

BENZOTRIAZOLE GLYCOSIDES FROM GLYCALs \*)

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Bowles and Robins (1) have shown the possibility of utilizing glycals for the synthesis of nucleosides in a fusion process, thus verifying the suggestion put forward by this group (2) in a model study with 2,3-dihydropyran and 2,3-dihydrofuran. More recently (3), they have described the synthesis of 9-(2'-desoxyribofuranosyl)-purines by fusion of 3,4-di-O-acetyl-D-arabinal with different purines, in the presence of an acidic catalyst.

Our interest in the synthesis of benzotriazole N-glycosides as potential anti-cancer agents led us (4) to the verification that both benzotriazole and 5,6-dimethyl- and 5,6-dichlorobenzotriazole react with 2,3-dihydro-4H-pyran and 2-acetoxymethyl-3,4-dihydro-2H-pyran, in ethyl acetate and in the presence of an acidic catalyst, yielding the corresponding 1-(2-tetrahydropyranyl)- and 1-(6-acetoxymethyl-2-tetrahydropyranyl) benzotriazoles respectively.

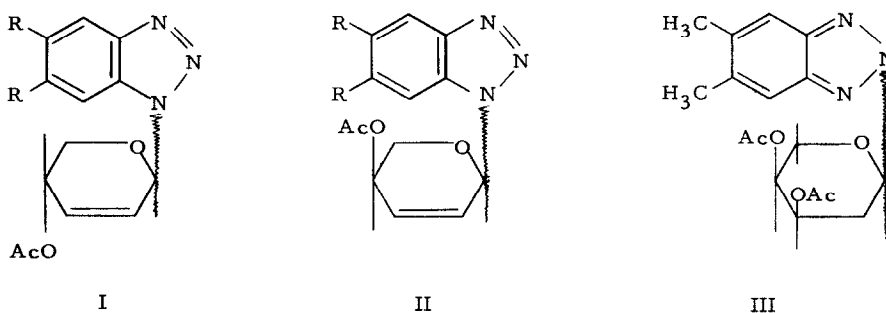
In an attempt to extend this reaction by employing glycals, the reactions of 3,4-di-O-acetyl-D-xylal and 3,4-di-O-acetyl-L-arabinal with benzotriazole and 5,6-dimethylbenzotriazole have been studied, in ethyl acetate and in the presence of trifluoroacetic acid. The results obtained in these conditions are somewhat different from those described by Robins et al. (3) for purines, in their fusion method.

Therefore, when 1.19 g (0.01 mol) of benzotriazole and 2 g (0.01 mol) of 3,4-di-O-acetyl-

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\*) This paper comprises part VII of the series "Anticancerosos potenciales". Preceding paper, part VI, M. Lora-Tamayo, R. Madroñero and C. Ochoa, *Anales real soc. españ. Fis. y Quím.*, (in press).

D-xylal (5), dissolved in 35 ml of ethyl acetate which contains 4-5 drops of trifluoroacetic acid, were heated in a sealed tube at 110°C for 15-16 hours, 1 g of a crystalline product of melting point 144-145°C was obtained, to which we have assigned the structure of 1-(4-O-acetyl-2,3-dideoxy-D-glycero-pent-2-enosyl)benzotriazole <sup>\*)</sup> (I, R=H) on the basis of its analysis and UV and NMR spectra (cf. table 1) and by analogy with certain reactions described by Ferrier (6), in which, an allylic transposition with the loss of one mol of acetic acid was produced, during the addition of glycal.



Similar behaviour shows the 3,4-di-O-acetyl-L-arabinal (7) which by reacting in the same experimental conditions with benzotriazole leads to 1-(4-O-acetyl-2,3-dideoxy-L-glycero-pent-2-enosyl)benzotriazole (II, R=H), with a 40% yield. Its UV and NMR spectra are identical to that of I (R=H), but its rotation is of opposite sign (cf. table 1).

