

erism, one can conclude that the N-H groups in these pyrimidines are *not* involved in the electron transfer reactions of these electron adducts. Hence, electron transfer probably occurs from the $\dot{C}(OH)$ and $\dot{C}(O^-)$ ketyl groups of these pyrimidines.

The electron adduct to cytosine ($pK_a^1 = 4.6$ and 12.2) at pH 9.2 is found to transfer 100% to acceptors and to have a very low redox potential; see Figure 5c and Table II.

Rates of Electron Transfer Reactions. In the process of determining the efficiency of electron transfer from the various radicals from pyrimidine bases to a number of acceptors, the formation kinetics of $\cdot A^-$ (or $\cdot A^-H^+$) radicals, reaction 2, can be monitored. These k_2 rates are pseudo-first-order dependent on the concentration of A. Table III presents a selection of the rates^{4,5,17} of electron transfer to a few acceptors A. These rates are the experimentally observed values and are not corrected for the back reaction. In most cases the correction is quite small.

It can be noted that (a) the intermediates produced from the reaction with OH radicals have k_2 values of $\sim 2-5 \times 10^9 M^{-1} sec^{-1}$, for acceptors having relatively

high redox potentials, *i.e.*, $E_A^{\circ 1} > E_{RH}^{\circ 1}$. These rates are close to being diffusion controlled. These rates are also slightly higher for the basic forms of the donor radicals compared to the acid forms, and (b) the electron adducts to pyrimidines also have k_2 values of $\sim 2-5 \times 10^9 M^{-1} sec^{-1}$. It is somewhat surprising that these electron transfer rates are not higher than those from the OH adducts to pyrimidines.

Conclusions

It is clear that a knowledge of the redox potentials of the free radicals produced from pyrimidines in aqueous solution can be of great value in understanding and interpreting the various observations previously reported in the literature. The $\cdot TH$ and $\cdot UH$ radicals (produced by H atom abstraction from dihydropyrimidines) are stronger reducing agents than the $\cdot T-OH$ and $\cdot U-OH$ radicals (produced by OH addition to the pyrimidines). The very low redox potentials of the electron adducts to pyrimidines make these intermediates powerful reducing agents. It suggests and supports postulated mechanisms of electronic conductivity through DNA and biopolymers.

Thermochemical Isotope Effects. Chloroform/Chloroform-*d* and Acetone/Acetone-*d*₆ in Selected Solvents

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Abstract: Isotope effects on the heats of solution of the isotopic pairs chloroform/chloroform-*d* and acetone/acetone-*d*₆ have been measured in a variety of solvents at 25°. While both positive and negative isotope effects have been observed for the heats of solution of these solutes, the transfer of the deuterated compound from cyclohexane (at infinite dilution) to other solvents is in every case more exothermic than the transfer of the parent compound.

Thermochemical isotope effects have been studied in a number of ways. The most common type of investigation has dealt with the properties of a pure compound, such as melting point, boiling point, vapor pressure, heat of vaporization, etc. There is a growing body of data on the change in the thermochemical properties of a solute (at high dilution) caused by isotopic substitution on the solvent. Virtually all of this work has involved H₂O and D₂O as solvents. In a few cases, the effect of substitution of deuterium for hydrogen on one or both components of a binary system has been studied with respect to the integral mixing properties. Benjamin and Benson² compared the heats of mixing of the water-methanol and heavy water-methanol-*d* systems. Rabinovich and Nikolaev³ measured the vapor pressures of the acetone-chloroform and acetone-chloroform-*d* systems to obtain the isotope effect on the excess free energy of mixing, and Morcom

and Travers⁴ studied heats of mixing in these systems to obtain the isotope effect on the heat of mixing. These investigations have led to the general conclusion that substitution of a deuterium atom for hydrogen increases the strength and/or the degree of hydrogen bonding.

