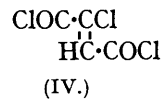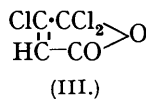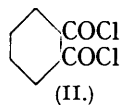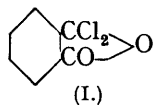## 6. *Phthalyl Fluoride.*

By Arthur T. Dann, William Davies, Arthur N. Hambly, Richard E. Paul, and George S. C. Semmens.

Ott (*Ber.*, 1922, **55**, 2115) has shown that the two " tetrachlorides " of phthalic acid are tautomerides, although the interconversion is very slow.   He had previously established (*Annalen*, 1912, **392**, 274) the conditions necessary for the interconversion of cyclic and acyclic phthalyl chloride (I and II, respectively), but did not prove that these substances are tautomeric forms.   Since it is possible that the fluorine atom, being lighter and smaller than the chlorine atom, might favour tautomeric change, *phthalyl fluoride* has been pre-

pared, most readily by heating acyclic phthalyl chloride (II) with sodium fluoride. Phthalyl fluoride appears to be obtainable only in one form, this having the acyclic structure (as II). It is unaffected by the prolonged action of heat, with or without aluminium fluoride or antimony fluoride, but is converted by aluminium chloride into cyclic phthalyl chloride, so that, if benzene also is present, diphenylphthalide is formed.

Evidence for the constitution of phthalyl fluoride has been obtained in three ways. (1) By parachor determinations. Hitherto the parachor of an acyl fluoride has not been ascertained, but the difficulty expected owing to the action of the fluoride on glass has been easily surmounted. The values obtained by using Sugden's constants (" The Parachor and Valency," 1930; J., 1932, 760) are 318·9 and 304·2 for acyclic phthalyl fluoride (as II) and cyclic phthalyl fluoride (as I) respectively, whereas the experimental values are 315·6 and

$$\begin{array}{cccc}
\text{CCl}_2\!\!>\!\!\text{O} & \text{COCl} & \text{ClC·CCl}_2\!\!>\!\!\text{O} & \text{ClOC·CCl} \\
\text{CO} & \text{COCl} & \text{HC—CO} & \text{HC·COCl} \\
\text{(I.)} & \text{(II.)} & \text{(III.)} & \text{(IV.)}
\end{array}$$

315·4. The discrepancy (3·4) between the theoretical value (318·9) and the observed values may be due to a strain effect on the ortho-position of the type suggested by Mumford and Phillips (J., 1929, 2112). This possibility is supported by the fact that *p*-toluenesulphonyl fluoride gives a practically theoretical parachor (338·5), whereas the *o*-isomeride gives 333·4 and 333·6 instead of the theoretical parachor of 339·0. It is also conceivable that a coordination ring compound may be produced in certain *o*-fluoro-derivatives.

(2) By a study of the rate of the " unimolecular " reaction of excess of methyl or *iso*propyl alcohol with phthalyl fluoride, the two phthalyl chlorides, benzoyl fluoride and chloride, and chloromaleyl and chlorofumaryl chlorides (III and IV, respectively). Phthalyl fluoride is initially more reactive towards methyl alcohol than the two cyclic chlorides or than benzoyl fluoride, but the rates can be considered to be approximately equal. On the other hand, acyclic phthalyl chloride (II) reacts about 200 times as rapidly as phthalyl fluoride with *iso*propyl alcohol, and, when this alcohol is used, benzoyl chloride is 500 times as reactive as benzoyl fluoride. These measurements agree in showing that in all probability phthalyl fluoride has the acyclic structure (as II).

(3) By comparing the reaction of phthalyl fluoride and the two phthalyl chlorides with aniline, and by means of other reactions. Although the chemical evidence is not so decisive as that obtained from the parachor and the rate of reaction determinations, it also indicates that phthalyl fluoride is as (II).

