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The isochroman- and 1,3-dihydroisobenzofuran-annulation on carbohydrate templates via [2+2+2]-cyclotrimerization and synthesis of some tricyclic nucleosides

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ABSTRACT

The synthesis of enantiopure tricyclic systems comprising isochroman or dihydroisobenzofuran units integrated with sugar templates has been documented. The alkyne cylotrimerization reaction has been employed with easily accessible sugar diynes for the key bicyclic ring construction and thus a provision to alter the functional groups on the newly formed aromatic rings. By selecting two representative trimerization products, we have synthesized the tricyclic nucleosides by simple synthetic manipulations.

1. Introduction

Access to collections of distinctive small molecules is an important aspect in the realm of chemical genetics and for identifying new therapeutic candidates.[1] Several philosophies addressing an ensemble of target molecules either in a forward or a backward sense have been put forward with the ultimate aim of providing flexible and diverse routes that have the potential of addressing both the number and function with ease.[2–4] Designing effective routes to construct complex cyclic structures through transition metal catalyzed reactions has been recognized as an attractive strategy for delivering molecular diversity. In this respect, cycloaddition reactions are considered to be strategically useful, where more than one carbon–carbon or carbon–heteroatom bonds are formed.[5]

We have been exploring the synthesis of a variety of homochiral complex small molecules and also of diverse natural products by employing the transition metal catalyzed reactions on easily available carbohydrate derivatives.[6] In particular, we have been focusing on the [2+2+2]-cyclotrimerization reaction and its application on sugar templates.[7–12] The [2+2+2]-cycloaddition reactions are characterized by high synthetic efficiency (the formation of several C–C and/or C–heteroatom bonds in a single step), complete atom economy, and the availability of a wide range of catalysts that tolerate a myriad of protecting/functional groups.[13] The utility of this reaction is exemplified in the synthesis of a variety of complex natural products consisting of aromatic rings.[14]

The scope of the cyclotrimerization reaction on sugar templates has been less explored and limited mainly to the synthesis of *C*-aryl glycosides.[9–11] An early example in this context is an expedient synthesis of spirocyclic *C*-arylglycoside whose framework is closely related to that of papulacandins by McDonald and co-workers.[9] Recently, Yamamoto and co-workers,[10] and Kotora and co-workers[11] have independently reported a [2+2+2]-cyclotrimerization approach for the synthesis of *C*-aryl ribosides and *C*-aryldeoxyribosides, respectively. In this context, recently we have documented a [2+2+2]-cyclotrimerization on a sugar derived building block for constructing enantiomeric tricyclic molecular skeletons consisting of isochroman units.[8] One such building block has been examined for its suitability in the preparation of a tricyclic nucleoside by simple synthetic manipulations. Considering the simplicity of the [2+2+2]-alkyne cyclotrimerization combined with our interest in exploiting simple carbohydrate building blocks for constructing useful molecular diversity, we intend to further explore this reaction for building modified sugar (spiro)-annulated tricyclic homochiral scaffolds; we also intend to explore the further utilization of these scaffolds for the synthesis of tricyclic nucleosides.

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The two structural units that we have intended to append on sugar skeletons are the isochroman (3,4-dihydro-1*H*-benzo[*c*]pyran)[15] and 1,3-dihydroisobenzofuran,[16] as these are present in a wide range of natural products and also in commercially available drugs (Fig. 1). We have selected the diynes **1** and **2**–**4** (Fig. 2) for a linear isochromannulation and for the spiro-isobenzofurannulation, respectively.[17] Our proposed strategy is shown in Figure 2.

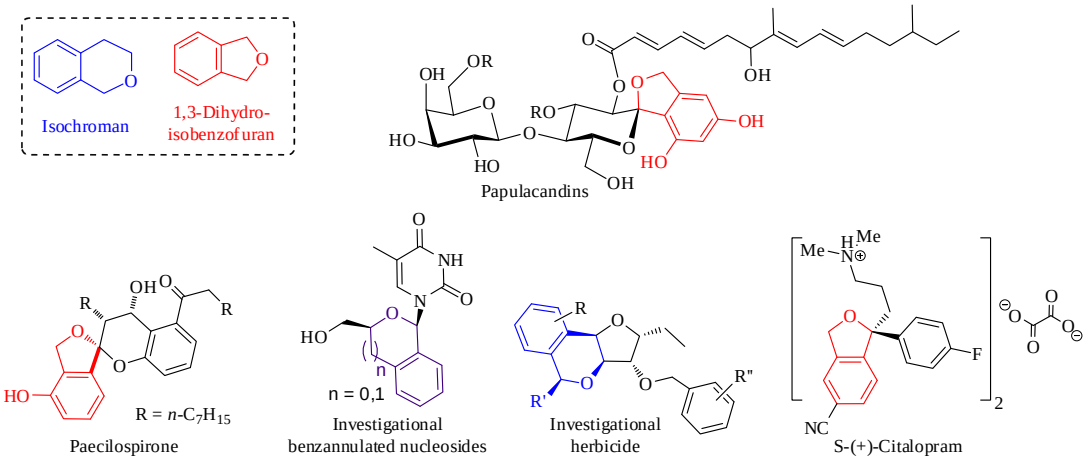


Figure 1. Natural products and/or (investigational) drugs with isochroman and 1,3-dihydroisobenzofuran rings.

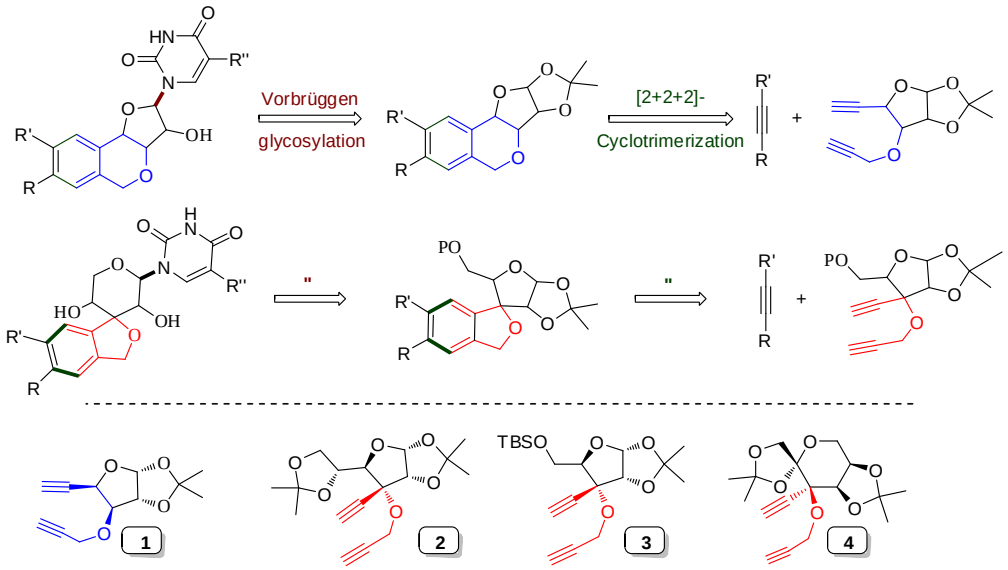
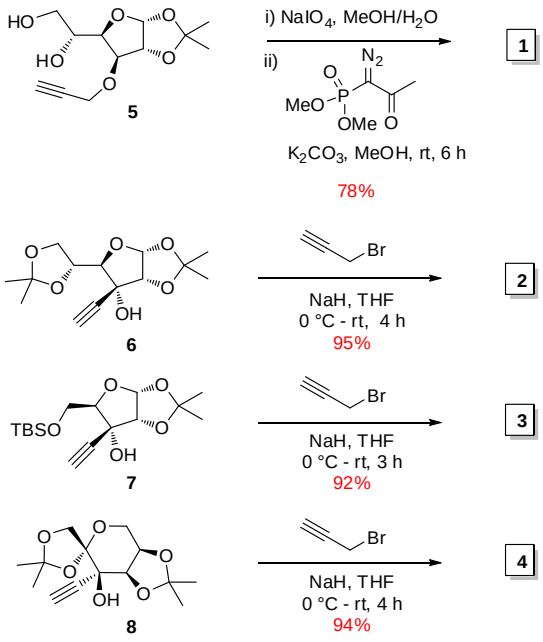


Figure 2. The intended [2+2+2]-cyclotrimerization approach for benzopyranannulation and isobenzofuranulation on sugar templates, glycosidation with pyrimidine base, and the selected sugar diyne substrates **1**–**4**.

2. Results and discussion

Scheme 1 describes the synthesis of the key diynes **1**–**4**. The diyne **1** was prepared from the known diol **5**[18] in 78% overall yield through sodium metaperiodate mediated cleavage and subsequent Ohira–Bestmann alkynylation[19] of the intermediate aldehyde. The diynes **2**–**4** were prepared by simple propargylation of the known alkynols **6**,[6e] **7**,[6e] and **8**,[20] respectively.

With the fully elaborated diyne framework **1**–**4** in place, we first examined the cyclotrimerization of diyne **1** (Table 1, entry 1) with 2-butyne-1,4-diol by employing some commonly used trimerization catalysts. We found that the reactions with Wilkinson's catalyst ($[RhCl(PPh_3)_3]$)[21] were smooth and gave the corresponding tricyclic compound **9** in 61% yield. The optimized conditions for this reaction involve the heating of the diyne with the diol in toluene/ethanol mixture (4:1) at 80 °C. The spectral and analytical data of **9** were in accordance with the assigned structure. In the NOESY spectrum, the observed cross peaks between C(4)–H and the aromatic ring proton at δ 7.24 has helped in assigning the ratios of the regiomeric compounds resulting from unsymmetric alkynes. To illustrate the flexibility of our strategy, several mono- and disubstituted alkynes were employed as the substrates (Table 1, entries 2–10). With acetylene (entry 2) and dimethyl acetylene dicarboxylate (entry 4) as the substrates, the cyclotrimerization reaction proceeded effectively at 80 °C in a sealed tube to afford **10** and **12** in 65% and 45% yields, respectively. Interestingly, the reaction of **1** with dimethyl acetylene dicarboxylate did not proceed at different temperatures under atmospheric pressure. Next sterically crowded alkynes such as dodec-6-yne (entry 5), bis-(trimethylsilyl)acetylene (entry 6) and diphenyl acetylene (entry 7) are employed for the trimerization reaction with the diyne **1**. The reactions are sluggish and no identifiable products could be



Scheme1. Synthesis of diynes **1**–**4**.

isolated. The cyclotrimerization of diyne **1** with the monosubstituted alkynes, such as phenyl acetylene (entry 8), *N*-propargyl phthalimide (entry 9), and 1-hexadecyne (entry 10) gave inseparable regiomeric mixtures **13**–**15**, respectively in good yields.[22]

Next, the cyclotrimerization of diyne **2** with various symmetric-disubstituted and monosubstituted alkynes were investigated and the results are given in Table 1 (entries 11–20). We examined the cyclotrimerization of diyne **2** and butyne-1,4-diol under conditions similar to those used in the reaction with diyne **1**. The reaction was clean and gave the corresponding spiro-dihydroisobenzofurannulated derivative **16** in 68% yield (Table 1, entry 11). The structure of compound **16** was assigned with the help of ^{1}H, ^{13}C NMR and other analytical data. In the ^{1}H NMR spectrum of **16**, two aromatic–H appeared as singlets at δ 7.09 and δ 7.27. The characteristic C(1′)–H and C(2′)–H of the furanose ring appeared as a doublets at δ 5.99 and δ 4.39 ($J_{1,2}$=3.5 Hz), respectively. The C(4)–H appeared downfield (δ 4.27) as doublet with J=8.5 Hz. The observed cross peaks between benzylic CH_2 and the aromatic ring proton at δ 7.27 in the NOESY spectrum was helpful in assigning the ratios of the regiomeric compounds resulting from unsymmetric alkynes (Fig. 3)

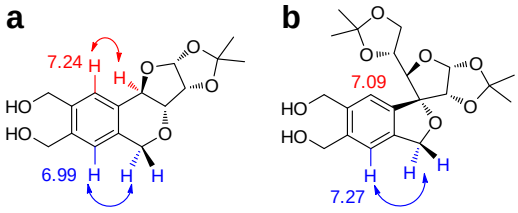
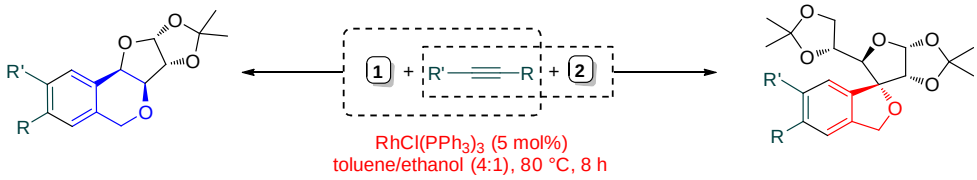
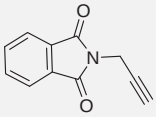


Figure 3. Observed through spatial contacts in the NOESY spectra of compounds (a) **9** and (b) **16**.

The results of the cyclotrimerization of diynes **1** and **2** with various symmetric-disubstituted and monosubstituted alkynes are given in Table 1 (entries 11–20). In the case of sterically crowded alkynes, such as bis-(trimethylsilyl)acetylene (entry 16) and

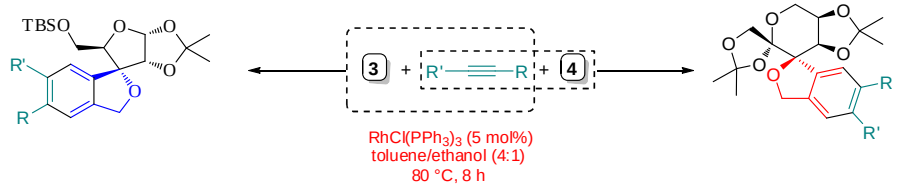
Table 1
Cyclotrimerization of diynes **1** and **2** with various symmetrically disubstituted and monosubstituted alkynes



Entry	Product (s)	Yield	Alkyne	Entry	Product (s)	Yield (%)
1	**9** (R=R′=CH_2OH)	61%	HOH_2C—≡—CH_2OH	11	**16** (R=R′=CH_2OH)	68
2	**10** (R=R′=H)	65%	H—≡—H	12	**17** (R=R′=H)	76
3	**11** (R=R′=CH_2OAc)	57%	$AcOH_2C$—≡—CH_2OAc	13	**18** (R=R′=CH_2OAc)	65
4	**12** (R=R′=CO_2Me)	45%	MeO_2C—≡—CO_2Me	14	**19** (R=R′=CO_2Me)	52
5	No product	—	*n*-C_5H_{11}—≡—*n*-C_5H_{11}	15	**20** (R=R′=C_5H_{11})	43
6	No product	—	TMS—≡—TMS	16	Diyne self trimerization	—
7	No product	—	Ph—≡—Ph	17	Diyne self trimerization	—
8	**13a** (R=Ph,R′=H) **13b** (R=H,R′=Ph) (1:4)	72%	≡—Ph	18	**21a** (R=Ph,R′=H) **21b** (R=H,R′=Ph) (1:3)	69
9	14a (R=CH_2NPhth,R′=H) **14b** (R=H,R′=CH_2NPhth) (1:3)	67%		19	**22a** (R=CH_2NPhth,R′=H) **22b** (R=H,R′=CH_2NPhth) (2:3)	72%
10	**15a** (R=*n*-$C_{14}H_{29}$,R′=H) **15b** (R=H,R′=*n*-$C_{14}H_{29}$) (1:1)	49%	*n*-$C_{14}H_{29}$—≡	20	**23a** (R=*n*-$C_{14}H_{29}$,R′=H) **23b** (R=H,R′=*n*-$C_{14}H_{29}$) (1:1)	52%

diphenyl acetylene (entry 17) we observed the dimerized products of diyne **2** (see Supplementary data for the NMR). Whereas, the cyclotrimerization of **2** with the other sterically crowded alkyne dodec-6-yne (entry 15), gave the expected product **20** in moderate yield. Similar to the diyne **1**, the trimerization reaction of the diyne **2** with phenyl acetylene (entry 18), *N*-propargyl phthalimide (entry 19), and 1-hexadecyne (entry 20) gave inseparable regiomeric mixtures **21**–**23**, respectively in good yields.[22] Next, we examined the scope of trimerization with diynes **3** and **4**. The results of the trimerization of diynes **3** and **4** with selected alkynes are given in Table 2.

