Synthesis of Biologically Potent $\alpha$-aminophosphonates Derivatives by Nano-catalyst

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ABSTRACT

$\alpha$-Aminophosphonate and their derivatives are biologically potent and have received considerable attention in a recent research scenario. The main reason is that they show intriguing biological activity. $\alpha$-Aminophosphonate derivatives are gaining a lot of importance in medicinal chemistry due to their application as enzyme inhibitors, herbicides, antibiotics, pharmaceutical agents and inhibitors of Excitatory Post-Synaptic Potential (EPSP) synthesis, and HIV Protease. It is also important in anti-cancer, anti-HIV, antithrombotic and antibacterial, antioxidant activity. Unfortunately, these compounds have certain limitation such as extraction, purification, of bioactive molecule and their minimum yields. For this reason, many scientists have been orienting their research towards the synthesis of molecules as a new tool to overcome this problems he prime focus of this work is the combination of three reactant derivative of benzaldehyde derivative of aniline, and diethyl phosphonate to form $\alpha$-aminophosphonates derivatives by multicomponent reaction (KFR). The novel nano-catalyst i.e. polyaniline-doped with manganese (PAni-Mn) was prepared. The catalyst shows excellent catalytic activity, high yields, short reaction times, easy synthesis. The PAni was fully characterized by X-ray diffraction, TEM, SEM, and FT-IR technique.

Keyword: $\alpha$-Aminophosphonates, EPSP, (PAni-MN), TEM, SEM, FT-IR.

INTRODUCTION

$\alpha$-Aminophosphonate is a valuable part of organo-phosphorus compounds due to their similarity in structure and properties to $\alpha$-amino acids$^1$. It plays an important role in several field including organic synthesis and various potential applications$^2$. Nowadays researchers have been attentively move towards pesticide, biochemistry and medicinal chemistry last few years because they show biological activity. Some $\alpha$-aminophosphonate show activity against tumor$^3$, activity against microbes$^4$, they inhibit the enzyme$^5$, they act an antiviral agent$^6$, some of the $\alpha$-aminophosphonates containing alkoxyethyl moieties shows antiviral bioactivity$^7$. The Kabachnik-Field reaction and the Pudovic reaction are the two major routs to synthesizing the biologically
potent α-Aminophosphonates. In the first reaction (Phospha-Manich) it contains three component condensation including aldehyde or ketone, a mine and diethyl phosphate8-9. In the second, it contains imines with >P(O)H reagent10. The classical version of the “Phospha-Manich” reaction was discovered by independently Kabachnik and fields more than sixty years ago11-12.

The researchers, while synthesizing of α-aminophosphonates used catalyst i.e. efficient Amberlight IRC-74813. An Extremely Efficient Three-Component (KFR) using oxidizing agent Magnesium Perchlorate 14, Zirconium(IV) compounds 15, The Efficient catalyst NbCl5 16, The efficient anthem sulphuric acid 17, Promiscuous Lipase catalyzed (NiSO4.6H2O) a new P-C bond formation in (MCR) Tin(II) compound as catalyst for (KFR)19.

The derivatives of α-Aminophosphonates synthesized by Multicomponent condensation through Kabachnik-Field Reaction12, are widely explained with a variety of catalysts. Now we have recently reporte the nano (PAni-Mn) catalyst as a novel catalyst used to form α-Aminophosphonates. The (PAni-Mn) Nano catalyst was used for the first time in Kabachnik-Field Reaction for α-Aminophosphonates synthesis. During the last decade, Polyaniline had great importance in the catalytic field20-21. The doping of the polyanilinewith metal increases the catalytical activity 22. The Fe-polyaniline composite Nano-fiber catalystfor chemo selective hydrolysis ofoxime23. In proposed work first prepares polyaniline, doping should be done with the help of MnCl2. The synthesized Nano material i.e. the nano catalyst (PAni-Mn) is utilized for preparation of α-aminophosphonates derivatives.KFR involes condensation of primary or secondary amines, carbonyl compounds i.e. aldehyde or ketones and dialkyl phosphite24. The Nano catalyst gives a high yield, short reaction time, it provides high surface area, increased catalytical activity. The synthesized Nano–catalyst was fully characterized by X-ray Diffraction, HR-TEM, FEG-SEM, FTIR.

