An Unusual Dienone–Phenol Rearrangement of a *p*-Quinol

G. G. I. Moore* and A. R. Kirk

Department of Chemistry, Riker Research Laboratories, 3M Company, St. Paul, Minnesota 55101

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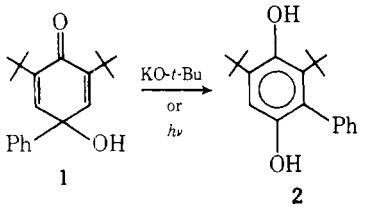
Acid-catalyzed reactions of 2,6-di-*tert*-butyl-4-hydroxy-4-phenylcyclohexadien-1-one (**1**) do not give the normal dienone–phenol rearrangement products. Instead, **1** is converted by Ac_2O, HOAc, CF_3CO_2H, and HCl to 4-biphenylol derivatives in which one *t*-Bu is replaced by the solvent-derived nucleophile. In contrast, **1** was reduced by aqueous HBr and HI to 3,5-di-*tert*-butyl-4-biphenylol (**19**). HBr in HOAc led to transient formation of **19**, followed by bromination to the *o*-bromobiphenylol. Conditions designed to yield the catechol (aqueous H_2SO_4, $HClO_4$, and CF_3CO_2H) gave instead equimolar mixtures of **19** and 3-*tert*-butyl-5-phenyl-*o*-benzoquinone, in effect a disproportionation. Methanolysis gave the quinol methyl ether at 25 °C and the *o*-methoxybiphenylol at reflux. These findings are consistent with initial loss of the 4-hydroxy group from **1** to give the carbonium ion (III).

Nishinaga et al. have recently reported base- and light-induced reactions of 2,6-di-*tert*-butyl-*p*-quinols, including the 4-phenyl derivative (**1**).[1] Acyloin rearrangement resulted in the 3-phenylhydroquinone (**2**), one of the two types of

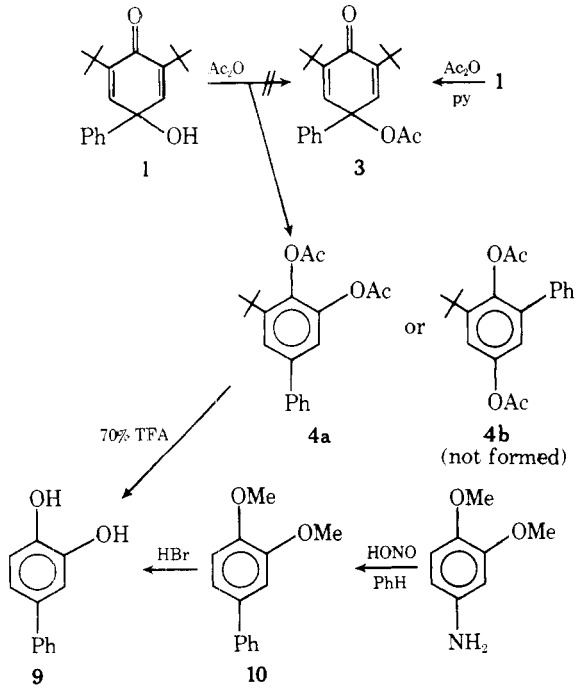


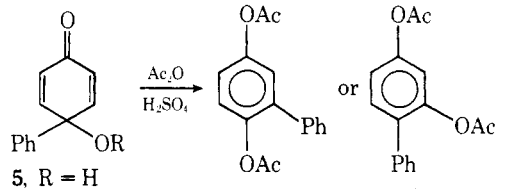
1 2

product normally expected from acid-catalyzed dienone–phenol rearrangements.[2] The other type also involves migration from position 4 to 3, to give resorcinols. We have been studying acid-induced reactions of **1**, with results surprisingly distinct from the dienone–phenol reaction of nonhindered *p*-quinols.

Attempted acetylation of **1** using Ac_2O in the absence of base gave a slow conversion not to **3** but instead to a product containing one *t*-Bu and two OAc groups (Scheme I). Use of $Eu(fod)_3$ NMR shift reagent showed that the two ring hydrogens were meta to one another (J = 2 Hz). This suggested either **4a** or **4b** as the structure, in which a 4 substituent on **1** has replaced a 2-*t*-Bu group. However, the dienone–phenol rearrangement of unhindered quinols on treatment with

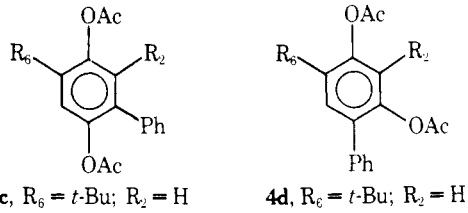
Scheme I





5, R = H
7, R = OAc
6 (from 5)
8 (from 7)

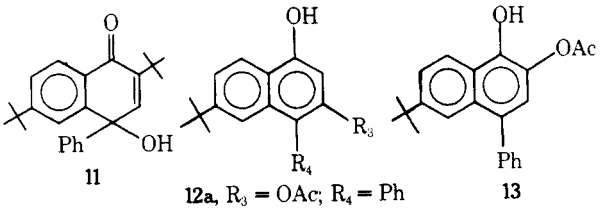
H_2SO_4–Ac_2O involves migration to the 3 position, much as seen in the base-induced reaction of **1** to **2**. Thus, 4-phenylquinol (**5**) is reported to give the product of phenyl migration (**6**) and the acetate (**7**) the product of OAc migration (**8**).[3] (The use of H_2SO_4–Ac_2O on **1** did not change the product or speed



4c, R_6 = *t*-Bu; R_2 = H
e, R_6 = H; R_2 = *t*-Bu
4d, R_6 = *t*-Bu; R_2 = H
f, R_6 = H; R_2 = *t*-Bu

of the reaction relative to the original Ac_2O procedure.) This analogy would suggest isomers **4c** or **4d** from the reaction of **1** (or less probably, **4e** or **4f** by extrusion of the less hindered *t*-Bu).

However, the shifted NMR ruled against **4c–f** (these do not have meta H) and provided the following evidence favoring **4a** over **4b**. The relative chemical shifts in $CDCl_3$ vs. $CDCl_3$–$Eu(fod)_3$ of the CH_3CO– groups (δ 2.29 and 2.37 to δ 3.16 and 3.20) were accompanied by a larger shift of one of the aryl H (δ 7.3–7.5 to δ 7.8 and 8.36). This suggested that only one aryl H is ortho to an OAc. Conclusive proof of isomer **4a** came on de-*tert*-butylation[4] of **4a** in hot 70% CF_3CO_2H (TFA) to 4-phenylcatechol (**9**). This proved to be identical with authentic material made via **10** from 4-aminoveratrole (Scheme I). Woodgate and Fitchett have reported that **11** (the benzo analogue of **1**) yields **12a** on treatment with H_2SO_4–Ac_2O,



ruling out the other 4 → 3 product **12b** by spectral data.[5] They did not consider **13**, equally consistent with the data and highly probable by analogy with our results.

