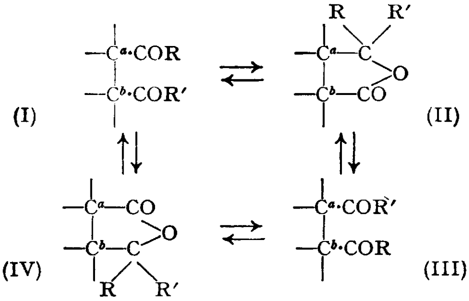
100. *Ring–Chain Tautomerism in the Acid Halides of the Half-esters of Dibasic Acids.*

By B. H. Chase and D. H. Hey.

A study has been made of the formation of ester acid chlorides derived from 1-methyl hydrogen 4-nitrophthalate, 1-methyl and 2-methyl hydrogen 3-nitrophthalate, and the acid methyl esters of αα-diphenyl-succinic and -glutaric acids. By an investigation of the products of various reactions of these ester acid chlorides, partial rearrangement has been shown to occur in all cases, giving rise to derivatives of the isomeric ester acid chloride formed by interchange of the ester and acid chloride groups. A number of analogous cases in the literature have been discussed, and a mechanism for the reaction proposed. Some confusion in the literature concerning the structure of certain compounds obtained by methods involving ester acid chlorides has been resolved.

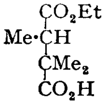
The existence of ring–chain tautomerism in the diacid halides of certain dibasic acids is well established. The diacid chlorides of phthalic acid and of succinic acid, for example, exhibit typical tautomeric properties which are represented by the equilibrium between the two structures (I) and (II), where R and R′ are Cl. The occurrence of similar tautomeric properties in the acid chlorides of the half-esters of dibasic acids, *e.g.*, (I) $\rightleftarrows$ (II), where R is OAlk and R′ is Cl, has not hitherto been generally recognised, although there is considerable experimental evidence which can only be interpreted satisfactorily on the basis of the existence of such tautomeric forms.

Systems in which R and R′ are not identical differ from those of the diacid chlorides of dibasic acids in that, provided the molecule of the parent dicarboxylic acid is itself dissymmetric by the possession of some structural feature which will differentiate the atoms C^a and C^b, the cyclic tautomeride (II) now allows ring fission to occur with formation of a second open-chain form (III). This in turn leads to a second ring form (IV), which completes the cycle. The experimental proof of existence of the two tautomerides (I) and (II) in the acid chlorides of dibasic acids depends largely on evidence obtained from the chemical reactions of these two forms which lead to fundamentally different structures, but in the series of the acid chlorides of the half-esters it is possible to utilise the reactions of the isomeric open-chain forms (I) and (III). Failure to recognise the existence of this type of tautomerism has led in the past to much confusion, and a number of reactions in which such half-ester acid chlorides have been used require reinvestigation. Any investigation of such reactions, however, depends in the first instance on the availability of reliable methods for the preparation of the isomeric half-esters (I and III; R = OAlk, R′ = OH) of unambiguous constitution. Much of the confusion on the subject in the literature can be traced to the use of half-esters of doubtful identity.

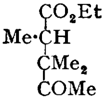


The existence of ring–chain tautomerism in the systems under discussion requires that the two carboxyl groups in the parent acid should be in close spatial proximity so that a stable ring can be formed. Examples of this phenomenon are therefore to be sought in the aliphatic series in derivatives of succinic, glutaric, and adipic acids and in the aromatic series in derivatives of *o*-dicarboxylic acids.

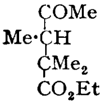
1 : 2-*Dicarboxylic Acid Series*.—In the succinic acid series Bardhan (*J.*, 1928, 2604) obtained both ethyl αββ-trimethyl-lævulate (VI) and ethyl ααβ-trimethyl-lævulate (VII) from the action of methylzinc iodide on the acid chloride of the β-ethyl ester (V) of ααβ-trimethylsuccinic acid. The concomitant formation of the two isomeric esters (VI) and (VII) from the half-ester (V) can be explained by the existence of the cyclic tautomeric system represented by the forms (I), (II), (III), and (IV). Bardhan, however, attributed the formation of the second keto-ester to the presence of the isomeric half-ester in his starting material. On the other hand, Anschütz and Drugman (*Ber.*, 1897, **30**, 2651) have reported the conversion of the acid chlorides of the two isomeric half-esters of mesaconic acid into the corresponding ester-anilides and ester-*p*-toluidides but record the formation of one product only in each case. In this instance the *trans*-relationship of the two carboxyl groups precludes the formation of a cyclic tautomeride. Anschütz (*Annalen*, 1907, **354**, 117) also carried out a Friedel–Crafts reaction between benzene and each of the isomeric acid chloride half-esters of phenylsuccinic acid and again reported the formation of a single ketonic product in each case. Salmon-Legagneur and Soudan (*Compt. rend.*, 1944, **218**, 681), however, state that the acid chlorides (VIII; R = alkyl) of the β-alkyl esters of αα-diphenylsuccinic acid readily rearrange to those of the α-alkyl esters (IX) during the course of preparation by the action of thionyl chloride on the


$\begin{array}{l} CO_2Et \\ Me\cdot CH \\ CMe_2 \\ CO_2H \end{array}$

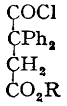
(V)


$\begin{array}{l} CO_2Et \\ Me\cdot CH \\ CMe_2 \\ COMe \end{array}$

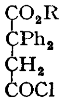
(VI)


$\begin{array}{l} COMe \\ Me\cdot CH \\ CMe_2 \\ CO_2Et \end{array}$

(VII)

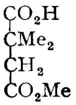

$\begin{array}{l} COCl \\ CPh_2 \\ CH_2 \\ CO_2R \end{array}$

(VIII)

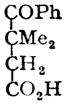

$\begin{array}{l} CO_2R \\ CPh_2 \\ CH_2 \\ COCl \end{array}$

(IX)

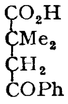
(β-)half ester. They further claim that such rearrangement can be avoided by treatment of the dry silver salt of the acid ester with thionyl chloride in cold ethereal solution. After reaction between the acid chloride prepared from the β-methyl ester (X) of αα-dimethylsuccinic acid and benzene in the presence of aluminium chloride Rothstein and Saboor (*J.*, 1943, 427) isolated, not the expected β-benzoyl-β-methylbutyric acid (XI), but the isomeric β-benzoyl-αα-dimethylpropionic acid (XII), whereas Rosambo (*Ann. Chim.*, 1923, **19**, 335), using the acid chloride of the (β-)ethyl ester of the same acid and ethylzinc iodide, obtained ethyl ββγ-trimethyl-lævulate (XIII). Bardhan (*J.*, 1928, 2593) has reported the formation of methyl 1-acetyl*cyclo*pentylacetate (XIV) by the action of methylzinc chloride on the acid chloride from the half-ester (XV), but, when Sen-Gupta (*J. Indian Chem. Soc.*, 1934, **11**, 392) used the same ester acid chloride in a Friedel–Crafts reaction with benzene, he obtained a ketone which has since been shown (Saboor, *J.*, 1945, 923) to be 1-phenacyl*cyclo*pentane-1-carboxylic acid (XVI) which yields a lactone, and not the expected 1-benzoyl*cyclo*pentylacetic acid. The work of Blaise (*Bull. Soc. chim.*, 1899, **21**, 715) and of Haworth and King (*J.*, 1914, **105**, 1348) on the ester acid chlorides of αα-dimethylsuccinic acid contains no indication of rearrangement, but the half-esters used by these workers were of uncertain identity. A further example of the rearrangement in this series has recently been provided by Turner, Bhattacharyya, Graber, and Johnson (*J. Amer. Chem. Soc.*, 1950, **72**, 5654) in their improved synthesis of bisdehydrodoisynolic acid.


$CO_2H\cdot CMe_2\cdot CH_2\cdot CO_2Me$

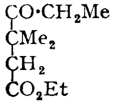
(X)


$COPh\cdot CMe_2\cdot CH_2\cdot CO_2H$

(XI)

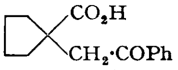

$CO_2H\cdot CMe_2\cdot CH_2\cdot COPh$

(XII)


$CO\cdot CH_2Me\cdot CMe_2\cdot CH_2\cdot CO_2Et$

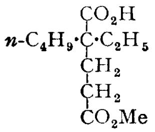
(XIII)

(XV) (XIV)

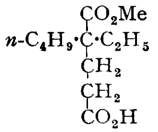


(XVI)

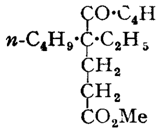
1 : 3-*Dicarboxylic Acid Series.*—In the glutaric acid series Cason (*J. Org. Chem.*, 1948, **13**, 227) has reported that when the isomeric half-esters (XVII) and (XVIII) of α-*n*-butyl-α-ethylglutaric acid are each converted into their acid chlorides by means of thionyl chloride and then treated with 2 : 4 : 6-tribromoaniline in boiling xylene, the same anilide is obtained in low yield in each case. It was inferred that a mixture of the two isomeric ester acid chlorides had been obtained in both cases but that only that from the unhindered carboxylic acid had reacted with the base. Confirmatory evidence for this hypothesis was obtained from the action of di-*n*-butylcadmium on the two acid chlorides, which gave in each case a mixture of the isomeric keto-esters (XIX) and (XX). Ställberg-Stenhagen (*J. Amer. Chem. Soc.*, 1947, **69**, 2568) has reported that when an optically active methyl hydrogen β-methylglutarate (XXI) is converted into the acid chloride by means of thionyl chloride and then recovered by hydrolysis racemisation takes place. Racemisation can be avoided, however, by the use of oxalyl chloride in benzene solution, or of *pure* thionyl chloride at temperatures below 30°. It is inferred that the use of less pure thionyl chloride


$CO_2H\cdot C(n\text{-}C_4H_9)(C_2H_5)\cdot CH_2\cdot CH_2\cdot CO_2Me$

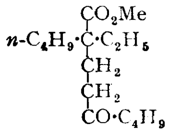
(XVII)


$CO_2Me\cdot C(n\text{-}C_4H_9)(C_2H_5)\cdot CH_2\cdot CH_2\cdot CO_2H$

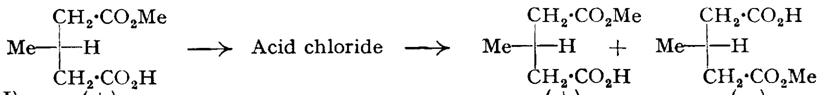
(XVIII)


$CO\cdot C_4H_9\cdot C(n\text{-}C_4H_9)(C_2H_5)\cdot CH_2\cdot CH_2\cdot CO_2Me$

(XIX)

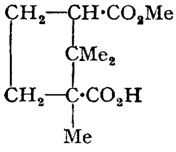

$CO_2Me\cdot C(n\text{-}C_4H_9)(C_2H_5)\cdot CH_2\cdot CH_2\cdot CO\cdot C_4H_9$

(XX)



(XXI) (+) (+) (−)

or of higher temperatures leads to rearrangement and, hence, racemisation. Ställberg-Stenhagen suggests that rearrangement occurs through the formation of the anhydride. It may be noted that Cason (*loc. cit.*) was able to reduce the extent of his rearrangement but was not able to eliminate it entirely by the use of low temperatures and purified thionyl chloride. Qudrat-i-Khuda (*J.*, 1930, 206) has suggested that the *ortho*- and *allo*-methyl hydrogen camphorates, which had previously been assigned the structures (XXII) and (XXIII) respectively, were in fact stereoisomerides. This conclusion was based largely on the claim that the acid chloride of either ester gave (*a*) the same keto-ester on treatment with methylzinc iodide and (*b*) only the *allo*-ester on hydrolysis. Bredt (*J. pr. Chem.*, 1932, **133**, 89), however, maintained that the two compounds were structural isomerides, which could undergo rearrangement through the chloro-methoxy-lactone (XXIV), a view which was later confirmed by Salmon-Legagneur (*Bull. Soc. Sci. Bretagne*, 1938, **15**, 189), who showed that each half-ester could be converted into a mixture of both through the acid chloride. The difficulties experienced by Haller and Blanc (*Compt. rend.*, 1905, **141**, 697) in the preparation of the anilides and *p*-toluidides of the *ortho*- and *allo*-camphoric acids must be attributed to the existence of this rearrangement.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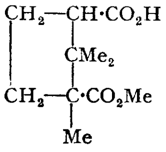
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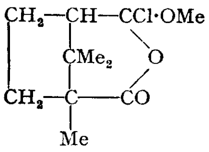

