Diisobutylphenol

Synthesis - Structure - Properties - Derivatives

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DIISOBUTYLPHENOL (*p-tert*-octylphenol) which was first prepared in this laboratory in 1929 (*41*) under the author's supervision (*31*, *32*, *33*, *40*, *41*) in the course of systematic investigations concerning the addition of phenols to various unsaturated compounds (*31–47*), is now manufactured on an industrial scale.[1] For this reason investigations in regard to its structure and its physical, chemical, and physiological properties, as well as to the preparation of a large number of derivatives (*35*) became desirable. The results of these investigations are given here.

Unlike the preparation of the previously reported isomeric normal and secondary octylphenols involving the Fries-Nencki-Clemenssen process (*50*) and the condensation of methylhexyl ketone with phenol, respectively (*8*), diisobutylphenol is prepared by condensing diisobutylene directly with phenol under the influence of a cationoid condensing agent, such as mineral acids (concentrated sulfuric acid, dry hydrogen chloride gas, phosphoric acid, *21*, etc.), or metal salts with acid reaction (the halides of aluminum, boron, copper, iron, phosphorus, tin, zinc, etc.) (*19*).

Other direct methods involve abnormal carbon alkylation (*4*, *19*), Claisen rearrangement (*7*), and the condensation of diisobutylene hydrohalides (*6*, *16*, *26*) with phenol in the presence of suitable catalysts, essentially at low temperatures; otherwise, *p-tert*-butylphenol is the main reaction product (*19*).

Notwithstanding the many possible methods of preparation of diisobutylphenol, the starting material is always diisobutylene; and the study of this compound, especially of its addition reactions, reveals the structure of the side chain in this octylphenol. It has been shown that the major components of commercial diisobutylene obtained in the polymerization of isobutylene (the latter a by-product in the petroleum cracking process and hence easily available) are 2,4,4-trimethyl-1-pentene and 2,4,4-trimethyl-2-pentene (*6*, *10*, *15*, *20*, *27*, *28*, *56–58*). Nevertheless, it has been repeatedly observed that upon addition of hydrogen bromide, only one product is formed—namely, 2-bromo-2,4,4-trimethylpentane with bromine adding to the tertiary carbon atom (*6*, *26*, *49*), as follows:

$$\left.\begin{matrix}(CH_3)_3CCH{=}C(CH_3)_2\\ (CH_3)_3CCH_2C(CH_3){=}CH_2\end{matrix}\right\} \text{Diisobutylene} \xrightarrow{+\,HBr} (CH_3)_2\overset{\displaystyle Br}{\overset{|}{C}}CH_2C(CH_3)_3$$

2-Bromo-2,4,4-trimethylpentane (diisobutylene hydrobromide)

Diisobutylphenol, or *p-tert*-octylphenol, is one of the few new phenols discovered in America within the last decade and now manufactured on a large industrial scale. The physical, chemical, and physiological properties of this phenol are described, and conclusive proof of its structure is given. Scores of new derivatives have been prepared, including new dyestuffs, a new salicylic acid and aspirin analog, new long-chain substituted alicyclic compounds, as well as a similarly substituted aliphatic dibasic acid and numerous types of aromatic compounds; all of them possess the diisobutyl radical in the side chain. The diisobutylphenol and consequently all its derivatives are prepared from phenol and diisobutylene, a formerly little utilized by-product, obtained in the petroleum cracking process.

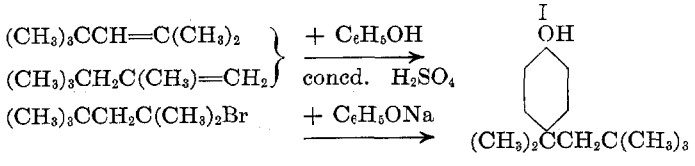
Since phenol always adds to a double bond in a manner similar to that of halogen acids (*39*, *44*, *46*), and since there is no reason why addition should take place differently in this case, it appears certain that the phenyl group is in the same position as would be occupied by the bromine—namely, at the tertiary carbon atom. Thus the analogous 2-(*p*-hydroxyphenyl)-2,-4,4-trimethylpentane is formed. This is further substantiated by the fact that when any of the tertiary diisobutylene hydrohalides (chloride, bromide, and iodide) was condensed with phenol or with sodium phenolate, it yielded no ether but the same alkylated phenol (*4*, *19*, *30*).

In this manner the structure of the side chain in diisobutylphenol was deducible, but it had to be proved whether substitution had taken place in either the ortho or para position to the phenolic hydroxyl group. For this purpose, direct as well as indirect methods of structure proof were applied.

