Carbohydrate Research, 216 (1991) 461–473
Elsevier Science Publishers B.V., Amsterdam

Cycloaddition of nitrile oxides to 3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*ribo*-hex-5-enofuranose*

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(Received January 2nd, 1991; accepted for publication April 25th, 1991)

ABSTRACT

Benzonitrile oxide and ethoxycarbonylformonitrile oxide cyclo-added to the title compound to afford a mixture of 3-substituted (phenyl or ethoxycarbonyl) (5*R*)- (**6**) and (5*S*)-5-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-tetrofuranos-4-yl)-2-isoxazoline (**7**). The π-facial selectivity of the reactions was low (~1:1) compared with that (9:1) for the corresponding D-*xylo* isomer of the title compound, which yielded the D-*xylo* isomers (**2** and **3**, respectively) of **6** and **7**. The structures of the 3-phenyl derivatives **2a** and **6a** were determined by X-ray crystallography.

INTRODUCTION

The cycloaddition of nitrile oxides to alkenes, to yield 2-isoxazolines (4,5-dihydroisoxazoles), has long been a subject of interest[1]. More recently, the topic has received renewed attention in view of the now widespread use[2] of nitrile oxide/isoxazoline chemistry for the synthesis of natural products and analogues.

Of particular significance for the application of this method in carbohydrate syntheses is the control of π-facial selectivity for the reaction of nitrile oxides with unsaturated sugars. The cyclo-addition[3–5] of nitrile oxides to D-*xylo*-hex-5-enofuranoses, *e.g.*, **1a**, is highly diastereoselective (73–93% d.e.) in favour of adducts (**2**) with *erythro* stereochemistry at C-4,5 over the *threo* isomers **3**. Such *erythro* selectivity for the cycloaddition to allyl ethers has been rationalised[5,6] in terms of an "inside alkoxy effect" that involves the allylic oxygen (in this case, O-4 of **1a**). De Amici *et al.*[5] have also considered the possible role of the homoallylic oxygen (*i.e.*, O-3). In order to test this latter hypothesis, the D-*ribo* isomer (**4**) of **1a** has been prepared, which has inverted stereochemistry at C-3, and the selectivity of its reactions with benzonitrile oxide ($PhC\equiv N^+-O^-$) and ethoxycarbonylformonitrile oxide ($EtO_2CC\equiv N^+-O^-$) have been compared with those of **1a**.

* Dedicated to Professor Grant Buchanan on the occasion of his 65th birthday.
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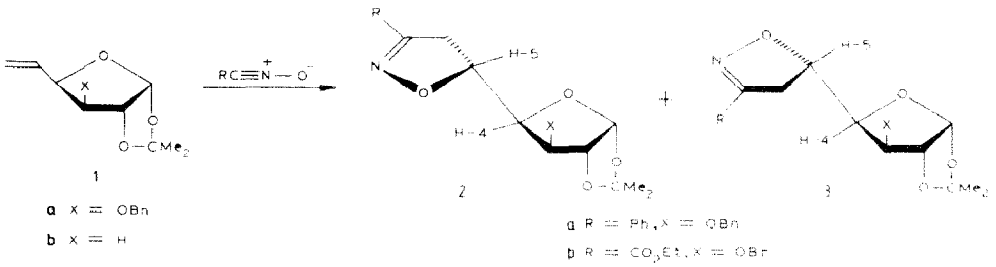
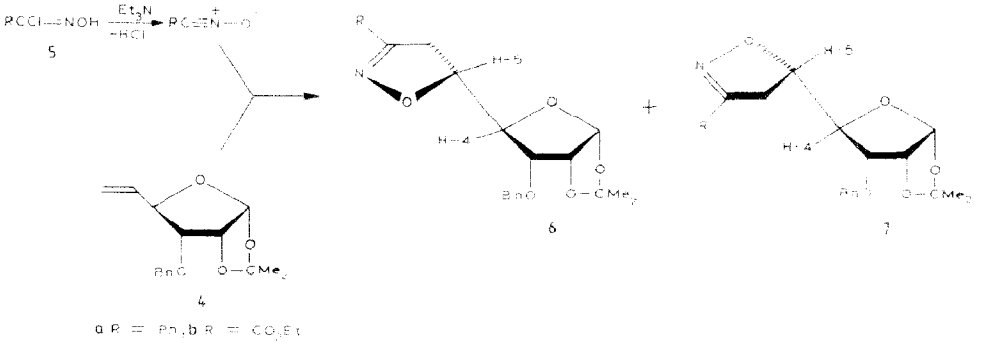
0008-6215/91/$03.50



RESULTS AND DISCUSSION

Benzonitrile oxide, generated *in situ* by dehydrochlorination of the corresponding hydroximoyl chloride **5a**, was reacted with 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-hex-5-enofuranose (**4**). Chromatography of the mixture of products gave 3,4-diphenylfurazan *N*-oxide, formed by dimerisation of the nitrile oxide[8], and a mixture of the diastereomeric isoxazolines **6a** and **7a** in a combined yield of 70% after recrystallisation.



The products were characterised by their analytical and spectroscopic properties. Although the adducts were not separable by chromatography, they were readily distinguishable by their ^{1}H-n.m.r. spectra (Table I), which indicated the ratio 42:58 on the basis of the integrated intensities of the signals for H-1 at δ 5.77 and 5.72. A small quantity of the minor isomer, purified by repeated recrystallisation from chloroform, was shown by X-ray analysis to have the *R* configuration at C-5, corresponding to an *erythro* structure at C-4,5 (Fig. 1a).

