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AN EFFICIENT METHOD FOR THE DEBUTYLATION OF *o*- AND *p*-t-BUTYLPHENOLS AND FOR THE HYDROLYSIS OF ARYL ACETATES

[PROTECTIVE GROUP; QUINONES]

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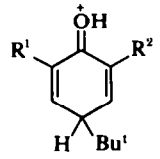
Abstract—t-Butyl groups can be removed from mono-, di-, or tri-t-butylphenols by refluxing with 70% trifluoroacetic acid. In the same way sterically hindered as well as unhindered aryl acetates can be hydrolysed.

In connexion with our studies on the Thiele-Winter acetoxylation of quinones[1] we required a synthesis of 2-bromo-3-phenylbenzo-1,4-quinone. The phenylation of 2-bromobenzoquinone gave a very difficultly separable mixture of the three isomers, of which the desired isomer was the minor product[2] (*cf.* the phenylation of 2-chlorobenzoquinone[3]). The fact that a t-Bu group will protect not only the position it occupies but also the adjacent one[4] suggested the possibility of a synthesis via 2-t-butyl-5-phenyl hydroquinone. The latter was made by treatment of phenylhydroquinone with t-butyl acetate using conc sulphuric acid as catalyst. As expected, bromination of the butylated biphenyl gave the desired compound **9** in which the bromine is *ortho* to the phenyl group: bromination of phenylhydroquinone itself gives the *para* isomer. Our attempts to remove the t-Bu group by transalkylation onto resorcinol were unsuccessful. Some debromination but very little if any debutylation occurred even after heating the reaction mixture at *ca* 110° for periods of a few hours up to 7 days with varying amounts of *p*-toluenesulphonic acid as catalyst (*cf* Ref 5).

At about this time we had found[1b] that hydrolysis of 4-t-butyl-6-methylpyrogallol triacetate **12** with trifluoroacetic acid (TFA)[6] was accompanied by de-t-butylation (Table). This observation suggested a possible method for the debutylation of compound **9** and indeed, when the latter was heated with 70% TFA, it underwent dealkylation. Surprisingly it underwent debromination as well, however with 20% TFA dealkylation only occurred thereby giving 2-bromo-3-phenylhydroquinone in 80% yield. Oxidation of this compound then gave the desired quinone. Thus this route, involving a protective group, provides a more convenient method for the preparation of 2-bromo-3-phenylbenzoquinone than the arylation method.

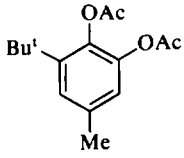
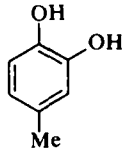
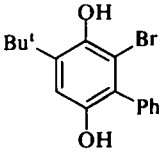
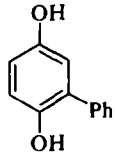
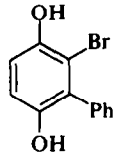
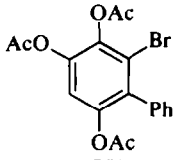
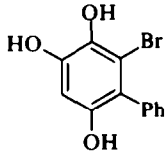
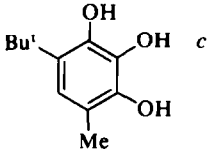
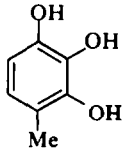
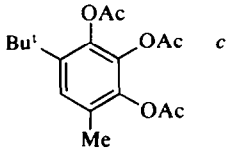
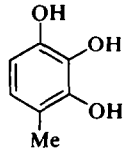
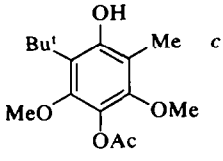
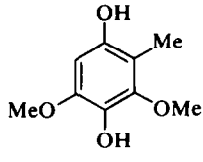
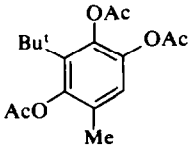
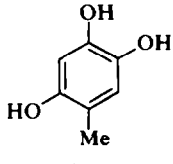
The successful debutylation of compound **9** by TFA led us to examine the use of this reagent for the dealkylation of other butyl phenols and for the hydrolysis of aryl acetates. The results are summarised in the Table. In all but three examples (compounds **5**, **10**, and **18**) the yields are excellent, although no attempt was made to find the optimum conditions. The partial debutylation of compounds **16** to **18** shows that dealkylation occurs much more easily with *ortho*- than with *para*-t-butyl-phenols, no doubt because debutylation removes the steric compression which is greater in the former than in the latter. With aryl acetates (see **8**, **12**, **13**, and **14**) it is probable that hydrolysis precedes dealkylation. The hydrolysis of the sterically hindered acetoxy groups in compounds **8**, **10**, **12**, **13**, and **14** is noteworthy.

After the completion of our work, Svanholm and Parker[7] published their kinetic studies which showed that TFA is a very effective catalyst for the t-butylation of phenols. They also studied the rearrangement of 2,6-di-t-butylphenol to the 2,4-isomer, and the de-t-butylation of 2,4,6-tri-t-butylphenol to 2,4-di- and 4-mono-t-butylphenol, also 2,6-di-t-butyl-*p*-cresol to 2-t-butyl-*p*-cresol. Under their conditions (100% TFA at room temperature) Svanholm and Parker found that *ortho*-debutylation occurred very rapidly but that *para*-debutylation did not occur. The mechanism which they favour for *ortho*-debutylation is not applicable to *para*-debutylation and we suggest that the latter occurs via the Wheland-type intermediate (A).



