

[CONTRIBUTION FROM THE GULF RESEARCH & DEVELOPMENT CO.]

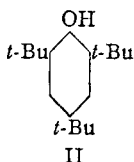
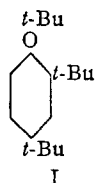
The Hindered Phenols

BY GORDON H. STILLSON, DAVID W. SAWYER¹ AND CHARLES K. HUNT²

When gaseous isobutylene is passed into phenol at 50–60°, in the presence of a catalytic amount of concentrated sulfuric acid, a white, crystalline product (m. p. 130–131°) is obtained in yields as high as 90%. This compound is insoluble in aqueous and customary alkali solutions and fails to give the customary phenol coloration with aqueous or alcoholic ferric chloride solution.

The formation of alkylphenols and phenyl alkyl ethers has been reported as resulting from the addition of olefins to phenols in the presence of concentrated sulfuric acid.³ Nuclear alkylations (4- and 2,4-) have been brought about by treating phenols with isobutylene in the presence of phosphoric acid,^{3c} apparently without the formation of ethers. The preparation of di- and tri-alkylphenols through the reaction of phenols and cresols with alcohols in the presence of acidic catalysts, a reaction which is generally thought to proceed through the intermediate conversion of the alcohol to an olefin, has been reported also.⁴ In many of the investigations which are described in the literature the differentiation of polyalkylphenols from alkylphenyl alkyl ethers has depended upon differences in alkali solubility. Misconceptions arising from dependence on this property alone will be apparent from the discussion which follows.

The isobutylene-phenol condensation product prepared by us had on analysis an empirical formula (C₁₈H₃₀O) which would correspond to a phenol nucleus to which had been added, in some way, three *t*-butyl groups. Thus there are two possible configurations to consider:



All of the preliminary tests pointed toward the ether structure (I), although a sensitive spot test for phenols (see Experimental Part) gave a positive reaction of high intensity. On the assumption that the compound was an ether, efforts were

(1) Present address: Aluminum Research Laboratories, New Kensington, Pennsylvania.

(2) Present address: Sharples Chemicals Inc., Wyandotte, Michigan.

(3) (a) Koenigs, *Ber.*, **23**, 3145 (1890); (b) Niederl and Natelson, *THIS JOURNAL*, **53**, 272 (1931); (c) Niederl, Natelson and Beekman, *ibid.*, **55**, 2571 (1933); (d) Niederl and Riley, *ibid.*, **56**, 2412 (1934); (e) Ipatieff, Pines and Friedman, *ibid.*, **60**, 2495 (1938); (f) Niederl, *Ind. Eng. Chem.*, **30**, 1269 (1938).

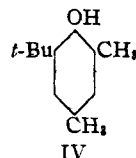
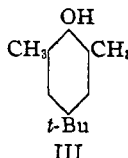
(4) (a) Meyer and Bernhauer, *Monatsh.*, **53-54**, 733 (1920); (b) Tchitchibabine, *Compt. rend.*, **198**, 1239 (1934); (c) Calcott, Tinker and Weinmeyer, *THIS JOURNAL*, **61**, 1010 (1939).

made to rearrange it to its isomeric trialkylphenol.⁵ All such attempts were futile; either the original compound was recovered or a partially dealkylated product was obtained. All attempts to form *t*-butyl 2,4-di-*t*-butylphenyl ether (I) from 2,4-di-*t*-butylphenol by the Williamson reaction and other direct methods⁶ resulted in failure.

Later a product identical to that formed by the isobutylene-phenol condensation was prepared through a Friedel-Crafts reaction in which *t*-butyl chloride reacted with phenol in the presence of anhydrous aluminum chloride. This reaction, commonly used to bring about nuclear substitution, was considered as evidence favoring the phenolic structure (II).

