flask. A weak flow of hydrogen was let pass through the apparatus and the solution was heated gently, so that only small quantities of isopropyl alcohol distilled. When benzophenone was added, the precipitation of acetone 2,4-dinitrophenylhydrazone began after five minutes; in the case of camphor, after ten minutes. When cafesterol was added, even after four hours we did not observe precipitation. Then we interrupted the experiment and by decomposition of the aluminum isopropylate with 10% sodium hydroxide and extraction with ether, we isolated cafesterol, m. p. 154–155°, after recrystallization from petroleum ether.

Summary

The partial hydrogenation of cafesterol acetate with Raney nickel confirms the existence of only two carbon–carbon double bonds. The oxidation of cafestan-triol with periodate yields formaldehyde. One hydroxy group of cafesterol can be split off, whereby a new double bond is formed. The inert oxygen atom seems to be present as an oxide ring rather than as a keto group.

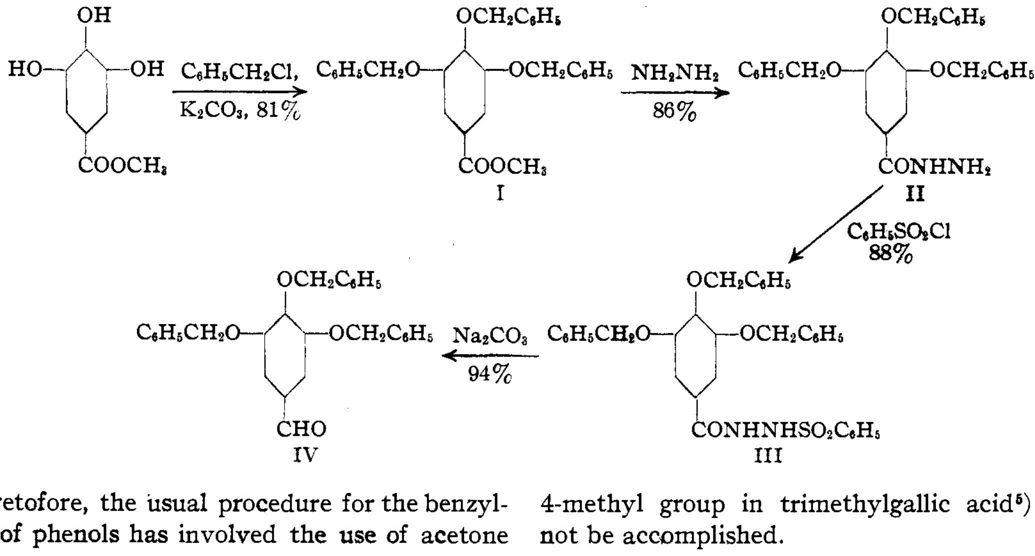
SAO PAULO, BRAZIL RECEIVED AUGUST 17, 1942

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Gallaldehyde Tribenzyl Ether

BY R. O. CLINTON AND T. A. GEISSMAN

Studies in the flavanone series being carried out in this Laboratory have necessitated the synthesis of certain flavanones containing the 3′,4′,5′-trihydroxyphenyl group. Since this group could not be introduced by the use of gallaldehyde[1] in the usual Claisen–Schmidt condensation, due not only to the difficulty of obtaining the aldehyde in sizable quantities, but to its great instability in basic solution, it became necessary to prepare the analogous aldehyde in which the hydroxy groups were protected by labile benzyl ether groups. This was accomplished through use of the McFadyen–Stevens synthesis,[2] as shown in the accompanying diagram.



Heretofore, the usual procedure for the benzylation of phenols has involved the use of acetone as solvent,[3] thus imposing a low maximum temperature upon the reaction, and necessitating long reaction periods. As a rule the yields obtainable by this method are low. It has been found in the present work that the substitution of acetophenone for acetone as solvent, with an increase in temperature, enables the reaction to be completed in a few hours, and with a greatly increased yield.

Both methyl and benzyl tris-benzylgallate were readily saponified to the corresponding acid.[4] The latter compound could be debenzylated to give gallic acid by heating with acids; however, removal of but one benzyl group, namely, that in the 4-position (in analogy with the loss of the 4-methyl group in trimethylgallic acid[5]), could not be accomplished.

