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Anilkumar R. Kore [a] , Sucheta V. Patil [a] & Manikrao M. Salunkhe [a]

[a] Department of Chemistry , Shivaji University , Kolhapur, 416 004, India

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SILYLATION OF 5'-O-DMT-2'-DEOXYNUCLEOSIDES USING DIBENZO [18] CROWN-6 AND PTC

Anilkumar R. Kore, Sucheta V. Patil and Manikrao M. Salunkhe*
Department of Chemistry, Shivaji University,
Kolhapur 416 004, India

ABSTRACT

3'O-silylated derivatives of 5'-O-DMT-2'deoxynucleoside (2) were synthesized in high yield by reaction of 5'-O-DMT-2'-deoxynucleosides (1) with tert-butyl dimethylsilylchloride using sodium hydride, benzyltriethylammonium chloride [TEBA] and a catalytic amount of dibenzo-[18]-crown-6 [DB-18-C-6] or 15-crown-5 [15-C-5] under mild reaction conditions.

INTRODUCTION

Trimethylsilyl derivatives of nucleosides and nucleotides were initially prepared in order to render these highly polar, high melting compounds sufficiently volatile for gas-liquid chromatography.[1]

The stable tert-butyldimethylsilyl protective group introduced by Corey[2] has enhanced the utility of silyl groups as hydroxyl masking agents. Ogilvie[3] evaluated various silyl chlorides for blocking hydroxyl functions of the nucleosides. Tenerally silyl derivatives are stable to base and hydrazine hydrate, conditions usually employed for the removal of acylprotecting groups. They are deblocked easily by treating with tetrabutyl ammonium fluoride in tetrahydrofuran. In addition mass spectroscopy can be used to identify silylated nucleosides and nucleotides[4].

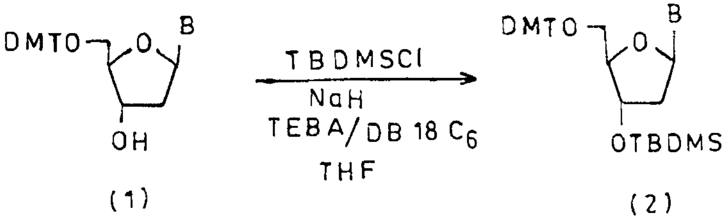
Ogilvie[5] reported that in the 2'-deoxynucleoside series, tert butyldimethylsilyl chlorides showed preference for the 5'-hydroxyl functions over 3'-hydroxyl in forming the monosubstituted derivatives because of the bulk of the silylating agent. The 5'-O-silyl ethers in turn, were found to be more acid labile than the 3'-isomers.

The preparation of the silyl derivatives of nucleosides with TBDMSCl and imidazole in DMF involves separation of various silylated products with low yields of 3'-O-silylated derivatives.[3]

Also in another method reaction of N-acyl-5'-O-(4,4'4' dimethoxytrityl)-2-deoxyribonucleoside in dry tetrahydrofuran with TBDMSCl in presence of pyridine and powdered silvernitrate shows lower yields even at longer reaction times.[3] Our interest in the synthesis of chiraly pure phosphorothioate oligodeoxy nucleotides led us to investigate the simple and efficient method for the silylation of 5'-O-DMT-2-deoxynucleosides.

Here 3'-O silylated derivatives of 5'-O-DMT-2'-deoxy nucleosides (2) were synthesized in short time and high yield by reaction of 5'-O-DMT-2'-deoxy nucleosides (1) with tert-butyl dimethyl silyl chloride using sodium hydride, benzyltriethylammonium chloride (TEBA) and a catalytic amount of dibenzo-[18]-crown-6 [DB-18-C-6] or 15-crown-5 under mild reaction conditions. It is also observed that 15-Crown-5 is also equally effective in catalyzing the above reaction.

Conducting the reaction without either the phase transfer reagent or 18-crown-6 resulted in lower chemical yield than with both catalysts.



DMT - dimethoxytrityl

B - a) thymidine
b) N-benzoyl adenine
c) N-benzoyl cytosine
d) N-isobutyryl guanine

TBDMSCl tert-butyldimethyl silyl chloride

SCHEME

The nucleophilicity of the alkoxyanions is enhanced by both catalysts and hence the O-alkylation reaction is completed within 30 min.

EXPERIMENTAL

TLC : Kodak plates, Silica gel 60 F 254, layer thickness 0.1 mm; detection by U.V. and exposure to HCl vapours. U.V. spectra were recorded on a Shimadzu model 160-A. Proton magnetic resonance spectra (^{1}H NMR) were recorded on a Hitachi R-600 FT nmr instrument.

Synthesis of 3'-O-silylated-5'-O-DMT-2'-deoxynucleosides

General Procedure :

A 0.1 m mol solution of 5'-O-DMT-2'-deoxynucleoside [Glen Research Corporation, U.S.A.] in dry THF was added dropwise to a suspension of sodium hydride (50% in mineral oil, 0.15 m mol) in THF with stirring at 0°C. After the mixture was stirred for 0.5 h, TEBA (4 mg) and Dibenzo-18

TABLE

Starting material	Yield (%)	max (nm) CH_2Cl_2	Rf values Pet ether:Ethyl acetate (80 : 20)	MP (°C)
2a	90	234.4	0.70	63-64
2b	93	233.0	0.70	90-91
2c	90	233.6	0.72	89-90
2d	91	234.4	0.70	125-126

-crown-6 or 15-crown-5 (2 mg) were added in one portion. Then TBDMSCl (0.2 m mol) in THF was added dropwise over 10 min. The resulting reaction mixture was warmed slowly to room temperature and stirred for 0.5 h. The reaction was carried out in round bottom flask under nitrogen, closed by rubber septa. Addition of reagents and control of the progress (TLC) of the reaction was achieved by using syringes.

The reaction mixture was washed with aqueous $NaHCO_3$ and brine. Organic layer was dried with sodium sulphate and evaporated. The crude material was purified by chromatography over silica gel eluting with pet ether-ethyl acetate (1:1). The products obtained were characterized by ^{1}H-NMR, U.V. and comparison with authentic samples.[6]

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REFERENCES

1. Y. Sasaki and T. Hashizume, Anal. Biochem., 1966, 16, 1.
2. E.J. Corey and A. Venkateswarlu, J. Am. Chem. Soc., 1972, 94, 6190.
3. K.K. Ogilvie, Can. J. Chem., 1973, 51, 3799.
4. J. McCloskey, A.M. Lawson, K. Tsuboyama, P.M. Krueger, and R.N. Stillwell. J. Am. Chem. Soc., 1968, 90, 4182.
5. K.K. Ogilvie, E.A. Thompson, M.A. Quilliam, and J.B. Westmore, Tetrahedron Lett., 1974, 2865.
6. Thomas Horn and MicKey S. Urdea, Nucleic Acids Research, 1989, 17, 6959.

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