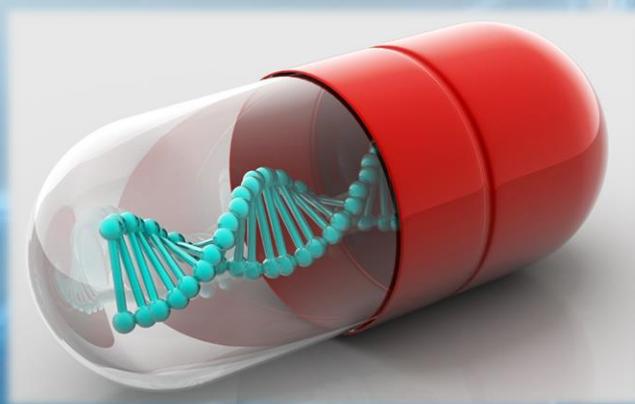


## Reagents for Nucleic Acid Synthesis



### ***Product features***

- Lineup of ancillary reagents for phosphoramidite method
- Provides products with guaranteed low water content based on advanced dehydration technology
- Customizable composition and scale-up
- Labels in different colors by reagent type to avoid mix-ups

### **Product Line-up**

- Deblocking Reagents
- Activators
- Capping Reagents
- Oxidation Reagents
- Sulfurizing Reagents
- Phosphoramidites
- Solvents
- Purification Products
- Common Chemicals

# Contents

**Introduction, Nucleic acid synthesis** p. 1-4

---

**Ancillary Reagents** p. 5-12

---

- Deblocking Reagents
- Activators
- Capping Reagents
- Oxidation Reagents
- Sulfurizing Reagents
- ÄKTA oligopilot Reagents

**Phosphoramidites** p. 13-14

---

**Dehydrated solvents** p. 15

---

**Reagents for amidite synthesis** p. 16

---

- Tritylation Reagents
- Base Reagents
- Silylation Reagents
- Phosphorylation Reagents

**Cleavage / Deprotection Reagents** p. 17-18

---

- Cleavage/Deprotection of nucleobase moieties
- Deprotection of phosphate moieties
- Deprotection of 2' protecting group

**Purification Products** p. 19-20

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- Solid-Phase Extraction Column
- HPLC Column
- Eluents

**Common Chemicals** p. 21

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- Drying Traps

# Introduction, Nucleic acid synthesis

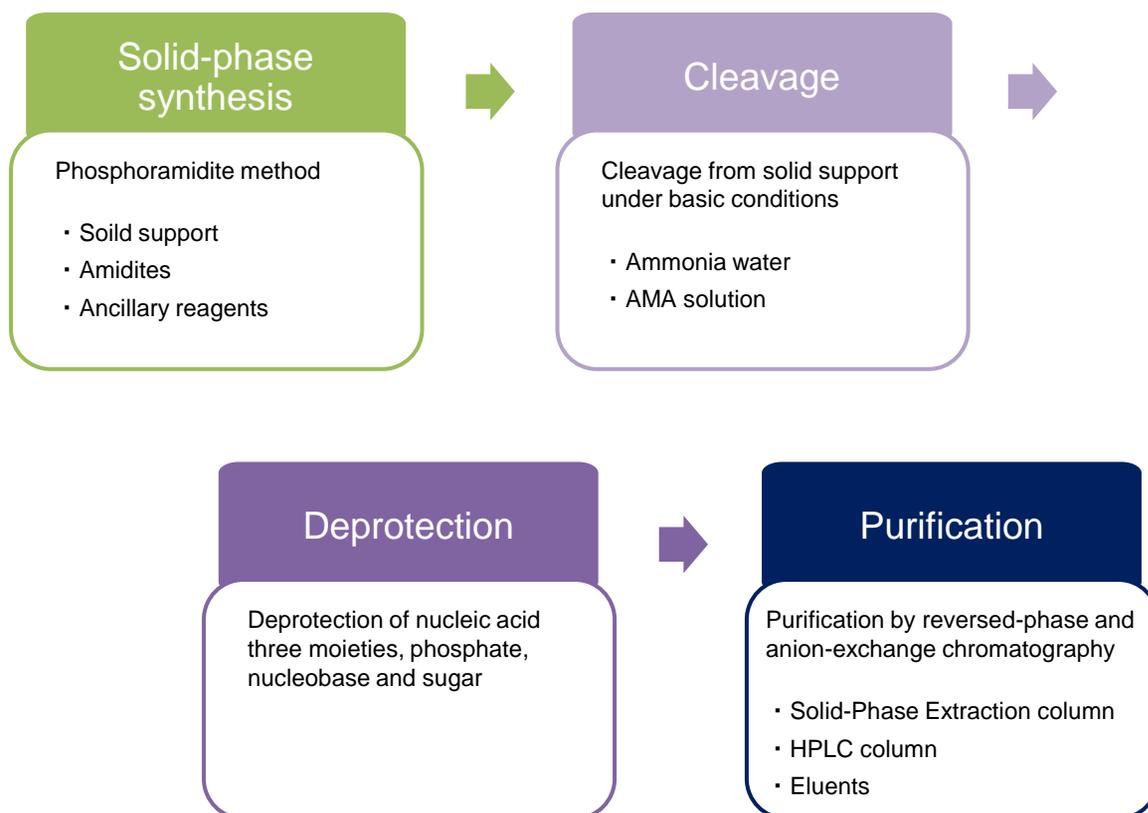
## Introduction

Our lineup of nucleic acid synthesis reagents focuses on ancillary reagents and dehydration solvents for use in the synthesis of oligonucleotides using the phosphoramidite method. We provide reagents of suitable quality for nucleic acid synthesis by leveraging our unique liquid preparation, synthesis, dehydration, and analysis technologies developed over years of reagent manufacturing.

## Nucleic acid

“Nucleic acids” are a collective term for deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). Its constituent molecule is an oligonucleotide, a structure of bases, sugars, and phosphates linked by phosphodiester bonds. “Nucleic acid medicine,” which has attracted considerable attention in recent years, uses DNA and RNA molecules, which are the carriers of genetic information in living organisms, as drugs. There is a high expectation that this approach will lead to next-generation drugs because they can act on biological molecules that cannot be targeted by conventional small-molecule agents or antibody drugs.<sup>1)</sup> Another characteristic is that oligonucleotides, the main component of “nucleic acid drugs,” can be manufactured by organic synthesis (mainly solid-phase synthesis) using an automated synthesizer.

