69. *The Stabilities of Complexes of Thallium*(I) *and the Alkali Metals with Uramildiacetic Acid.*

By H. Irving and J. J. R. F. da Silva.

Uramildiacetic acid, H_3Ur, has been shown to form a stable salt, H_3Ur,NaH_2Ur,H_2O, and its acid dissociation constants have been determined at various temperatures. The stabilities of complexes formed between the anion, Ur^{3-}, and univalent cations have been measured potentiometrically at 20°, 27°, 34°, and 39° by using tetramethylammonium hydroxide as titrant and tetramethylammonium nitrate to provide the salt background ($\mu =$ 0·1M). The stabilities of the 1 : 1 complexes increase in the order $K^+ <$ $Na^+ < Li^+ < Tl^+ < H^+$. The metal complexes are all stabilized by favourable (negative) enthalpy changes which increase in magnitude with ionic radius; the entropy changes are negative and large in the case of potassium and thallium.

The validity of the procedure for precipitating lead as its iodide after masking of thallium(I) with EDTA is examined and the use of uramildi-acetic acid is shown to offer no advantages.

Although EDTA forms stronger complexes than uramildiacetic acid with most bivalent ions, the situation is reversed for the alkali metals and for beryllium which forms a very stable complex with log $K_{\text{BeUr}} = 10\cdot36$.

ALTHOUGH a number of solid co-ordination compounds of the lighter alkali metals with oxygen-donor ligands have been described [1] they are all extensively dissociated in water,

[1] Sidgwick, " The Chemical Elements and their Compounds," Oxford Univ. Press, 1950, p. 99.

and formation constants for species persisting in aqueous solution have been measured for complexes formed with only the most powerful complexing agents such as nitrilotri-acetic acid (NITA) and ethylenediaminetetra-acetic acid (EDTA).[2]

From the point of view of size and charge the univalent thallium ion, Tl^+, most closely resembles the ions K^+ and Rb^+, but the stability constants of its complexes with halide ions (log $K_{TlF} = 0.1$, log $K_{TlCl} = 0.68$, log $K_{TlBr} = 0.93$) show that it has a definite tendency to behave as a class (b) metal.[3] The classification of thallium(III) as a class (b) metal is unambiguous.[3,4] The greater deforming power of Tl^+ than of K^+, a consequence of its very different electronic structure, enables it to form more stable complexes with multidentate ligands (Table 1).

TABLE 1.

Values for the logarithm of the stability constants of complexes of some univalent ions with nitrilotriacetic acid and ethylenediaminetetra-acetic acid.

Ion	log K (EDTA)	log K (NITA)
Na^+	1.66 *	2.1,† 1.22 ‡
Li^+	1.79 * §	3.28,† 2.51 ‡
Tl^+	5.81,¶ 6.55 ‡	3.44,¶ 4.74 ‡

* Potentiometric at 20° and $\mu = 0.1$ (KCl); Schwarzenbach and Ackermann, *Helv. Chim. Acta*, 1947, **30**, 1798. † Potentiometric at 20° $\mu \longrightarrow 0$; Schwarzenbach, Kampitsch, and Steiner, *Helv. Chim. Acta*, 1945, **28**, 828. ‡ Potentiometric at 20° and $\mu = 0.1$ (KNO₃). Irving and da Silva, unpublished results. § Wänninen (Thesis, Åbo, 1960) reports log $K_{LiY} = 3.1$ ($\mu = 0.1$) for $H_5Y = $ triethylenetetraminepenta-acetic acid. ¶ Polarographic at 25° and $\mu = 1—1.4$M-KNO₃; Bouten and Verbeck, *Analyt. Chim. Acta*, 1957, **17**, 339.

The values quoted for Tl^+ cannot readily be compared with those for the alkali metals which were obtained under very different conditions. A study of the stability of these univalent ions under strictly comparable conditions seemed worthwhile and in this paper we report measurements with the complexone, uramildiacetic acid (I), chosen because Schwarzenbach *et al.* had found that it forms complexes with lithium and sodium of quite exceptional stability.[5,6] The insolubility of thallous chloride precludes the use of potassium chloride as a medium for a constant salt background, and the probability that thallous complexes have strengths comparable with those of potassium ions demands the use of non-complex-forming cations (*e.g.*, tetramethylammonium ions) both in the titrant and in the salt background.

