ing fraction (0.4 g., b.p. 190–210°/0.05 mm.) or from the dark brown distillation residue.

Fourth experiment. A solution of 5.3 g. (0.05 mole) of benzaldehyde in 15 ml. of tetrahydrofuran was added dropwise, over a period of 3 hr., to a stirred solution of 0.050 mole of triphenylsilyllithium in the same solvent. Heat was evolved during the addition, and the solution gave only a weak Color Test I[6] after the addition was complete. Subsequent to hydrolysis with dilute acid and addition of ether, the mixture was filtered to give 7.92 g. (62%) of hexaphenyldisilane, m.p. 355–358°. The organic layer of the filtrate was worked up in the same manner as in the third experiment. There was obtained 3.2 g. (58%) of 1,2-dihydroxy-1,2-diphenylethane, m.p. 105–117° (mixture of isomers, identified by their infrared spectrum), and 0.6 g. (4.1%) of benzyloxytriphenylsilane, m.p. 83–84°, identified by a mixed melting point. No crystalline compound was isolated from the distillation residue.

When in two more experiments, benzaldehyde was added rapidly to triphenylsilyllithium (1:1 ratio), hexaphenyldisilane was isolated in 21 and 40% yields, respectively.

Reactions of triphenylsilylpotassium.[14] *A. With benzaldehyde.* A solution of 2.1 g. of benzaldehyde in 20 ml. of ether was added rapidly to 0.02 mole of a triphenylsilylpotassium suspension in ether in which the excess of alloy had been removed by amalgamation.[15] Some heat was evolved during the addition. After 48 hr. of stirring, the brown mixture was hydrolyzed and filtered to separate 2.6 g. (77%) of tetraphenylsilane, m.p. 232–234° (mixed m.p.). From the ethereal solution there was obtained a solid residue, melting over the range 85–125°. Several recrystallizations from ethanol gave 0.34 g. (16%) of 1,2-dihydroxy-1,2-diphenylethane, m.p. 138–139° and 0.6 g. (11%) of triphenylsilanol, m.p. 150–151°.

The experiment was repeated using 1,2-dimethoxyethane as the solvent. Under these conditions, a 77% yield of tetraphenylsilane was obtained.

B. With other carbonyl compounds. No addition products have been isolated so far from the reaction of triphenylsilylpotassium with hexamethylacetone, Michler's ketone, benzalacetophenone, paraldehyde, and benzalaniline. From the reaction of triphenylsiylpotassium with formaldehyde the products were triphenylsilylmethanol[4] and a small amount of a compound, m.p. 119–120°. The infrared spectrum of the compound indicated the presence of a carbonyl group and aliphatic hydrogen in the molecule, and the absence of hydroxyl and Si—O groups. Duplicate analyses gave 75.69 and 75.82% carbon and 5.70 and 5.67% hydrogen. The structure of this product has not yet been determined.

From the reaction of triphenylsilylpotassium with paraformaldehyde, a compound was obtained, m.p. 128–130°. Its infrared spectrum indicated the presence of a Si—O grouping and the absence of —OH in the molecule. The structure has not yet been established.

Anal. Found: C, 78.68, 78.58; H, 6.42, 6.29; Si, 9.82.

C. With di-p-tolylcarbinol. A solution of 2.1 g. (0.01 mole) of di-*p*-tolylcarbinol in 30 ml. of ether was added rapidly to an amalgamated suspension of 0.02 mole of triphenylsilylpotassium[15] in ether. After 48 hr. of stirring the reaction mixture was hydrolyzed and filtered to separate 3.2 g. of insoluble residue. Two recrystallizations from benzene yielded 2.2 g. (65%) of tetraphenylsilane,[11] m.p. 233–235°. (mixed m.p.). From the ethereal layer 0.5 g. (9%) of triphenyl silanol was isolated, m.p. 148–150°.

Under corresponding conditions, the reaction of benzhydrol with triphenylsilylpotassium yielded 80% of tetraphenylsilane.[11]

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Synthesis of 2-Isopropyl-4-methoxyphenol[1]

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Alkyl-4-methoxyphenols are important intermediates in the synthesis of alkyl-substituted thyroxine analogs. Although 2-isopropyl-4-methoxyphenol has been reported,[3] its synthesis and properties have not been described.