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(1) Rosenmund and Zetzsche, *Ber.*, **51**, 594 (1918); Rosenmund and Pfannkuch, *ibid.*, **55**, 2357 (1922).

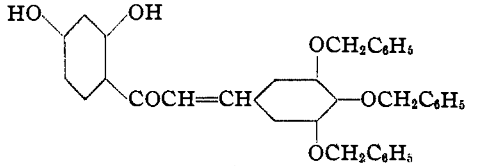
(2) McFadyen and Stevens, *J. Chem. Soc.*, 584 (1936).

(3) Baker and co-workers, *ibid.*, 77 (1929); 1924 (1939).

(4) Schöpf and Winterhalder, *Ann.*, **544**, 62 (1940).

(5) Graebe and Martz, *Ber.*, **36**, 216 (1903); *Ann.*, **340**, 220 (1905).

Gallaldehyde tribenzyl ether condensed readily with resacetophenone to yield the corresponding 2',4'-dihydroxy-3,4,5-tris-benzyloxychalcone, V.



V

Experimental

All melting points are corrected.

Methyl Tris-benzylgallate (I).—Into a 3-liter 3-necked flask equipped with mechanical stirrer, thermometer, and dropping funnel was introduced 59.0 g. (0.32 mole) of recrystallized methyl gallate[4,6] (dried at 120°) and 250 ml. of dry, redistilled acetophenone. The mixture was heated in an oil-bath at 100° with stirring until all of the ester was in solution, 142 g. (1.03 moles) of powdered potassium carbonate (dried at 140°) was added in one portion, and the temperature of the mixture raised to 140°. While maintaining the mixture at this temperature, 130 g. (1.03 moles) of redistilled benzyl chloride was added dropwise with stirring over a period of one and one-half hours. Heating with stirring at 140–150° was continued for an additional seven hours, at the end of which period the deep orange mixture was steam distilled to remove the acetophenone and excess benzyl chloride. The residue was transferred to a separatory funnel and, after removal of the brown viscous lower layer, the aqueous layer was extracted with two 100-ml. portions of benzene. The benzene extracts were combined with the major fraction and the whole treated while wet with 10 g. of Norite and boiled a few minutes. Filtration and evaporation of the benzene gave 130 g. of crude, cream-colored product. In order to remove unreacted or partially benzylated methyl gallate, the crude material was triturated at room temperature for three hours with a solution of 15 g. of potassium hydroxide in 600 ml. of a 4:1 methanol–water mixture, filtered, washed well with methanol, and finally with water. After drying and recrystallizing from benzene–ligroin there was obtained 118 g. (81%) of white product, m. p. 87–89°. A small portion after two recrystallizations from benzene–ligroin gave small, brilliant white needles, m. p. 89.5–90.0°.

Anal. Calcd. for $C_{29}H_{26}O_5$: C, 76.63; H, 5.77. Found: C, 76.35; H, 5.90.

Benzyl Tris-benzylgallate.—Benzylation of 10.0 g. (0.059 mole) of dry, recrystallized gallic acid in 50 ml. of acetophenone with 48.6 g. (0.38 mole) of benzyl chloride and 67.0 g. (0.49 mole) of potassium carbonate, under the above conditions, gave 18.0 g. of crude benzyl tris-benzylgallate. After treatment with aqueous-methanolic potassium hydroxide and two crystallizations from ligroin (Norite), there was obtained 14.8 g. (47%) of long, slender white needles, m. p. 90.0–90.5°.

Anal. Calcd. for $C_{35}H_{30}O_5$: C, 79.24; H, 5.69. Found: C, 79.23; H, 5.84.

Gallic Acid Tribenzyl Ether.—Saponification of either methyl or benzyl tris-benzylgallate with aqueous-alcoholic sodium hydroxide gave 80–90% yields of gallic acid tribenzyl ether. The compound crystallized from benzene–ligroin in white cottony needles, m. p. 196.0–196.5° (lit.[4] 187°).

Anal. Calcd. for $C_{28}H_{24}O_5$: C, 76.34; H, 5.49; neut. eq., 440.5. Found: C, 76.23; H, 5.72; neut. eq., 437.5.

Attempts to decarboxylate gallic acid tribenzyl ether by the usual methods were unsuccessful.

