Tetrahedron. Vol. 26, pp 973 to 1000. Pergamon Press 1970. Printed in Great Britain

AROMATIC REARRANGEMENTS IN THE BENZENE SERIES[1]—I

THE FRIES REARRANGEMENT OF PHENYL BENZOATE: THE BENZOYLATION OF PHENOL

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(*Received in the UK* 3 *January* 1969; *Accepted for publication* 25 *September* 1969)

Abstract The rearrangement of phenyl benzoate by anhydrous aluminium bromide in homogeneous solution in chlorobenzene, and the benzoylation of phenol by benzoyl bromide under the same conditions, have been investigated. Mechanisms for the reactions are suggested and discussed, and the relationship between the rearrangement and acylation reactions, under selected conditions, is established. Under the above selected conditions, the rearrangement of phenyl benzoate by one molar proportion of catalyst is shown to proceed simultaneously by two mechanisms. The first of these processes leads exclusively to *ortho*-migration, and is probably intramolecular, proceeding via a π-complex. The second mechanism by which rearrangement occurs is also that of the corresponding acylation reaction, is described as "pseudo-intramolecular", leads to ortho- and para-migration, and probably proceeds via an ion-pair-type intermediate.

This work is described in the wider context of a theory of the mechanism of the rearrangement of suitably constituted aromatic compounds. Published work on the mechanism of the Fries rearrangement is also discussed.

IT HAS been suggested[2a,b] that suitably constituted aromatic compounds might undergo rearrangement via a mechanism similar to that proposed to explain the course of the benzidine rearrangement.[3] Aromatic molecules structurally comparable with hydrazobenzene should be capable of undergoing rearrangement under the influence of Lewis acid catalysts through a "sandwich-type" π-complex intermediate, as proposed in the case of hydrazobenzene itself (Fig. 1).

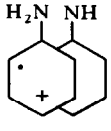

FIG. 1

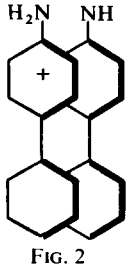

FIG. 2

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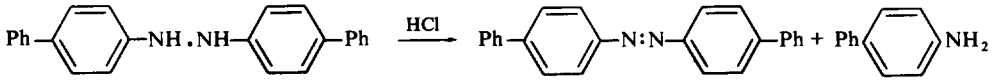
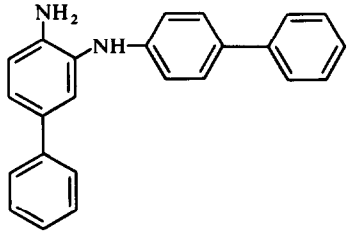
Addition of the second proton[4] causes the π-complex to "unfold" to give the products of the rearrangement.[5] It was further suggested[2a,b] that the presence of bulky substituents in the two *para*-positions of the suitably constituted aromatic compounds mentioned above might prevent such intramolecular rearrangements by interfering sterically with the formation of the postulated "sandwich-type" π-complexes (Fig. 2). There will also be repulsion between the π-electron clouds of the phenyl groups in the 4- and 4'-positions.[6]

Support for this view may be found in the report[7] that 4-hydrazobiphenyl did not undergo the benzidine rearrangement when heated with concentrated hydrochloric acid, but instead underwent disproportionation to 4-azobiphenyl and 4-aminobiphenyl:

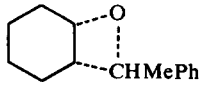


Repetition[8,9] of this reaction showed that the original findings were correct. However, a very recent re-investigation[10] of the rearrangements of 4,4'-disubstituted hydrazobenzenes showed that in the presence of hydrogen chloride in aqueous ethanol, 4-hydrazobiphenyl rearranged to a limited extent, although the major reaction was still disproportionation. The extent of rearrangement decreased with increasing temperature, being 25% at 0°, (with 75% disproportionation), and 12% at 25°, (with 88% disproportionation). The rearrangement product was believed to be the orthosemidine:

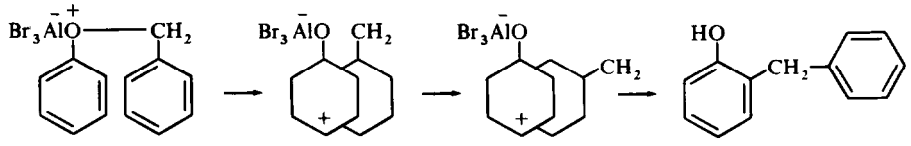


The rearrangement of benzyl phenyl ether by anhydrous aluminium bromide in homogeneous solution in chlorobenzene, occurring very rapidly to give principally *o*-benzylphenol, is most probably intramolecular.[11] Similarly,[12] *dl*-α-phenylethyl phenyl ether gave 85% *ortho*-, and 15% *para*- rearrangement products under these conditions, and (−)α-phenylethyl *p*-tolyl ether rearranged to the *ortho*- (α-phenylethyl)-*p*-cresol, with ca. 76% retention of optical purity, the stereochemical results being in accord with the proposed intramolecularity of the reaction.

The extreme ease of the rearrangements (that of benzyl phenyl ether being complete in 5 seconds at −40°) rules out a simple π-complex mechanism, or any mechanism involving a strained transition state, such as:



as similar intermediates could be formed equally well by other alkyl groups. The above benzyl ether rearrangements proceed much more readily than those of simple alkyl phenyl ethers, and the intramolecular rearrangement must be very easy to outweigh any possible intermolecular mechanism involving the very stable benzyl carbonium ion. Thus, here, too, the "sandwich" π-complex is a possible intermediate:



There is a possibility,[2a,b] therefore, that a similar mechanism may operate in the rearrangements of other molecules having two aromatic rings linked by a pair of atoms, i.e. in the rearrangements of compounds such as (I):

Ph—X—Y—Ph (I) where $X = CH_2$, $Y = S$;
$X = CH_2$, $Y = NH$;
$X = CO$, $Y = S$;
$X = CO$, $Y = O$; etc.

Recently, Miller[13] has proposed that the completely intramolecular rearrangement of *p*-quinamines has a mechanism very closely resembling that proposed[3] for the benzidine rearrangement, viz. involving a "sandwich" π-complex intermediate.

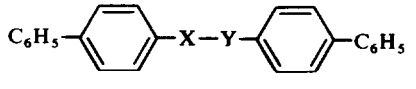
A test[14] of the above theory of the mechanism of such rearrangements involves a comparison of the *ortho/para* ratio for the rearrangement process with the *ortho/para* ratio for the reverse process, i.e. an acylation or alkylation reaction, depending on the natures of X and Y above. Thus in the case of phenyl benzoate, (I, X = CO, Y = O), the two reactions are:

1. Rearrangement: PhCOOPh $\xrightarrow{AlBr_3}$ HO—C$_6$H$_4$—COPh $\quad \frac{ortho/para}{\text{ratio} = r.}$

2. Acylation: PhOH + PhCOBr $\xrightarrow{AlBr_3}$ HO—C$_6$H$_4$—COPh $\quad \frac{ortho/para}{\text{ratio} = a.}$

A much higher value for *r* than for *a* may be regarded as an indication that an intramolecular path is important in the rearrangement process, as compared with the acylation process, (or alkylation in other reactions).

A second test of the above theory involves the attempted rearrangements of compounds of type I above substituted in both *para*-positions by phenyl groups, i.e. compounds of the type II:



(II) X and Y are the same as in (I) above.

to see whether the bulky *para*-substituents prevent, or interfere with, the rearrangement reaction.

Intramolecular rearrangements of the type described above should be most favoured in homogeneous solutions in non-polar solvents—e.g. with anhydrous aluminium bromide in chlorobenzene.

This paper describes the investigation of the rearrangement of phenyl benzoate, and the reverse (acylation) process, under such conditions. Part II[15] of this series describes the investigation of the rearrangement of the corresponding 4,4'-diphenyl-substituted ester, i.e. II, (X = CO, Y = O).

Mechanism of the Fries rearrangement—previous work

Four main reviews[16–19] have appeared. Early work on the mechanism is well covered by Blatt[16] and Prajer;[18] Gerecs[19] has considered some more recent work. Blatt[17] has also dealt with practical aspects of the reaction. We shall indicate here only very briefly the present state of opinion about the mechanism of this important reaction.

Controversy about the inter- or intra- molecularity of the reaction has continued since the 1920's, the problem being exacerbated by the wide variety of reaction conditions used by the many workers in this field.

Recent workers have supported each of the three main mechanisms proposed prior to 1940,[16, 18] or combinations of them. Thus Ralston *et al.*[20] supported the intermolecular mechanism of Skraup and Poller[21] and Cox;[22] Schönberg and Mustafa,[23] Hauser and Man,[24] and Bisanz[25] supported the bimolecular mechanism of Rosenmund and Schnurr;[26] and Klamann[27] has given a rather more modern interpretation of this mechanism. Dewar[28] and Ogata and Tabuchi[29] have supported the proposal of von Auwers[30a,b] that the rearrangement was truly intramolecular.

Gershzon[31] originally suggested that the Fries rearrangement was a combination of intramolecular and intermolecular processes leading respectively to *ortho*- and *para*- migration. This viewpoint was also taken by Illari,[32] Baddar *et al.*,[33] and Baltzly *et al.*[34] (Klamann's mechanism[27] is also a combination of intra- and intermolecular reactions). Cullinane *et al.*[35] interpreted the rearrangement as proceeding intramolecularly through a catalyst-ester complex, which could also give an ion-pair, the two halves of which then reacted with one another. Furka and Szell[36a,b] agreed with some of Cullinane's findings, but also suggested that hydrogen chloride, formed during the rearrangement, participated in the latter.

Amin and Shah[37] first suggested that the proton played an important part in the Fries rearrangement, and Gerecs *et al.*[19, 38] later investigated this possibility. They stated that proton catalysis played an essential part in the Fries rearrangement, the *ortho*- and *para*- rearrangements being affected to different degrees by altering the proton concentration, from which one can infer a difference in their mechanisms. Gerecs proposed[19] that in the case of lower proton concentrations, an *ortho*-directed intramolecular rearrangement of a catalyst-ester complex (e.g. $PhOC(R)=\overset{+}{O}—\bar{A}lCl_3$) occurred. The formation of a protonated catalyst-ester complex, $Ar\overset{+}{O}HC(R)=\overset{+}{O}—\bar{A}lCl_3$, could favour an intermolecular reaction leading to *para*-migration, (see later).

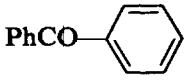
A detailed survey of all the above work is given in Ref. 1.

The Fries rearrangement of phenyl benzoate, and the benzoylation of phenol: previous work

Several workers have investigated the rearrangement of phenyl benzoate and the benzoylation of phenol under diverse conditions. A brief outline of their work follows.

Phenyl benzoate, heated with anhydrous aluminium chloride in the absence of a solvent, at 140° and higher temperatures, rearranges exclusively[26, 38–40] or predominantly[35, 41] to 4-hydroxybenzophenone. (Some workers' observations are contradictory: compare Ref. 35 and Refs 26, 39). Titanium tetrachloride[35] and anhydrous ferric chloride[42] in the absence of a solvent, also gave predominantly *para*-rearrangement.

Phenol and benzoyl chloride, heated with anhydrous aluminium chloride, gave phenyl benzoate and 4-hydroxybenzophenone.[43] In carbon disulphide, the ketoester



was also formed.[40] The ketoester was also obtained[44] when phenyl benzoate, (obtained by heating together phenol and benzoyl chloride), benzoyl chloride, and zinc chloride were heated together.

The ketoester was isolated from the aluminium chloride catalysed rearrangement of phenyl benzoate in ethylene chloride, and was converted to 4-hydroxybenzophenone when heated in the above solvent with phenol and aluminium chloride.[24]

Rearrangement of phenyl benzoate in homogeneous solution in nitrobenzene, using anhydrous aluminium chloride or titanium tetrachloride,[35] gave 2- and 4-hydroxybenzophenone, (*ortho/para* ratio ca. 0·1 with both catalysts). Benzoylation of phenol with benzoyl chloride under similar conditions gave similar results[45] (*ortho/para* ratio ca. 0·08 with both catalysts). Baltzly,[34] using less aluminium chloride for the rearrangement (in homogeneous solution in nitrobenzene), obtained *ortho/para* ratios of ca. 0·13 and 0·28, depending on the temperature and time of reaction.