Our first sample of uramildiacetic acid prepared according to the recorded instructions [5] gave an anomalous titration curve [Fig. 1; abscissa scale (a)], which was reproducible even after the sample had been recrystallized repeatedly from de-ionized water. The titration curve for this reagent in the presence of an equivalent amount of zinc ion was also anomalous (Fig. 1). After ignition, this sample of complexone left an alkaline residue and ultimate analysis showed that it was in fact a salt of the desired uramildiacetic acid, of composition H_3Ur,NaH_2Ur,H_2O (where $Ur = C_8H_7O_6N_3$) somewhat analogous to potassium quadroxalate, $H_2Ox,KHOx$ ($Ox = C_2O_4$). This result was confirmed on reconsideration of the original titration curves which were found to be consistent with those calculated for an equimolecular mixture of a dibasic acid NaH_2Ur and a tribasic acid H_3Ur [Fig. 1; abscissa scale (b)]. The ease of formation of the sodium salt and its ability to withstand recrystallization without change of composition may explain the difficulties reported in the preparation of pure samples of uramildiacetic acid and some of its derivatives, and of uramil-7-monoacetic acid.[5]

Recrystallization of the acid sodium salt from dilute perchloric acid gave the desired

[2] " Stability Constants of Metal-ion Complexes," *Chem. Soc. Special Publ.*, No. 6, Part I, 1957.
[3] Ahrland, Chatt, and Davies, *Quart. Rev.*, 1958, **12**, 265.
[4] Carleson and Irving, *J.*, 1954, 4390.
[5] Schwarzenbach, Kampitsch, and Steiner, *Helv. Chim. Acta*, 1946, **29**, 364.
[6] Schwarzenbach and Biedermann, *Helv. Chim. Acta*, 1948, **31**, 456.

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free uramildiacetic acid (I; H_3Ur) immediately. This acid could also be obtained directly by the procedure of Schwarzenbach *et al.* if a large excess of mineral acid was used when precipitating the complexone from the alkaline solution resulting from the condensation of uramil with sodium chloroacetate.

Analytical data for our sample of uramildiacetic acid and its molecular weight by titration agree best with the formula H_3Ur, for an anhydrous acid. However, the corresponding data for Schwarzenbach's preparation [5] pointed to its being the monohydrate H_3Ur,H_2O: that there was no loss of weight after it had been heated for 8 hr. at 0·005 mm. was taken to indicate the extreme stability of this hydrate. The analytical data for Schwarzenbach's compound agree more closely with the requirements of our sodium salt
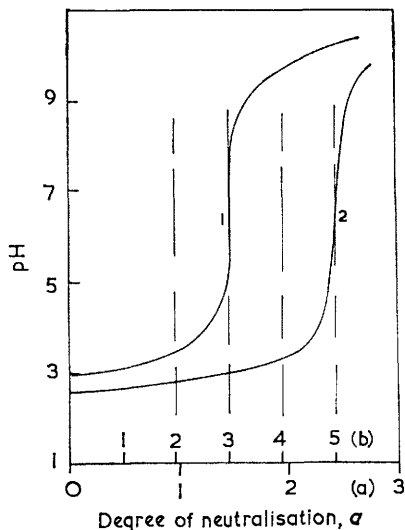

FIG. 1. Titration curves for the acid sodium salt H_3Ur,NaH_2Ur,H_2O (0·277 g./l.). (1) Reagent alone. (2) Reagent with an equivalent amount of zinc ions. (a) Scale on the assumption that the material was pure uramildiacetic acid, H_3Ur; (b) scale on the assumption that the material is a sodium salt, H_3Ur, NaH_2Ur,H_2O.

H_3Ur,NaH_2Ur,H_2O than with those of the monohydrate H_3Ur,H_2O (Table 2). However, it is difficult to reconcile this with the titration results and the fact that the sample was stated to be ash-free after six recrystallizations from water.

The neutralization curve of (anhydrous) uramildiacetic acid was determined by

TABLE 2.

Analytical data (%) for preparations of uramildiacetic acid.

	C	H	N	Calc. for:		C	H	N
Present sample	37·1	3·6	15·95	H_3Ur.....................		37·1	3·5	16·2
Schwarzenbach's sample [5]	34·35	3·69	15·02	H_3Ur,H_2O		34·7	4·0	15·2
				H_3Ur,NaH_2Ur,H_2O		34·4	3·4	15·0

potentiometric titration and its (stoicheiometric) dissociation constants defined by $K_1 = [H^+][H_2Ur^-]/[H_3Ur]$, $K_2 = [H^+][HUr^{2-}]/[H_2Ur^-]$, and $K_3 = [H^+][Ur^{3-}]/[HUr^{2-}]$ were calculated as follows. It can shown that

$$R[H^+]^3 + (R-1)K_1[H^+]^2 + (R-2)K_1K_2[H^+] + (R-3)K_1K_2K_3 = 0, \quad (1)$$

