water (300 ml.) and the suspension filtered hot. After washing and drying, the residue (open chain dihydrazide) weighed 0.64 g. (15%). The filtrate was shaken with Norit, filtered, acidified with glacial acetic acid (10 ml.), and chilled. The resultant microcrystalline precipitate weighed 2.92 g. (79%) and melted at 347.3–350.3° cor. with decomposition. Further reprecipitation from alkali by acidification, followed by recrystallization from ethylene glycol, raised the melting point only to 348.5–350.5° cor. dec.

Anal. Calcd. for $C_{11}H_7O_2N_3S$: N, 17.1; neut. equiv., 245.2. Found: N, 17.3, 17.2; neut. equiv., 263.1.

This cyclohydrazide was very insoluble in water, slightly soluble in hot acetic acid (about 0.5 g. in 125 ml.), more soluble in hot ethylene glycol (0.5 g. in 50 ml.). With ferric chloride, its saturated aqueous solution gave a faint pink color but did not reduce ammoniacal silver nitrate even on heating. It was soluble in dilute sodium hydroxide, sodium carbonate, ammonium hydroxide or in warm pyridine.

Another otherwise similar preparative run which was heated only seventeen hours gave 69% of cyclohydrazide and 27% of open chain dihydrazide.

The cyclohydrazide failed to show any significant chemiluminescence on oxidation with potassium ferricyanide in dilute alkali containing hydrogen peroxide.

2-Phenyl-5-carbethoxythiazole.—The sodium salt of the (enolic) ethyl α-formyl-α-chloroacetate (3.45 g., 0.02 mole) and thiobenzamide (2.74 g., 0.02 mole) were refluxed in absolute alcohol (15 ml.) for one hour. The precipitated sodium chloride was filtered from the hot deep red solution which on dilution with water (15 ml.) and refrigeration deposited a crystalline precipitate. After drying the product weighed 1.71 g. (37%) and melted 62.8–64.3° cor. Recrystallization from 70% acetone and then from petroleum ether gave colorless rods, m. p. 64.8–65.8° cor.

The same compound was also obtained in somewhat lower yield by using ethyl α-formyl-α-chloroacetate in place of its sodium salt, or in 89% yield from 2-phenylthiazole-5-carboxylic acid chloride (see below) by boiling with absolute alcohol for five minutes. The products from all three methods were identical as shown by the method of mixed melting points.

Anal. Calcd. for $C_{12}H_{11}O_2NS$: N, 6.00. Found: N, 5.93, 5.96.

2-Phenylthiazole-5-carboxylic Acid (VIII).—A sample of 2-phenyl-5-carbethoxythiazole (2.33 g., 0.01 mole) was saponified by refluxing for one and one-half hours with a solution of potassium hydroxide (0.7 g.) in methanol (25 ml.). Cooling in a refrigerator for two hours gave 2.25 g. (93%) of the corresponding potassium salt. This was largely dissolved in water (25 ml.) at room temperature, shaken with Norit, filtered and acidified with concentrated hydrochloric acid (1 ml.). After filtering, washing and drying the fine white crystals of free acid weighed 1.79 g. (87% from ester) and melted 190.5–192.5° cor. with gas evolution. Recrystallization from acetone and then benzene raised the melting point to 192–193° cor. with gas evolution.

Anal. Calcd. for $C_{10}H_7O_2NS$: N, 6.83; neut. equiv., 205.2. Found: N, 6.74, 6.86; neut. equiv., 207.6.

2-Phenylthiazole-5-carboxylic Acid Chloride.—This was obtained in 82.4% yield by boiling the acid (0.31 g.) with thionyl chloride (4 ml.) until a clear solution resulted (two minutes), and evaporating excess reagent in a stream of dry air. Recrystallization from hot ligroin gave 0.28 g. of acid chloride of m. p. 125.3–126.5° cor.

2-Phenylthiazole-5-carboxylic Acid Amide.—The above acid chloride was finely powdered, warmed with concentrated ammonium hydroxide (5 ml.) and stood overnight. The product weighed 0.24 g. (92% yield), melted 212.5–213.5° cor. and this melting point was unchanged by recrystallization from benzene. From 50% alcohol, however, the amide separated in lustrous white rods melting at 213.7–214.5° cor.

Anal. Calcd. for $C_{10}H_8ON_2S$: N, 13.7. Found: N, 13.6, 13.4.

Summary

1. The cyclic hydrazide of 2-phenylthiazole-4,5-dicarboxylic acid was prepared and its capacity to show chemiluminescence on oxidation with potassium ferricyanide in dilute alkali containing hydrogen peroxide found negligible.

2. Pyrolysis of 2-phenylthiazole-4,5-dicarboxylic acid and of its potassium acid salt has been found to give 2-phenylthiazole-4-carboxylic acid and potassium 2-phenylthiazole-4-carboxylate, respectively.

