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Several sugar-triazole derivatives were synthesized and characterized by spectroscopic techniques. Interaction of the sugar-triazoles with CT-DNA has been explored which revealed that all the compounds could interact with CT-DNA through groove binding was further supported by the docking analysis.
Design and synthesis of sugar-triazole based uracil appended sugar-imine derivatives – An application in DNA binding studies

Arasappan Hemamalini, Ettayapuram Ramaprasad Azhagiya Singam, Sathish kumar Mudedla, Venkatesan Subramanian, Thangamuthu Mohan Das

Several sugar-triazole derivatives were synthesized and characterized by spectroscopic techniques. Interaction of the sugar-triazoles with CT-DNA has been explored which revealed that all the compounds could interact with CT-DNA through groove binding was further supported by the docking analysis.

Introduction

DNA is the material of inheritance and control the structure and function of cells. Recently, there has been an emerging interest in the studies related to the interaction of small molecules with nucleic acid because of their relevance in the development of new reagents for biotechnology and medicine. General, DNA molecule is a target for plethora of anticancer and antiviral drugs that form covalent and non-covalent adducts with major or minor groove of DNA. DNA still represents one of the principal targets in drug development strategies designed to produce novel therapeutics for diseases such as cancer. In particular, CT-DNA is a natural DNA, widely used in the studies of DNA binding anticancer agents. It is polymer of alternate sugar-phosphate sequence with low protein and high polymerized skeleton. Since DNA is an important cellular receptor, many compounds exert their antitumor effects through binding to DNA thereby changing its replication and inhibiting cell growth. However, appending carbohydrate moiety to drug candidates to form new drugs, offers great potential in increasing the solubility of the molecule and minimizing the toxicity and enhancing the solubility. A potential benefit of this approach leads freely available pendant form of carbohydrate to interact with transport and metabolic pathways in the body. The investigation of drug-DNA interaction is important for understanding the molecular mechanism of drug action and also for the design of specific DNA targeted drug. The interaction of small molecules with DNA involves either electrostatic interaction or groove binding or intercalative binding. In addition, glucopyranosyltriazoles display a diverse biological activities such as anti-tumor, anti-viral and anti-tuberculosis agents. Furthermore, many N-substituted-uracil derivatives possess biological activity. N-Glycosides of substituted uracils are widely used in therapy, mainly as antiviral and antineoplastic agents. In continuation of our research in the area of carbohydrate chemistry, this paper deals with the synthesis and characterization of uracil appended triazole based sugar-imine derivatives which exhibits DNA binding property. To the best of our knowledge there is no report in the literature of any uracil appended sugar-triazole derivatives.

Results and discussion

Synthesis and characterization of sugar-triazole derivatives

1,3-Dipolar cycloaddition was applied to synthesize the sugar-triazole derivatives. 2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosylazide, 1 was synthesized from D-glucose by following the literature procedure. O-Alkylation of various aromatic α-hydroxy-aldehydes led to the formation of O-propargylated derivatives, 2-5 in excellent yield. CuAAC of the O-propargyl-aldehyde with sugar-azide was promoted by CuSO₄·5H₂O as catalyst and sodium ascorbate as reducing agent in a mixture of solvent [THF:H₂O, 1:1] resulted 74-85% of the corresponding sugar-triazole derivatives, 6-9. All the synthesized triazoles were confirmed by spectral techniques. Formation of the triazole-product, 7 was confirmed from NMR spectroscopic technique where a sharp singlet at δ 7.9 ppm corresponds to the triazole proton. 13C NMR spectrum of compound 7 exhibited characteristic signals at δ 144 and 122 ppm respectively which were assigned to the C4 and C5 carbon atoms of the triazole ring corroborated well with the proposed structure. Formation of the 1,4-regiosomer is confirmed from the difference in the chemical shift value of C4 and C5 of the triazole moiety which is around 23 ppm.
NMR spectrum of compound 7 also notably exhibited a large coupling constant for the H-1 signal ($J_{H1,H2} \sim 9$ Hz), indicating a trans-diaxial orientation of H-1 and H-2 as expected for a β-D-configured glucopyranose moiety. Optimization of experimental condition and spectroscopic data are given in Table 1 [See ESI for more details].

