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A concise pathway to synthesize a novel class of pyrido(2,3-*d*)pyrimidine-*C*-β-D-glycosides

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ABSTRACT

A concise pathway to synthesize a novel class of nine different pyrido(2,3-*d*)pyrimidine-*C*-β-D-glycosides is reported. Formation of Michael adduct as an intermediate followed by heterocyclization are the key steps and the products were characterized by different spectral studies. β-Anomeric forms of C-glycosides were assigned from ^{1}H NMR spectroscopy.

1. Introduction

In modern synthetic organic chemistry, development of a novel and efficient method for the construction of several mono as well as poly heterocyclic scaffolds is one of the current areas of research interest.[1] Pyrido(2,3-*d*)pyrimidine derivatives, being an important class of *N*-heterocycles display several potential biological activities, such as tyrosine kinase inhibition,[2] dihydrofolate reductase inhibition,[3] STa induced cGMP synthesis inhibition,[4] anti-bacterial,[5] anti-inflammatory[6] and in vitro cytotoxic activities.[7] In particular, naturally occurring compounds viz., sangivamycin (**1**) containing pyrrolo(2,3-*d*)pyrimidine nucleoside and its simple homologue pyrido(2,3-*d*)pyrimidine nucleoside (**2**) were found to possess anti-leukaemic activity (Fig. 1).[8,9] Moreover, the beneficial properties of basic and electron-withdrawing nature of *N*-heterocyclic compounds make them a more attractive biological target more effectively than carbocyclic compounds. In this connection the anti-tumour activity of benz[*a*]anthraquinone chromophore of 3,4-dihydro-8-hydrotetraphene-1,7,12(2*H*)-trione (**3**) was enhanced by modifying one of its aromatic methine groups to afford 3,4-dihydro-8-hydroxybenzo[*j*]phenanthridine-1,7,12(2*H*)-trione (**4**) (Fig. 1)[10] which possesses more potent anti-tumour activities. Thus these structural motifs acquire great attention in the field of pharmaceutical chemistry.

Indeed, some of the carbohydrate derivatives like flavone C-glycosides,[11] from natural origins as well as the synthetic macrocyclic lactones having a *C*-linkage[12] were also reported to possess good therapeutic profiles viz., solubility, in vivo stability, target-binding affinity and cell permeability.[13] Thus the studies pertaining to heterocyclic carbohydrate derivatives with *C*-linkage have received increasing attention not only among synthetic organic chemists but also among medicinal chemists. Although the synthesis of several pyrido(2,3-*d*)pyrimidine derivatives was carried out by different synthetic strategies and reported in the literature,[1,14–16] all those methods lead to the formation of the core moiety linked with aromatic systems. Among them, a few of the synthetic strategies involve Michael addition of α-,β-unsaturated ketones with aminouracil, reaction of 2-amino-3-cyano-4,5,6-disubstitutedpyridines with carbonyl compounds and a selective condensation of aminopyrimidine with propiophenone hydrochlorides. Therefore, by considering the importance of *N*-heterocyclic based C-glycosides including other glycosides,[17,18] viz., *N*-glycosylamine, *O*-glycosides and their various biological and material applications, our present study focuses on the concise pathway to synthesize the novel class of pyrido(2,3-*d*)pyrimidine-*C*-β-D-glycosides. Moreover, to the best of our knowledge this is the first report on studies on pyrido(2,3-*d*)pyrimidine based C-glycosides.

2. Results and discussion

Aldol condensation of (4,6-*O*-butylidene-β-D-glucopyranosyl)propan-2-one (**5**) with various substituted aromatic aldehydes (**6a–i**) resulted in the formation of the corresponding α-,β-unsaturated-*C*-β-glycosidic ketones (**7a–i**) in 80–95% yield (Scheme 1). Although the synthesis and characterization of sugar chalcones, **7a**, **7d**, **7e** and **7g** were already reported in the literature,[19] details about compounds **7b**, **7c**, **7f**, **7h** and **7i** are presented in the

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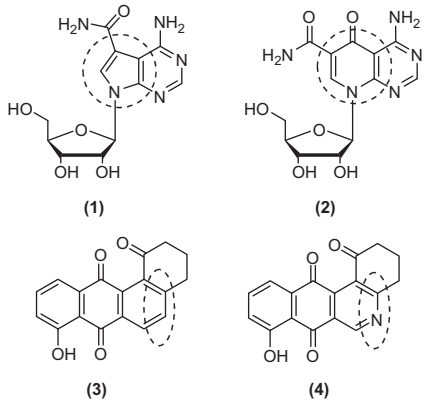
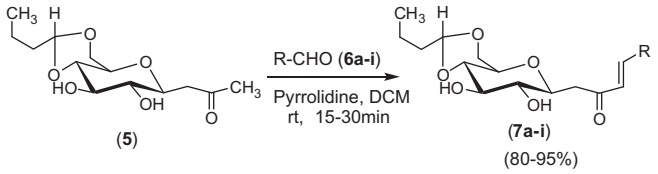


Figure 1. Molecular structures of 4-amino-7-(tetrahydro-3,4-dihydroxy-5-(hydroxymethyl)furan-2yl)-7*H*-pyrrolo[2,3-*d*]pyrimidine-5-carboxamide (**1**) and its homologue, 4-amino-5,8-dihydroxy-8-(tetrahydro-3,4-dihydroxy-5-(hydroxymethyl)furan-2yl)-5-oxopyrido-[2,3-*d*]pyrimidine-6-carboxamide (**2**), 3,4-dihydro-8-hydrotetraphene-1,7,12(2*H*)-trione (**3**) and 3,4-dihydro-8-hydroxybenzo[*j*]phenanthridine-1,7,12(2*H*)-trione (**4**). Encircled shows the comparison between the naturally occurring compound (**1**) with synthetic one (**2**) and also among the synthetic derivatives (**3** and **4**).



(a)R=Ph, (b)R=4-OMePh, (c)R=4-MePh, (d)R=Piperonal, (e)R=3,4-di-OMePh, (f)R=4-ClPh, (g)R=4-FPh, (h)R=3-BrPh, (i)R=Pyrrole,

Scheme 1. Synthesis of α-,β-unsaturated-*C*-β-glycosides.

experimental section. Pyrimidine based heterocyclic derivatives (**9a–i**) were synthesized by the condensation of α-,β-unsaturated-*C*-β-glycosidic ketones (**7a–i**) with 6-amino-1,3-dimethyluracil (**8**) (Scheme 2). In order to obtain the expected products in good yield, the reaction was carried out using different bases, such as KOH, NaOH, NaOEt, Et_3N in different solvents, such as EtOH and THF. The reaction condition was optimized to get 7-(4,6-*O*-butylidene-β-D-glucopyranosyl-1-methyl)-1,3-dimethyl-5-phenylpyrido(2,3-*d*)pyrimidine-2,4-dione (**9a**) and the details about the optimized reaction conditions are given in Table 1.

