

THE CONFIGURATION AT THE ANOMERIC CARBON OF THE ETHYNYLATED  
PRODUCTS OF 2,3,5-TRI-O-BENZOYL-D-RIBOFURANOSYL BROMIDE  
WITH MERCURIC AND CUPROUS PHENYLETHYNYLIDES

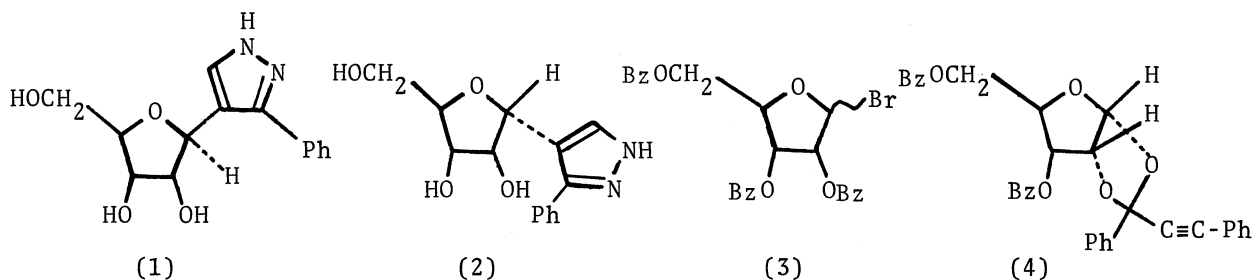
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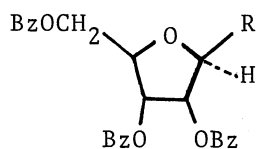
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The substituent at the anomeric carbon of the major product of the ethynylation, one of the 1-phenyl-2-(2,3,5-tri-O-benzoyl-D-ribofuranosyl)-ethynes, have chemically been proved to be  $\beta$ -oriented. In the NMR spectra of 2,3-isopropylidene-ribofuranose derivatives the coupling constant of  $C_1$ -H has been observed to be approximately 4 Hz in the 1- $\alpha$ -substituted anomers and almost negligible in the 1- $\beta$ -substituted anomers.

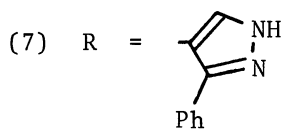
In the recent report on the synthesis of 3-phenyl-4-(1- $\beta$ - and 1- $\alpha$ -D-ribofuranosyl)pyrazoles (1) and (2), a new type of C-nucleosides, <sup>1)</sup> the configuration at the anomeric carbon of the former has tentatively been assigned as  $\beta$  on the basis of the general rule of the predominant formation of the  $\beta$ -anomer by substitution of tri-O-benzoylribofuranosylbromide (3) through heavy metal process.<sup>2),3)</sup> Treatment of (3) with cuprous phenylethynylide has given the ketal (4) [32% yield] and a small amount of 1-phenylethynylated product, the latter being identical with the major product (5) [ $[\alpha]_D^{20}$  -60.5° (c = 0.61 in  $CHCl_3$ ); NMR  $\delta$  (ppm in  $CDCl_3$ ): 5.19 (1H, d,  $J_{1,2}$  = 2.2 Hz,  $C_1$ -H)] which was obtained on reaction of (3) with mercuric phenylethynylide together with a small amount of the anomer (6) [m.p. 89-91°;  $[\alpha]_D^{22}$  +87.9° (c = 0.67 in  $CHCl_3$ )]. The addition of diazomethane on (5), followed by debenzoylation has furnished (1) [m.p. 92-93°] and the same procedure on the minor  $C_1$ -ethynylated product (6) has furnished the corresponding  $\alpha$ -anomer (2) [m.p. 103-105°].<sup>1)</sup>



