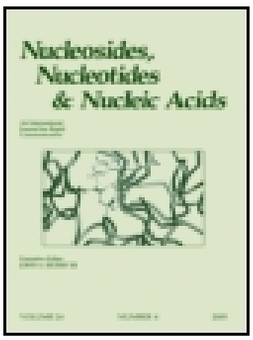

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Copper(II)nitrate catalyzed regioselective protection of primary alcohols with 4,4′-dimethoxytrityl and 2,7-dimethyl-9-phenyl xanthen-9-yl groups in nucleosides and carbohydrates

Srishylam Penjarla[a,b], S. Rajendra Prasad[a], Dhande Sudhakar Reddy[a], Shyamapada Banerjee[a], Santhosh Penta[b], and Yogesh S. Sanghvi[c]

[a]Research & Development, Sapala Organics Private Ltd., IDA Mallapur, Hyderabad, India; [b]Chemistry Department, National Institute of Technology, Raipur G.E. Road, Raipur, Chhattisgarh, India; [c]Process Chemistry, Rasayan Inc., Encinitas, CA, USA

ABSTRACT

Regioselective protection of primary hydroxyl group in nucleoside and carbohydrate analogs was accomplished using dimethoxytrityl alcohol (DMTr-OH) or dimethylpixyl alcohol (DMPx-OH) in presence of copper(II)nitrate as a Lewis acid catalyst. Excellent selectivity was observed for the protection of primary hydroxyl group over secondary while glycosidic bond remain unaffected. Utility of this methodology was further exemplified via DMTr- and DMPx-protection of alipahtic acyclic and cyclic diols.

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nucleosides; protecting groups; regioselectivity; lewis acid catalysis; DMTr-group and DMPx-group

Introduction

The design and synthesis of chemically modified nucleosides has led to the discovery of several antiviral and anticancer drugs. Often synthesis of these molecule requires multiple protection and deprotection steps before final compound could be assembled. The use of a protecting group triggers two extra synthetic steps which must be clean, facile, selective and high yielding to be attractive for practical applications. Our longstanding interest in design and application of protecting groups that are useful for nucleoside transformations has motivated us to develop new and improved protocols.[1] Since DMTr-protecting group[2] has become one of the workhorse for oligonucleotide synthesis and DMPx continues to generate interest, we decided to further explore methodologies for their installation in an efficient manner. In 2012, we reported[3] on large-scale synthesis of DMPx-OH and its convenient installation using tri(pentafluorophenyl)borane (TPB) as a Lewis acid. Although this study offered us a method for nucleoside protection, the high cost of TPB discouraged further usage for scale-up. Additionally, this protocol was limited

CONTACT Shyamapada Banerjee banerjee.s@sapalaorganics.com Research & Development, Sapala Organics Pvt. Ltd., Plot No-146B & 147, IDA Mallapur, Hyderabad, Telangana, 500076, India.

for installation of DMPx-group. Therefore, we explored the possibility of identifying another Lewis acid that is affordable and works equally well for installation of both DMTr- and DMPx groups. Herein, we are pleased to describe our finding and utility of copper(II)nitrate as a Lewis acid catalyst that enabled us not only protection but also deprotection of both DMTr- and DMPx groups in an efficient manner.

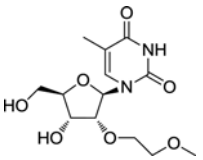
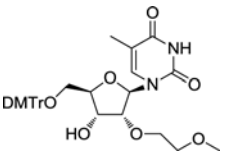
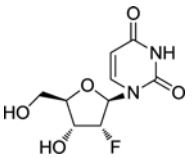
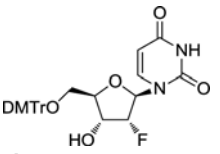
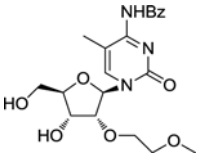
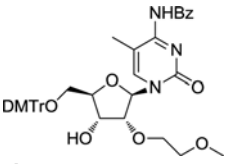
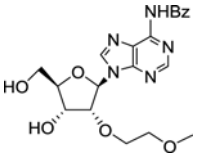
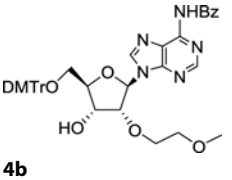
Results and discussion

The conventional protocol for the protection of a nucleoside with dimethoxytrityl group involves treatment of nucleoside with DMTr-Cl in the presence of excess pyridine serving as a base and solvent.[2] This procedure is not environmentally friendly given the fact that pyridine is classified as a toxic solvent and used in large excess. The high cost, storage and anhydrous handling of DMTr-Cl makes this procedure less attractive for large-scale applications. Often times, the selectivity of DMT-protection is not exquisite furnishing undesired bis-DMTr-protected nucleosides which requires chromatographic separation. These limitations of DMTr-Cl were driving force for our current study to develop an improved protocol where we could extend our original finding of TPB as Lewis acid catalyst.[3] The high cost and suboptimal yield obtained with TPB[4] sparked our interest in search for a better Lewis acid catalyst with wider utility.

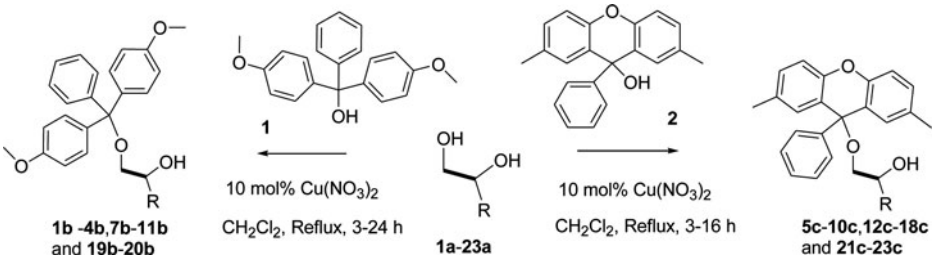
In order to develop an improved protocol that is mild, eco-friendly and economical, we sought after alternative Lewis acid catalysts.[5–8] After screening several metal salts, we selected three nitrates (copper, nickel and silver) for the current study. First, we tested the solubility of the $Cu(NO_3)_2$, $Ni(NO_3)_2$ and $AgNO_3$ in various solvents and found dichloromoethane to be ideal for dissolution of the Lewis acid and the starting materials. The evaluation of best catalyst was performed in parallel with four nucleoside substrates **1a**-**4a** listed in Table 1. No progress in the reaction or product formation at room temperature was observed. Therefore, the reaction mixture was heated to reflux until maximum conversion was accomplished for each substrate. The results indicated that when copper(II)nitrate was employed as the catalyst, best conversion and highest yields were obtained compared to the use of $Ni(NO_3)_2$ and $AgNO_3$ as catalysts. Use of 10 mol% catalyst offered most efficient conversion in shortest reaction time. More importantly, the 5′-*O*-protection was regioselective and all products **1b**-**4b** were isolated as homogeneous solid after chromatography (Scheme 1).

