[Contribution from the Kedzie Chemical Laboratory,
Michigan State College]

ORIENTATION IN THE PHOSPHORIC ACID-CATALYZED ALKYLATION OF ORTHO-CRESOL[1, 2]

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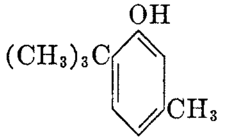
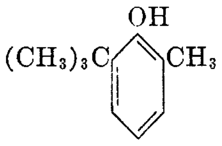
Received October 27, 1949

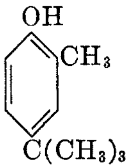
In connection with a research program on the *ortho*-alkylphenols and their derivatives (1) it was of interest to reinvestigate the orientation described by Chichibabin (2) when *o*-cresol was alkylated with *tert*-butyl alcohol in the presence of phosphoric acid. A careful examination of the product obtained when *m*-cresol was similarly alkylated showed that the *tert*-butyl group entered the ring *ortho* to the hydroxyl and *para* to the methyl, yielding



Chichibabin, reasoning by analogy, assumed that the product obtained from *o*-cresol, *tert*-butyl alcohol, and phosphoric acid was 6-*tert*-butyl-*o*-cresol (I).



I



II

Other workers have claimed that when zinc chloride (3) or aluminum chloride (4) was used as the catalyst, the product was 4-*tert*-butyl-*o*-cresol (II). If phosphoric acid acts uniquely to give *ortho* alkylation, then this behavior is worthy of further investigation; if not, the error[3] should be corrected.

Structure I claimed by Chichibabin is one which belongs to the class of compounds known as partially hindered phenols (5, 6). Such substances are known to be insoluble in 10% aqueous alkali, whereas Chichibabin isolated his product *via* extraction with dilute aqueous alkali. Furthermore, it has been shown (1) that *o*-*tert*-butylphenol readily rearranges to the *para* isomer in the presence of 100% phosphoric acid. It was believed, therefore, the Chichibabin's product had, in fact, structure II.

The hydrogenation of I has been reported (7) but its synthesis was not given. The properties of two *tert*-butyl-*o*-cresols of undetermined structure have also been reported (8).

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[1] The material herein presented is taken from the M.S. thesis of Edwin A. Haglund, Michigan State College, August 1949.

[2] Presented before the Organic Division at the Atlantic City meeting of the American Chemical Society, September 1949.

[3] See, for example, Heilbron, *Dictionary of Organic Compounds*, Oxford University Press, New York, N. Y., 1943, Vol. I, p. 284, which ascribes to 6-*tert*-butyl-*o*-cresol the properties and method of preparation described by Chichibabin.

An authentic sample of I was synthesized according to the scheme which had been used previously (1) to prepare *o*-*tert*-butylphenol. Reduction of III was carried out in an alkaline medium, thus avoiding migration of the *tert*-butyl group.

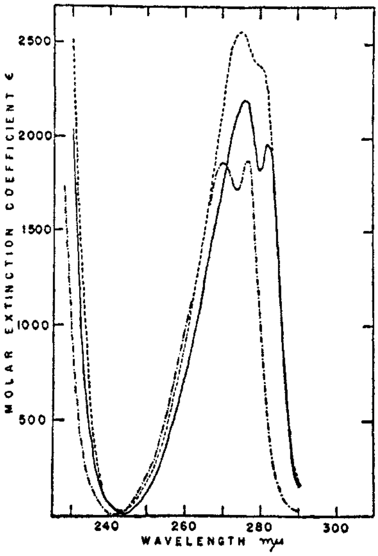
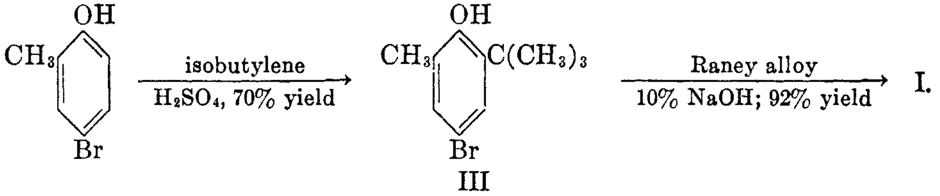


FIGURE 1. ULTRAVIOLET ABSORPTION SPECTRA: ———, 2.35 × 10^{-4} *M* 4-*tert*-butyl-*o*-cresol (II); —·—·—, 2.67 × 10^{-4} *M* 6-*tert*-butyl-*o*-cresol (I); - - - -, 2.37 × 10^{-4} *M* 4, 6-di-*tert*-butyl-*o*-cresol; all in cyclohexane solvent.



The boiling point of I was about 10° below that of the product obtained by alkylation of *o*-cresol according to Chichibabin's precedure. Furthermore, I was insoluble in 10% sodium hydroxide and did not give the characteristic phenol test with ferric chloride. No derivative could be prepared by the conventional methods [save the bromo derivative (III)] whereas the alkylation product of Chichibabin readily yielded a crystalline aryloxyacetic acid. That I was a partially hindered phenol and not an ether was indicated by a positive reaction in the sensitive spot test for phenols with phosphomolybdic acid and ammonium hydroxide (9) and the fact that its ultraviolet absorption spectrum (Figure 1) was very similar to that of phenol. Furthermore, under the conditions used to prepare III, any ether, if formed, would have rearranged (10) to the alkyl phenol.

