Potentiometric and Theoretical Studies of Stability Constants of Glyoxime Derivatives and their Nickel, Copper, Cobalt and Zinc Complexes

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Abstract

The dissociation constants of 1,2-bis(4-methylpiperazine)glyoxime (BMPGH2) and 1,2-bis(4-benzylpiperazine)glyoxime (BBPGH2) were determined in 0.1 mol dm^{-3} NaCl and 0.001 mol dm^{-3} HCl at 25 °C potentiometrically. pK_a values of BMPGH2 and BBPGH2 were obtained as 2.91, 6.79, 7.97, 10.00 and 3.46, 5.89, 6.77, 9.76, respectively. The protonation order of nitrogen atoms in the BMPGH2 and BBPGH$_2$ were determined using Semi-empirical AM1 method. In various pH conditions, the different complexes formulated as MH_6L_2, MH_5L_2, MH_4L_2, MH_3L_2, MH_2L_2, MHL_2, ML_2, $MH_{-1}L_2$, and $MH_{-2}L_2$ were formed with titration of ligand and Cu, Co, Ni and Zn ions.

Key words: 1,2-bis(4'-methylpiperazine)glyoxime, 1,2-bis(4'-benzylpiperazine)glyoxime, dissociation constant, stability constants, SUPERQUAD, AM1 method

Introduction

Recently, the high stability of the complexes prepared with *vic*-dioxime ligands have been extensively used for various purposes including model compounds for vitamin B$_{12}$ analytical and medicinal chemistry, pigments.[1,2] Schrauzer has found that this kind of complexes exhibits semiconductor property.[3] An investigation[4] has been done about spectrometric and potentiometric characterizations of these kinds of compounds and stability constants with divalent metal ions.

Stability constants of metals complexes have been determined by many different methods such as spectroscopy[5] and potentiometry.[4] It is well-known that the simplest electroanalytical technique for determination of stability constants is potentiometric titration system used for the glass electrode. SUPERQUAD,[6] a powerful computer program, was used in the evaluation of data obtained from this technique. In the literature, the synthesis of *vic*-dioximes and their various derivatives have been a subject of study for a long period of time.[7] In these studies, it is reported that *vic*-dioximes have three isomers, syn-, anti-, and amphi- forms, depending on the position of –OH groups in molecule.[7–9]

In the present work, we investigated the dissociation constants of 1,2-bis(4-methylpiperazinegl yoxime), (BMPGH2) and 1,2-bis(4-benzylpierazinegly oxime); (BBPGH2) and the stability constants of their complexes with Ni, Cu, Co and Zn potentiometrically and theoretically (AM1 method).

Results and Discussion

Dissociation Constants

The structures of BMPGH2 and BBPGH2 compounds are given in Scheme 1a and 1b. Potentiometric titrations of these compounds with NaOH were performed in 0.1 mol dm^{-3} NaCl at 25 °C. The titration curves of the ligands are given in Figure 1.

Four pK_a values for each protonated ligand have been calculated by SUPERQUAD using titration data (Table 1). pK_a values of the ligands are expected to be similar to each other because of having similar chemical structures, except for benzyl and methyl groups. But, there is a small difference among pK_a values because of different inductive properties of benzyl and methyl groups.

Four protonated species formulated as LH_4, LH_3, LH_2 and LH were observed during titration processes. The species distribution curves of BMPGH2 and BBPGH2 are shown in Figure 2a and 2b.

