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Synthesis of Some Acridin-9-Yl-Aryl-Thiourea and their Antimicrobial Study

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Abstract

As a part of systematic investigation, synthesis and antimicrobial activity some acridine derivatives have been achieved by using N-aryl-isothiocynatewhich on condensation with 9-aminoacridine hydrochloride afforded 1-acridin-9-yl-3-aryl-thioureas. Constitutions of synthesized compounds have been delineated on the basis of IR and ^{1}H-NMR spectral studies. The title compounds were found to be sufficient activity when screened for their antimicrobial activity against the microorganisms like S. typhi, E. coli, and S. aureus.

Keywords: Acridine, 1-acridin-9-yl-3-aryl-thiourea, antimicrobial activity.

Introduction

Acridine is heterocyclic nucleus containing nitrogen have been under investigation for a long time because of their important properties. It plays an important role in various medicines because of found to possess wide biological activity. Acridine and its derivatives are characterised by blue or green fluorescence showed by solution of its salts[1]. Antimicrobial property of acridine and its derivative was discovered by Ehrlich and Benda in 1917 [2]. The acridinyl derivatives such as 1-acridin-9yl-3-aryl thiourea[3], synthesis, structural properties and antimicrobial activities have been reported earlier. The literature survey revealed that the acridine derivatives have been found to possess potent anti-tumour[4], anti-tuberculosis[5], anti-hilmintics[6] and anti-cancer[7] properties. New method is been reported in view of utility of N-aryl isothiocynatein the synthesis of 1-acridin-9-yl-3-aryl-thiourea by using microwave radiation[8].

Materials and Methods

The melting points of all synthesized compounds were determine on Thieles tube apparatus using paraffin oil bath and were uncorrected. The structures of synthesized compounds were elucidated on the basis of elemental analysis, IR and ^{1}H-NMR spectral studies. IR spectra recorded on Perkin-Elmer spectrophotometer in the range 4000-400cm^{-1} in nujol hydrocarbon. ^{1}H-NMR, spectra were recorded with TMS as internal standard using DMSO-d^6 as solvents. Microwave oven GMG20E 08 SLGX used, Purity of the compounds checked on silica gel-G plates by TLC.

***Preparation of phenyl isothiocynate* (3a)**:

The phenyl isothiacynate**(3a)** was prepared by treatment of freezing mixture of ammonia and carbon disulphide (0.1M) in a round bottom flask, in this stirring mixture run aniline **(1a)** (0.1M) and stirr for further 30 min. A heavy precipitate of ammonium phenyl dithiocarbamate**(2a)** separates out as salt. Transfer this salt to R. B. Flask containing 100 ml solution of lead nitrate, lead sulphite is precipitates. On steam distillation of this mixture into a receiver containing 0.5M H_2SO_4 separates the oil, dry it over anhydrous calcium chloride and collect as a phenyl isothiocynates**(3a)**. This reaction was extended to synthesize other substituted aryl isothiocynate**(3b-g)** using substituted aryl amine **(1b-g)** by reported method.

***Preparation of 1-acridin-9-yl-3-phenyl thiourea* (4a)**:

1-acridin-9-yl-3-phenyl thiourea (4a) has been prepared by condensation of9-aminoacridine hydrochloride with phenyl isothiocynate**(3a)** in a basic medium under microwave radiation for 2min. in solvent free condition. The reaction was successful in terms of yield and was completed within 2 min. afforded 1-acridin-9-yl-3-aryl-thiourea. It was crystallized from ethanol and identified as a 1-acridin-9-yl-3-phenyl thiourea **(4a).**

Table 1. Analytical data of MW assisted synthesis of 1-acridin-9-yl-3-aryl thiourea **(4a)**

Entry	R	Mol. formula	Mol. wt.	Yield
4a	C_6H_5-	$C_{20}H_{15}N_3S$	329	76%
4b	*o*-H_3C-C_6H_4-	$C_{21}H_{17}N_3S$	343	70%
4c	*m*- H_3C-C_6H_4-	$C_{21}H_{17}N_3S$	343	72%
4d	*p*- H_3C-C_6H_4-	$C_{21}H_{17}N_3S$	343	64%
4e	*o*-Cl-C_6H_4-	$C_{20}H_{14}N_3SCl$	363	80%
4f	*m*-Cl-C_6H_4-	$C_{20}H_{14}N_3SCl$	363	74%
4g	*p*-Cl- C_6H_4-	$C_{20}H_{14}N_3SCl$	363	72%

Preparation of 1-acridin-9yl-3-phenyl-thiourea

(**4a**): IR (KBr): 1550, 1342, 758, 483 cm^{-1} ;^{1}H-NMR ($CDCl_3$) : δ 7.14-7.46 (10H, m); Anal. Calcd. : C, 74.12; N, 12.92; S, 9.14. Found: C, 72.12; N, 12.76; S, 9.1

Preparation of 1-acridin-9yl-3-(2-methyl-phenyl)-thiourea

(**4b**): IR (KBr) : 1538, 1332, 763, 458 cm^{-1}; ^{1}H-NMR ($CDCl_3$) : δ 6.90-7.39 (9H, m), 2.32 (3H, s); Anal. Calcd. : C, 74.58; N, 12.86; S, 9.94. Found: C, 73; N, 12.68; S, 9.3.

Preparation of 1-acridin-9yl-3-(3-methyl-phenyl)-thiourea

(**4c**): IR (KBr) : 1550, 1338, 755, 470 cm^{-1}; ^{1}H-NMR ($CDCl_3$) : δ 6.98-7.40 (9H, m), 2.38 (3H, s); Anal. Calcd. : C, 74.58; N, 12.86; S, 9.94. Found: C, 73; N, 12.68; S, 9.3.

