Agr. Biol. Chem., **40** (4), 801～803, 1976

Synthesis of Fluorinated Diaryl Ketones, Substituted Phenoxymethyl-5′-fluoro-2′-methoxyphenylketones and Their Thiosemicarbazones as Potential Fungicides†

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Received March 17, 1975

The fungistatic properties of some fluorinated ketones have been studied by Tehon[1] against *Macrosporium sarcinaeforme*. Thiosemicarbazones of many ketones and chalkones have been found to possess antifungal and antibacterial properties.[2] Keeping this in view we have prepared several fluorinated ketones by the Friedel-Crafts acylation. Attempt has also been made to combine the toxicity of a ketone molecule with that of the thiosemicarbazide which possesses a toxophoric >N–C(=)–S– grouping. The fluorinated ketones were, therefore, converted into their thiosemicarbazones by condensation with thiosemicarbazide in alcohol.[3]

EXPERIMENTAL

All melting points are uncorrected.

TABLE I. FLUORINATED DIARYL KETONES AND SUBSTITUTED PHENOXYMETHYL-5′-FLUORO-2′-METHOXYPHENYL KETONE

S. No.	Compound	mp/bp °C	Yield %	Molecular formula	C % Found	C % Calcd.	H % Found	H % Calcd.
1	4′-Bromophenyl-2-fluorophenyl-K	165～70/5 mm	64	$C_{13}H_8BrFO$	55.2	55.9	2.6	2.8
2	4′-Chlorophenyl-2-fluorophenyl-K	121～122	31	$C_{13}H_8ClFO$	61.7	62.2	3.1	3.4
3	4-Fluoro-3-methylphenyl-4′-chlorophenyl-K	122～123	71	$C_{13}H_{10}ClFO$	66.6	67.2	3.7	4.0
4	2-Fluoro-5-methylphenyl-4′-chlorophenyl-K	234	78	$C_{14}H_{10}ClFO$	66.5	67.2	3.8	4.0
5	4-Fluoro-3-methylphenyl-2′-chlorophenyl-K	118	82	$C_{14}H_{10}ClFO$	66.5	67.2	3.8	4.0
6	2-Fluoro-5-methylphenyl-2′-chlorophenyl-K	123	83	$C_{14}H_{10}ClFO$	66.8	67.2	3.9	4.0
7	2-Fluoro-5-methylphenyl-2′-fluorophenyl-K	157/1 mm	52	$C_{14}H_{10}F_2O$	71.9	72.4	4.2	4.3
8	2-Fluoro-5-methylphenyl-4′-fluorophenyl-K	179	89	$C_{14}H_{10}F_2O$	71.9	72.4	4.1	4.3
9	4-Fluoro-3-methylphenyl-4′-fluorophenyl-K	155	92	$C_{14}H_{10}F_2O$	71.8	72.4	4.0	4.3
10	2-Fluoro-5-methylphenyl-phenyl-K	106～107	64	$C_{14}H_{11}FO$	78.0	78.5	4.9	5.1
11	4-Fluoro-3-methylphenyl-phenyl-K	99	89	$C_{14}H_{11}FO$	77.9	78.5	4.9	5.7
12	2-Fluoro-5-methylphenyl-benzyl-K	183/1 mm	75	$C_{15}H_{13}FO$	78.3	78.9	5.3	5.7
13	4-Fluoro-3-methylphenyl-benzyl-K	62～63	85	$C_{15}H_{13}FO$	78.3	78.9	5.4	5.7
14	2-Fluoro-5-methylphenyl-4′-methoxyphenyl-K	145	35	$C_{15}H_{13}FO_2$	72.2	72.8	5.0	5.2
15	Phenoxymethyl-5′-fluoro-2′-methoxyphenyl-K	126	42	$C_{15}H_{13}FO_3$	68.8	69.2	4.8	5.0
16	2-Chlorophenoxymethyl-5′-fluoro-2′-methoxyphenyl-K	210～220/2 mm	51	$C_{15}H_{12}ClFO_3$	67.3	67.9	3.9	4.1
17	4-Nitrophenoxymethyl-5′-fluoro-2′-methoxyphenyl-K	97	49	$C_{15}H_{12}FNO_5$	58.7	59.0	3.7	3.9
18	4-Chlorophenoxymethyl-5′-fluoro-2′-methoxyphenyl-K	83	62	$C_{15}H_{12}ClFO_3$	67.3	67.9	3.9	4.1

N.B.: K denotes ketone.

† Studies in Organic Fluorine Compounds. Part III.

Fluorinated ketones. An appropriate hydrocarbon (0.01 M) in carbon disulphide was subjected to Friedel-Crafts reaction with an acid chloride (0.01 M) in the presence of anhydrous aluminium chloride (0.015 M). The mixture was kept at room temperature for twenty four hours and subsequently refluxed for two hours. Carbon disulphide was distilled off and the residue decomposed with ice cold dilute HCl. The product separating out was extracted with ether, washed with water and dried over anhydrous sodium sulphate. The excess ether was distilled off and the product obtained recrystallised from aqueous ethanol. The fluorinated ketones thus synthesised have been listed along with their relevant data in Table I.

Thiosemicarbazones. A solution of an appropriate ketone (0.01 M) in ethanol was treated with an ethanolic solution of thiosemicarbazide (0.011 M). The mixture was refluxed for twenty to thirty minutes and cooled when the thiosemicarbazone crystallised out. The thiosemicarbazones thus prepared are recorded with their relevant data in Table II.