**Synthesis and characterization of uracil appended sugar-imine derivatives**

Different sequences of the reaction were tried for the synthesis of uracil appended sugar-imine derivatives. Among the different sequences, O-alkylation followed by CuAAC and Schiff base formation resulted in a good yield where the other sequence of the reaction resulted in only diminished yield of the product. However, the reaction of 6-amino-3,5-N,N-dimethyluracil, 10 with sugar-triazole derivative bearing an aldehyde using ethanol as solvent under neutral condition did not give the expected sugar-imine product and it may be due to the very poor solubility of 10. When the same reaction was carried out in the presence of concentrated HCl at room temperature resulted in the sugar-imine derivatives, 11-14 in 35-58% yield (Scheme 1 and Scheme 2). Under the given reaction condition, ester group in the sugar moiety is completely hydrolyzed. In this case, HCl has not only improved the solubility of the reaction mixture which facilitated the reaction but also utilized for the deprotection of the acetyl group simultaneously, thus resulted in a water soluble sugar-imine derivatives. The structures of resulting sugar-imine derivatives were characterized using FT-IR, $^1$H and $^{13}$C NMR spectral techniques and elemental analysis. Details about the synthesis of sugar-imine derivatives are shown in Scheme 1 and 2.

The formation of imine core in compound, 12 is confirmed from the appearance of peak at 1667 cm$^{-1}$ in FT-IR spectrum. $^1$H NMR spectrum of compound, 12, revealed a sharp singlet at δ 8.0 ppm attributed to the methine proton and the product formation was further confirmed from the $^{13}$C NMR spectrum by the appearance of a peak at δ 165 ppm which corresponds to the imine carbon. Based on the literature,$^{19}$ the stereochromism of the imine group is assigned as trans geometry because it is well known that the trans product is much more stable than the corresponding cis form. The triazole proton resonated as a singlet at δ 7.6 ppm and its corresponding carbons (C5 and C4) observed at δ 148 and 124 ppm respectively.

![Scheme 2 Synthesis of sugar-imine derivative, 14.](image)

The difference between C4 and C5 carbon is found to be 24 which confirms the formation of 1,4-regiosomeric triazole product. It also notably exhibited a large coupling constant for the H-1 signal ($J_{H1,H2} \sim 9.3$ Hz), indicating a trans-diaxial orientation of H-1 and H-2 as expected for a β-D-configured glucopyranose moiety.$^{18}$ During the course of the reaction, the ester group which is actually the protecting group is cleaved in acidic condition. Hence, the disappearance of acetyl group peak in $^1$H NMR and carbonyl group peak in the $^{13}$C NMR has been observed and it further confirms the formation of deprotected sugar-imine derivatives. Details about the experimental condition and spectroscopic data are provided in Table 2 [See ESI for more details].

**DNA binding studies**

The application of electronic absorption spectroscopy in DNA binding studies is one of the most useful techniques$^{20}$ as the observed changes in the spectra may give evidence of the existing interaction and its mode.$^{21}$ Absorption spectrum of the compounds, 6-8 and 11-13 is compared with and without DNA. The binding study was carried out for sugar-imine derivatives, 11-13 and its precursors, 6-8. The derivatives$^{19}$ were titrated against calf-thymus DNA at different concentrations. Absorption band profile obtained during the titration experiment is shown in Figure 1. The absorbance was recorded for each addition of DNA. In order to eliminate the absorbance that arises due to CT-DNA, an equal amount of the same was added to both the compound, as well as the reference solution.

