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Synthesis and reactions of some derivatives of (3,6*S*,9*R*,10*R*,11*S*)-1,4,7-trioxaspiro[5,5]undecane-3,9,10,11-tetrol: novel quasi-saccharides[1]

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Abstract

The title compound was obtained by reductive ozonolysis of allyl β-D-fructopyranoside. The synthesis and characterization of a number of C-3-substituted derivatives using conventional carbohydrate procedures is described. Some of the products may be of biological interest as carbohydrate mimics. The structures of two of the basic products (**8** and **9**) were substantiated by X-ray diffraction studies.

Keywords: Spiro-fructosides-quasisaccharides; Carbohydrate mimics; X-ray diffraction

1. Introduction

During structural studies on some glycerol derivatives of D-fructose, compounds **1** and **2** were subjected to periodate oxidation. Appropriate removal of the protecting functions from the products gave in each case, the same crystalline compound. The ^{1}H NMR spectrum of this material, presumed to be the glycolaldehyde (hydroxyacetaldehyde) fructoside **3**, did not contain signals expected for an aldehyde function at 9–10 ppm. Previous studies on glycosides of this type have suggested that they exist in the free aldehyde form (Holme and Hall, 1992), but with no supportive evidence, or as intramolecular cyclic hemiacetals (Cabaret and Wakselman, 1989). This particular study described a number of lipophilic derivatives obtained by reductive ozonolysis of allyl glycosides. The products were shown by ^{1}H NMR spectroscopy to be cyclic hemiacetals involving the C-2 hydroxyl group of the basic carbohydrate ring. It seemed likely that the product obtained during this current study was the *spiro* hemiacetal **4** ((3,6*S*,9*R*,10*R*,11*S*)-1,4,7-trioxaspiro[5,5]undecane-3,9,10,11-tetrol]. This would have resulted from the in situ cyclisation of the produced aldehyde group with the primary C-1 hydroxyl function of the fructopyranoside ring, although the alternative structure **5** involving OH-3 could not be precluded. Little is known of the fundamental properties of spiroacetals of this type which possess the equivalent of an anomeric reducing centre at C-3 of the spiroundecane system. The synthesis and some reactions of the bicyclic triol **6** were reported (Aamlid et al., 1987) but this compound lacks a reactive group at C-3. Many important natural products also have spiroacetal linkages in their structures (Martin et al., 1996). These include insect pheromones, antiparasitic agents and polyether antibiotics. It was decided to investigate some basic characteristic carbohydrate-type reactions of compound **4** in order to produce some 'quasi' saccharide[2] derivatives as potential carbohydrate mimics. There is considerable current interest in the glycobiology of saccharide mimics, especially those in which the interglycosidic linkages have been replaced by methylene groups (Sinaÿ, 1997). The results of this study are now presented.

2. Results and discussion

Reductive ozonolysis (O_3-Ph_3P) of the previously described (Raaijmakers et al., 1994) allyl β-D-fructopyrano-

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[2] The term 'quasi' is employed because others (Defaye and Garcia-Fernándes, 1994) have used the alternative term 'pseudo' to describe unusual oligosaccharides.

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Table 1
Crystal data and structure refinement for **9**

Identification code	Compound **9**
Empirical formula	$C_{16}H_{22}O_{11}$
Formula weight	390.34
Temperature	293(2) K
Crystal system, space group	Orthorhombic, $P2_12_12_1$
Unit cell dimensions (25 reflections $40.242 < \theta < 46.196$)	$a = 8.0281(2)$ Å; $\alpha = 90°$
	$b = 9.2525(2)$ Å; $\beta = 90°$
	$c = 25.4333(5)$ Å; $\gamma = 90°$
Volume	1889.19(8) Å^3
Z, calculated density	4, 1.372 Mg/m^3
Absorption coefficient	1.016 mm^{-1}
Diffractometer/scan	Enraf–Nonius CAD4/θ–2θ
Radiation/wavelength	Cu Kα (graphite monochr.)/1.54184 Å
F(000)	824
Crystal size	0.59 × 0.21 × 0.08 mm
θ range for data collection	3.48–69.87°
Index ranges	$0 <= h <= 9$, $-11 <= k <= 0$, $0 <= l <= 30$
Reflections collected	2069
Independent/observed reflections	2069/1905 ($[I_o > 2\sigma(I_o)]$)
Absorption correction	Semi-empirical from psi-scans (North et al., 1968)
Range of related transmission factors	0.931 and 1.145
Refinement method	Full-matrix least-squares on F^2
Computing	SHELXL-97 (Sheldrick, 1997)
Data/restraints/parameters	2069/0/289
Goodness-of-fit on F^2	1.049
SHELXL-97 weight parameters	0.0526 0.3441
Final R indices ($I > 2\sigma(I)$)	$R_1 = 0.0322$, $wR_2 = 0.0884$
R indices (all data)	$R_1 = 0.0355$, $wR_2 = 0.0914$
Extinction coefficient	0.0068(5)
Largest difference: peak and hole	0.169 and −0.159 e Å^{-3}

side (**7**) also produced compound **4** in excellent yield (87.5%). The product, a mixture of isomers, was acetylated (acetic anhydride–pyridine) in the usual manner to give a mixture of the two 'anomeric' peracetates **8** and **9** in a 1:2 ratio, a portion of the material was separated by column chromatography. In keeping with simple carbohydrate convention compound **8** was assigned the α configuration, in which the C-3 acetoxy group (3*R*) assumes an axial disposition. Compound **9**, likewise, was the C-3 (*S*) acetoxy derivative with an equatorial (β) disposition. These assignments were confirmed by X-ray structural analyses on compounds **8** and **9** (see Figs. 1 and 2, Tables 1–10). Acetylation of **4** using acetic anhydride–sodium acetate gave a mixture of **8** and **9** in a 1:3 ratio (GLC), which was not separated. Treatment of compound **4** with *p*-nitroaniline in the conventional manner (Guthrie and Honeyman, 1960) gave the crystalline *p*-nitrophenylamino derivative **10** which had an unusually high positive specific rotation, +281°, for a derivative of β-D-fructopyranose. It was assigned the α-configuration on the basis of this value and by supportive ^{1}H NMR data. The signals for the C-3 proton coupling with the NH group appeared as a doublet–doublet 5.03 ppm in DMSO-D_6. This reduced to an approximate broad doublet when the spectrum was determined in DMSO-D_6–D_2O, as a result of partial exchange with the NH group. It is well known that glycosylamines can anomerise under these conditions. Compound **10** was characterized by acetylation

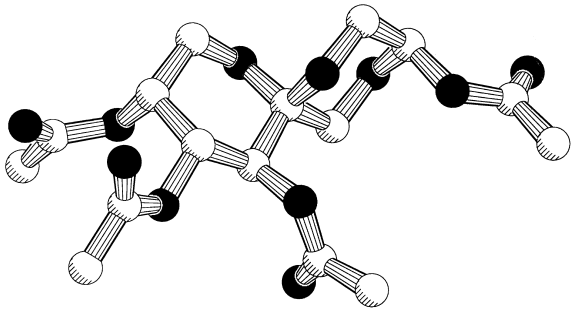


Fig. 1. PLUTON drawing of the X-ray structure **8** (Spek, 1995).

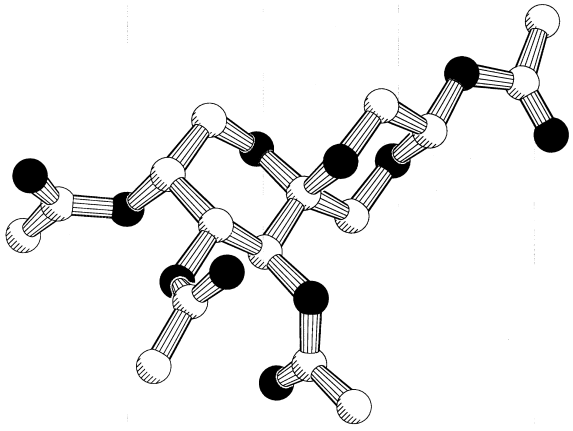


Fig. 2. PLUTON drawing of the X-ray structure **9** (Spek, 1995).

