Tetrahedron Vol. 48, No. 43, pp. 9553-9560, 1992
Printed in Great Britain

0040-4020/92 $5.00+.00

D-Xylofuranose: Conversion to its' 3,5-Oxetane via an Unusual Reductive Displacement of Phthalimide and Subsequent Regioselective Ring Opening.

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(*Received in UK 26 August* 1992)

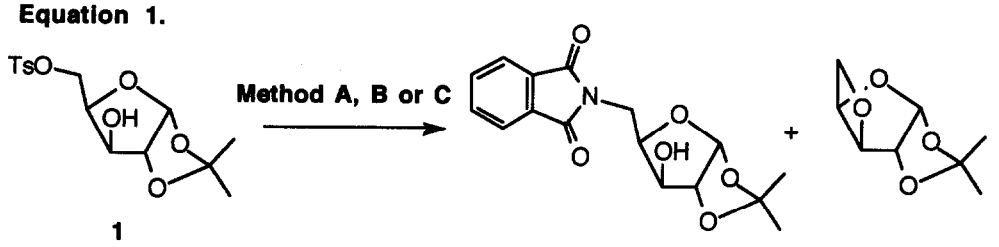
Abstract: 3,5-anhydro-1,2-O-isopropylidene-α-D-xylofuranose has been prepared from the corresponding 5-phthalimido derivative in quantitative yield, and its' formation involves an unusual phthalimide substitution in the presence of sodium borohydride in methanol. A mechanism is proposed for this unusual cyclisation, which involves initial activation of the phthalimide. Subsequent Lewis-acid catalysed ring openings have been achieved in a regiospecific manner.

As part of a programme aimed at utilising D-xylose as a starting material for the synthesis of certain nitrogen containing natural products, we had occasion to prepare the 5-tosylate derivative **1**[1]. Attempts to carry out a substitution of the tosylate of **1** with one (**Method A**) and two (**Method B**) equivalents of potassium phthalimide afforded the expected substituted product **2** in each case; however, the oxetane **3**[2] was also obtained [**2** : **3** = 2 : 1 and 1 : 1 respectively, quantitive total yield] (**Equation 1**). Expecting that the oxetane **3** would behave as a precursor of **2**, and other useful synthetic intermediates by regioselective ring opening[2b,3,4] with nucleophiles under Lewis-acid conditions[3], we examined the formation of the oxetane **3** under various conditions. We report herein the results of these investigations, the unusual and efficient substitution of phthalimide to form oxetane **3** under reducing conditions and the subsequent Lewis-acid catalysed ring opening of the oxetane.

In order to check if the increased amount of oxetane **3** obtained from **Method B** was due to base catalysed cyclisation of phthalimide **2**, **2** was treated separately with excess potassium phthalimide in N,N-dimethylformamide (DMF) and sodium methoxide in methanol. Phthalimide **2** was found to be stable under either of both these conditions. As expected, phthalimide is a poor leaving group and oxetane **3** does not result from direct cyclisation of **2**, despite the proximity of the phthalimide group to the hydroxy group. Phthalimide **2** is also stable to excess sodium methoxide in methanol, despite the high yield of the oxetane **3** obtained when tosylate **1** is treated with sodium methoxide under identical conditions. Therefore, proximity of the hydroxy group to the potential leaving group (phthalimide) alone is not sufficient to cyclise phthalide **2** to oxetane **3**. The result of the increased yield of oxetane **3** in **Method B** (**Equation 1**) is consistent with more rapid direct cyclisation of tosylate **1** under higher base concentration.

However, having prepared the phthalimide **2**, we attempted to reduce the imide moiety to generate the free amine **4** (**Equation 2**) using sodium borohydride in methanol and sodium borohydride in ethanol (followed by hydrolysis)[5]. To our surprise, the phthalimide was converted in quantitive yield to the oxetane **3** under these conditions, despite having already demonstrated the lack of reactivity of the phthalimide group to displacement by the hydroxy group using sodium methoxide in methanol.

