Table III—Antibacterial Activity of Some Xanthones and Benzophenones against *Escherichia coli* (K12) and *Streptococcus faecalis* (8043)

Number	Compound	—ID_{50}, moles/l.— *E. coli*	*S. faecalis*
I[a]		$>10^{-3}$	1×10^{-5} [b]
XV[c]		$>10^{-3}$	9×10^{-4}
XVII[c]		$>10^{-3}$	8×10^{-5}
XIX		$>10^{-3}$	1×10^{-3}
XX[c]		—[d]	—[d]
XXI[e]		3×10^{-4}	3×10^{-5} [f]
XXV		$>10^{-3}$	$>10^{-3}$
XXVII[e]		1×10^{-3}	9×10^{-5}
XXXI[c]	1,8-Dihydroxyxanthone (6)	$\gg 10^{-3}$	$\gg 10^{-3}$
XXXII	2,2′,3,3′-Tetrahydroxybenzophenone (5, 6)	6×10^{-5} [b]	1×10^{-5} [b]

[a] Suspension. [b] One hundred percent inhibition at 10^{-3} *M*. [c] Compound precipitated when test solution was added to medium. [d] No effect at 10^{-5} *M*; at 10^{-3} *M*, a 36% growth enhancement was observed. [e] No effect at 10^{-5} *M*; at 10^{-3} *M*, an 81% growth enhancement was observed. [f] One hundred percent inhibition at 10^{-4} *M*.

XXXII) showed borderline activity (ID_{50} values of about 10^{-5} *M*) against one or the other of these organisms.

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Synthesis and Antifungal Activity of Polyhalophenyl Esters of *p*-Sulfamoylcarbanilic Acid

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Abstract □ Several polyhalophenyl esters of *p*-sulfamoylcarbanilic acid were prepared and tested for antifungal activity against *Candida albicans*, *Penicillium notatum*, and *Aspergillus niger*. Pentachloro-, tribromo-, and triiodophenyl esters were found to be the most active.

Keyphrases □ *p*-Sulfamoylcarbanilic acid, polyhalophenyl esters—synthesized and screened as potential antifungal agents □ Antifungal agents, potential—synthesis and screening of polyhalophenyl esters of *p*-sulfamoylcarbanilic acid

Recently, it was reported that polyhalophenyl esters of *p*-substituted carbamic acids as well as polyhalophenyl esters of pyridyl- and quinolyl-4-carbamic acids (1, 2) showed significant antifungal activities.

In the present work, a series of polyhalophenyl esters of *p*-sulfamoylcarbanilic acid was prepared by interaction of *p*-sulfamoylbenzoyl azide and the appropriate phenol in boiling toluene or xylene (Scheme I).

$$p\text{-}NH_2SO_2C_6H_4CON_3 + ArOH \xrightarrow[\text{or xylene}]{\text{boiling toluene}} p\text{-}NH_2SO_2C_6H_4NHCOOAr + N_2$$

Scheme I

The physical data of all new compounds are reported in Table I. The antifungal activity of all compounds was determined[1] *in vitro* against *Candida albicans* 1959-2, *Penicillium notatum* 154-3, and *Aspergillus niger* A-23. Concentrations of 5, 10, and 25 mcg./ml. of each compound were used.

Compounds II–IV were dissolved in acetone, Compounds I and V were dissolved in 60% ethanol, and Compounds VI–XI were dissolved in 96% ethanol, all at concentrations of 5 mg./10 ml. These solutions were diluted with hot culture medium to the desired concen-

[1] Using BBL Sabouraud dextrose agar medium. The microorganisms were obtained from the Department of Parasitology, Public Health Institute, Iran.

Table I—Physical Constants of Substituted Polyhalophenyl Esters of *p*-Sulfamoylcarbanilic Acid

