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[A0032]

A Versatile Synthetic Precursor for Introduction of Specific N^6-Modifications in 2,6-Diaminopurine Nucleosides: N^2-Acetyl-2',3',5'-tri-*O*-acetyl-N^6-(1,2,4-triazol-1-yl)-2,6-diaminopurine-9--D-ribofuranoside

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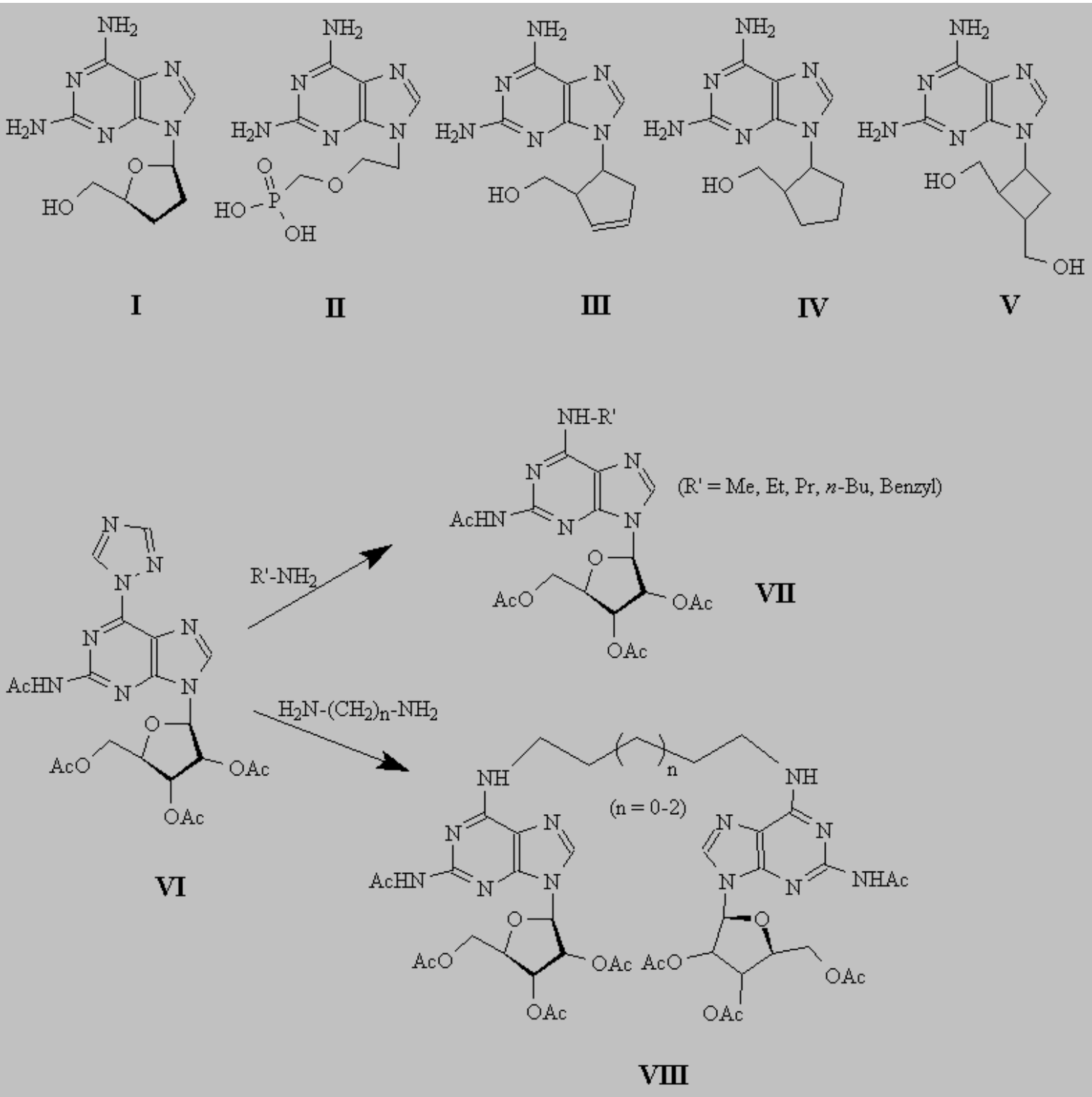
2,6-Diaminopurines as well as their nucleoside and nucleotide analogues have attracted considerable attention in recent years as potential antiviral and antitumor compounds. Some of these compounds have already been shown to be potent anti-HIV agents, including 2',3'-dideoxy-2,6-diaminopurine-9--D-ribofuranoside (**I**), the acyclic nucleotide analogue 9-[2-(phosphonylmethoxyethyl)]-2,6-diaminopurine (**II**), and the three carbocyclic nucleoside analogues (±)-*cis*-[4'-(2,6-diamino-9*H*- purin-9-yl)-2-cyclopentenyl]carbinol (**III**), (±)-*cis*-[3'-(2,6-diamino-9*H*-purin-9-yl)cyclopentyl] carbinol (**IV**), and (±)-9-[2',3'-bis(hydroxymethyl)]cyclobutyl-2,6-diaminopurine (**V**). As part of a program to improve profiles of drug efficiency and toxicity of 2,6-diaminopurine nucleoside analogues, it became necessary to explore the structure-activity relationships (SAR) via specific modifications at the N^6-position of 2,6-diaminopurine ring. However, all available conventional methods to accomplish this goal, including the alkylation of the N^6-amino group of 2,6-diaminopurine riboside or the displacement of a halogen group of 2-amino-6-chloropurine riboside yielded intractable mixtures of products and/or poor yields. We report here the synthesis of a versatile, highly reactive precursor (**VI**), which upon reaction with amine nucleophiles, gave the desired, specifically N^6-modified 2,6-diaminopurinepurine nucleosides (**VII**) in high yields. In addition, the reaction of **VI** with polymethylenediamines afforded the polymethylene-bridged dimers of 2,6-diaminopurine nucleosides (**VIII).**



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