If the compound in question is a phenol, the activity of its phenolic hydroxyl must be retarded in some way. At first it was thought that the cryptophenol concept of J. B. Niederl^{8f} might account for such inactivity. The term "cryptophenol" has been applied by Niederl to alkylphenols, which, through the presence of certain higher alkyl substituents, are sparingly soluble in dilute aqueous alkali; *p*-diisobutylphenol is given as an example. However, the cryptophenols do give a coloration with alcoholic ferric chloride solution and dissolve in Claisen solution (350 g. KOH in 250 g. of water, made up to one liter with methanol); our compound has no effect on alcoholic ferric chloride and is not even slightly soluble in Claisen solution.

Inactivation of the phenolic hydroxyl group could be brought about by steric hindrance⁷ or the "ortho effect."⁸ It is conceivable that *t*-butyl groups occupying the two positions ortho to the hydroxyl group might interfere with the normal functions of that group. This is substantiated somewhat by considering the properties of the two isomers



2,6-Dimethyl-4-*t*-butylphenol (III) is soluble in 10% sodium hydroxide solution while 2,4-di-

(5) Niederl and Natelson, *THIS JOURNAL*, **54**, 1068 (1932); Smith, *ibid.*, **56**, 849, 3718 (1933); **56**, 717, 1419 (1934).

(6) Claisen, *Ann.*, **418**, 78 (1919); Sowa, Hinton and Nieuwland, *ibid.*, **54**, 2019 (1932); Smith, *ibid.*, **55**, 3718 (1933); Kranzfelder and Sowa, *ibid.*, **59**, 1490 (1937).

(7) Meyer and Sudborough, *Ber.*, **27**, 510, 1580, 3146 (1894); Meyer, *ibid.*, **28**, 1254 (1895); van Loon and Meyer, *ibid.*, **29**, 839 (1896).

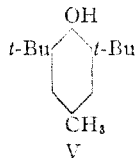
(8) Watson, "Modern Theories of Organic Chemistry," Oxford University Press, Oxford, 1941, pp. 241-243.

TABLE I
 HINDERED PHENOLS

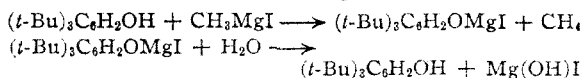
Compound	Em- pirical formula	M. p. uncor., °C.	Boiling point °C.	Mm.	Analyses, %						Benzoate ^a M. p., °C.
					Carbon		Hydrogen		Found		
					Calcd.	Found	Calcd.	Found	Calcd.	Found	
2,4,6-Tri- <i>t</i> -butylphenol	C ₁₈ H ₃₀ O	130-131	136	10	82.38	82.49	82.38	11.53	11.66	11.76	171.5-172.5
2,6-Di- <i>t</i> -butyl-4-methylphenol	C ₁₅ H ₂₄ O	70	132.5-133.5	11	81.77	81.60	81.78	10.97	11.08	11.10	138
2,6-Di- <i>t</i> -butyl-4-ethylphenol	C ₁₆ H ₂₆ O	44	134	10	81.98	81.93	81.89	11.19	11.19	11.23	161
2,6-Di- <i>t</i> -butyl-4- <i>t</i> -amylphenol	C ₁₉ H ₃₂ O	47	135-138	6	82.53	82.52	82.36	11.68	11.65	11.73	130-131
2,6-Di- <i>t</i> -butyl-4-cyclohexylphenol	C ₂₀ H ₃₂ O	98-99	83.26	83.13	83.01	11.22	11.10	11.24	180-181
2,6-Di- <i>t</i> -butyl-4-phenylphenol	C ₂₀ H ₂₈ O	101-102	146-151	2	85.04	85.23	85.11	9.33	9.21	9.30	175-176
2,6-Di- <i>t</i> -butyl-4-diisobutylphenol	C ₂₂ H ₃₈ O	45	127	1	82.94	82.96	83.04	12.03	12.13	12.16	99-100
2,6-Di- <i>t</i> -butyl-4-benzylphenol	C ₂₁ H ₂₈ O	61.5-62	164-166	3	85.07	85.08	84.97	9.53	9.64	9.50	108-108.5
2,6-Di- <i>t</i> -amyl-4-methylphenol	C ₁₇ H ₂₈ O	Liquid	136-144	5	82.18	82.33	82.47	11.37	11.44	11.46
2,6-Di- <i>t</i> -amyl-4- <i>t</i> -butylphenol	C ₂₀ H ₃₄ O	Liquid	117	7	82.68	82.77	82.86	11.81	11.79	11.90
2,4,6-Tri- <i>t</i> -amylphenol	C ₂₁ H ₃₆ O	Liquid	124-126	2	82.81	82.81	82.82	11.93	11.81	11.87
2- <i>t</i> -Butyl-4-methyl-6- <i>t</i> -amylphenol	C ₁₈ H ₂₈ O	Liquid	70-74	1.5	81.98	81.91	82.03	11.19	11.19	11.21	102.5
2,4-Di- <i>t</i> -butyl-6-phenylphenol	C ₂₀ H ₂₈ O	56-67	130-133	0.5	85.04	84.92	84.96	9.33	9.52	9.66	162-163
2,4-Di- <i>t</i> -butyl-6-cyclohexylphenol	C ₂₀ H ₃₂ O	80	83.26	83.10	11.22	11.24	202-203
2,4-Di- <i>t</i> -amyl- <i>t</i> -butylphenol	C ₂₀ H ₃₄ O	Liquid	114-115	1.5	82.71	82.95	82.96	11.81	11.65	11.63	81-83
2,4-Di- <i>t</i> -amyl-6-cyclohexylphenol	C ₂₂ H ₃₆ O	Liquid	177	5	83.46	83.27	83.21	11.48	11.41	11.41	121-122

