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Regioselective synthesis of *C*-nucleosides by 1,3-dipolar cycloaddition of arylnitrile oxides to 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose

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ABSTRACT

The synthesis of 3-aryl-5-(1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-2-isoxazoline (**3**) from arylnitrile oxides and 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose (**1**) is described. The 1,3-dipolar cycloaddition reactions give mainly anti-adducts (≥95% π-facial stereoselectivity).

INTRODUCTION

Naturally occurring *C*-nucleosides, such as formycin, formycin B, showdomycin, and pyrazomycin, are antibiotics and many also exhibit anticancer and antiviral activities. These properties have stimulated interest in the synthesis of analogues[1]. 2-Isoxazolines (4,5-dihydroisoxazoles) are versatile sources of the functionality present in natural products[2] and there is renewed interest in their synthesis via 1,3-dipolar cycloaddition of nitrile oxides to alkenes, particularly on the factors that influence stereo- and regio-selectivity[3].

In a continuation of our effort[4–8] to utilise heterocyclic compounds as dipolarophiles in 1,3-dipolar cycloaddition reactions, we have investigated 5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose (**1**). Although the formation[9] of **1** and some aspects of its chemistry have been investigated, only the cycloadditions of benzonitrile oxide (**2a**) and 2,4,6-trimethylbenzonitrile (mesitonitrile) oxide[10] (**2p**) to **1** and its 3-*O*-benzyl derivative[11] have been described. The stereoselectivity of the cycloaddition of nitrile oxides to 3-*O*-substituted derivatives of **1** has been discussed by De Micheli and co-workers[10]. We now report that **1** undergoes highly stereoselective cycloaddition reactions with numerous arylnitrile oxides.

RESULTS AND DISCUSSION

Cycloadditions of **1** with the substituted benzonitrile oxides **2a–2o**, generated *in situ*, were conducted under standard conditions by the Huisgen method[3], using a molar

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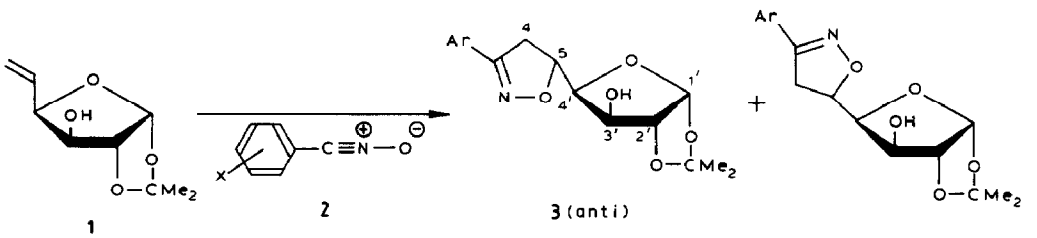

1 2 3 (anti) 4 (syn)

a	X = H	i	X = 4-F
b	X = 4-Me	j	X = 4-Cl
c	X = 4-OMe	k	X = 2-Cl
d	X = 2-OMe	l	X = $2,4-Cl_2$
e	X = $3,4-OCH_2O$	m	X = $3,4-Cl_2$
f	X = $3,4,5-(OMe)_3$	n	X = 3-Cl
g	X = $4-NO_2$	o	X = $2,6-Cl_2$
h	X = $3-NO_2$	p	X = $2,4,6-Me_3$

excess of the 1,3-dipole, whereas the stable mesitonitrile oxide (**2p**) was used as such[3]. The major products were the anti-cycloadducts **3** together with small proportions of the syn-cycloadducts (**4**) and the diarylfuroxans that resulted from dimerisation of the nitrile oxide. The formation of furoxans indicated **1** to be less reactive than other terminal alkenes.

