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A newly synthesized macrocyclic dithioxamide receptor for phosphate sensing

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Abstract

Polyvinyl chloride (PVC) based membranes using macrocyclic dithioxamide receptor (**I**) derived from isophthaloyl dichloride and dithioxamide have been prepared and explored as HPO_4^{2-}-selective sensors. Effect of various plasticizers viz., bis(2-ethylhexyl) sebacate (DOS), dibutylphosphate (DBP), tri-*n*-butylphosphate (TBP), *O*-nitrophenyl octyl ether (NPOE), tris(2-ethylhexyl)phosphate (TEHP) and a cation excluder, tridodecylmethylammonium chloride (TDDMACl) was studied in detail and improved performance was observed at several instances. Optimum performance was observed with the membrane having (**I**)-PVC–TDDMACl–NPOE in the ratio 2:33:1.5:63.5 (w/w). The sensor works satisfactorily in the concentration range 1.7×10^{-6} to 1.0×10^{-2} M (detection limit 0.2 ppm) with Nernstian compliance (29.6 mV/decade of activity) at pH 8.0 with a fast response time of about 8 s. The potentiometric selectivity coefficient values as determined by the matched potential method (MPM) and the fixed interference method (FIM) indicate selective response for HPO_4^{2-} in presence of interfering ions. The sensor exhibits adequate shelf life (∼2 months) with good reproducibility (S.D. ± 0.4 mV). The sensor was also used successfully in the potentiometric titration of HPO_4^{2-} with Ba^{2+}.

Keywords: Phosphate; Membrane; Ion selective sensor; Receptor

1. Introduction

Phosphorous, a key nutrient in living organisms is involved in several biological and environmental processes. Extensive input of phosphate due to over fertilization and from industrial and domestic waste water pollution results in eutrophication, a process that often is accompanied by growth of toxic algae [1,2]. The European Union regulatory directives set the limit of 0.1 ppm P–PO_4^{3-} as an indicator level for problematic algal growth. Although many analytical methods for phosphate have been reported, most of phosphate compounds are quantified by spectrophotometric methods using the formation of molybdenum blue. This system is complicated and remains unsuitable for application to automated sensing and feed back control. Automated flow analysis is another technique which is currently used for the detection of phosphate in water samples [3]. It is expensive in labor, equipment and produces toxic laboratory waste. A reliable, low cost, quick and portable analytical technique is the need of the day and such requirements are greatly met with ion sensors.

The primary requirement for the preparation of an ion sensor is that the electroactive material to be used in the membranes should exhibit strong affinity for a particular ion and poor affinity to others. Organotin compounds have shown high affinity toward phosphate ions and therefore a number of liquid and solvent polymeric membrane sensors based on these compounds have been reported [4–9]. However, these sensors exhibit poor selectivity, high response time, short lifetime and are not sensitive enough for measuring phosphate ions at lower concentrations (<1 ppm). In addition to these, a number of phosphate-selective sensors based on cobalt phthalocyanine [10], polyamines [11,12], uranyl salophene [13,14], vanadyl salen [15], guanidinium [16], thiourea [17,18] and calixarene [19] receptors have been described.

In recent times, intensive research has been directed towards the preparation of a variety of selective receptors for anions. These have included pyrroles, amides, thioamides, lewis acids and metalloreceptors [20,21]. Among these, thioamide receptors have shown strongest affinity for highly hydrophilic phosphate

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ions [22,23]. Evidence from ^{1}H NMR spectroscopy suggests that these receptors bind phosphate ions through hydrogen bonds which are directional in character and correct orientations of these provide selective anion recognition [24,25]. Keeping this in view, we have synthesized a cyclic bis-dithioxamide receptor containing strong hydrogen bond donor sites and employed it for developing phosphate sensor. The results of these investigations are presented in this communication and show that the sensor of the synthesized receptor has turned out to be a selective and sensitive sensor for phosphate.