Several workers have investigated the effects of isotopic substitution on equilibrium constants for formation of hydrogen bonds. Singh and Rao⁵ observed very large isotope effects for hydrogen bonds of phenol and phenol-*d* with various bases in carbon tetrachloride, reporting both positive and negative isotope effects. Pluorde⁶ investigated a similar series of bases and in every case found the ratio K_D/K_H to be greater than unity. Creswell and Allred⁷ studied the hydrogen bonds of fluoroform and fluoroform-*d* with tetrahydrofuran in cyclohexane and found $K_D/K_H = 1.04$ at 25°, with the complex formation 130 cal/mol more exothermic for the deuterated compound.

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As part of a continuing investigation of thermochemical isotope effects,⁸⁻¹⁰ we have measured the heats of solution of the isotopic pairs chloroform/chloroform-*d* and acetone/acetone-*d*₆ in a variety of liquids ranging from "inert" solvents such as cyclohexane and carbon tetrachloride to "active" solvents such as ethers, alcohols, and water (acetone only in water). Our results support the general conclusion that the substitution of deuterium for hydrogen in chloroform stabilizes the interactions of chloroform with active solvents. An analysis of this stabilization has been attempted for hydrogen bonds of chloroform with pyridine, acetone, *p*-dioxane, and THF. Similar effects are observed for heats of solution of acetone/acetone-*d*₆, but it is not possible at present to state whether this effect is due to simple solvent-solute interactions or to more complex interactions affecting the keto-enol equilibrium of acetone.

Experimental Section

Materials. Matheson Coleman and Bell (MCB) spectroquality chloroform was analyzed by gas chromatography and was found to contain about 0.3% of an impurity having the same retention time as carbon tetrachloride. For measurements involving chloroform as solvent, this material was used without further purification. The impurity was reduced to an undetectable level by distillation on a spinning band column for chloroform to be used as solute. Heats of solution of the distilled and untreated materials agreed to within 0.3% in *p*-dioxane and in 2-propanol.

Two lots of chloroform-*d* were used, both with deuterium content indicated as greater than 99.8%, supplied by Mallinckrodt and by Stohler Isotope Chemicals (SIC). The isotopic purities were confirmed by nmr analysis. Gas chromatograms of both samples showed a single peak. Heats of solution measured with samples from the two lots in various solvents were in excellent agreement.

MCB spectroquality acetone was analyzed by glc and was found to contain 2-propanol as the major impurity, amounting to approximately 0.1% by volume. This material was used without further purification for acetone to be used as solvent. For studies with acetone as the solute, this impurity was reduced to an undetectable level by distillation on the spinning band column.

SIC acetone-*d*₆, labeled as having an isotopic purity of greater than 99.5%, was used without further purification. Nmr analysis indicated an isotopic purity of 99.9 ± 0.3%, and the gas chromatogram showed a single peak.

Cyclohexane, carbon tetrachloride, and *p*-dioxane were Fisher Certified (99+ mol %). Tetrahydrofuran (THF) was MCB chromatography (99+ mol %), and methanol, 2-propanol, and pyridine were MCB spectroquality. All were used without further purification. Water and ethanol were conductivity grade.

Calorimetry. The calorimeter and sample handling techniques have been described previously.¹⁰⁻¹² The volume of solvent in each experiment was approximately 300 ml. Solute sample size ranged from 0.5 to 5 ml, except for measurements on the mixing of chloroform-*d* with chloroform and acetone-*d*₆ with acetone, in which samples of 10-15 ml were used. Observed enthalpy changes were generally in the range 5-15 cal and were corrected for the bulb-breaking effect (0.02 ± 0.01 cal). A vapor correction was made since some of the solute existed as vapor in the unfilled portion of the sample bulb. Vapor pressures and heats of vaporization for the hydrogen compounds were also used for the deuterium compounds in making this correction. The total correction for the vapor space was always less than 5 cal/mol. All measurements were made at 25.0 ± 0.1°.

