International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.5, No.4, pp 2051-2056, April-June 2013

Synthesis And Biological Evaluation Of 1-(4-P-Toluidino)-6-(Diphenylamino)-1,3,5-Triazine 2-yl- 3-Methyl -2,6- Diphenyl Piperidine-4-One.

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Abstract: Triazine is the chemical species of six-membered heterocyclic ring compound with three nitrogens replacing carbon-hydrogen units in the benzene ring structure. The names of the three isomers indicate which of the carbon- hydrogen units in the benzene ring position of the molecules have been replaced by nitrogens called 1,2,3-triazines. The triazine derivative of 1-(4-p-toludino)-6-(diphenylamino)-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one was synthesized by condensation method by using various amines. The final synthesized compound structure elucidated by spectral analysis and screened for antibacterial and antifungal activity using different strains of bacteria and fungi by turbidometric method at different concentration. Result showed marked anti-bacterial and anti-fungal activity with increasing the concentration and 250 µg revealed equal to standard drug ciprofloxacin in antibacterial activity.
Keywords: Triazine, Diphenylamine, spectral analysis, anti-microbial and anti-fungal.

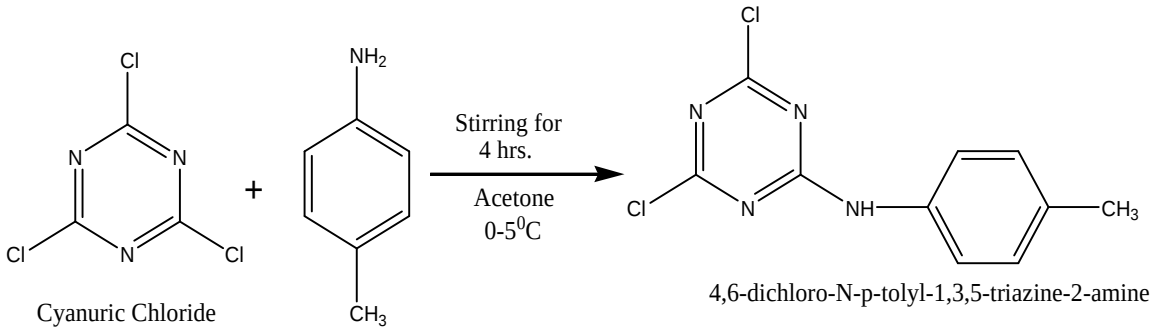
Introduction[1-6]:

Triazine is the chemical species of six-membered heterocyclic ring compound with three nitrogens replacing carbon-hydrogen units in the benzene ring structure.The names of the three isomers indicate which of the carbon- hydrogen units in the benzene ring position of the molecules have been replaced by nitrogens called 1,2,3-triazines.1,2,4-triazines and 1,3,5-triazine respectively.

Materials and Methods[1-6]:

Scheme of the work:

Step 1: Synthesis of 4,6-dichloro-N-p-tolyl-1,3,5-triazine-2-amine.

