Asymmetric Hydrogenation of Ethyl 2-Oxo-2-Phenylacetate with Chiral Platinum Loaded on Carbon Fiber

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Abstract- **The asymmetric hydrogenation of ethyl 2-oxo-2-phenylacetate is studied using platinum loaded carbon fiber (Pt/CF) catalyst with cinchonidine as a chiral modifier. Carbon fiber used as supporting material and functionalize by different chemical reagent that introduce oxygenated group on carbon surface. Pt/carbon fiber catalyst have been synthesized and characterized by TEM, SEM and XRD technique for asymmetric synthesis. Good catalytic conversion has been shown by heterogeneous catalyst and enantiomeric (ee = 99%) product was investigated by NMR and HPLC.**

Keywords- Cinchonidine, carbon fiber, Pt, acetic acid, Ketoester.

I. INTRODUCTION

Optically pure products have a great importance in many field such as used in food (in additives), pharmaceutical and agrochemical industries. So this thinks emphasis us to the enlargement of catalytic system that provides optically pure compounds[1, 2]. Among various optically active molecules, α-hydroxyesters have attracted considerable attention due to their importance in the synthesis of natural products and biologically active compounds [3]. α-Hydroxyesters are key intermediates of drug molecules,[4-6] e.g. Cefamandole antibiotic is recommended for the treatment of bacterial infection, [7] (Scheme 1). The asymmetric hydrogenation of α-ketoesters in presence of a metal catalyst is an excellent way to access chiral α-hydroxyesters [8-13]. In majority of asymmetric syntheses, homogenous catalysis show good catalytic conversion and enantioselectivity [8-15]. However, heterogeneous catalysis is desirable [16, 17] due to some drawbacks associated with homogenous catalysis such as tedious product purification, and separation and recycling of catalyst [18-20].

Heterogeneous catalysis is often associated with low catalytic activity and poor enantioselectivity [21-23]. The absorption of substrate on the catalyst surface varies with its structure. In case, greater affinity of chiral modifier towards the support surface or lower absorption of substrate may affect the activity of the catalyst. Non-effective communication between the catalyst and the chiral modifier

results in the formation of racemic products [19]. Therefore, there is demand of time to design efficient asymmetric heterogeneous catalysts. The idea of using supporting materials is to achieve an effective dispersion of the metal nanoparticles that increases the optimal performance and decreases the amount of expensive metal being used, and thus total catalyst expenses drop. Supporting materials for such catalysts should possess some unique properties like inertness towards direct participation in the reaction, stability under regeneration and reaction conditions, tunable surface area, adequate mechanical properties, and physical form. Creation of a chiral atmosphere and activation of solid support surface are the keys to produce good chiral heterogeneous catalysts [24, 25]. In this regard, several attempts have been made in past few decades by varying metal, chiral compound and support material [26-28]. Silica, alumina and titanium oxide are some common supporting materials and were replaced by a carbon support due to their easy availability, environmental acceptability, corrosion resistance, unique surface properties, thermal and chemical stability [29, 30].

Ortio et al. first reported the enantioselective hydrogenation of α-ketoesters using cinchona-modified Pt/Al_2O_3 catalysts [29-32]. Later, several researchers investigated the effect of solvent, modifier, metal and hydrogen pressure. Most of studies were based on understanding of interaction between substrate and modifier. With an increasing demand of effective heterogeneous catalytic system, it is required to design a efficient supporting material with optimum surface area. The carbon allotropes such as carbon nanotubes, graphene, activated carbon and carbon fiber are good candidates to eligible for supporting materials due to their tunable surface area, electrical conductivity, tailor-made porosity and sustainable chemical and thermal stability [33-36]. Recently, Sharma et.al. have been reported good enantioselective Pt (0)/MNNT-catalyzed hydrogenation reaction (at high pressure) of α-ketoester [28]. Out of various carbon allotropes, carbon fiber has been used for preparing heterogeneous catalysts, where carbon fiber was functionalized by different chemical agents [33, 35, 36].

