reaction was then carried out exactly like that with the enol ether of the *t*-butyl adduct. As in that experiment, the second fraction obtained in the crystallization from aqueous methanol was a solid which took the form of colorless needles after repeated recrystallization from methanol. Further purification was effected by sublimation at 165° (0.3 mm.). The melting point of the pure 2-*t*-amyl-4-*t*-butyl-2,3-dihydrophenyl duryl ketone is 115–116°, yield 0.5 g. (23%).

Anal. Calcd. for $C_{26}H_{38}O$: C, 85.19; H, 10.45. Found: C, 85.05; H, 10.48.

The infrared spectrum of this compound contains bands assignable to a hindered conjugated carbonyl group (1642 cm.$^{-1}$) and to a system of conjugated ethylenic double bonds (1567 cm.$^{-1}$).

(c) **2,4-Di-*t*-butyl-2,3-dihydrophenyl Duryl Ketone.**—To a *t*-butylmagnesium chloride reagent, prepared from 0.72 g. of magnesium and 4.0 ml. of *t*-butyl chloride in 25 ml. of ether, was added a solution of 3.25 g. of the enol methyl ether of the *t*-butyl adduct in 40 ml. of benzene. After being stirred for 3 minutes, the reaction mixture was decomposed with cold dilute hydrochloric acid. The organic layer was dried over magnesium sulfate and the solvents were evaporated. The residue was fractionally crystallized from aqueous methanol. The initial fractions consisted of unchanged starting material and a red oil, but 1.2 g. of yellow solid precipitated in the following fractions. After sublimation at 130–140° (0.04 mm.), the 2,4-di-*t*-butyl-2,3-dihydrophenyl duryl ketone crystallized from methanol as fine colorless needles which melted at 129.5–130.5°, yield 0.8 g. (22%). A mixed melting point with an authentic sample, prepared by adding *t*-butylmagnesium chloride to *p*-*t*-butylphenyl duryl ketone, was not depressed.

Anal. Calcd. for $C_{25}H_{36}O$: C, 85.17; H, 10.29. Found: C, 85.31; H, 10.49.

The infrared spectrum contains bands at 1645 and 1574 cm.$^{-1}$ assignable to a hindered conjugated carbonyl group and a system of conjugated ethylenic double bonds, respectively.

URBANA, ILLINOIS

[Contribution from the Research Laboratory, Dominion Rubber Co., Ltd.]

t-Butyl as a Blocking Group in the Synthesis of *o*-Hydroxybenzophenones

By Marshall Kulka

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A method has been developed for the synthesis of *o*-hydroxybenzophenones (VIII) utilizing *t*-butyl as a blocking group. *p*-*t*-Butylanisole was condensed with various aroyl chlorides to yield a series of 2-methoxy-5-*t*-butylbenzophenones (VI). These were then simultaneously de-*t*-butylated and demethylated to VIII in high yields by prolonged heating in benzene solution with four moles of aluminum chloride. Milder conditions, which preferentially de-*t*-butylated *p*-*t*-butylphenoxyethanol (I) to phenoxyethanol (II), caused only the demethylation of VI to 2-hydroxy-5-*t*-butylbenzophenones (VII).

The migration of the alkyl and especially the *t*-butyl group is a well-known phenomenon. Poly-*t*-butylbenzenes are dealkylated to *t*-butylbenzene when heated in benzene solution with aluminum chloride.[1] The Friedel–Crafts reaction between *p*-di-*t*-butylbenzene and acetyl chloride occurs after partial dealkylation to form *p*-*t*-butylacetophenone in 72% yield.[2] Smith has reported that heating under reflux a benzene solution of one mole of *p*-*t*-butylphenol with two-thirds of a mole of aluminum chloride resulted in a mixture of phenol and *t*-butylbenzene.[3] A similar migration of the *t*-butyl group to a foreign nucleus occurs with *p*-*t*-butylphenoxyethanol (I) which under conditions similar to those used by Smith gives phenoxyethanol (II) in 78% yield and *t*-butylbenzene (III) in 50% yield (see Experimental). *p*-*t*-Butylanisole can be converted to anisole with aluminum chloride and directly to phenol with hydriodic acid.[4]

$$\underset{\text{I}}{p\text{-}(CH_3)_3CC_6H_4OCH_2CH_2OH} + C_6H_6 \longrightarrow \underset{\text{II}}{C_6H_5OCH_2CH_2OH} + \underset{\text{III}}{(CH_3)_3CC_6H_5}$$

