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Note

1-(2,3-*O*-Isopropylidene-α- and -β-D-ribofuranosyl)-4,5-di-(methoxycarbonyl)-1,2,3-triazoles: An exception to the Δδ criterion for configurational assignment

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We recently synthesized 1-[2,3-*O*-isopropylidene-5-*O*-(*p*-nitrobenzoyl)-α- and -β-D-ribofuranosyl]-4,5-di-(methoxycarbonyl)-1,2,3-triazoles (**1** and **2**) from the corresponding ribofuranosyl azides[1]. Anomeric configurational assignments were based on the criteria of anomeric proton (H-1′) chemical shift[2] and $J_{1',2'}$ values[2b,3] (see Table I), and the configurational assignments for the precursor D-ribofuranosyl azides. As triazole **1** and its β anomer were now available, we decided to deacylate the 5′-hydroxyl group and check our configurational assignments against the Δδ criterion[4].

TABLE I

CHEMICAL SHIFT AND COUPLING-CONSTANT DATA[a]

Triazole	*δH-1′*	$J_{1',2'}$ *(Hz)*	*δCH₃*	*Δδ*
1	6.85	5	1.00, 1.27	0.27
2	6.67	0	1.43, 1.60	0.27
3	6.76	5	0.97, 1.27	0.30
4	6.48	1	1.39, 1.58	0.19

[a] Measured in $CDCl_3$, at 90 MHz.

Deacylation of triazoles **1** and **2** with methanolic sodium methoxide, followed by chromatography on silica gel, gave the unprotected triazoles **3** and **4** in 89 and 91% yield, respectively. As with **1** and **2**, the H-1′ resonance for **3** occurs at lower field (δ 6.76) than that for **4** (δ 6.48). Furthermore, the H-1′ resonances for both **3** and **4** are doublets, with $J_{1',2'}$ 5 and 1 Hz, respectively. Although the H-1′ chemi-

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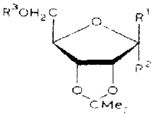
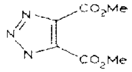
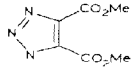
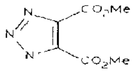
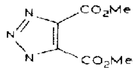


	R^1	R^2	R^3
1	H		$COC_6H_4NO_2$-*p*
2		H	$COC_6H_4NO_2$-*p*
3	H		H
4		H	H

cal-shifts and $J_{1',2'}$ values confirmed that **3** is the α and **4** the β anomer, the $\Delta\delta$ values for the isopropylidene methyls of **3** and **4** (see Table I) are useless for assigning anomeric configuration, as both **3** and **4** have $\Delta\delta > 0.15$ p.p.m. According to the $\Delta\delta$ criterion, $\Delta\delta < 0.15$ p.p.m. is indicative of the α configuration, whereas $\Delta\delta > 0.15$ p.p.m. is indicative of the β configuration.

Thus α anomer **3**, having a $\Delta\delta$ value of 0.30 p.p.m. [which, in addition to being greater than 0.15 p.p.m., is also greater than the $\Delta\delta$ value (0.19 p.p.m.) for its β anomer **4**], appears to be the first reported exception to the $\Delta\delta$ criterion for α-D-ribofuranosyl nucleosides. Most recently, some 6-substituted β-D-ribofuranosylpyrimidines having $\Delta\delta$ values < 0.15 p.p.m. have been reported[5] as exceptions to the $\Delta\delta$ criterion.

It is not clear why triazole **3** should be an exception, as other α-D-ribofuranosyltriazoles are known [4,6] to have $\Delta\delta$ values of < 0.15 p.p.m. However, these triazole nucleosides have either been of the benzotriazole type[4] or 5'-*O*-substituted[6]; the latter should be excluded, as the $\Delta\delta$ criterion is known[4] to be unreliable with 5'-*O*-substituted nucleosides.

Thus, when assigning anomeric configurations to triazole nucleosides, it should be borne in mind that α-D-ribofuranosyltriazoles in which the triazole moiety is monocyclic may not adhere to the $\Delta\delta$ criterion.

EXPERIMENTAL

General. — Optical rotations were measured with a Schmidt and Haensch polarimeter. Column chromatography was performed on Silica Gel 60 (E. Merck, 70–230 mesh). I.r. spectra were recorded with a Perkin–Elmer Model 137 spectrophotometer. N.m.r. spectra were recorded at 90 MHz with a Varian EM390 spectrometer, with Me_4Si as the internal standard.

*1-(2,3-*O*-Isopropylidene-β-*D*-ribofuranosyl)-4,5-di-(methoxycarbonyl)-1,2,3-triazole* (**4**). — To a solution of *p*-nitrobenzoate **2** (105 mg, 0.2 mmol) in dry methanol (1 mL) was added 0.05M methanolic sodium methoxide (3 mL), and the solution was magnetically stirred for 10 h at room temperature and evaporated to dryness under diminished pressure; the residue was chromatographed on a column (1.5 × 40 cm) of silica gel with 9:1 (v/v) chloroform–ethanol, to give **4** as a homogeneous syrup (65 mg, 91%); $[\alpha]_D^{25}$ −93.9° (c 3.38, $CHCl_3$); $\nu_{max}^{CHCl_3}$ 1725 cm^{-1}; n.m.r. data ($CDCl_3$): δ 1.39 and 1.58 (2 s, 6 H, CMe_2), 3.87 (br t, 2 H, $J_{4',5'a} \simeq J_{4',5'b} = 4.5$ Hz, H-5'a,5'b), 3.97 (s, 3 H, OMe), 4.03 (s, 3 H, OMe), 4.46 (td, 1 H, $J_{3',4'}$ 2 Hz, H-4'), 5.00 (dd, 1 H, $J_{2',3'}$ 6 Hz, H-3'), 5.60 (dd, 1 H, $J_{1',2'}$ 1 Hz, H-2'), and 6.48 (d, 1 H, H-1').

*1-(2,3-*O*-Isopropylidene-α-*D*-ribofuranosyl)-4,5-di-(methoxycarbonyl)-1,2,3-triazole* (**3**) was prepared, as for **4**, as a homogeneous syrup in 89% yield; $[\alpha]_D^{25}$ −55.0° (c 1.1, $CHCl_3$); $\nu_{max}^{CHCl_3}$1725 cm^{-1}; n.m.r. data ($CDCl_3$): δ 0.97 and 1.25 (2 s, 6 H, CMe_2), 3.99 (s, 6 H, 2 OMe), 3.65–3.97 (m, 2 H, H-5'a,5'b), 4.78–5.23 (m, 3 H, H-2',3',4'), and 6.76 (d, 1 H, $J_{1',2'}$ 5 Hz, H-1').

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