

STUDIES ON THE HEAVY METAL REMOVAL EFFICIENCY AND ANTIBACTERIAL ACTIVITY OF 2-(DIPHENYLPHOSPHINO)AMINOPYRIDINE

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The solvent extraction of metal picrates such as Ni²⁺, Cu²⁺, Co²⁺, Pb²⁺ and Cd²⁺ from the aqueous to the organic phase was studied using 2-(diphenylphosphino)aminopyridine (Ph₂PNHpy). The effects of parameters including the pH of the aqueous phase and the ligand solution volume were investigated to determine the extraction ability of the ligand for metal ions. The results showed that the extraction percentages of metal ions were high at low pH values. The antibacterial activity of the aminophosphine was also screened against *Escherichia coli* (*E. coli*) ATCC 25922, *Staphylococcus aureus* (*S. aureus*) ATCC 25923, *Pseudomonas syringae* pv. *tomato* (*P. syringae*) DC300, *Salmonella enterica* serotype *Typhmuri*um (*S. typhmuri*um) SL 1344 and *Streptococcus mutans* (*S. mutans*) ATCC 25175. From the studies of antibacterial activity, it was observed that the ligand exhibited a potent inhibitory effect against all Gram-negative and Gram-positive bacteria with a diameter of inhibition zone ranging from 3.86 to 18.10 mm. The aminophosphine ligand (Ph₂PNHpy) should be considered as a suitable bio-active molecule for antimicrobial material design and next-generation, non-toxic drug fabrication. The Ph₂PNHpy obtained may have the potential for use as an antimicrobial additive for bioengineering applications.

Keywords: aminophosphines; heavy metals; solvent extraction; antibacterial activity

ИСПИТУВАЊЕ НА ЕФИКАСНОСТА НА ОТСТРАНУВАЊЕ НА ТЕШКИ МЕТАЛИ И АНТИБАКТЕРИСКОТО ДЕЈСТВО НА 2-(ДИФЕНИЛФОСФИНО)АМИНОПИРИДИН

Испитувана е екстракцијата на металните пикрати на Ni²⁺, Cu²⁺, Co²⁺, Pb²⁺ и Cd²⁺ од водни раствори до органската фаза со употреба на 2-(дифенилфосфино)аминопиридин (Ph₂PNHpy). Беше испитано влијанието на параметрите како што се рН на водната фаза и волуменот на растворот на лигандот за да се определи способноста на лигандот за екстракција на метални јони. Резултатите покажуваат дека уделот на екстракција е поголем при пониски вредности на рН. Антибактериска активност на аминоксфинот беше испитана на *Escherichia coli* (*E. coli*) ATCC 25922, *Staphylococcus aureus* (*S. aureus*) ATCC 25923, *Pseudomonas syringae* pv. *tomato* (*P. syringae*) DC300, *Salmonella enterica* serotype *Typhmuri*um (*S. typhmuri*um) SL 1344 и на *Streptococcus mutans* (*S. mutans*) ATCC 25175. Од истражувањето на антибактериската активност беше утврдено дека лигандот има силно инхибиторно дејство врз сите Грам-негативни и Грам-позитивни бактерии со пречник на инхибиторна зона во опсегот од 3,86 до 18,10 mm. Аминоксфинскиот лиганд (Ph₂PNHpy) треба да се земе предвид како соодветна биомолекула за дизајнирање на антимикробни материи и производство на нетоксични лекови од следна генерација. Добиениот Ph₂PNHpy може да има потенцијал како антимикробен адитив за биоинженерски апликации.

