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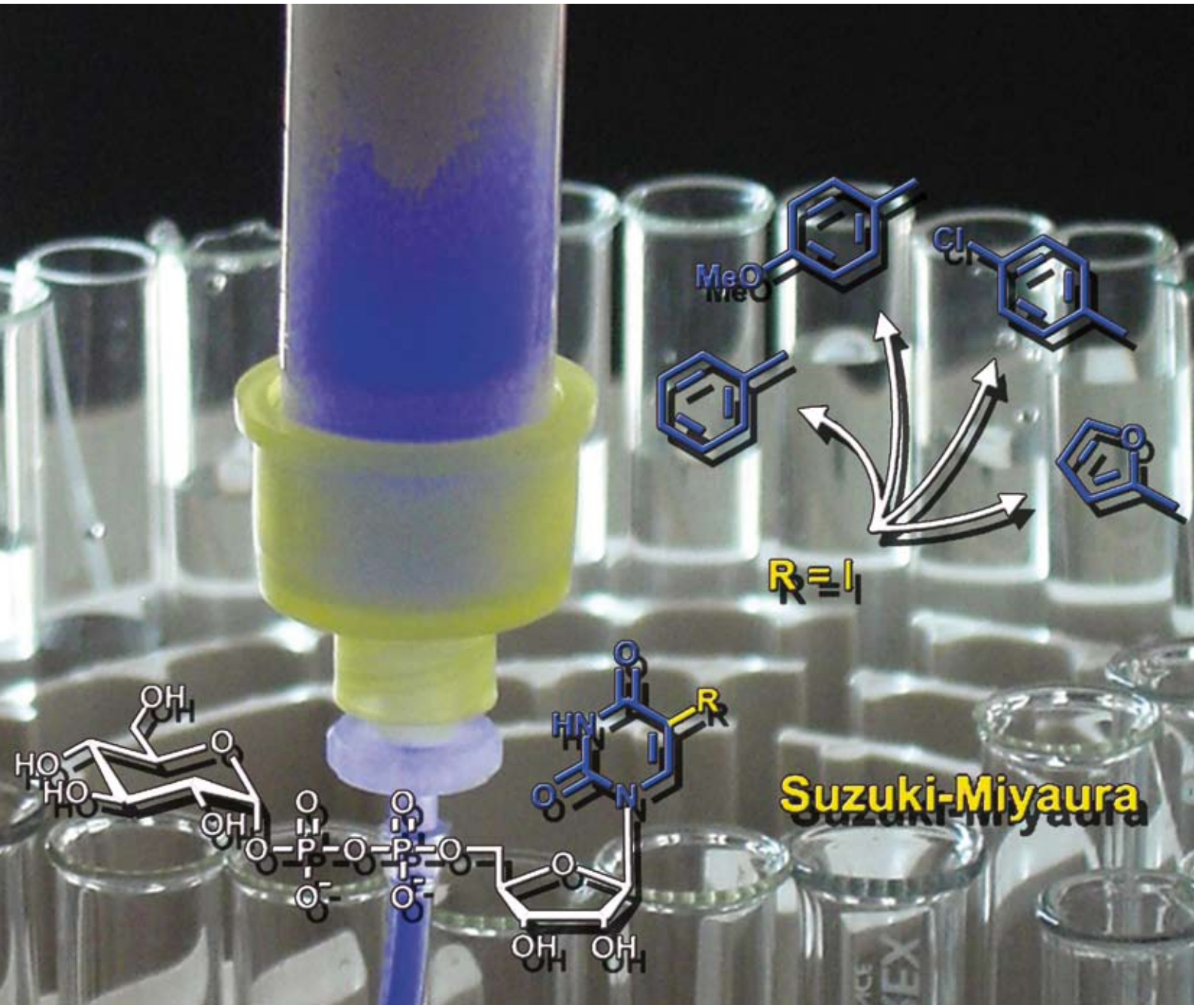

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Novel derivatives of UDP-glucose: concise synthesis and fluorescent properties†

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A series of novel 5-substituted UDP-glucose derivatives with interesting fluorescent properties and potential applications as sensors for carbohydrate-active enzymes is reported. An efficient synthesis of the target molecules was developed, centred around the Suzuki–Miyaura reaction of (hetero)arylboronic acids with 5-iodo UDP-glucose. Interestingly, the optimised cross-coupling conditions could also be applied successfully to 5-bromo UMP, but not to 5-bromo UDP-glucose.

Introduction

UDP-Sugars‡ like UDP-glucose (Fig. 1) and UDP-galactose are the natural donor substrates for a large number of carbohydrate-active enzymes, including glycosyltransferases and epimerases.[1] Many of these UDP-sugar-dependent enzymes are involved in important biological processes, such as the biosynthesis of blood group determinants,[2] the assembly of cell-surface glycoconjugates and cell wall components in (myco)bacteria[3a,b] and fungi,[3c] and galactose metabolism in trypanosomes.[4] Structural analogues of naturally occurring UDP-sugars are therefore sought after as inhibitor candidates and molecular tools for the investigation of these enzymes and processes.

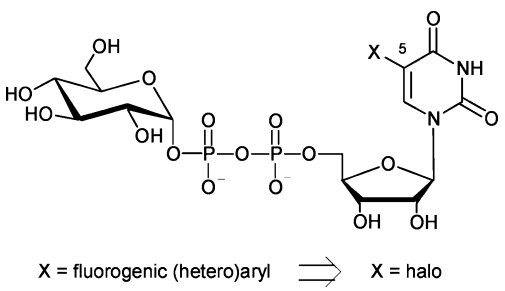

Fig. 1 UDP-glucose (X = H), and general synthetic strategy towards novel, fluorescent analogues.

Of particular interest in this context are fluorescently labelled UDP-sugars, which can be used in operationally simple glycosyltransferase bioassays. Previously, several UDP-sugars with a fluorophore connected *via* a linker to either the sugar[5,6] or, in one case, the nucleobase[6] have been described. The synthetic preparation of these analogues is usually carried out by multi-step synthesis from a fluorescently labelled precursor. Frequently, this approach involves lengthy protection–deprotection sequences, suffers from low overall yields, and is lacking the synthetic flexibility required for efficient analogue synthesis. In addition, the steric bulk of many conventional fluorophores may compromise the biological activity of the labelled UDP-sugars.[6]

As part of an ongoing effort to develop fluorescence-based glycosyltransferase assays, we have designed a novel type of fluorescent UDP-sugar with a compact, fluorogenic substituent at the uracil base (Fig. 1). Our target design was inspired by the recent discovery that uracil nucleosides and nucleotides with a small, heterocyclic substituent in position 5 possess interesting fluorescent properties.[7] We reasoned that this concept can also be applied to UDP-sugars, providing sugar-nucleotides sufficiently "auto-fluorescent" as to obviate the need for a bulky fluorophore.

Our synthetic strategy for the target 5-substituted UDP-sugars was devised with maximum structural flexibility in mind (Fig. 1). The fluorogenic aryl and heteroaryl substituents can be installed at the uracil base of a suitable halogenated precursor using Suzuki–Miyaura cross-coupling chemistry.[8] Taking advantage of recent advances in Pd-catalysed reactions in aqueous media,[9] we sought to carry out the cross-coupling directly on a preassembled 5-halo UDP-sugar substrate, in the final step of the synthesis. This approach facilitates analogue synthesis, thus allowing the rapid optimisation of biological and fluorescent properties.