Direct methods of structure proof involved oxidation of this phenol and of its derivatives (*2*, *12*, *14*, *22*). The direct oxidation of the diisobutylphenol, which was carried out by fusion with potassium hydroxide and separately with sodium hydroxide (to avoid possible rearrangements) in the presence

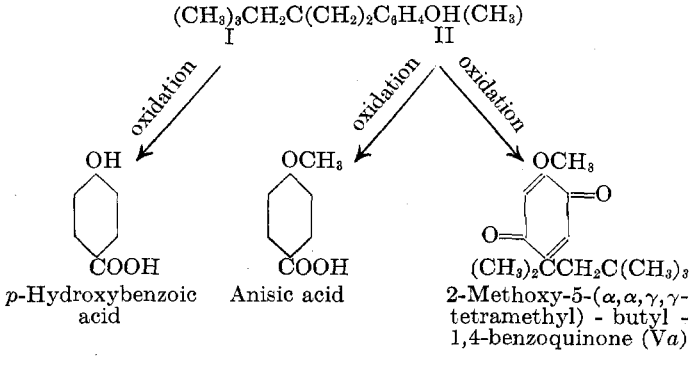
[1] Röhm and Haas Company, Philadelphia, Pa.

of oxidizing agents, such as copper oxide, manganese dioxide, or lead peroxide, yielded *p*-hydroxybenzoic acid (*48*). This acid was conclusively identified by quantitative analysis, melting point, and mixed melting point with a standard sample. No salicylic acid could be obtained. Then in diisobutylphenol the diisobutyl group must be in a position para to the phenolic hydroxyl group as follows:



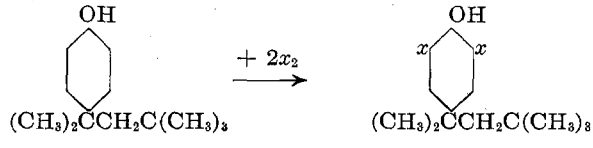
Diisobutylphenol or *p-tert*-octylphenol or 2-(*p*-hydroxyphenyl) - 2,4,4 - trimethylpentane or *p*-($\alpha,\alpha,\gamma,\gamma$ - tetramethylbutyl) - phenol

Similarly the oxidation of the ethers (methyl) No. II*a* in Tables I and II, and ethyl, II*b* of diisobutylphenol with chromic acid anhydride in glacial acetic acid solution (*4*), yielded the 2-alkoxy-5- (α, α, γ, γ-tetramethyl)-butyl-1,4-benzoquinones (methoxy, V*a*, and ethoxy, V*b*, together with small amounts of anisic and *p*-ethoxybenzoic acid, respectively; thus once more the above structure is verified:

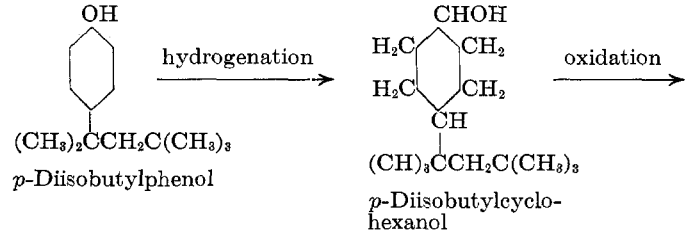


p-Hydroxybenzoic acid — Anisic acid — 2-Methoxy-5-($\alpha,\alpha,\gamma,\gamma$-tetramethyl) - butyl - 1,4-benzoquinone (V*a*)

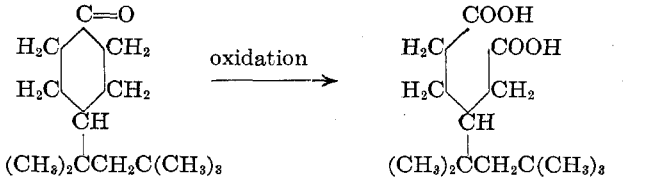
The fact that only one single disubstituted product (dichloro, VI*b*; bromonitro, VII*b*; dinitro, VII*c*; dimethylol, IX*a*) could be obtained (Körner's rule) was another positive indication of the above structure—i. e.,



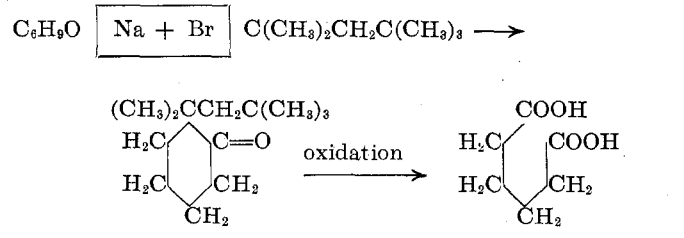
A new and rather unique additional structure proof was effected as follows: The diisobutylphenol was hydrogenated and the resulting *p*-diisobutylcyclohexanol was oxidized to the corresponding cyclohexanone (*45*). The oxime of this ketone was not identical with the oxime of α-diisobutylcyclohexanone, the latter having been prepared by the interaction of diisobutyl hydrobromide with the sodium salt of cyclohexenol (*46*). Further oxidation of both cyclic ketones yielded in the first case the new β-diisobutyladipic acid (*45*), and in the latter, adipic acid itself (*46*), shown graphically as follows:



p-Diisobutylphenol — *p*-Diisobutylcyclohexanol

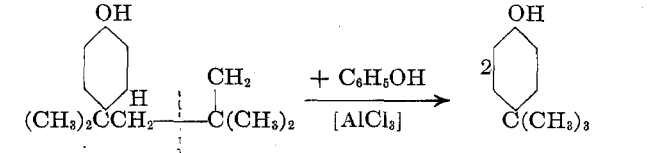


γ-Diisobutylcyclohexanone (oxime, m. p. 152° C.) — β-Diisobutyladipic acid (m. p. 134° C.)



