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Synthesis of glyco-1-ynitols via 1,1-dibromo-1-alkenes from partially and unprotected aldoses

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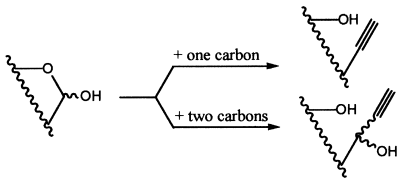
Abstract—We report the synthesis of 1,1-dibromo-1-alkenes from partially and unprotected aldoses and the synthesis of glyco-1-ynitols from these dibromocompounds. The 1,1-dibromo-1-alkenes were obtained by the reaction of dibromomethyl-triphenylphosphonium bromide in the presence of zinc in refluxing 1,4-dioxane. As an example, when the reaction is performed on 2-deoxy-5-*O*-trityl-D-ribofuranose (**1**) the corresponding 1,1-dibromo-1-olefin, (2*R*,3*S*)-6,6-dibromo-1-*O*-trityl-hex-5-ene-1,2,3-triol (**12**), is obtained in 89% yield. These smooth reaction conditions led also to the achievement of the other olefins from other sugars with good yields (44–90%). The reaction of these olefins with *n*-butyllithium in THF at low temperature afforded the corresponding alkynes. So the reaction of (2*R*,3*S*)-6,6-dibromo-1-*O*-trityl-hex-5-ene-1,2,3-triol (**12**) with this alkyllithium reagent led to (2*R*,3*S*)-1-*O*-trityl-hex-5-yne-1,2,3-triol (**23**) in 87% yield. Other glyco-1-ynitols were obtained with satisfying yields (64–87%).

1. Introduction

The branched-chain or chain-elongated carbohydrates are still subjects of interest, like the constructions of poly-hydroxylated carbocycles containing six or more carbons. Achieving the synthesis of such compounds is always a challenge to organic chemists, since they occur frequently in a number of natural products, which have remarkable biological activities. Since an ethynyl group is a useful and versatile functional group for chain-elongation or in cyclisation reaction to obtain carbocycles, we have begun studies on the transformation of carbohydrates into glyco-1-ynitols.[1] Alkynes can be used as radical acceptor in free-radical cyclisation,[2] in ring closing metathesis (RCM) reactions,[3] cycloisomerisation reactions,[4] or when transformed into the corresponding acetylides, they can be coupled with a variety of electrophiles such as halides,[5] epoxides,[6] carbonyl compounds,[7] etc.

Such glyco-1-ynitols can be obtained from monosaccharides with a one or two carbons chain elongation (Scheme 1). In fact, when an acetylide is reacted with the hemiacetal form of an aldose, it leads to a two carbons chain elongation.[8] In counterpart, this reaction creates a new asymmetric center. Contrary to a one-carbon chain elongation that needs the use of phosphoranes or phosphonates. Indeed, Toma described the achievement of glyco-1-ynitols via 1-chloro-1-alkenes.[9]



Scheme 1.

And recently, we described the action of a phosphonate, using an Ohira-modified procedure, on aldoses to give glyco-1-ynitols too.[1] But, for the best of our knowledge, a protection of hydroxyl group is a necessary step before using such strategies. Recently, Rassat described the synthesis of acetylenics via 1,1-dibromo-1-alkenes from aromatic and aliphatic aldehydes.[10] These dibromo-compounds were prepared by the condensation of aldehydes with dibromomethylenetriphenylphosphorane generated in situ from dibromomethyl-triphenylphosphonium[11] bromide (2 equiv.) and *t*-BuOK (2 equiv.) in THF at room temperature. A few years ago, we tuned a Wittig type reaction that allowed us to work on free carbohydrates. When aldoses were reacted with methylbromoacetate or bromoacetonitrile, *n*-tributyl-phosphine and zinc, these gave the corresponding *E* unsaturated Wittig products with good yields and high stereoselectivity.[12] Furthermore this procedure suppressed side reactions. As a result of these studies, we concluded that it would be of great value to transpose such smooth conditions to reactions with dibromomethyl-triphenylphosphonium bromide. This goal was achieved by overcoming some difficulties, and we report herein an efficient method for olefination of aldoses having free hydroxyl groups to 1,1-dibromo-1-alkenes,[13]

Keywords: dibromomethyl-triphenylphosphonium bromide; zinc; 1,1-dibromo-1-alkenes; glyco-1-ynitols.

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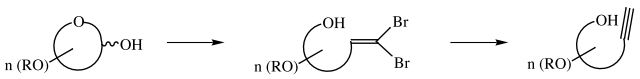
which can be useful precursor of glyco-1-ynitols that we have also synthesized (Scheme 2).

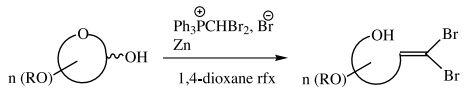


R : H, protecting group

Scheme 2.

2. Results and discussion

2.1. Synthesis of 1,1-dibromo-1-alkenes from partially and unprotected aldoses (Scheme 3, Table 1)

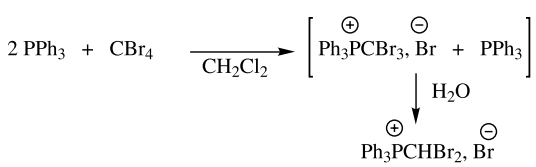


R : H, protecting group

Scheme 3.

We have applied Rassat conditions to substrates previously studied in our laboratories that had failed to react. When the reaction was allowed to reflux an inseparable mixture was obtained, the exception was in the case of 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose (**11**) in which case a clean product was obtained. As a result of these findings we studied the use of zinc that would allow the preparation of the ylide in situ.[13]

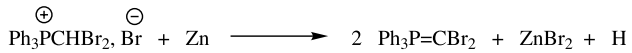
Reaction with derivatives of D*-ribose* **1**–**4**: reaction of 2-deoxy-5-*O*-trityl-D-ribofuranose (**1**) with dibromomethyl-triphenylphosphonium bromide in presence of zinc in refluxing 1,4-dioxane afforded the corresponding 1,1-dibromo-1-olefin (**12**): (2*R*,3*S*)-6,6-dibromo-1-*O*-trityl-hex-5-ene-1,2,3-triol. The conclusion that this was the product of reaction was established by analysis of its NMR and mass spectrometry data. In its NMR spectra three characteristic resonances were observed at 134.8 and 90.4 ppm, attributed respectively to C_{-5} and C_{-6} and 6.48 ppm attributed to H_{-5}. Optimisation of these conditions was necessary in order to obtain a clean and high yielding reaction. The dibromomethyl-triphenylphosphonium bromide was obtained under a modified Ramirez procedure[14] (Scheme 4). We found that it was necessary for the product to be recrystallised prior to its subsequent use otherwise undesirable by-products were formed in the reaction. The salt's structure was confirmed by NMR and mass spectrometry. In its mass spectra (FAB-MS) three characteristic ions at *m/z* 433, 353 and 275 were observed and attributed to $C_{19}H_{16}Br_2P^+$, $C_{19}H_{15}BrP^+$ and $C_{19}H_{16}P^+$, respectively.



Scheme 4.

