

Organic heterocyclic compounds as ionophores: recent progress in potentiometric sensing

Nataliya Korol ^{1,*}, Dzhosiya Molnar ^{2,3} and Mikhailo Slivka ¹

¹Organic chemistry department, Uzhhorod National University, Pidhirna street,46, 88000, Uzhhorod, Ukraine

²Department of hotel and restaurant business, Mukachevo State University, Uzhhorodska Street, 26, 89608, Mukachevo, Ukraine

³Ferenc Rákóczi II Transcarpathian Hungarian Institute, 6 Kossuth Sq., Beregovo, 90200, Ukraine

(Received February 20, 2025; Revised March 17,2025; Accepted March 18, 2025)

Abstract: This review article provides a comprehensive analysis of the advancements in organic heterocyclic compounds as ionophores for potentiometric sensors over the past decade. It highlights their critical role in modern analytical chemistry and their impact on sensor performance. Various classes of heterocyclic ionophores—including five-membered monoheterocyclic compounds (e.g., pyrazole and 1,2,4-triazole derivatives), pyridine derivatives, condensed heterocyclic compounds (such as indoles, quinazolines, cucurbiturils, benzimidazoles, benzothiazoles, carbazoles, and thiazines), Schiff bases, and macroheterocyclic compounds—are systematically reviewed. Special emphasis is placed on the design, synthesis, and optimization of these ionophores within polymer-based and PVC membrane electrodes, along with their key performance parameters such as linear concentration ranges, detection limits, response times, and ion selectivity. By analyzing research findings from the last 10 years, this review underscores the advantages of organic heterocyclic ionophores in terms of selectivity, stability, and versatility, making them highly suitable for applications in environmental monitoring, clinical diagnostics, food safety, and industrial analysis. Additionally, emerging trends and ongoing challenges in potentiometric sensor development are discussed, offering insights into future research directions in this rapidly evolving field.

Keywords: Ionophores; potentiometric sensors; ion-selective electrodes; PVC membrane electrodes; sensor selectivity; macroheterocyclic compounds. ©2025 ACG Publication. All right reserved.

1. Introduction

Organic heterocyclic compounds play a crucial role in modern analytical chemistry [1, 2]. Their unique chemical structures, combined with their ability to interact selectively with a range of ions, make them invaluable as ionophores—key functional components in sensors designed to deliver exceptional selectivity and sensitivity [3–7].

In potentiometric analysis, ionophores are integral to determining a sensor's ability to selectively target specific ions. Organic heterocyclic compounds are particularly well-suited for this function due to several distinct properties: their polarizability and the presence of heteroatoms, which promote the formation of strong ion complexes [8]; their structural versatility, enabling fine-tuning of chemical properties to address specific analytical challenges [9]; and their long-term stability, which ensures both sensor durability and the reliability of measurements over time [10].

Ionophores are specialized molecules that facilitate the selective transport or binding of specific ions, playing a crucial role in ion-selective electrodes (ISEs) [11-13]. They function by forming reversible complexes with target ions, thereby enabling highly selective ion recognition. Depending on their structural framework, ionophores can be classified as neutral carriers, charged carriers, or

* Corresponding author: E-Mail: nataliya.korol@uzhnu.edu.ua, Phone: + 38 0957043456.

Organic heterocyclic compounds as ionophores

macrobicyclic compounds such as crown ethers and cryptands. Their effectiveness is largely influenced by factors such as ligand geometry, the presence of electron-donating or withdrawing groups, and the rigidity or flexibility of the molecular backbone. These characteristics dictate the binding affinity and selectivity toward particular cations or anions, making ionophores indispensable in the development of highly responsive and accurate potentiometric sensors.

Significant advancements include the development of functional derivatives such as pyrazoles [14, 15], thiazoles [16, 17], and triazoles [18, 19], which have demonstrated high selectivity toward alkali metal cations, alkaline earth metal cations, heavy metals, and certain anions.

This review offers a comprehensive overview of the application of organic heterocyclic compounds as ionophores in potentiometric methods, highlighting key research advancements from the past decade.

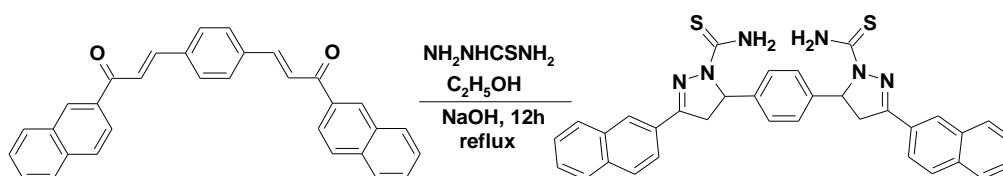
2. Literature Review

2.1. Pyrazole Derivatives

A research group [20] developed a novel polyvinyl chloride (PVC)-based membrane potentiometric sensor for the determination of chromium(III) ions. In this sensor, 5,5'-(1,4-phenylene)bis(3-(naphthalen-1-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide) was used as a neutral ionophore. The optimal membrane composition included the ionophore, potassium tetrakis(4-chlorophenyl)borate (KTPClPB), dibutyl phthalate (DBP), and PVC in a ratio of 5.5:1.5:55:38 (mg). The sensor featured a working concentration range of 1.0×10^{-5} – 1.0×10^{-1} mol/L, detection limit of 1.7×10^{-6} mol/L, response time of 8 seconds, and operation over a pH range of 5.0–11.0.

The sensor demonstrated excellent selectivity for chromium(III) ions compared to other investigated cations, including alkali, alkaline earth, heavy, and transition metals. Moreover, it exhibited good reusability and stability.

The study further showed that this sensor could be employed as an indicator electrode in the quantitative determination of Cr^{3+} ions by potentiometric titration with ethylenediaminetetraacetic acid (EDTA). The titration was successfully applied to samples of industrial water, distilled water, and wastewater. The ionophore was synthesized according to Scheme 1.



Scheme 1. Synthesis of the ionophore 5,5'-(1,4-phenylene)bis(3-(naphthalen-1-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide).

In a subsequent study, the same research group [21] developed a solid-state contact potentiometric membrane electrode based on bis-1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one (Fig. 1) as an ionophore for the selective detection of Hg^{2+} ions. The electrode's performance was evaluated over a mercury ion concentration range of 1.0×10^{-2} to 1.0×10^{-6} mol/L, showing excellent linearity ($R^2 = 0.9997$) with a detection limit of 1.2×10^{-7} mol/L. It maintained high selectivity for Hg^{2+} ions, unaffected by other ions, and exhibited a potential change of 62.0 ± 2.0 mV for each tenfold increase in mercury(II) ion concentration. The electrode's potentiometric response was stable in the pH range of 3.0 to 10.0. Similar to the earlier pyrazole-based sensor, this electrode was successfully used to determine mercury(II) in various water samples and as an indicator electrode in the potentiometric titration of mercury(II) ions with EDTA.