Studies show that using sodium ethoxide as catalyst in THF/EtOH (3:1) solvent mixture at room temperature resulted in better yield (entry 11, Table 1). Spectral data, reaction time and

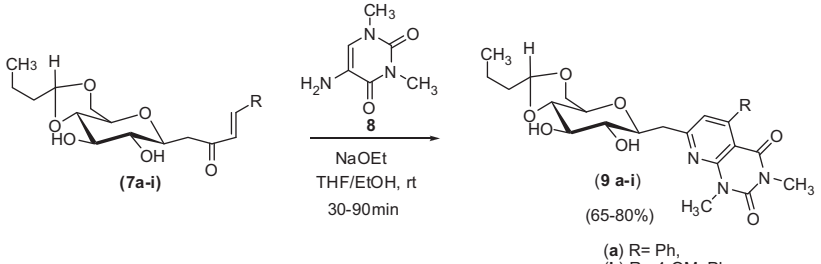
Table 1
Optimization of reaction condition for compound, **9a**

Entry	Solvent ratio of THF/EtOH	Condition	Temp (°C)	Yield (%)
1	0:1	KOH	60	—[a]
2	0:1	NaOH	60	—[a]
3	0:1	Et_3N	60	—[a]
4	1:0	KOH	rt	32
5	1:0	NaOH	rt	32
6	1:0	Et_3N	rt	—[b]
7	0:1	NaOEt	60	—[a]
8	1:0	NaOEt	rt	58
9	1:1	NaOEt	rt	60
10	2:1	NaOEt	rt	63
11	3:1	NaOEt	rt	73

[a] Resulted in formation of decomposed product.
[b] Reaction was not successful.

percentage of yield for different pyrimidine sugar heterocyclic derivatives (**9a–i**) are provided in Table 2.

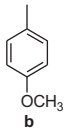
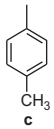
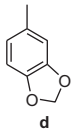
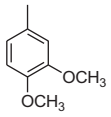
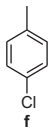
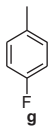
Structural elucidation of the expected product formation was established on the basis of its spectroscopic data. ^{1}H NMR spectra of α-,β-unsaturated-*C*-β-glycosides (**7a–i**) showed the signals around 7.30–6.59 ppm for alkenic proton (Alk-H_a), adjoining the carbonyl group and 7.80–7.30 ppm for the alkenic proton (Alk-H_b), adjoining the aromatic moiety their corresponding carbon peaks in ^{13}C NMR were observed in the region of 135.25–120.27 ppm and 147.97–141.71 ppm respectively. Moreover the observation of a larger coupling constant (J = 15.9–16.2 Hz) showed the existence of '*E*' isomeric forms in sugar chalcones. In particular, ^{1}H NMR spectral studies of the 7-(4,6-*O*-butylidene-β-D-glucopyranosyl-1-methyl)-1,3-dimethyl-5-phenylpyrido(2,3-*d*)pyrimidine-2,4-dione (**9a**) confirmed the formation of the pyridopyrimidine core moiety by the appearance of a sharp singlet (δ 6.91 ppm) corresponding to the methine proton and it was further confirmed by the disappearance of doublet (δ 6.78 ppm) corresponding to the alkenic proton of sugar chalcone, (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-phenylbut-3-en-2-one (**7a**). In addition, NMR spectral analysis of all the sugar-heterocyclic derivatives [**9**(**a–i**)] confirmed the formation of the pyridopyrimidyl core. Appearance of a characteristic peak [^{1}H NMR: singlet, δ 7.58–6.75 ppm; ^{13}C NMR: δ 126.84–122.17 ppm] corresponding to the "Py-*CH*" confirmed the presence of pyridopyrimidyl core in all the products [**9**(**a–j**)]. Although the starting material **8** exhibited two sharp singlets in the range of 3.32–3.18 ppm in ^{1}H NMR and 28.99–26.91 ppm in ^{13}C NMR, the corresponding peaks in the sugar-heterocyclic products were shifted to higher frequencies, 3.85–3.30 ppm in ^{1}H NMR & 30.15–28.41 ppm in ^{13}C NMR respectively. Diastereotopic proton of the methylene group which links



(**a**) R= Ph,
(**b**) R= 4-OMePh,
(**c**) R= 4-MePh
(**d**) R= Piperonal,
(**e**) R= 3,4-diOMePh
(**f**) R= 4-ClPh
(**g**) R= 4-FPh
(**h**) R= 3-BrPh
(**i**) R= Pyrrole

Scheme 2. Synthesis of pyrido(2,3-*d*)pyrimidine derivatives (**9a–i**).

Table 2
Spectral data, reaction time and percentage of yield for different pyrimidine sugar heterocyclic derivatives (**9a–i**)

Entry	R **6/7/9**(**a–i**)	NMR (δ in ppm) **9**		Reaction time (min)	Yield (%) **9**
		^{1}H [Py-*CH*]	^{13}C [Py-*CH*]		
1	 **a**	6.92	122.68	30	73
2	 **b**	6.83	122.79	35	82
3	 **c**	6.91	122.78	30	81
4	 **d**	6.79	122.17	60	72
5	 **e**	6.75	122.86	65	79
6	 **f**	6.81	122.46	30	86
7	 **g**	6.89	122.68	30	82
8	 **h**	6.88	122.40	90	67
9	 **i**	7.58	126.84	90	75

pyridopyrimidyl core moiety and protected sugar in the products, **9**(**a–i**) was found to appear at δ.3.04–2.80 ppm as a doublet of doublet and the corresponding ^{13}C NMR spectra exhibited a peak at δ 45.49–40.82 ppm further confirming the formation of the heterocyclic core moiety. Moreover, the saccharide skeletal proton of sugar-chalcones showed peaks in the range of 5.29–2.95 ppm, the corresponding sugar-heterocyclic products **9**(**a–i**) appeared in the region of δ 5.30–3.12 ppm. The appearance of the anomeric proton as a doublet of triplets at δ 4.04–3.78 ppm with a large coupling constant of J = 9.3–7.2 Hz supports the existence of a sugar moiety in the β-anomeric form. This is further supported by the observation of peaks at δ 75.39–70.67 ppm in the ^{13}C NMR spectrum. The condensation takes place between the chalcone moiety and the amine group of the heterocycle. Such condensation does not alter the chemical shift of the acetal proton. In addition the appearance of quaternary carbon peaks for the sugar-heterocyclic products **9**(**a–i**) in the region of δ 157.16–152.73 ppm, δ 151.60–147.82 ppm and δ 107.89–106.18 ppm showed the presence of four bridged quaternary carbons in the pyridopyrimidine core moiety. Although the two carbonyl carbon peaks of the starting material 8 were observed in δ 161.99 ppm and 151.57 ppm, in the corresponding products **9**(**a–i**) it was observed in the range of δ 167.08–161.97 ppm and d 155.47–151.53 ppm. Furthermore the FT-IR spectra of the sugar heterocyclic derivatives (**9a–i**) showed bands around the region of 1713–1690, 1659–1628, 1597–1589 and 1558–1535 cm^{-1} which correspond to $\nu_{C=O}$, $\nu_{C=O}$, $\nu_{C=N}$, $\nu_{C=C}$ groups confirming the formation of pyridopyrimidyl core moiety and it was again proved from the disappearance of bands in the range of 1744–1682 and 1628–1582 cm^{-1} which correspond to $\nu_{C=O}$, $\nu_{C=C}$ groups of the sugar chalcones (**7a–i**). Absorption spectral studies of both pyridopyimidine derivatives [**9b**,**c**,**f**,**i**] and their corresponding precursors [**7b**,**c**,**f**,**i**] showed that the characteristic bands for the product around 323 and 375 nm were absent in the precursor spectrum. Molar absorbance coefficients (ε_{max}) of the chalcone core moiety were observed around 16.2×10^3 M^{-1} cm^{-1} whereas for the pyridopyrimidine core moiety, it was observed around 34.0×10^3 M^{-1} cm^{-1}. Red shift of the absorbance band (λ_{max}) of the chalcones, which corresponds to

