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Synthesis of higher-carbon sugars by addition of organometallic reagents to aldehydes or lactols derived from carbohydrates

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Abstract—The addition of different Grignard or lithium organometallic reagents to lactols (**1**, **6**, **21**) or aldehydes (**10**), derived from D-glucose or D-mannose, to give the new higher-carbon sugars (**2**, **3**, **7**–**9**, **13**–**19**, **22** and **23**) is reported.

1. Introduction

The addition of organometallic reagents to aldehydes, ketones or lactols is one the best known, used and exploited methods for the synthesis of branched-chain or higher-carbon sugar derivatives.[1] This is a simple reaction which usually affords high stereoselection and convenient chemical yields of the desired products. Although it is difficult to predict the stereochemical outcome (the *syn*/*anti* ratio) of these processes, there is a plethora of dispersed and useful results in literature which allow us to generalize some general trends.[2] Some examples are shown in Scheme 1. A marked preferred *anti* selectivity has been reported in the Grignard addition to 2,3-*O*-isopropylidene derivatives in the manno-[3] (Eq. (1), Scheme 1) or in the addition of Grignard and lithium reagents in the ribo- series[4] (Eq. (2), Scheme 1). Conversely, in the addition of lithium reagents to manno- 2,3-*O*-isopropylidene derivatives, a reversal of this stereoselectivity has been reported (Eq. (3), Scheme 1).[5,3c] These trends have also been confirmed in other 2,3-*O*-isopropylidene derivatives in furanose templates.[2a,6] The same applies to precursors in the D-threose or D-erythrose[8] (Eq. (4), Scheme 1) series: major *anti* products have been obtained, independently of the organometallic agents used. An interesting, very synthetically useful and highly stereoselective protocol is also the one-carbon homologation protocol described by Dondoni: for α-alkoxy aldehydes only *anti* adducts have been observed (Eq. (5), Scheme 1).[9] The addition of 1,3-dithiane has also been extensively studied by several authors: major *syn* isomers have been obtained (Eq. (6), Scheme 1);[10] in addition, they have always found higher values for $J_{1,2}$ in *syn* products than in the similar *anti* compounds. This same preference (*syn* induction) has been reported in the reaction of organocopper compounds with 2,3-*O*-isopropylidene-D-glyceraldehyde.[11] The use of organozinc reagents has also been studied affording variable mixtures of the *syn*/*anti* products, the reaction being very substrate-dependent.[12] Another relevant type of substrates submitted to organometallic addition have been the free aldehydes derived from sugars or the *O*-perbenzylated lactols. With open-chain free aldehydes the addition of Grignard reagents gives major *syn* products, a situation which has been reversed to give major *anti* products by using magnesium bromide as additive (Eq. (1), Scheme 2).[13] The addition of vinyl species to *O*-perbenzylated aldopentoses described by Nicotra has afforded consistent major *syn* isomers from D-arabino, D-ribo and D-xylo precursors, but major *anti* isomers from D-lyxo derivatives (Eq. (2), Scheme 2).[14] In Fig. 1 we show some *syn*/*anti* adducts with the reported vicinal coupling between the newly formed and the pre-existing stereocenters. In most of these examples a correlation with a known stereochemically pure compound, or a simple chemical transformation leading to some 'cyclic' derivative, where an inequivocal spectroscopic proof, such as a nOe effect or a vicinal coupling constant, could be applied, has been used to assign the *syn*/*anti* stereochemical outcome of the organometallic addition. In fact, this strategy has been used sometimes for the synthesis of *C*-glycosides[4] or azasugars[15] from intermediates obtained via the organometallic addition to aldehydes or imines, respectively.

In summary, from all the reported data and results[1–15] we can conclude that the addition of organometallic reagents to lactols or aldehydes derived from carbohydrates is very complex, highly dependent on the reaction conditions, *O*-protecting groups, and that each new transformation[16] has to be carefully analyzed by chemical transformations and or by very well contrasted ^{1}H NMR spectroscopic data.

From the mechanistic point of view, it is important to highlight that the formation of major *anti* products has been

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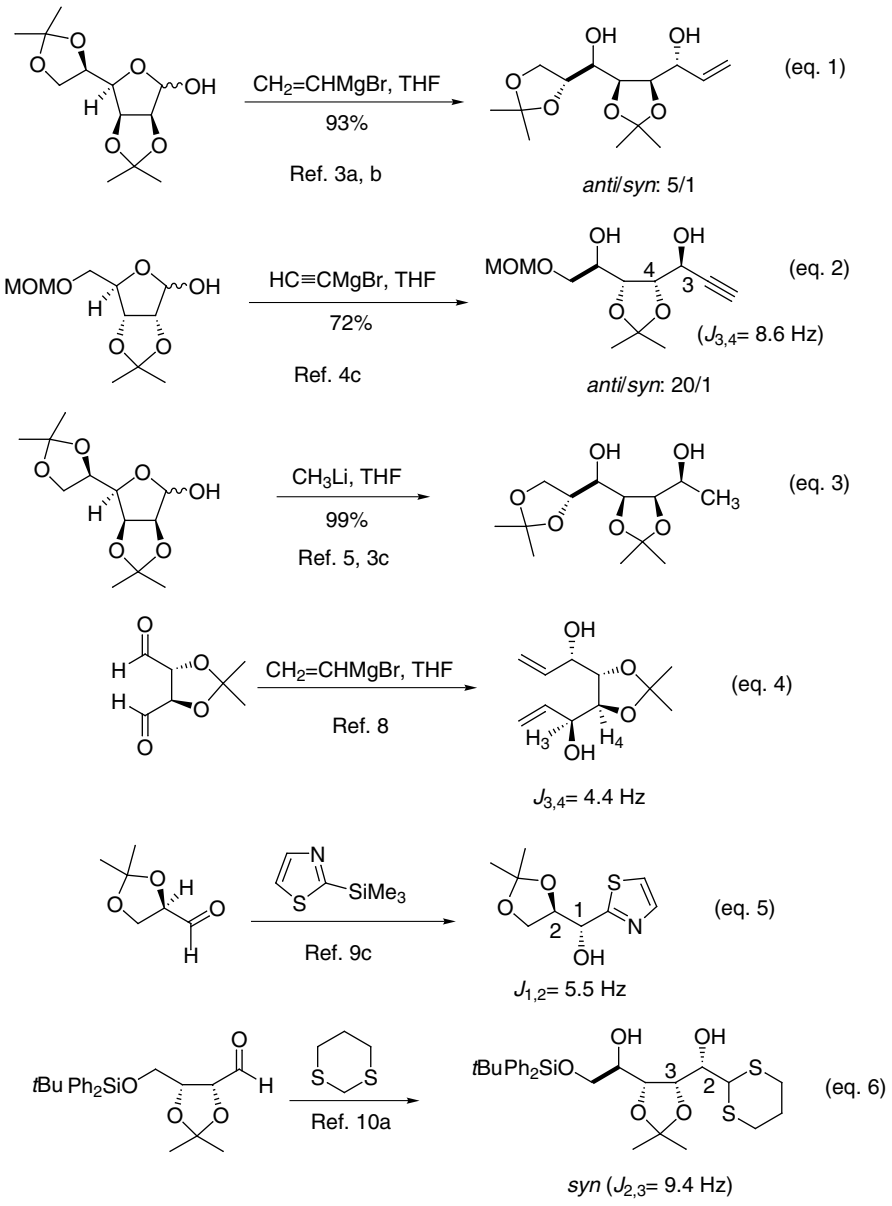


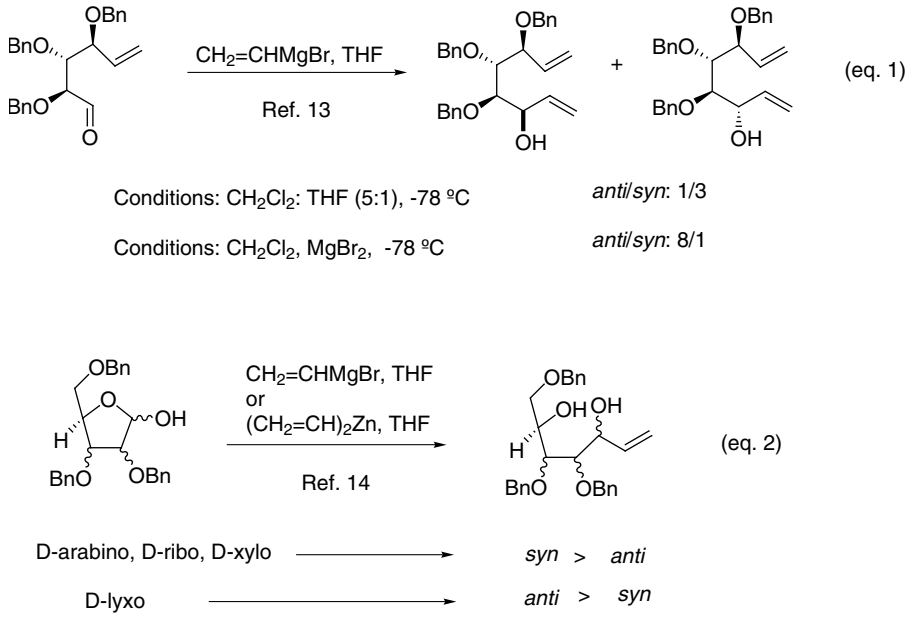
Scheme 1. Addition of organometallic reagents to sugar derivatives.

explained by assuming a chelation or nonchelation control in a Felkin–Ahn model (Fig. 2).[17,18]

In the course of our recent work we have analyzed the reactivity of some organometallic reagents with several aldehydo-sugars or lactols for the preparation of higher-carbon sugars. In this account we show and discuss the results we have obtained in these protocols.

