



Cite this: *Org. Biomol. Chem.*, 2024, **22**, 4922

# Synthesis, characterization and photophysical studies of dual-emissive base-modified fluorescent nucleosides†‡

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A straightforward and efficient methodology has been employed for the synthesis of a diverse set of base-modified fluorescent nucleoside conjugates via Cu(I)-catalysed cycloaddition reaction of 5-ethynyl-2',3',5'-tri-*O*-acetyluridine/3',5'-di-*O*-acetyl-2'-deoxyuridine with 4-(azidomethyl)-*N*<sup>9</sup>-(4'-aryl)-9,10-dihydro-2*H*,8*H*-chromeno[8,7-*e*][1,3]oxazin-2-ones in <sup>t</sup>BuOH to afford the desired 1,2,3-triazoles in 92–95% yields. Treatment with NaOMe/MeOH resulted in the final deprotected nucleoside analogues. The synthesized 1,2,3-triazoles demonstrated a significant emission spectrum, featuring two robust bands in the region from 350–500 nm (with excitation at 300 nm) in fluorescence studies. Photophysical investigations revealed a dual-emissive band with high fluorescence intensity, excellent Stokes shift (140–164 nm) and superior quantum yields (0.068–0.350). Furthermore, the electronic structures of the synthesized triazoles have been further verified by DFT studies. Structural characterization of all synthesized compounds was carried out using various analytical techniques, including IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, <sup>1</sup>H–<sup>1</sup>H COSY, <sup>1</sup>H–<sup>13</sup>C HETCOR experiments, and HRMS measurements. The dual-emissive nature of these nucleosides would be a significant contribution to nucleoside chemistry as there are limited literature reports on the same.

Received 8th May 2024,  
Accepted 16th May 2024  
DOI: 10.1039/d4ob00749b  
rsc.li/obc

## 1. Introduction

For over half a century, modified nucleosides have found applications in the field of nucleic acid chemistry.<sup>1</sup> The significance of modified nucleosides was immensely acknowledged in the year 2023 for modifying the nucleoside base. Katalin Karikó and Prof. Drew Weissmann received the Nobel Prize for modifying the nucleoside base, in particular a uridine base with a pseudo uridine. The realm of fluorescent analogues for nucleic acid bases has grown considerably in recent times due to the non-emissive nature of canonical bases in nucleic acids.<sup>2</sup> The fascination towards fluorescent nucleosides featuring modified bases is due to their extraordinary responsiveness to the microenvironment, making them potent tools for inves-

tigating the structural intricacies of nucleic acids. Moreover, they serve as powerful molecules for elucidating the biological processes of nucleic acids, including replication, transcription, recombination, and repair.<sup>3–10</sup>

Diverse modified nucleosides with extended conjugation have been synthesized and successfully utilized in DNA labeling due to their inherent fluorescent character (Fig. 1)<sup>11–17</sup> In general, the 5-position of pyrimidines is a favourable site for transformation because substituents introduced here tend to be accommodated well in the major groove without obstructing the Watson–Crick face.<sup>6,18</sup>

Fluorescent coumarin analogues have been extensively employed in various applications such as laser dyes,<sup>19</sup> fluorescent labels,<sup>20</sup> chemo-sensors,<sup>21</sup> and organic light-emitting diodes.<sup>22</sup> The inherent limitations of the unsubstituted coumarin fluorophore, notably its small Stokes shift, pose challenges in various applications such as fluorescent molecular probes.<sup>23,24</sup> Dihydro-oxazines are known for their compact nature, improving the Stokes shift values, which have made them promising candidates for application as fluorescent probes.<sup>25</sup> To overcome these drawbacks and enhance the utility of the coumarin scaffold as a fluorescent probe with larger Stokes shift values, we have coupled dihydro[1,3]oxazine with coumarin derivatives.

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† We dedicate this article to the fond memory of our beloved Late Prof. Ashok K. Prasad.

‡ Electronic supplementary information (ESI) available. CCDC 2343787. For ESI and crystallographic data in CIF or other electronic format see DOI: <https://doi.org/10.1039/d4ob00749b>

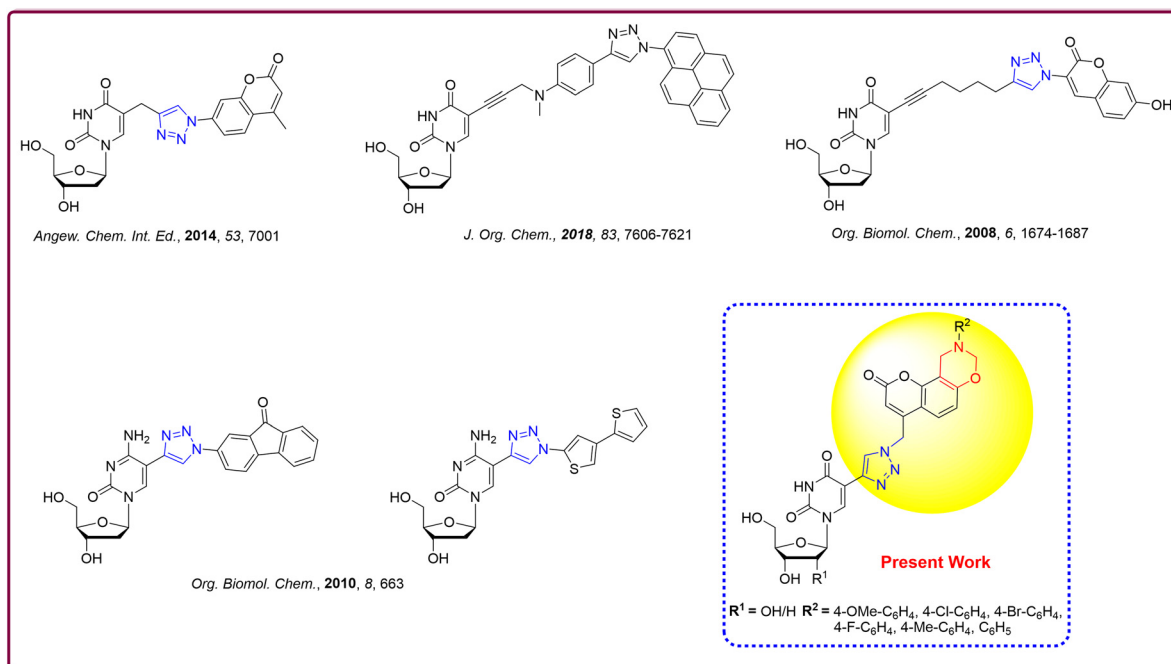


Fig. 1 Some literature reports for fluorescent base modified triazole nucleosides.

Furthermore, most environment-sensitive fluorescent nucleosides exhibit single-band emission and often lack microenvironment sensitivity and have low quantum yields.<sup>26,27</sup> Introducing two-band emission allows for ratio-metric sensing through emission ratios.<sup>28</sup> However, dual emissive fluorophores are rare due to synthesis challenges. Thus, dual emission-based biomolecular sensing, particularly in DNA analysis, remains poorly investigated.<sup>17,29</sup> Developing dual-emissive modified nucleosides is an unavoidable research area for detecting DNA microenvironment changes.

In continuation of our research efforts on developing modified fluorescent nucleosides,<sup>30–32</sup> we aimed to develop dual-emissive fluorescent nucleosides with better fluorescence properties. For this purpose, we designed oxazine-coupled coumarin-based triazole-linked<sup>33</sup> modified nucleosides.<sup>14,34–36</sup> Herein, we present the synthesis and comprehensive fluorescence, photophysical and DFT studies on our newly synthesized novel fluorophores.

## 2. Results and discussion

### 2.1 Chemistry

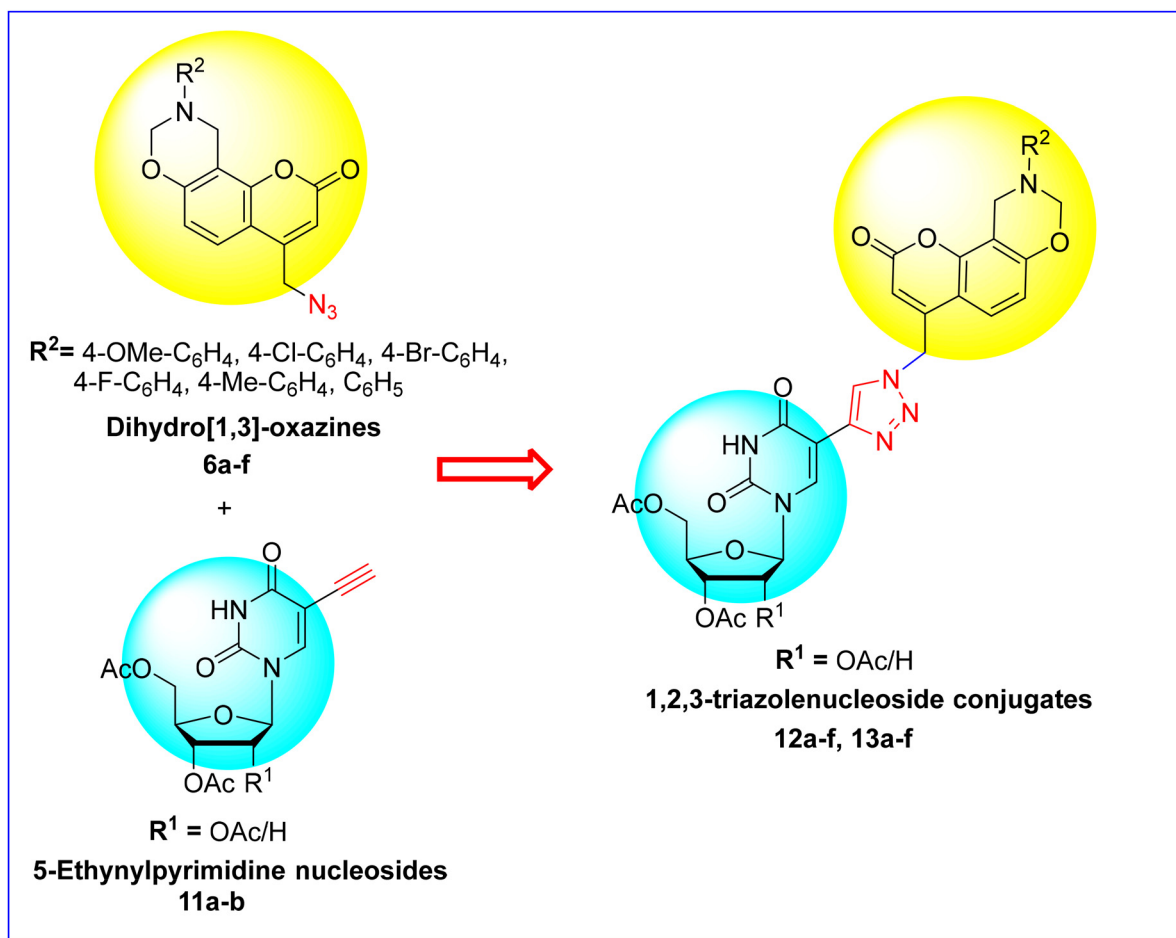
It was envisioned that our desired fluorophores could be obtained by the reaction of dihydro[1,3]-oxazines **6a–f** with 5-ethynyl-2',3',5'-tri-*O*-acetyl-2'-deoxyuridine **11a** or 3',5'-di-*O*-acetyl-2'-deoxyuridine **11b** through a copper(i)-catalyzed Huisgen (3 + 2) cycloaddition reaction (Scheme 1).

The first aim of this study was to construct a series of *N*-substituted-dihydro[1,3]-oxazine derivatives integrated onto the aryl ring of 7-hydroxy-4-azidomethyl coumarin **4**. Our

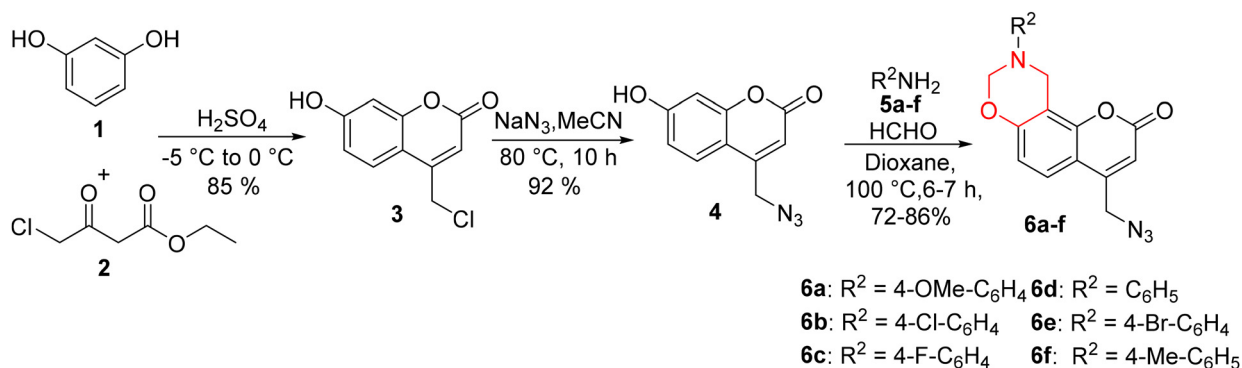
objective was to effectively combine the two motifs in order to generate a molecule with a high Stokes shift value. Consequently, we successfully synthesized the dihydro[1,3] oxazine analogues **6a–f** in good yields (Scheme 2).

To synthesize compounds **6a–f**, the precursor 7-hydroxy-4-chloromethylcoumarin **3** was initially prepared using the Pechmann condensation reaction of ethyl 4-chloroacetoacetate **2** and resorcinol **1** in the presence of conc. sulphuric acid.<sup>37</sup> The 7-hydroxy-4-chloromethylcoumarin **3** thus obtained on being treated with NaN<sub>3</sub> in MeCN at 80 °C resulted in the formation of 7-hydroxy-4-azidomethylcoumarin **4**.<sup>38</sup> Thereafter, six coumarin based dihydro[1,3]-oxazines were synthesized in 72–86% yields by following the Mannich-type condensation reaction of 7-hydroxy-4-azidomethylcoumarin **4** with formaldehyde and primary amines **5a–f** in 1,4-dioxane at 100 °C, as described in Scheme 2.<sup>39</sup>

The structure of the dihydro[1,3]-oxazine **6f** was further confirmed by its single crystal X-ray structural analysis (Fig. 7). Furthermore, the thus synthesized dihydro[1,3]-oxazines were subjected to the Cu(i)-catalyzed reaction. Initially, the click reaction<sup>40,41</sup> was carried out between the coumarin-based dihydro[1,3]-oxazine **6a** and 5-ethynyl-2',3',5'-tri-*O*-acetyl-2'-deoxyuridine **11a**. The reaction was performed in the presence of sodium ascorbate and CuSO<sub>4</sub>·5H<sub>2</sub>O in a solvent mixture of THF : *t*-BuOH : H<sub>2</sub>O (1 : 1 : 1) at ambient temperature, following the procedure outlined in the literature.<sup>42</sup> The reaction using the specified solvent system did not lead to complete consumption of the reactants even after 24 hours. Subsequently, the click reaction between the coumarin-based dihydro[1,3]-oxazine **6a** and 5-ethynyl-2',3',5'-tri-*O*-acetyl-2'-deoxyuridine **11a** was explored in different solvents and at various temperatures to



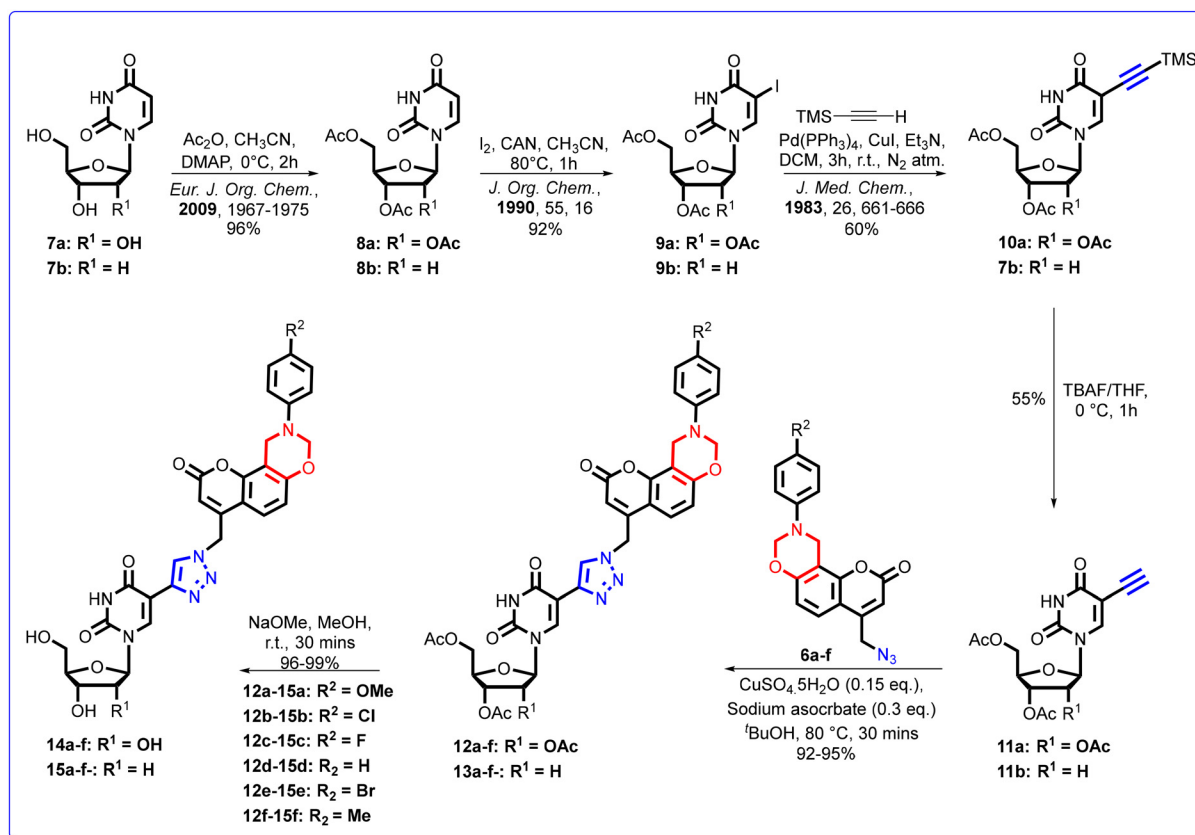
**Scheme 1** Precursors for fluorescent coumarin-triazole nucleoside conjugates.