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Pristine carbon fiber are chemically inactive [21, 23], making them difficult substrate for the attachment of metal nanoparticles. For chemical activation, functionalisation of carbon fiber is the first step before preparing heterogeneous Pt/CF catalyst. Functionalisation means oxidative treatment of carbon fiber with HNO_3, HCl or H_2O_2 and introducing carboxyl (-COOH), hydroxyl (-OH) and carbonyl (-C=O) groups on the surface of carbon fiber [24, 37]. These functional groups have been played an important role in facilitating the binding, embedding or stacking of nanoparticles on the carbon fiber. Functionalized carbon support has been shows acidic character due to the presence of above mentioned functional groups. In activated carbon fiber, it is easier for metal nanoparticles to make contact on their external walls by combining with different functional groups present over there.

Current study involves the use of Pt/CF catalyst for asymmetric hydrogenation of ethyl 2-oxo-2-phenylacetate in the presence of cinchonidine as chiral modifier. The remarkable and unexpected influence of surface properties of functionalized carbon fiber, and effect of % Pt loading on the catalytic performance have been discussed.
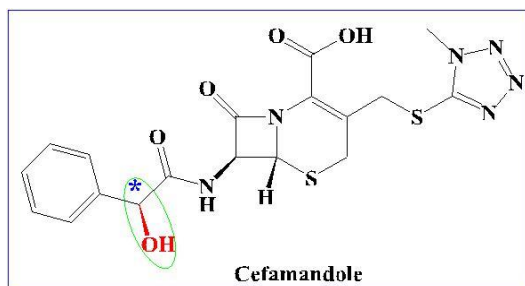
Shceme 1. Pharmaceutical derivative of ethyl 2-oxo-2-phenylacetate.

II. EXPERIMENT

A. Materials

Chloroplatinic acid (Aldrich 37.50%), carbon fiber (Auro carbon industry), ethyl 2-oxo-2-phenylacetate, (sigma Aldrich) acetic acid (Fisher scientific) and ethanol (commercial grade) were obtained locally. Oxidizing agent like HNO_3, H_2O_2, KOH, NaOH, H_3PO_4 and H_2SO_4 were obtained commercially.

B. Typical preparation method of Pt/CF catalyst

Functionalisation of carbon surface fig. 1: 0.5 g of carbon fiber was refluxed under constant stirring in 45ml of HNO_3[38], H_2O_2, H_3PO_4 and H_2SO_4 at 70°C. Now carbon fiber was extracted by centrifugation at 3000 rpm followed by washing with water and ethanol. Later the washed carbon fiber was dried at 80°C for 24 h. The wet chemical method has been used for preparing metal support on carbon fiber[26, 27].

The functionalized carbon fiber were immersed in an aqueous solution of Pt metal salt (H_2PtCl_6) and sonicated

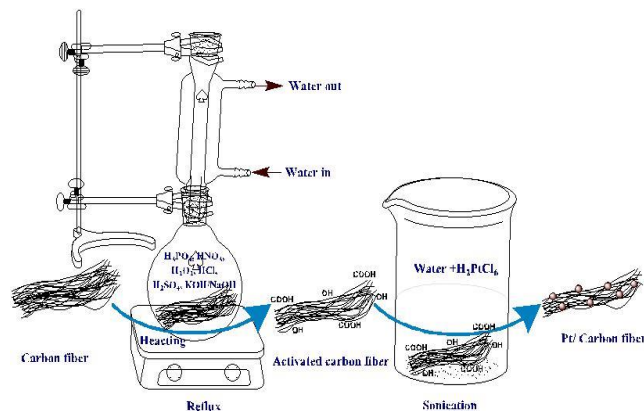
Figure 1. Typically catlysts preparation from Pt/CF

This slow drying method, Pt nanoparticles tinted on carbon surface. Sodium formate solution (42 mg mL-1) have been used for reducing of Pt metal at 100 °C for 1 h, and then the carbon fiber was filtered, washed with deionised water, and dried at 80 °C for 16 h.
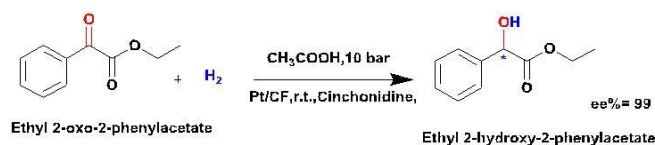

Figure 2. Typically asymmertric hydrogenation reaction of ethyl 2-oxo-2-phenylacetate.

