityl)-3′-enesulfone derivative of adenosine (18) : The key intermediate, 2′,3′-O-anhydroadenosine **13**[30] was opened up by a nucleophilic attack with 4-toluenethiolate in hot methanol to give 3′-O-tolylthio derivative **14** as the major product. Compound **14** was first trimethylsilylated (TMS-Cl in dry pyridine) followed by benzoylation and a hydrolysis step to give compound **15** in 70 % overall yield. Compound **15** was oxidized by m-chloroperbenzoic acid in dichloromethane to give the corresponding 3′-*xylo*-toluenesulfonyl derivative **16** in 93% yield. The 5′-hydroxy group of the sulfone **16** was subsequently protected with 4-methoxytrityl [MMTr] group to give **17** in 92% yield. The 5′-protected sulfone **17** was then treated with mesyl chloride in pyridine solution at 0 - 4 °C for 24 h. The product that was formed was isolated in 81% yield and was characterized to be 5′-protected-3′-enesulfone **18.** Clearly, the mesylation of C-2′ hydroxyl functions of **4** and **17** gave the corresponding 2′-O-mesylates as the intermediate which underwent instanteneous base catalyzed cis-β-elimination to give the 3′-enesulfones **5** and **18.**

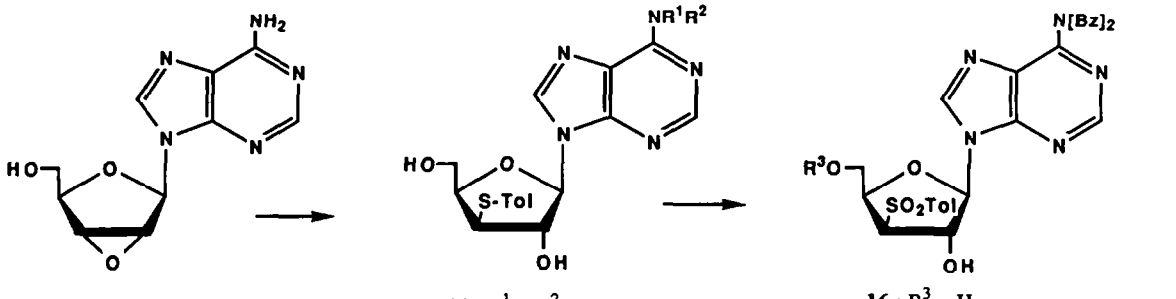
Nucleophilc addition reaction (Michael reaction) to the 3′-enesulfones [5, 6 & 18] : Nucleophilc addition reaction to the electron-deficient double bond constitute the main chemistry of α,β-unsaturated sulfones. An extensive series of papers describing such nucleophilic additions of amines, thiolates, alkoxides etc. has been published[58-69]. The trans-addition process giving the cis-adduct is the most commonly encountered pathway in allenic-[60], propargyllic-[60] and α,β–enesulfones[60]. The mechanism of the stereochemical pathways of addition of a nucleophile such as p-toluenesulfide to 1-p-tolylsulfonylcyclohexene[62] is opposite to that in the 1-p-tolylsulfonylcyclopentene[63]. While, in the former[62], the stereoselective Michael reaction gives the thermodynamically less stable cis-adduct upon a trans-addition process, but, in the latter[63], it is the steric strain in the cis-cyclopentyl system that dictates a cis-addition process to produce the trans-adduct. Reaction of methylamine with **5** at RT gave a 5:1 mixture of trans- and cis-adducts [**7b** + **9b**]; the latter reaction at 50 °C, however, produced a 1:2 mixture of **7b** and **9b**, respectively. Reaction of **5** with nitromethane, under the influence of a base, gave corresponding trans-isomer **7k** as the major product and the cis-isomer **9k** as the minor product in 11:1 ratio. The reaction of **5** with benzylamine at 20 °C was completely stereospecific giving only the trans-adduct **7d**. Similarly, the reactions of **5** with aqueous dimethylamine, pyrrolidine, piperidine, morpholine and glycine methyl ester at 20 °C gave the corresponding trans-adducts [**7c,e-i**] as the sole product in moderate to high yields. The reaction of **5** in aqueous ammonia has been studied at different temperatures in order to investigate the relative stabilities of the intermediates **27** and **28**. It turned out that at 20 °C, a 2:1 mixture of trans- versus cis-adduct, **7a** & **9a** respectively, was isolated; on the other hand, the reaction at 0 °C produced a 12:1 mixture while at 75 °C, the distribution of trans- versus cis-product were respectively 2:3. This shows that the trans-addition process giving the cis-adduct is prefered at a higher temperature while the cis-addition process to give the trans-adduct is clearly prefered at a lower temperature. The temperature-dependent formation of cis- versus trans-adduct was of considerable help in the isolation of pure diastereomer **7j** formed in the conjugate addition reaction of the malonate ion with compond **5**. In this particular reaction, both diastereomers (*ribo* & *xylo*) were formed at RT which had almost identical chromatographic properties and consequently caused considerable separation problems in our attempts to isolate a pure diastereomer. It turned out that we could easily circumvent this separation problem by performing the reaction at 0 °C when the pure trans-adduct **7j** was only formed which was isolated in 66% yield. Reaction of pyrrolidin-1-yl-cyclohexene with the enesulfone **5**, upon a hydrolytic work up, gave the C-3′ distereospecific trans-adducts **7i(R)** and **7i(S)**. ^{1}H-NMR data clearly showed that the products **7i(R)** and **7i(S)** were formed due to the assymmetric cyclohexyl-carbon. The stereochemical configurations of the cyclohexyl-carbons in **7i(R)** and **7i(S)** were assigned tentatively basing on the characteristic diamagnetic anisotropic effect of the cyclohexyl-keto function (at the C-2′) on either H-1′ or H-2′. Thus in one of the of the diastereomers **7i(S)**, the H-1′ [δ 6.24] was more deshielded and H-2′ [δ 2.55] was more shielded than the corresponding protons in the other diastereomer [δ



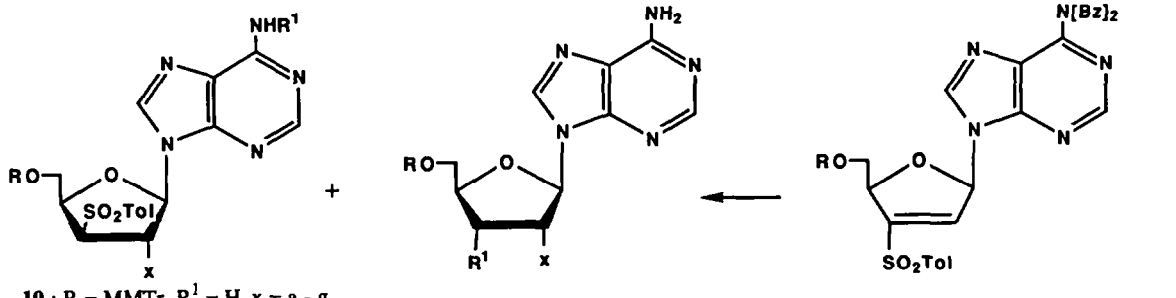
1 3 4 5 : R = Tr 6 : R = H



7 : R = Tr, x = a - k
8 : R = H, x = a - k
9 : R = Tr, x = a,b,k
10 : R = H, x = a,b,k
11 : R = Tr, x = a - g
12 : R = H, x = a - g

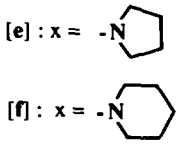


13
14 : $R^1 = R^2 = H$
15 : $R^1 = R^2 = Bz$
16 : $R^3 = H$
17 : $R^3 = MMTr$



18 : R = MMTr
19 : R = MMTr, R^1 = H, x = a - g
20 : R = MMTr, R^1 = COPh, x = j
21 : R = H , R^1 = H, x = a - g
22 : R = H, R^1 = COPh, x = j
23 : R = MMTr, R^1 = H, x = OH
24 : R = MMTr, $R^1 = SO_2Tol$, x = a, b, c
25 : R = H, $R^1 = SO_2Tol$, x = a, b, c
26 : R = MMTr, R^1 = H, x = a, f, g

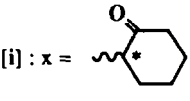
[a] : x = $-NH_2$;
[b] : x = $-NHCH_3$;
[c] : x = $-N(CH_3)_2$;
[d] : x = $-NHCH_2Ph$;



[e] : x =
[f] : x =

[g] : x =

[h] : x = $-NHCH_2CO_2CH_3$



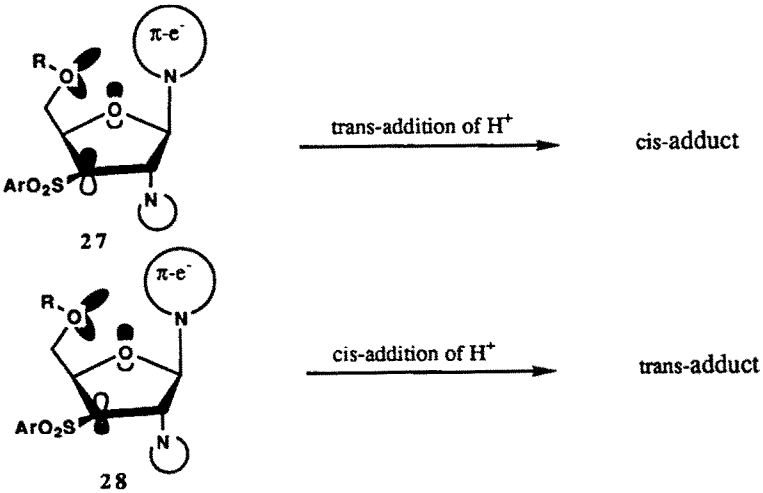
[i] : x =

[j] : x = $-CH(CO_2CH_3)_2$
[k] : x = $-CH_2NO_2$

H-1′ : 6.06 & δ H-2′ : 2.74]. Such characteristic changes in chemical shifts suggests the stereochemical proximity of the cyclohexyl-carbonyl group either to H-1′ or H-2′ due to the S or R configuration of the chiral cyclohexyl-carbon at C-2′. Upon these considerations[64,65] and the inspection of a molecular model, the S configuration is tentatively proposed for cyclohexyl-carbon at C-2′ for **7i(S)** and R configuration for **7i(R)**. Clearly, more specific experiments are required in order to assign the above configurations unambiguously. Treatment of compound **18** with aq. ammonia, aq. methylamine, aq. dimethylamine at 50 °C afforded a mixture of cis and trans isomers. In case of amino-adducts [**19a** & **24a**] and dimethylamino-adducts [**19c** & **24c**] the ratios of isomers are ca. 1:1, for methylamino-adducts [**19b** & **24b**], the ratio is ca. 1:4 respectively. Benzylamine, pyrrolidine, piperidine and morpholine reacted with the substrate **18** to give only trans-isomers [**19d-g**]. During the course of these latter reactions partial debenzoylation of the aglycone took place and complete debenzoylation was achieved by heating the reaction mixtures at ca. 50 °C. Dimethylmalonate anion reacted smoothly with the substrate **18** to give the monobenzoylated trans-isomer **20j**. Since it was not possible to obtain **20j** in a pure form, it was detritylated to give pure **22j** in 74% overall yield from **18**. Attempted reactions with nitromethane, pyrrolidin-1-cyclohexene and glycine methyl ester gave inseparable mixtures in each case. Aqeous 0.1 M sodium hydroxide was found to react with the purine-enesulfone **18**. Surprisingly, under an identical reaction condition, the pyrimidine-enesulfone **5** was completely unreactive. The major product isolated in the reaction of **18** with aq. NaOH, followed by an aqeous ammonia treatment, was identified as to be **23** (48 %) by comparison (NMR) with an authentic sample prepared by the debenzoylation of compound **17**.

Stereochemical course and the distribution of the cis- versus trans-adducts [**8a-d** versus **10a-b**] in the conjugate addition of aq. ammonia, aq. methylamine, aq. dimethylamine, benzylamine and carbanion of nitromethane to the 5′-hydroxy-3′-ene- sulfone **6** was almost identical to the products [**7a-d** versus **9a-b**] obtained in the corresponding reactions with the 5′-O-protected-3′-enesulfone **5**. These suggest the the bulky 5′-O-trityl group in **5** did not have any steric control on the diastereoselective nucleophilc conjugate addition reactions.

The mechanism and steric course of nucleophilc addition reaction to a α,β-unsaturated sulfones such as **5**, **6** or **18** is, as expected, substantially controlled by the relative thermodynamic stabilities of transition states **27** and **28** due to the steric and electronic environment around the planar α-sulfone carbanion[70-74]: [A] steric effect due to the bulk of the 2′-substituent[63], and [B] stereoelectronic influence by (i) the polarization of the p orbital of the chiral planar C-3′ carbanion because of the assymmetric orientation of the sulfone-oxygens[70-74], (ii) electronic repulsions between non-donating $O^{4'}$-oxygen-lone pair on the β-face [the donating lone-pair being antiperiplanar with respect to the glycosidic bond by anomeric effect] and the planar α-sulfone carbanion at C-3′, (iii) electronic repulsion between $O^{5'}$-lone pairs and the C-3′carbanion, and (iv) electronic repulsion between π–electrons of the aglycone and the carbanion. Presumably, the formation of a chiral anion at C-3′ would be favoured in a steric orientation in which its p orbital is polarized [δ^-] on the α-side in order to minimize any of the above cooperative steric and electronic interactions through the space. Thus the above electronic repulsions would polarize the p-lobes of the C-3′ carbanion as shown in structure **28** rather than in an unfavoured form shown in **27** [the dark lobes represent δ^-]. Apparently, the reason for obtaining the cis-adducts in the reactions of ammonia and methylamine with the 3′-enesulfones **5** and **18** is perhaps due to the destabilization of the C-3′ carbanion, as shown in **28**, by the electronic repulsion between the lone-pair of relatively unhindered, free-rotating C-2′ amino and methylamino substituents and the C-3′ carbanion. The lone-pair of more bulky C-2′amino-substituents, such as benzylamino, piperdino, pyrrolidino, morpholino, is presumably apart from the C-3′ carbanion in **28** and, therefore, do not contribute effectively to its destabilization. This effect is cooperative with the steric bulk of the 2′-substituent and the 3′-sulfone group. It should be however noted that above rational does not explain the following observations: (1) reaction of dimethylamine with the 3′-enesulfone **5** at 50 °C gave only the trans-adduct but with **18** produced a 1:1 mixture of cis- and trans-adducts; (2) reaction of conjugate base of nitromethane with **5** produced a 1:10 mixture of cis-



and trans-adducts; (3) reaction of **18** with sodium dimethylmalonate gave only trans-adduct while with **5** produced a 1:5 mixture of cis- and trans-adducts. Clearly, there are other steric and electronic factors that also play important roles in the final distribution of cis- versus trans-aducts. The assymmetric environment, owing to the stereochemical configuration of C-1′ and C-4′, should render the diastereotopic olefin faces of the vinyl groups in **5, 6** and **18** electronically dissimilar leading to a bias for nucleophilic addition at C-2′ one to the other. Unequivocal spectroscopic characterization (*vide infra*) however has established that the stereochemical course of the nucleophilic attack at C-2′ is always from the less sterically and electronically demanding α-face of the pento-enefuranosyl ring. This is presumably due to the steric and electronic hindrance on the β-face from the π-electron rich bulky aglycone and the $O^{4'}$ and $O^{5'}$ lone-pairs. Such diastereospecific nucleophilic attacks from the α-face have been also observed during the reduction of the 2′-keto function of appropriately protected 2′-ketonucleosides by the hydride ion generated from $NaBH_4$ [78] or $Li(Et)_3BH$[80]. Ueda et al. has also doccumented such stereoselective α-attack by other soft carbon-nucleo-philes[44-47], except one example[42,43].

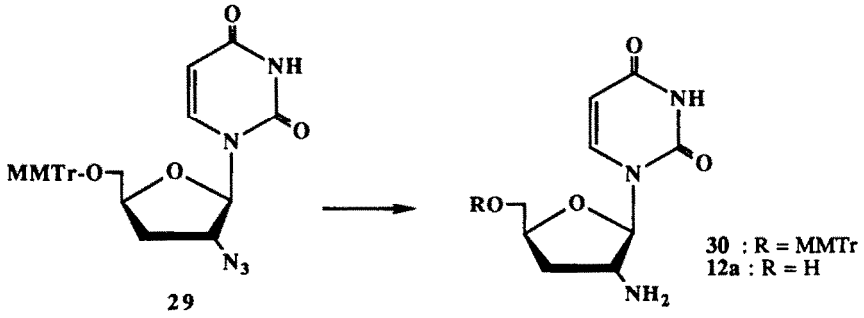
Distinction between cis- versus trans-adducts owing to their respective R and S configuration at C-3′ was conveniently achieved, both in pyrimidine and purine nucleoside derivatives, on the basis of following observations by ^{1}H-NMR spectroscopy: (1) One of the 5′-methylene protons (H-5′ or H-5") was more shielded than the other in the cis-adducts, and, as a result, the methylene protons were well separated. On the other hand the "upfield" H-5′ or H-5" absorption observed in the cis-adducts were found to be deshielded by ~0.5 - 0.8 ppm, along with a further deshielding (~0.2 ppm) of the "downfield" 5′-methylene proton in the trans-adducts, as compared to the cis-adducts, due to the magnetic anisotropy of the arenesulfonyl or benzylsulfonyl group in the *xylo*-configuration. (2) Owing to the trans- (*xylo*) orientation of the sulfonyl group, the H-5 proton in the pyrimidine nucleosides and both H-8 and H-2 protons in purine nucleosides were more downfield than the corresponding cis-adduct. (3) In the cis-adducts (*ribo*), the H-1′ was always more deshielded than the corresponding trans-adducts (*xylo*) owing to the diamagnetic anisotropy by the sulfonyl group (note that both H-1′ and the C-3′ sulfonyl group are on the α-face in the cis-adducts). (4) The $J_{1',2'}$ of the trans-adducts were always smaller (0.4 - 2 Hz) than the the corresponding coupling constant in the cis-adducts. It follows from the above observations that as a result of specific difference in configuration of the sulfonyl group (R versus S) at C-3′, one observes a specific shielding or deshielding patterns for H-5, H-8, H-2, H-5′, H-5" and H-1′ in all purine and pyrimidine nucleosides studied. Thus $\Delta\delta$[(H-1′) - (H-5)] and $\Delta\delta$[(H-6) - (H-5)] in trans-adducts of pyrimidine nucleosides are smaller than the corresponding cis-adducts. The $\Delta\delta^*$[(H-8) - (H-1′)] and $\Delta\delta^{\#}$[(H-2) - (H-1′)] and particularly the sum of $\Delta\delta^*$ & $\Delta\delta^{\#}$ in the trans-adducts of purine nucleosides have been found to be larger than in the corresponding cis-adducts. Similarly, the $\Delta\delta$[(H-5′) - (H-5")] are larger in the cis-adducts than in the corresponding trans-adducts in all pyrimidine and purine nucleosides studied in this work.

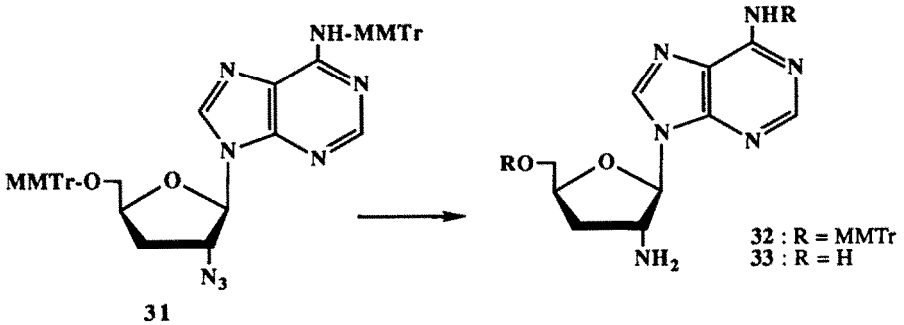
Deprotection of the 5′-acid labile protecting group from pure diastereomers 7, 9, 19 & 24 : The 5′-O-trityl group from **7g - 7i** could be easily removed by a brief treatment in boiling 80 % aqueous acetic acid (10 min) to give the corresponding 5′-hydroxy derivatives **8g - 8i** in 70 - 90% yields. However upon an identical treatment to compounds **7a - 7f** under the above deprotection condition the 5′-hydroxy-3′-enesulfone **6** was recovered as a major product (ca. 80%). Clearly, a β-elimination of the 2′-amine-protonated species of **7a - 7f,** in conjunction with the deprotection of the 5′-O-trityl group, took place. Deprotection of the 5′-trityl group from **7e** and **7f** in 80% aq. acetic acid at 20 °C took 2 days for completion and gave the 5′-hydroxy derivatives **8e** and **8f** in ca. 70% yield. In our search for an optimum condition for deprtotection of the 5′-O-trityl group, we subjected compounds **7a, 7e, 7f** and **7j** to the treatments of 2% trifluoroacetic acid in dichloromethane solution at 0 °C ; under this condition the 5′-O-trityl group could be cleanly and selectively removed in a shorter reaction time (ca. 4 h) giving pure products **8a, 8e, 8f** and **8j** in good yields. Compounds **19a-g** and **24a-c** were deprotected with 80% aqueous acetic acid (9-12 h at 20 °C) to give compounds **21a-g** and **25a-c**, respectively, in moderate to good yields.