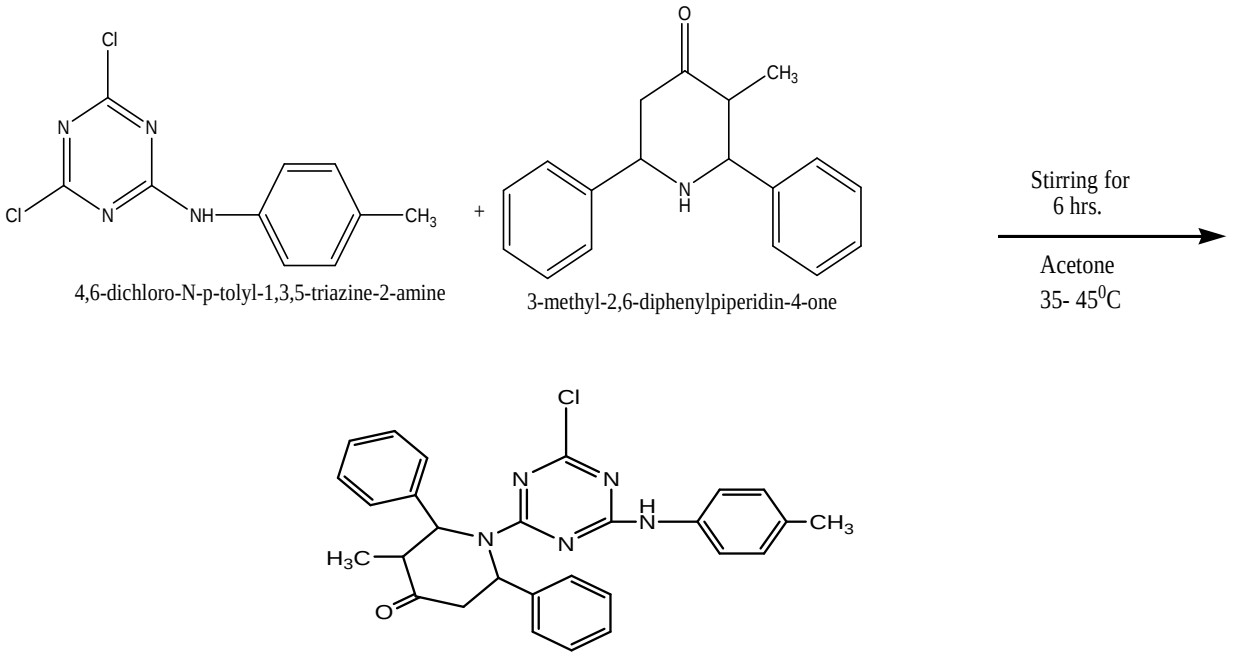


Cyanuric Chloride p-methyl aniline

4,6-dichloro-N-p-tolyl-1,3,5-triazine-2-amine

The Chlorine atom of 2, 4, 6-trichloro-1, 3, 5-triazine was replaced by nucleophillic reagent eg. P-methylaniline. 4,6-dichloro-N-p-tolyl-1,3,5-triazine-2-amine has been prepared by treating 2,4,6-trichloro-1,3,5-triazine in acetone with p-methylaniline at 0-5°c and stirring for 4 hrs.

Step 2: Synthesis of 1-(4-(p-toluidino)-6-chloro-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one.



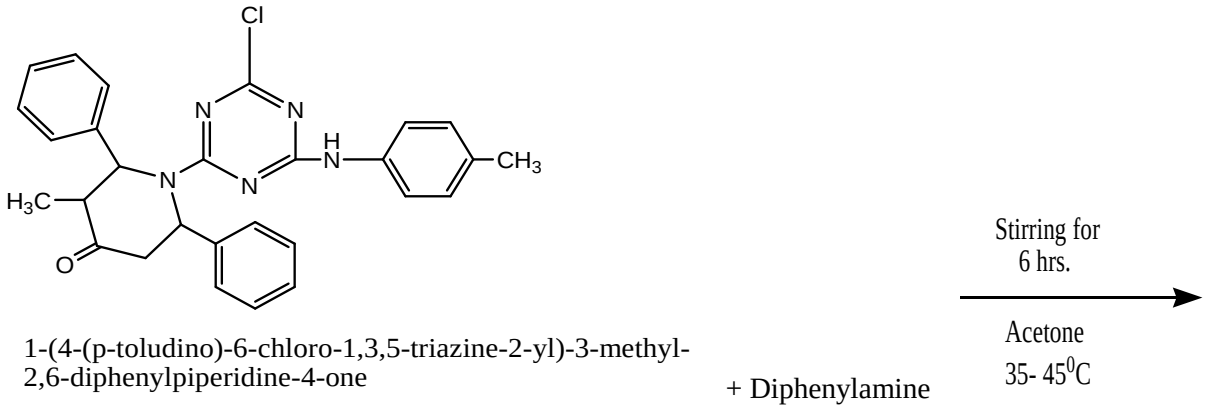
4,6-dichloro-N-p-tolyl-1,3,5-triazine-2-amine