We then explored the effect of other organic and inorganic acids on **1**. Hot HOAc converted **1** to monoacetate **14** within

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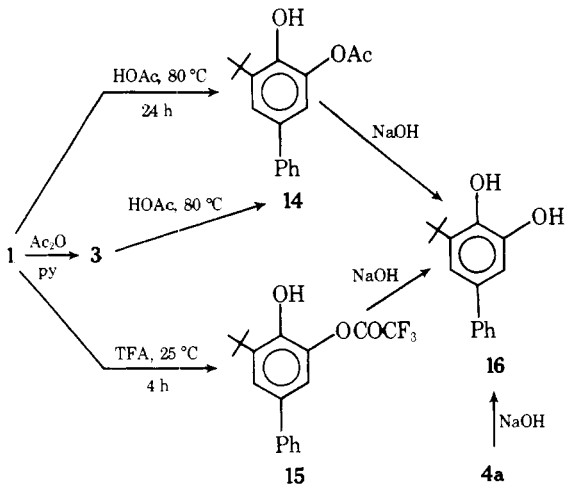
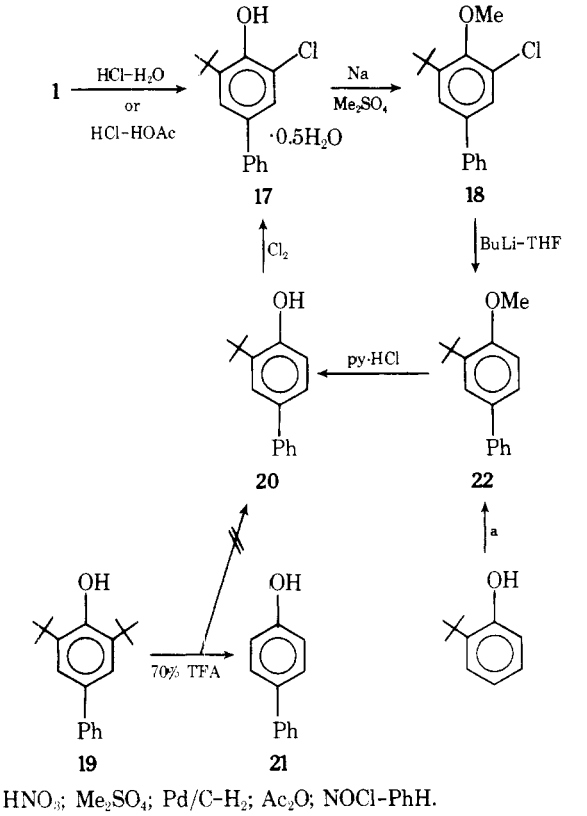
Scheme II



Scheme III

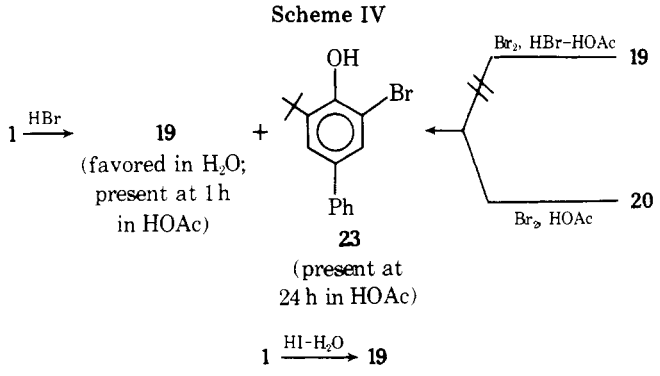


[a] HNO_3; Me_2SO_4; Pd/C-H_2; Ac_2O; NOCl-PhH.

24 h, while ambient TFA yielded **15** (assumed structure, difficult to purify because of ready hydrolysis to **16**) (Scheme II). Both **14** and the crude **15** on basic hydrolysis gave the same catechol (**16**) as did diacetate **4a.** The position of the Ac group on **14** was defined by the sharp NMR resonance at δ 5.6 ($CDCl_3$), which we find characteristic of the hindered phenolic OH. Catechol **16** showed the sharp δ 5.6 and a broad δ 4.85 resonance. Acetate **3**, prepared by acetylation of **1** in pyridine,[6] also yielded monoacetate **14** in hot HOAc.

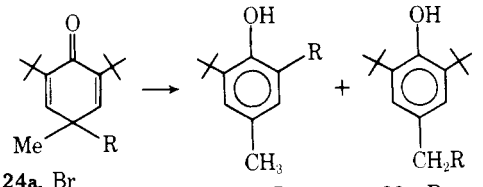
Treatment of **1** with inorganic acids gave even more surprising results (Scheme III). A slurry of **1** in concentrated HCl gave chlorophenol **17** as the hemihydrate. Both ^{13}C NMR and MS support this structure. Attempts to remove this water by azeotropic distillation and various drying agents all failed, which raised the possibility that, rather than the hemihydrate of **17**, this was some other molecule containing covalent -OH. Methylation yielded ether **18**, consistent with the proposed structure, but because of the tenacity of the water and to prove the location of the Cl we sought an alternative synthesis of **17.**

Scheme IV



Several attempts to selectively remove one *t*-Bu group from **19** failed to give **20;** only the completely dealkylated biphenylol (**21**) could be isolated. Subsequently, 2-*tert*-butylphenol was converted to ether **22.** This was identical with the product obtained by treating chloro ether **18** with BuLi in THF. This, while not confirmatory, is strong evidence for structure **17.** Confirmation came when pyridine HCl demethylation of **22** yielded **20,** and this was chlorinated to material identical with **17.** HCl (gas) in HOAc likewise transformed **1** into **17.**

These results are consistent with the reactions of **1** with HOAc and with TFA, i.e., migration from position 4 to 2. However, treatment of **1** with 48% HBr-H_2O gave primarily *reduction* to **19** (Scheme IV). (This reduction is also effected by $LiAlH_4$ and by hydrogenation over 5% Pd/C.) TLC and LC indicated traces of the 2-bromo derivative (**23**), subsequently prepared by bromination of **20.** The crude HBr-H_2O reaction mixture gave a strong starch-iodide test, indicative of Br_2 formation. This suggested initial reduction to **19,** followed by bromination. To test this, we ran the reaction in the presence of excess cyclohexene, using HBr in HOAc to achieve homogeneity. In this solvent, in the absence of cyclohexene, the reaction course changed; at short times the product was **19,** but by 22 h only bromide **23** was present. Cyclohexene led to the formation of dibromocyclohexane (by GLC) and prevented the formation of **23.** Bromination of **19** in both NaOAc-HOAc and 30% HBr-HOAc gave a complex mixture, casting some doubt on the intermediacy of molecular bromine. Cyclohexene had no effect on the HCl-HOAc conversion of **1** to **17.** Similar results have been reported in the analogous 4-methylcyclohexadienone system (**24**).