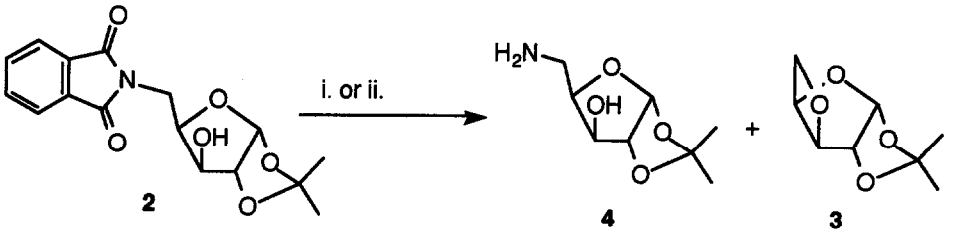
Equation 1.



1 2 3

A; 1 mol equiv. potassium phthalimide, DMF, 150 °C, 5h	66	:	33 %
B; 2 mol equiv. potassium phthalimide, DMF, 150 °C, 5h	50	:	50 %
C; NaOMe, MeOH, RT, 14h			82 %[2]

Equation 2.



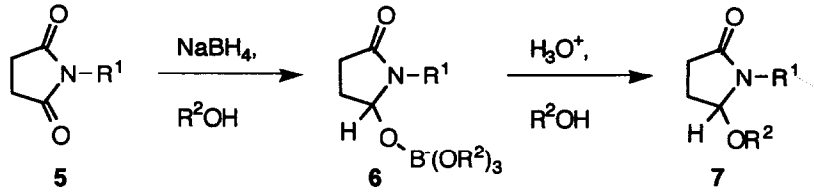
2 4 3

i; $NaBH_4$, MeOH, 14h, RT, then 10 % HCl	0	:	100 %
ii; $NaBH_4$, EtOH, 14h, RT, then 10 % HCl	0	:	100 %

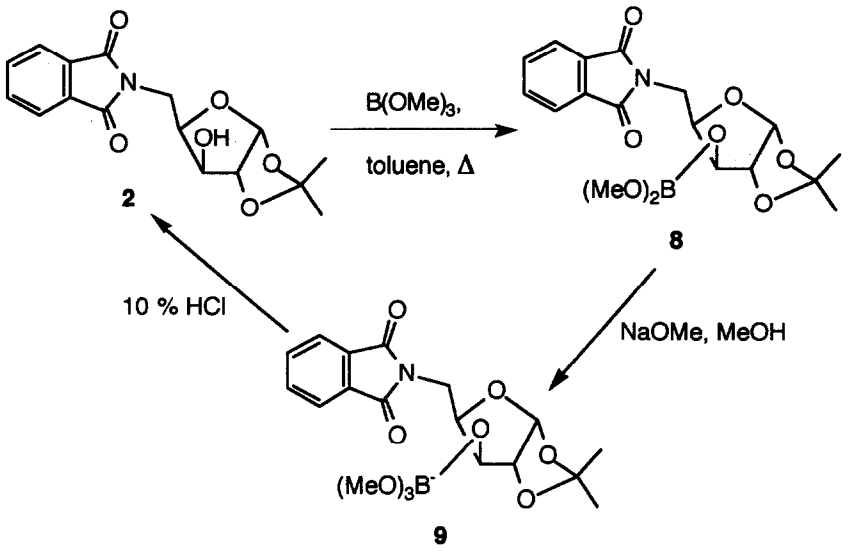
As far as we are aware, this is the first example of the substitution of a phthalimide to form an oxetane and we believe that the cyclisation of phthalimide **2** to the oxetane **3** procedes via initial reduction of the imide, as demonstrated by the following observations: Firstly, phthalimide itself could not be isolated from either of the reactions in **Equation 2**, only small quantities (ca. 30 %) of the crude reduced phthalimide-derived product **12** was isolated from the reaction mixture after repeated extractions of the aqueous extracts with diethylether [i.r. stretch (C:O) of 1707 cm^{-1} for **12** versus 1760 cm^{-1} for phthalimide itself]. Secondly, although reduction of phthalimide may occur after cyclisation of **2**, we know that **2** is stable to methoxide (*vide supra*) suggesting that reduction occurs prior to cyclisation. Thirdly, it is well known[5] that imides of general structure **5** can be rapidly reduced by addition of one hydride equivalent from sodium borohydride in alcohol solvents, the result of which would be a borate ester of type **6** (**Equation 3**). Usually, acidic hydrolysis of the intermediate **6** is employed to derive alkoxy lactam **7**. Fourthly, borohydride rather than borate plays a necessary role in the cyclisation of phthalimide **2**, as shown by the fact that when phthalimide **2** was treated with excess trimethylborate under azeotropic conditions (toluene) to remove methanol (deriving borate ester **8**[6]), treated with sodium methoxide in methanol (deriving "ate"-complex **9**), cyclisation fails to occur (**Equation 4**) and phthalimide **2** is recovered after acidic hydrolysis of the borate ester.

