

the melting point of a sample of the hydrocarbon prepared according to Gomberg.²⁷

Summary

The reaction of a methyl Grignard reagent with substances of the type of 10-acetoxyanthrone-9 results in the replacement of the acetoxy group by an alkyl radical, as well as addition to the carbonyl group, with the eventual production of

(27) Gomberg, *Ber.*, **39**, 2963 (1906).

9,10-dimethylantracene. This apparently novel replacement reaction of acyloxyanthrones seems to be attributable to the special reactivity of the acyloxy group, and an analogy has been found in the smooth reaction of triphenylmethyl acetate with methylmagnesium bromide to give α, α, α -triphenylethane.

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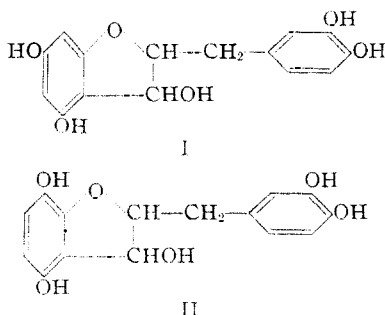
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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Coumaran Derivatives. IX. Synthesis of 3,4,6,3',4'-Pentahydroxy-2-benzylcoumaran

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From a study of the degradation products of quebracho tannin, Nñez² suggested that the tannin was a mixture of 3,4,6,3',4'-pentahydroxy-2-benzylcoumaran (I) and 3,4,7,3',4'-pentahydroxy-2-benzylcoumaran (II). These structures



differ markedly from those suggested by other investigators³ for the tannins in quebracho and also from the general structure of phlobatannins⁴ to which class quebracho belongs. The above structures also differ from fisetin, ellagic acid and gallic acid which Perkin and Gunnell⁵ isolated from quebracho.

The present report describes the synthesis of a compound with structure I and its comparison with some of the fractions obtained from quebracho powder.

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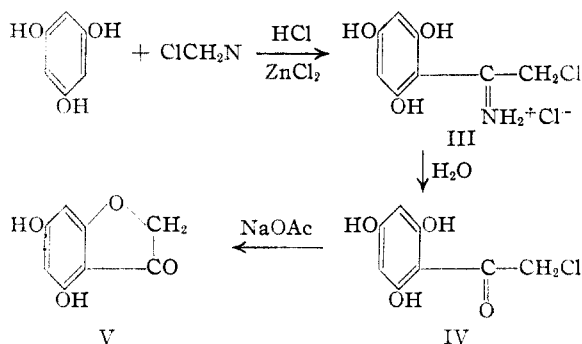
(2) Nñez, *Annales Assoc. Quim. Argentina*, **24**, 159 (1936).

(3) Arata, *Ann. Socied. Cientif. Argentina* (1878), (1879); Franke, *Pharm. Zentr.*, **47**, 887 (1906); Körner and Pertermann, *Deut. Gerbzeit.*, no. 117 (1904); Nierenstein, *Ber.*, **40**, 4575 (1907); *Collegium*, **69** (1905), 141 (1906); Einbeck and Jablonski, *Ber.*, **54**, 1084 (1921); **56**, 1906 (1923); Freudenberg and Maitland, *Ann.*, **510**, 193 (1934).

(4) Russell, *Chem. Rev.*, **17**, 155 (1935).

(5) Perkin and Gunnell, *J. Chem. Soc.*, **69**, 1303 (1896).

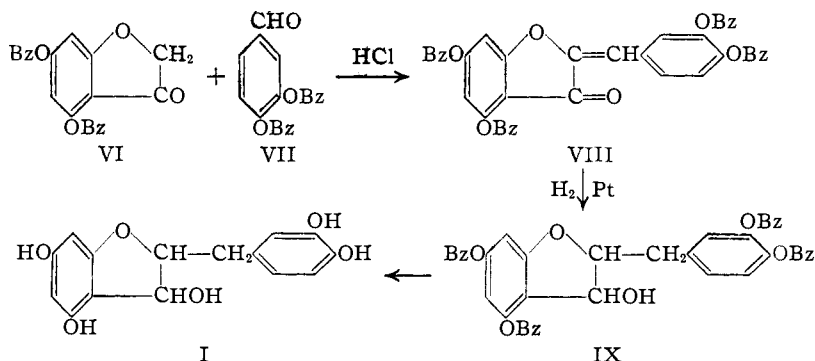
A Hoesch⁶ reaction between phloroglucinol and chloroacetonitrile produced 2,4,6-trihydroxyphenyl chloromethylketimide hydrochloride (III), which readily hydrolyzed to 2,4,6-trihydroxy- α -chloroacetophenone (IV). Ring closure by treatment with sodium acetate⁷ produced 4,6-dihydroxycoumaran-3-one (V). Attempts to condense