Table 2
Atomic coordinates($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **9**

	x	*y*	*z*	*U*(eq)
O(1)	−607(2)	−2496(2)	−8631(1)	42(1)
C(2)	−1589(3)	−3730(3)	−8774(1)	50(1)
C(3)	−3404(3)	−3341(3)	−8747(1)	47(1)
O(4)	−3747(2)	−2153(2)	−9082(1)	49(1)
C(5)	−2772(3)	−916(3)	−8943(1)	45(1)
C(6)	−928(3)	−1277(2)	−8953(1)	38(1)
O(7)	−499(2)	−1537(2)	−9482(1)	44(1)
C(8)	1210(3)	−1958(3)	−9552(1)	48(1)
C(9)	2396(3)	−823(3)	−9352(1)	44(1)
C(10)	1984(3)	−457(3)	−8785(1)	42(1)
C(11)	156(3)	−49(2)	−8743(1)	38(1)
O(20)	−4315(2)	−4509(2)	−8962(1)	59(1)
C(20)	−6778(5)	−5741(4)	−9149(2)	94(1)
O(21)	−6553(3)	−3910(3)	−8494(1)	91(1)
C(21)	−5938(4)	−4633(3)	−8824(1)	61(1)
O(30)	−217(2)	244(2)	−8200(1)	47(1)
C(30)	−849(6)	1775(5)	−7497(1)	95(1)
O(31)	−948(5)	2501(2)	−8392(1)	117(1)
C(31)	−694(4)	1608(3)	−8075(1)	62(1)
O(40)	2965(2)	761(2)	−8611(1)	53(1)
C(40)	4536(6)	2049(4)	−7990(2)	94(1)
O(41)	3834(4)	−431(3)	−7904(1)	103(1)
C(41)	3776(3)	648(3)	−8149(1)	60(1)
O(50)	2174(2)	473(2)	−9669(1)	51(1)
C(50)	3007(4)	2146(3)	−10306(1)	63(1)
O(51)	4799(2)	347(3)	−9954(1)	78(1)
C(51)	3460(3)	911(3)	−9964(1)	47(1)

U(eq) is defined as one-third of the trace of the orthogonalized U_{ij} tensor.

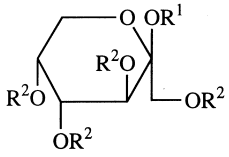
(pyridine–acetic anhydride) in the usual manner to give the tri-*O*-acetate **11**.

Treatment of a mixture of compounds **8** and **9** with 33% solution of hydrogen bromide in glacial acetic acid gave the bromide **12** as a syrup (94%). It is noteworthy that **12** was not stable when stored as a syrup, but could be kept for considerable periods (ca. 3 months) in dichloromethane solution at 0°C without deterioration. The assigned 3*R* (α) configuration of this derivative was based on the comparatively low negative rotational value (−40°) and on its ^{1}H NMR spectrum. Treatment of **12** with excess methanol in the presence of anhydrous sodium carbonate for 30 min, followed by column chromatography (hexane–ethylacetate, 1:1), yielded two crystalline products. The first of these was the 'β' glycoside **13** obtained in 49% yield, which was followed by the α-anomer **14** (21%). It was of interest that **13** and **14** were produced so readily compared with more complicated Koenigs–Knorr type conditions (Igarashi, 1977). When the glucopyranosyl bromide **15** (Bárczai-Martos and Körösy, 1950) was treated under similar conditions it was found (TLC) that little or no glycosidation occurred during a period of 15 h and that a complex mixture of products were produced gradually over the following 72 h. Many of these probably resulted from the gradual de-acetylation of the starting material.

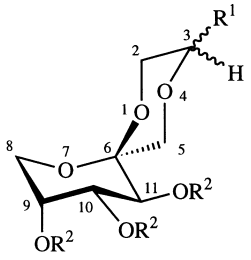
An alternative procedure for obtaining 'quasi' glycosides by alkylation of the C_3–OH group was then investigated. Treatment of compound **4** in aqueous 1,2-dimethoxyethane with benzyl chloride and potassium hydroxide in the presence of a catalytic quantity of 18-crown-6 at 70°C for 7 h gave, after column chromatography, the benzyl derivative **16** (71%). The assigned configuration of C-3 was again based on specific rotational and spectral characteristics. It seemed unusual that little alkylation of the fructosyl ring hydroxyl groups had occurred under these conditions. treatment of **4** with methyliodide in a similar manner gave, after acetylation of the crude product in the usual manner (acetic anhydride–pyridine), a mixture (GLC) of compounds **13** and **14** in a ratio of 8:1. The mixture was not separated. Acetal syntheses are known (Schmitz, 1958; Kuhn and Trischmann, 1961) in which the anion of the hemiacetal is alkylated under basic conditions. Although this approach is not generally used for the synthesis of simple glycosides, a recent study (Ewing et al., 1997) demonstrated that effective glycosidation of several monosaccharides could be achieved under basic conditions using a variety of benzyl bromides. A method of base promoted anomeric *O*-alkylation of protected sugars with alkyl triflates has also been described (Schmidt, 1989). A triflate is not always a convenient reagent and the necessity of a suitably blocked substrate also makes this procedure less attractive.

An alternative popular method of glycoside synthesis is the trichloroacetamidate procedure (Schmidt and Kinzy, 1994). The stereoselective *O*-activation of the anomeric centre of carbohydrate derivatives as trichloroacetamido compounds normally proceeds easily. Their subsequent reaction with alcohols, including other carbohydrate derivatives under mildly acidic conditions provides an efficient route to many types of glycosides. It was decided to investigate this approach with derivatives of **3** for obtaining a trisaccharide analogue.

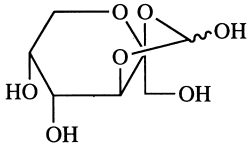
Brief treatment (10 min) of the bromide **12** with aqueous sodium hydrogen carbonate gave the free hemiacetal **17** with trichloroacetonitrile in 89% yield as a non-crystalline foam. Treatment of **17** with trichloroacetonitrile in the presence of sodium hydride gave the 3(*R*)-trichloroacetamidate (**18**, 72%) as a syrup. This material was treated with 1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**19**, Verhart et al., 1992) in the presence of boron trifluoride etherate at −72°C to give crystalline **20** in 32% yield after column chromatography. When compound **17** was treated with trichloroacetonitrile in the presence of anhydrous potassium carbonate the alternative 3(*S*)-trichloroacetamidate **21** was obtained in 65.5% yield. Reaction of **21** with the diacetal **19** in the above manner also yielded compound **20** (21%), which was identical with the material obtained from the isomeric **18**. The formation of the 'α'-linked compound **20** from the two trichloroacetamidates **18** and **21** is not fully understood. Its production from the 'β'-linked compound **18** would have been expected (Schmidt and Kinzy, 1994) assuming the



1 $R^1 = CH_2CH(OH)CH_2OH$, $R^2 = Ac$
2 $R^1 = CH_2CH(OH)CH_2OH$, $R^2 = Bn$
3 $R^1 = CH_2CHO$, $R^2 = H$
7 $R^1 = OCH_2CHCH_2$, $R^2 = H$



4 $R^1 = OH$, $R^2 = H$
6 $R^1 = R^2 = H$
17 $R^1 = OH$, $R^2 = Ac$



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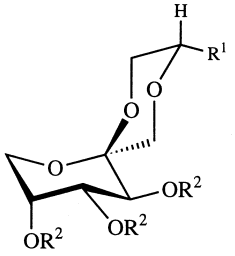
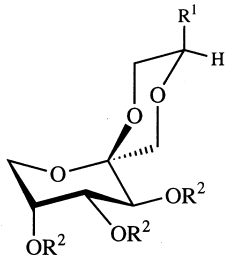
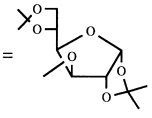
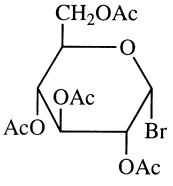




