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Thermodynamic properties of peptide solutions. Part 12. Enthalpies of dilution of aqueous solutions of some glycyl dipeptides at 298.15 K

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Abstract

Enthalpies of dilution at 298.15 K of aqueous solutions of the dipeptides glycyl-L-valine, glycyl-D-leucine, glycyl-L-asparagine, glycyl-L-threonine, glycyl-DL-threonine and glycyl-DL-serine have been determined using flow microcalorimetry. The results obtained were used to determine the enthalpic interaction coefficients that characterise pair interactions of the peptides in aqueous solution. These coefficients were compared with those for other dipeptides and also with those for some amino acids.

Keywords: Calorimetry; Excess molar enthalpy; Heat of dilution; Microcalorimetry; Peptide; Zwitterion

1. Introduction

In order for a globular protein to be functional in aqueous solution, the protein must fold into its unique three-dimensional native structure. Protein folding is the final step in the overall process of gene expression. The linear polymer of amino acid residues assembled by the cell machinery spontaneously folds into a specific three-dimensional conformation [1]. This folding process, which is not yet understood, is often referred to as the 'protein folding problem' [1-3].

A thorough understanding of this folding process requires a knowledge of the interactions that are responsible for stabilising the native protein structure in aqueous solution. Interactions between the solvent and various functional groups

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on the protein, along with the various non-covalent bonding interactions among protein constituent groups, are very important factors that determine the folded conformation of a globular protein [4, 5]. As proteins are large complex molecules, small solutes that incorporate some of the structural features found in proteins have been used as models for specific aspects of proteins in aqueous solution. The investigation of solute–solute and solute–water interactions for these model compounds in aqueous solution can assist in the understanding of the important interactions that determine protein stability [6, 7].

In some of our earlier work [8–10], we determined the enthalpic interaction coefficients for the intermolecular interactions in aqueous solution of some small peptides with a single alanyl side-chain. The results indicated that interactions involving the side-chain are significant in the overall interaction of the peptides [10]. In order to investigate the contributions of other side-chains to the pair interactions of peptides, we report herein the enthalpic interaction coefficients at 298.15 K for the intermolecular interactions in aqueous solution of the glycyl dipeptides glycyl-D-leucine, glycyl-L-valine, glycyl-L-asparagine, glycyl-L-threonine, glycyl-DL-threonine and glycyl-DL-serine. The results obtained are compared with those for other dipeptides and also with those for some amino acids.

2. Experimental

All the dipeptides were obtained from Sigma (St. Louis, USA). Details of the purification and analyses of the dipeptides glycyl-L-asparagine, glycyl-DL-threonine dihydrate, and glycyl-DL-serine monohydrate have been reported in earlier papers [11, 12]. Glycyl-L-threonine was recrystallised from water + ethanol to give a crystalline hydrate. Using alkalimetric titrations [9, 13], the relative molar mass of the hydrate was determined to be 211.7 ± 1 which is in good agreement with that expected for a dihydrate ($M_r = 212.20$). The purity was also confirmed by elemental analyses: found: C, 34.2%; H, 7.6%; N, 12.9%; calculated for $C_6H_{16}O_6N_2$: C, 34.0%; H, 7.6%; N, 13.2%. The optical purity was checked using an Optical Activity Ltd. polarimeter type AA-10: $[\alpha]_D^{19}$ $-16.8°$ ($c = 1$, H_2O); compare $[\alpha]_D^{25}$ $-16.2°$ ($c = 2$, H_2O) [14]. Glycyl-L-valine and glycyl-D-leucine were recrystallised from water + ethanol. The purity of each peptide was confirmed by alkalimetric titration and by elemental analyses. Glycyl-L-valine found: C, 48.3%; H, 8.1%; N, 16.2%; calculated for $C_7H_{14}O_3N_2$: C, 48.3%; H, 8.1%; N, 16.1%; glycyl-D-leucine found: C, 51.0%; H, 8.7%; N, 14.7%; calculated for $C_8H_{16}O_3N_2$: C, 51.1%; H, 8.6%; N, 14.9%. Measurements of the optical rotations gave glycyl-L-valine, $[\alpha]_D^{25}$ $-20.8°$ ($c = 0.5$, H_2O); compare $[\alpha]_D^{25}$ $-19.9°$ ($c = 2$, H_2O) [15]; glycyl-D-valine, $[\alpha]_D^{21}$ $+34.9°$ ($c = 1.0$, H_2O); compare $[\alpha]_D^{20}$ $+37.6°$ (H_2O) [15]. The water used to prepare solutions was deionised and glass-distilled. Solutions were prepared by mass and corrections were made for air buoyancy.

