

# UnyLinker™ NittoPhase® Solid Support

## A Superior Universal Support for Small to Large Scale Oligonucleotide Synthesis

Nitto Denko Corporation and Kinovate Life Sciences, Inc. are pleased to announce the launch of UnyLinker loaded NittoPhase® Solid Support for Oligonucleotide Synthesis. This exciting new development combines market leading performance of NittoPhase® with the superior universal linker technology developed at Isis Pharmaceuticals to create a universal support with a proven track record of outstanding yields and purity from lab to commercial scale at a highly competitive cost.

### Features:

- Fully compatible with standard reagents and synthesis conditions
- Standard DMT group and deprotecting conditions
- Coupling efficiency  $\geq 99\%$
- Results in 3'-OH oligonucleotides
- Compatible with various chemistries to synthesize RNA oligonucleotides
- Highly competitive cost

### Advantages:

- Eliminates need to utilize multiple succinates
- Improved oligonucleotide quality
- Consistency of quality from batch to batch
- Reduced cost through streamline of inventory to one solid support
- Greater simplicity of inventory management & QC
- Does not contribute any atom to API – Product need not be classified as a starting material, greatly reducing regulatory requirements

### Applications:

- Phosphodiester DNA Oligonucleotides
- Phosphorothioate DNA Oligonucleotides
- 2'-O-Alkyl Oligonucleotides
- siRNA Oligonucleotides (under optimization)
- LNA and other modified Oligonucleotides
- Labeled Oligonucleotides

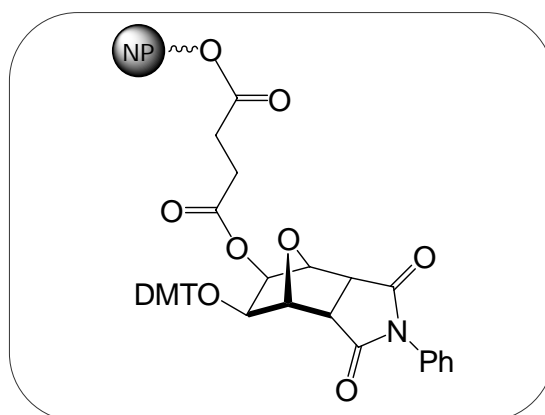


Fig. 1: Structure of UnyLinker® loaded NittoPhase®

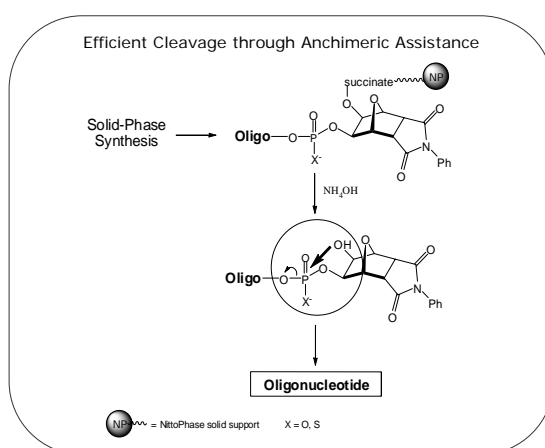


Fig. 2: Proposed Mechanism of cleavage reaction

## Performance:

### Comparative Syntheses at Lab Scale (1 mmol)

#### UnyLinker on NittoPhase®

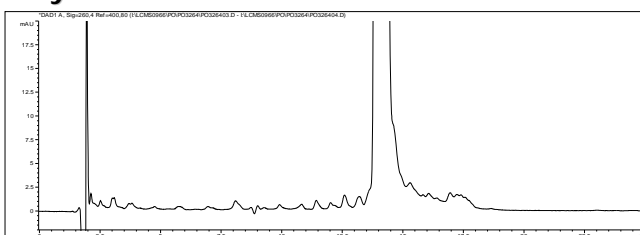


Fig 3. Ion-pair HPLC analysis of crude oligonucleotide

Sequence: Isis MOE 5-10-5 Gapmer  
Backbone: Phosphorothioate diester  
Length: 20-mer  
Support Loading: 207  $\mu$  mol/g  
Scale: 1 mmol  
Synthesizer: ÅKTA Oligopilot™100  
Column: 24 ml fixed bed column  
Crude Full Length: 75%  
Purified Yield: 4.50 mg/ $\mu$  mol  
P=O: 1.7%  
N-1: 1.4%  
Shortmer: 1.6%  
Full Length: 95.8%  
Longmer: 2.5%

#### MOE MeC Succinate on Support A

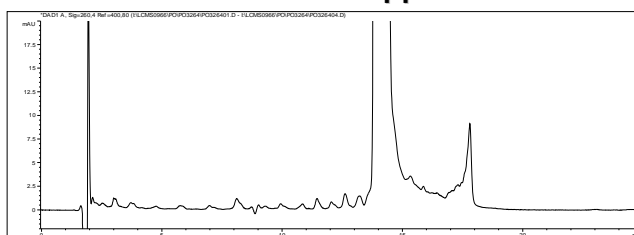


Fig 4. Ion-pair HPLC analysis of crude oligonucleotide

Sequence: Isis MOE 5-10-5 Gapmer  
Backbone: Phosphorothioate diester  
Length: 20-mer  
Support Loading: 201  $\mu$  mol/g  
Scale: 1 mmol  
Synthesizer: ÅKTA Oligopilot™100  
Column: 24 ml fixed bed column  
Crude Full Length: 74%  
Purified Yield: 3.99 mg/ $\mu$  mol  
P=O: 2.7%  
N-1: 0.8%  
Shortmer: 1.5%  
Full Length: 94.3%  
Longmer: 4.2%

### Commercial Scale Synthesis (220 mmol)

Sequence: Isis PS Oligonucleotide  
Backbone: Phosphorothioate diester  
Length: 20-mer  
Support Loading: 200  $\mu$  mol/g  
Scale: 500 mmol  
Synthesizer: ÅKTA OligoProcess™  
Column: TechniKrom® 60cm variable bed height column, 11.6L bed column  
Crude Full Length: 85%  
Purified Yield: +5% (vs Support A)  
P=O: 1.6%  
N-1: 0.4%

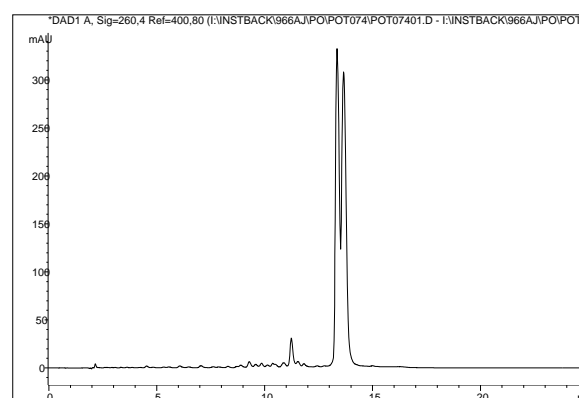


Fig 4. Ion-pair HPLC analysis of crude oligonucleotide



Kinovate Life Sciences, Inc. 501 Via del Monte, Oceanside CA, 92054  
Tel: 1-760-521-6684 Fax: 1-760-435-7050 Web: www.kinovate.com

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