The corresponding reaction of **4** with ethoxycarbonylformonitrile oxide, generated by dehydrochlorination of the hydroximoyl chloride, afforded a mixture of the isoxazolines **6b** and **7b** in the ratio 51:49. It was not possible to assign individual peaks in the ^{1}H-n.m.r. spectrum of the mixture from the integrated intensities, because of the similar proportions of the isomers. However, analysis was achieved by homonuclear Hartmann–Hahn correlation spectroscopy (HOHAHA)[9] in which sufficient relayed

TABLE I

Selected ^{1}H-n.m.r. data[a] for the isoxazolines **2, 3, 6,** and **7**

Compound	*Chemical shifts (δ, p.p.m.)*							*Coupling constants (J, Hz)*						
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6a*	*H-6b*	*1,2*	*2,3*	*3,4*	*4,5*	*5,6a*	*5,6b*	*6a,6b*
9a	5.77	4.54	3.84	4.17	5.05	3.42	3.30	3.7	4.4	8.8	2.1	6.7	11.6	16.6
10a	5.72	4.57	4.07	4.14	4.85	3.49	3.37	3.7	4.3	8.8	2.3	7.7	11.4	16.5
9b	5.72	4.56	3.65	4.17	5.01	3.19	3.05	3.6	4.3	8.9	2.1	7.7	12.0	18.0
10b	5.68	4.56	3.98	4.05	4.85	3.29	3.21	3.6	4.2	8.9	2.2	7.8	11.7	18.0
2a	5.94	4.64	4.14	4.23	5.10	3.55	3.45	3.7	<1	3.1	8.2	7.5	9.8	17.2
3a	6.05	4.70	4.05	4.34	4.99	2.87	3.20	3.9	<1	3.9	7.6	8.3	10.9	16.8
2b	5.87	4.57	4.01	4.22	5.01	3.34	3.19	3.7	<1	3.4	6.7	7.8	11.0	18.2
3b	6.00	4.65	4.00	4.27	5.03	2.82	3.14	3.6	<1	3.9	7.7	8.9	11.5	17.8

[a] For solutions in $CDCl_3$.

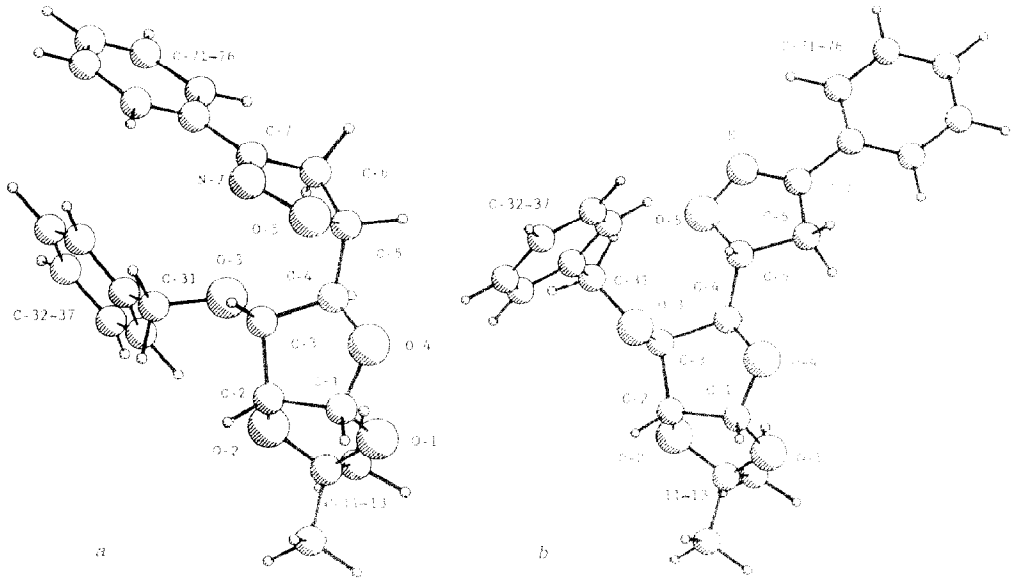


Fig. 1. Perspective drawings of (*a*) isoxazoline **6a** and (*b*) isoxazoline **2a**

correlations were observed (Fig. 2) to allow the connectivities for both components to be established unambiguously. Comparison of the spectral parameters for the isoxazolines with those for the corresponding benzonitrile oxide adducts allowed the major adduct (51%) to be identified as **6b** with the *R* configuration at C-5. Thus, the minor isomer was **7b**.

The reactions of the above nitrile oxides with 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose (**1a**) were re-examined. The reported[5] preference for the formation of the adducts **2**, with *erythro* stereochemistry at C-4,5, was confirmed. Cycloaddition of benzonitrile oxide to **1a** afforded a 90:10 mixture (^{1}H-n.m.r. data) of the isoxazolines **2a** and **3a** in a combined yield of 95%. The isomers were isolated by chromatography and the structure of the major product (**2a**) was determined by X-ray crystallography (Fig. 1b). Traces of 3,5-diphenyl-1,2,4-oxadiazole and 3,4-diphenylfurazan *N*-oxide were isolated as by-products[8]. Likewise, ethoxycarbonylformonitrile oxide reacted with **1a** to give a 75% combined yield of the isoxazolines **2b** and **3b** in the ratio 86:14 (^{1}H-n.m.r. data).