Клучни зборови: аминоксфини; тешки метали; екстракција со растворувач; антибактериска активност

1. INTRODUCTION

Heavy metal ions are extensively used in industrial applications and are among the most common environmental pollutants [1, 2]. Some metals, such as Fe, Zn, Cu, Co, Cr, Mn and Ni, play an essential role in metabolism for humans and animals in trace amounts, but higher concentrations can cause toxicity and health hazards [3, 4]. Others, such as Pb and Cd, are not suitable for biological functions and can cause many health complications, even at very low concentrations [5–7]. Waste materials containing heavy metals are considered hazardous materials. Heavy metal ion contamination of water is one of the most important environmental concerns. The heavy metal ions in wastewater are detrimental to soil, underground water and surface water, with destructive effects on ecology and the health of animals and humans if not properly treated [8]. Therefore, the recovery of heavy metals is necessary and important to protect the environment. In recent years, various methods for heavy metal removal have been extensively studied due to the potential health and ecological hazards. Among the available processing alternatives, solvent extraction offers a convenient solution to the problem and has been widely used for the extraction and separation of heavy metals from the aqueous phase [6, 9, 10]. Solvent extraction techniques are among the most studied method for the recovery of various metals ions from different sources due to their ease, simplicity, speed and wide scope [11, 12].

There are a number of efficient reagents used for metal extraction, most notably organophosphorus compounds [13–23] and amines [24]. The synergistic extraction of these divalent transition metal ions with mixtures of neutral organophosphorus extractants and amine extractants has been reported previously [25].

Aminophosphine ligands containing direct P–N bonds may be constructed in large quantities through the use of relatively simple condensation processes and from inexpensive starting materials [26]. Despite this, there are limited studies focusing on the potential use of aminophosphines, that combine neutral organic phosphorus derivatives and amines, in the extraction of metal ions [27]. In this study, bidentate aminophosphine ligand, 2-(diphenylphosphino)aminopyridine (Ph_2PNHpy), that incorporates both pyridyl and phosphine groups was investigated as a ligand in the solvent extraction of metal picrates such as Ni^{2+} , Cu^{2+} , Co^{2+} , Pb^{2+} and Cd^{2+} from water. Furthermore, it is known that both pyridine [28–31] and

aminophosphine derivatives [32–34] have exhibited a variety of biological activities. Consequently, the antibacterial effects of the aminophosphine containing a pyridyl group were investigated in Gram-positive and Gram-negative bacteria.

2. RESULTS AND DISCUSSION

2-(diphenylphosphino)aminopyridine was prepared as described previously by reacting 2-aminopyridine with chlorodiphenylphosphine in the presence of triethylamine (Fig. 1) [35]. The spectroscopic data are consistent with those reported in the literature [36].

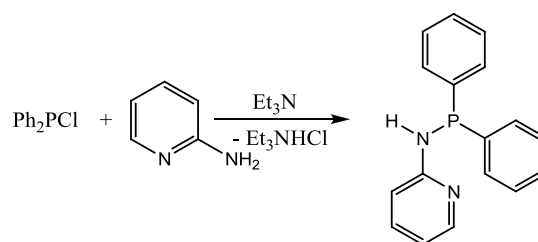


Fig. 1. Synthesis of 2-(diphenylphosphino)aminopyridine

The metal ion binding properties of 2-(diphenylphosphino)aminopyridine were investigated using solvent extraction experiments in order to determine the extractability of metal ions including Ni^{2+} , Cd^{2+} , Cu^{2+} , Co^{2+} and Pb^{2+} from the aqueous phase to the organic phase. Dichloromethane has a high dielectric constant and is favoured for the extraction of metal ions. Also, the aminophosphine ligand (Ph_2PNHpy) was completely soluble in dichloromethane. Therefore, dichloromethane was chosen as the solvent for the extraction procedure. The results related to the extractability of the abovementioned metal picrates from the aqueous phase to the organic phase are given in Table 1. The maximum extraction percentage (E%) values of Ni^{2+} , Cd^{2+} , Co^{2+} and Pb^{2+} picrates were 97.9%, 99.3%, 98.5% and 97.1%, respectively, at pH 2, while the maximum E% value of copper picrate was 94.5 % at pH 5.

