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Synthesis, Identification and Characterization of N-(4-Aminophenyl) Acetamide Molecule

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Abstract: ***N-(4-aminophenyl) acetamide molecule is a compound used in pharmaceutical industry and colour and medications industry. This semi-product is important because it is used to make N-(4-hydroxiphenyl) acetamide molecule or paracetamol. Reaction of nitro group reduction (-NO_2) to amino group (-NH_2) is one of the most significant reactions of aromatic compounds. Within the experimental research the synthesis of N-(4-aminophenyl) acetamide was done utilizing appropriate metals and acids. Catalysts that were used are iron (Fe) and zinc (Zn). Synthetizedp-aminoacetanilide is analysed utilizing FTIR, UV/VIS, TLC and MS method. In addition, crystal analysis was done utilising optical microscopy method.***

Keywords: N-(4-aminophenyl) acetamide, synthesis, FTIR, UV/VIS, MS

1. Introduction

N-(4-aminophenyl) acetamide is synthetic semi-product with molecule formula $C_8H_{10}N_2O$, mass of 150,1 g/mol. Melting point is from 164 to 165 ^{0} C.[1]CAS number is 122-80-5 and pK is 14,75.N-(4-aminophenyl) acetamide molecule is present in crystals from pink to brown colour, needle shaped. It is melted in cold and hot water, alcohol, ether. Molecule structure of N-(4-aminophenyl) acetamide is shown in the *Image 1*. Aromatic compound comprises benzene core with present acetamide (-NH-CO-CH_3) and amino (-NH_2) group at position (1,4).

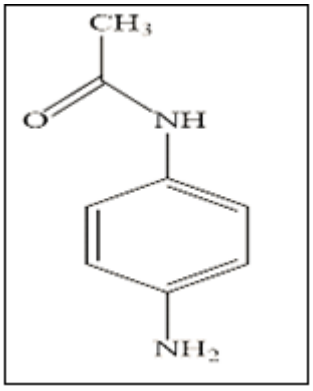

Image 1: Molecule structure N-(4-aminophenyl) acetamide

Reduction process of organic compounds or functional group is characterised by partial or complete acceptance of electrons. In organic chemistry, reduction reaction is used in terms of hydrogen addition to unsaturated groups, e.g. olefin bonds, carbonyl groups, aromatic systems or in terms of substitution of some group with hydrogen.[2] To obtain amines, different methods and agents are used, and one of them is the method with metals and acids. Those reactions are fierce and usually make amines as final products. [3]N-(4-nitrophenyl) acetamide is initial molecule in the first step of reduction reaction, which reacts with appropriate chloride acid (HCl) and zinc (Zn) catalyser producing N-phenylacetamide ammonium-ion (H_3C-CO-NH-C_6H_5-NH_3^+). Further reaction is reacting of N-phenylacetamide ammonium-ion with sodium-hydroxide (NaOH) to remove the proton, thus making the final product N-(4-aminophenyl) acetamide. Reaction is shown in two steps in the *Image 2*.