α-Diisobutylcyclohexanone (oxime, m. p. 147–148° C., mixed m. p. 123–125° C.) — Adipic acid

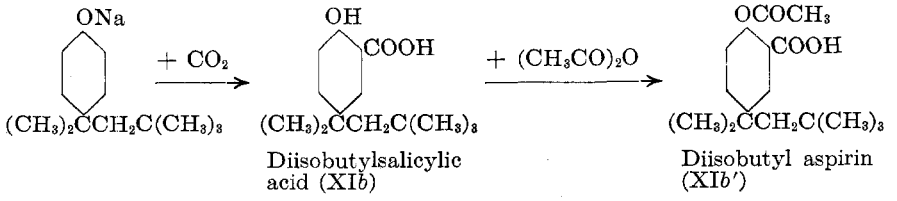
Still another structure proof included the treatment of molar mixtures of diisobutylphenol and carbolic acid with aluminum chloride, forming *p-tert*-butylphenol (*54*, *55*). This appears to be a reaction which amounts to a reversal of the polymerization of isobutylene to diisobutylene, and which thus gives rise to interesting electronic postulations (*21*):



p-Diisobutylphenol — *p-tert*-Butylphenol

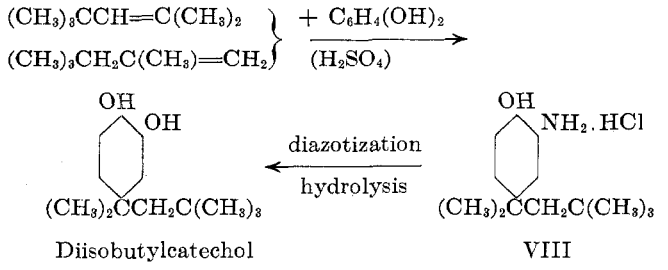
The following derivatives of *p*-diisobutylphenol (I) were prepared:

Ethers: methyl (II*a*), ethyl (II*b*), benzyl (II*c*), and menaphthyl (II*d*).
Esters: acetate (III*a*), benzoate (III*b*), and *p*-nitrobenzoate (III*c*).
Urethans: phenyl (IV*a*) and α-naphthyl (IV*b*).
Quinones: methoxy (V*a*), its mono- and dioxime (V*a'* and V*a''*), and ethoxy (V*b*).
Halogen: mono- and dichloro (VI*a* and *b*), monobromo (VI*c*).
Nitro: mononitro, sodium salt (VII*a*) and benzoate (VII*a'*); nitrobromo (VII*b*) and dinitro (VII*c*).
Amino: monoamino hydrochloride (VIII).
Methylol (*52*): dimethylol (IX), its monomethyl ether (IX*a*) and tribenzoate (IX*b*).
New azo dyestuffs (*25*) (X*a-k*) were prepared using the more common aromatic amines.
Acids: such as phenoxyacetic acid (XI*a*), salicylic acid (XI*b*) and its acetyl derivatives (diisobutyl aspirin, XI*b'*), monosulfonic acid (sodium salt, XI*c*, and methyl ether, XI*c'*); disulfonic acid and its disodium salt (XI*d*) have also been made; the diisobutyl salicylic acid (XI*b*) was prepared by the conventional Kolbe method as follows (*1*):



Application of the Reimer-Tiemann reaction to diisobutylphenol resulted in the formation of the corresponding salicyl aldehyde homolog (XII) of which the semicarbazone (XII*a*), the phenyl hydrazone (XII*b*), and the 2,4-dinitrophenyl hydrazone (XII*c*) were prepared (*24*).

Diazotization of the monoamino hydrochloride (VIII), followed by hydrolysis, produced diisobutylcatechol (*53*), a product of high bactericidal activity; it was identical with the compound prepared by condensing catechol directly with diisobutylene in the presence of sulfuric acid (*41*) as follows:



Preparation of *p*-Diisobutylphenol in the Laboratory (*11*)

In a 250-cc. Erlenmeyer flask are placed 10 grams of phenol and 10 grams of diisobutylene (boiling point 101–103° C.). The mixture is warmed to dissolve the phenol and then cooled to about 10° C. One cubic centimeter of concentrated sulfuric acid (specific gravity 1.84) is added at once. This generates enough heat to bring the mixture up to about 50° C. and form a homogeneous solution. It is then thoroughly shaken and quickly cooled to about 10° C. The reaction mixture is set aside and allowed to stand at room temperature overnight, after which the entire reaction mass usually becomes crystalline and forms a solid cake. One hundred cubic centimeters of water are then added to the product, and the inhomogeneous mixture is heated to about 90° C.

The Erlenmeyer flask is stoppered, and the hot mixture is shaken thoroughly to break up the molten mass into fine droplets and to extract all water-soluble products (unreacted phenol, sulfuric acid, and sulfonic acids). It is cooled, and upon standing at room temperature, crystallization sets in again. The crystals are filtered through a fluted filter paper and placed on a porous plate. The yield is 17 grams. The compound is best recrystallized from either diisobutylene or petroleum ether.

Manufacture of *p*-Diisobutylphenol (*18*)

A vessel is chosen which is resistant to sulfuric acid, such as any glass, enameled, or lead-lined kettle, fitted with a rapidly rotating stirrer. In the vessel is placed a mixture of substantially equimolecular quantities of phenol and diisobutylene—for example, 940 pounds phenol and 1120 pounds diisobutylene. To this mixture, which is cooled to 15–18° C., 40 pounds of 96 per cent sulfuric acid are added gradually in a slow stream, with constant and vigorous agitation.