(XXIV)

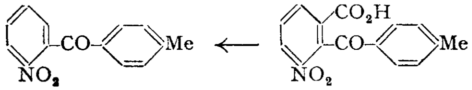
The reactions of ester acid chlorides in the 1 : 2- and more particularly the 1 : 3-dicarboxylic acid series have frequently been used in synthetic work in the steroid field for converting an acid ester into the next higher homologue by the Arndt–Eistert method (Litvan and Robinson, *J.*, 1938, 1997; Bachmann, Cole, and Wilds, *J. Amer. Chem. Soc.*, 1940, **62**, 834 and subsequent papers). In none of the many examples recorded has any evidence of rearrangement been reported and in many cases the yields of the required product are high. This may be attributed to the wide use made of oxalyl chloride, in place of thionyl chloride or phosphorus pentachloride, for the preparation of the acid chloride, or to the use of purified thionyl chloride under mild experimental conditions (cf. Ställberg-Stenhagen, *loc. cit.*). On the other hand, when unpurified thionyl chloride or phosphorus pentachloride has been used, low yields and difficulties in purification have sometimes been reported (cf. Litvan and Robinson, *loc. cit.*; Marker and Rohrmann, *J. Amer. Chem. Soc.*, 1940, **62**, 901; etc.).

1 : 4-*Dicarboxylic Acid Series.*—In the adipic acid series no examples of rearrangement have so far come to light. No reference to rearrangement was reported by Palfray (*Ann. Chim.*, 1923, **20**, 331), who prepared the phenyl ester of homocamphoric acid by the action of sodium phenoxide on the acid chloride. Litvan and Robinson (*loc. cit.*) obtained hydrocamphorylacetic acid in 53% yield by means of an Arndt–Eistert reaction on the half-ester of homocamphoric acid and recorded no evidence of rearrangement.

o-*Dicarboxylic Acids.*—Several examples of rearrangement have been recorded with the acid chlorides of half-esters in the aromatic series. Hayashi, Turuoka, Morikawa, and Namikawa (*Bull. Chem. Soc. Japan*, 1936, **11**, 191) reported the reaction of the acid chloride from 1-methyl hydrogen 3-nitrophthalate (XXV) on benzene in the presence of aluminium chloride and obtained after hydrolysis an acid, m. p. 236—237°, which they regarded as 6-nitrobenzophenone-2-carboxylic acid (XXVI). The acid chloride prepared from the isomeric half-ester (XXVII) on similar treatment gave an acid, m. p. 160—161°, regarded as 3-nitrobenzophenone-2-carboxylic acid (XXVIII), together with


(XXV) (XXVI) (XXVII) (XXVIII)

a small quantity of the higher-melting isomeric acid (XXVI), the formation of which they ascribed to the rearrangement of the acid chloride. These results, however, were in direct contrast to the earlier work of Lawrance (*J. Amer. Chem. Soc.*, 1920, **42**, 1875) who, using the corresponding isomeric 1- and 2-ethyl hydrogen 3-nitrophthalates, obtained nitrobenzophenonecarboxylic acids melting at 157—160° and 220—221°, respectively. Lawrance (*ibid.*, 1921, **43**, 2578) also submitted the acid chlorides from both 1- and 2-ethyl hydrogen 3-nitrophthalates to a Friedel–Crafts reaction with toluene and obtained from the former an acid, m. p. 123—126°, regarded as 4′-methyl-6-nitrobenzophenone-2-carboxylic acid (XXIX) and from the latter an acid, m. p. 262—265°, regarded as the isomeric 4′-methyl-3-nitrobenzophenone-2-carboxylic acid (XXX). Later, Mitter and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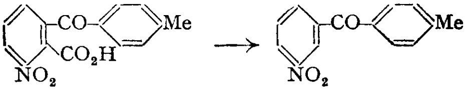
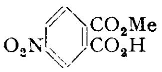

(XXX)

Sarkar (*J. Indian Chem. Soc.*, 1930, **7**, 619) obtained an acid claimed to be 4′-methyl-6-nitrobenzophenone-2-carboxylic acid, m. p. 218—219°, by the condensation of 3-nitrophthalic anhydride with toluene in the presence of aluminium chloride. More recently, Blicke and Otsuki (*J. Amer. Chem. Soc.*, 1941, **63**, 1945) have prepared a range of 1-alkyl 2-dialkylaminoalkyl 3-nitrophthalates by reactions involving ester acid chlorides, but no reference is made to any rearrangements.

Hayashi and Nakayama (*J. Soc. Chem. Ind. Japan*, 1933, **36**, 203B) also submitted the acid chloride derived from 1-methyl hydrogen 4-nitrophthalate (XXXI) to a Friedel–Crafts reaction with chlorobenzene and obtained both 4′-chloro-5-nitrobenzophenone-2-carboxylic acid (XXXII; R = Cl) and 4′-chloro-4-nitrobenzophenone-2-carboxylic acid (XXXIII; R = Cl). By means of a Friedel–Crafts reaction between 4-nitrophthalic anhydride and toluene, Lawrance (*J. Amer. Chem. Soc.*, 1921, **43**, 2579) obtained an acid, m. p. 100—105°, which was also obtained from the acid chloride from 1-methyl hydrogen 4-nitrophthalate (XXXI) and toluene and was therefore regarded as 4′-methyl-5-nitrobenzophenone-2-carboxylic acid (XXXII; R = Me). Repetition of Lawrance's work on the anhydride of 4-nitrophthalic acid and toluene by Mitter and Sarkar (*loc. cit.*) gave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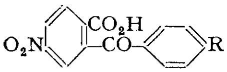
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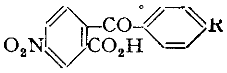
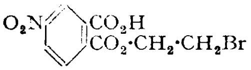

(XXXIII)

a methylnitrobenzophenonecarboxylic acid, m. p. 170—171°. The same reaction in the hands of Hayashi and Nakayama (*J. Soc. Chem. Ind. Japan*, 1934, **37**, 238B) gave an acid, m. p. 217—218°, together with a second acid, m. p. 190—191°, regarded as 4′-methyl-4-nitrobenzophenone-2-carboxylic acid (XXXIII; R = Me).

An unambiguous example of rearrangement in the 4-nitrophthalic acid series is provided by the work of Blicke and Castro (*J. Amer. Chem. Soc.*, 1941, **63**, 2437), who attempted to convert 1-2′-bromoethyl hydrogen 4-nitrophthalate (XXXIV) by means of its acid chloride into 1-2′-diethylaminoethyl 2-methyl 4-nitrophthalate (XXXV) but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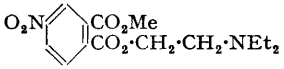
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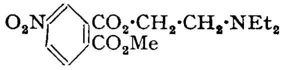

(XXXVI)

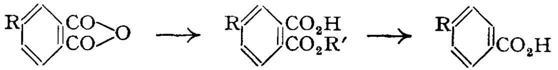
obtained instead the isomeric 2-2′-diethylaminoethyl 1-methyl 4-nitrophthalate (XXXVI), identical with the product obtained directly from 1-methyl hydrogen 4-nitrophthalate and 2-diethylaminoethyl chloride. Similar results were obtained with the ethyl, propyl, *iso*propyl, and *iso*butyl esters, and the authors concluded that they had obtained 2-2′-bromoethyl hydrogen 4-nitrophthalate and not the corresponding 1-ester in the initial reaction between 2-bromoethyl alcohol and 4-nitrophthalic anhydride. This, however, is contrary to the normal course followed in the reactions of 4-nitrophthalic anhydride, as shown in the work of Wegscheider *et al.* (*Monatsh.*, 1903, **24**, 805; 1905, **26**, 1093) as well as in that of Blicke and Castro themselves. It seems highly probable that the anomalous stage resides not in the formation of the acid ester from the anhydride but rather in the formation and behaviour of the ester acid chloride. A further example of rearrangement in the 4-nitrophthalic acid series has been provided by Hey and Walker (*J.*, 1948, 2214), who showed that treatment of the acid chloride derived from 1-methyl hydrogen 4-nitrophthalate (XXXI) with alkaline hydrogen peroxide gave two isomeric peroxides, which on decomposition in boiling benzene solution yielded methyl 4- and 5-nitrodiphenyl-2-carboxylate, (XXXVIII) and (XXXVII) respectively.

(XXXVII)

(XXXVIII)

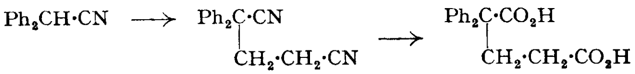
Hayashi, Turuoka, Morikawa, and Namikawa (*Bull. Chem. Soc. Japan*, 1936, **11**, 184) have reported the preparation of the acid chlorides of 1-methyl hydrogen 3-methylphthalate and of 2-methyl hydrogen 4-methylphthalate and their reaction with benzene in the presence of aluminium chloride. The formation of one ketonic acid only was reported in each reaction, on the structure of which the constitutions of the original half-esters were based. Friedel–Crafts reactions have been reported by Kirpal (*Monatsh.*, 1909, **30**, 355; 1910, **31**, 295) and Halla (*ibid.*, 1911, **32**, 747) on the acid chloride of the isomeric half-esters of cinchomeronic and quinolinic acids and no example of rearrangement has been recorded. The experimental detail is, however, sparse and unambiguous proof of the constitutions of the products is lacking.

Preparation of Half-esters.—The following methods have been used for the preparation of half-esters of unambiguous constitution. 1-Methyl hydrogen 3-nitrophthalate, 2-methyl hydrogen 3-nitrophthalate, and 1-methyl hydrogen 4-nitrophthalate were prepared by established methods, but a new route was developed for 2-methyl hydrogen 4-nitrophthalate. Nitration of *o*-toluic acid by van Scherpenzeel's method (*Rec. Trav. chim.*, 1901, **20**, 173) gave a mixture of nitrotoluic acids from which by esterification and fractional crystallisation methyl 2-methyl-5-nitrobenzoate was obtained. Oxidation of the latter with neutral potassium permanganate gave 2-methyl hydrogen 4-nitrophthalate. An attempt was made to prepare 2-methyl hydrogen 4-aminophthalate by the hydrogenolysis of 1-benzyl 2-methyl 4-nitrophthalate, but the action of benzyl alcohol on 4-nitrophthalic anhydride (XXXIX; R = NO_2) appeared to give a mixture of the two isomeric monobenzyl esters, from which on fractional crystallisation only the pure 1-benzyl ester (XL; R = NO_2, R′ = Ph·CH_2) was obtained in low yield. The constitution of this ester was established by decarboxylation with copper chromite, followed by hydrolysis, which gave *p*-nitrobenzoic acid (XLI; R = NO_2). Treatment of 4-chlorophthalic anhydride (XXXIX; R = Cl) with methyl alcohol also appeared to give a mixture of the two isomeric half-esters, from which only the 1-methyl ester (XL; R = Cl, R′ = Me) could be isolated in pure form. Dry distillation of the silver salt, followed by hydrolysis, gave *p*-chlorobenzoic acid (XLI; R = Cl). 1-Methyl hydrogen 4-nitro*iso*phthalate was obtained by esterification of 4-nitro*iso*phthalic acid prepared by the oxidation of 4-nitro-*m*-xylene, and 4-methyl hydrogen 2-nitroterephthalate was similarly obtained in good yield by the oxidation of 2-nitro-*p*-xylene and subsequent esterification (cf. Noyes, *Amer. Chem. J.*, 1888, **10**, 482).



