TABLE II

CHROMATOGRAPHY OF PRODUCTS FROM HYDROLYSIS OF IV

Solvent	R_f values: Hydrolysis product	Uridine	IV
A[a]	0.46	0.46	
B[a]	0.49	0.49	
Ethyl acetate[b]	0.015	0.015	0.35
Dioxane[b]	0.73	0.72	0.87
Tetrahydrofuran[b]	0.63	0.63	0.83

[a] Paper chromatography. [b] Thin layer chromatography on silica sheets.

N-Benzoyladenosine 2′,3′-Carbonate.—A solution made from 0.371 g (1 mmole) of N-benzoyladenosine[15] and 0.300 g (1.5 mmole) of *p*-nitrophenyl chloroformate and 10 ml of dry pyridine was stirred for 3 days at room temperature and then mixed with 150 ml of cold ether. The resulting precipitate was dissolved in a minimum volume of ethanol and chromatographed on silica gel by elution successively with ethyl acetate, ethyl acetate-tetrahydrofuran (9:1, v/v), and tetrahydrofuran. The ether solution was concentrated to a volume of ~2 ml and also chromatographed on silica gel with the same solvents. From the ethyl acetate fractions was obtained a total of 0.200 g (50%) of N-benzoyladenosine 2′,3′-carbonate, mp 164–165.5°; principal bands in the infrared were at 5.57, 5.92, 6.18, and 6.29 μ.

Anal. Calcd for $C_{18}H_{15}N_5O_6$: C, 54.42; H, 3.80; N, 17.62. Found: C, 54.35; H, 3.74; N, 17.59.

From the pure tetrahydrofuran fractions was recovered 0.160 g of N-benzoyladenosine. On the basis of the benzoyladenosine unrecovered the yield of N-benzoyladenosine 2′,3′-carbonate was 90%.

N-Benzoyl-5′-O-trityladenosine 2′,3′-Carbonate.—A solution of 0.30 g (1.1 mmole) of triphenylmethyl chloride and 0.300 g (0.75 mmole) of N-benzoyladenosine 2′,3′-carbonate in 10 ml of pyridine was stirred for 7 days at room temperature and then poured onto crushed ice. The gummy precipitate which formed was taken up in chloroform and the aqueous solution was extracted twice with chloroform. After drying with sodium sulfate, the chloroform solutions were combined and concentrated. Recrystallization of the resulting gum from ethyl acetate gave 0.350 g (73%) of N-benzoyl-5′-O-trityladenosine 2′,3′-carbonate, mp 134–135° with prior softening. After further purification by chromatography on silica gel with ethyl acetate, the product melted at 134–135.5° and exhibited bands in the infrared spectrum at 5.56, 5.92, 6.2, 9.2, and 14.2 μ.

Anal. Calcd for $C_{37}H_{29}N_5O_6$: C, 68.08; H, 4.57; N, 10.95. Found: C, 68.61; H, 4.46; N, 11.00.

R_f values for chromatography of the adenosine derivatives on silica thin layer slides are presented in Table III.

TABLE III

THIN LAYER CHROMATOGRAPHIC DATA FOR ADENOSINE DERIVATIVES

Solvent	N-Benzoyl-adenosine	N-Benzoyl-adenosine 2′,3′-carbonate	N-Benzoyl-5′-O-trityladenosine 2′,3′-carbonate
Ethyl acetate	0.05	0.45	0.83
Acetonitrile	0.15	0.71	0.84
Acetone	0.55	0.83	0.98
Ethanol	0.64	0.72	0.75
Dioxane	0.68	0.80	0.87

---

[15] Prepared by procedure of R. H. Hall, *Biochemistry*, **3**, 769 (1964).

Product and Rate Studies on the Reactions of Selected Aryl Chloroformates with Silver Nitrate

MATTHEW J. ZABIK[1] AND ROBERT D. SCHUETZ

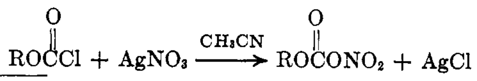
Department of Chemistry and the Institute of Biology and Medicine, Michigan State University, East Lansing, Michigan

Received March 18, 1966

The reactions of 13 aryl chloroformates prepared from phosgene and various phenols with silver nitrate in acetonitrile were examined. The reaction products, obtained in high yield from the 4-substituted phenyl chloroformates, were 4-substituted 2-nitrophenols. The 2,6-disubstituted phenyl chloroformates yielded two products; the expected 4-nitro-2,6-disubstituted phenols and biphenylquinones, while the 2,4,6-trimethylphenyl chloroformate yielded, as the major product, a substituted stilbenequinone. At equal molar concentrations the initial reaction rates of the 4-substituted phenyl chloroformates with silver nitrate at 10, 21, and 31° were second order. With a fivefold molar excess of silver nitrate, the initial rates at 21° were pseudo first order. The change in entropy, ΔS^*, was negative ranging from −40.7 for the 4-nitro to −5.1 for the 4-methoxy substituent. Good Hammett correlation was obtained for ρ values of 1.5017 (10°), 1.1482 (21°), and 0.9211 (31°) for the reactions at equal molar concentrations of reactants and 0.9383 (21°) for the reaction with excess silver nitrate.

Wolfrom and Chaney[2] in 1961, reported an attempt to prepare phenyl nitrate by the interaction of phenyl chloroformate with silver nitrate. They obtained *o*-nitrophenol in a 65% yield as a rearrangement product instead of the expected aryl nitrate. Since their initial report, no further studies on this aromatic chloroformate rearrangement reaction have appeared in the literature. The present investigation was undertaken to obtain information concerning the products and kinetics of the reactions of aryl chloroformates with silver salts to consider possible mechanisms for this type of rearrangement reaction.

Considerable research has been reported on the reactions of aliphatic chloroformates and some bears on on the reactions of aryl chloroformates with silver salts. Boschan,[3] in 1959, reported the preparation, in high yields, of aliphatic nitrate esters from the reaction of silver nitrate with aliphatic chloroformates. He demonstrated that 75% of the alkyl-oxygen (R–O) bond in the chloroformate remained intact by O^{18}-labeling experiments and that the reaction proceeded mainly with retention of configuration (70% retention, 30% inversion) in the migrating R group. Hence, it was postulated that an SN1 type of decomposition of this intermediate was operative with some action also occurring by an ionic mechanism. Mortimer[4] in a study of alkyl nitratocarbonates, found that reaction 2 paralleled roughly reaction 1 in velocity at moderate temperature (40°), but was much slower than 1 below 0°.



$$\mathrm{RO\overset{\overset{\displaystyle O}{\|}}{C}Cl + AgNO_3 \xrightarrow{CH_3CN} RO\overset{\overset{\displaystyle O}{\|}}{C}ONO_2 + AgCl} \qquad (1)$$

---

[1] Abstracted in part from the Ph.D. Dissertation of M. J. Zabik, Michigan State University, 1965.

