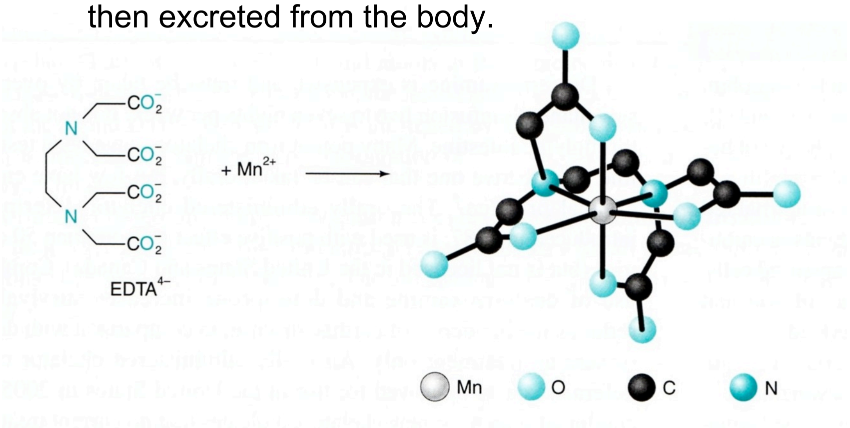
Chelation therapy

Calcium-disodium EDTA is approved for the removal of lead by the Food and Drug Administration (FDA). The drug bind to heavy metals in the body and prevent them from binding to other agents. They are then excreted from the body.



Metal-Chelate Complexes (Sec. 11-1)

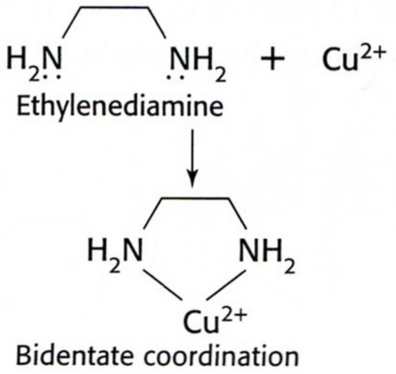
metal		chelating ligand (ligand, chelate)		metal-complex (Ag-complex)
Ag^+	+	$2\ :\bar{C}{\equiv}N:$	$\rightleftharpoons$	$(:N{\equiv}C{-}Ag{-}C{\equiv}N:)^-$
Lewis acid (electron pair acceptor)		Lewis base (electron pair donor)		Complex ion

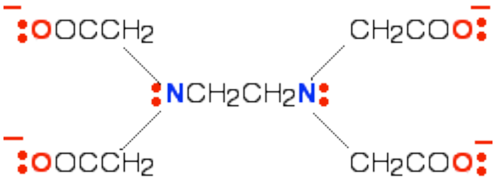
Coordination number, n, describes the number of sites on the metal ion that form a complex. Typical values are 4 and 6, with 7 or 8 being much less common.

Ligand - ion or molecule that forms a complex with the metal ion by donating a pair of electrons. Examples - NH_3, H_2O, CN^-, Cl^-, I^-, SCN^-, $H_2NCH_2CH_2NH_2$, R-COOH,

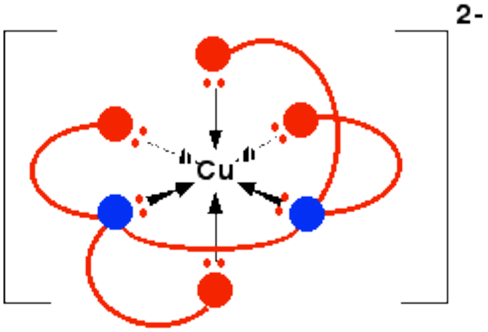
Monodentate
One electron donor atom per ligand
e.g. NH_3, Cl^-

Polydentate
More than one donor atom per ligand
Fewer ligands needed to complex the metal
eg. Ethylene diammine $H_2NCH_2CH_2NH_2$ (en)
Ethylenediamminetetraacetic acid (EDTA)





the EDTA^{4-} ion



the [Cu(EDTA)]$^{2-}$ ion

Chelate effect – single multidentate ligand forms a more stable metal metal complex that are more stable than those formed by several individual ligands with the same ligand atom.

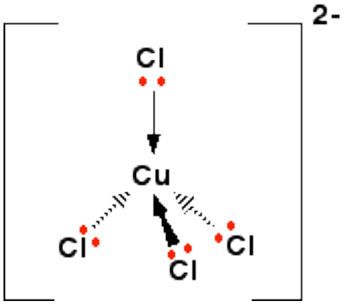
Examples:

$$Cd(H_2O)_6^{2+} + 4\ (CH_3)_2NH \rightleftharpoons Cd\ (H_2O)_2((CH_3)_2NH)_4^{2+} + 4\ H_2O \qquad \beta_4 = 3\times10^6$$

$$Cd(H_2O)_6^{2+} + 2\ en \rightleftharpoons Cd\ (H_2O)_2(en)_2^{2+} + 4\ H_2O \qquad \beta_2 = 2\times10^{10}$$

Water typically not shown, and not used in calculation.
Chelate effect is driven by entropy effects.

Complex Equilibria



Stepwise formation constants:

$M+L \leftrightarrows ML \qquad K_{f1}=[ML] / ([M][L])$

$ML +L \leftrightarrows ML_2 \qquad K_{f2}=[ML_2] / ([ML][L])$

$ML_2+L \leftrightarrows ML_3 \qquad K_{f3}=[ML_3] / ([ML_2][L])$

$ML_3+L \leftrightarrows ML_4 \qquad K_{f4}=[ML_4] / ([ML_3][L])$

Cumulative formation constants

$M+L \leftrightarrows ML \qquad \beta_1= K_{f1}$

$M +2L \leftrightarrows ML_2 \qquad \beta_2 = [ML_2]/([M][L]^2)=K_{f1}K_{f2}$

$M +3L \leftrightarrows ML_3 \qquad \beta_3 = [ML_3]/([M][L]^3)=K_{f1}K_{f2}K_{f3}$

$M +4L \leftrightarrows ML_4 \qquad \beta_4 = [ML_4]/([M][L]^4) = K_{f1}K_{f2}K_{f3}K_{f4}$

Formation Constant or stability constant (K_f) - constant for equilibrium between metal and ligands to form metal ligand complex.