Table 2
Cyclotrimerization of diynes **3** and **4** with mono- and disubstituted alkynes

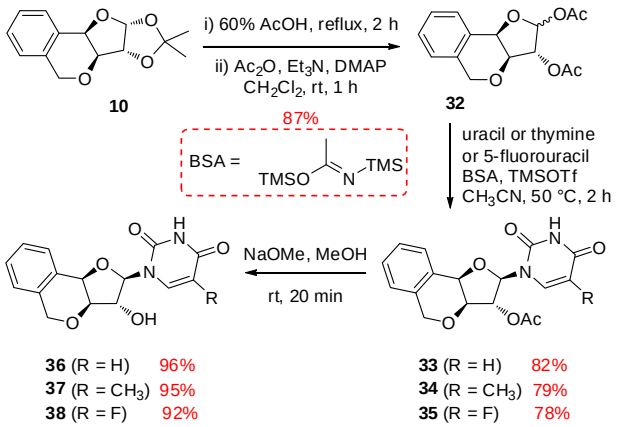


Entry	Product(s)	Yield	Alkyne	Entry	Product (s)	Yield
1	**24** (R=R′=H)	72%	H—≡—H	5	**28** (R=R′=H)	73%
2	**25** (R=R′=CH_2OAc)	60%	$AcOH_2C$—≡—CH_2OAc	6	**29** (R=R′=CH_2OAc)	65%
3	**26** (R=R′=CO_2Me)	67%	MeO_2C—≡—CO_2Me	7	**30** (R=R′=CO_2Me)	67%
4	**27a** (R=Ph,R′=H) **27b** (R=H,R′=Ph) (1:3)	78%	≡—Ph	8	**31a** (R=Ph,R′=H) **31b** (R=H,R′=Ph) (3:1)	75%

3. Synthesis of modified nucleosides

Considering the importance of modified nucleosides in antiviral and anticancer drug discovery programs,[23] we intended to carry out glycosylation of the cyclotrimerization products with easily available pyrimidine nucleobases, which should effectively address the synthesis of either conformationally restricted[24] or spiroannulated nucleosides.[25] We examined the feasibility of the synthesis of modified tricyclic nucleosides by employing isochroman **10**. The isochroman derivative **10** was subjected to acid catalyzed acetonide hydrolysis using acetic acid followed by acetylation of the hydrolyzed derivative by using acetic anhydride and Et_3N in dichloromethane to afford a 1:1 anomeric mixture of **32** (Scheme 2). Next, we proceeded to synthesize tricyclic nucleosides using **32**. The treatment of **32** with uracil, thymine, and 5-fluorouracil under modified Vorbrüggen[26] conditions afforded the protected nucleosides **33**–**35**, respectively. The structures of the protected nucleosides **33**–**35** were assigned with the help of extensive NMR spectroscopy studies. The C(1′)–H and C(2′)–H of the furanose ring appeared as doublets at δ 6.16 and δ 5.22 (J=1.6 Hz), respectively revealing the anomeric configuration as β. The assigned β-configuration of the glycosidic linkage was further confirmed by single crystal X-ray analysis of **33** (Fig. 4a).[27–29]

Subjecting **33**–**35** to Zemplen's deacetylation gave the tricyclic nucleosides **36**–**38** in excellent yields. The structural integrity and β-configuration of compound **36** were established with the help of



Scheme 2. Synthesis of benzopyrannulated nucleosides.

COSY and NOESY. For example, in the ^{1}H NMR spectrum of **36**, the characteristic C(1′)–H and C(2′)–H of the furanose ring appeared at δ 5.89 (s) and 4.52 (s), respectively. In the NOESY experiments of **36** (Fig. 5a), C(4)–H showed spatial interaction with C(3′)–H as well as with C(1′)–H. A similar β-configuration was assigned for **37** and **38** by comparing their chemical shifts and coupling constants with those of **36**. The β-configuration was confirmed by single crystal X-ray analysis of **37** (Fig. 4b).[27]

We executed a similar sequence of reactions with *C*(3)–spirobenzofurannulated ribose derivative **24** (Scheme 3). Global deprotection of **24** by heating in 60% acetic acid at the reflux temperature for 2 h gave the corresponding lactols, which was subsequently subjected to acetylation using acetic anhydride and Et_3N in dichloromethane to afford **39** in 83% yield in two steps (Scheme 3). In the ^{1}H NMR spectrum of **39**, C(1)–H appeared as a doublet at δ 6.04 with an 8.5 Hz coupling constant. The C(3)–H also appeared as a doublet at δ 5.31 with an J=8.2 Hz and the two C(5)–H_2 as a doublet at δ 4.01 (J=8.1 Hz). The large coupling constants observed indicated the formation of a β-pyranoside framework during the peracetylation of the intermediate lactols.[30] Next we proceeded to carry out the synthesis of tricyclic nucleosides using **39**. The treatment of **39** with uracil, thymine, and 5-fluorouracil under conditions similar to those employed for the glycosylation of **32** afforded the protected nucleosides **40**–**42**. The structures of the protected nucleosides **40**–**42** were assigned with the help of extensive NMR spectroscopy studies. The anomeric proton of **40** resonated as a doublet at δ 5.72 with a coupling constant J=8.2 Hz in the ^{1}H NMR spectrum. The assigned β-configuration of the glycosidic linkage and the pyranose form of the sugar ring were further confirmed by single crystal X-ray analysis of **40** (Fig. 4c).

Subjecting **40**–**42** to Zemplen's deacetylation afforded the tricyclic spironucleosides **43**–**45**. The structural integrity and β-configuration of compound **44** were established with the help of COSY

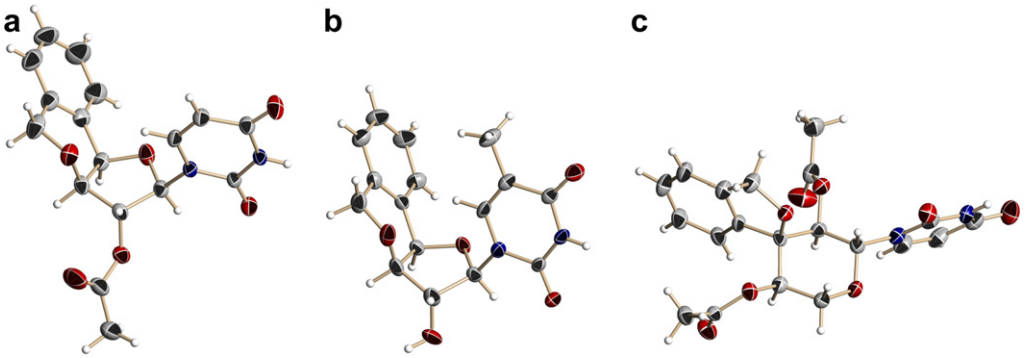


Figure 4. ORTEP Structures of (a) compound **33** (b), Compound **37** and (c) compound **40**.

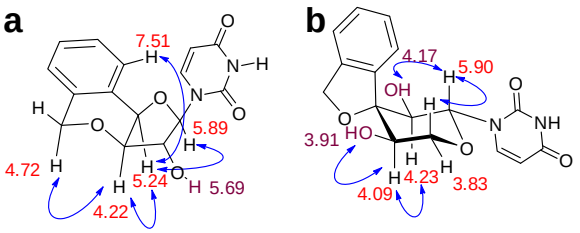
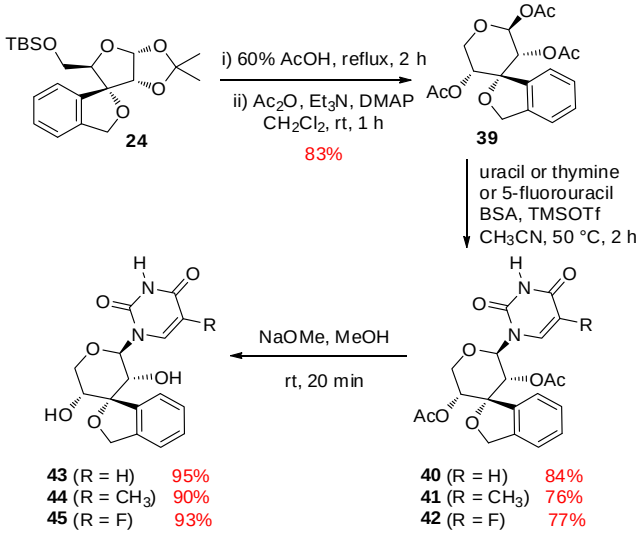


Figure 5. Observed through spatial contacts in the NOESY spectra of compounds (a) **36** and (b) **44**.



Scheme 3. Synthesis of spiro-isobenzofurannulated nucleosides.

and NOESY experiments. For example, in the ^{1}H NMR spectrum of **44**, the characteristic C(1′)–H and C(2′)–H of the pyranose ring appeared at δ 5.90 (d) and 4.23 (t), respectively, with $J_{1,2}$=9.5 Hz. The C(2′)–OH resonated as a doublet at 4.17 ppm (J=9.2 Hz), indicating a strong intramolecular hydrogen bonding,[31] and C(4′)–H appeared as a ddd (δ 4.09 ppm, J=10.8, 8.8, 5.5 Hz). In the NOESY experiments spectrum of **44** (Fig. 5b), C(1′)–H showed spatial interaction with C(4′)–H and C(2′)–OH, thus confirming the assigned β-configuration. A similar β-configuration was assigned for **43** and **45** by comparing their chemical shifts and coupling constants with those of **44**.

In summary, we have demonstrated the application of the [2+2+2]-cyclotrimerization reaction to the synthesis of enantiopure tricyclic systems comprising the isochroman or dihydroisobenzofuran units integrated with a sugar ring. The regioselectivity is one of the drawbacks of terminal alkynes. By selecting a representative trimerization product from each family, we synthesized tricyclic nucleosides by simple synthetic manipulations. Considering the importance of modified nucleosides (antiviral agents, antisense therapeutic and diagnostic agents) in medicinal chemistry programs, the results from the present investigation could be further explored for a strategic construction of related small molecule libraries. Work in this direction is ongoing in our laboratory.

4. Experimental

4.1. General methods

Air and/or moisture sensitive reactions were carried out in anhydrous solvents under an argon atmosphere in oven-dried glassware. All anhydrous solvents were distilled prior to use: Toluene from Na and benzophenone; CH_2Cl_2 and DMF from CaH_2; MeOH and EtOH from Mg cake. Commercial reagents were used without purification. Column chromatography was carried out by using Spectrochem silica gel (100–200 mesh). Optical rotations were determined on a Jasco DIP-370 digital polarimeter. Specific optical rotations $[\alpha]_D$ are given in 10^{-1} deg cm^2 g^{-1}. ^{1}H and ^{13}C NMR spectroscopy measurements were carried out on Bruker AC 200 MHz or Bruker DRX 400 MHz spectrometers, and TMS was used as internal standard. The ^{1}H and ^{13}C NMR chemical shifts are reported in parts per million downfield from tetramethylsilane and the coupling constants (J) are reported in Hertz (Hz). The following abbreviations are used to designate signal multiplicity: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad. The multiplicity of the ^{13}C NMR signals was assigned with the help of DEPT spectra and the terms s=singlet, d=doublet, t=triplet, and q=quartet represent C (quaternary), CH, CH_2, and CH_3, respectively. Mass spectroscopy was carried out on an API QStar Pulsar (Hybrid Quadrupole-TOF LC/MS/MS) spectrometer. Elemental analysis data were obtained on a Thermo Finnigan Flash EA 1112 Series CHNS Analyzer.

*4.1.1. 1,2-O-Isopropylidene-3-O-propargyl-α-D-xylo-hexofuranose (**1**).* To a solution of diol **5** (1.5 g, 5.8 mmol) in methanol (25 mL) and water (2 mL), $NaIO_4$ (1.4 g, 7.0 mmol) was added and stirred for 30 min at room temperature. The mixture was filtered through Celite and concentrated under reduced pressure. The residue was extracted with ethyl acetate, washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford an intermediate aldehyde (1.2 g). To a suspension of the above aldehyde (1.2 g, 7.9 mmol) and K_2CO_3 (1.4 g, 10.3 mmol) in methanol (30 mL), Ohira–Bestmann reagent (1.85 g, 9.5 mmol) was added at room temperature and stirred for 6 h. The reaction mixture was concentrated under reduced pressure, and the crude material was partitionated between water and ethyl acetate. The organic phase was separated, dried (Na_2SO_4), and concentrated under reduced

pressure. The purification of residue by silica gel column chromatography (7% ethyl acetate in petroleum ether) gave **1** (920 mg, 78% yield) as a colorless oil; R_f (25% ethyl acetate/pet. ether) 0.45; $[\alpha]_D^{25}$ +33.7 (*c* 1.3, $CHCl_3$); IR ($CHCl_3$) ν: 3291, 2990, 2938, 2120, 1455, 1376, 1347, 1254, 1218, 1164, 1078, 1028, 952, 861, 758, 667 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 1.30 (s, 3H), 1.47 (s, 3H), 2.46 (t, *J*=2.4 Hz, 1H), 2.55 (d, *J*=2.3 Hz, 1H), 4.17 (d, *J*=3.0 Hz, 1H), 4.40 (t, *J*=2.2 Hz, 2H), 4.60 (d, *J*=3.8 Hz, 1H), 4.80 (t, *J*=2.6 Hz, 1H), 5.91 (d, *J*=3.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 26.1 (q), 26.7 (q), 58.0 (t), 70.2 (d), 75.4 (d), 76.5 (d), 77.1 (s), 78.8 (s), 81.8 (d), 82.7 (d), 104.5 (d), 111.9 (s) ppm; ESI-MS (*m*/*z*): 223.2 (5%, $[M+H]^+$), 240.3 (15%, $[M+NH_4]^+$), 245.2 (100%, $[M+Na]^+$), 261.2 (6%, $[M+K]^+$). Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.82; H, 6.38.

