593. *Acid Dissociation Constants of the Ammonium Group in 2-Aminoethanol, 2-Aminoethyl Phosphate, and 2-Aminoethyl Sulphate.*

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The thermodynamic acid dissociation constants of the ammonium group in 2-aminoethanol, 2-aminoethyl phosphate, and 2-aminoethyl sulphate * have been determined from e.m.f. measurements in cells without liquid junction, by using hydrogen and silver–silver, chloride electrodes, at 5°, 15°, 25°, 35°, and 45°. Equations in temperature have been fitted to the results and the thermodynamic quantities associated with these dissociations evaluated and critically compared. An attempt is made to divide them into " environmental " and " non-environmental " components and to interpret the former in terms of the electrostatic interactions between the solute species and water.

After our investigation of the first two dissociations of 2-aminoethyl dihydrogen phosphate[1] it was of interest to extend this work to the third dissociation of this compound (ammonium group) and to related compounds, so that the effect of esterification of 2-aminoethanol with groups of various charge types could be investigated. Consequently chloride-containing buffer solutions of these compounds were used in cells without liquid junction of the type:

$$\text{Pt, H}_2\text{ (1 atm.)}|\text{R·NH}_3^+\ (m_1),\ \text{R·NH}_2\ (m_2),\ m_{\text{Cl}^-}|\text{AgCl,Ag} \qquad (1)$$

where m_1, m_2, and m_{Cl^-} are molal concentrations. From the e.m.f.'s of these cells, values of pwH were derived:

$$\text{pwH} = [F(E - E_0)/\boldsymbol{R}T \ln 10] + \log m_{\text{Cl}^-} = -\log a_{\text{H}^+}\gamma_{\text{Cl}^-}. \qquad (2)$$

The values of pK_a are related to pwH as follows:

$$\text{p}K_a = \text{pwH} + \log \frac{m_{\text{R·NH}_3^+}}{m_{\text{R·NH}_2}} + \log \frac{\gamma_{\text{R·NH}_3^+}\gamma_{\text{Cl}^-}}{\gamma_{\text{R·NH}_2}}, \qquad (3)$$

where the activity coefficient term is represented by[2]

$$-\log \frac{\gamma_{\text{R·NH}_3^+}\gamma_{\text{Cl}^-}}{\gamma_{\text{R·NH}_2}} = \Sigma z_i^2 A I^{\frac{1}{2}} + BI + CI^{\frac{3}{2}}, \qquad (4)$$

where Σz_i^2 is the sum of the squares of the charges on the ionic species in the numerator of the left-hand side of eqn. (4) minus the square of the charge on the species in the denominator. Σz_i^2 is +2 for 2-aminoethanol, 0 for 2-aminoethyl sulphate, and −2 for 2-aminoethyl phosphate. Corrections were applied for the hydrolysis of the basic species

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* In this paper 2-aminoethyl phosphate and 2-aminoethyl sulphate are used to include all the ionic species of 2-aminoethyl dihydrogen phosphate and 2-aminoethyl hydrogen sulphate present in any given solution.

[1] Clarke, Datta, and Rabin, *Biochem. J.*, 1955, **59**, 209.

and for complex-formation with silver ions where necessary.[2] The hydroxide-ion concentration was calculated from: $m_{\mathrm{OH^-}} = \text{antilog}\,[\mathrm{pwH} - \mathrm{p}K_{\mathrm{w}}]$, where $\mathrm{p}K_{\mathrm{w}}$ is the negative logarithm of the ion product of water calculated from Robinson and Stokes's equation.[3] The stability constants for the silver complexes were taken from an earlier paper.[4]

The thermodynamic value of $\mathrm{p}K_a$ was found by extrapolating to zero ionic strengths the function

$$y = \mathrm{pwH} + \log \frac{m_{\mathrm{R\cdot NH_3^+}}}{m_{\mathrm{R\cdot NH_2}}} - \Sigma z_i^2 A I^{\frac{1}{2}} = \mathrm{p}K_a - BI - CI^{\frac{3}{2}}, \qquad (5)$$

which is obtained by combining eqns. (3) and (4). The constants B and C are empirical parameters. The extrapolation was carried out by fitting experimental values of y to the above equation by least squares. The thermodynamic $\mathrm{p}K_a$'s were fitted to the Harned and Robinson equation [5]:

$$\mathrm{p}K_a = A/T - D + CT, \qquad (6)$$

from which the thermodynamic quantities associated with the ionisations were then derived in the usual way.

RESULTS AND DISCUSSION

The e.m.f.'s, the molalities, the ionic strengths, and the extrapolation functions y from eqn. (6) are given in Tables 1—3. The observed and the calculated values of $\mathrm{p}K_a$, the constants of eqns. (5) and (6), and the standard errors are collected in Tables 4—6. The thermodynamic functions, including those for taurine,[6] are in Table 7. The dissociation constants of 2-aminoethanol between 0° and 50° were determined by Bates and Pinching; [7] the constants were redetermined in the present investigation to see whether our method of extrapolation, for buffer solutions containing an additional salt, would give the same values. We used the hydrochloride partly neutralised with sodium hydroxide so that a certain amount of sodium chloride was present, whereas in Bates and Pinching's work pure base neutralized with hydrochloric acid was employed. This is important because, with the other compounds investigated here, it is inevitable that another salt is present. The error [8] is about the same in the two sets of results and amounts to $\pm 0{\cdot}004$ pK unit. As the maximum difference between the calculated values from the two sets is 0·005 pK unit, the agreement is satisfactory.

