Lech Chmurzyński

Department of General Chemistry, University of Gdańsk, ul. Sobieskiego 18, 80-952 Gdańsk, Poland
Received December 30, 1998

Acid dissociation constant, pK_a, of protonated pyridine, determined in the polar protophobic aprotic solvent, acetone, has been compared with pK_a values of the pyridinium ion in a variety of other polar solvents including aprotic protophobic ones, acetonitrile, benzonitrile, nitrobenzene, nitromethane, and propylene carbonate, in the protophilic aprotic dimethyl sulfoxide and N,N-dimethylformamide, as well as in the amphiprotic methanol. On the basis of the set of these pK_a values, the effect of the medium on the basicity of pyridine is discussed. Further, based on the cationic homoconjugation constants of pyridine conjugated with the pyridinium cation in the non-aqueous solvents, the tendency of pyridine towards homoconjugation reactions has also been discussed. Finally, both the basicity of pyridine and its tendency towards cationic homoconjugation has been compared with analogous properties of pyridine N-oxide.

Pyridine, on account of its specific structure and acid-base properties, belongs to the most interesting organic N-bases. Its basicity in both aqueous solutions [1,2] and non-aqueous media [3-5] has been extensively studied. Hence in the chemical literature one can find dissociation constants of its protonated form (expressed as pK_a values):

$$PyH^+ + SH \rightleftarrows Py + SH_2^+ \qquad (1)$$
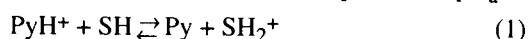
both in water [6-8] and non-aqueous solvents [9-13]. In the above-mentioned equation Py stands for the pyridine molecule and SH for a polar solvent molecule. However, the literature values of the constants differ markedly. For instance, the pK_a values of the pyridinium ion in water ranges significantly from 4.38 [14] to 5.42 [15]. The reason for this discrepancy lies in different methods used for the determination of the values. Generally, there is a lack of evidence for those pK_a values which were determined by a particular procedure, thus making impossible comparison of the equilibrium constants. Hence, the primary objective of this study was to determine the pK_a value of the pyridinium cation in one of the most basic polar protophobic aprotic solvents, acetone, and its comparison with pK_a values in other non-aqueous solvents by using the same technique of potentiometric titration. The following solvents were tested: acetonitrile, benzonitrile, nitrobenzene, nitromethane, and propylene carbonate as the polar protophobic aprotic ones, the polar protophilic dimethyl sulfoxide and N,N-dimethylformamide, as well as the polar amphiprotic methanol.

In the media favorable for attaining cationic homoconjugation equilibria in the system pyridine (Py) - conjugate cationic acid of Py (PyH$^+$) with subsequent formation of a homocomplexed cation PyHPy$^+$:

$$PyH^+ + Py \rightleftarrows PyHPy^+ \qquad (2)$$
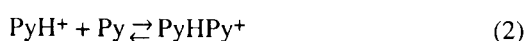
the potentiometric method enabled simultaneous determination of both the acid dissociation constant and the equilibrium constant of the homoconjugation reaction. This provided a basis for discussion of the influence of the solvent polarity and basicity on the equilibrium of the cationic homoconjugation reactions occurring in solution.

Further, the acid-base equilibrium constants for the Py/PyH$^+$ system were compared with analogous constants characterizing the acid-base properties of a system with pyridine N-oxide. In this way, acid-base properties of the two compounds representing classes of monocyclic amines and their N-oxides could be compared.

