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SYNTHESIS OF *C*-SUBSTITUTED TRIAZOLES, ISOXAZOLES, AND PYRAZOLES BY 1,3-DIPOLAR CYCLOADDITION TO ACETYLENIC SUGARS

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ABSTRACT

Addition of phenyl azide to 3,5-di-*O*-acetyl-6,7-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-hept-6-ynofuranose (**1**) and subsequent saponification gave a 4-substituted 1-phenyl-1,2,3-triazole derivative (**3**) whose optical rotatory dispersion (o.r.d.) curve was positive. The α-D-*gluco* analog (**5**) of **1** similarly gave the 5-epimer (**7**) of **3**; its o.r.d. curve was negative. Both **3** and **7** were degraded to the known 1-phenyl-1,2,3-triazole-4-carboxaldehyde. Similarly, addition of 2,4,6-trimethylbenzonitrile *N*-oxide to **1** or **5** gave the corresponding, crystalline 3-mesitylisoxazoles as single products; ^{13}C-n.m.r. spectroscopy was used to establish the orientation of addition. Related 3-mesitylisoxazoles (**11** and **13**) were obtained from 1,2:3,4-di-*O*-isopropylidene-D-*glycero*-α-D-*galacto*-oct-7-ynopyranose (**10**) and its L-*glycero* 6-epimer (**12**), respectively; **11** showed the expected, large levorotation, and the 6-epimer **13** was also levorotatory. Benzonitrile (*N*-phenyl)imine, prepared *in situ* from 1-(α-chlorobenzylidene)-2-phenylhydrazine and base, did not react with **10** (or its 6-epimer **12**), but did react with the 6-keto analog to give a 5-substituted 1,3-diphenyl-1,2-diazole.

INTRODUCTION

There has been considerable interest in synthetic routes to heterocycles *C*-substituted by a sugar residue[3], because of the discovery of natural *C*-nucleosides showing carcinostatic or antiviral activity; such agents include formycin[4], formycin B (ref. 5), showdomycin[6], and pyrazomycin[7]. As part of a general study of the applications of acetylenic sugars in synthesis, this report describes the use of pairs of chain-terminal acetylenic-sugar derivatives, epimeric at the propargylic position, in cycloaddition reactions to (*a*) study the feasibility of such reactions within a carbohydrate matrix, (*b*) examine the regioselectivity of the reactions, and (*c*) investigate the

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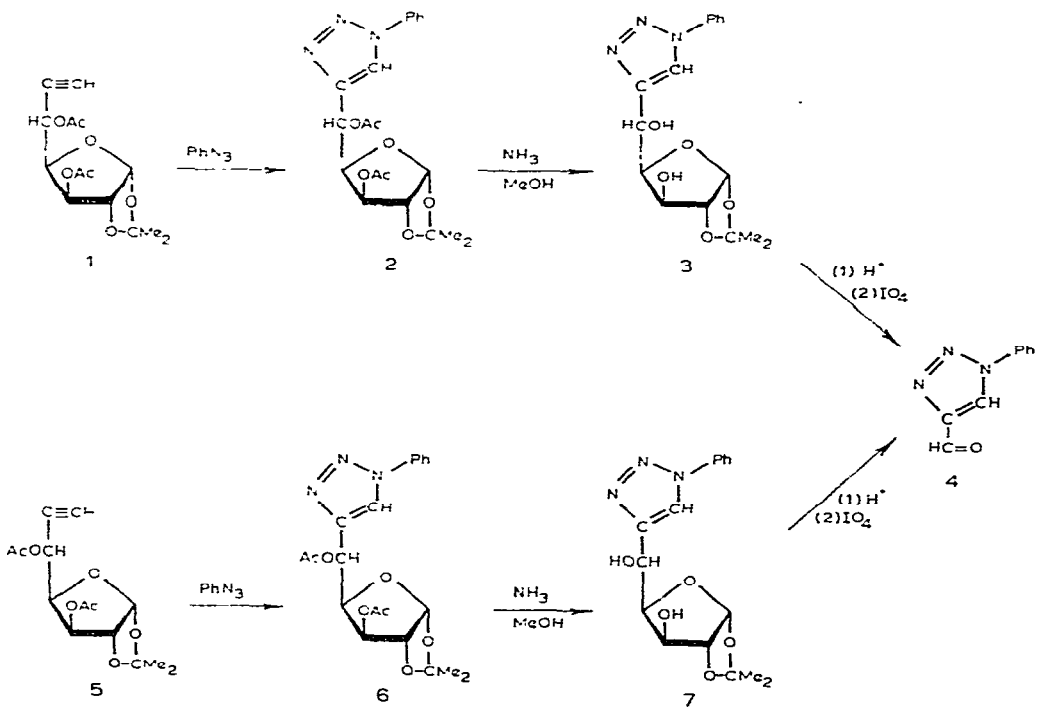
chiroptical properties of the products as a function of the chirality at the asymmetric center α-disposed to the heterocycle, whose stereochemistry is defined from the established stereochemistry of the precursor acetylene.

Acetylenes are known to be good 1,3-dipolarophiles in 1,3-cycloaddition reactions[8], and acyclic acetylenic-sugar derivatives have already been employed in this laboratory in such reactions, with use of phenyl azide to generate *C*-(sugar-substituted)-1,2,3-triazoles[9,10]; it was shown that 4-substituted 1-phenyl-1,2,3-triazoles are the main products[9,10], and small proportions of the 5-substituted analogs may also be formed[20].