As can be seen from the data in Table 1, the ligand had a high extraction efficiency for the metal ions. Aminophosphines containing direct P–N bonds are "soft-hard hybrid donor" ligands. Moreover, the introduction of the additional "soft donor" (nitrogen of the pyridine ring) to the structure enhances the extraction ability of the ligand toward soft and borderline metal cations such as Cd^{2+} , Ni^{2+} , Cu^{2+} , Co^{2+} and Pb^{2+} [37]. Although 2-(diphenylphosphino)aminopyridine displays a va-

riety of coordination modes to metal centres, the ligand prefers simple chelation over bridging or monodentate P-bound coordination modes, and forms a strong five-membered P,N chelate [26, 36, 38–41]. In our experiments, the high extraction efficiency of this ligand can be explained by the chelate effect of the two donors. Also, it is known

that 2-(diphenylphosphino)aminopyridine exists as hydrogen bonded dimers and can form hydrogen-bonded metal complexes [33, 36, 42]. Because the relative stability of the metal complexes is affected, the hydrogen bonds also play an important role in the solvent extraction of metal ions [43].

Table 1

Effect of the pH of the aqueous phase on the extraction of 2×10^{-4} M metal picrates

pH	E%				
	Ni ²⁺	Cd ²⁺	Cu ²⁺	Co ²⁺	Pb ²⁺
2	97.9 ± 0.2	99.3 ± 0.3	88.9 ± 7.4	98.5 ± 0.2	97.1 ± 2.3
3	90.6 ± 0.4	89.6 ± 0.3	92.9 ± 1.4	98.2 ± 0.2	95.4 ± 0.6
4	87.2 ± 2.0	88.0 ± 0.8	94.2 ± 1.1	96.1 ± 0.6	85.6 ± 0.4
5	95.2 ± 0.2	84.4 ± 3.3	94.5 ± 0.5	93.4 ± 0.4	78.2 ± 1.3
6	79.1 ± 1.9	80.6 ± 5.1	67.2 ± 6.8	92.9 ± 6.0	77.7 ± 6.1
7	83.4 ± 0.2	69.3 ± 2.5	67.8 ± 11.4	82.7 ± 8.9	77.1 ± 9.3
8	71.1 ± 1.0	61.0 ± 3.2	81.6 ± 3.6	72.7 ± 2.4	63.9 ± 6.5
9	75.1 ± 1.8	57.1 ± 1.7	87.2 ± 6.0	56.8 ± 1.5	51.1 ± 1.7
10	22.7 ± 2.4	55.7 ± 5.9	75.2 ± 3.3	54.7 ± 2.9	48.2 ± 3.0

In our previous paper [27], we reported the maximum E% values of lead, copper and nickel picrates for *N*-(diphenylphosphino)-4-methylpiperazin-1-amine as 71.8%, 74.7% and 76.9%, respectively. Experimental results revealed that the bidentate ligand 2-(diphenylphosphino)aminopyridine showed better efficiency and affinity for Cu²⁺, Ni²⁺ and Pb²⁺ ions with respect to the monodentate ligand *N*-(diphenylphosphino)-4-methylpiperazin-1-amine.

The metal ion extraction was studied with the simultaneous determination of metal ions in the aqueous phase at different pH levels. The pH level was clearly an important parameter in the extraction process of metal ions. Table 1 shows the dependence of recovery on the pH of the solution. According to our results, 2-(diphenylphosphino)aminopyridine was effective for the extraction of metal ions at pH 2. In most industrial processes cadmium is present in acidic solutions, and therefore it is necessary to use an extractant that can extract cadmium under these conditions [44]. Nickel is found in both leach liquors from ores and in secondary sources at a lower pH. Most of the work in hydrometallurgy is focused on extracting metals at pH values as low as possible [45]. Mixtures of extractants have been employed by different investigators to extract Ni²⁺, Co²⁺, Pb²⁺ and Cd²⁺ at relatively low pH (1–3) [46–48], however,

there are few single extractants that can extract metal ions efficiently at lower pH values. Most extractants are used commercially and are not effective for the recovery of these metals in a highly acidic medium (pH < 4) [45, 46, 49–55]. 2-(diphenylphosphino)aminopyridine showed good efficiency and affinity for metal ions at pH 2 according to the results obtained, making it suitable for solvent extractions in acidic media.

