Table VI. Distillation Results for Low Boiling Products from Acetolysis of 5-Methoxy-1-pentyl *p*-Bromobenzenesulfonate (I) at 75.0°

Fraction	Bp, °C	$n^{35}D$	Wt, g	Components	THP,[a,b] %
(a) Products from Acetolysis of I					
1	57–59	1.3625	1.06	MeOAc–THP	4
2	59–88.5	1.3706	0.49	MeOAc–THP	18
3	88.5–107	1.4031	0.54	THP–AcOH	67
4	107–116	1.3985	1.20	THP–AcOH	57
5	116–117.5	1.3730	1.20	THP–AcOH	3
Recovered yield of THP, 1.21 g (57%)					
Recovered yield of MeOAc, 1.42 g (67%)					
(b) Control Experiment[c]					
1	88–90	1.4174	1.00	THP–AcOH	99
2	90–106	1.4125	0.50	THP–AcOH	87
3	106–117.5	1.3861	0.80	THP–AcOH	30
4	117.5	1.3725	0.50	THP–AcOH	
Recovered yield of THP, 1.7 g (62%)					

[a] Abbreviation for tetrahydropyran. [b] Estimated from the refractive indices of the fractions. [c] In the control experiment, *p*-toluenesulfonic acid was used in place of *p*-bromobenzenesulfonic acid.

In an effort to estimate the total acetolysis yield of these low boiling products, a 10.22-g (0.03 mole) quantity of bromobenzenesulfonate I in 100 ml of acetic acid was solvolyzed at 75.0° for 75 hr. After this the cooled solution was neutralized with 1.65 g of sodium carbonate and 2.5 g of acetic anhydride was added to ensure anhydrous conditions. The fraction boiling below 117.5° was collected by slow distillation of the refluxing acetic acid solution through the 45-cm, helices-packed column. Total refluxing time at a kettle temperature of 118.5° was 6 hr. This fraction was carefully refractionated through a highly efficient 8.0 mm × 80 cm concentric tube column. Five fractions which proved to be binary mixtures of methyl acetate and tetrahydropyran, and tetrahydropyran and acetic acid were collected. The compositions of these mixtures were estimated from their refractive indices since it was shown experimentally with known mixtures that plots of refractive index *vs.* wt % composition were linear for both MeOAc–THP and AcOH–THP binary systems. The results including the estimated yields are listed in Table VI.

In order to get a better estimate of the actual yield of tetrahydropyran a control run was carried out under the acetolysis conditions. This consisted of dissolving 2.69 g (0.03 mole) of freshly distilled tetrahydropyran in 100 ml of an acetic acid solution 0.028 *M* in *p*-toluenesulfonic acid and keeping the mixture at 75.0° for 48 hr. During this time the solution became yellowish brown. Following this the solution was worked up exactly as described for the acetolysis solution of I. The distillation fractions with compositions are listed in Table VI. As indicated, the recovered yield of tetrahydropyran was 62%.

Using the control experiment as a correction factor, an over-all yield of 77% tetrahydropyran is estimated for the acetolysis of I.

Total Ethanolysis of 5-Methoxy-1-pentyl *p*-Bromobenzenesulfonate (I). A solution of 8.43 g (0.025 mole) of I in 250 ml of anhydrous ethanol was kept at 75.0° for 15 hr (12 half-lives). Following this the solution was cooled to room temperature and the *p*-bromobenzenesulfonic acid was neutralized with the calculated amount (0.58 g) of sodium. After standing for a few hours the solid was removed by filtration, and the ethanol was removed by distillation through a 45-cm, glass-helices-packed column. The residue was taken up in ether and filtered to remove the remaining sodium *p*-bromobenzenesulfonate. After evaporating off the ether, the concentrate was distilled through a 15-cm Vigreux column to afford 2.15 g (58.8%) of high boiling product, bp 101–102° (81 mm), $n^{25}D$ 1.4088.

Anal. Calcd for $C_8H_{18}O_2$: C, 65.71; H, 12.41. Found: C, 65.41; H, 12.36.

This material had an infrared spectrum identical with the spectrum for authentic 1-methoxy-5-ethoxypentane. Only one component was found according to gas chromatography.