Results and discussion

Table 1 lists pK_a values for the pyridinium cation in the polar non-aqueous solvents, and, whenever the cationic homoconjugation equilibria were set up, the homoconjugation constant values. For the sake of comparison, analogous equilibrium constants for acid-base systems involving pyridine N-oxide in respective solvents are included in the Table 1. Inspection of these values has led to the following conclusions referring to pyridine:

i) Pyridine turned out to be a stronger base in the protophilic aprotic solvents than in water, for instance, in acetonitrile even by approximately 7 units on the pK_a scale (pK_a for the pyridinium ion in water is 5.25 [6]). This difference in strength can be attributed to different solvation capacities of the solvents. Protophobic solvents do solvate cationic acid conjugated with pyridine, but not the pyridine itself. In the amphiprotic methanol the basicity of pyridine is comparable with that in water, the respective pK_a values in methanol and water being 5.13 (Table 1) and 5.25. On the other hand, in aprotic protophilic solvents pyridine is, by approximately 2 pK_a units, a weaker base.

ii) In all solvents studied, pyridine is a stronger base (by 1.5 - 3.5 pK_a units) than its N-oxide. The difference is larger, the weaker the basicity of the aprotic solvent, generally by 1 - 3 units lower than in water where it approaches 5 units (pK_a of pyridine in water is 5.25, whereas pK_a of pyridine N-oxide in water is 0.79 [6]).
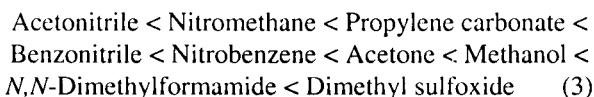
Table 1

Acid dissociation constants, pK_a, of the pyridinium ion and logarithms of the cationic homoconjugation constants, log K_{BHB+}, of the ion and free pyridine in polar non-aqueous solvents, at 298.15 K and ionic strength of the order of 10^{-3}. For comparison, analogous constants for the pyridine N-oxide system are provided. Standard deviations in parentheses.

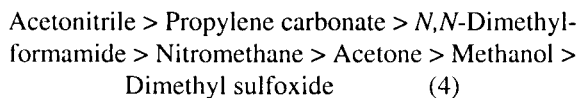| Solvent	Pyridine		Pyridine N-oxide	
	pK_a	log K_{BHB+}	pK_a	log K_{BHB+}
Acetone	6.97(0.01)	0.53(0.91)[a]	5.11(0.02)[a]	2.69(0.02)[a]
Acetonitrile [b]	12.47(0.01)	0.63(0.97)	10.04(0.01)	3.22(0.01)
Nitromethane [c]	12.16(0.10)	1.83(0.03)	8.66(0.07)	3.69(0.01)
Propylene carbonate [d]	11.64(0.01)	[e]	8.55(0.02)	3.08(0.08)
Benzonitrile [f]	11.3(0.74)	[e]	9.18(0.08)	3.57(0.05)
Nitrobenzene [g]	8.11(0.05)	1.05(0.33)	6.99(0.07)	3.67(0.06)
N,N-Dimethylformamide [h]	3.57(0.06)	[e]	1.68(0.46)	[e]
Dimethyl sulfoxide [h]	3.29(0.01)	[e]	1.63(0.18)	[e]
Methanol [i]	5.13(0.02)	1.99(0.03)	2.69(0.03)	[e]
Water [j]	5.25		0.79	

[a] The value of constant from ref 17. [b] The constant values from ref 18. [c] The constant values from ref 19. [d] The constant values from ref 20. [e] Homoconjugation constant value could not be determined from potentiometric measurements. [f] The constant values from ref 21. [g] The constant values from ref 22. [h] The constant values from ref 23. [i] The constant values from ref 24. [j] The pK_a values from ref 6.

