# Potentiometric investigation of the stability of palladium(II) complex of pralidoxime chloride in aqueous solution*

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**Abstract**: The formation of a complex between palladium(II) chloride and pralidoxime chloride (PAM-2Cl) has been studied by means of potentiometric pH measurements. The real stability constant of the complex in aqueous medium of ionic strength 0.3 M (KCl) at 25.0°C was log $K_s$ = 7.29. This value was close to that (log $K_s$ = 7.02) obtained previously by spectrophotometric methods after appropriate correction with respect to the corresponding value of the acidic constant of PAM-2Cl (p$K_a^c$ = 8.05), which was also determined under the same experimental conditions.

**Keywords**: *Pralidoxime chloride; palladium(II) complex; acidic constant; stability constant; potentiometric determination.*

## Introduction

Although hundreds of pyridinium oximes have been tested as antidotes, in combination with atropine, in experimental organophosphorus (nerve gases, pesticides) poisoning [1, 2], only three of these, PAM-2Cl, obidoxime chloride and TMB-4 are used in clinical medicine [3–5].

The values of the acidic constants (p$K_a$) are of prime importance for the reactivating efficiency of oximes. According to the same authors [5–7], the p$K_a$ should be such that a sufficient amount of the ionized form of oxime is present at physiological pH. The optimal p$K_a$ value of pyridinium oximes has been estimated to be about 8, although oxime HI-6 (p$K_a$ = 7.2) is an excellent reactivator [8].

Earlier spectrophotometric studies [9] showed that PAM-2Cl in reaction with Pd(II) forms complex of stoichiometric composition 1:1. The present report concerns the determination of the real stability constant (log $K_s$) of this complex by potentiometric pH measurements during titration with sodium hydroxide.

## Experimental

### Reagents

PAM-2Cl was of the same origin as that of previous work [9]. All other chemicals were of analytical grade (Merck); boiled double-dis-tilled water was used to prepare solutions for potentiometric determinations.

### Solutions

For the potentiometric determination of log $K_s$, a standard solution of PAM-2Cl (4 × $10^{-3}$M) was prepared freshly by dissolving the accurately weighed solid substance in boiled and cooled double-distilled water. Standard palladium(II) chloride solution (2.0 × $10^{-2}$ M) was prepared and standardized as described [10]; the ionic strength was adjusted with 2 M potassium chloride. For the titrations, 0.165 or 0.090 M sodium hydroxide (carbonate-free) was used; the concentrations were determined by titrating with a standard solution of potassium hydrogen phthalate.

### Apparatus

A PHM-62 Standard pH-meter (Radio-meter, Copenhagen) equipped with a com-bined electrode (GK 2401B) was used (accur-acy ±0.01 pH units). The response of the electrode was checked against: hydrogen phthalate, pH 4.01 (Radiometer S 1316); hydrogen phosphate, pH 7.00 (Radiometer S 1326); sodium tetraborate, pH 9.18 (Radio-meter S 1336); and hydrochloric acid, pH 1.00 (Merck) standard buffer solutions. The elec-trode was calibrated in the pH range 2.0–3.5 using solutions of known concentrations of

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HCl at a constant ionic strength (0.3 M KCl). On the basis of these data the correction factor was calculated for converting the measured $pH_{GE}$ values into the concentration of $H_3O^+$ ions in the investigated systems of the same ionic strength ($pH_{GE} - pc_H = 0.07$; $pc_H = -\log H_3O^+$) [11, 12]. For the potentiometric titrations, a TTT 60 titrator with an autoburette ABU 12 (Radiometer, Copenhagen) was used (accuracy ±0.001 ml). An Ultra-Thermo-stat Medigen (Dresden) was used for maintaining a constant temperature (25 ± 0.1°C) during the titrations. The $pK_a^c$ and log $K_s$ values were calculated using an EPSON HX-20.

