Oligo Modifications

Nuclease Resistance Introduction

Like cellular DNA and RNA, synthetic oligonucleotides are prone to degradation once introduced into the cell or body fluids. Such degradation is due to the ubiquitous presence of nuclease enzymes (both exonucleases and endonucleases), as well as chemical instability (particularly for RNA). Under normal cellular conditions, this leads to fast in vivo degradation of oligos and a short half-life (1). In addition, the ease with which RNAse, being very stable, can contaminate laboratory equipment and benchtop surfaces means that RNA is susceptible to degradation under normal laboratory conditions as well. To reduce or eliminate this susceptibility, nuclease-resistant modifications (for example, phosphorothiolation or 2'-OMethyl RNA bases) can be introduced into oligonucleotides slated for in vivo and/or regular benchtop work.

Nuclease Resistance Design Protocols

Nuclease Resistant Oligos for In vivo Applications and Design Considerations

While oligonucleotides are quickly degraded (typically within 15-30 minutes) by nucleases in both in vitro and in vivo contexts, the need to incorporate nuclease resistance into oligonucleotides is critically important for in vivo applications. Within serum or the cell, oligonucleotides can be degraded by both endo- and exonucleases. In serum, the 3'-exonucleases are of greatest concern (7), while within the cell, both 3'- and 5'-exonucleases are problematic (8). Endonucleases can also be an issue in those cases where the oligo contains a restriction site.

Based on the above, designing a nuclease-resistant oligonucleotide for in vivo applications primarily involves modifying it so as to protect it from exonucleases, while minimizing potential deleterious side-effects (such as reduced duplex stability, increased toxicity, or induction of off-target biological effects). The simplest and most cost-effective way to do this is to design the oligo as a 'gapmer', in which the linkages of the three end-most 5'- and 3'-bases are phosphorothiolated, with the remaining bases in the middle having native phosphorodiester linkages. Such phosphorothiolated 'gapmers' are highly resistant to both 5'- and 3'-exonuclease degradation. In addition, because phosphorothiolation lowers the binding affinity of the oligo for its target (Tm of the oligo-target duplex is lowered between 0.5C and 1.5C per linkage, depending on sequence), use of only six such linkages often yields an acceptable balance between nuclease resistance and binding affinity (if increased binding affinity is required, other modifications can also be incorporated into the oligo, such as 2'-fluoro pyrimidines, 2'-O-methyl RNA bases, or C5-propyne pyrimidines). Finally, since large numbers of phosphorothiolate linkages can be toxic (due to the presence of sulfur), using only a small number of such linkages in an oligo minimizes cellular toxicity.

If phosphorothiolation is not desired, other modifications can be used. One option is to use methylphosphonates instead of phosphorothiolation for the 5'- and 3'-end positions of the 'gapmer'. Methylphosphonates lower an oligo's binding affinity more than phosphorothiolation, however, so the use of additional modifications, such as 2'-fluoro-pyrimidines, is advisable to counteract this effect. More commonly, the substitution of 2'-O-methyl RNA bases at some or all positions of an oligo is used as an alternative to phosphorothiolation. Since the nuclease resistance conferred by 2'-O-methyl RNA lies between that of standard bases (no resistance) and phosphorothiolation (highly resistant), extensive/complete 2'-O-methylation is frequently chosen when a high level of nuclease resistance is required. 2'-O-methylation also confers higher binding affinity (that is, higher duplex Tm) to the oligo for its target, a desirable property, in many cases.

Nuclease Resistance Applications

For antisense or RNAi applications, incorporation of modifications conferring nuclease resistance is essentially indispensable and such modifications are used intensely. The most popular modification used for this purpose is phosphorothiolation, in which a phosphodiester backbone linkage is replaced by a phosphothiolate linkage. Such linkages are highly resistant to nuclease degradation, but they also lower duplex stability by about 0.5C per phosphorothioate linkage. However, judicious use of this modification (for example, placing them only at the three endmost bases of each end of the oligo to minimize exonuclease degradation) can produce excellent nuclease resistance while still maintaining reasonably good duplex stability (2). 2'-O Methyl (or other 2'-O-substituted) RNA bases also confer nuclease resistance to an oligo, and have the added benefit of increasing duplex stability as well (3,4). However, duplexes formed between oligos having 2'-OMethyl bases at all positions and RNA are incapable of activating RNase H activity (3), and this fact must be kept in mind if the user wishes to use such oligos for antisense applications. Recently, "mirror-image" (L)-nucleotide base phosphoramidites have become available as well. Oligonucleotides containing (L)-nucleotides are completely immune to nuclease attack at the incorporated positions (5). While (L)-nucleotides also do not base pair with natural (D)-nucleotides (6), they still could potentially be incorporated in, for example, the stems of molecular beacons to protect them from degradation by exonucleases.

References

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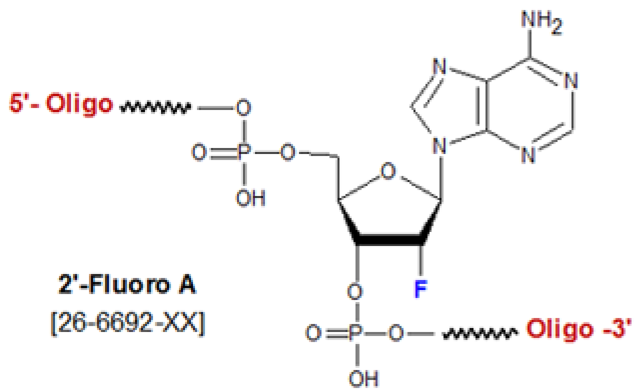
Modificaton Code List

Modification	Code	Catalog Number
2'-Fluoro deoxyadenosine (2'-F-A)	[fA]	26-6692
2'-Fluoro deoxycytosine (2'-F-C)	[fC]	26-6463
2'-Fluoro deoxyguanosine (2'-F-G)	[fG]	26-6693
2'-Fluoro deoxyuridine (2'-F-U)	[fU]	26-6462
2'-O methyl adenosine A	[mA]	27-6410A
2'-O methyl cytosine C	[mC]	27-6410C
2'-O methyl guanosine G	[mG]	27-6410G
2'-O methyl uridine U	[mU]	27-6410U
3'-dA (2'-5' linked)	[3dA2-5]	26-6490
3'-dC (2'-5' linked)	[3dC2-5]	26-6491
3'-dG (2'-5' linked)	[3dG2-5]	26-6492
3'-dT (2'-5' linked)	[3dT2-5]	26-6493
3'-O methyl bases (2'-5' linked)	[3OmN]	27-6458N
3'-O methyl rA (2'-5' linked)	[3OmA]	27-6458A
3'-O methyl rC (2'-5' linked)	[3OmC]	27-6458C
3'-O methyl rG (2'-5' linked)	[3OmG]	27-6458G
3'-O methyl rU (2'-5' linked)	[3OmU]	27-6458U
3'-rA (2'-5' linked)	[3rA2-5]	26-6682
3'-rC (2'-5' linked)	[3rC2-5]	26-6911
3'-rG (2'-5' linked)	[3rG2-5]	26-6912

3'-rU (2'-5' linked)	[3rU2-5]	26-6913
L-DNA dA (beta L)	[L-dA]	26-6941
L-DNA dC (beta L)	[L-dC]	26-6942
L-DNA dG (beta L)	[L-dG]	26-6943
L-DNA dT (beta L)	[L-dT]	26-6944
L-RNA rA	[L-rA]	27-6941
L-RNA rC	[L-rC]	27-6942
L-RNA rG	[L-rG]	27-6943
L-RNA rU	[L-rU]	27-6944
Ethoxy Phosphate dA	[EoP-dA]	26-6641A
Ethoxy Phosphate dC	[EoP-dC]	26-6641C
Ethoxy Phosphate dG	[EoP-dG]	26-6641G
Ethoxy Phosphate dT	[EoP-dT]	26-6641T
Methoxy Phosphate dA	[MoP-dA]	26-6642A
Methoxy Phosphate dC	[MoP-dC]	26-6642C
Methoxy Phosphate dG	[MoP-dG]	26-6642G
Methoxy Phosphate dT	[MoP-dT]	26-6642T
Phosphorothioate [Ps]	[Ps]	26-6401
propyne dC	[pdC]	26-6501
propyne dU	[pdU]	26-6502

2'-F-A

Category	Nuclease Resistance
Modification Code	fA
Reference Catalog Number	26-6692
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	331.2



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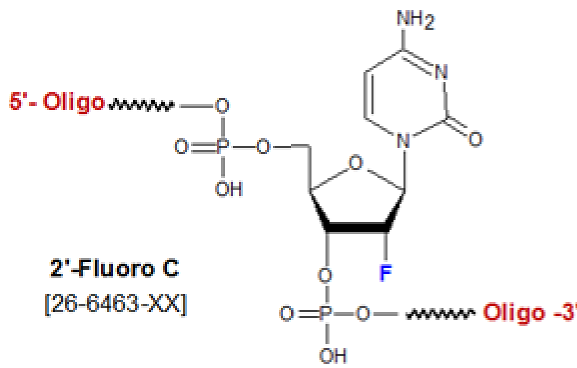
2'-F-C

