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TETRAHEDRON

A New Route to the Synthesis of Pyrazole and Pyrimidine C-Nucleoside Derivatives

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Abstract: A new route to the synthesis of pyrazole and pyrimidine C-nucleosides, which involves as the key step a metal promoted reaction of β-D-ribofuranosyl ketoesters with alkyl cyanoformates is described. 2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl cyanide **1** reacts with α-bromoesters, in the presence of zinc dust, to give β-D-ribofuranosyl-enaminoesters **2** which are hydrolysed with 1N hydrochloric acid to β-ketoesters **3**. The reactions of β-ketoesters **3** with alkyl cyanoformates, in the presence of tin(IV) chloride or of catalytic amounts of metal acetylacetonates, afford β-D-ribofuranosyl enaminoketoesters **4**. These compounds react with benzylhydrazine and acetamidine to give pyrazole and pyrimidine C-nucleosides (**6**,**7**). © 1999 Elsevier Science Ltd. All rights reserved.

The metal-promoted reactions of β-dicarbonyl compounds with nitriles afford β-enaminodiones resulting from the formation of a new carbon-carbon bond between the intercarbonyl methylene group of the dicarbonyls and the nitrile cyano group.[1,2] This reaction was applied to the synthesis of heterocycles such as amino pyridines, amino quinolines[3] and tetronic acid derivatives.[4] More recently, we demonstrated that β-ethoxycarbonyl-β-enaminodiones, obtained by the metal-catalysed reaction of alkyl acetoacetates with alkyl cyanoformates,[5] are useful intermediates for the synthesis of a number of heterocycles: pyrazole, isoxazole and pyrimidine *ortho*-dicarboxylic acid derivatives have been obtained in high yield and in very mild experimental conditions.[6]

These results prompted us to investigate the metal promoted reactions of protected β-D-ribofuranosyl ketoesters with alkyl cyanoformates in order to obtain C-glycosyl enaminodicarbonyls as intermediates of C-nucleosides, a class of compounds showing antiviral and antitumoral activities.[7] In this paper we report on a new synthesis of β-D-ribofuranosyl ketoesters, their functionalisation by metal promoted and metal catalysed reactions with alkyl cyanoformates and subsequent cyclisation of the obtained intermediates with ambident nucleophiles to afford pyrazole and pyrimidine C-nucleoside derivatives.[8]

Results and discussion

Although ribofuranosyl β-ketoesters are known in the literature,[9] we developed a new synthetic route to such compounds, in order to obtain higher yields of the desired products, possibly as only *beta* anomers. With this aim, 2,3,5-tri-O-benzoyl-β-D-ribofuranosyl cyanide **1**, prepared from the corresponding commercially

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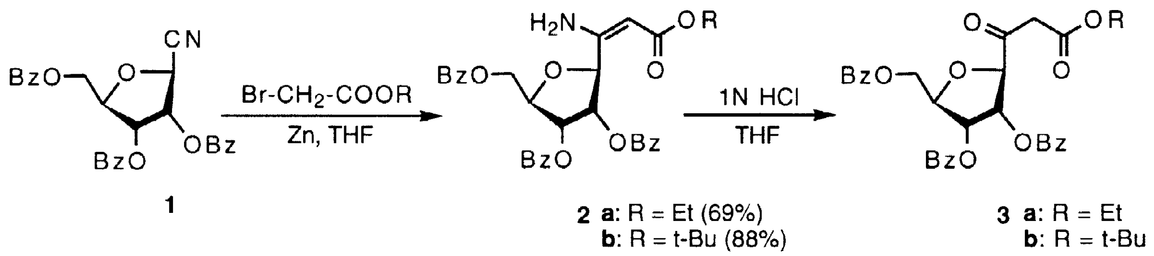
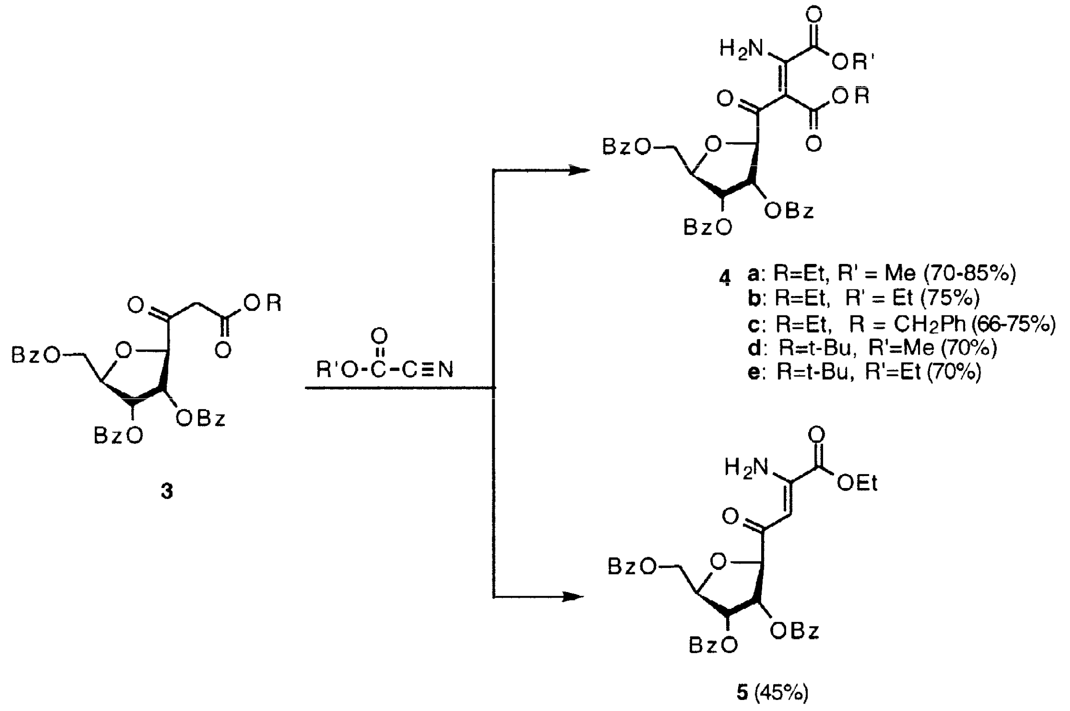
available 1-O-acetate,[10] was reacted with ethyl or *tert*-butyl bromoacetate in the presence of zinc dust in boiling tetrahydrofuran, under the Blaise reaction conditions,[11] to give the β-D-ribofuranosyl enaminoketoesters **2a,b** in good yield.



Compounds **2a,b** were easily hydrolysed to β-D-ribofuranosyl ketoesters **3a,b** by treatment with dilute hydrochloric acid in tetrahydrofuran. Enaminoketoesters **2** are solid foams showing no great stability, however they can be stored in a refrigerator for no more than a week. Ketoesters **3** are less stable and have to be used as soon as possible after their preparation.

