1007. *Errors Inherent in Competitive Methods of Determining Stability Constants of Mononuclear Complexes.*

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Formation equilibria of co-ordination compounds are often found by means of competitive reactions between the central group under study and another auxiliary species which forms, with the ligand, compounds of known stability. The effects of the errors in the assumed values of the constants of the reference system, and in the measured physical property, on the accuracy of the formation curve of the system under examination are analyzed. Methods are suggested of minimizing the errors.

MUCH attention has been devoted to determination of the stability constants of complexes.[1] The present paper deals with the conditions to be maintained in order to minimize errors. We begin with a study of the propagation of the errors introduced from the various sources into the data, *e.g.*, $\bar{n}$ and pA, used for calculation of the formation constants.

Suppose, for simplicity, that the formation of mononuclear complexes between a metal ion and a basic ligand is being studied by competitive methods, *i.e.*, by introducing in the solution a second cation which forms, with the ligand, complexes of known stability, and Bjerrum's "formation function" [2] is used. Such a method requires: (*a*) a knowledge of the basicity constant(s) of the ligand if the competitive ion is the hydrogen ion, or the stability constant(s) of the complexes formed by the ligand and the competitive metal ion, when a second metal cation is used; (*b*) determination of a physical property (generally pH, or pM if the antagonist ion is the proton or a metal ion) which permits calculation of the concentration of the free ligand; and (*c*) that the formation function may be expressed as follows:

$$\bar{n}_{M'} = \frac{\sum_{1}^{N} n\beta_n[A]^n}{\sum_{0}^{N} \beta_n[A]^n} = \frac{C_A - \dfrac{(C_H - [H^+] + K_{H_2O}[H^+]^{-1})}{\bar{n}_H}}{C_{M'}}, \tag{1}$$

if the antagonist ion is the proton;

or

$$\bar{n}_{M'} = \frac{\sum_{1}^{N} n\beta_n[A]^n}{\sum_{0}^{N} \beta_n[A]^n} = \frac{C_A - \bar{n}_{M''}C_{M''} - [A]}{C_{M'}}, \tag{1a}$$

if the antagonist ion is another metal ion and protonation of the ligand may be neglected because of the acidity of the medium. In expressions (1) and (1a), $\bar{n}_{M'}$ and $\bar{n}_{M''}$ represent the average number of ligands attached to a metal ion of the type under study and to the competitive metal cation, respectively; $\bar{n}_H$ is the average number of hydrogen ions bound to ligand that is not bound to the metal ion examined; [A] and [H$^+$] are the molar concentrations of the free ligand and hydrogen ion, respectively, in the equilibrated solution; C_A, $C_{M''}$, and $C_{M'}$ are the total analytical concentrations of ligand, competitive ion, and metal ion under study, respectively.

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[1] See, *e.g.*, Rossotti and Rossotti, "The Determination of Stability Constants," McGraw-Hill Book Co., Inc., New York, 1961.

[2] Bjerrum, "Metal Ammine Formation in Aqueous Solution," P. Haase and Son, Copenhagen, 1941.

If the ligand is a monoprotonic base and the antagonist ion is the proton, the average number of ligands bound to the central group is:

$$\bar{n}_{\mathrm{M}'} = \left\{C_{\mathrm{A}} - (C_{\mathrm{H}} - [\mathrm{H}^+])\left(1 + \frac{K_{\mathrm{AH}}}{[\mathrm{H}^+]}\right)\right\}\Big/C_{\mathrm{M}'}, \tag{2}$$

and the concentration of the free ligand, expressed as the exponent ligand is:

$$\mathrm{pA} = \mathrm{p}K_{\mathrm{AH}} - \log\{(C_{\mathrm{H}} - [\mathrm{H}^+])/[\mathrm{H}^+]\}. \tag{3}$$

