

### Summary

When ethyl furylacrylate is treated with bromine, an unstable dibromo addition compound is formed which readily loses hydrogen bromide to give ethyl 5-bromofurylacrylate. The isolation and analysis of this intermediate dibromo compound is advanced as supplementary evidence for the prior formation of addition compounds in substitution reactions of aromatic types.

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## SOME DERIVATIVES OF DIPHENYL SULFIDE AND DIPHENYL ETHER

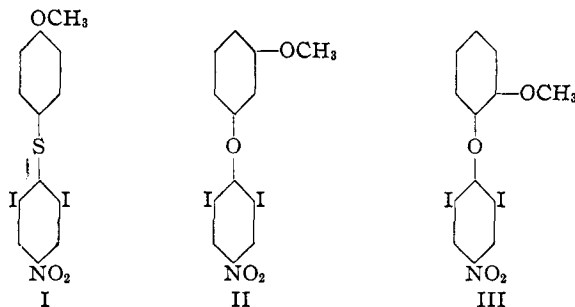
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The importance of the diaryl sulfide and diaryl oxide groupings in compounds which have therapeutic value has been demonstrated in the important work of T. B. Johnson<sup>1</sup> and C. R. Harington,<sup>2</sup> respectively. For this reason it was considered of interest to synthesize some sulfur ether analogs (Formula I) of 2,6-di-iodo-4-nitro-4'-methoxydiphenyl ether and its reduction compound 2,6-di-iodo-4-amino-4'-methoxydiphenyl ether. The latter compounds are intermediates in Harington and Barger's synthesis of thyroxine.<sup>2</sup> It was also considered of importance to prepare some oxygen ether isomers (Formulas II and III) of the above-mentioned compounds, *viz.*, 2,6-di-iodo-4-nitro-3'-methoxydiphenyl ether, 2,6-di-iodo-4-nitro-2'-methoxydiphenyl ether and the corresponding amino compounds.

The ultimate aim in view was to synthesize a sulfur ether analog of thyroxine<sup>3</sup> and also two oxygen ether isomers of thyroxine. Because this



<sup>1</sup> Hilbert and Johnson, *THIS JOURNAL*, **51**, 1526 (1929); Bass and Johnson, *ibid.*, **52**, 1146 (1930).

<sup>2</sup> Harington, *Biochem. J.*, **20**, 293, 300 (1926); Harington and Barger, *ibid.*, **21**, 169 (1927).

<sup>3</sup> This work is now in progress.

was a rather extensive field of investigation, and because of the departure of the junior author from this Laboratory, it was decided to report the work up to date.

In this work the authors have followed, in the main, the methods outlined by Harington and Barger.<sup>2</sup> The two isomers of hydroquinone monomethyl ether, *viz.*, guaiacol and resorcinol monomethyl ether, were condensed with 3,4,5-tri-iodonitrobenzene. The yields of the compounds produced, however, were much smaller than the yield of the corresponding hydroquinone monomethyl ether compound reported by Harington and Barger.<sup>2</sup> The yield in each case, which was really disappointing, apparently falls off as the methoxy group moves from position 4' to position 2'. The use of copper dust and longer periods of refluxing seemed to produce no beneficial results. The reduction of the nitro compounds to the amines was found to be a smooth reaction. For the purpose of identifying the amines, the acetyl derivatives and in some cases the benzoyl derivatives were prepared. The hydrochlorides of the amines were also prepared as a necessary step to subsequent diazotization.

The interaction of 3,4,5-tri-iodonitrobenzene and *p*-methoxythiophenol gave a fairly good yield of the sulfur ether compound. In fact, the yield was comparable to that of Harington's yield of 2,6-di-iodo-4-nitro-4'-methoxydiphenyl ether. Again the experimental conditions, with slight modifications, were those of Harington and Barger.<sup>2</sup> The sulfur ether compound was reduced, the amine acetylated and converted into the hydrochloride without difficulty.

Since these compounds have been prepared by standard methods, only the preparation of 2,6-di-iodo-4-nitro-4'-methoxydiphenyl sulfide will be described. The general properties, analytical data and some of the yields of these substances are given in the tables.