4.2. General procedure for the O-propargylation and synthesis of diynes 2–4

To a suspension of alcohol **6** (8.0 g, 28 mmol), NaH (1.7 g, 42 mmol) in DMF (60 mL), propargyl bromide (3 mL, 34 mmol) was added drop-wise at 0 °C. The reaction mixture was allowed to warm to room temperature, stirred for 2 h, quenched with slow addition of cold water at 0 °C and extracted with ethyl acetate. The combined organic layer was washed with water, dried over Na_2SO_4, concentrated, and purified by silica gel column chromatography (10% ethyl acetate in light petroleum) to give **2** (8.5 g, 95%) as a white powder.

*4.2.1. 1,2:5,6-Di-O-isopropylidene-3-C-ethynyl-3-O-propargyl-α-D-allofuranose (**2**).* Colorless oil; R_f (30% ethyl acetate/pet. ether) 0.55; $[\alpha]_D^{25}$ +23.2 (*c* 2.3, $CHCl_3$); IR ($CHCl_3$) ν: 3306, 3018, 2991, 2937, 2112, 1456, 1384, 1309, 1217, 1166, 1135, 1076, 1030, 990, 844, 758 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 1.34 (s, 6H), 1.42 (s, 3H), 1.58 (s, 3H), 2.41 (t, *J*=2.4 Hz, 1H), 2.75 (s, 1H), 4.04–4.11 (m, 3H), 4.31 (t, *J*=5.8 Hz, 1H), 4.41 (dd, *J*=2.4, 9.1 Hz, 2H), 4.62 (d, *J*=3.5 Hz, 1H), 5.76 (d, *J*=3.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 25.4 (q), 26.6 (q), 26.9 (q), 26.9 (q), 54.7 (t), 66.2 (t), 74.4 (d), 74.5 (s), 78.2 (s), 79.7 (s), 80.4 (s), 81.0 (s), 81.2 (d), 83.4 (d), 104.0 (d), 109.2 (s), 113.8 (s) ppm; ESI-MS (*m*/*z*): 323.3 (6%, $[M+H]^+$), 340.4 (6%, $[M+NH_4]^+$), 335.4 (100%, $[M+Na]^+$). Anal. Calcd for $C_{12}H_{14}O_4$: C, 63.34; H, 6.88. Found: C, 63.19; H, 7.01.

*4.2.2. 1,2-O-Isopropylidene-5-O-(tert-butyldimethylsilyl)-3-C-ethynyl-3-O-propargyl-α-D-ribofuranose (**3**).* The procedure used for the preparation of **2** was used with alkynol **7** (5 g, 16 mmol) to prepare diyne **3** (5.1 g, 92%) as a white solid. Mp: 105–110 °C; R_f (20% ethyl acetate/pet. ether) 0.50; $[\alpha]_D^{25}$ +40.6 (*c* 1.1, $CHCl_3$); IR ($CHCl_3$) ν: 3307, 2955, 2931, 2885, 2858, 2110, 1473, 1375, 1254, 1132, 1047, 876 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 0.06 (s, 6H), 0.88 (s, 9H), 1.33 (s, 3H), 1.57 (s, 3H), 2.44 (t, *J*=2.4 Hz, 1H), 2.66 (s, 1H), 3.81–3.97 (2dd, *J*=3.9, 11.2 Hz, 2H), 4.15 (dd, *J*=3.9, 6.7 Hz, 1H), 4.32 (dd, *J*=2.4, 14.6 Hz, 1H), 4.45 (dd, *J*=2.4, 14.6 Hz, 1H), 4.59 (d, *J*=3.6 Hz, 1H), 5.82 (d, *J*=3.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ −5.4 (q), −5.2 (q), 18.3 (s), 25.9 (q, 3C), 26.8 (q), 26.9 (q), 54.5 (t), 63.0 (t), 74.5 (d), 77.8 (d), 79.4 (s), 79.5 (s), 80.6 (s), 81.7 (d), 82.8 (d), 104.3 (d), 113.6 (s) ppm; ESI-MS (*m*/*z*): 367.5 (5%, $[M+H]^+$), 389.5 (100%, $[M+Na]^+$), 405.5 (67%, $[M+K]^+$). Anal. Calcd for $C_{19}H_{30}O_5Si$: C, 62.26; H, 8.25. Found: C, 62.12; H, 8.37.

*4.2.3. 1,2:4,5-Di-O-isopropylidene-3-C-ethynyl-3-O-propargyl-α-D-psicopyranose (**4**).* The procedure used for preparing **3** was used with alkynol **8** (2 g, 16 mmol), affording diyne **4** (2.1 g, 94%) as a white solid. Mp: 104–106 °C; R_f (30% ethyl acetate/pet. ether) 0.45; $[\alpha]_D^{25}$ −139.5 (*c* 1.6, $CHCl_3$); IR ($CHCl_3$) ν: 3271, 2989, 2939, 2114, 1458, 1255, 1094, 1015, 981 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 1.34 (s, 3H), 1.44 (s, 3H), 1.48 (s, 3H), 1.55 (s, 3H), 2.41 (t, *J*=2.4 Hz, 1H), 2.73 (s, 1H), 3.97–4.08 (m, 2H), 4.19–4.28 (m, 2H), 4.43 (d, *J*=9.3 Hz, 1H), 4.48 (d, *J*=6.2 Hz, 1H), 4.53 (d, *J*=2.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz): 25.2 (q), 25.9 (q), 26.2 (q), 26.2 (q), 56.3 (t), 61.2 (t), 71.3 (d), 73.0 (t), 74.5 (d), 74.9 (s), 77.6 (d), 77.6 (s), 79.0 (d), 80.3 (d), 105.5 (s), 109.9 (s), 112.2 (s) ppm; ESI-MS (*m*/*z*): 345.3 (100%, $[M+Na]^+$), 361.3 (73%, $[M+K]^+$). Anal. Calcd for $C_{17}H_{22}O_6$: C, 63.34; H, 6.88. Found: C, 63.19; H, 6.97.

4.3. Representative procedures for the [2+2+2]-cyclotrimerization reactions of diynes 1–4

Procedure A: A solution of diyne **1** (0.5 mmol) and alkyne (1.5 mmol) in 4:1 toluene/ethanol (12 mL) was degassed with dry argon for 20 min. To this, Wilkinson's catalyst [$RhCl(PPh_3)_3$] (0.03 mmol) was added, and the mixture was heated at 80 °C for 6 h and then allowed to cool to room temperature. The solvent evaporated under reduced pressure. The residue was purified by silica gel chromatography to procure the cyclotrimerization product.

Procedure B: A solution of diyne **1** (0.5 mmol) and alkyne (1.5 mmol) in toluene/ethanol (12 and 3 mL, respectively) in a sealed tube was degassed with dry argon for 20 min; thereafter, Wilkinson's catalyst [$RhCl(PPh_3)_3$] (0.03 mmol) was introduced and the tube sealed by fusion. The sealed tube was transferred into a steel bomb and heated at 80 °C for 4 h. After cooling to room temperature, the tube was broken and the mixture was transferred into a round-bottom flask and concentrated under reduced pressure. The residue was purified by silica gel chromatography (ethyl acetate in petroleum ether) to give the cyclotrimerization product.

Procedure C: A solution of diyne **1** (0.5 mmol) in toluene (10 mL) was degassed with dry acetylene for 20 min; then, Wilkinson's catalyst [$RhCl(PPh_3)_3$] (0.03 mmol) was introduced into the mixture. The reaction mixture was sealed with septum and a copper wire and cooled to −78 °C, and acetylene gas was condensed by continuous bubbling for 25 min. The reaction was transferred into steel bomb, heated at 80 °C for 4 h, and then allowed to cool to room temperature. The solvent was evaporated under reduced pressure. The residue was purified by silica gel chromatography (ethyl acetate in petroleum ether) to afford the cyclotrimerized product.

*4.3.1. 1,2-O-Isopropylidene-4-C,3-O-[o-{(3,4-bis(hydroxymethyl))} phenylenemethylene]-α-D-xylotetrofuranose (**9**).* Following procedure B, the cyclotrimerization of diyne **1** (120 mg, 0.54 mmol) and butynediol (140 mg, 1.6 mmol) gave **9** (102 mg, 61%) as a viscous oil; R_f (30% ethyl acetate/pet. ether) 0.30; $[\alpha]_D^{25}$ +28.0 (*c* 1.2, $CHCl_3$); IR ($CHCl_3$) ν: 3401, 3016, 2932, 1624, 1438, 1216, 1080, 1017, 898 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 1.35 (s, 3H), 1.58 (s, 3H), 3.90 (br s, 2H), 4.09 (d, *J*=2.3 Hz, 1H), 4.48–4.55 (m, *J*=12.7 Hz, 3H), 4.58 (d, *J*=15.1 Hz, 1H), 4.59 (d, *J*=12.7 Hz, 1H), 4.67 (d, *J*=3.8 Hz, 1H), 4.70 (d, *J*=15.1 Hz, 1H), 4.90 (d, *J*=2.3 Hz, 1H), 5.93 (d, *J*=3.8 Hz, 1H), 6.99 (s, 1H), 7.24 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 26.1 (q), 26.7 (q), 62.7 (t, 2C), 67.0 (t), 73.1 (d), 79.8 (d), 84.4 (d), 104.9 (d), 111.7 (s), 124.6 (d), 128.4 (s), 130.9 (d), 134.4 (s), 138.2 (s), 140.2 (s) ppm; ESI-MS (*m*/*z*): 309.4 (3%, $[M+H]^+$), 331.3 (100%, $[M+Na]^+$), 347.3 (4%, $[M+K]^+$). Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.33; H, 6.54. Found: C, 62.12; H, 6.68.

*4.3.2. 1,2-O-Isopropylidene-4-C,3-O-(o-phenylenemethylene)-α-D-xylotetrofuranose (**10**).* Following the general procedure C, the cyclotrimerization of diyne **1** (150 mg, 0.68 mmol) afforded **10** (109 mg, 65%) as a viscous oil; R_f (25% ethyl acetate/pet. ether) 0.55; $[\alpha]_D^{25}$ +21.6 (*c* 1.5, $CHCl_3$); IR ($CHCl_3$) ν: 3018, 2927, 1612, 1458, 1376, 1216, 1164, 1091, 1020, 920 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 1.28 (s, 3H), 1.50 (s, 3H), 4.07 (d, *J*=2.4 Hz, 1H), 4.59 (d, *J*=14.9 Hz, 1H), 4.60 (d, *J*=3.8 Hz, 1H), 4.71 (d, *J*=14.9 Hz, 1H), 4.88 (d, *J*=2.4 Hz, 1H), 5.89 (d, *J*=3.8 Hz, 1H), 6.94–6.99 (m, 1H), 7.17–7.23 (m, 2H),

7.35–7.42 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 26.3 (q), 26.9 (q), 67.4 (t), 73.5 (d), 80.1 (d), 84.7 (d), 105.2 (d), 111.6 (s), 124.2 (d), 127.4 (d), 128.7 (d), 129.5 (s), 130.7 (d), 134.8 (s) ppm; ESI-MS (*m*/*z*): 266.3 (36%, $[M+NH_4]^+$), 271.3 (100%, $[M+Na]^+$). Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50%; Found: C, 67.88; H, 6.59%.

*4.3.3. 1,2-O-Isopropylidene-4-C,3-O-[o-{3,4-bis(acetyloxymethy)} phenylenemethylene]-α-D-xylotetrofuranose (**11**).* The general procedure A was followed. Diyne **1** (100 mg, 0.45 mmol) and diacetate of 2-butyne-1,4-diol (230 mg, 1.4 mmol) were used to obtain **11** (101 mg, 57%) as colorless oil; R_f (30% ethyl acetate/pet. ether) 0.35; $[\alpha]_D^{25}$ +6.8 (*c* 1.1, $CHCl_3$); IR ($CHCl_3$) ν: 3020, 2932, 2854, 1740, 1614, 1454, 1244, 1064, 1118, 1104, 1081, 1022, 896 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.35 (s, 3H), 1.58 (s, 3H), 2.06 (s, 3H), 2.09 (s, 3H), 4.15 (d, *J*=2.3 Hz, 1H), 4.65 (d, *J*=15.2 Hz, 1H), 4.69 (d, *J*=3.8 Hz, 1H), 4.79 (d, *J*=15.2 Hz, 1H), 4.97 (d, *J*=2.2 Hz, 1H), 5.14, 5.16 (2s, 4H), 5.97 (d, *J*=3.8 Hz, 1H), 7.11 (s, 1H), 7.55 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 20.8 (q), 20.9 (q), 26.2 (q), 26.8 (q), 63.2 (t), 63.3 (t), 67.0 (t), 72.9 (d), 79.9 (d), 84.5 (d), 105.1 (d), 111.6 (s), 125.7 (d), 129.9 (s), 131.7 (d), 133.8 (s), 134.9 (s), 135.1 (s), 170.3 (s), 170.4 (s) ppm; ESI-MS (*m*/*z*): 410.5 (37%, $[M+NH_4]^+$), 415.4 (100%, $[M+Na]^+$), 431.4 (5%, $[M+K]^+$). Anal. Calcd for $C_{20}H_{24}O_8$: C, 61.22; H, 6.16%. Found: C, 61.15; H, 6.29.