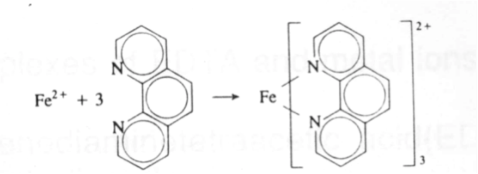
$$K_f = \frac{\left[Cd\left((CH_3)_2NH\right)_4^{2+}\right]}{[Cd^{2+}]\left[(CH_3)_2NH\right]^4} \qquad K_f = \frac{\left[Cd(en)_2^{2+}\right]}{[Cd^{2+}][en]^2}$$

Analytical Uses of Coordination Compounds

(1) Formation of colored substances

The formation of a colored compound can be used to indicate the presence of a specific metal ion and/or determine its concentration in a sample.

calcium titration



colorless red

2) Chemical masking

A masking agent decreases the concentration of a free metal ion to a level where a particular interfering reaction will not occur.

e.g., Cu^{2+} and I^- titration reaction can be interfered by Fe^{3+}. The addition of F^- will eliminate the interference.

$Fe^{3+} + 6\ F^- \rightarrow FeF_6^{3-}$
$FeF_6^{3-} + I^- \rightarrow$ no reaction

(3) Titrating metal ions

Multidentate ligands are exceptionally useful titrants for metal ions.

The titration of metal ions with monodentate ligands is not very successful. (indistinct multi-step endpoints; weak titration reaction)

e.g., EDTA is a hexadentate ligand.
- exists in 7 protonated forms
H_6Y^{2+} , H_5Y^+ , H_4Y , H_3Y^- , H_2Y^{2-} , HY^{3-} , and Y^{4-}

Advantages of EDTA over other multidentate ligands:

- complex stoichiometry of is 1:1;
- large K_f for most metals
- fast complexation kinetics for most metals
- selectivity controlled by pH
- $Na_2H_2Y{\cdot}2H_2O$, a reagent of high solubility, is considered as a good primary standard
- reliable methods for determining the end point
- metal-EDTA complexes are very soluble in water

EDTA Complexes (Sec. 11-2)

- Fractional composition equations are important for EDTA complex equilibria.

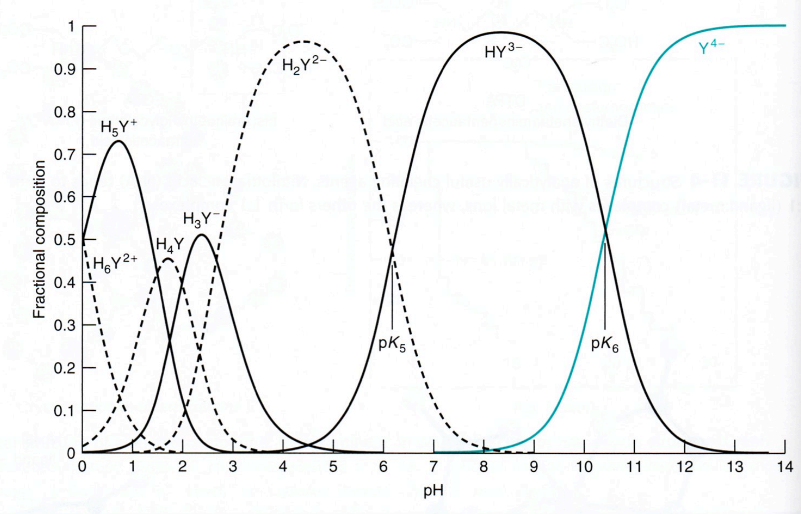


FIGURE 11-7 Fractional composition diagram for EDTA.

Taking the fully deprotonated form, Y^{4-}:

$$M^{x+} + Y^{4-} \rightleftharpoons MY^{x-4} \qquad K_f = \frac{[MY^{x-4}]}{[M^{x+}][Y^{4-}]} \quad \text{(formation constant)}$$

$$\alpha_{Y^{4-}} = \frac{[Y^{4-}]}{[\text{EDTA}]} \quad \text{or} \quad \alpha_{Y^{4-}} = \frac{[Y^{4-}]}{F_{\text{EDTA}}}$$

(Eqn. 11-4)

$$\alpha_{Y^{4-}} = \frac{K_1K_2K_3K_4K_5K_6}{[H^+]^6 + [H^+]^5K_1 + [H^+]^4K_1K_2 + [H^+]^3K_1K_2K_3 + [H^+]^2K_1K_2K_3K_4 + [H^+]K_1K_2K_3K_4K_5 + K_1K_2K_3K_4K_5K_6}$$

Most EDTA is not Y^{4-} below pH 10.4.
Instead we express $[Y^{4-}]$ as:

$$[Y^{4-}] = \alpha_{Y^{4-}}[\text{EDTA}]$$

$$K_f = \frac{[MY^{x-4}]}{[M^{x+}]\alpha_{Y^{4-}}[\text{EDTA}]}$$

$$K'_f = \alpha_{Y^{4-}}K_f = \frac{[MY^{x-4}]}{[M^{x+}][\text{EDTA}]}$$

TABLE 11-1 Values of $\alpha_{Y^{4-}}$ for EDTA at 25°C and $\mu = 0.10$ M

pH	$\alpha_{Y^{4-}}$
0	1.3×10^{-23}
1	1.4×10^{-18}
2	2.6×10^{-14}
3	2.1×10^{-11}
4	3.0×10^{-9}
5	2.9×10^{-7}
6	1.8×10^{-5}
7	3.8×10^{-4}
8	4.2×10^{-3}
9	0.041
10	0.30
11	0.81
12	0.98
13	1.00
14	1.00