The nature of the extracted species was studied by evaluating the distribution ratio of metal picrates in the aqueous and organic phases. In this system, log*D* versus pH were plotted (Fig. 2), where *D* is the distribution ratio of the concentration of each metal picrate. As shown in Figure 2, there was a deviation from linearity. This may be due to the different complexing effects and/or formation of protonated species of the ligand during extraction from the acidic solution.

The effect of ligand volume (organic phase) on the extraction of metal picrates was studied to determine the optimum value required for extraction. Table 2 shows the dependence of the recovery on the ligand solution volume (organic phase). The optimum ligand volume was determined as 2 ml at pH 2. The extraction percentage values of Ni, Cd, Cu, Co and Pb picrates were 97.9%, 99.3%, 88.9%, 98.5% and 97.1%, respectively, when 2 ml of the solution of aminophosphine was used for the

extraction. E% values for Ni, Cd, Co and Pb picrates were quantitative. As shown in Table 2, the

ligand volume did not significantly affect the recovery of metal ions.

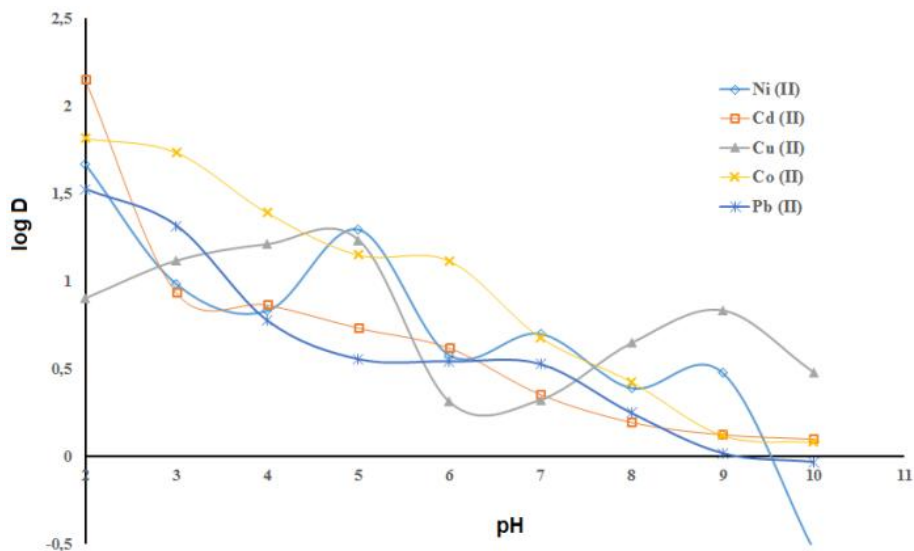


Fig. 2. Relationship between pH and logD

Table 2

Effect of ligand solution volume on the extraction of metal picrates

Ligand solution volume (ml)	%E				
	Ni ²⁺	Cd ²⁺	Cu ²⁺	Co ²⁺	Pb ²⁺
2	97.92 ± 0.1	99.30 ± 0.3	88.90 ± 7.4	98.50 ± 0.2	97.10 ± 2.3
4	97.30 ± 0.1	96.91 ± 1.2	76.08 ± 7.8	92.86 ± 0.4	94.95 ± 1.2
6	96.40 ± 0.3	97.10 ± 1.2	82.75 ± 2.4	93.11 ± 0.8	94.74 ± 0.5
8	95.68 ± 0.5	97.49 ± 0.9	83.14 ± 0.7	93.11 ± 0.6	95.13 ± 1.1
10	96.30 ± 0.3	95.56 ± 1.9	82.35 ± 1.8	90.23 ± 1.4	91.27 ± 0.3

Table 3

Quantitative antimicrobial assay results (zone of growth inhibition) of 2-(diphenylphosphino)aminopyridine at different concentrations

