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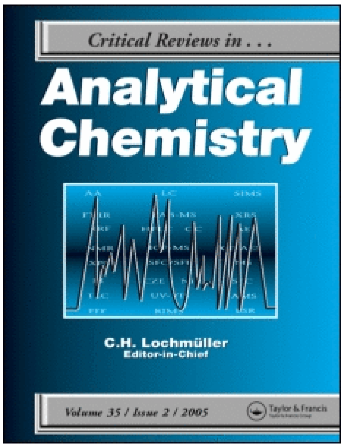

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Mariusz Kluska[a]
[a] Institute of Chemistry, University of Podlasie, Siedlce, Poland

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Analytical Techniques in Determination of Biologically Active Organosilicons of the ES-Silanate Group

Mariusz Kluska
Institute of Chemistry, University of Podlasie, Siedlce, Poland

An attempt of synthesis of information concerning chosen organosilicon compounds of the group of electrostatically stabilized (ES)-silanates is described. All hypercoordinated organosilicon derivatives show biological activity. This activity is very important for the whole ecosystem. Some of these compounds easily hydrolyze; it causes various difficulties during their isolation from different matrices and while preparing the samples to chromatographic analysis. Hypercoordinated ES-silanates can be determinate by the use of high performance liquid chromatography (HPLC) as well as capillary electrophoresis.

Keywords ES-silanates, organosilicon compounds, biological activity, HPLC, capillary electrophoresis

INTRODUCTION

More and more widespread application of silicon reagents in organic synthesis rises to arousing scientist's interest in chemistry of hypercoordinated organosilicon compounds. Because of the ability of chain formation, silicon can be proposed as a base of life, alternative to carbon.

ES-silanates are examples of hypercoordinated compounds. They are particularly interesting for their structure, properties and wide potentiality of application. Reviews published until now referring to the ES-silanate chemistry described methods of synthesis, results of investigation of geometry and electronic structure of these compounds (1, 2). Chemists interest in this group of molecules increases from year to year, similarly as the number of papers dedicated to these compounds.

Practically, there is no information concerning chromatographic separation and isolation of ES-silanates. Therefore, this paper is an attempt of synthesis of information describing such interesting group, of hypercoordinated compounds. Particular attention was paid to properties and analytical methods of this group. In addition to classical chromatographic methods electromigration techniques were taken into consideration, because hypercoordinated compounds are able to ionize.

Reliability, good accuracy and precision of determination characterize capillary electromigration techniques. Capillary isotachophoresis (ITP) is more and more often applied in analytical laboratories. Great efficiency and short time of separation are reasons why the ITP method can compete not only with HPLC, but also with other analytical techniques (3, 4).

PHYSICAL PROPERTIES OF SILICON

Berzelius obtained silicon from silica for the first time in 1822. It takes the seventh place among the most common elements of the universe. After oxygen, silicon is the main constituent of the earth, the amount of silicon is larger than the amount of all other elements. Depending on the method, silicon can be isolated in a form of grey, hard and fragile crystals or as brown powder. Both forms have the same crystallographic structure (of the diamond type), but differ by the dimension of crystals.

All living (not dried) plants contain soluble silicon derivatives, which can be assimilated by the human organism. In the biggest amount they appear in horsetail (Equisetum arvense), horse foot (Tussilago farfara), couch-grass (Agropyrum repens) and wild strawberry (Fragaria vesca). Another important source of silicon for the human organism is milk and its products.

CHEMICAL PROPERTIES OF ORGANOSILANATES

Organosilicon chemistry started more than 100 years ago in 1846, when Ebelman first obtained organic silicon derivative, i.e., tetraethoxysilane. Organosilicon compounds contain in its molecules tetravalent silicon atoms connected with hydrogen, carbon, halogen, and oxygen or nitrogen atoms (5).

In 1863, Charles Friedel and James M. Crafts obtained the first organochlorosilane—tetrathylsilane, by the reaction of diethylzinc with silicon tetrachloride (6). Ladenburg, who brought into practice sodium alkyls and mercury alkyls as reagents for

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Address correspondence to Mariusz Kluska, Institute of Chemistry, University of Podlasie, 54 3-Maja St, 08-110 Siedlce, Poland. E-mail: kluskam@ap.siedlce.pl

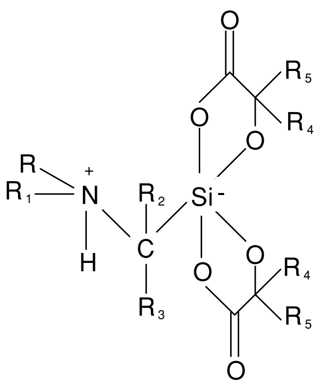


FIG. 1. General structure of ES-silanates.

the preparation of organic derivatives of silicon developed their method in the next decade, then Pape applied the Wurtz reaction. At the end of the 19th century a turn was caused by the use of the Grignard reaction to the synthesis of different organic silicon preparations. Despite it, Frederic Stanley Kipping is considered as a father of classical chemistry of silicon organic compounds (7, 8).

This class of compounds was investigated with variable intensity and in close connection with the development of carbon compounds chemistry. However, works of a Russian scientist, e.g., the papers of Andranov, once more caused interest in organosilicon chemistry and its turbulent development (9).

Since 1965, about 14,000 organosilicon compounds were reported. At present the rate of their preparation is still increasing. This increase is based on the wide potentiality of application of organosiloxane elastomers, resins and liquid polymers. Also, there are possibilities of modification of organic and inorganic substances by the substitution of organosilyl groups (9).

In the period of 2 years after the appearance of electric field compensation theory (10), in 1981, on the base of theoretical studies, aminiomethylspirobi(1-sila-2,5-dioxacyclopentanon)ate, the first example of a new class of organosilicon hypercoordinated compounds, was synthesized.

In 1994, Reinhold Tacke obtained a new class of compounds, which were named, electrostatically stabilized silanates (ES-silanates), with the general formula as shown in Figure. 1 (2). The synthesis of the first ES-silanate describes the scheme (Figure. 2). Since 1994, the interest concerning this class of compounds has significantly increased. Syntheses of compounds containing, carbon atom bonded with four silicon atoms out were carried with success (11).

Silicon, similarly to carbon, can form big molecules, even polymers (silicones and siloxanes). However, Si-C bonds are formed harder than C-C bonds and because of great silicon affinity to oxygen, more often Si-O bonds (siloxanes) can be observed. In organosilicon molecules Si-N-Si bonds (silazanes) also appear or seldom Si-S-Si (silathianes). The most important groups of organosilicon compounds are: silicon hydrocarbons (alkyl- or arylsilanes), halosilanes (methylchlorosilane), silanols (trimethylsilanol), siloxanes (hexamethylsiloxane), silyl esters (trimethylsilyl acetate), silylamines (trisilylamine), and silicone polymers.

Properties of the above, mentioned groups are similar to the properties of carbon compounds containing analogous functional groups. The Si-Si bond is less stable than the C-C bond; however, the Si-O bond is more stable than the C-O bond. For these reasons silanes containing a branched chain consisting of silicon atoms are not stable. On the other hand, silicone polymers containing chains and nets with Si-O-Si bonds are very resistant. They are obtained as products of hydrolysis of adequate dichloro- or trichlorosilanes (5).

