*Chebulinic Acid. Part II.**

By R. D. Haworth and L. B. de Silva.

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In agreement with Schmidt's formula (I; R = H) for chebulic acid, it has been shown (*a*) that a synthetic mixture of racemates of the γ-lactone (III; R = OH) of 1-hydroxybutane-1 : 2 : 3 : 4-tetracarboxylic acid gave 2·6 mols. of oxalic acid on oxidation with permanganate and (*b*) that 5 : 6 : 7-trimethoxy*iso*coumarin-3-carboxylic acid (IX; R = H) and succinic acid are products of pyrolysis of trimethylchebulic acid in presence of copper powder. Other pyrolytic products include optically active and inactive methyl esters, $C_{17}H_{18}O_8$, and the constitution of the former is discussed in light of the available chemical and spectroscopic evidence.

Our interest in chebulinic acid, the crystalline constituent of myrobalans, was aroused by a suggestion by Schmidt and Mayer (*Annalen*, 1951, **571**, 1) that " split acid " (now known as chebulic acid) (Schmidt, Lademann, and Himmele, *Chem. Ber.*, 1952, **85**, 408), a hydrolysis product of chebulinic acid, was an *iso*coumarin derivative of structure (I; R = H), which may be derived from ellagic acid by oxidative degradation of one of the phenolic rings. In view of the possibility of a relation between chebulic acid (I; R = H) and galloflavin, for which the *iso*coumarin structure (II) was tentatively suggested by Haworth and McLachlan (*J.*, 1952, 1583), we investigated chebulic acid; our oxidation (Part I *) of trimethylchebulic acid (I; R = Me) with potassium ferricyanide to 3 : 4 : 5-trimethoxyphthalic acid confirmed the structure of the aromatic moiety. Further evidence in this direction was obtained in the present work when it was found that oxalic, succinic, and trimethylgallic acid were produced by fusing trimethylchebulic acid with potassium hydroxide.

Schmidt and Mayer (*loc. cit.*) oxidised trimethylchebulic acid with permanganate to a lactonic tribasic acid (III; R = OH), the structure of which was supported by reasons summarised in Part I. More recently Schmidt, Mayer, and Wick (*Chem. Ber.*, 1953, **86**, 488) synthesised the two racemates of the isomeric γ-lactone (IV) of 2-hydroxybutane-1 : 2 : 3 : 4-tetracarboxylic acid, and showed that whilst the lactonic acid (III; R = OH)

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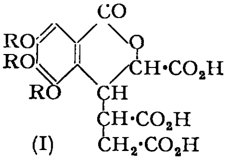
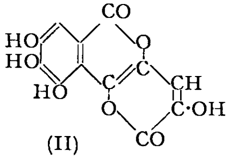
* *J.*, 1951, 3511, is now regarded as Part I.

gave 2·58 mols. of oxalic acid when oxidised with permanganate, the synthetic lactone (IV) yielded only 0·32 mol. More direct confirmatory evidence for structure (III; R = OH) has now been obtained by the synthesis of an oily mixture of racemates having this structure (III; R = OH). Tetraethyl propane-1 : 1 : 2 : 3-tetracarboxylate was isolated during these experiments, and a compound, possibly α-dicarbamoylmethylsuccinimide (V), was prepared by the action of ammonia on tetraethyl propane-1 : 1 : 2 : 3-tetracarboxylate. Wislicenus and Schwanhausser (*Annalen*, 1897, **297**, 107) prepared triethyl 4 : 5-dioxo*cyclo*pentane-1 : 2 : 3-tricarboxylate (VI) by the action of diethyl oxalate on triethyl carballylate in presence of sodium ethoxide, and Gault (*Compt. rend.*, 1910, **150**, 1341) reported the formation of a mixture of (VI) and triethyl ethoxalyltricarballylate (VII) without specifying reaction conditions. In the Experimental section we describe conditions which reduce the proportion of the *cyclo*pentanedione derivative (VI) to a minimum and, although the tetraethyl ester (VII) could not be purified because decarbonylation to tetraethyl propane-1 : 1 : 2 : 3-tetracarboxylate took place on heating, it was readily reduced by hydrogen in the presence of Raney nickel to the γ-lactone (III; R = OEt) of triethyl 1-hydroxybutane-1 : 2 : 3 : 4-tetracarboxylate. Although a crystalline triamide (III; R = NH_2) was prepared, this triethyl ester (III; R = OEt) and the hygroscopic acid obtained from it by hydrolysis are probably racemic mixtures. The hygroscopic acid (III; R = OH) was readily oxidised with alkaline permanganate, and the production of 2·6 mols. of oxalic acid confirm the structural views of Schmidt and Mayer (*loc. cit.*) concerning the hydroxybutanetetracarboxylic acid derived from chebulic acid.