[2] A. Chaney and M. L. Wolfrom, *J. Org. Chem.*, **26**, 2998 (1961).

[3] R. Boschan, *J. Am. Chem. Soc.*, **81**, 3341 (1959).

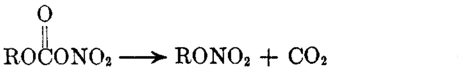
[4] G. A. Mortimer, *J. Org. Chem.*, **27**, 1876 (1962).

TABLE I

PHYSICAL DATA. ARYL CHLOROFORMATES

Chloroformate	Bp, °C (mm)	Mp, °C	$n^{19}D$	C=O, cm^{-1}	Yield, %	Ref
p-Methoxyphenyl	49 (0.27)	...	1.5110	1778	96.3	..
p-Methylphenyl	109 (30.0)	...	1.5110	1780	98.1	*a*
p-Phenylphenyl	120 (4)	39–40	...	1780	91.8	*b*
Phenyl	83 (12)	...	1.5007	1780	96.7	*c*
p-Bromophenyl	80 (2.0)	...	1.5583	1780	91.8	..
p-Chlorophenyl	108 (19.0)	...	1.5401	1769 + 1788	95.1	*d*
p-Nitrophenyl	159–162[e] (19.0)	81–81.5[f]	...	1765	70.2	*g*
2,4,6-Trimethylphenyl	64 (3)	...	1.5114	1777	95.5	..
2,6-Dimethylphenyl	71–62 (5.5–6.0)	...	1.4993	1777	85.4	*h*
2,6-Diisopropylphenyl	89 (2.8)	...	1.5001	1781	98.8	..
α-Naphthyl	130–132 (5.0)	...	...	1778	82.8	*d*
β-Naphthyl	158 (9.7)	65–65.5	...	1777	92.0	*i*

[a] F. K. Beilstein, "Handerbuch der Organischen Chemie, Vol. 6, 1923, p 159. [b] R E. Oesper, M. Boker, and W. A. Cook, *J. Am. Chem. Soc.*, **47**, 2609 (1925). [c] J. H. Barnes, M. V. A. Chapman, P. H. McCrea, P. G. Marshall, and P. A. Walsh, *J. Pharm. Pharmacol.*, **13**, 39 (1961). [d] A. Einhorn and L. Rothlauf, *Ann. Chem.*, **382**, 252 (1911). [e] Decomposes violently on distillation. [f] Recrystallized from petroleum ether. [g] L. C. Raifork and G. O. Inman, *J. Am. Chem. Soc.*, **56**, 2609 (1934). [h] Footnote *a*, p 412. [i] M. A. Long and G. M. Forker, "Handbook of Chemistry," 9th ed, Handbook Publishers, Inc., Sandusky, Ohio, 1956, p 634.



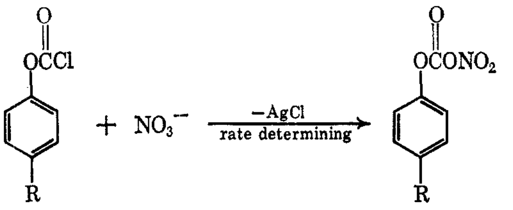
$$\mathrm{RO\overset{\displaystyle O}{\overset{\|}{C}}ONO_2 \longrightarrow RONO_2 + CO_2} \qquad (2)$$

Boschan[3] further reported that cholesteryl chloroformate reacts with silver trifluoroacetate to yield cholesteryl trifluoracetate (77%). An example of a similar type of a rearrangement was reported by Norris[5] in which dialkylcarbamyl chlorides react with silver nitrate to yield dialkylnitramines (14–48%) as the main product.

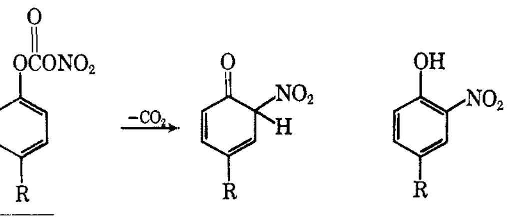
In the aliphatic chloroformate rearrangement reactions thus far reported, it is postulated that the reaction proceeds in two stages: reaction of the nitrate ion with the chloroformate to yield a nitratocarbamate and silver chloride followed by rearrangement of the nitratocarbamate to the nitrate ester and carbon dioxide.

Results and Discussion

The main conclusions based on data reported here on the rearrangement of aryl chloroformates by silver nitrate in acetonitrile are that the major products are 2-nitro-4-substituted phenols; a free-radical mechanism is not operative nor is an intermolecular mechanism; the reaction rate is enhanced by the addition of pyridine; the initial reaction rate is second order at equal molar concentrations of reactants but is pseudo first order in the presence of excess silver nitrate; the entropy change, ΔS^*, is negative; and the value of the Hammett ρ is positive. The observations suggest that the mechanism for the rearrangement of *p*-substituted phenyl chloroformate with silver nitrate in acetonitrile is a two-step sequence(eq 3 and 4), with the first step being rate controlling.



(3)



(4)

The aryl chloroformates were readily obtained, in 0.5 *M* quantities, by the addition of N,N-dimethylaniline to a solution of the phenol and phosgene in benzene as a reaction media. Distillation of the aryl chloroformates with the exception of *p*-nitrophenyl chloroformate gave yields of pure products in the range 85.4–98.8%. On two successive attempts to distil the *p*-nitrophenyl chloroformate at high vacuum (0.1 mm), it decomposed violently. However, it was readily purified by recrystallization from petroleum ether (bp 30–60° *r* 70.2%). Table I summarizes the physical properties of the aryl chloroformates prepared.

Reinvestigation of the reaction of phenyl chloroformate with silver nitrate[2] showed that a mixture of nitrated products was formed consisting of 65–70% *o*-nitrophenol plus 15–20% *p*-nitrophenol, with no *m*-nitrophenol being detectable in the reaction products. In this and subsequent reactions, acetonitrile was the choice of reaction solvents since it dissolves both the chloroformate and the silver nitrate yielding a homogeneous reaction solution.

The reactions of the *para*-substituted phenyl chloroformates were conducted at 20° on a 0.05-mole basis. The *para* substituents included methyl, methoxy, phenyl, bromo, chloro, and nitro. The products obtained in each case were 4-substituted 2-nitrophenols, produced in yields of 72.8–99.1%. Table II summarizes data for these reactions.

These reactions were rerun using a fivefold excess of silver nitrate. They proceeded considerably faster than with equal molar quantities of reactants as evidenced by visual observation of the rate of silver chloride precipitation. Increased initial concentration of silver nitrate and enhanced reaction rate had no major effect on the yields of the 4-substituted 2-nitrophenols (Table II).