β-D-Ribofuranosyl ketoester **3a** was then reacted with methyl, ethyl or benzyl cyanoformate in the presence of a stoichiometric amount of tin(IV) chloride at room temperature to afford, after treatment with saturated sodium hydrogen carbonate solution, β-ethoxycarbonyl-β-enaminodiones **4a-c**.[12]



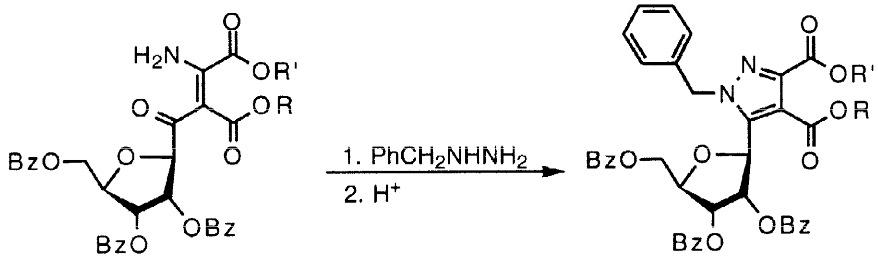
The tin (IV) chloride promoted reaction between *tert*-butyl β-ketoester **3b** and ethyl cyanoformate gave only the degradation product **5**. The formation of this compound can be explained by the lability of the *tert*-butyl ester moiety in the acidic medium derived from the presence of tin(IV) chloride, which leads to the elimination of *tert*-butyl group followed by decarboxylation.

On the basis of this result, we tried to react compounds **3a,b** with alkyl cyanoformates in the presence of a catalytic amount of metal acetylacetonates. The concentration of the reactants plays a crucial role in this kind of reaction: with diluted reaction mixtures the formation of the desired products is too slow to be practically useful. However at high concentration of the glycosyl derivatives **3** viscous solutions, in which it is impossible to obtain a good dispersion of the catalyst, are formed. Therefore, the reactions were carried out in the minimum amount of solvent necessary to obtain a non-viscous solution of compounds **3**, with a 2-2.5-fold excess of cyanoformates and in the presence of metal acetylacetonate (5 mol%). The best results were obtained when the reactions were carried out in dichloromethane with Ni(II) or Cu(II) acetylacetonate as the catalyst stirring the reaction mixture at room temperature for 1-5 days. Ni(II) acetylacetonate gave good results in terms of yields, but the presence of brown-coloured impurities which were difficult to remove often contaminated the products. Instead, with Cu(II) acetylacetonate as the catalyst, the yields were still good, and the dark blue-green colour of the reaction mixtures was removed by washing the solution of the crude products in ethyl acetate with dilute aqueous hydrochloric acid. This procedure allowed us to obtain compounds **4a-c** in yields comparable with those obtained in the presence of tin(IV) chloride, and represented the only possible entry to compounds **4d,e**.

Compounds **4** exist in solution as an equilibrium mixture of two unseparable geometric isomers, as can be seen from the ^{1}H-NMR spectra in $CDCl_3$. This behaviour can be explained by the structure of the vinylogous amide of these compounds: the partial C-C double bond character allows a slow conversion of the two possible geometric isomers, each of them being stabilized by an intramolecular hydrogen bond between a hydrogen atom of the amino group and an oxygen carbonyl atom.

Compounds **4** were then reacted with ambident nucleophiles such as benzylhydrazine and acetamidine.

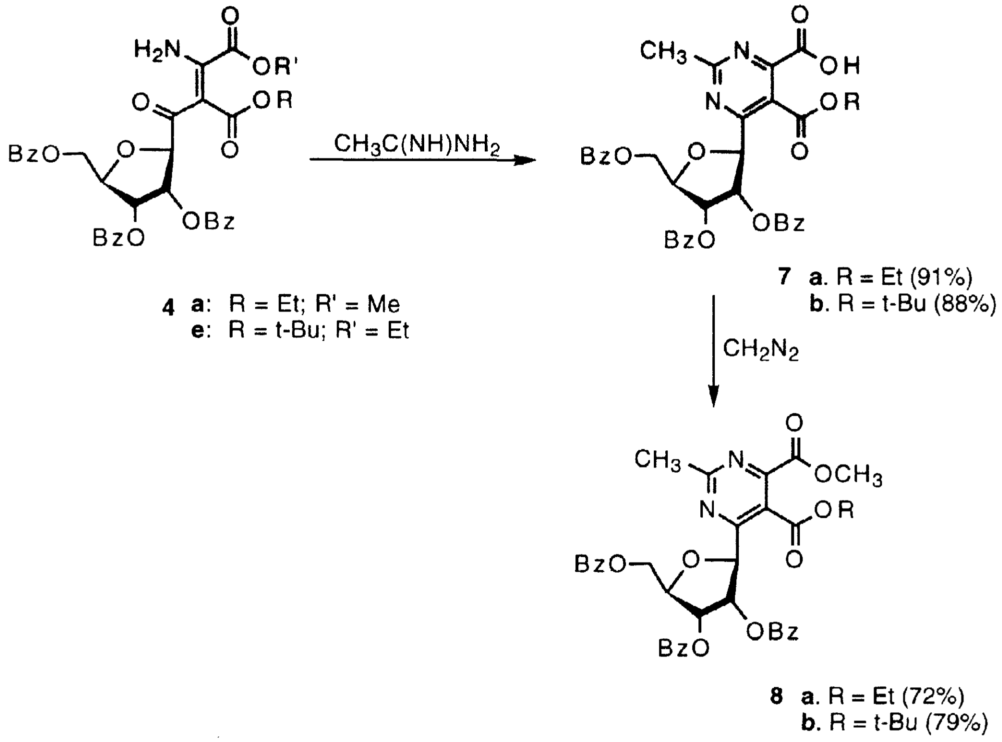
The reactions of compounds **4a,c,e** with benzylhydrazine were carried out in diethyl ether for 4-6 h. The ^{1}H-NMR spectrum of the reaction mixture showed the formation of intermediates. Their ^{13}C-NMR spectra showed the disappearance of the ketonic carbon atom, but did not show the resonances attributable to the pyrazole ring. Treatment of these intermediates with a drop of sulphuric acid in diethyl ether afforded the pyrazole C-nucleosides **6a-c** in good yield. In these reactions two isomeric pyrazole derivatives could be obtained, *i.e.* the pyrazole-3,4-dicarboxylic acid esters (**6**) and the isomeric 4,5-dicarboxylic acid esters. The ^{13}C-NMR spectra of the obtained compounds showing two resonances at *ca.* 140 and 142 ppm for the C-3 and C-5 carbon atoms of pyrazole ring, which is in agreement with previously reported ^{13}C-NMR spectra of pyrazole 3,4-dicarboxylic acid diesters,^{6} demonstrate that the obtained derivatives have the structure of the pyrazole C-nucleosides (**6**).



4 **a**: R = Et; R' = Me
c: R = Et; R' = CH_2Ph
e: R = t-Bu; R' = Et

6 **a**. R = Et; R' = Me (73%)
b. R = Et; R' = CH_2Ph (71%)
c. R = t-Bu; R' = Et (73%)

In similar reactions compounds **4a,d**, treated with acetamidine at room temperature for 3-5 h, gave the pyrimidine monocarboxylic acid C-nucleosides **7a,b** in which the ester group linked to the carbon atom *alpha* to the nitrogen atom of the pyrimidine ring was selectively hydrolysed. For better characterisation, these compounds were transformed in the corresponding methyl esters **8a,b** by reaction with diazomethane.