8 $R^1 = OAc$, $R^2 = Ac$
10 $R^1 = NH$-C$_6$H$_4$-NO_2, $R^2 = H$
11 $R^1 = NH$-C$_6$H$_4$-NO_2, $R^2 = Ac$
12 $R^1 = Br$, $R^2 = Ac$
14 $R^1 = OCH_3$, $R^2 = Ac$
16 $R^1 = OBzl$, $R^2 = H$
18 $R^1 = NHC(O)CCl_3$, $R^2 = Ac$
20 $R^1 =$  , $R^2 = Ac$

9 $R^1 = OAc$, $R^2 = Ac$
13 $R^1 = OCH_3$, $R^2 = Ac$
21 $R^1 = NHC(O)CCl_3$, $R^2 = Ac$



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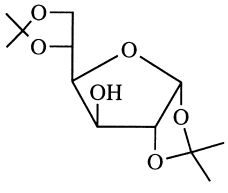

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usual S_N2-type reaction course, whereas from **21** it would require an S_N1-type mechanism. These usually only occur in the presence of polar (donor) solvents and when stronger catalysts are employed. Further studies would be required to clarify these points.

The results obtained during this preliminary study show that the C-3 hemiacetal group of compound **4** behaves in much the same fashion as a normal carbohydrate anomeric group. Further investigations of some of these reactions and the biological evaluation of the products as carbohydrate mimics are currently in progress.

3. Experimental

3.1. General

Melting points were determined on a Reichert Thermopan microscope and are uncorrected. Optical rotations were measured with a Perkin-Elmer 241 automatic polarimeter on approximately 1% solutions in the solvents indicated at 20°C. TLC was performed on silica gel plates (Merck F_{254}) and column chromatography on silica gel 60 (Merck 70-230 mesh) using the solvent combinations indicated, GLC was

Table 3
Bond lengths (Å) and angles (°) for **9**

O(1)–C(6)	1.417(2)
O(1)–C(2)	1.434(3)
C(2)–C(3)	1.502(4)
C(3)–O(20)	1.415(3)
C(3)–O(4)	1.418(3)
O(4)–C(5)	1.430(3)
C(5)–C(6)	1.518(3)
C(6)–O(7)	1.411(2)
C(6)–C(11)	1.527(3)
O(7)–C(8)	1.437(3)
C(8)–C(9)	1.506(4)
C(9)–O(50)	1.457(3)
C(9)–C(10)	1.517(3)
C(10)–O(40)	1.445(3)
C(10)–C(11)	1.519(3)
C(11)–O(30)	1.439(3)
O(20)–C(21)	1.354(3)
C(20)–C(21)	1.479(4)
O(21)–C(21)	1.182(4)
O(30)–C(31)	1.356(3)
C(30)–C(31)	1.483(4)
O(31)–C(31)	1.173(3)
O(40)–C(41)	1.348(3)
C(40)–C(41)	1.489(4)
O(41)–C(41)	1.177(4)
O(50)–C(51)	1.338(3)
C(50)–C(51)	1.481(4)
O(51)–C(51)	1.195(3)
C(6)–O(1)–C(2)	112.75(16)
O(1)–C(2)–C(3)	109.3(2)
O(20)–C(3)–O(4)	105.00(18)
O(20)–C(3)–C(2)	107.5(2)
O(4)–C(3)–C(2)	110.2(2)
C(3)–O(4)–C(5)	111.43(16)
O(4)–C(5)–C(6)	110.71(19)
O(7)–C(6)–O(1)	111.80(18)
O(7)–C(6)–C(5)	106.95(17)
O(1)–C(6)–C(5)	110.01(18)
O(7)–C(6)–C(11)	108.75(18)
O(1)–C(6)–C(11)	106.66(16)
C(5)–C(6)–C(11)	112.73(19)
C(6)–O(7)–C(8)	113.35(16)
O(7)–C(8)–C(9)	111.9(2)
O(50)–C(9)–C(8)	108.07(19)
O(50)–C(9)–C(10)	108.42(19)
C(8)–C(9)–C(10)	109.81(19)
O(40)–C(10)–C(9)	110.30(19)
O(40)–C(10)–C(11)	108.14(19)
C(9)–C(10)–C(11)	109.46(18)
O(30)–C(11)–C(10)	108.38(18)
O(30)–C(11)–C(6)	110.93(17)
C(10)–C(11)–C(6)	109.93(19)
C(21)–O(20)–C(3)	117.5(2)
O(21)–C(21)–O(20)	122.6(3)
O(21)–C(21)–C(20)	126.7(3)
O(20)–C(21)–C(20)	110.7(3)
C(31)–O(30)–C(11)	117.31(19)
O(31)–C(31)–O(30)	122.9(2)
O(31)–C(31)–C(30)	126.4(3)
O(30)–C(31)–C(30)	110.6(3)
C(41)–O(40)–C(10)	118.03(19)
O(41)–C(41)–O(40)	123.1(3)
O(41)–C(41)–C(40)	125.3(3)
O(40)–C(41)–C(40)	111.5(3)
C(51)–O(50)–C(9)	117.73(18)
O(51)–C(51)–O(50)	123.4(2)
O(51)–C(51)–C(50)	124.8(2)
O(50)–C(51)–C(50)	111.9(2)

Table 4
Anisotropic displacement parameters ($Å^2 \times 10^3$) for **9**

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O(1)	46(1)	40(1)	41(1)	6(1)	−7(1)	−2(1)
C(2)	55(2)	41(1)	54(1)	−1(1)	−6(1)	−2(1)
C(3)	53(1)	47(1)	41(1)	−5(1)	−2(1)	−9(1)
O(4)	46(1)	51(1)	50(1)	1(1)	−9(1)	−2(1)
C(5)	44(1)	44(1)	46(1)	1(1)	−4(1)	2(1)
C(6)	44(1)	41(1)	29(1)	3(1)	−2(1)	2(1)
O(7)	47(1)	55(1)	31(1)	−2(1)	−2(1)	3(1)
C(8)	51(1)	52(1)	40(1)	−2(1)	6(1)	6(1)
C(9)	42(1)	47(1)	45(1)	10(1)	4(1)	7(1)
C(10)	42(1)	41(1)	42(1)	6(1)	−6(1)	−1(1)
C(11)	44(1)	42(1)	27(1)	4(1)	−2(1)	1(1)
O(20)	59(1)	54(1)	63(1)	−15(1)	−3(1)	−11(1)
C(20)	79(2)	60(2)	142(3)	−12(2)	−39(2)	−14(2)
O(21)	64(1)	82(2)	127(2)	−25(2)	21(1)	−10(1)
C(21)	53(2)	44(1)	85(2)	1(1)	−10(1)	−5(1)
O(30)	59(1)	53(1)	30(1)	−2(1)	−1(1)	0(1)
C(30)	128(3)	110(3)	46 91)	−27(2)	−3(2)	27(3)
O(31)	221(4)	70(1)	59(1)	−2(1)	1(2)	63(2)
C(31)	80(2)	63(2)	43(1)	−13(1)	−5(1)	11(2)
O(40)	56(1)	49(1)	56(1)	8(1)	−10(1)	−14(1)
C(40)	95(3)	92(2)	96(3)	−14(2)	−22(2)	−34(2)
O(41)	135(2)	86(2)	88(2)	26(1)	−62(2)	−27(2)
C(41)	55(2)	71(2)	55(1)	1(1)	−11(1)	−9(1)
O(50)	48(1)	57(1)	50(1)	18(1)	10(1)	9(1)
C(50)	77(2)	61(2)	51(1)	14(1)	11(1)	0(2)
O(51)	50(1)	88(1)	96(2)	31(1)	19(1)	4(1)
C(51)	50(1)	49(1)	41(1)	1(1)	6(1)	−5(1)

The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11} + \ldots + 2hka^*b^*U_{12}]$.

performed with a Hewlett-Packard 5890 gas chromatograph, a fused-silica capillary column (25 m) coated with HP-1 cross-linked methyl silicone (gumphase) operating at 100–150°C ($t = 0$ min, 100°C, isothermal, $t = 5$ min, 5°C min^{-1}) and nitrogen as the carrier gas at 2 ml min^{-1} was used. ^{1}H NMR spectra were recorded with Bruker AC-100 (100 MHz, FT), Bruker AC-300 (300 MHz, FT) or Bruker AM-400 (400 MHz, FT) spectrometers on solutions in $CDCl_3$ (internal Me_4Si) or D_2O unless stated otherwise. ^{13}C NMR spectra were recorded with Bruker AC-100 or Bruker AM-400 spectrometers operating at 25, 75 and 100 MHz in $CDCl_3$ (internal Me_4Si) or D_2O (external, 1,4-dioxan at 67.8 ppm). Solvents were dried and purified using conventional procedures.

