

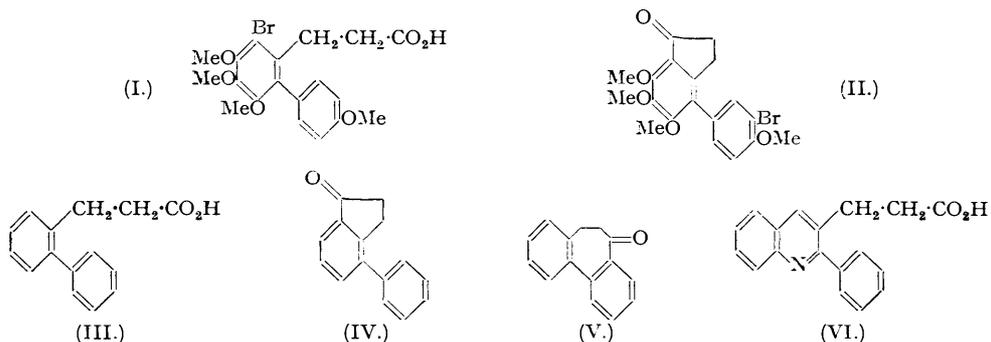
## 30. Colchicine and Related Compounds. Part IX.

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In Part V (*J.*, 1945, 176) it was shown that a degradation product of colchicine, deamino-colchicol methyl ether, is a derivative of dibenzcycloheptatriene, and a synthesis of this parent hydrocarbon was described in Part VI (*J.*, 1947, 746). The present communication records the preparation and cyclisation of  $\beta$ -2-diphenylpropionic acid (III) and some of its derivatives with a view to determine whether this type of method is adaptable to the synthesis of dibenzcycloheptadiene derivatives related to colchicine. In agreement with the conclusions of von Braun and his collaborators, the main product of cyclisation of (III) was found to be 4-phenylindanone (IV), but there was also formed, albeit in yields of less than 10%, the seven-membered ring ketone (V). The cyclisation of various methoxylated derivatives of (III) was also examined, but in no other case was evidence of seven-membered ring formation obtained. The ketone (V) was also synthesised from diphenic acid. Poor yields at an early stage discouraged attempts to extend the method to the synthesis of derivatives of (V).

Observations are recorded on the desulphuration of thiol esters of some aromatic acids by means of Raney nickel.

THE course, (I)  $\longrightarrow$  (II), taken by the Friedel-Crafts reaction when applied to the acid chloride of (I) (Barton, Cook, and Loudon, Part VIII, *J.*, 1949, 1079; Huang, Tarbell, and Arnstein, *J. Amer. Chem. Soc.*, 1948, 70, 4181) is probably determined by a combination of orienting influences and steric factors. Considered from the point of view of cyclisation to a 7-membered ring, the methoxylation pattern is unfavourable: in particular, the position of the methoxyl group in the disubstituted nucleus is unfortunate, since the directive powers of the substituent are not enlisted to offset the steric difficulty which is implicit in the rule that, *ceteris paribus*, a 5-membered ring is formed in preference to a 7-membered ring. Because of the importance of dibenzcycloheptadienones in the chemistry of colchicine we have now investigated the direction of ring-closure in several compounds related to (I).

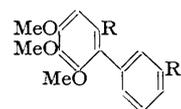
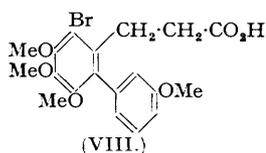
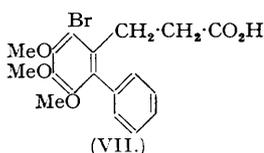


Von Braun and Manz (*Annalen*, 1929, 468, 258) have reported that the indanone (IV) is the sole product of cyclising (III) by the Friedel-Crafts reaction. Their conclusion, however, is based on very unconvincing evidence: the indanone (IV) is described as an oil, alleged to be homogeneous because it afforded a sharp-melting semicarbazone (no analyses are given), and

identified only through oxidation with nitric acid which appeared to yield a nitrated derivative of phthalic acid as judged from a qualitative nitrogen test and a fluorescein reaction. For re-investigation, diphenyl-2-aldehyde was conveniently prepared from the acid by the McFadyen-Stevens process (*J.*, 1936, 584) and was condensed with malonic acid to  $\beta$ -2-diphenylacrylic acid (cf. Zaheer and Faseeh, *J. Indian Chem. Soc.*, 1944, 21, 381). Hydrogenation of the latter acid using a palladium catalyst gave the required  $\beta$ -2-diphenylpropionic acid (III) which, however, was markedly different from the compound described by von Braun *et al.* Repetition of the method of preparation used by these authors, and based on the condensation of 2-bromo-methyldiphenyl (here obtained by an alternative method) with ethyl sodiomalonate, showed that the properties which they ascribe to (III) correspond with the properties now found for (2-diphenylmethyl)malonic acid. The latter acid, when heated, afforded a sample of (III) which was identical with the material produced by our first method of preparation.

Cyclisation of (III) by the Friedel-Crafts reaction gave a crystalline solid as main product, together with some oil. The solid was identified as 4-phenylindanone (IV) by oxidation with potassium permanganate to 3-phenylphthalic acid and conversion of the latter into fluorenone-1-carboxylic acid of which an authentic specimen was available. A portion of the oil was oxidised with sodium dichromate in acetic acid, and the formation of phenanthraquinone and of diphenic acid clearly indicated the presence of some dibenzcycloheptadienone (V) (cf. Part VI, Cook, Dickson, and Loudon, *J.*, 1947, 746). This was confirmed when the remainder of the oil was treated with 2:4-dinitrophenylhydrazine and, from the resulting mixture, the 2:4-dinitrophenylhydrazone of (V) was isolated. The total quantity of (V) in the cyclisation product was small—less than 10%.

As an alternative to the Friedel-Crafts type of cyclisation, the action of anhydrous hydrogen fluoride on the acids (I) and (III) was examined. By this means (III) was again converted into a mixture of (IV) and (V), the presence of the latter being inferred from the isolation of phenanthraquinone following oxidation. Frank, Fanta, and Tarbell (*J. Amer. Chem. Soc.*, 1948, 70, 2314) state that (I) does not undergo cyclisation when treated with hydrogen fluoride, but we now find that it affords a mixture of (II) and the debrominated indanone (II; H for Br), apparently formed by displacement and either migration or elimination of the bromo-substituent. Accordingly, in the respective cases, the Friedel-Crafts and the hydrogen fluoride method of cyclisation appear to produce essentially similar results and, when applied to (I), the latter method has the advantages of giving more easily separable products in better total yield (cf. Part VIII, *loc. cit.*). The production of (V) from (III) encourages the hope that dibenzcycloheptadienones may be synthesised by this method when favourable orienting influences are present, but it is relevant to add that Borsche and Sinn (*Annalen*, 1939, 538, 283) were unable to obtain the 7-membered cyclic ketone by cyclisation of (VI) although in this case a 5-membered ring was not formed.