^a Carbon and hydrogen results for all benzoates in agreement with calculated values.

methyl-6-*t*-butylphenol (IV) is not. The compound represented by IV has the same alkyl substituents as that represented by III; therefore the difference in alkali solubility cannot be attributed to the nature of the substituents but must be influenced in some way by their positions on the ring. While IV can be dissolved in Claisen solution, the substitution of a *t*-butyl group for the remaining *o*-methyl group results in a compound, 2,6-di-*t*-butyl-4-methylphenol (V), which is insoluble in aqueous or alcoholic alkali of any strength.



To confirm the belief that the isobutylene-phenol condensation product in question is a "hindered phenol," its latent phenolic properties were demonstrated in a number of ways. Metallic sodium has no effect on anhydrous petroleum ether or diethyl ether solutions of the compound, even at reflux temperatures. However, liquid ammonia solutions take up one equivalent of metallic sodium, accompanied by the precipitation of a salt, and the original compound may be recovered by hydrolyzing this salt. Furthermore, methane corresponding to one active hydrogen atom⁹ is evolved when a di-*n*-butyl ether solution of the condensation product reacts with an excess of methylmagnesium iodide. Hydrolysis of the magnesium salt gives the original compound.



After the presence of a replaceable hydrogen atom was established, the logical next step was the formation of a derivative. Attempts to prepare acetates or benzoates by the methods usually

(9) Zerewitloff, *ber.*, **40**, (1907); **45**, 2387 (1912).

applicable to phenols were unsuccessful, probably because of the insolubility of the compound in aqueous and alcoholic alkali solutions; but when an anhydrous petroleum ether suspension of the sodium salt formed in liquid ammonia was refluxed with benzoyl chloride, a crystalline solid (m. p. 171-172°) which gave a satisfactory analysis for the benzoate was isolated in very low yield. Later it was found that a mixture of the sodium and potassium salts can be prepared very readily shaking an anhydrous diethyl ether solution of the compound with sodium-potassium alloy, a liquid at ordinary temperatures. Treatment of the salt mixture with benzoyl chloride gives excellent yields of a benzoate identical with that obtained through the sodium salt formed in liquid ammonia. Finally it was discovered that the benzoate in liquid ammonia solution undergoes cleavage to the original compound and benzoic acid upon treatment with two equivalents of metallic sodium.