In most cases, heats of solution were measured by adding successive samples of the solute to an aliquot of solvent in a single series of measurements. The concentration dependence was small

but readily apparent in most cases. Our data were fitted to eq 1 in

$$\Delta H^{\text{soln}} = \Delta H^\circ + b\bar{m} \quad (1)$$

order to evaluate the standard heat of solution (ΔH°), and standard deviations were calculated as

$$\sigma^2 = (N - 2)^{-1} \sum_{i=1}^N (\Delta H_i^{\text{soln}} - \Delta H^\circ - b\bar{m}_i)^2 \quad (2)$$

with

$$\bar{m} = (m_0 + m_i)/2 \quad (3)$$

ΔH^{soln} is the observed enthalpy change (per mole of solute added) on adding an increment of solute to a solution containing solute at an initial molality m_0 , forming a solution of molality m_i . The parameters ΔH° and b were determined by the method of least squares, and ΔH° is taken to represent the standard (infinite dilution) heat of solution of the solute in a particular solvent. Our results are presented in Table I, in which we list values of ΔH° , b , σ , and the number of data points. The results of 138 measurements are reported here. An additional seven measurements were discarded because of differences of more than 6 standard deviations from the remainder of the set. Using these techniques, we occasionally observe low results, presumably due to leakage of the sample bulb or possibly to the trapping of a small amount of the solute in the side arm. Values of b are given only to illustrate the magnitude of the dilution effect. Because of the very small range of composition covered and the relatively small dilution effects, we attach very little significance to these values. Values of standard deviations are indicative only of precision and not of the accuracy of our standard heats of solution. Because of solvent impurities, calibration uncertainties, etc., we regard these standard heats as accurate to about (1% + σ). However, since most of these effects will be common to the heats of solution of both isotopic isomers, we consider the differences in the heats of solution of these isotopic isomers to have accuracies comparable to the combined standard deviations of the individual heats of solution.

There are very few studies available for comparison of our heats of solution. The mixing properties of nonelectrolytes have commonly been studied as integral heats of mixing, and the data are usually presented in the form of eq 4, from which heats of solution may be

ΔH^{mixing} (per mole of mixture) =

$$X_1 X_2 \sum_{r=0}^q C_r (X_2 - X_1)^r \quad (4)$$

calculated. In terms of the parameters of eq 4, the standard heat of solution of component 1 at infinite dilution in solvent 2 is

$$(\Delta H^\circ_1)_2 = \sum_{r=0}^q C_r \quad (5)$$

and the standard heat of solution of component 2 at infinite dilution in solvent 1 is

$$(\Delta H^\circ_2)_1 = \sum_{r=0}^q C_r (-1)^r \quad (6)$$

However, the mixing data on which the parameters of eq 4 are based contain very few measurements at high dilutions, and heats of solution calculated from such equations are not very reliable. Where possible, we have compared our results to standard heats calculated from mixing data, and in every case we found reasonable agreement.

In some cases, mixing data have been presented in terms of an ideal associated solution model. McGlashan and Rastogi¹³ considered the chloroform-*p*-dioxane system in terms of a 1:1 and a 2:1 (two molecules of chloroform to one of dioxane) complex. They report equilibrium constants of 1.11 mf⁻¹ and 1.24 mf⁻² at 50° and heats of complex formation of -2.01 and -3.61 kcal/mol. Assuming these heats of formation to be independent of temperature, we project equilibrium constants of 1.44 mf⁻¹ and 1.99 mf⁻² at 25°, using the van't Hoff equation. From these data, we calculate -1185 cal/mol for the heat of solution of chloroform in *p*-dioxane at 25°, compared with our value of -1182 cal/mol.

