

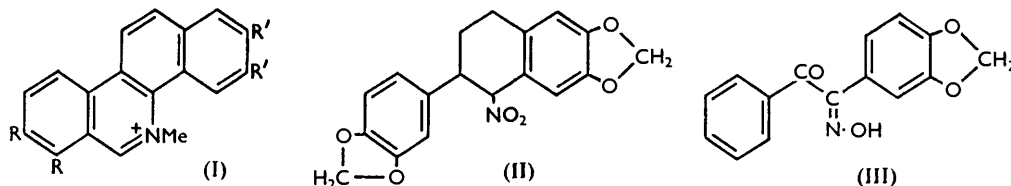
### 531. Some Synthetical Investigations in isoCoumarin Chemistry.

By J. B. JONES and A. R. PINDER.

Preliminary experiments on possible new routes to the *Chelidonium* alkaloids are described, and syntheses of some derivatives of naphtho(1' : 2' - 3 : 4)isocoumarin are outlined.

DEGRADATIVE studies of chelerythrine (I; R = OMe, R'R' = O<sub>2</sub>CH<sub>2</sub>) and sanguinarine (I; RR = R'R' = O<sub>2</sub>CH<sub>2</sub>), two of the four principal alkaloids of *Chelidonium majus*, showed that the bases were derived from 1 : 2-benzophenanthridine.<sup>1</sup> The major contribution towards the synthesis of the alkaloids has been made by Robinson and his co-workers,<sup>2</sup> who have synthesised several compounds closely related to chelerythrine. These investigations recently culminated in a total synthesis of chelerythrine chloride.<sup>3</sup>

The object of the investigations described here, which were begun before the chelerythrine synthesis was announced, was to explore possible alternative routes to these alkaloids.



Recent studies of Diels-Alder type additions between  $\omega$ -nitrostyrenes and buta-1 : 3-diene and its homologues<sup>4</sup> suggested that the compound (II), a possible intermediate in the synthesis of bases of type (I), might be formed by addition of 3 : 4-methylenedioxy- $\omega$ -nitrostyrene to 3 : 4-methylenedioxy-styrene. Model experiments with  $\omega$ -nitrostyrene and 3 : 4-methylenedioxy-styrene were, however, discouraging. This failure, under a variety of conditions, recalls that of Hudson and Robinson,<sup>5</sup> who were unable to obtain a normal adduct from maleic anhydride and 3 : 4-methylenedioxy-styrene, and is presumably explicable by the deactivating influence of the *p*-alkoxyl group on the double bond in the latter.

The observation that  $\omega$ -hydroxyiminoacetophenone and benzenediazonium chloride condense to form benzil monoxime<sup>6</sup> suggested that possible intermediates such as (III)

<sup>1</sup> Henry, "The Plant Alkaloids," Churchill, London, 1949, p. 277; Manske and Holmes, "The Alkaloids," Academic Press, New York, 1954, Vol. IV, Chapter 35.

<sup>2</sup> Richardson, Robinson, and Seijo, *J.*, 1937, 835; Bailey and Robinson, *Nature*, 1949, **164**, 402; *J.*, 1950, 1375; Bailey, Robinson, and Staunton, *Nature*, 1950, **165**, 235; *J.*, 1950, 2277.

<sup>3</sup> Bailey and Worthing, *J.*, 1956, 4535.

<sup>4</sup> Wildman and Wildman, *J. Org. Chem.*, 1952, **17**, 581; Mason and Wildman, *J. Amer. Chem. Soc.*, 1954, **76**, 6194.

<sup>5</sup> Hudson and Robinson, *J.*, 1941, 715.

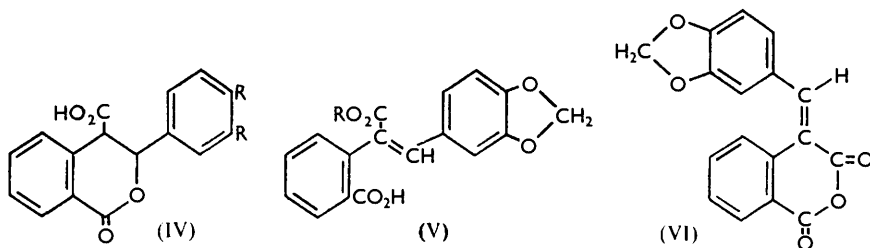
<sup>6</sup> Kanno, *J. Pharm. Soc. Japan*, 1953, **73**, 118.

were derivable by an analogous condensation, but attempts to condense  $\omega$ -hydroxyiminoacetophenone with 3 : 4-methylenedioxybenzenediazonium chloride were unsuccessful.