Previously, we and others have described the cross-coupling of various unprotected purine[10] and pyrimidine[11] nucleotides. Recently, we have also reported the first example for the Suzuki–Miyaura reaction of an unprotected GDP-sugar.[12] However, to the best of our knowledge no cross-coupling reactions with unprotected UDP-sugars are known in the literature. This gap illustrates the substantial challenge associated with the use of UDP-sugars as cross-coupling substrates, due to the intrinsic susceptibility of *e.g.* the glycosyl phosphate linkage to hydrolytic cleavage.

Herein, we report the first successful Suzuki–Miyaura reaction of an unprotected 5-halo UDP-sugar. We describe the development of cross-coupling conditions compatible with the use of sugar-nucleotide substrates and investigate the parameters important for cross-coupling reactivity. We show, for the first time, that these conditions can also be applied to the efficient cross-coupling

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† Electronic supplementary information (ESI) available: ^{1}H, ^{13}C and ^{31}P NMR spectra for sugar-nucleotides **6a**, **6b**, **7a–d** and selected nucleosides and nucleotides; UV absorbance spectra for **6b** and **7a–d**. See DOI: 10.1039/b805216f

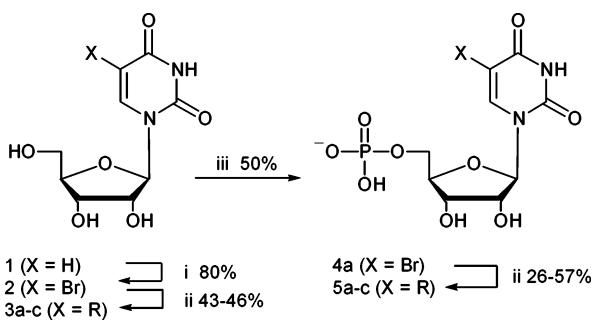
‡ Abbreviations: GDP guanosine diphosphate; UDP uridine diphosphate; UMP uridine monophosphate; TPPTS tris(3-sulfonatophenyl)phosphine trisodium salt.

of 5-bromouracil nucleotides. Using this methodology, we have prepared a series of four 5-(hetero)aryl UDP-glucose derivatives from a single synthetic precursor. These novel UDP-glucose analogues show interesting and differential fluorescent properties and may be useful for the development of glycosyltransferase bioassays. The synthetic method is robust and flexible, and may be applicable to the efficient preparation of other fluorescent UDP-sugars also.

Results and discussion

An important objective of the present study was the identification of suitably mild reaction conditions for the Suzuki–Miyaura cross-coupling of unprotected 5-halo UDP-sugars in aqueous solution. We decided to establish a suitable cross-coupling protocol using uracil nucleosides and nucleotides first, before attempting the more challenging cross-coupling of the corresponding sugar-nucleotides. We were particularly interested in using 5-bromouracil nucleosides and (sugar-)nucleotides as cross-coupling substrates, despite their potentially lower cross-coupling reactivity compared to the 5-iodo congeners, as the uracil base can be brominated selectively in position 5 under mild, aqueous conditions.[13] In principle, this would allow us to combine bromination and cross-coupling reaction in a one-pot, two-step procedure[12] in aqueous media, thus opening a very efficient synthetic route towards the target 5-(hetero)aryl UDP-glucose derivatives from commercially available UDP-glucose. However, while there is precedent for the cross-coupling of unprotected 5-iodouracil nucleotides[11] and nucleosides,[14] no examples have been reported for the successful use of the corresponding 5-bromo derivatives as Suzuki–Miyaura substrates.

The substrates required for the cross-coupling reaction, 5-bromouridine **2** and 5-bromo UMP **4a**, were prepared from uridine *via* Kumar's bromination method[13] and an adaptation of the original Yoshikawa protocol for the 5′-selective phosphorylation of unprotected nucleosides (Scheme 1).[15] The use of proton sponge[16] during this reaction helped accelerate the phosphorylation reaction, which is known to require prolonged reaction times for uracil nucleosides,[15] as well as suppress a potential bromine–chlorine exchange reaction in position 5.[16b]



Scheme 1 *Reagents and conditions*: i) NBS, NaN_3, 1,2-DME–H_2O, rt, 5 h; ii) Na_2Cl_4Pd (1 mol%), TPPTS (2.5 mol%), R-$B(OH)_2$, K_2CO_3, H_2O, 60 °C, 3 h; iii) $POCl_3$, proton sponge, MeCN, −5 °C, 4 h. For substituents R and individual yields see Table 1.

For the Suzuki–Miyaura cross-coupling of 5-bromouracil nucleosides and nucleotides, we initially investigated the suitability of a catalytic system composed of the water-soluble Pd source Na_2Cl_4Pd, the water-soluble phosphine ligand TPPTS‡[14b] and K_2CO_3 as the base. Reactions were carried out at 60 °C for 3 h, as we were concerned that elevated temperature and prolonged reaction times may promote decomposition under the basic conditions (*e.g.* by cleavage of the glycosidic bond). Under these conditions, the cross-coupling of both nucleoside **2** and nucleotide **4a** did afford the desired 5-aryl derivatives (Table 1). However, none of the cross-coupling reactions went to completion, and the cross-coupled products **3a–c** and **5a–c** were isolated in generally low to moderate yields. The problem of unsatisfactory yields due to incomplete conversion was further exacerbated by the loss of material during purification of the polar reaction products by chromatography. In order to improve the isolated yields, we therefore set out to identify a more reactive catalytic system for the cross-coupling of 5-bromo UMP **4a**.

Table 1 Suzuki–Miyaura coupling of 5-bromouridine **2** and 5-bromo UMP **4a** with various arylboronic acids R-$B(OH)_2$[a]

Entry	Substrate	Product	R	Yield[b] (%)
1	**2**	**3a**	Phenyl	45
2	**2**	**3b**	4-Methylphenyl	46
3	**2**	**3c**	4-Chlorophenyl	43
4	**4a**	**5a**	Phenyl	57
5	**4a**	**5b**	4-Methylphenyl	27
6	**4a**	**5c**	4-Chlorophenyl	26

[a] See Scheme 1 for structures. [b] Isolated yields.

The cross-coupling of **4a** with phenylboronic acid was chosen as a model reaction for the optimisation of ligand and catalytic base (Table 2). Neither an increase in the amount of K_2CO_3 (entries 1–3) nor use of a stronger base (entries 4–6) improved cross-coupling efficiency. However, replacement of K_2CO_3 with Cs_2CO_3 resulted in a substantially higher yield of 5-phenyl UMP **5a** (entry 7). No decomposition or side reactions were observed under these conditions, and any loss of material occurred only during purification by ion-pair chromatography. The use of additional equivalents of Cs_2CO_3 gave a reduced isolated yield (entry 8), as previously observed for K_2CO_3 and NaOH. This finding may be due to the deprotonation of the 5-bromouracil ring in position 3 in the presence of a large excess of base, deactivating the heterocycle for the cross-coupling reaction and/or facilitating coordination of the palladium catalyst.[14b] The superiority of Cs_2CO_3 over K_2CO_3 in the cross-coupling of 5-bromo UMP appears to be independent

Table 2 Optimisation of conditions for the Suzuki–Miyaura coupling of 5-bromo UMP **4a** with phenylboronic acid[a]