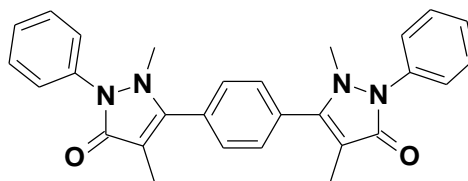


Figure 1. The structure of the ionophore is 5,5'-(1,4-phenylene)bis(1,5-dimethyl-2-phenyl-1,2-dihydro-3H-pyrazol-3-one)

2.2. Triazole Derivatives

A new PVC membrane electrode for the determination of Bi^{3+} ions has been developed, as described in [22]. This electrode is based on 5-(3,4,5-trimethoxyphenyl)-4-amino-1,2,4-triazole-3-thiol (Fig. 2) as the ionophore and uses *o*-nitrophenyl octyl ether (*o*-NPOE) as a plasticizer. The sensor demonstrated a Nernstian response for Bi^{3+} ions over a concentration range of 5.0×10^{-7} to 1.0×10^{-2} mol/L, with a slope of 19.8 mV/decade. It operated within a pH range of 3.0–6.0, had a response time of 6 seconds, and maintained consistent performance for at least five weeks. Additionally, it exhibited good selectivity against a wide range of alkali, alkaline earth, transition, and heavy metal ions. The electrode was successfully employed as an indicator in the potentiometric titration of Bi^{3+} ions with EDTA and in the determination of Bi^{3+} content in gastric preparations.

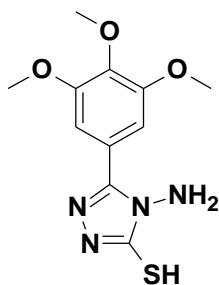


Figure 2. The structure of the ionophore is 5-(3,4,5-trimethoxyphenyl)-4-amino-1,2,4-triazole-3-thiol

2.3. Pyridine Derivatives

Heterocyclic compounds based on pyridine and urea (Fig. 3) that contain hydrogen bond donor/acceptor groups have been employed as ionophores in polymer membrane ion-selective electrodes for the determination of hydrosulfide and hydrosulfate anions [23]. Optimization of the membrane components—such as the choice of lipophilic additives and plasticizers—led to ion-selective electrodes that exhibit a Nernstian response for hydrosulfide/hydrosulfate with enhanced selectivity toward lipophilic anions and halides (Fig. 4). For the determination of hydrogen sulfate in water samples, these optimized electrodes demonstrated good reversibility and improved detection limits, featuring a linear response in the range of 5×10^{-5} M to 1×10^{-2} M and a detection limit of 1×10^{-6} M.

Organic heterocyclic compounds as ionophores

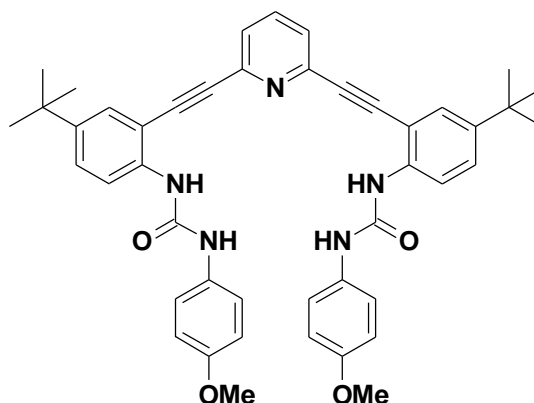


Figure 3. The structure of the ionophore is N,N' -{pyridine-2,6-diylbis[(ethyne-2,1-diyl)(4-tert-butylphenyl)-2,1-diyl]}bis(N' -(4-methoxyphenyl)urea)

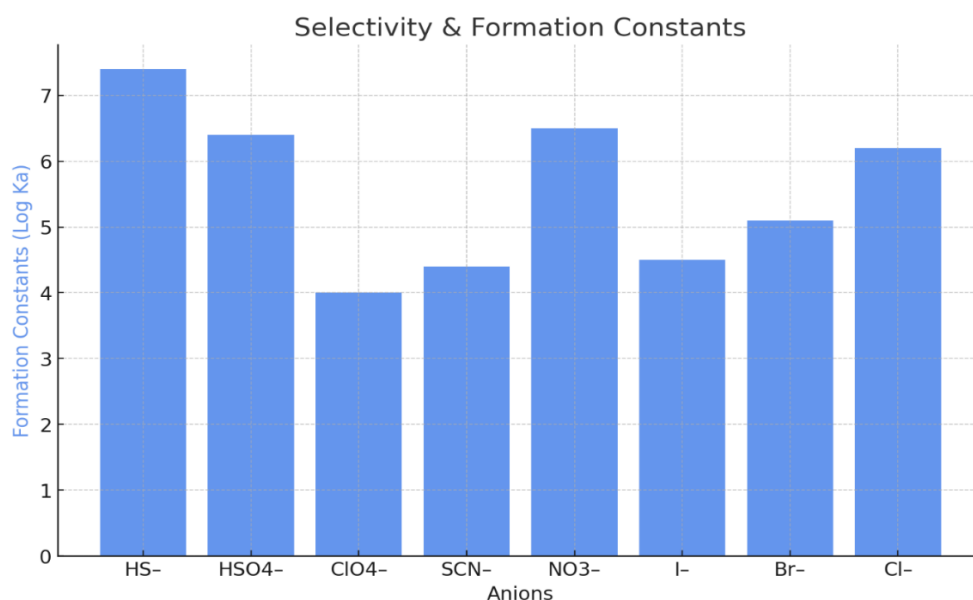
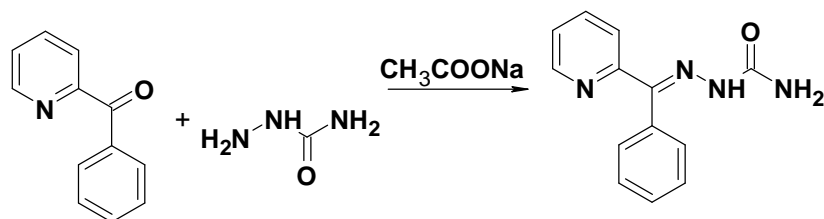


Figure 4. Results of the potentiometric determination of anions using the ionophore N,N' -{pyridine-2,6-diylbis[(ethyne-2,1-diyl)(4-tert-butylphenyl)-2,1-diyl]}bis(N' -(4-methoxyphenyl)urea)

In another study, the authors [24] fabricated and investigated a new polyvinyl chloride (PVC) membrane electrode that utilizes 2-benzoylpyridine semicarbazone as the ionophore, dioctyl phthalate as the plasticizer, and sodium tetraphenylborate (NaTBP) as an additive for the selective determination of Zn(II) ions. The optimal membrane composition was determined to be 30% PVC, 58% plasticizer, 8% NaTBP, and 4% 2-benzoylpyridine semicarbazone. The ionophore was synthesized following the reaction scheme shown in Scheme 2. The sensor exhibited a linear response over the concentration range of 1.0×10^{-2} to 4.56×10^{-6} M, a detection limit of 2.28×10^{-6} M, and a response time of less than 10 seconds. Moreover, the electrode maintained stable performance for at least six months and was successfully applied to the analysis of fruit and vegetable samples.



