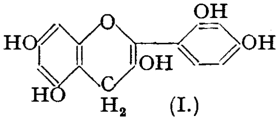
336. *Experiments on the Synthesis of Cyanomaclurin.*

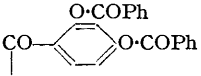
By Eric L. Fonseka.

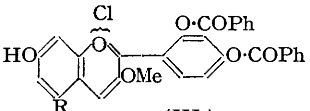
ω-Methoxy-2 : 4-dibenzoylresacetophenone (II, R = H) does not undergo the Mannich reaction, thereby excluding a proposed synthesis of the cyanomaclurin nucleus from (I, R = $CH_2 \cdot NEt_2$) and phloroglucinol. Catalytic reduction of the *flavylium* salt (III, R = H) apparently to the *flaven* (IV, R = H), indicated an alternative route, but the hydrogenation product of O-5 : 2′ : *4′-tribenzoyl-*O*-3-methylmorinidin chloride* (III, R = O·COPh), which resembled cyanomaclurin in its colour reactions, could not be recrystallised.

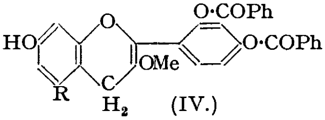
In the course of experiments on the synthesis of cyanomaclurin (I) (see also Bhalla and Rây, *J.*, 1933, 288; Mitter and Saha, *J. Indian Chem. Soc.*, **1934, 11**, 257; Mitter and Maitra, *ibid.*, **1936, 13**, 236), attempts have been made to prepare a Mannich base, *e.g.* (II, R = $CH_2 \cdot NEt_2$), which, on condensation with phloroglucinol, would be expected to give a cyanomaclurin derivative. Despite the use of a wide variety of conditions, ω-methoxy-2 : 4-dibenzoylresacetophenone (II, R = H) failed, however, to undergo the Mannich reaction.

An alternative route was therefore examined, depending on the catalytic reduction of an appropriate flavylium salt. In order to explore the method, experiments were first carried out with *7-hydroxy-2′ : 4′-dibenzoyloxy-3-methoxyflavylium chloride* (III, R = H), which was prepared from β-resorcylaldehyde, ω-methoxy-2 : 4-dibenzoylresacetophenone (II, R = H), and hydrogen chloride in ethyl acetate solution. Reduction in acetic acid in presence of Willstätter's platinum catalyst gave a product analysing as a *sesquihydrate* of the flaven (IV, R = H), and showing with alkali and with concentrated sulphuric acid the colour reactions associated with the cyanomaclurin nucleus.


(I.)


(II.)


(III.)


(IV.)

Similarly, the condensation of 2-benzoylphloroglucinaldehyde with (II, R = H) gave the well-defined O-5 : 2′ : *4′-tribenzoyl-*O*-3-methylmorinidin chloride* (III, R = O·COPh), which also absorbed two mols. of hydrogen on catalytic reduction. The crude substance likewise exhibited the colour reactions of cyanomaclurin, but all attempts to recrystallise the product for analysis were unsuccessful.

Experimental.

ω-Methoxy-2 : 4-dibenzoylresacetophenone (II, R = H).—Recrystallised ω-methoxyresacetophenone (Slater and Stephen, *J.*, 1920, 312) (13·2 g.) was dissolved in pyridine (65 c.c., redistilled over potassium hydroxide) and the solution cooled in ice while pure benzoyl choride (24·5 g.) was added with vigorous stirring during 20 minutes. Stirring was continued for ½ hour longer, by which time the smell of benzoyl chloride had practically disappeared, and the mixture left over-night. It was then poured on a mixture of crushed ice and dilute sulphuric acid, with stirring all the time; a lemon-yellow oil separated, which gradually grew more viscous and finally solidified. The solid was collected, and washed first with cold diluted sulphuric acid and then with water. Recrystallised twice from alcohol, the *dibenzoate* (25 g.) separated in flat needles, m. p. 74—75°, which gave no reaction with ferric chloride (Found, after drying over calcium chloride in a vacuum desiccator: C, 70·8; H, 4·5. $C_{23}H_{18}O_6$ requires C, 70·8; H, 4·6%).