That the product obtained by the alkylation of *o*-cresol was the 4-isomer (II) was indicated by the facts that (a) compound I, when treated with either sulfuric or phosphoric acid, rearranged to give a product in all respects identical with the alkylation product and (b) its absorption spectrum (Figure 1) shows the shift of about 6 mμ toward the longer wavelengths characteristic of *para*-alkylphenols (1). This point is further illustrated in Table I, in which the similar positions of the peaks in the spectra of unsubstituted and *ortho*-alkylphenols are contrasted with the spectra of the *para*-alkylphenols. It is to be noted that 4,6-di-*tert*-butyl-*o*-cresol also exhibits this shift (Figure 1) although the peaks are broader and overlap, as one would expect of the more highly substituted compound. Thus, sterically hindering the hydroxyl group does not appreciably effect this spectral shift.

TABLE I

MAXIMA IN THE ULTRAVIOLET ABSORPTION SPECTRA OF SOME PHENOLS

	PEAK 1		PEAK 2		REF.
	mμ	ε	mμ	ε	
Phenol	271	2130	278	1847	1
o-Cresol	271	2140	278	2040	11
o-*tert*-Butylphenol	271	2014	278	2018	1
6-*tert*-Butyl-*o*-cresol (I)	270	1865	277	1876	Fig. 1
p-Cresol	278	2180	284	1860	11
p-*tert*-Butylphenol	277	2130	283	2054	1
Alkylation product (II) (4-*tert*-Butyl-*o*-cresol)	276	2200	282	1957	Fig. 1
4,6-Di-*tert*-butyl-*o*-cresol	275	2557	(280)	2384	Fig. 1

It is concluded, therefore, that the alkylation of *o*-cresol according to the procedure of Chichibabin leads to a product with structure II.

EXPERIMENTAL

4-Bromo-6-tert-butyl-o-cresol (III). A solution of 140 g. (0.75 mole) of 4-bromo-*o*-cresol (m.p. 63–64°, 4-bromo-2-methylphenoxyacetic acid) m.p. 122–123°) in 200 cc. of benzene was alkylated with isobutylene and 5 cc. of concentrated sulfuric acid at 65° using a procedure similar to that of Stillson, Sawyer, and Hunt (5). It was necessary to use an excess of isobutylene (about 1.4 moles) and a reaction time of about five hours in order to obtain maximum yields. Under these conditions, 128 g. (70.0%) of III were obtained, b.p. 130–135° at 11 mm.; recrystallized from petroleum ether, m.p. 49–50°.

Anal. Calc'd for $C_{11}H_{15}BrO$: Br, 32.89. Found: Br, 32.75 (Parr).

The compound was insoluble in 10% aqueous sodium hydroxide and did not yield a phenoxyacetic acid derivative by the usual procedure.

6-tert-Butyl-o-cresol (I). When 11.1 g. (0.0457 mole) of III was treated with 30 g. of Raney nickel-aluminum alloy and 300 cc. of 10% sodium hydroxide according to the procedure of Schwenk, *et. al.* (12) and Hart (1) it yielded 6.9 g. (92.0%) of I, b.p. 225–227° at 740 mm.

Anal.[4] Calc'd for $C_{11}H_{16}O$: C, 80.3; H, 9.80.
Found: C, 80.34; H, 10.08.

I was insoluble in 10% aqueous sodium hydroxide and gave a negative color test with

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[4] This analysis was performed by the Clark Microanalytical Laboratory, Urbana, Illinois. The other analyses were performed by E.A.H.

ferric chloride. With phosphomolybdic acid and ammonium hydroxide, a blue color appeared (9).

Alkylation of o-cresol. *o*-Cresol (54 g.) was treated with a total of 200 g. of 100% phosphoric acid and 40 g. of *tert*-butyl alcohol for eight hours at 60–65° according to the procedure of Chichibabin (2). Instead of using Chichibabin's tedious procedure of isolation of the sodium phenoxide, the reaction mixture was poured into 2 liters of water and extracted with ether. Extraction of the ether layer with 10% sodium hydroxide, acidification, extraction with ether, drying over calcium chloride, removal of the solvent, and distillation of the product yielded 52 g. (63.4%) of alkylation product, [4-*tert*-butyl-*o*-cresol (II)] b.p. 235–237° at 740 mm. Treatment with chloroacetic acid yielded the 2-methyl-4-*tert*-butylphenoxyacetic acid, m.p. 101.5–102.0°.

Anal. Calc'd for $C_{13}H_{18}O_3$: Neut. equiv., 222. Found: Neut. equiv., 221.5.

The alkylation product gave a positive ferric chloride test and a positive phenol spot test (9).

Rearrangement of I. The homogenous mixture of one cc. of I with five drops of concentrated sulfuric acid was warmed gently for five minutes, then poured on ice, and extracted with petroleum ether. After washing with sodium carbonate and evaporation of the solvent, a liquid remained which was soluble in 2% aqueous sodium hydroxide and yielded a phenoxyacetic acid derivative, m.p. 99–100°; mixture with the same derivative of the alkylation product, m.p. 97–100°.

Two cc. of I treated with 100% phosphoric acid at 65–70° for eight hours, with constant stirring, also yielded some II (phenoxyacetic acid derivative, m.p. 97–100°) as well as some unchanged I.

The ultraviolet absorption spectra were determined with a Beckman spectrophotometer, model DU, using 1-cm. quartz cells. The cyclohexane solvent was freed of benzene by passage through silica gel, followed by fractionation.

SUMMARY

1. The product obtained from the phosphoric acid-catalyzed alkylation of *o*-cresol with *tert*-butyl alcohol is 4-*tert*-butyl-*o*-cresol and not 6-*tert*-butyl-*o*-cresol as stated in the literature.

2. The chemical properties and absorption spectra of these compounds are discussed.

EAST LANSING, MICH.

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