The ease of elimination of the *t*-butyl group from an aromatic nucleus suggested its use as a blocking group in substitution reactions. In the Friedel–Crafts reaction with aroyl chlorides, anisole is attacked at the *ortho* and *para* positions to form a mixture of *o*- and *p*-hydroxybenzophenone with the latter predominating. In order to prepare exclusively *o*-hydroxybenzophenone, it would be necessary to suppress the formation of the *para* isomer by first introducing a blocking group into the *para* position of anisole and then removing it after the Friedel–Crafts reaction. The purpose of this investigation was to evaluate the *t*-butyl as a blocking group in the synthesis of *o*-hydroxybenzophenones.

A series of 2-methoxy-5-*t*-butylbenzophenones (VI) (Table I) was first prepared by heating *p*-*t*-butylanisole (IV) with the appropriate acid chloride V in *sym*-tetrachloroethane as solvent and a trace of zinc chloride. Then VI was treated with aluminum chloride under the conditions which sufficed for the conversion of I to II and III but no de-*t*-butylation occurred. Demethylation of VI to VII was the only reaction as evidenced by the fact that the resulting product was difficultly alkali-soluble and yielded the starting material VI on methylation with dimethyl sulfate. No de-*t*-butylation could be effected in boiling benzene nor boiling toluene. Simultaneous de-*t*-butylation and demethylation to VIII was achieved finally by heating VI with four moles of aluminum chloride in benzene solution at 65–70° for 45 hours. Under the same conditions VII yielded VIII.

The fate of the *t*-butyl group has not been established definitely. In contrast to the formation of *t*-butylbenzene (III) during the de-*t*-butylation of I under the milder conditions, the formation of an alkali-insoluble higher-boiling liquid mixture accompanies the de-*t*-butylation of VI and VII to VIII under the prolonged treatment. It must be presumed that this higher-boiling by-product is

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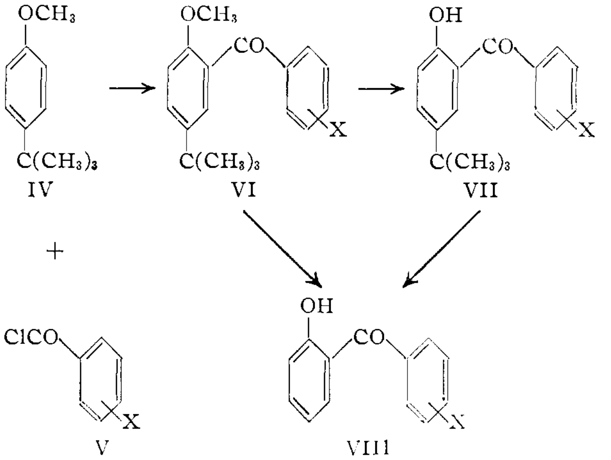
(1) E. Boedtker and O. M. Halse, *Bull. soc. chim.*, **19**, 444 (1916); *C. A.*, **11**, 938 (1917).

(2) G. F. Hennion and S. F. deC. McLeese, This Journal, **64**, 2421 (1942).

(3) R. A. Smith, *ibid.*, **59**, 899 (1937).

(4) B. M. Dubinin, *Zhur. Obshchei Khim.*, **18**, 2145 (1948); *C. A.* **43**, 3804 (1949).



formed from *t*-butylbenzene by alkylation and isomerization. In support of this is the fact that *t*-butylbenzene does not survive the 45-hour benzene–aluminum chloride treatment.

The scope of this de-*t*-butylation reaction is indicated in Table III. All of the benzophenones VI were de-*t*-butylated to VIII in high yields except 2,2′-dimethoxy-5-*t*-butylbenzophenone which suffered a side reaction to form xanthone. It will be noted that the *t*-butyl is eliminated in preference to the methyl group from VI (X = 4′-CH_3). A few attempts to apply the de-*t*-butylation reaction outside the ketone range did not meet with success. 2-Nitro-4-*t*-butylanisole under the conditions which converted I to II and III yielded only 2-nitro-4-*t*-butylphenol,[5] while under the more drastic conditions, tars were the major products. 2,2′-Dimethoxy-5,5′-di-*t*-butyldiphenylmethane, which was prepared from *p*-*t*-butylanisole and formaldehyde, when heated with four moles of aluminum chloride and benzene for 45 hours yielded a complex mixture of products which was not investigated further. 2,4′-Dimethoxy-3′-nitro-5-*t*-butyldiphenylmethane gave tars under these conditions.