3.2. 3,6S,9R,10R,11S-1,4,7-Trioxaspiro[5,5]undecane-3,9,10,11-tetrol (**4**)

A stirred, cooled (− 78°C) solution of allyl *β*-D-fructopyranoside (**7**, 18.0 g, 82 mmol) in water (45 ml) and methanol (450 ml) was subjected to ozonolysis until analysis (TLC, dichloromethane–methanol, 4:1, v/v) indicated the absence of compound **7** and a permanent blue coloration had developed. Nitrogen gas was then bubbled through the mixture for approx. 10 min, whereon it was treated with triphenylphosphine (21.48 g, 82 mmol), set aside at

Table 5
Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters (Å^2 $\times 10^3$) for **9**

	x	*y*	*z*	*U*(eq)
H(2A)	−1300(4)	−4500(3)	−8482(12)	67(9)
H(2B)	−1310(3)	−4060(3)	−9154(10)	45(7)
H(3)	−3750 93)	−3090(3)	−8403(10)	46(7)
H(5A)	−3060(4)	−580(3)	−8585(11)	53(7)
H(5B)	−3030(4)	−190(3)	−9222(12)	59(8)
H(8A)	1310(3)	−2110(3)	−9931(11)	50(7)
H(8B)	1450(3)	−2860(3)	−9358(10)	45(7)
H(9)	3570(4)	−1190(3)	−9396(10)	57(8)
H(10)	2210(3)	−1280(3)	−8564(9)	41(6)
H(11)	−80(3)	780(3)	−8951(9)	37(6)
H(20A)	−7768	−6064	−8973	140
H(20B)	−6041	−6546	−9201	140
H(20C)	−7069	−5333	−9483	140
H(30A)	229	1966	−7349	142
H(30B)	−1291	902	−7349	142
H(30C)	−1584	2565	−7420	142
H(40A)	5107	1931	−7661	142
H(40B)	3677	2764	−7951	142
H(40C)	5312	2357	−8254	142
H(50A)	3929	2804	−10328	95
H(50B)	2059	2637	−10161	95
H(50C)	2739	1798	−10651	95

−78°C for 30 min, and then allowed to attain room temperature gradually. The mixture was concentrated in vacuo, treated with water (100 ml), set aside at 5°C for 18 h, during which time triphenylphosphine oxide (23.0 g) crystallized out and which was collected by filtration and washed with water (100 ml). The combined filtrate and washings were concentrated in vacuo and the resultant crystalline material was recrystallized from ethanol to yield pure **4** (15.9 g, 87.5%), m.p. 172.5–174.5°C, $[\alpha]_D$ − 125° (H_2O, constant after 24 h). Anal. calcd. for $C_8H_{14}O_7$: C, 43.25; H, 6.35. Found: C. 42.77; H, 6.28. ^{1}H NMR (300 MHz, D_2O) δ: 4.96 (d, 0.42H, J = 1.9 Hz, H-3$_{ax}$), 4.89 (dd, 0.58H, J = 2.9 and J = 9.2 Hz, H-3$_{eq}$), 4.29 (d, 0,42H, J = 12.1 Hz, H-11$_{ax}$), 3.99 (d, 058H, J = 12.3 Hz, H-11$_{eq}$), 3.14–3.32 (m, 8H, remaining H)[3]. ^{13}C NMR (75 MHz, D_2O): δ 97.20, 96.29, 92.07, 88.71, 70.41, 70.19, 70.12, 69.40, 68.18, 64.64, 64.57, 63.61, 63.13, 60.99 ppm.

3.3. (3R,6S,9R,10R,11S)-3,9,10,11-Tetra-acetoxy- and (3S,6S,9R,10R,11S)-3,9,10,11-tetra-acetoxy-1,4,7-trioxaspiro[5,5]undecanes **8** *and* **9**

A cooled (0°C), stirred solution of compound **4** (9.30 g, 42 mmol) in dry pyridine (100 ml) was treated with acetic

[3] The equatorial/axial proton ratios varied with time.

Table 6
Crystal data and structure refinement for **8**

Identification code	Compound **8**
Empirical formula	$C_{16}H_{24}O_{12}$
Formula weight	408.35
Temperature	293(2) K
Crystal system, space group	Monoclinic, P2$_1$
Unit cell dimensions (25 reflections $36.525 < \theta < 45.359$)	a = 8.7436(3) Å; $\alpha = 90°$
	b = 7.89530(18) Å; $\beta = 102.623(9)°$
	c = 14.6467(4) Å $\gamma = 90°$
Volume	986.67(5) Å^3
Z, calculated density	2, 1.374 Mg/m^3
Absorption coefficient	1.034 mm^{-1}
Diffractometer/scan	Enraf–Nonius CAD4/θ–2θ
Radiation/wavelength	Cu Kα (graphite monochr.)/1.54184 Å
F(000)	432
Crystal size	0.54 × 0.21 × 0.08 mm
θ range for data collection	3.09–69.88°
Index ranges	$0 <= h <= 10$, $0 <= k <= 9$, $-17 <= l <= 17$
Reflections collected	2117
Independent/observed reflections	1995 (R_{int} = 0.0140)/1884 ($[I_o > 2\sigma(I_o)]$)
Absorption correction	Semi-empirical from psi-scans (North et al., 1968)
Range of related transmission factors	0.973 and 1.053
Refinement method	Full-matrix least-squares on F^2
Computing	SHELXL-97 (Sheldrick, 1997)
Data/restraints/parameters	1995/1/298
Goodness-of-fit on F^2	1.057
SHELXL-97 weight parameters	0.1155, 0.1449
Final R indices ($I > 2\sigma(I)$)	R_1 = 0.0492, wR_2 = 0.1468
R indices (all data)	R_1 = 0.0513, wR_2 = 0.1499
Extinction coefficient	0.010(2)
Largest difference: peak and hole	0.278 and −0.475 e Å^{-3}

Table 7
Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **8**

	x	*y*	*z*	*U*(eq)
O(1)	−8255(3)	−1364(3)	−7780(2)	47(1)
C(2)	−7479(5)	−2971(5)	−7691(3)	54(1)
C(3)	−6085(4)	−2934(5)	−8146(2)	51(1)
O(4)	−5041(3)	−1631(4)	−7776(2)	54(1)
C(5)	−5799(4)	−12(5)	−7861(3)	49(1)
C(6)	−7240(4)	−6(5)	−7433(2)	44(1)
O(7)	−6683(3)	−119(4)	−6456(2)	54(1)
C(8)	−7915(5)	−102(6)	−5954(2)	57(1)
C(9)	−8792(4)	1542(5)	−6095(2)	52(1)
C(10)	−9432(4)	1842(5)	−7137(2)	47(1)
C(11)	−8168(4)	1643(5)	−7690(2)	44(1)
O(20)	−6684(3)	−2695(3)	−9125(2)	51(1)
C(20)	−6639(5)	−3046(9)	−10696(3)	78(1)
O(21)	−4516(3)	−3867(5)	−9448(2)	78(1)
C(21)	−5800(4)	−3257(6)	−9710(3)	60(1)
O(30)	−8914(2)	1612(3)	−8663(1)	49(1)
C(30)	−9182(5)	2392(8)	−10231(3)	75(1)
O(31)	−7265(4)	3600 95)	−8976(2)	78(1)
C(31)	−8341(4)	2657(5)	−9243(2)	52(1)
O(40)	−9991(3)	3571(4)	−7304(2)	54(1)
C(40)	−11731(6)	5794(7)	−7250(4)	84(2)
O(41)	−12265(3)	2866(5)	−6947 92)	79(1)
C(41)	−11411(4)	3926(6)	−7139(3)	60(1)
O(50)	−7701(3)	2876(4)	−5732(2)	60(1)
C(50)	−6906(7)	5311(9)	−4836 94)	98(2)
O(51)	−9416(5)	4018(9)	−5010(4)	141(2)
C(51)	−8149(5)	4010(7)	−5168(3)	69(1)
O(100)	−4910(15)	4110(2)	−6397(10)	284(6)