**Scheme 2** Synthesis of coumarin-based dihydro[1,3]-oxazines **6a-f**.

optimize both the yield and efficiency of the reaction. It was observed that the reaction afforded 95% product yield in neat *t*BuOH at 80 °C.<sup>32,43</sup> Subsequently, the click reaction involving coumarin-based dihydro[1,3]-oxazines **6a-f** and the 5-ethynyl-2',3',5'-tri-*O*-acetyl-2'-deoxyuridine **11a** or 3',5'-di-*O*-acetyl-2'-deoxyuridine **11b** was performed in *t*BuOH at 80 °C. The resultant

oxazine coupled coumarin-based 1,2,3-triazole conjugates **12a-f** and **13a-f** were obtained in 92–95% yields (Scheme 3). Furthermore, the deacetylation of the nucleoside conjugates **12a-f** and **13a-f** was carried out using NaOMe in MeOH at 25 °C, resulting in the desired 1,2,3-triazole nucleoside conjugates **14a-f** and **15a-f** in quantitative yields (Scheme 3).



**Scheme 3** Synthesis of oxazine coupled coumarin-based 1,2,3-triazole conjugates **12a–f**, **13a–f**, **14a–f** and **15a–f**.

The structures of all the known compounds were confirmed by comparison of their spectral data with those reported in the literature.<sup>32,37,38,44,45</sup> The structures of the newly synthesized compounds **6a–f**, **12a–f**, **13a–f**, **14a–f** and **15a–f** were unambiguously established on the basis of their spectral (IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, <sup>1</sup>H-<sup>1</sup>H COSY NMR, <sup>1</sup>H-<sup>13</sup>C HETCOR NMR, NOESY NMR, DEPT-135 NMR and HRMS) data analysis. The hydroxyl groups present in the sugar moiety of the target compounds **14a–f** and **15a–f** were confirmed by <sup>1</sup>H NMR spectra using D<sub>2</sub>O exchange experiments (see the ESI†).

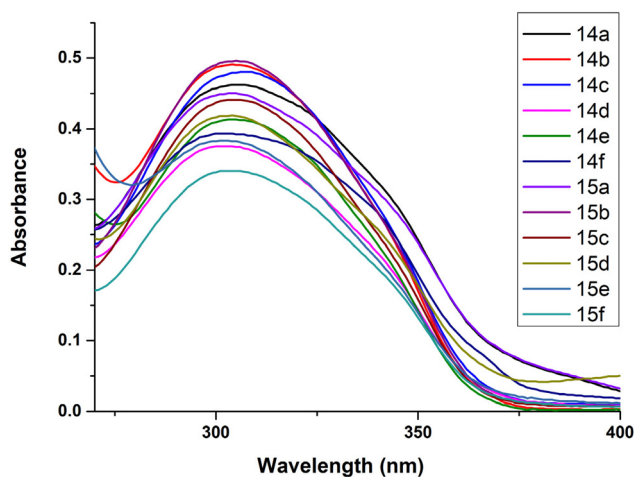
## 2.2. Photophysical characterization

Fluorescence is the physical property of a compound in which absorbed light is emitted and the extent of emission determines the fluorescence intensity. Numerous modified fluorescent nucleoside analogues have been explored for the study of the local structure and dynamics of nucleic acids. The synthesized compounds herewith have extended conjugations and thus their fluorescence properties were explored.

Photophysical studies of the synthesized nucleoside analogues, **14a–f** and **15a–f**, were carried out in DMSO. Attempts to perform the experiments in other solvents failed due to the poor solubility of these compounds.

**2.2.1. Absorption spectra.** The absorption spectra of the starting materials **11a** and **11b** were recorded in DMSO at  $2 \times 10^{-5}$  M concentration. No characteristic peak was observed in

the emission spectra. However, when the absorption spectra of the 1,2,3-triazoles **14a–f** and **15a–f** were recorded in DMSO at the same concentration at 25 °C (Fig. 2), a distinct peak at around 300 nm was observed with high absorption for all the compounds. A broad band was observed, which could be poss-



**Fig. 2** UV/Vis absorption spectra for compounds **14a–f** and **15a–f** in DMSO at  $2 \times 10^{-5}$  M concentration.

ibly due to the extended conjugation at the C-5 position of the nucleoside.

**2.2.2 Emission spectra.** The fluorescence spectra of the 1,2,3-triazoles **14a–f** and **15a–f** were recorded in DMSO at  $2 \times 10^{-5}$  M concentration at 25 °C (Fig. 3). Excitation of the nucleosides at  $\lambda_{\text{abs}}$  value = 300 nm resulted in maximum fluorescence of the compounds. The emission spectra of each compound depicted two strong bands at 360–380 nm and 450–480 nm and thus these nucleosides exhibited a dual-emissive behaviour. The electron donating group at the C-4''' position in **14a** and **14f** resulted in an increase in the fluorescence intensity, while those with electron withdrawing groups at the C-4''' position, *i.e.*, **14b**, **14c** and **14e**, were found to have lower values of fluorescence intensity. In the case of 2'-deoxyuridine analogues **15a–f**, the highest fluorescence intensity was observed for compound **15d**, followed by **15a** and lower values for **15b**, **15c** and **15e**. All the synthesized compounds exhibited high Stokes shift values (140–164 nm). Fluorescent nucleosides with high Stokes shift values have an added advantage as the possible spectral overlap of the absorption and emission spectra is eliminated and fluorescence can thus be easily detected.<sup>46</sup>

**2.2.3. Quantum yield calculations.** Furthermore, the fluorescence quantum yields ( $\Phi_F$ ) of the 1,2,3-triazole conjugates **14a–f** and **15a–f** were calculated by using the following equation with quinine sulphate as the reference ( $\Phi_{\text{st}} = 0.54$  in 0.1 M  $\text{H}_2\text{SO}_4$ ):

$$\Phi_F = \Phi_{\text{st}} \times S_{\text{u}}/S_{\text{st}} \times A_{\text{st}}/A_{\text{u}} \times n_{\text{Du}}^2/n_{\text{Dst}}^2$$

here,  $\Phi_F$  = emission quantum yield of the synthesized compounds **14a–f** and **15a–f**,  $\Phi_{\text{st}}$  = emission quantum yield of the standard,  $S_{\text{st}}$  = integrated emission band area of the standard,  $S_{\text{u}}$  = integrated emission band area of the samples,  $A_{\text{st}}$  = absorbance of the standard at the excitation wavelength,  $A_{\text{u}}$  = absorbance of the samples at the excitation wavelength,  $n_{\text{Dst}}$  =

solvent refractive index of the standard, and  $n_{\text{Du}}$  = solvent refractive index of the sample.

The subscripts 'u' and 'st' are used to denote the unknown samples and the standard, respectively. The quantum yields thus calculated are tabulated in Table 1.

The compounds exhibited varied trends of fluorescence properties. The quantum yield values ranged from 0.068–0.350, the highest being 0.350 for compound **14a**. The high quantum yields of these compounds can be attributed to the extended conjugation at the C-5 position of the nucleoside. Furthermore, derivatives with electron withdrawing substituents, *i.e.*, **14b**, **14c**, **14e**, **15b**, **15c** and **15e**, exhibited lower values of quantum yields while those with electron donating substituents at the C-4''' position resulted in higher quantum yields. Moreover, since H-bonding often exerts a strong influence on the fluorescence quantum yield, we may attribute the small differences observed in the ribo- vs. the deoxyribo-version to the extra OH group at the C-2' position in the case of the ribose version, which is absent in the case of the deoxyribose one.

**2.2.4. Solvatochromism.** Although the photophysical study of the nucleosides **14a–f** and **15a–f** was carried out only in DMSO due to their limited solubility in other organic solvents, we performed detailed solvatochromic studies of fluorophores **6a–f** in five different organic solvents, acetonitrile, MeOH, chloroform, DMSO, and 1,4-dioxane (Fig. 4 and 5), to study the effect of change of solvent polarity on the photophysical properties of these fluorophores.

The absorption and emission spectra of fluorophores **6a–f** were recorded in acetonitrile, MeOH, chloroform, DMSO, and 1,4-dioxane. The absorption spectra of all the compounds exhibited almost a similar pattern, that is, two absorption bands in the range 234–262 nm and 302–326 nm, in all the studied solvents (Fig. 4) except DMSO, wherein the lower wavelength peak was concealed by the absorption of the solvent.

A distinct hypsochromic shift was observed in the emission spectra of **6a–f** for 1,4-dioxane (292–293 nm), while a distinct bathochromic shift was observed for chloroform (390–416 nm) (Table 2). Also, high values of Stokes shift were observed in the case of chloroform (146–174 nm) while lowest values were observed in the case of 1,4-dioxane (35–58 nm). Moreover, the highest value of quantum yield was observed in the case of 1,4-dioxane (0.194–0.498) for each of the compounds **6a–f**. The highest fluorescence intensity was observed in the case of 1,4-dioxane for all the compounds. The emission wavelength, quantum yield, Stokes shift values and the molar absorption coefficient of compounds **6a–f** in different solvents are tabulated in Table 2.

**2.2.5. Theoretical calculations/frontier molecular orbitals.** We next carried out the quantum mechanical calculations of the synthesized molecules for better understanding of their electronic structures using the Gaussian 09 program.<sup>47</sup> The GaussView program<sup>48</sup> was used to visualize the molecular structures. The DFT computations employed the B3LYP functional with the Becke's gradient-exchange correction<sup>49</sup> along with the Lee–Yang–Parr correlation functional.<sup>50</sup> The geometry

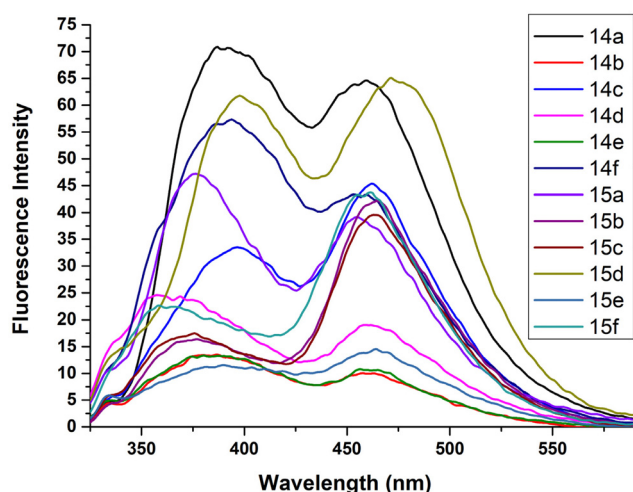
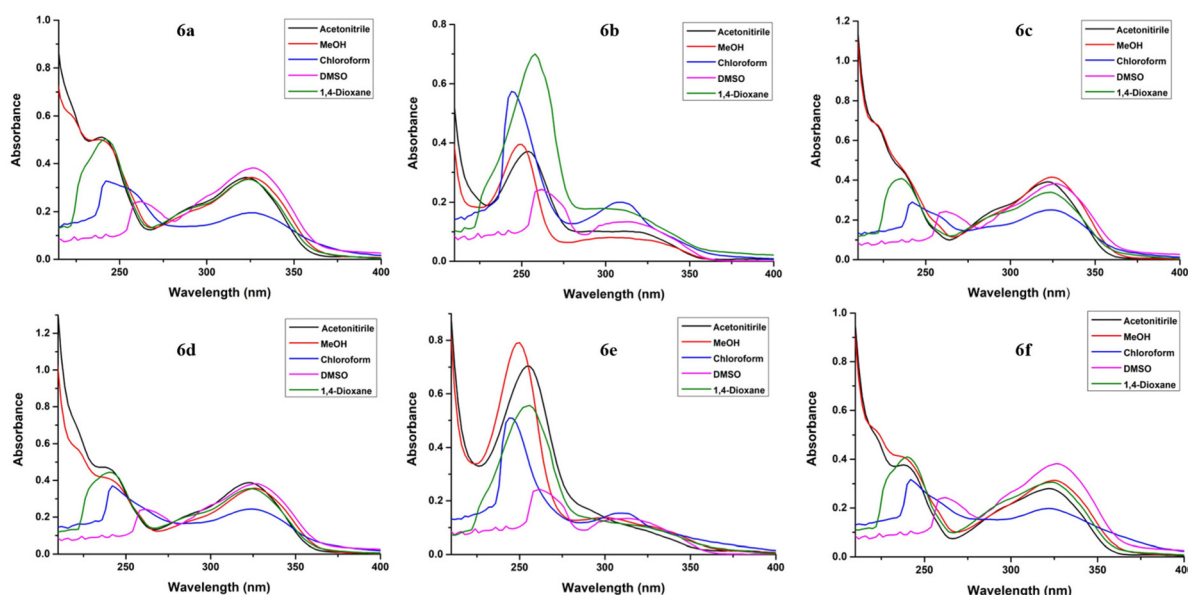


Fig. 3 Emission spectra for compounds **14a–f** and **15a–f** in DMSO at  $2 \times 10^{-5}$  M concentration (excitation at  $\lambda_{\text{ex}} = 300$  nm).



**Table 1** Emission spectra data for 1,2,3-triazoles **14a–f** and **15a–f**

Compound no.	Absorbance $\lambda_{\text{abs}}$ (nm)	Emission $\lambda_{\text{em}}$ (nm)	Stokes shift (nm)	Quantum yield ( $\Phi_F$ )	Extinction coefficient $\epsilon$ ( $\text{M}^{-1} \text{cm}^{-1}$ )
<b>14a</b>	310	392/460	150	0.350	22 850
<b>14b</b>	311	380/463	152	0.068	24 350
<b>14c</b>	310	396/462	152	0.150	23 600
<b>14d</b>	306	368/458	152	0.159	18 750
<b>14e</b>	315	390/465	150	0.082	20 450
<b>14f</b>	313	393/453	140	0.226	19 650
<b>15a</b>	309	376/454	145	0.261	22 350
<b>15b</b>	310	377/464	154	0.109	24 500
<b>15c</b>	309	375/463	154	0.150	21 850
<b>15d</b>	307	397/471	164	0.243	20 800
<b>15e</b>	306	390/463	157	0.093	19 100
<b>15f</b>	310	358/461	151	0.254	16 900

**Fig. 4** UV/Vis absorption spectra for fluorophores **6a–f** in acetonitrile, MeOH, chloroform, DMSO and 1,4-dioxane at  $2 \times 10^{-5}$  M concentration.