Desulfonation at C-3′ : Finally, the 3′-tolylsulfonyl group from isomeric mixture **[7a-b + 9a-b]** and pure isomers **[7c-g]** were removed by 6% Na-Hg in dry methanol[75] at RT to give 5′-O-trityl-2′,3′-dideoxy-2′-substituted nucleosides **11** in ca. 30% yield. The poor yields in the above desulfonation reactions is both due to competing elimination to give 2′,3′-dideoxy-β–D-glyceropentofuranosyl uridine and also due to cleavage of the glycosidic bond. Attempted desulfonation of some of the adenosine derivatives **[19a + 24a, 19f & 19g]** afforded the desired compounds **26a, 26f** and **26g** respectively in very poor yields. Two different reaction conditions, magnesium-methanol (50 °C, overnight)[77] and 6% Na-Hg in methanol (0 °C, ca. 1.5 - 3 h)[75], were employed for this purpose. Thus the treatment of a mixture of compounds **19a** and **24a** with Mg-MeOH or Na-Hg gave compound **26a** in 14 and 23% yields respectively. Compound **19f** could be converted to compound **26f** in 17% yield with Na-Hg. The Mg-MeOH promoted desulfonation afforded compound **26g** from **19g** in only 13% yield. Compound **11a-g** have been subsequently deprotected by boiling in 80% aq. acetic acid for 10 min to give compounds **12a-g** in ca. 90% yields. The 5′-O-MMTr group of compound **26a** was deprotected by 80% aq. acetic acid at 20 °C to give compound **33** in order to compare its spectral data with that of an authentic specimen prepared by an independent route (*vide infra*).

Evidence for the stereochemistry at C-2′ : That the addition of ammonia took place stereospecifically from the α-face of the 3′-enesulfones **5** and **18** were unequivocally established by comparing the C-2′ammonium acetate of **12a** and compound

33 with the authentic products obtained by independent syntheses [see experimental section for details]. An attempt to carry out a free radical deoxygenation reaction[79] on 1-(5′-O-monomethoxytrityl-3′-O-phenylthiocarbonyl-2′-deoxy-2′-azido)uracil was not successful in our hand. We then turned our attention to the elegant reaction designed by Kawana et al. involving a 3′-deoxygenative [1,2] hydride shift for the preparation of appropriately protected 3′-deoxy-2′-*threo* derivatives of adenosine[55]





and cytidine[56]. Using this procedure, authentic 2′,3′-dideoxy-2′-ammonium acetate of uridine **12a** [**29** → **30** → **12a**] and compound **33** [**31** → **32** → **33**] were prepared which were found to be spectroscopically (^{13}C- & ^{1}H-NMR) and chromatographically identical to the products obtained through Michael addition reactions.

Assessment of the configurations at the C-2' and C-3' by conformational analysis using ^{1}H-NMR spectroscopy : Beside the evidences presented above on the configurations of the 2'- and 3'-carbons (*i.e.* the 2' substituent is on the α–face ["down"] while the sulfone group is either *threo* ("up") or *erythro* ("down") at the 3′-position leading to two diastereomers), we have confirmed these assignments by an independent method. We reasoned that since the vicinal couplings of the sugar moiety (*i.e.* $^{3}J_{1',2'}$, $^{3}J_{2',3'}$ and $^{3}J_{3',4'}$) are interdependent on the conformation of the pentose ring it should be possible to assess if a given sugar with given J coupling constants is either in an *arabino-*, *ribo-*, *lyxo-* or *xylo* configuration[81]. Altona et al. have developed the concept of pseudorotation[82-84] where the sugar conformation can be well defined by the puckering amplitude ν_m and the phase angle of pseudorotation (P). The conformation is then described as an equilibrium between *two* conformers N (C2'-*exo* / C3'-*endo*) and S (C2'-*endo* / C3'-*exo*) with a respective value of ν_m and P[82,83]. A program has also been written (PSEUROT) which allows the calculation of the percentage of N (or S) conformers, P_N, P_S, ν_{mN}, ν_{mS}, (where ν_{mN} and ν_{mS} stand for the puckering amplitude of the conformers N and S respectively, and P_N and P_S stand for the phase amplitude of the conformers N and S respectively) from the coupling constants[85]. Clearly, the goal of our investigation is to determine the model which gives the best fit for a low root mean square (r.m.s) with our compounds assuming a usual conformational state. An examination of the conformation around the C-4' and C-5' bond can also throw some light on the configuration at the 3'-position[85-90,39,41]. Different conformational analysis of (modified) nucleosides have shown that the percentage of γ+ population is directly influenced by the position and the nature of the substituent on C-3'[87-89,39,41]. Thus when a methyl group is linked to C-3' the amount of γ+ population is very high (>50%) because of the preferred equatorial position of the methyl group ("up" or "down")[39,41,88]. On the other hand, an electronegative substituent at C-3' (such as OH, N3) has a drastic effect on γ+ population according to its configuration ("up" or "down")[7,9,87,89]. Accordingly, when the electronegative substituent is "down" the γ+ is still high (>50%) while in the "up" configuration the percentage of γ+ is found to be lower than 30% (γ_t is, in this case, usually high, ~45%). This is true in both purine and in pyrimidine nucleosides. The population of three rotamers about the exocyclic C-4' and C-5' bond is estimated from the J4',5' and J4',5" coupling constants using the method of Haasnoot *et al.*[90]. When the values for J4',5' and J4',5" are not possible

to extract from the apparent spectrum due to overlaps of absorptions or ambigous assignment between 5' and 5" one can use the "sum rule"[90,92] to obtain, the population of p+ in good approximation: $p(\gamma+) = \frac{13.3 - \Sigma}{9.7}$, [where Σ represents ($J_{4',5'} + J_{4',5''}$)]. Consequently, when a pair of C-3' diastereomers was available [C-3´ benzylsulfonyl in **7k** & **9k** instead of C-3´-(4-toluenesulfonyl), detailed spectroscopic data not shown]], the measurement of $P(\gamma+)$ clearly shows that the two isomers correspond to a different configurations of the sulfone group on C-3'. This clearly shows that the C-3' is the isomeric center for the addition reaction accross the double bond. Interestingly, in the pair of diastereomers **7i(S)** and **7i(R)**, which have the epimeric cyclohexanone group as the 2'-substituent, we found a similar γ+ population (23.7 and 24.7%) substantiating our earlier conclusion (*vide supra*) that the isomeric products **7i(S)** and **7i(R)** are most probably due to the additional assymmetric center of the cyclohexyl-carbon which is assumed to be always on the α-face (*vide supra*). Such estimates of γ+ population confirmed that when the above Michael reactions gave only one product, it was the *xylo* sulfone adduct which was formed. The absence of the 5´-O-trityl group in compound **8i(R)** also partly diminshed the γ+ population (11.3%) as compared to the 5´-O tritylated precursor **7i(R)** (γ+ 24.7%).

Once the configuration of the C-3' center has been achieved using the p(γ+) rule, the determination of the configuration of the C-2' can be obtained, as mentioned previously, by a complete conformational analysis of the pentose ring[82-85]. Such a study was performed on a few pairs of products (C-3´-benzylsulfonyl in **7k** & **9k** instead of C-3´-(4-toluenesulfonyl), **7i(S)** & **7i(R)**, **19a** & **24a**). The correction of the electronegativity of the substituents (including the β effect) was performed[82,86]. A "good" fitting is described as a low r.m.s obtained with P and ν_m, for both conformers N and S, lying in the "normal range"[85]. Accordingly, only the *ribo-* and the *xylo*-type gave an r.m.s close to zero, while the r.m.s, with the *lyxo-* or *arabino*-type, was found to be larger than one. Therefore the C-2' substituent should be always on the α-face and the C-3´ sulfone group should be either *threo* or *erythro*.

Independent of the above study, we have also performed NOE experiments. The H-6 or H-8 proton should be much closer to the substituent at the C-2' position when it is in the β-face of the pentofuranose ring and the aglycone is in the *anti* conformation[92]. We chose the pair of compounds [C-3´-benzylsulfonyl in **7k** & **9k** instead of C-3´-(4-toluenesulfonyl)] since it would allow the detection of the enhancement of either H2' or the protons of CH_2NO_2 group depending upon its configuration. An irradiation of H-6 of the uracil moiety showed that it was only H-2' and H-5 which were affected in the above compounds. This clearly confirmed our earlier assignments (*vide supra*) that the configuration of the CH_2NO_2 group at C-2' is indeed *erythro* ("down").

EXPERIMENTAL

^{1}H-NMR spectra were recorded (in δ scale) with Jeol 90 Q and JNM GX 270 spectrometer at 90 and 270 MHz respectively, using TMS (0.0 ppm) or CH_3CN (set at 2.0 ppm in D_2O solutions). ^{13}C-NMR were recorded at 22.5 and 67.9 MHz using both ^{1}H-coupled and ^{1}H-decoupled and INEPT modes. UV absorption spectra were recorded with Varian-Cary 2200 instrument; Jeol DX 303 instrument was used for recording mass spectra. TLC was carried out using Merck pre-coated silica gel F_{254} plates. The column chromatographic separations were carried out using Merck G60 silica gel.

1-(5'-0-trityl-3'-deoxy-3'-(4-toluene)thio-β-D-arabinofuranosyl)uracil (3): To a suspension of sodium methoxide (11.9 g, 220 mmol) in methanol (200 ml) was added to 4-toluenemercaptan (24.8 g, 200 mmol) at 0 °C. After 30 min, compound **1** (7.2g, 15.4 mmol) was added and the mixture was heated under reflux for 20 h. Solvent was removed under vaccum and the residue dissolved in ethyl acetate (300 ml), which was washed two times with aqueous sodium hydroxide (1M, 50 ml each). Organic phase was evaporated to dryness, the syrup was triturated with petroleum ether three times (300 ml each) and then was separated on a silica gel column to give **3** (5.05 g, 55%). ^{1}H-NMR ($CDCl_3$) : 7.99 (d, $J_{5,6}$ = 8.0 Hz, 1H) H-6; 7.31 (m, 19H) arom; 6.07 (d, $J_{1',2'}$ = 5.3 Hz,1H) H-1´; 5.23 (d, 1H) H-5; 4.87 (m, 1H) H-4´; 4.50 (m, 1H) H-2´; 3.72 (m, 3H) H-3´,H-5´ and H-5"; 2.28 (s, 3H) $\underline{CH_3}$Ph. ^{13}C-NMR ($CDCl_3$): 141.9 (d, J_{CH} = 185.3 Hz) C-6; 101.1 (d, J_{CH} = 177.4 Hz) C-5; 85.1 (d, J_{CH} = 170.7 Hz) C-1´; 81.0 (d, J_{CH} = 151.7 Hz) C-4´; 75.5 (d, J_{CH} = 148.2 Hz) C-2´; 62.0 (t, J_{CH} = 143.8 Hz) C-5´; 50.4 (d, J_{CH} = 146.0 Hz) C-3´; 21.0 (q) $\underline{CH_3}$Ph..

1-(5'-0-trityl-3'-deoxy-3'-toluenesulfonyl-β-D-arabinofuranosyl)uracil (4): To a solution of compound **3** (3.1g, 5.24 mmol) in dichloromethane (100 ml) was added m-chloroperbenzoic acid (85%, 3.60 g, 17.7 mmol). Stirring was continued for 2 h. Upon disappearence of the starting material, the mixture was washed with saturated aqueous solution of sodium thiosulfate (100 ml) and then aqueous sodium bicarbonate (100 ml). Organic phase was evaporated and separated on a silica gel column to give **4** (3.25g, 99%) ^{1}H-NMR ($CDCl_3$+CD_3OD): 7.75 (d, $J_{5,6}$ = 8.1 Hz, 1H) H-6; 7.75 and 7.27 (m, 19H) arom; 6.06 (d, $J_{1',2'}$ = 4.8 Hz, 1H) H-1´; 5.32 (d, 1H) H-5; 4.97 (t, $J_{2',3'}$ = 4.8 Hz, 1H) H-2´; 4.47 (m, 1H) H-4´; 3.96 (m, 1H) H-3´; 3.33 (m, 2H) H-5´, H-5"; 2.41 (s, 3H) $\underline{CH_3}$Ph. ^{13}C-NMR ($CDCl_3$+ CD_3OD): 142.0 (d, J_{CH} = 180.8 Hz) C-6; 101.8 (d, J_{CH} = 176.3 Hz) C-5; 85.8 (d, J_{CH} = 169.6 Hz) C-1´; 75.9 (d, J_{CH} = 152.8 Hz) C-4´; 71.4 (d, J_{CH} = 151.6 Hz) C-2´; 69.5 (d, J_{CH} = 149.4 Hz) C-3´; 63.0 (t, J_{CH} = 144.9 Hz) C-5´; 21.5 (q, J_{CH} = 126.5 Hz) $\underline{CH_3}$Ph;

1-(5'-trityl-2',3'-dideoxy-3'-toluenesulfonyl-β-D-glyceropent-2-enofuranosyl)uracil (5): To a solution of compound **4** (3.25 g. 5.21 mmol) in dry pyridine (80 ml) was added methylsulfonyl chloride (1.16 ml, 15 mmol) at 0 °C. The mixture was kept at 0 °C overnight. Water (2 ml) was added and the reaction was heated at 40 °C for 2 h. The cold solution was then poured into a ice cold water with vigorous stirring. Filtered and the solid was washed generouesly with water till free

of pyridine. The mixture was then purified on a silica gel column to give **5**, (2.27g, 72%). ^{1}H-NMR ($CDCl_3$): 7.68 (d, $J_{5,6}$ = 8.1 Hz, 1H) H-6; 7.30 (m, 19H) arom; 7.02 (dd, $J_{1',2'}$ = 1.7 Hz, $J_{1',4'}$ = 3.9 Hz, 1H) H-1'; 6.56 (t, $J_{2',4'}$ = 1.7 Hz, 1H) H-2'; 4.98 (m, 1H) H-4'; 4.59 (d, 1H) H-5; 3.71 (m, 2H) H-5', H-5"; 2.43 (s, 3H) CH_3Ph. ^{13}C- NMR ($CDCl_3$): 140.5 (d, J_{CH} = 186.5 Hz) C-6; 102.5 (d, J_{CH} = 178.5 Hz) C-5; 87.2 (d, J_{CH} = 173.0 Hz) C-1'; 83.9 (d, J_{CH} = 153.9 Hz) C-4'; 62.8 (t, J_{CH} = 142.7 Hz) C-5'; 21.5 (q) CH_3Ph.

Preparations of 7a and 9a: Compound **5** (200 mg, 0.33 mmol) was treated with aqueous ammonia (32%, 10 ml) in dioxane (10 ml) at 50 °C for 2 h. The solution was evaporated and co-evaporated with absolute ethanol to dryness and the residue was separated on a silica gel column to give **7a** (94 mg, 46%) and **9a** (77 mg, 37%). **Compound 7a**: ^{1}H-NMR ($CDCl_3$): 7.63 (d, $J_{5,6}$ = 8.2 Hz, 1H) H-6; 7.31 (m, 19H) arom; 5.77 (d, $J_{1',2'}$ = 5.1 Hz, 1H) H-1'; 5.68 (d, 1H) H-5; 4.59 (m, 1H) H-4'; 3.82-3.61 (m, 4H) H-2', H-3', H-5' and H-5"; 2.41 (s, 3H) CH_3Ph. ^{13}C-NMR ($CDCl_3$): 139.5 (d, J_{CH} = 180.7 Hz) C-6; 102.3 (d, J_{CH} = 175.8 Hz) C-5; 89.7 (d, J_{CH} = 168.4 Hz) C-1', 77.9 (d, J_{CH} = 151.4 Hz) C-4'; 70.6 (d, J_{CH} = 146.2 Hz) C-3'; 62.7 (t, J_{CH} = 149.7 Hz) C-5'; 59.2 (d, J_{CH} = 139.2 Hz) C-2'; 21.5 (q) CH_3Ph. **Compound 9a**: ^{1}H-NMR ($CDCl_3$): 7.66 (d, $J_{5,6}$ = 8.1 Hz, 1H) H-6; 7.32 (m, 19H) arom; 6.08 (d, $J_{1',2'}$ = 5.9 Hz, 1H) H-1'; 5.36 (d, 1H) H-5; 4.55 (m, 1H) H-4'; 3.97 (m, 2H) H-2' and H-3'; 3.49 (2xd, $J_{4',5'}$ = 2.6 Hz, 1H) H-5'; 2.84 (2xd, 1H) H-5"; 2.42 (s, 3H) CH_3Ph. ^{13}C-NMR ($CDCl_3$): 139.7 (d, J_{CH} = 183.5 Hz) C-6; 102.5 (d, J_{CH} = 177.0 Hz) C-5; 90.1 (d, J_{CH} = 166.1 Hz) C-1'; 78.3 (d, J_{CH} = 153.2 Hz) C-4'; 71.3 (d, J_{CH} = 155.0 Hz) C-3'; 63.2 (t, J_{CH} = 144.0 Hz) C-5'; 59.7 (d, J_{CH} = 142.8 Hz) C-2'; 21.5 (q) CH_3Ph. MS (FAB$^-$): calc. for (M-H)$^-$ 622.2012, found 622.1962.

Preparation of 7b and 9b: Compound **5** (606 mg, 1 mmol) was treated with aqueous methylamine (40%, 20 ml) in dioxane (20 ml) at room temperature over night. The solvent was evaporated and co-evaporated with absolute ethanol to dryness and the residue was separated on a silica gel column to give **7b** (394 mg, 62%) and **9b** (84 mg, 13%). **Compound 7b**: ^{1}H-NMR ($CDCl_3$) 7.79 (d, $J_{5,6}$ = 8.1Hz, 1H) H-6; 7.31 (m, 19H) arom; 5.80 (d, 1H) H-5; 5.73 (d, $J_{1',2'}$ = 3.4 Hz, 1H) H-1'; 4.56 (m, 1H) H-4'; 4.00-3.60 (m, 2H) H-5',H-5"; 3.43 (m, 2H) H-2', H-3'; 2.41 (s, 3H) CH_3Ph; 1.93 (s, 3H) NCH_3. ^{13}C-NMR ($CDCl_3$): 140.2 (d, J_{CH} = 183.1 Hz) C-6; 102.3 (d, J_{CH} = 175.8 Hz) C-5; 89.3 (d, J_{CH} = 166.0 Hz) C-1'; 79.2 (d, J_{CH} = 150.2 Hz) C-4'; 68.6 (d, J_{CH} = 141.6 Hz) C-2'; 68.4 (d, J_{CH} = 142.6 Hz) C-3'; 62.7 (t, J_{CH} = 144.0 Hz) C-5'; 33.5 (q) NCH_3; 21.5 (q) CH_3Ph. **Compound 9b**: ^{1}H-NMR ($CDCl_3$): 7.71 (d, $J_{5,6}$ = 8.4 Hz, 1H) H-6; 7.32 (m, 19H) arom; 6.05 (d, $J_{1',2'}$ = 6.6 Hz, 1H) H-1'; 5.30 (d, 1H) H-5; 4.55 (m, 1H) H-4'; 3.85 (m, 1H) H-3'; 3.53 and 3.13 (m, 3H) H-2', H-5' and H-5"; 2.48 and 2.44 (2xs, 6H) CH_3Ph and NCH_3. ^{13}C- NMR ($CDCl_3$): 139.6 (d, J_{CH} = 184.3 Hz) C-6; 102.4 (d, J_{CH} = 178.2 Hz) C-5; 87.5 (d, J_{CH} = 170.9 Hz) C-1'; 77.7 (d, J_{CH} = 151.5 Hz) C-4'; 67.3 (d, J_{CH} = 140.3 Hz) C-2'; 63.5 (t, J_{CH} = 139.1 Hz) C-5'; 63.1 (d, J_{CH} = 145.3 Hz) C-3'; 35.2 (q) NCH_3; 21.6 (q) CH_3Ph.