During the addition of the acid and shortly afterwards, there is a tendency for the temperature to rise to 30–35° C., and the mixture becomes completely fluid. The reaction mixture is cooled with stirring, so that a temperature of 20–25° C. is reached as quickly as possible. Then 110 pounds of 96 per cent sulfuric acid are added slowly to give a total of 150 pounds (0.15 mole) during 20–30 minutes, while the temperature is held at 20–25° C. After about an hour and a half of stirring, crystals of diisobutylphenol begin to separate out, and the mixture gradually becomes more viscous. Finally the reaction mixture sets to a hard crystalline cake. The latter is broken up, and the crystals are removed and washed thoroughly with water to extract sulfuric acid and traces of sulfonic acids or unchanged phenol. The crude technical diisobutylphenol forms colorless needlelike crystals with a faint camphorlike odor. The yield is about 90 to 95 per cent of the theoretical. No diisobutylphenyl ether is obtained.

Other Condensation Methods (*19*)

In general, the preparation of diisobutylphenol involves the addition of a cationoid catalyzer to equimolar mixtures of phenol and diisobutylene, with or without an inert diluent. The amount of the catalyzer used and the temperature employed vary with the chemical nature of the condensing agent. For example, for concentrated sulfuric acid, 0.15 to 0.3 molar quantities at room temperature (20–25° C.) are sufficient, and the yield is 90–95 per cent. For a metal salt, such as cupric chloride, 1 mole and refluxing of the reaction mixture are necessary; the yield is about 30 per cent. In much poorer yields (about 10 per cent), *p*-diisobutylphenol can be prepared from diisobutylene hydrohalides (chloride, bromide, and iodide) and phenol (or sodium phenolate) at room temperature. At higher temperatures *p-tert*-butylphenol is the main reaction product.

In all condensation methods not involving sulfuric acid as the condensing agent, the purification procedures of Behaghel and Freiensehner (*3*) and others (*28*, *29*) were employed. The condensation product was first washed with water, then separated and dissolved in toluene. The toluene extract was thoroughly treated with Claisen solution (*7*), a mixture of equal parts by volume of 50 per cent aqueous potassium hydroxide solution and methanol. These Claisen solution extracts were combined, once more extracted with toluene, and then acidified with dilute hydrochloric acid (10 per cent), causing the separation of a phenolic oil. This oil was dried and subjected to fractional distillation. The fractions consisted largely of *p*-diisobutylphenol, unreacted phenol, *p-tert*-butylphenol, and triisobutyl- and tetraisobutylphenol. Examination of the neutral products contained in the toluene extracts showed the presence of unreacted diisobutylene, together with its higher polymers, tri- and tetra-isobutylene, and other aliphatic polymeric hydrocarbons.

Repeated attempts to isolate in these condensations the isomeric ether (the *tert*-diisobutylphenyl ether), particularly in condensations where a diisobutyl hydrohalide and sodium phenolate were used as well as in the case where sulfuric acid was employed as a catalyst, resulted in failure. This appears to be in harmony with the observations of Ipatieff and co-workers (*21*) and in contrast to earlier postulations (*13*, *40*, *41*). Thus, in agreement with Ipatieff it can be repeated that "ether formation is not necessarily an intermediate step in nuclear alkylations with olefins."

TABLE I. PHYSICAL CONSTANTS OF DIISOBUTYLPHENOL AND ITS DERIVATIVES

No.	Compound	M. P. °C.	B. P. (760 Mm.) °C.
I	Diisobutylphenol, or *p-tert*-octylphenol, or 2-(*p*-hydroxyphenyl)-2,4,4-trimethylpentane	83–84	280–283
II:	Ethers:		
a	Methyl[a]	...	272
b	Ethyl[b]	...	280
c	Benzyl[c]	106	...
d	Menaphthyl[c]	99	...
III:	Esters:		
a	Acetate[d]	...	122–4 (1 mm.)
b	Benzoate[e]	81–83	...
c	*p*-Nitrobenzoate[e]	115	...
IV:	Urethans:		
a	Phenyl[f]	145–147	...
b	α-Naphthyl[g]	116	...
V:	Quinones:		
a	Methoxy[h]:	155	...
a'	Oxime	169	...
a''	Dioxime	183	...
b	Ethoxy[i]	135	...
VI:	Halogen:		
a	Monochloro[j]	27–29	...
b	Dichloro[k]	44–46	...
c	Monobromo[l]	30–32	...
VII:	Nitro:		
	Mononitro[m]		
a	Na salt	Decomposed	...
a'	Benzoate	98– 99	...
b	Nitrobromo	136	...
c	Dinitro[n]	68	...
VIII:	Amino[o]:		
	Monoamino hydrochloride	210	...
IX:	Methylol[p]:		
	Dimethylol	70	...
a	Monomethyl ether[q]	105	...
b	Tribenzoate[r]	108–111	...
X:	Azo dyes:		
	2'-Hydroxy-5'-(α,α,γ,γ-tetramethyl)-butyl	...	...
a	4-Nitroazobenzene	161	...
b	Azobenzene-4-sulfonic acid	305 (decomposed)	...
c	2-Chloroazobenzene	98	...
d	2,5-Chloroazobenzene	105	...
e	4-Methoxyazobenzene	115	...
f	4-Acetylaminoazobenzene	165	...
g	2,5-Diethoxy-4-benzoylaminobenzene	165	...
h	4-Methyl-2-nitroazobenzene	137	...
i	Benzeneazonaphthalene-4-sulfonic acid	315 (decomposed)	...
j	Benzene-(2-azo-2)-toluene-(5-azo-2)-toluene	136	...
k	Diphenyl-4,4-bis-azo-2-(4-α,α,γ,γ-tetramethyl)-1-butylphenol	168	...
XI:	Acids:		
a	Phenoxyacetic[t]	108–109	...
b	Salicylic[u]	157–158	...
b'	Acetylsalicylic[v]	*99–100*	...
c	Monosulfonic (Na salt)[w]	Decomposed	...
c'	Monosulfonic (Me ether)	Decomposed	...
d	Disulfonic (di-Na salt)[w]	Decomposed	...
XII:	Aldehyde[x]:	50	296
a	Semicarbazone	228	...
b	Phenylhydrazone	169	...
c	2,4-Dinitrophenylhydrazone	185	...