The reaction of *isocoumarins* with ammonia or a primary amine to give *isoquinolones*<sup>7</sup> (*isocarbotyrls*), and the conversion of other lactones into lactams under similar conditions,<sup>8</sup> are well-known transformations, and it seemed that a more profitable route to the benzophenanthridine bases might be *via* a naphtho*isocoumarin*.

Müller's observation<sup>9</sup> that the sodium enolate of homophthalic anhydride and benzaldehyde condense to form the dihydro*isocoumarin* (IV; R = H) appeared an interesting starting point. We have repeated this condensation and found the properties and infrared absorption of the product to be in agreement with this formula assigned to it by Müller. When benzaldehyde was replaced by piperonaldehyde in this condensation, the product was the analogue (IV; RR = O<sub>2</sub>CH<sub>2</sub>): and if condensation is effected with sodamide in liquid ammonia isolation of the sodium enolate and the long reaction period are obviated.

Loewenthal and Pappo<sup>10</sup> have obtained the acid (IV; R = H) by a Stobbe-type condensation between benzaldehyde and dimethyl homophthalate, the product being cyclised with hydrobromic-acetic acids. We have condensed piperonaldehyde with the same ester and obtained methyl  $\alpha$ -*o*-carboxyphenyl-3 : 4-methylenedioxybenzenecinnamate (V; R = Me), but attempts to cyclise this compound or the corresponding dicarboxylic acid (V; R = H) led to extensive decomposition, presumably because of the sensitivity of the methylenedioxy-group to acids. When the acid (V; R = H), m. p. 233°, was warmed with acetic anhydride it yielded an orange-yellow anhydride, m. p. 197°, presumably identical with the compound (m. p. 196°) obtained by Buu-Hoï<sup>11</sup> by the condensation of piperonaldehyde with homophthalic anhydride in the presence of piperidine. Inspection of molecular models shows that this compound must have the *cis*-configuration (VI);\*



in the corresponding *trans*-isomer there is considerable steric interference between the methylenedioxyphenyl group and the anhydride ring. Mild alkaline hydrolysis of the anhydride afforded an acid, m. p. 180°, isomeric with the original acid. The two acids appear to be geometrical isomers; models show that the hydrolysis of the anhydride ring removes the steric interference, both *cis*- and *trans*-forms of the acid (V; R = H) being stereochemically possible. In the ultraviolet spectrum the acid of m. p. 233° shows a principal maximum at 320  $\mu$ , and the acid of m. p. 180° a much weaker one at 315  $\mu$ . Generally, *trans*-compounds absorb at longer wavelengths and with greater intensity than their *cis*-isomers,<sup>12</sup> and on this evidence we assign the *trans*-configuration to the acid of m. p. 233° and the *cis* to the acid of m. p. 180°.

\* The prefix *cis* is used to denote that the two benzene rings are on the same side of the plane of the double bond.

<sup>7</sup> Gabriel, *Ber.*, 1885, **18**, 2433, 3470; 1886, **19**, 830, 1653.

<sup>8</sup> Meyer, *Monatsh.*, 1899, **20**, 717; Späth and Lintner, *Ber.*, 1936, **69**, 2927; Wiley *et al.*, *J. Amer. Chem. Soc.*, 1953, **75**, 4482; 1954, **76**, 625.

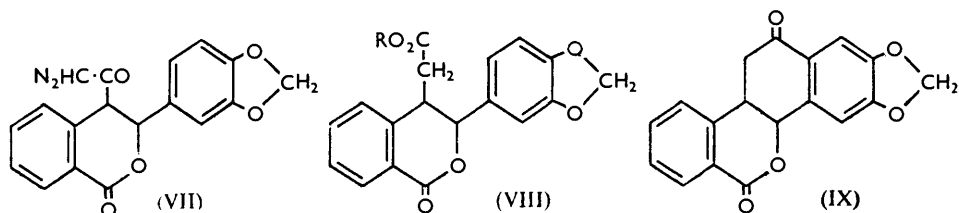
<sup>9</sup> Müller, *Annalen*, 1931, **491**, 251.

<sup>10</sup> Loewenthal and Pappo, *J.*, 1952, 4799.

<sup>11</sup> Buu-Hoï, *Compt. rend.*, 1940, **211**, 330, 563, 643.

