In Wirklichkeit handelt es sich aber nicht um eine einzige Reaktion, vielmehr um einen komplexen Vorgang. Er besteht darin, daß während der Verbrennung (-128 kcal) von 180 g Glucose für die Bildung von 1370 g lebendiger Zellsubstanz (s. o.) aus Nährstoff chemische und physikalische Arbeit geleistet wird. Dies bedeutet, daß 1 g Trockensubstanz 252 cal entspricht. Dieser Wert ist mit 1 g pro 461 cal Gärungswärme bei anaerober Vermehrung von Bäckerhefe zu vergleichen.

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Preparation and Fungicidal Properties of Some Arylthioalkanoyl- and (Arylsulphonyl)-aceto-hydroxamic Acids

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Some (phenylthio)- and (phenylsulphonyl) acetohydroxamic acids which are substituted in the *para*-position of the benzene ring, as well as α- and β-(phenylthio) propionyl hydroxamic acids have been synthesized. The compounds were tested for their fungicidal activity against *Rhizoctonia solani* and *Fusarium sp.* The (phenylthio) acetohydroxamic acids investigated were found to possess fungicidal properties. Whereas the fungicidal activity of α-(phenylthio) propionyl hydroxamic acid was comparable with that of (phenylthio) acetohydroxamic acid, the β-(phenylthio) propionyl hydroxamic acid was found to be biologically inactive. On the other hand, the corresponding phenylsulphonyl compounds did not show any fungitoxic activity, and some of them, unexpectedly and strikingly, led to promotion of mycelial growth of the fungi tested.

The fungicidal activity of (phenylthio) acetohydroxamic acids has been recently demonstrated by ZAYED et al. [1]. (4,5-Dimethoxy-2-nitrophenylthio)- (I_a) and (2,5-dimethoxy-4-nitrophenylthio) acetohydroxamic acid (I_b) were found to possess significant fungicidal properties against the phytopathogenic mould *Rhizoctonia solani*. The inhibition of the mycelial growth was obviously due to the hydroxamic acid group, as the corresponding carboxylic acids were inactive. It seemed, therefore, of interest to extend this work and investigate the effect of chemical structure on the biological activity of arylthioalkanoyl hydroxamic acids. These compounds would be expected to possess significant fungitoxic effects, since the parent arylthioalkanoic acids are known to inhibit the mycelial growth of several fungi [2, 3].

In the present work, a number of *p*-substituted (phenylthio)- (II_{a-e}) and (phenylsulphonyl) acetohydroxamic acids (II_{f-j}), as well as α-(III) and β-(phenylthio) propionyl hydroxamic acids (IV) have been prepared. These compounds were investigated for their effect on the mycelial growth of *Rhizoctonia solani* and *Fusarium sp.* The *p*-substituents in the benzene ring were chlorine, bromine, methyl and methoxyl groups.

Experimental

The hydroxamic acids were prepared from the corresponding methyl esters of (arylthio) acetic acids by the action of alkaline hydroxylamine in methanol at 40 °C [1]. They are colourless crystalline substances, easily soluble in alcohol and in dilute sodium hydroxide solution. Their aqueous or alcoholic solutions give an intense violet colour with ferric chloride solution and a bright green ppt. with copper acetate solution in acetic acid. The properties and analytical data of the hydroxamic acids are listed in Table I. All compounds were tested in concentrations of 10^{-3}, 10^{-4} and 10^{-5} M. The biological tests were carried out as described by ZAYED et al. [1]. Compounds II_{a-e} and II_{g-h} were tested as their potassium salts, after, being recrystallised from 90% methanol. The other compounds were investigated as the free acids, which possessed considerable solubility in water.

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Hydroxamic acid	m. p.[a] [°C]	Solvent of crystallisn.	Yield [%]	Mol. formula	Analysis							
					Calculated [%]				Found [%]			
					C	H	N	S	C	H	N	S
II_a	97–98	Water	60	$C_8H_9NO_2S$	52.44	4.95	7.64	17.49	52.16	4.82	7.85	17.23
II_b	143–144	Water	85	$C_8H_8BrNO_2S$	36.65	3.07	5.34	12.23	36.47	3.24	5.09	11.89
II_c	133–134	aq. methanol	81	$C_8H_8ClNO_2S$	—	—	6.43	14.73	—	—	6.18	14.58
II_d	83–85	Water	75	$C_9H_{11}NO_3S$	—	—	6.57	15.03	—	—	6.31	14.76
II_e	112–114	aq. methanol	70	$C_9H_{11}NO_2S$	—	—	7.10	16.25	—	—	6.88	16.37
II_f	158	Ethanol	65	$C_8H_9NO_4S$	44.64	4.21	6.51	14.89	44.81	4.20	6.35	15.21
II_g	154	Benzene	88	$C_8H_8BrNO_4S$	—	—	4.76	10.90	—	—	4.68	11.25
II_h	153–155	Water	79	$C_8H_8ClNO_4S$	—	—	5.61	12.84	—	—	5.52	12.81
IIi	88–90	aq. ethanol	70	$C_9H_{11}NO_5S$	—	—	5.71	13.07	—	—	5.91	12.81
IIj	115–116	aq. ethanol	72	$C_9H_{11}NO_4S$	—	—	6.11	13.98	—	—	6.23	13.74
III	92–94	petroleum ether (60–80°)	55	$C_9H_{11}NO_2S$	54.79	5.62	7.10	16.25	54.81	5.66	6.98	16.57
IV	86	Benzene	65	$C_9H_{11}NO_2S$	—	—	7.10	16.25	—	—	6.83	16.41

Table I. Analytical data of the hydroxamic acids. a) Melting points are uncorrected.

