REACTIONS OF HALOMETAL ALKOXIDES

XXI. A New Method of Synthesizing Sulfides of the Thiophene Series*

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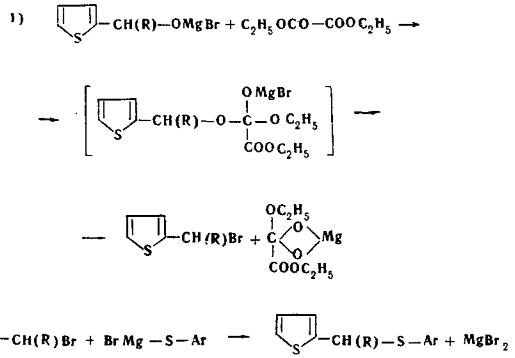
Aryl thenyl and aryl aryl-α-thienylmethyl sulfides have been obtained by the action of oxalic acid esters on an equimolecular mixture of bromomagnesium thienyl or aryl α-thienyl carbinolates and bromomagnesium thiophenolates (or thionaphtholates). Derivatives of the sulfides, sulfoxides and sulfones, are also described.

In previous publications [1,2] a new and convenient method for synthesizing unsymmetrical sulfides of the aromatic series has been described which consists of the reaction of halomagnesium alkoxides of primary and secondary aromatic alcohols with halomagnesium thiophenolates in the presence of esters of formic or oxalic acid. The method is based on a reaction discovered previously [3–5] in which the action of the esters mentioned above on halomagnesium carbinolates of the aromatic series leads to halogen derivatives. If this reaction is carried out in the presence of a halomagnesium thiophenolate, the latter reacts with the halogen derivative which leads to the formation of sulfides. The conditions for carrying out the reactions are so mild that it is suitable even for obtaining sulfides of the furan series [6].

In the present paper it is shown that this method can also be used for the synthesis of sulfides of the thiophene series.



where R = H or Ar′

The halomagnesium alkoxides required for the synthesis of the sulfides can be obtained not only from the previously-synthesized carbinols but also by organomagnesium synthesis directly in the process of preparation of the sulfide. In this case, the reaction mixture contains the previously prepared halomagnesium carbinolate. Only an excess of the Grignard reagent sufficient for the subsequent conversion of the thiophenol into the halomagnesium thiophenolate is necessary. The sulfides so synthesized have been oxidized to sulfoxides and sulfones with 30% hydrogen peroxide [7,8]. All the sulfides and also the sulfoxides and sulfones have been obtained for the first time (see Tables 1 and 2).

In spite of the fact that some of the sulfoxides (p-tert-butylphenyl phenyl-α-thienylmethyl, p-chlorophenyl phenyl-α-thienylmethyl, o-methoxyphenyl phenyl-α-thienylmethyl, and o-methoxyphenyl p-tolyl-α-thienylmethyl sulfoxides) each have two centers of asymmetry and consequently can form two racemates, constant melting points were obtained after only three recrystallizations.

EXPERIMENTAL*

Synthesis of sulfides from previously synthesized alcohols. In the usual manner, 0.2 mole of ethylmagnesium or propylmagnesium bromide was prepared in a three-necked flask fitted with a reflux condenser, stirrer with seal, and dropping funnel, and with the flask cooled in ice-water, a mixture of 0.1 mole of an alcohol and 0.1 mole of a thiophenol dissolved in three times the volume of anhydrous ether was added dropwise. The resulting mixture was heated for 10–15 minutes with the ether boiling to complete the formation of the bromomagnesium carbinolate and the thiophenolate. After the addition of 0.1 mole of diethyl oxalate, the reaction mixture was again heated in the water bath until the initially viscous precipitate had crystallized (2–4 hr) and was then hydrolyzed with water and 10% acetic acid. In order to eliminate the thiophenol that had not reacted, the ethereal layer, after separation from the aqueous layer, was washed with 10% NaOH solution and then with water, after which it was dried with anhydrous Na_2SO_4, the solvent was distilled off, and the sulfide formed was purified by vacuum distillation or by recrystallization from ethanol.

