gave 8.3 g. (64% yield) of jagged blades, m.p. 141.5–142°. This was assigned structure II as 5-amino-3-chloropyridazine on the basis that it caused marked depression of the melting point of I when admixed with it, and that sodium amide is known to cause rearrangements.

Anal. Calcd. for $C_4H_4ClN_3$: C, 37.08; H, 3.11; Cl, 27.57. Found: C, 37.40; H, 3.13; Cl, 27.51.

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Synthesis of Mercaptophenols and Alkyl Derivatives

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Received May 12, 1959

We were interested in studying the behavior of mercaptophenols, containing both phenolic and aromatic mercaptan groups, in free radical processes. The use of a number of thiohydroquinones as polymerization inhibitors has been described by us in a recent patent.[1] A review of the literature indicated relatively few mercaptophenols having a thiocatechol or thiohydroquinone configuration have been described.[2–6] These compounds were usually prepared by reduction of the corresponding sulfonyl chloride.

A synthetic procedure is described in this report based on sulfurization of a phenol with sulfur monochloride. The crude sulfurization product, containing a mixture of monosulfide, disulfide, and polysulfide, is subjected to pressure hydrogenation using supported MoS_2 as a catalyst. The disulfides and polysulfides are reduced to the corresponding thiol.

A study was made of the sulfurization reaction using 2,6-xylenol as a prototype, aimed at maximizing the yield of thiol. The preferred sulfurization procedure was applied to phenol. Thiohydroquinone was recovered. Since thiocatechol was not detected, it was assumed that sulfurization occurred exclusively in the para position. The thiol derived from *o*-cresol was assigned a thiohydroquinone structure. The thiols of 2,4-xylenol, 4-*t*-butyl-*o*-cresol, 6-*t*-butyl-*o*-cresol, 2-*t*-butyl-*p*-cresol, 2-*t*-amylphenol, 2,6-diisopropylphenol, and 2,6-di-*t*-butylphenol were produced by the sulfurization-hydrogenation procedure. All the resulting mercaptophenols except the mercaptans derived from phenol and 2,6-xylenol are new compounds.

(1) U. S. Patent **2,810,765**, M. B. Neuworth and E. B. Hotelling, October 22, 1957.

(2) R. Leuckart, *J. prakt. Chem.*, (2), **41**, 179 (1870).

(3) G. Schwarzenbach and H. Egli, *Helv. Chim. Acta*, **17**, 1176 (1934).

(4) T. Zincke and K. Arnold, *Ber.*, **50**, 116 (1917).

(5) P. Karrer and P. Leiser, *Helv. Chim. Acta*, **27**, 678 (1934).

(6) E. Katscher and H. Lehr, *Monatsh.*, **64**, 236 (1934).

EXPERIMENTAL

Starting materials. 2,6-Xylenol and 2,4-xylenol were purchased from Reilly Tar and Chemical Co. Both materials were redistilled and shown to be pure by infrared analysis. 2-*t*-Amylphenol was obtained from Sharples Chemicals, Inc., and used without further purification. 2,6-Diisopropylphenol and 2,6-di-*t*-butylphenol were purchased from Aldrich Chemical Co., and used without further purification.

6-*t*-Butyl-*o*-cresol and 4-*t*-butyl-*o*-cresol were synthesized by sulfuric acid–catalyzed butylation of *o*-cresol with isobutylene. 6-*t*-Butyl-*o*-cresol was obtained by fractionation of the crude butylation mixture, boiling point 118° (20 mm.). 4-*t*-Butyl-*o*-cresol, the higher boiling isomer, was similarly recovered, boiling point 132° (20 mm.). 2-*t*-Butyl-*p*-cresol was formed by sulfuric acid–catalyzed butylation of excess *p*-cresol with isobutylene. The desired product distilled at 125–126° (20 mm.) and had a melting point of 51°.

Sulfurization-hydrogenation procedure. The preferred sulfurization-hydrogenation procedure was carried out as follows:

The apparatus consisted of a 1-l., 4-neck round-bottom flask equipped with heating mantle, stirrer, thermometer well, gas inlet tube, and dropping funnel with pressure equalizer, a reflux condenser and drying tube. One mole of 2,6-xylenol was dissolved in 500 ml. of carbon tetrachloride, containing 1 g. of sulfur. Dry nitrogen gas was bubbled slowly through the apparatus. Seventy-four g. (0.55 mole, 10% excess) of sulfur monochloride (Matheson technical) is dissolved in 200 ml. of carbon tetrachloride. Toluene may be used as the solvent instead of carbon tetrachloride with no loss in yield. The sulfur monochloride solution is added slowly through the dropping funnel with continued efficient stirring and nitrogen sweeping, and at such a rate that the reaction temperature does not exceed 30°. This addition generally requires 1 hr. When it is complete the solution is heated to reflux, held at this temperature for 30 min., and then allowed to cool to room temperature with continued stirring and nitrogen sweeping.