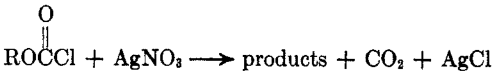
The *para*-substituted phenyl chloroformate reactions with silver nitrate were also examined in the presence of pyridine. The reaction is considerably accelerated. A reaction started at an initial temperature of 20° with an equal molar amount (0.05 mole) of pyridine

---

(5) W. P. Norris, *J. Am. Chem. Soc.*, **81**, 3346 (1959).

TABLE II

PRODUCT DATA. REACTION OF *para*-SUBSTITUTED PHENYL AND NAPHTHYL CHLOROFORMATES WITH SILVER NITRATE

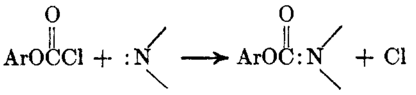


$$\mathrm{RO\overset{O}{\overset{\|}{C}}Cl + AgNO_3 \longrightarrow products + CO_2 + AgCl}$$

R	Product	Recrystn solvent	Mp, °C	Reaction	Yield, %			Ref
					Product	AgCl	CO_2	
p-Methoxyphenyl	2-Nitro-4-methoxyphenol	90–120° ligroin	79–80	1[a]	82.7	98.8	88.3	*b*
				2[c]	83.4	98.9	87.3	
				3[d]	90.8	97.6	88.2	
p-Methylphenyl	2-Nitro-4-methylphenol	Amyl alcohol	31–32	1	89.0	98.9	93.2	*e*
				2	94.4	97.7	90.1	
				3	90.1	99.3	92.7	
p-Phenylphenyl	2-Nitro-4-phenylphenol	Ethyl ether	65–66	1	99.1	99.8	97.2	*f*
				2	98.6	98.8	92.3	
				3	95.3	96.8	98.1	
Phenyl	2-Nitrophenol and	Ethyl ether	44.5–45.0	1	67.3 (*o*), 18.9 (*p*)	98.6	95.2	*g*
	4-Nitrophenol			2	69.3 (*o*), 22.4 (*p*)	99.3	96.5	
			113.5–114.0	3	69.1 (*o*), 18.3 (*p*)	97.3	97.3	
p-Bromophenyl	2-Nitro-4-bromophenol	Ethyl ether	88–89	1	97.7	99.0	98.5	*h*
				2	98.0	99.1	98.4	
				3	95.3	95.2	97.3	
p-Chlorophenyl	2-Nitro-4-chlorophenol	Ethyl ether	86.5–87.0	1	87.2	97.7	90.3	*i*
				2	92.6	98.1	91.5	
				3	92.2	96.3	95.5	
p-Nitrophenyl	2,4-Dinitrophenol	Ethyl ether	110.3–112.7	1	93.5	95.4	94.1	*j*
				2	95.1	98.4	95.1	
				3	93.9	96.7	94.0	
α-Naphthyl	2-Nitro-1-naphthol	Ethyl alcohol	128.0–128.5	1	66.6	97.5	73.2	*k*
β-Naphthyl	1-Nitro-2-naphthol	Water	103–104	1	38.6	91.9	83.2	*l*

[a] Reaction 1, equal concentrations of reactants. [b] Table I, footnote *h* [c] Reaction 2, equal concentrations of reactants plus 0.01 ml of pyridine. [d] Reaction 3, fivefold excess of silver nitrate. [e] Table I, footnote *i*. [f] Table I, footnote *a*, p 243. [g] Table I, footnote *a*, p 238. [h] Table I, footnote *i*, p 524. [i] Table I, footnote *a*, p 615. [j] Table I, footnote *a*, p 653. [k] M. Matzer, R. P. Kurkjy and R. J. Cotter, *Chem. Rev.*, **64**, 645 (1964). [l] Reference 7.

added, reached its reflux temperature in 0.5 min, and was complete in 2 min. This reaction time was short compared to the 3 or 4 hr required for the same reaction conducted in the absence of pyridine. It is well known[6] that tertiary amines form complexes with aryl chloroformates, and this suggests that the rate-determining step, in the rearrangement of aryl chloroformates with



$$\mathrm{ArO\overset{O}{\overset{\|}{C}}Cl + :N\!\!\lessdot \longrightarrow ArO\overset{O}{\overset{\|}{C}}:N\!\!\lessdot + Cl}$$

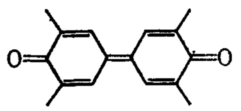
silver nitrate, is the initial attack by nitrate ions on the chloroformate. The presence of pyridine assists in the ionization of the C–Cl bond by nucleophilic attack on the carbonyl carbon, thus enhancing the reaction rate. It was also found that only a trace (0.001 ml) of pyridine is required for a large rate enhancement, suggesting that the pyridine is regenerated and reused by successive chloroformate molecules, thus, acting as a catalyst.

The fact that the product yields in these rearrangement reactions were quite high recommends them as a good preparative procedure for obtaining *o*-nitrophenols.

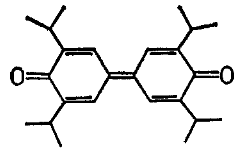
Similar reactions involving the naphthyl chloroformates were also conducted at 20° on a 0.05-mole scale. These yielded 28.6% of 1-nitro-2-naphthol and 66.6% of 2-nitro-1-naphthol from β- and α-naphthyl chloroformates, respectively. In each case some black amorphous intractable material was also obtained.

Reactions of aryl chloroformates with substituents blocking the *ortho* positions were conducted to determine whether only the *para* product would result if reaction occurred. Aryl chloroformates studied included 2,6-dimethyl- and 2,6-diisopropylphenyl chloroformates. The highly hindered, *ortho*-blocked 2,6-di-*t*-butylphenyl chloroformate, an obvious choice for this examination, unfortunately could not be prepared, probably due to steric hindrance.

On reaction with silver nitrate, 2,6-dimethylphenyl chloroformate yielded 4-nitro-2,6-dimethylphenol (*para* rearrangement, mp 172–173°) and 0.78 g of a dark red compound which decomposed at 224°. This was identified as 3,5,3′,5′-tetramethyl-(4,4′)-diphenoquinone, a quinone dimer.[7]



The 2,6-diisopropylphenyl chloroformate, under the same reaction conditions, yielded 4-nitro-2,6-diisopropylphenol (73%) and again a small amount of a dark red compound identified as 3,5,3′5′-tetraisopropyl-(4,4′)-diphenoquinone, mp 214°.[7]



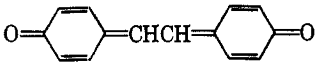
---

(6) M. Matzner, R. P. Kurkjy, and R. J. Cotter, *Chem. Rev.*, **64**, 645 (1964).