the π–π^* transition of enones has been observed in the range of 320–350 nm to 323–382 nm, further confirming the product formation. Thus the absorbance studies showed the formation of the expected products (see Supplementary data for details). It was presumed that the path of the reaction involves the formation of Michael adduct as an intermediate which then subsequently underwent heterocyclization to furnish the expected pyridopyrimidine derivatives. In general, the aromatic substrate bearing electron releasing group at the 4th position is known to activate these types of reactions.[20] Thus, the results corresponding to the formation of these products in yield further proved the observed trend (Table 2) that is, activation of these types of reactions by the electron releasing groups such as $-CH_3$, $-OCH_3$, –Cl, –F at the 4th position of aromatic core moiety. In addition, the preliminary investigation of sugar heterocyclic compounds such as **9c, 9f, 9g** and **9i** towards the anti-oxidant activity using the literature reported protocols[21,22] exhibited the moderate anti-oxidant activities with maximum inhibitory activity of 65.28% for **9c** and minimum inhibitory activity of 51.89% for **9f** (see Supplementary data for details).

3. Conclusion

In summary, a series of pyrido(2,3-*d*)pyrimidine-*C*-β-D-glycosides were synthesized in 65–80% yield with an efficient synthetic strategy accomplished by the formation of Michael adduct as an intermediate followed by heterocyclization and characterized by using NMR spectroscopic and elemental analyses. The existence of β-anomeric forms of the products were studied through ^{1}H NMR spectroscopy. Functional group transformation was identified by FT-IR studies. UV–visible spectral studies showed characteristic bands corresponding to the heterocyclic core moiety. The present study not only pioneers the novel class of compounds in carbohydrate chemistry but also provides an attractive and simple operational method for the construction of biological analogue pyrido(2,3-*d*)pyrimidine-*C*-β-D-glycosides as it is evidenced from the preliminary biological investigation.

4. Experimental section

4.1. General methods

All aromatic aldehydes were purchased from Sigma Aldrich, Bangalore, India. D-Glucose, butyraldehyde, acetylacetone, sodium bicarbonate and sodium sulphate were obtained from SRL, India with high purity. Sodium ethoxide was prepared through standard procedure.[23] Melting points were uncorrected. Dry solvents, such as THF and absolute ethanol used in the reaction were purchased from Sd-fine, India. The column chromatography was performed on Silica Gel (100–200) mesh. 4,6-*O*-Butylidene-D-glucopyranose and (4,6-*O*-butylidene-β-D-glucopyranosyl)propan-2-one (**5**) were synthesized by adopting the literature procedure.[24–28] NMR spectra were recorded with a Bruker DRX 300 MHz spectrometer with $CDCl_3$ and DMSO-d_6 as solvents. Chemical shift values are referenced with internal TMS. ABB-Bomem FT-IR spectrometer was used for recording IR spectra. Absorption studies were carried out with the UV–visible spectrophotometer 1800 Shimabzu, Japan. Elemental analysis was performed using Thermoquest microanalyser. Optical Density was measured using Eleco UV–Visible Double Spectrophotometer at 517 nm. While assigning spectral data several abbreviations were used and these include 'Ar' for aromatic, 'Ace' for acetal, 'Sac' for saccharide, 'Py' for pyridopyrimidine moiety, 'Pyr' for pyrrole and 'H_a & H_b' for the diasteretopic protons present in the methylene linker. Alk-H_a and Alk-H_b represent the alkenic protons of sugar chalcones.

4.2. Synthesis of α-,β-unsaturated-*C*-β-glycosides (7a–i)

The synthesis of α-,β-unsaturated-*C*-β-glycosidic compounds **7a**, **7d**, and **7e** were carried out by using literature procedures.[19,28–30] Similar procedure was adopted for the synthesis of the compounds **7**(**b**–**c**) and **7**(**f**–**i**). Spectral data and procedures are as follows:

4.2.1. Physicochemical and spectral data for (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(4-methoxy)phenylbut-3-en-2-one (7b)

The reaction of (4,6-*O*-butylidene-β-D-glucopyranosyl)propan-2-one (**5**) (1 mmol, 0.274 g) with *p*-methoxybenzaldehyde (**6b**) (1.2 mmol, 0.163 g) in the presence of organo-catalyst such as pyrrolidine (30 mol %) using DCM as a solvent afforded the compound, **7b** in 85% yield. Mp: 185–189 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6, ppm): δ 7.52–7.45 (m, 3H, Ar-*H*, Alk-H_b), 6.87 (d, 2H, J = 9 Hz, Ar-*H*), 6.61 (d, 1H, J = 16.2 Hz, Alk-H_a), 4.49 (t, 1H, J = 5.1 Hz, Ace-*H*), 4.09–4.04 (dd, 1H, J = 3.9 Hz, J = 9.9 Hz, Sac-*H*), 3.91–3.80 (dt, 1H, J = 3 Hz, J = 8.7 Hz, Ano-*H*), 3.80 (s, 3H, Ar-OCH_3), 3.64 (t, 1H, J = 8.7 Hz, Sac-*H*), 3.40–3.18 (m, 4H, Sac-*H*), 3.12–3.06 (m, 1H, Sac-*H*), 2.85–2.77 (dd, 1H, J = 8.4 Hz, J = 7.5 Hz, CH_2, H_a), 1.63–1.55 (m, 2H, CH_2), 1.35 (q, 2H, J = 7.5 Hz, CH_2). 0.86 (t, 3H, J = 7.5 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6, ppm): δ 198.01 (*C*O), 161.63 (Ar-*C*), 143.11 (Alk-*C*H), 130.08 (Ar-*C*H), 130.08 (Ar-*C*H), 127.06 (Ar-*C*), 124.26 (Alk-*C*H,), 114.40 (Ar-*C*H), 102.34 (Ace-*C*H), 80.49 (Sac-*C*H), 76.48 (Sac-*C*H), 75.14 (Sac-*C*H), 74.75 (Sac-*C*H), 70.57 (Sac-*C*H), 68.36 (Sac-CH_2), 55.38 (Ar-OCH_3), 43.27 (*C*H_2), 36.24 (*C*H_2), 17.42 (*C*H_2), 13.89 (*C*H_3). IR υ(cm^{-1}): 3502.47, 3394.97, 2954.73, 2869.87, 2360.70, 1712.66, 1627.80. Anal. Calcd for $C_{21}H_{28}O_7$: C, 64.27; H, 7.19. Found: C, 64.18; H, 7.25.

