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The Friedel-Crafts Acylation of Aromatic Halogen Derivatives. Part The Benzoylation of Chlorobenzene 111.†

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The Friedel-Crafts benzoylation of chlorobenzene leads to mixtures of o- (3-12%), m- (0.1-4%), and p- (84-97%) chlorobenzophenones and benzophenone (0-8%). The effects of solvent, catalyst, mode of addition, temperature, and duration of the reaction have been examined. The reactivity ratio of chlorobenzene : benzene has been found to be 0.0260 in nitrobenzene solution at 25°, leading to the partial rate factors $o_t = 0.00328$, $m_{\rm f} = 0.00016$, and $p_{\rm f} = 0.150$.

THE benzoylation of chlorobenzene was first reported by Kollarits and Merz,¹ who obtained p-chlorobenzophenone with benzoic acid and phosphoric oxide. Aluminium chloride was later used as the catalyst² and near quantitative yields of ketone have been reported.³⁻⁵ Some o-chlorobenzophenone (up to 12% yield) appears to be a normal product.^{4,6} More recently, Koike and Okawa⁷ reported the formation of *m*-chlorobenzophenone in up to 21% yield, and the absence of the *o*-isomer. Whereas the Friedel-Crafts acetylation of chlorobenzene has been quantitatively studied,⁸ precise information on the benzoylation reaction is scant.⁹

In the present work, the Friedel-Crafts benzoylation

† Parts I and II are considered to be R. B. Girdler, P. H. Gore, and J. A. Hoskins, J. Chem. Soc. (C), 1966, 518; and P. H. Gore and P. A. Goodman, Zh. Organ. Khim., 1967, 3, 1145, respectively.

¹ M. Kollarits and V. Merz, Ber., 1873, **6**, 536. ² P. Wegerhoff, Annalen, 1889, 252, 6.

³ M. Gomberg and L. H. Cone, Ber., 1906, 39, 3278; cf. P. J. Montagne, Rec. Trav. chim., 1907, 26, 262.

4 H. P. Newton and P. H. Groggins, Ind. Eng. Chem., 1935,

F. Smeets and J. Verhulst, Bull. Soc. chim. belges, 1952, 61, 694. 6

P. J. Montagne, Rec. Trav. chim., 1908, 27, 336; P. J. Montagne and S. A. Koopal, Rec. Trav. chim., 1910, 29, 138.

of chlorobenzene was investigated under a wide variety of conditions. The reaction products were freed from polymeric by-products by passage through alumina, and were then analysed quantitatively by g.l.c. Table 1 shows the isomer distributions found in Perrier¹⁰ benzoylations in six solvents, mostly at 100° and 125°. Only trace amounts (0.8-3%) of the *m*-isomer were observed. In every case the proportion of the p-isomer exceeds 86%. At 100° the 2p:o isomer ratio ranges from benzoyl chloride (27.4:1) to o-dichlorobenzene (14.4:1). These ratios are typical for Friedel-Crafts benzoylations of monosubstituted benzene derivatives; thus, for toluene the ratio has been found to be 18.6:1 in ethylene chloride,¹¹ 19.2:1 in benzoyl chloride,¹² and

¹⁰ P. H. Gore, 'Friedel-Crafts and Related Reactions,' ed. G. A. Olah, Interscience, New York, 1964, vol. III, part 1, p. 4.

¹¹ H. C. Brown and G. Marino, J. Amer. Chem. Soc., 1959,

81, 3308. ¹² H. C. Brown and F. R. Jensen, J. Amer. Chem. Soc., 1958, 80, 2296.

J. Amer. Chem. Soc., 1964, 86, 2198. • H. C. Brown and F. R. Jensen, J. Amer. Chem. Soc., 1958,

^{80, 2296.}

25.4:1 in nitrobenzene.¹³ In chlorobenzene solvent 3.1% of the total ketones was shown to be benzophenone; trace amounts were found in other solvents, but not in nitrobenzene. Dehalogenoacylations have been observed before in Friedel-Crafts reactions. Thus, Sulzbacher and Bergmann ¹⁴ observed the formation of a 15% yield of 2-ethylhexanophenone (the major product)

TABLE 1

The influence of the solvent on the benzoylation of chlorobenzene, catalysed by aluminium chloride