All species have broad protonation space between pH 2–10 except for LH_2. When pH increases, the protonated ligands lose the protons and convert to the other forms as seen in Figure 2. The concentration levels of LH_4, LH_3, LH and L form above 90%, while LH_2 is 50%. The free ligand (L) starts to form at pH 8 and reaches its maximum at pH 11 (90–95%).

a

1,2-Bis(4-methylpiperazine)glyoxime (BMPGH2)

b

1,2-Bis(4-benzylpiperazine)glyoxime (BBPGH2)
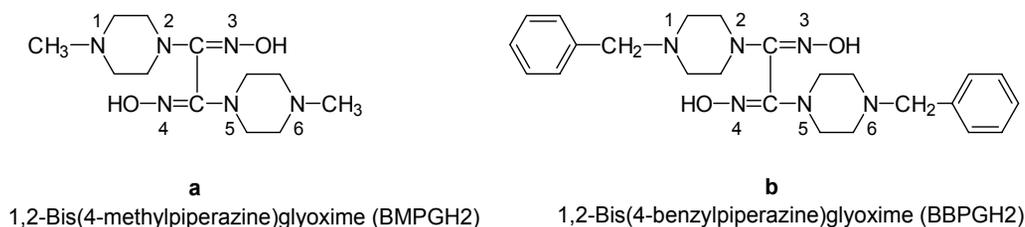
Sheme 1
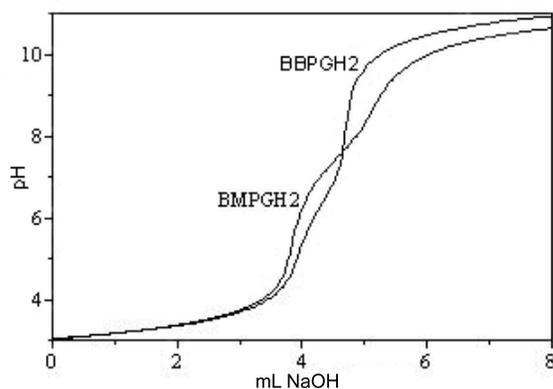
Figure 1. Potentiometric titration curve of the ligands.

Table 1. Dissociation constants (pK_a) of the ligands studied at 25 °C in aqueous NaCl (I = 0.100 mol dm^{-3}).

Ligand	Species	pK_a Values
BMPGH2	LH$_4$	2.91±0.06
	LH$_3$	6.79±0.06
	LH$_2$	7.97 ±0.06
	LH	10.00±0.04
BBPGH2	LH$_4$	3.46±0.03
	LH$_3$	5.89±0.01
	LH$_2$	6.77±0.01
	LH	9.76±0.01
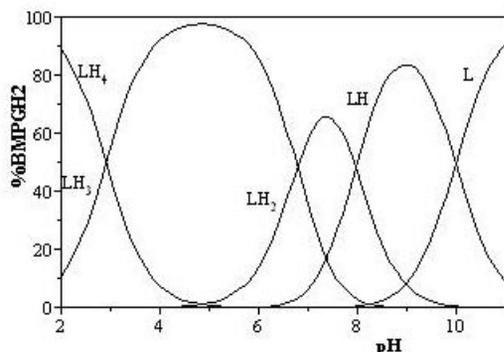
(a)
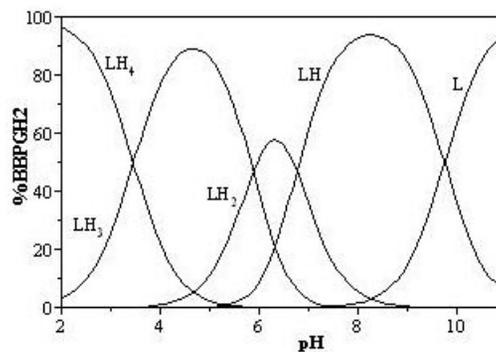
(b)

Figure 2. Distribution curves of a) BMPGH2 and b) BBPGH2.

There are six nitrogens and two hydroxyl groups in the BBPGH2 and the BMPGH2 as seen in Scheme 1. The pK_a values of BMPGH2 (2.91, 6.79, 7.97 and 10.00) and BBPGH2 (3.46, 5.89, 6.77 and 9.76) belong to the nitrogen atoms in the ligands. However, there is no information about pK_a values for hydroxide groups of glyoximes.[10–14]

Theoretical Calculation

The determination of the protonation order of these compounds is not possible with experimental methods such as NMR, IR, and UV. So, in this study, theoretical calculations were done to determine

Table 2. The calculated H$_f$ and TE values with AM1 method for BBPGH2 and BMPGH2 (their monoprotonated forms).