Scheme 2. Synthesis of the ionophore 2-benzoylpyridine semicarbazone.

Authors [25] prepared PVC-based ion-selective membranes by combining CP-DPA, dibutyl phthalate (or dioctyl phthalate), PVC, and THF. Within the 1×10^{-2} to 1×10^{-5} mol/L range, the electrodes exhibited near-Nernstian responses, with slopes of 57.2 ± 1.3 mV/decade (dibutyl phthalate) and 61.6 ± 1.2 mV/decade (dioctyl phthalate). The lower detection limits, determined from the intersections of extrapolated linear segments of the calibration plots, were 5.7×10^{-6} M for the DBP-based electrode and 8.0×10^{-6} M for the DOP-based electrode. Response times were approximately 30 s for concentrations between 10^{-5} and 10^{-2} M, and about 60 s in the 10^{-7} to 10^{-5} M range. Over a three-week period, the electrodes retained Nernstian slopes (varying by no more than ± 2 mV/decade), though by the end of this interval the detection limit shifted to 10^{-3} M CP chloride.

The same research group [26] developed the ionic associate (IA) of cetylpyridinium chloride (CPC) and tetraphenylborate (TPhB) which served as the ionophore. Validation of the fabricated electrode was carried out by examining its response in CPC and sodium dodecyl sulfate (DDS) solutions over a concentration range of 10^{-7} to 10^{-1} mol/L. The electrode displayed a near-theoretical slope of approximately 58 mV/decade and linear behavior from 10^{-5} to 10^{-1} mol/L. Notably, the electrode exhibited high sensitivity toward cationic surfactants and various lipophilic anions, resulting in a substantial potential jump at the equivalence point suitable for potentiometric titration. Perrhenate, bichromate, tungstate, periodate, vanadate, and perchlorate yielded significant potential changes, they did not produce the classic titration curve below 10^{-4} mol/L; however, these ions can still be analyzed in more concentrated solutions. In the case of labile complexes, optimal ligand concentrations favored the formation of mono-, di-, or tri-charged anionic species, which yielded the maximum analytical signal. Among the organic anions investigated, those of higher lipophilicity produced pronounced endpoint potential breaks. For instance, in solutions of 10^{-4} mol/L and above, a substantial potential break was observed starting from picrate. Consequently, the tested anions were placed in the following lipophilicity (selectivity) order: dipicrylaminate \geq tetraphenylborate $>$ $[P(W_2O_7)_6]^{7-}$ $>$ hexadecyl sulfate $>$ $[BiI_4]^-$ $>$ $[TlBr_4]^-$ $>$ $[HgI_4]^{2-}$ $>$ $[AuCl_4]^-$ $>$ $[Hg(SCN)_4]^{2-}$ $>$ dodecyl sulfate $>$ lauric sulfate \geq $[Zn(NCS)_4]^{2-}$ \geq $[TiCl_4]^-$ \geq $[IrCl_6]^{2-}$ \geq $[HgBr_4]^{2-}$ $>$ $[TaF_7]^{2-}$ $>$ picrate $>$ $[Co(NCS)_4]^{2-}$ $>$ MnO_4^- $>$ $[HgCl_4]^{2-}$ \geq $[Fe(CN)_6]^{4-}$ \geq $[Fe(CN)_5NO]^{2-}$ $>$ ReO_4^- \geq $[Fe(CN)_6]^{3-}$ $>$ $[PdCl_4]^{2-}$ $>$ $Cr_2O_7^{2-}$ $>$ WO_4^{2-} $>$ IO_4^- \geq VO_3^- \geq $[BF_4]^-$ \geq 4-tert-butylbenzene-1-sulfonate \geq ClO_4^- $>$ butyl xanthate \geq disulfine Blue VN 150 \geq SCN^- $>$ I^- \geq mesitylenesulfonate \geq salicylate $>$ MoO_4^{2-} \geq Br^- \geq lignosulfonate $>$ sebacate \geq IO_3^- \geq 4-nitrobenzoate \geq NO_3^- \geq $[FeCl_4]^-$ \geq SeO_3^{2-} \geq $S_2O_3^{2-}$ \geq ClO_3^- \geq $[SiF_6]^{2-}$ \geq p-toluenesulfonate \geq SeO_4^{2-} \geq sulfanilate.

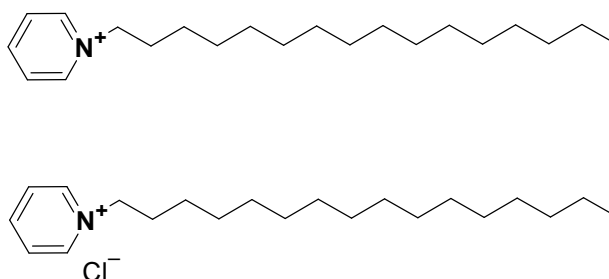


Figure 5. The structure of cetylpyridinium anion (above) and cetylpyridinium chloride

2.4. Indole

Solid-state potentiometric sensors for calcium determination were developed by the authors of [27]. These sensors were constructed by depositing a thin film composed of polymer membranes onto

Organic heterocyclic compounds as ionophores

gold electrodes pre-coated with the conducting polymer poly(3,4-ethylenedioxythiophene), which served as an ion-to-electron transducer. More than 40 sensor variants were investigated, each containing varying amounts of different ionophores—with and without anionic lipophilic additives. Indole derivatives (Fig. 6) were examined as ionophores, and the resulting sensors were used to determine calcium concentrations in blood serum. The results correlated well with those obtained from a standard electrolyte analyzer in a clinical laboratory.

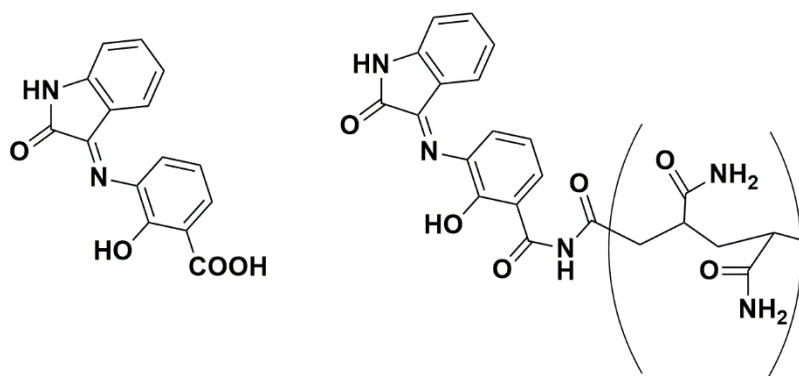


Figure 6. Chemical structures of ionophores – derivatives of 2-hydroxy-3-[(E)-(2-oxo-1,2-dihydro-3H-indol-3-ylidene)amino]benzoic acid

2.5. Quinazoline

Quinazolines and their derivatives are important chromophores with favorable electrochemical properties for use in ion-selective sensors [28]. Their metal complexes have demonstrated significant electrochemical behavior as ionophores or electroactive substances when incorporated into various polymer membranes (Fig. 7). Quinazoline derivatives have been utilized as ionophores within a PVC matrix to fabricate potentiometric ion-selective electrodes for the determination of analytes such as butralin, hydroxylamine, and nitrite, as well as heavy metal ions like Fe^{3+} and Th^{4+} . These electrodes have been successfully applied to samples of food products, drinking water, beverages, fertilizers, and industrial soils.