where $R = (aC_A + [H^+] - [OH^-])/C_A$, and C_A is the concentration of ligand acid and a the degree of neutralization by alkali during the course of the titration. Since (Fig. 1) pK_1 and pK_2 were obviously close in magnitude whereas pK_3 was much larger, values for the first two dissociation constants were obtained by solving sets of equations,

$$R[H^+]^2 + (R-1)K_1[H^+] + (R-2)K_1K_2 = 0, \quad (2)$$

for experimental results in the range $0 > a > 2$. This was done most conveniently by transforming eqn. (2) into the equivalent linear forms

$$\frac{(1 - R)[H^+]}{R - 2} = \frac{R[H^+]^2}{(R - 2)} \cdot \frac{1}{K_1} + K_2 \tag{3}$$

and

$$\frac{(2 - R)}{R[H^+]^2} = \frac{(R - 1)}{R[H^+]} \cdot \frac{1}{K_2} + \frac{1}{K_1 K_2} \tag{3a}$$

and solving them by a least-squares treatment to obtain K_1 and K_2 as the reciprocals of the calculated slopes. K_3 was calculated from the equation

$$K_3 = \{R[H^+]^3 + (R - 1)K_1[H^+]^2 + (R - 2)K_1 K_2[H^+]\}/(3 - R)K_1 K_2$$

by making use of the values of K_1 and K_2 previously obtained. This gives a more accurate value for K_3 than the use of the approximate equation $K_3 = (R - 2)[H^+]/(3 - R)$.

<div align="center">TABLE 3.</div>

<div align="center">Dissociation constants of uramildiacetic acid at 20°.</div>

	pK_1	pK_2	pK_3
Present work, $\mu = 0.1$M	1.7 ± 0.3 *	2.67 ± 0.03 *	9.63 ± 0.03 †
$\mu \longrightarrow 0$ (calc.)	1.9	3.1	10.33
Schwarzenbach's values valid for $\mu = 0$	2.86 ‡	3.76 ‡	10.44

* By using potassium hydroxide as titrant and 0.1M-potassium nitrate as the salt background. † By using tetramethylammonium hydroxide as titrant and 0.1M-tetramethylammonium nitrate as salt background. ‡ Values obtained by using tetramethylammonium hydroxide as titrant with no additional salt background and calculated to zero ionic strength (ref. 5). The values for pK_1 and pK_2 were interchanged in the original paper,[5] but this obvious error was corrected in ref. 2.

The values of pK_1 and pK_2 reported in Table 3 were obtained by using carbonate-free potassium hydroxide as the titrant and potassium nitrate to maintain the ionic strength constant at 0.1M and for the salt bridge to the saturated calomel electrode. Since potassium ions might themselves form complexes with the reagent the value of pK_3 was obtained from titrations in which tetramethylammonium hydroxide was employed as the titrant and 0.1M-tetramethylammonium nitrate for the salt background and in the bridge to the calomel reference electrode.

To check the reliability of this procedure neutralization curves for ethylenediamine-tetra-acetic acid and for nitrilotriacetic acid were obtained under each of the two conditions. The titration curves could be completely superimposed in the last two buffer regions, showing that any differences in junction potential or activity coefficients when potassium ions are replaced by tetramethylammonium ions are undetectable in the region where the formation of metal complexes might become appreciable.

As already pointed out by Schwarzenbach *et al.*[5] the values of pK_1 and pK_2 correspond in magnitude to the ionization of carboxylic protons, whilst that of pK_3 corresponds to the ionization of a proton from an ammonium ion. Schwarzenbach *et al.* explain the high acidity of the species H_2Ur^- as a consequence of the enolization of a 1-hydroxyl group accompanied by the migration of a proton to give a species which we should represent as a resonance hybrid (IIa). It is not, however, obvious whether the parent acid should be represented as (I) alone or in equilibrium with the isomer (Ib) or the resonance hybrid (Ic). In any event the removal of the first proton would give (IIa). The possibility of complete enolization of all three C=O groups in (I) to give a fully aromatic ring (as in Id or obvious modifications of this structure) appears unlikely from our studies with 1-methyl- and 1,3-dimethyl-uramildiacetic acid [8] which closely resemble the parent acid (I) although tautomeric changes involving the imino-hydrogen atoms have been inhibited.

[7] Stein, Gregor, and Spoerri, *J. Amer. Chem. Soc.*, 1956, **78**, 6185.
[8] Irving and da Silva, unpublished work.