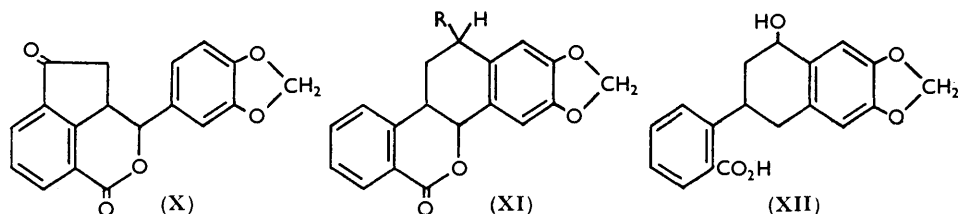
<sup>12</sup> Gillam and Stern, "An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry," Arnold, 1954, pp. 232—246; Braude, *J.*, 1949, 1902.

With thionyl chloride the lactonic acid (IV;  $RR = O_2CH_2$ ) gave the acid chloride in poor yield only, the main product being the anhydride (VI). Phosphorus pentachloride, on the other hand, afforded the chloride in good yield. With diazomethane this yielded the crystalline diazo-ketone (VII), which was smoothly converted into the homologous



methyl ester (VIII;  $R = Me$ ) by silver benzoate in methanol containing triethylamine.<sup>13</sup> Hydrolysis gave the acid (VIII;  $R = H$ ), which, in contrast to its lower homologue, yielded its chloride readily with thionyl chloride. Cyclisation of this with stannic chloride afforded the naphthoisoquinoline (IX). That the cyclisation had occurred in the expected direction (involving the reactive *para*-position of the methylenedioxybenzene ring) was proved by the presence of a strong band in the infrared absorption spectrum of the ketone at  $1664\text{ cm}^{-1}$ , characteristic of an  $\alpha\beta$ -unsaturated carbonyl group in a six-membered ring,<sup>14a</sup> thus ruling out the possible alternative structure (X). The somewhat low wave-number of this band may perhaps be accounted for by the influence of the methylenedioxy-substituent (cf. methoxyanthraquinones<sup>14b</sup>).

Attempts were made to reduce the ketone (IX) to the compound (XI;  $R = H$ ). Clemmensen's method caused extensive decomposition and the ketone could not be condensed with ethanedithiol, under the usual conditions, to form a thioketal, so that Mozingo's desulphurisation technique<sup>15</sup> could not be applied. Hydrogenation of the ketone in the presence of palladium-charcoal promoted with perchloric acid<sup>16</sup> gave an acidic product  $C_{18}H_{16}O_5$ , indicating reductive cleavage of the lactone ring. This product was not ketonic and showed ultraviolet absorption similar to that of benzoic acid,<sup>17</sup> a



hydroxyl band could not be detected in the infrared absorption curve, probably because the compound, which we formulate as (XII), is monomeric so that the alcoholic hydroxyl band is masked by a strong carboxyl band in the  $3400\text{ cm}^{-1}$  region.

Reduction of the ketone (IX) with potassium borohydride afforded the alcohol (XI;  $R = OH$ ), obtained in two modifications. Dehydrogenation of this compound resulted in the elimination of water and the formation of 6':7'-methylenedioxy-naphtho(1':2'-3:4)isocoumarin (XIII;  $R^1 = R^2 = H$ ,  $R^3R^4 = O_2CH_2$ ), unfortunately in very poor yield, the structure of the product being confirmed by its chemical properties and infrared

<sup>13</sup> Cf. Newman and Beal, *J. Amer. Chem. Soc.*, 1950, **72**, 5163.

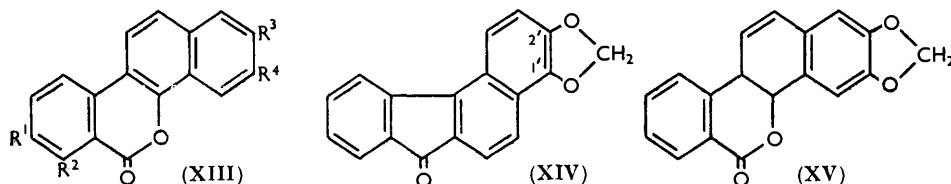
<sup>14</sup> (a) Cf. Grove and Willis, *J.*, 1951, 877; (b) Wiles and Thomas, *J.*, 1956, 4811.

<sup>15</sup> Mzingo *et al.*, *J. Amer. Chem. Soc.*, 1943, **65**, 1013, 1477.

