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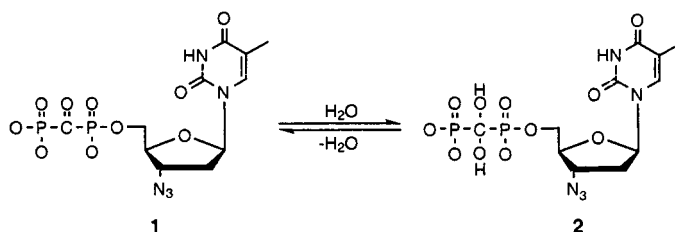
CARBONYLBISPHOSPHONATE ANALOGUES OF NUCLEOSIDE 5'-DIPHOSPHATES

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A new type of nucleotide analogue is described, in which the α,β -phosphoric anhydride oxygen of a nucleoside 5'-diphosphate is replaced by a carbonyl group. As an example, we have prepared the carbonylbisphosphonate analogue (**1**) of 3'-azido-3'-deoxythymidine 5'-diphosphate (AZT diphosphate) utilizing PyBOP-promoted, or preferably Mitsunobu-type coupling of AZT with a suitably protected bisphosphonate precursor. The ultimate product **1** was isolated by reverse-phase HPLC, and characterized by NMR (^{31}P , ^{13}C , ^1H), UV-visible spectroscopy and HRMS. In aqueous solution, it undergoes reversible, pH-dependent conversion to a hydrate adduct (**2**), identified by its ^{31}P NMR resonance (δ 15 ppm). As expected, the equilibrium is displaced to the hydrate form at acidic pH and when excess Mg^{2+} is added.



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