Next, the utility of $Cu(NO_3)_2$ as a catalyst for DMTr-protection was further tested with five substrates **7a**-**11a** with diverse structures furnishing **7b**-**11b** in high yields (71–90%; Table 2). Interestingly, the DMTr-protection of small molecules **7a**-**11a** was regioselective and found to be more efficient than the nucleosides substrate. The scope and application of this reaction was further evaluated for installation of DMPx-group.

Table 1. Catalyst screening experiments for 4,4′-dimethoxytritylation of nucleosides.

Entry	Starting Material	Product[a]	Catalysts	Time (h)	Yield[b] (%)	m.p. (°C)
1	 **1a**	 **1b**	$Cu(NO_3)_2$ $Ni(NO_3)_2$ $AgNO_3$	6 16 16	70 61 55	88–90
2	 **2a**	 **2b**	$Cu(NO_3)_2$ $Ni(NO_3)_2$ $AgNO_3$	8 16 16	50 35 40	118–120
3	 **3a**	 **3b**	$Cu(NO_3)_2$ $Ni(NO_3)_2$ $AgNO_3$	9 16 16	65 45 50	107–110
4[c]	 **4a**	 **4b**	$Cu(NO_3)_2$ $Ni(NO_3)_2$ $AgNO_3$	16 16 16	30 16 20	119–121

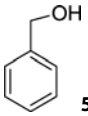
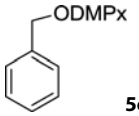
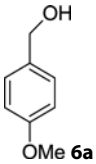
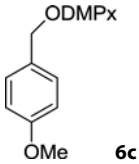
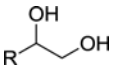
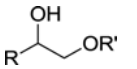
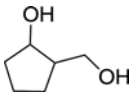
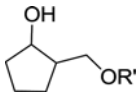
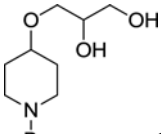
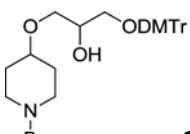
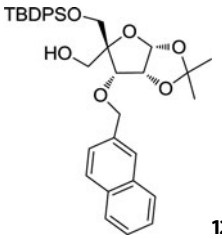
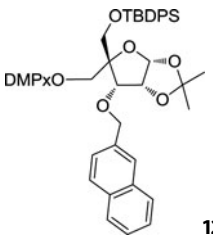
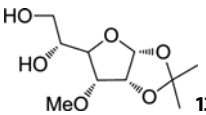
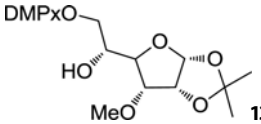
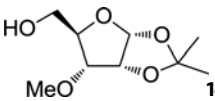
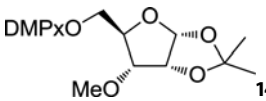
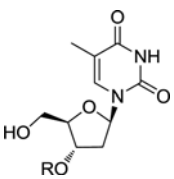
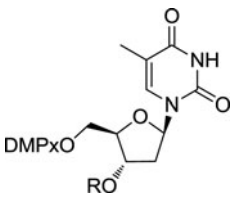
Reaction conditions: Substrate (1.0 mmol), DMTrOH (1.1 mmol) and $Cu(NO_3)_2$ (10 mol%) in dichloromethane (10 mL) under reflux condition.
[a] All the products were characterized by ^{1}H NMR and mass spectral analysis.
[b] Isolated yields after chromatography.
[c] The low yield is attributed to the low solubility of **4a** in dichloromethane



Scheme 1. $Cu(NO_3)_2$ catalysed protection of diols with 4, 4′-dimethoxytrityl alcohol **1** and DMPx alcohol **2**.

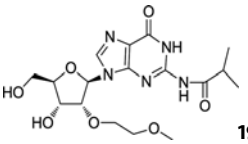
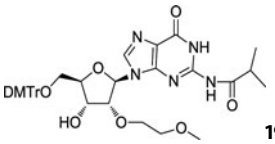
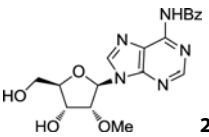
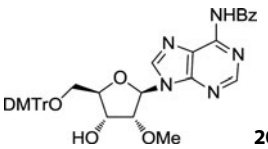
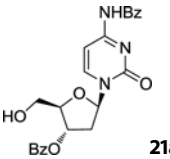
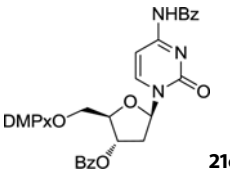
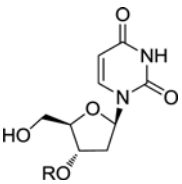
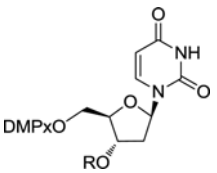
Previously we reported[3] on DMPx-protected compounds being crystalline in nature offering effortless isolation. Given the importance of DMPx-group, we extended the new $Cu(NO_3)_2$ catalyzed reaction for installation of DMPx on a variety of molecules. Gratifyingly, the reaction of electronically and structurally

Table 2. 4,4′-Dimethoxytritylation & DMPx protection of diverse substrates.

Entry	Starting Material	Time (hrs)	Product[a]	(Yield %)[b]	m.p. (°C)
1	 **5a**	6	 **5c**	83	119–120
2	 **6a**	6	 **6c**	72	99–102
3	 R = CH_3	6	 R = CH_3, R′ = DMTr **7b**	80	… ….
4	**7a**	4	R = CH_3, R′ = DMPx **7c**	51	115–117
5		3	R = C_2H_5, R′ = DMTr **8b**	90	… ….
6	R = C_2H_5 **8a**	4	R = C_2H_5, R′ = DMPx **8c**	60	120–123
7	R = CH_2NHBz **9a**	8	R = CH_2NHBz, R′ = DMTr **9b**	78	… ….
8		16	R = CH_2NHBz, R′ = DMPx **9c**	73	93–95
9	 **10a**	4	 R′ = DMTr **10b**	78	… ….
10	**10a**	12	R′ = DMPx **10c**	67	122–125
11	 **11a**	5	 **11b**	71	… ….
12	 **12a**	6	 **12c**	86	136–138
13	 **13a**	4	 **13c**	65	92–95
14	 **14a**	8	 **14c**	67	150–153
					

(*Continued on next page*)

Table 2. Continued.