<sup>16</sup> Cf. Rosenmund and Karg, *Ber.*, 1942, **75**, 1850; Kindler *et al.*, *ibid.*, 1943, **76**, 308; Baker and Jenkins, *J. Amer. Chem. Soc.*, 1946, **68**, 2102; Johnson and Graber, *ibid.*, 1950, **72**, 925.

<sup>17</sup> Ref. 12, p. 126.

absorption. The ultraviolet absorption curve was closely similar to that of the tetramethoxy-analogue synthesised by Bailey and Worthing.<sup>3</sup> An accompanying dehydrogenation product was a neutral compound  $C_{18}H_{10}O_3$ , which was not lactonic and showed ketonic properties. Its ultraviolet absorption curve resembled closely that of 3 : 4-benzofluorenone,<sup>18</sup> and the presence of a diaryl ketone grouping was indicated by the appearance



in the infrared spectrum of a band at  $1693\text{ cm}^{-1}$ , the position of which is probably modified by the methylenedioxy-substituent.<sup>14b,19</sup> On these grounds structure (XIV) is proposed for the compound.

Treatment of the alcohol (XI;  $R = OH$ ) with hydrogen chloride or phosphorus tribromide or pentachloride gave the anhydro-compound (XV), which showed no hydroxyl band in the infrared spectrum. Attempts to dehydrogenate this compound were equally discouraging, the same two products being obtained in very poor yield.

#### EXPERIMENTAL

Ultraviolet absorption spectra were determined on methanol solutions, and infrared spectra for Nujol mulls, unless otherwise stated.

4-Carboxy-3 : 4-dihydro-3-(3 : 4-methylenedioxyphenyl)isocoumarin (IV;  $RR = O_2CH_2$ ).—(a) Homophthalic anhydride was prepared by dehydration of homophthalic acid,<sup>20</sup> obtained by oxidation of indene.<sup>21</sup> The anhydride (4.0 g.), in the minimum quantity of warm, dry benzene, was added dropwise with swirling to an ethereal 0.13M-solution of triphenylmethylsodium (690 c.c., 1 mol.)<sup>22</sup> under nitrogen. The yellow enolate was collected, washed with ether, suspended in dry ether (50 c.c.), and shaken with a solution of piperonaldehyde (7.5 g.) in dry ether (50 c.c.) under nitrogen at room temperature for 7 days.<sup>23</sup> Water (100 c.c.) was then added and the aqueous layer separated and acidified. The liberated acid was collected and crystallised from 50% acetic acid, from which it separated in rhombic prisms of the monohydrate (1.6 g.) (Found: C, 61.9; H, 4.1.  $C_{17}H_{12}O_6 \cdot H_2O$  requires C, 61.8; H, 4.2%), which at  $100^\circ$  *in vacuo* gave the anhydrous acid, m. p.  $180^\circ$  (decomp.) (Found: C, 65.1; H, 4.0.  $C_{17}H_{12}O_6$  requires C, 65.4; H, 3.9%),  $\nu_{\max}$ . 1704 (lactone-CO), 1735 (carboxyl-CO), and  $3175\text{ cm}^{-1}$  (OH). With ethereal diazomethane the acid afforded the methyl ester, rhombic prisms (from methanol), m. p.  $145\text{--}145.5^\circ$  (Found: C, 66.2; H, 4.2.  $C_{18}H_{14}O_6$  requires C, 66.3; H, 4.3%),  $\nu_{\max}$ . 1720 (lactone-CO) and  $1730\text{ cm}^{-1}$  (ester CO) (no OH band).

(b) To liquid ammonia (600 c.c.) containing ferric nitrate (0.2 g.) sodium (2.4 g.; 1.05 atom.) was added gradually in small pieces, with stirring. When the metal had dissolved homophthalic anhydride (16.2 g., 1 mol.) in dry benzene (600 c.c.) was added dropwise, followed by piperonaldehyde (15 g.) in dry benzene (100 c.c.), with stirring throughout. Next morning water (200 c.c.) was added and the aqueous layer separated and acidified with 5N-hydrochloric acid. The liberated acid (22 g.) crystallised from 50% acetic acid as the monohydrate, which when dried at  $100^\circ$  *in vacuo* had m. p.  $180^\circ$  (decomp.) alone or mixed with the product obtained as in (a).

<sup>18</sup> Friedel and Orchin, "Ultraviolet Spectra of Aromatic Compounds," Wiley, 1951, curve 434.

<sup>19</sup> Bellamy, "The Infrared Spectra of Complex Molecules," Methuen, London, 1954, pp. 114, 119; Jones and Sandorfy in "Techniques of Organic Chemistry," Interscience Publ. Inc., New York, 1956 Vol. IX, p. 450.