(I)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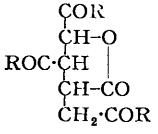
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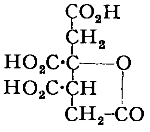
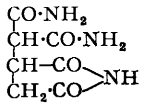

(IV)

These results may be interpreted on the basis of the *iso*coumarin structure (I; R = H) for chebulic acid, as suggested by Schmidt and Mayer (*loc. cit.*), but structure (VIII) is equally consistent with them. The latter γ-lactone structure however is probably excluded by our measurements of the infra-red absorption spectra of chebulic acid derivatives. Trimethyl trimethylchebulate (Schmidt, Heintzeler, and Mayer, *Chem. Ber.*, 1947, **80**, 514) shows a single broad band with a peak at 1740 cm.$^{-1}$, and points of 50% absorption between 1700 and 1790 cm.$^{-1}$; and trimethylchebulic triamide, m. p. 254° (decomp.) (Schmidt and Mayer, *loc. cit.*), has a sharp band at 1727 cm.$^{-1}$, and a broad intense band at 1666—1695 cm.$^{-1}$. The latter is probably due to the amide-carbonyl group (Grove and Willis, *J.*, 1950, 877), and the high-frequency bands are ascribable to six-membered ring lactonic structures such as (I).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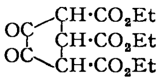
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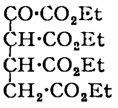
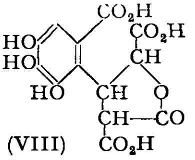


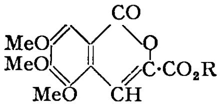
$$\begin{array}{l} CO{\cdot}CO_2Et \\ CH{\cdot}CO_2Et \\ CH{\cdot}CO_2Et \\ CH_2{\cdot}CO_2Et \end{array}$$

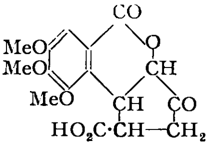
(VII)


(VIII)

Numerous attempts to dehydrogenate trimethylchebulic acid (I; R = Me) with palladium, sulphur, or selenium were abortive, and the lactone ring was not affected by sodium bismuthate or potassium cyanide. Decarboxylation with copper or copper chromite in boiling quinoline gave oils, but very interesting results have been obtained by pyrolysis of trimethylchebulic acid with copper powder at 260—290°/0·5 mm. An oily sublimate was obtained, and, after methylation with diazomethane, the ester mixture was separated by distillation followed by chromatography on a charcoal column into (*a*) methyl 5 : 6 : 7-trimethoxy*iso*coumarin-3-carboxylate (IX; R = Me), m. p. 154—155°, (*b*) an optically active methyl ester (A), m. p. 149°, of a keto-lactonic acid, $C_{16}H_{16}O_8$, possibly (XI), and (*c*) an optically inactive ketonic methyl ester (B), $C_{17}H_{18}O_8$, m. p. 141°. The methyl 5 : 6 : 7-trimethoxy*iso*coumarin-3-carboxylate (IX; R = Me) was converted into the corresponding acid (IX; R = H), from which the acid chloride and ethyl ester were prepared, and these product were identified by comparison with the corresponding synthetic substances described in the following paper. The production of the ester (IX; R = Me) during the pyrolysis is readily interpreted on the basis of Schmidt's formula (I; R = H) for chebulic acid as a type of reversed Michael reaction. In agreement with this, the most volatile fraction Y (p. 3615) of the pyrolysis products yielded, on hydrolysis, a small amount of solid which gave a green fluorescence with resorcinol and concentrated sulphuric acid, indicative of succinic acid.