The obtained results show that the β-D-ribofuranosyl enaminoketoesters **4**, easily obtained by metal promoted or metal catalysed reactions of glycosyl ketoesters **3** with alkyl cyanoformates, are useful intermediates for the synthesis of pyrazole and pyrimidine C-nucleosides which were obtained in good yield and only as *beta* anomers, opening a new route to an efficient synthesis of heterocyclic C-nucleosides.

EXPERIMENTAL

Mp.s were determined on a "Kofler" apparatus and are uncorrected. IR spectra were recorded on FT-IR Perkin-Elmer Paragon 500 spectrometer. NMR spectra were recorded on Bruker AC (200 MHz) spectrometer. Chemical shifts are given in ppm (δ) with respect to tetramethylsilane and coupling constants (J) are in Hertz. Glass plates "Merk Kieselgel 60" F 245 were used for thin layer chromatography. Silica gel "ICN Silica 32-60, 60 Å" was used for column chromatography.

2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl cyanide (**1**)^{10}

To a stirred solution of tri-O-benzoyl-β-D-ribofuranosyl acetate (1.009 g, 2 mmol) and trimethylsilyl cyanide (1 ml, 8 mmol) in dry acetonitrile (15 ml), a few drops of boron trifluoride etherate were added. The reaction mixture was stirred at room temperature under argon atmosphere for 3 min and treated with saturated sodium hydrogen carbonate solution (10 ml). The suspension was extracted several times with ethyl ether, the combined organic layers were washed with brine and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure afforded a yellow oil. Rapid stirring with the minimum amount of methanol at 0°C gave colourless crystals, 799 mg (yield 85%), mp 78-80°C, lit^{10a} mp 77-80°C; $[\alpha]_D$ + 23.9 (c=0.5, $CHCl_3$), lit^{10a} $[\alpha]_D$ +23.8 (c=0.5, $CHCl_3$); IR (KBr); 2200 (weak), 1730, 1270,1240 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 4.60-4.76 (m, 3H,

OCH_2, H-4), 5.98 (d, 1H, J=4.0 Hz, H-1), 5.86 (m, 1H, H-2, or H-3), 6.01 (m, 1H, H-2 or H-3), 7.31-7.58 (m, 9H, Ph), 7.90-8.09 (m, 4H, Ph), 8.10-8.15 (m, 2H, Ph); ^{13}C-NMR ($CDCl_3$) δ 63.19 (t, J=149 Hz, OCH_2), 69.45 (d, J=161 Hz, CH), 71.86 (d, J=155 Hz, CH), 74.46 (d, J=161 Hz, CH), 80.87 (d, J=151 Hz, CH), 115.82 (s, CN), 128.16 (s, Ph), 128.38 (s, Ph), 129.79 (d, Ph), 129.85 (d, Ph), 133.46 (d, Ph), 133.86 (d, Ph), 134.03 (d, Ph), 164.88 (s, COO), 165.10 (s, COO), 166.16 (s, COO).

***Ethyl 3-amino-3-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-propenoate* (2a)**

To a suspension of zinc dust (586 mg, 9 mmol) in dry THF heated under reflux, a few drops of ethyl bromoacetate were added. After a green colour had appeared (*ca.* 15 min), the β-D-ribofuranosyl cyanide (**1**) was added (706 mg, 1.5 mmol) in one portion. The remaining bromoacetate was added dropwise over 40 min (total amount of bromoacetate: 0.66 ml, 6 mmol). The reaction mixture was cooled at room temperature, treated with saturated sodium hydrogen carbonate solution and filtered on celite. The filtrate was extracted several times with ethyl ether, the combined organic layers were washed with brine and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure and at temperature < 30°C afforded a pale yellow oil, which was purified by column chromatography (flash chromatography, SiO_2, ethyl ether/light petroleum 4:6): colourless solid foam, 585 mg (yield 69%); $[\alpha]_D$ –5.3 (c=1.4, $CHCl_3$); IR (KBr): 3480, 3370, 1730, 1630, 1280 cm^{-1}; ^1H-NMR ($CDCl_3$) δ: 1.23 (t, 3H, J=7.1 Hz, $CH_2\mathit{CH_3}$), 4.10 (q, 2H, J=7.1 Hz, $\mathit{CH_2}CH_3$), 4.62-4.88 (m, 4H, H-1', H-4', OCH_2), 4.89 (s, 1H, CH), 5.51-5.59 (m, 2H, H-2', H-3'), 7.30-7.60 (m, 10H, Ph, NH), 7.70-8.20 (m, 7H, Ph, NH); ^{13}C-NMR ($CDCl_3$) δ: 14.56 (q, J=125 Hz, $CH_2\mathit{CH_3}$), 58.96 (t, J=143 Hz, OCH_2), 63.50 (t, J=148 Hz, OCH_2), 71.71 (d, J=154 Hz, CH), 76.24 (d, J=157 Hz, CH), 80.17 (d, J=149 Hz, CH), 81.24 (d, J=155 Hz, CH), 82.65 (d, J=164 Hz, CH), 128.55 (d, Ph), 128.61 (s, Ph), 128.67 (s, Ph), 129.35 (s, Ph), 129.81 (d, Ph), 133.50 (d, Ph), 133.72 (d, Ph), 158.25 (s, C-NH_2), 165.36 (s, COO) 165.67 (s, COO), 166.48 (s, COO), 170.03 (s, COO). Found: C, 66.40; H, 5.10; N, 2.40. $C_{31}H_{29}NO_9$ requires C, 66.54; H, 5.22; N, 2.50.

***tert-Butyl 3-amino-3-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-propenoate* (2b)**

This compound was obtained following the procedure described for the synthesis of **2a** with the following modifications: molar ratio β-D-ribofuranosyl cyanide/*tert*-butyl bromoacetate/zinc dust: 1 : 2.5 : 3; reaction time: 30 min. Yield: 88%, colourless solid foam, $[\alpha]_D$ –5.5 (c=1.4, $CHCl_3$); IR (KBr): 3480, 3340, 1740, 1620,1260 cm^{-1}; ^1H-NMR ($CDCl_3$) δ: 1.45 (s, 9H, C-Me_3), 4.62-4.76 (m, 4H, H-1', H-4', OCH_2), 4.83 (s, 1H, CH), 5.58-5.70 (m, 2H, H-2', H-3'), 7.30-7.60 (m, 9H, Ph), 7.90-8.10 (m, 6H, Ph), 6.20-8.00 (br, 2H, NH_2); ^{13}C-NMR ($CDCl_3$) δ: 28.51 (q, J=125 Hz, C-$\mathit{Me_3}$), 63.49 (t, J=148 Hz, OCH_2), 71.64 (d, J=155 Hz, CH), 76.27 (d, J=162 Hz, CH), 78.71 (s, *C*Me_3), 79.91 (d, J=149 Hz, CH), 81.84 (d, J=153 Hz, CH), 84.59 (d, J=166 Hz, CH), 128.48 (d, Ph), 128.54 (d, Ph), 128.63 (d, Ph), 128.80 (s, Ph), 128.98 (s, Ph), 129.35 (s, Ph), 129.75 (d, Ph), 133.41 (d, Ph), 133.61 (d, Ph), 133.65 (d, Ph), 157.27 (s, C-NH_2), 165.28 (s, COO), 165.63 (s, COO), 166.39 (s, COO), 169.84 (s, COO). Found: C, 67.60; H, 5.45; N, 2.31. $C_{33}H_{33}NO_9$ requires C, 67.45; H, 5.66; N, 2.38.

