Polymerisation and Related Reactions involving Nucleophilic Aromatic Substitution. Part 2.[1] The Rates of Reaction of Substituted 4-Halogenobenzophenones with the Salts of Substituted Hydroquinones

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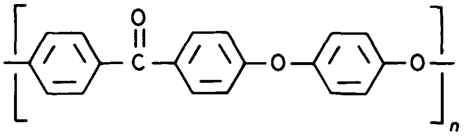
4-X-4′-Fluorobenzophenones undergo the expected nucleophilic substitution reactions with the alkali-metal salts of 4-Y-4′-hydroxydiphenyl ethers at 140 °C in diphenyl sulphone as solvent: the Hammett ρ value is 1.02 for the X substituents and -0.34 for the Y substituents. The order of reactivity of the alkali metal salts is Cs > K > Na. The related reaction of fluorobenzophenone with potassium 4-Z-phenolates under the same conditions gives a ρ value of -2.28. This result has been used to calculate the corresponding rate coefficients for the reaction of the mono- and di-potassium salts of hydroquinone with fluorobenzophenone.

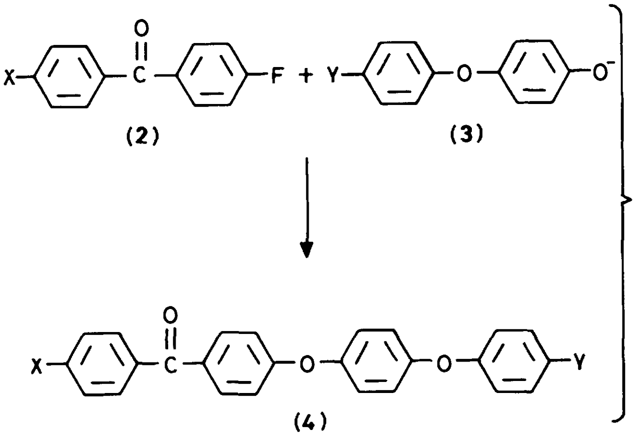
The work described here extends the study of substitution in the halogen derivatives of benzophenone to the use of salts of substituted hydroquinones as nucleophiles. In basic media, 4,4′-dihalogenobenzophenones and hydroquinone react together to form a polymer[2] with the repeating unit shown in structure (**1**); this polymer is made by I.C.I. with the trade name Victrex PEEK. As before,[1] the purpose of the present work was to obtain information on the rate coefficients for the stages of the polymerisation by the use of linear free energy relationships.



(1)

The plan of the work follows that described for the salts of hydroxybenzophenones in Part 1 and diphenyl sulphone was again used as the solvent but the much increased reactivity of the salts of the hydroquinone derivatives led to a number of changes and complications. Reactions with oxygen and with impurities in the diphenyl sulphone are more important and we have had to consider more carefully the possibility of reaction through radical intermediates. Because of the increased reactivity, the reactions have been studied at lower temperatures (usually 140 °C).

Stability of the Reactants.—Much of the work has been done with the fluoro compounds (**2**) and the potassium phenolates (**3**) shown in equation (1). As shown previously, the fluoro compounds (**2**) are perfectly stable under the reaction conditions but, with some samples of diphenyl sulphone, there was evidence of a small decrease in the concentration of the phenolate before the fluoro compound was added. The reason for this was never fully established but it could derive from the presence of a very small concentration (*ca.* 10^{-4} mol kg^{-1}) of a highly reactive impurity. Purification of the solvent did not prove an effective way of eliminating this initial reaction and so allowance was made for it in the kinetic analysis (see below).



(1)

Kinetics and Mechanism.—A solution of an alkali-metal salt of a derivative of hydroquinone was prepared under nitrogen in diphenyl sulphone as solvent using the apparatus described previously.[1] After the solution had been stirred for *ca.* 20 min, a weighed amount of the required fluoro compound was added and samples were then extracted at appropriate times. The progress of the reaction was followed from the changes in the u.v. spectra of solutions of these samples in a 1:1 mixture of methanol and dimethyl sulphoxide acidified with acetic acid. Under these conditions, the absorption of product (**4**) is much greater than that of the starting material. For the reaction in equation (1) with X = H, Y = Me, the final absorbance was in close agreement with that expected from the spectrum of a pure sample of product (**4**).