C. Catalytic hydrogenation

Catalytic asymmetric hydrogenation reaction was performed in a Berghof HR-100 high pressure vessel equipped with a teflon container (fig.2). Before reaction all Pt loaded catalysts were pre-treated in tubular furnace under flowing hydrogen for 3h at 300 ^{0}C. In reaction mixture (30 mg) Pt catalyst, (4 mg) chiral modifier, (1.5 ml) acetic acid was premixed in teflon vessel under hydrogen and after 10 min, (75 µl) ethyl 2-oxo-2-phenylacetate was introduce in reaction mixture. Now teflon vessel put in high pressure reactor and create vacuumed in teflon vessel followed by purged with hydrogen 2-3 times to remove the air, and filled to desire pressure. The magnetic stirring was set at 900 rpm for 24 h at room temperature. After completion of reaction, catalyst was removed by centrifuge and organic product was separated by column chromatography using new hexane as eluent.

D. Characterization

An X-ray diffractometer, D8 advance (Bruker,U.S.A.) ,using Cu Kα1 (λ = 1.54056 A˚) as the radiation source was used for to ascertain the quality and crystalline nature of carbon fiber as opposed to amorphous carbon materials with tube current and voltage 40 mA and 40 kV respectively.
Material spectrum range is 2Ө = 20-80˚ with 0.02

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increment. Catalysts morphology was studied using scanning electron microscopy (SEM, EVO18 special edition Carl Ziess) with an accelerating voltage of 20 kV. SEM has been used to investigate the surface morphology of different Pt/CF catalysts, prepared from different activation method. The product conversion and enantioselectivity monitored by NMR spectroscopy and HPLC column respectively. Nuclear magnetic resonance spectra (1H NMR) were recorded on a Bruker 500 spectrometer operating at 500MHz for 1H (CDCl$_3$). Chemical shift for 1H NMR spectra are reported as δ in parts per million (PPM) downfield from SiMe$_4$ (δ 0.0) and relative to the signal of chloroform-d (δ7.26, singlet). HPLC analysis of the reaction mixture was carried out using a WATERS (Ireland) system equipped with normal phase CHIRALPAK IA (Lot No.IA00CE-QA008) columns (0.46 cm*25 cm). The columns were thermostated at 30˚C and the eluent (90:10 v/v mixture of n-hexane/iso-propanol) was supplied at a flow rate of 1 mL/min.

III. RESULT AND DISCUSSION

Functionalized carbon fiber and Pt/CF catalyst were characterized by XRD in fig. 3. The pattern (Intensity counts versus two theta) shows peaks at 2θ = 25.90, 42.70 and 53.50 corresponding to the (002), (100), and (004) planes reflection, respectively which can be attributed to the planes of carbonized carbon. In case of Pt/CF, three major peaks at about 39.68˚, 46.4˚ and 67.7˚ were believed to correspond to diffractions from the (111), (200), and (220) planes of the face-centered cubic lattice of Pt metal. XRD of Pt/CF showed disappearance of plane (100) belonged to functionalized carbon surface.
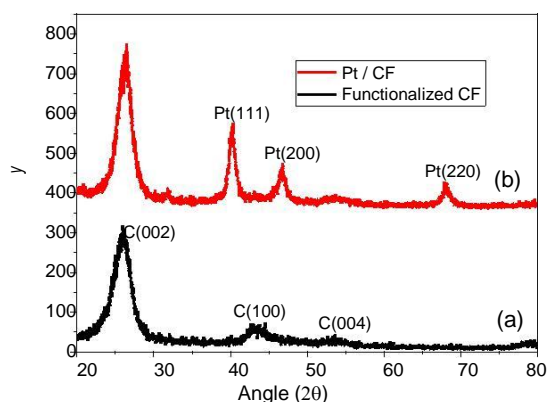

