

Antifungal activity of bicyclic heterocyclic-1,2-diazole

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Received 6 July 1999; revised 6 December 1999

A novel series of heterocyclic-1,2 diazole namely N¹-iso nicotinoyl-5, 5'- dimethyl cyclohexane -4-(sulpha/ substituted phenylazo) -1,2- diazoles have been synthesized. The compounds were screened for the anti-fungal properties against building fungi. The fungal species used for this purpose were *Aspergillus niger* and *Pencillium frequentans*. It was found that out of a series of 25 compounds, fourteen have shown significant fungicidal properties against both the above species. Minimum inhibition concentration was observed between 100 and 200 ppm for most of the compounds.

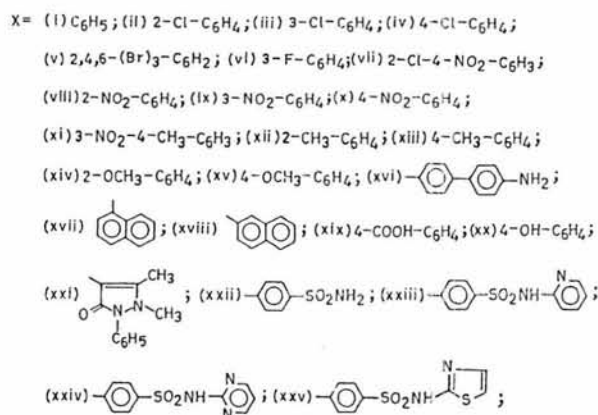
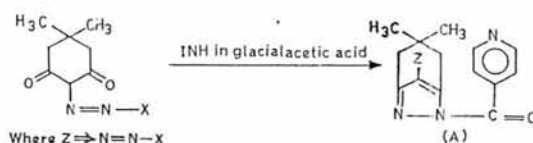
Fungi are highly diverse and versatile organisms adapted to all kinds of environments. A few species of fungi are pathogenic and produce diseases in all living beings. Some fungi occupy very specialized ecological niches, within buildings. They disfigure the buildings and may even damage to its structure and materials¹. They may also affect the health of occupants. In the mouldy buildings volatile metabolites produced by fungi are responsible for the musty odour. Due to their inhalation a range of symptoms of ill health are produced². These include headache, eye, nose and throat irritation, nausea fatigue and respiratory infection³. If *Aspergillus* grow in body cavities they may produce fungus ball of aspergilloma, causing tuberculosis⁴. A systematic research work is started in these laboratories to identify the fungal spp. of the buildings and to control them with safer methods⁵.

Organic compounds containing at least one heterocyclic atom in the ring are known as heterocyclic compounds. One of their important member diazole and its derivatives are extensively used as pesticides⁶⁻⁸. As reported in literature they found to have very good fungicidal properties also^{9,11}. A novel series of bicyclic heterocyclic -1,2-diazole namely N¹-iso nicotinoyl-5,5'- dimethyl cyclohexane -4-(sulpha/ substituted phenylazo) -1,2- diazoles have been synthesized (Scheme-I) and studied for their termiticidal activity¹². The present paper deals with the study of these compounds for their fungicidal activity against *Aspergillus niger* and *Pencillium frequentans*.

The synthesized compounds were tested for fungus resistance as per method reported in American Society for Testing & Materials Standards (1962-6)¹³.

However, the minimum inhibition concentration (MIC) was determined by taking six concentrations of each synthesized compound, viz. 50, 100, 200, 300, 400 and 500 ppm for the study. Each concentration was taken in sterilized culture medium and inoculated it for 48 hr. with *Aspergillus niger* and *Pencillium frequentans* separately. The diameter of every fungal colony was measured. The minimum concentration showing complete inhibition of the tested fungal spp was taken as minimum inhibition concentration (MIC). The results are recorded in Table 1.

As shown in Table 1, the growth of *Aspergillus niger* was appeared upto only 50 ppm concentration in case of compounds V, VIII, XII, XV, XVIII, XX and XXI. The growth was appeared 7 mm in case of compound XXI, while in case of compound VIII the growth of *Aspergillus niger* was 27 mm. In all other compounds the growth was between 7-27 mm. There



was no growth at 100 ppm of this fungal species in all the above compounds. Therefore, MIC of the above compounds is 100 ppm.