The combined yields of the cycloaddition products were good, but only the preponderant anti-adducts **3a–3p** were isolated pure after column chromatography. The structures of the diastereomers were assigned by correlation of the n.m.r. data (^1H and ^{13}C, and n.O.e. effects) with those of **3a**, the anti-structure of which has been established[10] by X-ray crystallography. The assignment of the relative stereochemistry at C-4,5 in the products of the cycloaddition of nitrile oxide to olefins, based only on ^1H- and ^{13}C-n.m.r. analysis data, is not straightforward[12,13]. Comparison of the n.m.r. data for **3b–3o** with those of **3a** and known[10] **3p** indicated that the cycloadditions are anti-selective and give **3** as the major product. As reported by others[14–16], the chemical shifts of the resonances for C-5,6 decreased and those of the resonances for H-4,5 increased on passing from the anti to the syn products.

The diastereoselectivity of the above cycloaddition reactions was high and virtually independent of the nature of the nitrile oxide. This finding supports the results of Houk *et al.*[17,18] who found that the anti/syn ratio in the cycloadditions of nitrile oxides to alkenes having a chiral centre in the allylic position varied little with steric or electronic changes in the nitrile oxide moiety. The preponderance of the anti-isomers **3a–3p** is as expected on the basis of experimental[12–16] and theoretical[17–18] results obtained for related reactions. Thus, De Micheli and co-workers[10] found that benzonitrile oxide (**2a**) and mesitonitrile oxide (**2p**) cycloadded to **1** to give the anti-adducts **3a** (86.6%) and **3p** (78.2%), respectively, with π-facial stereoselectivity. The anti/syn ratio for **3** and **4** was $\geqslant$95:5. Our results accord with observations on related systems reported by others[10–19].

The stereochemical outcome of the cycloaddition has been rationalised[18] in terms of the "inside alkoxy effect".

The mass spectra of **3a**, **3b**, and **3j** contained, in addition to peaks for the molecular ion, peaks for fragments that corresponded to retro-1,3-dipolar cycloadditions, which is characteristic of many cycloaddition products.

EXPERIMENTAL

General methods. — Melting points were determined on a Kofler hot-plate apparatus and are uncorrected. Optical rotations were measured at 20° with a Perkin–Elmer 141 polarimeter. Reactions were monitored by t.l.c. on Silica Gel F_{254} (Lachema) with methanol–benzene (1:4), with detection by u.v. light and/or by exposure to iodine vapour. Column chromatography was performed on silica gel (Lachema, 230–400 mesh). All solvents were distilled from the appropriate drying agents. The ^{1}H- and ^{13}C-n.m.r. spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si) with a Varian VXR 300 spectrometer. U.v. spectra were obtained with a M-40 spectrometer (Zeiss) on solutions in methanol. Mass spectra were obtained with an A.E.I. MS 902 S apparatus with a direct inlet system.

Chlorides of benzenehydroximic acids were prepared by chlorination[20] of the corresponding benzaldoximes in chloroform, chlorides of methoxybenzenehydroximic acid were obtained by treatment of the oximes with nitrosyl chloride[21], and 2,4,6-trimethylbenzonitrile oxide[22] and **1**[9] were prepared as described.

Standard procedures for the preparation of the isoxazolines **3** *and* **4**. — A solution of dry triethylamine (22 mmol) in ether (30 mL) was added dropwise at −5 to 0° to a stirred, cooled solution of the corresponding benzenehydroximic acid chloride (20 mmol) and **1** (1.86 g, 10 mmol) in dry ether (30 mL) over 2 h. Each mixture was stirred overnight at room temperature, filtered from triethylammonium chloride, and concentrated *in vacuo*. Column chromatography (methanol–benzene, 1:4) of each residue on silica gel and crystallisation from methanol then gave **3**. The cycloaddition of 2,4,6-trimethylbenzonitrile oxide involved heating a mixture of the nitrile oxide (20 mmol) and **1** (1.86 g, 10 mmol) in dry benzene (30 mL) at 80° for 4 h. The mixture was then cooled and worked-up as described above.

The following compounds were prepared in this manner.