4,6-dihydroxycoumaran-3-one with protocatechuic aldehyde did not yield definite crystalline products. However, the dibenzoate (VI) of the coumaran and of protocatechuic aldehyde (VII) readily condensed to give an excellent yield of 4,6,3',4'-tetrabenzoyloxy-2-benzal-coumaran-3-one (VIII). Catalytic reduction with hydrogen and platinum oxide-platinum black at 25° and 4 atmospheres pressure produced a compound which analyzed for 4,6,3',4'-tetra-benzoyloxy-2-benzylcoumaran-3-ol (IX). Saponification with alkali in a nitrogen atmosphere and acidification yielded 3,4,6,3',4'-pentahydroxy-2-benzylcoumaran (I). When compound VIII was reduced in the presence

(6) Hoesch, *Ber.*, **48**, 1122 (1915).

(7) Auwers and Pohl, *Ann.*, **405**, 243 (1914).



of hydrochloric acid, which has been found to promote the reduction⁸ of the carbonyl group, more than two moles of hydrogen was absorbed due to the reduction of some of the aromatic rings.⁹ Hydrolysis of the product, however, yielded the same pentahydroxy derivative (I). The latter was characterized by its analysis, determination of hydroxyl groups,¹⁰ and by the preparation of the pentaacetate as a derivative.

Commercial quebracho powder (60% actual tannins) was subjected to three different extraction procedures, based on the methods described in the literature,³ in an effort to obtain compounds corresponding to the tannins. These methods yielded amorphous products varying in color from pink to red and decomposing at temperatures ranging from 250–350°. They retained inorganic salts very tenaciously and always left a residue on combustion. The acetylated and benzoylated derivatives of the tannin, prepared by various methods, were also amorphous compounds which decomposed at relatively high temperatures, 190–270°. Up to the present time no procedure has been found which yields a pure compound; all of the fractions and their derivatives behaved like complex mixtures.

The synthetic 3,4,6,3',4'-pentahydroxy-2-benzylcoumaran (I) and its acetate are crystalline compounds which melt at 259–262° and 173–174°, respectively. They are quite different from any of the fractions obtainable from quebracho powder.

Experimental

2,4,6-Trihydroxy- α -chloroacetophenone.—A modification of Sonn's¹¹ procedure was used. In a 2-liter, 3-necked, round-bottomed flask equipped with a mercury-sealed stirrer, a reflux condenser, a 250-cc. separatory funnel, and

an inlet tube for hydrogen chloride, were placed 100 g. of phloroglucinol, 20 g. of anhydrous zinc chloride and 400 cc. of anhydrous ether. Dry hydrogen chloride was passed into the stirred mixture. After all the zinc chloride and phloroglucinol had gone into solution with the formation of two liquid layers, a solution of 30 g. of chloroacetonitrile in 200 cc. of anhydrous ether was added to the mixture dropwise. Stirring was continued for six hours and the introduction of hydrogen chloride

for ten hours. The mixture was allowed to stand overnight. The ether was decanted from the yellow solid which had formed. After two washings with 100 cc. of anhydrous ether, the yellow imine hydrochloride was hydrolyzed by the addition of 500 g. of ice and heating at 100° for one hour. On cooling, 56 g. of a pink voluminous precipitate separated. Concentration of the decanted ether solutions yielded some additional crude product. Recrystallization and decolorization with Darco from water yielded 71 g. (88%) of a light tan product, m. p. 188–191° (d.).