3. A number of compounds related to 2-phenylthiazole-4,5-dicarboxylic acid and 2-phenylthiazole-5-carboxylic acid have been described.

CAMBRIDGE, MASSACHUSETTS RECEIVED JUNE 22, 1943

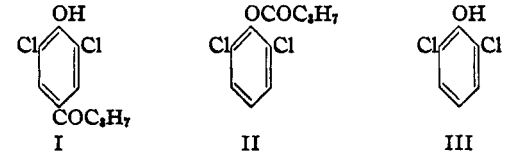
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

The Effect of Changes in the Acyl Group on the Fries Reaction with Esters of 2,6-Dichlorophenol and 2,6-Dimethylphenol

BY D. S. TARBELL AND PAUL E. FANTA

The Fries reaction of phenyl esters has been employed extensively in the synthesis of acylphenols. Most of the studies[1] of the effect of changes in structure on the reaction have been concerned with substituents in the phenoxyl group, rather than changes in the acyl radical. The present paper deals with the behavior of a series of esters of 2,6-dichloro- and 2,6-dimethylphenol when treated with aluminum chloride, and the results reported may be of some interest in connection with the general question of the Fries reaction.

This study was suggested by some previous observations[2] in the synthesis of 3,5-dichloro-4-hydroxybutyrophenone (I) from 2,6-dichlorophenyl butyrate (II).



I II III

The ester II, when treated with aluminum chloride in nitrobenzene solution at room temperature

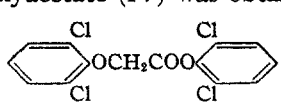
(1) For a summary of this topic, see Blatt, *Chem. Rev.*, **27**, 429 (1940), and Vol. I of Adams' "Organic Reactions," John Wiley and Sons, New York, N. Y., 1942, pp. 342–369.

(2) Tarbell and Wilson, THIS JOURNAL, **64**, 1066 (1942).

for a day, was cleaved in part to 2,6-dichlorophenol (III), and the remainder was recovered unchanged. These conditions in other cases favor migration of the acyl group to the *para* position.[3] The desired product I was obtained when the ester was heated with aluminum chloride at 140–150° without solvent, conditions which are recommended for rearrangement to the *ortho* position.[3]

It was found in the present work that the amount of cleavage of the ester II in nitrobenzene at room temperature was somewhat less than that previously reported; the cleavage was increased by adding small amounts of water or dry hydrogen chloride, so that variations are probably due to changes in the quality of the aluminum chloride.

The esters studied are listed in Table I, and include alkyl, chloro and phenyl substituted acetic esters. They were prepared from the phenol and acid chloride in pyridine solution, except in the case of the chloroacetates. The chloroacetyl chlorides react more rapidly with pyridine to form an ether-insoluble material (which is probably a betaine)[4] than they do to form the phenolic ester.[5] However, satisfactory yields of the esters were obtained by treating the dry potassium salt of the phenol with an excess of the chloroacetyl chloride in dry ether. When this method was applied to the preparation of 2,6-dichlorophenyl chloroacetate, a few per cent. of 2,6-dichlorophenyl 2,6-dichlorophenoxyacetate (IV) was obtained; it was



IV

identified by saponification to the expected products.

Since the low temperature nitrobenzene technique did not bring about rearrangement of the butyrate II or of the trimethylacetate, the esters in Table I were tested for ability to rearrange by heating without solvent with aluminum chloride at temperatures over 100°. The results are summarized in Table II, which lists the optimum conditions found for the formation of the hydroxyketones. In general, more drastic conditions than the optimum favored the production of dark resins, while conditions milder than the optimum yielded larger quantities of cleavage products and unreacted ester.

From the table, it is evident that increasing substitution of the α-hydrogens in 2,6-dichlorophenyl acetate by chlorine atoms, methyl groups or phenyl groups decreases the possibility of obtaining the Fries reaction. This is shown most strikingly by the series propionate, isobutyrate, trimethylacetate. There are several possible reasons for this effect.

The possibility that steric hindrance prevents the Fries reaction is untenable, because the mesitoate of 2,6-dichlorophenol gives the Fries reaction just as smoothly as the benzoate.[6] Other explanations of the effect of branching of the acyl group may be profitably considered in connection with the general question of the mechanism of the Fries reaction.