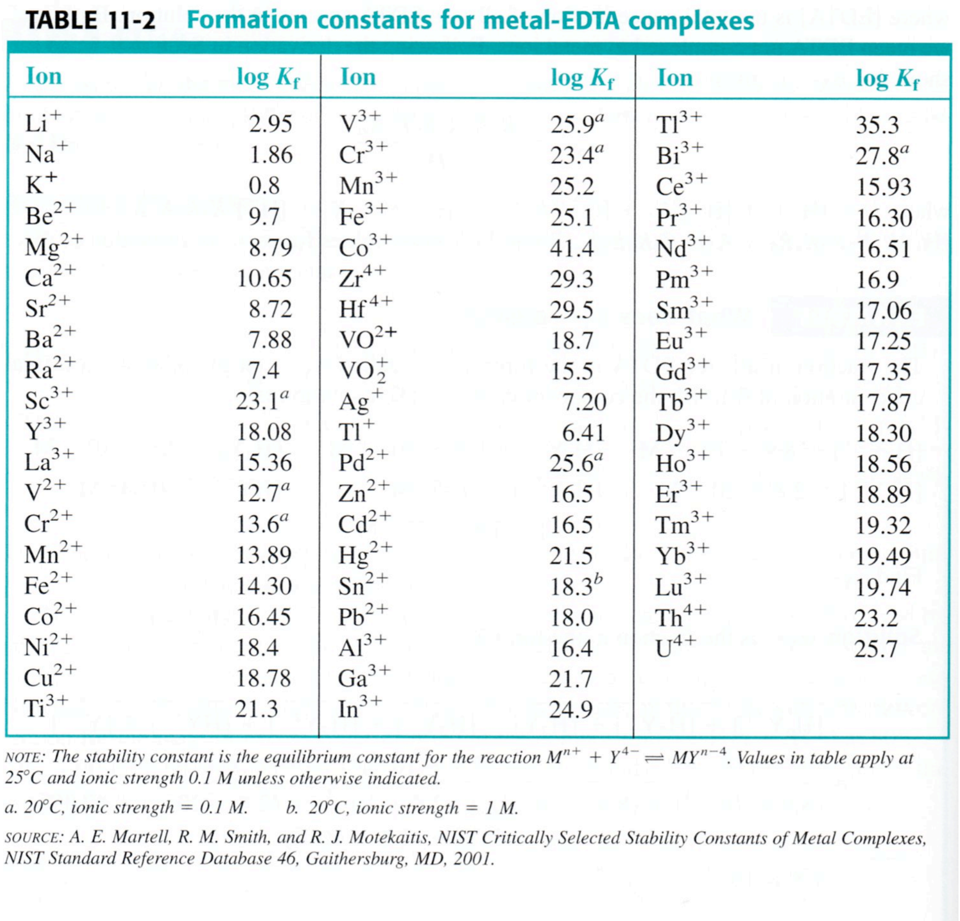


TABLE 11-2 Formation constants for metal-EDTA complexes

Ion	log K_f	Ion	log K_f	Ion	log K_f
Li^+	2.95	V^{3+}	25.9^a	Tl^{3+}	35.3
Na^+	1.86	Cr^{3+}	23.4^a	Bi^{3+}	27.8^a
K^+	0.8	Mn^{3+}	25.2	Ce^{3+}	15.93
Be^{2+}	9.7	Fe^{3+}	25.1	Pr^{3+}	16.30
Mg^{2+}	8.79	Co^{3+}	41.4	Nd^{3+}	16.51
Ca^{2+}	10.65	Zr^{4+}	29.3	Pm^{3+}	16.9
Sr^{2+}	8.72	Hf^{4+}	29.5	Sm^{3+}	17.06
Ba^{2+}	7.88	VO^{2+}	18.7	Eu^{3+}	17.25
Ra^{2+}	7.4	VO_2^+	15.5	Gd^{3+}	17.35
Sc^{3+}	23.1^a	Ag^+	7.20	Tb^{3+}	17.87
Y^{3+}	18.08	Tl^+	6.41	Dy^{3+}	18.30
La^{3+}	15.36	Pd^{2+}	25.6^a	Ho^{3+}	18.56
V^{2+}	12.7^a	Zn^{2+}	16.5	Er^{3+}	18.89
Cr^{2+}	13.6^a	Cd^{2+}	16.5	Tm^{3+}	19.32
Mn^{2+}	13.89	Hg^{2+}	21.5	Yb^{3+}	19.49
Fe^{2+}	14.30	Sn^{2+}	18.3^b	Lu^{3+}	19.74
Co^{2+}	16.45	Pb^{2+}	18.0	Th^{4+}	23.2
Ni^{2+}	18.4	Al^{3+}	16.4	U^{4+}	25.7
Cu^{2+}	18.78	Ga^{3+}	21.7		
Ti^{3+}	21.3	In^{3+}	24.9		

NOTE: The stability constant is the equilibrium constant for the reaction $M^{n+} + Y^{4-} \rightleftharpoons MY^{n-4}$. *Values in table apply at 25°C and ionic strength 0.1 M unless otherwise indicated.*

a. 20°C, ionic strength = 0.1 M. b. 20°C, ionic strength = 1 M.

SOURCE: A. E. Martell, R. M. Smith, and R. J. Motekaitis, NIST Critically Selected Stability Constants of Metal Complexes, NIST Standard Reference Database 46, Gaithersburg, MD, 2001.

Example: The formation constant for FeY^- is 1.3×10^{25}. Calc the conc of free Fe^{3+} in solutions of 0.10 M FeY^- at pH 8.00 and at pH 2.00. (α_{Y4-} at pH 8.00 is 5.6×10^{-3}; α_{Y4-} at pH 2.00 is 3.3×10^{-14})

	Fe^{3+} +	EDTA ⇌	FeY^-
Initial:	0	0	0.10 M
Equil:	X	X	0.10 M - X

$$K_f' = \frac{[FeY^-]}{[Fe^{3+}][EDTA]} = \frac{0.10-X}{X^2}$$

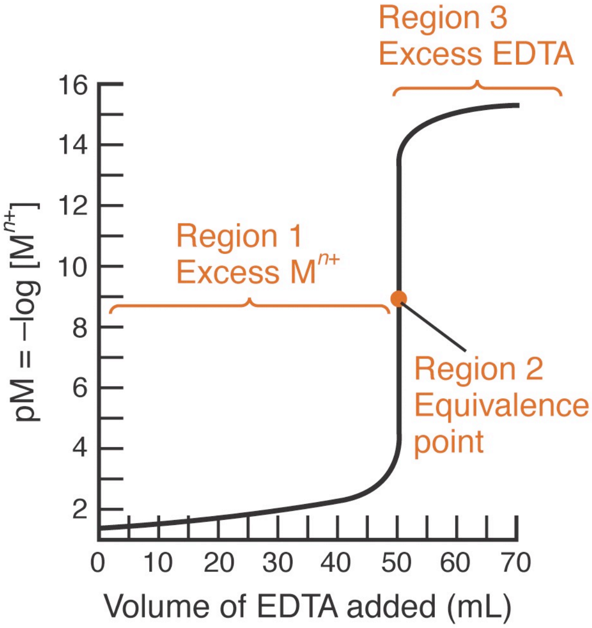
At pH 8.00, $K_f' = \alpha_{Y4-} K_f = 4.2\times10^{-3} \times 1.3\times10^{25} = 5.4_6\times10^{22}$
Since $K_f' > 10^4$, $0.10/X^2 = 5.4_6\times10^{22}$
$X = 1.4\times10^{-12}$ M = $[Fe^{3+}]$