When our results are extrapolated to zero ionic strength with the full Debye–Hückel equation to represent the activity coefficient term, the parameter for the closest approach of the ions (a^*), found by minimising the variance about the extrapolation lines, lies between 0 and the impossible value of -5 at 45°. This compares with $a^* = 1$ found by Bates and Pinching. For our results, the thermodynamic pK's found by using the Debye–Hückel equation with $a^* = 0$ (*i.e.*, the limiting law) are much higher than those found from eqn. (5), by between 0·004 and 0·015 pK unit. Both methods of extrapolation appear to fit the results almost equally. For instance, for our results at 25°, the variance about the line of eqn. (5), $\Sigma\Delta^2/(n-3)$, is $2{\cdot}15 \times 10^{-6}$, where Δ is the difference between the experimental value at a given ionic strength and the value predicted by the equation and n is the number of points; while for the line obtained by using the Debye–Hückel equation the minimum value for the variance about the line, $\Sigma\Delta^2/(n-2)$, is $2{\cdot}60 \times 10^{-6}$. The errors of the intercepts, calculated by standard statistical methods, are $\pm 0{\cdot}003_9$ and

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[2] Datta and Grzybowski, *Trans. Faraday Soc.*, 1958, **54**, 1179.

[3] Robinson and Stokes, " Electrolyte Solutions," Butterworths Scientific Publ., London, 1955, p. 496.

[4] Datta and Grzybowski, *J.*, 1959, 1091.

[5] Harned and Robinson, *Trans. Faraday Soc.*, 1940, **36**, 973.

[6] King, *J. Amer. Chem. Soc.*, 1953, **75**, 2204.

[7] Bates and Pinching, *J. Res. Nat. Bur. Stand.*, 1951, **46**, 349.

[8] Please, *Biochem. J.*, 1954, **56**, 196.

TABLE 1.

2-Aminoethanol: molalities and ionic strengths of solutions, e.m.f.'s of cell (1) (abs.v) and extrapolation functions y [eqn. (5)].

m_1 = molality of 2-aminoethanol hydrochloride; m_2 = molality of KOH;
$y = \text{pwH} + \log(m_1 - m_2 + m_{\text{OH}^-})/(m_2 - m_{\text{OH}^-})$; $I = m_1 + m_{\text{OH}^-}$.

	10^2m_1	2·0747	2·5939	3·2378	3·7093	4·3657	5·0094$_9$	5·5829$_5$	6·2961$_5$	7·4018	8·0371$_5$	8·3030
	10^2m_2	0·9229	1·1538	1·4402	1·6499$_5$	1·9419	2·2283	2·4834	2·8006	3·2924	3·5750	3·6933
Temp.												
5°	10^5E	88 805	88 363	87 923	87 634	87 308$_5$	87 044	86 822$_5$	86 590	86 264	86 115$_5$	86 053
	y	10·2655	10·2820	10·2983	10·3048	10·3164	10·3281	10·3349	10·3449	10·3560	10·3648	10·3677
	10^2I	2·077	2·597	3·241	3·712	4·369	5·013	5·586	6·299	7·405	8·041	8·306
15	10^5E	88 736	88 277	87 827	87 531	87 188	86 921	86 685	86 447	86 113	85 954	85 887
	y	9·9391	9·9554	9·9726	9·9797	9·9902	10·0031	10·0088	10·0193	10·0310	10·0389	10·0413
	10^2I	2·078	2·597	3·241	3·713	4·369	5·013	5·587	6·300	7·406	8·041	8·307
25	10^5E	88 603	88 131	87 662$_5$	87 357	87 004	86 728	86 482	86 238	85 893$_5$	85 728	85 657
	y	9·6346	9·6513	9·6680	9·6752	9·6860	9·6989	9·7043	9·7151	9·7270	9·7347	9·7368
	10^2I	2·078	2·598	3·242	3·713	4·370	5·014	5·587	6·300	7·406	8·042	8·307
35	10^5E	88 409	87 925	87 439	87 125	86 763	86 475	86 224	85 972	85 613	85 439	85 368
	y	9·3493	9·3666	9·3829	9·3904	9·4017	9·4141	9·4200	9·4309	9·4423	9·4495	9·4520
	10^2I	2·078	2·598	3·242	3·713	4·370	5·014	5·587	6·301	7·406	8·042	8·308
45	10^5E	88 135	87 661$_5$	87 154$_5$	86 839$_5$	86 471	86 166$_5$	85 908	85 652$_5$	85 289	85 089	85 034$_5$
	y	9·0783	9·0998	9·1153	9·1242	9·1363	9·1476	9·1536	9·1652	9·1777	9·1817	9·1872
	10^2I	2·079	2·598	3·242	3·714	4·370	5·014	5·588	6·301	7·407	8·042	8·308

TABLE 2.

2-Aminoethyl phosphate: molalities and ionic strengths of solutions, e.m.f.'s of cell (1) (abs.v), and extrapolation functions y [eqn. (5)].

m_1 = molality of 2-aminoethyl dihydrogen phosphate; m_2 = molality of NaOH; m_3 = molality of KCl;
$y = \text{pwH} + \log(2m_1 - m_2 + m_{\text{OH}^-})/(m_2 - m_1 - m_{\text{OH}^-})$; $I = 2m_2 - m_1 + m_3 - m_{\text{OH}_5}$.

Set I.