The enthalpies of dilution were determined using an LKB 10700-1 flow microcalorimeter. The apparatus and procedures used were the same as those described in earlier papers [16, 17].

3. Results

The enthalpies of dilution were analysed using a molality expansion of the excess enthalpy. The excess enthalpy per kg of solvent H^E of a binary aqueous solution is defined by [18]

$$H^E = H - h_w^* - mH_2^\infty \tag{1}$$

where H is the enthalpy of a solution containing 1 kg of water and m moles of the solute, h_w^* is the specific enthalpy of water, and H_2^∞ is the partial molar enthalpy of the solute at infinite dilution. The excess enthalpy can be expressed as a power series in the solution molality [7, 19]

$$H^E = h_{xx}m^2 + h_{xxx}m^3 + \ldots \tag{2}$$

where h_{xx} is the enthalpic interaction coefficient which characterises the interaction between pairs of solvated solute molecules and h_{xxx} contains, at least notionally, contributions from triplet interactions [7]. Equation (2) can be rearranged to give

$$H^E(m) = H^E/m = h_{xx}m + h_{xxx}m^2 + \ldots \tag{3}$$

where $H^E(m)$ is the excess enthalpy per mole of solute for a solution of molality m. For the dilution of a solution of initial molality m_i to give a solution of final molality m_f, the molar enthalpy of dilution $\Delta_{dil}H_m$ is given by [19, 20]

$$\Delta_{dil}H_m = H^E(m_f) - H^E(m_i) \tag{4}$$

From Eqns. (3) and (4), it follows that

$$\Delta_{dil}H_m = h_{xx}(m_f - m_i) + h_{xxx}(m_f^2 - m_i^2) + \ldots \tag{5}$$

The values of $\Delta_{dil}H_m$ for solutions of the dipeptides, together with the initial and final molalities, are given in Table 1. For each solute, the $\Delta_{dil}H_m$ data were fitted to Eq. (5) using the weighted least-squares procedure described previously [9, 17]. Values of the h coefficients together with their uncertainties are given in Table 2. Table 2 also contains values of an agreement index R that gives a measure of the overall agreement between the experimental $\Delta_{dil}H_m$ values and those calculated using Eq. (5). The expression used to calculate R is given by

$$R^2 = \sum_i w_i[Y_i(\text{obs}) - Y_i(\text{calc})]^2 \Big/ \sum_i w_i[Y_i(\text{obs})]^2 \tag{6}$$

where Y_i(obs) and Y_i(calc) refer respectively to the experimental enthalpy of dilution and that calculated using Eq. (5), and w_i is the weighting factor for Y_i(obs) [17]. The values of R given in Table 2 indicate that a polynomial in molality with two h coefficients gives a satisfactory representation of the experimental $\Delta_{dil}H_m$ data. For comparison, h coefficients for the peptides glycylglycine and glycyl-DL-alanine are also given in Table 2.

The enthalpic interaction coefficients for the dipeptide glycyl-L-leucine in aqueous solution at 298.15 K have been reported recently [21]. These results