5-(1,2-*O*-Isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-3-phenyl-2-isoxazoline (**3a**, 51%), m.p. 191–192°, $[\alpha]_D$ −157° (chloroform); lit.[10] m.p. 195–196°, $[\alpha]_D$ −136° (*c* 0.9, methanol), R_F 0.58 (methanol–benzene, 1:4). N.m.r. data: ^{1}H, δ 7.40–7.70 (m, 5 H, Ph), 5.97 (d, 1 H, $J_{1',2'}$ 4.0 Hz, H-1'), 5.03 (dd, 1 H, $J_{4',5'} = J_{4,5} = 8.0$ Hz, H-5), 4.43 (d, 1 H, $J_{3',4'}$ 3.0 Hz, H-3'), 4.18 (dd, 1 H, H-4'), 3.51 (d, 2 H, H-4), 1.35 and 1.45 (2 s, each 3 H, CMe_2); ^{13}C, δ 157.23 (s, C-3), 130.35, 129.13, 129.03, 126.88 (aromatic C), 111.95 (s, CMe_2), 105.19 (d, C-1'), 85.48 (d, C-5), 81.24 (d, C-4'), 77.59 (d, C-2'), 74.56 (d, C-3'), 38.76 (t, C-4), 26.82 and 26.17 (2 q, CMe_2). Mass spectrum: *m/z* 3.05 ($M^{+\cdot}$).

5-(1,2-*O*-Isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-3-(4-methylphenyl)-2-isoxazoline (**3b**, 65%), m.p. 170°, $[\alpha]_D$ −108° (*c* 0.9, methanol), R_F 0.44 (methanol–

benzene, 1:4); λ_{max} 261 nm (log ε 3.08). N.m.r. data: ^{1}H, δ 7.18 and 7.54 (2 d, each 2 H, aromatic), 5.98 (d, 1 H, $J_{1',2'}$ 4.0 Hz, H-1'), 5.06 (dd, 1 H, $J_{4',5'} = J_{4,5} = 8.0$ Hz, H-5), 4.61 (d, 1 H, H-2'), 4.42 (d, 1 H, $J_{3',4'}$ 3.0 Hz, H-3'), 4.25 (dd, 1 H, H-4'), 3.50 (d, 2 H, H-4), 2.36 (s, 3 H, Me), 1.32 and 1.49 (2 s, each 3 H, CMe_2); ^{13}C, δ 157.16 (s, C-3), 140.34, 129.95, 128.41, 126.24 (aromatic), 111.64 (s, CMe_2), 105.02 (s, C-1'), 85.41 (d, C-5), 90.95 (d, C-4'), 77.46 (d, C-2'), 74.0 (d, C-3'), 38.16 (t, C-4), 26.69 and 26.03 (2 q, CMe_2), 21.35 (q, Me). Mass spectrum: *m/z* 319 (M^+).

Anal. Calc. for $C_{17}H_{21}NO_5$: C, 63.9; H, 6.6; N, 4.4. Found: C, 64.1; H, 6.6; N, 4.8.

5-(1,2-*O*-Isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-3-(4-methoxyphenyl)-2-isoxazoline (**3c**, 55%), m.p. 175°, $[\alpha]_D$ −73° (*c* 0.8, methanol), R_F 0.58 (methanol–benzene, 1:4); λ_{max} 272 nm (log ε 3.25). N.m.r. data: ^{1}H, δ 6.95 and 7.62 (2 d, each 2 H, aromatic), 5.98 (d, 1 H, $J_{1',2'}$ 3.9 Hz, H-1), 5.02 (dd, 1 H, $J_{4',5} = J_{4,5} = 8.0$ Hz, H-5), 4.58 (d, 1 H, H-2'), 4.42 (d, 1 H, $J_{3',4'}$ 3.0 Hz, H-3'), 4.18 (dd, 1 H, H-4'), 3.85 (s, 3 H, OMe), 3.50 (d, 2 H, H-4), 1.31 and 1.48 (2 s, each 3 H, CMe_2); ^{13}C, δ 156.85 (s, C-3), 161.18, 132.03, 128.41, 114.12 (aromatic), 111.84 (s, CMe_2), 105.11 (d, C-1'), 85.49 (d, C-5), 81.15 (d, C-4'), 77.23 (d, C-2'), 74.25 (d, C-3'), 55.33 (q, OMe), 38.76 (t, C-4), 26.77 and 26.12 (2 q, CMe_2).

