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A FACILE METHOD FOR DETRITYLATION OF 5'-O-DIMETHOXY-TRITYL-3'-O-tert-BUTYLDIMETHYLSILYL-2'-DEOXYNUCLEOSIDES

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Abstract : The dimethoxytrityl group can be removed effectively from 5'-O-dimethoxytrityl-3'-O-tert-butyl dimethylsilyl-2'-deoxynucleosides and their N-acyl derivatives by using sulfonated crosslinked (1% DVB) polystyrene in dichloromethane-methanol (97.5 : 2.5,v/v) without causing depurination. It has been observed that solvent and percentage of crosslinking plays important role in these reactions.

INTRODUCTION

The dimethoxytrityl (DMT) group has been extensively employed to protect the 5'-hydroxyl function in nucleoside chemistry.^{1,2} Earlier reports showed that 2 % benzenesulfonic acid² or 2 % toluenesulfonic acid³ in chloroform-methanol (7 : 3,v/v) removes Cirrentgroup from the above protected nucleosides causing

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depurination. Dichloroacetic acid in dichloromethane⁴ is effective in achieving rapid detritylation with minimum loss of N-benzoyladenine. However, it can cause burns to skin and clothing and should always be used in hood.

RESULTS AND DISCUSSION

Our interest in nucleotide chemistry and polymeric reagents prompted us to study detritylation by use of sulfonated crosslinked polystyrene resin.



We were surprised to find that the detritylation with commercial resin Dowex 50W-X8 (5 meq/gm) in dichloromethane-methanol (70 : 30,v/v) was complete in 1.5 h but the product could not be isolated except II-A (approx. 20 %) (Entry 1). We thought that the solvent has an important role due to which the product could not be isolated. When the reaction was carried out under similar conditions only in dichloromethane, the detritylation was not observed. However, using dichloromethane-methanol (97.5 : 2.5, v/v) the optimum detritylation product was isolated in the range of 45 to 70 % in case of resin Dowex 50W-X8 (Entry 2) and 0 to 35 % in case of gel type resin Amberlite IR-120 (4.4 meq / gm) which was also 8% crosslinked with divinylbenzene (Entry 3). In case of sulfonated crosslinked (1 %) gel type (4.9 meq/gm) (Entry 4) and macroporous (4.6 meq/gm) (Entry 5) polystyrene resins effective detritylation was achieved in less than 30 min with quantitative isolation of products, without depurination using solvent system dichloromethane -methanol (97.5 : 2.5, v/v) (Table).

This method has the advantage over the other acidic catalysts used as the resin is filtered off immediately after the reaction and does not remain in contact with the product during work-up, thus avoiding depurination and possible glycosidic cleavage. The better results with lower crosslinking reagent (1%) could be explained on the basis of increased swelling ratio which allows quantitative isolation of products.

Entry	II-A		II-B		II-C		II-D	
No.	Time ^a	Yield ^b						
	(h)	(%)	(h)	(%)	(h)	(%)	(h)	(%)
1	1.5	20	1.5	-	2.5	102*	1.8	-
2	2.5	70	2.5	69	4.5	46	3.0	63
3	2.5	35	2.5	30	3.5	-	3.0	25
4	0.33	95	0.33	93	0.6	90	0.4	91
5	0.16	90	0.16	88	0.33	86	0.25	88

TABLE : Detritylation of 5'-0-DMT-3'-0-tert-butyldimethylsilyl-2'-deoxynucleosides by sulfonated polystyrene resins :

a : Estimate of detritylation times by thin layer chromatography

b : Isolated yields

EXPERIMENTAL

Procedure for sulfonation of polystyrene resin :

The 1 % crosslinked gel type or macroporous polystyrene resin (5 gm) was kept overnight in sulphuric acid (20 ml). The residual sulphuric acid was diluted by slow addition of water (to avoid too rapid swelling of the resin which may cause shattering). The diluted acid was filtered off, the beads were washed with water till free from excess of acid and dried under vacuum at 45° C over P_{205}° . The cation exchange capacity⁵ was found to be 4.9 meq/gm for gel type and 4.6 meq/gm for macroporous polystyrene resins.

Procedure for detritylation of 5'-O-DMT-3'-TBDMS-2'deoxynucleosides (I) :

To a solution of 5'-O-DMT-3'-TBDMS-2'-deoxynucleoside (I) (0.1 mmol) in 20 ml dichloromethanemethanol (97.5 : 2.5,v/v) sulfonated polystyrene resin (10 mmol) was added and stirred at room temperature until TLC analysis (pet ether : ethyl acetate, 1:1,v/v) indicated completion of the reaction. Then the resin was filtered off and washed with dichloromethane. The combined organic layer was dried over anhydrous sodium sulphate and evaporated under reduced pressure. The crude material was purified by silica gel column chromatography eluting with pet ether - ethyl acetate (1:1,v/v). The products obtained were characterized by ¹H NMR and comparision with authentic sample.

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