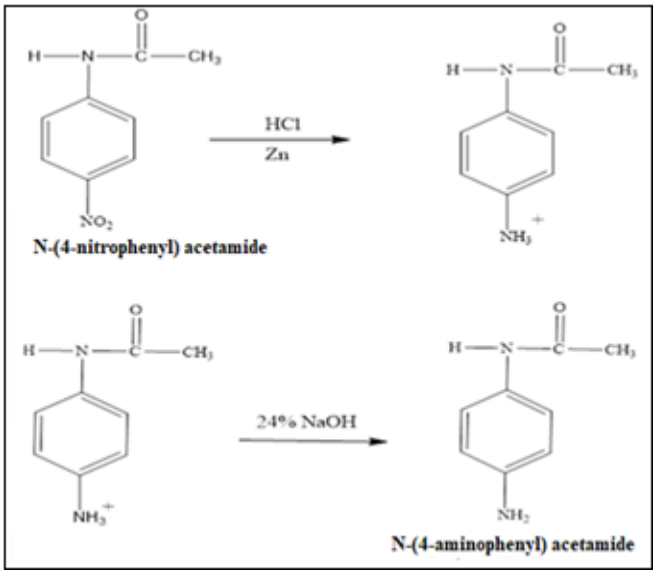

Image 2: Reduction reaction in making N-(4-aminophenyl) acetamide

Nitro group (NO_2) is stable to numerous reagents and is easily reduced in aromatic compounds to amino group (NH_2). Reduction with iron (fe) and acid catalyser is highly selective under mild conditions [4]and is used to reduce aromatic nitro groups (NO_2)to N-(4-nitrophenyl) acetamide. This reaction is called Bechamp reduction. In organic reactions, at some compounds comprising the groups sensitive to acid orbase, it

is necessary to carefully adjust pH to avoid dilution and side reactions. To avoid unfavourable conditions of reduction reaction, such as decrease in speed and yield of reaction, diluted acids are used at higher temperature. Reduction reaction is done in combination with iron chips (Fe) and diluted vinegar acid (CH_3COOH), which is used as solvent. Initial reactant N-(4-nitrophenyl) acetamide reacts with diluted vinegar acid (CH_3COOH) and iron metal (Fe) as catalyser *(Image 3.)* producing N-(4-aminophenyl) acetamide molecule.

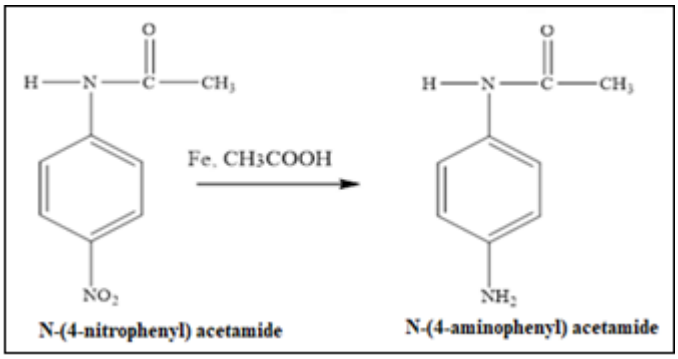

Image 3: Bechamp reduction reaction while composing N-(4-aminophenyl) acetamide

Iron (Fe) is used as catalyser, to speed up and improve reaction yield, while diluted acid melts N-(4-nitrophenyl) acetamide thus enabling metal to react at appropriate temperature to the final product N-(4-aminophenyl) acetamide. Reduction mechanism with metal is shown at the following reaction in the *Image 4.*

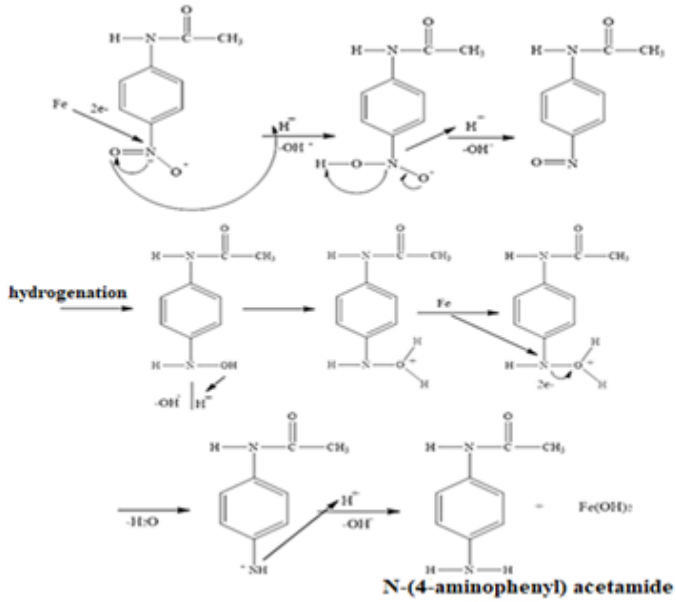

Image 4: Reduction mechanism with iron metal (Fe)

2. Experimental Part

2.1 Chemicals

The following chemicals are used in experimental researches:

