Synthesis, Crystal Structure, and Cytotoxicity of New Methyl-Substituted Oxaliplatin Anologues.

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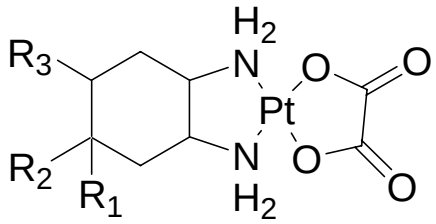
Oxaliplatin, [(*R*,*R*)-cyclohexane-1,2-diamine]oxalatoplatinum(II), has been the first platinum drug to prove clinical activity in an inherently cisplatin-resistant malignancy, i.e. colorectal cancer. The steric demand and/or the lipophilicity of the cyclohexane ring are structural requirements for the specific pharmacological properties of oxaliplatin [1] Derivatization of the cyclohexane ring might result in a marked effect on the antitumor activity. Previous results clearly indicated that the introduction of small substituents exhibits a positive influence on the cytotoxicity even when using racemic mixtures instead of the pure enantiomers (compare oxaliplatin) [2]. Herein, we present the synthesis of several new methyl-substituted *trans*-cyclohexane-1,2-diamine derivatives with methyl group(s) at different position on the cyclohexane ring and the oxaliplatin-analogous complexes.



R_1	R_2	R_3
CH_3	H	H
CH_3	CH_3	H
CH_3	H	CH_3

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[2] M. Galanski, A. Yasemi, S. Slaby, M. A. Jakupec, V. B. Arion, M. Rausch, A. A. Nazarov, B. K.Keppler, *Eur. J. Med. Chem.* 2004, 39(8), 707-714