2. Experimental

2.1. Reagents

All reagents were of analytical grade and used without further purification. Isophthaloyl dichloride, dithioxamide, triethylamine (Et_3N), tridodecylmethylammonium chloride (TDDMACl), tris(hydroxymethyl)aminomethane (Tris), bis(2-ethylhexyl)sebacate (DOS) and high molecular weight polyvinyl chloride (PVC), Aldrich, USA; *O*-nitrophenyl octyl ether (NPOE), Acros Organics, Belgium; tri-*n*-butylphosphate (TBP), BDH, England; tris(2-ethylhexyl) phosphate (TEHP), E. Merck, Germany; dibutyl phthalate (DBP), Reidel, India were used as obtained. Analytical reagent-grade tetrahydrofuran (THF) and sulphuric acid were obtained from Ranbaxy, India. Standard solutions and buffers were prepared with double distilled water. Working solutions of different concentrations were prepared by diluting 0.1 M stock solutions.

2.2. Synthesis of bis-dithioxamide receptor (*I*)

The solution of isophthaloyl dichloride (204 mg, 2 mmol) in 5 mL of dry THF was added dropwise to the mixture of Et_3N (0.28 mL), dithioxamide (120 mg, 2 mmol) and 200 mL of dry THF over a period of 5 min. After continuous stirring for 24 h, the mixture was filtered and filtrate evaporated. The solid residue obtained was purified by crystallization from THF to yield (**I**) (72%), orange solid (Scheme 1). mp 260–261 °C; IR: υ(–C=O, amide) = 1693 cm^{-1}, υ(–NH) = 3426 cm^{-1}; Anal. calcd. for $C_{20}H_{12}N_4O_4S_4$: C, 48.0; H, 2.4; N, 11.2; S, 25.6. Found: C, 47.9; H, 2.5; N, 11.3, S, 25.4; ^{1}H NMR (300 MHz, DMSO), δ: 12.24 (s, 4H), 8.12 (s, 2H), 7.80 (d, 4H), 7.42 (t, 2H).

2.3. Preparation of membranes

The PVC based membranes were prepared by dissolving appropriate amounts of (**I**), TDDMACl, plasticizers (DOS, TEHP, TBP, DBP and NPOE) and PVC in THF (10 mL). After complete dissolution of all the components and thorough mixing, homogeneous mixture was poured into polyacrylate rings placed on a smooth glass plate. THF was allowed to evaporate for about 24 h at room temperature. To obtain membranes with reproducible characteristics, the solvent evaporation was carefully controlled otherwise morphology and thickness of the membranes shows significant variation which ultimately affected the sensor response. The transparent membranes of 0.5 mm thickness were removed carefully from the glass plate. A 5 mm diameter piece was cut out and glued to one end of a "Pyrex" glass tube. The membranes thus prepared were equilibrated for 2 days in 0.1 M HPO_4^{2-} solution.

2.4. Potential measurement and apparatus

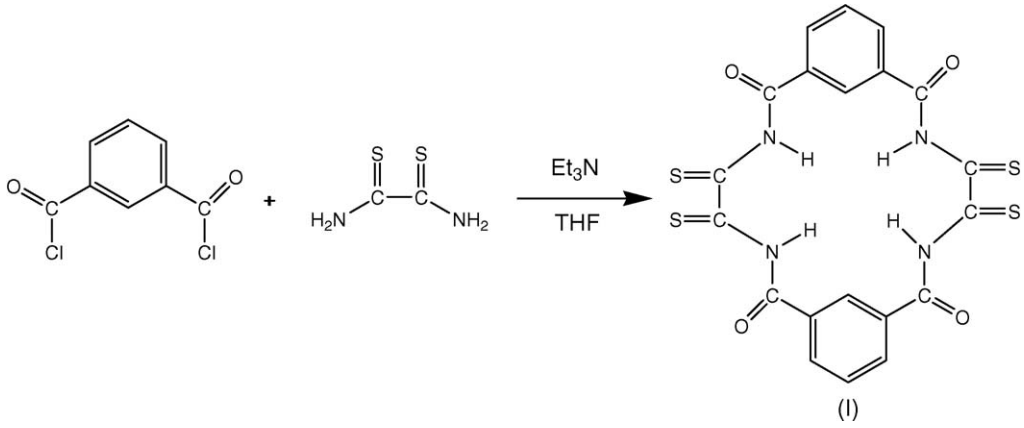
The potential and pH measurements were carried out at 25 ± 0.1 °C with a digital potentiometer (Model 5652 A, ECIL, India) and Century Microvoltmeter (Model CVM 301, India) by setting up the following cell assembly, employing saturated calomel electrodes (SCE) as a reference electrodes.