Preparation of 7c: It was prepared in the same way as discribed for **7b**. Yield (94%). ^{1}H-NMR ($CDCl_3$): 7.92 (d, $J_{5,6}$ = 8.0 Hz, 1H) H-6; 7.33 (m, 19H) arom; 6.17 (d, $J_{1',2'}$ = 4.9 Hz, 1H) H-1'; 5.85 (d, 1H) H-5; 4.02 (m, 2H) H-3' and H-4'; 3.54 (m, 3H) H-2', H-5' and H-5"; 2.41 (s, 3H) CH_3Ph; 2.06 (s, 6H) NMe_2. ^{13}C- NMR ($CDCl_3$): 140.7 (d, J_{CH} = 183.1 Hz) C-6; 103.7 (d, J_{CH} = 177.0 Hz) C-5; 83.1 (d, J_{CH} = 168.2 Hz) C-1'; 78.7 (d, J_{CH} = 151.9 Hz) C-4'; 71.8 (d, J_{CH} = 142.5 Hz) C-2'; 64.2 (d, J_{CH} = 144.1 Hz) C-3'; 62.8 (t, J_{CH} = 140.4 Hz) C-5'; 41.3 (q) NCH_3; 21.5 (q) CH_3Ph;

Preparation of 7d: Compound **5** (280 mg, 0.46 mmol) was treated with benzylamine (1 ml, 20 mmol) in dichloromethane (9 ml) overnight at room temperature, then the mixture was partitioned between dichloromethane (40 ml) and water (20 ml). The organic phase was then washed with water (20 ml), evaporated, and separated on a silica gel column to give **7d**. Yield 96%. ^{1}H-NMR ($CDCl_3$): 7.69 (d, $J_{5,6}$ = 8.2 Hz, 1H) H-6; 7.30 (m, 19H) arom; 5.83 (d, $J_{1',2'}$ = 4.2 Hz, 1H) H-1'; 5.75 (d, 1H) H-5; 4.54 (m, 1H) H-4'; 3.98 (m, 1H) H-3'; 3.55 (m, 3H) H-2',H-5' and H-5"; 3.37 (s, 2H) NCH_2Ph; 2.41 (s, 3H) CH_3Ph. ^{13}C-NMR ($CDCl_3$): 140.2 (d, J_{CH} = 184.3 Hz) C-6; 102.4 (d, J_{CH} = 177.0 Hz) C-5; 89.4 (d, J_{CH} = 168.5 Hz) C-1'; 78.9 (d, J_{CH} = 148.9 Hz) C-4'; 69.5 (d, J_{CH} = 142.8 Hz) C-2'; 66.3 (d, J_{CH} = 144.0 Hz) C-3'; 62.7 (t, J_{CH} = 143.6 Hz) C-5'; 51.0 (t, J_{CH} = 139.8 Hz) NCH_2Ph; 21.5 (q) CH_3Ph.

Preparation of 7e: Compound **5** (300 mg, 0.5 mmol) was treated with pyrrolidine (825 µl, 10 mmol) in tetrahydrofuran (3 ml). The mixture was stirred for 1 h when all starting material disappeared. All volatile materials were evaporated and co-evaporated with toluene till dryness. Then the mixture was separated on a silica gel column to give **7e** (330 mg, 97%). ^{1}H-NMR ($CDCl_3$): 9.68 (br., 1H) NH; 7.96 (d, $J_{5,6}$ = 8.1 Hz, 1H) H-6; 7.32 (m, 19H) arom; 6.22 (d, $J_{1',2'}$ = 5.4 Hz, 1H) H-1'; 5.85 (d, 1H) H-5; 4.29 (m, $J_{3',4'}$ = 6.1 Hz, $J_{4',5'}$ = 7.3 Hz, $J_{4',5"}$= 1.7 Hz, 1H) H-4'; 3.54 (m, 2H) H-2', H-3'; 2.40 (s, 3H) CH_3Ph; 2.32 (br., 4H) NCH_2; 1.65 (br., 4H) NCH_2CH_2; ^{13}C-NMR ($CDCl_3$): 140.9 (d J_{CH} = 181.2 Hz) C-6; 103.5 (d, J_{CH} = 178.2 Hz) C-5; 87.0 (s) Ph_3C; 85.0 (d, J_{CH} = 167.2 Hz) C-1'; ; 78.3 (d, J_{CH} = 144.0 Hz) C-4'; 69.3 (d, J_{CH} = 141.6 Hz) C-2'; 66.5 (d, J_{CH} = 144.0 Hz) C-3'; 62.5 (t, J_{CH} = 140.0 Hz) C-5'; 50.4 (t, J_{CH} = 140.4 Hz) NCH_2; 22.8 (t) NCH_2CH_2; 21.4 (q, J_{CH} = 134.8 Hz) $PhCH_3$.

Preparation of 7f: Compound **5** (400 mg, 0.66 mmol) was treated with piperidine (1.3 ml, 13.2 mmol) in tetrahydrofurane (6 ml) at room temperature for 5 h. All volatile materials were evaporated and co-evaporated with toluene to dryness. Then the mixture was separated on a silica gel column to give **7f** (yield 445 mg, 98%). ^{1}H-NMR: 9.53 (br.1H) NH; 7.85 (d, $J_{5,6}$ = 8.1 Hz, 1H) H-6; 7.30 (m, 19H) arom.; 6.22 (d, $J_{1',2'}$ = 5.4 Hz, 1H) H-1'; 4.14 (m, 1H) H-4'; 3.97 (m, 1H) H-5'; 3.57 (m, 2H) H-2', H-3', 3.48 (m, 1H) H-5"; 2.41 (s,3H) CH_3Ph; 2.23 (br.4H) NCH_2; 1.32 (br.6H) $NHCH_2CH_2CH_2$ ^{13}C-NMR ($CDCl_3$): 140.5 (d,J_{CH} = 185.3 Hz) C-6: 103.5 (d, J_{CH} = 178.3 Hz) C-5: 87.1 (s) Ph_3C: 82.0 (d, J_{CH} =167.3 Hz) C-1'; 78.4 (d, J_{CH} = 146.5 Hz) C-4 '; 72.3 (d, J_{CH} = 139.1 Hz) C-2'; 64,4 (d, J_{CH} = 144.0 Hz) C-3', 62.6 (t, J_{CH} = 141.6 Hz) C-5'; 50.3, 25.6, 23.6, for piperidinyl; 21,4 (s) $PhCH_3$.

Preparation of 7g: Compound **5** (400 mg, 0.66 mmol) was treated with morpholine (1.15 ml, 13.2 mmol) in tetrahydrofurane (6 ml) at room temperature overnight. All volatile materials were evaporated and co-evaporated with toluene to dryness. The mixture was then separated on a silica gel column to give **7g** (450 mg, 98%). ^{1}H-NMR ($CDCl_3$):9.53 (br.1H) NH; 7.85 (d, $J_{5,6}$ = 8.3 Hz, 1H) H-6; 7.31 (m,19H) arom.; 6.20 (d, $J_{1',2'}$ = 5.1 Hz, 1H) H-1'; 5.85 (d,1H) H-5; 4.04 (m,1H) H-4'; 3.97 (m,1H) H-5'; 3.55 (m, 7H) H-2', H-3', H-5'' and OCH_2; 2.41 (s, 3H) CH_3Ph; 2.35 (br,4H) NCH_2; ^{13}C-NMR ($CDCl_3$): 140.0 (d, J_{CH} = 189.8 Hz) C-6; 103.8 (d, J_{CH} = 176.7 Hz) C-5; 87.2 (s) Ph_3C; 82.7 (d, J_{CH} = 171.9 Hz) C-1'; 78.5 (d, J_{CH} = 152.8 Hz) C-4'; 71.6 (d, J_{CH} = 139.3 Hz) C-2'; 63.8 (d, J_{CH} = 143.1 Hz) C-3'; 66.3 (t, J_{CH} = 144.2 Hz) OCH_2; 62.6 (t, J_{CH} = 142.6Hz) C-5'; 49.7 (t) NCH_2; 21.4 (q) $PhCH_3$.

Preparation of 7h: The mixture of compound **5** (760 mg, 1.25 mmol), methyl glycinate hydrochloride (1.56 g, 12.5 mmol) and 1.8-diazabicyclo[5.4.0]undec-7-ene (DBU) (1.9 ml, 12.5 mmol) in dry dimethylsulfoxide (10 ml) was

stirred under argon at room temperature overnight. The reaction mixture was partitioned between ethyl acetate (60 ml) and water (30 ml). The aqueous phase was then extracted with ethyl acetate (3 x 40 ml). The combined organic phase was washed with water (2 x 20 ml), organic phase was dried and evaporated to dryness. The mixture was then purified on a silica gel column to give **7h** (510 mg, 59%). ^{1}H-NMR ($CDCl_3$): 9.41 (br, 1H) NH; 7.68 (d, $J_{5,6}$ = 8.5 Hz, 1H) H-6; 7.32 (m,19H) arom.; 5.84 (d, $J_{1',2'}$ = 4.5 Hz, 1H) H-1'; 5.82 (d, 1H) H-5; 4.50 (m, $J_{4',5'}$ = 9.0 Hz, $J_{4',5''}$ = 1.7 Hz,1H) H-4'; 3.82 (dd, $J_{5',5''}$ = 10.2 Hz, 1H) H-5'; 3.72 (m, 2H) H-2',H-3'; 3.60 (s, 3H) CO_2CH_3; 3.40 (dd, 1H) H-5"; 3.10 (dd, Jgem = 18.1 Hz, 2H) CH_2CO_2Me; 2.40 (s, 3H) CH_3Ph; ^{13}C-NMR ($CDCl_3$) : 172.0 (s) CO_2R; 140.0 (d, J_{CH} = 185.1 Hz) C-6; 102.8 (d, J_{CH} = 175.8 Hz) C-5; 88.5 (d, J_{CH} = 167.2 Hz) C-1'; 87.1 (s) Ph_3C; 78.6 (d, J_{CH} = 149.2 Hz) C-4'; 70.0 (d, J_{CH} = 144.1 Hz) C-2'; 66.0 (d, J_{CH} = 148.9 Hz) C-3'; 62.5 (t, J_{CH} = 144.0 Hz) C-5'; 51.7 (q, J_{CH} = 147.7 Hz) CO_2CH_3; 47.7 (t, J_{CH} = 136.8 Hz) CH_2CO_2Me; 21.5 (q) CH_3Ph.

Preparation of 7i(R) and 7i(S): To a solution of compound **5** (600 mg, 0.99 mmol) in dry tetrahydrofuran (5 ml) was added fresh distilled pyrrolidin-1-cyclohexene (1.5 g, 10 mmol) under argon. The mixture was stirred at room temperature for 3 h and then was heated at reflux for 1 h. Water (2 ml) was added to the mixture and which was kept at reflux for another hour. All volatile materials were evaporated and co-evaporated with toluene to dryness. The residue was separated on a silica gel column to give **7i(R)** (276 mg, 39%) and **7i(S)** (236 mg, 34%). **Compound 7i(R):** ^{1}H-NMR ($CDCl_3$): 9.16 (br., 1H) NH; 7.79 (d, $J_{5,6}$ = 8.1 Hz, 1H) H-6; 7.32 (m, 19H) arom.; 6.06 (d, $J_{1',2'}$ = 5.7 Hz, 1H) H-1'; 5.84 (d, 1H) H-5; 4.81 (m, $J_{3',4'}$ = 6.6 Hz, $J_{4',5'}$ = 10.3 Hz, $J_{4',5''}$ = 2.1 Hz, 1H) H-4'; 3.91 (dd, $J_{5',5''}$ = 11.0 Hz, 1H) H-5'; 3.58 (dd, $J_{2',3'}$ = 4.4 Hz, 1H) H-3'; 3.29 (dd, 1H) H-5"; 2.74 (m, 2H) H-2',-CHC=O; 2.41 (s, 3H) CH_3Ph; 2.40-1.25 (m, 8H) $COCH_2CH_2CH_2CH_2$; ^{13}C-NMR ($CDCl_3$) :211.1 (s) -CO-; 140.2 (d, J_{CH} = 187.1 Hz) C-6; 103.1 (d, J_{CH} = 178.2 Hz) C-5; 86.9 (s) Ph_3C; 85.0 (d, J_{CH} = 168.5 Hz) C-1'; 79.3 (d, J_{CH} = 147.7 Hz) C-4'; 66.9 (d, J_{CH} = 145.2 Hz) C-3'; 50.9 (d, J_{CH} = 126.1 Hz) HCC=O; 48.0 (d, J_{CH} = 133.0 Hz) C-2'; 41.8, 31.0, 26.8 and 24.6 for $COCH_2CH_2$ CH_2CH_2; 21.5 (q) CH_3Ph; **Compound 7i(S):** ^{1}H-NMR ($CDCl_3$): 9.15 (br, 1H) NH; 7.81 (d, $J_{5,6}$ = 8.0 Hz, 1H) H-6; 7.30 (m, 19H) arom; 6.24 (d, $J_{1',2'}$ = 6.6 Hz, 1H) H-1'; 5.84 (d,1H) H-5; 4.76 (m, $J_{3',4'}$ = 7.1 Hz, $J_{4',5'}$ = 9.5 Hz, $J_{4',5''}$ = 2.2 Hz, 1H) H-4'; 3.85 (dd, Jgem = 11.0 Hz, 1H) H-5'; 3.59 (dd, $J_{2',3'}$ = 4.9 Hz, 1H) H-3'; 3.22 (dd, 1H) H-5"; 2.55 (m, 1H) H-2'; 2.41 (s, 3H) CH_3Ph; 2.50-1.25 (m, 9H) for cyclohexanonyl ; ^{13}C-NMR ($CDCl_3$): 211.5 (s) -CO- ; 140.6 (d, J_{CH} = 179.7 Hz) C-6; 103.6 (d, J_{CH} = 179.7 Hz) C-5; 86.9 (s) Ph_3C; 84.1 (d, J_{CH} = 170.7 Hz) C-1'; 78.3 (d, J_{CH} = 150.5 Hz) C-4'; 68.3 (d, J_{CH} = 140.4 Hz) C-3', 62.7 (t, J_{CH} = 143.8 Hz) C-5'; 51.5 (d, J_{CH} = 128.0 Hz) HCCO-; 48.1 (d, J_{CH} = 128.0 Hz) C-2'; 42.1, 31.7, 26.8, and 25.2 for $COCH_2CH_2CH_2CH_2$; 21.4 (q) CH_3Ph.

Preparation of 7j: To a suspension of sodium hydride (80% in mineral oil, 150 mg, 5 mmol) in dry tetrahydrofuran (8 ml) was added dimethyl malonate (650 mg, 2 mmol) slowly under argon. After stirring for 20 min, compound **5** (606 mg, 1 mmol) in tetrahydrofuran (3 ml) was added. The mixture was stirred at 0 °C for 48 h and then poured into a saturated aqueous solution of ammonium chloride (30 ml). It was extracted with dichloromethane (3 x 30 ml) and the organic phase was evaporated. The residue was separated on a silica gel column to give **7j**. Yield 66 %. ^{1}H-NMR ($CDCl_3$): 7.74 (d, $J_{5,6}$ = 8.4 Hz, 1H) H-6; 7.30 (m, 19H) arom; 6.15 (d, $J_{1',2'}$ = 6.5 Hz, 1H) H-1'; 5.85 (d, 1H) H-5; 4.59 (m, 1H) H-4'; 4.10 (m, 1H) H-3'; 3.84 (m, 2H) H-5', H-5"; 3.73 (s, 6H) OCH_3; 3.23 (m, 2H) H-2' and -$CHCO_2Me$; 2.39 (s, 3H) CH_3Ph. ^{13}C NMR ($CDCl_3$): 139.9 (d, J_{CH} = 181.9 Hz) C-6; 103.4 (d, J_{CH} = 175.8 Hz) C-5; 85.0 (d, J_{CH} = 167.3 Hz) C-1'; 79.0 (d, J_{CH} = 153.8 Hz) C-4'; 66.2 (d, J_{CH} = 145.2 Hz) C-3'; 63.0 (t, J_{CH} = 147.7 Hz) C-5'; 53.1 (q, J_{CH} = 141.6 Hz) OCH_3; 50.8 (d, J_{CH} = 133.1 Hz) $CHCO_2Me$; 45.9 (d, J_{CH} = 147.6 Hz) C-2'; 21.5 (q) CH_3Ph.

Preparation of 7k and 9k: To a suspension of potassium tert-butoxide (248 mg, 2.1 mmol) in nitromethane (15 ml) was added compound **5** (635 mg, 1.05 mmol) and the mixture was stirred overnight at room temperature. The mixture was poured into saturated aqueous solution of ammonium chloride (30 ml), which was extracted with ethyl acetate (3 x 30 ml). Organic phase was evaporated and separated on a silica gel column to give **7k** and **9k**. **Compound 7k** (64 %): ^{1}H-NMR ($CDCl_3$): 7.73 (d, $J_{5,6}$ = 8.3 Hz, 1H) H-6; 7.30 (m, 19H) arom; 6.00 (d, $J_{1',2'}$= 5.3 Hz, 1H) H-1'; 5.81 (d, 1H) H-5; 4.51 (d, 2H) CH_2NO_2; 4.35 (m, 1H) H-4'; 4.01-3.66 (m, 2H) H-5', H-5"; 3.66 (m, 1H) H-3'; 3.08 (m, 1H) H-2'; 2.42 (s, 3H) CH_3Ph; ^{13}C-NMR ($CDCl_3$): 139.5 (d, J_{CH} = 180.0 Hz) C-6; 103.1 (d, J_{CH} = 180.7 Hz) C-5; 85.4 (d, J_{CH} = 168.5 Hz) C-1'; 79.3 (d, J_{CH} = 161.8 Hz) C-4'; 73.7 (t, J_{CH} = 141.9 Hz) CH_2NO_2; 66.0 (d, J_{CH} = 139.2 Hz) C-3'; 62.5 (t, J_{CH} = 147.7 Hz) C-5'; 46.2 (d, J_{CH} = 146.5 Hz) C-2'; 21.6 (q) CH_3Ph. **Compound 9k** (5 %): ^{1}H-NMR ($CDCl_3$): 7.72 (d, $J_{5,6}$ = 8.1 Hz, 1H) H-6; 7.30 (m, 19H) arom; 6.35 (d, $J_{1',2'}$ = 9.5 Hz, 1H) H-1'; 5.57 (d, 1H) H-5; 5.46 and 4.80 (2 x dd, $J_{2'}$, CH_2NO_2 = 6.0 Hz, 2H) CH_2NO_2; 4.30 (m, 1H) H-4'; 4.05 and 3.43 (2 x dd, $J_{4',5'}$= 2.6 Hz, 2H) H-5', H-5"; 3.71 (m, 2H) H-2',H-3'; 2.41 (s, 3H) CH_3Ph. ^{13}C-NMR ($CDCl_3$): 138.6 (d, J_{CH} = 182.0 Hz) C-6; 103.4 (d, J_{CH} = 177.4 Hz) C-5; 85.7 (d, J_{CH} = 162.9 Hz) C-1'; 78.0 (d, J_{CH} = 150.5 Hz) C-4'; 69.8 (t, J_{CH} = 151.1 Hz) CH_2NO_2; 64.2 (d, J_{CH} = 151.6 Hz) C-3'; 63.8 (t, J_{CH} = 144.3 Hz) C-5'; 44.6 (d, J_{CH} = 139.3 Hz) C-2'; 21.6 (q) CH_3Ph.

Preparation of 6: Compound **5** (450 mg, 0.74 mmol) was heated under refluxed in aqueous acetic acid (80%, 20 ml) for 10 min. All valotile matierals were evaporated and co-evaporated with absolute ethanol to dryness. The residue was separated on a silica gel column to give **6** (243 mg. Yield 90%. ^{1}H-NMR ($CDCl_3$) 7.92 (d, $J_{5,6}$ = 8.3 Hz, 1H) H-6; 7.82 and 7.40 (m, 4H) arom; 6.97(d, $J_{1',2'}$ = 2.6 Hz, 1H) H-1'; 6.53 (t, 1H) H-2'; 5.71 (d, 1H) H-5; 4.87 (m, 1H) H-4'; 3.99 (m,2H) H-5', H-5"; 2.45 (s) CH_3Ph. ^{13}C-NMR ($CDCl_3$): 140.6 (d, J_{CH} = 184.3 Hz) C-6; 102.8 (d, J_{CH} = 177.4 Hz) C-5; 87.5 (d, J_{CH} = 173.0 Hz) C-1'; 85.6 (d, J_{CH} = 150.6 Hz) C-4'; 62.1 (t, J_{CH} = 143.9 Hz) C-5'; 21.6 (q) CH_3Ph.

Preparation of 8a and 10a: They were prepared from **6** by Michael addition with ammonia as described for the preparation of **7a** & **9a**. **Compound 8a** (62%): ^{1}H-NMR (CD_3OD+D_2O): 7.89 (d, $J_{5,6}$ = 8.3 Hz, 1H) H-6; 7.85-7.53 (m, 4H) arom; 5.91 (d, 1H) H-5; 5.80 (d, $J_{1',2'}$ = 5.6 Hz, 1H) H-1'; 4.62 (m, 1H) H-4'; 4.11 (m, 3H) H-3', H-5' and H-5"; 3.80 (t, $J_{2',3'}$ = 5.4 Hz, 1H) H-2'; 2.48 (s, 3H) CH_3Ph. ^{13}C-NMR (CD_3OD+D_2O): 142.4 (d, J_{CH} = 184.3 Hz) C-6; 103.7 (d, J_{CH} = 178.3 Hz) C-5; 91.2 (d, J_{CH} = 169.7 Hz) C-1'; 80.9 (d, J_{CH} = 153.8 Hz) C-4'; 71.8 (d, J_{CH} = 146.5 Hz) C-3'; 61.8 (t, J_{CH} = 151.4 Hz) C-5'; 60.7 (d, J_{CH} = 144.1 Hz) C-2'; 22.1 (q) CH_3Ph. MS (FAB$^-$): Calc. for (M-H)$^-$ 380.0916, found 380.0925. **Compound 10a** (10%): 1H-NMR (CD_3OD + $CDCl_3$): 7.91 (d, $J_{5,6}$ = 8.2 Hz) H-6; 7.89 and 7.51 (m, 4H) arom; 6.15 (d, $J_{1',2'}$ = 7.1 Hz, 1H) H-1'; 5.80 (d, 1H) H-5; 4.46 (m, 1H) H-4'; 4.20 (m, 2H) H-2', H-3'; 3.70 (2xd, $J_{4',5'}$ = 2.7 Hz, 1H) H-5'; 3.20 (2xd, 1H) H-5"; 2.50 (s, 1H) CH_3Ph. ^{13}C-NMR (DMSO): 140.3 (d, J_{CH} = 182.0 Hz) C-6; 102.3 (d, J_{CH} = 177.5 Hz) C-5; 88.0 (d, J_{CH} = 171.6 Hz) C-1'; 77.6 (d, J_{CH} = 151.7 Hz) C-4'; 64.5 (d, J_{CH} = 143.8 Hz) C-3'; 62.5 (t, J_{CH} = 141.6 Hz) C-5'; 57.7 (d, J_{CH} = 140.4 Hz) C-2'; 21.2 (q) CH_3Ph. MS (FAB$^-$): calc. for (M-H)$^-$ 380.0916, found 380.0924.