Entry	Ligand[b]	Base	Yield[c] (%)
1	TPPTS	K_2CO_3 (2 eq.)	57
2	TPPTS	K_2CO_3 (5 eq.)	23
3	TPPTS	K_2CO_3 (10 eq.)	0
4	TPPTS	NaOH (2 eq.)	0
5	TPPTS	NaOH (5 eq.)	17
6	TPPTS	NaOH (10 eq.)	0
7	TPPTS	Cs_2CO_3 (2 eq.)	71
8	TPPTS	Cs_2CO_3 (10 eq.)	18
9	Buchwald ligand	Cs_2CO_3 (2 eq.)	53
10	Kirschning ligand	Cs_2CO_3 (2 eq.)	34

[a] See Scheme 1 for structures; other conditions: Na_2Cl_4Pd (1 mol%), H_2O, 60 °C, 2 h. [b] 2.5 mol%. [c] Isolated yields.

from the nature of the leaving group, as similar observations have previously been reported for the cross-coupling of 5-iodouridine nucleotides.[11b]

Next, we investigated the influence of alternative ligands, in combination with Na_2Cl_4Pd as the Pd source, on cross-coupling efficiency. Neither a water-soluble, phosphine-based ligand recently introduced by the Buchwald group for the cross-coupling of aryl chlorides and sterically hindered aryl bromides in water,[17a] nor a water-insoluble, 4-pyridine-aldoxime-based ligand developed by Kirschning and coworkers[17b] offered any advantage over TPPTS (Table 2, entries 9 and 10). From these reactions, **5a** was isolated in slightly or clearly lower yield.

Following optimisation of the catalytic system, we required 5-bromo UDP-glucose **6a** as the sugar-nucleotide substrate for the Suzuki–Miyaura cross-coupling (Scheme 2). We envisaged to prepare **6a** from the corresponding nucleoside monophosphate **4a** and glucose-1-phosphate. This approach involves activation of the phosphate group in **4a** in the form of *e.g.* the phosphoromorpholidate, followed by acid-catalysed formation of the pyrophosphate bond. Previously, we have successfully used $MnCl_2$ as a catalyst for this type of transformation in the synthesis of GDP-sugars.[12] However, while the conversion of nucleotide **4a** into its morpholidate proceeded smoothly, all attempts to react this morpholidate under $MnCl_2$-catalysis with glucose-1-phosphate to UDP-sugar **6a** failed. We finally resorted to activating nucleotide **4a** with the classical carbonyldiimidazole method.[18] Thus, **4a** was converted into the corresponding imidazolide and reacted *in situ* with glucose-1-phosphate, to provide sugar-nucleotide **6a** in 38% yield.

With both the optimised catalytic system and the required substrate for the cross-coupling in hand, we attempted the direct Suzuki–Miyaura reaction of UDP-sugar **6a** with phenylboronic acid (Scheme 2). Surprisingly, this reaction was unsuccessful under our optimised conditions (Table 3, entry 1). No cross-coupling product could be detected by TLC after 4 hours at 50 °C when decomposition of the sugar-nucleotide set in and the reaction was stopped. The lack of cross-coupling reactivity of sugar-nucleotide **6a** was particularly intriguing as the corresponding 5-bromouracil nucleoside **2** and nucleotide **4a** had both proved to be sufficiently reactive under these conditions.

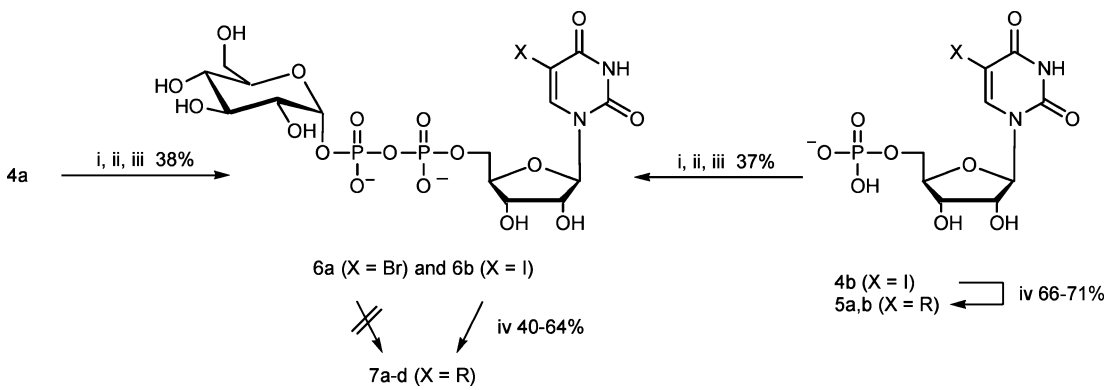
It is well known that (hetero)aryl iodides are generally more reactive in cross-coupling reactions than the corresponding bromide analogues.[19] Faced with the non-reactivity of **6a**, we therefore selected 5-iodo UDP-glucose **6b** as an alternative cross-coupling substrate, in order to gain access to the target 5-(hetero)aryl UDP-glucose derivatives (Scheme 2). In analogy to the synthesis of **6a**, **6b** was prepared from the corresponding nucleoside monophosphate **4b** and glucose-1-phosphate using the carbonyldiimidazole method. Gratifyingly, and in contrast to the unsuccessful cross-coupling of **6a**, the reaction of 5-iodo UDP-glucose **6b** with phenylboronic acid proceeded smoothly to afford 5-phenyl UDP-glucose **6a** in 64% yield after 1 h (Table 3, entry 2). To determine the scope of the reaction conditions, we then synthesised a small family of UDP-glucose derivatives with different aromatic and heteroaromatic substituents at position 5 (Table 3, entries 3–5). The cross-coupling reactions were successful with both electron-rich and electron-deficient (hetero)aromatic boronic acids, and the desired 5-substituted UDP-glucose derivatives **7b–d** were obtained in 40–58% isolated yield.

Table 3 Suzuki–Miyaura coupling of **4b**, **6a**, and **6b** with various arylboronic acids R-B(OH)$_2$[a]

Entry	Substrate	Product	R	Yield[b] (%)
1	**6a**	**7a**	Phenyl	0
2	**6b**	**7a**	Phenyl	64
3	**6b**	**7b**	4-Methoxyphenyl	58
4	**6b**	**7c**	4-Chlorophenyl	57
5	**6b**	**7d**	2-Furyl	40
6	**4b**	**5a**	Phenyl	71
7	**4b**	**5b**	4-Methylphenyl	66

[a] See Scheme 2 for structures. [b] Isolated yields.

At this point, we decided to carry out further experiments in order to better understand the differential cross-coupling reactivity of sugar-nucleotides **6a** and **6b**. It seemed to us that in the light of the successful cross-couplings with 5-bromouracil derivatives **2** and **4a**, the lack of reactivity observed for **6a** could not be explained by the potentially limited leaving group quality of the bromo substituent alone. Therefore, 5-iodo UMP **4b** was prepared from 5-iodouridine and reacted with phenylboronic acid, for direct comparison both with its 5-bromo congener **4a** and with the corresponding sugar-nucleotide **6b** (Table 3, entry 6). From this reaction, 5-phenyl UMP **5a** was obtained in 71% yield after 3 h, similar to the cross-coupling results obtained with both **4a**



Scheme 2 *Reagents and conditions*: i) carbonyldiimidazole, DMF, rt, 3 h; ii) MeOH; iii) glucose-1-phosphate, DMF, rt, 24 h; iv) Na_2Cl_4Pd (2.5 mol%), TPPTS (6.25 mol%), Cs_2CO_3, R-B(OH)$_2$, H_2O, 50 °C, 1 h. For substituents R and individual yields see Table 3.

and **6b**. The similar cross-coupling behaviour of 5-bromo UMP **4a**, 5-iodo UMP **4b**, and 5-iodo UDP-glucose **6b** suggests that neither a bromo leaving group, nor the sugar-nucleotide nature of the substrate are *per se* an obstacle to cross-coupling success.

