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Sonogashira reactions of α- and β-1-ethynyl-2-deoxyribosides: synthesis of acetylene-extended C-nucleosides

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ABSTRACT

An improved practical protocol for the synthesis of both anomers of 1-ethynyl-2-deoxiribosides **1** was developed. The Sonogashira coupling of ethynyldeoxyribosides **1** with various aryl- and heteroaryl halides was carried out under various conditions. It was found that the use of copper-free coupling protocols could reduce the oxidative dimerisation in favour of arylalkynyldeoxyriboside formation.

1. Introduction

Since its discovery, the Sonogashira reaction[1] has made an incredible impact on the construction of various molecules and has become a favourite synthetic tool in organic synthesis.[2] Although a great deal of work has been devoted to the exploration and explanation of factors influencing the course of the Sonogashira reaction, there are a number of interesting issues, such as reactivity of various alkynyl substrates, that should be addressed and clarified. One typical example is the reactivity of 1-ethynylsaccharides that are potential candidates for the synthesis of various C-glycoside or C-nucleoside derivatives. Among them α- and β-anomers of 1-ethynyldeoxyribosides **1** (Fig. 1) are of special interest, because they could serve as starting materials for the synthesis of various *C*-2′-deoxyribosides that could be used for the extension of the genetic alphabet,[3] or for the construction of acetylene-extended unnatural DNA.[4] Despite their importance, no reliable and efficient synthesis of these crucial intermediates is available and the current syntheses suffer from low yields, lack of selectivity, and difficult separation of anomers. Recently, several groups entered this area and studied the behaviour of various 1-ethynyldeoxyribosides **1** in transition-metal promoted reactions such as the Pauson–Khand reaction,[5] cyclotrimerizations,[6,7] and also the Sonogashira coupling reaction.[8–12] For the Sonogashira reaction, the majority of these studies concerned just the use of specific substrates (usually only β-1-ethynyldeoxyriboside) or the synthesis of specific targets and did not assess the scope of the reaction.

Owing to the different spatial arrangement of the alkynyl moiety in α- and β-anomers of 1-ethynyldeoxyriboside derivatives, it is reasonable to surmise that both anomers might display different reactivity patterns. Indeed, we observed that during the cyclotrimerisation under Rh-catalysis, α-1-ethynydeoxyriboside **1αa** tended to dimerise to the corresponding 1,4-bis(deoxyribosyl)but-1-yn-3-ene as a side reaction. On the other hand, β-1-ethynydeoxyriboside **1βa** was completely devoid of this behaviour under the same reaction conditions affording the cyclotrimerisation products.[7] In a similar fashion, coupling of **1αa** with 3-iodopropenoic acids was plagued by oxidative dimerisation of the alkyne to 1,4-bis(deoxyribosyl)buta-1,3-diyne in up to 60% yield. Interestingly, no such tendency was observed for **1βa**.[12] On the other hand, oxidative dimerisation of **1βb** to the corresponding diyne (up to 50%) was observed by some[9] but not others.[8,10,11]

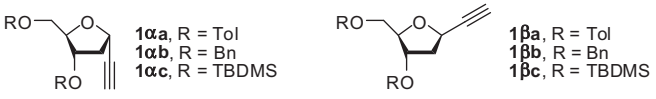

Figure 1. *O*-Protected 1-ethynyldeoxyribosides **1**.

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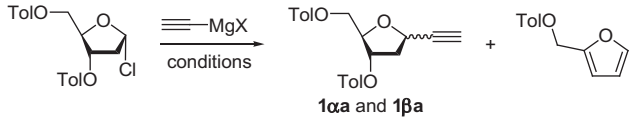
In view of these observations, we decided to improve the synthesis of **1** and to investigate the Sonogashira reaction of **1αa** and **1βa** with various aryl- and heteroaryl halides under several sets of reaction conditions.

2. Results and discussion

Prior to the coupling study, we wanted to address the issue of α- and β-1-ethynydeoxyribosides **1αa** and **1βa** preparation. It was reported that these compounds could be easily prepared by the reaction of the corresponding α-halogenose with ethynylmagnesium bromide in 60–70% isolated yields (along with minor amounts of the furan derivative).[7,13] However, the major product formed was the α-anomer **1αa** and the separation of the anomeric mixture into individual anomers required the use of preparative HPLC. At the outset we tried to affect the anomeric ratio in favour of the β-anomer **1βa** by carrying out the coupling reaction of ethynylmagnesium bromide with halogenose in the presence of various transition-metal catalytic systems such as Pd (Entries 1–6), Ni[14] (Entry 7), Co[15] (Entries 8 and 9), Fe[16] (Entries 10 and 11), and Cu[17] (Entry 12) salts (Table 1).

Table 1
The reaction of halogenose with ethynylmagnesium bromide



1αa and **1βa**

Entry	Catalytic system[a] (mol %)	Solvent	α/β[b]	Yield[c] (%)
1	$Pd(dba)_2$ (5), PPh_3 (50)	THF	2/1	38 (13)
2	$Pd(PPh_3)_4$ (10)	THF	1/1	30 (15)
3[d]	$Pd(PPh_3)_4$ (5)	THF	1/1	33 (6)
4	$Pd(OAc)_2$ (10), PCy_3 (10)	THF/NMP[e]	2/1	8 (10)
5	$PdCl_2(MeCN)_2$ (10), PPh_3 (20)	THF	1/1	25 (10)
6[d]	$PdCl_2(MeCN)_2$ (5) PPh_3 (10)	THF	1/1	28 (6)
7	$Ni(acac)_2$ (10)	THF	2/1	45 (15)
8	$Co(acac)_3$ (14)	THF	2/1	28 (9)
9	$Co(acac)_3$ (40)	TMEDA	—	0 (7)
10	$Fe(acac)_3$ (10)	THF	2/1	18 (19)
11	$FeCl_3$ (5)	TMEDA	2/1	7 (2)
12	$CuCl_2$ (5)	THF		9 (5)
13[f]	No added catalyst	THF	2/1	80 (5)

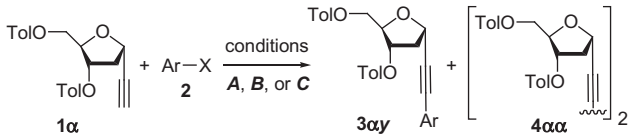
[a] Typical reaction conditions: halogenose (1 equiv), ethynylmagnesium bromide (1.5 equiv), 20 °C unless otherwise noted. (Ethynylmagnesium bromide was added in one portion).
[b] Anomeric ratio **1αa**/**1βa**.
[c] Isolated yield of ethynyldeoxyriboside (anomeric mixture). Isolated yield of the furan by-product in parentheses.
[d] Reaction was run at −20 °C (1.1 equiv of halogenose), and using a slow addition of ethynylmagnesium bromide (2 equiv).
[e] 1/1 mixture.
[f] Ethynylmagnesium chloride was used instead of bromide.

Although the presence of the Pd catalysts led to an increase in the proportion of the **1βa** in a few cases (e.g., Entries 2, 3, 5, and 6), the overall yield of both anomers did not surpass 38% (Entry 1). The highest yield of the desired products (45%) was achieved in the presence of the Ni-catalyst (Entry 7). Regarding the catalysis by Fe, Co, or Cu compounds, it proceeded with low efficiency with respect to the alkynylation selectivity as well as to the combined yields of **1αa** and **1βa** (Entries 8–12). Although the effort to affect coupling by transition-metal catalysis failed, we found that by using ethynylmagnesium chloride, instead of the bromide, the overall isolated yield of both anomers of **1a** could be reproducibly increased up to 80%, while the amount of the furan derivative was suppressed to 5% (Entry 13). It should be also added that using of ethynylmagnesium chloride in the transition-metal catalysed reactions did not have any positive effect on the product distribution and essentially the same results were obtained with ethynylmagnesium bromide.