The thermodynamic dissociation constant, K_3^T for the species HUr^{2-} (III) is related to the stoicheiometric value by the expression $K_3^T = K_3 f_1 f_3 / f_2$ where f_n is the activity coefficient for the relevant n-valent ion. By introducing Davies's approximation for

(Ia ; H₃Ur)

(Ib)

−H⁺

(Ic)

−H⁺

(IIa ; H₂Ur⁻)

(Id)

−H⁺

(III ; HUr²⁻)
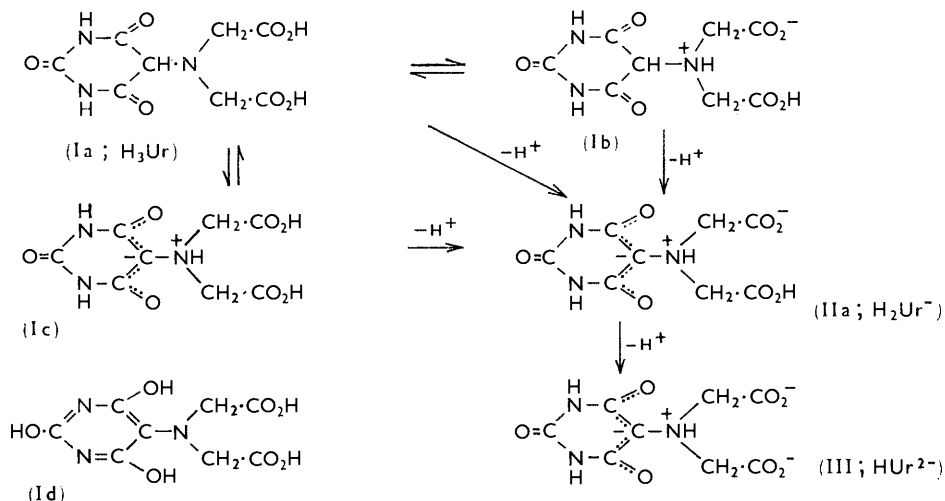
activity coefficients [9] this reduces to $pK_3^T = pK_3 + 0.70$ for $\mu = 0.1$M, whence $pK_3^T = 10.33$, in fair agreement with Schwarzenbach's value of 10.44 derived from potentiometric measurements in a medium of low ionic strength.

TABLE 4.

Values of log K_{ML} for the species ML at 20°.

Ion	Uramildiacetic acid (I; H₃Ur)			Ethylenediaminetetra-acetic (H₄Y)
	$\mu = 0.1$M	$\mu \longrightarrow 0$		$\mu = 0.1$M
Lithium	4·90	5·61 *	5·40 †	2·79 ‡
Sodium	2·72	3·33 *	3·32 †	1·66 ‡
Potassium	1·23	1·94 *	—	0 ᶜ
Thallium(I)	5·99	6·70 *	—	6·47 §
Lead(II)	~12 §	—	—	18·3 ‡

   * Calc. from present data for 0·1 μ by using Davies's expression for activity coefficients. † Schwarzenbach's results (ref. 5). ‡ Ref. 2. § Irving and da Silva.[8]

Titration curves for uramildiacetic acid in the presence of various univalent cations (Fig. 2) clearly demonstrate that complexes of appreciable stability are formed even by potassium ions and that the order of increasing stability is $K^+ < Na^+ < Li^+ < Tl^+$. Stability constants are summarized in Table 4 together with values reported for complexes of EDTA. Data for the lead(II) ion are also included. The stability constants K_{ML} were calculated from the equation

$$K_{ML} = (C_A - \alpha_H[L])/(C_M - C_A + \alpha_H[L]), \qquad (4)$$

where $\qquad \alpha_H = 1 + ([H^+]/K_3) + ([H^+]^2/K_2 K_3) + ([H^+]^3/K_1 K_2 K_3)$

and $[L] = K_1 K_2 K_3 \{(3-a)C_A - [H^+] + [OH^-]\}/(3[H^+]^3 + 2K_1[H^+]^2 + K_1 K_2[H^+])$.

Přibil has developed a method for the separation of thallium(I) and lead(II) that uses EDTA to mask the lead while the more weakly complexed thallous ion is precipitated

   [9] Davies, *J.*, 1938, 2093.

in the form of its very sparingly soluble iodide.[10] The advantages of replacing EDTA by a reagent that forms even weaker complexes with thallium are intuitive, but the unsuitability of uramildiacetic acid for this purpose will be seen by the following analysis of the conditions. If $K_{TlI(sol.)}$ and $K_{PbI_2(sol.)}$ are the solubility products of thallous and lead iodides and K_{TlL} and K_{PbL} the stability constants of 1 : 1 complexes with a given complex-forming agent (charges being omitted for clarity), then at the point when the
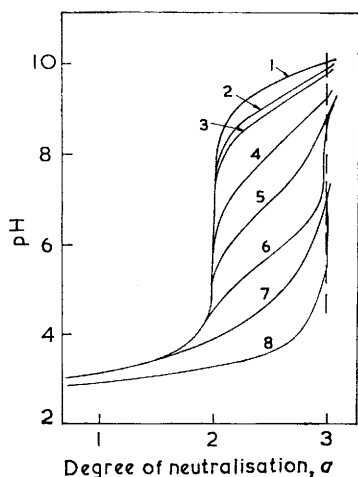

FIG. 2. Titration curves for uramildiacetic acid, alone and in the presence of various univalent and bivalent ions.

