METKINEN
chemistry

2-'DEOXY-2'-FLUORONUCLEOSIDES & DERIVATIVES

Synthetic RNA oligonucleotides, incorporating 2'-Deoxy-2'-fluoro-nucleosides (2'-F-RNA) find constantly increasing applications in research and new drug development. Among important areas of their application are such as design and synthesis of efficient and stable siRNAs, aptamers, anti-microRNAs (Antagomirs) as well as general use for affinity purification of RNA-binding proteins.

Today Metkinen Chemistry offers more than 99% pure purine 2'-fluoronucleosides, prepared by bioconversion of synthetic 2'-F-uridine, using evolved recombinant E.coli strains. These strains, in turn are grown on the media, incorporation only ingredients, derived from yeast and vegetable. That means that in the production process no secondary reagents of animal source (either BSE certified or non- BSE certified) are employed at any stage of 2'-F- A and G preparation. Hence, we guarantee the complete absence of ANY BSE/TSE risk, associated with our 2'-F-nucleosides and derivatives.

In addition to purine 2'-F-nucleosides, we offer a full set of 2'-F-nucleoside CE-phosphoramidites for chemical synthesis and a full set of 2'-F-nucleoside 5'-triphosphates for enzymatic preparation of 2'-F-RNA. Our latest addition to series of 2'-fluoronucleoside derivatives – 2'-F-nucleoside bound solid supports for 2'-F-RNA oligosynthesis, complements the range of these compounds and opens up a full spectrum of 2'-F-RNA applications.

In the talk titled "Translating RNAi," Dr. Manoharan (Alnylam) presented new data related to the effective delivery of RNAi therapeutics. Dr. Manoharan showed that among the numerous carbohydrate modifications to improve the drug-like properties of siRNAs, 2'-Fluoro modifications consistently provided increased target binding affinity, endonuclease stability, and, importantly, reduced immune response. In addition, it is the only modification compared to other carbohydrate modifications, including locked nucleic acid, or LNA, that preserves RISC activity when used in both sense and antisense strands. Data presented included the following: Synthetic 2'-Fluoro modified siRNAs are significantly more stable, thermodynamically and to nucleases in biological fluids, and can increase the efficacy of siRNAs approximately 2-fold in vivo; and 2'-Fluoro modified siRNA targeting Factor VII was found to produce no immuno-stimulatory response, whereas a corresponding unmodified siRNA could stimulate IFN-alpha and TNF-alpha in vitro.

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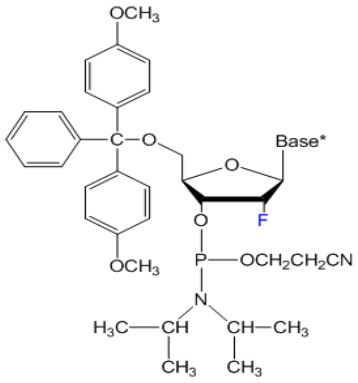
2'-Deoxy-2'-fluoronucleoside-3'-CE Phosphoramidites

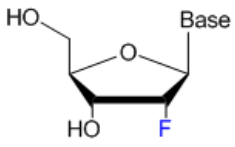


Base* = bzAde, ibGua, acCyt, Ura

Cat no	Product	Purity	Package
203-50	2’-Deoxy-2’-Fluoroguanosine-3’-CE-phosphoramidite	> 95%	0.1 g – 1 kg
203-51	2’-Deoxy-2’-Fluoroadenosine-3’-CE-phosphoramidite	> 95%	0.1 g – 1 kg
203-52	2’-Deoxy-2’-Fluorouridine-3’-CE-phosphoramidite	> 95%	0.1 g – 1 kg
203-53	2’-Deoxy-2’-Fluorocytidine-3’-CE-phosphoramidite	> 95%	0.1 g – 1 kg

Purine 2'-Deoxy-2'-fluoronucleosides

Purine 2'-Fluoro-2'deoxynucleosides are obtained via biotransformation. They are extra pure and efficiently priced.



Base = Ade, Gua

Cat no	Product	Cas No	Purity	Package
203-15	2’-Deoxy-2’-Fluoroguanosine	125291-17-0	≥ 99%	0.1 g – 1 kg
203-17	2’-Deoxy-2’-Fluoroadenosine	64183-27-3	≥99%	0.1 g – 1 kg

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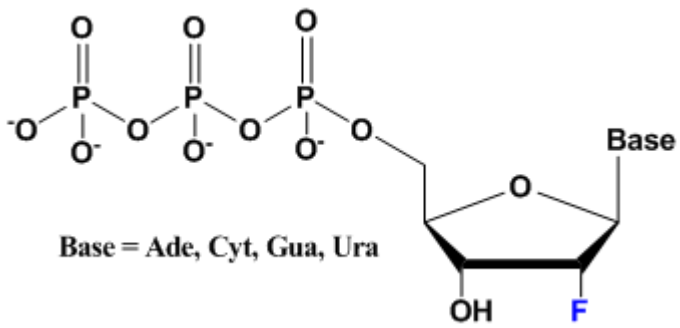
2'-DEOXY-2'-FLUORONUCLEOSIDE 5'-TRIPHOSPHATES



Oligonucleotides, incorporating 2'-F-nucleoside units are widely employed in RNA and aptamer research. 2'-Deoxy-2'-fluoronucleoside 5'-triphosphates are popular products for various applications: PCR, DNA- and RNA-polymerase, reverse transcriptase based assays, etc. Nowadays these compounds find diverse use in siRNA and Aptamer research.