At pH 2.00, $K_f' = \alpha_{Y4-} K_f = 2.6\times10^{-14} \times 1.3\times10^{25} = 3.3_8\times10^{11}$
Since $K_f' > 10^4$, $0.10/X^2 = 3.3_8\times10^{11}$
$X = 5.4\times10^{-7}$ M = $[Fe^{3+}]$

EDTA Titration Curve

Region 1 - excess M^{x+}

$[M^{x+}]$ = (Moles unreacted M^{x+}) / (total vol)



Region 2 - Equivalence point

- dissociation of MY

	M^{n+} + Y^{4-}	⇌	$MY^{(n-4)-}$
Initial	0	0	F_{MY}
Equil	x	x	F_{MY}-x

$K'_f \approx F_{MY} / x^2$

$$[M^{n+}] = \sqrt{\frac{F_{MY^{(n-4)-}}}{K_f'}}$$

Region 3 - Excess titrant

M is due to back reaction

$$[M^{n+}] = \frac{F_{MY^{(n-4)-}}}{K_f \alpha_{Y^{4-}} [EDTA]_{xs}}$$

Example: A 25 mL sample containing 0.025 M $Ca(NO_3)_2$ is titrated with 0.020 M EDTA at pH 10.00. K_f (CaY^{2-})= 5.01×10^{10} and α_{Y4-} at pH 10.00 is 0.30. Calc pCa after addition of **a)** 0 mL, **b)** 20 mL, **c)** 31.25 mL, **d)** 45 mL of EDTA.

a) Before EDTA is added, V_{EDTA} = 0,

pCa = -log[Ca^{2+}] = -log(0.025) = 1.60

b) After 20 mL EDTA is added, V_{EDTA} = 20 mL, there is a reaction.

	Ca^{2+}	+ EDTA	→ CaY^{2-}
Initial:	0.025Mx25mL = 0.62_5 mmol	0.020Mx20mL = 0.40 mmol	0
Final:	0.62_5 – 0.40 = 0.22_5 mmol	0	0.40 mmol

[Ca^{2+}] = 0.225 mmol/(25 mL + 20 mL) = 0.0050 M

pCa = -log 0.0050 = 2.30

c) After 31.25 mL EDTA is added, V_{EDTA} = 31.25 mL

	Ca^{2+}	+	EDTA	$\rightarrow$	CaY^{2-}
Initial:	0.025Mx25mL = 0.62_5 mmol		0.020Mx31.25mL = 0.62_5 mmol		0
Equil:	0		0		0.62_5 mmol

$C_{CaY2-} = 0.62_5$ mmol/(25 mL + 31.25 mL) = 0.011_1 M
Use conditional formation equilibrium to calc free Ca^{2+}.

	Ca^{2+}	+	EDTA	$\rightleftharpoons$	CaY^{2-}
Initial:	0		0		0.0111
Equil	x		x		0.0111 – x

$K_f' = (0.011_1M – X)/X^2$

At pH 10.00, $K_f' = \alpha_{Y4-} K_f = 0.30 \times 5.01 \times 10^{10} = 1.50 \times 10^{10}$

Since $K_f' > 10^4$, $0.011_1M/X^2 = 1.50 \times 10^{10}$
$X = 8.6_0 \times 10^{-7}$ M = $[Ca^{2+}]$
pCa = $-\log(8.60 \times 10^{-7}M) = 6.07$

d) After 45 mL EDTA is added, V_{EDTA} = 45 mL, there is a reaction.

	Ca^{2+}	+	EDTA	$\rightarrow$	CaY^{2-}
Initial:	0.025M x 25mL = 0.625 mmol		0.020M x 45mL = 0.90 mmol		0
Final:	0		0.90-0.625 = 0.275 mmol		0.625 mmol

The solution contains EDTA and CaY^{2-}. All free Ca^{2+} are from the dissociation of CaY^{2-}.
C_{EDTA} = 0.275 mmol/(25 mL + 45 mL) = 0.00393 M
C_{CaY2-} = 0.625 mmol/(25 mL + 45 mL) = 0.00694 M

We use conditional formation equilibrium to calc free Ca^{2+}.

	Ca^{2+}	+	EDTA	=	CaY^{2-}
Initial:	0		0.00393M		0.00694M
Final:	X		0.00393+X		0.00694 – X

$K_f' = (0.00694 – X)/[X(0.00393+X)]$

At pH 10.00, $K_f' = \alpha_{Y4-} K_f = 0.30 \times 5.01 \times 10^{10} = 1.50 \times 10^{10}$