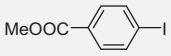
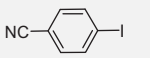
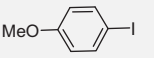
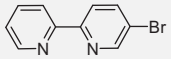
Having both anomers of **1a** in sufficient amounts, our attention turned to the coupling reaction of **1** with organic halides. In order to find the best reaction conditions for the Sonogashira coupling, three variants of the reaction were used: (i) condition ***A*** (classical conditions: $PdCl_2(CH_3CN)_2$, PPh_3, CuI, Et_3N),[1] (ii) copper-free condition ***B*** ($PdCl_2(CH_3CN)_2$, Cs_2CO_3, dicyclohexyl-(2′,4′,6′-triisopropyl-biphenyl-2-yl)-phosphine),[18] and (iii) copper-free condition ***C*** ($PdCl_2(CH_3CN)_2$, Cs_2CO_3, 2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl). All reactions were run until full consumption of one of the starting materials (monitored by TLC).

Initially, the Sonogashira reaction of α-1-ethynyldeoxyriboside **1αa** with various aryl halides was studied. The results are summarized in Table 2. The coupling with three substituted phenyl iodides **2a**–**2c** (Entries 1–3) proceeded under both conditions giving the corresponding products **3αa**–**3αc** in acceptable isolated yields. Somewhat better yields were obtained under copper-free conditions (conditions ***B***, 43–53% isolated yields) than under classical conditions (conditions ***A***, 35–43% isolated yields). Moreover, under condition ***A*** the coupling was plagued by oxidative dimerisation of α-1-ethynyldeoxyriboside to the corresponding diyne **4αα** (5–15%). To avoid this undesirable side reaction, further reactions were run only under conditions ***B*** or ***C***. The coupling with 2- and 3-iodothiophenes **2d** and **2e** gave the expected products **3αd** and **3αe** in mediocre yields of 24% and 25%, respectively. The

Table 2
The reaction of **1αa** with various organyl halides **2**



1α **3αy** Ar **4αα**

Entry	**2**, Ar-X	**3αy**	Cond.[a]	Yield[b] (%)
1		**3αa**	***A*** (20 h) ***B*** (2 h)	35 53
2		**3αb**	***A*** (0.5 h) ***B*** (2 h)	43 48
3		**3αc**	***A*** (1 h) ***B*** (2.5 h)	41 43
4		**3αd**	***B*** (6 h)	24
5		**3αe**	***B*** (10 h)	25
6		**3αf**	***B*** (3 h)	73
7		**3αg**	***B*** (6 h) ***B*** (18 h)[c]	33 61
8		**3αh**	***B*** (30 h)	41
9		**3αi**	***B*** (8 h) ***C*** (5 h)	29 30
10		**3αj**	***B*** (5 h)	17

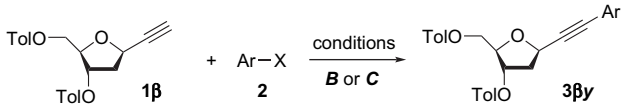
[a] The reaction time is in parentheses.
[b] Isolated yields.
[c] 3-Bromopyridine was used.

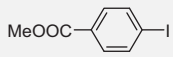
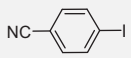
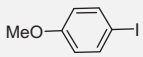
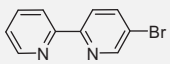
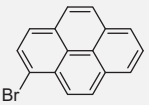
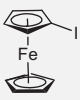
reaction with 2-iodopyridine **2f** gave a good 73% yield of **3αf**. Surprisingly, the reaction with 3-iodopyridine **2g** gave rise to the expected product **3αg** in only 33% yield, whereas the use of 3-bromopyridine gave **3αg** in 61% yield. The reaction with 3-bromobipyridine **2h** proceeded to give **3αh** in 41% yield. The coupling with 1-bromopyrene **2i** was carried out under two conditions (**B** and **C**), in both cases the corresponding product **3αi** was obtained in comparable yields of 29% and 30%, respectively. Finally, the coupling with iodoferrocene **2j** proceeded to give the ferrocenyl derivative **3αj** in 17% isolated yield. An attempt to prepare this compound by using an alternative approach based on alkyne-alkyne metathesis of α-1-propyn-1-yldeoxyriboside with propynylferrocene[19] did not yield any amount of the expected product.

In the next stage, we studied the coupling with the β-anomer **1βa** (Table 3). The reaction with aryl iodides **2a**–**2b** proceeded well to give the corresponding products **3βa**–**3βb** in good yields of 57 and 47%, respectively. Surprisingly, the coupling with **2c** afforded **3βc** a poor yield of 13%. The reactions with 2- and 3-iodothiophenes **2d** and **2e** gave the expected products **3βd** and **3βe** in mediocre yields of 32% and 41%, respectively. Coupling of 2-iodopyridine **2f** gave **3βf** in 33% yield. Gratifyingly, the change of the reaction conditions to ***C*** led to the increase in the yield to 70%. The reaction with 3-iodopyridine **2g** gave rise to the expected product **3βg** in 50% yield (the use 3-bromopyridine gave **3βg** in 43% yield). The coupling with 3-bromobipyridine **2h** proceeded to give **3βh** in a low yield of 19%. The reaction with 1-bromopyrene **2i** gave rise to **3βi** in 36% under conditions ***C***. Finally, the coupling with iodoferrocene **2j** gave the ferrocenyl derivative **3βj** in 20% yield. It should be also emphasised that oxidative dimerisation of **1βa** to the corresponding diyne like in the case of the α-anomer was not observed in any of the cases.

Although the isolated yields might seem to be in lower range, in all cases the starting compounds **1αa** and **1βa** were fully consumed. It should be pointed out that each reaction was accompanied by the formation of tar like material, probably by oligomerisation of the alkyne. Because it is well known that alkynes can be oligomerised in Pd-complex based catalytic systems,[20,21] **1αa** was allowed to react under conditions ***B*** at 80 °C for 4 h. After this period of time the alkyne disappeared and a small amount diyne **4ααα** (8%) and a polymeric material (56%) were isolated from the reaction mixture. ^{1}H NMR spectroscopic analysis clearly showed the presence of the deoxyribose moiety. This experiment proved that a part of the starting material is consumed by undesirable oligomerisations.

Table 3
The reaction of **1βa** with various organyl halides **2**



Entry	**2**, Ar-X	**3βy**	Cond.[a]	Yield[b] (%)
1		**3βa**	***B*** (2.5 h)	57
2		**3βb**	***B*** (3 h)	47
3		**3βc**	***B*** (15 h)	13
4		**3βd**	***B*** (4 h)	32
5		**3βe**	***B*** (6 h)	41
6		**3βf**	***B*** (8 h) ***C*** (12 h)	33 70
7		**3βg**	***B*** (6.5 h) ***B*** (8 h)[c]	50 43
8		**3βh**	***B*** (15 h)	19
9		**3βi**	***B*** (8 h) ***C*** (5 h)	29 36
10		**3βj**	***B*** (12 h)	20

[a] The reaction time is in parentheses.
[b] Isolated yields.
[c] 3-Bromopyridine was used.