Category	Nuclease Resistance
Modification Code	fC
Reference Catalog Number	26-6463
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	307.17



2'-Fluoro C
[26-6463-XX]

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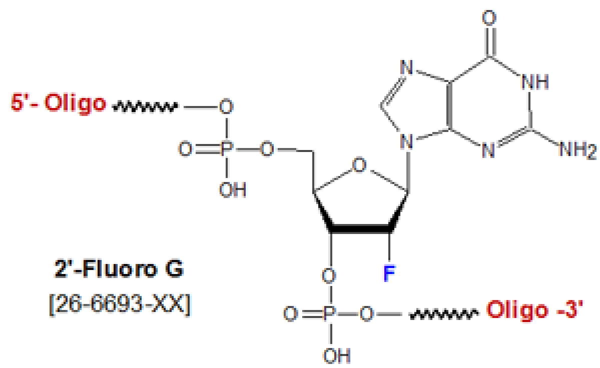
2'-F-G

Category	Nuclease Resistance
Modification Code	fG
Reference Catalog Number	26-6693
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	347.16



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[26-6693-XX]

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2'-F-U

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Modification Code	fU
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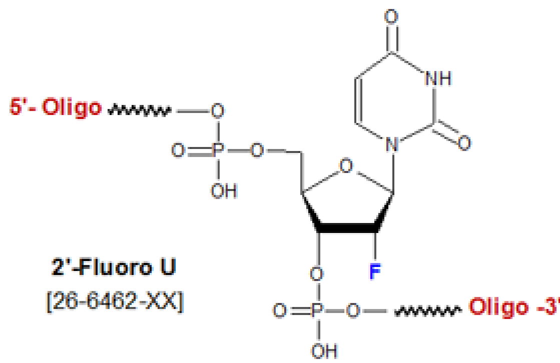
3 Prime	Y
Internal	Y
Molecular Weight(mw)	308.16



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REFERENCES:

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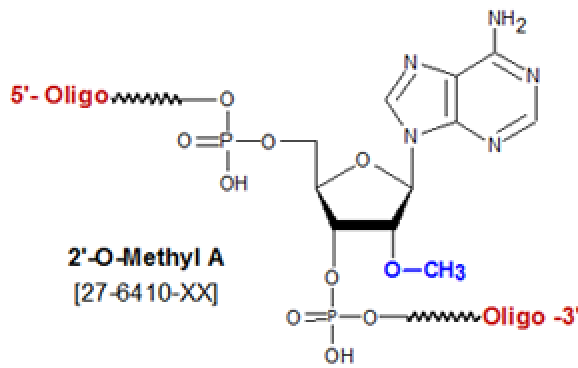
5. Allerson, C.R.; et al. Fully 2'-modified oligonucleotide duplexes with improved in vitro potency and stability compared to unmodified small interfering RNA. *Journal of Medicinal Chemistry* (2005), **48**: 901-904.

2'-O methyl A

Category	Nuclease Resistance
Modification Code	mA
Reference Catalog Number	27-6410A
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	343.24



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Modification

Duplex Stability [Tm Increase]

Nuclease Resistance Locked Analog Bases Increased [2- 4C per substitution] Increased 2-Amino-dA Increased [3.0C per substitution] Similar to DNA C-5 propynyl-C Increased [2.8C per substitution] Increased C-5 propynyl-U Increased [1.7C per substitution] Increased 2'-Fluoro Increased [1.8C per substitution] Increased 5-Methyl-dC Increased [1.3C per substitution] Similar to DNA 2'-O Methyl Increased Increased Phosphorothioate Slightly decreased Increased

genelink.com/oligo_modifications_reference/OMR_mod_category_intro.asp?mod_sp_cat_id=19 >Click here for complete list of duplex stability modifications

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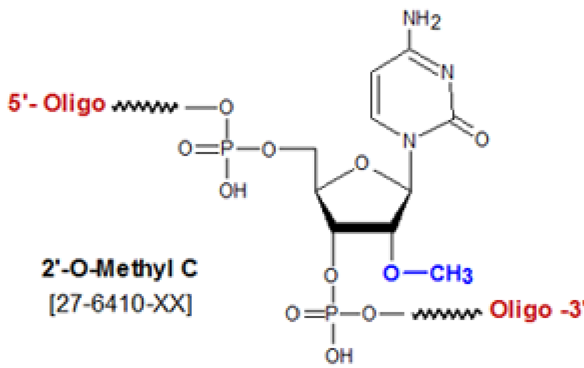
2'-O methyl C

Category	Nucleases Resistance
Modification Code	mC
Reference Catalog Number	27-6410C
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	319.21



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genelink.com/oligo_modifications_reference/OMR_mod_category_intro.asp?mod_sp_cat_id=19 >Click here for complete list of duplex stability modifications

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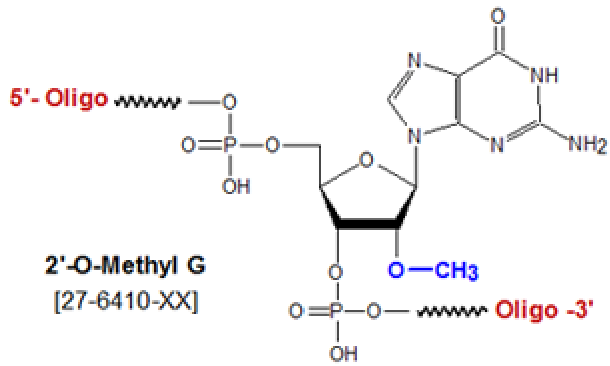
2'-O methyl G

Category	Nuclease Resistance
Modification Code	mG
Reference Catalog Number	27-6410G
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	359.24



2'-O-Methyl G
[27-6410-XX]

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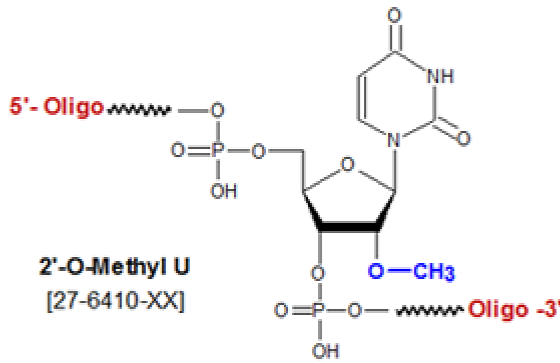
2'-O methyl U

Category	Nuclease Resistance
Modification Code	mU
Reference Catalog Number	27-6410U
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	320.2



2'-O-Methyl U
[27-6410-XX]

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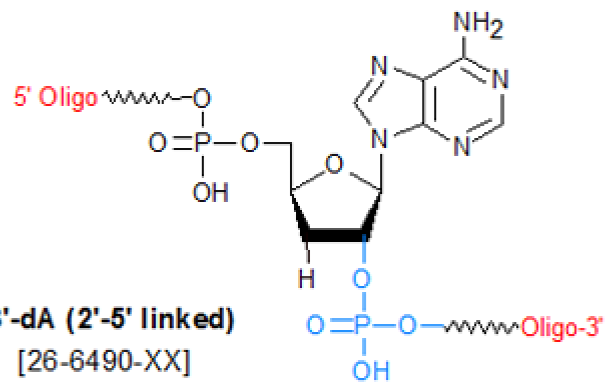
3'-dA (2'-5' linked)

Category	Antisense
Modification Code	3dA2-5
Reference Catalog Number	26-6490
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	313.21



3'-dA (2'-5' linked)
[26-6490-XX]

3'-deoxy bases (2'-5' linked) are deoxy at the 3' position of the ribose, instead of at the usual 2'-position (**note: All four deoxy and ribo versions the 2'-5' linked A, C, G and T or U are available from Gene Link**). 3'-deoxynucleotide (2',5'-linked) modifications are used to substitute 2'-5' phosphodiester linkages for the usual 3'-5' phosphodiester linkages at some or all positions of an oligo. Oligonucleotides containing all, or primarily, 2',5'-phosphodiester linkages selectively bind to complementary single-stranded 3',5'-RNA over comparable 3,5'-DNA (1,2). This property means that DNA oligos containing such linkages could be useful in either anti-sense applications or as ssRNA-specific probes.

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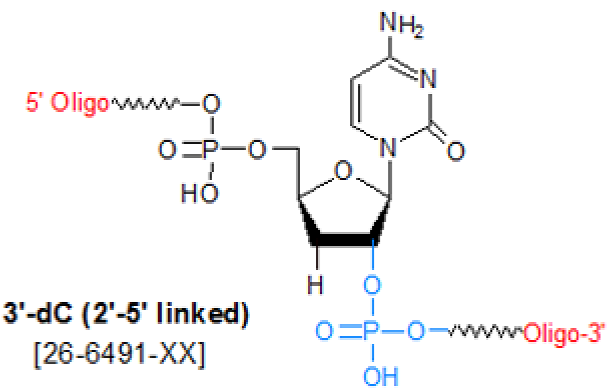
3. Sinha, S.; Kim, P.H.; Switzer, C. 2,5-Linked DNA Is a Template for Polymerase-Directed DNA Synthesis. *J. Am. Chem. Soc.* (2004), **126**: 3310-3317.