	10^2m_1	0·4023	0·5547	0·7236	0·3981	0·5525	0·7226	0·9191	1·1754	1·2823	1·4697
	10^2m_2	0·5371	0·7406	0·9661	0·5315⁻	0·7376	0·9647	1·2271	1·5693	1·7120	1·9621
	10^2m_3	0·7940	1·0948	1·4282	0·7857	1·0905	1·4262	1·8141	2·3200	2·5309	2·9006
Temp.											
5°	10^5E	94 545	93 180	93 811	94 565	93 825	93 202	92 614	92 027	91 812	91 458
	y	11·14455	11·13571	11·12754	11·14411	11·13700	11·13103	11·12195	11·11696	11·11411	11·10673
	10^2I	1·45499	2·00977	2·62319	1·43924	2·00180	2·62145	3·33769	4·27170	4·66117	5·34394
15	10^5E	94 715	93 970	93 326	94 735	93 985	93 349	92 743	92 141	91 915	91 554
	y	10·83310	10·82486	10·81641	10·83261	10·82607	10·82016	10·81039	10·80554	10·80178	10·79498
	10^2I	1·45261	2·00777	2·62319	1·43737	1·99980	2·61939	3·33562	4·26959	4·65908	5·34184
25	10^5E	94 855	94 098	93 440	94 881	94 115	93 463	92 839	92 219	91 987	91 616
	y	10·54872	10·54057	10·53196	10·54936	10·54210	10·53563	10·52516	10·51985	10·51611	10·50933
	10^2I	1·45079	2·00582	2·62118	1·43551	1·99784	2·61736	3·33358	4·26753	4·65702	5·33978
35	10^5E	94 967	94 201	93 526	94 994	94 213	93 548	92 902	92 268	92 028	91 648
	y	10·28780	10·28034	10·27108	10·28858	10·28090	10·27446	10·26261	10·25758	10·25351	10·24690
	10^2I	1·44909	2·00397	2·61927	1·43381	1·99602	2·61545	3·33169	4·26558	4·65508	5·33783
45	10^5E	95 033	94 265	93 579	95 076	94 281	93 605	92 936	92 285	92 036	91 656
	y	10·04416	10·03897	10·03023	10·04794	10·04020	10·03426	10·02096	10·01573	10·01119	10·00629
	10^2I	1·44769	2·00237	2·61758	1·43232	1·99440	2·61373	3·32998	4·26383	4·65334	5·33603

	10^2m_1	1·6558	1·8451	2·0047	2·1315	2·3096	2·5540
	10^2m_2	2·2106	2·4633	2·6764	2·8457	3·0835	3·4098
	10^2m_3	3·2680	3·6416	3·9566	4·2069	4·5584$_8$	5·0409
Temp.							
5°	10^5E	91 153		90 675	90 513	90 300	90 062
	y	11·10141		11·09540	11·09196	11·08734	11·08701
	10^2I	6·02234		7·29374	7·75603	8·40514	9·29574
15	10^5E	91 238	90 947	90 742	90 578	90 356	90 111
	y	10·78933	10·78367	10·78271	10·77983	10·77480	10·77458
	10^2I	6·02026	6·71009	7·29169	7·75397	8·40310	9·29370
25	10^5E	91 290	90 991	90 779	90 610	90 381	90 125
	y	10·50351	10·49793	10·49682	10·49394	10·48886	10·48805
	10^2I	6·01821	6·70805	7·28964	7·75193	8·40107	9·29168
35	10^5E	91 308	91 007	90 786	90 613	90 373	90 111
	y	10·24024	10·23578	10·23418	10·23145	10·22567	10·22513
	10^2I	6·01630	6·70610	7·28770	7·74999	8·39917	9·28976
45	10^5E	91 274	90 989	90 765	90 585	90 325	90 063
	y	9·99416	9·99378	9·99271	9·98964	9·98170	9·98243
	10^2I	6·01472	6·70435	7·28593	7·74823	8·39751	9·28804

TABLE 2 (*continued*)

Set II.

	10^2m_1	0·3909	0·4600	0·5752	0.7486	1·1339	1·5081	1·9004	0·6825	0·9385	1·3301
	10^2m_2	0·6267	0·7374$_9$	0·9222	1·2001	1·8178	2·4178	3·0457	1·0942	1·5046	2·1324
	10^2m_3	0·3908	0·4599	0·5752$_7$	0·7484$_9$	1·1337	1·5079	1·9002	0·6824	0·9384	1·3299$_6$
Temp.											
5°	10^6E	98 519	98 209	97 751	97 198	96 260	95 594	95 038	97 394$_8$	96 683	95 883
	y	11·15528	11·15375	11·14763	11·14218	11·12777	11·11836	11·10964	11·14425	11·13238	11·12114
	10^2I	1·22415	1·44487	1·81335	2·36823	3·60313	4·80312	6·06121	2·15665	2·97706	4·23243
15	10^5E	98 783	98 467	98 000	97 447	96 496	95 817	95 247	97 645	96 927	96 109
	y	10·84435	10·84175	10·83457	10·83014	10·81618	10·80673	10·79800	10·83214	10·82097	10·80905
	10^2I	1·21997	1·44048	1·80869	2·36314	3·59758	4·79736	6·05534	2·15168	2·97169	4·22681
25	10^5E	99 018	98 699$_5$	98 226	97 666	96 699	96 004	95 422	97 864$_7$	97 139	96 303
	y	10·56029	10·55748	10·54961	10·54519	10·53093	10·52108	10·51224	10·54684	10·53604	10·52352
	10^2I	1·21602	1·43626	1·80417	2·35823	3·59222	4·79178	6·04964	2·14693	2·96651	4·22134
35	10^5E	99 224$_5$	98 904	98 420	97 855	96 877	96 164$_8$	95 568	98 055	97 321	96 469
	y	10·29884	10·29649	10·28724	10·28334	10·26976	10·25911	10·25007	10·28450	10·27416	10·26140
	10^2I	1·21250	1·43243	1·80011	2·35373	3·58716	4·78655	6·04428	2·14261	2·96174	4·21624
45	10^5E	99 398	99 079$_6$	98 582	98 018	97 011	96 286	95 684$_8$		97 476	96 598
	y	10·05595	10·05487	10·04420	10·04210	10·02638	10·01604	10·00857		10·03324	10·01856
	10^2I	1·20959	1·42919	1·79669	2·34978	3·58296	4·78207	6·03947		2·95750	4·21185

TABLE 3.