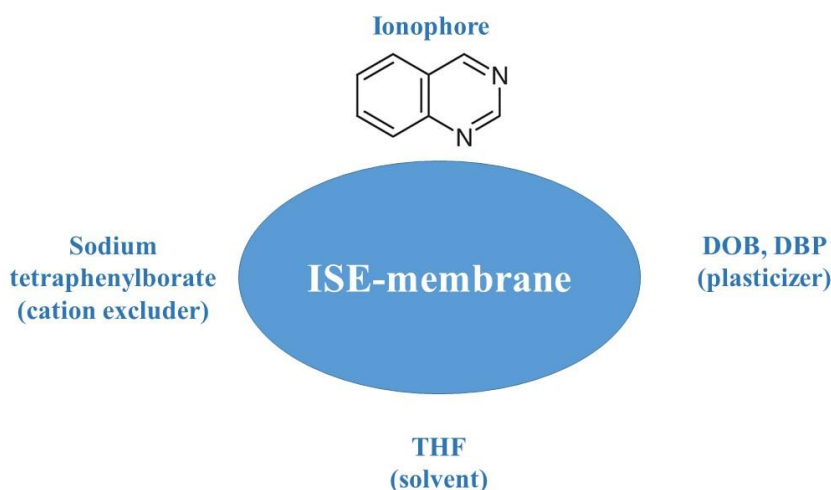


Figure 7. Composition of the ion-selective membrane as investigated in [25].

2.6. Cucurbituril

In study [29], the authors described a method for determining activated biogenic amines by combining ion-pair chromatography with potentiometric detection for food quality control. To fabricate an aminoselective electrode, cucurbit[6]uril (Fig. 8) was used as the ionophore. Biogenic amines were separated using a C18 column with gradient elution, employing a mobile phase containing lithium formate buffer, acetonitrile, and sodium butanesulfonic acid as an ion-pairing agent. This method enabled the simultaneous detection of ten biogenic amines—methylamine, ethylamine, putrescine, cadaverine, histamine, spermidine, spermine, tyramine, phenylethylamine, and tryptamine. Analysis of tomato samples yielded recovery rates between 85.8% and 108.5%, confirming the method's high accuracy. Thus, the proposed system represents an attractive, rapid, and environmentally friendly approach for the determination of biogenic amines in food products.

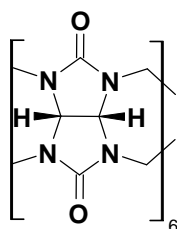
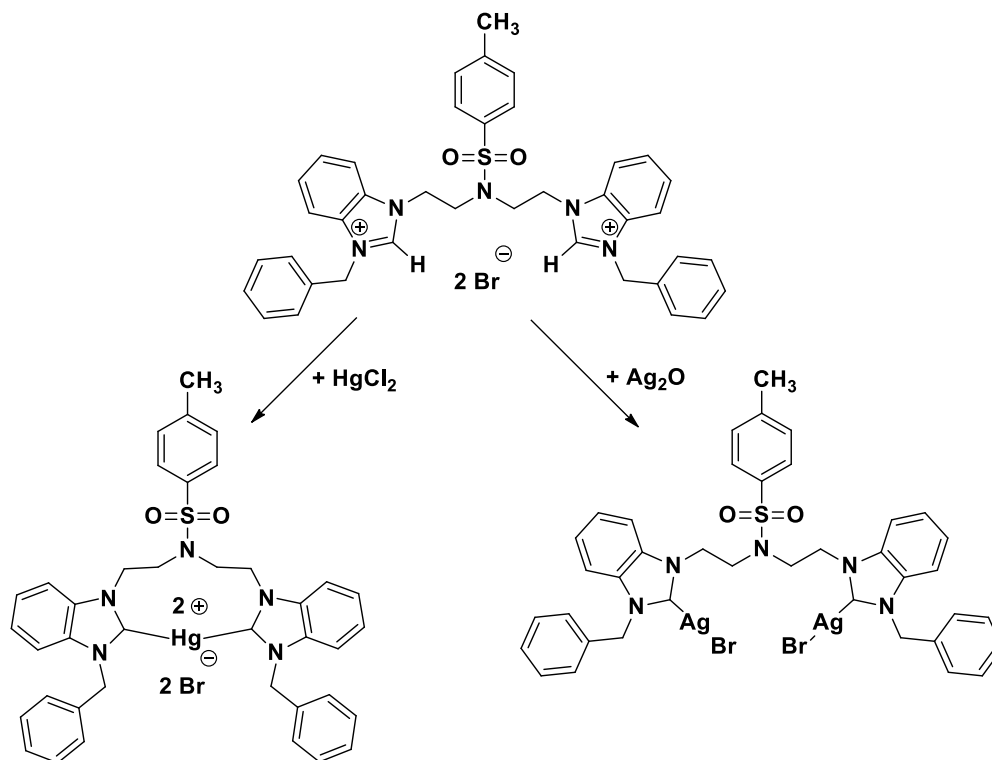


Figure 8. Chemical structure of cucurbit[6]uril

2.7. Benzimidazole

A group of authors [30] developed a novel potentiometric, self-plasticizing polypyrrole sensor for the determination of Hg^{2+} cations based on a bidentate bis-NHC ligand. The ionophore, bis[1-benzylbenzimidazolymethyl]-4-methylbenzenesulfonamide bromide (NHCL) (Scheme 3), was successfully synthesized and characterized using various physicochemical methods. The optimized electrode exhibited a Nernstian response for Hg^{2+} ions over the range of 1.0×10^{-6} to 1.0×10^{-2} M, with a detection limit of 2.5×10^{-7} M and a response time of approximately 20 seconds at room temperature. This membrane sensor was effectively applied for determining various concentrations of mercury(II) in real samples. In a subsequent study [31], the same ionophore was employed for the first time in the determination of Ag^+ ions. Spectrophotometric studies revealed a 1:2 stoichiometry for the NHCL: Ag^+ complex in DMSO (Scheme 3). The electrode exhibited a linear response for Ag^+ in the range of 2.5×10^{-6} to 1.0×10^{-1} M, with a detection limit of 2.00×10^{-6} M, a response time of approximately 20 seconds, and a working pH range of 3.5–9.0. It was successfully applied to the direct determination of Ag^+ in tap water and standard samples with satisfactory accuracy and precision.