The weight of evidence about this reaction supports the view that it is an intermolecular process, and not a true intramolecular rearrangement.[7] Two possible mechanisms have been considered. The ester may be split to form an acid chloride, followed by acylation

$$\begin{aligned} &RCOOAr + AlCl_3 \longrightarrow RCOCl + ArOAlCl_2 \\ &RCOCl + ArOAlCl_2 \longrightarrow RCOAr'OH + AlCl_3 \quad (1) \end{aligned}$$

The alternative mechanism involves an intermolecular acylation[8] as follows

$$\begin{aligned} &2\ RCOOAr + AlCl_3 \longrightarrow \\ &\qquad RCOAr'OCOR + ArOAlCl_2 + HCl \\ &RCOAr'OCOR + ArOAlCl_2 \longrightarrow \\ &\qquad 2\ RCOAr'OH + AlCl_3 \quad (2) \end{aligned}$$

The best piece of evidence in support of mechanism 1 is the observation of Cox[7b] that *m*-cresyl butyrate heated with aluminum chloride in diphenyl ether yields some 4-butyryl diphenyl ether, in addition to the expected product. In a similar experiment using 2,6-dichlorophenyl trimethylacetate (V), an ester which we have been unable to rearrange under any conditions, we obtained a small yield of trimethylacetyl diphenyl ether (VI), along with a large amount of 2,6-dichlorophenol, but no rearrangement product was found. If the ester had been cleaved as postulated in the first step of mechanism 1, a good yield of the trimethylacetyl diphenyl ether should have been obtained, as was actually the case when diphenyl ether was treated with trimethylacetyl chloride under the same conditions.

A more plausible explanation of these (and of Cox's) results is that the ester itself acts as the acylating agent

(3) (a) Rosenmund and Schnurr, *Ann.*, **460**, 56 (1928); (b) Ralston, McCorkle and Bauer, *J. Org. Chem.*, **5**, 645 (1940).

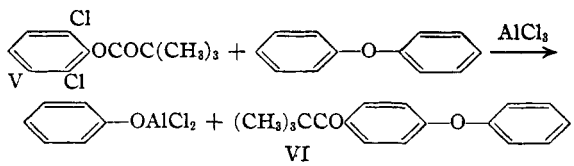
(4) Gerichten, *Ber.*, **15**, 1251 (1882).

(5) A trial run with chloroacetyl chloride and 2,6-dichlorophenol showed that long refluxing of the acid chloride with the phenol in the absence of any condensing agent gave only a poor yield of ester. Phenols which are not di-ortho substituted give good yields of the respective chloroacetates by this method; Fries and Finck, *Ber.*, **41**, 4271 (1908); Fries, Hasselbach and Schröder, *Ann.*, **405**, 368 (1914).

(6) Fuson, Scott and Speck, THIS JOURNAL, **63**, 2845 (1941), have noted that *p*-tolyl mesitoate and the 2,6-xylate undergo the Fries reaction readily.

(7) Refs. 3a, 3b; (a) Skraup and Poller, *Ber.*, **57**, 2033 (1924); (b) Cox, THIS JOURNAL, **52**, 352 (1930); (c) Fieser and Bradsher, *ibid.*, **58**, 1738, 2337 (1936). Some unconvincing arguments in favor of the intramolecular mechanism are given by (d) v. Auwers and Mauss, *Ann.*, **464**, 293 (1928).

(8) Schönberg and Mustafa, *J. Chem. Soc.*, 79 (1943), have isolated ketone esters of the type RCOAr'OCOR from the action of phosphorus pentoxide on phenyl esters; they did not show, however, that these compounds would acylate phenols under the conditions of the Fries reaction. It should be noted that the ketone esters are vinylogs of anhydrides, and hence should be good acylating agents.



The poor yield given by the ester is doubtless due to the fact that it undergoes side-reactions other than acylation, with the decomposition of the acyl group and the formation of the phenol.

The failure of this ester to give the Fries reaction is probably due in part to the unreactive character of the phenolic nucleus, with two chlorine atoms *meta* to the position where substitution must take place. Previous studies of the Fries reaction have usually employed quite reactive phenols which give rapid nuclear substitution (*m*-cresol, thymol, carvacrol, etc.).

The increasing substitution of methyl groups on the α-carbon of the esters would be expected to hinder the Fries reaction, whether it goes by mechanism 1 or 2. It is known that the rate of alcoholysis[9] of RCOCl decreases sharply as R changes from methyl to *t*-butyl, and doubtless the rate of acylation of a phenolic nucleus by $(CH_3)_3$-CCO- whether by the cleavage product $(CH_3)_3$-CCOCl (route 1) or by the ester (2), would be slow also. In the presence of aluminum chloride, trimethylacetyl chloride is decomposed under very mild conditions[10]

$$(CH_3)_3CCOCl \xrightarrow{AlCl_3} CO + HCl + C_4H_8 \text{ (polymer)}$$

It seems very probable that the ester $(CH_3)_3$-$CCOOC_6H_3(Cl)_2$ might decompose in an analogous manner when heated with aluminum chloride

$$(CH_3)_3CCOOC_6H_3(Cl)_2 \longrightarrow CO + C_4H_8 \text{ (polymer)} + HOC_6H_3(Cl)_2$$

This idea is supported by the observation[11] that trimethylacetic and other acids with a tertiary carbon adjacent to the carboxyl give a high yield of carbon monoxide when heated with phosphorus pentoxide. Primary and secondary acids yield less carbon monoxide and some carbon dioxide. This decomposition to yield carbon monoxide must take place through the formation of a phosphoric ester, which then decomposes. The sulfuric ester of trimethylacetic acid decomposes to yield carbon monoxide.[10]

The removal of the branching in the acyl group to the β-position allows the Fries reaction to take place, although in poor yield, as shown by the *t*-butylacetate (Table II). The same striking difference in behavior between trimethylacetic and *t*-butylacetic acids is shown in Whitmore's work, in which *t*-butylacetic acid gives practically no carbon monoxide.