Preparation of 8b and 10b: They were prepared from **6** by Michael addition with methylamine as described for **7b** and **9b**. **Compound 8b** (48%): ^{1}H-NMR (CD_3OD): 7.98 (d, $J_{5,6}$ = 8.1 Hz, 1H) H-6; 7.79 and 7.42 (m, 4H) arom; 5.83 (d, 1H) H-5; 5.76 (d, $J_{1',2'}$ = 4.6 Hz, 1H) H-1'; 4.53 (m, 1H) H-4'; 4.24 (d, $J_{4',5'}$ = 6.3 Hz, 2H) H-5', H-5"; 3.77 (m, $J_{2',3'}$ = 3.3 Hz, $J_{3',4'}$ = 6.3 Hz, 1H) H-3'; 3,41 (m, 1H) H-2'; 2.48 (s, 3H) $\underline{CH_3}$Ph; 1.82 (s, 3H) NCH_3. ^{13}C-NMR (CD_3OD): 140.3 (d, J_{CH} = 184.2 Hz) C-6; 102.6 (d, J_{CH} = 176.3 Hz) C-5; 88.5 (d, J_{CH} = 167.3 Hz) C-1'; 80.0 (d; J_{CH} = 149.2 Hz) C-4'; 68.2 (d, J_{CH} = 151.7 Hz) C-2'; 67.6 (d, J_{CH} = 149.4 Hz) C-3'; 60.5 (t, J_{CH} = 146.0 Hz) C-5'; 32.7 (q, J_{CH} = 138.2 Hz) NCH_3; 21.4 (q) $\underline{CH_3}$Ph. MS (FAB$^-$): calc. for (M-H)$^-$ 394.1073, found 394.1076. **Compound 10b** (30%): ^{1}H-NMR (CD_3OD+$CDCl_3$) : 7.85 (d, $J_{5,6}$ = 8.2 Hz, 1H) H-6; 7.85 and 7.42 (m, 4H) arom; 5.97 (d, $J_{1',2'}$ = 6.8 Hz, 1H) H-1'; 5.72 (d, 1H) H-5; 4.53 (m, 1H) H-4'; 4.17 (m, 1H) H-3'; 3.75 (m, 1H) H-2'; 3.82 and 3.35 (m, 2H) H-5', H-5"; 2.48 (s, 3H) NCH_3; 2.44 (s, 3H) $\underline{CH_3}$Ph. ^{13}C-NMR ($CDCl_3$+CD_3OD): 140.9 (d, J_{CH} = 182.0 Hz) C-6; 102.2 (d, J_{CH} = 178.6 Hz) C-5; 88.7 (d, J_{CH} = 171,9Hz) C-1'; 78.9 (d, J_{CH} = 151.6 Hz) C-4'; 66.0 (d, J_{CH} = 142.7 Hz) C-2'; 62.6 (d, J_{CH} = 142.7 Hz) C-3'; 62.2 (t, J_{CH} = 143.2 Hz) C-5'; 34.8 (q, J_{CH} = 135.4 Hz) NCH_3, 21.3 (q) CH_3Ph. MS (FAB$^-$): calc. for (M-H)$^-$ 394.1073, found 394.1052.

Preparation of 8c: It was prepared from **6** by Michael reaction with dimethylamine as described for **7b**. Yield 69%. ^{1}H-NMR ($CDCl_3$): 8.09 (d, $J_{5,6}$ = 8.2 Hz, 1H) H-6; 7.81 and 7.40 (m, 4H) arom; 6.18 (d, $J_{1',2'}$ = 6.1 Hz, 1H) H-1'; 5.88 (d, 1H) H-5; 4.39 (m, 1H) H-4'; 4.22 (m, 2H) H-5', H-5"; 3.97 (t, $J_{2',3'}$ = 5.0 Hz, 1H) H-3'; 3.57 (m, 1H) H-2'; 2.46 (s, 3H) $\underline{CH_3}$Ph; 1.97 (s, 6H) NCH_3. ^{13}C-NMR ($CDCl_3$): 140.4 (d, J_{CH} = 183.1 Hz) C-6; 103.9 (d, J_{CH} = 177.0 Hz) C-5; 82.6 (d, J_{CH} = 167.2 Hz) C-1'; 79.4 (d, J_{CH} = 158.9 Hz) C-4'; 71.5 (d, J_{CH} = 136.7 Hz) C-2'; 64.0 (d, J_{CH} = 141.1 Hz) C-3'; 61.4 (t, J_{CH} = 138.9 Hz) C-5'; 40.7 (q, JCH = 129.4 Hz) NCH_3; 21.6 (q) $\underline{CH_3}$Ph. MS (FAB$^-$): calc. for (M-H)$^-$ 408.1229, found 408.1227.

Preparation of 8d: It was prepared from **6** by Michael reaction with benzylamine as described for **7d**. Yield 68%. ^{1}H-NMR($CDCl_3$) 7.86 (d, $J_{5,6}$ = 8.0Hz, 1H) H-6; 7.79 and 7.33 (m, 9H) arom; 5.98 (d, $J_{1',2'}$ = 5.1 Hz, 1H) H-1'; 5.78 (d, 1H) H-5; 4.65 (m, 1H) H-4'; 4.39 (t, $J_{2',3'}$ = 5.5 Hz, $J_{3',4'}$ = 5.5 Hz, 1H) H-3'; 4.13 (m, 2H) H-5', H-5"; 3.69 (m, 1H) H-2'; 3.45 (s, 2H) N$\underline{CH_2}$Ph; 2.48 (s, 3H) $\underline{CH_3}$Ph. ^{13}C- NMR ($CDCl_3$) 140.1 (d, J_{CH} = 181.8 Hz) C-6; 102.5 (d, J_{CH} = 178.2 Hz) C-5; 88.3 (d, J_{CH} = 170.6 Hz) C-1'; 79.5 (d, J_{CH} = 144.0 Hz) C-4'; 68.6 (d, J_{CH} = 141.6 Hz) C-3'; 65.2 (t, J_{CH} = 142.3 Hz) C-5'; 60.3 (t, J_{CH} = 150.0 Hz) N$\underline{CH_2}$Ph; 50.1 (d, J_{CH} = 141.6 Hz) C-2'; 21.1 (q) $\underline{CH_3}$Ph.

Preparation of 8e: Compound **7e** (70 mg, 0.103 mmol) was treated with trifluoroacetic acid (3 ml, 2% in dichloromethane) at 0 °C for 3 h. The mixture was poured into a cold solution of sodium bicarbonate (15 ml) which was then extracted with dichloromethane (3 x 30 ml). Organic phase was evaporated and then the residue was purified by a preparative TLC to give **8e** (35 mg, 78%). ^{1}H-NMR ($CDCl_3$) : 9.38 (br, 1H) NH; 8.11 (d, $J_{5,6}$ = 8.3 Hz, 1H) H-6; 7.72 and 7.40 (2xd, 4H) arom; 6.21 (d, $J_{1',2'}$ = 5.8 Hz, 1H) H-1'; 5.87 (d, 1H) H-5; 4.43 (m, $J_{3',4'}$ = 4.6 Hz, $J_{4',5'}$ = 4.9 Hz, 1H) H-4'; 4.19 (d, 2H) H-5', H-5"; 3.94 (dd, $J_{2',3'}$ = 4.8 Hz, 1H) H-3'; 3.56 (dd, 1H) H-2'; 2.49 (s, 3H) CH_3Ph; 2.17 (br, 4H) NCH_2; 1.54 (br, 4H) $NCH_2\underline{CH_2}$; ^{13}C-NMR ($CDCl_3$): 147.0 (d, J_{CH} = 184.3 Hz) C-6; 103.9 (d, J_{CH} = 177.5 Hz) C-5; 83.8 (d, J_{CH} = 164.0 Hz) C-1'; 79.2 (d, J_{CH} = 151.6 Hz) C-4'; 68.9 (d, J_{CH} = 139.3 Hz) C-2'; 66.0 (d, J_{CH} = 143.7 Hz) C-3'; 60.9 (t, J_{CH} = 144.9 Hz) C-5'; 50.0 (t) NCH_2; 22.9 (t) $NCH_2\underline{CH_2}$; 21.6 (q) CH_3Ph. MS (FAB$^-$) : calc. for (M-H)$^-$ 434.1386, found 434.1419.

Preparation of 8f: **7f** (150 mg, 0.22 mmol) was treated with trifluoroacetic acid (7 ml, 2% in dichloromethane) in the same way as described for **7e**, yield (77 mg, 78%). ^{1}H-NMR (CD_3OD + D_2O) : 8.04 (d, $J_{5,6}$ = 8.1 Hz, 1H) H-6; 7.84 and 7.45 (2xd, 4H) arom; 6.17 (d, $J_{1',2'}$ = 6.6 Hz, 1H) H-1'; 5.84 (d, 1H) H-5; 4.35 (m, 1H) H-4'; 4.33 (m, 1H) H-3'; 4.18 (m, 2H) H-5',H-5"; 3.50 (dd, $J_{2',3'}$ = 6.9 Hz, 1H) H-2'; 2.46 (s, 3H) CH_3Ph; 2.22 (br, 4H) NCH_2; 1.23 (br, 6H) $NCH_2\underline{CH_2}\underline{CH_2}\underline{CH_2}$; ^{13}C-NMR ($CD_3OD$+$D_2O$) : 140.7 (d, J_{CH} = 183.1 Hz) C-6; 102.7 (d, J_{CH} = 178.6 Hz) C-5; 81.3 (d, J_{CH} = 167.4 Hz) C-1'; 79.0 (d, J_{CH} = 152.8 Hz) C-4'; 71.8(d, J_{CH} = 139.3 Hz) C-2', 63.6 (d, J_{CH} = 143.8 Hz) C-3'; 60.1 (t, J_{CH} = 146.0 Hz) C-5'; 49.5, 24.9 and 23.0 for piperidinyl; 20.4 (q) CH_3Ph; MS (FAB$^-$) : calc. for (M-H)$^-$ 448.1542, found 448.1516.

Preparation of 8g: Compound **7g** (160 mg, 0.23 mmol) was heated under reflux in aqueous acetic acid (6 ml, 80%) for 10 min. All volatile materials were evaporated and co-evaporated with toluene to dryness. the residue was then separated on a silica gel column to give **8g** (75 mg, 72%). ^{1}H-NMR ($CDCl_3$) : 8.06 (d, $J_{5,6}$ = 8.1 Hz, 1H) H-6; 7.79 and 7.41 (2xd, 4H) arom; 6.21 (d, $J_{1',2'}$ = 6.6 Hz, 1H) H-1'; 5.89 (d, 1H) H-5; 4.33-4.12 (m, 4H) H-3'', H-4', H-5', H-5"; 3.60 (m, 1H) H-2'; 3.31 (br, 4H) OCH_2; 2.48 (s,3H) CH_3Ph; 2.24 (br,4H) NCH_2; ^{13}C-NMR ($CDCl_3$): 140.2 (d, J_{CH} = 183.1 Hz) C-6; 103.8 (d, J_{CH} = 177.4 Hz) C-5; 81.8 (d, J_{CH} = 167.8 Hz) C-1'; 77.0 (d, J_{CH} = 149.4 Hz) C-4'; 71.3 (d, J_{CH} = 141.6 Hz) C-2'; 66.1 (d, J_{CH} = 138.1 Hz) OCH_2; 63.4 (d, J_{CH} = 144.8 Hz) C-3'; 60.9 (t, J_{CH} = 144.9Hz) C-5'; 49.1 (t) NCH_2; 21.4 (q) CH_3Ph. MS (FAB$^-$) : calc. for (M-H)$^-$ 450.1335 found 450.1292.

Preparation 8h: It was prepared from **7h** (170 mg, 0.24 mmol) in the same way as described for **8g**, yield (85 mg, 77%). ^{1}H-NMR (CD_3OD+D_2O): 7.96 (d, $J_{5,6}$ = 8.4 Hz, 1H) H-6; 7.79 and 7.47 (2xd, 4H) arom; 5.88 (d, 1H) H-5; 5.86 (d, $J_{1',2'}$ = 5.4Hz, 1H) H-1'; 4.54 (m, 1H) H-4'; 4.22 and 4.10 (m, 2H) H-5',H-5"; 4.14 (m, 1H) H-3'; 3.66 (m, 1H) H-2'; 3.54 (s, 3H) OMe; 2.90 (dd, Jgem = 18.1 Hz, 2H) $\underline{CH_2}CO_2R$; 2.47 (s, 3H) CH_3Ph; ^{13}C-NMR (CD_3OD+D_2O) : 173.5 (s) - $\underline{CO_2}CH_3$; 142.1 (d, J_{CH} = 181.8 Hz) C-6; 103.5 (d, J_{CH} = 178.6Hz) C-5; 89.6 (d, J_{CH} = 166.2 Hz) C-1'; 81.5 (d, J_{CH} = 152.8 Hz) C-4'; 70.3 (d, J_{CH} = 146.1 Hz) C-2'; 66.7 (d, J_{CH} = 142.6 Hz) C-3'; 61.6 (t, J_{CH} = 144.9 Hz) C-5'; 52.4 (q) - $CO_2\underline{CH_3}$; 47.8 (t) NCH_2; 21.7 (q) CH_3Ph; MS (FAB$^-$) : calc. for (M-H)$^-$ 452.1128, found 452.1098.

Preparation of 8i(R): It was prepared from **7i(R)** (200 mg, 0.28 mmol) in the same way as described for **8g**, yield (121 mg, 92%). ^{1}H-NMR ($CDCl_3$): 9.94 (br, 1H) NH; 7.94 (d, $J_{5,6}$ = 8.3 Hz,.1H) H-6; 7.74 and 7.38 (2xd, 4H) arom;

6.03 (d, $J_{1',2'}$ = 6.6 Hz, 1H) H-1'; 5.86 (d, 1H) H-5; 4.85 (m, $J_{3',4'}$ = 6.3 Hz, $J_{4',5'}$ = 6.3 Hz, 1H) H-4'; 4.21 (d, 2H) H-5', H-5"; 3.79 (dd, $J_{2',3'}$ = 4.2 Hz, 1H) H-3'; 2.71 (m, 1H) H-2'; 2.46 (s, 3H) CH_3Ph; 2.28-1.48 (m, 9H) cyclohexanonyl; ^{13}C-NMR ($CDCl_3$) : 211.8 (s) CO; 140.1 (d, J_{CH} = 182.6 Hz) C-6; 103.2 (d, J_{CH} = 177,0 Hz) C-5; 84.6 (d, J_{CH} = 167.3 Hz) C-1'; 80,4 (d, J_{CH} = 151.7 Hz) C-4'; 66.4 (d, J_{CH} = 145.7 Hz) C-3'; 66.8 (t, J_{CH} = 144.0 Hz) C-5'; 49.9 (d, J_{CH} = 133.1 Hz) HCCO; 48.0 (d, J_{CH} = 139.2 Hz) C-2'; 41.5, 29.7, 26.6 and 24.6 for -$COCH_2CH_2$ CH_2CH_2; 21.4 (q) CH_3Ph. MS (FAB^-) : calc. for $(M-H)^-$ 461.1382, found 461.1411.

Preparation of 8i(S): It was prepared from **7i(S)** (230 mg, 0.33 mmol) in the same way as described for **8g**, yield (140 mg, 93%). ^{1}H-NMR ($CDCl_3$): 7.97 (d, $J_{5,6}$ = 8.1 Hz, 1H) H-6; 7.76 and 7.41 (2xd, 4H) arom.; 6.21 (d, $J_{1',2'}$ = 6.9 Hz, 1H) H-1'; 5.88 (d, 1H) H-5; 4.76 (m, $J_{3',4'}$ = 5.7 Hz, $J_{4',5'}$ = 6.8 Hz, 1H) H-4'; 4.15 (d, 2H) H-5', H-5"; 3.86 (dd, $J_{2',3'}$ = 6.7 Hz, 1H) H-3'; 2.50 (m, 4H) H-2', CH_3Ph; 2.30-1.30 (m, 9H) cyclohexanonyl; ^{13}C- NMR ($CDCl_3$) : 211.8 (s) CO; 140.9 (d, J_{CH} = 183.0 Hz) C-6; 103.9 (d, J_{CH} = 177.1 Hz) C-5; 84.3 (d, J_{CH} = 170.9 Hz) C-1'; 79.2 (d, J_{CH} = 151.9 Hz) C-4'; 67.7 (d, J_{CH} = 145.2 Hz) C-3'; 60.9 (d, J_{CH} = 145.3 Hz) C-5'; 50.8 (d,J_{CH} = 133.1 Hz) HCCO-; 48.5 (d, J_{CH} = 139.9 Hz) C-2'; 42.0, 31.7, 26.7 and 25.2 for-$CO\underline{CH_2}\underline{CH_2}\underline{CH_2}\underline{CH_2}$; 21.5 (q) CH_3Ph. MS (FAB^-) : calc. for $(M-H)^-$ 461.1382, found 461.1406.

Preparation of 8j: Compound **7j** (230 mg, 0.31 mmol) was treated with trifluoroacetic acid (10ml, 2% in dichloromethane) at room temperature for 1 h. Then triethylamine (2 ml) was added and the mixture was evaporated. The residue was separated on a silica gel column to give **8j** (110 mg, 71%). ^{1}H-NMR ($CDCl_3$) 7.90 (d, $J_{5,6}$ = 8.3 Hz, 1H) H-6; 7.77 and 7.42 (m, 4H) arom; 6.24 (d, $J_{1',2'}$ = 6.1 Hz, 1H) H-1'; 5.86 (d, 1H) H-5; 4.56 (m, 1H) H-4'; 4.11 and 3.77 (m, 3H) H-3', H-5' and H-5"; 3.67 and 3.64 (2xs, 6H) OCH_3; 3.49 (d, $J_{CH,2'}$ = 5.4 Hz, 1H) $\underline{CH}CO_2Me$; 3.14 (m, 1H) H-2'; 2.47 (s, 3H) $\underline{CH_3}Ph$. ^{13}C-NMR ($CDCl_3$): 139.9 (d, J_{CH} = 184.3 Hz) C-6; 103.6 (d, J_{CH} = 177.0 Hz) C-5'; 84.6 (d, J_{CH} = 166.0 Hz) C-1'; 79.9 (d, J_{CH} = 156.2 Hz) C-4'; 66.0 (d, J_{CH} = 138.0 Hz) C-3'; 60.8 (t, J_{CH} = 145.9 Hz) C-5'; 53.1 (q, J_{CH} = 147.8 Hz) OCH_3; 50.7 (d, J_{CH} = 129.4 Hz) $\underline{CH}CO_2Me$; 46.1 (d, J_{CH} = 133.1 Hz) C-2'; 21.5 (q) $\underline{CH_3}Ph$. MS (FAB^-): calc. for $(M-H)^-$ 495.1073, found 495.1079.

Preparation 8k and 10k: Compound **6** (140 mg, 0.31 mmol) was added to a suspension of potassium tert-butoxide (135 mg, 1.2 mmol) in nitromethane (10 ml) and the mixture was stirred overnight at room temperature. The mixture was poured into saturated aqueous solution of ammonium chloride (20 ml), which was extracted with nitromethane (4 x 20 ml). Organic phase was evaporated and separated on a silica gel column to give **8k** (92 mg, 58%) and **10k**(10 mg, 4%).