		Chlorobe	Benzo-		
Solvent	Temp.	0	3n	Þ	phenone (%)
PhCl	100°	7.2	1.9	87.8	3.1
	125	$7 \cdot 6$	$2 \cdot 0$	87.3	$3 \cdot 1$
(CHCl ₂) ₂	100	7.5	$2 \cdot 0$	90.3	0.2
	125	8.7	$2 \cdot 5$	88.6	0.2
o-Cl ₂ C ₆ H ₄	100	12.0	1.9	86.1	<0.1*
-	125	10.6	3.0	86·4	<0.1*
BzCl	100	6.7	1.0	$92 \cdot 1$	<0.1
DI NIG	125	9.9	1.7	88.4	< 0.1
$PhNO_2$	100	8.0	1.0	91.0	0
(011 01)	125	9.0	1.3	89.7	0
$(CH_2CI)_2 \dots$	75	7.2	0.8	92.0	< 0.1

* In addition to 100 parts of chlorobenzophenones, the mixture contained $6\cdot 8$ parts (at 100°), or $12\cdot 0$ parts (at 125°) of 3,4-dichlorobenzophenone.

by the action of 2-ethylhexanoyl chloride on bromobenzene, in the presence of aluminium chloride. Bardone¹⁵ found that the extent of debromination which accompanied acylation in the reaction between 3,5-dinitrobenzoyl chloride and bromobenzene varied with the solvent, concentration, and pressure. Related debromobenzoylations have also been observed with 9-bromo- and 9,10-dibromo-anthracene.¹⁶ Analogous dechloroacylations have not been reported before. In the experimental procedure here used contact of chlorobenzene with free aluminium chloride is avoided. Presumably, chlorobenzene, when used as a solvent (i.e. in large excess), permits by-products to accumulate, which the other solvents do not. In fact it would require only trace formation of benzene from chlorobenzene. either by a catalysed disproportionation ¹⁷ or a catalysed protodechlorination, to account for the observed 3.1%yield of benzophenone (based on the amount of benzoyl chloride undergoing reaction). Alternatively, benzophenone could arise from the chlorobenzophenones first formed by a protodechlorination. It is difficult to see, however, why this process should be important only in one particular solvent. Since both disproportionation and protodechlorination have been shown to be very slow in the presence of anhydrous aluminium chloride,¹⁷ the formation of benzophenone in our system by either route seems unlikely. The most likely alternative appears to be a reaction in which entry of the acyl group occurs synchronously with the departure of the chlorine

atom from the same carbon atom. The formation of substantial amounts of benzophenone only with chlorobenzene as solvent appears to confirm this.

When *o*-dichlorobenzene was used as solvent a byproduct, 3,4-dichlorobenzophenone, was formed; this ketone derives from a competition by the comparatively inert ¹⁸ solvent, present in excess.

The results obtained on changing the addition sequence in this acylation are given in Table 2. The three main

TABLE	2
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The influence of the addition sequence on the benzoylation of chlorobenzene, catalysed by aluminium chloride, at 100°

		Chloro	Benzo-		
	Addition		(%)		phenone
Solvent	sequence *	0	111	Þ	- (%)
Chlorobenzene	Р	$7 \cdot 2$	1.9	87.8	$3 \cdot 1$
	в	4.5	1.7	92.3	1.5
	E	4.9	1.6	91.4	$2 \cdot 1$
Nitrobenzene	Р	8.0	$1 \cdot 0$	91·0	0
	в	11.1	$2 \cdot 2$	86.7	< 0.1
	E	10.2	$2 \cdot 0$	87.8	<0.1
* F	P = Perrier, 2	B = Bou	veault,	E = Elbi	s.

acylation procedures,¹⁰ those due to Perrier, Bouveault, and Elbs, were studied at 100° both in chlorobenzene, which, though a poor solvent for aluminium chloride, is a good solvent for the acylating complex and the catalyst-ketone complex,¹⁹ and nitrobenzene, which is a good solvent for all three species. The changes in isomer distribution are minor, as might be expected for a substrate of low reactivity. It is apparent that free aluminium chloride, which is present as such initially both in the Bouveault and Elbs procedures, will form a complex with the basic benzoyl chloride molecules before it can act to an appreciable extent on the chlorobenzene. Again, benzophenone is a significant by-product only when chlorobenzene is used as solvent. In the acylation of chlorobenzene the Perrier procedure leads to maximal formation of the o- and m-isomers with chlorobenzene as solvent, and to minimal with nitrobenzene.

