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INVESTIGATION OF THE REACTION OF SULFUR WITH ORGANIC COMPOUNDS

IX. A New Method for Synthesizing 5-Aryl-1,2-dithiol-3-thiones*

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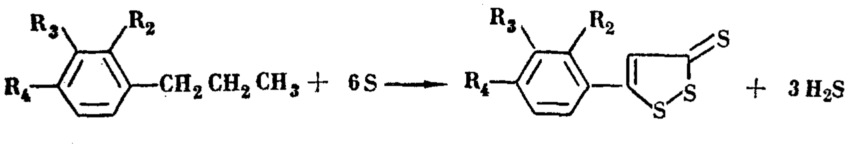
A new method for synthesizing 5-aryl-1, 2-dithiol-3-thiones is worked out. It is based on sulfuration of nuclear-substituted n-propylbenzenes in the presence of mercaptobenzothiazole.

The basic method of synthesizing 5-aryl-1, 2-dithiol-3-thiones (II) is the reaction of sulfur with aryl olefins [2–9], 9], or phosphorus pentasulfide with esters of β-ketocarboxylic acids and ketones [10–12]. However, in a number of cases, the possibilities of using these methods are limited, since the starting materials are expensive and not readily accessible, and low yields are characteristic. At the same time, II, especially 5-(p-methoxyphenyl)-1,2-dithiol-3-thione, has found application in medicine as a liver and gall bladder stimulant [13–17]. Because of this, the search for new synthetic routes to II is of definite interest.

An attempt to prepare 5-phenyl-1, 2-dithiol-3-thione by the action of sulfur on n-propylbenzene was unsuccessful [18]. It must be assumed that this failure was due to the low temperature at which the reaction was carried out (160° C), as one of us [19] previously observed that it was possible to sulfurate a n-alkyl chain linked to a benzene ring in the case of n-butyl benzene, which sulfur converted to 2-phenylthiophene. Actually, we succeeded in showing that a 30–40% yield of 5-aryl-1, 2-dithiol-3-thione (II) is obtained when sulfur reacts with nuclear substituted n-propylbenzenes (I) in the presence of mercaptobenzothiazole catalyst [20].



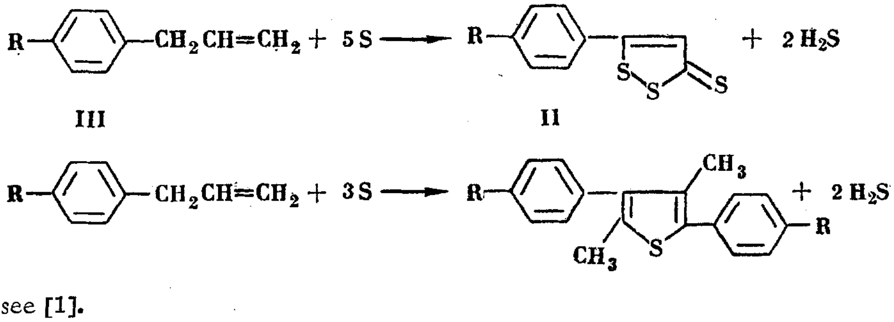
I II

(R_2 = H; R_3, R_4 = alkyl, alkoxyl, etc.)

Other catalysts, e.g., diphenylguanidine, mercuracetamide, which give good results in the synthesis of 4-aryl-1, 2-dithiol-3-thiones from cumene and its derivatives [21], lead to marked resinification, so that the yield of II is negligible. The yields of II are favorably affected by carrying out the reaction in media which are inert to sulfur (mesitylene, 1, 2, 4-trichlorobenzene). It did not prove possible to obtain the corresponding II (R_2 = R_4 = H) by the action of sulfur on n-propylbenzene.

With an o-substituted n-propylbenzene (e.g., o-propyltoluene), the reaction with sulfur leads to resinification, and it is not possible to isolate the corresponding II. A similar picture is found in the action of sulfur on o-substituted isopropylbenzenes [21].