![Figure 1](image)

For compounds, 6-8 and 11-13 the absorption bands were observed in the range from 240-375 nm which corresponds to $n-\pi^*$/$\pi-\pi^*$ transitions. On increasing the concentration of CT-DNA, there was a concomitant decrease in the absorption intensity – hypochromism for all the six derivatives. This hypochromic effect is suggestive for the compound possessing a higher propensity for DNA binding. It indicates that the interaction of compounds, 6-8 and 11-12 with DNA takes place by the direct formation of a novel complex with double-helical DNA. In general, the compound binding with DNA through intercalation results in hypochromism due to the intercalative mode involving a strong stacking interaction of the planar aromatic chromophore of the compound with the base pairs. But there are also few non-intercalators which results in both hyperchromism or hypochromism.$^{22}$ Out of the
six derivatives, the binding mode of uracil appended sugar-imine derivatives, 11-13 found to be almost same as that of the simple sugar-triazole derivatives, 6-8. This observation shows that the uracil appended sugar imine derivatives and also its precursors to be a good binder with CT-DNA. Irrespective of the substituent in the aromatic ring, the binding constant found to be almost similar. Since the molecule is non-planar and the hypochromism from the absorption studies obviously suggest that the compounds 6-8 and 11-13 are most likely to interact with DNA through a mode of groove binding with DNA. It was further confirmed from their binding constant values.

Figure 1 Absorption titration spectra of compounds: (a-c), sugar triazoles, 6-8, (d-f), sugar imines, 11-13 (10 x 10^6 M) with CT-DNA (0-250 x 10^-6 M); The arrow indicates the change in the absorbance upon increasing amount of CT-DNA; Inset plot of [DNA]/(ε_a - ε_f) Vs [DNA].

For the quantitative investigation of the binding strength of the sugar imine derivative, 11-13 and its precursors, 6-8 with CT-DNA, UV spectrophotometric titration was performed. The intrinsic binding constant (K_b) was calculated from the following equation:

\[
{[DNA]} / (\epsilon_a - \epsilon_f) = {[DNA]} / (\epsilon_b - \epsilon_f) + 1 / (K_b [\epsilon_b - \epsilon_f])
\]

Where, [DNA] represents the concentration of DNA and the apparent absorption coefficients \(\epsilon_a\), \(\epsilon_f\) and \(\epsilon_b\) correspond to A_{abs}/[ligand], the extinction coefficient of compound and the extinction coefficient of the compound in the fully DNA-bound form, respectively.

A plot of [DNA]/ (\epsilon_a - \epsilon_f) versus [DNA], gives 1/(\epsilon_b - \epsilon_f) as slope and 1/(K_b [\epsilon_b - \epsilon_f]) as the intercept. The intrinsic binding constant K_b is calculated as the ratio between slope and intercept. The determined K_b value for sugar imine derivatives, 11-13 is found to be 4.8 ± 0.4 x 10^3, 4.7 ± 0.5 x 10^3 and 4.8 ± 0.4 x 10^3 M^-1 respectively which indicates that the uracil-appended sugar-imine derivative is capable of binding moderately with CT-DNA. The K_b value for its precursor, 6-8 is 9.9 ± 0.4 x 10^3, 9.2 ± 0.3 x 10^3 and 6.4 ± 0.3
x 10^7 M^{-1} respectively. Ethidium bromide which is an excellent DNA binder binds with CT-DNA in the range of 10^7 whereas all the synthesized molecules shows the binding constants in the range of 10^3. These results suggested that both the sugar-imine derivatives, 11-13 and its precursor, 6-8 binds moderately with CT-DNA. The titration experiment is repeated thrice and the error graph plotted for the average values is represented in Figure 2.

![Figure 2 Error graph for the compound, 6-8 and 11-13; Values are mean ± S. D., n=3.](image)

Since the sugar-imine-derivative and its precursors are non-planar, it is assumed that they may have groove binding with DNA. Based on the present studies, the synthesized uracil-appended sugar-imine derivative exhibit a groove binding with DNA and hence may found to have applications in the field of medicine.

While designing sugar-triazole and sugar-imine derivatives, bioactive centres and binding centres has been incorporated and these synthesized sugar derivatives may find applications in the field of medicine. The binding nature and the binding sites of the synthesized molecules are confirmed from the docking analysis.