3'-dC (2'-5' linked)

Category	Antisense
Modification Code	3dC2-5
Reference Catalog Number	26-6491
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	289.18



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3'-dG (2'-5' linked)

Category	Antisense
Modification Code	3dG2-5
Reference Catalog Number	26-6492
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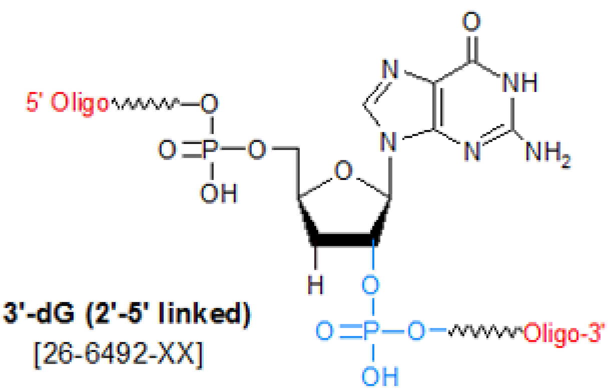
3 Prime	Y
Internal	Y
Molecular Weight(mw)	329.21



3'-dG (2'-5' linked)
[26-6492-XX]

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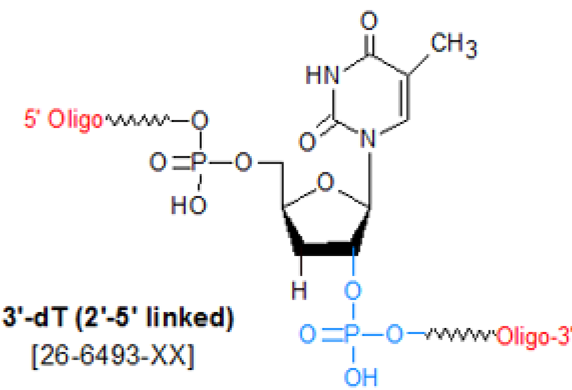
3'-dT (2'-5' linked)

Category	Antisense
Modification Code	3dT2-5
Reference Catalog Number	26-6493
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	304.2



3'-dT (2'-5' linked)
[26-6493-XX]

3'-deoxy bases (2'-5' linked) are deoxy at the 3' position of the ribose, instead of at the usual 2'-position (**note: All four deoxy and ribo versions the 2'-5' linked A, C, G and T or U are available from Gene Link**). 3'-deoxynucleotide (2',5'-linked) modifications are used to substitute 2'-5' phosphodiester linkages for the usual 3'-5' phosphodiester linkages at some or all positions of an oligo. Oligonucleotides containing all, or primarily, 2',5'-phosphodiester linkages selectively bind to complementary single-stranded 3',5'-RNA over comparable 3,5'-DNA (1,2). This property means that DNA oligos containing such linkages could be useful in either anti-sense applications or as ssRNA-specific probes.

Bhan *et al.* (2) studied the potential for 2',5'-linked DNA oligos as anti-sense molecules. High selectivity for 3',5' RNA over 3',5' DNA was observed, presumably due to the 2',5'-linkages destabilizing duplexes formed with 3',5' DNA more than those formed with 3',5'-RNA (for 2',5' DNA:3',5' RNA duplexes, Delta Tm is only about ~0.5 deg C per 2',5' linkage substitution). Phosphorothiolation (which confers nuclease resistance) of 2'-5' linkages lowers the Tm of 2',5' DNA:3',5' RNA duplexes even less, ~ 0.2 deg C per phosphorothiolated 2, '5'-linkage substitution. (by contrast, phosphorothiolation of a 3',5' linkage lowers the Tm of 3',5' DNA:RNA duplexes by 0.5 to 2.0 degC). Thus, 2',5'-linked DNA oligos show both high selectivity and good duplex stability for RNA target sequences. However, 2',5'-linked DNA oligos, whether phosphorothiolated or not, do not support RNAse H activity when bound to complementary RNA. But, substitution of six or seven contiguous 3',5' phosphorothiolate linkages into a 2',5' phosphorothiolated oligo at an appropriate place (that is, making a 2',5'/3',5' phosphorothiolated chimera restores the oligo's ability to support RNAse H activity. Furthermore, 2',5'-linked DNA oligos, whether phosphorothiolated or not, show little or no non-sequence specific binding to cellular proteins (by contrast, 3',5' DNA oligos show considerable levels of such binding.

In summary, this research suggests that 2',5'/3',5' phosphorothiolated chimeric oligos, in which 6-7 of the linkages are 3',5' to ensure that it can support RNAse H activity, have considerable potential as anti-sense reagents, due to their high selectivity for complementary RNA targets, and minimal non-sequence specific binding to cellular proteins.

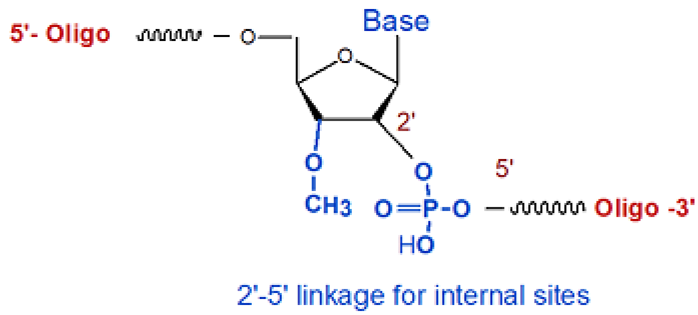
In 2004, Sinha and co-workers showed that 2',5'-linked DNA has some capability to function as a template for polymerase-directed DNA synthesis of the complementary strand (3).

The authors showed several polymerases, and HIV reverse transcriptase, can successfully use a string of 2-4 2',5'-linked DNA nucleotides as a template to synthesize its complementary strand with high fidelity, and speculated that the polymerases were serving as a "template for the template", i.e., compensating for structural deficiencies in the 2',5'-linked DNA that, in non-enzymatic contexts, would preclude genetic information transfer for 2',5'-linked DNA. **References**

1. Giannaris, P.A.; Damha, M.J. Oligoribonucleotides containing 2',5'-phosphodiester linkages exhibit binding selectivity for 3',5'-RNA over 3',5'-ssDNA. *Nucleic Acids Res* (1993), **21**: 4742-4749.
2. Bhan, P.; Bhan, A.; Hong, M.K.; Hartwell, J.G.; Saunders, J.M.; Hoke, G.D. 2',5'-linked oligo-3'-deoxyribonucleoside phosphorothioate chimeras: thermal stability and antisense inhibition of gene expression. *Nucleic Acids Res.* (1997), **25**: 40-41.
3. Sinha, S.; Kim, P.H.; Switzer, C. 2,5-Linked DNA Is a Template for Polymerase-Directed DNA Synthesis. *J. Am. Chem. Soc.* (2004), **126**: 3310-3317.

3'-O methyl bases

Category	Antisense
Modification Code	3OmN
Reference Catalog Number	27-6458N
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	386.55



3'-O-Methyl Base
[27-6458N-XX]

Mixed base N has a setup charge of $250.00 per order.

Antisense Oligos (ODN) & siRNA Oligo Modifications
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3'-O methyl bases (3'-Ome) form a 2'-5' phosphodiester linkage when placed internally. A single 3'-O methyl base modification at the 3' end will have a hydroxyl group at the 2' end and 3'-O methyl at the 3' end, this will prevent the oligo from extension by polymerases.

3'-O methyl bases (3'-Ome)-(2'-5' linked), are used to substitute 2'-5' phosphodiester linkages for the usual 3'-5' phosphodiester linkages at some or all positions of an oligonucleotide. Oligonucleotides containing all, or primarily, 2', 5'- phosphodiester linkages selectively bind to complementary single-stranded 3', 5'- RNA over comparable 3', 5'- DNA. Presumably this selectively is a consequence of the 2', 5'- linkages destabilizing duplexes formed with 3', 5'- DNA more than those formed with 3', 5'-RNA, leading to 2'-5'- RNA:3', 5'- DNA duplexes having much lower Tm than the corresponding 2'-5'- RNA:3'- 5'-RNA duplexes. This property means that RNA oligos containing such linkages could be useful in anti-sense applications, as ssRNA-specific probes, or as ligands for affinity purification of cellular RNA.
Antisense oligonucleotides (ASOs) and small interfering RNA (siRNA) are both recognized therapeutic agents for the silencing of specific genes at the posttranscriptional level. Chemical modifications, particularly 2'-O-(2-Methoxyethyl)-oligoribonucleotides (2'-O-MOE bases) and 2'-OMethyl bases are commonly used to confer nuclease resistance to an oligo designed for anti-sense, siRNA or aptamer-based research, diagnostic or therapeutic purposes, when specific 2'-OH is not required.
Nuclease resistance can be further enhanced by phosphorothiolation of appropriate phosphodiester linkages within the oligo. These modifications confers nuclease resistance, high binding affinity towards complementary RNA, reduced unspecific protein binding and extended half-life in tissues.
Gapmers. Currently, the mainstream of the ASO is gapmer design ASOs. Gapmer design oligonucleotides, contain two to five chemically modified nucleotides (LNA, 2'-O methyl or 2'-O-MOE RNA) as 'wings' at each terminus flanking a central 5- to 10-base 'gap' of DNA, enable cleavage of the target mRNA by RNase H, which recognizes DNA/RNA heteroduplexes.