4,6-Dihydroxycoumaran-3-one.—The above chloro-ketone had previously been converted to the coumaranone by long boiling with water¹¹ but it was found that the general method developed by Auwers and Pohl¹² for other coumaranones worked better. A mixture of 60 g. of 2,4,6-trihydroxy- α -chloroacetophenone, 70 g. of sodium acetate and 600 cc. of 95% ethanol was heated under reflux for five hours. After about one-half of the alcohol had been removed by distillation, the solution was poured into 1 liter of ice water. The salmon-colored precipitate was removed by filtration. Additional crude product was obtained by saturation of the filtrate with sodium chloride, extraction with ether, and evaporation of ether from the extract. Decolorization with Darco and recrystallization from water yielded 47 g. (95%) of a light pink product, which melted with decomposition at 255–260°. It has been described by Sonn.¹¹

3,4-Dibenzyloxybenzaldehyde.—Fifty grams of protocatechuic aldehyde was dissolved in 500 cc. of 10% sodium hydroxide. The solution was shaken in a tightly stoppered bottle with ice and 125 cc. of benzoyl chloride until a yellow precipitate had formed. The product was washed thoroughly with water and recrystallized from 95% ethanol. The dibenzoate, obtained in 62% yield, consisted of white crystals, melting at 96–97° which agrees with the report by Hayduck.¹³

4,6-Dibenzyloxy-3-one.—To a solution of 33.2 g. of 4,6-dihydroxycoumaran-3-one in 1 liter of acetone and 250 cc. of water was added a solution of 75 g. of potassium carbonate in 375 cc. of water. After the addition of 60 cc. of benzoyl chloride, two liquid layers formed and a crystalline precipitate started to form almost immediately in the upper layer. The mixture was heated gently for about fifteen minutes until no more precipitate appeared to be forming. The precipitate was removed by filtration

(8) Shriner and Witte, *THIS JOURNAL*, **63**, 1108 (1941).

(9) Brown, Durand and Marvel, *ibid.*, **58**, 1544 (1936).

(10) Freed and Wynne, *Ind. Eng. Chem., Anal. Ed.*, **8**, 278 (1936).

(11) Sonn, *Ber.*, **50**, 1262 (1917).

(12) Auwers and Pohl, *Ann.*, **405**, 243 (1914).

(13) Hayduck, *Ber.*, **36**, 2930 (1903).

and recrystallized from benzene; white plates, m. p. 166–167°; yield 42 g. (56%).

Anal. Calcd. for $C_{22}H_{14}O_6$: C, 70.59; H, 3.74. Found: C, 70.79; H, 3.85.

4,6,3',4'-Tetrabenzoyloxy-2-benzalcoumaran-3-one.—A solution of 3.75 g. of 4,6-dibenzoyloxy coumaran-3-one and 4 g. of 3,4-dibenzoyloxybenzaldehyde in 225 cc. of glacial acetic acid was shaken with 3 cc. of concentrated hydrochloric acid in a stoppered bottle at room temperature for forty-eight hours. The light greenish-yellow precipitate was removed by filtration and washed with water, m. p. 188–192°; yield 6.5 g. (92%). This compound was reduced without further purification. When the filtrate from the reaction mixture was poured into water, an additional yield of crude product was obtained which was recrystallized from glacial acetic acid. The total yield was nearly the theoretical.

Anal. Calcd. for $C_{13}H_{20}O_{10}$: C, 73.50; H, 3.70. Found: C, 73.79; H, 3.87.

4,6,3',4'-Tetrabenzoyloxy-2-benzylcoumaran-3-ol.—(A) Three and one-half grams of 4,6,3',4'-tetrabenzoyloxy-2-benzalcoumaran-3-one was dissolved in 50 cc. of dioxane. After the addition of 0.1 g. of platinum oxide, the solution was shaken under 37 pounds of hydrogen at 25° for twelve hours. The platinum catalyst was removed by filtration, and the almost colorless filtrate was poured into 400 cc. of water. After standing in the refrigerator overnight, the precipitate was removed by filtration. The product was a white, gummy material which was recrystallized from 500 cc. of absolute ethanol. About 1.5 g. (23%) of white crystals was obtained; m. p. 138–140°.

Anal. Calcd. for $C_{18}H_{30}O_{10}$: C, 73.09; H, 4.25. Found: C, 73.17; H, 4.25.

(B) The reduction of the tetrabenzoate was also carried out using glacial acetic acid as the solvent and using the same amounts of material and catalyst, and also the same temperature and pressure as given above in (A). The reduction was complete in one hour, but difficulty was experienced in purifying the product. After removal of the platinum by filtration, the filtrate was poured in 1 liter of water. The white, flocculent precipitate was removed by filtration, washed with water, and dried over calcium chloride and potassium hydroxide *in vacuo*. The crude product melted over a wide range, 60 to 80°. In order to purify it, 6 g. was dissolved in 100 cc. of ether. Slow evaporation of the ether yielded white crystals which melted at 135–137°, lower than the product obtained by reduction in dioxane. No depression of the melting point occurred when the samples were mixed. It should be pointed out that the reduction product may contain diastereoisomeric forms because of the two asymmetric carbon atoms.

