[Chem. Pharm. Bull. 20(2) 258—261 (1972)]

UDC 546.212.03 : 547.831.03 : 547.581.2-26.04

Effect of Water on Charge-Transfer Complexations[1]

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(Received July 9, 1971)

The effects of water on charge-transfer (CT) transition energy, $h\nu_{CT}$, and the equilibrium constant, K_C, for complexations of chlorpromazine hydrochloride with *p*-xyloquinone and sodium N,N-dimethyl-*p*-aminobenzoate with sodium anthraquinone-2-sulfonate were investigated in aqueous ethanol, aqueous dioxane, or water. With an increase in water content of the media, $h\nu_{CT}$ decreased and K_C increased markedly. Especially high correlations were recognized between $h\nu_{CT}$ and water content, and between log K_C and logarithm of dielectric constant of the media. From the results, mechanism of the effects of water was speculated. It may be concluded that water does not obstruct but promotes the CT complexations presumably by specific and non-specific effects.

In aqueous media, several complexations of pharmaceutical and biochemical interest are known which can well be explained by the occurrence of charge-transfer (CT) between reacting species.[3] On a theoretical basis, Yomosa[4] has suggested that enzyme-substrate complexes may generally be CT complexes formed in the aqueous media of living systems. The authors[5] have supported the suggestion by the findings that the bacteriostatic activity of sulfonamides and the rate of enzymatic acetylation of aniline derivatives are related to the electron-donating ability of the substrates. On the other hand, the question has often been raised as to whether or not CT can really be occurred in aqueous media. In fact, it is not generally known that typical CT complexing as usually seen in non-aqueous media can be observed also in aqueous solvents. In such circumstance, the present study has been made to clarify whether water promotes or obstructs the formation of CT complexes. For this purpose, the influences of water added in ethanol or dioxane solutions have been investigated on the CT transition energy, $h\nu_{CT}$,[6] and the equilibrium constant, K_C, for some donor-acceptor systems.

Experimental

Materials——*p*-Xyloquinone (XQ), sodium anthraquinone-2-sulfonate (AQS), and sodium N,N-dimethyl-*p*-aminobenzoate (DMAB) were of analytical grade from commercial sources. Chlorpromazine hydrochloride (CPZ) was kindly supplied by Shionogi & Co., Ltd. They were purified by recrystallization or redistillation, and their melting or boiling points were found to be similar to those listed in chemical handbooks and literatures.

Measurement of Absorption Spectra——The visible spectra were recorded with a Shimadzu model MPS-50L multipurpose spectrophotometer in 1 cm or 5 cm cells at room temperature.

Measurement of the Wave-Length of CT Band——The difference spectra of mixtures of CPZ (0.1—0.2M) with XQ (8×10^{-3}—2×10^{-2}M) *vs.* XQ and DMAB (10^{-2}M) with AQS (2×10^{-3}M) *vs.* AQS in ethanol or dioxane

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[1] *a*) This forms Part IX of "Spectroscopic Studies on Molecular Interactions"; *b*) Part VIII: I. Moriguchi, S. Fushimi, and N. Kaneniwa, *Chem. Pharm. Bull.* (Tokyo), **19**, 2132 (1971); *c*) Presented in part before the 90th Annual Meeting of Pharmaceutical Society of Japan, Sapporo, July 1970.

[2] Location: *Hatanodai, Shinagawa-ku, Tokyo, 142, Japan.*

[3] S. Hata, *Farumashia*, **4**, 796 (1968); M. Florkin and E.H. Stotz, "Comprehensive Biochemistry," Vol. **22**, Elsevier Publ. Co., Amsterdam, 1967.

[4] S. Yomosa, *Prog. Theor. Phys.*, **40**, *Suppl.* 249 (1967).

[5] I. Moriguchi and N. Kaneniwa, *Chem. Pharm. Bull.* (Tokyo), **17**, 2554 (1969); I. Moriguchi, S. Fushimi, and N. Kaneniwa, *ibid.*, **18**, 1553 (1970).