Alkyl 3-oxo-3-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-propanoate (3)

To a solution of alkyl 3-amino-3-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl) propenoate **2** in THF, 1M HCl was added (*ca.* 1.5 ml of solvent and 0.3 ml of HCl/100 mg of compound **2**) and the mixture was stirred at room temperature for 4-6 h (see below). Saturated sodium hydrogen carbonate was then added and the mixture was extracted several times with ethyl ether. The combined organic layers were washed with brine, dried (Na_2SO_4) and evaporated under reduced pressure without heating. Compounds **3** are very unstable and were used immediately after their preparation without any further purification.

Following this general procedure, the following compounds were obtained:

Ethyl 3-oxo-3-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-propanoate **(3a)**

This compound was obtained from ethyl 3-amino-3-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl) propenoate (**2a**); reaction time: 6 h. Colourless syrup; IR (neat) 1730, 1610, 1450, 1270, 1110 cm^{-1}; ^{1}H-NMR (DMSO-d$_6$) δ: 1.22 (t, 3H, J=7.0 Hz, CH_2CH_3), 3.80 (s, 2H, CH_2), 4.04 (q, 2H, J=7.0 Hz, CH_2CH_3), 4.45-4.65 (m, 2H, OCH_2), 4.65-4.80 (m, 1H, H-4'), 4.65 (d, 1H, J=4.6 Hz, H-1'), 5.67 (m, 1H, H-2' or H-3'), 5.90 (m, 1H, H-2' or H-3'), 6.82-7.68 (m, 10 H, Ph), 7.82-8.09 (m, 5H, Ph); ^{13}C-NMR (DMSO-d6) δ: 13.81 (CH_2CH_3) 45.47 (CH_2), 60.69 (OCH_2), 63.86 (OCH_2), 71.70 (CH), 72.55 (CH), 79.17 (CH), 84.70 (CH), 128.52 (Ph), 128.66 (Ph), 128.74 (Ph), 129.24 (Ph), 133.48 (Ph), 133.75 (Ph), 133.85 (Ph), 164.54 (2 COO), 165.45 (COO), 166.79 (COO), 200.97 (CO).

tert-Butyl 3-oxo-3-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-propanoate **(3b)**

This compound was obtained from *tert*-butyl 3-amino-3-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl) propenoate (**2a**); reaction time: 4 h. Colourless syrup; IR (neat): 1730, 1610, 1450, 1270, 1100 cm^{-1}; ^{1}H-NMR (DMSO-d$_6$) δ: 1.45 (s, 9H, t-Bu), 3.75 (s, 2H, CH_2), 4.61-4.73 (m, 3H, OCH_2, H-4'), 4.57 (d, 1H, J=4.5 Hz, H-1'), 5.65-5.75 (m, 1H, H-2' or H-3'), 5.87-5.91 (m, 1H, H-2' or H-3'), 7.20-7.50 (m, 10H, Ph), 7.82-8.09 (m, 5H, Ph).

Reactions of ethyl-3-oxo-3-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-propanoate (2a) with alkyl cyanoformates in the presence of stoichiometric amounts of tin (IV) chloride

To a 1M solution of tin(IV) chloride in dichloromethane (0.6 ml, 0.6 mmol), a solution of ethyl 3-oxo-3-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-propanoate (**3a**) (0.5 mmol) and the alkyl cyanoformate (0.6 mmol) in dry dichloromethane (3 ml) was added. The reaction mixture was stirred at room temperature under argon atmosphere for 15 min-2.5 h (see below), diluted with ethyl acetate and treated with saturated sodium hydrogen carbonate (5 ml) with stirring for 15 min. The suspension was filtered on celite; the layers were separated, the aqueous layer was extracted with ethyl acetate and the combined organic layers were washed with brine, dried (Na_2SO_4) and evaporated under reduced pressure to give a residue which was purified by column chromatography.

Following this general procedure, the following compounds were obtained:

Methyl 2-amino-3-ethoxycarbonyl-4-oxo-4-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-2-butenoate **(4a)**

This compound was obtained from reaction of **3a** with methyl cyanoformate (reaction time 15 min) in 70% yield (calculated on compound **2a**) after purification by flash chromatography (silica gel, ethyl ether/light petroleum 8:2) as colourless solid foam. IR (KBr): 3344, 1727, 1601,1271, 1121 cm^{-1}; ^{1}H-NMR ($CDCl_3$): two geometric isomers are present in 2:1 ratio. Major isomer, δ: 1.17 (t, 3H, J=7.0 Hz, CH_2CH_3), 3.82 (s, 3H, OMe), 4.10 (m, 2H, CH_2CH_3), 4.70-4.75 (m, 3H, OCH_2, H-4'), 5.63 (d, 1H, J=1.7 Hz, H-1') 5.60-5.70 (m, 1H, H-2' or H-3'), 6.07 (m, 1H, H-2' or H-3'), 6.90 (br, 1H, NH), 7.20-8.10 (m, 15 H, Ph), 10.80 (br, 1H, NH); minor isomer shows resonances at δ: 1.19 (t, 3H, J=7.0 Hz, CH_2CH_3), 3.87 (s, 3H, OMe), 4.10 (m, 2H, CH_2CH_3), 4.70-4.75 (m, 3H, OCH_2, H-4'), 5.43 (d, 1H, J=1.9 Hz, H-1'), 5.60-5.71 (m, 1H, H-2' or H-3'), 6.00 (m, 1H, H-2' or H-3'), 6.20 (br, 1H, NH), 7.22-8.09 (m, 15H, Ph), 8.80 (br, 1H, NH); ^{13}C-NMR ($CDCl_3$): major isomer shows resonances at δ: 13.94 (CH_2CH_3), 53.36 (OMe), 61.13 (OCH_2), 64.54 (OCH_2), 72.48 (CH), 74.25 (CH), 78.46 (CH), 84.41 (CH), 99.90 (C-3), 128.29 (Ph), 128.47 (Ph), 128.52 (Ph), 128.86 (Ph), 129.22 (Ph), 129.33 (Ph), 129.72 (Ph), 129.76 (Ph), 129.82 (Ph), 133.01 (Ph), 133.35 (Ph), 133.40 (Ph), 158.95 (C-NH$_2$), 164.09 (COO), 164.39 (COO), 165.19 (COO) 165.27 (COO), 166.51 (COO), 194.55 (CO); minor isomer shows resonances at δ: 14.13, 53.80, 60.86, 65.86, 72.27, 74.53, 78.46, 86.36, 100.23, 154.81, 165.32, 166.29, 166.35, 167.20, 196.47. Found: C, 63.10; H, 4.70; N, 2.25. $C_{34}H_{31}NO_{12}$ requires C, 63.25; H, 4.84; N, 2.17.

