

# The Effect of Selected Organometallic Compounds on Membrane Voltage

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## Abstract

Our work studied the effect of selected organometallic chloride compounds on electrical properties of membrane, in the form of hydrophilic filters impregnated with lauric acid. The presence of the compounds in the membrane surroundings induced a quick increase of the membrane voltage that decreased more slowly after reaching the maximum value, and stabilized after a lapse of a specified period of time. In the case of triphenyltin, the voltage changed direction during measurement and stabilized in negative values. Based on the results obtained, it was found that the effectiveness of the interaction of the compounds studied with the membrane is highest in the case of triphenyltin chloride. The change of voltage polarization in the case of triphenyltin may denote that chlorine ions released in the dissociation process penetrated the other side the membrane.

**Keywords:** organometallic compounds, model membranes, trans-membrane voltage

## Introduction

Organometallic compounds are present in the natural human environment. They are contained in products of industrial processes and pesticides [1]. The toxicity of those compounds is related to their accumulation degree in cells of living organisms [2-10] and their actions include blocking metabolic processes [5-8], disorders of barrier functions of intestine epithelial cells [9], and induction of the apoptosis of nerve cells [10]. Hydrophobic properties of amphiphilic organometallic compounds, including phenyltin chlorides, phenyllead chlorides and aliphatic tin chloride examined in the work, demonstrated their high affinity with the lipid phase of cell membranes. Organometallic compounds also affect physical parameters of model membranes [11-13]. Based on literature, we know that they change the degree of anion permeability through the bilayer lipid membrane (BLM) [13-15], and also structural and dynamic parameters of liposome membranes [16-21].

The aim of this work was to study the effect of selected organometallic tin and lead chlorides on electrical properties of model membranes, in the form of filters impregnated with butyl ester of the lauric acid. The method of electric tests of lipid membrane properties applied in this work proved to be a very sensitive tool for detection of activity of dissociating organometallic compounds.

## Material and Methods

Our work studied the effect of selected (tin and lead) chlorides, aromatic hydrocarbon derivatives, and aliphatic tin chloride (Table 1) on electric parameters of membranes in the form of filters from the Synpor Company (Czech Republic), pore diameter 1.5  $\mu\text{m}$ , thickness 50  $\mu\text{m}$ , impregnated with the lauric acid butyl ester. The impregnation consists of dropping 0.03 ml of ester butyl lauric acid on the filter placed between teflon chambers. The surface area of the filter was 0.196  $\text{cm}^2$ . The quality of impregnations was estimated on the basis of the impedance measurements performed using a Motech 4090 RLC bridge.

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Table 1. Chemical structure of the compounds studied.

Compound name	Chemical structure
Tripropyltin chloride (TriPT)	$(C_3H_7)_3SnCl$
Triphenyltin chloride (TPhT)	$(C_6H_5)_3SnCl$
Triphenyllead chloride (TPhL)	$(C_6H_5)_3PbCl$

Table 2. Maximum voltages  $U_m$  and stabilization voltage  $U_s$  read 60 minutes after introducing the TriPT admixture to the measurement chamber (for different concentrations of the compound).

Concentration in the measurement compound C [ $\mu M$ ]	Maximum voltage $U_m$ [mV]	Stabilization voltage $U_s$ [mV]
75	49.1	28.7
150	66.8	12.2
375	96.8	8.9
750	119.8	5.6
1500	142.2	2.7

Table 1 shows chemical formulas of the studied compounds.

The experimental system consisted of two chambers (measurement chamber 1 and reference chamber 2) divided by membrane M (Fig. 1) [22]. Chambers 1 and 2 were connected by salt bridges with indirect chambers 3 and 4. Electrodes Ag/AgCl were immersed in chambers 3 and 4 by agency of which, using an electrometer of the company Keithley 6517, membrane voltage was measured. The measurement started from filling in all chambers with a water solution of KCl of 10 mM concentration. After stabilization of identical electrolyte levels in chambers connected by salt bridges, admixtures of studied compounds dissolved in dimethylformamide (DMF) were added to the measurement chamber and measurements of trans-membrane voltage induced by the presence of the admixtures depending on time were conducted.