Moreover, as has been stated, the pK_a values of the pyridinium ion in water and methanol are comparable, while with pyridine N-oxide they differ by almost two units. It can thus be concluded that the weak differentiating capacity of methanol is even much weaker with respect to substituted pyridines than to their N-oxides.

iii) Inspection of the pK_a values of the pyridinium cation within the set of polar solvents shows that its acidic strength increases in the following series:

Acetonitrile < Nitromethane < Propylene carbonate <
Benzonitrile < Nitrobenzene < Acetone < Methanol <
N,N-Dimethylformamide < Dimethyl sulfoxide   (3)

The above series is nearly identical with that established [25] for the cation conjugated with pyridine N-oxide (see Table 1). On the other hand this sequence is different than that arranged on the basis of declining capacity to differentiate the strength of cationic acids [26] which is as follows:

Acetonitrile > Propylene carbonate > N,N-Dimethyl-
formamide > Nitromethane > Acetone > Methanol >
Dimethyl sulfoxide   (4)

The differences in basicity of the heterocyclic N-bases and their N-oxides in polar solvents are due to differences in solvation capacity of the solvents relative to cationic acids conjugated with these bases and to the free bases. The tendency towards variation in basicity of the N-bases can be related to differences in solvent basicities in the qualitative grounds only, as the crucial feature affecting the pK_a values of the compounds are autoionization constants of the solvents. Furthermore, the autoionization constants do not always change proportionally to the donicity numbers (i.e., basicities) of the solvents.

Inspection of the equilibrium constants for the homoconjugation of the pyridinium cation with free pyridine in the non-aqueous media considered, allows for the following conclusions to be drawn:

i) The constants for this equilibrium are undeterminable in some media. Those solvents in which the constants are determinable can be arranged in the following series of declining tendency to cationic homoconjugation:

Methanol > Nitromethane > Nitrobenzene >
Acetonitrile > Acetone   (5)
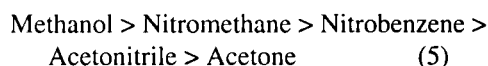
ii) The capacity of formation of the homocomplexed cation by pyridine in protophobic aprotic solvents is much weaker than that showed by pyridine N-oxide. While the logarithms of the homoconjugation constants of the N-oxide fall within the range 2.7 - 3.7, those of pyridine are in some solvents either undeterminable potentiometrically (propylene carbonate) or their values are burdened with standard deviations greater than the constants themselves (acetonitrile, acetone). Only for the solvents with the lowest basicity (nitromethane, nitrobenzene), could accurate homoconjugation constants for pyridine-containing systems be calculated (log K_{BHB+} in nitromethane is 1.83 and log K_{BHB+} in nitrobenzene equals to 1.05), whereas for the pyridine N-oxide systems their values are 3.69 and 3.67, respectively. It can thus be concluded that in polar aprotic solvents the formation constants of pyridine homocomplexes are on average two orders of magnitude lower than those of cations of homocomplexed N-oxides.

iii) The equilibrium constant for this reaction in amphiprotic methanol (log K_{BHB+} = 1.99) is higher than in the protophobic solvents where the highest value (log K_{BHB+} = 1.83) was found in nitromethane. Furthermore,

it should be noted that the cationic homoconjugation process in methanol is more pronounced with heterocyclic amines than with their N-oxides, unlike the case of protophobic aprotic solvents where just the opposite is true. The homoconjugation constant for the pyridine system is comparable with those for the most basic pyridine N-oxides and trimethylamine N-oxide which are of the same order of magnitude (around 2 on the logarithmic scale [24]), whereas for the pyridine N-oxide the constant could hardly be determined, its logarithm being around 1 [24]:

iv) in protophilic aprotic solvents, like dimethyl sulfoxide and N,N-dimethylformamide, the cationic homoconjugation equilibrium is not attained at all in both systems (pyridine and its N-oxide).

On this basis the groups of the solvents can be ranked after decreasing cationic homoconjugation constants as follows: amphiprotic > aprotic protophobic > aprotic protophilic.

With protophobic solvents, the lower homoconjugation constants in acetone than, for instance, in nitromethane can be interpreted as an outcome of stronger solvation of acid constituents of the hydrogen-bonded complexes by the more basic acetone, which results in weakening of the hydrogen bonding. Consequently, the complex becomes more labile in acetone. The much larger differences in the tendency towards cationic homoconjugation on going from the protophobic nitromethane to the protophilic N,N-dimethylformamide are due to strong interactions between the N,N-dimethylformamide molecules and the basic constituent of the complex (pyridine). The more basic solvent molecules form heterocomplexes with the pyridinium ion thus preventing the formation of homocomplexed cations.