This report describes the use of two pairs of acetylenic sugar derivatives, readily obtained by ethynylation of aldehydo sugar precursors and stereochemically characterized at the propargylic position, as model 1,3-dipolarophiles, and examines their reactions with three types of 1,3-dipolar species. The acetylenes used were 3,5-di-*O*-acetyl-6,7-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-hept-6-ynofuranose (**1**) and its 5-epimer (**5**), both available[1,11] in a number of steps from D-glucose, and 1,2:3,4-di-*O*-isopropylidene-α-D-*glycero*-D-*galacto*-oct-7-ynopyranose (**10**) and its 6-epimer (**12**), both available[12] from D-galactose as the precursor. Three types of 1,3-dipolar species were used: phenyl azide is shown to react with **1** and **5** to give mainly 4-substituted 1-phenyl-1,2,3-triazoles, and 2,4,6-trimethylbenzonitrile *N*-oxide reacts to give 5-substituted 3-mesitylisoxazole derivatives with both **1** and **5** and both **10** and **12**. Neither of the pairs of acetylenic sugar derivatives reacted with benzonitrile



(*N*-phenyl)imine, but this 1,3-dipolar species did react with the 6-ketone (**14**) obtained[2,13] by oxidation of **10** or **12**, and a 5-substituted 1,3-diphenylpyrazole was obtained.

The optical rotatory dispersion spectra of the heterocyclic adducts are discussed in relation to the stereochemistry at the chiral center adjacent to the heterocycle.

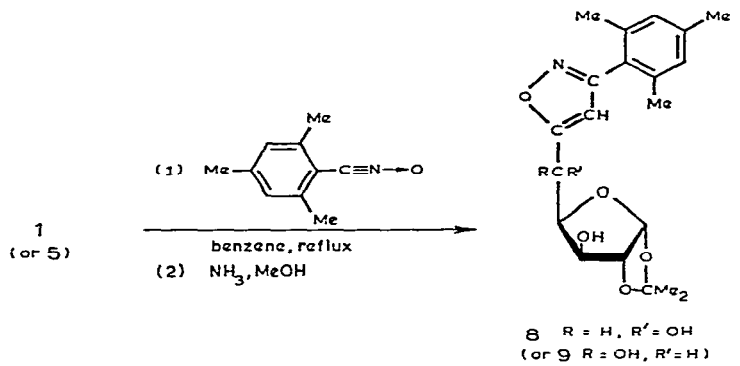
RESULTS AND DISCUSSION

Each of the acetylenic sugar derivatives **1** and **5** reacted with phenyl azide during 2 h at 100° to give the corresponding 4-substituted 1-phenyl-1,2,3-triazole derivatives **2** and **6**, respectively; the latter was obtained crystalline. Deacetylation of **2** and **6** with methanolic ammonia gave the corresponding diols **3** and **7**, both crystalline, in 64 and 57% overall yields from the acetylenic precursors **1** and **5**. Completion of the cycloaddition reaction was readily monitored by disappearance of the acetylenic C≡C absorption in the infrared spectra. The ^{1}H-n.m.r. spectra of both **2** and **6** showed a single, low-field singlet (at 8.08 and 8.05 p.p.m. respectively), assigned to H-5 of the triazole ring by comparison with previous data[9]; the products isolated were single isomers. Confirmation that they were substituted through C-4 was achieved by degradation of **3** and **7** by acid-catalyzed deacetonation followed by oxidation with 4 molar equivalents of periodate, to give a crystalline product (m.p. 98–99°) identified in each instance (by direct comparison) as the known[9,10] 1-phenyl-1,2,3-triazole-4-carboxaldehyde (**4**), and clearly differentiated by m.p. and X-ray diffractogram from the isomeric 5-carboxaldehyde[10] (m.p. 77–78°) used as a reference sample.

The favored transition-state for the cycloaddition is evidently the one in which the substituted end of the azide group is aligned with the unsubstituted end of the acetylene. In previous work[10] with a less-hindered acetylene, a minor proportion of the 5-substituted addition-product was isolated, but no direct evidence for such minor products was obtained in the present two reactions. The products **3** and **7** showed strong u.v. absorption near 245 nm, corresponding closely with values reported[9] for related 1,2,3-triazoles.

Nitrile oxides are 1,3-dipolar species that are known[8] to react with acetylenes to afford isoxazole derivatives, and this reaction was explored with the pairs of acetylenes **1** and **5**, and **10** and **12**, by use of 2,4,6-trimethylbenzonitrile *N*-oxide[14] (mesitylnitrile *N*-oxide). The *β*-L-*ido* acetylene **1** reacted with mesitylnitrile *N*-oxide in boiling benzene during 15 min to give, after *O*-deacetylation of the product, 71% of a crystalline adduct, the isoxazole **8**. Only one isomer was isolated, and its structure was deduced from its ^{1}H- and ^{13}C-n.m.r. spectra. After deuterium exchange of the hydroxyl protons, the ^{1}H-n.m.r. spectrum showed no acetylenic proton, but a 2-proton singlet (6.82 p.p.m.) and a 1-proton singlet (6.23 p.p.m.) could be attributed to the aromatic protons on the mesityl group and on C-4 of the isoxazole ring, respectively, The indicated orientation of addition was anticipated from steric considerations, and the low-field position of the aromatic H-4 signal lent weight to

this supposition. More-direct evidence was provided by the natural-abundance-^{13}C spectrum of **8** (see Table III). The chemical shifts of H-1,2,3,4, and 5 of the sugar portion were essentially the same in the spectra of the precursor acetylene (**1**) and the isoxazole product (**8**), and each gave rise to a singlet in the broad-band, ^1H-decoupled spectrum, and to a doublet in the off-resonance, ^1H-decoupled spectrum, as expected



8 R = H, R' = OH
(or **9** R = OH, R' = H)

from the presence of a methine proton at each of these carbon atoms. Signals of the three carbon atoms in the isoxazole portion were readily assigned by reference to the corresponding chemical-shifts for model isoxazole rings[15] having substituents at C-3, C-4, and C-5. The signals of C-3 and C-5 appear at lower field than that of C-4, because of the electron-withdrawing effects of oxygen and nitrogen. These signals appeared as singlets in the broad-band, ^1H-decoupled spectra, but off-resonance, ^1H-decoupling caused the high-field, isoxazole-ring signal (104.3 p.p.m., C-4) to appear as a doublet, whereas the low-field signals (162.5 and 173 p.p.m., C-3 and C-5) remained as singlets, thus establishing that C-3 and C-5 are carbon-substituted, whereas C-4 had a hydrogen substituent.

