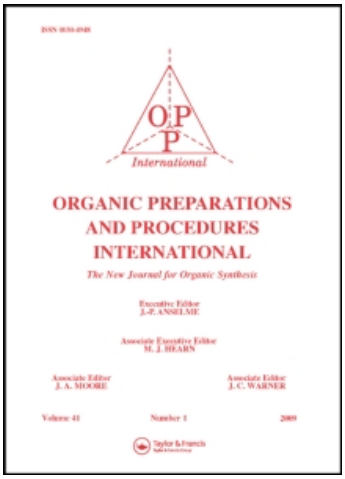

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POSITIONAL PROTECTIVE GROUPS VIII. PREPARATION OF 2-HYDROXY-3,2'-DIMETHYLDIPHENYL ETHER WITH *T*-BUTYL GROUP AS A POSITIONAL PROTECTIVE GROUP

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POSITIONAL PROTECTIVE GROUPS VIII.[1] PREPARATION OF 2-HYDROXY-3,2'-DIMETHYLDIPHENYL ETHER WITH t-BUTYL GROUP AS A POSITIONAL PROTECTIVE GROUP.

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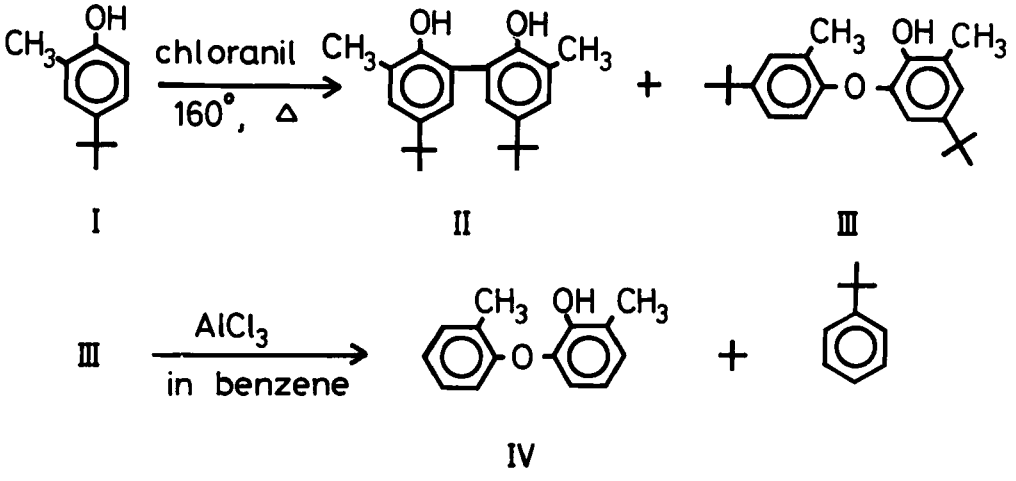
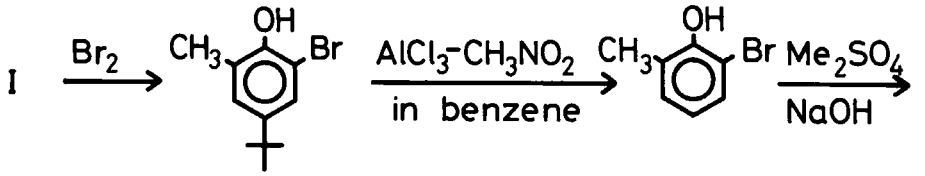
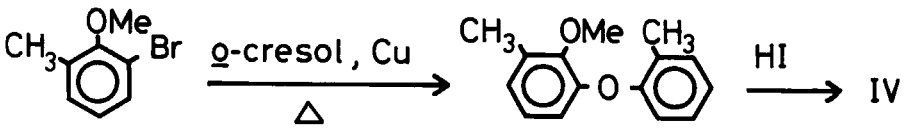
The oxidative coupling of 4-t-butyl-o-cresol (I) by chloranil to 5,5'-di-(t-butyl)-3,3'-dimethyl-2,2'-dihydroxybiphenyl (II), previously reported[2] with VCl_4 as the coupling agent, has been investigated. The transalkylation of 2-hydroxy-5,4'-di-(t-butyl)-3,2'-dimethylbiphenyl (II) formed as a by-product, was studied in order to establish its structure and to deter-



mine if the t-butyl group could serve as a positional protective group for the synthesis of diaryl ethers.

When I was heated with chloranil at 160° for 1 hr, II and III were obtained in 39 and 15% yields respectively. The structure of III was confirmed by its spectral data and the result of its $AlCl_3$ catalyzed transalkylation[3] to afford 2-hydroxy-3,2'-dimethyldiphenyl ether (IV) and t-butylbenzene in 76 and 78% yields respectively. An authentic sample of IV was prepared as shown below.