*4.3.4. 1,2-O-Isopropylidene-4-C,3-O-[o-{3,4-bis(methoxycarbonyl)} phenylenemethylene]-α-D-xylotetrofuranose (**12**).* Following the general procedure B, the cycloaddition of diyne **1** (120 mg, 0.54 mmol) and dimethyl acetylene dicaboxylate (230 mg, 1.6 mmol) gave **12** (89 mg, 45%) as colorless oil; R_f (30% ethyl acetate/pet. ether) 0.34; $[\alpha]_D^{25}$ +8.7 (*c* 1.4, $CHCl_3$); IR ($CHCl_3$) ν: 3022, 2994, 2955, 2847, 1726, 1620, 1578, 1437, 1215, 1163, 1093, 1045, 895 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.35 (s, 3H), 1.56 (s, 3H), 3.83 (s, 3H), 3.88 (s, 3H), 4.16 (d, *J*=2.4 Hz, 1H), 4.66 (d, *J*=15.6 Hz, 1H), 4.68 (d, *J*=3.8 Hz, 1H), 4.83 (d, *J*=15.6 Hz, 1H), 4.95 (d, *J*=2.4 Hz, 1H), 5.94 (d, *J*=3.8 Hz, 1H), 7.38 (s, 1H), 7.91 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 26.2 (q), 26.8 (q), 52.5 (q), 52.7 (q), 66.8 (t), 72.5 (d), 79.9 (d), 84.5 (d), 105.2 (d), 111.8 (s), 124.8 (d), 130.4 (s), 131.6 (d), 132.5 (s), 132.6 (s), 138.3 (s), 166.8 (s), 167.6 (s) ppm; ESI-MS (*m*/*z*): 365.4 (29%, $[M+H]^+$), 387.4 (100%, $[M+Na]^+$), 403.4 (11%, $[M+K]^+$). Anal. Calcd for $C_{18}H_{20}O_8$: C, 59.34; H, 5.53. Found: C, 59.48; H, 5.70.

*4.3.5. 1,2-O-Isopropylidene-4-C,3-O-[o-(3- or 4-phenyl)phenylenemethylene]-α-D-xylotetrofuranose (**13a**/**13b**).* The general procedure A was followed. Diyne **1** (120 mg, 0.54 mmol) and phenyl acetylene (0.2 mL, 1.6 mmol) were used to procure a mixture of **13a** and **13b** (126 mg, 72%) as reddish oil; R_f (30% ethyl acetate/pet. ether) 0.53; IR ($CHCl_3$) ν: 3019, 2926, 1679, 1488, 1453, 1384, 1163, 1019 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.30 (s, 3H), 1.53 (s, 3H), 4.12 (d, *J*=2.3 Hz, 1H), 4.62–4.82 (m, *J*=3.8, 15.5 Hz, 3H), 4.94, 4.95 (2d, *J*=2.3 Hz, 1H), 5.88, 5.92 (2d, *J*=3.8 Hz, 1H), 7.18–7.53 (m, 8H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 26.2 (q), 26.8 (q), 67.2 (t), 67.4 (t), 73.3 (d), 73.6 (d), 80.0 (d), 80.1 (d), 84.6 (d), 104.7 (d), 105.1 (d), 111.5 (s), 111.9 (s), 122.9 (d), 124.7 (d), 126.2 (d), 127.0 (d), 127.1 (d), 127.4 (d), 127.5 (d), 128.3 (d), 128.4 (s), 128.4 (d) 128.8 (d), 129.2 (d), 129.8 (s), 130.9 (d), 131.6 (d), 133.6 (s), 135.1 (s), 140.3 (s), 140.4 (s), 140.5 (s), 141.7 (s) ppm; ESI-MS (*m*/*z*): 347.4 (100%, $[M+Na]^+$), 363.4 (34%, $[M+K]^+$). Anal. Calcd for $C_{20}H_{20}O_4$: C, 74.06; H, 6.21. Found: C, 73.93; H, 6.38.

*4.3.6. 1,2-O-Isopropylidene-4-C,3-O-[o-(3- or 4-phthalimidomethyl) phenylenemethylene]-α-D-xylotetrofuranose (**14a**/**14b**).* Following the general procedure A, the cyclotrimerization of diyne **1** (130 mg, 0.59 mmol) and propargyl phthalamide (325 mg, 1.8 mmol) afforded a mixture of **14a** and **14b** (160 mg, 67%) as a viscous oil; R_f (30% ethyl acetate/pet. ether) 0.43; IR ($CHCl_3$) ν: 3017, 2924, 2854, 1770, 1714, 1460, 1376, 1247, 1164, 1088, 1019, 947 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.26 (s, 3H), 1.48 (s, 3H), 4.02 (d, *J*=2.2 Hz, 1H), 4.53 (d, *J*=15.6 Hz, 1H), 4.56 (d, *J*=3.6 Hz, 1H), 4.64–4.89 (m, 4H), 5.84, 5.86 (2d, *J*=3.6 Hz, 1H), 6.90–7.05 (m, 1H), 7.27–7.44 (m, 2H), 7.59–7.65 (m, 2H), 7.72–7.76 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 26.2 (q), 26.2 (q), 26.9 (q), 41.2 (t), 41.3 (t), 67.1 (t), 67.2 (t), 73.2 (d), 73.3 (d), 80.0 (d), 80.0 (d), 84.6 (d), 84.6 (d), 105.1 (d), 111.5 (s), 111.6 (s), 123.4 (d), 124.6 (d), 127.8 (d), 128.5 (d), 128.5 (d), 128.9 (d), 129.2 (d), 129.8 (s), 130.7 (d), 131.0 (d), 132.1 (s), 132.2 (s), 133.9 (d), 134.0 (d), 134.4 (s), 135.2 (s), 135.6 (s), 136.9 (s), 167.7 (s), 167.7 (s) ppm; ESI-MS (*m*/*z*): 425.4 (15%, $[M+NH_4]^+$), 430.5 (100%, $[M+Na]^+$). Anal. Calcd for $C_{23}H_{21}NO_6$: C, 67.80; H, 5.20; N, 3.44. Found: C, 68.01; H, 5.43; N, 3.28.

*4.3.7. 1,2-O-Isopropylidene-4-C,3-O-[o-(3- or 4-tetradecyl)phenylenemethylene]-α-D-xylotetrofuranose (**15a**/**b**).* General procedure B was followed. Diyne **1** (100 mg, 0.45 mmol) and 1-hexadecyne (300 mg, 1.4 mmol) were used to afford a mixture of **15a** and **15b** (98 mg, 49%) as a colorless oil; R_f (30% ethyl acetate/pet. ether) 0.56; IR ($CHCl_3$) ν: 3017, 2926, 2854, 1619, 1465, 1375, 1245, 1090, 865 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 0.86 (t, *J*=6.6 Hz, 3H), 1.25 (br s, 23H), 1.36 (s, 3H), 1.53–1.58 (m, 4H), 2.52–2.61 (m, *J*=3.7, 7.3 Hz, 2H), 4.13 (d, *J*=2.4 Hz, 1H), 4.64 (d, *J*=15.1 Hz, 1H), 4.67 (d, *J*=3.6 Hz, 1H), 4.76 (d, *J*=15.1 Hz, 1H), 4.93 (d, *J*=2.3 Hz, 1H), 5.97 (d, *J*=3.7 Hz, 1H), 6.85–6.97 (m, 1H), 7.09 (d, *J*=7.8 Hz, 1H), 7.30–7.39 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 4.2 (q), 22.7 (t), 26.3 (q), 26.9 (q), 29.3 (t), 29.4 (t), 29.4 (t), 29.6 (t), 29.6 (t), 29.7 (t), 31.4 (t), 32.0 (t), 35.6 (t), 35.9 (t), 67.3 (t), 67.5 (t), 73.5 (d), 73.7 (d), 80.1 (d), 80.1 (d), 84.7 (d), 105.2 (d), 111.5 (s), 111.5 (s), 124.1 (d), 124.1 (d), 126.6 (s), 127.6 (d), 128.9 (d), 129.1 (s), 130.4 (d), 130.5 (d), 131.9 (s), 134.5 (s), 142.1 (s), 143.6 (s) ppm; ESI-MS (*m*/*z*): 462.7 (27%, $[M+NH_4]^+$), 467.7 (100%, $[M+Na]^+$). Anal. Calcd for $C_{28}H_{44}O_4$: C, 75.63; H, 9.97. Found: C, 75.80; H, 10.12.

*4.3.8. 1,2:5,6-Di-O-isopropylidene-3-C,3-O-[o-{(3,4-bis(hydroxymethyl))}phenylenemethylene]-α-D-allofuranose (**16**).* By following procedure A, cycloaddition of diyne **2** (100 mg, 0.31 mmol) and 2-butyne-1,4-diol (80 mg, 0.93 mmol) gave **16** (86 mg, 68%) as colorless oil; R_f (20% ethyl acetate/pet. ether) 0.28; $[\alpha]_D^{25}$ −4.8 (*c* 1.2, $CHCl_3$); IR ($CHCl_3$) ν: 3412, 2989, 2935, 2875, 1438, 1374, 1330, 1217, 1123, 1074, 1022, 872, 842, 754, 724, 695, 667 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.11 (s, 3H), 1.36 (s, 3H), 1.38 (s, 3H), 1.68 (s, 3H), 3.23 (br s, 2H), 3.55 (dt, *J*=5.5, 8.5 Hz, 1H), 3.79 (dd, *J*=5.9, 8.5 Hz, 1H), 3.93 (dd, *J*=4.7, 8.6 Hz, 1H), 4.27 (d, *J*=8.5 Hz, 1H), 4.39 (d, *J*=3.5 Hz, 1H), 4.71 (d, *J*=12.2 Hz, 1H), 4.73 (d, *J*=12.2 Hz, 1H), 4.79 (d, *J*=12.0 Hz, 2H), 5.16 (d, *J*=12.3 Hz, 1H), 5.23 (d, *J*=12.3 Hz, 1H), 5.99 (d, *J*=3.5 Hz, 1H), 7.09 (s, 1H), 7.27 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 25.4 (q), 26.2 (q), 26.7 (q), 26.8 (q), 63.4 (t), 63.7 (t), 67.4 (t), 73.3 (t), 73.8 (d), 79.3 (d), 84.3 (d), 93.8 (s), 103.5 (d), 109.3 (s), 113.5 (s), 122.6 (d), 122.6 (d), 137.8 (s), 139.0 (s), 140.2 (s), 140.9 (s) ppm; ESI-MS (*m*/*z*): 431.5 (100%, $[M+Na]^+$). Anal. Calcd for $C_{21}H_{28}O_8$: C, 61.75; H, 6.91. Found: C, 61.87; H, 6.99.

*4.3.9. 1,2:5,6-Di-O-isopropylidene-3-C,3-O-(o-phenylenemethylene)-α-D-allofuranose (**17**).* General procedure C was followed. Diyne **2** (120 mg, 0.37 mmol) was used to obtain **17** (100 mg, 76%) as a viscous oil; R_f (20% ethyl acetate/pet. ether) 0.30; $[\alpha]_D^{25}$ +12.9 (*c* 1.9, $CHCl_3$); IR ($CHCl_3$) ν: 3019, 2939, 1461, 1375, 1216, 1165, 1074, 1034, 1017, 929, 845, 873, 757 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.03 (s, 3H), 1.29 (s, 3H), 1.31 (s, 3H), 1.61 (s, 3H), 3.47 (dt, *J*=5.5, 8.3 Hz, 1H), 3.70 (dd, *J*=5.8, 8.5 Hz, 1H), 3.84 (dd, *J*=5.1, 8.5 Hz, 1H), 4.20 (d, *J*=8.3 Hz, 1H), 4.32 (d, *J*=3.5 Hz, 1H), 5.09 (d, *J*=12.0 Hz, 1H), 5.18 (d, *J*=12.0 Hz, 1H), 5.88 (d, *J*=3.5 Hz, 1H), 7.02 (dd, *J*=1.2, 7.7 Hz, 1H), 7.16–7.33 (m, *J*=1.2, 7.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 25.4 (q), 26.3 (q), 26.7 (q), 26.9 (q), 67.4 (t), 73.4 (t), 73.8 (d), 79.4 (d), 84.3 (d), 93.7 (s), 103.5 (d), 109.0 (s), 113.3 (s), 121.3 (d), 121.4 (d), 127.3 (d), 128.7 (d), 137.4 (s), 140.4 (s) ppm; ESI-MS (*m*/*z*): 371.0 (100%, $[M+Na]^+$). Anal. Calcd for $C_{19}H_{24}O_6$: C, 65.50; H, 6.94. Found: C, 65.37; H, 6.69.

*4.3.10. 1,2:5,6-Di-O-isopropylidene-3-C,3-O-[o-{3,4-bis(acetyloxymethyl)}phenylenemethylene]-α-D-allofuranose (**18**).* Starting from

diyne **2** (150 mg, 0.46 mmol) and diacetate of 2-butyne-1,4-diol (237 mg, 1.4 mmol) and following procedure A, **18** (129 mg, 65%) was obtained as colorless oil; R_f (30% ethyl acetate/pet. ether) 0.42; $[\alpha]_D^{25}$ −8.4 (*c* 1.3, $CHCl_3$); IR ($CHCl_3$) ν: 3019, 2939, 1739, 1610, 1461, 1384, 1375, 1332, 1216, 1165, 1074, 1034, 1017, 929, 845, 757 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 1.10 (s, 3H), 1.34 (s, 3H), 1.36 (s, 3H), 1.66 (s, 3H), 2.08, 2.09 (2s, 6H), 3.50 (ddd, *J*=4.6, 5.7, 8.5 Hz, 1H), 3.79 (dd, *J*=4.7, 8.5 Hz, 1H), 3.91 (dd, *J*=4.7, 8.5 Hz, 1H), 4.23 (d, *J*=8.5 Hz, 1H), 4.34 (d, *J*=3.6 Hz, 1H), 5.09–5.24 (3d, *J*=12.1 Hz, 6H), 5.94 (d, *J*=3.6 Hz, 1H), 7.08 (s, 1H), 7.29 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 20.9 (q, 2C), 25.5 (q), 26.4 (q), 26.8 (q), 26.9 (q), 63.4 (t), 63.7 (t), 67.4 (t), 73.3 (t), 73.8 (d), 79.2 (d), 84.3 (d), 93.8 (s), 103.4 (d), 109.2 (s), 113.5 (s), 122.6 (d), 123.0 (d), 133.9 (s), 135.6 (s), 138.2 (s), 141.3 (s), 170.3 (s, 2C) ppm; ESI-MS (*m*/*z*): 493.3 (4%, $[M+H]^+$), 510.4 (20%, $[M+NH_4]^+$), 515.3 (100%, $[M+Na]^+$). Anal. Calcd for $C_{25}H_{32}O_{10}$: C, 60.97; H, 6.55. Found: C, 60.82; H, 6.71.