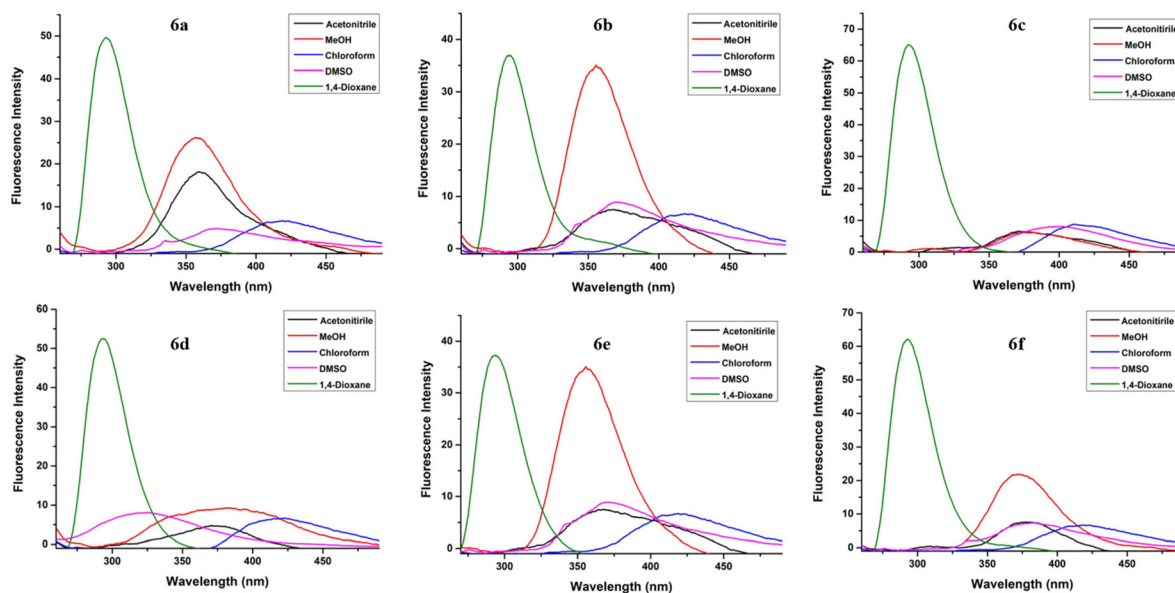
optimizations utilized the B3LYP/6-311++G(d,p) basis set.<sup>51</sup> The absence of negative vibrational modes in all the optimized structures confirmed their stability as stationary points throughout the optimization process.<sup>52</sup>

The resulting band gaps as well as the energies of the HOMO and LUMO were determined from the optimized structures (Fig. 6 and Table S1, see the ESI†). The band gaps range from 0.122 to 0.133 eV in DMSO. Understanding these orbital energies is crucial as they reflect the chemical behaviour of the molecules. The HOMO and LUMO orbital structures of compounds **14a** and **15a** are shown in Fig. 6 while those for the other compounds are detailed in Table S1 in the ESI†. In general, the LUMO is a typical electron acceptor, correlated with electron affinity (EA) while the HOMO is a typical electron donor, correlated with ionization potential (IP). The values of the HOMO–LUMO energy gap serve as useful indicators for a molecule's chemical reactivity. The reduction in this gap elucidates the potential charge transfer interactions within the compounds under study, attributed to the strong electron-

withdrawing capabilities of certain functional groups. For efficient charge separation, the localization of the HOMO on the donor moiety and the LUMO on the acceptor moiety is considered pertinent.<sup>53</sup> In this study, the coumarin and the triazole ring comprised the LUMO whilst the oxazine ring formed the HOMO, irrespective of its substituents.

These orbital contour diagrams distinctly suggest the generation of the charge-separated state by the transitions from the highest occupied molecular orbital to the lowest occupied molecular orbital. Moreover, these transitions can be attributed to be the intramolecular charge transfer (ICT) interactions from the donor to the acceptor moieties. Additionally, the significant overlap between the HOMO and LUMO implies effective electron donation and withdrawal properties for the donor and acceptor, respectively. Consequently, this strong overlap enhances the ICT between the donor and acceptor, thereby facilitating fluorescence exhibited by these compounds.

After optimizing the structures, the TDDFT method, known as the time-dependent density functional theory, was then



**Fig. 5** Emission spectra for fluorophores **6a–f** in acetonitrile, MeOH, chloroform, DMSO and 1,4-dioxane at  $2 \times 10^{-5}$  M concentration (excitation at  $\lambda_{\text{ex}} = 250$  nm).

**Table 2** Emission spectra data for fluorophores **6a–f** in acetonitrile, MeOH, chloroform, DMSO and 1,4-dioxane at  $2 \times 10^{-5}$  M concentration

Compound no.	Properties	Solvent				
		Acetonitrile	MeOH	Chloroform	DMSO	1,4-Dioxane
<b>6a</b>	Absorbance $\lambda_{\text{abs}}$ (nm)	240	238	242	262	242
	Emission $\lambda_{\text{em}}$ (nm)	358	357	416	370	292
	Stokes shift (nm)	118	119	174	108	50
	Quantum yield ( $\Phi_{\text{F}}$ )	0.064	0.025	0.009	0.004	0.257
	Extinction coefficient $\epsilon$ ( $\text{M}^{-1} \text{cm}^{-1}$ )	14 100	19 750	16 350	12 150	25 150
<b>6b</b>	Absorbance $\lambda_{\text{abs}}$ (nm)	254	250	245	261	258
	Emission $\lambda_{\text{em}}$ (nm)	365	356	392	368	293
	Stokes shift (nm)	111	106	147	107	35
	Quantum yield ( $\Phi_{\text{F}}$ )	0.080	0.026	0.013	0.010	0.498
	Extinction coefficient $\epsilon$ ( $\text{M}^{-1} \text{cm}^{-1}$ )	18 550	19 750	28 700	12 150	35 000
<b>6c</b>	Absorbance $\lambda_{\text{abs}}$ (nm)	238	239	242	262	234
	Emission $\lambda_{\text{em}}$ (nm)	370	371	410	397	292
	Stokes shift (nm)	132	132	168	135	58
	Quantum yield ( $\Phi_{\text{F}}$ )	0.187	0.022	0.007	0.008	0.365
	Extinction coefficient $\epsilon$ ( $\text{M}^{-1} \text{cm}^{-1}$ )	7900	12 400	14 550	11 800	20 200
<b>6d</b>	Absorbance $\lambda_{\text{abs}}$ (nm)	240	241	242	260	240
	Emission $\lambda_{\text{em}}$ (nm)	375	374	416	321	293
	Stokes shift (nm)	135	124	174	61	53
	Quantum yield ( $\Phi_{\text{F}}$ )	0.083	0.025	0.004	0.006	0.268
	Extinction coefficient $\epsilon$ ( $\text{M}^{-1} \text{cm}^{-1}$ )	12 650	15 900	18 550	12 250	22 200
<b>6e</b>	Absorbance $\lambda_{\text{abs}}$ (nm)	255	249	244	260	254
	Emission $\lambda_{\text{em}}$ (nm)	347	343	390	393	292
	Stokes shift (nm)	92	94	146	133	38
	Quantum yield ( $\Phi_{\text{F}}$ )	0.001	0.017	0.010	0.014	0.194
	Extinction coefficient $\epsilon$ ( $\text{M}^{-1} \text{cm}^{-1}$ )	35 150	39 550	25 450	12 350	27 650
<b>6f</b>	Absorbance $\lambda_{\text{abs}}$ (nm)	239	238	242	259	240
	Emission $\lambda_{\text{em}}$ (nm)	375	372	414	382	292
	Stokes shift (nm)	136	134	172	123	52
	Quantum yield ( $\Phi_{\text{F}}$ )	0.051	0.105	0.009	0.012	0.332
	Extinction coefficient $\epsilon$ ( $\text{M}^{-1} \text{cm}^{-1}$ )	9150	14 350	15 850	11 900	20 500

employed to calculate the vertical excited state energies as well the oscillator strengths ( $f$ ) for the electronic transitions of compound **13a**.<sup>54</sup> The TDDFT calculations were conducted on

the optimized ground state geometries utilizing the 6-31++G(d, p) basis set. Subsequently, the absorption spectra was generated based on the obtained data (Fig. S78, see the ESI†). The

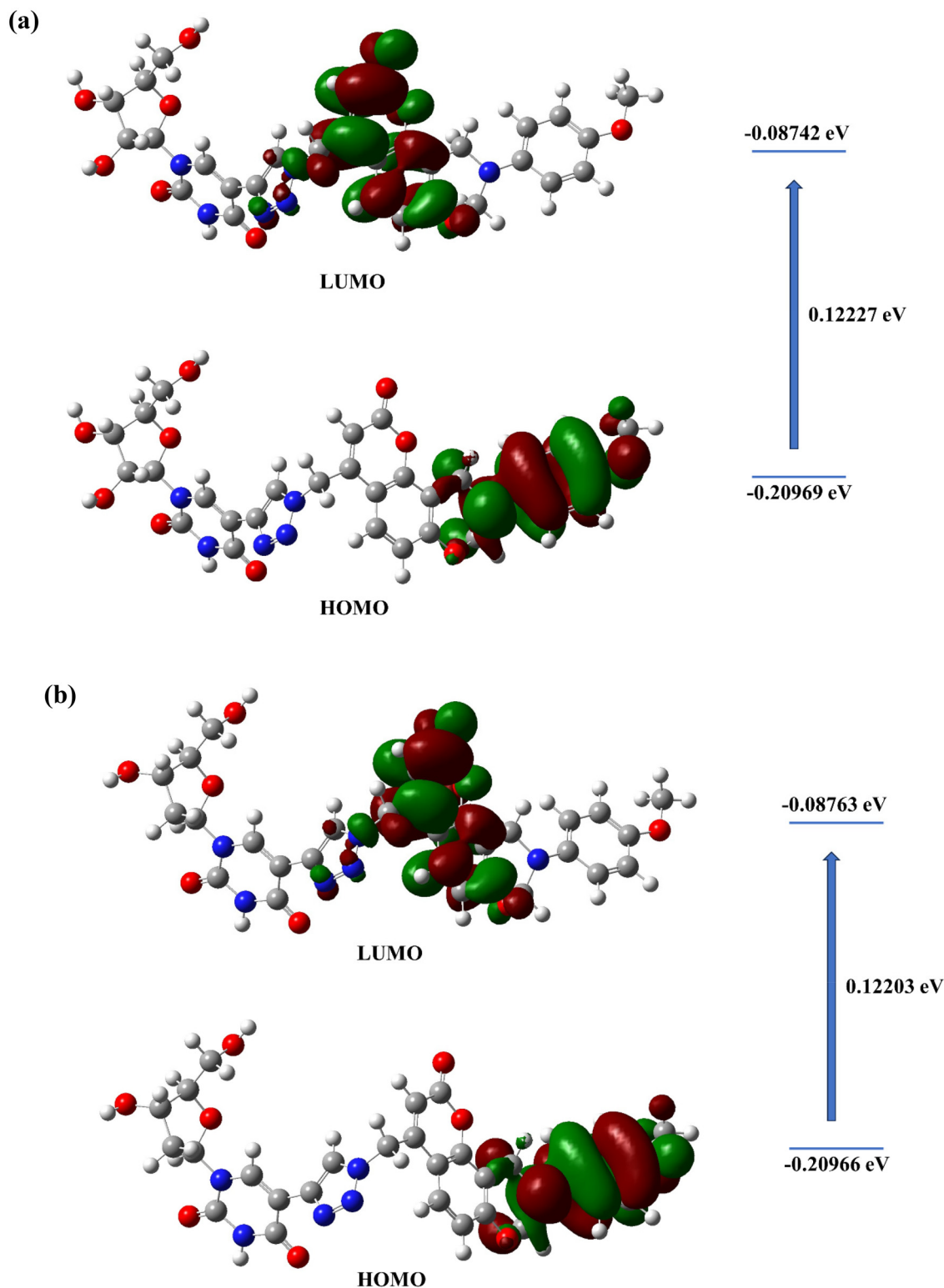


Fig. 6 HOMO–LUMO frontier molecular orbitals for nucleosides (a) 14a and (b) 15a calculated using the Gaussian 09 program package.

observed difference between the theoretical and experimental results can be attributed to the fact that realistically, the experimental results belong to solution which comprises several inter- and intramolecular interactions.

**2.2.6. Comparative discussion.** In this research, the quantum yield and Stokes shift values of the base-modified synthesized fluorescent nucleosides were investigated alongside those of the literature reported derivatives of pyrimidine fluo-



rescent nucleosides. The results demonstrated that the newly synthesized base-modified fluorescent nucleosides exhibited superior quantum yield and Stokes shift values when compared to their known pyrimidine fluorescent triazole counterparts

(Table 3).<sup>12,14,17</sup> These findings suggest the potential for enhanced fluorescence properties in the newly developed nucleosides, highlighting their promise for applications in various fields such as molecular imaging and biosensing.

**Table 3** Comparison of various photophysical parameters of compound **14a** with some reported C-5 modified pyrimidine nucleosides

Structure	Absorbance $\lambda_{\text{abs}}$ (nm)	Emission $\lambda_{\text{em}}$ (nm)	Stokes shift (nm)	Quantum yield ( $\Phi_F$ )	Extinction coefficient $\epsilon$ ( $\text{M}^{-1} \text{cm}^{-1}$ )	Solvent
	328, 343	387, 400, 494	nr	0.054	nr	Dioxane
	347	476	nr	0.32	21 300	MeOH
	320	385	65	0.0055	nr	EtOH
	320	380	60	0.0062	nr	EtOH
	310	392/460	150	0.350	22 850	DMSO

nr: not reported.

### 3. Conclusion

In light of the significance of triazole-linked fluorescent nucleosides, we herein present the synthesis of novel dihydro [1,3]oxazine-coumarin-based-1,2,3-triazole nucleoside analogues *via* the copper(I)-catalyzed Huisgen (3 + 2) cycloaddition reaction. Subsequently, comprehensive fluorescence and photophysical studies were also performed for the thus synthesized derivatives. The fluorophores **6a–f** demonstrated variations in the fluorescence properties with changes in solvent polarity. The higher quantum yield values ranged from 0.194 to 0.498, with the highest fluorescence intensity observed in 1,4-dioxane. Notably, the highest quantum yield of 0.498 was recorded for compound **6b**. Moreover, in our study, we witnessed a dual-emission phenomenon for all the synthesized nucleoside analogues, presenting the distinct advantage for DNA sensing in contrast to the commonly employed single-band fluorescent nucleosides. The electronic structure of these nucleosides was thoroughly investigated using the Density Functional Theory (DFT). We hypothesize that certain modified nucleosides among these could prove to be excellent candidates for fluorophores, given their substantial Stokes shifts and high quantum yields. Furthermore, to thoroughly assess the dual-emissive properties of these modified nucleosides within the oligonucleotide framework, it is necessary to synthesize oligonucleotides that incorporate these modified nucleosides.

