INFLUENCE OF PHENOL ACIDITY AND SOLVENT POLARITY WITH PHENOL—RETINAL SCHIFF BASE HYDROGEN BONDS — THERMODYNAMIC PARAMETERS OF BOND FORMATION AND PROTON TRANSFER

H. SCHMIDEDER, O. KASENDE*, H. MERZ, P. P. RASTOGI** and G. ZUNDEL Physikalisch-Chemisches Institut der Universität, D-8000 München 2 (F.R.G.) (Received 30 March 1987)

ABSTRACT

Phenol—butylamine Schiff base 1:1 systems are studied in methylcylohexane solutions. The thermodynamic data $(\Delta H^0 \text{ and } \Delta S^0)$ of the hydrogen bond formation and of the proton transfer in the OII····N $\Rightarrow O^{-}$ ···II*N bonds are determined using IR spectroscopy. In all systems studied these hydrogen bonds show large proton polarizability since double-minimum proton potentials are present, whereby the deeper well is at the N. The amounts of the negative ΔH_{PT}^0 and ΔS_{PT}^0 values increase in proportion to the $\Delta p K_a$ (p K_a of the protonated Schiff base minus p K_a of the phenol).

For one phenol-Schiff base system the thermodynamic quantities were determined using a variety of solvents of different polarity. The amounts of the negative ΔH_{PT}^0 and ΔS_{PT}^0 values increase with increasing polarity of the solvent.

A retinal Schiff base is the chromophore in visual pigment proteins (rhodopsin and bacteriorhodopsin). On the basis of our experimental results conclusions are presented concerning proton transfer processes between the side group of the amino acid tyrosine (which is a phenolic group) and the retinal Schiff base in the protein.

INTRODUCTION

Hydrogen bonds with a double-minimum proton potential show large proton polarizability [1-3]. The proton can easily be shifted in these hydrogen bonds by a local electrical field. The presence of such hydrogen bonds is indicated by continua in the infrared spectra [4-6]. Furthermore, bands of two distinct species can be found in the IR spectra, arising, for instance, from the two proton limiting structures of the equilibrium $OH \cdots N \Rightarrow$ $O^- \cdots H^+N$. From the IR spectra the concentrations of both proton limiting structures and hence the proton-transfer equilibrium constant can be determined. According to van't Hoff, from the temperature dependence of these equilibria the thermodynamic quantities, standard enthalpy ΔH^0 and standard entropy ΔS^0 of the proton transfer can be obtained. In the same way the

^{*}Present address: Faculté des Sciences, Université de Kinshasa, Zaire.

^{**}Present address: Department of Chemistry, Lucknow University, Lucknow, India.

thermodynamic quantities of the hydrogen bond formation can be determined. In this paper we present the investigation of hydrogen bonds formed between chlorinated phenols (Ar—OH) and butylamine retinal Schiff base (NBuRet)



With these hydrogen bonds proton-transfer equilibria Ar—OH···NBuRet \Rightarrow ArO⁻···H⁺NBuRet can be studied as a function of the ΔpK_a (pK_a of the protonated Schiff base minus pK_a of the phenol). It is well known that in the case of proton-transfer equilibria, according to Huyskens [7, 8], linear relations are found between ΔG_{PT} and the ΔpK_a values. Furthermore, with phenol—octylamine systems a similar linear relation has been found [9] between ΔH_{PT} and the Onsager parameter $P_o = (\epsilon - 1)/(2\epsilon + 1)$, whereby the latter is representative of the strength of the reaction field casued by the arrangement of the solvent molecules around the structures [10].

Such a retinal Schiff base is the chromophore in visual pigments (rhodopsin and bacteriorhodopsin). Hence the data presented are of interest regarding proton-translocation processes in such systems.

EXPERIMENTAL

Substances

n-Butylamine retinal Schiff base was prepared by condensation of n-butylamine (from Merck, p.s. quality) and all-*trans* retinal (from Fluka, p.s. quality), according to ref. 12. The phenols were purified by sublimation.

IR spectroscopy

IR spectra were taken with a grating spectrophotometer 325, Bodenseewerk Perkin—Elmer. For the samples a cell with silicon windows was used that is described elsewhere [9]. In the reference beam of the spectrophotometer a cell was placed that contained pure solvent. With this cell a layer of variable thickness could be adjusted in order to compensate for the solvent bands. The spectra were digitized by a microcomputer and transferred to the Leibniz-Rechenzentrum, Munich, for band evaluation.

Temperature control

A copper pipe was fixed to the sample cell through which a refrigerant was pumped, controlled by a thermostat (Lauda). The actual temperature at the cell was measured using a PT-100 resistor.