TABLE IA

## DERIVATIVES OF DIPHENYL SULFIDE

No.	Compound	Solvent	Yield, %	Crystal form
1	2,6-Di-iodo-4-amino-4'-methoxy-	(Et) <sub>2</sub> O	64	Gray-white needles
2	2,6-Di-iodo-4-acetylamino-4'-methoxy-	AcOH	Nearly quant.	Nearly colorless needles
3	Hydrochloride of 2,6-di-iodo-4-amino-4'-methoxy-	....	Nearly quant.	Colorless flakes

TABLE IB

## DERIVATIVES OF DIPHENYL SULFIDE

No.	Formula	M. p., °C. (corr.)	Analyses			
			Calcd.	Found		
1	C <sub>13</sub> H <sub>11</sub> ONSI <sub>2</sub>	172-173	I 52.5	I 52.4	I 52.6	
2	C <sub>13</sub> H <sub>13</sub> O <sub>2</sub> NSI <sub>2</sub>	230	I 48.38	I 48.4	I 48.2	
3	C <sub>13</sub> H <sub>12</sub> ONSClI <sub>2</sub>	Decomp. 200	HCl 7.02	HCl 7.27	HCl 7.35	

TABLE IIA  
 DERIVATIVES OF DIPHENYL ETHER

No.	Compound	Solvent	Yield, %	Crystal form
1	2,6-Di-iodo-4-nitro-2'-methoxy	Acetone or AcOH	25	Light gray needles
2	2,6-Di-iodo-4-nitro-3'-methoxy	AcOH	45-50	Yellow needles
3	2,6-Di-iodo-4-amino-2'-methoxy	Benzene	60	Light gray needles
4	2,6-Di-iodo-4-amino-3'-methoxy	(Et) <sub>2</sub> O	60	Light pink needles
5	2,6-Di-iodo-4-acetylamino-2'-methoxy	AcOH	Nearly quant.	White needles
6	2,6-Di-iodo-4-acetylamino-3'-methoxy	Dil. AcOH	Nearly quant.	White needles
7	2,6-Di-iodo-4-benzoylamino-2'-methoxy	EtOH	.....	White needles
8	2,6-Di-iodo-4-benzoylamino-3'-methoxy	EtOH	.....	White needles
9	Hydrochloride of 2,6-di-iodo-4-amino-2'-methoxy	.....	Nearly quant.	Gray-white flakes
10	Hydrochloride of 2,6-di-iodo-4-amino-3'-methoxy	.....	Nearly quant.	Gray flakes

 TABLE IIB  
 DERIVATIVES OF DIPHENYL ETHER

No.	Formula	M. p., °C. (corr.)	Analyses	
			Calcd.	Found
1	C <sub>13</sub> H <sub>9</sub> O <sub>4</sub> NI <sub>2</sub>	149-150	I 51.1	I 51.15 51.44
2	C <sub>13</sub> H <sub>9</sub> O <sub>4</sub> NI <sub>2</sub>	139-140	I 51.1	I 51.1 51.3
3	C <sub>13</sub> H <sub>11</sub> O <sub>2</sub> NI <sub>2</sub>	178-179	I 54.4	I 54.3 54.7
4	C <sub>13</sub> H <sub>11</sub> O <sub>2</sub> NI <sub>2</sub>	124-125	I 54.4	I 54.3 54.2
5	C <sub>15</sub> H <sub>13</sub> O <sub>3</sub> NI <sub>2</sub>	227-228	I 49.9	I 49.8 49.7
6	C <sub>15</sub> H <sub>13</sub> O <sub>3</sub> NI <sub>2</sub>	177-178	I 49.9	I 49.7 50.2
7	C <sub>20</sub> H <sub>15</sub> O <sub>3</sub> NI <sub>2</sub>	239-240	I 44.4	I 44.4 44.6
8	C <sub>20</sub> H <sub>15</sub> O <sub>3</sub> NI <sub>2</sub>	201-202	I 44.4	I 43.9
9	C <sub>13</sub> H <sub>12</sub> O <sub>2</sub> NCII <sub>2</sub>	236-237 (decomp.)	HCl 7.24	HCl 7.14 7.08
10	C <sub>13</sub> H <sub>12</sub> O <sub>2</sub> NCII <sub>2</sub>	132-134 (decomp.)	HCl 7.24	HCl 7.32 7.37