The anticipated regiospecificity of the nitrile oxide cycloaddition was thus confirmed: it is consistent with that expected from steric and electronic considerations[16].

The scope of the mesitylnitrile oxide reaction was extended to the 5-epimer (**5**) of **1**, which gave, in a similar way, the crystalline isoxazole **9**. Likewise, the C_8 acetylenes **10** and **12** underwent cycloaddition with mesitylnitrile *N*-oxide to give the corresponding isoxazole derivatives **11** and **13**, respectively, in ~70% yield; compound **11** was crystalline, and **13** was a syrup. Details of the characterization of these products are given in the Experimental section and in Tables I and II. The ^1H-n.m.r. data showed low-field patterns for the aromatic signals very similar to those discussed for **8**. The two 6-epimers showed appreciable differences in the value of $J_{5,6}$, 8.0 Hz for **11** and 5.5 Hz for **13**, evidently the result of the steric bulk of the isoxazole substituent relative to the 6-hydroxyl group; this behavior contrasts with that observed for the acetylenic precursors[12], where the couplings for the two epimers are very similar in magnitude and do not permit differentiation of the epimers.

TABLE I

CHEMICAL SHIFTS OF PROTONS

Compd.	*Solvent*	*Chemical shifts (p.p.m.), from 100-MHz spectra*[a]								
		H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*Ar*	CMe_2	*Other*
2	$CDCl_3$	5.99 d	4.50 d	5.14 d	5.07 dd	6.26 d		7.40–7.76 (Ph) 8.08 s (hetero)	1.48 1.33	2.01 (OAc)
3	$(CD_3)_2CO$[b,c]	6.07 d	4.41 d	4.10 d	4.32 dd	5.20 d		7.70–8.06 (Ph) 8.40 s (hetero)	1.48 1.22	
6	$CDCl_3$	5.93 d	4.52 d	5.56 d	5.06 dd	6.15 d		7.40–7.78 (Ph) 8.05 s (hetero)	1.48 1.24	2.01 (OAc) 1.96
7	$(CD_3)_2CO$[b,c]	6.10 d	4.48 d	4.24 d	4.44 dd	5.26 d		6.68–8.08 (Ph) 8.40 s (hetero)	1.40 1.24	
8	$CDCl_3$[b]	5.91 d	4.38 d	4.21 d	4.32 dd	5.20 d		6.82 s (Ph) 6.23 s (hetero)	1.36 1.18	2.19 (Ar-CH_3) 2.00 (2) (Ar-CH_3)
9	$(CD_3)_2CO$[b,c]	5.95 d	4.63 d	4.41 d	4.45 dd	5.20 d		6.96 s (Ph) 6.40 s (hetero)	1.28 1.44	2.08 (2) (Ar-CH_3) 2.26 (Ar-CH_3)
11	$CDCl_3$	5.53 d	4.32 dd	4.65 dd	4.46 dd	4.13 dd	5.09 d	6.89 s (Ph) 6.31 s (hetero)	1.42 (2) 1.28 1.24	2.23 (Ar-CH_3) 3.75 (OH) 2.06 (2) (Ar-CH_3)
13	$CDCl_3$[b]	5.59 d	4.35 dd	4.64 dd	4.29 dd	4.14 dd	5.21 d	6.90 s (Ph) 6.34 s (hetero)	1.45 (2) 1.27 (2)	2.25 (Ar-CH_3) 2.07 (2) (Ar-CH_3)
15	C_6D_6	5.52 d	4.12 dd	4.38 dd	4.52 dd	4.72 d		7.04–8.00 (Ph and hetero)	1.34 1.27 1.02 1.00	

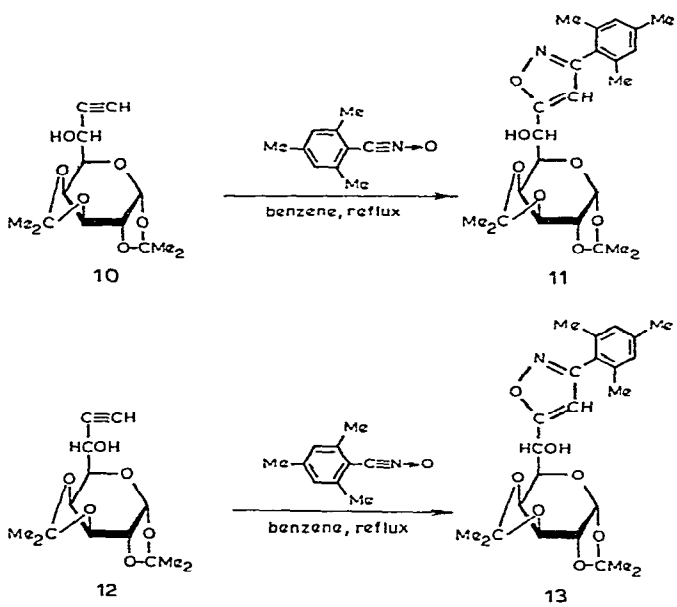
[a]First-order values are given. Observed multiplicities: d, doublet; dd, doublet of doublets; m, multiplet; s, singlet. [b]Under proton–deuterium exchange, the OH or NH signal disappears. [c]External tetramethylsilane as standard.

