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Note

Thermodynamics of proton dissociation in mixed aqueous media:

I. pK_a, $\Delta G°$, $\Delta H°$ and $\Delta S°$ values for proton-ligand stability constants of several N-*m*-tolyl-*p*-substituted benzohydroxamic acids

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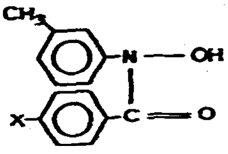
A great deal of work has been done on the synthesis and investigation of hydroxamic acids and their analogous compounds, the effect of substituents on their complexing properties and their application to analytical chemistry. A knowledge of proton–ligand stability constants is essential for elucidation of metal–ligand constants and their thermodynamic parameters for correlation and studying the reaction with metal ions.

In the present investigation the thermodynamic proton–ligand stability constants (ionisation constants, pK_a) of several N-m-tolyl-*p*-substituted benzohydroxamic acids (I) in 10, 20, 30, 40, 45, 50, 60 and 70% v/v dioxane water media are determined at 25 and 35°C. The thermodynamic parameters $\Delta G°$, $\Delta H°$ and $\Delta S°$ are discussed.



(I)

EXPERIMENTAL

Chemicals and apparatus

p-Dioxane (B.D.H., AnalaR) was purified by the method of Weissberger[1]. Tetrabutyl ammonium hydroxide (E. Merck) was purified[2] and used as a titrant. Pure distilled water redistilled over alkaline potassium permanganate and freed from carbon dioxide was used throughout this investigation.

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A Radiometer pH meter, equipped with shielded glass and calomel electrodes, was used for pH measurements.

Hydroxamic acids

The hydroxamic acids were synthesised as described elsewhere[3,4]. They were recrystallised before use and dried over P_2O_5 under vacuum. Their purity was checked by m.p., elemental analysis and infrared spectrometry.

Determination of proton–ligand stability constants

A three-necked, flat bottomed, titration cell with an inlet for nitrogen equipped with a glass electrode, calomel electrode and a microburrette was employed. 0.5 mole of hydroxamic acid was transferred to the titration cell and was dissolved in a dioxane–water mixture of desired composition, the initial volume being 47.5 ml in all the studies.

Before any titration was carried out, the titration cell containing the solution was placed in the thermostat for about 15 min to attain its temperature. Nitrogen gas presaturated with thermostated solvent of appropriate composition, was passed through the solution and titration carried out after 15 min, adding 0.5 ml aliquots of 0.1 M tetrabutyl ammonium hydroxide each time and noting the highest pH meter reading that did not drift.

The calculation method for thermodynamic proton–ligand stability constants is described in detail elsewhere[5,6].

Thermodynamic parameters

From the thermodynamic proton–ligand stability constants at two different temperatures the charge in free energy, $\Delta G°$, heat content or enthalpy, $\Delta H°$, and entropy, $\Delta S°$ associated with the ionisation equilibrium, i.e., $HA \rightleftharpoons H^+ + A^-$ (HA = hydroxamic acid), can be readily evaluated on the basis of the following equations:

The standard free energy change, $\Delta G°$, is given by eqn (1)

$$\Delta G° = 2.303\, RT\, pK_a \tag{1}$$

For simplicity eqn (1) can be written as:

$$\text{At } 25\,°\text{C}, \Delta G°_{(298.2\,°\text{C})} = 1.365\, pK_a \text{ (in kcal)} \tag{1a}$$

$$\text{At } 35\,°\text{C}, \Delta G°_{(308.2\,°\text{C})} = 1.411\, pK_a \text{ (in kcal)} \tag{1b}$$

The expression for standard enthalpy change $\Delta H°$, is obtained by integration of the Van't Hoff equation at two temperatures, T_1 and T_2

$$\log K_2/K_1 = \Delta H° \frac{(T_2 - T_1)}{T_1 T_2} \tag{2}$$

From the proton–ligand stability constants (ionisation constants) at two temperatures, the standard enthalpy change, $\Delta H°$, is estimated using equation (2).