The amorphous solid (5) was oxidized with potassium permanganate in acetic acid at 40° to give carboxylic acid (9a) [20% yield; amorphous solid;  $[\alpha]_D^{22} +39.7^\circ$  ( $c = 0.67$  in  $\text{CHCl}_3$ ); UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm ( $\log \epsilon$ ): 230 (4.36), 275 (3.37); IR  $\nu_{\text{max}}^{\text{CHCl}_3}$  ( $\text{cm}^{-1}$ ): 1721 ( $\text{C=O}$ ), 1270, 1120, 1105, 1094]. Methylation of (9a) with diazomethane in ether gave colorless solid (9b) [theoretical yield;  $[\alpha]_D^{19} +18.1^\circ$  ( $c = 1.63$  in  $\text{CHCl}_3$ ); NMR  $\delta$  (ppm in  $\text{CDCl}_3$ ): 3.78 (3H, s,  $-\text{CO}_2\text{CH}_3$ ), 4.73 (3H, m,  $\text{C}_5\text{-H}$ ,  $\text{C}_6\text{-H}_2$ ), 4.84 (1H, d,  $J_{2,3} = 4.0$  Hz,  $\text{C}_2\text{-H}$ ), 5.79 (1H, m,  $\text{C}_4\text{-H}$ ), 5.98 (1H, dd,  $J_{2,3} = 4.0$  Hz,  $J_{3,4} = 5.2$  Hz,  $\text{C}_3\text{-H}$ ), 7.22-8.24 (15H, m, aromatic)]. Oxidation of the anomer (6) in the same manner afforded carboxylic acid (10) [20% yield; amorphous solid;  $[\alpha]_D^{19} -494.6^\circ$  ( $c = 1.86$  in  $\text{CHCl}_3$ ); UV  $\lambda_{\text{max}}^{\text{EtOH}}$  nm ( $\log \epsilon$ ): 230 (4.36), 275 (3.37); IR  $\nu_{\text{max}}^{\text{CHCl}_3}$  ( $\text{cm}^{-1}$ ): 1720 ( $\text{C=O}$ ), 1270, 1110, 1095]. The carboxylic acid (9a) and the ester (9b) were completely identical with the specimens prepared according to Bobeck's procedure from 2,3,5-tri-O-benzoyl- $\beta$ -D-ribofuranosyl cyanide,<sup>2)</sup> which had been proved to be  $\beta$ -oriented in relationship with the natural oxoformycin.<sup>2),4),5)</sup> This fact offers unambiguous proof on the configuration at the anomeric carbon of the ribofuranosylethyne (5), and consequently of the C-nucleoside (1).

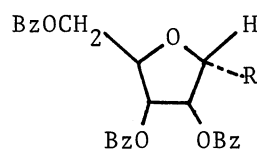


(5) R =  $-\text{C}\equiv\text{C}-\text{Ph}$

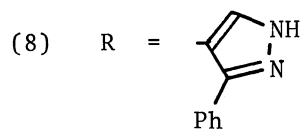


(9a) R =  $-\text{CO}_2\text{H}$

(9b) R =  $-\text{CO}_2\text{CH}_3$



(6) R =  $-\text{C}\equiv\text{C}-\text{Ph}$



(10) R =  $-\text{CO}_2\text{H}$

$\beta$ - and  $\alpha$ -Ribofuranosylethynes (5) and (6) were, then, debenzoylated with ammonia to triols (11) [amorphous solid] and (12) [m.p. 92-93°], which were treated with acetone in the presence of p-toluenesulfonic acid to 2,3-acetonides (13) [m.p. 67-69°; IR  $\nu_{\text{max}}^{\text{CHCl}_3}$  ( $\text{cm}^{-1}$ ): 1380, 1370] and (14) [m.p. 104-106°; IR  $\nu_{\text{max}}^{\text{CHCl}_3}$  ( $\text{cm}^{-1}$ ): 1380, 1370], respectively. These were converted into the monoacetates (15) and (16) and to the monobenzoates (17) and (18), which were hydrogenated into the  $\text{C}_1$ -phenethyl derivatives (19) and (20), respectively. The TABLE I summarizes the NMR data of the  $\beta$ - and  $\alpha$ -anomeric 2,3-isopropylidene derivatives.