Substance	% * inhibition or promotion in mycelial growth** of					
	Rhizoctonia solani			*Fusarium sp.*		
	10^{-3} M	10^{-4} M	10^{-5} M	10^{-3} M	10^{-4} M	10^{-5} M
II_a	82	28	10	45	9	+ 4
II_b	100	26	18	100	38	22
II_c	98	50	12	64	25	21
II_d	74	22	15	55	35	20
II_e	88	25	19	38	37	30
II_f	+ 105	0	25	+ 2	4	4
II_g	+ 60	+ 69	+ 54	+ 32	+ 36	+ 31
II_h	+ 180	+ 130	+ 110	+ 80	+ 41	+ 25
IIi	+ 270	+ 320	+ 300	+ 103	+ 43	+ 7
IIj	+ 10	8	9	+ 7	+ 2	10
III	79	65	58	43	26	7
IV	+ 5	0	3	17	13	8

Table II. Biological activity of arylthioalkanoyl- and (phenylsulphonyl) aceto-hydroxamic acids on the mycelial growth of *Rhizoctonia solani* and *Fusarium sp.* * Data are mean of 4 replicates. ** + = Promotion.

Biological Results

The effect of the hydroxamic acids on the growth of the phytopathogenic moulds *Rhizoctonia solani* and *Fusarium sp.* has been studied. From the results obtained in table II, the following conclusions may be drawn concerning the relation between the fungitoxic effect and the constitution of the investigated hydroxamic acids. The results show that the (phenylthio) acetohydroxamic acids were effective in inhibiting the growth of the tested fungi, whereas the phenylsulphonylanalogues were ineffective. At a concentration of 10^{-3} M, compounds II_{a-c} and II_e were in general more effective on *Rhizoctonia* than on *Fusarium*. The presence of a halogen atom in the *para*-position of the benzene ring apparently increased the fungicidal effect against both species; whereas a methyl or a methoxyl group did not affect significantly the biological activity.

Previous studies on phenoxyacetohydroxamic acids have shown that a halogen atom [4, 5] or a methyl group [6] in the *para*-position of the benzene ring increases the fungicidal activity. The relative activating influence of these substituents declined in

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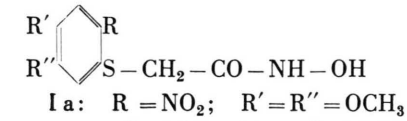
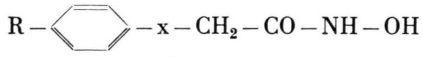


$$S-CH_2-CO-NH-OH$$

Ia: $R = NO_2$; $R' = R'' = OCH_3$

b: $R' = NO_2$; $R = R'' = OCH_3$



$$-x-CH_2-CO-NH-OH$$

IIa: $R = H$; $x = S$

b: $R = Br$; $x = S$

c: $R = Cl$; $x = S$

d: $R = OCH_3$; $x = S$

e: $R = CH_3$; $x = S$

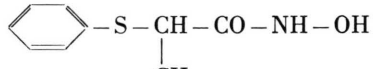
f: $R = H$; $x = SO_2$

g: $R = Br$; $x = SO_2$

h: $R = Cl$; $x = SO_2$

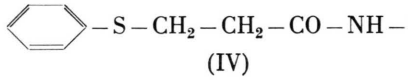
i: $R = OCH_3$; $x = SO_2$

j: $R = CH_3$; $x = SO_2$



$$-S-CH(CH_3)-CO-NH-OH$$

(III)



$$-S-CH_2-CH_2-CO-NH-OH$$

(IV)

the order $Br < Cl < CH_3$. Such defined conclusions cannot be drawn from the present investigation with the arylthio-analogues.

α-(phenylthio)propionyl hydroxamic acid (III) was found to possess significant fungicidal properties. This indicates that an α-substituent does not decrease the fungitoxic effect. Similar findings have been demonstrated with aryloxyalkanoic acids and their arylthio-analogues [2]. The insertion of another CH_2 group between the S atom and the hydroxamic acid group as in IV resulted in the almost complete disappearance of biological activity.

The transformation of the thio-group into the sulphonylgroup in II_f and II_j resulted also in the complete disappearance of the biological activity. In the case of II_{g-i}, the biological activity was reversed by the transformation $S \rightarrow SO_2$. Thus it was found that compounds II_{g-i} promote the fungal growth up to 300 per cent. The promotion was more obvious in *Rhizoctonia solani*.