

4'-Thiophosphoramidite

The structures of nucleic acid therapeutics are often chemically modified at the base, phosphate, and sugar moieties to achieve enhanced nuclease resistance and improved hybridization property.

4'-Thionucleic acids are nucleic acids (DNA, RNA) chemically modified at the sugar moiety, exhibiting higher duplex-forming ability and greater nuclease resistance compared to their natural counterparts.¹⁾

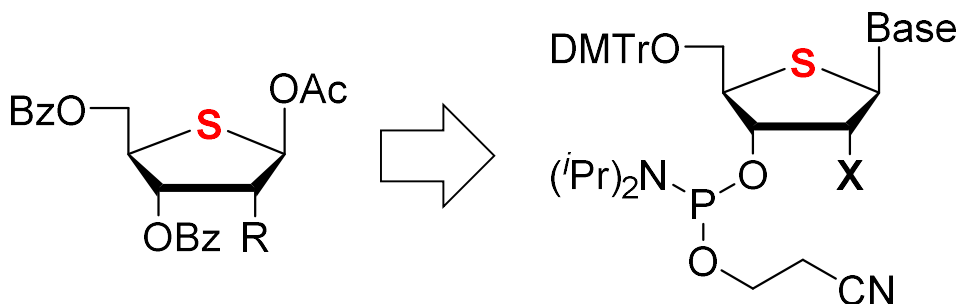
Features of 2'-modified-4'-thioDNA and RNA

- Excellent ability to form stable duplexes with complementary RNA¹⁾
- High nuclease resistance^{2,3)}
- Biological equivalence to natural nucleic acids (2'-OH)

4'-Thionucleosides, the building blocks of 4'-thionucleic acids, are modified nucleosides in which the oxygen atom at the 4' position of the sugar is replaced by a sulfur atom.

We offer a wide range of 4'-thio- compounds useful for the synthesis of 4'-thionucleic acids.

What We Offer



R = OBz, F

Base = A(Bz), G(*i*Bu), C(Bz), U
X = OTBDMS, OMe, OMOE, F

Our Strengths in 4'-Thiophosphoramidite synthesis

- We have efficient manufacturing technology⁴⁾ for the 4'-thioribose backbone, enabling cost-effective production of intermediates.
- These intermediates can be converted into a variety of amidites.

We offer custom synthesis of 2'-Modified-4'-thiophosphoramidite.

Please feel free to contact us for inquiries regarding substituted compounds or 4'-thioribose intermediates.

Attention: We are unable to provide samples to customers who intend to use them in the US.

Properties of 4'-thioRNA : Duplex formation and stability¹⁾

Thermal stabilities of the complementary duplexes

Table 2. Thermodynamic parameters for duplex formation determined from UV melting and DSC measurements^{a,b}

Duplex	UV melting T_m (°C)	DSC T_m (°C)	ΔH° (kcal mol ⁻¹)	ΔS° (cal mol ⁻¹ K ⁻¹)	ΔG° (37°C) (kcal mol ⁻¹)
RNA1 : RNA2	66.2 ± 0.2	53.9 ± 1.3	-85.2 ± 3.1	-263.2 ± 9.7	-3.58 ± 0.37
thioRNA1 : RNA2	74.5 ± 0.3	66.9 ± 0.1	-100.8 ± 0.9	-299.4 ± 2.8	-7.90 ± 0.21
thioRNA1 : thioRNA2	>99	91.0 ± 0.6	-126.9 ± 1.0	-350.8 ± 3.2	-18.1 ± 0.1
RNA1 : DNA1	51.6 ± 0.1	43.9 ± 0.2	-87.8 ± 2.2	-279.5 ± 9.8	-0.98 ± 0.99
thioRNA1 : DNA1	45.5 ± 0.9	35.9 ± 0.1	-61.7 ± 2.2	-200.8 ± 14.3	3.31 ± 0.37

^aErrors reflect standard deviation from three independent experiments.

^bExperimental conditions are described in Materials and Methods.

5' -r (AGUCCGAAUUCACGU) -3' : RNA1 and thioRNA1
3' -r (UCAGGCUUAAGUGCA) -5' : RNA2 and thioRNA2
3' -d (TCAGGCTTAAGTGCA) -5' : DNA 1

Figure 3. Sequences of RNA, 4'-thioRNA and DNA

The resulting T_m values showed that the thioRNA:RNA and thioRNA:thioRNA duplexes had higher T_m value than the natural RNA:RNA or RNA:DNA duplexes.



4'-thioRNA formed a thermally stable duplex with the complementary RNA

Supporting Information: Synthesis and physical properties of 4'-thioRNA

Properties of 4'-thioRNA : Nuclease stability²⁾

As is well known, MeRNA is highly resistant against ribonuclease (RNase) digestion due to methylation of the 2'-hydroxy groups.