4.2.2. Physicochemical and spectral data for (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(4-methyl)phenylbut-3-en-2-one (7c)

The reaction of (4,6-*O*-butylidene-β-D-glucopyranosyl)propan-2-one (**5**) (1 mmol, 0.274 g) with *p*-methylbenzaldehyde (**6c**) (1.2 mmol, 0.144 g) in the presence of organo-catalyst, such as pyrrolidine (30 mol %) using DCM as a solvent afforded the compound, **7c** in 86% yield. Mp: 178–182 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6, ppm,): δ 7.67–7.48 (m, 3H, Ar-*H*, Alk-H_b); 7.30 (d, 2H, J = 7.5 Hz, Ar-*H*) 6.82 (d, 1H, J = 15.9 Hz, Alk-H_a), 4.65–4.62 (m, 1H, Ace-*H*), 4.21–4.18 (m, 1H, Sac-*H*), 4.04–3.98 (m, 1H, Ano-*H*), 3.76 (t, 1H, J = 8.4 Hz, Sac-*H*), 3.53–3.32 (m, 4H, Sac-*H*), 3.28–3.22 (m, 2H, Sac-*H*), 2.98–2.90 (dd, 1H, J = 8.1 Hz, J = 15.6 Hz, CH_2, H_a), 2.48 (s, 1H, CH_3), 1.73–1.72 (m, 2H, CH_2) 1.52 (q, 2H, J = 7.2 Hz, CH_2), 1.00 (t, 3H, J = 7.2 Hz, CH_3). ^{13}C NMR (75MHZ, $CDCl_3$ + DMSO-d_6, ppm): δ 192.75 (*C*O), 137.88 (Ar-*C*H), 135.72 (Ar-*C*), 126.39 (Alk-*C*H), 124.38 (Ar-*C*H), 123.03 (Ar-*C*H), 120.27 (Alk-*C*H), 97.01 (Ace-*C*H), 75.24 (Sac-*C*H), 71.23 (Sac-*C*H), 69.82 (Sac-*C*H), 69.48 (Sac-*C*H), 65.31 (Sac-*C*H), 63.07 (Sac-CH_2), 38.02 (*C*H_2), 30.97 (*C*H_2), 16.18 (Ar-*C*H_3), 12.13 (*C*H_2), 8.62 (*C*H_3). IR υ(cm^{-1}): 3402.18, 2962.44, 2869.87, 2360.70, 1720.38, 1627.80. Anal. Calcd for $C_{21}H_{28}O_6$: C, 67.00; H, 7.50. Found: C, 66.94; H, 7.57.

4.2.3. Physicochemical and spectral data for (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(4-chlorophenyl)but-3-en-2-one (7f)

The reaction of (4,6-*O*-butylidene-β-D-glucopyranosyl)propan-2-one (**5**) (1 mmol, 0.274 g) with *p*-chlorobenzaldehyde (**6f**) (1.2 mmol, 0.168 g) in the presence of organo-catalyst such as pyrrolidine (30 mol %) using DCM as a solvent afforded the compound, **7f** in 90% yield. Mp: 186–191 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6, ppm): δ 7.83–7.79 (m, 3H, Ar-*H*, Alk-H_b), 7.69–7.66 (d, 2H, J = 8.1 Hz, Ar-*H*), 7.05 (d, 1H, J = 16.2 Hz, Alk-H_a), 5.29 (br, 1H, Sac-O*H*), 5.04 (br, 1H, Sac-O*H*), 4.83 (t, 1H, J = 5.1 Hz, Ace-*H*), 4.39–4.35

(dd, 1H, J = 3.9 Hz, J = 10.2 Hz, Sac-*H*), 4.22–4.15 (dt, 1H J = 2.4 Hz, J = 9 Hz, Ano-*H*), 3.93 (t, J = 8.7 Hz, 1H, Sac-*H*), 3.73–3.67 (m, 1H, Sac-*H*), 3.64–3.41 (m, 5H, Sac-*H*), 3.17–3.09 (dd, 1H, J = 8.7 Hz, J = 15.9 Hz, CH_2, H_a), 1.96–1.88 (m, 2H, CH_2), 1.72 (q, 2H, J = 7.2 Hz, CH_2), 1.20 (t, 3H, J = 7.2 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6, ppm): δ 202.60 (*C*O), 146.18 (Alk-*C*H), 140.89 (Ar-*C*), 137.82 (Ar-*C*), 134.30 (Ar-*C*H), 133.90 (Alk-*C*H,), 131.70 (Alk-*C*H), 106.98 (Ace-*C*H), 85.37 (Sac-*C*H), 81.40 (Sac-*C*H), 79.65 (Sac-*C*H), 79.39 (Sac-*C*H), 75.36 (Sac-*C*H), 73.05 (Sac-*C*H_2), 48.24 (*C*H_2), 41.00 (CH_2), 22.14 (*C*H_2), 18.69 (*C*H_3). IR υ(cm^{-1}): 3417.61, 2962.44, 2869.87, 2360.70, 1743.52, 1627.80. Anal. Calcd for $C_{21}H_{25}ClO_6$: C, 60.53; H, 6.35. Found: C, 60.44; H, 6.28.

4.2.4. Physicochemical and spectral data for (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(3-bromo)phenylbut-3-en-2-one (7h)

The reaction of (4,6-*O*-butylidene-β-D-glucopyranosyl)propan-2-one (**5**) (1 mmol, 0.274 g) with *m*-bromobenzaldehyde (**6h**) (1.2 mmol, 0.222 g) in the presence of organo-catalyst such as pyrrolidine (30 mol %) using DCM as a solvent afforded the compound, **7h** in 85% yield. Mp: 180–185 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6, ppm): δ 7.64–7.56 (m, 4H, Ar-*H*, Alk-H_b), 7.40 (t, 1H, J = 7.8 Hz, Ar-*H*), 6.87 (d, 1H, J = 16.2 Hz, Alk-H_a), 4.65 (t, 1H, J = 4.5 Hz, Ace-*H*), 4.22–4.17 (m, 1H, Sac-*H*), 4.04–3.98 (m, 1H, Ano-*H*), 3.76 (t, 1H, J = 8.4 Hz, Sac-*H*), 3.55–3.24 (m, 4H, Sac-*H*), 2.98–2.90 (dd, 2H, J = 8.4 Hz, J = 15 Hz, CH_2, H_a), 1.77–1.73 (m, 2H, CH_2), 1.55 (q, 2H, J = 7.2 Hz, CH_2), 1.02 (t, 3H, J = 7.2 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6, ppm): δ 192.75 (*C*O), 135.68 (Ar-*C*), 131.33 (Alk-*C*H), 127.77 (Ar-*C*H), 125.48 (Ar-*C*H), 125.17 (Ar-*C*H), 122.29 (Ar-*C*H,), 121.61 (Alk-*C*H), 117.57 (Ar-*C*), 96.91 (Ace-*C*H), 75.19 (Sac-*C*H), 71.19 (Sac-*C*H), 69.69 (Sac-*C*H), 69.39 (Sac-*C*H), 65.28 (Sac-*C*H), 62.97 (Sac-*C*H_2), 38.28 (*C*H_2), 30.92 (*C*H_2), 12.06 (*C*H_2), 8.59 (*C*H_3). IR υ(cm^{-1}): 3409.90, 2962.44, 2869.87, 2360.70, 1743.52, 1627.80. Anal. Calcd for $C_{21}H_{25}BrO_7$: C, 54.43; H, 5.71. Found: C, 54.34; H, 5.76.