1, NMe$_4$NO$_3$. 2, K$^+$ (100 : 1). 3, Na$^+$ (10 : 1). 4, Li$^+$ (1 : 1). 5, Tl$^+$ (1 : 1). 6, LiBr. 7, Mg^{2+}. 8, Be^{2+}.
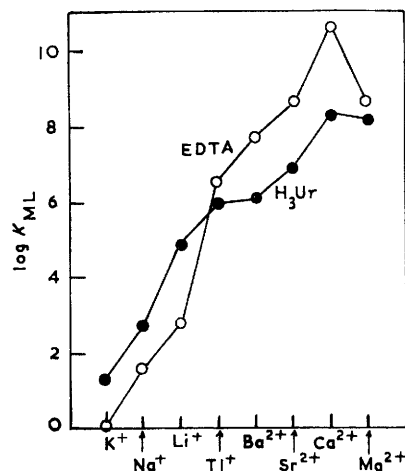
FIG. 3. A comparison of the stabilities of complexes of metals with uramildiacetic acid (filled circles) with those of ethylene-diaminetetra-acetic acid (open circles). Data valid for 20° and $\mu = 0.1$M. Values for alkaline-earth complexes from ref. 8. Values for EDTA from ref. 2.

solution is saturated with respect to thallous iodide and lead iodide is just about to be precipitated,

$$r = \frac{\text{Total concentration of lead in solution}}{\text{Total concentration of thallium in solution}}$$

$$= \frac{[\text{Pb}] + [\text{PbL}]}{[\text{Tl}] + [\text{TlL}]} = \frac{K_{PbI_2(sol.)}}{[\text{I}^-]K_{TlI(sol.)}} \cdot \frac{(1 + K_{PbL}[\text{L}])}{(1 + K_{TlL}[\text{L}])}.$$

It follows that the separation will be improved by (a) decreasing [I$^-$], (b) increasing [L], and (c) making the *ratio* of stability constants K_{PbL}/K_{TlL} as large as possible. Although replacing EDTA by uramildiacetic acid does effect a small decrease in K_{TlL} there is a disproportionately larger decrease in the *ratio* of stability constants from $10^{11.8}$ to 10^6.

Although our (unpublished) results for the stability constants of complexes of bivalent metals with uramildiacetic acid are consistently slightly higher than those reported by Schwarzenbach *et al.*,[5] there is no question that all such complexes are weaker than those formed by the corresponding ion and EDTA. This is not surprising since EDTA acts normally as a quinquedentate or sexidentate ligand, whereas uramildiacetic acid appears (from an examination of models) to act as a ter- or quadri-dentate ligand although the possibility of both the 4- and the 6-oxygen atom's being involved together with the terdentate grouping $-$N(CH$_2$·CO$_2$H)$_2$ cannot quite be excluded. It is therefore all the

[10] Přibil, *Coll. Czech. Chem. Comm.*, 1951, **16**, 86.

more remarkable that the complexes of univalent thallium with both EDTA and uramildiacetic acid are so similar in strength, and that EDTA forms weaker complexes than uramildiacetic acid with the other univalent ions of lithium, sodium, and potassium (Fig. 3). The complex of EDTA with silver (log $K_{AgY} = 7\cdot11$) is a little stronger than that with thallium(I). We were, however, unable to study complex formation between silver ions and uramildiacetic acid, for mixtures of the components rapidly decomposed.

On the hypothesis that in contrast to the behaviour of EDTA the structure of uramildiacetic acid might favour the chelation of small ions, or ions preferring tetrahedral co-ordination, we have made a preliminary study of its reaction with beryllium(II). The titration curve (Fig. 2) indicates much stronger complex-formation than in the case of magnesium and we find log $K_{BeUr} = 10\cdot36$. Beryllium is often supposed not to form a complex with EDTA, and this complexone is commonly used to mask other elements in the separation and determination of beryllium.[11] Unlike all other bivalent ions, its hydroxide can be precipitated by aqueous ammonia in the presence of EDTA. However, the fact that a large excess of ammonia must be added for complete precipitation suggests that a complex does exist, and recent work on the extraction of beryllium from aqueous solutions of EDTA by a 0·1M-solution of 8-hydroxyquinoline in chloroform is reported [12] to yield $K_{BeY} = 9\cdot27$, a stability greater than that for the magnesium complex (8·7) and approaching that for the most stable complex of the alkaline-earth metals, *viz.*, calcium (log $K_{CaY} = 10\cdot26$).[2] The greater sequestering effect of uramildiacetic acid must depend partly on the higher stability of the beryllium complex and partly on the smaller value of the last dissociation constant of this ligand ($pK_3 = 9\cdot63$) compared with that of EDTA ($pK_4 = 10\cdot26$) which makes a relatively higher concentration of the free ligand, Ur^{3-}, available for complex-formation at a pH below that at which competition between beryllium and hydroxyl ions leads to precipitation. The analytical potentialities of this reaction are under investigation.

