454. *Stereochemical Aspects of Aromatic Substitution. Part II.* Derivatives of* tert.*-Butylbenzene.*

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An attempt has been made to introduce bromine atoms into positions 2 : 6 in reactive *tert.*-butylbenzene derivatives. In no example studied was it possible to introduce more than one bromine atom.

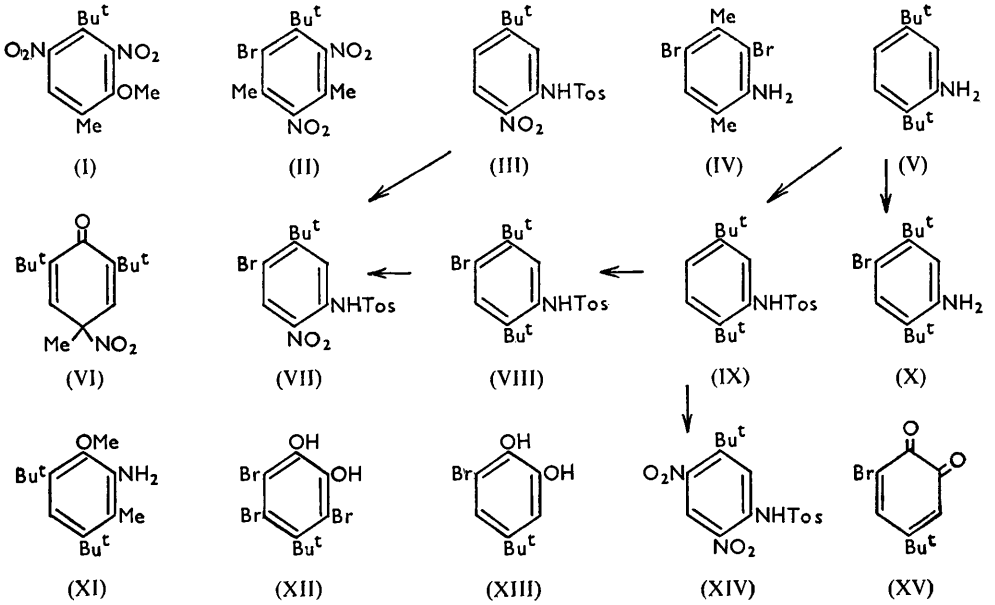
Although many derivatives of *tert.*-butylbenzene are known in which the *tert.*-butyl group has a nitro-group on each side, *e.g.*, (I),[1] or even a halogen atom and a nitro-group, *e.g.*, (II),[2] no examples appear to exist in which this group is flanked by two chlorine or

* Part I, preceding paper.

[1] Carpenter, Easter, and Wood, *J. Org. Chem.*, 1951, **16**, 586.
[2] Carpenter and Easter, *ibid.*, 1954, **19**, 77.

two bromine atoms. Using ordinary space-filling models it is impossible to construct molecules of this type and it was thought of interest to attempt the preparation of such bromo-compounds.

m-tert.-Butylaniline was first selected for study because steric hindrance effects appear to be negligible in *m*-toluidine and its derivatives. *m*-Toluidine and its benzenesulphonyl and toluene-*p*-sulphonyl derivative can be readily tribrominated. 4-Chloro-3-methylbenzenesulphonanilide undergoes chlorination in the 2-position instead of in the more exposed 6-position [3] and even on bromination gives a mixture of the 2- and the 6-bromo-compound, both of which are readily converted into the 2 : 6-dibromo-derivative. It



would be expected, therefore, that, except on steric grounds, 3-*tert.*-butyl-*N*-toluene-*p*-sulphonylaniline would readily yield an analogous tribromo-derivative. It was found, however, that only a dibromo-derivative was produced even when a very large excess of *N*-bromosuccinimide was employed. Similarly *m-tert.*-butylaniline could be smoothly mono- and di-brominated but with excess of bromine gave a resin. In these reactions position 6 is first entered.