Using the conditions of Meyer and Bernhauer[4] as well as lower temperatures, our attempts at alkylation of 4-methoxyphenol with isopropyl alcohol in the presence of sulfuric acid resulted in a low yield (3%) of 2-isopropyl-4-methoxyphenol. Alkylation with isopropyl alcohol in the presence of 85% phosphoric acid[5] yielded a mixture from which pure 2-isopropyl-4-methoxyphenol, as characterized by ultraviolet absorption spectra, could not be separated by fractional distillation.

Because of the low yields and side reactions obtained in acid-catalyzed alkylations, a more specific synthesis of the compound and its 2-alkyl congeners was sought. 4-Aminophenols have been obtained from phenols by nitrosation and ammonium sulfide reduction[6] or by coupling with diazotized sulfanilic acid followed by sodium hydrosulfite reduction.[7] Oxidative hydrolysis of the diazonium salts of aminophenols yielded quinones[6] which have been reduced to hydroquinones with

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TABLE I

YIELDS AND PROPERTIES OF 2-ALKYL-4-METHOXYPHENOLS

Phenol (Me = methyl, iP = isopropyl)	1,4-Quinone Yield, %	1,4-Quinone M.P., °C.	1,4-Hydroquinone Yield, %	1,4-Hydroquinone M.P., °C.	4-Methoxyphenol Yield, %	4-Methoxyphenol M.P. or B.P., °C./mm.
2,3-diMe[a]	46	53–55[b]	79	219–220 (dec.)[c]	18	95–96[d]
2,5-diMe	87	122–124[e]	78	208–209[f]	24	89–91[g]
2-iP	60	34–36[h]	82	129–131[i]	40	136–141/12[j]
2-iP, 5-Me	84	44–45[k]	79	141–142[l]	26	155–157/23[m]

[a] The synthetic sequence was carried out on 2,3-dimethylphenol by Mr. Pushkar N. Kaul. [b–m] Lit. m.p. or b.p., ° C./mm.: [b] 55,[11] 56.5–57.5[12]; [c] 221 (dec.),[11] 223–224 (dec.)[12]; [d] 95–97[12]; [e] 123[13]; [f] 210,[13] 208[14]; [g] 90[15]; [h] 28[16]; [i] 130–131,[16] 147–148;[17] [j] 118–119/4.5;[18] [k] 43–45[6]; [l] 140;[14] [m] 155–156/25.[19]

sodium hydrosulfite.[8] Monomethylation of hydroquinones has been carried out using dimethylsulfate.[9,10]

Although 2,3-dimethylphenol, 2,5-dimethylphenol, and thymol were nitrosated and reduced to the 4-aminophenols according to the procedure of Kremers, Wakeman, and Hixon,[6] all attempts to nitrosate 2-isopropylphenol failed. Coupling of 2-isopropylphenol with diazotized sulfanilic acid followed by reduction yielded 2-isopropyl-4-aminophenol which was characterized as the triacetate. As compiled in Table I, diazotization and steam distillation of 2-alkyl-4-aminophenols yielded the corresponding quinones which were reduced to hydroquinones and methylated to yield 2-alkyl-4-methoxyphenols. With the exception of 2-isopropyl-4-methoxyphenol, syntheses of these compounds have been reported. However, the method described herein constitutes a general synthetic sequence for this type of compound. In addition, the cryptophenolic properties noted for 2-isopropylphenols required a different purification procedure than for 2-methylphenols which exhibited normal phenolic properties. The 1,4-dimethoxy and 4-methoxy derivatives of 2-isopropylhydroquinone and 2-isopropyl-5-methylhydroquinone (thymohydroquinone) were extracted with ether from the alkaline methylation mixture and separated by fractional distillation. The 1,4-dimethoxy derivatives of 2,3- and 2,5-dimethylhydroquinone were extracted from the alkaline methylation mixture. Following acidification, 2,3- and 2,5-dimethylhydroquinone and their monomethylethers were extracted. These were separated by virtue of the insolubility of the hydroquinones in hot hexane. Other synthetic details were carried out as described in the Experimental section for the conversion of 2-isopropyl-1,4-quinone to 4-methoxy-2-isopropylphenol.