Kearns¹⁴ treated his data for the chloroform-acetone system in

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Table I. Heats of Solution and Derived Quantities at 25.0°

Solvent (S)	Isotope	Obsd	ΔH° , cal/mol	b^a	σ , cal/mol	$(\Delta H^\circ_D - \Delta H^\circ_H)_S$	$\Delta(\Delta H^\circ_{D/H})_{I \rightarrow S}^b$
Chloroform/Chloroform- <i>d</i>							
Acetone	H	4	-1202	18	1	-34	-40
	D	4	-1236	69	2		
THF	H	4	-2015	-216	9	-33	-39
	D	4	-2048	-50	9		
<i>p</i> -Dioxane	H	6	-1182	-59	3	-18	-24
	D	6	-1200	-75	3		
Pyridine	H	4	-1317	-47	2	-18	-24
	D	4	-1335	119	4		
MeOH-2-PrOH (50:50) (v:v)	H ^c	3	-1286	220	1	-14	-20
	D	4	-1300	224	2		
2-Propanol	H	4	-843	535	3	-13	-19
	D	4	-856	554	3		
Methanol	H ^c	3	-1145	189	1	-10	-16
	D	6	-1155	102	7		
Carbon tetrachloride	H	4	224	-48	1	0	-6
	D	4	224	-52	1		
Chloroform	H		(0)			1	-5
	D	1	1				
Cyclohexane	H	5	662	-108	3	6	
	D	4	668	-100	1		
Acetone/Acetone- <i>d</i> ₆							
Water	H	3	-2382	-100	5	-22	-194
	D	3	-2404	-59	5		
EtOH-water (35:65) (v:v)	H	5	251	-49	6	-19	-191
	D	4	232	-78	1		
Ethanol	H	4	-1192	-208	1	-9	-181
	D	4	-1183	-154	6		
Pyridine	H	4	65	19	1	-2	-174
	D	4	63	-16	1		
Acetone	H		(0)			4	-168
	D	1	4				
<i>p</i> -Dioxane	H	4	244	-93	2	13	-159
	D	4	257	-88	2		
Chloroform	H	2	-2046	0	1	61	-111
	D	2	-1985	0	1		
Carbon tetrachloride	H	4	707	-926	2	96	-76
	D	4	803	-931	6		
Cyclohexane	H	4	2397	542	4	172	
	D	4	2569	1124	5		

^a $\Delta H^{\text{soln}} = \Delta H^\circ + b\bar{m}$ (eq 1). ^b $\Delta(\Delta H^\circ_{D/H})_{I \rightarrow S} = (\Delta H^\circ_D - \Delta H^\circ_H)_S - (\Delta H^\circ_D - \Delta H^\circ_H)_I$; I = cyclohexane. ^c Determined by Mr. E. L. Taylor.

terms of the ideal associated solution model, again with both 1:1 and 2:1 complexes. He reports equilibrium constants 0.967 mf^{-1} and 1.117 mf^{-2} and heats of complex formation -2.42 and -3.29 kcal/mol for the 1:1 and 2:1 complexes, respectively, at 25°. From these data, we calculate -1190 cal/mol for the heat of solution of chloroform in acetone and -1950 cal/mol for the heat of solution of acetone in chloroform, compared with our values of -1202 and -2046 cal/mol. Morcom and Travers⁴ present their data for the integral heats of mixing of chloroform and acetone in terms of eq 4. Their parameters give -901 and -1939 cal/mol for the heats of solution of chloroform in acetone and acetone in chloroform. Since their data contain no measurements with mole fractions of either component less than 0.2, the discrepancy between these extrapolated values and our results is not surprising. Morcom and Travers also measured heats of mixing of acetone and chloroform-*d*. Again, heats of solution calculated from their parameters are in acceptable but not impressive agreement with our results. The isotope effect on the heat of solution of chloroform in acetone calculated from their data is in direct opposition to our observations. From their data, we calculate that the solution of chloroform-*d* in acetone is about 50 cal/mol more endothermic than that of chloroform, while we observe this difference to be 34 cal/mol exothermic. However, since in all of their measurements the heat of mixing for the deuterated system was more negative than that of the normal system at the same composition, this discrepancy is almost certainly due to their lack of measurements at very small mole fractions of chloroform and chloroform-*d*.