### 4. Experimental

All chemicals and solvents were purchased from Alfa Aesar, Thermo Fisher Scientific, India Pvt. Limited, Sigma-Aldrich Chemicals Pvt. Limited, India and from local commercial sources and were used without any further purification unless otherwise specified. Solvents for column chromatography were dried and distilled prior to use. Solvents were removed under reduced pressure using a rotary evaporator, followed by further removal of the residual solvent under high vacuum. Column chromatography was performed on silica gel (100–200 mesh). Melting points were determined on a Buchi M-560 instrument and are uncorrected. HRMS analysis was carried out using an Agilent G6530AA LC Q-TOF mass spectrometer using the ESI method. The IR spectra of compounds were recorded on a PerkinElmer model 2000 FT-IR spectrometer and are expressed as wavenumber ( $\text{cm}^{-1}$ ). The  $R_f$  values of compounds are reported from the analytical TLC study using the specified solvents and 0.25 mm silica gel 60  $F_{254}$  plates that were visualized by UV irradiation or by charring with a 5% alcoholic sulfuric acid solution. The  $^1\text{H}$ - and the  $^{13}\text{C}$ - and other 2D NMR spectra were recorded on JEOL alpha-400 and Bruker-Avance Neo 400 FT-NMR spectrometers by using tetramethylsilane (TMS) as the internal standard. The chemical shift values are on the  $\delta$  scale and the coupling constant ( $J$ ) are in Hz. Absorption spectra were recorded between 200 nm and 600 nm using a PerkinElmer UV/Vis spectrometer Lambda 45 at a scan speed

240  $\text{nm min}^{-1}$ . All measurements were carried out in PEUV/Vis spectroscopy cells (1 cm). HPLC grade solvents were used for all solution preparation.

#### 4.1. General procedure for the synthesis of 4-(azidomethyl)- $N^9$ -(4'-aryl)-9,10-dihydro-2H,8H-chromeno[8,7-e][1,3]oxazin-2-ones (**6a–f**)

A solution of primary amines **5a–f** (1.1 mmol) in dioxane (5 mL) was treated with formalin solution (2.5 mmol). The resulting mixture was stirred at room temperature for 3–5 h. Subsequently, 7-hydroxy-4-azidomethylcoumarin **4** (1 mmol) and a catalytic amount of DMAP were added to the reaction mixture. The reaction was then stirred at 100 °C until complete consumption of the reactants (the progress of the reaction was examined by thin layer chromatography). After the completion of the reaction, the solvent was evaporated under reduced pressure and the crude product was purified by using silica gel column chromatography using ethylacetate and hexane as the solvent to obtain the desired compounds **6a–f** in 72–86% yields.

**4.1.1 4-(Azidomethyl)- $N^9$ -(4'-methoxyphenyl)-9,10-dihydro-2H,8H-chromeno[8,7-e][1,3]oxazin-2-one (**6a**).** It was obtained as a yellow solid. Yield: 0.28 g (78%).  $R_f$  = 0.48 (30% ethyl acetate in petroleum ether); melting point = 140–142 °C; IR (KBr,  $\text{cm}^{-1}$ ): 2116, 1732, 1517, 1412, 1298, 1143, 1057, 926, 781, 719;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.29 (d,  $J$  = 8.8 Hz, 1H, ArH), 7.10–7.07 (m, 2H, ArH), 6.82–6.79 (m, 3H, ArH), 6.33 (s, 1H, C-3H), 5.38 (s, 2H,  $\text{CH}_2$ ), 4.73 (s, 2H,  $\text{CH}_2$ ), 4.47 (d,  $J$  = 1.0 Hz, 2H,  $\text{CH}_2\text{N}_3$ ), 3.74 (s, 3H,  $\text{OCH}_3$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  160.5 (C=O), 158.0 (ArC), 155.4 (ArC), 151.6 (ArC), 149.2 (ArC), 141.7 (ArC), 122.8 (ArC), 120.8 (ArC), 114.6 (ArC), 114.1 (ArC), 111.1 (ArC), 110.5 (C-3), 109.3 (ArC), 81.1 ( $\text{CH}_2$ ), 55.6 ( $\text{OCH}_3$ ), 50.8 ( $\text{CH}_2\text{N}_3$ ), 46.9 ( $\text{CH}_2$ ); HRMS (ESI):  $m/z$  calculated for  $\text{C}_{19}\text{H}_{17}\text{N}_4\text{O}_4^+ [\text{M} + \text{H}]^+$ : 365.1250, found: 365.1255.

**4.1.2 4-(Azidomethyl)- $N^9$ -(4'-chlorophenyl)-9,10-dihydro-2H,8H-chromeno[8,7-e][1,3]oxazin-2-one (**6b**).** It was obtained as a yellow solid. Yield: 0.28 g (75%).  $R_f$  = 0.52 (30% ethyl acetate in petroleum ether); melting point = 134–136 °C; IR (KBr,  $\text{cm}^{-1}$ ): 2100, 1715, 1591, 1488, 1360, 1307, 1248, 1157, 1091, 916, 796, 713;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.31 (d,  $J$  = 8.8 Hz, 1H, ArH), 7.22 (d,  $J$  = 8.7 Hz, 2H, ArH), 7.06 (d,  $J$  = 8.7 Hz, 2H, ArH), 6.79 (d,  $J$  = 8.8 Hz, 1H, ArH), 6.35 (s, 1H, C-3H), 5.40 (s, 2H,  $\text{CH}_2$ ), 4.78 (s, 2H,  $\text{CH}_2$ ), 4.48 (d,  $J$  = 1.0 Hz, 2H,  $\text{CH}_2\text{N}_3$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  160.2 (C=O), 157.7 (ArC), 151.5 (ArC), 149.0 (ArC), 146.4 (ArC), 129.3 (ArC), 127.3 (ArC), 123.0 (ArC), 119.9 (ArC), 114.0 (ArC), 111.3 (ArC), 110.7 (C-3), 109.0 (ArC), 79.8 ( $\text{CH}_2$ ), 50.8 ( $\text{CH}_2\text{N}_3$ ), 46.5 ( $\text{CH}_2$ ); HRMS (ESI):  $m/z$  calculated for  $\text{C}_{18}\text{H}_{14}\text{ClN}_4\text{O}^+ [\text{M} + \text{H}]^+$ : 369.0754, found: 369.0772.

**4.1.3 4-(Azidomethyl)- $N^9$ -(4'-fluorophenyl)-9,10-dihydro-2H,8H-chromeno[8,7-e][1,3]oxazin-2-one (**6c**).** It was obtained as a yellow solid. Yield: 0.25 g (72%).  $R_f$  = 0.53 (30% ethyl acetate in petroleum ether); melting point = 124 °C; IR (KBr,  $\text{cm}^{-1}$ ): 2118, 1711, 1556, 1414, 1336, 1222, 1154, 1071, 879, 743;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.30 (d,  $J$  = 8.8 Hz, 1H, ArH), 7.08 (dd,  $J$  = 9.1 Hz, 4.6 Hz, 2H, ArH), 6.94–6.79 (m, 2H, ArH), 6.78 (d,  $J$  = 8.8 Hz, 1H, ArH), 6.33 (s, 1H, C-3H), 5.36 (s, 2H,  $\text{CH}_2$ ), 4.74 (s, 2H,  $\text{CH}_2$ ), 4.47 (s, 2H,  $\text{CH}_2\text{N}_3$ );  $^{13}\text{C}$  NMR

(CDCl<sub>3</sub>, 100 MHz):  $\delta$  160.4 (C=O), 159.7 (ArC), 157.9 (ArC), 157.3 (ArC), 151.5 (ArC), 149.2 (ArC), 144.3 (ArC), 144.3 (ArC), 123.0 (ArC), 120.7 (ArC), 120.6 (ArC), 116.1 (ArC), 115.9 (ArC), 114.1 (ArC), 111.3 (ArC), 110.7 (C-3), 109.1 (ArC), 80.6 (CH<sub>2</sub>), 50.8 (CH<sub>2</sub>N<sub>3</sub>), 46.9 (CH<sub>2</sub>); HRMS (ESI):  $m/z$  calculated for C<sub>18</sub>H<sub>14</sub>FN<sub>4</sub>O<sub>3</sub><sup>+</sup> [M + H]<sup>+</sup>: 353.1050, found: 353.1059.

**4.1.4 4-(Azidomethyl)-N<sup>9</sup>-phenyl-9,10-dihydro-2H,8H-chromeno[8,7-e][1,3]oxazin-2-one (6d).** It was obtained as a yellow solid. Yield: 0.27 g (82%).  $R_f$  = 0.56 (30% ethyl acetate in petroleum ether); melting point = 129 °C; IR (KBr, cm<sup>-1</sup>): 2110, 1709, 1595, 1495, 1388, 1296, 1242, 1205, 1158, 1037, 894, 840, 753, 685; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta$  7.30–7.26 (m, 3H, ArH), 7.15–7.12 (m, 2H, ArH), 6.98–6.94 (m, 1.0 Hz, 1H, ArH), 6.78 (d,  $J$  = 8.8 Hz, 1H, ArH), 6.34 (d,  $J$  = 1.0 Hz, 1H, C-3H), 5.44 (s, 2H, CH<sub>2</sub>), 4.82 (s, 2H, CH<sub>2</sub>), 4.47 (s, 2H, CH<sub>2</sub>N<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz):  $\delta$  160.5 (C=O), 158.5 (ArC), 151.5 (ArC), 149.2 (ArC), 147.9 (ArC), 129.5 (ArC), 122.9 (ArC), 122.2 (ArC), 118.6 (ArC), 117.7 (ArC), 114.1 (ArC), 111.2 (C-3), 109.4 (ArC), 80.0 (CH<sub>2</sub>), 50.8 (CH<sub>2</sub>N<sub>3</sub>), 46.4 (CH<sub>2</sub>); HRMS (ESI):  $m/z$  calculated for C<sub>18</sub>H<sub>15</sub>N<sub>4</sub>O<sub>3</sub><sup>+</sup> [M + H]<sup>+</sup>: 335.1144, found: 335.1151.

**4.1.5 4-(Azidomethyl)-N<sup>9</sup>-(4'-bromophenyl)-9,10-dihydro-2H,8H-chromeno[8,7-e][1,3]oxazin-2-one (6e).** It was obtained as a yellow solid. Yield: 0.36 g (86%).  $R_f$  = 0.54 (30% ethyl acetate in petroleum ether); melting point = 131–132 °C; IR (KBr, cm<sup>-1</sup>): 2106, 1732, 1464, 1341, 1224, 1138, 1057, 923, 787, 707; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta$  7.37–7.36 (m, 1H, ArH), 7.35–7.34 (m, 1H, ArH), 7.31 (d,  $J$  = 8.9 Hz, 1H, ArH), 7.02–7.01 (m, 1H, ArH), 7.00–6.99 (m, 1H, ArH), 6.78 (d,  $J$  = 8.8 Hz, 1H, ArH), 6.34 (s, 1H, C-3H), 5.39 (s, 2H, CH<sub>2</sub>), 4.78 (s, 2H, CH<sub>2</sub>), 4.47 (d,  $J$  = 0.9 Hz, 2H, CH<sub>2</sub>N<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz):  $\delta$  160.3 (C=O), 157.8 (ArC), 151.5 (ArC), 149.1 (ArC), 147.0 (ArC), 132.4 (ArC), 123.0 (ArC), 120.3 (ArC), 114.8 (ArC), 114.1 (ArC), 111.4 (ArC), 110.7 (C-3), 109.1 (ArC), 79.7 (CH<sub>2</sub>), 50.9 (CH<sub>2</sub>N<sub>3</sub>), 46.5 (CH<sub>2</sub>); HRMS (ESI):  $m/z$  calculated for C<sub>18</sub>H<sub>14</sub>BrN<sub>4</sub>O<sub>3</sub><sup>+</sup> [M + H]<sup>+</sup>: 413.0249, found: 413.0266.

**4.1.6 4-(Azidomethyl)-N<sup>9</sup>-(4'-methylphenyl)-9,10-dihydro-2H,8H-chromeno[8,7-e][1,3]oxazin-2-one (6f).** It was obtained as a yellow solid. Yield: 0.28 g (79%).  $R_f$  = 0.63 (30% ethyl acetate in petroleum ether); melting point = 118–120 °C; IR (KBr, cm<sup>-1</sup>): 2103, 1726, 1550, 1478, 1336, 1317, 1231, 1129, 1064, 921, 771, 725; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz):  $\delta$  7.20 (d,  $J$  = 8.8 Hz, 1H, ArH), 6.99–6.97 (m, 4H, ArH), 6.70 (d,  $J$  = 8.8 Hz, 1H, ArH), 6.25 (s, 1H, C-3H), 5.33 (s, 2H, CH<sub>2</sub>), 4.70 (s, 2H, CH<sub>2</sub>), 4.39 (d,  $J$  = 0.8 Hz, 2H, CH<sub>2</sub>N<sub>3</sub>), 2.18 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz):  $\delta$  160.2 (C=O), 157.7 (ArC), 151.5 (ArC), 149.0 (ArC), 146.4 (ArC), 129.3 (ArC), 127.3 (ArC), 123.0 (ArC), 119.9 (ArC), 114.0 (ArC), 111.3 (ArC), 110.7 (C-3), 109.0 (ArC), 79.8 (CH<sub>2</sub>), 50.8 (CH<sub>2</sub>N<sub>3</sub>), 46.5 (CH<sub>2</sub>), 20.6 (CH<sub>3</sub>); HRMS (ESI):  $m/z$  calculated for C<sub>19</sub>H<sub>16</sub>N<sub>4</sub>NaO<sub>3</sub><sup>+</sup> [M + Na]<sup>+</sup>: 371.1120, found: 371.1104.

**4.2. General procedure for the synthesis of N<sup>1</sup>-(9'''-(4''-substituted)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(2',3',5'-tri-O-acetyl- $\beta$ -D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole conjugates (12a–f and 13a–f)**

A mixture of freshly synthesized dihydro[1,3]oxazines **6a–f** (1.2 mmol) and 5-ethynyl-2',3',5'-tri-O-acetyl/3',5'-di-O-acetyl-2'-

deoxyuridines **11a–b** (1.0 mmol) was stirred at 80 °C in <sup>t</sup>BuOH (20 mL). Subsequently, a solution of sodium ascorbate (0.40 mmol) in H<sub>2</sub>O was added followed by the addition of CuSO<sub>4</sub>·5H<sub>2</sub>O (0.20 mmol) solution in H<sub>2</sub>O. The progress of the reaction was monitored by TLC. After the completion of the reaction (as observed by TLC), the solvent was evaporated under reduced pressure and the crude product was purified by using silica gel column chromatography using methanol in chloroform as the solvent system to obtain the desired compounds **12a–f** and **13a–f** in 92–95% yields.

**4.2.1 N<sup>1</sup>-(9'''-(4'''-Methoxy)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(2',3',5'-tri-O-acetyl- $\beta$ -D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (12a).** It was obtained as a bright yellow solid. Yield: 0.72 g (95%).  $R_f$  = 0.32 (5% methanol in chloroform); melting point = 252 °C; IR (KBr, cm<sup>-1</sup>): 3318, 3074, 2937, 2840, 1680, 1602, 1514, 1465, 1377, 1217, 1102, 1043, 895, 826, 593; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz):  $\delta$  11.88 (s, 1H, N-3''H), 8.58 (s, 1H, C-5H), 8.47 (s, 1H, C-6''H), 7.66–7.63 (m, 1H, ArH), 7.11–7.06 (m, 2H, ArH), 6.86–6.79 (m, 3H, ArH), 6.11–6.08 (d,  $J$  = 5.3 Hz, 1H, C-1''H), 5.98 (s, 2H, CH<sub>2</sub>), 5.68 (s, 1H, ArH), 5.52–5.49 (m, 1H, C-2''H), 5.49–5.48 (m, 2H, CH<sub>2</sub>), 5.41–5.37 (m, 1H, C-3''H), 4.67 (s, 2H, CH<sub>2</sub>), 4.39–4.36 (m, 1H, C-4''H), 4.32–4.29 (m, 2H, C-5''H), 3.66 (s, 3H, OCH<sub>3</sub>), 2.14 (s, 3H, OCOCH<sub>3</sub>), 2.11 (s, 3H, OCOCH<sub>3</sub>), 2.06 (s, 3H, OCOCH<sub>3</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz)  $\delta$  170.0 (C=O), 170.0 (C=O), 169.9 (C=O), 161.6 (ArC), 160.0 (ArC), 158.1 (ArC), 154.9 (ArC), 151.5 (ArC), 151.3 (ArC), 150.1 (ArC), 141.6 (ArC), 139.5 (C-4), 137.0 (C-6''), 124.2 (C-5), 124.2 (ArC), 120.4 (ArC), 115.0 (ArC), 113.8 (ArC), 110.6 (ArC), 110.5 (ArC), 109.2 (ArC), 106.2 (ArC), 88.2 (C-1''), 81.2 (CH<sub>2</sub>), 80.0 (C-4''), 72.9 (C-2''), 70.5 (C-3''), 63.6 (C-5''), 55.7 (OCH<sub>3</sub>), 49.7 (CH<sub>2</sub>), 45.6 (CH<sub>2</sub>), 21.1 (OCOCH<sub>3</sub>), 20.9 (OCOCH<sub>3</sub>), 20.8 (OCOCH<sub>3</sub>); HRMS (ESI):  $m/z$  calculated for C<sub>36</sub>H<sub>34</sub>N<sub>6</sub>O<sub>13</sub><sup>+</sup> [M]<sup>+</sup>: 758.2184, found: 758.2140.