Entry	Starting Material	Time (hrs)	Product[a]	(Yield %)[b]	m.p. (°C)
15	R = Bz **15a**	4	R = Bz **15c**	83	138–142
16	R = THP **16a**	3	R = THP **16c**	88	92–96
17	R = TBDPS **17a**	8	R = TBDPS **17c**	85	93–95
18	R = Bn **18a**	5	R = Bn **18c**	76	… ….
19	 **19a**	24	 **19b**	40	118–120
20	 **20a**	24	 **20b**	40	… ….
21	 **21a**	6	 **21c**	86	160–164
22	 R = H **22a**	5	 R = H **22c**	40	140–146
23	R = Bz **23a**	6	R = Bz **23c**	70	130–133

Reaction conditions:Substrate (1.0 mmol), DMTrOH/DMPxOH (1.1 mmol) and $Cu(NO_3)_2$ (10 mol%) in dichloromethane (10 mL) under reflux condition.
[a]All the products were characterized by ^1H NMR and mass spectral analysis.
[b]Isolated yields after chromatography.

diverse aromatic compounds **5a** and **6a**, aliphatic compounds **7a**-**11a** with DMPx-OH (**2**) in presence of $Cu(NO_3)_2$ furnished the expected products in excellent yields (Table 2). We were delighted to observe that compounds protected with DMPx-group induced crystallinity whereas same compounds protetced with DMT-group did not crystallize. The potential of synthesizing crystalline compounds via the protection with DMPx was further explored with carbohydrates **12a**-**14a** as substrates. As expected, all three DMPx-protected **12c**-**14c** were isolated as crystalline products.

The compatability of these reaction conditions in presence of other sensitive protecting group was confirmed when compounds **12a**-**18a** and **21a**-**23a** were selectively converted to pixylated ethers **12c**-**18c** and **21c**-**23c**, repectively. It is noteworthy that the acetonide, ether, benzyl, THP, Nap, benzoyl and TBDMS protecting groups were not disturbed during protection with DMPx-group (Table 2, entry 8–15 and 21–23). Two base protected purine nucleosides **19a** and **20a** were also

Table 3. Deprotection of DMTr and DMPx ether with $Cu(NO_3)_2$ in methanol at room temperature.

Entry	Starting Material	Products[a]	Method-A Time (min)	Method-B Time (min)	(Yield %)[b]
1	**2b**	**2a**	45	15	93
2	**3b**	**3a**	60	20	90
3	**17c**	**17a**	180	45	95

Reaction conditions: Method-A: Substrate (1.0 mmol), and $Cu(NO_3)_2$ (10 mol%) in Methanol (5 mL); Method-B: Substrate (1.0 mmol), and $Cu(NO_3)_2$. (10 mol%) and triethyl silane (3.0 mmol) in Methanol (5 mL).
[a]All the products were characterized by ^{1}H NMR and mass spectral analysis.
[b]Isolated yields.

transformed successfully into 5′-*O*-DMTr-protected nucleosides **19b** and **20b**, respectively. The stability of wide range of acid sensitive and base labile groups demonstrated that $Cu(NO_3)_2$ catalyzed reaction is mild enough to leave the orthogonal protecting groups unharmed during protection of a hydroxyl group with DMTr- or DMPx-groups.

The deprotection of DMTr- and DMPx groups is well established under acidic conditions which invariably is a cause for depurination resulting in loss of product yield.[9–12,14] Although deprotection of pixyl-group could be accomplished via photolysis, it requires special equipment and may cause cross-linking in pyrimidine nucleosides. Therefore, deprotection under mild conditions at room temperature would be a desirable reaction to develop. In this vein, we examined the use of $Cu(NO_3)_2$ catalyzed deprotection in protic solvents. We were pleased to discover that methanol as a solvent served the purpose of deprotecting both DMTr- and DMPx-groups in an expeditious manner (Table 3). As expected, the deprotection of DMPx-group was found to be relatively slower than the deprotection of DMTr-group. The overall deprotection rate could be further enhanced by using triethylsilane as a cation scavenger (Method B in Table 3).[13] The highly efficient protocol may find applications toward mild deprotection of DMTr-group from an oligonucleotide post DMTr-on purificaiton.

Conclusion

In summary, we have developed a practical and efficient synthetic protocol for the selective protection of primary hydroxyl group over secondary using DMTr-OH or DMPx-OH as protecting reagents and copper(II)nitrate as Lewis acid catalyst. The protocol is tolerant to a variety of functional groups offering additional arsenal to the repertoire of protecting groups. The use of more stable and easy to handle DMTr-OH and DMPx-OH offers the convenience and advantage over conventional DMTr-Cl and DMPx-Cl that are relatively less stable and more expensive. Therefore, this protocol is expected to offer an economical way for synthesis of DMTr- and crystalline DMPx-protected molecules on large-scale. Facile and efficient deprotection of both DMTr- and DMPx-protected nucleosides was also accomplished under mild conditions.

Experimental

General synthetic procedure for 4, 4′-dimethoxytrityl alcohol (1)

Anisole (21.6 g, 0.2 mol,) and benzotrichloride (19.5 g, 0.1 mol) were placed in a three necked RB flask, equipped with a reflux condenser and mechanical stirrer, and attached a funnel for addition of solid. The flask was cooled in an ice-bath and aluminium chloride (10.6 g, 0.08 mol) was added in small portions to the contents of the flask at such rate that the reaction mixture does not reflux during addition. The addition took nearly 1.5 h. The ice–bath was removed 15 min after all the solid had been added and the reaction was allowed to proceed without further cooling. When the evolution of the gas subsided (nearly 2h). The reaction mixture was poured into a mixture of crushed ice (300 g) and conc. sulphuric acid (300 ml) and stirred vigorously. The two layers were separated. The aqueous layer was extracted with ethylacetate (1 × 100 ml). The combined organic extracts were further washed with conc. Sulphuric acid (50 ml) and the solvent removed on rotary evaporator to give gummy substance, which was steam distilled to remove any residual anisole. The distillate was dissolved in hexane and dried over Na_2SO_4 and allow stand the solution for crystallization to give DMT-OH **1** (27.8 g, 85%) as white color solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.68 (s, 1H), 3.79 (s, 6H), 6.83 (d, $J = 9.0$ Hz, 4H), 7.17 (d, $J = 9.0$ Hz, 4H), 7.29 (m, 5H).

MS: 303 (M +).

