Introduction of Phosphine-Gold(I) Precursors into a Cys-modified Enkephalin Neuropeptide as Part of Solid Phase Peptide Synthesis

Judy Caddy[a], Ulrich Hoffmanns[b], and Nils Metzler-Nolte[b,c]

[a] Project AuTEK, Mintek, Private Bag X 3015, Randburg 2125, South Africa
[b] Institute of Pharmacy and Molecular Biotechnology, University of Heidelberg, Im Neuenheimer Feld 364, 69120 Heidelberg, Germany
[c] New address: Department of Chemistry and Biochemistry, Ruhr-Universität Bochum, Universitätsstraße 150, 44801 Bochum, Germany

Reprint requests to Prof. Dr. N. Metzler-Nolte. E-mail: Nils.Metzler-Nolte@ruhr-uni-bochum.de

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The synthesis and full characterization of a series of (triphenylphosphine)gold complexes with thiol-containing amino acids and peptides is reported. Boc-Cys-Au(PPh_3) was prepared in solution by reaction of Boc-Cys-OH with (Ph_3P)AuCl. The related Ac-Cys-Au(PPh_3) and an Au derivative of the cysteine-modified neuropeptide enkephalin (Enk), [Cys]^5-Au(PPh_3)-Enk, were prepared on the resin, using the orthogonal trityl-protecting group on Cys. For comparison, the metal-free [Cys]^5-Enk and an *S-tert*-butyl-protected [Cys]^5-Enk were also prepared. Most noteworthy, gold complexation works best when carried out on the resin, and the gold thiolate survives cleavage from the resin under optimized conditions. The new conjugates were comprehensively characterized, including 1D and 2D NMR spectroscopy, and mass spectrometry. Along with characteristic changes in the ^{1}H and ^{13}C NMR spectra, ^{31}P NMR spectra reveal a characteristic downfield shift of *ca.* 5 ppm upon complexation of the Au(PPh_3)-fragment to Cys, which is also pertinent in the Au-labelled [Cys]^5-Enk.

Key words: Enkephalin, Gold Compounds, Medicinal Inorganic Chemistry, Peptides