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PharmTech
International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol.2, No.1, pp 205-208, Jan-Mar 2010

New Schiff bases derivatives containing anthracene and 1,3,4-thidiazole moieties: Synthesis and fungicidal activity

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Abstract:
New 5-[1-(anthracen-9(10H)-ylideneamino)-2-(1H-imidazol-5-yl)ethyl]-1,3,4-thiadiazol-2-amine 3 has been synthesized from condensation reaction of N-anthracen-9(10H)-ylidenehistidine 2 with thiosemicarbazide in phosphorusoxy chloride. The prepared compounds were characterized by FTIR spectroscopy, electronic spectroscopy, ^{1H}NMR and ^{13C}NMR. Preliminary in *vitro* tests for fungicidal activity show that prepared compounds display good activity to *Gibberela*, *Cercospora arachidicola*, *Physolospora piricola* and *Fusarium oxysporum*.
Keywords: Schiff bases, 1,3,4-thiadiazole, spectral studies, fungicidal activity.

Introduction

Schiff bases are used as substrates in the preparation of a number of industrial and biologically active compounds *via* closure, cycloaddition and replacement reactions. Moreover, Schiff bases are also known to have biological activities such as antimicrobial, antifungal, antitumor, and as herbicides [1]. Schiff bases have also been employed as ligands for complexation of metal ions [2]. On the industrial scale, they have a wide range of applications such as dyes and pigments [3]. The incorporation of the imidazole nuclei is an important synthetic strategy in drug discovery. Many imidazoles have been prepared as pharmacological agents Azomycine, Clotrimazole, Miconazole, Ergothionine, Clonidine and Moxonidine [4]. One of the most important applications of imidazole derivatives is their used as reline material for treatment of denture stomatities [5]. On the other hand, heterocyclic compounds possessing 1,3,4-thiadiazole ring system show antifungal, bacteriostatic, anthelmintic [6] effect as well as depression effect on central nervous system [7]. Palaska et al. reported 1,3,4-thiadiazole derivatives that exhibited analgesic and anti-inflammatory activities [8].

Materials and methods

***Synthesis of N-anthracen-9(10H)-ylidenehistidine* 2**

A mixture of anthrone **1** (0.012mol, 2.71g), 15ml glacial acetic acid and L-histidine (0.012mol, 1.86g) was heated under reflux for 10 h. The reaction mixture was filtered off and recrystalized from ethanol.

***Synthesis of 5-[1-(anthracen-9(10H)-ylideneamino)-2-(1H-imidazol-5-yl)ethyl]-1,3,4-thiadiazol-2-amine* 3**

A mixture of compound **2** (0.015mol, 5.69g) and an equivalent amount of thiosemicarbazide (0.015mol, 1.37g) in $POCl_3$ (25ml) was refluxed in a water bath for 10-12 h. After evaporating under reduced pressure, a solid product was obtained. This was recrystalized from chloroform to afford the desired product.

