Ionic liquid promoted and mediated green preparation of arylbispyranylmethane and pyran derivatives and their hybrid with a pyrimidine nucleoside

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The utilisation of an ionic liquid–[bmim][BF_4] as both reaction medium and promoter for the reaction between aldehyde and 4-hydroxy-6-methylpyran-2-one is described. Without any added catalyst, this reaction was realised efficiently to give arylbispyranylmethane derivatives in high yields. Alternatively, when this reaction was carried out in the presence of acetic anhydride, fused pyran derivatives were obtained. These two novel procedures have advantages such as an environmentally benign nature, high efficiency, simple operation process and mild reaction conditions. As an application, these procedures were used in the preparation of novel 5-substituted pyrimidine nucleoside derivatives with potential antiviral activities.

Keywords: ionic liquid, arylbispyranylmethane, pyran derivatives, 5-substituted pyrimidine nucleoside, green chemistry

Room temperature ionic liquids (RTILs) have gained wide popularity for their increasing use as greener reaction media due to their unique properties such as non-volatility, non-flammability, excellent chemical and thermal stability, and recyclability.[1,2] Their high polarity and their ability to solubilise both inorganic and organic compounds can result in enhanced rates of chemical processes and can provide higher selectivities compared to conventional solvents.[3,4] Moreover, ionic liquids are simple and inexpensive to prepare and easy to recycle and their properties can be fine-tuned by changing the anion or the alkyl group attached to cation. Recently, how to use ILs to promote the selectivity of various organic reactions and to dramatically influence the outcome of chemical reactions has attracted much attention.[5]

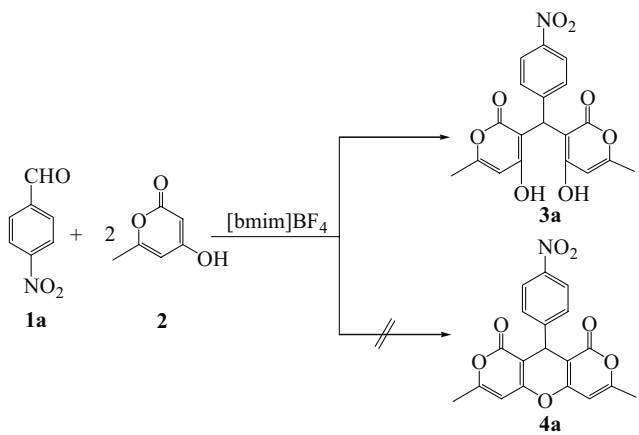
Substituted pyrans are biologically interesting compounds due to their antibacterial,[6] antitubercular,[7] antiproliferation and antitumor activities.[11] Particularly, pyrano ring fused to a polycyclic system such as acridone[12,13] and xanthone[11] exhibits interesting cytotoxic and antitumor properties. Among them, dipyrano[4,3-*b*:3,4-*e*]pyran system has created lots of interest and several preparative procedures have been reported. Classically, they were prepared through a two-step procedure from aldehyde and 4-hydroxy-6-methylpyran-2-one using toxic reagents such as triphenylphosphine, diethyl azodicarboxylate, and benzene.[12] Recently, Tu, Gao and coauthors reported two improved procedures either by employing KF/Al_2O_3 as catalyst under traditional heating conditions;[13] or by employing microwave irradiation with glycol as energy-transferring agent without catalyst.[14] It was also reported by Gao *et al*.[15] that dipyrano[4,3-*b*:3,4-*e*]pyran could be obtained by reacting aldehyde and 4-hydroxyl-6-methylpyran-2-one in acetic anhydride for 10–12 hours. On the other hand, arylbispyranylmethane derivatives have been shown to exhibit anticoagulant activity,[16] being also structurally related to the well known anticoagulant 3,3'-methylenebis (4-hydroxycoumarin). For their preparation, they were usually obtained from the reaction of 4-hydroxy-6-methylpyran-2-one with corresponding aldehyde under the catalysis of organic bases.[17,18] In view of the increasingly important role played by greener chemistry in the field of organic chemistry, we find it is of interest to develop more efficient and environmentally benign methods for the preparation of both dipyrano[4,3-*b*:3,4-*e*]pyran and arylbispyranylmethane derivatives.