Table 1
Enthalpies of dilution of aqueous solutions of dipeptides at 298.15 K

m_i in mol kg^{-1}	m_f in mol kg^{-1}	$\Delta_{dil}H_m$ [a] in J mol^{-1}	m_i in mol kg^{-1}	m_f in mol kg^{-1}	$\Delta_{dil}H_m$ [a] in J mol^{-1}	m_i in mol kg^{-1}	m_f in mol kg^{-1}	$\Delta_{dil}H_m$ [a] in J mol^{-1}
Glycyl-L-asparagine								
0.2088	0.1036	234.2 (0.9)	0.1560	0.0517	241.4 (1.0)	0.1035	0.0517	123.8 (1.2)
0.2088	0.0689	318.0 (1.6)	0.1560	0.0776	178.9 (0.9)	0.0911	0.0304	147.4 (1.0)
0.1959	0.0973	221.1 (0.9)	0.1372	0.0455	216.1 (0.9)	0.0911	0.0456	109.2 (0.9)
0.1959	0.0647	298.7 (1.2)	0.1372	0.0683	161.0 (0.8)	0.0756	0.0253	123.0 (1.1)
0.1798	0.0894	205.1 (1.2)	0.1222	0.0406	195.7 (2.2)	0.0756	0.0379	91.4 (1.0)
0.1798	0.0595	278.5 (1.4)	0.1222	0.0609	141.5 (0.9)	0.0643	0.0322	77.5 (1.5)
						0.0643	0.0214	105.0 (1.3)
Glycyl-D-leucine								
0.3163	0.1027	−302.2 (1.8)	0.2298	0.1133	−164.4 (1.3)	0.1119	0.0558	−75.3 (0.8)
0.3163	0.1551	−227.8 (3.0)	0.2097	0.0688	−195.2 (1.2)	0.1119	0.0372	−100.8 (2.3)
0.2799	0.0912	−265.1 (1.9)	0.2097	0.1039	−147.9 (1.0)	0.0961	0.0480	−62.1 (0.6)
0.2799	0.1375	−201.6 (1.0)	0.1809	0.0898	−128.8 (0.8)	0.0961	0.0319	−86.5 (1.0)
0.2549	0.0832	−239.5 (1.4)	0.1582	0.0524	−145.2 (1.0)	0.0798	0.0266	−72.0 (1.5)
0.2549	0.1255	−183.0 (2.4)	0.1582	0.0787	−112.8 (0.8)	0.0798	0.0399	−51.5 (0.7)
0.2298	0.0752	−217.6 (2.6)	0.1340	0.0668	−91.7 (2.1)			
Glycyl-L-valine								
0.3001	0.1478	−123.3 (1.1)	0.2199	0.1087	−92.2 (0.9)	0.1596	0.0527	−86.4 (2.8)
0.3001	0.0981	−168.2 (1.2)	0.2199	0.0723	−124.7 (1.3)	0.1399	0.0696	−58.1 (0.4)
0.2798	0.1380	−116.5 (1.4)	0.2002	0.0992	−85.2 (0.4)	0.1399	0.0463	−74.3 (0.5)
0.2798	0.0916	−157.9 (1.6)	0.2002	0.0659	−112.5 (0.6)	0.1199	0.0597	−50.0 (0.8)
0.2598	0.1283	−106.1 (0.5)	0.1798	0.0892	−75.6 (0.5)	0.1199	0.0397	−67.6 (1.2)
0.2390	0.1182	−98.7 (0.5)	0.1798	0.0593	−99.1 (0.5)	0.1000	0.0499	−44.2 (0.9)