RESULTS AND DISCUSSION

We investigated 1:1 mixtures of phenols (see Table 1) with butylamine retinal Schiff base $[pK_a = 5.99, \text{ from ref. 12}]$ in methylcyclohexane solution as a function of temperature. The spectra of one system are shown, for example, in Fig. 1. For comparison the spectrum of the pure 2,4,5-trichlorophenol is given.

The association equilibria

The hydrogen-bond-formation equilibrium is determined from the integrated abosrbance of ν_{OH} of the non-hydrogen-bonded phenols observed in the region 3550-3525 cm⁻¹ (Fig. 1). This band is calibrated using the integrated absorbance of a pure phenol solution (represented by · · · ·). Examples of van't Hoff plots are shown in Fig. 2. The slight deviation from linearity shows that within the large temperature range in which the systems are studied, ΔH_B^0 of the hydrogen-bond formation is not completely independent of the temperature. Nevertheless, from these van't Hoff plots, the thermodynamic data given in Table 2 can be obtained, since the deviation from linearity of the curves is small.

The proton transfer equilibria

Figure 3 shows the band of ν C=N of the non-protonated Schiff base at 1622 cm⁻¹ and that of the protonated one at 1662 cm⁻¹. In the following the band at 1662 cm⁻¹ is used to determine the position of the equilibria whereby the integrated absorbance of this band in the case of the hydrochloride (represented by ----) is used for calibration. To justify this procedure we studied the tetrachloroaurate salt of the Schiff base. The absorbance of this band is the same as that of the hydrochloride within experimental error. This result shows that the absorbance of this band is independent of the strength of the hydrogen bond.

TABLE 1

List of phenols used

Phenols	Supplier	Purity	pK_a
2,4.6-Trichlorophenol	Fluka	99%	5,99
2,4,5-Trichlorophenol	Fluka	99 %	6.72
2,6-Dichlorophenol	Merck	98%	6.78
2,3,4-Trichlorophenol	EGA-Chemie	97%	6.91
2,3-Dichlorophenol	Merck	98%	7.71
2,4-Dichlorophenol	Merck	96%	7.9
3,4-Dichlorophenol	EGA-Chemie	97%	8.62

All values taken from ref. 11.



Fig. 1. IR spectra of 2,4,5-trichlorophenol—butylamine retinal Schiff base 1:1 system, 27 mM in methylcyclohexane: layer thickness d = 0.66 mm; temperature. $-\cdot - \cdot -$, 30° C; ----, -35.7° C; ----, -49° C. For comparison the spectrum of the pure phenol (concentration 20 mM in methylcyclohexane is given ($\cdot \cdot \cdot \cdot$ line). The regions in which the spectra are masked by two intense solvent bands are omitted.



Fig. 2. Van't Hoff plots regarding hydrogen-bond parameters of the systems: (a, left) 2,4,5-trichlorophenol-NBuRet; (b, right) 2,3-dichlorophenol-NBuRet.

Correct thermodynamic data are only obtained if they are independent of the concentration. Therefore, the concentration dependence of these data was studied, as described in the next section, in the case of the 2,4,6-trichlorophenol—NBuRet system. Table 3 shows that the thermodynamic data are concentration independent if the concentrations are lower than 25.0 mM.

From the integrated absorbance of $\nu C=NH^+$ at 1662 cm⁻¹ the thermodynamic data of the proton-transfer equilibria are determined. They are given in Table 4. The van't Hoff plots of two examplex are shown in Fig. 4. In the case of the 3,4-dichlorophenol--NBuRet system the band of $\nu C=NH^+$ could not be evaluated quantitatively since the change of $\nu C=NH^+$ with temperature

TABLE 2

Thermodynamic data of the formation of the hydrogen bonds between the phenols and NBuRet

Phenols	∆pK _a	∆H [©] B (kJ mol ⁻¹)	$\Delta S^{\circ}_{\mathbf{B}}$ (J mol ⁻¹ K ⁻¹)	$\Delta G^{\circ}_{\mathbf{B}}(22^{\circ}\mathrm{C})$ (kJ mol ⁻¹)
2,4,6-Trichlorophenol	0.0	-51.3	-144.3	-8.7
2,4,5-Trichlorophenol	-0.73	-47.2	-116.2	-13.0
2.6-Dichlorophenol	-0.79	-30.2	-71.4	-9.1
2,3,4-Trichlorophenol	-0.98	-47.7	-122.6	-11.5
2,3-Dichlorophenol	-1.72	-47.6	-128.7	-9.6
2,4-Dichlorophenol	-1.91	-39.2	-95.2	-11.1