- Vinegar acid (CH_3COOH), Semikem
- Concentrated chloride acid (HCl) Semikem
- Sodium carbonate (Na_2CO_3) Semikem
- Sodium-hydroxide (NaOH) Semikem
- Zink powder (Zn) Semikem
- Iron chips (Fe) Semikem
- Potassiumcarbonate (K_2CO_3) Semikem
- Distilled and re-distilled water

2.2 Experimental procedure

a) Method 1. Fe/CH_3COOH

Within the second step, iron chips are added to the flask with round-shaped bottom, 40% vinegar acid (CH_3COOH) and distilled water (H_2O), reaction mixture is refluxed by mixing it in magnetic mixer until it boils. N-(4-nitrophenyl) acetamide is added and reaction is continued by mixing it for about 2,5 hours. After that, flask needs to cool down in icy bath to 70°C, adding to it the sodium carbonate (Na_2CO_3). Solution is cooled to avoid iron precipitation at the temperature higher than the mentioned one. After adding sodium carbonate (Na_2CO_3) and establishing base environment, the obtained sample is steamed until it is dry. After steaming, brownish-violet crystals are formed, which represent N-(4-aminophenyl) acetamide compound.

b) Method 2. Zn/ HCl

N-(4-nitrophenyl) acetamide is added to the flask with round-shaped bottom and concentrated chloride (HCl) acid is added by stirring it in magnetic mixer. After that, zinc powder is added gradually, and the whole mixture is poured to the glass with ice to reduce the temperature. Reaction mixture is heated in water bath until melted. 24% NaOH solution is gradually added, mixture is extracted in funnel and is tested using pH paper to check if it is of base environment. Once the layers are separated, small quantity of potassium carbonate (K_2CO_3) is added and the sample is steamed until dry. The obtained crystals are of brownish-violet colour and they represent synthetized N-(4-aminophenyl) acetamide.

2.3. Methods

Analysis of N-(4-aminophenyl) acetamide molecule is done utilizing the following methods:

- Interpretation of spectrum of synthetized N-(4-aminophenyl) acetamide samples is analysed at Perkin Elmer BX FT-IR spectrophotometer at 2 cm^{-1} resolution and wave length range from 4000 to 450 cm^{-1}.
- Melting point is done at the machine Melting-Point Meter-KSPI, 360°C.
- Analysis of UV spectrum of N-(4-aminophenyl) acetamide is done at Perkin Elmer Lambda UV/VIS 25 spectrophotometer at wave length range from 200 to 400 nm.
- Mass spectrum of N-(4-aminophenyl) acetamide is analysed at spectrometer LC-MS/MS Agilent Technologies.

- Analysis of synthetized N-(4-aminophenyl) acetamide is done utilizing thin-layer chromatography with stationary phase of silica jelly plate (20x20) and mobile phase of ethylacetate-hexane (50:50). Visualization of sample was done in Camag UV cabinet with the lamp at 254 nm.
- Samples are analysed at microscope Leica, model 2500D, working on the principle of transmitted polarized light. While making micro photographs, Nikolo's prisms were placed vertically (XPL). Samples are diluted in water and DMSO, with previous resting period of about 4-6hours.

3. Results and Discussion

The synthesis is based on reduction of N-(4-nitrophenyl) acetamide molecule to N-(4-aminophenyl) acetamide. Two metals were used in reduction reaction, zinc (Zn) and iron (Fe). Iron (Fe) as one of the most significant elements can build numerous oxidation conditions (from -2 to +6), is multiple as such and useful in organic synthesis. Zink (Zn) is cheap and easily available metal of low toxicity and therefore is used often in chemical catalysis. The *Image 5.*shows the reduction reaction yield of synthetized samples of N-(4-aminophenyl) acetamide with two catalysers (Zn, Fe). Reduction of N-(4-nitrophenyl) acetamide catalysed by iron (Fe) in presence of vinegar acid (CH_3COOH) achieves the average value of yield (32,38%) of N-(4-aminophenyl) acetamide compared to the reaction catalysed with zinc(Zn) in presence of chloride acid (HCl) with (33,29%). The obtained results for reaction yield and coincidence percent are shown in the *Images6. and 7.* with 95% N-(4-aminophenyl) acetamide, where initial reactant was used, commercial 99% N-(4-nitrophenyl) acetamide. After aluminium, iron is the second metal by quantity in the Earth core, so it is acceptable from environmental and economic aspect. Attention is more and more paid to researches and improvement of conditions for reaction with iron metal, so therefore it is selected as catalyser in this synthesis. By choosing the synthetic step of reduction with selected reaction terms, iron metal and vinegar acid, N-(4-aminophenyl) acetamideis synthetized with somewhat lower yield (*Image 7.*) and coincidence percentage *(Image 8.)*, of about 84,65% compared to 99% N-(nitrophenyl) acetamide.