[6] h is the Planck constant, and ν_{CT} the frequency of CT band.

containing varied concentrations of water were recorded with a Hitachi model EPS-3T spectrophotometer in 1 cm or 5 cm cells at room temperature, and the wave length of CT band, λ_{CT}, was determined. The value of $h\nu_{CT}$ was obtained from λ_{CT}.

Determination of Equilibrium Constant——A Hitachi model 139 or model EPS-3T spectrophotometer was employed for the measurements of absorbances at λ_{CT} for the donor-acceptor mixtures in various media at 30°. The concentrations of the donors and the acceptors were as follows: 2×10^{-3}—8×10^{-2}M for CPZ, 6.7×10^{-3}—1.3×10^{-2}M for XQ, 2×10^{-3}—1×10^{-2}M for DMAB, and 2×10^{-3}M for AQS. The value of K_C was calculated by the method previously described.[7]

Measurement of Refractive Index——The refractive indices of aqueous ethanol and aqueous dioxane were measured at 30° with an Atago model 302 Abbe-type refractometer.

Result and Discussion

Although a number of donors and acceptors are known to form stable CT complexes in non-aqueous solvents,[8] most of them are insoluble or, even if soluble, liable to be converted into colored substances[9] or led to chemical reactions through CT complexes[10] in aqueous media. However, CPZ-XQ and DMAB-AQS systems were found to form rather stable complexes in aqueous solvents such as more than 24% (v/v) ethanol or 20—60% (v/v) dioxane for CPZ-XQ system, and less than 15% (v/v) ethanol or water for DMAB-AQS system.

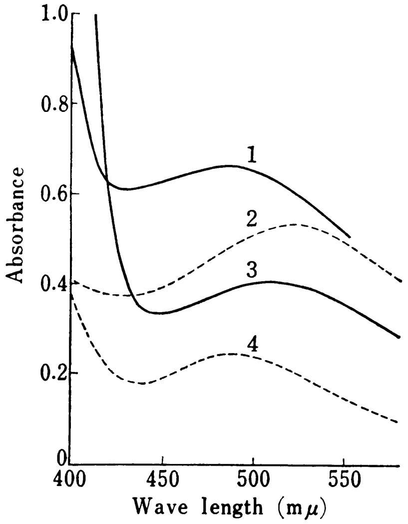

Fig. 1. Spectra of CPZ-XQ and DMAB-AQS Systems

1. CPZ (1.2×10^{-1}M) with XQ (8×10^{-3}M) in aqueous 20% (v/v) dioxane (1 cm cell)
2. XQ (8×10^{-4}M) with NaOH (0.035%) in aqueous 20% (v/v) dioxane (1 cm cell)
3. DMAB(10^{-2}M) with AQS(2×10^{-3}M) in water (5 cm cell)
4. AQS (1.7×10^{-3}M) with NaOH (0.07%) in water (1 cm cell)

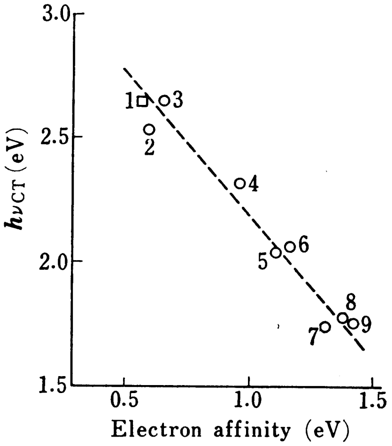

Fig. 2. Plots of $h\nu_{CT}$ for CPZ-XQ and Chlorpromazine-Benzoquinone Systems *vs.* Electron Affinity of the Acceptors[a]

1: CPZ-XQ system in aqueous 50% (v/v) dioxane

2–9: chlorpromazine-benzoquinone systems (benzoquinones: 2. *p*-benzoquinone (BQ), 3. methyl-BQ, 4. chloro-BQ, 5. 2,5-dichloro-BQ, 6. 2,6-dichloro-BQ, 7. trichloro-BQ, 8. *p*-chloranil, 9. *p*-bromanil) in acetonitrile

a) The values of $h\nu_{CT}$ except for CPZ-XQ system were taken from Ref. 13, and the values of electron affinity from Ref. 14.

