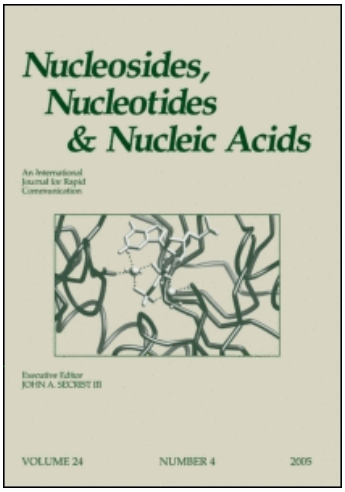

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The Synthesis of Pyrazol0[3,4-*c*]Pyridine C-Nucleosides

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THE SYNTHESIS OF PYRAZOLO[3,4-*c*]PYRIDINE C-NUCLEOSIDES

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Abstract: The synthesis of two members of the pyrazolo[3,4-*c*]pyridine C-nucleoside family is accomplished utilizing the 1,3-dipolar cycloaddition reaction of a diazo-ribofuranosyl derivative and an appropriate allenic diester.

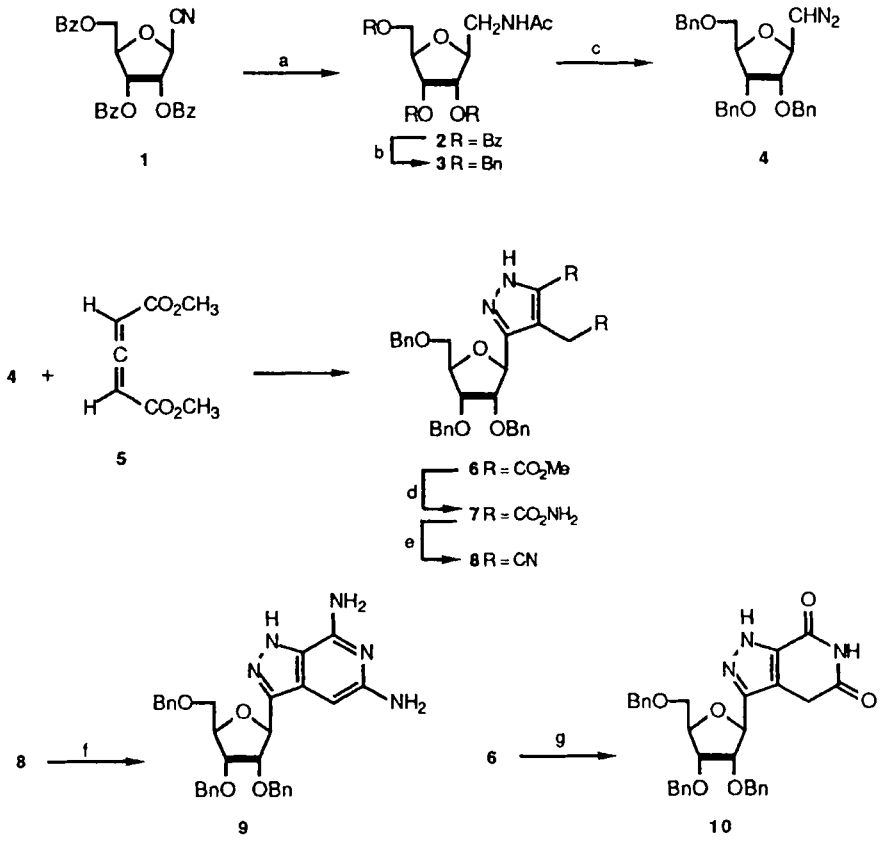
The pyrazolo[3,4-*c*]pyridine family of C-nucleosides represents an interesting and novel class of compounds, which are analogs of the biologically active 3-deazapurine N-nucleosides. Studies in our laboratory have indicated that compounds of this type can be synthesized from 2,5-anhydro-3,4,6-tri-O-benzyl-1-deoxy-1-diazo-D-allitol (**4**) and an allenic diester, specifically, dimethyl 2,3-pentadienedioate (**5**). This is illustrated herein.

The synthesis of **4** began with 2,5-anhydro-3,4,6-tri-O-benzoyl-β-D-allononitrile (**1**),[1] which was reduced with sodium trifluoroacetoxyborohydride[2] and the resultant product acetylated with acetic anhydride to give 1-acetamido-2,5-anhydro-3,4,6-tri-O-benzoyl-1-deoxy-D-allitol (**2**)[3] (colorless syrup, 70% from **1**). The benzoyl protecting groups of **2** were removed with sodium methoxide and the product reprotected with benzyl chloride to give 1-acetamido-2,5-anhydro-3,4,6-tri-O-benzyl-1-deoxy-D-allitol (**3**)[4] (64% from **2**). The desired diazo derivative (**4**) was formed by the method of Acton *et al.*[4] and allowed to react with dimethyl 2,3-pentadienedioate (**5**)[5] to give **6** (colorless syrup, 85% from **3**).

The diamino pyrazolo[3,4-*c*]pyridine **9** (light tan solid, mp 165-168 °C) was obtained from **6** by forming the diamide **7** (light brown syrup, 95%), dehydrating **7** with trifluoroacetic anhydride to the dinitrile **8** (colorless syrup, 79%), and ring closure of **8** with NH_3/NH_4Cl(cat.) at 160 °C (38%) in a stainless steel reaction vessel.

The dioxo pyrazolo[3,4-*c*]pyridine **10** (colorless syrup) was obtained in 48% yield by ring closure of **6** with $NaNH_2/NH_3$ at -40 °C.

The debenzylation of **9** and **10** is currently being pursued.



a) i. $NaBH_3OCOCF_3$, 28 °C, THF; ii. AC_2O, Et_3N, 28 °C THF.
b) i. NaOMe/MeOH, 25 °C; ii. BnCl, KOH, DMSO, 15 °C.
c) N_2O_4, 0 °C; KOH, Et_2O, 0 °C.
d) NH_3/MeOH, 120 °C, 14h.
e) $(CF_3CO)_2O$, pyridine, THF.
f) NH_3/NH_4Cl, 160 °C.
g) $NaNH_2/NH_3$, -40 °C.

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