Anal. Calc. for $C_{17}H_{21}NO_6$: C, 60.8; H, 6.3; N, 4.2. Found: C, 60.5; H, 6.5; N, 4.6.

5-(1,2-*O*-Isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-3-(2-methoxyphenyl)-2-isoxazoline (**3d**, 51%), m.p. 151–152°, $[\alpha]_D$ −30° (*c* 0.8, methanol) R_F 0.6 (methanol–benzene, 1:4); λ_{max} 252 (log ε 2.79) and 297 nm (log ε 2.49). N.m.r. data: ^{1}H, δ 6.90–7.75 (m, 4 H, aromatic), 5.90 (d, 1 H, $J_{1',2'}$ 4.0 Hz, H-1'), 4.93 (dd, 1 H, $J_{4',5'} = J_{4,5} = 7.9$ Hz, H-5), 4.52 (d, 1 H, H-2), 4.33 (d, 1 H, $J_{3',4'}$ 3.0 Hz, H-3'), 4.15 (dd, 1 H, H-4'), 3.79 (s, 3 H, OMe), 3.55 (d, 2 H, H-4), 1.30 and 1.45 (2 s, each 3 H, CMe_2); ^{13}C, δ 157.43 (s, C-3), 156.69, 135.96, 131.27, 129.22, 128.22, 120.42 (aromatic), 111.27 (s, CMe_2), 104.95 (d, C-1'), 85.33 (d, C-5), 80.92 (d, C-4'), 77.24 (d, C-2'), 73.84 (d, C-3'), 55.28 (q, OMe), 40.74 (t, C-4), 26.64 and 25.99 (2 q, CMe_2).

Anal. Calc. for $C_{17}H_{21}NO_6$: C, 60.8; H, 6.3; N, 4.2. Found: C, 61.0; H, 5.9; N, 4.3.

5-(1,2-*O*-Isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-3-(3,4-methylenedioxyphenyl)-2-isoxazoline (**3e**, 45%), m.p. 166–167°, $[\alpha]_D$ +1° (*c* 0.8, methanol), R_F 0.66 (methanol–benzene, 1:4); λ_{max} 283 nm (log ε 2.92). N.m.r. data: ^{1}H, δ 6.85–7.45 (m, 3 H, aromatic), 6.06 (d, 1 H, $J_{1',2'}$ 4.0 Hz, H-1'), 6.00 (s, 2 H, OCH_2O), 5.03 (dd, 1 H, $J_{4',5'} = J_{4,5} = 8.0$ Hz, H-5), 4.60 (d, 1 H, H-2'), 4.40 (d, 1 H, $J_{3',4'}$ 3.1 Hz, H-3'), 4.25 (dd, 1 H, H-4'), 3.60 (d, 2 H, H-4), 1.30 and 1.48 (2 s, each 3 H, CMe_2); ^{13}C, δ 157.05 (s, C-3), 149.48, 146.78, 128.75, 128.15, 125.72, 121.54 (aromatic), 110.57 (s, CMe_2), 105.06 (d, C-1'), 102.32 (t, OCH_2O), 85.35 (d, C-5), 80.69 (d, C-4'), 78.20 (d, C-2'), 74.10 (d, C-3'), 40.67 (t, C-4), 26.75 and 26.11 (2 q, CMe_2).

Anal. Calc. for $C_{17}H_{19}NO_7$: C, 58.4; H, 5.4; N, 4.0. Found: C, 58.1; H, 5.8; N, 3.8.

