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SHORT COMMUNICATION

FUNGICIDAL ACTIVITY OF SOME FLUOROAROMATIC COMPOUNDS

R. H. SHILEY, J. L. FORSBERG*, R. S. PERRY*, D. R. DICKERSON AND G. C. FINGER

Illinois State Geological Survey, Urbana, Illinois 61801 (U.S.A.)
*Illinois State Natural History Survey, Urbana, Illinois 61801 (U.S.A.)

In 1954, 1-fluoro-3-methyl- and 1,3-difluoro-4,6-dinitrobenzene were prepared in the Illinois State Geological Survey laboratory and tested for fungicidal activity by the Applied Botany and Plant Pathology Section of the Illinois State Natural History Survey. The compounds were very effective in preventing Fusarium rot of gladiolus corms.[1]

Recent success with the potassium fluoride-halogen exchange reaction on polychlorobenzenes[2] made available some fluoro intermediates that are easily convertible to compounds for further fungicidal research. Therefore, a new program was started to determine the fungicidal potency of fifty-one fluoroaromatic compounds on five different fungi.

Table 1 lists the results of the tests on three fungi Stromatinia gladioli (Column I), Fusarium oxysporum f. gladioli (Column II), and Curvularia trifolii f. sp. gladioli (Column III), which cause rot of gladiolus corms. The test results with Thielaviopsis basicola (Column IV), which attacks poinsettia plants, and Ceratocystis ulmi (Column V), which causes Dutch Elm Disease in the American Elm, are also listed.

A compound effective at less than 10 ppm would be considered as being highly potent, and those that were effective at 10 to 200 ppm

TABLE 1 FLUOROAROMATIC COMPOUNDS AS FUNGICIDES

Compound	Effectiveness against fungi[a] I ppm	A[f]	II ppm	B	III ppm	C	IV ppm	D	V ppm	E	VI[b]	Mp. °C	Analysis Found (Calcd.)	Synthesis Method[c]	Time/temp. h/°C	Solvent[d]	Benzene intermediate[e]
Dinitrobenzenes																	
1,3F2,5Cl4,6-*	12.5	3	25	5	111.1	10	20	6	25	2	5	132.5	C 26.10(26.40); H 0.1(0)	1a	0.5/50-98	1	1,3F2,5Cl2
1,2F3Cl4,6-*	50	8	12.5	1	50	5	12.5	5	25	3	4	60.0	C 30.43(30.21); H 0.48(0.42)	1b	0.5/35-80	2	1,2F3Cl
1,4F2Cl3,5-*	20	5	100	10	142.8	--	33.3	8	142.8	--	--	70.0	C 30.47(30.21); H 0.71(0.42)	1b	0.5/50-130	3	1,4F2Cl
1,3F2Cl4,6-*	100	--	100	--	100	9	100	--	100	9	--	62.5	C 30.51(30.21); H 0.28(0.42)	1c	25/90	4	1,3F2Cl4(NO_2)
1F2,3Cl4,6-*	50	9	12.5	2	100	8	12.5	4	25	4	6	47.0	C 28.36(28.26); H 0.38(0.40)	1b	0.5/35-80	2	1F2,3Cl2
1F2,6Cl3,5-	25	6	100	9	125	--	50	--	100	--	10	94.0					
1,2,3F4,6-*	142.8	--	111.1	--	125	--	83.3	--	111.1	--	--	70.0	C 32.69(32.45); H 0.38(0.45)	1b	2.5/90	5	1,2,3F4(NO_2)
1,3,5F2,4-	62.5	--	66.6	8	83.3	6	37	9	<33.3	7	9	53.5					
1F3Br4,6-	66.6	--	41.6	7	35.7	3	11.1	3	33.3	8	7	92.0					
1F2Cl4,5-*	>250	--	300	--	500	--	250	--	>250	--	--	63.0	C 32.96(32.67); H 0.77(0.92)	1c	3/45-90	5	1F2Cl
1F3Cl4,6-	<12.5	1	25.6	6	35.7	2	10.5	1	26.3	5	3	77.0					
1F3I4,6-*	<12.5	2	20	3	40	4	22.2	7	31.25	6	1	99.0	C 23.28(23.10); H 0.66(0.65)	2	2/56	6	1F3Br4,6(NO_2)2
1,3F4,6-	<16.6	4	22.2	4	33.3	1	<20	2	20	1	2	73.5					
1F2,4-	100	--	250	--	125	--	50	--	250	--	--	133/2[g]					
1F2(CH_3)3Cl4,6-*	<50	7	100	--	83.3	7	<50	10	100	10	8	84.0	C 36.18(35.84); H 1.74(1.72)	1d	4/15-50	7	1F2(CH_3)3Cl
Phenols																	
2,3Cl4,6(NO_2)2*	250	--	100	--	250	--	<100	--	100	11		94.5	C 28.51(28.48); H 0.81(0.80)	1e	0.5/20-90	2	1F2,3Cl2
2F4,6(NO_2)2	100	--	125	--	250	--	100	--	250	--		102.0					
4F2,6(NO_2)2	50	10	125	--	250	--	100	--	125	--		51.0					
3,4F2,6(NO_2)*	500	--	1000	--	1000	--	1000	--	>1000	--		59.5	C 40.97(41.16); H 1.82(1.73)	1f	4/25	8	1,2,4F3
Phenoxyacetic acids																	
4F2,6(NO_2)2	166.6	--	250	--	200	--	142.8	--	166.6	--		161.0					
2F4(NO_2)	166.6	--	142.8	--	200	--	90.9	--	125	--		140.0					
3F6(NO_2)	250	--	250	--	250	--	142.8	--	125	--		156.0					