2. Results and discussion

The first substrate studied was the commercially available tetra-*O*-benzyl-D-glucopyranose (**1**). After some experimentation suitable conditions were found to promote an efficient addition reaction using phenylethynylmagnesium bromide (1.0 M in THF) (see Section 3). As shown in Scheme 3 two compounds, **2** and **3**, were isolated in 88% overall yield. The ratio of these isomers in the crude reaction mixture was 37/63, respectively. All new molecules showed excellent analytical and spectroscopic data, in good agreement with their structures. Extensive ^{1}H NMR, ^{1}H–^{1}H COSY and HMQC experiments allowed us to assign the chemical and vicinal coupling constants. We have tentatively assigned as *syn* the relative stereochemistry to the major isomer **3**, and the *anti* to the minor product **2**. In fact, the analogous derivatives 3,4,5,7-tetra-*O*-benzyl-1-deoxy-D-*glycero*-D-gulo-heptitol (*anti* product: $J_{1,2}$=6 Hz) and 1,3,4,5-tetra-*O*-benzyl-7-deoxy-D-*glycero*-L-gulo-heptitol (*syn* product: $J_{1,2}$=2.9 Hz) (Fig. 3) show vicinal coupling constants at the newly formed stereocenters[19a] very similar to the values found by us in compound **2** (*anti*) ($J_{3,4}$=4.6 Hz; δ H-3: 4.88) and in compound **3** (*syn*) ($J_{3,4}$=2.9 Hz; δ H-3: 4.67), respectively. This fact is also in agreement with the reactivity of vinylmagnesium bromide with the 'stereochemically analogous' 2,3,5-tri-*O*-benzyl-xylo-D-furanose described by Nicotra, favouring the formation of major *syn* adducts (see Fig. 1, compounds **D2** and **D4** and Eq. (2), Scheme 2).[14]



Scheme 2. Addition of organometallic reagents to free aldehydes or *O*-perbenzylated aldoses.

As expected from literature data,[3] in very mild and careful reaction conditions, preferential functionalization in the *O*-propargyl side chain in the major product **3** (*syn*) lead to the C-3/*O*-monobenzyloxycarbonyl (**4**) and C-3/*O*-monobenzoyl (**5**) derivatives. Unfortunately, the reaction of compound **3** with tosyl chloride or methanosulfonyl chloride,[4b] or under Mitsunobu conditions[4f,g] as described, to give the 'cyclic' derivatives was very complex[4b] or gave no reaction at all,[4f,g] and one of the expected and known resulting *C*-glycosides[19b] (Fig. 4) was not obtained.

With these results in mind we turned our attention to lactol **6** obtained from D-glucose diethyl dithioacetal as described.[20] The reaction of this product with vinylmagnesium bromide (1.0 M in THF) at 0°C afforded compounds **7** and **8** in 45% yield, as a mixture of two isomers, in a 3:7 ratio,

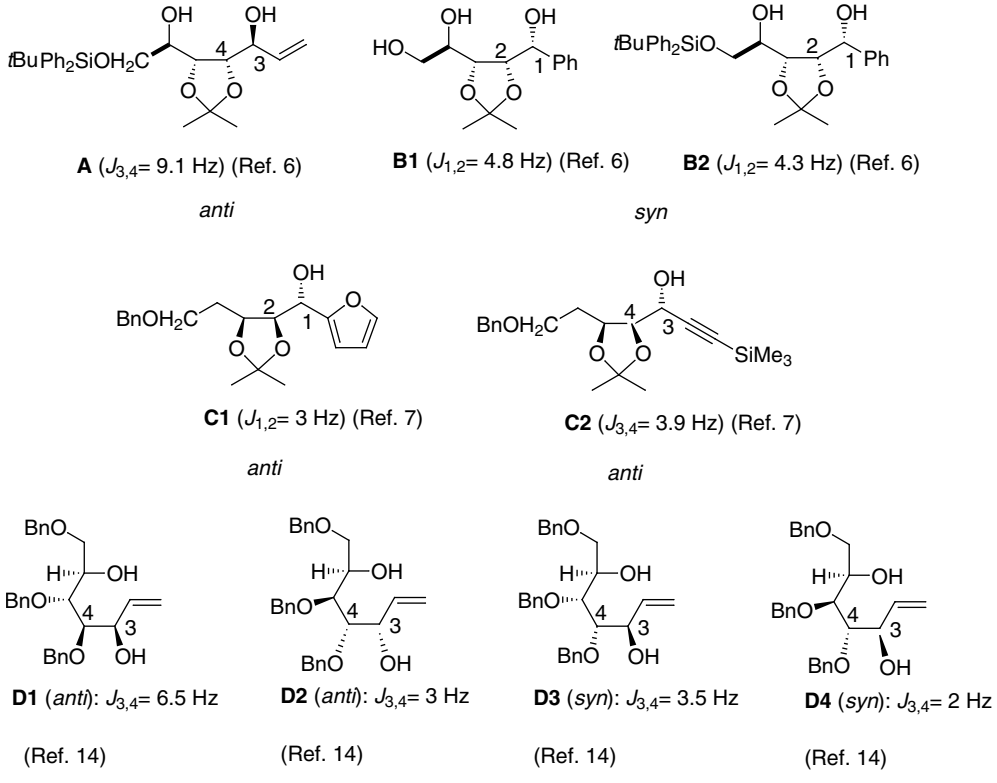


Figure 1. Some examples of *anti* and *syn* products obtained from carbohydrate derivatives with the reported vicinal coupling constants at the newly formed stereocentres.

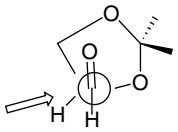
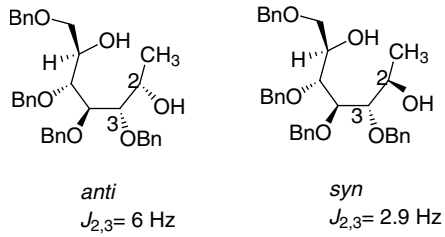


Figure 2. Felkin–Ahn model for the formation of *anti* products during the organometallic addition to aldehydes (Ref. 17).

respectively, which we could only partially separate: only major product **8** (*anti*) was isolated pure (Scheme 4). Performing the reaction at −78°C, in the same conditions, the yield was quite similar, but the ratio of isomers increased to 1:4, the *anti* isomer being again the major isomer in the mixture. The assignment of *anti* to the major isomer was tentatively made by comparison of the reactivity observed for the analogous D-glucose derivative **10**, which gives major *anti* derivatives **14** or **19** (see below, Scheme 6), a very well known stereochemical outcome in Dondoni's chemistry.[9] It is interesting to note that in the ^{1}H NMR spectrum, upon addition of D_2O, pure major **8** (*anti*) compound showed a vicinal coupling constant $J_{3,4}$ equal to 5.1 Hz; this value is very similar to the same vicinal coupling constant observed in analogous derivatives obtained from related D-glucose precursor **10** [see below, Scheme 6, compounds **14** (*anti*) and **19** (*anti*)]. Unfortunately, the ^{1}H NMR of the mixture, H-3 (*syn*) was overlapping other signals and an inequivocal analysis of this signal was not possible.

The same substrate (**6**) after addition of phenylethynylmagnesium bromide (1.0 M in THF) at rt afforded a mixture of **9** (*syn*) and **9** (*anti*) isomers in 67% yield (91% taking into account the recovered starting material), in 1 to 4 ratio, respectively, which we were unable to separate. However in the ^{1}H NMR spectrum of the mixture the signals for H-3 were clearly detected, appearing as triplets with identical vicinal coupling constants for H-3/OH and H-3/H-4. For the major isomer **9** (*anti*) we could observe δ H-3 at 4.88, with $J_{3,4}$=3.6 Hz, while for the minor isomer **9** (*syn*) we could observe δ H-3 at 4.68, with $J_{3,4}$=5.4 Hz. In this case the assignment as *anti* to the major isomer rests by comparison with compounds **15** (*syn*) and **16** (*anti*) (see below, Scheme 6), whose absolute configuration at the newly formed stereocenters has been inequivocally demonstrated by transforming **16** (*anti*) into 'cyclic' derivatives.[21] Note that in these examples the vicinal coupling constants in the *syn* isomers are higher than in the *anti*, the opposite observed in compounds **9**. This is a clear case where the



anti
$J_{2,3}$= 6 Hz

syn
$J_{2,3}$= 2.9 Hz

Figure 3. 3,4,5,7-Tetra-*O*-benzyl-1-deoxy-D-*glycero*-D-gulo-heptitol (*anti* product) and 1,3,4,5-tetra-*O*-benzyl-7-deoxy-D-*glycero*-L-gulo-heptitol (*syn* product) (Ref. 19a).