For measurements at 25 and 35°C equation (2) can be simplified as:

$$\Delta H^\circ = 42.07\,\Delta pK_a\ (\text{kcal}) \tag{2a}$$

where

$$\Delta pK_a = pK_{a(25\,^\circ C)} - pK_{a(35\,^\circ C)}$$

Standard enthalpy change, ΔS°, is computed from the Gibbs–Helmholtz eqn (3)

$$\Delta S^\circ = \frac{\Delta G^\circ - \Delta H^\circ}{T} \tag{3}$$

At 25 and 35°C eqn (3) can be reduced to the following forms:

$$\text{At } 25\,^\circ\text{C};\quad -\Delta S^\circ\ (\text{kcal}) = 3.354\times 10^{-3}\,(\Delta G^\circ - \Delta H^\circ) \tag{3a}$$

$$\text{At } 35\,^\circ\text{C};\quad -\Delta S^\circ\ (\text{kcal}) = 3.244\times 10^{-3}\,(\Delta G^\circ - \Delta H^\circ) \tag{3b}$$

RESULTS AND DISCUSSION

The thermodynamic pK_a for the several hydroxamic acid in 10–70% dioxane water media at 25 and 35°C are given in Table 1. These values are accurate to ±0.02 but not beyond ±0.03 in any case. The thermodynamic parameters are given in Table 2.

TABLE 1

THERMODYNAMIC PROTON–LIGAND STABILITY CONSTANTS OF HYDROXAMIC ACIDS

The average pK_a generally falls with a sprd of ±0.02 unit but not beyond ±0.03 in any case.

Hydroxamic acid	*Dioxane % (v/v)*								
	0[a]	*10*	*20*	*30*	*40*	*45*	*50*	*60*	*70*
H	8.62 (8.54)[b]	9.02 (8.86)	9.38 (9.25)	9.84 (9.75)	10.38 (10.34)	10.78 (10.65)	11.12 (11.07)	12.11 (11.96)	13.38 (13.23)
CH_3	8.69 (8.60)	ins[c] (ins)	ins (ins)	9.93 (9.86)	10.56 (10.46)	10.91 (10.80)	11.33 (11.23)	12.28 (12.20)	13.66 (13.55)
CH_3O	8.77 (8.66)	9.22 (9.00)	9.53 (9.43)	10.03 (9.92)	10.64 (10.53)	11.01 (10.90)	11.42 (11.30)	12.42 (12.30)	13.79 (13.67)
F	8.56 (8.44)	8.93 (8.78)	9.32 (9.20)	9.83 (9.72)	10.46 (10.32)	10.85 (10.63)	11.20 (11.06)	12.30 (12.06)	13.63 (13.42)
Cl	8.45 (8.29)	8.81 (8.66)	9.22 (9.08)	9.73 (9.53)	10.34 (10.18)	10.70 (10.56)	11.12 (10.92)	12.15 (11.96)	13.53 (13.38)
Br	8.46 (8.28)	8.80 (8.64)	9.21 (9.07)	9.73 (9.52)	10.33 (10.16)	10.69 (10.56)	11.10 (10.92)	12.14 (11.94)	13.52 (13.37)
NO_2	8.10 (7.90)	8.45 (8.25)	8.87 (8.68)	9.38 (9.18)	10.00 (9.80)	10.37 (10.18)	10.79 (10.59)	11.71 (11.50)	13.09 (12.90)

[a] Extrapolated values. [b] The values in parenthesis are at 35°C. [c] ins = the hydroxamic acids are insoluble in the solvent.

TABLE 2

FREE ENERGY, ENTHALPY AND ENTROPY CHANGES FOR IONISATION OF N-*m*-TOLYL-*p*-SUBSTITUTED BENZOHYDROXAMIC ACIDS

ΔG° and ΔH° in kcal mol^{-1}; ΔS° in cal mol^{-1} K^{-1}; first value at 25 °C and second at 35 °C.