Usually all the phosphodiester linkages are converted to phosphorothioate.

Delivery. The development of effective delivery systems for antisense oligonucleotides is essential for their clinical therapeutic application. The most common delivery system involves a relatively hydrophobic molecule that can cross the lipid membrane. The following list of modifications are suitable for delivery system in addition to cell penetrating peptides.

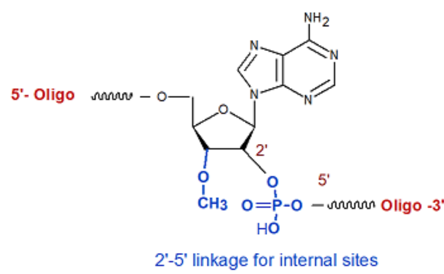
Cholesterol

Tocopherol (alpha-tocopherol, a natural isomer of vitamin E)

PEG

3'-O methyl rA

Category	Antisense
Modification Code	3OmA
Reference Catalog Number	27-6458A
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	343.24



3'-O-Methyl A
[27-6458A-XX]

Antisense Oligos (ODN) & siRNA Oligo Modifications
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3'-O methyl bases (3'-Ome) form a 2'-5' phosphodiester linkage when placed internally. A single 3'-O methyl base modification at the 3' end will have a hydroxyl group at the 2' end and 3'-O methyl at the 3' end, this will prevent the oligo from extension by polymerases.

3'-O methyl bases (3'-Ome)-(2'-5' linked), are used to substitute 2'-5' phosphodiester linkages for the usual 3'-5' phosphodiester linkages at some or all positions of an oligonucleotide. Oligonucleotides containing all, or primarily, 2', 5'-phosphodiester linkages selectively bind to complementary single-stranded 3', 5'- RNA over comparable 3', 5'- DNA. Presumably this selectively is a consequence of the 2', 5'- linkages destabilizing duplexes formed with 3', 5'- DNA more than those formed with 3', 5'-RNA, leading to 2'-5'- RNA:3', 5'- DNA duplexes having much lower Tm than the corresponding 2'-5'-RNA:3'- 5'-RNA duplexes. This property means that RNA oligos containing such linkages could be useful in anti-sense applications, as ssRNA-specific probes, or as ligands for affinity purification of cellular RNA.
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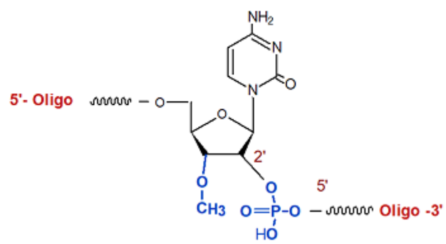
Cholesterol
Tocopherol (alpha-tocopherol, a natural isomer of vitamin E)
PEG

3'-O methyl rC

Category	Antisense
Modification Code	3OmC
Reference Catalog Number	27-6458C
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	319.21



3'-O-Methyl C
[27-6458C-XX]

Antisense Oligos (ODN) & siRNA Oligo Modifications
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3'-O methyl bases (3'-Ome) form a 2'-5' phosphodiester linkage when placed internally. A single 3'-O methyl base modification at the 3' end will have a hydroxyl group at the 2' end and 3'-O methyl at the 3' end, this will prevent the oligo from extension by polymerases.

3'-O methyl bases (3'-Ome)-(2'-5' linked), are used to substitute 2'-5' phosphodiester linkages for the usual 3'-5' phosphodiester linkages at some or all positions of an oligonucleotide. Oligonucleotides containing all, or primarily, 2', 5'-phosphodiester linkages selectively bind to complementary single-stranded 3', 5'- RNA over comparable 3', 5'- DNA. Presumably this selectively is a consequence of the 2', 5'- linkages destabilizing duplexes formed with 3', 5'- DNA more than those formed with 3', 5'-RNA, leading to 2'-5'- RNA:3', 5'- DNA duplexes having much lower Tm than the corresponding 2'-5'-RNA:3'- 5'-RNA duplexes. This property means that RNA oligos containing such linkages could be useful in anti-sense applications, as ssRNA-specific probes, or as ligands for affinity purification of cellular RNA.
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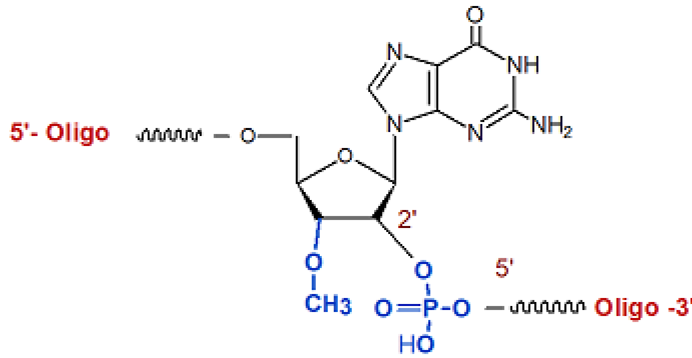
Cholesterol

Tocopherol (alpha-tocopherol, a natural isomer of vitamin E)

PEG

3'-O methyl rG

Category	Antisense
Modification Code	3OmG
Reference Catalog Number	27-6458G
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	359.24



2'-5' linkage for internal sites

3'-O-Methyl G

[27-6458G-XX]

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3'-O methyl bases (3'-Ome)-(2'-5' linked), are used to substitute 2'-5' phosphodiester linkages for the usual 3'-5' phosphodiester linkages at some or all positions of an oligonucleotide. Oligonucleotides containing all, or primarily, 2', 5'-phosphodiester linkages selectively bind to complementary single-stranded 3', 5'- RNA over comparable 3', 5'- DNA. Presumably this selectively is a consequence of the 2', 5'- linkages destabilizing duplexes formed with 3', 5'- DNA more than those formed with 3', 5'-RNA, leading to 2'-5'- RNA:3', 5'- DNA duplexes having much lower Tm than the corresponding 2'-5'-RNA:3'- 5'-RNA duplexes. This property means that RNA oligos containing such linkages could be useful in anti-sense applications, as ssRNA-specific probes, or as ligands for affinity purification of cellular RNA.
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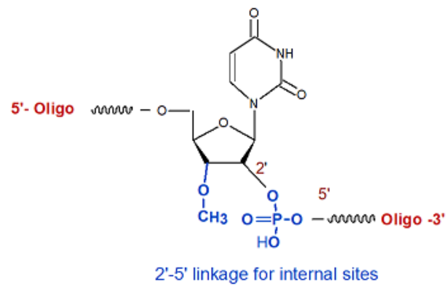
Tocopherol (alpha-tocopherol, a natural isomer of vitamin E)

PEG

3'-O methyl rU

Category	Antisense
Modification Code	3OmU
Reference Catalog Number	27-6458U
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	320.2



3'-O-Methyl U
[27-6458U-XX]

Antisense Oligos (ODN) & siRNA Oligo Modifications
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3'-O methyl bases (3'-Ome) form a 2'-5' phosphodiester linkage when placed internally. A single 3'-O methyl base modification at the 3' end will have a hydroxyl group at the 2' end and 3'-O methyl at the 3' end, this will prevent the oligo from extension by polymerases.

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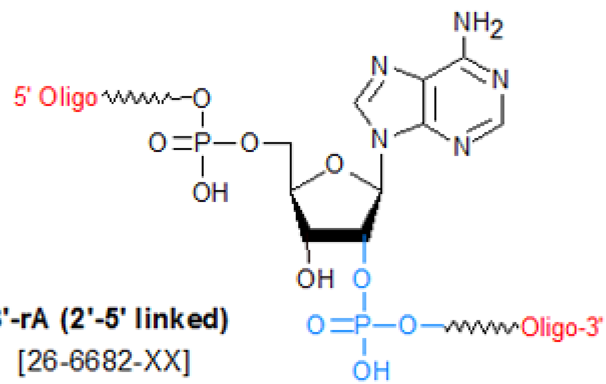
Cholesterol
Tocopherol (alpha-tocopherol, a natural isomer of vitamin E)
PEG

3'-rA (2'-5' linked)

Category	Minor Bases
Modification Code	3rA2-5
Reference Catalog Number	26-6682
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	329.24



3'-rA (2'-5' linked)
[26-6682-XX]

3'-riboadenosine (3'-rA)-(2'-5' linked), and the other three 3'-ribonucleotide (2',5'-linked) modifications are used to substitute 2'-5' phosphodiester linkages for the usual 3'-5' phosphodiester linkages at some or all positions of an oligonucleotide. Oligonucleotides containing all, or primarily, 2',5'-phosphodiester linkages selectively bind to complementary single-stranded 3',5'-RNA over comparable 3',5'-DNA (1). Presumably this selectively is a consequence of the 2',5'-linkages destabilizing duplexes formed with 3',5'-DNA more than those formed with 3',5'-RNA, leading to 2'5'-RNA:3',5'-DNA duplexes having much lower Tm than the corresponding 2'5'-RNA:3',5'-RNA duplexes. This property means that RNA oligos containing such linkages could be useful in anti-sense applications, as ssRNA-specific probes, or as ligands for affinity purification of cellular RNA.

