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SYNTHESIS OF 6,2'-METHYLENE-CYCLOURIDINES

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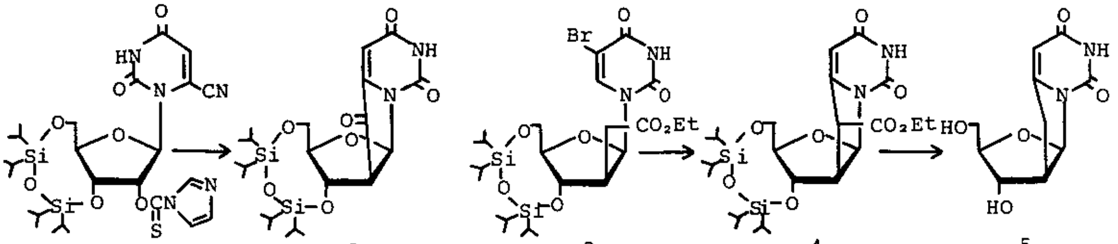
Cyclonucleosides are conformationally fixed models of ordinary nucleosides. As a part of our studies on the synthesis of carbon-bridged cyclonucleosides,[1] we have recently synthesized a variety of C-cyclouridines fixed in the anti-form.[2] Our synthetic method involved two step carbon-carbon bond formations on nucleoside structure. Carbon functionality which would construct carbon-bridge itself was first introduced into the base moiety or sugar moiety and then cyclization process was followed. At the present time, we undertook the synthesis of 6,2'-methylene-cyclouridines fixed in the high anti conformation on the basis of this synthetic methodology.

Treatment of 6-cyanouridine derivative(1) with Bu$_3$SnH and AIBN gave a desired product(2) but the yield was poor. Alternatively, reaction of 2'-carbon-branched 5-bromouridine derivative(3) with a strong base proceeded successfully to give a cyclonucleoside(4) via the addition of 2"-carbanion to the C-6 followed by the elimination of hydrogen bromide. De-ethoxycarbonylation and deprotection of 4 furnished 2'-deoxy-6,2'-methylene-cyclouridine(5). The synthesis of 2'-hydroxy compound of 5 will also be discussed.



1 2 3 4 5

1. A. Matzuda, K. Niizuma and T. Ueda, Chem. Pharm. Bull., 28, 876 (1980) and Refs.

2. T. Ueda, S. Shuto, T. Sano, H. Usui and H. Inoue, Nucleic Acids Res. Symp. Series, No. 11, 5 (1982).