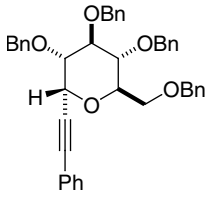


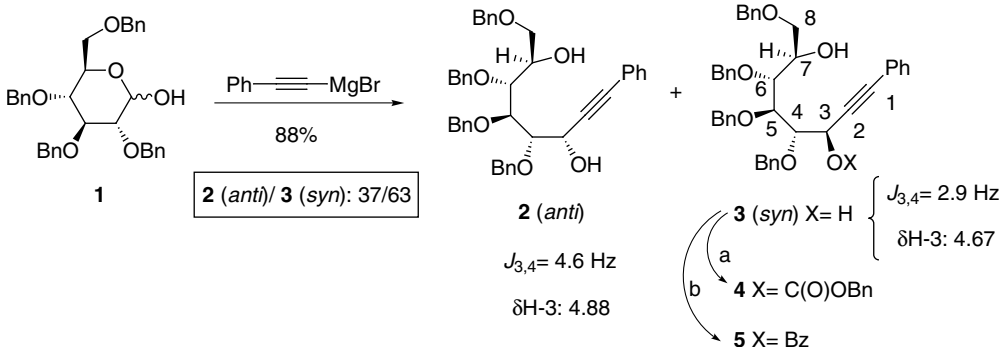
Figure 4. (2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyransoyl) phenylacetylene (Ref. 19b).

value of the coupling constants for stereochemical assignments have to be used with caution.

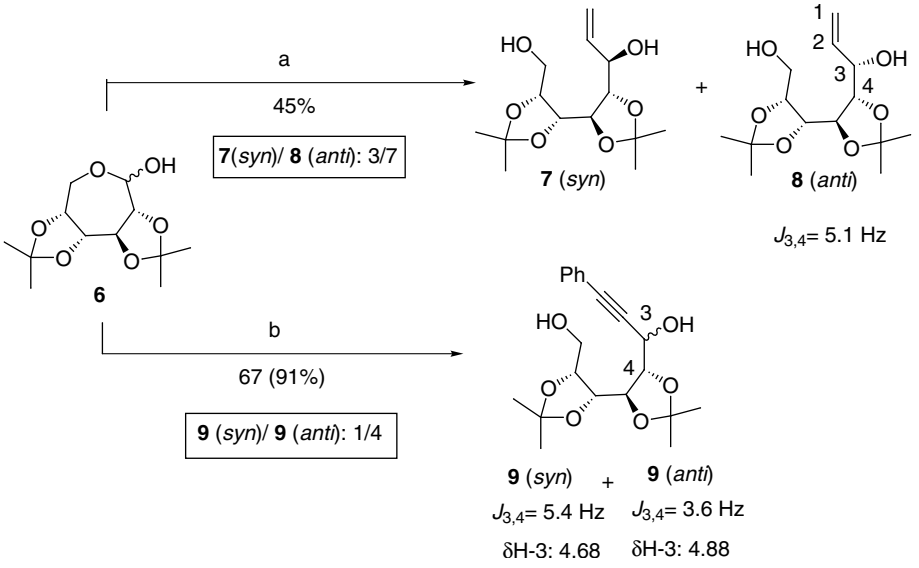
Next we turned out our attention to the organometallic additions to iodoaldehyde **10**. This compound has been easily prepared from alcohol **11**,[22] via iodide **12** as shown in Scheme 5.

Vinylmagnesium bromide addition to aldehyde **10** at 0°C gave the expected compounds **13** (*syn*) and **14** (*anti*) in 81% yield, showing that the iodine atom was quite stable to the present conditions (Scheme 6). The ratio of isomers *syn* and *anti* was 1 to 4, respectively. We only could isolate pure the major product **14** (*anti*), which in the ^{1}H NMR spectrum showed a vicinal coupling constant for H-3/H-4 equal to 4.4 Hz, in good agreement with the value observed for compound **8** (*anti*) (see above). Unfortunately, during the chromatography for the purification, the rest of the mass for this reaction was a mixture of products **13** (*syn*) and **14** (*anti*) whose ^{1}H NMR spectrum made difficult to analyze the $J_{3,4}$ (*syn*).

The addition of phenylethynylmagnesium bromide to compound **10** in the usual conditions afforded the mixture



Scheme 3. Addition of pehnylethynylmagnesium bromide to hemiacetal **1** at rt. *Reagents*: (a) CIC(O)OBn, py (63%); (b) CIBz, py (77%).



Scheme 4. Addition of Grignard reagents to hemiacetal **6**. *Reagents*: (a) Vinylmagnesium bromide, 0°C; (b) Phenylethynylmagnesium bromide, 0°C.

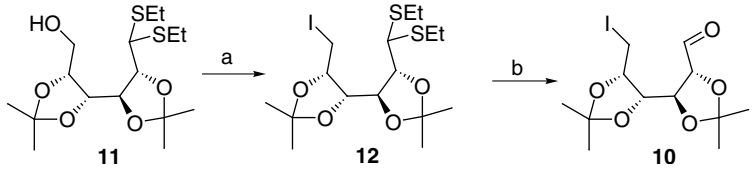
of compound **15** and **16**, in 73% overall yield and 3/7 ratio, respectively (Scheme 6). Only pure major **16** (*anti*) isomer was isolated pure. In agreement with the observed data for adducts **9** (*anti*) (see below, Scheme 4) compound **16** (*anti*) showed in the ^{1}H NMR spectrum a vicinal coupling constant between H-3 (4.83 ppm) and H-4 equal at 3.3 Hz; in the mixture of **15** (*syn*) and **16** (*anti*) we could analyze H-3 for **15** (*syn*) at 4.70 ppm as a doublet of doublets with $J_{3,4}$=4.4 Hz, $J_{3,OH}$=5.6 Hz.

The final assignment as *anti* to the major isomers **14** and **16** has been inequivocally demonstrated by transforming them into 'cyclic' derivatives, where the relative stereochemistry at the newly formed stereocenters has been established by spectroscopic data and nOe effects.[21]

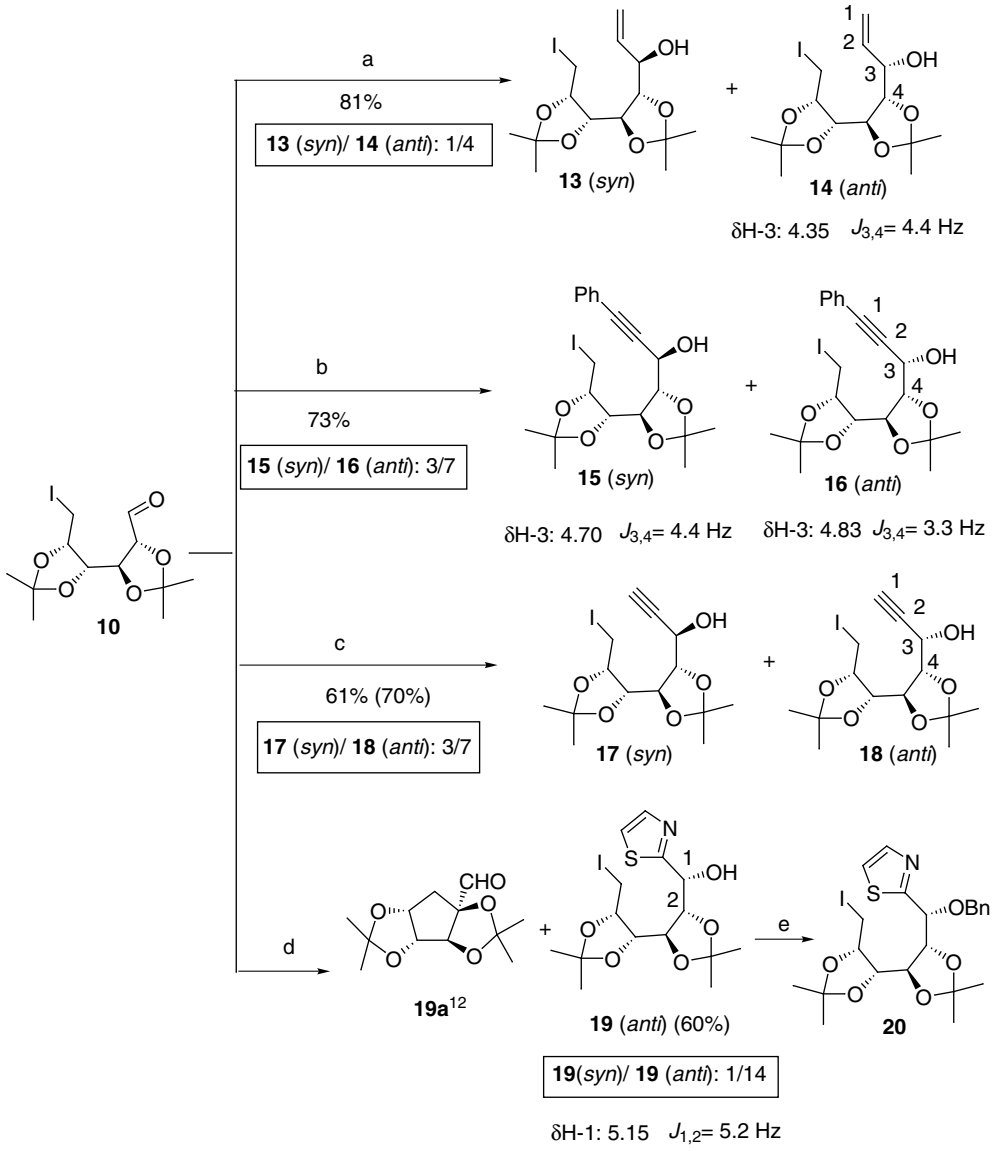
The addition of ethynylmagnesium bromide to compound **10** in the standard conditions gave an unseparable mixture of compounds **17** (*syn*) and **18** (*anti*) in 61% yield (70% taking into account the recovered starting material), in a 3 to 7 ratio, respectively (Scheme 6). Unfortunately, in the ^{1}H NMR spectrum protons H-3 and H-4 appeared as complex multiplets, and the inequivocal assignment was impossible. In addition to the assigned signals for the major **18** (*anti*) isomer, in the ^{1}H NMR and in the ^{13}C NMR spectra of the mixture we could also identify some specific signals for the minor **17** (*syn*) isomer: 4.30 (d, $J_{6,7}$=6.7 Hz, 1H, H-6), 4.17 (d, $J_{4,5}$=4.0 Hz, 1H, H-5), 3.40 (d, $J_{7,8}$=7.0 Hz, 2H, 2H-8), 2.81 (d, $J_{3,OH}$=6.3 Hz, 1H, OH), 2.55 (d, $J_{1,3}$=2.2 Hz, 1H, –C≡C–H) ppm, and 81.1 (q, –*C*≡C–H), 79.2 (q, –C≡*C*–H), 77.9 (C-7), 75.2 (C-4), 75.1 (C-5), 74.8 (C-6), 62.4 (C-3), 2.5 (C-8) ppm. In this case, the assignment of *anti* as the major isomer was tentatively made by comparison with the other related cases obtained from the same precursor (**10**) (see above).