It is known that the outcome of Suzuki–Miyaura reactions is strongly influenced by steric parameters, *e.g.* the accessibility of the substrate for the palladium–ligand catalytic complex.[19a] In order to investigate the possibility that **6a**, but not **6b**, may in solution adopt a conformation which restricts access of the palladium–ligand catalytic complex, we carried out a comparative conformational analysis of both sugar-nucleotides. In NOESY experiments with **6a**, NOE contacts were observed between protons H-6 and protons H-3′ (major NOE), H-1′ and H-5′ (Fig. 2). The close spatial proximity between H-6 and H-5′ strongly suggests a global conformation for this sugar-nucleotide in which the uracil base is oriented *anti* to the ribose ring, similar to the conformation of the 5-unsubstituted parent UDP-glucose.[20] In contrast, NOESY results for **6b** indicate that in solution, the 5-iodo congener exists predominantly in the *syn* conformation. For **6b**, a strong NOE signal was observed between protons H-6 and H-2′ and a weaker one between H-6 and H-1′, while no NOE contact was seen between H-6 and H-3′ or H-5′. In the *syn* conformation, the 5-iodo substituent in **6b** is pointing away from the glucose diphosphate group, and the 5 position is easily accessible for the Pd catalyst. Such easy access may not be granted in the *anti* conformation preferred by the 5-bromo analogue **6a**, where the 5-bromo substituent is facing towards the bulky glucose diphosphate moiety. Thus, the superior cross-coupling reactivity of **6b** may be attributed, at least in part, to the capacity of the bulky iodo substituent in **6b** to induce a conformation which is favourable for the insertion of the reactive Pd species during the oxidative addition step.

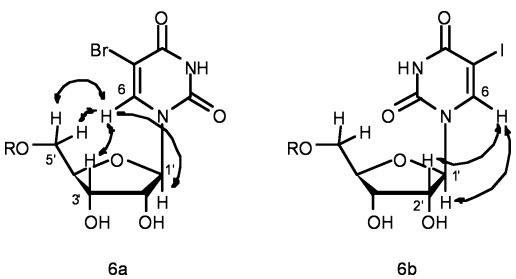


Fig. 2 Diagnostic NOE interactions, suggesting an *anti* conformation for **6a**, and a *syn* conformation for **6b** (R = glucosyl-1-diphosphate).

While 5-substituted uracil nucleosides and nucleotides have been used previously as fluorescent probes,[7] no fluorescent sugar-nucleotides of this type have so far been reported. In order to assess the suitability of the new 5-substituted UDP-glucose derivatives as fluorescent sensors, we have recorded UV absorbance and fluorescence spectra for **6b** and **7a–d**. The UV absorbance spectra of all 5-substituted UDP-glucose analogues show a low energy absorbance band, which lies at ~280 nm for the 5-phenyl derivatives (**7a–c**), at 287 nm for 5-iodo UDP-glucose **6b**, and at 314 nm for 5-(2-furyl) UDP-glucose **7d**.† In aqueous solution, all analogues were fluorescence emissive upon excitation at the absorbance maximum (Fig. 3). As expected, their fluorescent properties are strongly influenced by the nature of the substituent in position 5 (Table 4). While 5-iodo UDP-glucose **6b** is almost non-fluorescent, the 5-(hetero)aryl-substituted derivatives are weakly (**7a** and **7c**) or strongly (**7b** and **7d**) fluorescent. Among the three phenyl-substituted derivatives, the electron-rich 4-methoxy analogue **7b** stands out with its relatively large Stokes shift and strong fluorescence emission. Only **7d**, whose furan substituent is known as a strong fluorescence emitter[7] but more difficult to install than a phenyl substituent (*cf.* Table 3 for yields), can compare with **7b** in terms of fluorescence intensity. Of the new UDP-glucose derivatives presented herein, **7b** and **7d** may therefore be particularly useful as biological sensors for carbohydrate-active enzymes, and investigations into their biological activity are currently under way.

Table 4 Fluorescence spectroscopic properties of UDP-Glc derivatives

Compound	λ_{ex}/nm	λ_{em}/nm	Stokes shift[a]/cm^{-1}
6b	287	377	8318
7a	278	403	11157
7b	278	444	13449
7c	281	398	10462
7d	314	437	8963

[a] Stokes shift = $(1/\lambda_{ex} - 1/\lambda_{em})$.

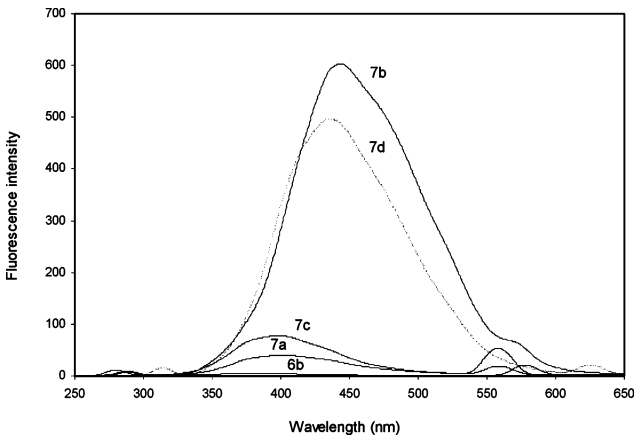


Fig. 3 Fluorescence emission spectra for UDP-glucose derivatives **6b** and **7a–d** in H_2O (c = 100 μM in H_2O).

Conclusions

In this study, we have shown that installation of an aromatic or heteroaromatic substituent at position 5 of UDP-glucose yields a novel type of fluorescent analogue, whose fluorescent properties can be modulated by the nature of the fluorogenic substituent. We have developed an efficient synthetic route towards the target molecules *via* Suzuki–Miyaura cross-coupling of 5-iodo UDP-glucose **6b**, which may be applicable to the preparation of other fluorescent UDP-sugars also. Interestingly, under otherwise identical conditions the cross-coupling reaction was unsuccessful with 5-bromo UDP-glucose **6a** as the substrate. Results from NOESY experiments suggest that the differential cross-coupling reactivity of 5-bromo UDP-glucose **6a** and its 5-iodo congener **6b** is due at least in part to conformational differences between the two sugar-nucleotides in solution. Investigations into the biological properties of the novel UDP-sugars described herein are currently

under way, and results from these studies will be reported in due course.