During the course of these investigations, it was established that activation of the zinc was an important point. In cases where activation of the zinc was insufficient, the reaction did not proceed to completion. For an efficient and high yielding reaction, we found that it was essential that an oxidation–reduction process must be used to prepare the zinc. The activated zinc used in these studies[12] was prepared by the reaction of zinc chloride with lithium metal,[15] as a dispersion in mineral oil, with ether as the solvent. Since this type of activated lithium was not commercially available, it was necessary to change our experimental conditions. In the studies, we have substituted the lithium by a dispersion of sodium metal in mineral oil furthermore, in order to facilitate the reaction we used monoglyme as the solvent. A modification was also introduced to the extraction of zinc dust (for more details see Section 3). This modification for the activation of the zinc metal did not reduce its activity in the reactions reported herein.

Using this modified procedure and a fourfold excess of the phosphonium salt and a fourfold excess of zinc good yields of **12** (89%) were obtained. The necessity for this excess of reagents is possibly due to a sluggish reaction of the substrates. During the reaction of methylbromoacetate or bromoacetonitrile and *n*-tributylphosphine in presence of zinc on aldoses,[12] the ylide was obtained, in situ, by action of zinc on the phosphonium salt. In a similar way the dibromomethylenetriphenylphosphorane was prepared from the corresponding phosphonium salt by action of activated zinc (Scheme 5). Using these conditions the reaction proceeded smoothly and no by-products were detected during the course of the reaction.



Scheme 5.

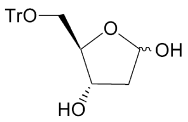
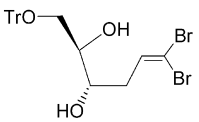
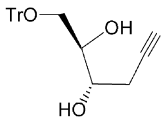
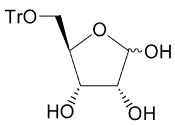
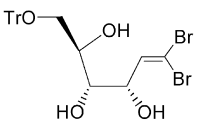
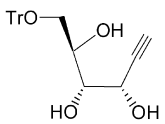
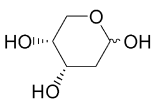
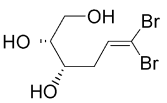
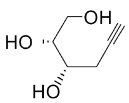
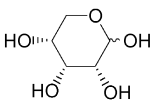
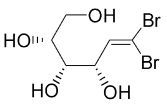
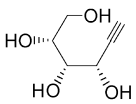
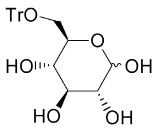
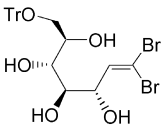
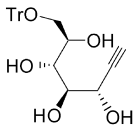
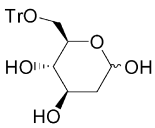
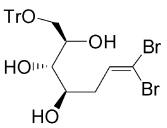
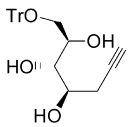
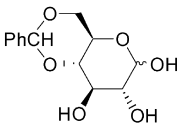
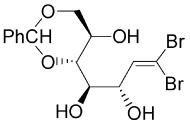
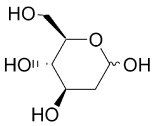
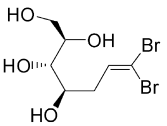
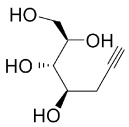
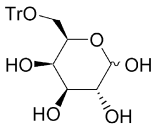
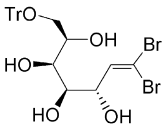
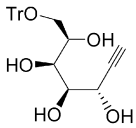
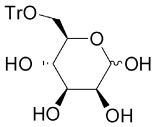
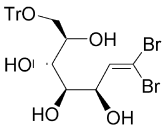
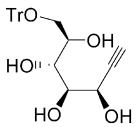
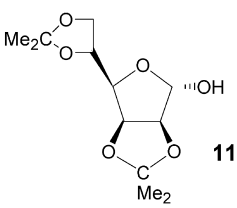
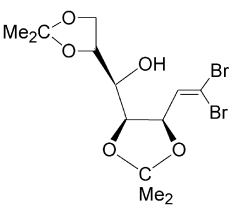
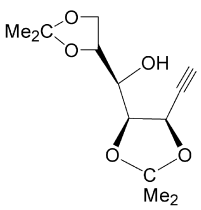
A Wittig type reaction on 5-*O*-trityl-D-ribofuranose (**2**) afforded the expected olefin (**13**), (2*R*,3*S*,4*S*)-6,6-dibromo-1-*O*-trityl-hex-5-ene-1,2,3,4-tetrol, in 77% yield. The NMR data of the product are characteristics resonances at 138.0 and 92.0 ppm attributed respectively to C_{-5} and C_{-6}. In the ^1H NMR the resonance at 6.64 ppm was attributed to H_{-5}.

In the case of a substrate with one more hydroxyl group than that in **1**, the reaction time became long. Furthermore, we observed that deprotection of hydroxyl group was occurring as evidenced by the takes formation of $ZnBr_2$ in the reaction mixture.

This procedure has been utilised for 2-deoxy-D-ribose (**3**) and D-ribose (**4**), resulting in the formation of the corresponding 1,1-dibromo-1-alkenes **14** and **15**, obtained in 54 and 48% yield, respectively. NMR and mass spectrometry confirmed the structure of these olefins. The poor yields for these cases may be due to the fact that the starting materials are scarcely soluble in 1,4-dioxane resulting in prolonged reaction times and degradation of the products.

Reaction with derivatives of D*-glucose* **5**–**8**: the reaction of derivatives of D-glucose with dibromomethyl-triphenyl-phosphonium bromide in presence of zinc in refluxing 1,4-dioxane afforded corresponding 1,1-dibromo-1-olefins **16**–**19** in yields about 60%.

Table 1. 1,1-Dibromo-1-alkenes and glyco-1-ynitols obtained from partially and unprotected aldoses

Starting materials	1,1-Dibromo-1-alkenes	Yields[a] (%)	Glyco-1-ynitols	Yields[a] (%)
 **1**	 **12**	89	 **23**	87
 **2**	 **13**	77	 **24**	84
 **3**	 **14**	54	 **25**	80
 **4**	 **15**	48	 **26**	71
 **5**	 **16**	56	 **27**	60
 **6**	 **17**	63	 **28**	67
 **7**	 **18**	60		
 **8**	 **19**	60	 **29**	86
 **9**	 **20**	44	 **30**	85
 **10**	 **21**	76	 **31**	69
 **11**	 **22**	90	 **32**	64

[a] Isolated yields.

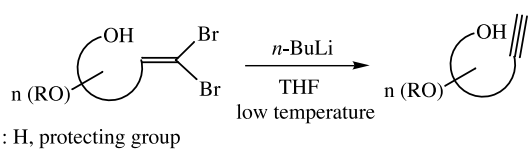
Reaction with 6-O-trityl-D-galactose **9**: when 6-*O*-trityl-D-galactose **9** was reacted with dibromomethyl-triphenylphosphonium bromide (5 equiv.) in the presence of zinc (5 equiv.) in refluxing 1,4-dioxane for 90 min, this led to the formation of the corresponding olefin **20** in a yield of 44%. The known sluggishness of derivatives of the D-galactose and a slowly deprotection of hydroxyl group during the reaction could explain the poorer yield.

Reaction with derivatives of D-mannose **10** and **11**: similar chemistry with 6-*O*-trityl-D-mannose **10** resulted in the formation of the expected 1,1-dibromo-1-alkene **21** in 76% yield. A Wittig type reaction on 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose **11** and dibromo-methyltriphenylphosphonium bromide in the presence of zinc in refluxing 1,4-dioxane led to **22** being formed in a yield of 90%. The use of Rassat conditions with dibromomethyltriphenylphosphonium bromide and *t*-BuOK in THF, failed to afford the corresponding dibromolefins when aldoses having a free hydroxyl group present were employed as substrates. However 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose **11** resulted in the production of the olefin **22** under Rassat conditions, in a yield of 89%. These experiments confirmed that Rassat conditions are only applicable to carbohydrates that do not bear a free hydroxyl group.