Phosphorus pentoxide in nitrobenzene solution converted phenyl benzoate mainly to the ketoester (III).[23] Polyphosphoric acid as reaction medium and catalyst gave, depending on conditions, 4-hydroxybenzophenone in poor yield,[46] or this same phenol in higher yield, and the ketoester.[47] Condensation of phenol and benzoic acid in this medium gave a trace of phenyl benzoate, and appreciable quantities of 4-hydroxybenzophenone and the ketoester.[46] Traces of 2-hydroxybenzophenone have been formed in rearrangement and acylation reactions in polyphosphoric acid.[48a, b]

Less common catalysts have been used. A fused mixture of sodium and aluminium chlorides rapidly converted either phenyl benzoate or phenol and benzoic acid into the same mixture of 2- and 4-hydroxybenzophenones, (*ortho/para* ratio 0·31).[49] Hydrogen fluoride converted phenyl benzoate to 4-hydroxybenzophenone,[50] whilst boron trifluoride gave the same product from benzoic acid and phenol.[51] This latter reaction proceeded through the ester,[51] as earlier suggested.[52]

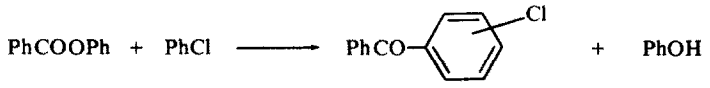
Very recently, photochemical rearrangements[53a, b, 54–56] of phenyl benzoate have been effected, to give 2- and 4-hydroxybenzophenone. The *ortho/para* ratio in these homolytic reactions is generally higher than in the heterolytic rearrangements, and the photochemical process is generally agreed to be intramolecular.

The above work is described in detail in Ref. 1.

The Fries rearrangement of phenyl benzoate and the benzoylation of phenol—present investigations

Synthetic and analytical work involved in the present investigation is described in the Experimental section of this paper, with the method used for carrying out the reactions. Detailed accounts of apparatus, syntheses, and analytical procedures are given in Ref. 1. The results of the present investigations, and their interpretations, will now be considered.

The rearrangement of phenyl benzoate by anhydrous aluminium bromide in homogeneous solution in chlorobenzene produced 2- and 4-hydroxybenzophenone, and, under suitable conditions, (see below), 2- and 4-chlorobenzophenone, as the principal products of interest. The formation of the chlorobenzophenones should be accompanied by the production of an equivalent (molar) amount of phenol:



and one might reasonably expect the formation of phenol and benzoic acid to occur.

Late in the investigation, 4-benzoylphenyl benzoate, PhCO—C$_6$H$_4$—OCOPh (hereafter referred to simply as "the ketoester") was also found, (see below). The above comments apply equally to the acylation of phenol by benzoyl bromide in the presence of anhydrous aluminium bromide in homogeneous solution in chlorobenzene: phenyl benzoate was also a product of the acylation process.

All the reactions investigated were performed at 110°. Two sets of rearrangement reactions were carried out, one using one mole of catalyst per mole of ester, and one using two moles of catalyst per mole of ester: the 1:1 and 2:1 rearrangement reactions respectively. Two sets of acylation reactions were carried out, one in which one mole each of benzoyl bromide, phenol, and catalyst were used, and one in which one mole each of benzoyl bromide and phenol, and two moles of catalyst, were used: the 1:1:1 and 2:1:1 acylation reactions respectively. The chlorobenzophenones were formed only in the 2:1 rearrangement and 2:1:1 acylation reactions, but not in the 1:1 rearrangement and 1:1:1 acylation reactions.

RESULTS

Before beginning the rearrangement and acylation reactions, it was first established that phenyl benzoate did not undergo a non-catalysed thermal rearrangement under the reaction conditions, by submitting a sample of the ester to the rearrangement procedure, omitting the catalyst, and analysing the product in the normal way. 98% of the phenyl benzoate was recovered unchanged, and no other products were found. (Skraup and Beng[57] claimed to have observed a thermal rearrangement with some esters, but their findings were not substantiated by von Auwers and Mauss[58]). Thus, under the reaction conditions used, we are considering a genuine catalysed rearrangement.

The possibility of the reversal of the rearrangement of phenyl benzoate, (i.e. the reversion of the hydroxybenzophenone rearrangement products to the ester), and the possibility of the interconversion of the reaction products, were also examined.

(The only known examples[59] of the reverse Fries transposition refer to suitably substituted hydroxyketones, not to the unsubstituted ones dealt with in this investigation). The principal reaction products (2- and 4- chloro- and 2- and 4- hydroxybenzophenone) were heated in homogeneous solution in chlorobenzene with anhydrous aluminium bromide under the usual reaction conditions, and then submitted to the usual analytical procedure (Experimental). The recoveries of the above four compounds were 100·4, 98·9, 97·9 and 99·7% respectively, and no other products were found. (An earlier spectrophotometric investigation had given similar results, showing also that phenol present in the reaction products was unchanged by the catalyst. It also showed that if a large excess of catalyst was used in the reaction, (e.g. a catalyst-ester molar ratio of 3 : 1), some destruction of 2-hydroxybenzophenone

TABLE 1. REARRANGEMENT REACTIONS ONE MOLE OF ESTER, ONE MOLE OF CATALYST
(the 1 : 1 rearrangement reaction)

PhOBz (mole-%)	82·5	77·0	61·6	45·5	36·8	28·2
2-OH (mole-%)	5·5	9·6	16·4	23·1	27·4	31·1
4-OH (mole-%)	3·0	6·1	13·1	20·8	26·5	30·7
2-OH/4-OH	1·83	1·57	1·25	1·11	1·03	1·01
2-OH + 4-OH (mole-%)	8·5	15·7	29·5	43·9	53·9	61·8
Reaction time (hr)	1	2	4	6¼	8	10
PhOBz decomposed (mole-%)	17·5	23·0	38·4	54·5	63·2	71·8

TABLE 2. ACYLATION REACTIONS ONE MOLE OF PHENOL, ONE MOLE OF BENZOYL BROMIDE, ONE MOLE OF CATALYST
(the 1 : 1 : 1 acylation reaction)

PhOBz (mole-%)	70·1	54·0	39·8	28·2	19·6
2-OH (mole-%)	9·6	16·6	21·6	25·7	28·9
4-OH (mole-%)	12·6	20·9	27·8	33·7	39·7
2-OH/4-OH	0·76	0·79	0·78	0·76	0·73
2-OH + 4-OH (mole-%)	22·2	37·5	49·4	59·4	68·6
Reaction time (hr)	2	4	6	8	10
PhOBz decomposed (mole-%)	29·9	46·0	60·2	71·8	80·4

TABLE 3. REARRANGEMENT REACTIONS ONE MOLE OF ESTER, TWO MOLES OF CATALYST
(the 2 : 1 rearranagement reaction)

PhOBz (mole-%)	14·9	9·0	3·8	2·8	1·8	0·9
2-Cl (mole-%)	1·7	1·9	2·0	2·0	2·0	2·0
4-Cl (mole-%)	17·4	20·7	22·2	22·6	23·7	22·2
2-OH (mole-%)	17·1	21·5	23·6	24·8	24·9	24·5
4-OH (mole-%)	24·9	31·7	39·3	42·4	43·7	43·6
2-Cl/4-Cl	0·098	0·092	0·090	0·088	0·084	0·090
2-OH/4-OH	0·69	0·68	0·60	0·59	0·57	0·56
2-Cl + 4-Cl (mole-%)	19·1	22·6	24·2	24·6	25·6	24·2
2-OH + 4-OH (mole-%)	42·0	53·2	62·9	67·2	68·6	68·1
Reaction time (hr)	¼	½	1	1½	2	2½

TABLE 4. ACYLATION REACTIONS ONE MOLE OF PHENOL, ONE MOLE OF BENZOYL BROMIDE, TWO MOLES OF CATALYST
(the 2:1:1 acylation reaction)

PhOBz (mole-%)	12·9	6·1	2·4	1·2	0·7	0·6
2-Cl (mole-%)	1·9	2·1	1·9	1·9	2·0	1·9
4-Cl (mole-%)	21·1	23·1	21·8	21·7	22·8	22·1
2-OH (mole-%)	13·1	16·3	18·9	19·9	20·6	20·7
4-OH (mole-%)	29·8	37·8	45·9	49·3	48·1	49·7
2-Cl/4-Cl	0·090	0·091	0·087	0·088	0·088	0·086
2-OH/4-OH	0·44	0·43	0·41	0·40	0·43	0·42
2-Cl + 4-Cl (mole-%)	23·0	25·2	23·7	23·6	24·8	24·0
2-OH + 4-OH (mole-%)	42·9	54·1	64·8	69·2	68·7	70·4
Reaction time (hr)	¼	½	1	1½	2	2½

occurred, but no isomerization). The above work also showed that the silylation process in the analytical method had no effect on those reaction products not capable of being silylated, and that the analytical process as a whole was satisfactory.

The results of the rearrangement and acylation reactions investigated are given in Tables 1–4. Yields are expressed as mole-percentages, based, for the rearrangement reactions, on the phenyl benzoate taken, and for the acylation reactions, on either the benzoyl bromide or phenol taken, as exactly equivalent molar quantities of the last two compounds were used. The results given in Tables 1–4 above are average values calculated from the results of several experiments (Experimental). Phenyl benzoate, phenol, 2- and 4-chloro-, and 2- and 4- hydroxy- benzophenone are all abbreviated respectively as follows:

PhOBz, PhOH, 2-Cl, 4-Cl, 2-OH, 4-OH.

(In Table 1, the "mole-% phenyl benzoate decomposed" is the difference between the mole-% phenyl benzoate left at the end of the reaction (i.e. the experimentally determined quantity) and 100 mole-%. In Table 2, the "mole-% phenyl benzoate decomposed" is again the difference between 100 mole-% and the experimentally determined amount of phenyl benzoate left at the end of the reaction. In this second case, therefore, there is an implicit assumption that the acylation reaction gives the hydroxybenzophenones entirely through a prior esterification process, followed by a rearrangement reaction. In an attempt to determine whether this was the only mode of formation of the hydroxybenzophenones, the 1:1:1 acylation reaction was

TABLE 5. ACYLATION REACTIONS ONE MOLE EACH OF PHENOL, BENZOYL BROMIDE, AND ALUMINIUM BROMIDE

PhOBz (mole-%)	91·3	92·8	90·7	90·5
2-OH (mole-%)	0·7	0·8	0·8	0·9
4-OH (mole-%)	3·1	3·4	3·7	3·6
2-OH/4-OH	0·23	0·24	0·22	0·25
Return (mole-%)	95·1	97·0	95·2	95·0
Reaction time (min)	2		2	

repeated using a very short reaction time (2 min). (Extrapolation back to zero time of graphs of the amounts of various products formed against time is not satisfactory, because the measurements are not infinitely accurate). The results shown in Table 5 were obtained. Thus, the 1:1:1 acylation reaction produces the hydroxybenzophenones almost entirely, (if not exclusively), through the ester).

The poor overall returns in some of the reactions, shown in Tables 3 and 4, i.e. those in which reaction times were $\frac{1}{4}$ hr and $\frac{1}{2}$ hr, were originally attributed to the conversion of appreciable amounts of the ester to phenol and benzoic acid. A check showed that the amounts of benzoic acid formed were too small to account for the low returns in the above cases. The only other reasonable possibility was that the ketoester (III) was also present in the reaction products. This was found to be so, the ketoester being positively identified (Experimental). It was not possible to carry out a rigorously quantitative determination of the amounts of ketoester present in the mixtures, (Experimental), but approximate values were obtained, and these show definite trends. In the 1:1 rearrangement and 1:1:1 acylation reactions, the amount of ketoester formed was always very small, and increased slightly to ca. 2 mole-% in the longer reactions. However, in the 2:1 rearrangement and 2:1:1 acylation reactions, the amount of ketoester formed in the shortest reactions (i.e. the $\frac{1}{4}$-hr reactions) was ca. 5–10 mole-%, but decreased to a mere trace in the longer reactions. (The amounts of ketoester given above are probably a little lower than the true ones). The significance of these observations is described later.