The reactions just described seem to furnish conclusive evidence that the compound under investigation is the trialkylphenol, 2,4,6-tri-*t*-butylphenol. Certainly none of them can be associated with an ether structure. Apparently a new class of compounds, the hindered phenols, has been encountered. In the alkylation of phenols with alcohols and olefins, compounds of this type doubtless have been prepared by other investigators, but were not recognized because of their unusual chemical properties. Other tri-substituted phenols found to have chemical properties similar to those of 2,4,6-tri-*t*-butylphenol are listed, with some of their properties, in Table I.

Hindrance of the phenol hydroxyl group by alkyl substituents in the two ring positions adjacent to it seems to reach its full effect starting with tertiary butyl groups. All of the 2,6-di-*t*-butyl-4-alkylphenols studied were insoluble in alcoholic alkali solution. 2,6-Di-*n*-butyl-4-alkylphenols, which cannot be prepared by the methods described in this paper, were not investigated.

TABLE II
 CRYPTOPHENOLS

Compound	Empirical formula	M. p. uncor., °C.	Boiling point		Analyses, %				Benzoate ^a M. p., °C.		
			°C.	Mm.	Calcd.	Carbon Found	Hydrogen Found	Calcd.			
2,4-Dimethyl-6- <i>t</i> -butylphenol	C ₁₂ H ₁₈ O	Liquid	129-131	19	80.83	80.66	80.57	10.19	10.26	10.40	88
2,4-Di- <i>t</i> -butyl-6-methylphenol	C ₁₈ H ₂₄ O	52.5	113	8	81.77	81.67	81.84	10.97	10.97	10.07	133.5
2,4-Di- <i>t</i> -butyl-6-ethylphenol	C ₁₈ H ₂₄ O	30	82-84	1	81.98	81.91	81.89	11.19	11.16	11.16	134-135
2,4,6-Tri-isopropylphenol	C ₁₅ H ₁₈ O	Liquid	81-84	1	81.77	81.71	81.65	10.97	11.01	10.90	137
2,6-Di- <i>s</i> -butyl-4-methylphenol	C ₁₈ H ₂₄ O	Liquid	153-155	20	81.77	81.71	81.67	10.97	11.12	11.00	104-105

^a Carbon and hydrogen results for all benzoates in agreement with calculated values.

2,6-Di-*s*-butyl-4-methylphenol was found to be soluble in Claisen solution and gives a positive phenol test with ferric chloride solution. Judging by the only *o*-phenyl trisubstituted phenol studied (2,4-di-*t*-butyl-6-phenylphenol), the phenyl group has a hindering effect comparable to that of the tertiary butyl group. On the basis of present evidence the cyclohexyl group would be placed in the same category.

2,4,6-Triisopropylphenol and the other trialkylphenols which appear in Table II are insoluble in dilute aqueous sodium hydroxide solutions but are soluble in Claisen solution, and therefore might be classed as cryptophenols. It is difficult to say definitely whether these solubility characteristics are attributable to the presence of higher alkyl groups which decrease solubility in aqueous alkali solutions generally, or to partial retardation of the phenolic properties by steric effects; both factors may be responsible. Certainly in the isomeric compounds III and IV the degree of alkali insolubility appears to be influenced strongly by the position of the *t*-butyl group relative to the hydroxyl group.

Tertiary amyl groups in the two ortho positions render the resulting trialkylphenols immune to the action of alcoholic or aqueous alkali, sodium in liquid ammonia, or sodium-potassium alloy suspended in anhydrous ether. As a consequence it has been impossible so far to form benzoyl derivatives of 2,6-di-*t*-amyl-4-methylphenol, 2,6-di-*t*-amyl-4-*t*-butylphenol, and 2,4,6-tri-*t*-amylphenol.