**Docking studies**

There has been increasing interest in the usage of docking methods in order to study binding of molecules to DNA. The structures of ligands (6-8 and 11-13) were optimized using density functional theory (DFT) with Becke’s three parameter hybrid exchange functional and the Lee-Yang-Parr correlation functional (B3LYP) and 6-31G(d,p) basis set was used. The geometry optimization was carried out without any geometrical constraints. To ensure that the optimized geometries correspond to true minima on the potential energy surface, vibrational frequencies were computed using DFT (B3LYP/6-31G(d,p)). Partial atomic charges for all atoms in the complexes were calculated using B3LYP/6-31G(d,p) level of theory. All these calculations were carried out using Gaussian 09 package. For docking studies the structural coordinates of DNA was obtained from the protein data bank (pdb id: 202D). In the docking analysis, the binding site was assigned across the entire minor and major grooves of the DNA molecule. As the docking module primarily imparts ligand flexibility and considers the receptor macromolecule as a rigid entity. The docking was performed to find the most stable and favorable orientation. All dockings were performed as blind dockings (blind docking refers to the use of a grid box which is large enough to encompass any possible ligand receptor complex) using Auto Dock Vina 1.0. The obtained data from docking was examined by PYMOL software. The most favorable docked orientation was depicted in Figure 3. It is very obvious from the result that all the compounds interact with DNA moderately. Interestingly, the sugar-triazole derivatives exhibits higher binding affinity compared to that of the sugar-imine derivatives which is in corroboration with the experimental results. Furthermore, the mode of binding of the sugar-triazole ligands (6-8) and the sugar imine derivatives (11-13) with DNA was revealed from the Figure 3. Due to the difference in the orientation of both the sugar-triazole and sugar-imine derivatives, there exist difference in the hydrogen bonding interaction with CT-DNA (See ESI) and hence there is a difference in the values of binding constant.

![Figure 3 Docked pose of compounds with CT-DNA: a, b and c are sugar-triazoles, 6, 7 and 8; d, e and f are sugar imines, 11, 12 and 13.](image)

The docking studies of the so synthesized ligands clearly showed the importance of mode of action through the interaction between sugar and DNA. From Figure 3 it can be seen that the ligands bound to the minor grooves of DNA. The molecular modeling study shows that all the six ligands bind DNA preferably through groove mode.

**Conclusion**

Several triazole based sugar-triazole and sugar-imine derivatives were synthesized and characterized using different spectral techniques. The interaction of the synthesized sugar-imine derivative, 11-13 along with its precursors, (sugar triazoles), 6-8 with CT-DNA is carried out using absorption spectroscopic technique. Binding constant is calculated and surprisingly, the results showed that the sugar triazole derivatives binds moderately with CT-DNA compared to that of the corresponding sugar-imine derivatives and the nature of binding is also revealed from their binding constant values as groove mode, which was further supported from the results obtained from docking analysis. Docking analysis revealed the binding of the compound with CT-DNA mostly in the minor groove.
**Experimental section**

**General methods**

D-Glucose, propargylbromide, various hydroxaldehydes and 6-amino-3,5-N,N-dimethylylacil and sodium azide were purchased from Sigma-Aldrich Chemicals Pvt. Ltd., USA and were of high purity. Other reagents, such as hydrochloric acid, hydrogenbromide in aceticacid, potassiumcarbonate, and solvents (AR grade) such as tetrhydrofuran, DMF were obtained from Sd-fine, India, in high purity and were used without any purification. Zincchloride, copper(II)carbonate, sodiumsulphate were obtained from Loba-chemie, India. Aceticanhydride was purchased from Fischer Chemicals Pvt. Ltd., India. CT-DNA was purchased from Genei, Bangalore, India. The stock solutions were stored at 4°C and were used not more than 4 days. All the experiments involving interaction of the compounds with DNA were carried out in doubly distilled water buffer containing 5 mM Tris-HCl (tris(hydroxymethyl)-aminomethane) and 50 mM NaCl. The solvents were purified according to standard methods. Column chromatography was performed on silica gel (100-200 mesh). NMR spectra were recorded on a Bruker DRX 300 MHz instrument in either CDCl$_3$ or DMSO-$d_6$. Chemical shifts were referenced to internal TMS. Absorption titration studies were carried out on 1800 Shimadzu UV spectrophotometer in the range 190-800 nm. Electro-spray ionization mass spectrum was recorded using WATERS-Q-TOF Premier-HAB213 spectrometer. Optical rotation was performed using Rudolf research analytical Autopol I polarimeter. Elemental analysis was performed using Perkin-Elmer 2400 series CHNS/O analyzer.

