703. *The* ortho : para-*Ratio in Aromatic Substitution. Part II.*[1] *Chlorination with t-Butyl Hypochlorite.*

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Reports that t-butyl hypochlorite gives rise to very high *ortho* : *para*-ratios in chlorination of monosubstituted benzenes have been shown to be erroneous. It has been found that in acid solutions the attacking entity is the highly reactive chlorinium ion (Cl^+), whereas in non-acidic conditions it is molecular chlorine, to which t-butyl hypochlorite slowly decomposes. A number of reactions reported in the literature have been interpreted in the light of these findings. The reaction of molecular chlorine with phenol in solution has been found to give *o*-chlorophenol in 74% yield; reaction of t-butyl hypochlorite with the phenoxide ion, when the attacking species is almost certainly hypochlorous acid, forms *o*- and *p*-chlorophenol in a ratio of 4 : 1. Possible explanations for these phenomena are advanced.

IN order to elucidate further the factors which govern the *ortho* : *para*-ratio in aromatic substitution,[1] we have investigated the reactions of t-butyl hypochlorite with a number of monosubstituted benzenes. We chose the reactions of this compound because of reports that it gives rise to unusually high *ortho* : *para*-ratios of chloro-derivatives with benzenoid compounds.[2-5] It was of interest to see whether the behaviour of t-butyl hypochlorite was related to that of acetyl nitrate, which also gives high yields of *ortho*-substituted derivatives in reactions with monosubstituted benzenes.[1]

The nature of the species responsible for chlorination in many of the reactions of t-butyl hypochlorite with organic compounds is known. Chlorination of methylene groups in allylic systems,[6] and of methyl groups in toluene and substituted toluenes,[7] by t-butyl hypochlorite has been shown to involve attack by chlorine atoms. Olefins react with the reagent in aqueous solution in the presence or absence of acid to form chlorohydrins,[8,9] and in alcoholic solution to form chlorohydrin ethers,[9] and these reactions are analogous to the two-stage ionic addition of molecular chlorine in such solvents.[10] In its reactions with benzenoid compounds, however, t-butyl hypochlorite resembles neither atomic nor molecular chlorine. Toluene, which is substituted in the side-chain by chlorine atoms, and which forms *o*- and *p*-chlorotoluenes in a ratio of about 3 : 2 with molecular chlorine,[11] is reported to form 93% of *o*-chlorotoluene with t-butyl hypochlorite in acid solution.[4] Chlorobenzene is likewise reported[4] to form *o*- and *p*-dichlorobenzene in a ratio of 4 : 1, whereas it does not react with molecular chlorine except in the presence of a halogen carrier. Anisole[4] and phenol[3] are reported to give *o*-chloro-derivatives in 87% and 94% yield, respectively, with t-butyl hypochlorite, as compared with 21%[12] and 50%[13] for chlorination by molecular chlorine.

From these reports, it appeared that t-butyl hypochlorite may chlorinate aromatic compounds by a different mechanism from that of "normal" chlorinations. Free-radical reactions with aromatic compounds customarily give high *ortho* : *para*-ratios,[14]

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[1] Part I, Norman and Radda, *J.*, 1961, 3030.
[2] Anbar and Ginsburg, *Chem. Rev.*, 1954, **54**, 925.
[3] Clark, *Chem. News*, 1931, **143**, 265.
[4] Anbar, Ph.D. Thesis, Hebrew University, Jerusalem, 1953; quoted in ref. 2.
[5] Ginsberg, *J. Amer. Chem. Soc.*, 1951, **73**, 2723.
[6] Walling, Jacknow, and Thaler, Abstracts, 136th A.C.S. Meeting, Atlantic City, N.J., 1959.
[7] Jacknow, *Diss. Abs.*, 1960, **21**, 55.
[8] Hanby and Rydon, *J.*, 1946, 114.
[9] Irwin and Hennion, *J. Amer. Chem. Soc.*, 1941, **63**, 858.
[10] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons, London, 1953.
[11] Brown and Stock, *J. Amer. Chem. Soc.*, 1957, **79**, 5175.
[12] Jones and Richardson, *J.*, 1956, 3939.
[13] Holleman and Rinkes, *Rec. Trav. chim.*, 1909, **28**, 408.
[14] Williams, "Homolytic Aromatic Substitution," Pergamon Press, London, 1960.