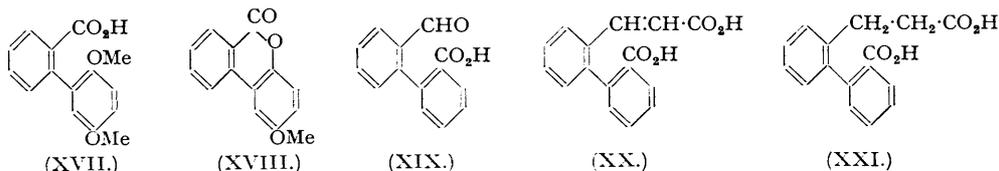
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| (IX; R = CO <sub>2</sub> H, R' = H.)                                   | (X; R = CO <sub>2</sub> H, R' = OMe.)                                     |
| (XI; R = CHO, R' = H.)   | (XII; R = CHO, R' = OMe.)   |
| (XIII; R = CH:CH-CO <sub>2</sub> H, R' = H.)                           | (XIV; R = CH:CH-CO <sub>2</sub> H, R' = OMe.)                             |
| (XV; R = CH <sub>2</sub> :CH <sub>2</sub> -CO <sub>2</sub> H, R' = H.) | (XVI; R = CH <sub>2</sub> :CH <sub>2</sub> -CO <sub>2</sub> H, R' = OMe.) |

In order to ascertain whether the position of the methoxyl group in the disubstituted nucleus materially affects the course of the reaction (I)  $\longrightarrow$  (II), the two acids (VII) and (VIII) were synthesised and examined. The syntheses followed the lines already described for (I) (Part VIII, *loc. cit.*) and involved condensations of 1-phenyl- and 1-methoxyphenyl-3:3-dimethyl-triazene with methyl 3:4:5-trimethoxybenzoate to form the methyl esters of the acids (IX) and (X) respectively (for by-products, cf. Experimental). Cyclisation of these acids by warming with thionyl chloride yielded fluorenone derivatives, a pair of isomers which were not individually oriented being obtained from the acid (X). Reduction of (IX) and (X) to the respective aldehydes (XI and XII) and subsequent conversion into the acrylic (XIII and XIV) and propionic acids (XV and XVI) were effected by standard methods. Bromination of (XV) and (XVI) gave the bromo-acids (VII) and (VIII), respectively. On cyclisation with hydrogen fluoride each of the acids (XV) and (XVI) gave a corresponding indanone derivative, and the failure of the

cyclisation products to furnish (coloured) phenanthraquinones in the oxidation test indicated the absence of dibenzcycloheptadienones. The same test was again negative when applied to the cyclisation products of the bromo-acids (VII) and (VIII). The former acid, when cyclised by either the Friedel-Crafts or the hydrogen fluoride method, gave only gummy products which were probably mixtures. On the other hand, (VIII) was cyclised by hydrogen fluoride to a brominated indanone which, on debromination, afforded 5 : 6 : 7-trimethoxy-4-m-methoxyphenyl-indan-1-one, already obtained by direct cyclisation of (XVI). Accordingly, it may be concluded that, in this case at least, cyclisation is achieved by displacement and migration of bromine, and that in neither case is there any significant tendency to form a 7-membered ring.

It is noteworthy that the displacement and migration of bromine, encountered in these cyclisations to indanone derivatives, finds its counterpart in the isomerisation which accompanies cyclisation of  $\beta$ -(9-s-octahydroanthranyl)propionic acid to 1'-keto-9 : 10-cyclopenteno-s-octahydrophenanthrene (Badger, Carruthers, Cook, and Schoental, *J.*, 1949, 169). In the latter case it is a saturated carbon chain which migrates, and in both types hydrogen fluoride is an effective agent.

2' : 5'-Dimethoxydiphenyl-2-carboxylic acid (XVII), prepared through the methyl ester by condensing 1-(*o*-carboxymethoxyphenyl)-3 : 3-dimethyltriazene and 1 : 4-dimethoxybenzene, was next examined in the hope of applying the synthetic procedure to a case favourable to 7-membered ring formation. The project, however, failed since the ester was recovered unchanged from all attempts to convert it by reaction with hydrazine hydrate into the hydrazide. Moreover, even mild treatment of (XVII) with thionyl chloride yielded the lactone (XVIII) of 2'-hydroxy-5'-methoxydiphenyl-2-carboxylic acid.



A different approach to the synthesis of the unsubstituted ketone (V) was made starting from diphenic anhydride. This reacted with hydrazine hydrate to form the half hydrazide of diphenic acid, which with benzenesulphonyl chloride afforded the *N*-benzenesulphonyl derivative. The latter was also obtained by the direct action of benzenesulphonylhydrazide on diphenic anhydride and by an adaptation of the McFadyen-Stevens process gave the aldehydo-acid (XIX) in rather poor yield. Condensation of (XIX) with malonic acid yielded an unsaturated dibasic acid (XX) which was hydrogenated by use of a palladium catalyst to the corresponding saturated acid (XXI). From this acid by heating (*a*) the barium salt alone or (*b*) the sodium salt with acetic anhydride there was obtained in each case a gum which afforded the 2 : 4-dinitrophenyl-hydrazone of (V). The method, however, is inferior to the synthesis of (V) recently reported by Rapoport and Williams (*J. Amer. Chem. Soc.*, 1949, 61, 1774) who prepared the same acid (XXI) in several stages from phenanthraquinone mono-oxide and achieved a more satisfactory cyclisation through the corresponding dinitrile by means of Ziegler's procedure.

In course of the foregoing synthetic work the frequent need of reducing a carboxylic acid to the corresponding aldehyde prompted some investigation of reductive desulphuration of thiolcarboxylic esters by means of Raney nickel. Wolfrom and Karabinos (*J. Amer. Chem. Soc.*, 1946, 68, 1455) report the formation of aldehydes in this way, whilst Prelog *et al.* (*Helv. Chim. Acta*, 1946, 29, 684) recommend the process for the preparation of primary alcohols. The results of our experiments show the prevalence of reduction beyond the aldehyde stage as well as the incidence of side reactions, but the activity of the catalyst may well be the critical factor determining the nature of the product (cf. Spero, McIntosh, and Levin, *J. Amer. Chem. Soc.*, 1948, 70, 1907) and requires further inquiry. Previous workers have confined their attention to thiol esters derived from methane-, ethane-, or toluene- $\omega$ -thiol, but it seems probable that in many cases these malodorous thiols may be replaced by thiophenols such as thio-*p*-cresol which was mainly used in the present connection.

By use of Raney nickel as prepared by Mozingo (*J. Amer. Chem. Soc.*, 1943, 65, 1015) the half thiol-ester from diphenic anhydride and thio-*p*-cresol was converted into 2'-hydroxymethyl-diphenyl-2-carboxylic acid, and *p*-tolyl *o*-carboxymethoxythiolbenzoate [*o*-C<sub>6</sub>H<sub>4</sub>(CO<sub>2</sub>Me)·CO·S·C<sub>7</sub>H<sub>7</sub>] yielded phthalide. A test experiment on *p*-tolyl thiolbenzoate showed the formation of benzaldehyde (*ca.* 10%) and benzyl alcohol (23%); moreover, examination of the more volatile

products from ethyl thiolbenzoate revealed unexpectedly the presence of much benzene. Both *ethyl* and *p-tolyl* 3 : 4 : 5-trimethoxythiolbenzoate afforded 3 : 4 : 5-trimethoxybenzyl alcohol (40%) together with 1 : 2 : 3-trimethoxybenzene (20—30%) and the formation of these products was largely independent of the conditions or of the thiol-ester used. The results, therefore, show that scission of the original carboxyl group may accompany desulphuration and reduction, and it may be recalled that similar competitive processes have been noted in connection with the Rosenmund reduction of acid chlorides (Späth, *Monatsh.*, 1919, **40**, 129; Rosenmund, *Zetsche*, and Heise, *Ber.*, 1921, **54**, 638) where again the activity of the catalyst is of paramount importance.