0.2390	0.0785	−133.4 (0.8)	0.1596	0.0793	−65.8 (0.4)	0.1000	0.0332	−56.8 (2.6)
Glycyl-L-threonine								
0.2591	0.1281	88.1 (0.4)	0.1900	0.0944	65.3 (1.0)	0.1536	0.0764	52.7 (0.3)
0.2591	0.0851	116.8 (0.5)	0.1900	0.0628	87.4 (1.3)	0.1425	0.0472	71.4 (0.5)
0.2388	0.1181	81.9 (0.3)	0.1785	0.0590	84.2 (0.4)	0.1425	0.0709	50.5 (0.3)
0.2388	0.0785	109.1 (0.6)	0.1785	0.0887	61.2 (0.3)	0.1269	0.0421	61.2 (0.3)
0.2281	0.1130	76.9 (0.4)	0.1700	0.0562	82.0 (0.5)	0.1201	0.0399	57.7 (0.9)
0.2281	0.0751	102.4 (1.0)	0.1700	0.0844	59.5 (0.3)	0.1201	0.0599	41.3 (0.6)
0.2172	0.1076	75.0 (0.3)	0.1609	0.0800	54.9 (0.3)	0.1096	0.0364	55.3 (0.6)
0.2172	0.0715	100.3 (0.5)	0.1609	0.0533	73.7 (0.5)	0.0910	0.0455	34.6 (0.4)
0.2015	0.1000	70.1 (1.1)	0.1536	0.0509	74.2 (0.4)	0.0910	0.0303	44.9 (0.5)
Glycyl-DL-threonine								
0.2706	0.0891	124.3 (0.6)	0.1888	0.0625	92.1 (1.5)	0.1429	0.0475	72.7 (0.9)
0.2706	0.1340	95.0 (1.4)	0.1888	0.0939	68.7 (0.6)	0.1429	0.0713	53.9 (0.5)
0.2278	0.0753	110.6 (1.2)	0.1689	0.0560	82.1 (0.6)	0.1249	0.0415	61.6 (0.7)
0.2278	0.1131	80.2 (0.6)	0.1689	0.0841	60.0 (0.6)	0.1249	0.0623	46.4 (0.9)
0.2037	0.0674	99.5 (1.3)	0.1562	0.0518	75.9 (0.6)	0.1118	0.0559	41.3 (0.8)
0.2037	0.1013	73.2 (0.4)	0.1562	0.0778	55.5 (0.5)	0.1118	0.0372	54.6 (0.7)
Glycyl-DL-serine								
0.2984	0.0984	243.1 (1.5)	0.2030	0.0673	175.6 (0.7)	0.1425	0.0475	122.4 (1.7)
0.2984	0.1481	178.7 (1.1)	0.2030	0.1011	125.9 (0.6)	0.1425	0.0712	90.2 (0.9)
0.2703	0.0893	222.8 (1.3)	0.1868	0.0932	114.5 (0.9)	0.1266	0.0632	78.8 (1.0)
0.2703	0.1344	164.1 (1.3)	0.1868	0.0621	159.4 (1.0)	0.1266	0.0421	109.7 (1.1)
0.2459	0.1224	148.9 (0.8)	0.1712	0.0855	107.3 (0.8)	0.1137	0.0568	70.5 (1.1)
0.2459	0.0814	204.5 (1.2)	0.1712	0.0570	148.1 (0.7)	0.1137	0.0379	101.6 (1.3)
0.2183	0.1088	133.5 (0.9)	0.1527	0.0509	132.4 (0.9)	0.0838	0.0280	76.4 (1.4)
0.2183	0.0724	182.7 (1.3)	0.1527	0.0763	96.4 (0.8)	0.0838	0.0419	55.2 (1.3)