A 5-ml quantity of a 0.1 *M* solution of I in ethanol was solvolyzed at 75.0° for 13 half-lives. After cooling to 25°, the calculated amount of sodium was added. The neutralized solution was distilled to dryness and the ethanol distillate analyzed for tetrahydropyran by gas chromatography. A 2 m × 0.6 mm stainless steel column packed with 30% by weight Carbowax 1500 on sieved 40–60 mesh Firebrick was used. The yield of tetrahydropyran was 40.8% of theoretical. The accuracy of this was checked by analysis of a known solution made up to the same concentration.

The Influence of the R Group on the Brominative Formation of 4-Bromo-4-R-2,6-di-*t*-butylcyclohexadienones from the Corresponding Phenols[1]

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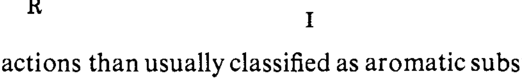
Contribution from the Department of Chemistry of the University of Rome, Rome, Italy. *Received March 28, 1967*

Abstract: The rate constants for the reaction of some 4-substituted 2,6-di-*t*-butylphenols with bromine in acetic acid solution to give *p*-cyclohexadienones derivatives have been determined at 25°. The data provide information on the scarcely known substituent effects at the point of attack where a geminal position is developed and are discussed in relation to the mechanism of both aromatic substitutions and nonconventional aromatic reactions.

A widely accepted mechanism for a great number of electrophilic aromatic substitutions involves the formation of a benzenonium ion (I) as a reactive intermediate (eq 1). On decomposition of I, normal substitution products are formed if R is a good leaving group.[2] However, the scope of eq 1 includes more reactions than usually classified as aromatic substitutions



I

(1)

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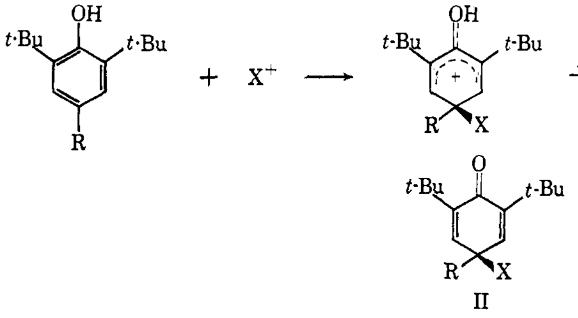
(1) Part V in the series: Nonconventional Paths in Electrophilic Aromatic Reactions.

(2) See, for example, R. O. C. Norman and R. Taylor, "Electrophilic Substitution in Benzenoid Compounds," Elsevier Publishing Co., Amsterdam, 1965, Chapters 9 and 10.

because there is an increasing number of recognized cases whereby decomposition of I leads to nonconventional products. As long as the formation of I is rate determining for the over-all process, the reaction kinetics do not depend on whether the subsequent decomposition occurs in the conventional way or not.[3]

In cyclohexadienone formation[4] (eq 2) C–X bond making and sp² → sp³ hybridization change are expectedly involved in the rate-determining step probably without appreciable contribution of O–H bond breaking. We have chosen this reaction in order to consider kinetic aspects supposedly common to ordinary aromatic substitutions. This paper is concerned with the influence of the nature of the group R on the rate of attack by the electrophilic reagent. Both polar and steric effects involved in a system of this kind where a varying substituent group is placed right on the reaction site are far less known than those involved in the familiar *ortho*, *meta*, and *para* positions. The problem has received some attention in aromatic substitutions by comparison of leaving group effects on reaction rates.[5,6] The alternative approach proposed here is characterized by the fact that reactivity data for reaction 2 are free from any influence of the C_{Ar}–R bond breaking possibly affecting aromatic substitution.



(2)

Results and Discussion

As with 2,6-di-*t*-butylphenol[7] (R = H), reaction 2 can be conveniently studied by a spectrophotometric method on the basis of the characteristic absorption maximum of the formed dienone at 250–252 mμ. Second-order rate constants were evaluated from the early part of the reaction (up to 2–4% change) since the kinetics are eventually complicated by the decomposition of the dienone to phenolic derivatives. The *k* values thus obtained were found to be independent of the initial concentration of the reactants in the observed range of 5×10^{-5} to 2×10^{-4} *M*. The results are reported in Table I. In 98% aqueous acetic acid the dienone formation shows a fivefold rate increase as compared to the reaction in the anhydrous solvent and, also, appears to be less affected by the subsequent decomposition of the product presumably because of a smaller solvent effect on the latter reaction.

