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Abstract

Full Text

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SYNTHESIS OF S-SUBSTITUTED ISOTHIURONIUM DERIVATIVES BY THE ACTION OF THIOUREA ON ETHERS

Salts of S-substituted isothiuronium bases are an important class of organosulfur compounds; their preparation by the action of thiourea on halohydrocarbons is widely used for the identification of halogen derivatives. S-Benzylisothiuronium chloride and certain analogous compounds are also often used for the identification of carboxylic and sulfonic acids.

Hydrolysis of salts of isothiuronium compounds leads to the synthesis of mercaptans, and chlorination gives sulfochlorides. We have developed a synthesis of α-chloro-ω-sulfocarboxylic acids by conjugate chlorination of isothiuronium salts of the structure:

$$\mathrm{CCl_2{=}CH(CH_2)_{nSC}(=NH)NH_2 \cdot HX}$$

in anhydrous formic acid (^{1}).

Compounds containing the isothiuronium group are widely studied as physiologically active substances.

In the present work we have shown that certain ethers, on interaction with thiourea in anhydrous formic acid, form S-substituted isothiuronium compounds according to the scheme:

$$\mathrm{ROR_1 + SC(NH_2)_2 \xrightarrow{HCOOH} RSC(=NH)NH_2 \cdot HCOOH + [R_1OH].}$$

The isothiuronium compounds were isolated by us in the form of picrates. Apparently, the reaction proceeds through the intermediate formation of dialkylhydroxonium formates $\mathrm{(RR_1\overset{\oplus}{O}H)O\overset{\ominus}{O}CH}$, whose interaction with thiourea may proceed, depending on the structure of the starting ether, by either an S_N1 or an S_N2 mechanism, similarly to reactions of other nucleophilic compounds with ethers (^{2}). This is confirmed by the fact that in glacial acetic acid, which is incapable of forming oxonium compounds with ethers (^{3}), reaction of the latter with thiourea does not take place.

The reaction of thiourea with ethyl allyl ether, 1,1-dichloro-5-ethoxypentene, tetrahydrofuran, and tetrahydropyran was carried out at 100°. Under these conditions the yield of picrates of S-substituted isothiuronium compounds did not exceed 35% of theoretical.* From the first two ethers, picrates of S-allylisothiuronium and S-(5,5-dichloropentenyl)-isothiuronium, respectively, were obtained. The structures of these compounds were proved by independent synthesis—by the action of thiourea on allyl chloride and on 1,1,5-trichloropentene-1. From tetrahydrofuran, the picrate of S-(4-formoxybutyl)-isothiuronium was obtained $[\mathrm{HCOO{-}(CH_2)_4SC(=NH)NH_2 \cdot C_6H_2(NO_2)_3OH}]$. This structure of the picrate was confirmed by its IR spectrum, which showed the presence of a frequency characteristic of the C=O group in esters, and by hydrolysis with formation of the corresponding picrate of S-(4-hydroxybutyl)-isothiuronium $[\mathrm{HO(CH_2)_4SC(=NH)NH_2 \cdot C_6H_2(NO_2)_3OH}]$. In the case of tetrahydropyran, the picrate of S-(5-hydroxypentyl)-isothiuronium, a hydrolysis product, was isolated. The IR spectra of the picrates S-(4-hydroxybutyl)isothiuronium and S-(5-hydroxypentyl)isothiuronium showed the absence of the C=O frequency of an ester group.

It should be emphasized that the reaction found is new for ethers and may find application for the purposes of identification and proof of the structure of substances containing C–O–C groups.

Experimental Part

S-allylisothiuronium picrate $[CH_2 = CH{-}CH_2SC(=NH)NH_2 \cdot C_6H_2(NO_2)_3OH]$. A solution of 5 g of ethyl allyl ether and 4.5 g of thiourea in 30 ml of anhydrous formic acid was heated in a sealed glass ampoule on a boiling water bath for 20 hours. Formic acid was distilled off from the reaction mixture in vacuo. There remained 6.5 g of an oily product containing unreacted thiourea. From a solution of 1 g of this mixture in alcohol, the picrate was obtained by adding an excess of picric acid; for complete precipitation of the picrate a small amount of water was added. Yield 0.55 g (17% of theory), m.p. 147–148°. A mixed sample with an authentic specimen gave no depression of the melting point.

S-(5,5-dichloropentenyl)isothiuronium picrate $[CCl_2 = CH{-}(CH_2)_3SC(=NH)NH_2 \cdot C_6H_2(NO_2)_3OH]$ was obtained from 10.4 g of 1,1-dichloro-5-ethoxypentene and 4.3 g of thiourea as described in the preceding experiment. The picrate separates as an oil, which gradually crystallizes. Yield of crude product 21% of theory, m.p. 123–124° (after two recrystallizations from alcohol). A mixed sample with an authentic specimen [4] showed no depression of the melting point.

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* In the present work we did not set ourselves the task of finding the optimal conditions of synthesis.

S-(4-formoxybutyl)isothiuronium picrate $[HCOO(CH_2)_4SC(=NH)NH_2 \cdot C_6H_2(NO_2)_3OH]$. A solution of 5 g of tetrahydrofuran and 7.3 g of thiourea in 30 ml of anhydrous formic acid was heated in a sealed glass ampoule on a boiling water bath for 10 hours. Formic acid was distilled off from the reaction mixture in vacuo; residue 14 g. From 1 g of this mixture, dissolved in acetone, 0.76 g of picrate was obtained. Yield 35% of theory, m.p. 140–141° (after one recrystallization from acetone).

$C_{12}H_{15}O_9N_5S$. Found, %: C 35.58, 35.78; H 4.04, 3.92; N 17.08, 17.09
Calculated, %: C 35.55; H 3.73; N 17.27

By boiling the picrate of the formoxy derivative with aqueous ethyl alcohol, the picrate of the corresponding hydroxy derivative $[HO(CH_2)_4SC(=NH)NH_2 \cdot C_6H_2(NO_2)_3OH]$ was obtained, m.p. 197–198° (after two recrystallizations from alcohol).

$C_{11}H_{15}O_8N_5S$. Found, %: C 34.79, 34.80; H 3.81, 3.95; N 18.13, 18.29
Calculated, %: C 35.01; H 4.00; N 18.56

S-(5-hydroxypentyl)isothiuronium picrate $[HO(CH_2)_5SC(=NH)NH_2 \cdot C_6H_2(NO_2)_3 \cdot OH]$ was obtained from 5 g of tetrahydropyran and 4.3 g of thiourea with subsequent hydrolysis similarly to that described in the preceding experiment, m.p. 152–153° (from acetone).

$C_{12}H_{17}O_8N_5S$. Found, %: C 36.21, 36.39; H 4.08, 4.11; N 18.78, 18.45
Calculated, %: C 36.82; H 4.37; N 17.89

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