Discussion

Chloroform/Chloroform-*d*. The heat of solution may

be considered to arise from four contributions: (a) the breaking of solute-solute interactions, (b) the formation of solvent-solute interactions, (c) the breaking of solvent-solvent interactions, and (d) an effect on solvent-solvent interactions caused by the presence of the solute. Of these contributions, the latter two can be expected to be the least affected by substitution of deuterium atoms for one or more of the hydrogen atoms of the solute, though in the case of highly structured solvents such as water and alcohols, these contributions could be rather large. For a relatively inert solvent, there should be little isotope effect on the formation of solvent-solute interactions, and the difference between the heats of solution of the isotopic isomers should be primarily due to differences in the breaking of solute-solute interactions in the pure liquids. A clearer measurement of this effect might be gained from the isotope effect on the heat of vaporization of the solute, but this measurement would require extreme precision. In this discussion, we will assume that there is no isotope effect on the heats of solution of these vapors in an inert solvent such as cyclohexane and that the isotope effect on the heats of solution of these liquids in cyclohexane is the same as the isotope effect on the heats of vaporization. In order to provide some test of this assumption,

we measured the temperature dependence of the vapor pressures of acetone and acetone- d_6 by the isoteniscope method. From these experiments, we calculated that the vaporization of acetone- d_6 is 150 ± 90 cal/mol more endothermic than the vaporization of acetone. The isotope effect on the heat of solution of acetone in cyclohexane was found to be 170 cal/mol.

The isotope effect on heats of solution in an "active" but not self-associating solvent can be attributed mainly to differences in both solute-solute interactions and solvent-solute interactions. The solute-solute effect can be removed by subtraction of the isotope effect on the heats of solution in an inert solvent (I) from the isotope effect in an active solvent (S). This difference is more properly described as the isotope effect on the enthalpy of transfer of the solute from the inert solvent to the active solvent and should be primarily due to differences in the interactions of the isotopic isomers with the active solvent. These differences are listed in column 8 of Table I as $\Delta(\Delta H^\circ_{D/H})_{I \rightarrow S}$, with

$$\Delta(\Delta H^\circ_{D/H})_{I \rightarrow S} = (\Delta H^\circ_D - \Delta H^\circ_H)_S - (\Delta H^\circ_D - \Delta H^\circ_H)_I \quad (7)$$

I = cyclohexane

The quantity $\Delta(\Delta H^\circ_{D/H})_{I \rightarrow S}$ is negative in every solvent studied, indicating that the deuterated compound interacts more strongly with these solvents than does the parent compound. Of course, self-association of some of the solvents may contribute significantly to this isotope effect.

Chloroform is known to form hydrogen bonds with acetone, THF, *p*-dioxane, and pyridine. The isotope effect on the enthalpy of transfer of chloroform from cyclohexane to these solvents is probably due to a change in both the degree of hydrogen bonding and the strength of the hydrogen bonds. If the effect $\Delta(\Delta H^\circ_{D/H})_{I \rightarrow S}$ is attributed entirely to hydrogen bond effects, one can write

$$\Delta(\Delta H^\circ_{D/H})_{I \rightarrow S} = (f_D)_S \Delta H^\circ_{D-S} - (f_H)_S \Delta H^\circ_{H-S} \quad (8)$$

in which $(f_D)_S$ and $(f_H)_S$ represent the fractions of the solute molecules involved in hydrogen bonds at infinite dilution in the solvent S, and ΔH°_{D-S} and ΔH°_{H-S} are the enthalpies of formation of the hydrogen bonds of the solvent with the deuterium and hydrogen compounds. The fractions $(f_D)_S$ and $(f_H)_S$ are related to the equilibrium constants for hydrogen bond formation (mole fraction basis) K_{D-S} and K_{H-S} by

$$\begin{aligned} (f_D)_S &= K_{D-S}/(1 + K_{D-S}) \\ (f_H)_S &= K_{H-S}/(1 + K_{H-S}) \end{aligned} \quad (9)$$

and these equilibrium constants are related to thermodynamic properties for formation of hydrogen bonds.