The effect of different catalysts in the acylation is summarised in Table 3. Six Lewis acids were investigated in the reaction in nitrobenzene at 100° , both with the Perrier and the Elbs method. Again, only minor variations in isomer distribution were observed. The Elbs procedure gives the greater proportion of benzophenone with most catalysts. The values obtained with stannic chloride appear high; however, since formation of the chlorobenzophenone is very slow with this catalyst, the side reaction is able to compete. This observation is similar to that for reactions with aluminium chloride carried out at comparatively low temperature (see below; Table 4). The overall reactivities of the catalysts follow the sequence

$$\operatorname{AlCl}_3 \sim \operatorname{SbCl}_5 \sim \operatorname{FeCl}_3 > \operatorname{ZrCl}_4 > \operatorname{TiCl}_4 > \operatorname{SnCl}_4,$$

P. H. Gore and J. A. Hoskins, J. Chem. Soc., 1964, 5666.
 G. A. Olah, W. S. Tolyesi, and R. E. A. Dear, J. Org. Chem.,

¹⁸ P. A. Goodman and P. H. Gore, unpublished.

¹⁹ H. F. Bassilios, S. M. Makar, and A. Y. Salem, Bull. Soc. chim. France, 1954, [5], **21**, 72.

¹³ H. C. Brown, B. A. Bolto, and F. R. Jensen, J. Org. Chem., 1958, **23**, 417; H. C. Brown, and H. L. Young, J. Org. Chem., 1957, **22**, 719.

¹⁴ M. Sulzbacher and E. Bergmann, J. Org. Chem., 1948, 13, 303.

¹⁵ F. Bardone, Compt. rend., 1953, 236, 828.

¹⁷ G. A. Olah, W. S. Tolyesi, and R. E. A. Dear, *J. Org. Chem.*, 1962, **27**, 3441.

TABLE 3

The influence of the catalyst on the benzovlation of chlorobenzene in nitrobenzene at 100°, using the Perrier and Elbs addition procedures

	Addition	Chlore	Benzo-		
Catalyst	sequence *	0	m	Ь	(%)
AICI	n	ě o	1.0		(70)
AICI3	P E	3.0	1.0	91.0	-01
01 01	E	10.2	2.0	81.8	< 0.1
SDCI5	\mathbf{P}	8.1	1.4	90.5	< 0.1
	E	8.6	$2 \cdot 1$	89·3	< 0.1
FeCl ₃	Р	7.6	1.4	91 ·0	< 0.1
	E	6.9	1.4	91.3	0.4
SnCl.	Р	7.0	1.4	88.2	3.4
-	E	6.7	1.0	87.4	4.9
TiCl	Р	7.6	1.5	90.3	0.7
•	E	$7 \cdot 2$	1.2	89.5	$2 \cdot 1$
ZrCl	\mathbf{P}	9.7	1.9	87.7	0.7
•	E	7.5	1.3	90·0	$1 \cdot 2$
	* P	- Perrie	$\cdot \mathbf{E} \Rightarrow \mathbf{E}$	hs	

which differs in detail from more quantitative studies of chloride catalysts, as in the acetylation of toluene,²⁰ the benzoylation of toluene,²¹ or the benzoylation of anthracene.16

The effect of temperature on the benzovlation of chlorobenzene in nitrobenzene solution was studied, with aluminium chloride as catalyst, in the range $0-175^{\circ}$ (Table 4). The Perrier procedure was here used, no

TABLE 4

The effect of temperature on the benzoylation of chlorobenzene in nitrobenzene at 100°, catalysed by aluminium chloride and using the Perrier addition procedure

Chlorob	enzophenc	ones (%)	
0	m	Þ	Benzophenone (%)
3.1	0.1	85.5	8.4
$4 \cdot 2$	0.2	94.6	1.2
5.6	0.3	94 ·4	< 0.1
7.7	0.6	91 .7	< 0.1
8.0	1.0	91 ·0	0
9.0	1.3	89.7	0
10.6	2.0	87.4	0
11.8	$3 \cdot 8$	84.4	0
	Chlorob 0 3·1 4·2 5·6 7·7 8·0 9·0 10·6 11·8	$\begin{array}{c cccc} c & m \\ \hline o & m \\ \hline 3\cdot1 & 0\cdot1 \\ 4\cdot2 & 0\cdot2 \\ 5\cdot6 & 0\cdot3 \\ 7\cdot7 & 0\cdot6 \\ 8\cdot0 & 1\cdot0 \\ 9\cdot0 & 1\cdot3 \\ 10\cdot6 & 2\cdot0 \\ 11\cdot8 & 3\cdot8 \end{array}$	o m p $3 \cdot 1$ $0 \cdot 1$ $85 \cdot 5$ $4 \cdot 2$ $0 \cdot 2$ $94 \cdot 6$ $5 \cdot 6$ $0 \cdot 3$ $94 \cdot 4$ $7 \cdot 7$ $0 \cdot 6$ $91 \cdot 7$ $8 \cdot 0$ $1 \cdot 0$ $91 \cdot 0$ $9 \cdot 0$ $1 \cdot 3$ $89 \cdot 7$ $10 \cdot 6$ $2 \cdot 0$ $87 \cdot 4$ $11 \cdot 8$ $3 \cdot 8$ $84 \cdot 4$