## Synthesis of oligonucleotide by solid-phase synthesis ~ Purification flow



# Nucleic Acid Synthesis Method

## Phosphoramidite method

The traditional method for synthesizing oligonucleotides is called the phosphoramidite method, which is a form of solid-phase synthesis that involves the addition of a phosphoramidite monomer (monoamide of phosphite diester) to a solid-phase support. The fundamental reaction to bind the amidite, which is a nucleic acid monomer, consists of 4 steps:

Step 1 detritylation → Step 2 amidite coupling reaction → Step 3 capping reaction → Step 4 oxidation or sulfurization. A cycle consisting of these 4 steps is repeated until the desired strand length is obtained (see Figure 1). An automated synthesizer is used for this reaction.

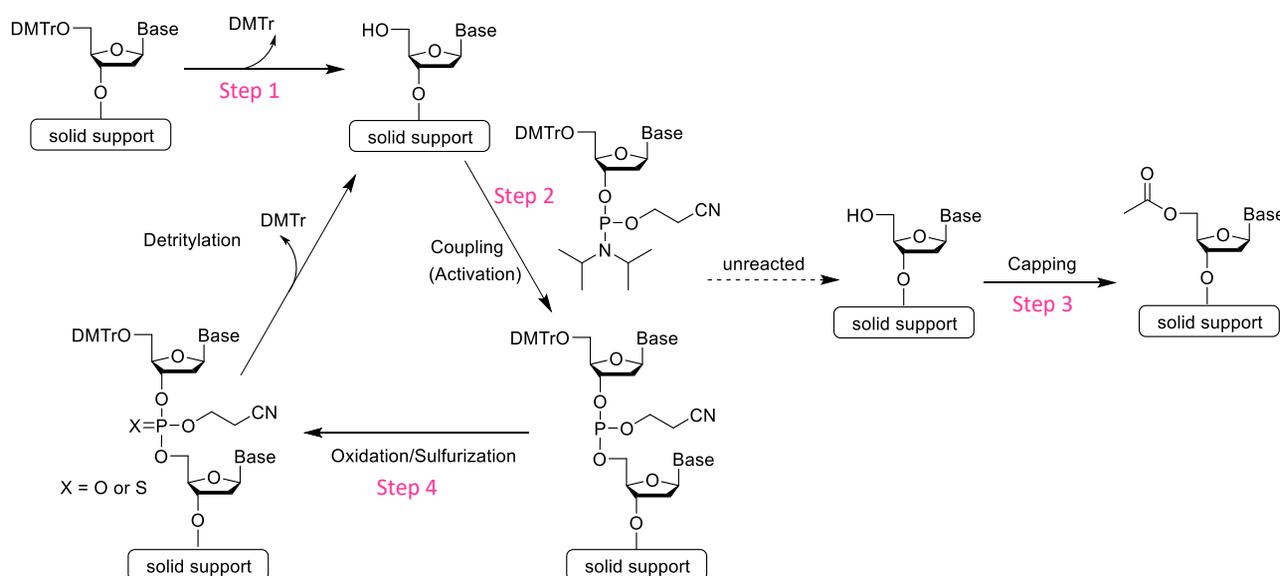
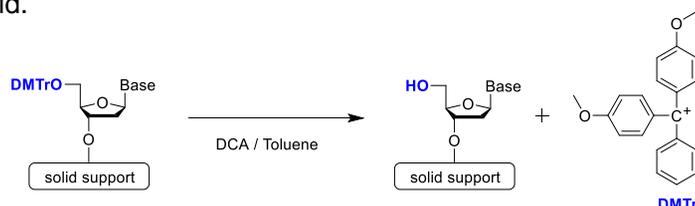


Fig 1. Reaction mechanism of phosphoramidite method

## Reactions and reagents for the phosphoramidite method<sup>2)</sup>

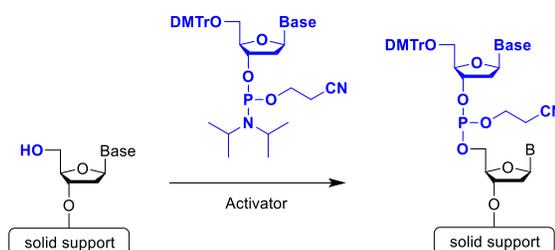
### Step 1 Detritylation

Step 1 is detritylation. 4,4'-Dimethoxytrityl group (DMTr group) is often used to protect the hydroxy group at the 5' position. Since the trityl cation is stabilized by two methoxy groups, it can be easily cleaved by treatment with a weak acid. Dichloroacetic acid or trichloroacetic acid is used as the acid.



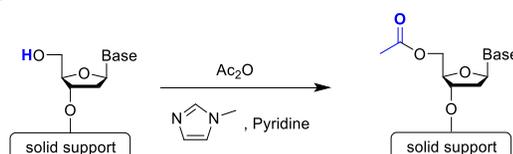
### Step 2 Coupling Reaction (Activation)

Step 2 is the coupling reaction. Condensation occurs between the nucleotide unit to be bound and the nucleoside on the solid support or the oligonucleotide being synthesized. In general, 5-Benzylthio-1*H*-tetrazole (BTT), 5-Ethylthio-1*H*-tetrazole (ETT), or 4,5-Dicyanoimidazole (DCI) is used to activate phosphoramidite.



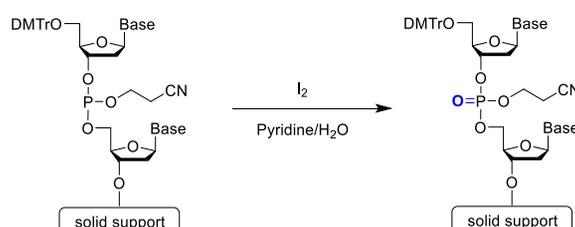
### Step 3 Capping Reaction

Step 3 is the capping reaction. In the phosphoramidite method, an incomplete oligo that has one less base than the desired oligonucleotide may be formed if the coupling reaction does not progress completely and proceeds to the next step with an unreacted hydroxy group remaining. Therefore, the 5'-OH group of the unreacted strand is acetylated to prevent elongation reaction.



### Step 4 Oxidation

Step 4 is oxidation. A phosphite ester bond is formed during phosphoramidite coupling. This is slightly unstable and may cause a side reaction during further elongation reactions. To prevent this, it is converted into a stable phosphate ester. Iodine (I<sub>2</sub>) is the most commonly used oxidizing reagent.