(XXXIX) (XL) (XLI)

αα-Diphenylsuccinic acid was prepared by Salmon-Legagneur's method (*Compt. rend.*, 1939, **208**, 1507) from diphenylacetonitrile. The Fischer–Speier esterification of the acid gave a mixture of the β-ester and the diester. Partial hydrolysis of the latter gave the α-ester. A much improved method has been developed for the preparation of the homologous αα-diphenylglutaric acid (XLIII). Condensation of diphenylacetonitrile with acrylonitrile gave αα-diphenylglutarodinitrile (XLII) in excellent yield, which on hydrolysis gave the acid (XLIII) :



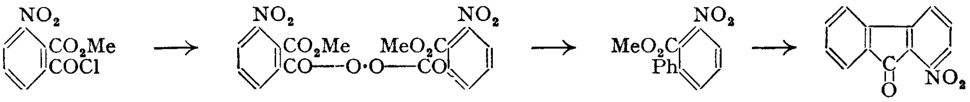
$$Ph_2CH{\cdot}CN \longrightarrow \underset{CH_2{\cdot}CH_2{\cdot}CN}{Ph_2C{\cdot}CN} \longrightarrow \underset{CH_2{\cdot}CH_2{\cdot}CO_2H}{Ph_2C{\cdot}CO_2H}$$

(XLII) (XLIII)

Following the previous example, Fischer–Speier esterification now gave a mixture of the γ-methyl ester and the diester, which on partial hydrolysis gave the α-methyl ester (cf. Salmon-Legagneur, *Compt. rend.*, 1941, **213**, 182).

Reactions of Half-esters.—In order to detect any rearrangement in the acid chlorides of the half-esters of dibasic acids described above, the most suitable reactions in the aromatic series were found to be (*a*) the formation of peroxides followed by their decomposition in boiling benzene solution, and (*b*) the formation of aromatic ketonic acids by means of Friedel–Crafts reactions with benzene or toluene. In the latter method the presence of *o*-nitro-groups is disadvantageous (see Thomas, " Anhydrous Aluminium Chloride in Organic Chemistry," 1941, pp. 252, 255), and aliphatic tertiary acid chlorides tend to react abnormally in giving rise to the elimination of carbon monoxide. In the aliphatic series reactions with a secondary base such as methylaniline or diethylamine can be used.

3-*Nitrophthalic Acid Series.*—Attempts to prepare a peroxide from 1-methyl hydrogen 3-nitrophthalate failed but the isomeric 2-methyl ester (cf. XLIV), by use of phosphorus pentachloride or pure thionyl chloride followed by alkaline hydrogen peroxide, gave the peroxide (XLV) in almost quantitative yield. Decomposition of the peroxide in boiling benzene solution gave a mixture of 2-methyl hydrogen 3-nitrophthalate (cf. XLIV) and methyl 3-nitrodiphenyl-2-carboxylate (XLVI). Hydrolysis of the latter to the free acid and treatment with concentrated sulphuric acid gave the hitherto unknown 1-nitrofluorenone (XLVII), which was reduced and acetylated to give 1-acetamidofluorenone, identical with the product obtained by the Hofmann degradation of the amide of fluorenone-1-carboxylic acid (Huntress, Pfister, and Pfister, *J. Amer. Chem. Soc.*, 1942, **64**, 2847) followed by acetylation. The high yields obtained in the preparation of this peroxide and its reaction with benzene, coupled with the absence of any isomeric compounds, shows that little rearrangement, if any, can have taken place. The possibility of limited rearrangement cannot be entirely excluded, since it is known that the isomeric acid chloride does not appear to form a peroxide.



(XLIV) (XLV) (XLVI) (XLVII)

The action of the acid chloride derived from 1-methyl hydrogen 3-nitrophthalate on benzene in the presence of aluminium chloride yielded an oily product in only 16% yield, which on hydrolysis gave two crystalline isomeric keto-acids, m. p.s 161·5—162·5° and 236—237°. In a similar reaction using the acid chloride derived from 2-methyl hydrogen 3-nitrophthalate the product, obtained in 75% yield, was mainly a methyl ester, m. p. 94·5°, which on hydrolysis gave the lower-melting acid obtained from 1-methyl hydrogen 3-nitrophthalate, while hydrolysis of the ester contained in the mother-liquors gave a small quantity of the higher-melting acid. The lower-melting acid gave 3-nitrobenzophenone on decarboxylation and must therefore be 3-nitrobenzophenone-2-carboxylic acid (XXVIII). The higher-melting acid must be 6-nitrobenzophenone-2-carboxylic acid (XXVI). The relationship of these results to those of previous workers is shown by the m. p.s in Table 1.

The constitutions assigned to these keto-acids by Hayashi *et al.* were based on those of the acid esters used and these are now shown to be in agreement with the results obtained on decarboxylation. The constitutions assigned by Lawrance, however, who isolated only one acid in each case, are reversed, and it is difficult to give any logical reason for this confusion, since the work of Bogert and Boroschek (*J. Amer. Chem. Soc.*, 1901, **23**, 746), to which reference is made for the original half-esters used, is clear and unequivocal. Lawrance also showed that the higher-melting keto-acid gave *o*-nitrobenzoic acid on alkaline fusion, whereas the lower-melting acid gave *m*-nitrobenzoic acid, but no reliable inference can be drawn from these observations. In the light of the results now presented, the structures assigned by Lawrance must be reversed both for the two nitrobenzophenone-carboxylic acids and for the two aminobenzophenone-carboxylic acids which he obtained from them.

TABLE 1.

	Benzophenone-2-carboxylic acid :			Benzophenone-2-carboxylic acid :	
Starting ester	6-nitro-	3-nitro-	Starting ester	6-nitro-	3-nitro-
1-Ethyl (*a*)	157—160° (decomp.)	None	2-Ethyl (*a*) ...	None	220—221° (decomp.)
			2-Methyl (*b*) ...	236—237°	160—161 (main)
1-Methyl (*b*) ...	236—237	None	2-Methyl (*c*) ...	236—238	162·5—163·5 (main)
1-Methyl (*c*) ...	236—237	161·5—162·5°			

(*a*) Lawrance, *J. Amer. Chem. Soc.*, 1920, **42**, 1875. (*b*) Hayashi, Turuoka, Morikawa, and Namikawa, *Bull. Chem. Soc. Japan*, 1936, **11**, 191. (*c*) This paper.

The action of the acid chloride prepared from 1-methyl hydrogen 3-nitrophthalate on toluene in the presence of aluminium chloride gave a mixture of esters consisting largely of the methyl ester of 4′-methyl-6-nitrobenzophenone-2-carboxylic acid. Hydrolysis of the ester gave the free acid (XXIX), m. p. 219·5—220·5°, the structure of which was proved by decarboxylation to give 4′-methyl-2-nitrobenzophenone. Fractional crystallisation of the mother-liquors gave a second ester in very small yield, which gave an acid, m. p. 211—212°. This acid and its methyl ester on admixture depressed the melting points of both 4′-methyl-6- and -3-nitrobenzophenone-2-carboxylic acid and their methyl esters respectively. This acid must therefore be regarded as a derivative of 2′- or 3′-methylbenzophenone. The presence of the isomeric 4′-methyl-3-nitrobenzophenone-2-carboxylic acid (XXX) was not detected in the reaction product. In a similar reaction with 2-methyl hydrogen 3-nitrophthalate the resulting mixture of esters consisted largely of the methyl ester of 4′-methyl-3-nitrobenzophenone-2-carboxylic acid, hydrolysis of which gave the free acid, m. p. 188—189° (XXX), which was smoothly decarboxylated to 4′-methyl-3-nitrobenzophenone. No other isomeride was isolated. It seems likely, by analogy with the results of the corresponding reactions with benzene, that in both of these reactions with toluene some rearrangement has occurred but the isolation of the rearranged product was rendered difficult owing to the presence of additional isomerides, which arise from reactions at the *ortho*- and *meta*-positions with regard to the methyl group. There is considerable confusion in the literature with regard to the methylnitrobenzophenone-carboxylic acids, and Table 2 shows by the m. p.s that the present results are in agreement with those of Mitter and Sarkar for the one isomer prepared by them and are in total disagreement with those of Lawrance.

TABLE 2.

	4′-Methylbenzophenone-2-carboxylic acid :			4′-Methylbenzophenone-2-carboxylic acid :	
Starting compound	6-nitro-	3-nitro-	Starting compound	6-nitro-	3-nitro-
Anhydride (*a*) ...	122—126° *	262—265° *	Anhydride (*b*) ...	218—219° †	None
1-Ethyl ester (*a*)...	123—126° *	None	1-Methyl ester (*c*)	219·5—220·5° ‡	None isolated
2-Ethyl ester (*a*)	None	262—265° *	2-Methyl ester (*c*)	None isolated	188—189°

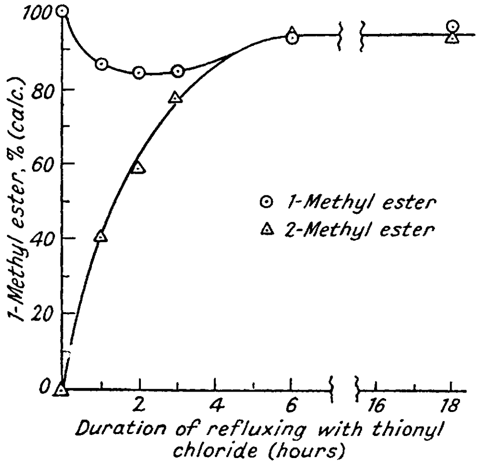
(*a*) Lawrance, *J. Amer. Chem. Soc.*, 1921, **43**, 2578. (*b*) Mitter and Sarkar, *J. Indian Chem. Soc.* 1930, **7**, 619. (*c*) This paper.

* With decomp. † Yellow. ‡ Colourless.

Experiments were also carried out on the preparation of the phenyl esters of 1-methyl and of 2-methyl hydrogen 3-nitrophthalate by means of the acid chlorides. The former half-ester gave largely 1-methyl 2-phenyl 3-nitrophthalate and the latter largely 2-methyl 1-phenyl 3-nitrophthalate, which confirms the fact that in this series little rearrangement appears to have taken place. There was, however, qualitative evidence of some rearrangement, and an attempt was therefore made to determine whether an equilibrium is set up by utilising the different rates of esterification of the two isomeric half-esters.

A weighed quantity of each acid ester was converted into the acid chloride under standard conditions, "crude" thionyl chloride being used in order to favour rearrangement. After rapid removal of the excess of thionyl chloride, the product was hydrolysed with aqueous sodium hydrogen carbonate, and the mixture of half-esters recovered. The determination of the composition of the product was effected by means of esterification with methyl alcohol and sulphuric acid under standard conditions. The esterification of the sterically hindered 1-methyl ester under these conditions gave only 7·2% of the neutral dimethyl ester, whereas the less hindered 2-methyl ester gave 93·7% of the neutral dimethyl ester. It thus follows that a mixture of half-esters will give a value for the percentage unesterified between 92·8 and 6·3%. On the not unreasonable assumption that the presence of one isomeride does not substantially affect the rate of esterification of the other, the composition of any mixture of half-esters can be determined from the percentage of unesterified material by simple proportion using the known values for the pure esters.

Isomerisation of the acid chlorides of the two methyl hydrogen 3-nitrophthalates.