The keto-ester B gave crystalline phenyl- and 2 : 4-dinitrophenyl-hydrazones, but further experiments on it await accumulation of more material. Considerable progress has however been made in elucidating the constitution of the ester (A), although a final solution has not been reached. The derived acid, $C_{16}H_{16}O_8$, gave a crystalline *p*-nitrobenzyl ester, and titration showed the presence of a lactone group in addition to the carboxyl group. Oxidation of the acid with potassium ferricyanide gave 3 : 4 : 5-trimethoxyphthalic acid, but as the methyl ester A did not react with ferric chloride or 3 : 5-dinitrobenzoyl chloride and gave a negative Zerewitinoff test hydroxyl groups were absent. The methyl ester however gave a crystalline phenylhydrazone and a red amorphous 2 : 4-dinitrophenylhydrazone, proving the presence of a ketonic group and accounting for the eighth oxygen atom. The high optical rotation and sparing solubility in water of the ester and the acid suggest that further ring formation has occurred during the pyrolysis of trimethylchebulic acid (I; R = Me). If the *iso*coumarin ring remains undisturbed, structure (X) may be advanced for the acid, $C_{16}H_{16}O_8$, but (XI), (XII), or (XIII) must be considered if the original lactone ring is ruptured during the pyrolysis. All attempts to decarboxylate the acid or to prepare benzylidene, *p*-nitrobenzylidene, piperonylidene, and *iso*nitroso-derivatives were unsuccessful, although the latter failures are not regarded as excluding the presence of a keto-methylene group. The acid, $C_{16}H_{16}O_8$, was recovered after being heated with palladium–charcoal in boiling *p*-cymene, but it was dehydrogenated to $C_{16}H_{14}O_8$ by selenium dioxide. Unfortunately small amounts of material only were available and any conclusions must be regarded as provisional and requiring confirmation. But the properties of $C_{16}H_{14}O_8$ are consistent with the α-naphthol structure (XIV; R = H), which is derivable from the α-tetralone formula (XI) for the acid A, $C_{16}H_{16}O_8$. Thus in alkaline solution the acid $C_{16}H_{14}O_8$ gave a red azo-dye with benzenediazonium chloride, and on methylation with diazomethane gave a product $C_{18}H_{18}O_8$ which did not react with ketonic reagents and is regarded as (XIV; R = Me). The acid $C_{16}H_{14}O_8$ lost carbon dioxide on melting, but unfortunately the yellow resinous product could not be purified. The α-tetralone structure (XI) is also supported by the red colour shown by the amorphous 2 : 4-dinitrophenylhydrazone and by an infra-red spectroscopic study of the acid, $C_{16}H_{16}O_8$, its methyl ester, phenylhydrazone, and disodium salt made by Mr. H. J. V. Tyrrell to whom we are greatly indebted for the results in the annexed Table and their interpretation.


(IX)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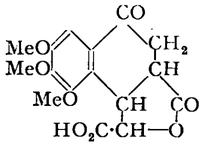
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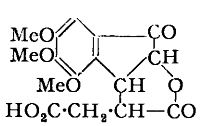
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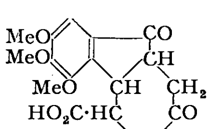
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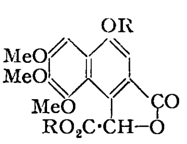
(XIV)

Infra-red absorption of the acid A, $C_{16}H_{16}O_8$ (*cm.*$^{-1}$).

