SYNTHESIS OF PHYSIOLOGICALLY ACTIVE COMPOUNDS OF THE THIOSEMICARBAZONE SERIES AND DERIVATIVES

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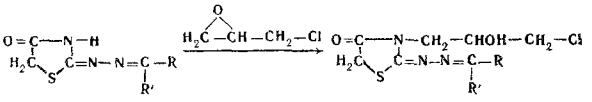
With a view to discovering new plant growth regulators, a series of thiosemicarbazones and derivatives of thiazolidine-2-4-dione were synthesized. Reaction of epichlorohydrin with derivatives of thiazolidine-2, 4-dione without a substituent at position 3 gives 3-(β-hydroxy-γ-chloropropyl) derivatives of thiazolidine-2, 4-dione-2-hydrazone.

Thiosemicarbazones are synthesized by treating the free, or 4 substituted thiosemicarbazides with the appropriate carbonyl compounds in the ordinary way [1] (Table 1). 4-Substituted thiosemicarbazides were prepared by reacting hydrazine with isothiocyanates [2], or by treating primary aromatic amines with carbon disulfide, sodium chloroacetate, and hydrazine hydrate [3].

A series of derivatives of thiazolidine-2,4-dione-2-hydrazone are synthesized by condensing thiosemicarbazones with monochloroacetic acid by analogy with [4–6]. (Table 2). They are colorless or yellow crystalline high-melting substances, insoluble in water, but soluble in organic solvents.

The addition reaction between epichlorohydrin and some derivatives of thiazolidine-2,4-dione has now been studied.



In the presence of a suitable hydrogen atom, addition of epichlorohydrin takes place at the nitrogen of the thiazolidine ring. If the hydrogen is replaced by various groups addition does not take place. The addition products (Table 2) are crystalline compounds soluble in dioxane, acetone and benzene, slightly soluble in ethanol, and insoluble in water.

Some of the thiosemicarbazones obtained possess marked herbicidal activity. The products of condensing them with monochloroacetic acid lacked phytophysiological activity.

EXPERIMENTAL

3-(β-Furfuralacetone-γ-chloropropyl)thiazolidine-1,4-dione-2-hydrazone. A mixture of 2.5 g (0.01 mole) thiazolidine-2,4-dione-2-hydrazone, 0.92 g (0.01 mole) epichlorohydrin, and 100 m*l* EtOH was refluxed for 3 hr, the products cooled, and the solid filtered off, washed with water, and recrystallized from EtOH + water. Yield 70%. The other epichlorohydrin derivatives (Table 2) were crystallized from EtOH or benzene.

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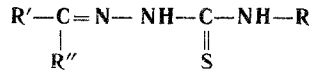
Table 1

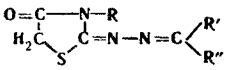
Thiosemicarbazones of Ketones



R	R′COR″	Mp, °C	Formula	Element	Found, %	Calculated, %
H	n-Butyl p-chlorophenylglyoxylate	155—156	$C_{13}H_{16}ClN_3O_2S$	Cl	11.02	11.29
H	4-Carboxyfluorenone	250 (decomp)	$C_{15}H_{11}N_3O_2S$	N	14.13	14.14
C_6H_5	Furfuralacetone	162—164	$C_{15}H_{15}N_3OS$	N	14.68	14.73
Allyl	Fluorenone	143—144	$C_{17}H_{15}N_3S$	N	14.24	14.33
C_6H_5	Fluorenone	174—176	$C_{20}H_{15}N_3S$	N	12.42	12.76
C_6H_5	4-Carboxyfluorenone	>300	$C_{21}H_{15}N_3O_2S$	N	11.23	11.26
p-Hydroxyphenyl	4-Carboxyfluorenone	280—282	$C_{21}H_{15}N_3O_3S$	N	10.48	10.79
β-Naphthyl	Benzalacetone	164—166	$C_{21}H_{18}N_3S$	N	12.53	12.20

Table 2

Derivatives of Thiazolidin-2,4-dione-2-hydrazone



R	R′COR″	Mp, °C	Formula	Element	Found, %	Calculated, %
H	Cyclopentanone	215—217	$C_8H_{11}N_3OS$	N	20.98	21.31
H	p-Chloroacetophenone	184—186	$C_{11}H_{10}ClN_3OS$	Cl	13.23	13.29
H	Furfuralacetone	197—199	$C_{11}H_{11}N_3O_2S$	N	16.99	16.86
H	p-Methylacetophenone	191—193	$C_{12}H_{13}N_3OS$	N	16.73	17.00
H	Diisobutyl ketone	121—123	$C_{12}H_{21}N_3OS$	N	16.89	16.47
H	Benzalacetophenone	180—182	$C_{13}H_{13}N_3OS$	N	16.56	16.21
p-Hydroxyphenyl	Furfural	263—265	$C_{14}H_{11}N_3O_3S$	N	13.83	13.95
C_6H_5	Cyclopentanone	214—216	$C_{14}H_{15}N_3OS$	N	15.44	15.38
Allyl	Cinammaldehyde	104—106	$C_{15}H_{15}N_3OS$	S	10.84	11.22
H	Fluorenone	231—233	$C_{16}H_{11}N_3OS$	S	10.79	10.92
p-Hydroxyphenyl	Benzaldehyde	284—286	$C_{16}H_{13}N_3O_2S$	N	13.63	13.50
H	4-Carboxyfluorenone	250(decomp)	$C_{17}H_{11}N_3O_3S$	N	12.10	12.46
C_6H_5	p-Chloroacetophenone	227—229	$C_{17}H_{14}ClN_3OS$	Cl	10.02	10.31
C_6H_5	Furfuralacetone	190—192	$C_{17}H_{15}N_3O_2S$	N	12.73	12.92
β-Naphthyl	Furfural	203—205	$C_{18}H_{13}N_3O_2S$	N	12.43	12.53
C_6H_5	Benzalacetophenone	237—239	$C_{19}H_{17}N_3OS$	N	12.97	12.53
p-Hydroxyphenyl	Fluorenone	281—283	$C_{22}H_{15}N_3O_2S$	N	10.74	10.90
β-Hydroxy-γ-chloropropyl	Furfuralacetone	166—168	$C_{14}H_{16}ClN_3O_3S$	Cl	10.68	10.36
"	p-Methylacetophenone	200—202	$C_{15}H_{18}ClN_3O_2S$	Cl	10.73	10.44
"	Benzalacetophenone	183—185	$C_{16}H_{18}ClN_3O_2S$	Cl	9.92	10.08
"	Fluorenone	204—206	$C_{19}H_{16}ClN_3O_2S$	Cl	9.56	9.20