The acid chlorides from 1-methyl and 2-methyl hydrogen 3-nitrophthalate were prepared with five different times of refluxing and the products were treated as described above. The results, expressed in the figure, show that the acid chloride of the 1-methyl ester has undergone maximum rearrangement after 2 hours' refluxing and approaches a steady value at about 96% of 1-methyl ester on prolonged heating. The 2-methyl ester approaches asymptotically the same value. This phenomenon is probably due to the formation of the diacid chloride on prolonged heating, which on hydrolysis to the diacid would simulate the behaviour of the 1-methyl ester, which it yields on esterification. The formation of this diacid chloride prevents the realisation of a true equilibrium between the two isomeric acid chlorides.

4-*Nitrophthalic Acid Series.*—Reactions in the 4-nitrophthalic acid series were confined to those of the more accessible 1-methyl ester. The acid chloride, prepared with purified thionyl chloride, was converted into the peroxide, as described by Hey and Walker (*loc. cit.*), the decomposition of which in boiling benzene gave a mixture of the methyl esters of 5- and 4-nitrodiphenyl-2-carboxylic acid (XXXVII) and (XXXVIII). Hydrolysis and subsequent ring closure with concentrated sulphuric acid gave both 3- and 2-nitrofluorenone. Rearrangement had thus taken place, and similar results were obtained when phosphorus pentachloride was used in place of thionyl chloride. These results are therefore similar to those previously reported by Hey and Walker (*loc. cit.*), who used unpurified thionyl chloride. When the same acid chloride (prepared with phosphorus pentachloride) was allowed to react with benzene in the presence of aluminium chloride the product consisted largely of methyl 4-nitrobenzophenone-2-carboxylate, the product of rearrangement, with a smaller quantity of the methyl ester of 5-nitrobenzophenone-2-carboxylic acid. Hydrolysis gave the corresponding acids (XXXIII; R = H) and (XXXII; R = H). These experiments show the existence of appreciable rearrangement which was not eliminated even by the use of purified thionyl chloride and by working at temperatures below 30° both in the preparation of the acid chloride and in the subsequent reaction with benzene. This result is in contrast to the experience of Ställberg-Stenhagen (*loc. cit.*) with the half-esters of β-methylglutaric acid. In the Friedel–Crafts reaction, however, the possibility of rearrangement after the addition of the aluminium chloride cannot be excluded.

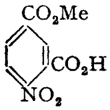
Analogous results were obtained in the reaction between the acid chloride from 1-methyl hydrogen 4-nitrophthalate (prepared with purified thionyl chloride) and toluene in the presence of aluminium chloride, which gave a mixture of esters from which both 4′-methyl-4-nitrobenzophenone-2-carboxylic acid (XXXIII; R = Me) and 4′-methyl-5-nitrobenzophenone-2-carboxylic acid (XXXII; R = Me) were obtained on hydrolysis. The former acid gave 4′-methyl-4-nitrobenzophenone on decarboxylation, whereas the latter gave 4′-methyl-3-nitrobenzophenone. The reports in the literature concerning these acids are again confused, as shown by the m. p.s in Table 3. The present results are in agreement with those of Hayashi and Nakayama. The acid obtained by Mitter and Sarkar is probably a mixture, since their amino-acid obtained on reduction was converted into the known 6-methylalizarin (Mitter and Biswas, *J. Indian Chem. Soc.*, 1928, **5**, 775).

TABLE 3.

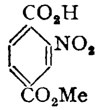
Starting compound	4′-Methylbenzophenone-2-carboxylic acid: 5-nitro-	4′-Methylbenzophenone-2-carboxylic acid: 4-nitro-	Starting compound	4′-Methylbenzophenone-2-carboxylic acid: 5-nitro-	4′-Methylbenzophenone-2-carboxylic acid: 4-nitro-
Anhydride (*a*) ...	100—105° *	Trace	Anhydride (*c*) ...	217—218°	190—191°
1-Methyl ester (*a*)	101—105 *	None	1-Methyl ester (*d*)	217·5—218·5	192—193
Anhydride (*b*)	170—171	Trace			

(*a*) Lawrance, *J. Amer. Chem. Soc.*, 1921, **43**, 2579. (*b*) Mitter and Sarkar, *J. Indian Chem. Soc.*, 1930, **7**, 619. (*c*) Hayashi and Nakayama, *J. Soc. Chem. Ind. Japan*, 1934, **37**, 238. (*d*) This paper.
* With decomposition.

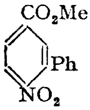
iso*Phthalic and Terephthalic Acid Series*.—Reactions carried out with 1-methyl hydrogen 4-nitro*iso*phthalate (XLVIII) and with 4-methyl hydrogen 2-nitroterephthalate (XLIX) showed no evidence of rearrangement. Thus, the acid chloride prepared from 1-methyl hydrogen 4-nitro*iso*phthalate on treatment with aniline gave only one product, presumably the anilide of 1-methyl hydrogen 4-nitro*iso*phthalate. Conversion of the same acid chloride into the peroxide and decomposition of the latter in boiling benzene gave only methyl 6-nitrodiphenyl-3-carboxylate (L), which on hydrolysis and decarboxylation gave 2-nitrodiphenyl. In similar manner the acid chloride prepared from 4-methyl hydrogen 2-nitroterephthalate gave a peroxide, which underwent decomposition in boiling benzene to give methyl 2-nitrodiphenyl-4-carboxylate (LI). The free acid was obtained on hydrolysis.



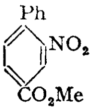
(XLVIII)



(XLIX)



(L)

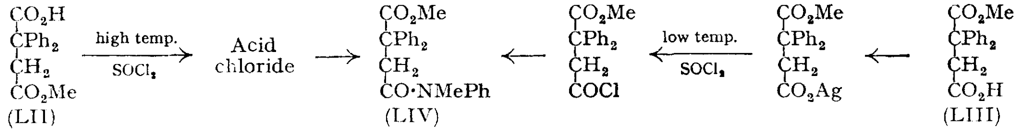


(LI)

Succinic and Glutaric Acid Series.—Reactions were restricted to the methyl esters of αα-diphenyl-succinic and -glutaric acids.

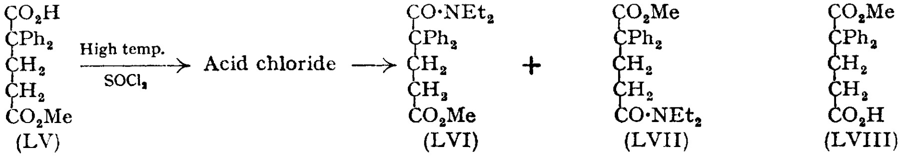
When the acid chloride prepared from the β-methyl ester (LII) of αα-diphenylsuccinic acid was treated with aniline the only product isolated was αα*N*-triphenylsuccinimide, probably formed during recrystallisation (cf. Salmon-Legagneur and Soudan, *loc. cit.*). When the aniline was replaced by methylaniline, in order to exclude the possibility of cyclisation, two products were obtained, namely, the methyl ester of an *N*-methyl-αα-diphenylsuccinanilide, m. p. 150—150·5°, and the bis-(*N*-methylanilide), m. p. 156°. In order to ascertain the exact structure of the former, recourse was had to the silver salt technique of Salmon-Legagneur and Soudan (*loc. cit.*), who showed that when ester acid chlorides are prepared by the action of thionyl chloride at low temperatures on the dry silver salt of the half-ester, the resulting ester acid chloride has the expected structure and rearrangement is entirely suppressed. When the α-methyl ester of αα-diphenylsuccinic acid (LIII) was converted in this manner into the acid chloride and then treated with methylaniline, two products were obtained, namely, an ester *N*-methylanilide, m. p.

150° (LIV), identical with the compound prepared as described above from the β-methyl ester, and an unidentified neutral compound, m. p. 166—167°.

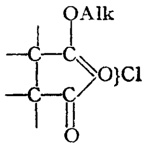


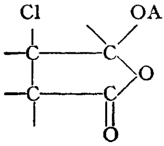
The application of the silver salt technique to the β-methyl ester (LII) of αα-diphenylsuccinic acid led only to inconclusive results, presumably owing to steric hindrance in the acid chloride. The formation of the same ester-anilide (LIV) by these two routes indicated that rearrangement must occur in one of them. In agreement with Salmon-Legagneur and Soudan, it seems most likely that rearrangement occurs in the high-temperature reaction with thionyl chloride. The absence of a second isomeric ester-anilide from the high-temperature reaction does not exclude the possibility of the existence of a mixture of the two acid chlorides, since the β-ester α-acid chloride is sterically hindered.

In similar manner, when the γ-methyl ester of αα-diphenylglutaric acid (LV) was converted into the acid chloride with hot thionyl chloride and then treated with diethylamine, two isomeric ester diethylamides, (LVI) and (LVII), were obtained. When the silver salt of the α-methyl ester (LVIII) of αα-diphenylglutaric acid was treated with cold thionyl chloride and then with diethylamine, one ester diethylamide only was obtained which was identical with one of the diethylamides prepared by the former method and which presumably has the structure of the α-methyl ester (LVII) of *NN*-diethyl-αα-diphenylglutaramide. The application of the silver salt technique to the γ-methyl ester again led to inconclusive results, presumably owing to the reluctance of the hindered acid chloride to react with the secondary base. These results again indicate that rearrangement occurred when the γ-ester was treated with hot thionyl chloride.



Mechanism of the Rearrangement.—The absence of the evidence of the occurrence of any rearrangement with the acid chlorides of the half-esters of substituted *iso*phthalic and terephthalic acids suggests that the change is intramolecular rather than intermolecular and involves a cyclic intermediate. It is possible to visualise three types of intermediate, namely, (*a*) the anhydride of the dicarboxylic acid, (*b*) an oxonium chloride (LIX), and (*c*) an alkoxy-chloro-lactone (LX). Ställberg-Stenhagen (*loc. cit.*) regards the anhydride

(LIX)




(LX)

as the essential intermediate in her reactions with derivatives of β-methylglutaric acid, but this suggestion cannot be applied to the reactions of 1-methyl hydrogen 4-nitrophthalate which yield mainly derivatives of 2-methyl hydrogen 4-nitrophthalate. The action of methanol on 4-nitrophthalic anhydride is known to lead almost quantitatively to the formation of the 1-methyl ester (Wegscheider and Lipschitz, *Monatsh.*, 1900, **21**, 805). An oxonium salt has been suggested by Prelog and Heimbach-Juhasz (*Ber.*, 1941, **74**, 1702) as an intermediate in the closely related isomerisation of γ-ethoxybutyryl and δ-ethoxyvaleryl chlorides to ethyl γ-chlorobutyrate and ethyl δ-chlorovalerate respectively. The lactone intermediate has been suggested by Bredt (*loc. cit.*), Salmon-Legagneur (*Bull. Soc. Sci. Bretagne*, 1938, **15**, 189), and Hayashi, Turuoka, and Nakayama (*J. Chem. Soc.*

Japan, 1935, **56**, 1096) for the reactions of specific half-ester halides, and the results now reported would appear to support the view that this mechanism is general. Such a theory is in agreement with the better-known examples of the tautomerism shown by the diacid halides of phthalic and succinic acids, and also with the closely related rearrangements studied by Meyer (*Monatsh.*, 1904, **25**, 477), Johnson and Goldman (*J. Amer. Chem. Soc.*, 1945, **67**, 430), and Badger, Campbell, Cook, Raphael, and Scott (*J.*, 1950, 2326). Evidence for lactone formation in the action of alcohols on *o*-dicarboxylic anhydrides has also been provided by Hirshberg, Lavie, and Bergman (*J.*, 1951, 1030).

EXPERIMENTAL

(M. p.s are uncorrected. Microanalyses are by Drs. Weiler and Strauss, Oxford.)

Preparation of Half-esters.

1-Methyl hydrogen 3-nitrophthalate, m. p. 163·5—164°, was prepared in 71% yield by the method of Cohen, Woodroffe, and Anderson (*J.*, 1916, **109**, 222). 2-Methyl hydrogen 3-nitrophthalate, m. p. 152·5—153·5°, was prepared in 67% yield by the method of Dickinson, Crosson, and Copenhaver (*J. Amer. Chem. Soc.*, 1937, **59**, 1094). 1-Methyl hydrogen 4-nitrophthalate, m. p. 131·5—132·5°, was obtained in 93% yield as described by Wegscheider and Lipschitz (*Monatsh.*, 1900, **21**, 805).