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7) I. Moriguchi and N. Kaneniwa, *Chem. Pharm. Bull.* (Tokyo), 17, 2173 (1969).

8) G. Briegleb, "Elektronen-Donator-Acceptor-Komplexe," Springer Verlag, Berlin, 1961; L.J. Andrews and R.M. Keefer, "Molecular Complexes in Organic Chemistry," Holden-Day, Inc., San Francisco, 1964; R.S. Mulliken and W.B. Person, "Molecular Complexes," John Wiley & Sons, Inc., New York, 1969.

9) In the presence of sufficient amounts of water, *p*-chloranil, *p*-benzoquinone, and 2,6-dichloro-*p*-benzoquinone in organic solvents such as alcohols, acetone, and dioxane were observed to become reddish brown at 30°.

10) I. Moriguchi, S. Fushimi, and N. Kaneniwa, *Chem. Pharm. Bull.* (Tokyo), *in press.*

Curves 1 and 3 in Fig. 1 are examples of their absorption spectra: for CPZ-XQ system in 20% (v/v) dioxane and DMAB-AQS system in water, respectively. The absorption bands at 485 mμ and 513 mμ are due to neither the donors nor the acceptors, and also different from those[11] for alkaline solutions of the acceptors. The alterations of intensity of the bands were observed to be reversible according to the change of temperature. Moreover, as shown in Fig. 2, the obtained value of $h\nu_{\mathrm{CT}}$ for CPZ-XQ system in 50% (v/v) dioxane[12] exactly falls on the plotted line of $h\nu_{\mathrm{CT}}$ for chlorpromazine-benzoquinone systems in acetonitrile[13] against electron affinity[14] of the acceptors. These findings suggest the formation of CT complexes in CPZ-XQ and DMAB-AQS systems.

TABLE I. CT Properties of CPZ-XQ Complex in Aqueous Ethanol

Water content (% (v/v))	λ_{CT} (mμ)	$h\nu_{\mathrm{CT}}$ (eV)	$K_{\mathrm{C}}(30°)$ (M^{-1})	n_{D}^{30}	log $D^{a)}$
0.5	*ca.* 440	*ca.* 2.818	0.84	1.3581	1.387
10	450	2.756	0.94	1.3610	1.484
20	455	2.725	1.10	1.3618	1.559
30	457	2.713	1.25	1.3608	1.623
40	460	2.696	1.59	1.3591	1.679
50	468	2.650	2.13	1.3565	1.731
60	480	2.583	3.13	1.3529	1.775
67	485	2.557	4.00	1.3495	1.799
76	487	2.546	4.12	1.3449	1.828

a) *D* at 25°, Ref. 13

TABLE II. CT Properties of CPZ-XQ Complex in Aqueous Dioxane

Water content (% (v/v))	λ_{CT} (mμ)	$h\nu_{\mathrm{CT}}$ (eV)	$K_{\mathrm{C}}(30°)$ (M^{-1})	n_{D}^{30}	log $D^{a)}$
40	462	2.684	0.86	1.3864	1.389
50	465	2.667	1.21	1.3783	1.515
60	469	2.650	1.59	1.3690	1.613
70	474	2.622	2.34	1.3591	1.698
80	485	2.557	3.51	1.3503	1.770

a) *D* at 30°, Ref. 13

TABLE III. CT Properties of DMAB-AQS Complex in Aqueous Ethanol and Water

Water content (% (v/v))	λ_{CT} (mμ)	$h\nu_{\mathrm{CT}}$ (eV)	$K_{\mathrm{C}}(30°)$ (M^{-1})	n_{D}^{30}	log $D^{a)}$
85	510	2.431	21.5	1.3399	1.856
92	512	2.422	31.8	1.3363	1.874
100	513	2.417	67.4	1.3324	1.895

a) *D* at 25°, Ref. 13

Thus, CPZ-XQ system in aqueous ethanol and aqueous dioxane, and DMAB-AQS system in aqueous ethanol and water were investigated for the determination of λ_{CT}, $h\nu_{\mathrm{CT}}$, and K_{C} by

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[11] Those seemed to be for anion radicals of the acceptors, but this was not confirmed.

