

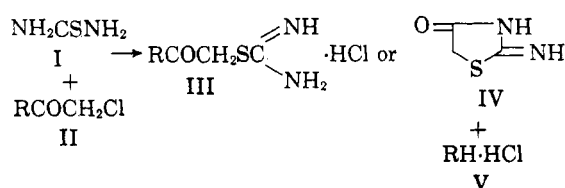
isothiuronium salt [III, R = (C₃H₇)₂N] and a 21% yield of pseudothiohydantoin (IV). In 95% ethanol at 25°, the dipropylamide and thiourea afforded a 57% yield of the isothiuronium salt and 17% yield of IV. In refluxing ethanol, none of III [R = (C₃H₇)₂N] was isolated but rather an 86% yield of IV and a 74% yield of dipropylamine hydrochloride. III [R = (C₃H₇)₂N] was converted to IV in refluxing ethanol.⁴ 2-Chloro-*N,N*-diethylacetamide and thiourea in benzene at 80° for 2 hrs gave a 51.8% yield of IV.


Ethyl chloroacetate and thiourea gave a 57% yield of III (R = C₂H₅O) and 26% yield of IV (as the hydrochloride) at 25° in ethanol, and a 62% yield of III (R = C₂H₅O) and a 14% yield of IV·HCl in DMF at 25°. A slightly higher yield of the isothiuronium salt was obtained when the reaction was carried out for only 4 hr. rather than 24 hr. at 25° in ethanol.

The data, summarized in Table I, clearly indicate that solvents have no appreciable effect on the course of reaction of I and II, and that the amounts of III and IV formed are dependent on reaction temperature. Temperatures of about 25–30° favor the formation of the isothiuronium salts (III) while temperatures of about 80° favor the formation of IV.

TABLE I

REACTION OF THIOUREA WITH 2-HALOACETAMIDES AND 2-HALOACETATES



R	Solvent	Temp., °C.	Time, Hr.	% Yield	
				III	IV
(C ₂ H ₅) ₂ N	C ₆ H ₆	80	2.0	—	51.8 ^a
(C ₃ H ₇) ₂ N	EtOH	80	1.5	—	86.0 ^b
	DMF	30	18.0	75.0	20.7
	EtOH	25	23.0	57.0	17.3
	DMF	30	20.0	59.0	— ^c
C ₂ H ₅ O ^d	EtOH	25	24.0	56.8	25.6 ^f
	DMF	25	24.0	61.8	14.1 ^f
	DMF	25	4.0	70.4	— ^c
^e	EtOH	80	3.0	—	79–82 ^f

^a 45.5% yield of diethylamine hydrochloride isolated.

^b 74% yield of dipropylamine hydrochloride isolated. ^c Attempt to isolate IV was unsuccessful. ^d With esters, IV is isolated as the hydrochloride (IV HCl) which on treatment with NaOAc gives IV. ^e Data from reference 6. ^f Yield of IV HCl.

EXPERIMENTAL

Thiourea and ethyl chloroacetate. The procedure used in the reactions of thiourea with 2-chloroacetates and 2-chloroacetamides⁷ is illustrated by this typical example. A solu-

tion of 15.2 g. (0.2 mole) of thiourea and 24.5 g. (0.2 mole) of ethyl chloroacetate in 100 ml. of DMF was stirred at 25° for 24 hr. One liter of acetone was added to the clear solution and the precipitated solid was filtered; wt. 32.8 g. This was dissolved in 200 ml. of absolute ethanol and 4.3 g. (14.1% yield) of pseudothiohydantoin hydrochloride was recovered by filtration of the alcohol insoluble material. The alcohol filtrate, diluted with 1.5 liters of ethyl acetate, afforded 24.5 g. (61.8% yield) of the isothiuronium hydrochloride [III, R = C₂H₅O], m.p. 110° (dec.).