*Potentiometric determination of $pK_a^c$*

Quantities of 0.0173 g of PAM-2Cl were transferred into a special double-walled thermostatted vessel; after addition of 3.0 ml of 2 M KCl, the solutions were diluted to 20.00 ml with double-distilled water and titrated with 0.165 M NaOH. Before the start of each titration a stream of nitrogen was passed through the solution and the inert atmosphere was kept constant during the titration. The neutralization region ($a = 0.2$–0.8) was used for the determination of $pK_a^c$ as described by Djatlova [13]. The value of $pK_w^c = 13.74$ ($\mu = 0.3$ M) was used.

*Potentiometric determination of log $K_s$*

*Titrations.* PAM-2Cl–ligand (L) was titrated with 0.09 M NaOH first in the presence of a constant Pd(II) concentration of 5 × $10^{-4}$ M (0.50 ml; 2 × $10^{-2}$ M) in molar ratios 1L–1Pd(II), 2L–1Pd(II) and 4L–1Pd(II) using 2.50, 5.0 and 10.0 ml of PAM-2Cl standard solution, respectively, and then in the absence of Pd(II). The pH of the solution of the ligand alone was adjusted to that of the mixture with Pd(II) (3.14) using 0.51 M HCl because of the acidity of Pd(II) solution itself.

The titrations were carried out at 25 ± 0.1°C at constant ionic strength (0.3 M) obtained by addition of 3.0 ml of 2 M KCl. The solutions were diluted to a total volume ($V_o$) of 20.0 ml, with double-distilled water, whether metal was present or not. Before the start of each titration a stream of nitrogen was passed through the solution and the inert atmosphere was kept constant during the titration.

*Calculations.* The equations of Albert [14] were used with some modifications. The free

ligand concentration [L] was calculated from the equation:

$$[L] = \frac{(1 - a) \cdot c_{L_{corr}} - c_H + c_{OH}}{c_H/K_a^c}, \quad (1)$$

where $a$ is the degree of titration calculated from $a = V_{NaOH} \cdot c_{NaOH}/c_L \cdot V_{oc}$; $c_{L_{corr}}$ is the initial concentration of ligand corrected at each point on the titration curve as $c_{L_{corr}} = c_L \cdot V_o/V_{oc} + V_{NaOH}$; $K_a^c$ = acidic constant of PAM-2Cl; $c_{OH}$ was omitted from the calculations because $pc_H$ was in the range 3.61–5.01. The value $V_{oc}$ represents the starting point for the calculations, determined for each pair of titration curves where the difference of $pc_H$ between the ligand alone and the complex becomes significant.

The function $\bar{n}$ is the average number of ligands bound to one metal atom and is calculated from [L] using equation (2):

$$\bar{n} = (c_{L_{corr}} - \alpha[L])/c_{M_{corr}}, \quad (2)$$

in which $\alpha = 1 + c_H/K_a^c$; $c_{M_{corr}}$ is the total metal ion concentration initially present in the solution corrected by $c_{M_{corr}} = c_M \cdot V_o/V_{oc} + V_{NaOH}$.

The value of log $K_s$ can be calculated using the method of least squares by plotting values of $\bar{n}/(\bar{n} - 1)[L]$ against the corresponding values of $(2 - \bar{n})[L]/(\bar{n} - 1)$ to yield a straight line of which the intercept is $-K_s$ if a 1:1 complex is formed.

The value of the conditional stability constant (log $K_s'$) of the PAM-2Cl–Pd(II) complex [9] was corrected with respect to the $pK_a^c$ of PAM-2Cl and the $pc_H$ according to equation (3):

$$\log K_s = \log K_s' + \log c_H - \log K_a^c. \quad (3)$$

**Results and Discussion**

Although the $pK_a$ value of PAM-2Cl could be derived from the literature [4] (8.0 at 20°C), it was considered preferable to determine the $pK_a$ under the same experimental conditions as those to be used in complex formation studies, because this value has a remarkable influence on the free ligand concentration [L]. The concentration acidic constant ($pK_a^c$) of PAM-2Cl at $\mu = 0.3$ M (KCl) was obtained from 29 equidistant points on the titration curve. PAM-

2Cl was titrated twice with an initial concentration of $5 \times 10^{-3}$ M. The $pK_a^c$ calculations were performed in the neutralization region ($a = 0.182 - 0.792$). The mean value of $pK_a^c$ was 8.05.