Table I. Rate Data for the Bromination of 2,6-Di-*t*-butyl-4-R-phenols at 25°

	k_2, l. mole^{-1} sec^{-1}	
R	Anhydrous AcOH	98% aq AcOH
Hydrogen	4.79[a]	25.1
Methyl	1.28	7.29
t-Butyl	1.30	6.41
Bromine	$<1 \times 10^{-4}$ [b]	$<9 \times 10^{-6}$ [c]

[a] de la Mare, *et al.*,[7] have reported k_2 = 5.00 l. mole^{-1} sec^{-1}. [b] At 7.5×10^{-3} *M* concentration in both reactants no evidence of formation of dienones was obtained after 17 hr. [c] At 4×10^{-2} *M* in phenol and 2×10^{-3} *M* in Br_2 no change in optical density in 24 hr within experimental error.

The solvent effect on dienone formation is in agreement with the charge type of the reaction and is analogous to what is found in aromatic bromination (bromo deprotonation). It is worth noting that the analogy also involves the kinetic form in the concentration range stated above, as a third-order term in aromatic bromination only appears at higher concentrations.[8]

The effect of R on the rate of reaction 2, by which a geminal position is developed, is expected to be of two kinds, polar and steric. The resonance effect can be neglected with the groups (alkyl, Br) under examination, as it is slight in the ground state and zero in the transition state. At such a short distance, polar effects should be stronger than those observed were the R group located in any other position of the ring relative to the reaction site. On comparing groups of similar size, CH_3 and Br, polar effects are held responsible for the rate enhancement relation $k_{CH_3}/k_{Br} > 830{,}000$ as obtained from Table I. Although polar effects from aromatic ring positions decrease in the order *ortho* > *meta* > *para*, the largest k_{CH_3}/k_{Br} ratio should be found when R is located in the *meta* position, where the least resonance effect should be felt. The only available value of this kind, 6000, concerns the bromination of R-substituted mesitylenes.[9] A more closely related structural situation to compare with is presumably offered by the electrophilic addition to olefins,[10] when R is changed at the point of attack to the double bond. However, apart from any special mechanistic features involved in the mode of attack of the halogen in this reaction, a proper quantitative comparison of Br *vs.* CH_3 does not seem to be available.

The effect of replacing H with an alkyl group offers several points of interest. The observed reactivity order is H > $CH_3 \simeq C(CH_3)_3$ and is apparently a combination of polar and steric effects which are assumed to act in opposite directions. The k_H/k_{CH_3} ratio, even though greater than unity, involves a small factor (3.7). This is a clean-cut measure of the ease, relative to hydrogen, at which an electrophile can attack a ring position occupied by such a familiar substituent as a CH_3 group. Thus, in agreement with the proposed mechanism of "electrophilic" side-chain halogenation,[11] methylbenzenes are indeed vulnerable to attack

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[8] P. B. D. de la Mare and J. H. Ridd, "Aromatic Substitution," Butterworth and Co., Ltd., London, 1959, p 124.

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at CH_3 positions nearly as easily as at H positions, other reactivity conditions being equal (long-range orientation effects, etc.).

The reactivity ratio remains practically unchanged on going from k_H/k_{CH_3} to $k_H/k_{C(CH_3)_3}$ and does not reveal any dramatic effect of the large size of the *t*-butyl group. Increase in the steric requirements of this group is believed to be balanced by an increase in the electron-repelling polar effect. Probably, the absolute steric requirements of the reaction are not as large as might be expected because the bulky group is bound to change from a coplanar aromatic position to a noncoplanar geminal position. It is of interest to note that in methanol addition to the double bond in the series $(CH_3)_2C{=}CHR$, which apparently proceeds *via* carbonium ions of the type $(CH_3)_2C^+{-}CH_2R$, the reactivity ratios $H:CH_3:C(CH_3)_3$ are in the order 2.6:1:1.8.[12] Despite the smaller steric requirements of electrophilic hydrogen as compared to halogen, this order is of comparable magnitude to the one observed here (3.7:1:1).

In aromatic bromination by "positive" bromine the ease of replacement of the *t*-butyl group is 1.4 times as great as that of hydrogen.[5] On the other hand, from data concerning aromatic chlorination by Cl_2,[13] it appears that hydrogen is replaced faster than *t*-butyl by factors of 1.5 (*p*-R-*t*-butylbenzene) and 1.9 (*p*-R-toluene). In any case, in these reactions, if allowance is made for the different halogenating species involved, the *t*-butyl group can be taken nearly as a good leaving group as hydrogen.