5-(1,2-*O*-Isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-3-(3,4,5-trimethoxyphenyl)-2-isoxazoline (**3f**, 54%), m.p. 162–163°, $[\alpha]_D$ +28° (*c* 0.9, methanol), R_F 0.46 (methanol–benzene, 1:4); λ_{max} 278 nm (log ε 2.71). N.m.r. data: ^{1}H, δ 7.79 (s, 2 H, aromatic), 5.85 (d, 1 H, $J_{1',2'}$ 3.8 Hz, H-1'), 4.95 (dd, 1 H, $J_{4',5} = J_{4,5} = 7.9$ Hz, H-5), 4.45 (d,1 H, H-2'), 4.28 (d,1 H, $J_{3',4'}$ 3.0 Hz, H-3'), 4.15 (dd, 1 H, H-4'), 3.80, 3.75, and 3.70 (3 s,

each 3 H, 3 OMe), 3.65 (d, 2 H, H-4), 1.20 and 1.38 (2 s, each 3 H, CMe_2); ^{13}C, δ 156.82 (s, C-3), 153.31, 152.95, 139.42, 124.53 (aromatic), 111.49 (s, CMe_2), 103.84 (d, C-1'), 85.32 (d, C-5'), 80.69 (d, C-4'), 77.64 (d, C-2'), 73.75 (d, C-3'), 60.57 (q, OMe), 55.91 (q, OMe), 37.76 (t, C-4), 26.53 and 25.86 (2 q, CMe_2).

Anal. Calc. for $C_{19}H_{25}NO_8$: C, 57.7; H, 6.3; N, 3.5. Found: C, 57.3; H, 6.7; N, 3.2.

5-(1,2-*O*-Isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-3-(4-nitrophenyl)-2-isoxazoline (**3g**, 58%), m.p. 156–157°, $[\alpha]_D$ −111° (*c* 0.8, methanol), R_F 0.51 (methanol–benzene, 1:4); λ_{max} 224 (log ε 2.79) and 306 nm (log ε 2.85). N.m.r. data: ^1H, δ 7.80 and 8.18 (2 d, each 2 H, aromatic), 5.90 (d, 1 H, $J_{1',2'}$ 4.0 Hz, H-1'), 5.10 (dd, 1 H, $J_{4',5} = J_{4,5} =$ 8.0 Hz, H-5), 4.55 (dd, 1 H, H-2'), 4.31 (d, 1 H, $J_{3',4'}$ 3.0 Hz, H-3'), 4.20 (dd, 2 H, H-4'), 3.45 (dd, 2 H, H-4), 1.30 and 1.45 (2 s, each 3 H, CMe_2); ^{13}C, δ 156.00 (s, C-3), 148.50, 131.54, 127.47, 119.23 (aromatic), 111.49 (s, CMe_2), 104.50 (d, C-1'), 84.99 (d, C-5), 81.20 (d, C-4'), 75.73 (d, C-2'), 73.91 (d, C-3'), 37.12 (t, C-4), 26.60 and 26.05 (2 q, CMe_2).

Anal. Calc. for $C_{16}H_{18}N_2O_7$: C, 54.8; H, 5.1; N, 8.0. Found: C, 54.4; H, 4.7; N, 7.7.

5-(1,2-*O*-Isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-3-(3-nitrophenyl)-2-isoxazoline (**3h**, 65%), m.p. 163–165°, $[\alpha]_D$ −125° (*c* 0.9, methanol), R_F 0.45 (methanol–benzene, 1:4); λ_{max} 259 nm (log ε 3.18). N.m.r. data: ^1H, δ 7.55–8.40 (m, 4 H, aromatic), 5.90 (d, 1 H, $J_{1',2'}$ 4.0 Hz, H-1'), 5.10 (m, 1 H, $J_{4',5} = J_{4,5} =$ 8.0 Hz, H-5), 4.65 (d, 1 H, H-2'), 4.35 (d, 1 H, $J_{3',4'}$ 3.0 Hz, H-3'), 4.20 (dd, 1 H, H-4'), 3.5 (dd, 2 H, H-4), 1.31 and 1.45 (2 s, each 3 H, CMe_2). ^{13}C, δ 155.68 (s, C-3), 148.25, 132.34, 131.42, 129.79, 121.48, 119.34 (aromatic), 111.54 (s, CMe_2), 104.48 (d, C-1'), 84.39 (d, C-5), 81.12 (d, C-4'), 75.73 (d, C-2'), 74.00 (d, C-3'), 37.35 (t, C-4), 26.70 and 26.06 (2 q, CMe_2).