Again, since the dibromo-derivative (IV) is very readily prepared from 2 : 5-xylidine it appeared of interest to examine the bromination of 2 : 5-di-*tert.*-butylaniline (V). Monobromination either of the base or of its toluene-*p*-sulphonyl derivative (IX) occurred very readily, leading to almost quantitative yields of, probably, compounds (X) and (VIII) respectively. Further bromination was not smooth : bromine was absorbed but only oils were obtained and it appears likely that partial or total replacement of *tert.*-butyl groups had occurred since on nitration of either bromo-derivative (VIII) or (IX) one *tert.*-butyl group is displaced by a nitro-group, giving probably compounds (VII) [alternatively prepared from (III)] and (XIV).

It was then hoped to examine the bromination of the di-*tert.*-butyl-amine (XI), which appeared to be available from commercial 2 : 4-di-*tert.*-butyl-5-methylphenol by nitration, methylation, and reduction. However, on nitration only 4 : 6-di-*tert.*-butyl-3-methyl-2 : 4-dinitro*cyclo*hexa-2 : 5-dienone, 6-*tert.*-butyl-3-methyl-2 : 4-dinitrophenol, and 3-methyl-2 : 4 : 6-trinitrophenol could be isolated, in agreement with similar experiments by Albert and Sears.[4] A compound (VI), analogous to the first mentioned, was prepared

[3] Raper, Thompson, and Cohen, *J.*, 1904, **85**, 375.
[4] Albert and Sears, *J. Amer. Chem. Soc.*, 1954, **76**, 4979.

from 2 : 6-di-*tert.*-butyl-4-methylphenol, but this underwent decomposition without simple displacement, owing to the inability of the methyl group to be expelled as methylene. By starting, however, with 2 : 4-di-*tert.*-butyl-5-methylphenyl methyl ether a mononitro-derivative could be isolated, in somewhat small yield, and this was reduced to the amine (XI). This base reacted with bromine in acetic acid to give only oils; its toluene-*p*-sulphonyl derivative was unchanged even after treatment with such a vigorous brominating agent as *N*-bromosuccinimide in pyridine.

4-*tert.*-Butylcatechol might by analogy with catechol be expected to yield a tribromo-derivative (XII). Although mono-bromination went very smoothly, to give probably (XIII), further bromination resulted in complex mixtures from which only tri- and tetra-bromocatechols could be isolated. Interaction with nitric acid gave only the quinone (XV), more advantageously prepared by use of nitrous acid.

Experimental

2 : 4-*Dibromo*-5-*methyl*-N-*toluene*-p-*sulphonylaniline* was obtained by addition of bromine (2 mols.) in chloroform to a solution of *N*-toluene-*p*-sulphonyl-*m*-toluidine in chloroform, warming to expel hydrogen bromide, and dilution of the solution with light petroleum. After repeated recrystallisation from acetic acid or ethanol it formed prisms, m. p. 152° (Found: C, 40·3; H, 2·9. $C_{14}H_{13}O_2NSBr_2$ requires C, 40·1; H, 3·1%), and was slowly dissolved by cold sulphuric acid to give 2 : 4-dibromo-5-methylaniline, which formed needles, m. p. 75°, from ethanol (acetyl derivative, m. p. 172°, from acetic acid).[5]

Iodine monochloride (up to 10 mols.) did not react with the sulphonyl derivative in cold pyridine in 1—3 days.

2 : 4 : 6-*Tribromo*-3-*methyl*-N-*toluene*-p-*sulphonylaniline* was obtained in almost theoretical yield by the addition of *N*-bromosuccinimide (3 mols.) to a solution of *N*-toluene-*p*-sulphonyl-*m*-toluidine in pyridine. It crystallised from acetic acid in prisms, m. p. 171° (Found: C, 34·0; H, 2·7. $C_{14}H_{12}O_2NSBr_3$ requires C, 33·8; H, 2·4%), and was rapidly dissolved by cold sulphuric acid to give 2 : 4 : 6-tribromo-*m*-toluidine, m. p. 102°, alone or mixed with a sample prepared by Cohen and Dutt's method [6] (acetyl derivative, m. p. 208°; Blanksma [7] gives m. p. 205°).