U(eq) is defined as one-third of the trace of the orthogonalized U_{ij} tensor.

anhydride (80 ml), set aside at room temperature for 20 h and processed in the usual manner. A solution of the resultant material in ether (100 ml) was set aside (2 h), and the resultant material collected by filtration. Analysis (GLC) of the material indicated a mixture of compounds **8** and **9** (1:2). Column chromatography (hexane–ethyl acetate, 3:2, v/v) of a portion (1.06 g) of the foregoing product gave compound **9** (0.695 g, 52%), m.p. 160.5–162°C (aqueous MeOH), $[\alpha]_D$ −177°C ($CHCl_3$). Anal. calcd. for $C_{16}H_{22}O_{11}$: C, 49.23; H, 5.68. Found: C, 49.34; H, 5.65%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.93 (dd, 1H, $J_{3,2a} = 8.7$ Hz, $J_{3,2b} = 4.7$ Hz, H-3), 5.39–5.27 (m, 3H, H-9, H-10, H-11), 4.02–3.66 (m, 6H), 2.15–1.99 (4s, each 3H, actyl H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.33 (2*x*), 169.95, 164.41, 95.55, 88.81, 68.88, 68.54, 67.63, 65.76, 61.82, 59.66, 20.94 (2*x*), 20.70, 20.61 ppm. Continued elution then gave material that was a mixture (GLC), followed by compound **8** (144 mg, 11%), m.p. 171–172.5°C (aqueous ethanol), $[\alpha]_D$ −79° ($CHCl_3$). Anal. calcd. for $C_{16}H_{22}O_{11}$: C, 49.23; H, 5.68. Found: C, 48.99; H, 5.64%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.92 (d, 1H, $J_{10,11} = 10.3$ Hz and $J_{10,9} = 3.5$ Hz), 5.37 (m, 1H, H-9), 5.19 (d, 1H, $J_{11,10} = 10.3$ Hz, H-11), 4.06 (dd, 1H, $J_{2a,2b} = 12.3$ Hz and $J_{2a,3} = 2.1$ Hz, H-2a), 3.92 (dd, 1H, $J_{8a,8b} = 13.1$ Hz and $J_{8a,9} = 1.3$ Hz, H-8a), 3.87 (d, 1H, $J = 12$ Hz, H-5a), 3.85 (dd, 1H, $J_{8b,8a} = 13.1$ Hz and $J_{8b,9} = 1.7$ Hz, H-8b), 3.76 (d, 1H, $J = 12.3$ Hz, H-2b), 3.57 (d, 1H, $J = 12.0$ Hz, H-5b), 2 (4s, each 3H, acetyl H). ^{13}C NMR (75 MHz, $CDCl_3$): 170.24, 170.08, 169.78, 169.35, 95.16,87.62, 68.86, 67.43, 67.36, 61.56, 61.49, 60.91, 20.86 (2*x*), 20.60 and 20.52 ppm.

Colorless transparent crystals of **8** suitable for X-ray diffraction studies were obtained from ethyl acetate solution by slow evaporation of the solvent. Colorless transparent crystals of **9** suitable for X-ray diffraction studies were obtained from a methanol/water solution by slow cooling of the solvent. Single crystals were mounted in air on a glass fibre. Intensity data were collected at room temperature. An Enraf-Nonius CAD4 single-crystal diffractometer was used, Cu Kα radiation (λ = 1.54184 Å), θ–2θ scan mode. Unit cell dimensions were determined from the angular setting of 25 reflections. Intensity data were corrected for Lorentz and polarization effects. Semi-empirical absorption correction (psi-scans) (North et al., 1968) was applied.

Crystal data for compound **9** (see Tables 1–5): $C_{16}H_{22}O_{11}$, $M_r = 390.34$, orthorhombic, spacegroup $p2_12_12_1$, $a = 8.0281(2)$, $b = 9.2525(2)$, $c = 25.4333(5)$, $V = 1889.19(8)$ Å^3, $Z = 4$, ρ(calcd) = 1.372 g/cm^3. Crystal data for compound **8** (see Tables 6–10): $C_{16}H_{24}O_{12}$, $M_r = 408.35$, monoclinic, spacegroup $p2_1$, $a = 8.7436(3)$, $b = 7.89530(18)$, $c = 14.6467(4)$, $V = 986.67(5)$ Å^3, $Z = 2$, ρ(calcd) = 1.374 g/cm^3. The structures were solved by the program CRUNCH (de Gelder et al., 1993) and were refined with standard methods (refinement against F^2 of all reflections with SHELXL97 (Sheldrick, 1997) with anisotropic parameters for the nonhydrogen atoms. The hydrogen atoms of the methyl groups were refined as rigid rotors with idealized sp^3 hybridization and a C–H bond length of 0.97 Å to match maximum electron density in a difference Fourier map. All other hydrogens were initially placed at calculated positions and were freely refined subsequently.

Final *R*-indices for **9**: $R_1 = 0.0322$ (for 1905 reflections considered observed ($I > 2\sigma(I)$)), $wR_2 = 0.0914$ (all data) for all 289 parameters.

Final *R*-indices for **8**: $R_1 = 0.0492$ (for 1995 reflections considered observed ($I > 2\sigma(I)$)), $wR_2 = 0.1499$ (all data) for all 298 parameters.

PLUTON drawings (Spek, 1995) of the X-ray structures are shown in Figs. 1 and 2.

3.4. (3R,6S,9R,10R,11S)-3-p-Nitrophenylamino-1,4,7-trioxaspiro[5,5]undecane-9,10,11-triol (**10**)

A stirred solution of compound **4** (0.9 g, 4.05 mmol) in ethanol (10 ml) was treated with *p*-nitroaniline (0.55 g, 4.05 mmol) and glacial acetic acid (0.5 ml) and heated at 70°C for 30 min, The mixture was concentrated in vacuo to approximately half the volume, set aside at room temperature for 1 week, and the crystalline material collected by filtration, washed with a small volume (approx. 4 ml) of ethanol to give compound **10** (1.124 g, 81%), m.p. 223°C, $[\alpha]_D$ +281° (CH_2Cl_2–MeOH, 1:1). Anal. calcd. for