## Purification process of nucleic acid

The oligonucleotide synthesized by solid-phase synthesis is retained on the solid support and is thus cleaved using a base. The protecting groups that were introduced into reactive substituent groups during oligonucleotide synthesis cycles to avoid their participation in coupling are deprotected to complete the reaction. After cleavage and deprotection, the crude material is separated and purified by reversed-phase or anion-exchange chromatography to obtain the desired oligonucleotide.<sup>3)</sup>

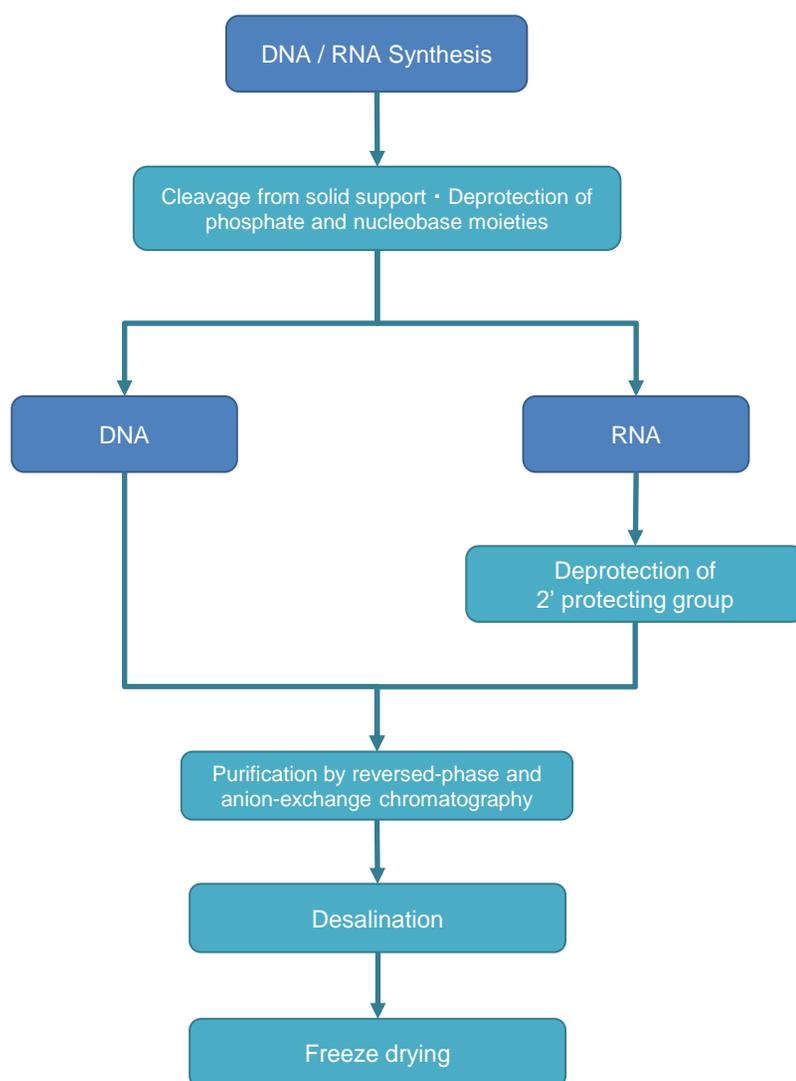


Fig 2. Separation/purification process after DNA/RNA synthesis

# Ancillary reagents

- Features**
- Lineup of ancillary reagents for phosphoramidite method
  - Provides products guaranteed to have a low water content based on advanced dehydration technology
  - Supports customization of concentration and composition
  - Supports scale-up and mass production



Fig 3. Reagent bottles and rabel colors.

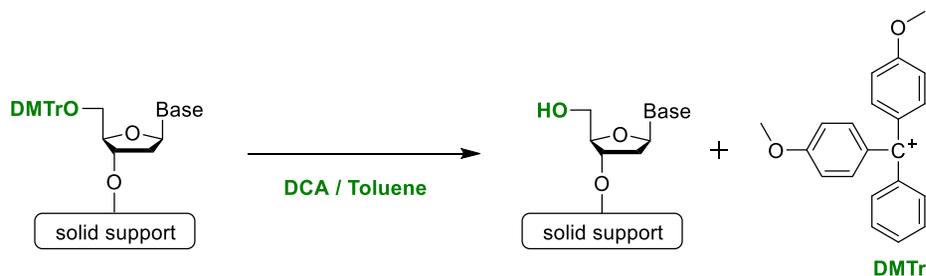
## Labels of different colors used for each reagent type to avoid mix-ups

 <p><b>Deblocking Reagents</b></p>	 <p><b>Activators</b></p>	 <p><b>Capping Reagents (Cap A)</b></p>
		
 <p><b>Capping Reagents (Cap B)</b></p>	 <p><b>Oxidation Reagents</b></p>	 <p><b>Sulfurizing Reagents</b></p>
		

## Cap connection between reagent bottles and automated synthesizers

- The glass gallon container used for our 3 L packaging does not fit the bottle cap provided with ÄKTA oligopilot. Before use, transfer it to a container with the GL45 screw thread.

## Deblocking Reagents



### Toluene

Code No.	Product Name	Pkg. Size	Water Content	Storage Condition
045-34445	Deblocking Solution [Dichloroacetic Acid-Toluene (3:97)]	500 mL	≤ 200ppm	Keep at RT
043-34441		3 L		
047-34525	Deblocking Solution [Dichloroacetic Acid-Toluene (5:95)]	500 mL	≤ 500ppm	Keep at RT
045-34521		3 L		
040-34515	Deblocking Solution [Dichloroacetic Acid-Toluene (10:90)]	500 mL	≤ 0.1%	Keep at RT
048-34511		3 L		

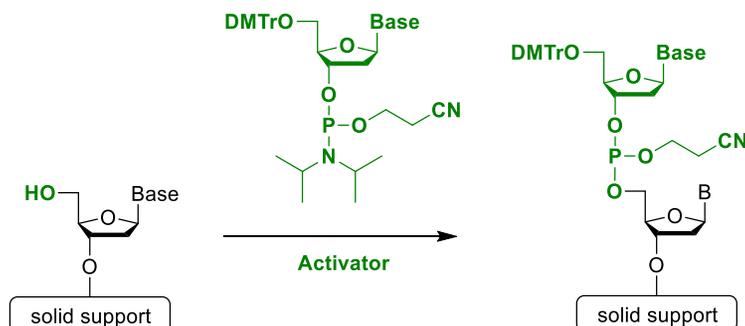
### DCM

Code No.	Product Name	Pkg. Size	Water Content	Storage Condition
048-28923	Deblocking Solution-1 (3w/v% Trichloroacetic Acid, Dichloromethane Solution)	1 L	≤ 40ppm	Keep at RT
042-28921		3 L		
042-28926		3 Lx4		