Organosilicon derivatives with a coordination number higher than four belong to the group of hypercoordinated compounds. Their preparation is based on the ability of silicon to coordinate ligands containing groups of atoms with easily accessible electron pairs (12–21).

Suitable aminomethyl derivatives of trialkoxysilane are substrates to the synthesis of ES-silanates. Significant attitude of this method are conditions of this reaction aminomethyltrialkoxysilanes are not sensitive to various impurities and can crystallize from aqueous solution.

Published information reports many examples of obtaining ES-silanates by the use of various aminotrialkoxysilane derivatives (22).

In the last several years, syntheses and structures of a number of zwitterionic λ^5Si-silanates and λ^5Si, λ^5Si-disilanates,

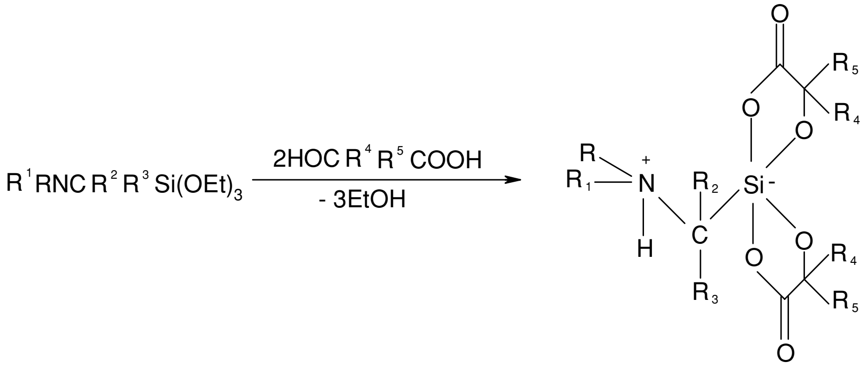


FIG. 2. General reaction schema of ES-silanate preparation.

containing SiO_4C structures, were reported. Systematic research is carried out concerning the chemistry of molecular λ^5Si-silanates (18, 23–26). Due to X-ray spectroscopy investigations, shapes and lengths of bonds between atoms in ES-silanates were determined. Also, electronic spectra made in visible and ultraviolet ranges, which gave information about orbital energy and shapes of molecules, were helpful. Their interpretation enabled determination of crystal structures.

Pentacoordinated organosilicon compounds have a structure of trigonal bipyramid with an equatorial arrangement of the Si-C bond. Two Si-O bonds have axial and two equatorial arrangements. Axial Si-O bonds (with oxygen atoms in the apexes of the pyramids), called apical, are longer and weaker than the rest—the equatorial bonds, which mark the bases of the pyramids. The investigations confirmed the presence of pentacoordinated silicon atoms and tetracoordinated nitrogen atoms (23).

Great electronegativity, the same origin of axial ligands and differences in charges of didonor oxygen atoms cause the spirocyclic anion to form a more stable (for pentacoordinated silicon compounds) trigonal bipyramid shape (27).

Spirocyclic zwitterionic λ^5Si–silanates contain in the molecule pentacoordinated silicon atoms (with formally negative charge) and tetracoordinated nitrogen atoms (with formally positive charge). Therefore, molecules of ES-silanates are neutral.

Properties of the Si-O bond are very important for the chemistry of pentacoordinated silicon. Because of its polarity, the oxygen atom can stabilize more than four coordination numbers on the silicon atom (23).

IMPORTANCE OF SILICON DERIVATIVES FOR ECOSYSTEM

Biological Activity

Silica is a basic and necessary constituent for growth and extension of living organisms. But mechanisms of silicon transport are not entirely understandable. Biogenic silica has various functions. Sea organisms, i.e., diatoms, radiolarian and sponges, use it as a protection against plunderers. Silica forms called plant fossils improve structural stability, photosynthetic ability and defensive strength of higher plants. Perhaps precipitation (by bacteria) irons containing silica covers enabled the survival of archaic forms of life on the earth, when it was exposed to intensive UV radiation. Higher (including human) organisms need silica for the formation of bones and connective tissue. Increasing facts show that silica serves as a detoxification agent against dissolved aluminum (28).

Numerous organosilicon compounds show biological activity. Some of them are very toxic (usually are selective) and they are used for fighting against rodents (5).

The literature exactly describes triorganosilyl derivatives of some biologically active heterocyclic bases and uridine (29). The evaluation of the influence of 2,4,6-tris-(*tert*-butylmethylsilyl)barbituric acid on the central nervous system and anti-cancer activity of 5-O-*tert*-butyldimethylsilyluridine was investigated. The results of biological tests, which were carried out on mice and rats, were compared with the results obtained for non-silylated precursors. Locomotors activity, muscle tension, influences on mind processes and tests of Porsolt were tested. The last test can be count to so-called screening tests widely used in pharmacology, which investigate single reactions. Tested animals must show a certain kind of behavior or do a certain activity. In these kinds of tests only one or a few a parameters can be counted, e.g., time of a reaction, without detailed analysis of complex behavior. This procedure enables quick investigation of a big number of animals by the use of standard, easily accessible instrumentation (29). It was confirmed that tris(*tert*-butylmethylsilyl)barbituric acid showed stronger sedative activity than barbituric acid. It showed also stronger influence on mind processes, completely removing regressive amnesia and intensification of psychotropic activity. Silylated barbituric acid showed slightly higher antistress activity in the Porsolt test. Both acids have low toxicity, but the silylated derivative has a, lower index of acute toxicity. It was also confirmed that 5-O-*tert*-butyldimethylsilyluridine in the contrary to uridine is characterized by anti-cancer activity decreasing development of muscle fibroma in human lungs, mice fibroblasts and isolated cancer cells.

Triorganosilyl derivatives of biologically active substances are very good medical agents because of the hydrolytic lability of Si-N and Si-O bond (29). By-products of the hydrolysis are not overly toxic. Silylation of compounds increases their lipophility. Owing to this fact, triorganosilicon drugs can cure pathological processes, which demand the use of intracellular penetration (30). The efficiency of this activity depends on the speed of silylated compounds hydrolysis (29).

In order to determinate the relation between structure, physicochemical properties and biological activity, a series of neutral organosilicon complexes of oxorene (V) with mixed ligands were synthesized and their lipophile nature was tested (31). Complexes were investigated in relation to their neuronotropic properties and acute toxicity *in vivo* (i.e., tested immediately on living animals or plant organisms). The investigation included consideration of an influence of a nature of ligands (monodonors and tridonors) on the biological properties. Activity of these compounds towards the central nervous system was evaluated on the base of tests concerning anoxemia, narcosis caused by ethanol and hexenal, excessive functional activity caused by phenamine, convulsion caused by corasol, electroshocks and regressive amnesia. It became evident that these compounds showed sedative activity, prolongation of mice life in anoxemia condition, showed anti-convulsive activity, reduced excessive functional activity caused by phenamine and inhibited appearance of regressive amnesia (31).

Introduction of triphenylsiloxyl subsistent to a complex of (2-hydroxyethanothiolate)-3-thapentane increases the length of time of narcosis executed by hexenal but decreases it when narcosis was caused by ethanol. Though trimethylsilyl group introduction (and the increase of lipophility) is of little importance on anoxemia index, the time of narcosis duration after the use of ethanol or hexenal and anti-convulsive activity of hydroxycomplex are significantly changed. Investigations of acute toxicity of these compounds confirm a tendency towards toxicity decrease after introducing, a trialkylsilyl group. It is generally known that the efficiency of psychotropic drugs is closely connected with their ability to cross the barrier between blood and brain, which depends not only on structure parameters but also in appreciable rate on the lipopohility of tested compounds (31).