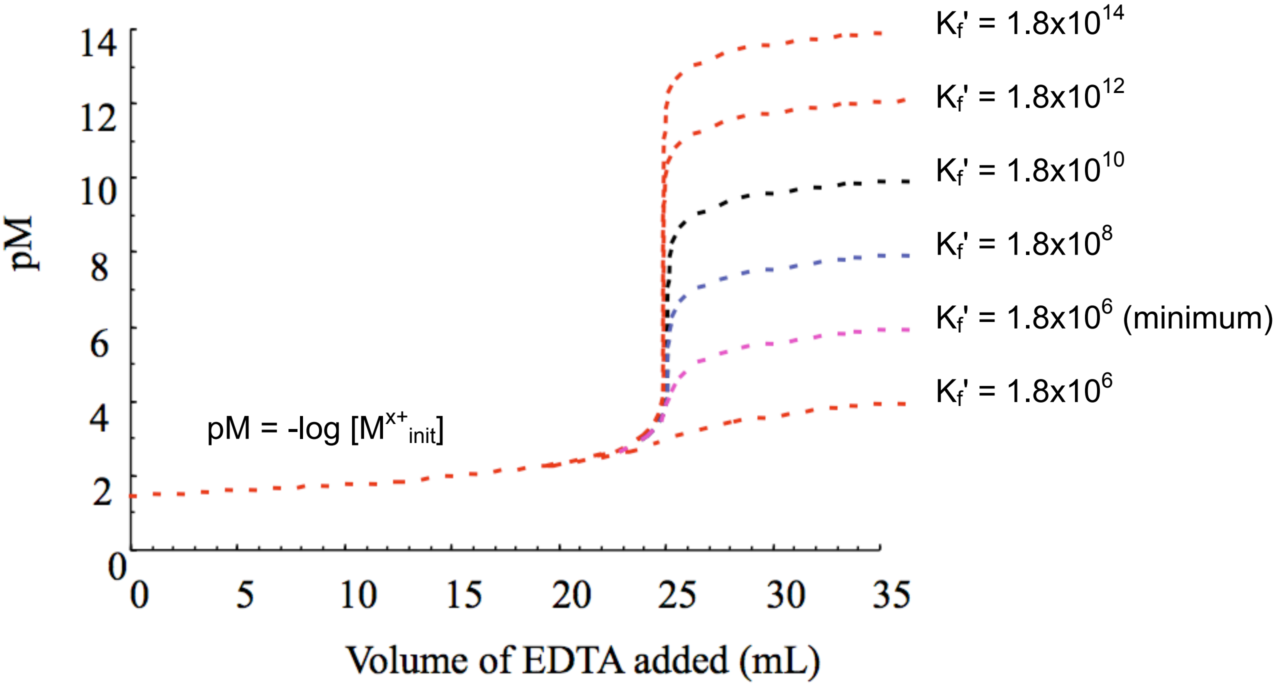
Since $K_f' > 10^4$, 0.00694-X = 0.00694 and 0.00393+X=0.00393
So $0.00694/(X \bullet 0.00393) = 1.50 \times 10^{10}$
$X = 1.18 \times 10^{-10} = [Ca^{2+}]$
pCa = $-\log(1.18 \times 10^{-10}) = 9.93$

Effect of K_f' on sharpness

Conditions: $\alpha_{M^{x+}}$ = constant; K_f or $\alpha_{Y^{4-}}$ allowed to vary.

Example: 50.0 mL of 0.040 M metal ion titrated with 0.080 M EDTA. $\alpha_{M^{x+}} = 1$

$$\text{Plotting the curve: } [\mathrm{M}^{x+}] = \frac{F_{\mathrm{MY}^{y-}}}{\mathrm{K_f}\alpha_{\mathrm{Y}^{4-}}[\mathrm{EDTA}]}$$



Question: What pH should be used for titrating calcium with EDTA? Show all calculations. $K_f(\mathrm{CaY^{2-}}) = 10^{10.65}$

$$K'_f = \alpha_{Y^{4-}} K_f \quad \text{or} \quad \alpha_{Y^{4-}} = K'_f / K_f$$

$K_{f\,(\mathrm{CaY2-})} = 10^{10.65} = 4.4_7\text{x}10^{10}$

Minimum K_f' for EDTA titration = 10^6

$K_f' \geq 10^6 = \alpha_{Y4-} K_{f(\mathrm{CaY2-})}$

$\alpha_{Y4-} \geq 10^6 / K_{f(\mathrm{CaY2-})} = 10^6 / 4.4_7\text{x}10^{10}$

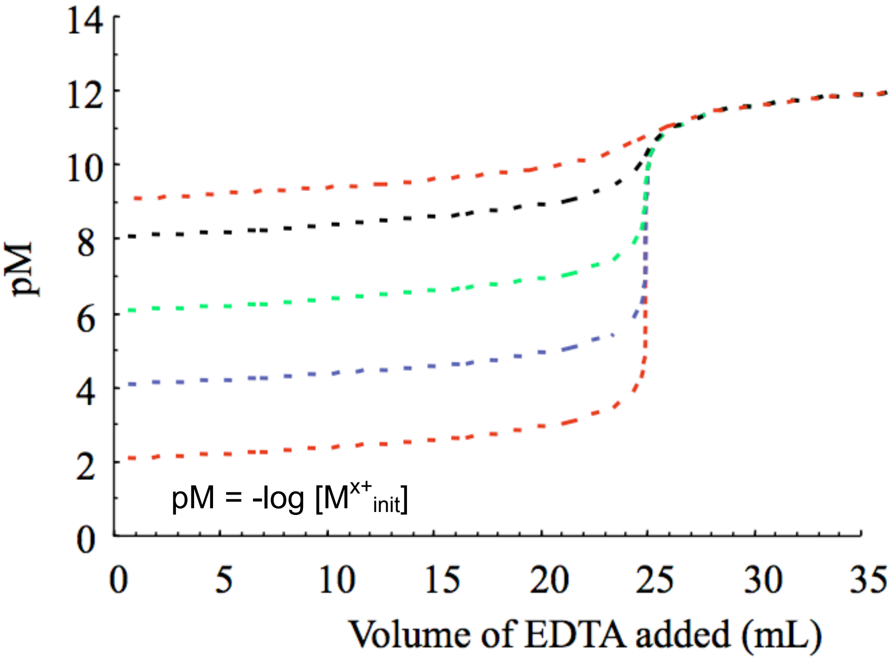
$\geq 2.2_4\text{x}10^{-5}$

Based on the table, the pH should be > 6 or 6.5

Effect of Metal Concentration on sharpness
Conditions: $K'_f = 1.8 \times 10^{12}$; 50.0 mL of M^{x+}

$$[M^{x+}] = \frac{F_{MY^{y-}}}{K_f \alpha_{Y^{4-}} [EDTA]} \qquad pM = -\log [M^{x+}]$$

[EDTA]	$[M^{x+}]$
2×10^{-9} M	10^{-9}M
2×10^{-8} M	10^{-8}M
2×10^{-6} M	10^{-6}M
2×10^{-4} M	10^{-4}M
2×10^{-2} M	10^{-2}M



Metal Ion Conc should be ≥ 10^{-6} M for titration to work

Auxiliary Complexing Agents (Ligands) (Sec. 11-5)