Table 8
Bond lengths (Å) and angles (°) for **8**

O(1)–C(6)	1.414(4)
O(1)–C(2)	1.431(5)
C(2)–C(3)	1.512(5)
C(3)–O(4)	1.403(5)
C(3)–O(20)	1.428(4)
O(4)–C(5)	1.433(5)
C(5)–C(6)	1.525(4)
C(6)–O(7)	1.409(4)
C(6)–C(11)	1.537(5)
O(7)–C(8)	1.431(4)
C(8)–C(9)	1.499(6)
C(9)–O(50)	1.442(5)
C(9)–C(10)	1.524(4)
C(10)–O(40)	1.453(4)
C(10)–C(11)	1.515(4)
C(11)–O(30)	1.432(4)
O(20)–C(21)	1.348(4)
C(20)–C(21)	1.479(6)
O(21)–C(21)	1.205(5)
O(30)–C(31)	1.355(4)
C(30)–C(31)	1.489(5)
O(31)–C(31)	1.196(5)
O(40)–C(41)	1.345(4)
C(40)–C(41)	1.503(7)
O(41)–C(41)	1.195(6)
O(50)–C(51)	1.334(5)
C(50)–C(51)	1.497(8)
O(51)–C(51)	1.180(60
C(6)–O(1)–C(2)	113.1(2)
O(1)–C(2)–C(3)	110.8(3)
O(4)–C(3)–O(20)	110.8(3)
O(4)–C(3)–C(2)	111.3(3)
O(20)–C(3)–C(2)	106.9(3)
C(3)–O(4)–C(5)	111.8(2)
O(4)–C(5)–C(6)	112.0(3)
O(7)–C(6)–O(1)	111.6(3)
O(7)–C(6)–C(5)	106.5(2)
O(1)–C(6)–C(5)	111.1(3)
O(7)–C(6)–C(11)	110.4(3)
O(1)–C(6)–C(11)	107.3(2)
C(5)–C(6)–C(11)	109.9(3)
C(6)–O(7)–C(8)	112.9(2)
O(7)–C(8)–C(9)	110.9(3)
O(50)–C(9)–C(8)	107.7(3)
O(50)–C(9)–C(10)	108.9(3)
C(8)–C(9)–C(10)	109.7(3)
O(40)–C(10)–C(11)	105.4(3)
O(40)–C(10)–C(9)	110.6(3)
C(11)–C(10)–C(9)	111.6(2)
O(30)–C(11)–C(10)	107.9(2)
O(30)–C(11)–C(6)	109.3(3)
C(10)–C(11)–C(6)	111.4(3)
C(21)–O(20)–C(3)	117.4(3)
O(21)–C(21)–O(20)	123.5(3)
O(21)–C(21)–C(20)	125.8(3)
O(20)–C(21)–C(20)	110.7(3)
C(31)–O(30)–C(11)	117.6(3)
O(31)–C(31)–O(30)	123.1(3)
O(31)–C(31)–C(30)	126.2(4)
O(30)–C(31)–C(30)	110.6(3)
C(41)–O(40)–C(10)	117.1(3)
O(41)–C(41)–C(40)	127.0(4)
O(40)–C(41)–C(40)	110.0(4)
C(51)–O(50)–C(9)	117.3(3)
O(51)–C(51)–O(50)	122.7(5)
O(51)–C(51)–C(50)	125.4(5)
O(50)–C(51)–C(50)	111.7(4)

Table 9
Anisotropic displacement parameters (Å^2 × 10^3) for **8**

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
0(1)	43(1)	50(1)	52(1)	−1(1)	17(1)	−2(1)
C(2)	59(2)	51(2)	56(2)	5(2)	19(2)	2(2)
C(3)	50(2)	49(2)	54(2)	1(1)	11(1)	5(2)
O(4)	40(1)	60(2)	61(1)	−4(1)	9(1)	6(1)
C(5)	38(1)	55(2)	55(2)	−3(2)	15(1)	1(1)
C(6)	39(1)	53(2)	41(1)	−3(1)	11(1)	−1(1)
O(7)	50(1)	68(2)	43(1)	−2(1)	9(1)	9(1)
C(8)	65(2)	69(2)	41(2)	8(2)	19(1)	7(2)
C(9)	51(2)	65(2)	46(2)	−2(2)	21(1)	−1(2)
C(10)	44(1)	51(2)	48(2)	2(1)	15(1)	4(1)
C(11)	41(1)	52(2)	40(1)	−3(1)	10(1)	−1(1)
O(20)	50(1)	57(1)	51(1)	−3(1)	17(1)	7(1)
C(20)	71(2)	110(4)	61(2)	−9(2)	27(2)	3(3)
O(21)	57(1)	92(2)	90(2)	−2(2)	30(1)	17(2)
C(21)	54(2)	67(2)	66(2)	−7(2)	24(2)	2(2)
O(30)	45(1)	59(1)	42(1)	1(1)	10(1)	−1(1)
C(30)	74(2)	101(4)	48(2)	11(2)	10(2)	5(2)
O(31)	103(2)	69(2)	65(2)	2(2)	27(2)	−27(2)
C(31)	60(2)	49(2)	49(2)	2(1)	17(1)	9(2)
O(40)	50(1)	54(1)	60(1)	1(1)	19(1)	8(1)
C(40)	75(3)	82(3)	96(3)	2(3)	21(2)	32(3)
O(41)	53(1)	98(2)	91(2)	8(2)	29(1)	7(2)
C(41)	44(2)	80(3)	55(2)	2(2)	14(1)	13(2)
O(50)	56(1)	75(2)	53(1)	−15(1)	20(1)	0(1)
C(50)	90(3)	102(4)	90 93)	−38(3)	−7(3)	4(3)
O(51)	104(3)	161(5)	181(5)	−99(4)	84(3)	−16(3)
C(51)	67(2)	83(3)	58(2)	−18(2)	16(2)	11(2)
O(100)	278(12)	225(14)	314(15)	23(12)	−10(11)	−25(11)

The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11} + \ldots + 2hka^*b^*U_{12}]$.

$C_{14}H_{18}N_2O_8$: C, 49.12; H, 5.30; N 8.18. Found: C, 49.12; H 5.36; N, 8.01%. ^{1}H NMR (300 mHz, DMSO-D_6): δ 8.05 (d, 2H, $J = 9.2$ Hz, aromatic H), 7.96 (d, 1H, $J = 6.6$ Hz, NH), 6.88 (d, 2H, $J = 9.2$ Hz, aromatic H), 5.03 (dd, 1H, $J =$ 6.3 Hz and $J = 2.5$ Hz, H-3), 4.64 (d, 1H, $J = 5.9$ Hz, OH), 4.58 (d, 1H, $J = 3.7$ Hz, OH), 4.45 (d, 1H, $J = 8.2$ Hz, OH), 4.02 (m, 2H), 3.71 (m, 1H), 3.64–3.51 (m, 4H), 3.30–3.15 (m, 2H).

3.5. (3R,6S,9R,10R,11S)-3-p-Nitrophenylamino-9,10,11-triacetoxy-1,4,7-trioxaspiro[5,5]undecane (**11**)

A sample (165 mg) of the foregoing material in anhydrous pyridine (1.5 ml) was treated with acetic anhydride (1 ml), stored overnight at room temperature, and processed in the usual manner to give **11** (148 mg, 65.5%), m.p. 188–197°C (ethanol), $[\alpha]_D$ −151° ($CHCl_3$). Anal. calcd. for $C_{20}H_{22}N_2O_{11}$: C, 51.28; H, 5.10; N, 5.98. Found: C, 51.44; H, 5.13; N, 5.96%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.13 (m, 2H, aromatic H), 6.78 (m, 2H, aromatic H), 5.62 (d, 1H, $J = 7.2$ Hz, N–H), 5.41 (dd, 1H, $J = 3.5$ Hz and $J =$ 10.3 Hz, H-10), 5.30 (m, 1H, H-9), 5.18 (d, $J = 10.3$ Hz, H-11), 5.07 (dd, 1H, $J = 2.4$ Hz and $J = 11.7$ Hz, H-3), 4.29 (dd, 1H, $J = 2.7$ Hz and $J = 11.7$ Hz, H-2a), 3.95 (dd, 1H, $J =$ 1.3 Hz and $J = 13.1$ Hz, H-8a), 3.87 (dd, 1H, $J = 13.1$ Hz,

