Intercalators Introduction

DNA intercalators in general are polycyclic, aromatic, planar molecules capable of fitting in between nucleic acid base pairs (1). Incorporation of intercalators into oligonucleotides allows the modified oligos to be cross-linked (in the case of psoralen) to complementary nucleic acid strands, or to show an increase in subsequent duplex or triplex stability (in the case of acridine).

Intercalators Design Protocols

Under Development. Please inquire here

Intercalators Applications

Currently, DNA intercalators are used in both antisense work and structural studies. For example, incorporation of acridine into oligos is attractive for antisense applications, because intercalation of acridine into the DNA-RNA duplex significantly increases the Tm (that is, enhances duplex stability) without affecting target specificity (2). Consequently, it becomes possible to use much shorter oligos as antisense moieties. Incorporating psoralen into oligos is attractive for cross-linking studies into nucleic acid secondary structure and protein-nucleic acid interactions. For more information on the uses of psoralen, see the applications section of the Cross-Linkers modification category.

References

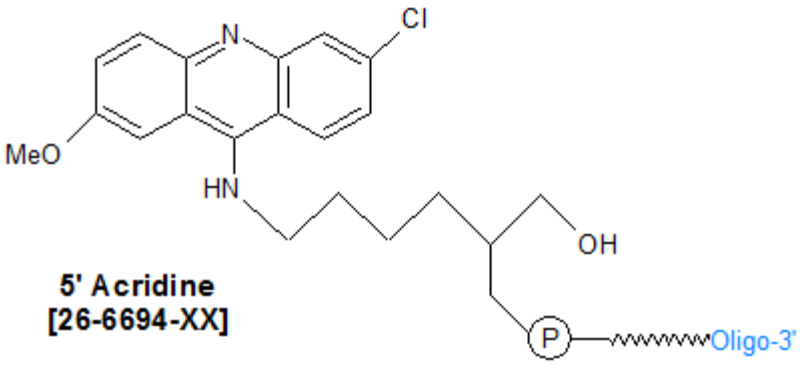
(1) Sinha, R., Islam, M.M., Kakali, B., Gopinatha, S.K., Banerjee, A., Maiti, M. The binding of DNA intercalating and non-intercalating compounds to A-form and protonated form of poly(rC)-poly(rG): Spectroscopic and viscometric study. Bioorg. & Medic. Chem. (2006), 14: 800-814.
(2) Fukui, K., Tanaka, K. The Acridine Ring Selectively Intercalated into a DNA Helix at Various Types of Abasic Sites: Double Strand Formation and Photophysical Properties. Nucleic Acids Res. (1996), 24: 3962-3967.
(3) Salson-Behmoaras, T., Tocque, B., Rey, I., Casslgnol, M., Thuong, N-T., Helene, C. Short modified antisense oligonucleotides directed against Ha-ras point mutation induce selective cleavage of the mRNA and inhibit T24 cells proliferation. EMBO J. (1991), 10: 1111-1118.

Modificaton Code List

Modification	Code	Catalog Number
Acridine	[Acrd]	26-6694
Psoralen C6-5'	[Pso-C6-5]	26-6686

Acridine

Category	Intercalators
Modification Code	Acrd
Reference Catalog Number	26-6694
5 Prime	Y
3 Prime	Y
Internal	Y
Molecular Weight(mw)	450.86



5' Acridine
[26-6694-XX]

Acridine is classified as a DNA intercalating agent. Labeling of DNA oligos with acridine allows them to rapidly and stably intercalate into a target dsDNA molecule, adding increased stability to the double helix (1). In addition, incorporation of acridine to the 3'-end of an oligo confers a high level of exonuclease resistance to that end (2). Thus, oligos labeled with acridine may be useful in applications involving oligo hybrids requiring higher levels of stability.