As a continuation of our research interest in the development of novel methods for the preparation of various biologically important heterocyclic compounds by using ionic liquids as novel reaction medium and promoter,[19-22] we now report our preliminary results on the novel preparation of arylbispyranylmethane (**3**) and dipyrano[4,3-*b*:3,4-*e*]pyran (**4**) from aldehyde (**1**) and 4-hydroxy-6-methylpyran-2-one (**2**) in an ionic liquid–1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF_4]) acting as a recyclable solvent and promoter.

Results and discussion

Firstly, 4-nitrobenzaldehyde (**1a**) was used as model substrate to test if our envisioned method works. Thus, **1a** (0.5 mmol) and 4-hydroxy-6-methylpyran-2-one (**2**, 1 mmol) were treated with [bmim][BF_4] (Scheme 1) and the mixture was stirred at ambient temperature. The reaction took place slowly at room temperture to give a solid product, which was collected by suction and then submitted to identification. NMR and MS spectra showed that the product was **3a**, bis(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3yl)(4-nitrophenyl)methane, not **4a** (Scheme 1). Firstly, ESI MS showed a molecular weight of 385 for **3a** instead of 367 for **4a**. Secondly, ^{1}H NMR spectrum showed two broad singlet at 10.81 and 10.94 ppm with one proton each corresponding to the two OH groups. Finally, the structure was further confirmed by comparison with the authentic product prepared with known method.

Efforts were made to improve the reaction in terms of yield and reaction period. By varying the reaction temperature, it was found that when it was run at 80 °C, all the starting materials were consumed in 2 h and **3a** was obtained in a yield of 95%. Considering its simple procedure, high efficiency and its being free of added basic catalyst, this method is expected



Scheme 1

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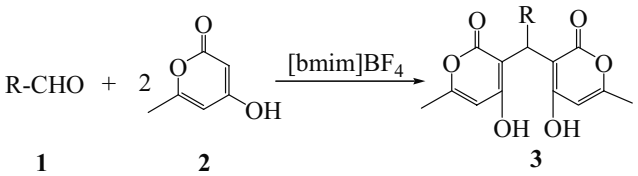


Scheme 2

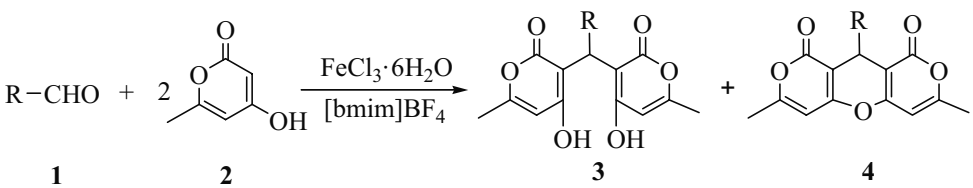
to be developed as a novel alternative for the preparation of arylbis(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)methane derivatives. Thus, several aldehyde substrates were treated with **2** in [bmim][BF_4] to explore its scope and generality (Scheme 2). It turned out that all the aldehydes studied, with either electron-donating group or electron-withdrawing group, reacted with **2** smoothly and efficiently to give compound **3** in good yields. The results are listed in Table 1.

It should be noted that dipyrano[4,3-*b*:3,4-*e*]pyran (**4**) were not formed from **1** and **2** in [bmim][BF_4] without catalysts. Bearing in mind that $FeCl_3{\cdot}6H_2O$ could efficiently promote similar condensation cyclisation processes in [bmim][BF_4],[23-24] we then made further efforts by employing catalytic amount of $FeCl_3{\cdot}6H_2O$ as an additional promoter to get compound **4**. However, it turned out that in the presence of 20 mol% $FeCl_3{\cdot}6H_2O$, the reaction between **1a** and **2** at 80°C gave a mixture of **3a** and **4a**. With a higher temperature and an increased amount of $FeCl_3{\cdot}6H_2O$, the reaction did not improve significantly in terms of selectivity for **4a**.