Fungicidal activity

The fungicidal activity of ten ketones and nine

TABLE II. THIOSEMICARBAZONES

S. No	Compound	mp °C	Yield %	Molecular formula	N %		S %	
					Found	Calcd.	Found	Calcd.
1	4′-Bromophenyl-2-fluorophenyl-KT	159	32	$C_{14}H_{11}BrFN_3S$	11.5	11.9	8.9	9.1
2	4′-Chlorophenyl-2-fluorophenyl-KT	111	38	$C_{11}H_{11}ClFN_3S$	13.0	13.3	10.1	10.4
3	4-Fluoro-3-methylphenyl-4′-chlorophenyl-KT	152~153	57	$C_{15}H_{13}ClFN_3S$	12.8	13.1	9.8	9.9
4	2-Fluoro-5-methylphenyl-4′-chlorophenyl-KT	211	46	$C_{15}H_{13}ClFN_3S$	12.7	13.1	9.7	9.9
5	4-Fluoro-3-methylphenyl-2′-chlorophenyl-KT	273	31	$C_{15}H_{13}ClFN_3S$	12.8	13.1	9.7	9.9
6	2-Fluoro-5-methylphenyl-2′-chlorophenyl-KT	197	31	$C_{15}H_{13}ClFn_3S$	12.9	13.1	9.8	9.9
7	2-Fluoro-5-methylphenyl-2′-fluorophenyl-KT	191	36	$C_{15}H_{13}F_2N_3S$	13.5	13.8	10.3	10.5
8	2-Fluoro-5-methylphenyl-4′-fluorophenyl-KT	190	38	$C_{15}H_{13}F_2N_3S$	13.4	13.8	10.2	10.5
9	4-Fluoro-3-methylphenyl-4′-fluorophenyl-KT	195	53	$C_{15}H_{13}F_2N_3S$	13.4	13.8	10.4	10.5
10	2-Fluoro-5-methylphenyl-phenyl-KT	90~91	31	$C_{15}H_{14}FN_3S$	14.2	14.6	10.9	11.2
11	4-Fluoro-3-methylphenyl-phenyl-KT	75	38	$C_{15}H_{14}FN_3S$	14.2	14.6	11.0	11.2
12	2-Fluoro-5-methylphenyl-benzyl-KT	114	45	$C_{16}H_{16}FN_3S$	13.6	13.9	10.4	10.6
13	4-Fluoro-3-methylphenyl-benzyl-KT	130	53	$C_{16}H_{16}FN_3S$	13.5	13.9	10.3	10.6
14	2-Fluoro-5-methylphenyl-4′-methoxyphenyl-KT	173	46	$C_{16}H_{16}FN_3OS$	12.9	13.2	9.9	10.1
15	Phenoxymethyl-5′-fluoro-2′-methoxyphenyl-KT	157	50	$C_{16}H_{16}FN_3O_2S$	12.4	12.6	9.3	9.6
16	2-Chlorophenoxymethyl-5′-fluoro-2′-methoxyphenyl-KT	162	56	$C_{16}H_{15}ClFN_3O_2S$	11.1	11.4	8.3	8.7
17	4-Nitrophenoxymethyl-5′-fluoro-2′-methoxyphenyl-KT	134	51	$C_{16}H_{15}FN_4O_4S$	14.5	14.8	8.1	8.5
18	4-Chlorophenoxymethyl-5′-fluoro-2′-methoxyphenyl-KT	108	66	$C_{16}H_{15}ClFN_3O_2S$	11.1	11.4	8.4	8.7

N.B.: KT denotes ketone thiosemicarbazone.

TABLE III. FUNGICIDAL ACTIVITY

Compound No.[a]	Average percentage inhibitions after 96 hr concentrations used		
	1 : 1000	1 : 10000	1 : 100000
3 of Table I	100.00	54.76	16.66
4 —	100.00	100.00	100.00
5 —	100.00	100.00	40.47
8 —	100.00	92.85	64.28
10 —	100.00	100.00	100.00
14 —	69.04	54.76	35.71
15 —	72.57	50.91	28.75
16 —	100.00	100.00	30.34
17 —	100.00	90.47	62.54
18 —	100.00	100.00	33.34
2 of Table II	100.00	50.00	21.42
3 —	100.00	100.00	33.33
4 —	100.00	52.37	23.80
12 —	100.00	52.37	33.33
14 —	100.00	100.00	35.71
15 —	80.52	60.95	45.23
16 —	85.98	77.12	54.76
17 —	100.00	100.00	71.25
18 —	100.00	100.00	60.23

[a] Number refer to those in Tables I and II and number of replications=3.

thiosemicarbazones has been evaluated against *Aspergillus niger* by agar plate technique[4,5] at three different concentrations namely 1 : 1000, 1 : 10,000 and 1 : 100,000. The average percentage inhibitions of radial growths of mycelial colonies by various compounds are recorded in Table III. The compounds 4, 8, 10 and 17 of Table I and 16, 17 and 18 of Table II were found active even at low concentrations.

Acknowledgement. One of the authors (AKS) is grateful to the University Grants Commission, New Delhi, for the award of a Junior Research Fellowship. The authors thank Dr. R. P. Rastogi, Professor and Head, Chemistry Department, University of Gorakhpur, Gorakhpur (U.P.), India, for providing all departmental facilities.

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