3. Conclusion

We showed that 1-ethynyldeoxyribose derivatives undergo Sonogashira reaction with various aryl, heteroaryl, and metallocenyl derivatives to give the cross-coupling products in reasonable yields. The data obtained clearly show that the reaction course could be controlled in individual cases by the conditions employed (e.g., the change of phosphine, Table 3, Entry 6), as well as the nature of the aryl halide (e.g., switching from the iodide to the bromide resulted in higher yield, Table 2, Entry 7). In addition, we showed that the alkynes are prone to oligomerisation under the reaction conditions used diminishing the overall yield of the desired cross-coupling products. However, since the oligomeric products are not chromatographically mobile, the desired products can be easily isolated. Worth of mention is the different susceptibility to oxidative dimerisation of **1αa** and **1βa** to give the corresponding diynes.[7b] The obtained results clearly indicate that individual approach to each cross-coupling reaction should be considered in order to achieve the efficient coupling with high yields of the desired products. The final arylalkynyl derivatives can be considered as novel acetylene-extended C-nucleosides with tunable properties.

4. Experimental

4.1. General procedure for the coupling of halogenose with ethynylmagnesium bromide in the presence of transition-metal catalysts

Reactions were performed under a protective atmosphere of argon in dried 50 mL microwave vials. A 0.5 M THF solution of ethynylmagnesium chloride (194 mg, 3.0 mL, 1.5 mmol) was added to a solution of halogenose (388 mg, 1 mmol), catalyst, and ligand in THF, NMP or TMEDA (8–10 mL) and the reaction mixture was maintained at 20 °C for 3 h. The reaction mixture was quenched with 1 M HCl, extracted with EtOAc (3×10 mL), the combined organic fractions were washed with water (10 mL), brine (10 mL), and dried over $MgSO_4$. The volatiles were removed under reduced pressure and column chromatography of the residue on silica gel (40/1 toluene/acetone) yielded products (details are given in the Supplementary data).

4.2. Reaction of halogenose with ethynylmagnesium chloride

A 0.5 M THF solution of ethynylmagnesium chloride (194 mg, 3.0 mL, 1.5 mmol) was added to a solution of halogenose (388 mg, 1 mmol) and the reaction mixture was maintained at 20 °C for 3 h. The reaction mixture was quenched with 1 M HCl, extracted with EtOAc (3×10 mL), the combined organic fractions were washed

with water (10 mL), brine (10 mL), and dried over $MgSO_4$. The volatiles were removed under reduced pressure and column chromatography of the residue on silica gel (40/1 toluene/acetone) yielded 302 mg (80%) of 2/1 mixture of the α- and β-anomer. The spectroscopic characteristics were in agreement with the previously reported data.[7a]

4.3. General procedure for the classical Sonogashira reaction (conditions *A*)

Et_3N (27 mg, 37 μL, 0.26 mmol) was added to a solution of $PdCl_2(CH_3CN)_2$ (3.4 mg, 13 μmol), PPh_3 (7.0 mg, 26 μmol), CuI (5.0 mg, 26 μmol), **1αa** (50.0 mg, 0.13 mmol), and **2a**–**2c** (0.13 mmol) in dry THF (3 mL) and the reaction mixture was maintained at 20 °C until the starting material disappeared. Then the reaction mixture was quenched with 1 M HCl, extracted with EtOAc (3×20 mL), combined organic fractions were washed with H_2O (10 mL), brine (10 mL), and dried over $MgSO_4$. The volatiles were removed under reduced pressure and column chromatography of the residue on silica gel (hexane/EtOAc) gave the desired products.

4.4. General procedure for the copper/free Sonogashira reaction (conditions *B*)

Reactions were performed under a protective atmosphere of argon in dried microwave vials. A solution of $PdCl_2(CH_3CN)_2$ (3.4 mg, 13 μmol), dicyclohexyl-(2′,4′,6′-triisopropyl-biphenyl-2-yl)-phosphine (19.0 mg, 40 μmol), Cs_2CO_3 (112.0 mg, 0.35 mmol), **1αa** or **1βa** (50 mg, 0.13 mmol) and **2a**–**2j** (0.13 mmol) in dry acetonitrile (3 mL) was heated to 80 °C for 2–30 h. Then the reaction mixture was quenched with H_2O and the acetonitrile was removed under reduced pressure. Residue was dissolved in EtOAc (10 mL), washed with H_2O (2×10 mL), brine (10 mL), and dried over $MgSO_4$. The volatiles were removed under reduced pressure and column chromatography of the residue on silica gel (hexane/EtOAc) afforded the desired products.

4.5. General procedure for the copper/free Sonogashira reaction (conditions *C*)

Reactions were performed under a protective atmosphere of argon in dried microwave vials. A solution of $PdCl_2(CH_3CN)_2$ (3.4 mg, 13 μmol), 2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl (19.0 mg, 40 μmol), Cs_2CO_3 (112.0 mg, 0.35 mmol), **1αa** or **1βa** (50 mg, 0.13 mmol) and **2f**, **2i** (0.13 mmol) in dry acetonitrile (3 mL) was heated to 80 °C for 5–12 h. Then the reaction mixture was quenched with H_2O and the acetonitrile was removed under reduced pressure. Residue was dissolved in EtOAc (10 mL), washed with H_2O (2×10 mL), brine (10 mL), and dried over $MgSO_4$. The volatiles were removed under reduced pressure and column chromatography of the residue on silica gel (hexane/EtOAc) afforded the desired products.

*4.5.1. 1α-[(4-Methoxycarbonylphenyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3αα**). Conditions A.* Methyl 4-iodobenzoate **2a** (35 mg, 0.13 mmol), reaction time 20 h. Column chromatography (3/1 hexane/EtOAc) afforded 12 mg (35%) of the title compound as an orange solid and 5 mg (14%) of **4αα** as a dark brown oil. *Conditions B.* Methyl 4-iodobenzoate **2a** (35 mg, 0.13 mmol), reaction time 2 h. Column chromatography (3/1 hexane/EtOAc) afforded 28 mg (53%) of the title compound as an orange solid. Mp 89–91 °C; $[\alpha]_D^{20}$ +30 (*c* 0.51, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 2.38 (s, 3H), 2.39 (s, 3H), 2.46–2.52 (m, 1H), 2.69 (ddd, *J*=8.4, 8.2, 5.1 Hz, 1H), 3.92 (s, 3H), 4.50 (dd, *J*=12.0, 4.8 Hz, 1H), 4.56 (dd, *J*=12.0, 3.9 Hz, 1H), 4.66–4.70 (m, 1H), 5.22 (dd, *J*=7.8, 2.7 Hz, 1H), 5.55–5.59 (m, 1H), 7.10–7.15 (m, 2H), 7.20–7.26 (m, 4H), 7.42–7.48 (m, 2H), 7.91–7.99 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7 (2C), 39.6, 52.2, 64.3, 68.8, 75.8, 82.4, 84.8, 91.3, 126.8, 126.9, 127.2, 128.2, 129.1 (2C), 129.2 (2C), 129.4 (2C), 129.7 (2C), 129.8 (2C), 131.6 (2C), 143.9, 144.1, 166.1, 166.2, 166.5; IR (neat) ν 3069, 3022, 2997, 2953, 2920, 1718, 1704, 1609, 1402, 1268, 1170, 1050, 1017, 959, 770, 687 cm^{-1}; HRMS (EI) *m*/*z* for $C_{31}H_{28}O_7$ calcd 512.1835, found 512.1820. R_f (3/1 hexane/EtOAc)=0.40.