**4.2.2 N<sup>1</sup>-(9'''-(4'''-Chloro)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(2',3',5'-tri-O-acetyl- $\beta$ -D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (12b).** It was obtained as a yellowish white solid. Yield: 0.71 g (93%).  $R_f$  = 0.36 (5% methanol in chloroform); melting point = 214 °C; IR (KBr, cm<sup>-1</sup>): 3037, 2833, 1747, 1711, 1692, 1604, 1496, 1363, 1267, 1225, 1218, 1100, 1059, 1047, 876, 817, 581; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  11.83 (s, 1H, N-3''H), 8.54 (s, 1H, C-5H), 8.43 (s, 1H, C-6''H), 7.63–7.59 (m, 1H, ArH), 7.25–7.21 (m, 2H, ArH), 7.17–7.13 (m, 2H, ArH), 6.83–6.79 (m, 1H, ArH), 6.07–6.04 (m, 1H, C-1''H), 5.93 (s, 2H, CH<sub>2</sub>), 5.66 (s, 1H, ArH), 5.52 (s, 2H, CH<sub>2</sub>), 5.48–5.44 (m, 1H, C-2''H), 5.37–5.33 (m, 1H, C-3''H), 4.71 (s, 2H, CH<sub>2</sub>), 4.35–4.32 (m, 1H, C-4''H), 4.28–4.24 (m, 2H, C-5''H), 2.09 (s, 3H, OCOCH<sub>3</sub>), 2.06 (s, 3H, OCOCH<sub>3</sub>), 2.02 (s, 3H, OCOCH<sub>3</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz)  $\delta$  170.7 (C=O), 170.0 (C=O), 170.0 (C=O), 161.6 (ArC), 160.0 (ArC), 157.9 (ArC), 151.2 (ArC), 151.2 (ArC), 150.1 (ArC), 146.9 (ArC), 139.5 (C-4), 137.0 (C-6''), 129.5 (C-5), 125.6 (ArC), 124.3 (ArC), 124.2 (ArC), 120.1 (ArC), 113.9 (ArC), 110.8 (ArC), 110.7 (ArC), 109.2 (ArC), 106.2 (ArC), 88.2 (C-1''), 80.0 (CH<sub>2</sub>), 79.9 (C-4''), 72.9 (C-2''), 70.5 (C-3''), 63.6 (C-5''), 49.7 (CH<sub>2</sub>), 45.1 (CH<sub>2</sub>), 21.1 (OCOCH<sub>3</sub>), 20.9 (OCOCH<sub>3</sub>),

20.8 (OCOCH<sub>3</sub>); HRMS (ESI):  $m/z$  calculated for C<sub>35</sub>H<sub>32</sub>ClN<sub>6</sub>O<sub>12</sub><sup>+</sup> [M + H]<sup>+</sup>: 763.1761, found: 763.1760.

**4.2.3 N<sup>1</sup>-(9''-(4'''-Fluoro)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(2',3',5'-tri-O-acetyl-β-D-ribofuranos-1'-(2',4'-dioxo-3',4'-dihydropyrimidin))-1,2,3-triazole (12c).** It was obtained as a yellow solid. Yield: 0.69 g (92%).  $R_f$  = 0.34 (5% methanol in chloroform); melting point = 222–226 °C; IR (KBr, cm<sup>-1</sup>): 2982, 2918, 1693, 1596, 1504, 1454, 1368, 1221, 1045, 879, 811, 757, 581; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  11.89 (s, 1H, N-3''H), 8.60–8.58 (m, 1H, C-5H), 8.49–8.47 (m, 1H, C-6''H), 7.70–7.64 (m, 1H, ArH), 7.20–7.17 (m, 1H, ArH), 7.11–7.05 (m, 2H, ArH), 6.95–6.91 (m, 1H, ArH), 6.89–6.84 (m, 1H, ArH), 6.11–6.08 (m, 1H, C-1'H), 5.98 (s, 2H, CH<sub>2</sub>), 5.70–5.65 (m, 1H, ArH), 5.55–5.51 (m, 2H, CH<sub>2</sub>), 5.51–5.48 (m, 1H, C-2'H), 5.42–5.38 (m, 1H, C-3'H), 4.73 (s, 1H, C-4'H), 4.39–4.34 (m, 2H, CH<sub>2</sub>), 4.33–4.29 (m, 2H, C-5'H), 2.14 (s, 3H, OCOCH<sub>3</sub>), 2.11 (s, 3H, OCOCH<sub>3</sub>), 2.06 (s, 3H, OCOCH<sub>3</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz)  $\delta$  170.7 (C=O), 170.0 (C=O), 170.0 (C=O), 161.6 (ArC), 160.0 (ArC), 158.0 (ArC), 151.5 (ArC), 151.2 (ArC), 150.1 (ArC), 144.6 (ArC), 139.4 (C-4), 137.0 (C-6''), 124.3 (C-5), 124.2 (ArC), 120.5 (ArC), 120.4 (ArC), 116.3 (ArC), 116.1 (ArC), 113.8 (ArC), 110.7 (ArC), 110.6 (ArC), 109.1 (ArC), 106.2 (ArC), 88.2 (C-1'), 80.7 (CH<sub>2</sub>), 80.0 (C-4'), 72.9 (C-2'), 70.5 (C-3'), 63.6 (C-5'), 49.7 (CH<sub>2</sub>), 45.5 (CH<sub>2</sub>), 21.1 (OCOCH<sub>3</sub>), 20.9 (OCOCH<sub>3</sub>), 20.8 (OCOCH<sub>3</sub>); HRMS (ESI):  $m/z$  calculated for C<sub>35</sub>H<sub>32</sub>FN<sub>6</sub>O<sub>12</sub><sup>+</sup> [M + H]<sup>+</sup>: 747.2057, found: 747.2054.

**4.2.4 N<sup>1</sup>-(9''',10'''-Dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(2',3',5'-tri-O-acetyl-β-D-ribofuranos-1'-(2',4'-dioxo-3',4'-dihydropyrimidin))-1,2,3-triazole (12d).** It was obtained as a yellow solid. Yield: 0.68 g (94%).  $R_f$  = 0.36 (5% methanol in chloroform); melting point = 238–240 °C; IR (KBr, cm<sup>-1</sup>): 3082, 1686, 1598, 1506, 1447, 1364, 1214, 1103, 1049, 894, 820, 748, 691; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  11.84 (s, 1H, N-3''H), 8.54 (s, 1H, C-5H), 8.43 (s, 1H, C-6''H), 7.63–7.58 (m, 1H, ArH), 7.23–7.18 (m, 2H, ArH), 7.14–7.10 (m, 2H, ArH), 6.88–6.83 (m, 1H, ArH), 6.83–6.79 (m, 1H, ArH), 6.07–6.04 (m, 1H, C-1'H), 5.93 (s, 2H, CH<sub>2</sub>), 5.64 (s, 1H, ArH), 5.53 (s, 2H, CH<sub>2</sub>), 5.48–5.43 (m, 1H, C-2'H), 5.37–5.33 (m, 1H, C-3'H), 4.72 (s, 2H, CH<sub>2</sub>), 4.35–4.31 (m, 1H, C-4'H), 4.28–4.24 (m, 2H, C-5'H), 2.09 (s, 3H, OCOCH<sub>3</sub>), 2.06 (s, 3H, OCOCH<sub>3</sub>), 2.02 (s, 3H, OCOCH<sub>3</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz)  $\delta$  170.7 (C=O), 170.0 (C=O), 170.0 (C=O), 161.6 (ArC), 160.0 (ArC), 158.1 (ArC), 151.5 (ArC), 151.3 (ArC), 150.1 (ArC), 147.9 (ArC), 139.5 (C-4), 137.0 (C-6''), 129.8 (ArC), 124.2 (C-5, ArC), 121.8 (ArC), 118.4 (ArC), 113.9 (ArC), 110.7 (ArC), 110.5 (ArC), 109.3 (ArC), 106.2 (ArC), 88.2 (C-1'), 80.2 (CH<sub>2</sub>), 80.0 (C-4'), 72.9 (C-2'), 70.5 (C-3'), 63.6 (C-5'), 49.7 (CH<sub>2</sub>), 45.0 (CH<sub>2</sub>), 21.1 (OCOCH<sub>3</sub>), 20.9 (OCOCH<sub>3</sub>), 20.8 (OCOCH<sub>3</sub>); HRMS (ESI):  $m/z$  calculated for C<sub>35</sub>H<sub>33</sub>N<sub>6</sub>O<sub>12</sub><sup>+</sup> [M + H]<sup>+</sup>: 729.2151, found: 729.2129.

**4.2.5 N<sup>1</sup>-(9''-(4'''-Bromo)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(2',3',5'-tri-O-acetyl-β-D-ribofuranos-1'-(2',4'-dioxo-3',4'-dihydropyrimidin))-1,2,3-triazole (12e).** It was obtained as a yellowish white solid. Yield: 0.77 g (95%).  $R_f$  = 0.35 (5% methanol in chloroform); melting point = 275 °C; IR (KBr, cm<sup>-1</sup>): 3156,

2993, 2829, 1692, 1603, 1479, 1454, 1366, 1215, 1103, 1058, 1006, 887, 812, 581; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  11.86 (s, 1H, N-3''H), 8.59–8.58 (m, 1H, C-5H), 8.49–8.46 (m, 1H, C-6''H), 7.69–7.64 (m, 1H, ArH), 7.42–7.37 (m, 2H, ArH), 7.17–7.13 (m, 2H, ArH), 6.89–6.84 (m, 1H, ArH), 6.12–6.08 (m, 1H, C-1'H), 5.98 (s, 2H, CH<sub>2</sub>), 5.73–5.70 (m, 1H, ArH), 5.56 (s, 2H, CH<sub>2</sub>), 5.53–5.49 (m, 1H, C-2'H), 5.42–5.38 (m, 1H, C-3'H), 4.76 (s, 2H, CH<sub>2</sub>), 4.39–4.36 (m, 1H, C-4'H), 4.33–4.29 (m, 2H, C-5'H), 2.15–2.14 (m, 3H, OCOCH<sub>3</sub>), 2.12–2.10 (m, 3H, OCOCH<sub>3</sub>), 2.08–2.06 (m, 3H, OCOCH<sub>3</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz)  $\delta$  170.7 (C=O), 170.0 (C=O), 169.9 (C=O), 161.6 (ArC), 160.0 (ArC), 157.9 (ArC), 151.5 (ArC), 151.2 (ArC), 150.1 (ArC), 147.3 (ArC), 139.5 (C-4), 137.0 (C-6''), 132.4 (ArC), 129.3 (C-5), 124.2 (ArC), 120.5 (ArC), 113.9 (ArC), 113.4 (ArC), 110.8 (ArC), 109.2 (ArC), 106.2 (ArC), 88.2 (C-1'), 80.0 (CH<sub>2</sub>), 79.8 (C-4'), 72.9 (C-2'), 70.5 (C-3'), 63.6 (C-5'), 49.7 (CH<sub>2</sub>), 45.1 (CH<sub>2</sub>), 21.1 (OCOCH<sub>3</sub>), 20.9 (OCOCH<sub>3</sub>), 20.8 (OCOCH<sub>3</sub>); HRMS (ESI):  $m/z$  calculated for C<sub>35</sub>H<sub>32</sub>BrN<sub>6</sub>O<sub>12</sub><sup>+</sup> [M + H]<sup>+</sup>: 807.1256, found: 807.1265.

**4.2.6 N<sup>1</sup>-(9''-(4'''-Methyl)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(2',3',5'-tri-O-acetyl-β-D-ribofuranos-1'-(2',4'-dioxo-3',4'-dihydropyrimidin))-1,2,3-triazole (12f).** It was obtained as a yellow solid. Yield: 0.69 g (93%).  $R_f$  = 0.38 (5% methanol in chloroform); melting point = 198 °C; IR (KBr, cm<sup>-1</sup>): 3302, 2921, 1693, 1602, 1506, 1435, 1371, 1223, 1092, 1039, 878, 814, 760, 711; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  11.87 (brs, 1H, N-3''H), 8.58 (s, 1H, C-5H), 8.47 (s, 1H, C-6''H), 7.66–7.63 (m, 1H, ArH), 7.05–7.04 (m, 4H, ArH), 6.85–6.82 (m, 1H, ArH), 6.11–6.08 (m, 1H, C-1'H), 5.97 (s, 2H, CH<sub>2</sub>), 5.69–5.68 (m, 1H, ArH), 5.53–5.51 (m, 2H, CH<sub>2</sub>), 5.51–5.49 (m, 1H, C-2'H), 5.41–5.38 (m, 1H, C-3'H), 4.71 (s, 2H, CH<sub>2</sub>), 4.39–4.36 (m, 1H, C-4'H), 4.33–4.29 (m, 2H, C-5'H), 2.18 (s, 3H, OCOCH<sub>3</sub>), 2.14 (s, 3H, OCOCH<sub>3</sub>), 2.11 (s, 3H, CH<sub>3</sub>), 2.06 (m, 3H, OCOCH<sub>3</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz)  $\delta$  170.7 (C=O), 170.0 (C=O), 169.9 (C=O), 161.6 (ArC), 160.0 (ArC), 158.1 (ArC), 151.5 (ArC), 151.2 (ArC), 150.1 (ArC), 145.6 (ArC), 139.5 (C-4), 137.0 (C-6''), 130.8 (C-5), 130.2 (ArC), 124.2 (ArC), 118.6 (ArC), 113.8 (ArC), 113.4 (ArC), 110.6 (ArC), 109.3 (ArC), 106.2 (ArC), 88.2 (C-1'), 80.6 (CH<sub>2</sub>), 80.0 (C-4'), 72.9 (C-2'), 70.5 (C-3'), 63.6 (C-5'), 49.7 (CH<sub>2</sub>), 45.2 (CH<sub>2</sub>), 21.1 (OCOCH<sub>3</sub>), 20.9 (OCOCH<sub>3</sub>), 20.8 (OCOCH<sub>3</sub>), 20.6 (CH<sub>3</sub>); HRMS (ESI):  $m/z$  calculated for C<sub>36</sub>H<sub>35</sub>N<sub>6</sub>O<sub>12</sub><sup>+</sup> [M + H]<sup>+</sup>: 743.2307, found: 743.2295.