Compound Number	R	Yield, %	Melting Point	Formula	Analysis, %	Calc.	Found
I	Ethyl	70	235°[a]	$C_9H_{12}N_2O_4S$	C	44.26	44.10
					H	4.91	5.11
II	Phenyl	25	160°[b]	$C_{13}H_{12}N_2O_4S$	C	53.42	53.10
					H	4.10	3.90
III	*p*-Tolyl	40	215°[b]	$C_{14}H_{14}N_2O_4S$	C	55.08	55.15
					H	4.59	4.62
IV	*p*-Nitrophenyl	20	235–236°[b]	$C_{13}H_{11}N_3O_6S$	C	48.29	48.26
					H	3.40	3.48
V	*p*-Chlorophenyl	50	225°[a]	$C_{13}H_{11}Cl_2N_2O_4S$	C	47.77	47.80
					H	3.36	3.32
VI	2,4-Dichlorophenyl	70	240°[a]	$C_{13}H_{10}Cl_2N_2O_4S$	C	43.21	43.10
					H	2.77	2.80
VII	2,4,5-Trichlorophenyl	40	212°[a]	$C_{13}H_9Cl_3N_2O_4S$	C	39.44	39.15
					H	2.27	2.30
VIII	2,4,6-Trichlorophenyl	30	215°[a]	$C_{13}H_9Cl_3N_2O_4S$	C	39.44	39.42
					H	2.27	2.24
IX	2,4,6-Tribromophenyl	60	230°[a]	$C_{13}H_9Br_3N_2O_4S$	C	29.48	29.51
					H	1.70	1.65
X	2,4,6-Triiodophenyl	70	220°[a]	$C_{13}H_9I_3N_2O_4S$	C	23.28	23.32
					H	1.34	1.32
XI	Pentachlorophenyl	70	195°[a]	$C_{13}H_7Cl_5N_2O_4S$	C	33.58	33.58
					H	1.93	1.89

[a] Recrystallized from ethanol plus water. [b] Recrystallized from acetone.

Table II—Antifungal Activity of Some Polyhalophenyl Esters of *p*-Sulfamoylcarbanilic Acid[a]

Compound	*Penicillium notatum* 5 mcg./ml.	*Penicillium notatum* 10 mcg./ml.	*Penicillium notatum* 25 mcg./ml.	*Candida albicans* 5 mcg./ml.	*Candida albicans* 10 mcg./ml.	*Candida albicans* 25 mcg./ml.	*Aspergillus niger* 5 mcg./ml.	*Aspergillus niger* 10 mcg./ml.	*Aspergillus niger* 25 mcg./ml.
IX	—	—	+	—	—	+	—	+	2+
X	—	+	2+	+	2+	2+	+	2+	2+
XI	+	2+	2+	2+	2+	2+	—	2+	2+

[a] — equals no inhibition, 2+ equals complete inhibition.

trations and autoclaved at 120° for 2 hr. Five replicates of each concentration were prepared. The antifungal activities of pentachloro-, tribromo-, and triiodophenyl esters are reported in Table II. The antifungal activities of all other compounds were insignificant. The pentachlorophenyl ester was the most active of this series.

EXPERIMENTAL[1]

p-Sulfamoylbenzoylhydrazide was prepared according to Shimizu *et al.* (3).

Preparation of *p*-Sulfamoylbenzoyl Azide—To an ice-cold solution of 2.15 g. (10 mmoles) of *p*-sulfamoylbenzoylhydrazide in 50% acetic acid (25 ml.), a 5% aqueous solution of 0.69 g. (10 mmoles) of sodium nitrite was added with stirring. The resulting precipitate was filtered, washed with cold water, and dried to give 1.92 g. (85%) of *p*-sulfamoylbenzoyl azide, m.p. 100° dec.

Preparation of *p*-Sulfamoylcarbanilic Acid Ethyl Ester—A solution of *p*-sulfamoylbenzoyl azide, 2.26 g. (10 mmoles), in 15 ml. of ethanol was refluxed for 4 hr. The reaction mixture was diluted with water, the resulting precipitate was filtered, and the solid was recrystallized from aqueous ethanol to give 1.70 g. (70%) of the title compound, m.p. 235°; NMR (CF_3CO_2H): τ 9.2 (t, 3H,CH_3), 6.1 (q, 2H, CH_2), 2.7 (q, 4H, ArH), and 2.3 (s, 2H, NH_2).

Preparation of *p*-Sulfamoylcarbanilic Acid Pentachlorophenyl Ester—A solution of 0.452 g. (2 mmoles) of *p*-sulfamoylbenzoyl azide and 0.355 g. (2 mmoles) of pentachlorophenol in 20 ml. of dry toluene was gently refluxed for 4 hr. After evaporation of the solvent under reduced pressure, the residue was recrystallized from 96% ethanol to give 0.650 g. (70%) of the title compound, m.p. 195°; IR (KBr) ν_{max}: 3400, 3320 (C—H and N—H), 1700 (C=O), 1595, 1540 (carbamate)(C—H), 1415, 1390, 1210, 1060 (C—H), 1300, and 1152 (SO_2NH_2) cm.$^{-1}$.

All other carbanilic acid derivatives were prepared similarly (Table I).

[1] Melting points were taken on a Kofler hot-stage microscope and are uncorrected. The IR spectra were determined with a Leitz model III spectrograph. NMR spectra were obtained on a Varian A 60A instrument.

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