## EXPERIMENTAL.

*Diphenyl-2-aldehyde from the 2-Carboxylic Acid.*—Methyl diphenyl-2-carboxylate (14.8 g.), heated under reflux with hydrazine hydrate (98% ; 25 g.) and ethanol (30 c.c.) for 5 hours, afforded the *hydrazide*, as colourless needles, m. p. 136.5°, from methanol (Found : C, 73.8; H, 5.6.  $C_{13}H_{12}ON_2$  requires C, 73.6; H, 5.7%). The product (9.6 g.) in pyridine (40 c.c.) was treated at 0° with benzenesulphonyl chloride (8.2 g.) and the whole was left for 3 hours at room temperature before it was added to a mixture of ice and hydrochloric acid. The resulting *benzenesulphonhydrazide* of diphenyl-2-carboxylic acid formed colourless needles, m. p. 173.5°, from methanol (Found : C, 64.8; H, 4.6.  $C_{19}H_{16}O_3N_2S$  requires C, 64.8; H, 4.6%). A solution of the above sulphonhydrazide (14.3 g.) in ethylene glycol (70 c.c.) was treated at 160° with anhydrous sodium carbonate (21 g.) and after 80 seconds the reaction was quenched by pouring the mixture into hot water. The required aldehyde, recovered in ether, had b. p. 162°/12 mm.; the yield was 55%, based on the acid.

*1-o-Tolyl-3 : 3-dimethyltriazen.*—*o*-Toluidine (32.1 g.) in concentrated hydrochloric acid (108 c.c.) and water (72 c.c.) was diazotised at 0° with a concentrated aqueous solution of sodium nitrite (21 g.) and the resulting solution was added with stirring to an ice-cold solution of dimethylamine (33% ; 48 g.) in 30% aqueous sodium carbonate (300 c.c.). The required *triazen*, b. p. 128—129°/12 mm., was recovered from a dried and washed benzene extract (Found : C, 66.1; H, 7.8.  $C_9H_{13}N_3$  requires C, 66.3; H, 8.0%).

2-Methyldiphenyl was obtained in poor yield by the following procedure : Glacial acetic acid (40 c.c.) was gradually added to a boiling solution of the above triazen (45 g.) in benzene (400 c.c.) and the whole was heated under reflux for 16 hours. The resulting solution was washed in turn with water, dilute hydrochloric acid, dilute alkali, and again with water. Fractionation of the dried benzene solution gave 2-methyldiphenyl, b. p. 128—130°/15 mm. (9%), and neutralisation of the acid washings gave indazole (21%), m. p. 144—145° (Found : C, 71.5; H, 5.0; N, 23.8. Calc. for  $C_7H_6N_2$  : C, 71.2; H, 5.1; N, 23.7%).

2-Bromomethyldiphenyl was prepared in 65% yield by adding (2 hours) a solution of bromine (4.1 g.) in carbon tetrachloride (12 c.c.) to a strongly irradiated, boiling solution of 2-methyldiphenyl (4.1 g.) in the same solvent (25 c.c.) which contained a trace of iodine and was covered with a layer of water (6 c.c.). After further heating ( $\frac{1}{2}$  hour), the cooled solution was washed in turn with sulphurous acid, dilute sodium carbonate, and water before being dried and concentrated. The required product distilled at 168—172°/11 mm. (von Braun and Manz record b. p. 166°/11 mm.).

*(2-Diphenylmethyl)malonic Acid.*—The corresponding diethyl ester, prepared as described by von Braun and Manz (*loc. cit.*), was hydrolysed by potassium hydroxide in boiling ethanol-water. After distillation of the ethanol and extraction of the diluted solution with ether, the aqueous residue was acidified and the precipitated oil was extracted with much boiling water from which the *acid* slowly crystallised, having m. p. 125.5—127.5° (decomp.); it was dried at 65° *in vacuo* (Found : C, 71.1; H, 5.1.  $C_{16}H_{14}O_4$  requires C, 71.1; H, 5.2%).

*$\beta$ -2-Diphenylpropionic Acid (III).*—(a)  $\beta$ -2-Diphenylacrylic, m. p. 196°, prepared essentially as described by Zaheer and Faseeh (*loc. cit.*) who give m. p. 202°, was dissolved (6.2 g.) in glacial acetic acid (450 c.c.) and was hydrogenated using palladium-black as catalyst (0.3 g.) at ordinary temperature and pressure. Absorption was complete in 2 $\frac{1}{2}$  hours and the product, recovered from the solvent, had m. p. 110—113°. Methylation with diazomethane in ether gave the *methyl ester*, b. p. 181.5—182°/10 mm. (Found : C, 80.1; H, 6.5.  $C_{16}H_{16}O_2$  requires C, 80.0; H, 6.7%), from which the *acid* was recovered by hydrolysis and formed plates, m. p. 112.5—113°, from aqueous acetic acid (Found : C, 79.8; H, 6.0.  $C_{15}H_{14}O_2$  requires C, 79.7; H, 6.2%). (b) The same acid, m. p. and mixed m. p. 111—113°, was obtained when 2-diphenylmethylmalonic acid was heated at 130° until evolution of carbon dioxide ceased and the product was crystallised from benzene-petroleum.

*4-Phenylindanone (IV).*—2-Diphenylpropionic acid (2 g.) suspended in pure dry benzene (20 c.c.) was treated with phosphorus pentachloride (2 g.), shaken until solution of the acid was complete, and left at room temperature for one hour. The acid chloride, recovered after evaporation under reduced pressure, was dissolved in dry carbon disulphide (4 c.c.), powdered aluminium chloride (3 g.) was added, and the whole was left protected from moisture at 0° for 3 days. Dilute hydrochloric acid was added and after distillation in steam to remove the residual liquor was extracted with ether from which, when washed with dilute alkali, dried, and evaporated, a gum was recovered. The gum distilled at 130—135°/10 mm. (yield 75%) and crystallised in the receiver; recrystallisation from ethanol-water gave rectangular prisms of 4-phenylindanone (yield 45%), initially melting at 69°, but changing on storage to m. p. 86° (Found : C, 86.7; H, 5.6.  $C_{15}H_{12}O$  requires C, 86.5; H, 5.8%), while the mother-liquor of the crystallisation was worked up as described below. 4-Phenylindanone formed a 2 : 4-dinitrophenyl-hydrazone (referred to as "A" below) as scarlet needles, m. p. 243—245° (decomp.), from acetic acid (Found : C, 65.1; H, 4.3.  $C_{21}H_{16}O_4N_4$  requires C, 65.0; H, 4.1%), and a *semicarbazone* as colourless platelets, m. p. 225—229° (decomp.) from 2-ethoxyethanol (von Braun and Manz, *loc. cit.*, record m. p. 192°) (Found : C, 72.3; H, 5.6; N, 15.7.  $C_{16}H_{15}ON_3$  requires C, 72.5; H, 5.7; N, 15.9%).