Table 3. Comprehensive investigation of nuclease stability of chemically modified OligoNucleotides (ONs)^a

ON	S1 nuclease		SVPD	50% human plasma	
	$t_{1/2}^b$	$t_{1/2}^c$	$t_{1/2}$	$t_{1/2}$	Degradation pattern
RNA1	25.4 ± 7.2 s	–	6.0 ± 0.6 min	< 10 s	Endo
DNA1	7.4 ± 1.9 s	–	3.1 ± 0.1 min	46.8 ± 7.0 min	Exo
MeRNA1	>24 h	224 ± 47.6 min	5.3 ± 1.5 min	187 ± 22.6 min	Exo
SRNA1	76.8 ± 25.2 min	–	54.4 ± 2.5 min	65.7 ± 8.0 min	Endo
Me-SRNA1	>24 h	>24 h	79.2 ± 8.7 min	1631 ± 60.8 min	Exo
FRNA1	1.1 ± 0.1 min	–	5.8 ± 1.2 min	53.2 ± 3.5 min	Exo
RNA2	13.0 ± 2.4 s	–	4.3 ± 0.4 min	< 10 s	Endo
DNA2	6.6 ± 1.3 s	–	2.7 ± 0.3 min	31.0 ± 1.7 min	Exo
FRNA2	20.8 ± 0.4 s	–	6.0 ± 1.0 min	51.9 ± 3.1 min	Exo
SRNA2	12.6 ± 1.7 min	–	12.8 ± 3.5 min	< 10 s	Endo
F-SRNA2	6.5 ± 0.5 min	–	21.0 ± 3.6 min	120 ± 10.5 min	Exo
MeRNA2	>24 h	136 ± 11.5 min	4.5 ± 1.1 min	435 ± 12.9 min	Exo

^aErrors reflect standard deviation from three independent experiments.

^bONs were treated with 0.17 U/μL S1 nuclease.

^cONs were treated with 51 U/μL S1 nuclease.

ON1s; RNA1, MeRNA1, SRNA1, Me-SRNA1, and FRNA1

5' –AGUCCGAAUUCACGU– 3'

ON2s; RNA2, FRNA2, SRNA2, F-SRNA2, and MeRNA2

5' –ACUCCUAAUUCACAU– 3'

Figure 4. Sequences of modified ONs.

2'-OMe-4'-thioRNA exhibits higher nuclease resistance than 2'-OMe-RNA

References

- 1) Hoshika, S., Minakawa, N. and Matsuda, A. : *Nucleic Acid Res.*, **32** (13), 3815 (2004).
- 2) Takahashi, M., Minakawa, N. and Matsuda, A. : *Nucleic Acid Res.*, **37**, 1353 (2009).
- 3) Saito, Y., Hashimoto, Y., Arai, M., Tarashima, N., Miyazawa, T., Miki, K., Takahashi, M., Furukawa, K., Yamazaki, N., Matsuda, A., Ishida, T. and Minakawa, N. : *ChemBioChem*, **15**, 2535 (2014).
- 4) JP Patent Application No. 5970550 (FUJIFILM Corporation)
- 5) Our experimental data

Listed products are intended for laboratory research use only, and not to be used for drug, food or human use. Please visit each region's website for product information. This leaflet may contain products that cannot be exported to your country due to regulations. Bulk quote requests for some products are welcomed. Please contact us.

Japan
FUJIFILM Wako Pure Chemical Corporation
 1-2, Doshomachi 3-Chome, Chuo-ku, Osaka 540-8605, Japan
 ffwk-cserservice@fujifilm.com
 labchem-wako.fujifilm.com

Chinese Mainland
FUJIFILM Wako (Guangzhou) Trading Corporation
 Room 3002, 3003, 3011, 30/F., Dong Shan Plaza,
 69 Xian Lie Middle Road, Yuexiu District, Guangzhou, 510095, China
 wkgz.info@fujifilm.com
 labchem.fujifilm-wako.com.cn

The Americas
FUJIFILM Biosciences
 2501 Pullman Street, Santa Ana, CA 92705, USA
 supportfilsilssupport@fujifilm.com
 fujifilm-biosciences.fujifilm.com

Hong Kong SAR
FUJIFILM Wako Chemicals (Hong Kong) Limited
 Units 9-12 and 15-18, Level 28, Tower 1, The Millennium,
 98 How Ming Street, Kwun Tong, Kowloon, Hong Kong
 wkhk.info@fujifilm.com
 labchem.fujifilm-wako.com.cn

Europe, Middle East, and Africa
FUJIFILM Wako Chemicals Europe GmbH
 Fuggerstr 12, 41468 Neuss, Germany
 labchem_wkeu@fujifilm.com
 labchem-wako.fujifilm.com

Other Areas
fujifilm.com/ffwk/en/about/partners/labchem