An interesting feature in the amphiprotic methanol is the observed enhanced tendency towards cationic homoconjugation of pyridine, representing heterocyclic amines, in relation to substituted pyridine N-oxides. The tendency is opposite to those observed in aprotic solvents, both protophobic and protophilic [10]. This feature will be addressed in subsequent contributions.

EXPERIMENTAL

Pyridine was purified by vacuum distillation. Simple perchlorate of pyridine was prepared by mixing together equivalent quantities of a 72% aqueous perchloric acid (Merck Co.) and base in methanol. The mixture was vacuum concentrated. The residue was filtered off, washed twice with chloroform and dried in vacuum over phosphorus pentoxide. Picric acid and tetraethylammonium chloride (both Fluka AG) were purified by triple crystallization from ethanol. Tetraethylammonium picrate and perchlorate were obtained by mixing together equimolar quantities of the purified picric acid or 72% aqueous perchloric acid solution with 25% tetraethylammonium hydroxide (Fluka AG) in ethanol. The salts were crystallized twice from ethanol. Tetra-butylammonium picrate was obtained by mixing together equimolar quantities of the purified picric acid with 25% tetra-butylammonium hydroxide in methanol. Tetra-butylammonium perchlorate was obtained by mixing together equimolar quantities of 72% aqueous perchloric acid solution with 25% tetra-butylammonium hydroxide in methanol. Both salts were crystallized twice from ethanol. Tetra-butylammonium chloride (Serva Co.) was purified by triple crystallization from a 1:1 mixture acetonitrile and ethyl acetate. 2,6-Dinitrophenol (Fluka AG) was purified by triple crystallization from methanol. Tetra-butylammonium 2,6-dinitrophenolate was obtained in the same way as tetra-butylammonium picrate. The salt was crystallized twice from ethyl acetate. Acetone (Aldrich Chemical Co.) was purified by the standard procedure: in the first stage the solvent was heated under reflux with potassium permanganate and subsequently dried with anhydrous calcium sulfate, then the solvent was redistilled with the exclusion of air humidity. The purified acetone had a specific conductivity of the order of 2×10^{-7} S cm^{-1}.

The e.m.f. measurements of the cell:

indicator glass electrode | system studied || modified calomel electrode

were run by an OP-208 digital potentiometer (Radelkis) with the accuracy of ± 0.1 mV. An OP-7183 (Radelkis) indicator glass electrode and an OP-08303 (Radelkis) reference calomel electrode were used. The reference calomel electrode, modified by replacing the aqueous potassium chloride solution by a 0.1 mol dm^{-3} acetone solution of tetra-butylammonium chloride, was placed in a shortened salt bridge filled with 0.01 mol dm^{-3} tetra-butylammonium perchlorate solution in acetone. The e.m.f. measurements of the pyridine perchlorate - pyridine system in acetone were run at a constant ionic strength. The solution containing pyridine perchlorate at a concentration of about 10^{-3} mol dm^{-3} was titrated with the solution containing the base (pyridine) at a concentration of about 10^{-2} mol dm^{-3} and pyridine perchlorate at the same concentration as that of the titrand (about 10^{-3} mol dm^{-3}) to keep the formal ionic strength constant for all titration points. The electromotive force (e.m.f.) was recorded for each titration point, after electrode relaxation (i.e., when the measured potential was stable).

