

## Synthesis of platinum(II) complexes with some 1-methylnitropyrazoles and in vitro research on their cytotoxic activity.

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### Streszczenie

A series of eight novel platinum(II) complexes were synthesized by the reaction of the appropriate 1-methylnitropyrazole derivatives with  $K_2PtCl_4$  and characterized by elemental analysis, ESI MS spectrometry,  $^1H$  NMR,  $^{195}Pt$  NMR, IR and far IR spectroscopy. Thermal isomerization of cis-dichloridobis(1-methyl-4-nitropyrazole)platinum(II) **1** to trans-dichloridobis(1-methyl-4-nitropyrazole)platinum(II) **2** has been presented, and the structure of the compound **2** has been confirmed by X-ray diffraction method. Cytotoxicity of the investigated compounds was examined in vitro on three human cancer cell lines (MCF-7 breast, ES-2 ovarian and A-549 lung adenocarcinomas) and their logP was measured using a shake-flask method. The trans complex **2** showed better antiproliferative activity than cisplatin for all the tested cancer cell lines. Additionally, trans-dichloridobis(1-methyl-5-nitropyrazole)platinum(II) **4** has featured a lower  $IC_{50}$  value than reference cisplatin against MCF-7 cell line. To gain additional information that may facilitate the explanation of the mode of action of tested compounds cellular platinum uptake, stability in L-glutathione solution, influence on cell cycle progression of HL-60 cells and ability to apoptosis induction were determined for compounds **1** and **2**.

### Słowa kluczowe

nitropyrazoles-Pt(II)complexes, synthesis, structural analysis, LogP, cellular platinum uptake, antiproliferative activity, normoxia-hypoxia, L-glutathione (GSH), cell cycle, X-ray crystallography

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