24a, Br
b, Cl
c, OO-*t*-Bu

25a, Br
b, Cl

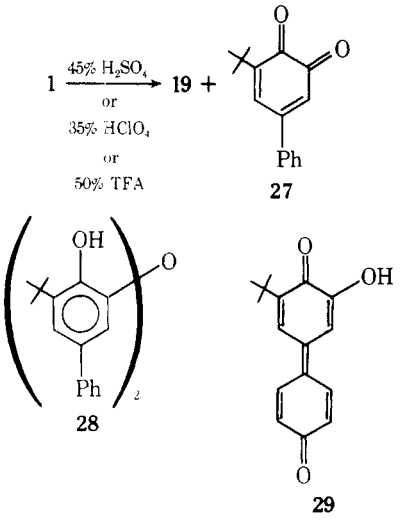
26a, Br
b, H

Ershov and Volod'kin showed that bromide **24a** reacted with HCl and HBr to give mixtures of **25a** and **26a.**[7] The initial product was **26b,** and the brominating species was interceptable. Starnes found that HCl treatment of **24b** and **24c** gave **25b** and that the reaction of **24b** did not involve a trappable chlorinating species.[8]

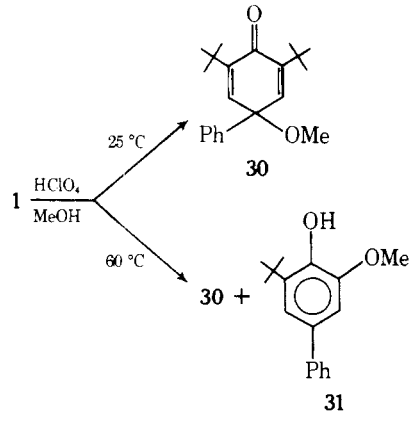
Aqueous HI caused only reduction of **1** to **19.**

The above results led us to expect that acids such as H_2SO_4 and $HClO_4$ would lead to catechol **16,** with no reduction to **19.** A slurry of **1** in 20% H_2SO_4 did not change, but use of 45% H_2SO_4 and 35% $HClO_4$ led to mixtures of **19** and quinone **27** (Scheme V). No catechol (**16**) was isolated, but in subsequent experiments trace amounts were detected by LC. Catechol **16** proved stable to both 45% H_2SO_4 and 35% $HClO_4$. This, and the roughly equal amounts seen initially, suggested that the

Scheme V



Scheme VI



observed products result from reaction between **16** formed in situ and **1**, in effect a disproportionation. Scaleup and further repetitions using LC analysis showed the reaction to be more complex and poorly reproducible, probably because of the extreme hydrophobicity of **1**. Thus, two new products (tentatively assigned structures **28** and **29**) were isolated from a large scale run; further small scale runs showed that **28** could be the *major* product in 45% H_2SO_4. In an effort to minimize the heterogeneity problem, we turned to aqueous TFA. We hoped that the hydrolytically labile trifluoroacetate **15**, if formed, would rapidly give **16** and thus allow a similar reaction course as seen with H_2SO_4 and $HClO_4$. This proved true in 70% TFA and 50% TFA. The reaction mixtures were still heterogeneous, but mixing seemed better and reproducibility was good. The 50% TFA conditions led to a 47:53 molar ratio (by GLC) of **19**/**27**, which favors the disproportionation concept. No **28** or **29** was seen.

Treatment of **1** with a catalytic amount of $HClO_4$ in MeOH at 25 °C led to the quinol ether (**30**), previously prepared by Muller from **19** and bromine in HOAc–MeOH.[9] Repetition at reflux led to the slow formation of the 2-methoxy compound (**31**) (Scheme VI).

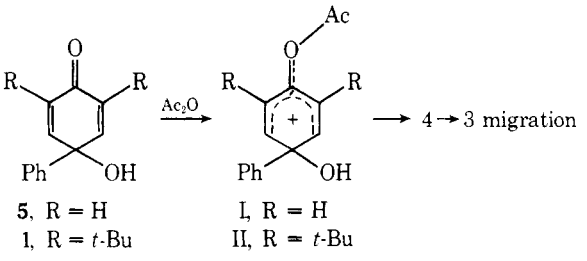
Discussion

Several unusual acid-induced reactions of **1** were discovered. Our initial interest was the abnormal dienone–phenol rearrangement, but this led to the discovery of the quinol ether formation, competing reductions, and the apparent disproportionation. A satisfactory rationalization of these data is outlined in Scheme VII.

The normal dienone–phenol rearrangement of nonhindered quinols such as **5** is thought to involve acetylation at the carbonyl oxygen to give cation I. Migration then occurs from

Scheme VII

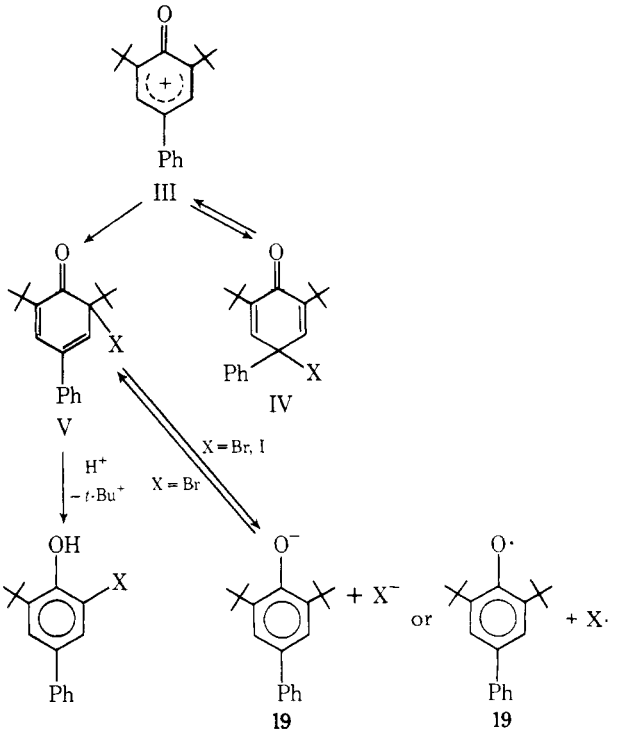
Normal Dienone–Phenol



5, R = H
1, R = *t*-Bu

I, R = H
II, R = *t*-Bu

Present Case



position 4 to 3, with the relative migratory aptitudes AcO > Ph > HO. Acetylation of the 4-hydroxy group is considered sterically unfavored. In the case of **1**, we propose that the ortho *tert*-butyl groups render attack at the carbonyl (which would give II, analogous to I) even less favorable than attack at the 4-hydroxy (to give acetate **3** and thence by solvolysis cation III). The sluggishness of the H_2SO_4–Ac_2O reaction of **1** is consistent with this interpretation (requiring several days at 100–110 °C vs. hours at 20 °C reported for quinols **5** and **7**). Subsequently, cation III can intercept a nucleophile to give intermediates IV and V. Involvement of the latter structure is implicit in the formation of 2-substituted products. The former is directly demonstrated by the isolation of the quinol ether (**30**). Reversibility of the III–IV reaction is indicated by the acetolysis of **3** and by the methanolysis of **30** at reflux. Extrusion of the *tert*-butyl cation from V then leads to the observed 2-substituted phenols. This seems unambiguous for X = CH_3CO_2 and CF_3CO_2. The hydrohalic acid reactions of **1** are more complex, but can be rationalized in terms of initial formation of cation III and intermediates IV and V.

