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

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

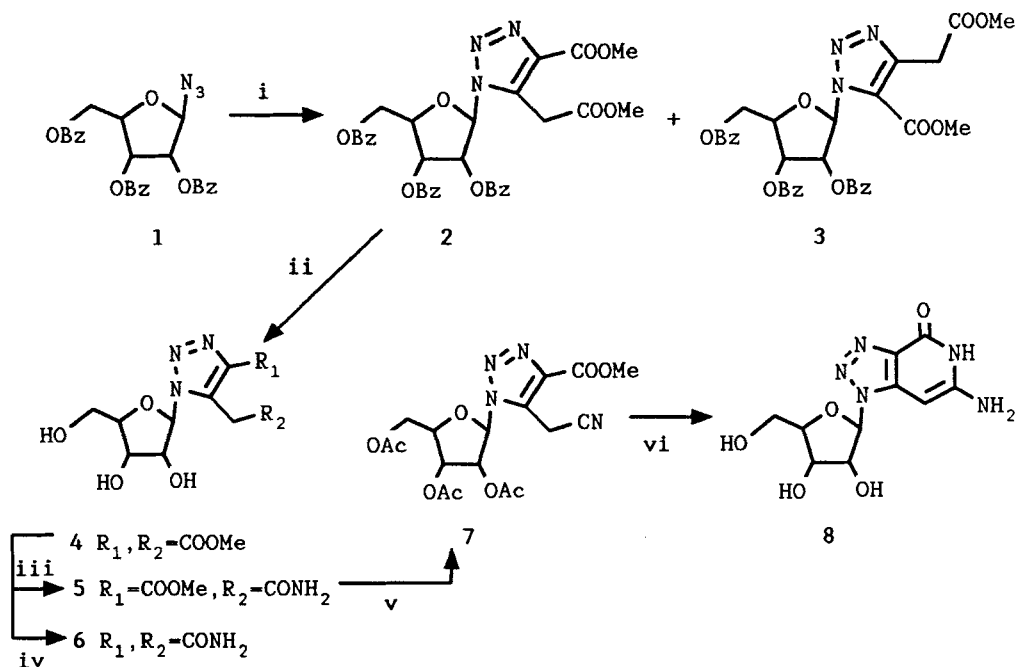
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Abstract: 8-aza-3-carbaguanosine **8** has been prepared via 1,3-dipolar cycloaddition of the azide **1** with dimethyl 1,3-allenedicarboxylate, followed by a ring closure procedure utilizing simple methods.

We expected much easier entry into the title class of compounds utilizing allenic esters as dipolarophiles instead of previously used 4-hydroxy-2-butyrate¹. Thus, the reaction of **1**³ with dimethyl 1,3-allenedicarboxylate⁴ 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 ¹H-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 isomers¹. 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. Acetylation⁶ of the sugar hydroxyl groups of **5** and subsequent dehydration of the amide group by (CF₃CO)₂O⁷ afforded the nitrile **7** (56%). Although absent in an IR spectrum, the nitrile group is readily observable in a ¹³C-NMR spectrum (δ = 115.01 ppm in DMSO-*d*₆). Ring closure according to the earlier procedure² gave a 32% yield of

8-aza-3-carbaguanosine **8** with spectral data (^1H - 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 $(\text{CF}_3\text{CO})_2\text{O}$, pyridine, THF, 1h; vi) liq. NH_3

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3. An improved preparation of **1** is submitted for publication.
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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 $\text{CH}_2\text{Cl}_2/\text{EtOAc}$ 20:1). Only **2** could be obtained in a pure state upon treatment of appropriate fractions with 2-PrOH (48% isol. yield, mp $110\text{--}111.5^\circ\text{C}$ from MeOH).
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