• For preparation at the time of use, use the following reagent

Code No.	Product Name	Pkg. Size	Water Content	Storage Condition
200-02402	Trichloroacetic Acid	25 g	—	Keep at RT
202-02401		100 g		
204-02405		500 g		
044-31235	Dichloromethane, Super Dehydrated	500 mL	≤ 10ppm	Keep at RT
048-31233		3 L		
040-16653	Dichloroacetic Acid	25 mL	—	Keep at RT
044-16656		500 mL		
204-17915	Toluene, Super Dehydrated	500 mL	≤ 10ppm	Keep at RT
206-17914		3 L		

## Activators



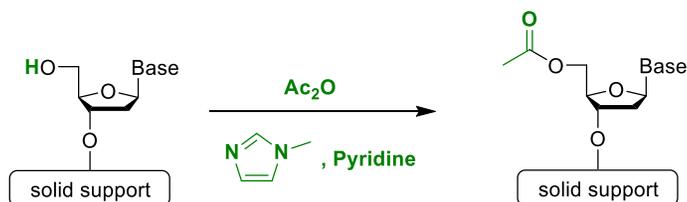
### Powder / Solid

Code No.	Product Name	Structure	CAS RN®	Pkg. Size	Water Content	Storage Condition
044-34851	4,5-Dicyanoimidazole		1122-28-7	5 g	≤300ppm	Keep at RT
042-34852				25 g		
046-34855				500 g		
051-09491	5-Ethylthio-1 <i>H</i> -tetrazole		89797-68-2	5 g	≤300ppm	Keep at RT
059-09492				25 g		
053-09495				500 g		
130-19221	<i>N</i> -Methylbenzimidazolium Trifluoromethanesulfonate		361447-89-4	5 g	≤300ppm	Keep at RT
138-19222				25 g		
161-29041	<i>N</i> -(Phenyl)imidazolium Trifluoromethanesulfonate		361447-81-6	5 g	≤300ppm	Keep at RT
169-29042				25 g		

### Solution

Code No.	Product Name	Structure	CAS RN®	Pkg. Size	Water Content	Storage Condition
013-19685	Activator Solution-1 (0.25 mol/L 4,5-Dicyanoimidazole, Acetonitrile Solution)		1122-28-7	500 mL	≤30ppm	Keep at RT
011-19681				3 L		
011-19701	Activator Solution-2 (0.45 mol/L 1 <i>H</i> -Tetrazole, Acetonitrile Solution)		288-94-8	3 L	≤30ppm	Keep at RT
015-20015	Activator Solution-3 (0.25 mol/L 5-Benzylthio-1 <i>H</i> -tetrazole, Acetonitrile Solution)		21871-47-6	500 mL	≤30ppm	Keep at RT
013-20011				3 L		
010-19695	Activator Solution-4 (0.25 mol/L 5-Ethylthio-1 <i>H</i> -tetrazole, Acetonitrile Solution)		89797-68-2	500 mL	≤30ppm	Keep at RT
012-19699				2.5 L		
018-19691				3 L		
012-19694				3 Lx4		

## Capping Reagents



### THF

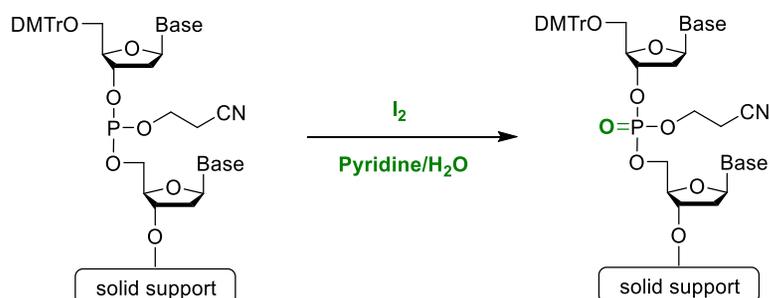
Code No.	Product Name	Pkg. Size	Water Content	Storage Condition
036-18991	Cap A Solution-1 (10vol% Acetic anhydride/Tetrahydrofuran Solution)	3 L	≤ 100ppm	Keep at RT
032-18993		3 Lx4		
033-19001	Cap B Solution-1 [Tetrahydrofuran/1-Methylimidazole/Pyridine (8:1:1) Solution]	3 L	≤ 100ppm	Keep at RT
039-19003		3 Lx4		
030-19011	Cap A Solution-2 [Tetrahydrofuran/Acetic Anhydride/Pyridine (8:1:1) Solution]	3 L	≤ 100ppm	Keep at RT
034-19014		3 Lx4		
037-19021	Cap B Solution-2 (10vol% 1-Methylimidazole/Tetrahydrofuran Solution)	3 L	≤ 100ppm	Keep at RT
031-19024		3 Lx4		

### Acetonitrile

Code No.	Product Name	Pkg. Size	Water Content	Storage Condition
036-25385	Cap B1 Solution [Acetic Anhydride-Acetonitrile (4:6)]	500 mL	—	Keep at RT
034-25381		3 L		
039-25635	Cap B2 Solution [Pyridine-Acetonitrile (6:4)]	500 mL	≤ 100ppm	Keep at RT
033-25633		3 L		
039-25375	Cap B2 Solution [2,6-Lutidine-Acetonitrile (6:4)]	500 mL	≤ 100ppm	Keep at RT
031-25374		2.5 L		
037-25371		3 L		
034-25401	Cap B Solution [Acetic Anhydride-2,6-Lutidine-Acetonitrile (2:3:5)]	3 L	—	Keep at RT



## Oxidation Reagents



### THF

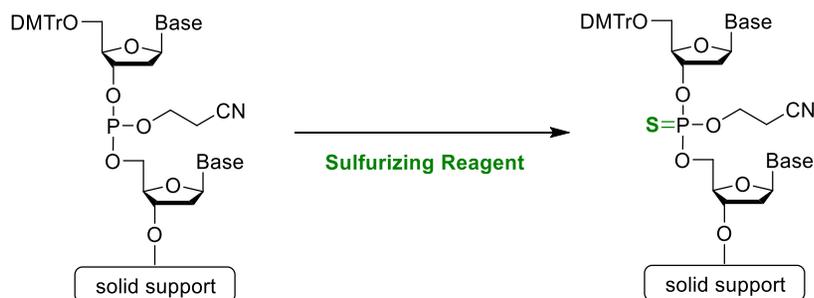
Code No.	Product Name	Pkg. Size	Water Content	Storage Condition
156-02451	Oxidizing Solution-2 [0.1 mol/L I <sub>2</sub> · THF:Pyridine:Water(78:20:2)Solution]	3 L	—	Keep at RT
152-02453		3 Lx4		

