H-phosphonamidites are deoxynucleoside amidites modified such that, when incorporated into an oligonucleotide, that base position will have an H-phosphonate backbone linkage instead of the standard phosphodiester linkage. In the H-phosphonate linkage, one of the oxygen bound to the phosphorus atom in a phosphodiester linkage has been replaced by hydrogen. H-phosphonate-modified oligos are typically synthesized when a researcher wants to prepare a S-35 radiolabeled phosphorothioate linkage (1). For the radiolabeled phosphorothioate, an H-phosphonate linkage is incorporated at the desired position using phosphoramidite chemistry, and then S-35 is used to replace the hydrogen atom via a sulfurization reaction (2). For the phosphoroamidate, N,N-dimethylaminoethylamine is reacted with the H-phosphonate to form the substituted linkage. Phosphoroamidates, being a cationic linkage, may provide nuclease resistance and improved cell permeability (3).

References