As a further resort, acetic anhydride were used since, as mentioned previously, Gao *et al*.[15] reported that compounds like **4a** could be obtained by reacting **1a** and **2** in refluxing acetic anhydride. Thus, the reaction was run again in [bmim][BF_4] in the presence of acetic anhydride. It turned out that in the presence of 0.2 mL acetic anhydride, reaction of **1a** (1 mmol) and **2** (2 mmol) at 100 °C gave **4a** in a yield of 72% in 3 h. This result is in remarkable contrast to that with $FeCl_3{\cdot}6H_2O$ as a promoter or without any additives at all. Moreover, studies with more acetic anhydride than 0.2 mL gave no remarkable improvements. To study the generality of the above procedure, other aldehyde substrates were also tried (Scheme 4). It turned out that in the presence of acetic anhydride all aldehydes studied reacted with **2** efficiently to give compound **4** in moderate to good yields. The results were listed in Table 2. Note that compared with the literature method,[12] this procedure needs much less amount of acetic anhydride and much shorter reaction period to obtain comparable results, thus remarkably alleviated its impact to the environment.

Recently we have pursued a chemistry-driven strategy for the discovery of lead nucleoside molecules with antiviral activity.[25-27] Our approach to new antivirals has been guided by the following considerations: (a) since the privileged structure of nucleosides has led to a variety of efficacious antiviral agents, the nucleosides scaffold is an excellent point of departure in the search for new antiviral drugs; (b) other privileged molecular scaffolds exist, like fused pyran and arylbis-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)methane derivatives, have spawned a significant number of drugs and other biologically active agents, and can be used to discover molecular "masterkeys". As a part of our ongoing program, we are interested in the preparation of novel pyrimidine nucleoside-fused pyran (**4i**, Scheme 5) and pyrimidine nucleoside-bis(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl) methane hybrid (**3i**, Scheme 5) with the aim of getting new chemical entities with synergic effects on its biological activities.

Thus, a mixture of 5-formyl-2'-deoxyuridine (**1**, Scheme 5) and **2** was stirred in [bmim]BF_4 with or without acetic



Scheme 3

Table 1 Preparation of **3** in [bmim][BF_4]

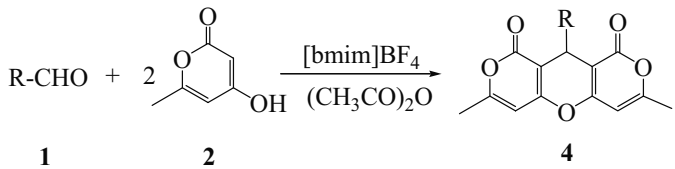
Entry	R	Product	Reaction time/h	Temperature/°C	Yield/%[a, b]
1	4-$NO_2C_6H_4$	**3a**	2	80	95
2	C_6H_5	**3b**	3	80	88
3	4-FC_6H_4	**3c**	2	80	90
4	4-ClC_6H_4	**3d**	2	80	91
5	4-$CH_3C_6H_4$	**3e**	3	80	85
6	4-$CH_3OC_6H_4$	**3f**	4	80	83
7	4-NCC_6H_4	**3g**	2	80	95
8	4-$F_3CC_6H_4$	**3h**	2	80	96

[a]Isolated yield; [b]**1**: 1 mmol, **2**: 2 mmol.

Table 2 Preparation of **4** in [bmim][BF_4] with acetic anhydride

Entry	R	Product	Reaction time/h	Temperature/°C	Yield/%[a,b]
1	4-$NO_2C_6H_4$	**4a**	3 (10~12)[15]	100	72 (58)[15]
2	C_6H_5	**4b**	4 (10~12)[15]	100	63 (60)[15]
3	4-FC_6H_4	**4c**	3	100	66
4	4-BrC_6H_4	**4d**	3 (10~12)[15]	100	62 (66)[15]
5	4-$CH_3C_6H_4$	**4e**	4 (10~12)[15]	100	60 (56)[15]
6	2-ClC_6H_4	**4f**	4 (10~12)[15]	100	58 (61)[15]
7	4-NCC_6H_4	**4g**	3	100	73
8	2-$F_3CC_6H_4$	**4h**	3	100	80

[a]Isolated yield; [b]**1**: 1 mmol, **2**: 2 mmol, acetic anhydride: 0.2 mL.