*Oxidation.* A well-stirred emulsion of the indanone (IV) (0.2 g.) in a little dilute sodium hydroxide

at 100° was treated portionwise with 6% aqueous potassium permanganate until the pink colour persisted. Excess of permanganate (2 c.c.) was now added and the whole was maintained at 100° for 1 hour. After acidification and treatment with sulphur dioxide the insoluble product was collected, washed with water, reprecipitated from alkali, and again collected. Sublimation at 120°/2 mm. furnished 3-phenylphthalic anhydride, m. p. 145°, from benzene-petroleum (Found: C, 74.9; H, 3.5. C<sub>14</sub>H<sub>8</sub>O<sub>3</sub> requires C, 75.0; H, 3.6%), from which 3-phenylphthalic acid, m. p. 169—171°, was obtained on hydrolysis (Heilbron *et al.*, *J.*, 1938, 1386, give m. p. 181°). For identification, the latter was cyclised by warming for 10 minutes in concentrated sulphuric acid from which dilution with water yielded fluorenone-1-carboxylic acid, m. p. and mixed m. p. with an authentic specimen 190—191°, from ethanol-water.

*Detection of Dibenzcycloheptadienone (V).*—The mother-liquor from the crystallisation of 4-phenylindanone gave a colourless gum on evaporation. (i) One portion of the gum (0.3 g.) in acetic acid (3 c.c.) was heated under reflux for 1 hour with a solution of sodium dichromate (1.3 g.) in acetic acid (3.5 c.c.). A chloroform extract of the diluted solution was washed with aqueous sodium hydroxide, dried, and concentrated. The gummy neutral residue gave crystals of phenanthraquinone, m. p. and mixed m. p. 204—205°, from chloroform (diazine, from *o*-phenylenediamine, m. p. and mixed m. p. 216—219°). The alkaline liquor gave, on acidification, diphenic acid, m. p. and mixed m. p. 216—219°. (ii) The residual gum (0.28 g.) was treated with 2:4-dinitrophenylhydrazine (0.3 g.) in ethanol-sulphuric acid and the well-washed precipitate was dissolved in the minimum quantity of hot acetic acid. On cooling, the aforementioned 2:4-dinitrophenylhydrazone "A", m. p. and mixed m. p. 243° (decomp.), crystallised, and the filtrate when kept overnight deposited a second dinitrophenylhydrazone, m. p. 230—233° (decomp.) depressed to 220—226° by admixture with "A". The residual mother-liquor was now concentrated to half its volume and was seeded with "A". After 2 hours the resulting deposit of slightly impure "A" was filtered off and the filtrate was then seeded with the second dinitrophenylhydrazone, of which a further crop accrued. The combined crops of the second material were crystallised from acetic acid, forming orange-red needles of m. p. 236—238° (decomp.) raised to 238—240° by admixture with the 2:4-dinitrophenylhydrazone of (V) (Cook, Dickson, and Loudon, *loc. cit.*) and depressed to 216—224° (decomp.) by admixture with "A".

*Cyclisation of (III) with Hydrogen Fluoride.*—The acid (III) (0.84 g.) was dissolved in hydrogen fluoride (*ca.* 10 c.c.) which was then allowed to evaporate in absence of moisture. The residue, after treatment with cold dilute sodium hydroxide, was recovered in ether and gave 4-phenylindanone (IV), m. p. and mixed m. p. 86—87°, from ethanol (yield 79%). The mother-liquor from the crystallisation gave, on concentration, a yellow gum which when oxidised (*cf.* above) with sodium dichromate in acetic acid afforded phenanthraquinone, m. p. and mixed m. p. 201—204°, after sublimation; diazine from *o*-phenylenediamine, m. p. and mixed m. p. 216—217°.

*Cyclisation of β-(5-Bromo-2:3:4:4'-tetramethoxy-6-diphenyl)propionic Acid with Hydrogen Fluoride.*—The neutral solid (0.38 g.), obtained by treating (I) (1 g.) with hydrogen fluoride as above, was crystallised from petroleum (b. p. 40—60°) and gave, as first crop, warty nodules of the bromo-ketone (II) (0.014 g.), (micro-)m. p. and mixed m. p. 141.5°, which was debrominated to 5:6:7-trimethoxy-4-*p*-methoxyphenylindan-1-one (*cf.* Part VIII, *loc. cit.*), (micro-)m. p. and mixed m. p. 84—86°. This compound [oxime, (micro-)m. p. 216°] was also obtained as a second crop of needles from the petroleum mother-liquor of the bromo-ketone.

*2:3:4-Trimethoxydiphenyl-6-carboxylic Acid (IX).*—Methyl 3:4:5-trimethoxybenzoate (265 g.) and 1-phenyl-3:3-dimethyltriazen (53 g.) were slowly treated with acetic acid (70 c.c.) at 100° and the whole was heated at 100° for 16 hours. The resulting dark liquid, dissolved in chloroform, was thoroughly washed in turn with dilute hydrochloric acid, water, dilute sodium hydroxide, and again with water, and recovered. Unchanged ester was distilled off up to 185°/10 mm. and the residue was combined with similar residues obtained by renewed interaction of the recovered ester with fresh triazen. In all, 110 g. of the triazen were used in three runs and the crude trimethoxybenzoate finally recovered weighed 200 g. The combined higher-boiling residues on fractional distillation gave: (a) a small quantity of unchanged ester, b. p. 180—186°/10 mm.; (b) the main, partly solid fraction, b. p. 186—205°/10 mm.; (c) an oily fraction, b. p. 204—214°/10 mm. Fractions (b) and (c) when rubbed each with half its volume of methanol gave solids which were combined (24 g.) and crystallised from methanol (50 c.c.). The resulting crystalline mixture was swirled in the solvent, the lighter material (solid B) was collected by decantation, and the mother-liquor was used for renewed treatment of the heavier constituent. The latter, after further crystallisation from methanol, afforded methyl 2:3:4-trimethoxydiphenyl-6-carboxylate (15 g.), m. p. 71—72° (Found: C, 67.6; H, 5.7. C<sub>17</sub>H<sub>18</sub>O<sub>5</sub> requires C, 67.5; H, 5.95%), which was hydrolysed by 50% aqueous potassium hydroxide in methanol to the corresponding acid (IX), m. p. 196° from methanol (Found: C, 66.95; H, 5.6. C<sub>16</sub>H<sub>16</sub>O<sub>5</sub> requires C, 66.7; H, 5.6%), and was regenerated from this acid by diazomethane in ether; m. p. and mixed m. p. 71—73°. The combined gums, recovered from the various methanol mother-liquors of the above separation, gave small additional quantities of the products after redistillation and re-treatment, while the final methanol mother-liquors on heating with aqueous alkali gave in addition to some non-saponifiable oil (discarded) a small quantity of the above acid, m. p. 191—193°.

