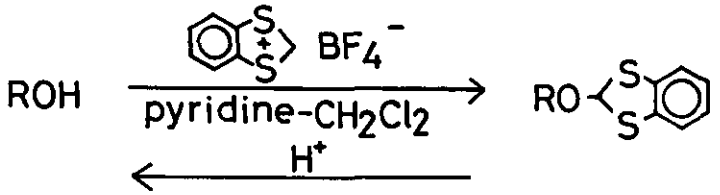
BENZODITHIOL-2-YL AS A NEW HYDROXYL PROTECTING GROUP IN NUCLEOSIDES

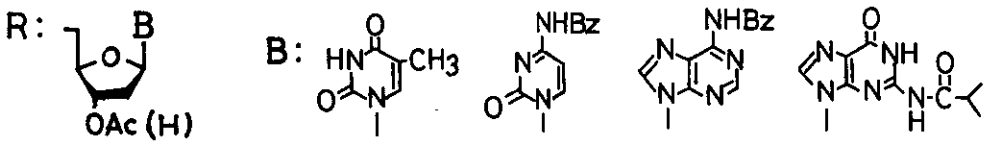
Mitsuo Sekine and Tsujiaki Hata

Department of Life Chemistry, Tokyo Institute of Technology,
Nagatsuta, Midoriku, Yokohama 227, Japan

For the synthesis of complicated molecules such as oligonucleotides, protecting groups that are stable under alkaline conditions and can be removed under mildly acidic conditions are quite useful. Here, we report the benzodithiol-2-yl group, i.e., a new type of acid-labile protecting group for nucleoside hydroxyl groups.

The benzodithiol-2-yl (BDT) group can be easily introduced into nucleoside hydroxyl groups in high yields by employing 1,3-benzodithiolium tetrafluoroborate (BDTF) in the presence of pyridine in methylene chloride. Upon treatment of N-protected deoxyribonucleosides with BDTF in pyridine, selective protection of the primary hydroxyl groups with the BDT group has been achieved.





The BDT group was smoothly cleaved from the protected nucleosides by treatment with 80% acetic acid at room temperature for 3 h. The stability of the BDT group was compared with those of previously known acid-labile protecting groups under the conditions of 80% acetic acid at room temperature. Consequently, the BDT group was found to be situated between the 4-methoxytetrahydroxy-4-yl and 4-monomethoxytrityl groups or nearer the latter group.

This new protecting group was successfully applied to the synthesis of oligothymidylates and uridylyl(5'→3')uridine where it was used as the 5'- and 2'-hydroxyl protecting groups, respectively.