*4.5.2. 1,4-Bis[1α-1,2-dideoxy-3,5-di-O-(4-toluoyl)-D-ribofuranos-1-yl]butadiyne (**4αα**).* $[\alpha]_D^{20}$ +44 (*c* 0.3, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 2.34 (m, 2H), 2.37 (s, 6H), 2.41 (s, 6H), 2.61–2.71 (ddd, *J*=13.8, 7.8, 6.6 Hz, 2H), 4.46–4.61 (m, 2H), 4.50–4.58 (m, 4H), 5.04 (dd, *J*=8.1, 2.4 Hz, 2H), 5.50–5.53 (m, 2H), 7.19–7.25 (m, 8H), 7.90–7.93 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7 (4C), 39.5 (2C), 64.1 (2C), 68.7 (2C), 69.7 (2C), 75.5 (2C), 79.0 (2C), 82.6 (2C), 126.6 (2C), 126.9 (2C), 129.1 (4C), 129.2 (4C), 129.7 (4C), 129.9 (4C), 143.9 (2C), 144.1 (2C), 166.1 (2C), 166.2 (2C); IR (neat) ν 3063, 3034, 2952, 2923, 2851, 1720, 1613, 1452, 1375, 1309, 1271, 1179, 1106, 1078, 1017, 837, 751, 695 cm^{-1}; HRMS (EI) *m*/*z* for $C_{46}H_{42}O_{10}$ calcd 755.2856, found 755.2844. R_f (3/1 hexane/EtOAc)=0.72.

*4.5.3. 1α-[(4-Cyanophenyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3αb**). Conditions A.* 4-Iodobenzonitrile **2b** (30 mg, 0.13 mmol), reaction time 0.5 h. Column chromatography (5/1 hexane/EtOAc) afforded 27 mg (43%) of the title compound as a yellow solid and 3.0 mg (5%) of **4αα** as dark brown oil. *Conditions B.* 4-Iodobenzonitrile **2b** (30 mg, 0.13 mmol), reaction time 2 h. Column chromatography (5/1 hexane/EtOAc) afforded 30 mg (48%) of the title compound as a yellow solid: mp 111–112 °C; $[\alpha]_D^{20}$ +29 (*c* 0.51, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 2.40 (s, 3H), 2.41 (s, 3H), 2.45–2.48 (m, 1H), 2.70 (ddd, *J*=13.8, 6.6, 6.3 Hz, 1H), 4.50 (dd, *J*=12.0, 4.8 Hz, 1H), 4.55 (dd, *J*=12.0, 4.2 Hz, 1H), 4.66–4.71 (m, 1H), 5.21 (dd, *J*=7.8, 2.7 Hz, 1H), 5.54–5.60 (m, 1H), 7.10–7.14 (m, 2H), 7.20–7.26 (m, 2H), 7.43–7.48 (m, 2H), 7.55–7.59 (m, 2H), 7.90–7.92 (m, 2H), 7.93–7.95 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7 (2C), 39.5, 64.2, 68.7, 75.8, 82.5, 84.0, 92.9, 111.9, 118.3, 126.8, 126.9, 127.2, 129.1 (2C), 129.2 (2C), 129.7 (2C), 129.8 (2C), 131.9 (2C), 132.2 (2C), 143.9, 144.2, 166.1, 166.2; IR (neat) ν 3719, 3697, 3621, 2957, 2219, 1710, 1611, 1274, 1111, 1083, 752, 690, 668 cm^{-1}; HRMS (EI) *m*/*z* for $C_{30}H_{25}NO_5$ calcd 479.1733, found 479.1733. R_f (5/1 hexane/EtOAc)=0.24.

*4.5.4. 1α-[(4-Methoxyphenyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3αc**). Conditions A.* 1-Iodo-4-methoxy-benzene **2c** (31 mg, 0.13 mmol), reaction time 1 h. Column chromatography (5/1 hexane/EtOAc) afforded 26 mg (41%) of the title compound as a yellowish-brown oil and 5.0 mg (8%) of **4αα** as a dark brown oil. *Conditions B.* 1-Iodo-4-methoxy-benzene **2c** (31 mg, 0.13 mmol), reaction time 2.5 h. Column chromatography (5/1 hexane/EtOAc) afforded 27 mg (43%) of the title compound as a yellowish-brown oil: $[\alpha]_D^{20}$ +10 (*c* 0.48, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 2.38–2.40 (m, 1H) (overlapped with CH_3–Tol signal), 2.40 (s, 3H), 2.41 (s, 3H), 2.68 (ddd, *J*=13.7, 8.1, 6.9 Hz, 1H), 3.79 (s, 3H), 4.50 (dd, *J*=11.8, 4.9 Hz, 1H), 4.56 (dd, *J*=11.8, 4.0 Hz, 1H), 4.66–4.70 (m, 1H), 5.20–5.22 (m, 1H), 5.53–5.56 (m, 1H), 6.80–6.83 (m, 2H), 7.11–7.15 (m, 2H), 7.20–7.25 (m, 2H), 7.30–7.35 (m, 2H); 7.90–7.92 (m, 2H), 7.93–7.97 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7 (2C), 39.8, 64.4, 55.3, 69.0, 75.9, 82.1, 85.6, 86.8, 113.8 (2C), 114.6, 127.0 (2C), 129.1 (2C), 129.2 (2C), 129.8 (2C), 129.9 (2C), 133.3 (2C), 143.8, 144.0, 159.7, 166.3 (2C); IR (neat) ν 3035, 2958, 2923, 2834, 2224, 1723, 1711, 1607, 1511, 1456, 1267, 1179, 1105, 1013, 835, 150 cm^{-1}; MS (FAB) *m*/*z* 213 (10), 135 (8), 119 (100), 91 (18). R_f (5/1 hexane/EtOAc)=0.26.

*4.5.5. 1α-[(2-Thienyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3αd**). Conditions B.* 2-Iodothiophene **2d** (28 mg, 15 μL, 0.13 mmol), reaction time 6 h. Column chromatography (3/1

hexane/EtOAc) afforded 15 mg (24%) of the title compound as a dark brown viscous oil: $[\alpha]_D^{20}$ +13 (*c* 0.3, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 2.40 (s, 3H), 2.41 (s, 3H), 2.43–2.46 (m, 1H), 2.67 (ddd, *J*=13.9, 8.1, 6.9 Hz, 1H), 4.49 (dd, *J*=12.0, 4.8 Hz, 1H), 4.55 (dd, *J*=12.0, 3.9 Hz, 1H), 4.64–4.70 (m, 1H), 5.22 (dd, *J*=8.1, 3.0 Hz, 1H), 5.53–5.59 (m, 1H), 6.95 (dd, *J*=5.1, 3.6 Hz, 1H), 7.17–7.25 (m, 2H) (overlapped with $CDCl_3$ and H-*m*-Tol signal), 7.17–7.29 (m, 4H); 7.90–7.95 (m, 2H), 7.96–8.00 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7 (2C), 39.6, 64.3, 69.0, 75.8, 78.9, 82.4, 92.0, 122.4, 126.9, 127.0, 127.4 (2C), 129.1 (2C), 129.2 (2C), 129.7 (2C), 129.9 (2C), 132.4, 143.9, 144.0, 166.2, 166.3; IR (neat) ν 3419, 3104, 3071, 2952, 2855, 2221, 1930, 1793, 1616, 1509, 1456, 1409, 1376, 1209, 1130, 996, 853, 759, 710, 666 cm^{-1}; HRMS (EI) *m*/*z* for $C_{27}H_{24}O_5S$ calcd 460.1344, found 460.1331. R_f (3/1 hexane/EtOAc)=0.56.