Anal. Calc. for $C_{16}H_{18}N_2O_7$: C, 54.8; H, 4.5; N, 8.0. Found: C, 54.7; H, 4.9; N, 7.9.

3-(4-Fluorophenyl)-5-(1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-2-isoxazoline (**3i**, 65%), m.p. 170–171°, $[\alpha]_D$ −139° (*c* 0.9, methanol), R_F 0.6 (methanol–benzene, 1:4); λ_{max} 265 nm (log ε 3.10). N.m.r. data: ^1H, δ 7.40 and 7.61 (2 d, each 2 H, aromatic), 5.95 (d, 1 H, $J_{1',2'}$ 4.0 Hz, H-1'), 5.05 (dd, 1 H, $J_{4',5} = J_{4,5} =$ 8.0 Hz, H-5), 4.59 (d, 1 H, H-2'), 4.40 (d, 1 H, $J_{3',4'}$ 3.0 Hz, H-3'), 4.17 (dd, 1 H, H-4'), 3.47 (d, 2 H, H-4), 1.30 and 1.45 (2 s, each 3 H, CMe_2); ^{13}C, δ 156.44 (s, C-3), 136.28, 129.03, 128.11, 127.68 (aromatic), 111.95 (s, CMe_2), 105.16 (d, C-1'), 85.52 (d, C-5), 81.04 (d, C-4'), 77.94 (d, C-2'), 74.30 (d, C-3'), 38.28 (t, C-4), 26.83 and 26.17 (2 q, CMe_2).

Anal. Calc. for $C_{16}H_{18}FNO_5$: C, 54.4; H, 4.3; N, 5.5 Found: C, 54.2; H, 4.5; N, 5.1.

3-(4-Chlorophenyl)-5-(1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-2-isoxazoline (**3j**, 52%), m.p. 180–181°, $[\alpha]_D$ −17° (*c* 0.9, methanol), R_F 0.52 (methanol–benzene, 4:1); λ_{max} 266 nm (log ε 3.14). N.m.r. data: ^1H, δ 7.40 and 7.65 (2 d, each 2 H, aromatic), 5.98 (d, 1 H, $J_{1',2'}$ 4.1 Hz, H-1'), 5.05 (dd, 1 H, $J_{4',5} = J_{4,5} =$ 8.0 Hz, H-5), 4.60 (d, 1 H, H-2'), 4.42 (d, 1 H, $J_{3',4'}$ 2.5 Hz, H-3'), 4.23 (dd, 1 H, H-4'), 3.45 (d, 2 H, H-4), 1.30 and 1.45 (2 s, each 3 H, CMe_2); ^{13}C, δ 156.85 (s, C-3), 136.53, 129.79, 128.76, 127.95 (aromatic), 112.24 (s, CMe_2), 105.47 (d, C-1'), 85.85 (d, C-5), 81.38 (d, C-4'), 78.28 (d, C-2'), 74.67 (d, C-3'), 38.70 (t, C-4), 27.26 and 26.60 (2 q, CMe_2). Mass spectrum: *m/z* 341.339 ($M^{+\cdot}$).

Anal. Calc. for $C_{16}H_{18}ClNO_5$: C, 56.5; H, 5.3; N, 4.1. Found: C, 56.6; H, 5.3; N, 4.2.