The factors just mentioned do not explain the failure of chlorine or phenyl substituted acyl groups to give a smooth shift. Trichloroacetyl chloride decomposes in the same way[10] as the trimethylacetyl chloride, but at a much slower rate, when treated with aluminum chloride. The alcoholysis of RCOCl proceeds more rapidly as the number of α-chlorine atoms is increased,[9] in contrast to the effect of methyl substitution, and hence this factor is not the cause for the behavior of the phenyl and chlorine-substituted acids. A more plausible explanation is that as the number of electron-attracting groups on the α-carbon atom increases, the oxygens of the esters become less basic, *i. e.*, they form less stable complexes with aluminum chloride or resist the attack of this acidic reagent. The rate of acid hydrolysis of esters is known to be decreased by increasing chlorine-substitution on the α-carbon,[12] which decreases the electron availability at the oxygen atoms and hence decreases the tendency of the acid catalyst to coördinate.

A possible explanation for the failure to isolate the trichloromethyl ketones from the trichloroacetates is that they were formed, but were cleaved by base to chloroform and the corresponding acid[13] during isolation. The acids were not isolated, however, and hence it is unlikely that the ketones were formed.

Because of the usefulness of boron fluoride as a catalyst, we investigated the action of this compound on 2,6-dichlorophenyl propionate, which rearranges readily with aluminum chloride.[14] Boron fluoride readily formed a solid complex with the ester, which was unstable at 100°; no rearrangement product was obtained, even when the complex was heated in a sealed tube at 200°. This negative result with boron fluoride is doubtless due to the instability of the complex and the lack of reactivity of the chlorine-substituted aromatic nucleus.

The esters of 2,6-dimethylphenol in Table I were prepared to see if failure to give the Fries reaction was due to the two *ortho* chlorines, which, incidentally, make the 2,6-dichloro-4-acylphenols very strongly acidic compounds. These compounds give good neutral equivalents, and can be readily extracted by sodium bicarbonate. The esters of 2,6-dimethylphenol showed no notable differences in behavior compared to the dichlorophenyl esters, and it was not possible to get any rearrangement product from the trimethylacetate or the trichloroacetate, although the isobutyrate rearranged in high yield.

Experimental[15]

2,6-Dichlorophenol was prepared by the method previously described.[2] The acids and acid chlorides were pre-

(9) Leimu, *Ber.*, **70**, 1040 (1937).

(10) Böeseken, *Rec. trav. chim.*, **29**, 94 (1910).

(11) Whitmore and Crooks, THIS JOURNAL, **60**, 2078 (1938).

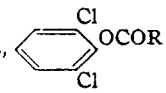
(12) Timm and Hinshelwood, *J. Chem. Soc.*, 862 (1938).

(13) Fuson and Bull, *Chem. Rev.*, **15**, 275 (1934); Houben and Fischer, *J. prakt. Chem.*, (2) **123**, 263 (1929).

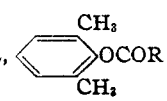
(14) Several workers have mentioned the use of boron fluoride in the Fries reaction without giving details: Meerwein, *Ber.*, **66**, 411 (1933); Smith and Haller, THIS JOURNAL, **56**, 237 (1934); German patent 637,808 (*Chem. Zentr.*, **108**, I, 4581 (1937)); v. Auwers, Pötz and Noll, *Ann.*, **535**, 228 (1938).

(15) All melting points corrected; analyses by Robert Bauman. We are indebted to Wilbur Kirchgessner for preliminary experiments.