The crude disulfide is freed of solvent by distillation under low vacuum to a pot temperature of 120°/50 mm. (A water aspirator is the only practical source of vacuum, due to the exceedingly corrosive nature of the vapors.) The dark viscous residue is dissolved in toluene while still hot. It is then charged into a hydrogenation bomb constructed of Type 316 stainless steel, treated with 10% by weight of molybdenum disulfide (supported on alumina pellets; Davison Catalyst TS-55-3668), and hydrogenated at 140° (cold hydrogen pressure 1800 p.s.i.) until no further gas uptake is observed.

The hydrogenation product, after cooling to room temperature, is filtered to remove catalyst. The filtrate is distilled on a $^3/_4 \times 24$ in. Vigreaux column; approximately 15% of the 2,6-xylenol is recovered. The yield of 4-mercapto-2,6-xylenol, based on xylenol consumed, is 49%; it is accompanied by a 5% yield of 4-chloro-2,6-xylenol. The remainder of the product is high-boiling yellow oil, presumably mostly 4,4′-thiobis-(2,6-xylenol), plus an intractable tarry residue.

Discussion of results. The preferred sulfurization conditions were applied to phenol followed by hydrogenation of the crude sulfurization mixture. Thiohydroquinone,[7] a solid, melting point 32–35°, was recovered in 19% yield. The lower boiling analog, thiocatechol, could not be detected, indicating sulfurization occurs exclusively in the para position. Sulfurization-hydrogenation of *o*-cresol yielded a crystalline thiol,[8] m.p. 39–42°, in 28% yield. This com-

(7) Boiling point 149–150° (25 mm.). *Anal.* Calcd. for C_6H_6OS: C, 57.11; H, 4.79; S, 25.41. Found: C, 56.90; H, 4.95; S, 24.95. Ref. (4) reports the synthesis of thiohydroquinone, m.p. 29–30°, b.p. 144–146° (20 mm.).

(8) Calcd. for C_7H_8OS: C, 59.98; H, 5.75; S, 22.87. Found: C, 59.65; H, 5.75; S, 23.22.

TABLE I

SYNTHESIS OF ALKYL MERCAPTOPHENOLS, YIELDS AND PROPERTIES

Starting Phenol	Mercaptan	Yield	M.P.[a]	B.P. (mm.)	Formula	Analysis	
						Calculated	Found
2,4-Xylenol	6-Mercapto	48	37–39[b]	99–100 (6.5)	$C_8H_{10}OS$	C, 62.30; H, 6.53; S, 20.79	C, 62.59; H, 6.65; S, 20.20
2,6-Xylenol	4-Mercapto	49	85–87[c]	137–138 (10)	$C_8H_{10}OS$	C, 62.30; H, 6.53; S, 20.79	C, 62.48; H, 6.40; S, 20.21
6-*t*-Butyl-*o*-cresol	4-Mercapto	42	Oil	134–135 (5)	$C_{11}H_{16}OS$	C, 67.29; H, 8.22; S, 16.33	C, 67.26; H, 8.21; S, 16.34
4-*t*-Butyl-*o*-cresol	6-Mercapto	40	Oil	124–125 (5)	$C_{11}H_{16}OS$	C, 67.29; H, 8.22; S, 16.33	C, 67.33; H, 8.20; S, 15.80
2-*t*-Butyl-*p*-cresol	6-Mercapto	41	40–42	118–118.5 (5.5)	$C_{11}H_{16}OS$	C, 67.29; H, 8.22; S, 16.33	C, 67.21; H, 8.40; S, 15.75
2-*t*-Amylphenol	4-Mercapto	40	Oil	140–141 (5)	$C_{11}H_{16}OS$	C, 67.29; H, 8.22; S, 16.33	C, 67.16; H, 8.33; S, 15.93
2,6-Di-isopropylphenol	4-Mercapto	30	Oil	82–90 (0.2)	$C_{12}H_{18}OS$	C, 68.57; H, 8.64	C, 68.51; H, 8.43
2,6-Di-*t*-butylphenol	4-Mercapto	31	65–69	85–97 (0.2)	$C_{14}H_{18}OS$	C, 70.54; H, 9.31	C, 71.13; H, 9.44

[a] All melting points corrected. [b] Reported[6] erroneously to melt at 91–93°C. This is probably the monosulfide. The monosulfide was recovered from the residue m.p. 95–98°C. Calcd. for $C_{16}H_{18}O_2S$: C, 70.03; H, 6.61; S, 11.68. Found: C, 70.02; H, 6.79; S, 11.57. [c] Reported[5] m.p. is 86°.