Aminomethyltrialkoxysilanes belong to an important group of substances, which can serve as substrates in a reaction of obtaining hypercoordinated ES-silanates. Compounds of this type are biologically active and their properties approximate to the properties of natural compounds. Research concerning biological activity of this group is still continuing (14, 15).

These aminomethyltrialkoxysilanes, which contain a nitrogen atom bonded with methyl or butyl groups, are important in preparation of repellents (22). Repellent activities of N,N-dibutylamino-N-methyltrialkoxysilanes, with different alkoxy groups, were exactly investigated. It was noted that an exchange of etoxy group for butoxy increased the repellent activity.

More and more often in a synthesis of new compounds based on natural systems, their potential application and biological activity is considered. The preparation of different kinds of ES-silanates. can serve as an example λ^5Si–[(morpholinio)methyl]bisglycolic(2-)-O^1,O^2]silanate is used as a stimulator of plant growth (in concentrations of 0.0005–0.002 mole/L) (32). This compound is appropriated in agriculture for acceleration of growth and development of cultivated plants, especially Graminae and Cucurbitaceae.

Recently, many various organosilicon compounds are efficient agents assigned to biological regulation of plant organisms (32). Substances with the most similar properties to reported compounds, i.e., growth stimulating, are silatranes. But they have some disadvantages (32): they belong to the class of chloro-organic compounds, therefore there is a possibility of formation of toxic for the environment degradation products; very low solubility in water, high hydrolytic unstableness; and permanent hydrolysis of silatranes causes changes of chemical composition, which makes it impossible to refer obtained results to defined chemical compounds.

The most favorable growth-stimulating agent should not have these disadvantages. It should possess a wide spectrum of activity; it should be effective towards the main kinds of cultivated plants (increase of germination, increase of plant development and of general crop) but not toxic to the environment.

These suggestions were taken into account during preparation of λ^5Si–[(morpholinio)methyl]bisglycolic(2-)-O^1,O^2]silanate [33]. This compound is the first example of a new class of organosilicon—ES-silanates. It is stable in aqueous solutions; its properties are similar to the properties of natural compounds.

The mention of the above properties of this compound, more encouraging than in case of silatranes, caused further investigation of its biological activity. Then, the genetic activity of its aqueous solution (concentration 0.0005–0.002 mole/L) towards plant and animal cells was determined as low. This fact shows that such a solution is ecologically safe (33). It was used also in order to improve germination, to increase energy of germination, to accelerate development and formation of the root system and the growth of the over ground parts of plant. Also observed shorter vegetation time and larger crops, especially in case of root crops (21). Stableness, solubility in water, lack of toxicity, lack of mutagenic activity and high biological activity of tested 0.0005–0.002 mole/L solution of the tested λ^5Si – silanate promises its wide application in the future.

Potential applications of ES-silanates connected with their biological activity were described (34–36). In addition to pentacoordinated silicon compounds exist heptacoordinated derivatives, Hoszczawa silanates. In this case oxygen atoms of carbonyl and hydroxyl groups of oxalic acid (37) server as electron donors.

It is supposed that transport of silicon in biological systems is based on hypercoordinated silicon compounds (38). Therefore, investigated pentacoordinated silicon derivatives can be interesting as model systems (23).

Experimental confirmation of the possibility of electrostatic stabilization of ES-silanate molecules changes a view upon chemistry of compounds containing a Si-O bond. It opens a way to numerous earlier unknown classes of chemical substances. New classes are starting points to originate new substances, systems, materials, composites, new technical solutions and qualitatively new level of science and technology. New, specific biological properties can be expected and, consequently, so can possible effects on diseases presently incurable or difficult to cure (27).

Some hypercoordinated silicon compounds are used for transferring of chirality's from the silicon to the carbon atom and can serve as models for biological transport processes of silicon [39]. The life on earth can be considered as a pyramid, with a base made of the simplest organisms, in particular microflora, which is a silicon-based form of life (40). The absence of silicon causes inhibiting of growth and development of plants. For higher plants the importance of the level of silicon decreases, but still remains important, even for human organisms (41).

Silicon takes part in a cycle in the earth's crust, which includes participation of homologues of lower classes of organisms. A biochemical silicon cycle begins with the weathering of minerals and process of soil formation. Weathering is connected mainly with biochemical activity of organisms. Influence of living organisms on minerals initiates the soil formation (42). Therefore, one of the most important points of the soil formation process is an insertion of silicon in the cycle, which is connected with its transformation into a soluble form. For this reason, during the last century many chemists attempted to synthesize a Si-O bond containing silicon compounds resistant to hydrolysis and neutral and soluble in water. Unfortunately, it is impossible to create in an aqueous medium and at room temperature neutral monomers of organosilicon compounds with alkoxy- or acyloxygroups near to the silicon atom. This problem was successfully solved due to a theory of compensation of electric molecular field in the 1980s (27). At that time, homologues of a new class of chemical compounds, electric stabilized silanates (so-called ES-silanates) were synthesized. They are the only existing neutral, water soluble, hydrolytic stable silicon compounds containing Si-O-C bonds (27, 43–45).

The presence of silicon in the cycle of life and catalysis of biogeochemical processes is essential for the soil formation. Possible mechanisms of introducing of silicon into the cycle of life can be investigated by the use of organosilicon compounds containing Si-O-C bonds. It was proven that maximum electric stabilization of molecules by the coordination of particular substituents and functional groups bonded with the silicon atom belongs to main forces, which liberate this element from minerals. ES-silanates can serve as examples. The mechanism of maximum electric stabilization of molecule electric fields can be effectively utilized by the microflora for assimilation and transformation of one form of silicon into another, its transport, etc. (42).

Information enclosed in the literature shows that hypercoordinated siliconorganic complexes can be formed in biologically connected liquids (28). Proof of an existence of transition organosilicon complex was also reported, generated during the cycle of the organism life. It was confirmed that hypercoordinated organosilicon compounds play an important part in assimilation and transport of silica through biological systems. The existence of such complexes can explain other questions concerning biogeochemistry of silicon, i.e., stability of dissolved silica in concentrated biological liquids, biofractionation of silicon isotopes and fractionation of germane from the mixture with silicon (28).

Organosilicon compounds containing pentacoordinated silicon can effectively increase solubility of silicon, transport this element through tissues and accumulate it in places of destination.

APPLICATION OF ORGANOSILICON COMPOUNDS

Organosilicon compounds are often applied in organic synthesis: substituents containing silicon became important in stabilizing transitive metal derivatives and lower oxidation states of main group metals. Besides, new organosilicon transitive compounds were generated, which contained multiple bonds between the silicon atom and carbon, nitrogen, oxygen and sulfur.