MATERIALS AND METHODS

Materials
All chemicals are used in these experiments, which are supplied by Sigma Aldrich with high purity.

Synthesis of polyaniline
The chemical oxidation methods were used for PANI-ES synthesis lower than (5ºC). mL Aniline (mL) was dissolved in Hydrochloric acid (70 mL, 1.5 M) his mixture is kept in an ice bath to maintain the temperature below 4-5 ºC. The 10 g Oxidizing agent Ammonium Per Sulfate (APS) was dissolved in deionized water. The solution of APS was added drop by drop into monomer solution. This mixture was stirred with a magnetic stirrer up to 4-5 hours25. The polymerization process is carried out, at the end of the polymerization reaction, the green color Polyaniline was formed, washed 2-3 times with D.W. and methanol. Finally, the dark-green composite powder is dried at 70ºC in a hot air oven, for 10-12 hours. The final product was grounded to form a green powder (Figure 1).

Fig. 1. Structure of Polyaniline

Preparation of Polyaniline Nano-catalyst
After formation of polyaniline Emeraldine salt (ES), the accurate amount of solution of manganese chloride MnCl2 slowly and carefully dissolved in polyaniline. The polyaniline manganese chloride solution was kept for stirring with the help of a round bottom flask and Magnetic stirrer (700 RPM) for about 5 hours. After filtration, the product washed 3 times with deionized water and three times with ethanol. The prepared nano catalyst was kept in a hot air oven for 6 h at 70-80ºC. In this method the nano particles of Mn was uniformly distributed in polyaniline26-27. There is formation of a nano catalyst having a dark green color (Figure 2).

Fig. 2. Freshly PAni-Mn Nano catalyst prepared

RESULT AND DISCUSSION

Polyaniline (X-RD) Analysis
The X-RD technique is used to determine the crystalline nature of polyaniline. ThePANI-ES
gives three different peaks at room temperature i.e. 20.1, 25.3, 26.7°C, respectively as shown in Fig. 2. Polymer is semi-crystalline in nature as the pattern shows sharp peaks due to the presence of Benzenoid and quinonoid groups in the polyaniline28. The sharp peak is observed in the XRD spectrum 2θ=25.2550 The interplanar distance value obtained is 3.35Å0. Hence the average crystallite size is calculated on the basis of the Debye Scherer Equation. (D=kλ/βcosθ) in this equation 1) D=average size of crystallite 2) k=0.89 (Shape of factor), λ=(1.54Å0), β=full width at half maximum; θ=angle of diffraction29.

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The average crystallite size value obtained is 1.387 nm on the basis of XRD data given in Table 1.

### Table 1: Polyaniline data of XRD

| Pos[°2θ] | Height [cts] | FWHM[°2θ] | d-Spacing[Å] | Rel.Int[%] |
|---------|-------------|-----------|--------------|-----------|
| 25.255  | 17.32       | 1         | 3.53544      | 100.00    |

**SEM Characterization**

The main objective of scanning electron microscopy is to determine morphological features and surface characteristics of the compounds. The instruments used JEOL JSM-7600F FEG-SEM. Morphology of polyaniline (ES) shows fibrous in nature particle size is around 1μm, 100μm. This shows that the material is in good shape having high surface area, nano fibre which is used for further application. at high temperature polyaniline (ES), tends to form nano-rod like structure. The factors such as polymerization process, polymerization rate, growth of polymers and solvent interfacial tension are also involved in the formation of nano rods30.