A series of dibromoolefins were obtained under our optimised conditions: the yields were excellent with 2-deoxy-5-*O*-trityl-D-ribofuranose **1** (89%) and 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose **11** (90%), but were slightly lower with partially and unprotected substrates (44–77%). These yields are also satisfactory for free aldoses: 54% from 2-deoxy-D-ribose **3**, 48% from D-ribose **4** and 60% from 2-deoxy-D-glucose **8**. With other substrates, a deprotection of hydroxyl groups takes place when the reaction time is too long and by the way undesirable by-products appears. After being isolated, these 1,1-dibromoolefins have been used to synthesize glyco-1-ynitols.

2.2. Synthesis of glyco-1-ynitols from 1,1-dibromo-1-alkenes (Scheme 6, Table 1)

Having been successful with these substrates, we chose to study the synthesis of glyco-1-ynitols from these 1,1-dibromo-1-alkenes. A number of reagents were investigated for this transformation. In our search for a reagent that would be compatible with a range of substrates we investigated this type of chemistry using magnesium metal,[16] zinc dust[17] and in the presence of *t*-BuOK[10] as a base. Unfortunately all of these proved to be ineffective, however using *n*-BuLi, we were able to effect both dehalogenation, to form the desired acetylene, in addition to forming the terminal olefin as a result of further reduction.



R : H, protecting group

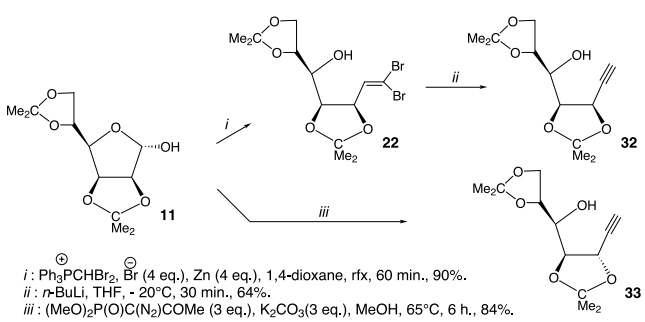
Scheme 6.

Reaction with 1,1-dibromo-1-alkenes **12**–**15**: the reaction of compounds **12** and **13** with an excess of *n*-butyllithium (5 equiv.) in THF at low temperature (−70°C) afforded the corresponding glyco-1-ynitols **23** and **24** in pretty good yields (around 85%). NMR, IR and mass spectrometry have established the structure of these alkynes. We extended these reaction's conditions to obtain glyco-1-ynitols that do not bear hydroxyl-protecting groups. The reaction of olefin **14** with *n*-butyllithium led to (2*R*,3*S*)-hex-5-yne-1,2,3-triol **25** being formed in an isolated yield of 80%. Analogously the olefin **15**, (2*R*,3*S*,4*S*)-hex-5-yne-1,2,3,4-tetrol **26** was obtained in 71% yield.

Reaction with 1,1-dibromo-1-alkenes **16**–**19**: when these reaction's condition were applied to the olefins **16**, **17** and **19**, the corresponding glyco-1-ynitols (2*R*,3*R*,4*R*,5*S*)-1-*O*-trityl-hept-6-yne-1,2,3,4,5-pentol **27**, (2*R*,3*S*,4*R*)-1-*O*-trityl-hept-6-yne-1,2,3,4-tetrol **28** and (2*R*,3*S*,4*R*)-hept-6-yne-1,2,3,4-tetrol **29** were obtained in 60, 67 and 86% yields, respectively. On the other hand, reaction of the olefin **18**, under the same conditions, resulted in only trace quantities of the desired alkyne. In this instance, 80% of the starting material was recovered from the reaction mixture along with degradation products.

Reaction with 1,1-dibromo-1-alkene **20**: the reaction of *n*-BuLi on olefin **20**, at low temperature, afforded the corresponding glyco-1-ynitol **30**, (2*R*,3*S*,4*R*,5*S*)-1-*O*-trityl-hept-6-yne-1,2,3,4,5-pentol, in 85% yield.

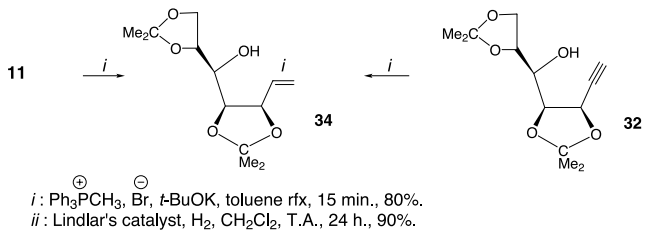
Reaction with 1,1-dibromo-1-alkenes **21** and **22**: as in the case of olefins **16** and **20**, the reaction of *n*-BuLi on olefin **21** afforded the corresponding glyco-1-ynitol **31**, the (2*R*,3*R*,4*R*,5*R*)-1-*O*-trityl-hept-6-yne-1,2,3,4,5-pentol, in 69% yield. A similar compound obtained by reaction of a phosphonate with **22**, has already been described.[1] By comparing NMR data, it appeared that the two compounds were different (Scheme 7).



Scheme 7.

We have proposed that an epimerisation takes place at the α-carbon of the final product. Analysis of the NMR spectra did not enable the structures **32** and **33** to be established unequivocally. Evidence that these structures were in deed these was obtained by correlation with material prepared using an alternative approach for their synthesis. Thus, treatment of 2,3:5,6-di-*O*-isopropylidene-α-D-manno-furanose **11** with the methylenetriphenylphosphorane[18] gave the olefin **34** (Scheme 8) which was identical in all respects with the olefin that we have prepared by the reduction of alkyne

32 under the Lindlar's conditions (Scheme 8). During the reaction with the phosphonate, an epimerisation takes place at carbon 5 of the final product.



Scheme 8.

In summary, the use of zinc in Wittig type reactions provides a ready access to 1,1-dibromo-1-alkenes derivatives from aldoses. These dibromocompounds were used for the synthesis of glyco-1-ynitols. Contrary to the one-pot method that we described in preceding report, we have obtained the glyco-1-ynitols on partially and unprotected aldoses in satisfactory yields.

3. Experimental

3.1. General

Unless otherwise specified, materials were purchased from commercial suppliers and used without further purification. THF was distilled from lithium aluminium hydride immediately before use. Acetonitrile was distilled from calcium hydride under argon. Moisture-sensitive reactions were conducted in oven-dried glassware under an argon atmosphere. Flash chromatography was carried out on Kieselgel 60 (230–400 mesh, Merck) and analytical thin-layer chromatography (TLC) was performed on E. Merck glass-backed silica gel sheets (Silica Gel 60 F_{254}). Melting points were determined with a Büchi 535 digital melting point apparatus and are uncorrected. Optical rotations were measured with a Jasco DIP-370 digital polarimeter using a sodium lamp (λ=589 nm). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker WB 300 spectrometer, respectively, at 300 and 75 MHz. Spectra were recorded in $CDCl_3$, CD_3OD, C_5D_5N or D_2O as solvent, and chemicals shifts (δ) were expressed in ppm relative to residual $CHCl_3$ or an internal standard. All ^{13}C NMR signals were assigned through C,H-correlated spectra. IR spectra were recorded as neat films (NaCl cell) and KBr pellets for solids on a Nicolet 205. Microanalyses were performed at the Service de Microanalyse de l'Université de Champagne-Ardenne in Reims. Infusion electrospray mass spectra in the positive ion mode were obtained on an updated (3.6 GHz TDC) Micromass Q-TOF hybrid quadrupole/time-of-flight instrument, equipped with a pneumatically assisted electrospray ion source (Z-spray).