(7) T. Berreras, M.S. Thesis, Michigan State University, 1965.

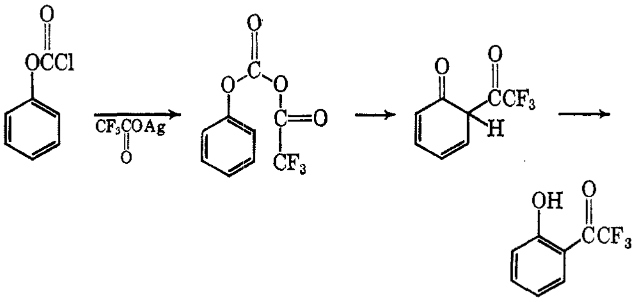
Formation of the *p*-nitro compound as the major product indicates that *para* rearrangement is essentially unhindered by blocking the *ortho* positions. Further, the product yields obtained from the dimethyl and diisopropyl compounds suggests that there is little or no effect on the *para* rearrangement as a result of the size of groups in the *ortho* positions.

The reaction of 2,4,6-trimethyphenyl chloroformate with silver nitrate was run to determine whether the nitro group would enter the *meta* position. As this reaction proceeded, dark red crystals separated from solution with the precipitation of the silver chloride. The red crystalline product melted at 245° and was identified as 3,5,3′,5′-tetramethyl-(4,4′)-stilbenequinone.



Reactions of aryl chloroformates with silver salts of acetic and trifluoroacetic acid were conducted under the same experimental conditions as were those with silver nitrate to determine whether acetyl or trifluoroacetyl groups would enter the aromatic nucleus similarly to the nitro group. With silver acetate, the only products obtained were nonacylated phenols (90% yields).

When silver trifluoroacetate was used, a substituted phenyl trifluoromethyl ketone was obtained in 95% yield. Conceivably this reaction could proceed through the same type of mechanism postulated for the reaction with silver nitrate. The carbonyl carbon of the trifluoromethyl acetate is more positive, owing to the three fluorine atoms ($-I$) than is the acetate carbonyl and should participate more readily in the postulated rearrangement mechanism. This could explain why silver acetate failed to yield rearrangement products in these reactions. There is some similarity between the nitro and the trifluoromethyl group in that in such a rearrangement both have positive charges on the central atom involved in the migration (nitrogen and carbonyl carbon atoms, respectively). Thus, it appears that this is a prerequisite for this type of a rearrangement to occur.



Experiments were conducted in which *p*-methoxyphenol- or *p*-methoxyphenoxide were added to *p*-phenylphenyl chloroformate and silver nitrate in acetonitrile media to determine whether a nitronium ion (NO_2^+) was formed in the reaction sequence which in turn reacted with the methoxyaryl ring in an intermolecular process. The sole product isolated in these experiments was 2-nitro-4-phenylphenol in greater than 90% yields. However, some difficulty was encountered with sodium *p*-methoxyphenoxide, in that it instantly reacted with silver nitrate to yield a black precipitate, which slowly (12 hr) underwent a color change to a light cream material. Thus, the over-all mechanism for the reaction between *p*-phenylphenyl chloroformate and silver nitrate may be changed and the results of these trapping experiments must be taken with reservation. Nevertheless, the results of both experiments showed that an intermolecular reaction had not occurred. These results, however, do not rule out the possibility of a closely bound ion pair where the NO_2^+, if formed, could not have participated in an intermolecular reaction mechanism.

The reaction between *p*-phenylphenyl chloroformate and silver nitrate was also conducted in the presence of α-methylstyrene and galvinoxyl to determine if the reaction proceeded by a free-radical process. In separate experiments galvinoxyl and α-methylstyrene were added at the initiation of the reaction and in each case the yield of 4-phenyl-2-nitrophenol ranged between 94 and 98%. These observations rule out a free-radical mechanism being operative in the rearrangement reaction under the experimental conditions used in these studies. However, these results do not rule out the possibility that the nitrate carbonate decomposition could involve the formation of caged radicals which would not be detected by galvinoxyl or α-methylstyrene.

Experiments were conducted to determine whether other nitrate salts such as lead nitrate or mercuric nitrate would react with aryl chloroformates to yield the same products as the reactions with silver nitrate. In all cases the only product obtained was the unsubstituted phenol corresponding to the original aryl chloroformate. These results indicate that the silver ion must have a specific role in the reaction. Reactions conducted using equal molar (0.05 mole) concentrations of silver nitrate and aryl chloroformate with a fivefold excess of silver sulfate showed no increase in reaction rate or any change in reaction order from reactions conducted in the absence of excess silver sulfate. Thus, any role the silver ion plays in the reaction is not involved in the rate-determining step.

Quantitative determinations of the carbon dioxide liberated in the rearrangement reactions of the aryl chloroformates were carried out on the reactions run at 20°. The results are summarized in Table II. They indicate that the amount of carbon dioxide liberated corresponds closely with the percentage yield of the nitrated phenol products.

A semiquantitative determination of the very high yield of silver chloride obtained in all cases indicates that chlorine from the chloroformate is removed as chloride ions. This strongly suggests that the first step is quantitative and that subsequent steps (elimination of carbon dioxide) may or may not be, depending on the particular chloroformate involved.

Determination of the reaction rates of the *para*-substituted phenyl chloroformates was followed by measuring the rate of disappearance of the 1777-cm^{-1} chloroformate carbonyl peak in the infrared. The *para*-substituted phenyl chloroformates were all found to obey Beer's law at the concentrations used in this work.

Results of the kinetic determinations at reaction temperatures of 10, 21, and 31° and at equal molar concentrations of reactants were plotted for second-order kinetics (Figures 1–3). Several conclusions can be

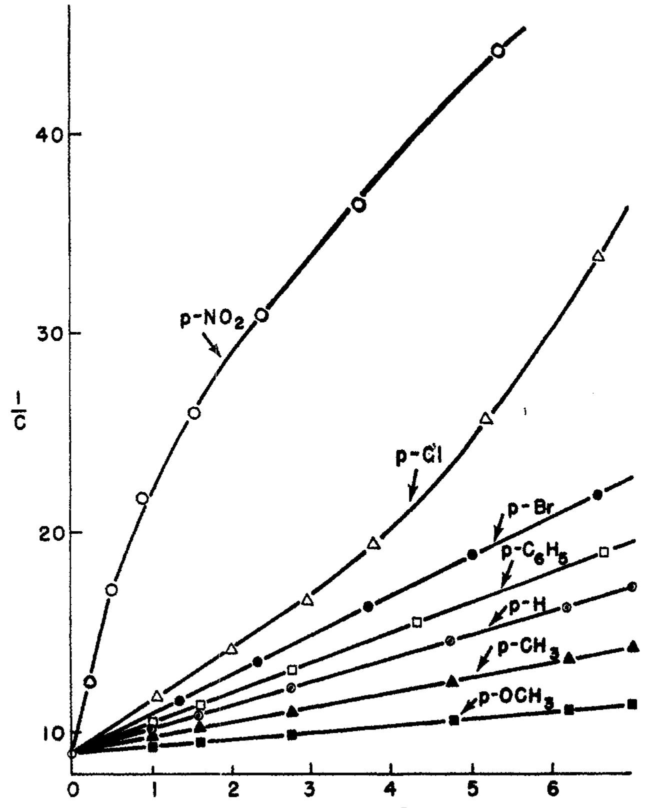


Figure 1.—Second-order kinetic plots for the reactions of *p*-substituted phenyl chloroformate with silver nitrate (equal molar concentrations) at 10°.