**DNA binding experiments**

CT-DNA was dissolved in Tris-buffer (Tris-HCl pH 7.2) and the stock solution was stored at 4°C and was stable for several days. A solution of CT-DNA in water gave a ratio of UV absorbance at 260 and 280 nm, $A_{260}/A_{280}$ of 1.89-2.01, indicating that DNA was sufficiently free of protein. The concentration of DNA was determined from the UV absorbance at 260 nm using the extinction coefficient $e_{260} = 6600$ M$^{-1}$·cm$^{-1}$. The absorbance titration was performed at a fixed concentration of compound, 6-8 and 11-13 and varying the concentration of double stranded CT-DNA. Upon additions in each cuvette (sample and blank) of a same aliquot of CT-DNA, the samples were shaken and left in equilibrium for 2 minutes before recording each spectrum.

**General procedure for the synthesis of sugar-triazole derivatives (6-9):**

To a solution of acetylenic compounds, 2-5 (1 equiv.) in a 1:1 (V/V) mixture of THF: HO (10 ml) were added 2,3,4,6-tetra-O-acetyl-sugar-azide, 1 (1.2 equiv.), CuSO$_4$·5H$_2$O (0.2 equiv.), sodium ascorbate (0.4 equiv.). After stirring the reaction mixture for a given period of time, it was then extracted with chloroform and washed with saturated NH$_4$Cl, water and brine solution. Organic layer was collected, dried over anhydrous Na$_2$SO$_4$ and concentrated to dryness under vacuum. The crude mixture was purified by column chromatographic technique.

**Spectral data of 1-(2,3,4,6-tetra-O-acetyl-$eta$-D-glucopyranosyl)-4-(2-formyl-1-phenoxymethyl)-1H-1,2,3-triazole (6):**

Compeund, 6 was obtained by the CuAAC of 2-propynoxybenzaldehyde, 2 (0.16 g, 1 mmol) and sugar-azide, 1 (0.45 g, 1.2 mmol) as a colourless solid; $M_p$ 146-148 °C; Yield: 0.45 g (85%); $[a]$_{26}^{20} -0.48$ (c 1, CHCl$_3$); $R_f$ = 0.5 (Hexane-EtOAc, 40:60); $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 10.48 (s, 1H, -CHO), 7.92 (s, 1H, Trz-H), 7.87 (d, $J = 7.5$ Hz, 1H, Ar-H), 7.58 (t, $J = 7.6$ Hz, 1H, Ar-H), 7.15-7.06 (m, 2H, Ar-H), 5.91-5.88 (m, 8H, Sac-H, 1), 5.45-5.42 (m, 2H, Sac-H-2, 3), 5.35 (s, 2H, -OCH$_3$), 5.29-5.26 (m, 1H, Sac-H-4), 4.32 (dd, $J_{4,6a} = 4.8$ Hz, $J_{5,6a} = 12.6$ Hz, 1H, Sac-H-6a), 4.16 (dd, $J_{4,6b} = 1.8$ Hz, $J_{5,6b} = 12.6$ Hz, 1H, Sac-H-6b)

**Spectral data of 1-(2,3,4,6-tetra-O-acetyl-$eta$-D-glucopyranosyl)-4-(4-formyl-2-methoxy-1-phenoxymethyl)-1H-1,2,3-triazole (7):**

Compound, 7 was obtained by the CuAAC of 3-methoxy-4-propynoxybenzaldehyde, 4 (0.19 g, 1 mmol) and sugar-azide, 1 (0.45 g, 1.2 mmol) as a colourless solid.