Colour reactions have been advocated for the differentiation of isomeric acyl dichlorides such as (I) and (II), but the experiments carried out in connexion with phthalyl fluoride indicate that such reactions must be used and interpreted with caution. Pfeiffer (*Ber.*, 1922, **55**, 415) detects the presence of a compound containing the group O:C·C:C·C:O by its conversion into coloured quinhydrone-like compounds in the presence of guaiacol, etc. He thus successfully differentiates cyclic (I) from acyclic (II) phthalyl chloride; and it is now found that chlorofumaryl chloride (IV) under the same conditions instantly gives a deep yellow colour, whereas chloromaleyl chloride (III), as his theory demands, produces no colour. On the other hand, only a very faint yellow colour is obtained from phthalyl fluoride ,which contains the above reactive group, whereas succinyl chloride (neither possible form of which can have the above colour-producing group) instantly gives a bright yellow. The colour reaction of von Braun (*Ber.*, 1922, **55**, 1308) is scarcely more decisive. When the condensation of phthalyl fluoride with the piperidine salt of piperidyldithiocarbamic acid is carried out in a cold ethereal suspension, the liquid has only a very faint yellow colour and the precipitate is practically colourless, whereas with (II) both precipitate and solution are bright yellow. After standing over-night, the product from phthalyl fluoride is essentially phthalyl-*NN'*-dipiperidide (m. p. 56—66° instead of 52—54°), although it does contain a small quantity of a sulphur compound. It is evident that for the determination of constitution by the above colour reactions it is necessary that both forms of the acyl halides should be isolated, and strictly comparative tests carried out.

This investigation has incidentally shown that lack of activity of acyl halides, as far as

alcohols, and presumably water, are concerned, is accompanied by enhanced lachrymatory power : the two cyclic chlorides (I) and (III) are far more lachrymatory than their acyclic isomerides (II and IV), and benzoyl fluoride is more lachrymatory than benzoyl chloride.

The formula (III) given to chloromaleyl chloride is that accepted by Ott (*Annalen, loc. cit.*, p. 253), although it is possible that the compound has the structurally isomeric formula with the single chlorine atom attached to the α-carbon atom of the double bond. Such a structure, however, would probably not seriously invalidate the comparisons based on the lactonic structure of the compound.

<div align="center">EXPERIMENTAL.</div>

Preparation of Phthalyl Fluoride.—(1) Acyclic phthalyl chloride (50 c.c.) and ZnF_2 (35 g.) are shaken in a glass flask at 60° for 20 min.; the phthalyl fluoride (5 g.) is extracted in light petroleum (b. p. 40—60°). Cyclic phthalyl chloride (m. p. 85—88°) can be used at a high temperature, but the yield is very poor.

(2) In an inclined Pt distilling flask to which is attached, by means of a rubber stopper, a Cu air-condenser provided with a $CaCl_2$ drying-tube, ordinary phthalyl chloride (55 g.) and NaF (30 g.) are heated (oil-bath) to 250°, and then gradually, with occasional shaking, to 300° during 48 hr. It is difficult to prevent the rubber stopper from becoming damaged, with consequent formation of some phthalic anhydride. The cooled product is extracted in C_6H_6, recovered (free from chlorine compounds), and distilled from a glass flask under reduced press. The *phthalyl fluoride*, thus largely purified from the higher-boiling phthalic anhydride, separates from light petroleum (b. p. 40—60°) in small colourless prisms or massive crystals, m. p. 42—43°. Yield, 24·5 g.; 53% of the theoretical. Its approx. b. p.'s are 135°/54 mm., 142°/65 mm., 224—236°/ 760 mm., all taken in glass, the distillation at ordinary press. being accompanied by considerable reaction between the fluoride and the glass.

Analysis. Schiemann and Pillarsky's method (*Ber.*, 1929, **62**, 3043) gives low and very variable results for carbon. An alc. solution of the fluoride is boiled in a Pt flask for 24 hr. with excess of NaOH, and the unused alkali titrated with HCl aq. The neutralised solution is made faintly alkaline with Na_2CO_3, and CaF_2 pptd. by excess of $CaCl_2$ aq., heated to decompose the calcium phthalate, washed with warm dil. AcOH, gently ignited, and weighed (Found : 4 mols. NaOH hydrolysed 169·1 g. of fluoride; F, 22·5, 21·8. $C_8H_4O_2F_2$ requires M, 170; F, 22·35%).

Phthalyl fluoride is lachrymatory, especially when hot. It is much more slowly converted into phthalic anhydride by atmospheric moisture than is either form of phthalyl chloride; it can even, in small quantities, be distilled in steam, but the hydrolysis is extensive. The pure fluoride in the solid state has little action on glass at the ordinary temp., and even when molten the reaction is slow.