Organic heterocyclic compounds as ionophores



Scheme 3. Synthesis of the ionophores bis[1-benzyl-benzimidazolymethyl]-4-methylbenzenesulfonamide bromides.

2.8. Benzothiazole

Benzothiazole-based chelating ionophores such as 1,3-bis[2-(1,3-benzothiazol-2-yl)-phenoxy]propane (L1) and 1,2'-bis[2-(1,3-benzothiazol-2-yl)-phenoxy]2-ethoxyethane (L2) (Fig. 9) were synthesized and evaluated as neutral ionophores for Cu^{2+} ion-selective electrodes [32]. The study involved constructing various electrode types, including PVC-based electrodes, coated graphite electrodes, and pyrolytic graphite electrodes with membrane coatings. The electrode with a composition of 1,2'-bis[2-(1,3-benzothiazol-2-yl)-phenoxy]2-ethoxyethane:PVC:1-chloronaphthalene:sodium tetraphenylborate in the ratio 6:39:53:2 exhibited the best potentiometric characteristics. Comparative studies showed that the pyrolytic graphite electrode with this coating achieved a low detection limit of 6.30×10^{-9} mol/L, a Nernstian slope of 29.5 mV/decade, and a response time of 9 seconds, while maintaining stable performance for up to 5 months. This sensor was successfully applied to detect Cu^{2+} ions in water, soil, and medicinal herb samples and was also used as an indicator electrode in the potentiometric titration of Cu^{2+} with EDTA.

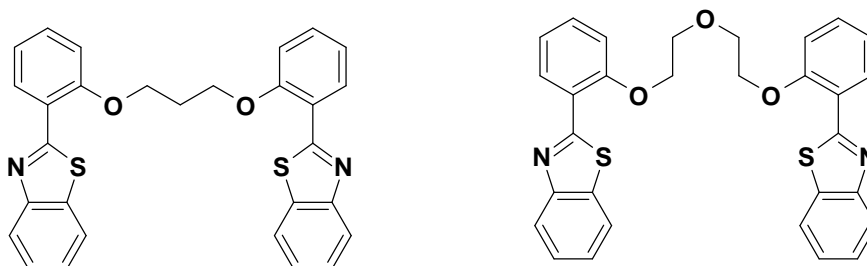
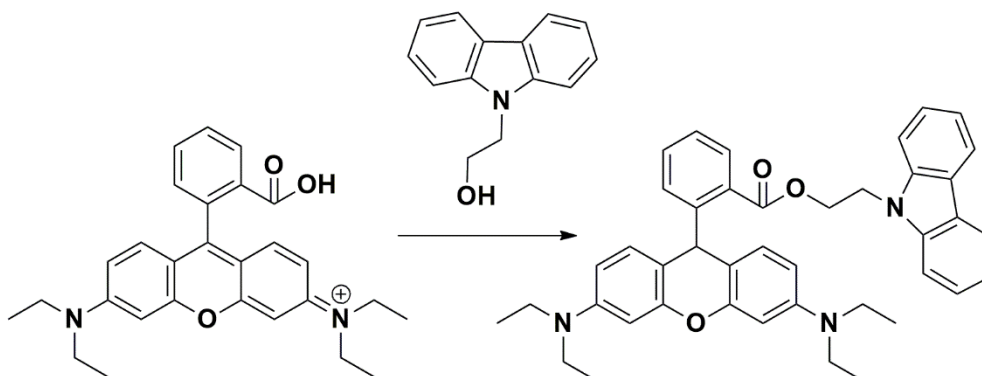


Figure 9. Chemical structures of 1,3-bis[2-(1,3-benzothiazol-2-yl)phenoxy]propane (left) and 1,2'-bis[2-(1,3-benzothiazol-2-yl)phenoxy]2-ethoxyethane (right)

2.9. Carbazole

An ionophore was reported to be synthesized via the esterification of rhodamine B with 9H-carbazole-9-ethanol (Scheme 4), and the resulting compound was electropolymerized by cyclic voltammetry [33]. The resulting polymer was deposited on both ITO glass and screen-printed electrodes. For the ITO/glass system, the selective response toward mercury(II) ions was observed over the range of 10^{-2} M to 10^{-9} M, with a detection limit of 6.4×10^{-9} M. For the screen-printed electrode system, the response range was 10^{-2} M to 10^{-11} M, with a detection limit of 2.02×10^{-12} M.



Scheme 4. Synthesis of the ionophore – a derivative of 9H-carbazole-9-ethanol.

2.10. Thiazine

The complexation of 2,3-dihydro-1H-phenothiazin-4(5aH)-one (Fig. 10) with 14 different cations was investigated using density functional theory in [34]. Initially, the structures of the ligand, the cations, and their respective complexes were geometrically optimized. Subsequently, IR calculations were performed to determine the enthalpy of formation and Gibbs free energy values. The results indicated that 2,3-dihydro-1H-phenothiazin-4(5aH)-one forms the strongest and most stable complex with Cr^{3+} , as evidenced by the lowest enthalpy change, confirming an exothermic complexation process (Fig. 11). These findings suggest that this heterocyclic compound is a promising electroactive substance for developing a Cr^{3+} -selective potentiometric electrode. All calculations were carried out using density functional theory at the B3LYP/6-31G(d) level.