EXPERIMENTAL

2-Isopropyl-4-methoxyphenol. (*A*) *Alkylation in the presence of sulfuric acid.*[4] 4-Methoxyphenol (62 g., 0.5 mole) dissolved in isopropyl alcohol (38.5 ml., 0.5 mole) was added slowly (4 hr.) to well stirred sulfuric acid (75% v./v., 500 ml.) kept at 74°. The non-steam distillable residue, extracted with benzene and subsequently petroleum ether, yielded a base soluble (*N* sodium hydroxide) extract which was acidified, extracted with ether, and dried. Removal of the ether left 4 g. of a yellow oil from which was obtained 2.5 g. (3%) of 2-isopropyl-4-methoxyphenol, b.p. 105° (1 mm.), n_D^{24} 1.5320 (Lit. b.p. 118–119°/4.5 mm.[18]).

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.14; H, 8.34. Two moles of 4-methoxyphenol, dissolved in 2 moles of isopropyl alcohol were introduced during 3 hr., at 45° into 1200 ml. (75% v./v.) of well stirred sulfuric acid. Fractionation of the reaction mixture gave 2-isopropyl-4-methoxyphenol 8.3 g. (3%), b.p. 252–253°, n_D^{22} 1.5305, log ϵ_{max} = 3.523 (292 mμ) and log ϵ_{min} = 2.065 (252 mμ).

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.39; H, 8.57.

(*B*) *Alkylation in the presence of phosphoric acid.*[5] To 4-methoxyphenol (62 g., 0.5 mole) in phosphoric acid (86.2%, 200 ml.) at 155°, isopropyl alcohol (38.5 ml., 0.5 mole) was added over a period of 4 hr., stirred an additional 3 hr. at 112° and separated with base (2.5*N* sodium hydroxide, 300 ml.) into 2 fractions. The base soluble fraction, after acidification and ether extraction, gave 37.0 g. of an oily residue which yielded 2.1 g., b.p. 93–95°, 5.0 g., b.p. 96–105°, and 6.2 g., b.p. 107–115° when fractionated at 1 mm. Ultraviolet spectra indicated the presence of impurities in these fractions.

2-Isopropyl-4-aminophenol. Sulfanilic acid (132 g., 0.75 mole) was diazotized,[7] the diazotized solution added in the presence of 600 g. of ice to 2-isopropylphenol (b.p. 211.5–212.5°, 102 g., 0.75 mole) in sodium hydroxide (165 g., 4.1 moles in 900 ml. water) and refrigerated overnight. The solution of azo compound was warmed to 45° on the steam bath and reduced with technical sodium hydrosulfite (about 1.5 moles). The yellow aminophenol was filtered under nitrogen and washed with 1% sodium hydrosulfite solution. A

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small portion of the aminophenol (0.7 g.) was dissolved in benzene, precipitated with ligroin, filtered, and dried. 2-Isopropyl-4-aminophenol, m.p. 126.5–128° (dec.), was unstable in the presence of air and its hydrochloride was too hygroscopic to be characterized. Acetylation[20] yielded the triacetyl derivative,[21] m.p. 99.5–100.5° (from petroleum ether).

Anal. Calcd. for $C_{15}H_{19}NO_4$: C, 64.96; H, 6.91. Found: C, 65.29; H, 6.74.

2-Isopropyl-1,4-quinone. The aminophenol was treated with stannous chloride and hydrochloric acid as described in the preparation of 1,4-aminonaphthol hydrochloride,[7] diluted with water (4000 ml.), diazotized with sodium nitrite (170 g.) and concentrated sulfuric acid (110 ml.), heated to 60° and steam-distilled.[6] Filtration and subsequent ether extraction of the steam distillate yielded 67 g. (60% based on the starting phenol) of 2-isopropyl-1,4-quinone, m.p. 34–36° (lit. m.p. 28°[16]).

2-Isopropyl-1,4-hydroquinone. To a vigorously stirred solution of 2-isopropyl-1,4-quinone (118 g., 0.78 mole) in ether (300 ml.) technical sodium hydrosulfite (191 g., about 1 mole) in water (400 ml.) was added gradually. After stirring (3 hr.) the ether phase was separated and the aqueous phase extracted with ether (2 × 100 ml.). The residue left after evaporation of the ether extracts was recrystallized from benzene, giving 98 g. (82%) 2-isopropyl-1,4-hydroquinone, m.p. 127–128°. A sample, recrystallized twice from benzene and sublimed, colorless needles, m.p. 129–131° (lit. m.p. 130–131°[16], 147–148°[17]).

