[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF SWARTHMORE COLLEGE]

ARYLSULFONYL METHYLISOTHIOUREAS

EDWARD H. COX

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One of the reactions by which we attempted to prepare the arylsulfonyl ureas (1) was through the hydrolysis of the corresponding arylsulfonyl methylisothioureas. This reaction had already been successfully carried out in the pyrimidine series, when the ethylthiol group was transformed into the carbonyl group by means of warm dilute hydrochloric acid solution. In particular, Wheeler (2) and his co-workers converted 2-ethylthiol-6-oxypyrimidine-5-carboxylic acid to uracil-5-carboxylic acid. Ethyl mercaptan was the by-product. Several of the analogous derivatives of the arylsulfonyl methylisothiourea series have now been prepared and the hydrolysis of these has been studied. We were not able to prepare any pure specimens of the arylsulfonyl ureas by the hydrolysis of the corresponding isothiourea derivatives. While the amount of methyl mercaptan was in all cases practically quantitative, the main product proved to be a mixture of the arylsulfonyl amide and the arylsulfonyl urea.

The sulfonylisothioureas have not been recorded in the literature, and furthermore it has now been shown that the *p*-aminobenzenesulfonyl methylisothiourea has value in the treatment of streptococcal infection in mice. It is, therefore, considered of value to record some of the compounds of this series.[1]

EXPERIMENTAL PART[2]

Since the procedure for the condensation of the various sulfonyl chlorides with the methylisothiourea is practically the same for all the compounds prepared, only the detailed account of preparation of the *p*-acetaminobenzenesulfonyl methylisothiourea will be given. The hydrolysis of this is also described. The melting points and analyses are given in tabular review.

Preparation of p-*acetaminobenzenesulfonyl methylisothiourea.* In a three-liter flask provided with a motor stirrer were placed 400 g. of anhydrous potassium carbonate and one liter of acetone to which had been added 300 cc. water. The suspension was stirred and cooled in an ice-bath. To this was added a mixture of 153 g. (1.1 moles) of methylisothiourea sulfate and 234 g. (1.0 mole) of *p*-acetaminobenzenesulfonyl chloride[3] over a period of half an hour. After the addition, the ice-bath was removed and the reaction mixture stirred for four hours. The reaction contents were then poured while stirring into four liters of water, filtered, and washed with water. When dried, the crude product weighed 228 g. (80%). After crystallization from dilute acetic acid, small colorless needles were deposited which melted at 230–232°.

Preparation of p-*aminobenzenesulfonyl methylisothiourea.* Two hundred grams of *p*-

[1] Private communication from Professor Perrin H. Long, The Johns Hopkins Medical School.

[2] The author wishes to express this thanks to Mr. S. M. Raymond who prepared and analyzed some of the compounds.

[3] Grateful acknowledgement is made to the Monsanto Chemical Company for its generous supply of *p*-acetaminobenzenesulfonyl chloride.

acetaminobenzenesulfonyl methylisothiourea (crystallized once from dilute acetic acid) was suspended in 1200 cc. of 7% hydrochloric acid solution. The flask was lowered into a boiling water-bath and mechanically stirred until solution took place (30–45 mins.). The solution was then treated with charcoal, filtered while hot, and the filtrate diluted with one-half volume of water (to prevent the crystallization of the hydrochloride salt). It was then cooled in an ice-bath and made alkaline with ammonia (stirring). The crude product was filtered, washed, and dried (128 g., 75% yield). After a specimen was twice crystallized from dilute acetic acid it melted at 183–185° (colorless white needles).

TABLE

ARYLSULFONYL METHYLISOTHIOUREAS

$ArSO_2NHC(SCH_3)=NH$.

Ar.	M.P., °C.	FORMULA	NITROGEN %	
			Calc'd	Found
Benzene	159–160	$C_8H_{10}N_2O_2S_2$	12.16	12.23
Toluene	118–119	$C_9H_{12}N_2O_2S_2$	11.46	11.35
o-Xylene	136–137	$C_{10}H_{14}N_2O_2S_2$	10.84	11.04
m-Xylene	137–138	$C_{10}H_{14}N_2O_2S_2$	10.84	10.64
p-Xylene	144–145	$C_{10}H_{14}N_2O_2S_2$	10.84	10.60
p-Acetaminobenzene	230–232	$C_{10}H_{13}N_3O_3S_2$	14.62	14.81
p-Aminobenzene	183–185	$C_8H_{11}N_3O_2S_2$	17.13	17.06

SUMMARY

The preparation of arylsulfonyl methylisothioureas has been described, with particular reference to the preparation of *p*-acetaminobenzene sulfonyl and *p*-aminobenzenesulfonyl methylisothioureas.

The latter substance shows value in cases of streptococcal infection in mice, and it is to be further investigated in this connection.

SWARTHMORE, PA.

REFERENCES

(1) COX AND RAYMOND, *J. Am. Chem. Soc.*, **63**, 300 (1941).
(2) WHEELER, JOHNSON, AND JOHNS, *Am. Chem. J.*, **37**, 394 (1907).