Asian Journal of Chemistry; Vol. 28, No. 5 (2016), 954-956

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2016.19277

Synthesis, Characterization and Biological Studies of Ethynyl Nickelocene

MUHAMMAD ARSHAD RAZA[1], MUHAMMAD PERVAIZ[1], AYOUB RASHEED[1], HINA MUSTAFA[2] and AHMAD ADNAN[1,*]

[1]Department of Chemistry, Government College University, Lahore, Pakistan
[2]Department of Biochemistry, Government College University, Lahore, Pakistan

*Corresponding author: Tel/Fax: +92 4237164058; E-mail: adnan_biochem@yahoo.com

Received: 14 April 2015; *Accepted*: 8 January 2016; *Published online*: 30 January 2016; AJC-17724

The titled compound (ethenyl nickelocene) containing nickel as central metal ion was synthesized. The reaction methodology was divided in two steps. The organometallic compound was characterized by FT-IR, Mass spectrometry and X-ray crystallographic studies. The compound was subjected for antimicrobial activities in order to check the influence against different bacteria (*Escheria coli*, *staphylococcus aureus* and *Bacillus subbtilis*) and fungal strains (*Alternaria alternate*, *Aspergillus flavus* and *Aspergillus niger*). The results showed remarkable influence of ethynyl nickelocene against bacterial and fungal strains.

Keywords: Ethynyl nickelocene, Antimicrobial activities.

INTRODUCTION

The major practical technologies of our universe is found to be use the methodology of click chemistry in different reactions that uses only the most practical and reliable chemical transformations. The main biological processes like proteomics and DNA research with the help of bioconjugation reactions are increasingly found to be dependent on click chemistry [1,2]. A powerful reaction of copper(I)-catalyzed1,2,3-triazole formation has been reported [3]. This reaction was proceeded by reacting acetylene and azides under appropriate reaction conditions.

The azide alkynes click reaction also known as Sharpless click reactions [3] is a novel rediscovery of a reaction which meets the different requirements of affixation of ligands on to polymers by sing post modification processes. The present work is mainly focussed on precursor of click chemistry, related to the reaction itself, thus a focus on making carbon-heteroatom bonds must be accompanied by the use of pre-formed carbon-carbon bonds [4]. The best and most energetic, of these building blocks are olefins and acetylenes. In this article, we report a synthesis of new organometallic compound *viz*., ethynyl nickelocene (**I**) which contains olefinic and acetylene bonds.

EXPERIMENTAL

Analytical reagent grade chemicals and solvents including nickelocene, amino acid azides, copper iodide, sodium azide, dimethyl formamide, methyl nitrile and diisopropyl ethylene amine were purchased from Sigma-Aldrich, Lab Scan and Acros Organics. All chemicals and solvents were used without any further purification. Melting points were taken by electro-thermal open capillary method and hence are uncorrected.

Synthesis of ethynyl nickelocene: Equimolar quantities of nicklocene (1.78 g, 0.01 mol) and acetic anhydride (1.02 g, 0.01 mol) were reacted in a three necked round bottom flask fitted with magnetic stirrer in the presence of phosphoric acid. The whole mixture was refluxed for 5-7 h and the solvent was removed by rotary evaporator. The acetyl nikelocene formed was separated and dried. In the second step, dimethyl formamide (25 mL, 0.32 mol) and acetyl nikelocene (22.8 g, 0.1 mol) were reacted in a three neck round bottom flask. Inert atmosphere was provided by nitrogen gas and system was subjected to ice bath in order to provide cooling up to 0 °C. The reaction mixture was stirred for 2 h and cooled again up to 0 °C with inert atmosphere of nitrogen. Now added 25 mL phosphorus oxychloride drop wise with great care. The mixture was stirred again at 0 °C for 2 h. The whole mixture was kept under cooling and stirred vigorously for 1 h along with 75 mL of diethyl ether under inert atmosphere. After stirring the reaction mixture was neutralized with sodium acetate (116 g, 0.55 mol) and aqueous media was created by adding 10 mL of distilled water. Two layers (organic and aqueous) formed were separated followed by stirring for 3 h at room temperature. The aqueous layer was extracted several times with 100 mL of diethyl ether. The organic layer was washed carefully with sodium bicarbonate solution (100 mL) and distilled water (100 mL). The organic layer was dried over sodium sulphate, filtered