2-Aminoethyl sulphate: molalities and ionic strengths of solutions, e.m.f.'s of cell (1), and extrapolation functions y [eqn. (5)].

m_1 = molality of 2-aminoethyl hydrogen sulphate; m_2 = molality of NaOH; m_3 = molality of KCl; $y = \text{pwH} + \log(m_1 - m_2 + m_{\text{OH}^-})/(m_2 - m_{\text{OH}^-})$; $I = m_2 + m_3$.

	10^2m_1	0·9044$_8$	1·0591	1·3968	1·7798	2·2487	2·7750	3·1477
	10^2m_2	0·4307	0·5043	0·6651	0·8475	1·0708	1·3214$_9$	1·4989
	10^2m_3	0·4762	0·5576	0·7354	0·9371	1·1839	1·4611	1·6573
	10^2I	0·9069	1·0619	1·4006	1·7846	2·2548	2·7826	3·1562
Temp.								
5°	y	9·77110	9·77376	9·77416	9·77641	9·78011	9·78286	9·78533
	10^5E	89 904	89 542	88 883	88 316	87 777	87 289	87 001
15	y	9·46961	9·47269	9·47261	9·47452	9·47876	9·48106	9·48321
	10^5E	90 014	89 642	88 957	88 368	87 813	87 305	87 005
25	y	9·18880	9·19252	9·19264	9·19404	9·19880	9·20065	9·20237
	10^5E	90 063	89 682	88 975	88 363	87 792	87 264	86 951
35	y	8·92644	8·93089	8·93138	8·93348	8·93736	8·93965	8·94092
	10^5E	90 055	89 666	88 938	88 310	87 715	87 172	86 846
45	y	8·68142	8·68703	8·68781	8·68928	8·69289	8·69523	8·69545
	10^5E	89 995	89 601	88 852	88 200	87 584	87 024	86 681

	10^2m_1	3·5495	4·0149$_7$	4·5894	4·8755	5·3189	5·7574	6·2274$_8$
	10^2m_2	1·6903	1·9119$_6$	2·1854$_9$	2·3218	2·5329	2·7417	2·9656
	10^2m_3	1·8689	2·1139	2·4164	2·5670	2·8004$_7$	3·0314	3·2788
	10^2I	3·5592	4·0259	4·6018	4·8888	5·3334	5·7731	6·2444
Temp.								
5°	y	9·78525	9·78798	9·78966	9·79178	9·79208	9·79184	9·79490
	10^5E	86 713	86 433	86 122	85 989	85 782	85 591	85 420
15	y	9·48355	9·48608	9·48757	9·48935	9·48990	9·48976	9·49251
	10^5E	86 709	86 418	86 095	85 955	85 742	85 545	85 366
25	y	9·20339	9·20577	9·20764	9·20850	9·20912	9·20896	9·21177
	10^5E	86 649	86 347	86 015	85 865	85 645	85 441	85 256
35	y	8·94228	8·94386	8·94608	8·94663	8·94791	8·94789	8·95025
	10^5E	86 536	86 219	85 878	85 721	85 498	85 288	85 094
45	y	8·69778	8·69925	8·70142	8·70072	8·70367	8·70409	8·70598
	10^5E	86 367	86 039	85 687	85 517	85 297	85 083	84 880

TABLE 4.

2-Aminoethanol: the constants B and C of eqn. (5) and the values of pK_a.

pK_a (obs.) was obtained from eqn. (5), pK_a (calc.) from eqn. (6); pK_a (Bates) are the values quoted by Bates and Pinching.[7] pK_a (calc.) = $2309{\cdot}66/T + 2{\cdot}9209 - 0{\cdot}0039152T$; $\sigma_{\text{av.}}$ is the average standard error of the intercepts [pK_a (obs.)] of eqn. (5) and V (log K) is the variance about the curve of eqn. (6); Δ = pK_a (calc.) − pK_a (obs.).

Temp.	pK_a (obs.)	$10^4\sigma$	B	C	pK_a (calc.)	$10^4\Delta$	pK_a (Bates)
5°	10·1362	39	0·385	0·888	10·135	−10	10·133
15	9·8062	40	0·270	1·311	9·808	+17	9·803
25	9·4994	39	0·270	1·410	9·500	+5	9·496
35	9·2117	36	0·252	1·577	9·209	−23	9·209
45	8·9336	55	−0·216	2·936	8·935	+11	8·940
		av. 42			$\surd[V (\log K)] = 2{\cdot}3 \times 10^{-3}$.		$\surd[V (\log K)] = 1{\cdot}3 \times 10^{-3}$.

TABLE 5.