Fig. 3. IR spectra: layer thickness d = 0.24 mm; ——, NBuRet, 50 mM in methylcyclohexane; ——, H*NBuRetCl⁻, 25 m in butylchloride. The regions in which the spectra are masked by two intense solvent bands are omitted.

was too small. However, the band of $\nu C=NH^+$ increases noticeably with decreasing temperature. This result proves that ΔH_{PT}^0 is still negative. The values of this system given in Table 4 are extrapolated values taken from Figs 5 and 6. In these figures the ΔH_{PT}^0 and ΔS_{PT}^0 values are shown as a function of the ΔpK_a . Linear relationships were found between the thermodynamic quantities and the ΔpK_a values.

In the spectra shown in Fig. 1, the band of $\nu C=N$ at 1622 cm^{-1} as well as the band of $\nu C=NH^+$ at 1662 cm^{-1} are observed. This result shows that a double-minimum proton potential is present in the $OH\cdots N \Rightarrow O^-\cdots H^+N$ bonds. This result is confirmed in the following since with all systems IR continua are observed. With all systems studied, ΔH_{PT}^0 is negative. In the classical approximation ΔH_{PT}^0 is the difference between the two minima. Thus, the negative ΔH_{PT}^0 values show that with all systems the deeper well of the proton potential is at the N. TABLE 3

Concentration dependence of the thermodynamic data of the 2,4,6-trichlorophenol-NBuRet system

Concentration (mM)	$\Delta H_{\rm PT}^{0}$ (kJ mol ⁻¹)	$\Delta S_{\mathrm{PT}}^{0}$ (J mol ⁻¹ K ⁻¹)
68.5	-14.4	-73.4
25.0	-26.2	129.2
12.9	-22.9	-125.5
8.0	-23.8	-132.1



Fig. 4. Van't Hoff plots regarding the proton transfer equilibrium in the hydrogen bond: (a, left) 2,4,5-trichlorophenol-NBuRet; (b, right) 2,3-dichlorophenol-NBuRet.

TABLE 4

Thermodynamic data of the proton transfer in phenol-NBuRet 1:1 complexes in methylcyclohexane solution

Phenol	ΔpK_{a}	∆ <i>H</i> ⁰ _{PT} (kJ mol ⁻¹)	Δ <i>S</i> ^o _{PT} (J mol ⁻¹ K ⁻¹)	∆G _{PT} (at 22°C) kJ mol ⁻¹)
2,4,6-Trichlorophenol	0.0	-24.9	-130.1	13.5
2,4,5-Trichlorophenol	-0.73	-17.4	-94.9	10.6
2,6-Dichlorophenol	-0.79	-19.1	-106.0	12.2
2,3,4-Trichlorophenol	-0.98	-16.9	-93.1	10.6
2.3-Dichlorophenol	-1.72	-11.1	-73.2	10.5
2,4-Dichlorophenol	-1.91	-9.0	-67.0	10.8
3,4-Dichlorophenol	-2.63	-3.0	-46.0	10.6

In the spectra of the solutions in Fig. 1, intense IR continua are observed. The same is true with the other systems. Thus, all phenol—Schiff base hydrogen bonds studied show large proton polarizability caused by proton fluctuation within these hydrogen bonds. Furthermore, Fig. 1 shows that the intensity of the continuum increases with decreasing temperature. This result



Fig. 5. ΔH_{PT}^0 as a function of ΔpK_a (pK_a of H⁺NBuRet - pK_a of the phenol).



Fig. 6. ΔS_{PT}° as a function of $\Delta p K_a$.

is true with all systems studied as shown by Table 5. In this table, in all systems the absorbance of the continua at 1560 cm⁻¹ is summarized as a function of temperature. The result that the intensity of the IR continua, casued by heteroconjugated hydrogen bonds with large proton polarizability,

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Absorptivity coefficient of the continuum ϵ_c at 1960 cm⁻¹ as a function of the temperature of the phenol–NBuRet systems