free aluminium chloride therefore being present in the system at any time. The results show certain trends: (a) a decrease of the percentage of p-isomer, (b) a substantial increase in the proportion of o- and m-isomers, and (c) a sharp decrease in dechlorobenzoylation, all with increase in temperature. These variations were also observed over the narrower range 100-125° in the solvents chlorobenzene, s-tetrachloroethane, and benzoyl chloride (Table 1). The variations in isomer proportions formed can be used to estimate differences in Arrhenius activation energies at the o-, m-, and p-positions in chlorobenzene. If it can be assumed that the mechanisms at the three substituent positions are the same, and that differences in rates are due only to changes in activation energies, *i.e.* with a constant pre-exponential factor, then e.g. $\sqrt[6]{p}-\sqrt[6]{0} = e^{E_o - E_p/RT}$. Plots of the

\log_{10} of the product ratios vs. $1/T$ gave satisfactory
straight lines, from which the relationships were derived:
$E_{o} = E_{p} + 1.9$ (±0.1) kcal./mole, $E_{m} = E_{p} + 5.4$
(± 0.2) kcal./mole, $E_m = E_o + 3.3$ (± 0.2) kcal./mole.
These results are satisfactorily self-consistent, but doubt
remains about the correctness of the assumptions. The
results here found disprove the results obtained by
Koike and Okawa. ⁷

It was observed that reactions carried out for a long time in ethylene chloride tended to give tarry by-products. Shortening the duration resulted in satisfactory yields of a much cleaner product, but also in a change in isomer distribution (Table 5). The product after a 10 min. reaction period contained only ca. 4% of the o-isomer, whereas the eventual proportion is nearly

TABLE 5

The effect of duration of reaction on the benzovlation of chlorobenzene in ethylene chloride at 75°

Duration	Yield	Chlorobe	Benzo-		
(hr.)	(%)	0-	m-	p-	phenone (%)
0.16	1.0	$4 \cdot 2$	1.5	90.5	3.8
1	10	5.5	1.0	90.5	$3 \cdot 0$
2	52	7.5	$1 \cdot 1$	90.7	0.7
5	72	7.9	0.7	91.4	< 0.1
25	ca. 45	$7 \cdot 2$	0.8	92.0	< 0.1

double that value. It may be noted that again conditions which result in small yields of ketones produce relatively high proportions of benzophenone. The change of isomer composition with time is possibly due to a slow, aluminium chloride-catalysed, chlorineisomerisation.22

The rate of the Friedel-Crafts benzoylation of chlorobenzene relatively to benzene was determined, from a duplicate competitive experiment, in nitrobenzene solution at 25° (Table 6). Brown and Jensen⁹ have

TABLE 6

Relative rate data for the benzoylation of chlorobenzene in nitrobenzene at 25°

Reactivity ratio	Isomer distri- bution (%)			Partial rate factors		
$(k_{\rm chlorobenzene}/k_{\rm benzene})$	6	m	₽`	ot	$m_{\rm f}$	Pt `
$\left. \begin{smallmatrix} 0 \cdot 0263 \\ 0 \cdot 0258 \end{smallmatrix} ight\} 0 \cdot 0260$	$4 \cdot 2$	$0 \cdot 2$	95 ∙6	0.00328	0.00016	0.150

reported a relative rate of 0.0115, and $p_i = 0.0690$ for the benzoylation of chlorobenzene in benzoyl chloride solution at 25°. These values differ from ours not alone because of the difference in the solvent; the earlier values⁹ could only have been approximate. A rate constant for chlorobenzene was determined only at 70° and a rate for 25° found by extrapolation, using a value for the entropy of activation (-27 e.u.) found for the benzoylation of benzene (or toluene). It had further been assumed,⁹ wrongly, that acylation would occur

²¹ F. R. Jensen and H. C. Brown, J. Amer. Chem. Soc., 1958, 80, 3039. ²² K. R. Buck, N. M. Scollick, and D. Simpson, Chem. and

²⁰ O. C. Dermer and R. A. Billmeier, J. Amer. Chem. Soc., 1942, **64**, 464; O. C. Dermer, D. M. Wilson, F. M. Johnson, and V. H. Dermer, J. Amer. Chem. Soc., 1941, 63, 2881.