	BMPGH2		BBPGH2	
	Total Energy (kcal/mol)	H$_f$	Total Energy (kcal/mol)	H$_f$
1N-H	–86549.22	190.41	–124512.08	230.13
2N-H	–86546.02	193.61	–124489.75	253.45
3N-H	–86553.30	186.32	–124486.09	257.11

protonation order of nitrogen atoms in the ligands. The formation heats (H$_f$) and the total energies (TE) of various protonated species of ligands were calculated by Semi-Empirical AM1 method and given in Table 2.

Table 3. The calculated H_f and TE values with AM1 method for BMPGH2 and BBPGH2; a) diprotonated forms, b) tri protonated forms and c) four protonated forms.

		BMPGH2			BBPGH2	
		T.E. (kcal/mol)	$\underline{H_f}$		TE (kcal/mol)	$\underline{H_f}$
a)	3N-1N	–86640.87	413.67	1N-2N	–124579.55	478.56
	3N-2N	–86590.83	463.70	1N-3N	–124595.94	462.17
	3N-4N	–86631.59	422.94	1N-4N	–124619.29	438.82
	3N-5N	–86638.75	415.79	1N-5N	–124618.25	439.86
	3N-6N	–86661.84	392.69	1N-6N	–124632.91	425.20
b)	3N-6N-1N	–86709.61	659.83	1N-6N-2N	–124659.37	713.65
	3N-6N-2N	–86647.26	722.18	1N-6N-3N	–124677.35	695.66
	3N-6N-4N	–86664.72	704.72	1N-6N-4N	–124676.42	696.59
	3N-6N-5N	–86660.37	709.08	1N-6N-5N	–124669.36	703.65
c)	3N-6N-1N-2N	–86612.42	1071.92	1N-6N-3N-2N	–124591.41	1096.51
	3N-6N-1N-4N	–86649.00	1035.34	1N-6N-3N-4N	–124625.04	1062.88
	3N-6N-1N-5N	–86657.23	1027.12	1N-6N-3N-5N	–124629.24	1058.68

According to the calculated H_f and TE values, the first protonation of BMPGH2 and BBPGH2 are on 3N and 1N, respectively. It was also determined the protonation orders for the second, third and fourth protonation with H_f and TE values as shown in Table 3.

According to the calculated results, the protonation orders of nitrogen atoms are 3N, 6N, 1N and 5N for BMPGH21N and 1N, 6N, 3N and 5N for BBPGH2. There are differences in these orders due to different inductive effects of benzyl and methyl groups in the ligands.

In conclusion, according to the data obtained from the theoretical calculations, it can be proposed that the pK_a values, 2.91 (LH_4), 6.79 (LH_3), 7.97 (LH_2) and 10.00 (LH) belong to 3N, 6N, 1N and 5N in BMPGH2, respectively. Similarly, 3.46 (LH_4), 5.89 (LH_3), 6.77 (LH_2) and 9.76 (LH) belong to 1N, 6N, 3N and 5N in BBPGH2, respectively.

Stability Constants of Metal Complexes

The complex solutions were titrated with standard NaOH solution to determine the stability constants of complexes formed by divalent metal ions (M) and the ligands (L). The titration curves are given in Figure 3a and 3b. There are two end points in the titration curves. Although the experimental conditions are similar, their end points are different from each other because of the various degree of hydrolysis of the metal ions. When the hydrolysis degree of M is increased, the end point of the complex system shifts to right.[4] The interactions of M with L (1:2) lead to form ML_2 type complexes. The same ratio was found between M and similar ligands in literature.[4,10,14,15]

The data obtained from M-BMPGH2 and BBPGH2 titrations have been evaluated using SUPERQUAD program and the species distribution curves obtained from calculations are given in Figure

4a–4h. Various complexes formulated as MH_6L_2, MH_5L_2, MH_4L_2, MH_3L_2, MH_2L_2, MHL_2, $MH_{-1}L_2$, and $MH_{-2}L_2$ between the ligands and the metal ions are formed depending on pH.