3.2. Preparation of reagents

3.2.1. Preparation of dibromomethyl-triphenylphosphonium bromide. Carbon tetrabromide (it must be a colourless solid) (16.4 g, 49.4 mmol) was added to a solution of triphenylphosphine (26 g, 99.1 mmol) in methylene chloride (240 mL). The solution was stirred for 15 min at room temperature. Water (8 mL) was added to this resulting red reaction. After 15 min of vigorous magnetic stirring, the aqueous layer was separated of CH_2Cl_2. The organic layer was dried and evaporated under reduced pressure to syrup. The salt was precipitated by addition of acetonitrile. The yellow powder obtained was filtered, dried under vacuum and resolubilised in CH_2Cl_2 (500 mL) and re-evaporated to syrup and reprecipitated by addition of acetonitrile. The white powder obtained was filtered, dried under vacuum and recrystallised from dry acetonitrile freshly distillate on $CaCl_2$ at reflux temperature. The solution was filtered hot and the dibromomethyl-triphenyl-phosphonium bromide recrystallised was filtered and dried under vacuum. It was stable at least 6 months if stored at −20°C under an inert atmosphere. Mp 143–148°C, lit.[19] 144–147°C; ^{13}C NMR ($CDCl_3$): δ 30.1 (d, J=48.0 Hz), 116.7 (d, J=87.7 Hz), 130.6 (d, J=12.8 Hz), 134.9 (d, J=9.8 Hz), 136.4 (d, J=2 Hz).

3.3. General procedure for the activation of zinc—by using lithium

The lithium dispersion (~30 wt% in mineral oil, sodium content ~0.5%) (1.388 g, 60 mmol) was weighed directly into a 250 mL round bi-necked flask. This flask was then fitted with a magnetic stirrer, rubber septum and reflux condenser attached to a balloon of argon gas. To the lithium was added 10 mL of dry Et_2O. The mixture was stirred and the flask was immersed in a water bath. $ZnCl_2$, 1.0 M solution in Et_2O (30 mL, 30 mmol) was added dropwise by syringe through the septum. The mixture was stirred for 5 h at room temperature. The flask was then immersed in an ice-water bath and the mixture was quenched with absolute ethanol and filtered. The zinc was washed successively with water (2 L), acetone (200 mL) then Et_2O (100 mL). The zinc was dried at hot (100°C) under vacuum over night. It must be used quickly by using sodium: the sodium dispersion (~40 wt% in mineral oil) must be used instead of the lithium. The activation's procedure was the same, only the solvent was modified: using ethylene glycol dimethylether instead of ethyl ether. And when the zinc was filtered, before the addition of water, ethanol must be completely removed, and addition of *n*-hexane is needed. During water washing, it is essential to remove the floating.

3.4. Preparation of 1,1-dibromo-1-alkenes (NMR data, see Tables 2 and 3)

General procedure 1: an anhydrous 1,4-dioxane (1 mL for 0.05 mmol) solution of starting material, zinc (4.4 equiv.) and dibromomethyl-triphenylphosphonium bromide (4 equiv.) was stirred under an argon atmosphere and allowed to reflux. The reaction was monitored by TLC, and after completion the mixture was cooled to room temperature and filtered on glass-frit. After concentration, the crude residue was purified by flash chromatography to give the 1,1-dibromo-1-alkene.

3.4.1. (2*R*,3*S*)-6,6-Dibromo-1-*O*-trityl-hex-5-ene-1,2,3-triol 12. The compound was prepared by general procedure 1 from 2-deoxy-5-*O*-trityl-D-ribofuranose **1** (0.5 g, 1.33 mmol). The reaction was completed after 40 min. The crude residue was purified by flash chromatography

Table 2. ^{13}C NMR data for 1,1-dibromo-1-alkenes derivatives of aldoses

Olefins	^{13}C chemical shifts δ (ppm)											
	C-1	C-2	C-3	C-4	C-5	C-6	C-7	*C*Ph$_3$	*C*HPh	*C*(CH$_3$)$_2$	C(*C*H$_3$)$_2$	Ph
12[a]	64.3	72.4	71.5	36.4	134.8	90.4	–	87.3	–	–	–	143.4–128.5–128.0–127.3
13[b]	66.0	72.0[d]	74.4[d]	73.3	138.0	92.0	–	87.0	–	–	–	144.1–129.0–127.8–127.1
14[b]	63.6	74.9	70.7	37.2	136.6	89.0	–	–	–	–	–	–
15[b]	63.9	72.4	74.2	73.5	138.2	92.5	–	–	–	–	–	–
16[b]	66.7	72.2	72.5	72.5	74.8	139.8	92.5	87.7	–	–	–	145.4–129.9–128.9–127.9
17[b]	67.2	69.4	73.7	72.1	37.3	135.3	95.0	87.0	–	–	–	143.8–129.1–128.9–127.4
18[b]	71.5	70.8	81.2	60.6	73.0	138.3	92.0	–	101.3	–	–	138.3–128.8–128.0–126.6
19[c]	64.9	72.8	74.1	69.7	38.7	141.7	89.6	–	–	–	–	–
20[a]	61.0	70.0	72.2[d]	73.5[d]	72.4	138.3	92.6	87.7	–	–	–	143.4–129.0–128.5–127.7
21[a]	68.0	73.2	71.1[d]	71.2[d]	73.5	142.9	91.4	87.0	–	–	–	145.3–129.5–129.1–124.1
22[a]	67.2	76.5	70.6	76.5	78.0	135.8	92.4	–	–	109.4 109.1	27.3–27.0 25.7–24.7	

[a] In $CDCl_3$.
[b] In CD_3OD.
[c] In C_5D_5N.
[d] No assignment.