3-methyl-2,6-diphenylpiperidin-4-one

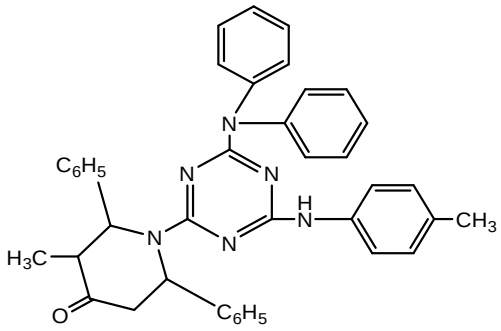
1-(4-(p-toludino)-6-chloro-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one

1-(4-(p-toludino)-6-chloro-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one has been prepared by treating 4,6-dichloro-N-p-tolyl-1,3,5-triazine-2-amine in acetone with 3-methyl-2,6-diphenylpiperidine-4-one.

Step 3: Synthesis of 1-(4-p-toluidino)-6-(diphenylamino)-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one.



1-(4-(p-toludino)-6-chloro-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one + Diphenylamine



1-(4-(*p*-toluidino)-6-(diphenylamino)-1,3,5-triazin-2-yl)-3-methyl-2,6-diphenylpiperidin-4-one

Compound -2 (1-(4-(p-toluidino)-6-chloro-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one) (0.01 mole) was dissolved in acetone (50 ml) then it was added to Diphenylamine (0.01 mole) in acetone (50 ml) and contents are to be stirred for 3 hours at 85-90°C poured in to ice water and neutralized with sodium carbonate solution to get the product. Then it was filtered, washed, dried, and recrystallized from ethanol.

Physical charecterization:

- ✓ Molecular formula : $C_{40}H_{36}N_6O$
- ✓ Molecular weight (gm) : 616.75
- ✓ Soluble in Methanol, Ethanol, DMSO and DMF.
- ✓ Melting point : 205ºC
- ✓ Melting points were determined using Veego Digital melting point apparatus.
- ✓ The purity of synthesis compound was monitored on TLC.
- ✓ Absorbent used : Precoated Silica gel- G plate
- ✓ Mobile Phase : Chloroform : Methnol (3:7)
- ✓ R_f value: 0.71

Biological screening

Antibacterial activity

The synthesized compounds were screened for *invitro* antimicrobial activity by Turbidimetric method. This method was used for determining the selective effectiveness of the antibacterial activity. The standard antibiotic selected for study of the antibacterial activity was ciprofloxacin. The activity was compared with standard ciprofloxacin drug.

Material Used

Nutrient broth, Sterile borosil boiling test tube, Sterile test tube, Sterile pipettes and Sterile cotton swabs.

Bacteria

In the present study the following bacteria were used.

A. *Escherichia coli* (Gram – ve)
B. *Bacillus subtillus* (Gram + ve)
C. *Staphylococcus aureus* (Gram + ve)

Antifungal activity

Turbidometric method by using Sabouraund dextrose broth

The synthesized compounds were screened for *invitro* antimicrobial activity by Turbidimetric method. This method was used for determining the selective effectiveness of the antifungal activity. The standard antibiotic selected for study of the antifungal activity was ketoconazole. The activity was compared with standard ciprofloxacin drug.

Material Used

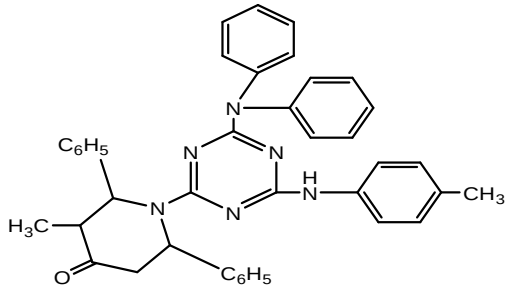
Sabouraud dextrose broth, sterile borosil boiling test tube, Sterile test tube, Sterile pipettes and Sterile cotton swabs.