2-Aminoethyl phosphate: the constants B and C of eqn. (5) and the values of pK_a (third dissociation).

pK_a (obs.) was obtained from eqn. (5) and pK_a (calc.) from eqn. (6).

pK_a (calc.) = $2998{\cdot}17/T - 1{\cdot}3841 + 0{\cdot}0065963T$; $\sigma_{\text{av.}}$ is the average standard error of the intercepts [pK_a (obs.)] of eqn. (5), and V (log K) is the variance about the curve of eqn. (6); Δ = pK_a (calc.) − pK_a (obs.).

Temp.		pK_a (obs.)	$10^4\sigma$	B	C	pK_a (calc.)	$10^4\Delta$
5°	Set 1	11·2269	17	−3·081	4·557	11·2294	+25
	Set 2	11·2330	14	−3·348	5·674		−36
15	Set 1	10·9180	20	−3·065	4·477	10·9213	+33
	Set 2	10·9223	13	−3·387	5·631		−10
25	Set 1	$10{\cdot}6364_7$	11	−3·028	4·339	10·6383	+18
	Set 2	10·6400	12	−3·359	5·466		−17
35	Set 1	$10{\cdot}3784_7$	19	−2·977	4·148	10·3779	−6
	Set 2	10·3796	14	−3·432	5·577		−17
45	Set 1	10·1363	23	−3·249	4·873	10·1381	+18
	Set 2	10·1388	21	−3·477	5·541		−7
			av. 16			$\sqrt{[V (\log K)]} = 2{\cdot}5 \times 10^{-3}$.	

TABLE 6.

2-Aminoethyl sulphate: the constants B and C of eqn. (5) and the values of pK_a (second dissociation).

pK_a (obs.) was obtained from eqn. (5) and pK_a (calc.) from eqn. (6).

pK_a (calc.) = $2530{\cdot}12/T + 0{\cdot}2782 + 0{\cdot}00140175T$; $\sigma_{\text{av.}}$ is the average standard error of the intercepts [pK_a (obs.)] of eqn. (5), and V (log K) is the variance about the curve of eqn. (6); Δ = pK_a (calc.) − pK_a (obs.).

Temp.	pK_a (obs.)	$10^4\sigma$	B	C	pK_a (calc.)	$10^4\Delta$
5°	9·7638	4	1·055	−2·276	9·764	+2
15	9·4628	4	1·017	−2·205	9·462	−4
25	9·1821	4	1·066	−2·412	9·182	−2
35	8·9201	3	1·128	−2·633	8·921	+5
45	8·6768	5	1·004	−2·200	8·677	−2
		av. 4			$\sqrt{[V (\log K)]} = 5{\cdot}0 \times 10^{-4}$.	

TABLE 7.

Thermodynamic quantities for the amino-dissociations of 2-aminoethanol, 2-aminoethyl phosphate, 2-aminoethyl sulphate, and taurine.[6]

	ΔG^0 (kJ mole^{-1})					ΔH^0 (kJ mole^{-1})				
Temp.	5°	15°	25°	35°	45°	5°	15°	25°	35°	45°
2-Aminoethanol	53·972	54·107	54·227	54·332	54·421	50·02	50·44	50·88	51·34	51·80
2-Aminoethyl phosphate ...	59·799	60·249	60·725	61·225	61·751	47·63	46·91	46·17	45·41	44·62
2-Aminoethyl sulphate ...	51·996	52·201	52·412	52·628	52·849	46·36	46·21	46·05	45·89	45·72
Taurine	51·082		52·308		52·407	42·52		41·84		41·12
	$\sigma\Delta G^0$ (kJ mole^{-1})					$\sigma\Delta H^0$ (kJ mole^{-1})				
2-Aminoethanol..............	0·023		0·017		0·023	0·80		0·23		0·84
2-Aminoethyl phosphate ...	0·014		0·010		0·014	0·48		0·14		0·50
2-Aminoethyl sulphate......	0·007		0·005		0·007	0·22		0·07		0·24
	$-\Delta S^0$ (J mole^{-1} deg.$^{-1}$)					$\Delta C_p{}^0$ (J mole^{-1} deg.$^{-1}$)				
Temp.	5°	15°	25°	35°	45°	5°	15°	25°	35°	45°
2-Aminoethanol	14·22	12·72	11·22	9·72	8·22	41·7	43·2	44·7	46·2	47·7
2-Aminoethyl phosphate ...	43·8	46·3	48·8	51·3	53·9	−70·3	−72·8	−75·3	−77·8	−80·4
2-Aminoethyl sulphate......	20·26	20·79	21·33	21·87	22·40	−14·9	−15·5	−16·0	−16·5	−17·1
Taurine	30·8		33·1		35·5	32·7		35·0		37·4
	$\sigma\Delta S^0$ (J mole^{-1} deg.$^{-1}$)					$\sigma\Delta C_p{}^0$ (J mole^{-1} deg.$^{-1}$)				
2-Aminoethanol..............	2·70		0·76		2·70	36		39		41
2-Aminoethyl phosphate ...	1·60		0·45		1·60	21		23		24
2-Aminoethyl sulphate......	0·86		0·23		0·86	11		12		12

$0{\cdot}001_3$ pK unit respectively. The difference here is more apparent than real since the latter figure is derived on the assumption that the Debye–Hückel equation is a simple linear relation, no account being taken of the uncertainty introduced by the arbitrary parameter a^*; it is not a true measure of the error and a valid comparison cannot, therefore, be made. It appears, however, that since the variances about the extrapolation lines are very nearly equal in both methods of extrapolation the errors of the intercepts must be comparable and near that for eqn. (5). When Bates and Pinching's results at 25° are extrapolated by means of our eqn. (5) the intercept is $9{\cdot}496_7$, to be compared with $9{\cdot}498_0$ obtained by Bates and Pinching using the full Debye–Hückel equation. This, together with the excellent agreement between the two sets of results mentioned above, seems to indicate that eqn. (5) is of more general applicability in systems of this sort, than is the full Debye–Hückel equation.

