of $17\alpha,20\alpha$-dihydroxy-4-pregnene-3-one (III) and $17\alpha,20\beta$-dihydroxy-4-pregnene-3-one (IV). The $17\alpha,20$-glycols (III and IV) were separated by paper chromatography using the solvent system benzene-formamide[3] (formamide diluted with an equal volume of methanol). Although it was previously shown[4] that reduction of 17α-hydroxy-20-keto-steroids with lithium aluminum hydride affords predominantly the $17\alpha,20\alpha$-dihydroxy epimer, we have observed in the present instance that the $17\alpha,20\beta$-isomer constitutes the major product (70%). By a similar reduction of a 17α-hydroxy-progesterone derivative Romo *et al.*[5] have obtained only the $17\alpha,20\beta$-dihydroxy epimer IV. However, it has been possible for us to isolate the $17\alpha,20\alpha$-dihydroxy epimer in 30% yield, and as expected it was more polar than the $17\alpha,20\beta$-dihydroxy epimer[4a] and the molecular rotation was lower than its $17\alpha,20\beta$-isomer IV.

EXPERIMENTAL[6]

Melting points. All melting points were determined on samples dried under high vacuum at 60° for 24 hr. and were uncorrected.

Absorption spectra. The ultraviolet absorption spectra were determined in methanol on a Cary Recording Spectrophotometer (Model 11 MS). The infrared absorption spectra were determined in potassium bromide disks on a Perkin-Elmer infrared spectrometer (Model 21).

Optical rotations. All optical rotations were measured in chloroform solution.

Lithium aluminum hydride reduction of I. A solution of 2 g. of 17α-hydroxyprogesterone (I) in 60 ml. of tetrahydrofuran was added with stirring to 3.5 g. of lithium aluminum hydride in 110 ml. of tetrahydrofuran over a period of 15 min., and the mixture was then heated under reflux for 2 hr. The excess reagent was decomposed by addition of ethyl acetate. A saturated solution of sodium sulfate was then added until the precipitate began to adhere to the sides of the flask. Finally 20 g. of solid sodium sulfate was added and the solution was filtered from the salts. Evaporation of the filtrate gave 2 g. of a mixture of epimeric 4-pregnene-3ξ, $17\alpha,20\xi$-triols (II) as a crystalline solid. Without further purification this mixture was subjected to manganese dioxide oxidation.

Manganese dioxide oxidation of the mixture of triols II. To a solution of 2 g. of the mixture of aforementioned triols in 100 ml. of tetrahydrofuran 10 g. of manganese dioxide[7] was added and stirred at room temperature (25°) for 4 hr. The solution was then filtered from the catalyst and after evaporating the solvent, 1.8 g. of a mixture of 17α, 20α-dihydroxy-4-pregnene-3-one (III) and $17\alpha,20\beta$-dihydroxy-4-pregnene-3-one (IV) was obtained as a solid.

Separation of III and IV by paper chromatography. One gram of the mixture of III and IV was chromatographed on 200 Whatman No. 1 paper grams in the solvent system benzene-formamide[3] (formamide diluted with an equal volume of methanol) for 5 hr. The positions of III and IV were demonstrated by means of a 2,4-dinitrophenylhydrazene reagent[7] and iodine reagent.[8] Both compounds reacted with the 2,4-dinitrophenylhydrazene reagent to give orange colors on the paper, whereas the iodine reagent gave a blue color with the more polar $17\alpha,20\alpha$-dihydroxy-4-pregnene-3-one (III) and a brown color with the less polar $17\alpha,20\beta$-dihydroxy-4-pregnene-3-one (IV). The compounds were then separately eluted from the papers with a mixture of equal volumes of methanol and chloroform. The solvent was evaporated under a stream of nitrogen *in vacuo* at 45° in each case and the residue was crystallized. $17\alpha,20\alpha$-Dihydroxy-4-pregnene-3-one (III) which was obtained in 30% yield crystallized from methanol as stout needles, m.p. 208–210°, $(\alpha)_D^{22°}$ $+20.4°$, M_D $+ 67.7°$; $\lambda_{max}^{CH_3OH}$ 242 mμ, $\epsilon = 19{,}210$), ν_{max}^{KBr} 3483, 2965, 1660, and 1615 cm.$^{-1}$

Anal. Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.71. Found: C, 75.70; H, 9.53.