Compound 8k: ^{1}H-NMR (DMSO): 7.84 (d, $J_{5,6}$ = 8.2 Hz, 1H) H-6; 7.79 and 7.50 (m, 4H) arom; 6.07 (d, $J_{1',2'}$ = 6.4 Hz, 1H) H-1'; 5.87 (d, 1H) H-5; 5.10 (t, $J_{4',5'}$ = 5.7 Hz, $J_{3',4'}$ = 5.7 Hz, 1H) H-4'; 4.83 and 4.43 (2xm, $J_{2'}$, $\underline{CH_2}NO2$ = 7.9 Hz, 2H) CH_2NO_2; 4.36 (m, 1H) H-3'; 3.87 (m, 2H) H-5', H-5"; 3.14 (m, 1H) H-2'; 2.42 (s, 3H) $\underline{CH_3}Ph$. ^{13}C-NMR (DMSO): 139.6 (d, J_{CH} = 181.9 Hz) C-6; 103.3 (d, J_{CH} = 175.8 Hz) C-5; 84.6 (d, J_{CH} = 173.4 Hz) C-1'; 79.9 (d, J_{CH} = 151.4 Hz) C-4'; 74.2 (t, J_{CH} = 144.0 Hz) $\underline{CH_2}NO_2$; 64.7 (d, J_{CH} = 151.4 Hz) C-3'; 59.6 (t, J_{CH} = 145.2 Hz) C-5'; 44.2 (d, J_{CH} = 134.2 Hz) C-2'; 21.2 (q) $\underline{CH_3}Ph$. MS (FAB^-): calc. for $(M-H)^-$ 424.0815, found 424.0800. **Compound 10k:** ^{1}H-NMR (CD_3OD): 7.97 (d, $J_{5,6}$ = 8.2 Hz, 1H) H-6; 7.85 and 7.51 (m, 4H) arom; 6.32 (d, $J_{1',2'}$ = 9.7 Hz, 1H) H-1'; 5.76 (d, 1H) H-5; 5.25 and 4.95 (m, 2H) CH_2NO_2; 4.34 (m, 2H) H-3', H-4'; 3.70 (m, 1H) H-2'; 3.62 (2xd, $J_{4',5'}$ = 2.4 Hz, $J_{5',5"}$ = 12.5 Hz, 1H) H-5'; 3.10 (2xd, 1H) H-5"; 2.47 (s, 3H) $\underline{CH_3}Ph$. ^{13}C-NMR (CD_3OD): 141.4 (d, J_{CH} = 184.3 Hz) C-6; 103.9 (d, J_{CH} = 177.4 Hz) C-5; 87.2 (d, J_{CH} = 167.4 Hz) C-1'; 80.8 (d, J_{CH} = 151.6 Hz) C-4'; 78.0 (t, J_{CH} = 144.5 Hz) $\underline{CH_2}NO_2$; 65.8 (d, J_{CH} = 144.9 Hz) C-3'; 63.8 (t, J_{CH} = 148.3 Hz) C-5'; 45.5 (d, J_{CH} = 130.5 Hz) C-2'; 21.7 (q) $\underline{CH_3}Ph$. MS (FAB^-): calc. for $(M-H)^-$ 424.0815, found 424.0809.

Removal of 4-toluenesulfonyl group from nucleosides 7a-g & 9a-b *(general procedure)*: To a stirred suspension of toluenesulfone nucleosides (1 mmol) in dry methanol (10 ml), anhydrous disodium hydrogen phosphate (8 mmol) was added and followed by sodium amalgam (Na 6%, 8 mmol) in portions over 1 h. Stirring was continued for another 5 h when all starting material disappearred. The reaction mixture was filtered and the solid was washed with dichloromethane (3 x 40 ml). Lipophilic phases were pooled and washed with saturated aqueous solution of EDTA (20 ml). Organic phase was separated and evaporated to a syrup which was purified on a silica gel column to give 3'-deoxy nucleosides **11a-g.**

Preparation 11a: It was prepared from **7a** and **9a** following the general procedure. Yield 30%. ^{1}H-NMR ($CDCl_3$): 7.98 (d, $J_{5,6}$ = 8.1 Hz, 1H) H-6; 7.33 (m, 15H) arom; 5.65 (d, $J_{1',2'}$ = 1.7 Hz, 1H) H-1'; 5.33 (d, 1H) H-5; 4.60 (m, 1H) H-4'; 3.64 (m, 1H) H-2'; 3.45 (m, 2H) H-5', H-5"; 1.95 (m, 2H) H-3', H-3". ^{13}C-NMR ($CDCl_3$): 139.9 (d, J_{CH} = 180.9 Hz) C-6; 101.4 (d, J_{CH} = 168.2 Hz) C-5; 92.9 (d, J_{CH} = 167.3 Hz) C-1'; 79.9 (d, J_{CH} = 159.6 Hz) C-4'; 63.7 (t, J_{CH} = 145.3 Hz) C-5'; 58.4 (d, J_{CH} = 144.0 Hz) C-2'; 33.6 (t, J_{CH} = 135.5 Hz) C-3'.

Preparation of 11b: It was prepared from **7b** and **9b** following the general procedure. Yield 47%. ^{1}H-NMR ($CDCl_3$): 8.03 (d, $J_{5,6}$ = 8.3 Hz, 1H) H-6; 7.35 (m, 15H) arom; 5.80 (s, 1H) H-1'; 5.32 (d, 1H) H-5; 4.54 (m, 1H) H-4'; 3.46 (m, 2H) H-5', H-5"; 3.35 (m, 1H) H-2'; 2.51 (s, 3H) NCH_3; 2.02 (m, 2H) H-3'. ^{13}C-NMR ($CDCl_3$): 139.9 (d, J_{CH} = 178.2 Hz) C-6; 101.3 (d, J_{CH} = 175.8 Hz) C-5; 90.3 (d, J_{CH} = 170.9 Hz) C-1'; 79.8 (d, J_{CH} = 141.6 Hz) C-4'; 66.7 (d, J_{CH} = 142.9 Hz) C-2'; 63.5 (t, J_{CH} = 141.6 Hz) C-5'; 34.1 (q) NCH_3; 31.1 (t, J_{CH} = 133.7 Hz) C-3';

Preparation of 11c: Yield 45%. ^{1}H-NMR ($CDCl_3$): 7.86 (d, $J_{5,6}$ = 8.2 Hz, 1H) H-6; 7.35 (m, 15H) arom; 6.08 (d, $J_{1',2'}$ = 4.4 Hz, 1H) H-1'; 5.32 (d, 1H) H-5; 4.33 (m, 1H) H-4'; 3.43 (m, 2H) H-5'and.H-5"; 3.11 (m, 1H) H-2'; 2.36 (s, 6H) NCH_3; 2.16 (q, $J_{2',3'}$ = 7.7 Hz, $J_{3',4'}$ = 5.5 Hz, 2H) H-3', H-3". ^{13}C NMR ($CDCl_3$): 140.4 (d, J_{CH} = 180.6 Hz) C-6; 102.1 (d, J_{CH} = 177.0 Hz) C-5; 87.2 (d, J_{CH} = 172.1 Hz) C-1'; 78.7 (d, J_{CH} = 146.4 Hz) C-4'; 70.7 (d, J_{CH} = 137.7 Hz) C-2'; 64.2 (t, J_{CH} = 142.8 Hz) C-5'; 42.7 (q, J_{CH} = 134.3 Hz) NCH_3; 28.3 (t, J_{CH} = 133.1 Hz) C-3'.

Preparation 11d: Yield 45%. ^{1}H-NMR ($CDCl_3$): 8.01 (d, $J_{5,6}$ = 8.1 Hz, 1H) H-6; 7.30 (m, 20H) arom; 5.85 (d, $J_{1',2'}$ = 1.8 Hz, 1H) H-1'; 5.27 (d, 1H) H-5; 4.55 (m, 1H) H-4'; 3.92 (s, 2H) $N\underline{CH_2}Ph$; 3.61 (m, 1H) H-2'; 3.46 (m, 2H) H-5', H-5"; 1.98 (m, 2H) H-3', H-3". ^{13}C NMR ($CDCl_3$): 139.6 (d, J_{CH} = 182.0 Hz) C-6; 101.3 (d, J_{CH} = 176.0 Hz) C-5; 90.9 (d, J_{CH} = 172.5 Hz) C-1'; 80.0 (d, J_{CH} = 145.0 Hz) C-4'; 64.2 (d, J_{CH} = 144.0 Hz) C-2'; 63.5 (t, J_{CH} = 142.0 Hz) C-5'; 51.4 (t, J_{CH} = 133.0 Hz) $N\underline{CH_2}Ph$; 31.9 (t, J_{CH} = 132.0 Hz) C-3'. MS (FAB^-): Calc.for $(M-H)^-$ 558.2393, found 558.2415.

Preparation 11e: Yield 28%. ^{1}H-NMR ($CDCl_3$) : 9.75 (br, 1H) NH; 7.94 (d, $J_{5,6}$ = 8.0 Hz, 1H) H-6; 7.32 (m, 15H) arom; 6.10 (d, $J_{1',2'}$ = 2.9 Hz, 1H) H-1'; 5.30 (d, 1H) H-5; 4.46 (m, $J_{3',4'}$ = 7.1 Hz, 1H) H-4'; 3.53 (dd, $J_{4',5'}$ = 3.4 Hz, $J_{5',5''}$ = 11.5Hz, 1H) H-5'; 3.32 (dd, $J_{4',5''}$ = 2.7 Hz, 1H) H-5"; 3.07 (m, $J_{2',3'}$ = 7.3 Hz, 1H) H-2'; 2.67 (br, 4H) NCH_2; 2.18 (m, 2H) H-3', H-3"; 1.78 (br, 4H) $NCH_2\underline{CH_2}$; ^{13}C- NMR ($CDCl_3$) : 140.5 (d, J_{CH} = 184.3 Hz) C-6; 101.7 (d, J_{CH} = 177.9 Hz) C-5; 88.6 (d, J_{CH} = 171.8 Hz) C-1'; 87.2 (s) Ph_3C; 78.9 (d, J_{CH} = 148.3 Hz) C-4'; 70.0 (d, J_{CH} = 137.0 Hz) C-2'; 64.1 (t, J_{CH} = 142.6 Hz) C-5'; 52.1 (t) NCH_2; 30.6 (t, J_{CH} = 132.0 Hz) C-3'; 23.2 (t) $NCH_2\underline{CH_2}$.

Preparation of 11f: Yield 26%. ^{1}H-NMR ($CDCl_3$) 9.32 (br, 1H) NH; 7.76 (d, $J_{5,6}$ = 8.3Hz, 1H) H-6; 7.34 (m, 15H) arom; 6.15 (d, $J_{1',2'}$ = 4.9Hz, 1H) H-1'; 5.32 (d, 1H) H-5; 4.33 (m, $J_{3',4'}$ = 7.1Hz, 1H) H-4'; 3.36 (m, $J_{4',5'}$ = 2.6 Hz, 2H) H-5', H-5"; 3.20 (m, $J_{2',3'}$ = 7. 3 Hz, 1H) H-2'; 2.57 (br, 4H) NCH_2; 2.19 (t, 2H) H-3',H-3"; 1.53 (br, 6H) $NCH_2\underline{CH_2CH_2CH_2}$. ^{13}C- NMR ($CDCl_3$): 140.4 (d, J_{CH} = 180.6 Hz) C-6; 102.1 (d, J_{CH} = 174.0Hz) C-5; 87.1(s) Ph_3C; 86.0 (d, J_{CH} = 167.2 Hz) C-1'; 78.2 (d, J_{CH} = 146.5 Hz) C-4'; 69.9 (d, J_{CH} = 140.4 Hz) C-2'; 64.9 (t, J_{CH} = 141.6 Hz) C-5'; 51.0 (t) NCH_2; 27.8 (t, J_{CH} = 131.8 Hz) C-3'; 25.4 and 24.0 for $NCH_2\underline{CH_2CH_2}$.

Preparation of 11g: Yield 28%. ^{1}H-NMR ($CDCl_3$): 9.90 (br, 1H) NH; 7.87 (d, $J_{5,6}$=8.3Hz, 1H) H-6; 7.30 (m, 15H) arom; 6.10 (d, $J_{1',2'}$ = 3.6 Hz, 1H) H-1'; 5.33 (d, 1H) H-5; 4.36 (m, $J_{3',4'}$ = 6.6 Hz, $J_{4',5'}$ = 3.7 Hz, $J_{4',5''}$ = 2.8 Hz, 1H) H-4'; 3.73 (t, 4H) OCH_2; 3.43 (dd, $J_{5',5''}$ = 10.9 Hz, 1H) H-5'; 3.39 (dd, 1H) H-5"; 3.16 (m, $J_{2',3'}$ = 6.8 Hz, 1H) H-2'; 2.63 (m, 4H) NCH_2; 2.18 (dd, 2H) H-3'; ^{13}C-NMR ($CDCl_3$) : 140.3 (d, J_{CH} = 184.2 Hz) C-6; 102.1 (d, J_{CH} = 177.4) C-5; 87.2 (d, J_{CH} = 167.4 Hz) C-1'; 87.2(s) Ph_3C; 78.6 (d, J_{CH} = 149.4 Hz) C-4'; 70.4 (d, J_{CH} = 138.2 Hz) C-2'; 64.3 (t, J_{CH} = 142.7 Hz) C-5'; 66.6 (t) OCH_2; 51.0 (t) NCH_2; 27.8 (t, J_{CH} = 130.3 Hz) C-3'.

Detritylation of 11 to 12 (*general procedure*): Compound **11** was heated under reflux in 80% aqueous solution of acetic acid (40 ml / mmol) for 10 min. All volatile materials were evaporated and the syrup was co-evaporated twice with toluene and then with ethanol to dryness. The residue was partitioned between dichloromethane (30 ml) and water (30 ml). The aqueous phase was washed with dichloromethane (3 x 10 ml). The combined organic phase was extracted with water (15 ml), the aqueous phases were pooled and evaporated to dryness to give **12**.

Preparation of 12a: It was prepared from **11a**, yield 94%. *This compound was found to be spectroscopically identical to the compound obtained by an authentic route from* **29**.

Preparation of 12b: Yield 81.8%. ^{1}H-NMR (D_2O): 7.85(d, $J_{5,6}$=8.1Hz, 1H) H-6; 5.99(d, $J_{1',2'}$=3.2 Hz, 1H) H-1'; 5.81(d, 1H) H-5; 4.43(m, 1H) H-4'; 3.75(m,3H) H-2',H-5'and H-5"; 2.63(s, 3H) NCH_3; 2.23(m,2H) H-3',H-3". ^{13}C-NMR (D_2O): 142.6(d, J_{CH}=184.3Hz) C-6; 103.4(d, J_{CH}=179.7Hz) C-5; 89.3(d, J_{CH}=169.6Hz) C-1'; 81.9(d, J_{CH}=157.3Hz) C-4'; 6lt 5.0(d, J_{CH} =157.3Hz) C-2'; 63.3(t, J_{CH}=143.2Hz) C-5'; 33.5(q,J_{CH}=140.4Hz) NCH_3; 30.4(t, J_{CH}=132.1Hz) C-3'. MS (FAB^+): calc. for $(M+H)^+$ 242.1141, found 242.1163.

Preparation of 12c: Yield 94%. ^{1}H-NMR (D_2O): 7.81 (d, $J_{5,6}$ = 8.5 Hz, 1H) H-6; 6.16 (d, $J_{1',2'}$ = 4.8 Hz, 1H) H-1'; 5.84 (d, 1H) H-5; 4.38 (m, 1H) H-4'; 3.93 (m, 1H) H-2'; 3.72 (m, 2H) H-5', H-5"; 2.73 (s, 6H) NCH_3; 2.32 (m, 2H) H-3', H-3". ^{13}C-NMR (D_2O): 142.3 (d, J_{CH} = 184.2 Hz) C-6; 103.6 (d, J_{CH} = 180.8 Hz) C-5; 87.1 (d, J_{CH} = 169.6 Hz) C-1'; 81.2 (d, J_{CH} = 151.7 Hz) C-4'; 69.9 (d, J_{CH} = 152.8 Hz) C-2'; 63.2 (t, J_{CH} = 143.2 Hz) C-5'; 42.3 (q, J_{CH} = 142.3 Hz) NCH_3; 27.8 (t, J_{CH} = 134.2 Hz) C-3'. MS (FAB^+): calc. for $(M+H)^+$ 256.1297, found 256.1318.

Preparation of 12d: Yield 70%. ^{1}H-NMR ($CDCl_3$ + CD_3OD): 8.0 (d, $J_{5,6}$ = 8.3 Hz, 1H) H-6; 5.85 (d, $J_{1',2'}$ = 3.2 Hz, 1H) H-1'; 5.67 (d, 1H) H-5, 4.44 (m, 1H) H-4'; 3.87 (s, 2H) $N\underline{CH_2}Ph$; 3.79 (m, $J_{4',5'}$ = 3.1 Hz, 2H) H-5', H-5"; 3.43 (m, 1H) H-2'; 2.02 (m, 2H) H-3', H-3". ^{13}C-NMR ($CDCl_3$+CD_3OD): 140.5 (d, J_{CH} = 186.7 Hz) C-6; 101.2 (d, J_{CH} = 177.0 Hz) C-5; 90.7 (d, J_{CH} = 170.9 Hz) C-1'; 80.7 (d, J_{CH} = 147.7 Hz) C-4'; 63.4 (d, J_{CH} = 144.4 Hz) C-2'; 62.1 (t, J_{CH} = 142.4 Hz) C-5'; 51.1 (t, J_{CH} = 134.9 Hz) $N\underline{CH_2}Ph$; 31.1 (t, J_{CH} = 131.3 Hz) C-3'. MS (FAB^+): calc. for $(M+H)^+$ 318.1454, found 318.1459.

Preparation of 12e: Yield 94%. ^{1}H-NMR (CD_3OC+D_2O): 8.05 (d, $J_{5,6}$ = 8.1 Hz, 1H) H-6; 6.09 (d, $J_{1',2'}$ = 4.9 Hz, 1H) H-1'; 5.70 (d, 1H) H-5; 4.31 (m, $J_{3',4'}$ = 7.1 Hz, $J_{4',5'}$ = 3.5 Hz, $J_{4',5''}$ = 2.7 Hz, 1H) H-4'; 3.82 (dd, $J_{5',5''}$ = 12.2 Hz, 1H) H-5', 3.59 (dd, 1H) H-5"; 3.22 (m, $J_{2',3'}$ = 7.1 Hz, 1H) H-2'; 2.72 (br, 4H) NCH_2; 2.23 (m, 2H) H-3'; 1.83 (br, J_{CH} = 168.4 Hz) C-1'; 80.9 (d, J_{CH} = 148.2 Hz) C-4'; 70.1 (d, J_{CH} = 140.4 Hz) C-2'; 64.2 (t, J_{CH} = 141.5 Hz) C-5'; 53.5 (t) NCH_2; 31.9 (t, J_{CH} = 133.6 Hz) C-3'; 24.2 (t) $NCH_2\underline{CH_2}$. MS (FAB^-) : calc. for $(M-H)^-$ 280.1297, found 280.1315.

Preparation of 12f: Yield 95%. ^{1}H-NMR (CD_3OD+D_2O): 7.99 (d, $J_{5,6}$ = 8.1 Hz, 1H) H-6; 6.14 (d, $J_{1',2'}$ = 5.6 Hz, 1H) H-1'; 5.72 (d, 1H) H-5; 4.24 (m, $J_{3',4'}$ = 7.1Hz, $J_{4',5'}$ = 3.4 Hz, $J_{4',5''}$ = 2.9 Hz, 1H) H-4'; 3.77 (dd, $J_{5',5''}$ = 11.9 Hz, 1H) H-5'; 3.57 (dd, 1H) H-5"; 3.33 (m, $J_{2',3'}$ = 7.6 Hz, $J_{2',3''}$ = 7.1 Hz, 1H) H-2'; 2.65 (br, 4H) NCH_2; 2.23 (t, 2H) H-3'; 1.57 (br, 6H) $NCH_2\underline{CH_2CH_2CH_2}$. ^{13}C- NMR ($CD_3OD$+$D_2O$): 142.8 (d, J_{CH} = 183.1 Hz) C-6; 103.0 (d, J_{CH} = 177.5 Hz) C-5; 87.7 (d, J_{CH} = 169.6 Hz) C-1'; 80.7 (d, J_{CH} = 149.5 Hz) C-4'; 70.5 (d, J_{CH} = 140.4 Hz) C-2'; 64.5 (t, J_{CH} = 142.1 Hz) C-5'; 29.5 (t, J_{CH} = 132.5 Hz) C-3'; 52.5, 26.2 and 24.6 for peperidinyl. MS (FAB^-) : calc. for $(M-H)^-$ 294.1454, found 294.1444.

Preparation of 12g: Yield 92%. ^{1}H-NMR (CD_3OD+D_2O): 8.05 (d, $J_{5,6}$ = 8.1 Hz, 1H) H-6; 6.07 (d, $J_{1',2'}$ = 5.1 Hz, 1H) H-1'; 5.71 (d, 1H) H-5; 4.25 (m, $J_{3',4'}$ = 6.6 Hz, $J_{3'',4'}$ = 2.2 Hz, 1H) H-4'; 3.80 (dd, $J_{4',5'}$ = 3.9 Hz, $J_{5',5''}$ = 12.1 Hz, 1H) H-5'; 3.59 (dd, $J_{4',5''}$ = 2.9 Hz, 1H) H-5"; 3.68 (m, 4H) OCH_2; 3.12 (m, $J_{2',3'}$ = 6.1 Hz; $J_{2',3''}$ = 5.6 Hz, 1H) H-2'; 2.59 (br, 4H) NCH_2; 2.17 (m, 2H) H-3',H-3"; ^{13}C- NMR (CD_3OD+D_2O) : 142.8 (d, J_{CH} = 186.4 Hz) C-6; 102.9 (d, J_{CH} = 176.3 Hz) C-5; 88.4 (d, J_{CH} = 166.2 Hz) C-1'; 81.0 (d, J_{CH} = 149.4 Hz) C-4'; 70.9 (d, J_{CH} = 139.2 Hz) C-2'; 67.8 (t) OCH_2; 64.4 (t, J_{CH} = 142.6 Hz) C-5'; 52.3 (t) NCH_2; 29.2 (t, J_{CH} = 132.0 Hz) C-3'. MS (FAB^-) : calc. for $(M-H)^-$ 296.1247, found 296.1243.