Finally, aldehyde **10** was submitted to reaction with 2-(trimethylsilyl)thiazole. Not unexpectedly, we isolated only one compound (**19**) (Scheme 6) to whom the *anti* stereochemistry at carbons C-1 and C-2 was assigned based on well known precedent.[9] In fact, the observed $J_{1,2}$=5.2 Hz is in good agreement with the reported analogous vicinal coupling constant (5.5 Hz) for (1*R*)-2,3-*O*-isopropylidene-1-(2-thiazolyl)-D-glycitol (Eq. (5), Scheme 1).[9c]

We wanted also to test the reactivity of lithium reagents with these type of lactols. It is well known for instance that the reaction of methyllithium with 2,3:5,6-bis-*O*-isopropylidene-α-D-mannofuranose (**21**)[23] gives exclusively *syn* product (Eq. (3), Scheme 1),[5] while the reaction with methylmagnesium bromide affords a major *anti* compound.[3c] In our case we have submitted the hemiacetal **21**[23] to reaction with lithium phenylacetylide, and have obtained products **22** (*syn*) and **23** (*anti*) in 82% yield, in a 2.6 to 1 ratio, respectively (Scheme 7). After separation by chromatography, the usual analytical and spectroscopic data allowed us to determine the structure of these compounds. Major isomer showed a vicinal coupling constant for H-3 and H-4 equal to 6.8 Hz, while minor isomer showed a vicinal coupling constant for H-3 and H-4 equal to 4.9 Hz, showing that in this case and as expected[5] the major isomer is *syn*. In this case, the assignment of *syn* to the major isomer was tentatively made by comparison with the other related



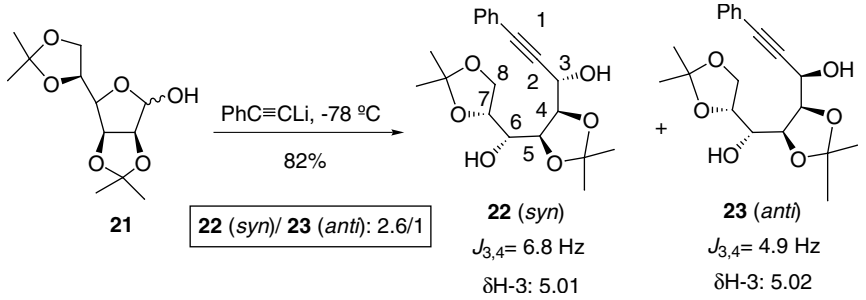
Scheme 5. Synthesis of precursor **10**. *Reagents*: (a) I_2, Ph_3P, toluene, imidazole (70%); (b) HgO, $HgCl_2$, acetone (75%).



Scheme 6. Addition of organometallic reagents to aldehyde **10**. *Reagents*: (a) Vinylmagnesium bromide, 0°C; (b) Phenylethynylmagnesium bromide, 0°C; (c) Ethynylmagnesium bromide, 0°C; (d) 2-(Trimethylsilyl)thiazole, 0°C; (e) (from **19**) NaH, BnBr (92%).

cases obtained by Corey[5] and other authors[3c] with the same precursor.

In summary, we have described the synthesis of higher-carbon sugars from readily available hemiacetals or free aldehydes, derived from D-glucose or D-mannose, by reaction with Grignard or lithium reagents. Yields were usually good with moderate stereoselectivities ranging from 1 to 4 or 2 to 1, in favor of *anti* isomers when using Grignard reagents, while for lithium species the stereoselectivity was reversed. The best result was obtained with any doubt using Dondoni's formyl homologation method.[9] The



Scheme 7. Addition of lithium phenylacetylide to hemiacetal **21**.

resulting products are useful building blocks for further synthetic manipulation, and they will serve us in future developments in our laboratory.[21]

3. Experimental

3.1. General methods

Reactions were monitored by TLC using precoated silica gel aluminium plates containing a fluorescent indicator (Merck, 5539). Detection was done by UV (254 nm) followed by charring with sulfuric–acetic acid spray, 1% aqueous potassium permanganate solution or 0.5% phosphomolybdic acid in 95% EtOH. Anhydrous Na_2SO_4 was used to dry organic solutions during work-ups and the removal of solvents was carried out under vacuum with a rotary evaporator. Flash column chromatography was performed using silica gel 60 (230–400 mesh, Merck) and hexane/ethyl acetate mixtures as eluent unless otherwise stated. ^{1}H spectra were recorded with a Varian VXR-300(400)S spectrometers, using tetramethylsilane as internal standard and ^{13}C NMR spectra were recorded with a Bruker WP-200-SY. Values with (*) can be interchanged. For the DEPT experiments (q=quaternary carbon; d=*C*H; t=*C*H_2).

3.2. General method for the addition of Grignard reagents

To a solution of the substrate in the appropriate dry solvent, at the selected temperature, under argon, the commercial available Grignard reagent (4.0 equiv.) was slowly added. The reaction was stirred at the indicated temperature and monitored by TLC; when the reaction was complete, the mixture was quenched by addition of aqueous saturated solution of ammonium chloride, the solvent was removed, the residue diluted wih ethyl acetate, washed with brine, dried, filtered and evaporated to give a crude which was submitted to chromatography eluting with hexane/ethyl acetate mixtures.

3.2.1. 4,5,6,8-Tetra-*O*-benzyl-1,2-dideoxy-1-phenyl-D-*glycero*-D-gulo-oct-1-ynitol (2 *anti*) and 4,5,6,8-tetra-*O*-benzyl-1,2-dideoxy-1-phenyl-D-*glycero*-D-*ido*-oct-1-ynitol (3 *syn*). Following the *General method for the addition of organometallic reagents* compound **1** (1 g, 1.85 mmol), dissolved in dry toluene (18 mL), was treated with phenylethynylmagnesium bromide (15 mmol, 1.0 M in THF, 8 equiv.) at rt, for 24 h, to give compound **2** (*anti*) (164 mg), a mixture of **2** and **3** (376 mg, ratio: 17/83, respectively) and compound **3** (*syn*) (524 mg), after chromatography (hexane/ethyl acetate: 88/12). Overall yield: 1.0 g (88%). **2** (*anti*): oil; $[\alpha]_D^{25}=+21$ (*c* 0.4, $CHCl_3$); IR (film) ν 3445 (OH), 3063, 3030, 2867, 2211 (C≡C), 1598, 1490, 1453, 1071, 1027 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42–7.21 (m, 25H, aromat.), 4.88 (m, 1H, H-3), 4.84/4.83 (AB system, *J*=11.3 Hz, 2H, OC*H*$_2$Ph), 4.77 (s, 2H, OC*H*$_2$Ph), 4.62/4.50 (AB system, *J*=11.3 Hz, 2H, OC*H*$_2$Ph), 4.59/4.57 (AB system, *J*=12 Hz, 2H, OC*H*$_2$Ph), 4.30 (t, $J_{5,6}=J_{4,5}=4.6$ Hz, 1H, H-5), 4.02–3.99 (m, 1H, H-7), 3.96 (t, $J_{4,3}=J_{4,5}=4.6$ Hz, 1H, H-4), 3.90 (dd, $J_{6,7}=7.1$, $J_{6,5}=4.6$ Hz, 1H, H-6), 3.68–3.60 (m, 2H, 2H-8), 3.30 (d, *J*=7.5 Hz, 1H, OH–C3), 2.89 (d, *J*=4.6 Hz, 1H, OH–C7); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.2, 138.0, 137.9, 137.6 (q, OCH_2*Ph*), 131.9 (d, 2 C, *Ph*–C≡C), 129.0–128.0 (23 C, aromat.), 122.7 (q, *Ph*–C≡C), 88.3, 86.6 (q, Ph–*C*≡*C*), 79.5 (2 C, C-4, C-5), 77.2 (C-6), 71.5 (C-7), 73.8, 73.6 (2 C), 73.6 (4 C, O*C*H_2Ph), 71.2 (C-8), 63.3 (C-3); MS (70 eV) *m/z* 403 (18), 295 (13), 253 (32), 193 (44), 182 (17), 131(26), 103 (13), 91 (100), 65 (12). Anal. calcd for $C_{42}H_{42}O_6$: C, 78.48; H, 6.59. Found: C, 78.30; H, 6.81. **3** (*syn*): oil; $[\alpha]_D^{25}=-8$ (*c* 0.7, $CHCl_3$); IR (film) ν 3435 (OH), 3030, 2922, 2233 (C≡C), 1598, 1490, 1454, 1357, 1210, 1070, 1027 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43–7.21 (m, 25H, aromat), 4.96/4.88 (AB system, *J*=11 Hz, 2H, OC*H*$_2$Ph), 4.79/4.68 (AB system, *J*=11.2 Hz, 2H, OC*H*$_2$Ph), 4.67 (m, 1H, H-3), 4.56/4.51 (AB system, *J*=11 Hz, 2H, OC*H*$_2$Ph), 4.59/4.52 (AB system, *J*=11.8 Hz, 2H, OC*H*$_2$Ph), 4.12–4.09 (m, 1H, H-7), 4.11 (dd, $J_{5,4}=7.2$, $J_{5,6}=3.3$ Hz, 1H, H-5), 4.07 (dd, $J_{4,5}=7.2$, $J_{4,3}=2.9$ Hz, 1H, H-4), 3.82 (dd, $J_{6,7}=7.2$, $J_{6,5}=3.3$ Hz, 1H, H-6), 3.66 (dd, $J_{8,8'}=9.9$, $J_{8,7}=3.5$ Hz, 1H, H-8), 3.64 (dd, $J_{8,8'}=9.9$, $J_{8',7}=4.9$ Hz, 1H, H-8′), 3.07–3.05 (m, 2H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.0, 137.9, 137.7, 137.4 (q, OCH_2*Ph*), 131.6 (d, 2 C, *Ph*–C≡C), 128.4–127.7 (23 C, aromat.), 122.4 (q, *Ph*–C≡C), 84.4, 85.5 (q, Ph–*C*≡*C*), 81.8 (C-5), 78.8 (C-7), 76.9 (C-6), 75.4, 74.9, 73.3, 73.0 (4 C, O*C*H_2Ph), 71.0 (C-8), 70.7 (C-4), 63.2 (C-3); MS (70 eV) *m/z* 403 (15), 295 (11), 253 (25), 205 (13), 193 (39), 182 (15), 181 (75), 131 (25), 91 (100), 65 (13). Anal. calcd for $C_{42}H_{42}O_6$: C, 78.48; H, 6.59. Found: C, 78.41; H, 6.80.

