

Products

dA-Thiophosphoramidite

5'-Dimethoxytrityl-N-benzoyl-2'-deoxy-Adenosine, 3'-[(- thiobenzoylethyl)-(1-pyrrolidinyl)]-thiophosphoramidite, M.W.: 959.7

dC-Thiophosphoramidite

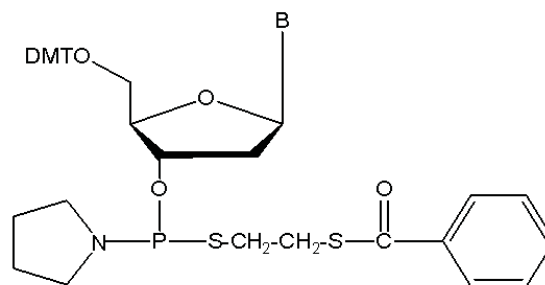
5'-Dimethoxytrityl-N-benzoyl-2'-deoxy-Cytidine, 3'-[(- thiobenzoylethyl)-(1-pyrrolidinyl)]-thiophosphoramidite, M.W.: 950.7

dG-Thiophosphoramidite

5'-Dimethoxytrityl-N-isobutyryl-2'-deoxy-Guanosine, 3'-[(- thiobenzoylethyl)-(1-pyrrolidinyl)]-thiophosphoramidite, M.W.: 936.7

T-Thiophosphoramidite

5'-Dimethoxytrityl-2'-deoxy-Thymidine, 3'-[(- thiobenzoylethyl)-(1-pyrrolidinyl)]-thiophosphoramidite, M.W.: 841.6



1. B=dA^{Bz} 3. B=dG^{iBu}

2. B=dC^{Bz} 4. B=T

Description:

Thiophosphoramidites are activated modified nucleotides which effect the substitution of the two internucleotide non-bridging oxygen atoms with sulfur. The result is a nucleic acid analog with an internucleotide phosphorodithioate linkage that is achiral.

Applications:

PS2 analogues have been successfully used as aptamers for a variety of protein targets including activated-protein 1 (AP-1) as well as transcription factor NFκB for which the PS2-ODN demonstrated 150 picomolar Kd with a dissociation time >12 hours. PS2-ODNs demonstrate up to 300 times greater binding affinity for proteins than oligos without PS2 linkages with no loss of their aptamer specificity.

In addition, PS2-ODNs have been investigated as potential antisense compounds and have exhibited the ability to interfere with the expression of erbB-2 mRNA associated with breast cancer; to induce B-cell proliferation and differentiation; and to potently inhibit HIV-1 reverse transcription activity as well as viral replication. The inhibition is dependent upon both the number of dithioate linkages as well as the length of dithioate oligomer analog. A comparative analysis with phosphorothioate equivalents indicates that dithioates are much better inhibitors and are able to inhibit at relatively short oligomer length. Inhibition of HIV-1 reverse transcriptase by dithioate oligodeoxynucleotides appears to be a general phenomenon as use of any of the nucleotide base sequences examined inhibits its activity.

Bottle Sizes

100 mole
250 mole
500 mole
1000 mole

Usage parameters on oligo synthesizers:

Coupling: Double couplings

Deprotection: no changes needed from standard DNA methods

Storage: refrigerated, dry

Stability in solution: 2-3 days

Concentration on Synthesizer: 0.1 mM

Purification of PS2 oligos

Strong anion exchange liquid chromatography for high resolution analysis and purification at pH 8. The thiocyanate, SCN⁻, as eluting ion can be used for oligos containing a high percentage of phosphorodithioate linkages.

● Patent Reference:

U.S. Patent Number: 5,218,088 "Process for Preparing Dithiophosphate Oligonucleotide Analogs Via Nucleoside Thiophosphoramidite Intermediates"

Selected Literature References:

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