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The NMR study of biologically active metallated alkanol ammoinium ionic liquids

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ABSTRACT

The ^{1}H, ^{13}C, ^{15}N, and ^{111}Cd NMR spectra of a series of metallated alkanol ammonium ionic liquids (MAIL) series [n $N(CH_2CH_2OH)_3M]^+ \cdot mX^-$, where M = Cd, Mg, Zn, Fe, Rh; X = Cl, $OOCCH_3$, obtained in a wide range of temperatures of the studied samples, have been analyzed. It is found that, under biomimetic conditions (H_2O, 25 °C), the compounds studied exist as mono- bi- and the tricyclic structures, which are in equilibrium. Shift of the equilibrium depends upon nature of a metal and effects all the parameters of the NMR spectra. Peculiarities of ligand exchange, typical for the studied compounds, have been studied in a wide range of temperatures. It is found that the NMR data can be used to control structure of the compounds formed in the course of synthesis.

1. Introduction

The complexation of triethanolamine – tris(2-hydroxyethyl) amine (TEA) with various transition metals has a long history [1–3], but research on the syntheses, X-ray structures [4–8], compound characterizations and their applications still are of interest [9,10]. The corresponding complexes have found applications in various fields such as buffers, catalysts, inhibitors, ion exchangers, additives in building materials, electroplating, dyes, glassy semiconductor materials, etc.

The interaction of transition metal ions with triethanolamine results in the formation of high-spin complexes in which TEA usually acts as a tridentate (N, O, O′) ligand [11]. However TEA may also act as a tetradentante (N, O, O′, O″) ligand, then geometrical demands enforce high coordination numbers of the metal ions have large ionic radii [12]. Complexes in which triethanolamine acts as a tetradentate ligand are known as atranes, [3.3.3.0] tricyclic systems in which two bridgehead atoms are bridged by three-atom moieties. The formation of the intramolecular dative coordination N → M bond constitutes the basis for their specific properties in various contexts.

Earlier, we have shown that the reaction of biogenic (i.e. participating in organism activity) 2-hydroxyethylamines with biologically active arylchalcogenylacetic acids affords the salts $[N(CH_2CH_2OH)_3H]^+ \cdot {}^-OOCCH_2YAr$; ($Y = O, S, SO_2$), where cation has tricyclic atrane structure with $N^+ \rightarrow H$ bond [13], which can be considered as proton alkanol ammonium liquids (PAILs) [14]. The PAILs obtained possess high pharmacological activity surpassing that of the parent acids and alkanol amines. They also exhibit adaptogenic, antitumor, heamopoesis-stimulating and immunomodulating properties, increase the resistance of animals to hypobaric hypoxia, hyper - and hypothermia, intoxications, action of ultrasound and microwave radiation [15] and they are effective stimulants of many biological process [16].

The essential metals (Ca, Mg, Co, Ni, Zn, etc.) are present in enzymes and vitamins providing the organism with necessary trace elements [17]. We have assumed that the changing of N^+H-proton in PAIL by essential metals can lead to new class of biologically active compounds. To reach this goal, we have synthesized a series of metallated alkanol ammonium ionic liquids (MAILs) via the reaction of 2-hydroxyethylamines with metal salts (Scheme 1).

One of the peculiarities of salts (ionic liquids), PAIL and MAIL belong to the above-mentioned, is their ionic conductance. The electric conduction of series of synthesized PAILs in the solutions

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$$n\,N(CH_2CH_2OH)_3 + MX_m \xrightarrow[1\text{-}8\ h]{25\text{-}50^{\circ}C} (N(CH_2CH_2OH)_3)_nM^{m+}\,mX^{-}$$

78-97 %

$n=1, 2;\ m=1, 2$

M = Na, Mg, Ca, Mn, Fe, Co, Ni, Cu, Zn, Rh

$X = Cl, OOCCH_3, OOCCH_2YAr;\ Y = O, S, SO_2$

Scheme 1. The reaction of 2-hydroxyethylamines with metal salts.

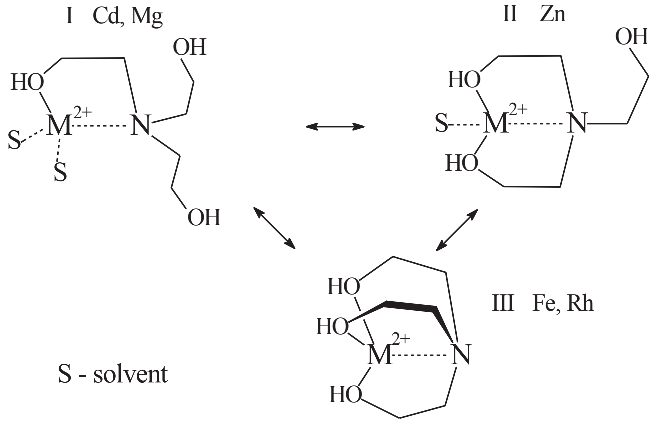
has been preliminarily researched. It is revealed that their 0.1 N aqueous and ethanolic solutions possess electric conductivity. It is established that the value is linearly increasing with the growth of concentration of PAIL and MAIL in the solution.