<sup>20</sup> Price, Lewis, and Meister, *J. Amer. Chem. Soc.*, 1939, **61**, 2762.

<sup>21</sup> Cooney and Whitmore, *ibid.*, 1944, **66**, 1237.

<sup>22</sup> "Organic Reactions," Vol. I, p. 286.

<sup>23</sup> Cf. Müller, *Annalen*, 1931, **491**, 260.

*Methyl  $\alpha$ -o-Carboxyphenyl-3 : 4-methylenedioxybenzylidene* (V; R = Me).<sup>24</sup>—Dimethyl homophthalate<sup>25</sup> (4.2 g.) in dry methanol (25 c.c.) was added gradually to a solution of sodium methoxide prepared by dissolving sodium (0.46 g.) in dry methanol (25 c.c.). Piperonaldehyde (3.0 g.) in dry methanol (15 c.c.) was then added and the mixture refluxed on the water-bath for 3 hr. The solvent was evaporated under reduced pressure and the residual syrup taken up in water (50 c.c.) and acidified with 5*N*-hydrochloric acid. The acid (6.3 g.) was collected and crystallised from benzene, in rhombic prisms, m. p. 173.5° (Found: C, 65.5; H, 4.5; OMe, 9.0. C<sub>18</sub>H<sub>14</sub>O<sub>6</sub> requires C, 66.3; H, 4.3; OMe, 9.5%). Hydrolysis of the product (3.3 g.) by refluxing 2*N*-sodium hydroxide (30 c.c.) for 2 hr. gave, after acidification, *trans*- $\alpha$ -piperonylidenehomophthalic acid (2.8 g.), which separated from 70% acetic acid in cubes, m. p. 233° (decomp.) (Found: C, 65.3; H, 3.8. Calc. for C<sub>17</sub>H<sub>12</sub>O<sub>6</sub>: C, 65.4; H, 3.9%). Buu-Hoï<sup>11</sup> gives m. p. 235°. The acid had an infrared absorption band at 1678 cm.<sup>-1</sup> (CO) and an ultraviolet absorption max. at 320 m $\mu$  ( $\epsilon$  15,700). Attempts to cyclise both the above products to 4-carboxy-3 : 4-dihydro-3-(3 : 4-methylenedioxyphenyl)isocoumarin (IV; RR = O<sub>2</sub>CH<sub>2</sub>) by hydrobromic-acetic acids<sup>10</sup> led to extensive decomposition.

*$\alpha$ -Piperonylidenehomophthalic Anhydride* (VI).—The above dicarboxylic acid (0.3 g.) was refluxed for 30 min. with acetic anhydride (5 c.c.). The solution was evaporated to dryness *in vacuo*. The residual orange anhydride (0.17 g.) crystallised from benzene in feathery orange needles, m. p. 197° (Buu-Hoï<sup>11</sup> gives m. p. 196°) (Found: C, 69.7; H, 3.4. Calc. for C<sub>17</sub>H<sub>10</sub>O<sub>5</sub>: C, 69.4; H, 3.4%). Hydrolysis of the anhydride (0.1 g.) by refluxing 2*N*-sodium hydroxide (10 c.c.) for 30 min. gave *cis*- $\alpha$ -piperonylidenehomophthalic acid (0.1 g.), which separated from 50% acetic acid in very pale yellow needles, m. p. 180° (decomp.) (Found: C, 65.6; H, 4.25. C<sub>17</sub>H<sub>12</sub>O<sub>6</sub> requires C, 65.4; H, 3.9%),  $\lambda_{\text{max}}$ . 315 m $\mu$  ( $\epsilon$  10,300),  $\nu_{\text{max}}$ . 1685 cm.<sup>-1</sup> (CO).

*4-Chlorocarbonyl-3 : 4-dihydro-3-(3 : 4-methylenedioxyphenyl)isocoumarin*.—The dry lactonic acid (IV; RR = O<sub>2</sub>CH<sub>2</sub>) (25 g.) and phosphorus pentachloride (20.8 g.) were mixed and kept at room temperature for 8 hr. Phosphorus oxychloride was removed *in vacuo* at room temperature and the residue crystallised from benzene, from which the acid chloride separated in rhombic prisms (17.7 g.), m. p. 141—142° (Found: C, 62.1; H, 3.6. C<sub>17</sub>H<sub>11</sub>O<sub>5</sub>Cl requires C, 61.7; H, 3.3%). When warmed with methanol the product afforded the corresponding methyl ester, m. p. 141—142°, alone or mixed with the ester obtained by the action of diazomethane on the parent acid (see above). With thionyl chloride the lactonic acid afforded mainly  $\alpha$ -piperonylidenehomophthalic anhydride (see above).

