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Biochemical Reactions Through Charge Transfer Complex Formation or Ion Pair Formation

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It is, perhaps, generally believed that many biological reactions take place in vivo through intermolecular charge transfer complex formation [1-3]. Although, there has been so far, no direct evidence for the existence of a charge transfer complex, in vivo, its existence has been invoked to explain some biological reactions and actions of certain drugs[1-3].

It may be noted that biological reactions occur under homogeneous as well as heterogeneous conditions; while it is assumed that these reactions involve aqueous phase. In the laboratory, relevant or similar reactions are studied in vitro. Thus the conclusions drawn from in vitro reactions are assumed to be valid for in vivo reactions. One thus must demonstrate the existence of the CT complex in vitro, if the claim for the existence of the CT complex in vivo to be true. One only needs to study properties of a charge transfer complex in aqueous phase and determine the nature of this CT complex.

We embarked upon this study by carrying out some studies on a well established charge transfer complex, 1-ethyl-4-carbomethoxy pyridinium iodide (PyI)[1,4,5]. This particular compound is of particular interest because of its relevance to some biological reactions[1]. The behaviour of two co-enzymes, NAD$^+$ and NADP$^+$, and reaction of NAD. radical may be considered under this perspective[1]. We have studied PyI and also its perchlorate salt, the former a CT complex, the latter an ionic salt, to compare their properties.

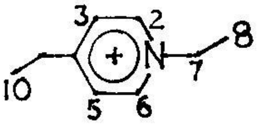
The CT optical absorption spectrum of PyI is strongly dependant upon the solvent. In fact this property of PyI led Kosower to propose a solvent polarity parameter Z-value, for various solvents[1,4,6]. Interestingly, while Z-value of most of the solvents could be obtained directly from the observed absorption spectrum, for water it was obtained indirectly[6]. Neither (directly observed) CT spectrum for this compound (PyI) was reported in water[6], nor was it observed in the present studies. The question thus arises whether this compound, (PyI), occurs as CT complex in water. The failure to observe the C-T absorption spectrum of PyI in water was attributed to the existence of very strong $\pi \rightarrow \pi^*$ transition of pyridinium ring.

We resorted to an alternative but equally effective technique for studying the properties of this charge transfer complex. We used NMR spectroscopy to study PyI. The NMR spectra of both PyI and the perchlorate salts were recorded in a series of solvents including water, and the chemical shift noted[5]. It is evident from NMR data (collected in the table) that, while the structure of the two compounds, PyI and the perchlorate salt, differ substantially in chloroform, they are practically identical in water. This gives us direct proof that the pyridi-

Table: Proton NMR Spectral data of Pyridinium iodide, PyI, and Perchlorate in Chloroform and Water[a]

Solvent/Position		CH(2,6)	CH(3.5)	CH_2(7)	CH_3COO(10)	CH_3(8)
$CHCl_3$	Iodide	9.72;9.62	8.59;8.49	5.35;5.21; 5.10;4.58	4.08	1.97;1.84; 1.60
	Perchlorate	9.05;8.95	8.44;8.38	4.91;4.82; 4.67;4.54	3.98	1.82;1.67; 1.57
D_2O	Iodide	9.72;9.62	9.10^b	c	4.69	2.46;2.36; 2.24
	Perchlorate	9.71;9.61	9.08^b	c	4.68	2.45;2.31; 2.22

(a) δ-values (b) broad (c) Under H_2O impurity (?) around 5.30 (d) 1-ethyl-4-car-bomethoxypyridinium ring (Py^+)



nium iodide and the pyridinium perchlorate have exactly the same structure in water, both of them exist as ion pair, may be solvent separated ion pair.

NMR is an extremely sensitive probe to monitor the change in environment in a molecule and gives information regarding the structure and geometry of molecules. This sensitive probe (NMR) identifies the nature of pyridinium iodide and compares it with perchlorate salt which exists as ion pair in chloroform as well as in water.

Thus if a well established intermolecular charge transfer complex 1-ethyl-4-carbomethoxy pyridinium iodide does not exist as CT complex in aqueous system, then how can one be sure about the existence of other CT complex in a (biological) system involving an aqueous phase. However, absence of CT complex formation does not preclude the biological reactions through formation of an ion pair, in the form of which PyI exists in aqueous system.

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