Table 10
Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($Å^2 \times 10^3$) for **8**

	x	*y*	*z*	*U*(eq)
H(2A)	−8250(6)	−3900(8)	−8070(4)	76(15)
H(2B)	−7060(4)	−3210(5)	−7000(2)	39(8)
H(3)	−5530(5)	−4090(6)	−7980(3)	56(11)
H(5A)	−6280(5)	310(6)	−8510(3)	57(11)
H(5B)	−5090(4)	840(5)	−7500(3)	40(9)
H(8A)	−7500(4)	−210(6)	−5330(3)	51(10)
H(8B)	−8510(6)	−1090(8)	−6220(3)	71(14)
H(9)	−9580(5)	1580(7)	−5790(3)	58(10)
H(10)	−10380(5)	980(7)	−7450(3)	62(12)
H(11)	−7430(4)	2490(5)	−7590(2)	35(8)
H(20A)	−7720	−2792	−10720	118
H(20B)	−6566	−4075	−11033	118
H(20C)	−6173	−2135	−10974	118
H(30A)	−8472	1928	−10581	112
H(30B)	−9580	3456	−10500	112
H(30C)	−10037	1621	−10250	112
H(40A)	−10760	6406	−7087	126
H(40B)	−12404	6136	−6846	126
H(40C)	−12231	6034	−7888	126
H(50A)	−7181	5973	−4347	147
H(50B)	−6817	6037	−5348	147
H(50C)	−5922	4755	−4602	147

$J = 1.3$ Hz, H-8b), 3.74 (d, 1H, $J = 11.6$ Hz, H-2b), 3.72 (d, 1H, $J = 12.4$ Hz, H-5a), 3.47 (d, 1H, $J = 12.4$ Hz, H-5b), 2.17–2.00 (3s, each 3H, acetyl H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.27, 169.95, 169.67, 150.45, 139.82, 126.12 (2*x*), 112.61 (2*x*), 95.54, 75.23, 68.85, 67.55, 67.39, 62.24, 61.57, 59.90, 20.89, 20.60, 20.56 ppm.

3.6. (3R,6S,9R,10R,11S)-3-Bromo-9,10,11-triacetoxy-1,4,7-trioxaspiro[5,5]undecane (**12**)

A stirred solution of a mixture of compounds **8** and **9**, vide supra (0.5 g) in 33% hydrogen bromide solution in glacial acetic acid (0.5 ml) was maintained at room temperature for 10–15 min. The mixture was treated with dichloromethane (30 ml) and ice-water (20 ml). The separated organic layer was washed sequentially with ice cold saturated aqueous sodium hydrogen carbonate solution and ice-water, dried (Na_2SO_4) and concentrated in vacuo to give **12** (0.49 g, 94%) as a syrup, $[\alpha]_D$ − 39° ($CHCl_3$). ^{1}H NMR (100 MHz, $CDCl_3$): δ 6.37 (d, 1H, $J = 17$ Hz, H-3), 5.40–5.10 (m, 3H, H-9,10,11), 4.27 (dd, 1H, $J = 2$ Hz and $J = 12$ Hz, H-2), 4.13–3.53 (m, 5H), 2.20–2.00 (3s, each 3H, acetyl H).

*3.7. (3S,6S,9R,10R,11S)-3-Methoxy-9,10,11-triacetoxy-1,4,7-trioxaspiro[5,5]undecane (**13**) and (3R,6S,9R,10R,11S)-3-methoxy-9,10,11-triacetoxy-1,4,7-trioxaspiro[5,5]undecane (**14**)*

A mixture of compounds **8** and **9** (1.0 g, 2.56 mmol) was treated and processed as described above and the resulting compound **12** (1.05 g, 100%), treated with methanol (20 ml) followed by anhydrous sodium carbonate (1.03 g) and then stirred at room temperature for 30 min. The mixture was diluted with dichloromethane (20 ml), filtered, the organic layer washed with dichloromethane (10 ml) and the combined filtrate and washings concentrated in vacuo. Column chromatography (hexane–ethyl acetate, 2:1, v/v) gave compound **13** (448 mg, 48%), mp 133.5–135°C (di-isopropylether) $[\alpha]_D$ − 199° ($CHCl_3$). Anal. calcd. for $C_{15}H_{22}O_{10}$: C, 49.72; H, 6.12. Found: C, 49.91; H, 6.06%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.35 (m, 2H, H-9,10), 5.27 (d, 1H, $J = 10.1$ Hz, H-11), 4.61 (dd, 1H, $J_{3,4a} = 13.2$ Hz and $J_{3,4b} = 8.4$ Hz, H-3), 3.96 (dd, 1H, $J_{8a,8b} = 13.2$ Hz and $J_{8a,9} = 1.2$ Hz, H-8a), 3.77 (m, 3H, H-8b,2a,5), 3.68 (d, 1H, $J = 12.4$ Hz, H-5b), 3.53 (dd, 1H, $J_{2b,3} = 8.4$ Hz and $J_{2b,2a} = 11.6$ Hz, H-2b), 3.45 (s, 3H, OCH_3), 2.15–1.99 (3s, each 3H, acetyl H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.31 (2*x*), 169.89, 97.18, 95.46, 68.98,68.62, 67.74, 64.96, 61.59, 61.13, 55.84, 20.92, 20.72 and 20.59 ppm.

Continued elution then gave **14** (192 mg, 21%) which was recrystallized from aqueous propan-2-ol, m.p. 174.5–175°C, $[\alpha]_D$ − 56.8° ($CHCl_3$). Anal. calcd. for $C_{15}H_{22}O_{10}$: C, 49.72; H, 6.12. Found: C, 49.89; H, 6.05%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.39 (m, 2H, H-9,10), 5.19 (d, 1H, $J_{11,10} = 10.2$ Hz, H-11), 4.53 (d, 1H, $J = 2.0$ Hz, H-3), 3.96 (dd, 1H, $J_{2a,3} = 2.2$ Hz and $J_{2a,2b} = 11.8$ Hz, H-2a), 3.93 (dd, 1H, $J_{8a,9} = 1.4$ Hz and $J_{8a,8b} = 13.1$ Hz, H-8a), 3.85 (dd, 1H, $J_{8b,9} = 1.7$ Hz and $J_{8b,8a} = 13.1$ Hz, H-8b), 3.81 (d, 1H, $J = 11.8$ Hz, H-5a), 3.71 (d, 1H, $J = 11.8$ Hz, H-2b), 3.46 (d, 1H, $J = 11.8$ Hz, H-5b), 3.43 (s, 3H, OCH_3), 2.16–1.98 (3s, each 3H, acetyl H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.45, 170.45, 170.29, 169.77, 95.24, 94.34, 69.04, 67.62, 67.52, 61.93, 61.38, 59.91, 55.12, 20.90, 20.73, 20.54.

3.8. (3S,6S,9R,10R,11S)-3-Benzyloxy-1,4,7-trioxaspiro[5,5]undecane-9,10,11-triol (**16**)

A stirred solution of compound **4** (223 mg, 1 mmol) in 1,2-dimethoxyethane (5 ml) and water (5 ml) was treated sequentially with potassium hydroxide (156 mg, 2.78 mmol), benzyl chloride (0.25 g, 1.97 mmol) and 18-crown-6 (5 mg). The mixture was maintained at 70°C for 7 h, set aside at room temperature for 50 h, diluted with water (40 ml), extracted with ether (2 × 20 ml), and the aqueous layer concentrated in vacuo. Column chromatography (dichloromethane–methanol 6:1, v/v) gave compound **16** (222 mg, 71%), m.p. 147.5–151.5°C (ethyl acetate), $[\alpha]_D$ − 201° ($CHCl_3$). Anal. calcd. for $C_{15}H_{20}O_7$: C, 57.69; H, 6.45. Found: C, 57.56; H, 6.46%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31 (m, 5H, aromatic H), 4.87 (d, 1H, $J = 11.8$ Hz, benzylic H), 4.79 (dd, 1H, $J = 4.5$ Hz and $J = 8$ Hz, H-3), 4.58 (d, 1H, $J = 11.8$ Hz, benzylic H), 3.98 (m, 2H), 3.87–3.77 (m, 4H), 3.73–3.58 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.08 (1*x*), 128.38 (2*x*), 127.82 (3*x*), 95.86, 95.69, 70.05 (2*x*), 69.70, 69.21, 66.17, 63.53 and 61.73 ppm.