Reactions. When phthalyl fluoride (1 part) is heated with $AlCl_3$ (1 part) in C_6H_6 (40 parts) for 3 hr. on the water-bath, a 60% yield of diphenylphthalide, m. p. 117°, is obtained. Both phthalyl chlorides react in this way (Copisarow, *J.*, 1917, **111**, 10). Phthalyl and benzoyl fluoride both react very slowly with boiling anhyd. formic acid, whereas acyclic phthalyl chloride reacts below 25°, and cyclic phthalyl chloride below 40°, to produce CO and HCl. The action of phthalyl fluoride in C_6H_6 towards NH_3 aq. at the ordinary temp. closely resembles that of both the phthalyl chlorides, *o*-cyanobenzoic acid, m. p. 184°, being formed, and this is converted into phthalimide on heating. When phthalyl fluoride (1·7 g.) in C_6H_6 (80 c.c.) is poured into aniline (4·65 g.; 25% excess) in C_6H_6 (80 c.c.), a copious ppt. is produced in several sec.; this, after being washed with C_6H_6, EtOH, and cold H_2O and dried in vac. over P_2O_5, has m. p. 253—255° and is pure phthalyldianilide * in more than 90% yield. Phthalyldianilide is, under

* Ott (*Annalen, loc. cit.*, p. 285) gives m. p. 230—231°, and it is true that when either phthalyl chloride is mixed with aniline in C_6H_6 or Et_2O and the product kept for some time, the anilide, purified as above, does melt at about 231°. But when cryst. from EtOH, the dianilide melts at 253—255°. The discrepancy is due to the fact that phthalyl chloride contains some phthalic anhydride (cf. Pfeiffer, *loc. cit.*, p. 429), and the condensation product of aniline with phthalic anhydride contaminates the product. This is proved by taking ordinary liquid phthalyl chloride (which gives the anilide, m. p. 231°, as above described) and filtering off the reaction product with aniline instantly, before the anhydride has reacted. The ppt. is washed as described for the fluoride, and the m. p. is also the same (253—255°), without any recrystn. having taken place. The m. p. varies several degrees according to the rate of heating. Hoogenwerff and van Dorp (*Rec. trav. chim.*, 1902, **31**, 344) have described the other source of error in the literature, namely, the conversion of phthalyldianilide (m. p. 251°) into phthalanil (m. p. 205°) by crystn. from an acid medium.

C

the above conditions, instantly produced from acyclic phthalyl chloride, whereas many min. elapse before appreciable pptn. occurs from cyclic phthalyl chloride. As benzoyl fluoride under the above conditions reacts instantly and almost completely to form benzanilide, it follows that phthalyl fluoride has the same type of constitution and is as (II).

Preparation and Purification of Reagents for Rate of Reaction Measurements and Parachor Determinations.—The two phthalyl chlorides are prepared after Ott's method (" Organic Syntheses," XI, p. 88) and have the properties therein described. The small quantity of phthalic anhydride present is estimated by determining the Cl content and also the alkali required for complete hydrolysis, and allowance is made for the phthalic anhydride impurity in weighing the chlorides for the velocity of reaction measurements. Benzoyl fluoride is made by adding benzoyl chloride (50 g.) to ZnF_2 (30 g., dried at 180°) in a Cu distilling flask, heating the mixture for $\frac{1}{2}$ hr. at 150°, and distilling the fluoride from an oil-bath at 195°, 30·5 g., b. p. 155—156°, being obtained (yield, 69%). NaF requires much longer heating, but gives a better yield. Benzoyl fluoride boils at 155—156°/760 mm. (Found on complete hydrolysis : 0·6970 g. required 30·46 c.c. of 0·3688N-NaOH. Calc., 30·47 c.c.). Benzoyl chloride (corr. b. p. 196·2—196·5°/761·3 mm.) is obtained analytically pure by fractionation of Kahlbaum's reagent. Pure succinyl chloride boils at 114—116°/55 mm., and pure chlorofumaryl chloride (made after Perkin, J., 1888, **53**, 695) has b. p. 96—96·5°/40 mm. The latter (36 g.) is converted after Ott (*Annalen, loc. cit.,* p. 256) into chloromaleyl chloride (23 g.; b. p. 104—104·5°/50 mm., and m. p. 11—12° after several crystns.). The middle fractions of thoroughly purified and dried methyl and *iso*propyl alcohols, boiling within 0·2°, have been used throughout. *o*- and *p*-Toluenesulphonyl fluorides are prepared after Davies and Dick (J., 1931, 2106) and the *o*- is completely freed from the *p*-isomeride by preferential oxidation with CrO_3 in AcOH.