Reduction by HI and HBr–H_2O occurs on extrusion of positive halogen (or halide radical) and V (or IV) to give the anion (or radical) of **19**. With HCl and HBr–HOAc, the *tert*-butyl cation is lost to give the 2-halophenol. The cyclohexene experiments suggest the bromination to be more complex, involving the initial reduction to **19** and subsequent bromination to V (X = Br) and then loss of *t*-Bu. It is tempting to speculate that HBr converts **1** initially to IV (X = Br), which loses Br^+ to form **19**, and this brominates to give V (X = Br). The HCl reactions seem to fit direct solvolysis.

The H_2SO_4 and $HClO_4$ reactions likewise fit the overall scheme, with the added complication that the initial product (catechol **16**) can reduce unreacted quinol to form **19** and quinone **27.**

The well-known stability of the phenoxyl radical corresponding to **19** requires consideration of the alternative radical pathway for all steps. Preliminary ESR experiments in which **1** and various acids were mixed at room temperature and then placed in the cavity showed no signal at 25 °C or at −80 °C for HCl/HOAc or HBr–HOAc. Possibly, the reaction is too fast, and more sophisticated experiments are planned.

Experimental Section

Melting points were determined on a Thomas-Hoover Uni-Melt in open capillary tubes and are uncorrected. LC analyses were done on a Waters M-6000 using a C_{18} Poropak column with 0.5 mL/min 1% HOAc–1.5 mL/min CH_3CN. Microanalyses were performed by the 3M Central Research Analytical Section. Abbreviations: PhH, benzene; PE, petroleum ether; Hex, hexane.

2,6-Di-*tert*-butyl-4-hydroxy-4-phenyl-2,5-cyclohexadien-1-one (1). A solution of 660 g (3.0 mol) of 2,6-di-*tert*-butyl-*p*-benzoquinone in 2.5 L of Et_2O was chilled in ice, and 1050 mL (3.0 mol) of 2.86 M PhMgBr in Et_2O was added over 0.5 h. After 1 h, the dark mixture was quenched with 0.5 L of 20% HCl, the Et_2O separated, and the aqueous layer extracted with 200 mL of Et_2O. The combined organic layers were dried ($MgSO_4$) and concentrated to a solid. Trituration with PE at −20 °C left 675 g (75%) of **1** as an off-white solid, mp 140–143 °C. Recrystallization from PhH–Hex (1:1) gave a white solid, mp 142–143 °C (lit.[9] 137–138 °C). The NMR ($CDCl_3$) showed *t*-Bu at δ 1.27, OH at δ 2.55, =CH at δ 6.55, and Ph as a multiplet at δ 7.15–7.45. Anal. Calcd for $C_{20}H_{26}O_2$: C, 80.5; H, 8.8. Found: C, 80.8; H, 8.9.

Reaction of 1 with Ac_2O. 3-*tert*-Butyl-4,5-diacetoxybiphenyl (4a). A solution of 8.0 g (26.8 mmol) of **1** in 100 mL of Ac_2O was heated on steam (90–100 °C) for 72 h. An aliquot at 24 h showed no reaction by TLC (silica gel, PhH) and melting point. At 72 h, the dark mixture was quenched in H_2O and extracted twice with 100 mL of CH_2Cl_2, and the organic layers were dried ($MgSO_4$) and concentrated. The resulting oil was dissolved in hexane and chilled (−20 °C). Beige crystals formed (6.8 g, 78%), mp 113–116 °C. Recrystallization from PhH–Hex (1:1) gave **4a** as a white solid, mp 116–117 °C. The NMR ($CDCl_3$) showed *tert*-Bu at δ 1.40 (*A* = 9.0), CH_3CO_2 at δ 2.29 and 2.37 (*A* = 6.0), and Ar as a multiplet at δ 7.3–7.5 (*A* = 7.0). Addition of Eu(fod)$_3$ shifted the *t*-Bu to δ 1.75, the CH_3CO_2 to δ 3.16 and 3.20, H-2 to δ 7.83 (d, *J* = 2 Hz), H-6 to δ 8.36 (d, *J* = 2 Hz), and Ph to δ 7.3–7.6. The *J* = 2 Hz indicates that H-2 and H-6 are meta. Both CH_3CO shift about equally, but only one H shifts substantially, indicating that only one H is ortho to an acetoxy group, arguing for **4a** over **4b.** Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.6; H, 6.8. Found: C, 73.5; H, 6.8.

4-Phenylcatechol (9) from 4a. Using the technique of McOmie et al.,[4] a solution of 6.0 g (18.4 mmol) of **4a** and 10 mg of Na dithionite in 150 mL of 70% TFA was heated at reflux under N_2 for 24 h. The orange solution was quenched in H_2O and extracted with CH_2Cl_2 as above to give a solid. Trituration with PE left 3.2 g (93%) of **9** as a tan solid, mp 135–139 °C. Recrystallization from PhH–Hex (1:1) gave white crystals, mp 137–139 °C. This material was identical with that made from 4-aminoveratrole (IR, NMR, and mixture melting point).

4-Phenylcatechol (9) from 4-Aminoveratrole. 4-Aminoveratrole (50.3 g, 0.328 mol) was mixed with 81.5 mL of concentrated HCl, chilled, and treated with 22.6 g (0.328 mol) of $NaNO_2$ in 50 mL of H_2O. The resulting solution was vigorously stirred with 300 mL of PhH while slowly adding a chilled solution of 40 g (1.0 mol) of NaOH in 200 mL of H_2O. Gas evolution ceased by 2 h, and the PhH layer was worked up to a dark oil. Chromatography on 300 g of silica gel with PhH gave 12.4 g of an oil, assumed to be 4-phenylveratrole (**10**). This was mixed with 38 g (0.225 mol) of 48% HBr–H_2O and 100 mL of HOAc and heated at reflux for 2 days. Extraction with CH_2Cl_2 gave a solid which was recrystallized from PhH–Hex (1:1) twice to give 4.0 g (37%) of **9** as an off-white solid, mp 136–137.5 °C (lit.[10] 138–140 °C). Anal. Calcd for $C_{12}H_{10}O_2$: C, 77.4; H, 5.4. Found: C, 77.1; H, 5.4.

