Synthesis and Spectral Studies of 1,2,4 -Tiazine Derivatives

Dushyant Kumar & Manju Kumari
Deptt. Of Chemistry,Y.N. College , Dighwara, J.P. Unviersity, Chapra (Bihar)

Received: February 20, 2019 Accepted: March 24, 2019

ABSTRACT: *The 1,2,4- trazine derivatives were obtained through a multi-stepsreactions using tricyclic ketone, anthrone as starting materials . All derivatives were characterized by using spectroscopic method such as IR, NMR- Spectra , X-ray diffraction and elemental analysis. All derivatives were primary in vitro Screened for their antipocterial activity against gram positive and gram negative bacteria by drug diffusion method.*

Key Words: *Triazine , KMnO4 ,Ethanol , IR, NMR – Spectra.*

INTRODUCTION

Hydrazides deriavative compounds have been described as useful building blocks for the assembly of different types of heterocyclic rings . A large number of aliphatic, alicyclic, aromatic and heterocyclic carbohydrazides, their derivatives and related compounds are reported to present a plethora ofbiological activities Thus, various carbohy drazides were found to be useful as medicaments especially in the treatment of inflammatory and autoimmune diseases. osteoarthritis, respiratory diseases, cardiovascular diseases, fever, hemorrhage Carbohydrazides and derivative compounds exhibited antifungal antiviral bacteriostatic antiparasite antituberculous, psychotropic, and insecticidal activities. The 1,2,4-triazine derivatives have been synthesized and screened in *vitro*/*vivo*, thus revealing their varied biochemical, biological, pharmacological or cellular activities These facts encouraged us to synthesize 1,2,4-triazine derivatives.

MATERIAL AND METHODS

***Synthesis of N-anthracen-9(10H)-ylidene-4-methylpyridine-2-amine* 1**

A mixture of anthrone (0.012 mol), 15 ml glacial acetic acid and 2-amino-4-methylpyridine (0.012 mol) was heated under reflux for 10 hrs. The reaction mixture was filtered off and recrystalized from ethanol.

***Synthesis of 2-(anthracen-9(10H)-ylideneamino)-4-carboxylic acidpyridine* 2**

Compound **1** (0.05 mol) is added to a solution of (0.05 mol) of potassium permanganate and (0.05 mol) of sodium carbonate in (25 ml) water and the mixture is heated under reflux until the color of the permanganate has disappeared (15 hrs). The reaction mixture was filtered while still hot to get rid of the MnO_2 precipitate. The cooled filtrate is acidified with sulphuric acid (20 %), the carboxylic acid precipitate is filtered off, washed with a little cold water and used without further purification.

***Synthesis of ethyl 2-(anthracen-9(10H)-ylideneamino)pyridine -4-carboxylate* 3**

A mixture of the acid **2** (0.01 mol), abs. ethanol (10 ml), and few drops of conc. sulfuric acid was refluxed for 10 hrs, the reaction mixture was cooled to room temperature and then in the refrigerator for 5 hrs. The solid product was filtered off washed and recrystalized from ethanol.

***Synthesis of 2-(anthracen-9(10H)-ylideneamino)pyridine-4-carbohydrazide* 4**

A mixture of ester **4** (0.012 mol) and hydrazine hydrate (0.02 mol) was refluxed for 5 hrs, then absolute ethanol (15 ml) was added and refluxed for further 8 hrs. The separated precipitate was filtered and washed with cold water.

***Synthesis of 2-(4-(anthracen-9(10H)-ylideneamino)-4-(1,6-dihydro-1,2,4-triazin-5(2 H)-one)pyridine* 5**

Compound **4** (0.01 mol) and chloroacetamide (0.01 mol) were mixed together in (20 ml) absolute ethanol. The reaction mixture was refluxed for 24 hrs, the solvent was reduced to one third its volume under reduced pressure. The crude product was obtained by filtration, washed with water and recrystalized from chloroform.

RESULTS AND DISCUSSION

I.R. SPECTROSCOPY

The FTIR spectrum of N-anthracen-9(10H)-ylidenehistidine 1 showed disappearance of ketone C=O bands at 1715 cm^{-1} which confirm the conversion of compound 1 to 2-(anthracen-9(10H)-ylideneamino)-4-

carboxylic acidpyridine **2**. The compound 2 has carboxylic and and C=O stretching vibration at 1735 cm^{-1} In the spectra of ethyl2-(anthracen-9(10H)-ylideneamino) pyridine -3-carboxylate **3**, 2-(anthracen-9(10H)-ylideneamino)pyridine-4- carbohydrazide **4** and 2-(4-(anthracen-9(10H)-ylideneamino)-4-(1,6-dihydro-1,2,4-triazin-5(2 H)-one)pyridine **5**, the bands at 1723, 3324-3256 and1685 cm^{-1} were assigned to the stretching of ester C=O, -$NHNH_2$ and amide C=O groups, respectively. Table 1 lists the stretching frequency (υ) for some of the characteristics groups exhibited by the synthesized compounds.