[12] Its dielectric constant (34.5 at 20°) is close to that of acetonitrile (37.5 at 20°).

[13] R. Foster and P. Hanson, *Biochim. Biophys. Acta*, **112**, 482 (1966).

[14] G. Briegleb, *Angew. Chem.*, **76**, 326 (1964).

the CT bands. The values obtained are listed in Table I, II, and III, along with refractive index, n_D, and logarithm of dielectric onstant,[15] log D, of the solvents. n_D and log D are considered to be typical solvent parameters for CT complexations.[1b] It is clearly seen that $h\nu_{CT}$ decreases and K_C increases with an increase in water content of the media. Consequently, it can be said that water promotes the formation of CT complexes in those systems investigated. The values of n_D and log D also appear to be related to both $h\nu_{CT}$ and K_C.

For elucidation of the promoting effect of water, the correlation coefficients of n_D and log D as well as water content with $h\nu_{CT}$ and with log K_C for CPZ–XQ system were calculated from the whole data obtained in aqueous ethanol and aqueous dioxane, because n_D and log D are generally related to water content in one kind of solvent-water system. The results are listed in Table IV, indicating that significant correlations exist there except for n_D with $h\nu_{CT}$, and the correlation coefficients are especially high for water content with $h\nu_{CT}$ and for log D with log K_C. The highly significant correlation of log D with log K_C is interpreted as being due to the stabilization of CT complexes by solvations and CT forces, both of which may be dominant in the solvents of higher D value among a number of forces probably contributing to CT complex formation.[1b] The reason for the high correlation of water content with $h\nu_{CT}$ is uncertain. Some specific effects of water, such as specific hydration[16] of the more polar structure of the excited state of CT complexes compared with that of ground state, may account for the high correlation.

TABLE IV. Correlation Coefficients of Water Content, n_D, and log D of Solvents with $h\nu_{CT}$ and with log K_C for CPZ–XQ Complexation in Aqueous Ethanol and Aqueous Dioxane

	Correlation coefficients[a]	
	with $h\nu_{CT}$	with log K_C
Water content	$-0.959^{b)}$	$0.861^{b)}$
n_D^{30}	0.429	$-0.723^{c)}$
log D	$-0.857^{b)}$	$0.954^{b)}$

a) 14 samples *b*) significant at the 0.001 level *c*) significant at the 0.01 level

In addition, K_C values for CT complexes of benzene derivatives with silver ion in water and in equimolar water–methanol mixture were collected from the literatures.[17] It was recognized that the K_C values in water were about 2 to 3 times as high as those in aqueous methanol. This may provide additional support for the promoting effect of water on CT complexations.

Thus, it may be concluded from these results that water does not obstruct but promotes the CT complexations. Presumably two kinds of mechanism may account for the promoting effect of water: specific one such as specific hydration, and non-specific one such as enhancing D value of the media. Although the number of examples demonstrated here seems rather small, there was no exception for the above conclusion.

In this paper, special attention has mainly been paid to the formation of usual CT complexes, *e.g.*, "outer complexes" according to Mulliken's classification.[18] The effect of water on the formation of "inner complexes" or further, on the formation of CT reaction products will be demonstrated in later papers.

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15) G. Akerlöf and O.A. Short, *J. Am. Chem. Soc.*, **58**, 1241 (1936); M.L. Huérou and C. Guerillot, *Compt. Rend.*, **258**, 2549 (1964).

16) L.P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, 1970, Chapter 8.

17) L.J. Andrews and R.M. Keefer, *J. Am. Chem. Soc.*, **71**, 3644 (1949); **72**, 5034 (1950); N. Ogimachi, L.J. Andrews, and R.M. Keefer, *ibid.*, **78**, 2210 (1956).

18) R.S. Mulliken, *J. Am. Chem. Soc.*, **74**, 811 (1952); **76**, 3869 (1954).