The use of TFA for de-t-butylation of butylphenols and for the hydrolysis of aryl acetates has three main advantages over previous methods,[4]

Table. Summary of dealkylations with 70% trifluoroacetic acid

No.	Butylphenol or aryl acetate	Product[a]	Time (h)	Yield (%)
1	2-t-Butyl-6-methyl	2-Methylphenol	16	74
2	4-t-Butyl-2-methyl	2-Methylphenol	46	70
3	2-t-Butyl-5-methyl	3-Methylphenol	18	98
4	2-t-Butyl-4-methyl	4-Methylphenol	50	90
5	4-t-Butyl-2-hydroxy	Catechol	90	37
6	2-t-Butyl-4-hydroxy-6-methyl	Methylhydroquinone	14	76
7	2-t-Butyl-4-hydroxy-5-phenyl	Phenylhydroquinone	22	90
8			16	74
9			28	64
	"		3[b]	80
10			12	43
11	 *c*		14	96
12	 *c*		16	96
13	 *c*		18	71
14			4	68
15	2,6-Di-t-butyl-4-methyl	4-Methylphenol	20	94

Table—*Continued*

No.	Butylphenol or aryl acetate	Product[a]	Time (h)	Yield (%)
16	2,4-Di-t-butyl	4-t-Butylphenol	36	82
		Phenol		16
17	2,4-Di-t-butyl-6-hydroxy	4-t-Butylcatechol	8	94
18	2,4,6-Tri-t-butyl	4-t-Butylphenol	40	56
		Phenol		21

[a]The identity of the products was confirmed by their IR and NMR spectra, and, in most cases, by comparison with authentic specimens.
[b]In this experiment 20% trifluoroacetic acid was used.
[c]The preparation of these compounds is given in Ref 1*b*.

namely the high yields, relatively mild conditions, and the great ease of isolation of the products (Experimental) which avoids the necessity of extracting phenols from aqueous solutions.

EXPERIMENTAL

NMR spectra were measured in $CDCl_3$ with a Varian HA100 spectrometer. Silica-gel (MFC) was used for column chromatography and silica-gel grade G or H for TLC.

General procedure for de-t-butylation. The butylphenol (1·0 g) and sodium dithionite (*ca* 50 mg) in 70% TFA (30 ml) was boiled under reflux (in a fume-cupboard) until debutylation was complete. This was determined by removing one drop of the reaction mixture every few hours and analysing it *either* by TLC (using $CHCl_3$ or $CHCl_3$/EtOAc as eluent and by spraying with ceric sulphate) *or* by following the diminution of the t-Bu peak in the NMR spectrum.

At the end of the reaction the solvents were removed by a rotary evaporator. The residue was dissolved in $CHCl_3$ then the soln was filtered (to remove $Na_2S_2O_4$) and again evaporated to dryness. The product was purified by chromatography on a column of silica-gel (150 g) with $CHCl_3$ as eluent. If necessary, further purification was effected by TLC with $CHCl_3$ or any other suitable solvent.

2-t-Butyl-5-phenylhydroquinone (**7**). Reduction of 2-phenylbenzo-1,4-quinone[8] with $Na_2S_2O_4$ in aqueous MeOH gave 2-phenylhydroquinone (51% after purification by chromatography). A stirred mixture of the hydroquinone (2·7 g), t-butyl acetate (15 ml), and conc H_2SO_4 (0·25 ml) was heated at 65° for 8 h. The mixture was then poured into water and the product was collected in ether. It was purified by chromatography in benzene followed by TLC with benzene again as eluent. The butyl phenylhydroquinone (1·6 g, 47%) formed fluffy needles, m.p. 114–115° (from benzene/light petroleum), NMR τ 2·6–2·7 (m, Ph), 3·07 (s, ArH), 3·41 (s, ArH), 5·15 (s, OH), 5·35 (s, OH), 8·57 (s, Bu^t). (Found: M^+, 242·133. $C_{16}H_{18}O_2$ requires: *M*, 242·131).

2-Bromo-6-t-butyl-3-phenylhydroquinone (**9**). A soln of Br_2 (0·56 g) in $CHCl_3$ (17 ml) was added dropwise to a stirred soln of the butylhydroquinone (1·5 g) in $CHCl_3$ (20 ml). The soln was stirred for 7 h, then the solvent was removed. The residue was purified by chromatography then TLC with benzene as eluent and thereby gave the bromo product (1·3 g, 68%) as plates, m.p. 119·5–120° (from light petroleum), m.p. 119·5–120°, NMR, τ 2·5–2·8 (m, Ph), 3·16 (s, ArH), 4·55 (s, OH), 5·82 (s, OH), and 8·59 (s, Bu^t). Found: C, 59·82; H, 5·32; Br, 24·61. $C_{16}H_{17}BrO_2$ requires: C, 59·83; H, 5·33; Br, 24·88%).

2-Bromo-3-phenylbenzo-1,4-quinone. Debutylation of **9** gave 2-bromo-3-phenylhydroquinone, m.p. 130–131°, NMR, τ 2·4–2·8 (m, Ph), 2·98 and 3·06 (AB q, H-5 and H-6), 4·74 (s, OH), and 5·46 (s, OH). (Found: C, 54·56; H, 3·64; Br, 30·40. $C_{12}H_9BrO_2$ requires: C, 54·37; H, 3·42; Br, 30·15%).

Ferric chloride hexahydrate (0·5 g) was added in portions to a stirred soln of 2-bromo-3-phenylhydroquinone (45 mg) in EtOH (10 ml). Stirring was continued for 1 h then the mixture was diluted with water (30 ml) and extracted with ether. The crude product was separated by TLC in $CHCl_3$ and gave starting material (15 mg) and 2-bromo-3-phenylbenzoquinone (20 mg, 43%) as orange needles, m.p. 104–106°. The compound was identical (m.p. and IR spectrum) with material made by phenylation of 2-bromobenzoquinone.[2]

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