TABLE 5.

The variation with temperature of the acid dissociation constants and metal stability constants of uramildiacetic acid at 0·1M-ionic strength.

Temperature (c)	20°	27°	34°	39°
Hydrogen, pK_1	1·7 ± 0·3	1·82	1·90	2·21
pK_2	2·67 ± 0·02	2·83	2·88	2·90
pK_3	9·63 ± 0·03	9·47	9·38	9·31
Lithium	4·90 ± 0·02	4·70	4·57	4·60
Sodium	2·72 ± 0·01	2·54	2·42	
Potassium	1·23 ± 0·03	1·00	0·81	0·70
Thallium	5·99 ± 0·02	5·76	5·41	5·33

Plots of log K_{ML} against $1/T°$ (absolute) were sensibly linear and led to the thermodynamic parameters summarized in Table 6.

To throw light on the unusually high stability of complexes of uramildiacetic acid with univalent ions we have made a preliminary study of the thermodynamics of the reactions by using data calculated from values for the stabilities of proton- and metal-complexes obtained by potentiometric titrations at a series of temperatures. Although it was appreciated that the accuracy would be much below that of measurements in which the enthalpy changes are obtained by direct calorimetry, it was hoped that at least the sign and approximate magnitude of the enthalpy and entropy terms could be established. The results of the measurements are summarized in Table 5.

The most striking result is that all the metal complexes are stabilized by a negative enthalpy change and that the entropy changes are invariably opposed to complex formation. Although the stabilization by the favourable enthalpy change increases in the

[11] Schwarzenbach, " Complexometric Titrations," trans. Irving, Methuens, London, 1957, p. 89.
[12] Starý, *Analyt. Chim. Acta*, in the press.

order $Li^+ < Na^+ < K^+$, the opposing entropy effect increases in the same order but more rapidly, thus leading to the reversal of order of stabilities. The stability of many 1 : 1 metal complexes is due to a favourable (positive) net entropy change resulting from the circumstances that the entropy increase due to the liberation of water from the hydrated cation and the hydrated ligand on complex-formation exceeds the concomitant loss in configurational entropy of the ligand and that due to the reduction in the number of reacting molecules (from two to one). It is significant that the net entropy change with complexes of uramildiacetic acid is almost zero for the heavily hydrated lithium ion and that unfavourable values of ΔS are most negative with the largest ions (K^+ and Tl^+), which will be the least hydrated. The loss of configurational entropy when the anion, Y^{4-}, of EDTA forms a metal complex would be expected to be greater than that with the simpler and less flexible anion Ur^{3-}, and consequently ΔS for the overall reaction with any particular cation should be more negative: provided the enthalpy changes were of the same magnitude this could explain or at least contribute to the lower stability of complexes of EDTA.

The sum $\Delta S + S^\circ$ of the entropy change in the reaction and the standard entropy, S°, of the hydrated cation is a measure of the entropy, S_{ML}°, of the 1 : 1 complex since it differs from this only by a constant term, S_L°, the entropy of the anionic species Ur^{3-} itself.[13] This sum might well be expected to be constant for all cations if the ligand formed a cage-like structure completely enveloping the metal and thus forming complexes having the same tendency to solvate: alternatively, a progressive variation with ionic radius might occur. Certainly $\Delta S + S^\circ$ decreases with ionic radius, r, for hydrogen and the alkali metals, but the position of Tl^+ is anomalous. Care and Staveley [13] noted similar anomalies between pairs of ions of comparable size and charge (*e.g.*, Sr^{2+} and Pb^{2+}) when discussing complexes of EDTA and point out that the thermodynamic properties of complexes can scarcely be determined by size factors alone but must depend on the nature of the interaction between the metal ion and the nitrogen and oxygen atoms of the ligand. Thus the ligational enthalpy changes (Table 6) are roughly a linear function (not reproduced) of

TABLE 6.

Thermodynamic data for reactions of uramildiacetic acid with univalent ions.

