

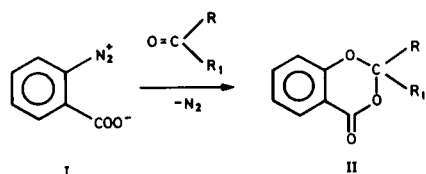
## Isocoumarin Tricyclic Derivatives from Benzenediazonium Salts

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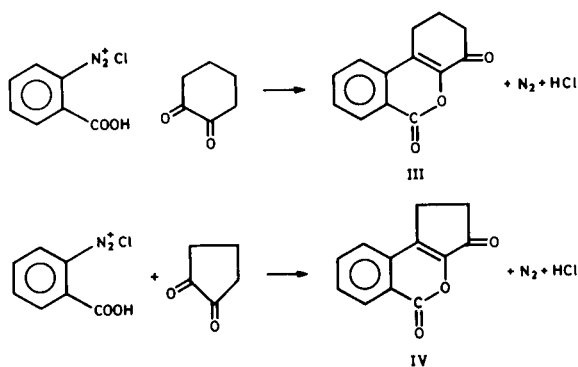
In the course of our studies on the reactions of benzenediazonium carboxylate (I) with carbonyl compounds (1,2) we had observed a nucleophilic attack of the carbonyl oxygen on the aromatic carbon (1) leading to the formation of benzodioxanones, according to the following scheme:



Analogous additions have also been obtained with thio-benzophenone (3) and phenylisocyanide (4). These reactions are likely to involve the intermediacy of carbonium ions (as ion pairs), whereas aryne-type reactions occur with  $\alpha,\beta$ -unsaturated aldehydes (5,6).

We now wish to report a new synthesis of isocoumarin tricyclic derivatives which involves a nucleophilic attack of the carbon atom of a keto-enolic system to the aromatic carbon.

Tricyclic lactone derivatives of isocoumarin (III and IV) are obtained from cyclohexane-1,2-dione or cyclopentane-1,2-dione, according to the equations:



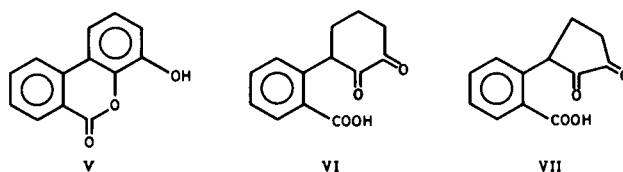
Substituents like 4-chloro or 4-nitro may be present on the diazonium salt. All the compounds obtained had not been described previously.

The reaction was carried out at atmospheric pressure and at a temperature of about 40° by simply dissolving the

diketone in the aqueous solution resulting from the diazotization of anthranilic acid.

Cyclohexane-1,3-dione gave cyclohexane-1,2,3-trione 2-*o*-carboxyphenylhydrazone, which was the expected product from the reaction of diazonium salts with methylene active compounds.

Compound III was converted to V (4-hydroxy-6*H*-dibenzo[*b,d*]pyran-6-one) by dehydrogenation with Pd/C as catalyst. Compounds III and IV were soluble in 10% sodium hydroxide giving rise to the sodium salts of acids VI and VII.



Acid VI was not isolated because acidification of the corresponding Na-salt gives the lactone again. On the contrary, VII is stable as the free acid. It also was cyclized to the original lactone. The acid is mainly under the enolic form as shown by hydroxyl absorption in the infrared and by the fact that only four aliphatic protons are revealed by nmr.

We were unable to find products corresponding to *O*-attack of the  $\alpha$ -diketones on the aromatic carbon.

The course of the reaction can be explained by a nucleophilic attack of the enolic carbon of the cyclic diones on the aromatic carbon. Phenols are known to react with the diazonium salts of anthranilic acid to give 6*H*-dibenzo[*b,d*]pyran-6-ones (7,8) but no reaction of ketoenolic systems has been described so far.

## EXPERIMENTAL (10)

1,2,3,4-Tetrahydro-6*H*-dibenzo[*b,d*]pyran-4,6-dione (III).

