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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.

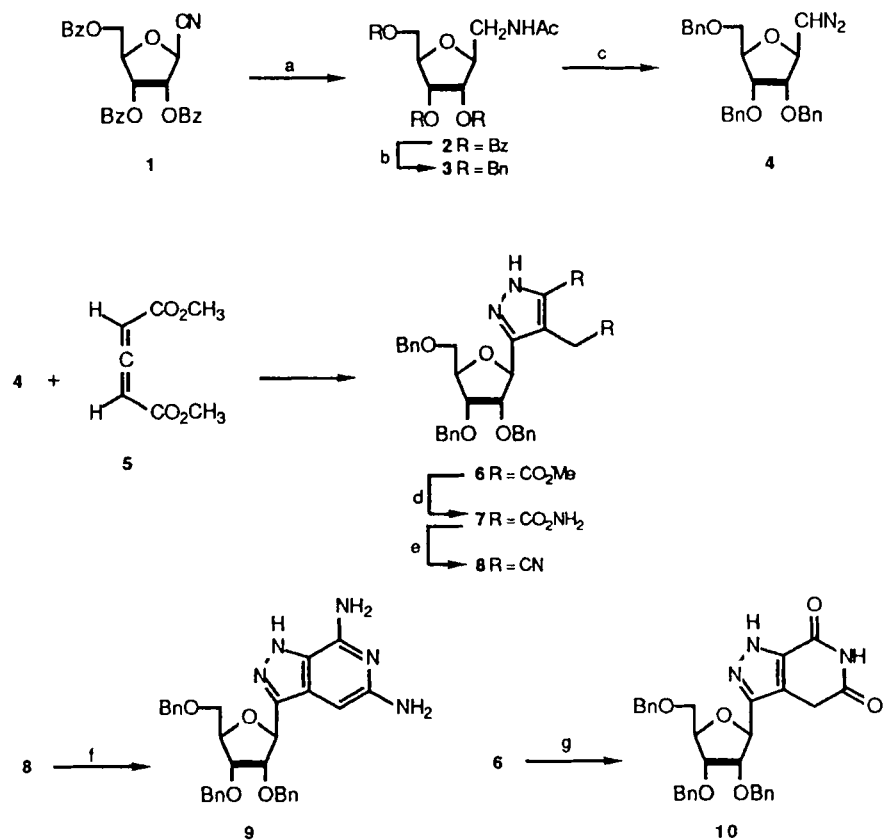
The pyrazolo[3,4-*c*]pyridine family of C-nucleosides represents an interesting and novel class of compounds, which are analogs of the biologically active 3-deazapurine N-nucleosides. Studies in our laboratory have indicated that compounds of this type can be synthesized from 2,5-anhydro-3,4,6-tri-O-benzyl-1-deoxy-1-diazo-D-allitol (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 trifluoroacetoxyborohydride² 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 NH₃/NH₄Cl(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 NaNH₂/NH₃ at -40 °C.

The debenzylation of 9 and 10 is currently being pursued.



- a) i. NaBH₃OCOCF₃, 28 °C, THF; ii. AC₂O, Et₃N, 28 °C THF.
 b) i. NaOMe/MeOH, 25 °C; ii. BnCl, KOH, DMSO, 15 °C.
 c) N₂O₄, 0 °C; KOH, Et₂O, 0 °C.
 d) NH₃/MeOH, 120 °C, 14h.
 e) (CF₃CO)₂O, pyridine, THF.
 f) NH₃/NH₄Cl, 160 °C.
 g) NaNH₂/NH₃, -40 °C.

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