Ind., 1964, 494.

exclusively at the p-position. Our value for the relative rate chlorobenzene/benzene falls within the range of values (0.0115-0.35) determined for a number of electrophilic substitution reactions.²³

EXPERIMENTAL

Materials.—The chlorobenzophenones were obtained by standard Friedel-Crafts acylations of excess of benzene with the corresponding acyl chloride: o-chlorobenzophenone, m.p. 43°, m-chlorobenzophenone, m.p. 82—83°, and p-chlorobenzophenone, m.p. 75.5°. The chlorobenzene used was gas-chromatographically pure.

Gas Chomatography.—Analyses were carried out routinely on a glass column (1 m. \times 0.3 cm.) packed with 10% Apiezon L on Celite, operated at 185° with argon carrier gas, flow rate 60 ml./min. Sample size was approximately 2×10^{-5} g. The competitive acylations were analysed on a stainless steel column (2 m. $\times \frac{1}{8}$ in. o.diam.), packed with 4% Carbowax 20M on Chromosorb P, operated at 200° with nitrogen carrier gas, with inlet pressure 10 lb./sq. in. Sample size was approximately 0.5 µl. Mass corrections were applied where appropriate. Kováts retention indices ²⁴ were determined on 10% Apiezon L on Celite, at 175°, with argon at 30 ml./min.; the values were benzophenone 1677, o-chlorobenzophenone 1768, m-chlorobenzophenone 1826, and p-chlorobenzophenone 1844.

Specimen Friedel-Crafts Acylations.—(a) Perrier method. To a stirred mixture of aluminium chloride (5.9 g.) and nitrobenzene (20 ml.), benzoyl chloride (6.2 g.) was added. The mixture was then heated to the appropriate temperature, and chlorobenzene (5.0 g.) was then quickly added. The reaction was continued until evolution of hydrogen chloride had practically ceased. The mixture was poured

²³ L. M. Stock and H. C. Brown, 'Advances in Physical Organic Chemistry,' ed. V. Gold, Academic Press, London, 1963, vol. I, ch. 2.

on ice (50 g.)-10N-hydrochloric acid (20 ml.); the organic layer was separated and washed with 3N-hydrochloric acidand then with water. The solvent was removed by steam distillation to leave a solid product, a portion (*ca.* 1 g.) of which was dissolved in benzene and chromatographed on alumina; the combined eluates were evaporated, and the residue analysed by g.l.c.

(b) Bouveault method. Aluminium chloride (5.9 g.) and chlorobenzene (5.0 g.) were added to nitrobenzene (20 ml.) and the mixture was stirred and heated to the desired temperature. Benzoyl chloride (6.2 g.) was then added rapidly. Further treatment was as under (a).

(c) Elbs method. Chlorobenzene $(5 \cdot 0 \text{ g.})$, nitrobenzene (20 ml.), and benzoyl chloride (6·2 g.) were mixed, stirred, and heated to the desired temperature. Aluminium chloride (5·9 g.) was then added rapidly. Further treatment was as under (a).

Competitive Benzoylation of Chlorobenzene and Benzene in Nitrobenzene at 25°.—Aluminium chloride (4 g., 1 mol.) was dissolved in nitrobenzene (10 ml.) and benzoyl chloride (4.2 g., 1 mol.) added, and the vessel placed in a thermostatted bath at 25°. Benzene (3.47 g., 1.5 mol.) and chlorobenzene (5.0 g., 1.5 mol) in nitrobenzene (10 ml.) were added rapidly, and the mixture was set aside at 25° for 8 days. The mixture was then poured into cold 3N-hydrochloric acid (70 ml.), the organic layer was separated and washed with 3N-hydrochloric acid and water, and then dried (CaCl₂). A sample (4 g.) was then passed through a short column of alumina, and the ketones were eluted with benzene. Most of the benzene was then distilled off, and the residue was analysed by g.l.c. In calculating relative reactivities allowance was made for the normal formation of some benzophenone from chlorobenzene under the reaction conditions.

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²⁴ E. Kováts, *Helv. Chim. Acta*, 1958, **41**, 1915; 1959, **42**, 2709; L. S. Ettre, *Analyt. Chem.*, 1964, **36**, 31A.