Because of the initial reaction of some of the phenolate with the solvent, and because of some uncertainty over the purity of some of the phenolates, the kinetic runs for each pair of reactants were carried out at least twice; once with insufficient of the fluoro compound and once with excess of this reagent, the initial concentration of phenolate ions being held effectively constant. This enabled the initial concentration of phenolate ions to be determined from the relative changes in absorbance in the two runs (see Experimental section). When the initial concentrations of phenolate ions are calculated in this way, good second-order kinetics are observed (first-order with

Table 1. Evidence on the kinetic order of the reaction in equation (1; X = H; Y = H). Temperature 140 °C

10^2 [ArOK] / mol kg^{-1}	10^2 [ArF] / mol kg^{-1}	$10^2 k_2$ / kg mol^{-1} s^{-1}
0.877	2.00	37.3
0.887	0.476	35.4
0.676	0.498	40.5
2.01	0.495	21.4

Table 2. The effect of the metal ion on the second-order rate coefficient (k_2) for the reaction in equation (1; X = H, Y = H). Temperature 140 °C

Metal ion (M)	10^2 [ArOM] / mol kg^{-1}	$10^2 k_2$ / kg mol^{-1} s^{-1}
Na^+	0.91	5.5
K^+	0.882	36.4
Cs^+	0.766	76.4

Table 3. The variation of the second-order rate coefficient (k_2) with temperature for the reaction of the phenolate (3; Y = OPh) with (a) 4-fluorobenzophenone and (b) 4-chlorobenzophenone. For (a), [ArOK] 0.0086 mol kg^{-1}; for (b), [ArOK] 0.0064 ± 0.003 mol kg^{-1}

Reaction	T/°C	$10^2 k_2$ / kg mol^{-1} s^{-1}
(a)	140	27.5
(a)	155	62.5
(a)	170	105.1
(a)	200	355*
(b)	140	0.27*
(b)	185	5.7
(b)	200	13.5
(b)	215	31.7

* Calculated from the Arrhenius plots.

Table 4. Activation parameters for the reactions listed in Table 3

Reaction	E / kJ mol^{-1}	log A	$\Delta H^‡$ / kJ mol^{-1}	$\Delta S^‡$ / J mol^{-1} K^{-1}
(a)	68.2	8.08	65.7	−98.7
(b)	106.3	10.87	103.8	−45.1

Table 5. The variation of the second-order rate coefficient (k_2) with the structure of the reactants in equation (1). Temperature 140 °C

X	Y	10^2 [ArOK] / mol kg^{-1}	$10^2 k_2$ / kg mol^{-1} s^{-1}
Cl	H	0.517	71.6
H	H	0.882	37.3
PhO	H	0.873	34.3
MeO	H	0.887	18.8
H	Me	0.870	44.8
H	Cl	0.807	30.3
H	PhCO	0.862	27.5

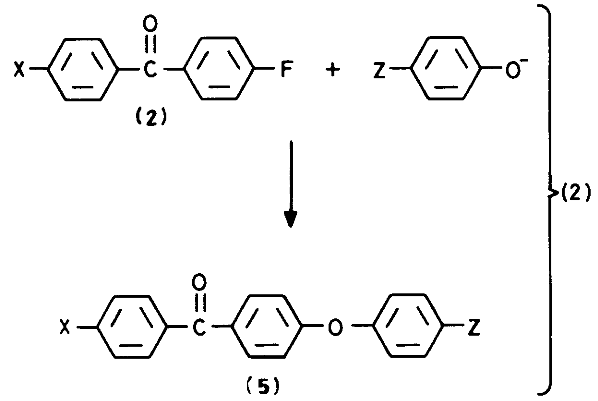
respect to each reagent) throughout a given run for all runs using the potassium phenolates. The results will be discussed in terms of these second-order rate coefficients (k_2).

The results for the reaction of 4-fluorobenzophenone with the phenolate ion (3; Y = Me) are given in Table 1. The first two results confirm that the order with respect to the fluoro compound is unity. The last three results show that the order with respect to the phenolate ions appears to be less than unity. The form of the variation of k_2 with the concentration of phenolate ions accords with that reported in Part 1 and attributed there to ion association. Studies on the variation of the second-order rate coefficient with the cation present (Table 2) support this interpretation, for the caesium salt is more reactive than the sodium salt by a factor of 13.9. The kinetic runs carried out with the sodium salt showed considerable distortion from second-order kinetics, and approximated more closely to a first-order kinetic form, presumably because changes in the extent of ion association during a kinetic run are then more important. The relative reactivity of the caesium and sodium salts must therefore be dependent on the concentrations used.

Table 6. The variation of the second-order rate coefficient (k_2) with the structure of the reactants in equation (2; X = H). Temperature 140 °C

Z	10^2 [ArOK] / mol kg^{-1}	$10^2 k_2$ / kg mol^{-1} s^{-1}
MeO	0.741	126.0
PhO	0.882	36.4
Cl	0.868	14.5
PhCO	0.800	(0.25)*

* Calculated from the results in Part 1.