Gallhydrazide Tribenzyl Ether (II).—A mixture of 65.0 g. (0.143 mole) of methyl tris-benzylgallate, 200 ml. of butyl cellosolve, and 17.5 g. of 85% hydrazine hydrate (0.30 mole) was refluxed for seven hours under an air condenser, in such a manner that the liberated methyl alcohol was permitted to distill from the top of the condenser. The reaction product was poured into one liter of ice-water, mixed well and filtered. After washing with ice-water and drying, the crude hydrazide (64.4 g.) was boiled for fifteen minutes with 250 ml. of benzene, cooled, filtered and washed with benzene. There was thus obtained 56.0 g. (86%) of white, nearly pure product. From the benzene filtrate and washings was recovered 8.1 g. of methyl tris-benzylgallate.

The hydrazide was extremely difficult to purify free from small traces of the methyl ester. For analysis a small portion was extracted several times with hot 1:1 benzene–ligroin, and recrystallized three times from acetone–water as long, slender white needles, m. p. 137.0–137.5°.

Anal. Calcd. for $C_{28}H_{26}O_4N_2$: N, 6.16. Found: N, 6.00.

Benzenesulfonylgallhydrazide Tribenzyl Ether (III).—A solution of 40.0 g. (0.088 mole) of gallhydrazide tribenzyl ether in 350 ml. of anhydrous pyridine was treated dropwise, with stirring, with 19.4 g. (0.11 mole) of redistilled benzenesulfonyl chloride, added over a period of forty-five minutes. The temperature of the reaction mixture was kept at 20–25° by means of external cooling. The light brown reaction product was stirred at room temperature for an additional four hours, transferred to a Claisen flask, and the pyridine removed in so far as possible on the steam-bath at 15–20 mm. The residue was washed by decantation with two 300-ml. portions of 2% hydrochloric acid solution. One crystallization from benzene with Norite decolorization gave 46.0 g. (88%) of white product, m. p. 163–165°. A sample recrystallized from aqueous alcohol gave short, brilliant white needles, m. p. 165.0–165.5°.

Anal. Calcd. for $C_{34}H_{30}O_6N_2S$: C, 68.67; H, 5.08. Found: C, 68.65; H, 5.20.

Gallaldehyde Tribenzyl Ether (3,4,5-Tris-benzyloxybenzaldehyde) (IV).—A mixture of 43.0 g. (0.072 mole) of benzenesulfonylgallhydrazide tribenzyl ether and 400 ml. of technical ethylene glycol in a three-liter flask was heated to 160° (thermometer in mixture) in an oil-bath. The compound dissolved completely. Forty-five grams (0.42 mole) of technical powdered anhydrous sodium carbonate was added in one portion. When the violent effervescence had subsided (*ca.* two minutes), the flask was removed from the oil-bath and 200 ml. of water was added cautiously to the hot solution, followed by a liter of ice water and 50 ml. of 10% sodium hydroxide solution. After mixing well, the mixture was set in the ice chest for five hours, filtered,

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(6) Mauthner, *J. prakt. Chem.*, **133** [2] 121 (1932).

and washed well with ice-water. One crystallization from aqueous alcohol with Norite decolorization gave 28.9 g. (94%) of brilliant, slender white needles of the aldehyde, m. 104.0–104.5°.

Anal. Calcd. for $C_{28}H_{24}O_4$: C, 79.22; H, 5.70. Found: C, 79.09; H, 5.83.

Gallaldehyde tribenzyl ether could not be smoothly debenzylated in the presence of alcoholic acids to yield gallaldehyde, or in the presence of acetic anhydride–hydrochloric acid, to yield gallaldehyde triacetate, due to extensive decomposition.

Gallaldoxime Tribenzyl Ether.—The oxime was prepared by treating the aldehyde with hydroxylamine hydrochloride in pyridine–absolute alcohol solution,[7] and crystallizing the product from benzene and from alcohol as long, slender white needles (from alcohol), m. p. 140.0–140.5°.

Anal. Calcd. for $C_{28}H_{25}O_4N$: C, 76.52; H, 5.73. Found: C, 76.35; H, 5.97.

Gallaldehyde Tribenzyl Ether 2,4-Dinitrophenylhydrazone.—To 10 ml. of a saturated solution of 2,4-dinitrophenylhydrazine in glacial acetic acid was added 100 mg. of the aldehyde, the mixture was refluxed for fifteen minutes, and the insoluble hydrazone filtered hot. The crude product was washed on the filter with warm glacial acetic acid and with three 15-ml. portions of hot alcohol. Crystallization from a large volume of acetone gave small, brilliant scarlet needles, m. p. 214.0–214.5°.