and concentrated by using rotary evaporator. Crystals of 2-formyl-1-chlorovinyl nikelocene were obtained after drying. Another three neck round bottom flask was engaged and 2-formyl-1-chlorovinyl nikelocene (26 g, 0.95 mol) and 1,4-dioxane (300 mL) were refluxed for 1 h in a refluxing system containing heating oil bath. The reaction mixture was poured in to the beaker containing ice and neutralized with 1 N HCl solution. The mixture was engaged with separating funnel containing 100 mL *n*-hexane in order to separate organic phase. The extracted organic phase was washed, filtered, dried and concentrated by rotary evaporator (**Scheme-I**). The crude product in the form of ethynyl nikelocene was purified by chromatographic tools. The physical properties of the synthesized compound are shown in Table-1.

TABLE-1
PHYSICAL PROPERTIES OF ETHYNYL NICKELOCENE

Compound nature	Solid
m.w.	212.89
m.f.	$NiC_{12}H_{10}$
m.p. (°C)	29.44
Solubility	Insoluble in water
Physical appearance	Light greenish in colour

RESULTS AND DISCUSSION

Crystallization of ethynyl nickelocene in triple component solvent system: The most successful method was adopted by using a combination of three solvents system in order to get fine crystals of ethenyl nickelocene. Three different individual solvents were employed for the crystallization but none of them was good enough to dissolve the compound and ultimately to weigh down the crystallization of the compound. Three component solvents system (ethanol, toluene, ethyl acetate: 50, 10 and 40 %, respectively) was adopted to significantly enhance the solubility [5]. Results were inspiring because the solubility was improved when 0.5 g ethynyl nickelocene was experienced which may be due to strong intermolecular interactions between the solvents and the solute particles.

FT-IR: The FT-IR spectrum of ethenyl nickelocene was recorded in the range of 4000-400 cm^{-1} as KBr pallets. The assignment has been prepared on basis of reported work [6]. In IR spectra of the compound, bending vibrations for CH group (methine) of alkenes were observed at 772 cm^{-1}, 1002 cm^{-1}. Bending vibrations for C=C group of aromatic rings was observed at 1550 cm^{-1}. Similarly, stretching vibrations for CH group of aromatic ring were observed at 1425 cm^{-1} and 3075 cm^{-1}. The CH stretching vibrations for triple bond of alkyne group was observed at 3312 cm^{-1}.

Mass analysis: The molecular ion peak of the compound was observed at *m/z* 212.69 which is not the base peak (Fig. 1). The disintegration pattern showed that the molecular ion fragment was disintegrated by the cleavage of acetylene resulting in the fragment peak at *m/z* 188.The fragment pattern of the molecule was also observed by the cleavage of 1,3-pentadiene and fragment was observed at *m/z* 123 which is also a base peak. The further cleavage of 1,3-pentadiene gave fragments at *m/z* 98 and 58 by the cleavage of ethylene and acetylene groups respectively. The isotopic peak after the cleavage of acetylene group was observed for nickelocene at *m/z* 190.