In M-BMPGH2 system, the main complexes for Ni, Cu, Co and Zn are NiH_5L_2, CuH_6L_2 (and CuH_2L_2), CoH_7L_2 (and CoH_2L_2) and ZnH_5L_2 (and ZnL_2) respectively. Their concentration ranges are about 90% except for ZnH_5L_2. Although Co, Zn, and Cu complexes are formed after pH 5, Ni complexes are formed after pH 2. The other intermediate complexes such as MH_3L_2, MH_2L_2 and MHL_2 have also been observed due to smaller titrant additions (0.03–0.04 mL) in the titrations. Intermediate complexes NiH_3L_2, CuH_3L_2 and $CoHL_2$ are at the lowest level (15–20%) between pH 6–9. After pH 8, hydroxide group bound to M ions. Therefore, $M(OH)L_2$ and $M(OH)_2L_2$ complexes formed, as seen in Figure 4. By increasing pH level, one nitrogen is protonated each time and the functional group bound the corresponding metal ions. The protonated mononuclear complexes undergo simple deprotonation reactions at high pH values.

In M-BBPGH2 system, the main complexes were NiH_3L_2, CuH_5L_2 (and CuL_2), CoH_6L_2 and ZnH_6L_2 (and ZnL_2). Their concentration levels were above 80%. The other properties of complex species were similar to M-BMPGH2. However, only Cu complexes exist between pH 3–5 in Cu-BBPGH2.

After obtaining the dissociation constants for BMPGH2 and BBPGH2, overall stability constants have been calculated at the same way. The $\log\beta$ values obtained from these calculations for all M-ligand complexes are given in Table 4. The stability constants of the complexes (ML_2) decrease in the orders of Zn>Ni>Cu>Co for M-BMPGH2 system and Cu>Ni>Zn>Co for M-BBPGH2 system. Stability constants of M-BMPGH2 are higher than those of M-BMPGH2. A comparison of stability constants

Table 4. Stability constant data for the complexation of Cu, Ni, Co and Zn with BMPGH2 and BBPGH2 at 25 °C in aqueous NaCl ($I = 0.100$ mol dm^{-3}) $\beta_{pqr} = [M_pL_qH_r]/[M]^p[L]^q[H]^r$.

Complex	βpqr	Ni	Cu	Co	Zn
M-BMPGH2	102	19.42±0.03	19.21±0.02	19.17±0.02	22.81±0.03
	112	28.77 ±0.02	29.28±0.03	28.16±0.05	31.90 ±0.02
	122	37.47 ±0.06	38.73 ±0.02	38.17±0.02	–
	132	44.84 ±0.07	45.85±0.05	46.31±0.01	48.92±0.02
	142	52.48 ±0.08	53.40±0.02	54.01±0.01	56.57±0.02
	152	58.11 ±0.07	60.32 ±0.02	61.05±0.02	64.04±0.02
	162	60.85 ±0.07	66.28 ±0.02	68.23±0.01	70.13±0.03
	172	–	–	74.07±0.02	73.13±0.02
	1–22	0.37±0.01	–2.08 ±0.01	–1.53±0.03	2.18±0.03
M-BBPGH2	102	18.41±0.03	18.82±0.03	14.47±0.03	17.07±0.04
	112	–	26.18±0.05	–	24.48 ±0.01
	122	36.30 ±0.06	–	32.77±0.06	32.65±0.03
	132	45.42 ±0.03	39.71±0.04	41.37±0.01	48.60±0.04
	142	52.63 ±0.06	46.49±0.05	48.14±0.03	–
	152	58.87 ±0.05	52.21 ±0.05	54.44±0.05	55.64±0.03
	162	64.45 ±0.07	55.72 ±0.07	59.51±0.06	61.50±0.04
	172	67.78 ±0.03	–	–	65.16±0.05
	1–12	8.73±0.02	9.42 ±0.03	3.99±0.04	7.66±0.04
	1–22	–0.66±0.01	–0.88 ±0.02	–5.41±0.02	–2.56±0.03