[a] The estimated uncertainty of each $\Delta_{dil}H_m$ is given in parentheses.

Table 2
Enthalpic coefficients of Eq. (5) for aqueous solutions of some dipeptides at 298.15 K

Dipeptide	h_{xx} in J kg mol^{-2} [a]	h_{xxx} in J kg^2 mol^{-3} [a]	R
Glycylglycine [b]	−796 (5)	173 (8)	–
Glycyl-DL-alanine [c]	−39 (3)	68 (2)	–
Glycyl-L-valine	824 (3)	–	0.018
Glycyl-D-leucine	1310 (17)	272 (53)	0.015
Glycyl-L-asparagine	−2528 (14)	970 (57)	0.006
Glycyl-DL-serine	−1378 (17)	431 (54)	0.015
Glycyl-DL-threonine	−788 (12)	263 (42)	0.015
Glycyl-L-threonine	−764 (10)	261 (37)	0.018

[a] Standard deviations are given in parentheses. [b] From ref. 16. [c] From ref. 21.

($h_{xx} = 1505(5)$ J kg mol^{-2}, $h_{xxx} = -145(18)$ J kg^2 mol^{-3}) differ considerably from those determined in this work for the D isomer.

For the solute glycyl-DL-threonine, the coefficients given in Table 2 have been derived by treating the mixture of optical isomers as a single solute. An alternative approach, which has been used in studies of chiral interactions in aqueous solutions [22–24], is to treat mixtures of DL isomers as ternary solutions. The excess enthalpy per kg of solvent of a solution containing the D and L isomeric forms of a solute at molalities m_D and m_L respectively is given by

$$H^E = h_{LL}m_L^2 + 2h_{LD}m_Lm_D + h_{DD}m_D^2 + h_{LLL}m_L^3 + 3h_{LLD}m_L^2m_D + 3h_{LDD}m_Lm_D^2 + h_{DDD}m_D^3 + \ldots \quad (7)$$

It is possible to recast Eq. (7) in terms of the osmolality m, $m = m_L + m_D$, where $m_L = y_Lm$, $m_D = y_Dm$, and y_L and y_D are respectively the mole fractions of the L and D isomers. Equation (7) thus becomes

$$H^E = m^2[h_{LL}y_L^2 + 2h_{LD}y_Ly_D + h_{DD}y_D^2] + m^3[h_{LLL}y_L^3 + 3h_{LLD}y_L^2y_D + 3h_{DDL}y_D^2y_L + h_{DDD}y_D^3] + \ldots . \quad (8)$$

From Eqs. (2) and (8) it follows that

$$h_{xx} = h_{LL}y_L^2 + 2h_{LD}y_Ly_D + h_{DD}y_D^2 \quad (9)$$

and

$$h_{xxx} = h_{LLL}y_L^3 + 3h_{LLD}y_L^2y_D + 3h_{DDL}y_D^2y_L + h_{DDD}y_D^3 \quad (10)$$

For equimolar mixtures of D and L isomers, the pairwise enthalpic coefficient is given by

$$h_{xx} = (h_{LL} + 2h_{LD} + h_{DD})/4 \quad (11)$$

Given the h_{xx}, h_{LL} and h_{DD} values, the cross coefficient h_{LD} can be derived using Eq. (11). The coefficient h_{DD} for the depeptide glycyl-D-threonine has not been deter-

mined. However, as it has been shown [23, 24] that the h_{DD} and h_{LL} values for some amino acids and their derivatives are the same, within experimental uncertainties, which is as expected, it is reasonable to assume that $h_{LL} = h_{DD}$ for glycylthreonine. The results for glycylthreonine in Table 2 give a cross coefficient of $h_{LD} = -812(34)$ J kg mol^{-2}. This heterotactic coefficient is almost the same, within the combined uncertainties, as the homotactic coefficient h_{LL}. It would appear that chiral recognition is not particularly significant for the dipeptide glycylthreonine.

4. Discussion

As the enthalpic coefficient h_{xxx} contains contributions from multiple interactions and as such is difficult to interpret [7, 25], we will discuss only the h_{xx} coefficients which give a measure of pair associations between solvated solute molecules.

For the dipeptides with apolar side-chains, the h_{xx} coefficients increase with an increase in the number of carbon atoms in the side-chain. In Fig. 1, the homotactic coefficients for these dipeptides and that for diglycine are plotted against the number of equivalent methylene groups in the side-chain, n_{CH_2}. The usual approach of assuming that methyl and methyne groups are equivalent to 1.5 and 0.5 methylene groups, respectively, has been used to determine the n_{CH_2} values [26, 27]. For these dipeptides there is an approximately linear relationship between the h_{xx} coefficients and n_{CH_2}. For comparison, the analogous plot for the α-amino acids is also included in Fig. 1 [24, 28]. The result is qualitatively similar to that observed for the dipeptides. Better linear relationships between h_{xx} and n_{CH_2} are in fact

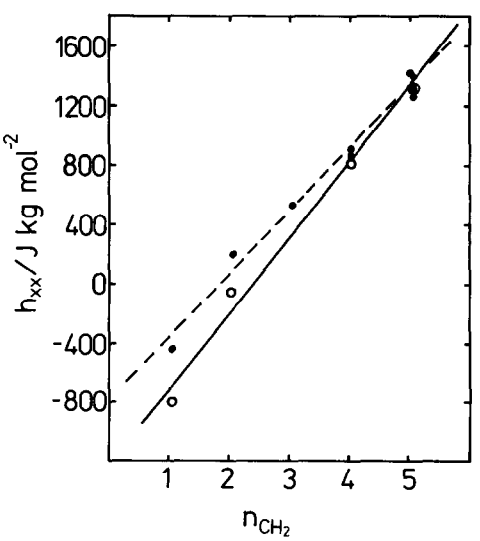

Fig. 1. The pairwise enthalpic interaction coefficients for α-amino acids and dipeptides with apolar side-chains versus the number of equivalent methylene groups in the side-chain: –○–, glycyl dipeptides; – – ● – –, α-amino acids.