4.2.5. Physicochemical and spectral data for (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-pyrrolobut-3-en-2-one (7i)

The reaction of (4,6-*O*-butylidene-β-D-glucopyranosyl)propan-2-one (**5**) (1 mmol, 0.274 g) with pyrrole-2-carboxaldehyde (**6i**) (1.2 mmol, 0.114 g) in the presence of organo-catalyst such as pyrrolidine (30 mol %) using DCM as a solvent afforded the compound, **7i** in 85% yield. Mp: 192–196 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6, ppm): δ 11.45 (br, 1H, Pyr-N*H*), 7.80 (d, 1H, J = 16.2 Hz, Alk-H_b), 7.30 (br, 1H, Pyr-*H*), 6.93–6.88 (m, 2H, Pyr-*H*, Alk-H_a), 6.59 (br, 1H, Pyr-*H*), 5.27 (br, 1H, Sac-O*H*), 5.03 (br, 1H, Sac-O*H*), 4.89 (t, 1H, J = 5.1 Hz, Ace-*H*), 4.45–4.41 (dd, 1H, J = 3.9 Hz, J = 9.9 Hz, Sac-*H*), 4.27–4.21 (dt, 1H, J = 2.4 Hz, J = 9.3 Hz, Ano-*H*), 3.97 (t, 1H, J = 8.7 Hz, Sac-*H*), 3.79–3.72 (m, 2H, Sac-*H*), 3.66–3.52 (m, 6H, Sac-*H*), 3.10–3.07 (dd, 2H, J = 8.7 Hz, J = 15 Hz, CH_2, *Ha*), 2.02–1.91 (m, 2H, CH_2), 1.78 (q, 2H, J = 7.2 Hz, CH_2), 1.27 (t, 3H, J = 7.2 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6,): δ 202.67 (*C*O), 147.58 (Alk-*C*H), 139.23 (Pyr-*C*), 135.25 (Alk-*C*H), 133.71 (Pyr-*C*H), 133.05 (Pyr-*C*H), 131.34 (Pyr-*C*H), 106.93 (Ace-*C*H), 85.47 (Sac-*C*H), 81.51 (Sac-*C*H), 79.67 (Sac-*C*H), 79.44 (Sac-*C*H), 75.40 (Sac-*C*H), 73.06 (Sac-*C*H_2), 48.19 (*C*H_2), 41.03 (*C*H_2), 22.12 (*C*H_2), 18.72 (*C*H_3). IR υ(cm^{-1}): 3355.89, 2962.44, 2869.87, 1681.80, 1581.51. Anal. Calcd for $C_{18}H_{25}NO_6$: C, 61.52; H, 7.17; N, 3.99. Found: C, 61.44; H, 7.25, N, 4.10.

4.3. General procedure for the reaction of (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-phenylbut-3-en-2-one derivatives with 6-amino-1,3-dimethyluracil

6-Amino-1,3-dimethyluracil (1.2 mmol) was added in the solvent mixture containing 15 mL of dry THF and 5 mL of absolute ethanol and then the freshly prepared sodium ethoxide (1–3 mmol) solution was added slowly. Finally (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-phenylbut-3-en-2-one derivatives (1 mmol) were dissolved portion wise and the mixture was allowed to stir at room temperature for 30–90 min. The course of the reaction was monitored through thin layer chromatography. After the completion of the reaction the solvent was evaporated under reduced pressure and excess of sodium ethoxide was neutralized with 10% of HCl. Then the reaction mixture was washed with saturated $NaHCO_3$ solution and extracted with chloroform. The extracted organic layer was dried with anhydrous Na_2SO_4 and concentrated to give a crude product which was further purified with the help of column chromatography.

4.3.1. Physicochemical and spectral data for 7-(4,6-*O*-butylidene-β-D-glucopyranosyl-1-methyl)-1,3-dimethyl-5-phenylpyrido(2,3-*d*)pyrimidine-2,4(1*H*,3*H*)-dione (9a)

The reaction of 6-amino-1,3-dimethyluracil (**8**) (1.2 mmol, 0.186 g) with (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-phenylbut-3-en-2-one (**7a**) (1 mmol, 0.362 g) in the presence of sodium ethoxide (1 mmol, 0.068 g) as a base at room temperature for 30 min afforded a white solid of compound, **9a** in 73% yield. Mp: 174–178 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.45–7.43 (m, 3H, Ar-*H*), 7.29–7.28 (m, 2H, Ar-*H*), 6.92 (s, 1H, Py-*H*), 4.52 (t, 1H, J = 5.1 Hz, Ace-*H*), 4.08–4.03 (dd, 1H, J = 3.9 Hz, J = 10.2 Hz, Sac-*H*), 3.92–3.86 (dt, 1H, J = 3.3 Hz, J = 9 Hz, Ano-*H*), 3.76 (s, 3H, NCH_3, Sac-*H*), 3.48–3.41 (m, 4H, Sac-*H*), 3.36 (m, 3H, NCH_3, Sac-*H*), 3.31–3.23 (m, 2H, Sac-*H*), 3.04 2.96 (dd, 1H, J = 7.8 Hz, J = 14.7 Hz, CH_2, H_a), 1.66–1.59 (m, 2H, CH_2), 1.41 (q, 2H, J = 7.5 Hz, CH_2), 0.91 (t, 3H, J = 7.5 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 162.16 (Py-*C*O), 160.48 (Py-*C*), 154.67 (Py-*C*), 151.53 (Py-*C*), 151.41 (Py-*C*O) 139.17 (Ar-*C*), 128.20 (Ar-*C*H), 127.80 (Ar-*C*H, 3*C*), 122.68 (Py-*C*H), 106.37 (Py-*C*), 102.49 (Ace-*C*H), 80.56 (Sac-*C*H), 78.56 (Sac-*C*H), 75.17 (Sac-*C*H), 74.41 (Sac-*C*H), 70.74 (Sac-*C*H), 68.29 (Sac-*C*H_2), 40.94 (*C*H_2), 36.22 (*C*H_2), 30.20 (NCH_3), 28.46 (NCH_3), 17.45 (*C*H_2), 13.91 (*C*H_3). IR υ(cm^{-1}): 3517.90, 3417.61, 2964.44, 2869.87, 2360.70, 1697.23, 1658.66, 1589.23, 1558.37. Anal. Calcd for $C_{26}H_{31}N_3O_7$: C, 62.76; H, 6.28; N, 8.45. Found: C, 62.67; H, 6.22; N, 8.56.

4.3.2. Physicochemical and spectral data for 7-(4,6-*O*-butyli dene-β-D-glucopyranosyl-1-methyl)-5-(4-methoxyphenyl)-1,3-dimethylpyrido(2,3-*d*)pyrimidine-2,4(1*H*,3*H*)-dione (9b)