DISCUSSION AND INTERPRETATION OF THE RESULTS

The following points are significant:

1. The 1:1 rearrangement reaction differs from all the other three processes in that (i) it is the only reaction in which the *ortho/para* ratio for the hydroxybenzophenones is greater than 1; and (ii) this *ortho/para* ratio varies considerably with time (from ca. 1·8 to ca. 1·0 over the period studied), an approximately constant value of about 1 being finally attained.

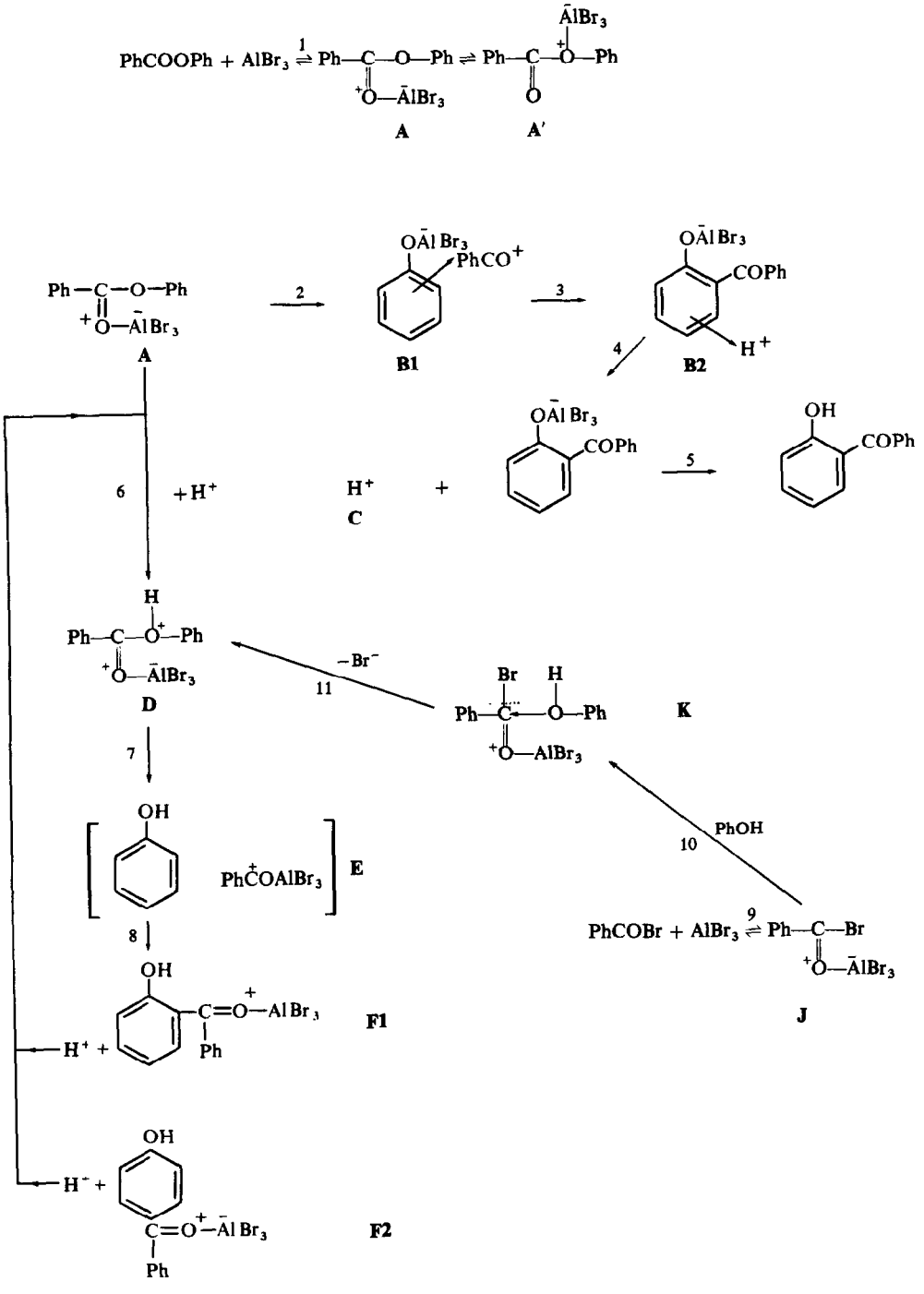
2. The *ortho/para* ratio in the 1:1:1 acylation process (which proceeds mainly, if not exclusively, through the ester), is constant, (other than at the very beginning of the reaction), and ca. 0·76. This constancy implies that the 2- and 4-hydroxyketones are being formed in reactions of the same order, (Wegscheider's test[60]).

3. In the 2:1 rearrangement reaction, the *ortho/para* ratio (for the hydroxybenzophenones) varies from ca. 0·69 to ca. 0·56, and this variation may be genuine; and not merely the result of experimental error. In the 2:1:1 acylation reaction, the *ortho/para* ratio (for the hydroxybenzophenones) is essentially constant (ca. 0·42), implying that the hydroxybenzophenones are formed in reactions of the same order.[60] In both these reactions, the *ortho/para* ratios for the hydroxyketones are less than 1, and the *ortho/para* ratios for the chlorobenzophenones are lower still, (ca. 0·09), and constant, indicating that in both processes the chloroketones are formed in reactions of the same order.[60] The absolute values of the amounts of the chlorobenzophenones (and hence the *ortho/para* ratios for these compounds) formed in these two reactions are similar.

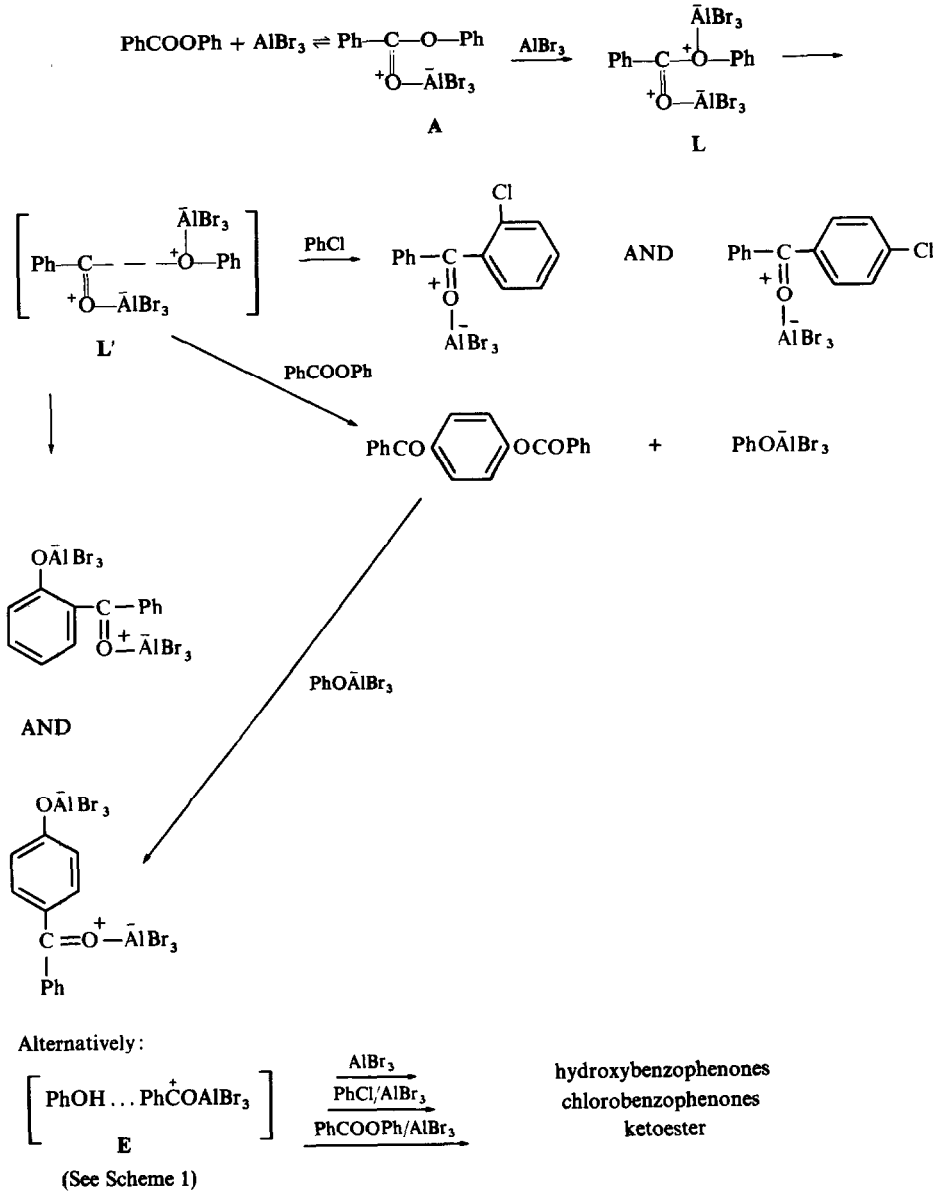
4. The total yield of hydroxybenzophenones obtained from the 1:1:1 acylation process is a little greater than that from the 1:1 rearrangement reaction, but there is

SCHEME 1

Proposed mechanisms of the 1:1 rearrangement and 1:1:1 acylation reactions



SCHEME 2
Proposed mechanisms of the 2:1 rearrangement reaction

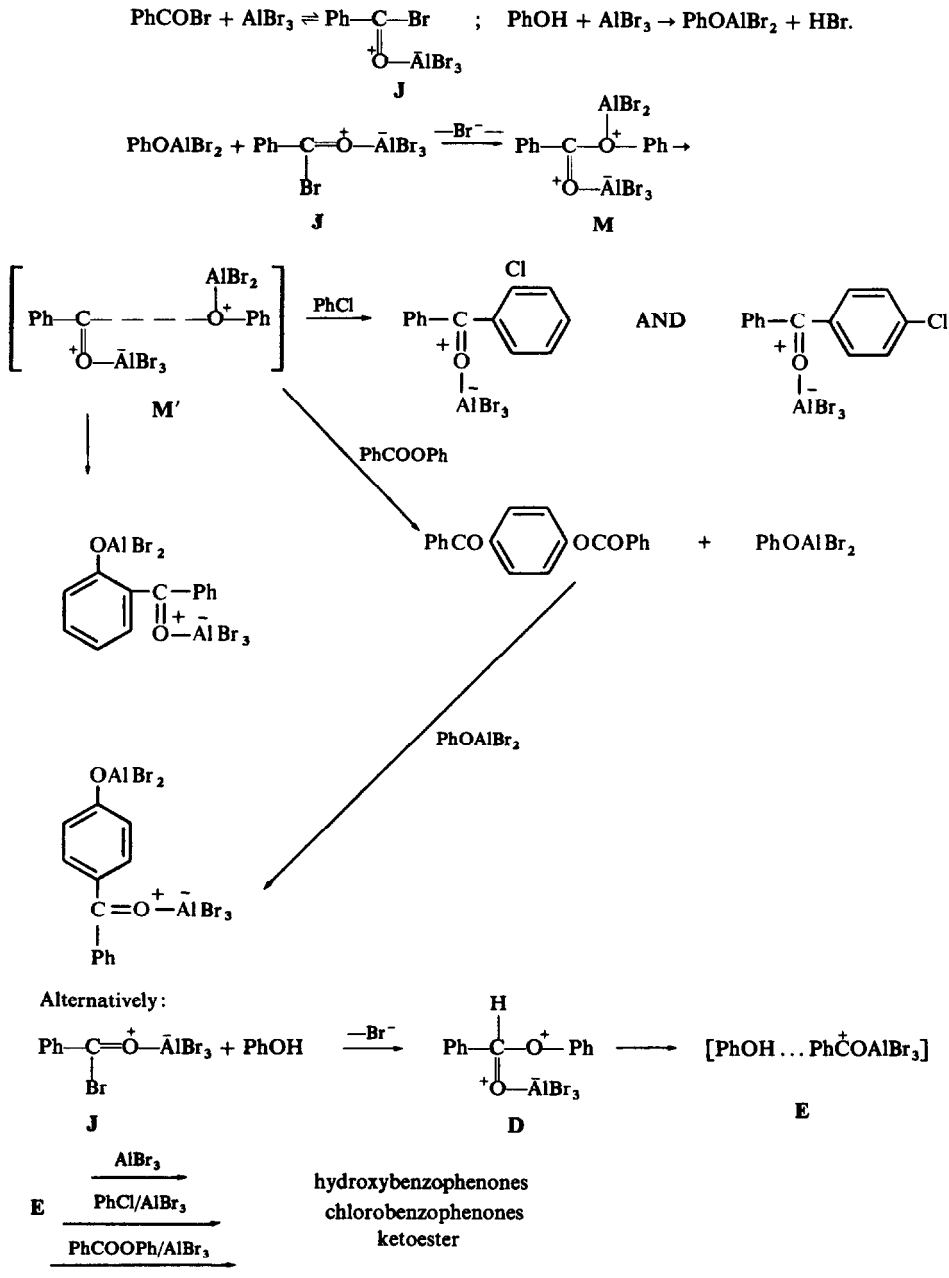


very little difference between the 2:1 rearrangement and 2:1:1 acylation reactions in this respect.