The uncertainties in $\bar{n}_{\mathrm{M}'}$ and pA are related to the uncertainties in the values of the dissociation constant K_{AH} of the protonated ligand and the values of the hydrogen-ion concentration $[\mathrm{H}^+]$. The error in $[\mathrm{H}^+]$ depends both on the error in the experimental measurements and on the error in the preliminary calibration by which the correspondence between e.m.f. and hydrogen-ion concentration was established, for the medium being used. Assuming that the stoicheiometric concentrations are exact and considering $\mathrm{p}K_{\mathrm{AH}}$ and pH as variable instead of K_{AH} and $[\mathrm{H}^+]$, we may write:

$$\mathrm{d}\bar{n}_{\mathrm{M}'} = \left(\frac{\partial\bar{n}_{\mathrm{M}'}}{\partial\mathrm{p}K_{\mathrm{AH}}}\right)_{\mathrm{p}[\mathrm{H}^+]}\mathrm{dp}K_{\mathrm{AH}} + \left(\frac{\partial\bar{n}_{\mathrm{M}'}}{\partial\mathrm{p}[\mathrm{H}^+]}\right)_{\mathrm{p}K_{\mathrm{AH}}}\mathrm{dp}[\mathrm{H}^+]; \tag{4}$$

$$\mathrm{dpA} = \left(\frac{\partial\mathrm{pA}}{\partial\mathrm{p}K_{\mathrm{AH}}}\right)_{\mathrm{p}[\mathrm{H}^+]}\mathrm{dp}K_{\mathrm{AH}} + \left(\frac{\partial\mathrm{pA}}{\partial\mathrm{p}[\mathrm{H}^+]}\right)_{\mathrm{p}K_{\mathrm{AH}}}\mathrm{dp}[\mathrm{H}^+]. \tag{5}$$

By differentiation of equations (2) and (3) successively with respect to K_{AH} and $[\mathrm{H}^+]$ and transformation to the variables $\mathrm{p}K_{\mathrm{AH}}$ and $\mathrm{p}[\mathrm{H}^+]$, the following expressions for the respective finite changes are obtained:

$$(\Delta\bar{n}_{\mathrm{M}'})_{[\mathrm{H}^+]} = \frac{2{\cdot}303K_{\mathrm{AH}}}{C_{\mathrm{M}'}}\left(\frac{C_{\mathrm{H}} - [\mathrm{H}^+]}{[\mathrm{H}^+]}\right)\Delta\mathrm{p}K_{\mathrm{AH}} \tag{6}$$

$$= \frac{2{\cdot}303[\mathrm{A}]}{C_{\mathrm{M}'}}\Delta\mathrm{p}K_{\mathrm{AH}} \tag{6a}$$

$$(\Delta\bar{n}_{\mathrm{M}'})K_{\mathrm{AH}} = -\frac{2{\cdot}303}{C_{\mathrm{M}'}}\left[\frac{C_{\mathrm{H}}\,.\,K_{\mathrm{AH}} + [\mathrm{H}^+]^2}{[\mathrm{H}^+]}\right]\Delta\mathrm{p}[\mathrm{H}^+] \tag{7}$$

$$= -\frac{2{\cdot}303}{C_{\mathrm{M}'}}\left(K_{\mathrm{AH}} + [\mathrm{A}] + \frac{C_{\mathrm{H}}\,.\,K_{\mathrm{AH}}}{K_{\mathrm{AH}} + [\mathrm{A}]}\right)\Delta\mathrm{p}[\mathrm{H}^+] \tag{7a}$$

$$(\Delta\mathrm{pA})_{[\mathrm{H}^+]} = \Delta\mathrm{p}K_{\mathrm{AH}}. \tag{8}$$

$$(\Delta\mathrm{pA})K_{\mathrm{AH}} = -\frac{C_{\mathrm{H}}}{C_{\mathrm{H}} - [\mathrm{H}^+]}\Delta\mathrm{p}[\mathrm{H}^+] \tag{9}$$

$$= -\frac{K_{\mathrm{AH}} + [\mathrm{A}]}{[\mathrm{A}]}\Delta\mathrm{p}[\mathrm{H}^+]. \tag{9a}$$

The error $\Delta\mathrm{p}[\mathrm{H}^+]$ is casual, while $\Delta\mathrm{p}K_{\mathrm{AH}}$ is systematic and may have a larger and less controllable effect on the values of the data necessary for the computation of the stability constants.