7-*Hydroxy*-2′ : 4′-*dibenzoyloxy*-3-*methoxyflavylium Chloride* (III, R = H).—Well-dried ω-methoxy-2 : 4-dibenzoylresacetophenone (1·18 g.) was dissolved in dry ethyl acetate (30 c.c.). Resorcylaldehyde (0·63 g., dried in a vacuum over sulphuric acid) was added and the mixture warmed to complete solution. The clear liquid was cooled in ice and saturated with dry hydrogen chloride for 2 hours, care being taken to prevent access of moisture. A deep orange-red solution was obtained which was left in a tightly corked flask in the ice chest for 2 days. The *flavylium* salt separated as a red solid which crystallised from hot glacial acetic acid in flat, rectangular, orange prisms (Found, in air-dried substance: C, 62·1; H, 4·4; Cl, 6·2; OMe, 5·4. $C_{30}H_{21}O_7Cl,3H_2O$ requires C, 61·8; H, 4·6; Cl, 6·1; OMe, 5·3%).

7-*Hydroxy*-2′ : 4′-*dibenzoyloxy*-3-*methoxyflaven* (IV, R = H).—The flavylium salt (1 g.) dissolved in glacial acetic acid (160 c.c.) was placed in a hydrogenation flask with the platinum catalyst (0·1 g.). The absorption of hydrogen, which was fairly rapid up to 35 c.c., slowed down considerably and after 24 hours reached 45 c.c. (2H requires 36 c.c.), while the deep orange-red solution turned light brown. The reduced solution was diluted with a large quantity of ether and the ethereal extract, after being washed with ice water, sodium bicarbonate solution, and then again with ice water, was dried ($CaCl_2$) and the ether removed under reduced pressure at room temperature. A faintly pink solid was obtained which, after repeated precipitations with dry petrol from an ethereal solution, was crystallised from a mixture of these two solvents. The crystals were faintly yellow, and on treatment with sodium hydroxide in the cold gave a blue dichroic solution which turned green on standing. With concentrated sulphuric acid, a claret-red solution was obtained (Found, in substance dried in a vacuum over calcium chloride: C, 69·0; H, 4·6. $C_{30}H_{22}O_7,1·5H_2O$ requires C, 69·2; H, 4·7%).

O-5 : 2′ : 4′-*Tribenzoyl*-O-3-*methylmorinidin Chloride* (III, R = O·COPh).—Pure dry ω-methoxy-2 : 4-dibenzoylresacetophenone (5 g.) was dissolved in dry ethyl acetate (100 c.c.), and 2-benzoylphloroglucinaldehyde (3·2 g.) added. The mixture was warmed to ensure complete solution and filtered. The clear solution, cooled in ice, was saturated with dry hydrogen chloride for 3 hours. A small quantity of the sparingly soluble benzoylphloroglucinaldehyde separated and was removed. The clear deep red solution was left in the ice chest for 3 days, but no flavylium salt separated. It was then poured into dry ether, and the solid which separated was collected and washed with dry ether. The *salt* was deep red with a green reflex; unlike the resorcinol analogue it was readily soluble in glacial acetic acid. It was crystallised from methyl cyanide, separating in flat orange rectangular plates (Found, in substance dried over sulphuric acid: C, 66·6; H, 3·82; Cl, 5·1. $C_{37}H_{25}O_9Cl,H_2O$ requires C, 66·6; H, 4·05; Cl, 5·3%).

The flavylium salt (1 g.) was dissolved in glacial acetic acid (60 c.c.), Willstätter's platinum catalyst (0·1 g.) added, and the solution shaken with hydrogen. The quantity of hydrogen taken up was 34 c.c. (2H requires 34 c.c.). The solution changed in colour from dark orange-red to light brownish-red which darkened considerably in contact with air. It was quickly filtered into ice–water, and the faintly pink solid collected, washed with water, and dried in a vacuum over calcium chloride. In dilute sodium hydroxide solution a faint green colour was observed, which on heating became bright blue, while concentrated sulphuric acid dissolved it to yield a crimson solution.

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