Reaction of 1 with HOAc. 3-Acetoxy-5-*tert*-butyl[1,1′-biphenyl]-4-ol (14). A solution of 5.0 g (16.7 mmol) of **1** in 100 mL of HOAc was heated on steam for 24 h. The deep red solution was quenched in H_2O and extracted with CH_2Cl_2, and this extract was washed well with H_2O, dried ($MgSO_4$), and concentrated to 4.2 g of dark oil. This was chilled in PE at −20 °C to give 3.5 g (73%) of tan crystals, mp 133–136 °C. Recrystallization from Hex gave **14** as a white solid, mp 134–136 °C. The NMR ($CDCl_3$) showed *t*-Bu at δ 1.45 (*A* = 9.0), CH_3CO_2 at δ 2.3 (*A* = 3.2), OH at δ 5.5 (*A* = 1.0), and ArH at δ 7.2–7.5 (*A* = 7.3). Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.0; H, 7.1. Found: C, 76.2; H, 7.3.

Reaction of 1 with TFA. 3-*tert*-Butyl-5-trifluoroacetoxy[1,1′-biphenyl]-4-ol (15). Addition of 100 mL of TFA to 10.0 g (33.5 mmol) of **1** caused the immediate formation of a dark solution. At 10 min, the reaction was quenched in H_2O and worked up to give an oil. Chilling at −20 °C in PE left a violet solid: 6.0 g (53%); mp 95–100 °C; a mixture by TLC.

Hydrolysis with dilute NaOH gave catechol **16** (by melting point and IR) as below.

3-*tert*-Butyl-5-phenylcatechol (16). A mixture of 6.0 g (18.4 mmol) of **4a,** 4.0 g (50 mmol) of 50% NaOH, and 200 mL of 25% EtOH was heated at reflux for 3 h under N_2. Treatment with dilute HCl and extraction with CH_2Cl_2 gave an oil. This was chilled at −20 °C in Hex to give a tan solid (3.7 g, 83%), mp 91–94.5 °C. Recrystallization from Hex gave **16** as pink needles, mp 100–101 °C.

In a similar fashion, 6.0 g (21.1 mmol) of **14** yielded 3.8 g (75%) of crude **16,** recrystallized to mp 100–101 °C.

The NMR ($CDCl_3$) showed *t*-Bu at δ 1.43 (*A* = 6.1), broad OH at δ 4.85 (*A* = 1.0), sharp OH at δ 5.60 (*A* = 1.0), CH at δ 6.88 and 7.08 (doublets, *J* = 2.5 Hz, *A* = 2.0), and ArH at δ 7.2–7.5 (*A* = 5.1). Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.3; H, 7.5. Found: C, 79.3; H, 7.3.

4-Acetoxy-2,6-di-*tert*-butyl-4-phenyl-2,5-cyclohexadien-1-one (3). A mixture of 50 mL of Ac_2O–20 mL of pyridine was treated with 12.0 g (40 mmol) of **1** (no exotherm), and the resulting solution was stirred for 2 days. This was quenched in ice water, and the oil was scratched until it solidified. The solid was collected and washed with H_2O, dried in CH_2Cl_2 over $MgSO_4$, and concentrated at room temperature. (A prior run decomposed partially at this stage at 60–70 °C.) Recrystallization twice from PE gave 7.6 g (56%) of **3** as a yellow solid, mp 88.5–92 °C. The NMR ($CDCl_3$) showed *t*-Bu at δ 1.37, CH_3CO_2 at δ 2.27, H-3 and H-5 at δ 6.77, and Ph at δ 7.43. Anal. Calcd for $C_{22}H_{28}O_3$: C, 77.6; H, 8.3. Found: C, 77.6; H, 8.3.

A solution of 1.5 g (4.4 mmol) of **3** in 50 mL of HOAc was heated on steam for 17 h. The solution was concentrated to a dark oil, which on chilling gave 1.1 g (88%) of **14,** mp 131–135 °C, identical with pure **14** by IR and TLC.

Reaction of 1 with HCl. 3-*tert*-Butyl-5-chloro[1,1′-biphenyl]-4-ol Hemihydrate (17). A mixture of 5.0 g (16.7 mmol) of **1** and 100 mL of concentrated HCl was stirred with a bar magnet. Within 20 min, the solid changed to a yellow oil. By 3 h, the reaction was complete (TLC, $CHCl_3$ on silica gel). Extraction twice with 40 mL of CH_2Cl_2, washing with H_2O, drying over $MgSO_4$, and concentration gave 4.6 g of yellow oil. Chilling in 25 mL of PE at −20 °C gave 3.2 g (73%) of **17** hemihydrate as white crystals, mp 55–70 °C. Further recrystallization and drying (under vacuum at 60 °C, in refluxing benzene, or in PE with 4A molecular sieves) did not improve the melting point. The NMR ($CDCl_3$) showed *t*-Bu at δ 1.45, H_2O at δ 1.55, OH at δ 5.9, and Ar at δ 7.3–7.6. Anal. Calcd for $C_{16}H_{17}ClO{\cdot}0.5H_2O$: C, 71.2; H, 6.7. Found: C, 71.4; H, 6.7.

A solution of 5.0 g of **1** in 100 mL of HCl (gas)–saturated HOAc was quenched in H_2O–ice at 1 h to give 4.5 g (100%) of **17** hemihydrate, mp 62–80 °C, identical with the above by IR and NMR.

A solution of 2.0 g (6.7 mmol) of **1** in 75 mL of HOAc was treated with 10 mL of cyclohexene and then 25 mL of HCl (gas)–saturated HOAc. Quenching in H_2O, extraction with CH_2Cl_2, and concentration yielded only **17,** by TLC and GLC (2 ft OV-210, 180 °C).

3-*tert*-Butyl-5-chloro-4-methoxybiphenyl (18). A solution of 26.7 g (0.10 mol) of **17** hemihydrate in 250 mL of glyme was added to 2.4 g (0.104 mol) of Na, and the mixture was warmed on steam after the vigorous initial reaction. This was treated with 25.6 g (0.2 mol) of Me_2SO_4, causing an exotherm and formation of a white precipitate. After 0.5 h, the mixture was quenched and extracted with CH_2Cl_2, giving an oil. Distillation yielded 24.0 g (87%) of **18** as a viscous, colorless liquid, bp 160–164 °C/0.6 mm. The NMR ($CDCl_3$) showed *t*-Bu at δ 1.53, CH_3O at δ 4.07, and ArH at δ 7.4–7.6. Anal. Calcd for $C_{17}H_{19}ClO$: C, 74.3; H, 7.0. Found: C, 74.3; H, 6.8.

