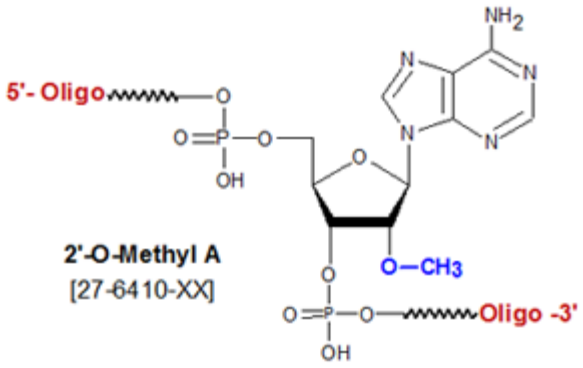
Oligo Modifications

For research use only. Not for use in diagnostic procedures for clinical purposes.

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



Antisense Oligos (ODN) & siRNA Oligo Modifications
Click here for more information on antisense modifications, design & applications.

2'-O-Methyl bases are classified as a 2'-O-Methyl RNA monomer. 2'-O-Methyl nucleotides are most 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 internucleotide linkages within the oligo.

The hydrogen bonding behavior of a 2'-O-Methyl RNA/RNA base pair is closer to that of an RNA/RNA base pair than a DNA/RNA base pair. Consequently, the presence of 2'-O-Methyl nucleotides **improves duplex stability**. Indeed, incorporation of a 2'-O-Methyl nucleotide into an anti-sense oligo (resulting in a 2'-O-Methyl RNA/DNA chimeric), lead to a **increase** in the Tm of its duplex with RNA, relative to that formed by an unmodified anti-sense DNA oligo, **of 1.3^{O}C per 2'-O-Methyl RNA residue added** (2). Moreover, from a synthesis standpoint, the coupling efficiency of 2'-O-Methyl phosphoramidites are higher than those of RNA monomers, resulting in higher yield of full-length oligos.
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

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

ASO's and siRNA Modifications.
Click this link to view ASO's and siRNA Modifications.

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.

References

1. Cotton, M.; Oberhauser, B.; Burnar, H. *et al.* 2'O methyl and 2'O ethyl oligoribonucleotides as inhibitors of the in vitro U7 snRNP-dependent messenger-RNA processing event. *Nucleic Acids Res.* (1991) , **19**:2629-2635.
2. Kawasaki, A.M. *et al.*, Uniformly modified 2'-deoxy-2'-fluoro phosphorothioate oligonucleotides as nuclease resistant antisense compounds with high affinity and specificity for RNA targets, *Journal of Medicinal Chemistry* (1993), **36**: 831-841.