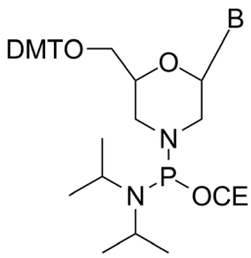
Morpholino Amidates

ChemGenes is pleased to offer Exceptional Quality of Morpholino Phosphoramidate monomers for synthesis of Morpholino Phosphoramidate Oligomers (PMOs)

Introduction:

Phosphorodiamidate morpholinos (PMOs) are chemically modified oligonucleotides (ODNs) wherein the 2′-deoxyribonucleosides and phosphate linkages of canonical DNA are substituted with morpholino rings and phosphorodiamidate linkages respectively. They have been researched extensively in oligonucleotide therapeutics as potential steric blocking agents for the treatment of various genetic disorders. PMOs exhibit high hybridization affinity to complementary RNA, possess excellent enzymatic stability both in vitro and in vivo and elicit low immunogenicity leading to acceptable toxicokinetic profiles in mammalian models. The ability of PMOs to effectively function as steric blockers arises from their ability to specifically bind complementary RNA both in vitro and in vivo.

Morpholinos block small (~25 base) regions of the base-pairing surfaces of ribonucleic acid (RNA). Morpholinos are six-membered rings which may provide higher conformational rigidity when incorporated into an oligonucleotide (ODN) backbone.



B	Protection	Catalog#	Packing Size
Adenine	*N*-Bz	ANP-3751	250mg, 500mg, 1g
Cytosine	*N*-Bz	ANP-3752	250mg, 500mg, 1g
Guanine	*N*-*i*Bu	ANP-3753	250mg, 500mg, 1g
Thymine	N/A	ANP-3754	250mg, 500mg, 1g

Bulk quantities available : 10 g, 100 g, Please enquire.

Figure 1. Structure of Morpholino amidates

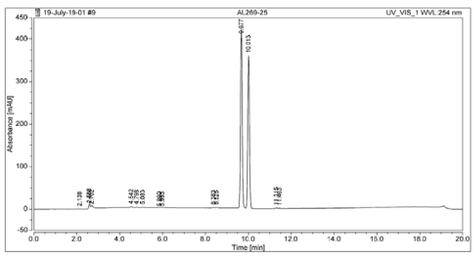


Figure. 2. UHPLC of G Morpholinophosphoramidate, Purity 100%

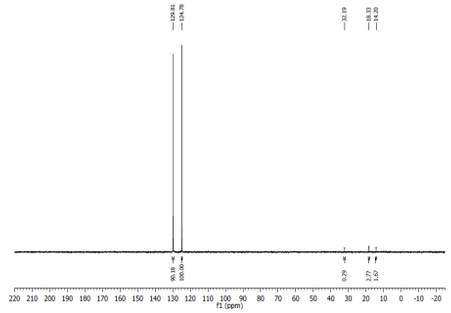


Fig. 3. 31^{P}-NMR of G Morpholinophosphoramidate, purity100%

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Morpholino Amidates

Application of Morpholino oligos and their therapeutic potentials:

Morpholino oligos are specific, soluble, non-toxic, stable, and effective antisense oligonucleotide suitable for development as therapeutics and currently in clinical trials. Efficacy of Morpholino oligos in humans has been shown in clinical trials for Duchenne muscular dystrophy. The splice modifying Morpholino eteplirsen has partially restored function to the dystrophin protein, enough to show significant clinical benefit on a six-minute walk test versus the untreated control group.

Blocking translation- Morpholinos can bind to the 5'-untranslated region of messenger RNA (mRNA), and can interfere with progression of the ribosomal initiation complex from the 5' cap to the start codon.

Modifying pre-mRNA splicing- Morpholinos can prevent splice-directing small nuclear ribonucleoproteins (snRNP) complexes from binding introns of pre-mRNA, blocking the splice lariat structure, interfering with the binding of splice regulatory proteins such as splice silencers[1] and splice enhancers [2] there by interfering with pre-mRNA processing steps.

Morpholinos can block miRNA activity [3][4] and maturation.[5] Fluorescein-tagged Morpholinos along with fluorescein-specific antibodies that could be used as probes for in-situ hybridization to miRNAs [6] Morpholinos can also block ribozyme activity .[7]

Gene knockdown by morpholino- The morpholino-modified antisense oligonucleotides are primarily used in animal embryonic systems for the 'knock-down' of gene function

Intron retention using RNA-targeting thiomorpholino antisense oligonucleotides.[8]

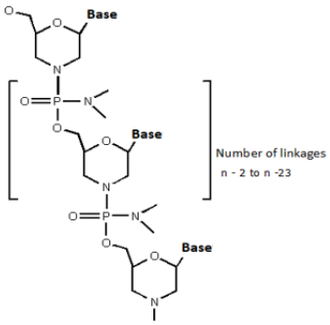

Figure 4. The Synthesis of Morpholinophosphoramidate Oligonucleotides

References:

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12. Guide for Morpholino Users: Toward Therapeutics J Drug Discov Develop and Deliv. 2016; 3(2): 1023. Gene Tools, LLC, USA *Corresponding author: Moulton JD, Gene Tools, LLC, 1001 Summerton Way, Philomath, Oregon 97370, USA.

The subject products are available from ChemGenes Corp., thanks to a license agreement for Morpholino Oligonucleotide Synthesis Technology developed by University of Colorado, Boulder (10)(11).