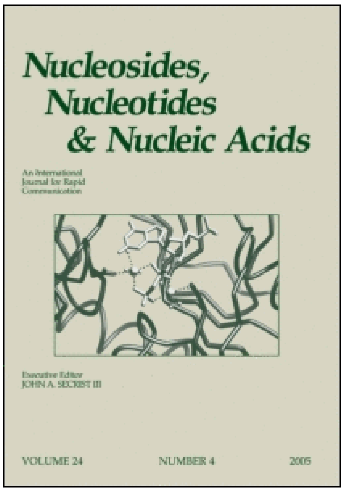

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

The Synthesis of v-Triazolo[4,5-c]pyridine Nucleosides

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To cite this Article Sscaron, A. , timac, Townsend, L. B. and Kobe, J.(1991) 'The Synthesis of v-Triazolo[4,5-c]pyridine Nucleosides', Nucleosides, Nucleotides and Nucleic Acids, 10: 1, 727 — 728

To link to this Article: DOI: 10.1080/07328319108046583

URL: http://dx.doi.org/10.1080/07328319108046583

NUCLEOSIDES & NUCLEOTIDES, 10(1-3), 727-728 (1991)

THE SYNTHESIS OF *v*-TRIAZOLO[4,5-*c*]PYRIDINE NUCLEOSIDES

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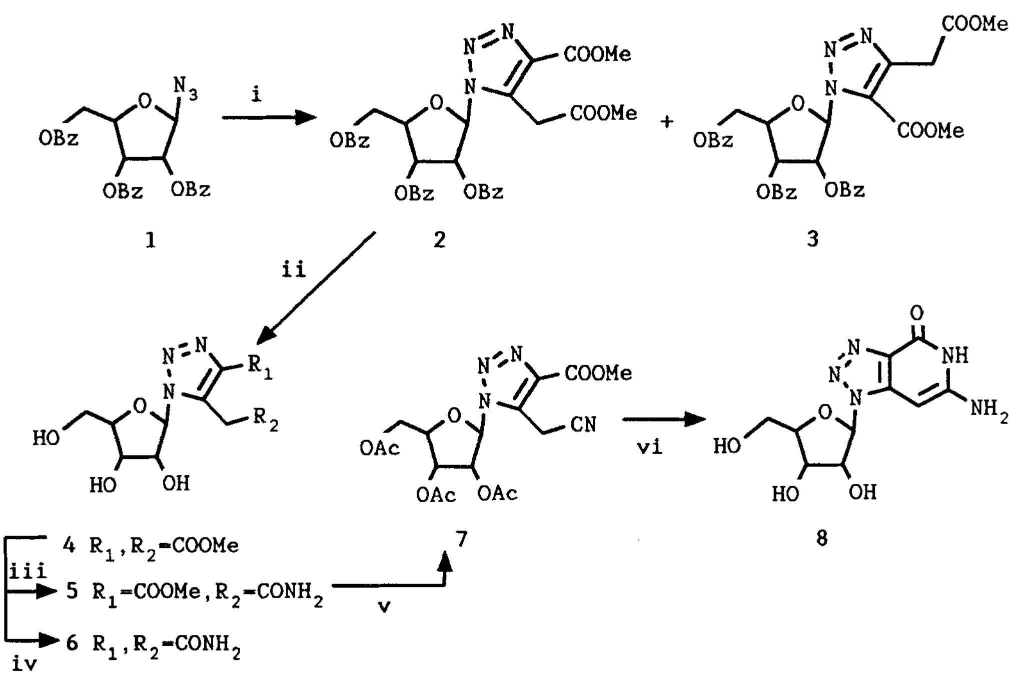
Abstract: 8-aza-3-carbaguanosine **8** has been prepared *via* 1,3-dipolar cycloaddition of the azide **1** with dimethyl 1,3-allenedicarboxylate, followed by a ring closure procedure utilizing simple methods.

We expected much easier entry into the title class of compounds utilizing allenic esters as dipolarophiles instead of previously used 4-hydroxy-2-butynoate[1]. Thus, the reaction of **1**[3] with dimethyl 1,3-allenedicarboxylate[4] provided **2** as a principal cycloadduct (77%), accompanied by minor amounts of its positional isomer **3** (11%) and presumably an 1:2 adduct (12%)[5]. Orientation of the acetate side chain in **2** and **3** was confirmed by ^{1}H-NMR techniques. The chemical shift of H-1 is at 0.77 ppm downfield for **3** (δ_{H-1}= 7.13 ppm, $J_{1,2}$= 1.5 Hz) as compared with **2** (δ_{H-1}= 6.36 ppm, $J_{1,2}$= 1.95 Hz), a characteristic feature of such isomers[1]. Deprotection of **2** to the diester **4** and subsequent treatment with methanolic ammonia gave either the monoamide **5** or the diamide **6**, depending on the reaction conditions. Acetylation[6] of the sugar hydroxyl groups of **5** and subsequent dehydration of the amide group by $(CF_3CO)_2O$[7] afforded the nitrile **7** (56%). Although absent in an IR spectrum, the nitrile group is readily observable in a ^{13}C-NMR spectrum (δ= 115.01 ppm in DMSO-d_6). Ring closure according to the earlier procedure[2] gave a 32% yield of

8-aza-3-carbaguanosine **8** with spectral data (^{1}H- and ^{13}C-NMR, IR) identical to those reported previously[1,2].



i) dimethyl 1,3-allenedicarboxylate, toluene, 67°C, 7d; ii) NaOMe/MeOH; iii) NH_3/MeOH, 0°C, 4h; iv) NH_3/MeOH, r.t.,12h; v) Ac_2O, DMAP, MeCN; then $(CF_3CO)_2O$, pyridine, THF, 1h; vi) liq. NH_3

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5. Dimethyl 1,3-allenedicarboxylate (2 mole equiv.) was added in several portions to a solution of **1** in a small amount of toluene at 67°C over 7d. Unreacted **1** (25%) and the products were isolated by chromatography on silica gel (eluants CH_2Cl_2 and CH_2Cl_2/EtOAc 20:1). Only **2** could be obtained in a pure state upon treatment of appropriate fractions with 2-PrOH (48% isol. yield, mp 110-111.5°C from MeOH).
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