SCE/internal solution (0.01 M, HPO_4^{2-})/membrane/test solutions/SCE.

IR spectra were recorded on Perkin-Elmer 1600 series FT-IR spectrophotometer. ^{1}H NMR spectra were recorded on a Bruker AC 300 MHz spectrophotometer. The melting points were determined on Buchi SMP 20 melting point apparatus. Elemental analysis was performed with Vario EL III instrument.

3. Results and discussions

In preliminary investigations, potentiometric response of the sensors having membrane of composition (w/w) (**I**): TDMACl:PVC (2:1.5:33) was tested for a number of anions.



Scheme 1. Synthesis of bis-dithioxamide receptor (**I**).

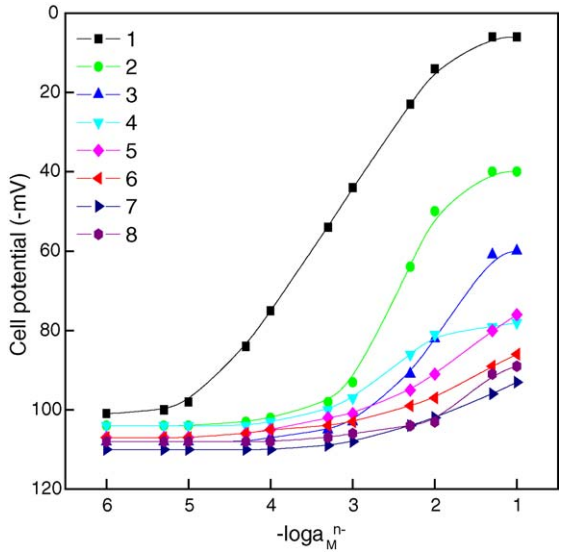


Fig. 1. Response of the bis-dithioxamide receptor based membranes (without plasticizer) at pH 8.0 to (1) monohydrogenphosphate, (2) acetate, (3) sulphate, (4) bicarbonate, (5) nitrate, (6) perchlorate, (7) iodide and (8) thiocynate.

In these studies, pH was maintained at 8.0 by using 0.01 M Tris–H_2SO_4 buffer solution. The potential response of various sensors is shown in Fig. 1. Among the anions, the best response was observed for HPO_4^{2-} ions, therefore, the ionophore was selected as suitable sensor material for HPO_4^{2-}-selective sensor.

3.1. Working concentration range and slope

The potentials of the membranes of (**I**) were investigated as a function of HPO_4^{2-} activity in the range of 1.0×10^{-7} to 1.0×10^{-1} M and the results obtained are shown in Fig. 2. From this plot, the working concentration ranges and slopes

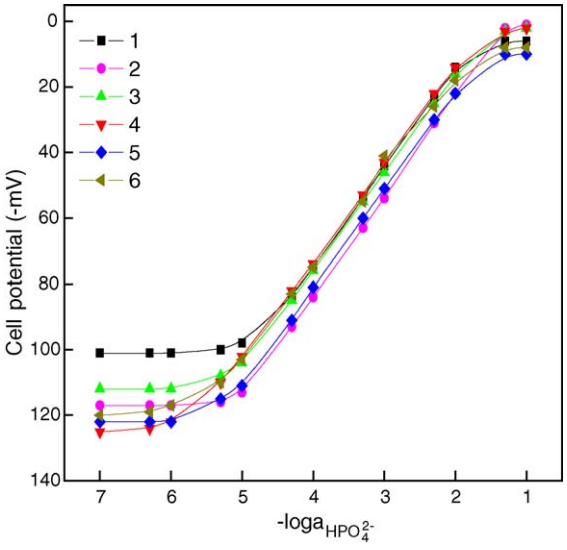


Fig. 2. Variation of membrane potential with activity of HPO_4^{2-} ions of PVC based membranes of (**I**) without plasticizer (1), with plasticizer, DOS (2), TEHP (3), NPOE (4), DBP (5), TBP (6).