Solid B (2.2 g.) was separated by crystallisation from methanol into a small, sparingly soluble fraction consisting of nacreous platelets, m. p. 210°, probably of *p*-terphenyl (Found: C, 93.6; H, 6.15. Calc. for C<sub>18</sub>H<sub>14</sub>: C, 93.9; H, 6.1%), and a relatively soluble fraction (1.5 g.) of m. p. 156° (Found: C, 70.6; H, 5.65. C<sub>10</sub>H<sub>16</sub>O<sub>4</sub> requires C, 70.6; H, 5.9%), which is probably methyl 2:6-dimethoxydiphenyl-4-carboxylate (*cf.* Part VIII, *loc. cit.*). The latter compound was hydrolysed by aqueous potassium hydroxide in methanol to the corresponding acid, m. p. 237° from methanol (Found: C, 69.8; H, 5.7. C<sub>12</sub>H<sub>14</sub>O<sub>4</sub> requires C, 69.8; H, 5.4%).

*2:3:4-Trimethoxyfluorenone.*—The acid (IX) (0.3 g.) was dissolved and gently warmed (10 minutes) in thionyl chloride. The solvent was distilled off; the residual ketone formed long orange needles, m. p. 113°, from methanol (Found: C, 70.8; H, 5.2. C<sub>16</sub>H<sub>14</sub>O<sub>4</sub> requires C, 71.1; H, 5.2%). It yielded a 2:4-dinitrophenylhydrazone as fluffy red needles, m. p. 211°, from acetic acid (Found: C, 58.4; H, 3.8. C<sub>22</sub>H<sub>18</sub>O<sub>7</sub>N<sub>4</sub> requires C, 58.7; H, 4.0%).

2 : 3 : 4-Trimethoxydiphenyl-6-aldehyde (XI).—2 : 3 : 4-Trimethoxydiphenyl-6-carboxyhydrazide, colourless needles of m. p. 156° from methanol (Found : C, 63.7; H, 5.9.  $C_{16}H_{18}O_4N_2$  requires C, 63.8; H, 6.0%), was prepared by heating the methyl ester of (IX) (16.7 g.) and 90% hydrazine hydrate (31 c.c.) in methanol (60 c.c.) for 8 hours. Addition of benzenesulphonyl chloride (9.2 g.) to its solution in cold pyridine (14.1 g. in 84 c.c.), followed after 1 hour by pouring into iced hydrochloric acid, yielded the benzenesulphonyl derivative, m. p. 162—163° (from methanol) (Found : C, 59.4; H, 4.9.  $C_{22}H_{22}O_6N_2S$  requires C, 59.7; H, 5.0%). A solution of the latter (18.5 g.) in ethylene glycol (150 c.c.) at 160° was treated with anhydrous sodium carbonate and, after 100 seconds, the reaction was quenched with boiling water. The required aldehyde, recovered from an alkali-washed ethereal extract, formed almost colourless plates, m. p. 92—93°, from methanol (Found : C, 70.6; H, 5.7.  $C_{16}H_{16}O_4$  requires C, 70.6; H, 5.9%).

$\beta$ -2 : 3 : 4-Trimethoxy-6-diphenylacrylic Acid (XIII).—A solution of the above aldehyde (9.3 g.) and malonic acid (7.4 g.) in dry pyridine (20 c.c.) containing a few drops of piperidine was heated first at 100° (4 hours) and then under reflux (15 minutes). After cooling, pouring into iced hydrochloric acid, and extraction with ether, the required acid was recovered from aqueous alkali and formed small needles, m. p. 165°, from acetic acid-water (2 : 1) (Found : C, 68.7; H, 5.6.  $C_{18}H_{18}O_5$  requires C, 68.8; H, 5.8%).

$\beta$ -2 : 3 : 4-Trimethoxy-6-diphenylpropionic Acid (XV).—This acid was prepared by hydrogenating a solution of (XIII) (9.6 g.) in acetic acid (330 c.c.) over palladium-black (0.6 g.). After filtration and recovery the acid formed colourless plates, m. p. 121—122°, from acetic acid-water (1 : 1) (Found : C, 68.7; H, 6.3.  $C_{18}H_{20}O_5$  requires C, 68.7; H, 6.3%). Methylation with diazomethane in ether gave the methyl ester as cubes, m. p. 56°, from light petroleum (b. p. 40—60°) (Found : C, 69.3; H, 6.8.  $C_{19}H_{22}O_5$  requires C, 69.1; H, 6.7%).

5 : 6 : 7-Trimethoxy-4-phenylindan-1-one.—This ketone was obtained as neutral product in colourless needles of m. p. 74° from petroleum (b. p. 60—80°) (Found : C, 72.9; H, 6.0.  $C_{18}H_{18}O_4$  requires C, 72.5; H, 6.0%) when the acid (XV; 0.5 g.) was treated with hydrogen fluoride. It formed an oxime, m. p. 200°, from ethanol (Found : C, 68.9, H, 6.0.  $C_{18}H_{19}O_4N$  requires C, 69.0; H, 6.1%). Oxidation of the crude product gave no evidence of the formation of a coloured phenanthraquinone derivative.

$\beta$ -(5-Bromo-2 : 3 : 4-trimethoxy-6-diphenyl)propionic Acid (VII).—A solution of bromine (0.1 c.c.) in dry chloroform (2.5 c.c.) was added to a solution of (XV) (0.63 g.) in the same solvent (12.5 c.c.) and, after 3 hours at room temperature, the crude product was recovered from the (water-washed) solution. It was purified by conversion into the sparingly soluble sodium salt by concentrated aqueous sodium hydrogen carbonate. The bromo-acid was regenerated by dilute hydrochloric acid, forming colourless plates, m. p. 164—165°, from acetic acid-water (1 : 1) (Found : C, 54.7; H, 4.8.  $C_{18}H_{18}O_5Br$  requires C, 54.7; H, 4.8%) and affording, with diazomethane in ether, the methyl ester, m. p. 95—96° (from methanol) (Found : C, 55.7; H, 5.0.  $C_{19}H_{21}O_5Br$  requires C, 55.6; H, 5.1%).

Attempts to cyclise (VII).—(a) The neutral gum obtained from (VII) by treatment with hydrogen fluoride remained resinous after reaction with Girard's reagent-r and hydrolysis of the product. It afforded a bright red 2 : 4-dinitrophenylhydrazone, but was not converted into a solid by debromination with hydrogen in presence of palladised strontium carbonate. (b) The acid (0.7 g.) in dry benzene (10 c.c.) was shaken with phosphorus pentachloride (0.4 g.). Volatile materials were removed under reduced pressure and the residue was treated with carbon disulphide (3 c.c.) and aluminium chloride (0.6 g.). After 2 days at 0° dilute hydrochloric acid was added, the solvent was removed in steam, and the neutral product was recovered from chloroform as a gum. This did not yield a solid on debromination.

Neither of the (debrominated) gums showed any trace of a phenanthraquinone derivative when oxidised with sodium dichromate in acetic acid.