*4.3.11. 1,2:5,6-Di-O-isopropylidene-3-C,3-O-[o-{3,4-bis(methoxycarbonyl)}phenylenemethylene]-α-D-allofuranose (**19**).* Procedure B was followed. Diyne **2** (150 mg, 0.46 mmol) and dimethyl acetylene dicarboxylate (0.4 mL, 2.7 mmol) were used to afford **19** (112 mg, 52%) as colorless oil; R_f (30% ethyl acetate/pet. ether) 0.40; $[\alpha]_D^{25}$ −10.2 (*c* 0.9, $CHCl_3$); IR ($CHCl_3$) ν: 3021, 2989, 2954, 1735, 1621, 1579, 1383, 1219, 1165, 1125, 1075, 1053, 985, 922, 843, 755 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 1.08 (s, 3H), 1.34, 1.36 (2s, 6H), 1.65 (s, 3H), 3.46 (ddd, *J*=4.4, 5.5, 9.1 Hz, 1H), 3.82 (s, 2H), 3.89 (s, 6H), 4.19 (d, *J*=9.1 Hz, 1H), 4.37 (d, *J*=3.6 Hz, 1H), 5.15 (d, *J*=12.9 Hz, 1H), 5.24 (d, *J*=12.9 Hz, 1H), 5.97 (d, *J*=3.6 Hz, 1H), 7.39 (s, 1H), 7.57 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 25.2 (q), 26.2 (q), 26.6 (q), 52.6 (q), 53.2 (q, 2C), 67.5 (t), 73.0 (t), 73.6 (d), 79.3 (d), 84.1 (d), 93.8 (s), 103.3 (d), 109.3 (s), 113.4 (s), 121.9 (d, 2C), 131.6 (s), 133.0 (s), 140.9 (s), 144.1 (s), 167.2 (s), 167.4 (s) ppm; ESI-MS (*m*/*z*): 487.0 (100%, $[M+Na]^+$). Anal. Calcd for $C_{23}H_{28}O_{10}$: C, 59.48; H, 6.08. Found: C, 59.59; H, 6.02.

*4.3.12. 1,2:5,6-Di-O-isopropylidene-3-C,3-O-[3,4-di(n-pentyl)phenylenemethylene]-α-D-allofuranose (**20**).* Following procedure B, using diyne **3** (130 mg, 0.4 mmol) and 6-dodecyne (0.34 mL, 1.6 mmol), a mixture of **20** (84 mg, 43%) was obtained as colorless oil; R_f (35% ethyl acetate/pet. ether) 0.34; $[\alpha]_D^{25}$ +18.7 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) ν: 2986, 2930, 2859, 1620, 1331, 1249, 1218, 1075, 873 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 0.89 (2 t, *J*=6.7 Hz, 6H), 1.11 (s, 3H), 1.24–1.38 (m, 15H), 1.58 (s, 3H), 1.67 (s, 3H), 2.11 (t, *J*=7.6 Hz, 4H), 3.48–3.59 (m, 1H), 3.76 (dd, *J*=5.8, 8.4 Hz, 1H), 3.91 (ddd, *J*=4.6, 6.2, 8.4 Hz, 1H), 4.22 (d, *J*=8.4 Hz, 1H), 4.33 (d, *J*=3.6 Hz, 1H), 5.12 (d, *J*=12.0 Hz, 1H), 5.21 (d, *J*=12.0 Hz, 1H), 5.82 (d, *J*=3.6 Hz, 1H), 7.09 (s, 1H), 7.31 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 14.0 (q, 2C), 22.5 (t), 22.5 (t), 25.4 (q), 25.5 (q), 26.6 (q), 26.7 (q), 28.0 (t), 28.3 (t), 28.8 (t), 30.3 (t), 31.2 (t), 31.5 (t), 67.3 (t), 73.3 (t), 73.8 (d), 83.3 (d), 84.4 (d), 93.7 (s), 103.4 (d), 109.1 (s), 113.3 (s), 120.9,(d), 120.9 (d), 121.6 (s), 137.9 (s), 139.3 (s), 139.7 (s) ppm; ESI-MS (*m*/*z*): 511.2 (100%, $[M+Na]^+$). Anal. Calcd for $C_{29}H_{44}O_6$: C, 71.28; H, 9.08. Found: C, 71.40; H, 9.26.

*4.3.13. 1,2:5,6-Di-O-isopropylidene-3-C,3-O-[o-(3- or 4-phenyl)phenylenemethylene]-α-D-allofuranose (**21a**/**21b**).* General procedure A was followed. Diyne **2** (110 mg, 0.33 mmol) and phenyl acetylene (0.2 mL, 1.9 mmol) were used to afford a mixture of **21a** and **21b** (98 mg, 69%) as reddish oil; R_f (30% ethyl acetate/pet. ether) 0.42; IR ($CHCl_3$) ν: 3020, 2991, 2936, 1620, 1375, 1215, 1165, 1974, 1044, 1028, 873, 843 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 1.13 (s, 3H), 1.38 (s, 3H), 1.40 (s, 3H), 1.69 (s, 3H), 3.56–3.68 (m, 1H), 3.80, 3.84 (2dd, *J*=5.7, 8.5 Hz, 1H), 3.95 (dd, *J*=8.5, 4.9 Hz, 1H), 4.31 (br d, *J*=8.3 Hz, 1H), 4.42, 4.44 (2d, *J*=3.6, Hz, 1H), 5.21 (d, *J*=12.1 Hz, 1H), 5.29 (d, *J*=12.1 Hz, 1H), 5.98, 6.00 (2d, *J*=3.6 Hz, 1H), 7.15 (d, *J*=7.9 Hz, 1H), 7.29–7.60 (m, 7H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 25.5 (q), 26.3 (q), 26.7 (q), 26.9 (q), 67.3 (t), 67.4 (t), 73.3 (t), 73.4 (t), 73.9 (d), 79.4 (d), 84.4 (d), 93.7 (s), 93.7 (s), 103.5 (d), 103.5 (d), 109.1 (s), 113.3 (s), 113.3 (s), 120.0 (d), 120.0 (d), 121.6 (d), 121.7 (d), 126.6 (d), 127.1 (d), 127.6 (d), 127.9 (d), 128.8 (d), 128.8 (d), 136.5 (s), 138.4 (s), 139.5 (s), 140.5 (s), 140.5 (s), 141.0 (s), 141.3 (s), 142.1 (s) ppm; ESI-MS (*m*/*z*): 447.8 (100%, $[M+Na]^+$). Anal. Calcd for $C_{25}H_{28}O_6$: C, 70.74; H, 6.65. Found: C, 70.79; H, 6.82.

*4.3.14. 1,2:5,6-Di-O-isopropylidene-3-C,3-O-[o-(3- or 4-phthalimidomethyl)phenylenemethylene]-α-D-allofuranose (**22a**/**22b**).* By following procedure A, cycloaddition of diyne **2** (130 mg, 0.4 mmol) and propargyl phthalamide (224 mg, 1.2 mmol) gave a mixture of **22a** and **22b** (147 mg, 72%) as a viscous oil; R_f (35% ethyl acetate/pet. ether) 0.32; IR ($CHCl_3$) ν: 3020, 2991, 2936, 1771, 1716, 1395, 1216, 1074, 1024 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 1.07 (s, 3H), 1.31, 1.35 (2s, 6H), 1.64, 1.66 (2s, 3H), 3.45–3.55 (m, 1H), 3.72–3.80 (m, 1H), 3.84–3.93 (m, 1H), 4.22 (dd, *J*=3.4, 8.4 Hz, 1H), 4.32 (dd, *J*=3.5, 9.6 Hz, 1H), 4.85 (s, 2H), 5.09 (d, *J*=12.1 Hz, 1H), 5.18 (d, *J*=12.1 Hz, 1H), 5.88, 5.98 (2d, *J*=3.6 Hz, 1H), 7.00–7.30 (m, 2H), 7.34–7.42 (m, 1H), 7.68–7.75 (m, 2H), 7.80–7.87 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 25.4 (q), 26.3 (q), 26.4 (q), 26.7 (q), 26.9 (q), 26.9 (q), 41.2 (t), 41.4 (t), 67.3 (t), 67.4 (t), 73.2 (t), 73.8 (d), 73.8 (d), 79.2 (d), 79.3 (d), 84.3 (d), 93.6 (s), 93.7 (s), 103.4 (d), 103.5 (d), 109.0 (s), 109.1 (s), 113.3 (s), 121.6 (d), 121.6 (d), 122.1 (d), 123.4 (d), 128.0 (d), 129.2 (d), 132.0 (s), 134.0 (d), 135.8 (s), 137.1 (s), 137.2 (s), 138.1 (s), 140.2 (s), 141.2 (s), 167.7 (s) ppm; ESI-MS (*m*/*z*): 508.4 (7%, $[M+H]^+$), 525.4 (27%, $[M+NH_4]^+$), 530.3 (100%, $[M+Na]^+$). Anal. Calcd for $C_{28}H_{29}NO_8$: C, 66.26; H, 5.76; N, 2.76. Found: C, 66.30; H, 5.82; N, 2.70.

*4.3.15. 1,2:5,6-Di-O-isopropylidene-3-C,3-O-[o-(3- or 4-tetradecyl)phenylenemethylene]-α-D-allofuranose (**23a**/**23b**).* Procedure B was followed. Diyne **2** (120 mg, 0.37 mmol) and 1-hexadecyne (248 mg, 1.1 mmol) were used to afford a mixture of **23a** and **23b** (105 mg, 52%) as a colorless oil; R_f (25% ethyl acetate/pet. ether) 0.45; IR ($CHCl_3$) ν: 3019, 2987, 2927, 2855, 1618, 1458, 1373, 1249, 1217, 1167, 1074, 1025, 873 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 0.87 (t, *J*=6.4 Hz, 3H), 1.10 (s, 3H), 1.24 (br s, 20H), 1.34–1.36 (m, 7H), 1.53–1.59 (m, 3H), 1.67 (s, 3H), 2.61 (t, *J*=7.6 Hz, 2H), 3.54 (2d, *J*=5.4, 7.9 Hz, 1H), 3.72 (2dd, *J*=5.8, 8.4 Hz, 1H), 3.88 (2dd, *J*=5.2, 8.4 Hz, 1H), 4.26, 4.27 (2d, *J*=7.9 Hz, 1H), 4.36, 4.37 (2d, *J*=3.6 Hz, 1H), 5.10 (d, *J*=11.8 Hz, 1H), 5.19 (d, *J*=11.8 Hz, 1H), 5.92, 5.95 (2d, *J*=3.6 Hz, 1H), 6.83, 7.03 (2s, 1H), 6.95, 7.07 (2d, *J*=7.7 Hz, 1H), 7.10, 7.11 (2d, *J*=7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): 14.1 (q) 22.7 (t), 25.5 (q), 26.4 (q), 26.7 (q), 27.0 (q), 29.3 (t), 29.4 (t), 29.5 (t), 29.6 (t), 29.7 (t), 31.6 (t), 31.8 (t), 32.0 (t), 35.9 (t), 67.2 (t), 67.3 (t), 73.4 (t), 73.4 (t), 73.9 (d), 79.5 (d), 79.5 (d), 84.4 (d), 84.4 (d), 93.6 (s), 93.6 (s), 103.5 (d), 103.6 (d), 109.0 (s), 113.3 (s), 121.1 (d), 121.2 (d), 121.2 (d), 121.2 (d), 127.7 (d), 129.0 (d), 134.8 (s), 137.7 (s), 137.8 (s), 140.7 (s), 142.4 (s), 143.7 (s) ppm; ESI-MS (*m*/*z*): 567.1 (100%, $[M+Na]^+$). Anal. Calcd for $C_{33}H_{52}O_6$: C, 72.76; H, 9.62. Found: C, 72.59; H, 9.78.

*4.3.16. 1,2-O-Isopropylidene-5-O-(tert-butyldimethylsilyl)-3-C,3-O-(o-phenylenemethylene)-α-D-ribofuranose (**24**).* By following procedure C, cycloaddition of the diyne **3** (200 mg, 0.55 mmol) with acetylene gave **24** (152 mg, 71%) as a colorless oil; R_f (20% ethyl acetate/pet. ether) 0.28; $[\alpha]_D^{25}$ +36.4 (*c* 1.1, $CHCl_3$); IR ($CHCl_3$) ν: 3077, 3019, 2955, 2930, 2858, 1608, 1462, 1383, 1255, 1167, 1087, 1049, 939 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ −0.09, −0.08 (2s, 6H), 0.80 (s, 9H), 1.36 (s, 3H), 1.69 (s, 3H), 3.30 (dd, *J*=5.2, 11.1 Hz, 1H), 3.54 (dd, *J*=6.5, 11.1 Hz, 1H), 4.35 (d, *J*=3.6 Hz, 1H), 4.46 (dd, *J*=5.2, 6.5 Hz, 1H), 5.17 (d, *J*=12.5 Hz, 1H), 5.23 (d, *J*=12.5 Hz, 1H), 5.99 (d, *J*=3.6 Hz, 1H), 7.16 (dd, *J*=1.6, 7.5 Hz, 1H), 7.24 (d, *J*=7.5 Hz, 1H), 7.29–7.40 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ −5.9 (q), −5.8 (q), 17.9 (s), 25.5 (q, 3C), 26.1 (q), 26.6 (q), 61.9 (t), 73.0 (t), 79.8 (d), 83.6 (d), 93.1 (s), 103.4 (d), 112.9 (s), 121.0 (d), 121.4 (d), 127.3 (d), 128.4 (d), 136.9 (s), 139.4 (s) ppm; ESI-MS (*m*/*z*): 410.7 (47%,

$[M+NH_4]^+$), 415.3 (100%, $[M+Na]^+$), 431.3 (67%, $[M+K]^+$). Anal. Calcd for $C_{21}H_{32}O_5Si$: C, 64.25; H, 8.22. Found: C, 64.32; H, 8.14.

*4.3.17. 1,2-O-Isopropylidene-5-O-(tert-butyldimethylsilyl)-3-C,3-O-[o-{3,4-bis(acetyloxymethyl)} phenylenemethylene]-α-D-ribofuranose (**25**).* Procedure A was followed. Diyne **3** (150 mg, 0.41 mmol) and diacetate of 2-butyne-1,4-diol (209 mg, 1.2 mmol) were used to obtain **25** (132 mg, 60%) as colorless oil; R_f (25% ethyl acetate/pet. ether) 0.32; $[\alpha]_D^{25}$ +25.0 (*c* 2.6, $CHCl_3$); IR ($CHCl_3$) *ν*: 3020, 2930, 2857, 1745, 1626, 1472, 1375, 1221, 1078, 1023, 874, 838, 756, 667 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): *δ* −0.11, −0.10 (2s, 6H), 0.76 (s, 9H), 1.34 (s, 3H), 1.66 (s, 3H), 2.07, 2.08 (2s, 6H), 3.27 (dd, *J*=5.2, 11.0 Hz, 1H), 3.53 (dd, *J*=6.6, 11.0 Hz, 1H), 4.31 (d, *J*=3.6 Hz, 1H), 4.42 (dd, *J*=5.2, 6.5 Hz, 1H), 5.09–5.22 (m, 6H), 5.97 (d, *J*=3.6 Hz, 1H), 7.17 (s, 1H), 7.28 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): *δ* −5.7 (q), −5.6 (q), 18.2 (s), 20.8 (q), 25.7 (q, 3C), 25.8 (q), 26.3 (q), 26.7 (q), 61.9 (t), 63.3 (t), 63.5 (t), 73.0 (t), 79.7 (d), 83.6 (d), 93.3 (s), 103.5 (d), 113.3 (s), 122.5 (d), 123.2 (d), 134.1 (s), 135.5 (s), 137.8 (s), 140.4 (s), 170.4 (s), 170.4 (s) ppm; ESI-MS (*m*/*z*): 554.6 (36%, $[M+NH_4]^+$), 559.5 (100%, $[M+Na]^+$), 575.5 (35%, $[M+K]^+$). Anal. Calcd for $C_{27}H_{40}O_9Si$: C, 60.42; H, 7.51. Found: C, 60.29; H, 7.67.