TABLE II

FIRST-ORDER PROTON–PROTON COUPLING CONSTANTS

Compd.	*Solvent*	*Coupling constants (Hz), from 100-MHz spectra*				
		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$
2	$CDCl_3$	3.5	0	3.0	8.5	
3	$(CD_3)_2CO$[a]	3.5	0	3.0	8.0	
6	$CDCl_3$	3.5	0	3.0	9.0	
7	$(CD_3)_2CO$[a]	3.5	0	3.0	9.0	
8	$CDCl_3$[a]	3.5	0	2.8	5.6	
9	$(CD_3)_2CO$[a]	3.5	0	2.5	8.5	
11	$CDCl_3$	4.8	2.7	8.0	1.9	8.0
13	$CDCl_3$[a]	4.5	2.5	8.0	1.9	5.5
15	C_6D_6	5.0	2.4	8.0	2.0	

[a]Spectra were simplified by proton–deuterium exchange.

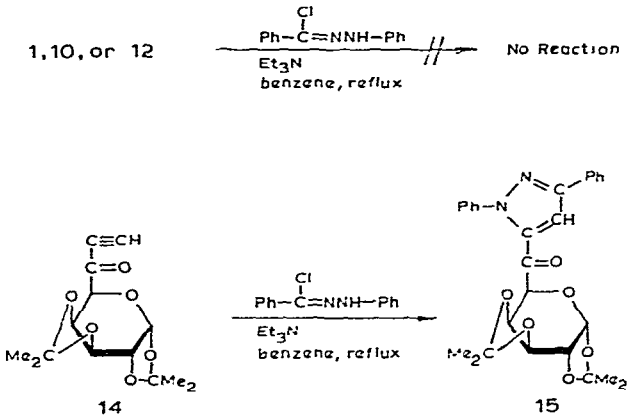


Strong u.v. maxima were observed for the isoxazoles near 272 and 222 nm.

Nitrile imines are reported[8] to react with acetylenes to give pyrazoles, and this reaction was evaluated with use of benzonitrile (*N*-phenyl)imine ($PhC{\equiv}N{\rightarrow}NHPh$), generated *in situ* by treating 1-(α-chlorobenzylidene)-2-phenylhydrazine[17] with triethylamine. No reaction occurred when the acetylenes **1**, **10**, or **12** were used, and the starting acetylenes were recovered almost quantitatively. However, oxidation of

either **10** or **12** to the corresponding 6-ketone[2,13] **14** furnished a precursor that reacted readily with the reagent in dry, boiling benzene to give the corresponding pyrazole derivative **15** in 71% yield. It has been suggested by Huisgen and co-workers[17] that such a conjugated system lowers the activation energy and thus enhances the reactivity of the dipolarophile in the cycloaddition reaction. Only one product was isolated, absorbing in the u.v. at 250 and 296 nm, and the orientation assigned is that expected on the basis of steric effects[8,17,18].

The 100-MHz, ^{1}H-n.m.r. spectrum of **15** in chloroform-*d* showed an uninterpretable multiplet for all protons except H-1. In benzene-d_6, however, **15** gave a first-order spectrum. The H-1 signal gave the expected doublet ($J_{1,2}$ 5.0 Hz) at



5.52 p.p.m., and doublets of doublets appeared at 4.12, 4.38, and 4.52 p.p.m., respectively, for H-2, 3, and 4. The H-5 signal, a doublet at 4.72 p.p.m., occurs downfield of its position for the acetylenes **10** and **12**. The signal of the methine proton of the pyrazole ring was obscured by the phenyl-group resonances, so that direct information on the pyrazole moiety was not available from the ^{1}H-n.m.r. spectrum.

However, the substitution-mode of the pyrazole ring was readily deduced from the ^{13}C-n.m.r. spectrum (see Table III). By comparing the spectrum with that of model compounds[19] having substituents at C-3, C-4, and C-5, it was possible to assign the low-field signals (at 152.0 and 140.2 p.p.m.) to C-3 and C-5 of the pyrazole ring, as these carbon atoms are deshielded by the nitrogen atoms. These signals remained as singlets on off-resonance, ^{1}H-decoupling, indicating that both carbon atoms were substituted, whereas the C-4 signal (at 110 p.p.m.) became a doublet, indicating that C-4 is hydrogen-substituted, and verifying the proposed mode of cyclization.

The optical rotatory dispersion (o.r.d.) spectra of the 5-epimeric triazole derivatives **3** and **7**, the isoxazole derivatives **8** and **9**, and the 6-epimeric isoxazole derivatives **11** and **13**, were examined (see Fig. 1), in order to determine whether these stereochemically identified compounds would show clear correlation with the Generalized Heterocycle Rule[20] relating chirality at the α-position of a substituted heterocycle with the sign of optical rotation and the optical rotatory dispersion

TABLE III

^{13}C CHEMICAL SHIFTS[a] FOR COMPOUNDS 8 AND 15

Compound	*Phenyl*	*CMe_2*	*Sugar chain*			*Heterocyclic ring*				
			C-1	*C-2,3,4,5*	*C-6*	*C-5'*	*C-3'*	*C-4'*	*CMe_2*	*Ar-CH_3*
8	139.3 137.7 129.0	112.1	106.0 d	86.7 d 82.9 d 75.8 d 66.7 d[b]		173.0 s	162.5 s	104.3 d	27.2 26.5	21.1 20.3
15	133.3 129.5 129.3 129.1 128.7 126.4 126.1	110.5 109.5	97.4 d	74.1 d 73.7 d 72.0 d 71.2 d	186.9 s	152.0 s	140.2 s	110.0 d	26.3 25.0	

[a]Spectra were recorded at 22.6 MHz in acetone-d_6, with broad-band, proton decoupling, and chemical shifts are expressed in p.p.m. downfield of the ^{13}C resonance of tetramethylsilane. Primed numbers refer to carbon atoms of the heterocyclic, aromatic ring. The multiplicities (d, doublet; s, singlet) refer to appearance of signals upon off-resonance, ^1H-decoupling. [b]The C-5 resonance.