N-*Benzenesulphonyl*-4-*chloro*-3-*methylaniline*.—Sulphuryl chloride (8 g., 1·2 mols.) was added to *N*-benzenesulphonyl-*m*-toluidine (11·8 g.). The vigorous reaction was completed on a steam-bath and the excess of sulphuryl chloride removed under reduced pressure. The product, recrystallised from acetic acid and then ethanol, had m. p. 129—130° (8 g.). Raper, Thompson, and Cohen,[3] who used sodium hypochlorite as chlorinating agent, give m. p. 130°.

Bromination of N-*Benzenesulphonyl*-4-*chloro*-3-*methylaniline*.—Bromine (1·7 mols.) was added to the compound (2·6 g.), dissolved in chloroform, the mixture heated under reflux, and the solvent removed. The product, recrystallised from acetic acid and then chloroform, had m. p. 121—123° (Found: C, 43·1; H, 3·0. $C_{13}H_{11}O_2NBrClS$ requires C, 43·4; H, 3·1%). From the mother-liquor was isolated an isomeride, which after repeated recrystallisation from chloroform, had m. p. 128—129°, markedly depressed on admixture with the previous compound (Found: C, 43·3; H, 2·9%). It is probable that the major product, m. p. 121—123°, is the 2-*bromo*-4-*chloro*-5-*methyl derivative* and the other the 2-*bromo*-4-*chloro*-3-*methyl derivative*.

Bromination of N-*Benzenesulphonyl*-2-*bromo*-4-*chloro*-5-*methylaniline*.—To the compound (0·24 g.) in pyridine was added *N*-bromosuccinimide (0·12 g.). After 1 hr. the mixture was decomposed by addition of hydrochloric acid and the product recrystallised from acetic acid, to give N-*benzenesulphonyl*-2 : 6-*dibromo*-4-*chloro*-3-*methylaniline*, m. p. 189—191° (Found: C, 35·4; H, 2·0. $C_{13}H_{10}O_2NBr_2ClS$ requires C, 35·5; H, 2·3%). The same compound was obtained by bromination of the isomeride (above).

N-*Benzenesulphonyl*-2 : 4-*dichloro*-3-*methylaniline*.—*N*-Benzenesulphonyl-*m*-toluidine (1·32 g.) was added to sulphuryl chloride (1·73 g.), and the mixture warmed on a steam-bath for 5 min. Excess of sulphuryl chloride was removed under diminished pressure and the residue recrystallised from acetic acid and then ethanol, giving crystals, m. p. 114° (Raper, Thompson, and Cohen [3] give m. p. 114°).

N-*Benzenesulphonyl*-6-*bromo*-2 : 4-*dichloro*-3-*methylaniline*.—*N*-Bromosuccinimide (1·13 g.)

[5] Nevile and Winther, *Ber.*, 1880, **13**, 971.
[6] Cohen and Dutt, *J.*, 1914, **105**, 515.
[7] Blanksma, *Chem. Weekblad*, 1909, **6**, 717.

was added to *N*-benzenesulphonyl-2 : 4-dichloro-3-methylaniline (1·89 g.) in pyridine and, after some time, the mixture decomposed by addition of hydrochloric acid. The *product*, after recrystallisation from chloroform, had m. p. 177—178° (Found : C, 39·4; H, 2·4. $C_{13}H_{10}O_2NBrCl_2S$ requires C, 39·5; H, 2·5%).