We therefore suggest that the mechanism of cyclisation of phthalimide **2** to oxetane **3** occurs as shown in **Scheme 1**, i.e. initial reduction of the imide of **2** providing a borate "ate"-

Equation 3.



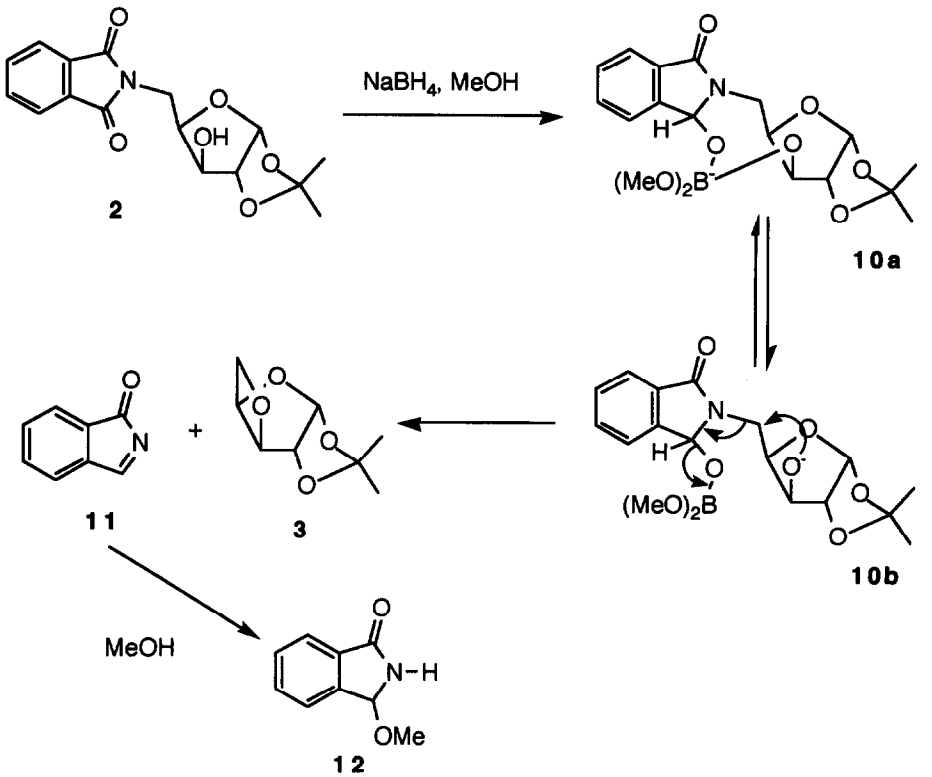
Equation 4.



complex possibly possessing structure **10a**. The complex **10a** can also exist in equilibrium with its' open-chain, uncomplexed form **10b** which can be followed by cyclisation of the now activated leaving group by the deprotonated hydroxy function of **10b**. The phthalimide derived acyl imine **11** rapidly reacts with methanol to give the alkoxy lactam **12** as the by-product. This result raises the possibility of using imides as "armable" leaving groups for the preparation of small rings under reducing, basic conditions.

Since oxetane **3** has been regioselectively ring opened under basic conditions at C-5 using sulphur[2a] and cuprate[4a] nucleophiles, we briefly examined the ring opening of **3** under Lewis-acidic conditions. Oxetanes can be efficiently ring opened under strongly Lewis-acidic conditions ($TiCl_4$ or ZnI_2) at the more substituted carbon[3] (analogous to an S_N1 process). Less Lewis-acidic (BF_3), non-Lewis-acidic and basic conditions, however favour S_N2-like ring opening at the least hindered carbon of oxetanes[4]. If oxetane **3** could be ring-opened under strongly Lewis-acidic conditions in an S_N1 manner, the xylo-configuration could be inverted at C-3 to a ribo-configuration. However one might expect that approach of a nucleophile from the same side of the furanose ring as the acetonide would be disfavoured, due to dipolar and steric repulsions of the C-2 oxygen moiety.