**4.2.7 N<sup>1</sup>-(9''-(4'''-Methoxy)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(3',5'-di-O-acetyl-β-D-ribofuranos-1'-(2',4'-dioxo-3',4'-dihydropyrimidin))-1,2,3-triazole (13a).** It was obtained as a yellow solid. Yield: 0.65 g (93%).  $R_f$  = 0.30 (5% methanol in chloroform); melting point = 226 °C; IR (KBr, cm<sup>-1</sup>): 3414, 2927, 1683, 1586, 1511, 1414, 1226, 1097, 1034, 825, 760, 647; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  11.82 (brs, 1H, N-3''H), 8.61–8.56 (m, 1H, C-5H), 8.46–8.43 (m, 1H, C-6''H), 7.66–7.52 (m, 2H, ArH), 7.11–7.06 (m, 2H, ArH), 6.85–6.80 (m, 2H, ArH), 6.29–6.25 (m, 1H, C-1'H), 5.97 (s, 2H, CH<sub>2</sub>), 5.68–5.63 (m, 1H, ArH), 5.49–5.47 (m, 1H, C-3'H), 5.27–5.24 (m, 1H, C-4'H), 4.67 (s, 2H, CH<sub>2</sub>), 4.33–4.24 (m, 4H, CH<sub>2</sub>, ArH), 3.66 (s, 3H, CH<sub>3</sub>), 2.51–2.44 (m,



1H, C-2'H), 2.44–2.40 (m, 1H, C-2'H), 2.14 (s, 3H, OCOCH<sub>3</sub>), 2.09 (s, 3H, OCOCH<sub>3</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz) δ 170.9 (C=O), 170.6 (C=O), 161.6 (ArC), 160.0 (ArC), 158.1 (ArC), 154.9 (ArC), 151.5 (ArC), 151.3 (ArC), 150.1 (ArC), 141.6 (ArC), 139.7 (C-4), 136.1 (C-6''), 124.2 (C-5), 124.0 (ArC), 120.4 (ArC), 115.4 (ArC), 115.0 (ArC), 113.8 (ArC), 110.6 (ArC), 109.2 (ArC), 105.9 (ArC), 85.5 (C-1'), 82.2 (C-4'), 81.8 (CH<sub>2</sub>), 74.7 (C-3'), 64.3 (C-5'), 55.7 (OCH<sub>3</sub>), 49.7 (CH<sub>2</sub>), 45.6 (CH<sub>2</sub>), 37.3 (C-2'), 21.3 (OCOCH<sub>3</sub>), 21.1 (OCOCH<sub>3</sub>); HRMS (ESI): *m/z* calculated for C<sub>34</sub>H<sub>33</sub>N<sub>6</sub>O<sub>11</sub><sup>+</sup> [M + H]<sup>+</sup>: 701.2202, found: 701.2187.

**4.2.8 N<sup>1</sup>-(9'''-(4'''-Chloro)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(3',5'-di-O-acetyl-β-D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (13b).** It was obtained as a yellowish white solid. Yield: 0.65 g (92%). *R*<sub>f</sub> = 0.33 (5% methanol in chloroform); melting point = 210 °C; IR (KBr, cm<sup>-1</sup>): 3350, 2933, 1611, 1571, 1441, 1360, 1232, 1108, 1049, 873, 754, 717; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ 11.80 (brs, 1H, N-3''H), 8.61–8.55 (m, 1H, C-5H), 8.48–8.42 (m, 1H, C-6''H), 7.68–7.62 (m, 1H, ArH), 7.42–7.36 (m, 2H, ArH), 7.17–7.11 (m, 2H, ArH), 6.89–6.83 (m, 1H, ArH), 6.31–6.23 (m, 1H, C-1'H), 6.00–5.95 (s, 2H, CH<sub>2</sub>), 5.71–5.66 (m, 1H, ArH), 5.55 (m, 2H, CH<sub>2</sub>), 5.27–5.22 (m, 1H, C-3'H), 4.75 (s, 2H, CH<sub>2</sub>), 4.32–4.28 (m, 1H, C-4'H), 4.28–4.23 (m, 2H, C-5'H), 2.46–2.37 (m, 2H, C-2'H), 2.13 (s, 3H, OCOCH<sub>3</sub>), 2.08 (s, 3H, OCOCH<sub>3</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz) δ 170.9 (C=O), 170.6 (C=O), 161.6 (ArC), 160.0 (ArC), 157.9 (ArC), 151.5 (ArC), 151.3 (ArC), 150.1 (ArC), 147.2 (ArC), 139.7 (C-4), 136.1 (C-6''), 132.4 (ArC), 124.3 (C-5), 124.0 (ArC), 120.5 (ArC), 113.9 (ArC), 113.4 (ArC), 110.6 (ArC), 109.2 (ArC), 105.9 (ArC), 85.5 (C-1'), 82.2 (C-4'), 79.8 (CH<sub>2</sub>), 74.7 (C-3'), 64.3 (C-5'), 49.7 (CH<sub>2</sub>), 45.0 (CH<sub>2</sub>), 37.3 (C-2'), 21.3 (OCOCH<sub>3</sub>), 21.1 (OCOCH<sub>3</sub>); HRMS (ESI): *m/z* calculated for C<sub>33</sub>H<sub>30</sub>ClN<sub>6</sub>O<sub>10</sub><sup>+</sup> [M + H]<sup>+</sup>: 705.1706, found: 705.1728.

**4.2.9 N<sup>1</sup>-(9'''-(4'''-Fluoro)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(3',5'-di-O-acetyl-β-D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (13c).** It was obtained as a yellowish brown solid. Yield: 0.63 g (92%). *R*<sub>f</sub> = 0.32 (5% methanol in chloroform); melting point = 194–196 °C; IR (KBr, cm<sup>-1</sup>): 3288, 1687, 1597, 1512, 1453, 1382, 1228, 1096, 1039, 817, 608, 552; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ 11.82 (brs, 1H, N-3''H), 8.57–8.56 (m, 1H, C-5H), 8.44–8.43 (m, 1H, C-6''H), 7.67–7.64 (m, 1H, ArH), 7.21–7.16 (m, 2H, ArH), 7.10–7.05 (m, 2H, ArH), 6.87–6.84 (m, 1H, ArH), 6.28–6.25 (m, 1H, C-1'H), 5.97 (s, 2H, CH<sub>2</sub>), 5.69–5.67 (m, 1H, ArH), 5.53 (m, 2H, CH<sub>2</sub>), 5.26–5.24 (m, 1H, C-3'H), 4.73 (s, 2H, CH<sub>2</sub>), 4.31–4.29 (m, 1H, C-4'H), 4.28–4.25 (m, 2H, C-5'H), 2.46–2.44 (m, 1H, C-2'H), 2.43–2.40 (m, 1H, C-2'H), 2.14 (s, 3H, OCOCH<sub>3</sub>), 2.09 (s, 3H, OCOCH<sub>3</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz) δ 170.9 (C=O), 170.6 (C=O), 161.6 (ArC), 160.0 (ArC), 158.0 (ArC), 151.5 (ArC), 151.3 (ArC), 150.1 (ArC), 144.6 (ArC), 139.7 (C-4), 136.1 (C-6''), 124.3 (C-5), 124.0 (ArC), 120.5 (ArC), 120.4 (ArC), 116.3 (ArC), 116.1 (ArC), 113.9 (ArC), 110.7 (ArC), 110.5 (ArC), 109.1 (ArC), 105.9 (ArC), 85.5 (C-1'), 82.2 (C-4'), 80.7 (CH<sub>2</sub>), 74.7 (C-3'), 64.3 (C-5'), 49.7 (CH<sub>2</sub>), 45.5 (CH<sub>2</sub>), 37.3 (C-2'), 21.3 (OCOCH<sub>3</sub>), 21.1 (OCOCH<sub>3</sub>); HRMS (ESI): *m/z* calculated for C<sub>33</sub>H<sub>30</sub>FN<sub>6</sub>O<sub>10</sub><sup>+</sup> [M + H]<sup>+</sup>: 689.2002, found: 689.2041.

**4.2.10 N<sup>1</sup>-(9'''-(10'''-Dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(3',5'-di-O-acetyl-β-D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (13d).** It was obtained as a yellow solid. Yield: 0.63 g (94%). *R*<sub>f</sub> = 0.34 (5% methanol in chloroform); melting point = 246 °C; IR (KBr, cm<sup>-1</sup>): 2889, 2106, 1720, 1585, 1495, 1359, 1302, 1251, 1162, 1097, 914, 797, 713; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ 11.81 (brs, 1H, N-3''H), 8.57–8.55 (m, 1H, C-5H), 8.44–8.43 (m, 1H, C-6''H), 7.66–7.62 (m, 1H, ArH), 7.27–7.22 (m, 2H, ArH), 7.17–7.14 (m, 2H, ArH), 6.92–6.89 (m, 1H, ArH), 6.86–6.82 (m, 1H, ArH), 6.28–6.24 (m, 1H, C-1'H), 5.96 (s, 2H, CH<sub>2</sub>), 5.67–5.64 (m, 1H, ArH), 5.57 (m, 2H, CH<sub>2</sub>), 5.26–5.23 (m, 1H, C-3'H), 4.76 (s, 2H, CH<sub>2</sub>), 4.30–4.29 (m, 1H, C-4'H), 4.27–4.25 (m, 2H, C-5'H), 2.46–2.43 (m, 1H, C-2'H), 2.43–2.41 (m, 1H, C-2'H), 2.13 (s, 3H, OCOCH<sub>3</sub>), 2.08 (s, 3H, OCOCH<sub>3</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz) δ 170.9 (C=O), 170.6 (C=O), 161.6 (ArC), 160.0 (ArC), 158.0 (ArC), 151.5 (ArC), 151.3 (ArC), 150.1 (ArC), 144.6 (ArC), 139.7 (C-4), 136.1 (C-6''), 124.3 (C-5), 124.0 (ArC), 120.5 (ArC), 120.4 (ArC), 116.3 (ArC), 116.1 (ArC), 113.9 (ArC), 110.7 (ArC), 110.5 (ArC), 109.1 (ArC), 105.9 (ArC), 85.5 (C-1'), 82.2 (C-4'), 80.7 (CH<sub>2</sub>), 74.7 (C-3'), 64.3 (C-5'), 49.7 (CH<sub>2</sub>), 45.5 (CH<sub>2</sub>), 37.3 (C-2'), 21.3 (OCOCH<sub>3</sub>), 21.1 (OCOCH<sub>3</sub>); HRMS (ESI): *m/z* calculated for C<sub>33</sub>H<sub>31</sub>N<sub>6</sub>O<sub>10</sub><sup>+</sup> [M + H]<sup>+</sup>: 671.2096, found: 671.2111.

**4.2.11 N<sup>1</sup>-(9'''-(4'''-Bromo)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(3',5'-di-O-acetyl-β-D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (13e).** It was obtained as a yellowish brown solid. Yield: 0.69 g (93%). *R*<sub>f</sub> = 0.33 (5% methanol in chloroform); melting point = 249 °C; IR (KBr, cm<sup>-1</sup>): 3054, 2811, 1707, 1687, 1599, 1492, 1228, 1052, 817, 602, 554; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ 11.76 (brs, 1H, N-3''H), 8.57–8.50 (m, 1H, C-5H), 8.45–8.38 (m, 1H, C-6''H), 7.64–7.59 (m, 1H, ArH), 7.38–7.32 (m, 2H, ArH), 7.13–7.07 (m, 2H, ArH), 6.85–6.79 (m, 1H, ArH), 6.28–6.19 (m, 1H, C-1'H), 5.98–5.90 (m, 2H, CH<sub>2</sub>), 5.69–5.63 (m, 1H, ArH), 5.52 (m, 2H, CH<sub>2</sub>), 5.24–5.18 (m, 1H, C-3'H), 4.71 (s, 2H, CH<sub>2</sub>), 4.28–4.24 (m, 1H, C-4'H), 4.23–4.19 (m, 2H, C-5'H), 2.43–2.40 (m, 1H, C-2'H), 2.39–2.36 (m, 1H, C-2'H), 2.10 (s, 3H, OCOCH<sub>3</sub>), 2.04 (s, 3H, OCOCH<sub>3</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz) δ 170.9 (C=O), 170.6 (C=O), 161.6 (ArC), 160.0 (ArC), 157.9 (ArC), 151.5 (ArC), 151.3 (ArC), 150.1 (ArC), 147.2 (ArC), 139.7 (C-4), 136.1 (C-6''), 132.4 (ArC), 124.3 (C-5), 124.0 (ArC), 120.5 (ArC), 113.9 (ArC), 110.8 (ArC), 110.6 (ArC), 109.2 (ArC), 105.9 (ArC), 85.5 (C-1'), 82.2 (C-4'), 79.8 (CH<sub>2</sub>), 74.7 (C-3'), 64.3 (C-5'), 49.7 (CH<sub>2</sub>), 45.0 (CH<sub>2</sub>), 37.3 (C-2'), 21.3 (OCOCH<sub>3</sub>), 21.1 (OCOCH<sub>3</sub>); HRMS (ESI): *m/z* calculated for C<sub>33</sub>H<sub>30</sub>BrN<sub>6</sub>O<sub>10</sub><sup>+</sup> [M + H]<sup>+</sup>: 749.1201, found: 749.1179.

**4.2.12 N<sup>1</sup>-(9'''-(4'''-Methyl)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(3',5'-di-O-acetyl-β-D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (13f).** It was obtained as a yellow solid. Yield: 0.63 g (92%). *R*<sub>f</sub> = 0.35 (5% methanol in chloroform); melting point = 217 °C; IR (KBr, cm<sup>-1</sup>): 1689, 1597, 1509, 1444, 1361, 1226, 1103, 1045, 814; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz) δ 11.81 (brs, 1H, N-3''H), 8.59–8.55 (m, 1H, C-5H), 8.46–8.42 (m, 1H, C-6''H), 7.66–7.62 (m, 1H, ArH), 7.07–7.02 (m, 4H, ArH),



6.85–6.82 (m, 1H, ArH), 6.29–6.24 (m, 1H, C-1'H), 5.97 (m, 2H, CH<sub>2</sub>), 5.67–5.61 (m, 1H, ArH), 5.53 (s, 2H, CH<sub>2</sub>), 5.27–5.23 (m, 1H, C-3'H), 4.71 (s, 2H, CH<sub>2</sub>), 4.33–4.29 (m, 1H, C-4'H), 4.27–4.25 (m, 2H, C-5'H), 2.48–2.39 (m, 2H, C-2'H), 2.18 (s, 3H, CH<sub>3</sub>), 2.15 (s, 3H, OCOCH<sub>3</sub>), 2.09 (s, 3H, OCOCH<sub>3</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz)  $\delta$  170.9 (C=O), 170.6 (C=O), 161.6 (ArC), 160.0 (ArC), 158.1 (ArC), 151.5 (ArC), 151.3 (ArC), 150.1 (ArC), 145.6 (ArC), 139.7 (C-4), 136.1 (C-6'), 130.2 (ArC), 124.2 (C-5), 124.0 (ArC), 118.6 (ArC), 113.8 (ArC), 113.0 (ArC), 110.6 (ArC), 110.4 (ArC), 109.3 (ArC), 105.9 (ArC), 85.5 (C-1'), 82.2 (C-4'), 80.5 (CH<sub>2</sub>), 74.7 (C-3'), 64.3 (C-5'), 49.7 (CH<sub>2</sub>), 45.2 (CH<sub>2</sub>), 37.3 (C-2'), 21.3 (OCOCH<sub>3</sub>), 21.1 (OCOCH<sub>3</sub>), 20.6 (CH<sub>3</sub>); HRMS (ESI): *m/z* calculated for C<sub>34</sub>H<sub>33</sub>N<sub>6</sub>O<sub>10</sub><sup>+</sup> [M + H]<sup>+</sup>: 685.2253, found: 685.2280.

#### 4.3. General procedure for the synthesis of *N*<sup>1</sup>-(9'''-(4'''-substituted)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-( $\beta$ -D-ribofuranos-2'-deoxy- $\beta$ -D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole conjugates (14a–f and 15a–f)

To a solution of *N*<sup>1</sup>-(9'''-(4'''-substituted)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(2',3',5'-tri-*O*-acetyl/3',5'-di-*O*-acetyl- $\beta$ -D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole conjugates (12a–f/13a–f, 1.0 mmol) in methanol, NaOMe (2.2 mmol) was added. The reaction mixture was allowed to stir at 25 °C for 10–15 minutes. After the completion of the reaction (as monitored by TLC), the reaction was neutralized with serralite (H<sup>+</sup>) resin. The solution was filtered through a cotton plug and the solvent was evaporated under vacuum. The crude product thus obtained was purified by silica gel column chromatography using methanol in chloroform as the solvent system to afford the desired products 14a–f and 15a–f in quantitative yields.