In most cases the hindered phenols are formed in good yields at reaction temperatures between 60 and 70°. Occasionally it is found necessary, in order to obtain satisfactory yields, to carry out the alkylation at 20° or lower. The reaction is exothermic, and precautions usually must be taken to hold the temperature within the limits desired. If operating in the 60 to 70° range it is advisable to apply heat toward the end of the reaction by means of a hot-water-bath. With gaseous alkylating agents best results are obtained when the gas is dispersed finely in the liquid by passing it upward past the blades of the stirrer. A convenient and efficient vessel for this purpose is described in the discussion of experimental procedures. Temperature control and stirring are maintained until a gain in weight of from 0.1 to 0.9 mole in excess of the amount of alkylating agent required theoretically is observed. With

liquid alkylating agents such as trimethylethylene, the phenol is placed in a three-necked, round-bottom reaction flask equipped with reflux condenser, sealed stirrer, and dropping funnel. The alkylating agent is added slowly, using an excess of 0.2 mole over the calculated amount. Stirring and heating are continued for four to five hours from the time addition of the olefin begins. Concentrated (96%) sulfuric acid amounting to 5% of the weight of the phenol is used as the catalyst and is mixed with the phenolic compound before the alkylation is begun.

In distilling the hindered phenols, extreme care must be taken to remove all acidic materials from the distillation charge if one or both of the ortho positions are occupied by butyl groups or higher. If this precaution is not observed, dealkylation will take place, with the partial or total loss of the ortho substituents.¹⁰

Although the hindered phenols, through oxidation, tend to become discolored when allowed to stand exposed to the atmosphere for any length of time, they may be stored in a vacuum desiccator almost indefinitely without appreciable deterioration. Extremely pure samples appear to be considerably more stable toward oxidation than impure ones. As a class they are insoluble in hot or cold water but dissolve readily in all of the common organic solvents.

Acknowledgment.—The authors wish to acknowledge the many contributions made to this work by various members of the Chemical Staff of this Laboratory, and to give full recognition to the fact that the earlier work of Dr. Donald R. Stevens and co-workers of the Mellon Institute of Industrial Research opened the way for this investigation.

Experimental¹¹

The Reaction Vessel.—The design of the Pyrex reaction vessel used for most of the phenol alkylations involving gaseous olefins is shown in Fig. 1. A gas passed into this vessel through a tube at the bottom is immediately broken up into fine bubbles by the stirrer and dispersed in the reaction mixture. Because of the slender, cylindrical shape of the vessel the dispersed bubbles must pass upward through a relatively tall column of liquid, thereby prolonging the time of contact between liquid and gas. A side neck at the top is fitted with a reflux condenser, and the motor-driven glass stirrer is fitted with a mercury seal.

2,4,6-Tri-*t*-butylphenol.—A. Sulfuric acid catalyst: Phenol (66 g. or 0.7 mole), with 3.3 g. of concentrated sul-

(10) Stevens, *Ind. Eng. Chem.*, **35**, 655 (1943).

(11) Microanalyses by James M. Fulton, Ralph O. Clark, and Lincoln T. Jenkins.

furic acid, was dissolved in 35 ml. of benzene in the alkylation vessel. Pure isobutylene (118 g. or 2.1 mole) was passed through the solution for seven hours during which time the temperature was held at 50° by means of a water-

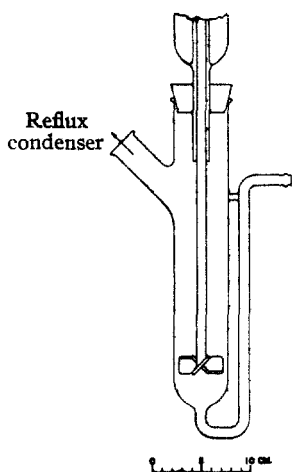


Fig. 1.—Reaction vessel for phenol alkylation.

95% ethyl alcohol, melted at 130–131°. The boiling point of the pure compound was found to be 136° at 10 mm. pressure.

Anal. Calcd. for $C_{18}H_{20}O$: C, 82.38; H, 11.53. Found: C, 82.49, 82.38; H, 11.66, 11.76.

