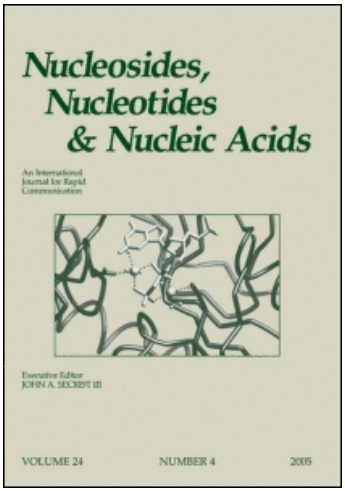

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

A Novel Approach for the Synthesis of *seco* C-Nucleoside Analogues

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To cite this Article Awad, Laila F. and Ashry, El Sayed H. El(1999) 'A Novel Approach for the Synthesis of *seco* C-Nucleoside Analogues', Nucleosides, Nucleotides and Nucleic Acids, 18: 4, 557 — 558
To link to this Article: DOI: 10.1080/15257779908041493
URL: http://dx.doi.org/10.1080/15257779908041493

NUCLEOSIDES & NUCLEOTIDES, 18(4&5), 557–558 (1999)

A NOVEL APPROACH FOR THE SYNTHESIS OF *seco* C-NUCLEOSIDE ANALOGUES

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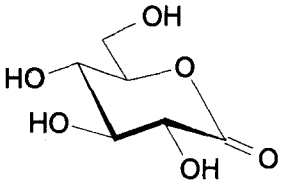
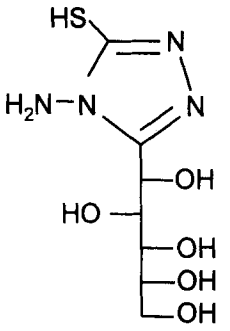
ABSTRACT: The synthesis of 4-amino-3-(D-gluco- or D-galacto-pentitol-1.yl)-5-mercapto-1,2,4-triazoles and their conversion to the respective 6-methyl-3-(1,2,3,4,5-penta-O-acetyl-pentitol-1-yl)1,2,4-triazolo[3,4-b]1,3,4-thiadiazoles have been achieved. The vicinal coupling constants were used to deduce the favored conformations.

The biological properties exhibited by 4-amino-5-mercapto-3-substituted-1,2,4-triazoles and 3,6-disubstituted-1,2,4-triazolo[3,4-b]1,3,4-thiadiazoles have made them important chemotherapeutic targets[1,2]. The substitution at the 3- and 6-positions lowered the toxicity of some of these heterocycles. Continuing our interest in the synthesis of *seco* nucleosides[3-5], we have synthesized a number of *seco* C-nucleosides having alditolyl residues linked to these heterocycles which may increase their transportation in biological systems. The synthesis has been achieved by heating D-glucono-1,5-lactone with thiocarbohydrazide in pyridine to give **1** in 81% yield (m.p. 201-202°C). Treatment of **1** with acetic anhydride gave **2** in 63% yield (m.p. 123-125°C). Similarly, the D-galacto analogues were prepared, but in this case the N-acetyl derivative of the D-galacto analogue of **1** could be isolated indicating its intermediacy in the reaction. These reactions were extended successfully to the D-glycero-D-gulo analogues. Reaction of **1** or its analogues with benzoyl chloride caused their cyclization to the respective triazolo-thiadiazole derivatives. On the other hand, reaction of thiocarbohydrazide with galactaric acid or its 2,3,4,5-tetra-O-acetyl derivative did





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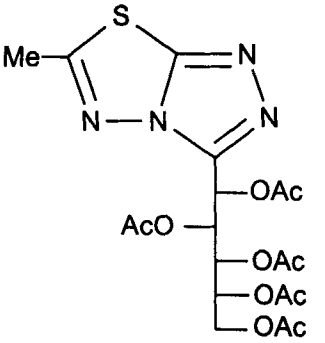

2

not go to completion, and a mixture of products was obtained which could be separated, in the latter case, to give 4-amino-5-mercapto-3-methyl-1,2,4-triazole in addition to galactaric acid and the starting material. The extended zigzag conformations of **2** and its D-galacto analogue have been deduced from the vicinal coupling constants in their ^{1}H NMR spectra. On the other hand, a sickle conformation was deduced for the D-glycero-D-gulo analogue

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