

LETTERS  
TO THE EDITOR

## Bioactive Metalated (2-Hydroxyethyl)ammonium Ionic Liquids

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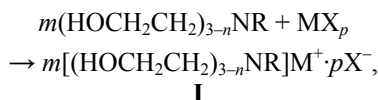
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We have shown earlier that the reaction of biogenic (2-hydroxyethyl)amines with the biologically active aryl(indolyl)oxy(sulfanyl)(sulfonyl)acetic acids results in the non-toxic pharmacologically active protic ionic liquids  $(\text{HOCH}_2\text{CH}_2)_{3-n}\text{N}^+\text{H}^-\text{OOCCH}_2\text{O}(\text{S})(\text{SO}_2)(\text{Ind})\text{Ar}$ ,  $n = 0-2$  [1].

We presumed that the substitution of the  $\text{N}^+\text{H}^-$  proton in these compounds by a biogenic metal [2] may lead to the significant changes in their biological properties. The reaction of (2-hydroxyethyl)amine with the metal salts of hydrochloric, acetic and aryl(indolyl)oxy(sulfanyl)(sulfonyl)acetic acid yields the metalated (2-hydroxyethyl)ammonium ionic liquids.



R = H, CH<sub>3</sub>; M = Na, Mg, Ca, Mn, Fe, Co, Ni, Cu, Zn, Rh; X = Cl, OOCCH<sub>3</sub>, OOCCH<sub>2</sub>O(S)(SO<sub>2</sub>)(Ind)Ar;  $m = 1, 2$ ;  $n = 0-2$ ;  $p = 2, 3$ .

By the primary screening of the biological activity, the resulting ionic liquids **Ia–Ic** [X = OOCCH<sub>3</sub>, M = Zn (**a**), Ni (**b**), Co (**c**)] possess the growth-regulating activity. Thus, the aqueous solutions of compound **Ia** ( $10^{-4}$ – $10^{-6}$  M) stimulates, and compounds **Ib**, **Ic** ( $10^{-3}$ – $10^{-4}$  M) inhibit the cell growth activity of the sugar cane culture [3]. The ionic liquids (M = Zn, Co, Ni, Mn, Mo, Fe, Rh; X = Cl, OOCCH<sub>3</sub>) were investigated for the immune activity. Some non-toxic ionic liquids (LD<sub>50</sub> 4000 mg kg<sup>-1</sup>) were revealed affecting the integral factors of the immune response: the antibody production, cellular immunity, and anti-proliferative properties. Thus, the cobalt compounds in

the doses of 1–10 mg kg<sup>-1</sup> inhibit the spontaneous Con-A and PWM-stimulated proliferation of the spleen T-cells *in vitro*. The Fe<sup>+3</sup> derivatives exhibit a stimulating effect on these cells. The Co and Rh compounds show the selective immunoactive properties: they stimulate either the humoral or cellular immune response. This makes them promising precursors of new drugs. The compound, where M = Zn and X = OOCCH<sub>2</sub>OC<sub>6</sub>H<sub>4</sub>-CH<sub>3</sub>-2 activating tryptophanyl-tRNA synthetase exhibits an anti-sclerotic activity (150% compared to a control).

The resulting ionic liquids are viscous liquids or powders soluble in water. Their composition and structure was confirmed by the <sup>1</sup>H NMR, <sup>13</sup>C, <sup>15</sup>N, IR spectroscopy and elemental analysis.

**General procedure.** The alcoholic solution of the corresponding (2-hydroxyethyl)amine and a metal salt (1:1 or 2:1) was stirred at 65°C for 8 h. Then the solvent was removed. The residue was washed with ether and dried in a high vacuum over P<sub>2</sub>O<sub>5</sub>.

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