Table 1
Composition of PVC membranes of bis-dithioxamide receptor (**I**) and performance characteristics of HPO_4^{2-}-selective sensors based on them

Sensor no.	Percentage (w/w) of various components in membranes									Working concentration range (M)	Slope (mV/decade of activity)	Response time (s)
	(**I**)	PVC	TDDMACl	DOS	TEHP	NPOE	DBP	TBP				
1	2	33	1.5							1.0×10^{-5} to 1.0×10^{-2}	29.0	30
2	2	33	1.5	63.5						7.9×10^{-6} to 1.0×10^{-2}	29.0	22
3	2	33	1.5		63.5					6.3×10^{-6} to 1.0×10^{-2}	30.0	16
4	2	33	1.5			63.5				1.7×10^{-6} to 1.0×10^{-2}	29.6	8
5	2	33	1.5				63.5			4.0×10^{-6} to 1.0×10^{-2}	30.5	15
6	2	33	1.5					63.5		2.8×10^{-6} to 1.0×10^{-2}	29.0	12

have been determined and compiled in Table 1. It should be noted that in the entire concentration range, the pH of test solution was adjusted to 8.0 (by using 0.01 M Tris–H_2SO_4 buffer) in order to ensure the existence of monohydrogenphosphate as predominant species. A perusal of data presented in Table 1 indicates that the sensor no. 1 having membrane without plasticizer exhibited a narrow working concentration range of 1.0×10^{-5} to 1.0×10^{-2} M with a slope 29.0 mV/decade of activity. The sensitivity, linearity, and selectivity obtained for a given ionophore depend significantly on the membrane composition and nature of plasticizer used [26]. Further, it has been shown that the presence of appropriate amount lipophilic cationic additives in the anion selective membrane sensors is necessary to introduce perm selectivity. Thus, several membranes of varying plasticizers (DOS, TEHP, NPOE, DBP and TBP)/cation excluder (TDDMACl)/PVC/carrier (**I**) ratios were tested. The optimum membrane ingredient showing the most sensitive, reproducible, and stable results was obtained with a plasticizer/PVC ratio of ~1.9 together with 2% ionophore and 1.5% cation excluder (Table 1). Of the five plasticizers added, the best performance characteristics are obtained with the membrane having NPOE plasticizer (sensor no. 4). This sensor exhibits widest working concentration range 1.7×10^{-6} to 1.0×10^{-2} M (detection limit 0.2 ppm) with the slope of 29.6 mV/decade of activity.

3.2. Response time and lifetime

Response time of the sensor has been determined by measuring the time required to achieve a steady potential for 1.0×10^{-4} M solution, when HPO_4^{2-} concentration was increased 10-fold from 1.0×10^{-5} to 1.0×10^{-4} M and is given in Table 1. Among all the sensors, the sensor no. 4 exhibited lowest response time of 8 s. The sensing behavior of the membrane electrode remained unchanged when the potentials recorded either from low to high concentrations or vice versa.

The sensors worked satisfactorily over a period of 2 months without showing any significant change in the value of slope or working concentration range. They were stored in 0.1 M HPO_4^{2-} solutions, when not in use. The standard deviation of potentials for 15 measurements at a fixed concentration of 1.0×10^{-3} M was found to be ±0.4 mV, while that of slope was ±0.5 mV. Since, sensor no. 4 exhibited the widest working concentration range, stable potential response and smallest response time, the same was chosen for further studies.

