SHORT PAPER

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Deacetylation of 2′-O-Ts-3′,5′-di-O-acetylpurine nucleosides via a free radical reaction

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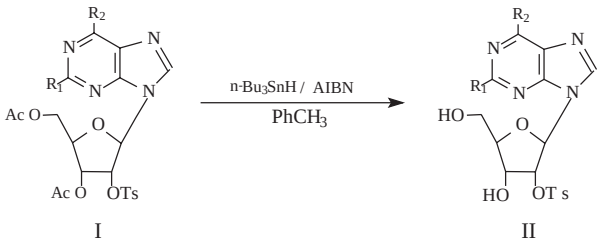
A new method for deprotecting acetyl groups of blocked purine nucleosides has been established by using tri-*n*-butyltin hydride (*n*-Bu_3SnH) in the presence of α, α'-azobisisobutyronitrile (AIBN) without affecting OTs group.

Keywords: *n*-Bu_3SnH, AIBN, deacetylation, free radical

The protection and deprotection of hydroxyl groups as esters are one of the most common procedures used in nucleoside chemistry. The acetyl ester is among the most useful protecting groups.[1]

The methods for the deacetylation of nucleoside derivatives are versatile, and can be divided into two categories: base hydrolysis, for example, using methanolic ammonia,[2] NaOH[3], NaOMe/MeOH[4], $H_2NNH_2{\cdot}H_2O$[5]; acid hydrolysis, for example, using HCl in methanol.[6] To our knowledge, reductive cleavage of acetyl group using tri-*n*-butyltin hydride (*n*-Bu_3SnH) to deprotect without affecting an OTs group has not been reported.[7]

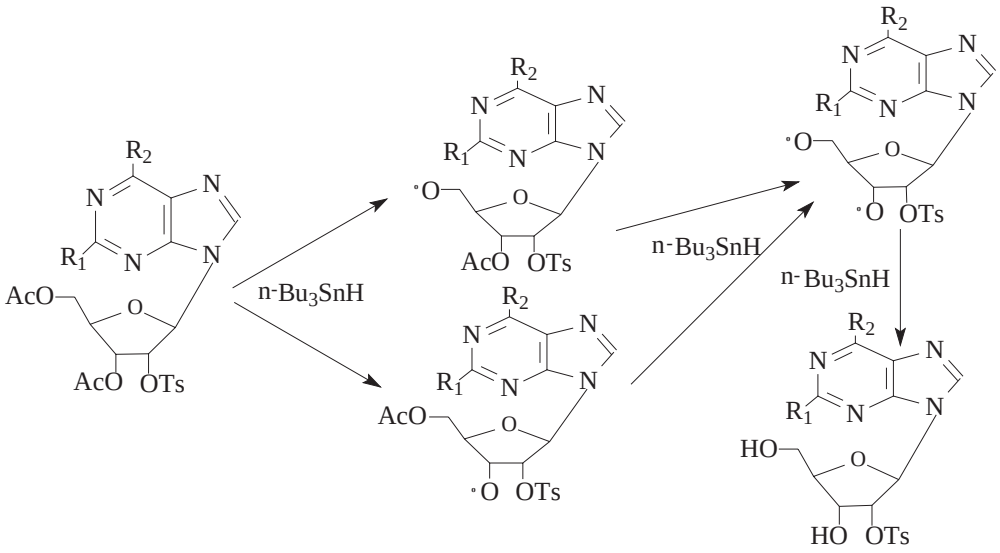
We wished to synthesise 3',5'-di-O-acetyl-2'-deoxy-adenosine starting from 2'-OTs-3',5'-di-O-acetyladenosine,[8] through reductive cleavage of OTs group with tri-*n*-butyltin hydride in toluene at 75°C and α,α'-azobisisobutyronitrile (AIBN) as initiator. Our attempt was unsuccessful. However, to our surprise, after heating 2'-OTs-3',5'-di-O-acetyl adenosine with *n*-Bu_3SnH and AIBN in benzene for 6h at 75° without any change, and allowing the temperature to rise to 100°C, the reaction began to occur. The colour of the solution began to become yellow and four spots appeared on TLC. After 48h, TLC showed that the reaction was complete (only one spot), ^{1}H NMR, LC-MS and Elemental analysis confirmed that the product was 2'-OTs-adenosine. This reaction was reproducible. This result has attracted our interest.