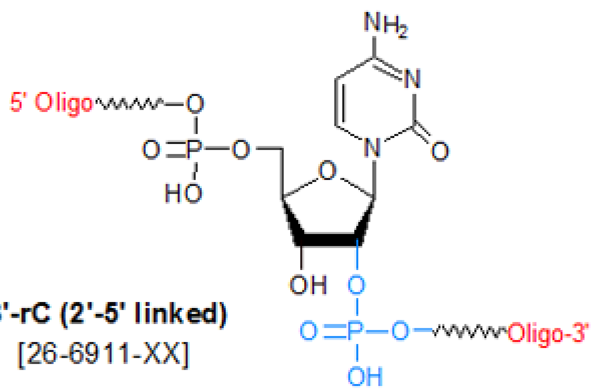
A interesting application of the 3'-rA-(2',5'-linked) modification is as an activator for 2-5A dependent RNAse to direct it to cleave unique RNA sequences (2). In this approach, the 5'-phosphorylated, 2',5'-linked tetramer p5'A2'p5'A2'p5'A2'p5'A (abbreviated "2-5A" as covalently linked to anti-sense oligo, resulting in the chimera (2-5A:AS). The AS sequence of 2-5A:AS bound to a particular ssRNA target sequence, and he 2-5A activator sequence activated 2-5A-dependent RNA, causeing it to cleave the target after UpUp and UpA motifs. Selectively targeted destruction of ssRNA in vivo via this approach has potential applications for therapeutic control of gene expression in such diseases as cancer, viral infections, and certain genetic disorders. **References**

1. Giannaris, P.A.; Damha, M.J. Oligoribonucleotides containing 2',5'-phosphodiester linkages exhibit binding selectivity for 3',5'-RNA over 3',5'-ssDNA. *Nucleic Acids Res* (1993), **21**: 4742-4749.
2. Torrence, P.F.; Maitra, R.K.; Lesiak, K.; Khamnei, S.; Zhou, A.; Silverman, R.H. Targeting RNA for degradation with a (2'-5') oligoadenylate-antisense chimera. *Proc. Natl. Acad. Sci. USA* (1992), **90**: 1300-1304.

Gene Link™

3'-rC (2'-5' linked)

Category	Minor Bases
Modification Code	3rC2-5
Reference Catalog Number	26-6911
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	305.18



3'-rC (2'-5' linked)
[26-6911-XX]

3'-ribocytidine (3'-rC)-(2'-5' linked), and the other three 3'-ribonucleotide (2',5'-linked) modifications are used to substitute 2'-5' phosphodiester linkages for the usual 3'-5' phosphodiester linkages at some or all positions of an oligonucleotide. Oligonucleotides containing all, or primarily, 2',5'-phosphodiester linkages selectively bind to complementary single-stranded 3',5'-RNA over comparable 3',5'-DNA (1). Presumably this selectively is a consequence of the 2',5'-linkages destabilizing duplexes formed with 3',5'-DNA more than those formed with 3',5'-RNA, leading to 2'5'-RNA:3',5'-DNA duplexes having much lower Tm than the corresponding 2'5'-RNA:3',5'-RNA duplexes. This property means that RNA oligos containing such linkages could be useful in anti-sense applications, as ssRNA-specific probes, or as ligands for affinity purification of cellular RNA.

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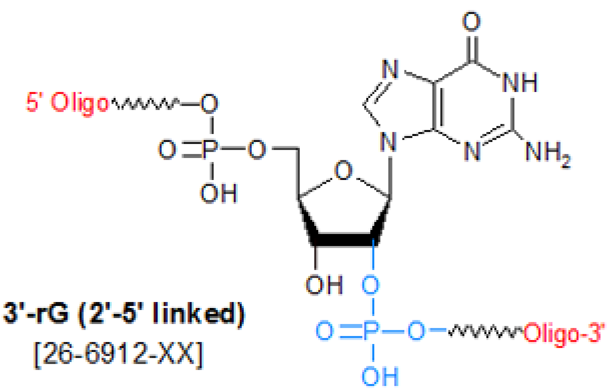
2. Torrence, P.F.; Maitra, R.K.; Lesiak, K.; Khamnei, S.; Zhou, A.; Silverman, R.H. Targeting RNA for degradation with a (2'-5') oligoadenylate-antisense chimera. *Proc. Natl. Acad. Sci. USA* (1992), **90**: 1300-1304.

3'-rG (2'-5' linked)

Category	Minor Bases
Modification Code	3rG2-5
Reference Catalog Number	26-6912
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	345.21



3'-rG (2'-5' linked)
[26-6912-XX]

3'-riboguanosine(3'-rG)-(2'-5' linked), and the other three 3'-ribonucleotide (2',5'-linked) modifications are used to substitute 2'-5' phosphodiester linkages for the usual 3'-5' phosphodiester linkages at some or all positions of an oligonucleotide. Oligonucleotides containing all, or primarily, 2',5'-phosphodiester linkages selectively bind to complementary single-stranded 3',5'-RNA over comparable 3',5'-DNA (1). Presumably this selectively is a consequence of the 2',5'-linkages destabilizing duplexes formed with 3',5'-DNA more than those formed with 3',5'-RNA, leading to 2'5'-RNA:3',5'-DNA duplexes having much lower Tm than the corresponding 2'5'-RNA:3',5'-RNA duplexes. This property means that RNA oligos containing such linkages could be useful in anti-sense applications, as ssRNA-specific probes, or as ligands for affinity purification of cellular RNA.

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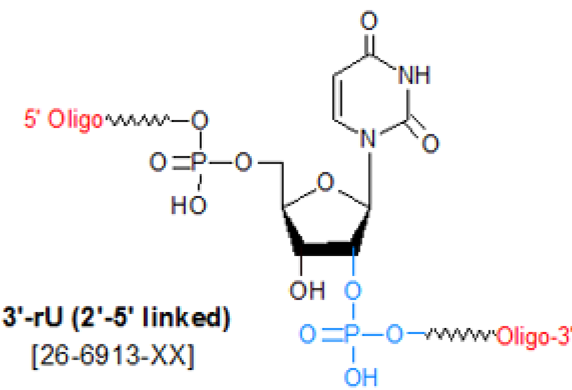
3'-rU (2'-5' linked)

Category	Minor Bases
Modification Code	3rU2-5
Reference Catalog Number	26-6913
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	306.17



3'-rU (2'-5' linked)
[26-6913-XX]

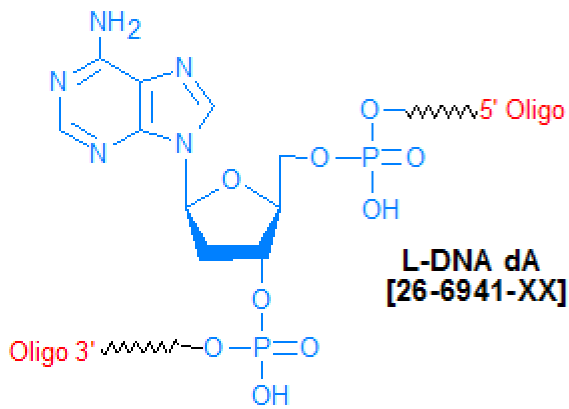
3'-ribouridine (3'-rU)-(2'-5' linked), and the other three 3'-ribonucleotide (2',5'-linked) modifications are used to substitute 2'-5' phosphodiester linkages for the usual 3'-5' phosphodiester linkages at some or all positions of an oligonucleotide. Oligonucleotides containing all, or primarily, 2',5'-phosphodiester linkages selectively bind to complementary single-stranded 3',5'-RNA over comparable 3',5'-DNA (1). Presumably this selectively is a consequence of the 2',5'-linkages destabilizing duplexes formed with 3',5'-DNA more than those formed with 3',5'-RNA, leading to 2'5'-RNA:3',5'-DNA duplexes having much lower Tm than the corresponding 2'5'-RNA:3',5'-RNA duplexes. This property means that RNA oligos containing such linkages could be useful in anti-sense applications, as ssRNA-specific probes, or as ligands for affinity purification of cellular RNA.