$17\alpha,20\beta$-Dihydroxy-4-pregnene-3-one (IV) was obtained in 70% yield and crystallized from acetone as prisms, m.p. 204–205.5°, $(\alpha)_D^{22}$ $+ 72.7°$, M_D $+ 241.6°$, $\lambda_{max}^{CH_3OH}$241 mμ (ϵ = 16,030), ν_{max}^{KB} 3465, 2960, 1660, and 1615 cm.$^{-1}$

Anal. Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.71. Found: C, 75.93; H, 9.70. [Lit.[5] m.p. 201–204°, $(\alpha)_D^{20}$ $+68.2°$, λ_{max} 240 mμ (log ϵ, 4.29).]

The mixture melting point of III and IV showed depression and melted over a range 190–198°.

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DEPARTMENT OF PHYSIOLOGY AND BIOCHEMISTRY
SOUTHWEST FOUNDATION FOR RESEARCH AND EDUCATION
SAN ANTONIO, TEX.

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Reactions of Vanillin and Its Derived Compounds. XXX.[1] The Reduction of 4,4′-Dibenzyloxy-3,3′-dimethoxybenzil

IRWIN A. PEARL

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Earlier studies on the synthesis of 4,4′-dihydroxy-3,3′-dimethoxybenzophenone from vanillil (4,4′-dihydroxy-3,3′-dimethoxybenzil) (I)[2] indicated that the bisbenzyl ether of vanillil, 4,4′-dibenzyloxy-3,3′-dimethoxybenzil (II) was more amenable to rearrangement with alkali than was the parent I. This greater specific reactivity of bisbenzyl ethers led to the preparation of bisbenzyl ethers of several reduction products of I needed for preparative studies related to products isolated from lignosulfonate oxidation mixtures.[3–5] The present paper

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[1] For paper XXIX of this series, see *J. Org. Chem.*, **25**, 1449 (1960).

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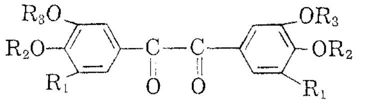
reports the preparation of the bisbenzyl ethers of several reduction products of I by the reduction of II.

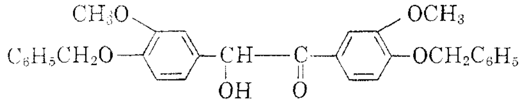
Reduction of II under conditions previously employed for the reduction of I[6] gave three monomolecular reduction products of II, but there appeared to be very little correlation between reductions of II and those of I, syringil (III),[7] and 3,3′-4,4′-tetrahydroxybenzil (IV).[1]

EXPERIMENTAL[8]

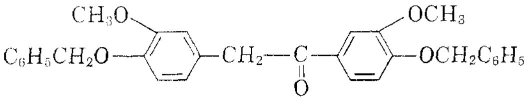
4,4′-Dibenzyloxy-3,3′-dimethoxybenzoin (V). A solution of 10 g. of II[2] in 150 ml. of glacial acetic acid was heated to boiling, removed from the source of heat, and treated with an excess (10 g.) of reduced iron powder. The mixture was shaken for approximately 15 min. during which time the color of the solution changed from yellow to brown. The mixture was filtered, and the brown filtrate was diluted with ten volumes of water. The resulting white precipitate was filtered, washed with water, and allowed to air dry to yield 7.2 g. of yellowish horny solid. This product was recrystallized from methanol and from ethanol to yield colorless crystals of V melting at 110–111° and not depressing a mixed melting point with authentic V prepared by condensing *O*-benzylvanillin with potassium cyanide.[2] The ultraviolet absorption spectrum showed the following maxima:
λ_{max} 232 mμ, ϵ 25680; λ_{max} 280 mμ, ϵ 14250; λ_{max} 310 mμ, ϵ 10103.



