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Extended Abstract
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Organic Chemistry : 2018- Preparation of novel nucleoside analogues from cyclobutane precursors as potential antiviral agents - Edward Lee-Ruff

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Cyclobutanes represent strained compounds which exhibit chemical reactivity not encountered with unstrained ring systems. These properties have been exploited in their capacity as synthetic intermediates. Cyclobutane nucleosides as oxetanocin analogs have been shown to exhibit antiviral and other biological activities. Our interests in cyclobutanone chemistry has prompted investigations into the preparation of novel cyclobutane nucleoside analogs. We report in this paper the synthesis of novel cyclobutanols2 and 3 from its precursor 1. The coupling of 6-chloropurine with 1 gives two regioisomers consisting of the N-9 and N-7 ketones with the latter formed as the major product.

Nucleoside analogues are an important class of antiviral agents now used in the treatment of infection with human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis virus C (HCV), cytomegalovirus (CMV), herpes simplex virus (HSV) and varicella-zoster infection (VZV). A nascent DNA chain terminating by natural nucleosides and work like nucleoside analogs look. These agents are generally safe and well-tolerated because they are used by viral, but not human, DNA replication in polymerases. In fact, nucleoside analogues are a large class of agents that include cancer drugs (cytarabine, gemcitabine, mercaptopurine, azacytidine, cladribine, decitabine, fluorouracil, floxuridine, fludarabine, nelarabine), and rheumatic diseases (azathioprine, and bacterial) .

The nucleoside analogues used to treat HIV infection are often called reverse transcriptase inhibitors (NRTIs). However, they have activity against DNA-dependent and RNA-dependent DNA polymerases. They are thought to inhibit viral replication by several mechanisms, either by competitive viral polymerase, or by the termination of the DNA chain. Many analogues of antiviral nucleosides are blocked at the 3 hydro hydroxyl group of deoxyribonucleic acid, a nascent DNA molecule that causes the degradation of failure.

The other antiviral nucleoside analogues are negative enantiomers (L forms: lamivudine, emtricitabine, telbivudine) of natural nucleosides (form D) and interfere with replication, partly due to viral causes or added to the DNA molecule. Nucleoside analogs that are phosphorylated at the 5 'site are often called nucleotide analogs, but this distinction is artificial because these agents (tenofovir and adefovir) are also nucleoside analogs. These structural properties of nucleoside analogs are important because they can be used by human polymerases and incorporated into RNA or DNA .

These agents can be used against the hepatitis B virus, the hepatitis C virus, herpes simplex and HIV. Once phosphorylated, they function as antimetabolites by being sufficiently similar to nucleotides to be incorporated into growing strands of DNA; But they act as chain terminators and stop the viral DNA polymerase. They are not specific to viral DNA and are also affected by mitochondrial DNA. For this reason, they have side effects such as removal of bone marrow. There is a large family of nucleoside reverse transcriptase inhibitors, since DNA production by reverse transcriptase is very different from normal human DNA, so it is possible to design nucleoside analogues which are preferentially incorporated into the first ones.

The marine world contains about half of all species. The vast expanse of the ocean and its unique environment are responsible for the exceptional chemical and biological diversity of marine organisms, with 300,000 species described and much more to study. The fact that less than 0.01% to 0.1% of microbial species in the ocean are known to the marine organisms and their active chemical constituents for many avenues. Almost all types of marine organisms, including algae, sea squirts, bacteria, corals, fungi and sponges, have been subjected to scientific review for their natural products.

Historically, the pivotal role of mushrooms in different aspects of human life is very pronounced and this is true even in the marine world. Marine fungi belong to the phyla Ascomycota, Bacidomycota, Chytridiomycota, Deuteromycota and Zygomycota. The evolution of these heterotrophic eukaryotes to degrade different solid

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substrates helps them to recycle dead plants (for example, lignan and cellulose) and animal tissues (for example, chitin and keratin) through the ecosystem. Investigations of marine fungi have begun to occur mainly in the marine environment. The tolerance of certain terrestrial species to the conditions of the marine ecosystem, including their salt concentration, has made them powerful pathogens in the marine world. For example, The pathogenicity of the genera Aspergilus and Fusarium solani has contributed to the mortality of the Caribbean fan and to the various marine crustaceans of infection. In addition, blue crabs, lobster eggs and farmed crabs were reportedly infected with Lagenidium callinectes.

Instead of the pathogenicity of certain species of marine fungi, mutual interactions are the dominant types of relationship found in marine fungi. The marine fungi of the life strongly depend on their symbiotic relationships with other marine organisms such as algae and marine invertebrates. For example, Turgidosculum ulcers can only be grown in the thallus of Blidingia minima, a green alga. In addition, the marine environment of different species of Penicillium and Aspergillus are isolated from the sponges. The isolation of these species requires the collection of support material or the host marine organism. As a result, extraction of sample preservation from marine fungi surveys faces a serious obstacle

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