Scheme 1.



This expectation was born out by the experiments outlined in **Equation 5** and **Table 1**. Thus, under all the conditions examined (**Table 1**), oxetane **3** could be regiospecifically ring-opened at the least-hindered C-5 postion only, affording the xylo-configuration products **13**. It is noteworthy that all yields are unoptimised and 300 MHz ^{1}H n.m.r. analysis of the crude reaction mixtures showed no evidence for any other products.

Ring opening to afford bromide **13a** was straight forward using borontrifluoride-bromotrimethylsilane (Entry 1, **Table 1**), and the identical product **13a** was obtained, rather than **13b**, when attempting to ring open with vinylmagnesiumbromide-borontrifluoride. Oxetane **3** is resistant to ring-opening by vinylmagnesium bromide alone, therefore **13a** results from borontriflouride catalysed ring opening with bromide ion (Entry 2). When titanium(IV) chloride was used as the catalyst, competitive ring opening was observed. Thus, azidotrimethylsilane-titanium(IV) chloride gave a mixture of ring opened products **13c** and **13d**, with azide being the more efficient nucleophile (Entry 3). The problem of competitive ring opening could be avoided though by using borontrifluoride-azidotrimethylsilane (Entry 4).

The oxetane **3** required a strong Lewis-acid to give sufficient activation for ring opening. When oxetane **3** was treated with titanium(IV) isopropoxide-azidotrimethylsilane, no reaction occurred over several hours at room temperature (Entry 5). Attempts to use weak nucleophiles to

Equation 5.

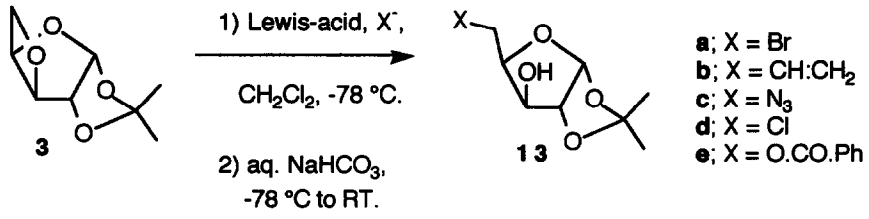
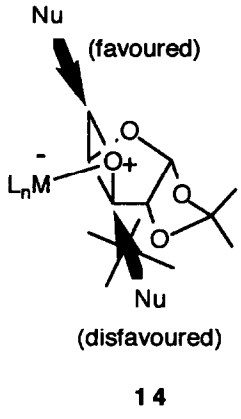


Table 1.

Entry	Lewis-acid	Nucleophile X^-	Product(s)[a] **13**	Yield[f] %
1	$BF_3.Et_2O$	Me_3SiBr	**13a**[b]	60
2	$BF_3.Et_2O$		**13a**[b]	51
3	$TiCl_4$	Me_3SiN_3	**13c**[c] **13d**[d]	57 22
4	$BF_3.Et_2O$	Me_3SiN_3	**13c**[c]	56
5	$Ti(O^iPr)_4$	Me_3SiN_3	No reaction	
6	$TiCl_4$	None	**13d**[d]	48
7	$TiCl_4$	$PhCO_2H$	**13d**[e]	43



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a, See reference 6. b, See reference 7. c, See reference 8. d, See reference 9.
e,See reference 10. f, All yields are isolated yields, after SiO_2 chromatography.

ring open the oxetane **3** catalysed by strong Lewis-acids were uniformly unsuccessful, as exemplified by Entry 7, attempts to isolate benzoate **13e** by ring opening with benzoic acid resulted not in **13e**, but the chloride **13d** which is the result of direct attack of the oxetane **3** by titanium(IV) chloride (see Entry 6). All the results shown in **Table 1** can be interpreted in terms of an S_N2-type ring opening of a Lewis-acid activated oxetane complex of type **14**, which avoids severe repulsions between the C-2 oxygen function and the incoming nucleophile.

Experimental.

Dry tetrahydrofuran was freshly distilled from benzophenone and sodium, under argon, immediately prior to use. Dichloromethane was distilled over calcium hydride. Light petroleum refers to the fraction boiling in the range 40-60 °C.