Ph ₂ PNHPy concentration (mol.l ⁻¹)	Inhibition zone diameter [mm]				
	Gram negative bacteria			Gram positive bacteria	
	<i>E.coli</i>	<i>P.syringae</i>	<i>S.typhmuriium</i>	<i>S.aureus</i>	<i>S.mutans</i>
1·10 ⁻⁸	6.21	3.86	5.85	4.91	6.25
1·10 ⁻⁷	9.47	5.12	8.32	6.29	9.78
1·10 ⁻⁶	11.28	6.27	11.74	8.22	12.32
1·10 ⁻⁵	14.84	7.58	14.27	9.16	15.27
1·10 ⁻⁴	16.32	9.27	18.10	11.48	17.12
Control: DMSO	0.0	0.0	0.0	0.0	0.0
Gentamicin	11.87	11.68	11.52	12.36	11.92
Ampicillin	12.26	10.21	12.92	11.84	12.48

The antibacterial activity of 2-(diphenylphosphino)aminopyridine at various concentrations was evaluated against Gram-positive and Gram-negative bacteria using the disc diffusion method. More than one organism was tested to increase the chance of detecting antibacterial activities. The compound was insoluble in water, so the assay was carried out using dimethylsulfoxide (DMSO) as solvent. DMSO was also used as a control to confirm that it did not inhibit bacterial growth. Commercially available standard drugs ampicillin and gentamicin were used as antibacterial controls and the results of the disc diffusion assay are summarized in Table 3. The presence of an inhibition zone clearly indicated the antibacterial effect of aminophosphine. The ligand showed high antibacterial activity against the investigated Gram-positive and Gram-negative bacteria. The amount of ligand tested for antibacterial activity was essential. As shown in Table 3, the antibacterial activity of the aminophosphine increased with increasing ligand concentration. The antibacterial activities of the aminophosphine at concentrations of 10^{-5} M and 10^{-4} M were found to be higher than those of standard antibiotics against *E. coli*, *S. typhmuri*um and *S. mutans*.

3. MATERIALS AND METHODS

Reactions were routinely carried out using Schlenk-line techniques under pure dry nitrogen gas. Solvents were dried and distilled prior to use. All other chemicals used were of analytical grade and did not require further purification. ^{31}P - $\{^1\text{H}\}$ and ^1H NMR spectra were taken on a Bruker UltraShield-400 spectrophotometer. Infrared spectra were recorded on a Perkin Elmer FT-IR System Spectrum BX. Spectrophotometric measurements were performed using a Shimadzu UV-160 A UV-vis spectrophotometer.

3.1. Preparation of

2-(diphenylphosphino)aminopyridine

Ph_2PNHpy was synthesised as in a previously reported procedure [35]. A mixture of 2-aminopyridine (3.75 g, 39.84 mmol) and triethylamine (5.5 ml, 39.68 mmol) was dissolved in tetrahydrofuran (20 ml). The solution was cooled to 0 °C and Ph_2PCl (7.3 ml, 39.70 mmol) was slowly added. The reaction mixture was stirred for 6 h. After this time, the ammonium salt was separated by filtration and the solvent was removed under vacuum. The oily residue obtained was dissolved in tetrahydrofuran and precipitated with

diethylether, producing 7.5 g of white powder (68% yield). Found (calc. for $\text{C}_{17}\text{H}_{15}\text{PN}_2$): C, 73.67 (73.37); H, 5.21 (5.43); N, 9.83 (10.07). ^1H NMR (CDCl_3 , δ , ppm): 5.36 (d, NH, 1H, $J_{\text{PH}}=8\text{Hz}$), 6.72 (t, $\text{C}_{5\text{-H}}$, 1H), 7.04 (d, $\text{C}_{3\text{-H}}$, 1H), 7.28–7.50 (m, Ph, $\text{C}_{4\text{-H}}$, 11H), 8.11 (d, $\text{C}_{6\text{-H}}$, 1H). ^{31}P - $\{^1\text{H}\}$ NMR (CDCl_3 , δ , ppm): 25.86 (s). IR (cm^{-1}): 918 (PN), 1434 (PPh), 3117 (NH), 1599 (C=N).