As an example, in Fig. 1 are reported plots of the functions (6), (7), and (9) against pA. Constant parameters are: $\Delta\mathrm{p}K_{\mathrm{AH}}$ and $C_{\mathrm{M}'}$ (part I); C_{H}, $C_{\mathrm{M}'}$, K_{AH}, and $\Delta\mathrm{p}[\mathrm{H}^+]$ (part II); $\mathrm{p}K_{\mathrm{AH}}$ (part III).

Equation (6) shows that $\Delta\bar{n}_{\mathrm{M}'} < \Delta\mathrm{p}K_{\mathrm{AH}}$ for all values of $C_{\mathrm{M}'} > 2{\cdot}303[\mathrm{A}]$, but increases rapidly when $C_{\mathrm{M}'} < 2{\cdot}303[\mathrm{A}]$. From the curves of the part I, obtained by assuming $|\Delta\mathrm{p}K_{\mathrm{AH}}| = 0{\cdot}01$, it is evident that for $C_{\mathrm{M}'} = 10^{-3}\mathrm{M}$ good determinations of $\bar{n}_{\mathrm{M}'}$ are possible when $pA > 3$, but that when $pA < 3$ a higher concentration of the salt of the metal is necessary to yield reliable results.

The behaviour of the function $|\Delta n_{M'}|_{K_{AH}} = f(pA)$ is more complex if one considers the effect of an error in the $p[H^+]$ value on the value of $\bar{n}_M$, as a function of the pA value. In this case it is necessary to take simultaneously into account the values of C_H, $C_{M'}$, K_{AH}, and $\Delta p[H^+]$. In part II of Fig. 1 are shown two cases: the pK_{AH} of the ligand is 6 (solid curves a and c) or 3 (broken curves b and d), while the $C_{H'}$'s are 10^{-3}M (curves a, b) and 10^{-2}M (curves c, d); $|\Delta p[H^+]|$ is 0·01 and $C_{M'}$ is 10^{-3}M. From the examination of these curves it may be deduced that, for complexes whose formation curve extends beyond $pA = 3$ it is convenint to use, when possible, a low concentration of mineral acid, and the choice of $C_{M'}$ is not very important; for $pA < 3$, in order to obtain reliable results, rather high concentrations of the metal salt must be used while the value of C_H is not very important. For $[A] \gg K_{AH}$ the coefficient of $\Delta p[H^+]$ of equation (7a) becomes $-2{\cdot}303[A]/C_{M'}$; and, therefore, $[A]/C_{M'} < 1$ is a condition to be fulfilled in order to get good values of $\bar{n}_{M'}$. If $[A] \ll K_{AH}$ the coefficient of $\Delta p(H^+)$ becomes $-2{\cdot}303(K_{AH^+} + C_H)/C_{M'}$; and for $K_{AH} < C_H$ it is necessary to use solutions with $C_H/C_{M'}$ not exceeding unity.