General synthetic procedure for 2, 7-dimethyl-9-phenyl xanthen-9-ol (2)

To the 250 mL 3-neck RB flask charged di-*p*-tolylether (10 g, 50.43 mmol), benzoic acid (7.39 g, 60.52 mmol) and $ZnCl_2$ (19.73 g, 144.73 mmol) in $POCl_3$ (15 mL) and stirred mechanically for few minutes. Then the reaction mixture heated up to 95°C and allowed to stir for 4h. After 4h, color of the reaction mixture turned into dark brown and unable to stir. Then the above reaction mixture cooled to 0°C and quenched with crushed ice (40 g) while mechanically stirring. To the above reaction mixture added H_2O (150 ml) and allowed to stir at RT for 16h.The obtained solid suspension filtered through Buchner funnel and the solid cake washed with H_2O (3 × 50 mL) followed by hexane (2 × 100 mL) to get crude DMPx-OH. This crude solid re-dissolved in EtOAc (200 mL) and taken into separating flask and washed with sat $NaHCO_3$ (2 × 50 mL), the organic layer dried over Na_2SO_4 and evaporated the solvent on rotary evaporator to get off-white color DMPx-OH **2** (10.37 g, 68%).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.24 (s, 6H), 2.55 (s, 1H), 7.07 (m, 4H), 7.12 (t, $J = 0.8$ Hz, 2H), 7.19 (m, 1H), 7.29 (m, 2H), 7.40 (dd, $J1 = 8.3$, 1.1 Hz, 2H).

MS: 285.6 (M +).

General experimental procedure for the 4, 4′-dimethoxytritylation and pixylation of diols 1a-23a

To a mixture of diol **1a-23a** (1.0 mmol) and dimethoxy triphenylmethonol **1 or 2** (1.1 mmol) in dichloromethane (10 mL), 10 mol % of $Cu(NO_3)_2.H_2O$

(copper(II)nitrate monohydrate is highly oxidizing and irritant) was added and the blue heterogeneous reaction mixture refluxed for 3–24 h. After completion of the starting material **1a-23a**, (monitored by TLC), the reaction mixture was diluted with dichloromethane and washed with water (1 × 10 mL) and brine (1 × 10 mL). The organic layer was dried over Na_2SO_4 and evaporated to get crude product. The crude compound was purified by column chromatography (30% ethylacetate in hexane to 80% ethylacetate in hexane) to afford compound **1b-4b 17b-11b & 19b-20b or 5c-10c, 12c-18c & 21c-23c**.

4,4′-Dimethoxytritylation of 2′-O-methoxyethyl-thymidine (1b)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.414 (s, 3H), 3.385 (s, 3H), 3.509–3.650 (m, 5H),3.792 (s, 6H), 4.030–4.047 (m, 1H), 4.058–4.135 (m, 2H), 4.421–4.461 (m, 1H), 6.014–6.024 (d, $J = 4.0$ Hz, 1H), 6.826–6.849 (d, $J = 9.2$ Hz, 4H), 7.219–7.648 (m, 9H), 7.651 (s, 1H), 8.238 (br s, NH, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 11.7, 29.6, 30.6, 55.2, 58.9, 62.4, 69.2, 70.2, 71.2, 82.8, 83.6, 86.8, 87.3, 110.9, 113.2, 127.1, 127.9, 128.1, 130.0, 135.2, 135.4, 135.5, 144.3, 150.2, 158.6, 163.6.

MS: 641 (M + Na).

4,4′-Dimethoxytritylation of 2′deoxy-2′-fluorouridine (2b)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.887 (s, 1H), 2.960 (s, 1H), 3.519–3.554 (m, 1H), 3.626–3.660 (m, 1H), 3.802 (s, 6H), 4.078–4.096 (m, 1H), 4.524–4.574 (m, 1H), 4.968–5.107 (m,1H), 5.324 – 5.343 (d, $J = 7.6$ Hz, 1H), 6.099–6.060 (d, 1H), 6.834–6.870 (dd, $J = 2.8$, 4.4 Hz, 4H), 7.235–7.390 (m, 8H), 7.905–7.927 (d, $J = 8.8$ Hz, 1H), 8.153 (br s, NH, 1H).

^{13}C NMR (100MHz, $CDCl_3$) δ: 29.6, 55.2, 60.4, 61.0, 68.8, 69.0, 82.2, 87.2, 87.4, 87.7, 87.7, 92.9, 94.7, 102.4, 113.3, 127.2, 128.0, 130.0, 130.1, 134.9, 135.1, 139.9, 144.1, 149.7, 158.7, 162.7.

MS: 549.57 (M + H).

4, 4′-Dimethoxytritylation of N^4-benzoyl -2′-O-methoxyethyl-5-methyl cytidine (3b)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.597 (s, 3H), 3.386 (s, 3H), 3.423–3.652 (m, 5H), 3.778 (s, 6H), 4.083–4.130 (m, 3H), 4.441–4.487 (m, 1H), 6.035–6.043 (d, $J = 3.2$ Hz, 1H), 6.866–6.840 (dd, $J = 1.2$, 9.2 Hz, 4H), 7.232–7.539 (m, 12H), 7.864 (br s, NH, 1H), 8.282–8.301 (d, $J = 7.2$ Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.8, 55.2, 58.9, 62.2, 69.1, 70.3, 71.7, 83.0, 83.6, 86.8, 87.9, 111.9, 113.2, 127.1, 128.02, 128.09, 128.1, 129.8, 130.1, 132.4, 135.2, 135.4, 136.7, 144.3, 158.6, 159.7.

MS: 722 (M + H).

4, 4′-Dimethoxytritylation of 2′-O-methoxyethyl- N^6-benzoyl -adenosine (4b)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.373 (s, 3H), 3.386–3.652 (m, 5H), 3.778 (s, 6H),3.95 (m, 1H), 4.10–4.20 (m, 2H), 4.041–4.054 (t, $J = 5.2$ Hz, 1H), 6.200–6.208 (d, $J =$

3.2 Hz, 1H), 6.589–6.609 (d, J = 8.0 Hz, 2H), 6.792–6.864 (m, 6H), 7.056–7.083 (dd, J = 5.6 Hz, 2H), 7.160–7.523 (m, 12H), 7.986 (br s, NH, 1H), 8.30 (s, 1H).

MS: 732 (M + H).

2, 7-Dimethyl-9-phenyl xanthen-9-yl protection of benzyl alcohol (5c)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.206 (s, 6H), 4.060 (s, 2H), 7.061–7.081 (m, 6H), 7.148–7.185 (m, 1H), 7.246–7.252 (m, 2H), 7.284–7.321 (m, 4H), 7.444–7.463 (d, 2H).

MS: 392 (M + H).