Anal. Calcd. for $C_{34}H_{28}O_7N_4$: C, 67.54; H, 4.67. Found: C, 67.48; H, 4.87.

2',4'-Dihydroxy-3,4,5-tris-benzyloxychalcone (V).—A mixture of 5.0 g. (0.012 mole) of gallaldehyde tribenzyl ether, 1.82 g. (0.012 mole) of resacetophenone, 40 ml. of alcohol, and 10 g. of 50% potassium hydroxide solution was refluxed on the steam-bath for two hours, and then allowed to stand overnight. The deep red reaction product was poured into 150 ml. of ice water, the mixture was acidified to litmus with dilute hydrochloric acid, filtered and the precipitate was washed well with water. After three crystallizations from ligroin (Norite) and two recrystallizations from dilute alcohol, there was obtained 1.87 g. (28%) of small, light yellow needles, m. p. 160–161°.

Anal. Calcd. for $C_{36}H_{30}O_6$: C, 77.40; H, 5.41. Found: C, 77.48; H, 5.64.

Summary

The preparation of gallaldehyde tribenzyl ether involving an improved procedure for benzylation has been described. Gallaldehyde tribenzyl ether has been condensed with resacetophenone to yield the corresponding chalcone.

LOS ANGELES, CALIF.

RECEIVED SEPTEMBER 28, 1942

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[7] Shriner and Fuson, "Identification of Organic Compounds," 2nd ed., John Wiley and Sons, New York, N. Y., p. 167.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

Tertiary Alkyl Primary Amines, $RR'R''CNH_2$. II

BY HENRY R. HENZE, BRUCE B. ALLEN[1] AND WILLIAM B. LESLIE

Utilization of the Grignard reaction through interaction of a nitrile and an organomagnesium halide has long been a standard procedure for the preparation of ketones. Hence, the failure[2] to obtain the anticipated ketone from reaction between ethoxyacetonitrile and allylmagnesium bromide was a distinct surprise; the product was shown to be a carbinamine of structure $C_2H_5OCH_2C(CH_2CH{=}CH_2)_2NH_2$. Equally surprising was the discovery that the ketimine formed from ethoxyacetonitrile and *n*-propylmagnesium bromide was able to react with allylmagnesium bromide to yield, after hydrolysis, another carbinamine, $C_2H_5OCH_2C(CH_2CH_2CH_3)(CH_2CH{=}CH_2)NH_2$. We have continued our study of this reaction to ascertain whether it is limited to utilization of alkoxynitriles.

In the present investigation it is clear that allylmagnesium bromide is able to react not only with alkoxyalkyl cyanides, but also with alkyl cyanides, with aralkyl cyanides, and with alkenyl cyanides to yield the corresponding carbinamines, $RR'R''CNH_2$. Likewise, allylmagnesium bromide has been caused to react with the addition product formed from interaction of *n*-butoxyacetonitrile and *n*-butylmagnesium bromide to produce another carbinamine.

Experimental

Preparation of Alkyl-, Alkoxyalkyl-, Aralkyl- and Alkenyldiallylcarbinamines.—The tertiary alkyl primary amines of these types were prepared from essentially those proportions of Grignard reagent and organic cyanide, and by the method previously described,[2] namely, one molar equivalent of a nitrile was caused to react with two molar equivalents of allylmagnesium bromide under anhydrous conditions, and then the resulting addition product was decomposed with ammonium chloride solution. The cyanides employed were *n*-butoxyacetonitrile,[3] *n*-butyronitrile,

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[1] Present address: Tubize-Chatillon Co., Rome, Ga.

[2] Allen and Henze, THIS JOURNAL, **61**, 1790 (1939).

[3] This nitrile was obtained by the method of Gauthier [*Compt. rend.*, **143**, 831 (1906)] from cuprous cyanide and *n*-butyl chloromethyl ether, the latter being formed when *n*-butanol, formaldehyde and dry hydrogen chloride were combined according to the procedure of Henry [*Bull. soc. chim.*, [2] **44**, 458 (1885)]. The nitrile was purified by distillation under diminished pressure, b. p. 79° (30 mm.).