TABLE I

ESTERS OF 2,6-DICHLOROPHENOL, 

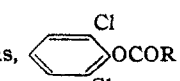
R	B. p., °C.	$n^{25}D$	d^{25}_{25}	Formula	Calcd., % C	Calcd., % H	Found, % C	Found, % H
C_2H_5	113–115 (0.5 mm.)	1.5210	1.2844	$C_9H_8Cl_2O_2$	49.3	3.7	49.4	3.7
$(CH_3)_2CH$	130–130.5 (3 mm.)	1.5128	1.2384	$C_{10}H_{10}Cl_2O_2$	51.5	4.3	51.2	4.3
$(CH_3)_3C$	130–132 (3 mm.)	1.5068	1.2025	$C_{11}H_{12}Cl_2O_2$	53.4	4.9	53.3	5.0
$(CH_3)_3CCH_2$	114–116 (1 mm.)	1.5074	1.1790	$C_{12}H_{14}Cl_2O_2$	55.2	5.4	55.2	5.5
$ClCH_2$	115–116 (2 mm.)	1.5452	1.4609	$C_8H_6Cl_3O_2$	40.1	2.1	40.0	2.3
Cl_2CH	113–114 (0.5 mm.)	1.5456	1.5231	$C_8H_4Cl_4O_2$	35.1	1.5	35.3	1.5
Cl_3C	119–120 (1 mm.)	1.5474	1.5837	$C_8H_3Cl_5O_2$	31.1	1.0	31.3	1.0
$C_6H_5CH_2$	167–172 (2 mm.)	1.5704	1.2903	$C_{14}H_{10}Cl_2O_2$	59.8	3.6	60.1	3.7
$(C_6H_5)_2CH$	M. p. 132–133			$C_{20}H_{14}Cl_2O_2$	67.2	3.9	67.5	4.0
C_6H_5	M. p. 74–74.5			$C_{12}H_8Cl_2O_2$	58.4	3.0	58.7	3.1
2,4,6-$(CH_3)_3C_6H_2$	M. p. 84.5–85.5			$C_{16}H_{14}Cl_2O_2$	62.1	4.6	62.4	4.7

ESTERS OF 2,6-DIMETHYLPHENOL, 

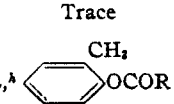
$(CH_3)_2CH$	126–128 (22 mm.)	1.4872	0.9879	$C_{12}H_{16}O_2$	75.0	8.4	74.7	8.4
$(CH_3)_3C$	80–83 (0.5 mm.)	1.4838	0.9717	$C_{13}H_{18}O_2$	75.7	8.8	75.7	8.9
Cl_3C	M. p. 58.5–59.5			$C_{10}H_9Cl_3O_2$[a]	44.9	3.4	45.2	3.6

[a] Calcd.: Cl, 39.8. Found (Parr bomb): Cl, 39.8.

TABLE II

REARRANGEMENT OF 2,6-DICHLOROPHENYL ESTERS, 

R[a]	Time of heating, hours	Temp., °C.	Rearrangement, %[b]	Phenolic material, %	Unreacted ester, %[c]	Total accounted for, %
C_2H_5	2	135–145	87	7	3	97
	3[d]	195–210	0	Trace	77	77
$(CH_3)_2CH$	4.5	130–135	42	32	14	88
$(CH_3)_3C$	0.25	120	0	71[e]	29	100
	1	155	[f]			
$(CH_3)_3CCH_2$	2	135–145	28	5	25	58
$ClCH_2$	2.5	112–114	77	2	15	94
Cl_2CH	2	134	9	Trace	79	88
Cl_3C	5	110	0	2	70	72
	3	137	[f]			
$C_6H_5CH_2$	4	112	26	[g]	28	54
$(C_6H_5)_2CH$	0.17	100	0			
	2	125–130	[f]	0		
C_6H_5	2.5	154	71	<10	10	91
2,4,6-$(CH_3)_3C_6H_2$	1	155	79	Trace	10	89

ESTERS OF 2,6-DIMETHYLPHENOL,[h] 

$(CH_3)_2CH$	3.5	125	94	0	0	94
$(CH_3)_3C$	2	120	[i]			
	6	122–125	[f]			
Cl_3C	5	102–105	[f]	0	78	
	4.5	120–125	[j]			

[a] For R = CH_3 and n-C_3H_7, see ref. 2. [b] Calculated from weight of crude material extracted by sodium carbonate or sodium bicarbonate. [c] Calculated from weight of neutral material, which usually contained other products in addition to ester. [d] Using boron trifluoride instead of aluminum chloride. [e] Shown to be mainly 2,6-dichlorophenol. [f] Only black, unworkable tars obtained. [g] Resinous material containing trace of 2,6-dichlorophenol obtained. [h] For several straight-chain esters of this phenol, which rearrange in good yield, see v. Auwers and Mauss, ref. 20; v. Auwers and Janssen, *Ann.*, **483**, 44 (1930). [i] An impure compound was obtained from this fraction in small amount as the 2,4-dinitrophenylhydrazone, but it could not be purified. [j] More tar and less unreacted ester obtained than in preceding run.

pared by standard methods. **t-Butylacetic acid** was prepared in 61% yield by the haloform reaction on methyl neopentyl ketone,[16] and had the following properties: b. p. 180–185°, $n^{20}D$ 1.4122. The methyl neopentyl ketone was prepared in poor yield by oxidation of diisobutylene with chromic acid at 50–90°.

The esters in Table I were prepared from the phenol and acid chloride or anhydride in pyridine by the usual method. The preparation of the chloroesters was carried out by the following method.