2, 7-Dimethyl-9-phenyl xanthen-9-yl protection of p-methoxybenzyl alcohol (6c)

^{1}HNMR (400 MHz, $CDCl_3$) δ: 2.217 (s, 6H), 3.797 (s, 3H), 3.985 (s, 2H), 6.843–6.865 (d, J = 8.8 Hz, 2H), 7.061–7.081 (m, 6H), 7.137–7.271 (m, 5H), 7.421–7.442 (m, 2H).

MS: 422 (M + H).

4, 4′-Dimethoxytritylation of propane-1, 2-diol (7b)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.093 (m, 3H), 2.371–2.379 (d, 1H), 2.959–3.003 (t, 1H), 3.105–3.171 (m, 1H), 3.794 (s, 6H), 3.936–4.011 (m, 1H), 6.821–6.844 (m, 4H), 7.162–7.238 (m, 1H), 7.232–7.327 (m, 6H), 7.420–7.438 (d, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 18.9, 55.1, 67.0, 68.7, 85.9, 113.0, 126.7, 127.7, 128.0, 129.0, 130.0, 135.9, 136.0, 144.8, 158.4.

MS: 377 (M – H).

2, 7-Dimethyl-9-phenyl xanthen-9-yl protection of Propane-1, 2-diol (7c)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.04 – 1.06 (d, J = 6.8 Hz, 3H), 2.21 (s, 6H), 2.25–2.26 (d, J = 3.2 Hz, 1H), 2.80–2.84 (t, J = 8.6 Hz, 1H), 2.92–2.95 (dd, J = 2.8, 9.2 Hz, 1H), 3.90–3.95 (m, 1H), 6.94 (s, 1H), 7.04–7.08 (m, 4H), 7.16 –7.20 (m, 1H), 7.25–7.29 (m, 2H), 7.37–7.39 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 18.8, 20.8, 66.9, 68.5, 75.6, 116.0, 122.4, 126.4, 126.4, 126.5, 127.8, 129.1, 130.1, 130.15, 132.6, 132.7, 148.8, 149.3.

MS: 383 (M + Na).

4, 4′-Dimethoxytritylation of butane-1, 2-diol (8b)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.863–0.901 (t, 3H), 1.408–1.478 (m, 2H), 2.992–3.034 (dd, 1H), 3.156–3.188 (dd, 1H), 3.670–3.721 (m,1H), 3.794 (s, 6H), 6.812–6.850 (m, 4H), 7.160–7.234 (m, 1H), 7.272–7.328 (m, 6H), 7.420–7.441 (dd, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 9.9, 26.3, 55.1, 67.1, 72.3, 85.9, 113.0, 126.7, 127.7, 128.1, 129.1, 130.0, 136.01, 136.09, 144.8, 158.4.

MS: 415 (M + Na).

2, 7-Dimethyl-9-phenyl xanthen-9-yl protection of butane-1, 2-diol (8c)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.82–0.86 (t, J = 7.2 Hz, 3H), 1.38–1.45 (m, 2H), 2.16–2.17 (d, J = 4.4 Hz, 1H), 2.20–2.21 (d, 6H), 2.84–2.88 (m, 1H), 2.97–3.00 (m,

1H), 3.61–3.67 (m, 1H), 6.94 (s, 2H), 7.03–7.08 (m, 4H), 7.16–7.19 (m, 1H), 7.25–7.29 (m, 2H), 7.37 –7.38 (d, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 9.8, 20.8, 26.2, 66.7, 72.2, 75.5, 116.6, 122.4, 126.4, 126.5, 127.8, 129.1, 130.09, 130.1, 132.6, 132.6, 132.7, 148.9, 149.

MS: 397 (M + Na)

4, 4′-Dimethoxytritylation of N-(2, 3-dihydroxypropyl) benzamide (9b)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.228–3.243 (d, 2H), 3.422–3.486 (m, 2H), 3.768 (s, 6H), 4.093–4.146 (m, 3H), 6.502–6.530 (m, 1H), 6.801–6.823 (m, 4H), 7.158–7.222 (m, 1H), 7.257–7.319 (m, 5H), 7.376–7.429 (m, 4H), 7.471–7.508 (m, 1H), 7.645–7.667 (d, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 21.0, 22.6, 43.2, 55.1, 64.7, 70.1, 86.3, 113.1, 126.8, 126.9, 127.9, 128.4, 129.9, 131.5, 134.0, 135.6, 144.5, 158.5, 168.5.

MS: 496 (M – H).

2, 7-Dimethyl-9-phenyl xanthen-9-yl protection of N-(2, 3 dihydroxypropyl) benzamide (9c)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.17–2.19 (d, 6H), 2.98–3.06 (m, 3H), 3.37–3.43 (m, 1H), 3.72 –3.78 (m, 1H), 3.95 (br s, 1H), 6.37 (br s, 1H), 6.92 (s, 2H), 7.03–7.10 (m, 4H), 7.18–7.21 (m, 1H), 7.27–7.29 (m, 2H), 7.37–7.41 (m, 4H), 7.47–7.50 (m, 1H),7.61- 7.63 (d, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.7, 29.6, 43.0, 64.5, 69.9, 75.9, 116.14, 116.19, 122.0, 122.1, 126.4, 126.6, 126.9, 127.8, 128.4, 129.01, 129.1, 130.2, 131.5, 132.6, 132.5, 134.0, 148.4, 149.3, 168.5.

MS: 478.1 (M – H).

4, 4′-Dimethoxytritylation of 2-(hydroxymethyl) cyclopentanol (10b)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.150–1.159 (m, 1H),1.081–1.159 (m, 2H), 1.734–1.782 (m, 2H), 1.896- 1.937 (m, 1H), 2.079- 2.095 (m, 1H), 2.594–2.598 (d, 1H), 2.918–2.963 (t,1H), 3.305–3.340 (m, 1H), 3.795 (s, 6H),3.925–3.937 (d, 2H), 6.821–6.843(d, 4H),7.296–7.318 (d, 5H), 7.403–7.423 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.4, 26.4, 33.6, 47.6, 55.1, 66.8, 78.1, 86.1, 113.0, 126.6, 127.7, 128.0, 129.0, 129.9, 135.9, 136.1, 144.8, 158.3.

MS: 441 (M + Na).