Anthranilic acid (2.4 g., 0.0175 mole) dissolved in 3.6 ml. of water and 3.6 ml. of concentrated hydrochloric acid was diazotized at 0° with 1.26 g. (0.0182 mole) of sodium nitrite dissolved in 5 ml. of water by the usual procedure.

Cyclohexane-1,2-dione (5 g., 0.0463 mole) was added to the aqueous solution of the diazonium salt in a 100 ml. round-bottomed

flask. The solution was stirred at 40-45° for 8 hours, then water was added and the solution was extracted with chloroform. Chloroform and cyclohexane-1,2-dione were recovered by distillation under reduced pressure. On adding diethyl ether to the distillation residue, 1.65 g. (0.0077 mole) of product (yield 44%) separated as yellowish solid. The compound was crystallized from methanol, m.p. 247-249° (10); ir (chloroform) 1740 ( $\delta$ -lactone) and 1690  $\text{cm}^{-1}$  ( $\alpha,\beta$ -unsaturated cyclohexanone); nmr (trifluoroacetic acid) 1.5-2.5  $\tau$  (m, 4H, aromatic), 6.6-7.3  $\tau$  (m, 4H,  $\text{CH}_2\text{CO}$ ,  $\text{CH}_2\text{C}=\text{C}$ ), 7.3-7.9  $\tau$  (m, 2H,  $\text{CH}_2$ );  $M^+$  = 214.

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{10}\text{O}_3$ : C, 72.89; H, 4.71. Found: C, 72.60; H, 4.90.

1,2-Dihydro-3*H*,5*H*-cyclopenta[*b*]benzo[*d*]pyran-3,5-dione (IV).

Under the same conditions described before, 5 g. (0.052 mole) of cyclopentane-1,2-dione were caused to react with the diazonium salt of anthranilic acid (2.4 g., 0.0175 mole). A yellowish solid product (1.3 g., 0.0065 mole) was obtained (yield: 37%) m.p. 226-227° from methanol; ir (chloroform) 1743 ( $\delta$ -lactone) and 1720  $\text{cm}^{-1}$  ( $\alpha,\beta$ -unsaturated cyclopentanone); nmr (trifluoroacetic acid) 1.3-2.3  $\tau$  (m, 4H, aromatic), 6.5-7  $\tau$  (m, 4H,  $\text{CH}_2\text{CH}_2$ );  $M^+$  = 200.

*Anal.* Calcd. for  $\text{C}_{12}\text{H}_8\text{O}_3$ : C, 71.99; H, 4.03. Found: C, 72.32; H, 3.92.

Chloro-1,2-dihydro-3*H*,5*H*-cyclopenta[*b*]benzo[*d*]pyran-3,5-dione (IV, 8-chloro).

A cold solution of 3 g. (0.0174 mole) of 4-chloroanthranilic acid in 30 ml. of acetic acid was stirred into 1.26 g. (0.0182 mole) of sodium nitrite dissolved in 6 ml. of concentrated sulfuric acid at 0° and the mixture kept at this temperature until diazotization was complete (10-30 minutes). Diethyl ether was stirred gradually into the mixture. Diazonium sulphate separated. Under the same conditions described before, 5 g. (0.052 mole) of cyclopentane-1,2-dione were reacted with the diazonium sulphate dissolved in 5 ml. of water and 1.5 ml. of concentrated hydrochloric acid. A solid product (1.3 g., 0.0055 mole) was obtained (yield 31%), m.p. 203-205° (from methanol); ir (chloroform) 1749 and 1720  $\text{cm}^{-1}$ ; nmr (trifluoroacetic acid) 1.4-1.7  $\tau$  (m, 1H,  $\text{CH}-\text{Cl}$ ), 1.95-2.3  $\tau$  (m, 2H, aromatic), 6.5-7.5  $\tau$  (m, 4H,  $\text{CH}_2\text{CH}_2$ ).

*Anal.* Calcd. for  $\text{C}_{12}\text{H}_7\text{ClO}_3$ : C, 61.42; H, 3.00; Cl, 14.95. Found: C, 61.26; H, 3.16; Cl, 14.82.