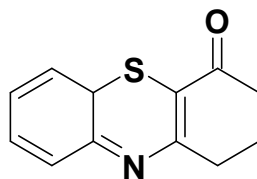


Figure 10. Chemical structure of 2,3-dihydro-1H-phenothiazin-4(5aH)-one

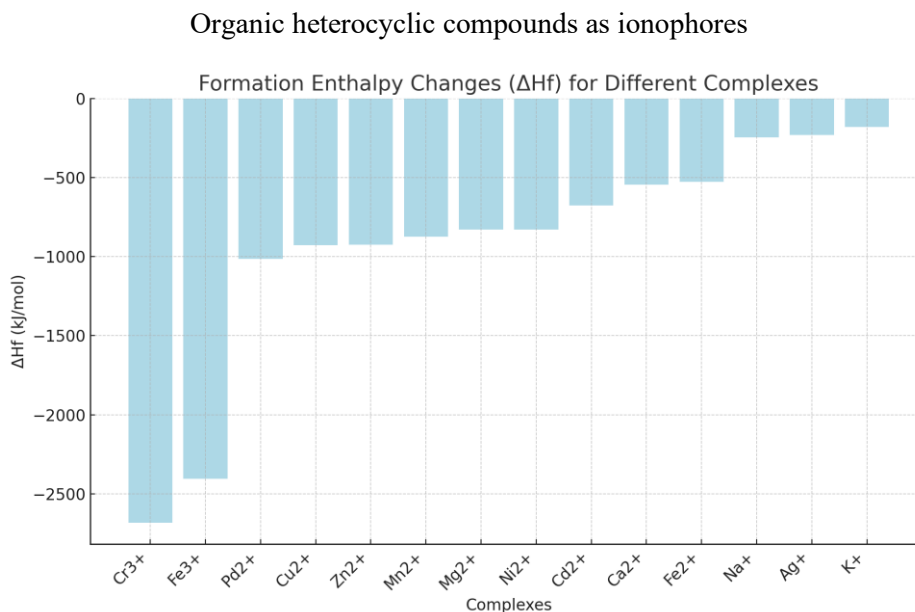


Figure 11. Enthalpy change values for the complexes studied

2.11. Schiff Bases

Schiff base derivatives featuring pseudocavities with various heteroatoms (O, N, and S) were designed, synthesized, and evaluated for their ability to detect different metal ions [35]. Ultraviolet and fluorescence studies showed that all three receptors (Fig. 12) were highly responsive to Cu^{2+} ions, while the thiophene-containing compound also exhibited sensitivity toward Hg^{2+} ions. Electrochemical experiments revealed Cu^{2+} detection limits ranging from 1.41×10^{-7} M to 9.8×10^{-7} M, and the detection limit for Hg^{2+} using the thiophene-containing receptor was 5.61×10^{-8} M. The sensors, constructed on carbon electrodes, were successfully tested on groundwater samples.

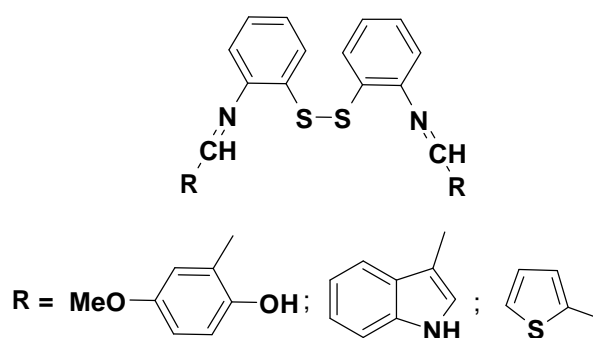


Figure 12. Chemical structures of the studied Schiff bases

2.12. Diazacyclooctadecane

A novel PVC membrane sensor for the quantitative determination of cerium(III) was fabricated using 4,13-didecyl-1,7,10,16-tetraoxa-4,13-diazacyclooctadecane (cryptofix22DD) (Fig. 13) as the ionophore [36]. The sensor exhibits a linear response over the concentration range of 1.0×10^{-6} to 1.0×10^{-1} M, a Nernstian slope of 18.0 ± 1.0 mV/decade, a detection limit of 9.7×10^{-7} M, and a response time of 5 seconds. It maintains stable performance for up to two months without significant potential drift. The sensor shows high selectivity for Ce^{3+} ions over various alkali, alkaline earth, and transition metal cations, operating effectively in a pH range of 2.0–11.0. It was also successfully used as an indicator electrode in the potentiometric titration of Ce^{3+} with EDTA and sodium iodide solutions.

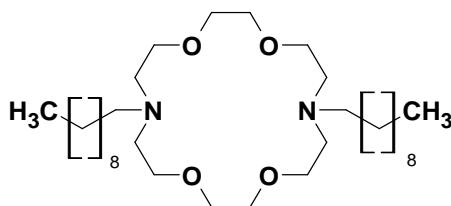


Figure 13. Chemical structure of 4,13-didecyl-1,7,10,16-tetraoxa-4,13-diazacyclooctadecane (cryptofix22DD)

2.13. Chiral Lariat Esters of Monoaza-15-Crown-5

Chiral lariat esters of monoaza-15-crown-5 (Fig. 14), attached to a 1,2-O-isopropylidene- α -D-glucufuranoside unit, were synthesized and investigated as ionophores. Their ability to extract alkali metal and ammonium picrates from a dichloromethane–water system was studied. Plasticized PVC membrane electrodes were fabricated using a triphenylmethyl (trityl) ether derivative based on α -D-glucufuranoside. One of the resulting lariat esters exhibited high selectivity for Ag^+ ions [37].

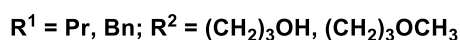
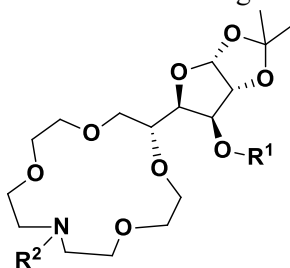


Figure 14. Chemical structures of monoaza-15-crown-5 lariat esters

2.14. Calixpyrrole

A receptor based on an aryl-substituted calix[4]pyrrole featuring a monophosphonate bridge (Fig. 15) exhibits significant affinity for creatinine and its cationic form [38]. The receptor functions by incorporating the target molecule into its polar aromatic cavity and establishing specific three-dimensional interactions. When embedded in an appropriate polymer membrane, it acts as an ionophore. On this basis, a highly sensitive and selective potentiometric sensor was developed for the rapid, simple, and cost-effective determination of creatinine levels in biological fluids such as urine or plasma.

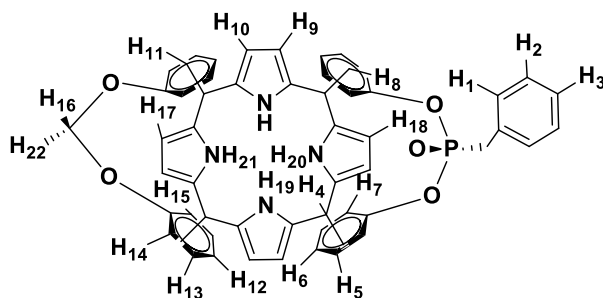


Figure 15. Chemical structure of an aryl-substituted calix[4]pyrrole with a monophosphonate bridge

Organic heterocyclic compounds as ionophores

2.15. Oxovanadate(IV) Complexes of Heteromacrocyclic Compounds

PVC membrane electrodes based on oxovanadate(IV) complexes of heteromacrocyclic compounds (Fig. 16) were fabricated as novel iodine-selective ionophores for ion-selective electrodes (ISEs) [39]. The optimized membrane composition consisted of PVC (28.1 wt.%), plasticizer (69.3 wt.%), ionophore (2.6 wt.%), and a cation scavenger (15 mol% relative to the ionophore). The electrode comprising tetraphenylporphyrin oxovanadium(IV) with 2-nitrophenyl octyl ether (o-NPOE) as the membrane solvent and tetradodecylammonium chloride (TDDACl) as the cation scavenger demonstrated the best performance. It exhibited a wide concentration range from 5.0×10^{-7} to 2.1×10^{-2} M, a Nernstian slope of -59.02 mV/decade, and excellent ion selectivity toward I^- ions over perchlorate ions ($I^-/ClO_4^- = 91$).