2, 7-Dimethyl-9-phenyl xanthen-9-yl protection of 2-(hydroxymethyl) cyclopentanol (10c)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.05- 1.13 (m, 1H), 1.47–1.61 (m, 2H), 1.66 –1.77 (m, 2H), 1.84–1.92 (m, 1H), 2.22- 2.23 (d, 6H), 2.82–2.86 (t, $J = 9$ Hz, 1H), 3.04 –3.07 (q, $J = 4.8$, 8.4 Hz, 1H), 3.88–3.93 (m, 1H), 6.96–7.36 (m, 11H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.8, 21.6, 26.4, 33.8, 47.7, 66.3, 78.1, 115.09, 115.9, 122.4, 122.6, 126.2, 126.4, 127.9, 129.0, 129.9, 130.0, 132.5, 132.6, 149.0, 149.3, 149.4.

MS: 423 (M + Na).

4, 4′-Dimethoxytritylation of tert-butyl 4-(2,3-dihydroxypropoxy) piperidine-1-carboxylate (11b)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.254 (s, 9H), 1.472–1.516 (m, 2H), 1.758 (s, 2H), 2.423–2.437 (d, 2H), 3.047–3.111 (m, 2H), 3.161–3.28 (m, 2H), 3.422–3.576 (m, 4H), 3.655 (m, 2H), 3.789 (s, 6H), 3.880–3.920 (m, 1H), 6.814–6.836 (d, 4H), 7.211–7.229 (m, 1H),7.284–7.323 (m, 6H),7.414–7.433 (d, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.4, 30.9, 55.1, 64.1, 70.0, 75.0, 79.4, 86.0, 113.0, 126.7, 127.7, 128.1, 130.0, 135.9, 144.7, 158.4.

MS: 600 (M + Na).

2,7-Dimethyl-9-phenyl xanthen-9-yl protection of 5-O-(tert-Butyldiphenylsilyl)-4-C-hydroxymethyl-1,2-O-isopropylidene-3-O-(2-naphthyl- α -D-tribofuranose (12c)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.93 (s, 9H), 1.01 (s, 3H), 1.24 (s, 3H), 1.87 (s, 3H), 1.20 (s, 3H), 3.25–3.28 (d, J = 10.4 Hz, 1H), 3.44–3.47 (d, J = 10 Hz, 1H), 3.54–3.57 (d, J = 11.2 Hz, 1H), 4.23–4.26 (d, J = 11.2 Hz, 1H), 4.47–4.48 (d, J = 5.2 Hz, 1H), 4.53–4.60 (m, 2H), 4.71–4.79 (d, J = 12.4 Hz, 1H), 5.77–5.78 (d, J = 3.2 Hz, 1H), 6.64 (s, 1H), 6.96–7.82 (m, 28H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 19.21, 20.50, 20.66, 26.18, 26.34, 26.74, 64.25, 65.67, 75.53, 75.37, 79.42, 87.91, 104.27, 113.33, 115.91, 122.47, 125.41, 125.86, 126.00, 126.06, 126.3, 127.60, 127.63, 127.69, 127.93, 128.10, 129.08, 129.63, 129.73, 132.20, 132.99, 135.24, 135.42, 135.73, 149.20, 149.44, 149.54.

MS: 284.9 (DMPx +)

2,7-Dimethyl-9-phenyl xanthen-9-yl protection of (R)-1-((3aR,5R,6R,6aR)-6-methoxy-2, 2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)ethane-1, 2-diol (13c)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.33 (s, 3H), 1.54 (s, 3H), 2.21 (s, 6H), 2.37–2.38 (d, J = 2.8 Hz, 1H), 3.02–3.08 (m, 2H), 3.26 (s, 3H), 3.64–3.67 (q, J = 13.2 Hz, 1H), 3.91–3.95 (dd, J = 3.6, 8.8 Hz, 1H), 4.05–4.09 (m, 1H), 4.59–4.61 (t, J = 4 Hz, 1H), 5.69–5.70 (d, J = 3.6 Hz, 2H), 6.95–6.97 (d, 2H), 7.02–7.07 (m, 4H), 7.15–7.19 (m, 1H), 7.24–7.28 (m, 2H), 7.37–7.40 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.7, 20.8, 26.4, 26.7, 57.8, 63.5, 70.2, 75.9, 77.1, 77.9, 79.8, 103.8, 112.8, 115.9, 116.0, 122.2, 122.4, 126.4, 127.7, 129.10, 129.15, 130.03, 130.09, 132.5, 132.6, 148.7, 149.2, 149.4.

MS: 541 (M + Na).

2,7-Dimethyl-9-phenyl xanthen-9-yl protection of ((3aR,5R,6R,6aR)-6-methoxy-2, 2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-5-yl)methanol (14c)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.28 (s, 3H), 1.41 (s, 3H), 2.19 (s, 6H), 2.96–3.00 (dd, J = 4.4,10.4 Hz, 1H), 3.12–3.14 (m, 1H), 3.27 (s, 3H), 3.64–3.67 (dd, J = 4.4, 9.6 Hz, 1H), 3.85–3.86 (m, 1H), 4.71–4.73 (t, J = 4 Hz, 1H), 5.77–5.78 (d, J = 4.4 Hz, 1H), 6.93–6.94 (d, J = 3.6 Hz, 2H), 7.15–7.30 (m, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.4, 26.4, 26.5, 57.0, 62.0, 74.9, 76.1, 76.8, 79.6, 103.8, 111.6, 116.0, 116.1, 122.2, 125.6, 126.5, 128.0, 128.4, 130.2, 132.3, 148.6, 148.7, 149.0.

MS: 511.23 (M + Na).

2, 7-Dimethyl-9-phenyl xanthen-9-yl protection of 2′-deoxy 3′-O-benzoyl-thymidine (15c)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.64 (s, 3H), 2.19 (s, 3H), 2.22 (s, 3H), 2.56–2.68 (m, 2H), 3.29–3.37 (m, 2H), 4.22–4.23 (d, $J = 2$ Hz, 1H), 5.61–5.6 (t, $J = 3.6$ Hz, 1H), 6.48–6.51 (m, 1H), 6.92 (s, 1H), 7.06–7.47 (m, 12H), 7.57–7.60 (t, 1H), 7.82 –7.83 (d, 1H), 8.00–8.02 (d, $J = 7.2$ Hz, 2H), 8.20 (br s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 11.9, 20.7, 38.4, 63.3, 75.4, 76.8, 83.7, 84.3, 111.5, 116.2, 121.4, 121.7, 126.1, 126.9, 128.1, 128.4, 128.8, 129.2, 129.6, 130.4, 130.5, 132.9, 133.2, 133.4, 135.3, 148.2, 149.1, 149.7, 150.4, 163.6, 165.6.

MS: 629 (M – H).