1-*Benzyl Hydrogen* 4-*Nitrophthalate*.—4-Nitrophthalican hydride (16·4 g.) was boiled under reflux for 1 hour with benzyl alcohol (10·0 g.) in dry benzene (50 c.c.). After removal of the solvent under reduced pressure, the residue was taken up in ether (50 c.c.) and extracted with 5% aqueous sodium carbonate. Acidification of the alkaline extracts precipitated the crude half-ester as a pale yellow oil, which solidified at 0° (23·6 g.; m. p. 90—120°). Repeated crystallisation from benzene–light petroleum (b. p. 80—100°) gave 1-*benzyl hydrogen* 4-*nitrophthalate* in white prisms, m. p. 142—143·5° (Found: C, 59·6; H, 4·0. $C_{15}H_{11}O_6N$ requires C, 59·8, H, 3·7%). No pure isomeric acid ester could be obtained by fractional crystallisation of the filtrates. A portion of the acid ester (1·8 g.), copper chromite (1·8 g.), and redistilled quinoline (10 c.c.) were stirred for 1 hour at 160—170°. The cooled mixture was diluted with ether (20 c.c.), filtered from catalyst, and thoroughly extracted with 5N-hydrochloric acid and then with 5% aqueous sodium carbonate. Distillation of the ether yielded a brown oil (1·8 g.), which only partly solidified at 0° and appeared to contain nitrobenzene. The oily residue was boiled under reflux for 2 hours with a mixture of glacial acetic acid (6 c.c.), concentrated sulphuric acid (3 c.c.), and water (1·5 c.c.). The cooled solution was diluted with water and extracted with ether, and the ethereal extract washed with 5% aqueous sodium carbonate. Acidification of the alkaline extract, ether-extraction, and distillation of the ether gave *p*-nitrobenzoic acid (0·3 g.). Three recrystallisations from water yielded the pure acid, m. p. 235—237°, undepressed on admixture with an authentic specimen.

2-*Methyl Hydrogen* 4-*Nitrophthalate*.—Methyl 2-methyl-5-nitrobenzoate (5·0 g.) [prepared by nitration of *o*-toluic acid and subsequent esterification as described by van Scherpenzeel (*Rec. Trav. chim.*, 1901, **20**, 173)], potassium permanganate (12·5 g.), magnesium sulphate (5·3 g.), and water (250 c.c.) were vigorously stirred at 80—90° for 3 hours. The hot mixture was filtered at the pump, the residue was washed with hot water (100 c.c.), and the combined aqueous solutions were cooled and extracted with ether. Evaporation of the ethereal solution yielded unchanged ester (1·4 g.). Acidification of the alkaline solution and ether-extraction gave the crude 2-methyl ester (2·1 g.), m. p. 129—135°, raised on recrystallisation from benzene and subsequently from water to 141·5—143·5°. Wegscheider, Kusy, and Dubrav (*Monatsh.*, 1903, **24**, 827) recorded m. p. 140—142°.

1-*Methyl Hydrogen* 4-*Chlorophthalate*.—4-Chlorophthalic anhydride (16·0 g.) in absolute methanol (20 c.c.) was boiled under reflux for ½ hour. Removal of the methanol under reduced pressure yielded a colourless oil (18·7 g.), which solidified to a sticky white solid when kept. Five recrystallisations from benzene–light petroleum (b. p. 80—100°) gave 1-methyl hydrogen 4-chlorophthalate in colourless needles, m. p. 104—105° (Found: C, 50·7; H, 3·2. Calc. for $C_9H_7O_4Cl$: C, 50·4; N, 3·3%). Hayashi, Furusawa, and Turuoka [*J. Soc. Chem. Ind., Japan*, 1941, **44**, No. 11, 436B (Supp. Bdg.)] quote m. p. 107·5°. A portion of the acid ester (2·0 g.) was converted into the silver salt (2·7 g., 90%), and the latter dry-distilled at 40 mm. On the bath-temp. being raised to 250° a colourless oil (1·0 g.) distilled. The distillate, after being kept for 12 hours in 5% sodium hydrogen carbonate (2 c.c.) to remove any anhydride, was recovered by ether-extraction and boiled under reflux for 2 hours with a solution of potassium hydroxide (1·0 g.) in 40% aqueous alcohol (15 c.c.). The cooled solution was diluted with water (20 c.c.), extracted with ether, and acidified. The crude precipitate (0·6 g.; m. p. 175—200°) on sublimation and recrystallisation from dilute acetic acid yielded *p*-chlorobenzoic acid, m. p. 232—235°, raised to 238—241° on admixture with an authentic specimen, m. p. 239—241°.

1-*Methyl Hydrogen* 4-*Nitro*iso*phthalate.*—The addition of *m*-xylene to fuming nitric acid at 0° (Harmsen, *Ber.*, 1880, **13**, 1558; Holleman and Huisinger, *Rec. Trav. chim.*, 1908, **27**, 267) gave rise to considerable quantities of undesirable polynitro-compounds. Inversion of the procedure proved satisfactory and only traces of polynitro-compounds were formed. The reaction product was distilled with steam, the first fraction consisting of *m*-xylene ($d < 1$) being rejected, and then redistilled under reduced pressure; the product had b. p. 142—148°/48 mm. (yield 58%). Crude 4-nitro*iso*phthalic acid from the oxidation of 4-nitro-*m*-xylene (Axer, *Monatsh.*, 1920, **41**, 159) was esterified with methanol–sulphuric acid. The acidic product separated from benzene in colourless prisms (45%), m. p. 153·5° (Axer, *loc. cit.*, gives m. p. 154°).

4-*Methyl Hydrogen* 2-*Nitroterephthalate.*—2-Nitro-*p*-xylene (99·5 g.) and water (4 l.) were vigorously stirred at 80—90°, and potassium permanganate (469 g.) added in 8 portions during 3 hours. Stirring and heating were continued for a further 5 hours, the solution decolorised with sodium hydrogen sulphite and filtered, and the residue washed with hot water (1 l.). The combined aqueous solutions were concentrated to 500 c.c., acidified, and cooled to 0°, and the crude 2-nitroterephthalic acid was filtered off. Ether-extraction of the filtrates gave a further quantity of acid. The total yield was 104 g., m. p. 260° (cf. Noyes, *Amer. Chem. J.*, 1888, **10**, 485). The crude acid, on esterification with methanol–sulphuric acid, gave a neutral fraction (36 g.) which yielded dimethyl 2-nitroterephthalate (18·0 g.; m. p. 71·5°), and an acidic fraction, which yielded 4-methyl hydrogen 2-nitroterephthalate (56 g.; m. p. 134·5—136°). Wegscheider (*Monatsh.*, 1902, **23**, 407) records m. p. 73—74° and m. p. 133·5—135°, respectively.

The α- *and the* β-*Methyl Ester of* αα-*Diphenylsuccinic Acid.*—αα-Diphenylacetonitrile (Robb and Schultz, *Org. Synth.*, **28**, 55) was converted into ethyl β-cyano-ββ-diphenylpropionate (69%; m. p. 104—105°) by Salmon-Legagneur's method (*Compt. rend.*, 1939, **208**, 1507). Hydrolysis with aqueous-alcoholic potassium hydroxide and subsequently with concentrated hydrochloric acid–acetic acid yielded αα-diphenylsuccinic acid (75%), m. p. 169—170°. Salmon-Legagneur (*loc. cit.*) gives m. p. 197—199° with softening at 170°, but does not record a yield. Dry hydrogen chloride was passed for 2½ hours into a solution of αα-diphenylsuccinic acid (23·8 g.) in absolute methanol (60 c.c.) gently boiling under reflux. The majority of the excess of alcohol was then removed under reduced pressure, and the cooled residue taken up in ether. Extraction of the ether with excess of 10% aqueous sodium carbonate and acidification of the alkaline extract precipitated the β-methyl ester as a colourless oil, which solidified (15·3 g.) and was dried at 100°. Recrystallisation from benzene–light petroleum (b. p. 80—100°) gave β-methyl hydrogen αα-diphenylsuccinate in colourless prisms, m. p. 140·5—142°. Salmon-Legagneur (*loc. cit.*) records m. p. 141—143°, but no yield. Distillation of the ether from the neutral fraction (see above) gave dimethyl αα-diphenylsuccinate (9·9 g.) as a white crystalline solid, m. p. 85·5—88°. A sample crystallised from light petroleum (b. p. 80—100°) in rosettes of prisms, m. p. 86—88·5°. Salmon-Legagneur (*loc. cit.*) records m. p. 82—83°. The dimethyl ester (9·8 g.) was boiled under reflux for ½ hour with methanol (30 c.c.) containing potassium hydroxide (1·9 g.). Methanol (15 c.c.) was then distilled off, water (30 c.c.) added, and the solution extracted with ether. Distillation of the ether gave unchanged dimethyl ester (5·0 g.). Acidification of the aqueous solution precipitated the methyl ester (4·3 g.), m. p. 175—181°. Two recrystallisations from benzene–light petroleum (b. p. 80—100°) gave the pure ester, m. p. 179·5—181°. Salmon-Legagneur (*loc. cit.*) records m. p. 183—184°.

αα-*Diphenylglutarodinitrile.*—To a stirred solution of diphenylacetonitrile (19·3 g.) in *tert.*-butyl alcohol (50 c.c.) containing 1 c.c. of 30% methanolic potassium hydroxide was added acrylonitrile (redistilled, 8·0 g.). The temperature was maintained at 50° first by warming, then by controlled addition of the acrylonitrile. After complete addition (20 minutes) the temperature was kept at 50° for a further 3 hours. Water (100 c.c.) was then added, and the cooled mixture extracted with ether. The dried extract (Na_2SO_4) was freed from solvent by distillation under reduced pressure. The residual pale yellow oil solidified and recrystallisation from ethanol yielded αα-*diphenylglutarodinitrile* (20·1 g.) in colourless prisms, m. p. 71·5—72·5° (Found: C, 83·2; H, 5·9. $C_{17}H_{14}N_2$ requires C, 82·9; H, 5·7%).

The α- *and the* γ-*Methyl Ester of* αα-*Diphenylglutaric Acid.*—αα-Diphenylglutarodinitrile (10·4 g.) was boiled under reflux for 36 hours with acetic acid (20 c.c.) and concentrated hydrobromic acid (40 c.c.). The cooled solution was poured on ice (200 g.), and the fawn-coloured solid filtered off (11·7 g.) and dried *in vacuo* (m. p. 158—172°). The solid was boiled under reflux for 4 hours with potassium hydroxide (50 g.) in water (50 c.c.), and the cooled solution poured into water (150 c.c.) and acidified. The white precipitate was filtered off and recrystallised from aqueous acetic acid. The acid (10·4 g.) separated in colourless needles, m. p. 195—197°. Salmon-Legagneur (*Compt. rend.*, 1941, **213**, 183) records m. p. 183° and Trivedi, Phalnikar, and Nargund (*J. Univ. Bombay*, 1942, **10**, Part 5, 136) quote m. p. 193—194° for αα-diphenylglutaric acid. The acid (10·4 g.) was esterified as for the corresponding succinic acid (see above). The γ-methyl ester separated from benzene–light petroleum (b. p. 80—100°) in colourless prisms (7·3 g.). The m. p. on drying at 100° was 110—112°, but prolonged drying at 100° *in vacuo* raised it to 124—125°, and subsequent recrystallisation and drying to 125—125·5°. Salmon-Legagneur (*Compt. rend.*, 1941, **213**, 183) records m. p. 108°. Distillation of the ether from the neutral fraction yielded the dimethyl ester (3·3 g.), m. p. 53—55°. Salmon-Legagneur records 64—65°. The dimethyl ester (3·3 g.) was boiled under reflux for ½ hour with potassium hydroxide (0·65 g.) in methanol (30 c.c.). The mixture, worked up as above, yielded unchanged dimethyl ester (1·2 g.), and the α-methyl ester (1·6 g.) in colourless prisms, m. p. 127—129·5°, unchanged by prolonged drying *in vacuo*. Salmon-Legagneur records m. p. 129° for this ester.

