Friedel-Crafts reaction. 3,5-Dimethyl-4-isoxazolylcarboxylic acid was prepared by the method of Claisen[4] and converted to the acid chloride, b.p. 85°/10 mm., in 90% yield.

The acid chlorides were converted to the following ketones in over 90% yield, using typical Friedel-Crafts procedures (Table I).

The ketones were converted to the following carbinols in 80–85% yield, using lithium aluminum hydride in ether (Table II).

Table III summarizes the physical and biological data for the aminoethers described.

SMITH, KLINE AND FRENCH LABORATORIES
PHILADELPHIA, PA.

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Improved Procedure for Preparation of Aromatic Thiols[1]

E. CAMPAIGNE AND S. W. OSBORN

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The preparation of aromatic thiols from the corresponding aryl ethyl xanthates by alkaline hydrolysis has not been satisfactory in many instances. Yields are relatively low due to loss by oxidation, and to incomplete hydrolysis in the case of hindered xanthates. Although Tarbell and Fukushima[2] report yields of 63–75% in the case of *m*-tolyl ethyl xanthate, we have been unable to duplicate these yields with more hindered compounds. In our hands the conventional method gave at best a yield of only 49% in the case of 2,6-dimethylthiophenol, and even poorer yields in the case of *o*-thiocresol (39%) and *o*-phenylthiophenol (21%). In the latter case, even prolonged hydrolysis (24 hr.), followed by isolation as the disulfide to avoid apparent loss observed in isolation of the less stable thiol, gave at best a 58% yield.

Djerassi, *et al.*,[3] obtained excellent yields of aliphatic mercaptans by reduction of xanthates with lithium aluminum hydride. They also demonstrated that this method was applicable to aryl xanthates by the conversion of *o*-aminophenol *via* the ethyl xanthate to *o*-mercaptophenol in 64% over-all yield, which compares favorably with the variable yields of 30–70% for this compound reported by Greenwood and Stevenson,[4] using alkaline hydrolysis of the xanthate.

Reduction of the xanthates by lithium aluminum hydride proved to be a much more effective method for preparing hindered aromatic thiols. Yields of 84–89% were consistently obtained. For example, reduction of *o*-biphenyl ethyl xanthate with lithium aluminum hydride gave an 84% yield of pure *o*-phenylthiophenol, while even better yields were obtained in the preparation of 2,6-dimethylthiophenol (86%) and *o*-thiocresol (89%) by the reduction of their respective xanthates. With lithium aluminum hydride, the thiol was obtained directly, since loss through oxidation was avoided. Moreover, the method of isolation was both faster and simpler than by alkaline hydrolysis. The by-products of this reductive cleavage were not isolated, but methyl mercaptan was obviously present.

Pure *o*-phenylthiophenol and 2,6-dimethylthiophenol have not previously been reported. These were characterized and converted to their respective disulfides and to their 2,4-dinitrophenyl sulfides.

EXPERIMENTAL

o-Thiocresol (*lithium aluminum hydride method*). *o*-Tolyl ethyl xanthate was prepared by the method of Bourgeois.[5] Fifty-three and five-tenths grams (0.5 mole) of *o*-toluidine was diazotized and added dropwise to 60 g. (0.375 mole) of technical potassium ethyl xanthate. The crude *o*-tolyl ethyl xanthate was extracted with ether and the ethereal solution, after washing with sodium carbonate solution and then with water, was carefully dried over anhydrous sodium sulfate to be used directly without further purification.

The lithium aluminum hydride reduction required a good hood. To 1 l. of anhydrous ether contained in a 3-liter, three necked flask, 19 g. (0.5 mole) of lithium aluminum hydride was added. The resulting slurry was stirred rapidly while the ethereal solution of *o*-tolyl ethyl xanthate was added dropwise at such a rate that the ether refluxed gently without external cooling. Stirring was continued at room temperature for 1 hr. after the addition was complete. One hundred fifty ml. of water was then added dropwise (very carefully!) at such a rate that only a small amount of ether escaped from the reflux condenser. The mixture became thick during this addition and efficient stirring was necessary. Five hundred ml. of 10% sulfuric acid was then added carefully from the separatory funnel to dissolve the precipitated alumina. The ether layer was separated and the aqueous phase extracted twice with ether. The combined ether solutions were washed thoroughly with water and dried over anhydrous calcium chloride. The ether was removed under reduced pressure and the residual thiol was distilled through a short fractionating column. The yields of colorless *o*-thiocresol was 55.2 g. (89% based on *o*-toluidine), b.p 104° (48 mm.).

Alkaline hydrolysis of o-tolyl ethyl xanthate. For comparison purposes the crude xanthate, obtained by evaporation of the ethereal solution described above was hydrolyzed in alcoholic potassium hydroxide, by the conventional method.[2] Although Bourgeois reports adequate yields in the hydrol-

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(3) C. Djerassi, M. Gorman, F. X. Markley, and E. B. Oldenburg, *J. Am. Chem. Soc.*, **77**, 568 (1955).

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ysis of *o*-tolyl ethyl xanthate by this method,[5] the yield obtained in our experiments was not more than 37%, based on the starting material, *o*-toluidine.

2,6-Dimethylthiophenol. Application of the lithium aluminum hydride reduction described above using 60.5 g. (0.5 mole) of 2,6-dimethylaniline as the starting material yielded 59.4 g. (86% overall) of colorless 2,6-dimethylthiophenol, b.p. 111° (25 mm.), n_D^{25} 1.5712, d^{25} 1.038.

