SULFONES OF THE 3-PYRROLIN-2-ONE SERIES: SYNTHESIS AND BIOLOGICAL ACTIVITY

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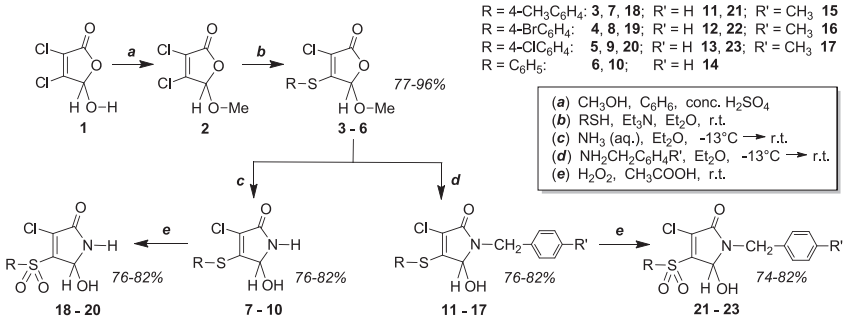
Nitrogen-containing heterocycles attract considerable attention of researchers due to the presence among them of a large number of physiologically active substances and potential drugs. In this study we developed a facile approach to the preparative synthesis of novel sulfonyl derivatives of 5-hydroxy-3-pyrrolin-2-one **18**–**23** from commercially available mucochloric acid **1** based on the following steps: 1) thiilation of 3,4-dichloro-5-methoxy-2(5*H*)-furanone **2** in the presence of triethylamine, 2) ammonolysis and amination reactions of thioethers **3**–**6**, 3) oxidation of 3-pyrrolin-2-one thioderivatives **7**–**17** to sulfones with excess 33% hydrogen peroxide in acetic acid at room temperature.



The ability of the synthesized compounds **1**–**23** to inhibit the growth and the biofilm formation by various bacteria was studied. The minimal concentrations of sulfones **18**–**23** required for the complete inhibition of growth and for the biofilm formation by *Staphylococcus aureus* and *Staphylococcus epidermidis* were determined. It is shown that these furanones do not possess mutagenic and cytotoxic activity at concentrations which inhibit the growth of bacteria and biofilm formation.

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ENCAPSULATION OF MACROMOLECULAR BIOTECHNOLOGICAL PRODUCTS (PROTEINS AND POLYNUCLEOTIDES) INTO THE BIODEGRADABLE POLYMER PARTICLES

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The study of macromolecular biotechnological products (proteins and polynucleotides) entrapment into the biodegradable polymer particlesis of significant interest because it allows solving of various biochemical and pharmaceutical problems. One of such issues is the development of systems for targeted delivery of bio macromolecules into diseased tissues and organs. The formation of such polymer systems could be performed via double emulsion method. This method includes the primary emulsification of an aqueous solution of the protein (or other biomolecule) in the oil phase, which represents the solution of biodegradable aliphatic polyester in volatile organic solvent (dichloromethane, ethyl acetate, acetone) and further formation of double “water in oil in water” emulsion with application of the excess of aqueous phase, containing polymer stabilizer. Then the gradual removal of organic solvent occurs by evaporation or diffusion mechanism. This processes result in the formation of a suspension of polymer particles, which contain the encapsulated protein into their internal cavity.

However, due to the fact that the effect of the w/o/w encapsulation procedure on protein stability and structure has only been studied on occasion, many issues are not clear. The main difficulty of this method is to determine the conditions which allow one to keep the structure of the double emulsion, specifically water in oil in water and prevent the association of internal and external aqueous phases. Such a phase merger inevitably leads to a decrease in encapsulation efficiency (EE). Therefore, this research was aimed at optimizingthe conditions for obtaining biodegradable particles by the double emulsionto increase the EE. The protein release kinetics and its dependence on polyester structure were also of particular interest.

In this work we have studied the influence of experimental conditions on encapsulation efficiency of model protein - bovine serum albumin (BSA). For this purpose we have synthesized polylactic acid (PLA, MW = 15 000) copolymerof lactic and glycolic acids (PLGA, MW = 20 000), polypentadecalactone (PPDL, MW = 24 000), and polycaprolactone (PCL, MW = 21 000). The stabilizers choice and organic solvent removal mechanism were tuned in order to maximize the BSA EE. Also the concentration of stabilizer and pH of second water phase were varied in order to obtain a stable