The reaction of 6-amino-1,3-dimethyluracil (**8**) (1.2 mmol, 0.186 g) with (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(4-methoxyphenyl)but-3-en-2-one (**7b**) (1 mmol, 0.392 g) in the presence of sodium ethoxide (1 mmol, 0.068 g) as a base at room temperature for 35 min afforded light yellowish a white solid of compound **9b** in 82% yield. Mp: 175–179 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.17 (d, 2H, J = 8.4 Hz, Ar-*H*), 6.88 (d, 2H, J = 8.7, Ar-*H*), 6.83 (s, 1H, Py-*H*), 4.46 (t, 1H, J = 4.8 Hz, Ace-*H*), 4.24 (br, 1H, Sac-*H*), 3.97–3.94 (m, 2H, Sac-*H*, Ano-*H*), 3.81–3.78 (m, 4H, NCH_3, Sac-*H*), 3.68 (s, 3H, Ar-OCH_3), 3.37–3.33 (m, 3H, Sac-*H*), 3.30 (s, 3H, NCH_3), 3.19–3.18 (m, 2H, Sac-*H*), 2.88–2.80 (dd, 1H, J = 8.7 Hz, J = 14.7 Hz, CH_2, H_a), 1.57–1.54 (m, 2H, CH_2), 1.34 (q, 2H, J = 7.2 Hz, CH_2), 0.83 (t, 3H, J = 7.2 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 162.52 (Py-*C*O), 160.69 (Py-*C*), 159.63 (Ar-*C*), 154.14 (Py-*C*), 151.56 (Py-*C*), 151.45 (Py-*C*O), 131.30 (Ar-*C*), 129.50 (Ar-*C*H), 122.79 (Py-*C*H), 113.19 (Ar-*C*H), 106.11 (Py-*C*), 102.39 (Ace-*C*H), 80.49 (Sac-*C*H), 78.81 (Sac-*C*H), 75.16 (Sac-*C*H), 74.74 (Sac-*C*H), 70.67 (Sac-*C*H), 68.33 (Sac-*C*H_2), 55.24 (Ar-OCH_3), 40.82 (*C*H_2), 36.25 (*C*H_2), 30.15 (NCH_3), 28.41 (NCH_3), 17.43 (*C*H_2), 13.91 (*C*H_3). IR υ(cm^{-1}): 3494.76, 3448.47, 2962.44, 2869.87, 2360.70, 1704.95, 1658.66, 1589.23, 1550.65. Anal. Calcd for $C_{27}H_{33}N_3O_8$: C, 61.47; H, 6.30; N, 7.96. Found: C, 61.37; H, 6.35; N, 7.86.

4.3.3. Physicochemical and spectral data for 7-(4,6-*O*-butylidene-β-D-glucopyranosyl-1-methyl)-5-(4-methylphenyl)-1,3-dimethylpyrido(2,3-*d*)pyrimidine-2,4(1*H*,3*H*)-dione (9c)

The reaction of 6-amino-1,3-dimethyluracil (**8**) (1.2 mmol, 0.186 g) with (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(4-methylphenyl)but-3-en-2-one (**7c**) (1 mmol, 0.376 g) in the presence of sodium ethoxide (1 mmol, 0.068 g) as a base at room temperature for 30 min afforded a white solid of compound **9c** in 81% yield. Mp: 198–203 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.25 (d, 2H, J = 9.6 Hz, Aro-*H*), 7.18 (d, 2H, J = 8.1 Hz, Ar-*H*), 6.91 (s, 1H, Py-*H*), 4.52 (t. 1H, J = 5.1 Hz, Ace-*H*), 4.08–4.03 (dd, 1H, J = 3.6 Hz, J = 10.2 Hz, Sac-*H*), 3.92–3.85 (dt, 1H, J = 3.3 Hz, J = 8.4 Hz, Ano-*H*), 3.75 (s, 3H, NCH_3), 3.48–3.41 (m, 3H, Sac-*H*), 3.37 (s, 3H, NCH_3), 3.31–3.20 (m, 3H, Sac-*H*), 3.04–2.97 (dd, 1H, J = 7.5 Hz, J = 14.7 Hz, CH_2, H_a), 2.42 (s,3H, -CH_3), 1.66–1.59 (m, 2H, CH_2), 1.41 (q, 2H, J = 7.5 Hz, CH_2), 0.91 (t, 3H, J = 7.5 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 162.02 (Py-*C*O), 160.52 (Py-*C*), 154.85 (Py-*C*), 151.55 (Py-*C*), 151.42 (Py-*C*O), 138.18 (Ar-*C*), 136.14 (Ar-*C*), 128.54 (Aro-*C*H), 127.81 (Ar-*C*H), 122.78 (Py-*C*H), 106.41 (Py-*C*), 102.47 (Ace-*C*H), 80.50 (Sac-*C*H), 78.56 (Sac-*C*H), 75.14 (Sac-*C*H), 74.41 (Sac-*C*H), 70.71 (Sac-*C*H), 68.29 (Sac-*C*H_2), 40.93 (*C*H_2), 36.22 (*C*H_2), 30.19 (N*C*H_3), 28.46 (N*C*H_3), 21.38 (Ar-*C*H_3), 17.45 (*C*H_2), 13.91 (*C*H_3). IR υ(cm^{-1}): 3517.90, 3417.61, 2962.44, 2969.87, 2360.70, 1697.23, 1658.66, 1589.23, 1550.65. Anal. Calcd for $C_{27}H_{33}N_3O_7$: C, 63.39; H, 6.50; N, 8.21. Found: C, 63.45; H, 6.42; N, 8.16.

4.3.4. Physicochemical and spectral data for 5-(benzo[*d*]dioxol-5-yl)-7-(4,6-*O*-butylidene-β-D-glucopyranosyl–1-methyl)-1,3-dimethylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (9d)

The reaction of 6-amino-1,3-dimethyluracil (**8**) (1.2 mmol, 0.186 g) with (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(3,4-dioxanephenyl)-but-3-en-2-one (**7d**) (1 mmol, 0.402 g) in the presence of sodium ethoxide (1 mmol, 0.068 g) as a base at room temperature for 60 min afforded a light yellowish solid of compound **9d** in 72% yield. Mp: 132–137 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.83 (s, 1H, Py-*H*), 6.79 (s, 1H, Ar-*H*), 6.69–6.68 (m, 2H, Ar-*H*), 5.95 (s, 2H, OCH_2O), 4.45 (t. 1H, J = 5.1 Hz, Ace-*H*), 4.00–3.96 (dd, 1H, J = 3.9 Hz, J = 9.6 Hz, Sac-*H*), 3.78–3.84 (dt, 1H, J = 3.9 Hz, J = 7.2 Hz, Ano-*H*), 3.70–3.65 (m, 4H, NCH_3, Sac-*H*), 3.40–3.33 (m, 1H, Sac-*H*), 3.30 (s, 3H, NCH_3), 3.29–3.15 (m, 3H, Sac-*H*), 2.95–2.88 (dd, 1H, J = 7.8 Hz, J = 14.7 Hz, CH_2, H_a), 1.59–1.52 (m, 2H, CH_2), 1.34 (q, 2H, J = 7.2 Hz, CH_2), 0.84 (t, 3H, J = 7.2 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 162.14 (Py-*C*O), 160.44 (Py-*C*), 154.26 (Py-*C*), 151.60 (Py-*C*), 151.37 (Py-*C*O), 147.78 (Ar-*C*), 147.15 (Ar-*C*), 132.77 (Ar-*C*), 122.77 (Py-*C*H), 121.55 (Ar-*C*H), 109.02 (Ar-*C*H), 107.90 (Ar-*C*H), 106.41 (Py-*C*), 102.49 (Ace-*C*H), 101.29 (O*C*H_2O), 80.52 (Sac-*C*H), 78.59 (Sac-*C*H), 75.18 (Sac-*C*H), 74.41 (Sac-*C*H), 70.71 (Sac-*C*H), 68.29 (Sac-*C*H_2), 40.90 (*C*H_2), 36.22 (*C*H_2), 30.19 (N*C*H_3), 28.46 (N*C*H_3), 17.44 (*C*H_2), 13.88 (*C*H_3). IR υ(cm^{-1}): 3510.19, 3394.47, 2962.44, 2877.58, 2360.70, 1704.95, 1658.66, 1589.23, 1558.37. Anal. Calcd for $C_{27}H_{33}N_3O_9$: C, 59.88; H, 5.77; N, 7.76. Found: C, 59.80; H, 5.71; N, 7.66.