Each e.m.f. measurement in the system studied was preceded by the determination of the characteristic of the glass electrode. The linearity of the response of the glass electrode versus the modified calomel electrode in acetone was checked by means of the standardizing system: tetra-butylammonium picrate - picric acid (the pK_a value of picric acid in acetone is 6.3 [16]) at a constant ionic strength. 0.001 Mol dm^{-3} tetra-butylammonium picrate solution was titrated by the solution containing picric acid and tetra-butylammonium picrate at a concentration of 0.01 mol dm^{-3} and 0.001 mol dm^{-3}, respectively in order to keep the formal ionic strength constant.

Solutions for potentiometric measurements were prepared on the volume basis. All potentiometric measurements were run at 298.1 ± 0.1 K.

REFERENCES AND NOTES

[1] L. D. Hansen and E. A. Lewis, *Anal. Chem.*, **43**, 1393 (1971).

[2] I. R. Bellobano and P. Beltrame, *J. Chem. Soc. (B)*, 1047 (1969).

[3] Z. Dega-Szafran and M. Szafran, *J. Chem. Soc., Perkin Trans. 1*, 195 (1982).

[4] S. Kuna, Z. Pawlak and M. Tusk, *J. Chem. Soc., Faraday Trans I*, **78**, 2685 (1982).

[5] Z. Dega-Szafran and E. Dulewicz, *Org. Mag. Res.*, **16**, 214 (1981).

[6] D. D. Perrin, Dissociation Constants of Organic Bases in Aqueous Solutions, Butterworths, London, 1965, pp 1-473.

[7] J. J. Christensen, L. D. Hansen and R. M. Izatt, Handbook of Proton Ionization Heats and Related Thermodynamic Quantities, Brigham Young University, Provo, Utah, 1976, pp 1-269.

[8] R. A. Abramovich and E. M. Smith, Pyridine and its Derivatives, John Wiley, New York, 1974 pp 1-451.

[9] J. F. Coetzee, *Progr. Phys. Org. Chem.*, **4**, 45 (1967).

[10] L. Chmurzyński, Solvent Effect on Acidic-Basic Interactions of Pyridine N-Oxide Derivatives, University of Gdańsk, Gdańsk, 1994, pp 1-127.

[11] Z. Pawlak and A. A. Hampton, *Thermochim. Acta*, **59**, 313 (1982).

[12] F. J. Coetzee, G. R. Padmanabhan and G. P. Cunningham, *Talanta*, **11**, 93 (1964).

[13] A. Wawrzynów, Ph. D. Thesis, University of Gdańsk, Gdańsk, 1985.

[14] L. Sacconi, P. Paoletti and M. Ciampolini, *J. Amer. Chem. Soc.*, **82**, 3831 (1960).

[15] R. W. Green, *Aust. J. Chem.*, **22**, 721 (1969).

[16] C. M. French and J. G. Roe, *Trans Faraday Soc.*, **49**, 314 (1953).

[17] L. Chmurzyński and A. Liwo, *J. Chem. Soc., Faraday Trans. 1*, **87**, 3853 (1991).

[18] L. Chmurzyński, A. Wawrzynów and Z. Pawlak, *Electrochim. Acta*, **35**, 665 (1990).

[19] L. Chmurzyński, *J. Chem. Soc., Faraday Trans. 1*, **87**, 1729 (1991).

[20] A. Wawrzynów and L. Chmurzyński, *J. Chem. Thermodyn.*, **30**, 313 (1998).

[21] L. Chmurzyński and G. Wawrzyniak, *Pol. J. Chem.*, **66**, 333 (1992).

[22] L. Chmurzyński, A. Liwo and P. Barczyński, *Anal. Chim. Acta*, **335**, 147 (1996).

[23] L. Chmurzyński and Z. Warnke, *Aust. J. Chem.*, **46**, 185 (1993).

[24] L. Chmurzyński, *J. Sol. Chem.*, **21**, 171 (1992).

[25] L. Chmurzyński, L. *Anal. Chim. Acta*, **321**, 237 (1996).

[26] L. Chmurzyński, L. *Anal. Chim. Acta*, **326**, 267 (1996).