[CONTRIBUTION FROM RESEARCH AND DEVELOPMENT DIVISION, CONSOLIDATION COAL COMPANY]

Ring Alkylation of Aromatic Thiols[1]

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A procedure has been developed for ring alkylation of thiophenols based on boron trifluoride–catalyzed reaction with isobutylene or by disproportion of the appropriate *t*-butyl sulfide with the parent thiol. The *t*-butyl derivatives of thiophenol, *o*-thiocresol, and 2,6-dimethylthiophenol have been prepared. Substitution occurs exclusively *para*. Therefore, thiophenols substituted in the *para* position, *e.g.*, *p*-thiocresol, do not yield any ring-substituted product. Reaction of thiophenol with propylene produced *o*-isopropylthiophenol in low yield. Ethylation of thiophenol did not occur using this technique.

Ring alkylation of aromatic thiols with olefins is difficult because of the reactivity of the thiol group and the stability of resulting alkyl sulfides. The resistance of sulfides to cleavage[4] by acid catalysts was compared with their oxygen analogs by Tarbell. The aluminum chloride–catalyzed ring alkylation of thiophenol, *o*-thiocresol, and *o*-ethyl thiophenol with *t*-butyl alcohol or *t*-amyl mercaptam was claimed in a recent patent.[5] The properties of the resulting alkyl derivatives were not described.

We have succeeded in the ring alkylation of thiophenol, *o*-thiocresol, and 2,6-thioxylenol with isobutylene or by disproportionation of the appropriate *t*-butyl sulfide with the parent thiol. Boron trifluoride was used as a catalyst. Substitution occurs exclusively *para*.[6] Reaction of thiophenol with propylene produced isopropylthoiphenol in low yield. The isopropylthiophenol appears to be entirely *ortho*-substituted. Ethyl thiophenols could not be synthesized by this technique.

EXPERIMENTAL

Starting materials. Thiophenol (99% minimum purity) was purchased from Evans Chemetics, Inc.

o-Thiocresol and *p*-thiocresol were purchased from Eastman Kodak Co. (White Label) and used without further purification.

2,6-Thioxylenol was synthesized by the procedure of Bartkus *et al.*,[6] thiol content 99%.

The *t*-butyl thioethers were synthesized by the procedure of Ipatieff *et al.*,[7] using equal weights of 75% sulfuric acid and thiophenol with a slight molar excess of isobutylene. The reaction was carried out in an autoclave. Essentially quantitative yields of thioethers were obtained. The crude thioether was purified by distillation, a center cut being retained for further synthesis.

The reactants and catalyst were added at room temperature to a 300-ml. Aminco rocking autoclave or a 2 l. stirred Parr autoclave depending on the scale of operation. After the reaction was completed, the catalyst was neutralized. The thiols were extracted with aqueous sodium hydroxide in a nitrogen atmosphere. The sodium hydroxide extract was neutralized with sulfuric acid. The organic layer was washed with water and azeotropically dried with toluene. The dried product was fractionated *in vacuo* on a 25 × 120 cm. Vigreux distillation column. The caustic insoluble fraction was analyzed by distillation.

DISCUSSION OF RESULTS

An interesting facet of this study was the observation that boron fluoride does not form stable complexes with aromatic thiols. A saturated solution of boron trifluoride in thiophenol at room temperature contains less than 2% boron fluoride. Reaction of a saturated solution with isobutylene will occur in an open system for a short time. The excess olefin sweeps out the boron trifluoride, and the reaction stops. Simultaneous addition of boron fluoride and olefin permits reactions to be carried out at 1 atm. The use of a pressure vessel is much more efficient in minimizing the amount of boron trifluoride required.

A series of experiments was carried out in which equimolar amounts of *t*-butyl phenyl sulfide and thiophenol were treated with 10% boron trifluoride in an autoclave. The temperature was varied from 80 to 140°. Yields of 4-*t*-butyl thiophenol varied from 58% to 81% based on sulfide charged. The major by-product is 4-*t*-butylphenyl *t*-butyl sulfide. A reaction temperature of 80° for 4 hr. appears optimum based on the recovery of 4-*t*-butyl thiophenol in 81% yield. No *o*-*t*-butyl thiophenol could be detected by precision fractionation. In order to show that an open *para* position was required for ring alkylation, *t*-butyl-*p*-tolyl sulfide was treated with *p*-thiocresol at 80°. No reaction occurred; the starting material was recovered unchanged. Reaction of the *t*-butyl thioether of 2,6-thioxylenol with an equimolar amount of 2,6-thioxylenol produced 4-*t*-butyl-2,6-dimethylthiophenol in 55% yield.

