

NOTE**Synthesis of Some 'N' Bridgehead Heterocycles Containing Quinoxaline and 1,2,4-Triazole and Their Antifungal and Antitubercular Activity**

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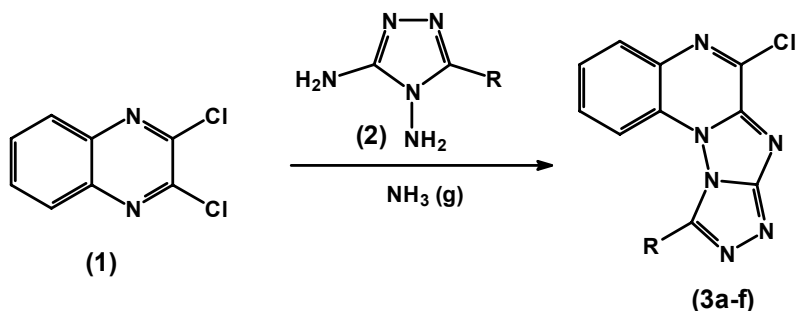
2,3-Dichloroquinoxaline reacted with 5-substituted 3,4-diaminotriazole afforded 3-substituted quinoxalino(2,1b)-1,2,4-triazolo(5,1c)-5-substituted-1,2,4-triazole. The structures were supported by spectral studies and evaluated for their antifungal and antitubercular activities.

Key Words: Quinoxaline, Triazole, Antitubercular.

Literature studies reveal that both quinoxaline¹ and triazole² cores possess similar biological activities like antibacterial, antifungal and antitubercular activities. In connection with other observation regarding the antimicrobial potency of 'N' bridgehead heterocycles, the present work has been undertaken on synthesis of the same, containing both quinoxaline and 1,2,4-triazole and to perform their antimicrobial screening for their antifungal and antitubercular activities. Both 2,3-dichloroquinoxaline³ (**1**) and 5-substituted 1,2,4-triazole (**2**) were synthesized as reported method⁴. Compounds **1** and **2** were subjected to fusion reaction to yield 3-substituted quinoxalino(2,1b)-1,2,4-triazolo-(5,1c)-5-substituted-1,2,4-triazole (**3a-f**) (**Scheme-I**). All the synthesized compounds shown bathochromic shift on λ_{\max} determination that confirms the cyclization and increased conjugation. Further, it was supported by absence of -NH₂ stretching band (3467 cm⁻¹) at IR spectra of **3a-f**.

Melting points were determined by open capillary method. The purity was confirmed by appearance of single spot on TLC. Benzene and acetone at the ratio of 3:1 was used as irrigant. IR spectra (KBr, cm⁻¹) were recorded on Shimadzu IR-460 spectrophotometer. ¹H NMR spectra were recorded using TMS as internal standard and measured in δ ppm.

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Scheme-I

General procedure for the synthesis of 3-chloroquinoxalino(2,1b)-1,2,4-triazolo(5,1c)-5-substituted-1,2,4-triazole (3a-f): 2,3-Dichloroquinoxaline (1) (0.02 mol) and 5-substituted 3,4-diamino-1,2,4-triazole (2) (0.02 mol) in DMF was refluxed at 150 °C for 6-8 h, until the evolution of ammonia get ceased. The resultant reaction mixture was cooled and kept under refrigeration for overnight. The formed crystals were filtered and recrystallized from ethanol.

3a: 3-Chloroquinoxalino(2,1b)-1,2,4-triazole (5,1c)-5-methyl-1,2,4-triazole, m.p. 142 °C, yield: 74 %, λ_{max} : 337 nm, R_f : 0.9. IR (KBr, ν_{max} , cm^{-1}); 3105, 3039 (C-H), 1617 (C=N), 1559 (C=C), 990 (C-Cl), 767 (C-H out of plane deformation). ^1H NMR (δ ppm); 3.2 (3H, s, -CH₃), 7.2-7.8 (4H, m, Ar-H). Mass (EI); 258 (M^+ , 20 %), 57 (base peak, 100 %).

Antimicrobial activity: All the compounds (3a-f) were subjected to antifungal and antitubercular screening by agar plate disc diffusion method⁵ and Microplate alamar blue assay (MABA)⁶, respectively. *Aspergillus niger* and *Mycobacterium tuberculosis* H₃₇Rv were used for antifungal and antitubercular screening, respectively. At 100 $\mu\text{g}/\text{disc}$ concentration, the compound 3c (23 mm zone of inhibition) and compound 3d (21 mm zone of inhibition) were found to shown comparable antifungal activity that of standard clotrimazole. Among the series, the compound 3c found to exhibit 77 % inhibition followed by compound 3f with 72 % inhibition against *Mycobacterium tuberculosis* H₃₇Rv while rest of the compounds were found to exhibit % inhibition in between 47-53 (Table-1).

The results revealed that 2-chloro phenyl substitution at N-bridgehead triazolo quinoxaline system increases the antimicrobial spectrum towards both antifungal and antitubercular activity. The benzene sulfonic acid substitution enhances the activity in antitubercular spectrum but not with antifungal spectrum.

TABLE-1
RESULTS OF ANTIMICROBIAL ACTIVITY

Compd.	R	<i>A. niger</i> (100 µg/disc)	<i>M. tuberculosis</i> H ₃₇ Rv (6.25 µg/mL)
3a	-CH ₃	14	48
3b	-C ₆ H ₅	13	47
3c	-2(Cl)-C ₆ H ₄	23	77
3d	-4(NH ₂)-C ₆ H ₄	16	52
3e	-2(OH)-C ₆ H ₄	18	53
3f	-2(OH)-5(SO ₃ H)C ₆ H ₃	17	72
Clotrimazole	-	25	-

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