N^6,N^6-dibenzoyl-9-[3'-deoxy-3'-(p-toluenethio)-β-D-xylofuranosyl]adenine (15): A mixture of sodium methoxide (5.49 g, 100 mmol) and p-thiocresol (18.7 g, 150 mmol) in methanol (200 ml) was stirred at 20 °C until a clear solution was obtained. Compound **13** (5 g, 20 mmol) was added to the mixture and was heated under reflux overnight. The reaction mixture was cooled and all volatile matters were removed in vacuuo. The residue was purified on silica gel. It was dissolved in dry pyridine (200 ml). Chlorotrimethylsilane (25 ml, 200 mmol) was added and the mixture was stirred at 20 °C.

After 2 h, benzoyl chloride (23 ml, 200 mmol) was added and the stirring was continued. After 3 h, the reaction mixture was worked up in the usual way. The residue was purified on a silica gel column and the product was collected as a yellow foam. Yield: 8.1 g (70%). ^{1}H-NMR ($CDCl_3$ + CD_3OD) : 8.6 (s, 1H) H-8 ; 8.29 (s, 1H) H-2; 7.86 - 7.08 (m, 14H) arom.; 5.79 (d, $J_{1',2'}$ = 6.6 Hz, 1H) H-1'; 4.85 (dd, $J_{1',2'}$ = 6.6 Hz, 1H, $J_{2',3'}$ = 9.3 Hz, 1H) H-2'; 4.57 (m, 1H) H-4'; 3.99 (m, 1H) H-3'; 3.89 (m, 2H) H-5', H-5"; 2.31 (s, 3H) -CH_3. ^{13}CNMR ($CDCl_3$) : 90.3 (d, J_{CH} = 162.5 Hz) C-1'; 81.7 (d, J_{CH} = 146.5 Hz) C-4'; 77.5 (d, J_{CH} = 147.7 Hz) C-2'; 62.7 (t, J_{CH} = 143.4 Hz) C-5'; 54.8 (d, J_{CH} = 141.6 Hz) C-3'; 20.9 (q, J_{CH} = 125.7 Hz) -CH_3.

N^6,N^6-dibenzoyl-9-[3'-deoxy-3'-(p-toluenesulfonyl)-β-D-xylofuranosyl]adenine (16): m-Chloroperbenzoic acid (4.8 g, 28 mmol) was added to a solution of compound **15** (4 g, 7 mmol) in dichloromethane (35 ml) and the solution was stirred for 1 h at 20 °C. Reaction was worked up in the usual way. The product was purified on silica gel. Yield: 4 g (93%). ^{1}H-NMR ($CDCl_3$ + CD_3OD) : 8.68 (s, 1H) H-8; 8.59 (s, 1H) H-2; 7.8 - 7.4 (m, 14H) arom.; 5.97 (d, $J_{1',2'}$ = 5.8 Hz, 1H) H-1'; 5.1 (dd, $J_{1',2'}$ = 5.8 Hz, $J_{2',3'}$ = 8.2 Hz, 1H) H-2'; 4.71 (m, 1H) H-4'; 4.19 (m, 3H) H-3', H-5', H-5". ^{13}C-NMR ($CDCl_3$) : 89.9 (d, J_{CH} = 168.5 Hz) C-1'; 80.1 (d, J_{CH} = 153.8 Hz) C-4'; 75.7 (d, J_{CH} = 146.5 Hz) C-2'; 69.3 (d, J_{CH} = 136.7 Hz) C-3'; 61.8 (t, J_{CH} = 141.6 Hz) C-5'; 21.6 (q, J_{CH} = 125.0 Hz) -CH_3.

N^6,N^6-dibenzoyl-9-[3'-deoxy-3'-(p-toluenesulfonyl)-5'-O-(MMTr)-β-D-xylofuranosyl]adenine (17): Compound **16** (4.3 g, 7 mmol) was dried by co-evaporation with pyridine and was dissolved in the same solvent (70 ml). 4-methoxytrityl chloride (4.3 g, 14 mmol) was added and the solution was stirred for 24 h at 20 °C. After usual work up the compound was purified on silica gel column. Yield 5.7 g (92%). ^{1}H-NMR ($CDCl_3$ + CD_3OD) : 8.52 (s, 1H) H-8; 8.34 (s, 1H) H-2; 7.86-6.79 (m, 28H) arom.; 5.9 (d, $J_{1',2'}$ = 4.4 Hz,1H) H-1'; 5.02 (t, $J_{1',2'}$ = 4.4 Hz, $J_{2',3'}$ = 4.6 Hz, 1H) H-2'; 4.7 (m, 1H) H-4'; 4.07 - 3.6 (m, 6H) H-3', H-5', H-5", -OCH_3; 2.39 (s, 3H) -CH_3. ^{13}C-NMR ($CDCl_3$) : 90.5 (d, J_{CH} = 163.6 Hz) C-1'; 79.5 (d, J_{CH} = 162.3 Hz), 76.8 (d, J_{CH} = 151.4 Hz), 70.2 (d, J_{CH} = 140.4 Hz) C-2', C-3', C-4'; 63.1 (t, J_{CH} = 143.4 Hz) C-5'; 55.2 (q, J_{CH} = 144.0 Hz) -OCH_3; 21.6 (q, J_{CH} = 125.0 Hz) -CH_3.

N^6,N^6-dibenzoyl-9-[3'-deoxy-3'-(p-toluenesufonyl)-5'-O-(MMTr)-β-D-glyceropent-2-enofuranosyl]-adenine (18): Compound **17** (5.5 g, 6.3 mmol) was dissolved in pyridine (63 ml) and the solution was cooled down in an ice bath. Methanesulfonyl chloride (9.6 ml, 126 mmol) was added and the resulting solution was left at 0 - 4 °C for 24 h. The reaction mixture was worked up in the usual way. The product was then purified on a silica gel column. Yield 4.45 g (81%). ^{1}H-NMR ($CDCl_3$) : 8.48 (s, 1H) H-8; 8.01 (s, 1H) H-2; 7.86-7.16 (m, 27H) arom., H-1'; 6.85 (t, $J_{1',2'}$ = 1.7 Hz, $J_{2',4'}$ = 2.2 Hz, 1H) H-2'; 6.66 (d, 2H) arom.; 5.24 (m, 1H) H-4'; 3.71 (s, 3H) -OCH_3; 3.41 (m, 2H) H-5', H-5"; 2.43 (s, 3H) -CH_3. ^{13}C-NMR ($CDCl_3$) : 87.5 (d, J_{CH} = 170.9 Hz) C-1'; 85.3 (d, J_{CH} = 151.9 Hz) C-4'; 63.9 (t, J_{CH} = 142.8 Hz) C-5'; 21.7 (q) -CH_3. MS (FAB^+): calc. for $(M+H)^+$ 868.2805, found 868.2829.

Preparations of 19a & 24a: Aqueous ammonia (37%, 1 ml) was added to a solution of compound **18** (0.3 g, 0.35 mmol) in dioxane (2.4 ml). The resulting solution was heated at 50 ° for 3 h. It was cooled and all volatile matters were removed in vacuuo. The residue was taken in chloroform (50 ml) and washed with water (25 ml). Organic layer was dried on $MgSO_4$ and evaporated to dryness. The dichloromethane solution of the residue, which was a mixture to two compounds in almost 1:1 ratio (EtOAc:EtOH:Et3N 8:1:1, v/v/v), was loaded on a silica gel column made of the same solvent. The compound corresponding to the higher Rf was eluted with 2% ethanol in dichloromethane. Appropriate fractions were collected and evaporated to afford compound **24a** as a white glass. Yield: 0.1 g (42%). ^{1}H-NMR ($CDCl_3$+CD_3OD) : 8.16 (s, 1H) H-8; 7.99 (s, 1H) H-2; 7.69-6.78 (m, 18H) arom.; 6.06 (d, $J_{1',2'}$ = 7.3 Hz, 1H) H-1'; 4.84 (t, $J_{1',2'}$ = 7.3 Hz, $J_{2',3'}$ = 7.9 Hz,1H) H-2'; 4.56 (m, 1H) H-4'; 4.15 (dd, $J_{2',3'}$ = 7.9 Hz, $J_{3',4'}$ = 4.6 Hz, 1H) H-3'; 3.79 (s, 3H) -OCH_3; 3.44, 2.78 (m, 2H) H-5', H-5"; 2.41 (s, 3H) -CH_3. ^{13}C-NMR ($CDCl_3$+CD_3OD) : 90.2 (d, J_{CH} = 159.9 Hz) C-1'; 78.0 (d,J_{CH} = 152.6 Hz) C-4'; 65.0 (d, J_{CH} = 162.4 Hz) C-3'; 63.5 (t, J_{CH} = 145.9 Hz) C-5'; 57.9 (d, J_{CH} = 159.9 Hz) C-2'. Further elution of the column with 4% ethanol in dichloromethane afforded compound **19a** as white foam. Yield: 0.11 g (46%). ^{1}H-NMR ($CDCl_3$+CD_3OD): 8.25 (s, 1H) H-8; 8.12 (s, 1H) H-2; 7.3-6.8 (m, 18H) arom.; 5.92 (d, $J_{1',2'}$ = 5.8 Hz, 1H) H-1'; 4.59 (m, 1H) H-4'; 4.19 (t, $J_{1',2'}$ = 5.8 Hz, $J_{2',3'}$ = 6.8 Hz, 1H) H-2'; 3.81 (m, 6H) H-3', H-5', H-5", -OCH_3; 2.42 (s, 3H) -CH_3. ^{13}C-NMR ($CDCl_3$+CD_3OD) : 90.2 (d, J_{CH} = 158.7 Hz) C-1'; 78.5 (d, J_{CH} = 140.0 Hz) C-4'; 71.5 (d, J_{CH} = 145.3 Hz) C-2' or C-3'; 63.5 (t, J_{CH} = 149.0 Hz) C-5'; 59.7 (d, J_{CH} = 139.3 Hz) C-3' or C-2'.

Preparations of 19b & 24b: Compound **18** (0.43 g, 0.5 mmol) was treated with aqueous solution of methylamine (40%, 1 ml) in tetrahydrofuran (1.2 ml) in the same way as described for amino compounds. Purification on a silica gel column afforded compound **24b** as white foam. Yield 0.22 g (65%). ^{1}H-NMR ($CDCl_3$) : 8.14 (s, 1H) H-8; 7.89 (s, 1H) H-2; 7.73-6.78 (m, 18H) arom.; 6.11 (d, $J_{1',2'}$ = 8.0 Hz, 1H) H-1'; 4.71 (t, $J_{1',2'}$ = 8.0 Hz, $J_{2',3'}$ = 7.6 Hz, 1H) H-2'; 4.47 (m, 1H) H-4'; 4.08 (dd, $J_{2',3'}$ = 7.6 Hz, $J_{3',4'}$ = 3.0 Hz, 1H) H-3'; 3.79 (s, 3H) -OCH_3; 3.57, 2.96 (m, 2H) H-5', H-5"; 2.41 (s, 6H) -CH_3, -$NHCH_3$. ^{13}C-NMR : ($CDCl_3$) 88.5 (d, J_{CH} = 168.2 Hz) C-1'; 77.8 (d, J_{CH} = 150.1 Hz), 64.9 (d, J_{CH} = 141.6 Hz), 63.6 (d, J_{CH} = 146.5 Hz) C-2', C-3', C-4'; 63.6 (t, J_{CH} = 143.5 Hz) C-5'; 35.7 (q, J_{CH} = 130.3 Hz) -NCH_3.Compound **19b:** Yield: 0.05 g.(15%). ^{1}H-NMR ($CDCl_3$ + CD_3OD): 8.31 (s, 1H) H-8; 8.29 (s, 1H) H-2; 7.61 - 6.77 (m, 14H) arom.; 6.0 (d, $J_{1',2'}$ = 4.4 Hz, 1H) H-1'; 4.57 (m, 1H) H-4'; 4.1 -3.5 (m, 7H) H-2', H-3', H-5', H-5",-OCH_3; 2.4 (s, 3H) -CH_3; 1.99 (s, 3H) -$NHCH_3$. ^{13}C-NMR ($CDCl_3$): 88.4 (d, J_{CH} = 163.6 Hz) C-1'; 79.3 (d, J_{CH} = 152.6 Hz), 69.2 (d, J_{CH} = 140.4 Hz), 68.8 (d, J_{CH} = 140.4 Hz) C-2', C-3', C-4'; 63.0 (t, J_{CH} = 144.0 Hz) C-5'; 33.7 (q) -NCH_3.

Preparations of 19c & 24c: Compound **18** (0.43 g, 0.5 mmol) was treated with aqueous solution of dimethylamine (40%, 2 ml) in tetrahydrofuran (2 ml) in the same way as described for amino compounds. Two isomers, which were formed in an approximate ratio of 1:1 (tlc, EtOAc:EtOH:Et3N 8:1:1) were separated by silica gel column chromatography. Compound **24c** : Yield 0.11 g (31%). ^{1}H-NMR ($CDCl_3$) : 8.17 (s, 1H) H-8; 7.93 (s, 1H) H-2; 7.79-6.78 (m, 18H) arom.; 6.42 (d, $J_{1',2'}$ = 7.1 Hz, 1H) H-1'; 4.76 (m, 1H) H-4'; 4.38 (t, $J_{1',2'}$ = 7.1 Hz, $J_{2',3'}$ = 7.3 Hz, 1H) H-2'; 4.14 (dd, $J_{2',3'}$ = 7.3 Hz, $J_{3',4'}$ = 3.7 Hz, 1H) H-3'; 3.79 (s, 3H) -OCH_3; 3.56, 3.11 (m, 2H) H-5', H-5"; 2.43 (s, 3H) -CH_3; 2.15 (s, 6H) -$N(CH_3)_2$. ^{13}C-NMR ($CDCl_3$) : 84.9 (d, J_{CH} = 169.7 Hz) C-1'; 77.7 (d, J_{CH} = 151.4 Hz) C-4'; 69.2 (d, J_{CH} = 145.3 Hz), 65.6 (d, J_{CH} = 147.7 Hz) C-2', C-3'; 64.6 (t, J_{CH} = 142.8 Hz) C-5'; 43.6 (q, J_{CH} = 134.8 Hz) -$N(CH_3)_2$. Compound **19c:** Yield: 0.12 g (34%). ^{1}H-NMR ($CDCl_3$+CD_3OD) : 8.48 (s, 1H) H-8; 8.32 (s, 1H) H-2; 7.6-6.8 (m, 18H) arom.; 6.24 (d, $J_{1',2'}$ = 4.9 Hz, 1H) H-1'; 4.19-3.65 (m, 8H) H-2', H-3', H-4',H-5', H-5", -OCH_3; 2.41 (s, 3H) -CH_3; 2.04 (s, 6H) -

$N(CH_3)_2$. ^{13}C-NMR ($CDCl_3$) : 83.7 (d, J_{CH} = 158.7 Hz) C-1'; 80.0 (d, J_{CH} = 149.9 Hz), 73.8 (d, J_{CH} = 144.0 Hz), 64.4 (d, J_{CH} = 141.6 Hz) C-2', C-3', C-4'; 63.0 (t, J_{CH} = 147.7 Hz) C-5'; 41.5 (q, J_{CH} = 134.8 Hz) -$N(CH_3)_2$.

Preparation of 19d: Benzylamine (2 ml, 20 mmol) was added to a solution of compound **18** (0.43 g, 0.5 mmol) in dichloromethane (10 ml). The solution was stirred overnight at 20 ° and then heated at 50 ° for 3 h. It was cooled and diluted with chloroform (25 ml). The chloroform solution was washed with aqueous solution of citric acid (10%, 3 x 25 ml) and then dried on magnesium sulfate. It was then filtered and the filtrate was evaporated to dryness. The compound was then purified on a silica gel column to give the title compound as off white foam. Yield: 0.35 g (91%). ^{1}H-NMR ($CDCl_3$) : 8.34 (s, 1H) H-8, 8.15 (s, 1H) H-2; 7.26-6.82 (m, 23H) arom.; 6.08 (d, $J_{1',2'}$ = 4,9 Hz, 1H) H-1'; 4.55 (m, 1H) H-4';; 3.96 (m, 2H) H-2',H-5' or H-5"; 3.79 (s, 3H) -OCH_3; 3.6 (m,2H) H-3', H-5' or H-5"; 3.41 (s, 2H) -NCH_2; 2.39 (s, 3H) -CH_3. ^{13}C-NMR ($CDCl_3$) : 88.7 (d, J_{CH} = 152.8 Hz) C-1'; 79.1 (d, J_{CH} = 142.6 Hz) C-4'; 70.2 (d, J_{CH} = 131.4 Hz) C-3'; 66.3 (d, J_{CH} = 133.7 Hz) C-2'; 63.0 (t, J_{CH} = 132.0 Hz) C-5'; 50.9 (t, J_{CH} = 124.1 Hz) -NCH_2.

Preparation of 19e: Compound **18** (0.43 g, 0.5 mmol) was treated with pyrrolidine (0.8 ml, 10 mmol) in tetrahydrofuran (10 ml) for 3 days at 20 ° and then heated at 60 ° for 4 h. All volatile matters were removed in vacuuo and the residue was dissolved in chloroform (30 ml). the solution was washed with aqueous solution of citric acid (10%, 3 x 25 ml) and dried on magnsium sulfate. It was filtered and the filtrate was evaporated to dryness. The compound was then purified on a silica gel column. Yield: 0.29 g (80%).^{1}H-NMR ($CDCl_3$) : 8.53 (s, 1H) H-8; 8.38 (s, 1H) H-2; 7.66-6.78 (m, 18H) arom.; 6.28 (d, [illegible] (t, J_{CH} = 136.2 Hz), 23.0 (t, J_{CH} = 132.4 Hz) pyrrolidine.

Preparation of 19f: A solution of compound **18** (0.43 g, 0.5 mmol) in tetrahydrofuran (10 ml) was treated with piperidine (1 ml, 10 mmol) for 2 days at 20 ° and then at 60 ° for 1 day. It was worked up and purified in the same way as reported for pyrrolidino compound. Yield: 0.32 g (87%). ^{1}H-NMR ($CDCl_3$) : 8.43 (s, 1H) H-8; 8.36 (s, 1H) H-2; 7.63-6.78 (m, 18H) arom.; 6.28 (d, $J_{1',2'}$ = 5.4 Hz, 1H) H-1'; 4.41-3.57 (m, 8H) H-2', H-3', H-4',H-5', H-5", -OCH_3; 2.4 (s, 3H) -CH_3; 2.22 (br, 4H), 1.32 (br, 6H) piperidine. ^{13}C-NMR ($CDCl_3$) : 82.3 (d, J_{CH} = 170.9 Hz) C-1'; 79.6 (d, J_{CH} = 147.7 Hz), 73.8 (d, J_{CH} = 130.6Hz), 64.1 (d, J_{CH} = 144.0 Hz) C-2', C-3', C-4'; 62.8 (t, J_{CH} = 146.5Hz) C-5'; 50.2 (t, J_{CH} = 134.3 Hz), 25.4 (t, J_{CH} = 126.9 Hz), 23.6 (t, J_{CH} = 125.1 Hz) piperidine.

Preparation of 19g: A solution of compound **18** (0.43 g, 0.5 mmol) in tetrahydrofuran (10 ml) was treated with morpholine (0.9 ml, 10 mmol) for 3 days at 20 ° and then at 60 ° for 2 days. It was worked up and purified in the same way as reported for pyrrolidino compound. Yield: 0.34 g (91%). ^{1}H-NMR ($CDCl_3$) : 8.44 (s, 1H) H-8; 8.36 (s, 1H) H-2; 7.65-6.78 (m, 18H) arom.; 6.25 (d, $J_{1',2'}$ = 5.4 Hz, 1H) H-1'; 4.16-3.66 (m, 8H) H-2'; H-3'; H-4', H-5', H-5", -OCH_3; 3.47 (br, 4H) morpholine; 2.41 (s, 3H) -CH_3; 2.23 (br, 4H) morpholine. ^{13}C-NMR ($CDCl_3$) : 82.9 (d, J_{CH} = 170.9 Hz) C-1'; 79.7 (d, J_{CH} = 139.1 Hz), 73.6 (d, J_{CH} = 144.0 Hz), 64.4 (d, J_{CH} = 141.6 Hz) C-2', C-3', C-4'; 66.5 (t, J_{CH} = 144.6 Hz) morpholin; 62.9 (t, J_{CH} = 148.9 Hz) C-5'; 50.0 (t, J_{CH} = 131.8 Hz) morpholine.