Potentiometric titration with NaOH of the ligand alone and of the mixture with Pd(II) was performed first in a molar ratio of 1:1, because previous spectrophotometric studies [9] showed that a complex of this stoichiometric composition had been formed. Because of the acidity of palladium(II) chloride solution the selected concentration was $5 \times 10^{-4}$ M. Higher concentrations would decrease the pH below 3 where the complex is not formed.

An oxime group is amphiprotic. The oxime nitrogen atom is weakly basic [15, 16] ($pK$ (=$\overset{+}{N}HOH$) $\ll 2$) and the hydroxyl group is weakly acidic [17]. This was confirmed by calculating the value of the average number of protons bound per mole of the oxime ($\bar{n}_{tot}$) according to the formation function method [18], from the titration curve of PAM-2Cl with NaOH obtained from a strongly acidic solution (pH = 1.78, adjusted with 0.5073 M HCl). The value of $\bar{n}_{tot}$ (from 1 to 0) provides

evidence for binding of the free nigroten atom with Pd(II).

Titration curves for the metal alone, for the complex in different molar ratios with respect of PAM-2Cl, and for the ligand alone are presented in Fig. 1. The diagram attached to Fig. 1 shows the dependence on pH of the percentage of mole fraction of each molecular species of PAM-2Cl; it is evident that oxime is present completely in molecular form even at pH 6.45 where the conditional stability constant was obtained [9]. The pH values are calculated according to equation (4):

$$pH = pK_a^c + \log \frac{c_I}{100 - c_I}, \qquad (4)$$

on the basis of $pK_a^c = 8.05$, where $c_I$ represents the concentration of the ionized species expressed as a percentage.

From the results of the titrations of the complex with different molar ratios only one complex of composition 1:1 was observed. The value of the average number of ligands bound to one metal atom ($\bar{n}$) reaches 1 for values of the degree of titration (a) of 0.95, 0.49 and 0.24
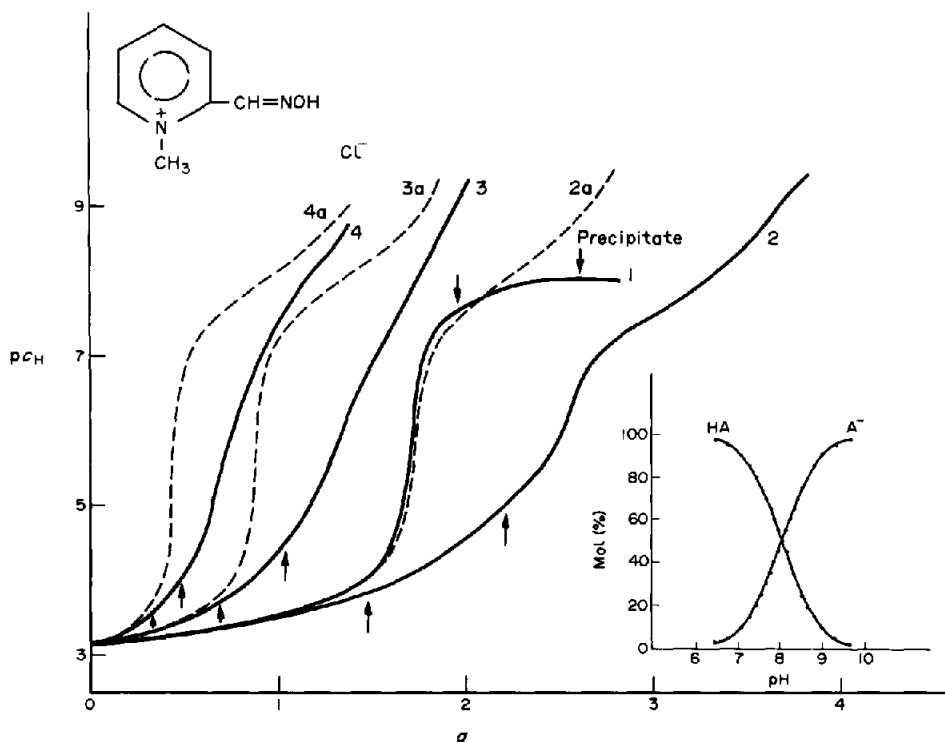