B. Aluminum chloride catalyst: Ninety-four grams of phenol and 160 g. of *t*-butyl chloride were weighed into a three-necked flask fitted with a reflux condenser, a thermometer, and a sealed, electrically-driven stirrer. Six grams of anhydrous aluminum chloride was added and the mixture was stirred at 20–30°. After five hours the temperature was raised to 60–70°, an additional 160 g. of *t*-butyl chloride and 6 g. of aluminum chloride were added, and the mixture was stirred for twenty-four hours. The cooled reaction mixture was poured onto cracked ice and extracted with ether. The ether layer was washed with water until neutral to litmus, dried over anhydrous sodium sulfate, and freed of ether by distillation at room temperature under reduced pressure.

The solvent-free residue (275 g.), a dark-brown liquid, was distilled at 10 mm. pressure. The first fraction, a liquid (52 g., b. p. 92–120°), yielded *p*-*t*-butylphenol (m. p. 98–100°) when dissolved in petroleum ether and chilled; the second fraction (63 g., b. p. 120–130.5°), also a liquid, was identified as mainly 2,4-di-*t*-butylphenol (m. p. 56–57°); and the third fraction (58 g., b. p. 130.5–140°) was a solid which, after recrystallization from petroleum ether, melted at 130–131°. A mixture with 2,4,6-tri-*t*-butylphenol prepared as in (A) melted at 130°.

Anal. Calcd. for $C_{18}H_{20}O$: C, 82.38; H, 11.53. Found: C, 82.31, 82.46; H, 11.63, 11.70.

Spot Test for Hindered Phenols.¹²—A few crystals or one drop of the sample are placed in a small porcelain crucible or "spot plate" and dissolved in a few drops of 95% ethyl alcohol. To the alcoholic solution is added a drop of 2% phosphomolybdic acid solution, followed by two drops of concentrated ammonium hydroxide solution. In the presence of a phenol or hindered phenol a deep blue color develops. This test will detect as little as one part of 2,4,6-tri-*t*-butylphenol in 8,500 parts of alcoholic solution.

Formation and Hydrolysis of Salts of 2,4,6-Tri-*t*-butylphenol.—**Method A:** Some 300 ml. of liquid anhydrous ammonia was condensed onto 5 g. of 2,4,6-tri-*t*-butylphenol at –60 to –70° and atmospheric pressure. The compound

was sparingly soluble, even when the ammonia was warmed to its boiling point. Metallic sodium was added to the solution in small portions until 0.5–0.6 g. had been consumed, after which the permanent blue color of the solution indicated the presence of an excess of the metal; theoretically, 0.52 g. of sodium would have been required to displace the phenolic hydrogen atom. As the sodium reacted, the alkylphenol gradually went into solution until, with the appearance of the blue color, no solid remained. The ammonia was allowed to evaporate overnight.

The white residue left in the reaction vessel after the evaporation of the ammonia was covered with petroleum ether and treated with a petroleum ether solution of absolute alcohol in order to destroy excess sodium. When the evolution of hydrogen had ceased, water and finally dilute hydrochloric acid were added. The petroleum ether layer was separated, washed with water until neutral, and dried over anhydrous sodium sulfate. All but approximately 5 ml. of the solvent was evaporated at 80–90 mm. pressure. Upon cooling, crystals (m. p. 129°) separated from the remaining solution. Recrystallized from 95% ethyl alcohol, these crystals melted at 131° and did not depress the melting point (130–131°) of pure 2,4,6-tri-*t*-butylphenol.

Method B: A mixture of the sodium and potassium salts of 2,4,6-tri-*t*-butylphenol was formed by shaking 10 g. of the alkylphenol with 4 g. of sodium-potassium alloy. The alloy, a liquid at room temperature, was made up in the proportion of two parts of sodium to five parts of potassium.¹³ The alkylphenol was dissolved in anhydrous diethyl ether (500 ml.) in a 1000-ml. distilling flask, the alloy was introduced, and the mixture was shaken for seven hours after displacing the air in the flask with dry nitrogen. The hydrogen evolved was vented through the side-arm of the flask, which was connected to a mercury pressure-relief valve by means of a rubber tube. The salts, which commenced to precipitate almost immediately, were removed on a Büchner funnel when the reaction was complete.