π-Facial selectivity. The ratios of products for the above cycloadditions are compared in Table II. The low selectivities observed for the D-*ribo*-hex-5-enofuranose derivative **4** is in marked contrast to the substantial *erythro* preference for the *xylo* isomer **1a**. The 3-deoxy analogue **1b** also afforded mainly *erythro* products[5]. These results demonstrate that the "inside alkoxy effect" exerted by O-4 is *not* the sole factor that governs selectivity, and that homoallylic groups may either reinforce or counteract the effect of the allylic group.

Structures of the isoxazolines. The structures of the *erythro* products **2a** and **6a**

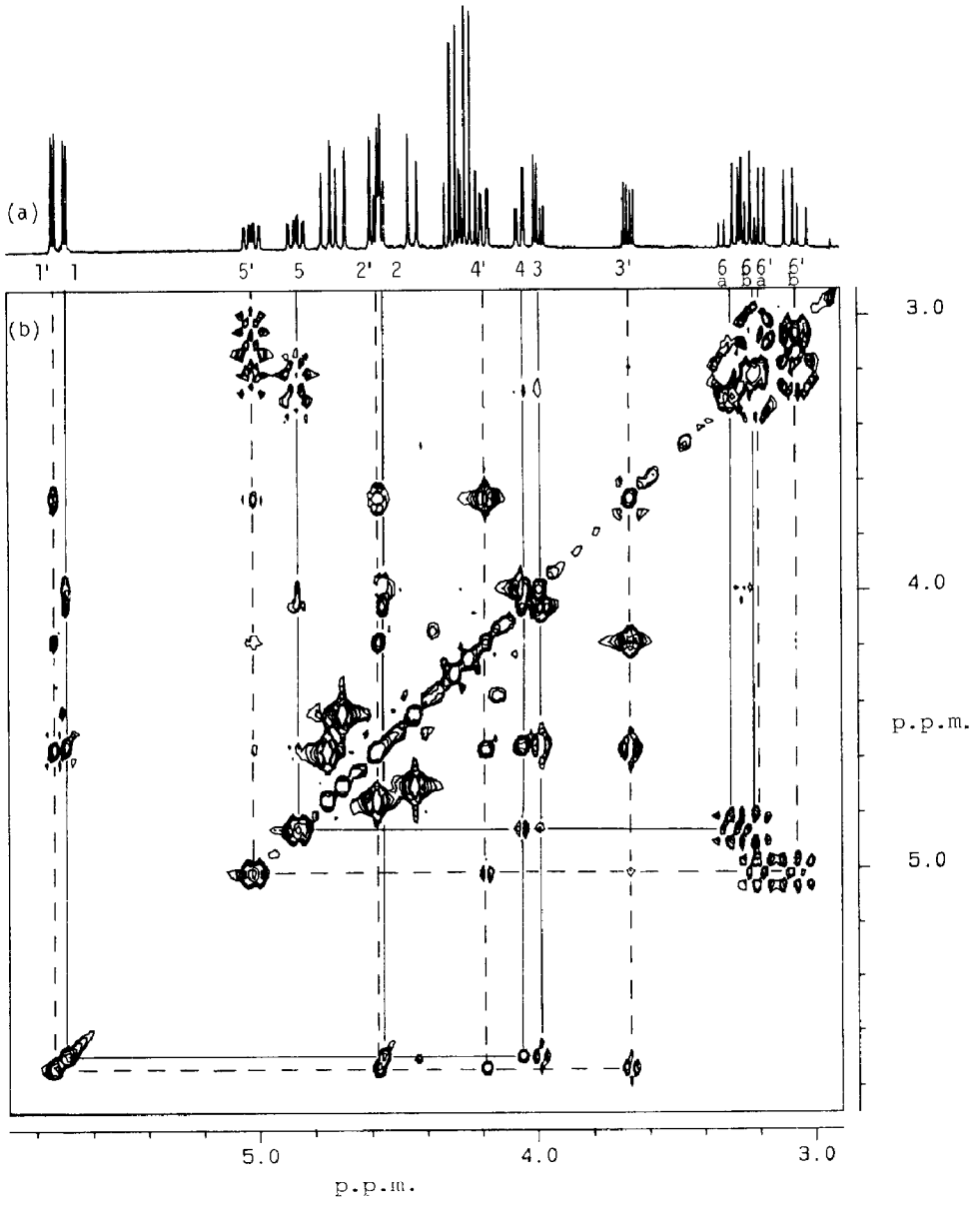


Fig. 2. (*a*) ^{1}H-N.m.r. spectrum of the mixture of **6b** and **7b**; (*b*) HOHAHA correlation spectrum of the same mixture, using the MLEV17 spin-locking sequence[9] for 60 ms; spectral width, 2 kHz in each dimension; 256 increments; Gaussian weighting (LB = −1.5; GB = 0.1) in f2 and sine-bell squared shifted by $\pi/6$ weighting in f1, and zero filling in each dimension to a 1 K × 512 data-point matrix before transformation; repetition time, 2 s. Correlations for the ring protons: **6b**——; **7b**----------.

TABLE II

π-Facial selectivity for the cycloaddition of nitrile oxides to **1a** and **4**

Substrate	*Nitrile oxide*	*Isoxazolines* (%)	
		erythro	threo
4	PhCNO	42	58
4	EtO$_2$CCNO	51	49
1a	PhCNO	90	10
		94[a]	6
1a	EtO$_2$CCNO	86	14
		84[b]	16
1a	MesCNO[c]	74[b]	26

[a] 2,4,6-Trimethylbenzonitrile oxide. [b] Ref. 5.

are compared in Fig. 1. Selected torsion angles involving hydrogen atoms are given in Table III, and other crystallographic data in Tables IV–IX.

