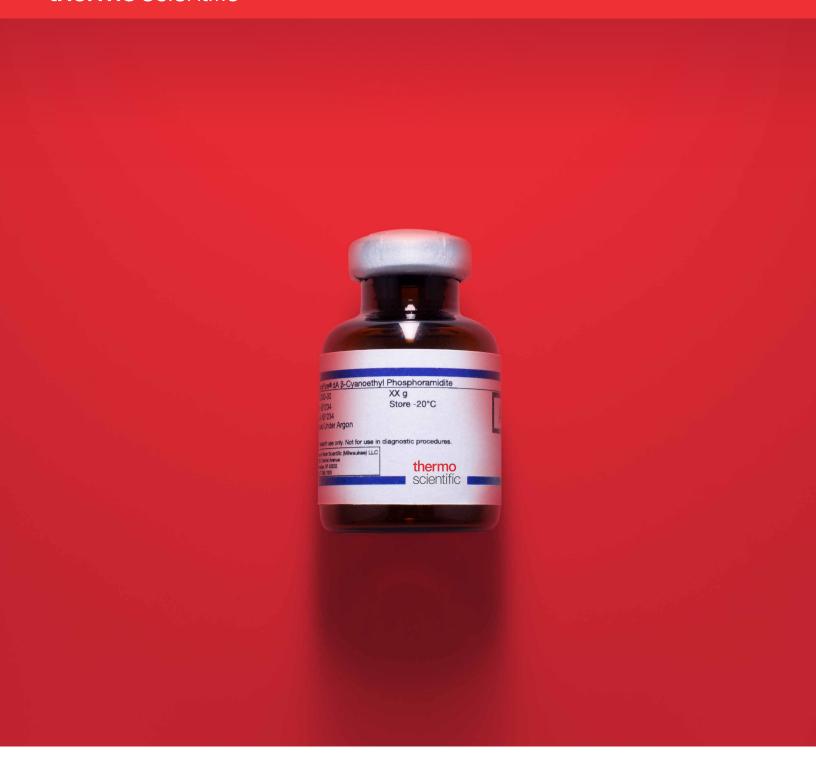
### thermo scientific



Phosphoramidites for oligonucleotide synthesis



# TheraPure DNA and RNA phosphoramidites

Thermo Scientific™ DNA and RNA phosphoramidites are built to meet the varying needs of oligonucleotide manufacturers for the development of therapeutic, diagnostic, and research applications. A broad range of options are available, including CRO/CMO services, custom analytics, alternative protection chemistries, active moieties, and base modifications.

#### **Reliable quality**

- Manufactured in an ISO 9001–registered facility since 1995
- Controlled and documented processes provide consistent product quality with full traceability

#### Flexible supply

- Bulk or pack sizes to fit most commercially available synthesizers are ready for prompt delivery
- Extensive manufacturing experience enables us to meet your scale-up requirements, from grams to metric tons

#### **Solid commitment**

- Over 30 years of experience with growing capabilities to meet market needs
- Continued development and advancement of critical analytics
- Investments in increased capacity

#### Large selection of base protection options

		Base protection options						
	Base	Benzoyl (Bz)	Isobutyryl (iBu)	Isopropylphenoxyacetyl (iPrPAC)	Phenoxyacetyl (PAC)	Acetyl (AC)	Dimethylaminoformamidine (DMF)	Custom
	А	•			•			•
DNA phosphoramidites	С	•	•			•		•
DNA phosphoralillules	G		•	•			•	•
	5mC	•						•
	А	•			•			•
RNA phosphoramidites	С					•		•
	G		•	•		•		•
2'-OMe RNA phosphoramidites	А	•			•			•
	С					•		•
	G		•	•		•		•
	А	•						•
2'-Fluoro RNA phosphoramidites	С					•		•
	G		•					•

Originally designed specifically to meet the needs of oligonucleotide-based therapeutics development, Thermo Scientific<sup>™</sup> TheraPure<sup>™</sup> phosphoramidites are now important for molecular assay and gene synthesis applications, which both benefit from low levels of critical impurities.