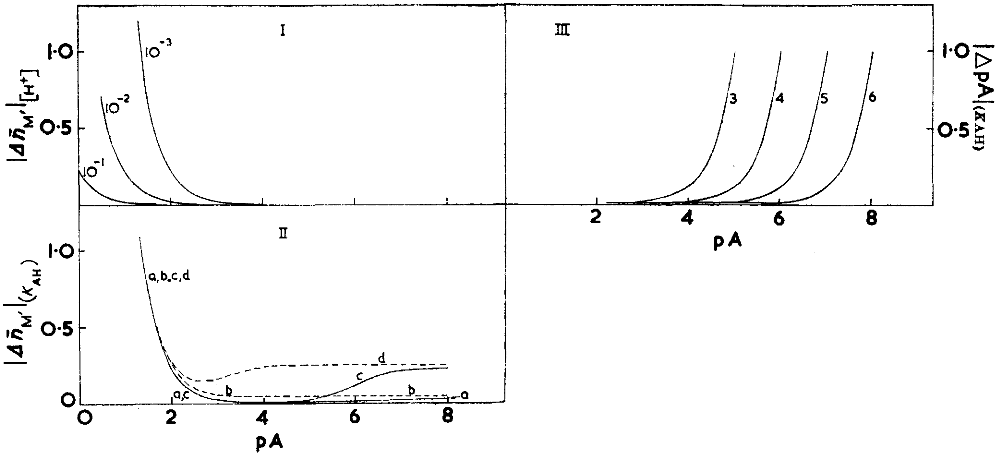

FIG. 1. Shape of the functions: (I) $|\Delta\bar{n}_{M'}|_{[H^+]} = f(pA)$ for $|\Delta pK_{AH}| = 0{\cdot}01$, numerals on the curves indicating the values (M) of $C_{M'}$; (II) $|\Delta\bar{n}_{M'}|_{(K_{AH})} = f(pA)$ for $|\Delta p[H^+]| = 0{\cdot}01$ and $C_{M'} = 10^{-3}$M, with (a) $pK_{AH} = 6$, $C_H = 10^{-3}$M, (b) $pK_{AH} = 3$, $C_H = 10^{-3}$M, (c) $pK_{AH} = 6$, $C_H = 10^{-2}$M, and (d) $pK_A = 3$, $C_H = 10^{-2}$M; and (III) $|\Delta pA|_{(K_{AH})} = f(pA)$ for $|\Delta p[H^+]| = 0{\cdot}01$, the numerals on the curves indicating pK_{AH}.

Finally, from the curves of the part III (Fig. 1) it follows that a pA value of the same order of magnitude as $(pK_{AH} + 1)$ is a rather sharp upper limit to the range of application of the pH-metric technique to the study of mononuclear complexes between metal ions and monoprotonic basic ligands, because of the way in which an error in $p[H^+]$ affects the pA value. This source of error cannot be reduced because (i) $\Delta pA = f(\Delta p[H^+])$ is independent of the composition of the medium and (ii) the uncertainty in $p[H^+]$ is hardly less than 0·01.

To conclude: the pH-metric method is suitable when the useful part of the formation curve lies at $pA < pK_{AH}$; however, when $pA \ll pK_{AH}$, a concentration $C_{M'} > 2{\cdot}303[A]$ must be used. It is anyway very likely that, at small values of pA, the representative points in the ($\bar{n}_{M'}$–pA) plane will be rather scattered as a consequence of the casual errors in the $p[H^+]$ measurements, even if one works with a high concentration of metal salt and has reason to believe that the acid constant of the reference system is accurately known. This is due to the very critical dependence of $\bar{n}_{M'}$ on $\Delta p[H^+]$ and ΔpK_{AH}. Because of this, the values of pA at half-values of $\bar{n}_{M'}$ cannot be taken as zero-order values of the logarithms of the formation constants to be used in an iterative procedure, and one cannot reliably deduce the types of complexes which may be formed by inspecting the formation curve alone. This is true especially in cases in which a shift of the formation curve itself with the change of the total concentration of metal ion is observed.*

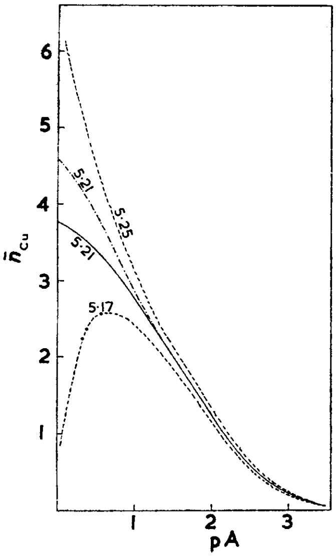

FIG. 2.