*4-Diazoacetyl-3 : 4-dihydro-3-(3 : 4-methylenedioxyphenyl)isocoumarin* (VII).—The above acid chloride (17.6 g.) in dry benzene (240 c.c.) was added dropwise, with swirling, to a cooled solution of diazomethane (4.5 g.) in dry ether (160 c.c.).<sup>26</sup> After being kept overnight at 0° the crystalline *diazo-ketone* was collected (17.2 g.). A sample crystallised from dioxan-ether in rhombic prisms, m. p. 149° (decomp.) (Found: C, 64.5; H, 3.9. C<sub>18</sub>H<sub>12</sub>O<sub>5</sub>N<sub>2</sub> requires C, 64.3; H, 3.6%).

*4-Methoxycarbonylmethyl-3 : 4-dihydro-3-(3 : 4-methylenedioxyphenyl)isocoumarin* (VIII; R = Me).—Dry silver benzoate (2.5 g.) in anhydrous triethylamine (50 c.c.) was filtered and added portionwise during 30 min. to the above diazo-ketone (11.2 g.) in dioxan-methanol (1 : 1; 400 c.c.) at room temperature, with shaking.<sup>13</sup> Nitrogen was evolved and the solution darkened. A little "Norit" was added and the solution boiled for 2 min.; it was then filtered and concentrated under reduced pressure. The residual gum was purified by chromatography in benzene-light petroleum (b. p. 40—60°) on alumina, with elution with benzene. Evaporation of the eluate afforded a syrup which solidified on trituration with methanol. The ester separated from methanol in feathery needles, m. p. 116° (6.7 g.) (Found: C, 67.6, 67.4; H, 4.9, 4.8. C<sub>19</sub>H<sub>16</sub>O<sub>6</sub> requires C, 67.1; H, 4.7%).

*4-Carboxymethyl-3 : 4-dihydro-3-(3 : 4-methylenedioxyphenyl)isocoumarin* (VIII; R = H).—(a) The foregoing methyl ester (3.4 g.) was refluxed for 30 min. with a mixture of glacial acetic acid, concentrated hydrochloric acid, and water (3 : 1 : 1 by vol.; 60 c.c.). The solution was cooled, diluted, and extracted with ether. The extract was washed several times with sodium hydrogen carbonate solution, and the combined aqueous layers were acidified with 5*N*-hydrochloric acid. The solid was collected, washed with water, and crystallised from 50% acetic acid. *4-Carboxymethyl-3 : 4-dihydro-3-(3 : 4-methylenedioxyphenyl)isocoumarin*

<sup>24</sup> Cf. Loewenthal and Pappo, ref. 10; Dieckmann, *Ber.*, 1914, **47**, 1428.

<sup>25</sup> Sheehan and O'Neill, *J. Amer. Chem. Soc.*, 1950, **72**, 4614.

<sup>26</sup> *Org. Synth.*, 1935, **15**, 4.

separated in feathery needles, m. p. 172.5° (Found: C, 65.9, 66.1; H, 4.2, 4.65.  $C_{18}H_{14}O_6$  requires C, 66.3; H, 4.3%),  $\nu_{\max}$ . 1678 (probably internally hydrogen-bonded carboxyl-carbonyl group) and 1724  $cm^{-1}$  (lactone-carbonyl group).

(b) The same ester (0.6 g.) was refluxed for 2 hr. with 2N-sodium hydroxide (15 c.c.). Concentrated hydrochloric acid (5 c.c.) and glacial acetic acid (5 c.c.) were then added and the mixture refluxed for a further 30 min. The acid (0.5 g.), isolated by the same procedure as in (a), crystallised from 50% acetic acid in rhombic prisms, m. p. 163—164° (Found: C, 66.5; H, 4.4%). When a solution of this acid in 50% acetic acid was inoculated with a crystal of the acid of m. p. 172.5°, crystals of m. p. 172.5° were obtained. The infrared absorption spectra of the two acids were identical.