Experimental

General

All chemicals were obtained commercially and used as received unless stated otherwise. TLC was performed on precoated aluminium plates (Silica Gel 60 F_{254}, Merck). Compounds were visualized by exposure to UV light. NMR spectra were recorded at 298 K on a Varian VXR 400 S spectrometer or on a Bruker Avance DPX-300 spectrometer. Chemical shifts (δ) are reported in ppm and, for solutions in D_2O, are referenced to methanol (δ_H 3.34, δ_C 49.50). Coupling constants (J) are reported in Hz. Resonance allocations were made with the aid of COSY and HSQC experiments. NOESY measurements were carried out with a relaxation delay of 1.000 s and a mixing time of 0.200 s. High resolution electrospray ionisation mass spectra (HR ESI-MS) were obtained on a Finnigan MAT 900 XLT mass spectrometer at the EPSRC National Mass Spectrometry Service Centre, Swansea. UV absorbance measurements were carried out on a Perkin Elmer Lambda 25 UV/VIS spectrometer. Fluorescence spectra were recorded on a PerkinElmer LS-45 spectrometer at ambient temperature. Samples were measured in aqueous solution at a concentration of 100 μM in a quartz micro fluorescence cell (path length 1.0 cm). Preparative chromatography was performed on a Biologic LP chromatography system equipped with a peristaltic pump and a 254 nm UV Optics Module under the following conditions.

Purification method 1. Ion-pair chromatography was performed using Lichroprep RP-18 resin, gradient 0–10% MeCN against 0.05 M TEAB (triethylammonium bicarbonate) over 480 mL, flow rate 5 mL min^{-1}. Product-containing fractions were combined and reduced to dryness. The residue was co-evaporated repeatedly with methanol to remove residual TEAB.

Purification method 2. Anion exchange chromatography was performed using a Macro prep 25Q resin, gradient 0–100% 1 M TEAB (pH 7.3) against H_2O over 480 mL, flow rate 5 mL min^{-1}. Product-containing fractions were combined and reduced to dryness. The residue was co-evaporated repeatedly with methanol to remove residual TEAB.

5-Bromouridine (2)

N-Bromosuccinimide (1.6 g, 9.0 mmol) was added to a stirred suspension of uridine **1** (2.0 g, 8.2 mmol) in 1,2-dimethoxyethane (100 mL) at 25 °C. The mixture was stirred for 5 minutes. To the clear solution was added a solution of sodium azide (2.15 g, 32 mmol) in water (6.0 mL). The reaction turned bright yellow, accompanied by the separation of a colourless oil. The yellow colour disappeared slowly while the oily material remained. After stirring for 2 h, TLC (30% methanol in chloroform, Rf 0.62; Rf_{SM} 0.45) showed complete conversion of starting material. The solvents were removed under vacuum to give a pale yellow, amorphous solid. The crude material was purified by column chromatography (silica; 15% methanol in $CHCl_3$). Initially, a colourless oil was obtained which was dried under vacuum overnight to give a white solid. Recrystallisation from dry ethanol gave 5-bromouridine **2** as white crystals in 80% yield (2.11 g). δ_H (400 MHz, DMSO-d_6) 3.49–3.71 (2H, m, H-5′), 3.82–3.86 (1H, m, H-4′), 3.92 (1H, t, J = 5.6 Hz, H-3′), 4.03 (1H, dd, J = 3.6 and 5.2 Hz, H-2′), 5.05 (1H, d, J = 5.1 Hz, OH-3′), 5.26 (1H, t, J = 4.6 Hz, OH-5′), 5.41 (1H, d, J = 4.2 Hz, OH-2′), 5.70 (1H, d, J = 3.9 Hz, H-1′), 8.46 (1H, s, H-6), 11.80 (1H, s, NH); δ_C (75.5 MHz, DMSO-d_6) 60.2 (C-5′), 69.3 (C-3′), 74.0 (C-2′), 84.8 (C-4′), 88.6 (C-1′), 95.9 (C-5), 140.4 (C-6), 150.3 (C-2), 159.5 (C-4). m/z (ESI) 322.9872 $[M + H]^+$, $C_9H_{12}O_6N_2Br^{79}$ requires 322.9873.

General method A: Suzuki–Miyaura cross-coupling of 5-bromouridine

A 2-necked round bottom flask with 5-bromouridine **2** (1 eq.), arylboronic acid (1.5 eq.) and K_2CO_3 (2 eq.) was purged with N_2. Upon addition of TPPTS (0.025 eq.), Na_2Cl_4Pd (0.01 eq.) and degassed H_2O (5 mL) the mixture turned orange in colour. The reaction was stirred under N_2 for 3 h at 60 °C, turning brown–black. Once the starting material was fully consumed, the reaction mixture was cooled to room temperature. The pH was adjusted to 7 with HCl 1% and the reaction mixture was filtered through Celite. The solvents were removed to give a white powder, which was purified by column chromatography (silica; gradient of 0–15% methanol in chloroform).

5-Phenyluridine (3a). The title compound was prepared from **2** (50 mg, 155 μmol) and phenylboronic acid according to general method A. After recrystallisation from absolute ethanol, **3a** was obtained in colourless crystals in 45% yield (22.4 mg). δ_H (400 MHz, DMSO-d_6) 3.52–3.68 (2H, m, H-5′), 3.84–3.88 (1H, m, H-4′), 3.97–4.14 (2H, m, H-2′, H-3′), 5.07 (1H, d, J = 4.8 Hz, OH-3′), 5.20 (1H, t, J = 4.5 Hz, OH-5′), 5.41 (1H, d, J = 5.4 Hz, OH-2′), 5.82 (1H, d, J = 3.0 Hz, H-1′), 7.24–7.56 (5H, m, Ph), 8.25 (1H, s, H-6), 11.5 (1H, br s, NH); δ_C (75.5 MHz, DMSO-d_6) 60.5 (C-5′), 69.3 (C-3′), 74.7 (C-2′), 84.6 (C-4′), 88.2 (C-1′), 108.3 (C-5), 127.7, 127.9, 128.0 (Ph), 137.6 (C-6), 147.2 (C-2), 162.0 (C-4). m/z (ESI) 321.1081 $[M + H]^+$, $C_{15}H_{17}O_6N_2$ requires 321.1087.

5-(4-Methylphenyl)uridine (3b). The title compound was obtained from **2** (50 mg, 155 μmol) and 4-methylphenylboronic acid according to general method A in 46% yield (24.0 mg). δ_H (400 MHz, DMSO-d_6) 2.30 (3H, s, Me), 3.50–3.72 (2H, m, H-5′), 3.82–3.90 (1H, m, H-4′), 3.96–4.05 (1H, m, H-3′), 4.07–4.15 (1H, m, H-2′), 5.10 (1H, s, OH-3′), 5.22 (1H, s, OH-5′), 5.44 (1H, s, OH-2′), 5.86 (1H, d, J = 4.5 Hz, H-1′), 7.17 (2H, d, J = 6.6 Hz, *m*Ph), 7.43 (2H, d, J = 8.4 Hz, *o*Ph), 8.24 (1H, s, H-6′), 11.42 (1H, br s, NH). δ_C (75.5 MHz, DMSO-d_6) 20.6 (Me), 60.3 (C-5′), 69.6 (C-3′), 73.9 (C-2′), 84.7 (C-4′), 88.2 (C-1′), 113.4 (C-5), 127.8, 128.7, 130.3, 136.5 (Ph), 137.7 (C-6), 150.3 (C-2), 162.3 (C-4). m/z (ESI) 335.1236 $[M + H]^+$, $C_{16}H_{19}O_6N_2$ requires 335.1238).