Ethyl 2-amino-3-ethoxycarbonyl-4-oxo-4-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-2-butenoate (**4b**)

This compound was obtained from the reaction of **3a** with ethyl cyanoformate (reaction time 1 h) in 75% yield (calculated on compound **2a**) after purification by flash chromatography (silica gel, ethyl acetate/light petroleum 1:2) as colourless solid foam. IR (KBr): 3350, 1730, 1600,1260 cm^{-1}; ^{1}H-NMR (DMSO-d$_6$) δ: 1.06 (t, 3H, J=7.0 Hz, $CH_2\mathit{CH_3}$), 1.25 (t, 3H, J=7.0 Hz, $CH_2\mathit{CH_3}$), 3.90-4.10 (m, 2H, $\mathit{CH_2}CH_3$), 4.22 (q, 2H, J=7.0 Hz, $\mathit{CH_2}CH_3$), 4.40-4.80 (m, 3H, OCH$_2$, H-4'), 5.42-5.63 (m, 1H, H-2' or H-3'), 5.57 (d, 1H, J=1.7 Hz, H-1'), 5.71-5.85 (m, 1H, H-2' or H-3'), 7.12-7.93 (m, 15H, Ph), 9.60 (br, 1H, NH), 10.60 (br, 1H, NH). ^{13}C-NMR (DMSO-d$_6$) δ: 13.51 (q, J= 126 Hz, $CH_2\mathit{CH_3}$), 13.64 (q, J=126 Hz, $CH_2\mathit{CH_3}$), 60.03 (t, J=142 Hz, OCH$_2$), 61.97 (t, J=144 Hz, OCH$_2$), 64.40 (t, J=149 Hz, OCH$_2$), 72.30 (d, J=152 Hz, CH), 74.04 (d, J=164 Hz, CH), 77.53 (d, J=148 Hz, CH), 83.48 (d, J=157 Hz, CH), 96.43 (s, C-3), 128.48 (d, Ph), 128.76 (d, Ph) 129.05 (d, Ph), 129.12 (d, Ph), 129.21 (d, Ph), 133.25 (d, Ph), 133.58 (d, Ph), 133.71 (d, Ph), 161.72 (s, C-NH$_2$), 163.12 (s, COO), 164.48 (s, COO), 164.71 (s, COO), 165.37 (s, COO), 165.93 (s, COO), 193.66 (s, CO). Found: C, 63.60; H, 5.10; N, 2.25. $C_{35}H_{33}NO_{12}$ requires C, 63.73; H, 5.04; N, 2.12.

Benzyl 2-Amino-3-ethoxycarbonil-4-oxo-4-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-2-butenoate (**4c**)

This compound was obtained from the reaction of **3a** with benzyl cyanoformate (reaction time 2.5 h) in 66% yield (calculated on compound **2a**) after purification by flash chromatography (silica gel, ethyl acetate/light petroleum 1:2) as colourless solid foam. IR (KBr); 3339, 1727, 1601, 1270 cm^{-1}; ^{1}H-NMR(CDCl$_3$): two geometric isomers are present in 2:1 ratio. Major isomer, δ: 1.07 (t, 3H, J=7.1 Hz, $CH_2\mathit{CH_3}$), 3.85-4.05 (m, 2H, $\mathit{CH_2}CH_3$), 4.61-4.82 (m, 3H, OCH$_2$, H-4'), 5.25 (s, 2H, OCH$_2$Ph), 5.61 (d, 1H, J=1.5 Hz, H-1'), 5.65-5.75 (m, 1H, H-3') 6.08 (dd, 1H, J=4.8 and 1.5 Hz, H-2'), 6.72 (br, 1H, NH), 7.20-8.12 (m, 20H, Ph), 10.75 (br, 1H, NH); minor isomer shows resonances at δ: 1.21 (t, 3H, J=7.0 Hz, $CH_2\mathit{CH_3}$), 4.10-4.25 (m, 2H, $\mathit{CH_2}CH_3$), 4.63-4.82 (m, 3H, OCH$_2$, H-4'), 5.30 (s, 2H, OCH$_2$-Ph), 5.33 (d, 1H, J=2.2 Hz, H-1'), 5.60-5.61 (m, 1H, H-2' or H-3'), 5.99 (m, 1H, H-2' or H-3'), 6.15 (br, 1H, NH), 7.22-8.13 (m, 20H, Ph), 8.70 (br, 1H, NH). Found: C, 66.50; H, 4.95; N, 1.90. $C_{40}H_{35}NO_{12}$ requires C, 66.57; H, 4.89; N, 1.94.

Ethyl 2-amino-4-oxo-4-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-2-butenoate (**5**)

This compound was obtained from the reaction of **3b** with ethyl cyanoformate (reaction time 15 min) in 45% yield (calculated on compound **2b**) after purification by flash chromatography (silica gel, ethyl acetate/light petroleum 1:3) as a colourless oil. IR (KBr): 3340, 1735, 1640, 1255 cm^{-1}; ^{1}H-NMR (CDCl$_3$) δ: 1.20 (t, J=7.0 Hz, 3H, $CH_2\mathit{CH_3}$), 4.00-4.25 (m, 2H, OCH$_2$), 4.50-4.70 (m, 2H, H-1' and H-4'), 4.70-4.85 (m, 2H, OCH$_2$), 5.70-5.76 (m, 1H, H-2' or H-3'), 5.80-5.86 (m, 1H, H-2' or H-3'), 6.17 (br, 1H, NH), 6.32 (s, CH), 7.25-7.58 (m, 9H, Ph), 7.81-8.07(m, 6H, Ph), 9.24 (br, 1H, NH). Found: C, 65.50; H, 4.90; N, 2.30. $C_{32}H_{29}NO_{10}$ requires C, 65.41; H, 4.97; N, 2.38.

Reactions of alkyl 3-oxo-3-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-propanoate (3) with alkyl cyanoformates in the presence of catalytic amounts of metal acetylacetonates

***Methyl 2-amino-3-ethoxycarbonyl-4-oxo-4-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-2-butenoate* (4a)**

To a solution of ethyl 3-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-3-oxo-propanoate **3a** (230 mg, 0.4 mmol) and methyl cyanoformate (0.05 ml, 0.62 mmol) in dry dichloromethane (0.3 ml), [Ni(acac)$_2$] (5 mg, 0.02 mmol) was added and the mixture was stirred at room temperature under argon atmosphere for 4 days. The reaction mixture was diluted with ethyl acetate (10 ml), filtered on celite and concentrated under reduced pressure to afford a yellow oil which was purified by flash chromatography (silica gel, ethyl ether/light petroleum 8:2): colourless solid foam, 230 mg (yield 85%, calculated on compound **2a**); mp, IR and ^{1}H-NMR spectra identical with those of compound **4a** described before.

Following this procedure, with modifications reported below, the following compounds were prepared:

***Benzyl 2-Amino-3-ethoxycarbonyl-4-oxo-4-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-2-butenoate* (4c)**

This compound was obtained by reaction of ethyl 3-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-3-oxo-butenoate **3a** with benzyl cyanoformate in the presence of [Ni(acac)$_2$] 5 mol% (reaction time: 7 days) in 75% yield (calculated on compound **2a**) after purification by flash chromatography (silica gel, ethyl acetate/light petroleum 1:2) as colourless solid foam; IR and ^{1}H-NMR identical to that of the compound **4c** described before.

