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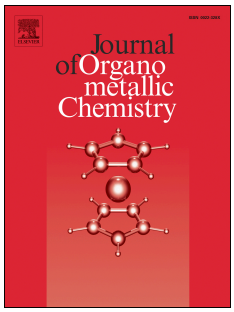

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Nitro-imidazoles in Ferrocenyl Alkylation Reaction. Synthesis, Enantiomeric Resolution and *in Vitro* and *in Vivo* Bioeffects

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Ferrocenylalkyl nitro-imidazoles (**4a-h**, **5a-h**) were prepared *via* the regiospecific reaction of the *α*-(hydroxy)alkyl ferrocenes, FcCHR(OH) (**1a–h**; Fc=ferrocenyl; R=H, Me, Et, Pr, *i*-Pr, Ph, *ortho*-Cl-Ph, *ortho*-I-Ph), with nitro-imidazoles in aqueous organic medium (H_2O-CH_2Cl_2) at room temperature in the presence of HBF_4, within several minutes in good yields. X-ray structural data for racemic (*R*,*S*)-1-*N*-(benzyl ferrocenyl)-2-methyl-4-nitroimidazole (**5f**) were determined. The resulting enantiomers were resolved into enantiomers by analytical HPLC on modified amylose or cellulose chiral stationary phases. The viabilities of **4b**, **4d**, **5b**, **5c** *in vitro*, and in experiments *in vivo* antitumor effects of 1-*N*-ferrocenylethyl-4-nitroimidazole (**4b**) against murine solid tumor system Ca755 carcinoma were evaluated.

Keywords: ferrocene compounds; nitro-imidazoles; enantiomeric resolution; X-ray crystal structure; toxicity *in vitro*; bioactivity *in vivo*

1. Introduction

The conjugation of nitrogen-containing hetero cycles with ferrocene represents perspective directions for design and synthesis of bioactive compounds with different types of activities including antianemic, tuberculostatic, antimalarial, antimicrobic and antiproliferative [1–10]. The antiproliferative activity has been especially investigated by numerous research groups [10–15].

Among heterocycles, azoles and especially imidazole cause a high interest because represent essential components of DNA, RNA, histidine amino acid or drugs [10–14,16-20]. On the other

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