Ion	$-\Delta G$ (20°)	$-\Delta H$	ΔS	S°	$\Delta S + S^\circ$	r (Å)
Hydrogen	12.89 ± 0.05	6.9	$+19 \pm 2$	0.0	19 ± 2	—
Lithium	6.55 ± 0.04	7.0	-1 ± 5	3.4	2 ± 5	0.60
Sodium	3.64 ± 0.02	8.7	-18 ± 2	14.4	-4 ± 2	0.95
Potassium	1.65 ± 0.04	11.8	-35 ± 2	24.5	-10 ± 2	1.33
Thallium	8.02 ± 0.03	15.4	-25 ± 4	30.4	5 ± 4	1.44

$1/r$, save in the case of Tl^+ for which complex formation is more exothermic than would be expected purely from its radius. However, the electronic structure of this ion is such as to produce greater deforming power than an alkali-metal cation of the same radius, and the greater stability of its complexes than of those of potassium can then be correlated with the greater enthalpy decrease on complex-formation. That thallium(i) has a greater tendency than the alkali metals to form bonds to nitrogen is an additional reason why all the univalent ions cannot be treated as a single series.

EXPERIMENTAL

Preparation of the Acid Sodium Salt, NaH_5Ur_2,H_2O.—Chloroacetic acid (20 g., 0·21 mole), previously neutralized with 5N-sodium hydroxide was added to uramil (10 g., 0·07 mole) and 5N-sodium hydroxide (14·0 ml., 0·07 mole), whereupon a light red suspension was obtained which was heated to boiling. 5N-Sodium hydroxide (28 ml., 0·14 mole) was added at such a rate that the pH remained between 8 and 10 (30 min.). The reaction was quite rapid during

[13] Care and Staveley, *J.*, 1956, 4571.

the first 15 min. and most of the solid dissolved. After all the base had been added a light orange solution was obtained and no change in alkalinity was observed even at the b. p. during the next 10 min.

This solution (A) was cooled in an ice–salt mixture and acidified with concentrated hydrochloric acid (20 ml.). The solid that separated was collected and recrystallized from hot water (60 ml.), a white product being obtained (12·58 g., 70%) which became red if left in moist air.

After two further recrystallizations from water, the product (B) was titrated with carbonate-free potassium hydroxide solution, alone and in the presence of zinc ions (Fig. 1). The titration curves were not changed after material B had been repeatedly recrystallized from water (Found: C, 34·8; H, 3·6; N, 14·9; Na, 4·1. $C_{16}H_{17}O_{14}N_6Na,H_2O$ requires C, 34·4; H, 3·4; N, 15·0; Na, 4·1%).

Preparation of Uramildiacetic Acid (I; H_3Ur).—Sodium ions were removed from an aqueous solution of material B by passage through a cation-exchange resin in the hydrogen-ion form. Concentration of the effluent gave pure uramildiacetic acid. This was obtained more conveniently by recrystallization of material B from dilute perchloric acid, or directly from the solution A by the addition of a large excess of acid. Recrystallization was best effected from dilute perchloric acid. Neither the *product* nor its aqueous solution showed changes of colour on being kept [Found: C, 37·1; H, 3·6; N, 15·95%; M (by titration), 259. $C_8H_9O_7N_3$ (*i.e.*, H_3Ur) requires C, 37·1; H, 3·5; N, 16·2%; M, 259·2].

Tetramethylammonium Hydroxide and Nitrate.—The preparation of carbonate-free tetramethylammonium hydroxide was based on that devised by Schwarzenbach and Biedermann for the preparation of the carbonate-free solutions of potassium hydroxide.[14] Freshly precipitated silver oxide was carefully washed with boiling de-ionized water and allowed to react with a little less than the equivalent amount of tetramethylammonium iodide dissolved in boiled-out water in an apparatus from which carbon dioxide could be excluded. After being shaken for 2 hr. the mixture was filtered in the same apparatus through sintered glass; a clear solution of tetramethylammonium hydroxide was then obtained. This was shown to be absolutely free from carbonate.

Tetramethylammonium nitrate was prepared by neutralization of the hydroxide with " AnalaR " nitric acid, followed by concentration of the solution until crystallization occurred. The crystals were collected and recrystallized twice from 80% alcohol.

After a preliminary standardization the solution of carbonate-free tetramethylammonium hydroxide was made up to 0·1M with respect to cations by adding the calculated amount of tetramethylammonium nitrate.

The absence of silver and other metals in both reagents was verified by testing them with diphenylthiocarbazone.

De-ionized Water.—Laboratory distilled water was passed through a mixed-bed ion-exchange resin.

Metal Solutions.—All the metal salts were of " AnalaR " grade. Laboratory lithium bromide was recrystallized several times from water; the concentration of its solutions was determined by the Volhard method.

