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Note

Thioamides. XI.* The Preparation of 5-Bromo-2-thiofuramides

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A number of 5-bromo-2-furamides, obtained from 5-bromo-2-furoyl chloride and ammonia or various amines, have been converted to corresponding thioamides by thiation with phosphorus pentasulfide in dry dioxane.

Unlike relatively numerous examples of thioamides derived from pyromucic acid (2-furancarbonic acid)[1], only a limited number of corresponding compounds with the furan nucleus carrying functional groups like nitro[2] or halogen[3] has been described as yet. While halogenation of various thioamides led to desulfurized products[4] it was shown that thiobenz- and thiofur- halogenarylamides could be conveniently prepared by thiation of corresponding halogenamides with phosphorus pentasulfide[5].

In the present paper we describe the preparation of thioamides derived from 5-bromo-2-furoic acid which have been of interest in our studies of the chemical properties of thiofuramides and compounds of potential biological activity.

5-Bromo-2-furamides (Table I) used as starting material were prepared from 5-bromo-2-furoylchloride[6] and ammonia or an appropriate amine by the modified Schotten-Baumann procedure.

The thioamides listed in Table II were prepared in very good yields by thiation of corresponding amides with phosphorus pentasulfide in dry dioxane; they are well crystallized yellow compounds soluble in usual organic solvents but practically insoluble in water.

EXPERIMENTAL

The melting points are uncorrected.

The Preparation of 5-Bromo-2-furamides I—VII

The solution of 5-bromo-2-furoylchloride** in dioxane (Method *A*) or benzene (Method *B*) was added dropwise with stirring and cooling into a slight excess of a corresponding amine in 10% aqueous NaOH. The exceptions were I and IV which were prepared by addition of a dioxane solution of 5-bromo-2-furoylchloride into a large excess of ammonium hydroxide or aniline respectively (Method *C*). The crude products were obtained by filtration (Method *A* and *C*) or by evaporating the separated benzene layer (Method *B*), and recrystallized from an appropriate solvent.

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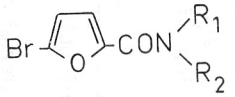
** Prepared from 5-bromo-2-furancarbonic acid[7] and thionylchloride according to Raiford and Huey[6].

TABLE I

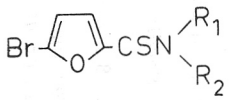
5-Bromo-2-furamides



No	R_1	R_2	Method	Yield %	Recryst. from[a]	M p.[b] °C	Formula	*Anal.* calc'd / found		
								% C	% H	%N
I	H	H	*C*	77	b	145—146[c]	$C_5H_4BrNO_2$			
II	H	CH_3	*A*	86	c	107—108	$C_6H_6BrNO_2$	35.32 35.43	2.96 3.23	6.87 6.79
III	CH_3	CH_3	*A*	94	d	95—96	$C_7H_8BrNO_2$	38.56 38.68	3.70 3.84	6.42 6.19
IV	H	C_6H_5	*C*	95	e	143—144[d]	$C_{11}H_8BrNO_2$			
V	H	4-$CH_3 \cdot C_6H_4$	*B*	98	e	106—107	$C_{12}H_{10}BrNO_2$	51.45 51.29	3.60 3.58	5.00 5.32
VI	H	4-$CH_3O \cdot C_6H_4$	*B*	88	f	139—140	$C_{12}H_{10}BrNO_3$	48.67 48.41	3.40 3.69	4.73 4.61
VII	C_2H_5	C_6H_5	*A*	93	f	147—148	$C_{13}H_{12}BrNO_2$	53.08 52.98	4.11 4.18	4.76 5.00

TABLE II

5-Bromo-2-thiofuramides



	R_1	R_2	Reaction conditions Temp.[a] °C	Time (Min.)	Yield %	Recryst. from[b]	M. p.	Formula	*Anal.* calc'd / found % C	% H	% N	% S
VIII	H	H	90—95	30	61	c	108—109	C_5H_4BrNOS	29.14 29.28	1.96 2.13	6.80 6.68	15.56 15.85
IX	H	CH_3	100—105	15	82	d	49—50	C_6H_6BrNOS	32.74 32.92	2.75 2.72	6.36 6.52	14.57 14.51
X	CH_3	CH_3	80—85	10	90	e	87—88	C_7H_8BrNOS	35.91 35.89	3.44 3.30	5.98 5.90	13.70 13.99
XI	H	C_6H_5	100—105	15	80	d	95—96	$C_{11}H_8BrNOS$	46.82 46.85	2.86 2.83	4.96 4.96	11.36 11.62
XII	H	4-$CH_3 \cdot C_6H_4$	85—90	20	91	d	89—90	$C_{12}H_{10}BrNOS$	48.66 48.78	3.40 3.43	4.73 4.68	10.83 10.41
XIII	H	4-$CH_3O \cdot C_6H_4$	80—90	30	80	d	134—135	$C_{12}H_{10}BrNO_2S$	46.17 46.13	3.23 3.16	4.49 4.23	10.27 9.90
XIV	C_2H_5	C_6H_5	100—105	15	90	e	93—94	$C_{13}H_{12}BrNOS$	50.33 50.66	3.90 4.01	4.52 4.33	10.34 9.84

[a] Temperature of the oil bath; [b] c = carbon tetrachloride; d = diluted ethanol; e = ethanol.

The Preparation of 5-Bromo-2-Thiofuramides VIII—XIV

To a solution of 5-bromo-2-furamide (I—VII 5—50 M moles) in dry preheated dioxane, phosphorus pentasulfide (0.5 mole pro mole of amide) was added. The reaction mixture was heated near the boiling point of the solvent, while an intimate contact of reactants was maintained by stirring. After the reaction was over the mixture was filtered into 5—10 volumes of water. In most cases the oily product soon crystallized. If there was no crystallization (as in XI) the oil was taken into ether, the organic layer separated and after drying with anhydrous magnesium sulphate the solvent was evaporated. The product was in each case dissolved in 10% aqueous sodium hydroxide, and the filtered solution carefully neutralized with 10% hydrochloric acid. Exceptions were X and XIV where re-precipitation had been omited.

5-Bromo-2-thiofuramide (VIII) (Via *nitrile*)

Into the solution of 5-bromo-2-furonitrile[9] (2.5 g., 1.45 M mole) in 5 ml. dry saturated ethanolic solution of ammonia containing a few drops of triethylamine, dry hydrogen sulfide was bubbled during 6 hrs. The reaction mixture was diluted with 20 ml. of water and the yellow precipitate (2.25 g., 75%) recrystallized from benzene; prisms, m. p. 108—109°. The mixed melting point with the sample obtained by thiation of I (Table II) was undepressed.

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IZVOD

Tioamidi. XI. Priprava tioamida koji se odvode od 5-brom-2-furankarbonske kiseline

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Opisana je priprava do sada nedovoljno istraženih tioamida koji se odvode od 5-brom-2-furankarbonske kiseline. Pokazano je da se ovakvi tioamidi (Tabela II VIII—XIV) mogu uspješno pripraviti tiiranjem odgovarajućih amida (Tabela I I—VII) pomoću fosfornog pentasulfida u dioksanu.

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