2,6-Dichlorophenyl Chloroacetate and 2,6-Dichlorophenyl 2,6-Dichlorophenoxyacetate (IV).—To 22.1 g. of potassium 2,6-dichlorophenolate in a 200-cc. flask provided with a ground glass condenser, 25.0 g. (100% excess) of chloroacetyl chloride was added slowly. When the vigorous reaction had subsided, 100 cc. of anhydrous ether was added, and the mixture was refluxed gently for thirty minutes. Water (50 cc.) was added cautiously to hydrolyze unchanged acid chloride; after addition of 100 cc. of ether, the ether solution was washed with several portions of aqueous alkali, dried and the solvent evaporated. The resulting crystals were separated from the oil by filtration, washed with cold ether and recrystallized from 25 cc. of ether, yielding 1.0 g. (5%) of 2,6-dichlorophenyl 2,6-dichlorophenoxyacetate (IV) as white prisms, m. p. 153–153.5°.

Anal. Calcd. for $C_{14}H_8O_3Cl_4$: C, 45.9; H, 2.2. Found: C, 45.8; H, 2.4.

Distillation of the oil yielded 15.9 g. (61%) of 2,6-dichlorophenyl chloroacetate, whose physical constants are given in Table I. A 28% yield of this ester was obtained by refluxing a solution of 2,6-dichlorophenol in a 40% excess of chloroacetyl chloride for twenty-six hours.

2,6-Dichlorophenoxyacetic Acid.—This compound was formed by hydrolysis of 2,6-dichlorophenyl 2,6-dichlorophenoxyacetate (IV), and was also prepared from 2,6-dichlorophenol and chloroacetic acid by the usual method[17]; both samples were identical, as shown by m. p. and mixed m. p. The compound crystallizes from water as white, silky needles, m. p. 134.5–135°.

Anal. Calcd. for $C_8H_6Cl_2O_3$: C, 43.5; H, 2.7. Found: C, 43.4; H, 2.9.

Potassium 2,6-Dichlorophenolate.—2,6-Dichlorophenol (32.6 g.) was added to a solution of 11.2 g. of potassium hydroxide in 100 cc. of methanol. Toluene (100 cc.) was added and the solution was distilled until the condensate became clear. Upon cooling the residue, the salt separated as a light purple, granular solid, which was collected by filtration and dried in an oven for twelve hours. Analysis for potassium gave too low a value, but the salt was used without further purification.

2,6-Dimethylphenyl trichloroacetate was prepared in 50% yield by refluxing sodium 2,6-dimethylphenolate with 100% excess trichloroacetyl chloride in benzene.

Procedure for the Fries Reaction[18]

A. 3,5-Dichloro-4-hydroxypropiophenone.—Anhydrous aluminum chloride (3.66 g., 10% excess) was added to a solution of 5.48 g. of 2,6-dichlorophenyl propionate in 10 cc. of carbon disulfide. The solvent was evaporated and the residue was heated in an oil-bath for two hours at 135–145°. The dark, resinous reaction complex was decomposed by warming with dilute hydrochloric acid and taken up in 100 cc. of ether. The ether solution was washed with dilute hydrochloric acid and extracted with several portions of 10% sodium bicarbonate solution. Acidification of the combined extracts with hydrochloric acid and saturation with sodium chloride precipitated a white solid, which was extracted with a single 100-cc. portion of ether. The ether extract was dried and evaporated, giving 4.75 g. (87%) of a white solid, which was recrystallized from 90–100° petroleum ether to give white needles, m. p. 110–111°.

Anal. Calcd. for $C_9H_8O_2Cl_2$: C, 49.3; H, 3.7. Found: C, 49.0; H, 3.8.

The ether solution remaining after the sodium bicarbonate extractions was extracted with 10% sodium hydroxide solution, dried and evaporated to give 0.17 g. (3%) of unreacted ester. The sodium hydroxide extract gave upon acidification with hydrochloric acid about 0.3 g. (7%) of phenolic material.

B. 3,5-Dichloro-4-hydroxyisobutyrophenone was prepared similarly, and obtained as white needles from petroleum ether, m. p. 112–113°.

Anal. Calcd. for $C_{10}H_{10}Cl_2O_2$: C, 51.5; H, 4.3. Found: C, 51.6; H, 4.5.

The neutral material was impure unreacted ester, $n^{25}D$ 1.5161. From the sodium hydroxide soluble fraction (46%) only a trace of 2,6-dichlorophenol could be isolated by distillation.

C. 3,5-Dichloro-4-hydroxy-t-butylacetophenone.—The ester yielded 70% of a red oil which was recrystallized successively from petroleum ether and dilute alcohol to give 28% of white plates, m. p. 94–95.5°.

Anal. Calcd. for $C_{12}H_{14}Cl_2O_2$: C, 55.2; H, 5.4. Found: C, 54.9; H, 5.6.

Impure ester ($n^{25}D$ 1.5194) and phenolic material were by-products.

D. 3,5,α-Trichloro-4-hydroxyacetophenone was obtained in 77% yield as a slightly brown solid, which, upon recrystallization from benzene–petroleum ether, yielded glistening white plates, m. p. 120–121°.