### THF free

Code No.	Product Name	Pkg. Size	Water Content	Storage Condition
150-03515	Oxidizing Solution [Iodine Solution (abt. 0.05 mol/L)][Pyridine:Water(9:1)]	500 mL	—	Keep at RT
158-03516		2.5 L		
158-03511		3 L		

## Sulfurizing Reagents

Chemical modifications of the nucleic acid phosphate moiety include phosphorothioate modification where O (oxygen atom) is substituted by S (sulfur atom). In nucleic acid medicine, sulfurizing modification is used mainly for antisense drugs.<sup>4)</sup> Phosphorothioate synthesis is achieved by having a sulfurizing reagent act on the phosphite ester formed by a coupling reaction.



### Powder / Solid

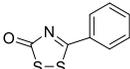
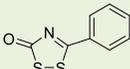
Code No.	Product Name	Structure	CAS RN®	Pkg. Size	Water Content	Storage Condition
324-72121	3 <i>H</i> -1,2-Benzodithiol-3-one 1,1-Dioxide 【Beaucage reagent】		66304-01-6	500 mg	—	Keep at 2-10 degrees C.
027-19422	Bis(phenylacetyl) Disulfide 【PADS】		15088-78-5	25 g	—	Keep at RT
021-19425				500 g		
166-28251	5-Phenyl-3 <i>H</i> -1,2,4-dithiazol-3-one		7047-10-1	5 g	≤200ppm	Keep at 2-10 degrees C.
164-28252				25 g		
168-28255				500 g		



The most commonly used reagent, DDTT, is highly crystalline and hardly dissolves in acetonitrile, the reaction solvent. Therefore, acetonitrile is spiked with pyridine to increase its solubility. On the other hand, 5-phenyl-3*H*-1,2,4-dithiazole-3-one shows favorable solubility in acetonitrile and is thus a convenient sulfurizing reagent that can be used pyridine-free.

## Sulfurizing Reagents

### Solution

Code No.	Product Name	Structure	CAS RN®	Pkg. Size	Water Content	Storage Condition
199-18751	Sulfurizing Solution (0.05 mol/L 5-Phenyl-3 <i>H</i> -1,2,4-dithiazol-3-one, Acetonitrile Solution)		7047-10-1	100 mL	—	Keep at RT
191-18755				500 mL		
192-18741	Sulfurizing Solution (0.1 mol/L 5-Phenyl-3 <i>H</i> -1,2,4-dithiazol-3-one, Acetonitrile Solution)		7047-10-1	100 mL	—	Keep at RT
194-18745				500 mL		

Our sulfurizing solutions are distributed after the stability of the compound in organic solvents is confirmed.

#### [Notes]

1. Sulfurizing reagents manufactured by FUJIFILM Wako Pure Chemical Corporation or FUJIFILM Wako Chemical Corporation are distributed for research-only purposes. If you are seeking products for commercial use, please refer to the related patents of the compound.
2. Code No. 324-72121 is distributed as a non-standard product without specific limitations on its use. Please refer to related patents of the compound if you intend to use it for nucleic acid synthesis.

## Reagents for ÄKTA oligopilot

### Features

- Composition for automated synthesizer ÄKTA oligopilot (Cytiva)
- Free from THF which may cause deterioration of the synthesizer flow channel
- Can be supplied from laboratory to industrial scale



Fig 4. ÄKTA oligopilot

Code No.	Product Name	Pkg. Size	Water Content	Storage Condition
<b>Deblocking Reagents</b>				
043-34441	Deblocking Solution [Dichloroacetic Acid-Toluene (3:97)]	3 L	≤200ppm	Keep at RT
045-34521	Deblocking Solution [Dichloroacetic Acid-Toluene (5:95)]	3 L	≤500ppm	Keep at RT
048-34511	Deblocking Solution [Dichloroacetic Acid-Toluene (10:90)]	3 L	≤1000ppm	Keep at RT
<b>Activators</b>				
011-19681	Activator Solution-1 (0.25 mol/L 4,5-Dicyanoimidazole, Acetonitrile Solution)	3 L	≤30ppm	Keep at RT
011-19701	Activator Solution-2 (0.45 mol/L 1 <i>H</i> -Tetrazole, Acetonitrile Solution)	3 L	≤30ppm	Keep at RT
013-20011	Activator Solution-3 (0.25 mol/L 5-Benzylthio-1 <i>H</i> -tetrazole, Acetonitrile Solution)	3 L	≤30ppm	Keep at RT
012-19699	Activator Solution-4 (0.25 mol/L 5-Ethylthio-1 <i>H</i> -tetrazole, Acetonitrile Solution)	2.5 L	≤30ppm	Keep at RT
<b>Capping Reagents</b>				
034-25381	Cap B1 Solution [Acetic Anhydride-Acetonitrile (4:6)]	3 L	—	Keep at RT
033-25633	Cap B2 Solution [Pyridine-Acetonitrile (6:4)]	3 L	≤100ppm	Keep at RT
031-25374	Cap B2 Solution [2,6-Lutidine-Acetonitrile (6:4)]	2.5 L	≤100ppm	Keep at RT
034-25401	Cap B Solution [Acetic Anhydride-2,6-Lutidine-Acetonitrile (2:3:5)]	3.0 L	—	Keep at RT
<b>Oxidation Reagents</b>				
158-03516	Oxidizing Solution [Iodine Solution (abt. 0.05mol/L)][Pyridine:Water(9:1)]	2.5 L	—	Keep at RT

## Provides high-quality phosphoramidite

### Features

- Supports small scale to bulk scale
- Supplies company-specific products in containers compatible with each synthesizer, such as ABI, Expedite, MerMade, and ÄKTA oligopilot

## Modified phosphoramidite

Nucleic acid drugs have chemical modifications of the nucleobase, phosphate, or sugar moiety for functional improvements, such as acquisition of nuclease resistance and improvement of binding affinity to target nucleic acids. Modifications of the sugar moiety include 2'-position modifications and bridging modifications.

