



Physicochemical Studies on Preparation, Properties and Characterization of Salts of weak acids and weak bases

Dr. Mukesh Kumar Sharma

Assistant Professor,

University Department of Chemistry,

Lalit Narayan Mithila University, Darbhanga, Bihar, India.

E-mail: mukesh82kumarsharma@gmail.com

Abstract: This work needs effective research on the physicochemical studies on preparation and characterization of salts of weak acids and weak bases. In this research several salts of this kind such as ammonium acetate, ammonium formate, ammonium carbonate, etc. were prepared and analysed. The P^H of such salt solutions were also examined. Their several laboratorial and industrial uses are also discussed in this field due to their potential to modify physicochemical properties such as solubility, stability and dissolution rate. However, their utility is often limited by disproportionation, where the salt reverts to its less soluble free acid or free base forms below or above a critical P^H . The study focuses on the systematic preparation such as neutralization, solvent evaporation and mechanochemical grinding and characterization was performed using multi-technique approach.

Key Words: weak acids, weak bases, salts, ammonium, acidic, basic, P^H .

1. INTRODUCTION: Salt formation is a fundamental strategy used in chemistry and pharmaceutical sciences to modify the physicochemical and biopharmaceutical properties of ionizable compound. The salts of weak acids and weak bases exhibit unique behavior that differs significantly from salts of strong acids and strong bases. Salt solutions of this category are generally neutral having P^H nearly equal to 7. However, some salt solutions are acidic and basic also. The salts of weak acids and weak bases are formed by the neutralization reaction of a weak acid and a weak base in which proton transfer occurs slightly. The extent of salt formation is governed by the difference in ionization constant of acid and base. The practical importance of the salts lie in their solubility, dissolution rate, stability and crystallinity. Unlike salts of strong acids and strong bases, the salts of this category are highly susceptible to disproportionation. Components and Nature of Salts are tabled as:

Table:1

Salt	Weak Acid	Weak Base	Nature
Ammonium Acetate	Acetic Acid $K_a = 1.8 \times 10^{-5}$	Ammonia $K_b = 1.8 \times 10^{-5}$	Neutral
Ammonium Formate	Formic Acid $K_a = 1.8 \times 10^{-4}$	Ammonia $K_b = 1.8 \times 10^{-5}$	Slightly Acidic
Ammonium Carbonate	Carbonic Acid $K_a = 4.3 \times 10^{-7}$	Ammonia $K_b = 1.8 \times 10^{-5}$	Slightly Basic
Ammonium Bicarbonate	Carbonic Acid $K_a = 1.8 \times 10^{-5}$	Ammonia $K_b = 1.8 \times 10^{-5}$	Basic
Ammonium Sulfide	Hydrosulfuric Acid $K_a = 9.1 \times 10^{-8}$	Ammonia $K_b = 1.8 \times 10^{-5}$	Basic
Ammonium Benzoate	Benzoic Acid $K_a = 6.3 \times 10^{-5}$	Ammonia $K_b = 1.8 \times 10^{-5}$	Slightly Acidic
Pyridinium Acetate	Acetic Acid	Pyridine	Acidic



	$K_a = 1.8 \times 10^{-5}$	$K_b = 1.7 \times 10^{-9}$	
Anilinium Acetate	Acetic Acid $K_a = 1.8 \times 10^{-5}$	Aniline $K_b = 4.3 \times 10^{-10}$	Acidic

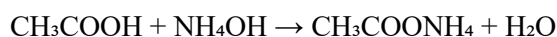
2. General Methods of Preparation:

- Neutralization Method: In this method both the acid and base are dissolved in a suitable solvent and mixed with each other in a stoichiometric proportion resulting in the formation of a salt and water.
e.g. Acid + Base $\rightarrow$ Salt + Water
- Solvent Evaporation: Both the components are dissolved in a suitable solvent in stoichiometric ratio and stirred and then evaporated to get crystals of salt.
- Precipitation Method: If the solubility of salt formed is low, then solution of both the acid and base is mixed in a definite ratio which results the formation of precipitate of the salt.
- P^H adjustment: The P^H is adjusted in such a way that the P^H for weak acid should be greater than its P^H_{max} or the P^H for weak base should be less than its P^H_{max} to ensure salt stability and avoid disproportionation.

