SYNTHESIS OF 2,3,3a,8a-TETRAHYDROFURO[2,3-b] BENZOFURAN-2-ONE FROM COUMARIN

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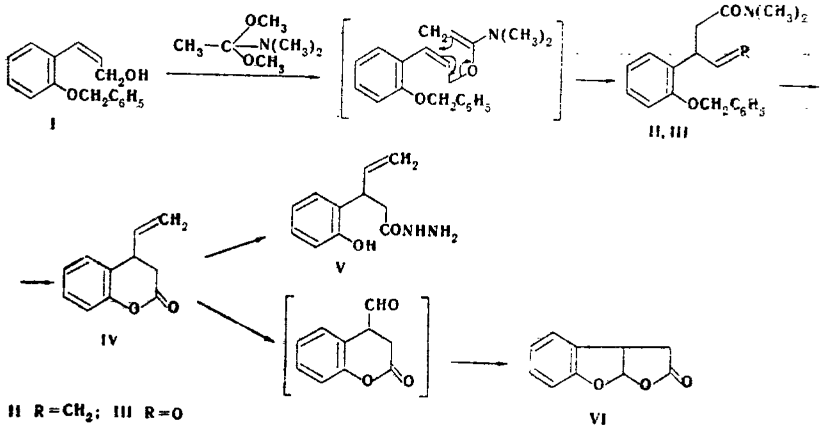
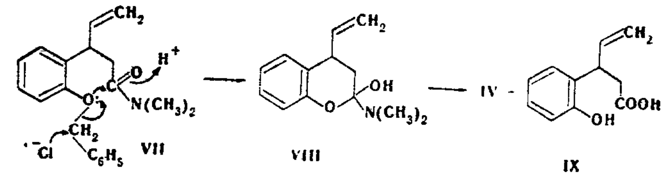
4-Vinyl-3,4-dihydrocoumarin, which is obtained in two steps from 3-(2-benzyloxyphenyl)allyl alcohol, was converted to 2,2,3a,8a-tetrahydrofuro[2,3-b]benzofuran-2-one by oxidation and rearrangement.

The three-ring 3a,8a-dihydrofuro[2,3-b]benzofuran system is the basis of natural physiologically active compounds, of which the toxins of lower fungi – aflatoxin B_1 and sterigmatocystin [1] – are the most well-known compounds. Several methods for the synthesis of the indicated heterocyclic system have been described [2-4]. In the present paper we propose yet another approach to the synthesis of a simple representative of this three-ring system – 2,3,3a,8a-tetrahydrofuro[2,3-b]benzofuran-2-one (VI).





Allyl alcohol I, which is readily obtained from coumarin, underwent Claisen rearrangement [5] on heating with dimethylacetamide dimethylacetal to give unsaturated amide II. Dilute hydrochloric acid in warm aqueous dioxane readily saponified amide II with simultaneous splitting out of a benzyl group in the form of benzyl chloride. A mixture of lactone IV and the corresponding phenolic acid IX was formed as a result of these transformations, according to IR spectroscopic and thin-layer chromatography (TLC) data. Because of the ease of lactonization of this phenolic acid, we were unable to isolate it. The mixture obtained from the reaction was treated with phosphorus oxychloride in pyridine to complete the lactonization. Lactone IV was readily opened by the action of hydrazine hydrate in the cold to give hydrazide V, which was also used for the characterization of the vitreous high-boiling IV. Allyl alcohol I is also a viscous high-boiling vitreous substance, which was characterized in the form of the dinitrobenzoyl derivative. Unstable aldehyde III was characterized in the form of the dinitrophenylhydrazone. Oxidation of dihydrocoumarin IV with iodic acid in the presence of a catalytic

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amount of osmium tetroxide and subsequent heating in acetic acid to bring about rearrangement of the formyllactone [3] gave desired product VI.

The astonishing ease of the II→IX transformations is most likely explained by anchimeric assistance [6] of the benzyloxy and carboxamide groups, as shown by formulas VII and VIII in the above scheme. This should also explain the inertness of II during attempts to reduce the amide function with lithium diethoxyaluminum hydride by the method in [7]. In this case the shielding of the carbonyl carbon atom by the free electron pair of the benzyloxy group hinders attack by the hydride ion.

In an attempt to change the order of the steps, we oxidized II to formylamide III, and subjected the latter to debenzylation by hydrogenation on palladinized carbon and by means of boron tribromide. However, we did not observe the formation of VI, and no other substances whatsoever were identified.

EXPERIMENTAL

All of the melting points (which were not corrected) were determined with a Kofler apparatus. The spectral data were obtained with UR-10, Specord UV-dis, and RS-60 spectrometers. The purity of the noncrystalline substances was monitored by TLC on Silufol in benzene–ether systems with various component ratios.