Acknowledgment.—The author is indebted to Miss Gisela Rotermann for the microanalyses.

Experimental

De-*t*-butylation of *p*-*t*-Butylphenoxyethanol (I).—To a solution of *p*-*t*-butylphenoxyethanol (I) (65 g.) in dry benzene (250 ml.) was added reagent grade aluminum chloride (68 g.) and the reaction mixture was then stirred and heated at 55–60° for five hours. The dark solution was poured into a mixture of ice and concentrated hydrochloric acid. The benzene layer was separated, washed with dilute hydrochloric acid and with water and then the solvent was removed. Fractional distillation of the residue yielded two main fractions. The first (25 g. or 50%) boiled at 167–170° and had the same refractive index as *t*-butylbenzene (III). The second fraction (36 g. or 78%) boiled at 120–124° (12 mm.) and had the same refractive index as phenoxyethanol (II). A portion of this fraction when treated with *p*-chlorobenzenesulfonyl chloride and pellet sodium hydroxide yielded **2-phenoxyethyl *p*-chlorobenzenesulfonate** which melted at 101–102° alone or in admixture with the ester prepared from authentic phenoxyethanol (II) and *p*-chlorobenzenesulfonyl chloride.

Anal. Calcd. for $C_{14}H_{13}O_4ClS$: C, 53.75; H, 4.16. Found: C, 54.17, 54.14; H, 3.99, 4.07.

De-*t*-butylation of *p*-*t*-Butylanisole.—This on treatment as above yielded a colorless liquid boiling at 153–168°. On careful fractional distillation the mixture was separated into anisole and *t*-butylbenzene.

2-Methoxy-5-*t*-butylbenzophenones (VI).—These compounds which are listed in Table I were prepared from *p*-*t*-butylanisole (IV) and the appropriate acid chloride V by the method which follows.

A solution of *p*-*t*-butylanisole (100 g.), benzoyl chloride (85 g.), *sym*-tetrachloroethane (150 ml.) and zinc chloride (0.2 g.) was heated under reflux for 40 hours. The solvent was removed from the dark solution and the residue was distilled, b.p. 208–210° (12 mm.). The distillate (132 g.) which solidified on standing was crystallized from methanol yielding white prisms (107 g. or 66%), m.p. 61–62°.

Oxime of 2-Methoxy-5-*t*-butylbenzophenone.—A solution of 2-methoxy-5-*t*-butylbenzophenone (2.5 g.), ethanol (30 ml.), hydroxylamine hydrochloride (2 g.) and potassium acetate (2 g.) was heated under reflux for 16 hours. The ethanol was removed, the residue dissolved in benzene, the solution washed with water and then concentrated to a small volume and cooled. The white crystals (2.5 g.) melted 136–137° after drying *in vacuo*. *Anal.* Calcd. $C_{18}H_{21}NO_2$: C, 76.32; H, 7.42. Found: C, 76.41, 76.49; H, 7.00, 7.06. This compound on standing liquefied and liberated nitrogen oxide gas.

2-Hydroxy-5-*t*-butylbenzophenones (VII).—These compounds which are listed in Table II were prepared from the corresponding methyl ethers VI by the method which follows.

To a solution of 2-methoxy-5-*t*-butylbenzophenone (38 g.) in dry benzene (150 ml.) was added aluminum chloride (20 g.) and the reaction mixture was stirred and heated at 50–60° for five hours. The dark solution was added to cold dilute hydrochloric acid, the benzene layer was washed with dilute hydrochloric acid and with water and the solvent removed. The residue distilled at 195–197° (12 mm.) and the distillate which solidified was crystallized from methanol to yield yellow prisms (22 g. or 63%), m.p. 67–68°. This compound on prolonged methylation with dimethyl sulfate and boiling dilute aqueous alkali yielded a white compound which did not depress the melting point of 2-methoxy-5-*t*-butylbenzophenone.