Titration Technique.—Titrations of the ligand acid (100 ml.; concentration C_A) in the presence of potassium, sodium, or tetramethylammonium nitrates (10 ml. of 1·200M-solution) and either metal salt solution (10 ml.; concentration C_M) or water (10 ml.) were carried out potentiometrically with carbonate-free tetramethylammonium hydroxide solution. The hydrogen-ion concentration was measured with the aid of a " Radiometer " pH-meter type PHM4 with a glass electrode and a saturated calomel reference electrode. Both the titration and the reference electrode vessels were thermostatically controlled at 20° by circulating water through a jacket, and a Laitinen type of bridge was used. The glass electrode was calibrated by titrating a solution of perchloric acid in 0·1M-potassium nitrate; the deviation in the low-pH zone was less than 0·004 pH unit. For higher pH values the electrode was tested by using it to determine the last dissociation constant of various polybasic acids. *o*-Carboxyphenylimino-diacetic acid, nitrilotriacetic acid, and ethylenediaminetetra-acetic acid were used to cover the pH range 6·5—10·5. The values obtained were, respectively, 7·754, 9·74, and 10·25 which agree well with those previously reported in the literature for the same experimental conditions.

The third dissociation constant of uramildiacetic acid and the stability constants of its

[14] Schwarzenbach and Biedermann, *Helv. Chim. Acta*, 1948, **31**, 331.

lithium complexes were determined with tetramethylammonium nitrate to provide the salt background; with thallium(I), both tetramethylammonium and potassium nitrate were used with the same results. For lithium and thallium the molar ratio of acid to metal was 1 : 1. For sodium and potassium the ratio 1 : 100 was used and consequently the determinations were carried in a medium consisting of 0·1M-sodium and -potassium nitrate, respectively. To prove that changes in this ratio did not introduce systematic errors due to differences in junction potentials or in activity coefficients, and that the low value of $\bar{n}$ obtained did not adversely affect the subsequent calculation, complex-formation with sodium was studied also with a molar ratio of 1 : 10. Similar experiments were carried out with the more unfavourable case of lithium bromide. The two calculated constants were 4·90 ± 0·02 (from the titration of 0·001M-Li$^+$ and 0·001M-ligand in 0·0999M-tetramethylammonium nitrate) and 4·87 ± 0·03 (from the titration of 0·001M-ligand in 0·100M-lithium bromide); the difference is within the experimental error. This result was confirmed with other ligands.

The following titration results are typical of those performed at various temperatures.

Titration of uramildiacetic acid alone at 20° in 0·1M-KNO$_3$. $C_A = 1\cdot078 \times 10^{-3}$. The degree of neutralization (the ratio of the number of mols. of alkali added per mol. of acidic ligand is denoted by the symbol a.

a	0·0	0·206	0·412	0·619	0·825	1·031	1·237	1·443	1·650	1·753	1·856	1·959	2·062
pH	2·845	2·897	2·952	3·018	3·095	3·183	3·295	3·440	3·660	3·825	4·090	7·784	8·504

Titration of uramildiacetic acid, $C_A = 9\cdot768 \times 10^{-4}$M in the presence of various metals added as solutions of concentration C_M. Temperature 20°. With the dilute solutions of lithium, sodium, and thallium, tetramethylammonium nitrate was present to bring the ionic strength up to 0·1M.

Ion	C_M	pH values at various degree of neutralization, a								
*	0	8·290	8·885	9·175	9·378	9·545	9·690	9·820	9·944	10·057
K$^+$	1·200	7·674	8·458	8·780	9·005	9·187	9·352	9·525	9·688	9·850
Na$^+$	1·200	6·540	7·230	7·560	7·800	8·003	8·204	8·418	8·678	9·010
Li$^+$	1·200	4·629	5·038	5·321	5·555	5·762	5·975	6·210	6·531	7·254
Li$^+$	0·0108	6·450	7·100	7·468	7·768	8·050	8·325	8·610	8·875	9·180
Tl$^+$	0·010	5·490	6·080	6·432	6·741	7·015	7·317	7·676	8·153	8·810
	a	2·045	2·159	2·272	2·386	2·500	2·613	2·727	2·840	2·954

* 0·1M-(NMe$_4$)NO$_3$ only.

Ion	C_M	($C_A = 9\cdot670 \times 10^{-4}$M)								
Na$^+$	0·100	7·650	8·160	8·450	8·662	8·840	9·000	9·157	9·310	9·470
	a	2·068	2·167	2·265	2·364	2·462	2·561	2·659	2·758	2·856

THE DEPARTMENT OF INORGANIC AND STRUCTURAL CHEMISTRY,
THE UNIVERSITY OF LEEDS.