Control measurements of the voltage performed for water solutions of KCl containing different amounts of DMF, also with DMF concentrations higher than those applied in the rest of present work, indicated that DMF does not induce the membrane potential.

## Results and Discussion

Fig. 2 shows the dependence of membrane voltage on time that has lapsed after the introduction of tripropyltin chloride (TriPT) into the measurement chamber (Table 1). The measurements were conducted for 5 different concentrations of TriPT.

The introduction of TriPT to the measurement chamber resulted in a quick increase of membrane voltage until reaching the maximum; then the voltage decreased much slower and it stabilized after ca. 60 minutes. The maximum values of voltages  $U_m$  and stabilization voltages  $U_s$  are demonstrated in Table 2.

Table 2 shows that as the concentration of TriPT rose, voltage  $U_m$  increased, whereas  $U_s$  decreased (Table 2). Moreover, the location of voltage maxima moved toward shorter time  $t$  and more quickly reached voltage stabilization. A similar effect was observed in works [23, 24], in which the compound TriPT was dissolved in methanol. The appearance of the voltage maxima is apparently a result of two processes shifted in time: penetration of positive (hydrophobic) ions  $(C_3H_7)_3Sn^+$  inside membranes (generated as a result of TriPT dissociation), which results in an increase of voltage, and then negative (hydrophilic) ions  $Cl^-$  (voltage drop).

Fig. 3 shows the dependence of the membrane voltage on time for different concentrations of triphenyltin chloride (TPhT) (Table 1).

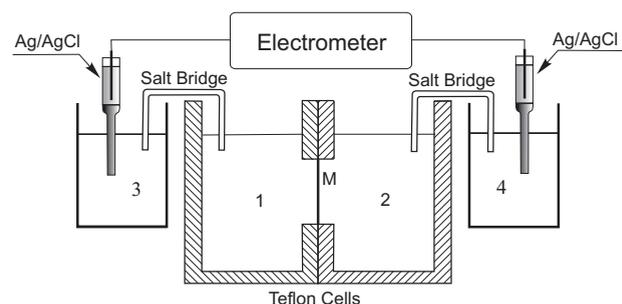


Fig. 1. Measuring system: 1 - measurement chamber, 2 - reference chamber, 3 and 4 - indirect chambers, M - membrane, Ag/AgCl - silver-silver chloride electrode.

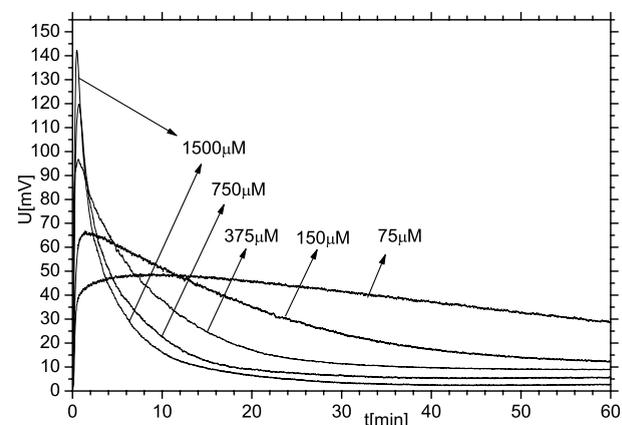


Fig. 2. Dependence of membrane voltage  $U$  on time  $t$  for different concentrations of the TriPT admixture in the measurement chamber.

The presence of TPhT in the measurement chamber resulted in the occurrence of the membrane voltage that increased as time lapsed until reaching the maximum value  $U_m$ . Similarly as in the case of TriPT, as the concentration of the compound rose, values of  $U_m$  increased and their location shifted toward shorter times (Fig. 3).

Table 3 shows that membrane voltage decreased to zero after reaching maximum value  $U_m$  and then changed to the opposite sign, and in case of this compound they stabilized in negative values. In the case of the lowest of the applied concentrations (75  $\mu\text{M}$ ), the stabilization voltage approached zero and did not change the polarization direction. The obtained results may indicate that above certain concentration, hydrophilic ions  $(\text{C}_6\text{H}_5)_3\text{Sn}^+$  generated in the dissociation process of the compound TPhT penetrate inside the membrane and modify its structure; as a result, it ceases to be an impermeable barrier for hydrophilic ions  $\text{Cl}^-$ . Therefore, ions  $\text{Cl}^-$ , under the influence of the concentration difference, will apparently penetrate from the measurement chamber (higher concentration) into the reference chamber (lower concentration), resulting in a change of polarization of the membrane voltage.