### Experimental Part

**2,6-Di-iodo-4-nitro-4'-methoxydiphenyl Sulfide, III.**—Fifty grams (0.1 mole) of 3,4,5-tri-iodo-nitrobenzene<sup>2,4</sup> and 14 g. (0.1 mole) of *p*-methoxythiophenol<sup>5</sup> were added to 250 cc. of boiling methyl ethyl ketone. To this mixture was added 30 g. of finely powdered, anhydrous potassium carbonate. After heating under a reflux condenser and in a current of hydrogen gas for five hours, the mixture was filtered. On cooling the filtrate, the bright yellow crystals of the pure nitro compound were obtained. On

<sup>4</sup> Kalb, Schweizer, Zellner and Berthold, *Ber.*, 59, 1869 (1926).

<sup>5</sup> Prepared from *p*-anisidine by the method of Leuckart, *J. prakt. Chem.*, 41, 179 (1890).

evaporating the mother liquor the yield was increased. It was readily crystallized from acetone or methyl ethyl ketone. It melted at 138–139° (corr.) and the yield was 30 g. or 60%.

*Anal.* Calcd. for  $C_{18}H_{19}O_3NSI_2$ : I, 49.5. Found: I, 49.7, 49.2.

### Summary

1. Some new derivatives of diphenyl sulfide and diphenyl ether have been prepared.
2. This work, with the possibility of leading to thyroxine-like compounds, is being continued.

EDMONTON, ALBERTA, CANADA

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

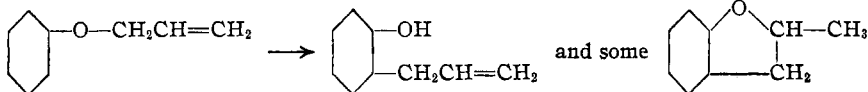
## THE PYROLYSIS OF ALLYL ARYL SULFIDES

BY CHARLES D. HURD AND HARRY GREENGARD

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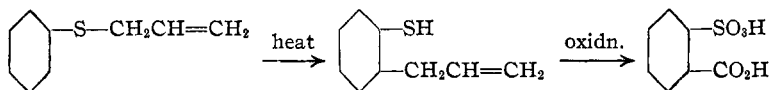
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The most striking property of allyl aryl ethers is their rearrangement<sup>1</sup> into *o*-allylphenols when they are heated. In some instances small yields of the isomeric methylcoumaranes have been observed as by-products. Allyl phenyl ether, for example, rearranges into *o*-allylphenol (80% yield) and 2-methylcoumarane (5% yield) by refluxing for six hours.



By analogy, one would infer that allyl aryl thioethers should rearrange similarly, if an ortho position is available, into *o*-allylthiophenols. Small amounts of dihydrothionaphthenes, the sulfur analogs of the coumaranes, might also be anticipated.

This problem has been approached by studying allyl phenyl sulfide and allyl *p*-tolyl sulfide, both of which were prepared in nearly quantitative yields from allyl bromide and the sodium salt of the aryl mercaptan. Allyl phenyl sulfide gradually undergoes rearrangement into *o*-allylthiophenol by refluxing, as witnessed by the increase in the boiling temperature during six hours from 207 to 240°. The *o*-allylthiophenol was identified by analysis of its lead salt, and by oxidation into *o*-sulfobenzoic acid



There is some evidence for the belief that a small amount of the hitherto undescribed 2-methyl-2,3-dihydrothionaphthene, A, was also formed during

<sup>1</sup> For a survey of this topic, see Hurd, "The Pyrolysis of Carbon Compounds," The Chemical Catalog Co., Inc., New York, 1929, pp. 214–228.