*4.5.6. 1α-[(3-Thienyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3αe**). Conditions B.* 3-Iodothiophene **2e** (28 mg, 13 μL, 0.13 mmol), reaction time 10 h. Column chromatography (3/1 hexane/EtOAc) afforded 15 mg (25%) of the title compound as a dark brown viscous oil: $[\alpha]_D^{20}$ +14 (*c* 0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.41 (s, 3H), 2.42–2.50 (m, 1H), 2.67 (ddd, *J*=13.8, 7.8, 6.9 Hz, 1H), 4.51 (dd, *J*=11.7, 4.5 Hz, 1H), 4.55 (dd, *J*=11.7, 3.9 Hz, 1H), 4.65–4.68 (m, 1H), 5.19 (dd, *J*=7.8, 3.0 Hz, 1H), 5.54–5.58 (m, 1H), 7.06 (dd, *J*=5.1, 0.9 Hz, 1H), 7.12–7.17 (m, 2H), 7.20–7.25 (m, 2H), 7.24–7.28 (m, 1H) (overlapped with H-*m*-Tol signal), 7.39 (dd, *J*=3.0, 0.9 Hz, 1H), 7.91–8.00 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7 (2C), 39.7, 64.4, 69.0, 75.8, 80.8, 82.2, 87.9, 121.6, 125.2 (2C), 126.9, 127.0, 129.1 (2C), 129.2 (2C), 129.7 (2C), 129.9 (2C), 130.2, 143.9, 144.0, 166.2, 166.3; IR (neat) ν 3394, 2928, 1726, 1707, 1612, 1454, 1275, 1179, 1109, 1019, 750 cm^{-1}; HRMS (EI) *m*/*z* for $C_{27}H_{24}O_5S$ calcd 460.1344, found 460.1356. R_f (3/1 hexane/EtOAc)=0.60.

*4.5.7. 1α-[(2-Pyridyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3αf**). Conditions B.* 2-Iodopyridine **2f** (27 mg, 14 μL, 0.13 mmol), reaction time 3 h. Column chromatography (3/1 hexane/EtOAc) afforded 44 mg (73%) of the title compound as a dark brown viscous oil: $[\alpha]_D^{20}$ +25 (*c* 0.72, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 2.37 (s, 3H), 2.41 (s, 3H), 2.51–2.57 (m, 1H), 2.71 (ddd, *J*=13.8, 8.4, 2.7 Hz, 1H), 4.51 (dd, *J*=11.7, 5.4 Hz, 1H), 4.56 (dd, *J*=11.7, 3.6 Hz, 1H), 4.65–4.70 (m, 1H), 5.19 (dd, *J*=7.8, 3.0 Hz, 1H), 5.54–5.58 (m, 1H), 7.09–7.13 (m, 2H), 7.20–7.25 (m, 2H), 7.35–7.40 (m, 2H), 7.58–7.62 (m, 1H), 7.90–7.94 (m, 2H), 7.94–8.02 (m, 2H), 8,62 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7 (2C), 39.5, 64.3, 68.7, 75.7, 82.5, 82.8, 91.7, 123.2, 126.9, 127.0, 128.2, 129.1 (2C), 129.2 (2C), 129.7 (2C), 129.9 (2C), 136.5, 142.4, 143.9, 144.0, 149.5, 166.2 (2C); IR (neat) ν 3419, 3035, 2939, 2588, 2362, 1930, 1732, 1615, 1508, 1409, 1288, 1130, 917, 843, 760, 691 cm^{-1}; HRMS (EI) *m*/*z* for $C_{28}H_{25}NO_5$ calcd 455.1733, found 455.1723. R_f (3/1 hexane/EtOAc)=0.18.

*4.5.8. 1α-[(3-Pyridyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3αg**). Conditions B.* 3-Iodopyridine **2g** (27 mg, 0.13 mmol), reaction time 6 h. Column chromatography (3/1 hexane/EtOAc) afforded 20 mg (33%) of the title compound as a yellow viscous oil: $[\alpha]_D^{20}$ +26 (*c* 0.50, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.41 (s, 3H), 2.47–2.53 (m, 1H), 2.71 (ddd, *J*=13.8, 7.5, 7.2 Hz, 1H), 4.50 (dd, *J*=12.0, 4.8 Hz, 1H), 4.56 (dd, *J*=12.0, 3.9 Hz, 1H), 4.65–4.70 (m, 1H), 5.23 (dd, *J*=8.1, 2.7 Hz, 1H), 5.54–5.58 (m, 1H), 7.13–7.17 (m, 2H), 7.20–7.26 (m, 2H), 7.22–7.31 (m, 1H), 7.71 (d, *J*=7.8 Hz, 1H), 7.90–7.97 (m, 4H), 8.55–8.70 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 22.6, 39.5, 64.2, 68.7, 75.8, 81.8, 82.4, 92.4, 120.2, 123.3, 126.8, 126.9, 129.1 (2C), 129.2 (2C), 129.7 (2C), 129.8 (2C), 139.5, 143.9, 144.2, 147.9, 151.4, 166.1, 166.2; IR (neat) ν 3415, 3034, 2925, 2855, 1930, 1793, 1735, 1612, 1509, 1408, 1288, 1125, 997, 841, 758, 706, 691 cm^{-1}; HRMS (EI) *m*/*z* for $C_{28}H_{25}NO_5$ calcd 455.1733, found 455.1726. R_f (3/1 hexane/EtOAc)=0.16. *Reaction with 3-bromopyridine*. 3-Bromopyridine **2g** (21 mg, 14 μL, 0.132 mmol) reaction time 18 h. Column chromatography (3/1 hexane/EtOAc) afforded 37 mg (61%) as a yellow viscous oil.

*4.5.9. 1α-[(2,2′-Bipyridyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3αh**). Conditions B.* 5-Bromo-[2,2′]bipyridine **2h**[22] (27 mg, 0.13 mmol), reaction time 30 h. Column chromatography (1/1 hexane/EtOAc) afforded 29 mg (41%) of the title compound as a yellow viscous oil: $[\alpha]_D^{20}$ +13 (*c* 0.67, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 2.37 (s, 3H), 2.41 (s, 3H), 2.50–2.56 (m, 1H), 2.73 (ddd, *J*=13.8, 2.4, 2.8 Hz, 1H), 4.52 (dd, *J*=12.0, 4.8 Hz, 1H), 4.57 (dd, *J*=12.0, 3.9 Hz, 1H), 4.69–4.73 (m, 1H), 5.26 (dd, *J*=8.1, 3.0 Hz, 1H), 5.56–5.59 (m, 1H), 7.13–7.22 (m, 4H), 7.30 (ddd, *J*=7.5, 4.8, 0.9 Hz, 1H), 7.76 (dd, *J*=8.4, 2.1 Hz, 1H), 7.80–7.85 (m, 1H), 7.90–7.99 (m, 4H), 8.36 (d, *J*=8.4 Hz, 1H), 8.40 (d, *J*=8.1 Hz, 1H), 8.67–8.73 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7 (2C), 39.6, 64.3, 68.8, 75.8, 82.5, 82.6, 92.6, 119.6, 120.3, 121.5, 124.0, 126.8, 126.9, 129.1 (2C), 129.3 (2C), 129.7 (2C), 129.8 (2C), 137.2, 139.6, 143.9, 144.2, 149.0, 151.7, 154.8, 155.2, 166.1, 166.2; IR (neat) ν 3419, 3050, 2957, 2855, 1727, 1611, 1587, 1542, 1409, 1281, 1212, 1180, 1112, 1021, 1002, 916, 886, 873, 852, 798, 691, 662 cm^{-1}; HRMS (*m*/*z*) for $C_{33}H_{28}N_2O_5$ calcd 532.1998, found 532.2010. R_f (1/1 hexane/EtOAc)=0.73.