Figure 3. XRD spectra of (a) Functionalize CF (b) Pt/CF

SEM image was taken with low or high magnification to investigate the loading of Pt particle dispersed on the carbon fiber. Fig.4 presented the low magnification SEM to reflect the morphology of the carbon fiber/silver nanocomposites in which carbon fiber dispersed on silver tape. Dispersion of Pt nanoparticles have been depended on functionalized carbon fiber. For example, we found that when carbon fiber was treated with KOH and NaOH then there is no Pt particle loading, it means above bases are unable to functionalize the

carbon fiber (fig. 4 a, b). When we functionalized carbon fiber with dilute HCl, H$_3$PO$_4$ and H$_2$O$_2$ then 2.6%, 3%, and 3.1% Pt loading were obtained, respectively with agglomeration of particles (fig. 4 (c), (d), (e)). In fig 4((f), (g), (h)) high dispersion of Pt nanoparticles with high %Pt loading has been showed when carbon fiber was treated with HNO$_3$, H$_2$SO$_4$ and mixture of HNO$_3$+H$_2$SO$_4$, respectively. The EDX measurements have been used to confirm the % Pt loading and the atomic components on the surface of the catalyst. However, it was not expected to get the exact atomic ratio of the metal because of partial oxygen contribution comes from the oxygen-containing functional groups, such as carbonyl or carboxyl groups on the surface of carbon fiber. In case of functionalized carbon surface, carbon (0.277 Kev) and oxygen (0.525 Kev) EDX peak have been obtained, after loading of Pt on carbon fiber surface; Pt peaks were obtained at 2.048 KeV and 9.441

KeV due to M line and Lα line respectively. TEM image [fig. 5 a, b, c and d] reported the shape and allocation of nanoparticles on the surface of the support. The average size and diameters of the nanoparticles were determined from TEM images. Particularly, TEM was employed to observe the loading state of the platinum. Specifically, TEM images indicated the surface of the fiber coated, decorated or embedded with the nanoparticles.

One the catalyst was well characterized, a most significant reaction for application i.e. asymmetric hydrogenation was chosen. For this purpose, the reaction conditions were optimized and carried out hydrogenation reaction of ethyl 2-oxo-2-phenylacetate using Pt/CF catalyst. Theses optimal reaction conditions were used to screen activity of other Pt/CF catalysts prepared. In the current studies, for ease of comparison, we have used 5% platinum on carbon fiber. Catalytic performance of Pt/carbon fiber activated by different chemical reagent demonstrated in Table 1. It was observed that different %Pt loading on carbon fiber gave different conversion (Table 1). Enantiomeric product was investigated by NMR and HPLC. The optical yield was expressed as the enantiomeric excess (ee) of R-(+) enantiomer.

$$Ee\% = ([R]-[S])*100/ ([R] +[S])$$

NMR data has been recorded for ethyl 2-hydroxy-2-phenylacetate (Fig.6) 1H NMR; δH (500 MHz; CDCl$_3$; Me$_4$Si) 1.21 (3 H, t, J 7.45 Hz, CH$_3$), 4.21 (2 H, q, J 3.45 Hz, CH$_2$), 5.19 (1 H, s, CH), 7.29(5 H, m, J 6.85 Hz, C$_4$H$_5$), ppm; 13C NMR (CDCl$_3$, 125 MHz): 14.0, 61.6, 72.8, 126.8, 127.5, 129.5, 138.2, 173.7 ppm; $[\alpha]D^{20°C}$ = +10 (c 0.1 in chloroform). The retention time of (+)-R- ethyl 2-hydroxy-2-phenylacetate and (-)-S- ethyl 2-hydroxy-2-phenylacetate are 3.5 and 6.1 min., (Fig. 7) respectively.
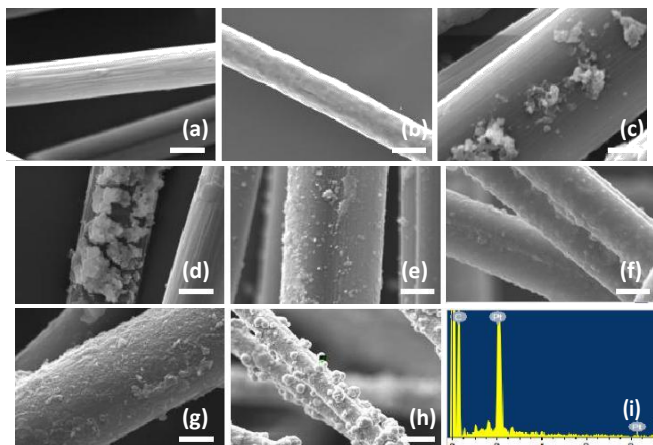
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Figure 4. SEM image of carbon fiber surface at 5μm (a) fuctionalized CF (b) Pt/CF (fuctionalized with NaOH/KOH) (c) Pt/CF (functionalized with dilute HCl) (d) Pt/ CF (functionalized with H₃PO₄) (e) Pt/ CF (functionalized with H₂O₂) (f) Pt/CF (functionalized with HNO₃) (g) Pt/CF (functionalized with H₂SO₄) (h) Pt/CF (functionalized with H₂SO₄) (i) Pt/CF (functionalized with H₂SO₄) (i) EDX spectrum image of Pt/CF.
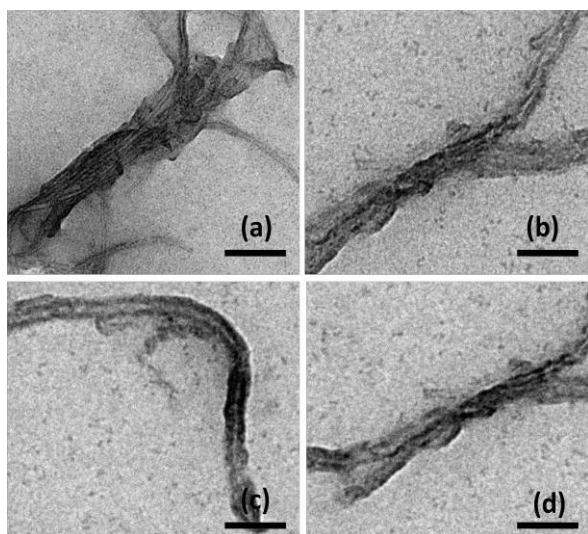