Reactions of Half Esters.

Peroxide of 2-*Methyl Hydrogen* 3-*Nitrophthalate with Benzene.*—2-Methyl hydrogen 3-nitrophthalate (22·5 g.) was boiled under reflux for 1 hour with purified thionyl chloride (25 c.c.; b. p. 75—76°) which had been fractionated over quinoline and refractionated over linseed oil. Removal of the excess of thionyl chloride under reduced pressure gave the acid chloride in white needles. To a stirred solution of the acid chloride in chloroform (40 c.c.) was added a solution of sodium hydroxide (4·5 g.) in water (10 c.c.), followed by hydrogen peroxide (20-vol.; 60 c.c.). The temperature was kept at 0—5° for 1½ hours. The bulky white precipitate was filtered off and dried *in vacuo*. A further 0·8 g. was obtained by addition of methanol (200 c.c.) to the chloroform layer. The total yield of the *peroxide* was 19·9 g. (purity by titration, 98·3%). The peroxide (18·5 g.) was boiled under reflux for 18 hours with benzene (100 c.c.). The cooled solution on extraction with 5% aqueous sodium carbonate and acidification of the extracts gave crude 2-methyl hydrogen 3-nitrophthalate (8·9 g.), m. p. 148—152°. Distillation of the benzene gave an orange solid, which distilled at 135—145°/3 × 10^{-2} mm., to give *methyl* 3-*nitrodiphenyl*-2-*carboxylate* as a colourless oil (9·3 g.), which solidified. Crystallisation from aqueous alcohol gave colourless prisms, m. p. 121·5—122·5° (Found: C, 65·5; H, 4·3. $C_{14}H_{11}O_4N$ requires C, 65·4; H, 4·3%). The methyl ester (8·7 g.) on hydrolysis with 5% potassium hydroxide in aqueous alcohol yielded 3-*nitrodiphenyl*-2-*carboxylic acid* (7·4 g.) in colourless prisms, m. p. 200·5—201·5° from aqueous alcohol (Found: C, 64·4; H, 3·9. $C_{13}H_9O_4N$ requires C, 64·2; H, 3·7%). The crude 3-nitrodiphenyl-2-carboxylic acid (6·6 g.) was powdered and stirred with concentrated sulphuric acid (20 c.c.) (5 minutes), the temperature raised to 60° for 5 minutes, and the mixture poured on ice (100 g.). The yellow precipitate was filtered off, washed well with 5% sodium carbonate solution, then with water, and dried at 100°. The 1-*nitrofluorenone* (5·9 g.) melted at 187—188°, raised on sublimation under reduced pressure and recrystallisation from benzene to 188·5—189·5° (lemon-yellow prisms) (Found: C, 69·1; H, 3·2. $C_{13}H_7O_3N$ requires C, 69·3; H, 3·1%). Finely powdered 1-nitrofluorenone (2·0 g.) was boiled under reflux with alcohol (120 c.c.) and ammonia (*d* 0·88; 15 c.c.). Hydrogen sulphide was passed in for 3 hours, during which the fluorenone dissolved. The solution, concentrated to 25 c.c., was diluted with water (125 c.c.) and filtered. The orange residue was 6 times extracted with boiling 3N-hydrochloric acid (25 c.c. portions). Basification of the filtered extract with ammonia precipitated 1-aminofluorenone (1·43 g.) as an orange solid, m. p. 114—117°, raised on recrystallisation from aqueous alcohol and subsequently from light petroleum (b. p. 80—100°) to 118·5—119·5° (orange plates and needles, the latter transforming sharply into the former near the m. p.). The acetyl derivative formed yellow needles, m. p. 138—139°, from aqueous alcohol or light petroleum (b. p. 80—100°) (Huntress, Pfister, and Pfister, *J. Amer. Chem. Soc.*, 1942, **64**, 2847, record m. p. 118—118·5° for 1-aminofluorenone and 138—138·3° for the acetyl derivative).

The use of phosphorus pentachloride in the preparation of the acid chloride from 2-methyl hydrogen 3-nitrophthalate led to rather lower yields of peroxide, but the latter when decomposed in benzene and submitted to the above series of reactions yielded only 1-nitrofluorenone,

m. p. 188·5—189·5°, identical with that obtained above. No trace of the isomeric 4-nitro-compound could be detected.

Friedel–Crafts Reaction (*Benzene*) *with* 1-*Methyl Hydrogen* 3-*Nitrophthalate*.—1-Methyl hydrogen 3-nitrophthalate (15 g.) was boiled under reflux for 1½ hours with purified thionyl chloride (25 c.c.), and the excess of chloride removed under reduced pressure. The acid chloride in dry thiophen-free benzene (75 c.c.) was added dropwise to a stirred suspension of freshly ground aluminium chloride (20 g.) in dry thiophen-free benzene (75 c.c.). The temperature was kept at 0—5° during the addition (1 hour); the colour of the mixture changed through green to dark blue and finally almost to black. The mixture was stirred for a further hour, kept at room temperature overnight, and decomposed with ice (200 g.) and concentrated hydrochloric acid (50 c.c.). A considerable quantity of insoluble material was filtered off. The benzene layer, washed well with dilute acid and with 5% aqueous sodium carbonate, on removal of solvent and distillation of the residue, gave a viscous yellow oil (4·8 g.). This oil was boiled under reflux for ½ hour with methanol (20 c.c.) (in order to remove anhydride), diluted with ether (100 c.c.), and extracted with 5% aqueous sodium carbonate. Distillation of the ether yielded a viscous yellow oil (3·0 g.) which was boiled under reflux for 18 hours with 10% aqueous potassium hydroxide (40 c.c.). The solution was cooled, diluted with water, extracted with ether, acidified, and re-extracted with ether. Distillation of the ether from the second dried extract yielded a brown solid (2·5 g.). One recrystallisation from 80% acetic acid yielded 6-nitrobenzophenone-2-carboxylic acid (0·5 g.), m. p. 223—233°, raised on recrystallisation from aqueous acetic acid to 236—237° (colourless needles) (Hayashi *et al.*, *Bull. Chem. Soc. Japan*, 1936, **11**, 191, quote m. p. 236—237°). The mother-liquors on concentration yielded first a further quantity of the same acid and then 3-nitrobenzophenone-2-carboxylic acid in colourless needles (0·3 g.), m. p. 160—162°, raised on subsequent recrystallisation to 161·5—162·5°. Hayashi *et al.* quote m. p. 160—161°. The latter acid (0·19 g.) was stirred with copper chromite (0·5 g.) in quinoline (5 c.c.) at 165—175°. The product, worked up as for 1-benzyl hydrogen 4-nitrophthalate, on recrystallisation from alcohol gave 3-nitrobenzophenone (0·087 g.) in colourless needles, m. p. 93·5—94·5°. Geigy and Koenigs (*Ber.*, 1885, **18**, 2401) quote m. p. 94—95°.

Friedel–Crafts Reaction (*Benzene*) *with* 2-*Methyl Hydrogen* 3-*Nitrophthalate*.—2-Methyl hydrogen 3-nitrophthalate (15 g.) was converted into the acid chloride and treated with aluminium chloride in benzene as for the 1-methyl ester. The product distilled at 170—180°/2 × 10^{-2} mm. as a pale yellow oil (15·3 g.). After removal of anhydride as above, the residue (14·3 g.) solidified on trituration with methanol to a white solid, m. p. 85—95°. Two recrystallisations from methanol gave pure *methyl* 3-*nitrobenzophenone*-2-*carboxylate* (12·0 g.) in colourless prisms, m. p. 93·5—94·5° (Found: C, 63·4; H, 3·7. $C_{15}H_{11}O_5N$ requires C, 63·2; H, 3·9%). Hydrolysis of the ester with concentrated hydrochloric acid containing a little dioxan yielded 3-nitrobenzophenone-2-carboxylic acid in long colourless prisms, m. p. 162·5—163·5°, undepressed on admixture with the acid, m. p. 161·5—162·5°, obtained from the 1-methyl ester. The mother-liquors from the recrystallisation of methyl 3-nitrobenzophenone-2-carboxylate yielded on evaporation a viscous light brown oil, which was boiled under reflux for 8 hours with concentrated hydrochloric acid (20 c.c.), water (10 c.c.), and dioxan (1 c.c.). The acidic product (0·8 g.) on recrystallisation from aqueous acetic acid gave 6-nitrobenzophenone-2-carboxylic acid (0·2 g.) in colourless needles, m. p. 236—238°, identical with the corresponding compound obtained from the isomeric acid ester.

Friedel–Crafts Reaction (*Toluene*) *with* 1-*Methyl Hydrogen* 3-*Nitrophthalate*.—The acid ester (15 g.) was converted into the acid chloride, and the Friedel–Crafts reaction carried out as previously but with dry toluene in place of benzene. The reaction mixture, worked up as before, gave on distillation a pale yellow oil (6·7 g.; b. p. 175—195°/1·5 × 10^{-2} mm.). After removal of any 3-nitrophthalic anhydride by treatment with methanol, the residue (6·0 g.) largely solidified. Recrystallisation from ethanol yielded pure *methyl* 4′-*methyl*-6-*nitrobenzophenone*-2-*carboxylate* (3·5 g.) in colourless prisms, m. p. 162—163° (Found: C, 64·4; H, 4·6. $C_{16}H_{13}O_5N$ requires C, 64·2; H, 4·3%). The mother-liquors on fractional crystallisation from ethanol gave an unidentified *isomer* (0·15 g.) in colourless prisms, m. p. 107·5—108·5° (Found: C, 64·4; H, 4·5%), which depressed the m. p. of both methyl 4′-methyl-6- and -3-nitrobenzophenone-2-carboxylate. Methyl 4′-methyl-6-nitrobenzophenone-2-carboxylate (2·0 g.; m. p. 162—163°) was boiled under reflux for 1 hour with a mixture of concentrated sulphuric acid (6 c.c.), water (3 c.c.), and acetic acid (10 c.c.). The cooled solution was diluted and extracted with ether, and the ethereal extract washed with 5% aqueous sodium carbonate. Acidification of the alkaline extract gave 4′-methyl-6-nitrobenzophenone-2-carboxylic acid

(1·85 g.) as a fawn-coloured crystalline powder, m. p. 217·5—218·5°, raised on recrystallisation from aqueous acetic acid to 219·5—220·5° (colourless prisms) (see also Table 2, p. 560). The above acid (1·0 g.) on decarboxylation with copper chromite and quinoline at 165—185° (3 hours) yielded 4′-methyl-2-nitrobenzophenone (0·74 g.), m. p. 151—153°, raised on recrystallisation from aqueous alcohol to 154—155° (large flattened needles). Boëtius and Römisch (*Ber.*, 1935, **68**, 1931) quote m. p. 155°.

The isomeric ester (m. p. 107·5—108·5°; 0·09 g.) obtained above yielded on acid hydrolysis an unidentified *acid* (0·07 g.), m. p. 206·5—210°, raised on recrystallisation from aqueous acetic acid to 211—212° (colourless needles) (Found: C, 63·5; H, 3·8. $C_{15}H_{11}O_5N$ requires C, 63·2; H, 3·9%). The acid depressed the m. p. of both 4′-methyl-6-nitrobenzophenone-2-carboxylic acid (m. p. 220·5°) and of 4′-methyl-3-nitrobenzophenone-2-carboxylic acid (m. p. 189°) and must be, therefore, 2′(or 3′)-methyl-3(or 6)-nitrobenzophenone-2-carboxylic acid.