N-*Benzenesulphonyl-4-bromo-3-methylaniline*.—A solution of *N*-benzenesulphonyl-*m*-toluidine (4 g.) and bromine (2·9 g.) in chloroform was boiled for 2 hr. and then the solvent was distilled off. The *product*, crystallised first from ethanol and then acetic acid, gave rectangular plates, m. p. 129—130° (Found : C, 48·1; H, 3·5. $C_{13}H_{12}O_2NBrS$ requires C, 47·9; H, 3·7%).

Attempted Preparation of p-tert.-*Butylaniline by the Curtius Reaction*.—(*a*) *p-tert.*-Butylbenzoic acid was dissolved in a slight excess of thionyl chloride and the product, b. p. 138°/15 mm., dissolved in acetone and agitated with aqueous sodium azide. The mixture was diluted with water and extracted with benzene. The extract was heated on a steam-bath with 3N-sodium hydroxide for 2 hr. and the benzene removed in steam (no amine appeared to be present in the steam-distillate). The non-volatile solid was extracted with hot acetic acid and the residue crystallised from 2-ethoxyethanol, yielding needles of *di-(p-tert.-butylphenyl)urea*, m. p. 292° (decomp.) (Found : C, 78·2; H, 8·4. $C_{21}H_{28}ON_2$ requires C, 77·8; H, 8·6%). The acetic acid extract yielded crystals of pp′-*di*-tert.-*butylbenzanilide*, which after two recrystallisations from ethanol formed needles, m. p. 158° (Found : C, 81·4; H, 8·5; N, 4·7. $C_{21}H_{27}ON$ requires C, 81·5; H, 8·7; N, 4·5%). This compound was alternatively prepared by the interaction of *p-tert.*-butylaniline with *p-tert.*-butylbenzoyl chloride. (*b*) *p-tert.*-Butylbenzoyl chloride (10 c.c.) and sodium azide (5 g.) were boiled together in benzene for 5 hr. 3N-Sodium hydroxide (25 c.c.) was then added and heating continued for several hours. The product was then worked up as under (*a*) and with an identical result.

p-tert.-*Butylacetanilide*.—*p-tert.*-Butylbenzoic acid (40 g.) was dissolved in a slight excess of thionyl chloride, and the excess removed. The product, without further purification, was introduced into ammonia solution (200 c.c.; *d* 0·88) and the resultant amide filtered off and dried (m. p. 168°). This was added slowly to hypobromite solution prepared from bromine (18 c.c.) and sodium hydroxide (72 g.). When dissolution had occurred the product was slowly heated to 100° and then distilled in steam. The resultant oil was separated and acetylated, to give *p-tert.*-butylacetanilide, m. p. 168—171° (24 g.). This was converted into *m-tert.*-butylaniline by the method of Carpenter, Easter, and Wood ;[1] this base with toluene-*p*-sulphonyl chloride in pyridine gave m-tert.-*butyl*-N-*toluene*-p-*sulphonylaniline*, which crystallised from ethanol in prisms, m. p. 118° (Found : C, 67·5; H, 6·8. $C_{17}H_{21}O_2NS$ requires C, 67·3; H, 6·9%). This sulphonanilide in chloroform with bromine (1 mole) gave the 2-*bromo*-5-tert.-*butyl derivative* (Found : C, 53·8; H, 5·3. $C_{17}H_{20}O_2NSBr$ requires C, 53·4; H, 5·2%), which crystallised from ethanol in prisms, m. p. 131°, alone or mixed with a specimen prepared from 1-bromo-4-*tert.*-butyl-2-nitrobenzene, kindly supplied by Mr. J. E. L. S. Platou. *N*-Bromosuccinimide (2—5 mols.) was added to this monobromo-derivative in pyridine. The product was 2 : 4-*dibromo*-5-tert.-*butyl*-N-*toluene*-p-*sulphonylaniline*, which crystallised from acetic acid in needles, m. p. 151° (Found : C, 44·2; H, 4·0. $C_{17}H_{19}O_2NSBr_2$ requires C, 44·2; H, 4·1%).