* *p*: number of metal, *q*: number of hydrogens (positive values) or hydroxides (negative values), *r*: number of ligands in the complex.
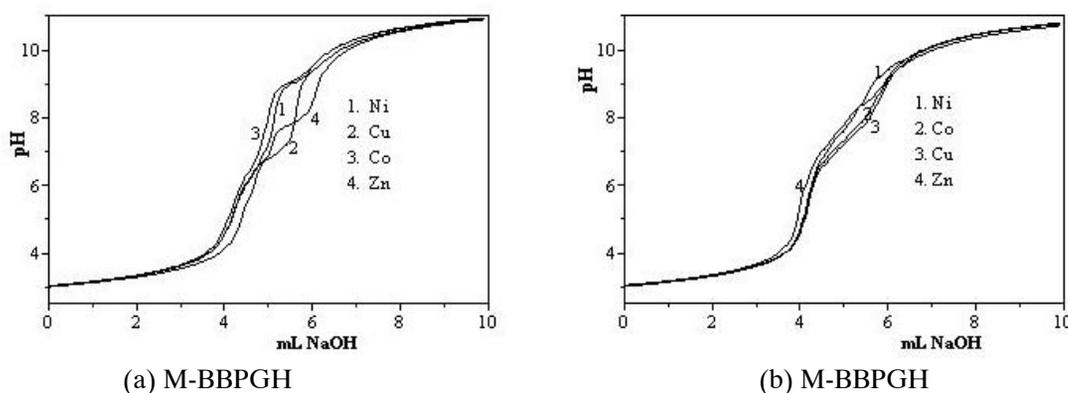
(a) M-BBPGH

(b) M-BBPGH

Figure 3. Titration curves for a) M-BBPGH2 and b) M-BMPGH2.

of the Ni complexes with these two ligands (logβ[Ni-(BMPGH2)$_2$]=19.42, logβ [Ni-(BBPGH)$_2$]=18.41) indicates that the imino groups (=N-OH) in the ligand plays an important role on the stability of mononuclear complex formation.

relatively more stable complexes were formed between M and BMPGH2 in the bases of ML$_2$ species.

Conclusions

The dissociation constant values (pK_a) were determined as 2.91, 6.79, 7.97 and 10.00 for BMPGH2 and 3.46, 5.89, 6.77 and 9.76 for BBPGH2 in acidic medium, respectively. The protonation order of nitrogen atoms in the BMPGH2 and BBPGH$_2$ were determined using Semi-empirical AM1 method. The stability constants of the various complexes from MH$_6$L$_2$ to MH$_{-2}$L$_2$ were calculated using SUPERQUAD. The

