ChemPubSoc Europe

DOI: 10.1002/slct.201701111

Chemistry SELECT Full Papers

Organic & Supramolecular Chemistry

Microwave-Assisted Synthesis of *C*-4′-(1,5-disubstituted)-triazole-spiro-α-L-arabinofuranosyl Nucleosides

Pallavi Rungta,[a] Priyanka Mangla,[a] Vipin K. Maikhuri,[a] Sunil K. Singh,[a, b] and Ashok K. Prasad*[a]

The synthesis of *C*-4′-(1,5-disubstituted)-triazole-spiro-α-L-arabinofuranosyl nucleosides has been achieved in a regio- and stereospecific manner by using intramolecular Huisgen 1,3-dipolar cycloaddition reaction. The synthesis of these nucleosides necessitates the possession of azide and alkyne moieties in the same molecule, which is being employed as the precursor. Thus, the crucial step in the synthesis of targeted compound is the preparation of 1,2,3-tri-*O*-acetyl-5-azido-5-deoxy-4-*C*-propynyl-α,β-L-arabinofuranose and its conversion to corresponding nucleosides via nucleobase coupling. The microwave heating of such tailor made nucleoside precursors furnishes the targeted spironucleosides, which combines conformational-restriction concept with a triazole structural feature highly sought in drug design.

Introduction

A vibrant area of synthetic organic chemistry is represented by structurally modified nucleosides. This class of selective compounds is vulnerable to the treatment of those diseases where the diseased state differs from the normal state with regard to the enzymes involved in the processing of nucleic acids.[1] These enzymes generally require strict conformational behaviour of the furanose ring with respect to the geometry. Viral diseases are recognized to often fit these criteria. These fascinating interdependencies have prompted several research groups to undertake the preparation of modified nucleosides that feature restrictions in conformational flexibility in order to attain a more optimal level of puckering.[2] Many bicyclic nucleoside analogues with restricted conformation have thus been designed and synthesized aiming at finding new and better anti-viral drugs.[3]

The Huisgen 1,3-dipolar cycloaddition between azide and alkyne leading to 1,5-substitued triazole moiety has gained considerable attention due to its vast biological applications.[4] Notably, several members of the 1,2,3-triazole family have shown gripping biological properties[5], and the triazole moiety with its novel structural features and physiochemical properties is regarded as a privileged structure in drug design and discovery (Figure 1, **1–4**).[6–10] When customized nucleosides possessing alkyne and azide moieties disposed in the same

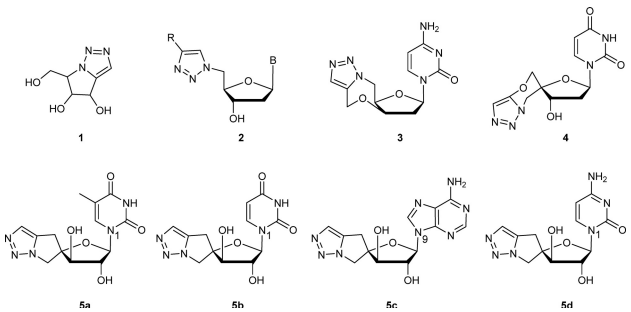

Figure 1. Structures of some of the triazole containing nucleosides **1–4** and targeted *C*-4′-(1,5-disubstituted)-triazole-spiro-α-L-arabinofuranosyl nucleosides **5 a-d.**

nucleosides are heated, they undergo intramolecular Huisgen cycloaddition to furnish 1,5-disubstituted triazole compounds. Such nucleosides induce the antiviral properties of the triazole ring along with conformational restriction due to spiro ring present in the molecule.[10–11] In this article we have described the design and successful synthesis of novel *C*-4′-(1,5-disubstituted)-triazole-spiro-α-L-arabinofuranosyl nucleosides **5 a-d** under microwave irradiation, which enhances reaction yields and also accelerates the rate of the cycloaddition reaction (Figure 1).[12]

Results and Discussion

The synthesis of targeted compound 4-*C*-methylene,5-deoxy-5-*C*-(1,2,3-triazol-1,5-diyl)-α-L-arabinofuranosyl nucleosides **5 a-d** requires a key precursor unifying both azide and alkyne groups

[a] *P. Rungta, P. Mangla, V. K. Maikhuri, Dr. S. K. Singh, Prof. A. K. Prasad*
Bioorganic Laboratory,
Department Of Chemistry
University Of Delhi
Delhi-110 007, India
E-mail: ashokenzyme@gmail.com
[b] *Dr. S. K. Singh*
Department Of Chemistry,
KM College
University Of Delhi
Delhi-110 007, India

Supporting information for this article is available on the WWW under https://doi.org/10.1002/slct.201701111