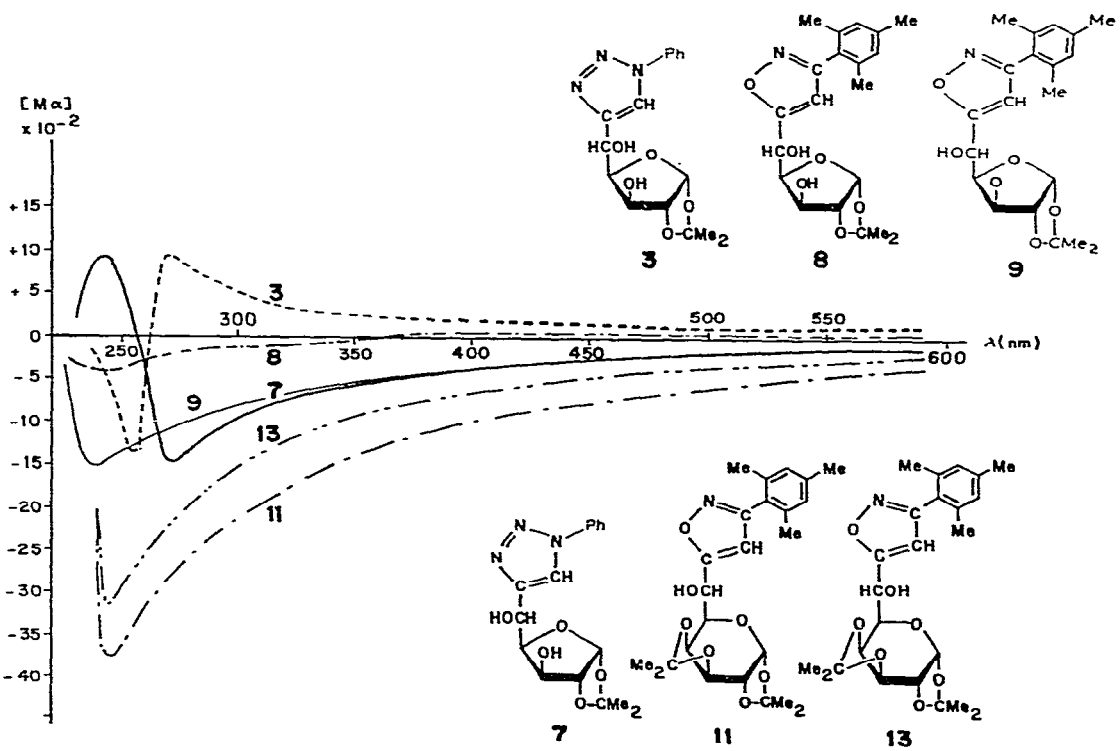


Fig. 1. The optical rotatory dispersion spectra of the adducts 3, 7, 8, 9, 11, and 13 in methanol.

spectrum. Emergence of a distinct correlation could be of value as a general method for stereochemical characterization of optically active propargyl alcohols of unknown configuration.

The L-*ido* triazole **3**, which has the α-hydroxyl group on the right in the orientation visualized for application of the Generalized Heterocycle Rule[20], is dextrorotatory at the sodium D-line ($[\alpha]_D^{25}$ +17° in methanol) and becomes more dextrorotatory at shorter wavelengths, exhibiting a positive Cotton effect at ~265 nm. The D-*gluco* triazole **7**, having OH-5 on the left in similar orientation, shows exactly the opposite behavior: it is levorotatory ($[\alpha]_D$ −39° in methanol), its levorotation increases at shorter wavelengths, and it gives a negative Cotton effect at ~260 nm. This behavior is in exact concordance with the Generalized Heterocycle Rule[20], and is also adhered to (at least at the D line) by the corresponding acetates **2** and **6**, which are respectively dextrorotatory and levorotatory in chloroform. Other examples of triazoles have been noted[10] where the hydroxyl derivatives follow the rule but the acetates do not.

The D-*glycero*-D-*galacto* isoxazole derivative **11**, having the α-hydroxyl group on the left in the standard orientation, is levorotatory ($[\alpha]_D^{25}$ −80° in methanol), and shows increasing levorotation at shorter wavelengths, exhibiting a negative extremum at 242 nm. However, its 6-epimer **13**, having the α-hydroxyl group on the right of the chain in the standard orientation, is not dextrorotatory as might have been predicted from the rule, but is also levorotatory ($[\alpha]_D^{25}$ −45° in methanol), and shows a negative o.r.d. curve having a negative extremum at 242 nm; the magnitude of the levorotation is lower than that of **11** at all wavelengths, but it remains negative nevertheless.

The isoxazole **8** also has its α-hydroxyl group on the right in the standard orientation. It is very weakly dextrorotatory ($[\alpha]_D$ +2° in methanol), but its rotation becomes negative at shorter wavelengths, and a negative extremum of low amplitude is reached at 240 nm. This, again, is at variance with the Generalized Heterocycle Rule[20] and indicates that, whereas some measure of confidence may be placed in use of the rule with the triazole derivatives having the α-hydroxyl group unsubstituted, its application to the isoxazole derivatives is not directly evident. The 5-epimer (**9**) of **8** is, however, more levorotatory than **8** at all wavelengths.

A recent extension[21] of the Generalized Heterocycle Rule, developed to predict the sign of the Cotton effect for nitrogen heterocycles attached to alditol residues, considers the direction of the dipole-moment vector of the heterocycle in relation to the orientation of the sugar chain in the most stable conformation. It is possible that, with suitable additional examples, a satisfactory interpretation of the chiroptical behavior of the isoxazole derivatives reported here may be achieved by use of this extended rule[21].

