SYNTHESIS OF 3,5-DI-IODOSALICYLTHIOBENZANILIDES AND SALICYLTHIOTOLUIDIDES

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2-Acetoxy-3,5-di-iodo-4' R_2 — benzanilides obtained from 2-acetoxy-3,5-di-iodobenzoyl chloride in reaction with aniline (p-iodoaniline, p-nitroaniline) and o-acetoxy-benztoluidides obtained from o-acetoxy-benzoyl chloride in reaction with o(m,p)-toluidines (Table I), have been converted to corresponding acetoxythioamides by thiation with phosphorus pentasulfide in dry organic solvent (Table II). By alkaline hydrolysis (ln NaOH) the acetyl group was eliminated and hydroxythioamides were obtained (Table III).

As a continuation of our examinations in the field of the hydroxythioamides and in connection with the already reported conclusions[1–4] we have synthetized 3,5-di-iodosalicylthiobenzanilides and salicylthiotoluidides (Table III).

The component to begin with were 3,5-di-iodosalicylic acid[5] and o-hydroxybenzoic acid in which the hydroxyl group was protected by an acetyl group. The acetoxyderivatives were further treated by thionyl chloride in dry solvent giving appropriates acetoxybenzoyl chlorides[6].

The compounds (Table I) which appears to have been formed as a result of the modified Schotten-Baumman method have been obtained by refluxing dioxane (Pyridine) solutions of acetoxybenzoyl chlorides and aniline (p-iodoaniline, p-nitroaniline), o(m,p)-toluidine[7,8].

The compounds (Table II) were prepared in good yields by thiation of benzanilides and benztoluidides with phosphorus pentasulfide in dry dioxane (pyridine, xylole)[9–11].

By alkaline hydrolysis the compounds (Table III) were formed. They are well crystallized, yellow compounds which have been of great interest in our investigations as substances with antifugal and antibacterial activity.

EXPERIMENTAL

The melting points are uncorrected

The preparation of compounds 1—6

To a solution of 2-acetoxy-3,5-di-iodobenzoyl chloride or 2-acetoxybenzoyl chloride (fresh prepared) in dry dioxane (pyridine) was added in drops and by mechanical stirring at room temperature, the solution of

aniline (p-iodoaniline, p-nitroaniline, o(m,p)-toluidine) in dry dioxane. The mixture was kept three hours at room temperature with occasionnal stirring. When the reaction was completed, the mixture was cooled slowly and poured into ice water. The product was filtered by suction, washed with water and dried. The resulting crude acetoxyderivate recrystallized from an appropriate solvent.

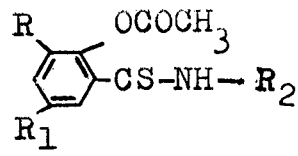
The preparation of compounds 7—12

2-acetoxybenzanilides or 2-acetoxybenztoluidides were disloved in 6—10 ml dry dioxane (pyridine, xylole), heated on a oil bath, and phosphorus pentasulfide was added in two portions. The reaction mixture was refluxed at temperature of 120—130°C for about 30 minutes. The reaction mixture was poured into water and after staying over night the resulting product was filtered, washed with water, dried and recrystallized from an appropriate solvent.

The preparation of compounds 13—18

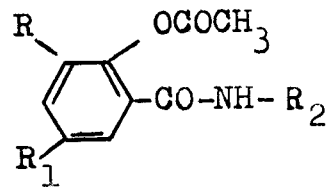
A mixture of 0,002 mole — 2-acetoxythiobenzanilides or 2-acetoxythiobenztoluidides and 15—20 ml of ln NaOH (aqueous sodium hydroxyde) was heated on a water bath for 10—30 minutes at the temperature of 60—70°C. The alkali solution (pH 8—9) was filtered and after cooling was acidified with ln HCl to pH 5—6. Yellow precipitate was obtained, filtered, washed and air dried. By recrystallization from appropriate solvent yellow crystalls were formed, which are soluble in usual organic solvent, yellow crystalls werre formed, which are soluble in usual organil solvents, but practically insoluble in water.