Auxiliary ligand – added to solution to stabilize (i.e., keep in solution) the analyte

e.g., titrating metal under alkaline conditions

$Zn^{2+} + 2\,OH^- \rightarrow Zn(OH)_2 \downarrow$ at pH=10

$Zn(OH)_{2\,(s)} + EDTA \rightarrow$ no or slow reaction

Criteria for auxiliary ligand:
- form water soluble complexes
- form weaker complex than titrant
- form a stronger complex than interferent (OH^-)
- kinetically labile

e.g., $Zn^{2+} + 4\,NH_3 \rightarrow Zn(NH_3)_4^{2+}$

$Zn(NH_3)_4^{2+} + EDTA \rightarrow ZnY^{2-} + 4\ NH_3$ (fast reaction)

Complex Equilibria

Overall reaction and equilibrium expression for complexation of Zn^{2+} by NH_3 is:

$Zn^{2+} + 4\ NH_3 \rightleftharpoons [Zn(NH_3)_4]^{2+}$

- Stepwise formation constants:

$Zn^{2+} + NH_3 \leftrightarrows ZnNH_3^{2+}$ $K_1 = 151$
$ZnNH_3^{2+} + NH_3 \leftrightarrows Zn(NH_3)_2^{2+}$ $K_2 = 178$
$Zn(NH_3)_2^{2+} + NH_3 \leftrightarrows Zn(NH_3)_3^{2+}$ $K_3 = 204$
$Zn(NH_3)_3^{2+} + NH_3 \leftrightarrows Zn(NH_3)_4^{2+}$ $K_4 = 91$

- Cumulative formation constants

$Zn^{2+} + NH_3 \leftrightarrows ZnNH_3^{2+}$ $\beta_1 = K_1 = 151$
$Zn^{2+} + 2NH_3 \leftrightarrows Zn(NH_3)_2^{2+}$ $\beta_2 = K_1K_2 = 2.69\times10^4$
$Zn^{2+} + 3NH_3 \leftrightarrows Zn(NH_3)_3^{2+}$ $\beta_3 = K_1K_2K_3 = 5.48\times10^6$
$Zn^{2+} + 4NH_3 \leftrightarrows Zn(NH_3)_4^{2+}$ $\beta_4 = K_1K_2K_3K_4 = 5.0\times10^8$

Question: Calculate the conditional formation constant for the reaction of Zn^{2+} with EDTA in 0.0030 M NH_3 and pH 9.00. $K_{f,ZnY} = 2.9\times10^{16}$. α_{Y4-} (pH 9.0) = 0.041. $K_1 = 320$, $K_2 = 91$, $K_3 = 20$, and $K_4 = 6.2$.

$Zn^{2+} + Y^{4-} \rightleftharpoons ZnY^{2-}$ $K_f = 2.9\times10^{16}$

Zn^{2+}
$Zn(NH_3)^{2+}$
$Zn(NH_3)_2^{2+}$
$Zn(NH_3)_3^{2+}$
$Zn(NH_3)_4^{2+}$

H_6Y^{2+}
H_5Y^{+}
H_4Y
H_3Y^{-}
H_2Y^{2-}
HY^{3-}
Y^{4-}

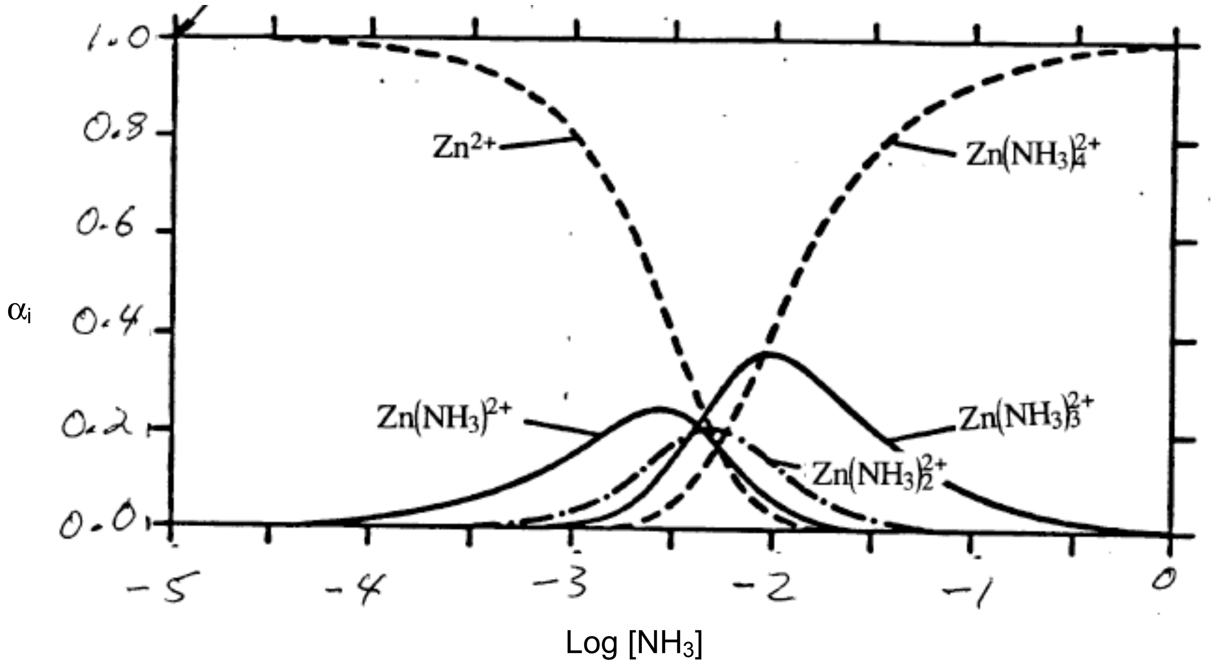
$[Y^{4-}] = \alpha_{Y4-}F_{EDTA}$

Fractional composition of Zn^{2+} (α_{Zn2+}) = fraction of Zn^{2+} in a specific form

$$\alpha_{Zn^{2+}} = \frac{[Zn^{2+}]}{F_{Zn}} \qquad \alpha_{Zn(NH_3)_4{}^{2+}} = \frac{[Zn(NH_3)_4{}^{2+}]}{F_{Zn}}$$

$$\alpha_{Zn^{2+}} = \frac{1}{1 + K_1[NH_3] + K_1K_2[NH_3]^2 + K_1K_2K_3[NH_3]^3 + K_1K_2K_3K_4[NH_3]^4}$$

$$\alpha_{Zn^{2+}} = \frac{1}{1 + \beta_1[NH_3] + \beta_2[NH_3]^2 + \beta_3[NH_3]^3 + \beta_4[NH_3]^4}$$



