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Studies in Organic Fluorine Compounds Part I. Synthesis of Some N-Substituted Fluorobenzamides as Potential Fungicides Ashok K. Srivastava^a & Suresh C. Bahel^a ^a Chemistry Department, University of Gorakhpur, Gorakhpur (U.P.), India Published online: 09 Sep 2014.

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Studies in Organic Fluorine Compounds Part I. Synthesis of Some N-Substituted Fluorobenzamides as Potential Fungicides

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vaecides and rodenticides. The effective part of the molecule was found to be the CH₂F group.³⁾ The introduction of fluorine and other halogens in the aromatic nucleus also confers fungicidal activity⁴⁾ on the unsubstituted aromatic compounds.

Studies on the halogenated amides made by Mitchell⁵ have revealed that the biological activity could be attributed both to the presence of an amide group in the side chain of the aromatic nucleus and the position and degree of halogenation in the benzene nucleus.

These views have been supplemented by the studies made on the amides of fluorophenoxy acids^{6,8)} and N-

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Saunders¹⁾ and Bergmann *et al.*²⁾ have extensively investigated substituted fluoroacetamides of the type FCH₂CONHR as contact insecticides, potential larsubstituted fluorobenzamides.^{7,8} Johnson *et al.*⁹ have reported N,N-dialkyl and aminoalkyl benzamides as topical mosquito repellents.

Keeping these observations in view we have synthesised, as possible fungicides, N-substituted fluorobenzamides¹⁰ from *m*-fluorobenzoic acid, 4-fluoro-3-

TABLE I. AMIDES OF FLUOROBENZOIC ACIDS

$\begin{array}{c} R_2 \longrightarrow -C - N - R \\ U & H \\ R_1 \end{array}$								
S. No.	R	R ₁ R	D	mp/bp °C	Yield %	Molecular formula	% N	
			\mathbf{K}_2				Found	Calcd.
1	<i>n</i> -Butyl	F	Н	110/15 mm	67	C ₁₁ H ₁₄ FNO	7.00	7.17
2	3,4-Dichlorophenyl	F	Η	$123 \sim 124$	86	$C_{13}H_8Cl_2FNO$	4.80	4.92
34)	p-Bromophenyl	F	\mathbf{H}	167~168	74	C13H9BrFNO	4.75	4.76
4	<i>m</i> -Chlorophenyl	F	H	62	53	C ₁₃ H ₉ ClFNO	5.70	5.61