Table 2
Selectivity coefficients of sensor no. 4 as determined by the matched potential method (MPM) and the fixed interference method (FIM) at pH 8.0

Interfering ion (M)	Selectivity coefficient ($K^{pot}_{HPO_4^{2-},M}$)	
	MPM	FIM
SCN^-	8.6×10^{-3}	8.9×10^{-3}
ClO_4^-	4.5×10^{-3}	4.6×10^{-3}
SO_4^{2-}	1.6×10^{-2}	1.4×10^{-2}
CH_3COO^-	2.8×10^{-2}	3.0×10^{-2}
I^-	4.2×10^{-3}	4.4×10^{-3}
BrO_3^-	8.1×10^{-4}	8.4×10^{-4}
CrO_4^{2-}	9.8×10^{-4}	9.7×10^{-4}
MnO_4^-	9.0×10^{-4}	9.2×10^{-4}
NO_3^-	5.0×10^{-3}	5.3×10^{-3}
F^-	1.0×10^{-3}	1.2×10^{-3}
Cl^-	3.7×10^{-3}	4.0×10^{-3}
HCO_3^-	6.9×10^{-3}	7.3×10^{-3}
HSO_4^-	7.8×10^{-3}	8.1×10^{-3}
Br^-	2.7×10^{-3}	3.1×10^{-3}

3.3. Selectivity determination

When measuring real samples by ion sensors, the response of the sensor to the primary ion can be affected by the presence of other ions of the same charge sign. Potentiometric selectivity coefficients K^{ij}_{pot}, which are generally defined with reference to the Nikolsky–Eisenman equation, are commonly used as the quantitative expression of the ability of the sensor to respond primarily to the analyte ion in the presence of interfering ions. Several experimental methods such as the 'separate solution' (SSM), the 'fixed interference' (FIM) and the 'matched potential' (MPM) methods are described for the determination of selectivity coefficients [27]. In this study, potentiometric selectivity coefficients of the proposed sensor were determined by the MPM and the FIM. In the MPM, the primary ion activity was increased from 2.0×10^{-5} to 4.0×10^{-5} M and activity of interfering ions was experimentally determined. However, in the FIM, concentration of interfering ion was kept at 1.0×10^{-2} M. The values of selectivity coefficient so determined are compiled in Table 2. A value of 1.0 of selectivity coefficient indicates equal response to primary and interfering ions. As it is seen, the sensor exhibits selective response toward HPO_4^{2-} ion and follows selectivity pattern for several anions in the order of $HPO_4^{2-} > CH_3COO^- > SO_4^{2-} > HSO_4^- > HCO_3^- > NO_3^- > ClO_4^- > I^- > SCN^- > Cl^- > Br^- > F^- >$

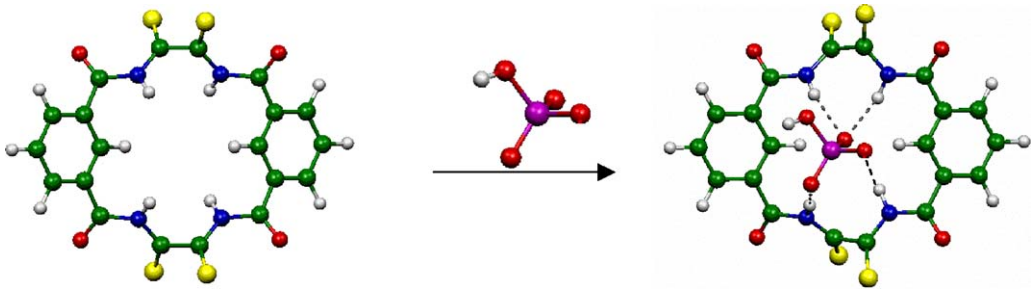


Fig. 3. Binding mechanism of monohydrogenphosphate ion through hydrogen bonds of bis-dithioxamide receptor generated by applying semiempirical AM1 method of Hyperchem programme.