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Prodigiosin Hydrochloride¹

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Efimenko and co-workers³ have claimed the isolation of prodigiosin hydrochloride from *Serratia marcescens* through a process involving chromatography of the bacterial pigment. Identification of the compound, which is described as red needles melting at 149°, rests solely upon analysis for carbon and hydrogen and apparently its absorption spectrum, λ_{max} 538–539 m μ ⁴ (presumably in ethanol). In a previous paper⁵ we described the isolation of a magenta colored solid, m.p. 150.0–150.5° (dec.), from a powdered sugar chromatogram of the mixture resulting from the reaction of prodigiosin perchlorate with sodium hydroxide. At that time the similarity in the properties of the two products was noted. We have now established that the compound isolated by us is definitely prodigiosin hydrochloride. The substance gives a positive Beilstein test and elemental analyses are in good agreement with the calculated values for the hydrochloride, C₂₀H₂₆ON₃Cl. The ultraviolet-visible absorption spectrum is like that for prodigiosin perchlorate⁵ with a main absorption maximum in isopropyl alcohol at 540 m μ ($\epsilon = 7.07 \times 10^4$) and a second very much weaker maximum at 294 m μ ($\epsilon = 1.08 \times 10^4$). The addition of aqueous sodium hydroxide to a solution of the magenta colored solid in isopropyl alcohol gave a mixture exhibiting absorption like that for prodigiosin with λ_{max} 468 m μ ($\epsilon = 4.2 \times 10^4$). The observed⁵ maximum

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(3) O. M. Efimenko, G. A. Kutnesova, and P. A. Yakimov, *Biokhimiya*, **21**, 416 (1956).

(4) Estimated by us from reported curve.

(5) A. J. Castro, A. H. Corwin, F. J. Waxham, and A. L. Beilby, submitted for publication in *J. Org. Chem.*

absorption for pure prodigiosin in isopropyl alcohol occurs at $466\text{ m}\mu$ ($\epsilon\ 4.3 \times 10^4$). Moreover, a mixture of the magenta solid with prodigiosin hydrochloride, m.p. $148.5\text{--}150.0^\circ$ (dec.), prepared from prodigiosin, showed no depression of the melting point and the infrared spectra for the two hydrochlorides are identical.

We attribute the presence of the hydrochloride in our chromatogram to an artifact arising from the introduction of traces of hydrogen chloride, or hydrochloric acid, during working up the mixture derived from the perchlorate. We were able to isolate 33.3 mg. of pure hydrochloride from the reaction of 2.00 g. of prodigiosin perchlorate with sodium hydroxide. Aside from operational losses, this corresponds to a yield of 2% and the combination of prodigiosin with 3.4 mg. of hydrogen chloride.

The compound described by the Russian workers is apparently identical with ours, as far as a comparison can be made. However, it should be pointed out that their product was derived by way of a process wherein the bacterial pigment was treated in one step with sodium hydroxide. We have observed an immediate change in color from that for the acid derivative (red) to that for the free base (orange) when sodium hydroxide is added to an isopropyl alcohol solution of the salt. Therefore, it cannot be unequivocally concluded from the earlier work that prodigiosin hydrochloride is a bacterial product. While it is possible that the conditions employed in the earlier study may have permitted incomplete reaction of any hydrochloride present, it would seem that another explanation, such as used to explain our results, should be considered.

EXPERIMENTAL

Magenta solid derived from prodigiosin perchlorate. The solid was isolated and purified as has already been described.⁵

Anal. Calcd. for $\text{C}_{20}\text{H}_{26}\text{ON}_2\text{Cl}$: C, 66.74; H, 7.28; N, 11.68; Cl, 9.86. Found: C, 66.90; H, 7.51; N, 11.56; Cl, 9.68.

The ultraviolet-visible absorption spectra were determined with a Beckman Model DU spectrophotometer. The spectrum for the magenta solid was measured using a solution containing 0.928 mg. of the compound per 100 ml. of isopropyl alcohol solution. The spectrum for the free base derived from the magenta solid was measured using the mixture obtained by adding 0.20 ml. of 0.507*N* aqueous sodium hydroxide to 9.80 ml. of a solution having 1.240 mg. of the magenta colored solid per 100 ml. of isopropyl alcohol solution.