NMR SPECTROCOPY

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 the synthesized compounds lend further support to suggested formation of 2-(4-(anthracen-9(10H)-ylideneamino)-4-(1,6-dihydro-1,2,4-triazin-5(2 H)-one)pyridine **5**. The most characteristic evidence support the formation of compound **5** was the two singlet peaks at δ 8.40 and 8.53 ppm due to the N-H protons, which further characterized by D_2O exchange. Furthermore, there are a multiple signals of the aromatic protons resonances at 6.42-7.89 ppm.

Table 3 shows the most relevant ^{13C}NMR data. Due to scan solubility of the synthesized compounds, their spectra were recorded in [$_2H^6$] DMSO. The –CH_3 peak of N-anthracen-9(10H)-ylidene-4-methylpyridine-2-amine **1** appeared at 12.63 ppm. Furthermore, the C=O resonances group of 2-(anthracen-9(10H)-ylideneamino)-4-carboxylicacidpyridine**2**, ethyl 2-(anthracen-9 (10H)-ylideneamino)pyridine-4-carboxylate**3**,2-(anthracen-9 (10H) ylideneamino) pyridine -4-carbohydrazide **4**and 2-(4-(anthracen-9(10H)-ylideneamino)-4-(1,6-dihydro-1,2,4-triazin-5(2 H)-one)pyridine **5** appeared at 173.46, 171.25, 170.26 and 169.83 ppm, respectively .

Table .1 Absorption bands of the synthesized compounds 1 to 5.

Comp.	O-H	-NHNH2	N-H	Aromatic protons	Aliphatic protonns	C=O	C=N
1	-	-	-	3069	2943,2857	-	1610
2	2421	-	-	3054	-	1735	1611
3	-	-	-	3067	2952,2864	1723	1612
4	-	33243256	3172	3063	-	1680	1610
5	-		3176	3060	-	1685	1613

Table .2 "NMR data (δ,ppm) of all compounds prepared 1 to 5

Comp.	-CH3	-CH2-	Aromatic protons	N-H	-NH2	O-H
1	1.34	-	6.56-7.74	-	-	-
2	-	-	6.58-7.83	-	-	9.54
3	1.52	2.03	6.57-7.75	-		-
4	-	-	6.54-7.62	8.42	8.89	-
5	-	-	6.56-7.70	8.40.853	-	-

Table .3 ^{13C} NMR data (δ,ppm) of Syntherized. compounds prepared 1 to 5

Comp.	-CH3	-CH2-	-C=N-	Aromatic protons	C=O
1	12.63	13.31	40.15	13.67-143.29	-
2	-	13.42	41.13	132.68-142.20	143.46
3	12.54	13.38	40.59	133.53-144.21	171.25
4	-	13.43	40.76	134.39-143.22	170.26
5	-	13.46	40.78	132.65-142.89	169.83

ANTIMICROBIAL ACTIVITY

All the compounds 1-5 were in vitro screened for their antibacterial activity against Gram- positive and Gram negative bacteria by the drug diffusion method . All the derivative compounds were tested at 100 µg/ml and 250 µg/ml concentration. The data are summarized in Table 4 , and show that all compounds display certain antibacterial activity.

Table 4 . Antibacaterial activity of the synthesized.compounds 1 to 5

Zone of inhibition in mm Middle												
Comp.	S aurenus		S. epidermidis		B. Subitilis		K. Pneumoniae		E. Coli		P. aeruginosa	
	100	200	100	200	100	200	100	200	100	200	100	200
	µg	µg	µg	µg	µg	µg	µg	µg	µg	µg	µg	µg

1	+	+	+	+++	++	++	++	++	+++	++	++	++
2	++	+++	+	+	+	+++	++	++	+	+	++	++
3	+	+	++	+	++	+	+	+	++	+++	+++	+
4	++	+	+	+++	+++	++	+	+		+	+	+
5	+++	+++	++	++	++	+++	+++	++	+	+	+	+++

Here ,+++ = high activity, , ++= Moderate activity, + = low activity,

CONCLUSION

We have described the synthesis and 1,2,4- triazine derivative compounds 1-5 . These compounds showed in vitro growth inhibitory activity against the tested organisms comparable. The all above data revealed that with slight modifications in the structure one can plan for the drug design.

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