observed if the points for glycine and diglycine, neither of which possess a side-chain, are omitted from the respective plots in Fig. 1.

The Savage and Wood group additivity method has been widely used in the analyses of enthalpic pair coefficients [7, 26, 27]. This approach assumes that when two solute molecules interact, every functional group on one molecule interacts with every group on the other molecule and that each interaction has a characteristic enthalpy. The total pairwise interaction is given by the sum of all various group interactions

$$h_{xy} = \sum_{ij} n_i^x n_j^y H_{ij} \tag{12}$$

where n_i^x is the number of type i groups on molecule x, n_j^y is the number of type j groups on molecule y, and H_{ij} is the enthalpy of the ij interaction. In order to apply this additivity approach, it is necessary to divide each molecule into a number of functional groups. The dipeptides with apolar side-chains can be considered to comprise equivalent methylene groups, a peptide group and a group, symbolised E, that combines the charged $-\overset{+}{N}H_3$ and $-CO_2^-$ functional groups. Using these groups, the pair enthalpic coefficient is given by

$$h_{xx} = H_{E\text{-}E} + 2H_{pep\text{-}E} + H_{pep\text{-}pep} + 2n_{CH_2}(H_{CH_2\text{-}E} + H_{CH_2\text{-}pep}) + n_{CH_2}^2 H_{CH_2\text{-}CH_2} \tag{13}$$

This result suggests that if hydrophobic interactions are significant in the pairwise interaction, there should be a quadratic dependence of h_{xx} on the number of equivalent methylene groups. Our interpretation of the approximately linear trend shown in Fig. 1 is that the hydrophobic term in Eq. (13) is negligible compared with the terms that arise from the interactions of the equivalent methylene groups with the E group and the peptide group.

The application of this group contribution approach assumes that the pair interaction is not dominated by one, or more, particular interactions. For zwitterionic amino acids and peptides in aqueous solution this may not be the case. The most probable configuration in the pairwise interaction of the glycyl dipeptides is one where the positively charged amino group interacts with the negatively charged carboxyl group of the second molecule. If these electrostatic interactions are dominant then the molecules will tend to associate 'side-on' as illustrated in Fig. 2. Using such a 'dominant interaction model' and assuming that only nearest neighbour interactions need be considered, then a linear relationship between h_{xx} and the number of equivalent methylene groups in the functional unit $-CH(R)-$, where R

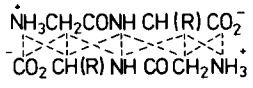

Fig. 2. A probable arrangement of zwitterionic dipeptides in a pair association. The dotted lines represent the nearest neighbour group interactions that are likely to be dominant in such a pair interaction.

is an apolar side-chain, would indeed be expected. Some recent studies on the α-amino acids with apolar side-chains have shown the importance of charge–charge interactions in the pair association of zwitterionic species [24, 28]. In water as the solvent, interactions between oppositely charged groups are favourable and, as shown in Fig. 1, h_{xx} is an approximately linear function of n_{CH_2}. However, in the mixed solvent (H_2O/1 mol dm^{-3} HCl), where the charge–charge interactions in the pair association of the α-amino acids are repulsive, there is a quadratic dependence of h_{xx} on the number of equivalent methylene groups in the side-chain of the amino acid [28]. With the disappearance of the dominant zwitterionic–zwitterionic interaction, the significance of the interactions between the hydrophobic side-chains is enhanced [28, 29].