Chlorosilanes and alkoxysilanes, which are basic substrates to polysiloxanes and modified silica gels, also belong to the organosilicon compounds. Silicons (polydimethylsiloxanes, PDMS) are known for their particular properties, i.e., high thermal stability, resistance against hard weather conditions, hydrophobicity, thermal resistance, dielectric properties, coating ability, surface activity and adhesiveness (5). These properties make them precious for various industrial applications and cause their presence in consumer goods. Organosilicon polymers (popularly called silicones) are widely applied: starting from cosmetics, through medical applications (e.g., implants), up to the architecture and chemical industry (paints, rubber, and elastomers) (7).

Products based on PDMS are applied in electric, electronic, motorization, textile, pharmaceutical, cosmetic and architectural industry, in rubber, glass, and plastics production (46). Potential human contact with silicones exists in a place of work, during production processes as well as during normal exploitation of silicone containing goods. Among them are, e.g., silicone implants and catheters, balsams for care of body, products for hair care, antiperspirants, glues, tightening masses, antifoam agents, polishing pastes, and waxes (46, 47).

PDMS penetrate to many food products (and were extracted from them): defatted powder milk, milk beverages, ketchup, jam, sugar and fruit juice (48). Many silanols, including dimethylsilandiol (DMSD), were extracted from aqueous and biological samples, e.g., from urine, blood and plasma (49). Silanols is an important group of organosilicon compounds. They are formed during degradation of polymeric siloxanes in living organisms and in the environment. Silicones are also used in laboratories as solvents, tightening rings, etc. In gas chromatography, gas chromatography (GC) and mass spectrometry gas chromatography (MSGC) stationary phases based on PDMS are commonly used (50).

Organosilicon compounds are widely applied in medicine. In the early 20th century the first organosilicon compounds with anti-cancer properties were synthesized. In 1962, Woronkow discovered a new class of organosilicon compounds—silatranes. Papers appeared concerning biological activity of these compounds (51) 7 years later.

Multi-directional methods of synthesis based on organosilicon reagents enabled improvment of technology of production of antibiotics, which possessed extraordinary activity against gram-positive and gram-negative bacteria.

Silicones are materials with great influence on the stomatology development. Different kinds of silicones are applied, due to their properties (as materials, which can be sterilized, by warming in temperatures over 200°C or by radiation and in most cases neutral towards living tissue). Silicones applied in stomatology are especially raffinated for their differentiated properties, in order to remove all possible impurities.

In the stomatological practice silicones are most often used as squeezing materials of various thicknesses. They are used during preparation of double-layer impress. Thin (soft) silicones are used in surgical practice to litter a denture after removing of cancer or after mechanic injury. Soft silicones are also used for operated patients in order to prepare external artificial parts of face. They are accessible in various colors and can be mixed, obtaining the most suitable result (5).

Hydrophobic silicones were shown to be very efficient in the protection of buildings and other objects against destructive water activity. For more than 40 years they have been applied as a barrier against moisture in architectural materials. Siloxanes are optimum bases for protective coatings. Organosilicon compounds increase resistance of concrete and iron-concrete against corrosion and low temperature. Chemical structure of organosilicon compounds causes their high effectiveness as protective and impregnating architecture materials.

Silanes and polysiloxanes have been applied as hydrophobic agents for many years. On the other hand, the recently intensive use of oligomeric siloxanes is observed. They have attitudes of both aforementioned groups. The high efficiency and ability of penetration characterize them; they form stable bonds with architecture materials. For these reasons oligomeric siloxanes are the optimum base of impregnation emulsions (5).

Organosilicon compounds are used also in preservation of antiques. Rarely they are used as heat carriers, for warming or cooling of heating installations, nuclear energetic devices, etc. (5).

Hypercoordinated silicon compounds are used in a similar way, as other organosilicon compounds. Aminomethyltrialkoxysilanes, which are substrates to hypercoordinated ES-silanates, are applied as corrosion inhibitors. A new, efficient method of inhibiting corrosion is based on the addition of aminomethyltrialkoxysilanes to paints. Considering the increased attack of a polluted environment on steel constructions, bridges, etc., research in this area seems to be of great importance. Other adequate aminomethyl derivatives of trialkoxysilane are used as hardeners (instead of epoxide resin) to glass fiber production (52).

Research in the area of high-duty materials caused increased interest in polymers and silicon-based substances. Aminomethyltrialkoxysilanes as polyfunctional organosilicon monomers were used for the preparation of crosslinked plastics (52).

Silsesquioxanes, which belong to ES-silanates, show very interesting properties. They can be used as membrane materials to optical fiber production or as substrates to ceramic material production. On the other hand, after adequate modification, they can bind catalysts and mesogens, leading to liquid crystals. They form with polymer compounds able to emit light (50).

In organic synthesis hypercoordinated silicon compounds are used for simulation of different steps of the reaction of nucleophile substitution S_N2 (Nu: → Si–X, where substituent X is a leaving group and Nu: is a nucleophile). During this reaction course the silicon atom coordination changes from 4+1 into 3+2 (in the transition state) and then into 1+4 (3).

PREPARATION OF SAMPLES TO ANALYSIS

Organosilicon compounds with increased coordination are intensively investigated because of their potential biological activity. Pentacoordinated silicon compounds with characteristic-spirocyclic ligand of $–O^1$, O^2 type, λ^5-silanates belong to this group. These compounds show zwitterionic structure with tetracoordinated nitrogen atom and pentacoordinated silicon atom (SiO_2C_2 ring system). Some of them easily hydrolyze. It causes numerous difficulties during their isolation from various matrices and preparation of the samples for chromatographic analysis. For this reason, during the whole analytic procedure only high purity, anhydrous solvents should be used.

Another problem is connected with the ability to modify column packing surface by some organosilicon derivatives. It causes additional difficulties during isolation and chromatography determination process.

Immense development of specific packing caused solid phase extraction (SPE) to become the most often used method of isolation of different substances from various matrices. However, remains the most popular separation and determination technique high performance liquid chromatography (HPLC) (53–57). Recently, optimization of determination conditions for some ES-silanates by HPLC methods and capillary electrophoresis (CE) (58–61) was reported.

Preparation of samples for the analysis usually requires primary isolation of an analyzed compound from a complex matrix, especially when it concerns the HPLC technique. Samples of solution subjected to capillary electrophoretic analysis do not require concentration. Categories of concentration of analyzed compounds can be significantly different. ES-silanates are stabilized electrostatically and hydrolytically stable. For these reasons water and DMSO can be used for ES-silanate extraction.