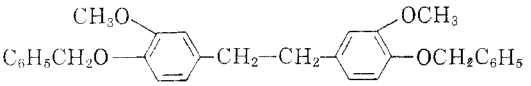
I. $R_1 = R_2 = H; R_3 = CH_3$
II. $R_1 = H; R_2 = C_6H_5CH_2; R_3 = CH_3$
III. $R_1 = OCH_3; R_2 = H; R_3 = CH_3$
IV. $R_1 = R_2 = R_3 = H$



V



VI



VII

Anal. Calcd. for $C_{30}H_{28}O_6$: C, 74.36; H, 5.83. Found: C, 74.33; H, 5.92.

V was also prepared by reduction of II with tin granules in boiling glacial acetic acid in the presence of a few crystals of mercuric chloride.

4,4′-Dibenzyloxy-3,3′-dimethoxydeoxybenzoin (VI). A warm (65°) solution of 10 g. of II in 150 ml. of glacial acetic acid was treated with 10 g. of zinc dust, and the mixture was shaken. After a few minutes, decolorization was complete. The mixture was heated on the steam bath for 30 min. and filtered hot. The filtrate was cooled and diluted with ten volumes of water. The precipitate was filtered, washed with water, and air dried to yield 7.6 g. of colorless crystals melting at 142–143°. Recrystallization from methanol and then from ethanol yielded crystals of pure VI melting at 144–145° and having the following maxima in its ultraviolet absorption spectrum: λ_{max} 230 mμ, ϵ 26350; λ_{max} 27 mμ, ϵ 14920; λ_{max} 305 mμ, ϵ 10320. The ultraviolet spectrum was almost identical with that for V, thus establishing the similarity of the structure between the benzylated guaiacyl units in the compounds.

Anal. Calcd. for $C_3OH_{28}O_5$: C, 76.90; H, 6.02. Found: C, 76.91; H, 6.41.

4,4′-Dibenzyloxy-3,3′-dimethoxybibenzyl (VII). A mixture of 4 g. of II and 400 ml. of 95% ethanol was heated to boiling and removed from the source of heat. The hot mixture was treated with 20 g. of granulated zinc and then with concentrated hydrochloric acid in small portions. Each addition of acid caused the mixture to boil, and boiling was allowed to subside before the next addition. After approximately 75 ml. of acid had been added, the yellow color of the solution disappeared. The colorless mixture was filtered, and the zinc was washed with a little hot ethanol. The crystalline precipitate which separated on cooling was filtered and recrystallized from acetic acid to yield colorless crystals (3.0 g.) of VII melting at 129–130° and having the following maxima in its ultraviolet absorption spectrum: λ_{max} 230 mμ, ϵ 18900; λ_{max} 280 mμ, ϵ 6910. VII has a strong white fluorescence under ultraviolet light.

Anal. Calcd. for $C_{30}H_{30}O_4$: C, 79.27; H, 6.65. Found: C, 79.26; H, 7.12.

VII was also prepared in almost quantitative yield by reduction of II with amalgamated zinc and hydrochloric acid in ethanolic solution.

Unsuccessful reductions of II. Attempted reductions of II with granulated tin and hydrochloric acid, Raney nickel in alkaline solution, sodium hydrosulfite in alkaline solution, magnesium amalgam in acetic acid solution, and aluminum amalgam in acetic acid solution under conditions reported previously[6,7,9] resulted in either the recovery of starting material or in the production of unidentified mixtures.

THE INSTITUTE OF PAPER CHEMISTRY
APPLETON, WIS.

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Amide Derivatives of D-Glucosamine

WILLIAM A. BONNER AND PHILIP I. MCNAMEE[1]

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In connection with a problem requiring the availability of sulfur-containing amide derivatives of D-glucosamine we have been interested in the development of a simple, acceptable-yield procedure for the *N*-acylation of *O*-acetylated D-glucosamine with a variety of acyl functions. Bergmann and Zervas[2] as well as Link and co-workers[3]

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[1] The authors are indebted to the U. S. Army Medical Research and Development Command (Contract DA-49-193-MD-2070) for its generous support of this investigation.

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