Preparation of 20: Sodium hydride (80% in oil, 0.15 g, 5 mmol) was added to dimethyl malonate (1.2 ml, 10 mmol) in tetrahydrofuran (10 ml). The mixture was stirred at 20 ° until almost all the solid disappears. Compound **18** (0.43 g, 0.5 mmol) was added to it and the resulting solution was stirred for 6 h at 20 °. All volatile matters were removed in vacuuo and the residue was dissolved in ethylacetate (30 ml). It was washed with saturated solution of $NaHCO_3$ (3 x 25 ml). The organic layer was dried on magnesium sulfate, filtered and evaporated to dryness. The residue was treated with aqueous acetic acid (80%, 25 ml) for 4 h at 20 °. All volatile matters were removed and the residue was purified on a silica gel column. The title compound was isolated as a white powder. Yield: 0.23 g (74%). ^{1}H-NMR ($CDCl_3$) : 8.78 (s, 1H) H-8; 8.65 (s, 1H) H-2; 8.11-7.36 (m, 9H) arom.; 6.55 (d, $J_{1',2'}$ = 6.35 Hz, 1H) H-1'; 4.64 (m, 1H), 4.2 (m, 3H), 3.62 (m, 5H) H-2', H-3', H-4', H-5', H-5", -OCH_3, malonate -CH-; 3.29 (s, 3H) -OCH_3; 2.47 (s, 3H) -CH_3. ^{13}C-NMR ($CDCl_3$+CD_3OD) : 84.5 (d, J_{CH} = 162.4 Hz) C-1'; 80.8 (d, J_{CH} = 157.4 Hz), 66.4 (d, J_{CH} = 147.7 Hz), 50.4, 46.9 (d, J_{CH} = 155.0 Hz) C-2', C-3', C-4', malonate -CH-; 61.3 (t, J_{CH} = 146.5 Hz) C-5'; 53.0 (q, J_{CH} = 152.6 Hz) -OCH_3. MS (FAB$^+$): calc. for $(M+H)^+$ 624.1762, found 624.1741.

Preparation of 23: Compound **18** (0.43 g, 0.5 mmol) was dissolved in dioxane (10 ml). Aqueous solution of sodium hydroxide (1 M, 1 ml) was added and the mixture was stirred at 20 ° for 2 h. Dichloromethane (50 ml) was added, organic layer separated and washed with aqueous solution of citric acid (10%, 25 ml). Organic layer was dried over magnesium sulfate, filtered and the filtrate was dried in vacuuo. The major product was isolated by column chromatography. The compound was dissolved in minimum volume of tetrahydrofuran and saturated solution of ammonia in methanol (25 ml) was added. The mixture was stirred overnight at 20 °. All volatile matters were removed and the residue was purified on silica gel column to afford the title compound as white foam. Yield: 0.16 g (48%). ^{1}H-NMR ($CDCl_3$+$CD3O_D$) : 8.14 (s, 1H) H-8; 8.06 (s, 1H) H-2; 7.8-6.76 (m, 18H) arom.; 6.05 (d, $J_{1',2'}$ = 3.9 Hz, 1H) H-1'; 5.1 (dd, $J_{1',2'}$ = 3.9 Hz, $J_{2',3'}$ = 6.3 Hz, 1H) H-2', 4.9 (m, 1H) H-4'; 4.28 (t, $J_{2',3'}$ = 6.3 Hz, $J_{3',4'}$ = 6.6 Hz, 1H) H-3'; 3.78 (s, 3H) -OCH_3; 3.62,3.23 (ddd, 2H) H-5', H-5"; 2.42 (s, 3H) -CH_3. ^{13}C-NMR ($CDCl_3$+CD_3OD) : 90.4 (d, J_{CH} = 167.2 Hz) C-1'; 78.5 (d, J_{CH} = 153.8 Hz), 74.7 (d, J_{CH} = 151.4 Hz) C-2', C-4'; 64.9 (d, J_{CH} = 144.0 Hz) C-3'; 63.4 (t, J_{CH} = 141.6 Hz) C-5'. MS (FAB$^+$): calc. for $(M+H)^+$ 678.2386, found 678.2360.

General procedure for the removal of 5'-O-MMTr group from 19 & 24: Compounds **19a-g** and **24a-c** (0.4 mmol each) were treated with aqueous acetic acid (80%, 25 ml) for 9-12 h at 20 °. After completion of the reaction (tlc) all volatile matters were removed *in vacuuo*. Residual acetic acid was removed by repeated coevaporation with ethanol and toluene. The residues were purified on silica gel columns to afford compounds **21a-g** and **25a-c** respectively.

Compound 25a Yield: 0.11 g (68%). ^{1}H-NMR (DMSO-d_6, 80°) : 8.39 (s, 1H) H-8; 8.27 (s, 1H) H-2; 8.02, 7.61 (dd, 4H) arom.; 6.09 (d, $J_{1',2'}$ = 7.3 Hz, 1H) H-1'; 4.72-4.33 (m, 3H) H-2', H-3', H-4'; 3.87-3.36 (m, 2H) H-5', H-5"; 2.55 (s, 3H) -CH_3. ^{13}C-NMR (DMSO-d_6) : 89.1 (d, J_{CH} = 163.6 Hz) C-1'; 78.6 (d, J_{CH} = 151.4 Hz), 64.7 (d, J_{CH} = 148.9 Hz), 57.2 (d, J_{CH} = 146.5 Hz) C-2', C-3', C-4'; 62.9 (t, J_{CH} = 144.6 Hz) C-5'; 21.2 (q, J_{CH} = 129.4 Hz) -CH_3. MS (FAB$^+$) : calc. for $(M+H)^+$ 405.1345, found 405.1344. **Compound 21a** Yield : 0.1 g. (62%) ^{1}H-NMR ($CDCl_3$+ CD_3OD) : 8.37 (s, 1H) H-8; 8.23 (s, 1H) H-2; 7.85 , 7.43 (dd, 4H) arom.; 5.83 (d, $J_{1',2'}$ = 6.6 Hz, 1H) H-1'; 4.6-3.97 (m, 5H) H-2',H-3', H-4', H-5', H-5"; 2.48 (s, 3H) -CH_3. ^{13}C-NMR : (DMSO-d_6) : 87.9 (d, J_{CH} = 163.6 Hz) C-1'; 79.4 (d, J_{CH} = 155.0 Hz), 69.6 (d, J_{CH} = 146.5 Hz), 58.1 (d, J_{CH} = 141.6 Hz) C-2', C-3'; C-4'; 60.6 (t, J_{CH} = 144.0 Hz) C-5'; 21.2 (q, J_{CH} = 125.7 Hz) -CH_3. MS (FAB+): calc. for $(M+H)^+$ 405.1345, found 405.1336. **Compound 25b:** Yield: 0.14 g

(84%).^{1}H-NMR : ($CDCl_3$+CD_3OD) : 8.23 (s, 1H) H-8; 8.01 (s, 1H) H-2; 7.89, 7.46 (dd, 4H) arom.; 6.03 (d, $J_{1',2'}$ = 7.6 Hz, 1H) H-1'; 4.52-4.34 (m, 3H) H-2'; H-3'; H-4'; 3.87, 3.19 (ddd, 2H) H-5', H-5"; 2.5 (s, 3H) -CH_3; 2.3 (s, 3H) -NCH_3. ^{13}C-NMR ($CDCl_3$+CD_3OD) : 90.9 (d, J_{CH} = 166.0 Hz) C-1'; 80.6 (d, J_{CH} = 150.1 Hz), 66.7 (d, J_{CH} = 144.0 Hz), 64.3 (d, J_{CH} = 144.0 Hz) C-2', C-3', C-4'; 63.9 (t, J_{CH} = 142.2 Hz) C-5'; 35.7 (q) -$NHCH_3$; 21.7 (q) -CH_3. MS (FAB^+): calc. for $(M+H)^+$ 419.1502, found 419.1519. **Compound 25c** : Yield: 0.17 g (98%).^{1}H-NMR ($CDCl_3$+CD_3OD) : 8.23 (s, 1H) H-8; 8.16 (s, 1H) H-2; 7.89, 7.39 (dd, 4H) arom.; 6.47 (d, $J_{1',2'}$ = 7.1 Hz, 1H) H-1'; 4.81 (m, $J_{4',5'}$ = 1.7 Hz, 1H) H-4'; 4.29-4.13 (m, 2H) H-2', H-3'; 3.95, 3.44 (ddd, $J_{4',5'}$ = 1.7 Hz, $J_{4',5"}$ = 1.9 Hz, $J_{5',5"}$ = 12.8 Hz, 2H) H-5', H-5"; 2.48 (s, 3H) -CH_3; 2.04 (s, 6H) -$N(CH_3)_2$. ^{13}C-NMR (CD_3OD+$CDCl_3$) : 87.5 (d, J_{CH} = 166.0 Hz) C-1'; 79.7 (d, J_{CH} = 150.1 Hz) C-4'; 69.8 (d, J_{CH} = 140.4 Hz), 66.4 (d, J_{CH} = 147.7 Hz) C-2', C-3'; 64.5 (t, J_{CH} = 144.0 Hz) C-5'; 43.9 (q) -$N(CH_3)_2$; 21.7 (q) -CH_3. MS (FAB^+): calc. for $(M+H)^+$ 433.1658, found 433.1635. **Compound 21c.** Yield: 0.16g. (92%). ^{1}H-NMR (CD_3OD+$CDCl_3$) : 8.62 (s, 1H) H-8; 8.25 (s, 1H) H-2; 7.87, 7.45 (dd, 4H) arom. ; 6.23 (d, $J_{1',2'}$ = 5.6 Hz, 1H) H-1'; 4.49-4.25 (m, 4H) H-3', H-4', H-5', H-5"; 3.93 (dd, $J_{1',2'}$ = 5.6 Hz, $J_{2',3'}$ = 3.7 Hz; 1H) H-2'; 2.48 (s, 3H) -CH_3; 1.98 (s, 6H) -$N(CH_3)_2$. ^{13}C-NMR : (CD_3OD+$CDCl_3$) : 83.9 (d, J_{CH} = 163.6 Hz) C-1'; 81.6 (d, J_{CH} = 151.4 Hz), 74.1 (d, J_{CH} = 150.1 Hz), 64.4 (d, J_{CH} = 143.0 Hz) C-2', C-3', C-4'; 61.5 (t, J_{CH} = 142.9 Hz) C-5'; 41.3 (q) -$N(CH_3)_2$; 21.8 (q) -CH_3. MS (FAB^+): calc. for $(M+H)^+$ 433.1658, found 433.1684. **Compound 21d:** Yield: 0.19 g (96%).^{1}H-NMR ($CDCl_3$ + CD_3OD) : 8.36 (s, 1H) H-8; 8.24 (s, 1H) H-2: 7.76, 7.35 (dd, 4H) toluyl; 7.11- 6.76 (m, 4H) benzyl; 6.03 (d, $J_{1',2'}$ = 4.9 Hz, 1H) H-1'; 4.58 (m, 1H), 4.22-4.05 (m, 6H) H-2', H-3', H-4'; H-5', H-5"; 3.27 (s, 2H) benzyl -CH_2-; 2.45 (s, 3H) -CH_3. ^{13}C-NMR ($CDCl_3$+CD_3OD) : 88.6 (d, J_{CH} = 164.8) C-1'; 80.7 (d, J_{CH} = 156.2 Hz), 69.6 (d, J_{CH} = 139.1 Hz), 65.8 (d, J_{CH} = 128.5 Hz) C-2'; C-3'; C-4'; 61.4 (t, J_{CH} = 144.0 Hz) C-5'; 50.6 (t, J_{CH} = 134.9 Hz) -CH_2. MS (FAB^+): calc. for $(M+H)^+$ 495.1815, found 495.1828. **Compound 21e:** Yield: 0.11 g (61%).^{1}H-NMR ($CDCl_3$+CD_3OD) : 8.61 (s, 1H) H-8; 8.28 (s, 1H) H-2; 7.84, 7.39 (dd, 4H) arom.; 6.29 (d, $J_{1',2'}$ = 5.1 Hz, 1H) H-1'; 4.74-4.02 (m, 4H) H-3', H-4', H-5', H-5"; 3.81 (dd, $J_{1',2'}$ = 5.1 Hz, $J_{2',3'}$ = 3.6 Hz, 1H) H-2'; 2.47 (s, 3H) -CH_3; 2.18, 1.56 (br, 8H) pyrrolidine. ^{13}C-NMR ($CDCl_3$+CD_3OD) : 84.2 (d, J_{CH} = 166.0 Hz) C-1'; 80.3 (d, J_{CH} = 153.8 Hz), 71.4 (d, J_{CH} = 141.6 Hz), 66.6 (d, J_{CH} = 145.3 Hz) C-2', C-3', C-4'; 60.8 (t, J_{CH} = 144.0 Hz) C-5'; 50.4 (t), 22.7 (t) pyrrolidine; 21.5 (q) -CH_3. MS (FAB^+): calc. for $(M+H)^+$ 459.1815, found 459.1830. **Compound 21f:** Yield: 0.15 g (74%).^{1}H-NMR (CD_3OD+$CDCl_3$) : 8.58 (s, 1H) H-8; 8.24 (s, 1H) H-2; 7.88, 7.46 (dd, 4H) arom.; 6.27 (d, $J_{1',2'}$ = 6.3 Hz, 1H) H-1'; 4.58-4.21 (m, 4H) H-3', H-4', H-5', H-5"; 4.06 (t, 1H) H-2'; 2.47 (s, 3H) -CH_3; 2.18 (br, 4H), 1.22 (br, 6H) piperidine. ^{13}C-NMR (CD_3OD + $CDCl_3$) : 82.4 (d, J_{CH} = 166.0 Hz) C-1'; 81.0 (d, J_{CH} = 161.1 Hz), 74.1 (d, J_{CH} = 142.8 Hz), 64.4 (d, J_{CH} = 146.5 Hz) C-2', C-3', C-4'; 61.6 (t, J_{CH} = 146.5 Hz) C-5'; 50.8 (t), 25.9 (t), 24.0 (t) piperidine; 21.7 (q) -CH_3. MS (FAB^+): calc. for $(M+H)^+$ 473.1971, found 473.1978. **Compound 21g:** Yield: 0.14 g (77%).^{1}H-NMR (CD_3OD+$CDCl_3$) 8.64 (s, 1H) H-8; 8.28 (s, 1H) H-2; 7.9, 7.46 (dd, 4H) arom.; 6.28 (d, $J_{1',2'}$ = 6.1 Hz, 1H) H-1'; 4.47-4.23 (m, 4H) H-3', H-4', H-5', H-5"; 4.05 (t, $J_{1',2'}$ = 6.1 Hz, $J_{2',3'}$ = 5.1 Hz, 1H) H-2'; 3.3 (m, 4H) morpholine; 2.48 (s, 3H) -CH_3; 2.24 (m, 4H) morpholine. ^{13}C-NMR (CD_3OD+$CDCl_3$) : 83.6 (d, J_{CH} = 164.8 Hz) C-1'; 81.9 (d, J_{CH} = 147.7 Hz), 74.2 (d, J_{CH} = 145.0 Hz), 64.7 (d, J_{CH} = 145.3 Hz) C-2'; C-3'; C-4'; 62.2 (t, J_{CH} = 144.0 Hz) C-5'; 67.5 (t), 50.4 (t) morpholine.MS (FAB^+): calc. for $(M+H)^+$ 475.1764, found 475.1781.

9-[2',3'-Dideoxy-2'(R)-2'-amino-5'-0-(MMTr)-β-D-glycero-pentofuranosyl]adenine (26a): Compounds **19a** + **24a** (1.4 g, 2.0 mmol) was dissolved in minimum amount of dry tetrahydrofuran. Dry methanol (20 ml) and disodium hydrogen phosphate (2.3 g, 16.5 mmol) were added and the mixture was cooled down to 0-4 °. Sodium amalgam (6%, 6.3 g, 16.5 mmol of sodium) was added and the mixture was stirred vigorously at 0-4 ° for 3 h. The mixture was filtered through celite bed and the bed was washed several times with tetrahydrofuran. The solution was diluted with chloroform (150 ml) and it was washed with aqueous solution of citric acid (10%, 3 x 25 ml). The organic layer was dried on magnesium sulfate, filtered and the filtrate was evaporated to dryness. The residue was purified on silica gel. Yield. 0.25 g (23%). ^{1}H-NMR ($CDCl_3$+CD_3OD) : 8.26 (s, 1H) H-8 ; 8.12 (s, 1H) H-2; 7.29-6.81 (m, 14H) arom.; 5.96 (d, $J_{1',2'}$ = 2.4 Hz, 1H) H-1'; 4.71 (m, 1H) H-4'; 4.0 (m, 1H) H-2'; 3.79 (s, 3H) -OCH_3; 3.42 (m, 2H) H-5', H-5"; 2.2 (m, 2H) H-3', H-3". ^{13}C-NMR (CD_3OD+$CDCl_3$).: 93.0 (d, J_{CH} = 166.0 Hz) C-1'; 80.5 (d, J_{CH} = 146.5 Hz) C-4'; 65.4 (t, J_{CH} = 141.6 Hz) C-5'; 58.2 (d, J_{CH} = 147.7 Hz) C-2'; 34.5 (t, J_{CH} = 138.0 Hz) C-3'. MS (FAB^+): calc. for $(M+H)^+$ 523.2458, found 523.2486.

9-[2',3'-Dideoxy-2'(R)-2'-(1-piperidino)-5'-0-(MMTr)-β-D-glycero-pentofuranosyl]adenine.(26f): Compounds **19f** (1.1 g, 1.5 mmol) were converted to the title compound in 3 h following the procedure described for the preparation of compound **26a**. Yield: 0.15 g (17%). ^{1}H-NMR ($CDCl_3$) : 8.27 (s, 1H) H-8; 7.97 (s, 1H) H-2; 7.29 - 6.78 (m, 14H) arom.; 6.26 (d, $J_{1',2'}$ = 4.6 Hz, 1H) H-1'; 5.88 (bs, 2H) -NH_2; 4.47 (m, 1H) H-4'; 3.78 (m, 4H) H-2', -OCH_3; 3.29 (m, 2H) H-5', H-5"; 2.55 (m, 4H) piperidine; 2.33 (m, 2H) H-3', H-3"; 1.54 (m, 6H) piperidine.^{13}C-NMR ($CDCl_3$) : 87.2 (d, J_{CH} = 163.6 Hz) C-1'; 79.3 (d, J_{CH} = 155.0 Hz) C-4'; 69.9 (d, J_{CH} = 137.9 Hz) C-2'; 65.9 (t, J_{CH} = 142.2 Hz) C-5'; 55.1 (q) -OCH_3; 51.7 (t) piperidine; 29.9 (t, J_{CH} = 131.8 Hz) C-3'; 25.8 (t), 24.1 (t) piperidine. MS (FAB^+): calc. for $(M+H)^+$ 591.3083, found 591.3071.

9-[2',3'-Dideoxy-2'(R)-2'-(4-morpholino)-5'-0-(MMTr)-β-D-glycero-pentofuranosyl]adenine (26g): A mixture of magnesium turnings (0.24 g, 10 mmol) in dry methanol (20 ml) was heated under stirring at 50 °C until the evolution of hydrogen started. **19g**, (0.75 g, 1 mmol) was added to the mixture and it was stirred at 50 ° for 24 h. It was cooled, poured into an aqueous solution of ammonium chloride (10%, 100 ml) and stirred for a while. The aqueous solution was extracted with chloroform (3 x 25 ml). Organic layers were pooled together, dried on $MgSO_4$, filtered and the filtrate was dried under vacuuo. The residue was purified on silica gel column . Yield: 0.15 g (13%).^{1}H-NMR ($CDCl_3$+ CD_3OD) :

[redacted]

morpholine; 65.5 (t, J_{CH} = 142.8 Hz) C-5'; 55.1 (q) -OCH_3; 51.1 (t) morpholine; 29.4 (t, J_{CH} = 131.8 Hz) C-3'. MS (FAB^+): calc for $(M+H)^+$ 593.2876, found 593.2844.

1-[5′-O-(MMTr)-2′,3′-dideoxy-2′(R)-2′-azido-5′-O-(MMTr)-β–D-glycero-pentofuranosyl]uracil (29): 1-[3′-deoxy-2′(S)-2′-O-methanesulfonyl-5′-O-(MMTr)-β-D-glycero-pentofuranosyl]uracil, prepared using an identical procedure described for cytidine (ref. 56) (579 mg, 1mmol) was dissolved in dry DMF (10ml / mmole) and sodium azide (325 mg,5 mmol) was added.After stirring for 1 hour at 115 °C. An usual work up and a column chromatographic purification gave **29** as a white foam in 87% yield. ^{1}H-NMR ($CDCl_3$): 8.82 (s, 1H) H-3; 8.03 (d, 1H, $J_{5,6}$ = 8.3 Hz) H-6; 7.54 to 6.75,aromatic protons; 5.87 (bs, 1H) H-1′; 5.32 (dd, 1H, $J_{3',5}$ = 2.2 Hz) H-5; 4.45 (m, 1H) H-4′; 4.30 (m, 1H) H-2′; 3.80 (s, 3H) OCH_3; 3.50 (ddd, 2H, $J_{4',5'}$ = 2.7 Hz, $J_{4',5''}$ = 3.0Hz, $J_{5',5''}$ = 11.5 Hz) H-5′and H-5′′; 2.08 (m, 2H, $J_{3',3''}$ = 13.4 Hz) H-3′ and H-3′′. ^{13}C-NMR ($CDCl_3$): 163.0 (d, J_{CH} = 11 Hz) C-4; 159.2 (m) OCH_3-bearing carbon; 150.6 (d, J_{CH} = 8.5 Hz) C-2; 144.7, 144.4, 135.2, 130.7, 128.7, 128.1, 127.3, aromatic carbons; 135.2 (d, J_{CH} = 184.0 Hz) C-6; 113.4 (d, J_{CH} = 184.0 Hz) carbons ortho to OCH_3; 101.4 (d, J_{CH} = 174.6 Hz) C-5; 90.2 (d, J_{CH} = 176.4 Hz) C-1′; 87.1 (s) quaternary carbon of MMTr; 80.7 (d, J_{CH} = 152.6 Hz) C-4′; 66.7 (d, J_{CH} = 156.3 Hz) C-2′; 63.6 (t, J_{CH} = 139.2 Hz) C-5′; 54.9 (t, J_{CH} = 144 Hz) OCH_3; 31.2, C-3′.UV (95% EtOH): 263nm (ε = 10900), MS (FAB$^-$): calc. for (M-H)$^-$ 524.1934, found 524.1916.