Table 3
Comparison of the selectivity coefficients of different HPO_4^{2-}-selective sensors

References	log $K^{pot}_{HPO_4^{2-},M}$								
	SCN^-	ClO_4^-	I^-	Cl^-	SO_4^{2-}	NO_3^-	CH_3COO^-	CrO_4^{2-}	Br^-
[4]	+0.6	NM	−0.6	−2.5	NM	−1.7	−2.3	NM	−1.8
[5]	NM	NM	−0.7	−2.2	NM	−1.5	−2.0	NM	−2.0
[6]	NM	NM	−0.04	−3.0	−4.3	−2.4	−3.2	NM	−2.2
[7]	−0.8	−2.3	−0.7	−1.5	−2.7	−2.5	NM	NM	−1.4
[11]	NM	NM	NM	−1.0	−0.2	−0.3	NM	NM	NM
[15]	−3.4	−3.1	−3.7	−3.1	−4.3	−3.7	−4.3	NM	−3.1
[16]	NM	+13	+8.8	−0.5	−1.8	+4.1	−1.4	NM	+ 1.8
[19]	−1.0	−0.3	NM	−1.0	−1.3	−1.0	NM	NM	NM
Sensor no. 4	−2.0	−2.3	−2.4	−2.0	−1.8	−2.3	−1.5	−3.0	−2.3

NM: not mentioned.

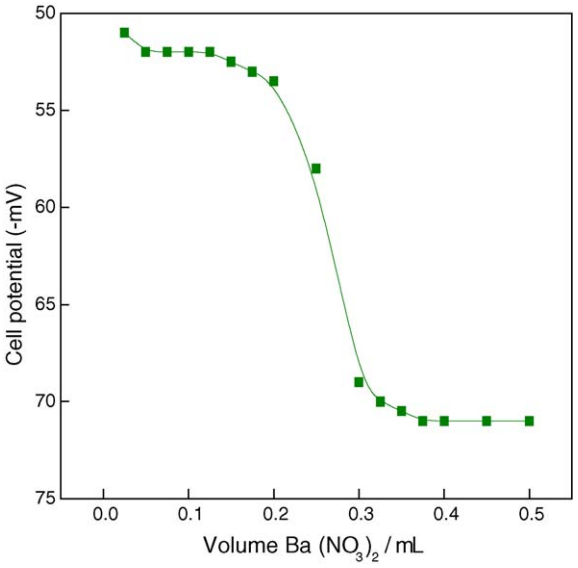


Fig. 4. Potentiometric titration curve of 1.0×10^{-3} M HPO_4^{2-} solution (25 mL) with $\times 10^{-1}$ M $Ba(NO_3)_2$.

$CrO_4^{2-} > MnO_4^- > BrO_3^-$. This anti-Hofmeister selectivity response pattern clearly reveals the mechanism of recognition of HPO_4^{2-} which takes place via hydrogen bonds of the ionophore (**I**) (Fig. 3). In Table 3, the selectivity coefficients for diverse anions of the proposed sensor are compared with the reported phosphate-selective sensors. It is seen that the selectivity of the proposed sensor towards HPO_4^{2-} is comparable in some cases [6,15] and better than almost all reported sensors [4,5,7,11,16,19]. The sensor shows good selectivity over several other anions such as MnO_4^-, CrO_4^{2-} and BrO_3^- that have not been reported for the other electrodes.

4. Analytical application

The electrode was also used to determine the end-point in the potentiometric titration of HPO_4^{2-} with $Ba(NO_3)_2$. A 25 mL solution of 1.0×10^{-3} M HPO_4^{2-} was titrated against 1.0×10^{-1} M $Ba(NO_3)_2$ solution at pH 8.0. The titration plot obtained (Fig. 4) is of standard sigmoid shape and the end-point corresponds to 1:1 stoichiometry of barium-monohydrogenphosphate complex. Therefore, the sensor can be successfully used as an indicator electrode for determining HPO_4^{2-} by potentiometric titration.

5. Conclusions

A bis-dithioxamide receptor performed well as electroactive material in the development of a phosphate-selective sensor since it shows less interference from thiocyanate, perchlorate and iodide than previously designed sensors. Among the various membranes prepared, the sensor no. 4 having membrane with composition (w/w) (**I**) (2%): PVC (33%):NPOE (63.5%):TDDMACl (1.5%) displays widest working concentration range of 1.7×10^{-6} to 1.0×10^{-2} M (detection limit 0.2 ppm) with Nernstian compliance of 29.6 mV/decade of activity. It was found to be chemically and physically stable, and generated steady potential in 8 s with high reproducibility. The sensor could be put to analytical use both by direct potentiometry as well as potentiometric titration.

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