3-*tert*-Butyl-4-methoxybiphenyl (22) from 18. A solution of 20.0 g (72.8 mmol) of **18** in 100 mL of THF was treated dropwise with 32 mL (73 mmol) of 2.29 M *n*-BuLi in Hex. After the initial exotherm, the mixture was heated at reflux for 2 h, cooled, treated with dilute HCl, and extracted with Et_2O. The resulting oil was distilled to 10.0 g of **22,** a colorless liquid, bp 155–160 °C/0.35 mm. This was triturated with PE at −20 °C, giving **22** as a white solid, mp 79–81 °C. The NMR ($CDCl_3$) showed *t*-Bu at δ 1.43, CH_3O at δ 3.83, and ArH at δ 6.8–7.7. Anal. Calcd for $C_{17}H_{20}O$: C, 85.0; H, 8.4. Found: C, 84.8; H, 8.5.

3-*tert*-Butyl-4-methoxybiphenyl (22) from 2-*tert*-Butyl-

phenol. By the method of Hewgill and Middleton,[11] 150.2 g (1.0 mol) of 2-*tert*-butylphenol in 115 mL of HOAc was added over 2 h to a solution of 112 mL of concentrated HNO_3 in 365 mL of HOAc. The mixture was quenched on ice and the precipitate recrystallized from EtOH–H_2O to give 65.0 g (33%) of 2-*tert*-butyl-4-nitrophenol as a yellow solid, mp 141–143 °C (lit.[12] 144–145 °C). The NMR ($CDCl_3$) showed *t*-Bu at δ 1.43, H-6 at δ 6.87 (d, J = 8.6 Hz), H-5 at δ 7.73 (q, J = 8.6 and 2.4 Hz), H-3 at δ 8.1 (d, J = 2.4 Hz), and OH broad at δ 10.0. A solution of 47.1 g (2.05 mol) of Na in 1 L of MeOH was treated with a slurry of the above phenol (400 g, 2.05 mol) in 1 L of MeOH, the MeOH was removed under vacuum, and the resulting Na salt was dissolved in 1 L of diglyme and treated with 260 g (2.06 mol) of Me_2SO_4. After heating at 140 °C for 5 h, the mixture was quenched in H_2O and extracted with CH_2Cl_2. Distillation yielded 385 g (90%) of 2-*tert*-butyl-4-nitroanisole as a yellow oil, bp 120 °C/0.14 mm. Recrystallization from Hex gave mp 62–64 °C (lit.[13] 62–63 °C). This was dissolved in 600 mL of EtOH and reduced over 10% Pd/C in a Parr apparatus. The product was distilled to 279 g (84%) of 2-*tert*-butyl-4-aminoanisole, bp 118 °C/0.1 mm. Of this, 100 g (0.558 mol) was acetylated with 100 mL of Ac_2O in HOAc on steam. The mixture was quenched in H_2O and the product collected (125 g, 100%). Recrystallization from EtOH–H_2O gave 3-*tert*-butyl-4-methoxyacetanilide, mp 128–129 °C (lit.[14] 126.5–129 °C).

A solution of 44.3 g (0.20 mol) of the above acetanilide, 100 mL of Ac_2O, and 27 g (0.27 mol) of KOAc in 200 mL of HOAc was treated dropwise at 0 °C with a solution of 20 g (0.30 mol) of NOCl in 150 mL of Ac_2O. The yellow mixture was quenched in ice–H_2O, and the *N*-nitrosoacetanilide was extracted into two 500-mL portions of PhH. This was dried briefly over $MgSO_4$ and warmed on steam over Na_2SO_4 overnight. Distillation gave 14.0 g (29%) of **22**, bp 155–165 °C/0.35 mm. Recrystallization from PE gave **22**, mp 79–81 °C, identical with that made from **18** by IR and mixture melting point.

3-*tert*-Butyl[1,1′-biphenyl]-4-ol (20). A mixture of 9.4 g (39.1 mmol) of **22** and 20 g of pyridine HCl was heated at 220 °C for 2 h. The brown mixture was cooled, quenched in H_2O, and extracted with CH_2Cl_2. Distillation yielded 8.0 g (90%) of **20**, bp 140–145 °C/0.25 mm. This oil was chilled in Hex at −20 °C to give 6.4 g (72%) of **20** as a colorless solid, mp 41–43 °C (lit.[15] 40–42 °C). The NMR ($CDCl_3$) showed *t*-Bu at δ 1.45, OH broad at δ 4.8, H-5 at δ 6.73 (d, J = 8 Hz), and the remaining ArH at δ 7.2–7.6. Anal. Calcd for $C_{16}H_{18}O$: C, 84.9; H, 8.0. Found: C, 84.3; H, 8.0.

Reaction of 1 with HBr–H_2O. 3,5-Di-*tert*-butyl[1,1′-biphenyl]-4-ol (19). A slurry of 5.0 g (16.7 mmol) of **1** in 100 mL of 48% HBr–H_2O was stirred for 5 h with a bar magnet. TLC (silica gel, PhH) showed no **1** left. Filtration yielded 4.8 g (102%) of crude **19**, mp 93–96 °C. Recrystallization from Hex gave 2.9 g (60%), mp 101–102 °C. The NMR ($CDCl_3$) showed *t*-Bu at δ 1.45, OH at δ 5.0, and ArH at δ 7.2–7.5. The mother liquor gave a strong starch–iodide test. This material was identical by mixture melting point, IR, and NMR with material derived from 17.2 g (0.1 mol) of 4-biphenylol (**21**), 20 g (0.36 mol) of isobutene, and 0.5 g of H_2SO_4 at 80 °C in an autoclave for 15 h. This product was recrystallized from PE to give 9.5 g (33%) of **19**, mp 101–103 °C. Anal. Calcd for $C_{20}H_{26}O$: C, 85.0; H, 9.3. Found: C, 85.3; H, 9.2.

Reaction of 1 with HBr–HOAc. 3-Bromo-5-*tert*-butyl[1,1′-biphenyl]-4-ol Hemihydrate (23). A solution of 1.0 g (3.3 mmol) of **1** in 20 mL of 30% HBr–HOAc (initially chilled to 10 °C) was stirred at 27 °C for 24 h. At 1 h, TLC (silica gel, Hex) showed a mixture of **19**, **23**, and unreacted **1**. At 24 h, only **23** was present. Quenched in H_2O, the solution yielded 0.66 g (63%) of **23**, mp 54–8 °C, identical by IR and NMR with that prepared from **20** below. Repetition in the presence of 8 mL of cyclohexene showed only **19** as the product, by NMR and TLC.