*4.5.10. 1α-[(1-Pyrenyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3αi**). Conditions B.* 1-Bromopyrene **2i** (46 mg, 0.16 mmol), reaction time 8 h. Column chromatography (5/1 hexane/EtOAc) afforded 28 mg (29%) of the title compound as a yellow viscous oil. *Conditions C.* 1-Bromopyrene **2i** (46 mg, 0.16 mmol), reaction time 5 h. Column chromatography (5/1 hexane/EtOAc) afforded 29 mg (30%) of the title compound as a yellow viscous oil: $[\alpha]_D^{20}$ −84 (*c* 0.28, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 2.15 (s, 3H), 2.41 (s, 3H), 2.63–2.72 (m, 1H), 2.84 (ddd, *J*=14.8, 8.0, 1.2 Hz, 1H), 4.58 (dd, *J*=11.6, 4.8 Hz, 1H), 4.65 (dd, *J*=11.6, 4.0 Hz, 1H), 4.80–4.86 (m, 1H), 5.46 (dd, *J*=8.0, 2.1 Hz, 1H), 5.62–5.70 (m, 1H), 6.88 (d, *J*=8.0 Hz, 2H), 7.23 (d, *J*=8.0 Hz, 2H) (overlapped with $CDCl_3$ signal), 7.90–8.10 (m, 10H), 8.14–8.20 (m, 2H), 8.44–8.47 (d, *J*=9.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 21.6, 40.1, 64.4, 69.3, 76.0, 82.4, 84.8, 93.9, 117.0, 124.2, 124.3, 124.4, 125.3, 125.5, 125.6, 126.2, 126.8, 127.0, 127.2, 128.2, 128.3, 128.9 (2C), 129.2 (2C), 129.7 (2C), 129.9 (2C), 130.9, 131.1, 131.4, 132.0, 143.9, 144.0, 166.3, 166.4; IR (neat) ν 2956, 2929, 2857, 2845, 1721, 1712, 1610, 1455, 1413, 1270, 1177, 1105, 1021, 848, 752 cm^{-1}; HRMS (EI) *m*/*z* for $C_{39}H_{30}O_5$ calcd 579.2171, found 579.2184. R_f (5/1 hexane/EtOAc)=0.30.

*4.5.11. 1α-[1-Ferrocenyl]ethynyl-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3αj**). Conditions B.* 1-Iodoferrocene **2j** (34 mg, 0.13 mmol), reaction time 5 h. Column chromatography (5/1 hexane/EtOAc) afforded 13 mg (17%) of the title compound as a dark brown viscous oil: $[\alpha]_D^{20}$ +39 (*c* 0.35, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 2.38–2.45 (m, 1H), 2.41 (s, 3H), 2.42 (s, 3H), 2.68 (ddd, *J*=13.9, 7.8, 6.8 Hz, 1H), 4.17 (s, 5H), 4.17–4.20 (m, 2H), 4.36–4.39 (m, 2H), 4.51 (dd, *J*=11.4, 3.9 Hz, 1H), 4.55 (dd, *J*=11.4, 3.9 Hz, 1H), 4.63–4.67 (m, 1H), 5.10 (dd, *J*=7.8, 3.3 Hz, 1H), 5.51–5.55 (m, 1H), 7.19–7.26 (m, 4H), 7.90–8.00 (m, 4H); ^{13}C NMR (75 MHz, C_6D_6) δ 22.0, 22.1, 40.6, 65.3, 66.1, 69.6, 69.9 (2C), 70.9 (5C), 72.5 (2C), 77.1, 83.1, 85.0, 86.5, 129.0, 129.5, 130.0 (2C), 130.1 (2C), 130.8 (2C), 131.0 (2C), 144.1, 144.5, 166.7, 166.8; IR (neat) ν 3380, 2958, 2918, 2229, 1723, 1612, 1506, 1451, 1375, 1272, 1179, 1019, 829, 752 cm^{-1}; HRMS (EI) *m*/*z* for $C_{33}H_{30}FeO_5$ calcd 562.1443, found 562.1450. R_f (5/1 hexane/EtOAc)=0.31.

*4.5.12. 1β-[(4-Methoxycarbonylphenyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3βa**). Conditions B.* Methyl 4-iodobenzoate **2a** (35 mg, 0.13 mmol), reaction time 2.5 h. Column chromatography (5/1 hexane/EtOAc) afforded 39 mg (57%) of the title compound as a yellow solid: mp 114–117 °C; $[\alpha]_D^{20}$ −16

(*c* 0.77, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 2.43 (s, 3H), 2.56–2.59 (m, 2H), 3.92 (s, 3H), 4.55 (dd, *J*=12.0, 4.0 Hz, 1H), 4.58 (dd, *J*=12.0, 4.8 Hz, 1H), 4.62 (ddd, *J*=6.4, 4.0, 1.5 Hz, 1H), 5.10–5.15 (m, 1H), 5.58–5.61 (m, 1H), 7.15–7.22 (m, 2H), 7.24–7.29 (m, 2H), 7.40–7.46 (m, 2H), 7.90–7.96 (m, 2H), 7.95–8.05 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7 (2C), 39.9, 52.2, 64.4, 68.8, 76.4, 82.7, 85.1, 89.9, 126.7, 126.9, 127.1, 129.1 (2C), 129.2 (2C), 129.4 (2C), 129.7 (2C), 129.8 (2C), 129.9 (2C), 131.7, 143.8, 144.2, 165.9, 166.3, 166.5; IR (neat) ν 2949, 2920, 2852, 1722, 1613, 1436, 1369, 1272, 1180, 1108, 1016, 839, 755, 692 cm^{-1}; HRMS (EI) *m*/*z* for $C_{31}H_{28}O_7$ calcd 513.1913, found 513.1893. R_f (5/1 hexane/EtOAc)=0.30.

*4.5.13. 1β-[(4-Cyanophenyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3βb**). Conditions B.* 4-Iodobenzonitrile **2b** (30 mg, 0.13 mmol), reaction time 3 h. Column chromatography (5/1 hexane/EtOAc) afforded 30 mg (47%) of the title compound as a yellow solid: mp 126–127 °C, $[\alpha]_D^{20}$ −63 (*c* 0.30, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.43 (s, 3H), 2.57–2.60 (m, 2H), 4.47 (ddd, *J*=6.8, 4.4, 2.4 Hz, 1H), 4.53 (dd, *J*=12.0, 4.4 Hz, 1H), 4.60 (dd, *J*=12.0, 4.4 Hz, 1H), 5.10–5.15 (m, 1H), 5.59–5.61 (m, 1H), 7.15–7.23 (m, 2H), 7.24–7.29 (m, 2H), 7.42–7.45 (m, 2H), 7.53–7.58 (m, 2H), 7.90–7.97 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 21.7, 39.8, 64.3, 68.6, 76.3, 82.8, 84.2, 91.4, 111.9, 118.3, 126.7, 127.0, 127.2, 129.1 (2C), 129.2 (2C), 129.7 (2C), 129.8 (2C), 131.9 (2C), 132.3 (2C), 143.8, 144.3, 165.9, 166.2; IR (neat) ν 2933, 2851, 2221, 1711, 1610, 1502, 1448, 1283, 1264, 1176, 1122, 840, 751, 669 cm^{-1}; HRMS (EI) *m*/*z* for $C_{30}H_{25}NO_5$ calcd 480.1811, found 480.1796. R_f (5/1 hexane/EtOAc)=0.22.

*4.5.14. 1β-[(4-Methoxyphenyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3βc**). Conditions B.* 1-Iodo-4-methoxy-benzene **2c** (31 mg, 0.13 mmol), reaction time 15 h. Column chromatography (5/1 hexane/EtOAc) afforded 8.5 mg (13%) of the title compound as a yellow viscous oil: $[\alpha]_D^{20}$ −26 (*c* 0.35 $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.42 (s, 3H), 2.53–2.57 (m, 2H), 3.81 (s, 3H), 4.43 (ddd, *J*=9.2, 6.8, 4.4 Hz, 1H), 4.52 (dd, *J*=11.8, 1.6 Hz, 1H), 4.58 (dd, *J*=11.8, 1.6 Hz, 1H), 5.08–5.13 (m, 1H), 5.56–5.58 (m, 1H), 6.80–6.84 (m, 2H), 7.15–7.20 (m, 2H), 7.22–7.27 (m, 2H), 7.30–7.35 (m, 2H), 7.89–7.95 (m, 2H), 7.93–7.98 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7 (2C), 39.5, 55.3, 64.4, 69.0, 75.9, 82.1, 86.8, 113.8 (2C), 127.0 (2C), 129.0 (2C), 129.1 (2C), 129.0 (2C), 129.1 (2C), 129.7 (2C), 133.3 (2C), 143.8, 143.9, 166.3 (2C); IR (neat) ν 2959, 2923, 2852, 1719, 1608, 1506, 1458, 1413, 1374, 1261, 1177, 1102, 1021, 797, 752, 669 cm^{-1}; HRMS (EI) *m*/*z* for $C_{30}H_{28}O_6$ calcd 485.1964, found 485.1976. R_f (5/1 hexane/EtOAc)=0.26.