V

Our results indicate that the t-butyl group can be useful as a positional protective group in the preparation of diaryl ethers since transalkylation of the t-butyl group occurred without cleavage of the ether bonds. In addition, IV may easily be obtained in two steps from I, albeit in low yield, while the authentic synthesis gave essentially the same yield of IV but in five steps.

EXPERIMENTAL

General Experimental.- All melting points are uncorrected. IR spectra were measured as KBr pellets on a Nippon Bunko IR-A spectrophotometer and NMR spectra were determined at 60MHz with a Hitachi R-20 NMR spectrometer with TMS as an internal standard. 4-t-butyl[4]- and 4-butyl-6-bromo-2-methylphenol[5] by the reported method. Commercial grade chloranil was used without purification. $AlCl_3$ was purified by sublimation just prior to use.

Oxidative coupling reaction of I with chloranil.- A mixture of 20 g (122 mmoles) of I and 16.9 g (60.5 mmoles) of chloranil was heated at 160° for 1 hr, then the reaction mixture was cooled to room temperature and was extracted with 200 ml of petroleum ether (bp. 35-60°) leaving 12.8 g (85%) of tetrachlorohydroquinone. The extract was concentrated to one-tenth its volume and the residual solution was chromatographed on alumina with benzene as the eluent to afford 7.7 g (39%) of II[2] and 2.97 g (15%) of III. The starting material, I was recovered in 22% of yield.

III: bp. 164° / 2 mmHg, pale yellow liquid.

Anal. Calcd for $C_{22}H_{30}O_2$: C, 80.93; H, 9.26.

Found: C, 81.01; H, 9.29.

IR cm^{-1}: 3560 (νOH). NMR ($CDCl_3$) δ ppm: 1.16 (9H, s, $C(CH_3)_3$), 1.27 (9H, s, $C(CH_3)_3$), 2.23 (6H, s, CH_3), 5.28 (1H, s, OH) and 6.75-7.09 (5H, m, aromatic protons).

Transalkylation reaction of III.- After a solution of 100 mg (0.38 mmole) of III in 3 ml of benzene in the presence of 170 mg (1.27 mmole) of $AlCl_3$ was shaken at 50° for 1 hr, the reaction mixture was quenched with 10 ml of 6N HCl and extracted with three times with 5 ml of benzene. The benzene solution was dried over sodium sulfate and the solvent and small amount of the produced t-butylbenzene were distilled in vacuo, affording

66 mg (76%) of IV ; it was purified by the preparative gas chromatographic method to yield a colorless liquid.

Anal. Clacd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59.
Found: C, 78.76; H, 6.64.

IR cm^{-1}: 3500 (νOH). NMR ($CDCl_3$) δ ppm: 2.25 (6H, s, CH_3), 5.41 (1H, s, OH) and 6.16-7.36 (7H, m, aromatic protons).

6-Bromo-2-methylphenol[6] and 6-bromo-2-methylanisole.- A mixture of 15 g (62 mmoles) of 6-bromo-4-t-butyl-o-cresol and $AlCl_3$-CH_3NO_2 (10 g/18 g) catalyst[7] in 170 ml of benzene was shaken at 50° for 30 min and the reaction mixture was quenched with 150 ml of 6N HCl and the organic layer was separated. The water layer was extracted twice with 100 ml of benzene and the combined organic solution was extracted three times with 10% NaOH solution. The alkaline solution was acidified with 10% hydrochloric acid and extracted three times with 50 ml of benzene. The benzene solution was dried over sodium sulfate and distilled under reduced presure affording 7.6 g (66%) of 6-bromo-2-methylphenol, bp. 86-90°/ 20 mmHg, lit.[8], bp. 206-207°/ 740 mmHg. When it was treated with dimethyl sulfate in alkaline solution under usual condition[9], 6-bromo-2-methylanisole was obtained in 78% yield.

2-Methoxy-3,2'-dimethyldiphenyl ether.- A mixture of the potassium salt of o-cresol [prepared from 1.6 g (15 mmoles) of o-cresol and 0.6 g of K in 6.5 ml of MeOH], 3.00 g (15 mmoles) of 6-bromo-2-methylanisole and 40 mg of Cu powder was heated at 160° for 3 hr and then at 190° for additional 3.5 hr. The reaction mixture was extracted with diethyl ether and the ethreal solution (dried over sodium sulfate) was evaporated

and the residue was distilled to give 1.3 g (38%) of 2-methoxy-3,2'-dimethyldiphenyl ether (VI), bp. 120/2 mmHg.

Demethylation of 2-methoxy-3,2'-dimethyldiphenyl ether.- A mixture of 200 mg of VI (0.88 mmole) and hydroiodic acid (d:1.7) 1.6 g was heated at 170° for 3 hr, the reaction mixture was extracted with diethyl ether and the ethereal extract was dried over sodium sulfate. Evaporation of the solvent in vacuo afforded 150 mg (80%) of a pale yellow liquid which was identical in all respects with IV described above.

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* To whom inquiries should be sent.

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