Thus, the 1:1 rearrangement reaction is the "odd" process of the four reactions examined, in that it is the only reaction in which *ortho*-migration predominates over *para*-migration, at least for part of the reaction, and it is also the only reaction for which the *ortho/para* ratio for the hydroxybenzophenones varies drastically with time.

In Schemes 1–3, the proposed mechanisms of the four reactions studied are depicted, individual parts of the Schemes being discussed below. Reactions involving one and two molar proportions respectively of catalyst are considered separately, as a detailed analysis of the 1:1 rearrangement and the 1:1:1 acylation reactions is possible.

SCHEME 3
Proposed mechanisms of the 2:1:1 acylation reaction



In the 1:1 rearrangement reaction (Scheme 1) the first step (reaction 1) is the rapid and reversible[61] formation of a catalyst-ester complex (**A**).[29, 34, 35, 36a, b, 61] (The complex (**A**) is shown with the catalyst attached to the carbonyl O atom,[61, 62] but may be represented as having the catalyst co-ordinated to the delocalized p-π-electron system, as a whole, if preferred).

This complex then undergoes an exclusively *ortho*-directed rearrangement, consistent with an intramolecular migration involving a π-complex intermediate, (i.e. via (**B1**) and (**B2**), reactions 2, 3 and 4: hydrolysis (reaction 5) at the end of the reaction giving 2-hydroxybenzophenone). The occurrence of this exclusively ortho-oriented rearrangement is justified below, on the basis of the experimental data obtained, and the process is referred to subsequently as the "first-stage" reaction.

As a result of this ortho-rearrangement, a proton is liberated in the substitution of the nucleus by the benzoyl group, (reaction 4), and this proton (**C**) allows an alternative, faster, rearrangement mechanism to operate.

The complex (**A**) accepts this proton at its second nucleophilic centre,[19] and the protonated complex (**D**) then undergoes rearrangement to 2- and 4- hydroxybenzophenone. This process is referred to subsequently as the "second-stage" reaction. The actual mechanism of this process is uncertain. The absence of attack on the solvent under these reaction conditions is not sufficient proof of the intramolecularity of this reaction,[63] and may be merely a consequence of the lower reactivity, i.e. insufficient nucleophilicity, (see the discussion of the 2:1 rearrangement reaction below), of the chlorobenzene molecule, compared with that of the phenol moiety in the intermediate **E**, towards the (cationoid) acylating moiety in **E**. The structure **E** merely represents an intermediate in which there is a (partial) separation of the protonated complex (**D**) into two fragments, which recombine to give 2- and 4-hydroxybenzophenone without any attack on the solvent). (The formation of small amounts of the ketoester (see earlier) in this reaction is most probably the result of the fact that reaction 1 (Scheme 1) is reversible, although the equilibrium lies well to the right. Acylation of the ester molecule is easier than acylation of the chlorobenzene molecule, the latter molecule being the less nucleophilic of the two. Acylation of the catalyst-ester complex (**A**) seems unlikely; (this view is also taken by Baltzly *et al.*[64]). The fact that the quantity of ketoester formed increases with increasing reaction time, whilst still remaining small, is probably an indication that the ketoester is not an intermediate in the 1:1 rearrangement reaction, but a side-product, in contrast to its role in the 2:1 rearrangement reaction—see below).

The *ortho/para* ratio for the second-stage reaction is shown below to be the same as that for the 1:1:1 acylation reaction, i.e. ca. 0·8. This is low for an intramolecular rearrangement proceeding through a π-complex intermediate, which would normally be expected to give predominantly, if not exclusively, *ortho*-migration.[65] (Ogata and Tabuchi,[29] who studied the rearrangement of phenyl acetate catalysed by anhydrous aluminium chloride in homogeneous solution in nitrobenzene, explained their results in terms of an intramolecular migration, to both *ortho*- and *para*- positions, involving a π-complex intermediate. Their *ortho/para* ratios for this reaction (ca. 0·4/60°; 0·64/80°) seem low for such a process. In this context, compare the intramolecular rearrangement of N-nitroamines,[66] the rearrangement of benzyl phenyl ether studied by Tarbell and Petropoulos,[11] and the rearrangements of alkyl aryl ethers studied by Dewar and Puttnam.[67] Compare also the percentages of *ortho*-

and *para*- products, formed in various (intermolecular) electrophilic substitution reactions undergone by phenol, listed in the Table on p. 259 of the Ref. 66—thus, for nitration, the *ortho/para* ratio is 0·67, and for chlorination, nearly as high as 1).

However, on the basis of the experimental data, we cannot say that the second-stage reaction is not intramolecular, and in a non-polar solvent such as chlorobenzene (dielectric constant 5·6/25°[68]) the intermediacy of free ions in this reaction is questionable. Thus the second-stage reaction is shown as proceeding through an ion pair-type intermediate (E). The detailed mechanism of the second stage reaction is not material to the following argument which justifies the duality of mechanism, described above, in the 1:1 rearrangement reaction, and the exclusive *ortho*-orientation of the first-stage reaction.

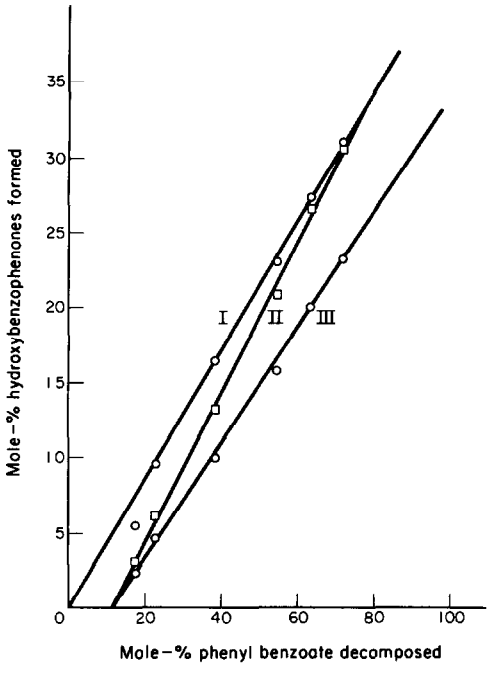


FIG. 3

If the mole-% of phenyl benzoate decomposed in the 1:1 rearrangement reaction is plotted as abscissa, and the mole-% of 2-hydroxybenzophenone and mole-% of 4-hydroxybenzophenone formed in the same reaction are separately plotted as ordinates, Fig. 3 is obtained. Curves I and II refer to 2- and 4- hydroxybenzophenone respectively. Curve I is a straight line passing through the origin; Curve II is a straight line making an appreciable intercept on the mole-%-ester decomposed axis. This means that the 4-hydroxybenzophenone is not being formed at the beginning of the reaction: that there is an initial phase of the reaction during which only 2-hydroxybenzophenone is being formed, and that the formation of 2-hydroxybenzophenone begins at the start of the reaction. It is shown below that the quantities of 2-hydroxybenzophenone formed at a given time as a result of the first-stage reaction can be

calculated, and hence the amounts of 2-hydroxybenzophenone formed as a result of the second-stage reaction can also be found. If these latter values are plotted on the above graph as ordinates, Curve III of Fig. 3 is obtained: a straight line intersecting the mole-%-ester decomposed axis at the same point as Curve II, the line for 4-hydroxybenzophenone. Thus, the earlier statements are justified. There is an initial reaction giving only 2-hydroxybenzophenone, followed by a (faster—see below) reaction giving both 2- and 4-hydroxybenzophenone.

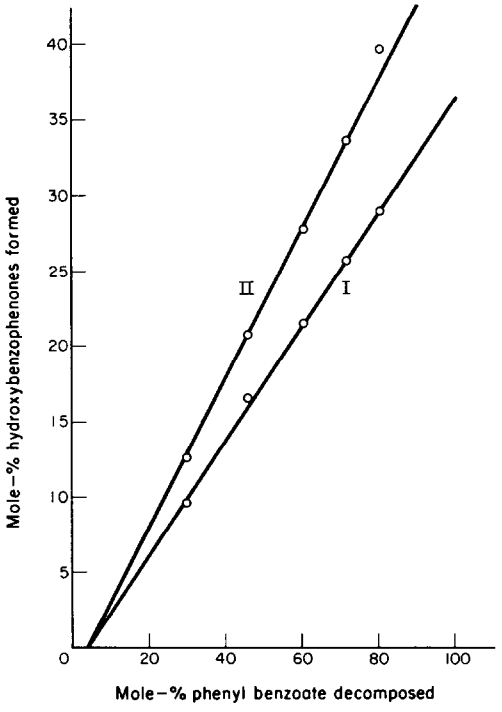


FIG. 4

(The first point on Curve I, i.e. total 2-hydroxybenzophenone formed, lies off the straight line, because at this time there is a predominant contribution from the first-stage reaction to the overall amount of 2-hydroxybenzophenone. For the other points, there is a predominant contribution from the second-stage reaction).

The values of mole-%-phenyl benzoate converted are obtained by difference, using only the experimentally determined values of mole-% phenyl benzoate found at the end of the reaction.

If a similar procedure is followed with the results of the 1:1:1 acylation reaction, Fig. 4 is obtained, Curves I and II referring to 2- and 4- hydroxybenzophenone respectively. The straight lines obtained both intersect the mole-%-ester decomposed axis together, very near the origin. Thus, both the 2- and 4- hydroxyketones are formed simultaneously in this reaction.

The observed decrease, with increasing time, of the *ortho/para* ratio in the 1:1 rearrangement reaction, is due to the fact that the second-stage reaction is faster than the first-stage reaction, because there is a better leaving group in the protonated catalyst-ester complex (**D**), i.e. $PhC\overset{+}{O}\bar{A}lBr_3 \ldots \overset{+}{O}HPh$, than in the catalyst-ester complex (**A**), i.e. $PhC\overset{+}{O}\bar{A}lBr_3 \ldots OPh$. The rate of the first-stage reaction will naturally decrease with increasing time as the catalyst-ester complex (**A**) undergoes rearrangement and is consumed, but superimposed on this decrease in reaction rate is a further decrease, due to the conversion of the complex (**A**) to the protonated complex (**D**), and the (faster) consumption of **D** by its conversion to 2- and 4- hydroxybenzophenone. This production of 2- and 4- hydroxybenzophenone also produces more protons, (Scheme 1, reaction 8), and so the second-stage reaction might be considered autocatalytic.

Thus, the form of the variation with time of the amount of 2-hydroxybenzophenone formed in the first-stage reaction will be similar to the curve in Fig. 5.