but although it has been suggested that chlorination with t-butyl hypochlorite involves radical intermediates [15] (a theory which is discussed in greater detail below), it is doubtful whether direct replacement of hydrogen atoms attached to aromatic nuclei by halogen atoms takes place except under extremely vigorous conditions.[16]

We have redetermined the products obtained in the chlorination by t-butyl hypochlorite of anisole, toluene, chlorobenzene, and phenol, studying these reactions in different solvents and in the presence and absence of acid. We have also investigated the chlorination of the phenoxide ion with t-butyl hypochlorite, and the chlorination of all these aromatic compounds with molecular chlorine and with the chlorinium (Cl^+) ion. The reactions were carried out at 25°, and gas chromatography was used to determine the ratios of chloro-isomers, control experiments with synthetic mixtures showing that the analytical method was accurate to $\pm 2\%$. To minimise disubstitution, the extent of chlorination was always small.

Anisole.—Results for the chlorinations are set out in Table 1. Contrary to the report [4] that anisole forms 87% of the *o*-chloro-derivative when treated with t-butyl hypochlorite in acetic acid and sulphuric acid, we found that the *p*-chloro-derivative predominates. The values for the *ortho* : *para*-ratios obtained with this reagent fall into two groups, dependent on the presence or absence of acid. Further, chlorination occurs to a considerable extent in acid solution in a few minutes, whereas chlorination in the absence of acid is extremely slow.

TABLE 1. *Chlorination of anisole.*

Conditions		Orientation (%) * *o*-	*p*-
t-Butyl hypochlorite in:	carbon tetrachloride	23·0	77·0
	dioxan	20·0	80·0
	acetonitrile	20·5	79·5
	t-butanol	20·1	79·9
	acetic acid	33·5	66·5
	acetic acid–sulphuric acid	35·5	64·5
Chlorine in CCl_4		20·5	79·5
Chlorinium ion in H_2O		34·9	65·1

* No *m*-chloroanisole was obtained.

TABLE 2. *Chlorination of chlorobenzene.*

Conditions	*o*-	Orientation *m*- *	*p*-
t-Butyl hypochlorite in acetic acid	44·9	1·1	54·0
t-Butyl hypochlorite in acetic acid–sulphuric acid	44·1	1·4	54·5
Chlorinium ion in carbon tetrachloride–water	39·7	1·6	58·7

* See Experimental.

The reactions carried out in the absence of acid give the same *ortho* : *para*-ratios as those obtained with molecular chlorine, our value for which is recorded in Table 1 and which agrees with the value reported previously.[12] In these conditions, t-butyl hypochlorite therefore has the same selectivity as molecular chlorine. Thus, either the reagents responsible for chlorination are the same, or they are different but by chance have the same selectivity.[17] The second alternative is an unlikely coincidence, for molecular chlorine, which is a far more powerful chlorinating agent than hypochlorous acid,[18] should similarly be a more powerful, and therefore less selective, reagent than t-butyl hypochlorite, since the reactivity of a carrier (Cl–X) of electrophilic chlorine decreases as the electron-withdrawing power of X decreases.[19] t-Butyl hypochlorite

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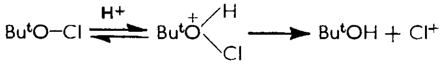
[15] Pausacker and Scroggie, *Austral. J. Chem.*, 1959, **12**, 430, 748.
[16] Ref. 14, p. 120.
[17] Brown and Smoot, *J. Amer. Chem. Soc.*, 1956, **78**, 6255; Nelson, *J. Org. Chem.*, 1956, **21**, 145.
[18] Soper and Smith, *J.*, 1926, 1582.
[19] de la Mare and Ridd, "Aromatic Substitution," Butterworths Scientific Publications, London, 1959, p. 128.

decomposes if kept at room temperature, its infrared spectrum developing a band at 3350 cm.$^{-1}$ characteristic of the hydroxyl group; and, whereas the hypochlorite, when freshly distilled, gives no precipitate with aqueous silver nitrate, it does so after a day at room temperature. These facts are consistent with the slow decomposition of the hypochlorite to chlorine, and we conclude that it is this which is the chlorinating species in non-acidic conditions.