[a] Prepared by interaction of the sodium salt of No. I with methyl iodide in alcoholic solution. Insoluble in Claisen solution, soluble in cold concentrated sulfuric acid with the gradual formation of the monosulfonic acid (XIc'). Concentrated nitric acid has no effect, even on prolonged boiling. Sp. gr., 0.927 (28° C.); n_D^{25}, 1.5026 (*4*).

[b] Prepared like II*a*, using ethyl iodide. Solubility the same as II*a*. Sp. gr., 0.916 (23° C.); n_D^{25}, 1.4884 (*4*).

[c] Prepared by treating the sodium salt of No. I with benzyl and menaphthyl chloride, respectively (*5*).

[d] Prepared by treating No. I with either acetic acid anhydride or acetyl chloride. Sp. gr., 0.9245 (24° C.); n_D^{25}, 1.4660 (*34*).

[e] Prepared from No. I and benzoyl- and *p*-nitrobenzoyl chloride, respectively (*34*).

[f] Prepared from No. I and phenyl isocyanate.

[g] Prepared from No. I and α-naphthyl isocyanate.

[h] Prepared by oxidizing *IIa with chromic acid* anhydride in glacial acetic acid solution. Golden yellow crystals are formed. The mono- and dioxime (*Va'*, *a''*) were prepared by the conventional methods (*4*).

[i] Prepared similar to *Va* by oxidizing II*b*. Golden yellow crystals.

[j] Prepared from No. I and 1 mole of sulfuryl chloride (*34*, *48*). Phenol coefficient, 118. Exhaustive nitration yielded 2-chloro-4,6-dinitrophenol (m. p., 108° C.).

[k] Prepared from No. I and 2 moles of sulfuryl chloride (*34*, *48*). Phenol coefficient, 69.

[l] Prepared from No. I and calculated amounts of bromine at 85° C. (*34*, *48*). Phenol coefficient, 25. Nitration with 1 mole nitric acid in glacial acetic acid yielded VII*b*. Exhaustive nitration gave 2-bromo-4,6-dinitrophenol (m. p. 118° C.).

[m] Prepared from 1 mole of No. I dissolved in glacial acetic acid and 1 mole of concentrated nitric acid (oily product). The sodium salt is red and quite insoluble in water. Crystalline benzoate (VII*a*) was prepared by the Schotten-Baumann reaction (*51*).

[n] Prepared from 1 mole of No. I dissolved in glacial acetic acid and 2 moles of concentrated nitric acid (*51*). Phenol coefficient, *10*; yellow crystals. This compound was found to possess no hyperthermic action (*9*).

[o] Prepared by the reduction of VII*a* with tin and hydrochloric acid (*51*). Diazotization and subsequent hydrolysis yielded diisobutylcatechol, melting at 107° C. (*53*).

[p] Prepared by mixing No. I with 20 per cent sodium hydroxide and 40 per cent formaldehyde solution, and allowing the mixture to stand for 1 week (*52*). Exhaustive nitration yielded picric acid (*52*).

[q] Prepared from IX by methylation with dimethyl sulfate or methyl iodide (*52*).

[r] Prepared from IX with benzoyl chloride (*52*).

[s] Diazotization of No. I with: *p*-nitroaniline (*a*); sulfanilic acid (*b*); 2-chloroaniline (*c*); 2,5-dichloroaniline (*d*); anisidine (*e*); *p*-acetylphenylenediamine (*f*); *p*-benzoylphenylenediamine (*g*); *o*-nitro-*p*-toluidine (*h*); naphthionic acid (*i*); aminoazotoluene (*j*); and benzidine (*k*) (*25*).

[t] Because of the insolubility of the sodium salt of No. I, the reaction had to be modified by dissolving No. I in Claisen solution and treating this solution with chloro- or bromoacetic acid, or by treating a suspension of the sodium salt of No. I in alcohol with sodium bromoacetate and refluxing the mixture (*34*, *48*).

[u] 206 grams of No. I were dissolved in 1.5 liters of xylene in a three-necked round-bottomed flask provided with a reflux condenser and an inlet tube for the introduction of dry carbon dioxide. While the solution was boiling and while a slow stream of carbon dioxide was passing through the solution, 44 grams of sodium metal were slowly added over a period of 9 hours. The reaction mixture was then allowed to cool in carbon dioxide atmosphere. The xylene was decanted off and the precipitate extracted with hot water. The water solution was acidified, and the precipitated diisobutylsalicylic acid was recrystallized *from alcohol* (*1*). Diisobutylsalicylic acid was also prepared by subjecting the dry sodium salt of No. I to carbon dioxide under pressure.