*4.5.15. 1β-[(2-Thienyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3βd**). Conditions B.* 2-Iodothiophene **2d** (28 mg, 15 μL, 0.13 mmol), reaction time 4 h. Column chromatography (3/1 hexane/EtOAc) afforded 20 mg (32%) of the title compound as a dark brown solid: mp 95–96 °C; $[\alpha]_D^{20}$ −55 (*c* 0.32, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.42 (s, 3H), 2.54–2.57 (m, 2H), 4.44 (ddd, *J*=6.8, 4.4, 2.0 Hz, 1H), 4.52 (dd, *J*=11.6, 4.4 Hz, 1H), 4.57 (dd, *J*=11.6, 4.4 Hz, 1H), 5.10–5.15 (m, 1H), 5.56–5.58 (m, 1H), 6.95 (dd, *J*=5.2, 3.6 Hz, 1H), 7.19 (dd, *J*=6.0, 4.8 Hz, 1H), 7.19–7.23 (m, 2H), 7.24–7.27 (m, 1H) (overlapped with $CDCl_3$ and H-*m*-Tol signals), 7.24–7.27 (m, 2H), 7.90–7.98 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 21.7, 39.8, 64.5, 68.9, 76.5, 79.3, 82.6, 90.6, 122.2, 126.8, 126.9, 127.0, 127.6, 129.1 (2C), 129.2 (2C), 129.7 (2C), 129.8 (2C), 132.7, 143.7, 144.2, 165.9, 166.3; IR (neat) ν 2958, 2923, 2851, 1717, 1613, 1454, 1372, 1268, 1179, 1100, 1021, 840, 751, 666 cm^{-1}; HRMS (EI) *m*/*z* for $C_{27}H_{24}O_5S$ calcd 461.1423, found. 461.1442. R_f (5/1 hexane/EtOAc)=0.36.

*4.5.16. 1β-[(3-Thienyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3βe**). Conditions B.* 3-Iodothiophene **2e** (28 mg, 13 μL, 0.13 mmol), reaction time 6 h. Column chromatography (5/1 hexane/EtOAc) afforded 25 mg (41%) of the title compound as a viscous oil: $[\alpha]_D^{20}$ −35 (*c* 0.32, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.42 (s, 3H), 2.53–2.57 (m, 2H), 4.44 (ddd, *J*=6.8, 4.4, 2.4 Hz, 1H), 4.55 (dd, *J*=12.0, 0.8 Hz, 1H), 4.58 (dd, *J*=12.0, 1.2 Hz, 1H), 5.07–5.12 (m, 1H), 5.56–5.59 (m, 1H), 7.07 (dd, *J*=4.8, 1.2 Hz, 1H), 7.16–7.19 (m, 2H), 7.24–7.27 (m, 1H) (overlapped with $CDCl_3$ and H-*m*-Tol signals), 7.24–7.27 (m, 2H), 7.42–7.48 (m, 1H), 7.90–7.98 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 21.8, 39.9, 64.5, 68.9, 76.5, 81.2, 82.6, 86.5, 121.3, 125.2, 126.8, 127.1, 129.1 (2C), 129.2 (2C), 129.4 (2C), 129.7 (2C), 129.8, 129.9, 143.7, 144.2, 165.9, 166.3; IR (neat) ν 2965, 2911, 1715, 1608, 1267, 1480, 1105, 1021, 840, 782, 749 cm^{-1}; HRMS (EI) *m*/*z* for $C_{27}H_{24}O_5S$ calcd 461.1423, found 461.1408. R_f (5/1 hexane/EtOAc)=0.36.

*4.5.17. 1β-[(2-Pyridyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3βf**). Conditions B.* 2-Iodopyridine **2f** (27 mg, 14 μL, 0.13 mmol), reaction time 8 h. Column chromatography (2/1 hexane/EtOAc) afforded 19 mg (33%) as a grey solid. *Conditions C.* 2-Iodopyridine **2f** (27 mg, 14 μL, 0.13 mmol), reaction time 12 h. Column chromatography (2/1 hexane/EtOAc) afforded 42 mg (70%) of the title compound as a grey solid: mp 105–107 °C; $[\alpha]_D^{20}$ −42 (*c* 0.4, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6) δ 1.94 (s, 3H), 2.00 (s, 3H), 2.05–2.34 (m, 1H), 2.26–2.36 (m, 1H), 4.23–4.26 (m, 1H), 4.43 (dd, *J*=10.4, 4.8 Hz, 1H), 4.47 (dd, *J*=10.4, 5.2 Hz, 1H), 4.87 (dd, *J*=8.6, 5.6 Hz, 1H), 5.35–5.37 (m, 1H), 6.45–6.48 (m, 1H), 6.80–6.82 (s, 1H), 6.85–6.88 (m, 2H), 6.90–6.94 (m, 2H), 7.02–7.04 (m, 1H), 8.00–8.02 (m, 2H), 8.17–8.21 (m, 2H), 8.34–8.37 (m, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 22.0, 22.1, 40.4, 65.4, 69.6, 77.6, 83.8, 86.6, 88.3, 115.3, 123.4, 127.9 (2C), 130.0 (4C), 130.8 (2C), 130.9 (2C), 136.2, 144.0, 144.2, 144.6, 150.9, 166.3, 166.8; IR (neat) ν 3040, 2950, 2917, 1721, 1610, 1584, 1464, 1428, 1407, 1368, 1269, 1183, 1105, 1021, 989, 779, 755, 692 cm^{-1}; HRMS (EI) *m*/*z* for $C_{28}H_{25}NO_5$ calcd 456.1811, found 456.1826. R_f (1/1 hexane/EtOAc)=0.61.

*4.5.18. 1β-[(3-Pyridyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3βg**). Conditions B.* 3-Iodopyridine **2g** (27 mg, 0.13 mmol), reaction time 6.5 h. Column chromatography (1/1 hexane/EtOAc) afforded 30 mg (50%) of the title compound as a yellow viscous oil: $[\alpha]_D^{20}$ −26 (*c* 0.27, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 2.42 (s, 3H), 2.57–2.60 (m, 2H), 4.47 (ddd, *J*=6.4, 4.4, 2.4 Hz, 1H), 4.54 (dd, *J*=11.6, 4.4 Hz, 1H), 4.58 (dd, *J*=11.6, 4.4 Hz, 1H), 5.10–5.13 (m, 1H), 5.59–5.61 (m, 1H), 6.99 (s, 1H), 7.17–7.21 (m, 2H), 7.23–7.27 (m, 2H), 7.70 (d, *J*=7.6 Hz, 1H), 7.90–7.94 (m, 2H), 7.95–7.99 (m, 2H), 8.59 (br s, 1H), 8.64 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 21.7, 39.9, 64.3, 68.6, 76.4, 82.3, 82.8, 90.8, 120.2, 126.7, 127.0, 129.1 (2C), 129.2 (2C), 129.6 (2C), 129.7 (2C), 139.3, 143.8, 144.3, 145.8, 148.3, 151.7, 165.9, 166.3; IR (neat) ν 2965, 2911, 1715, 1608, 1267, 1480, 1105, 1021, 840, 782, 749 cm^{-1}; HRMS (ESI) *m*/*z* for $C_{28}H_{25}NO_5$ calcd 456.1811, found 456.1826. R_f (1/1 hexane/EtOAc)=0.68. *Reaction with 3-bromopyridine.* 3-Bromopyridine **2g** (21 mg, 14 μL, 0.132 mmol) reaction time 8 h. Column chromatography (3/1 hexane/EtOAc) afforded 26 mg (43%) as a yellow viscous oil.