	3-μ region	6-μ region				
Acid	No free OH band	1795	1742	1656	1587	1488
Me ester	,,	1789	1751	1684	1592	1488
Phenylhydrazone of ester	,,	1795	1751	Absent	1608	1492
Na_2 salt	Undissociated OH	Absent	Absent	1661	1621	1590

In the acid there were three bands which might reasonably be identified as carbonyl frequencies, *viz.*, 5·57, 5·74, and 6·04 μ. On esterification, the greatest change occurred in the band of lowest frequency, but since this disappeared from the spectrum of the phenylhydrazone of the ester it must be assigned to the ketonic-carbonyl group. This assignment is confirmed by the persistence of this band in the spectrum of the disodium salt. The frequency (1684 cm.$^{-1}$) of this band in the ester spectrum is the best guide to the nature of the ketonic group; it is too low for *cyclo*pentanone structures such as (X), (XII), (XIII), but fits well with that expected for the keto-group in structure (XI). Both the bands of higher frequency disappeared from the spectrum of the disodium salt, and must therefore be associated with the acid- and lactone-carbonyl groups. The band of highest frequency (1795 cm.$^{-1}$) can be assigned most plausibly to a γ-lactone structure (Grove and Willis, *loc. cit.*) as in (XI), leaving 1742 cm.$^{-1}$ as the acid-carbonyl frequency. Although this is unduly high for a solid dimeric acid, no unbonded-hydroxyl frequency was detected and these observations, together with the large shift of the keto-group frequency on passing from the acid to the ester, are not readily explicable at the moment.

When the acid $C_{16}H_{16}O_8$ was treated with thionyl chloride, it gave, in small yield, an acid chloride, m. p. 204—205°, but as the original acid, $C_{16}H_{16}O_8$, was not recoverable therefrom, some more profound structural change probably took place. Alkaline hydrolysis of the chloride gave an isomeric acid $C_{16}H_{16}O_8$, which separated with one molecule of water of crystallisation, and decomposition of the chloride with methyl alcohol gave a methyl ester, m. p. 227—228°, differing from the methyl ester, m. p. 149°, obtained by pyrolysis of trimethylchebulic acid. A satisfactory explanation cannot be advanced from the available evidence, but it is hoped to examine these reactions more fully in further work.

EXPERIMENTAL

Infra-red Spectra.—Substances were examined as mulls in Nujol. Spectra were obtained with a Grubb-Parsons S. 3*A* spectrometer.

Chebulinic Acid.—This has usually been isolated by extraction of powdered myrobalans with aqueous alcohol. The use of acetone (4·5 vols.) as a solvent was found advantageous. The acetone extract was concentrated to about one-seventh of its volume, diluted with seven volumes of water, and filtered from ellagic acid and other insoluble matter; the filtrate gradually deposited chebulinic acid, which was collected, washed with ether, and crystallised from water, forming needles (5—10%, varying with origin of the myrobalans).

Trimethylchebulic Acid (I; R = Me).—Isolation of chebulic acid as thallium salt (Freudenberg and Fick, *Ber.*, 1920, **53**, 1728; Schmidt, Heintzeler, and Mayer, *loc. cit.*) was tedious and Schmidt and Mayer's method (*loc. cit.*) of isolation of trimethylchebulic acid [Found : equiv. (cold), 132·0, (hot), 100·5. Calc. for $C_{17}H_{18}O_{11}$: equiv. (cold), 132·8; (hot), 99·6] was more satisfactory.

Trimethyl trimethylchebulate, prepared with diazomethane in ether–acetone, was a pale yellow oil, b. p. 200—205°/0·001 mm. (Found : C, 54·3; H, 5·7; OMe, 42·0. Calc. for $C_{20}H_{24}O_{11}$: C, 54·5; H, 5·5; OMe, 42·3%), which yielded trimethylchebulic triamide as prisms, m. p. 254—255° (decomp.) (Found : C, 51·8; H, 5·5; N, 10·8. Calc. for $C_{17}H_{21}O_8N_3$: C, 51·6; H, 5·3; N, 10·6%).