[v] Prepared by refluxing XI*b* with acetic acid anhydride or acetyl chloride (*1*).

[w] Prepared by treating No. I with 1 mole (XI*c*) or 2 moles (XI*d*) equivalent of concentrated sulfuric acid and warming the mixture on a steam bath until the material became water soluble. The sodium salt of the monosulfonic acid (XI*d*) is quite insoluble in water (*34*, *48*).

[x] Eighty grams of sodium hydroxide were dissolved in 80 cc. of water. Into this solution 100 grams of No. I (half mole) were introduced. Hot ethanol was added to the mixture with vigorous shaking until a clear solution resulted. To this solution 120 grams of chloroform were added in 10-cc. portions during the course of an hour and a half. The temperature of the reaction mixture was kept at 60–65° C. throughout the addition. Precipitation of sodium chloride took place rapidly. After 2 hours the mixture was cooled and acidified with hydrochloric acid and filtered. The alcohol was distilled off and the residue extracted with ether. The ether extract was dried with *anhydrous sodium sulfate*; then the ether was distilled off and the residue fractionally distilled at atmospheric pressure. The compound was purified through its phenylhydrazone derivative (XII*b*). This product was prepared by adding calculated amounts of phenylhydrazine to a solution of the aldehyde in ethyl alcohol. The phenylhydrazone was hydrolyzed by refluxing its alcoholic solution with phosphoric acid to which a small amount of formaldehyde (0.25 per cent) had been added, or by refluxing its alcoholic solution with a formaldehyde solution. The hydrolysis was followed by steam distillation. The semicarbazone (XII*a*) and the 2,4-dinitrophenylhydrazone (XII*c*) were prepared employing the conventional methods (*24*).

Properties

PHYSICAL. Pure diisobutylphenol is a colorless, odorless crystalline solid with a melting point of 84° C. Its crystals are birefringent under crossed Nicol prisms, show rectangular extinction, and exhibit the phenomenon of the polarization cross.

The phenol is volatile with steam. It is practically insoluble in cold and hot water, as well as in dilute alkali, but is soluble in Claisen solution (*7*), which is a mixture of equal parts of methanol and 50 per cent aqueous potassium hydroxide solution. These solubility characteristics place it under the group of "cryptophenols" (*3*). It is very soluble in most organic solvents, such as alcohol, ether, chloroform, carbon tetrachloride, acetone, and benzene. It is soluble only to a limited extent in the lower aliphatic hydrocarbons,

TABLE II. FORMULAS AND ANALYSES[a]