Table 3. ^{1}H NMR data for 1,1-dibromo-1-alkenes derivatives of aldoses

Olefins	^{1}H chemical shifts δ (ppm) and ^{1}H coupling constants J (Hz)											
	H-1 ($J_{1-1'}$)	H-1′ (J_{1-2})	H-2 ($J_{1'-2}$)	H-3 (J_{2-3})	H-4 (J_{3-4})	H-4′ ($J_{3-4'}$)	H-5 ($J_{4-4'}$)	H-5′ (J_{4-5})	H-6 ($J_{4'-5}$)	C*H*Ph ($J_{4-5'}$)	C_6H_5 ($J_{5-5'}$)	(CH$_3$)$_2$C	
												J_{5-6}	$J_{5'-6}$
12[a]	3.30 dd 10.1	3.41 dd 3.9	3.70 m 3.9	3.80 m	2.20 m	2.20 m	6.48 t	– 7.1	– 7.1	–	7.2–7.4 m	–	
13[b]	3.40 m	3.40 m	3.74 m	3.74 m	4.54 dd 8.8	–	6.64 d	– 1.2	–	–	7.2–7.4 m	–	
14[b]	3.74 ddd 15.0	3.58 dd 3.8	3.45 ddd 6.3	3.60 ddd 7.0	2.53 ddd 3.5	2.28 ddd 8.5	6.72 t 15.5	– 6.9	– 6.9	–	–	–	
15[b]	3.75 dd 11.3	3.60 m 4.6	3.55 m	3.60 m	4.54 dd 4.2	–	6.68 d	– 8.8	–	–	–	–	
16[b]	3.29 dd 9.5	3.36 dd 6.1	3.95 m 3.7	3.67 dd 7.6	3.81 dd 1.8	–	4.46 dd	– 6.2	6.61 d	–	7.2–7.4 m	– 8.6	
17[b]	3.30 m	3.30 m	3.82 m	3.50 dd 2.0	4.15 q 7.2	–	3.30 m	3.30 m	6.50 t	–	7.2–7.4 m	– 6.9	6.9
18[b]	4.35 dd 10.6	3.55 dd 5.3	3.90 m 1.6	3.90 m	3.80 dd 1.4	–	4.55 dd	– 7.8	6.61 d	5.52s	7.2–7.4 m	– 8.9	
19[c]	4.47 dd 11.3	4.34 dd 3.4	4.54 m 5.6	4.09 dd 8.2	4.63 ddd 1.4	–	2.90 m	2.70 ddd 7.1	6.92 t	– 4.9	– 12.1	– 7.0	7.0
20[a]	3.41 dd 9.7	3.30 dd 4.6	4.05 m 6.0	3.63 m	3.63 m	–	4.55 d	–	6.64 d	–	7.2–7.4 m	– 8.2	
21[a]	3.95 dd 9.0	3.74 dd 2.2	4.70 m 6.3	4.70 m	4.70 m	–	5.15 dd	– 7.5	7.13 d	–	7.2–7.4 m	– 8.0	
22[a]	4.02 m	4.02 m	4.02 m	3.42 dd 7.6	4.50 dd 1.4	–	4.91 t	– 7.7	6.78 d	–	–	1.61–1.12s 7.7	

[a] In $CDCl_3$.
[b] In CD_3OD.
[c] In C_5D_5N.

(97:3 CH_2Cl_2–EtOAc) to afford **12** (0.626 g, 89%) as a syrup: $[\alpha]_D^{28}=-9$ (*c* 1.10, CH_2Cl_2); R_f 0.31 (75:25 hexane–EtOAc); IR ($CHCl_3$) ν 2974 and 1636 cm^{-1}; anal. calcd for $C_{25}H_{24}Br_2O_3$: C, 56.41; H, 4.54. Found: C, 56.83; H, 4.45; EI MS *m/z* $[M+Na]^+$ 554.9; $[MM+Na]^+$ 1086.8.

3.4.2. (2*R*,3*S*,4*S*)-6,6-Dibromo-1-*O*-trityl-hex-5-ene-1,2,3,4-tetrol 13. The compound was prepared by general procedure 1 from 5-*O*-trityl-D-ribofuranose **2** (0.5 g, 1.27 mmol). The reaction was completed after 45 min. Purification of the residue by flash chromatography (90:10 CH_2Cl_2–EtOAc) led to **13** (0.537 g, 77%) as a syrup: $[\alpha]_D^{28}=+67$ (*c* 1.00, CH_2Cl_2); R_f 0.55 (8:2 CH_2Cl_2–$(CH_3)_2CO$); IR ($CHCl_3$) ν 2980 and 1650 cm^{-1}; anal. calcd for $C_{25}H_{24}Br_2O_4$: C, 54.76; H, 4.41. Found: C, 54.42; H, 4.67; EI MS *m/z* $[M+Na]^+$ 570.9; $[MM+Na]^+$ 1118.8.

3.4.3. (2*R*,3*S*)-6,6-Dibromo-hex-5-ene-1,2,3-triol 14. The compound was prepared by general procedure 1 from 2-deoxy-D-ribose **3** (0.25 g, 1.86 mmol). The reaction was completed after 25 min. Purification of the residue by two consecutive flash chromatographies (97:3 CH_2Cl_2–MeOH, then 5:95 hexane–EtOAc) gave **14** (0.29 g, 54%) as a powder: mp 98–100°C; $[\alpha]_D^{23}=-21$ (*c* 0.96, MeOH); R_f 0.59 (85:15 CH_2Cl_2–MeOH); IR (film) ν 2980 and 1636 cm^{-1}; anal. calcd for $C_6H_{10}Br_2O_3$: C, 24.85; H,

3.47. Found: C, 25.06; H, 3.32; EI MS *m/z* $[M+Na]^+$ 312.9; $[MM+Na]^+$ 602.8.

3.4.4. (2*R*,3*S*,4*S*)-6,6-Dibromo-hex-5-ene-1,2,3,4-tetrol 15. The compound was prepared by general procedure 1 from D-ribose **4** (0.35 g, 2.33 mmol). The reaction was completed after 40 min. Purification of the residue by flash chromatography (92:8 CH_2Cl_2–MeOH) gave **15** (0.340 g, 48%) as a syrup: $[\alpha]_D^{24}=+80$ (*c* 0.98, MeOH); R_f 0.63 (8:2 CH_2Cl_2–MeOH); IR ($CHCl_3$) ν 2975 and 1636 cm^{-1}; anal. calcd for $C_6H_{10}Br_2O_4$: C, 23.55; H, 3.29. Found: C, 23.89; H, 3.18; EI MS *m/z* $[M+Na]^+$ 328.9; $[MM+Na]^+$ 634.8.

3.4.5. (2*R*,3*R*,4*R*,5*S*)-7,7-Dibromo-1-*O*-trityl-hept-6-ene-1,2,3,4,5-pentol 16. The compound was prepared by general procedure 1 from 6-*O*-trityl-D-glucose **5** (0.5 g, 1.18 mmol). The reaction was completed after 60 min. The crude residue was purified by flash chromatography (7:3 CH_2Cl_2–EtOAc) to give, after precipitation of salt with Et_2O, **16** (0.380 g, 56%) as a syrup: $[\alpha]_D^{30}=+7$ (*c* 1.01, $CHCl_3$); R_f 0.58 (9:1 CH_2Cl_2–MeOH); IR ($CHCl_3$) ν 2980 and 1640 cm^{-1}; Anal. calcd for $C_{26}H_{26}Br_2O_5$: C, 54.00; H, 4.53. Found: C, 54.22; H, 4.85; EI MS *m/z* $[M+Na]^+$ 601.0; $[MM+Na]^+$ 1178.9.

3.4.6. (2*R*,3*S*,4*R*)-7,7-Dibromo-1-*O*-trityl-hept-6-ene-1,2,3,4-tetrol 17. The compound was prepared by general procedure 1 from 2-deoxy-6-*O*-trityl-D-glucose **6** (0.5 g, 1.23 mmol). The reaction was completed after 65 min. Purification of the residue by flash chromatography (1:1 hexane–EtOAc) afforded **17** (0.449 g, 63%) as a syrup: $[\alpha]_D^{25}=+15$ (*c* 1.00, CH_2Cl_2); R_f 0.57 (85:15 CH_2Cl_2–$(CH_3)_2CO$); IR ($CHCl_3$) ν 2990 and 1655 cm^{-1}; anal. calcd for $C_{26}H_{26}Br_2O_4$: C, 55.53; H, 4.66. Found: C, 55.89; H, 4.45; EI MS *m/z* $[M+Na]^+$ 584.9; $[MM+Na]^+$ 1146.8.