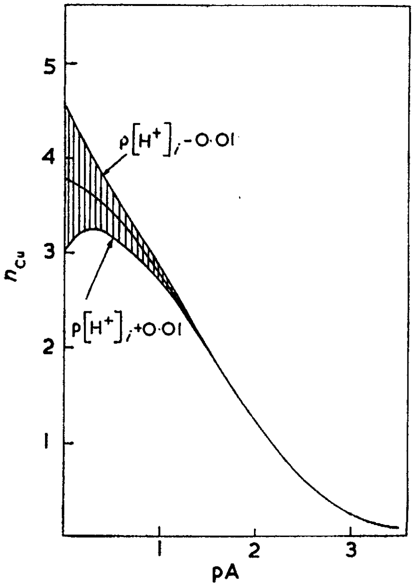

FIG. 3.

FIG. 2. Formation curves of copper (II)–pyridine complexes.

——, Calc. by using $\log \beta_1 = 2{\cdot}41$, $\log \beta_2 = 4{\cdot}29$, $\log \beta_3 = 5{\cdot}43$, and $\log \beta_4 = 6{\cdot}03$ (ref. 4). — • — • —, Calc. by using these values for $\log \beta_1, \ldots, \log \beta_4$, and $\log \beta_5 = 6{\cdot}43$. – – –, Two representative curves obtained by assuming (a) for C_H and C_{Cu} the values 0·1M and 0·03M used by Bruhelman *et al.*,[3] (b) for $[H^+]$ the values derived as stated in the text, (c) for C_A the values calculated from equation (2) and, for each pA value the $\bar{n}_{Cu}$ value obtained from the general expression for $\bar{n}$ [left-hand part of equation (1)] with the above values for $\beta_1, \ldots, \beta_4$.

Figures on the curves indicate pK_{AH}. For pK_{AH} of the pyridinium ion at 25° the following values have been reported: 5·18 (Murman and Basolo, *J. Amer. Chem. Soc.*, 1955, **77**, 3485); 5·17 (Brown and Mihm, *ibid.*, p. 1723); 5·25 (Linnel, *J. Org. Chem.*, 1960, **25**, 290); 5·12 (at 20°) Hughes, Jellinek, and Ambrose, *J. Phys. Chem.*, 1949, **53**, 410); 5·16 (at 20°) (Albert, Goldacre, and Phillips, *J.*, 1948, 2240). For concentration function $pK^c{}_{AH}$ (at 25°) values reported are: 5·21 (ref. 4); 5·45 (ref. 3); 5·51 (ref. 5); 5·29 (solution 0·04M) (Jaffé and Doak, *J. Amer. Chem. Soc.*, 1955, **77**, 4441); 5·23 (solution 0·016M) (Albert *et al.*, *loc. cit.*). Other data, calculated by the approximation $pK_{AH} = pH$ at half-neutralization, lack precise meaning.

FIG. 3. The central curve is the formation curve of copper(II)–pyridine drawn with the constants: $\log \beta_1 = 2{\cdot}41$, $\log \beta_2 = 4{\cdot}29$, $\log \beta_3 = 5{\cdot}43$, $\log \beta_4 = 6{\cdot}03$.[4] The shaded area indicates the zone within which the experimental points would fall if obtained under the following conditions: $C_H = 0{\cdot}1M$, $C_{Cu} = 0{\cdot}03M$ (refs. 3, 5), and $pK_{AH} = 5{\cdot}21$. ΔpK_{AH} is assumed to be zero and the error in the $p[H^+]$ measurements $\pm 0{\cdot}01$.

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* Examination of the curves ($n_{M'}$–pA) at different concentrations of metal salt may be still useful, even in case of unfavourable condition ($pA \ll pK_{AH}$) as a very sensitive, though indirect, test of the accuracy of the value of the acidity constant of the ligand. The requirements are, of course, that all complexes which are formed are mononuclear and that their formation proceeds up to a well-defined co-ordination number.

Let us consider, for example, the copper(II)-pyridine complexes, whose stability constants were determined by Bruhelman and Verhoek[3] by pH-metric measurements, by Bjerrum and Nielsen[4] by spectrophotometric measurements, and by Leussig and Hansen[5] by distribution and pH-metric measurements (see Table). According to Bruhelman and Bjerrum the cupric ion may co-ordinate with up to four molecules of pyridine, and according to Leussing and Hansen may exist also a complex with five ligand molecules.