Experimental

Reagents

All reagents were of analytical quality and were used without further purification. BBMGH2 and BMPGH2 were synthesised and characterized according to Macit et al.[16] Sodium hydroxide (Merck), potassium hydrogen phthalate (Fluka), were dried at 110 °C before use. HCl, CuCl$_2$, ZnCl$_2$, CoCl$_2$.6H$_2$O and NiCl$_2$.6H$_2$O were purchased from Merck. For the solutions, CO$_2$-free deionized water was obtained with an aquaMAX^{TM}-*Ultra* water purification system (Young Lin Inst.). Its resistivity was 18.2 MΩcm^{-1}.
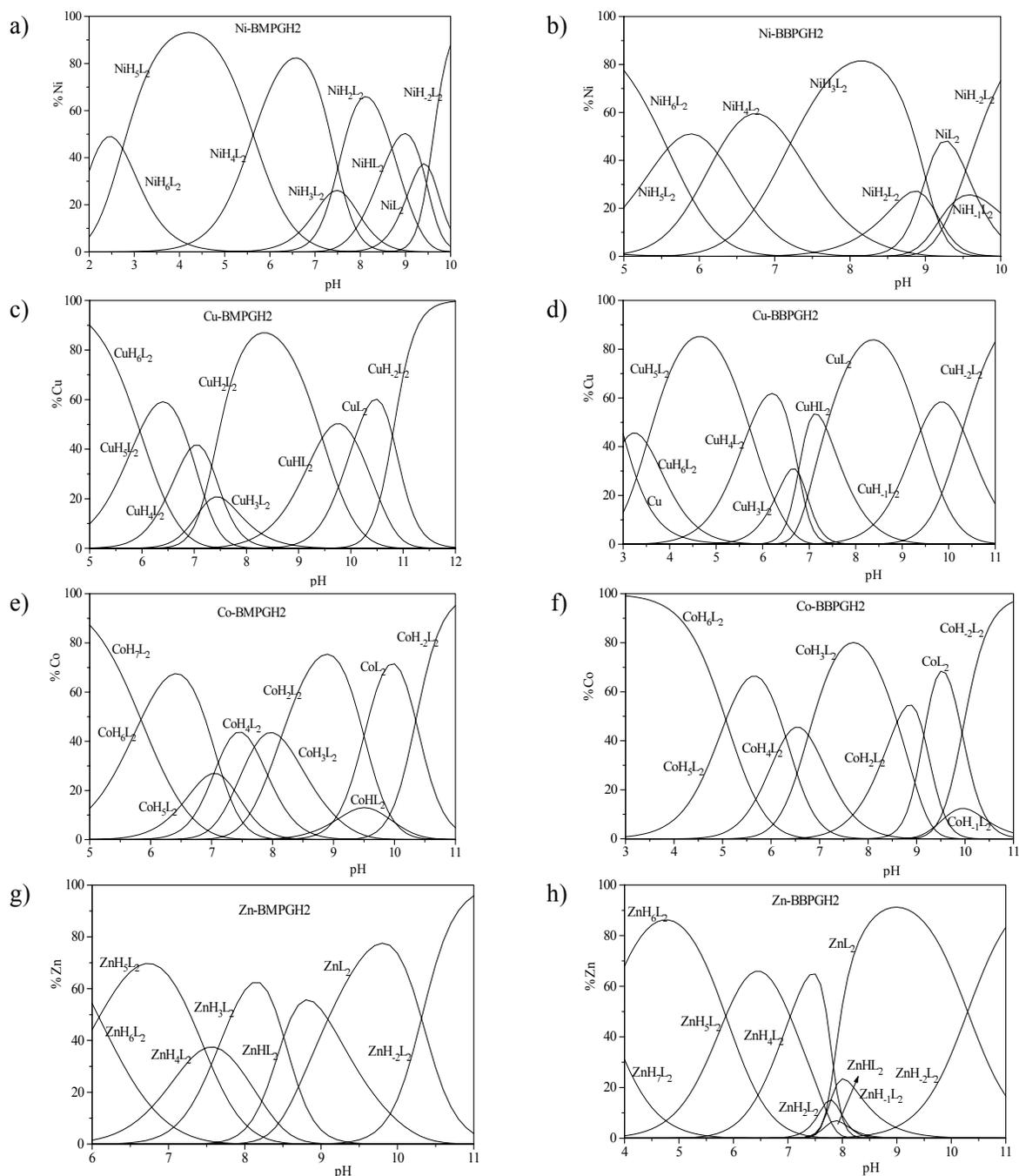
Figure 4. Species distribution curves for the following systems: a) Ni-BMPGH2, b) Ni-BBPGH2, c) Cu-BMPGH2, d) Cu-BBPGH2, e) Co-BMPGH2, f) Co-BBPGH2, g) Zn-BMPGH2 and h) Zn-BBPGH.