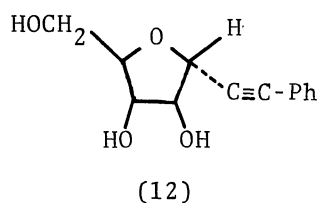
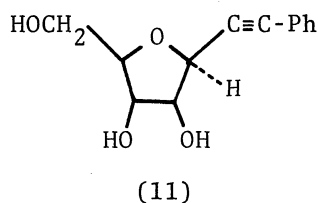


TABLE I. NMR Spectral Data of 2,3-Isopropylidene Derivatives (13) - (20).

C o m p o u n d s			Chemical Shifts of $\text{C}_1\text{-H}$ (ppm)	$J_{1,2}$ Values (Hz)	Chemical Shifts of $>\text{C}-\text{CH}_3$ (ppm)	$\Delta\delta$ - Values of $>\text{C}-\text{CH}_3$ (ppm)
$\text{R}^1$	$\text{R}^2$					
	(13)	H - $\text{C}\equiv\text{C}-\text{Ph}$	4.80-4.99	*	1.32, 1.50	0.18
	(15)	Ac - $\text{C}\equiv\text{C}-\text{Ph}$	4.77	0	1.35, 1.52	0.18
	(17)	Bz - $\text{C}\equiv\text{C}-\text{Ph}$	4.87	0	1.37, 1.55	0.18
	(19)	Bz - $\text{CH}_2\text{CH}_2\text{Ph}$	3.97	*	1.33, 1.52	0.19
	(14)	H - $\text{C}\equiv\text{C}-\text{Ph}$	5.01	4.1	1.33, 1.55	0.22
	(16)	Ac - $\text{C}\equiv\text{C}-\text{Ph}$	4.81	4.4	1.34, 1.55	0.21
	(18)	Bz - $\text{C}\equiv\text{C}-\text{Ph}$	5.07	4.1	1.39, 1.62	0.23
	(20)	Bz - $\text{CH}_2\text{CH}_2\text{Ph}$	3.87	3.6	1.33, 1.50	0.17

\*) Obscured by overlapping with the signals of  $\text{C}_2\text{-H}$  and  $\text{C}_3\text{-H}$ .

Ph =  $-\text{C}_6\text{H}_5$ , Ac =  $\text{CH}_3\text{CO}-$ , Bz =  $\text{C}_6\text{H}_5\text{CO}-$ .

In connection with the determination of the configuration at the anomeric carbon of 1-C-substituted riboses by NMR spectroscopy, Maehr and co-workers have

recently reported on the empirical study concerning to the coupling constants of the vicinal protons on a rigidly condensed bicyclic system with a five-membered ring of 2,3-acetone ketal.<sup>7),8),9),10)</sup> The TABLE I shows that the C-1 proton was split into a doublet ( $J_{1,2} = \text{ca. } 4 \text{ Hz}$ ) by the vicinal proton at C<sub>2</sub> in the  $\alpha$ -substituted ribose derivatives (14), (16), (18) and (20), on the other hand, the coupling of the C<sub>1</sub>-H with the C<sub>2</sub>-H in the  $\beta$ -substituted derivatives (15) and (17) was negligible. With respect to the chemical shift differences ( $\Delta\delta$ -value) of the two methyl groups at the isopropylidene moiety of the both anomers Igolen and co-workers observed a smaller difference for the  $\alpha$ -anomers of some C-nucleosides.<sup>9),10),11)</sup> As shown in the TABLE I  $\Delta\delta$ -values of the two methyl groups were 0.18-0.19 ppm for the  $\beta$ -anomers and 0.21-0.23 ppm for the  $\alpha$ -anomers and these values were not large enough to be useful to identify the both anomers. The discrepancy between the values in C-nucleosides and the ethynylated compounds seems to be likely the results of the reverse anisotropic effects of the pi-systems of hetero-aromatic group and those of the acetylenic linkage.

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