**Figure 1**
Potentiometric titration curves of Pd(II) alone (curve 1) $c_{Pd(II)} = 5 \times 10^{-4}$ M; and in the presence of PAM-2Cl in molar ratios of PAM-2Cl–Pd(II) of 1:1 (curve 2); 2:1 (curve 3); and 4:1 (curve 4) with the corresponding curves of ligand–PAM-2Cl alone (2a, 3a and 4a). The arrows denote the intervals for calculation. The attached diagram shows the dependence on pH of the percentage mole fraction of each species.

in respect of molar ratios 1PAM-2Cl-1Pd(II), 2PAM-2Cl-1Pd(II) and 4PAM-2Cl-1Pd(II), respectively. The confirmatory results were obtained by plotting values of $\bar{n}$ against p[L]; such curves have been termed "formation curves" by Bjerrum [19] (Fig. 2). They provide evidence as to whether the reaction under consideration is stepwise or not. Since both curves showed an inflection point at a value of $\bar{n}$ of about 1, it was concluded that only the 1:1 complex was formed. Figure 3 represents the formation curves of the PAM-2Cl-Pd(II) complex for all molar ratios with values $\bar{n}$ up to 1.
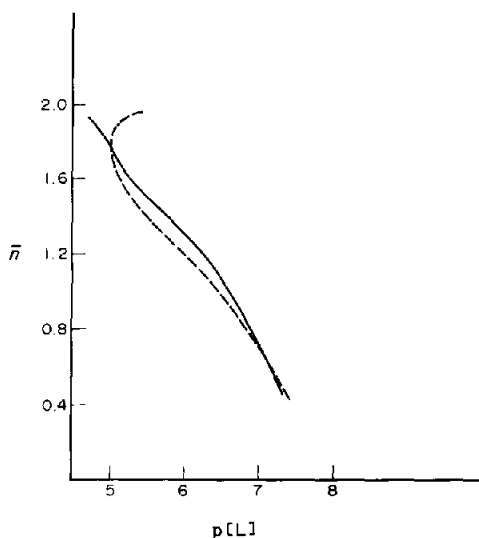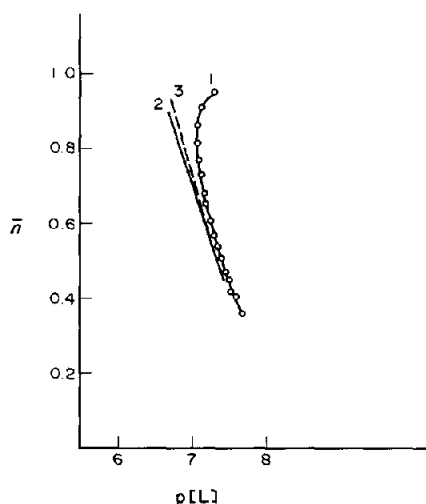


**Figure 3**
The formation curves of PAM-2Cl-Pd(II) complex for molar ratios: 1PAM-2Cl-1Pd(II) (curve 1); 2PAM-2Cl-1Pd(II) (curve 2) and 4PAM-2Cl-1Pd(II) (curve 3).

The values of log $K_s$ obtained for 1:1, 2:1 and 4:1 molar ratios of PAM-2Cl-Pd(II) were 7.29, 7.31 and 7.29, respectively. The summarized results for the titration of 2PAM-2Cl-1Pd(II) are shown in Table 1. The value of 7.29 is close to that (log $K_s$ = 7.02) obtained after correction of log $K'_s$ = 5.35 (Sommer's method) according to equation (3).

Calculations according to the formation function method [18] for titration of the complex [ratio 1PAM-2Cl-1Pd(II)] show that the acidity of the oxime group increases markedly with co-ordination of the oxime nitrogen atom to Pd(II), since the value obtained for the $pK_a^c$



**Figure 2**
The formation curves of PAM-2Cl-Pd(II) complex for molar ratios 2PAM-2Cl-1Pd(II) (broken line) and for 4PAM-2Cl-1Pd(II) (solid line).