Friedel–Crafts Reaction (*Toluene*) *with* 2-*Methyl Hydrogen* 3-*Nitrophthalate*.—The 2-methyl ester (9·0 g.) was employed as for the 1-methyl ester (above). The product distilled at 160—180°/9 × 10^{-3} mm., to give a pale yellow oil (11·0 g.), which solidified on trituration with methanol. Six recrystallisations from methanol gave pure *methyl* 4′-*methyl*-3-*nitrobenzophenone*-2-*carboxylate* (5·1 g.) in colourless prisms, m. p. 114—115° (Found: C, 64·2; H, 4·4. $C_{16}H_{13}O_5N$ requires C, 64·2; H, 4·3%). No pure isomeric ester could be isolated by fractional crystallisation of the mother-liquors, or by fractional crystallisation of the corresponding acids. Methyl 4′-methyl-3-nitrobenzophenone-2-carboxylate (4·0 g.) was boiled under reflux for 4 hours with acetic acid (12 c.c.), sulphuric acid (8 c.c.), and water (4 c.c.). The product, worked up as previously, gave unchanged ester (0·5 g.) and an *acid* (2·9 g.), which crystallised from aqueous acetic acid in long colourless prisms, m. p. 186—188°, raised on recrystallisation to 188—189° (Found: C, 63·3; H, 3·8. $C_{15}H_{11}O_5N$ requires C, 63·2; H, 3·9%) (see also Table 2, p. 560). The above acid (1·0 g.) on decarboxylation with copper chromite and quinoline (2 hours at 175°) gave 4′-methyl-3-ntrobenzophenone 0·67 g.), m. p. 112·5—114°, undepressed on admixture with an authentic specimen, m. p. 112·5—114°, prepared by Limpricht and Lenz's method (*Annalen*, 1895, **286**, 307).

1-*Methyl* 2-*Phenyl* 3-*Nitrophthalate*.—The acid chloride, prepared as described above from 1-methyl hydrogen 3-nitrophthalate (7·5 g.), in chloroform (25 c.c.), was cooled to 0°, and an ice-cold solution of phenol (4·5 g.) in 5% aqueous sodium hydroxide (50 c.c.) added with vigorous stirring. The mixture was stirred for a further hour, then set aside overnight, and the organic layer then washed with water, dried, and distilled free from solvent. 1-*Methyl* 2-*phenyl* 3-*nitrophthalate* separated from methanol in colourless prisms (6·3 g.), m. p. 123·5—124·5° (Found: C, 59·9; H, 3·5. $C_{15}H_{11}O_6N$ requires C, 59·8; H, 3·7%). The filtrates on storage for 48 hours deposited a few crystals, m. p. 160—162°, which proved to be 1-methyl hydrogen 3-nitrophthalate. The residue was taken up in ether and washed with 5% sodium carbonate solution, and the ether distilled off from the dried (Na_2SO_4) extract. The residue (1·0 g.) did not solidify on storage or on trituration.

2-*Methyl* 1-*Phenyl* 3-*Nitrophthalate*.—The 2-methyl ester (4·5 g.) was employed as described above for the 1-methyl ester. The product, on crystallisation from aqueous methanol, gave 2-*methyl* 1-*phenyl* 3-*nitrophthalate* (3·2 g.) in colourless prisms, m. p. 108·5—109·5° (Found: C, 60·1; H, 3·6. $C_{15}H_{11}O_6N$ requires C, 59·8; H, 3·7%). The filtrates on dilution precipitated an oil, which did not solidify on long storage at 0°. The m. p. of the crystalline product was strongly depressed on admixture with that prepared from the 1-methyl ester.

Kinetic Studies of 1-*Methyl and* 2-*Methyl Hydrogen* 3-*Nitrophthalate*.—The two monomethyl esters (5·00 g.) were separately heated under reflux with unpurified thionyl chloride (20 c.c.) for a known time. After removal of excess of thionyl chloride as rapidly as possible on the water-bath under reduced pressure, the residue was treated with 10% aqueous sodium hydrogen carbonate (100 c.c.) and boiled gently under reflux for 15 minutes, more bicarbonate being added, if necessary, to maintain an excess. The resulting mixture, cooled to 0°, was made acid with concentrated hydrochloric acid and thoroughly extracted with ether. Distillation of the ether from the dried extract gave the mixture of half-esters, which was dried at 100° under reduced pressure before esterification. The esterification was carried out by boiling under reflux for 24 hours with absolute methanol (25 c.c.) containing concentrated sulphuric acid (2·5 c.c.). The cooled solution was diluted with water (50 c.c.) and extracted with ether, and the ethereal extract was washed with 5% aqueous sodium carbonate (4 × 30 c.c.). Removal of the ether in a tared flask gave the neutral fraction (diester), whereas acidification of the carbonate washings, extraction with ether, and removal of the solvent gave the acid fraction (monoester). Both fractions were dried at 100° under reduced pressure before being weighed.

The proportions of the 1-methyl and 2-methyl esters present in the product obtained on hydrolysis of the acid chloride were calculated from a knowledge of the proportions of acid and neutral esters obtained by the application of the procedure outlined above to each of the pure half-esters. Thus, the 1-methyl ester (5·00 g.) gave 4·533 g. of acid ester and 0·374 g. of neutral ester. The latter is equivalent to 225/239 × 0·374 g. = 0·352 g. of acid ester, and thus the total acid ester recovered is 4·885 g. The percentage of acid ester in the total recovered material, *i.e.*, the percentage unesterified, is 4·533/4·885 × 100 = 92·8%. In similar manner, when the pure 2-methyl ester was used, the percentage unesterified was 6·3%. If it is assumed that the rate of esterification in each case is unaffected by the presence of the isomeric half-ester, the percentage of 1-methyl ester in any mixture of the two isomeric half-esters is given by $P = 100(U - 6{\cdot}3)/(92{\cdot}8-6{\cdot}3)$, where U is the percentage of half-ester unesterified after 24 hours. The results obtained in this way are shown in the figure.

Peroxide of 1-*Methyl Hydrogen* 4-*Nitrophthalate* (cf. Hey and Walker, *J.*, 1948, 2217).—1-Methyl hydrogen 4-nitrophthalate (22·5 g.) was boiled under reflux for 1 hour with purified thionyl chloride (20 c.c.), and the excess of chloride removed under reduced pressure. The semi-solid acid chloride was converted into the peroxide, and the latter decomposed in boiling benzene (200 c.c.). The neutral product on distillation gave a pale yellow oil (8·2 g.; b. p. 130—145°/1·5 × 10^{-2} mm.), which did not completely solidify on storage. The product was hydrolysed with 10% aqueous sodium hydroxide, and the crude acid (7·9 g.) stirred with concentrated sulphuric acid (20 c.c.) at 30—40° until dissolution was complete. The reaction mixture was poured on ice, basified with sodium hydroxide, and filtered. The crude mixture of nitrofluorenones (5·0 g.) was sublimed under reduced pressure (approx. 200°), to yield lemon-yellow prisms (3·1 g.), m. p. 182—190°. Fourteen recrystallisations from benzene gave 3-nitrofluorenone (0·1 g.) in yellow needles, m. p. 231—232°. Ray and Barrick (*J. Amer. Chem. Soc.*, 1948, **70**, 1492) quote m. p. 236°. Laborious fractional crystallisation of the mother-liquors yielded 2-nitrofluorenone (0·05 g.) in yellow needles, m. p. 218—219°, undepressed on admixture with an authentic specimen, m. p. 219° (Heilbron, Hey, and Wilkinson, *J.*, 1938, 115). The m. p. was strongly depressed on admixture with the 3-nitrofluorenone obtained above. The use of phosphorus pentachloride in place of thionyl chloride in the preparation of the acid chloride led to a similar yield of peroxide (65%, purity 98%). Decomposition in benzene and fractional crystallisation of the nitrofluorenone mixture led to the isolation of both 2-nitrofluorenone (m. p. 219—220°) and 3-nitrofluorenone (m. p. 230—231·5°).

Friedel–Crafts Reaction (*Benzene*) *with* 1-*Methyl Hydrogen* 4-*Nitrophthalate.*—The acid ester (15 g.) in dry benzene (50 c.c.) was treated with phosphorus pentachloride (16·7 g.). After 1 hour at room temperature, the mixture was boiled under reflux for 15 minutes and the volatile products were removed under reduced pressure. The reaction with benzene was carried out as described for the 3-nitrophthalic acid esters. The product distilled at 150—170°/5 × 10^{-2} mm. to yield a pale yellow oil (8·9 g.), which solidified on trituration with methanol. Recrystallisation from methanol gave methyl 4-nitrobenzophenone-2-carboxylate in colourless prisms, m. p. 124—125°. Rainer (*Monatsh.*, 1908, **29**, 434) records m. p. 123·5—124°. Concentration of the mother-liquors yielded an oil from which no pure ester could be isolated. Acid hydrolysis of the crystalline ester gave 4-nitrobenzophenone-2-carboxylic acid in white plates, m. p. 214—215°. Rainer (*loc. cit.*) quotes m. p. 212° for this acid prepared by a Friedel–Crafts reaction upon the anhydride. The mother-liquors from the crystallisation of the ester were hydrolysed with boiling 4N-hydrochloric acid (100 c.c.; 12 hours). The acidic product (5·8 g.) on recrystallisation from aqueous ethanol (6 times) and from benzene–light petroleum (b. p. 60—80°) (3 times) gave 5-nitrobenzophenone-2-carboxylic acid in long colourless needles, m. p. 163—164°. Rainer (*Monatsh.*, 1908, **29**, 179) quotes m. p. 164—165° (corr.).

In an attempt to avoid rearrangement, the reaction was carried out as follows: The acid ester (7·5 g.) in dry ether (30 c.c.) was treated with purified thionyl chloride (10 c.c.). The temperature was slowly raised to 25° and kept thereat for 2 hours. Removal of the ether and excess of thionyl chloride at 25° under reduced pressure yielded the acid chloride as a viscous, fawn-coloured semi-solid. The condensation with benzene was carried out as before, but care was taken to ensure that the reaction temperature did not rise above 10° during 3 hours. Distillation of the product (5·15 g.), b. p. 150—160°/1·3 × 10^{-2} mm., followed by recrystallisation from methanol, gave methyl 4-nitrobenzophenone-2-carboxylate (2·0 g.), m. p. 124—125°.

Friedel–Crafts Reaction (*Toluene*) *with* 1-*Methyl Hydrogen* 4-*Nitrophthalate.*—The 1-methyl ester (22·5 g.) was converted into the acid chloride with purified thionyl chloride and submitted to the Friedel–Crafts reaction with toluene, as described above for the 3-nitrophthalates. The product (23·0 g.), b. p. 180—190°/0·35 mm., solidified. Recrystallisation from methanol

(8 times) gave *methyl 4′-methyl-4-nitrobenzophenone-2-carboxylate* (5·0 g.) in colourless prisms, m. p. 132—133° (Found: C, 64·5; H, 4·4. $C_{16}H_{13}O_5N$ requires C, 64·2; H, 4·3%). No pure isomeric ester could be obtained by fractional crystallisation of the mother-liquors, but a residue (A), m. p. 83—87°, was hydrolysed (see below). Acid hydrolysis yielded 4′-methyl-4-nitrobenzophenone-2-carboxylic acid, m. p. 191—192·5°, raised on recrystallisation from aqueous acetic acid to 192—193° (colourless prisms) (see also Table **3**, p. 562). Decarboxylation with copper chromite (2 hours at 190°), carried out as described above, gave 4′-methyl-4-nitrobenzophenone, m. p. 122—123°, in colourless needles from benzene–light petroleum (b. p. 80—100°). Limpricht and Samietz (*Annalen*, 1895, **286**, 321) record m. p. 122—124°. Acid hydrolysis of the ester residue (A) obtained above (1·5 g., colourless needles, m. p. 83—87°) gave crude 4′-methyl-5-nitrobenzophenone-2-carboxylic acid (1·35 g.), m. p. 189—212°. Recrystallisation from aqueous acetic acid yielded the pure acid in colourless prisms, m. p. 217·5—218·5° (see, further, Table 3). Decarboxylation of 4′-methyl-5-nitrobenzophenone-2-carboxylic acid yielded 4′-methyl-3-nitrobenzophenone (59%). The ketone separated from aqueous alcohol in a mixture of needles and prisms. The former changed into the latter at 110·5° and the homogeneous material melted at 113—114°, undepressed on admixture with an authentic specimen (Limpricht and Lenz, *Annalen*, 1895, **286**, 307).