2'-Fluoro (2'-F), 2'-O-methyl (2'-OMe), and 2'-O-methoxyethyl (2'-MOE) modifications are known 2'-position modifications. Kynamro<sup>®</sup>, a nucleic acid drug marketed in 2013, is a representative Gapmer-type antisense, which uses 2'-MOE at both ends (wing sites) of the oligo nucleic acid to increase binding affinity to the target RNA in addition to sulfurization to improve in vivo stability.<sup>4)5)</sup>

Bridging modifications were developed under the concept of "fixing the fluctuating conformation of the sugar moiety by bridging." The sugar moiety can be fixed to the RNA type (N type) by chemically modifying the 2'- and 4'-positions of the sugar moiety. This confers excellent binding affinity to the target complementary strand nucleic acid, and furthermore, steric hindrance due to bridging is expected to improve functionality including nuclease resistance. In 1997, 2',4'-BNA/LNA (bridged nucleic acid) was developed by Imanishi, Obika, and others from the School of Pharmaceutical Sciences, Osaka University.<sup>4)5)</sup>

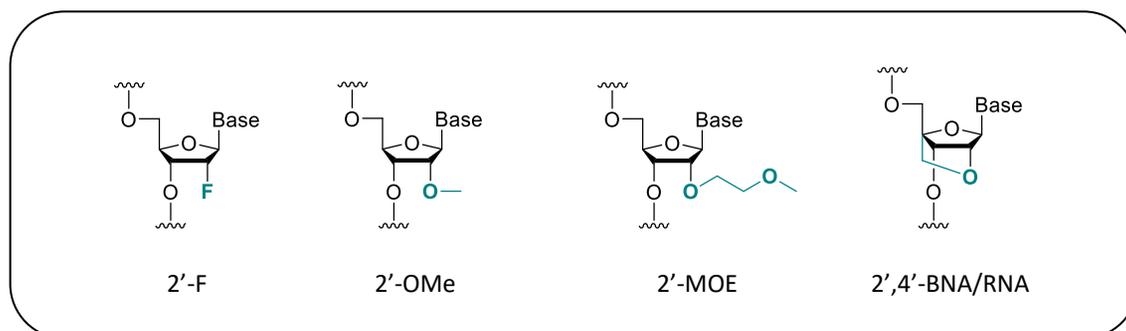
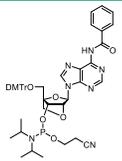
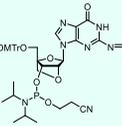
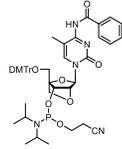
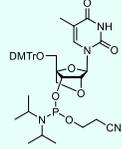


Fig 5. Structure of modified nucleic acids

## Locked Nucleic Acid

Code No.	Product Name	Structure	CAS RN®	Pkg. Size	Water Content	Storage Condition
128-06771	Locked Nucleic Acid-A(Bz) Cyanoethyl Phosphoramidite (mixture of isomers)		206055-79-0	1 g	≤0.5%	Keep at -20 degrees C.
124-06773				5 g		
125-06781	Locked Nucleic Acid-G(DMF) Cyanoethyl Phosphoramidite (mixture of isomers)		709641-79-2	1 g	≤0.5%	Keep at -20 degrees C.
121-06783				5 g		
122-06791	Locked Nucleic Acid-mC(Bz) Cyanoethyl Phosphoramidite (mixture of isomers)		206055-82-5	1 g	≤0.5%	Keep at -20 degrees C.
128-06793				5 g		
125-06801	Locked Nucleic Acid-T Cyanoethyl Phosphoramidite (mixture of isomers)		206055-75-6	1 g	≤0.5%	Keep at -20 degrees C.
121-06803				5 g		

We supply locked nucleic acids in containers (glass bottles) that meet our specifications.

# Dehydrated solvents

## Acetonitrile (Low moisture guaranteed)

### Features

- Water content  $\leq 10$ ppm guaranteed, optimal for nucleic acid synthesis due to minimal water content
- Absorbance guaranteed (260 nm, 280 nm, 400 nm)
- Can be supplied from laboratory to industrial scale

Code No.	Product Name	Pkg. Size	Water Content	Storage Condition
017-27111	Acetonitrile, Super Dehydrated	3 L	$\leq 10$ ppm	Keep at RT
015-27117		18 L		

### [ Notes ]

1. Acetonitrile is available in 3 L glass bottle and returnable container for larger volumes.
2. Returnable containers made 304 stainless steel. Coupler size is 18 L (2P on gas side, 3P on liquid side), 100L (3P on gas side, 4P on liquid side).
3. Please use up the reagents completely and return it to the agency immediately after use.



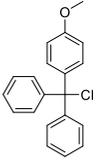
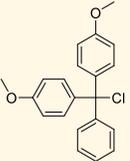
Fig 6. Image of container  
(left : 3L glass bottle, center / right : stainless containers)

In addition to acetonitrile, we provide solvents with guaranteed low water content for organic synthesis.

Code No.	Product Name	Pkg. Size	Water Content	Storage Condition
167-18455	Pyridine, Dehydrated	500 mL	$\leq 50$ ppm	Keep at RT
165-18451		3 L		
204-17915	Toluene, Super Dehydrated	500 mL	$\leq 10$ ppm	Keep at RT
206-17914		3 L		

# Reagents for amidite synthesis

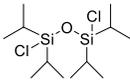
## Tritylation Reagents

Code No.	Product Name	Structure	CAS RN®	Pkg. Size	Storage Condition
130-19282	4-Methoxytrityl Chloride		14470-28-1	25 g	Keep at RT
132-19281				100 g	
046-34872	4,4'-Dimethoxytrityl Chloride		40615-36-9	25 g	Keep at RT
048-34871				100 g	

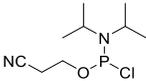
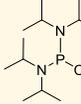
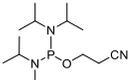
## Base Reagents

Code No.	Product Name	Pkg. Size	Storage Condition
059-05352	<i>N</i> -Ethyl-diisopropylamine 【DIPEA】	25 mL	Keep at RT
164-05312	Pyridine	25 mL	Keep at RT

## Silylation Reagents

Code No.	Product Name	Structure	CAS RN®	Pkg. Size	Storage Condition
043-34681	1,3-Dichloro-1,1,3,3-tetraisopropyl- <i>disiloxane</i>		69304-37-6	5 g	Keep at RT
041-34682				25 g	