TABLE I

2-METHOXY-5-*t*-BUTYLBENZOPHENONES (VI) PREPARED FROM *p*-*t*-BUTYLANISOLE (IV) AND THE APPROPRIATE BENZOYL CHLORIDE V

VI, X =	Yield, %	M.p., °C.	B.p. (12 mm.), °C.	Formula	Carbon, %		Hydrogen, %	
					Calcd.	Found	Calcd.	Found
H	66	61–62	208–210	$C_{18}H_{20}O_2$	80.61	80.34	7.46	7.25
4′-Cl	60		223–225	$C_{18}H_{19}O_2Cl$	71.40	71.58	6.28	5.90
						71.80		6.25
3′-Br	61		233–236	$C_{18}H_{19}O_2Br$	62.26	62.25	5.48	5.42
						62.61		5.14
2′-Cl	62	61–62	222–225	$C_{18}H_{19}O_2Cl$	71.40	71.66	6.28	6.21
2′-Br	68	72–73	225–230	$C_{18}H_{19}O_2Br$	62.26	62.52	5.48	5.56
						62.44		5.48
4′-OCH_3	60		238–239	$C_{19}H_{22}O_3$	76.51	76.26	7.38	7.03
						76.63		6.93
2′-OCH_3	50		225	$C_{19}H_{22}O_3$	76.51	76.65	7.38	7.14
4′-CH_3	76		222–225	$C_{19}H_{22}O_2$	80.85	80.74	7.80	7.83

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[5] A. W. Anish, U. S. Patent 2,429,178 (1947); *C. A.*, **42**, 618 (1948).

TABLE II

2-HYDROXY-5-*t*-BUTYLBENZOPHENONES (VII) PREPARED BY THE DEMETHYLATION OF THE METHYL ETHERS VI

VII, X =	Yield, %	M.p., °C.	B.p., 12 mm., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
H	63	67–68	195–197	$C_{17}H_{18}O_2$	80.31	80.38	7.08	6.93
4′-Cl	68	94–95	218–220	$C_{17}H_{17}O_2Cl$	70.70	71.17	5.89	5.60
3′-Br	75		225–227	$C_{17}H_{17}O_2Br$	61.27	61.84	5.10	5.03
2′-Cl	70		200–205	$C_{17}H_{17}O_2Cl$	70.70	70.41	5.89	5.53
2′-Br	80		208–212	$C_{17}H_{17}O_2Br$	61.27	60.89	5.10	4.94
4′-OCH$_3$	76	93–94	235	$C_{18}H_{20}O_3$	76.07	76.55	7.04	7.17
4′-CH$_3$	85	94–95	210–212	$C_{18}H_{20}O_2$	80.61	80.83	7.46	7.50

2-Hydroxybenzophenones (VIII).—These compounds which are listed in Table III were prepared by the de-*t*-butylation of VI by the method which follows.

TABLE III

2-HYDROXYBENZOPHENONES (VIII) PREPARED FROM 2-METHOXY-5-*t*-BUTYLBENZOPHENONES (VI)

VIII, X =	Yield, %	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
H	79	38–39	$C_{13}H_{10}O_2$				
4′-Cl	60	74–75	$C_{13}H_9O_2Cl$	67.10	67.13	3.87	3.75
3′-Br	60	77–78	$C_{13}H_9O_2Br$	56.32	55.97	3.25	3.26
2′-Cl	73	58–59	$C_{13}H_9O_2Cl$	67.10	67.02	3.87	3.97
2′-Br	75	76–77	$C_{13}H_9O_2Br$	56.32	56.72	3.25	3.40
4′-CH$_3$[a]	80	39–40	$C_{14}H_{12}O_2$				
4′-OH[b]	75	146–147	$C_{13}H_{10}O_3$				
2′-OH[c]	0						

[a] This compound when mixed with 2-hydroxy-4′-methylbenzophenone (VIII, X = 4′-CH$_3$) prepared from *o*-methoxybenzoyl chloride and toluene did not give a depression of the melting point. It did depress the melting of 2-hydroxybenzophenone. Ullmann and Goldberg[6] report a melting point of 61.5° for VIII (X = 4′-CH$_3$). The sample prepared by the author by their method melted at 39–40° and did not change after repeated recrystallizations. The possibility of dimorphism cannot be excluded. [b] This compound did not depress the melting point of VIII (X = 4′-OH) prepared from salicylic acid and phenol.[7] [c] The de-*t*-butylation of 2,2′-dimethoxy-5-*t*-butylbenzophenone gave a 3% yield of xanthone among other unidentified products. The xanthone must have been formed through dehydration of 2,2′-dihydroxybenzophenone.

