SYNTHESIS AND PROPERTY OF 5-(2,2-DIFLUOROVINYL)URACIL DERIVATIVES

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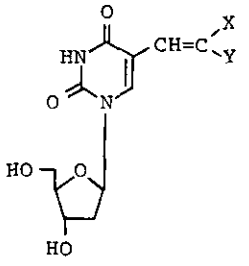
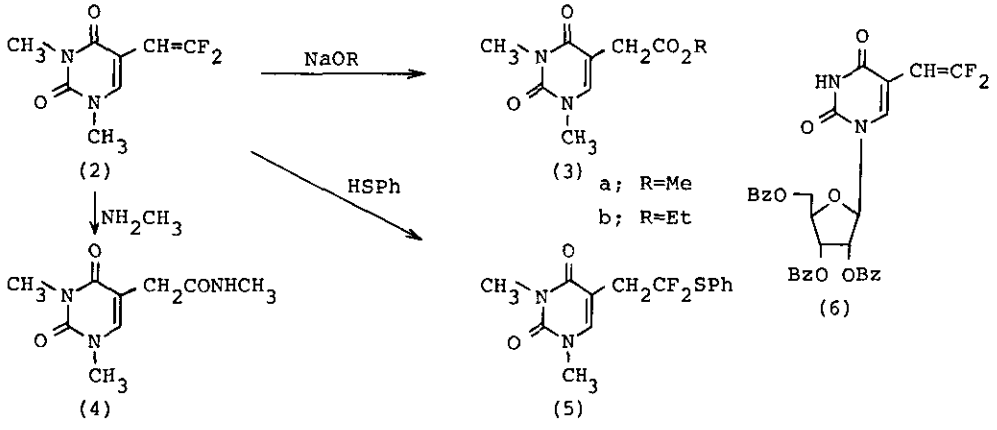
There has been great interest in 5-substituted pyrimidine nucleosides as potential antivirus and anticancer agents. Recently, it was found that 5-bromovinyl-2'-deoxyuridine(BVDU) was highly efficacious against herpes simplex virus type 1. In view of structural similarity to the BVDU, we planed to synthesize 5-(2,2-difluorovinyl)-2'-deoxyuridine(1). The present paper describes the results of the preliminary investigation on the synthesis and property of 5-(2,2-difluorovinyl)uracil derivatives.



BVDU; X=Br, Y=H
(1); X=Y=F

The reaction of 5-formyl-1,3-dimethyluracil with Ph_3P and $ClCF_2COONa$ in dry acetonitrile under argon resulted in the formation of 5-(2,2-difluorovinyl)-1,3-dimethyluracil(2) in 86% yield. Analogously, the reaction of 2',3',5'-tri-O-benzoyl-5-formyluridine with Ph_3P and $ClCF_2COONa$ afforded the corresponding 5-(2,2-difluorovinyl)uridine derivative(6).

Reactivities of (2) toward nucleophiles were observed to be higher than those of 5-bromovinyl-1,3-dimethyluracil. For example, treatment of (2) with NaOR(R=Me, Et) and methylamine gave the corresponding esters(3a, 3b) and amide (4) in high yields, respectively. The reaction of (2) with thiophenol led to the smooth formation of the adduct(5).



(2) (3) a; R=Me b; R=Et (4) (5) (6)