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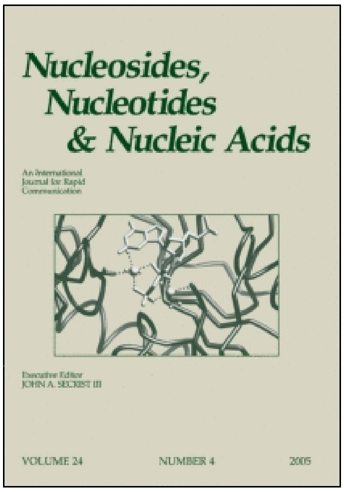

Nucleosides, Nucleotides and Nucleic Acids

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Covalent Analogues of Nucleobase-Pairs

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Covalent Analogues of Nucleobase-Pairs

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ABSTRACT

Covalently linked base pairs analogues consisting of purine-purine or purine-pyrimidine conjugates linked by carbon linkages of diverse length and configuration (ethylene, vinylene, acetylene and phenylene) were prepared.

Key Words: Purines; Pyrimidines; Nucleobases; Base-pairs.

Numerous covalently bounded purine and pyrimidine derivatives representing Watson-Crick base-pair models have been prepared and their properties as DNA cross-links, intercalators or fluorescent probes have been studied.[1] 6-Aryl- and 6-alkynylpurines display diverse types of biological activity.[2] Therefore, we have decided to combine these two classes of compounds to devise novel types of base-pairs or triplets analogues. Thus here we report the synthesis of a novel type of covalent base-pair analogues consisting of purine-purine or purine-pyrimidine conjugates

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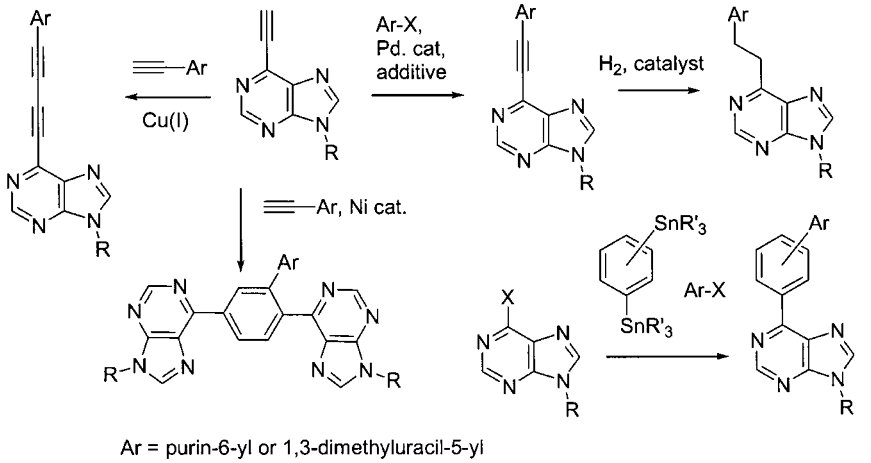

Ar = purin-6-yl or 1,3-dimethyluracil-5-yl

Scheme 1.

linked by carbon linkages of various length and configuration (ethylene, *E*- or *Z*-vinylene, acetylene, diacetylene and *m*- or *p*-phenylene) as well as benzenes bearing three purines or pyrimidines.

The synthesis of the derivatives with acyclic linkages was based on cross- or homo-coupling reactions of 6-halo- and/or 6-ethynylpurines (or pyrimidines) followed by partial or total hydrogenations. Ni-catalyzed cyclotrimerizations[3] of 6-ethynylpurines or 5-ethynyl-1,3-dimethyluracil gave 1,2,4-tris(purin-6-yl)- or 1,2,4-tris(1,3-dimethyluracil)benzenes.[4] The synthesis of the phenylene-linked base-pairs was based on cross-coupling reactions of phenylenebis(stannanes) with 6-halopurines and/or 5-halopyrimidines (Sch. 1). Preliminary biological activity screening showed a significant cytostatic activity of bis(purin-6-yl)acetylenes and -diacetylenes.[5]

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