The temperature dependence of the second-order rate coefficients for the reactions of 4-fluoro- and 4-chloro-benzophenone with the potassium phenolate (3; R = OPh) is shown in Tables 3 and 4. From an extrapolation of these results, the relative reactivity of the fluoro to the chloro compound is a factor of 101 at 140 °C, decreasing to 26 at 200 °C. The latter value is similar to that observed (31.4) for the reaction of the potassium salt of 4-phenoxy-4′-hydroxybenzophenone with these substrates at 200 °C. The replacement of the ArCO group by the ArO group in the nucleophile does not appear therefore to have produced any significant change in the reaction mechanism.

The dependence of the second-order rate coefficient on the structure of the reactants is shown in Table 5. In linear free energy plots using σ_p values, the variation of the substituent in the fluoro compound gives a ρ value of 1.02 (r 0.989) and the variation of the substituent in the phenolate gives a ρ value of −0.34 (r 0.978). Before plotting, a correction was applied to the result for X = Cl to give k_2 62.3 kg mol^{-1} s^{-1}; this allows for the lower phenolate ion concentration in this run.

The reactions in equation (1) provide models for the later stages of the polymerisation of hydroquinone with 4,4′-difluorobenzoquinone in alkaline media. However, the initial stages of these reactions must involve the much more reactive salts of hydroquinone itself and we originally intended to include these reactions in the kinetic analysis. Solutions of hydroquinone in methanol were therefore treated, under nitrogen, with the appropriate amounts of potassium hydroxide for the formation of the mono- and di-potassium salts; removal of the solvent then gave these salts as off-white solids. Unfortunately, these salts proved to be insufficiently soluble in diphenyl sulphone for kinetic studies to be attempted. We therefore turned to an estimate of the reactivity of these species by linear free energy relations using the compounds shown in equation (2). The results are given in Table 6 and the plot of $\log k_2$ against the σ_p^- values for the substituent gives a ρ value of -2.28 (r 0.993). The σ_p^- values are used here since the substituent and the reaction centre are in the same ring[3] but the difference between the σ_p and σ_p^- values arises only with the PhCO substituent.

Possible Radical Reactions.—The dianion ($C_6H_4O_2^{2-}$) in these salts of hydroquinone is known to be a strong electron donor, for alkaline solutions of hydroquinone and nitrobenzene give e.s.r. signals for both the semiquinone radical anion ($C_6H_4O_2^{\bullet -}$) and the radical anion of nitrobenzene.[4] Experiments were therefore carried out to see if electron transfer could be detected between the dianion of hydroquinone and the benzophenone derivatives used in the present work. The e.s.r. signal of the semiquinone radical anion could be easily detected in alkaline solutions of hydroquinone in diglyme or in a mixture of dimethyl sulphoxide and t-butyl alcohol (1:4) even when it was thought that oxygen had been excluded in the preparation of the solutions; however, no additional e.s.r. signals were seen when 4-fluorobenzophenone was present in the latter solution.

This result could arise because of the further reaction of the ketyl radicals produced by electron transfer to 4-fluorobenzophenone and so an attempt was made to detect the products of any radical reaction between hydroquinone and 4-chlorobenzophenone in basic media. The chloro compound was used because it would be more susceptible to substitution by the $S_{RN}1$ mechanism.[5] The reaction of hydroquinone with 4-chlorobenzophenone in the presence of potassium metal in dimethyl sulphoxide under nitrogen at room temperature did give a small yield (3%) of the expected product (**5**; X = H, Z = OH) after 24 h, but this is probably not more than could arise from direct nucleophilic substitution. Small yields of a number of other products were detected.[6]

Discussion

The kinetic form, substituent effects, and medium effects for the reactions in equation (1) are so similar to those described in Part 1 that no separate discussion is needed: these reactions are clearly direct nucleophilic substitutions with the attack of the nucleophile as the rate-determining step. In these reactions, the change from 4-hydroxybenzophenones to 4-hydroxydiphenyl ethers has increased the reactivity of the corresponding anions by a factor of *ca.* 100 (at 140 °C).