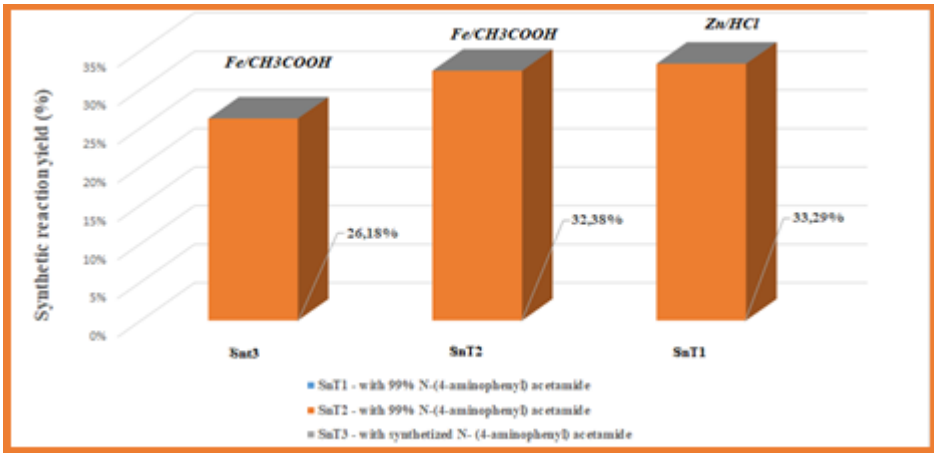

Image 6: Diagram of reaction yield of synthetized samples of N-(4-aminophenyl) acetamide

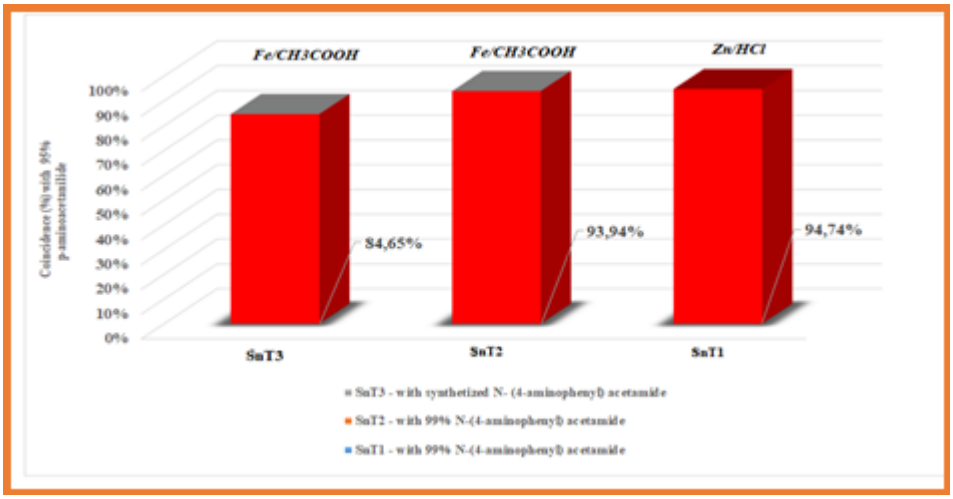

Image 7: FTIR characterization of synthetized samples of N-(4-aminophenyl) acetamide