Anal. Calcd. for $C_8H_5Cl_3O_2$: C, 40.1; H, 2.1. Found: C, 40.3; H, 2.1.

Treatment of the ketone with sodium hypoiodite gave 3,5-dichloro-4-hydroxybenzoic acid.[2]

The **2,4-dinitrophenylhydrazone,** fine, orange plates from dilute acetic acid, melts with decomposition at 221–223°.

Anal. Calcd. for $C_{14}H_9Cl_3N_4O_6$: C, 40.1; H, 2.2. Found: C, 40.2; H, 2.4.

Unreacted ester ($n^{25}D$ 1.5482) and a small amount of dark alkali-soluble resin were also obtained.

E. 3,5,α,α-Tetrachloro-4-hydroxyacetophenone was obtained from the sodium bicarbonate extract in 9% yield as an impure brown solid, which, after recrystallization from dilute alcohol (charcoal) and from petroleum ether, gave fine, white needles, m. p. 92.5–94.5°.

Anal. Calcd. for $C_8H_4Cl_4O_2$: C, 35.1; H, 1.5. Found: C, 35.5; H, 1.8.

Treatment with *p*-nitrophenylhydrazine gave, instead of a *p*-nitrophenylhydrazone, a good yield of **3,5-dichloro-4-hydroxyphenylglyoxal *p*-nitrophenylosazone,**[19] as fine, red-purple plates, insoluble in alcohol or glacial acetic acid; after recrystallization from nitrobenzene, it melted at 289.5–290° (heated stage).

Anal. Calcd. for $C_{20}H_{14}Cl_2N_6O_5$: C, 49.1; H, 2.9. Found: C, 49.2; H, 3.1.

The neutral residue from the rearrangement was 79% of unreacted ester ($n^{25}D$ 1.5472).

F. 3,5-Dichloro-4-hydroxyphenyl benzyl ketone was obtained as a red oil (26%) which, after crystallization from petroleum ether–benzene (charcoal), yielded 15% of yellow plates, m. p. 135–138°; recrystallization from dilute acetic acid yielded white needles, m. p. 136.5–138°.

Anal. Calcd. for $C_{14}H_{10}Cl_2O_2$: C, 59.8; H, 3.6. Found: C, 59.1; H, 3.9.

The ***p*-nitrophenylhydrazone,** yellow-orange needles melting at 227.5–228.5°, was obtained in good yield.

Anal. Calcd. for $C_{20}H_{15}Cl_2N_3O_3$: C, 57.7; H, 3.6. Found: C, 58.0; H, 3.7.

Some ester (less than 28%) and some alkali-soluble phenolic resin was obtained.

G. 3,5-Dichloro-4-hydroxybenzophenone was prepared by the usual procedure. Decomposition of the tough, resinous reaction complex was effected by heating with

(16) Homeyer, Whitmore and Wallingford, THIS JOURNAL, **55**, 4209 (1933), give b. p. 183°, $n^{20}D$ 1.4096 for *t*-butylacetic acid.

(17) Koelsch, *ibid.*, **53**, 304 (1931).

(18) Unless otherwise indicated, the time of heating and temperature for each ester are those specified in Table II.

(19) *Cf.* Bender, *Ber.*, **21**, 2496 (1888).

dilute hydrochloric acid for two days on the steam-bath. The product, obtained in 71% yield, was recrystallized from benzene–petroleum ether; fine, white needles, m. p. 145–146°.

Anal. Calcd. for $C_{12}H_8Cl_2O_2$: C, 58.4; H, 3.0. Found: C, 58.5; H, 3.1.

Ten per cent. each of impure unreacted ester and phenolic material was obtained.

H. 3,5-Dichloro-4-hydroxyphenyl mesityl ketone was obtained in 79% yield, and after recrystallization from dilute alcohol (charcoal), formed fine, white needles, m. p. 201.5–203°.

Anal. Calcd. for $C_{16}H_{14}Cl_2O_2$: C, 62.1; H, 4.6; neut. equiv., 309. Found: C, 62.1; H, 4.5; neut. equiv., 309, 310, 309.

I. 3,5-Dimethyl-4-hydroxyisobutyrophenone.—The ester yielded a red, crystalline reaction product which was decomposed by hot, dilute hydrochloric acid to give an oil which solidified on cooling. This product, when subjected to steam-distillation to remove unreacted ester,[20] yielded only a trace of solid in 100 cc. of distillate. The residue was crystallized from 50% alcohol in 94% yield, and upon recrystallization from petroleum ether–benzene gave white plates, m. p. 106.5–107°.

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 75.0; H, 8.4. Found: C, 75.0; H, 8.5.