3-Bromo-5-*tert*-butyl[1,1′-biphenyl]-4-ol Hemihydrate (23) from 20. A stirred mixture of 4.0 g (17.7 mmol) of **20**, 1.5 g (18.3 mmol) of NaOAc, and 80 mL of HOAc was treated dropwise with 2.9 g (19 mmol) of Br_2 in 5 mL of HOAc. The reaction was quenched at 20 h and extracted with CH_2Cl_2. The resulting solid was recrystallized from MeOH–H_2O to give 4.0 g (72%) of **23**, mp 60–70 °C, as a colorless solid. The melting point was not improved by repeated recrystallizations. The NMR ($CDCl_3$) showed *t*-Bu at δ 1.47, H_2O at δ 1.57, OH at δ 5.95, and ArH at δ 7.4–7.7. Anal. Calcd for $C_{16}H_{17}BrO{\cdot}0.5H_2O$: C, 61.1; H, 5.8. Found: C, 61.0; H, 5.8.

Reaction of 1 with HI. A mixture of 5.0 g (16.7 mmol) of **1** in 100 mL of 48% HI–H_2O was stirred for 24 h with a bar magnet. Filtration gave 4.7 g (99%) of **19**, mp 99–100 °C, identified by IR and MS. No iodinated material was detected by MS.

Reaction of 1 with 35% $HClO_4$. A mixture of 5.0 g (16.7 mmol) of **1** and 100 mL of 35% $HClO_4$ was stirred for 24 h with a bar magnet at 28 °C. The dark red slurry was extracted with CH_2Cl_2. Chromatography on 100 g of 40–140 mesh silica gel gave three fractions. The first (200 mL of PhH) yielded 1.9 g (42%) of **19** after recrystallization from Hex, mp 100–102 °C, identical with authentic **19** by TLC, IR, and NMR. The second fraction (100 mL of PhH) was triturated with hexane to give 0.5 g (10%) of unreacted **1**, mp 116–119 °C. The third fraction (300 mL of acetone) yielded a red solid which was recrystallized from hexane to give 1.6 g (39%) of **27**, mp 119–121 °C (lit.[16] 116–118 °C). The NMR ($CDCl_3$) showed *t*-Bu at δ 1.48, H-4 at δ 6.50 (d, J = 2.0 Hz), H-6 at δ 7.20 (d, J = 2.0 Hz), and ArH at δ 7.45–7.6. Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.9; H, 6.7. Found: C, 80.0; H, 6.8.

Repetitions of this reaction showed trace amounts of catechol **16** by LC analysis. A slurry of 1.0 g of **16** in 20 mL of 35% $HClO_4$ did not change in 24 h (TLC).

Reaction of 1 with 45% H_2SO_4. A mixture of 20.0 g (67 mmol) of **1** and 300 mL of 45% H_2SO_4 was stirred for 24 h with a bar magnet. Chromatography as above gave 4.0 g (24%) of **19**, 2.3 g (12%) of unreacted **1**, and 4.2 g (26%) of **27**. However, repetition on 30 g gave a mixture (36.0 g) from which not only **19** and **27** were isolated, but also the byproducts **28** and **29** were found. Chromatography of 22 g gave 22 fractions (1–8, each 100 mL of PhH; 9–22, each 250 mL of PhH). Fractions 1–4 yielded 13.0 g of a solid. Sublimation of 10.4 g at 90 °C/0.3 mm gave 0.53 g of **19** and left a residue of 9.5 g, mp 135–138 °C. Recrystallization from Hex yielded 6.6 g of a colorless solid, mp 154–156 °C. This was assigned structure **28**, bis(3-*tert*-butyl-4-hydroxy[1,1′-biphenyl]-5) ether. The NMR ($CDCl_3$) showed *t*-Bu at δ 1.53 (singlet, A = 17.3), OH at δ 6.00 (A = 2.0), H-2 at δ 7.11 (J = 2 Hz, A = 2.0), and ArH at δ 7.35–7.6 (A = 12.0). The MS yielded a molecular weight of 466.25 (calcd 466.58). Anal. Calcd for $C_{32}H_{34}O_3$: C, 82.4; H, 7.4. Found: C, 82.9; H, 7.4.

Fractions 5 and 6 yielded 0.5 g after recrystallization from PE, mp 95–98 °C, tentatively identified as **29**, 3-*tert*-butyl-5-hydroxy[1,1′-bipheno]-4,4′-quinone. The NMR ($CDCl_3$) showed *t*-Bu at δ 1.43 (A = 9.0), OH at δ 6.82 (A = 1.0), and ArH at δ 7.4–7.5 (A = 6.0). The MS yielded a molecular weight of 256 (calcd 256.3). Anal. Calcd for $C_{16}H_{16}O_3$: C, 75.0; H, 6.3. Found: C, 75.3; H, 6.5.

Fractions 7–11 yielded 2.2 g of unreacted **1**. Fractions 12–22 yielded 4.3 g of **27**.

Reaction of 1 with 50% TFA. A mixture of 10.0 g (33.5 mmol) of **1** and 120 mL of 50% aqueous TFA was stirred for 24 h. TLC and GLC (2 ft OV-210, 200 °C) showed only **19** and **27**. Workup yielded 8.7 g of a dark oil. Two 1.0-g runs were also made. The GLC areas were 66% **19** and 34% **27** (±2%). A mixture of 0.604 mmol of **19** and 0.867 mmol of **27** (molar 41–59%) gave a GLC area of 60%: 40%. This allowed a correction of the reaction mixture to 47% **19** and 53% **27** (molar percent). A 10-g run using 90 mL of 50% TFA and 10 mL of 70% $HClO_4$ gave a 46:52 molar ratio of **19**/**27**.

Reaction of 1 with MeOH. 2,6-Di-*tert*-butyl-4-methoxy-4-phenyl-2,5-cyclohexadien-1-one (30) and 5-*tert*-Butyl-3-methoxy[1,1′-biphenyl]-4-ol Hemihydrate (31). A solution of 10.0 g (33.5 mmol) of **1** and 10 drops of 70% $HClO_4$ in 100 mL of MeOH was stirred for 24 h. The MeOH was evaporated and the residue extracted into Hex. Concentration to an oil and recrystallization from MeOH–H_2O gave 8.5 g (81%) of **30** as a white solid, mp 72–73 °C (lit.[9] 70–72 °C). The NMR ($CDCl_3$) showed *t*-Bu at δ 1.27, MeO at δ 3.34, H-3 and H-5 as a sharp singlet at δ 6.47, and Ph at δ 7.2–7.4. Anal. Calcd for $C_{21}H_{28}O_2$: C, 80.7; H, 9.0. Found: C, 80.4; H, 9.0.