**4.3.1 *N*<sup>1</sup>-(9'''-(4'''-Methoxy)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-( $\beta$ -D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (14a).** It was obtained as a yellow solid. Yield: 0.61 g (97%). *R*<sub>f</sub> = 0.24 (10% methanol in chloroform); melting point = 258 °C; IR (KBr, cm<sup>-1</sup>): 3393, 1683, 1586, 1500, 1495, 1452, 1377, 1232, 1039, 818; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  11.75 (brs, 1H, N-3''H), 9.25–9.21 (m, 1H, C-6''H), 8.69–8.66 (m, 1H, C-5''H), 8.60–8.55 (m, 1H, ArH), 7.94–7.87 (m, 1H, ArH), 7.57–7.52 (m, 2H, ArH), 7.08–7.03 (m, 2H, ArH), 6.99–6.95 (m, 1H, ArH), 6.04–6.00 (m, 1H, C-1'H), 5.93–5.88 (m, 2H, CH<sub>2</sub>), 5.70 (brs, 1H, OH), 5.44 (brs, 1H, OH), 5.19–5.14 (m, 2H, CH<sub>2</sub>), 4.18–4.14 (m, 1H, C-2'H), 4.04–4.00 (m, 1H, C-3'H), 3.93–3.89 (m, 1H, C-4'H), 3.81 (s, 3H, CH<sub>3</sub>), 3.66–3.61 (m, 2H, C-5'H), 3.51 (m, 2H, CH<sub>2</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz)  $\delta$  166.9 (ArC), 161.6 (ArC), 159.6 (ArC), 159.5 (ArC), 154.7 (ArC), 151.6 (ArC), 150.5 (ArC), 139.7 (C-4), 137.1 (C-6''), 129.9 (ArC), 124.3 (C-5), 124.0 (ArC), 123.2 (ArC), 115.3 (ArC), 109.6 (ArC), 108.6 (ArC), 106.8 (ArC), 105.6 (ArC), 88.4 (C-1'), 85.6 (C-4'), 74.3 (CH<sub>2</sub>), 70.7 (C-3'), 70.2 (C-2'), 61.5 (C-5'), 55.9 (CH<sub>3</sub>), 49.7 (CH<sub>2</sub>), 45.1 (CH<sub>2</sub>); HRMS (ESI): *m/z* calculated for C<sub>30</sub>H<sub>29</sub>N<sub>6</sub>O<sub>10</sub><sup>+</sup> [M + H]<sup>+</sup>: 633.1940, found: 633.1944.

**4.3.2 *N*<sup>1</sup>-(9'''-(4'''-Chloro)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-( $\beta$ -D-ribo-**

**furanos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (14b).** It was obtained as a yellow solid. Yield: 0.62 g (98%). *R*<sub>f</sub> = 0.26 (10% methanol in chloroform); melting point = 262–264 °C; IR (KBr, cm<sup>-1</sup>): 3307, 3153, 2928, 1686, 1591, 1495, 1459, 1400, 1317, 1257, 1044, 818; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  11.75 (brs, 1H, N-3''H), 8.69–8.67 (m, 1H, C-6''H), 8.58–8.55 (m, 1H, C-5''H), 7.73–7.66 (m, 1H, ArH), 7.30–7.26 (m, 1H, ArH), 7.21–7.18 (m, 1H, ArH), 7.10–7.05 (m, 1H, ArH), 6.96–6.85 (m, 1H, ArH), 6.75–6.65 (m, 1H, ArH), 5.98–5.94 (m, 2H, CH<sub>2</sub>), 5.93–5.90 (m, 1H, C-1'H), 5.74–5.69 (m, 1H, ArH), 5.62–5.48 (m, 2H, CH<sub>2</sub>), 5.48–5.40 (brs, 1H, OH), 5.15 (brs, 2H, OH), 4.84–4.68 (m, 2H, CH<sub>2</sub>), 4.18–4.14 (m, 1H, C-2'H), 4.03–4.01 (m, 1H, C-3'H), 3.93–3.91 (m, 1H, C-4'H), 3.66–3.59 (m, 2H, C-5'H); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz)  $\delta$  161.6 (ArC), 159.9 (ArC), 157.8 (ArC), 154.1 (ArC), 151.5 (ArC), 150.5 (ArC), 148.2 (ArC), 146.8 (ArC), 139.7 (C-4), 137.1 (C-6''), 129.5 (ArC), 128.9 (ArC), 125.5 (ArC), 124.0 (C-5), 120.0 (ArC), 113.8 (ArC), 112.9 (ArC), 110.8 (ArC), 109.1 (ArC), 105.6 (ArC), 88.4 (C-1'), 85.6 (C-4'), 79.9 (CH<sub>2</sub>), 74.3 (C-2'), 70.7 (C-3'), 61.5 (C-5'), 49.6 (CH<sub>2</sub>), 45.1 (CH<sub>2</sub>); HRMS (ESI): *m/z* calculated for C<sub>29</sub>H<sub>26</sub>ClN<sub>6</sub>O<sub>9</sub><sup>+</sup> [M + H]<sup>+</sup>: 637.1444, found: 637.1425.

**4.3.3 *N*<sup>1</sup>-(9'''-(4'''-Fluoro)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-( $\beta$ -D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (14c).** It was obtained as a yellow solid. Yield: 0.60 g (97%). *R*<sub>f</sub> = 0.26 (10% methanol in chloroform); melting point = 241–243 °C; IR (KBr, cm<sup>-1</sup>): 3314, 2718, 1684, 1596, 1512, 1455, 1396, 1338, 1269, 1211, 1103, 1054, 830, 644, 517; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  11.74 (brs, 1H, N-3''H), 8.69–8.66 (m, 1H, C-6''H), 8.58–8.55 (m, 1H, C-5''H), 7.72–7.67 (m, 1H, ArH), 7.22–7.05 (m, 2H, ArH), 7.02–6.98 (m, 1H, ArH), 6.94–6.88 (m, 2H, ArH), 6.71–6.66 (m, 1H, ArH), 5.99–5.94 (m, 2H, CH<sub>2</sub>), 5.93–5.89 (m, 1H, C-1'H), 5.73–5.66 (m, 1H, CH<sub>2</sub>), 5.54–5.46 (m, 1H, CH<sub>2</sub>), 5.16 (brs, 2H, OH), 4.25 (brs, 1H, OH), 4.18–4.14 (m, 1H, C-2'H), 4.04–4.01 (m, 1H, C-3'H), 3.93–3.90 (m, 1H, C-4'H), 3.67–3.58 (m, 4H, C-5'H, CH<sub>2</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz)  $\delta$  161.6 (ArC), 160.7 (ArC), 160.4 (ArC), 154.0 (ArC), 153.7 (ArC), 151.4 (ArC), 150.5 (ArC), 146.0 (ArC), 139.7 (C-4), 137.1 (C-6''), 125.1 (ArC), 124.0 (C-5), 120.4 (ArC), 120.4 (ArC), 116.3 (ArC), 116.0 (ArC), 115.7 (ArC), 115.5 (ArC), 113.4 (ArC), 113.3 (ArC), 113.1 (ArC), 113.0 (ArC), 109.8 (ArC), 109.6 (ArC), 105.6 (ArC), 88.5 (C-1'), 85.6 (C-4'), 74.3 (CH<sub>2</sub>), 70.7 (C-3', C-2'), 61.5 (C-5'), 49.7 (CH<sub>2</sub>), 36.4 (CH<sub>2</sub>); HRMS (ESI): *m/z* calculated for C<sub>29</sub>H<sub>26</sub>FN<sub>6</sub>O<sub>9</sub><sup>+</sup> [M + H]<sup>+</sup>: 621.1740, found: 621.1716.

**4.3.4 *N*<sup>1</sup>-(9'''-(4'''-Chloro)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-( $\beta$ -D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (14d).** It was obtained as a yellow solid. Yield: 0.58 g (96%). *R*<sub>f</sub> = 0.27 (10% methanol in chloroform); melting point = 216–220 °C; IR (KBr, cm<sup>-1</sup>): 1686, 1591, 1511, 1451, 1359, 1226, 1104, 1045, 807; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  11.74 (brs, 1H, N-3''H), 8.69–8.65 (m, 1H, C-6''H), 8.57–8.53 (m, 1H, C-5''H), 7.70–7.64 (m, 1H, ArH), 7.29–7.19 (m, 2H, ArH), 7.18–7.14 (m, 1H, ArH), 7.09–7.00 (m, 1H, ArH), 6.96–6.84 (m, 2H, ArH), 6.70–6.50 (m, 1H, ArH), 5.96 (m, 2H, CH<sub>2</sub>), 5.92–5.88 (m, 1H, C-1'H), 5.72–5.66 (m, 1H, CH<sub>2</sub>), 5.59–5.56 (m, 1H, CH<sub>2</sub>), 5.14 (brs, 1H, OH), 4.76 (brs,

1H, OH), 4.28 (brs, 1H, OH), 4.17–4.13 (m, 1H, C-2'H), 4.03–3.99 (m, 1H, C-3'H), 3.93–3.89 (m, 1H, C-4'H), 3.69–3.54 (m, 4H, C-5'H, CH<sub>2</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz)  $\delta$  161.6 (ArC), 160.0 (ArC), 158.0 (ArC), 151.5 (ArC), 151.2 (ArC), 150.5 (ArC), 149.3 (ArC), 147.9 (ArC), 139.7 (C-4), 137.1 (C-6''), 129.7 (ArC), 129.3 (ArC), 124.0 (C-5), 121.8 (ArC), 118.4 (ArC), 113.8 (ArC), 112.6 (ArC), 110.7 (ArC), 109.3 (ArC), 105.6 (ArC), 88.4 (C-1'), 85.6 (C-4'), 80.1 (CH<sub>2</sub>), 74.3 (C-3'), 70.7 (C-2'), 61.5 (C-5'), 49.6 (CH<sub>2</sub>), 45.0 (CH<sub>2</sub>); HRMS (ESI): *m/z* calculated for C<sub>29</sub>H<sub>27</sub>N<sub>6</sub>O<sub>9</sub><sup>+</sup> [M + H]<sup>+</sup>: 603.1834, found: 603.1859.

**4.3.5 N<sup>1</sup>-(9'''-(4''''-Bromo)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-( $\beta$ -D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (14e).** It was obtained as a yellow solid. Yield: 0.67 g (98%). *R*<sub>f</sub> = 0.28 (10% methanol in chloroform); melting point = 254 °C; IR (KBr, cm<sup>-1</sup>): 3324, 2741, 1644, 1531, 1415, 1367, 1332, 1258, 1123, 1035, 826, 643, 509; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  11.74 (brs, 1H, N-3''H), 8.67–8.66 (m, 1H, C-6''H), 8.56–8.54 (m, 1H, C-5H), 7.70–7.66 (m, 1H, ArH), 7.40–7.38 (m, 1H, ArH), 7.19–7.17 (m, 1H, ArH), 7.15–7.13 (m, 1H, ArH), 6.93–6.85 (m, 1H, ArH), 6.66–6.64 (m, 1H, ArH), 5.96–5.89 (m, 4H, CH<sub>2</sub>, C-1'H, ArH), 5.72–5.66 (m, 1H, CH<sub>2</sub>), 5.56–5.45 (m, 1H, CH<sub>2</sub>), 5.13 (brs, 1H, OH), 4.75 (brs, 1H, OH), 4.24 (brs, 1H, OH), 4.16–4.13 (m, 1H, C-2'H), 4.01–3.99 (m, 1H, C-3'H), 3.91–3.89 (m, 1H, C-4'H), 3.66–3.56 (m, 4H, C-5'H, CH<sub>2</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz)  $\delta$  161.6 (ArC), 160.4 (ArC), 154.1 (ArC), 150.5 (ArC), 148.6 (ArC), 147.2 (ArC), 139.7 (C-4), 137.1 (C-6''), 132.4 (ArC), 131.7 (ArC), 124.0 (C-5), 114.5 (ArC), 110.8 (ArC), 109.1 (ArC), 106.7 (ArC), 105.6 (ArC), 88.4 (C-1'), 85.6 (C-4'), 74.3 (CH<sub>2</sub>), 70.7 (C-2', C-3'), 61.5 (C-5'), 60.2 (CH<sub>2</sub>), 49.6 (CH<sub>2</sub>); HRMS (ESI): *m/z* calculated for C<sub>29</sub>H<sub>26</sub>BrN<sub>6</sub>O<sub>9</sub><sup>+</sup> [M + H]<sup>+</sup>: 681.0939, found: 681.1012.

**4.3.6 N<sup>1</sup>-(9'''-(4''''-Methyl)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-( $\beta$ -D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (14f).** It was obtained as a yellow solid. Yield: 0.60 g (98%). *R*<sub>f</sub> = 0.29 (10% methanol in chloroform); melting point = 235–237 °C; IR (KBr, cm<sup>-1</sup>): 3309, 2722, 1676, 1545, 1501, 1452, 1337, 1242, 1112, 1067, 805, 663, 503; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  11.71 (brs, 1H, N-3''H), 8.67–8.64 (m, 1H, C-6''H), 8.56–8.53 (m, 1H, C-5H), 7.68–7.63 (m, 1H, ArH), 7.40–7.33 (m, 1H, ArH), 7.04 (brs, 2H, ArH), 6.94–6.82 (m, 2H, ArH), 5.97–5.93 (m, 2H, CH<sub>2</sub>), 5.91–5.88 (m, 1H, C-1'H), 5.73–5.70 (m, 1H, ArH), 5.56–5.50 (m, 2H, CH<sub>2</sub>), 5.14 (brs, 2H, OH), 4.71 (brs, 1H, OH), 4.18–4.13 (m, 1H, C-2'H), 4.02–3.99 (m, 1H, C-3'H), 3.92–3.89 (m, 1H, C-4'H), 3.68–3.63 (m, 2H, C-5'H), 3.61–3.56 (m, 2H, CH<sub>2</sub>), 2.18 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz)  $\delta$  161.6 (ArC), 160.0 (ArC), 158.0 (ArC), 154.0 (ArC), 151.5 (ArC), 150.5 (ArC), 147.0 (ArC), 145.5 (ArC), 139.7 (C-4), 137.1 (C-6''), 130.1 (ArC), 129.7 (ArC), 124.0 (C-5), 118.6 (ArC), 112.9 (ArC), 109.9 (ArC), 109.6 (ArC), 109.2 (ArC), 105.6 (ArC), 88.4 (C-1'), 85.6 (C-4'), 74.3 (CH<sub>2</sub>), 70.7 (C-2', C-3'), 61.5 (C-5'), 49.7 (CH<sub>2</sub>), 45.1 (CH<sub>2</sub>), 20.5 (CH<sub>3</sub>); HRMS (ESI): *m/z* calculated for C<sub>30</sub>H<sub>29</sub>N<sub>6</sub>O<sub>9</sub><sup>+</sup> [M + H]<sup>+</sup>: 617.1991, found: 617.1997.

**4.3.7 N<sup>1</sup>-(9'''-(4''''-Methyl)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(2'-deoxy-**

**$\beta$ -D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (15a).** It was obtained as a yellow solid. Yield: 0.59 g (96%). *R*<sub>f</sub> = 0.25 (10% methanol in chloroform); melting point = 266 °C; IR (KBr, cm<sup>-1</sup>): 3275, 3071, 1672, 1586, 1489, 1446, 1254, 1174, 1040, 818; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  11.72 (brs, 1H, N-3''H), 8.66–8.60 (m, 1H, C-6''H), 8.60–8.52 (m, 1H, C-5H), 7.66–7.54 (m, 1H, ArH), 7.12–6.62 (m, 5H, ArH), 6.28–6.21 (m, 1H, C-1'H), 6.03–5.89 (m, 2H, CH<sub>2</sub>), 5.75–5.43 (m, 2H, CH<sub>2</sub>), 5.32 (brs, 1H, OH), 5.10–5.02 (m, 1H, ArH), 4.67–4.50 (m, 1H, C-3'H), 4.32–4.25 (m, 1H, C-4'H), 3.90–3.78 (m, 2H, CH<sub>2</sub>), 3.70–3.55 (m, 5H, C-5'H, CH<sub>3</sub>), 2.23–2.16 (m, 2H, C-2'H); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz)  $\delta$  161.6 (ArC), 160.0 (ArC), 159.6 (ArC), 158.0 (ArC), 154.8 (ArC), 151.5 (ArC), 150.1 (ArC), 141.6 (ArC), 139.8 (C-4), 136.8 (C-6''), 123.2 (ArC), 120.3 (ArC), 115.3 (ArC), 114.9 (ArC), 113.8 (ArC), 110.6 (C-5), 109.1 (ArC), 105.4 (ArC), 88.1 (C-4'), 85.2 (C-1'), 55.9 (CH<sub>2</sub>), 71.1 (C-3'), 61.8 (C-5'), 55.6 (CH<sub>3</sub>), 55.6 (CH<sub>2</sub>), 49.6 (CH<sub>2</sub>), 45.6 (C-2'), 40.5 (CH<sub>2</sub>); HRMS (ESI): *m/z* calculated for C<sub>30</sub>H<sub>29</sub>N<sub>6</sub>O<sub>9</sub><sup>+</sup> [M + H]<sup>+</sup>: 617.1991, found: 617.1981.