Preparation of 1-acridin-9yl-3-(4-methyl-phenyl)-thiourea

(**4d**): IR (KBr) : 1533, 1332, 760, 458 cm^{-1}; ^{1}H-NMR ($CDCl_3$) : δ 7.12-7.39 (9H, m), 2.29 (3H, s); Anal. Calcd. : C, 74.58; N, 12.86; S, 9.94. Found: C, 73; N, 12.68; S, 9.3.

Preparation of 1-acridin-9yl-3(2-chloro-phenyl)-thiourea

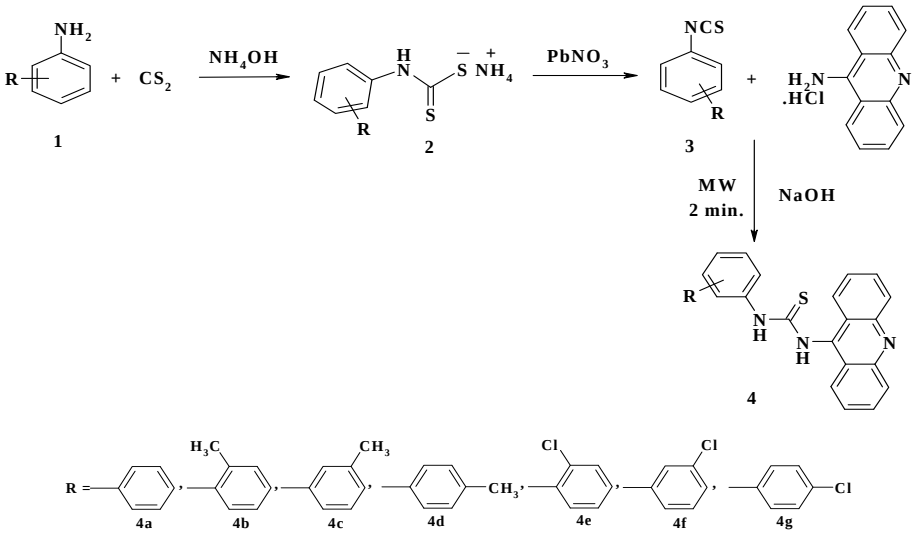
(**4e**): IR (KBr) : 1550, 1338, 764, 483 cm^{-1}; ^{1}H-NMR ($CDCl_3$) : δ 7.22-7.46 (9H, m); Anal. Calcd. : C, 69.32; N, 11.29; S, 10.90. Found: C, 66.32; N, 11.18; S, 9.6.

Preparation of 1-acridin-9yl-3-(3-chloro-phenyl)-thiourea

(**4f**): IR (KBr) : 1554, 1358, 751, 480 cm^{-1}; ^{1}H-NMR ($CDCl_3$) : δ 7.14-7.46 (9H, m); Anal. Calcd. : C, 69.32; N, 11.29; S, 10.90. Found: C, 66.32; N, 11.18; S, 9.6.

Preparation of 1-acridin-9yl-(4-chloro-phenyl)l-thiourea

(**4g**): IR (KBr) : 1550, 1340, 758, 483 cm^{-1}; ^{1}H-NMR ($CDCl_3$) : δ 7.22-7.46 (9H, m); Anal. Calcd. : C, 69.32; N, 11.29; S, 10.90. Found: C, 66.32; N, 11.18; S, 9.6.



Antimicrobial screening

The antimicrobial activities of all the synthesized compounds **(4a-g)** were performed using Kirby- Bauer method[10,11] against microorganisms like *S. typhi, E. coli* and *S. aureus.* The each well (diameter 10 mm) was loaded with 0.1 mL^{-1} of test compound solution in dimethyl sulphoxide, so that concentration of each test compound was 100µg mL^{-1}. The zones of inhibition of the compounds were recorded in mm after incubation for 24 h at 37^0Cclearly indicated that **(4e)** and **(4g)** were highly active against *E. coli* and moderately active against *S. aureus.* Majority of the compounds were found moderately active against *S. typhi*.

Table 2. Antimicrobial screening results of compounds **(4a-g)** with conc.100 mμ/ml

Microorganism	**4a**	**4b**	**4c**	**4d**	**4e**	**4f**	**4g**	**Chloramphenicol**
***S.typhi*(mm)**	21	19	17	17	20	17	19	19
***E. coli* (mm)**	19	18	17	18	20	19	21	22
***S. aureus*(mm)** 20	18	20	18	17	18	20	21	

Results and Discussion

Aryl isothiacynate[9] was prepared by running aryl amine (0.1M) in freezing mixture of ammonia and carbon disulphide (0.1M), stirred for further 30 min. A heavy precipitate of ammonium aryl dithiocarbamate separated transfer to a solution of lead nitrate, lead sulphite is precipitates. On steam distillation of this mixture into a receiver containing 0.5M H_2SO_4, oil separated from this mixture, dry over anhydrous calcium chloride and collect as an aryl isothiocynateswhich on condensation with 9-aminoacridine hydrochloride in a basic medium under microwave radiation for 2min. afforded 1-acridin-9-yl-3-aryl-thiourea. The bacterial organisms used were *S. typhi, E. coli*and *S. aureus*. Inhibition zone record of the compounds indicated that **(4e)** and **(4g)** were highly active against *E. coli* and moderately active against *S. aureus*.

Conclusion

The reported method is favourable to preserve the protocols of the green chemistry. We have been attempted the synthesis of 1-acridin-9-yl-3-aryl-thiourea and their antimicrobial study by using microwave energy without solvent andheating assembly with improved yield.

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