On the conventional assumption that the substituent effects in the substrate and nucleophile are additive,[1] the linear free energy plots for the variation of the substituents X and Y in equation (1) can be summarised by equation (3). In the same way, the kinetic studies on the reaction in equation (2) give rise to equation (4). Because of the effects of ion association, these equations are valid only for potassium phenolates and for initial concentrations of phenolate ions of *ca.* 10^{-2} mol kg^{-1}.

$$\log k_{X.Y} = 1.02\,\sigma_X - 0.34\,\sigma_Y - 0.428 \qquad (3)$$

$$\log k_{X.Z} = 1.02\,\sigma_X - 2.28\,\sigma_Z^- - 0.528 \qquad (4)$$

Equation (4) can be used to provide details of the reaction of hydroquinone with 4-fluorobenzophenone. The above work provides no evidence for a radical component in these substitution reactions, and the fluoro compounds would not be expected to react by an $S_{RN}1$ mechanism[5] so direct nucleophilic substitution will be assumed in the following discussion. The rate coefficient for the reaction of the monoanion ($C_6H_5O_2^-$) with 4-fluorobenzophenone can be estimated as 2.18 kg mol^{-1} s^{-1} by substitution of the appropriate σ_p value (-0.38)[7] in equation (4). Following the discussion in Part 1, a value of σ_p -1.2 has been taken for the O^- substituent in this medium. The corresponding value of k_2 for the dianion ($C_6H_4O_2^{2-}$) as calculated from equation (4) is then 1.6×10^2 kg mol^{-1} s^{-1} but, for the reaction with 4-flurobenzophenone, the value has to be multiplied by 2 to give 3.2×10^2 kg mol^{-1} s^{-1} because the dianion of hydroquinone has two equivalent reaction sites. It is clear from this result that, even if the dipotassium salt of hydroquinone had been sufficiently soluble, the direct study of the substitution could not have been carried out under the same conditions as for the other nucleophiles for, with reactant concentrations of *ca.* 10^{-2} mol kg^{-1}, the half-life would have been < 1 s.

Experimental

Materials.—4-Hydroxydiphenyl ether (**3**; Y = H) and 4-hydroxy-4′-methyldiphenyl ether (**3**; Y = Me) were prepared by the Ullmann ether synthesis[8] followed by demethylation.

A mixture of *p*-cresol (86.5 g, 0.8 mol) and sodium methoxide (42.4 g, 0.78 mol) in anhydrous pyridine (800 cm^3) was heated with stirring under nitrogen for 1 h. The methanol was then distilled off and *p*-bromoanisole (146.6 g, 0.78 mol) and copper(I) chloride (12 g, 0.12 mol) were added. After the mixture had been stirred under reflux for 13 h, pyridine was distilled off and the remainder, after cooling, was added to cold water and the mixture acidified with hydrochloric acid. The 4-methoxy-4′-methyldiphenyl ether formed was isolated by extraction with chloroform followed by distillation. This ether (27.8 g, 0.13 mol) was then demethylated[9] by heating with pyridinium chloride (89.7 g, 0.78 mol) under nitrogen for 5 h at 215 °C. The reaction mixture was then poured into hydrochloric acid (750 cm^3, 2.8%) and the 4-hydroxy-4′-methyldiphenyl ether formed was isolated by filtration. The product (23.4 g), after recrystallisation from aqueous methanol, had m.p. 72.7 °C (lit.,[10] 72—73 °C).

The reaction of phenol to form 4-hydroxydiphenyl ether was similar except that the demethylation was carried out by heating the 4-methoxydiphenyl ether (120 g) with aluminium chloride (78 g) to 130 °C for 1 h and then, after the addition of more aluminium chloride (15 g), to 150 °C for a further hour. The product, after recrystallisation from aqueous methanol, had m.p. 82.8—83.8 °C (lit.,[11] 83—85 °C), yield 31.2 g.

Several of the other compounds were prepared by the nucleophilic displacement of fluorine from fluorobenzophenones. For the preparation of 4-fluoro-4′-phenoxybenzophenone (**2**; X = PhO), a mixture of 4,4′-difluorobenzophenone (218.2 g, 1 mol) and potassium carbonate (70.4 g, 0.51 mol) in dimethylformamide (750 cm^3) was heated to 140 °C and a solution of phenol (47 g, 0.5 mol) in dimethylformamide was added dropwise over 4 h. After a further hour at 140 °C, the reaction mixture was poured into cold water and 4-fluoro-4′-phenoxybenzophenone was collected by filtration. After distillation under reduced pressure and recrystallisation from aqueous methanol, the product (92.6 g) had m.p. 98.7—100.5 °C (lit.,[12] 101.5—102 °C) (Found: C, 77.9; H, 4.5. Calc. for $C_{19}H_{13}FO_2$: C, 78.1; H, 4.5%).