These principles are strictly followed during the preparation of salts formed by the interaction of weak acids and weak bases.

Preparation of Ammonium Acetate:

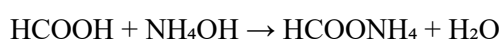
The common method used for the preparation of ammonium acetate is the neutralization reaction between the acetic acid and ammonia solution. This method is also used in laboratory for this preparation.



Procedure: During this preparation, the glacial acetic acid is taken in a beaker on ice bath. The dilute ammonium hydroxide solution is added to it dropwise with constant stirring. The addition is continued till P^H reaches to 6.8-7.2. The end point is not sharp because both the acid and base are weak. The P^H meter is used for accuracy. The solution is evaporated on a water bath at 60-70°C. The concentrated solution is cooled so that a white crystal of ammonium acetate is separated out which is filtered off quickly and dried in a vacuum desiccator over P_2O_5 or conc. H_2SO_4 . It is hygroscopic and deliquescent.

Preparation of Ammonium Formate:

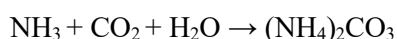
Ammonium formate is also prepared by neutralization reaction of Formic Acid with Ammonia. This is the standard and laboratory method of preparation ammonium formate.



Procedure: During this preparation 85-98% of formic acid taken in a conical flask. Work is done in fume hood. The flask is cooled in an ice bath. The dilute aqueous ammonia is added dropwise with stirring. Conc. NH_3 is avoided. The P^H is maintained to 6.0-6.5. The solution is evaporated under reduced pressure at $\leq 60^\circ\text{C}$ using a rotary evaporator because above 60°C ammonium formate is decomposed. On cooling concentrated solution deposits colourless, hygroscopic crystals which is filtered rapidly and dried in vacuum desiccator over P_2O_5 .

Preparation of Ammonium Carbonate:

Method 1: Ammonium Carbonate is prepared by the action of ammonia and carbon dioxide in presence of water.

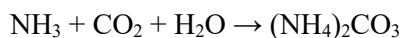


Procedure: A gas mixing chamber is set up in a fume hood. The ammonia and carbon dioxide gas in 2:1 ratio is pressed through a U-tube cooled to 0°C . A small amount of water vapour is added to the tube walls. A white crystalline solid of ammonium carbonate is deposited which is transferred to air tight container immediately to avoid its decomposition into ammonium bicarbonate.

Method 2: It is also prepared by the sublimation of ammonium chloride and calcium carbonate. When equimolar mixture of ammonium chloride and calcium carbonate is heated, following reaction occurs:



The NH_3 , CO_2 and H_2O recombine on cold surface to give ammonium carbonate.



Procedure: The equimolar mixture of dry ammonium chloride and calcium carbonate is taken in powdered form. The mixture is heated in a hard glass tube with delivery tube. A white sublimate of ammonium carbonate is collected to a receiver cooled in ice.

Preparation of Ammonium Bicarbonate:

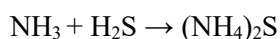
Ammonium bicarbonate is prepared by the absorption of carbon dioxide in aqueous ammonia solution.



Procedure: A dilute ammonia solution is prepared in a beaker. The carbon dioxide gas is bubbled slowly through the solution using a gas diffuser till the solution becomes saturated. A white crystal of ammonium bicarbonate is separated which is filtered quickly on Buchner funnel.

Preparation of Ammonium Sulphide:

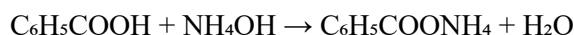
Ammonium sulphide is prepared by passing hydrogen sulphide gas through aqueous ammonia solution.



Procedure: A concentrated ammonia solution is taken in a flask having fume hood environment and cooled it to $0-10^\circ\text{C}$ in an ice bath. H_2S gas is bubbled slowly through ammonia solution till saturation using H_2S cylinder with regulator in which solution turns yellow to orange. A gas trap with NaOH is used to scrub excess of H_2S . For this preparation 2 moles of ammonia is used with 1 mole of hydrogen sulphide. The reaction is stopped when pH becomes nearly equal to 9.3 and solution becomes pale yellow.