Synthesis of sulfides with the simultaneous production of the alcohols. In order to obtain the bromomagnesium aryl α-thienyl carbinolate, ethereal solutions of 0.1 mole of α-thienylmagnesium bromide and 0.1 mole of an aromatic aldehyde were mixed in a flask with ice-water cooling. Simultaneously, in another flask, the bromomagnesium thiophenoxide was prepared by adding an ethereal solution of 0.1 mole of ethylmagnesium or propylmagnesium bromide to 0.1 mole of the thiophenol. The contents of the flasks were mixed and then 0.1 mole of diethyl oxalate was added to the mixture. The further operations have been described above.

Synthesis of the sulfoxides and sulfones. The aryl phenyl and aryl α-thienylmethyl sulfides were obtained by the oxidation of the sulfides with 30% hydrogen peroxide taken in 5–7% excess in glacial acetic acid at room temperature for 18–20 hr with subsequent dilution with water and, in some cases, neutralization of the solution with caustic alkali or sodium carbonate [7, 8]. All the sulfoxides obtained were isolated in the crystalline state or in the form of heavy oils which rapidly crystallized.

Phenyl thenyl and p-tert-butylphenyl thenyl sulfones were obtained by oxidizing the sulfoxides dissolved in acetic acid with 30% hydrogen peroxide for 1 1/2 hr in the boiling water bath. The other sulfones

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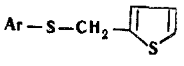
*For part XX, see [9].

*Students N. M. Bezdomnikova and Yu. A. Galishevskii took part in the experimental work.

Table 1

Aryl Thenyl and Aryl Aryl-α-thienylmethyl Sulfides



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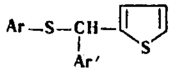

Reactants		Compound	Mp, °C;bp °C (pressure,mm)	Empirical formula	S, %		Yield, %
					found	calculated	
Benzaldehyde	Bromomagnesium thiophenolate	Phenyl phenyl-α-thienylmethyl sulfide	44—45	$C_{17}H_{14}S_2$	22.51	22.70	55
Phenyl α-thienyl carbinol	Thiophenol	Phenyl phenyl-α-thienylmethyl sulfide	45	$C_{17}H_{14}S_2$	22.55	22.70	80
Benzaldehyde	Bromomagnesium p-thiocresolate	p-Tolyl phenyl-α-thienylmethyl sulfide	53.5—54	$C_{18}H_{16}S_2$	21.50	21.62	58
Phenyl α-thienyl carbinol	p-Thiocresol	p-Tolyl phenyl-α-thienylmethyl sulfide	54	$C_{18}H_{16}S_2$	21.42	21.62	76
Phenyl α-thienyl carbinol	p-tert-Butylthiophenol	p-tert-Butylphenyl phenyl-α-thienylmethyl sulfide	42.7—43 (from methanol)	$C_{21}H_{22}S_2$	19.03	18.90	74
p-Tolualdehyde	o-Methoxythiophenolate	o-Methoxyphenyl p-tolyl-α-thienylmethyl sulfide	73	$C_{19}H_{18}OS_2$	19.45	19.66	44
p-Tolyl α-thienyl carbinol	o-Methoxythiophenol	o-Methoxyphenyl p-tolyl-α-thienylmethyl sulfide	73	$C_{19}H_{18}OS_2$	19.81	19.66	53
p-Tolyl α-thienyl carbinol	p-Chlorothiophenol	p-Chlorophenyl p-tolyl-α-thienylmethyl sulfide	69 (from petroleum ether)	$C_{18}H_{15}ClS_2$	19.51	19.30	89

Table 1 (Cont'd)