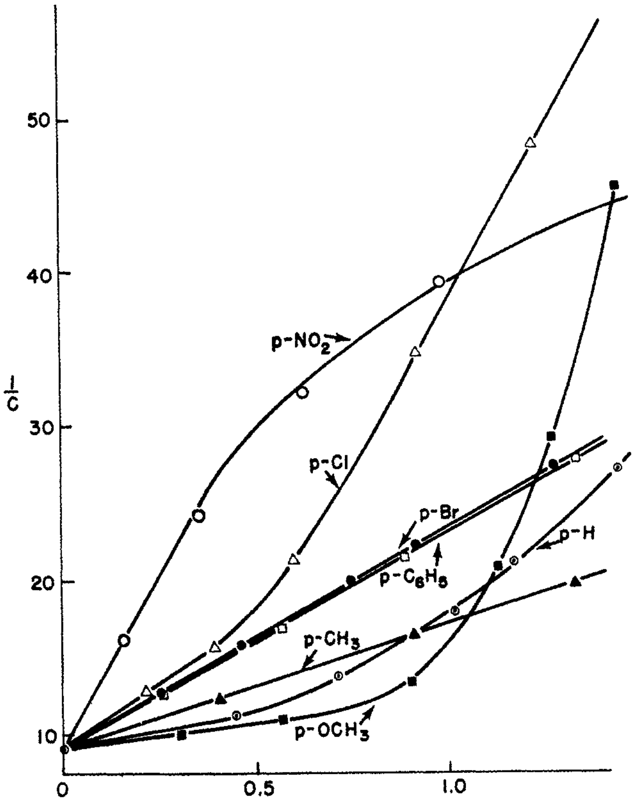


Figure 3.—Second-order kinetic plots for the reactions of *para*-substituted phenyl chloroformates with silver nitrate (equal molar concentrations) at 31°.

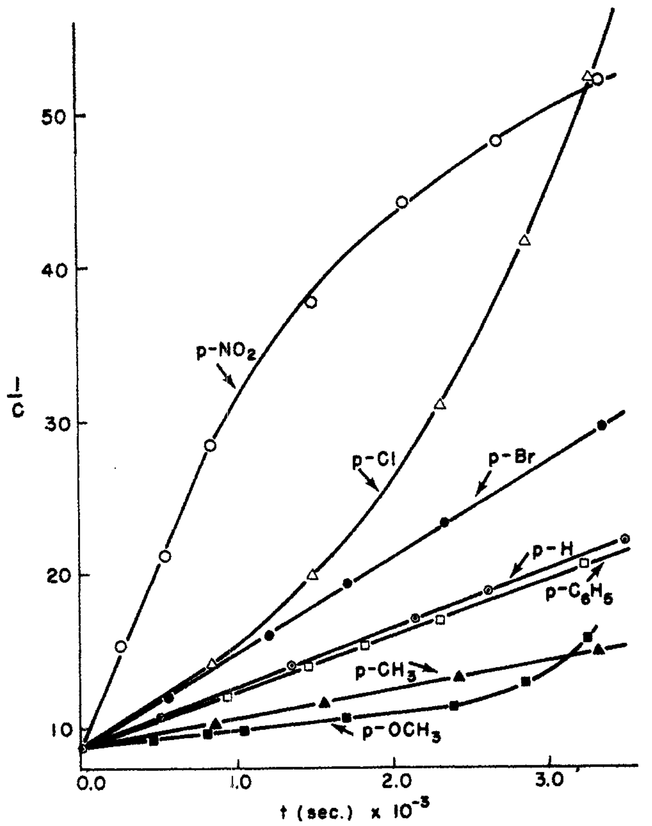


Figure 2.—Second-order kinetic plot for the reaction of *para*-substituted phenyl chloroformates with silver nitrate (equal molar concentration) at 21°.

drawn from these data. First, as the reaction temperature increased, the kinetic results became more erratic, especially at 31°. Secondly, the plots for the kinetic determinations at 10 and 21° are quite similar. These observations indicate strongly that no simple reaction order exists for the over-all reaction (0–100% completion). However, when the initial 20% of each of the kinetic curves is examined it is readily seen that these portions of the plots are straight-line functions following a second-order rate law. Further, it can also be seen that in the initial 20% of the reaction there is a definite increase in the reaction rate in going from *p*-methoxy- to *p*-nitrophenylchloroformates. Consequently, the following data and its discussion deals with the initial reaction rates (20% completion) and not to over-all rates of reaction. This is also true for the *p*-methyl- and *p*-phenylphenyl chloroformate reactions, even though these followed second-order kinetics to 90% completion at 10 and 21°.

Possibly the over-all kinetic abnormalities were due to autocatalytic effects of one of the products or to a surface area effect. To examine experimentally these possibilities kinetic determinations were conducted with reaction product or freshly precipitated silver chloride added at the initiation of the reaction, or finally with glass wool added to the reaction flask. None of these variables had an effect on the rate of the reaction. However, such observations fail to rule out effects which an unstable intermediate could have on the reaction rate. The effect of water in the reaction medium was also examined. Water decreased the reaction rate probably owing to the formation of a heterogeneous mixture (the chloroformate separates from the reaction solution on the addition of water).

