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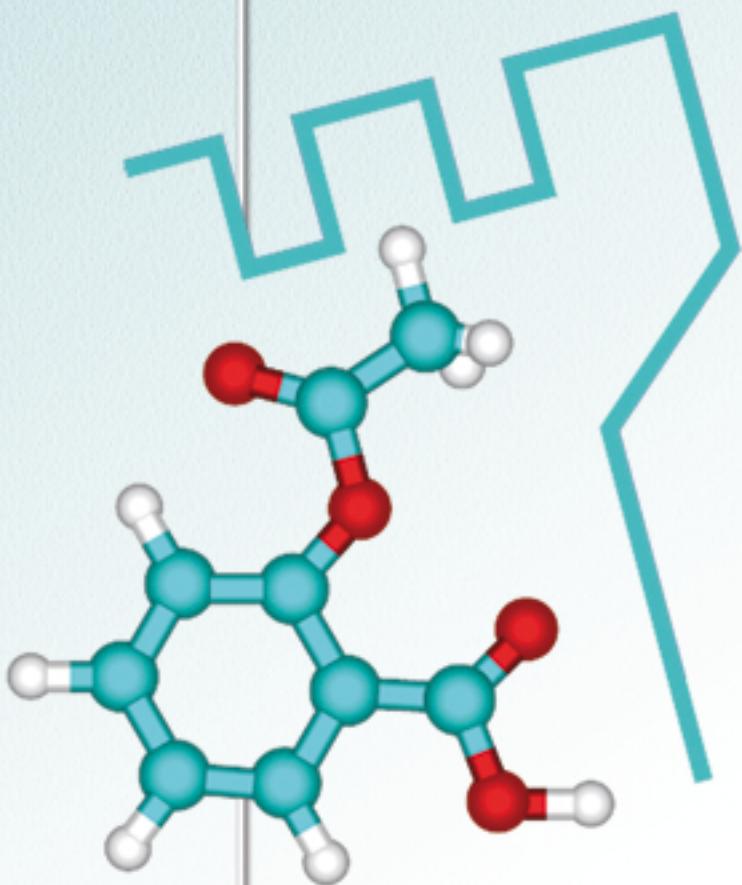


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FINAL PROGRAMME & ABSTRACT BOOK



KINETIC STUDY OF 2-MERCAPTOETHANOL ALKYLATION WITH THE ANTIPROLIFERATIVE AROYLACRILIC ACID PHENYLAMIDES

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Aroylacrylic acid phenylamides **1-13**, Figure 1, exert antiproliferative activity toward human tumour cell lines (HeLa, FemX, and k562) in the submicromolar to low micromolar concentrations.¹ The aim of this study was to find out whether the rate of the covalent adduct formation between **1-13** and the 2-mercaptoethanol (as a model of biomolecules reactive thiols) has significant impact on the overall potency of compounds. Spectrophotometrically, under the pseudo-first order conditions, we obtained second order rate constants² (k_2) for the Michael addition of 2-mercaptoethanol to **1-13**.

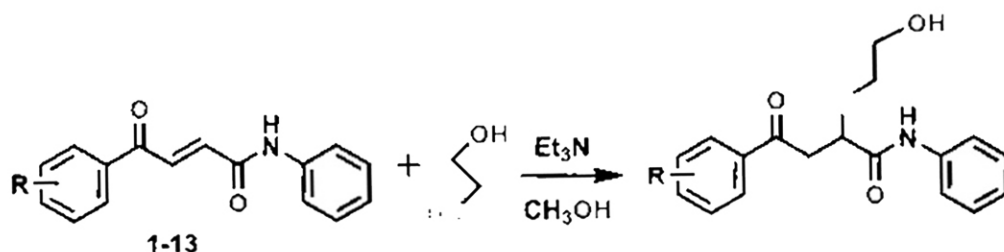


Figure 1. Michael addition of the 2-mercaptoethanol to **1-13**.

Michael-type addition of thiols to unsaturated ketones is the second-order reaction. Rate constants of thiol addition to the structurally similar chalcones are pH and substitution dependent.^{3,4} Correlations of the obtained k_2 with the Hammett substituent constants, with the atomic charges calculated on a DFT level (B3LYP/6-311G**) in the vacuum and by using an implicit solvent (MeOH) gave good results ($r = 0.92 - 0.98$). Along with this, with the aim to describe potency of **1-13**, rate constants were used as one of the descriptors and MLR correlations reported.

References:

- ¹ M. D. Vitorović-Todorović, A. Erić, S. B. Novaković, G. A. Bogdanović, B. J. Drakulić, submitted; ² R. A. Bartsch, B. R. Cho, *J. Am. Chem. Soc.*, 1979, **101**, 3587; ³ J. R. Dimmock, L. M. Smith, P. J. Smith, *Can. J. Chem.* 1980, **58**, 984; P. V. Korikov, N. P. Gerasimova, O. A. Moskovicov, E. M. Alov, N. A. Noznin, *Himija i himičiska tehnologija*, 2001, **44** (5), 19.