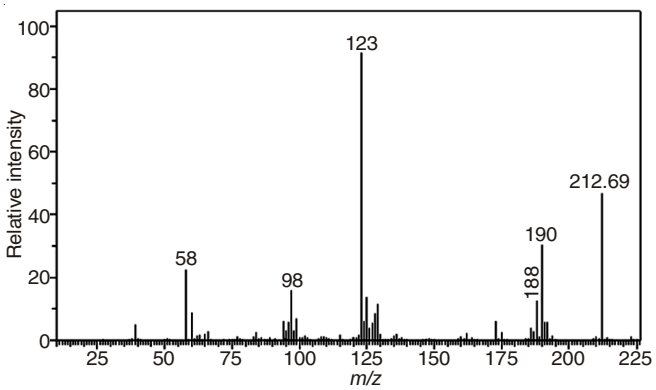
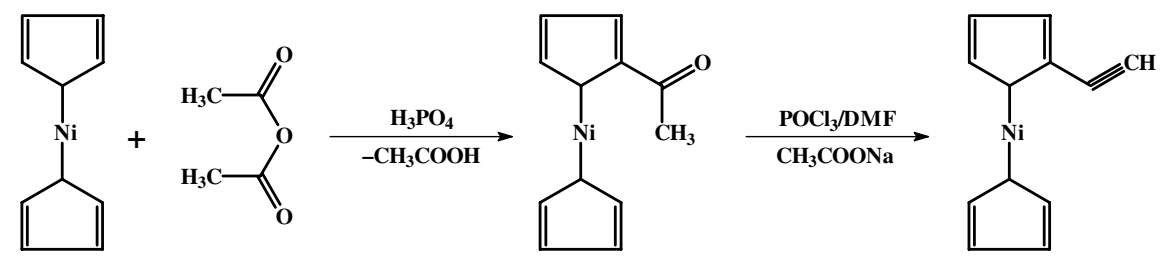


Fig: 1. Mass spectrum of ethynyl nickelocene

XRD analysis: The compound was characterized for XRD studies on Apex-II Bruker X-Ray diffractometer. The structure of the compound ($NiC_{12}H_{10}$) was confirmed by X-ray crystallography. The crystallographic data and atom numbering of the compound is shown in Table-2. The molecular structure, selected bond lengths and bond angles are shown in Table-3 and Fig. 2. The crystal structure justifies that compound contains one Ni metal Ni(1)[5] which is bonded to carbons atoms of the ring on both sides. The bond distances of Ni(1)–C(1) and Ni(1)–C(6) are 1. 3187 (1) nm and 1.3154 (1) nm, respectively which indicates that Ni(1)–C(1) and Ni(1)–C(6) are covalent bonds. Furthermore the both angles involving Ni center for C(1)–Ni(1)–C(6), C(6)–C(7)–Ni(1) and C(2)–C(1)–Ni(1) are 176 (11), 135.30 (11) and 135.14 (10), respectively.

Antibacterial activity of ethynyl nickelocene: The antimicrobial activity was determined by using disc diffusion method. The compound was tested for activity against *S. aureus, B. subtilis, E. coli* using rifamipicin as positive control.



Ethenyl nickelocene

Scheme-I

TABLE-2
CRYSTAL DATA FOR ETHYNYL NICKELOCENE

Mol. formula	$NiC_{12}H_{10}$
Formula weight	212
Crystal class	Monoclinic
Space group C	2/c
a	21.932(3)
b	6.0755(5)
c	14.208(2)
α	90
β	97.471(5)
γ	90
Colour	Green
Shape	Prism
Volume	1883.18(7)
Z	4
Radiation type	MoK_α
Wavelength	0.710730
Dx	1.62
θ max	28.32
H_{min}, H_{max}	-35, 35
K_{min}, K_{max}	-9, 8
L_{min}, L_{max}	-19, 19
R-factor	0.05
Max shift/su	0.0003
Weighted R-factor	0.08
Delta Rho min	-1.69
Delta Rho max	2.92
Reflections used	3328
Sigma (I) limit	-10.00
Number of parameters	191
Goodness of fit 1.096	1.096

TABLE-3
SELECTED BOND LENGTHS (nm) AND
ANGLES (°) FOR ETHYNYL NICKELOCENE

Ni(1)–C(1)	1.3387 (1)
Ni(1)–C(6)	1.3154 (1)
C(1)–Ni(1)–C (6)	176 (11)
C (6)–C(7)–Ni(1)	135.30 (11)
C (2)–C(1)–Ni(1)	135.14 (10)

