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(54) Title: BIOCONJUGATION REACTIONS FOR ACRYLYATING POLYETHYLENE GLYCOL REAGENTS

\[ \text{Activating agent} \]

\[ \begin{align*}
\text{mPEG} - O & \quad \text{NO}_2 \\
\text{H}_2\text{N} - \text{Protein} & \quad \text{Efficient reaction at neutral pH or pH ≤ 7}
\end{align*} \]

\[ \text{Sluggish reaction at neutral pH or pH < 8} \]

\[ \text{mPEG} - O - \text{N} - \text{Protein} \]

(57) Abstract: A method for conjugation of PEG to a protein in an aqueous solution at a pH less than or equal to about 7.0 or neutral pH comprising combining an activated PEG reagent and a protein in the presence of an activating agent at a pH of less than about 7.0 or neutral pH. In one embodiment, the method produces mixed populations of moderately PEGylated proteins, including 1:1, 2:1, and 3:1 PEGylated proteins.
A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K47/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, WPI Data, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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[ ] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

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Date of the actual completion of the international search
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Date of mailing of the international search report
02/11/2006

Name and mailing address of the ISA/

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Weikl, Martina
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<td>US 2004181035 A1</td>
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