#### **Control of critical impurities**

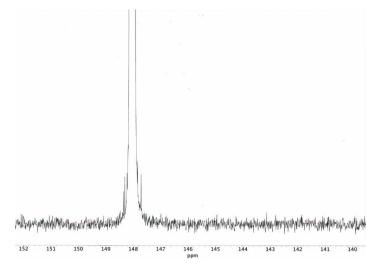
- Sum of nonprimary peaks at 140–150 ppm <0.3–0.5 mol % in <sup>31</sup>P NMR
- Reduced levels of noncritical impurities
- Reduced occurrence of critical impurities that can be incorporated during oligonucleotide synthesis

#### Control of residual solvents and water content

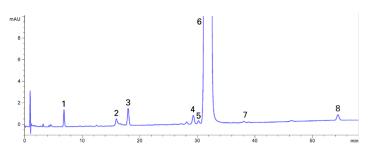
- Low residual solvents
- Low water content, which enables higher coupling efficiency and solution stability

#### **Security of supply**

- Multiple sources of critical raw materials
- Long-term supplier agreements, including access to safety stock and change notification



Typical NMR scan of a TheraPure RNA phosphoramidite.



Example of impurity profile of Thermo Scientific™ TheraPure™ 2'-TBDMS iBU rG Phosphoramidite by LC-MS.

Peak	Area (%)	Mass spec identification	Impurity classification
1	0.09	5'-DMTr-2'-TBDMS-3'-OH	Nonreactive, noncritical
2	0.05	5'-DMTr-2'-TBDMS 3'-phosphoramidate (VI)	Nonreactive, noncritical
3	0.13	5'-DMTr-2'-TBDMS 3'-H-phosphonate	Nonreactive, noncritical
4	0.08	5'-DMTr-2'-TBDMS 3'-H-phosphonate	Nonreactive, noncritical
5	0.02	3'-TBDMS 2'-phosphoramidite	Reactive and critical
6	99.51	5'-DMTr-2'-TBDMS 3'-phosphoramidite	Product
7	0.01	5'-modified trityl-2'-TBDMS 3'-phosphoramidite	Reactive, noncritical
8	0.07	5′,3′-Di-DMTr-2′-OH	Nonreactive, noncritical

# 2'-modified RNA phosphoramidites

2'-modified	Base						
phosphoramidites	A	С	G	Т	U		
2'-MOE	2'-MOE-A CEP	2'-MOE-5mC CEP	2'-MOE-G CEP	2'-MOE-T CEP			
2'-Fluoro	2'-Fluoro-Bz-A CEP	2'-Fluoro-Ac-C CEP	2'-Fluoro-iBu-G CEP		2'-Fluoro-U CEP		
			2'-Fluoro-Ac-G CEP				
2'-OMe	2'-OMe-Bz-A CEP	2'-OMe-Ac-C CEP	2'-OMe-iBu-G CEP		2'-OMe-U CEP		

#### 2'-MOE Phosphoramidites, TheraPure Grade

2'-O-methoxyethyl (MOE) modification offers:

- Nuclease resistance
- Fewer off-target effects
- Increased hybridization affinities

Key component of antisense-based oligonucleotides.

### 2'-Fluoro Phosphoramidites, TheraPure Grade

2'-Fluoro modification offers:

- Nuclease resistance
- Increased thermal stability of RNA duplexes

2'-O-methyl (OMe) modification offers:

- Nuclease resistance
- Fewer off-target effects
- Increased hybridization affinities

PAC-A and iPrPAC-G available for fast deprotection.

Key component of oligonucleotides designed for antisense, siRNA, aptamer, or gRNA-based applications.

# Dye-labeled and structural phosphoramidites

#### **Dye-labeled phosphoramidites**

Thermo Scientific™ DyLight™ fluorescent labels offer a brighter choice with spectrally distinct colors for oligonucleotide labeling, ideal for molecular assay applications and microarrays.

#### A broad range of labeling options

Phosphoramidites labeled with fluorophores (DY547, DY647, and DY677) with coupling efficiency, emission, and absorption spectra comparable to Cy®3, Cy®5, and Cy®5.5 dyes.

Fluorophore	λ <sub>max</sub> abs (nm)	Emission max
Fluorescein	494	520
FAM-6	494	520
DY3	548	562
DY5	645	662
DY547	548	562
DY549	557	568
DY647	645	662
DY677	684	698



Fluorescence intensity of PCR products with DyLight and Cy labels. PCR products were resolved by gel electrophoresis and visualized using a FluorChem™ Q imager (ProteinSimple) with Cy3 and Cy5 filters. The DyLight and Cy labels yield similar fluorescence intensity when used on PCR products.