3.2.2. 4,5,6,8-Tetra-*O*-benzyl-3-*O*-benzyloxycarbonyl-1,2-dideoxy-1-phenyl-D-*glycero*-D-*ido*-oct-1-ynitol (4). To a solution of compound (**3** *syn*) (280 mg, 0.44 mmol) in dry methylene chloride (5 mL), at 0°C, under argon, benzyl chloroformiate (0.06 mL, 0.44 mmol) and pyridine (0.04 mL, 0.44 mmol) were slowly added and the solution was stirred to rt. This operation was repeated three times after 28 h. The reaction was quenched after 48 h. The mixture was treated with water and extracted with methylene chloride and washed with brine. The organic layer was dried, filtered, the solvent was removed and the residue submitted to chromatography (hexane/ethyl acetate: 93/7) to give compound **4** (193 mg, 63%) and unreacted product **3** (31 mg). **4**: mp 75–78°C; $[\alpha]_D^{25}=-16$ (*c* 0.3, $CHCl_3$); IR (KBr) ν 3435 (OH), 3029, 2891, 2222 (C≡C), 1754 (C=O), 1496, 1453, 1381, 1357, 1267, 1050 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–7.19 (m, 30H, aromat.), 5.81 (d, $J_{3,4}=6.7$ Hz, 1H, H-3), 5.15/5.10 (AB system, *J*=11.9 Hz, 2H, OC*H*$_2$Ph), 4.89/4.72 (AB system, *J*=11.6 Hz, 2H, OC*H*$_2$Ph), 4.75/4.70 (AB system, *J*=11.2 Hz, 2H, OC*H*$_2$Ph), 4.55/4.48 (AB system, *J*=11.5 Hz, 2H, OC*H*$_2$Ph), 4.52/4.50 (AB system, *J*=11.9 Hz, 2H, OC*H*$_2$Ph), 4.18–4.12 (m, 2H, H-5, H-4), 4.01–3.99 (m, 1H, H-7), 3.85 (dd, $J_{6,7}=7.4$, $J_{6,5}=4.8$ Hz, 1H, H-6), 3.65 (dd, $J_{8,8'}=9.9$, $J_{8,7}=3.3$ Hz, 1H, H-8), 3.59 (dd, $J_{8,8'}=9.9$, $J_{8',7}=5.1$ Hz, 1H, H-8′), 2.92 (d, *J*=4.4 Hz, 1H, OH–C7); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.2 (O*C*O$_2$CH$_2$Ph), 139.0, 138.0, 137.8, 137.7 (q, OCH_2*Ph*), 135.0 (q, OCO$_2$CH_2*Ph*), 131.9 (d, 2 C, *Ph*–C≡C), 128.8–127.6 (28 C, aromat.), 121.8 (q, *Ph*–C≡C), 87.9, 83.7 (Ph–*C*≡*C*), 80.0 (C-5), 78.4 (C-7), 76.8 (C-6), 75.1, 74.6, 73.4, 73.4, 71.1 (5 C, 4×O*C*H_2Ph, OCO*C*H_2Ph), 69.9 (C-8), 71.4 (C-4), 70.2 (C-3); MS (70 eV) *m/z* 403 (10), 383 (11), 271 (10), 253 (18), 193

(22), 182 (11), 181 (60), 131 (18), 91(100), 77 (11), 65 (10). Anal. calcd for $C_{50}H_{48}O_8$: C, 77.30; H, 6.23. Found: C, 77.49; H, 6.16.

3.2.3. 4,5,6,8-Tetra-*O*-benzyl-3-*O*-benzoyl-1,2-dideoxy-1-phenyl-D-*glycero*-D-*ido*-oct-1-ynitol (5). To a solution of compound (**3** *syn*) (102 mg, 0.16 mmol) and 4-dimethylaminopyridine (20 mg) in dry pyridine (1.5 mL), at 0°C, under argon, benzoyl chloride (0.02 mL, 0.19 mmol) was slowly added in 10 min, and the solution was stirred to rt. This operation was repeated after 4 h. The reaction was quenched after 6 h. The solvent was eliminated and the residue was dissolved in ethyl acetate, washed with a 15% aqueous solution of sodium bicarbonate and brine. The organic layer was dried, filtered, the solvent was removed and the residue submitted to chromatography (hexane/ethyl acetate: 95/5) to give compound **5** (79 mg, 77%) and unreacted product **3** (16 mg). **5**: mp 92–95°C; $[\alpha]_D^{25}=-9$ (*c* 0.7, $CHCl_3$); IR (KBr) ν 3447 (OH), 3029, 2925, 2244 (C≡C), 1723, 1452, 1265, 1119, 1068, 1026 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.16–7.17 (m, 30H, aromat.), 6.20 (d, $J_{3,4}$=6.5 Hz, 1H, H-3), 4.99/4.82 (AB system, J=10 Hz, 2H, OCH_2Ph). 4.83 (s, 2H, OCH_2Ph), 4.52/4.50 (AB system, J=11.6 Hz, 2H, OCH_2Ph), 4.51/4.50 (AB system, J=11.7 Hz, 2H, OCH_2Ph), 4.32 (dd, $J_{4,3}$=6.5, $J_{4,5}$=4.5 Hz, 1H, H-4), 4.27 (t, $J_{5,4}=J_{5,6}$=4.6 Hz, 1H, H-5), 4.08–4.05 (m, 1H, H-7), 3.91 (dd, $J_{6,7}$=7.2, $J_{6,5}$=4.8 Hz, 1H, H-6), 3.69 (dd, $J_{8,8'}$=10.0, $J_{8,7}$=3.7 Hz, 1H, H-8), 3.64 (dd, $J_{8,8'}$=10.0, $J_{8',7}$=5.3 Hz, 1H, H-8′), 2.94 (d, J=4.6 Hz, 1H, OH/C-7); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.2 (O*C*OPh), 138.0, 137.8, 137.8, 137.7 (q, OCH_2*Ph*), 133.1–127.6 (30 C, aromat.), 129.7, 121.9 (q, *Ph*–C≡C), 86.9, 84.4 (q, Ph–*C*≡*C*) 81.1 (C5), 78.4 (C-7), 77.0 (C-6), 75.0, 74.7 (2 C), 73.3 (4 C, O*C*H_2Ph), 71.2 (C-4), 71.0 (C-8), 66.4 (C-3); MS (70 eV) *m*/*z* 403 (8), 253 (9), 234 (18), 205 (9), 197 (11), 193 (15), 181 (43), 106 (8), 91 (100), 77 (13). Anal. calcd for $C_{49}H_{46}O_7$: C, 78.80; H, 6.20. Found: C, 78.77; H, 6.16.

