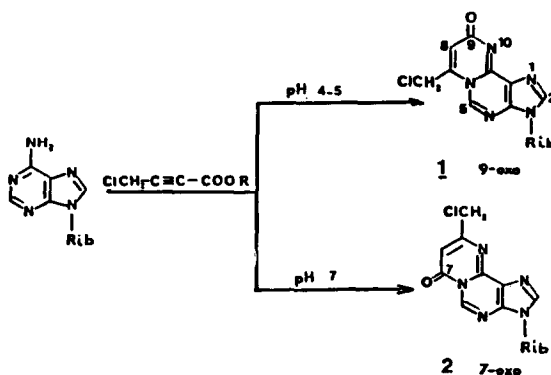


## A CONFORMATION-SPECIFIC CHEMICAL MODIFICATION OF NUCLEIC ACIDS

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Small molecules containing an adenine ring react under mild conditions with  $\alpha$ -acetylenic esters. Chlorotetrolic (4-chlorobutynoic) acid ester yields two isomeric products 1 and 2 [1-3].



However, in the case of nucleic acids, the nature of the isomer formed depends mainly on steric factors. Thus, treatment of poly(A) with methyl chlorotetrolate at pH 7 leads first to derivatives of type 1 instead of the normally expected 2 isomers. This chemical modification is accompanied by a gradual destacking of the bases which makes possible the formation of derivatives 2 in the later stages of the reaction when the conformation of the polynucleotide chain changed sufficiently.

In the case of tRNA<sup>Phe</sup> the reaction involves the anticodon loop and the 3'-end. In the anticodon region which has an ordered conformation with nearly normal base stacking [4], adenine bases are converted to derivatives of structure 1, while in the 3'-end in which the bases are only slightly stacked [4], isomers 2 are formed. Derivatives 1 and 2 have very different physical properties and can be easily identified e.g. by HPLC following hydrolysis of modified nucleic acids.