**Table 1**
Potentiometric determination of the stability constant[*] of PAM-2Cl-Pd(II) complex for the molar ratio 2PAM-2Cl-1Pd(II); $c_{PAM-2Cl}$ = 1 × $10^{-3}$ M; $c_{Pd(II)}$ = 5 × $10^{-4}$ M; $V_0$ = 20 ml; $V_{0c}$ = 20.14 ml; $pK_a^c$ = 8.05; temperature = 25 ± 0.1°C; μ = 0.30 M (KCl)

| 0.09 M NaOH (ml) | $pc_H$ | p[L] | [L] | $\bar{n}$ | $\dfrac{\bar{n}}{(\bar{n}-1)[L]}$ | $\dfrac{(2-\bar{n})[L]}{(\bar{n}-1)}$ | $a$ |
|---|---|---|---|---|---|---|---|
| 0.010 | 3.74 | 7.425 | 3.753 × $10^{-8}$ | 0.456 | −2.233 × $10^7$ | −1.065 × $10^{-7}$ | 0.045 |
| 0.020 | 3.81 | 7.366 | 4.307 × $10^{-8}$ | 0.491 | −2.238 × $10^7$ | −1.276 × $10^{-7}$ | 0.089 |
| 0.030 | 3.89 | 7.297 | 5.049 × $10^{-8}$ | 0.527 | −2.214 × $10^7$ | −1.574 × $10^{-7}$ | 0.134 |
| 0.040 | 3.98 | 7.219 | 6.036 × $10^{-8}$ | 0.568 | −2.184 × $10^7$ | −2.003 × $10^{-7}$ | 0.178 |
| 0.045 | 4.02 | 7.187 | 6.486 × $10^{-8}$ | 0.595 | −2.259 × $10^7$ | −2.253 × $10^{-7}$ | 0.201 |
| 0.050 | 4.07 | 7.145 | 7.164 × $10^{-8}$ | 0.618 | −2.264 × $10^7$ | −2.595 × $10^{-7}$ | 0.223 |
| 0.055 | 4.13 | 7.092 | 8.089 × $10^{-8}$ | 0.641 | −2.208 × $10^7$ | −3.063 × $10^{-7}$ | 0.246 |
| 0.060 | 4.18 | 7.051 | 8.884 × $10^{-8}$ | 0.669 | −2.280 × $10^7$ | −3.576 × $10^{-7}$ | 0.268 |
| 0.065 | 4.23 | 7.012 | 9.739 × $10^{-8}$ | 0.699 | −2.392 × $10^7$ | −4.217 × $10^{-7}$ | 0.291 |
| 0.070 | 4.29 | 6.962 | 1.093 × $10^{-7}$ | 0.729 | −2.463 × $10^7$ | −5.126 × $10^{-7}$ | 0.313 |
| 0.075 | 4.35 | 6.913 | 1.223 × $10^{-7}$ | 0.760 | −2.594 × $10^7$ | −6.328 × $10^{-7}$ | 0.335 |
| 0.080 | 4.42 | 6.854 | 1.401 × $10^{-7}$ | 0.792 | −2.712 × $10^7$ | −8.122 × $10^{-7}$ | 0.357 |
| 0.085 | 4.48 | 6.806 | 1.562 × $10^{-7}$ | 0.826 | −3.046 × $10^7$ | −1.055 × $10^{-6}$ | 0.379 |
| 0.090 | 4.55 | 6.749 | 1.779 × $10^{-7}$ | 0.861 | −3.480 × $10^7$ | −1.458 × $10^{-6}$ | 0.402 |

[*]$N$ = 14; $\bar{n}$ (0.456 − 0.861); intercept = −2.020 × $10^7$; $r$ = 0.98; log $K_s$ = 7.31.

is $5.08 \pm 0.6$. This is in accordance with literature data obtained for co-ordination of some other oximes with different metal ions [20, 21].

The results show that the potentiometric method enables an accurate and reproducible log $K_s$ value of PAM-Cl–Pd(II) complex to be determined, and also confirm the molar ratio of the complex obtained by spectrophotometric methods.

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