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Substituted γ-Lactones XVII (1). Synthesis of 3,4-Dihydrocoumarins by Hydrogenation of α-(2-Hydroxybenzylidene)-γ-lactones.

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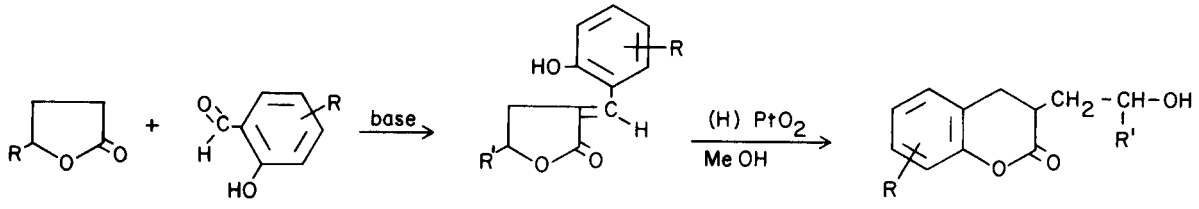
3,4-Dihydrocoumarins have been described from time to time in the literature. Their synthesis was accomplished either by catalytic reduction of coumarins (2), reduction of coumarins with Na-Hg (3) or cyclization of $R_1R_2C=CR_3CO_2Ar$ and $\phi CH=CH-CO_2Ar$ type compounds with $AlCl_3$ in CS_2 (4). The idea to cyclize β-(*o*-hydroxyphenyl)propionic acid recurs, starting with various precursors. Thus, the literature covers the cyclization of β-(2-methoxy-5-bromophenyl)propionic acid under Friedel-Crafts conditions (5) and the cyclization of 2-hydroxyphenylsuccinic acid in a high boiling solvent with phosphorus pentoxide yielding 4-substituted-3,4-dihydrocoumarins (6). Any phenol treated with an ester of the type $R_1R_2C=CR_3CO_2Me$ produces dihydrocoumarins (7) in the presence of acid catalysts. A 3,4-dihydrocoumarin is also found as a side product during the addition of vinylidene cyanide to *p*-chloroanisole and by refluxing the reaction product, 2-methoxy-5-chlorobenzylmalonitrile, with 48% HBr (8). Similarly, the δ-lactone of β-(*o*-hydroxyphenyl)propionic acid is obtained as a minor product by cyanoethylation of phenol in the presence of anhydrous aluminum chloride and dry hydrogen chloride (9). In addition, the hydrogenation of coumarilic acid yields β-(*o*-hydroxyphenyl)propionic acid which is cyclized to the δ-lactone (10). The patent literature describes the synthesis of 3,4-dihydrocoumarins from *o*-allylphenols (11) and the formation of 3-substituted-3,4-dihydrocoumarins starting with N-acetyl-4-hydroxybenz[c,d]indoline (12).

We recently described the synthesis of α-(oxo-1,2,3,4-tetrahydroquinolines (dihydrocarbostyrils) starting with substituted α-(2-aminobenzylidene)-γ-butyrolactones (13). Analogously, one should expect to obtain 3-substituted 3,4-dihydrocoumarins if one performs this reaction with condensation products of *o*-hydroxybenzaldehydes and γ-butyrolactones and subsequently hydrogenates the formed 2-(*o*-hydroxybenzylidene)-γ-butyrolactones.

As expected, the reaction went according to the above scheme. Several, so far unknown, 3-substituted-3,4-dihydrocoumarins were obtained. The structures of the 3,4-dihydrocoumarins reported here were further confirmed through IR- and UV- spectroscopy. All compounds of type II showed in the IR-spectrum an alcoholic OH-absorption between 3333-3445 cm^{-1}. The carbonyl group of the 3,4-dihydrocoumarins absorbed between 1770-1779 cm^{-1}. This finding agreed with the observation that γ, δ-unsaturated δ-lactones have a carbonyl absorption which is shifted unusually far towards higher frequencies (14). The ferric chloride color test for phenolic-groups was negative for all synthesized type II compounds, while all type I compounds showed a positive test with this reagent. As expected, the UV-spectra of the type II compounds did not exhibit an absorption maximum above 300 mμ, as is characteristic for coumarins (15). This reaction seems to be a general one and gives access to this type of compound from readily available starting material (16).