3-(2-Chlorophenyl)-5-(1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-2-isoxazoline (**3k**, 44%), m.p. 177–178°, $[\alpha]_D$ −10° (*c* 0.8, methanol), R_F 0.58 (methanol–benzene, 4:1); λ_{max} 244 nm (log ε 2.81). N.m.r. data: ^{1}H, δ 7.15–7.40 (m, 4 H, aromatic), 5.81 (d, 1 H, $J_{1',2'}$ 4.0 Hz, H-1'), 4.92 (dd, 1 H, $J_{4',5} = J_{4,5}$ = 8.0 Hz, H-5), 4.45 (d, 1 H, H-2), 4.21 (d, 1 H, $J_{3',4'}$ 3.0 Hz, H-3'), 4.15 (dd, 1 H, H-4'), 3.45 (dd, 2 H, H-4), 1.15 and 1.32 (2 s, each 3 H, CMe_2); ^{13}C, δ 156.82 (s, C-3), 132.27, 130.47, 130.11, 128.50, 126.64, 126.59 (aromatic), 111.22 (s, CMe_2), 104.76 (d, C-1'), 85.06 (d, C-5), 80.24 (d, C-4'), 78.31 (d, C-2'), 73.46 (d, C-3'), 39.56 (t, C-4), 26.50 and 25.86 (2 q, CMe_2).

Anal. Calc. for $C_{16}H_{18}ClNO_5$: C, 56.5; H, 5.3; N, 4.1. Found: C, 56.3; H, 5.0; N, 3.8.

3-(2,4-Dichlorophenyl)-5-(1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-2-isoxazoline (**3l**, 62%), $[\alpha]_D$ +1° (*c* 0.8, methanol), R_F 0.56 (methanol–benzene, 4:1); λ_{max} 263 nm (log ε 2.92). N.m.r. data: ^{1}H, δ 7.17–7.66 (m, 3 H, aromatic), 5.95 (d, 1 H, $J_{1',2'}$ 3.9 Hz, H-1'), 5.0 (dd, 1 H, $J_{4',5} = J_{4,5}$ = 8.0 Hz, H-5), 4.58 (d, 1 H, H-2'), 4.39 (d, 1 H, $J_{3',4'}$ 3.0 Hz, H-3'), 4.10 (dd, 1 H, H-4'), 3.48 (dd, 2 H, H-4), 1.32 and 1.43 (2 s, each 3 H, CMe_2); ^{13}C, δ 157.28 (s, C-3), 140.58, 130.29, 129.04, 128.96, 128.72, 126.86 (aromatic), 111.87 (s, CMe_2), 105.17 (d, C-1'), 85.52 (d, C-5), 81.18 (d, C-4'), 77.67 (d, C-2'), 74.35 (d, C-3'), 38.48 (t, C-4), 26.82 and 26.17 (2 q, CMe_2).

Anal. Calc. for $C_{16}H_{17}Cl_2NO_5$: C, 51.3; H, 4.5; N, 3.7. Found: C, 51.1; 4.7; N, 3.6.

3-(3,4-Dichlorophenyl)-5-(1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-2-isoxazoline (**3m**, 59%), m.p. 175–176°, $[\alpha]_D$ −1° (*c* 0.9, methanol), R_F 0.55 (methanol–benzene, 4:1); λ_{max} 269 nm (log ε 2.61). N.m.r. data: ^{1}H, δ 7.30–7.85 (m, 3 H, aromatic), 5.98 (d, 1 H, $J_{1',2'}$ 4.0 Hz, H-1'), 5.09 (dd, 1 H, $J_{4',5} = J_{4,5}$ = 8.0 Hz, H-5), 4.60 (d, 1 H, H-2'), 4.42 (d, 1 H, $J_{3',4'}$ 3.0 Hz, H-3'), 4.20 (dd, 1 H, H-4'), 3.48 (d, 2 H, H-4), 1.35 and 1.55 (2 s, each 3 H, CMe_2); ^{13}C, δ 157.00 (s, C-3), 131.26, 130.80, 128.62, 125.92, 119.61 (aromatic), 111.73 (s, CMe_2), 104.64 (d, C-1'), 84.94 (d, C-5), 80.96 (d, C-4'), 75.73 (s, C-2'), 73.40 (d, C-3'), 38.10 (t, C-4), 26.74 and 26.20 (2 q, CMe_2).