Scheme 4

anhydride at 80 °C. It turned out that just as other aldehyde substrates, the reaction of **1** with **2** underwent smoothly and afforded the desired products in good yields. The structure of **3i** and **4i** was fully characterised by their spectra data of NMR, MS and HRMS. The screen of their antiviral activities against various virus members is underway.

On the other hand, one of the goals in ionic liquids study is to identify the additional advantages they have over conventional organic solvent besides a greener nature. In this regard, it has been documented that compared with classical organic solvents, reactions carried out in ionic liquids possess the advantages of offering simpler operational process and/or enhanced reactivity and better yields. This was indeed demonstrated by comparing [bmim]BF_4 with several conventional volatile organic solvents including ethanol, methanol, toluene and THF. The following is the results (shown in Table 3) of investigations using **1a** and **2** as model substrates for the preparation of **3a**.

The results listed in Table 3 clearly showed that of the five solvents studied, [bmim][BF_4] gave the best result. Moreover, using [bmim][BF_4] as a reaction medium made the separation process much easier since in [bmim][BF_4] **3a** is in solid state and can be obtained with high purity through suction. On the other hand, with ethanol, methanol, toluene or THF as the reaction medium, it usually resulted in a complicated mixture and **3a** could only be obtained through tedious column chromatography.

In conclusion, two efficient and selective procedures have been developed for the preparation of arylbispyranylmethane or pyran derivatives respectively by using [bmim][BF_4] as both reaction medium and promoter with or without acetic anhydride. These two novel procedures have advantages of being environmentally benign, highly efficient, a simple operation process with mild reaction conditions.

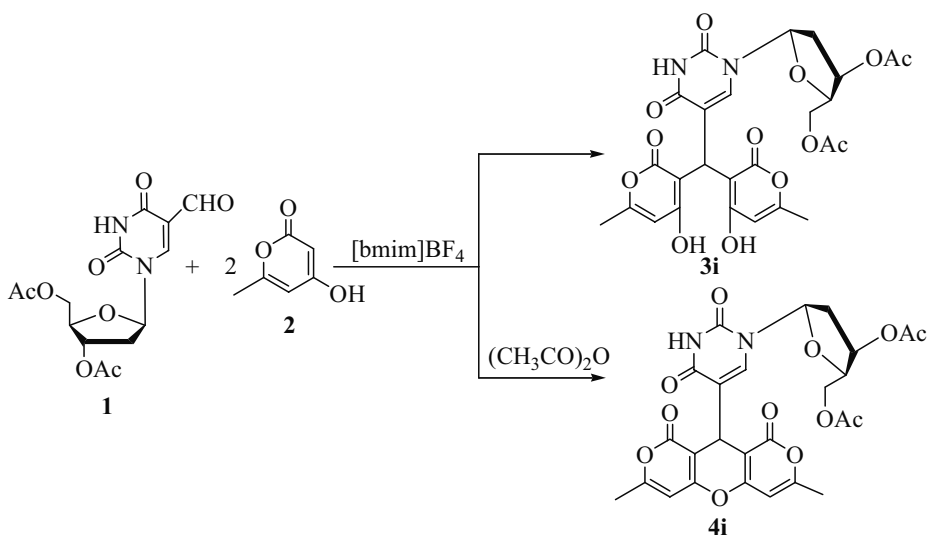
Experimental

Melting points were measured by a Kofler micromelting point apparatus and were uncorrected. ^{1}H NMR spectra were determined on a Bruker AC 400 spectrometer as $CDCl_3$ or DMSO-d_6 solutions. Chemical shifts (δ) were expressed in ppm downfield from the internal standard tetramethylsilane and coupling constants *J* were given in Hz. Mass spectra were obtained in ESI mode using a Bruker Esquire 3000 mass spectrometer. The HRMS (high resolution mass spectra) were performed on a JEOL HX 110A spectrometer. Elemental analyses were performed on an EA-1110 instrument.