All these data from aromatic substitution compare favorably with the relative ease of attack of molecular bromine in dienone formation and agree with the view that both aromatic substitution and dienone formation proceed by corresponding essentially similar transition states for their rate-determining steps. We may thus regard this comparison as an additional evidence for the benzenonium ion intermediate theory concerning most electrophilic aromatic substitution reactions.

Experimental Section

Materials. The solvent acetic acid was purified as previously described.[14] The following phenols were recrystallized commercial specimens (melting points are given in parentheses): 2,6-di-*t*-butylphenol (35.7–36.5°), 2,4,6-tri-*t*-butylphenol (130–130.5°), 2,6-di-*t*-butyl-4-methylphenol (68–68.5°). 2,6-Di-*t*-butyl-4-bromophenol (mp 82–82.5°; lit.[15] 83–83.5°) was prepared by bromination of 2,6-di-*t*-butylphenol in acetic acid and recrystallized from hexane.

4-Bromo-2,6-di-*t*-butylcyclohexa-2,5-dien-1-one (II, R = H) was prepared according to the procedure described by de la Mare, *et al.*,[7] mp 69–70°, λ_{max} 252 mμ (ϵ 14,000). 4-Bromo-4-methyl-2,6-di-*t*-butylcyclohexa-2,5-dien-1-one (II, R = CH_3) was prepared by the procedure of Volod'kin and Ershov,[16] mp 91.5–92°, λ_{max} 250 mμ (ϵ 14,000). 4-Bromo-4-*t*-butyl-2,6-di-*t*-butylcyclohexa-2,5-dien-1-one (II, R = $C(CH_3)_3$) was prepared by adding Br_2 to a suspension of 2,4,6-tri-*t*-butylphenol in aqueous acetic acid,[17] mp 80.5–81.5°, λ_{max} 250 mμ (ϵ 13,120). 4,4-Dibromo-2,6-di-*t*-butylcyclohexa-2,5-dien-1-one (II, R = Br) was obtained by brominating 2,6-di-*t*-butyl-4-bromophenol in ethyl ether and in the presence of pyridine,[18] mp 127–128°, λ_{max} 250 mμ (ϵ 13,500).

Kinetic Procedure. The kinetic measurements were carried out as described by de la Mare, *et al.*,[7] by the use of a spectrophotometer Unicam SP800. A typical kinetic experiment is reported in Table II. The rate constants were calculated from the slope of the initial linear portion of plots of $1/(OD_\infty - OD_t)$ *vs.* time; the precision was 10% or better.

In the case of 2,6-di-*t*-butyl-4-bromophenol the optical density at 250 mμ remained unchanged throughout the experiments (see Table I) and the analysis of bromine by iodometric titration showed that no halogen was used up. In order to see whether the observed unreactivity of this phenol was actually due to the establishment of a fast equilibrium shifted toward the reactants, the expected reaction product (compound II, R = Br) as synthesized by an independent route was made to react with HBr in 98% aqueous acetic acid. The reaction rate was determined by the decrease in optical density at 250 mμ and found to be *ca.* 0.2 l. mole^{-1} sec^{-1} (25°). Thus, the rate of the reverse reaction is so slow that it cannot be responsible for the observed lack of reaction of the phenol.

Table II. Kinetic Data for the Bromination of 2,6-Di-*t*-butyl-4-methylphenol in Anhydrous Acetic Acid at 25° [a]

Time, sec	OD,[b] 252 mμ	Time, sec	OD,[b] 252 mμ
50	0.280	110	0.340
60	0.290	125	0.360
70	0.300	140	0.375
80	0.310	165	0.400
90	0.320	180	0.415
100	0.330	200	0.440

[a] The concentration was 2.512 × 10^{-4} *M* in both reactants. [b] Determined with a spectrophotometer Unicam SP800. For the present experiment a k_2 value of 1.43 l. mole^{-1} sec^{-1} was obtained, the OD_∞ value being 3.517.

The optical density of 2,6-di-*t*-butyl-4-bromophenol was also found to be constant at 340 mμ, which indicates that an attack of Br_2 *ortho* to the hydroxyl group is unlikely and no 2,4-cyclohexadienone is formed.

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(12) See ref 10, p 43.

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