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First Report On The Synthesis Of 3-(4-Chloro-Phenyl)-2-Phenyl-3,4-Dihydro-2H-Benzo[E][1,3,2]- Oxazaphosphinine And Its Chalcogenides

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Abstract

The synthesis of 3-(4-Chloro-phenyl)-2-phenyl-3,4-dihydro-2H-benzo[e][1,3,2]-oxazaphosphinine by cyclization of 2-(4-Chloro-phenyl amino)-methyl-phenol with PhPCl2 and its chalcogenides is described.

Keywords: Oxazaphosphinine; Chalcogenides; Organophosphorus; Anti-tumor

Introduction

Organophosphorus compounds have widespread use mainly in agriculture, medicinal and biological field. They are used not only as insecticides but also as herbicides and plant growth regulators [1]. They have also been used as nerve agents in chemical warfare and as therapeutic agents, such as ecothiopate used in the treatment of glaucoma [2]. One of phosphorus heterocyclic compounds, cyclophosphamide has been shown to have very high anti-tumor activity contains oxazaphosphinine ring in it. Therefore, synthesis of such phosphorus-heterocycles is considered of great interest [3].

The organophosphorus compounds are used as chiral ligands in both research laboratory synthesis and industrial production. The development of many efficient chiral phosphorus ligands also allows the discovery of new mechanistic information of Rh- or Ru-catalyzed asymmetric hydrogenation [4,5]. Synthesis of flame retardants with low flammability and melt dropping limits is in urgent need now-a-days and gaining much attention [6] because they can be used as flame retardants for fabrics and plasticising and stabilising agents in the polymer/plastics industry. The synthesis of oxazaphosphinine and similar compounds are described in the literature [7,8]. We have reported [9-14] a number of such compounds containing benzodioxophosphinone, benzoxazaphosphinine and their chalcogenides.

In this paper we report the synthesis of 3-(4-Chloro-phenyl)-2-phenyl-3,4-dihydro-2H-benzo[e][1,3,2]- oxazaphosphinine and its chalcogenides.

Material and Methods

The solvents were received from Sigma Aldrich and CDH used with further purification according to literature [15] and the starting materials/reagents acquired from Sigma Aldrich and CDH used as received. Progress of reaction was monitored by ^{31}P-NMR. ^{31}P-NMR Spectra were measured ($CDCl_3$ solution) with JEOL RESONANCE spectrometer at 161.5MHz. Mass spectra were recorded on a Shimadzu GCMS- QP2010 Ultra mass spectrometer.

Phosphorus heterocyclic compounds are highly moisture and air sensitive, so all the reactions and manipulations were carried out in highly inert atmosphere with dry gases like nitrogen, helium and argon. Thermally unstable products were isolated by low temperature column chromatography with dried silica gel (60-120 mesh).

Procedure of the Preparation of Compounds

Synthesis of 2-(4-Chloro-phenyl amino)-methyl-phenol [1]: was prepared according to the literature [12].

Synthesis of 3-(4-Chloro-phenyl)-2-phenyl-3,4-dihydro-2H-benzo[e][1,3,2]- oxazaphosphinine [2]:

To a toluene (40ml) solution of 2-(4-Chloro-phenyl amino)-methyl-phenol (0.233gm, 1mmol), phenyldichlorophosphine (0.179gm, 1mmol) and triethyl-amine (0.202gm, 2mmol) were added under dry nitrogen atmosphere in round bottom schlenk

flask. After addition, the reaction mixture was kept on reflux for 2-3 hours. The salt thus formed was removed by filteration under nitrogen and the solvent was removed under reduced pressure to obtain semi solid material. The product thus obtained was isolated by low temperature column chromatography (mesh size 60-120 SiO_2, Temp. -5°C). Evaporation of the solvents of the fraction(70%DEE+30%PE) and recrystallization from diethyl ether at -5°C yielded 3-(4-Chloro-phenyl)-2-phenyl-3,4-dihydro-2H-benzo[e][1,3,2]-oxazaphosphinine, a yellow coloured semi solid compound. ^{31}P-NMR (161MHz, CDCl3): δ 112.1; MS (EI, 30eV) m/ z=338 (20 %, M^+), 57 (100%, base peak); ^{13}C-NMR(100MHz, $CDCl_3$): δ 158, 138, 129, 126, 120,118, 115; ^{1}H-NMR(400MHz, $CDCl_3$): δ 4.35(2H), δ 6-8(m, 13H).