Anal. Calcd. for $C_8H_{10}S$: S, 23.20; Found: S, 23.03.

When the crude 2,6-xylyl ethyl xanthate was hydrolyzed in the conventional manner,[2] the yield was 34 g. (49%) based on 60.5 g. (0.5 mole) of 2,6-dimethylaniline.

2,6-Dimethylphenyl disulfide. A solution of 6.9 g. (0.05 mole) of 2,6-dimethylthiophenol, in 15 ml. of ethanol, was treated with 6.7 g. (0.026 mole) of iodine. Upon stirring, the mixture became warm and the disulfide rapidly precipitated. The mixture was cooled and the disulfide was collected by filtration and washed with cold 80% ethanol, yielding 6.65 g. (97%) of light yellow crystals. After three recrystallizations from 80% ethanol, white needles weighing 5.3 g. (77%) were obtained.

Anal. Calcd. for $C_{16}H_{18}S_2$: S, 23.37; Found 23.13.

2,6-Dimethylphenyl 2,4-dinitrophenyl sulfide. A 2,4-dinitrophenyl sulfide was prepared from 2,6-dimethylthiophenol by treating an alcoholic solution of the thiol, containing an equivalent amount of sodium hydroxide solution, with an equimolar quantity of 2,4-dinitrochlorobenzene dissolved in alcohol. After recrystallization from ethanol, yellow needles were obtained which melted at 124.5–125°.

Anal. Calcd. for $C_{14}H_{12}O_4N_2S$: C, 55.25; H, 3.97. Found: C, 55.59; H, 4.01.

o-Phenylthiophenol. When 51.5 g. (0.25 mole) of finely ground *o*-aminobiphenyl hydrochloride was used as the starting material, and the crude xanthate cleaved with lithium aluminum hydride, 39.0 g. (84%) of *o*-phenylthiophenol was obtained, b.p. 105° (0.5 mm.), n_D^{25} 1.6403, d^{25} 1.076.

Anal. Calcd. for $C_{12}H_{10}S$: S, 17.21; Found: S, 16.94.

Alkaline hydrolysis of the crude xanthate prepared from 51.5 g. (0.25 mole) of *o*-aminobiphenyl hydrochloride yielded 9.8 g. (21%) of *o*-phenylthiophenol boiling at 104–105° (0.5 mm.).

o-Phenylthiophenol disulfide.[6] Oxidation with iodine of a crude sample of *o*-phenylthiophenol, prepared by the alkaline hydrolysis of *o*-biphenyl ethyl xanthate, gave the disulfide in 23% yield (based on the original amine). When an aqueous, alkaline solution of *o*-phenylthiophenol (prepared by alkaline hydrolysis of the xanthate for 24 hr. and worked up in the usual way[2]) was treated with equivalent quantities of 3% hydrogen peroxide or ammonium persulfate, the disulfide was obtained directly in 55 and 58% yields, respectively. It precipitated upon standing and was recrystallized from acetone to give pale yellow plates, m.p. 115.5–116°.

Anal. Calcd. for $C_{24}H_{18}S_2$: C, 77.80; H, 4.89; S, 17.31. Found: C, 77.52; H, 5.07; S, 17.21.

o-Biphenyl 2,4-dinitrophenyl sulfide. Treatment of an alkaline alcoholic solution of the above thiol with 2,4-dinitrochlorobenzene produced a yellow solid which, after recrystallization from ethanol, yielded yellow needles, m.p. 132.5–133°.

Anal. Calcd. for $C_{18}H_{12}O_4N_2S$: C, 61.35; H, 3.43. Found: C, 61.58; H, 3.46.

DEPARTMENT OF CHEMISTRY
INDIANA UNIVERSITY
BLOOMINGTON, IND.

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(6) Prepared by Dr. L. Ergener in these laboratories.

Some Azo Derivatives of 9-Ethylcarbazole

HENRY GILMAN AND JULIAN B. HONEYCUTT, JR.

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Since the first azo dye containing the carbazole nucleus was reported in 1888[1] a large number of dyes and pigments incorporating the carbazolylazo group have been prepared by the dyestuff industry. Cohn[2] and Freudenberg[3] give good accounts of the carbazole dyes while the more extensive coverages of Grimmel,[4] Lubs,[5] and Venkataraman[6] include carbazole derivatives in conjunction with other compounds making up the various classes of dyes.

The incentive for the preparation of 9-ethylcarbazole dyes was the reports by Farr[7,8] and Kruger[9,10] on the use of boron-containing compounds in brain tumor therapy. Kruger[10] used boronic acid azo dyes prepared by Snyder[11,12] in place of the borax used previously. We wished to synthesize carbazole derivatives which contained both the azo linkage and a boronic acid group. Two possibilities of preparing the desired compounds were considered. One was coupling diazotized aminobenzeneboronic acids, prepared by Johnson and coworkers,[13,14] with 9-ethylcarbazole and the other was condensing diazotized 3-amino-9-ethylcarbazole with hydroxybenzeneboronic acids.[14,15] Prior to use of the boron compounds range-finding experiments were performed with more readily available amines and phenols and we are now reporting the results of those experiments.

Diazotized 2,4-dinitroaniline and *p*-nitroaniline were sufficiently reactive to couple with 9-ethyl-

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