***Methyl 2-amino-3-tert-butyloxycarbonyl-4-oxo-4-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-2-butenoate* (4d)**

This compound was obtained by reaction of *tert*-butyl 3-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-3-oxo-propanoate **3b** with methyl cyanoformate in the presence of [Cu(acac)$_2$] 5 mol% (reaction time: 3 days) in 70% yield (calculated on compound **2b**) after purification by flash chromatography (ethyl ether/light petroleum 7:3) as colourless solid foam. IR (KBr): 3350, 1735, 1620, 1270 cm^{-1}; ^{1}H-NMR (CDCl$_3$): two geometric isomers are present in 3:2 ratio; major isomer, δ: 1.42 (s, 9H, CMe$_3$), 3.87 (s, 3H, OMe), 4.45-4.80 (m, 3H, OCH$_2$, H-4'), 5.71 (d, 1H, J=2.2 Hz, H-1'), 5.65-5.75 (m, 1H, H-2' or H-3'), 6.05-6.15 (m, 1H, H-2' or H-3'), 7.30-8.15 (m, 16H, Ph, NH), 10.56 (br, 1H, NH); minor isomer shows absorptions at δ: 1.50 (s, 9H, CMe$_3$), 3.90 (s, 3H, OMe), 4.45-4.80 (m, 3H, OCH$_2$, H-4'), 5.34 (d, 1H, J=2.1 Hz, H-1'), 5.55-5.65 (m, 1H, H-2' or H-3'), 6.05-6.15 (m, 1H, H-2' or H-3'), 6.25 (br, 1H, NH), 7.32-8.15 (m, 16H, Ph, NH), 8.60 (br, 1H, NH). Found: C, 64.10; H, 5.30; N, 2.15. $C_{36}H_{35}NO_{12}$ requires C, 64.18; H, 5.24; N, 2.08.

***Ethyl 2-Amino-3-tert-butyloxycarbonyl-4-oxo-4-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-2-butenoate* (4e)**

This compound was obtained by reaction of *tert*-butyl 3-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-3-oxo-butenoate **3b** with ethyl cyanoformate in the presence of [Cu(acac)$_2$] 5 mol% (reaction time 5 days) in 70% yield (calculated on compound **2b**) after purification by flash chromatography (silica gel, ethyl ether/light petroleum 7:3) as colourless solid foam. $[\alpha]_D$ –39.6 (c=0.88, CHCl$_3$); IR (KBr): 3400, 1740, 1610, 1260, 1120 cm^{-1}; ^{1}H-NMR (CDCl$_3$): two geometric isomers are present in 3:2 ratio; major isomer, δ: 1.20 (t, 3H, J=7.0 Hz, $CH_2\mathit{CH_3}$), 1.42 (s, 9H, CMe$_3$), 4.22-4.38 (m, 2H, OCH$_2$), 4.61-4.79 (m, 3H, OCH$_2$, H-4'), 5.66 (d, 1H, J=1.5 Hz, H-1'), 5.71-5.80 (m, 1H, H-2' or H-3'), 6.02-6.19 (m, 1H, H-2' or H-3'), 6.60 (br, 1H, NH), 7.20-8.02 (m, 15H, Ph), 10.60 (br, 1H, NH); minor isomer shows resonances at δ: 1.30 (t, 3H, J=7.0 Hz, $CH_2\mathit{CH_3}$), 1.49 (s, 9H, CMe$_3$), 4.22-4.41 (m, 2H, OCH$_2$), 4.61-4.83 (m, 3H, OCH$_2$, H-4'), 5.35 (d, 1H, J=1.7 Hz, H-1'), 5.7-5.8 (m, 1H, H-2' or H-3'), 6.0-6.2 (m, 1H, H-2' or H-3'), 6.10 (br, 1H, NH), 7.21-8.00 (m, 15H, Ph), 8.7 (br, 1H, NH). Found: C, 64.50; H, 5.50; N, 2.00. $C_{37}H_{37}NO_{12}$ requires C, 64.62; H, 5.42; N, 2.04.

Synthesis of pyrazole and pyrimidine C-nucleosides

***1-Benzyl-3-methoxycarbonyl-4-ethoxycarbonyl-5-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-pyrazole* (6a)**

To a cooled (0°C) solution of triethylamine (0.22 ml, 1.56 mmol) in ethyl ether (4 ml) benzylhydrazine dihydrochloride (152 mg, 0,78 mmol) was added and the suspension was stirred under argon atmosphere for 15 min. Methyl 2-amino-3-ethoxycarbonyl-4-oxo-4-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-2-butenoate **4a** (419 mg, 0.65 mmol) was then added in one portion. The mixture was stirred at 0°C for 15 min and the temperature was then slowly allowed to rise to room temperature. After 5 h the reaction mixture was diluted with ethyl ether and filtered; the resulting solution was washed with 1M HCl, brine and dried (Na_2SO_4). The solvent was removed under reduced pressure, to give a residue which was dissolved in ethyl ether (3 ml). The solution was added to a cooled (0°C) solution of one drop of concentrated sulphuric acid in 1 ml of ethyl ether. The mixture was stirred at 0°C for 15 min and at room temperature for further 15 min. The colourless solid so obtained was dissolved by adding ethyl acetate and the obtained solution was washed with saturated sodium hydrogen carbonate solution, brine, and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure afforded an oily solid which was purified by column chromatography (flash chromatography, silica gel, ethyl acetate/light petroleum 1:1): colourless crystals (ethyl acetate-light petroleum), 349 mg (yield 73%), mp 140-142 °C, $[\alpha]_D$ –40.7 (c=0.90, $CHCl_3$); IR (KBr): 1720, 1485, 1274 cm^{-1}; ^1H-NMR ($CDCl_3$) δ: 1.26 (t, 3H, J=7.0 Hz, $CH_2\mathit{CH_3}$), 3.90 (s, 3H, OMe), 4.20-4.43 (m, 2H, $O\mathit{CH_2}CH_3$), 4.52-4.61 (m, 1H, H-4'), 4.60-4.72 (m, 2H, OCH_2), 5.52, 5.62 (AB system, 2H, J=15.6 Hz, N-CH_2), 5.70 (d, J=2.1 Hz, 1H, H-1'), 5.69-5.73 (m, 2H, H-2', H-3'), 7.00-7.62 (m, 14H, Ph), 7.80-7.92 (m, 4H, Ph), 8.00-8.12 (m, 2H, Ph); ^{13}C-NMR ($CDCl_3$) δ: 13.97 (q, J= 126 Hz, $CH_2\mathit{CH_3}$), 52.43 (q, J=146 Hz, OMe), 55.32 (t, J=139 Hz, OCH_2), 61.39 (t, J=142 Hz, OCH_2), 63.84 (t, J=148 Hz, NCH_2), 71.44 (d, J=162 Hz, CH), 74.16 (d, J=158 Hz, CH), 74.59 (d, J=158 Hz, CH), 80.91 (d, J=149 Hz, CH), 115.68 (s, C-4), 126.58 (d, Ph), 128.11 (d, Ph), 128.37 (d, Ph), 128.48 (d, Ph), 128.63 (d, Ph), 128.85 (d, Ph), 129.37 (d, Ph), 129.71(d, Ph), 133.29 (d, Ph), 133.50 (d, Ph), 135.24 (s, Ph), 140.31 (s, C-3 or C-5), 142.75 (s, C-3 or C-5), 162.11 (s, COO), 162.83 (s, COO), 164.88 (s, COO), 165.16 (s, COO), 166.11 (s, COO). Found: C, 67.30; H, 4.90; N, 3.90. $C_{41}H_{36}N_2O_{11}$ requires C, 67.21; H, 4.95; N, 3.82.