2,6-Dichlorophenyl Butyrate (II) and Aluminum Chloride in Nitrobenzene at Room Temperature.—When 1.34 g. of the ester was allowed to stand for forty-eight hours at room temperature with 1.2 moles of aluminum chloride in 4 cc. of nitrobenzene, 20% of 2,6-dichlorophenol and 80% of unreacted ester were obtained. A similar run to which 20 mole-per cent. of water had been added gave 30% of the phenol and 70% unreacted ester, while another run in which dry hydrogen chloride was slowly bubbled through the reaction mixture for forty-eight hours gave 35% of the phenol and 65% unreacted ester.

2,6-Dichlorophenyl Trimethylacetate and Aluminum Chloride in Nitrobenzene at Room Temperature.—A run conducted as described above gave no rearrangement product after twenty-four hours, but resulted in 40% cleavage, 30% unreacted ester and some resinification as indicated by darkening of the solution.

2,6-Dichlorophenyl Propionate and Boron Trifluoride.—A solution of 1.00 g. of the ester in 5.74 g. of carbon tetrachloride in a glass tube was saturated with boron trifluoride at 0°. A white, crystalline precipitate appeared, and the gain in weight corresponded to an absorption of 87 mole per cent. of boron trifluoride. The tube was sealed and heated at 195–210° for three hours. Opening the tube and warming on the steam-bath caused most of the boron trifluoride to be expelled. The residue, a brown oil, was taken up in ether and extracted with sodium hydroxide solution; nothing was recovered from this extract. Drying and evaporation of the ethereal solution gave 0.77 g. (77%) of impure unreacted ester, brown oil, $n^{25}D$ 1.5230. A separate run indicated that the boron trifluoride–ester complex was rapidly and completedly decomposed by heating at 100° at atmospheric pressure.

2,6-Dichlorophenyl Trimethylacetate (V) and Aluminum Chloride in the Presence of Diphenyl Ether.[7b]—The ester (8.47 g.) was added dropwise to a stirred suspension of 330 mole per cent. of aluminum chloride in a solution of 5.83 g. of diphenyl ether in 40 cc. of carbon disulfide. The solution was refluxed for two hours, decomposed with dilute hydrochloric acid without removing the carbon disulfide and taken up in ether. Extraction with sodium bicarbonate followed by acidification gave no hydroxy ketone and only a trace of trimethylacetic acid. Extraction with sodium hydroxide solution followed by acidification gave 4.09 g. (73%) of 2,6-dichlorophenol (m. p. 64.5–66°). Drying and distillation of the ethereal residue at 2.5 mm. gave 6.87 g. of a mixture of unreacted ester and diphenyl ether, colorless oil b. p. 78–134°; 0.94 g. of impure 4-trimethylacetyl diphenyl ether, yellow oil, b. p. 134–163° and about 1.0 g. of brown resin which remained undistilled at 193°. Treatment of the impure 4-trimethylacetyl diphenyl ether with 2,4-dinitrophenylhydrazine gave 1.58 g. (99%) of the crude 2,4-dinitrophenylhydrazone. After two recrystallizations from aqueous acetic acid this was shown by m. p. (167.5–170°) and mixed m. p. (169.5–172°) to be a slightly impure form of the analytically pure material described below.

4-Trimethylacetyl diphenyl ether (VI) was prepared in 70% yield by the Friedel-Crafts reaction, using 2 moles of aluminum chloride in the usual procedure.[21] The ketone boils at 175° (3 mm.) to give a colorless oil which solidifies on cooling. It forms, on recrystallization from petroleum ether, large, white prisms melting at 52–52.5°.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 79.5; H, 7.4. Found: C, 79.9; H, 7.3.

The **2,4-dinitrophenylhydrazone,** prepared in the usual manner, forms yellow needles, m. p. 172–173° upon crystallization from aqueous acetic acid.

Anal. Calcd. for $C_{23}H_{22}N_4O_5$: C, 63.6; H, 5.1. Found: C, 63.6; H, 5.3.

Summary

1. A series of esters of 2,6-dichlorophenol and 2,6-dimethylphenol has been prepared and characterized. Their behavior on heating with aluminum chloride has been studied, and a number of new phenolic ketones characterized.

2. Replacement of the α-hydrogens of the acyl group by chlorine, phenyl or methyl tends to hinder the Fries reaction. The trimethyl-, trichloro- and diphenyl-acetates could not be rearranged, while the *t*-butylacetate rearranged in fair yield.

3. 2,6-Dichlorophenyl trimethylacetate yields some trimethylacetyl diphenyl ether when treated with aluminum chloride and diphenyl ether in carbon disulfide.

4. Boron trifluoride does not cause rearrangement of 2,6-dichlorophenyl propionate, which rearranges readily in the presence of aluminum chloride.

5. The results observed agree best with the idea that the Fries reaction involves a bimolecular acylation (mechanism 2).

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(20) v. Auwers and Mauss, *Ann.*, **460**, 240 (1928).

(21) "Organic Syntheses," Coll. Vol. I, 2nd ed., pp. 109–111.