Pseudo-first-order rate constant, at 21°, for the

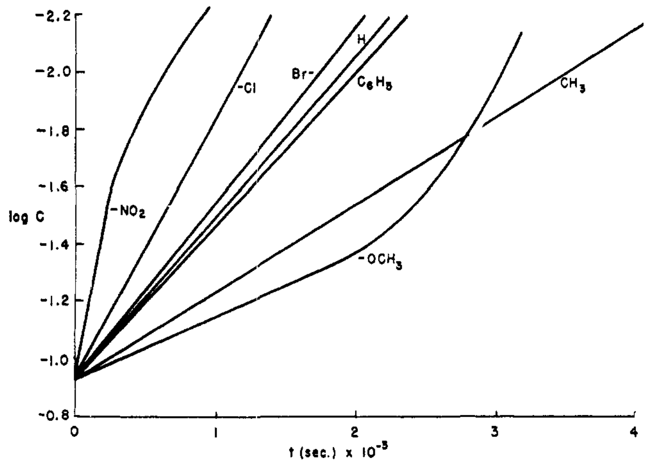


Figure 4.—Pseudo-first-order kinetic plot at 21° for the reaction of *para*-substituted phenyl chloroformate with a fivefold excess of silver nitrate.

reactions of the *para*-substituted phenyl chloroformates with silver nitrate were determined by flooding the reaction with a fivefold excess of silver nitrate (Figure 4). Under these reaction conditions first-order plots gave good straight lines for 80% of the reaction. As in the previous cases subsequent kinetic data were determined for the initial (20%) rates only. Obtaining pseudo-first-order kinetics under these reaction conditions indicates that silver nitrate is involved in the rate-determining step. Examination of the combined second- and pseudo-first-order kinetic data indicates that the first step in the reaction sequence is rate determining.

The activation parameters calculated from the kinetic data indicate that the particular substituent on the aromatic ring has a large effect on the over-all rate of reaction. Activation energies vary from 8.0 for *p*-nitro- to 18.8 kcal/mole for *p*-methoxyphenyl chloroformates (Table III).

Table III

Initial Rate Constants and Activation Parameters for the Reaction of *para*-Substituted Phenyl Chloroformates with Silver Nitrate

para substituent	Temp, °C	$k_1 \times 10^3$/ mole sec	E_a, kcal/mole	ΔS^*, eu
Hydrogen	10	1.12		
	21	3.79	18.8	−6.7
	31	5.01		
Methoxy	10	0.34		
	21	1.27	20.1	−5.1
	31	3.95		
Methyl	10	0.72		
	21	2.16	19.6	−6.1
	31	8.24		
Phenyl	10	1.40		
	21	3.62	19.0	−6.6
	31	14.82		
Bromo	10	1.84		
	21	5.81	16.8	−13.7
	31	14.74		
Chloro	10	2.68		
	21	6.62	14.6	−20.9
	31	16.34		
Nitro	10	16.41		
	21	23.52	8.0	−40.7
	31	44.41		

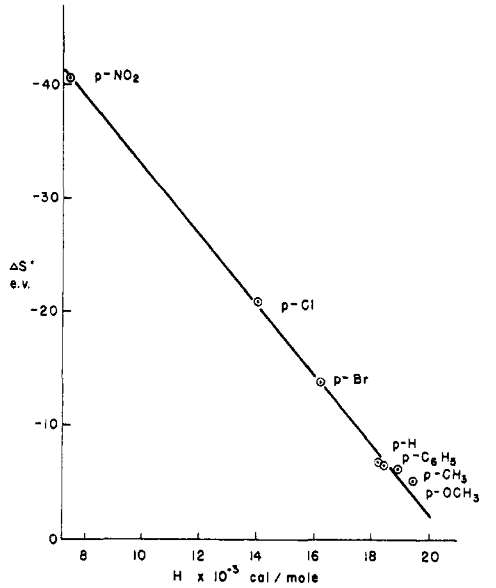


Figure 5.—Graph of ΔS^* *vs.* ΔH^* for the determination of the isokinetic temperature for the reaction of the *para*-substituted phenyl chloroformates with silver nitrate (equal molar concentrations); isokinetic temperature, T = 52.0°.

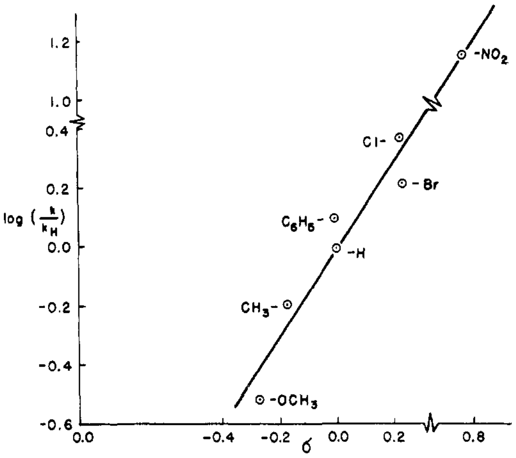


Figure 6.—Plot of the Hammett equation for the reaction of *para*-substituted phenyl chloroformates with silver nitrate (equal molar concentrations at 10° (ρ = 1.5017).

The negative entropy (ΔS^*) values indicate that there is a decrease in freedom of reactants with a very large ΔS^* difference between the *p*-methoxyphenyl (ΔS^* = −5.1) and *p*-nitrophenyl (ΔS^* = −40.7) chloroformates.

From the physical data an isokinetic temperature of 52.0° for the reaction was determined by plotting ΔS^* *vs.* ΔH^* (Figure 5), which is 21° above the maximum temperature used in the kinetic determinations and, thus, data for the Hammett relationship should be valid.

A Hammett plot of the rates at 10, 21, and 31° (equal molar concentration) gives a reasonably straight line where the *para*-substituent values are plotted *vs.* log (k/k_H). The values for ρ obtained were positive: 10°, 1.5017; 21°, 1.1482; 31°, 0.9211 (Figures 6–8). The magnitude of these positive values suggests that a negative charge of some magnitude is developed in the transition state. In the reactions with a fivefold ex-

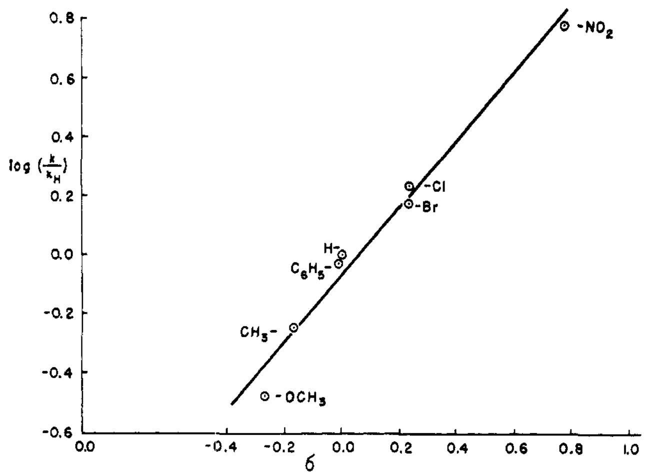


Figure 7.—Plot of the Hammett equation for the reaction of *para*-substituted phenyl chloroformates with silver nitrate (equal molar concentrations) at 21° (ρ = 1.1482).

