

Determination of Thermodynamic Functions for the Hydrogen Bonded Complexes Pyrrole-DMSO and Indole-DMSO

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〈Abstract〉

The enthalpies of formation for the hydrogen bonded complexes Pyrrol-DMSO and Indole-DMSO have been determined by the pure base and high dilution calorimetric methods and by IR spectroscopy. The agreement between all three methods for the enthalpy of the hydrogen bonded adducts is good, though it is considered that DMSO is a highly polar solvent.

수소결합착물 Pyrrole-DMSO와 Indole-DMSO의 생성엔탈피

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〈요 약〉

수소결합착물인 Pyrrole-DMSO와 Indole-DMSO에 대한 수소결합형성엔탈피를 순열기열계량법, 고희석 열계량법 및 적외선분광법으로 측정하여 비교하였다. DMSO가 극성이 큰 물질임에도 불구하고 수소결합착물의 생성엔탈피 값들은 측정방법에 의한 차이가 크지 않았다.

I. Introduction

In spite of the interest in the hydrogen bond due to its importance in biological processes, thermodynamic parameters for hydrogen bond formation by molecules of biological interest are lacking. One reason for this is that these compounds generally involve weak N—H...O or N—H...N linkages. The small formation constants for these hydrogen bonded adducts lead to inaccurate results of the thermodynamic parameters.

Most molecules which participate in biological process are complex. Thus the thermodynamics of hydrogen bond formation in model compounds has been studied in connection with the stru-

ctural stability of molecules of biological interest. ^(1,2) However, the use of model compounds does not lighten the difficulty in determining thermodynamic properties of weakly hydrogen bonded systems. The standard spectrophotometric analysis is pushed to its limits for the determination of formation constants and enthalpy changes as small as those encountered in these model compounds. Even high dilution calorimetric methods may produce large errors under these conditions. ^(3,4)

The pure base calorimetric method was proposed by Arnett et al. ⁽⁵⁾ in 1970 to deal with those cases where the formation constant for hydrogen bonded adducts was small or difficult to obtain. The pure base method has been shown to give enthalpies in good agreement

with the reliable result obtained by other investigators using different method of analysis.⁽³⁾ The advantage of the pure base method is on the fact that larger and more easily measured experimental heats of solution are used to calculate the enthalpy of formation.

II. Experimental

All of the compounds used in this study were commercially available. Baker Analyzed reagent grade carbon tetrachloride was distilled from calcium hydride through a column packed with glass helices. Karl Fischer titration, using an automatic titrator, showed that random samples of the carbon tetrachloride used generally contained less than 0.005% water. Aldrich Analyzed reagent pyrrole and dimethyl sulfoxide (DMSO) were dried over NaOH and distilled under nitrogen. Kanto analytical reagent grade indole was recrystallized to a constant melting point and dried in a vacuum oven. All compounds were purified until their properties agree well with accepted literature values.

Infra-red spectra were recorded on the Hilger & Watts Infragraph MK.2 IR Spectrophotometer. The methods of calculation is same as the one described by Spencer et al.⁽⁶⁾ Concentration were chosen so as to minimize the overlap of peaks. Pyrrole and indole concentration of about 0.01M and DMSO concentrations of 0.02M were used. Frequency measurements were made in 2- and 1-mm cells. The accuracy of measurement is made more difficult by the large frequency shifts which place the bonded absorbance close to the C—H absorption region. Enthalpy changes were calculated from the temperature dependence of the equilibrium constant.

The solution calorimeter was essentially that described originally by Arnett, et al.⁽⁷⁾ Its application to hydrogen bonding (ΔH) measurements and heats of protonation was as they they have previously reported.^(8,5) The sample

to be injected was brought to the same temperature as the solvent by equilibration in the temperature bath. samples (1~2m mol) were injected into 100 m liter of solvent. Injections were made into a minimum of three different freshly prepared volumes of solvent.

The errors involved in the measurements are reported here at the 95% confidence level.⁽⁹⁾

III. Results and Discussion

The equilibrium constants and enthalpies determined by infra-red spectroscopic methods for the formation of the pyrrole-DMSO and indole-DMSO complexes in carbon tetrachloride are given in table I. Frequency shift measured relative to the free acid. Equilibrium constants determined at 20 and 30°C. The reported error in the enthalpy is large in both cases and reflects the difficulty encountered with the spectroscopic measurements. For systems with small enthalpy changes the errors are magnified. Error estimate obtained from the slope of a least-squares plot of $\ln K$ vs. T^{-1} .