Figure 5. TEM image of Pt/CF catalysts at 50 μm.

Table 1. Asymmetric hydrogenation reaction of ethyl 2-oxo-2-henylacetate with various Pt/CF.

S. NO.	Chemical reagent	% Pt loading	ee* %
1	H₃PO₄	3	78
2	H₂O₂	3.1	78
3	HNO₃	4.5	95
4	HCl	2.6	60
5	H₂SO₄	4.0	85
6	KOH/NaOH	0.0	0
7	HNO₃+H₂SO₄	4.9	99

Proposed reaction condition (mmol): Ethyl 2-oxo-2-phenylacetate /acetic acid/cinchodine/time ::0.50/17.48/0.70/24h .*The product was inveastigated by column chromatography and specific rotation was observed of D-line.
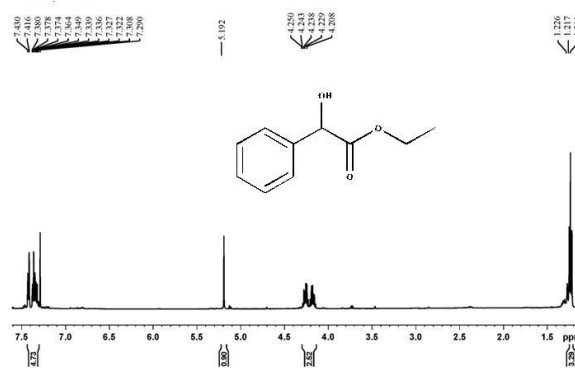

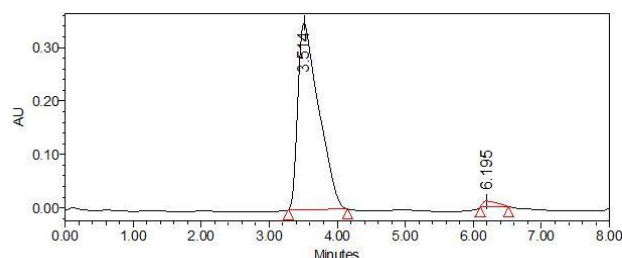Figure 6. NMR spectrum of ethyl 2-hydroxy-2-phenylacetate .

Figure 7. HPLC spectrum of ethyl 2-hydroxy-2-phenylacetate.

IV. CONCLUSION

In conclusion, carbon fiber have been functionalized from different chemical reagent and used for supporting materials for heterogeneous catalyst. Asymmetric heterogeneous catalysts have been prepared by Pt nanoparticles loading on carbon fiber. The prepared catalysts were characterized meticulously and were further used in enantioselectivity hydrogenation of ethyl 2-oxo-2-phenylacetate. The efficacy of the catalysis was confirmed by the good conversion factor and resultant enantioselectivity in the products as obtained at optimized reaction condition.

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