Prodigiosin hydrochloride. One hundred milligrams of prodigiosin, m.p. $152.0\text{--}153.0^\circ$ (dec.) was dissolved in about 15 ml. of petroleum ether and dry hydrogen chloride was added to the resulting solution until precipitation of the hydrochloride was complete. The mixture was stored in a refrigerator for an hour and the solid removed by filtration. After one recrystallization from a mixture of benzene and petroleum ether 65 mg. of magenta colored hydrochloride, m.p. $148.5\text{--}150.0^\circ$ (dec.) was obtained.

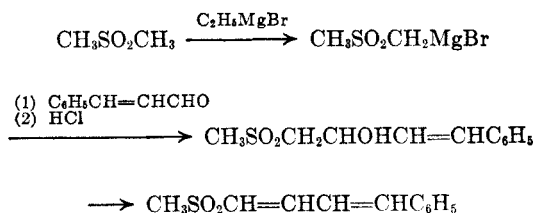
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Preparation of 1-Methylsulfonyl-4-phenyl-1,3-butadiene

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In connection with a study of conjugated sulfones, we required 1-methylsulfonyl-4-phenyl-1,3-butadiene. It was prepared by the following sequence:



EXPERIMENTAL

3-Hydroxy-4-methylsulfonyl-1-phenyl-1-butene. A solution of ethylmagnesium bromide (prepared from 4.5 g. of magnesium, 20.8 g. of ethyl bromide and 100 ml. of ether) was added to 16.5 g. (0.18 mole) of dimethyl sulfone in 750 ml. dry anisole. A bulky white precipitate separated. The mixture was stirred by means of a liquid-sealed mechanical stirrer and heated on a water bath for 3 hr. and then stirred at room temperature for a further 2 hr. A solution of 16.5 g. (0.125 mole) of freshly distilled cinnamaldehyde in 50 ml. dry anisole was then added rapidly and stirring continued at room temperature for 16 hr. The reaction product was hydrolyzed with hydrochloric acid (2.5*N*, 100 ml.). The aqueous layer was separated and extracted with two 25-ml. portions of benzene. The benzene extract together with the anisole layer was washed thrice with 50-ml. portions of a saturated solution of sodium chloride and dried over anhydrous sodium sulfate. The solvents were removed under reduced pressure, the solid residue collected and washed with a few ml. of light petroleum (b.p. $70\text{--}80^\circ$). The yield of the crude product was 25.2 g. (90%). It crystallized as colorless plates from benzene and melted at $111\text{--}112^\circ$.

Anal. Calcd. for $\text{C}_{11}\text{H}_{14}\text{O}_3\text{S}$: C, 58.4; H, 6.2; S, 14.2. Found: C, 58.4; H, 5.9; S, 14.4.

The *acetate*, prepared with acetic anhydride and pyridine, crystallized from ethanol as needles, m.p. $85\text{--}86^\circ$.

Anal. Calcd. for $\text{C}_{13}\text{H}_{18}\text{O}_4\text{S}$: C, 58.2; H, 6.0. Found: C, 58.8; H, 6.2.

The *benzoate*, prepared in the usual manner, crystallized from ethanol as needles, m.p. $146\text{--}147^\circ$.

Anal. Calcd. for $\text{C}_{18}\text{H}_{22}\text{O}_4\text{S}$: C, 65.4; H, 5.5. Found: C, 65.7; H, 5.7.

1-Methylsulfonyl-4-phenyl-1,3-butadiene. A suspension of 2 g. of the foregoing hydroxy unsaturated sulfone in 4 ml. of 85% phosphoric acid was heated under reflux for 15 min., cooled, and diluted with water. A pasty mass was thrown out. It was dissolved in 50 ml. of hot benzene and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave a yellow pasty mass which solidified after several days. The yield was 0.6 g. (32%). Recrystallization from ethanol gave colorless needles, m.p. $89\text{--}90.5^\circ$.

Anal. Calcd. for $\text{C}_{11}\text{H}_{12}\text{O}_2\text{S}$: C, 63.4; H, 5.8. Found: C, 63.1; H, 5.6.

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