Abstract

Syntheses of two series of 2'-sugar-modified pyrimido[4,5-*b*]indole nucleosides were developed. The synthetic strategy was based on functional group transformations of the 2'-hydroxy group of the 3',5'-protected ribonucleoside. The key intermediate was prepared via stereoselective nucleobase anion glycosylation of the known 4,6-dichloropyrimido[4,5-*b*]indole nucleobase with 2,3-*O*-isopropylidene-5-*O*-TBS-protected halogenose, subsequent deprotection under acidic conditions and protection of 3'- and 5'-hydroxy groups with Markiewicz reagent. Pyrimidoindole arabinonucleoside was then synthesized using a sequence of oxidation-reduction reactions of the 2'-hydroxy stereocenter. The synthesis of pyrimidoindole 2'-deoxy-2'-fluororibonucleoside was achieved by stereoselective S_N2 fluorination of the THP-protected arabinoside followed by acidic deprotection. For the biological activity testing, two series of 4-substituted arabinonucleosides and 2'-deoxy-2'-fluororibonucleosides were synthesized employing nucleophilic substitution or Pd-catalyzed cross-coupling reactions.