Fuming nitric acid (1 c.c.) in acetic acid (1 c.c.) was added to 2-bromo-5-*tert.*-butyl-*N*-toluene-*p*-sulphonylaniline (1 g.) in acetic acid (3 c.c.). On cooling, prisms were deposited which, recrystallised from acetic acid, gave the 4(?)-*nitro-derivative*, m. p. 144° (Found : C, 47·7; H, 4·5. $C_{17}H_{19}O_4BrS$ requires C, 47·8; H, 4·5%).

m-tert.-Butyl-*N*-toluene-*p*-sulphonylaniline by the same method gave the 2-*nitro*-5-tert.-*butyl derivative*, which crystallised from ethanol in needles, m. p. 103° (Found : C, 58·0; H, 5·4; N, 8·2. $C_{17}H_{20}O_4N_2S$ requires C, 58·6; H, 5·7; N, 8·1%). This nitro-derivative with excess of *N*-bromosuccinimide in pyridine gave an almost quantitative yield of 4-*bromo*-5-tert.-*butyl*-2-*nitro*-N-*toluene*-p-*sulphonylaniline* (VII) (Found : C, 47·7; H, 4·2. $C_{17}H_{19}O_4N_4BrS$ requires C, 47·8; H, 4·5%), which crystallised from ethanol or acetic acid in yellow prisms, m. p. 131°.

Bromination of m-tert.-*Butylaniline*.—(*a*) Bromine (1 mol.) in acetic acid was added to the base in acetic acid. The bromine was immediately decolorised and a white precipitate separated. On addition of water a colourless oil separated, which did not solidify. With acetic anhydride it gave 2-*bromo*-5-tert.-*butylacetanilide*, which crystallised from ethanol in needles, m. p. 127° (Found : C, 53·8; H, 5·7. $C_{12}H_{16}ONBr$ requires C, 53·3; H, 5·9%). (*b*) In a similar experiment but with bromine (3 mols.), the first precipitate redissolved. Addition of water gave a black resin. (*c*) The base in chloroform was added to bromine (3 mols.) in chloroform. The mixture remained clear but after some hours a precipitate had been formed. All the chloroform was distilled off and the residue decomposed with ammonia solution. The resultant oil was dissolved in acetic anhydride, the solution decomposed with water, and the product purified by

repeated recrystallisation from ethanol. 2 : 4-*Dibromo*-5-tert.-*butylacetanilide* was obtained in needles, m. p. 143° (Found : C, 41·6; H, 4·3. $C_{12}H_{15}ONBr$ requires C, 41·3; H, 4·3%).

2 : 5-*Di*-tert.-*butyl*-N-*toluene*-p-*sulphonylaniline* (IX), prepared by the interaction of the base [1] with toluene-*p*-sulphonyl chloride in pyridine, crystallised from acetic acid in plates, m. p. 164° (Found : C, 70·3; H, 7·9. $C_{21}H_{29}O_2NS$ requires C, 70·2; H, 8·1%). Addition of bromine (1 mol.) in chloroform to this in chloroform gave an almost quantitative yield of 4(?)-*bromo*-2 : 5-*di*-tert.-*butyl*-N-*toluene*-p-*sulphonylaniline* (VIII), which crystallised from acetic acid in needles, m. p. 179° (Found : C, 57·6; H, 6·2. $C_{21}H_{28}O_2NSBr$ requires C, 57·5; H, 6·4%). Addition of *N*-bromosuccinimide to a pyridine solution of this compound produced a resin.

4(?)-*Bromo*-2 : 5-*di*-tert.-*butylaniline* (X), prepared by the addition of an acetic acid solution of bromine (1 mol.) to a cold solution of 2 : 5-di-*tert.*-butylaniline in acetic acid, crystallised from ethanol in plates, m. p. 90° (Found : C, 59·0; H, 7·6. $C_{14}H_{22}NBr$ requires C, 59·1; H, 7·8%). This base in acetic acid reacted rapidly with bromine, but the only crystalline material recovered was the hydrobromide of the base; the majority had been converted into a violet paste.