Rates of Reaction of Alcohols with Phthalyl Fluoride and Related Compounds.—The rate of the reaction $R \cdot COX + R_1 \cdot OH = R \cdot CO \cdot OR_1 + HX$ at a definite temp. is ascertained by measurement of the hydrogen halide produced. After a definite interval of time 10 c.c. of the reaction mixture are run into 25 c.c. of H_2O and 25 c.c. of C_6H_6 so that the alc. solution first enters the C_6H_6 and passes through this to the aq. layer below. The flask is then stoppered and well shaken, the two layers are allowed to separate, and 20 c.c. are pipetted from the aq. layer and titrated with $N/50$-NaOH and phenolphthalein. The alkali titre is proportional to the hydrogen halide produced. This method is a great improvement on that used by Ott (*Annalen, loc. cit.,* p. 280), who adds his alc. solution first to H_2O and then extracts the mixture several times with his org. solvent.

With acyl fluorides the reaction is carried out in a Ag bottle and the portion withdrawn is shaken with H_2O and C_6H_6 in a bakelite bottle.* A glass pipette is used, as the action of the weak alc. HF on the pipette during the short time of transference is negligible. The fluoride, when solid is weighed in Ag foil, and when liquid in a stoppered Ag tube.

Comparative Reactivity of Methyl Alcohol with Phthalyl Fluoride, Cyclic Phthalyl Chloride, and Chloromaleyl Chloride at 30°.—The acid halide (approx. that required for 100 g. of MeOH) is weighed in a stoppered bottle or metallic container and kept in a desiccator while the amount of MeOH required to make the solution (1/12·5 g.-atom halogen per 1000 g. of MeOH) is heated in the thermostat to the required temp. The acyl halide and its container are then put in the alcohol, which is well shaken, and the results are timed from this point as zero. The cooling effect of the halide and container is negligible. The expt. has been repeated in each case.

Discussion of Results.—The results are summarised in the figure. Phthalyl fluoride (4) is at first more reactive towards methyl alcohol than either of the cyclic chlorides (2 and 3), and even towards the end of the reaction the rate is not much less than that for cyclic phthalyl chloride. Moreover, although not shown in the figure, a comparison of the rates of reaction of methyl alcohol at 20° with phthalyl fluoride, cyclic phthalyl chloride, and benzoyl fluoride has also been made, and the curves are very similar to the ones shown in the figure for 30°, the curve for benzoyl fluoride approximately replacing that for chloromaleyl chloride (2). The phthalyl fluoride curve (4) is the only one with a definite break, which occurs immediately after 50% of the fluoride has been used. This break is still more clearly indicated by plotting the logarithm of the concentration of the remaining fluoride against the time (curve inset). The ratio of the gradient of the first part to that of the

* Transparent bakelite apparatus for work with HF is obtainable from The Fisher Scientific Co., 709–717 Forbes St., Pittsburg, U.S.A.

second part of this log. curve is approximately 10 to 1. The possibility that this break is due to the formation of *o*-carbomethoxybenzoyl fluoride is being examined.

The curve for the reaction between an acyclic dicarboxyl halide and an alcohol appears not to have previously been obtained; a comparison in this respect between phthalyl fluoride and other acyclic dicarboxyl halides has therefore been attempted. As both succinyl and chlorofumaryl chloride are far too reactive, even towards *iso*propyl alcohol, for their reaction curves to be obtained, acyclic phthalyl chloride has been chosen.