5-(4-Chlorophenyl)uridine (3c). The title compound was obtained from **2** (20 mg, 62 μmol) and 4-chlorophenylboronic acid according to general method A in 43% yield (9.4 mg). δ_H (400 MHz, DMSO-d_6) 3.50–3.75 (2H, m, H-5′), 3.84–3.91 (1H, m, H-4′), 4.00–4.07 (1H, m, H-3′), 4.08–4.18 (1H, m, H-2′), 5.10 (1H, d, J = 3.9 Hz, OH-3′), 5.26 (1H, s, OH-5′), 5.46 (1H, d, J = 4.8 Hz, OH-2′), 5.82 (1H, d, J = 4.5 Hz, H-1′), 7.36–7.62 (4H, 2d, J = 8.4 and 8.7 Hz, Ph), 8.38 (1H, s, H-6′), 11.6 (1H, br s, NH); δ_C (75.5 MHz, DMSO-d_6) 60.1 (C-5′), 69.3 (C-3′), 74.0 (C-2′), 84.6 (C-4′), 88.5 (C-1′), 112.1 (C-5), 128.2, 129.6, 131.8, 132.1 (Ph),

138.6 (C-6), 150.2 (C-2), 162.1 (C-4). *m/z* (ESI) 355.0693 [M + H]$^+$, $C_{15}H_{16}O_6N_2Cl^{35}$ requires 355.0691.

5-Bromouridine-5′-monophosphate (4a)

A suspension of **2** (50 mg, 0.15 mmol) and proton sponge (199 mg, 0.9 mmol) in dry acetonitrile (3 mL) was cooled to −5 °C, and $POCl_3$ (58 μl, 0.6 mmol) was added dropwise. The orange-coloured reaction was stirred at −5 °C for 4 h, at which time TLC indicated near complete conversion (IPA–H_2O–NH_3 6 : 3 : 1; Rf 0.31; Rf_{SM} 0.71). The reaction was quenched with 50 mL of ice cold 0.2 M TEAB buffer. The pale orange solution was stirred for 1 h at 0 °C. After warming to 25 °C, the aqueous layer was washed with ethyl acetate (3×) and concentrated under reduced pressure. The crude residue was purified sequentially by purification methods 1 and 2 to provide **4a** in its triethylammonium salt form as a colourless, glassy solid in 50% yield (31.2 mg). δ_H (400 MHz, D_2O) 4.03–4.16 (2H, m, H-5′), 4.23–4.27 (1H, m, H-4′), 4.30 (1H, t, J = 4.8, H-3′), 4.34 (1H, t, J = 5, H-2′), 5.93 (1H, d, J = 4.8 Hz, H-1′), 8.24 (1H, s, H-6); δ_C (75.5 MHz, D_2O) 64.9 (C-5′), 70.3 (C-3′), 74.7 (C-2′), 84.2 (C-4′), 89.7 (C-1′), 97.7 (C-5), 141.3 (C-6), 152.0 (C-2), 162.7 (C-4); δ_P (121.5 MHz, D_2O) 7.5. *m/z* (ESI) 400.9391 [M − H]$^-$, $C_9H_{11}O_9N_2Br^{79}P$ requires 400.9393.

5-Iodouridine-5′-monophosphate (4b)

The title compound was prepared from 5-iodouridine[21] (480 mg, 1.3 mmol) by the procedure used in the synthesis of **4a**. The triethylammonium salt of **4b** was obtained as a colourless, glassy solid in 53% yield (307 mg). δ_H (400 MHz, D_2O) 3.96–4.10 (2H, m, H-5′), 4.20–4.27 (1H, m, H-4′), 4.31 (1H, t, J = 3.9 Hz, H-3′), 4.38 (1H, t, J = 5.1 Hz, H-2′), 5.92 (1H, d, J = 5.1 Hz, H-1′), 8.27 (1H, s, H-6); δ_C (75.5 MHz, D_2O) 64.8 (C-5′), 69.6 (C-5), 70.8 (C-3′), 74.6 (s, C-2′), 84.8 (d, J = 9.1 Hz, C-4′), 89.6 (C-1′), 147.1 (C-6), 152.8 (C-2), 164.3 (C-4); δ_P (121.5 MHz, D_2O) 7.6. *m/z* (ESI) 448.9255 [M − H]$^-$, $C_9H_{11}O_9N_2IP$ requires 448.9252.

General method B: Suzuki–Miyaura cross-coupling of 5-bromo UMP

A 2-necked round bottom flask with 5-bromouridine-5′-monophosphate **4a** (1 eq.), K_2CO_3 (2 eq.) and arylboronic acid (1.5 eq.) was purged with N_2. TPPTS (0.025 eq.), Na_2Cl_4Pd (0.01 eq.) and degassed H_2O (4 mL) were added, and the reaction was stirred under N_2 for 3 h at 60 °C. The reaction was cooled to room temperature, and the pH was adjusted to 7 with 1% HCl. The black suspension was concentrated under reduced pressure, and the residue was taken up in MeOH. The methanolic suspension was filtered through Celite, and the residue was washed with methanol. The combined filtrates were evaporated under reduced pressure, and the residue was purified using purification method 1.

5-Phenyluridine-5′-monophosphate (5a). The triethylammonium salt of the title compound was obtained as a glassy solid in 57% yield (11.5 mg) from **3a** (20 mg, 49.6 μmol) and phenylboronic acid according to general method B. δ_H (400 MHz, D_2O) 4.07–4.11 (2H, m, H-5′), 4.26–4.30 (1H, m, H-4′), 4.23 (1H, t, J = 4.8 Hz, H-3′), 4.45 (1H, t, J = 6.0 Hz, H-2′), 6.04 (1H, d, J = 5.6 Hz, H-1′), 7.42–7.54 (5H, m, Ph), 7.89 (1H, s, H-6); δ_C (75.5 MHz, D_2O) 65.1 (C-5′), 71.2 (C-3′), 74.6 (C-2′), 85.8 (C-4′), 89.8 (C-1′), 117.2 (C-5), 128.2, 129.4, 131.7 (Ph), 139.6 (C-6), 152.7 (C-2), 165.8 (C-4); δ_P (121.5 MHz, D_2O) 7.6. *m/z* (ESI) 399.0593 [M − H]$^-$, $C_{15}H_{16}O_9N_2P$ requires 399.0599.

5-(4-Methylphenyl)uridine-5′-monophosphate (5b). The triethylammonium salt of the title compound was obtained as a glassy solid in 27% yield (5.5 mg) from **3a** (20 mg, 49.6 μmol) and 4-methylphenylboronic acid according to general method B. δ_H (400 MHz, D_2O) 2.35 (3H, s, Me), 4.04–4.09 (2H, m, H-5′), 4.24–4.28 (1H, m, H-4′), 4.32 (1H, t, J = 4.6 Hz, H-3′), 4.44 (1H, t, J = 4.5 Hz, H-2′), 6.00 (1H, d, J = 4.5 Hz, H-1′), 7.29 (2H, d, J = 6.0, Ph), 7.39 (2H, d, J = 6.0 Hz, Ph), 7.80 (1H, s, H-6); δ_C (75.5 MHz, D_2O) 20.9 (Me), 65.0 (C-5′), 70.8 (C-3′), 74.1 (C-2′), 84.4 (C-4′), 89.4 (C-1′), 116.8 (C-5), 129.4, 130.1, 138.8 (Ph), 139.5 (C-6), 154.1 (C-2), 165.5 (C-4); δ_P (121.5 MHz, D_2O) 7.6. *m/z* (ESI) 413.0753 [M − H]$^-$, $C_{16}H_{18}O_9N_2P$ requires 413.0755.