Anilide of 1-*Methyl Hydrogen* 4-*Nitro*iso*phthalate*.—1-Methyl hydrogen 4-nitro*iso*phthalate (2·25 g.) was boiled under reflux for 2 hours with purified thionyl chloride. On removal of the excess of chloride under reduced pressure the acid chloride formed white needles. To the acid chloride in pyridine (6 c.c.) was added dropwise with shaking a solution of aniline (1·4 g.) in pyridine (5 c.c.). The crude anilide, isolated in the usual manner, was obtained as a fawn-coloured crystalline solid (2·6 g.), m. p. 165—168°. Recrystallisation from aqueous alcohol or benzene–light petroleum (b. p. 80—100°) gave the pure *anilide* in very pale yellow needles, m. p. 170·5—171·5° (Found: C, 60·2; H, 4·1. $C_{15}H_{12}O_5N_2$ requires C, 60·0; H, 4·0%). No trace of an isomeric ester anilide could be detected.

Peroxide of 1-*Methyl Hydrogen* 4-*Nitro*iso*phthalate*.—The acid ester (7·5 g.) was boiled under reflux for 2 hours with crude thionyl chloride and converted into the peroxide (6·5 g.) as described above for 2-methyl hydrogen 3-nitrophthalate. The peroxide (6·2 g.) was boiled under reflux for 21 hours with dry thiophen-free benzene (50 c.c.). The resultant red solution deposited, on cooling, crystals of the acid ester. After extraction with aqueous sodium carbonate, the benzene solution was dried ($CaCl_2$). Removal of the benzene and distillation of the residue yielded methyl 6-nitrodiphenyl-3-carboxylate (2·6 g.) as a pale yellow viscous oil, which did not solidify. Hydrolysis of the ester by refluxing it for 1½ hours with a mixture of acetic acid (10 c.c.), concentrated sulphuric acid (4 c.c.), and water (2 c.c.) gave 6-nitrodiphenyl-3-carboxylic acid (2·2 g.), which separated from aqueous acetic acid and from ethanol in bright yellow needles, m. p. 224·5—226°. France, Heilbron, and Hey (*J.*, 1939, 1292) recorded m. p. 220—221° (yellow plates) for this acid. The acid (1·5 g.) was decarboxylated with copper chromite in quinoline (3 hours at 200°) in the usual way. The acidic fraction gave unchanged acid (0·6 g.). The neutral fraction was extracted with hot light petroleum (b. p. 40—60°), and the extract concentrated. 2-Nitrodiphenyl was deposited in colourless prisms, m. p. 30°, raised on recrystallisation from the same solvent to m. p. 35—36°, undepressed on admixture with an authentic specimen, m. p. 36·5°.

Peroxide of 4-*Methyl Hydrogen* 2-*Nitroterephthalate*.—The acid ester (10·0 g.) was boiled under reflux for 2 hours with crude thionyl chloride (20 c.c.), the excess of the latter removed under reduced pressure, and the residual acid chloride in alcohol-free chloroform (30 c.c.) converted into the peroxide (9·5 g.) as for the *iso*phthalate. The peroxide (9·5 g.) in the form of a white powder was boiled under reflux for 18 hours with dry thiophen-free benzene (100 c.c.). The neutral fraction, worked up as for the *iso*phthalate, distilled at 155—165°/0·5 mm. to give a pale yellow viscous oil (4·3 g.), which did not solidify. The crude methyl 2-nitrodiphenyl-4-carboxylate was hydrolysed with sulphuric acid in aqueous acetic acid, to give the acid (3·7 g.), which separated from aqueous acetic acid and subsequently from benzene in yellow needles or plates, m. p. 190·5—192·5°, undepressed on admixture with an authentic specimen, m. p. 191°, prepared by Grieve and Hey (*J.*, 1932, 1894). The mother-liquors were evaporated to dryness and extracted with hot benzene. The extract yielded a small amount of 2-nitrodiphenyl-4-carboxylic acid. The residue, m. p. 259—263°, crystallised from water and subsequently from chloroform–ether–light petroleum (b. p. 80—100°) in colourless prisms, m. p. 270—271·5°, undepressed on admixture with authentic 2-nitroterephthalic acid.

Anilide from β-*Methyl Hydrogen* αα-*Diphenylsuccinate*.—The β-methyl ester (2·84 g.) was boiled under reflux for ½ hour with purified thionyl chloride. The acid chloride in dry benzene (20 c.c.) was treated with aniline (1·9 g.) in dry benzene, and the mixture shaken, kept overnight, and worked up in the usual way. The neutral fraction (3·1 g.) solidified when kept. Five successive recrystallisations from benzene–light petroleum and then from ethanol gave αα*N*-triphenylsuccinimide, m. p. 169·5—170·5° (Found: C, 80·3; H, 5·0. Calc. for $C_{22}H_{17}O_2N$: C, 80·7; H, 5·2%). Salmon-Legagneur and Soudan (*Compt. rend.*, 1944, **218**, 682) quote m. p. 163°.

Methylanilide from β-Methyl Hydrogen αα-Diphenylsuccinate.—To the acid chloride from the β-methyl ester (5·0 g.) in dry benzene (20 c.c.) were added methylaniline (2·5 g.) in dry benzene (10 c.c.) and pyridine (2 drops). The mixture was heated under reflux on the steam-bath for 1 hour and worked up in the usual manner. The neutral fraction (6·3 g.) was a fawn-coloured gum, which did not completely solidify on storage. The product was chromatographed on alumina. Elution with benzene yielded buff-coloured prisms (A) (2·12 g.), m. p. 140—147°, followed by a small amount of colourless gum (0·25 g.); elution with ether and with methanol yielded white prisms (B) (1·44 g.), m. p. 136—139°. The compound (A), on recrystallisation from benzene–light petroleum (b. p. 80—100°), gave the *methylanilide* of methyl αα-diphenylsuccinate in colourless prisms, m. p. 149·5—150·5° (Found: C, 77·1; H, 6·1. $C_{24}H_{23}O_3N$ requires C, 77·2; H, 6·2%). The fraction (B) separated from light petroleum (b. p. 80—100°) in thick prisms, m. p. 136—138° [mixed m. p. with (A) 117—128°], but further recrystallisation from benzene–light petroleum (b. p. 80—100°) gave *αα-diphenylsuccinobismethylanilide* in colourless plates, m. p. 155—156° (Found: C, 80·6; H, 6·2; N, 6·3. $C_{30}H_{28}O_2N_2$ requires C, 80·4; H, 6·3; N, 6·25%).

Synthesis of the α-Methyl Ester β-Methylanilide of αα-Diphenylsuccinic Acid (*Methyl αα-Diphenylsuccinomethylanilide*).—The silver salt (2·05 g.) of the α-methyl ester in dry ether (10 c.c.) at 0—10° was treated with purified thionyl chloride (1·0 g.) in dry ether (5 c.c.) containing pyridine (1 drop). After this had stood, with occasional shaking, at 0—10° for 5 minutes, methylaniline (0·6 g.) was added, and the mixture shaken at the same temperature for 10 minutes. Ether (25 c.c.) was then added, the mixture filtered, and the residue washed with dry ether (20 c.c.). The combined ethereal extracts, thoroughly washed with 5N-hydrochloric acid and with 5% aqueous sodium carbonate, were dried (Na_2SO_4), and the solvent was distilled off. The residue (1·8 g.) slowly solidified on trituration with light petroleum. Two recrystallisations from ethyl acetate–light petroleum (b. p. 80—100°) gave colourless prisms (0·19 g.), m. p. 154—166°, raised on recrystallisation from benzene–light petroleum to 166—167° (Found: C, 68·3; H, 4·8%). Concentration of the mother-liquors gave clusters of prisms (1·3 g.), m. p. 143—148°, raised on recrystallisation from benzene–light petroleum (b. p. 80—100°) to 149—150°. The m. p. was undepressed on admixture with the ester methylanilide (A) (above).

When the silver salt of the β-methyl ester (2·9 g.) was treated with thionyl chloride and with methylaniline as described above for the α-methyl ester, the neutral fraction on recrystallisation from benzene–light petroleum (b. p. 80—100°) gave only the *anhydride* of the β-methyl ester in prisms, m. p. 115—118° (Found: C, 74·0; H, 5·6. $C_{34}H_{30}O_7$ requires C, 74·2; H, 5·5%).

Diethylamide from γ-Methyl Hydrogen αα-Diphenylglutarate.—The γ-methyl ester (3·6 g.) was boiled under reflux for 1 hour with purified thionyl chloride (15 c.c.), and the excess of the latter removed under reduced pressure. The oily acid chloride in dry benzene (15 c.c.) was treated with diethylamine (2·0 g.) in dry benzene (15 c.c.). The mixture was boiled under reflux for 20 minutes, cooled, and thoroughly washed with acid and with 5% aqueous sodium carbonate. The residue (3·4 g.) after distillation of the benzene was chromatographed on an alumina column. Elution with benzene–light petroleum (b. p. 80—100°) yielded a pale yellow gum (1·80 g.). Subsequent elution with benzene and later with ether yielded a diethylamide of methyl hydrogen αα-diphenylglutarate (Diethylamide A) (1·53 g.) in colourless prisms, m. p. 99·5—100° from light petroleum (b. p. 80—100°) (Found: C, 75·0; H, 7·7. $C_{22}H_{27}O_3N$ requires C, 74·8; H, 7·6%), shown below to be *methyl* NN-*diethyl-αα-diphenylglutaramate*. The gummy fraction from the chromatogram was rechromatographed and the first of these new fractions (0·25 g.), m. p. 88—107°, was depressed on admixture with diethylamide A. The later fractions consisted entirely of more of the diethylamide A. The first fraction was thrice recrystallised from benzene–light petroleum and separated by hand into colourless prisms (27 mg.), m. p. 112—117°, and opaque prisms, m. p. 98—103°. The former, after recrystallisation from benzene–light petroleum, gave the isomeric diethylamide (Diethylamide B), m. p. 115·5—117·5° (Found: C, 74·5; H, 7·6. $C_{22}H_{27}O_3N$ requires C, 74·8; H, 7·6%), which, by exclusion, is *methyl* NN-*diethyl-γγ-diphenylglutaramate*.

Synthesis of γ-Diethylamide of α-Methyl Hydrogen αα-Diphenylglutarate (*Methyl* NN-*Diethyl-αα-diphenylglutaramate*).—To the silver salt of the α-methyl ester in dry ether was added purified thionyl chloride (1·2 g.) in dry ether (5 c.c.), the temperature being kept at 0—5°. After this had been kept, with occasional shaking, at 0—5° for 10 minutes, diethylamine (1·0 g.) in dry ether (5 c.c.) was added with cooling. The mixture was kept for 10 minutes at room temperature and worked up in the usual way. The neutral fraction (0·6 g.) was chromatographed on alumina. Elution with ether gave the diethylamide A (0·25 g.), m. p. 97—99°, raised on recrystallisation to 99—100° and undepressed on admixture with the diethylamide A obtained as above. No other product could be isolated.

When the silver salt technique, as outlined above, was applied to the γ-methyl ester only inconclusive results were obtained.

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