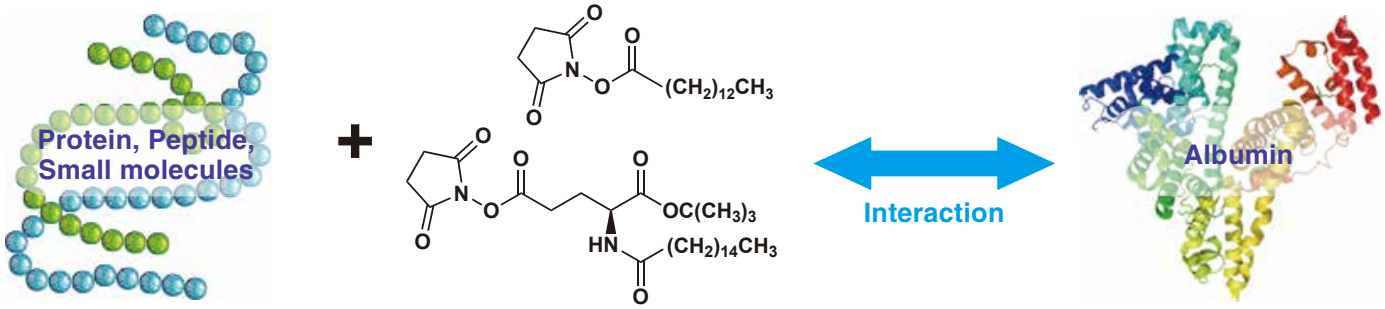
CHEMISTRY LIFE SCIENCE

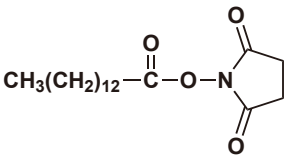
# Human-Serum-Albumin Binding Agents for Improvement of Pharmacokinetics

## Useful for Drug Kinetics Studies

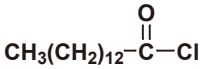



**In pharmaceuticals, pharmacokinetics is one of the important factors for drug efficacy. Pharmacokinetics of drugs and contrast agents is optimized by introducing fatty acids and some small molecules which have affinity with human serum albumin. Recently, several insulin drugs having a regulated half-life in blood by modification with fatty acids such as myristic acid or palmitic acid have been developed and approved. Fatty acid derivatives reported to bind with albumin are shown below. Diphenylcyclohexane derivatives are also presented. These reagents are available as building blocks for optimization of pharmacokinetics with peptides generally having a short half-life in blood.**

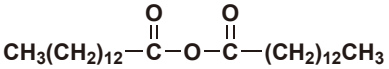
## Myristoylation Reagents



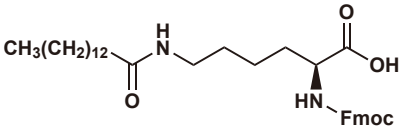
**Myristic Acid *N*-Succinimidyl Ester**
1g / 5g
[S0997]



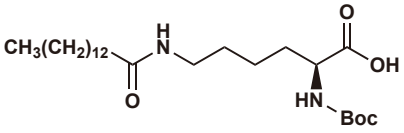
**Myristoyl Chloride**
25g / 400g
[T0086]



**Myristic Anhydride**
25g / 250g
[M0484]



**$N^{\alpha}$-Fmoc-$N^{\varepsilon}$-tetradecanoyl-L-lysine**
1g / 5g
[F1143]



**$N^{\alpha}$-Boc-$N^{\varepsilon}$-tetradecanoyl-L-lysine**
200mg / 1g
[B5366]

## Applications


1) Albumin binding of insulins acylated with fatty acids: characterization of the ligand-protein interaction and correlation between binding affinity and timing of the insulin effect *in vivo*
P. Kurtzhals *et al.*, *Biochem. J.* **1995**, *312*, 725. https://doi.org/10.1042/bj3120725
2) Insulin Mimetic Action of Synthetic Phosphorylated Peptide Inhibitors of Glycogen Synthase Kinase-3
B. Plotkin *et al.*, *J. Pharmacol. Exp. Ther.* **2003**, *305*, 974. https://doi.org/10.1124/jpet.102.047381
3) Design of the Novel Protraction Mechanism of Insulin Degludec, an Ultra-long-Acting Basal Insulin
I. Jonassen *et al.*, *Pharm. Res.* **2012**, *29*, 2104. https://doi.org/10.1007/s11095-012-0739-z
4) Myristic acid-modified thymopentin for enhanced plasma stability and immune-modulating activity
W. Su *et al.*, *Int. Immunopharmacol.* **2017**, *47*, 88. https://doi.org/10.1016/j.intimp.2017.03.025