5-(4-Chlorophenyl)uridine-5′-monophosphate (5c). The triethylammonium salt of the title compound was obtained as a glassy solid in 26% yield (5.5 mg) from **3a** (20 mg, 49.6 μmol) and 4-chlorophenylboronic acid according to general method B. δ_H (400 MHz, D_2O) 3.97–4.03 (2H, m, H-5′), 4.20–4.25 (1H, m, H-4′), 4.29 (1H, t, J = 4.7 Hz, H-3′), 4.43 (1H, t, J = 5.4 Hz, H-2′), 5.99 (1H, d, J = 5.7 Hz, H-1′), 7.40–7.55 (4H, m, Ph), 7.86 (1H, s, H-6); δ_C (75.5 MHz, D_2O), 65.0 (C-5′), 70.9 (C-3′), 74.3 (C-2′), 82.5 (s, C-4′), 89.6 (C-1′), 101.6 (C-5), 129.6, 129.9, 131.2 (Ph), 139.6 (C-6), 152.4 (C-2), 165.8 (C-4); δ_P (121.5 MHz, D_2O) 7.6. *m/z* (ESI) 433.0210 [M − H]$^-$, $C_{15}H_{15}O_9N_2Cl^{35}P$ requires 433.0209.

5-Bromouridine-5′-diphosphate-α-D-glucose (6a)

4a (43 mg, 0.11 mmol) was coevaporated with dry DMF (3×). Carbonyldiimidazole (35 mg, 0.21 mmol) was added and the flask was purged with N_2. Dry DMF (2 mL) was added, and the mixture was stirred at room temperature for 1 h. Once the formation of the phosphoroimidazolide was complete dry methanol (350 μL) was added to destroy excess carbonyldiimidazole. The reaction was stirred for 20 min, and the solvents were removed under reduced pressure. α-D-Glucose monophosphate (triethylammonium salt; 51 mg, 0.13 mmol) was coevaporated with DMF (3×) and dissolved in dry DMF (2 mL). Under N_2, this solution was added to the **4a**-imidazolide, and the reaction was stirred at room temperature for 24 h. Once TLC indicated complete consumption of the **4a**-imidazolide (IPA–H_2O–NH_3 6 : 3 : 1; Rf 0.40; Rf_{SM} 0.37; $Rf_{imidazolide}$ 0.71) all solvents were removed under reduced pressure, and the crude residue was purified sequentially by purification methods 1 and 2. The title compound was obtained in its triethylammonium salt form as a colourless, glassy solid in 38% yield (26 mg). δ_H (400 MHz, D_2O) 3.40–3.46 (1H, m, H-4″), 3.46–3.56 (1H, m, H-2″), 3.57–3.78 (4H, m, H-3″, H-5″ and H-6″), 4.20–4.26 (1H, m, H-5′), 4.26–4.30 (1H, m, H-4′), 4.34–4.40 (2H, m, H-2′, H-3′), 5.43 (1H, dd, J = 3.6 and 9.6 Hz, H-1″), 5.78 (1H, d, J = 4.4 Hz, H-1′), 8.06 (1H, s, H-6); δ_C (75.5 MHz, D_2O) 61.2 (C-6″), 65.9 (C-5′), 70.1 (C-4″), 70.4 (C-3′), 73.4 (C-2″), 73.7, 73.8 (C-3″/C-5″), 74.7 (C-2′), 84.2 (C-4′), 89.8 (C-1′), 96.6 (C-1″), 118.6 (C-5), 141.8 (C-6), 152.3 (C-2), 163.1 (C-4); δ_P (121.5 MHz, D_2O) −9.07 (d, J = 20.0 Hz), −7.57 (d, J = 22.2 Hz). *m/z* (ESI) 642.9586 [M − H]$^-$, $C_{15}H_{22}O_{17}N_2Br^{79}P_2$ requires 642.9583.

5-Iodouridine-5′-diphosphate-α-D-glucose (6b). The title compound was prepared from **4b** (137 mg, 0.30 mmol) by the procedure

used in the synthesis of **6a**. The triethylammonium salt of **6b** was obtained as a colourless, glassy solid in 37% yield (78 mg). δ_H (400 MHz, D_2O) 3.40–3.58 (2H, m, H-2″ and H-4″), 3.75–3.92 (4H, m, H-3″, H-5″ and H-6″), 4.18–4.25 (2H, m, H-5′), 4.25–4.29 (1H, m, H-4′), 4.32–4.42 (2H, m, H-2′, H-3′), 5.61 (1H, dd, $J = 3.6$ and 9.6 Hz, H-1″), 5.93 (1H, d, $J = 4.4$ Hz, H-1′), 8.25 (1H, s, H-6); δ_C (75.5 MHz, D_2O) 59.9 (C-5), 61.3 (C-6″), 66.0 (d, $J = 3.8$ Hz, C-5′), 70.2 (C-4″), 70.6 (C-3′), 72.6 (C-2″), 73.7, 73.8 (C-3″/C-5″), 74.7 (C-2′), 84.3 (d, $J = 9.1$ Hz, C-4′), 89.7 (C-1′), 96.6 (d, $J = 6.8$ Hz, C-1″), 147.0 (C-6), 152.8 (C-2), 164.4 (C-4); δ_P (121.5 MHz, D_2O) −9.21 (d, $J = 20.9$ Hz), −7.70 (d, $J = 21.1$ Hz). *m/z* (ESI) 690.9431 $[M - H]^-$, $C_{15}H_{22}O_{17}N_2IP_2$ requires 690.9444.

General method C: Suzuki–Miyaura cross-coupling of 5-iodouridine-5′-diphosphate-α-D-glucose

A 2-necked round bottom flask with 5-iodouridine-5′-diphosphate-α-D-glucose **6b** (20 mg, 0.029 mmol), Cs_2CO_3 (19 mg, 0.058 mmol) and arylboronic acid (0.043 mmol) was purged with N_2. TPPTS (0.9 mg, 1.8 μmol), Na_2Cl_4Pd (0.2 mg, 0.7 μmol) and degassed H_2O (4 mL) were added, and the reaction was stirred under N_2 for 1 h at 50 °C. Upon completion, the reaction was cooled to room temperature, and the pH was adjusted to 7 with 1% HCl. The black suspension was filtered through a membrane filter (0.45 μm). The filter was washed with H_2O, and the combined filtrates were evaporated under reduced pressure. The residue was purified sequentially by purification methods 2 and 1.