*General procedure for the preparation of arylbis(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)methane derivatives* (**3**)

To 1 mL of [bmim][BF_4] was added aldehyde (**1**, 1 mmol) and 4-hydroxy- 6-methylpyran-2-one (**2**, 2 mmol). The reaction mixture was stirred at 80 °C until a complete reaction (monitored by TLC). Then, the mixture was cooled to room temperature and 1 mL of 50% ethanol in water was added. The solids were collected by suction and rinsed with ethanol, and then dried to give **3** with high purity. The ionic liquid layer was dried at 100°C under reduced pressure to recover the ionic liquid.

*Bis(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)(4-nitrophenyl) methane* (**3a**): M.p. 215–217 °C (lit.[17] 214–217 °C); ^{1}H NMR ($CDCl_3$) δ: 2.32 (s, 6H, 2 × CH_3), 5.78 (s, 1H, CH), 6.11 (s, 2H, 2 × CH), 7.33



Scheme 5

Table 3 Preparation of **3a** in different solvents

Entry	Solvent	Temperature/°C	Product	Reaction time/h	Yield/%
1	[bmim][BF_4]	80	**3a**	2	95
2	Ethanol	Reflux	**3a**	3	45
3	Methanol	Reflux	**3a**	3	35
4	Toluene	80	**3a**	3	30
5	THF	Reflux	**3a**	3	35

(d, 2H, J = 8.8 Hz, ArH), 8.17 (d, 2H, J = 8.8 Hz, ArH), 10.81 (br s, 1H, OH), 10.94 (br s, 1H, OH); MS: m/z 408 $[M + Na]^+$.

*Bis(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)phenylmethane* (**3b**): M.p. 214–215 °C (lit.[17] 214–215 °C); ^{1}H NMR ($CDCl_3$) δ: 2.31 (s, 6H, 2 × CH_3), 5.78 (s, 1H, CH), 6.05 (s, 1H, CH), 6.12 (s, 1H, CH), 7.17–7.35 (m, 5H, ArH), 10.75 (br s, 1H, OH), 11.00 (br s, 1H, OH); MS: m/z 363 $[M + Na]^+$.

*(4-Fluorophenyl)bis(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl) methane* (**3c**): M.p. 202–204 °C; ^{1}H NMR ($CDCl_3$) δ: 2.31 (s, 6H, 2 × CH_3), 5.74 (s, 1H, CH), 6.09 (s, 2H, 2 × CH), 6.98–7.15 (m, 4H, ArH), 10.81 (br s, 1H, OH), 10.97 (br s, 1H, OH); ^{13}C NMR ($CDCl_3$) δ: 19.64, 34.20, 103.32, 115.19, 115.41, 127.99, 128.07, 130.96, 131.00, 160.37, 162.81; MS: m/z 381 $[M + Na]^+$. Anal. Calcd for $C_{19}H_{15}FO_6$: C, 63.69; H, 4.22. Found: C, 63.80; H, 4.12%.

*(4-Chlorophenyl)bis(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl) methane* (**3d**): M.p. 201–203 °C (lit.[17] 202–205 °C); ^{1}H NMR ($CDCl_3$) δ: 2.30 (s, 6H, 2 × CH_3), 5.76 (s, 1H, CH), 6.10 (s, 2H, 2 × CH), 7.03 (d, 2H, J = 8.8 Hz, ArH), 7.23 (d, 2H, J = 8.8 Hz, ArH), 11.2 (br s, 2H, 2 × OH); MS: m/z 397 $[M + Na]^+$.