Question 1: Calculate the conditional formation constant for the reaction of Zn^{2+} with EDTA in 0.0030 M NH_3 and pH 9.00. $K_{f,ZnY} = 3.2\times10^{16}$.
α_{Y4-} (pH 9.0) = 0.041 (from Table 11-1)

$Zn^{2+} + Y^{4-} \rightleftharpoons ZnY^{2-}$ $K_f = 2.9\times10^{16}$

$$K_f = \frac{[ZnY^{2-}]}{[Zn^{2+}][Y^{4-}]} = 2.9\times10^{16}$$

$$K_f = \frac{[ZnY^{2-}]}{\alpha_{Zn^{2+}}F_{Zn}\alpha_{Y4-}F_{EDTA}} \quad \text{since } \left[\mathrm{Zn}^{2+}\right] = \alpha_{Zn^{2+}}F_{Zn} \text{ and } \left[\mathrm{Y}^{4-}\right] = \alpha_{Y^{4-}}F_{EDTA}$$

$$K_f'' = \alpha_{Zn^{2+}}\alpha_{Y4-}K_f = \frac{[ZnY^{2-}]}{F_{Zn}F_{EDTA}}$$

$$\alpha_{Zn^{2+}} = \frac{1}{1+\beta_1[NH_3]+\beta_2[NH_3]^2+\beta_3[NH_3]^3+\beta_4[NH_3]^4} = 0.53 \quad \text{(when } [NH_3] = 0.003\text{ M)}$$

$K_f'' = \alpha_{Zn^{2+}}\alpha_{Y4-}K_f = 0.53\ (0.041)\ 3.2\times10^{16} = 6.9\times10^{14}$

Question 2: Calc the free Zn^{2+} concentration in a solution of 0.10 M ZnY^{2-} at pH 9.00 and with the presence of 0.0030 M NH_3.

With auxiliary ligand (NH_3) present, use K_f''.

	Zn(all forms)	+	EDTA	⇌	CdY^{2-}
Initial:	0		0		0.10 M
Final:	X		X		0.10 - X

$K_f'' = (0.10 - X)/X^2 = 6.9x10^{14}$ (from Ques. 1)

Since $K_f'' > 10^4$, $0.10 - X \cong 0.10$ so
$0.10M/X^2 = 4.8x10^{14}$ or $X = 1.4_4x10^{-8}$ M = F_{Zn} (i.e., formal conc of Zn)

$\alpha_{Zn^{2+}} = \frac{[Zn^{2+}]}{F_{Zn}}$, so $[Zn^{2+}] = \alpha_{Zn2+} F_{Zn} = 0.53 x 1.4_4x10^{-8} = 7.6x10^{-9}$ M

Question 3: Calc the free Zn^{2+} concentration in a solution of 0.10 M ZnY^{2-} at pH 9.00.
$K_{f,ZnY} = 3.2x10^{16}$. α_{Y4-} (pH 9.0) = 0.041.

Without auxiliary ligand present, use K_f'.

	Zn(all forms)	+	EDTA	⇌	CdY^{2-}
Initial:	0		0		0.10 M
Final:	X		X		0.10 - X

$K_f'' = (0.041)3.2x10^{16} = 1.3_1x10^{15} = (0.10 - X)/X^2$

Since $K_f'' > 10^4$, $0.10 - X \cong 0.10$ so
$1.3_1x10^{15} = 0.10M/X^2$ or $X = 8.7x10^{-9}$ M = $[Zn^{2+}]$

Summary for complexation rxn calculation:

- If there is an auxiliary ligand present, use K_f'' ($= \alpha_{Y4-} \alpha_{Zn2+} K_f$)
  and Zn (all forms) + EDTA ⇌ ZnY^{2-}
- If there is no auxiliary ligand present, use K_f' ($= \alpha_{Y4-} K_f$)
  and Zn^{2+} + EDTA ⇌ ZnY^{2+}

Types of EDTA Titrations (Sec. 11-7)

1) **Direct Titration**

- EDTA is used as the titrant for a solution of the analyte M_{an}
e.g., Ca^{2+} (analyte) + EDTA (titrant) $\rightarrow$ CaY^{2+}
- masking agents or auxiliary ligands may be used

masking agent: ligand that strongly complexes an interferent; e.g., F^- for Fe^{3+} in Cu in brass (fast, strong titration reaction, no side reactions, good end point)

mol EDTA used = mol analyte M_{an} in sample

2) **Back Titration**

- used when direct titration not possible
e.g., ppt of metal at pH needed to titration
slow titration reaction
no good indicator

- known excess of EDTA added to analyte solution of M_{an}

- the excess EDTA is titrated with another metal ion, M_{BT}
e.g., Hg^{2+} (analyte) + EDTA (excess) $\rightarrow$ HgY^{2-}
EDTA (leftover) + Mg^{2+} (titrant) $\rightarrow$ MgY^{2-}

mol EDTA added - mol M_{BT} used as titrant = mol analyte M_{an}

• back titrant M_{BT} must not displace M_{an} from the EDTA-M_{an} complex, i.e., $K_f'(M_{an}Y^{x-}) > 100 \times K_f'(M_{BT}Y^{x-})$

3) **Displacement Titration**

- used when no satisfactory indicator, e.g., titration of Hg^{2+}, Ag^+
- known excess of MgY^{2-} is added to analyte solution of M_{an},
e.g., $Hg^{2+} + MgY^{2-}$ (xs) $\rightarrow$ $HgY^{2-} + Mg^{2+}$ $\quad K_f'(HgY^{2-}) \gg K_f'(MgY^{2-})$

- freed Mg^{2+} is titrated with EDTA:
Mg^{2+} + EDTA (titrant) $\rightarrow$ MgY^{2-}

mol analyte (Hg^{2+}) = mol Mg^{2+} (free) = mol EDTA (titrant)

4) **Indirect Titration**

- known excess of metal ion is added to a sample to react with an anion to form a precipitate,
e.g., Ca^{2+} (excess) + CO_3^{2-} (analyte) $\rightarrow$ $CaCO_3 \downarrow$ + Ca^{2+} (left over)