In some respects, the structures of **2a** and **6a** are similar. The furanose ring in each compound adopts the E_4 envelope conformation with C-4 0.54 and 0.53 Å, respectively, below the plane C-1–C-2–C-3–O-4. For **6a**, the atoms C-6–C-7–N-7–O-5 in the isoxazoline ring are nearly coplanar (torsion angle 0.3°) with C-5 displaced by 0.30 Å. The corresponding angle for **2a** is 1.2° and the ring is more twisted, as evidenced by the H-5–C-5–C-6–H-6 torsion angles (Table III). The torsion angles for N-7–C-7–C-71–C-72 are 176.3° and 179.2°, respectively, indicating that the phenyl ring in each compound is almost coplanar with C-6–C-7–N-7–O-5.

The most significant differences between the two structures are in the region linking the two five-membered rings. For the D-*ribo* compound **6a**, the torsion angle H-4–C-4–C-5–H-5 is 70.6°, whereas that for the *xylo* isomer **2a** is 179.5°. Thus, the isoxazoline ring and its 3-phenyl substituent are rotated towards the BnO-3 of the furanose moiety in **6a**. These differences are reflected in the ^{1}H-n.m.r. spectra (Table I). For the *erythro* isomer **6a**, the $J_{4,5}$ value was 2.1 Hz, consistent with the 70.6° torsion angle in the crystal. The small $J_{4,5}$ value (2.3 Hz) for the major *threo* isomer **7a** indicated a similar conformation in solution. In contrast, for the *erythro* adduct **2a**, derived from **1a**, the $J_{4,5}$ value was 8.2 Hz and the torsion angle was 179.2°.

In other regards, the ^{1}H-n.m.r. data for the two series of isoxazolines were broadly

TABLE III

Selected torsion angles (°) (H-X–C-X–C-Y–H-Y) for **2a** and **6a**

Compound	*X,Y*					
	1,2	*2,3*	*3,4*	*4,5*	*5,6a*	*5,6b*
2a	7.0	86.8	38.9	179.5	124.4	1.5
6a	1.5	22.7	150.8	70.6	99.5	22.9

TABLE IV

Bond lengths with standard deviations in parentheses for **2a**

Bond	*Length, Å*	*Bond*	*Length, Å*
C-1–C-2	1.544(14)	C-11–C-13	1.474(14)
C-1–O-4	1.408(12)	C-11–O-2	1.439(12)
C-1–O-1	1.399(12)	O-3–C-30	1.444(11)
C-2–C-3	1.535(13)	C-30–C-31	1.500(13)
C-2–O-2	1.416(11)	C-5–C-6	1.513(14)
C-3–C-4	1.549(14)	C-5–O-5	1.489(13)
C-3–O-3	1.440(11)	C-6–C-7	1.475(15)
C-4–O-4	1.419(12)	C-7–N-7	1.285(14)
C-4–C-5	1.523(15)	C-7–C-71	1.502(14)
O-1–C-11	1.424(13)	N-7–O-5	1.414(11)
C-11–C-12	1.514(14)		

TABLE V

Bond angles with standard deviations in parentheses for **2a**

Bond	*Angle (°)*	*Bond*	*Angle (°)*
C-2–C-1–O-4	107.4 (8)	C-12–C-11–O-2	110.5 (8)
C-2–C-1–O-1	106.1 (8)	C-13–C-11–O-2	109.9 (8)
O-4–C-1–O-1	110.6 (8)	C-2–O-2–C-11	108.6 (7)
C-1–C-2–C-3	104.0 (8)	C-3–O-3–C-30	113.1 (7)
C-1–C-2–O-2	103.1 (7)	O-3–C-30–C-31	108.2 (7)
C-3–C-2–O-2	108.8 (7)	C-30–C-31–C-32	118.6 (8)
C-2–C-3–C-4	101.2 (7)	C-30–C-31–C-36	121.4 (8)
C-2–C-3–O-3	103.2 (7)	C-4–C-5–C-6	111.5 (9)
C-4–C-3–O-3	111.2 (7)	C-4–C-5–O-5	105.4 (8)
C-3–C-4–O-4	104.3 (8)	C-6–C-5–O-5	105.6 (8)
C-3–C-4–C-5	116.6 (8)	C-5–C-6–C-7	100.6 (8)
O-4–C-4–C-5	106.4 (8)	C-6–C-7–N-7	116.4 (10)
C-1–O-4–C-4	108.9 (7)	C-6–C-7–C-71	123.4 (9)
C-1–O-1–C-11	109.6 (7)	N-7–C-7–C-71	120.2 (10)
O-1–C-11–C-12	109.0 (8)	C-7–N-7–O-5	108.6 (8)
O-1–C-11–C-13	108.6 (8)	C-5–O-5–N-7	108.2 (7)
O-1–C-11–O-2	104.4 (8)	C-7–C-71–C-72	120.4 (8)
C-12–C-11–C-13	113.9 (8)	C-7–C-71–C-76	119.6 (8)

similar. For each compound, the isoxazoline ring protons give rise to a characteristic ABX system with the resonance of H-5, which is adjacent to the ring oxygen, having the highest chemical shift. The ^3J values of 10–12 Hz for the near-eclipsed protons H-5,6a, the 7–9 Hz *gauche* coupling for H-5,6b, and the geminal coupling of 16–18 Hz for H-6a,6b are typical of sugar isoxazolines[3]. In the furanose ring, the H-1 resonances for each pair of diastereomers were well resolved, despite their remoteness from the centre of asymmetry. For the adducts **6** and **7**, derived from **4**, the resonance for H-1 had a higher chemical shift in the *erythro* product **6**, whereas the order was reversed for the