**4.3.8 N<sup>1</sup>-(9'''-(4''''-Chloro)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(2'-deoxy- $\beta$ -D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (15b).** It was obtained as a yellow solid. Yield: 0.61 g (99%). *R*<sub>f</sub> = 0.26 (10% methanol in chloroform); melting point = 259–260 °C; IR (KBr, cm<sup>-1</sup>): 3186, 3004, 1659, 1581, 1440, 1387, 1257, 1048, 834; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  8.62–8.61 (m, 1H, C-6''H), 8.54–8.53 (m, 1H, C-5H), 7.67–7.61 (m, 1H, ArH), 7.40–7.38 (m, 1H, ArH), 7.17–7.15 (m, 1H, ArH), 7.14–7.12 (m, 1H, ArH), 6.88–6.84 (m, 1H, ArH), 6.67–6.64 (m, 1H, ArH), 6.25–6.22 (m, 1H, C-1'H), 5.96–5.94 (m, 1H, CH<sub>2</sub>), 5.92–5.90 (m, 1H, CH<sub>2</sub>), 5.56–5.53 (m, 2H, CH<sub>2</sub>), 4.75–4.74 (m, 1H, ArH), 4.29–4.22 (m, 3H, C-3'H, CH<sub>2</sub>), 3.86–3.84 (m, 1H, C-4'H), 3.60–3.59 (m, 2H, C-5'H), 2.20–2.17 (m, 2H, C-2'H); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>, 100 MHz)  $\delta$  161.2 (ArC), 160.2 (ArC), 159.5 (ArC), 157.4 (ArC), 151.0 (ArC), 150.7 (ArC), 149.7 (ArC), 146.7 (ArC), 139.4 (C-4), 136.4 (C-6''), 131.9 (ArC), 131.2 (ArC), 123.4 (ArC), 120.0 (ArC), 114.1 (ArC), 112.9 (ArC), 110.3 (ArC), 108.7 (C-5), 106.2 (ArC), 105.0 (ArC), 87.7 (C-4'), 84.8 (C-1'), 79.3 (CH<sub>2</sub>), 70.7 (C-3'), 61.4 (C-5'), 49.1 (CH<sub>2</sub>), 44.5 (C-2'), 35.6 (CH<sub>2</sub>); HRMS (ESI): *m/z* calculated for C<sub>29</sub>H<sub>26</sub>ClN<sub>6</sub>O<sub>8</sub><sup>+</sup> [M + H]<sup>+</sup>: 621.1495, found: 621.1491.

**4.3.9 N<sup>1</sup>-(9'''-(4''''-Fluoro)-9''',10'''-dihydro-2'''H,8'''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(2'-deoxy- $\beta$ -D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (15c).** It was obtained as a yellow solid. Yield: 0.59 g (98%). *R*<sub>f</sub> = 0.26 (10% methanol in chloroform); melting point = 208–210 °C; IR (KBr, cm<sup>-1</sup>): 3363, 3280, 2924, 1678, 1583, 1512, 1453, 1405, 1275, 1215, 1097, 1037, 824; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, 400 MHz)  $\delta$  11.71 (brs, 1H, NH), 8.63–8.62 (m, 1H, C-6''H), 8.56–8.54 (m, 1H, C-5H), 7.70–7.66 (m, 1H, ArH), 7.19–7.16 (m, 1H, ArH), 7.01–6.97 (m, 1H, ArH), 6.93–6.87 (m, 2H, ArH), 6.69–6.67 (m, 1H, ArH), 6.26–6.23 (m, 1H, C-1'H), 5.97–5.94 (m, 2H, CH<sub>2</sub>), 5.72–5.66 (m, 1H, CH<sub>2</sub>), 5.57–5.48 (m, 1H, CH<sub>2</sub>), 5.34 (brs, 1H, OH), 5.07 (brs, 1H, OH), 4.76–4.69 (m, 1H, ArH), 4.30–4.28 (m, 1H, C-3'H), 4.26–4.22 (m, 2H, CH<sub>2</sub>), 3.87–3.85 (m, 1H, C-4'H), 3.62–3.59 (m, 2H, C-5'H), 2.21–2.18 (m, 2H,

C-2'H);  $^{13}\text{C}$  NMR (DMSO- $d_6$ , 100 MHz)  $\delta$  161.7 (ArC), 160.8 (ArC), 160.4 (ArC), 155.9 (ArC), 154.0 (ArC), 151.4 (ArC), 150.1 (ArC), 146.0 (ArC), 139.8 (C-4), 136.8 (C-6''), 125.1 (ArC), 123.9 (ArC), 120.5 (ArC), 120.4 (ArC), 116.3 (ArC), 116.0 (ArC), 115.7 (ArC), 115.5 (ArC), 113.4 (ArC), 113.3 (ArC), 113.1 (ArC), 109.7 (C-5), 109.5 (ArC), 105.4 (ArC), 88.1 (C-4'), 85.2 (C-1'), 80.6 (CH<sub>2</sub>), 71.1 (C-3'), 61.8 (C-5'), 49.7 (CH<sub>2</sub>), 45.5 (C-2'), 36.4 (CH<sub>2</sub>); HRMS (ESI):  $m/z$  calculated for  $\text{C}_{29}\text{H}_{26}\text{FN}_6\text{O}_8^+ [\text{M} + \text{H}]^+$ : 605.1718, found: 605.1787.

**4.3.10  $N^1$ -(9''',10'''-Dihydro-2''H,8''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(2'-deoxy- $\beta$ -D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (15d).** It was obtained as a yellow solid. Yield: 0.57 g (98%).  $R_f$  = 0.27 (10% methanol in chloroform); melting point = 242 °C; IR (KBr,  $\text{cm}^{-1}$ ): 3276, 2946, 1648, 1565, 1417, 1405, 1266, 1043, 811, 524;  $^1\text{H}$  NMR (DMSO- $d_6$ , 400 MHz)  $\delta$  8.64–8.62 (m, 1H, C-6''H), 8.56–8.55 (m, 1H, C-5H), 7.71–7.65 (m, 1H, ArH), 7.27–7.16 (m, 2H, ArH), 7.07–7.00 (m, 2H, ArH), 6.91–6.85 (m, 1H, ArH), 6.72–6.68 (m, 1H, ArH), 6.56–6.48 (m, 1H, C-1'H), 6.26–6.23 (m, 1H, CH<sub>2</sub>), 5.97–5.93 (m, 2H, CH<sub>2</sub>), 5.59–5.56 (m, 1H, CH<sub>2</sub>), 4.80–4.73 (m, 1H, ArH), 4.32–4.23 (m, 3H, C-3'H, CH<sub>2</sub>), 3.88–3.85 (m, 1H, C-4'H), 3.62–3.60 (m, 2H, C-5'H), 2.22–2.18 (m, 2H, C-2'H);  $^{13}\text{C}$  NMR (DMSO- $d_6$ , 100 MHz)  $\delta$  161.7 (ArC), 160.7 (ArC), 160.0 (ArC), 158.0 (ArC), 155.7 (ArC), 154.2 (ArC), 150.1 (ArC), 149.4 (ArC), 139.8 (C-4), 136.8 (C-6''), 129.7 (ArC), 129.2 (ArC), 123.9 (ArC), 118.4 (ArC), 116.1 (ArC), 113.1 (C-5), 113.2 (ArC), 112.7 (ArC), 105.4 (ArC), 88.1 (C-4'), 85.2 (C-1'), 80.1 (CH<sub>2</sub>), 71.1 (C-3'), 61.8 (C-5'), 49.1 (C-2', CH<sub>2</sub>), 36.0 (CH<sub>2</sub>); HRMS (ESI):  $m/z$  calculated for  $\text{C}_{29}\text{H}_{27}\text{N}_6\text{O}_8^+ [\text{M} + \text{H}]^+$ : 587.1885, found: 587.1869.

**4.3.11  $N^1$ -(9''-(4''''-Bromo)-9''',10'''-dihydro-2''H,8''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(2'-deoxy- $\beta$ -D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (15e).** It was obtained as a yellow solid. Yield: 0.64 g (97%).  $R_f$  = 0.27 (10% methanol in chloroform); melting point = 229 °C; IR (KBr,  $\text{cm}^{-1}$ ): 3325, 3224, 2814, 1708, 1683, 1658, 1583, 1557, 1516, 1457, 1306, 1222, 1047, 820, 644, 517;  $^1\text{H}$  NMR (DMSO- $d_6$ , 400 MHz)  $\delta$  8.63–8.62 (m, 1H, C-6''H), 8.56–8.54 (m, 1H, C-5H), 7.69–7.61 (m, 1H, ArH), 7.42–7.38 (m, 1H, ArH), 7.19–7.15 (m, 1H, ArH), 7.15–7.13 (m, 1H, ArH), 6.89–6.85 (m, 1H, ArH), 6.68–6.65 (m, 1H, ArH), 6.26–6.23 (m, 1H, C-1'H), 5.97–5.95 (m, 1H, CH<sub>2</sub>), 5.94–5.91 (m, 1H, CH<sub>2</sub>),

5.59–5.52 (m, 2H, CH<sub>2</sub>), 4.76–4.74 (m, 1H, ArH), 4.30–4.21 (m, 3H, C-3'H, CH<sub>2</sub>), 3.87–3.85 (m, 1H, C-4'H), 3.62–3.59 (m, 2H, C-5'H), 2.21–2.18 (m, 2H, C-2'H);  $^{13}\text{C}$  NMR (DMSO- $d_6$ , 100 MHz)  $\delta$  161.7 (ArC), 160.7 (ArC), 159.9 (ArC), 157.8 (ArC), 151.5 (ArC), 151.2 (ArC), 150.1 (ArC), 147.2 (ArC), 139.8 (C-4), 136.8 (C-6''), 132.3 (ArC), 131.7 (ArC), 123.9 (ArC), 120.4 (ArC), 114.5 (ArC), 113.3 (ArC), 110.8 (ArC), 109.1 (C-5), 106.6 (ArC), 105.4 (ArC), 88.1 (C-4'), 85.2 (C-1'), 79.7 (CH<sub>2</sub>), 71.1 (C-3'), 61.8 (C-5'), 49.5 (CH<sub>2</sub>), 45.0 (CH<sub>2</sub>), 40.5 (C-2'), 36.0 (CH<sub>2</sub>); HRMS (ESI):  $m/z$  calculated for  $\text{C}_{29}\text{H}_{26}\text{BrN}_6\text{O}_8^+ [\text{M} + \text{H}]^+$ : 665.0990, found: 665.1005.

**4.3.12  $N^1$ -(9''-(4''''-Methyl)-9''',10'''-dihydro-2''H,8''H-chromeno[8''',7'''-e][1''',3''']oxazin-2'''-one-4'''-methyl)-C<sup>4</sup>-(2'-deoxy- $\beta$ -D-ribofuranos-1'-(2'',4''-dioxo-3'',4''-dihydropyrimidin))-1,2,3-triazole (15f).** It was obtained as a yellow solid. Yield: 0.58 g (97%).  $R_f$  = 0.28 (10% methanol in chloroform); melting point = 202 °C; IR (KBr,  $\text{cm}^{-1}$ ): 3296, 2932, 1672, 1589, 1506, 1446, 1399, 1268, 1043, 817;  $^1\text{H}$  NMR (DMSO- $d_6$ , 400 MHz)  $\delta$  11.72 (brs, 1H, NH), 8.63–8.62 (m, 1H, C-6''H), 8.56–8.54 (m, 1H, C-5H), 7.70–7.62 (m, 1H, ArH), 7.05–7.02 (m, 2H, ArH), 6.93–6.83 (m, 2H, ArH), 6.64–6.56 (m, 1H, ArH), 6.26–6.23 (m, 1H, C-1'H), 5.97–5.92 (m, 2H, CH<sub>2</sub>), 5.73–5.64 (m, 1H, CH<sub>2</sub>), 5.55–5.52 (m, 1H, CH<sub>2</sub>), 5.34–5.32 (m, 1H, ArH), 5.08–5.05 (m, 1H, C-3'H), 4.71 (brs, 1H, OH), 4.31–4.25 (m, 2H, CH<sub>2</sub>), 3.88–3.85 (m, 1H, C-4'H), 3.63–3.59 (m, 2H, C-5'H), 2.22–2.17 (m, 4H, C-2'H, CH<sub>3</sub>), 2.14–2.13 (m, 1H, C-2'H);  $^{13}\text{C}$  NMR (DMSO- $d_6$ , 100 MHz)  $\delta$  161.6 (ArC), 160.5 (ArC), 160.0 (ArC), 158.0 (ArC), 154.0 (ArC), 150.1 (ArC), 145.5 (ArC), 139.8 (C-4), 136.8 (C-6''), 130.8 (ArC), 130.1 (ArC), 129.7 (ArC), 123.9 (ArC), 118.6 (ArC), 112.9 (ArC), 110.6 (C-5), 109.2 (ArC), 105.4 (ArC), 88.1 (C-4'), 85.2 (C-1'), 80.5 (CH<sub>2</sub>), 71.1 (C-3'), 61.8 (C-5'), 49.7 (CH<sub>2</sub>), 45.1 (C-2'), 36.3 (CH<sub>2</sub>), 20.5 (CH<sub>3</sub>); HRMS (ESI):  $m/z$  calculated for  $\text{C}_{30}\text{H}_{29}\text{N}_6\text{O}_8^+ [\text{M} + \text{H}]^+$ : 601.2041, found: 601.2064.

#### 4.4. Single-crystal X-ray structural analysis

High-quality crystals of compound **6f** were obtained by slow evaporation of 5 : 1 methanol–chloroform solution at room temperature. The crystals were selected by careful examination under a polarizing microscope. Detailed experimental data for the X-ray crystallography of compound **6f** can be found in Table S2 (refer to the ESI†). The crystallographic data for com-

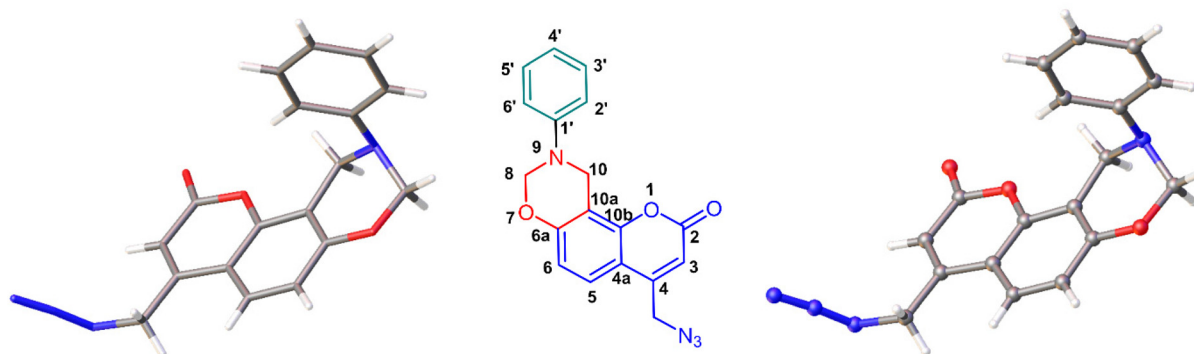


Fig. 7 X-Ray crystallographic structure of compound **6f**.

pound **6f** have been deposited with the Cambridge Crystallographic Data Centre, and a CCDC number has been assigned: 2343787 (Fig. 7).<sup>‡</sup>

## Conflicts of interest

The authors declare no competing financial interest.

## Acknowledgements

We appreciate the funding provided by the Institute of Imminence (IoE), University of Delhi which has contributed to further research and development. We appreciate the assistance provided by USIC and the Department of Chemistry, University of Delhi, for recording NMR, HRMS and IR data. Aditi Arora (SRF, File No. 09/0045(11270)/2021/EMR-I) and Sumit Kumar (SRF, File No. 09/045(1798)/2020-EMR-1) are grateful to the CSIR, New Delhi for fellowships.

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