Preparation of Ammonium Benzoate:

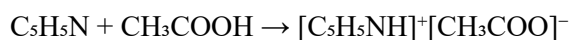
Ammonium Benzoate is prepared by the neutralization of Benzoic Acid with Ammonia solution. By this method it is prepared in laboratory also.



Procedure: Benzoic acid dissolved in ethanol-water mixture. A dilute NH_4OH is added to it dropwise with constant stirring. The mixture is kept warm because benzoic acid is precipitated in cold. The addition of ammonium hydroxide is continued till pH reaches 6.0–6.5. At equivalence, solution is nearly neutral. If solution is still cloudy, then it is warmed gently to dissolve unreacted benzoic acid and more NH_4OH is added. The clear solution is evaporated on water bath at $60-70^\circ\text{C}$ till crystals are obtained. Strong heating avoided because ammonium benzoate starts to decompose above 110°C . Now, it is cooled in ice bath then white crystalline ammonium benzoate separated out. It is filtered and washed with ice-cold ethanol to remove impurities, and dries in vacuum desiccator over P_2O_5 .

Preparation of Pyridinium Acetate:

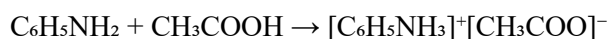
Pyridinium acetate is prepared by direct neutralization of Pyridine with Acetic Acid.



Procedure: The equimolar amount of pyridine and glacial acetic acid e.g. 79.1 g pyridine (1 mol) + 60.05 g glacial acetic acid (1 mol) is taken in fume hood environment in which glacial acetic acid cooled in an ice bath and pyridine is added to it dropwise with constant stirring. The reaction is exothermic. The temperature is kept less than 30°C and pH to 3.0–3.5. Solution becomes viscous and yellowish and on standing it is crystallized. It is dried in vacuum desiccator over P_2O_5 .

Preparation of Anilinium Acetate:

Anilinium acetate is prepared by the neutralization of Aniline with Acetic Acid.



Procedure: The glacial acetic acid is cooled in an ice bath and freshly distilled aniline is added dropwise with constant stirring in fume hood environment. The acetic acid and aniline is taken in equimolar ratio e.g. 60.05 g glacial acetic acid (1 mol) & 93.13 g aniline (1 mol). The temperature is maintained less than 30°C to prevent discoloration and formation of acetanilide and p^{H} nearly equal to 3.0. Solution becomes reddish-brown viscous liquid. Anhydrous anilinium acetate is unstable. It tends to stay as oily liquid but when cooled to 0°C it is solidified. It is dissolved in dry ether petroleum ether is added for precipitation. It is filtered quickly in dry atmosphere in vacuum desiccator over P_2O_5 . Following characteristics are examined during preparation:

Table:2

Salt	Appearance	Melting Point ($^{\circ}\text{C}$)	Boiling Point ($^{\circ}\text{C}$)
Ammonium Acetate	White crystalline solid	114	138
Ammonium Formate	White crystalline solid	116	180
Ammonium Carbonate	Colorless translucent crystalline solid	58	179.5
Ammonium Bicarbonate	White crystalline powder	42	143
Ammonium Sulfide	White crystalline solid	0	40
Ammonium Benzoate	White crystalline powder	198	255
Pyridinium Acetate	Pale yellow viscus liquid	11	115.3
Anilinium Acetate	Brown viscus liquid	30	184.4

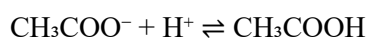
3. Buffer Action of Ammonium Acetate:

Buffer solution is a solution which resists any change in its p^{H} value on dilution or on addition of an acid or alkali. The process by which added H^+ and OH^- ions are removed so that p^{H} remains constant is known as buffer action.

For this test we take ammonium acetate. The p^{H} of aqueous solution of ammonium acetate is also 7. But the addition of 1 ml of M.HCl or 1 ml of M.NaOH solution to 1 litre of ammonium acetate solution does not decrease or increase its p^{H} and hence ammonium acetate solution acts as a buffer solution.