The species involved in chlorination by t-butyl hypochlorite in acid solution is almost certainly the chlorinium ion. The evidence for this is strong: (i) the *ortho* : *para*-ratio is the same as that obtained when chlorinium ion is the reagent; (ii) the smaller selectivity is indicative of a more reactive chlorinating agent; (iii) the kinetics of the reaction of t-butyl hypochlorite with mineral acid are consistent with the formation of chlorinium ion:[20]



$$\mathrm{Bu^tO{-}Cl} \underset{}{\overset{H^+}{\rightleftharpoons}} \mathrm{Bu^t\overset{+}{O}(H)Cl} \longrightarrow \mathrm{Bu^tOH} + \mathrm{Cl^+}$$

(iv) chlorination in acid solution occurs rapidly, as is consistent with the expected rapid production of the Cl^+ ion by the above mechanism.

Toluene.—We found that toluene reacts only to a small extent with t-butyl hypochlorite on its own, forming benzyl chloride. In the presence of 2,2′-azoisobutyronitrile, larger quantities of benzyl chloride are formed in a similar time. These observations are diagnostic of atomic chlorination, and, together with the evidence above that molecular chlorine is formed slowly by the decomposition of t-butyl hypochlorite in neutral solution, are consistent with this decomposition's occurring *via* chlorine atoms. With toluene, chlorine atoms bring about side-chain chlorination, and with anisole dimerisation of chlorine atoms to molecular chlorine is followed by electrophilic chlorination of this very reactive nucleus. In the presence of acid, toluene and t-butyl hypochorite form no benzyl chloride but give a mixture of chlorotoluenes which could not be resolved by gas chromatography.

Chlorobenzene.—Chlorobenzene does not react with t-butyl hypochlorite in the absence of acid, or with molecular chlorine. In acid solution a mixture of the three dichlorobenzenes was obtained in very nearly the same proportions as were produced by the chlorinium ion (Table 2). We were unable to confirm the report[4] that chlorobenzene forms the *o*-dichloro-compound in 80% yield in these conditions. The small difference between chlorination by the chlorinium ion and by hypochlorite may arise from the difference in the solvents used, for the solvent can have a marked effect on the *ortho* : *para*-ratios in aromatic substitutions.[21] To see if atomic chlorination by the hypochlorite might be responsible for the difference, chlorobenzene and the hypochlorite were treated with 2,2′-azoisobutyronitrile in the absence of acid, but no chlorination occurred. It seems likely, therefore, that the difference is not significant and that it is again the chlorinium ion which is responsible for chlorination in acid conditions.

TABLE 3. *Chlorination of phenol.*

Conditions	Orientation (%) *	
	o-	*p*-
t-Butyl hypochlorite in carbon tetrachloride	51·0	49·0
t-Butyl hypochlorite with sulphuric acid	50·8	49·2
Cl_2 in carbon tetrachloride	74·0	26·0
Cl_2 with molten phenol	39·5	60·5
Chlorinium ion in water	51·4	48·6

* No *m*-chlorophenol was obtained.

Phenol.—The orientations of monochlorophenols obtained by chlorinating phenol under various conditions are set out in Table 3. Our results for the chlorination of phenol with t-butyl hypochlorite disagree with those reported previously,[3] but resemble closely

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[20] Anbar and Dostrovsky, *J.*, 1954, 1094.

[21] Stock and Himoe, *Tetrahedron Letters*, 1960, **13**, 9.

those obtained with the chlorinium ion. The *ortho* : *para*-ratio is the same whether t-butyl hypochlorite is used with or without mineral acid. We conclude that phenol is itself acidic enough to generate the chlorinium ion with t-butyl hypochlorite, and that this, rather than the more slowly generated and less reactive molecular chlorine, is the attacking species.

We found that molecular chlorine reacts with phenol in carbon tetrachloride solution to give a surprisingly high *ortho* : *para*-ratio in the monochlorophenols. It has recently been reported [22] that molten phenol and chlorine form *o*- and *p*-chloro-derivatives in a ratio of 1 : 1·7. We confirmed this large difference in the *ortho* : *para*-ratios under these two conditions, and suggest the following explanation for it: in carbon tetrachloride solution the phenolic hydrogen forms a hydrogen bond with the chlorine molecule, resulting in polarisation of this molecule, its positively-polarised end being suitably placed for reaction at the *ortho*-position [see (I)]. Reaction then takes place by the electron shifts depicted in (II). In molten phenol, the phenolic hydrogen forms a hydrogen bond with the oxygen atom of an adjacent molecule and is not able to assist chlorination at the *ortho*-position.