The *Image 8.* shows the results of melting points of N-(4-aminophenyl) acetamide or p-aminoacetanilide samples ranging from 164,1 to 165°C, which complies with the data from literature.[1]

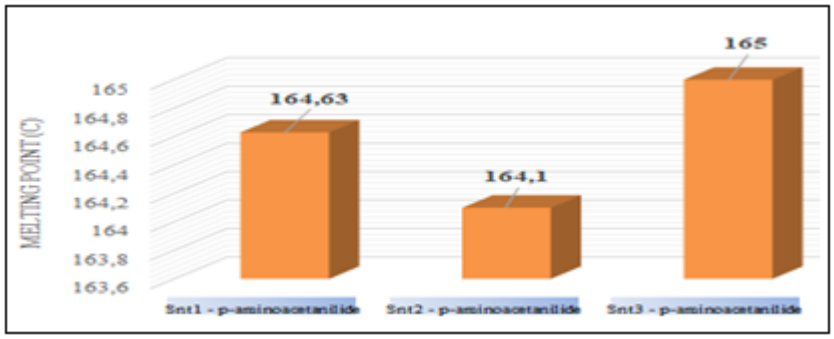

Image 8: Melting point (°C) of synthetized N-(4-aminophenyl) acetamide

FTIR characterization (*Image 8.*) of synthetic semi-product of N-(4-aminophenyl) acetamide is presented. Synthetized N-(4-aminophenyl) acetamide-Snt3 shows absorption peak of 3368,30-3280,36 cm^{-1}, where amide N-H stretch is present with mild movement of absorption bands towards bigger wave number compared to synthetized molecules Snt1 and Snt2 (*Image 8.*). At the spectrum of synthetized N-(4-aminophenyl) acetamide - Snt3 molecule there is no peak of aromatic (-CH) stretch compared to the spectrum of synthetized molecules Snt1 and Snt2 , which show the peaks in range from 3126,13 to 3061,36 cm^{-1}. Two absorption peaks in range from 1652,03 to 1597,87 cm^{-1} indicate presence of band of amide C=O stretch in spectrum of N-(4-aminophenyl) acetamide-Snt3 molecule, with mutual variation for presented absorption peaks of about 3 cm^{-1} compared with the spectrum of synthetized Snt1 and Snt2 molecules, which confirms the similarity of three spectra. Spectrum N-(4-aminophenyl) acetamide - Snt3 shows absorption peak at 1508, 56 and 1421,09 cm^{-1} which indicatespresence of absorption areas of aromatic stretch vibrations (C=C) in spectra Snt1 and Snt2 with minor differences of few cm^{-1}. In absorption area of vibration *v*(C-N) all three spectra of synthetized N-(4-aminophenyl) acetamide molecules are present. At spectrum of Snt3 molecule, absorption peak is shown at 1320, 83 cm^{-1}. Bending bands (N-H) at three spectra of synthetized molecules are present at 876,59 $cm^{-1}$for Snt3, 865,68 cm^{-1} for Snt1 and 864,43 cm^{-1} for Snt2. Band of strong aromatic C-H bending are present at 825,75 i 784,24 cm^{-1}[5]for the spectrum of Snt3 molecule, which complies with present bands at spectra of synthetized Snt1 and Snt2 molecules.