Product Note: All of our Triphosphates are lithium salts. They are are analyzed by NMR, UV, HPLC and are accompanied by a Product Data Sheet

Cat no	Product	Package
104-01	2'-Deoxy-2'-fluoroadenosine-5'-Triphosphate	10 µmol
104-02	2'-Deoxy-2'-fluorocytidine-5'-Triphosphate	10 µmol
104-03	2'-Deoxy-2'-fluoroguanosine-5'-Triphosphate	10 µmol
104-04	2'-Deoxy-2'-fluorouridine-5'-Triphosphate	10 µmol
104-05	2'-Deoxy-2'-fluoronucleoside-5'-Triphosphate Kit, containing 5 µmol of each	20 µmol (4x5 µmol)

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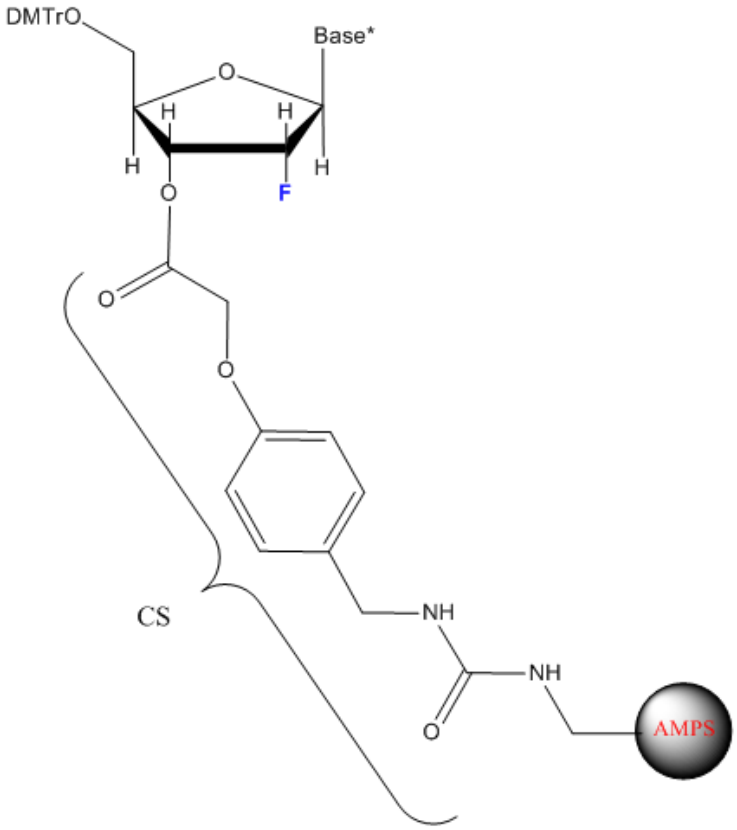
NEW 2'-F-NUCLEOSIDE BOUND SOLID SUPPORTS (F-CS-SUPPORTS)

The F-CS Solid Supports incorporate a new linker that allows 3-4 times faster cleavage of target oligonucleotide off the solid phase under the the regular cleavage/deprotection conditions. This feature make them indispensable, when UltraFAST Deprotection ULtraMILD Deprotection is necessary in order to insure the convenient isolation of modified and dye labelled oligonucleotides that appear not stable to deprotection with ammonium hydroxide or AMA at regular conditions (e.g. oligonucleotides, labled with Cy5 or Cy 5.5 dyes)

The novel F-CS supports appear absolutely similar, if not better than the conventional nucleoside bound supports (incorporating the traditional succinate linker) in terms of performance as solid phases for RNA Oligonucleotide synthesis. Noteworthy, the precise loading of the new linker on the solid phase is much easier to achieve when using the new Carbomoylation procedure, developed by Metkinen Chemistry (U.S. Patent Application Serial No 60/854,721 and International Patent Application No. PCT/FI2007/050575).



B*= bzAde, Thy, acCyt, ibuG; AMPS = macroporous aminomethyl polystyrene

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Catalogue numbers: 103-30FA, 103-30FG, 103-30FC, 103-30FU

Description: Chemically modified Macroporous Aminomethyl Polystyrene. White to off-white powder.

Storage of dry compound: 1 year at +4ºC

Loading: standard - 30 - 40 µmol/g; custom loading – from 5 to 80 µmol/g.

Oligosynthesis on CS supports: perform oligonucleotide assembly, using standard RNA protocols, recommended by your synthesizer manufacturer.

Cleavage: Cleave the oligo from the support using concentrated aqueous ammonium hydroxide at room temperature for 30 minutes. Alternatively, cleave the oligo from the support using concentrated aqueous ammonium hydroxide – 40 % aqueous methylamine (AMA) at room temperature for 15 minutes.

Deprotection AFTER Cleavage: Following the cleavage step, proceed with oligonucleotide deprotection using the conditions appropriate for removal of the protecting groups on the nucleobases.

REFERENCES

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