A interesting application of the 3'-rA-(2',5'-linked) modification is as an activator for 2-5A dependent RNAse to direct it to cleave unique RNA sequences (2). In this approach, the 5'-phosphorylated, 2',5'-linked tetramer p5'A2'p5'A2'p5'A2'p5'A (abbreviated "2-5A" as covalently linked to anti-sense oligo, resulting in the chimera (2-5A:AS). The AS sequence of 2-5A:AS bound to a particular ssRNA target sequence, and he 2-5A activator sequence activated 2-5A-dependent RNA, causeing it to cleave the target after UpUp and UpA motifs. Selectively targeted destruction of ssRNA in vivo via this approach has potential applications for therapeutic control of gene expression in such diseases as cancer, viral infections, and certain genetic disorders. **References**

1. Giannaris, P.A.; Damha, M.J. Oligoribonucleotides containing 2',5'-phosphodiester linkages exhibit binding selectivity for 3',5'-RNA over 3',5'-ssDNA. *Nucleic Acids Res* (1993), **21**: 4742-4749.
2. Torrence, P.F.; Maitra, R.K.; Lesiak, K.; Khamnei, S.; Zhou, A.; Silverman, R.H. Targeting RNA for degradation with a (2'-5') oligoadenylate-antisense chimera. *Proc. Natl. Acad. Sci. USA* (1992), **90**: 1300-1304.

L-DNA dA

Category	Others
Modification Code	L-dA
Reference Catalog Number	26-6941
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	313.2



L-DNA (beta stereoisomer deoxyribose that is same as in D-DNA)is the left-turning and mirror image version of natural DNA, as opposed to the naturally occurring right-turning version called D-DNA. L-DNA is more stable than D-DNA to enzymatic degradation by certain nucleases (1). Since the two enantiomers are identical in structure other than their chiral differences, their intrinsic physical properties are generally equal to each other. This includes duplex stability, solubility, and selectivity as D-DNA but form a left-helical double-helix. Because of its chiral difference, L-DNA does not bind to its naturally occurring D-DNA counterpart.

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Gene Link synthesizes L-DNA oligos with any combination of D-DNA bases including fluorescent dyes and all other available modifications.

L-DNA Applications References
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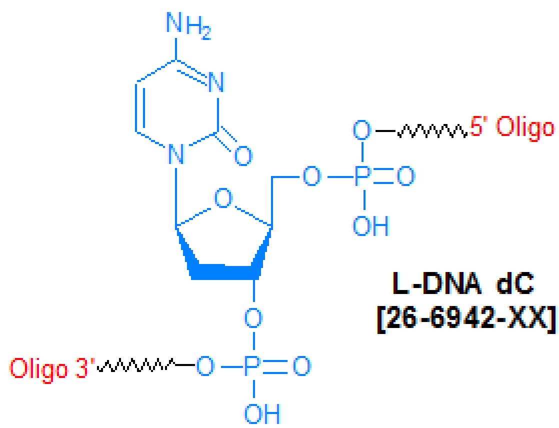
L-DNA dC

Category	Others
Modification Code	L-dC
Reference Catalog Number	26-6942
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	289.19



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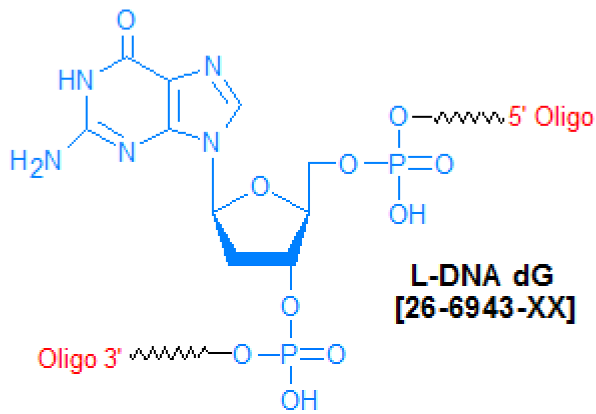
L-DNA dG

Category	Others
Modification Code	L-dG
Reference Catalog Number	26-6943
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	329.21



L-DNA dG
[26-6943-XX]

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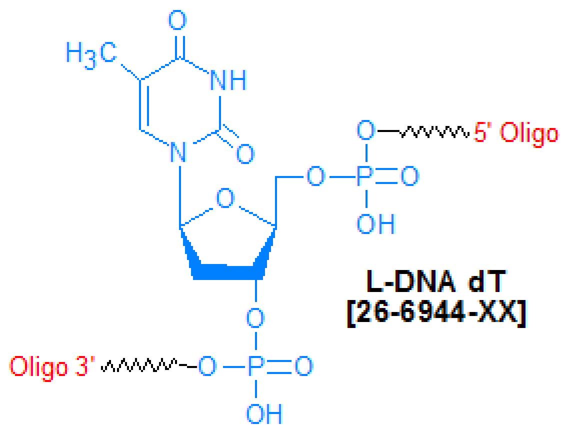
L-DNA dT

Category	Others
Modification Code	L-dT
Reference Catalog Number	26-6944
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	304.2



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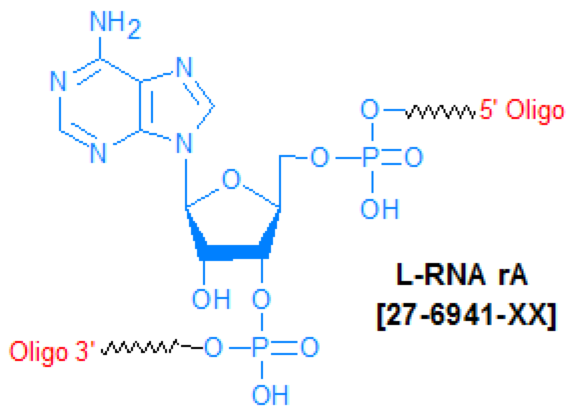
L-RNA rA

Category	Others
Modification Code	L-rA
Reference Catalog Number	27-6941
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	329.2



L-RNA rA
[27-6941-XX]

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L-DNA Applications

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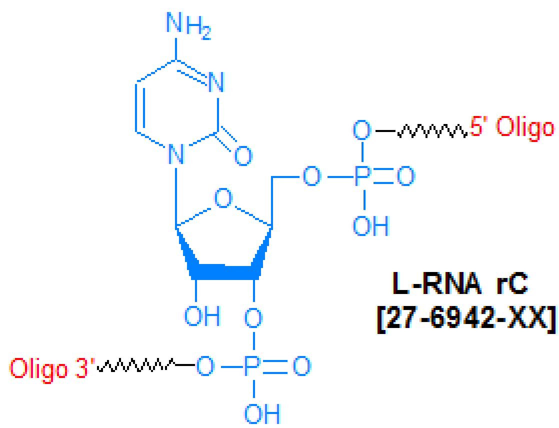
Chem. Sci., 2014,5, 1533-1537

L-RNA rC

Category	Others
Modification Code	L-rC
Reference Catalog Number	27-6942
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	305.19



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L-DNA Applications

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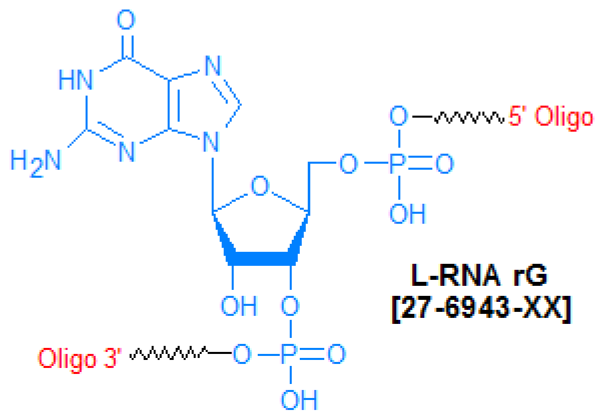
L-RNA rG

Category	Others
Modification Code	L-rG
Reference Catalog Number	27-6943
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	345.21



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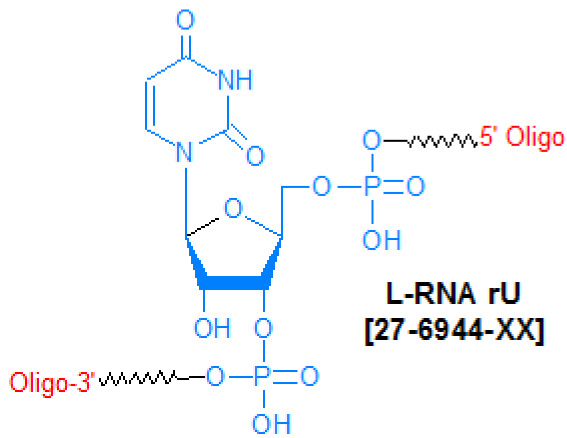
L-RNA rU

Category	Others
Modification Code	L-rU
Reference Catalog Number	27-6944
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	306.17



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L-DNA Applications

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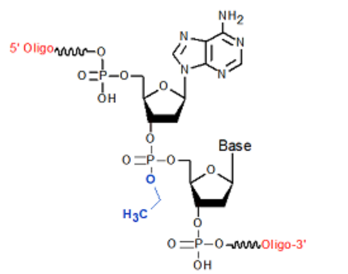
P-Ethoxy dA

Category	Antisense
Modification Code	EoP-dA
Reference Catalog Number	26-6641A
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	341.49



P-Ethoxy dA / Ethoxy Phosphate dA Oligo
[26-6641A-XX]

P-Methoxy (Methoxy Phosphate)[MoP] and P-Ethoxy (Ethoxy Phosphate) [EoP] modification has a setup charge of $250.00 per order for special synthesis reagents.