4.3.5. Physicochemical and spectral data for 7-(4,6-*O*-butylidene-β-D-glucopyranosyl-1-methyl)-5-(3,4-dimethoxyphenyl)-1,3-dimethylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (9e)

The reaction of 6-amino-1,3-dimethyluracil (**8**) (1.2 mmol, 0.186 g) with (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(3,4-dimethoxyphenyl)-but-3-en-2-one (**7e**) (1 mmol, 0.422 g) in the presence of sodium ethoxide (2 mmol, 0.136 g) as a base at room temperature for 65 min afforded a light yellowish solid of compound **9e** in 79% yield. Mp: 80–85 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.78–6.78 (m, 3H, Ar-*H*), 6.75 (s, 1H, Py-*H*), 4.45 (t. 1H, J = 5.1 Hz, Ace-*H*), 4.00–3.96 (dd, 1H, J = 3.6 Hz, J = 10.2 Hz, Sac-*H*), 3.86 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 3.70–3.65 (m, 4H, NCH_3, Sac-*H*), 3.42–3.34 (m, 3H, Sac-*H*), 3.31(s, 3H, -NCH_3), 3.27–3.13 (m, 3H, Sac-*H*), 2.97–2.89 (dd, 1H, J = 7.4 Hz, J = 14.7 Hz, CH_2, H_a), 1.59–1.52 (m, 2H,CH_2), 1.35 (q, 2H, J = 7.5 Hz, CH_2), 0.84 (t, 3H, J = 7.5 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 161.97 (Py-*C*O), 160.43 (Py-*C*), 154.52 (Py-*C*), 151.63 (Py-*C*), 151.41 (Py-*C*O) 149.23 (Ar-*C*), 148.30 (Ar-*C*), 131.53 (Ar-*C*), 122.86 (Py-*C*H), 120.72 (Ar-*C*H), 111.83 (Ar-*C*H), 110.51 (Ar-*C*H), 106.39 (Py-*C*), 102.49 (Ace-*C*H), 80.51 (Sac-*C*H), 78.56 (Sac-*C*H), 75.18 (Sac-*C*H), 74.46 (Sac-*C*H), 70.71 (Sac-*C*H), 68.29 (Sac-*C*H_2), 56.00 (Ar-O*C*H_3), 55.87 (Ar-O*C*H_3), 40.94 (*C*H_2), 36.22 (*C*H_2), 30.21 (N*C*H_3), 28.48 (N*C*H_3), 17.44 (*C*H_2), 13.90 (*C*H_3). IR υ(cm^{-1}): 3571.90, 3463.90, 2962.44, 2869.87, 2360.70, 1712.66, 1666.37, 1589.23, 1550.65. Anal. Calcd for $C_{28}H_{35}N_3O_9$: C, 60.31; H, 6.33; N, 7.54. Found: C, 60.41; H, 6.40; N, 7.44.

4.3.6. Physicochemical and spectral data for 5-(4-chlorophenyl)-7-(4,6-*O*-butylidene-β-D-glucopyranosyl-1-methyl)-1,3-dimethylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (9f)

The reaction of 6-amino-1,3-dimethyluracil (**8**) (1.2 mmol, 0.186 g) with (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(4-chlorophenyl)-but-3-en-2-one (**7f**) (1 mmol, 0.396 g) in the presence of sodium ethoxide (3 mmol, 0.276 g) as a base at room temperature for 30 min afforded a white solid of compound **9f** in 83% yield. Mp: 209–214 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.34 (d, 2H, J = 8.4 Hz, Ar-*H*), 7.15 (d, 2H, J = 8.4 Hz, Ar-*H*), 6.81 (s, 1H, Py-*H*), 4.45 (t. 1H, J = 4.8 Hz, Ace-*H*), 4.00–3.95 (dd, 1H, J = 3.6 Hz, J = 9.9 Hz, Sac-*H*), 3.82 (dt, 1H, J = 3 Hz, J = 7.5 Hz, Ano-*H*), 3.69–3.65 (m, 4H, NCH_3, Sac-*H*), 3.41–3.33 (m, 3H, Sac-*H*), 3.29 (s, 3H, NCH_3), 3.27–3.12 (m, 2H, Sac-*H*), 2.97–2.89 (dd, 1H, J = 8.1 Hz, J = 14.7 Hz, CH_2, H_a), 1.57–1.52 (m, 2H, CH_2), 1.34 (q, 2H, J = 7.5 Hz, CH_2), 0.84 (t, 3H, J = 7.5 Hz, CH_3), ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 162.47 (Py-*C*O), 160.50 (Py-*C*), 153.33 (Py-*C*), 151.60 (Py-*C*), 151.30 (Py-*C*O), 137.51 (Ar-*C*), 134.41 (Ar-*C*), 129.26 (Ar-*C*H), 128.07 (Ar-*C*H), 122.46 (Py-*C*H), 106.22 (Py-*C*), 102.50 (Ace-*C*H), 80.48 (Sac-*C*H), 78.53 (Sac-*C*H), 75.20 (Sac-*C*H), 74.35 (Sac-*C*H), 70.71 (Sac-*C*H), 68.27 (Sac-*C*H_2), 40.91 (*C*H_2), 36.21 (*C*H_2), 30.21 (N*C*H_3), 28.46 (N*C*H_3), 17.44 (*C*H_2), 13.90 (*C*H_3). IR υ(cm^{-1}): 3517.90, 3433.04, 2970.16, 2869.87, 2360.87, 1704.95, 1658.66, 1589.23, 1550.65. Anal. Calcd for $C_{26}H_{30}ClN_3O_7$: C, 58.70; H, 5.68; N, 7.90. Found: C, 58.61; H, 5.73; N, 8.00.

4.3.7. Physicochemical and spectral data for 5-(4-fluorophenyl)-7-(4,6-*O*-butylidene-β-D-glucopyranosyl-1-methyl)-1,3-dimethylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (9g)

The reaction of 6-amino-1,3-dimethyluracil (**8**) (1.2 mmol, 0.186 g) with (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(4-fluorophenyl)-but-3-en-2-one (**7g**) (1 mmol, 0.381 g) in the presence of sodium ethoxide (3 mmol, 0.276 g) as a base at room temperature for 30 min afforded a light yellowish solid of compound **9g** in 82% yield. Mp: 189–194 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.26–7.23 (m, 2H, Ar-*H*), 7.15–7.09 (m, 2H, Ar-*H*), 6.89 (s, 1H, Py-*H*), 4.52 (t. 1H, J = 4.8 Hz, Ace-*H*), 4.07–4.02 (dd, 1H, J = 3.6 Hz, J = 10.2 Hz, Sac-*H*), 3.93–3.86 (dt, 1H, J = 3.3 Hz, J = 9 Hz, Ano-*H*), 3.76–3.71 (m, 4H, NCH_3, Sac-*H*), 3.48–3.41 (m, 2H, Sac-*H*), 3.37 (s, 3H, NCH_3), 3.34–3.23 (m, 3H, Sac-*H*), 3.03–2.96 (dd, 1H, J = 8.1 Hz, J = 15 Hz, CH_2, H_a),1.66–1.59 (m, 2H, CH_2), 1.41 (q, 2H, J = 7.2 Hz, CH_2), 0.91 (t, 3H, J = 7.2 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 162.37 (Py-*C*O), 160.54 (Py-*C*), 153.59 (Py-*C*), 151.60 (Py-*C*), 151.31 (Py-*C*O), 134.97 (Ar-*C*), 134.92 (Ar-*C*), 129.80 (Ar-*C*H), 129.69 (Ar-*C*H), 122.68 (Py-*C*H), 115.03 (Ar-*C*H), 114.74 (Ar-*C*H), 106.32 (Py-*C*), 102.50 (Ace-*C*H), 80.50 (Sac-*C*H), 78.56 (Sac-*C*H), 75.19 (Sac-*C*H), 74.38 (Sac-*C*H), 70.70 (Sac-*C*H), 68.27 (Sac-*C*H_2), 40.90 (*C*H_2), 36.21 (*C*H_2), 30.21 (N*C*H_3), 28.46 (N*C*H_3), 17.44 (*C*H_2), 13.90 (*C*H_3). IR υ(cm^{-1}): 3517.90,