- filter out precipitate, and titrate remaining Ca^{2+} with EDTA

Mol CO_3^{2-} (analyte) = Mol Ca^{2+} added – Mol EDTA (titrant)

- Good for analyzing some anions that precipitate with certain metal ions: CO_3^{2-}, CrO_4^{2-}, S^{2-}, SO_4^{2-}

Endpoint Detection

- Colorimetric endpoint detection is most common
- Indicators are weak complexing agents that exhibit different colors in their complexed and uncomplexed forms.

$$M + In\ (\text{color B}) \rightarrow MIn\ (\text{color A})$$

- Titrant reacts with the free metal ion until no free metal is left.
- Titrant then complexes the metal in MIn complex

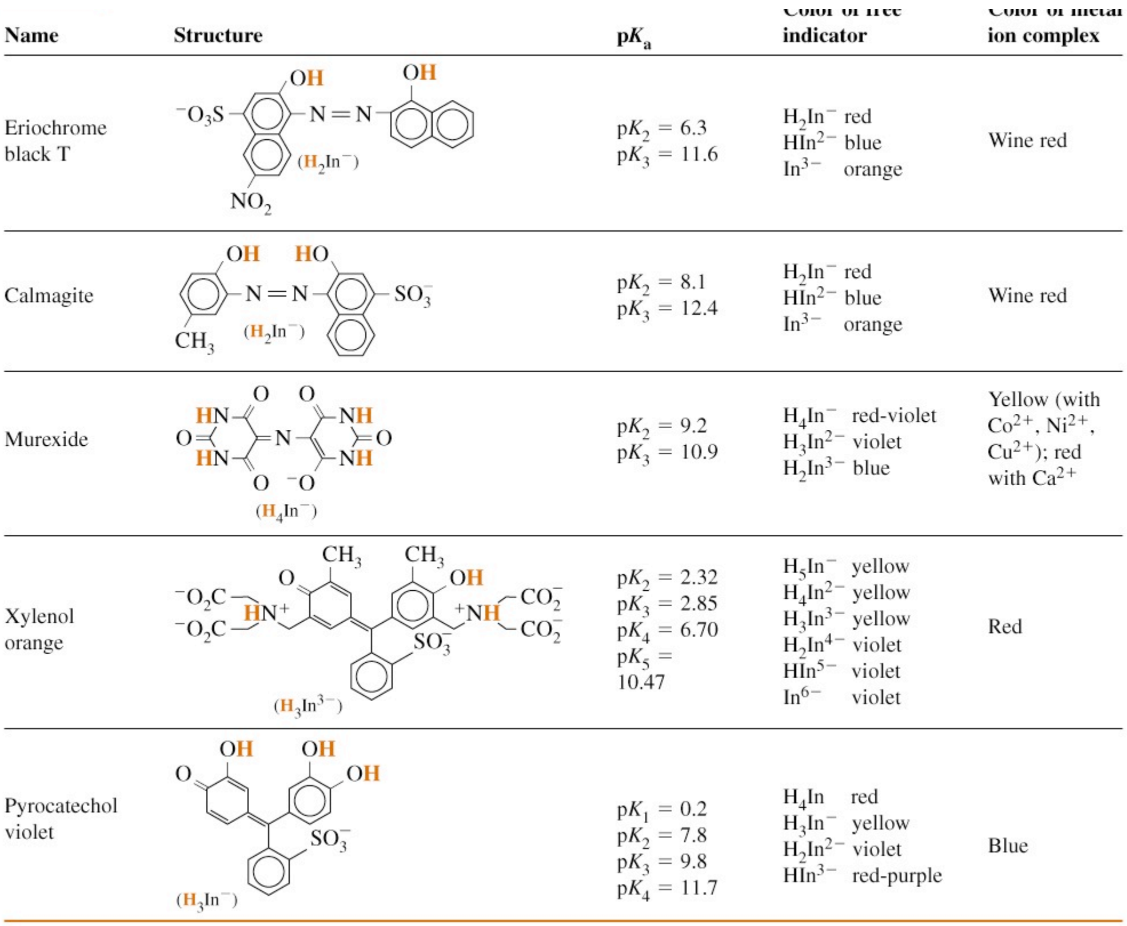
$$MIn\ (\text{color A}) + EDTA \rightarrow MY\ (\text{colorless}) + In\ (\text{color B})$$

- Visual transition range: our eye requires an order of magnitude or more change in conc:

$$10 \geq [MIn]/[In] \geq 0.1$$

- Note: controlling pH of the titration solution is very important;
  e.g., Xylenol orange at pH 5.5: end point color change from Yellow to Red;
  At pH 7.5: Violet to Red.

Table 11-3 Common metal ion indicators



Name	Structure	pK_a	Color of free indicator	Color of metal ion complex
Eriochrome black T	(H_2In^-)	$pK_2 = 6.3$ $pK_3 = 11.6$	H_2In^- red HIn^{2-} blue In^{3-} orange	Wine red
Calmagite	(H_2In^-)	$pK_2 = 8.1$ $pK_3 = 12.4$	H_2In^- red HIn^{2-} blue In^{3-} orange	Wine red
Murexide	(H_4In^-)	$pK_2 = 9.2$ $pK_3 = 10.9$	H_4In^- red-violet H_3In^{2-} violet H_2In^{3-} blue	Yellow (with Co^{2+}, Ni^{2+}, Cu^{2+}); red with Ca^{2+}
Xylenol orange	(H_3In^{3-})	$pK_2 = 2.32$ $pK_3 = 2.85$ $pK_4 = 6.70$ $pK_5 = 10.47$	H_5In^- yellow H_4In^{2-} yellow H_3In^{3-} yellow H_2In^{4-} violet HIn^{5-} violet In^{6-} violet	Red
Pyrocatechol violet	(H_3In^-)	$pK_1 = 0.2$ $pK_2 = 7.8$ $pK_3 = 9.8$ $pK_4 = 11.7$	H_4In red H_3In^- yellow H_2In^{2-} violet HIn^{3-} red-purple	Blue

- Thin black lines indicate the pH ranges the dyes are useful. In this range the color difference between In and the MIn complex can be observed.

  See text for indicator abbreviations.