P-Methoxy (Methoxy Phosphate)[MoP] and P-Ethoxy (Ethoxy Phosphate) [EoP] modified backbone oligos

P-Methoxy (Methoxy Phosphate), P-Ethoxy (Ethoxy Phosphate) and methyl phosphonate [mp] modified backbone oligos makes the phosphodiester linkage neutral charged. The solubility of the oligo in aqueous solutions slowly decreases with increasing modified linkages; consider incorporating as many standard phosphodiester linkages as well in the oligo. Increasing percentage of DMSO from 0.5 to 10% may be used to solubilize the oligo.
These oligonucleotides with neutral backbone displayed high nuclease resistance and improved cellular uptake (1). These are one of the favorable properties of antisense oligonucleotides. In addition to being neutral charge but also impart lipophilic character to the modified oligo.
. Gutierrez-Puente et al (2) used a P-ethoxy oligonucleotide (oligo), 20 bases long and specific for the translation initiation site of human Bcl-2 mRNA. This was incorporated into liposomes to increase its intracellular delivery. This oligo selectively inhibited Bcl-2 protein expression and induced growth inhibition in t(14;18)-positive transformed follicular lymphoma (FL) cell lines. They studied the inhibitory effects of shorter liposomal P-ethoxy oligos (7, 9, 11 or 15 mer) in order to determine the activity of different oligo chain lengths targeted to the same Bcl-2 mRNA. At 12 μM, all the oligos inhibited the growth of a FL cell line. They compared the 7-mer oligo with the 20-mer oligo. The two oligos inhibited Bcl-2 protein expression similarly: 66% and 60% for the 7- and 20-mer, respectively. The uptake and retention of both oligos were also very similar. Their results indicate that the Bcl-2 inhibitory activity is maintained with P-ethoxy antisense oligos ranging from 7 to 20 bases.

P-Methoxy (Methoxy Phosphate), P-Ethoxy (Ethoxy Phosphate) References

1. Roberts, T. C.; Langer, R.; Wood, M. J. A. (2020) Advances in oligonucleotide drug Delivery. Nature Reviews Drug Discovery 19: 673-694.
2. Gutierrez-Puente, Y.; Tari, A.M.; Ford, R.J.; Tamez-Guerra, R.; Mercado-Hernandez, R.; Santoyo-Stephano, M.; Lopez-Berestein, G. (2009) Cellular Pharmacology of P-ethoxy Antisense Oligonucleotides Targeted to Bcl-2 in a Follicular Lymphoma Cell Line.

Leukemia & Lymphoma 44: 1979-1985

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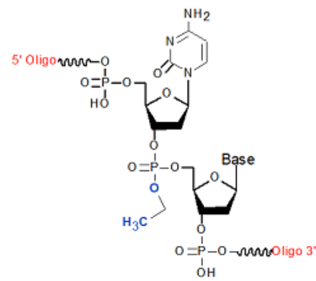
P-Ethoxy dC

Category	Antisense
Modification Code	EoP-dC
Reference Catalog Number	26-6641C
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	303.21



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[26-6641C-XX]

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P-Ethoxy dG

Category	Antisense
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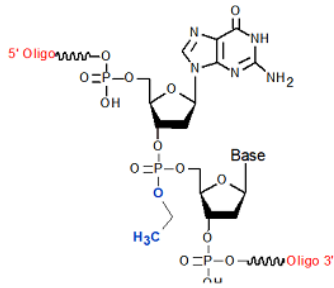
3 Prime	Y
Internal	Y
Molecular Weight(mw)	357.49



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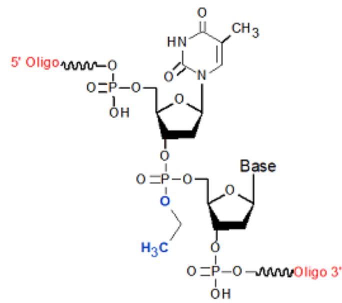
Click this link to view these modifications.

P-Ethoxy dT

Category	Antisense
Modification Code	EoP-dT
Reference Catalog Number	26-6641T
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	332.48



P-Ethoxy dT / Ethoxy Phosphate dT Oligo
[26-6641T-XX]

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Category	Antisense
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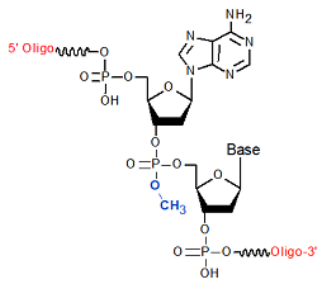
3 Prime	Y
Internal	Y
Molecular Weight(mw)	327.24



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Reference Catalog Number	26-6642C
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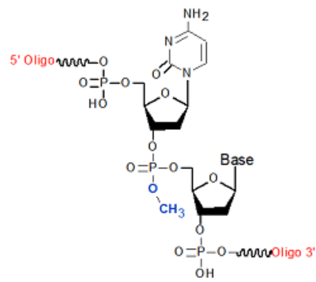
3 Prime	Y
Internal	Y
Molecular Weight(mw)	317.46



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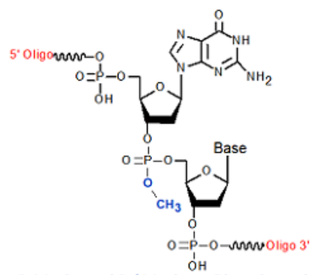
P-Methoxy dG

Category	Antisense
Modification Code	MoP-dG
Reference Catalog Number	26-6642G
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	343.24



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[26-6642G-XX]

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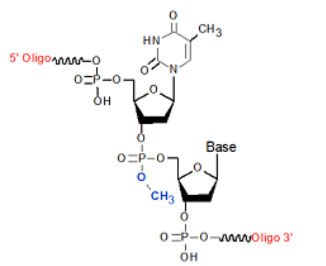
P-Methoxy dT

Category	Antisense
Modification Code	MoP-dT
Reference Catalog Number	26-6642T
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	318.23



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DNA analog in which the mesyl (methanesulfonyl) phosphoramidate group is substituted for the natural phosphodiester group at each internucleotidic position (2-5), the oligomers show significant advantages over the often-used DNA phosphorothioates in RNA binding affinity, nuclease stability, and specificity of their antisense action, which involves activation of cellular RNase H enzyme for hybridization-directed RNA cleavage. Biological activity of the oligonucleotide analog was demonstrated with respect to pro-oncogenic miR-21. A 22-nt anti-miR-21 mesyl phosphoramidate oligodeoxynucleotide specifically decreased the miR-21 level in melanoma B16 cells, induced apoptosis, reduced proliferation, and impeded migration of tumor cells, showing superiority over isosequential phosphorothioate oligodeoxynucleotide in the specificity of its biological effect. Lower overall toxicity compared with phosphorothioate and more efficient activation of RNase H are the key advantages of mesyl phosphoramidate oligonucleotides, which may represent a promising group of antisense therapeutic agents (1).

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3. Chelobanov,B.P., Burakova,E.A., Prokhorova, D.V., Fokina, A.A., Stetsenko,D.A. (2017) New oligodeoxynucleotide derivatives containing N-(methanesulfonyl)-phosphoramidate (mesyl phosphoramidate) internucleotide group. Russ. J. Bioorganic Chem. 43:664-668.
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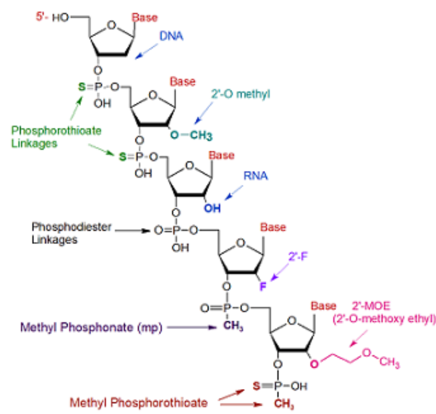
ASO's and siRNA Delivery. The development of effective delivery systems for antisense oligonucleotides is essential for their clinical therapeutic application. The most common delivery system involves a relatively hydrophobic molecule that can cross the lipid membrane. Cholesterol TEG, alpha-Tocopherol TEG (a natural isomer of vitamin E), stearyl and GalNAc modifications have been shown to effective for delivery of ASO's and siRNA in addition to cell penetrating peptides.

Click this link to view these modifications.

Phosphorothioate [Ps]

Category	Antisense
Modification Code	Ps
Reference Catalog Number	26-6401
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	16.06



The code for phosphorothioate linkage has been changed to [Ps] from [*]. Please do not use an asterisk "*" to denote phosphorothioate linkages. Standard phosphodiester linkages does not require a code. Antisense Oligos (ODN) & siRNA Oligo Modifications

Click here for more information on antisense modifications, design & applications.

Minimum Pricing Note that the above pricing for phosphorothioate linkages is for one site only. Minimum charges apply for 15 sites per oligo.