The solid on the filter was transferred to a beaker, where it was covered with anhydrous petroleum ether, and any excess alloy was destroyed by carefully adding a 20% petroleum ether solution of 95% ethyl alcohol. Hydrolysis of the salt was accomplished by the addition of dilute hydrochloric acid. The hydrocarbon layer was washed with water until the washings were neutral to litmus, dried over anhydrous sodium sulfate, and freed of solvent on a steam-bath. The solid residue was recrystallized from 95% ethyl alcohol and found to melt at 129–130°. A mixture with 2,4,6-tri-*t*-butylphenol melted at 130–130.5°.

2,4,6-Tri-*t*-butylphenyl Benzoate.—**Method A:** Metallic sodium (0.6 g.) was added slowly to anhydrous liquid ammonia (at its atmospheric boiling point) containing 6 g. of 2,4,6-tri-*t*-butylphenol. Addition of the last portion of sodium turned the solution deep blue, indicating that the metal was present in excess of the amount necessary for reaction with the phenol. The ammonia was allowed to evaporate overnight and the residual ammonia was removed by covering the solid residue with anhydrous petroleum ether and partially evaporating the ether. The residue was not soluble in the hydrocarbon.

Four grams of benzoyl chloride was added to the petroleum ether suspension and the mixture was refluxed for an hour in an atmosphere of dry nitrogen. An additional 4 g. of benzoyl chloride was introduced, and the mixture was heated for one and a half hours under reflux. Excess benzoyl chloride was destroyed by shaking the cooled solution with 10% potassium carbonate solution. The hydrocarbon solvent was removed by blowing air over the petroleum ether-carbonate mixture. The coagulated solid was collected on a filter and washed with 20% potassium carbonate solution and water. When recrystallized twice from 95% ethyl alcohol, this solid melted at 170–171°; yield (pure), 0.6 g. (7%).

Anal. Calcd. for $C_{25}H_{28}O_2$: C, 81.91; H, 9.36. Found: C, 82.09, 82.21; H, 9.45, 9.52.

(12) Platkonkaya, *J. App. Chem.* (U. S. S. R.), 10, 202 (1937); *C. A.*, 31, 4232 (1937).

(13) Birmingham, *Ind. Eng. Chem., Anal. Ed.*, 7, 53 (1935).

Method B: A mixture of the sodium and potassium salts of 2,4,6-tri-*t*-butylphenol was prepared as described previously. No attempt was made to destroy the excess alloy in the residue on the filter. The residue was washed with anhydrous ether, quickly transferred to a 1000-ml. round-bottom flask, and immediately covered with about 600 ml. of anhydrous petroleum ether. Ten grams of benzoyl chloride was added and the mixture was refluxed gently for eleven hours. Any alloy which remained was destroyed with an alcohol-petroleum ether solution; unreacted benzoyl chloride was decomposed by shaking with three 200-ml. portions of 5% sodium hydroxide solution. The hydrocarbon layer was washed with water until neutral, dried with anhydrous sodium sulfate, and freed of solvent by distillation under reduced pressure. The residue, after recrystallization from 95% ethyl alcohol, melted at 171.5–172.5°C; yield, 10 g. (72%). The melting point when mixed with the product from Method A was 171–172°.

Anal. Calcd. for $C_{23}H_{34}O_2$: C, 81.91; H, 9.36. Found: C, 81.99, 82.11; H, 9.19, 9.40.

Cleavage of Benzoate.—Liquid anhydrous ammonia (250–300 ml.) was condensed at -40 to -50° into a glass reaction vessel containing 8 g. of 2,4,6-tri-*t*-butylphenyl benzoate (Method B, above). Although the benzoate was sparingly soluble, the suspension in ammonia reacted with metallic sodium until 1.35 g. (2.7 gram atoms per mole of benzoate) had been consumed, and the final deep-blue color of the solution indicated an excess of metal. As the sodium reacted, the solid went into solution. Anhydrous petroleum ether (100 ml.) was added and the ammonia was allowed to evaporate. The excess sodium was then destroyed with a 50% solution of absolute ethyl alcohol in petroleum ether. Hydrolysis of any sodium salts was completed with dilute hydrochloric acid.