#### Structural phosphoramidites

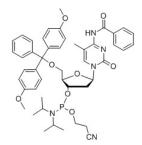
Modified oligonucleotides can be synthesized effortlessly with nonstandard, specialty phosphoramidites. These modified oligonucleotides are used as primers or probes, or in studies such as:

#### **Duplex stability**

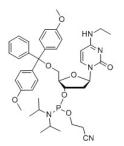
 Stability and melting point of oligonucleotide duplexes can be altered by incorporation of N4-ethyl dC,
5-methyl dC, dl, or dU into the oligonucleotide sequence

#### Mutagenesis

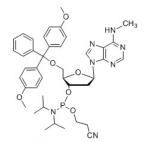
 Mutagenic effects from methylation of exocyclic amine can be studied by incorporation of N6-Methyl dA into the oligonucleotide sequence



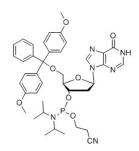
5-methyl dC phosphoramidite Formula weight: 848.0 g/mol



N4-ethyl dC phosphoramidite Formula weight: 757.9 g/mol



N6-methyl dA phosphoramidite Formula weight: 767.9 g/mol



dl phosphoramidite Formula weight: 754.8 g/mol

## Linker and spacer phosphoramidites

Put your oligonucleotides to work through 5' end and internal modifications.

#### **Amino modifiers**

- Suitable for attachment of amine-reactive entities, including fluorescent labels, tags, and other molecules
- Offered with MMT or TFA protection

#### Phosphorylation

- Increased stability; suitable for ligation applications
- Incorporation of phosphate group to 5' position of oligonucleotide

5'-aminohexyl linker phosphoramidite Formula weight: 590 g/mol

Phosphorylating phosphoramidite Formula weight: 657 g/mol

## Succinates and CPG synthesis supports

DNA succinates are ideal for derivatization of controlled pore glass (CPG), polystyrene, and other supports used in solid-phase oligonucleotide synthesis.

#### Standard base protection

- Standard base protection is available on stock items
- All succinates are formulated as TEA salts

RNA CPG synthesis supports are suitable for automated synthesis of RNA oligonucleotides.

#### Standard base protection

- RNA CPG synthesis supports are derivatized with 2'-TBDMS-protected base with 5'-DMT
- CPG support will not swell or shrink
- CPG support is inert to reagents during synthesis

#### **Custom services**

Custom manufacturing services are available to assist you in your development or scale-up of succinates and synthesis supports.

## OEM and custom nucleic acid chemistry

Our proven custom product development process is built to efficiently and effectively respond to your specific needs.

#### **Advanced project management**

- Customer involvement
- Dedicated cross-functional project team
- Project planning and execution tailored to each custom request
- Manufactured in an ISO 9001-registered facility
- Thoroughly documented processes provide consistent product quality with batch-to-batch consistency

#### **Custom chemistries and capabilities**

- Chemistries: triphosphate, phosphoramidite, and custom organics
- Fluorescent labeling compounds
- Modifiers and linkers
- Manufacturing from R&D to bulk scale
- Development of customized QC
- Customer-driven specifications
- · Custom filling, lyophilization, labeling, and packaging

#### **Customization options**

- Base or base protection modification
- Sugar modifications at 2' position
- Changes to phosphitylation, or phosphitylation of custom molecules
- 5' protection modification

- A. Dimethoxytrityl (DMT) substitution with alternate protecting groups
- B. Base = A, C, G, T, or U protection modifications or base modifications
- C. Sugar 2' position modifications and protection options
- D. Phosphoramidite, succinate, and support attachment and proprietary chemistries