Carbamates																
N(4Fph)et	333.3	--	333.3	--	333.3	--	142.8	--	142.8	--	56.0					
N(2,4,6F_3ph)ipr*	200	--	500	--	333.3	--	166.6	--	250	--	92.0	C 51.64(51.51); H 4.42(4.32)	3a	1/38	3	1,3,5$F_3$2(NH_2)
N(4Fph)ipr	83.3	--	500	--	333.3	--	125	--	125	--	88.0					
5-Pyrazolones																
1(3Fph)2,3(CH_3)$_2$-*	2000	--	>2000	--	>2000	--	>2000	--	>2000	--	87.0	C 64.45(64.07); H 5.52(5.38)	3b	3/110	9	1F3($NHNH_2$)
1(3CF_3ph)2,3(CH_3)$_2$-*	2000	--	>2000	--	>2000	--	>2000	--	>2000	--	102.0	C 56.55(56.25); H 4.53(4.33)	3b	3/110	9	1(CF_3)3($NHNH_2$)
Biphenyl																
3,3'$F_2$6,6'($OH)_2$	200	--	333.3	--	333.3	--	166.6	--	250	--	139.0					
Diphenyl sulfides																
3,3'$F_2$6(OH)6'(OCH_2COOH)*	1000	--	>2000	--	>2000	--	>2000	--	2000	--	119.5	C 54.22(53.85); H 3.47(3.23)[h]	3c	12/30	9	[i]
3,3'$F_2$6,6'($OCH_2COOH)_2$*	1000	--	2000	--	>2000	--	>2000	--	2000	--	197.0	C 52.02(51.89); H 3.54(3.27)	3c	24/95	10	[i]
Diphenyl sulfoxide																
3,3'$F_2$4,4'($OCH_3)_2$*	200	--	500	--	500	--	166.6	--	166.6	--	104.0	C 56.41(56.36); H 4.16(4.06)	3d	0.75/10-32	6	1F2Cl
1,2-Dithiolium iodide																
3(SCH_3)5(4Fph)*	1000	--	>1000	--	>1000	--	>1000	--	>1000	--	153.0d	C 32.41(32.44); H 2.27(2.18)	3e		11	[j]
Standard																
Mercuric chloride	>12.5		12.5		50		25		12.5							

[a] I Stromatinia gladioli II Fusarium oxysporum f. gladioli III Curvularia trifolii f. sp. gladioli IV Thielaviopsis basicola V Ceratocystis ulmi

[b] Rating of the overall effectiveness against all three fungi affecting gladiolus corms. (Column I, II, III.)