3-(2-Benzyloxyphenyl)-2-propenol (I). A 6.05-g (40 mmole) sample of 3-(2-hydroxyphenyl)-2-propenol [8] was benzylated with 7.67 g (45 mmole) of benzyl bromide in dimethylformamide (DMF) in the presence of anhydrous potassium carbonate at 20° for 24 h. Workup gave a viscous substance, which was fractionated at a bath temperature of 150-165° and a pressure of 0.04 mm to give a product with n_D^{25} 1.6026 in 70% yield. The dinitrobenzoate had mp 94-96° (from methanol). Found: C 63.6; H 4.3; N 6.3%. $C_{23}H_{18}N_2O_7$. Calculated: C 63.6; H 4.1; N 6.5%.

3-(2-Benzyloxyphenyl)-4-pentene-N,N-dimethylcarboxamide (II). A mixture of 5.68 g (24 mmole) of I, 4.3 g (35 mmole) of DMF dimethylacetal, and 56 ml of anhydrous diglyme was heated at 150° for 2 h, after which it was diluted with water and extracted with ether. The extract was dried, the solvent was evaporated, and the residue was chromatographed on 300 g of silica gel with elution by benzene–ether (4 : 1) to give 5.9 g (80%) of II with n_D^{20} 1.5720. IR spectrum, cm^{-1}: 1650 (C=C, CO). PMR spectrum: (CCl_4), δ, ppm: 2.40 d (J=6.5 Hz, 2H, CH_2), 2.62 s (6H, CH_3), 4.14 q (J=6 Hz, CH), 4.62 m (2H, $=CH_2$), 4.82 s (2H, benzyl CH_2), 5.91 m (CH), and 7.5 m (aromatic). Found: C 77.2; H 7.5; N 4.8%. $C_{20}H_{23}NO_2$. Calculated: C 77.7; H 7.4: N 4.5%.

3-(2-Benzyloxyphenyl)-3-formylpropane-N,N-dimethylcarboxamide (III). A total of 25 ml of 1% aqueous OsO_4 solution was added in an argon atmosphere to 3.96 g (12.8 mmole) of II in 125 ml of purified tetrahydrofuran (THF), after which the mixture was stirred at room temperature for 30 min. It was then cooled with ice and mixed with 6 g (26.4 mmole) of periodic acid dissolved in 25 ml of water, and the mixture was allowed to stand at 20-25° for 2.5 h. It was then neutralized with sodium bicarbonate solution and extracted with ether. The extract was dried, the solvent was removed, and the residual dark mass was chromatographed on 160 g of silica gel with benzene–ether (4 : 1) to give 2.97 g (73%) of III as an unstable oil. The dinitrophenylhydrazone had mp 140-142° (from benzene). Found: C 61.3; H 5.2; N 14.2%. $C_{25}H_{25}N_5O_6$. Calculated: C 61.1; H 5.1: N 14.3%.

4-Vinyl-3,4-dihydrocoumarin (IV). A 21.7-g sample of II was dissolved in 217 ml of a mixture of concentrated hydrochloric acid and dioxane (1 : 1), and the solution was heated and stirred on a boiling-water bath for 1 h. It was then cooled and diluted with water, and the mixture of IV and IX was extracted with ether. The extract was dried with anhydrous sodium sulfate and evaporated to dryness, and the residue was dissolved in 135 ml of pyridine. The pyridine solution was cooled and mixed, with stirring, with 7.5 g of phosphorus oxychloride, after which the mixture was allowed to stand at room temperature for 1 h. It was then diluted with water and extracted. The solvent and benzyl chloride were evaporated from the extract to give an oil. which was fractionated to give 4.9 g (40%) of IV as a colorless liquid that was distillable at a bath temperature of 138-140° at 0.1 mm. IR spectrum, cm^{-1}: 1645 (C=C) and 1770 (C=O). PMR spectrum (CCl_4), δ, ppm: 2.68 d (J=6.5 Hz, 2H, CH_2), 3.66 m (CH), 4.83-5.03 m (2H, $=CH_2$), 5.76 m (CH), and 7.1 m (aromatic). The hydrazide of V had mp 100-102° (from benzene). IR spectrum, cm^{-1}: 3260 (NH_2), 3160 (OH), 1640 (CO), and 1615 (C=C). Found: C 64.3; H 6.6; N 13.7%. $C_{11}H_{14}N_2O_2$. Calculated: C 64.1; H 6.8; N 13.6%.

2,3,3a,8a-Tetrahydrofuro[2,3-b]benzofuran-2-one (VI). A 35.4-ml sample of a 1% aqueous solution of osmium tetroxide was added with stirring in a nitrogen atmosphere to 3.16 g (18.2 mmole) of IV in 150 ml of purified THF, after which it was allowed to stand for 10 min. It was then mixed with a solution of 8.70 g (45.5 mmole) of periodic acid in 72.5 ml of water, and the mixture was allowed to stir for 3 h. It was then poured into water, and the mixture was extracted with ether. The ether extract was evaporated, the residual oil was dissolved in 41 ml of glacial acetic acid, and the solution was refluxed for 0.5 h. It was then diluted with water and extracted with ether. The extract was washed with sodium carbonate, dried, and evaporated, and the solid residue was recrystallized from alcohol to give VI, with mp 124-126°, in 68% yield. The IR, UV, and PMR spectra were in agreement with the spectra presented in [3].

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