*4.3.18. 1,2-O-Isopropylidene-5-O-(tert-butyldimethylsilyl)-3-C,3-O-[o-{3,4-bis(methoxycarbonyl)} phenylenemethylene]-α-D-ribofuranose] (**26**).* Following procedure B, cycloaddition of the diyne **3** (130 mg, 0.36 mmol) and dimethyl acetylene dicarboxylate (0.13 mL, 1.1 mmol) gave **26** (121 mg, 67%) as colorless oil; R_f (25% ethyl acetate/pet. ether) 0.38; $[\alpha]_D^{25}$ +6.6 (*c* 0.7, $CHCl_3$); IR ($CHCl_3$) *ν*: 3021, 2955, 2858, 1730, 1621, 1271, 1216, 1022 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz):*δ* −0.10 (2s, 6H), 0.76 (s, 9H), 1.33 (s, 3H), 1.66 (s, 3H), 3.25 (dd, *J*=5.7, 11.1 Hz, 1H), 3.57 (dd, *J*=6.2, 11.0 Hz, 1H), 3.89 (2s, 6H), 4.33 (d, *J*=3.7 Hz, 1H), 4.41 (t, *J*=5.9 Hz, 1H), 5.20 (s, 2H), 6.00 (d, *J*=3.7 Hz, 1H), 7.49 (s, 1H), 7.55 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): *δ* −5.7 (q), −5.6 (q), 18.2 (s), 25.7 (q, 2C), 26.3 (q), 26.7 (q), 52.8 (q), 52.9 (q), 61.6 (t), 72.9 (t), 79.5 (d), 83.5 (d), 93.5 (s), 103.5 (d), 113.5 (s), 121.9 (d), 122.5 (d), 131.7 (s), 133.2 (s), 140.6 (s), 143.4 (s), 167.2 (s), 167.7 (s) ppm; ESI-MS (*m*/*z*): 509.5 (11%, $[M+H]^+$), 526.6 (30%, $[M+NH_4]^+$), 531.5 (100%, $[M+Na]^+$), 547.5 (9%, $[M+K]^+$). Anal. Calcd for $C_{25}H_{36}O_9Si$: C, 59.03; H, 7.13. Found: C, 58.91; H, 7.20.

*4.3.19. 1,2:4,5-Di-O-isopropylidene-3-C,3-O-[o-(3- or 4-phenyl)phenylenemethylene]-α-D-ribopyranose] (**27a**/**27b**).* General procedure A was followed. Diyne **3** (130 mg, 0.36 mmol) and phenyl acetylene (0.2 mL, 1.8 mmol) were used to obtain a mixture of **27a** and **27b** (130 mg, 78%) as a reddish viscous oil; R_f (30% ethyl acetate/pet. ether) 0.42; IR ($CHCl_3$) *ν*: 3019, 2955, 2857, 1600, 1472, 1255, 1085, 1016, 837 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): *δ* −0.15, −0.14 (2s, 6H), 0.72 (s, 9H), 1.29, 1.30 (2s, 3H), 1.62 (s, 3H), 3.27–3.32 (2dd, *J*=5.2, 11.0 Hz, 1H), 3.51, 3.57 (2dd, *J*=6.6, 11.0 Hz, 1H), 4.32, 4.33 (2d, *J*=3.6 Hz, 1H), 4.40–4.43 (m, 1H), 5.13–5.19 (m, *J*=13 Hz, 2H), 5.94, 5.95 (2d, *J*=3.6 Hz, 1H), 7.14–7.31 (m, 2H), 7.36–7.50 (m, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz): *δ* −5.7 (q), −5.5 (q), 18.2 (s), 25.8 (q), 26.3 (q), 26.8 (q), 62.1 (t), 62.1 (d), 73.1 (t), 73.2 (t), 79.9 (d), 83.8 (d), 93.3 (s), 93.4 (s), 103.6 (d), 103.6 (d), 113.2 (s), 113.2 (s), 119.9 (d), 120.3 (d), 121.5 (d), 121.9 (d), 126.8 (d), 127.1 (d), 127.5 (d), 127.9 (d), 128.8 (d), 136.2 (s), 138.0 (s), 138.8 (s), 140.5 (s), 140.5 (s), 141.1 (s), 142.1 (s) ppm; ESI-MS (*m*/*z*): 492.0 (100%, $[M+Na]^+$), 508.0 (25%, $[M+K]^+$). Anal. Calcd for $C_{27}H_{36}O_5Si$: C, 69.20; H, 7.74. Found: C, 69.12; H, 7.81.

*4.3.20. 1,2:4,5-Di-O-isopropylidene-3-C,3-O-(o-phenylenemethylene)-α-D-psicopyranose (**28**).* General procedure C was followed. The cycloaddition of diyne **4** (150 mg, 0.47 mmol) with acetylene gave **28** (118 mg, 73%) as crystalline solid; R_f (20% ethyl acetate/pet. ether) 0.30; mp: 91–94 °C; $[\alpha]_D^{25}$ −183.5 (*c* 1.3, $CHCl_3$); IR ($CHCl_3$) *ν*: 3077, 3016, 2987, 2935, 2867, 1609, 1460, 1380, 1247, 1090, 1064, 979, 885 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): *δ* 1.32 (s, 6H), 1.52 (s, 3H), 1.59 (s, 3H), 3.46 (d, *J*=9.0 Hz, 1H), 4.08 (d, *J*=9.0 Hz, 1H), 4.25–4.29 (m, 3H), 4.48 (d, *J*=5.3 Hz, 1H), 5.11 (d, *J*=12.3 Hz, 1H), 5.23 (d, *J*=12.3 Hz, 1H), 7.19 (dd, *J*=7.2, 2.1 Hz, 1H), 7.27–7.41 (m, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): *δ* 25.6 (q), 25.7 (q), 26.1 (q), 26.6 (q), 59.8 (t), 71.1 (d), 72.5 (t), 73.7 (t), 76.6 (d), 86.7 (s), 106.6 (s), 109.3 (s), 112.8 (s), 120.5 (d), 123.5 (d), 127.3 (d), 128.7 (d), 138.2 (s), 140.7 (s) ppm; ESI-MS (*m*/*z*): 349.2 (9%, $[M+H]^+$), 366.2 (100%, $[M+NH_4]^+$), 371.2 (12%, $[M+Na]^+$), 387.2 (17%, $[M+K]^+$). Anal. Calcd for $C_{19}H_{24}O_6$: C, 65.50; H, 6.94. Found: C, 65.62; H, 7.03.

*4.3.21. 1,2:4,5-Di-O-isopropylidene-3-C,3-O-[o-{3,4-bis(acetyloxymethyl)}phenylenemethylene]-α-D-psicopyranose (**29**).* Following procedure A, cycloaddition of diyne **4** (130 mg, 0.4 mmol) and diacetate of 2-butyne-1,4-diol (206 mg, 1.2 mmol) gave **29** (130 mg, 65%) as a viscous oil; R_f (20% ethyl acetate/pet. ether) 0.35; $[\alpha]_D^{25}$ −111.43 (*c* 1.4, $CHCl_3$); IR ($CHCl_3$) *ν*: 3020, 2989, 2937, 1736, 1600, 1381, 1090, 980 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): *δ* 1.29 (s, 3H), 1.33 (s, 3H), 1.49 (s, 3H), 1.55 (s, 3H), 2.03 (s, 3H), 2.06 (s, 3H), 3.44 (d, *J*=9.0 Hz, 1H), 4.03 (d, *J*=9.0 Hz, 1H), 4.24–4.26 (m, 3H), 4.45 (d, *J*=5.3 Hz, 1H), 5.07–5.21 (m, *J*=12.5, 12.8 Hz, 6H), 7.23 (s, 1H), 7.42 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): *δ* 20.7 (q), 20.8 (q), 25.5 (q), 25.6 (q), 26.0 (q), 26.3 (q), 59.8 (t), 63.4 (t), 63.4 (t), 71.0 (d), 72.6 (t), 73.5 (t), 76.5 (d), 86.7 (s), 106.5 (s), 109.4 (s), 112.8 (s), 122.1 (d), 124.9 (d), 134.0 (s), 135.3 (s), 139.1 (s), 141.0 (s), 170.4 (s), 170.5 (s) ppm; ESI-MS (*m*/*z*): 510.8 (43%, $[M+NH_4]^+$), 515.7 (100%, $[M+Na]^+$), 531.7 (17%, $[M+K]^+$). Anal. Calcd for $C_{25}H_{32}O_{10}$: C, 60.97; H, 6.55. Found: C, 60.82; H, 6.68.

*4.3.22. 1,2:4,5-Di-O-isopropylidene-3-C,3-O-[o-{3,4-bis(methoxycarbonyl)}phenylenemethylene]-α-D-psicopyranose (**30**).* Cycloaddition of diyne **4** (130 mg, 0.4 mmol) and dimethyl acetylene dicarboxylate (0.15 mL, 1.2 mmol) following procedure B gave **30** (129 mg, 69%) as white solid; R_f (30% ethyl acetate/pet. ether) 0.40; mp: 78–81 °C; $[\alpha]_D^{25}$ −136.5 (*c* 0.8, $CHCl_3$); IR ($CHCl_3$) *ν*: 3019, 2990, 2938, 2874, 1779, 1730, 1622, 1437, 1383, 1216, 1091, 980, 877, 667 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): *δ* 1.30 (s, 3H), 1.35 (s, 3H), 1.50 (s, 3H), 1.57 (s, 3H), 3.41 (d, *J*=9.1 Hz, 1H), 3.86 (s, 3H), 3.88 (s, 3H), 4.06 (d, *J*=9.1 Hz, 1H), 4.25–4.28 (m, 3H), 4.45 (d, *J*=5.3 Hz, 1H), 5.14 (d, *J*=13.1 Hz, 1H), 5.26 (d, *J*=13.1 Hz, 1H), 7.49 (s, 1H), 7.82 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): *δ* 25.4 (q), 25.6 (q), 25.8 (q), 26.2 (q), 52.6 (q), 52.7 (q), 59.8 (t), 70.8 (d), 72.5 (t), 73.5 (t), 76.5 (d), 86.7 (s), 106.1 (s), 109.5 (s), 113.0 (s), 121.1 (d), 124.8 (d), 130.9 (s), 133.5 (s), 141.6 (s), 144.0 (s), 167.1 (s), 168.0 (s) ppm; ESI-MS (*m*/*z*): 465.5 (14%, $[M+H]^+$), 487.5(100%, $[M+Na]^+$), 503.5 (33%, $[M+K]^+$). Anal. Calcd for $C_{23}H_{28}O_{10}$: C, 59.48; H, 6.08. Found: C, 59.69; H, 6.14.

*4.3.23. 1,2:4,5-Di-O-isopropylidene-3-C,3-O-[o-(3- or 4-phenyl)phenylenemethylene]-α-D-psicopyranose (**31a**/**31b**).* General procedure A was followed. Diyne **4** (140 mg, 0.43 mmol) and phenyl acetylene (0.2 mL, 1.7 mmol) were used to procure a mixture of **31a** and **31b** (138 mg, 75%) as amorphous solid; R_f (25% ethyl acetate/pet. ether) 0.50; mp: 71–73 °C; IR ($CHCl_3$) *ν*: 3019, 2935, 1601, 1382, 1133, 1091, 879 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): *δ* 1.27, 1.28, 1.31 (3s, 6H), 1.48 (s, 3H), 1.56 (s, 3H), 3.49 (br d, *J*=9.0 Hz, 1H), 4.05, 4.07 (2d, *J*=9.0 Hz, 1H), 4.22–4.28 (m, 3H), 4.46, 4.49 (2d, *J*=5.3 Hz, 1H), 5.10, 5.11 (2d, *J*=12.3 Hz, 1H), 5.19, 5.24 (2d, *J*=12.3 Hz, 1H), 7.19–7.39 (m, 5H), 7.44–7.53 (m, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): *δ* 25.6 (q), 25.7 (q), 26.2 (q), 26.3 (q), 26.5 (q), 26.6 (q), 59.7 (t), 59.8 (t), 71.1 (d), 72.6 (t), 73.6 (t), 73.7 (t), 76.6 (d), 86.6 (s), 86.7 (s), 106.7 (s), 109.4 (s), 112.8 (s), 119.4 (d), 120.9 (d), 122.3 (d), 123.8 (d), 126.8 (d), 126.9 (d), 127.2 (d), 127.3 (d), 128.1 (d), 128.7 (d), 137.3 (s), 139.1 (s), 139.4 (s), 140.7 (s), 140.8 (s), 141.0 (s), 142.2 (s) ppm; ESI-MS (*m*/*z*): 425.7 (9%, $[M+H]^+$), 442.7 (53%, $[M+NH_4]^+$), 447.7 (100%, $[M+Na]^+$), 463.7

(16%, $[M+K]^+$). Anal. Calcd for $C_{25}H_{28}O_6$: C, 70.74; H, 6.65. Found: C, 70.52; H, 6.79.