EXPERIMENTAL

General methods. — Evaporations were performed on a rotary evaporator under diminished pressure (~15 mmHg, ~2 kPa) at 45°. Specific rotations were measured in a 1-dm tube with a Perkin–Elmer Model 141 photoelectric polarimeter.

and o.r.d. spectra were recorded with a Jasco Model 5 spectropolarimeter. Melting points were determined with a Thomas–Hoover "Unimelt" apparatus. I.r. spectra were recorded with a Perkin–Elmer Model 137 spectrophotometer. U.v. spectra were recorded with a Cary Model 14 spectrophotometer. ^{1}H-N.m.r. spectra were recorded at 100 MHz with a Varian HA-100 spectrometer, and the data are given in Tables I and II; for routine monitoring of reactions, a Varian A-60 60-MHz spectrometer was used. ^{13}C-N.m.r. spectra were recorded at 22.6 MHz with a Bruker HX-90 spectrometer, and the data are given in Table III. Chemical shifts refer to an internal standard of tetramethylsilane ($\delta = 0.00$) for organic solutions. Microanalyses were performed by W. N. Rond. X-Ray powder diffraction data give interplanar spacings, Å, for CuKα radiation. The camera diameter was 114.59 mm. Relative intensities were estimated visually; m, moderate; s, strong; v, very; w, weak. The strongest lines are numbered (1, strongest); double numbers indicate approximately equal intensities. T.l.c. was performed on Silica Gel G (E. Merck, Darmstadt, Germany), activated at 110°, as the adsorbent. Unless otherwise indicated, the developers used were *A*, 1:1 ether–petroleum ether (b.p. 30–60°) and *B*, 3:1 chloroform–ether. Detection was effected by spraying with sulfuric acid, unless specified otherwise. Column chromatography was performed with Silica Gel No. 7734 (0.05–0.2 mm mesh, E. Merck AG), with 1 g of the mixture to be separated per 30 g of adsorbent. The petroleum ether used was a fraction having b.p. 30–60°.

*3,5-Di-O-acetyl-1,2-O-isopropylidene-5-C-(1-phenyl-1,2,3-triazol-4-yl)-β-*L-ido-*pentofuranose* (**2**). — The L-*ido* alkyne[1] **1** (540 mg, 1.81 mmol) was heated with phenyl azide (1 mL, 9.31 mmol) for 2 h on a steam bath. The solution was then evaporated to a syrup that was dissolved in 1:1 petroleum ether–ether, and the solution passed through a small column of silica gel, to give the product, **2**, as a homogeneous glass: yield 512 mg (75%); $[\alpha]_D^{25}$ +48° (*c* 0.6, chloroform); R_F 0.17 (solvent *A*), 0.50 (solvent *B*); λ_{max}^{film} 3.55 (Ar–H), 5.70 (C=O), 6.20 (Ar), 6.65 (heterocyclic C=C), 7.28 (doublet, CMe_2), 13.10, and 14.50 μm (aryl).

Anal. Calc. for $C_{20}H_{23}N_3O_7$: C, 57.55; H, 5.51; N, 10.07. Found: C, 57.59; H, 5.68; N, 10.21.

*1,2-O-Isopropylidene-5-C-(1-phenyl-1,2,3-triazol-4-yl)-β-*L-ido-*pentofuranose* (**3**). — A solution of the diacetate **2** (300 mg) in methanol (20 mL) was saturated at 0° with dry ammonia; the flask was then stoppered, and refrigerated overnight. The solution was evaporated to dryness, and the residue triturated with ether–petroleum ether, to give crystalline compound **3**; yield (after recrystallization) 202 mg (86%); m.p. 148–149°, $[\alpha]_{589}^{25}$ +17°, $[\alpha]_{578}^{25}$ +17°, $[\alpha]_{546}^{25}$ +18°, $[\alpha]_{436}^{25}$ +32°, $[\alpha]_{365}^{25}$ +55° (*c* 1.0 methanol); λ_{max}^{MeOH} 245 nm (ε_{mM} 17.6); R_F 0.15 (solvent *B*), 0.70 (ether); λ_{max}^{KBr} 2.98 (OH), 3.38 (Ar–H), 6.24 (A$_1$), 6.68 (heterocyclic C=C), 7.22 (doublet, CMe_2), 13.05, and 14.50 μm (aryl); X-ray powder diffraction data: 9.21 m (3,3), 7.83 m, 7.02 s (2), 6.06 m (3,3), 5.38 m, 5.02 m (4,4,4), 4.82 m (4,4,4), 4.58 m (4,4,4), 3.89 vs (1), 3.65 w, 3.48 w, and 3.31 vw.

Anal. Calc. for $C_{16}H_{19}N_3O_5$: C, 57.66; H, 5.71; N, 12.61. Found: C, 57.64; H, 5.81; N, 12.90.

3,5-Di-O-acetyl-1,2-O-isopropylidene-5-C-(1-phenyl-1,2,3-triazol-4-yl)-α-D-gluco-pentofuranose (**6**). — Prepared from the acetylene[1] **5** (504 mg, 1.69 mmol) in the same way as for the L-*ido* analog **2**, and recrystallized from acetone–petroleum ether, the acetylated triazole **6** was obtained crystalline; yield 494 mg (70%); m.p. 216–217°, $[\alpha]_D^{25}$ −18.3° (*c* 0.7, chloroform); R_F 0.13 (solvent *A*), 0.45 (solvent *B*); λ_{max}^{KBr} 3.35 (Ar–H), 5.75 (C=O), 6.24 (Ar), 6.68 (heterocyclic C=C), 7.26 (doublet, CMe_2), 13.15, and 14.55 μm (aryl); X-ray powder diffraction data: 9.82 vs (1), 7.69 vw, 7.08 w, 6.23 w, 5.47 m (4,4), 5.06 s (2), 4.87 m (4,4), 4.50 w, 4.33 w, 3.81 m (3,3), and 3.42 m (3,3).

