

Dissociation Constants of Some Quinoline Derivatives in Mixed Solvent mixture

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ABSTRACT

The dissociation constants of some derivatives of quinoline have been determined by Calvin Bjerrum pH titration method in DMF–water (60:40 v/v) mixture at 308.15 K. It is observed that dissociation constant depends on the substituents present in the compound.

Keywords: Dissociation constant; quinoline derivatives; pH; DMF-water mixture

1. INTRODUCTION

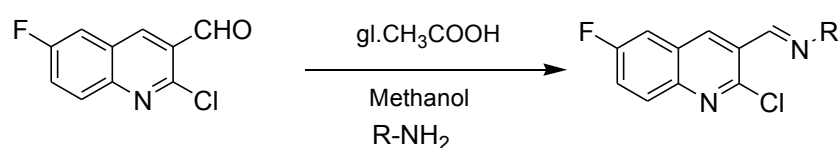
The dissociation constant provides useful information about structure, tautomeric equilibria, solvent– solute interactions etc. [1-3]. In continuation with our previous work, in the present paper dissociation constants of some derivatives of quinoline have been studied. Literature survey shows that various quinoline derivatives are known to have broad spectrum of biological activities [4–6], such as antifungal [7], antibacterial [8], antioxidant [9], antiparasitic [9], antimicrobial [10], anti tubercular [11], anticytotoxic [12], antiinflammatory [13, 14], antiviral [15], antiparasitic [15] etc. Some other pharmacological activities of these derivatives have also been reported by some workers [16-18].

Some new quinoline derivatives are synthesized and their dissociation constants have been determined in DMF–water mixtures by Calvin Bjerrum pH titration method at 308.15 K.

2. EXPERIMENTAL

Five new Quinoline derivatives are synthesized in the laboratory and the reaction scheme is:

REACTION SCHEME



The synthesized compounds were recrystallized and their purity was checked by thin layer chromatography. Further, the characterization was done by IR, NMR and mass spectral analysis. The physical constants of these derivatives are given in Table 1.

Dissociation constant: The chemical used were of AR grade. Solutions of nitric acid (1.0M), sodium hydroxide (0.5 M) and sodium nitrate (1.0 M) were prepared using Mill-Q water (Millipore Pvt. Ltd. Bangalore, India). The solutions of synthesized compounds (0.1 M) were prepared in DMF. An electrical balance (Mettler Toledo AB204-S) with an accuracy of ± 0.1 mg was used for solution preparation.

The Calvin Bjerrum pH titration method [19] was used to determine dissociation constants of synthesized compounds. For this, a Systronic pH meter (Model No. EQ 664) was used. The glass and saturated calomel electrodes were used as indicator and reference electrodes respectively. Before measurement, the pH meter was calibrated with buffer solution of known pH. The following sets of mixtures were prepared for titration:

(I) **Blank Solution:** It consists of 2 ml HNO_3 (0.1 M) + 4 ml water +30 ml DMF + 4.0 ml NaNO_3 (1.0 M).

(II) **Test solution:** It consists of 2 ml HNO_3 (0.1 M) + 4 ml water +28 ml DMF + 2.0 ml compound solution (0.1 M) + 4.0 ml NaNO_3 (1.0 M).

Thus, total volumes (V^0) in each set is equal 40.0 ml and DMF : water ratio 60 : 40 (v/v).

The above mentioned solutions were allowed to attain a constant temperature (308.15 K) and then titrated against standard sodium hydroxide solution (0.5 M) under an inert atmosphere of nitrogen. The change in the pH of solution with each addition of alkali was recorded.

3. RESULTS AND DISCUSSION

The pH values are plotted against volume of alkali added for both the solutions and from the two titration curves, the average number of protons associated with ligand (n_H) can be calculated by Irving and Rossotti equation:

$$n_H = Y - \frac{(V'' - V')(N^0 - E^0)}{(V^0 + V')T_L^0}$$

where Y is the number of displaceable protons per compound molecule. For the studied compounds, value of Y is one.

V' and V'' are the volume of alkali required at the same pH for both blank and compound titration curves respectively; V^0 is the initial volume of the test solution. N^0 , E^0 and T_L^0 are the initial concentration of the alkali, acid and compound respectively.

The values of n_H are found to be between 0 to 1 for all the compounds suggesting thereby the presence of one dissociable proton.

The dissociation constants of compounds were determined by two methods: average method and half-integral method. In average method, for each compound, the values of dissociation constants were evaluated at different pH using following equation:

$$\log pK = pH + \log \left[\frac{n_H}{(n_H - 1)} \right]$$

From these log pK values, the average value of pK was calculated and is reported in Table 1.

In half-integral method, n_H values are plotted against pH and the log pK values at $n_H = 0.5$ were evaluated for each compound and are given in Table 1.

It is observed from Table 1 that there is good agreement between the values evaluated by two methods.

Out of five compounds, SB-5 and SB-3 are more basic whereas SB-2 is least basic means more acidic. In all the compounds, central moiety is same but different substitutions are present as shown in Table 1. SB-5 contains 3-chloro and 4-fluoro groups whereas SB-3 contains 4-chloro group only. Thus, the more basic character of SB-5 and SB-3 may be due of positive resonating effect of halogen groups which donate lone pair of electrons to phenyl ring.

Table 1. Physical constants of Schiff bases.

S. No.	Compound Code	pK	
		Average method	Half-integral method
1	SB-1	11.09	11.10
2	SB-2	10.93	10.95
3	SB-3	11.37	11.40
4	SB-4	11.07	11.08
8	SB-5	11.40	11.38

*Acetone: Benzene: 2:8

Table 2. Dissociation constants (pK) of synthesized quinoline derivatives by Average and half-integral methods.

S. No.	Comp. code	R	Molecular formula	M. W (g/mol)	Rf value	M.P 0C	Yield %
1.	SB-1	4-OCH3-C6H4-	C17H12ClFN2O	314	0.53	192	62
2.	SB-2	4-CH3-C6H4-	C17H12ClFN2	298	0.52	168	65
3.	SB-3	4-Cl- C6H4-	C16H9Cl2FN2	319	0.47	217	55
4.	SB-4	2-OCH3-C6H4-	C17H12ClFN2	298	0.34	205	59
8.	SB-5	3-Cl-4-F-C6H3-	C16H8Cl2F2N2	337	0.44	211	69

The more acidic character of SB-2 is because of negative inductive effect of 4-CH₃ group. Thus, the presence of different substituent influences the dissociation of compound due to their different effects [20]. Similar results have been reported by earlier studies on pyrimidine compounds where polarity of substituent affects basicity of compounds [21]. SB-2 is followed by SB-1 and SB-4. Both SB-1 and SB-4 contain methoxy groups at para and ortho positions respectively.

Thus, it is concluded that ionization of compound depends on inductive effects of substituent present in the compound.

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