The only other accurate determination of the thermodynamic pK_a (at 25° only) is that of Sivertz, Reitmeier, and Tartar[9] from conductivity measurements. Their value of 9·500 is in excellent agreement with ours. Other determinations are quoted by Bates and Pinching.[7] The value of ΔH^0 for this ionisation is largely consistent with the reaction's being isoelectric and with the magnitude of pK_a.

ΔS^0, however, is rather more negative than might have been expected, as is found with the monomethylammonium dissociation, and possibly for the same reasons. In our paper on the ionisations of *N*-methylated glycine derivatives we suggested that the principal cause of the anomaly might be the so called " iceberg " effect.[10]

The thermodynamic quantities associated with the ionisations of the ammonium groups in 2-aminoethyl phosphate and 2-aminoethyl sulphate may be explained in terms of the changes in electrostatic interaction between the various acid–base species and the surrounding medium (water). The problem has been studied in the same way as for arginine and glycine.[10,11] Changes in thermodynamic quantities associated with the interaction of any charged species with the medium may be represented as follows:

$$\Delta G^0{}_{\text{el}} = p(1/D), \tag{7}$$

$$\Delta S^0{}_{\text{el}} = -p[\mathrm{d}/\mathrm{d}T\ (1/D)], \tag{8}$$

$$\Delta H^0{}_{\text{el}} = p[1/D - T\mathrm{d}/\mathrm{d}T\ (1/D)], \tag{9}$$

$$\Delta C_p{}^0{}_{\text{el}} = -p[T\mathrm{d}^2/\mathrm{d}T^2\ (1/D)]. \tag{10}$$

In each of these equations p is a constant characteristic of the charged species and the second factor is a known function of the dielectric constant.

For a molecule bearing several charges, it is most convenient to use Kirkwood's model, a sphere of uniform dielectric constant with the charges embedded at a fixed distance from the surface.[12] It is further assumed that the intramolecular dielectric constant is invariant with temperature, and terms involving it are not considered. For the calculation of p, it is necessary to know the " depth " of the charges, their relative distances, defined by the angles (θ_{kl}) between lines joining the charges to the centre of the spherical molecule, and the radius of the sphere. The problem is complicated by the many conformations that the molecule can assume in solution. However, it is reasonable to suppose that there is a time-average preferred conformation. In the absence of other data all that can be done is to make a guess on the basis of models. In this work, however, the structure of

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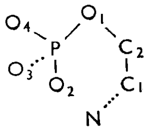
[9] Sivertz, Reitmeier, and Tartar, *J. Amer. Chem. Soc.*, 1940, **62**, 1379.

[10] Datta and Grzybowski, *Trans. Faraday Soc.*, 1958, **54**, 1188.

[11] Datta and Grzybowski, *Biochem. J.*, 1961, **78**, 289.

[12] Kirkwood, *J. Chem. Phys.*, 1934, **2**, 767.

2-aminoethyl phosphate was assumed to be similar to that of crystalline L-serine phosphate deduced from *X*-ray diffraction data by McCallum *et al.*[14]



The interatomic distances (to two decimal places) are as follows: C_1–C_2 1·53 Å; C_1–N 1·47 Å; C_2–O_1 1·47 Å; P–O_1 1·61 Å; P–O_2 1·52 Å; P–O_3 1·50 Å; and P–O_4 1·56 Å; there is also an intramolecular hydrogen bond between O_2 and N (N–O_2 2·79 Å). The chain O_4–P–O_1–C_2–C_1 is roughly coplanar, with the remaining atoms projecting away from it. This structure actually relates to the solid $^-HO_3P{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}NH_3^+$, *i.e.*, the acid species of the second dissociation. From the distances between phosphorus and the "free" oxygen atoms, it is apparent that two of the latter are approximately equivalent and presumably bearing the negative charge which resonates between them. It was then assumed that when a proton is lost (presumably from O_4), all three external oxygen atoms become equivalent with now two negative charges resonating among them, all P–O distances being ~1·5 Å.

To evaluate the electrostatic contribution to the thermodynamic functions, the two negative charges, considered in isolation, were assumed to lie at the centre of a sphere with a radius of 1·52 Å. Then, as in the treatment of the arginine dissociations, the free energy associated with such ion calculated from the Born equation[13] ($\Delta G_{el} = z^2e/2RD$) is equated to the appropriate self-energy term in the modified Kirkwood equation associated with this charge as part of the molecule:[11]

$$z^2e/RD = b/(b^2 - r^2),$$

where b is the radius of the spherical molecule, r the distance between the charge and the centre of the molecule, and R the radius of the "free" ion. A similar calculation can be made for the positive charge on the nitrogen atom (taking $R = 1{\cdot}40$ Å).[11] The average charge "depth" (average for $R^\pm$, R^{+2-}, and R^{2-}) is then found to be 0·84 Å for $b = 3{\cdot}50$ Å. This procedure is unjustified if the individual charges are associated with widely differing radii; with 2-aminoethyl phosphate, however, this is not the case. The shape of the molecule is ellipsoidal rather than spherical, and this value of b represents half the long axis. From the geometry of the molecule the P–N distance was calculated to be 3·31 Å and hence θ_{kl} for R^{+2-} is 76° 57′; p can now be evaluated. The details of the calculation have been given elsewhere.[11]

The value of p for the basic species ($NH_2{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}PO_3^{2-}$) can be obtained readily and its overall value for the ionisation

$$^+NH_3{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}PO_3^{2-} + H_2O \rightleftharpoons NH_2{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}PO_3^{2-} + H_3O^+$$

can be found [$p_{H_3O^+} = (7{\cdot}551 \times 10^5) - p = 1{\cdot}0518 \times 10^6$]. The corresponding "electrostatic" thermodynamic functions are given in Table 8.