1' : 2' : 3' : 4'-Tetrahydro-6' : 7'-methylenedioxy-4'-oxonaphtho(1' : 2'-3 : 4)isocoumarin (IX).—The above acid (3.25 g.), purified chloroform (60 c.c.), and purified thionyl chloride (2.4 g.) were refluxed on the water-bath for 45 min. Removal of the solvent and excess of thionyl chloride *in vacuo* gave a syrup which was dissolved in chloroform (100 c.c.), cooled, and treated with stannic chloride (5.2 g.), which was added dropwise at 0°, with shaking. After being kept overnight at this temperature the complex which had separated was decomposed with 5N-hydrochloric acid, and the chloroform layer separated, washed with dilute sodium hydroxide solution and water, dried, and evaporated. The crystalline ketone remaining separated from benzene or a large volume of ethanol in feathery needles, m. p. 229° (1.9 g.) (Found: C, 69.6; H, 4.0.  $C_{18}H_{12}O_5$  requires C, 70.1; H, 3.9%),  $\nu_{\max}$ . 1502 and 1603 (aromatic ring conjugated with carbonyl group), 1664 (conjugated CO group in six-membered ring), and 1706  $cm^{-1}$  (lactone-CO). The semicarbazone crystallised from ethanol in needles, m. p. 260—261° (decomp.) (Found: C, 62.7; H, 4.3.  $C_{19}H_{15}O_5N_3$  requires C, 62.5; H, 4.1%). The 2 : 4-dinitrophenylhydrazone separated from nitrobenzene in orange needles, m. p. 305° (Found: N, 11.9.  $C_{24}H_{16}O_8N_4$  requires N, 11.5%).

1' : 2' : 3' : 4'-Tetrahydro-4'-hydroxy-6' : 7'-methylenedioxy-naphtho(1' : 2'-3 : 4)isocoumarin (XI; R = OH).—A solution of potassium borohydride (0.14 g.) in 80% dioxan (25 c.c.) was mixed with the foregoing ketone (0.62 g.) in 80% dioxan (60 c.c.). After 1 hr. the solution was acidified with dilute sulphuric acid and poured into a large volume of water. The precipitate was collected and dried (0.56 g.); 1' : 2' : 3' : 4'-tetrahydro-4'-hydroxy-6' : 7'-methylenedioxy-naphtho(1' : 2'-3 : 4)isocoumarin separated from ethanol in prismatic needles, m. p. 167° (Found: C, 69.7; H, 4.5.  $C_{18}H_{14}O_5$  requires C, 69.7; H, 4.5%),  $\nu_{\max}$ . 1703 (lactone-CO) and 3400  $cm^{-1}$  (OH group hydrogen-bonded to CO). Under certain conditions the alcohol was obtained as a modification which had m. p. 182—183° (Found: C, 70.0; H, 4.7%); the two forms were interconvertible and gave identical infrared absorption curves.

Dehydrogenation of the Alcohol (XI; R = OH).—(a) The above hydroxyisocoumarin (0.82 g.) and 30% palladised charcoal<sup>27</sup> (0.24 g.) were heated at 220° under dry nitrogen for 1 hr. Water vapour was observed to be eliminated. The mixture was cooled and thoroughly extracted with boiling chloroform, and the solution filtered. Evaporation gave a yellowish-brown solid which was purified by chromatography on alumina in benzene solution. Chloroform-elution yielded 6' : 7'-methylenedioxy-naphtho(1' : 2'-3 : 4)isocoumarin (XIII; R<sup>1</sup> = R<sup>2</sup> = H, R<sup>3</sup>R<sup>4</sup> = O<sub>2</sub>CH<sub>2</sub>) (40 mg.), which separated from dioxan in cream needles, m. p. 254—255° (Found: C, 73.9; H, 3.3.  $C_{18}H_{10}O_4$  requires C, 74.5; H, 3.45%),  $\lambda_{\max}$ . 275 ( $\epsilon$  35,000), 307 ( $\epsilon$  12,400), and 335  $m\mu$  ( $\epsilon$  8500) (in CHCl<sub>3</sub>),  $\nu_{\max}$ . 1272 and 1720  $cm^{-1}$  (lactone-CO), 1502, 1573, 1600, 1613, and 1640  $cm^{-1}$  (aromatic rings) (no OH band). The product was readily soluble in warm dilute alkali.