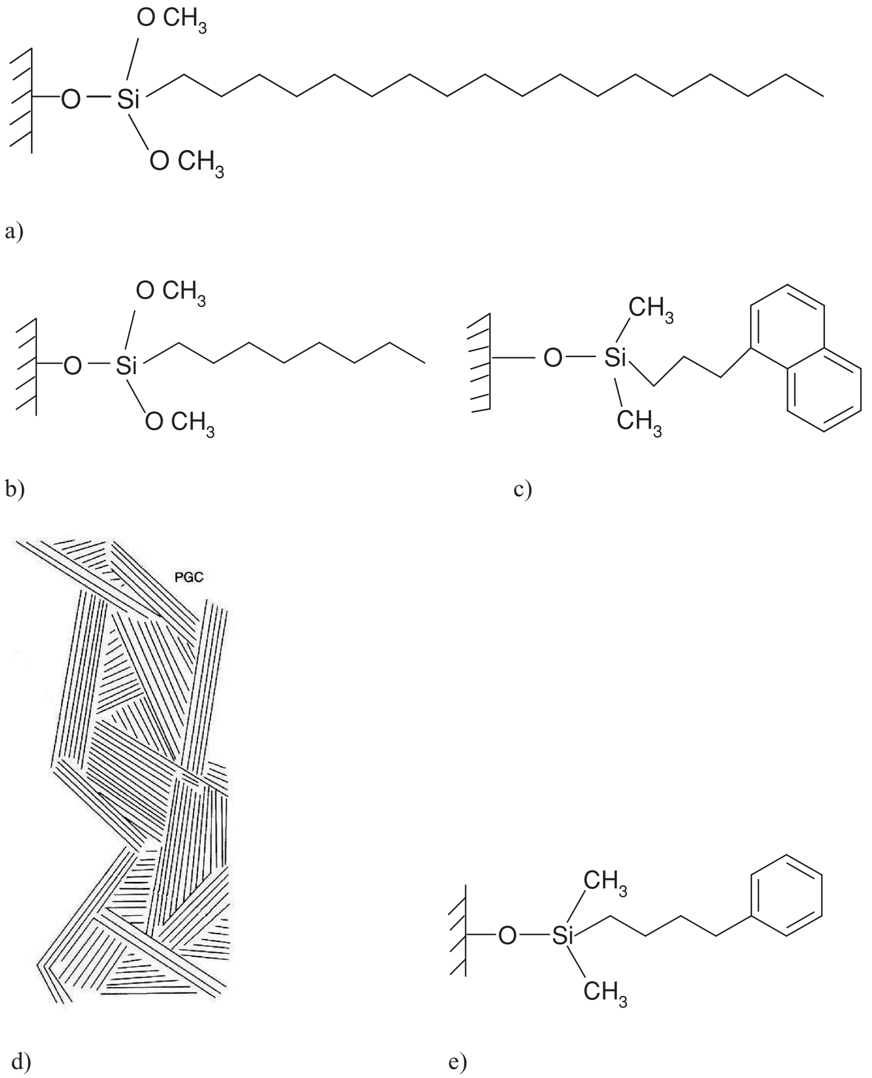
Analysis of biologically active substances is very important in pharmacy and medicine. Usually, in order to isolate and separate complex mixtures, it is necessary to use a selective column. Stability and reproducibility of an extractive column as well as chromatographic is essential for suitable analytic procedure. In chromatography and related techniques the choice of proper stationary phase and mobile phase, accordant for an analyzed substance is crucial.

SPE and HPLC packing are of different polarity. Most of them are based on silica, these used to extraction are similar to these used to chromatography method. The greatest importance has modified silica phase assigned to reverse phase systems (Figure. 3).

Retention process in reverse phase chromatography is based on specific and unspecific interactions between stationary phase, mobile phase and analyzed substance. Changes of type, composition and character of the mobile phase or changes of type, properties and topography of the stationary phase perform optimization of the chromatographic process (61, 62). Separation of a mixture by two-phase system depends on thermodynamic properties of this system.

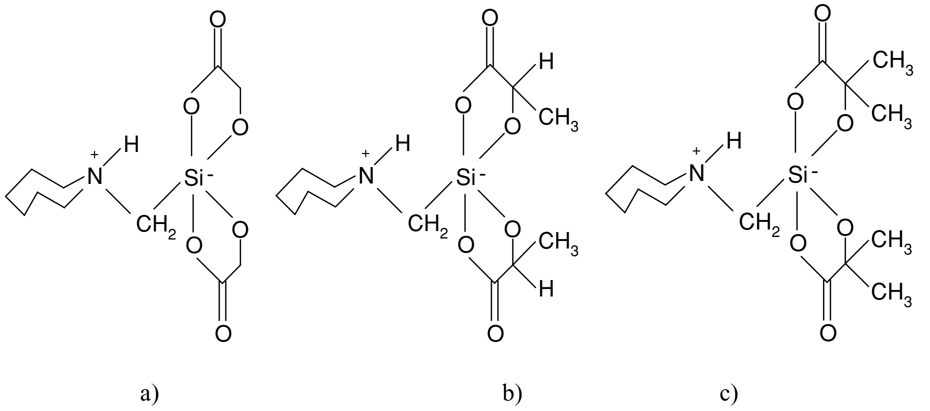
EXAMPLES OF CHROMATOGRAPHIC AND ISOTACHOPHORETIC ANALYSIS

CE is one of the techniques used for ES-silanates determination. Some of them were separated and determined using analysator (Fig. 4). The separation is based on the difference of electrophoretic mobility of analyzed ions.



a) b) c) d) e)

FIG. 3. Schema of chemically bonded stationary phases: a) octadecyl, b) octyl, c) naphthylpropyl, d) PGC, e) phenylbutyl.



a) b) c)

FIG. 4. Structures of members of homologic series of ES-silanates: a) 1-(N-Perhydroazepiniomethyl)[spirobi(1-sila-2,5-dioksacyklopentan-3-on)]at (ES-1), b) 1-(N-Perhydroazep-iniomethyl)[spirobi(1-sila-2,5-dioksa-4-methylcyklopentan-3-on)]at (ES-2), c) 1-(N-Perhydroazepiniomethyl)[spirobi(1-sila-2,5-dioksa-4,4-dimethylcyklopentan-3-on)]at (ES-3).

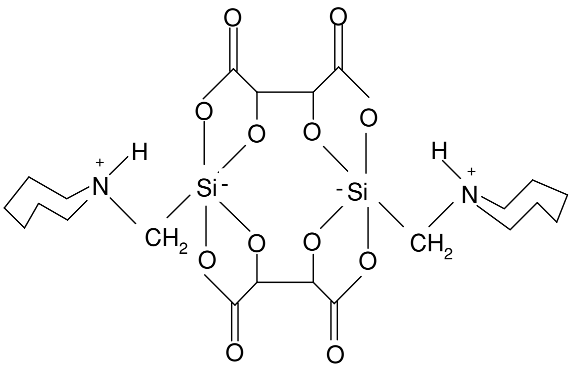


FIG. 5. Schema of the structure of the terminating electrolyte constituent used for ITP determination: 4,4′-bis{1-(Perhydroazepiniomethyl)[spirobi(1-sila-2,5-dioksacyklopentan-3-on)]at}.

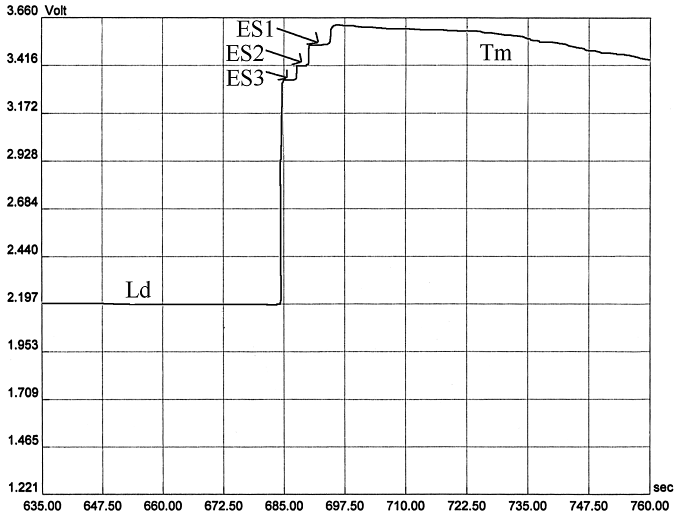


FIG. 6. Isotachophoregram of the mixture of λ^5 Si–[(azepinio)methyl]bis[glycolic(2-)-O^1, O^2]silanate (**ES-1**), λ^5 Si–[(azepinio)methyl]bis[lactic(2-)-O^1, O^2]silanate (**ES-2**), λ^5 Si–[(azepinio)methyl]bis[methyllactic(2-)-O^1, O^2]silanate (**ES-3**).