*Bis(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)(4-methylphenyl) methane* (**3e**): M.p. 186–187 °C; ^{1}H NMR ($CDCl_3$) δ: 2.20 (s, 6H, 2 × CH_3), 2.24 (s, 3H, CH_3), 5.93 (s, 1H, CH), 6.08 (s, 2H, 2 × CH), 6.86 (d, 2H, J = 8.0 Hz, ArH), 7.03 (d, 2H, J = 8.0 Hz, ArH), 11.70 (br s, 2H, 2 × OH); ^{13}C NMR ($CDCl_3$) δ: 19.52, 20.93, 33.91, 101.80, 102.17, 126.81, 129.12, 135.00, 136.75, 161.61, 166.77, 168.53; MS: m/z 377 $[M + Na]^+$. Anal. Calcd for $C_{20}H_{18}O_6$: C, 67.79; H, 5.12. Found: C, 67.90; H, 5.06%.

*Bis(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)(4-methoxyphenyl) methane* (**3f**): M.p. 173–175 °C (lit.[17] 174–176 °C); ^{1}H NMR ($CDCl_3$) δ: 2.27 (s, 6H, 2 × CH_3), 3.72 (s, 3H, OCH_3), 5.78 (s, 1H, CH), 6.05 (s, 2H, 2 × CH), 6.78 (d, 2H, J = 7.2 Hz), 7.13 (d, 2H, J = 7.2 Hz, ArH), 10.99 (br s, 2H, 2 × OH); MS: m/z 393 $[M + Na]^+$.

*(4-Cyanophenyl)bis(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl) methane* (**3g**): M.p. 201–203 °C; ^{1}H NMR (DMSO-d_6) δ: 2.18 (s, 6H, 2 × CH_3), 5.82 (s, 1H, CH), 6.03 (s, 2H, 2 × CH), 7.20 (d, 2H, J = 8.0 Hz, ArH), 7.67 (d, 2H, J = 8.0 Hz, ArH); ^{13}C NMR (DMSO-d_6) δ: 19.59, 35.70, 101.10, 101.38, 108.71, 119.53, 128.46, 132.23, 147.47, 161.72, 165.78, 168.09; MS: m/z 388 $[M + Na]^+$. Anal. Calcd for $C_{20}H_{15}NO_6$: C, 65.75; H, 4.14; N, 3.83. Found: C, 65.88; H, 4.02; N, 3.70%.

*Bis(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)(4-trifluoromethyl-phenyl)methane* (**3h**): M.p. 184–186 °C; ^{1}H NMR (DMSO-d_6) δ: 2.19 (s, 6H, 2 × CH_3), 5.87 (s, 1H, CH), 6.05 (s, 2H, 2 × CH), 7.23 (d, 2H, J = 8.0 Hz, ArH), 7.58 (d, 2H, J = 8.0 Hz, ArH); ^{13}C NMR (DMSO-d_6) δ: 19.58, 35.29, 101.36, 101.53, 125.21, 128.07, 146.12, 161.64, 165.95, 168.23; MS: m/z 431 $[M + Na]^+$. Anal. Calcd for $C_{20}H_{15}F_3O_6$: C, 58.83; H, 3.70. Found: C, 58.72; H, 3.80%.

*Bis(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)[4-(3,5-di-*O*-acetyl-2-deoxy-β-D-ribosyl)-1,2,3,4-tetrahydropyrimidin-5-yl]methane* (**3l**): M.p. 208–209 °C; ^{1}H NMR (DMSO-d_6) δ: 1.99 (s, 3H, CH_3), 2.06 (s, 3H, CH_3), 2.12 (s, 6H, 2 × CH_3), 2.15–2.18 (m, 1H, 2'-H1), 2.32–2.35 (m, 1H, 2'-H2), 4.02–4.05 (m, 2H, 5'-H), 4.15–4.17 (m, 1H, 4'-H), 5.11–5.13 (m, 1H, 3'-H), 5.23 (s, 1H, CH), 5.90 (s, 1H, CH), 5.91 (s, 1H, CH), 6.05–6.08 (m, 1H, 1'-H), 6.93 (s, 1H, CH), 11.26 (br s, 3H, NH, 2 × OH); MS: m/z 597 $[M + Na]^+$. HRMS (FAB) Calcd for $C_{26}H_{26}N_2O_{13}$: 575.1513 $(MH)^+$. Found: 575.1520.