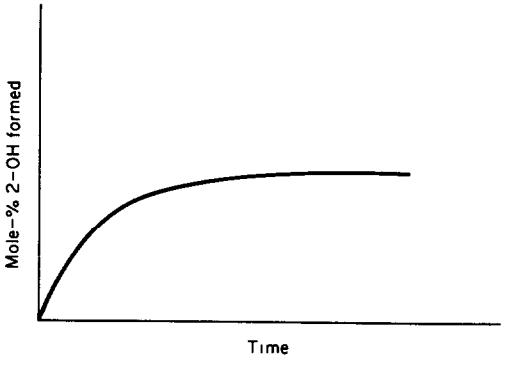


FIG. 5

The variation with time of the quantities of 2- and 4- hydroxybenzophenone formed in the second stage reaction will be similar to that in the 1:1:1 acylation reaction. The formation of the hydroxybenzophenones in the latter reaction proceeds mainly, if not exclusively, through the ester. The only difference between the reaction conditions for the 1:1 rearrangement and the 1:1:1 acylation reaction is the presence in the latter of hydrogen bromide, i.e. the presence of a proton, which is required for the second-stage process in the 1:1 rearrangement reaction.

A quantitative analysis of the 1:1 rearrangement reaction follows, in which the separate contributions of the first- and second- stage processes to the formation of hydroxybenzophenones can be calculated.

At time (t), let (x_1) be the amount of 2-hydroxybenzophenone formed in the first-stage reaction, and (x_2) and (y_2) the amounts of 2- and 4- hydroxybenzophenone respectively formed in the second-stage reaction. Let (r) be the measured *ortho/para* ratio for the overall rearrangement, i.e. the ratio of the experimentally determined amounts of 2- and 4- hydroxybenzophenone, and let (k_2) be the *ortho/para* ratio for the second-stage process only. By analogy with the 1:1:1 acylation reaction, (k_2) will be a constant.

Then:

$$\frac{x_1 + x_2}{y_2} = r$$

i.e.

$$\frac{x_1}{y_2} + k_2 = r \qquad (1)$$

The values of (y_2) and (r) are both measured. As a first approximation, it is assumed that (x_1) has reached a constant value after a reaction time of 8 hr, i.e. that the rate of the first-stage reaction has by this time fallen to zero.

The using the experimentally determined values in Table 1,

at 8 hr, $y_2 = 26{\cdot}5$ mole-%; $r = 1{\cdot}03$;
at 10 hr, $y_2 = 30{\cdot}7$ mole-%; $r = 1{\cdot}01$.

By substituting the above values into Eq. (1), the value obtained for (k_2) is **0·88**. The average of the experimental values for the *ortho/para* ratio in the 1:1:1 acylation reaction is 0·76, so that considering the approximation above, and the very small difference in the *ortho/para* ratios used in the above calculation, the agreement between the experimental and calculated results above is very good.

The contribution of the second-stage reaction to the overall formation of 2-hydroxybenzophenone can now be calculated, since (y_2) is known in each case, and using the (Experimental) value of 0·76 for (k_2), values of (x_2) are easily calculated, from $x_2 = k_2 y_2$. Values of (x_1) can then be obtained by subtracting values of (x_2) from the total measured amount of 2-hydroxybenzophenone. Table 6 gives the values of (x_1), (x_2), and (y_2) at different times. If values of (x_1) are plotted against time, a curve similar to that in Fig. 5 is obtained.

TABLE 6. CONTRIBUTION OF THE FIRST- AND SECOND-STAGE REACTIONS TO THE 1:1 REARRANGEMENT REACTION
(See also Table 1)

Time (hr)	1	2	4	6¼	8	10
4-OH (y_2)	3·0	6·1	13·1	20·8	26·5	30·7
2-OH (total)	5·5	9·6	16·4	23·1	27·4	31·1
2-OH (second stage-x_2)	2·3	4·6	10·0	15·8	20·1	23·3
2-OH (first-stage-x_1)	3·2	5·0	6·4	7·3	7·3	7·8

In the 1:1:1 acylation reaction, (Scheme 1), the first step is the reversible formation (reaction 9) of a benzoyl bromide-aluminium bromide complex, (**J**),[69,70] as the benzoyl halide and catalyst were always dispensed first. After addition of the phenol solution, esterification occurs. (The complexes formed from acyl halides and Lewis acid catalysts such as the anhydrous aluminium halides are effective esterification reagents[70]). Loss of bromide ion Br^- gives the protonated catalyst-ester complex (**D**) immediately, and the conversion of this to 2- and 4- hydroxybenzophenone occurs by the second-stage mechanism directly, there being no need (or opportunity) for the first-stage mechanism to operate, as the protonated complex is formed at the start. This is also indicated by Fig. 4.

In the 2:1 rearrangement reaction, (Scheme 2), the catalyst-ester complex (**A**) is again formed, but the second catalyst molecule now attaches itself to the second available nucleophilic centre in the phenyl benzoate molecule, the ether O atom, giving the complex **L**. This begins to break down, (**L'**), steric influences being more important in this case than in the case of the corresponding complex (**D**), where a proton is attached to the nucleophilic centre now linked to an aluminium bromide molecule. The potentially cationic part of **L'** is thus very susceptible to nucleophilic attack: by the potentially anionic part of **L'**, leading to the formation of hydroxybenzophenones; by a molecule of chlorobenzene, leading to the formation of chlorobenzophenones, (and, incidentally , to another fragment $PhO\bar{A}lBr_3$, which can in turn give rise to the hydroxybenzophenones); or by a molecule of phenyl benzoate, leading to the formation of the ketoester, which is subsequently converted to 4-hydroxybenzophenone, possibly through reaction with the fragment $PhO\bar{A}lBr_3$, referred to above. The ketoester should probably be considered as one true intermediate (among others) in the 2:1 rearrangement reaction, as the quantity of ketoester in the reaction products diminishes with increasing time.

Interpretation of this reaction in terms of the nucleophilicity of the molecules present in the reaction medium avoids postulating an ion such as $Ph—\overset{+}{C}=\overset{+}{O}—\bar{A}lBr_3$ as an intermediate, apart from the fact that a reaction medium of low polarity would in any case not favour the production of free ionic intermediates. The reactivity of the incipiently ionic structure **L'** is such that any sufficiently reactive nucleophile available is acylated—which explains why solvent acylation occurs, even the deactivated (towards electrophilic attack) chlorobenzene molecule being extensively acylated, whereas the corresponding intermediate (**E**) ($PhC\overset{+}{O}\bar{A}lBr_3 \ldots OHPh$) in the 1:1 rearrangement and 1:1:1 acylation reactions does not attack the solvent. Probably steric effects play a greater part in the 2:1 rearrangement and 2:1:1 acylation reactions, so that the incipient ionization of the intermediate complex proceeds further towards the formation of the very reactive, and hence unselective, cationic moiety, than in the other reactions. Equally, attack on the phenolic moiety is likely to be more rapid than in the 1:1 rearrangement and 1:1:1 acylation reactions.

The 2:1 rearrangement reaction may also proceed in part through the same mechanism as the 1:1 rearrangement reaction. Possibly the variation in the *ortho/para* ratio for the hydroxybenzophenones in the former reaction is an indication of a duality (or multiplicity) of mechanisms operating simultaneously.

In the 2:1:1 acylation reaction (Scheme 3), the first step is the formation of a catalyst-benzoyl bromide complex, which can then esterify the phenol present to give the protonated catalyst-ester complex (**D**) directly followed by conversion of this to the hydroxybenzophenones. However, the phenol is more probably present as $PhOAlBr_2$, and esterification of this will give **M**, (analogous to **L** in the 2:1 rearrangement reaction), which will begin to break down as in **M'**, (analogous to **L'** in the 2:1 rearrangement reaction), suffering nucleophilic attack to give the hydroxybenzophenones, the chlorobenzophenones, or the ketoester, exactly as in the 2:1 rearrangement reaction.

In the 2:1:1 acylation reaction, under the conditions used, it is difficult to determine from the evidence available whether direct acylation of the phenol molecule, or its aluminium bromide salt, occurs without prior esterification. The

ketoester is probably one intermediate in the 2:1:1 acylation reaction as in the 2:1 rearrangement reaction.

These latter two reactions do not lend themselves to a detailed analysis such as was possible for the 1:1 rearrangement reaction, because, under the reaction conditions used, the former reactions occur too quickly. They require study under conditions such that their rates are less, i.e. at a lower temperature. A plot of mole-%-hydroxybenzophenone formed against mole-%-phenyl benzoate decomposed in the 2:1 rearrangement reaction is of little value, because after the lapse of the smallest time interval used, ($\frac{1}{4}$ hr), 85% of the ester had already been converted to products.

The *ortho/para* ratio for the hydroxybenzophenones in the 2:1:1 acylation reaction is essentially constant (over the reaction period studied) and ca. 0·42. This is very little more than half the value of the *ortho/para* ratio (0·76) in the 1:1:1 acylation reaction. This may be rationalized in terms of steric hindrance of one of the *ortho*-positions in the fragment $PhOAlBr_2$ during its nuclear acylation, in the 2:1:1 acylation reaction, compared with the fragment PhOH in the 1:1:1 acylation reaction, (i.e. compare structures **E** and **M'**).

In the 2:1 rearrangement and 2:1:1 acylation reactions the chlorobenzophenones are formed in similar amounts. This may reasonably be expected, if the chloroketones result from nucleophilic attack by the chlorobenzene molecule on the intermediates **L'** and **M'**, which themselves differ very little.

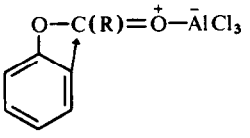
Thus, points 1–3 listed above have been dealt with, as has the occurrence, or non-occurrence, depending on conditions, of solvent acylation. Point 4 has also been accounted for in the above explanations, because the Friedel-Crafts reaction in the present context includes the Fries rearrangement, as the intermediate complex (**D**) is involved in both the 1:1 rearrangement and 1:1:1 acylation reactions. However, in the Friedel-Crafts, (i.e. the acylation), reaction, this complex is formed immediately. In the Fries, (i.e. the rearrangement), reaction, there is a time-lag before this intermediate is formed, and the slower first-stage mechanism must operate before the faster second-stage mechanism can. Hence, for a given reaction time, the overall conversion of starting materials to hydroxybenzophenones will be a little higher in the Friedel-Crafts reaction than in the Fries reaction, but 2-hydroxybenzophenone will be formed to a larger extent relative to 4-hydroxybenzophenone in the Fries rearrangement.

Thus, the theory of a "sandwich" π-complex intermediate, leading to a rapid predominantly (or exclusively) *ortho*-directed intramolecular rearrangement, appears untenable. Although we have proposed that an intramolecular, exclusively *ortho*-directed rearrangement occurs, i.e. the first-stage process of the 1:1 rearrangement reaction, this reaction is obviously not fast, (relative to the rearrangement of benzyl phenyl ether under similar conditions[11]), and is readily superseded by the second-stage mechanism of the 1:1 rearrangement reaction, i.e. the *ortho*- and *para*-directed rearrangement of the protonated catalyst-ester complex (**D**). The rearrangement of the 4,4'-diphenylsubstituted phenyl benzoate is dealt with in Part II[15] of this series.

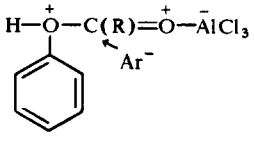
Under the influence of anhydrous aluminium bromide in homogeneous solution in chlorobenzene, benzyl phenyl ether rearranges[11] exclusively to *o*-benzylphenol, with concurrent cleavage to phenol and simultaneous benzylation of the solvent. For catalyst-ether molar ratios of 4:1 (or 2·5:1) the reaction is extremely rapid, being complete in less than 5 sec at −40°. With catalyst-ether molar ratios greater than 1:1, the initial rapid reaction gave the same initial amounts of *o*-benzylphenol and phenol,

but for ratios lower than 1:1, these amounts were decreased. In this ether molecule there is only one nucleophilic centre, i.e. formation of the complex $PhCH_2\overset{+}{O}(\bar{A}lBr_3)Ph$ represents the limit of the co-ordinating possibilities of the ether. In the case of phenyl benzoate however, excess of an electrophile (X) in the reaction mixture, beyond the one molar proportion of catalyst necessary to form the catalyst-ester complex (A), is taken up by this complex. Where (X) is H^+, as in the 1:1 rearrangement reaction, the second-stage mechanism of this reaction begins to operate. Where (X) is $AlBr_3$, as in the 2:1 rearrangement reaction, the reaction is far more rapid, but leads to different products. As soon as the catalyst-ester molar ratio of 1:1 is exceeded appreciably, solvent acylation occurs.