9-Nitro-1,2,3,4-tetrahydro-6*H*-dibenzo[*b,d*]pyran-4,6-dione (III, 9-nitro).

A cold solution of 3.18 g. (0.0174 mole) of 4-nitroanthranilic acid in 15 ml. of concentrated sulfuric acid was stirred into 1.26 g. (0.0182 mole) of sodium nitrite dissolved in 6 ml. of concentrated sulfuric acid and 30 ml. of acetic acid at 0° and the mixture kept at this temperature until diazotization was complete. Diethyl ether was added to the mixture. Diazonium sulphate separated. Under the same conditions described before, 5 g. (0.0463 mole) of cyclohexane-1,2-dione were reacted with the diazonium sulphate, dissolved in 5 ml. of water and 1.5 ml. of concentrated hydrochloric acid. A solid golden product (1 g., 0.0038 mole) was obtained. It was crystallized from methanol, m.p. 249-251° dec.; ir (chloroform) 1697 and 1747  $\text{cm}^{-1}$ .

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_9\text{NO}_5$ : C, 60.23; H, 3.47; N, 5.40. Found: C, 59.82; H, 3.75; N, 5.80.

4-Hydroxy-6*H*-dibenzo[*b,d*]pyran-6-one (V).

Compound III (0.41 g.) dissolved in 3 ml. of mesitylene were refluxed with 0.2 g. of 5% palladised charcoal in a slow stream of

dry carbon dioxide for 7 hours. After extraction with chloroform and filtration from the catalyst, evaporation of the solvent gave 0.3 g. of a white solid. It was crystallized from methanol, m.p. 181-182° (lit. 180-181° (9)).

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_8\text{O}_3$ : C, 73.58; H, 3.77. Found: C, 73.85; H, 3.84.

Treatment of V with diazomethane gave the corresponding methyl ether, m.p. 168-169° (lit. 168-169° (9)).

3-(*o*-Carboxyphenyl)cyclopentane-1,2-dione (VII).

Compound IV (0.3 g.) in 6 ml. of 10% sodium hydroxide was kept at room temperature for 20 minutes. The solution was washed with chloroform. On acidification with hydrogen chloride, 0.15 g. of a solid separated. The latter was crystallized from acetone. It cyclized to the original lactone simply by heating above 200°; ir (nujol) 3185 (OH), 1700 (COOH) and 1679 (CO)  $\text{cm}^{-1}$ ; nmr (trifluoroacetic acid) 1.4-2.4  $\tau$  (m, 4H, aromatic), 6.5-7.1  $\tau$  (m, 4H,  $\text{CH}_2\text{CH}_2$ );  $M^+$  = 218.

*Anal.* Calcd. for  $\text{C}_{12}\text{H}_{10}\text{O}_4$ : C, 66.05; H, 4.58. Found: C, 66.10; H, 4.91.

Cyclohexane-1,2,3-trione 2-*o*-Carboxyphenylhydrazone.

Under the same conditions described before, cyclohexane-1,3-dione (5 g., 0.0463 mole) and 5 ml. of water were allowed to react with the diazonium salt of anthranilic acid (2.4 g., 0.0175 mole). After extraction with chloroform, a yellow solid product (2.2 g., 0.0084 mole) was obtained by evaporation of most of the solvent and addition of diethyl ether. This compound was crystallized from water, m.p. 185-190° dec.; ir (chloroform) 1718-1684, 1636, 1603  $\text{cm}^{-1}$ ; nmr (hexadeuterodimethylsulfoxide) 2-3  $\tau$  (m, 4H, aromatic); 7-7.7  $\tau$  (m, 4H,  $\text{CH}_2\text{CH}_2$ ); 7.7-8.4  $\tau$  (m, 2H,  $\text{CH}_2$ ).

*Anal.* Calcd. for  $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}_4$ : C, 60.00; H, 4.61; N, 10.76. Found: C, 59.70; H, 4.64; N, 10.35.

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