3.4.7. (2*R*,3*R*,4*R*,5*S*)-7,7-Dibromo-1,3-*O*-benzylidene-hept-6-ene-1,2,3,4,5-pentol 18. The compound was prepared by general procedure 1 from 4,6-*O*-benzylidene-D-glucopyranose **7** (0.5 g, 1.86 mmol). The reaction was completed after 55 min. The crude residue was purified by flash chromatography (55:45 CH_2Cl_2–EtOAc) afforded **18** (0.473 g, 60%) as a syrup: $[\alpha]_D^{25}=+25$ (*c* 1.00, CH_2Cl_2); R_f 0.47 (1:1 hexane–EtOAc); IR ($CHCl_3$) ν 2985 and 1660 cm^{-1}; anal. calcd for $C_{14}H_{16}Br_2O_5$: C, 39.65; H, 3.80. Found: C, 39.61; H, 3.85; EI MS *m/z* $[M+Na]^+$ 446.9; $[MM+Na]^+$ 870.8.

3.4.8. (2*R*,3*S*,4*R*)-7,7-Dibromo-hept-6-ene-1,2,3,4-tetrol 19. The compound was prepared by general procedure 1 from 2-deoxy-D-glucose **8** (0.3 g, 1.83 mmol). The reaction was completed after 50 min. The crude residue was purified by flash chromatography (95:5 CH_2Cl_2–MeOH) to give, after precipitation of salt with MeOH, **19** (0.350 g, 60%) as a syrup: $[\alpha]_D^{28}=+20$ (*c* 1.00, MeOH); R_f 0.43 (85:15 CH_2Cl_2–MeOH); IR ($CHCl_3$) ν 2980 and 1655 cm^{-1}; anal. calcd for $C_7H_{12}Br_2O_4$: C, 26.27; H, 3.78. Found: C, 26.32; H, 3.74; EI MS *m/z* $[M+Na]^+$ 342.9; $[MM+Na]^+$ 662.8.

3.4.9. (2*R*,3*S*,4*R*,5*S*)-7,7-Dibromo-1-*O*-trityl-hept-6-ene-1,2,3,4,5-pentol 20. The compound was prepared by general procedure 1 from 6-*O*-trityl-D-galactose **9** (0.5 g, 1.18 mmol). The reaction was completed after 90 min. Purification of the residue by two consecutive flash chromatographies (99:1 CH_2Cl_2–MeOH, then 3:7 hexane–EtOAc) gave **20** (0.300 g, 44%): $[\alpha]_D^{24}=+94$ (*c* 0.61, CH_2Cl_2); R_f 0.61 (9:1 CH_2Cl_2–MeOH); IR ($CHCl_3$) ν 2980 and 1650 cm^{-1}; anal. calcd for $C_{26}H_{26}Br_2O_5$: C, 54.00; H, 4.53. Found: C, 54.21; H, 4.54; ES MS *m/z* $[M+Na]^+$ 601.0; $[MM+Na]^+$ 1178.9.

3.4.10. (2*R*,3*R*,4*R*,5*R*)-7,7-Dibromo-1-*O*-trityl-hept-6-ene-1,2,3,4,5-pentol 21. The compound was prepared by general procedure 1 from 6-*O*-trityl-D-mannose **10** (0.5 g, 1.18 mmol). The reaction was completed after 100 min. The crude residue was purified by two consecutive flash chromatographies (98:2 CH_2Cl_2–EtOAc, then 2:8 hexane–EtOAc) to afford **21** (0.520 g, 76%): $[\alpha]_D^{27}=+45$ (*c* 1.25, MeOH); R_f 0.35 (9:1 CH_2Cl_2–MeOH); IR ($CHCl_3$) ν 2980 and 1655 cm^{-1}; anal. calcd for $C_{26}H_{26}Br_2O_5$: C, 54.00; H, 4.53. Found: C, 54.37; H, 4.32; ES MS *m/z* $[M+Na]^+$ 601.1; $[MM+Na]^+$ 1178.9.

3.4.11. (2*R*,3*R*,4*R*,5*R*)-7,7-Dibromo-1,2:4,5-di-*O*-isopropylidene-hept-6-ene-1,2,3,4,5-pentol 22. The compound was prepared by general procedure 1 from 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose **11** (0.5 g, 1.92 mmol). The reaction was completed after 60 min. The crude residue was purified by flash chromatography (75:25 hexane–EtOAc) to afford **22** (0.715 g, 90%): $[\alpha]_D^{27}=+8$ (*c* 1.0, CH_2Cl_2); R_f 0.47 (75:25 hexane–EtOAc); IR ($CHCl_3$) ν 2975 and 1650 cm^{-1}; anal. calcd for $C_{13}H_{20}Br_2O_5$: C, 37.52; H, 4.84. Found: C, 37.37; H, 4.52; ES MS *m/z* $[M+Na]^+$ 438.9; $[MM+Na]^+$ 854.8.

This compound **22** was also obtained under Rassat conditions: anhydrous 1,4-dioxane (70 mL) was added to a mixture of dibromomethyl-triphenylphosphonium bromide (7.93 g, 15.4 mmol) and *t*-BuOK (1.68 g, 15 mmol) under argon atmosphere. The mixture was stirred at room temperature, and after 15 min, the 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose **11** (1 g, 3.85 mmol) was added. So the mixture was allowed to 60°C during 20 min as monitored by TLC. After the mixture was cooled to room temperature, it was filtered on glass-frit. After an extraction with CH_2Cl_2 and brine, the combined organic extracts was dried (Na_2SO_4) and concentrated. The crude residue was purified by flash chromatography (88:12 hexane–EtOAc) to afford **22** (1.43 g, 90%).

3.5. Preparation of glyco-1-ynitols (NMR data see Tables 4 and 5)

General procedure 2: To a THF (10 mL) solution of the 1,1-dibromo-1-alkene was added dropwise *n*-BuLi (2.5 M in hexanes, 5 equiv.) at −70°C under an argon atmosphere. After being stirred at low temperature for 25–30 min, the reaction mixture was warmed to room temperature, hydrolysed with brine and extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4) and concentrated. The crude residue was purified by flash chromatography to give the glyco-1-ynitol.

3.5.1. (2*R*,3*S*)-1-*O*-Trityl-hex-5-yne-1,2,3-triol 23. The compound was prepared by general procedure 2 from

Table 4. [13] C NMR data for *glyco*-1-ynitols

Glyco-1-ynitols	^{13}C chemical shifts δ (ppm)										
	C-1	C-2	C-3	C-4	C-5	C-6	C-7	*C*Ph$_3$	*C*(CH$_3$)$_2$	C(*C*H$_3$)$_2$	Ph
23[a]	64.9	71.2[d]	72.5[d]	23.5	81.0	71.2	–	87.8	–	–	144.1–129.0–128.4–127.6
24[b]	64.2	71.5	73.3	64.5	80.8	75.1	–	87.7	–	–	143.4–128.5–127.9–127.3
25[b]	63.5	74.0	70.7	23.3	81.2	71.3					–
26[b]	61.8	71.0[d]	73.0[d]	62.3	80.3	72.8	–	–	–	–	–
27[a]	65.5	71.6	75.0	72.0	64.4	82.5	74.9	87.3	–	–	142.2–129.3–128.3–127.5
28[a]	64.7	76.6	77.4	68.9	23.6	80.7	71.7	87.2	–	–	143.5–128.5–127.9–127.2
29[c]	63.5	71.4	72.0	68.8	23.3	82.2	71.5	–	–	–	–
30[b]	65.6	69.5	70.3	73.7	62.5	83.8	73.4	87.0	–	–	144.6–129.0–127.8–127.0
31[a]	65.1	72.0	71.3	72.0	65.5	82.6	75.7	87.5	–	–	144.0–130.9–129.1–128.4
32[a]	67.4	76.1	72.0	78.1	67.7	80.2	77.9	–	110.2 109.7	27.2–26.7 25.9–25.5	–
33[a]	66.1	75.7	69.3	80.7	66.3	80.4	74.7	–	110.4 109.0	26.4–26.2 25.7–24.9	–

[a] In $CDCl_3$.
[b] In CD_3OD.
[c] D_2O.
[d] No assignment.