T.l.c. was performed on Schleicher and Schull plastic or aluminium sheets coated with silica gel (F1500 LS254); the chromatograms were initially examined under u.v. light and then

developed either with iodine vapour or an ethanolic anisaldehyde (1.0 %) solution containing sulphuric acid (9 %) used as a spray and visualised by heating with a heat gun. Column chromatography was achieved under medium pressure, using Merck Kieselgel H (Type 60).

All anhydrous, low temperature reactions were carried out in glassware which was dried prior to use by storage in a glass oven maintained at 140 °C and cooled under a stream of argon. Evaporations were carried out using a Buchi rotary evaporator or Buchi cold-finger rotary evaporator. Kugelrohr distillations were carried out using a Buchi GKR-51 Kugelruhr apparatus.

M.p.'s were determined using an Electrothermal melting point apparatus and were uncorrected and optical rotations were recorded on a Optical Activity AA-1000 polarimeter. ^1H spectra were recorded at 200 or 300 MHz on a Bruker AC200 or AC300 n.m.r. spectrometers respectively. ^{13}C spectra were recorded at 75.6 MHz on a Bruker AC300. Both ^1H and ^{13}C spectra were recorded using $CHCl_3$ and $CDCl_3$ as internal standards respectively. I.r. spectra were recorded on a Perkin-Elmer 783 equipped with a PE600 data station and u.v. spectra were recorded on a Perkin-Elmer λ15 spectrometer. Electron impact (e.i.) (70 e.v.) and chemical ionisation (c.i.) spectra were recorded with a Kratos MS25. Fast atom bombardment (f.a.b.) spectra were recorded on a Kratos MS50, using a *meta*-nitrobenzylalcohol matrix and accurate mass determinations were carried out on a Kratos Concept IS spectrometer. Microanalyses were performed using a Carlo-Erba 1106 elemental analyser.

Preparation of 1,2-O-isopropylidine-5-deoxy-5-phthalimido-D-xylofuranose 2. 1,2-*O*-Isopropylidine-5-toluene-*p*-sulphonyl-α-D-xylofuranose **1**[1] (20.20 g, 0.60 mol) and potassium phthalimide (16 g, 0.85 mol) were stirred in dimethylformamide (250 ml) at 150 °C for 5 hours. The solution was diluted with ethyl acetate (500 ml) and washed with water (3 X 200 ml). Drying and evaporation of the organic layer gave 17 g of a crude product as a white crystalline solid. Recrystalllisation from ether gave 1,2-*O*-isopropylidine-5-deoxy-5-phthalimido-α-D-xylofuranose **2** (12.0 g, 66 %): m.pt. 109 °C; $[\alpha]_D^{24}$ 5.14 ° (c. 0.07, $CHCl_3$); υ_{max} (KBr disc) *inter alia* 3420 (br, OH), and 1383 and 1373 (CO) cm^{-1}; δ (^1H, 300 MHz, $CDCl_3$) 1.30 and 1.49 (each 3H, s, C.$\underline{Me}_2$), 3.53 (1H, dd, J = 8.8 and 14.8 Hz, C-5 H), 3.76 (2H, m, C-3 H and OH), 4.15-4.22 (2H, m, C-5 H and C-4 H), 4.61 (1H, d, J = 3.6 Hz, C-2 H), 5.95 (1H, d, J = 3.6 Hz, C-1 H), 7.78-7.75 and 7.89-7.86 (each 2H, m, 2 x 2 phthalimide H's) (addition of D_2O caused the signal at δ 3.76 to collapse to a d, J = 1.9 Hz); δ (^{13}C, 75.6 MHz, $CDCl_3$) 25.9 and 26.6 (2 x C.$\underline{Me}_2$), 34.8 (C-5), 73.8 (C-3), 78.1 (C-2), 84.7 (C-4), 104.7 (C-1), 111.6 (C.$\underline{Me}_2$), 123.6, 131.5, and 134.4 (each Ph C's), and 166.7 (C:O); m/z (e.i.) 320 (M^+ + H), 304 (M^+ - CH_3), and 43 (base peak, $C_3H_7^+$); Accurate m.s., $C_{16}H_{18}O_6N$ requires m/z 320.1134, found peak at m/z 320.1145.