Following this procedure, with the modifications reported below, the following compounds were synthesized:

***1-Benzyl-3-benzyloxycarbonyl-4-ethoxycarbonyl-5-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-pyrazole* (6b)**

Obtained from benzyl 2-amino-3-ethoxycarbonyl-4-oxo-4 (2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-2-butenoate **4c**, benzylhydrazine dihydrochloride and triethylamine in 71% yield after recrystallization (ethyl acetate-light petroleum) as colourless crystals, mp 134-136°C, $[\alpha]_D$ –36.3 (c=0.88, $CHCl_3$); IR (KBr): 1719, 1450,1273, 1209 cm^{-1}; ^1H-NMR ($CDCl_3$) δ: 1.10 (t, 3H, J= 7.1 Hz, $CH_2\mathit{CH_3}$), 4.09 (q, 2H, J=7.1 Hz, $\mathit{CH_2}CH_3$), 4.50-4.60 (m, 1H, H-4'), 4.60-4.70 (m, 2H, OCH_2), 5.35 (s, 2H, OCH_2), 5.49, 5.61 (AB system, 2H, J=15.2 Hz, NCH_2), 5.66 (s, 1H, H-1'), 5.62-5.75 (m, 2H, H-2', H-3'), 7.00-7.60 (m, 19H, Ph), 7.82-

7.91 (m, 4H, Ph), 8.00-8.11 (m, 2H, Ph); ^{13}C-NMR ($CDCl_3$) δ: 13.83 (q, J=126 Hz, Me), 55.31 (t, J=139 Hz, NCH_2), 61.39 (t, J=142 Hz, OCH_2), 63.87 (t, J=156 Hz, OCH_2), 67.21 (t, J=145 Hz, OCH_2), 71.45 (d, J=157 Hz, CH), 74.22 (d, J=158 Hz, CH), 74.67 (d, J=152 Hz, CH), 80.83 (d, J=149 Hz, CH), 115.61 (s, C-4), 126.64 (d, Ph), 128.13 (d, Ph), 128.37 (d, Ph), 128.50 (d, Ph), 128.65 (d, Ph), 128.86 (d, Ph), 129.39 (d, Ph), 129.73 (d, Ph), 133.29 (d, Ph), 133.50 (d, Ph), 135.25(s, Ph) 135.36 (s, Ph), 140.23 (s, C-3 or C-5), 142.79 (s, C-3 or C-5), 161.71 (s, COO), 162.89 (s, COO), 164.68 (s, COO), 165.15 (s,COO), 166.12 (s, COO). Found: C, 69.70; H, 5.05; N, 3.40. $C_{47}H_{40}N_2O_{11}$ requires C, 69.79; H, 4.98; N, 3.46.

***1-Benzyl-3-ethoxycarbonyl-4-tert-butoxycarbonyl-5-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-pyrazole* (6c)**

Obtained from *tert*-butyl 2-amino-3-ethoxycarbonyl-4-oxo-4-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-2-butenoate **4e**, benzylhydrazine dihydrochloride and triethylamine in 73% yield after recrystallization (ethyl ether-light petroleum) as colourless crystals, mp 137-39 °C, $[\alpha]_D$ –40.9 (c=0.96, $CHCl_3$); IR (KBr): 1723, 1708, 1546, 1275 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.44 (t, 3H, J=7.0 Hz, CH_2CH_3), 1.60 (s, 9H, CMe_3), 4.40-4.51 (m, 2H, OCH_2CH_3), 4.59-4.64 (m, 1H, H-4'), 4.74-4.78 (m, 2H, OCH_2), 5.54, 5.68 (AB system, 2H, J=15.0 Hz, NCH_2), 5.78-5.92 (m, 3H, H-1', H-2', H-3'), 7.08-7.62 (m, 14H, Ph), 7.90-7.96 (m, 4H, Ph), 8.09-8.12 (m, 2H, Ph); ^{13}C-NMR ($CDCl_3$) δ:14.29 (q, J=126 Hz, CH_2CH_3), 28.02 (q, J=126 Hz, CMe_3), 5.17 (t, J=140 Hz, OCH_2), 61.61 (t, J=146 Hz, OCH_2), 64.00 (t, J=148 Hz, NCH_2), 71.51 (d, J=151 Hz, CH), 74.16 (d, J=158 Hz, CH), 74.44 (d, J=158 Hz, CH), 81.01 (d, J=148 Hz, CH), 82.06 (s, CMe_3), 116.33 (s, C-4), 126.57 (d, Ph), 128.04 (d, Ph), 128.31 (d, Ph), 128.36 (d, Ph), 128.51 (d, Ph), 128.83 (d, Ph), 129.47 (d, Ph), 129.74 (d, Ph), 129.84 (d, Ph), 133.29 (d, Ph), 133.46 (d, Ph), 135.51 (s, Ph), 140.31 (s, C-3 or C-5), 143.92 (s, C-3 or C-5), 161.77 (s, COO), 162.27 (s, COO), 164.98 (s, COO), 165.21 (s, COO), 166.14 (s, COO). Found: C, 68.30; H, 5.45; N, 3.70. $C_{44}H_{42}N_2O_{11}$ requires C, 68.21; H, 5.46; N, 3.62.

Synthesis of pyrimidine C-nucleosides

To a cooled (0°C) solution of triethylamine (0.05 ml, 0.4 mmol) in dry dichloromethane acetamidine hydrochloride (38 mg, 0.4 mmol) was added and the mixture was stirred under argon atmosphere for 15 min. Alkyl 2-amino-3-alkoxycarbonyl-4-oxo-4-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-2-butenoate **4** was then added (0.34 mmol), followed by tetramethylguanidine (0.085 ml, 0.68 mmol). The reaction mixture was stirred for 4 h, and the temperature was allowed to rise from 0°C to room temperature. The solvent was removed under reduced pressure, the residue was dissolved in ethyl acetate and filtered. The solution was washed with 1M hydrochloric acid and brine and dried (Na_2SO_4). The solvent was evaporated under reduced pressure to give the product.

Following this procedure the following compounds were prepared:

***2-Methyl-6-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-pyrimidine-4,5-dicarboxylic acid-5-ethyl ester* (7a)**

This compound was obtained from methyl 2-amino-3-ethoxycarbonyl-4-oxo-4-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-2-butenoate **4a** in 91% yield (crude product) as pale yellow solid foam. IR (KBr): 3600-2400 (br), 1727, 1451, 1269 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.35 (t, 3H, J=7.2 Hz, CH_2CH_3), 2.79 (s, 3H, Me), 4.46 (q, 2H, J=7.2 Hz, OCH_2CH_3), 4.59-4.66 (m, 1H, H-4'), 4.8-4.9 (m, 2H, OCH_2), 5.59 (d, 1H, J=4.3 Hz, H-1'), 5.96-6.02 (m, 1H, H-2' or H-3'), 6.27-6.32 (m, 1H, H-2' or H-3'), 5.70-6.10 (br, 1H, COOH), 7.31-7.63 (m, 8H, Ph), 7.97-8.16 (m, 7H, Ph).