The hydrocarbon solution was extracted with two 100-ml. portions of sodium carbonate solution (20%). The extracts were combined with the aqueous layer from the hydrolyzed reaction mixture and evaporated to 150 ml. on a steam-bath. The concentrate was acidified with hydrochloric acid and extracted with ether. Evaporation of the ether left 0.6 g. of a white solid which, after recrystallization from water, melted at 120–121°. When mixed with pure benzoic acid the melting point was 121°, the melting point of the acid.

The petroleum ether layer from the reaction mixture was washed with water until neutral, dried with anhydrous sodium sulfate, and freed of solvent by distillation at 50–100 mm. pressure. The residue was distilled at 10 mm. and the fraction boiling at 139–140° (2.7 g.) crystallized in the receiver. This solid fraction was recrystallized from 70% ethyl alcohol; m. p. 128.5–129.5°. Admixed with pure 2,4,6-tri-*t*-butylphenol (m. p. 130–131°), the melting point was 129–130°.

Active Hydrogen Determination.—The active hydrogen apparatus consisted of a special reaction vessel fitted with a

built-in, solenoid-operated magnetic stirrer, a Lunge nitrometer with a mercury displacement system, and stop-cocks so arranged that the entire system could be evacuated and flushed with dried nitrogen before the determination. Methylmagnesium iodide prepared in anhydrous di-*n*-butyl ether solution was added to the sample (also in di-*n*-butyl ether solution) by the inversion of a retort-shaped bulb connected to the reaction vessel by means of a ground-glass joint. The reaction was carried on at 95–100° until the volume of methane collected reached a constant value.

In two determinations an excess of methylmagnesium iodide was added to di-*n*-butyl ether solutions containing 0.350 g. of pure 2,4,6-tri-*t*-butylphenol. Methane amounting to, respectively, 33.8 cc. and 34.3 cc. at 25° at 743.7 mm. was collected. These results agreed very well with the calculated value of 33.4 cc., the methane which theoretically should be evolved through the loss by the hindered phenol of one active hydrogen atom.

Hydrolysis of Grignard Addition Compound.—A solution of methylmagnesium iodide was prepared, using 10.7 ml. of methyl iodide, 4.5 g. of magnesium turnings, and 60 ml. of anhydrous di-*n*-butyl ether. The Grignard solution was added slowly, with stirring, to 15 g. of 2,4,6-tri-*t*-butylphenol dissolved in 60 ml. of anhydrous di-*n*-butyl ether. The temperature was held to approximately 25° by means of a water-bath. Methane was evolved and a white precipitate formed. The mixture was allowed to stand in an atmosphere of dry nitrogen for one hour, after which it was hydrolyzed with dilute hydrochloric acid. The ether layer was washed with water until the washings were neutral, and dried over anhydrous sodium sulfate. The residue remaining after evaporation of the ether was recrystallized from ethyl alcohol. Melting point and melting point of a mixture with pure 2,4,6-tri-*t*-butylphenol, 130°; yield (pure), 11.8 g. or 79%.

Anal. Calcd. for $C_{18}H_{26}O$: C, 82.38; H, 11.53. Found: C, 82.37, 82.50; H, 11.30, 11.67.

Summary

A new class of compounds, the hindered phenols, is characterized. These compounds are 2,4,6-tri-substituted phenols whose phenolic properties are hindered by the presence of *t*-butyl or other large hydrocarbon groups in the two positions ortho to the hydroxyl group. They are insoluble in aqueous or alcoholic alkali solutions and will not respond to any of the conventional tests and reactions of phenols. Methods for synthesis of the compounds and their derivatives are described, and evidence supporting the structures assigned is presented.

PITTSBURGH, PENNSYLVANIA

RECEIVED NOVEMBER 8, 1944