4-*Bromo*-5-tert.-*butyl*-2-*nitro*-N-*toluene*-p-*sulphonylaniline* (VII) was obtained by addition of fuming nitric acid (0·5 c.c.) in acetic acid (1 c.c.) to 4(?)bromo-2 : 5-di-*tert.*-butyl-*N*-toluene-*p*-sulphonylaniline (0·6 g.) in acetic acid (3 c.c.). The mixture was poured into water and the resultant gum crystallised from ethanol and then acetic acid, to give yellow prisms, m. p. 131°, identical with those described on p. 2343.

5-tert.-*Butyl*-2 : 4-*dinitro*-N-*toluene*-p-*sulphonylaniline* (XIV) was obtained by addition of fuming nitric acid (1 c.c.) in acetic acid (2 c.c.) to 2 : 5-di-*tert.*-butyl-*N*-toluene-*p*-sulphonylaniline (1 g.) in acetic acid (5 c.c.) at 70°. The mixture was poured into water and the resultant gum crystallised from ethanol and then acetic acid to give pale yellow prisms, m. p. 142° (Found : C, 51·7; H, 4·6. $C_{17}H_{19}O_6N_3S$ requires C, 51·9; H, 4·8%).

Nitration of 2 : 4-*Di*-tert.-*butyl*-5-*methylphenol*.—Fuming nitric acid (20 c.c.) in acetic acid (50 c.c.) was added to the compound (20 g.) in acetic acid (100 c.c.) cooled in ice. The mixture was filtered from crystalline 4 : 6-di-*tert.*-butyl-3-methyl-2 : 4-dinitro*cyclo*hexa-2 : 5-dienone, m. p. 91° (decomp.) (Found : C, 58·2; H, 7·2. Calc. for $C_{15}H_{22}O_5N_2$: C, 58·1; H, 7·1%), and the filtrate poured into water. The resultant oil soon became semisolid and it was separated, dried, and recrystallised from benzene–light petroleum. It gave 6-*tert.*-butyl-3-methyl-2 : 4-dinitrophenol in yellow prisms, m. p. 98° (Found : C, 52·3; H, 5·3. Calc. for $C_{11}H_{14}O_5N_2$: C, 52·0; H, 5·5%), soluble in hot aqueous sodium hydroxide to an orange solution which deposited needles on cooling. On introduction into fuming nitric acid there was a vigorous reaction and pouring the solution into water gave 2 : 4 : 6-trinitro-3-methylphenol, needles, m. p. 109° (from ethanol), in high yield.

When 2 : 4-di-*tert.*-butyl-5-methylphenyl methyl ether was nitrated as described by Carpenter, Easter, and Wood [1] the only easily isolable product was 4-*tert.*-butyl-3-methyl-2 : 6-dinitrophenyl methyl ether, m. p. 113°. When fuming nitric acid (10 c.c.) in acetic acid (50 c.c.) was added to 10 g. of the ether in acetic acid (100 c.c.) and the mixture cooled in ice and poured into water after 1 hr. semisolid material was obtained, which was solidified when rubbed with ethanol. The product (5·5 g.; m. p. *ca.* 75°) was crystallised from benzene to remove the more soluble 6-*tert.*-butyl-3-methyl-2 : 4-dinitrophenyl methyl ether, m. p. 84°. The less soluble material gave 4 : 6-*di*-tert.-*butyl*-3-*methyl*-2-*nitrophenyl methyl ether* as needles, m p. 140° (Found: C, 69·2; H, 9·1. $C_{16}H_{25}O_3N$ requires C, 68·8; H, 9·0%). 3 G. of this nitro-compound in 66% ethanol (30 c.c.) containing hydrochloric acid (1 c.c.) was boiled with iron powder (3 g.) for 24 hr. The product was extracted with ethanol, and the resultant solid recrystallised from ethanol. 3 : 5-*Di*-tert.-*butyl*-2-*methoxy*-6-*methylaniline* (XI) was obtained in needles, m. p. 110° (Found : C, 77·5; H, 10·7. $C_{16}H_{27}ON$ requires C, 77·1; H, 10·8%). This base reacted readily with bromine in acetic acid but gave only oils. With toluene-*p*-sulphonyl chloride in pyridine the base gave the *toluene*-p-*sulphonyl derivative*, prisms, m. p. 183° (from acetic acid) (Found : C, 68·4; H, 8·1. $C_{23}H_{33}O_3NS$ requires C, 68·5; H, 8·2%). This compound was recovered after treatment with excess of *N*-bromosuccinimide in pyridine, and with fuming nitric acid in acetic acid gave oils.