The formation curve of this system calculated by using Bjerrum's data has the form shown by the solid line in Fig. 2. For the same values of the hydrogen-ion concentration (calculated for each pA by assuming $pK_{AH} = 5{\cdot}21$ and $C_H = 0{\cdot}1$M) with slightly different pK_{AH} values one obtains the broken curves in Fig. 2. We may then conclude that, if several authors had found the same pH values for solutions with the same concentrations of mineral acid, cupric salt, pyridine, and inert salt, but had used different values for the acid dissociation constant of the ligand in obtaining the data necessary to draw the formation curve, they would have been led to different conclusions about the characteristics of this system.

Stability constants for copper(II)-pyridine complexes.

pK_{AH}	$\log k_1$	$\log k_2$	$\log k_3$	$\log k_4$	$\log k_5$	Medium	Ref.
5·45	2·52	1·86	1·31	0·85	—	H_2O; 0·5M-KNO_3; 25°	3
5·21	2·41	1·88	1·14	0·60	—	H_2O; 0·5M-pyridine-HNO_3; 25°	4
5·51	2·59	1·74	1·60	0·61	0·41	H_2O; 0·99M-KNO_3; 25°	5

The effect of an error of $\pm 0{\cdot}01$ in $p[H^+]$ is evident from Fig. 3. At $C_{Cu} = 0{\cdot}03$M, small errors in the potentiometric determination of the hydrogen-ion concentration in the solution have practically no effect so long as pA is greater than 1·6; but when pA becomes less than 1 it is almost impossible to obtain reproducible data unless the concentration of the cupric salt is much higher. In these conditions the effect of an error in pK_{AH} (Fig. 2) is much more serious. In fact, the effect of the errors in $p[H^+]$ can be reduced by making a large number of measurements and drawing the curve in such way that the algebraic sum of the deviations is as low as possible,* but, on the other hand, the systematic character of the error in pK_{AH} may considerably affect the values of the β_i, especially if the error is small and does not have very apparent effects. In Fig. 2 the dot-dashed curve is the "formation curve" calculated with the values of β_i given by Bjerrum and $\log k_5 = 0{\cdot}4$ (*i.e.*, $\log \beta_5 = 6{\cdot}03 + 0{\cdot}4 = 6{\cdot}43$). The deviation of this curve from that calculated by use of only the four values of the β_i's given by Bjerrum is less than that due to $\Delta pK_{AH} = +0{\cdot}04$. Therefore, if there are no other experimental data supporting the hypothesis of the formation of a quinqueco-ordinated complex, this cannot be deduced on the basis of the "best formation curve" only, nor, of course, can its stability constant be given.

The argument about the use of pH-metric measurements is substantially valid also for the case that instead of the proton the antagonist ion is a different metal ion M″ which forms with the ligand a number N of complexes of known stability constants.

Let $C_{M'}$ and $C_{M''}$ be the total stoicheiometric concentrations of the metal salt under examination and of the reference metal salt, and let [M″] be the molar concentration of the free antagonist ion, as determined potentiometrically. A criterion for the evaluation of

* In effect this procedure is not correct and it has been observed[6] that to draw a smoothed curve through a set of data can lead to erroneous results when the data have intermediate accuracy.

[3] Bruhelman and Verhoek, *J. Amer. Chem. Soc.*, 1948, **70**, 1401.

[4] Bjerrum and Nielsen, *Acta Chem. Scand.*, 1948, **2**, 297; Bjerrum, *Chem. Rev.*, 1950, **46**, 381.

[5] Leussig and Hansen, *J. Amer. Chem. Soc.*, 1957, **79**, 4270.