TABLE II

DERIVATIVES OF THE ALKYL MERCAPTOPHENOLS

Mercaptophenol	Derivative	M.P.[a]	Formula	Analysis	
				Calculated	Found
6-Mercapto-2,4-xylenol	1-(Oxyacetic acid)-6-thioacetic acid[9]	132 (dec.)	$C_{12}H_{14}O_5S$	C, 53.31; H, 5.22; eq. wt. 135	C, 53.23; H, 5.34; eq. wt. 132
	6-(2′,4′-Dinitrophenyl[10] thioether)	154–156	$C_{14}H_{12}O_5N_2S$	C, 52 49; H, 3.78	C, 52.15; H, 3.94
	6-(β-Thiopropionic[11] acid)	78–80	$C_{11}H_{14}O_3S$	C, 58.38; H, 6.23	C, 58.32; H, 6.32
4-Mercapto-2,6-xylenol	1-(Oxyacetic acid)-4-(thioacetic acid)	171–172 (dec.)	$C_{12}H_{14}O_5S$	C, 53.31; H, 5.22; eq. wt. 135	C, 53.42; H, 5.29; eq. wt. 136
	4-(2′,4′-Dinitrophenyl thioether)	191–193	$C_{14}H_{12}O_5N_2S$	C, 52.49; H, 3.78	C, 52.54; H, 4.00
	4-(β-Thiopropionic acid)	106–108	$C_{11}H_{14}O_3S$	C, 58.38; H, 6.23	C, 58.71; H, 6.14
6-Mercapto-4-*t*-butyl-*o*-cresol	6-(2′,4′-Dinitrophenyl thioether)	185–186	$C_{17}H_{18}O_5N_2S$	C, 56.34; H, 5.00; S, 8.85	C, 56.69; H, 5.16; S, 8.78
4-Mercapto-6-*t*-butyl-*o*-cresol	1-(Oxyacetic acid)-4-(thioacetic acid)	118–120 (dec.)	$C_{15}H_{20}O_5S$	C, 57.66; H, 6.45; S, 10.27	C, 58.01; H, 6.97; S, 10.08
6-Mercapto-2-*t*-butyl-*p*-cresol	1-(Oxyacetic acid)-6-(thioacetic acid)	140–141 (dec.)	$C_{15}H_{20}O_5S$	C, 57.66; H, 6.45; S, 10.27	C, 57.50; H, 6.79

[a] All melting points corrected.

pound is assigned a thiohydroquinone structure. The infrared spectrum of this compound, in the 5- to 6-micron region, corresponded to a benzene derivative with a 1,2,4 configuration.

This procedure was then applied to eight alkylphenols. The yields and properties of the resulting thiols are shown in Table I. Characterizing thiol derivatives of five of these thiols were prepared. Their melting points and analyses are presented in Table II.

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(9) Made by reaction of the disodium salt with bromoacetic acid.

(10) R. W. Bost, J. O. Turner, and R. D. Norton, *J. Am. Chem. Soc.*, **54**, 1985 (1932).

(11) E. A. Bartkus, E. B. Hotelling, and M. B. Neuworth, *J. Org. Chem.*, **22**, 1185 (1957).

11-Alkylated Steroids. III. Two Syntheses of 11-Methylhydrocortisone[1]

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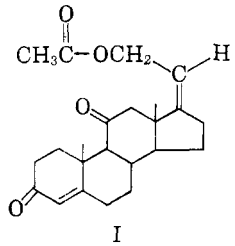
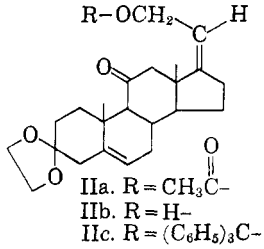
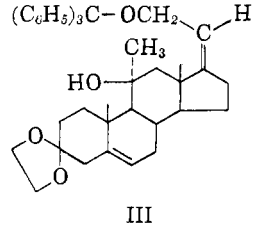
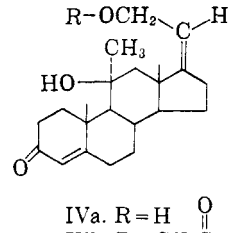
Received May 14, 1959