Anal. Calc. for $C_{16}H_{17}Cl_2NO_5$: C, 51.3; H, 4.5; N, 3.7. Found: C, 50.9; H, 4.4; N, 3.4.

3-(3-Chlorophenyl)-5-(1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-2-isoxazoline (**3n**, 61%), syrup, $[\alpha]_D$ −23° (*c* 0.9, methanol), R_F 0.58 (methanol–benzene, 4:1); λ_{max} 256 nm (log ε 3.11). N.m.r. data: ^{1}H, δ 7.29–7.60 (m, 4 H, aromatic), 5.87 (d, 1 H, $J_{1',2'}$ 4.0 Hz, H-1'), 4.92 (dd, 1 H, $J_{4',5} = J_{4,5}$ = 7.9 Hz, H-5), 4.49 (d, 1 H, H-2'), 4.34 (d, 1 H, $J_{3',4'}$ 3.0 Hz, H-3'), 4.07 (dd, 1 H, H-4'), 3.42 (dd, 2 H, H-4), 1.21 and 1.37 (2 s, each 3 H, CMe_2); ^{13}C, δ 157.22 (s, C-3), 130.65, 130.37, 129.37, 129.09, 129.04, 128.76 (aromatic), 111.97 (s, CMe_2), 105.19 (d, C-1'), 85.45 (d, C-5), 81.25 (d, C-4'), 77.55 (d, C-2'), 74.62 (d, C-3'), 38.82 (t, C-4), 26.81 and 26.16 (2 q, CMe_2).

Anal. Calc. for $C_{16}H_{18}ClNO_5$: C, 56.5; H, 5.3; N, 4.1. Found: C, 56.8; H, 5.5; N, 3.9.

3-(2,6-Dichlorophenyl)-5-(1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-2-isoxazoline (**3o**, 60%), syrup, $[\alpha]_D$ −66° (*c* 0.8, methanol), R_F 0.50 (methanol–benzene, 4:1); λ_{max} 266 nm (log ε 2.91). N.m.r. data: ^{1}H, δ 7.12–8.06 (m, 3 H, aromatic), 5.87 (d, 1 H, $J_{1',2'}$ 4.0 Hz, H-1'), 4.93 (dd, 1 H, $J_{4',5} = J_{4,5}$ = 8.0 Hz, H-5), 4.49 (d, 1 H, H-2')), 4.33

(d, 1 H, $J_{3',4'}$ 3.0 Hz, H-3'), 4.08 (dd, 1 H, H-4'), 3.40 (dd, 2 H, H-4), 1.27 and 1.36 (2 s, each 3 H, CMe_2); ^{13}C, δ 157.22 (s, C-3), 130.34, 129.63, 129.03, 126.07 (aromatic), 111.93 (s, CMe_2), 105.19 (d, C-1'), 85.47 (d, C-5), 81.22 (d, C-4'), 77.60 (d, C-2'), 74.53 (d, C-3'), 38.71 (t, C-4), 26.82 and 26.17 (2 q, CMe_2).

Anal. Calc. for $C_{16}H_{17}Cl_2NO_5$: C, 51.3; H, 4.5; N, 3.7. Found: C, 51.6; 4.5; N, 3.4.

5-(1,2-*O*-Isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-3-(2,4,6-trimethylphenyl)-2-isoxazoline (**3p**, 51%), m.p. 119–120° (lit.[10] m.p. 120–121°), $[\alpha]_D$ −161° (*c* 1.0, chloroform), R_F 0.58 (methanol–benzene, 4:1).

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