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Facile Synthesis of Base-Labile 2'-Deoxyribonucleosides: An Improved Synthesis of 2'-Deoxy-5-aza-Cytidine

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FACILE SYNTHESIS OF BASE-LABILE 2'-DEOXYRIBONUCLEOSIDES:

AN IMPROVED SYNTHESIS OF 2'-DEOXY-5-AZA-CYTIDINE

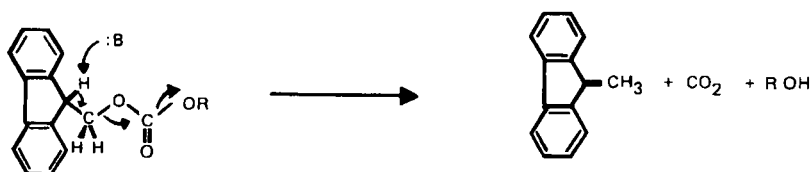
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Abstract: The use of the Fmoc group for the protection of the hydroxy functions of the sugar moiety gave an improved overall yield of 2'-deoxy-5-azacytidine (6 β), due to the mildly-basic conditions required for its removal from the protected nucleoside.

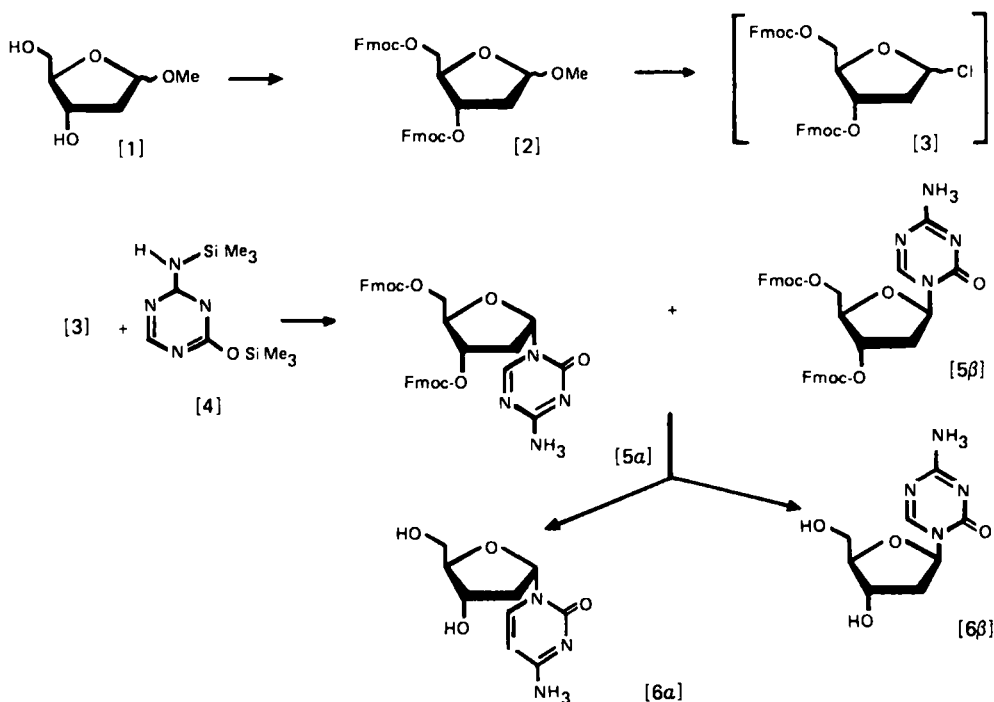
Recent reports describing the role of 2'-deoxy-5-azacytidine (6 β) in the regulation of gene expression through the inhibition of DNA methylation¹ have generated renewed interest in this nucleoside. 2'-deoxy-5-azacytidine was first synthesized in 1964 by a multistep procedure described by Pliml and Sorm². More recently, improved yields were obtained by a direct glycosylation procedure of silylated 5-azacytosine, or via a total synthesis, using glycosyl isocyanates as intermediates.

Our attempts at the synthesis of 2'-deoxy-5-azacytidine via the glycosylation procedure described by Piskala³, using the toluoyl group for protection of the sugar moiety, were largely unsuccessful, due to the hydrolysis of the product during the final deprotection procedure.

The use of the 9-fluorenylmethoxycarbonyl group (Fmoc) enabled us to overcome this problem. When used for the protection of hydroxyl groups, it may be conveniently removed by the action of triethylamine in dry pyridine via a β -elimination reaction.



The fully-deprotected crystalline product (6 β) was obtained from (5 α , β) by the action of 15 equivalents of triethylamine in dry pyridine after one hour at room temperature in a 36% yield⁴.



The use of the Fmoc group in nucleoside synthesis represents a significant improvement of the existing methodology. Our procedure should be applicable to the synthesis of numerous other nucleosides analogues, unobtainable by the standard route.

REFERENCES

1. Jones, P. A., (1985) *Pharmacol. Ther.*, **28**, 17-27.
2. Pliml, J. and Sorm, F., (1964) *Collect. Czech. Chem. Commun.*, **29**, 2576-2577.
3. Piskala, A.; Synackova, M.; Tomankova, H.; Fiedler, P. and Zizkovsky, V., (1978) *Nucleic Acids Res.*, **4**, 109-114.
4. Ben-Hattar, J. and Jiricny, J., (1986) *J. Org. Chem.*, **51**, 3211-3213.