Procedure

First, the ligands were dissolved in ethyl alcohol and then the solutions obtained were diluted with deionized water. The final concentration of the ligands was 2.10^{-3} mol dm^{-3} and their final water-ethyl alcohol ratio (v/v) was 96:4. Stock 0.025 mol dm^{-3} sodium hydroxide and 0.1 mol dm^{-3} hydrochloric acid solutions were prepared. Solutions of 0.001 mol dm^{-3} metals ions have been prepared from CuCl$_2$, ZnCl$_2$,

CoCl$_2$.6H$_2$O and NiCl$_2$.6H$_2$O. The ionic strength was adjusted at 0.1 mol dm^{-3} with sodium chloride. The potentiometric titrations were performed using Molspin pH meter™ with a Sentix 20 pH combination electrode (WTW, Weilheim). Temperature was controlled by a thermostat (DIGITERM 100, SELECTA) at 25.0 ± 0.1 °C. The titration vessel is double-wall glass and placed on the magnetic stirrer. It was cleaned with distilled

Table 5. Summary of the experimental parameters for the potentiometric stability constants measurements.

System	BBPGH2 and BMPGH2 with H, Cu, Ni, Co, and Zn in water
Solution composition	[L] range/mol dm^{-3} 0.001–0.002 [M] range/mol dm^{-3} 0.001 ionic strength/mol dm^{-3} 0.1 electrolyte NaCl
Experimental Method	Potentiometric titration in range pH 3–11 log β_{00-1} –13.98
T/°C	25.0
n_{tot}[a]	250
n_{tit}[b]	3
Method of calculation	SUPERQUAD
Titration system	MOLSPIN

[a] Number of titration points per titration. [b] Number of titrations per metal-ligand system. M: Metal ion, L: ligand, β: overall stability constant.

water and dried with a tissue before and after each titration. The vessel was kept closed by the lid, which contained three holes for the electrode, glass tubing for nitrogen purging and plastic tubing for alkali from the burette. The electrode was calibrated according to the instructions in the Molspin manual.[17] Air bubble was not allowed to syringe while filling with alkali solution. Before filling with solution, the syringe was washed several times with distilled water, and rinsed at least three times with the alkali. Titration was performed in triplicate, and the SUPERQUAD computer program[6] was used for calculation of protonation and stability constants. Summary of the experimental parameters for the potentiometric measurements were given in Table 5. Standard deviations quoted refer to random errors only. The pH data (250) were obtained after addition of 0.03 cm^3 increments of standardized NaOH solution. The pK_w values for the aqueous system at the ionic strength employed, defined as –log [H$^+$][OH$^-$], was obtained as 13.98. The theoretical calculations were performed by Semi-empirical(AM1) method.[18–22]

Acknowledgement

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Povzetek

Potenciometrično smo določili konstante disociacije 1,2-bis(4-methilpiperazin)glyoxima (BMPGH2) in 1,2-bis(4-benzilpiperazin)glyoxima (BBPGH2) v 0.1 mol dm^{-3} NaCl in v 0.1 mol dm^{-3} HCl pri 25 °C. Dobljene vrednosti pK_a BMPGH2 in BBPGH2 so 2.91, 6.79, 7.97, 10.00 in 3.46, 5.89, 6.77, 9.76. S semiempirično AM1 metodo smo določili vrstni red protonacije dušikovih atomov v BMPGH2 in v BBPGH2. Ob titraciji liganda z Cu, Co, in Zn ioni pri različnih vrednostih pH v raztopini obstajajo različni kompleksi: MH$_6$L$_2$, MH$_5$L$_2$, MH$_4$L$_2$, MH$_3$L$_2$, MH$_2$L$_2$, MHL$_2$, ML$_2$, MH$_{-1}$L$_2$, in MH$_{-2}$L$_2$.