We hope to discuss elsewhere the relationship between our work and other published related work, (see also Ref. 1 for a discussion of this matter), but will consider here Gerecs's interpretation of the mechanism of the Fries rearrangement, as this is of particular interest. Gerecs suggests[19] that *ortho*-migration occurs, in conditions of lower proton concentrations, as a result of intramolecular rearrangement of a catalyst-ester complex:



When a protonated catalyst-ester complex is formed, the proton induces a stronger polarization within the molecule, with a consequent weakening of the C—O bond, resulting in a greater distance between the two atoms. This can favour an intermolecular reaction, Ar^- being a nucleophilic centre in another ester molecule:



(Gerecs also emphasises[19] that a 2-hydroxyketone may be formed by intermolecular acylation.)

We interpret the matter differently, as in Scheme 1 above. In this, *ortho*-migration by intramolecular rearrangement of the catalyst-ester complex (A) is indicated, but the protonated catalyst-ester complex (D) gives rise to both *ortho*- and *para*-migration. It is possibly the use of the relatively non-polar chlorobenzene as solvent which allows a "pseudo-intramolecular" reaction to occur, (i.e. the two fragments of E recombine before they have separated to any great extent), whereas in a more polar solvent such as nitrobenzene, (dielectric constant 34·8/25°[68]), there may be an actual splitting of E, (i.e. of D, or even of A), resulting in an intermolecular rearrangement. In the 1:1 rearrangement and 1:1:1 acylation reactions, we should not suggest that nucleophilic attack by another ester molecule on the protonated complex (D) makes an important contribution to these processes. Our results indicate that the ketoester is a side-product, rather than an intermediate, in these two reactions. However, in the 2:1 rearrangement and 2:1:1 acylation reactions, nucleophilic attack by the ester on

the highly polarized intermediates L′ and M′ is part of our theory of the mechanism of these two reactions.

CONCLUSIONS

Our conclusions are as follows. Our work establishes that in the 1:1 rearrangement reaction, two mechanisms operate: an initial slower process, which is exclusively *ortho*-oriented, and a subsequent faster process, which is *ortho*- and *para*-oriented.

The fast, exclusively *ortho*-directed intramolecular rearrangement mechanism, involving a "sandwich" π-complex intermediate, proposed,[2a,b] is unlikely to be involved (see also Part II of this series[15]). However, it is very reasonable to interpret the first-stage process above as an intramolecular migration proceeding through a "normal" π-complex intermediate. The exclusive *ortho*-migration is consistent with such a mechanism.[65] The migrating group is monodentate,[71] and it is unlikely that a cyclic transition state, (such as that postulated[72] for the Claisen rearrangement, involving a 6-membered ring), could be involved in the migration of an acyl group, as it would require the formation of a highly-strained 4-membered ring.

The second-stage process above may not be truly intramolecular, though superficially appearing to be so. An ion-pair-type intermediate (Scheme 1) may plausibly be involved in this process.

The 1:1:1 acylation reaction occurs principally through prior esterification, followed by rearrangement in accordance with the second-stage mechanism above, which is a common feature of the rearrangement and acylation reactions involving only one mole of catalyst per mole of ester or of benzoyl halide or phenol.

The 2:1 rearrangement and 2:1:1 acylation reactions proceed too quickly under the conditions used to allow us to determine whether there is a similar duality of mechanisms in the former reaction as in the 1:1 rearrangement reaction. The 2:1:1 acylation reaction proceeds to some extent through a prior esterification.

The duality of mechanism operating in the 1:1 rearrangement reaction is a consequence of the presence in the ester of two nucleophilic centres, and the presence (in addition to that of the catalyst) in the reaction mixture of the electrophile H^+: immediately, in the case of the 1:1:1 acylation reaction; and after a time-lag, in the case of the 1:1 rearrangement reaction. This brings the question of the mechanism back to the views of von Auwers,[30a,b] who claimed that there is a difference between the Friedel-Crafts and Fries reactions, performed, as far as possible, under identical conditions. (The conditions used can never be identical, because different reactants are involved in the two processes.) Our work shows the following difference between the two processes: the Fries rearrangement and Friedel-Crafts reaction can both proceed by a mechanism, (i.e. the second-stage mechanism), common to both reactions, but the Fries rearrangement can also proceed, under selected conditions, by an individual mechanism, (i.e. the first-stage mechanism), of its own. The mutual relationship of these two named reactions is plainly established, and the above work may therefore be taken to justify the standpoint of von Auwers, though he himself was unable to do this.

Although other workers have suggested, and in some cases probably established, that there is a difference between the mechanisms of the *ortho*- and *para*-migrations, and though Gerecs has stated[19] that *ortho*-migration may occur by intermolecular acylation, we are the first to establish the duality of the mechanism of the *ortho*-

rearrangement, and to show that one of these mechanisms is common to both the *ortho*- and *para*-migrations under the particular conditions considered.

EXPERIMENTAL

Synthetic work. Anhyd $AlBr_3$ was synthesized from the elements, using 'AnalaR' Br_2, (obtained from Hopkin and Williams Ltd., Chadwell Heath, Essex), and 99·99%-pure Al.* The apparatus used was essentially that described by Nicholson, *et al.*,[73] but the $AlBr_3$ was distilled into Al-foil lined test-tubes, for ease in handling and dispensing. Details of the apparatus, including dimensions, (not given in the Ref. 73), and the synthesis and handling of the halide, are given in Ref. 1.

Chlorobenzene (the B.D.H. product, obtained from The British Drug Houses Ltd., Poole, Dorset), was dried over $CaCl_2$, and then fractionally distilled from P_2O_5 through a 14-plate glass column, packed with Fenske helices. The purified solvent boiled at 131·5-132°/758 mm, (cf. 131·7°/760 mm[68]), and its refractive index (Na light) was 1·5250/20°, (cf. 1·52481/20°, Na light[68]).

Phenol was the "AnalaR" product, (obtained from B.D.H.), used as bought. (Small amounts were removed from the main stock in a N_2-filled dry-box and transferred to a small container, from which the amounts required for a particular experiment were weighed out. The remaining material in the small container was not used subsequently for the acylation reactions, a fresh sample of the main supply being taken each time).

Benzoyl bromide, (the Eastman product, obtained through Kodak Ltd., Kirkby, Liverpool), was redistilled in a current of dry N_2, and dispensed in a N_2 filled dry-box. Phenyl benzoate was commercially available, (B.D.H.), and was re-crystallised from alcohol. The purified compound was powdered and and vacuum-dried. The pure ester melted at 70·5–71°, (cf. 71°[74]), and was chromatographically pure. 4-Bromobiphenyl was used extensively as an internal standard, in the GLC analysis of the products of the rearrangement and acylation reactions. The B.D.H. product was purified by distillation through a 38-plate glass column at 15 mm press, the b.p. being 173°. The first 5 ml of distillate from a 40–50 g sample of the bromo compound was discarded. The contents of the distillation flask and material held up in the column were recrystallized from light petroleum, (b.p. 40–60°), giving chromatographically pure material, m.p. 89–89·5°, (cf. 89°[74]).

Microanalyses were performed by Alfred Bernhardt, Mikroanalytisches Laboratorium, 5251 Elbach über Engelskirchen, Fritz-Pregl-Strasse 14–16, West Germany.

Where standard synthetic methods have been used, these are not described in detail. Complete details of all practical work, synthetic and analytical, are given in Ref. 1.

The hydroxy- and chloro-benzophenones involved in this work are listed in Table 7, with their m.ps, derivatives, etc. The parent ketones, and those derivatives marked with an asterisk, all gave the correct analytical figures, (given in Ref. 1), when subjected to elemental microanalysis. The main features of the methods of preparation of the compounds listed in Table 7 are outlined in Notes I–VII below: full details are given in Ref. 1.

I. 2-Hydroxybenzophenone was prepared (in 39% yield) from salicylic acid.† The acid was treated with $SOCl_2$ and DMF,[75] and the product used in a Friedel-Crafts acylation of benzene, in the presence of two molar proportions of anhyd $AlCl_3$ as catalyst.

Ullmann and Goldberg[76] synthesized 2-hydroxybenzophenone from 2-methoxybenzoic acid, and claimed[76] that under the reaction conditions used, demethylation occurred to give the free hydroxyketone. In our hands,[1] this method invariably gave a mixture, (of the hydroxyketone and its methyl ether), which is not readily separated.[1] Our synthesis using salicylic acid as starting material avoids the need for any such separation.

II. 3-Hydroxybenzophenone was prepared (in 55–60% yield) from 3-methoxybenzoic acid. This was treated with oxalyl chloride[77] in benzene, and the 3-methoxybenzoyl chloride produced was used in a standard Friedel-Crafts acylation of benzene, to give 3-methoxybenzophenone. (The methoxyketone is

* L.S.H. is grateful to the firm of Albert Cook & Son (Founders) Ltd., 273 Wincolmlee, Hull, for the gift of a piece of high-purity Al sheet, from which all the aluminium bromide used in this work was prepared.

† A similar synthesis of 2-hydroxybenzophenone from salicylic acid has recently been published, E. H. Charlesworth and P. Charleson, *Canad. J. Chem.* **46**, 1843 (1968). However, the synthesis mentioned above in our paper was first performed in May, 1961, by L.S.H. (Ref. 1). Details of an improved method similar to the above will be published separately.

TABLE 7. THE MONOHYDROXY- AND MONOCHLORO-BENZOPHENONES

Benzophenone[a]	m.p.[c] (°)	Derivatives and their m.ps[c] (°).
2-OH (I)[b]	37·5–38; (36–41[41,76,80a–c])	2, 4-DNP[d]: 245–247; (250[74]) p-nitrobenzyl ether: 123; (124–125[80b])
3-OH (II)	115; (114–115·5,[81] 116[76,82])	2, 4-DNP*: 274–275; benzoate*: 73–73·5
4-OH (III)	134; (134–136[44,74,80b,83a,b])	2, 4-DNP*: 227–228; (242[84]); benzoate: 112; (112·5[40,44,83a,b])
2-Cl (IV)	46; (43–46,[85a,b] 52–56[85c])	2, 4-DNP*: 168–169
3-Cl (V)	83; (81–84[85b])	2, 4-DNP*: 235
4-Cl (VI)	75; (75–78·4,[85b] 71[86])	2, 4-DNP*: 196; (223–224, 229–230[74])

[a] The abbreviations used for the names of the substituted benzophenones are the same as those used in Tables 1–4.

[b] The Roman numerals refer to the notes in the text dealing with the methods of preparation of the benzophenones.

[c] Melting points quoted in the literature, with the appropriate references, are given in brackets.

[d] 2,4-DNP = 2,4-Dinitrophenylhydrazone; (see note VII in the text).

Compounds marked with an asterisk were submitted to elemental analysis (see text).

not demethylated to any appreciable extent under the conditions used[76]). The methoxyketone was virtually quantitatively demethylated using one molar proportion of boron tribromide[78] in methylene chloride solution. (Boron tribromide is reported to react explosively with liquid water, with which it must not come into contact—see Ref. 1 for the original source of this information).

III. 4-Hydroxybenzophenone was commercially available, (Kodak, or L. Light & Co. Ltd.), as a "Practical" or "Technical" grade product, which was purified by boiling a solution of the hydroxyketone in chloroform with activated charcoal, filtering, and adding to the hot filtrate petroleum ether (boiling range 40–60°) in an amount just insufficient to cause precipitation of the phenol, which then crystallized cleanly as the solution cooled. (3-Hydroxybenzophenone was purified similarly).

IV. 2-Chlorobenzophenone was prepared (in 89% yield) from 2-chlorobenzoyl chloride (B.D.H.) and benzene via the Friedel-Crafts reaction.

V. 3-Chlorobenzoyl chloride was prepared (in 70% yield) similarly, starting from 3-chlorobenzoyl chloride (Aldrich, Technical grade).