*4.5.19. 1β-[(2,2′-Bipyridyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3βh**). Conditions B.* 5-Bromo-[2,2′]bipyridinyl **2h**[22] (31 mg, 0.13 mmol), reaction time 15 h. Column chromatography (1/1 hexane/EtOAc) afforded 13 mg (19%) of the title compound as a white solid: mp 43–45 °C; $[\alpha]_D^{20}$ −40 (*c* 0.68, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 2.43 (s, 3H), 2.59–2.62 (m, 2H), 4.47–4.50 (m, 1H), 4.56 (dd, *J*=11.6, 4.4 Hz, 1H), 4.61 (dd, *J*=11.6, 4.4 Hz, 1H), 5.12–5.16 (m, 1H), 5.59–5.62 (m, 1H), 7.16–7.19 (m, 2H), 7.23–7.27 (m, 2H), 7.31–7.38 (m, 1H), 7.78–7.84 (m, 2H), 7.95–8.00 (m, 4H), 8.36–8.39 (m, 2H), 8.66–8.71 (m, 2H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ 21.6, 21.7, 39.9, 64.3, 68.8, 76.4, 82.8, 82.9, 91.2, 120.1, 120.3, 121.5, 124.1, 125.3, 126.7, 127.0, 129.1 (2C), 129.2 (2C), 129.7 (2C), 129.8 (2C), 137.3, 139.7, 143.9, 144.3, 148.9, 151.8, 155.0, 166.0, 166.3; IR (neat) ν 2956, 2923, 2852, 1721, 1614, 1455, 1380, 1267, 1177, 1102, 1021, 800, 749, 672 cm^{-1}; HRMS (EI) m/z for $C_{33}H_{28}N_2O_5$ calcd 533.2076, found 533.2085. R_f (1/1 hexane/EtOAc)=0.68.

*4.5.20. 1β-[(1-Pyrenyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3βi**). Conditions B.* 1-Bromopyrene **2i** (28 mg, 0.13 mmol), reaction time 8 h. Column chromatography (5/1 hexane/EtOAc) afforded 22 mg (29%) of the title compound as a yellow viscous oil. *Conditions C.* 1-Bromopyrene **2i** (28 mg, 0.13 mmol), reaction time 5 h. Column chromatography (5/1 hexane/EtOAc) afforded 28 mg (36%) of the title compound as a yellow viscous oil. $[\alpha]_D^{20}$ −84 (*c* 0.28, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 2.24 (s, 3H), 2.43 (s, 3H), 2.69–2.81 (m, 2H), 4.54 (m, 1H), 4.63 (dd, *J*=12.0, 4.4 Hz, 1H), 4.67 (dd, *J*=12.0, 4.4 Hz, 1H), 5.34 (dd, *J*=9.2, 6.4 Hz, 1H), 5.68–5.70 (m, 1H), 7.06 (d, *J*=8.0 Hz, 2H), 7.25 (d, *J*=8.0 Hz, 2H) (overlapped with $CDCl_3$ signal), 7.96–8.10 (m, 10H), 8.16–8.21 (m, 2H), 8.46–8.49 (d, *J*=8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 21.7, 40.4, 64.5, 69.2, 76.6, 82.8, 85.0, 92.5, 116.7, 124.2, 124.3, 125.3, 125.6, 125.7, 126.2, 126.8, 127.1, 127.2, 128.3, 128.4, 129.0 (2C), 129.2 (2C), 129.7 (2C), 129.8 (2C), 130.9, 131.2, 131.4, 132.1, 143.6, 144.2, 166.0, 166.4; IR (neat) ν 3036, 2950, 2223, 1718, 1613, 1508, 1296, 1176, 1105, 1018, 911, 848, 749, 716, 687 cm^{-1}; HRMS (FAB) m/z for $C_{39}H_{30}O_5$ calcd 579.2172, found 579.2178. R_f (5/1 hexane/EtOAc)=0.32.

*4.5.21. 1β-[(1-Ferrocenyl)ethynyl]-1,2-dideoxy-3,5-di-O-(4-toluoyl)]-D-ribofuranose (**3βj**). Conditions B.* Iodoferrocene **2j** (41 mg, 0.13 mmol), reaction time 12 h. Column chromatography (5/1 hexane/EtOAc) afforded 15 mg (20%) of the title compound as a dark red viscous oil: $[\alpha]_D^{20}$ −25 (*c* 0.2, $CHCl_3$); ^1H NMR (400 MHz, C_6D_6) δ 1.96 (s, 3H), 2.00 (s, 3H), 2.15 (ddd, *J*=14.0, 6.1, 1.6 Hz, 1H), 2.30 (ddd, *J*=14.0, 9.6, 6.0 Hz, 1H), 3.86–3.90 (m, 1H), 4.05 (s, 5H), 4.24–4.27 (m, 2H), 4.34–4.37 (m, 2H), 4.47 (dd, *J*=11.6, 5.2 Hz, 1H), 4.51 (dd, *J*=11.6, 5.2 Hz, 1H), 4.93 (dd, *J*=9.6, 5.6 Hz, 1H), 5.40–5.44 (m, 1H), 6.86–6.90 (m, 2H), 6.91–6.95 (m, 2H), 8.00–8.04 (m, 2H), 8.16–8.20 (m, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ 22.0, 22.1, 41.0, 59.3, 65.6, 69.70 (2C), 69.9, 71.0 (5C), 72.6 (2C), 77.7, 83.6, 85.2, 85.6, 128.3 (2C), 130.0 (4C), 130.8 (2C), 130.9 (2C), 166.4, 166.8; IR (neat) ν 2959, 2923, 2851, 1914, 1715, 1506, 1455, 1270, 1174, 1105, 1018, 821, 752, 687, 669 cm^{-1}; HRMS (EI) m/z for $C_{33}H_{30}FeO_5$ calcd 562.14426, found 562.14148. R_f (5/1 hexane/EtOAc)=0.40.

4.6. Polymerization of 1αa (conditions *B*)

A solution of $PdCl_2(CH_3CN)_2$ (3.4 mg, 13 μmol), dicyclohexyl-(2′,4′,6′-triisopropyl-biphenyl-2-yl)-phosphine (19.0 mg, 40 μmol), Cs_2CO_3 (112.0 mg, 0.35 mmol), **1αa** (50 mg, 0.13 mmol) in dry acetonitrile (3 mL) was heated to 80 °C for 4 h (until the full consumption of the alkyne). Then the volatiles were removed under reduced pressure and column chromatography of the residue on silica gel (3/1 hexane/EtOAc) gave 5 mg (8%) of **4**, further elution with neat EtOAc yielded 28 mg (56%) of a brown viscous liquid: ^1H NMR (300 MHz, $CDCl_3$) δ 2.0–2.4, 4.2–4.7, 5.0–5.6, 6.7–7.2, 7.5–8.0, all are broad signals and correspond to characteristic signals of the protected deoxyribose moiety.

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Supplementary data

Copies of ^1H and ^{13}C NMR spectra of all new compounds and some experimental details can be found in the online version. Supplementary data associated with this article can be found in online version, at doi:10.1016/j.tet.2009.11.030.

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