TABLE VI

Torsion angles with standard deviations in parentheses for **2a**

	Angle (°)		*Angle (°)*
O-4 C-1 C-2 C-3	−4.5(10)	C-1 O-1 C-11 C-12	−94.5 (9)
O-4 C-1 C-2 O-2	109.0 (8)	C-1 O-1 C-11 C-13	140.8 (8)
O-1 C-1 C-2 C-3	−122.8 (8)	C-1 O-1 C-11 O-2	23.6(10)
O-1 C-1 C-2 O-2	−9.2 (9)	O-1 C-11 O-2 C-2	−30.0 (9)
C-2 C-1 O-4 C-4	−19.8(10)	C-12 C-11 O-2 C-2	87.1 (9)
O-1 C-1 O-4 C-4	95.5 (9)	C-13 C-11 O-2 C-2	−146.4 (8)
C-2 C-1 O-1 C-11	9.0(10)	C-3 O-3 C-30 C-31	176.3 (7)
O-4 C-1 O-1 C-11	−125.2 (8)	O-3 C-30 C-31 C-32	85.3(10)
C-1 C-2 C-3 C-4	24.2 (9)	O-3 C-30 C-31 C-36	−91.7(10)
C-1 C-2 C-3 O-3	−91.0 (8)	C-30 C-31 C-32 C-33	−177.0 (8)
O-2 C-2 C-3 C-4	−85.2 (8)	C-30 C-31 C-36 C-35	176.9 (8)
O-2 C-2 C-3 O-3	159.6 (7)	C-4 C-5 C-6 C-7	121.5 (9)
C-1 C-2 O-2 C-11	24.0 (9)	O-5 C-5 C-6 C-7	−7.5(10)
C-3 C-2 O-2 C-11	134.0 (8)	C-4 C-5 O-5 N-7	125.7 (8)
C-2 C-3 C-4 O-4	−36.6 (9)	C-6 C-5 O-5 N-7	−7.6(10)
C-2 C-3 C-4 C-5	−153.6 (9)	C-5 C-6 C-7 N-7	5.8(12)
O-3 C-3 C-4 O-4	72.5 (9)	C-5 C-6 C-7 C-71	174.3 (9)
O-3 C-3 C-4 C-5	−44.5(11)	C-6 C-7 N-7 O-5	1.2(13)
C-2 C-3 O-3 C-30	−147.0 (7)	C-71 C-7 N-7 O-5	−178.9 (8)
C-4 C-3 O-3 C-30	105.2 (8)	C-6 C-7 C-71 C-72	3.6(14)
C-3 C-4 O-4 C-1	35.9 (9)	C-6 C-7 C-71 C-76	−175.8 (9)
C-5 C-4 O-4 C-1	159.8 (8)	N-7 C-7 C-71 C-72	−176.3 (9)
C-3 C-4 C-5 C-6	−178.0 (8)	N-7 C-7 C-71 C-76	4.3(14)
C-3 C-4 C-5 O-5	−63.9(11)	C-7 N-7 O-5 C-5	4.1(11)
O-4 C-4 C-5 C-6	66.1(10)	C-7 C-71 C-72 C-73	−179.4 (8)
O-4 C-4 C-5 O-5	−179.8 (7)	C-7 C-71 C-76 C-75	179.4 (8)

TABLE VII

Bond lengths with standard deviations in parentheses for **6a**

Bond	*Length, Å*	*Bond*	*Length, Å*
C-1 C-2	1.482(10)	C-11 C-13	1.447(10)
C-1 O-4	1.386 (8)	C-11 O-2	1.385 (8)
C-1 O-1	1.382 (8)	O-3 C-31	1.414 (8)
C-2 C-3	1.513 (9)	C-31 C-32	1.452(10)
C-2 O-2	1.390 (9)	C-32 C-33	1.363(10)
C-3 C-4	1.440 (9)	C-32 C-37	1.334(10)
C-3 O-3	1.401 (8)	C-33 C-34	1.367(12)
C-4 O-4	1.405 (8)	C-34 C-35	1.336(14)
C-4 C-5	1.513(10)	C-35 C-36	1.307(14)
C-5 C-6	1.467(10)	C-36 C-37	1.396(12)
C-5 O-5	1.422 (9)	C-71 C-72	1.362(11)
C-6 C-7	1.418(10)	C-71 C-76	1.352(10)
C-7 N-7	1.267 (9)	C-72 C-73	1.394(13)
C-7 C-71	1.448(10)	C-73 C-74	1.309(15)
N-7 O-5	1.403 (8)	C-74 C-75	1.353(14)
O-1 C-11	1.426 (8)	C-75 C-76	1.345(12)
C-11 C-12	1.493(11)		