I II

R' = CH_3 and H R = various substituents

EXPERIMENTAL

Melting points are uncorrected. Microanalyses by A. Bernhardt, Mikroanalytisches Laboratorium im Max-Planck-Institut, Mühlheim/Ruhr, Germany.

Condensations.

The condensations were generally run as follows: the aldehyde (0.1 mole) and butyrolactone (0.2 mole) were dissolved in 100-150 ml. of benzene. Sodium methoxide (0.25 mole) was gradually added under cooling with ice salt bath. After stirring for a three-hour period, the solution was refluxed for an additional hour. The reaction mixtures were then decomposed with 10% sulfuric acid, and stirred continually for one hour. The precipitated product was filtered and the benzene layer washed with dilute sodium bicarbonate solution, then with water, and the benzene removed by distillation. The residue was recrystallized from ethanol or methanol. The following compounds were prepared according to this procedure: α-(2-Hydroxy-5-chlorobenzylidene)-γ-butyrolactone, m.p., 233°, yield 49%; *Anal.* Calcd. for $C_{11}H_9ClO_3$: C, 58.81; H, 4.04; Cl, 15.78. Found: C, 58.97; H, 4.09; Cl, 15.89. α-(2-Hydroxy-3,5-dichlorobenzylidene)-γ-butyrolactone, m.p., 188-189°, yield 54%; *Anal.* Calcd. for $C_{11}H_8Cl_2O_3$: C, 50.99; H, 3.11; Cl, 27.37. Found: C, 50.92; H, 3.25; Cl, 27.06. α-(2-Hydroxy-3,5-dibromobenzylidene)-γ-butyrolactone, m.p. 211-212°, yield 22%; *Anal.* Calcd. for $C_{11}H_8Br_2O_3$: C, 37.96; H, 2.32; Br, 45.93. Found: C, 38.11; H, 2.27; Br, 46.22. α-(2-Hydroxy-3,5-dichlorobenzylidene)-γ-valerolactone, m.p. 186-187°, yield 51%; *Anal.* Calcd. for $C_{12}H_{10}Cl_2O_3$: C, 52.77; H, 3.69; Cl, 25.96. Found: C, 52.78; H, 3.94; Cl, 25.86.

Hydrogenation.

The hydrogenations were performed by dissolving or suspending 5 g. of the condensation product in 150 ml. of methanol, adding 10% by weight of platinum oxide and shaking the mixture under 45 lbs. of hydrogen pressure in a Parr apparatus for 24 hours. The catalyst was removed by filtration, the solvent distilled and the residue worked up by crystallization or distillation. The following compounds were obtained: 3-(2-Hydroxyethyl)-3,4-dihydrocoumarin (76%), previously erroneously described as α-(2-hydroxybenzyl)-γ-butyrolactone (16). 3-(2-Hydroxyethyl)-3,4-dihydro-6-chlorocoumarin, b.p., 126-128° at 9 mm (18%). *Anal.* Calcd. for $C_{11}H_{11}ClO_3$: C, 58.29; H, 4.89. Found: C, 59.18; H, 4.23. 3-(2-Hydroxyethyl)-3,4-dihydro-6,8-dichlorocoumarin, m.p., 115-116°, (87%). *Anal.* Calcd. for $C_{11}H_{10}Cl_2O_3$: C, 50.60; H, 3.86; Cl, 27.16. Found: C, 50.69; H, 3.94; Cl, 26.97. 3-(2-Hydroxypropyl)-3,4-dihydro-6,8-dichlorocoumarin, m.p. 106-107°, (81%). *Anal.* Calcd. for $C_{12}H_{12}Cl_2O_3$: C, 52.38; H, 4.40; Cl, 25.77. Found: C, 52.42; H, 4.53; Cl, 25.62.

Besides the dihydrocoumarins, several other fractions were isolated but not identified. Better yields of dihydrocoumarins and less side-products can probably be obtained by using Raney copper as the hydrogenation catalyst, as was recommended for the hydrogenation of coumarins (17).

Acknowledgment.

This work was supported financially through grant RG-08797 by the National Institutes of Health, Washington, D.C. The authors appreciate the assistance of Mr. Tai-Chee Lee.

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Received August 14, 1964 Cincinnati, Ohio