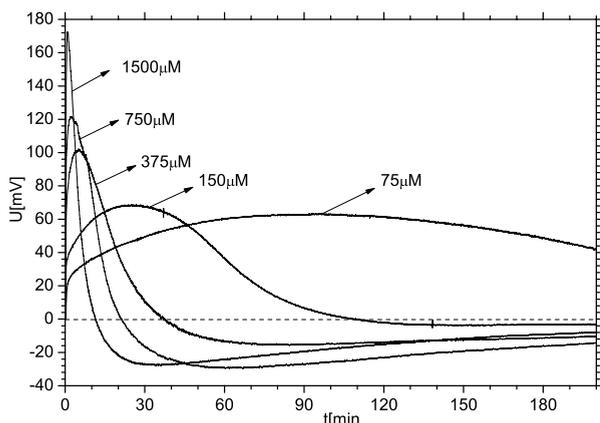


Fig. 3. Dependence of membrane voltage  $U$  on time  $t$  for different concentrations of the TPhT admixture in the measurement chamber.

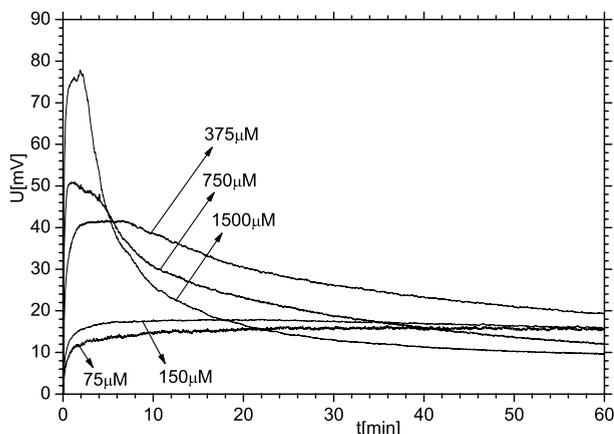


Fig. 4. Dependence of membrane voltage  $U$  on time  $t$  for different concentrations of the TPhL admixture in the measurement chamber.

Fig. 4 shows the dependence of the membrane voltage on time for different concentrations of triphenyllead chloride (TPhL) (Table 1).

The compound differed from TPhT only by lead replacing tin in its structure. With the two lowest concentrations of TPhL (75  $\mu\text{M}$  and 150  $\mu\text{M}$ ), membrane voltages stabilized at the level of several mV not reaching peak. The lack of voltage peak may denote that with such concentrations, the compound TPhL interacted only with the surface layer of the membrane. A similar effect was observed in the case of inorganic potassium chloride in work [23]. In higher concentrations of TPhL, membrane voltages reached maximum values (almost one-half than in the case of TPhT) and stabilized after ca. 60 minutes no changing polarization (Table 4).

The obtained results show much lower activity of the lead compound in interaction with the membrane in comparison with the analogical tin compound.

Fig. 5 shows a breakdown of dependences of membrane voltages on time for compounds applied in the tests with the lowest concentration amounting to 75  $\mu\text{M}$ . The figure shows clear diversification of the dynamics and volume of changes in membrane voltages induced by the presence of

Table 3. Maximum voltages  $U_m$  and stabilization voltage  $U_s$  read 200 minutes after introducing the TPhT admixture to the measurement chamber (for different concentrations of the compound).

Concentration in the measurement compound $C$ [ $\mu\text{M}$ ]	Maximum voltage $U_m$ [mV]	Stabilization voltage $U_s$ [mV]
75	63.6	41.9
150	68.7	-3.0
375	102.2	-10.3
750	121.7	-14.5
1500	172.4	-7.9

Table 4. Maximum voltages  $U_m$  and stabilization voltage  $U_s$  read 60 minutes after introducing the TPhL admixture to the measurement chamber (for different concentrations of the compound).