4.4. Synthesis of nucleosides 36–38

*4.4.1. 1,2-Di-O-acetyl-4-C-(o-phenylenemethylene)-β-D-xylo-tetrofuranose (**32**).* Compound **10** (700 mg, 2.82 mmol) in 60% acetic acid (20 mL) was heated under reflux temperature for 2 h. The reaction mixture was neutralized by slow addition of solid K_2CO_3 and extracted in ethyl acetate. Combined ethyl acetate extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The crude lactols (570 mg, 3.5 mmol) were dissolved in dry CH_2Cl_2 (15 mL). TEA (5 mL) and catalytic DMAP were added and the mixture was cooled to 0 °C. To this, acetic anhydride (0.77 mL, 8.22 mmol) was added and the contents were stirred at 0 °C for 1 h and then at room temperature for 1 h. The reaction mixture was quenched with cold 2 N HCl and extracted in CH_2Cl_2. Combined organic phase was washed with satd $NaHCO_3$ and water, dried over Na_2SO_4, and filtered and concentrated under reduced pressure. Purification of the residue by silica gel column chromatography (15% ethyl acetate in petroleum ether) gave a mixture of diacetates **32** (717 mg, 87% yield) as colorless oil; R_f (20% ethyl acetate/pet. ether) 0.30; IR ($CHCl_3$) ν: 3032, 2903, 1751, 1638, 1432, 1374, 1242, 1219, 1087, 1012, 925, 909 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 1.94, 2.12, 2.13, 2.16 (4s, 6H), 4.26 (d, J=3.9 Hz, 0.3H), 4.42 (dd, J=2.4, 4.3 Hz, 0.7H), 4.61 (2d, J=14.5 Hz, 1H), 4.79, 4.84 (2d, J=14.5 Hz, 1H), 5.03 (t, J=4.3 Hz, 1H), 5.30 (s, 0.3H), 5.36 (dd, J=2.4, 4.6 Hz, 0.7H), 6.16 (s, 0.3H), 6.52 (d, J=4.7 Hz, 0.7H), 7.06–7.13 (m, 1H), 7.26–7.32 (m, 2H), 7.42–7.50 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 20.4 (q), 20.7 (q), 20.9 (q), 21.0 (q), 66.5 (t), 66.9 (t), 72.7 (d), 75.7 (d), 77.7 (d), 78.8 (d), 79.2 (d), 81.6 (d), 94.4 (d), 99.6 (d), 124.2 (d), 124.4 (d), 127.6 (d), 128.4 (d), 128.6 (d), 129.5 (s), 129.9 (d, 2C), 130.0 (d), 130.3 (s), 134.3 (s), 134.8 (s), 168.9 (s), 169.1 (s), 169.2 (s), 169.4 (s) ppm; ESI-MS (m/z): 315.0 (100%, $[M+Na]^+$), 331.1 (10%, $[M+K]^+$). Anal. Calcd for $C_{15}H_{16}O_6$: C, 61.64; H, 5.52. Found: C, 61.50; H, 5.67.

*4.4.2. 1-[2-O-Acetyl-3-O,4-C-(o-phenylenemethylene)-β-D-xylo-tetrofuranosyl]uracil (**33**).* A solution of acetates **32** (100 mg, 0.34 mmol), uracil (77 mg, 0.68 mmol), and *N,O*-bis(trimethylsilyl) acetamide (0.42 mL, 1.71 mmol) in anhydrous CH_3CN (5 mL) was heated to reflux for 15 min. The reaction mixture was cooled to 0 °C and TMSOTf (0.12 mL, 0.68 mmol) was added. The reaction mixture was stirred at 50 °C for 2 h, quenched with cold aq $NaHCO_3$, and extracted with EtOAc. The combined organic layer was washed with water, dried over Na_2SO_4, and filtered and concentrated under reduced pressure. Purification of the residue by silica gel column chromatography (45% ethyl acetate in petroleum ether) afforded the nucleoside **33** (97 mg, 82% yield) as a crystalline solid; R_f (60% ethyl acetate/pet. ether) 0.35; mp: 214–216 °C; $[\alpha]_D^{25}$ −8.6 (c 1.0, $CHCl_3$); IR ($CHCl_3$) ν: 3241, 3032, 2927, 2253, 1750, 1686, 1461, 1371, 1320, 1268, 1225, 1108, 1066, 909 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 2.17 (s, 3H), 4.19 (d, J=2.6 Hz, 1H), 4.72 (d, J=15.2 Hz, 1H), 4.87 (d, J=15.2 Hz, 1H), 4.96 (d, J=2.6 Hz, 1H), 5.22 (d, J=1.6 Hz, 1H), 5.60 (dd, J=2.1, 8.2 Hz, 1H), 6.16 (d, J=1.6 Hz, 1H), 7.11 (dd, J=2.1, 8.2 Hz, 1H), 7.32–7.48 (m, 4H), 9.21 (br s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 20.7 (q), 67.3 (t), 75.4 (d), 78.8 (d), 81.7 (d), 89.3 (d), 102.5 (d), 124.4 (d), 127.8 (d), 127.9 (s), 129.4 (d), 130.6 (d), 134.1 (s), 140.5 (d), 150.2 (s), 163.1 (s), 169.2 (s) ppm; ESI-MS (m/z): 345.1 (6%, $[M+H]^+$), 367.0 (100%, $[M+Na]^+$). Anal. Calcd for $C_{17}H_{16}N_2O_6$: C, 59.30; H, 4.68; N, 8.14. Found: C, 59.09; H, 4.80; N, 8.26.

*4.4.3. 1-[2-O-Acetyl-3-O,4-C-(o-phenylenemethylene)-β-D-xylo-tetrofuranosyl]thymine (**34**).* Following the above procedure, the glycosylation of acetates **32** (100 mg, 0.34 mmol) with thymine (86 mg, 0.68 mmol) gave **34** (97 mg, 79% yield) as white solid; R_f (60% ethyl acetate/pet. ether) 0.35; mp: 192–194 °C; $[\alpha]_D^{25}$ −18.9 (c 1.0, $CHCl_3$); IR ($CHCl_3$) ν: 3196, 3019, 2927, 2851, 1752, 1697, 1466, 1372, 1270, 1228, 1110, 1061, 875 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 1.77 (d, J=1.1 Hz, 3H), 2.16 (s, 3H), 4.20 (d, J=2.7 Hz, 1H), 4.74 (d, J=15.2 Hz, 1H), 4.89 (d, J=15.2 Hz, 1H), 4.92 (d, J=2.1 Hz, 1H), 5.22 (d, J=2.0 Hz, 1H), 6.21 (d, J=2.1 Hz, 1H), 7.13 (dd, J=2.5, 7.3 Hz, 1H), 7.22 (d, J=1.1 Hz, 1H), 7.32–7.38 (m, 2H), 7.46 (dd, J=2.5, 7.2 Hz, 1H), 9.03 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 2.5 (q), 20.6 (q), 67.2 (t), 74.7 (d), 78.9 (d), 81.6 (d), 88.9 (d), 111.0 (s), 124.2 (d), 127.7 (d), 127.9 (s), 129.2 (d), 130.4 (d), 134.1 (s), 136.3 (d), 150.4 (s), 163.9 (s), 169.4 (s) ppm; ESI-MS (m/z): 359.3 (19%, $[M+H]^+$), 381.2 (100%, $[M+Na]^+$). Anal. Calcd for $C_{18}H_{18}N_2O_6$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.26; H, 4.98; N, 7.76.

*4.4.4. 1-[2-O-Acetyl-3-O,4-C-(o-phenylenemethylene)-β-D-xylo-tetrofuranosyl]-5-fluorouracil (**35**).* Following the procedure used for the preparation of **33**, glycosylation of acetates **32** (100 mg, 0.34 mmol) with 5-fluorouracil (89 mg, 0.68 mmol) gave the nucleoside **35** (96 mg, 78% yield) as a white solid; R_f (60% ethyl acetate/pet. ether) 0.31; mp: 194–196 °C; $[\alpha]_D^{25}$ +2.2 (c 1.1, $CHCl_3$); IR ($CHCl_3$) ν: 3239, 3109, 3078, 3024, 2925, 2894, 2853, 1752, 1715, 1466, 1373, 1345, 1268, 1224, 1091, 1072, 879 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 2.17 (s, 3H), 4.20 (d, J=2.5 Hz, 1H), 4.73 (d, J=15.2 Hz, 1H), 4.90 (d, J=15.2 Hz, 1H), 4.97 (d, J=2.5 Hz, 1H), 5.22 (d, J=1.4 Hz, 1H), 6.15 (t, J=1.6 Hz, 1H), 7.13 (dd, J=2.3, 6.4 Hz, 1H), 7.33–7.39 (m, 2H), 7.42–7.46 (m, 1H), 7.50 (d, J=6.32 Hz, 1H), 9.65 (br s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 20.5 (q), 67.1 (t), 75.4 (d), 78.4 (d), 81.5 (d), 89.4 (d), 124.8 (d, J=35.1 Hz), 125.2 (d), 127.5 (s), 127.7 (d), 129.4 (d), 130.5 (d), 133.9 (s), 140.8 (d, J=238.5 Hz), 149.0 (s), 156.4 (d, J=27.2 Hz), 169.4 (s) ppm; ESI-MS (m/z): 385.2 (100%, $[M+Na]^+$). Anal. Calcd $C_{17}H_{15}FN_2O_6$: C, 56.36; H, 4.17; N, 7.73. Found: C, 56.25; H, 4.29; N, 7.60.

*4.4.5. 1-[3-O,4-C-(o-Phenylenemethylene)-β-D-xylo-tetrofuranosyl] uracil (**36**).* A solution of **33** (80 mg, 0.36 mmol) and catalytic NaOMe in methanol (2 mL) was stirred at room temperature for 20 min. The reaction mixture was concentrated under reduced pressure and the crude was purified by silica gel column chromatography to afford the tricyclic nucleoside **36** (67 mg, 96% yield) as a white solid; R_f (70% ethyl acetate/pet. ether) 0.41; mp: 140–143 °C; $[\alpha]_D^{25}$ +60.4 (c 1.9, $CHCl_3$); IR ($CHCl_3$) ν: 3383, 3218, 3108, 3068, 2923, 2844, 2252, 1775, 1695, 1464, 1393, 1322, 1265, 1114, 1097, 1059, 999 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 4.22 (d, J=1.9 Hz, 1H), 4.52 (s, 1H), 4.64 (d, J=15.1 Hz, 1H), 4.72 (d, J=15.1 Hz, 1H), 5.24 (d, J=1.9 Hz, 1H), 5.48 (d, J=8.0 Hz, 1H), 5.65 (br s, 1H), 5.89 (s, 1H), 7.10 (dd, J=2.3, 8.1 Hz, 1H), 7.15 (d, J=8.0 Hz, 1H), 7.34–7.36 (m, 2H), 7.51 (dd, J=2.3, 8.1 Hz, 1H), 10.61 (br s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 66.9 (t), 77.1 (d), 80.1 (d), 80.7 (d), 94.2 (d), 101.1 (d), 124.3 (d), 127.8 (d), 128.8 (s), 129.2 (d), 130.8 (d), 134.3 (s), 140.7 (d), 151.1 (s), 164.2 (s) ppm; ESI-MS (m/z): 325.0 (100%, $[M+Na]^+$), 341.0 (7%, $[M+K]^+$). Anal. Calcd for $C_{15}H_{14}N_2O_5$: C, 59.60; H, 4.67; N, 9.27. Found: C, 59.52; H, 4.76; N, 9.18.

*4.4.6. 1-[3-O,4-C-O-(Phenylenemethylene)-β-D-xylo-tetrofuranosyl] thymine (**37**).* Deacetylation of **34** (70 mg, 0.2 mmol) following the procedure described above gave nucleoside **37** (57 mg, 95% yield) as crystalline solid; R_f (70% ethyl acetate/pet. ether) 0.45; mp: 177–179 °C; $[\alpha]_D^{25}$ +40.0 (c 1.0, MeOH); IR (Nujol) ν: 3392, 3220, 3065, 2924, 2854, 1668, 1462, 1377, 1270, 1099, 1062, 916 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 1.61 (d, J=1.0 Hz, 3H), 4.25 (d, J=2.6 Hz, 1H), 4.52 (s, 1H), 4.64 (d, J=15.2 Hz, 1H), 4.74 (d, J=15.2 Hz, 1H), 5.23 (d, J=2.6 Hz, 1H), 5.78 (br s, 1H), 5.93 (s, 1H), 6.97 (d, J=1.1 Hz, 1H), 7.08–7.13 (m, 1H), 7.33–7.38 (m, 2H), 7.47–7.54 (m, 1H), 10.62 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 2.4 (q), 66.8 (t), 76.8 (d), 80.2 (d), 80.8 (d), 93.8 (d), 109.2 (s), 124.2 (d), 127.8 (d), 128.9 (s), 129.1 (d), 130.7 (d), 134.3 (s), 137.0 (d), 151.0 (s), 164.7 (s) pp; ESI-MS (m/z): 339.1 (100%, $[M+Na]^+$),

355.1 (13%, $[M+K]^+$). Anal. Calcd for $C_{16}H_{16}N_2O_5$: C, 60.75; H, 5.10; N, 8.86. Found: C, 60.59; H, 4.97; N, 8.98.

*4.4.7. 1-[3-O,4-C-(o-Phenylenemethylene)-β-D-xylo-tetrofuranosyl]-5-fluorouracil (**38**).* Following the procedure used for the preparation of **36**, deacetylation of compound **35** (85 mg, 0.23 mmol) gave **38** (70 mg, 92% yield) as crystalline solid; R_f (70% ethyl acetate/pet. ether) 0.40; mp: 142–144 °C; $[\alpha]_D^{25}$ +58.5 (*c* 1.3, MeOH); IR (Nujol) *ν*: 3400, 3217, 3067, 2924, 2854, 1712, 1461, 1377, 1256, 1081, 964, 909, 761 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): *δ* 4.26 (d, *J*=2.6 Hz, 1H), 4.52 (s, 1H), 4.65 (d, *J*=15.1 Hz, 1H), 4.76 (d, *J*=15.1 Hz, 1H), 5.24 (d, *J*=2.6 Hz, 1H), 5.48 (br s, 1H), 5.87 (d, *J*=1.0 Hz, 1H), 7.11 (dd, *J*=2.2, 6.8 Hz, 1H), 7.22 (d, *J*=6.3 Hz, 1H), 7.31–7.41 (m, 2H), 7.50 (dd, *J*=2.2, 6.3 Hz, 1H), 10.84 (d, *J*=3.5 Hz, 1H); ^{13}C NMR ($CDCl_3$+methanol-d_4, 50 MHz): *δ* 66.7 (t), 76.4 (d), 80.1 (d, 2C), 92.9 (d), 124.1 (d), 125.1 (d, *J*=36.4 Hz), 127.5 (d), 128.1 (s), 129.0 (d), 130.3 (d), 133.9 (s), 139.5 (d, *J*=234.1 Hz), 149.1 (s), 157.7 (d, *J*=29.4 Hz), ppm; ESI-MS (*m*/*z*): 321.1 (4%, $[M+H]^+$), 343.1 (100%, $[M+Na]^+$), 359.0 (13%, $[M+K]^+$). Anal. Calcd for $C_{15}H_{13}FN_2O_5$: C, 56.25; H, 4.09; N, 7.75. Found: C, 56.37; H, 4.18; N, 7.83.