Explanation of buffer action of $\text{CH}_3\text{COONH}_4$:

Ammonium acetate, like other salts exists in the form of its ions, viz. NH_4^+ and CH_3COO^- ions. If an acid is added to this solution the H^+ ions furnished by the acid combine with acetate ions to form feebly dissociated molecules of acetic acid.



Since most of the H^+ ions added are taken up by acetate ions to form acetic acid, which itself is only slightly dissociated, the H^+ ion concentration (and hence the pH) of ammonium acetate solution changes only slightly. Now suppose, a base is added to ammonium acetate solution. The OH^- ions furnished by the base will be taken up by NH_4^+ ions to form feebly dissociated NH_4OH molecules.



Since most of the OH^- ions are taken up by NH_4^+ ions to form weakly dissociated NH_4OH . Therefore, there is very little change in the pH of ammonium acetate solution.

Hydrolysis of Salts:

Hydrolysis of salts is a process involving the action of water on a salt to form a mixture of acid and alkali. Thus, the hydrolysis of salt is the reverse of neutralization.



Salt + Water $\rightleftharpoons$ Acid + Base.

Applying law of mass action, the equilibrium constant, K is given as:

$$K = \frac{[\text{Acid}][\text{Base}]}{[\text{Salt}][\text{Water}]}$$

$$\text{or, } K \times [\text{Water}] = \frac{[\text{Acid}][\text{Base}]}{[\text{Salt}]}$$

$$\text{or, } K_h = \frac{[\text{Acid}][\text{Base}]}{[\text{Salt}]}$$

where K_h = Hydrolysis constant of salt.

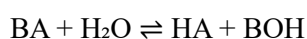
Degree of Hydrolysis:

It is the fraction (or percentage) of the total salt which is hydrolysed at equilibrium. For example, if 90% of a salt solution is hydrolysed, its degree of hydrolysis is 0.90 or as 90%. It is generally represented by 'h'.

Hydrolysis of Salts of a weak acid and a weak base:

Hydrolysis of this type of salts will form weak acid and weak base. The solution will be neutral and its p^H value will be 7.

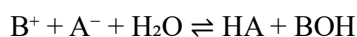
Consider BA as this type of salt which ionises as:



Acid Base

(weak) (weak)

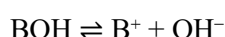
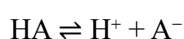
Hydrolysis of such salts can be written in terms of ions as follows:



Since, HA and BOH are weak species, they remain nearly undissociated. Hence,

$$\therefore K_h = \frac{[HA][BOH]}{[B^+][A^-]} \dots\dots\dots (1)$$

Now, let us also consider the dissociation of HA and BOH



$$\therefore K_a = \frac{[H^+][A^-]}{[HA]} \dots\dots\dots (2)$$

And,

$$K_b = \frac{[B^+][OH^-]}{[BOH]} \dots\dots\dots (3)$$

Also, we know that

$$K_w = [H^+][OH^-] \dots\dots\dots (4)$$

Dividing eqⁿ (4) by (2) and (3)

$$\begin{aligned} K_w / (K_a \times K_b) &= \frac{[H^+][OH^-][HA][BOH]}{([H^+][A^-][B^+][OH^-])} \\ &= \frac{[HA][BOH]}{[B^+][A^-]} \dots\dots\dots (5) \end{aligned}$$

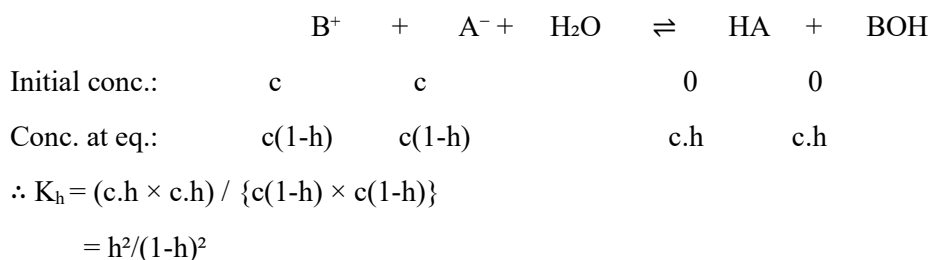
From eqⁿ (1) & (5), we have

$$K_h = K_w / (K_a \times K_b) \dots\dots\dots (6)$$

Degree of hydrolysis :-



If the degree of hydrolysis is 'h' when c moles of the salt is dissolved per litre of water, then



In case h is very small,

$$K_h = h^2$$

$$\text{Or, } h = \sqrt{K_h} \quad \dots\dots\dots (7)$$

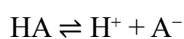
Thus, degree of hydrolysis of such salt is independent of concentration (i.e. dilution) of the salt.