$$-RT \ln K_{D-S} = \Delta G^\circ_{D-S} = \Delta H^\circ_{D-S} - T\Delta S^\circ_{D-S} \quad (10a)$$

$$-RT \ln K_{H-S} = \Delta G^\circ_{H-S} = \Delta H^\circ_{H-S} - T\Delta S^\circ_{H-S} \quad (10b)$$

$$-RT \ln (K_{D-S}/K_{H-S}) = \Delta(\Delta G^\circ_{D-S/H-S}) = \Delta(\Delta H^\circ_{D-S/H-S}) - T\Delta(\Delta S^\circ_{D-S/H-S}) \quad (11)$$

The isotope effect on the enthalpy of transfer of a solute

from an inert solvent to a hydrogen bonding solvent is actually due to two effects, an enthalpy effect and an entropy effect on the formation of the hydrogen bond. Separation of these effects on the basis of the data presented here is impossible. Even with supplementary data in the form of equilibrium constants, definitive separation of the contributions of enthalpy and entropy to the overall isotope effect can be quite difficult. Creswell and Allred⁷ studied the temperature dependence of the equilibrium constant for formation of hydrogen bonds of THF with fluoroform and fluoroform- d in mixtures of THF and cyclohexane and observed differences in both the enthalpies and entropies of formation of the hydrogen bonds. However, their data can be fitted almost as well by attributing the differences in these equilibrium constants solely to either a difference in the enthalpy term or in the entropy term. Curvefitting their data of $\ln(K_D/K_H)$ vs. $(1/T)$ gives $\Delta(\Delta H^\circ_{D/H}) = -132$ cal/mol and $\Delta(\Delta S^\circ_{D/H}) = -0.36$ cal/(deg mol), with a standard deviation in $\ln(K_D/K_H)$ of 0.015. If the effect is attributed entirely to enthalpy differences [setting $\Delta(\Delta S^\circ_{D/H}) = 0$], the enthalpy effect is found to be $\Delta(\Delta H^\circ_{D/H}) = -21$ cal/mol with a standard deviation in $\ln(K_D/K_H)$ of 0.018. Attributing the effect entirely to entropy differences [setting $\Delta(\Delta H^\circ_{D/H}) = 0$] gives $\Delta(\Delta S^\circ_{D/H}) = 0.07$ cal/(deg mol) and a standard deviation of 0.020. These parameterizations cannot be distinguished on the basis of "goodness of fit" unless the ratios of equilibrium constants can be determined with better than 2% accuracy. The relative accuracy of the three treatments cannot be distinguished with calorimetric data unless the isotope effect on the enthalpy of formation of hydrogen bonds can be determined to within about 50 cal/mol. For weak complexes, equilibrium constants are usually reported with 5-10% uncertainties, and values of ΔH° determined calorimetrically are generally reliable to 100-200 cal/mol. The investigation by Creswell and Allred indicates that there actually is an isotope effect on both the enthalpy and entropy of formation of hydrogen bonds between fluoroform and THF, but even with their very precise data, the separation of the two effects leaves very little margin for error.

Pimentel and McClellan¹⁵ discuss the compensating effects of $\Delta(\Delta H^\circ)$ and $\Delta(\Delta S^\circ)$ which tend to work against each other to make $\Delta(\Delta G^\circ)$ relatively insensitive to changes which might cause rather large effects in $\Delta(\Delta H^\circ)$ and $\Delta(\Delta S^\circ)$. This compensation applied to isotope effects can be stated mathematically as

$$\Delta(\Delta H^\circ_{D-S/H-S}) = \beta \Delta(\Delta S^\circ_{D-S/H-S}) \quad \beta \geq 0 \quad (12)$$

Estimates of the possible contributions of enthalpy and entropy to our results can be made on the basis of three special cases [(I) $\beta = \infty$, $\Delta(\Delta S^\circ_{D-S/H-S}) = 0$; (II) $\beta = 0$, $\Delta(\Delta H^\circ_{D-S/H-S}) = 0$; and (III) $\beta = T$, $\Delta(\Delta G^\circ_{D-S/H-S}) = 0$, $(K_{D-S}/K_{H-S}) = 1$] for the four solvents for which hydrogen bond data are available. We have used Kearns' data for chloroform-acetone,¹⁴ McGlashan and Rastogi's data for chloroform-*p*-dioxane,¹³ and Slejko, Drago, and Brown's¹⁶ data for

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(16) F. L. Slejko, R. S. Drago, and D. G. Brown, *J. Amer. Chem. Soc.*, **94**, 9210 (1972).