4.5. Synthesis of nucleosides 43–45

*4.5.1. 1,2,4-Tri-O-acetyl-3-C,3-O-(o-phenylenemethylene) β-D-ribopyranose (**39**).* The procedure for preparing **32** was repeated with compound **24** (600 mg, 1.53 mmol) to prepare the triacetates **39** (462 mg, 83% yield) as colorless oil R_f (30% ethyl acetate/pet. ether) 0.42; IR ($CHCl_3$) *ν*: 3025, 2952, 2872, 1751, 1611, 1463, 1371, 1265, 1070, 1039, 941, 755 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): *δ* 1.70 (s, 3H), 1.74 (s, 3H), 2.09 (s, 3H), 4.01 (d, *J*=8.1 Hz, 2H), 5.19 (d, *J*=12.0 Hz, 1H), 5.22 (d, *J*=12.0 Hz, 1H), 5.31 (d, *J*=8.5 Hz, 1H), 5.33 (t, *J*=8.4 Hz, 1H), 6.04 (d, *J*=8.5 Hz, 1H), 7.19 (d, *J*=7.87 Hz, 1H), 7.23–7.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz): *δ* 20.1 (q), 20.3 (q), 20.9 (q), 63.1 (t), 70.2 (d), 71.9 (d), 74.2 (t), 90.0 (s), 91.8 (d), 120.3 (d), 122.0 (d), 127.7 (d), 128.9 (d), 134.7 (s), 140.6 (s), 169.0 (s), 169.3 (s), 169.4 (s) ppm; ESI-MS (*m*/*z*): 387.2 (100%, $[M+Na]^+$), 403.2 (12%, $[M+K]^+$). Anal. Calcd for $C_{18}H_{20}O_8$: C, 59.34; H, 5.53. Found: C, 59.22; H, 5.60.

*4.5.2. 1-[2,4-Di-O-acetyl-3-C,3-O-(o-phenylenemethylene)-β-D-ribopyranosyl]uracil (**40**).* A procedure similar to the one used for the glycosylation of diacetate **32** was employed. Triacetates **39** (120 mg, 0.33 mmol) and uracil (74 mg, 0.66 mmol) were used to obtain nucleoside **40** (115 mg, 84% yield) as crystalline solid; R_f (50% ethyl acetate/pet. ether) 0.38; mp: 213–215 °C; $[\alpha]_D^{25}$ +52.7 (*c* 1.1, $CHCl_3$); IR ($CHCl_3$) *ν*: 3214, 3021, 2962, 2928, 2873, 1754, 1695, 1634, 1456, 1373, 1219, 1071, 1041, 810, 765 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): *δ* 1.57 (s, 3H), 1.70 (s, 3H), 4.01 (d, *J*=8.1 Hz, 2H), 5.14 (d, *J*=12.3 Hz, 1H), 5.22 (d, *J*=12.3 Hz, 1H), 5.25–5.33 (m, 2H), 5.72 (d, *J*=8.2 Hz, 1H), 6.15 (d, *J*=9.4 Hz, 1H), 7.12–7.27 (m, 4H), 7.39 (d, *J*=8.2 Hz, 1H), 9.10 (br s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): *δ* 19.8 (q), 20.2 (q), 64.4 (t), 69.8 (d), 71.2 (d), 74.2 (t), 79.5 (d), 89.6 (s), 103.1 (d), 120.5 (d), 121.4 (d), 127.7 (d), 129.0 (d), 134.3 (s), 139.7 (d), 140.6 (s), 150.5 (s), 163.0 (s), 169.3 (s), 169.6 (s) ppm; ESI-MS (*m*/*z*): 417.5 (40%, $[M+H]^+$), 439.5 (100%, $[M+Na]^+$), 455.5 (19%, $[M+K]^+$). Anal. Calcd for $C_{20}H_{20}N_2O_8$: C, 57.69; H, 4.84; N, 6.73. Found: C, 57.56; H, 4.94; N, 6.86.

*4.5.3. 1-[2,4-Di-O-acetyl-3-C,3-O-(o-phenylenemethylene)-β-D-ribopyranosyl]thymine (**41**).* Following the procedure used for the preparation of **33**, glycosylation of triacetates **39** (110 mg, 0.30 mmol) with thymine (76 mg, 0.60 mmol) gave compound **41** (99 mg, 76% yield) as a crystalline solid; R_f (50% ethyl acetate/pet. ether) 0.40; mp: 158–160 °C; $[\alpha]_D^{25}$ +20.0 (*c* 1.2, $CHCl_3$); IR ($CHCl_3$) *ν*: 3389, 3020, 2874, 1745, 1686, 1461, 1373, 1216, 1150, 1071, 1042, 985 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): *δ* 1.61 (s, 3H), 1.74 (s, 3H), 1.91 (s, 3H), 4.05 (dd, *J*=7.3, 9.1 Hz, 2H), 5.19 (d, *J*=12.1 Hz, 1H), 5.25 (d, *J*=12.1 Hz, 1H), 5.33 (dd, *J*=7.3, 9.1 Hz, 1H), 5.35 (d, *J*=9.5 Hz, 1H), 6.18 (d, *J*=9.5 Hz, 1H), 7.19–7.23 (m, 2H), 7.26–7.32 (m, 3H), 9.37 (br s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): *δ* 12.4 (q), 19.9 (q), 20.2 (q), 64.5 (t), 69.9 (d), 71.3 (d), 74.2 (t), 79.5 (d), 89.7 (s), 111.5 (s), 120.5 (d), 121.5 (d), 127.7 (d), 129.1 (d), 134.5 (s), 135.3 (d), 140.7 (s), 150.6 (s), 163.7 (s), 169.3 (s), 169.6 (s) ppm; ESI-MS (*m*/*z*): 431.2 (10%, $[M+H]^+$), 453.3 (100%, $[M+Na]^+$), 469.3 (8%, $[M+K]^+$). Anal. Calcd for $C_{21}H_{22}N_2O_8$: C, 58.60; H, 5.15; N, 6.51. Found: C, 58.76; H, 4.99; N, 6.63.

*4.5.4. 1-[2,4-Di-O-acetyl-3-C,3-O-(o-phenylenemethylene)-β-D-ribopyranosyl]-5-fluorouracil (**42**).* A procedure similar to the one used for the glycosylation of diacetate **32** was employed. Triacetates **39** (120 mg, 0.33 mmol) and 5-fluorouracil (86 mg, 0.66 mmol) gave compound **42** (110 mg, 77% yield) as a white solid; R_f (50% ethyl acetate/pet. ether) 0.42; mp: 216–218 °C; $[\alpha]_D^{25}$ +38.7 (*c* 1.5, $CHCl_3$); IR ($CHCl_3$) *ν*: 3217, 3084, 3023, 2930, 2874, 1732, 1673, 1463, 1373, 1219, 1072, 1043, 904 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): *δ* 1.58 (s, 3H), 1.71 (s, 3H), 4.03 (d, *J*=8.2 Hz, 2H), 5.15 (d, *J*=12.1 Hz, 1H), 5.21 (d, *J*=12.1 Hz, 1H), 5.32 (d, *J*=9.3 Hz, 1H), 5.38 (t, *J*=8.2 Hz, 1H), 6.12 (d, *J*=9.3 Hz, 1H), 7.12–7.21 (m, 3H), 7.24–7.28 (m, 1H), 7.53 (d, *J*=6.0 Hz, 1H), 9.81 (br s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): *δ* 19.8 (q), 20.2 (q), 64.4 (t), 69.7 (d), 71.3 (d), 74.2 (t), 80.0 (d), 89.6 (s), 120.5 (d), 121.3 (d), 124.2 (d, *J*=34.2 Hz), 127.7 (d), 129.1 (d), 134.3 (s), 140.4 (d, *J*=239.1 Hz), 140.6 (s), 149.2 (s), 157 (d, *J*=26.6 Hz), 169.5 (s), 169.8 (s) ppm; ESI-MS (*m*/*z*): 435.4 (20%, $[M+H]^+$), 452.47 (35%, $[M+NH_4]^+$), 457.44 (100%, $[M+Na]^+$). Anal. Calcd for $C_{20}H_{19}FN_2O_8$: C, 55.30; H, 4.41; N, 6.45. Found: C, 55.21; H, 4.50; N, 6.51.

*4.5.5. 1-[3-C,3-O-(o-Phenylenemethylene)-β-D-ribopyranosyl]uracil (**43**).* Deacetylation of **40** (90 mg, 0.22 mmol), as followed in the preparation of **36**, gave nucleoside **43** (68 mg, 95% yield) as a white solid; R_f (10% *i*-PrOH/CH_2Cl_2) 0.35; mp: 138–140 °C; $[\alpha]_D^{25}$ +56.5 (*c* 0.4, MeOH); IR (Nujol) *ν*: 3393, 3018, 2961, 2854, 1679, 1459, 1377, 1243, 1062 cm^{-1}; ^1H NMR (methanol-d<GK>$_4$, 200 MHz): *δ* 3.85 (t, *J*=10.8 Hz, 1H), 3.94 (dd, *J*=5.4, 10.8 Hz, 1H), 4.03 (dd, *J*=5.4, 10.8 Hz, 1H), 4.06 (d, *J*=9.5 Hz, 1H), 5.22 (d, *J*=11.8 Hz, 1H), 5.27 (d, *J*=11.8 Hz, 1H), 5.73 (d, *J*=8.1 Hz, 1H), 5.86 (d, *J*=9.5 Hz, 1H), 7.25 (dd, *J*=6.1, 1.55 Hz, 1H), 7.30–7.35 (m, 2H), 7.38–7.40 (m, 1H), 7.79 (d, *J*=8.1 Hz, 1H); ^{13}C NMR (methanol-d<GK>$_4$, 50 MHz): *δ* 68.8 (t), 71.4 (d), 72.7 (d), 75.8 (t), 83.7 (d), 93.9 (s), 103.2 (d), 121.8 (d), 122.3 (d), 128.6 (d), 129.4 (d), 139.5 (s), 142.9 (d), 143.0 (s), 152.9 (s), 166.1 (s) ppm; ESI-MS (*m*/*z*): 333.60 (19.12%, $[M+1]^+$), 355.60 (100%, $[M+Na]^+$), 371.57 (11.03%, $[M+K]^+$). Anal. Calcd for $C_{16}H_{16}N_2O_6$: C, 57.83; H, 4.85; N, 8.43. Found: C, 57.95; H, 4.98; N, 8.56.

*4.5.6. 1-[3-C,3-O-(o-Phenylenemethylene)-β-D-ribopyranosyl]thymine (**44**).* Deacetylation of **41** (80 mg, 0.19 mmol), as followed in the preparation of **36**, afforded nucleoside **44** (58 mg, 90% yield) as a crystalline solid; R_f (10% *i*-PrOH/CH_2Cl_2) 0.40; mp: 116–118 °C; $[\alpha]_D^{25}$ +30.0 (*c* 0.8, MeOH); IR (Nujol) *ν*: 3371, 3017, 2925, 2855, 1653, 1463, 1377, 1064, 762 cm^{-1}; ^1H NMR (acetone-d<GK>$_6$, 500 MHz): *δ* 1.85 (d, *J*=1.07 Hz, 3H), 3.83 (t, *J*=10.8 Hz, 1H), 3.91 (br d, *J*=8.8 Hz, C(4)-O*H*, 1H), 3.93 (dd, *J*=5.5, 10.8 Hz, 1H), 4.09 (ddd, *J*=10.8, 8.8, 5.5 Hz), 4.17 (d, *J*=8.5 Hz, C(2)–O*H*, 1H), 4.23 (dd, *J*=8.8, 9.5 Hz, 1H), 5.24 (d, *J*=11.7 Hz, 1H), 5.29 (d, *J*=11.7 Hz, 1H), 5.90 (d, *J*=9.5 Hz, 1H), 7.27–7.28 (m, 1H), 7.30–7.35 (m, 2H), 7.40–7.42 (m, 1H), 7.63 (q, *J*=1.1 Hz, 1H), 10.12 (br s, 1H); ^{13}C NMR (acetone-d<GK>$_6$, 50 MHz): *δ* 12.3 (q), 68.5 (t), 71.1 (d), 72.2 (d), 75.3 (t), 82.8 (d), 93.5 (s), 110.8 (s), 121.4 (d), 122.0 (d), 127.9 (d), 128.7 (d), 137.1 (d), 139.7 (s), 142.5 (s), 152.0 (s), 164.2 (s) ppm; ESI-MS (*m*/*z*): 369.1 (100%, $[M+Na]^+$), 385.2 (6%, $[M+K]^+$). Anal. Calcd for $C_{17}H_{18}N_2O_6$: C, 58.96; H, 5.24; N, 8.09. Found: C, 59.10; H, 5.06; N, 7.97.

*4.5.7. 1-[3-C,3-O-(o-Phenylenemethylene)-β-D-ribopyranosyl]-5-fluorouracil (**45**).* The deacetylation of compound **42** (90 mg, 0.21 mmol) was carried out according to the procedure used for the preparation of **36**, giving nucleoside **45** (67 mg, 93% yield) as a crystalline solid; R_f (10% *i*-PrOH/CH_2Cl_2) 0.40; mp: 153–155 °C;

$[\alpha]_D^{25}$ +44.0 (*c* 0.7, MeOH); IR (Nujol) ν: 3387, 3021, 2920, 2854, 1698, 1666, 1461, 1377, 1284, 1245, 1063, 914, 756 cm^{-1}; ^1H NMR (methanol-*d*<GK>$_4$, 200 MHz): δ 3.85 (t, *J*=10.9 Hz, 1H), 3.95 (dd, *J*=5.3, 10.7 Hz, 1H), 3.99–4.04 (m, 2H), 5.22 (d, *J*=11.9 Hz, 1H), 5.26 (d, *J*=11.9 Hz, 1H), 5.84 (dd, *J*=1.5, 9.5 Hz, 1H), 7.23–7.25 (m, 1H), 7.29–7.38 (m, 3H), 7.94 (d, *J*=6.5 Hz, 1H); ^{13}C NMR (methanol-*d*<GK>$_4$, 50 MHz): δ 68.5 (t), 71.0 (d), 72.5 (d), 75.6 (t), 83.6 (d), 93.5 (s), 121.6 (d), 121.9 (d), 124.4 (d, J=34.3 Hz), 128.4 (d), 129.2 (d), 139.0 (s), 141.7 (d, *J*=235.1 Hz), 142.5 (s), 151.2 (s), 159.1 (d, *J*=26.9 Hz) ppm; ESI-MS (*m*/*z*): 351.5 (18%, $[M+H]^+$), 373.5 (100%, $[M+Na]^+$). Anal. Calcd for $C_{16}H_{15}FN_2O_6$: C, 54.86; H, 4.32; N, 8.00. Found: C, 54.71; H, 4.48; N, 8.13.

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Supplementary data

^1H, ^{13}C spectra of selected compounds and 2D NMR spectra wherever applicable. Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.06.011. These data include MOL files and InChIKeys of the most important compounds described in this article.

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