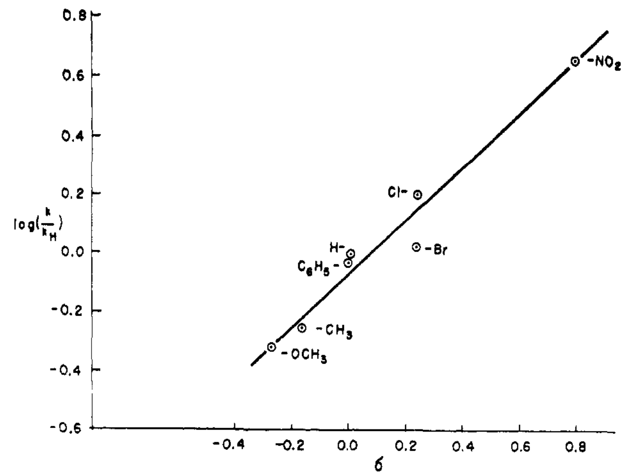


Figure 9.—Plot of the Hammett equation for the reaction of *para*-substituted phenyl chloroformates with a fivefold excess of silver nitrate at 21° (ρ = 0.9383).

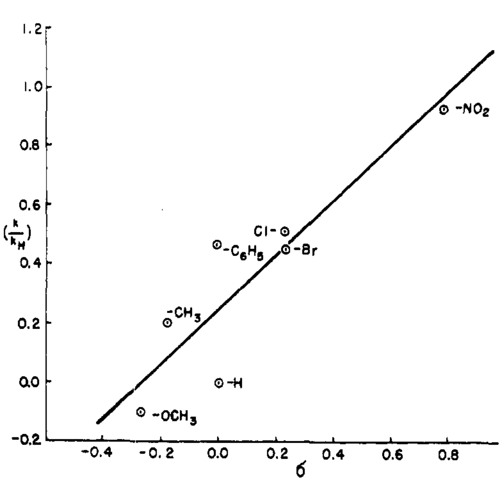


Figure 8.—Plot of the Hammett equation for the reaction of *para*-substituted phenyl chloroformates with silver nitrate (equal molar concentrations) at 31° (ρ = 0.9211).

cess of silver nitrate, a ρ value of 0.9383 was obtained (Figure 9), again indicating that a negative charge is formed in the transition state.

Experimental Section

Aryl Chloroformates.—In a typical preparation, a 1-l. three-necked flask fitted with two dropping funnels, a Dry Ice–acetone reflux condenser (methanolic potassium hydroxide and water traps connected to the condenser outlet), a magnetic stirrer, and immersed in a Dry Ice–acetone cooling bath, was charged with 325 ml of benzene, 62.07 g (0.50 mole) of *p*-methoxyphenol and cooled to 0°. Through the dropping funnels 67.8 ml of liquid phosgene was cautiously added to the stirred benzene solution of phenol, followed by 66.92 ml (0.50 mole) of N,N-dimethylaniline while maintaining the temperature at 0°. On adding the final milliliter of amine the reaction solution became a yellow slush. The mixture was set aside for 10 min and 50 ml of water was *cautiously* added in 5-ml portions. The benzene layer was separated, washed successively with dilute hydrochloric acid, dilute sodium hydroxide, and water, and dried over anhydrous magnesium sulfate. The benzene was removed and the crude product was distilled *in vacuo* to obtain 89.9 g (96.3%) of clear colorless *p*-methoxyphenyl chloroformate, bp 49° (0.27 mm), $n^{19}\text{D}$ 1.5237. Table I summarizes the properties of additional aryl chloroformates prepared.

Anal. Calcd for $C_8H_7ClO_3$: C, 51.50; H, 3.78; Cl, 19.00. Found: C, 51.80; H, 3.45; Cl, 18.82.

Product Analyses.—Reactions of the naphthyl- and *para*-substituted phenyl chloroformates with silver nitrate were conducted in a flask connected to a carbon dioxide absorption train. A solution (precooled to 20°) containing 11.77 g (0.05 mole) of *p*-bromophenyl chloroformate in 150 ml of acetonitrile was added to a solution (precooled to 20°) containing 8.50 g (0.05 mole) of silver nitrate in 150 ml of acetonitrile. The reaction temperature was maintained at 20° and a stream of nitrogen was passed through the apparatus during the reaction period. The reaction was complete after 20 hr as evidenced by the failure of precipitation when chloride ion was added to a aliquot of the clear reaction solution. The silver chloride was recovered by filtration, washed successively with two 20-ml portions of cold acetonitrile and two 10-ml portions of cold anhydrous ether, dried at 105° 2 hr, and weighed (7.10 g, 99.0%). The combined acetonitrile washings were added to the original filtrate and the acetonitrile was removed. The residue was dissolved in approximately 150 ml of anhydrous ethyl ether and decolorized with Norit. The volume of the ether solution was concentrated to 50 ml and chilled in an ice bath to obtain 7.8 g of yellow crystals; further concentration of the mother liquor to 15 ml and cooling yielded a second quantity of the crystalline solid (2.8 g). The combined yield of 2-nitro-4-bromophenol obtained was 10.60 g (97.7%), mp 88–89°, lit.[8] mp 89°.

The Dry Ice traps were set aside at room temperature for 1 hr, and the tared carbon dioxide absorption tube, packed with a 2:1 mixture of ascarite and anhydrous magnesium perchlorate, was reweighed and its gain in weight (2.2 g, 98.5%) was taken as equivalent to the weight of the carbon dioxide evolved during the reaction. Product data on the reactions of the naphthyl- and *para*-substituted phenyl chloroformate with silver nitrate are summarized in Table II.

Using the experimental procedure described above, 9.23 g (0.05 mole) of 2,6-dimethylphenyl chloroformate in 25 ml of acetonitrile was added to a solution containing 8.50 g (0.05 mole) of silver nitrate in 50 ml of acetonitrile. The reaction mixture was cooled by immersion in an ice bath to maintain the reaction temperature below 30°. After 14 hr of reaction the silver chloride was removed by filtration, washed successively with two 20-ml portions of acetonitrile and two 10-ml portions of anhydrous ether, dried at 105° for 90 min, and weighed (7.12 g, 99.2%). The combined acetonitrile washings were added to the filtrate and the mixture was decolorized. On cooling it yielded a yellow crystalline product which on recrystallization from methylene bromide gave 5.23 g (62.6%) of light yellow 4-nitro-2,6-dimethylphenol, mp 167.5–168.3°. A mixture melting point with authentic 4-nitro-2,6-dimethylphenol showed no depression, lit.[9] mp 169–170°.

Concentration of the mother liquor yielded 0.78 g of a dark red crystalline solid which decomposed at 224°. This was identified as 3,5,3′,5′-tetramethyl-(4,4′)-diphenoquinone.[7] The carbon dioxide evolved (83% yield) during the reaction was determined as previously described.

Reaction of 2,6-Diisopropylphenyl Chloroformate with Silver Nitrate.—Using the procedure already described, 8.9 g (0.05

---

[8] See Table I, footnote *a*.