TABLE VIII

Bond angles with standard deviations in parentheses for **6a**

Bond	*Angle (°)*	*Bond*	*Angle (°)*
C-2–C-1–O-4	107.5 (6)	O-1–C-11–C-13	110.8 (6)
C-2–C-1–O-1	104.8 (6)	O-1–C-11–O-2	103.6 (5)
O-4–C-1–O-1	109.9 (5)	C-12–C-11–C-13	114.8 (6)
C-1–C-2–C-3	102.7 (6)	C-12–C-11–O-2	109.5 (6)
C-1–C-2–O-2	105.5 (6)	C-13–C-11–O-2	111.7 (6)
C-3–C-2–O-2	110.6 (6)	C-2–O-2–C-11	108.0 (5)
C-2–C-3–C-4	104.0 (5)	C-3–O-3–C-31	112.8 (5)
C-2–C-3–O-3	113.3 (5)	O-3–C-31–C-32	108.0 (6)
C-4–C-3–O-3	109.9 (5)	C-31–C-32–C-33	120.1 (6)
C-3–C-4–O-4	103.7 (5)	C-31–C-32–C-37	120.3 (6)
C-3–C-4–C-5	116.6 (6)	C-33–C-32–C-37	119.6 (7)
O-4–C-4–C-5	108.3 (5)	C-32–C-33–C-34	119.4 (7)
C-1–O-4–C-4	106.9 (5)	C-33–C-34–C-35	120.9 (9)
C-4–C-5–C-6	111.8 (6)	C-34–C-35–C-36	119.8(10)
C-4–C-5–O-5	108.8 (6)	C-35–C-36–C-37	121.2 (9)
C-6–C-5–O-5	104.5 (6)	C-32–C-37–C-36	119.1 (8)
C-5–C-6–C-7	102.1 (6)	C-7–C-71–C-72	116.5 (7)
C-6–C-7–N-7	114.0 (6)	C-7–C-71–C-76	123.2 (6)
C-6–C-7–C-71	127.4 (6)	C-72–C-71–C-76	120.4 (7)
N-7–C-7–C-71	118.7 (6)	C-71–C-72–C-73	118.1 (8)
C-7–N-7–O-5	108.3 (6)	C-72–C-73–C-74	120.5 (9)
C-5–O-5–N-7	107.1 (5)	C-73–C-74–C-75	120.7(10)
C-1–O-1–C-11	107.2 (5)	C-74–C-75–C-76	120.4 (9)
O-1–C-11–C-12	105.7 (6)	C-71–C-76–C-75	119.8 (7)

adducts **2** and **3**. Other differences for the furanose protons, particularly the $J_{2,3}$ and $J_{3,4}$ values, can be attributed to the inversion of stereochemistry at C-3.

Thus, the cycloadditions of nitrile oxides to the α-D-*ribo*-hex-5-enofuranose derivative **4** are much less selective than the corresponding reactions with *xylo* isomer **1a**, an effect which emphasises the important role played by homoallylic as well as allylic groups.

EXPERIMENTAL

General. — T.l.c. was carried out on Silica Gel F_{254} (Merck) with detection by u.v. absorbance. Silica Gel 60 (Merck) was used for flash-column chromatography. Optical rotations were measured with a Perkin–Elmer 241 polarimeter. The ^{1}H- and ^{13}C-n.m.r. spectra were recorded with Bruker WP200 and WH360 spectrometers on solutions in $CDCl_3$ (internal Me_4Si). F.a.b.-mass spectra (glycerol matrix) were obtained with a Kratos MS50TC instrument. The by-products (3,5-diphenyl-1,2,4-oxadiazole, 3,4-diphenylfurazan *N*-oxide, and 3,4-diethoxycarbonylfurazan *N*-oxide) were identified by comparison (t.l.c., n.m.r.) with authentic samples[8].

Cycloaddition of benzonitrile oxide and ethoxycarbonylformonitrile oxide to 3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene-α-D-ribo- (**4**) *and -D-xylo-hex-5-enofuranose*

TABLE IX

Torsion angles with standard deviations in parentheses for **6a**

	Angle (°)		*Angle (°)*
O-4–C-1–C-2–C-3	3.1 (7)	C-6–C-7–N-7–O-5	0.3 (8)
O-4–C-1–C-2–O-2	119.0 (6)	C-71–C-7–N-7–O-5	−178.6 (6)
O-1–C-1–C-2–C-3	−113.8 (6)	C-6–C-7–C-71–C-72	2.0(11)
O-1–C-1–C-2–O-2	2.1 (7)	C-6–C-7–C-71–C-76	−178.9 (7)
C-2–C-1–O-4–C-4	−26.3 (7)	N-7–C-7–C-71–C-72	−179.2 (7)
O-1–C-1–O-4–C-4	87.3 (6)	N-7–C-7–C-71–C-76	0.1(11)
C-2–C-1–O-1–C-11	−21.2 (7)	C-7–N-7–O-5–C-5	−13.0 (7)
O-4–C-1–O-1–C-11	−136.5 (5)	C-1–O-1–C-11–C-12	147.9 (6)
C-1–C-2–C-3–C-4	20.1 (7)	C-1–O-1–C-11–C-13	−87.2 (7)
C-1–C-2–C-3–O-3	139.4 (5)	C-1–O-1–C-11–O-2	32.7 (6)
O-2–C-2–C-3–C-4	−92.1 (6)	O-1–C-11–O-2–C-2	−31.3 (7)
O-2–C-2–C-3–O-3	27.2 (7)	C-12–C-11–O-2–C-2	−143.7 (6)
C-1–C-2–O-2–C-11	18.5 (7)	C-13–C-11–O-2–C-2	88.0 (7)
C-3–C-2–O-2–C-11	128.8 (6)	C-3–O-3–C-31–C-32	−169.3 (5)
C-2–C-3–C-4–O-4	−36.1 (6)	O-3–C-31–C-32–C-33	62.9 (8)
C-2–C-3–C-4–C-5	−155.0 (6)	O-3–C-31–C-32–C-37	−117.8 (7)
O-3–C-3–C-4–O-4	−157.7 (5)	C-31–C-32–C-33–C-34	177.9 (7)
O-3–C-3–C-4–C-5	83.4 (7)	C-37–C-32–C-33–C-34	−1.4(11)
C-2–C-3–O-3–C-31	77.3 (7)	C-31–C-32–C-37–C-36	−177.6 (7)
C-4–C-3–O-3–C-31	−166.9 (5)	C-33–C-32–C-37–C-36	1.7(11)
C-3–C-4–O-4–C-1	39.5 (6)	C-32–C-33–C-34–C-35	0.2(13)
C-5–C-4–O-4–C-1	163.9 (5)	C-33–C-34–C-35–C-36	0.7(15)
C-3–C-4–C-5–C-6	−67.9 (8)	C-34–C-35–C-36–C-37	−0.4(16)
C-3–C-4–C-5–O-5	47.0 (8)	C-35–C-36–C-37–C-32	−0.8(14)
O-4–C-4–C-5–C-6	175.7 (6)	C-7–C-71–C-72–C-73	178.7 (8)
O-4–C-4–C-5–O-5	−69.4 (7)	C-76–C-71–C-72–C-73	−0.5(12)
C-4–C-5–C-6–C-7	98.9 (7)	C-7–C-71–C-76–C-75	179.6 (7)
O-5–C-5–C-6–C-7	−18.6	C-72–C-71–C-76–C-75	−1.3(11)
C-4–C-5–O-5–N-7	−99.8 (6)	C-71–C-72–C-73–C-74	1.1(14)
C-6–C-5–O-5–N-7	19.7 (7)	C-72–C-73–C-74–C-75	0.1(16)
C-5–C-6–C-7–N-7	11.9 (8)	C-73–C-74–C-75–C-76	−1.8(15)
C-5–C-6–C-7–C-71	−169.3 (7)	C-74–C-75–C-76–C-71	2.4(13)