The Phenoxide Ion.—t-Butyl hypochlorite and hypochlorous acid give very nearly the same ratio of *o*- and *p*-chloro-derivatives in their reactions with sodium phenoxide in alkaline solution (Table 4). Since it is known that t-butyl hypochlorite is hydrolysed by alkali to hypochlorous acid,[20] it is probably the latter which is the chlorinating species in each case.

The high *ortho* : *para*-ratio may be due to one of three causes: (i) The phenoxide ion is highly reactive to electrophiles at its *ortho*- and *para*-positions, and, according to the principle enunciated by Hammond,[23] the transition state in the rate-determinating step should resemble the ground state. The relative reactivities of the *ortho*- and *para*-positions should therefore depend on the relative electron densities at these positions in the ground state.[24] It is reasonable to suppose that the inductive effect of the negatively charged oxygen atom in the ion operates more powerfully on the *ortho*- than on the *para*-position, giving rise to the observed relative reactivities. (ii) Reaction in the *ortho*-position may be aided by hydrogen-bonding between the phenoxide ion and hypochlorous acid, as in the chlorination of phenol [see (III)]. This is consistent with the kinetic equation for the reaction of phenol with hypochlorous acid in alkaline solution: $v = k[PhO^-][HOCl]$.[18] (iii) The same effect could be brought about by co-ordination of the oxygen atom of hypochlorous acid to the cation of the metal phenoxide ion-pair [see (IV)]. The last mechanism is analogous to the explanations offered for the high *ortho* : *para*-ratios in reactions of the phenoxide ion with chloroform and alkali [25] and formaldehyde.[26]

TABLE 4. *Chlorination of the phenoxide ion.*

Conditions	Orientation (%) * *o*-	*p*-
t-Butyl hypochlorite in 4N-NaOH	78·9	21·1
Hypochlorous acid in water	80·7	19·3
t-Butyl hypochlorite in 15N-NaOH †	81·3	18·7
15N-KOH †	78·9	21·1
3·5N-$MeEt_3N\cdot OH$	63·0	37·0

* No *m*-chlorophenol was obtained. † These reactions were carried out at 50°, the remainder at 25°.

It is difficult to distinguish between these three mechanisms, although process (iii) is supported by the fact that triethylmethylammonium phenoxide, in which co-ordination

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[22] Bing, Kennard, and Matthews, *Austral. J. Chem.*, 1960, **13**, 317.

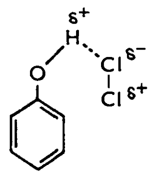
[23] Hammond, *J. Amer. Chem. Soc.*, 1955, **77**, 334.

[24] Knowles, Norman, and Radda, *J.*, 1960, 4885.

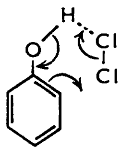
[25] Brady and Jakobovits, *J.*, 1950, 767.

[26] Peer, *Rec. Trav. chim.*, 1959, **78**, 851; 1960, **79**, 825.

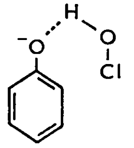
of oxygen to the cation cannot occur, gives a lower *ortho* : *para*-ratio on chlorination with hypochlorous acid. Moreover, whereas process (iii), involving electron-removal from hypochlorous acid, should give rise to a chlorinating species of enhanced electrophilic power, process (ii) should involve polarisation of the hypochlorous acid so that the chlorine atom becomes less electrophilic.



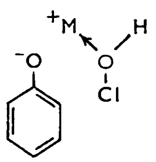
(I)



(II)



(III)



(IV)

From the results described above it is evident that t-butyl hypochlorite, contrary to previous reports, does not give rise to unusually high *ortho* : *para*-ratios in its reactions with anisole, phenol, and chlorobenzene. Its reactions are satisfactorily interpreted by supposing that, in the absence of acids, it decomposes slowly to molecular chlorine, and in the presence of acids it rapidly generates chlorinium ions. The ease of preparation of t-butyl hypochlorite,[27] and its ability to give chlorinating species of different selectivity, and the fact that it can be stored without noticeable decomposition at —40°, suggest its usefulness as a synthetic reagent.