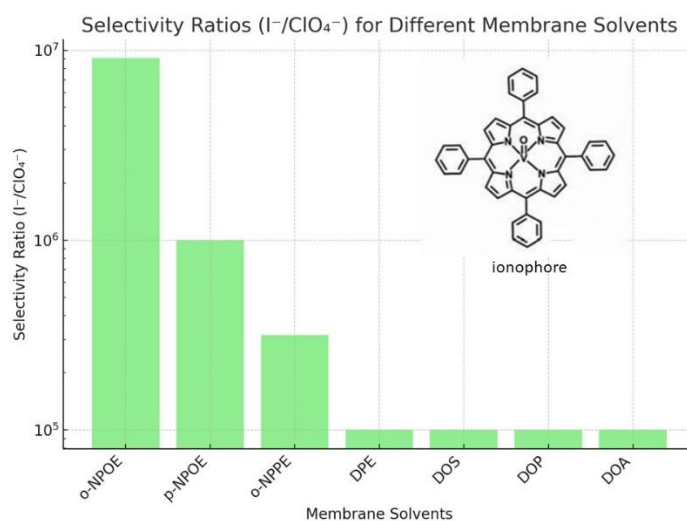


Figure 16. Hofmeister series of the studied anions and chemical structures of oxovanadates (IV) of heteromacrocyclic compounds

3. Conclusion

In summary, the extensive review of organic heterocyclic compounds as ionophores in potentiometric sensors underscores their pivotal role in advancing analytical methodologies. These compounds exhibit unique advantages—including high selectivity, enhanced stability, and the ability to fine-tune their chemical properties—that are critical for the development of efficient and reliable sensors. The integration of diverse heterocyclic structures into membrane electrodes has led to significant improvements in sensor performance, enabling precise detection of a wide range of analytes in environmental, clinical, and industrial settings. Despite the notable progress, challenges remain in the development of novel heterocyclic architectures and the further miniaturization of sensor systems. Future research should focus on addressing these challenges to harness the full potential of these ionophores, thereby paving the way for next-generation, high-performance analytical devices.

Acknowledgement

The authors would like to express our sincere gratitude to Troyasil HPLC Column Technologies for their valuable support and the possibility to publish this work.

ORCID

Nataliya Korol: [0000-0001-7155-1676](https://orcid.org/0000-0001-7155-1676)

Dzhosiya Molnar: [0000-0003-1063-013X](https://orcid.org/0000-0003-1063-013X)

Mikhailo Slivka: [0000-0003-4788-0511](https://orcid.org/0000-0003-4788-0511)

References

- [1] Anderson, R. G.; Nickless, G. Heterocyclic azo dyestuffs in analytical chemistry: A review. *Analyst* **1967**, *92*, 207–238.
- [2] Machado, M. E.; Nascimento, M. M.; Bahia, P. V. B.; Martinez, S. T.; de Andrade, J. B. Analytical advances and challenges for the determination of heterocyclic aromatic compounds (NSO-HET) in sediment: A review. *TrAC Trends Anal. Chem.* **2022**, *150*, 116586.
- [3] Otazo-Sánchez, E.; Pérez-Marín, L.; Estévez-Hernández, O.; Rojas-Lima, S.; Alonso-Chamarro, J. Aroylthioureas: New organic ionophores for heavy-metal ion selective electrodes. *J. Chem. Soc., Perkin Trans.* **2001**, *2*, 2211–2218.
- [4] Otazo-Sánchez, E.; Ortiz-del-Toro, P.; Estévez-Hernández, O.; Pérez-Marín, L.; Goicoechea, I.; Cerón Beltrán, A.; Villagómez-Ibarra, J. R. Aroylthioureas: New organic ionophores for heavy metal ion selective electrodes. A nuclear magnetic resonance study. *Spectrochim. Acta Part A: Mol. Biomol. Spectrosc.* **2002**, *58*, 2281–2290.
- [5] Herges, R.; Dikmans, A.; Jana, U.; Köhler, F.; Jones, P.; Dix, I.; Fricke, T.; König, B. Design of a neutral macrocyclic ionophore: Synthesis and binding properties for nitrate and bromide anions. *Eur. J. Org. Chem.* **2002**, 3004–3014.
- [6] Veljković, J.; Molčanov, K.; Kojić-Prodić, B.; Mlinarić-Majerski, K. Thiamacrocyclic lactones: New Ag(I)-ionophores. *J. Org. Chem.* **2008**, *73*, 9221–9227.
- [7] Jumal, J.; Yamin, B. M.; Ahmad, M.; Heng, L. Y. Mercury ion-selective electrode with self-plasticizing poly(n-butylacrylate) membrane based on 1,2-bis-(N'-benzoylthioureido)cyclohexane as ionophore. *APCBEE Procedia* **2012**, *3*, 116–123.
- [8] Choi, H. S.; Suh, S. B.; Cho, S. J.; Kim, K. S. Ionophores and receptors using cation- π interactions: collarenes. *Proc. Natl. Acad. Sci. USA* **1998**, *95*, 12094–12099.
- [9] Ferdani, R.; Gokel, G. W. Ionophores. In *Encyclopedia of supramolecular chemistry*; CRC Press: **2004**.
- [10] Buhlmann, P.; Umezawa, Y. Lifetime of ion-selective electrodes based on charged ionophores. *Anal. Chem.* **2000**, *72*, 1843–1852.
- [11] Mistlberger, G.; Crespo, G. A.; Bakker, E. Ionophore-based optical sensors. *Annu. Rev. Anal. Chem.* **2014**, *7*, 483–512.
- [12] Novilla, M. N. Chapter 78 – Ionophores. In *Veterinary toxicology: basic and clinical principles* **2018**, 1073–1092.
- [13] Ekinci, İ.B.; Chłodowska, A.; Olejnik, M. Ionophore toxicity in animals: A review of clinical and molecular aspects. *Int. J. Mol. Sci.* **2023**, *24*, 1696.
- [14] Colozza, N.; Casanova, A.; Fernández-Pérez, B. M.; Crespo, G. A.; Flores, G. A.; Kavallieratos, K.; de Gracia, J.; Ahlquist, M.; Cuartero, M. Insights into tripodal tris(pyrazolyl) compounds as ionophores for potentiometric ammonium ion sensing. *Chem. Electro. Chem.* **2022**, *9*, e202200716.
- [15] Săcărescu, L.; Chibac-Scutaru, A. L.; Roman, G.; Săcărescu, G.; Simionescu, M. Selective detection of metal ions, sulfites and glutathione with fluorescent pyrazolines: A review. *Environ. Chem. Lett.* **2023**, *21*, 561–596.
- [16] Kim, H.-S.; Kim, D.-H.; Kim, K. S.; Choi, J.-H.; Choi, H.-J.; Kim, S.-H.; Shim, J. H.; Cha, G. S.; Nam, H. Cation selectivity of ionophores based on tripodal thiazole derivatives on benzene scaffold. *Talanta* **2007**, *71*, 1986–1992.
- [17] Singhal, D.; Singh, A. K.; Upadhyay, A. Highly selective potentiometric and colorimetric determinations of Cobalt(II) ion using thiazole-based ligands. *Mater. Sci. Eng.* **2014**, *45*, 216–224.
- [18] Kumar, P.; Sharma, H. K.; Shalaan, K. G. Development of Chromium(III) selective potentiometric sensor by using synthesized triazole derivative as an ionophore. *J. Chem.* **2013**, 142752. doi:10.1155/2013/142752
- [19] Zahran, E. M.; Hua, Y.; Li, Y.; Flood, A. H.; Bachas, L. G. Triazolophanes: A new class of halide-selective ionophores for potentiometric sensors. *Anal. Chem.* **2010**, *82*, 368–375.
- [20] Isildak, Ö.; Özbek, O.; Gürdere, M. B. Development of a Chromium(III)-selective potentiometric sensor by using a synthesized pyrazole derivative as an ionophore in a PVC matrix and its applications. *J. Anal. Test.* **2020**, *4*, 273–280.
- [21] Isildak, O.; Yildiz, I.; Erenler, R.; Dag, B.; Isildak, I. Hg(II) ion-selective electrodes with PVC membranes based on bis-1,5-dimethyl-2-phenyl-1,2-dihydro-3h-pyrazol-3-one. *Bull. Chem. Soc. Japan* **2022**, *95*, 353–358.
- [22] Wang, H.-X.; Yan, Z.-N.; Wen, X.-L.; Kang, Y.-X.; Zhang, S.-Y. A Bismuth(III) PVC membrane ion selective electrode based on 5-(3,4,5-trimethoxyphenyl)-4-amino-1,2,4-triazole-3-thiol. *Chin. Chem. Lett.* **2015**, *26*, 1147–1149.