**Spectral data of 1-(2,3,4,6-tetra-O-acetyl-$eta$-D-glucopyranosyl)-4-(5-chloro-2-formyl-1-phenoxymethyl)-1H-1,2,3-triazole (8):**

Compound, 8 was obtained by the CuAAC of 5-chloro-2-propynoxybenzaldehyde, 3 (0.19 g, 1 mmol) and sugar-azide, 1 (0.44 g, 1.2 mmol) as a colourless solid.

**Spectral data of 1-(2,3,4,6-tetra-O-acetyl-$eta$-D-glucopyranosyl)-4-(2-formyl-1-phenoxymethyl)-1H-1,2,3-triazole (6):**

<table>
<thead>
<tr>
<th>Compound</th>
<th>mp</th>
<th>Yield</th>
<th>$[a]_{26}^{20}$</th>
<th>$R_f$</th>
<th>$^1$H NMR (300 MHz, CDCl$_3$):</th>
<th>$^1$C NMR (75 MHz, CDCl$_3$):</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>146-148 °C</td>
<td>0.45 g</td>
<td>-0.48 (c 1, CHCl$_3$)</td>
<td>0.5</td>
<td>$\delta$ 10.48 (s, 1H, -CHO), 7.92 (s, 1H, Trz-H), 7.87 (d, $J = 7.5$ Hz, 1H, Ar-H), 7.58 (t, $J = 7.6$ Hz, 1H, Ar-H), 7.15-7.06 (m, 2H, Ar-H), 5.91-5.88 (m, 8H, Sac-H, 1), 5.45-5.42 (m, 2H, Sac-H-2, 3), 5.35 (s, 2H, -OCH$<em>3$), 5.29-5.26 (m, 1H, Sac-H-4), 4.32 (dd, $J</em>{4,6a} = 4.8$ Hz, $J_{5,6a} = 12.6$ Hz, 1H, Sac-H-6a), 4.16 (dd, $J_{4,6b} = 1.8$ Hz, $J_{5,6b} = 12.6$ Hz, 1H, Sac-H-6b)</td>
<td>$\delta$ 190.9, 170.5, 169.9, 166.8, 160.9, 153.9, 128.7, 125.2, 121.5 (2C), 113.0, 85.8, 75.3, 72.5, 70.3, 67.7, 62.3, 61.5, 20.7, 20.5</td>
<td>20:1; Elemental analysis Anal. Calc. for C$_4$H$_7$NO$_5$: C, 54.03; H, 5.10; N, 7.88%. Found: C, 54.06; H, 5.14; N, 7.92.</td>
</tr>
</tbody>
</table>
bearing aldehyde, 7 (0.56 g, 1 mmol) and 6-amino-3,5,N-dimethyluracil, 10 (0.15 g, 1 mmol) as a colourless solid.  
Mp: 186-190 °C; Yield: 0.31 g (58%); [α]D 28 2.13 (c 1, H2O);  
1H NMR (300 MHz, CDCl3 + DMSO-d6): δ 8.01 (s, 1H, Imin-H), 7.69 (s, 1H, Trz-H), 6.93 (d, J = 9.0 Hz, 1H, Ar-H), 6.68 (bs, 2H, Ar-H), 5.69 (s, 1H, alk-H), 5.58 (d, J = 9.3 Hz, 1H, Ano-H-1), 5.32 (bs, 2H, Sac-H-2,3), 5.17 (s, 2H, -OCH2), 5.03-4.97 (m, 2H, Sac-H-4,6a), 4.47 (bs, 1H, Sac-H-6b), 3.94-3.80 (m, 1H, Sac-H-5), 3.71 (s, 3H, -OCH3), 3.44 (s, 6H, -NCH3); 13C NMR (75 MHz, CDCl3 + DMSO-d6): δ 168.0, 159.8, 157.5, 155.8, 153.9, 150.1, 148.4, 137.9, 127.9, 123.5, 118.6, 116.4, 92.8, 84.6, 83.0, 82.2, 77.3, 74.5, 67.3, 66.0, 60.7, 40.0, 34.8, 33.0; ESI-MS Calc. for C23H23N6O2: 532.19; m/z found, 533.20 [M+H]+; Elemental analysis Anal. Calc. for C23H22N6O2; C, 51.88; H, 5.30; N, 15.78%. Found: C, 51.92; H, 5.32; N, 15.82.  