**TEM (300kV) Characterization**

The TEM300kV can be used to study electron beams to image a Nano particle and generate highly magnified images. The Nano structure of the polyaniline is shown in the following micrographs on the basis of TEM analysis, the particle size of Polyaniline is very small, i.e. 1μm, 200nm, 50nm. It is spherical in shapes, having the rough surface.
Fig. 9. In a spectrum, the characteristic band observed at 3464-3727 cm$^{-1}$ as a result of nitrogen-hydrogen stretching. The polymers peak observed on 3232, 2923, 2852 cm$^{-1}$ as a result of asymmetric, symmetric carbon-hydrogen vibration. The C=C of aromatic ring Absorption spectra observed on 1663 cm$^{-1}$ is the result of C-H stretching in an aromatic compound. The IR spectrum band observed at 1468.59 cm$^{-1}$ corresponds to C=N stretching in ring aromatic compound. 1240-1299 cm$^{-1}$. The polymer absorption band of C-N stretching On the basis of this, it confirm the presence of amine group.

RESULT AND DISCUSSION

Following $\alpha$-Aminophosphonate derivatives were prepared.

**Diethyl-3-chlorophenylamino-4-hydroxy-3-methoxy-5-nitrophenyl methylphosphonates.**

M.F. C$_{18}$H$_{22}$ClN$_2$O$_7$P M.W= 444, dark brown color m.p. = 177-179°C, yield=88% $^1$HNMR(300MHz, DMSO-$d_6$) $\delta$; 10.3 (s, 1H, -OH), 8.90-6.58 (m, 6H, Ar-H), 5.02-xx (m, 1H,P-CH), 3.81 (q, 4H, P-OCH$_2$), 3.15 (s, 3H, -OCH$_3$), and 1.12 (8, 3H, -OCH$_3$) (t, H, -OCCH$_3$)./1162 MHz, 32 M/Z=444 and 446 with a 3:1 ratio for 31P-NMR.

**Diethyl (4-methoxyphenyl)-N-(Phenyl amino) methylphosphonate**

M.F. C$_{18}$H$_{24}$NO$_4$P M.W=349, dark yellow color m.p. = 57-59°C, yield=92% $^1$HNMR(300MHz, CDCl$_3$) $\delta$: 1.01-1.07(m,3H), 1.17-1.21(m, 3H), 3.71 (s,3H). 3.62-3.64, 3.84-3.88, 4.04-xx(m, 4H), 4.57-4.68 (m, 2H), 6.51-6.62(m, 3H), 6.76-8.00(m, 2H) and 7.0-xx(m,2H), 7.30-7.32(m, 2H). 31P-NMR (16.9 MHz, DMSO-$d_6$) With a 3:1 ratio, 30.6 M/Z equals 444 and 44638.

**Diethyl (2-chloro phenyl amino) nitrophenyl methyl (4-hydroxy-3-methoxy) phosphonate**

M.F. C$_{18}$H$_{22}$ClNO$_7$P M.W=408, brown color m.p. = 174-177°C, yield=87% $^1$HNMR(300MHz, CDCl$_3$) $\delta$: 8.20(s, 1H, ArH), 7.28(d, 1H, J=6.5 Hz, ArH), 6.989d, 1 h, J=6.5 Hz, ArH), 6.92 (d, 2H, J=6.5Hz, ArH) 6.70(s, 1H, ArH), 4.80 (d, 1H, JCHPO=23.7 Hz, CHP) 4.02-4.12(m, 2H, OCH$_2$CH$_3$), 3.95-3.98(m, 1H, OCH$_2$CH$_3$), 3.90 (s, 3H, OCH$_3$) 3.70-3.75(m, 1H, OCH$_3$CH$_2$), 3.16(t, 3H, J=6.4 Hz, CH$_2$), 1.15(t, 3h, J=6.4 Hz, CH$_3$) 31P-NMR (16.5 MHz, DMSO-$d_6$) at 30.4M/Z=440 and 44239.
CONCLUSION

Using the one-pot, three-component Kabachnik-field reaction, it was possible to synthesize novel derivatives of α-amino-phosphonates. The use of different types of aldehyde, substituted aniline and dialkyl phosphate under solvent free condition using a novel nano-catalyst (PAni-Mn). The nano catalyst doped polyaniline with manganese (PAni-Mn) has greater efficiency, simple reaction condition, easy to handle and efficient. The nano-catalyst was characterized by X-ray diffraction, HR-TEM, FEG-SEM, FTIR technique. All the prepared compounds were analyzed. It is worth mentioning that this catalyst is first used in the synthesis of α-aminophosphonates.

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