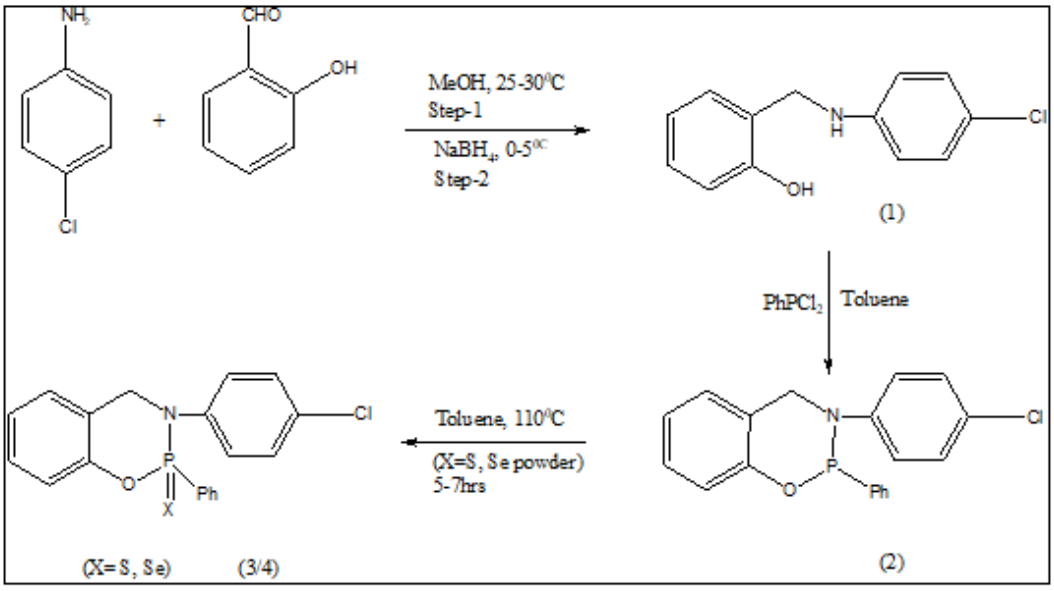
Synthesis of 3-(4-Chloro-phenyl)-2-phenyl-3,4-dihydro-2H-benzo[e][1,3,2]- oxazaphosphinine -2-sulphide [3]: A solution of 3-(4-Chloro-phenyl)-2phenyl-3,4-dihydro-2H-benzo[e][1,3,2]-oxazaphosphinine (0.34gm, 1mmol) and elemental sulphur (0.320gm, 10mmol) in dry toluene was added and heated at reflux for 5-6 hours. The resulting orange colour solution was filtered hot under nitrogen and concentrated under reduced pressure. The crude product thus obtained was isolated by low-temperature column chromatography (mesh size 60-120 SiO_2, Temp. -5°C) but could not be isolated in pure form. The synthesis of 3-(4-Chloro-phenyl)-2phenyl-3,4-dihydro-2H-benzo[e][1,3,2]-oxazaphosphinine-2-sulphide confirmed by ^{31}P-NMR and GC-MS. ^{31}P-NMR (161MHz, $CDCl_3$): δ 76.8; MS (EI, 30eV)m/ z=371(80%, M^+), 373 (100%, base peak).

Synthesis of 3-(4-Chloro-phenyl)-2-phenyl-3,4-dihydro-2H-benzo[e][1,3,2]- oxazaphosphinine -2-selenide [4]: A solution of 3-(4-Chloro-phenyl)-2-phenyl-3,4-dihydro-2H-benzo[e][1,3,2]-oxazaphosphinine (0.34gm, 1mmol) and selenium powder (0.77gm, 10mmol) in 20mL dry toluene was added and heated at reflux for 5-6 hours. The resulting reddish-brown solution was filtred hot under nitrogen and concentrated under reduced pressure. The crude product thus obtained was isolaed by low temperature column chromatography (mesh size 60-120 SiO_2, Temp. -5°C) but could not be isolated in pure form. The synthesis of 3-(4-Chloro-phenyl)-2-phenyl-3,4-dihydro-2H-benzo[e][1,3,2]-oxazaphosphinine-2-selenide was confirmed by ^{31}P-NMR and GC-MS. ^{31}P-NMR (161MHz, $CDCl_3$): δ 83.3; MS (EI, 30eV)m/ z=420.97(20%, M^+), 57 (100%, base peak).

Result and Discussion

Herein, we report synthesis of chalcogenides of 3-(4-Chloro-phenyl)-2-phenyl-3,4-dihydro-2H-benzo[e][1,3,2]-oxazaphosphinine (2). The 3-(4-Chloro-phenyl)-2-phenyl-3,4-dihydro-2H-benzo[e][1,3,2]-oxazaphosphinine was obtained from condensation of 2-(4-Chloro-phenyl amino)-methyl-phenol with dichlorophenylphosphine in equimolar quantities in presence of excess of triethylamine in dry toluene at reflux for 3 hours . The P-chalcogenides (3) and (4) were prepared by reacting 3-(4-Chloro-phenyl)-2-phenyl-3,4-dihydro-2H-benzo[e][1,3,2]-oxazaphosphinine with elemental sulphur and selenium powder in dry toluene at reflux. They were characterized by ^{1}H,^{13}C, ^{31}P NMR and GC-MS spectroscopic data. GC-MS of all the compounds exhibited molecular ion (M^+) and characterstics daughter ion peaks at their expected m/z values.

In the ^{1}H NMR spectra, the aromatic protons resonated in the region 6.84-8.06 as multiplets and aliphatic protons at 4.35ppm. Phosphorus resonance signals, P=S and P=Se were observed at 76.8 and 83.3, respectively. All values are in the range as reported in the literature [13] (Scheme 1).



Scheme-1

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Conclusion

In conclusion, a simple route for the synthesis of 3-(4-Chloro-phenyl)-2-phenyl-3,4-dihydro-2H-benzo[e][1,3,2]-oxazaphosphinine and its chalcogenides is described.

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