Compounds I, VI, VII, IX, XI, XIV, XVI, XVII and XXII gave growth *Aspergillus niger* up to only 100 ppm concentration. The growth in case of compound XXII at 50 ppm was 9 mm, while it reduced 2 mm at 100 ppm. In case of compound VII the growth of *Aspergillus niger* at 50 ppm was 30 mm while at 100 ppm it was 20 mm. In all the compounds the growth of fungal spp. was between 2-20 mm. In all the above compounds there was no growth of *Aspergillus niger* at 200 ppm, therefore, MIC of the above compounds is 200 ppm.

As shown in Table 1, the growth of *Penicillium frequentans* was appeared upto only 50 ppm

concentration in case of compounds V, VIII, X, XI, XIV, XVIII and XX. The growth was appeared 4 mm in case of compound XVIII, while in case of compound VIII the growth was 21 mm. In all other compounds the growth was between 4 - 21 mm. There was no growth at 100 ppm of this fungal species, hence MIC of the above compounds is 100 ppm.

Compound I, VI, IX, XV, XVI, XVII, XIX, XXI, XXII, XXIII and XXIV gave growth of *Penicillium frequentans* up to only 100 ppm dilution. The growth in case of compound XXII at 50 ppm was 5 mm while it reduced to 2 mm at 100 ppm whereas for the compound XIX the growth of *Penicillium frequentans* at 50 ppm was 19 mm while at 100 ppm it was 13 mm. In all the compounds the growth of fungal spp. was between 2-13 mm. There was no growth of

Table-1—Antifungal activity of N¹-Isonicotinoyl-5,5'-Dimethyl Cyclohexane-4-(z)-1,2-Diazole

S.No.	Substituted Group (X)	Diameter of fungus growth (mm) at various dilution (ppm)											
		<i>Aspergillus niger</i>						<i>Penicillium frequentans</i>					
		50	100	200	300	400	500	50	100	200	300	400	500
	Solvent	41	34	27	15			41	34	27	15		
I	Phenyl	18	12	x				15	10	x			
II	2-Chlorophenyl	31	28	20	8			22	16	12	6		
III	3-Chlorophenyl	28	20	15	5			14	9	5	x		
IV	4-Chlorophenyl	38	30	20	x			25	20	14	x		
V	2,4,6-Tribromophenyl	18	x					10	x				
VI	3-Fluorophenyl	15	8	x				9	4	x			
VII	2-Chloro-4-Nitrophenyl	30	20	x				16	11	7	x		
VIII	2-Nitrophenyl	27	x					21	x				
IX	3-Nitrophenyl	32	12	x				26	10	x			
X	4-Nitrophenyl	22	14	7	x			18	x				
XI	3-Nitro-4-Methylphenyl	18	4	x				10	x				
XII	2-Methylphenyl	15	x					20	11	3	x		
XIII	4-Methylphenyl	30	18	12	6			32	16	10	x		
XIV	2-Methoxyphenyl	13	5	x				10	x				
XV	4-Methoxyphenyl	11	x					16	12	x			
XVI	4-Aminodiphenyl	16	12	x				9	3	x			
XVII	1-Naphthylamine	14	4	x				11	5	x			
XVIII	2-Naphthylamine	10	x					4	x				
XIX	4-Carboxyphenyl	19	15	6	x			19	13	x			
XX	4-Hydroxyphenyl	12	x					9	x				
XXI	2,3 -dimethyl-1-phenyl pyrazolone	7	x					10	4	x			
XXII	2-Sulphonamidobenzene	9	2	x				5	2	x			
XXIII	N ¹ -2-pyridylsulphonamido benzene	19	13	6	3			15	10	x			
XXIV	N ¹ -2-pyrimidylsulphonamido benzene	22	10	6	x			10	5	x			
XXV	N ¹ -2-Thiazolyl sulphonamido benzene	25	14	9	5			17	10	4	2		

Penicillium frequentans at 200 ppm in all the above compounds. Therefore, MIC of the above compounds is 200 ppm.

The foregoing discussion concludes that bicyclic heterocyclic-1,2 diazoles synthesized and reported earlier have potential fungicidal properties. In the series of 25 such compounds studied compound I, V, VI, VIII, VIX, XI, XIV, XV, XVI, XVII, XVIII, XX, XXI, and XXII have shown promising anti-fungal properties on *Aspergillus niger* and *Pencillium frequentans*. Compounds V, VIII, XVIII, and XX have shown activity at 100 ppm while compounds I, VI, IX, XVI, XVII, and XXII have shown at 200 ppm. However, the XI, XIX, XV and XXI are active at 300 ppm.

The authors are grateful to Prof. R.N. Iyengar, Director, Central Building Research Institute, Roorkee for his constant encouragement and paper is published with his kind permission.

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