Substituent		*Dioxane % (v/v)*							
		10	*20*	*30*	*40*	*45*	*50*	*60*	*70*
H,	ΔG°	12.31	12.80	13.43	14.17	14.71	15.18	16.53	18.26
		12.50	13.05	13.76	14.59	15.02	15.62	16.88	18.67
(ΔH° 3.4),	$-\Delta S^\circ$	29.9	31.5	33.6	36.1	37.9	39.5	44.0	49.8
		29.5	31.3	33.6	36.3	37.7	39.6	43.7	49.5
CH_3,	ΔG°	ins	ins	13.55	14.14	14.89	15.47	16.76	18.65
				13.91	14.76	15.24	15.85	17.21	19.20
(ΔH° 3.8),	$-\Delta S^\circ$	ins	ins	32.7	34.7	37.2	39.1	43.5	49.8
				32.8	35.6	37.1	39.1	43.5	50.0
CH_3O,	ΔG°	12.45	13.01	13.69	14.52	15.03	15.59	16.59	18.82
		12.70	13.31	14.00	14.86	15.38	15.94	17.36	19.29
(ΔH° 4.6),	$-\Delta S^\circ$	26.3	28.2	30.5	33.3	35.0	36.9	40.2	47.7
		26.3	28.3	30.5	33.3	35.0	36.8	41.4	47.7
F,	ΔG°	12.19	12.72	13.42	14.28	14.81	15.29	16.79	18.60
		12.40	12.98	13.71	14.56	14.99	15.61	17.02	18.94
(ΔH° 5.1),	$-\Delta S^\circ$	23.8	25.6	27.9	30.8	32.6	34.2	39.2	45.3
		23.7	25.6	27.9	30.7	32.8	34.1	38.7	44.9
Cl,	ΔG°	12.03	12.59	13.28	14.11	14.61	15.18	16.58	18.47
		12.22	12.81	13.45	14.36	14.90	15.42	16.88	18.88
(ΔH° 6.7),	$-\Delta S^\circ$	17.9	19.8	22.1	24.9	26.5	28.4	33.1	39.5
		17.9	19.8	21.9	24.8	26.6	28.3	33.0	39.5
Br,	ΔG°	12.01	12.57	13.28	14.10	14.59	15.15	16.57	18.45
		12.19	12.80	13.43	14.34	14.90	15.41	16.85	18.87
(ΔH° 7.6),	ΔS°	14.8	16.7	19.1	21.8	23.4	25.3	30.1	36.4
		14.9	16.9	18.9	21.8	23.7	25.3	30.0	36.4
NO_2,	ΔG°	11.53	12.11	12.81	13.65	14.16	14.73	15.98	17.87
		11.64	12.25	12.95	13.84	14.36	14.94	16.22	18.20
(ΔH° 8.4),	$-\Delta S^\circ$	10.5	12.4	14.8	17.6	19.3	21.2	25.4	31.8
		10.5	12.5	14.8	17.6	19.3	21.2	25.4	31.8

A plot of p*K* vs. mole fraction of dioxane is linear and the values were extrapolated for aqueous media at both temperatures.

Errors caused in the determination of pK_a are reflected in the values of all thermodynamic functions. An estimate of the error is, therefore, necessary to show how reliable these results are. The pK_a values have been determined with a precision of ±0.02 to ±0.03 and hence the error in ΔG° is estimated to be between ±0.03 and ±0.04 kcal. It is apparent from eqn (2a) that an error of 0.01 in pK_a causes an error of 0.42 kcal in ΔH° while the magnitude error in ΔpK_a depends on the cancellation or addition of errors of an individual set of pK_a determined at two temperatures. In view of the inherent weakness of the method, no definite trends in the magnitude of the values of $\Delta H°$ with change of media could be observed[7]. Despite the relatively large errors in the value of $\Delta H°$ computed by the temperature coefficient method, the data are still of great significance for drawing certain valuable conclusions. In any case the positive value of $\Delta H°$ found in all solvent media and for all hydroxamic acids has a real significance; it implies that the ionisation process at 25°C is endothermic and will be exothermic only above T_{max}. Further, it is certain that the magnitude of change in $\Delta H°$ with change in media is relatively small and is within the range of experimental error. In the light of the above observation, it is justifiable as a first approximation, to assume that $\Delta H°$ is independent of solvent media at least in the narrow range of 0 to 0.33 mole fraction of dioxane of the present study. The fresh values of $\Delta H°$ for each hydroxamic acid were computed (at 0% dioxane) while the values calculated at each mole fraction of dioxane are deliberately omitted.

It is observed that there is a general tendency of increase in magnitude of $\Delta S°$ with increase in dioxane content of the solvent medium.

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