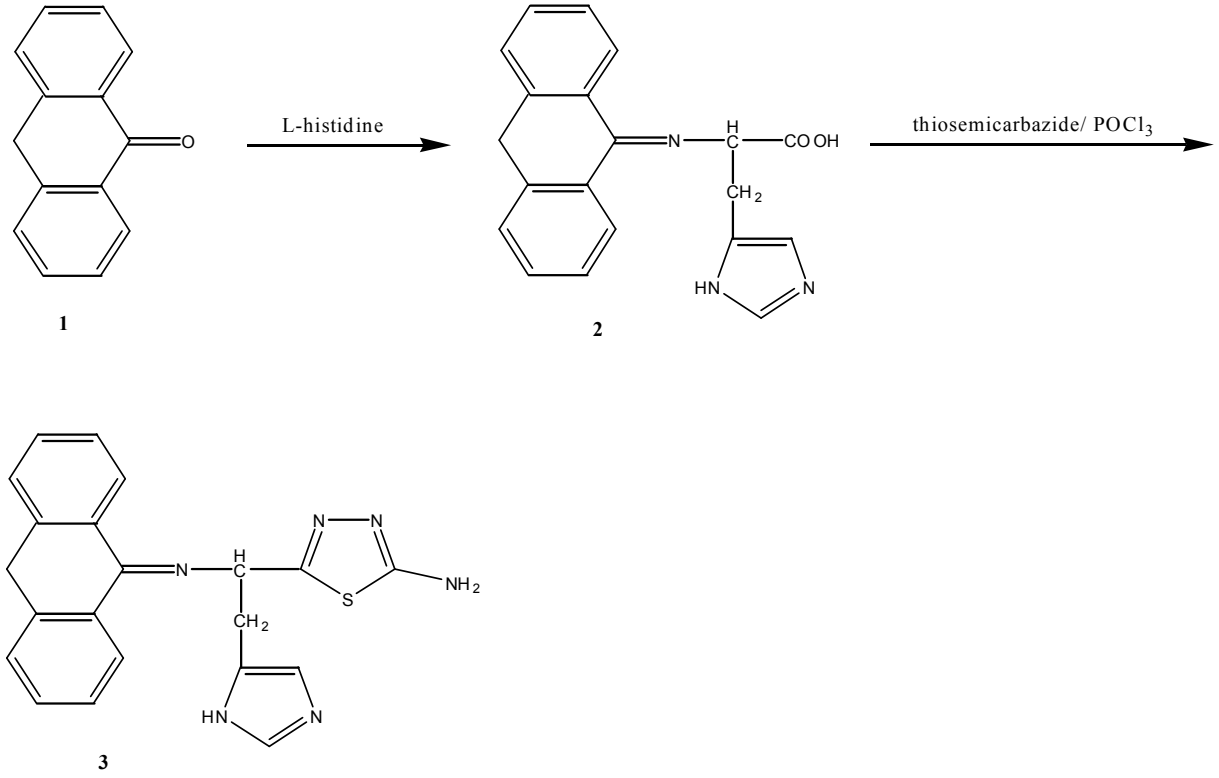
Instrumentation

Elemental C, H, N and S analysis were carried out on a Fison EA 1108 analyzer. Melting points were determined in open capillary tubes using an electrothermal 9300 digital melting point apparatus. The IR spectra of the compounds were recorded on Shimadzu FTIR-8300 spectrometer as KBr disc. The ^{1}H and ^{13}C nuclear magnetic resonance spectra were recorded on Fourier transform Bruker spectrometer, relative to the internal standard tetramethylsilane (TMS) and the chemical shifts are reported in part per million (ppm). ^{1}H-, ^{13}C-NMR and elemental analysis were made at Drug and Natural Product Department, University of Vienna, Australia.

Results and discussion

The 5-**[**1-(anthracen-9(10H)-ylideneamino)-2-(1H-imidazol-5-yl)ethyl]-1,3,4-thiadiazol-2-amine **3** was prepared by the reaction of anthron **1** with L-histidine in glacial acetic acid to give N-anthracen-9(10H)-ylidenehistidine **2** which turned into compound **3** through its reaction with thiosemicarbazide in phosphorous oxychloride.

Scheme 1.



Scheme 1

Table 1 shows the physical data for the starting material and the synthesized compounds. The purity of the ligand and its complexes were checked by TLC using silica gel-G as adsorbent.

Table 1. Physical data for the synthesized compounds

Comp.	Color	% Yield	M. P, ̊C	Found (Calcd.)%			
				C	H	N	S
1	Brown	85	152-154	84.99 (85.12)	8.72(7.54)	-	-
2	Yellow	80	130-132	72.79 (71.65)	7.70 (6.98)	11.07 (10.68)	-
3	White	90	170-172	66.33 (65.74)	6.96 (7.13)	19.34 (18.56)	7.38 (6.75)

Infra-red Spectroscopy

The IR spectra of the synthesized compounds were devoid of the band at 1715cm^{-1} due to the C=O stretching vibration of the conjugated ketones [9]. The IR spectra of N-anthracen-9(10H)-ylidenehistidine **2** showed characteristic bands at 3420, 1730 and 1625cm^{-1} assigned to υ(OH), υ(C=O) and Schiff base υ(C=N) [10] groups, respectively. In the IR spectrum of 5-**[**1-(anthracen-9(10H)-ylideneamino)-2-(1H-imidazol-5-yl)ethyl]-1,3,4-thiadiazol-2-amine **3**, the stretching bands derived from –OH and C=O of carboxylic acid were disappeared with the appearance of new two bands at 3345 and 3276 cm^{-1} due to asymmetric and symmetric stretching vibrations of –NH_2 group. This evidence clearly confirmed the formation of this compound had been take place. The IR data of the synthesized compounds are shown in Table 2.