VI. 4-Chlorobenzophenone was commercially available (B.D.H. or Hopkin & Williams) as a "Technical" grade product containing a red impurity, which was removed by boiling a solution of the chloroketone in petroleum ether (boiling range 40–60°) with activated charcoal, filtering, and allowing the ketone to crystallize.

VII. The 2,4-dinitrophenylhydrazones of the benzophenones were prepared using dimethylsulphoxide[79] as solvent. Those from the hydroxyketones were recrystallized from alcohol, those from the chloroketones from slightly aqueous acetic acid.

IR and UV absorption spectra of the monohydroxy- and monochloro- benzophenones are given in Ref. 1.

Rearrangement and acylation reactions—technique of the reactions

A detailed account of the techniques used in performing these reactions is given in Ref. 1: only some essential features of the procedures are described here.

The nature of the homogeneous reaction between phenyl benzoate, aluminium bromide, and chlorobenzene depends, among other factors, on the relative proportions of catalyst and ester, the reaction products altering when a catalyst-ester molar ratio greater than 1:1 is used, (see earlier). The necessary degree of accuracy in preparing and dispensing the various reactants was achieved by using weight-in-weight solutions of catalyst, ester, benzoyl bromide, and phenol, allowing the exact amounts of the required materials to be used.

In the rearrangement reactions, catalyst and ester were dissolved in five times their weight of chlorobenzene. In the acylation reactions, catalyst and benzoyl bromide were used in molal solns. When preparing

the phenol soln for use in an acylation reaction, the weight of chlorobenzene taken was adjusted to give a similar concentration of ester (assuming complete esterification of the phenol) as in the corresponding rearrangement reaction.

Catalyst and benzoyl bromide solns were dispensed in a N_2 filled dry-box, using safety pipettes. The phenyl benzoate and phenol solns were prepared in small thin-walled glass tubes, which were subsequently broken (by pointed glass rods) inside the larger glass tubes containing the catalyst (and, where appropriate, benzoyl bromide) solns. This solved the problems of transference and mixing of reactants, some of which were highly reactive and moisture sensitive.

Reactions were performed in duplicate, and repeated using freshly prepared solns of reactants.

The reaction tubes, (fitted with silica-gel drying tubes), were heated in a constant temp oil-bath (110 ± 0·15°) for the requisite time, then their contents were poured into cold dil HCl. The tubes were rinsed with water and ether, the washings being added to the respective hydrolysed reaction mixtures. Each mixture was extracted thoroughly with ether, and the ether extract washed with a little water and dried. The ether was then evaporated on the water-bath, the required amounts of the internal standards for the subsequent GLC analysis were added, a sample of the soln was silylated, (see later), and the products were then submitted to GLC.

Analytical work

Spectrophotometric work (in conjunction with column chromatography) is described in detail in Ref. 1. This work did not give reproducible quantitative results, but established the following points. (i) Chemical methods of separating the reaction products (i.e. by alkali extraction of phenolic material) could not be used, because of the hydrolysis of phenyl benzoate present in these products. (ii) 4-Chlorobenzophenone was first detected by spectroscopic means, isolated by column chromatography, and subsequently identified. (iii) The reaction products were shown to be unaffected by the catalyst, (see earlier), except that in the presence of a large excess of $AlBr_3$, 2-hydroxybenzophenone suffered some decomposition. (iv) At 20°, a soln of phenyl benzoate and three molar proportions of $AlBr_3$ returned, after 1 hr, a little over 90% of the ester. No hydroxybenzophenones seemed to be formed, but the smell of a benzoyl halide was detectable in the reaction products.

GLC solved most of the analytical problems involved in our investigations, and this phase of the work is described at length in Ref. 1, where detailed descriptions and diagrams of apparatus, calibration curves, etc., are all provided. Only the most important points are mentioned here.

The apparatus was of glass, with a vapour jacket as heater, on-column injection, (using a Hamilton 10 μl. syringe, type 701-N), and a flame-ionization detector. The amplifier was obtained from Gas Chromatography Ltd., (Boyn Valley Road, Maidenhead, Berkshire), and a Honeywell recorder, with a range of 0–2·5 mv, was used. The standard operating conditions used were as follows: glass columns, 6′ long, 4–5 mm internal diam, packed with 25% "Embaphase" silicone oil, (obtained from May & Baker Ltd., Dagenham, Essex), on 60–80 mesh Diatoport S, (kieselguhr which has been acid- and alkali-washed, and silanized), obtained from F & M Scientific Group, Hewlett Packard Ltd., 224 Bath Road, Slough, Buckinghamshire). The column temp was 193°, (dekalin as heating liquid), and the carrier gas was a mixture of 3 parts H_2 and 1 part N_2, admitted at 7 lb press. Filtered compressed air was fed to the detector at 600–800 ml min^{-1}: as long as the air flow-rate was greater than 400 ml min^{-1}, its actual value was not critical.

Quantitative analyses were made using peak-height ratios and the internal standard method.[87a,b] Calibration curves (peak-height ratios vs. weight ratios) for phenyl benzoate, 2- and 4- chloro and 2- and 4-hydroxybenzophenone were good straight lines. The internal standards used are described below.

Phenol present in the reaction products could not be determined quantitatively because of interference, even at lower column temps, by the other reaction products, preventing accurate measurement of peak heights.

As 3-hydroxybenzophenone was not formed in the rearrangement (or acylation) reactions, it provided a very suitable internal standard for the analysis of 2- and 4- hydroxybenzophenone. 4-Bromobiphenyl was a good internal standard for phenyl benzoate and 2- and 4- chlorobenzophenone.

As 4-hydroxybenzophenone tailed excessively, (at least for quantitative work), a derivative had to be used. Methylation was no solution, as 2-methoxybenzophenone and 4-chlorobenzophenone had the same retention times. However, trimethylsilylation provided the answer, converting all three monohydroxybenzophenones quantitatively to their trimethylsilyl ethers:

$$2ArOH + (Me_3Si)_2NH \rightarrow 2ArOSiMe_3 + NH_3$$

The best silylation technique was that of Grant and Vaughan,[88] which was applied as follows. A sealed tube containing one volume (ca. 0·2 ml) of the soln of the reaction products and internal standards, two volumes of hexamethyldisilazane, and a trace of HCl, was heated in a boiling water-bath for at least 1 hr, (generally about 4 hr). when trimethylsilylation of the hydroxybenzophenones was complete. This silylation procedure was superior to any others examined,[1] providing a stable sample for analysis. Any incompletely silylated material (i.e. any free hydroxybenzophenones) was readily detected by chromatography, and such a sample would be discarded, and a fresh one prepared. The reaction products, before silylation, were eluted in the following order (retention times in min in parentheses): phenyl benzoate, (14·5), 4-bromobiphenyl, (16·5), 2-hydroxy-, (19), 2-chloro-, (20·5), 4-chloro-, (24·5), 3-hydroxy-, (39·5), and 4-hydroxy-, (46·5), benzophenone. After silylation, the order became: phenyl benzoate, (14·5), 4-bromobiphenyl, (16·5), 2-chloro-, (20·5), 4-chloro-, (24·5), 2-trimethylsilyloxy-, (28), 3-trimethylsilyloxy-, (42), and 4-trimethylsilyloxy-, (55·5), benzophenone. Chromatograms are shown in Ref. 1. Thus trimethylsilylation solved the problems of tailing of 4-hydroxybenzophenone and insufficient resolution of 2-hydroxy- and 2-chlorobenzophenone. All peaks obtained were symmetrical and sharp.

Silylated samples (both calibration mixtures and mixtures of reaction products) were chromatographed 5 or 6 times, and the calculated peak-height ratios averaged. The performance of the chromatograph as a whole was checked by running calibration mixtures among the mixtures being analysed every 2 or 3 days. Any discrepancies between calculated and observed peak-height ratios were generally due to wear in the column packing, disappearing when the latter was renewed.

The ketoester, 4-benzoylphenyl benzoate, (see earlier), could be chromatographed on a 1′-column of 5% (M&B) "Embaphase" silicone oil, on (M&B) "Embacel", (acid-washed, 60–100 mesh), as solid support: the column was operated at 206°, with an inlet pressure of 4 lb. On this column, an authentic sample of the ketoester (4-hydroxybenzophenone benzoate) had a retention time of 11 min.

Several reaction mixtures were analysed on this column, and found to contain small amounts of a compound with the same retention time as the authentic ketoester. Two of the reaction mixtures which contained fairly appreciable amounts of the suspected ketoester were pooled, and the chlorobenzene was removed on the water-bath, under reduced press. (The residue was again chromatographed, merely to check that the suspected ketoester was still intact). A fraction of the residue was dissolved in a small amount of abs EtOH, and the soln applied to the top of a column of alumina, ca. 1″ × 8″. Elution with abs EtOH was continued, the hydroxybenzophenones, which were originally adsorbed as a deep yellow band at the top of the column, spreading a little way down the column.

The eluate was submitted to GLC on the usual column, (i.e. the 6′ column operated at 193°—see above), and the chromatogram showed peaks due to phenyl benzoate, 2- and 4- chlorobenzophenone. There were no peaks attributable to the hydroxybenzophenones, as these compounds were retained by the alumina column. 2N NaOH (3 ml) was added to the ethanolic eluate, and the whole soln warmed for 10 min on the water-bath. The soln was then acidified with 2N HCl, and a sample chromatographed. The chromatogram now showed no peak due to phenyl benzoate, since this had been hydrolysed, but more important, a peak with the same retention time as 4-hydroxybenzophenone, which is a hydrolysis product of the ketoester, was now shown. The combined evidence from the above chromatograms, together with the circumstances of the reaction, are sufficient evidence of the identity of the (hitherto merely suspected) ketoester.

The detector was calibrated approximately using weight-in-volume solns of authentic ketoester. (It was not possible at this stage to weigh another internal standard into the mixtures being analysed). When the reaction mixtures themselves were analysed, the amounts of ketoester found to be formed in the different reactions, though approximate, showed definite trends, the significance of which has already been discussed.

Acknowledgements—This work was begun in 1958 during the tenure of a Postgraduate Studentship, held at Queen Mary College, University of London. L.S.H. is grateful to London University for the award of this Studentship for the session 1958–9, and to the Local Education Authority, Hull, for a Major Award during the sessions 1959–60, (part), 1960–3. L.S.H. also wishes to thank Mr. (now Dr.) R. Dietz, his former colleague at Queen Mary College; Messrs. G. W. Nendick and D. H. Langford, Department of Chemistry & Biology, College of Technology, Hull; H. Jowitt, B.P. Chemicals, (U.K.) Ltd., Salt End, Hedon, near Hull; and D. W. Grant, Coal Tar Research Association, Oxford Road, Gomersal, near Leeds: with all of whom he had helpful discussions about different aspects of his work. L.S.H. is also grateful to the firm of Reckitt & Sons Ltd., Dansom Lane, Hull, and certain of their personnel, for providing facilities not originally available to him elsewhere.

REFERENCES

[1] This work was approved for the Ph.D. Degree of London University, and is taken from the Ph.D. Thesis (1967) of Lionel S. Hart.

[2] [a] M. J. S. Dewar, *Theoretical Organic Chemistry—Papers presented to the Kekule Symposium* pp. 179–208, *Aromatic Rearrangements.* Butterworths, London (1958);

[b] M. J. S. Dewar, *Molecular Rearrangements* (Edited by P. de Mayo) Chapter V, pp. 295–344. *Aromatic Rearrangements.* Interscience, New York, London (1963).

[3] M. J. S. Dewar, *Nature, Lond.* **156**, 784 (1945); *J. Chem. Soc.* 406 (1946); *The Electronic Theory of Organic Chemistry* Chapter XI, p. 225. O.U.P. London (1949) and Refs 2*a* and 2*b*.

[4] G. S. Hammond and H. J. Shine *J. Am. Chem. Soc.* **72**, 220 (1950).

[5] See p. 337 in Ref. 2*b*.

[6] See p. 336 in Ref. 2*b*.

[7] G. Friebel and B. Rassow, *J. prakt. Chem.* **63**, 444 (1901).

[8] F. Bell, J. Kenyon and P. H. Robinson, *J. Chem. Soc.* 1239 (1926).

[9] R. B. Carlin, personal communication to M. J. S. Dewar.