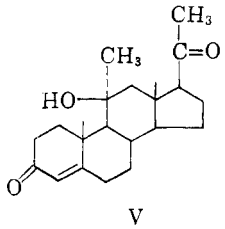
In our earlier report[1] of a synthesis of 11-methylhydrocortisone acetate (XIIa), we outlined the conversion of the known 21-hydroxypregna-4,17(20)-[*cis*]-diene-3,11-dione acetate[2] (I) to its ketal, 21-hydroxypregna-5,17(20)-[*cis*]-diene-3,11-dione 3-ethylene acetal acetate (IIa), which was hydrolyzed with aqueous methanolic potassium bicarbonate to the corresponding free alcohol (IIb). Treatment of the alcohol (IIb) with triphenylmethyl chloride in dry pyridine afforded the 21-trityl ether (IIc), which, on treatment with excess ethereal methyllithium, was converted to 11β-hydroxy-11-methyl-21-triphenylmethoxypregna-5,17(20)-[*cis*]-dien-3-one ethylene acetal (III). Efforts to substitute methyl Grignard reagent for methyllithium were unsuccessful, only unchanged IIc being recovered. Similarly, treatment of either the alcohol IIb or its acetate IIa with either methyl Grignard reagent or methyllithium gave only the alcohol IIb, with no evidence of addition to the 11-oxo group being observed. A consideration of the molecular model of IIb suggests that an initially formed 21-oxy anion, by virtue of its proximity to the 12β-hydrogen, facilitates enolization of the 11-oxo group. That the 5,6-double bond might also be implicated in some way in the mechanism of unreactivity was suggested by the failure of another 11-oxopregn-5-ene, namely pregn-5-ene-3,11,20-trione 3,20-bis(ethylene acetal)[3] (VI), to add methyllithium (see below). However, in the present case,


I


IIa. R = CH_3C–
IIb. R = H–
IIc. R = $(C_6H_5)_3C$–


III


IVa. R = H
IVb. R = CH_3C–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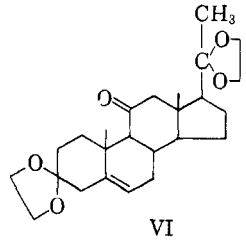
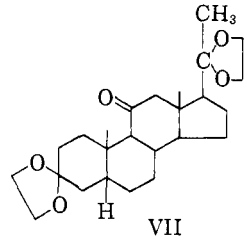
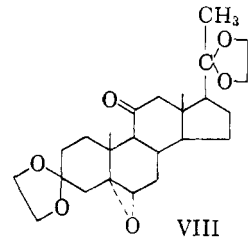
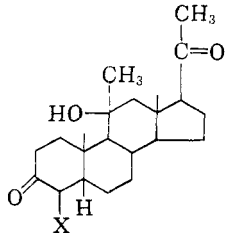
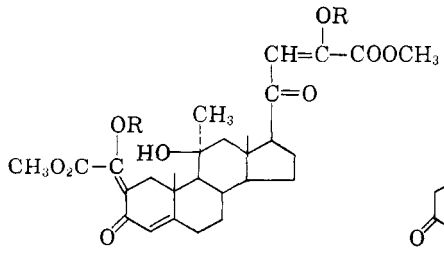
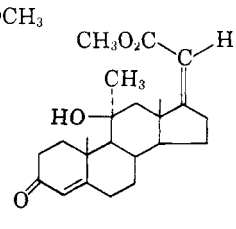

VI

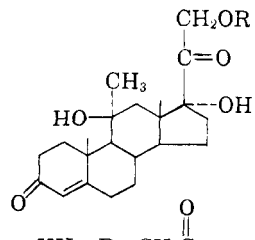

VII


VIII


IXa. X = H
IXb. X = Cl


Xa. R = Na
Xb. R = H


XI


XIIa. R = CH_3C–
XIIb. R = H

(1) Part of the material of this paper has appeared as a Preliminary Communication [G. S. Fonken and J. A. Hogg, *Tetrahedron*, **2**, 365 (1958)]. Preceding paper in this series: see ref. (8).

(2) J. A. Hogg, P. F. Beal, A. H. Nathan, F. H. Lincoln, W. P. Schneider, B. J. Magerlein, A. R. Hanze, and R. W. Jackson, *J. Am. Chem. Soc.*, **77**, 4436 (1955).