Table 2. Characteristic absorption bands for the synthesized compounds

Comp.	υ(O-H)	υ(NH_2)	υ(N-H)	υ(C-H) aromatic	υ(C-H) aliphatic	υ(C=O)	υ(C=N) Schiff base	υ(C-S)
1	-	-	-	3067	-	1715	-	-
2	3420	-	3238	3059	2932	1730	1625	-
3	-	3345, 3276	3232	3084	2945	-	1620	670

Nuclear magnetic resonance

The ^{1H}NMR spectra for all compounds were recorded in [$_2H^6$] DMSO using tetramethysilane as the internal standard. The data are compiled in Table 3. The conclusion drawn from ^{1H}NMR studies of a few compounds lend further support to suggested formation of 5-**[**1-(anthracen-9(10H)-ylideneamino)-2-(1H-imidazol-5-yl)ethyl]-1,3,4-thiadiazol-2-amine **3**. The spectrum also exhibit a singlet peaks at δ 8.23 and 8.79 ppm due to the N-H and –NH_2 protons, respectively, which further characterized by D_2O exchange. Furthermore, there are a multiple signals of the aromatic protons resonances at 6.52-7.90 [11].

Table 3. ^{1H}NMR spectral data (δ, ppm) for the synthesized compounds

Comp.	-CH_2-	aromatic protons	N-H	-NH_2	O-H
1	-	6.77-7.98	-	-	-
2	2.02	6.45-7.87	8.20	8.80	9.12
3	2.04	6.52-7.90	8.23	8.79	-

Table 4 shows the most relevant ^{13}C and ^{13C}NMR data, ^{13}C spectra were recorded in [$_2H^6$] DMSO. The C=O resonance group of N-anthracen-9(10H)-ylidenehistidine **2** appeared at 173.32 ppm while the spectrum of 5-**[**1-(anthracen-9(10H)-ylideneamino)-2-(1H-imidazol-5-yl)ethyl]-1,3,4-thiadiazol-2-amine **3** was devoid of the C=O peak. Beside this, the two thiadiazole carbons appear at δ 87.45 and 89.23ppm [12]. These observations lend further evidence to the proposed structure.

Table 4. ^{13C}NMR spectral data (δ, ppm) for the synthesized compounds

Comp.	-CH_2-	aromatic carbons	C=O
1	-	132.54-136.89	165.57
2	20.46	133.12-137.40	170.14
3	22.51	134.34-137.65	173.32

Biological activity

Preliminary in vitro tests for fungicidal activity of synthesized compounds have been carried out by the fungi growth inhibition method [13]. These compounds are dissolved in DMSO at a concentration of 50 ppm. The data are summarized in Table 5, and show that all compounds display certain activity at a low concentration. Moreover, compound **3** shows the highest inhibition percentage for *Physolospora piricola* (80.4%) in vitro.

Conclusion

The preparation procedure follow in this work for synthesis of the title compounds offers reduction in the reaction time, operation simplicity, cleaner reaction, easy work-up and improved yields. All spectroscopic analysis confirmed the proposed structures of these compounds. Biological activity data have shown that the synthesized compounds have a significant biological activity against *Gibberela*, *Cercosora arachidicola*, *Physolospora piricola* and *Fusarium oxysporum*.

Acknowledgement

The authors are acknowledge to Universiti Kebangsaan Malaysia for research funding # UKM-GUP-NBT-08-27-113 and UKM-OUP-NBT-28-145/2009, and to the supporting staffs from School of Chemical Sciences and Food Technology that has contributed greatly in this study.

Table 5. Fungicidal activities of synthesized compounds

Comp.	Inhibition Ratio (%) (50ppm)			
	Gibberela	***Cercosora arachidicola***	***Physolospora piricola***	***Fusarium oxysporum***
1	11.2	41.3	23.4	27.9
2	34.3	71.6	44.3	56.2
3	23.1	56.3	80.4	63.7

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