3.2.4. 1,2-Dideoxy-4,5:6,7-bis-*O*-(1-methylethylidene)-D-*glycero*-D-*ido*-oct-1-enitol (7 *syn*) and 1,2-dideoxy-4,5:6,7-bis-*O*-(1-methylethylidene)-D-*glycero*-D-gulo-oct-1-enitol (8 *anti*). Following the *General method for the addition of organometallic reagents* compound **6** (124 mg, 0.48 mmol) dissolved in dry THF (0. 4 mL) was treated with vinyl magnesium bromide (1.91 mL, 1.91 mmol, 1.0 M in THF, 4 equiv.) at 0°C, for 1 h, to give a mixture of compounds **7** (*syn*)+**8** (*anti*) (21 mg, 1:1) and pure compound **8** (*anti*) (20 mg), after chromatography (hexane/ethyl acetate: 75/25). Overall yield: 41 mg (45%). **8** (*anti*): oil; $[\alpha]_D^{25}=-41$ (*c* 0.3, $CHCl_3$); IR (film) ν 3419 (OH), 2986, 2936, 1645 (C=C), 1381, 1215, 1164, 1044 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.88 (ddd, $J_{1,2}$=17.3, $J_{1',2}$=10.7, $J_{2,3}$=5.1 Hz, 1H, H-2), 5.39 (dt, $J_{1,2}$=17.3, $J_{1,1'}=J_{1,3}$=1.5 Hz, 1H, H-1), 5.24 (dt, $J_{1',2}$=10.7, $J_{1,1'}=J_{1',3}$=1.5 Hz, 1H, H-1′), 4.36 (br s, $J_{2,3}=J_{3,4}$=5.1 Hz, 1H, H-3), 4.24–4.09 (m, 4H, H-4, 5, 6, 7), 3.75 (br s, 2H, 2H-8), 2.88 (br s, 1H, OH), 2.39 (br s, 1H, OH), 1.48, 1.44, 1.42, 1.33 [4 s, 2×OC$(CH_3)_2$O]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.4 (C-2), 116.9 (C-1), 109.9, 108.5 [2×O*C*$(CH_3)_2$O], 79.3/77.5 (C-6*, C-7*), 75.2/74.5 (C-4*, C-5*), 71.6 (C-3), 61.6 (C-8), 27.4, 26.9, 26.5, 25.5 [4 C, 2×OC(*C*$H_3)_2$]; MS (70 eV) *m*/*z* 273 (M^+-15, 32), 173 (24), 143 (11), 129 (10), 113 (11), 101 (22), 59 (100). Anal. calcd for $C_{14}H_{24}O_6$: C, 58.32; H, 8.39. Found: C, 58.30; H, 8.41.

3.2.5. 1,2-Dideoxy-4,5:6,7-bis-*O*-(1-methylethylidene)-1-phenyl-D-*glycero*-D-*ido*-oct-1-enitol (9 *syn*) and 1,2-dideoxy-4,5:6,7-bis-*O*-(1-methylethylidene)-1-phenyl-D-*glycero*-D-gulo-oct-1-ynitol (9 *anti*). Following the *General method for the addition of organometallic reagents* compound **6** (247 g, 0.95 mmol) dissolved in dry THF (0.66 mL) was treated with phenylethynyl magnesium bromide (3.8 mL, 3.8 mmol, 1.0 M in THF, 4 equiv.) at 0°C. The reaction was warmed at rt and after stirring for 5 h, the mixture was quenched. After work-up and chromatography (hexane/ethyl acetate: 75/25), recovered compound **6** (64 mg) and compound **9** {231 mg [67% yield (91%)], as a mixture of *syn* and *anti* isomers in 1 to 4 ratio, respectively, which we were unable to separate} were isolated. **9** (*syn*+*anti*): oil; IR (film) ν 3418 (OH), 2986, 2211 (C≡C), 1598, 1490, 1380, 1215, 1164 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (major isomer *anti*) 7.44–7.39/7.35–7.29 (m, 5H, *Ph*–C≡C), 4.88 (t, $J_{3,4}=J_{3,OH}$=3.6 Hz, 1H, H-3), 4.43 (dd, $J_{5,6}$=6.7, $J_{6,7}$=1.3 Hz, 1H, H-6), 4.41–4.25 (m, 3H, H-7,5,4), 3.80 (br s, 2H, 2H-8), 2.87 (br s, 2H, 2 OH), 1.52, 1.49, 1.48, 1.34 [4 s, 2×OC$(CH_3)_2$O]; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major isomer *anti*) 131.5 (d, 2 C, *Ph*–C≡C), 128.7/128.2 (d, 3 C, *Ph*–C≡C), 121.8 (q, *Ph*–C≡C), 110.2/108.5 [2×O*C*$(CH_3)_2$], 86.6, 85.9 (q, Ph–*C*≡*C*), 79.3, 77.4, 75.3, 74.6 (C-4,5,6,7), 62.0 (C-3), 61.5 (C-8), 27.1, 26.7, 26.6, 25.3 [4 C, 2×OC(*C*$H_3)_2$O]; MS (70 eV) *m*/*z* 362 (M^+, 1), 347 (M^+-15, 14), 231 (58), 185 (10), 173 (89), 157 (12), 143 (35), 129 (40), 115 (58), 59 (100). Anal. calcd for $C_{20}H_{26}O_6$: C, 66.32; H, 7.23. Found: C, 66.30; H, 7.52.

3.2.6. 6-Deoxy-6-iodo-2,3:4:5-bis-*O*-(1-methylethylidene)-D-glucose diethyldithioacetal (12). Alcohol **11**[11] (1 g, 2.7 mmol), dissolved in dry toluene (60 mL) was treated with triphenylphosphine (2.1 g, 8.2 mmol, 3 equiv.), imidazole (557 mg, 8.2 mmol, 3 equiv.) and iodine (1.3 g, 5.5 mmol, 2 equiv.), at reflux for 10 min. Then, the mixture was diluted with an aqueous saturated solution of $NaHCO_3$ and an 5% aqueous solution of $Na_2S_2O_3$. The organic layer was dried, filtered and evaporated. The residue was submitted to chromatography (hexane/ethyl acetate: 98/2) to give product **12** (911 mg, 70%): oil; $[\alpha]_D^{25}=-61$ (*c* 0.9, $CHCl_3$); IR (film) ν 2910, 2800, 1450, 1350, 1260, 1180, 1020 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.56 (q, $J_{4,5}=J_{5,6}=J_{5,6'}$=6.9 Hz, 1H, H-5), 4.42 (d, $J_{4,5}$=6.9 Hz, 1H, H-4), 4.32 (dd, $J_{1,2}$=5.4, $J_{2,3}$=7.9 Hz, 1H, H-2), 4.22 (d, $J_{2,3}$=7.9, 1H, H-3), 3.90 (d, $J_{1,2}$=5.4 Hz, 1H, H-1), 3.44 (d, $J_{5,6}$=7.0 Hz, 2H, 2H-6), 2.78–2.70 (m, 4H, 2×SCH_2CH$_3$), 1.50, 1.44, 1.43, 1.36 [4 s, 2×OC$(CH_3)_2$O], 1.27 (t, J=7.3 Hz, 6H, 2×SCH$_2$CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.9, 108.9 [2×O*C*$(CH_3)_2$O], 79.7 (C-3), 78.1 (C-5), 77.3 (C-2), 75.7 (C-4), 52.5 (C-1), 27.3, 26.9, 26.8, 25.3 [4 C, 2×OC(*C*$H_3)_2$], 25.4/25.2 (2×SCH_2CH$_3$), 14.4/14.3 (2×SCH$_2$CH_3), 3.2 (C-6); MS (70 eV) *m*/*z* 477 (M^++1, 2), 476 (M^+, 10), 357 (15), 341 (21), 299 (16),283 (83), 225 (46), 135 (100), 87 (24), 59 (18). Anal. calcd for $C_{16}H_{29}IO_4S_2$: C, 40.34; H, 6.14; S, 13.46. Found: C, 40.45; H, 6.09; S, 13.75.

3.2.7. 6-Deoxy-6-iodo-2,3:4:5-bis-*O*-(1-methylethylidene)-D-glucose (10). Iodide **12** (291 mg, 0.61 mmol) was dissolved in a mixture of acetone/water (9.5 mL, 1/18) and was treated with $HgCl_2$ (363 mg, 1.3 mmol, 2.2 equiv.) and HgO (278 mg, 1.28 mmol, 2.1 equiv.). After refluxing for 6 h, the mixture was cooled, hexane was added, and after stirring for 10 min at rt, the mass was filtered over Celite-545, washing the cake with acetone. The organic layer was evaporated, the residue was dissolved in methylene chloride and washed with a 5% aqueous solution of KI and brine. After drying, filtration, evaporation and chromatography (hexane/ethyl acetate: 4/1) compound **10** {^{1}H NMR (300 MHz, $CDCl_3$) δ 9.82 (d, $J_{1,2}$=1.7 Hz, 1H, H-1), 4.56 (q, $J_{4,5}$=$J_{5,6}$=$J_{5,6'}$=7.0 Hz, 1H, H-5), 4.38 (dd, $J_{1,2}$=1.7, $J_{2,3}$=7.9 Hz, 1H, H-2), 4.24 (dd, $J_{4,5}$=7.0, $J_{3,4}$=1.6 Hz, 1H, H-4), 4.18 (dd, $J_{2,3}$=7.9, $J_{3,4}$=1.6 Hz, 1H, H-3), 3.39 (dd, $J_{5,6}$=7.0, $J_{6,6'}$=1.1 Hz, 2H, 2H-6), 1.51, 1.43 (2 s), 1.38 [4 s, 2×OC$(CH_3)_2$O]} was isolated (170 mg, 75%) and immediately submitted to further reaction.