Distilllation of the mother liquor (Kugelrohr, 85 °C at 1.0 mmHg) (lit.[2b] m.p. 64 °C at 0.1 mmHg) gave 3,5-anhydro-1,2-O-isopropylidene-α-D-xylofuranose **3** (1.8 g, 19 %) as a clear liquid: $[\alpha]_D^{24}$ +11.9 (c. 0.75, $CHCl_3$) {lit.[2b] $[\alpha]_D^{20}$ +12.0 ° (c. 0.80, $CHCl_3$)}; δ (^1H, 300 MHz, $CDCl_3$) 1.36 and 1.40 (each 3H, s, C.$\underline{Me}_2$), 4.24 (1H, dd, J = 2 and 8 Hz, C-5 H), 4.73 (1H, d, J = 4 Hz, C-2 H), 4.74 (1H, dd, J = 4 and 8 Hz, C-5 H), 5.11 (1H, dt, J = 2 and 4 Hz, C-4 H), 5.20 (1H, d, J = 4 Hz, C-3 H), and 6.27 (1H, d, J = 4 Hz, C-1 H); δ (^{13}C, 75.6 MHz, $CDCl_3$) 27.0 and 27.8 (C.$\underline{Me}_2$), 78.2 (C-4), 78.4 (C-5), 84.5 (C-2), 87.4 (C-3), 108.1 (C-1), and 113.8 (C.$\underline{Me}_2$).

Formation of oxetane from phthalimido derivative 2. 1,2-*O*-Isopropylidine-5-deoxy-5-phthalimido-D-xylofuranose **2** (90 mg, 0.30 mmol) was stirred with sodium borohydride (45 mg, 1.30 mmol) in absolute ethanol (5 ml) at room temperature for 2 hours. The ethanol was evaporated to give 120 mg of a crude white product. ^1H n.m.r. showed complete conversion to 3,5-anhydro-1,2-O-isopropylidene-α-D-xylofuranose **3** (100 %), which was identical to the sample prepared in the previous experiment.

Preparation of bromide 13a with bromotrimethylsilane. Bromotrimethylsilane (0.12 g, 0.80 mmol) was added slowly to a stirred solution of oxetane **2** (0.12 g, 0.70 mmol) and $BF_3.OEt_2$ (0.10 ml, 0.70 mmol) (prequilibrated at -78 °C for 10 mins) in dichloromethane (30 ml). The solution was diluted with dichloromethane (30 ml) after 6 hours at -78 °C. The mixture was washed with water (3 x), dried ($MgSO_4$), and evaporated to give 0.170 g of a crude syrup.

Purification by silica gel chromatography (petroleum ether : ethyl acetate, 3 : 1 as eluant) gave 1,2-O-isopropylidene-5-deoxy-bromo-α-D-xylofuranose **13a** (0.095 g, 60 %) as a white crystalline solid: m.p. 99 °C (lit.[7] m.p. 93-94 °C); $[\alpha]_D^{24}$ -20 ° (c. 1.20, $CHCl_3$) {lit.[7] $[\alpha]_D^{20}$ -22.2 ° (c. 1.58, MeOH)}; υ_{max} (nujol mull)*inter alia* 3420 (br, OH) cm^{-1}; δ (^1H, 300 MHz, $CDCl_3$) 1.30 and 1.32 (each 3H, s, C.$\underline{Me}_2$), 3.50 (2H, m, 2 x C-5 H), 4.35-4.45 (3H, m, C-4, C-3 H and OH), 4.55 (1H, d, J = 4 Hz, C-2 H), and 5.96 (1H, d, J = 4 Hz, C-1 H) (addition of D_2O caused the signal at δ 4.35-4.45 to collapse to a 2H, m); δ (^{13}C, 75.6 MHz, $CDCl_3$) 26.1 and 26.7 (C.$\underline{Me}_2$), 26.6 (C-5), 74.4 (C-4), 80.0 (C-2), 84.8 (C-3), 105.3 (C-1), and 112.0 ($\underline{C}$.Me_2); m/z (ci) 272 and 270 (base peaks, M + NH_4^+), and 214 and 212 (M + NH_4^+ -C_3H_6O); Accurate m.s., $C_8H_{17}BrNO_4$ requires m/z 270.0341, found peak at m/z 270.0333.