3.2. Solvent extraction procedure

1×10^{-3} M aqueous solutions of the metal picrates were prepared according to literature [49]. 1×10^{-3} M solutions of 2-(diphenylphosphino)aminopyridine were prepared separately in dichloromethane and used as extractants. 2 ml of the extractant solution was added to a 10 ml volumetric flask that was then filled with dichloromethane. An organic solution (10 ml) containing 2 ml of ligand (1×10^{-3} M), an aqueous solution (10 ml) containing 2 ml of the metal picrate solution (1×10^{-3} M) and 8 ml of a buffer solution (for pH adjustment) were placed into a stoppered flask and stirred with a magnetic stirrer at 25 °C for 1 h in a water jacket. The mixture was allowed to settle for 30 min to allow for phase separation. After phase separation, the metal picrate extraction values (E%) in the aqueous phase were determined based on their absorbance by UV-Vis spectrophotometry using the following equation (Eq. 1).

$$E\% = \left[\frac{A_0 - A}{A_0} \right] \times 100 \quad (\text{Eq. 1})$$

where A_0 is the absorbance in the absence of the ligand and A denotes the absorbance in the aqueous phase after extraction.

The pH of the aqueous solutions was maintained at pH 2–10 using buffer solutions to investigate the effect of pH on E%. The extractant solutions with various volumes (2, 4, 6, 8 and 10 ml) were added to 10 ml volumetric flasks that were then filled with dichloromethane. Equal volumes (10 ml) of the organic solution and aqueous solution were used to investigate the effect of the ligand solution volume on the extraction of metal ions at pH 2.

3.3. Antibacterial activity studies

3.3.1. Microorganisms tested

Escherichia coli (*E. coli*) ATCC 25922, *Staphylococcus aureus* (*S. aureus*) ATCC 25923, *Pseudomonas syringae* pv. *tomato* (*P. syringae*) DC300, *Salmonella enterica* serotype *Typhmuri*um

(*S. typhmuri*) SL 1344 and *Streptococcus mutans* (*S. mutans*) ATCC 25175 were the microorganisms tested. Bacteria were maintained on Luria Bertoni (LB) agar culture medium at 4 °C. All the tested microorganisms were subcultured on appropriate medium at 37 °C for 24 h.

3.3.2. Activity assay

Antibacterial activities of the synthesized Ph₂PNHpy ligand against the Gram-positive and Gram-negative bacteria were determined using the disc diffusion method. 0.5 McFarland standard was used as a reference to adjust the turbidity of the microorganisms. The tested compound was dissolved in DMSO, which has no inhibition activity. Samples were sterilized by UV irradiation for 30 min before incubation. Microorganism suspensions of 100 µl were inoculated (1 × 10⁸ CFU/ml) onto Müller-Hinton medium. Filter discs (6 mm in diameter) containing various concentrations of the Ph₂PNHpy (10⁻⁸ M, 10⁻⁷ M, 10⁻⁶ M, 10⁻⁵ M and 10⁻⁴ M) were placed on inoculated Petri plates and incubated at 37 °C for 24 h. A DMSO-only disc was used as a negative control. Ampicillin and gentamicin were used as standard drugs for the bacteria. The diameter of the inhibition zone was calculated after incubation. All experiments were repeated in triplicate and mean values were calculated.

4. CONCLUSIONS

2-(diphenylphosphino)aminopyridine effectively extracted metal ions including Ni²⁺, Cu²⁺, Co²⁺, Pb²⁺ and Cd²⁺ from the aqueous phase to the organic phase. The maximum E% values of nickel, cadmium, cobalt and lead picrates were 97.9%, 99.3%, 98.5% and 97.1%, respectively, at pH 2, while the maximum E% value of copper picrate was 94.5% at pH 5. This makes the ligand suitable for solvent extraction at a low pH. The aminophosphine was also observed to have good antibacterial activity against *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 25923, *Pseudomonas syringae* pv. *tomato* DC300, *Salmonella enterica* serotype *Typhmuri* SL 1344 and *Streptococcus mutans* ATCC 25175.

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