From eqⁿ (6) & (7) we have,

$$h = \sqrt{(K_w / (K_a \times K_b))}$$

⇒ Calculation of hydrogen ion concentration:

In such cases, hydrogen ion concentration may be calculated from the following equation of weak acid HA



$$\text{Thus, } K_a = [H^+][A^-] / [HA]$$

$$\text{or, } [H^+] = (K_a \times [HA]) / [A^-]$$

$$= K_a \times (hc) / ((1-h)c)$$

$$= K_a \times h / (1-h)$$

Neglecting h as compared to unity

$$[H^+] = K_a \times h$$

Substituting the value of h

$$[H^+] = K_a \sqrt{(K_w / (K_a \cdot K_b))} = \sqrt{(K_w \cdot K_a / K_b)}$$

We know that,

$$p^H = -\log [H^+]$$

$$= -\log \sqrt{(K_w \times K_a / K_b)}$$

$$= -\log (K_w \times K_a / K_b)^{1/2}$$

$$= -1/2 \log K_w - 1/2 \log K_a + 1/2 \log K_b$$

$$= 1/2 pK_w + 1/2 pK_a - 1/2 pK_b$$

$$= 1/2 (pK_w + pK_a - pK_b)$$

If $pK_a = pK_b$ i.e. if the dissociation constants of the acid and base are equal

$p^H = 1/2 pK_w = 7$. Hence, in such cases i.e. when $pK_a = pK_b$, the solution will be neutral although the salt has undergone hydrolysis. In case $pK_a > pK_b$ i.e. when the acid is relatively weaker than the base, the solution will be alkaline because



pH will be more than 7. On the other hand, if $pK_a < pK_b$ i.e. when the acid is relatively stronger, the solution will be acidic because the p^H value will be less than 7.

4. Result:

The salts of this category are formed by the neutralization reaction of a weak acid and a weak base. These salt solutions are generally neutral having P^H nearly equal to 7. However, some salt solutions are acidic and basic also. They have low thermal stability and melting also accompanied by decomposition in some cases. They are soluble in water and solubility is generally higher than parent acids and bases. They behave as weaker electrolyte than salts of strong acids and strong bases. Some salt solutions have buffer action also. They are generally hygroscopic in nature due to ionic nature and hydrogen bonding and hence needs storage in desiccator.

Discussion on Result:

The results confirm that the formation of salts of weak acids and weak bases are the results of neutralization reaction and governed by Bronsted-Lorry theory and occurred by proton transfer. The FTIR data confirm proton transfer. The extent of proton transfer depends on the value of ΔpK_a by pK_a rule reported by Cruz-Cabeza. For this, following observations are cited:

- $\Delta pK_a > 4$: Generally, results in complete proton transfer, forming a salt.
- $\Delta pK_a < -1$: Generally, results in no proton transfer, forming a co-crystal.
- ΔpK_a between -1 and 4: The outcome is variable and can form either depending on solvation and the specific molecular environment

pK_a rule also determines the position of acid-base equilibria and whether a proton transfers to form a molecular salt. For this, following observations are cited:

- $\Delta pK_a > 0$: The reaction favours products.
- $\Delta pK_a < 0$: The reaction favours reactants.

In our results, some salts like ammonium acetate formed are stable crystalline solids while some are unstable and easily decomposed into parent acids and bases.

The aqueous solution of this category of salts is generally neutral having P^H nearly equal to 7. However, the P^H deviates in some cases. They have low melting point and thermal stability. Most of them are decomposed at 110-200°C. This is because heating reverses the proton transfer. They possess low lattice energy which makes sublimation of the salt easier. They have high hygroscopicity due to ionic surface and H-bonding. Due to ionic nature and H-bonding they are soluble in water, but solubility is low as compared to parent acid and base. Some of the salts have buffer action and hence used in laboratory. Some of them have also pharmaceutical uses.