These differences were not great; therefore, analysis of the silanates caused numerous difficulties. The next problem was to select an adequate terminating electrolyte for these compounds, a compound with low mobility. An ionic double salt 4,4′-bis{1-(Perhydroazepiniomethyl)[spirobi(1-sila-2,5-dioksacyklopentan-3-on)]at} was used for the determination of ES-silanates (Fig. 5) (60).

Elaboration of optimum conditions of separation and determination was confirmed by the obtained isotachophoregram (Figure. 6). Good separation for a mixture of three ES-silanates was achieved in 12 minutes.

High efficiency of separation in comparison with other electrophoretic methods and the short time of analysis cause capillary ITP, from many points of view, to compete not only with HPLC but also with other analytic techniques.

ITP allows the determination of chosen ES-silanates in an aqueous solution. The main attitude of this method is simultaneous determination of all macro- and micro-elements in a short time (up to 25 minutes) comparing with classical chromatographic methods. Preparation of samples is simple (only the dissolution in water), the method is cheap and is suitable for routine analyses. It can be considered as a green chemistry" technique, because toxic solvents or reagents are not used. Precision and accuracy of results obtained by the capillary ITP method is better than those obtained by classical methods.

The second technique used for ES-silanate determination was HPLC. Analyses were performed with detection at wavelength 325 nm, using anhydrous mobile phases: acetonitrile, methanol, and dichloromethane with different flow intensities. Five various stationary phases were applied: octadecyl, octyl, phenylbutyl, naphthylpropyl and PGC (Figure. 3) (58, 59).

The octadecyl column served as reference column. Mixtures of solvents with water were not considered because of long retention time.

The best results were obtained when pure acetonitrile was used as a mobile phase and a stationary phase was the naphthylpropyl column. The shortest retention time of the slowest (in homological series) derivative did not exceed 4 minutes.

In the case of PGC and the same mobile phase, retention time was slightly shorter, but the separation was unsatisfactory. Better selectivity yielded a phenylbutyl column but retention times of analyzed compounds were a few minutes longer (59).

The octyl phase was characterized by relatively long retention times, which at flow intensity 0.3 ml/min reached almost 110 minutes (at the same flow a naphthylpropyl column yielded retention time of merely 31 minutes). Proportional results were obtained using anhydrous methanol and anhydrous dichloromethane. However, these mobile phases yielded slightly longer retention times (58).

Decrease of flow intensity of the mobile phase caused significant prolongation of retention time for alkyl (i.e., octadecyl and octyl) columns. On the other hand, in case of aryl columns, this prolongation was negligible (Fig. 7).

The PGC column was characterized by a different surface structure than the remaining columns (Fig. 3). This obvious difference caused shorter retention times but lower selectivity. Therefore, the effect obtained on a naphthylpropyl column is the best among five tested columns (three columns belonging to the aryl group, two to the alkyl, which were considered as standard: octyl and octadecyl).

SUMMARY

To summarize, for the determination of hypercoordinated compounds, which belong to the ES-silanate group, HPCL as

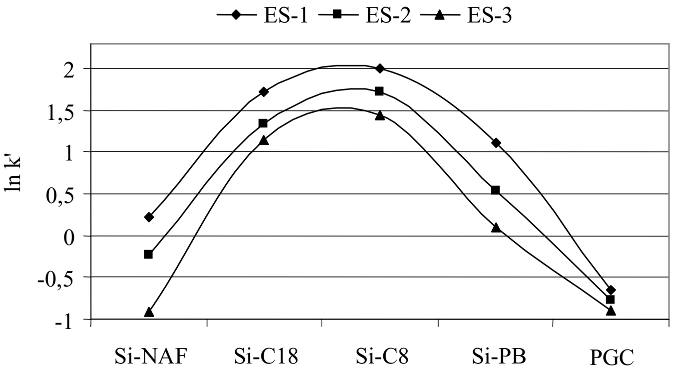


FIG. 7. Results of the separation of λ^5 Si–[(azepinio)methyl]bis[glycolic(2-)-O^1, O^2]silanate (**ES-1**), λ^5 Si–[(azepinio)methyl]bis[lactic(2-)-O^1, O^2]silanate (**ES-2**), λ^5 Si–[(azepinio)methyl]bis[methyllactic(2-)-O^1, O^2]silanate (**ES-3**) with the use of stationary phases Si-NAF (naphthylpropyl), Si-C_8 (octyl), PGC, Si-PB (phenylbutyl) and Si-C_{18}(octadecyl). The mobile phase: acetonitrile (100%).

well as can be applied. Separation of a mixture of compounds {1-(N-Perhydroazepiniomethyl)[spirobi(1-sila-2,5-diok-sacyklopentan-3-on)]at, 1-(N-Perhydroazepiniomethyl)[spirobi(1-sila-2,5-dioksa-4-methylcyklopentan-3-on)]at and 1-(N-Perhydroazepiniomethyl)[spirobi(1-sila-2,5-dioksa-4,4-dimet-hylcyklo pentan-3-on)]at} was successfully carried out. Optimum conditions of their separation and determination were elaborated using ITP with conductometric detection, despite small differences of electrophoretic mobility. A new terminating electrolyte containing 4,4′-bis{1-(Perhydroazepiniomethyl)[spirobi(1-sila-2,5-dioksacyklopentan-3-on)]at} was used for the analysis.

Optimum conditions of separation and determination of aforementioned ES-silanates by HPLC technique were also elaborated. Independently of a composition of a mobile phase, the naphthylpropyl phase was characterized by the highest selectivity. Besides, this phase affords possibilities for short retention times. The main reason for increased selectivity is an occurrence of additional interactions of π-electrons between the stationary phase and determined compounds. The PGC column was characterized by the shortest retention times of the tested compounds, but had unsatisfactory resolution. Slightly lower separation factors and longer retention times of analyzed ES-silanates showed octadecyl phase. Generally, retention times of analyzed compounds obtained by the use of aryl stationary phases were significantly shorter than retention times obtained by the use of alkyl phases.

This work was started in hopes that optimization of determination of these compounds by means of HPLC and CE technique could be useful in the development of silicon chemistry, especially for the investigation of biologic activity of organosilicon derivatives. This paper is an attempt of a synthesis of information concerning hypercoordinated compounds, which belong to the group of ES-silanates (biologically active) in order to help the research in the area of organosilicon chemistry.