3.9. (3RS,6S,9R,10R,11S)-3-Hydroxy-9,10,11-triacetoxy-1,4,7-trioxaspiro[5,5]undecane (**17**)

A stirred solution of the bromide **12** (493 mg, 12 mmol) in 1,2-dimethoxyethane (10 ml) was treated with sodium hydrogen carbonate (120 mg) followed by water (1 ml) and then set aside at room temperature for 10 min when analysis (TLC, hexane–ethyl acetate, 1:1, v/v) indicated the absence of **17**. The mixture was treated with dichloromethane (20 ml), dried (Na_2SO_4) and concentrated in vacuo to give **17** (372 mg, 89%) as a foam, $[\alpha]_D$ −117° (ethanol, 1 min). ^{1}H NMR (100 MHz, $CDCl_3$: δ 5.45–5.15 (m, 3H, H-9,10,11), 5.13–4.85 (m, 1H, H-3), 4.09–3.39 (m, 6H, H-2a,2b,5a,5b,8a,8b), 2.16–1.99 (3s, each 3H, acetyl H). ^{13}C NMR (25 MHz, $CDCL_3$): δ 170.38, 170.28, 169.25, 95.27, 94.53, 90.64, 78.35, 77.08, 75.81, 68.93, 67.76, 67.67, 67.51, 65.90, 62.69, 62.35, 61.29, 59.81, 20.57, 20.54 and 20.44 ppm.

3.10. (3R,6S,9R,10R,11S)-9,10,11-Ttriacetoxy-3-trichloroacetamido-1,4,7-trioxaspiro[5,5]undecane (**18**)

A stirred solution of compound **17** (650 mg, 1.87 mmol) in dry acetonitrile (10 ml) was treated sequentially with trichloroacetonitrile (0.65 ml) and sodium hydride (63 mg, 2.63 mmol) and set aside at room temperature for 20 min. The mixture was filtered through a layer (approx. 1 cm) of silica gel, the inorganic material washed with acetonitrile (2 × 5 ml) and the combined filtrate and washings concentrated in vacuo. Column chromatography (hexane–ethylacetate, 1:1, v/v) of the resultant material yielded compound **18** (665 mg, 725) as a foam, $[\alpha]_D$ −55° ($CHCl_3$). ^{1}H NMR (100 MHz, $CDCl_3$): δ 8.64 (bs, 1H, NH), 6.08 (bs, 1H, H-3), 5.50–5.07 (m, 3H, H-9,10,11), 4.23–3.55 (m, 6H, residual H), 2.17–1.99 (3s, each 3H, acetyl H).

3.11. (3S,6S,9R,10R,11S)-9,10,11-Triacetoxy-3-trichloroacetamido-1,4,7-trioxaspiro-[5,5]undecane (**21**)

A stirred mixture of compound **17** (530 mg, 1.52 mmol) and anhydrous potassium carbonate (536 mg) in dichloromethane (10 ml) was treated with trichloroacetonitrile (770 mg, 5.33 mmol). The mixture was set aside at room temperature for 6 h, filtered, the inorganic material washed with dichloromethane (2 × 5 ml), and the combined filtrate and washings concentrated in vacuo. Column chromatography (hexane–ethyl acetate–triethylamine, 50:50:1, v/v/v) of the crude product gave **21** (492 mg, 65.5%), $[\alpha]_D$ −154.5° ($CHCl_3$). ^{1}H NMR (100 MHz, $CDCl_3$): δ 8.64 (s, 1H, NH), 6.20 (dd, 1H, J = 5.6 Hz and J = 8.1 Hz, H-3), 5.37 (bs, 3H, H-9,10,11), 4.23–3.71 (m, 6H, residual H), 2.16–2.00 (3s, each 3H, acetyl H).

3.12. (3R,6S,9R,10R,11S)-3-O-(1′,2′;5′,6′-Di-O-isopropylidene-α-D-glucofurano-3′-yl)-9,10,11-triacetoxy-1,4,7-trioxaspiro[5,5]undecane (**20**)

A stirred, cooled (− 78°C) mixture of compound **18** (665 mg, 1.35 mmol), 1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (**19**, 351 mg, 1.35 mmol; Verhart et al., 1992) and molecular sieves 3 Å (1.0 g), maintained under N_2, was treated with 0.1 M boron trifluoride in dichloromethane (3.37 ml, 0.25 equiv.). The mixture was stirred at the same temperature for 3 h when potassium carbonate (400 mg), followed by dichloromethane (20 ml) and saturated sodium hydrogen carbonate solution (10 ml) were added and the mixture allowed to attain room temperature. The mixture was then filtered, the inorganic material washed with dichloromethane (2 × 5 ml), the combined filtrate and washings separated and the aqueous layer extracted with dichloromethane (10 ml). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo to give an oil (980 mg). Column chromatography (hexane–ethyl acetate, 2:1, v/v) of this material gave compound **19** (195 mg), m.p. 109–111°C, $[\alpha]_D$ −18° ($CHCl_3$), lit. (Verhart et al., 1992) m.p. 110°C, $[\alpha]_D$ −18.8° ($CHCl_3$) followed by compound **20** (255 mg, 32%) obtained as an oil which was crystallized from di-isopropyl ether (196 mg, 25%), m.p. 151–153.5°C, $[\alpha]_D$ −41° ($CHCl_3$). Anal calcd. for $C_{26}H_{38}O_{15}$: C, 52.88, H, 6.49. Found: C, 52.62; H, 6.55. ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ 5.85 (d, 1H, J = 3.6 Hz, H-1′), 5.39 (dd, 1H, $J_{10,9}$ = 3.5 Hz and $J_{10,11}$ = 10.4 Hz, H-10), 5.36 (m, 1H, H-9), 5.17 (d, 1H, $J_{11,10}$ = 10.4 Hz, H-11), 4.91 (d, 1H, $J_{3,2a}$ = 2.1 Hz, H-3), 4.51 (d, 1H, $J_{2',1'}$ = 3.6 Hz, H-2′), 4.27 (d, 1H, $J_{3'4'}$ = 2.9 Hz, H-3′), 4.20 (m, 1H, H-5′), 4.12 (dd, 1H, $J_{6'a,6'b}$ = 8.6 Hz and $J_{6'a,5'}$ = 6.0 Hz, H-6′a), 4.08 (dd, 1H, $J_{4',3'}$ = 2.9 Hz and $J_{4',5'}$ = 8.6 Hz, H-4′), 3.98 (dd, 1H, $J_{6'b,5'}$ = 5.2 Hz and $J_{6'b,6'a}$ = 8.6 Hz, H-6b), 3.93 (dd, 1H, $J_{2a,3}$ = 2.3 Hz and $J_{2a,2b}$ = 11.7 Hz, H-2a) (at 40°C), 3.90 (dd, 1H, $J_{8a,9}$ = 1.1 Hz, H-8a), 3.83 (d, 1H, $J_{5a,5b}$ = 11.8 Hz, H-5a), 3.82 (dd, 1H, $J_{8a,8b}$ = 13.1 Hz and $J_{8b,9}$ = 1.8 Hz, H-8b) (at 25°C), 3.70 (d, 1H, $J_{2b,2a}$ = 1.7 Hz, H-2b), 3.51 (d, 1H, J = 11.8 Hz, H-5b), 2.17–1.98 (3s, each 3H, acetyl H), 1.50–1.31 (4s, each 3H, CMe_2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.33, 170.27, 169.82, 112.14, 109.20, 105.24, 95.19, 94.16, 84.05, 81.34, 80.34, 72.46, 68.99, 67.73, 67.72, 67.53, 61.77, 61.44, 60.52, 26.90, 26.81, 26.27, 25.34, 20.95, 20.63 and 20.58 ppm.

In another experiment the trichloroacetamidate **21**, vide supra (232 mg, 0.471 mmol) was reacted with compound **19** (122 mg, 0.471 mmol) in the presence of boron trifluoride etherate and processed in the manner described above to give compound **20** (118 mg, 42%). The physical and spectral properties of which were identical with the above described material.

Crystallographic data (excluding structure factors) for the structures reported in this article have been deposited with the Cambridge Crystallographic Data Centre as

supplementary publication no. CCDC-101081. Copies of available material can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336033; e-mail: deposit@chemcrys.cam.ac.uk).

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