Table I



№	R	R_1	R_2	Yield %	Mp.°C	Formula	Analyse Calc. Found %C	%H	%N
1	J	J	phenyl	98	189—190	$C_{15}H_{11}J_2NO_3$	35,53 35,40	2,20 2,13	2,71 2,66
2	J	J	p-iodphe-nylene	97	198—199	$C_{15}H_{10}J_3NO_3$	28,50 28,40	1,60 1,45	2,22 2,10
3	J	J	p-nitrophe-nylene	98	209—210	$C_{15}H_{10}J_2N_2O_5$	32,64 32,41	1,83 1,70	5,08 4,98
4	H	H	o-tolyl	96	121—122	$C_{16}H_{15}NO_3$	71,36 71,24	5,61 5,70	5,20 5,15
5	H	H	m-tolyl	98	202—203	$C_{16}H_{15}NO_3$	71,36 71,20	5,61 5,53	5,20 5,10
6	H	H	p-tolyl	98	134—135	$C_{16}H_{15}NO_3$	71,36 71,18	5,61 5,71	5,20 5,24

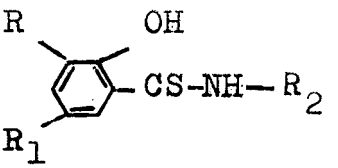
Table II



№	R	R_1	R_2	Yield%	Mp.°C	Formula	Analyse Calc. Found %C	%H	%N
7	J	J	phenyl	84	125—126	$C_{15}H_{11}J_2NO_2S$	34,45 34,31	2,13 2,00	2,68 2,73
8	J	J	p-iodphe-nylene	83	151—152	$C_{15}H_{10}J_3NO_2S$	27,76 27,61	1,56 1,43	2,10 2,04
9	J	J	p-nitrophe-nylene	85	197—198	$C_{15}H_{10}J_2N_2O_4S$	31,72 31,60	1,78 1,55	4,93 4,78
10	H	H	o-tolyl	80	105—106	$C_{16}H_{15}NO_2S$	67,42 67,32	5,31 5,36	4,92 4,80

11	H	H	m-tolyl	84	181—182	$C_{16}H_{15}NO_2S$	67,42 67,35	5,31 5,38	4,92 4,85
12	H	H	p-tolyl	95	84—85	$C_{16}H_{15}NO_2S$	67,42 67,34	5,31 5,35	4,92 4,86

Table III



№	R	R_1	R_2	Yield %	mp.°C	Formula	Analyse Calc. Found %C	%H	%N
13	J	J	phenyl	92	62—63	$C_{13}H_9J_2NOS$	32,46 32,33	1,89 1,71	2,91 2,82
14	J	J	p-iodphe-nylene	93	81—82	$C_{13}H_8J_3NOS$	25,76 25,60	1,33 1,20	2,32 2,12
15	J	J	p-nitraphe-nylene	94	97—98	$C_{13}H_8J_2N_2O_3S$	29,68 29,51	1,54 1,46	5,33 5,12
16	H	H	o-tolyl	92	84—85	$C_{14}H_{13}NOS$	69,19 69,25	5,39 5,40	5,76 5,80
17	H	H	m-tolyl	96	88—90	$C_{14}H_{13}NOS$	69,19 69,00	5,39 5,22	5,76 5,65
18	H	H	p-tolyl	99	138—140	$C_{14}H_{13}NOS$	69,19 70,05	5,39 5,40	5,76 5,72

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Р Е З И М Е

СИНТЕЗА НА 3,5-ДИ-ЈОДСАЛИЦИЛБЕНЗАНИЛИДИ И САЛИЦИЛ ТИОТОЛУИДИДИ

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Дадена е синтезата на некои тиоамиди, што се добиени од салицилната како и од 3,5-ди-јодсалицилната киселина. Синтезата се одвива преку три реакциони степени. Добиените ацетокси-анилиди, односно ацетокси-толуидиди (1-6 Табл. I/) со сулфурирање со фосфор (V) сулфид во сув органски растворувач (диоксан, пиридин, ксилол) преминуваат во соодветни ацетокси-тиодеривати (7-12 Табл. II/). Од нив, со умерена алкална хидролиза (1n NaOH), се добиени соодветни хидрокситиоанилиди, односно хидрокситиотолуидиди (13-18 Табл. III/).

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