Really, preliminary pharmacological studies have revealed that among triethanolamine-based ($MX_2 \cdot TEA$) MAILs there are compounds which increase or depress plants growth [18], protect animals from ethanol and carbon monoxide poisoning [19]. The named compounds possess pronounced immuno-modulating and antiproliferative properties [20]. For example, tris (2-hydroxyethyl)-amine-bis-(2-methylphenoxyacetate) zinc by 1.5 times increases the activity of tritophanyl-tRNA-synthesase enzyme, which exerts antiangiogenic and antiatherogenic action [21].

The present work is aimed at the NMR study of MAILs behavior in aqueous solutions, i.e. under the conditions modeling real processes occurring in live organisms. A special attention is paid to the effects of ligand exchange and possibility of controlling the structure of MAILs using NMR technique.

2. Experimental

The reaction mixture MX_2 with TEA (ratio of the reagents 1:1 or 1:2) in 20 ml of MeOH or H_2O was stirred at 20°C – 75°C for 1–5 h. The solvent was removed in a vacuum. The solid residue was



Scheme 3. Possible equilibrium states of MAILs in solution.

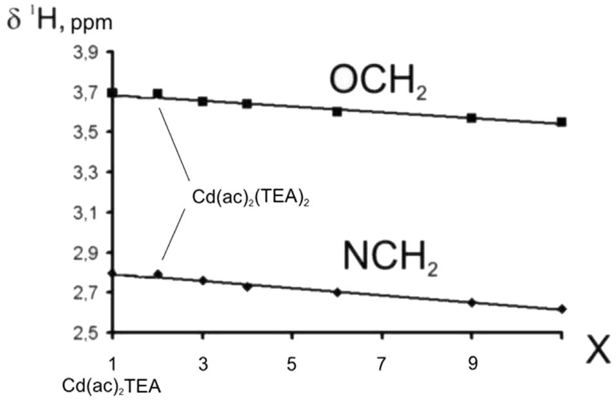
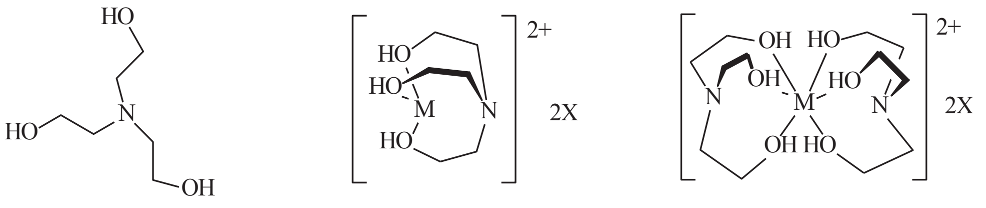


Fig. 1. Dependence of chemical shifts of OCH_2 and NCH_2 protons in the spectrum of $Cd(ac)_2TEA$ (**2**) upon the excess TEA (X – molar ratios TEA to $Cd(ac)_2$).

Table 1
^1H, ^{13}C and ^{15}N NMR spectral characteristics of TEA (**1**) and MAILS (**2**–**10**) in D_2O solution (T = 25 °C).

Compound		δ, ^1H ppm			δ, ^{13}C ppm (^1J(C,H), Hz)					δ, ^{15}N М.д.
		NCH_2	OCH_2	CH_3	NCH_2	OCH_2	Δ	CH_3	C=O	
1	TEA	2.62	3.55	–	55.63 (133.1)	58.85 (142.6)	3.22	–	–	−351.9
2	$Cd(ac)_2TEA$	2.78	3.69	1.82	55.07 (135.7)	57.21 (144.0)	2.14	22.67 (127.5)	181.60	−359.3
3	$Cd(ac)_2(TEA)_2$	2.70	3.61	1.79	55.17 (135.8)	57.31 (144.1)	2.14	22.65 (127.5)	181.62	−358.0
4	$MgCl_2(TEA)_2$	2.68	3.58	–	55.61 (134.7)	58.49 (143.1)	2.88	–	–	−349.9
5	$Zn(ac)_2TEA$	3.23	3.77	1.77	55.03 (143.0)	55.34 (145.7)	0.31	22.95 (127.6)	181.57	−342.7
6	$Zn(ac)_2(TEA)_2$	3.20	3.73	1.73	55.82 (142.8)	55.70 (145.9)	−0.12	22.93 (127.6)	181.58	−340.1
7	$ZnCl_2(TEA)_2$	3.16	3.76	–	55.46 (141.2)	56.11 (144.7)	0.65	–	–	−342.7
8	$FeCl_3(TEA)_2$	3.37	3.84	–	55.49 (143.8)	55.19 (144.5)	−0.30	–	–	–
9	$RhCl_3TEA$	3.38	3.83	–	55.34 (144.5)	55.04 (145.3)	−0.30	–	–	−339.6
10	$RhCl_3(TEA)_2$	3.57	4.04	–	55.40 (144.5)	55.00 (145.0)	−0.40	–	–	−340.2



TEA

MX_2TEA

$MX_2(TEA)_2$

1

(2 - 10)

$X = CH_3COO^-;\ Cl^-$

Scheme 2. The compounds included in this study.