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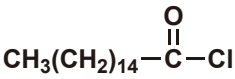
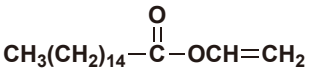
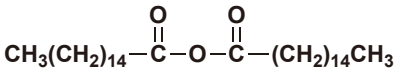
## Palmitoylation Reagents



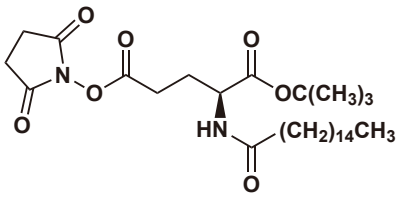
**Palmitoyl Chloride**
25mL / 500mL
[P0009]



**Vinyl Palmitate**
25mL / 500mL
[P0848]



**Palmitic Anhydride**
25g / 500g
[P0008]

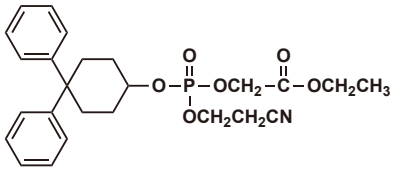


**1-*tert*-Butyl 5-(*N*-Succinimidyl) *N*-Palmitoyl-L-glutamate**
100mg
[B5390]

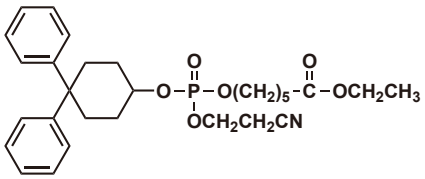
## Applications


1) Acylation of human insulin with palmitic acid extends the time action of human insulin in diabetic dogs
S. Myers *et al., Diabetes* **1997**, *46*, 637. https://doi.org/10.2337/diab.46.4.637
2) Potent Derivatives of Glucagon-like Peptide-1 with Pharmacokinetic Properties Suitable for Once Daily Administration
L. B. Knudsen *et al., J. Med. Chem.* **2000**, *43*, 1664. https://doi.org/10.1021/jm9909645
3) Lipidation of Cysteine or Cysteine-Containing Peptides Using the Thiol-Ene Reaction (CLipPA)
M. A. Brimble *et al., Eur. J. Org. Chem.* **2016**, 2608. https://doi.org/10.1002/ejoc.201501375

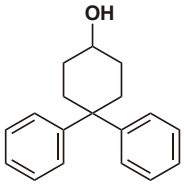

## Diphenylcyclohexane Derivatives



**Ethyl 2-[(2-Cyanoethoxy)-(4,4-diphenylcyclohexyloxy)-phosphoryloxy]acetate**
100mg / 500mg
[E1268]



**Ethyl 6-[(2-Cyanoethoxy)-(4,4-diphenylcyclohexyloxy)-phosphoryloxy]hexanoate**
100mg / 500mg
[E1313]



**4,4-Diphenylcyclohexanol**
1g / 5g
[D4973]

## Applications


1) MS-325: albumin-targeted contrast agent for MR angiography
R. B. Lauffer *et al., Radiology* **1998**, *207*, 529. https://doi.org/10.1148/radiology.207.2.9577506
2) The Effect of a Phosphodiester Linking Group on Albumin Binding, Blood Half-Life, and Relaxivity of Intravascular Diethylenetriaminepentaacetato Aquo Gadolinium(III) MRI Contrast Agents
T. J. McMurry *et al., J. Med. Chem.* **2000**, *45*, 3465. https://doi.org/10.1021/jm0102351
3) Phosphate ester serum albumin affinity tags greatly improve peptide half-life *in vivo*
K. Zobel, M. F. T. Koehler, *et al., Bioorg. Med. Chem. Lett.* **2003**, *13*, 1513. https://doi.org/10.1016/S0960-894X(03)00209-9
4) Conjugation to albumin-binding molecule tags as a strategy to improve both efficacy and pharmacokinetic properties of the complement inhibitor compstatin
J. D. Lambris *et al., ChemMedChem* **2014**, *9*, 2223. https://doi.org/10.1002/cmdc.201402212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