Fusion of Trimethylchebulic Acid with Potassium Hydroxide.—Trimethylchebulic acid (4·5 g.) was stirred with potassium hydroxide (30 g.) and water (15 c.c.); the temperature was raised to 100° in ½ hr., to 200° in the next ½ hr., and finally to 300° in the third ½ hr. The cooled melt was dissolved in water, acidified with concentrated hydrochloric acid, decolorised with charcoal, and extracted with ether. Removal of the ether left a brown residue which was taken up in hot water (50 c.c.), treated with charcoal, and filtered, and excess of calcium chloride was added. The insoluble calcium salt was decomposed with dilute sulphuric acid, and the acid, isolated with ether, crystallised from water in needles (0·6 g.), m. p. 109°, undepressed on admixture with hydrated oxalic acid. The filtrate from the calcium oxalate was acidified and the acid, isolated with ether, separated from a little water in needles (0·51 g.), m. p. 185°, undepressed on admixture with succinic acid. The aqueous mother-liquors were evaporated to dryness and the residue was dissolved in methyl alcohol (5 c.c.) and mixed with ethereal diazomethane. After 12 hr. the solvent was removed and the residue distilled at 0·3 mm. (bath-temp. 155—165°). The distillate separated from methyl alcohol in prisms (0·1 g.), m. p. 82°, undepressed on admixture with methyl trimethylgallate, m. p. 82°, and converted into trimethylgallic acid, m. p. 167°, by alkaline hydrolysis.

Propane-1 : 1 : 2 : 3-*tetracarboxylic Acid.*—The tetramethyl ester (*Org. Synth.*, 1925, **4**, 29) was refluxed with excess of 2N-sodium hydroxide for 1½ hr. The solution was acidified and the *acid*, isolated with ether, crystallised from acetic acid in needles, m. p. 144—145° (decomp.) (Found : C, 38·3; H, 3·8. $C_7H_8O_8$ requires C, 38·2; H, 3·6%).

α-Dicarbamoylmethylsuccinimide (V).—A methyl-alcoholic solution of tetraethyl propane-1 : 1 : 2 : 3-tetracarboxylate was saturated with ammonia and heated in a sealed tube at 100° for 24 hr. Removal of the solvent and crystallisation of the residue from hot water gave the *diamide* as prisms, m. p. 244—245° (decomp.) (Found : C, 42·4; H, 4·7; N, 21·4. $C_7H_9O_4N_3$ requires C, 42·2; H, 4·5; N, 21·1%).

Triethyl Ethoxalyltricarballylate (VII).—Triethyl tricarballylate (13·7 c.c.) was added to diethyl oxalate (7·8 c.c.) and potassium ethoxide (from potassium, 2·25 g.) in ether (10 c.c.). After 24 hr. water was added and the aqueous extract was acidified and extracted with ether. Removal of the solvent gave a pale yellow oil which slowly deposited triethyl 4 : 5-dioxo*cyclo*pentane-1 : 2 : 3-tricarboxylate (VI) which separated from ethyl alcohol in prisms (0·35 g.), m. p. 122—123° (Found : C, 53·5; H, 5·9. Calc. for $C_{14}H_{18}O_8$: C, 53·5; H, 5·7%). Wislicenus and Schwanhausser (*loc. cit.*) and Gault (*loc. cit.*) give m. p. 122—123° and 127° respectively. The osazone separated from alcohol in yellow needles, m. p. 162—163° (Found : C, 63·3; H, 6·0; N, 11·1. Calc. for $C_{26}H_{30}O_6N_4$: C, 63·2; H, 6·1; N, 11·3%). Wislicenus and Schwanhausser (*loc. cit.*) give m. p. 162—163°. The *quinoxaline* derivative crystallised from aqueous alcohol in yellow elongated prisms, m. p. 170—171° (Found : C, 62·2; H, 5·7; N, 7·1. $C_{20}H_{22}O_6N_2$ requires C, 62·2; H, 5·7; N, 7·3%).

Triethyl ethoxalyltricarballylate (VII), on distillation at 1 mm., gave tetraethyl propane-1 : 1 : 2 : 3-tetracarboxylate, b. p. 160—162/1 mm. (Found : C, 54·0; H, 7·4. Calc. for $C_{15}H_{24}O_8$: C, 54·2; H, 7·4%), which was hydrolysed by alkali to the tetracarboxylic acid melting at 144—145° with loss of carbon dioxide and formation of tricarballylic acid, m. p. 157—159°. The *methyl ether* of (VII), prepared by diazomethane in ether–acetone, was a yellow viscous oil, b. p. 170—175°/0·1 mm. (Found : C, 54·2; H, 7·0. $C_{17}H_{26}O_9$ require C, 54·5; H, 7·0%).