2-Isopropyl-4-methoxyphenol. To 2-isopropyl-1,4-hydroquinone (97 g., 0.64 mole) stirred at 9° in sodium hydroxide (4*N*, 350 ml.), dimethylsulfate (71.5 ml., 0.76 mole) was added over a period of 2.5 hr. and stirred for another hour at 9°.[9] The mixture was extracted with six 100-ml. portions of ether (extract I), acidified with 6*N* hydrochloric acid (250 ml.) and re-extracted with four 100-ml. portions of ether (extract II). Following removal of ether, distillation of extract I (81.3 g.) yielded 26.5 g. of 2-isopropyl-1,4-dimethoxybenzene, b.p. 122–124° (11 mm.), $n_D^{23} = 1.5130$. (Lit.[22] b.p. 114–116° (15 mm.) $n_D^{17} = 1.5105$).

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.50; H, 8.87. Further distillation of extract I yielded 27.2 g. (40%) of 2-isopropyl-4-methoxyphenol, b.p. 136–141° (12 mm.), $n_D^{23} = 1.5280$, log $\epsilon_{max} = 3.539$ (292 mμ) and log $\epsilon_{min} = 2.050$ (252 mμ) in 95% ethanol. (Lit.[18] 118–119°/4.5 mm.).

Anal. Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.03; H, 8.53. Extract II (in ether) was passed through a column of activated alumina, giving 34.2 g. of material, m.p. 110–122°, which was assumed to be impure isopropylhydroquinone.

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Synthesis of 2-Tolyl-1-ethynylcyclohexanols

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Tertiary acetylenic carbinols are often conveniently prepared by the reaction of an alkali metal acetylide with the appropriate ketone in liquid ammonia. Under these conditions sodium acetylide has been used successfully with cyclohexanone,[2,3] and with several methyl substituted cyclohexanones[3] to give the corresponding 1-ethynylcyclohexanols; lithium acetylide in liquid ammonia has been used with good results for a number of tertiary acetylenic carbinols.[4] Application of the above methods to 2-(*o*-tolyl)cyclohexanone resulted in poor yields of 2-(*o*-tolyl)-1-ethynylcyclohexanol with recovery of almost half of the unreacted starting ketone in each case. This low yield could result from the low solubility of the tolylcyclohexanone in liquid ammonia. Dropwise addition of an ether solution of 2-(*o*-tolyl)cyclohexanone to the sodium or lithium acetylide–liquid ammonia mixture resulted in precipitation of the solid ketone. Much better yields were obtained by treating 2-(*o*-tolyl)cyclohexanone with lithium aceytlide in purified, anhydrous methylal (dimethoxymethane) at room temperature. The three 2-tolyl-1-ethynylcyclohexanols were prepared by this method.

The fact that only one 3,5-dinitrobenzoate was obtained from each 2-tolyl-1-ethynylcyclohexanol is not considered a proof that only one isomer, either cis or trans, was obtained because the 3,5-dinitrobenzoates were not obtained quantitatively and there is always a possibility that one isomer could undergo dehydration under the conditions of esterification.

EXPERIMENTAL

The preparation of 2-(*o*-tolyl)-1-ethynylcyclohexanol illustrates the general procedure used for obtaining all three isomers. Anhydrous acetylene was bubbled through 300 ml. of anhydrous liquid ammonia (distilled after addition of sodium) and 1.1 g. (0.16 g. atom) of lithium metal was added in small pieces at such a rate that not much blue color was allowed to accumulate. When the lithium had all reacted 100 ml. of purified, anhydrous methylal was slowly added and the NH_3 was allowed to evaporate while bubbling acetylene slowly through the mixture. An additional 50-ml. portion of methylal was added to the resulting white, curdy mixture. A solution of 15 g. (0.08 mole) of 2-(*o*-tolyl)-cyclohexanone[5] in 60 ml. of methylal was added dropwise at room temperature with stirring and the mixture was stirred at room temperature for 16 hr. while passing a slow stream of acetylene through the mixture. The mixture was hydrolyzed by pouring into 400 ml. of ice water mixture containing 20 ml. of concentrated HCl. The mixture was extracted with ether, the ether solution washed with 5% sodium bicarbonate solution and dried over calcium sulfate. Removal of the ether gave 16.2 g. of oily substance which was treated with Girard T reagent giving 13.8 g. of nonketonic oily substance and 2 g. of unreacted ketone. Distillation of the oily sub-

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