REFERENCES

1. Böhme, S. Wiesner, and B. Günther, Easy access to chiral penta- and hexacoordinate silicon compounds. *Inorganic Chemistry Communications* 9 (2006): 806–809.
2. R. Tacke, J. Heermann, M. Pülm, and E. Gottfried, Zwitterionic λ^5Si-silicate with an almost ideal square-pyramidal Si coordination polyhedron: Synthesis and crystal structure analysis. *Monatshefte für Chemie* 130 (1999): 99–107.
3. J. G. Shackman, and D. Ross, Gradient elution isotachophoresis for enrichment and separation of biomolecules. *Analytical Chemistry* 79 (2007): 6641–6649.
4. R. Kocjan, *Analytical Chemistry* (PZWL, Warsaw, Poland, 2000).
5. G. Koerner, M. Schulze, and J. Weis, *Silicones: Chemistry and Technology* (Vulkan-Verlag, Essen, Germany, 1991).
6. T. J. Barton, Carbacyclic silanes, in *Comprehensive Organometallic Chemistry* eds. G. Wilkinson, F. G. A. Stone, an E. W. Abel (Pergamon, Harvard University, 1982), Ch. 9.2, 205–217.
7. F. S. Kipping, and J. E. Hackford, Organic derivatives of silicon. Part XIV. The preparation of tertiary silicol. *Journal of the Chemical Society* 99 (1911): 138–145.
8. H. Davies, and F. S. Kipping, Different methods of applying the Grignard reagents. *Journal of the Chemical Society* 99 (1911): 296–301.
9. E. G. Rochow, *The Chemistry of Silicon* (Pergamon, Harvard University, 1986), Ch. 15, 1431–1465.
10. N. Erchak, E. Lukevics, W. Motorykina, A. Kemme, and J. Bleidelis, Preparation of 1-morpholiniomethyl-1,1-spirobi(1-sila-2,5-dioxacyclopentanon-3) at. *A. c. 1059872 USSR*, No. 45 (1984): C239.
11. N. Erchak, and E. Lukevics, Preparation of morpholiniomethyl-spirobi(1-sila-2,5-dioxacyclopentanon-3) at. *A. c. 1439991 USSR*, No. 43 (1988): C268.
12. R. Tacke, J. Becht, O. Dannappel, R. Ahlrichs, U. Schneider, W. S. Sheldrick, J. Hahn, and F. Kiesgen, Zwitterionic spirocyclic λ^5 Si-silicates with two *cis*-1,2-diphenylethene-1,2-diolato(2–) ligands: Synthesis and structural characterization. *Organometallic* 15 (1996): 2060–2077.
13. R. Bertermann, A. Biller, M. Kaupp, M. Penka, O. Seiler, and R. Tacke, New zwitterionic spirocyclic λ^5Si-silicates with an SiX_4C skeleton ($X = S, O$) containing two ligands of the dithiolato(2-) or diolato(2-) type: Synthesis, structure, and bonding situation. *Organometallics* 22 (2003): 4104–4110.
14. N. Erchak, and E. Liepins, Homo[oxalic acid Si-(aminomethyl)Si, Si-diethoxysilanates] (Goshchava diethoxysilanatees) and process for their preparation. *USSR Patent SU N. 1710561*, (1991). [C.A. 117 (1991) 234244].
15. N. Erchak, and E. Liepins, Homo[oxalic acid Si-(N, N-dimethylaminiomethyl)-Si, Si-dihydroxysilanate]–Goshchava dihdroxysilanate and a method of preparing some. *USSR Patent SU N. 1685954*, (1991). [117 (1991) 910079].
16. R. Tacke, B. Pfrommer, K. Lunkenheimer, and R. Hirte, Zwitterionic (ammoniomethyl)-tetrafluorosilicates of the formula type $F_4SiCH_2NH_2(CH_2)_nMe$ (n=5B11) and $F_4SiCH_2NMe_2(CH_2)_5Me$: A new class of highly efficient surface-active compounds. *Organometallics* 17 (1998): 3670–3676.

17. R. Tacke, M. Pülm, and J. Heermann, Zwitterionic bis[citrato2B-O^3, O^4](morpholinio-methyl)germanate hydrate and its silicon analogue: Syntheses and crystal structure analyses. *Organometallics* 16 (1997): 5648–5652.
18. M. Kluska, An application of aryl stationary phases for separation of select organogermanium compounds. *Journal of Liquid Chromatography & Related Technologies* 31 (2008): 210–218.
19. R. Tacke, M. Pülm, J. Heermann, and I. Richter, (Ammoniomethyl)bis[salicylato(2B)-O^1, O^2]silicates: Zwitterionic spirocyclic λ^5Si-silicates with two six-membered SiO_2C_3 ring systems. *Organometallics* 17 (1998): 1663–1668.
20. G. Rima, J. Satge, R. Dagiral, C. Lion, H. Sentenac-Roumanou, M. Fatome, V. Roman, and J. Laval, A review on the radioprotective activity of organogermanium and organosilicon compounds. *Metal Based Drugs* 6 (1999): 49–56.
21. N. Erchak, and E. Liepins, SU N. 1710562, (1992) (USSR).
22. E. Lukevics, V. P. Dremowa, L. I. Simchenko, and M. G. Voronkov, Siloxazolidines with a pentacovalent silicon atom. *Chemistry of Heterocyclic Compounds* 13 (1977): 1037–1047.
23. R. Corriu, and P. Jutzi, *Tailor-Made Silicon-Oxygen Compounds: From molecules to Materials* (Braunschweig, Wiesbaden, 1996).
24. R. Tacke, J. Becht, O. Dannappel, M. Kropfgans, A. Lopez-Mras, M. Mühleisen, and J. Sperlich, *Progress in Organosilicon Chemistry, in Gordon and Breach Science Publishers* (Amsterdam, Holland, 1995).
25. D. Reichel, R. Tacke, P. G. Jones, G. Lambrecht, J. Gross, E. Mutschler, and M. Waelbroeck, Biological recognition of enantiomeric silanes and germanes: Syntheses and antimuscarinic properties of the enantiomers of the Si/Ge analogues cyclohexyl(hydroxymethyl)phenyl(2-piperidinoethyl)silane and -germane and their methiodides, in: *Organosilicon Chemistry II* eds. N. Auner and J. Weis, (VCH, Weinheim, 1996): 231–236.
26. E. Lukevics, L. Ignatovich, I. Shestakova, V. Romanov, S. Grinberg, J. Popelis, and I. Sleiksha, A new method for the synthesis of silicon- and germanium- containing 2-acetylfurans and 2- acetylthiophenes. *Chemistry of Heterocyclic Compounds* 43 (2007): 143–152.
27. N. Erchak, Chemistry of Furan Derivatives of 4B Group Elements (Riga, Latvia, 1990).
28. J. D. Kubicki and P. J. Heaney, Molecular orbital modeling of aqueous organosilicon complexes: Implications for silica biomineralization. *Geochimica et Cosmochimica Acta* 67 (2003): 4113–4121.
29. E. Lukevits, I. Segal, I. Birgele, and A. Zablotskaya, Silyl modification of biologically active compounds. *Chemistry of Heterocyclic Compounds* 34 (1998): 1076–1080.
30. M. Kluska, Some aspects of the analysis of biologically active organogermanium substances. *Critical Reviews in Analytical Chemistry* 38 (2008): 85–93.
31. A. Zablotskaya, I. Segal, A. Kemme, S. Germane, J. Popelis, E. Lukevics, R. Berger, and H. Spies, Silyl modification of biologically active compounds. Synthesis, structure, physicochemical and biological properties of some silicon-containing “3+1” oxorhenium(V) complexes. *Chemistry of Heterocyclic Compounds* 38 (2002): 477–489.
32. I. Lukjanchik, N. Erchak, M. Nistratov, and I. Makovey, Testing of mutagenic properties of ES-silanates using a method based on chromosomic aberration in meristematic plant cells. *Proceedings of International Scientific Conference: Biological Cycles*. (Brest, Byelorussia 1999).
33. L. Kinchak, A. Tarasiuk, and N. Erchak, Genetic activity of a new class of compounds in adaptation problem of organisms in changeable conditions. *Proceedings of Scientific International Conference: Ecology and Youth* (Homel, Byelorussia 1988).
34. Z. Rappoport, and Y. Apeloig, *The Chemistry of Organic Silicon Compounds* (New York, Wiley 1998).
35. R. Tacke, R. Bertermann, M. Penka, and O. Seiler, Easy access to chiral penta- and hexacoordinate silicon compounds. *Zeitschrift für Anorganische und Allgemeine Chemie* 629 (2003): 2415–2427.
36. E. Lukevics, A. F. Lapsina, G. Zelcans, A. Dauvarte, and A. Zidermane, Silatranes and their tricyclic analogs, in *The Chemistry of Organic Silicon Compounds*, ed. Zvi Rappaport (Wiley Interscience, Chichester-NewYork-Weinheim-Brisbane–Singapore-Toronto, 1998), Vol. II, Ch. 326: 1536–1597.
37. A. Szymanik, Synthesis and properties of 1-[(silanyl)methyl] azepane. *Master’s thesis* (University of Podlasie, Poland 2005).
38. C. W. Sullivan, *Silicon Biochemistry* (Wiley, Chichester, 1986).
39. R. Tacke, Easy access to chiral penta- and hexacoordinate silicon compounds. *Angewandte Chemie* (International Edition in English, 1999).
40. D. Evered and M. O’Connor, *Silicon Biochemistry: Ciba Foundation Symposium 121* Chichester-New York-Sydney-Toronto-Singapore, A. Wiley-Interscience Publication, 1986.
41. V. Leoni, and L. Fabiani, Aspetti nutrizionali della presenza della Silice nelle acque minerali e potabili. *La Rivista di Scienza dell’ Alimentazione* 4 (1999): 407–414.
42. М. П. Ярчак, Attempts of modeling of some soil forming processes. *Natural Environment of Polesie: Present Situation and Changes: Proceedings of the International Scientific Conference*, (Brest, Bielarus 2002): 57–60.
43. N. I. Erchak, Theoretical approach to electrostatic stabilization of molecules *in Abstracts of 10th International Symposium of Organosilicon Chemistry* (Poznan, Poland, 1993).
44. N. I. Erchak, Electrostatically stabilized silanates*in Abstracts of 11th International Symposium of Organosilicon Chemistry* (Université Montpellier II, France, 1996).
45. N. I. Erchak, Theory of electrostatic stabilization of molecules*in Abstracts of 13th International Conference on Organic Chemistry* (Warsaw, Poland, 2000).
46. G. M. Cameron, H. Haala, and A. L. Kuo, The use of volatile silicones in cosmetic applications. *Perfume Cosmetic A* 67 (1986): 384–396.
47. T. H. Lane, The manufacture and use of silicones, unpublished internal Dow Corning. *Technical Report I0000–44151* (1997).
48. M. Nishijima, M. Kanmuri, S. Takahashi, H. Kimamura, M. Nakazato, and Y. Kimura, Determination of dimethylpolysiloxane in foods by atomic absorption spectrophotometry. *Shokuhin Eiseigaku Zasshi 16, 110; through Chem. Abstr. 83, 145855f* (1975).