Spectral data of 1,3-dimethyl-6-[(E)-4-chloro-2-(1-(2,3,4,6-tetra-O-hydroxy-β-D-glucopyranosyl)-1-H,1,2,3-triazol-4-yl)methoxy]benzilideneamino]pyrimidine-2,4(1H,3H)-dione (13):  
Compound, 13 was obtained by the reaction of sugar-triazole bearing aldehyde, 8 (0.57 g, 1 mmol) and 6-amino-3,5,N-dimethyluracil, 10 (0.16 g, 1 mmol) as a colourless solid.  
Mp: 194-198 °C; Yield: 0.19 g (35%); [α]D 28 1.3 (c 1, H2O);  
1H NMR (300 MHz, CDCl3 + DMSO-d6): δ 7.93 (s, 1H, Imin-H), 7.67 (s, 1H, Trz-H), 7.15-7.12 (m, 2H, Ar-H), 6.88 (d, J = 8.1 Hz, 1H, Ar-H), 5.60 (bs, 2H, Alk-H, Sac-H-1), 4.97 (bs, 4H, -OCH2, Sac-H-2,3), 4.50 (bs, 1H, Sac-H-4), 3.91-3.87 (m, 2H, Sac-H-6a,6b), 3.76 (bs, 1H, Sac-H-5), 3.59 (s, 3H, -NCH3); 3.41 (s, 3H, -NCH3); 13C NMR (75 MHz, CDCl3 + DMSO-d6): δ 167.0, 159.8, 158.0, 155.7, 153.6, 150.0, 148.1, 136.5, 132.6, 131.2, 130.0, 126.9, 117.2, 92.8, 84.6, 82.3, 77.5, 75.4, 66.8, 66.1, 37.2, 34.7; Elemental analysis Anal. Calc. for C22H20ClN6O2: C, 49.21; H, 4.69; N, 15.65%. Found: C, 49.26; H, 4.73; N, 15.68.  
Spectral data of 1,3-dimethyl-6-[(E)-3-(1-(2,3,4,6-tetra-O-hydroxy-β-D-glucopyranosyl)-1-H,1,2,3-triazol-4-yl)methoxy]benzilideneamino]pyrimidine-2,4(1H,3H)-dione (14):  
Compound, 14 was obtained by the reaction of sugar-triazole bearing aldehyde, 9 (0.53 g, 1 mmol) and 6-amino-3,5,N-dimethyluracil, 10 (0.15 g, 1 mmol) as a colourless solid.  
Mp: 192-194 °C; Yield: 0.26 g (52%); [α]D 28 0.96 (c 1, H2O);  
1H NMR (300 MHz, CDCl3 + DMSO-d6): δ 8.01 (s, 1H, Imin-H), 7.50 (s, 1H, Trz-H), 7.28 (s, 1H, Ar-H), 7.14 (t, J = 7.7 Hz, 1H, Ar-H), 6.78-6.72 (m, 2H, Ar-H), 5.69 (s, 1H, Alk-H), 5.60 (d, J = 9.0 Hz, 1H, Ano-H-1), 5.24 (bs, 2H, Sac-H-2,3), 5.14 (s, 2H, -OCH2), 4.84 (bs, 2H, Sac-H-4,6a), 3.89-3.72 (m, 2H, Sac-H-6b,5), 3.53 (s, 3H, -NCH3), 3.42 (s, 3H, -NCH3); 13C NMR (75 MHz, CDCl3): δ 166.7, 160.7, 154.6, 146.9, 132.6, 127.6, 125.3, 120.6, 118.2, 116.6, 114.8, 90.3, 81.8, 85.1, 79.7, 78.9, 75.1, 72.0, 63.4, 38.3, 33.1, 31.6; Elemental analysis Anal. Calc. for C22H20N6O2: C, 52.59; H, 5.22; N, 16.73%. Found: C, 52.64; H, 5.27; N, 16.77.  
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Notes and references

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