***2-Methyl-6-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-pyrimidine-4,5-dicarboxylic acid-5-tert-butyl ester* (7b)**

This compound was obtained from *tert*-butyl 2-amino-3-ethoxycarbonyl-4-oxo-4-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-2-butenoate **4e** in 88% yield (crude product) as yellow solid foam. IR (KBr): 3600-2800 (br), 1728, 1560, 1270 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.55 (s, 9H, CMe_3), 2.71 (s, 3H, Me), 4.5-4.6 (m, 1H, H-4'), 4.79-4.86 (m, 2H, OCH_2), 5.61 (d, 1H, J=4.0 Hz, H-1'), 6.00-6.05 (m, 1H, H-2' or H-3'), 6.22-6.27 (m, 1H, H-2' or H-3'), 7.31-7.57 (m, 9H, Ph), 7.90-8.05 (m, 6H, Ph), 8.60-8.80 (br, 1H, COOH)

Esterification of pyrimidine C-nucleoside acid derivatives 7

To a cooled (0°C) solution of crude pyrimidine C-nucleoside derivative (*ca.* 0.25 mmol) in ethyl acetate (2 ml), a solution of diazomethane in diethyl ether was added until the evolution of gas was no longer detected. The mixture was then stirred at 0°C under argon atmosphere for 10 min. The excess of diazomethane was destroyed by careful addition of glacial acetic acid. The reaction mixture was then diluted with ethyl acetate (*ca.* 10 ml), washed with saturated sodium hydrogen carbonate, brine and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure gave a residue which was purified by flash column chromatography.

Following this general procedure, the following compounds were prepared:

***2-Methyl-6-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-pyrimidine-4,5-dicarboxylic acid 4-methyl-5-ethyl ester* (8a)**

This compound was obtained from crude 2-methyl-6-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-4,5-pyrimidinedicarboxylic acid-5-ethyl ester **7a** in 72% yield (calculated on **4a**) after purification by flash chromatography (silica gel, ethyl ether/light petroleum 7:3) as colourless crystals, mp 47-50°C, $[\alpha]_D$ –38.5 (c=1.0, $CHCl_3$), IR (KBr): 1728, 1561, 1451, 1268 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.30 (t, 3H, J=7.1 Hz, CH_2CH_3), 2.77 (s, 3H, Me), 3.96 (s, 3H, OMe), 4.37 (q, 2H, J=7.1 Hz, OCH_2CH_3), 4.58 (dd, 1H, J=12.8 and 5.7 Hz, H-4'), 4.73-4.81 (m, 2H, OCH_2), 5.67 (d, 1H, J=3.9 Hz, H-1'), 5.94 (dd, 1H, J=5.7 and 5.5 Hz, H-3'), 6.25 (dd, 1H, J=5.7 and 3.9 Hz, H-2'), 7.30-7.58 (m, 9H, Ph), 7.90-8.02 (m, 6H, Ph); ^{13}C-NMR ($CDCl_3$) δ: 13.88 (q, J=126 Hz, CH_2CH_3), 26.19 (q, J=127 Hz, Me), 53.60 (q, J=147 Hz, OMe), 62.63 (t, J=149 Hz, OCH_2), 63.88 (t, J=151 Hz, OCH_2), 72.63 (d, J=156 Hz, CH), 75.07 (d, J=163 Hz, CH), 80.34 (d, J=149 Hz, CH), 81.23 (d, J=153 Hz, CH), 122.96 (s, C-5), 128.45 (Ph), 128.49 (Ph), 128.54 (Ph), 128.99 (Ph), 129.17 (Ph), 129.69 (Ph), 129.83 (Ph), 133.22 (Ph), 133.56 (Ph), 155.24 (s, C-6), 164.49 (s, COO), 164.82 (s, COO), 165.27 (s, COO), 165.40 (s, COO), 166.16 (s, COO), 169.51 (s, C-2). Found: C, 64.70; H, 4.88; N, 4.10. $C_{36}H_{32}N_2O_{11}$ requires C, 64.67; H, 4.82; N, 4.19.

***2-Methyl-6-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-4,5-dicarboxylicacid-4-methyl-5-tert-butyl ester* (8b)**

This compound was obtained from crude 2-methyl-6-(2',3',5'-tri-O-benzoyl-β-D-ribofuranosyl)-pyrimidine-4,5-dicarboxylic-5-*tert*-butyl ester **7b** in 79% yield (calculated on **4d**) after purification by flash chromatography (silica gel, ethyl ether/light petroleum 7:3) as colourless crystals, mp 126-128°C, $[\alpha]_D$ –35.6 (c=1.11, $CHCl_3$); IR (KBr): 1735, 1559, 1454, 1274 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.54 (s, 9H, CMe_3), 2.75 (s, 3H, Me), 3.97 (s, 3H, OMe), 4.60 (dd, 1H, J=12.8 and 5.5 Hz, H-4'), 4.74-4.81 (m, 2H, OCH_2), 5.73 (d, 1H, J=3.8 Hz, H-1'), 6.00 (dd, J=5.4 and 5.6 Hz, 1H, H-3'), 6.27 (dd, 1H, J=5.4 and 3.8 Hz, H-2'), 7.30-7.57 (m, 9H, Ph), 7.91-8.01 (m, 6H, Ph); ^{13}C-NMR ($CDCl_3$) δ: 26.14 (q, J=128 Hz, Me), 27.87

(q, J=127 Hz, C*Me₃*), 53.47 (q, J=147 Hz, OMe), 63.93 (t, J=148 Hz, OCH_2), 72.83 (d, J=155 Hz, CH), 75.01 (d, J=156 Hz, CH), 80.16 (d, J=149 Hz, CH), 80.83 (d, J=153 Hz, CH), 84.29 (s, CMe_3), 123.96 (s, C-5'), 128.43 (Ph), 128.47 (Ph), 128.53 (Ph), 129.05 (Ph), 129.21 (Ph), 129.72 (Ph), 129.80 (Ph), 129.83 (Ph), 133.19 (Ph), 133.53 (Ph), 155.29 (C-4' or C-6'), 163.94 (s), 164.34 (s), 164.63 (s), 165.31 (s), 165.40 (s), 166.16 (5 COO, C-4' or C-6'), 169.15 (C-2'). Found: C, 65.40; H, 5.15; N, 4.10. $C_{38}H_{36}N_2O_{11}$ requires C, 65.51; H, 5.21; N, 4.02.

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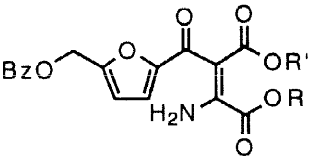
12. Together with the desired products **4**, the furan by-product **9** was isolated in 5-10% yield.



9

For instance, in the reaction of **3a** with ethyl cyanoformate compound **9** (R=R'=Et) was isolated as by-product in 5% yield. ^1H-NMR ($CDCl_3$) δ: 0.99-1.25 (m, 6H, 2 OCH_2CH_3), 4.06-4.19 (m, 4H, 2 OCH_2CH_3), 5.35 (s, 2H, OCH_2), 5.70 (br, 1H,NH), 6.59 (d, J=3.6 Hz, 1H, CH), 7.01 (d, J=3.6 Hz, 1H, CH), 7.40-7.58 (m, 3H, Ph), 8.01-8.06 (m, 2H, Ph), 8.40 (br, 1H, NH).