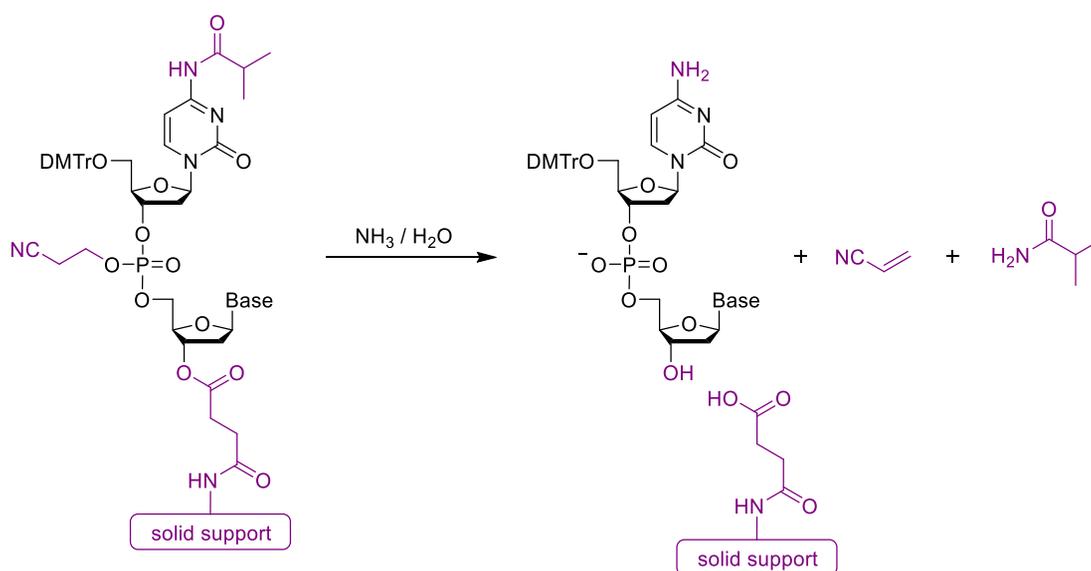
## Phosphorylation Reagents

Code No.	Product Name	Structure	CAS RN®	Pkg. Size	Storage Condition
037-25751	2-Cyanoethyl <i>N,N</i> -Diisopropylchloro phosphoramidite		89992-70-1	1 g	Keep at 2-10 degrees C.
033-25753				5 g	
028-19751	Bis(diisopropylamino) chlorophosphine		56183-63-2	5 g	Keep at 2-10 degrees C.
026-19752				25 g	
035-25671	2-Cyanoethyl <i>N,N,N,N</i> -Tetraisopropyl phosphordiamidite		102691-36-1	5 g	Keep at -20 degrees C.

# Cleavage / Deprotection Reagents

## Cleavage/Deprotection of nucleobase moieties

The crude oligonucleotide obtained by solid-phase synthesis remains bound to the solid support. After synthesis, it is cleaved from the solid support by ester hydrolysis with a base such as concentrated ammonia water. At the same time, the protecting group introduced into the amino group of the nucleobase moiety is removed under basic conditions. Instead of concentrated ammonia water, methylamine solution, AMA solution (a mixture of concentrated ammonia water and methylamine solution), or potassium carbonate/methanol solution may be used for this reaction depending on the type of protecting group.

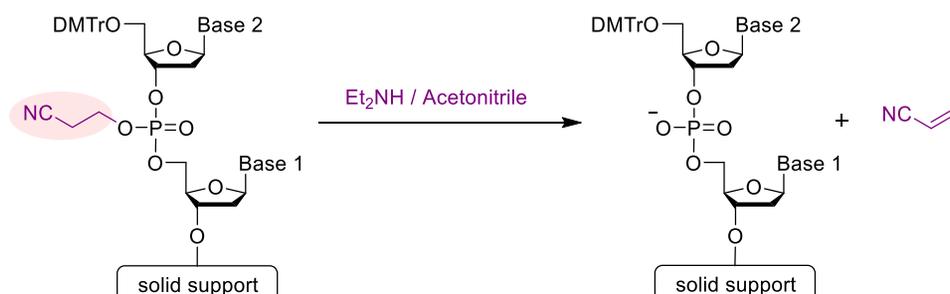


Code No.	Product Name	Pkg. Size	Storage Condition
017-03176	25% Ammonia Solution	500 mL	Keep at RT
132-01856	40% Methylamine Solution	500 mL	Keep at RT

## Deprotection of phosphate moieties

### I Deprotection of 2-cyanoethyl group

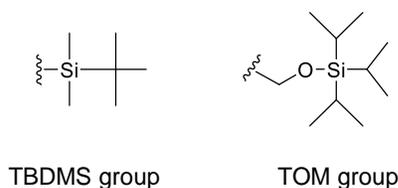
The 2-cyanoethyl group, which protects the phosphate moiety, generates acrylonitrile as a by-product when deprotected with concentrated ammonia water. Acrylonitrile may cause 2-cyanoethylation through addition reaction to the nucleobase moiety. As a method to avoid the side reaction of acrylonitrile, a weak base reagent such as diethylamine/acetonitrile solution, instead of generally used concentrated ammonia water, can be used to deprotect the 2-cyanoethyl group while maintaining binding with the solid support, followed by cleavage from the solid support and deprotection of the protecting group of the nucleobase moiety.



Code No.	Product Name	Pkg. Size	Storage Condition
045-34825	20% Diethylamine Acetonitrile Solution	500 mL	Keep at RT
017-27111	Acetonitrile, Super Dehydrated	3 L	Keep at RT

### Deprotection of 2' protecting group

For the purpose of RNA synthesis, the hydroxy group at the 2'-position of the sugar moiety is also protected. A *tert*-butyldimethylsilyl group (TBDMS group) or triisopropylsilyloxymethyl group (TOM group) is commonly used as the protecting group. Both TBDMS and TOM groups can be deprotected by treatment with fluoride ions such as tetrabutylammonium (TBAF) solution.<sup>3)</sup>



Code No.	Product Name	Pkg. Size	Storage Condition
208-20201	Tetrabutylammonium Fluoride, Tetrahydrofuran Solution (ca. 1 mol/L) 【TBAF】	100 mL	Keep at 2-10 degrees C.
200-20205		500 mL	
352-34922	Triethylamine Trihydrofluoride	25 g	Keep at RT
350-34923		100 g	

# Purification Products

Liquid chromatography-based nucleic acid separation is widely used for oligonucleotide purification and analysis. Reversed-phase chromatography is based on the principle of separation using differences in hydrophobicity and uses a support of silica gel C18. Anion-exchange chromatography is based on the principle of separation using the polyanionic nature of nucleic acids and uses a support of an anion-exchange resin (rigid polymer, etc.) that is positively charged to capture anions.<sup>3)</sup>

## Solid-Phase Extraction column (SPE column)

Solid-phase extraction is a separation and purification technique to extract and purify the target material using a small-sized column packed with a silica gel or polymer gel support. During oligonucleotide pretreatment, the synthesized crude material is passed through a simple reversed-phase resin column (solid-phase extraction column) for contaminant removal and detritylation. This technique is suitable for pretreatment of small-volume samples.

