

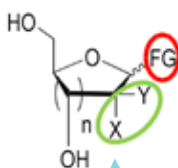


Phosphoramidites

Overview

Kolon has been supplying **refined high-purity APIs and Intermediates** using our core technology, **Sugar Chemistry**. Our sugar chemistry consists of (1) control of functional groups (2) various refinement & crystallization methods (3) scale-up experience.

KLS Sugar / Nucleoside Chemistry



Functional group: OBz, OAc, Cl, Br, etc

2-deoxy anilide: 400Ton/year

MDR: 10Ton/year

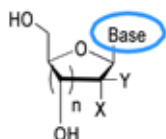
2-deoxy ribose: 400Kg/year

X, Y: H, OH, alkyl, Amine, Cl, Br, F, etc

1. 2'-modification

Monosaccharide derivatives
(Ribose, Glucose, Arabinose etc.)

2. Base modification

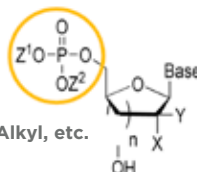


Base: Purine, Adenine, Cytosine, Uracil, Thymine, etc

Thymidine: 5Kg/Bx.

IPdR(New Drug): 8Kg/Bx

3. Phosphorylation

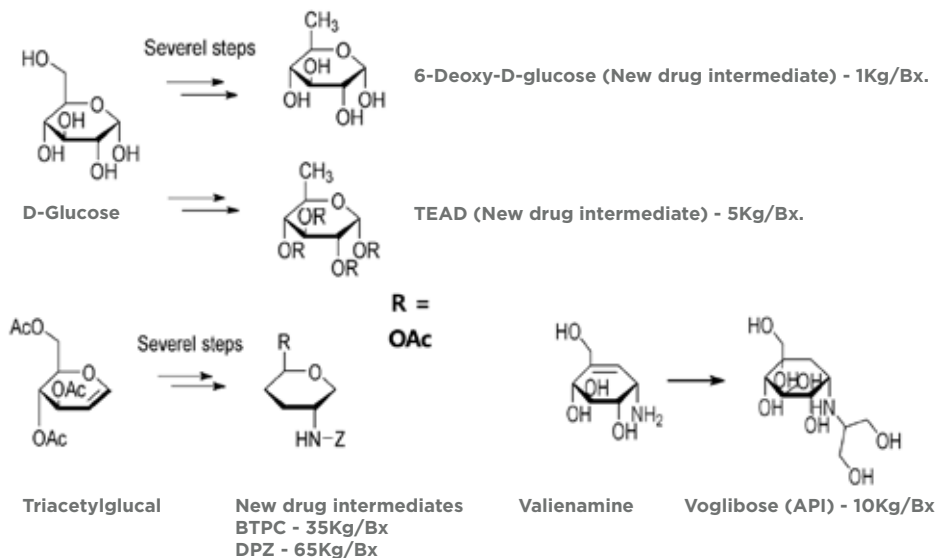


Z¹, Z²: H, OH, Alkyl, etc.

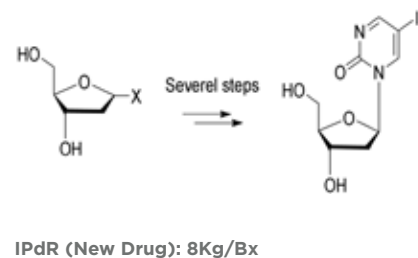
Phosphoramidate prodrug
Bucladesin: Lab Process

New Drug Intermediate / API

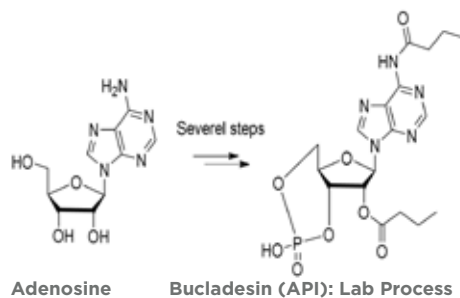
1. 2'-modification derivatives



2. Base modification



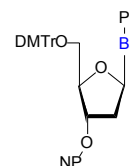
3. Phosphorylation



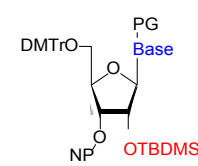
Product List

Kolon has completed the synthesis of **23 Phosphoramidites** through sugar/nucleoside chemistry. Each of them can incorporate flow chemistry, scale up, specific quality control and customization.

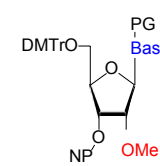
DNA Phosphoramidites



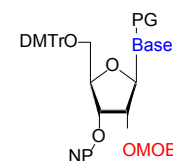
TBDMS-RNA Phosphoramidites



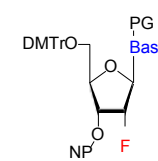
2'-Modified Phosphoramidites (2'-OMe)



2'-Modified Phosphoramidites (2'-O-MOE)



2'-Modified Phosphoramidites (2'-F)



Quality Control

As the basic quality control methods for Phosphoramidites, Kolon conducts **¹H NMR, ³¹P NMR, UV, TLC, HPLC, LC/MS, GC/MS and MASS Spectrum** are used for stricter management of impurities that has adverse effects on Oligo synthesis.

¹H NMR

³¹P NMR

UV -The UV test provides 4 values of data

TLC

HPLC
>98%

LC/MS

GC/MS

ESI-MS

Differentiation

- Securing product competitiveness through differentiated process development.
- Preoccupation of the market through early establishment of GMP process.

Stage 1. Fast Follower

- **Completion of general-purpose phosphoramidite development through competitor's product analysis.**
 - Continuously expanding the product portfolio with customer requests.
- **Promotion through collaboration with top 3 oligonucleotide makers around the world.**

Stage 2. Differentiation

- **Securing cost competitiveness through differentiated process development.**
 - Reduce manufacturing costs by developing switchable continuous manufacturing process suitable for small-scale multi-variety production.
 - Development of crystallization process to replace column process.
- **Diversification of Portfolio and development of customization.**
 - Development of a product line that can be used to manufacture oligonucleotides in the future (Diester, Triester, etc.).
 - Development of various product lines to meet customer needs (Back-bone modification, 5'-capping, etc.).

Stage 3. First Mover

- **It is scheduled to build a production facility of 300 kg per year in the Kilo-Lab Center in 2025.**
- **A production base of 3 MT per year will be established in the GMP plant in 2027.**
 - There is a high probability that regulation will be strengthened as the RNA market grows.