Interaction of 2 : 6-*Di*-tert.-*butyl*-4-*methylphenol with Nitric Acid*.—To the phenol (2 g.) in acetic acid (10 c.c.) was added fuming nitric acid (2 c.c.) in acetic acid (5 c.c.). The almost colourless precipitate was filtered off after ½ hr., dried, and crystallised from light petroleum, from which it formed needles, m. p. 98° (decomp.). It recrystallised also from aqueous ethanol but from acetic acid was converted into oily decomposition products. When it was boiled in toluene oxides of nitrogen were evolved and the solution became deep red. A small quantity of black crystals, m. p. 240° (decomp.), was deposited on cooling but the

major product was a very soluble, deep-red gum. With quinol in ethanol there was produced benzoquinone, and with *p*-chlorophenol in light petroleum 4-chloro-2-nitrophenol, m. p. 87°. The properties indicate that this compound is 2 : 6-*di*-tert.-*butyl*-4-*methyl*-4-*nitro*cyclo*hexa*-2 : 5-*dienone* (VI) (Found : C, 67·4; H, 8·7; N, 5·1. $C_{15}H_{23}O_3N$ requires C, 67·9; H, 8·7; N, 5·3%).

Bromination of 4-tert.-*Butylcatechol*.—Commercial 4-*tert*.-butylcatechol, recrystallised from light petroleum, gave needles, m. p. 56—57°. To this material (5 g.) in chloroform was added bromine (5 g.) in chloroform, and the mixture was evaporated to small bulk. On addition of light petroleum 3-*bromo*-5-tert.-*butylcatechol* (XIII) separated in needles (78%), m. p. 86° (Found : C, 49·3; H, 5·4. $C_{10}H_{13}O_2Br$ requires C, 49·0; H, 5·3%). Bromination in warm light petroleum gave a much lower yield.

Addition of bromine (1 mol.) to a solution of the above monobromo-derivative in chloroform resulted in a non-crystallisable mass. Use of bromine (2 mols.) led to the production in small yield of tetrabromocatechol (in one experiment a little tribromocatechol was isolated).

Fuming nitric acid (1 c.c.) in acetic acid (1 c.c.) was added to 3-bromo-5-*tert*.-butylcatechol (1 g.) in acetic acid (5 c.c.). After a few minutes the liquid was poured into water. The precipitate, crystallised from light petroleum, gave 3-*bromo*-5-tert.-*butyl*-o-*benzoquinone* (XV) as red prisms, m. p. 98—100° (Found : C, 49·4; H, 4·6. $C_{10}H_{11}O_2Br$ requires C, 49·4; H, 4·5%), which with *o*-phenylenediamine in acetic acid gave the *quinoxaline derivative* as pale yellow needles, m. p. 122° (from ethanol) (Found : N, 9·3. $C_{16}H_{15}N_2Br$ requires N, 8·9%).

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