1-m-Methoxyphenyl-3 : 3-dimethyltriazene.—A diazo-solution from *m*-anisidine (100 g.), concentrated hydrochloric acid (290 c.c.), water (200 c.c.), and sodium nitrite (56 g.) was added with stirring to a mixture of 25% dimethylamine (280 g.) and 30% aqueous sodium carbonate (800 c.c.) kept at 0°; the mixture was then stirred for 30 minutes and the product was extracted in benzene and recovered from the dried extract. The triazene distilled as a yellow liquid (114 g.), b. p. 161°/15 mm. (Found : C, 60.4; H, 6.9.  $C_9H_{13}ON_3$  requires C, 60.3; H, 7.25%).

2 : 3 : 4 : 3'-Tetramethoxydiphenyl-6-carboxylic Acid (X).—Starting from methyl 3 : 4 : 5-trimethoxybenzoate (165 g.), the above triazene (32 g.), and acetic acid (43 c.c.) and using in all 125 g. of the triazene in 4 runs as described for (IX), there were obtained recovered initial ester (94 g.) and the following higher-boiling fractions : (a) a small fraction, b. p. 185—215°/8 mm.; (b) a main fraction, b. p. 203—220°/0.5 mm. On rubbing these combined fractions with half their volume of methanol there was obtained a product, regarded as methyl 2 : 6 : 3'-trimethoxydiphenyl-4-carboxylate (cf. Part VIII, *loc. cit.*), m. p. 154—156°, from acetic acid (yield, 2 g.) (Found : C, 67.5; H, 5.7.  $C_{17}H_{18}O_5$  requires C, 67.5; H, 5.9%), which was hydrolysed by 50% potassium hydroxide in methanol to the corresponding acid, m. p. 215°, from acetic acid (Found : C, 65.9; H, 5.6. Found, after drying *in vacuo*/100° for 1 hour : C, 66.4; H, 5.2.  $C_{17}H_{16}O_5$  requires C, 66.7; H, 5.5%), and was regenerated from this acid by diazomethane in ether. The methanol mother-liquor from the foregoing ester contained a second (oily) ester which was hydrolysed to 2 : 3 : 4 : 3'-tetramethoxydiphenyl-6-carboxylic acid (X), colourless prisms, m. p. 134—135° (19 g.), from methanol-water (1 : 1) (Found : C, 64.2; H, 5.8.  $C_{17}H_{18}O_6$  requires C, 64.1; H, 5.8%).

2 : 3 : 4 : 6- and 2 : 3 : 4 : 8-Tetramethoxyfluorenone.—The residue obtained by heating (X) with thionyl chloride and distilling off excess of this reagent crystallised from methanol as a mixture of small lemon-coloured needles (A) and heavier, stout, golden needles (B). These were separated by swirling and decanting (A) with the mother-liquor. Fluorenone-A, m. p. 122° from methanol (Found : C, 68.1; H, 5.45.  $C_{17}H_{16}O_5$  requires C, 68.0; H, 5.3%), afforded a 2 : 4-dinitrophenylhydrazone as fluffy red needles, m. p. 236° from acetic acid (Found : C, 57.6; H, 4.1.  $C_{23}H_{22}O_8N_4$  requires C, 57.5; H, 4.2%). Fluorenone-B, m. p. 152—153° from methanol (Found : C, 68.2; H, 5.2.  $C_{17}H_{16}O_5$  requires C, 68.0; H, 5.3%), gave a 2 : 4-dinitrophenylhydrazone, m. p. 137° depressed by admixture with the isomer (Found : C, 57.8; H, 3.7%).

2 : 3 : 4 : 3'-Tetramethoxydiphenyl-6-aldehyde (XII).—This compound, crystallising in colourless

plates, m. p. 60—61°, from methanol (Found : C, 67.4; H, 5.8.  $C_{17}H_{18}O_5$  requires C, 67.5; H, 6.0%), and yielding a 2 : 4-dinitrophenylhydrazone, m. p. 192° (Found : C, 57.4; H, 4.7.  $C_{23}H_{22}O_8N_4$  requires C, 57.3; H, 4.6%), was prepared as described for (XI) via the hydrazide, m. p. 137—138° (Found : C, 61.6; H, 6.0.  $C_{17}H_{20}O_5N_2$  requires C, 61.45; H, 6.0%), and benzenesulphonhydrazide, m. p. 182—183°, of the acid (X) (Found : C, 58.5; H, 5.0.  $C_{23}H_{24}O_7N_2S$  requires C, 58.7; H, 5.1%). Under the conditions given, decomposition of the sulphonhydrazide was incomplete: the sulphonhydrazide was partly recovered from a chloroform extract of the reaction products by washing with 2N-sodium hydroxide, from which it was liberated by saturation with carbon dioxide and on renewed treatment yielded the aldehyde.

$\beta$ -(2 : 3 : 4 : 3'-Tetramethoxy-6-diphenyl)acrylic Acid (XIV).—This acid which formed colourless needles, m. p. 150—151°, from acetic acid : water (1 : 1) (Found : C, 66.2; H, 5.8.  $C_{19}H_{20}O_6$  requires C, 66.3; H, 5.8%), and the corresponding propionic acid (XVI), m. p. 90—91° (from dilute acetic acid) (Found : C, 65.7; H, 6.2.  $C_{19}H_{22}O_6$  requires C, 65.9; H, 6.4%), were obtained by the methods described for analogous cases.

5 : 6 : 7-Trimethoxy-4-m-methoxyphenylindan-1-one was obtained as neutral product from the treatment of the acid (XVI) with hydrogen fluoride. It formed thick colourless plates, m. p. 141—142°, from methanol (Found : C, 69.25; H, 6.1.  $C_{19}H_{20}O_5$  requires C, 69.5; H, 6.1%). An oxidation test on the cyclised material gave no evidence of formation of a phenanthraquinone derivative.

$\beta$ -(5-Bromo-2 : 3 : 4 : 3'-tetramethoxy-6-diphenyl)propionic Acid (VIII).—The bromo-acid, m. p. 163—164° (from acetic acid) (Found : C, 53.8; H, 4.8.  $C_{19}H_{21}O_4Br$  requires C, 53.65; H, 5.0%), was prepared from (XVI) as described for the compound (VII).

5 : 6 : 7-Trimethoxy-4-(?bromo-m-methoxyphenyl)indan-1-one.—Colourless plates, m. p. 115—116° (from methanol) (Found : C, 56.1; H, 4.7.  $C_{19}H_{19}O_5Br$  requires C, 56.0; H, 4.7%), of this ketone were obtained as neutral product by treating (VIII) with hydrogen fluoride. The gum, recovered from the methanol mother-liquor, did not afford evidence of formation of a phenanthraquinone derivative when oxidised with sodium dichromate in acetic acid.

Debromination. The above bromo-indanone (0.04 g.) in methanol (20 c.c.) was shaken (1 hour) with 2% palladised strontium carbonate in an atmosphere of hydrogen. Concentration of the filtered solution yielded 5 : 6 : 7-trimethoxy-4-m-methoxyphenylindan-1-one, m. p. and mixed m. p. 139—141°.