49. S. Varaprath, K. L. Salyers, K. P. Plotzke, and S. Nanavati, Extraction of octamethylcyclotetrasiloxane and its metabolites from biological matrices. *Analytical of Biochemistry* 256 (1998): 14–22.
50. S. Varaprath, D. H. Stutts, and G. E. Kozerski, A primer on the analytical aspects of silicones at trace levels-challenges and artifacts —A review. *Silicon Chemistry* 3 (2006): 79–102.
51. M. G. Voronkov, and K. A. Abzaeva, Genesis and evolution in the chemistry of organogermanium, organotin and organolead compounds.*The Chemistry of Organic Germanium, Tin and Lead Compounds* (Wiley, New York, 2002).
52. V. G. D'yakov, and A. V. Shreider, Corrosion control and selection of materials for refinery equipment. *Chemistry and Technology of Fuels and Oils* 12 (1976): 926–936.
53. B. Buszewski, R. Gadzała-Kopciuch, and M. Jaroniec, Chromatographic properties of mixed chemically bonded phases with alkylamide and aminopropyl ligands. *Journal of Liquid Chromatography & Related Technologies* 20 (1997): 2313–2325.
54. B. Buszewski, R. Gadzała-Kopciuch, M. Markuszewski, and R. Kaliszan, Chemically bonded silica stationary phases: Synthesis, physicochemical characterization, and molecular mechanism of reversed-phase HPLC retention. *Analytical Chemistry* 69 (1997): 3277–3284.
55. B. Buszewski, R. Gadzała-Kopciuch, R. Kaliszan, M. Markuszewski, M. T. Matyska, and J. J. Pesek, Polyfunctional chemically bonded stationary phases for reversed phase high performance liquid chromatography. *Chromatographia* 48 (1998): 615–622.
56. B. Buszewski, K. Krupczyřska, R. Gadzała-Kopciuch, G. Rychlicki, and R. Kaliszan, Evaluation of HPLC columns: A study on surface homogeneity of chemically bonded stationary phases. *Journal of Separation Science* 26 (2003): 313–321.
57. R. Gadzała-Kopciuch, M. Kluska, M. Weniak, and B. Buszewski, Silicon dioxide surfaces with aryl interaction sits for chromatographic applications. *Materials Chemistry and Physics* 89 (2005): 228–237.
58. M. Kluska, K. Pypowski, I. Chrząścik, R. Gadzała-Kopciuch, M. Michel, E. Liepinsh, and N. Erchak, High performance liquid chromatography of benzyl derivatives of ES-silanates. *Journal of Liquid Chromatography & Related Technologies* 31 (2008): 1195–1203.
59. M. Kluska, E. Liepinsh, K. Pypowski, and N. Erchak, Separation of azepinio-methyl derivatives of ES-silanates by the use of aryl stationary phases in HPLC. *Journal of Liquid Chromatography & Related Technologies* 31 (2008): 675–682.
60. M. Kluska, K. Pypowski, I. Chrząścik, T. Koval, and N. Erchak, Optimization of conditions of isotachophoretic separation and determination of new class of pentacoordinated silanes — λ^5–silanates, *Journal of Chromatographic Science* (2008) (in press).
61. M. Kluska, E. Liepinsh, K. Pypowski, I. Chrząścik, M. Michel, N. Erchak, Separation of chosen derivatives of Hoszczawa-silanates with taking advantage of π–π interactions. *Journal of Liquid Chromatography & Related Technologies* (2008) (in press).
62. R. Gadzała-Kopciuch, and B. Buszewski, Comparative study of hydrophobicity of octadecyl and alkylamide bonded phases using the methylene selectivity. *Journal of Separation Science* 26 (2003): 1273–1283.