These values may be compared with the "environmental" thermodynamic quantities (ΔG^0_{env}, etc.) which are calculated on the assumption that the experimental value of ΔC_p^0 is entirely due to electrostatic interactions. The reciprocal of the dielectric constant of water,[15] $1/D$, may be represented by the equation

$$1/D = a - bT + cT^2 = 8{\cdot}5756 \times 10^{-3} - 2{\cdot}9915 \times 10^{-5}T - 1{\cdot}4741 \times 10^{-7}T^2 \quad (11)$$

and

$$\Delta C_{p,\,el}^0 = p[-T\mathrm{d}^2/\mathrm{d}T^2(1/D)] = -2cTp. \quad (12)$$

Since from Harned and Robinson's equation ΔC_p^0 is equal to $-2\boldsymbol{R} \ln 10CT$, an "experimental" value of p may be obtained:

$$p_{exp.} = \boldsymbol{R} \ln 10C/c = 12{\cdot}987 \times 10^7C \text{ joules.}$$

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[13] Born, *Z. Phys.*, 1920, **1**, 45.

[14] McCallum, Robertson, and Sim, *Nature*, 1959, **184**, 1863.

[15] Malmberg and Maryott, *J. Res. Nat. Bur. Stand.*, 1956, **50**, 1.

TABLE 8.

The " electrostatic," " environmental," and " non-environmental " thermodynamic quantities associated with the acid dissociations of 2-aminoethyl phosphate, 2-aminoethyl sulphate, and taurine at 25°: the measured overall quantities are included for comparison.

(ΔG and ΔH in kJ mole^{-1}; ΔS and ΔC_p in J mole^{-1} deg.$^{-1}$.)

	2-Aminoethyl phosphate (2nd dissn.)	2-Aminoethyl phosphate (3rd dissn.)	2-Aminoethyl sulphate (2nd dissn.)	Taurine (2nd dissn.)
$\Delta G^0{}_{\text{el}}$	20·30	13·43	6·09	6·09
$\Delta H^0{}_{\text{el}}$	−7·20	−4·76	−2·16	−2·16
$\Delta S^0{}_{\text{el}}$	−92·2	−61·0	−27·6	−27·6
$\Delta C_p{}^0{}_{\text{el}}$	−139·7	−92·5	−41·9	−41·9
$\Delta G^0{}_{\text{env}}$	24·76	10·94	2·32	5·09
$\Delta H^0{}_{\text{env}}$	−8·78	−3·88	−0·82	−1·81
$\Delta S^0{}_{\text{env}}$	−112·5	−49·7	−10·6	−23·1
$\Delta C_p{}^0{}_{\text{env}}$	−170·4	−75·3	−16·0	−35·0
$\Delta G^0{}_{\text{non}}$	8·56	49·78	50·09	47·22
$\Delta H^0{}_{\text{non}}$	6·89	50·05	46·87	43·65
$\Delta S^0{}_{\text{non}}$	−5·6	0·9	−10·73	−10·0
ΔG^0	33·325	60·725	52·412	52·31 *
ΔH^0	−1·892	46·17	46·05	41·84 *
ΔS^0	−118·1	−48·8	−21·33	−33·1 *
$\Delta C_p{}^0$	−170·4	−75·3	−16·0	−35·0 *

* See King (ref. 6).

This can be used to calculate the environmental thermodynamic quantities from eqns. (7)—(10).

A similar calculation was made for the second ionisation of 2-aminoethyl phosphate, the same shape and dimensions of the ions and the same intercharge distances being assumed; in the acid species there is, of course, now only one negative charge centred on the phosphorus, and in the basic species, two:

$$\mathrm{H_2R^{\pm} + H_2O \rightleftharpoons H_3O^+ + HR^{+2-}};$$

p for this dissociation is $1{\cdot}5898 \times 10^6$. The results have been compared with the " environmental " quantities calculated from the experimental data of Clarke, Datta, and Rabin.[1] Table 8 shows that the calculated electrostatic and the experimentally determined " environmental " thermodynamic quantities are at least in good qualitative agreement. In view of the complexity of the ionic species involved and the approximate method of calculation employed, this may be regarded as satisfactory.

Kapustinsky [16] recently published a list of heats of hydration of a large number of ions. When those for 1+ cations are plotted against $1/r$ (r = crystal radius of an ion),[17] a smooth curve can be drawn from which $r_{\mathrm{H_3O^+}}$ can be obtained by interpolation as 0·81 Å, to be compared with 0·92 Å used in our previous work. It is interesting that interpolation of Pauling's table of crystal radii (with $r_{\mathrm{Li^+}}$ and $r_{\mathrm{Na^+}}$ or $r_{\mathrm{Na^+}}$ and $r_{\mathrm{K^+}}$) for a 1+ ion of mass 19 yields $r_{\mathrm{H_3O^+}} = 0{\cdot}86$ Å. If 0·81 Å is accepted as the correct value, the contribution to p in any of the above dissociations will increase by $0{\cdot}1025 \times 10^6$ J. This means that, at 25°, $\Delta G^0{}_{\text{el}}$ has to be diminished (made more negative) by 13·1 kJ, $\Delta S^0{}_{\text{el}}$ by 5·95 J/deg., $\Delta H^0{}_{\text{el}}$ by 0·46 kJ, and $\Delta C_p{}^0{}_{\text{el}}$ by 9·0 J/deg., which leads to somewhat better agreement with experiment.