2 : 5-Dimethoxydiphenyl-2'-carboxylic Acid (XVII).—Glacial acetic acid (60 c.c.) was slowly added to a melt of quinol dimethyl ether (160 g.) and 1-(*o*-carboxymethoxyphenyl)-3 : 3-dimethyltriazen (50 g.; cf. Elks and Hey, *J.*, 1943, 443) at 100° and the mixture was maintained at this temperature for 18 hours. The resulting dark liquid was dissolved in chloroform and, after being washed in turn with dilute hydrochloric acid, water, dilute sodium hydroxide and again with water, the solution was dried and concentrated. Distillation of the residue gave the following fractions: (i) quinol dimethyl ether (140 g.), b. p. 110—112°/10 mm.; (ii) a pale yellow oil (3 g.), b. p. 127—132°/10 mm.; (iii) a yellow oil (7 g.), b. p. 196—204°/10 mm., which when rubbed with methanol gave methyl 2 : 5-dimethoxydiphenyl-2'-carboxylate, m. p. 65° from methanol (Found : C, 70.6; H, 6.0.  $C_{16}H_{16}O_4$  requires C, 70.6; H, 5.9%); (iv) a viscous brownish gum, b. p. 205—215°/10 mm. with much decomposition, yielding a small quantity of unidentified needles, m. p. 291—293°, when rubbed with methanol; (v) a non-volatile residue which was dissolved in chloroform, washed with dilute hydrochloric acid and, combined with the residues from subsequent runs, concentrated, and redistilled, thereby slightly adding to fraction (iv). Fraction (ii), combined with the methanol mother-liquors from fractions (iii) and (iv), gave on hydrolysis (1 hour) with aqueous methanolic potassium hydroxide the acid (XVII), m. p. 155° (from methanol), which was also obtained by hydrolysing the pure methyl ester (Found : C, 69.9; H, 5.4.  $C_{15}H_{14}O_4$  requires C, 69.8; H, 5.4%).

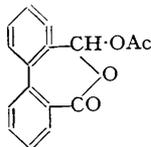
2-Hydroxy-5-methoxydiphenyl-2'-carboxylic Acid Lactone (XVIII).—The preceding acid (0.5 g.) in benzene (5 c.c.) and thionyl chloride (1.2 c.c.) was kept for 12 hours at room temperature. After removal of solvent under reduced pressure (temp. ca. 25°), the lactone was obtained as colourless crystals, m. p. 119—120°, from benzene (Found : C, 73.7; H, 4.4; OMe, 13.4.  $C_{14}H_{10}O_3$  requires C, 74.3; H, 4.4; OMe, 13.7%). It did not give a coloration to aqueous ferric chloride, was insoluble in cold alkali, but dissolved on heating and was regenerated on acidification.

Monobenzenesulphonhydrazide of Diphenic Acid.—(a) A suspension of the monohydrazide of diphenic acid (1.3 g.; m. p. with gas evolution 185°: cf. Labriola, *Chem. Zentr.*, 1938, II, 1770) in cold pyridine (4 c.c.) was treated with benzenesulphonyl chloride (0.9 g.) which was washed in with the aid of a further 2 c.c. of pyridine. After 12 hours at room temperature the yellow solution was added to dilute sulphuric acid, yielding the required product, m. p. 220° from ethanol-water (Found : C, 60.3; H, 4.1; N, 7.3.  $C_{20}H_{16}O_5N_2S$  requires C, 60.6; H, 4.0; N, 7.1%). With acetic anhydride and a trace of sulphuric acid or with acetic anhydride in pyridine it reacted to form an anhydro-acetyl derivative, m. p. 216° from acetic acid, which was insoluble in alkali (Found : C, 63.3; H, 3.9; N, 6.5.  $C_{22}H_{16}O_5N_2S$  requires C, 62.9; H, 3.8; N, 6.7%).

(b) Diphenic anhydride (6.6 g.) was added slowly with cooling to a solution of benzenesulphonhydrazide (5.1 g.) in pyridine (30 c.c.). After 12 hours the solid obtained on pouring into dilute hydrochloric acid yielded the above compound, m. p. and mixed m. p. 220°, from ethanol-water, as main product, while a second product—probably the isomeric *aa*-diacylhydrazide [ $C_{12}H_8(CO_2H)CO \cdot N(NH_2)SO_2Ph$ ]—m. p. 220° depressed to ca. 215° by admixture with the above compound, was obtained in small amount from the mother-liquor (Found : C, 60.8; H, 4.0; N, 6.9.  $C_{20}H_{16}O_5N_2S$  requires C, 60.6; H, 4.0; N, 7.1%).

2'-Formylidiphenyl-2-carboxylic Acid (XIX).—To a solution of the above benzenesulphonhydrazide (2 g.; main fraction) in ethylene glycol (20 c.c.) at 165° anhydrous sodium carbonate (25 g.) was added during 30 seconds and after a further 240 seconds the reaction was terminated by cautious addition of boiling water (100 c.c.). After cooling and filtering, unreacted hydrazide was precipitated by a stream of sulphur dioxide, and the resulting mother-liquor, on acidification with dilute sulphuric acid, gave the acid (XIX) in 40% yield, m. p. 132° from methanol-water (Found : C, 74.5; H, 4.4.  $C_{14}H_{10}O_3$  requires C, 74.4; H, 4.4%).

*ω*-Acetoxydiphenide (as annexed) was obtained when a solution of (XIX) in acetic anhydride containing a few drops of concentrated sulphuric acid was kept for 12 hours and then poured into water. After recovery from an alkali-washed ethereal extract, the neutral product had m. p. 125° from methanol (Found: C, 71.6; H, 4.3. C<sub>16</sub>H<sub>12</sub>O<sub>4</sub> requires C, 71.6; H, 4.5%). It was reconverted into (XIX) by warming (90 minutes) in dilute sulphuric-acetic acid.



*β*-(2'-Carboxy-2-diphenyl)acrylic Acid (XX).—A solution of the aldehydo-acid (XIX) (1.2 g.) and malonic acid (0.55 g.) in pyridine (6 c.c.), containing a few drops of piperidine, was heated first at 100° (1 hour) and then under reflux (15 minutes) before being cooled and poured into dilute hydrochloric acid. The oily product solidified and had m. p. 228° [Rapoport and Williams, *loc. cit.*, record m. p. 230—231° (corr.)], from dilute acetic acid (Found: C, 72.1; H, 4.5. Calc. for C<sub>16</sub>H<sub>12</sub>O<sub>4</sub>: C, 71.6; H, 4.5%). Its titre, determined in methanol solution, showed the compound to be dibasic (Found: equiv., 130. Calc.: equiv., 134).

*β*-(2'-Carboxy-2-diphenyl)propionic Acid (XXI).—The above acid, dissolved in acetic acid, was hydrogenated in presence of palladium-black at ordinary temperature and pressure. Hydrogenation was complete in 1½ hours and the product, recovered from the filtered solution, had m. p. 185° from aqueous acetic acid (Found: C, 71.1; H, 4.8. Calc. for C<sub>16</sub>H<sub>14</sub>O<sub>4</sub>: C, 71.1; H, 5.2%). Rapoport and Williams (*loc. cit.*) give m. p. 171—173° (corr.) (prepared by three distinct methods).