[c] Method: (1) Nitrations - Five volumes H_2SO_4 and 1.1 equivalents HNO_3 used. (a) H_2SO_4 sp gr 1.84: HNO_3 sp gr 1.49 (b) H_2SO_4 sp gr 1.84: HNO_3 sp gr 1.59 (c) H_2SO_4 sp gr 1.915: HNO_3 sp gr 1.49 (d) By-product from mononitration. H_2SO_4 sp gr 1.84: HNO_3 sp gr 1.42 (e) H_2SO_4 sp gr 1.915: HNO_3 sp gr 1.59, Exothermic (f) By-product, H_2SO_4 sp gr 1.84: HNO_3 sp gr 1.42. (2) Halogen exchange: NaI in acetone. (3) References to synthetic method. (a) Ref 5 (b) Ref 6 (c) Ref 7 (d) Ref 8 (e) Ref 9.

[d] Recrystallization solvents: (1) petroleum ether b.p. 90-110° (2) petroleum ether b.p. 90-110° and petroleum ether b.p. 30-60° (3) petroleum ether b.p. 30-60° (4) diethyl ether (5) carbon tetrachloride (6) ethyl alcohol (7) 3-fluorobenzotrifluoride (8) petroleum ether b.p. 30-60° and benzene (9) petroleum ether and benzene (10) methyl alcohol (11) acetonitrile

[e] Known compounds

[f] Columns A, B, C, D, and E individual fungus, effectiveness rating.

[g] Boiling point

[h] S(10.25); 10.57

[i] 3,3'-Difluoro-6,6'-dihydroxydiphenyl sulfide

[j] Ethyl 4-fluorocinnamate

* New compounds

would be considered as highly to fairly potent (Finger et al.[3]). Seven of the compounds tested have a fungicidal activity equal to or greater than that of mercuric chloride on one or more of the organisms tested. The test compounds are listed in Table 1. Their physical constants, methods of preparation, reaction conditions, and methods of purification are reported or indicated by reference.

The 10 compounds that are most effective against the five fungi are dinitro derivatives and are rated, from 1 through 10, from most active to least active, (Table 1). The ratings are listed in columns A, B, C, D, or E. Column VI gives the over-all effectiveness against the three fungi affecting gladiolus corms.

EXPERIMENTAL

Small scale syntheses were used to prepare the compounds. The yield data are not reported. Solid products were vacuum sublimed after recrystallization and before analysis.

The method used for screening the compounds was developed by J. L. Forsberg[4]. In this method, the test fungus is first grown on potato dextrose agar plates on which cotton threads have been spread. The infested threads are cut into small sections that are then suspended in an aqueous diacetone alcohol solution of the pure fungicide for 15-, 30-, 60-, and 120- minute periods. After these exposures, the sections of thread are placed on potato-dextrose agar plates and incubated at room temperature for 7 days. Growth of the fungus is recorded as + or -. Although determinations were made at all four exposure times, only the results of the 120-minute exposure are given in Table 1.

These results indicate in ppm the amount of the compound necessary to stop growth of the fungus after exposure to the potential fungicide.

In addition to the compounds listed in Table 1, tests were conducted on 19 other known compounds, but because of their poor activity (>200 ppm), these tests were not included in Table 1. These compounds are listed in groups as follows: dinitrobenzenes, 1F2,4,6 $Cl_3$3,5—, 1F2,4$Cl_2$3,5—, 1F4(COOH)2,6—; phenols, 2,4$F_2$6(NO_2)—, 2F6(NO_2)—, 3F6(NO_2)—,4F2(NO_2)—, 3(CF_3)2(NO_2)—, 3(CF_3)4(NO_2)—, 3(CF_3)—; phenoxyacetic acid, 4F2(NO_2)—; 5-pyrazalones, 1(3Fph)3(CH_3)—, 1(4Fph)3(CH_3)—, 1(4Fph)2,3(CH_3)$_2$—, 1(3CF_3ph)3(CH_3)—; biphenyl, 3,3'$F_2$4,4'(OH)$_2$: diphenyl sulfide, 3,3'$F_2$6,6'(OH)$_2$—; and ethyl cinnamates, 2F—, 4F—.

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