No crystallographic studies on 2-aminoethyl sulphate appear to have been made, but as models indicate its close similarity to 2-aminoethyl phosphate, the same structure as for the latter may be assumed as a first approximation. Thus the molecule is regarded

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[16] Kapustinsky, *Zhur. fiz. Khim.*, 1958, **32**, 1648.

[17] Pauling, " The Nature of the Chemical Bond," Cornell University Press, Ithaca, New York, 3rd Edition, 1960, p. 514.

as a sphere of 3·5 Å radius; the acid species has a single negative charge centred on the sulphur atom (the charge is assumed to resonate among the oxygen atoms around the sulphur) and a single positive charge on the nitrogen; the basic species has only the negative charge. Calculation similar to the above leads to $p_{\text{calc}} = 0{\cdot}4768 \times 10^6$ J. Now $p_{\text{exp}} = 0{\cdot}1820 \times 10^6$ J, and consequently the agreement between the "electrostatic" and "environmental" thermodynamic quantities in Table 8 is comparatively poor (qualitatively the two sets agree). However, the environmental quantities for taurine, which differs from 2-aminoethyl sulphate only in an intervening oxygen atom between the sulphur and the carbon atom, agree much better with experiment. Models show that the shapes of the two molecules differ little, taurine being a little smaller and more compact; it appears possible to bring one of the oxygen atoms and the quaternary nitrogen atom into somewhat closer juxtaposition than in 2-aminoethyl sulphuric acid. If we postulate that the environmental quantities are largely electrostatic, two interpretations of the results are possible: (*a*) the contribution of the 2-aminoethyl sulphate ion to the overall change in the electrostatic energy is smaller than expected; (*b*) that of the zwitter-ion is larger. The second interpretation appears the more likely, since a substantial difference in the behaviour of taurine ions and 2-aminoethyl sulphate ions is improbable. We are thus left with the implication that the mutual cancellation of the positive and the negative charges in the 2-aminoethyl hydrogen sulphate zwitter-ion does not take place to the extent postulated.

EXPERIMENTAL

2-Aminoethanol Hydrochloride.—2-Aminoethanol (B.D.H) was distilled and converted into the hydrochloride by dropping it slowly into bromine-free ~7N-hydrochloric acid. The resulting crystals were filtered off, washed, recrystallised, and dried in a desiccator over P_2O_5. The purity (99·63%, average of three determinations) of the material was checked by gravimetric estimation of the chloride content (as AgCl). Potentiometric titration gave a purity of 99·40% with a thermodynamic pK_a at 25° of 9·505 ± 0·009 (pH 9·2—10·0); formol titration gave a purity of 99·53%. The m. p. was 83·5—84·0° (cf. Gawriloff,[18] 75—77°). One stock solution containing 2-aminoethanol hydrochloride and sodium hydroxide was prepared from which eleven dilutions were made for use in the cells without liquid junction; the ionic strengths of these dilutions varied from ~0·02 to ~0·08. Since the hydrochloride is somewhat hygroscopic, its concentration in the stock solution was determined gravimetrically as silver chloride; the result corresponded to a purity of the initial solid of 99·58%. The concentration of the base in the stock solution was estimated by weight titration with hydrochloric acid and a 0·1% solution of Chlorophenol Red screened with 0·1% of Aniline Blue.

2-Aminoethyl Dihydrogen Phosphate.—This material was from the sample used by Clarke, Datta, and Rabin.[1] Two stock solutions containing 2-aminoethyl dihydrogen phosphate, sodium hydroxide, and potassium chloride were prepared. Sixteen dilutions were made from the first stock and ten from the second; the ionic strength range covered was ~0·01—~0·09.

2-Aminoethyl Hydrogen Sulphate.—A commercial sample (L. Light & Company, Colnbrook) was recrystallised from water and analysed by formol titration. Fourteen dilutions were prepared from one stock solution containing 2-aminoethyl hydrogen sulphate, sodium hydroxide, and potassium chloride, the ionic strengths being in the range 0·01—0·06.

Potassium Chloride.—"Analar" material was dissolved in water, the solution was chlorinated, and the solid was precipitated from solution by saturation with gaseous bromine-free hydrogen chloride. The salt was filtered off, dried at 160°, and fused in an atmosphere of dry nitrogen.

The preparation of carbonate-free sodium hydroxide, measurement of the e.m.f.'s of the cells without liquid junction, and measurement of temperature have been described previously.[19, 20]

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[18] Gawriloff, *Bull. Soc. chim. France*, 1925, **37**, 1651.

[19] Ashby, Crook, and Datta, *Biochem. J.*, 1954, **56**, 190.

[20] Clarke, Cusworth, and Datta, *Biochem. J.*, 1954, **58**, 146.

Fundamental Constants.—The values used in this work were those given by DuMond and Cohen.[21]

E_0 *of the Silver-Silver, Chloride Electrodes.*—The values of the E_0 of the Ag–AgCl electrodes were calculated from eqn. (4) of Bates and Bower.[22]

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[21] DuMond and Cohen, *Rev. Mod. Phys.*, 1953, **55**, 691.

[22] Bates and Bower, *J. Res. Nat. Bur. Stand.*, 1954, **53**, 283.