1-[2′,3′-Dideoxy-2′(R)-2′-amino-5′-O-(MMTr)-β–D-glycero-pentofuranosyl]uracil (30): Compound **29** (115 mg,0.22 mmol) was dissolved in 5ml of methanol ccontaining a suspension of Pd/C in an atmosphere of hydrogen gas.which slowly bubbled into the heterogeneous reaction mixture for 3 h.Thin layer chromatography at that time showed complete reduction of the azido group while cleavage of the 5′-O-monomethoxytrityl remained negligible.The catalyst was removed by filtration on a celite bed, the methanolic solution evaporated to dryness to give a foam which was purified by short column chromatography to give pure **30** in 79% yield. ^{1}H-NMR (CD_3COCD_3+CD_3OD): 8.15 (d, 1H, $J_{5,6}$ = 8.3 Hz) H-6; 5.91 (d, 1H, $J_{1',2'}$ = 1.7 Hz) H-1′; 5.35 (d, 1H)H-5; 4.71 (m, 1H, $J_{3',4'}$ = 5.6 Hz, $J_{3'',4'}$ = 5.1 Hz) H-4′; 4.40 (m, 1H, $J_{2',3'}$ =2 .3 Hz, $J_{2',3''}$ = 6.0 Hz) H-2′; 3.91 (s, 3H) OCH_3; 3.58 (m, 2H, $J_{4',5'}$ = 2.4 Hz) H-5′; 3.00 (bs, 2H exchangeable) 2′-NH_2; 2.57 (m, 2H) H-3′and H-3′′. ^{13}C-NMR(CD_3COCD_3): 166.4, C-4; 160.6, OCH_3-bearing carbon; 152.7, C-2; 142.3 (d, J_{CH} = 187 Hz) C-6; 145.8, 145.6, 136.5, 132.0, 129.9, 129.2, 128.5, aromatic carbons; 114.5 (dd, J_{CH} = 156 Hz, J_{CH} = 5 Hz) carbons ortho to OCH_3; 102.4 (d, J_{CH} = 177 Hz) H-5; 94.0 (d, J_{CH} = 171 Hz) C-1′; 88.6, quaternary carbon of monomethoxytrityl; 81.2 (d, J_{CH} = 150 Hz) C-4′; 65.7 (t, J_{CH} = 143 Hz) C-5′; 59.0 (d, J_{CH} = 142 Hz) C-2′; 34.7 (t, J_{CH} = 130 Hz) C-3′.UV (95% EtOH): 259nm (ε=8900). MS (FAB$^-$): calc. for (M-H)$^-$ 498.2029, found 498.2003.

1-(2′,3′-Dideoxy-2′(R)-2′-amino-β–D-glycero-pentofuranosyl)uracil (12a): Compound **30** was treated for 5 h with 80% acetic acid at 20 °C. After evaporation, redissolving of the glass in water and washing with diethyl ether, lyophilization of the aqueous extracts gave the ammonium acetate salt of **12a** in 83% yield. ^{1}H-NMR (D_2O): 7.83 (d, 1H, $J_{5,6}$ = 8.3 Hz); 5.95 (d, 1H, $J_{1',2'}$ = 3.9 Hz) H-1′; 5.82 (d, 1H) H-5; 4.50 (m, 1H) H-4′; 4.03 (m, 1H) H-2′; 3.73 (ddd, 2H, $J_{4',5'}$ = 2.9 Hz, $J_{4',5''}$ = 4.9 Hz, $J_{5',5''}$ = 12.5 Hz) H-5′and H-5′′; 2.24 (m, 2H) H-3′ and H-3′′; 1.85 (s, 3H) acetate.^{13}C-NMR (D_2O): 182.0 (s) acetate; 167.6 (d, J_{CH} = 11 Hz) C-4; 156.5 (d, J_{CH} = 7.3 Hz) C-2; 142.1 (d, J_{CH} = 185.6 Hz) C-6; 102.9 (d, J_{CH} = 178.2 Hz) C-5; 85.6 (d, J_{CH} = 170.9 Hz) C-1′; 81.5 (d, J_{CH} = 150.1 Hz) C-4′; 63.0 (t, J_{CH} = 143 Hz) C-5′; 56.1 (d, J_{CH} = 155 Hz) C-2′; 30.7 (t, J_{CH} = 131 Hz) C-3′; 23.5 (q) acetate. UV (water): 260 nm (pH 7), 301 nm (pH 1), 262 nm (pH 14).MS (FAB$^-$): calc. for (M-H)$^-$ 226.0828, found 226.0827. *This was identical to the Michael reaction product which was obtained from* **11a.**

N^6-(MMTr)-9-[2′,3′-dideoxy-2′(R)-2′-amino-5′-O-(MMTr)-β–D-glycero-pentofuranosyl]adenine (32): 1-[5′-O-(MMTr)-2′,3′-dideoxy-2′(R)-2′-azido-5′-O-(MMTr)-β-D-glycero-pentofuranosyl]adenine (**31**) (ref. 55) (1.4 g, 1.8 mmols) was dissolved in dry THF (20 ml) and added dropwise to a suspension of $LiAlH_4$ (760 mg) in the same solvent (10 ml).After stirring for 4 h under nitrogen, the reaction was worked up in the usual way and then purified by short column chromatography to give the title compound in 80% yield. ^{1}H-NMR ($CDCl_3$): 8.02 (s, 1H) H-8; 7.96 (s, 1H, H-2); 5.83 (d, 1H, $J_{1',2'}$ = 3.4 Hz) H-1′; 4.88 (m, 1H) H-4′; 4.01 (m, 1H) H-2′; 3.77 (s, 3H) OCH_3; 3.33 (d, 2H, $J_{4',5'}$ = 4.2 Hz) H-5′; 2.25 (m, 1H) H-3′; 1.95 (m, 1H) H-3′′; 1.75 (bs, 2H exchangeable) 2′-NH_2. ^{13}C-NMR($CDCl_3$): 158.5 and 158.2, OCH_3-bearing carbons of MMTr; 153.3 (d, J_{CH} = 12 Hz) C-6; 151.9 (d, J_{CH} = 201.4 Hz) C-2; 148.3, (s), C-4; 137.7 (d, J_{CH} = 210.2 Hz) C8; 137.1, 135.1, 130.2, 130.0, 128.7,128.2,127.7,126.8, 126.6, aromatic carbons of MMTr; 121.3 (m) C-5; 113.0 (d, J_{CH} = 159.9 Hz) carbons ortho to OCH_3 of MMTr; 92.7 (d, C-1′, J_{CH} = 176 Hz) C-1′; 86.5 (s) quaternary carbon of MMTr; 79.0 (d, J_{CH} = 151.2 Hz) C-4′; 65.3 (t, J_{CH} = 144 Hz) C-5′; 57.5 (d, J_{CH} = 142.8 Hz) C-2′; 55.1 (q, J_{CH} = 142.8 Hz) OCH_3; 35.5 (t, J_{CH} = 133.1 Hz) C-3′. MS (FAB$^+$): calc. for M^+ 794.3580, found 794.3552

9-[2′,3′dideoxy-2′(R)-2′-amino-β–D-glycero-pentofuranosyl]adenine (33): Compound **32** (200 mg,0.25 mmol) was treated with 80% acetic acid at room temperature for 60 h. Evaporation of the volatile matters, followed by dissolving the residue in water, washing the aqueous phase with ether and then lyophilization of the aqueous phase gave the ammonium acetate salt of **33**,which was desalted on a Dowex OH^- column to give **33** in a quantitative yield. ^{1}H-NMR (D_2O): 8.19 (s, 1H) H-8; 8.05 (s, 1H) H-2; 5.77 (d, 1H, $J_{1',2'}$ = 4.4 Hz) H-1′; 4.41 (m, 1H) H-4′; 3.90 (m, 1H) H-2′; 3.69 (ddd, 2H, $J_{4',5'}$ = 2.9 Hz, $J_{4',5''}$ = 4.1 Hz, $J_{5',5''}$ = 12.2 Hz) H-5′and H-5′′; 2.45 (m) H-3′and H-3′′ ^{13}C-NMR (D_2O): 156.0 (s) C-6; 153.2 (d, J_{CH} = 202.3 Hz) C-2; 142.8 (s) C-4; 140.6 (d, J_{CH} = 212 Hz) C-8; 119.3 (m) C-5; 92.5 (d, J_{CH} = 164.8 Hz) C-1′; 81.9 (d, J_{CH} = 151.4 Hz) C-4′; 65.0 (t, J_{CH} = 140.3 Hz) C-5′; 55.9 (d, J_{CH} = 138.1 Hz) C-2′; 35.6 (t, J_{CH} = 135.5 Hz) C-3′. UV (water): 259.5nm (pH 7), 255 nm (pH 1), 260 nm (pH 13). MS (FAB$^-$): calc. for (M-H)$^-$ 249.1100, found 249.1070. *The product obtained in this preparation was identical to the Michael reaction product which was prepared from* **26a.**

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REFERENCES

1. M. S. Hirsch and J. C. Kaplan, *Ann. Int. Med.* **103**, 750 (1985)

2. P. Chandra et. al., *Cancer Res.(suppl)*, **45**, 4677s, (1985)
3. E. de Clercq and J. Balzarini, *Antiviral Res. Suppl.*, **1**, 89, (1985)
4. R. K. Robins, *Chem. & Eng. News*, **64**, 28, (1986)
5. R. Dagani, *ibid*, **65**, 41, (1987)
6. R. Pauwels, M. Baba, J. Balzarini, P. Herdewijn, J. Desmyter, M. J. Robins, R. Zou, D. Madej and E. de Clercq, *Biochem. Pharm.*, **37**, 1317, (1988)
7. L. Vrang, H. Bazin, G. Ramaud, J. Chattopadhyaya and B. Öberg, *Antiviral Res.*, **7**, 139, (1987)
8. B. Eriksson, L. Vrang, H. Bazin, J. Chattopadhyaya and B. Öberg, *Antimicrobial agents and Chemotherapy*, **31**, 600, (1987)
9. H. Bazin, J. Chattopadhyaya,R. Datema, A-C. Ericson, G. Gilljam, N. G. Johansson, J. Hansen, R. Koshida, K. Moelling, B. Öberg, G. Ramaud, G. Stening, L. Vrang, B. Wahren and J-C. Wu, *Pharm. Biochem.*, (in press)
10. M. Ikehara and M. Hiroto, *Chem. Pharm. Bull.*, **26**, 2449, (1978)
11. R. Ranganathan and D. Larwood, *Tet. Lett.*, 4341, (1978)
12. R. Mengel and H. Wiender, *Chem. Ber.*, **109**, 433, (1976)
13. G. Kowollik and P. Langen, *Chem. Ber.*, **101**, 235, (1968)
14. L. Colla, P. Herdewijn, E. de Clercq, J. Balzarini and H. Vanderhaeghe, *Eur. J. Med. Chem.*, **20**, 295, (1985)
15. M. Hirata, *Chem. Pharm. Bull.*, **16**, 291, (1968)
16. T. Naito, M. Hirata, Y. Nakai, T. Kobayashi and M. Kanao, *Chem. Pharm. Bull.*, **16**, 285, (1968)
17. J. G. Moffatt and J. P. H. Verheyden, *J. Org. Chem.*, **37**, 2289, (1972)
18. G. Kowollik and P. Langen, *Z. Chem.*, **15**, 147, (1975)
19. U. Reichman, D. H. Hollenberg, C. K. Chu, K. A. Watanabe and J. J. Fox, *J. Org. Chem.*, **41**, 2042, (1976)
20. D. H. Hollenberg, K. A. Watanabe and J. J. Fox, *J. Med. Chem.*, **20**, 113, (1977)
21. *CA*, **69**: 107013; *CA*, **69**: 107014
22. T. Sasaki, K. Minamoto and N. Kidokoro, *Org. Prep. Proceed. Int.*, **5**, 75, (1973)
23. A. Mete, J. B. Hobbs, D. I. C.Scopes and R. F. Newton, *Tet. Lett.*, **26**, 97, (1985)
24. M. Ashwell, A.S. Jones and R. T. Walker, *Nucleic Acids Res.*, **15**, 2157, (1987)
25. *CA*, **87** : 102604
26. R. Mengel and H. Wiender, *Chem. Ber.*, **109**, 1395, (1976)
27. M. J. Robins, Y. Fouron and R. Mengel, *J. Org. Chem.*, **39**, 1564, (1974)
28. H. Bazin and J. Chattopadhyaya, *Chem. Script.*, **26**, 13 (1986)
29. J. F. Codington, R. Fecher and J. J. Fox, *J. Org. Chem.*, **27**, 163, (1962)
30. M. J. Robins, F. Hansske, N. H. Low and J. I. Park, *Tet. Lett.*, **25**, 367, (1984)
31. H. Bazin and J. Chattopadhyaya, *Synthesis*, 1108, (1985); A. Nyilas and J. Chattopadhyaya, *Synthesis*, 196 (1986)
32. K. Miyai, R.k. Robins and R. L. Tolman, *J. Med. Chem.*, **15**, 1092, (1972)
33. J. J. Fox, *Pure Appl.Chem.* **18**, 223, (1969)
34. D. M. Brown, D. B. Parihar, A. Todd and S. Varadarajan, *J. Chem. Soc.*, 3028, (1958)
37. S. Greenberg and J. G. Moffatt , *J. Am. Chem. Soc.*, **95**, 4016, (1973)
38. A Grouiller, H. Essadiq, H. Pacheco, S. Junthunen and J. Chattopadhyaya, *Angew. Chem. Int. Ed. Engl.*, **24**, 52, 1985
39. L. H Koole, H-M. Moody, H. M. Buck, A Grouiller, H. Essadiq, J-M. Vial and J. Chattopadhyaya, *Recueil des trav. Chim. pays-bas.*, **107**, 343, (1988)
40 A. Calvo-Mateo, M-J. Camarasa, A. Diaz-Ortiz and F. G. De las Heras, *Tet. Lett.*, **29**, 941, (1988)
41. J-M. Vial, L. H Koole and J. Chattopadhyaya, *Acta Chem. Scand. Ser. B* (in press)
42. A. Matsuda, K. Takenuki, H. Itoh, T. Sasaki and T. Ueda, *Chem. Pharm. Bull.*, **35**, 3967, (1987)
43. A. Matsuda, H. Itoh, K. Takenuki,T. Sasaki and T. Ueda, *Chem. Pharm. Bull.*, **36**, 945, (1988)
44 T. Ueda, S. Satoshi and I. Hideo, *Nucleosides and Nucleotides*, **3**, 173, (1984)
45. H. Usui and T. Ueda, *Chem. Pharm. Bull.*, **34**, 1518, (1986), *and references therein*
46 T. Sano, S. Shuto, H. Inone and T. Ueda, *Chem. Pharm. Bull.*, **33**, 3617, (1985), *and references therein*
47. T. Ueda, S. Satoshi, M. Satoh and I. Hideo, *Nucleosides and Nucleotides*, **4**, 401, (1985), *and references therein*
48. H. Hayakawa, H. Tanaka, N. Itoh, M. Nakajima, T. Miyasaka, K. Yamaguchi, and Y. Iitaka, *Chem. Pharm. Bull.*, **35**, 2605, (1987)
49. T. Sasaki, K. Minamoto, T. Sugiora and M. Niwa, *J. Org. Chem.*, **41**, 3138, (1976)
50. T. Sekiya and T. Ukita, *Chem. Pharm. Bull.*, **15**, 542, (1967)
51. W. W. Lee, A. Benitez, C. D. Anderson, L. Goodman and B. R. Baker, *J. Am. Chem. Soc.*, **83**, 1906, (1961)
52. S. Shuto, T. Iwano and H. Inoue and T. Ueda,*Nucleosides and Nucleotides*, **1**, 263, (1982)
53. P. Herdewijn, J. Balzarini, E. de Clercq, R. Pauwels, M. Baba, S. Broder and H. Vanderhaeghe, *J. Med. Chem.*, **30**, 1270, (1987)
54. C. J. Welch, H. Bazin and J. Chattopadhyaya, *Acta Chem. Scand.*, **B40**, 343, (1986)
55. M. Kawana and H. Kuzuhara, *Tet. Lett.*, **28**, 4075 (1987)
56. M. Kawana N. Yamasaki, M. Nishikawa and H. Kuzuhara, *Chem. Lett.*, 2419, (1987)
57. R. Datema (Astra Läkemedel AB, Södertälje, Sweden), *personal comm.*
58. P. D. Magnus, *Tetrahedron*, 33, 2019, (1977)
59. P. L. Fuchs and T. F. Braish, *Chem. Rev.*, **86**, 903, (1986)
60. S.T. McDowell and C.J.M. Stirling, J. Chem. Soc. (B) 348 (1967); 343 (1967) & 351 (1967);
61. B. M. Trost, *Bull. Chem. Soc. Jpn.*, **61**, 107, (1988)
62. W. E. Truce and A. J. Levy, *J. Am. Chem. Soc.*, **83**, 4641, (1961)
63. W. E. Truce and A. J. Levy, *J. Org. Chem.*, **28**, 679, (1963)
64. S. Fabrissin, S. Fatutta, N. Malusa, and A. Risaliti, *J. C. S. Perkin I*, 686, (1980)
65 S. Fabrissin, S. Fatutta, N. Malusa, and A. Risaliti, *J. C. S. Perkin I*, 109, (1981)
66 J-L. Fabre, M. Julia and J-N. Verpeaux, *Tet. Lett.*, **23**, 2469, (1982)
67. T. Agawa, Y. Yoshida, M. Komatsu and Y. Ohshrio, *J. C. S. Perkin I*, 751, (1981)
68. D. F. Taber and S. A. Saleh, *J. Org. Chem.*, **46**, 4819, (1981)
69. P. R. Hamann and P. L. Fuchs, *J. Org. Chem.*, **48**, 914, (1983)
70. F. G. Bordwell, J. C. Branca, C. R. Johnson and N. R. Vanier, *J. Org. Chem.*, **45**, 3884, (1980)
71. D. A. Bors and A. Streiwieser, *J. Am. Chem. Soc.*, **108**, 1397, (1986)
72. G. Boche, M. Marsch, K. Harms and G. M. Sheldrick, *Angew. Chem. Int. Ed. Engl.*, **24**, 573, (1985)
73. H-J. Gais, H. J. Linder and J. Volhardt, *Angew. Chem. Int. Ed. Engl.*, **24**, 859, (1985)

74. S. Wolfe, A. Stolow and L. A. Lajohn, *Tet. Lett.*, **24**, 4017, (1983)
75. N. A. Sasaki, C. Hashimoto and P. Potier, *Tet. Lett*, **28**, 6069, (1987)
76. C. Herdeis and C. Hartke, *Synthesis*, 76, (1988)
77. A. C. Brown and L. A. Carpino, *J Org. Chem.*, **50**, 1749, (1985)
78 F. Hansske, D. Madej, and M. J. Robins, *Tetrahedron*, **40**, 125, (1984)
79 M. J. Robins, J. S. Wilson and F. Hansske, *J. Am. Chem. Soc.*, **105**, 4059, (1983)
80 F. Hansske, and M. J. Robins, *J. Am. Chem. Soc.*, **105**, 6736, (1983)
81. F.A.A.M. de Leeuw and C. Altona, *J. Chem. Soc. Perkin II* p.376 (1982)
82. C.A.G. Haasnoot, F.A.A.M. de Leeuw and C. Altona, *Tetrahedron*, **36**, 2783 (1980)
83. C. Altona and M. Sundaralingam, *J. Am. Chem. Soc.* **94**, 8205 (1972)
84. C. Altona and M. Sndaralingam, *J. Am. Chem. Soc.*, **95**, 2333 (1973)
85. F.A.A.M. de Leeuw and C. Altona, *J. Comp. Chem.*, **4**, 428 (1983); Quantum Chemistry Programme Exchange No 463
86. C.A.G. Haasnoot, F.A.A.M. de Leeuw and C. Altona, *Org. Magn. Res.*, **15**, 43 (1981)
87. E. Westhof, H. Plach, I. Cuno, H.-D-Ludemann, *Nucl. Acids. Res.*, **4**, 939 (1977)
88. L.H. Koole, H.M. Buck, H. Bazin and J. Chattopadhyaya, *Tetrahedron*, **43**, 2989 (1987)
89. L.H. Koole, H.M. Buck, A. Nyilas and J. Chattopadhyaya, *Can. J. Chem.* **65**, 2089 (1987)
90. C.A.G. Hassnoot, F.A.A.M. de Leeuw, H.P.M. de Leeuw and C. Altona, *Recl. Trav. Chim. Pays-Bas.*, **98**, 576
91. L.H. Koole, H.M. Buck, J.-M. Vial and J. Chattopadhyaya, *Acta Chem. Scand. Ser. B* (in press)
92. C.S.M. Olsthhoorn, L.J. Bostelaar, J.H. van Boom and C. Altona, *Eur. J. Chem.* **112**, 95 (1980)