The decomposition of t-butyl hypochlorite to molecular chlorine almost certainly involves the formation of atomic chlorine. This decomposition has been investigated at high temperatures, where the products are consistent with an initial cleavage of the molecule to t-butoxy-radicals and chlorine atoms.[28] At the temperature of our reactions, a slow cleavage of the weak O–Cl bond is likely and is supported by the following observations: (*a*) The infrared spectrum of t-butyl hypochlorite slowly develops an absorption band at 3350 cm.$^{-1}$ characteristic of an alcohol and at the same frequency as the hydroxyl band in t-butyl alcohol, which could be due to t-butyl alcohol formed from the t-butoxy-radical. (*b*) The side-chain chlorination of toluene by the hypochlorite is catalysed by 2,2′-azoisobutyronitrile, which also catalyses other chlorinations involving chlorine atoms. (*c*) In the absence of acid, *o*- and *p*-methoxybenzaldehyde are oxidised by t-butyl hypochlorite to the corresponding acids.[29] This may take place by initial abstraction of aldehydic hydrogen by a radical formed by decomposition of the hypochlorite, corresponding to the well-established mechanism of autoxidation of aromatic aldehydes.

Other published observations of the behaviour of t-butyl hypochlorite may be interpreted in the light of our results. Thus benzene is chlorinated by the reagent in acetic acid solution but not in the absence of acid,[30] just as it is chlorinated by chlorinium ion but not by molecular chlorine. Acetanilide is chlorinated in the presence or absence of acid,[31] since it is reactive enough to be attacked by molecular chlorine. Finally, the observation that the nuclear chlorination of nitroanilines with t-butyl hypochlorite shows the characteristics of a free-radical reaction [15] is now understood, since the formation of the electrophilic chlorinating agent, molecular chlorine, itself depends on the generation of chlorine atoms from the hypochlorite.

EXPERIMENTAL

Materials.—t-Butyl hypochlorite [27] was stored at —40° and distilled (b. p. 78°) immediately before use. Toluene and phenol were " AnalaR " reagents, and anisole and chlorobenzene were purified by distillation.

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[27] Teeter and Bell, *Org. Synth.*, Vol. 32, p. 20.

[28] Yoffe, *Chem. and Ind.*, 1954, 963.

[29] Ginsburg, *J. Amer. Chem. Soc.*, 1951, **73**, 702.

[30] Clark, Ph.D. Thesis, Massachusetts Institute of Technology, 1931; quoted in ref. 3.

[31] Israelstam, *J. S. African Chem. Inst.*, 1956, **9**, 30.

m-Chloroanisole was prepared by methylation of *m*-chlorophenol with dimethyl sulphate. Gas chromatography indicated the presence of the *para*-isomer in *o*-dichlorobenzene, and this could not be removed by fractional distillation. Pure *o*-dichlorobenzene was obtained by the Sandmeyer reaction on *o*-chloraniline. The remaining chloro-derivatives of anisole, chlorobenzene, and toluene were commercial reagents. Their purities were checked by gas chromatography.

Chlorinations.—(a) *t-Butyl hypochlorite.* The procedure used is illustrated by the chlorination of anisole. Anisole (1·1 ml.) in a solvent (S) (3 ml.) was treated with t-butyl hypochlorite (1 ml.) in S (2 ml.). When the solvent was carbon tetrachloride, dioxan, acetonitrile, or t-butyl alcohol, the solution was kept for 2 days before being analysed. When it was acetic acid or acetic acid (3 ml.) containing 2N-sulphuric acid (1 ml.), the solution was neutralized after 15 min., extracted with ether, and analysed.

Chlorobenzene and toluene were treated similarly, and an additional experiment was carried out on each compound in carbon tetrachloride solution to which 2,2′-azoisobutyronitrile (1 mole %) was added.

Phenol was chlorinated similarly in carbon tetrachloride solution. In addition, phenol (0·75 g.) in 3 ml. of alkali (see Table 4) was treated with t-butyl hypochloride (0·5 ml.). The reactions were very vigorous, and after 10 min. the mixtures were neutralised with sulphuric acid and organic material was extracted into ether.