It was also of interest to investigate the reaction of sulfur with nuclear-substituted 1-phenylpropenes (III), since the yields of II which they give are quite small and do not exceed 20% [22]. Ordinarily, the reaction with sulfur is carried out using a 4-fold excess of the latter, and at 200–220° C. A considerable amount of thiophene is formed along with the II:



III II

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* For Part VIII see [1].

This makes it quite difficult to isolate and purify the II.

We investigated the reaction of sulfur with III in the presence of mercaptobenzothiazole catalyst, plus a solvent. In mesitylene, reaction could be brought about even at 180–185°C. Then, however, some excess of arylpropene had to be taken, to secure the necessary reaction mixture temperature, since there is practically no reaction at the boiling point (168°C) of mesitylene. It was not possible to recover unreacted III.

When 1, 2, 4-trichlorobenzene is used as the solvent the reaction proceeds at 210–215° C, so that it is unnecessary to use a catalyst. The II formed is precipitated on cooling the reaction products, and can easily be separated and purified. Still, it proved impossible to raise the yield of II to anything like that previously obtained.

Table 1 gives physical constants, analytical data, synthesis conditions, and yields for the 5-aryl-1, 2-dithiol-3-thiones prepared.

Table 1

5-Aryl-1, 2-dithiol-3-thiones (II, R_2 = H), and the Conditions Used for Synthesizing Them

Compound number	II		Molar ratio I:S:$C_6H_3Cl_3$	Reaction temperature, ° C	Reaction time, hr	Mp	Appearance of crystals	Formula	Found, %			Calculated, %			Yield, %	
	R_3	R_4							C	H	S	C	H	S	On the initial S	On the initial hydrocarbon
IV*	H	CH_3	1 : 1.5	186—189	20	118,3	Red needles	$C_{10}H_8S_3$	53.87	3.73	42.73	53.63	3.59	42.87	31	—
V*	H	OCH_3	1 : 6 : 2	214—217	8	107	Pale brown fluffy needles	$C_{10}H_8S_3O$	49.98	3.44	39.79	49.96	3.35	40.02	36.9	35.0
V	H	OCH_3	1**: 6 : 2	213—216	5	107	Chocolate-colored needles								24.8	20.7
VI*	—OCH_2O—		1 : 6 : 2	213—214	5	194	Chocolate-colored needles	$C_{10}H_6O_2S_3$	47.36	2.75	37.28	47.02	2.76	37.67	27.2	23.0
VII*	OCH_3	OH	1 : 6 : 2	213—216	4	181	Reddish-brown minute crystals	$C_{10}H_8O_2S_3$	46.50	3.35	37.12	46.82	3.15	37.52	11.3	9.7

* Reference mps: IV 120° [11]; VI 108.5° [4, 6]; VII 195° [4]; VIII 182° C [3].

** Anethole

Experimental

n-Propylbenzene. 30.0 g (1.3 g at) finely-divided sodium was covered with 150 ml dry ether, cooled, and a mixture of 95.0 g (0.6 mole) bromobenzene and 86.0 g (0.7 mole) n-propyl bromide added dropwise. After 24 hr the precipitate of NaBr was filtered off along with unreacted sodium, the ether distilled off and the residue distilled through a column. Yield of n-propylbenzene bp 158–159° C, n_D^{20} 1.4920, 39.1 g or 53.8% based on the starting bromobenzene.

p- and o-propyltoluene (Table 2) were similarly synthesized from the appropriate bromotoluenes.

p-Methoxy-n-propylbenzene (dihydroanethole). 59.0 g (0.4 mole) anethole was hydrogenated at 160° and 20–25 atm in the presence of 5 g Raney Ni. When hydrogen absorption had ceased (4 hr), the autoclave was opened, the products filtered, and distilled through a column. Yield of dihydroanethole 82–84° C (15 mm), n_D^{20} 1.4981 50.0 g, or 84% theory.