2, 7-Dimethyl-9-phenyl xanthen-9-yl protection of 2′-deoxy 3′-O-THP-thymidine (16c)

^{1}H NMR (400 MHz, $CDCl_3$) (Diastereomericmixture) δ: 1.43–1.59 (m, 4H), 1.65 (m, 6H), 1.66–1.86 (m, 8H), 2.18 (s, 6H), 2.22 (s, 6H), 2.29–2.36 (m, 1H), 2.46–2.51 (m, 1H), 3.09–3.12 (m, 1H), 3.15 –3.18 (m, 1H), 3.24–3.31 (m, 2H), 3.34–4.63 (m, 10H), 6.30 (q, $J = 6.8$ Hz, 2H), 6.90 (s, 2H), 6.98–7.53 (m,22H), 8.50 (br s, 2H, NH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.0, 19.2, 20.7, 25.2, 30.5, 30.6, 62.6, 75.6, 76.2, 84.8, 97.0, 98.4, 110.9, 111.0, 126.2, 126.2,126.8,128.0,128.5, 128.6, 128.9, 130.2, 132.7, 135.5, 148.4, 149.2, 149.2, 150.1, 163.5.

MS: 609 (M – H).

2, 7-Dimethyl-9-phenyl xanthen-9-yl protection of 2′-deoxy 3′-O-TBDPS-thymidine (17c)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.03 (s, 9H), 1.57–1.58 (d, $J = 0.8$ Hz, 3H),1.90 (s, 3H), 2.12 (s, 3H), 2.14–2.18 (m,1H), 2.40–2.45 (m, 1H), 2.58–2.62 (m, 1H), 2.98–3.02 (m, 1H), 3.87–3.88 (d, $J = 1.6$ Hz, 1H), 4.41–4.42 (d, $J = 5.2$ Hz, 1H), 6.49 (q, $J = 4.5$ Hz, 1H), 6.75–6.77 (d, $J = 9.6$ Hz, 2H), 7.00- 7.44 (m, 17H), 7.44–7.68 (m, 2H), 7.68 (s, 1H), 8.50 (br s, 1H, NH).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 11.9, 18.8, 20.5, 20.7, 26.8, 41.3, 74.4, 76.5, 85.1, 86.8, 110.8, 116.1, 121.4, 121.8, 126.1, 126.8, 127.7, 127.8, 127.9, 128.3, 128.9, 129.9, 129.9, 130.2, 130.4, 132.79, 133.0, 135.4, 135.5, 135.7, 148.3, 149.0, 149.6, 150.1, 163.62.

MS: 763 (M – H).

2, 7-Dimethyl-9-phenyl xanthen-9-yl protection of 2′-deoxy 3′-O-Bn-thymidine (18c)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.707 (s, 3H), 2.172 (s, 3H), 2.213 (s, 3H), 2.263–2.249 (m, 1H), 2.396–2.454 (m, 1H), 3.122–3.155 (m, 1H), 3.227–3.261 (m, 1H),

3.940–3.962 (m, 1H), 4.418–4.447 (m, 1H), 5.132 (s, 2H), 6.411 (t, $J = 5.7$ Hz, 1H), 6.887 (s, 1H), 6.941 (s, 1H), 7.052–7.327 (m, 12H), 7.488–7.505 (d, $J = 6.8$ Hz, 2H), 7.638 (s, 1H).

^{13}C NMR (100MHz,$CDCl_3$) δ: 12.97, 20.80, 29.67, 41.13, 44.40, 63.24, 72.61, 85.40, 85.78, 110.32, 116.22, 116.32, 121.55, 121.95, 126.32, 126.91, 127.58, 128.03, 128.35, 128.60, 129.08, 129.23, 130.41, 130.53, 132.80, 132.93, 133.62, 136.90, 148.18, 149.37, 149.66, 150.94, 163.42.

MS: 617 (M + H).

4, 4′-Dimethoxytritylation of 2′-O-methoxy ethyl- N^2-isobutyryl guanosine (MOE-G) (19b)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.667- 0.684 (d, 3H), 0.878–0.895 (d, 2H), 1.243–1.261 (m, 2H), 1.383–1.415 (m, 1H), 2.049 (s, 1H), 3.082–3.116 (m, 1H), 3.382 (s, 3H),3.449–3.765(m, 4H), 3.779(s, 6H),3.869–4.150 (m,1H),4.217(br s, 1H), 4.484–4.496 (d, 1H), 4.954–4.983 (t, $J = 6.8$ Hz, 1H), 5.838–5.856 (d, 1H), 6.777–6.824 (t, $J = 9.2$ Hz, 4H), 7.220–7.289 (m, 3H), 7.392–7.421 (m, 5H), 7.545–7.562 (d, 2H),7.795 (s, 1H).

^{13}C NMR (100MHz,$CDCl_3$) δ: 18.4, 18.5, 36.0, 55.2, 59.0, 63.7, 69.3, 69.9, 71.7, 81.3, 84.4, 86.2, 86.3, 113.2, 122.4, 127.1, 128.0, 129.9, 135.6, 136.0, 136.0, 144.9, 147.0, 148.2, 155.4, 158.7, 178.3.

MS: 714 (M + H).

4, 4′-Dimethoxytritylation of 2′-O-methoxy N^6-benzoyl –adenosine (20b)

^{1}H NMR (400 MHz, DMSO-d_6) δ: 3.221–3.316 (m, 3H), 3.402 (s, 3H), 3.424 (s, 1H),3.721 (s, 6H), 4.002–4.055 (m, 1H), 4.099–4.134 (m, 1H), 4.461–4.521 (m, 1H), 4.539–4.563 (t, $J = 4.8$ Hz, 1H), 5.365–5.380 (d, $J = 6.0$ Hz, 1H), 6.183–6.208(t, $J = 4.8$ Hz, 1H), 6.820–6.856 (m, 4H), 7.195–7.272 (m, 7H), 7.354–7.372 (d, $J = 7.2$ Hz, 2H), 7.539–7.576 (m, 3H), 7.635–7.653 (m, 1H), 8.035–8.056 (m, 2H),8.620 (s, 1H), 8.699 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.0, 20.7, 55.0, 57.7, 59.7, 63.5, 68.9, 81.7, 53.6, 85.5, 85.9, 86.1, 113.1, 125.9, 126.6, 127.6, 127.7, 128.5, 128.7, 129.2, 129.6, 132.4, 133.2, 135.4, 135.5, 138.8, 143.2, 144.8, 150.5, 151.7, 151.9, 158.0, 165.6.

MS: 688 (M + H).