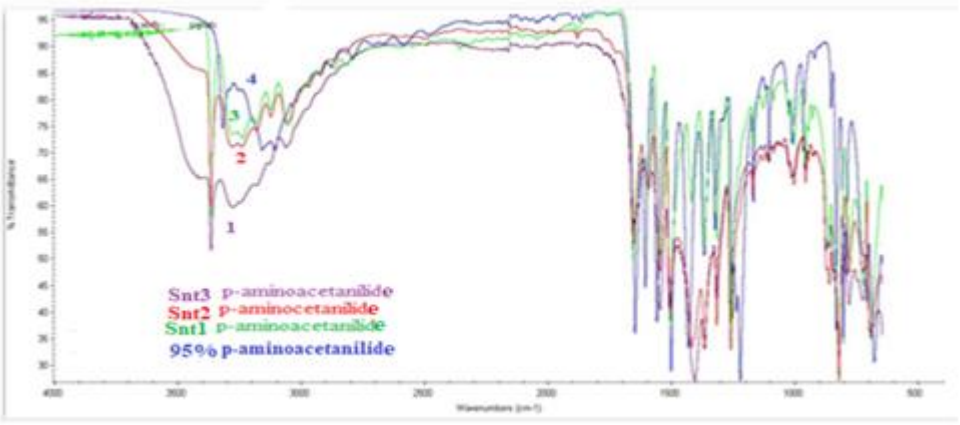

Image 9: FTIR spectrums of synthetized samples:
1. N-(4-aminophenyl) acetamide, 2. N-(4 aminophenyl) acetamide and 3.N-(4-aminophenyl) acetamide and 95% N-(4-aminophenyl) acetamide or p-aminoacetanilide

UV spectrum of synthetized N-(4-aminophenyl) acetamide molecule shows absorption peak at λ_{max} =246,41 nm and λ_{max} =206,05 nm (*Image 10*).

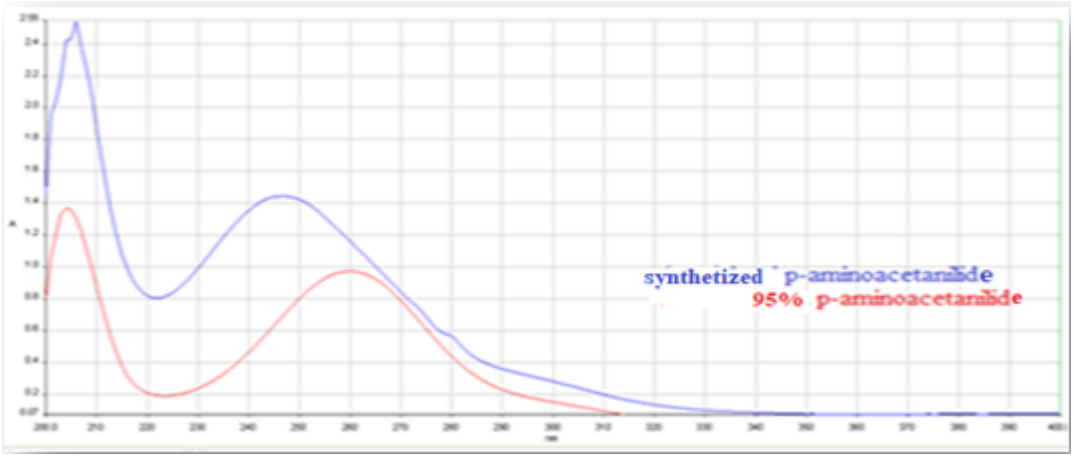

Image 10: UV spectrum of synthetized N-(4-aminophenyl) acetamideor p-aminoacetanilideand 95% N-(4-aminophenyl) acetamide

The results of characterization utilizing mass spectrometry of synthetic N-(4-aminophenyl) acetamide are also obtained *(Image 11.)*. Interpretation of mass spectrum shows the main molecule ion at m/z =151,1 (M+1), which complies with the data from literature.[6]In further fragmentation procedure, the fragmented peak is obtained at m/z=109,1 originating from the composed fragment (H_2N-C_6H_4-NH). Presented peaks at spectrum indicate successfully synthetized compound of N-(4-aminophenyl) acetamide. The peak of small intensity at the spectrum at m/z =353,3 indicates possible presence of impurities.

Image 11: Mass spectrum of synthetized N-(4-aminophenyl) acetamide

Results of thin-layer chromatographic analysis of reduction reaction are shown in the *Image 12*. Samples of synthetized N-(4-aminophenyl) acetamide with iron metal (Fe) (Rf =0,42), synthetized sample with zinc metal (Zn) (Rf=0,43) and 95% N-(4-aminophenyl) acetamide (Rf=0,45) are analysed. The obtained results of synthetized samples compared to 95% N-(4-aminophenyl) acetamide, indicate successfully synthetized N-(4-aminophenyl) acetamide molecule.

