MITSUNOBU REACTION ON PROTECTED DEOXYGUANOSINE AND GUANOSINE

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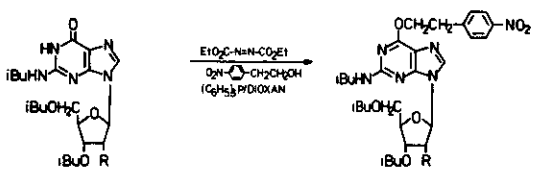
Syntheses of guanosine containing oligonucleotides reveal longstanding problems of various side reactions involving the amide function of the guanine moiety during phosphorylation and condensation reactions. We used the Mitsunobu reaction for protection of the O^6-position of deoxyguanosine and guanosine with the p-nitrophenylethyl group, which showed excellent properties for phosphate protection in oligonucleotide syntheses.

Treatment of N^2,3',5'-triisobutyroyl-2'-deoxyguanosine and N^2,2',3',5'-tetraisobutyroylguanosine respectively with diethyl azodicarboxylate, triphenylphosphine, and p-nitrophenylethanol in dioxane at room temp. led to the O^6-p-nitrophenylethyl derivatives in good yield. This blocking group could selectively be removed with 0.5 M DBU in pyridine in 40 min. to give the starting materials back. Conc. ammonia cleaved the sugar isobutyroyl groups to give N^2-isobutyroyl-O^6-p-nitrophenylethyl-deoxyguanosine and -guanosine. The introduction of p-nitrophenylethyl groups also increased the solubility of these derivatives considerably in organic solvents and led to easy purification. The advantages of these newly protected guanosine derivatives in oligonucleotide synthesis will be discussed.



iBu = $(CH_3)_2CHCO$
R = H, $(CH_3)_2CHCOO$