

The Crystal Structure of DL-Tryptophan Formate

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Tryptophan is one of the naturally occurring amino acids. It is a precursor of neurochemically important compounds and chemically related to a group of psychopharmaca. Several structure determinations of tryptophan derivatives have been carried out, *e.g.* glycyl-L-tryptophan dihydrate,¹ the serotonin-creatinine sulphate complex,² the hydrochloride and hydrobromide of L-tryptophan,³ and 5-hydroxy-DL-tryptophan.⁴ The purpose of the present X-ray analysis of the formate of DL-tryptophan was to examine a tryptophan derivative in which the accuracy of the measurement was not expected to be influenced by heavy atoms or statistical disorder, and to observe possible variations in the conformation of the alanine part of the molecule in different environments.

Crystals were formed by precipitation of DL-tryptophan from a formic acid solution with the use of diethyl ether. The crystal data are as follows: DL-tryptophan formate $C_{11}H_{13}N_2O_4 \cdot HCO_2$, monoclinic, space group $P2_1/c$; cell dimensions (with e.s.d. in parentheses): $a = 11.237$ (.003) Å, $b = 6.728$ (.002) Å, $c = 16.013$ (.003) Å, $\beta = 96.29^\circ$ (.01); density (measured) 1.37 g cm^{-3} , density (calculated) 1.38 g cm^{-3} , $Z = 4$.

Intensity data were collected on an automatic Picker diffractometer with graphite crystal monochromated $MoK\alpha$ radiation. 2234 reflections were recorded as observed ($I > 2\sigma(I)$) up to a 2θ value of 60° using the $\omega - 2\theta$ scanning mode.

The structure was solved by direct methods and refined by Fourier and least-squares calculations to a conventional R -factor of 0.05. Hydrogen atoms were localized and included in the refinements.

A schematic view of the structure as seen along the b axis is given in Fig. 1. The bond lengths and interbond angles indicated are not corrected for thermal effects; the estimated standard deviations are 0.002–0.003 Å for bond lengths and 0.1–0.2° for angles.

The indole part of the tryptophan ion is strictly planar, the largest displacement

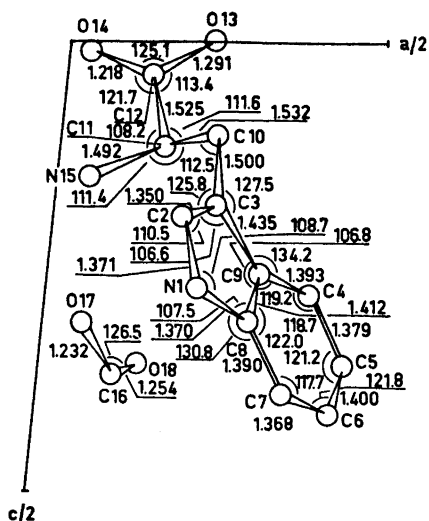


Fig. 1. Structure of tryptophan formate as seen along the b -axis.

from a least-squares plane (including also C10) being 0.004 Å. The angle between this plane and a plane through C3–C10–C11 is 74° . The dihedral angle C3–C10–C11–C12 is 174.5° , and the orientation of the C3–C10 bond is thus *anti* with respect to the $-COOH$ group on C11. This result differs from what was found for the hydrochloric salt in which both $-NH_3^+$ and $-COOH$ groups were found to be in *gauche* positions relative to the C(β)–C(γ) bond. The C–CO₂ arrangement is planar and the C11–N15 direction forms an angle of 4.3° with this plane.

There is an extensive network of hydrogen bonds throughout the crystal. O18 of the formate ion is acceptor in a rather short hydrogen bond (2.49 Å) from the hydroxyl oxygen atom (O13) of the amino acid. It is also acceptor in the hydrogen bond (3.01 Å) from the indole nitrogen atom. Three hydrogen atoms are bonded to the amino acid nitrogen atom which formally acts as the centre of positive charge in the tryptophan ion. There are two hydrogen bonds (2.79 and 2.81 Å) between this nitrogen atom and O17 atoms in different formic acid ions; a third hydrogen bond (3.03 Å) exists between N15 and an O14 atom in another tryptophan ion.

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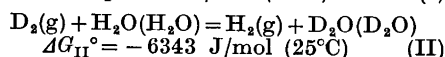
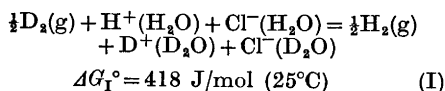
Solvent Deuterium Isotope Effects on Acid-Base Reactions. Part V. Assignment of Individual Ionic Contributions to Transfer Free Energies of Electrolytes from H₂O to D₂O

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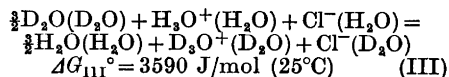
Relative equilibrium and rate constants of ionic and other reactions in light and heavy water include always the free energies of transfer of the reactants and products (or critical complexes) from H₂O to D₂O. This fact, which was early recognized by LaMer and his coworkers,¹ has been recently discussed by several authors.²⁻⁶ Although there are no exact thermodynamic methods of estimating single-ion thermodynamic quantities, fairly reasonable assumptions can be made in the present particular case. As shown below, this involves the pooling of data collected by several independent methods.

Accurate values based on careful experimental investigations are available for the standard free energy changes of reactions (I) and (II). Both values refer to standard states on the mole fraction

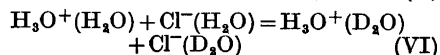
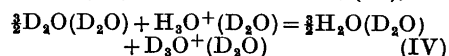


scale. The former value is that derived from EMF data by Gary, Bates and Robinson,⁷ the latter has been calculated here from the spectroscopic value for the corresponding gas phase reaction⁸ and the critically reevaluated ratio, 1.1483, of the vapor pressures of H₂O and D₂O at 25°C.⁹ The value thus obtained is seen to be fairly consistent with the early electrochemical value, -6300 J/mol, reported by Kingerley and LaMer.¹

It has been shown^{4,10} that the water molecules hydrogen-bonded to L₃O⁺ (L=H, D) must possess essentially the same isotope composition as the bulk water. Hence the classical H₃O⁺ model is a satisfactory approximation of the aqueous proton in so far as its isotope exchange equilibria are concerned. Adopting this model, the quantity $\Delta G_I^\circ - \frac{1}{2}\Delta G_{II}^\circ$ represents the standard free energy change of reaction (III).



Reaction (III) can be thought to be composed of three separate processes, (IV), (V) and (VI). The first of these, (IV), the



isotope exchange equilibrium between the hydronium ion and water, does not actually depend on whether this exchange reaction takes place in light or heavy water, owing to cancellation of the respective free energy terms. Experimentally measured values of its equilibrium constant^{4,5,10} provide confirmatory evidence on this point. Further, the standard free energy change for (V) must be close to zero as no deviations from the ideal mixture behavior have been detected in the solvent system in question.^{4,5,10} The last-mentioned process, (VI), involves the transfer of hydronium and chloride ions from light to heavy water.

The standard free energy change of reaction (IV) is, according to the best estimates of its equilibrium constant,^{3,5,10} 2760 J/mol at 25°C. This value and that of reaction (III) yields $\Delta G_{VI}^\circ = 830$ J/mol for reaction (VI) at the same temperature. The least accurate value involved in the whole derivation is un-