Organic heterocyclic compounds as ionophores

- [23] Li, L.; Du, P.; Zhang, Y.; Duan, Y.; Li, Y.; Qian, Y.; Zhang, P.; Guo, Q. Deploying hydrogen bond donor/acceptor on arylolethynyl scaffold I: PN-heterocycles and urea-based cleft ionophores for hydrosulfide/hydrosulfate selective electrodes. *Sensors Actuat. B. Chem.* **2021**, *345*, 130416.
- [24] Suman, S.; Singh, R. Zn(II)-selective poly(vinyl chloride) (PVC) membrane electrode based on Schiff base ligand 2-benzoylpyridine semicarbazone as an ionophore. *J. Polym. Eng.* **2020**, *40*, 842–847.
- [25] Fizer, M.; Fizer, O.; Sidey, V.; Marychuk, R.; Studenyak, Y. Experimental and theoretical study on cetylpyridinium dipicrylamide – A promising ion-exchanger for cetylpyridinium selective electrodes. *J. Mol. Str.* **2019**, *187*, 77–85.
- [26] Fizer, M.; Fizer, O.; Sidey, V.; Studenyak, Y. Predicting the end point potential break values: A case of potentiometric titration of lipophilic anions with cetylpyridinium chloride. *Microchem. J.* **2021**, *160*, 105758.
- [27] Abbas, M. N.; Magar, H. S. Highly sensitive and selective solid-contact calcium sensor based on Schiff base of benzil with 3-aminosalicylic acid covalently attached to polyacrylic acid amide for health care. *J. Solid State Electrochem.* **2018**, *22*, 181–192.
- [28] Mohan, C.; Robinson, J.; Negi, A. Ion-selective electrode (ISE) based on polyvinyl chloride membrane formed from heterocyclic quinazoline compounds as ionophore material. *Eng. Proceed.* **2023**, *48*, 10.
- [29] Gil, R. L.; Amorim, C. G.; Montenegro, M. S. B. S. M.; Araújo, A. N. Determination of biogenic amines in tomato by ion-pair chromatography coupled to an amine-selective potentiometric detector. *Electrochim. Acta* **2021**, *378*, 138134.
- [30] Said, N. R.; Rezayi, M.; Narimani, L.; Manana, N. S. A.; Alias, Y. A novel potentiometric self-plasticizing polypyrrole sensor based on a bidentate bis-NHC ligand for determination of Hg(II) cation. *RSC Adv.* **2015**, *5*, 76263–76274.
- [31] Said, N. R.; Rezayi, M.; Narimani, L.; Al-Mohammed, N. N.; Manana, N. S. A.; Alias, Y. A new N-heterocyclic carbene ionophore in plasticizer-free polypyrrole membrane for determining Ag⁺ in tap water. *Electrochim. Acta* **2016**, *197*, 10–22.
- [32] Singh, A. K.; Sahani, M. K.; Bandi, K. R.; Jain, A. K. Electroanalytical studies on Cu(II) ion-selective sensor of coated pyrolytic graphite electrodes based on n₂s₂o₂ and n₂s₂o₃ heterocyclic benzothiazole ligands. *Mater. Sci. Eng. C* **2014**, *41*, 206–216.
- [33] Şahutoğlu, A. K.; Kaya, I. Synthesis and a new Mercury(II) ion sensor application of conductive polymer containing rhodamine B. *React. Funct. Polym.* **2019**, *141*, 50–57.
- [34] Sarvestani, M. R. J.; Ahmadi, R. Evaluating the performance of 2,3-dihydro-1H-phenothiazine-4(5aH)-one as an ionophore in construction of a cation selective electrode by density functional theory. *Int. J. New Chem.* **2018**, *5*, 1–10.
- [35] Kaur, S.; Kaur, J.; Sharma, J.; Kaur, I. S–S bridged Schiff bases as versatile ionophores: Synthesis and application for electrochemical sensing of Copper(II) and Mercury(II). *Anal. Chim. Acta* **2024**, *1287*, 342122.
- [36] Mehranfar, F.; Ghaemi, A.; Tavakkoli, H. Highly selective and sensitive sensor based on 4,13-didecyl-1,7,10,16-tetraoxa-4,13-diazacyclooctadecane as a heterocyclic ionophore. *Int. J. Heterocycl. Chem.* **2016**, *6*, 1–70.
- [37] Rapi, Z.; Ozohanics, O.; Tóth, G.; Bako, P.; Hofler, L.; Nemcsok, T.; Kanya, N.; Keglevich, G. Syntheses and complexing ability of α-D-gluco- and α-D-xylofuranoside-based lariat ethers. *J. Incl. Phenom. Macrocycl. Chem.* **2016**, *85*, 19–32.
- [38] Guinovart, T.; Hernández-Alonso, D.; Adriaenssens, L.; Blondeau, P.; Martínez-Belmonte, M.; Rius, F. X.; Andrade, F. J.; Ballester, P. Recognition and sensing of creatinine. *Angew. Chem. Int. Ed.* **2016**, *55*, 2435.
- [39] Moriuchi-Kawakami, T.; Higashikado, A.; Hirahara, M.; Fujimori, K.; Moriuchi, T. Oxovanadium(IV) heteromacrocyclic complexes as ionophores for iodide-selective electrodes. *Chem. Lett.* **2024**, *53*, upad058.

A C G
publications

© 2025 ACG Publications