From the variation in the values of h_{xx} given in Table 2, it is clear that interactions involving the side-chains are quite significant in the dipeptide pair associations. The contributions that these interactions make to the values of h_{xx} depend on the nature of each side-chain. As outlined above, interactions involving apolar side-chains result in positive contributions to the value of h_{xx}. Based on the cosphere overlap model [18], where the overlap of the cospheres of solvated molecules results in the release of solvent to the bulk, a positive contribution would be expected. On pairwise association of the peptides there will be rearrangement of water molecules in the vicinity of the apolar side-chain due to overlap of the hydration spheres of various interacting groups. This solvent reorganisation is an endothermic process [30] and so the contribution to h_{xx} will be positive. As the side-chain is adjacent to the charged $-CO_2^-$ group in the dipeptide, there will also be a contribution to the value of h_{xx} through modulation of the charge–charge interaction between the amino and carboxyl groups in the pair interaction of the peptides [31].

The h_{xx} values for the dipeptides glycyl-L-asparagine and glycyl-DL-serine, which have hydrophilic side-chains, are large and negative. The hydroxyl and amidic functional groups on these side-chains can participate in hydrogen bonding [32]. If hydrogen bonding is important in molecular pair interaction then the contribution to h_{xx} should be negative [27, 30]. Because water can also hydrogen-bond to the side-chains, the negative contribution to the value of h_{xx} can be rationalised if the breaking of solute–water hydrogen bonds and the subsequent formation of solute–solute and solvent–solvent hydrogen bonds is a net exothermic process. The considerably more negative value of h_{xx} for glycyl-L-asparagine compared with that for glycyl-DL-serine is consistent with the large hydrogen bonding propensity of the $-CONH_2$ moiety.

The side-chain of glycyl-L-threonine ($-CH(OH)CH_3$) has both a hydroxyl group and an apolar group. The h_{xx} value for this peptide reflects a balance between a negative contribution due to the presence of the hydrophilic –OH group, and a positive contribution associated with interactions of the apolar groups on the side-chain. A similar result was observed for the amino acid L-threonine [33].

The dipeptides listed in Table 2 differ from their parent amino acids by a single glycyl unit ($-CH_2CONH-$) inserted between the amino group and the α-carbon atom of the amino acid. Given this structural similarity, it is of interest to see whether there is any relationship between the h_{xx} values for the α-amino acids (AA)

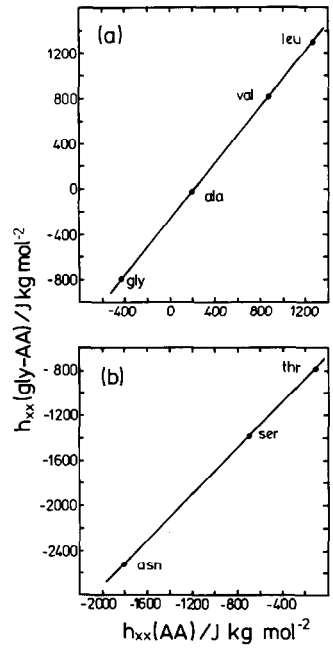

Fig. 3. The pairwise enthalpic interaction coefficients for the glycyl dipeptides, h_{xx}(gly-AA), versus those for the α-amino acids, h_{xx}(AA): (a), results for apolar side-chains; (b), results for polar side-chains.

and those for the corresponding dipeptides of sequence gly-AA. Figure 3 shows the h_{xx} values for the dipeptides given in Table 2 plotted against the h_{xx} values for the amino acids taken from the literature [17, 24, 33]. Good linear relationships are obtained if the results are grouped according to side-chain type; the results for hydrophobic side-chains, (h_{xx}(gly-AA) = (1.25 ± 0.03)h_{xx}(AA) − (269 ± 22), correlation coefficient $r = 0.9995$) are shown in Fig. 3(a) while those for hydrophilic side-chains (h_{xx}(gly-AA) = (1.03 ± 0.02)h_{xx}(AA) − (665 ± 26), $r = 0.9997$) are shown in Fig. 3(b). These results indicate that the contribution to h_{xx} from the addition of a glycyl unit to an amino acid with a hydrophilic side-chain differs from that for an amino acid with a hydrophobic side-chain.

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