*Cyclisation of (XXI).*—(a) The dry barium salt, heated in a sublimation apparatus at 360°/1 mm., yielded an oily sublimate which could not be induced to crystallise but afforded a 2 : 4-dinitrophenylhydrazone, (micro)-m. p. 220° from acetic acid, unchanged by further crystallisation or by admixture with the 2 : 4-dinitrophenylhydrazone of (V), (micro)-m. p. 237°. (b) The dry sodium salt (0.11 g.) was heated under reflux with acetic anhydride (2 c.c.) for 1 hour. The solvent was removed under reduced pressure and the residue was treated with dilute alkali and extracted with ether. The oil recovered from the ether yielded a crystalline 2 : 4-dinitrophenylhydrazone, (micro)-m. p. 234° and mixed m. p. 235° with the 2 : 4-dinitrophenylhydrazone of (V).

*p*-Tolyl 2-*o*-carboxyphenylthiolbenzoate was prepared by heating (90 minutes) a solution of diphenic anhydride (0.5 g.) and thio-*p*-cresol (0.34 g.) in pyridine at 70°. It solidified when the cooled solution was poured into dilute hydrochloric acid and had m. p. 147° (from methanol-water) (Found: C, 72.8; H, 4.6. C<sub>21</sub>H<sub>16</sub>O<sub>3</sub>S requires C, 72.4; H, 4.6%). On cooling a solution of the compound in warm dilute sodium hydroxide there was deposited a crystalline product of m. p. 88°, from which the thiol-ester was regenerated by dilute acid and which appeared to be a hydrated sodium salt (Found: C, 51.6; H, 5.5. C<sub>21</sub>H<sub>15</sub>O<sub>3</sub>SNa, 7H<sub>2</sub>O requires C, 51.6; H, 5.8%).

When treated as in the following case with Raney nickel the half thiol-ester yielded 2'-hydroxymethyl-diphenyl-2-carboxylic acid, m. p. 145—146° [from ether-light petroleum (b. p. 40—60°)], which was converted by heating at 110° for 1 hour into diphenide, m. p. and mixed m. p. 132° (Kenner and Turner, *J.*, 1911, 99, 2101, give m. p. 146° and 132°, respectively).

*p*-Tolyl *o*-Carbomethoxythiolbenzoate.—A solution of equivalent amounts of *o*-carbomethoxybenzoyl chloride and thio-*p*-cresol in cold pyridine was poured, after 12 hours, into iced dilute hydrochloric acid. The product, washed with alkali, dried, recovered in ether, and crystallised from methanol, had m. p. 58—59° (Found: C, 67.3; H, 4.9. C<sub>16</sub>H<sub>14</sub>O<sub>3</sub>S requires C, 67.1; H, 4.9%). A solution of this compound (1.5 g.) in 70% ethanol (30 c.c.) was heated under reflux with suspended Raney nickel (7.5 g.) for 90 minutes. After filtration, concentration, and an ineffective attempt to separate aldehydic material by means of sodium hydrogen sulphite solution, the resulting oil slowly solidified, giving crystals of m. p. and mixed m. p. with phthalide 71—72°.

*p*-Tolyl thiolbenzoate (2 g.) in 70% ethanol (40 c.c.) with Raney nickel (10 g.) in suspension was heated under reflux for 6 hours. On distillation from a water-bath the ethanol entrained some benzaldehyde, isolated as 2 : 4-dinitrophenylhydrazone (0.25 g.), m. p. and mixed m. p. 235°, whilst the residue afforded benzyl alcohol (0.25 g.), b. p. 178°/24 mm., characterised as the 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 110—112°.

Ethyl thiolbenzoate (9.5 g.) in 70% ethanol (180 c.c.) was heated under reflux with Raney nickel (54 g.) for 2 hours. The filtrate from the nickel was diluted with water and extracted with ether. The ether was removed through an efficient reflux column and the residue was cautiously treated with an excess of concentrated nitric acid, nitration being completed by heating under reflux for 1 hour. Nitrobenzene was isolated by distillation, b. p. 208—210°, and was identified by conversion (Raney nickel and hydrogen) into aniline, b. p. 180—182°, and thence into acetanilide and tribromoaniline. The yield of benzene, based on the aniline found, was 60%.

*p*-Tolyl 3 : 4 : 5-Trimethoxythiolbenzoate.—Thio-*p*-cresol (2.6 g.) in dry pyridine (14 c.c.) was treated with finely powdered 3 : 4 : 5-trimethoxybenzoyl chloride and the whole was heated at 80° for 1 hour. The cooled mixture was poured into iced hydrochloric acid and, after recovery in benzene, the thiol-ester formed colourless plates, m. p. 102° (Found: C, 64.2; H, 5.4. C<sub>17</sub>H<sub>14</sub>O<sub>4</sub>S requires C, 64.35; H, 5.4%).

*Reaction with Raney Nickel.*—(i) The thiol-ester (2.25 g.) in 70% ethanol (50 c.c.) containing Raney nickel (12 g.) in suspension was heated under reflux for 6 hours. After recovery and distillation there were obtained: (i) 1 : 2 : 3-trimethoxybenzene (0.24 g.), b. p. 80°/0.5 mm., m. p. 42—43° from petroleum (b. p. 40—60°), forming a *picrate*, golden needles of m. p. and mixed m. p. 79—80° (Found: C, 45.8; H, 3.8; N, 10.4. C<sub>15</sub>H<sub>10</sub>O<sub>3</sub>N<sub>3</sub> requires C, 45.4; H, 3.8; N, 10.6%), and further characterised by oxidation with dilute nitric acid to 2 : 6-dimethoxybenzoquinone, m. p. 246—248°; (ii) 3 : 4 : 5-trimethoxybenzyl alcohol (0.62 g.), b. p. 152—154°/0.5 mm., identified as the 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 147—148° (Cook, Graham, and Cohen, *J.*, 1944, 323) (Found: C, 52.3; H, 4.15. Calc. for C<sub>17</sub>H<sub>16</sub>O<sub>9</sub>N<sub>2</sub>: C, 52.1; H, 4.1%).

(ii) The thiol-ester (4 g.) in dioxan (40 c.c.) was treated with a suspension of Raney nickel (32 g.) in dioxan (40 c.c.). Heat was evolved and the reaction was completed by shaking for 1 hour at room temperature. 1 : 2 : 3-Trimethoxybenzene (0.705 g.) and 3 : 4 : 5-trimethoxybenzyl alcohol (1.05 g.) were again isolated as under (a).

Ethyl 3 : 4 : 5-trimethoxythiolbenzoate (7 g.), b. p. 185°/0.3 mm., m. p. 35—36° from light petroleum

(b. p. 40—60°) (Found : C, 56.3; H, 6.3.  $C_{12}H_{16}O_4S$  requires C, 56.3; H, 6.25%), treated as in experiment (i), gave 1 : 2 : 3-trimethoxybenzene (1.1 g.) and 3 : 4 : 5-trimethoxybenzyl alcohol (2.1 g.).

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