5-Phenyluridine-5′-diphosphate-α-D-glucose (7a). The triethylammonium salt of the title compound (TLC: IPA–H_2O–NH_3 6 : 3 : 1; Rf 0.58, Rf_{SM} 0.37) was obtained as a glassy solid in 64% yield (15.9 mg) from **6b** (20 mg, 29 μmol) and phenylboronic acid according to general method C. δ_H (400 MHz, D_2O) 3.38–3.46 (2H, m, H-2″ and H-4″), 3.71–3.92 (4H, m, H-3″, H-5″ and H-6″), 4.17–4.20 (2H, m, H-5′), 4.26–4.30 (1H, m, H-4′), 4.39 (1H, t, $J = 4.6$ Hz, H-3′), 4.47 (1H, t, $J = 5.4$ Hz, H-2′), 5.55 (1H, dd, $J = 3.2$ and 7.2 Hz, H-1″), 6.03 (1H, d, $J = 6.0$ Hz, H-1′), 7.4–7.6 (5H, m, Ph), 7.87 (1H, s, H-6); δ_C (75.5 MHz, D_2O) 61.0 (C-6″), 66.1 (C-5′), 69.9 (C-4″), 70.6 (C-3′), 72.2 (C-2″), 73.4, 73.6 (C-3″/C-5″), 74.0 (C-2′), 84.2 (C-4′), 89.3 (C-1′), 96.3 (C-1″), 117.0 (C-5), 129.2, 129.6, 132.4 (Ph), 139.3 (C-6), 152.4 (C-2), 165.6 (C-4); δ_P (121.5 MHz, D_2O) −9.26 (d, $J = 22.0$ Hz), −7.68 (d, $J = 20.4$ Hz). *m/z* (ESI) 641.0793 $[M - H]^-$, $C_{21}H_{27}O_{17}N_2P_2$ requires 641.0790.

5-(4-Methoxyphenyl)uridine-5′-diphosphate-α-D-glucose (7b). The triethylammonium salt of the title compound (TLC: IPA–H_2O–NH_3 6 : 3 : 1; Rf 0.58, Rf_{SM} 0.37) was obtained as a glassy solid in 58% yield (15.5 mg) from **6b** (20 mg, 29 μmol) and 4-methoxyphenylboronic acid according to general method C. δ_H (400 MHz, D_2O) 3.38–3.43 (1H, m, H-4″), 3.40–3.45 (1H, m, H-2″), 3.70–3.87 (4H, m, H-3″, H-5″ and H-6″), 3.86 (3H, s, Me), 4.16–4.21 (2H, m, H-5′), 4.27–4.31 (1H, m, H-4′), 4.39 (1H, t, $J = 4.6$ Hz, H-3′), 4.47 (1H, t, $J = 5.6$ Hz, H-2′), 5.54 (1H, dd, $J = 3.2$ and 7.2 Hz, H-1″), 6.03 (1H, d, $J = 6.0$ Hz, H-1′), 7.07 (2H, d, $J = 8.8$ Hz, *m*Ph), 7.49 (2H, d, $J = 8.8$ Hz, *o*Ph), 7.81 (1H, s, H-6); δ_C (75.5 MHz, D_2O) 56.0 (Me), 61.0 (C-6″), 66.1 (C-5′), 69.9 (C-4″), 70.6 (C-3′), 72.4 (C-2″), 73.4, 73.6 (C-3″/C-5″), 74.0 (C-2′), 84.2 (C-4′), 89.31 (C-1′), 96.3 (C-1″), 115.0 (*m*Ph), 116.6 (C-5), 125.2 (*i*Ph), 130.9 (*o*Ph), 138.5 (C-6), 152.4 (C-2), 159.7 (*p*Ph), 165.6 (C-4); δ_P (121.5 MHz, D_2O) −9.25 (d, $J = 20.2$ Hz), −7.62 (d, $J = 21.9$ Hz). *m/z* (ESI) 671.0909 $[M - H]^-$, $C_{22}H_{29}O_{18}N_2P_2$ requires 671.0896.

5-(4-Chlorophenyl)uridine-5′-diphosphate-α-D-glucose (7c). The triethylammonium salt of the title compound (TLC: IPA–H_2O–NH_3 6 : 3 : 1; Rf 0.58, Rf_{SM} 0.37) was obtained as a glassy solid in 57% yield (14.9 mg) from **6b** (20 mg, 29 μmol) and 4-chlorophenylboronic acid according to general method C. δ_H (400 MHz, D_2O) 3.39–3.44 (1H, m, H-4″), 3.42–3.47 (1H, m, H-2″), 3.71–3.92 (4H, m, H-3″, H-5″ and H-6″), 4.17–4.22 (2H, m, H-5′), 4.28–4.32 (1H, m, H-4′), 4.39 (1H, t, $J = 4.4$ Hz, H-3′), 4.47 (1H, t, $J = 5.6$ Hz, H-2′), 5.54 (1H, dd, $J = 2.8$ and 5.2 Hz, H-1″), 6.03 (1H, d, $J = 6.0$ Hz, H-1′), 7.45–7.58 (4H, m, Ph), 7.90 (1H, s, H-6); δ_C (75.5 MHz, D_2O) 61.1 (C-6″), 65.9 (C-5′), 69.9 (C-4″), 70.6 (C-3′), 72.3 (C-2″), 73.4, 73.6 (C-3″/C-5″), 74.1 (C-2′), 84.3 (C-4′), 89.3 (C-1′), 96.3 (C-1″), 115.9 (C-5), 129.5, 130.9, 134.4 (Ph), 139.3 (C-6), 152.3 (C-2), 165.4 (C-4); δ_P (121.5 MHz, D_2O) −9.27 (d, $J = 20.2$ Hz), −7.68 (d, $J = 21.8$ Hz). *m/z* (ESI) 675.0402 $[M - H]^-$, $C_{21}H_{26}O_{17}N_2Cl^{35}P_2$ requires 675.0401.

5-(2-Furyl)uridine-5′-diphosphate-α-D-glucose (7d). The triethylammonium salt of the title compound (TLC: IPA–H_2O–NH_3 6 : 3 : 1; Rf 0.58, Rf_{SM} 0.37) was obtained as a glassy solid in 40% yield (10.4 mg) from **6b** (20 mg, 29 μmol) and 2-furylboronic acid according to general method C. δ_H (400 MHz, D_2O) 3.39–3.44 (1H, m, H-4″), 3.42–3.47 (1H, m, H-2″), 3.70–3.93 (4H, m, H-3″, H-5″ and H-6″), 4.23–4.28 (2H, m, H-5′), 4.30–4.34 (1H, m, H-4′), 4.42 (1H, t, $J = 4.6$ Hz, H-3′), 4.49 (1H, t, $J = 5.6$ Hz, H-2′), 5.60 (1H, dd, $J = 3.6$ and 7.8 Hz, H-1″), 6.05 (1H, d, $J = 6.0$ Hz, H-1′), 6.55 (1H, d, $J = 3.2$ Hz, H-3 fur), 6.90 (1H, d, $J = 3.6$ Hz, H-2 fur), 7.60 (1H, s, H-4 fur), 8.21 (1H, s, H-6); δ_C (75.5 MHz, D_2O) 61.0 (C-6″), 66.3 (C-5′), 69.9 (C-4″), 70.6 (C-3′), 72.3 (C-2″), 73.5, 73.6 (C-3″/C-5″), 74.3 (C-2′), 84.3 (C-4′), 89.4 (C-1′), 96.3 (C-1″), 109.7 (C-2 fur), 112.2 (C-3 fur), 121.5 (C-5), 133.4 (C-6), 143.5 (C-4 fur), 146.1 (C-1 fur), 151.7 (C-2), 163.3 (C-4); δ_P (121.5 MHz, D_2O) −9.20 (d, $J = 20.2$ Hz), −7.62 (d, $J = 20.1$ Hz). *m/z* (ESI) 631.0586 $[M-H]^-$, $C_{19}H_{25}O_{18}N_2P_2$ requires 631.0583.

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