Anal. Calc. for $C_{20}H_{23}N_3O_7$: C, 57.55; H, 5.51; N, 10.07. Found: C, 57.48; H, 5.50; N, 10.16.

1,2-O-Isopropylidene-5-C-(1-phenyl-1,2,3-triazol-4-yl)-α-D-gluco-pentofuranose (**7**). — A solution of the diacetate **6** (400 mg) in methanol (20 mL) was saturated with dry ammonia at room temperature. The same isolation procedure as used for **3** gave **7** as a solid that was purified by recrystallization from acetone–petroleum ether; yield 260 mg (81%), m.p. 162–163°, $[\alpha]_{589}^{25}$ −39°, $[\alpha]_{578}^{25}$ −48°, $[\alpha]_{548}^{25}$ −55°, $[\alpha]_{436}^{25}$ −93°, $[\alpha]_{356}^{25}$ −151° (*c* 1.0 methanol); λ_{max}^{MeOH} 245 nm (ε_{mM} 18.4); R_F 0.1 (solvent *B*), 0.64 (ether); λ_{max}^{KBr} 2.90 (OH), 3.35 (Ar–H), 6.22 (Ar), 6.65 (heterocyclic C=C), 7.25 (doublet, CMe_2), 13.10, and 14.50 μm (aryl); X-ray powder diffraction data: 14.73 vw, 8.50 m (3,3), 6.23 w, 5.15 m (3,3), 4.92 vs (1), and 3.83 s (2).

Anal. Calc. for $C_{16}H_{19}N_3O_5$: C, 57.66; H, 5.71; N, 12.61. Found: C, 57.73; H, 5.74; N, 12.74.

1-Phenyl-1,2,3-triazole-4-carboxaldehyde (**4**). — Compound **3** (170 mg, 0.51 mmol) was dissolved in 1:1 ethanol–water (50 mL), and the solution was stirred with Amberlite IR-120 (H^+) cation-exchange resin (15 mL) overnight at room temperature. After removal of the resin, the solution was evaporated, to give a white, solid residue (142 mg). The latter was then suspended in water (30 mL) and sodium metaperiodate (440 mg, 2.05 mmol) was added. The mixture was stirred for 24 h at room temperature, and the resultant solid was filtered off. The aqueous filtrate was extracted with dichloromethane (2 × 30 mL), and the extract was dried (magnesium sulfate), and evaporated, to give a white solid. The combined solid residues were recrystallized from water–methanol to give the aldehyde **4** as needles: yield 56.5 mg (64%), m.p. 98–99°; X-ray powder diffraction data: 7.62 m, 5.12 vs (1), 4.19 m, 3.98 vw, 3.81 w, 3.56 m, 3.36 s (2,2), and 3.04 s (2,2).

This compound has been reported[22] to have m.p. 98°, and two independent routes to it in this laboratory have given material having m.p.[9] 99–100° and[10] 98–99°. The X-ray pattern of the present product was identical to that of a reference[9,10] sample.

A similar procedure was performed on the D-*gluco* isomer **7** (133 mg). The same product (**4**) was obtained; yield 48 mg (61%).

1,2-O-Isopropylidene-5-C-(3-mesitylisoxazol-5-yl)-β-L-ido-pentofuranose (**8**). — The acetylene[1] **1** (450 mg, 1.51 mmol) and 2,4,6-trimethylbenzonitrile *N*-oxide (245 mg, 1.52 mmol) were dissolved in benzene (15 mL), and the solution was boiled

gently for 15 min under reflux. After evaporation of the solvent, the resultant syrup was dissolved in methanol (30 mL), the solution was saturated at 0° with dry ammonia, and the flask was stoppered, and refrigerated overnight. The solvent was removed under diminished pressure, and the residue, dissolved in 1:1 ether–petroleum ether, was passed through a small column packed with silica gel, to give the isoxazole **8** as a solid; yield, 402 mg (71%), m.p. 123–124°, $[\alpha]_D^{25}$ +2° (*c* 1.0, methanol); λ_{max}^{MeOH} 272 (ε 562), 222 nm (ε_{mM} 13.2); R_F 0.17 (solvent *A*), 0.23 (solvent *B*); λ_{max}^{KBr} 2.88 (OH), 3.38 (Ar–H), 6.15 (Ar), 6.25 (heterocyclic C=C), and 7.25 μm (doublet,CMe_2); X-ray powder diffraction data: 14.36 m, 10.78 m (4,4,4), 8.75 vw, 7.62 w, 6.26 s (2,2), 5.35 w, 5.01 vs (1), 4.74 w, 4.50 s (2,2), 4.33 w, 4.20 s (3,3), 3.76 s (3,3), 3.61 m (4,4,4), and 3.48 m (4,4,4). For ^{13}C-n.m.r. data on compound **8**, see Table III.

Anal. Calc. for $C_{20}H_{25}NO_6$: C, 64.00; H, 6.66; N, 3.73. Found: C, 64.22; H, 6.89; N, 3.91.