(**1a**). — (*a*) A solution of triethylamine (325 mg, 3.2 mmol) in 1,2-dichloroethane (13 mL) was added over 36 h with a syringe to a solution of **4** (538 mg, 1.95 mmol) and benzohydroximoyl chloride[10] (455 mg, 2.9 mmol) in 1,2-dichloroethane (7 mL), and the mixture was stirred for a further 6 h. The precipitated triethylamine hydrochloride was removed, the filtrate was washed with water (25 mL), diluted with chloroform, and dried ($MgSO_4$), and the solvent was evaporated *in vacuo* to afford a yellow syrup. Dry flash-column chromatography (20–80% Et_2O in cyclohexane, gradient elution) yielded, first, 3,4-diphenylfurazan *N*-oxide and then a mixture (541 mg, 70%) of (5*R*)- (**6a**) and (5*S*)-5-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-tetrofuranos-4-yl)-3-phenyl-2-isoxazoline (**7a**), m.p. 85–86° (from cyclohexane), Mass spectrum: *m/z* 396 ($M^+ + 1$) (Found: C, 69.5; H, 6.2; N, 3.6. $C_{23}H_{25}NO_5$ calc.: C, 69.9; H, 6.3; N, 3.5%). For the ^1H-n.m.r. data, see Table I. The ratio **6a:7a** was determined as 42:58 from the integrated intensities of the signals for H-1 and H-5. Crystals suitable for X-ray analysis were

obtained by repeated recrystallisation from chloroform. The ^{1}H-n.m.r. spectrum of this sample showed it to be **6a**.

(*b*) Reaction of ethyl chloro-oximinoacetate[11] and **4** (1.0:1.4), following the procedure in (*a*), gave a 51:49 mixture of (5*R*)- (**6b**) and (5*S*)-5-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*ribo*-tetrofuranos-4-yl)-3-ethoxycarbonyl-2-isoxazoline (**7b**) isolated as an oil. Mass spectrum: *m/z* 392.17088 ($M^+ + 1$) (Calc. for $C_{20}H_{26}NO_7$: *m/z* 392.17091). The assignment of the ^{1}H-n.m.r. data was made from the TOCSY spectrum.

(*c*) Reaction of benzohydroximoyl chloride[10] and **1a**[7] (1.0:1.5) as in (*a*), with dry flash-column chromatography of the product, afforded in sequence 3,5-diphenyl-1,2,4-oxadiazole (2%), 3,4-diphenylfurazan-*N*-oxide (2%), **1a**, and then (5*R*)-5-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-3-phenyl-2-isoxazoline (**2a**, 89%), as needles, m.p. 121–124° (from Et_2O/hexane, 1:1), $[\alpha]_D^{21}$ −128° (*c* 2, chloroform); lit.[5] m.p. 125–127°. ^{13}C-N.m.r. data (50 MHz): δ 156.8 (C-7), 137.3, 129.3 (Ph*C*), 130.0, 127.9, 127.8, 127.7 (10 Ph*C*H), 111.8 (*C*Me$_2$), 105.1 (C-1), 82.8, 81.4, 80.5 (C-2,3,4), 77.1 (C-5), 72.6 (*C*H$_2$Ph), 31.3 (C-6), 26.7 and 26.1 (CH$_3$). Mass spectrum: *m/z* 396 ($M^+ + 1$). The final fraction contained (5*S*)-5-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-3-phenyl-2-isoxazoline (**3a**, 6%). ^{13}C-N.m.r. data (50 MHz): δ 156.1 (C-7), 136.7, 129.2 (Ph*C*H), 129.9, 128.5, 128.1, 127.9, 126.5 (10 Ph*C*H), 112.0 (*C*Me$_2$), 105.6 (C-1), 81.9, 81.8, 81.6 (C-2,3,4), 79.6 (C-5), 71.6 (*C*H$_2$Ph), 37.0 (C-6), 26.8 and 26.3 (CH$_3$). Mass spectrum: *m/z* 396.18107 ($M^+ + 1$) (Calc. for $C_{23}H_{26}NO_5$: *m/z* 396.18108). The ^{1}H-n.m.r. data for **2a** and **3a** are listed in Table I. The ratio **2a:3a** was 90:10 (^{1}H-n.m.r. data).