To a solution of 2-methoxy-5-*t*-butylbenzophenone (25 g.) in dry benzene (250 ml.) was added reagent grade aluminum chloride (50 g.) and the reaction mixture was heated at 65–70° for 45 hours. The dark mixture was poured into cracked ice containing hydrochloric acid and the benzene layer was separated and washed with dilute hydrochloric acid and with water. After removal of the solvent from the benzene solution, the product distilled at 170–185° (12 mm.) leaving a residue of 3 g. The distillate (24 g.) was dissolved in benzene and the solution was extracted exhaustively with 2% hot aqueous sodium hydroxide (approximately ten extractions with 350-ml. portions was necessary). The benzene solution contained 5 g. of alkali-insoluble oil which is probably a polyalkylated benzene. The intense yellow alkaline extract was acidified and extracted with benzene. Removal of the benzene from the extract left a yellow oil which solidified on cooling. Crystallization from methanol gave yellow prisms (14.6 g. or 79%) melting at 38–39°. These did not depress the melting point of 2-hydroxybenzophenone (VIII, R = H) prepared from *o*-methoxybenzoyl chloride and benzene.[6] The same compound (VIII, R = H) was obtained in 63% yield when 2-hydroxy-5-*t*-butylbenzophenone was subjected to the above de-*t*-butylation procedure.

The Conversion of the 2-Halo-2′-hydroxybenzophenones to Xanthone.—To a solution of 2-chloro- or 2-bromo-2′-hydroxybenzophenone (0.5 g.) in ethanol (5 ml.) was added potassium hydroxide (0.1 g.). The reaction mixture was heated until solution resulted and then the alcohol was distilled off. The residue was heated at 200° for five hours and then distilled at 12 mm. Crystallization of the distillate from methanol gave a white solid melting at 175–176° alone or in admixture with an authentic sample of xanthone. The yield in each case was 90%.

2-*t*-Butyl-9-xanthenone.—This was prepared from 2′-chloro- or 2′-bromo-2-hydroxy-5-*t*-butylbenzophenone by the method described for xanthone above. The impurities were sublimed out at 190° (12 mm.) and the residue was distilled at 1 mm. and crystallized from methanol giving white rhombohedra, m.p. 114–115°, yield 35%. *Anal.* Calcd. for $C_{17}H_{16}O_2$: C, 80.95; H, 6.35. Found: C, 81.37; H, 6.18.

2,2′-Dimethoxy-5,5′-di-*t*-butyldiphenylmethane.—Carpenter, Easter and Wood[8] chloromethylated *p*-*t*-butylanisole and obtained some 2-chloromethyl-4-*t*-butylanisole but did not isolate the diphenylmethane derivative.

A reaction mixture of *p*-*t*-butylanisole (40 g.), paraformaldehyde (4 g.) and ethylene dichloride (100 ml.) was stirred at 35° while hydrogen chloride gas was passed in for eight hours. The reaction mixture was washed with water, the solvent removed and the residue distilled. The fraction boiling at 220–250° (12 mm.) solidified and was crystallized from methanol to yield white prisms (17 g. or 40%) melting at 82–83°. *Anal.* Calcd. for $C_{23}H_{32}O_2$: C, 81.16; H, 9.41. Found: C, 81.42, 80.87; H, 9.27, 9.49.

In another experiment a 25% yield of the diphenylmethane derivative was obtained when *p*-*t*-butylanisole was stirred with excess 40% aqueous formaldehyde and concentrated hydrochloric acid for 12 hours at room temperature.

2,4′-Dimethoxy-3′-nitro-5-*t*-butyldiphenylmethane.—A mixture of *p*-*t*-butylanisole (20 g.), 3-nitro-4-methoxybenzyl chloride (20 g.) and zinc chloride (0.05 g.) was heated up on the steam-bath when a vigorous evolution of hydrogen chloride set in. The reaction mixture was heated on the steam-bath for five hours and then distilled. This yielded 18 g. of a viscous yellow liquid, b.p. 200° (0.3 mm.). *Anal.* Calcd. for $C_{19}H_{23}NO_4$: C, 69.28; H, 6.99. Found: C, 69.34, 69.14; H, 6.63, 6.80.

GUELPH, ONTARIO, CANADA

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