o-Tolyl	F	\mathbf{H}	$101 \sim 103$	61	$C_{14}H_{12}FNO$	6.20	6.11
<i>m</i> -Tolyl	F	\mathbf{H}	85	86	$C_{14}H_{12}FNO$	6.23	6.11
<i>p</i> -Anisyl	F	Η	106	84	$C_{14}H_{12}FNO_2$	5.62	5.71
α-Naphthyl	F	Η	146	88	$C_{17}H_{12}FNO$	5.12	5.28
n-Butyl	NO_2	F	$117 \sim 118$	62	$C_{11}H_{13}FN_2O_3$	11.80	11.60
p-Bromophenyl	NO_2	F	$178 \sim 180$	90	$C_{13}H_8BrFN_2O_3$	8.00	8.23
<i>p</i> -Chlorophenyl	NO_2	F	174	35	$C_{13}H_8ClFN_2O_3$	9.40	9.50
o-Chlorophenyl	\mathbf{NO}_2	F	164	64	$C_{13}H_8ClFN_2O_3$	9.36	9.50
<i>m</i> -Chlorophenyl	NO_2	F	172~173	86	$C_{13}H_8ClFN_2O_3$	9.32	9.50
Phenyl	NO_2	F	150~151	92	$C_{13}H_9FN_2O_3$	10.88	10.76
<i>p</i> -Tolyl	NO_2	F	165	76	$C_{14}H_{11}FN_2O_3$	10.30	10.21
o-Tolyl	NO_2	F	166~167	54	$C_{14}H_{11}FN_2O_3$	10.33	10.21
<i>p</i> -Anisyl	NO_2	F	169~171	86	$C_{14}H_{11}FN_2O_4$	9.51	9.65
p-Chlorophenyl	Br	\mathbf{F}	172~173	53	C ₁₃ H ₈ BrClFNO	4.12	4.26
o-Chlorophenyl	Br	\mathbf{F}	136~137	57	C ₁₃ H ₈ BrClFNO	4.14	4.26
p-Bromophenyl	Br	F	$148 \sim 149$	62	$C_{13}H_8Br_2FNO$	3.58	3.75
<i>p</i> -Tolyl	Br	F	169~170	43	C ₁₄ H ₁₁ BrFNO	4.38	4.54
<i>m</i> -Tolyl	Br	F	$180 \sim 181$	40	$C_{14}H_{11}BrFNO$	4.40	4.54
<i>p</i> -Anisyl	Br	F	122~123	37	$C_{14}H_{11}BrFNO_2$	4.37	4.32
	o-Tolyl m-Tolyl p-Anisyl α-Naphthyl n-Butyl p-Bromophenyl p-Chlorophenyl m-Chlorophenyl m-Chlorophenyl p-Tolyl o-Tolyl p-Anisyl p-Chlorophenyl p-Chlorophenyl p-Bromophenyl p-Tolyl p-Tolyl p-Tolyl p-Tolyl p-Tolyl p-Tolyl p-Tolyl p-Tolyl p-Tolyl p-Anisyl	o -TolylF m -TolylF m -TolylF p -AnisylF α -NaphthylF n -ButylNO2 p -BromophenylNO2 p -ChlorophenylNO2 o -ChlorophenylNO2 m -ChlorophenylNO2 m -ChlorophenylNO2 p -TolylNO2 p -TolylNO2 p -TolylNO2 p -ChlorophenylNO2 p -TolylNO2 p -TolylBr o -ChlorophenylBr p -ChlorophenylBr p -TolylBr m -TolylBr p -AnisylBr p -AnisylBr m -TolylBr p -AnisylBr p -AnisylBr m -TolylBr </td <td>o-TolylFHm-TolylFHp-AnisylFHa-NaphthylFHn-ButylNO2Fp-BromophenylNO2Fp-ChlorophenylNO2Fo-ChlorophenylNO2Fp-ChlorophenylNO2Fp-ChlorophenylNO2Fp-ChlorophenylNO2Fp-ChlorophenylNO2Fp-TolylNO2Fp-TolylNO2Fp-ChlorophenylBrFp-ChlorophenylBrFp-ChlorophenylBrFp-ChlorophenylBrFp-ChlorophenylBrFp-ChlorophenylBrFp-ChlorophenylBrFp-ChlorophenylBrFp-AnisylBrFp-TolylBrFp-AnisylBrFp-AnisylBrFp-AnisylBrFp-AnisylBrFp-AnisylBrF</td> <td>o-TolylFH$101 \sim 103$m-TolylFH85p-AnisylFH106a-NaphthylFH146n-ButylNO2F117 ~ 118p-BromophenylNO2F178 ~ 180p-ChlorophenylNO2F174o-ChlorophenylNO2F164m-ChlorophenylNO2F165o-ChlorophenylNO2F165p-TolylNO2F165o-TolylNO2F166 ~ 167p-AnisylNO2F166 ~ 167p-AnisylNO2F166 ~ 167p-AnisylNO2F169 ~ 171p-ChlorophenylBrF136 ~ 137p-TolylBrF148 ~ 149p-TolylBrF169 ~ 170m-TolylBrF169 ~ 170m-TolylBrF122 ~ 123</td> <td>o-TolylFH$101 \sim 103$61m-TolylFH$85$86p-AnisylFH$106$84α-NaphthylFH$106$84α-NaphthylFH$146$88n-ButylNO2F$117 \sim 118$62p-BromophenylNO2F$178 \sim 180$90p-ChlorophenylNO2F$174$35o-ChlorophenylNO2F$164$64m-ChlorophenylNO2F$164$64m-ChlorophenylNO2F$165$$76$o-TolylNO2F$165$$76$o-TolylNO2F$165$$76$o-TolylNO2F$166 \sim 167$$54$p-AnisylNO2F$169 \sim 171$$86$p-ChlorophenylBrF$136 \sim 137$$57$p-BromophenylBrF$148 \sim 149$$62$p-TolylBrF$169 \sim 170$$43$m-TolylBrF$180 \sim 181$$40$p-AnisylBrF$180 \sim 181$$40$</td> <td>o-TolylFH$101 \sim 103$61$C_{14}H_{12}FNO$m-TolylFH8586$C_{14}H_{12}FNO$p-AnisylFH10684$C_{14}H_{12}FNO_2$a-NaphthylFH14688$C_{17}H_{12}FNO$n-ButylNO2F117 ~ 11862$C_{11}H_{13}FN_2O_3$p-BromophenylNO2F178 ~ 18090$C_{13}H_8BrFN_2O_3$p-ChlorophenylNO2F17435$C_{13}H_8ClFN_2O_3$o-ChlorophenylNO2F172 ~ 17386$C_{13}H_8ClFN_2O_3$p-EnomophenylNO2F150 ~ 15192$C_{13}H_8ClFN_2O_3$p-TolylNO2F166 ~ 16754$C_{14}H_{11}FN_2O_3$o-TolylNO2F166 ~ 16754$C_{14}H_{11}FN_2O_3$p-AnisylNO2F169 ~ 17186$C_{14}H_{11}FN_2O_4$p-ChlorophenylBrF136 ~ 13757$C_{13}H_8BrClFNO$o-ChlorophenylBrF136 ~ 13757$C_{13}H_8BrClFNO$p-BromophenylBrF169 ~ 17043$C_{14}H_{11}BrFNO$p-TolylBrF169 ~ 17043$C_{14}H_{11}BrFNO$p-TolylBrF169 ~ 17043$C_{14}H_{11}BrFNO$p-TolylBrF169 ~ 17043$C_{14}H_{11}BrFNO$p-TolylBrF169 ~ 17043$C_{14}H_{11}BrFNO$p-TolylBrF<th< td=""><td>o-TolylFH$101 \sim 103$61$C_{14}H_{12}FNO$6.20m-TolylFH8586$C_{14}H_{12}FNO$6.23p-AnisylFH10684$C_{14}H_{12}FNO_2$5.62a-NaphthylFH14688$C_{17}H_{12}FNO$5.12n-ButylNO2F117 ~ 11862$C_{11}H_{13}FN_2O_3$11.80p-BromophenylNO2F178 ~ 18090$C_{13}H_8BrFN_2O_3$8.00p-ChlorophenylNO2F17435$C_{13}H_8ClFN_2O_3$9.40o-ChlorophenylNO2F172 ~ 17386$C_{13}H_8ClFN_2O_3$9.36m-ChlorophenylNO2F172 ~ 17386$C_{13}H_9FN_2O_3$10.88p-TolylNO2F16576$C_{14}H_{11}FN_2O_3$10.33p-TolylNO2F166 ~ 16754$C_{14}H_{11}FN_2O_3$10.33p-AnisylNO2F169 ~ 17186$C_{14}H_{11}FN_2O_4$9.51p-ChlorophenylBrF136 ~ 13757$C_{13}H_8BrClFNO$4.12o-ChlorophenylBrF136 ~ 13757$C_{13}H_8BrClFNO$4.14p-BromophenylBrF148 ~ 14962$C_{13}H_8BrClFNO$4.14p-BromophenylBrF169 ~ 17043$C_{14}H_{11}BrFNO$4.38m-TolylBrF168 ~ 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IR Spectral analyses ν_{max} in cm⁻¹



