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NOTE

Synthesis and Antimicrobial Activity of 1-(9′-Acridinyl)-5-(4-Substituted Phenyl) Tetrazoles

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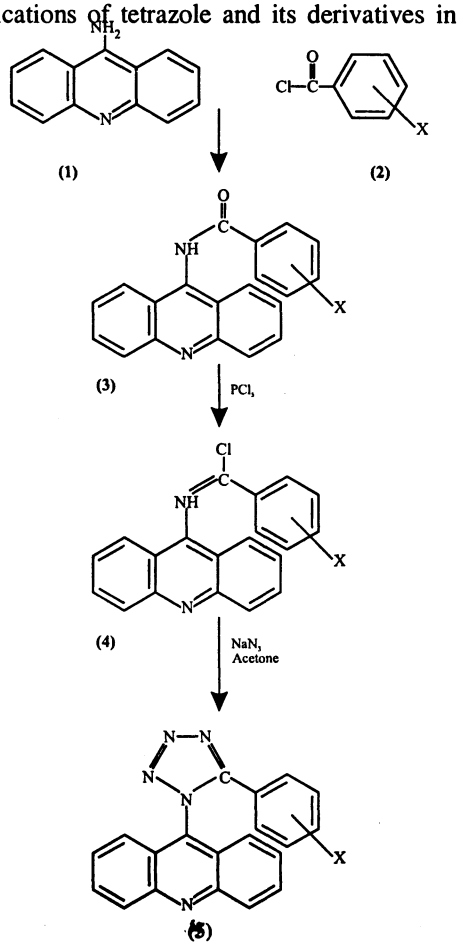
This paper reports the synthesis and antimicrobial activity of some 1-(9′-acridinyl)-5-(4-substituted phenyl) tetrazoles.

Key Words: Substituted tetrazoles, Antimicrobial activity.

Owing to the vast and wide applications of tetrazole and its derivatives in industries and industrial operations, and in the field of pharmacology as antiallergic, antifungal, antihypertensive, anti-inflammatory, herbicidal, central nervous system stimulant and photofog inhibitory substances, the advancement and development in the field of tetrazole chemistry by scientists in different fields including chemistry, pharmacology and medicine. Wittenberger[1] has published an article to focus recent progress in the syntheses and reactions of tetrazole and its derivatives. The syntheses and activity of the tetrazole-containing cephalosporin have been reported by Jung[2]. Yoshida and co-workers[3, 4] have found monocyclic β-lactams containing tetrazolyl moiety at N-1 as potential bactericidal agents. A similar study has also been made by Xiaoming and co-workers[5, 6]. Though there are a large number of references for the synthesis of biologically active tetrazoles, only very little work on record is found concerning the synthesis of tetrazole compounds carrying an acridine group, which is also a well known biologically active substance.



Scheme-1 (For **X** see Table-1)

In the present investigation, it is aimed at synthesizing some novel tetrazole derivatives containing acridine ring with a view to evaluate their antimicrobial activity. **Scheme-1** was proposed to synthesize novel tetrazole derivatives.

All melting points were uncorrected. The purity of the compounds was checked by TLC.

All the synthesized compounds were characterized by their physical and analytical data (Table-1).

Compound	X	m.p. (°C)	Yield (%)	m.f.	m.w.	Found(Calcd.)%		
						C	H	N
5a	-H	240	63	$C_{20}H_{13}N_5$	323	74.06 (74.30)	3.99 (4.02)	20.98 (21.67)
5b	*p*-CH_2	290	68	$C_{21}H_{15}N_5$	342	74.51 (74.78)	4.39 (4.45)	20.12 (20.77)
5c	*p*-CH_3	215	71	$C_{21}H_{15}N_5$	342	77.21 (77.06)	4.42 (4.59)	18.30 (18.35)
5d	*p*-NH_2	260	69	$C_{20}H_{14}N_6$	338	70.97 (71.01)	4.02 (4.14)	24.90 (24.85)
5e	*p*-Cl	176	67	$C_{20}H_{12}ClN_5$	357.5	66.89 (67.13)	3.41 (3.36)	19.75 (19.58)
5f	*p*-OH	189	72	$C_{20}H_{13}N_5O$	339	70.76 (70.80)	3.70 (3.83)	20.81 (20.65)
5g	*p*-OCH_3	265	70	$C_{21}H_{15}N_5O$	358	71.02 (71.39)	4.04 (4.25)	19.78 (19.83)
5h	*p*-NO_2	220	69	$C_{20}H_{12}N_5O_2$	354	69.61 (69.77)	3.52 (3.49)	17.58 (17.44)
5i	-3,4-dinitro	245	63	$C_{20}H_{11}N_7O_4$	399	57.98 (58.11)	2.59 (2.66)	23.08 (23.73)
5j	*o*-Cl	186	62	$C_{20}H_{12}ClN_5$	357.5	66.89 (67.13)	3.41 (3.36)	19.75 (19.58)