(b) *Chlorine.* Anisole (0·5 ml.) in carbon tetrachloride (4 ml.) was treated with carbon tetrachloride (2 ml.) saturated with chlorine. (This solution contained enough chlorine to react with approximately one-third of the anisole.[32]) After 30 min. the solution was washed with water to remove hydrogen chloride and then analysed. A similar procedure was used to chlorinate phenol in solution in carbon tetrachloride.

Phenol was also chlorinated by passing chlorine (30 ml./min.) into molten phenol (10 g.) at 60° for 15 min.

(c) *The chlorinium ion.* (i) [32] Chlorobenzene (1·1 ml.) was treated with silver perchlorate (1·5 g.), concentrated perchloric acid (10 ml.), and water (1·5 ml.). To the suspension was added carbon tetrachloride (4 ml.) saturated with chlorine. After 1 hr. silver chloride was removed by filtration, and the organic material was extracted into ether.

This method was unsuitable for anisole because, after removal of silver chloride, further chlorination occurred, presumably by molecular chlorine remaining in the carbon tetrachloride solution.

(ii) [33] Anisole (0·5 ml.) was added to a solution of hypochlorous acid [18] (50 ml.) containing silver perchlorate (2 g.) and perchloric acid (1·5 ml.). After 30 min. the solution was filtered and extracted with ether, and the ethereal solution treated immediately with sodium metabisulphite to prevent further chlorination. Phenol was treated similarly.

(d) *Hypochlorous acid.* Phenol (1 g.) and sodium hydroxide pellets (2 g.) were dissolved in water (10 ml.), and hypochlorous acid (75 ml.), prepared by the method of Soper and Smith [18] and purified by being shaken with mercuric oxide, was added. The solution was filtered from mercuric oxide, neutralised with dilute sulphuric acid, and extracted with ether.

TABLE 5. *Retention times of chloro-derivatives.*

	Retention times			
Compounds	*o*-Chloro (min.)	*m*-Chloro (min.)	*p*-Chloro (min.)	Column temp.
Chloroanisoles [a]	48	34	39	130°
Dichlorobenzenes	51	35	40	100
Chlorinated toluenes [b]				150

[a] 2,4-Dichloroanisole had retention time 60 min. [b] The three chlorotoluenes were not resolved, but had a retention time (4 min.) which was different from those of benzyl chloride (10 min.) and benzylidene chloride (26 min.).

Gas-chromatographic Analysis.—The column (203 cm. × 4·5 mm.) was packed with tritolyl phosphate (20% w/w) coated on Embacel and was operated at temperatures between 100° and 150° (see Table 5). Hydrogen (40 ml./min.) was used as the carrier gas, and detection was

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[32] Gorvin, *Chem. and Ind.*, 1951, 910.

[33] de la Mare, Ketley, and Vernon, *J.*, 1954, 1290.

by the flame-ionisation method. The detector was coupled to a Sunvic recorder which gave a linear response. Proportions of isomers in each reaction mixture were obtained from the Gaussian curves by the method reported previously,[24] injection of synthetic mixtures of isomeric chloro-compounds showing that areas were proportional to quantities.

Mixtures of chlorophenols could not be analysed directly. Instead, they were treated with diazomethane (prepared from Diazald) and the resulting mixtures of chloroanisoles were analysed. The methylation procedure was shown to be quantitative by analysing synthetic mixtures of chlorophenols in the same way.

TABLE 6. *Chlorination of anisole in acetic acid–sulphuric acid.*

			Orientation (%)	
Experiment	Analysis		*o*-Chloro	*p*-Chloro
1	1		35·6	64·4
	2		35·4	64·6
2	1		36·0	64·0
	2		35·2	64·8
		Mean	35·5	64·5

No peak with retention time corresponding to 2,4-dichloroanisole occurred in the chromatograms from any of the mixtures obtained by chlorinating anisole or phenol. This confirmed that there was no preferential loss of the *o*- or *p*-chloro-derivative by further chlorination.

Each analytical result in Tables 1—4 is the mean of two analyses of each of two products. Analytical accuracy is greater for mixtures of dichlorobenzenes, where complete resolution of the *ortho*- and *para*-isomers occurred, than for chloroanisoles, where the peaks formed by the isomers overlapped slightly. The figure recorded for the proportion of *m*-dichlorobenzene in each reaction can only be taken as indicative of an upper limit of 2% for the proportion of this isomer. Typical experimental results are shown in Table 6.

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