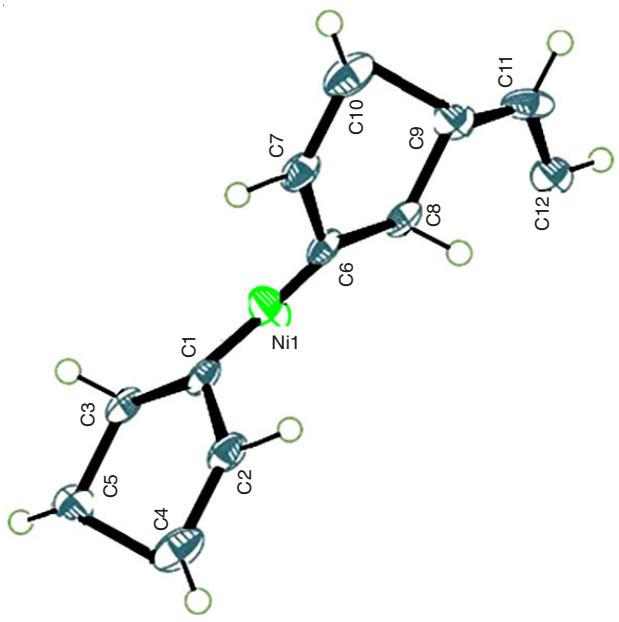


Fig. 2. Ellipsoid displacement view for the crystal structure of ethynyl nickelocene at 50 % probability level

The highest activity was shown against *B. subtilis* with zone 5.25 ± 0.957 mm. The activities against *E. coli* and *S. aureus* were average with zones 5.0 ± 0.816 and 4.5 ± 0.816, respectively. All results are given in comparison with standard drug (rifamipicin) which gave the zone 24.5 ± 0.577 mm (Table-4).

TABLE-4
ANTIBACTERIAL ACTIVITY OF ETHYNYL NICKELOCEN

Compounds	Tested microorganism diameter of inhibition zone (mm)		
	E. coli	*S. aureus*	*B. subtilus*
$NiC_{12}H_{10}$	5 ± 0.816	4.5 ± 0.816	5.25 ± 0.957
Standard	23 ± 2.061	24.5 ± 0.577	23.25 ± 0.816

Antifungal activity of ethynyl nickelocene: The synthesized compound was tested for activity against various fungus starins (*A. niger*, *A. alternata, A. flavus*) by using disc diffusion method. Fluconazol is used as standard drug. The highest activity was shown by compound ethynyl nickelocene against *A. flavus* with zone 5.25 ± 0.577. The activity against *A. niger* was nil and against *A. alternata* was average with zone 4.75 ± 1.825. The results are in comparison with standard drug (fluconazol) which gave the zone 24 ± 0.816 (Table-5).

TABLE-5
ANTIFUNGAL ACTIVITY OF ETHYNYL NICKELOCENE

Compounds	Tested microorganism diameter of inhibition zone (mm)		
	A. niger	*A. flavus*	*A. alternata*
$NiC_{12}H_{10}$	Nil	5.25 ± 0.577	4.75 ± 1.825
Standard	23.5 ± 0.577	23.25 ± 2.061	24 ± 0.816

ACKNOWLEDGEMENTS

The authors wish to thank Dr. Muhammad Wakeel Ahsan Chief Executive of Bhatti Scientifics Lahore, Pakistan, Mr. Faisal Hameed of Biochemika Int. Lahore, Pakistan and Mr. Basar-uz-Zaman Managing Director of Zeta Chemical Company Lahore, Pakistan for support in research work.

REFERENCES

1. K. Nwe and M.W. Brechbiel, *Cancer Biother. Radiopharm.*, **24**, 289 (2009).
2. H.C. Kolb, M.G. Finn and K.B. Sharpless, Angew. Chem. Int. Ed., 40, 2004 (2001).
3. V.V. Rostovtsev, L.G. Green, V.V. Fokin and K.B. Sharpless, *Angew. Chem. Int. Ed.*, **2002**, *41*, 2596-2599 (2002).
4. S.J. Black, D.E. Hibbs, M.B. Hursthouse, C. Jones, K.M. Abdul Malik and N.A. Smithies, *J. Chem. Soc., Dalton Trans.*, 4313 (1997).
5. C. Chen and P.A. Crafts, *Ind. Eng. Chem.*, **45**, 4816 (2006).
6. H. Nandivada, X. Jiang and J. Lahann, *Adv. Mater.*, **19**, 2197 (2007).