General procedure for the preparation of 3,6,9-trioxanthracene (**4**)
To 1 mL of [bmim][BF_4] were added aldehyde (**1**, 1 mmol), 4-hydroxy-6-methylpyran-2-one (**2**, 2 mmol) and 0.2 mL acetic anhydride. The reaction mixture was stirred at 100 °C till a complete reaction (monitored by TLC). Acetic anhydride was removed under reduced pressure and the mixture was cooled to room temperature. Then, 1 mL of 50% ethanol in water was added. The solids thus formed were collected and recrystallised from ethanol to give **4** with high purity.

*3,7-Dimethyl-10-(4-nitrophenyl)-1*H*,9*H*,10*H*-dipyrano[4,3-*b*:3,4-*e*]pyran-1,9-dione* (**4a**): M.p. 290–291 °C (lit.[13] 289–291 °C); ^{1}H NMR (DMSO-d_6) δ: 2.24 (s, 6H, 2 × CH_3), 4.71 (s, 1H, CH), 6.52 (s, 2H, 2 × CH), 7.56 (d, 2H, J = 8.8 Hz, ArH), 8.13 (d, 2H, J = 8.8 Hz, ArH); MS: m/z 390 $[M + Na]^+$.

*3,7-Dimethyl-10-phenyl-1*H*,9*H*,10*H*-dipyrano[4,3-*b*:3,4-*e*]pyran-1,9-dione* (**4b**): M.p. 295–296 °C (lit.[12] 297–298 °C); ^{1}H NMR (DMSO-d_6) δ: 2.23 (s, 6H, 2 × CH_3), 4.56 (s, 1H, CH), 6.30 (s, 2H, 2 × CH), 7.08–7.26 (m, 5H, ArH); MS: m/z 345 $[M + Na]^+$.

*3,7-Dimethyl-10-(4-fluorophenyl)-1*H*,9*H*,10*H*-dipyrano[4,3-*b*:3,4-*e*]pyran-1,9-dione* (**4c**): M.p. 274–276 °C; ^{1}H NMR (DMSO-d_6) δ: 2.23 (s, 6H, 2 × CH_3), 4.56 (s, 1H, CH), 6.47 (s, 2H, 2 × CH), 7.06–7.30 (m, 4H, ArH); ^{13}C NMR (DMSO-d_6) δ: 19.76, 33.19, 98.59, 102.25, 115.13, 115.20, 130.81, 130.89, 158.59, 161.91, 163.42; MS: m/z 363 $[M + Na]^+$. Anal. Calcd for $C_{19}H_{13}FO_5$: C, 67.06; H, 3.85. Found: C, 67.15; H, 3.78%.

*10-(4-Bromophenyl)-3,7-dimethyl-1*H*,9*H*,10*H*-dipyrano[4,3-*b*:3,4-*e*]pyran-1,9-dione* (**4d**): M.p. 294–295 °C (lit.[13] 293–295 °C); ^{1}H NMR (DMSO-d_6) δ: 2.25 (s, 6H, 2 × CH_3), 4.68 (s, 1H, CH), 6.39 (s, 2H, 2 × CH), 7.16 (d, 2H, J = 8.0 Hz, ArH), 7.38 (d, 2H, J = 8.0 Hz, ArH); MS: m/z 423 $[M + Na]^+$.

*3,7-Dimethyl-10-(4-methylphenyl)-1*H*,9*H*,10*H*-dipyrano[4,3-*b*:3,4-*e*]pyran-1,9-dione* (**4e**): M.p. 282–283 °C (lit.[13] 282–284 °C); ^{1}H NMR (DMSO-d_6) δ: 2.23 (s, 9H, 3 × CH_3), 4.51 (s, 1H, CH), 6.46 (s, 2H, 2 × CH), 7.06 (d, 2H, J = 8.0 Hz, ArH), 7.11 (d, 2H, J = 8.0 Hz, ArH); MS: m/z 359 $[M + Na]^+$.