[9] See Table I, footnote *a*, p 486.

mole) of 2,6-diisopropylphenyl chloroformate was allowed to interact with 8.50 g (0.05 mole) of silver nitrate. Following the product isolation described above, a dark reddish yellow solution was obtained. This was diluted to 125 ml in a volumetric flask with acetonitrile; and a 10-ml aliquot was chromatogramed on an acid-washed alumina column using acetonitrile as the eluent. The initial band to come off the column was dark yellow in color and on evaporation of the solvent yielded 8.2 g (73% yield) of 4-nitro-2,6-diisopropylphenol, mp 112°, lit.[10] mp 112°. A second band was obtained which yielded a dark red compound (1.2 g). It decomposed at 245° and was identified as 3,5,3′,5′-tetraisopropyl-(4,4′)-diphenoquinone. The yields of silver chloride and carbon dioxide in this reaction were 96.0 and 74.1%, respectively.

Reaction of 2,4,6-Trimethylphenyl Chloroformate with Silver Nitrate.—Using the procedures described, 20.0 g (0.10 mole) of 2,4,6-trimethylphenyl chloroformate was allowed to interact with 17.1 g (0.10 mole) of silver nitrate in 300 ml of acetonitrile. The reaction mixture was set aside for 24 hr at room temperature, then heated to 30°, and held at this temperature, for an additional 24 hr resulting in the formation of a dark red solution containing silver chloride and a red crystalline product. The silver chloride and red crystals were recovered by filtration. The latter were insoluble in the common organic solvents, and the silver chloride was separated from the red crystals with ammonium hydroxide. The red solid was washed with water and acetone to yield 4.73 g of a material which decomposed at 224–230°. It was identified as 3,5,3′,5′-tetramethyl-(4,4′)-stilbenequinone, lit.[11] mp 224–225°.

Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.16; H, 6.66.

Reaction of *p*-Phenylphenyl Chloroformate with Silver Nitrate in the Presence of Sodium *p*-Methoxyphenoxide.—To 4.5 g (0.025 mole) of silver nitrate in 150 ml of acetonitrile, precooled to 0°, was added a solution containing 5.82 g (0.025 mole) of *p*-phenylphenyl chloroformate in 50 ml of acetonitrile followed by a solution containing 3.65 g (0.025 mole) of sodium *p*-methoxyphenoxide in 25 ml of acetonitrile. A black precipitate formed immediately and the reaction mixture underwent a color change from light green to yellow. On being set aside for 10 hr, with stirring, the black precipitate turned to light yellow. Product isolation was conducted as in the studies of the other *para*-substituted phenyl chloroformates. The yield of 4-phenyl-2-nitrophenol obtained amounted to 5.23 g (97.3%), mp 65.5–66°, lit.[12] mp 66°. Additional investigations of rearrangement reactions with the aryloxide base as a catalyst were conducted. Here the experimental procedures described were used except that the sodium *p*-methoxyphenoxide was added 10 and 60 min after initiation of the reaction. Product yields of the expected products were 98.3 and 97.9%, respectively.

Reaction of 1-Substituted Phenyl Chloroformates with Silver Acetate.—To 0.25 mole of a *para*-substituted phenyl chloroformate in 25 ml of acetonitrile was added 0.25 mole of silver acetate in 25 ml of acetonitrile. A silver chloride precipitate immediately formed. The reaction mixture was stirred for 24 hr at room temperature. Product isolation was conducted as in the reactions of silver nitrate with aryl chloroformates previously described. In all cases only nonnitrated phenols were obtained.

Reaction of *p*-Phenylphenyl Chloroformate with Silver Trifluoroacetate.—On the addition of 1.28 g (0.0058 mole) of silver trifluoroacetate in 25 ml of acetonitrile to 1.36 g (0.0058 mole) of *p*-phenylphenyl chloroformate in 25 ml of acetonitrile, immediate precipitation of silver chloride occurred. After the reaction mixture had been set aside for 24 hr, the silver chloride was recovered by filtration, washed with acetonitrile and ether, dried at 106° for 2 hr, and weighed (0.75 g, 94%). The washings were added to the filtrate, and the solvents were removed, leaving a white solid, mp 95–105°. Recrystallization of this from 2:1 ether–pentane gave 1.51 g (98%) of a white crystalline solid, mp 98–103°. It was identified as 2-hydroxy-5-phenyl trifluoromethyl ketone, which decomposed on storage.

Anal. Calcd for $C_{14}H_9F_3O_2$: C, 63.16; H, 3.14; F, 21.41. Found: C, 63.46; H, 3.15; F, 22.01.

Reaction of *p*-Methoxyphenyl Chloroformate with Silver Nitrate in the Presence of Pyridine.—To a solution containing 0.1085 mole of *p*-methoxyphenyl chloroformate in 50 ml of acetonitrile was added 0.1085 mole of silver nitrate and 0.01 ml of pyridine. A rapid evolution of carbon dioxide occurred. The reaction was set aside for 2 hr and product isolation was carried out in the usual manner. The yields of silver chloride and 2-nitro-4-methoxyphenol were 98.9 and 83.4%, respectively.

Kinetic Determination of Reaction Rates of *para*-Substituted Phenyl Chloroformates with Silver Nitrate.—Reaction rates were determined by measuring the rate of disappearance of the chloroformate carbonyl absorption band at 1777 cm^{-1} in a Unicam S.P. recording infrared spectrophotometer using a variable-temperature infrared cell, with silver chloride windows.

In a typical kinetic determination a 50-ml aliquot of a standard *para*-substituted phenyl chloroformate was added to the reaction flask, magnetically stirred, and allowed to reach the bath temperature controlled to ±0.01° with a Thryratron electronic relay. The reaction solution was then injected with a 4-ml aliquot of a standardized silver nitrate solution. At predetermined time intervals, samples were filtered, withdrawn from the reaction flask, and injected into the sample cell. The carbonyl absorption was scanned and the time was noted at which minimum transmittance occurred. The sample was withdrawn from the cell with a hypodermic syringe and the cell was washed with acetonitrile. Acetonitrile was injected into the cell and the 100% transmittance point was determined; this point was redetermined after each sample was examined since silver chloride precipitated onto the cell windows during the measurements and thus affected the 100% transmittance point. In preparation for the next determination, the cell was dried by forcing dry air through it. By this procedure the rate of the disappearance of the chloroformate carbonyl peak could be accurately followed. Table I summarizes the absorption determination of the carbonyl band for the aryl chloroformates.

---

[10] T. J. Barnes and W. J. Tickenbottom, *J. Chem. Soc.*, 2615 (1961).

[11] See Table I, footnote *a*, p 706.

[12] See Table I, footnote *a*.