(b) A similar reaction with the hydroxyisocoumarin (0.26 g.) and 30% palladised charcoal (0.1 g.) at 270° for 30 min. gave, after purification by chromatography and elution with benzene, a compound which separated from dioxan in pale orange needles, m. p. 205° (40 mg.) (Found: C, 78.3; H, 3.9.  $C_{18}H_{10}O_3$  requires C, 78.8; H, 3.7%),  $\lambda_{\max}$ . 255 ( $\epsilon$  38,000), 280 ( $\epsilon$  40,000), and 351  $m\mu$  ( $\epsilon$  7800) (in CHCl<sub>3</sub>),  $\nu_{\max}$ . 1693, 1604, 1546, 1499, 1253, 954, 865, and 852  $cm^{-1}$ . This compound was insoluble in warm dilute alkali and gave a positive reaction towards Brady's reagent. It is considered to be 1' : 2'-methylenedioxy-3 : 4-benzofluorenone. Subsequent chloroform-elution of the column gave a small yield of 6' : 7'-methylenedioxy-naphtho(1' : 2'-3 : 4)isocoumarin, m. p. 254—255°, identical with that obtained as in (a).

Attempts to effect the dehydrogenation with palladised charcoal in boiling trichlorobenzene or with 5% rhodium-charcoal (Baker Platinum Co.) were unsuccessful.

<sup>27</sup> Linstead and Thomas, *J.*, 1940, 1130.

1' : 2'-Dihydro-6' : 7'-methylenedioxy-naphtho(1' : 2'-3 : 4)isocoumarin (XV).—The hydroxy-isocoumarin (XI; R = OH) (0.62 g.) in purified chloroform (100 c.c.) was cooled to 0° and a current of dry hydrogen chloride was passed into the solution for 30 min. After being washed with sodium hydrogen carbonate solution, the organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated under reduced pressure. The residual *anhydro-compound* (XV) crystallised from benzene in needles, m. p. 188° (0.5 g.) (Found: C, 73.9; H, 4.2. C<sub>18</sub>H<sub>12</sub>O<sub>4</sub> requires C, 74.0; H, 4.1%),  $\nu_{\max}$ . 1690 cm.<sup>-1</sup> (lactone-CO) (no hydroxyl band), soluble in warm dilute alkali. The same product was obtained by the action of phosphorus halides on the alcohol. On one occasion the action of hydrogen chloride afforded 4'-chloro-1' : 2' : 3' : 4'-tetrahydro-6' : 7'-methylenedioxy-naphtho(1' : 2'-3 : 4)isocoumarin (XI; R = Cl), rhombic prisms [from light petroleum (b. p. 40—60°)], m. p. 125—126° (decomp.) (Found: C, 65.8; H, 3.7. C<sub>18</sub>H<sub>13</sub>O<sub>4</sub>Cl requires C, 65.8; H, 4.0%), having an infrared absorption for lactone-CO at 1715 cm.<sup>-1</sup> but no hydroxyl band.

Dehydrogenation of the compound (XV) (0.4 g.) by 30% palladised charcoal (0.1 g.) at 220° for 45 min. under nitrogen gave, as major product (25 mg.), the compound of m. p. 205° obtained by dehydrogenation of the hydroxyisocoumarin (XI; R = OH), together with a trace of compound (XIII; R<sup>1</sup> = R<sup>2</sup> = H, R<sup>3</sup>R<sup>4</sup> = O<sub>2</sub>CH<sub>2</sub>).

*Catalytic Hydrogenation of 1' : 2' : 3' : 4'-Tetrahydro-6' : 7'-methylenedioxy-4'-oxonaphtho(1' : 2'-3 : 4)isocoumarin (IX).*—The ketone (0.1 g.) in glacial acetic acid (15 c.c.) containing 60% perchloric acid (0.2 c.c.) was shaken in hydrogen with 5% palladised charcoal<sup>28</sup> for 5 hr.<sup>16</sup> (absorption 2 mol.). The filtered solution was poured into ice-water, and the product collected and crystallised from 50% acetic acid, from which it separated in needles, m. p. 163—164° (Found: C, 70.7; H, 4.8. C<sub>18</sub>H<sub>16</sub>O<sub>5</sub> requires C, 69.3; H, 5.1%),  $\lambda_{\max}$ . 232 ( $\epsilon$  16,900), 276 ( $\epsilon$  5530), 295 ( $\epsilon$  4480), and 318 m $\mu$  ( $\epsilon$  3900),  $\nu_{\max}$ . 3400 cm.<sup>-1</sup> (intense; CO<sub>2</sub>H). The compound dissolved with effervescence in sodium hydrogen carbonate solution; it is formulated as 3-o-carboxyphenyl-1 : 2 : 3 : 4-tetrahydro-6 : 7-methylenedioxy-1-naphthol (XII).

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DEPARTMENT OF CHEMISTRY,  
UNIVERSITY COLLEGE, CARDIFF.

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<sup>28</sup> *Org. Synth.*, 1946, 26, 78.