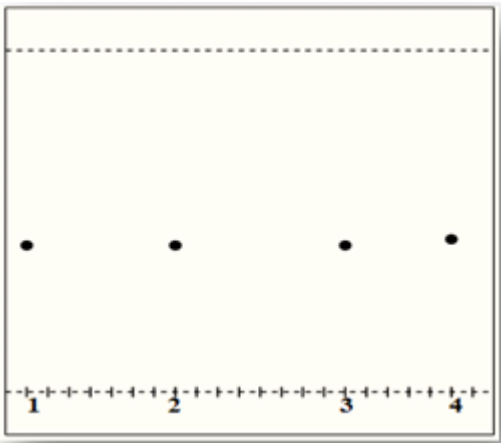

Image 12: Thin-layer chromatographic analysis of synthetized N-(4-aminophenyl) acetamide
1. Commercial N-(4-aminophenyl) acetamide Fe/CH_3COOH, 2. Synthetized N-(4-aminophenyl) acetamide Fe/CH_3COOH, 3. Synthetized N-(4-aminophenyl) acetamide Zn/HCl and 4. 95% N-(4-aminophenyl) acetamide

The *Image 13*. Shows physical-morphological characterization of synthetic product crystals of N-(4-aminophenyl) acetamide, which is compared with commercial N-(4-aminophenyl) acetamide, where similarity of needle shaped crystal is noticed [7]of lively interferenced colours, which complies with the data from literature.

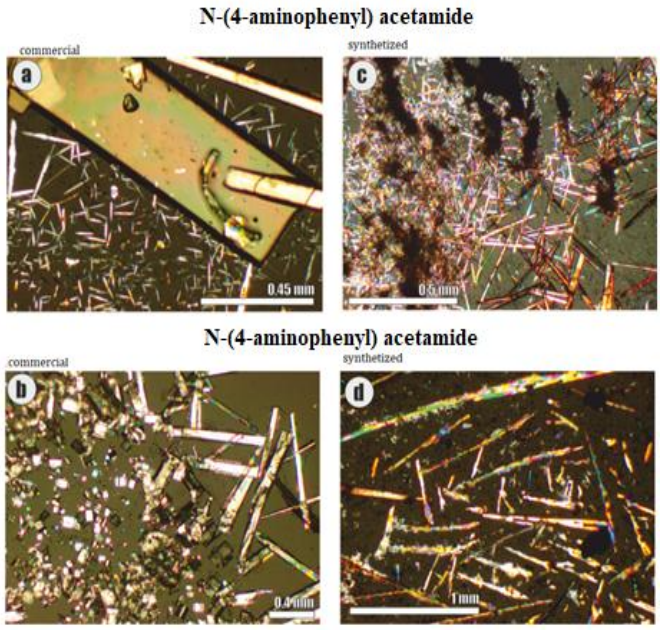

Image 13: Morphological appearance of crystals of N-(4-aminophenyl) acetamide molecule
a) N-(4-aminophenyl) acetamide commercial (DMSO), b) N-(4-aminophenyl) acetamide commercial (water), c) N-(4-aminophenyl) acetamide synthetized (DMSO) and d) c) N-(4-aminophenyl) acetamide synthetized (water)

4. Conclusion

- N-(4-aminophenyl) acetamideis synthetic semi-product and isused to compose N-(4-hydroxyphenyl) acetamide molecule or paracetamol, which is exceptionally important for pharmaceutical industry.
- The obtained experimental data indicate approximate yield results and FTIR coincidence of synthetized product in reduction reaction utilizing two catalysers (Fe and Zn). The obtained results encouraged further research in order to find better conditions using those two catalysers.
- Methods used in identification and characterization indicate successfully synthetized compound.
- Results of characterization with mass spectrometry indicate presence of main peak m/z =151,1 (M+1) of N-(4-aminophenyl) acetamide molecule, which complies with the data from literature.

5. Acknowledgement

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Author Profile

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