5. Conclusion:

The present study demonstrates that the salts of this category can be prepared successfully through neutralization followed by crystallization with proton transfer. However, their physicochemical behavior differs markedly from the salts of strong acids and strong bases. It is seen that the P^H value of such salt solutions is not equal to zero, but observed more or less than seven, depending upon the strength of parent acid and base. Thus, salts of this category may be basic or acidic. The hydrolysis of these salts is significant and degree of hydrolysis, K_h increases on dilution. The salts have low thermal conductivity, with low melting point usually accompanied by decomposition into parent acid and base. They have high hygroscopicity. They have low solubility as compared to parent acid and base. They also behave as equilibrium systems.

The salts of weak acids and weak bases have a wide application. Some salts possess buffer action and hence ammonium acetate and ammonium carbonate are used as buffer solutions and salts like pyridinium acetate is commonly used as electrolyte in laboratory. Some are used in agricultural field as fertilizer and in soil testing, e.g. ammonium citrate and ammonium acetate. Ammonium acetate is also used in complexometric titration of Fe^{3+} ion. Ammonium benzoate is used as precipitating agent for certain metal



ions. Some are used as preservatives. The salts of this category have a wide use in pharmaceutical field also.

REFERENCES:

1. Stahl, P.H., & Wermuth, C.G. (2011). Handbook of Pharmaceutical Salts. Wiley-VCH.
2. Black, S.N., et al. (2007). Structure, Solubility, Screening, and Synthesis of Molecular Salts. *J. Pharm. Sci.*, 96(5), 1053-1068.
3. Cruz-Cabeza, A.J. (2012). Acid–base crystalline complexes and pKa rule. *CrystEngComm*, 14(20), 6362-6365. DOI: 10.1039/C2CE26055G
4. Serajuddin, A.T.M. (2007). Salt formation to improve drug solubility. *Advanced Drug Delivery Reviews*, 59(7), 603-616.
5. Badawy, S.I.F., & Hussain, M.A. (2007). A study on the effect of salt form on the rate of disproportionation of salts of weak base. *Pharmaceutical Research*, 24(12), 2350-2359.
6. Stephenson, G.A., Aburub, A., & Woods T.A. (2011). Physical stability of salts of weak bases in the solid state. *Journal of Pharmaceutical Sciences*, 100(5), 1607-1617.
7. Zannou, E.A., Ji, Q., Joshi, Y.M., & Serajuddin, A.T.M. (2007). Stabilization of the melete salt of a basic drug by adjustment of microenvironmental P^H . *International Journal of Pharmaceutics*, 337(1-2), 210-218.
8. Puri, B.R., et al. (2016-2017). Principles of Physical Chemistry, Vishal Publication Co., 706-747.
9. Agarwal, O.P., et. al. (2008). Objective Chemistry, Jai Prakash Nath Publication (Meerut), 364-380.
10. Martin, A.N., et al. (2011). Physical Pharmacy and Pharmaceutical Sciences, 6th Ed., Lippincott, Ch. 13-14.
11. Nair, R., et al. (2012). Solid-state stability of pharmaceutical salts: hygroscopicity and disproportionation. *Int. J. Pharm.*, 432(1-2), 102-111.
12. Atkins, P. et al. (2018). Physical Chemistry. 11th Ed, Oxford, Ch. 6, 10
13. Aulton, M.E., Taylor, K.M.G. Aulton's Pharmaceutics: The Design and Manufacture of Medicines. 5th Ed, Elsevier, 2017. Ch. 5
14. Brittain, H.G. (2006). Polymorphism in Pharmaceutical Solids, 2nd Ed. Ch. 6.
15. Childs, S.L., Stahly, G.P., Park, A. (2007). The Salt-Cocrystal Continuum: The Influence of Crystal Structure on Ionization. *Mol. Pharmaceutics*, 4(3), 323-338.
16. Gordon, R.E., Ford, J.L. Thermal analysis of pharmaceutical salts. *Thermochimica Acta*, 1986, 108, 121-128.