3,4,6,3',4'-Pentahydroxy-2-benzylcoumaran.—(A) Saponification of the benzoylated compound followed the procedure of Russell and Todd¹⁴ for the hydrolysis of pentabenzoyloxy chalcones. A solution of 2.1 g. of 4,6,3',4'-tetrabenzoyloxy-2-benzylcoumaran-3-ol in 30 cc. of benzene and 70 cc. of ethanol was treated in a nitrogen atmosphere, dropwise, with 100 cc. of 2% aqueous potassium hydroxide, the alcohol and benzene being distilled off at a rate equal to the rate of addition of potassium hydroxide. After the addition of the potassium hydroxide

was complete (one hour), the orange solution was heated under reflux for one-half hour. After cooling, the solution was acidified with dilute hydrochloric acid, saturated with sodium chloride and extracted with ethyl acetate. The extract was dried (sodium sulfate), filtered, and the filtrate evaporated to dryness. The residue was extracted with benzene to remove benzoic acid, dissolved in acetone, filtered, and the filtrate evaporated to dryness. Crystallization from alcohol yielded small, pink crystals, m. p. 252–257°. Analysis revealed the presence of ash which was removed by solution of the product in anhydrous ether, filtration, evaporation, and recrystallization from 50% ethanol; m. p. 259–262° (d.); yield, 0.35 g. (41%).

Anal. Calcd. for $C_{15}H_{14}O_8$: C, 62.07; H, 4.83. Found: C, 62.43; H, 4.38.

Determination of hydroxyl groups by the acetic anhydride-pyridine method¹⁰ gave 27.9%; calculated for five hydroxyls in $C_{15}H_{14}O_8$, 29.3%.

(B) To a solution of 3.3 g. of 4,6,3',4'-tetrabenzoyloxy-2-benzalcoumaran-3-one in 300 cc. of glacial acetic acid was added 0.2 g. of platinum oxide and 1 cc. of concentrated hydrochloric acid. The mixture was shaken under 45 lb. of hydrogen. The platinum was removed by filtration, and the filtrate was poured into 1 liter of water. The resultant milky emulsion was saturated with sodium chloride and extracted with ether. The ether extract was dried over potassium hydroxide, which also served to remove any acetic acid present. After filtration, the ether solution was evaporated to dryness under reduced pressure. The residue was a yellow oil.

This oil was hydrolyzed, using exactly the same procedure as outlined above in the hydrolysis of 4,6,3',4'-tetrabenzoyloxy-2-benzylcoumaran-3-ol. The product was a white, crystalline compound, m. p. 258–261°, which caused no depression in the melting point of the compound prepared in the first reaction described above.

Anal. Calcd. for $C_{15}H_{14}O_8$: C, 62.07; H, 4.83. Found: C, 62.00; H, 4.43.

3,4,6,3',4'-Pentaacetoxy-2-benzylcoumaran.—A solution of 65 mg. of 3,4,6,3',4'-pentaacetoxy-2-benzylcoumaran in 2 cc. of a 20% solution of acetic anhydride in pyridine was heated under reflux for fifteen minutes. After dilution with 30 cc. of water, the solution was neutralized with 0.1 N sodium hydroxide. The tan precipitate was removed by filtration, washed with water, and recrystallized from ethanol, m. p. 173–174°; yield 80 mg. (71%).

Anal. Calcd. for $C_{23}H_{24}O_{11}$: C, 60.00; H, 4.80. Found: C, 60.57; H, 4.76.

Summary

Condensation of 4,6-dibenzoyloxy-coumaran-3-one with 3,4-dibenzoyloxybenzaldehyde yielded 4,6,3',4'-tetrabenzoyloxy-2-benzal-coumaran-3-one. Catalytic reduction of the latter produced 4,6,3',4'-tetrabenzoyloxy-2-benzylcoumaran-3-ol which was hydrolyzed to 3,4,6,3',4'-pentahydroxy-2-benzylcoumaran. This compound and its pentaacetate differed markedly from any of the fractions obtainable from quebracho powder.

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(14) Russell and Todd, *J. Chem. Soc.*, 1070 (1934).