4-Benzoyl-4′-hydroxydiphenyl ether (**2**; Y = PhCO) was prepared by the same method starting with 4-methoxyphenol

Table 7. The variation of the absorbance (A) at 300 nm with time for two kinetic runs on the reaction in equation (1; X = H, Y = H). Temperature 140 °C

[ArF] 2.0×10^{-2} mol kg^{-1}	[ArOK][a] 0.877×10^{-2} mol kg^{-1}	
Time (s)	A	$10^2 x$/mol kg^{-1}
0	0.063[b]	0
23	0.112	0.119
55	0.18	0.283
120	0.264	0.487
180	0.31	0.598
240	0.334	0.656
3 000	0.425	0.877
	k_2 37.3×10^{-2} kg mol^{-1} s^{-1}	
[ArF] 0.476×10^{-2} mol kg^{-1}	[ArOK][a] 0.887×10^{-2} mol kg^{-1}	
0	0.066[b]	0
20	0.074	0.019
60	0.091	0.061
120	0.118	0.126
180	0.13	0.155
240	0.148	0.199
300	0.168	0.247
360	0.177	0.269
540	0.202	0.33
720	0.223	0.381
6 600	0.262	0.476
	k_2 35.4×10^{-2} kg mol^{-1} s^{-1}	

[a] After correction for initial reaction (see text). [b] Obtained by extrapolation.

(62.1 g, 0.5 mol) and 4-fluorobenzophenone (100 g, 0.5 mol). 4-Benzoyl-4′-methoxydiphenyl ether obtained (24.3 g) was demethylated with pyridinium chloride (60 g) using the method described above. The product (19 g), after recrystallisation from aqueous methanol, had m.p. 108—109 °C (lit.,[13] 109 °C).

4-(4-Methylphenoxy)-4′-benzoyldiphenyl ether (**4**; X = H, Y = Me) was prepared by the same method using 4-hydroxy-4′-methyldiphenyl ether (4 g, 0.2 mol) and 4-fluorobenzophenone (4 g, 0.2 mol). After recrystallisation from aqueous methanol, the *product* (4.0 g) had m.p. 125 °C (Found: C, 82.0; H, 5.5. $C_{26}H_{20}O_3$ requires C, 82.1; H, 5.3%).

4-Chloro-4′-hydroxydiphenyl ether was provided by I.C.I. and the other reactants were either commercial products, recrystallised before use, or were prepared as described in Part 1. The alkali-metal phenolates were also prepared as described[1] but, although the analysis of the 'standard' phenolate (**3**; Y = H) was satisfactory, the analyses of a number of the others were 1—2% low for carbon. For all but one of the phenolates, the analyses by automatic titration showed purities of 95—99%; the exception (**3**; Y = Cl) was 87.7% pure.

Kinetics.—The kinetic runs were carried out as described in Part 1 except that the infinity readings were taken without raising the temperature, exactly 1 g of the extracted samples was used in the analysis, and the u.v. spectra of the extracted samples were measured in acidic solution.

After extraction, the sample (1 g) was dissolved in dimethyl sulphoxide (25 cm^3), a solution of acetic acid in methanol (0.5 cm^3, 0.1 mol dm^{-3}) was added, and the volume was brought to 50 cm^3 by the addition of methanol. This solution was then diluted by a further factor of 5 or 10 with methanol (depending on the reactants used). The extent of reaction was then determined from the change in the absorption at 300 nm using a similar solution prepared from the solvent (1 g) in the reference cell.

Because of the complications introduced by the initial reaction of some of the phenolate ions with the solvent and the possible impurities in some of the phenolates, the rate coefficient for a given pair of reactants was determined from a pair of kinetic runs, one carried out with insufficient of the fluoro compound and one with excess of the fluoro compound, the concentration of phenolate ions being very similar in both. In the run with excess of phenolate ions, the final absorbance was taken to derive from a concentration of product equal to the initial concentration of the fluoro compound. In the run with excess of fluoro compound, the true initial concentration of phenolate ions was determined from the absorbance change during reaction. This concentration was normally *ca.* 90% of that calculated from the weight of phenolate added to the reaction mixture and the same 'correction factor' was then used to calculate the initial concentration of phenolate ions in both runs. For the phenolate (**3**; Y = Me), this procedure was checked by determining the extinction coefficient of the pure product (**4**; X = H, Y = Me) at 300 nm (1.3095×10^4 dm^3 mol^{-1} cm^{-1}) and using this to compare the calculated absorption at the end of reaction for the fifth run in Table 5 (0.456) with that observed (0.455).

The details of the first two runs in Table 1 are illustrated in Table 7. In this Table, the values of x are calculated from the initial and final values of the absorbance (A) using equation (5)

$$x = (A_t - A_0)c/(A - A_0) \qquad (5)$$

where c is the lower of the two initial concentrations.

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