3.2.8. 1,2,8-Trideoxy-8-iodo-4,5:6,7-bis-*O*-(1-methylethylidene)-D-*glycero*-D-*ido*-oct-1-enitol (13 *syn*) and 1,2,8-trideoxy-8-iodo-4,5:6,7-bis-*O*-(1-methylethylidene)-D-*glycero*-D-gulo-oct-1-enitol (14 *anti*). Following the *General method for the addition of organometallic reagents* compound **10** (439 mg, 1.18 mmol) dissolved in dry THF (2.4 mL) was treated with vinyl magnesium bromide (1.6 mL, mmol, 1.0 M in THF, 4 equiv.) at 0°C, for 4 h (this protocol was repeated three times each hour), to give a mixture of compounds **13** (*syn*) and **14** (*anti*) (127 mg, in a 6:4 ratio) and pure compound **14** (*anti*) (255 mg), after chromatography (hexane/ethyl acetate: 93/7). Overall yield: 382 mg (81%). **14** (*anti*): oil; $[\alpha]_D^{25}$=−39 (*c* 0.3, $CHCl_3$); IR (film) ν 3500–3200 (OH), 2920, 2870, 1350, 1240, 1170, 1050 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88 (ddd, $J_{1,2}$=17.3, $J_{1',2}$=10.6, $J_{2,3}$=5.3 Hz, 1H, H-2), 5.41 (dt, $J_{1,2}$=17.3, $J_{1,1'}$=$J_{1,3}$=1.6 Hz, 1H, H-1), 5.25 (dt, $J_{1,2}$=10.6, $J_{1,1'}$=$J_{1',3}$=1.6 Hz, 1H, H-1′), 4.50 (q, $J_{6,7}$=$J_{7,8}$=$J_{7,8'}$=6.9 Hz, 1H, H-7), 4.37-4.33 (m, 1H, H-3), 4.18 (dd, $J_{6,7}$=6.9, $J_{5,6}$=0.8 Hz, 1H, H-6), 4.11 (dd, $J_{4,5}$=8.2, $J_{5,6}$=0.8 Hz, 1H, H-5), 4.05 (dd, $J_{4,5}$=8.2, $J_{3,4}$=4.4 Hz, 1H, H-4), 3.40 (d, $J_{7,8}$=6.9 Hz, 2H, 2H-8), 2.30 (br s, 1H, OH), 1.48, 1.41, 1.39, 1.34 [4 s, 2×OC$(CH_3)_2$O]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.7 (C-2), 116.7 (C-1), 100.9, 100.8 [2×O*C*$(CH_3)_2$O], 78.9 (C-4), 78.1 (C-7), 75.7 (C-6), 74.7 (C-5), 71.7 (C-3), 27.3, 26.8 (2 C), 25.4 [2×OC(*C*$H_3)_2$], 3.1 (C-8); MS (70 eV) *m*/*z* 383 (M^+−15, 24), 283 (27), 195 (15), 183 (18), 157 (26), 101 (41), 43 (100). Anal. calcd for $C_{14}H_{23}IO_5$: C, 42.24; H, 5.82. Found: C, 42.55; H, 5.67.

3.2.9. 1,2,8-Trideoxy-8-iodo-4,5:6,7-bis-*O*-(1-methylethylidene)-1-phenyl-D-*glycero*-D-*ido*-oct-1-ynitol (15 *syn*) and 1,2,8-trideoxy-8-iodo-4,5:6,7-bis-*O*-(1-methylethylidene)-1-phenyl-D-*glycero*-D-gulo-oct-1-ynitol (16 *anti*). Following the *General method for the addition of organometallic reagents* compound **10** (164 mg, 0.44 mmol) dissolved in dry THF (0.66 mL) was treated with phenylethynyl magnesium bromide (4.7 mL, 4.7 mmol, 1.0 M in THF, 4 equiv.) at 0°C. A mixture of compounds **15** (*syn*) and **16** (*anti*) (66 mg, in 6 to 4 ratio, respectively) and pure compound **16** (*anti*) (86 mg) (overall yield: 152 mg, 73%), after chromatography (hexane/ethyl acetate: 9/1) were isolated. **16** (*anti*): oil; $[\alpha]_D^{25}$=−10 (*c* 0.8, $CHCl_3$); IR (film) ν 3436 (OH), 2986, 2934, 2243 (C≡C), 1598, 1490, 1453, 1381, 1161, 1065 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46–7.31 (m, 5H, *Ph*–C≡C), 4.83 (dd, $J_{3,4}$=3.3, $J_{6,OH}$=4.6 Hz, 1H, H-3), 4.56 (q, $J_{6,7}$=$J_{7,8}$=$J_{7,8'}$=7.0 Hz, 1H, H-7), 4.45 (dd, $J_{6,7}$=7.0, $J_{5,6}$=0.9 Hz, 1H, H-6), 4.35 (dd, $J_{4,5}$=8.3, $J_{5,6}$=0.9 Hz, 1H, H-5), 4.30 (dd, $J_{4,5}$=8.3, $J_{3,4}$=3.3 Hz, 1H, H-4), 3.45 (d, $J_{7,8}$=7.0 Hz 2H, 2H-8), 2.62 (d, $J_{6,OH}$=4.6 Hz, 1H, OH), 1.53, 1.48, 1.47, 1.37 [4 s, 2×OC$(CH_3)_2$O]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.7 (d, 2 C, *Ph*–C≡C), 128.8 (d, C, *Ph*–C≡C), 128.4 (d, 2 C, *Ph*–C≡C), 121.9 (q, *Ph*–C≡C), 110.2/109.0 [2×O*C*$(CH_3)_2$], 87.1, 85.5 (q, Ph–*C*≡*C*), 78.9 (C-7), 78.1 (C-4), 75.8 (C-5), 74.8 (C-6), 62.1 (C-3), 27.2, 26.9, 26.8, 25.5 [4 C, 2×OC(*C*$H_3)_2$O], 3.1 (C-8); MS (70 eV) *m*/*z* 250 (1), 205 (100), 188 (52), 145 (39), 119 17), 73 (10). Anal. calcd for $C_{20}H_{25}IO_5$: C, 50.86; H, 5.34. Found: C, 50.77; H, 5.81.

3.2.10. 1,2,8-Trideoxy-8-iodo-4,5:6,7-bis-*O*-(1-methylethylidene)-D-*glycero*-D-*ido*-oct-1-ynitol (17 *syn*)+ 1,2,8-trideoxy-8-iodo-4,5:6,7-bis-*O*-(1-methylethylidene)-D-*glycero*-D-gulo-oct-1-ynitol (18 *anti*). Following the *General method for the addition of organometallic reagents* compound **10** (241 mg, 0.65 mmol) dissolved in dry THF (0.66 mL) was treated with ethynyl magnesium bromide (2.6 mL, 2.6 mmol, 1.0 M in THF, 4 equiv.) at 0°C. An unseparable mixture of compounds **17** (*syn*) and **18** (*anti*) (157 mg, in a 3 to 7 ratio, respectively) [overall yield: 61% (70%)], after chromatography (hexane/ethyl acetate: 85/15) were isolated: oil; IR (film) ν 3444 (OH), 3284, 2987, 2118 (C≡C), 1456, 1381, 1216, 1063 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major isomer **18** *anti*) 4.58–4.50 (m, 2H, H-3, H-7), 4.35 (dd, $J_{6,7}$=6.7, $J_{5,6}$=1.0 Hz, 1H, H-6), 4.22 (dd, $J_{4,5}$=8.2, $J_{5,6}$=1.0 Hz, 1H, H-5), 4.16–4.14 (m, 1H, H-4), 3.41 (d, $J_{7,8}$=7.0 Hz, 2H, 2H-8), 2.78 (d, $J_{3,OH}$=5.0 Hz, 1H, OH), 2.56 (d, $J_{1,3}$=2.3 Hz, 1H, –C≡C–H), 1.49, 1.43, 1.41, 1.35 [4 s, 2×OC$(CH_3)_2$O]; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major isomer **18** *anti*) 110.1/108.9 [2×O*C*$(CH_3)_2$], 80.7 (q, –*C*≡C–H), 78.6 (q, –C≡*C*–H), 78.0 (C-7), 75.8 (C-4), 75.4 (C-5), 74.9 (C-6), 61.6 (C-3), 27.0, 26.9, 26.7, 25.3 [4 C, 2×OC(*C*$H_3)_2$O], 2.8 (C-8); MS (70 eV) *m*/*z* 381 (M^+−15, 283 (28), 263 (11), 195 (34), 113 (22), 85 (32), 59 (100). Anal. calcd for $C_{14}H_{21}IO_5$: C, 42.44; H, 5.34. Found: C, 42.30; H, 5.63.

3.2.11. 6-Deoxy-6-iodo-2,3:4,5-bis-*O*-(1-methylethylidene)-1-(2-thiazolyl)-D-*glycero*-D-gulo-hexitol (19 *anti*). Compound **10** (197 mg, 0.53 mmol) dissolved in dry CH_2Cl_2 (1 mL) was treated with 2-(trimethylsily)thiazole (0.094 mL, 0.58 mmol, 1.1 equiv.) at 0°C, under argon. The reaction mixture was warmed and stirred to rt for 18 h. The solvent was removed and the residue was treated with Bu_4NF (0.53 mL, 1.1 M in THF) as usual until complete desilylation. The solvent was evaporated, diluted with water and extracted with CH_2Cl_2 several times. The organic layer was dried, filtered and evaporated. Flash chromatography (hexane/ethyl acetate: 9/1) gave compound **19** (*anti*) (141 mg, 60%) and the unexpected product **19a**[12] (9.3 mg, 7%). **19** (*anti*): oil; $[\alpha]_D^{25}$=−23 (*c* 0.2, $CHCl_3$); IR (film) ν 3435 (OH), 2986, 1630, 1508, 1381, 1161, 1068 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80/7.37 (AB system: 2 d, *J*=3.2 Hz, 2H, aromat.), 5.15 (dd, $J_{1,2}$=5.2,