No.	Formula	Calculated C	H	N	N.E.[b]	Na	Cl	MeO	Found C	H	N	N.E.[b]	Na	Cl	MeO
I:	$HOC_6H_4C(CH_3)_2CH_2C(CH_3)_3$ (1, 4)	81.55	10.68	...	...	...	...	...	81.50	10.75	...	...	...	...	...
II:															
a	$CH_3OC_6H_4C_8H_{17}$	81.82	10.91	...	...	...	...	...	81.87	10.85	...	...	...	...	...
b	$C_2H_5OC_6H_4C_8H_{17}$	82.06	11.11	...	...	...	...	...	82.10	11.28	...	...	...	...	...
c	$C_6H_5CH_2OC_6H_4C_8H_{17}$	85.13	9.45	...	...	...	...	...	85.38	9.69	...	...	...	...	...
d	$C_{10}H_7CH_2OC_6H_4C_8H_{17}$	87.21	8.14	...	...	...	...	...	86.84	8.71	...	...	...	...	...
III:															
a	$CH_3COOC_6H_4C_8H_{17}$	77.42	9.67	...	...	...	...	...	77.62	9.90	...	...	...	...	...
b	$C_6H_5COOC_6H_4C_8H_{17}$	81.29	10.32	...	...	...	...	...	81.45	10.51	...	...	...	...	...
c	$O_2NC_6H_4COOC_6H_4C_8H_{17}$	...	...	3.94	...	...	...	...	...	...	3.85	...	...	...	...
IV:															
a	$C_6H_5NHCOOC_6H_4C_8H_{17}$	77.53	8.30	4.31	...	...	...	...	77.54	8.20	4.33	...	...	...	...
b	$C_{10}H_7NHCOOC_6H_4C_8H_{17}$	...	...	3.73	...	...	...	...	...	...	3.85	...	...	...	...
V:															
a	$O:C_6H_2(OCH_3)(C_8H_{17}):O$	72.00	8.80	...	...	...	...	12.40	77.91	8.95	...	...	...	...	12.70
a'	$HON:C_6H_2(OCH_3)(C_8H_{17}):O$	...	...	5.28	...	...	...	...	...	...	5.28	...	...	...	...
a''	$HON:C_6H_2(OCH_3)(C_8H_{17}):NOH$	...	...	10.00	...	...	...	...	...	...	9.33	...	...	...	...
b	$O:C_6H_2(OC_2H_5)(C_8H_{17}):O$	72.72	9.09	...	...	...	...	...	72.51	9.23	...	...	...	...	...
VI:															
a	$HOC_6H_3(Cl)C_8H_{17}$	70.00	8.75	...	...	...	14.58	...	69.54	8.77	...	...	...	15.02	...
b	$HOC_6H_2(Cl_2)C_8H_{17}$	61.31	7.29	...	...	...	25.54	...	61.48	7.35	...	...	...	25.06	...
c	$HOC_6H_3(Br)C_8H_{17}$	58.94	7.36	...	...	...	...	...	58.44	7.15	...	...	...	...	...
VII:															
a	$NaOC_6H_3(NO_2)C_8H_{17}$	...	...	...	...	8.42	...	...	...	...	...	...	8.73	...	...
a'	$C_6H_5COOC_6H_3(NO_2)C_8H_{17}$	...	...	3.94	...	...	...	...	...	...	4.07	...	...	...	...
b	$HOC_6H_2(NO_2)(Br)C_8H_{17}$	...	...	4.26	...	...	...	...	...	...	4.97	...	...	...	...
c	$HOC_6H_2(NO_2)_2C_8H_{17}$	...	...	9.15	...	...	...	...	...	...	9.26	...	...	...	...
VIII:	$HOC_6H_3(C_8H_{17})NH_2.HCl$	...	...	5.40	...	...	...	...	...	...	5.38	...	...	...	...
IX:	$HOC_6H_2(C_8H_{17})(CH_2OH)_2$	70.86	10.24	...	...	...	...	...	71.17	10.12	...	...	...	...	...
a	$CH_3OC_6H_2(C_8H_{17})(CH_2OH)_2$	72.85	10.00	...	...	...	...	...	73.39	10.05	...	...	...	...	...
b	$C_6H_5COOC_6H_2(C_8H_{17})(CH_2OCOC_6H_5)_2$	76.82	6.57	...	...	...	...	...	76.41	6.87	...	...	...	...	...
X:															
a	$HOC_6H_3(C_8H_{17})N:NC_6H_4NO_2$	...	...	11.81	...	...	...	...	...	...	11.13	...	...	...	...
b	$HOC_6H_3(C_8H_{17})N:NC_6H_4SO_3H$	...	...	7.14	...	...	...	...	...	...	6.91	...	...	...	...
c	$HOC_6H_3(C_8H_{17})N:NC_6H_4Cl$	...	...	8.13	...	...	...	...	...	...	7.99	...	...	...	...
d	$HOC_6H_3(C_8H_{17})N:NC_6H_3Cl_2$	...	...	7.49	...	...	...	...	...	...	7.45	...	...	...	...
e	$HOC_6H_3(C_8H_{17})N:NC_6H_4OCH_3$	...	...	8.28	...	...	...	...	...	...	8.45	...	...	...	...
f	$HOC_6H_3(C_8H_{17})N:NC_6H_4NHCOCH_3$	...	...	11.44	...	...	...	...	...	...	11.57	...	...	...	...
g	$HOC_6H_3(C_8H_{17})N:NC_6H_2(OC_2H_5)_2NHCOC_6H_5$	...	...	8.12	...	...	...	...	...	...	8.15	...	...	...	...
h	$HOC_6H_3(C_8H_{17})N:NC_6H_3(NO_2)CH_3$	...	...	11.37	...	...	...	...	...	...	11.57	...	...	...	...
i	$HOC_6H_3(C_8H_{17})N:NC_{10}H_6SO_3H$	...	...	6.34	...	...	...	...	...	...	5.78	...	...	...	...
j	$HOC_6H_3(C_8H_{17})N:NC_6H_3(CH_3)N:NC_6H_4CH_3$	...	...	12.67	...	...	...	...	...	...	12.84	...	...	...	...
k	$(HOC_6H_3(C_8H_{17})N:NC_6H_4)_2$	...	...	11.37	...	...	...	...	...	...	11.57	...	...	...	...
XI:															
a	$HOOCCH_2OC_6H_4C_8H_{17}$	72.72	9.09	...	264	...	...	...	72.82	9.20	...	262	...	...	...
b	$HOC_6H_3(C_8H_{17})COOH$	72.00	8.80	...	250	...	...	...	72.12	8.93	...	253	...	...	...
b'	$CH_3COOC_6H_3(C_8H_{17})COOH$	69.86	8.22	...	292	...	...	...	70.01	8.34	...	289	...	...	...
c	$HOC_6H_3(C_8H_{17})SO_3Na$	...	...	...	...	7.46	...	...	...	...	...	...	7.57	...	...
c'	$CH_3OC_6H_3(C_8H_{17})SO_3H$	60.00	8.00	...	300	...	...	...	59.81	7.88	...	290	...	...	...
d	$HOC_6H_2(C_3H_7)(SO_3Na)_2$	...	...	...	...	11.20	...	...	...	...	...	...	11.30	...	...
XII:	$HOC_6H_3(C_8H_{17})CHO$	76.92	9.23	...	...	...	...	...	75.44	9.24	...	...	...	...	...
a	$HOC_6H_3(C_8H_{17})CH:N.NHCONH_2$	...	...	14.43	...	...	...	...	...	...	14.31	...	...	...	...
b	$HOC_6H_3(C_8H_{17})CH:NNHC_6H_5$	...	...	8.64	...	...	...	...	...	...	8.58	...	...	...	...
c	$HOC_6H_3(C_8H_{17})CH:NNHC_6H_3(NO_2)_2$	...	...	13.53	...	...	...	...	...	...	13.95	...	...	...	...