Anethole, safrole, and isoeugenol. These were commercially available CP materials. After distilling through a column, they had the constants give in Table 3.

5-(p-Tolyl)-1, 2-ditolyl-3-thione (IV). 28.0 g (0.21 mole) p-n-propyltoluene, 10.0 g (0.31 g at) S, and 0.1 g (0.0006 mole) mercaptobenzothiazole were refluxed together at 186–189° C for 20 hr. Then the products were cooled to 0–5° C for 2 hr. The crystals of IV precipitated were filtered off and washed with hexane-benzene (2 : 1). Yield of unpurified IV, 3.6 g (31%, based on the sulfur taken). Recrystallized from 75% AcOH, IV formed red needle-shaped crystals, mp 118.3° C.

5-(p-Methoxyphenyl)-1, 2-dithiol-3-thione (V). 10.0 g (0.067 mole) dihydroanethole, 12.5 g (0.39 g at) S, 20 g (0.13 mole) 1, 2, 4-trichlorobenzene, and 0.1 g (0.0006 mole) mercaptobenzothiazole were heated together at

Table 2

Starting Nuclear-substituted n-Propylbenzenes (I, R = H)

I		Bp°C (pressure mm)	n_D^{20}	Yield, %
R_2	R_4			
H	H	158—159 (760)	1.4920	54
H	CH_3	64—66 (10)	1.4928	52
CH_3	H	78—80 (12)	1.5103	41
H	CH_3O_3	82—84 (15)	1.4991	84

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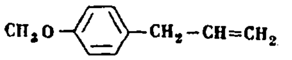
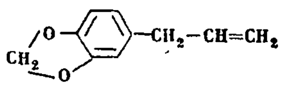
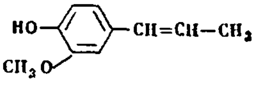
* New compound.

Table 3

Starting Arylpropenes (III)

III		Bp °C (pressure mm)	n_D^{20}
Anethole		115—117 (15)	1.5624
Safrole		105—107 (7)	1.5383
Isoeugenol		137—139 (15)	1.5740

214–217°C for 8 hr. On cooling the reaction products they deposited crystals of V, which were filtered off and washed with hexane-benzene (2:1). Yield of unpurified V 5.6 g (35.0% based on the starting dihydroanethole). Recrystallization from 4.2 g (26.3%) pure V, mp 107° C.

Synthesis of 5-(p-methoxyphenyl)-1,2-dithiol-3-thione (V) from anethole. a) 9.3 g (0.063 mole) anethole, 10.0 g (0.31 g at) S, and 19.0 g (0.12 mole) 1,2,4-trichlorobenzene were heated together at 213–216° C for 5 hr. On cooling, the reaction products deposited crystals of V which were filtered off and washed with hexane-benzene (2:1). Yield of unpurified V, 3.1 g (20.7%, based on the starting anethole). By recrystallizing from 75% AcOH, 2.7 g (18.0%) pure V was obtained, mp 107° C.

b) 7.2 g (0.05 mole) anethole, 6.2 g (0.05 mole) mesitylene, 5.0 g (0.15 g at) S, and 0.05 g (0.0003 mole) mercaptobenzothiazole were heated together at 180–185° for 5 hr. On cooling the reaction products, crystals of V separated, and these were filtered off, and washed with hexane-benzene (2:1). Yield of unpurified V, 2.3 g (19.9%, based on the anethole taken). Recrystallization from 75% AcOH gave 1.1 g (10.1%) pure V, mp 107° C.

Similarly, 5-(3,4-methylenedihydroxyphenyl) 1, 2-dithiol-3-thione (VI) and 5-(3-methoxy-4-hydroxyphenyl)-1,2-dithiol-3-thione (VII) were obtained from safrole and isoeugenol respectively.

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