Phosphorothioate Phosphorothioate modification is to the backbone linkage modifying the phosphodiester linkage to phosphorothioate. Replacing one non-bridging oxygen atom with sulfur atom in a DNA phosphodiester linkage creates a phosphorothioate [PS] linkage. This imparts considerable nuclease resistance and is used widely in the design of antisense oligonucleotides (ODN).
An antisense oligonucleotide refers to a short, synthetic DNA or RNA strand that is complementary in sequence to a short target sequence on a particular mRNA strand, which upon specific hybridization to its target induces inhibition of gene expression. The mechanism of inhibition is based on two properties: first, the physical blocking of the translation process by the presence of the short double-stranded region, and second, in the case of antisense DNA, the resulting DNA-RNA duplex is susceptible to cleavage by cellular RNase H activity, which degrades the mRNA and prevents proper translation. The latter property is the classic mode of action for antisense oligos. The former property can be used when it is necessary to design an antisense oligo with certain modifications that result in it not supporting RNase-H activity (1,2).

Phosphorothioate Chiral Rp and Sp Isomers
Modification of the phosphodiester linkage to phosphorothioate by replacing a non-bridging oxygen atom creates additional stereocenters. Each phosphorothioate substitution can be either an 'Sp' or 'Rp' conformation. As such, a fully phosphorothioate 20 nt antisense oligonucleotide will be a mixture of more than half a million different molecules.
Rp and Sp are the two stereoisomers of phosphorothioate [PS] linkages.

genelink.com/newsite/products/images/modificationimages/PO_PS_PS2_Phosphorothioate_Oligo_Linkages_V1.png" align="center">

Phosphorothioate References 1. Sazani, P., Kole, R. Therapeutic potential of antisense oligonucleotides as modulators of alternative splicing. (2003) J. Clin. Invest., 112: 481-486.
2. Juliano, R., Alam, Md.R., Dixit, V., Kang, H.(2008) Mechanisms and strategies for effective delivery of antisense and siRNA oligonucleotides. Nucleic Acids Res., 36: 4158-4171.
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Phosphorodithioate Linkages

Gene Link offers phosphorodithioate linkage modified DNA and 2'O methyl oligos. The phosphorodithioate linkage [PS2] are achiral and is a good substitute to obviate the disadvantage of phosphorothioate [PS] linkages that yield stereoisomers. Each phosphorothioate substitution can be either an "Sp" or "Rp" conformation. As such, a fully phosphorothioate 20 nt antisense oligonucleotide will be a mixture of more than half a million different molecules.

To avoid and/or reduce this type of complexity is to use achiral phosphorodithioates instead, where both non-bridged oxygen atoms are replaced with sulfurs. Phosphorodithioates share many of the desirable properties of phosphorothioates without the additional undesired stereocenters. (1,2) In addition, phosphorodithioates are even more stable to nucleases than their phosphorothioate counterparts.
Replacing two non-bridging oxygen atoms with sulfur atoms in a DNA phosphodiester linkage creates a phosphorodithioate (PS2) linkage (1). Like natural DNA, the phosphorodithioate linkage is achiral at phosphorus. This analog is completely resistant to nuclease degradation and forms complexes with DNA and RNA with somewhat reduced stabilities (2). Moreover, it has been found that PS2 oligos bind with a higher affinity than their phosphodiester analogue (2-6) suggesting that PS2 oligos may have additional utility in the form of sulfur-modified phosphate ester aptamers (thioaptamers) (3,6-8) for therapeutic and diagnostic applications.
The phosphorodithioate linkage (PS2) is both achiral and essentially resistant to nucleases. Previous studies have shown very interesting results which include observations that DNA with PS2 linkages activates RNase H in vitro, strongly inhibits human immunodeficiency virus (HIV) reverse transcriptase, induces B-cell proliferation and differentiation, and is completely resistant to hydrolysis by various nucleases. 2'OMe- RNA Thiophosphoramidites are RNA monomers designed to produce oligos combining the PS2 linkage with the 2'O-methyl ribose modification. These PS2-modified RNA oligos have potential for use in siRNAs and dithiophosphate aptamers (thioaptamers).
Phosphorodithioate References
1. W.S. Marshall, and M.H. Caruthers, Science, 1993, 259, 1564-70.
2. X. Yang, and E. Mierzejewski, New Journal of Chemistry, 2010, 34, 805-819.
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8. K. Bleicher, et al. Oligonucleotides comprising a phosphorodithioate internucleoside linkage. WO2019122279A1, Jun 27, 2019

Methyl phosphonate (mp) Methyl phosphonate (mp) modification makes the phoshodiester linkage neutral charged. The solubility of the oligo in aqueous solutions slowly decreases with increasing mp linkages; consider incorporating as many standard phosphodiester linkages as well in the oligo. Increasing percentage of DMSO from 0.5 to 10% may be used to solubilize the oligo.

Methyl phosphonoamidites are deoxynucleoside amidites modified such that, when incorporated into an oligonucleotide, that base position will have a (electrically neutral) methyl phosphonate backbone linkage instead of the standard (negatively charged) phosphodiester linkage. Oligos containing one or more methyl phosphonate linkages will be resistant to nuclease degradation at those positions, and the lack of charge improves intracellular transport. Because of these properties, methyl phosphonolated oligos have been explored as anti-sense reagents (1). However, since methyl phosphonate linkages lower the oligo's cellular uptake (2) as well as the Tm of the duplex formed with its RNA target (3), and, most importantly, also interferes with activation of RNase H activity (4), considerable care must taken in choosing which, and how many, methyl phosphonate linkages to incorporate into a putative anti-sense oligo. In that regard, we note that 2'-O-Methyl RNA oligos containing a single 3'-end methyl phosphonate "cap" (to eliminate 3'-exonuclease degradation) have been successfully used as anti-sense reagents (5). In addition, DNA extension primers containing such a "cap" have been used to characterize the nuclease activity of the yeast telomerase complex (6). Methylphosphonolated anti-sense oligos have also been used successfully to "mask" sites in U1 and U2 snRNPs required for spliceosome formation, and thus interfere with mRNA splicing (7). Many of the unique properties of methylphosphonolated oligos are due to the introduction of chirality into the phosphodiester backbone by the methyl group (8).

Methyl phosphonate (mp) References

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Oligo Modifications for ASO's and siRNA Delivery.

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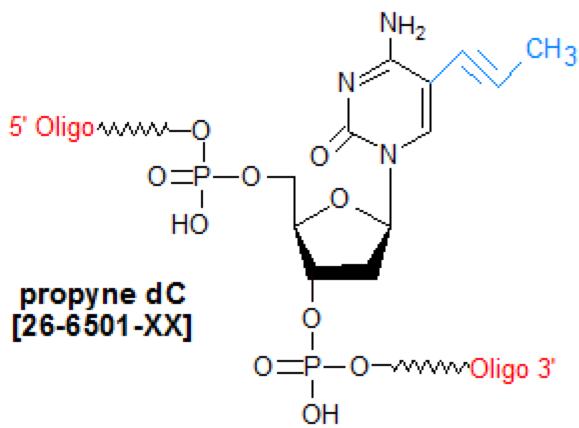
Click this link to view these modifications.

propyne dC

Category	Antisense
Modification Code	pdC
Reference Catalog Number	26-6501
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	327.23



propyne dC
[26-6501-XX]

It has been shown that C-5 propyne analogs of dC and dT when substituted in phosphorothioate oligonucleotide imparts greater inhibition of gene expression due to increased binding affinity to the target mRNA and increased stability. Based on the above information antisense oligonucleotide could either be Phosphorothioated at all diester linkages or combined with substitutions of dC and dT by C-5 propyne analogs pdC and pdU.
Modifications Increasing Duplex Stability and Nuclease Resistance

Modification

Duplex Stability [Tm Increase]

Nuclease Resistance Locked Analog Bases Increased [2- 4C per substitution] Increased 2-Amino-dA Increased [3.0C per substitution] Similar to DNA C-5 propynyl-C Increased [2.8C per substitution] Increased C-5 propynyl-U Increased [1.7C per substitution] Increased 2'-Fluoro Increased [1.8C per substitution] Increased 5-Methyl-dC Increased [1.3C per substitution] Similar to DNA 2'-O Methyl Increased Increased Phosphorothioate Slightly decreased Increased Click here for complete list of duplex stability modifications The use of propyne analogs is covered by patents and licensing agreements. The sale of propyne-modified oligos is for research use only. See license agreement*

Oligo Modifications

propyne dU

Category	Antisense
Modification Code	pdU
Reference Catalog Number	26-6502
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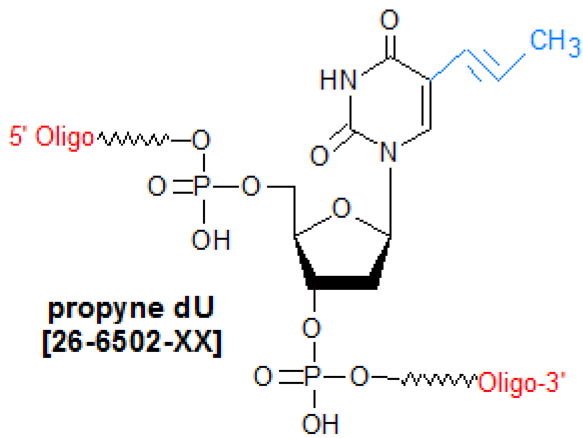
3 Prime	Y
Internal	Y
Molecular Weight(mw)	328.22



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