[a] All the analyses were performed microanalytically according to the procedures of Niederl and Niederl (*41A*).
[b] Neutralization equivalent.

such as petroleum ether, ligroin, or diisobutylene, which are therefore most suitable for the recrystallization of the phenol. Its solubility in water, alcohol, glycerol, and their aqueous solutions at room temperature, is as follows (*17*, *22*):

1 part dissolves in 60,000 parts water
in 20,000 parts 5% alcohol soln.
in 7,500 parts 10% alcohol soln.
in 5,000 parts 25% alcohol soln.
in 3,000 parts 30% alcohol soln.
in 2,000 parts 35% alcohol soln.
in 63 parts 50% alcohol soln.
in less than 1 part 95% alcohol
in 450 parts glycerol
in 6,000 parts 50% glycerol soln.

Equal parts of diisobutylphenol and soaps upon addition of water (1:500, 1:1000, 1:2000, and 1:3000) yield opalescent colloidal solutions, with small amounts of the phenol gradually settling out. With sulfonated oils (1 part of phenol to 5 parts of sulfonated oil) more stable solutions result. The latter solutions permit chemical transformations (diazotizations, as shown by X*a–k* (Tables I and II) in which aqueous media are required (*25*).

PHYSIOLOGICAL. Diisobutylphenol has good bactericidal and preserving properties; its phenol coefficient has been ascertained to be 158.

The 1:1000 30 per cent alcohol solution, diluted 1:3, kills *Staphylococcus aureus* in 15 seconds, and in a 1:10 dilution in 10 minutes. This same solution is bactericidal to *Bacillus typhosus* in full strength (1:1000) in both 5 minutes and 15 seconds. Its aqueous soap solutions, however, show a marked decrease in bactericidal action and lose it entirely in dilutions above 1:500. Exceptions are the aqueous solutions with sulfonated oils as dispersing agents which in dilutions up to 1:1000 still exhibit bactericidal activity (*51A*). Its toxicity has been found to be less than that of thymol. Five grams of this phenol per kg. of body weight are still not fatal (injections in oil) (*49A*).

CHEMICAL. Diisobutylphenol gives, essentially, all the known qualitative phenolic reactions; but on account of its insolubility in water and that of its salts (1 part of sodium salt dissolves in 3000 parts of water, 1 part of potassium salt in 2000 parts of water), the conventional tests require modifications to take into account this characteristic.

Its concentrated ethanol solution (0.2 cc.) gives an intense green color with a freshly prepared dilute ferric chloride solution (one drop). The dilute aqueous solutions of its potassium or sodium salt upon the addition of bromine water give, first, a green coloration and, in greater concentrations, a green precipitate. A trace of the phenol mixed with an equal amount of vanillin dissolved in concentrated sulfuric acid assumes a cherry red coloration upon heating on a steam bath, and subsequent dilution with water produces a lilac

coloration. Diazotization with *p*-nitroaniline (X*a*) gives, in very dilute solution, an orange coloration; with a more concentrated solution, a red coloration, and in still greater concentration, a red precipitate (melting point, 161° C.).

Oxidations

DIISOBUTYLPHENOL (*48*). Three hundred grams of sodium hydroxide pellets were heated to their melting point in an iron crucible; then 100 grams of diisobutylphenol were added, which caused the mixture to become hard as the result of the formation of the sodium salt. The heating of the alkaliphenol mixture was continued until partial liquefaction took place. Then 100 grams of powdered copper oxide were added in small quantities; the fusion mixture first assumed a blue, then brown, and finally a red coloration, indicating oxidation. All the while the fusion mixture was stirred. The contents of the crucible were then transferred to a beaker, dissolved in water, and filtered, leaving a residue of copper sponge and unchanged sodium phenolate. The filtrate was decomposed with hydrochloric acid and then extracted with ether. The ether extract was evaporated to dryness, and the residue treated with ammonium carbonate and filtered. This filtrate, containing the ammonium salt of *p*-hydroxybenzoic acid, was again decomposed with hydrochloric acid and once more extracted with ether. The ether extract was evaporated to dryness, and the residue was dissolved in boiling water, treated with decolorizing carbon (Norite), filtered, and allowed to crystallize. The yield was 1 to 2 per cent. The acid had a melting point of 210° C.; the mixed melting point with *p*-hydroxybenzoic acid was 210° C., and with salicylic acid, 135° C.

Treatment of diisobutylphenol with an excess of concentrated nitric acid yielded picric acid, which is likewise obtained from *p-tert*-butyl- and *p-tert*-amylphenol under similar reaction conditions.

ETHERS (*4*). Ten grams of the methyl ether of diisobutylphenol (II*a*) were dissolved in 50 cc. of glacial acetic acid. To this solution 500 cc. of glacial acetic acid containing 30 grams of chromic acid anhydride were added. A vigorous reaction set in immediately. As soon as the reaction had subsided, the mixture was placed on a steam bath for half an hour to complete the oxidation. When cold the oxidation mixture was poured into water, which caused the separation of a flocculent precipitate. This precipitate was filtered off and purified as in the above case of the alkali fusion of the free phenol. A number of salts (the lead and the ammonium salt) of the anisic acid thus isolated were also prepared and analyzed (melting point 176° C.; mixed melting point with anisic acid, 180° C.; with *o*-methoxybenzoic acid, 75° C.).

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