Attempted ring opening with vinylmagnesium bromide and $BF_3.OEt_2$. To a stirred, prequilibrated mixture of 3,5-anhydro-1,2-O-isopropylidene-α-D-xylofuranose **3** (0.13 g, 0.50 mmol), borontrifluoride etherate (0.30 ml, 0.50 mmol) and dichloromethane (15 ml) at -78 °C, was added vinylmagnesium bromide (1.0 ml of a 1M solution) (dropwise addition). The solution was allowed to warm to 0 °C, stirred for 2 hours, diluted with dichloromethane (40 ml), washed with water (2 x 50 ml), dried ($MgSO_4$), and evaporated to give a crude white crystalline solid (300 MHz ^1H n.m.r. showed a single product) (0.170 g). Recrystallisation from dichloromethane / petroleum ether gave bromide **13a** (0.133 g, 53 %), which was identical to the sample prepared in the previous experiment: m.p. 99.3 - 99.7 °C.

Preparation of azide 13c using titanium(IV) chloride. Azidotrimethylsilane (0.10 g, 0.90 mmol) was added slowly to a stirred -78 °C solution of 3,5-anhydro-1,2-O-isopropylidene-a-D-xylofuranose **3** (0.15 g, 0.80 mmol) and titanium(IV) chloride (0.10 ml, 0.80 mmol) in dichloromethane (30 ml). After warming to room temperature and stirring for 24 hours, the reaction was quenched by addition of triethanolamine (0.30 ml, 1.80 mmol), stirred vigorously for 30 mins and then filtered through Celite. Evaporation of the filtrate gave 0.34 g of a crude syrup. Purification by silica gel chromatography (chloroform : ether, 3 : 1 as eluant) gave two fractions. The first (0.110 g, 57 %) was identified as 1,2-O-isopropylidine-5-deoxy-5-azido-α-D-xylofuranose **13c**: m.p. 55-56 °C (lit. m.p.'s: 61-63 °C[8a]; 58.5 60 °C[8b]); $[\alpha]_D^{24}$ +86 ° (c. 0.060, $CHCl_3$) {lit.[8b] $[\alpha]_D^{21}$ +44 ° (c. 1.55, MeOH)}; υ_{max} (KBr disc)*inter alia* 3530 (br, OH), and 2150 (N_3) cm^{-1}; δ (^1H, 300 MHz, $CDCl_3$) 1.32 and 1.49 (each 3H, s, C.Me_2), 2.40 (1H, br s, OH), 3.61 (2H, m, N_3CH_2), 4.24 (1H, m, C3-H), 4.31-4.26 (1H, m, C4-H), 4.52 (1H, d, J = 3.5 Hz, C2-H), and 5.95 (1H, d, J = 3.5 Hz, C1-H), (addition of D_2O caused the signal at δ 2.40 to dissappear and the peak at 4.24 to collapse to a d, J = 3.2 Hz); δ (^{13}C, 75.1 MHz, $CDCl_3$) 26.1 and 26.7 (C.$\underline{Me}_2$), 39.3 (N_3CH_2), 74.2 (C-3), 80.0 (C-4), 84.7 (C-2), 105.1 (C-1) and 112.0 ($\underline{C}$.Me_2); m/z (ci) 233 (base peak, M^+ +NH_4), 216 (M^++ H), and 188 (M^+ - CH_2N_3); Analysis: $C_8H_{13}O_4N_3$ reqiures C, 44.7; H, 6.1; N, 19.5; found C, 44.8; H, 5.8; N, 19.2.

The second fraction (0.065 g, 31 %) was identified as 1,2-O-isopropylidine-5-deoxy-5-chloro-α-D-xylofuranose **13d**: m.p. 93-96 °C (lit. m.p. 91-92 °C[9b]); $[\alpha]_D^{24}$ -71.2 ° (c. 0.025, $CHCl_3$) {lit.[9b] $[\alpha]_D^{18}$ -26 °}; υ_{max} (KBr disc)*inter alia* 3500 (br, OH) cm^{-1}; δ (^1H, 300 MHz, $CDCl_3$) 1.32 and 1.50 (each 3H, s, C.Me_2), 1.97 (1H, br s, OH), 3.54-4.43 (2H, m, $ClCH_2$), 4.35-4.45 (2H, m, C3- and C4-H), 4.55 (1H, d, J = 3.5 Hz, C2-H), and 5.96 (1H, d, J = 3.5 Hz, C1-H), (addition of D_2O caused the signal at δ 1.97 to dissappear and the peak at 4.35-4.45 to collapse to a); δ (^{13}C, 75.1 MHz, $CDCl_3$) 26.1 and 26.7 (C.$\underline{Me}_2$), 39.3 ($ClCH_2$), 74.2 (C-2), 80.0 (C-4), 84.8 (C-3), 105.1 (C-1), and 112.0 ($\underline{C}$.Me_2); m/z (ci) 228 and 226 (base peaks, M + NH_4^+), and 170 and 168 (M + NH_4^+ -C_3H_6O); Accurate m.s., $C_7H_{10}O_4Cl$ requires m/z 193.0268, found peak at m/z 193.0668.