3433.04, 2970.16, 2869.87, 2360.70, 1704.95, 1658.66, 1596.94, 1558.37. Anal. Calcd for $C_{26}H_{30}FN_3O_7$: C, 60.57; H, 5.87; N, 8.15. Found: C, 60.50; H, 5.80; N, 8.21.

4.3.8. Physicochemical and spectral data for 5-(3-bromophenyl)-7-(4,6-*O*-butylidene-β-D-glucopyranosyl-1-methyl)-1,3-dimethylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (9h)

The reaction of 6-amino-1,3-dimethyluracil (**8**) (1.2 mmol, 0.186 g) with (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(3-bromophenyl)-but-3-en-2-one (**7h**) (1 mmol, 0.441 g) in the presence of sodium ethoxide (3 mmol, 0.276 g) as a base at room temperature for 90 min afforded a yellowish solid of compound **9h** in 67% yield. Mp: 72–76 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 7.55 (d, 1H, J = 7.8 Hz, Ar-*H*). 7.42 (s, 1H, Ar-*H*), 7.33–7.23 (m, 2H, Ar-*H*), 6.88 (s, 1H, Py-*H*), 4.53 (t, 1H, J = 5.1 Hz, Ace-*H*), 4.08–4.03 (dd, 1H, J = 3.9 Hz, J = 10.2 Hz, Sac-*H*), 3.93–3.86 (dt, 1H, J = 3 Hz, J = 8.7 Hz, Ano-*H*), 3.76–3.72 (m, 4H, NCH_3, Sac-*H*), 3.48–3.41 (m, 2H, Sac-*H*), 3.40–3.36 (s, 4H, NCH_3, Sac-*H*), 3.28–3.23 (m, 2H, Sac-*H*), 3.03–2.95 (dd, 1H, J = 8.1 Hz, J = 14.7 Hz, CH_2, H_a), 1.66–1.59 (m, 2H, CH_2), 1.41 (q, 2H, J = 7.2 Hz, CH_2), 0.91 (t, 3H, J = 7.2 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, ppm): δ 162.60 (Py-*C*O), 160.36 (Py-*C*), 152.73 (Py-*C*), 151.52 (Py-*C*), 151.32 (Py-*C*O), 141.11 (Ar-*C*), 131.15 (Ar-*C*H), 130.59 (Ar-*C*H), 129.22 (Ar-*C*H), 126.69 (Ar-*C*H), 122.40 (Py-*C*H), 121.86 (Ar-*C*), 106.18 (Py-*C*), 102.49 (Ace-*C*H), 80.48 (Sac-*C*H), 78.55 (Sac-*C*H), 75.20 (Sac-*C*H), 74.35 (Sac-*C*H), 70.70 (Sac-*C*H), 68.27 (Sac-*C*H$_2$), 40.91 (*C*H$_2$), 36.21 (*C*H$_2$), 30.21 (*C*H$_3$), 28.49 (*C*H$_3$), 17.44 (*C*H$_2$), 13.91 (*C*H$_3$)). IR υ(cm^{-1}): 3456.18, 2962.44, 2869.87, 2360.70, 1712.66, 1658.66, 1589.23, 1550.65. Anal. Calcd for $C_{26}H_{30}BrN_3O_7$: C, 54.17; H, 5.25; N, 7.29. Found: C, 54.27; H, 5.30; N, 7.36.

4.3.9. Physicochemical and spectral data for 7-(4,6-*O*-butylidene-β-D-glucopyranosyl-1-methyl)-1,3-dimethylpyrido-5-(1*H*-pyrrol-2yl)pyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (9i)

The reaction of 6-amino-1,3-dimethyluracil (**8**) (1.2 mmol, 0.186 g) with (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(1*H*-pyrrol-2yl)-but-3-en-2-one (**7i**) (1 mmol, 0.351 g) in the presence of sodium ethoxide (3 mmol, 0.276 g) as a base at room temperature for 90 min afforded a yellowish solid of compound **9i** in 75% yield. Mp: 192–196 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6, ppm): δ 7.58 (s, 1H, Py-*H*),. 7.19 (br, 1H, Pyr-*H*), 7.07 (br, 1H, Pyr-*H*), 6.45–6.46 (m, 1H, Py-*H*), 5.30 (d, 1H, J = 4.5 Hz, Sac-*OH*), 5.07 (d, 1H, J = 3.6 Hz, Sac-*OH*), 4.68 (t. 1H, J = 5.1 Hz, Ace-*H*), 4.16–4.12 (dd, 1H, J = 4.2 Hz, J = 10.3 Hz, Sac-*H*), 4.04–3.98 (dt, 1H, J = 2.1 Hz, J = 9.3 Hz, Ano-*H*), 3.85 (s, 3H, -NCH_3), 3.79–3.74 (m, 2H, Sac-*H*), 3.62 (s, 3H, NCH_3), 3.57–3.47 (m, 4H, Sac-*H*), 3.02–2.94 (dd, 1H, J = 9.3 Hz, J = 14.7 Hz, CH_2, H_a), 1.79–1.71(m, 2H, CH_2), 1.56(q, 2H, J = 7.2 Hz, CH_2), 1.05 (t, 3H, J = 7.2 Hz, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6, ppm): δ 167.89 (Py-*C*O), 167.08 (Py-*C*), 157.16 (Py-*C*), 155.47 (Py-*C*O), 147.82 (Py-*C*), 132.72 (Pyr-*C*), 126.84 (Py-*C*H), 123.28 (Pyr-*C*H), 118.84 (Pyr-*C*H), 115.07 (Pyr-*C*H), 107.89 (Py-*C*), 106.90 (Ace-*C*H), 85.51 (Sac-*C*H), 83.98 (Sac-*C*H), 79.68 (Sac-*C*H), 79.61 (Sac-*C*H), 75.39 (Sac-*C*H), 73.05 (Sac-*C*H$_2$), 45.49 (*C*H$_2$), 41.04 (*C*H$_2$), 35.32 (NCH_3), 33.76 (NCH_3), 22.12 (*C*H$_2$), 18.74 (*C*H$_3$). IR υ(cm^{-1}): 3456.18, 3132.17, 2962.44, 2877.58, 2360.70, 1689.52, 1627.80, 1596.94, 1535.22. Anal. Calcd for $C_{24}H_{30}N_4O_7$: C, 59.25; H, 6.22; N, 11.52. Found: C, 59.17; H, 6.27; N, 7.43.

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Supplementary data

Supplementary data (copy of all the spectra, optimization of reaction conditions) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.carres.2012.11.013.

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