Preparation of 9-aminoacridine: Albert and Ritchie[7] procedure was followed to synthesize 9-aminoacridine (**1**).

Preparation of acid chlorides: Various acid chlorides (**2**), such as benzoyl chloride, phenylacetyl chloride, 4-methylbenzoyl chloride, 4-aminobenzoyl chloride, 4-chlorobenzoyl chloride, 4-hydroxybenzoyl chloride, 4-methoxybenzoyl chloride, 4-nitrobenzoyl chloride, 3,5-dinitrobenzoyl chloride, 2-chlorobenzoyl chloride were prepared using the standard procedure.

General procedure for the preparation of amides

A known weight (0.02 mol) of acid chloride was added to a round-bottomed flask, containing a known volume (10 cm^3) of dry benzene. A known weight (0.02 mol) of 9-aminoacridine was added in small quantities at a time to the mixture with efficient hand shaking. The mixture was refluxed on a water bath for about

4 h. After cooling, it was diluted with water. The crude amide (**3**) was found and separated out. It was recrystallized from aqueous ethanol.

General procedure for the synthesis of 1-(9′-acridinyl)-5-substituted phenyl tetrazoles (5): A known weight of amide (**3**) was taken in a beaker and to it, a known weight (0.01 mol) of phosphorus pentachloride was added. The mixture was heated at 100°C until the evolution of hydrogen chloride fumes ceased. The reaction mixture was found to contain some unreacted phosphoryl chloride which was removed by distillation under reduced pressure. The resulting imidoyl chloride (**4**) was treated with an ice-cold solution, containing a known weight (0.02 mol) of sodium azide, a known volume (40 cm^3) of saturated sodium acetate solution and a known volume (60 cm^3) of acetone with constant stirring in sequence. The resulting reaction mixture was kept stirred overnight. Acetone was removed by distillation under reduced pressure. The residue was extracted with chloroform. After drying, the chloroform extract was concentrated to obtain the tetrazole (**5**). The separated crude product was recrystallized from a mixture of benzene and petroleum ether.

Antimicrobial activity: The tetrazole derivatives, *viz.*, 1-(9′-acridinyl)-5-(4-chlorophenyl)tetrazole (**5e**), 1-(9′-acridinyl)-5-(4-hydroxyphenyl)tetrazole (**5f**) and 1-(9′-acridinyl)-5-(4-methoxyphenyl)tetrazole **5g** were tested against micro-organisms, namely, *Escherichia coli, Salmonella spp., Staphylococcus aureus, Pseudomonas aeruginosa* and yeast using pour plate method. The results of the study show the absence of any viable count indicating higher antimicrobial activity of these compounds.

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REFERENCES

1. S.J. Wittenberger, *Organic Preparations and Procedures Int.*, **26**, 499 (1994).
2. F.H. Jung, EP 447118 A2 (18 Sep 1991); *Chem. Abstr.*, **116**, 6339C (1992).
3. C.Yoshida, K.Tanaka, R. Hattori, Y. Fukuoka, M. Komatsu, S. Kishimoto and I. Saikawa, *J. Antibiot.*,, **9**, 215 (1986).
4. C.Yoshida, K. Tanaka, Y. Todo, R. Hattori, Y. Fukuoka, M. Komatsu and Saikawa, *J. Antibiot.*, **39**, 90 (1986).
5. F. Xiaoming, C. Rong and C. Shaoyin, *Org. Prep. Proced. Int.*, **24**, 492 (1992).
6. F. Xiaoming and C. Rong, *Chem. Res. Chin. Uni.*, **8**, 315 (1992); *Chem. Abstr.*, **119**, 8746u (1993).
7. A. Albert and B. Ritchie, *Org. Synthesis*, 5 (1942).

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