*10-(2-Chlorophenyl)-3,7-dimethyl-1*H*,9H,10*H*-dipyrano[4,3-b:3,4-e]pyran-1,9-dione* (**4f**): M.p. 268–270 °C (lit.[13] 271–273 °C); ^{1}H NMR (DMSO-d_6) δ: 2.26 (s, 6H, 2 × CH_3), 4.82 (s, 1H, CH), 6.16 (s, 2H, 2 × CH), 7.16–7.59 (m, 4H, ArH); MS: m/z 379 $[M + Na]^+$.

*10-(4-Cyanophenyl)-3,7-dimethyl-1*H*,9*H*,10*H*-dipyrano[4,3-b:3,4-e]pyran-1,9-dione* (**4g**): M.p. 270–273 °C; ^{1}H NMR (DMSO-d_6) δ: 2.24 (s, 6H, 2 × CH_3), 4.64 (s, 1H, CH), 6.50 (s, 2H, 2 × CH), 7.47 (d, 2H, J = 8.0 Hz, ArH), 7.74 (d, 2H, J = 8.0 Hz, ArH); ^{13}C NMR (DMSO-d_6) δ: 19.78, 34.26, 98.61, 101.37, 110.24, 119.11, 130.21, 132.44, 147.89, 158.89, 162.84, 163.83; MS: m/z 370 $[M + Na]^+$. Anal. Calcd for $C_{20}H_{13}NO_5$: C, 69.16; H, 3.77; N, 4.03. Found: C, 69.02; H, 3.88; N, 3.92%.

*3,7-Dimethyl-10-(4-trifluoromethylophenyl)-1*H*,9*H*,10*H*-dipyrano[4,3-b:3,4-e]pyran-1,9-dione* (**4h**): M.p. 241–242 °C; ^{1}H NMR (DMSO-d_6) δ: 2.22 (s, 6H, 2 × CH_3), 5.54 (s, 1H, CH), 6.35 (s, 2H, 2 × CH), 7.33 (d, 2H, J = 8.0 Hz, ArH), 7.63 (d, 2H, J = 8.0 Hz, ArH); ^{13}C NMR (DMSO-d_6) δ: 19.74, 33.99, 103.26, 112.76, 125.45, 128.97, 144.27, 160.63, 161.29, 163.52, 163.73, 167.21; MS: m/z 413 $[M + Na]^+$. Anal. Calcd for $C_{20}H_{13}F_3O_5$: C, 61.54; H, 3.36. Found: C, 61.62; H, 3.51%.

*3,7-Dimethyl-10-[4-(3,5-di-*O*-acetyl-2-deoxy-β-D-ribosyl)-1,2,3,4-tetrahydropyrimidin-5-yl]-*1H,9H,10H*-dipyrano[4,3-b:3,4-e]pyran-1,9-dione* (**4i**): M.p. 152–154 °C; ^{1}H NMR (DMSO-d_6) δ: 2.08 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 2.17 (s, 6H, 2 × CH_3), 2.30–2.40 (m, 2H, 2'-H), 4.20–4.32 (m, 4H, 5'-H, 4'-H, CH), 5.23–5.25 (m, 1H, 3'-H), 6.15–6.17 (m, 1H, 1'-H), 6.40 (s, 2H, 2 × CH), 7.75 (s, 1H, CH), 11.36 (br s, 1H, NH); ^{13}C NMR (DMSO-d_6) δ: 19.77, 21.06, 21.20, 29.08, 36.76, 64.27, 74.66, 81.98, 85.19, 98.64, 99.03, 111.04, 139.82, 150.34, 159.95, 160.03, 161.98, 162.05, 163.24, 163.35, 170.60, 170.70; MS: m/z 579 $[M + Na]^+$. HRMS (FAB) Calcd for $C_{26}H_{24}N_2O_{12}$: 557.1407 $(MH)^+$. Found: 557.1413.

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