γ-Lactone (III; R = OEt) *of Triethyl* 1-*Hydroxybutane*-1 : 2 : 3 : 4-*tetracarboxylate.*—The ester (VII) (10 g.) was reduced in alcohol at 100°/100 atm. with Raney nickel (1·5 g.) during 12 hr. After removal of the catalyst and solvent, the residue yielded the *lactone* (III; R = OEt) as a colourless oil, b. p. 176—178°/0·3 mm. (Found : C, 53·5; H, 6·6. $C_{14}H_{20}O_8$ requires C, 53·2; H, 6·3%), which gave the acid (III; R = OH) as a hygroscopic oil. The triamide was prepared from a methyl-alcoholic solution of the ester (III; R = OEt) which was saturated with ammonia at −10° and kept at room temperature for 4 days. Then after 1 hour's refluxing the *amide* was collected. It separated from water in prisms, m. p. 244—245° (decomp.) (Found : C, 42·1; H, 5·1; N, 18·2. $C_8H_{11}O_5N_3$ requires C, 41·9; H, 4·8; N, 18·3%). The ester (III; R = OEt) (1·65 g.) was heated on the steam-bath for 2 hr. with N-sodium hydroxide (40 c.c.), cooled to room temperature, and mixed with 2N-sodium hydroxide (80 c.c.) and potassium permanganate (7·53 g.) in water (250 c.c.). After 12 hr., more N-sodium hydroxide (40 c.c.) was added and the solution heated for 2 hr. at 100°. Excess of permanganate was destroyed with methyl alcohol, the manganese dioxide was collected and washed with hot water, the concentrated filtrate and washings were acidified with acetic acid, and calcium chloride was added. The calcium oxalate was collected, washed, and dried at 110° (1·97 g.).

Pyrolysis of Trimethylchebulic Acid (I; R = Me).—The acid (I; R = Me) (7·6 g.) was heated with freshly precipitated copper powder (2·5 g.) at 260—290°/0·5 mm. The red sublimate (3 g.) was heated at 100° for 2 hr. with 2N-sodium hydroxide (30 c.c.) and, after acidification with 2N-sulphuric acid, tarry impurities were removed by filtration and the orange filtrate was extracted with ether for 48 hr. The ether was removed, and the residue was taken up in acetone (100 c.c.), mixed with excess of ethereal diazomethane, and after 12 hr. filtered and evaporated. The residual oil was distilled. The small fraction (Y) (0·2 g.) boiling below

150°/0·005 mm. was hydrolysed with sodium hydroxide, and the acid, isolated by continuous extraction with ether, gave the succinic acid reaction with resorcinol. The yellow viscous fraction (1·7 g.) of b. p. 204—208°/0·003 mm. yielded a colourless solid (A) when triturated with ether. The residual liquors were evaporated and the orange syrup (1·3 g.) was poured in benzene–light petroleum (b. p. 40—60°) (3 : 1; 150 c.c.) on to a charcoal column (2·5 × 14·5 cm.) and eluted (100-c.c. fractions). The preceding mixture (5 × 100 c.c.) removed a yellow oil. Benzene (fractions 6—10) removed ester A (see below). Benzene–ether (9 : 1) (fractions 11—18) removed a semi-solid material, whence fractional crystallisation from methyl alcohol afforded esters A and B. Benzene–ether (4 fractions, 3 : 1; 2 fractions, 1 : 1) removed oils. Ether and ether–acetone (9 : 1) (2 fractions each) removed nothing. Finally ether–acetone (1 : 1; fractions 29—35) removed the *iso*coumarin ester (IX; R = Me).

5 : 6 : 7-*Trimethoxy*iso*coumarin-3-carboxylic Acid* (IX; R = H).—Fractions 29—35 of the preceding separation, when combined and crystallised from methyl alcohol, gave *methyl* 5 : 6 : 7-*trimethoxy*iso*coumarin-3-carboxylate* (IX; R = Me) as needles (0·1 g.), m. p. 154—155° (Found: C, 57·2; H, 4·6. $C_{14}H_{14}O_7$ requires C, 57·2; H, 4·9%), undepressed on admixture with a synthetic specimen (see following paper). This ester (0·05 g.), refluxed for 4 hr. with 2N-sulphuric acid (4 c.c.) and acetic acid (1 c.c.), gave its *acid* (IX; R = H), needles (from alcohol), m. p. 262—264° (Found: C, 55·9; H, 4·4. $C_{13}H_{12}O_7$ requires C, 55·7; H, 4·3%), undepressed on admixture with a synthetic specimen.