Our Presep® DNA/RNA is a solid-phase extraction column suitable for oligonucleotide pretreatment. Type A uses a silica gel support and achieves high-efficiency and high-performance purification. It can be used as a sample pretreatment tool for HPLC or LC/MS analysis.

### Features

- Achieves high sample load
- Can load a sample volume 3 to 5 times larger than that of commercial pretreatment columns
- Excellent deprotection efficiency
- High purification capacity
- High recovery



Fig 7. Presep® DNA/RNA Type A

Code No.	Product Name	Pkg. Size	Storage Condition
290-36691	Presep® DNA/RNA Type A (85 mg/1 mL)	20 pieces	Keep at RT
296-36693	Synthetic scale : 0.2-0.5 $\mu$ mol	50 pieces	
290-36711	Presep® DNA/RNA Type A (255 mg/3 mL)	20 pieces	Keep at RT
296-36713	Synthetic scale : 1-1.5 $\mu$ mol	50 pieces	
292-36891	Presep® DNA/RNA Type A (1.0 g/15 mL)	10 pieces	Keep at RT
292-36911	Presep® DNA/RNA Type A (1.7 g/25 mL)	10 pieces	Keep at RT
299-36921	Presep® DNA/RNA Type A (5.1 g/70 mL)	10 pieces	Keep at RT
	Synthetic scale : 20-30 $\mu$ mol		

## HPLC column (ODS column)

Wakopak® Ultra Series C18 is a highly durable ODS column using high-purity spherical silica gel.

Code No.	Product Name	Pkg. Size	Storage Condition
235-02651	Wakopak® Ultra C18-5 $\Phi$ 4.6 mm $\times$ 150 mm (W)	1 piece	Keep at RT

## Eluents

A mixture of an organic solvent (acetonitrile, methanol, etc.) and a buffer (triethylamine-acetic acid, etc.) is used as an eluent for reversed-phase chromatography. As the buffer for nucleic acid separation, triethylamine-acetic acid, which is easily sublimated by freeze-drying, is generally used.<sup>3)</sup>

Code No.	Product Name	Pkg. Size	Storage Condition
019-08631	Acetonitrile	1 L	Keep at RT
015-08633		3 L	
202-13131	2 mol/L Triethylamine Acetate Solution pH 7.0 【 TEAA solution 】	200 mL	Keep at RT
085-06991	1,1,1,3,3,3-Hexafluoro-2-propanol	100 mL	Keep at RT
087-06995		500 mL	

The products listed below are buffer products for nucleic acid synthesis manufactured and distributed by Nippon Gene Co., Ltd. These products can be used as dissolution solvents for salts or nucleic acids to be added to nucleic acid solutions for ethanol precipitation. Since we provide a custom buffer manufacturing service, we can manufacture custom-made buffers according to your request.

Code No.	Product Name	Pkg. Size	Storage Condition
316-90081	3 M Sodium Acetate (pH 5.2)	100 mL	Keep at RT
314-90021	TE (pH8.0) [10 mmol/L Tris-HCl (pH 8.0)1 mmol/L, EDTA (pH 8.0)]	100 mL	Keep at RT
310-90023		100 mL×6	
316-90025		500 mL	
316-90101	Distilled Water, Deionized	100 mL	Keep at RT
312-90103		100 mL×6	
318-90105		500 mL	

## Drying traps

We offer zeolite packed in non-woven fabric pouches. By wrapping zeolite in non-woven fabric, crushed zeolite powder is prevented from being mixed into the solvent. After use, zeolite can be removed from the bottle with the non-woven fabric pouch, facilitating aftertreatment. Use these products for dehydration of amidite reagents or ancillary reagents.

- Shape: spherical
- 3 sizes: 3 g, 10 g, and 50 g  
⇒ Selectable according to container size
- Highly airtight aluminum outer bag (degassed inside aluminum bag)
- Non-woven fabric material: composite fiber of polypropylene/polyethylene



Fig 8. Zeolite pack each capacity

Code No.	Product Name	Pkg. Size	Storage Condition
261-02271	Zeolite Packs [Zeolite, Synthetic, A-3, Beads, 1.40-2.36 mm (8 - 12mesh)]  • Reference size of non-woven fabric 3 g : 60 mm×65 mm, 10 g : 120 mm×65 mm, 50 g : 120 mm×65 mm	3 g×20	Keep at RT
267-02273		10 g×20	
265-02274		50 g×10	

### 【Notes】

The moisture absorption capacity of synthetic zeolite is approximately 25% of its own weight. Add approximately 3 to 4 times the calculated amount of synthetic zeolite to your solvent.

Regular bottled products are also available. Please use them if non-woven fabric is not required.

Code No.	Product Name	Pkg. Size	Storage Condition
263-00575	Zeolite, Synthetic, A-3, Beads, 1.40 - 2.36 mm (8 - 12mesh)	500 g	Keep at RT
133-08645	Molecular Sieves 3A 1/8	500 g	Keep at RT
134-06095	Molecular Sieves 3A 1/16	500 g	Keep at RT

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- 2) [Biotechnology reagents] Baiotekunoroji shiyaku (in Japanese). The Chemical Daily Co., Ltd. (1989).
- 3) Hirao Ichiro., Kurumizaka Hitoshi., [Principles and protocols of nucleic acid experiments that can be selected according to purpose] Mokutekibetsu de eraberu kakusanjikken no genri to purotokoru (in Japanese). Yodosha Company, Ltd. (2011).
- 4) Takao Inoue., : *Drug Delivery System.*, 31-1, **10** (2016). (Japanese)
- 5) "*Development and Applications of Nucleic Acid Therapeutics*" ed. by Takeshi Wada., CMC Publishing Co.,Ltd. (2016). (Japanese)

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