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Phenol	$\Delta p K_{\mathbf{a}}$	_د (ا	mol ⁻¹ c	m ⁻¹) as	a funct	ion of th	e temper:	ature (°C)					
2,4,6-Trichlorophenol	0.0	T			4.1			-12.9	- 30.2	-41.8	51.0		
2,4,5-Trichlorophenol	-0.73	$_{T}^{\epsilon}$	30.0		35			64	26 - 35.7	46 - 49.0	45		
2,6-Dichlorophenol	-0.79	T_{c}^{ϵ}	48 30.0			-5.4		-19.2	49 35.9	55	50.0		
2,3,4-Trichlorophenol	-0.98	$r_c^{\epsilon_c}$	37	28.0		35 -8.1		37 -24.7	38 -38.9		41 - 50.6		
2,3-Dichlorophenol	-1.72	T_c^{ϵ}		31 29.7	2.5	28		44 	48	-42.9	37 53.5	-64.0	- 71.0
2,4-Dichlorophenol	-1.91	L_{e}^{e}	30.0	31	31		-12.9	33 —28.8		37 41.6	38	43	48
3,4-Dichlorophenol	-2.63	$t_c^{\epsilon_c}$	30			0.8	39	42 —26.0		44 42.0			
		εc				18		18		23			

increases with decreasing temperature is in very good agreement with recent calculations of the line spectra of a heteroconjugated hydrogen bond with a double-minimum energy surface [13].

Influence of solvent polarity

In the case of the 2,4-dichlorophenol—butylamine Schiff base systems the position of the proton-transfer equilibria were studied as a function of the polarity of the solvents. The thermodynamic data obtained are given in Table 6 together with the dielectric permittivity of the solvent and its Onsager parameter [10]. This table shows that the amounts of the negative ΔH_{PT}^0 and ΔS_{PT}^0 values increase with increasing polarity of the solvent. This result is expected since all $AH \cdots B \rightleftharpoons A^- \cdots H^+B$ equilibria in solutions are shifted to the right-hand side by the reaction field at the hydrogen bond. This reaction field is caused by the arrangement of the solvate molecules around this structure. The order of the solvate molecules is, however, higher around the polar structure and, thus, the reaction field shifts the equilibrium further to the right. With the systems presented here, however, no strict linear relation is observed between ΔH_{PT}^0 and the Onsager parameter.

CONCLUSIONS

In the case of all phenol-butylamine retinal Schiff base hydrogen bonds studied, $OH \cdots N \rightleftharpoons O^{-} \cdots H^+N$ equilibria are present in which, at least at low temperature, both proton-limiting structures have noticeable weight. A double-minimum proton potential occurs in these hydrogen bonds.

IR continua indicate that these hydrogen bonds show large proton polarizability due to proton motion. The intensity of these continua increases with decreasing temperature. This result is in good agreement with a recent theoretical treatment of a heteroconjugated hydrogen bond [13].

The value of ΔH_{PT}^0 of the proton-transfer equilibrium is always negative. Hence, in the classical approximation the deeper well of the double minimum

TABLE 6

Solvent	e	Po	$\Delta H_{\rm PT}^{\circ}$ (kJ mol ⁻¹)	$\Delta S_{\rm PT}^{0}$
•••••			((0 1101 11)
Methylcyclohexane	2.071	0.208	-9.0	-67.0
Tetrachlorodifluoroethane	2.4	0.241	-8.5	-70.4
Trichloroethane	3.4	0.308	-10.6	-89.4
Dibromomethane	7.77	0.405	-15.5	-92.5
Dichloromethane	9.08	0.422	-16.1	-93.3
Dichloroethane	10.65	0.433	-16.9	-94.6

Thermodynamic data of hydrogen-bonded complexes between 2,4-dichlorophenol and butylamine retinal Schiff base in various solvents

is always at the acceptor. The amounts of the negative ΔH_{PT}^0 and ΔS_{PT}^0 values increase in proportion to ΔpK_a , i.e., the pK_a value of the protonated Schiff base minus that of the phenol.

The study of the position of the proton-transfer equilibrium as a function of the polarity of the solvent has shown that with increasing polarity the amounts of the negative $\Delta H_{\rm PT}^0$ and $\Delta S_{\rm PT}^0$ values increase, a tendency which is expected with regard to the reaction field.

If a tyrosine—Schiff base hydrogen bond is present in visual pigment proteins, this bond corresponds to a cresol—butylamine Schiff base hydrogen bond. The extrapolation of the curves in Figs 5 and 6 shows that the $\Delta H_{\rm PT}^0$ value of such a hydrogen bond amounts to 9.2 kJ mol⁻¹ and $\Delta S_{\rm PT}^0$ amounts to 0. Hence, $\Delta G_{\rm PT}^0$ is 9.2 kJ mol⁻¹, i.e., the proton is preferentally present at the tyrosine in such a hydrogen bond. But it could be shifted by a local electrical field to the Schiff base since this hydrogen bond should show considerable proton polarizability.

ACKNOWLEDGEMENTS

Our thanks are due to the Deutsche Forschungsgemeinschaft and to the Fonds der Chemie for providing the facilities for this work. Two of us (O. K. and P. P. R.) are grateful to the Humboldt Foundation for grants.

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