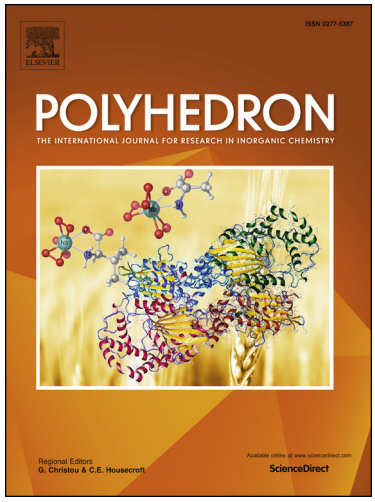

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Non-classical *N*-Metallated Pd(II) Pincer Complexes Featuring Amino Acid Pendant Arms: Synthesis and Biological Activity

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Abstract

A series of non-classical pincer ligands with the secondary amide central unit and amino acid pendant arms was obtained from 2-diphenylphosphanyl- and 2-methylsulfanylbenzoic acids and a range of amino acid derivatives (*S*-methyl-L-cysteine, L-methionine, and L-histidine methyl esters). In addition, the reactions of amino acid-functionalized chloroacetamides with *in situ* generated Ph_2PSK afforded their counterparts with an aliphatic ligand backbone. All the compounds obtained smoothly underwent direct cyclopalladation upon interaction with $PdCl_2(NCPh)_2$ under mild reaction conditions, resulting in *N*-metallated pincer complexes with 5,6- and 6,6-membered fused metallocycles. The realization of κ^3-*S,N,S*-, *S,N,N*- and *S,N,P*-coordination was unambiguously confirmed based on the IR and NMR spectroscopic data. In the case of the methionine-based thiophosphorylacetamide derivative, the unexpected selectivity in the formation of one complex diastereomer was observed in solution. The solid-state structures of some of the complexes obtained were also elucidated by X-ray crystallography. The preliminary investigations on cytotoxicity of the resulting palladocycles against HCT116, MCF7, and PC3 human cancer cell lines as well as HEK293 normal cells gave some insight into the structure–activity relationships for this relatively new type of potential anticancer agents. Some of the complexes demonstrated promising cytotoxic effects.

Key words: pincer complexes, palladium, functionalized amides, amino acids, cytotoxicity