Concentration in the measurement compound $C$ [ $\mu\text{M}$ ]	Maximum voltage $U_m$ [mV]	Stabilization voltage $U_s$ [mV]
75	16.5	15.6
150	18.0	15.8
375	41.5	19.4
750	50.8	12.0
1500	77.4	9.7

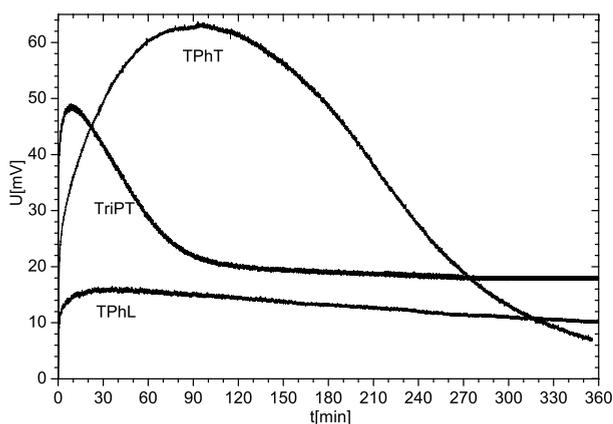


Fig. 5. Dependence of membrane voltage  $U$  on time  $t$  for compounds studied in the work of concentration amounting to  $75 \mu\text{M}$ .

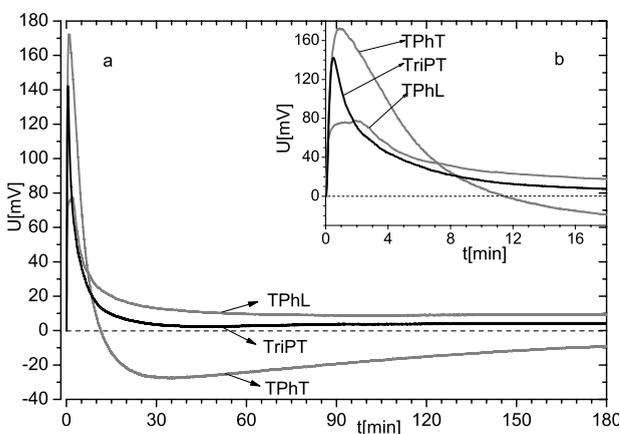


Fig. 6. Dependence of membrane voltage  $U$  on time  $t$  for compounds studied in the work of concentration amounting to  $1500 \mu\text{M}$  (Figures a and b shows dependences of  $U=f(t)$  in different time scales).

the examined compounds. The time after which the voltage peaks occurred in the presence of TriPT and TPhL in the measurement chamber amounted to ca. 10 and 30 minutes, accordingly, whereas in the case of TPhT ca. 95 minutes. From among the examined compounds, with concentration of  $75 \mu\text{M}$ , TPhT demonstrated the highest activity in interaction with examined membranes; TriPT was less active, whereas TPhL was least active.

Fig. 6. shows a breakdown of dependence of membrane voltages on time for compounds applied in the work whose concentration was highest and amounted to  $1500 \mu\text{M}$ .

With this concentration, all compounds generated high peaks of the membrane voltage. After reaching maximum, membrane voltages quickly dropped to zero and, in the case of TPhT, changed their polarization.

The obtained results show that the activity of the interaction of the examined compounds with lipid membranes is highest for the aromatic tin compound (TPhT); in particular, it is higher than the activity of the lead compound (TPhL), despite the identical structure of their molecules.

Similar conclusions are drawn from work [25] concerning interactions of triphenyltin and triphenyllead chlorides with lipid bilayers in which the  $^1\text{H-NMR}$  method was used to examine the effect of the compounds on structural and dynamic parameters of liposome membranes EYL (egg yolk lecithin).

The method of electric tests of lipid membrane properties applied in this work proved to be a very sensitive tool for detection of activity of dissociating organometallic compounds. The method can be useful for examination of interactions with membranes of organometallic compounds that differ by their chemical structure, and also the effect of the type of metal present in the structure on the interactions.

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