$J_{1,OH}$=3.3 Hz, 1H, H-1), 4.40 (dd, $J_{1,2}$=5.2, $J_{2,3}$=7.9 Hz, 1H, H-2), 4.33 (q, $J_{4,5}$=$J_{5,6}$=$J_{5,6'}$=6.7 Hz, 1H, H-5), 4.20 (dd, $J_{2,3}$=7.9, $J_{3,4}$=1.2 Hz, 1H, H-3), 3.67 (d, $J_{1,OH}$= 3.3 Hz, 1H, OH), 3.61 (dd, $J_{4,5}$=6.7, $J_{3,4}$=1.2 Hz 1H, H-4), 3.34 (d, $J_{5,6}$=6.7 Hz, 2H, 2H-6), 1.50, 1.47, 1.45, 1.31 [4 s, 2×OC(CH_3)$_2$O]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0 (q, aromat.), 142.1/119.1 (d, d, aromat.), 110.2/108.7 [2×O*C*(CH_3)$_2$], 79.2 (C-2), 78.0 (C-5), 75.4 (C-4), 75.2 (C-3), 71.4 (C-1), 27.2, 26.8 (2 C), 25.1 [4 C, 2× OC(*C*H_3)$_2$O], 3.5 (C-6); MS (70 eV) *m/z* 455 (M^+, 1), 440 (M^+−15, 60), 341 (25), 283 (100), 270 (18), 224 (37), 195 (14), 183 (25), 85 (18). Anal. calcd for $C_{15}H_{22}INO_5S$: C, 39.57; H, 4.87; N, 3.08; S, 7.04. Found: C, 39.44; H, 4.81; N, 2.87; S, 6.86.

3.2.12. 1-*O*-Benzyl-6-deoxy-6-iodo-2,5:4,5-bis-*O*-(1-methylethylidene)-1-(2-thiazolyl)-D-*glycero*-D-gulo-hexitol (20). Compound **19** (101 mg, 0.22 mmol) dissolved in dry THF (1 mL, 0.2 M), under argon and at 0°C, was treated with sodium hydride (13.3 mg, 0.33 mmol, 1.5 equiv.), a catalytic amount of tetrabutylammonium iodide and benzyl bromide (0.03 mL, 0.24 mmol, 1.1 equiv.). After stirring at rt for 15 h, when the reaction was complete some drops of AcOH were added and the mass was filtered over Celite-545. The solvent was evaporated, diluted with water, extracted with CH_2Cl_2 several times and washed with brine. The organic layer was dried, filtered and evaporated. Flash chromatography (hexane/ethyl acetate: 85:15) gave compound **20** (111 mg, 92%). **20**: oil; $[\alpha]_D^{25}$=−5 (*c* 0.4, $CHCl_3$); IR (film) ν 2986, 2934, 1498, 1380, 1161, 1082 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83/7.42 (AB system: 2 d, *J*=3.3 Hz, 2H, aromat.), 7.39–7.33 (m, 5H, $OCH_2C_6H_5$), 4.93 (d, $J_{1,2}$=5.3 Hz, 1H, H-1), 4.71/4.57 (AB system: 2 d, *J*=11.5 Hz, 2H, $OCH_2C_6H_5$), 4.51 (dd, $J_{1,2}$=5.3, $J_{2,3}$=8.0 Hz, 1H, H-2), 4.43 (q, $J_{4,5}$=$J_{5,6}$=$J_{5,6'}$= 7.0 Hz, 1H, H-5), 4.13 (dd, $J_{2,3}$=8.0, $J_{3,4}$=1.5 Hz, 1H, H-3), 3.94 (dd, $J_{4,5}$=6.9, $J_{3,4}$=1.5 Hz 1H, H4), 3.36 (d, $J_{5,6}$=7.0 Hz, 2H, 2H-6), 1.50, 1.47, 1.31 (2 C) [4 s, 2×OC(CH_3)$_2$O]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.5 (q, aromat.), 142.9/120.5 (d, d, aromat.), 137.2, 128.7, 128.5, 128.3 ($OCH_2C_6H_5$), 110.8/109.2 [2×O*C*(CH_3)$_2$], 79.6 (C-2), 79.0 (C-1), 78.3 (C-5), 76.3 (C-3), 75.7 (C-4), 72.8 ($OCH_2C_6H_5$), 27.3, 27.1 (2 C), 25.6 [4 C, 2×OC(*C*H_3)$_2$O], 3.6 (C-6); MS (70 eV) *m/z* 546 (M^+, 1), 530 (M^+−15, 57), 304 (26), 341 (84), 283 (67), 225 (39), 205 (51), 114 (71), 91 (100). Anal. calcd for $C_{22}H_{28}INO_5S$: C, 48.45; H, 6.21; N, 2.57; S, 5.88. Found: C, 48.40; H, 6.33; N, 2.41; S, 5.52.

3.2.13. 1,2-Dideoxy-4,5:7,8-bis-*O*-(1-methylethylidene)-1-phenyl-D-*glycero*-D-galacto-oct-1-ynitol (22 *syn*) and 1,2-dideoxy-4,5:7,8-bis-*O*-(1-methylethylidene)-1-phenyl-D-*glycero*-D-talo-oct-1-ynitol (23 *anti*). To a solution of phenylacetylene (1.8 mL, 16.1 mmol, 6 equiv.) in dry THF (12 mL), under argon and at −78°C, *n*-BuLi (10 mL, 16.1 mmol, 6 equiv.) was slowly added. After 15 min at this temperature, compound **21**[23] (700 mg, 2.69 mmol), dissolved in dry THF (1 mL), was added and the mixture was stirred at −78°C for 72 h. The reaction was quenched with aqueous saturated solution of ammonium chloride, diluted and extracted several times with ethyl acetate. The organic layer was washed with brine, dried, filtered, evaporated and the residue was submitted to chromatography (hexane/ethyl acetate: 85/15) to give products **22** (*syn*) (590 mg) and 23 (210 mg) (Total: 800 mg; overall yield: 82%). **22** (*syn*): oil; $[\alpha]_D^{25}$=−12 (*c* 0.2, $CHCl_3$); IR (film) ν 3600–3200 (OH), 2211 (C≡C), 1470, 1360, 1090 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45–7.42 (m, 2H, *Ph*–C≡C), 7.33–7.26 (m, 3H, *Ph*–C≡C), 5.01 (dd, $J_{3,4}$=6.8, $J_{3,OH}$=4.2 Hz, 1H, H-3), 4.52 (dd, $J_{5,6}$=0.7, $J_{4,5}$=7.3 Hz, 1H, H-5), 4.45 (t, $J_{4,5}$=$J_{3,4}$=6.8 Hz, 1H, H-4), 4.11–4.03 (m, 3H, 2H-8, H-7), 2.88 (d, $J_{3,OH}$=4.2 Hz, 1H, OH–C3), 2.60 (d, $J_{6,OH}$=7.9 Hz, 1H, OH–C6), 1.56, 1.44, 1.33, 1.31 [4 s, 2×OC(CH_3)$_2$O]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.8 (d, 2 C, *Ph*–C≡C), 128.8 (d, 1 C, *Ph*–C≡C), 128.3 (d, 2 C, *Ph*–C≡C), 125.0 (q, *Ph*–C≡C), 109.4/109.0 [2× O*C*(CH_3)$_2$], 80.0 (C-4), 79.6, 77.2 (q, Ph–*C*≡*C*), 76.1 (C-7), 75.2 (C-5), 69.9 (C-6), 67.1 (C-8), 62.0 (C-3), 26.8, 26.6, 25.3, 24.5 [4 C, 2×OC(*C*H_3)$_2$O]; MS (70 eV) *m/z* 362 (M^+, 1), 231 (65), 173 (98), 131 (33), 115 (66), 73 (37), 59 (100). Anal. calcd for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23. Found: C, 66.44; H, 7.42. **23** (*anti*): oil; $[\alpha]_D^{25}$=−12 (*c* 0.9, $CHCl_3$); IR (film) ν 3429 (OH), 2988, 2211 (C≡C), 1373, 1066 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45–7.42 (m, 2H, *Ph*–C≡C), 7.33–7.27 (m, 3H, *Ph*–C≡C), 5.02 (d, $J_{3,4}$=4.9 Hz, 1H, H-3), 4.54 (d, $J_{4,5}$=7.2 Hz, 1H, H-5), 4.43 (dd, $J_{4,5}$=7.2, $J_{3,4}$=4.9 Hz, 1H, H-4), 4.25–4.23 (m, 1H, H-6), 4.13–4.06 (m, 3H, H-7, 2H-8), 3.60–3.40 (br s, 2H, OH), 1.57, 1.42, 1.35, 1.34 [4 s, 2×OC(CH_3)$_2$O]; ^{13}C NMR (75 MHz, $CDCl_3$) δ 131.9 (d, 2 C, *Ph*–C≡C), 128.8 (d, 1 C, *Ph*–C≡C), 128.4 (d, 2 C, *Ph*–C≡C), 122.1 (q, *Ph*–C≡C), 109.6/108.9 [2×O*C*(CH_3)$_2$], 86.7, 85.6 (q, Ph–*C*≡*C*), 78.6 (C-4), 76.1 (C-7), 75.8 (C-5), 73.3 (C-6), 69.7 (C-8), 61.6 (C-3), 26.9, 26.6, 25.4, 24.9 [4 C, 2× OC(*C*H_3)$_2$O]; MS (70 eV) *m/z* 362 (M^+, 1), 347 (M^+−15, 10), 231 (52), 173 (84), 131 (37), 115 (64), 101 (60), 59 (100). Anal. calcd for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23. Found: C, 66.04; H, 7.02.

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