Scheme 1 Deacetylation of 2′-OTs-3′,5′-Di-O-acetylpurine nucleosides

To test the flexibility and generality of this reaction, we have extended it to a series of different purine nucleosides as shown in Scheme 1 and Table 1.

The chosen examples are spread from common 2'-OTs-3',5'-di -O-acetylpurine nucleosides (entry1, 2, 3 and 5) to the 2'-OTs-3',5'-di-O-acetylpurine nucleosides including free radical-sensitive chloro atom (entry 4). All these reactions gave good yields.



Scheme 2 Possible deacetylation mechanism of 2′-OTs-3′,5′-di-O-acetylpurine nucleosides

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1

Entry		Reaction time		Yield (purity by HPLC)
		75°C	100°C	
1	R_1=H R_2=NH_2	6h	48h	85.5% (94.5%)
2	R_1=NH_2 R_2=OH	6h	48h	83.4% (93.2%)
3	R_1=H R_2=OH	6h	48h	83.8% (93.9%)
4*	R_1=NH_2 R_2=Cl	4h	45h	76.9% (90.7%)
5	R_1=NH_2 R_2=NH_2	6h	48h	81.5% (91.9%)

* II : R_1=NH_2 R_2=H entries 1, 2, 3 and 5 II R_1, R_2 is the same as I
Purity is referred to the crude product.

Experimental

A typical procedure: 2'-OTs-3',5'-di-O-acetyl purine nucleoside (1mmol), freshly distilled anhydrous benzene (dried over sodium, 15ml), and AIBN (0.3mmol) were placed in a round bottom flask under a nitrogen atmosphere. The solution was degassed with oxygen-free N_2 for further 10min after slowly adding *n*-Bu_3SnH (13.6mmol) over 5–6 min while stirring at room temperature. The mixture was allowed to stand at 75°C for 6h[9] and then refluxed at 100°C for another 48h. After the reaction was complete (monitored by TLC), the mixture was cooled to room temperature and quenched with MeOH. The crude product was collected by filtration. The pure product was obtained by recrystallisation or through column chromatograph.

We are now investigating the specific mechanism of this procedure. A possible utilisation of a successive radical process was presumed, from one oxygen free radical to two oxygen free radicals during the reaction process (Scheme 2).

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References

1 T. Fuchs and R.R. Schmidt, *Synthesis*, 2000, 259.
2 J.P.H. Verheyden, D. Wagner and J.G. Moffatt, *J. Org. Chem.*, 1971, **36**, 250.
3 K.V.B. Rao, W.Y. Ren, J.H. Burchenal and R.S. Klein, *Nucleosides & Nucleotides*, 1986, **5**, 539.
4 A.L. Schwartz and L.M. Lerner, *J. Org. Chem.*, 1975, **40**, 24.
5 Y. Ishido, N. Nakazaki and N. Sakairi, *J. Chem. Soc. Perkin I*, 1979, 2088.
6 K.A. Watanabe, U. Reichman, C.K. Chu, D.H. Hollenberg and J.J. Fox, *J. Med. Chem.*, 1980, **23**, 1088.
7 A similar cleavage of benzoates by tin hydride has been reported. See: D.R. Kelly, J.G. Mahdi, *Tetrahedron Lett.*, 2002, **43**, 511.
8 Y. Ueno, C. Tanaka and M. Okawara, *Chem. Lett.*, 1983, 795.
9 For entry 4: After refluxing at 75°C for 4h, 2'-OTs-3',5'-di-O-acetyl-2-amino-6-chloropurine nucleoside was converted into 2'-OTs-3',5'-di-O-acetyl-2-aminopurine nucleoside.