2, 7-Dimethyl-9-phenyl xanthen-9-yl protection of 2′-deoxy, 3′-O- Bz-N^4 Bz-cytidine (21c)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.17 (s, 3H), 2.29 (s, 3H), 2.46–2.53 (m, 1H), 2.94 –2.98 (m, 1H), 3.23–3.26 (m, 1H), 3.33–3.36 (m, 1H), 4.34–4.35 (d, $J = 2.4$ Hz, 1H), 5.49–5.51 (t, $J = 2.8$ Hz, 1H), 6.92–6.94 (d, 2H), 7.07 –7.65 (m, 20H), 8.37–8.39 (d, 1H), 8.66 (br s, 1H).

^{13}C NMR (400 MHz, $CDCl_3$) δ: 20.6, 20.9, 39.6, 62.9, 74.7, 84.4, 87.3, 116.0, 116.2, 121.5, 121.6, 126.4, 126.9, 127.4, 127.9, 128.3, 128.9, 129.0, 129.1, 129.2, 129.6, 130.5, 132.9, 133.0, 133.1, 133.3, 144.3, 147.6, 149.4, 162.2, 165.5.

MS: 720 (M + H).

2,7-Dimethyl-9-phenylxanthen-9-yl protection of 2′-deoxyuridine (22c)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.21–2.23 (d, 6H), 2.44–2.50 (m, 1H), 2.88 (s, 1H), 2.95 (s, 1H), 3.09–3.13 (dd, $J = 3.6$, 10.8 Hz, 1H), 3.22–3.25 (dd, $J = 3.2$, 10.4 Hz, 1H), 3.96–3.99 (m, 1H), 4.41 (s, 1H), 5.60 –5.62 (d, $J = 8$ Hz, 1H), 6.26–6.29 (m, 1H), 6.83–6.90 (m, 2H), 7.05 –7.42 (m, 9H), 7.84–7.86 (d, $J = 8$ Hz, 1H), 8.54 (br s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.4, 150.3, 149.5, 149.4, 147.7, 140.0, 132.8, 132.7, 130.4, 130.3, 129.1, 128.9, 127.9, 127.7, 127.0, 126.9, 126.4, 121.8, 121.5, 116.1, 102.1, 86.1, 85.4, 71.8, 63.0, 41.3, 36.5, 31.4, 29.6, 20.8, 20.8, 14.0.

MS: 535.1 (M + Na).

2, 7-Dimethyl-9-phenyl xanthen-9-yl protection of 3′-O-Bz-2′-deoxyuridine (23c)

^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.19 (s, 3H), 2.22 (s, 3H), 2.47–2.54 (m, 1H), 2.67–2.72 (m, 1H), 3.25–3.34 (m, 2H), 4.25–3.73 (m, 1H), 4.03–4.05 (d, $J = 7.2$ Hz, 1H), 4.38–4.43 (m, 1H), 4.97–4.25 (d, 1H), 5.55–5.56 (d, $J = 5.2$ Hz,1H), 5.67–5.69 (d, $J = 8$ Hz, 1H), 6.40–6.44 (t, 1H), 6.85 (s, 1H), 6.919 (s, 1H), 7.06 –7.60 (m, 12H), 7.96–8.01 (t, 3H), 9.35 (bs,1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.7, 20.9, 38.8, 63.0, 74.7, 83.8, 85.1, 102.6, 116.1, 116.2, 121.5, 121.6, 126.4, 126.9, 127.9, 128.4, 128.8, 129.0, 129.1, 129.6, 130.4, 130.5, 132.8, 133.0, 133.4, 139.7, 147.5, 149.3, 149.5, 150.3, 163.3, 165.6.

MS: 615 (M – H).

General procedure for the deprotection of DMTr-ether and DMPx-ether (Method-A)

To a mixture of DMTr or DMPx-protected nucleosides (0.3 mmol) in MeOH (5 mL) was added 10 mol% of $Cu(NO_3)_2$ and stirred the reaction mixture at room temperature for given time (see Table 3). After completion of the reaction (monitored by TLC), solvents were distilled out on rotary evaporator to get crude product. The crude compound was purified by column chromatography using 60–120 silica gel and (ethyl acetate in hexane) to afford unprotected nucleosides summarized in Table 3.

General procedure for the deprotection of DMTr-ether and DMPx-ether(Method-B)

To a mixture of DMTr or DMPx-protected nucleosides (1.0 mmol) in MeOH (5 mL) was added, triethylsilane (3.0 mmol) and 10 mol% of $Cu(NO_3)_2$ and stirred the reaction mixture at room temperature for given time (see Table 3). After completion of the reaction (monitored by TLC), solvents were distilled out on rotary evaporator to get crude product. The crude compound was purified by column chromatography using 60–120 silica gel and (ethyl acetate in hexane) to afford unprotected nucleosides (Table 3).

^{1}H NMR (400 MHz, $CDCl_3$) δ: (Compound-2a) 3.568–3.599 (m, 1H), 3.742–3.773 (m, 1H), 3.862–3.880 (d, $J = 7.2$ Hz, 1H), 4.097–4.195 (m, 1H), 4.957–5.208 (m, 2H), 5.615 (t, $J = 8.0$Hz, 2H), 5.879–5.926 (dd, $J = 1.2$, 17.6 Hz, 1H), 7.905–7.926 (d, $J = 8.4$ Hz, 1H), 11.37 (s, 1H).

MS: 247.15 (M + H).

^{1}H NMR (400 MHz, $CDCl_3$) δ: (compound-3a) 2.112 (s, 3H), 3.054 (s, 1H), 3.403 (s, 3H), 3.524–3.618 (m, 2H), 3.678–3.813 (m, 3H), 3.970–3.996 (d, J = 10.4 Hz, 2H), 4.157 (s, 1H), 4.356 (s, 1H), 4.432 (s, 1H), 5.581–5.593 (d, J = 4.8 Hz, 1H), 7.426–7.464 (m, 2H), 7.525–7.550 (m, 2H), 8.304–8.324 (d, J = 8.0 Hz, 2H), 13.326 (br s, 1H).

MS: 420 (M + H) and 418 (M – H).

^{1}H NMR (400 MHz, $CDCl_3$) δ: (compound-17a) 1.09 (s, 9H), 1.86 (d, J = 1.2 Hz, 3H),1.93 (dd, J = 6.5, 4.2 Hz, 1H), 2.17 (m, 1H), 2.28 (dq, J = 13.4, 3.0 Hz, 1H), 3.24 (m, 1H), 3.63 (m, 1H), 3.98 (q, J = 2.8 Hz, 1H), 4.45 (m, 1H), 6.22 (m, 1H), 7.28 (d, J = 1.2 Hz, 1H), 7.40 (m, 4H), 7.46 (m, 2H), 7.64 (m, 4H), 8.05 (br s, 1H).

MS: 481 (M + H) and 479 (M – H).

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