Table 5. [1] H NMR data for *glyco*-1-ynitols

glyco-1-ynitols	^{1}H chemical shifts δ (ppm) and ^{1}H coupling constants J (Hz)													
	H-1 ($J_{1-1'}$)	H-1′ (J_{1-2})	H-2 ($J_{1'-2}$)	H-3 (J_{2-3})	H-4 (J_{2-4})	H-4′ (J_{3-4})	H-5 ($J_{3-4'}$)	H-5′ (J_{4-5})	H-6 ($J_{4'-5}$)	H-7 ($J_{4-5'}$)	C_6H_5 (J_{4-6})	C(*CH*$_3$)$_2$		
												$J_{4'-6}$	J_{5-7}	$J_{5'-7}$
23[a]	3.41 dd	3.44 dd	3.82 m	3.82 m	2.40 m	2.40 m	–	–	2.00 t	–	7.2–7.4 m	–		
	9.7	3.9	5.4								2.6	2.6		
24[b]	3.55 dd	3.45 dd	3.88 m	3.77 dd	4.63 dd	–	–	–	2.46 d	–	7.2–7.4 m	–		
	9.8	5.2	3.9	7.8		4.2					2.2			
25[b]	3.80 m	3.60 m	3.60 m	3.71 m	2.57 ddd	2.40 ddd			2.28 t					
						4.0	6.8				2.7	2.7		
26[b]	2.24 dd	2.14 m	2.14 m	2.14 m	3.04 m	–	–	–	2.29 m	–	–	–		
	10.8	1.4												
27[a]	3.38 m	3.33 m	4.10 q	3.93 m	3.93 m		4.50 dd			2.45 d		–		
		7.1	7.1	7.1				6.9					2.1	
28[a]	3.25 m	3.25 m	3.89 dd	3.70 dd	3.97 dt	–	2.50 m	2.50 m	–	2.00 d	7.2–7.4 m	–		
				6.0	5.6	1.8		6.8	6.8				2.6	5.3
29[c]	3.97 dd	3.58 m	3.66 m	3.58 m	3.97 dt	–	2.45 m	2.45 m	–	2.35 t	–	–		
	11.5	2.5				1.6		6.9					1.5	
30[b]	3.29 dd	3.00 dd	4.14 dt	3.85 dd	2.07 dd	–	4.62 t	–	–	2.45 d	7.2–7.4 m	–		
	9.0	6.3	6.3	1.0		8.6		2.4					2.4	
31[a]	3.42 dd	3.33 dd	3.98 q	4.26 d	3.89 d	–	4.56 dd	–	–	2.45 d	7.2–7.4 m	–		
	9.7	5.7	5.7	5.7				4.5					2.0	
32[a]	4.00 m	4.00 m	4.00 m	3.8 dd	4.15 dd		4.80 dd			2.60 d		1.41–1.25–1.22–1.21		
				7.5		4.5		6.1					1.9	
33[a]	3.60 m	3.60 m	3.60 m	3.40 m	4.15 dd		4.50 dd	–	–	2.50 d	–	1.23–1.15–1.14–1.10		
						2.3		7.6					2.1	

[a] In $CDCl_3$.
[b] In CD_3OD.
[c] In D_2O.

(2*R*,3*S*)-6,6-dibromo-1-*O*-trityl-hex-5-ene-1,2,3-triol **12** (0.626 g, 1.18 mmol). Purification of the residue by flash chromatography (99.5:0.5 CH_2Cl_2–EtOAc) furnished **23** (0.380 g, 87%): $[\alpha]_D^{25}$=+113 (*c* 1.10, CH_2Cl_2); R_f 0.4 (7:3 hexane–EtOAc); IR ($CHCl_3$) ν 3300 and 2100 cm^{-1}; anal. calcd for $C_{25}H_{24}O_3$: C, 80.62; H, 6.49. Found: C, 80.48; H, 6.64; ES MS *m*/*z* $[M+Na]^+$ 395.1; $[MM+Na]^+$ 767.3.

3.5.2. (2*R*,3*S*,4*S*)-1-*O*-Trityl-hex-5-yne-1,2,3,4-tetrol 24. The compound was prepared by general procedure 2 from (2*R*,3*S*,4*S*)-6,6-dibromo-1-*O*-trityl-hex-5-ene-1,2,3,4-tetrol **13** (0.507 g, 0.925 mmol). The crude residue was purified by flash chromatography (9:1 CH_2Cl_2–EtOAc) to give **24** (0.30 g, 84%): $[\alpha]_D^{28}$=+27 (*c* 1.0, CH_2Cl_2); R_f 0.54 (7:3 CH_2Cl_2–$(CH_3)_2CO$); IR ($CHCl_3$) ν 3300 and 2100 cm^{-1}; anal. calcd for $C_{25}H_{24}O_4$: C, 77.29; H, 6.22. Found: C, 77.43; H, 6.17; ES MS *m*/*z* $[M+Na]^+$ 411.1; $[MM+Na]^+$ 799.2.

3.5.3. (2*R*,3*S*)-Hex-5-yne-1,2,3-triol 25. The compound was prepared by general procedure 2 from (2*R*,3*S*)-6,6-dibromo-hex-5-ene-1,2,3-triol **14** (0.21 g, 0.724 mmol). The reaction mixture was quenched by addition of EtOH (5 mL). Purification of the residue by two consecutive flash chromatographies (95:5 CH_2Cl_2–MeOH, then 97:3 EtOAc–MeOH) gave **25** (0.075 g, 80%): R_f 0.4 (85:15 CH_2Cl_2–MeOH); IR ($CHCl_3$) ν 3300 and 2100 cm^{-1}; Anal.

calcd for $C_6H_{10}O_3$: C, 55.37; H, 7.74. Found: C, 55.70; H, 7.49; ES MS *m/z* $[M+Na]^+$ 152.9; $[MM+Na]^+$ 282.8.

3.5.4. (2*R*,3*S*,4*S*)-Hex-5-yne-1,2,3,4-tetrol 26. The compound was prepared by general procedure 2 from (2*R*,3*S*,4*S*)-6,6-dibromo-hex-5-ene-1,2,3,4-tetrol **15** (0.32 g, 1.05 mmol). The reaction mixture was quenched by addition of EtOH (5 mL). Purification of the residue by flash chromatography (88:12 CH_2Cl_2–MeOH) gave **26** (0.11 g; 71%) as a syrup: $[\alpha]_D^{24}=+20$ (*c* 1.0, MeOH); R_f 0.38 (8:2 CH_2Cl_2–MeOH); IR ($CHCl_3$) ν 3300 and 2100 cm^{-1}; anal. calcd for $C_6H_{10}O_4$: C, 49.31; H, 6.89. Found: C, 49.53; H, 6.75; ES MS *m/z* $[M+Na]^+$ 169.1; $[MM+Na]^+$ 315.2.