Fungal

In the percent study the following fungi were used.

- *Aspergillus niger*

Spectral analysis



IUPAC Name:

1-(4-(*p*-toluidino)-6-(diphenylamino)-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one

IR Interpretation

I.R. Spectral data (KBr discs) (in Cm^{-1})	
N-H str.	3382.58
C=N str.	1566.58
=C-H str.	3172.33
C=O str.	1722.67
C-N str.	1344.02
=C-H bending	1510.28

^{1}HNMR Interpretation

^{1}HNMR Spectral data Absorption position (in PPM)	
6.34 - 7.2	m, 24H, ArH
4.0	s, 1H, NH
2.35	s, 3H, CH_3
4.12	d, 1H, CH
4.13	t, 1H, CH
3.14	q, 1H, CH
3.10, 2.85	d, 2H, CH_2
1.16	d, 3H, CH_3

Results and discussion

Synthesis

The present study report the Synthesis of 1, 3, 5-Triazine derivatives. Nucleophilic substitution of Chloro group in Cyanuricchloride was carried out stepwise at different temperature by various amines. The first step involve the substitution of p-methylaniline and the next by 3-methyl-2,6-diphenyl piperidine-4-one. The final chloro group in the synthesized compound-2 was replaced by Diphenylamine. Since the report regarding this compound suggest a good bioactive moiety.

Physical Characterization

Melting point of the synthesize compound was taken in open capillary tubes and was uncorrected and were found to be in the range of 180-240°C.

TLC was performed using precoated silica gel plates of 0.25mm thickness. Eluents used were Chloroform, Methanol (3:7). Spots were visualized in U.V. light.

At room temperature solubility of newly synthesize compound were determined by various organic solvents and it was found that compound were freely soluble in DMSO, DMF, Methanol and Ethanol.

Anti-bacterial activity

The table shows the 250 µg/ml concentration having good antibacterial activity and equal to ciprofloxacin 100 µg/ml compare to other concentration. The compound most effective against gram^{-ve} microorganism compare to gram^{+ve}.

Sample	Bacteria	Concentration	% inhoibition of growth
Control	*Escherichia coli, Bacillus subtillus, Staphylococcus aureus*	------	0
1-(4-p-toludino)-6-(diphenylamino)-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one.	*Escherichia coli*	50 µg/ml	34.24
		100 µg/ml	47.39
		150 µg/ml	63.69
		200 µg/ml	69.31
		250 µg/ml	91.36
1-(4-p-toludino)-6-(diphenylamino)-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one.	*Bacillus subtillus*	50 µg/ml	33.28
		100 µg/ml	33.83
		150 µg/ml	46.57
		200 µg/ml	55.61
		250 µg/ml	62.32
1-(4-p-toludino)-6-	*Staphylococcus aureus*	50 µg/ml	24.65

(diphenylamino)-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one.		100 µg/ml	31.25
		150 µg/ml	45.65
		200 µg/ml	56.42
		250 µg/ml	61.24
Ciprofloxacin	*Escherichia coli*	100 µg/ml	82.35
Ciprofloxacin	*Bacillus subtillus*	100 µg/ml	65.47
Ciprofloxacin	*Staphylococcus aureus*	100 µg/ml	68.91

Anti-fungal activity

The below table revealed that activity increase with concentration

Sample	**Bacteria**	**Concentration**	**% inhoibition of growth**
Control	*Aspergillus niger*	------	0
1-(4-p-toludino)-6-(diphenylamino)-1,3,5-triazine-2-yl)-3-methyl-2,6-diphenylpiperidine-4-one.	*Aspergillus niger*	50 µg/ml	18.13
		100 µg/ml	23.46
		150 µg/ml	32.00
		200 µg/ml	39.72
		250 µg/ml	51.56
Ketaconazole	*Aspergillus niger*	100 µg/ml	82.67

Conclusion

In the present study we concluded that the triazine derivative of synthesized compound having good anti-bacterial activity then the antifungal and most effective against gram^{-ve} bacteria.

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