Table II. Estimates of the Isotope Effects on the Hydrogen Bonds of Chloroform

Solvent (S)	Case	$\Delta(\Delta H_{D-S/H-S}^\circ)$, cal/mol	$\Delta(\Delta S_{D-S/H-S}^\circ)$, cal/(deg mol)	K_D/K_H
Acetone $K_H = 0.97 \text{ mf}^{-1}$ $\Delta H_{H-S}^\circ = -2420 \text{ cal/mol}$	I	-26	(0)	1.04
	II	(0)	0.13	1.07
	III	-81	-0.27	(1.00)
THF $K_H = 5.5 \text{ mf}^{-1}$ $\Delta H_{H-S}^\circ = -3600 \text{ cal/mol}$	I	-23	(0)	1.04
	II	(0)	0.16	1.08
	III	-46	-0.15	(1.00)
<i>p</i> -Dioxane $K_H = 1.44 \text{ mf}^{-1}$ $\Delta H_{H-S}^\circ = -2010 \text{ cal/mol}$	I	-17	(0)	1.03
	II	(0)	0.10	1.05
	III	-41	-0.14	(1.00)
Pyridine $K_H = 8.6 \text{ mf}^{-1}$ $\Delta H_{H-S}^\circ = -4600 \text{ cal/mol}$	I	-15	(0)	1.03
	II	(0)	0.11	1.06
	III	-27	-0.09	(1.00)

chloroform-THF and chloroform-pyridine. The formation constants for the chloroform-THF and chloroform-pyridine hydrogen bonds were reported in units of reciprocal molarity at 27.3 and 9.5°, respectively. These were converted to units of reciprocal mole fraction using the density of the solvent (cyclohexane) at the reported temperatures then adjusted to the values at 25° using the reported enthalpy values in the van't Hoff equation, assuming that the enthalpies of formation of the hydrogen bonds were independent of temperature.¹⁷ The results of these calculations are shown in Table II. Case III is probably the least likely of the three cases, since ratios of equilibrium constants for hydrogen bond formation of deuterated compounds over those of hydrogen compounds have generally been found to be greater than unity. The other two cases give results comparable to the values calculated with the same assumptions from the data for fluoroform and fluoroform-*d* with THF.

In general, we conclude that substitution of deuterium for hydrogen in the chloroform molecule increases the strength of its hydrogen bonds by about 20 cal/mol and increases the equilibrium constant for the hydrogen bond by 3-8%.

(17) G. L. Bertrand, D. E. Oyler, U. G. Eichelbaum, and L. G. Hepler, *Thermochimica Acta*, **7**, 87 (1973).

Acetone/Acetone-*d*₆. As in the case of chloroform, the isotope effect on the enthalpy of transfer of acetone from cyclohexane to other solvents is negative for all of the solvents studied. Interpretation of our results for acetone and acetone-*d*₆ in terms of hydrogen bonding is tempting and might lead to some very interesting conclusions, particularly with respect to the strongly endothermic isotope effect on the heats of solution in cyclohexane. This effect coupled with the highly endothermic heats of solution in cyclohexane might lead one to speculate on self-association in liquid acetone. However, the solution properties of acetone are strongly affected by keto-enol tautomerism, which is probably also very strongly affected by deuterium substitution. The fraction of acetone molecules in the enol form is known to decrease with increasing solvent polarity, and the trends which we have observed for the isotope effect on heats of solution of acetone in various solvents might equally well be interpreted in terms of an isotope effect on hydrogen bonding, an isotope effect on keto-enol tautomerism, or both. Investigations of the isotope effects on these equilibria by other methods may allow separation of the two contributions to the isotope effect on heats of solution of acetone.

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