Table I : IR Spectroscopic Determination of Thermodynamic parameters for N—H...O Hydrogen Bonds in CCl_4 Solvent

Proton donor	Proton acceptor	$-\Delta H^\circ_{298}$ Kcal/mol	K_{298}	ν cm^{-1}
Pyrrole	DMSO	4.2 ± 0.5	14.7	175
Indole	DMSO	2.7 ± 0.5	5.1	129

The calorimetric pure base approach to the determination of enthalpy changes is independent of the equilibrium constant provide that the equilibrium constant is large enough to ensure complete complexation.⁽⁶⁾ According to the pure base method, if a small quantity of hydrogen bonding acid is injected into the base as a solvent, two contributions to the heat observed are involved; the heat due to hydrogen bonding and that heat term which might occur if there were no hydrogen bonding. If a proper model

compound is chosen, the hydrogen bonding heat term can be isolated. An inert reference solvent is chosen to correct for heats of solution of the acid and model compound. Then the enthalpy of formation may be calculated from

$$\Delta H = (\Delta H_s^a - \Delta H_s^m)_{\text{base}} - (\Delta H_s^a - H_s^m)_{\text{ref}} \quad (1)$$

where the superscripts *a* and *m* refer to acid and model compound respectively. Both the choice of model compound and reference solvent can influence the enthalpy calculated from equation (1). For solvent such as DMSO, pure base measurements may lead to higher calculated enthalpies than those found in CCl₄.

The high dilution calorimetric method⁽⁶⁾ assumes that if small quantity of acid or base is injected into a medium which contains a species capable of hydrogen bonding to the acid or base, the enthalpy of hydrogen bond formation may be found from

$$\Delta H_{\text{obs}} = JHCV \quad (2)$$

where ΔH_{obs} is the heat observed corrected for the heat of solution of the injected species, *C* is the concentration of the hydrogen bonded complex, and *V* is the total volume of the system. If the equilibrium constant, usually determined from infra-red spectroscopic measurements, is known *C* may be calculated and ΔH directly solved for by equation(2).

Table II : Heat of Solution at Infinite Dilution at 298°K (ΔH_s , Kcal/mol)

Solute	Solvent		
	CCl ₄	Cyclohexane	DMSO
Pyrrole	+2.22	+3.74	-2.29
<i>N</i> -Methylpyrrole	+0.38	+1.85	+0.10
Indole	+1.74	+3.25	-1.69
<i>N</i> -Methylindole	+0.44	+1.70	+0.14

Table II gives the heat of solution at infinite dilution for the acids and bases of this work. Table III lists the enthalpy of hydrogen bond formation calculated by the pure base method for the two reference solvents cyclohexane and

carbon tetrachloride. The model compounds chosen were *N*-methylpyrrole for pyrrole and *N*-methylindole for indole. The enthalpy values obtained for the two reference solvents are not markedly different within error limits. However, a clear trend is evident. The calculated enthalpy values are in all cases higher when cyclohexane is the reference solvent than for carbon tetrachloride. This results are attributed the difference in calculated enthalpy for the two reference solvents to an interaction of pyrrole with carbon tetrachloride.⁽¹⁰⁾

Table III : Enthalpy of Formation of N-H...O Bonds Calculated by the Pure Base Method (Kcal/mol of H⁺donor)

Adduct	Reference Solvent	
	CCl ₄	Cyclohexane
Pyrrole-DMSO	4.23	4.28
Indole-DMSO	2.74	2.81

Table IV : Comparison of Enthalpies of Hydrogen Bond Formation by Pure Base, High Dilution, and Spectroscopic Method ($-\Delta H$, Kcal/mol)

Adduct	Method		
	Pure base ^a	High dilution ^b	Spectroscopic
Pyrrole-DMSO	4.23	4.08	4.2±0.5
Indole-DMSO	2.74	2.67	2.7±0.5

a. Reference solvent is carbon tetrachloride.

b. Calculated from equation (2) using *K* given in Table I.

Table IV gives a comparison of the enthalpies obtained for the formation of the pyrrole-DMSO and indole-DMSO complexes by the pure base, high dilution, and spectroscopic method. There is the good agreement between the three methods for the enthalpy of the pyrrole-DMSO adduct, especially when it is considered that DMSO is a highly polar solvent.

It is the ultimate goal of the study of model compounds to be able to apply the results to more complex molecules. Although the model compounds of this work cannot be said to be

truly representative of the more complex molecules of biological interest, there is an ample hope for good estimates of the actual hydrogen bond strength formed by the molecules of biological interest.

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