3.5.5. (2*R*,3*R*,4*R*,5*S*)-1-*O*-Trityl-hept-6-yne-1,2,3,4,5-pentol 27. The compound was prepared by general procedure 2 from (2*R*,3*R*,4*R*,5*S*)-7,7-dibromo-1-*O*-trityl-hept-6-ene-1,2,3,4,5-pentol **16** (0.38 g, 0.658 mmol). The crude residue was purified by flash chromatography (7:3 CH_2Cl_2–EtOAc) to give **27** (0.166 g, 60%): $[\alpha]_D^{23}=+14$ (*c* 1.0, CH_2Cl_2); R_f 0.2 (6:4 CH_2Cl_2–EtOAc); IR ($CHCl_3$) ν 3300 and 2100 cm^{-1}; anal. calcd for $C_{26}H_{26}O_5$: C, 74.62; H, 6.26. Found: C, 74.77; H, 6.21; ES MS *m/z* $[M+Na]^+$ 441.1; $[MM+Na]^+$ 859.2.

3.5.6. (2*R*,3*S*,4*R*)-1-*O*-Trityl-hept-6-yne-1,2,3,4-tetrol 28. The compound was prepared by general procedure 2 from (2*R*,3*S*,4*R*)-7,7-dibromo-1-*O*-trityl-hept-6-ene-1,2,3,4-tetrol **17** (0.417 g, 0.742 mmol). The crude residue was purified by flash chromatography (96:4 CH_2Cl_2–$(CH_3)_2CO$) to give **28** (0.2 g, 67%): $[\alpha]_D^{23}=-14$ (*c* 1.0, CH_2Cl_2); R_f: 0.47 (85:15 CH_2Cl_2–$(CH_3)_2CO$); IR ($CHCl_3$) ν 3300 and 2100 cm^{-1}; anal. calcd for $C_{26}H_{26}O_4$: C, 77.58; H, 6.51. Found: C, 77.81; H, 6.32; ES MS *m/z* $[M+Na]^+$ 425.2; $[MM+Na]^+$ 827.4.

3.5.7. (2*R*,3*S*,4*R*)-Hept-6-yne-1,2,3,4-tetrol 29. The compound was prepared by general procedure 2 from (2*R*,3*S*,4*R*)-7,7-dibromo-hept-6-ene-1,2,3,4-tetrol **19** (0.337 g; 1.05 mmol). The reaction mixture was quenched by addition of EtOH (5 mL). Purification of the residue by flash chromatography (9:1 CH_2Cl_2–MeOH) gave **29** (0.145 g; 86%) as a syrup: $[\alpha]_D^{26}=-15$ (*c* 1.45, MeOH); R_f 0.38 (8:2 CH_2Cl_2–MeOH); IR ($CHCl_3$) ν 3300 and 2100 cm^{-1}; Anal. calcd for $C_7H_{12}O_4$: C, 52.49; H, 7.55. Found: C, 52.75; H, 7.41; ES MS *m/z* $[M+Na]^+$ 182.9; $[MM+Na]^+$ 342.8.

3.5.8. (2*R*,3*S*,4*R*,5*S*)-1-*O*-Trityl-hept-6-yne-1,2,3,4,5-pentol 30. The compound was prepared by general procedure 2 from (2*R*,3*S*,4*R*,5*S*)-7,7-dibromo-1-*O*-trityl-hept-6-ene-1,2,3,4,5-pentol **20** (0.292 g, 0.5 mmol). The reaction mixture was quenched by addition of EtOH (5 mL). The crude residue was purified by flash chromatography (97:3 CH_2Cl_2–MeOH) to give **30** (0.181 g, 85%): $[\alpha]_D^{24}=-11$ (*c* 1.4, MeOH); R_f 0.49 (85:15 CH_2Cl_2–MeOH); IR ($CHCl_3$) ν 3300 and 2100 cm^{-1}; anal. calcd for $C_{26}H_{26}O_5$: C, 74.62; H, 6.26. Found: C, 74.81; H, 6.15; ES MS *m/z* $[M+Na]^+$ 441.2; $[MM+Na]^+$ 859.4.

3.5.9. (2*R*,3*R*,4*R*,5*R*)-1-*O*-Trityl-hept-6-yne-1,2,3,4,5-pentol 31. The compound was prepared by general procedure 2 from (2*R*,3*R*,4*R*,5*R*)-7,7-dibromo-1-*O*-trityl-hept-6-ene-1,2,3,4,5-pentol **21** (0.52 g, 1 mmol). The crude residue was purified by flash chromatography (98:2 CH_2Cl_2–MeOH) to give **31** (0.260 g, 69%): $[\alpha]_D^{24}=-27$ (*c* 1.0, CH_2Cl_2); R_f 0.37 (85:15 CH_2Cl_2–MeOH); IR ($CHCl_3$) ν 3300 and 2100 cm^{-1}; anal. calcd for $C_{26}H_{26}O_5$: C, 74.62; H, 6.26. Found: C, 74.78; H, 6.19; ES MS *m/z* $[M+Na]^+$ 441.2; $[MM+Na]^+$ 859.4.

3.5.10. (2*R*,3*R*,4*R*,5*R*)-1,2:4,5-Di-*O*-isopropylidene-hept-6-yne-1,2,3,4,5-pentol 32. The compound was prepared by general procedure 2 from (2*R*,3*R*,4*R*,5*R*)-7,7-dibromo-1,2:4,5-di-*O*-isopropylidene-hept-6-ene-1,2,3,4,5-pentol **22** (0.715 g, 1.72 mmol). The crude residue was purified by flash chromatography (90:10 hexane–EtOAc) to give **32** (0.28 g, 64%): $[\alpha]_D^{24}=+13$ (*c* 1.0, CH_2Cl_2); R_f: 0.37 (75:25 hexane–EtOAc); IR ($CHCl_3$) ν 3300 and 2100 cm^{-1}; anal. calcd for $C_{13}H_{20}O_5$: C, 56.23; H, 7.86. Found: C, 56.42; H, 7.58; ES MS *m/z* $[M+Na]^+$ 279.1; $[MM+Na]^+$ 535.2.

3.5.11. (2*R*,3*R*,4*R*,5*S*)-1,2:4,5-Di-*O*-isopropylidene-hept-6-yne-1,2,3,4,5-pentol 33. MeOH (10 mL) was added to a mixture of 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose **11** (1 g, 3.84 mmol) and K_2CO_3 (1.59 g, 11.5 mmol). The mixture was stirred under an argon atmosphere and allowed to reflux. Dimethyl(1-diazo-2-oxopropyl)phosphonate (2.21 g, 11.5 mmol) was added dropwise during 6 h (syringe-pump). After the mixture was cooled to room temperature, it was filtered on glass-frit and concentrated. After an extraction with EtOAc/H_2O, the combined organic extracts was dried (Na_2SO_4) and concentrated. The crude residue was purified by flash chromatography (85:15 hexane–EtOAc) to afford **33** (0.83 g, 84%) as a syrup: $[\alpha]_D^{28}=-27$ (*c* 1.4, $CHCl_3$); R_f 0.31 (75:25 hexane–EtOAc); IR ($CHCl_3$) ν 3300 and 2100 cm^{-1}; anal. calcd for $C_{13}H_{20}O_5$: C, 56.23; H, 7.86. Found: C, 56.42; H, 7.58; ES MS *m/z* $[M+Na]^+$ 279.2; $[MM+Na]^+$ 535.4.

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