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nitrobenzoic acid¹¹ and 3-bromo-4-fluorobenzoic acid.¹²⁾

Twelve of these fluorobenzamides were assayed for their antifungal activity.

EXPERIMENTAL

All the melting points are uncorrected.

N-Substituted amides of fluorobenzoic acids A solution of the appropriate amine (0.02 M) in dry benzene was added dropwise, with frequent shaking to TABLE II. FUNGICIDAL ACTIVITY

Compound	Average percentage inhibition after 96 hr						
No. ^a	Co 1:1000	oncentrations 1:10,000	used 1:100,000				
2	100.00	100.00	100.00				
3	100.00	100.00	100.00				
4	100.00	100.00	87.61				
7	100.00	92.85	80.95				
8	100.00	100.00	78.57				
10	100.00	88.09	80.95				
11	80.95	75.81	75.61				
13	97.60	71.42	50.00				
18	64.28	52.38	33.33				
19	66.66	52.38	47.61				
20	66.66	61.92	57.14				

a solution of the acid chloride (0.01 м) in dry benzene. The reaction mixture was refluxed for two hours, left overnight, and then filtered. The precipitate was washed with a small quantity of warm benzene, which was then subsequently mixed with the original benzene extract from which the amide was obtained in the usual way.

The amides thus prepared are listed along with their relevant data in Table I.

To confirm their amide nature, some of the compounds were hydrolysed and the acids obtained were characterised by their melting points and neutralisation equivalents. In all cases the parent acids were obtained. For further structural confirmation the IR spectra of three representative compounds were taken and analysed. The spectral analyses have been reported in Table I.

Fungicidal activity. The antifungal activity of twelve compounds were evaluated against the fungus "Aspergillus niger" by agar plate technique¹³) at three different concentrations namely 1:1,000; 1:10,000 and 1:100,000. The average percentage inhibitions of radial growths of mycelial colonies by various compounds are recorded in Table II. The compounds No. 2, 3, 4, 7, 8, 10, 11, 13 and 20 were found active even at low concentrations.

^{a)} Numbers refer to those in Table I and number of replications = 3.

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