1,2-O-Isopropylidene-5-C-(3-mesitylisoxazol-5-yl)-α-D-gluco-pentofuranose (**9**). — Prepared from the acetylene[1] **5** (500 mg, 1.68 mmol) in the same way as for the L-*ido* analog **8**, and recrystallized from acetone–petroleum ether, the isoxazole **9** was obtained crystalline; yield 415 mg (66%), m.p. 154–156°, $[\alpha]_{589}^{25}$ −40°, $[\alpha]_{578}^{25}$ −42°, $[\alpha]_{546}^{25}$ −48°, $[\alpha]_{436}^{25}$ −84°, $[\alpha]_{365}^{25}$ −129° (*c* 1.0, methanol); λ_{max}^{MeOH} 272 (ε 640), 222 nm (ε_{mM} 15); R_F 0.15 (solvent *A*), 0.20 (solvent *B*); λ_{max}^{KBr} 2.85 (OH), 3.35 (Ar–H), 6.12 (Ar) 6.26 (heterocyclic C=C), and 7.20 μm (doublet, CMe_2); X-ray powder diffraction data: 12.98 vw, 11.32 w, 9.01 m (4), 7.02 s (2), 5.75 vs (1), 5.33 w (5,5,5), 4.55 w (5,5,5), 4.35 w (5,5,5), 4.15 m (3,3), and 3.86 m (3,3).

Anal. Calc. for $C_{20}H_{25}NO_6$: C, 64.00; H, 6.66; N, 3.73. Found: C, 63.84; H, 6.54; N, 3.72.

1,2:3,4-Di-O-isopropylidene-6-C-(3-mesitylisoxazol-5-yl)-D-glycero-α-D-galacto-hexopyranose (**11**). — A solution of the acetylenic derivative[1,2] **10** (284 mg, 1 mmol) and 2,4,6-trimethylbenzonitrile *N*-oxide (161 mg, 1 mmol) in benzene (20 mL) was boiled gently for 15 min under reflux. After evaporating off the solvent, the solid residue was dissolved in 1:1 ether–petroleum ether, and the solution passed through a small column of silica gel. Evaporation of the solvent from the effluent gave crystals of the pure product (**11**): yield 302 mg (68%), m.p. 163–164°, $[\alpha]_{589}^{25}$ −80°, $[\alpha]_{578}^{25}$ −96.4°, $[\alpha]_{546}^{25}$ −110.9°, $[\alpha]_{436}^{25}$ −185.4°, $[\alpha]_{365}^{25}$ −278.1° (*c* 1.1, methanol); λ_{max}^{MeOH} 272 (ε_{mM} 1.16), 222 nm (ε_{mM} 13.7); R_F 0.45 (solvent *A*), 0.50 (solvent *B*); λ_{max}^{KBr} 2.90 (OH), 3.38 (Ar–H), 6.20 (Ar), 6.30 (heterocyclic C=C), and 7.26 μm (doublet, CMe_2); X-ray powder diffraction data: 12.62 w, 9.50 vw, 7.89 vs (1), 6.60 s (2,2), 4.67 s (2,2), and 4.21 m.

Anal. Calc. for $C_{24}H_{31}NO_6$: C, 64.72; H, 6.96; N, 3.14. Found: C, 64.67; H, 7.11; N, 3.10.

1,2:3,4-Di-O-isopropylidene-6-C-(3-mesitylisoxazol-5-yl)-L-glycero-α-D-galacto-hexopyranose (**13**). — The method of preparation described in the preceding experiment, applied to the L-*glycero*-α-D-*galacto* derivative[1,2] **12** (284 mg), yielded the isoxazole derivative **13** as a syrup; yield 304 mg (68.5%); $[\alpha]_{589}^{25}$ −45°, $[\alpha]_{578}^{25}$ −55.°, $[\alpha]_{546}^{25}$ −62.5°, $[\alpha]_{436}^{25}$ −115°, and $[\alpha]_{365}^{25}$ −175° (*c* 0.8, methanol); λ_{max}^{MeOH} 272 (ε 890),

222 nm (ε_{mM} 13.5); R_F 0.41 (solvent *A*), 0.50 (solvent *B*); λ_{max}^{film} 2.85 (OH), 3.35 (Ar–H), 6.18 (Ar), 6.24 (heterocyclic C=C), and 7.25 μm (doublet, CMe_2).

Anal. Calc. for $C_{24}H_{31}NO_7$: C, 64.72; H, 6.96; N, 3.14. Found: C, 64.58; H, 7.23; N, 3.14.

5-C-[(1,3-Diphenylpyrazol-5-yl)carbonyl]-1,2:3,4-di-O-isopropylidene-α-D-galacto-pentopyranose (**15**). — The unsaturated ketone[2,13] **14** (389 mg, 1.38 mmol) and 322 mg (1.40 mmol) of 1-(α-chlorobenzylidene)-2-phenylhydrazine[17] were dissolved in dried benzene (5 mL); the solution was boiled for 2 min under reflux, and then triethylamine (1.0 mL, 7.15 mmol) was added. After 10 sec, precipitation of triethylamine hydrochloride began. After 1 h, the solvent was evaporated off, to give a brown syrup that was passed through a column packed with silica gel with 3:1 benzene–ether as the eluant. The product was obtained as a glass; yield 450 mg (71%). $[\alpha]_D^{25}$ −108° (*c* 0.6, methanol); λ_{max}^{MeOH} 250 (ε_{mM} 54.9), 296 nm (ε 8090); R_F 0.56 (solvent *A*), 0.67 (solvent *B*); λ_{max}^{film} 3.35 (Ar–H), 5.80, 5.92 (C=O), 6.20 (Ar) 6.68 (heterocyclic C=C), and 7.24 μm (doublet, CMe_2). For ^{13}C-n.m.r. data on **15**, see Table III.

Anal. Calc. for $C_{27}H_{28}N_2O_6$: C, 68.06; H, 5.88; N, 5.88. Found: C, 67.84; H, 6.06; N, 5.96.

Compounds **1**, **10**, and **12** were each treated with 1-(α-chlorobenzylidene)-2-phenylhydrazine under the same conditions as for compound **14**. No reaction was observed in any of the experiments, and the starting acetylenes were recovered almost quantitatively.

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