Repetition at reflux for 20 h gave a mixture containing both **30** and **31** by TLC. The MeOH was evaporated to leave a solid, which was recrystallized from MeOH–H_2O to give 10.8 g of a sticky yellow solid, mp 95–100 °C. Sublimation at 90 °C/0.25 mm and recrystallization of the lower portion of the sublimate from MeOH–H_2O gave **31** (6.0 g, 67%) as a white solid, mp 98–100 °C. The NMR ($CDCl_3$) showed *t*-Bu at δ 1.47, H_2O at δ 3.45, MeO at δ 3.93, OH at δ 6.05, H-2 at δ 7.00 (d, J = 2 Hz), H-6 at δ 7.17, and Ph at δ 7.3–7.6. Anal. Calcd for $C_{17}H_{22}O_2{\cdot}0.5H_2O$: C, 76.9; H, 8.0. Found: C, 76.3; H, 8.3.

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Registry No.—**1**, 24457-06-5; **3**, 68757-64-2; **4a**, 68757-65-3; **9**, 92-05-7; **10**, 17423-55-1; **14**, 68757-66-4; **15**, 69896-71-4; **16**, 68757-67-5; **17**, 68757-68-6; **18**, 68757-69-7; **19**, 2668-47-5; **20**, 42479-87-8; **21**, 92-69-3; **22**, 68757-70-0; **23**, 68757-71-1; **27**, 24456-99-3; **28**, 68757-72-2; **29**, 68757-73-3; **30**, 68757-74-4; **31**, 68757-75-5; 3,6-di-*tert*-butylquinone, 719-22-2; phenyl bromide, 108-86-1; acetic anhydride, 108-24-7; 4-aminoveratrole, 6315-89-5; 2-*tert*-butyl-4-nitrophenol, 6683-81-4; 2-*tert*-butyl-4-nitroanisole, 15353-20-5; 2-*tert*-butyl-4-aminoanisole, 35292-03-6; 3-*tert*-butyl-4-methoxyacetanilide, 68757-76-6; 3-*tert*-butyl-4-methoxy-*N*-nitrosoacetanilide, 68757-77-7; isobutene, 115-11-7.

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Synthesis and Reactions of (4,5-Dicarbomethoxy-1,3-dithiolyl)tributylphosphonium Tetrafluoroborate†

Masaru Sato, Nina C. Gonnella, and Michael P. Cava*

Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104

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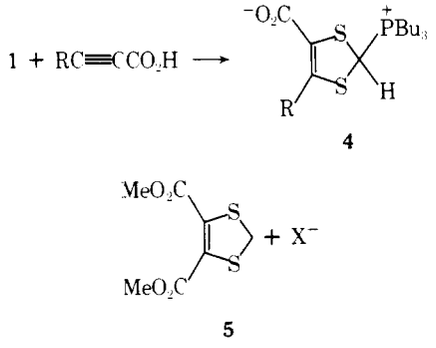
The title phosphonium salt (**7**) is readily prepared by the reaction of dimethyl acetylenedicarboxylate and fluoroboric acid with the adduct of carbon disulfide and tributylphosphine and serves as a stable precursor of the corresponding unstable phosphorane (**6**). A comparative study of the use of salt **7** in the Wittig reaction with various aldehydes and ketones is described. Attempts to effect the complete dehydrogenation of the bisfulvene **21** from cyclohexane-1,4-dione were unsuccessful.

In 1971, Hartzler reported that the carbon disulfide–tributylphosphine adduct (**1**) reacts with electron-deficient acetylenes to give poor yields of tetrathiafulvalenes. If adduct **1** is mixed with an aromatic aldehyde prior to the addition of the acetylene, excellent yields of 2-benzylidene-1,3-dithioles (**3**) are obtained, a result strongly suggesting the intermediacy of a highly reactive phosphorane **2**, the dipolar resonance contributor of which (**2b**) is a destablilized cyclic 8π-electron antiaromatic (Scheme I).[1] Additional support for this mechanism, as well as for a concerted 1,3-dipolar addition of **1** to the acetylene, was given by Pittman and Narita, who found that adduct **1** reacts smoothly with either propiolic acid or acetylenedicarboxylic acid to give a crystalline zwitterion (**4**).[2]

During the past few years, phosphoranes of the type **2** have become available in a very different manner from simple 1,3-dithiolium salts in cases where R equals H, alkyl, or a condensed benzene ring; these intermediates have proved very useful for the synthesis of a variety of dithiafulvenes,[3] as well as unsymmetrical tetrathiafulvalene derivatives.[4] This new method is not applicable, however, to the synthesis of phosphoranes containing electron-withdrawing groups since the required dithiolium salts (i.e., **5**) are not known.[5]

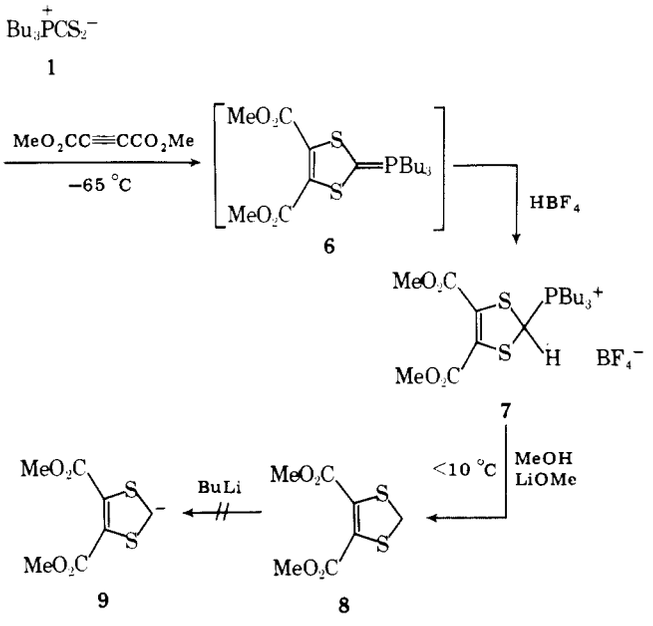
We now report a modification of the Hartzler reaction which provides a simple and convenient synthesis of the title phosphonium salt **7**, and which has enabled us to study in some detail the generation and Wittig reactions of the corresponding ester-substituted phosphorane **6**.



Results

When the carbon disulfide–tributylphosphine adduct (**1**) is treated with a mixture of dimethyl acetylenedicarboxylate and fluoroboric acid etherate at −65 °C, the initially produced phosphorane **6** is trapped by protonation, and the resulting cation can be isolated in yields of up to 72% as the stable, white, crystalline tetrafluoroborate **7**, mp 120–121 °C.

Treatment of salt **7** with dilute lithium methoxide in methanol at a low temperature, followed by an aqueous workup, led to a good yield (88%) of the previously unreported dephosphinated ester, 4,5-dicarbomethoxy-1,3-dithiole (**8**).



† Dedicated to Professor A. Dreiding on the occasion of his 60th birthday.

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