Comparative Reactivity of Phthalyl Fluoride and Acyclic Phthalyl Chloride towards Alcohols.—The rate of reaction of acyclic phthalyl chloride with methyl alcohol is too great for even approx. estimation (cf. Ott, *Annalen, loc. cit.*, p. 280). On the other hand, *iso*propyl alcohol, which is ideal for the phthalyl chloride measurements, reacts too slowly
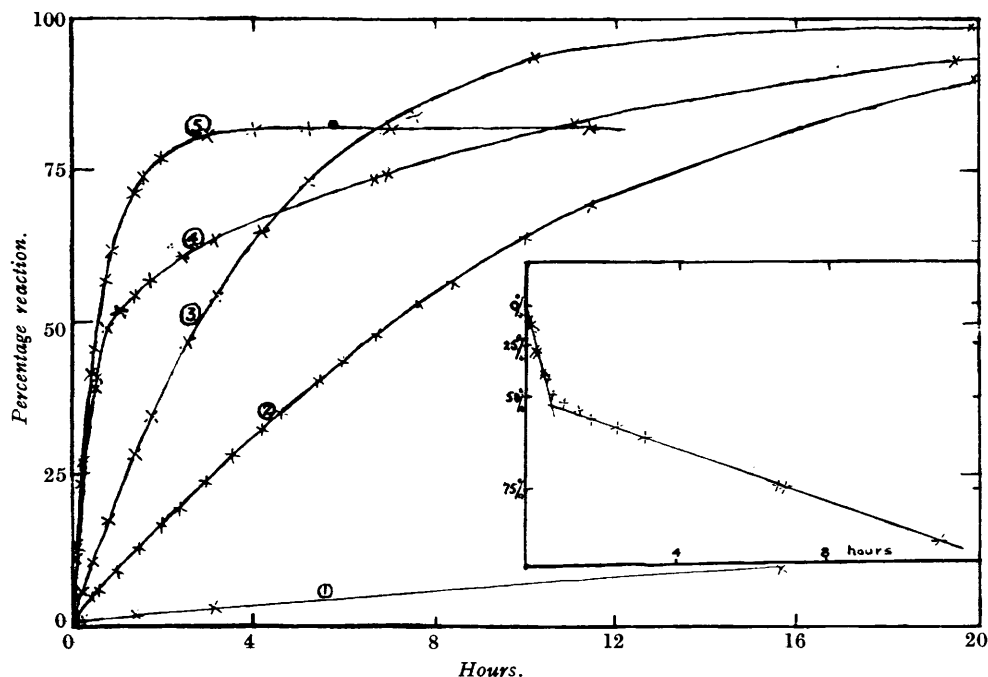
(1) *Phthalyl fluoride*–iso*Propyl alcohol.* (2) *Chloromaleyl chloride–Methyl alcohol.* (3) *Cyclic phthalyl chloride–Methyl alcohol.* (4) *Phthalyl fluoride–Methyl alcohol.* (5) *Acyclic phthalyl chloride*–iso*Propyl alcohol. All at* 30°.

Inset : $\log_{10}$ *concentration of phthalyl fluoride against time from curve* (4).

with phthalyl fluoride for accurate results to be obtained. *iso*Propyl alcohol nevertheless seems the most suitable alcohol available, and the reaction curves at 30° are given in the figure. In calculating the reaction velocities the zero of time is taken from a titre immediately after the reaction has begun.

For phthalyl fluoride $k = [1/t \cdot \log_{10} a/(a - x)]$ is about $5 \cdot 2 \times 10^{-5}$, and for the acyclic chloride it is about $9 \cdot 93 \times 10^{-2}$. The rate of reaction of *iso*propyl alcohol with acyclic phthalyl chloride is thus about 200 times greater than with phthalyl fluoride (see figure, curves 5 and 1, respectively). The curve for acyclic phthalyl chloride and *iso*propyl alcohol (5) is smooth and continuous, in contrast to that for phthalyl fluoride and methyl alcohol (4). The action of phthalyl fluoride on *iso*propyl alcohol is so slow that the resulting type of curve is not experimentally realisable, the initial portion of the curve (1) only being obtained.

The curve (5) for acyclic phthalyl chloride and *iso*propyl alcohol approaches an asymptote when less than 85% of the theoretical amount of hydrogen chloride has been formed. From 180 to 1301 minutes the increase in titre is from 16·44 c.c. (80·7%) to 16·84 c.c. (82·7%), whereas complete reaction demands 20·4 c.c. A similar phenomenon is noticeable with

phthalyl bromide and *iso*propyl alcohol, and will be discussed in a subsequent communication. The presence of phthalic anhydride in the phthalyl chloride does not explain the anomaly, because this is very small in amount, and because the 100% figure for the hydrogen chloride production is the amount actually obtainable by hydrolysis of the phthalyl chloride with excess of alcoholic alkali.