[10] H. J. Shine and J. P. Stanley, *J. Org. Chem.* **32**, 905 (1967); and earlier papers.

[11] D. S. Tarbell and J. C. Petropoulos, *J. Am. Chem. Soc.* **74**, 244 (1952).

[12] H. Hart and R. J. Elia, *Ibid.* **76**, 3031 (1954).

[13] B. Miller, *Tetrahedron Letters* 55 (1962); *J. Am. Chem. Soc.* **86**, 1127, 1135 (1964).

[14] See p. 308 in Ref. 2*b*.

[15] Following paper.

[16] A. H. Blatt, *Chem. Rev.* **27**, 413 (1940).

[17] A. H. Blatt, *Organic Reactions* **1**, 342 (1942).

[18] L. Prajer, *Wiadomosci Chemiczne*, **11**, 177 (1957).

[19] A. Gerecs, *Friedel-Crafts and Related Reactions*, (Edited by G. A. Olah) Volume III, Part I, Chapt. XXXIII, pp. 499–533. *The Fries Reaction.* Interscience, New York, London, Sydney (1964).

[20] A. W. Ralston, M. R. McCorkle and E. W. Segebrecht, *J. Org. Chem.* **6**, 750 (1941); and other papers, *J. Org. Chem.* 1940–1942.

[21] S. Skraup and K. Poller, *Ber. Dtsch. Chem. Ges.* **57**, 2033 (1924).

[22] E. H. Cox, *J. Am. Chem. Soc.* **52**, 352 (1930).

[23] A. Schönberg and A. Mustafa, *J. Chem. Soc.* 79 (1943); See also: D. S. Tarbell and P. E. Fanta, *J. Am. Chem. Soc.* **65**, 2169 (1943).

[24] C. R. Hauser and E. H. Man, *J. Org. Chem.* **17**, 390 (1952).

[25] T. Bisanz, *Rocz. Chem.* **30**, 87 (1956).

[26] K. W. Rosenmund and D. Schnurr, *Liebigs Ann.* **460**, 56 (1928).

[27] D. Klamann, *Ibid.* **583**, 63 (1953); *Chem. Abstr.* **49**, 1609 (1955).

[28] M. J. S. Dewar, *The Electronic Theory of Organic Chemistry* pp. 229–230. O.U.P., London (1949).

[29] Y. Ogata and H. Tabuchi, *Tetrahedron* **20**, 1661 (1964).

[30] [a] K. von Auwers and W. Mauss, *Liebigs Ann.* **464**, 293 (1928);

[b] K. von Auwers and W. Mauss, *Ber. Dtsch. Chem. Ges.* **61**, 1495 (1928).

[31] G. I. Gershzon, *J. Gen. Chem. USSR* **13**, 82 (1943); *Chem. Abstr.* **38**, 1220 (1944).

[32] G. Illari, *Gazzetta* **77**, 339 (1947); *Chem. Abstr.* **42**, 2948 (1948).

[33] A. F. Marey, F. G. Baddar, and W. I. Awad, *Nature, Lond.* **172**, 1186 (1953);
A. M. El-Abbady, F. G. Baddar and A. Labib, *J. Chem. Soc.* 1083 (1961); and earlier papers.

[34] R. Baltzly, W. S. Ide and A. P. Phillips, *J. Am. Chem. Soc.* **77**, 2522 (1955).

[35] N. M. Cullinane and B. F. R. Edwards, *J. Chem. Soc.* 2926 (1958), and earlier papers; See also papers by Cullinane *et al. Rec. Trav. chim.* 1959, 1960; and *J. Chem. Soc.* 1961.

[36] [a] A. Furka and T. Szell, *Ibid.* 2312 (1960);

[b] T. Szell and A. Furka, *Ibid.* 2321 (1960)

[37] G. C. Amin and N. M. Shah, *J. Univ. Bombay* **17A**, 5 (1948); *Chem. Abstr.* **43**, 6593 (1949).

[38] A. Gerecs and M. Windholz, *Naturwiss.* **42**, 414 (1955); and earlier papers in *Acta Chim. Acad. Sci. Hung.* 1953–5.

[39] F. F. Blicke and O. J. Weinkauff, *J. Am. Chem. Soc.* **54**, 330 (1932).

[40] A. Pieroni with S. Longhini, *Gazzetta* **62**, 387 (1932); *Chem. Abstr.* **26**, 4802 (1932).

[41] N. M. Cullinane, N. M. C. Morgan and C. A. J. Plummer, *Rec. Trav. Chim.* **56**, 627 (1937); *Chem. Abstr.* **31**, 6238 (1937).
[42] H. Huber and K. Brunner, *Monatsh.* **56**, 322 (1930).
[43] G. Heller, *Ber. Dtsch. Chem. Ges.* **46**, 1497 (1913).
[44] O. Döbner, *Liebigs Ann.* **210**, 246 (1881).
[45] N. M. Cullinane and B. F. R. Edwards, *J. Appl. Chem.* **9**, 133 (1959).
[46] H. R. Snyder and C. T. Elston, *J. Am. Chem. Soc.* **77**, 364 (1955).
[47] P. D. Gardner, *Ibid.* **77**, 4674 (1955).
[48] [a] K. Nakazawa and K. Kusuda, *J. Pharm. Soc. Japan* **75**, 257 (1955); *Chem. Abstr.* **50**, 1661 (1956);
[b] K. Nakazawa and S. Baba, *J. Pharm. Soc. Japan* **75**, 378 (1955); *Chem. Abstr.* **50**, 2510 (1956).
[49] D. B. Bruce, A. J. S. Sorrie and R. H. Thomson, *J. Chem. Soc.* 2403 (1953).
[50] K. Wiechert, *Newer Methods of Preparative Organic Chemistry* pp. 315–68, (pp. 344, 351). Interscience, New York (1948).
[51] K. Kindler, H. Oelschläger and P. Henrich, *Arch. Pharm.* **287**, 210 (1954).
[52] D. Kästner, *Newer Methods of Preparative Organic Chemistry*, pp. 249–313; (pp. 284-289, *The Fries Rearrangement*). Interscience, New York (1948); The original German text is in *Angew. Chem.* **54**, 273–281, 296–304, (1941).
[53] For reviews, see:
[a] V. I. Stenberg, *Org. Photochem.* **1**, 127 (1967);
[b] D. Bellus and P. Hrdlovic, *Chem. Rev.* **67**, 599 (1967).
[54] J. C. Anderson and C. B. Reese, *J. Chem. Soc.* 1781 (1963).
[55] W. M. Horspool and P. L. Pauson, *Ibid.* 5162 (1965).
[56] R. A. Finnegan and J. J. Mattice, *Tetrahedron* **21**, 1015 (1965);
See also: J. J. Mattice, *Chem. Abstr.* **67**, 21282s (1967).
[57] S. Skraup and E. Beng, *Ber. Dtsch. Chem. Ges.* **60**, 942 (1927).
[58] K. von Auwers and W. Mauss, *Ibid.* **61**, 416 (1928).
[59] See ref. 26; see also: N. M. Cullinane and B. F. R. Edwards, *J. Chem. Soc.* 434 (1958); J. F. Miquel, P. Miller and Ng. Ph. Buu-Hoi, *Bull. Soc. Chim. Fr* 633 (1956).
[60] See S. Glasstone; *Textbook of Physical Chemistry* (2nd Edition), pp. 1086–1087. Macmillan, London (1955).
[61] J. Göhring and B. P. Susz, *Helv. Chim. Acta* **49**, 486 (1966).
[62] D. S. Bystrov and V. N. Filimonov, *Dokl. Akad. Nauk SSSR* **131**, 338 (1960); *Chem. Abstr.* **55**, 11083 (1961).
[63] See p. 229 in Ref. 2b.
[64] See Ref. 34, footnotes on pp. 2523 and 2525.
[65] See pp. 307–308 in Ref. 2*b*.
[66] C. K. Ingold, *Structure and Mechanism in Organic Chemistry*, p. 625. Bell, London (1953).
[67] M. J. S. Dewar and N. A. Puttnam, *J. Chem. Soc.* 4080, 4086, 4090 (1959).
[68] *Techniques of Organic Chemistry*. Edited by A. Weissberger, E. S. Proskauer, J. A. Riddick and E. E. Toops, Jr. 2nd edition, Vol. VII. Interscience, New York, (1955).
[69] See particularly the many papers, listed in Ref. 1, by Susz, *et al.*, appearing mainly in *Helv. Chim. Acta* from 1954 onwards, e.g. **40**, 971 (1957); **43**, 424 (1960); **44**, 395, 943 (1961).
See also:
D. Cook, *Canad. J. Chem.* **37**, 48 (1959); H.-H. Perkampus and E. Baumgarten, *Ber. Bunsengesellschaft. Phys. Chem.* **68**, 496 (1964);
For a summary of the present position, see:
R. O. C. Norman and R. Taylor; *Electrophilic Substitution in Benzenoid Compounds*, Chapter VI, p. 174. Elsevier, London, New York and Amsterdam (1965).
[70] B. Mori, J. Göhring, D. Cassimatis and B. P. Susz, *Helv. Chim. Acta* **45**, 77 (1962).
[71] See pp. 295–296 in Ref. 2*b*.
[72] See H. J. Shine; *Aromatic Rearrangements*, Chapter II, p. 89. Elsevier, London, New York, Amsterdam (1967).
[73] D. G. Nicholson, P. K. Winter and H. Fineberg; *Inorg. Synth.* **3**, 33 (1950).
[74] *Dictionary of Organic Compounds* (4th Edition). Eyre & Spottiswoode, Spon, London (1965).
[75] H. H. Bosshard, R. Mory, M. Schmid and Hch. Zollinger; *Helv. Chim. Acta* **42**, 1653 (1959).
[76] F. Ullmann and I. Goldberg, *Ber. Dtsch. Chem. Ges.* **35**, 2811 (1902).

[77] R. Adams and L. H. Ulich, *J. Am. Chem. Soc.* **42**, 599 (1920).
[78] J. F. W. McOmie, M. L. Watts and D. E. West, *Tetrahedron* **24**, 2289 (1968).
[79] J. Parrick and J. W. Rasburn, *Canad. J. Chem.* **43**, 3453 (1965).
[80] [a] P. Cohn, *Monatsh.* **17**, 102 (1896);
[b] F. F. Blicke and O. J. Weinkauff, *J. Am. Chem. Soc.* **54**, 1446 (1932);
[c] M. Kulka, *Ibid.* **76**, 5469 (1954).
Additional Refs are listed in Ref. 1.
[81] P. Pfeiffer and E. Ochiai, *J. Prakt. Chem.* **136**, 125 (1933); *Chem. Abstr.* **27**, 1870 (1933).
[82] A. W. Smith, *Ber. Dtsch. Chem. Ges.* **24**, 4025 (1891).
[83] [a] S. Grucarevic and V. Merz, *Ibid.* **6**, 1245 (1873);
[b] O. Doebner and W. Stackmann, *Ibid.* **9**, 1918 (1876).
[84] *Organic Reagents for Organic Analysis* 2nd Edition. Hopkin & Williams, Chadwell Heath, Essex (1950).
[85] [a] E. Berliner, *J. Am. Chem. Soc.* **66**, 533 (1944);
[b] J. F. Bunnett and B. F. Hrutfiord, *J. Org. Chem.* **27**, 4152 (1962);
[c] K. von Auwers, M. Lechner and H. Bundesmann, *Ber. Dtsch. Chem. Ges.* **58**, 36 (1925); *Chem. Abstr.* **19**, 1405 (1925).
[86] E. von Meyer, *J. Prakt. Chem.* **82**, 538 (1910); *Chem. Abstr.* **5**, 1596 (1911).
Additional Refs., relevant to material covered by Refs 85 and 86 above, are listed in Ref. 1.
[87] [a] N. H. Ray, *J. Appl. Chem.* **4**, 21 (1954);
[b] E. H. Lee and G. D. Oliver, *Analyt. Chem.* **31**, 1925 (1959).
[88] D. W. Grant and G. A. Vaughan, *Gas Chromatography* 1962 (Edited by M. van Swaay), p. 305. Butterworths, London (1962).