Reactants		Compound	Mp, °C; bp °C (pressure, mm)	Empirical formula	S, %		Yield, %
					found	calculated	
Benzaldehyde	Bromomagnesium p-chlorothiophenolate	p-Chlorophenyl phenyl-α-thienylmethyl sulfide	44	$C_{17}H_{13}ClS_2$	20.19	20.20	60
Benzaldehyde	Bromomagnesium o-methoxythiophenolate	o-Methoxyphenyl phenyl-α-thienylmethyl sulfide	99	$C_{18}H_{16}OS_2$	20.59	20.58	60
Benzaldehyde	Bromomagnesium α-thionaphtholate	α-Naphthyl phenyl-α-thienylmethyl sulfide	65.5—66	$C_{21}H_{16}S_2$	19.28	19.21	52
p-Tolualdehyde	Bromomagnesium thiophenolate	Phenyl p-tolyl-α-phenylmethyl sulfide	52	$C_{18}H_{16}S_2$	21.50	21.62	55
p-Tolualdehyde	Bromomagnesium p-thiocresolate	p-Tolyl p-tolyl-α-thienylmethyl sulfide	68.5—69	$C_{19}H_{18}S_2$	20.60	20.65	77
p-Tolualdehyde	Bromomagnesium α-thionaphtholate	α-Naphthyl p-tolyl-α-thienylmethyl sulfide	87	$C_{22}H_{18}S_2$	18.78	18.50	44
α-Thienyl carbinol	Thiophenol	Phenyl α-thenyl sulfide[a]	152—153 (7)	$C_{11}H_{10}S_2$	30.92	31.08	72
α-Thienyl carbinol	p-Thiocresol	p-Tolyl α-thenyl sulfide[b]	164—165 (7)	$C_{12}H_{12}S_2$	28.97	29.10	64
α-Thienyl carbinol	p-tert-Butylthiophenol	p-tert-Butylphenyl α-thenyl sulfide[c]	187—188 (8)	$C_{15}H_{18}S_2$	24.81	24.89	67

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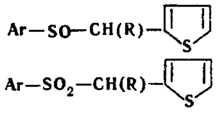
a) d_4^{20} 1.1909; n_D^{20} 1.6360; MR_D 62.09; Calculated 62.50; b) d_4^{20} 1.1585; n_D^{20} 1.6205; MR_D 66.85; Calculated 67.12; c) d_4^{20} 1.0994; n_D^{20} 1.5930; MR_D 80.78; Calculated 81.02.

Table 2

Sulfoxides and Sulfines of the Thiophene Series



Compound	Mp, • C	Solvent for recrystallization	Empirical formula	S, %		Yield, %
				found	calculated	
Phenyl α-thenyl sulfoxide	80	Petroleum ether	$C_{11}H_{10}OS_2$	28.72	28.84	98
Phenyl α-thenyl sulfone	138	Ethanol	$C_{11}H_{10}O_2S_2$	26.74	26.90	88
p-Tolyl α-thenyl sulfone	101	Gasoline	$C_{12}H_{12}O_2S_2$	25.32	25.41	99
p-tert-Butylphenyl α-thenyl sulfoxide	51	Petroleum ether	$C_{15}H_{18}OS_2$	22.91	23.03	82
p-tert-Butylphenyl α-thenyl sulfone	87	Gasoline	$C_{15}H_{18}O_2S_2$	21.75	21.78	90
p-tert-Butylphenyl phenyl-α-thienylmethyl sulfoxide	87.5—88	Ethanol	$C_{21}H_{22}OS_2$	17.90	18.08	72
p-Chlorophenyl phenyl-α-thienyl methyl sulfoxide	80	Methanol	$C_{17}H_{13}ClOS_2$	19.45	19.22	61
o-Methoxyphenyl p-tolyl-α-thienylmethyl sulfoxide	117	Ethanol	$C_{19}H_{18}O_2S_2$	18.90	18.85	53
o-Methoxyphenyl phenyl-α-thienylmethyl sulfoxide	113	Ethanol	$C_{18}H_{16}O_2S_2$	19.90	19.65	66
Phenyl phenyl-α-thienylmethyl sulfone	173—174 (decomp.)	Petroleum ether	$C_{17}H_{14}O_2S_2$	20.10	20.38	40
p-Tolyl phenyl-α-thienylmethyl sulfone	185—187 (decomp.)	Ethanol	$C_{18}H_{16}O_2S_2$	19.63	19.51	42
α-Naphthyl phenyl-α-thienylmethyl sulfone	193—195 (decomp.)	Ethanol	$C_{21}H_{16}O_2S_2$	18.60	18.39	43
p-Chlorophenyl p-tolyl-α-thienylmethyl sulfone	163—164	Petroleum ether	$C_{18}H_{15}ClO_2S_2$	17.54	17.41	41

were obtained by oxidizing the corresponding sulfides in acetic acid with 30% hydrogen peroxide at 30°–35° C for 20–24 hr.

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