(*d*) Reaction of ethyl chloro-oximinoacetate[11] and **1a** (1.0:1.5) by the procedure in (*a*) gave 3,4-diethoxycarbonylfurazan *N*-oxide (14%), then (5*R*)-5-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-3-ethoxycarbonyl-2-isoxazoline (**2b**, 63%) as needles, m.p. 63–65°, $[\alpha]_D^{21}$ −111° (*c* 1.5, chloroform); lit.[5] oil (Found: C, 61.3; H, 6.7; N, 3.5. $C_{20}H_{25}NO_7$ calc.: C, 61.4; H, 6.4; N, 3.6%). ^{13}C-N.m.r. data (50 MHz): δ 160.2 (*C*O$_2$Et), 151.8 (C-7), 136.9 (Ph*C*), 128.2, 127.7, 127.4 (5 Ph*C*H), 111.7 (*C*Me$_2$), 104.9 (C-1), 82.1, 81.2, 79.9 (C-2,3,4), 79.8 (C-5), 72.0 (*C*H$_2$Ph), 61.6 (*C*H$_2$CH$_3$), 36.0 (C-6), 26.5, 25.9 (CH$_3$), and 13.7 (CH$_2$*C*H$_3$). Mass spectrum: *m/z* 392 ($M^+ + 1$).

Eluted last was (5*S*)-5-(3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-tetrofuranos-4-yl)-3-ethoxycarbonyl-2-isoxazoline (**3b**, 12%), isolated as an oil, $[\alpha]_D^{21}$ +13° (*c* 2.5, chloroform) (Found: C, 61.6; H, 6.6; N, 3.5%). ^{13}C-N.m.r. data (50 MHz): δ 160.3 (*C*O$_2$Et), 151.3 (C-7), 136.9 (Ph*C*), 128.4, 128.1, 127.9, 127.7 (5 Ph*C*H), 112.1 (*C*Me$_2$), 105.6 (C-1), 82.1, 81.9, 81.7 (C-2,3,4), 81.2 (C-5), 71.7 (*C*H$_2$Ph), 61.8 (*C*H$_2$CH$_3$), 35.7 (C-6), 26.8, 26.3 (CH$_3$), and 13.9 (CH$_2$*C*H$_3$). Mass spectrum: *m/z* 392 ($M^+ + 1$). The ^{1}H-n.m.r. data for **2b** and **3b** are listed in Table IX. The ratio **2b:3b** was 86:14 (^{1}H-n.m.r. data).

Crystal structures of **2a** *and* **6a**. — Data for **2a**, where different from that for **6a**, are given in square brackets. Tables of bond lengths, angles, and torsion angles are shown in Tables IV–IX.

(*a*) *Crystal data*. $C_{23}H_{25}NO_5$, M = 395.4, orthorhombic, space group $P2_12_12_1$; a = 19.264(7) [10.295(4)], b = 11.505(4) [38.649(15)], c = 8.922(8) [5.299(4)] Å; V = 1977.4

[2108] Å^3 [from setting angles for 16 *hko* and 4 *001* data, $2\theta = 12$–$18°$, $\lambda = 0.71073$ Å], $Z = 4$, $D_{calc} = 1.328$ [1.246] g.cm^{-3}, $T = 22°$; colourless needle [lath], $0.3 \times 0.8 \times 1.0$ [$0.06 \times 0.12 \times 0.5$] mm; $\mu = 0.087$ mm^{-1}, $F(000) = 840$.

(*b*) *Data collection and processing.* STADI-2, two-circle diffractometer, graphite-monochromated Mo-K_α radiation, $T = 22°$, ω-scans with ω-range $(1.0 + 0.5\sin\mu/\tan\theta)°$, 1603 [3626] unique reflections ($2\theta_{max} \times 50°$, h: $0 \rightarrow 22$ [$-12 \rightarrow 12$], k: $0 \rightarrow 13$ [$0 \rightarrow 45$], l: $0 \rightarrow 10$ [$0 \rightarrow 6$]), giving 1381 [1240] with $F \geqslant 4\sigma(F)$ for use in all calculations. No significant crystal decay or movement was apparent*.

(*c*) *Structure solution and refinement.* Automatic direct methods[12] located all non-hydrogen atoms which were then refined anisotropically; hydrogen atoms were fixed in calculated positions with fixed temperature factors of $U = 0.07$ Å^2. At the final convergence, R and R_w were 0.070 and 0.079 [0.084, 0.024], respectively. $S = 1.20$ [1.04] for 263 refined parameters, and the final difference synthesis showed no peak or trough outside ± 0.25 [0.39] eÅ^{-3}. No absorption corrections were made. An empirical extinction parameter refining to $9.4(15) \times 10^{-8}$ was applied to **2a** only. The weighting scheme $w^{-1} = \sigma^2(F) + 0.00082\,[0.0]\,|F|^2$ gave satisfactory agreement analyses, and in the final cycle, the maximum shift over error was 0.09 [0.07]. Inlaid[13] atomic scattering factors were used, molecular geometry calculations utilised CALC[14], and the Figures were produced by PLUTO[15].

ACKNOWLEDGMENT

We thank the S.E.R.C. for financial support.

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