Preparation of azide 13c with azidotrimethylsilane and $BF_3.OEt_2$. 3,5-Anhydro-1,2-O-isopropylidene-α-D-xylofuranose **3** (35 mg, 0.25 mmol) in dichloromethane (20 ml) at -78 °C under argon, was treated with borontrifluoride etherate (0.040 ml, 0.32 mmol) followed by

azidotrimethylsilane (0.055 ml, 0.41 mmol). The reaction mixture was allowed to warm to room temperature, and treated a further 0.10 ml (0.80 mmol) of borontrifluoride etherate added. After 4h, the reaction mixture was diluted with dichloromethane, washed with dilute hydrochloric acid, saturated sodium hydrogencarbonate, and water, dried ($MgSO_4$) and evaporated to gave **13c** as a white solid (0.030 g, 56 %) and was identical to the sample previously prepared.

Ring opening of oxetane 3 with $TiCl_4$. A solution of titanium(IV) chloride (0.70 ml of a 1.0 M solution in dichloromethane) and 3,5-anhydro-1,2-O-isopropylidene-α-D-xylofuranose **3** (0.110 g, 0.68 mmol) in dichloromethane (15 ml) at -78 °C under argon, was stirred for 1 hour, allowed to warm to room temperature and stirred for a further 17 hours. Triethanolamine (0.20 ml, 1.50 mmol) was added, the resulting suspension was filtered through Celite and evaporated to give 0.150 g of a crude product. Purification by silica gel chromatography (diethyl ether : dichloromethane, 1:3 as eluant) afforded 1,2-O-isopropylidene-5-deoxy-5-chloro-α-D-xylofuranose **13d** as a colorless solid (0.052 g, 37 %): m.p. 93-96 °C (lit.[9b] m.p. 91-92 °C).

Attempted preparation of benzoate 13e. Titanium(IV) chloride (0.15 ml, 3.00 mmol) was added slowly to a stirred solution of oxetane **3** (0.50 g, 3.00 mmol) and benzoic acid (0.37 g, 3.20 mmol) in dichloromethane (15 ml) at -78 °C. The reaction mixture was allowed to warm to room temperature, stirred for 14 hours, diluted with dichloromethane, washed with water, dried ($MgSO_4$) and evaporated to give 0.30 g of a crude syrup (300 MHz ^1H n.m.r. showed a single product) which was crystallised from dichloromethane to give 0.26 g of chloride **13d** containing residual benzoic acid. Purification by silica gel chromatography (dichloromethane : ether, gradient elution) gave pure chloride **13d** (0.21 g, 43 %) which was identical to the sample prepared in the previous experiments (*vide supra*).

Acknowledgements.

We thank Ciba-Geigy Central Research, Manchester and the S.E.R.C. for a CASE studentship (to D.A.J.). We are grateful to Messers K. Walkling, for i.r. and u.v. spectra; C.R. Perkins, for m.s. spectra and Dr. R. Perry for elemental analyses.

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6. Borate **8** was surprisingly stable to hydrolysis, as evidenced by its 200MHz ^1H n.m.r. spectrum: δ ($CDCl_3$) 1.26 and 1.42 (each 3H, s, $C.Me_2$), 2.17 and 2.45 [each 3H, s, $B.(OMe)_2$], 4.00 (2H, dd, J = 1.0 and 5.0 Hz, $N.CH_2$), 4.32 (1H, dt, J = 3.0 and 5.0 Hz, C-4 H), 4.68 (1H, d, J = 3.5 Hz, C-2 H), 4.75 (1H, d, J = 3Hz, C-3 H), 5.85 (1H, d, J = 3.5 Hz, C-1 H), and 7.32-7.42 and 7.70-7.18 (each 2H, m, C_6H_4).
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