Acridine-labeled oligos containing a polypyrimidine sequence possess the ability to form triplex helices that are highly stable, and, due to their increased hydrophobicity, can pass through membranes more easily than normal oligos. Such oligos were used as anti-sense reagents to suppress c-myc protooncogene expression and control tumor growth in mice (3), and as a transcriptional repressor to the IL-2 Receptor (4).

Since acridine is a fluorescent dye, it can also be use to make dye-labeled oligos. An interesting such application is the use of acridine-labeled primers to study non-enzymatic-template-directed RNA synthesis to provide experimental support for theories concerning possible replication of genetic information by early life forms on Earth (5). **References**

1. Fukui, K., Tanaka, K. The Acridine Ring Selectively Intercalated into a DNA Helix at Various Types of Abasic Sites: Double Strand Formation and Photophysical Properties. *Nucleic Acids Res.* (1996), **24**: 3962-3967.
2. Gamper, H.B., Reed, M.W., Cox, T., Virosco, J.S., Adams, A.D., Gall, A.A., Scholler, J.K., Meyer, R.B. Facile preparation of nuclease resistant 3ï¿½ modified oligodeoxynucleotides. *Nucleic Acids Res.* (1993), **21**: 145-150.
3. Stewart, D.A., Xu, Xiaohou, Thomas, S.D., Miller, D.M. Acridine-modified, clamp-forming antisense oligonucleotides synergize with cisplatin to inhibit c-Myc expression and B16-F0 tumor progression.*Nucleic Acids Res.* (2002), **30**: 2565-2574.
4. Grigoriev, M., Praseuth, D., Robin, P., Hemar, A., Saison-Behmoaras, T., Dautry-Varsat, A., Thuong, N.T., Helene, C., Harel-Bellan, A. A Triple-Helix-forming Oligonucleotide-Intercalator Conjugate Acts as Transcriptional Repressor via Inhibition of NFkB Binding to Interleukin-2 Receptor alpha-Regulatory Sequence. *J. Biol. Chem.* (1992), **267**: 3389-3395.
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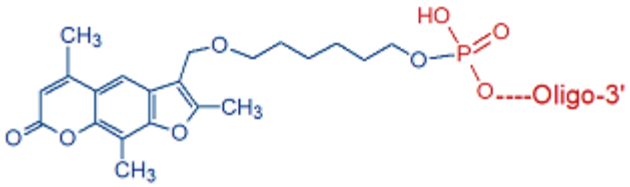
Helv. Chim. Acta (1998), 81: 1156-1180.

Psoralen C6-5'

Category	Intercalators
Modification Code	Pso-C6-5
Reference Catalog Number	26-6686
5 Prime	Y
3 Prime	N
Internal	N
Molecular Weight(mw)	420.4



5'-Psoralen C6

[26-6686-XX]

Psoralen C6 is a heterocyclic compound capable of intercalating between bases, and cross-link bases, in both double-stranded and triple-stranded DNA. It is attached to a C6 linker in order to facilitate a psoralen-modified oligonucleotide's ability to intercalate and cross-link with triple-stranded DNA. Psoralen is typically used as a ss/ds DNA intercalating or cross-linking reagent, for the purpose of probing nucleic acid secondary structure (1). Upon exposure to long wavelength UV light (350 nm), psoralen forms covalent cyclobutane linkages to thymidine. Psoralen can form two different types of adducts with thymidine. The first is a monoadduct, in which the psoralen moiety binds to one adjacent thymidine on the same or complimentary strand. The second is a diadduct, in which psoralen binds to two thymidines adjacent to it, either on the same or complimentary strand (2). Diadducts formed between adjacent thymidines are photo-reversable with short wavelength UV light (254 nm). In addition to cross-linking duplex DNA, Psoralen-C6 homopyrimidine oligos can be used to bind to a complementary homopurine-homopyrimidine duplex, to form a triple-helix that can then be cross-linked together at the triplex-duplex junction point (3). Psoralen-modified oligonucleotides are widely used as research tools; representative examples of such use are shown in these references (4,5). **References**

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