Direct *t*-butylation of thiophenol was explored. The results are shown in Table I. At 80°, the yield of 4-*t*-butyl thiophenol was 64%. The principal by-products are the *t*-butyl sulfide and the *t*-butyl sulfide of 4-*t*-butyl thiophenol. Higher molecular weight sulfides and diphenyl disulfide make up the higher boiling fraction. The results, while incomplete, suggest that under optimum conditions the same yield of 4-*t*-butyl-thiophenol could be obtained by direct alkylation as shown previously for the disproportionation of *t*-butyl phenyl sulfide. Direct alkylation of *o*-thiocresol at 80° produced a 44% yield of the 4-*t*-butyl derivative.

An authentic sample of 4-*t*-butyl thiophenol was synthesized by reaction of *t*-butylbenzene with chlorosulfonic acid. The resulting sulfonyl chloride was reduced using zinc and sulfuric acid. The crude thiol was distilled on a high efficiency fractionating column to produce a heart cut analyzing 97% *t*-butylthiophenol by silver nitrate titration.

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TABLE I

SYNTHESIS OF ALKYLATED THIOPHENOLS BY DIRECT ALKYLATION

Experiment	Temp., °C.	Time, Hr.	BF_3, Wt. %	Mol. Ratio Thiol/ Olefin	Conversion of Thiol, %	Yields, Mol. % Converted Thiol: Alkyl thiol	Alkyl aryl sulfide	Alkyl aryl alkyl sulfide
1	120	2	5	2.0	33	58	12	12
2	80	6	5	1.4	71	64	5	10
3 (*o*-thiocresol)	80	6	10	0.8	71	44	—	—
4 (propylene	80	5	6	1.1	48	19	32	—
5 (propylene)	140	4	9	1.2	76	14	40	9
6 (*p*-thiocresol-propylene)	80	2	10	0.5	45	25	14	21

TABLE II

PROPERTIES AND ANALYSES OF ALKYL THIOPHENOLS AND DERIVATIVES

Compound	Derivative	B.P., °C.	M.P., °C.[a]		Analysis: Calculated C	Calculated H	Calculated S	Found C	Found H	Found S
4-*t*-Butyl thiophenol		120 (20)[b]		$C_{10}H_{14}S$	72.23	8.48	19.28	72.10	8.40	19.77
	2,4-Dinitrophenyl sulfide		130.2–131.5	$C_{16}H_{16}O_4N_2S$	57.82	4.85		57.99	5.65	
4-*t*-Butyl, 2-methyl thiophenol		117 (10)		$C_{11}H_{16}S$	73.27	8.95	17.78	73.16	8.91	16.79
	2,4-Dinitrophenyl sulfide		140.5–142.5	$C_{17}H_{18}O_4N_2S$	58.94	5.24		58.60	5.25	
4-*t*-Butyl, 2,6-dimethyl thiophenol		126 (10)	44–46	$C_{12}H_{18}S$	74.17	9.33		74.28	9.36	
	2,4-Dinitrophenyl sulfide		192–193	$C_{18}H_{20}O_4N_2S$	59.98	5.60	8.90	60.24	5.72	8.00
t-Butyl-*p*-*t*-butylphenyl sulfide		132 (10)	49.5–51	$C_{14}H_{22}S$	75.61	9.97	14.41	75.23	10.01	14.25
2-Isopropyl, 4-methyl thiophenol		115 (20)		$C_{10}H_{14}S$	72.23	8.48		72.42	8.28	
2-Isopropylthiophenol		100 (20)		$C_9H_{12}S$	71.00	7.95	21.05	70.64	8.25	20.20

[a] All melting points corrected. [b] Distillation pressure, mm.

The boiling point agreed with the published value of Strating and Backer.[8] The infrared spectrum in the 5 to 6 μ region corresponds to a *para*-substituted benzene. Air oxidation of the thiol in the presence of ammonia produced the disulfide m.p. 88.5–89.5°, in agreement with the literature value.[9] In addition, a 2,4-dinitrophenyl sulfide was prepared by reaction with 2,4-dinitrochlorobenzene. The melting points of the disulfide and dinitrophenyl sulfide produced from the butylated thiophenol were identical to the respective values of the authentic samples. The mixed melting points of the appropriate pairs were undepressed.

Direct alkylation of thiophenol with propylene produced low yields of isopropyl thiophenol. (Cf. Experiments 4 and 5, Table I). Increasing the reaction temperature to 140° did not improve the yield. Substitution appears to be entirely *ortho*. The identity of the isopropyl thiophenol was established by comparison of the infrared spectrum with the spectra of authentic samples[10] of *ortho*- and *para*-isopropyl thiophenol.

While *t*-butylation of *p*-thiocresol was unsuccessful, propylation of *p*-thiocresol did yield 2-isopropyl-4-methylthiophenol in 25% yield.

The properties and analyses of the alkylated thiophenols and characterizing 2,4-dinitrophenyl sulfides are shown in Table II.

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(10) The authentic samples were prepared by Dr. R. J. Laufer, of our laboratory, by reacting the appropriate cumidines with potassium ethyl xanthate followed by reduction with lithium aluminum hydride.