A mild and efficient method for the preparation of 5′-dimethoxytrityl-2′-deoxynucleoside using poly(4-vinylpyridine)-costyrene

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5′-O-4,4′-Dimethoxytrityl-2′-deoxynucleosides have been synthesized in high yield by the reaction of 2′-deoxynucleosides with 4, 4′-dimethoxytrityl chloride in acetonitrile using poly (4-vinylpyridine)-costyrene (styrene 10%).

Progress on the chemical synthesis of oligonucleotide has culminated in the development of automated procedure for the synthesis of gene fragment. The success in the deoxynucleoside area is principally due to the early establishment of adequate and versatile protecting groups for amino and hydroxyl groups of the growing chain. However, direct DMT-protection of nucleosides have been carried out by using pyridine as a solvent. As pyridine is noxious and has a high boiling point, reaction work-up becomes difficult. Polymeric reagents offer advantage over homogenous catalyst such as the reagent can be easily separated from the reaction mixture, undesirable reactions can be avoided. Poly (4-vinylpyridine) is a polymeric reagent that replaces liquid pyridine as acid acceptor in aqueous and nonaqueous media for reactions that produce acids as a by-product.

Generically hydrogen chloride generated during esterification using acyl halides, from silylation of a primary alcohol with diphenyl i-butyl chlorosilane and mixed acid anhydride preparation from acyl halide were trapped on such type of polymer. Since the polymer is a solid, filtering it from the reaction mixture simplifies work-up. After recovery, the polymer can be regenerated and used in further reactions.

In continuation of our interest in polymeric reagents, we were prompted to study tritylation reaction by use of poly(4-vinylpyridine)-costyrene with different styrene content (Scheme I). The major factor influencing the nature of the polymeric reaction is the type of solvent used for the reaction. The compatibility of the two phases is an important factor governing such type of reaction. The solvent which are capable of swelling the polymer matrix and which are also able to dissolve the substrate are suitable for carrying out the reaction. In order to investigate the effect of solvent on the reactivity of the polymer, the reactions were carried out in acetonitrile, chloroform and benzene. We found that both the polymer, poly(2-vinylpyridine)-costyrene (styrene content 30%) and poly(4-vinylpyridine)-costyrene (styrene content 10%) were soluble in most of the solvents. However, poly(4-vinylpyridine)-costyrene (styrene content 10%) was insoluble in acetonitrile and benzene. Hence, only poly(4-vinyl pyridine)-costyrene (styrene content 10%) was used for reactions. The pyridine content of the polymer was determined by titration with HCl and was found to be 1.5 mmole s/g. It was observed that the reaction proceed very slowly in benzene than in acetonitrile.

![Scheme I](image-url)
The amount of poly(4-vinylpyridine)-costyrene does have much effect on the rate of reaction (0.3 mmole/g–0.75 mmole/g).

**Experimental**

Protected nucleosides were prepared as per reported procedure\(^1\). 4,4'-Dimethoxytrityl chloride (DMT-Cl) was purchased from Aldrich. Acetonitrile was refluxed with calcium hydride for 6 hr and then distilled under nitrogen and stored in air tight bottles over 4Å molecular sieves. Poly(2-vinylpyridine)-costyrene (styrene content 30%) and poly(4-vinylpyridine)-costyrene (styrene content 10%) were purchased from Aldrich Chemical Company, USA.

TLC was carried out using Kodak 13181 silica gel with Fluorescence indicator pre-coated plates.

**Synthesis of 5'-O-DMT-2'-O-deoxynucleoside.**

The general procedure for tritylation of nucleoside, involves treatment of appropriately protected nucleosides (0.1 mmole) in acetonitrile (dry) containing poly (4-vinylpyridine)-costyrene (styrene content 10%, 3 mmole) with 4,4'-dimethoxytrityl chloride (0.13 mmole) at room temperature until TLC analyses (Kodak 13181 silica gel precoated plates, ethyl acetate-pet. ether 7:3, v/v) indicated completion of reaction. The reaction mixture was cooled and triturated with cold diethyl ether. Then the polymer was filtered off and washed with CH\(_3\)CN. The combined organic layer was dried over anhydrous sodium sulfate and concentrated. The products were purified by a short silica gel column (ethyl acetate; pet. ether, 7:3, v/v) and were identified by UV, \(^1\)H NMR and comparison with authentic samples.

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**References**