The *chloride*, prepared from the acid (IX; R = H) and thionyl chloride (5 vols.), crystallised from benzene in needles, m. p. 163—164° (Found: C, 52·6; H, 3·7. $C_{13}H_{11}O_6Cl$ requires C, 52·3; H, 3·7%), and gave the *ethyl* ester (IX; R = Et), needles (from alcohol, m. p. 118° (Found: C, 58·5; H, 5·3. $C_{15}H_{16}O_7$ requires C, 58·4; H, 5·2%).

Ethyl 3 : 4-*Dihydro*-5 : 6 : 7-*trimethoxy*iso*coumarin*-3-*carboxylate*.—A solution of ethyl 5 : 6 : 7-trimethoxy*iso*coumarin-3-carboxylate (IX; R = Et) (1 g.) in glacial acetic acid (25 c.c.) was reduced at 50° in presence of 30% palladium–charcoal (0·1 g.), this requiring 48 hr. for completion. The reduced *ester* was distilled at 250° (bath)/0·1 mm. and then crystallised from alcohol in prisms, m. p. 84—85° (Found: C, 57·8; H, 5·9. $C_{15}H_{18}O_7$ requires C, 58·1; H, 5·8%), identical with a synthetic specimen described in the following paper. This ester was recovered after attempted dehydrogenation with 30% palladium–charcoal in boiling *p*-cymene.

The Optically Active Acid, $C_{16}H_{16}O_8$ (XI).—The ester (A) (0·5 g.) obtained by trituration with ether (above) was combined with fractions 6—10 (0·1 g.) and crystallised from methyl alcohol; the *methyl* ester (A) was obtained in prisms (0·5 g.), m. p. 149°, $[\alpha]_D^{20}$ +238° (*c*, 2·78 in $CHCl_3$) [Found: *M* (Rast), 345; C, 58·2; H, 5·1. $C_{17}H_{18}O_8$ requires *M*, 350; C, 58·3; H, 5·1%]. A further crop (0·05 g.), m. p. 149°, was obtained from the less soluble portions on fractionation of the combined fractions 11—18 from methyl alcohol. The *acid*, $C_{16}H_{16}O_8$ (XI), prepared by hydrolysis of methyl ester (A) by 2 hours' boiling with 2N-hydrochloric acid or methyl-alcoholic 3% potassium hydroxide, separated from hot water in rhombic prisms, m. p. 217°, $[\alpha]_D^{20}$ +221° (*c*, 1·36 in MeOH) [Found: equiv. (cold), 334, (hot), 168·5; C, 57·2; H, 4·8. $C_{16}H_{16}O_8$ requires equiv. (cold), 336, (hot), 168·5; C, 57·2; H, 4·8%]. Attempts to reduce it, to dehydrogenate it in presence of palladium or platinum catalysts, and to decarboxylate it with copper catalysts were unsuccessful. Oxidation of the acid (XI) with potassium ferricyanide (cf. *J.*, 1951, 3511) gave 3 : 4 : 5-trimethoxyphthalic acid, identified as anhydride, m. p. 144°, and *N*-methylimide, m. p. 127°. A methyl ester, m. p. 149°, identical with methyl ester (A), was prepared by the action of methyl-alcoholic hydrogen chloride or diazomethane on the acid (XI).