From the reactions between 5,6-dimethylbenzotriazole and 3,4-di-O-acetyl-D-xylal or 3,4-di-O-acetyl-L-arabinal, the corresponding optical isomers, 1-(4-O-acetyl-3,4-dideoxy-D-glycero-pent-2-enosyl)-5,6-dimethylbenzotriazole (I, R=CH<sub>3</sub>) and 1-(4-O-acetyl-2,3-dideoxy-L-glycero-pent-2-enosyl)-5,6-dimethylbenzotriazole (II, R=CH<sub>3</sub>) were obtained respectively. Some of its characteristics are summarized in table 1.

<sup>\*)</sup> Satisfactory elemental analysis data were obtained for all new compounds.

TABLE I

Compounds	M. p. <sup>a)</sup>	$[\alpha]_D$ c = 1% CHCl <sub>3</sub>	EtOH $\mu\mu$ ( $\epsilon$ ) max	NMR $\tau$ CDCl <sub>3</sub>
I R = H	144-145°C	+120.7	253.5 (7240) 280 (3950)	1.7-2.8 (4H, aromatic) 3.2-3.6 (1H, anomeric + 2H, vinylic) 4.79 (b s, 1H) 6.07 (b s, 2H) 7.88 (s, 3H)
I R = H	144-145°C	-122.4	254 (7040) 280 (3910)	1.7-2.8 (4H, aromatic) 3.2-3.6 (1H, anomeric + 2H, vinylic) 4.79 (b s, 1H) 6.07 (b s, 2H) 7.88 (s, 3H)
II R = CH <sub>3</sub>	147-148°C	+22.6	259 (7800) 280 (4630)	2.22 (b s, 1H, aromatic) 2.51 (b s, 1H, aromatic) 3.2-3.7 (1H, anomeric + 2H, vinylic) 4.4-4.8 (b m, 1H) 5.8-6.1 (b m, 2H) 7.59 (b s, 6H) 7.86 (s, 3H)
II R = CH <sub>3</sub>	147-148°C	-22.4	260 (7650) 289 (4460)	2.22 (b s, 1H, aromatic) 2.51 (b s, 1H, aromatic) 3.2-3.7 (1H anomeric + 2H, vinylic) 4.4-4.8 (b m, 1H) 5.8-6.1 (b m, 2H) 7.59 (b s, 6H) 7.86 (s, 3H)

a) All products crystallised from ethyl acetate-petroleum ether (50-70°C)

b) Compare with 1- and 2-alkylbenzotriazole spectra (8)

From the reaction between 5,6-dimethylbenzotriazole and 3,4-di-O-acetyl-L-arabinal another crystalline product was isolated in addition to the product II, (R = CH<sub>3</sub>). This product melts at 172-173<sup>o</sup>C (from ethyl acetate-petroleum ether) and  $[\alpha]_D = 87.4$ . We assigned to it the structure III on the basis of its analysis (Calc. for C<sub>17</sub>H<sub>21</sub>N<sub>3</sub>O<sub>5</sub>: C 58.79; H 6.05; N 12.10. Found C 58.49; H 5.75; N 12.19), UV spectrum ( $\lambda_{\text{max}}^{\text{EtOH}}$  284 m $\mu$ ,  $\epsilon = 12.000$ ;  $\lambda_{\text{max}}^{\text{EtOH}}$  294 m $\mu$ ,  $\epsilon = 10.400$ , which shows the union of the sugar at N<sub>2</sub>) and NMR spectrum (two acetyl groups at 7.84-7.88  $\tau$ ; triplet at 3.54  $\tau$ , corresponding to the anomeric proton; also a band at 2.34  $\tau$  corresponding to the two aromatic protons).

At present, we are carrying out a detailed study of these reactions with other glycols and heterocyclic bases, in order to determine its extension and limitations and to establish the configuration on the anomeric carbon atom. The results will be published later on.

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