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#### Ordering information

Product	Cat. No.
TheraPure DNA phosphoramidites	
TheraPure dA β-Cyanoethyl Phosphoramidite	27-2030
TheraPure dC β-Cyanoethyl Phosphoramidite	27-2032
TheraPure dG β-Cyanoethyl Phosphoramidite	27-2034
TheraPure DMF dG Phosphoramidite	27-1737
TheraPure dT β-Cyanoethyl Phosphoramidite	27-2036
TheraPure RNA phosphoramidites	
TheraPure PAC-rA Phosphoramidite	27-1803
TheraPure rU Phosphoramidite	27-1804
TheraPure Ac-rC Phosphoramidite	27-1805
TheraPure iPrPAC-rG Phosphoramidite	27-1806
TheraPure Bz-rA Phosphoramidite	27-1903
TheraPure iBu-rG Phosphoramidite	27-1906
TheraPure 2'-OMe phosphoramidites	
TheraPure 2'-OMe-Bz-A Phosphoramidite	27-2042
TheraPure 2'-OMe-Ac-C Phosphoramidite	27-2043
TheraPure 2'-OMe-U Phosphoramidite	27-2044
TheraPure 2'-OMe-iBu-G Phosphoramidite	27-2046
TheraPure 2'-MOE phosphoramidites	
TheraPure 2'-MOE-A Phosphoramidite	27-1019
TheraPure 2'-MOE-5mC Phosphoramidite	27-1020
TheraPure 2'-MOE-G Phosphoramidite	27-1022
TheraPure 2'-MOE-T Phosphoramidite	27-1021
TheraPure 2'-fluoro phosphoramidites	
TheraPure 2'-Fluoro-Bz-A Phosphoramidite	27-1601
TheraPure 2'-Fluoro-U Phosphoramidite	27-1602
TheraPure 2'-Fluoro-Acetyl-C Phosphoramidite	27-1604
TheraPure 2'-Fluoro-iBu-G Phosphoramidite	27-1607
Fast deprotect DNA phosphoramidites	
PAC-dA Phosphoramidite	27-1723
iBu-dC Phosphoramidite	27-1725
iPrPAC-dG Phosphoramidite	27-1726
DMF-dG Phosphoramidite	27-1737
Ac-dC Phosphoramidite	29-1727
Structural phosphoramidites	
dU Phosphoramidite	27-1738
dl Phosphoramidite	27-1744
N6-Me-dA Phosphoramidite	27-1746
5-Me-dC Phosphoramidite	27-1748
TFA Amino Linker Phosphoramidite	27-1792
Phosphorylating Phosphoramidite	27-1794
5'-Aminohexyl Linker Phosphoramidite	27-0035
N4-Ethyl-dC Phosphoramidite	27-1743
5'-Biotin Phosphoramidite	27-1793

Product	Cat. No.
TheraPure locked nucleic acids	
TheraPure Locked Nucleic Acid A (Bz) Phosphoramidite	27-1340
TheraPure Locked Nucleic Acid 5-Me-C (Bz) Phosphoramidite	27-1348
TheraPure Locked Nucleic Acid G (DMF) Phosphoramidite	27-1347
TheraPure Locked Nucleic Acid T Phosphoramidite	27-1346
Standard DNA phosphoramidites	
dA β-Cyanoethyl Phosphoramidite	27-1730
dC β-Cyanoethyl Phosphoramidite	27-1732
dG β-Cyanoethyl Phosphoramidite	27-1734
T β-Cyanoethyl Phosphoramidite	27-1736
5-Me-dC β-Cyanoethyl Phosphoramidite	27-1748
Standard RNA phosphoramidites	
Bz-rA Phosphoramidite	27-1403
rU Phosphoramidite	27-1404
Ac-rC Phosphoramidite	27-1405
iBu-rG Phosphoramidite	27-1406
Standard 2'-OMe phosphoramidites	
2'-OMe-PAC-A Phosphoramidite	27-1822
2'-OMe-Ac-C β-Cyanoethyl Phosphoramidite	27-1823
2'-OMe-U β-Cyanoethyl Phosphoramidite	27-1825
2'-OMe-iPrPAC-G Phosphoramidite	27-1826
2'-OMe-Bz-A β-Cyanoethyl Phosphoramidite	27-1842
2'-OMe-iBu-G β-Cyanoethyl Phosphoramidite	27-1846
DyLight dye-labeled phosphoramidites	
DyLight DY547 Phosphoramidite	SY6332
DyLight DY647 Phosphoramidite	SY6334
DyLight DY677 Phosphoramidite	SY6336
DyLight 3 Phosphoramidite	SY6333
DyLight 5 Phosphoramidite	SY6335
DyLight Fluorescein Phosphoramidite	27-1606
DyLight FAM-6 Phosphoramidite	27-1608
RNA CPG synthesis supports	
PAC-rA CPG Synthesis Support	SY6503
rU-CPG Synthesis Support	SY6504
Ac-rC CPG Synthesis Support	SY6505
iPrPAC-rG CPG Synthesis Support	SY6506
Succinates	
Bz-dA Succinate	27-0030
Bz-dC Succinate	27-0032
iBu-dG Succinate	27-0034
T Succinate	27-0036

Make us a part of your team—contact an OEM specialist at **thermofisher.com/amidites** 