The Rate of Reaction of Benzoyl Chloride and Fluoride with iso*Propyl Alcohol.*—Staudinger and Anthes (*Ber.*, 1913, **46**, 1417) have shown that towards water in moist ether the order of increasing activity of benzoyl halides is chloride, bromide, and iodide. For the purposes of this investigation the rates of reaction of benzoyl chloride and fluoride with *iso*propyl alcohol have been measured at 30·0°, and k for benzoyl fluoride is $5·1 \times 10^{-6}$, and for benzoyl chloride is $2·64 \times 10^{-3}$. The curves are smooth and regular, and from the above figures it follows that the chloride reacts about 500 times faster than the fluoride. Now it has been found that benzoyl fluoride is only somewhat less reactive (particularly during the middle and the latter part of the reaction) than is phthalyl fluoride towards methyl alcohol. Consequently it is to be expected that phthalyl fluoride, if acyclic, would be very much less reactive than the acyclic phthalyl chloride. On the other hand, if phthalyl fluoride has the cyclic form, it might be expected to be much less reactive than the corresponding chloride. Hence the series of reactions indicated in the figure, and the comparison of the rates of reaction of benzoyl fluoride and chloride, both indicate the acyclic nature of phthalyl fluoride.

Determination of the Parachor of Phthalyl Fluoride and Other Fluorides.—The surface tension measurements of phthalyl fluoride are made at 50° in the maximum bubble pressure cell of Sugden (J., 1924, **125**, 27) in a bath of benzyl benzoate the temp. of which is electrically controlled to 0·1°. The manometer containing pure *m*-xylene is in a separate thermostat at 30·0° (Sidgwick and Barkworth, J., 1931, 808), so the gauge factor remains constant throughout. The manometric heights are obtained with a cathetometer reading to 0·01 mm. Before each determination the cell is calibrated with pure C_6H_6.

The density determinations are carried out by means of a small pipette drawn out to a fine tip and provided at the other end with a small well-ground glass tap (see Sidgwick and Bayliss, J., 1930, 2027). With a pipette of about 3 c.c. capacity, density values are obtained easily reproducible to 0·1%. The action of pure phthalyl fluoride on the glass of the pipette is negligible under the above conditions.

It was anticipated that difficulties in determining the surface tension of acyl fluorides would arise, because a trace of SiF_4 formed from the glass would prevent true contact between the liquid and the glass surface. Moreover, any etching would alter the size and constants of the jets, and it has been found that when slight etching does occur the surface tension values diminish. The difficulty has been overcome by using slightly impure phthalyl fluoride during a preliminary determination; the surface tension values then fall off by about 15% during the expt., and the cell constant on recalibration is found to have changed accordingly. Then, when a pure specimen of phthalyl fluoride is used with these etched jets, the manometric head remains constant (within the usual experimental error) for more than 1 hr., and moreover the cell constant,

	Temp.	H, cm.	Cell const. $\times 10^3$.	γ, dynes/cm.	D.	[P]. Found.	[P]. Calc.
Phthalyl fluoride	50°	5·132	7·782	34·63	1·3065	315·6	{318·9 / 320·3*
,, ,, ...	50	5·096	7·790	34·45	1·3067	315·4	{304·2 / 305·6†
o Toluenesulphonyl fluoride	30·5	5·308	7·811	35·91	1·278	333·4	{339·0 / 339·7
,, ,, ,,	30·5	5·329	7·811	36·05	1·278	333·6	339·7
p-Toluenesulphonyl fluoride	60	5·023	7·417	33·04	1·233	338·5	{339·0 / 339·7

* Acyclic formula (as II). † Cyclic formula (as I).

redetermined after the fluoride has been removed, is not appreciably altered (see table). Subsequent determinations give values in good agreement with the first. The gauge factor is 838·8.

The lower value for each calc. parachor has been obtained from the constants in Sugden's

" Parachor and Valency." The upper value has been obtained by using the most recent value for the parachor of fluorine, 25·0, obtained by Allen and Sugden (J., 1932, 761).