The *phenylhydrazone* of the methyl ester separated from methyl alcohol in hexagonal prisms, m. p. 197—198° (Found: C, 62·6; H, 5·5; N, 6·3. $C_{23}H_{24}O_7N_2$ requires C, 62·7; H, 5·5; N, 6·4%). The p-*nitrobenzyl* ester, prepared by refluxing the acid (XI) (0·1 g.) in 1 mol. of N-sodium hydroxide for 1 hr. with *p*-nitrobenzyl bromide (0·067 g.) in alcohol, crystallised from aqueous alcohol in prisms, m. p. 122—123° (Found: C, 58·4; H, 4·5; N, 2·7. $C_{23}H_{21}O_{10}N$ requires C, 58·6; H, 4·5; N, 3·0%). The methyl ester (0·27 g.) was added to methyl alcohol (5 c.c.) saturated with ammonia at 10°; after 48 hr. at room temperature, propyl alcohol (5 c.c.) was added and the solution refluxed for 2 hr., after which the solvent was removed and the *amide* crystallised from water in prisms, m. p. 232—234° (decomp.) (Found: C, 57·2; H, 5·1; N, 4·2. $C_{16}H_{17}O_7N$ requires C, 57·3; H, 5·1; N, 4·2%).

Dehydrogenation of the Acid (XI) *with Selenium Dioxide*.—A solution of the acid (XI) (0·11 g.) and selenium dioxide (0·02 g.) in water (15 c.c.) was refluxed for 4 hr. The precipitated selenium was collected, and the *acid* which separated from the filtrate on cooling crystallised from glacial acetic acid in needles (0·05 g.), m. p. 210°, $[\alpha]_D^{20}$ +52·5° (*c*, 0·45 in methanol) (Found:

C, 57·2; H, 4·4. $C_{16}H_{14}O_8$ requires C, 57·5; H, 4·2%). The *methyl* ester, prepared by diazomethane, separated from methyl alcohol in elongated plates, m. p. 147° (Found: C, 59·4; H, 5·0. $C_{18}H_{18}O_8$ requires C, 59·7; H, 5·0%).

Action of Thionyl Chloride on the Acid (XI).—After the acid (XI) had been refluxed with excess of thionyl chloride for 30 min., the excess of thionyl chloride was removed and benzene added. The *acid chloride* which separated crystallised from benzene–light petroleum (b. p. 40—60°) in plates, m. p. 204—205° (decomp.) (Found: C, 54·2; H, 3·8. $C_{16}H_{15}O_7Cl$ requires C, 54·2; H, 4·2%). It was warmed with dilute sodium hydroxide until dissolution was complete; acidification gave an *acid*, which crystallised from aqueous alcohol in long needles. m. p. 198° (decomp.) (Found: C, 54·5; H, 5·3. $C_{16}H_{16}O_8,H_2O$ requires C, 54·2; H, 5·1%). The *methyl* ester, prepared by decomposition of the acid chloride with methyl alcohol, separated from methyl alcohol in needles, m. p. 227—228°, $[\alpha]_D^{20}$ +164 (*c*, 1·07 in MeOH) (Found: C, 58·5; H, 5·4. $C_{17}H_{18}O_8$ requires C, 58·3; H, 5·1%). The *ethyl* ester, prepared similarly in ethyl alcohol, crystallised in needles, m. p. 142° (Found: C, 59·4; H, 5·7. $C_{18}H_{20}O_8$ requires C, 59·3; H, 5·5%).

The Optically Inactive Methyl Ester (*B*).—This *product*, obtained from the more soluble portions during crystallisation of the combined fractions 11—18, separated from methyl alcohol in prisms (0·07 g.), m. p. 141°, $[\alpha]_D^{20}$ 0° (*c*, 0·38 in MeOH) (Found: C, 58·2; H, 5·1. $C_{17}H_{18}O_8$ requires C, 58·3; H, 5·1%), depressed to 110—113° on admixture with methyl ester (A). The *phenylhydrazone* crystallised from acetic acid in needles, m. p. 214° (Found: C, 62·5; H, 5·5; N, 6·4. $C_{23}H_{24}O_7N_2$ requires C, 62·7; H, 5·5; N, 6·4%), and the 2 : 4-*dinitrophenylhydrazone* crystallised from the same solvent in orange needles, m. p. 233—234° (Found: C, 51·9; H, 4·0; N, 10·7. $C_{23}H_{22}O_{11}N_4$ requires C, 52·1; H, 4·2; N, 10·6%).

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