[6] Sillén, *Acta Chem. Scand.*, 1956, **10**, 186.

the propagation of the errors is supplied by examining the dependence, on each variable, of the functions:

$$\Delta \mathrm{pA} = \mathrm{f}_1(\Delta \mathrm{pM}'', \Delta \log \beta_1, \Delta \log \beta_2, \ldots\ldots, \Delta \log \beta_n);$$

$$\Delta \bar{n}_{\mathrm{M}'} = \mathrm{f}_2(\Delta \mathrm{pM}'', \Delta \log \beta_1, \Delta \log \beta_2, \ldots\ldots, \Delta \log \beta_n);$$

which can be obtained by differentiating:

$$C_{\mathrm{M}''} = [\mathrm{M}''] + [\mathrm{M}''\mathrm{A}] + [\mathrm{M}''\mathrm{A}_2] + \ldots\ldots + [\mathrm{M}''\mathrm{A}_N] = [\mathrm{M}'']\left(1 + \sum_1^N \beta_n[\mathrm{A}]^n\right)$$

and
$$\bar{n}_{\mathrm{M}'} = \left(C_{\mathrm{A}} - \sum_1^N n\beta_n[\mathrm{M}''][\mathrm{A}]^n - [\mathrm{A}]\right)/C_{\mathrm{M}'}$$

successively with respect to β_1, β_2, ..., β_n, and $[\mathrm{M}'']$; one then proceeds as already described for the system H^+–M′–ligand.

From the equations that may be obtained in this way it follows that the uncertainty $|\Delta \mathrm{pA}|_{[\mathrm{M}'']}$ is of little practical importance at any value of pA, while the uncertainty $|\Delta \mathrm{pA}|_{\beta_1, \beta_2, \cdots, \beta_n}$ limits the applicability of the method to pA values $<(\log \beta_1 + 1)$ if $\Delta \mathrm{pM}'' = 0{\cdot}01$. The representative curves of the functions $(\Delta \mathrm{pA})_{\beta_1, \beta_2, \cdots, \beta_n} = \mathrm{f(pA)}$ are almost identical with the curves reported in part III of Fig. 1 if $\log \beta_1$ is taken as constant parameter instead of $\mathrm{p}K_{\mathrm{AH}}$. However, the range of useful measurements may, in this instance, be extended by using metal electrodes capable of a better accuracy than is normally achieved by the glass electrode and the other pH-measuring electrodes.

The relations giving the effect of errors in $\log \beta_1$ and pM″ on the values of $\bar{n}_{\mathrm{M}'}$ are more complex and the representative curves of equations of the type $(\Delta \bar{n}_{\mathrm{M}'})_{(\mathrm{M}''), \beta_1, \beta_2, \cdots, \beta_n} = \mathrm{f}(\Delta \log \beta_i)$ and $(\Delta \bar{n}_{\mathrm{M}'})_{\beta_1, \beta_2, \cdots, \beta_n} = \mathrm{f}(\Delta \mathrm{pM}'')$ may take different forms depending on the values of the β_i's of the reference system and on the composition of the solutions. However, the form of the equations suggests that, as a general rule, to reduce the error in $\bar{n}_{\mathrm{M}'}$ it is useful to use low concentrations of the salt of the reference metal and high concentrations of the salt of the metal under examination. This is indispensable when the range to be examined is at $\mathrm{pA} < 2{\cdot}5$. When formation of polynuclear species can be excluded, from examination of the curves of the propagation of the errors, it follows that, in general, it is more correct to increase the concentration of metal salt under study while the pA value is decreasing instead of taking data covering the whole formation curve at one metal concentration only.

Morcillo *et al.*[7] have studied the optimum concentrations for determination of the equilibrium constants; others[8] have defined the limits of the competitive method. Our examination of the propagation of the errors, *e.g.*, in $\mathrm{p}K_{\mathrm{AH}}$, emphasizes the caution with which experimental data collected in unfavourable conditions, must be treated, and the need, in such cases to examine the system by various methods.

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[7] Morcillo, Gallego, and Biorge, *Anales real. Soc. españ. Fís. Quím.*, 1958, **54**, 325; Bjerrum, "Metal Ammine Formation in Aqueous Solution," P. Haase and Son, Copenhagen, 1941, pp. 21, 22, 28.

[8] Ref. 2, pp. 21, 22, 28; also Rossotti and Rossotti, "The Determination of Stability Constants," McGraw-Hill, New York, 1961, p. 61.