210°. $[\alpha]_D^{25}$ +152° (c, 1.1 $CHCl_3$); $\lambda_{max.}^{CHCl_3}$ 2.72 and 6.21 μ.

Anal.—Calcd. for $C_{22}H_{36}N_2O$: C, 76.69; H, 10.53; N, 8.13. Found: C, 76.98; H, 10.15; N, 8.31.

4H-1,4-Benzothiazino[b-2,3]-17α-methyl-5α-androst-2-en-17β-ol (VII).—2α-Bromo-17α-methyl-5α-androstan-17β-ol-3-one (V) (6) (2.0 Gm., 0.005 *M*) was dissolved in 200 ml. of refluxing ethanol through which a stream of nitrogen was passed. After the addition of 2.0 ml. of freshly distilled *o*-aminobenzenethiol, the solution was refluxed 1 hr. and allowed to stand overnight at room temperature. The reaction mixture was concentrated by distillation under nitrogen, cooled, and the resulting yellow-white precipitate collected by filtration. The product was crystallized from methanol to yield 0.9 Gm. (42%) of VII as pale yellow crystals, m.p. 215–219.5°. $[\alpha]_D^{25}$ −7.9° (c, 1.0 $CHCl_3$); $\lambda_{max.}^{CHCl_3}$ 2.72, 2.90, 6.30, and 6.81 μ.

Anal.—Calcd. for $C_{26}H_{35}NOS$: C, 76.24; H, 8.61; N, 3.42; S, 7.83. Found: C, 76.22; H, 8.78; N, 3.48; S, 7.85.

1′,2′,3′,4′-Tetrahydropyrazino[e-2,3-]5α-cholest-2-ene (IX).—2α-Bromo-5α-cholestan-3-one (VIII) (6) (7.0 Gm., 0.015 *M*) and 7.0 ml. of ethylenediamine were dissolved in 200 ml. of 1:1 chloroform–ethanol and kept at room temperature for 7 days. The reaction mixture was evaporated to dryness and the solid residue was suspended in 50 ml. of methanol and filtered to obtain 5.3 Gm. (82%) of IX as pale yellow crystals, m.p. 157–159°. $[\alpha]_D^{25}$ +142° (c, 1.1 $CHCl_3$); $\lambda_{max.}^{CHCl_3}$ 3.00–3.10 and 6.21 μ.

Anal.—Calcd. for $C_{29}H_{50}N_2$: C, 81.62; H, 11.81; N, 6.57. Found: C, 82.13; H, 11.80; N, 6.89.

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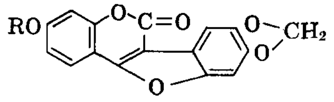
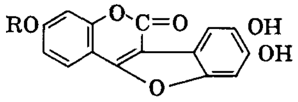
Synthesis of 7-Hydroxy-5′,6′-methylenedioxy-benzofurano (3′,2′:3,4) Coumarin (Medicagol)

By LEONARD JURD

Medicagol (I*a*) has been synthesized by hydrogen peroxide oxidation of 3-methoxy-6,7-methylenedioxy-2′,4′-dihydroxyflavylium chloride (V*b*).



I*a*, R = H
I*b*, R = Me



II*a*, R = Me
II*b*, R = H

MEDICAGOL, 7-hydroxy-5′,6′-methylenedioxy-benzofurano (3′,2′:3,4) coumarin (I*a*), co-occurs with the estrogenic benzofuranocoumarin, coumestrol (1), in alfalfa (2). A synthesis of medicagol methyl ether (I*b*) has now been reported by Fukui *et al.* (3). Modifying Wanzlick's elegant wedelolactone synthesis (4), these authors oxidized a mixture of 4-hydroxy-7-methoxycoumarin and catechol with potassium ferricyanide to give II*a*. This was methylenated to yield I*b*. The Japanese authors reported that attempts to methylenate selectively the trihydroxy compound II*b* to give I*a* were abortive. In their synthetic approach, Livingston *et al.* (2) also synthesized II*b* by Wanzlick's method. They found that methylenation of II*b* gave a mixture of products from which, by countercurrent separation and sublimation, a small quantity of medicagol was isolated (in approximately 5% yield). The recent publication of the Japanese work prompts the report of synthesis of medicagol (and its methyl ether) which is less equivocal than the above. The details of this synthesis, furthermore, may be of some use in devising possible approaches to erosnin III, a constituent of the seeds of yam beans (*Pachyrhizus erosus*) (5), and to pisatin (IV), an antifungal substance in garden peas (*Pisum sativm*) (6).

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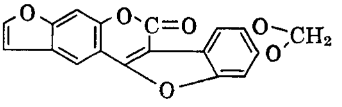
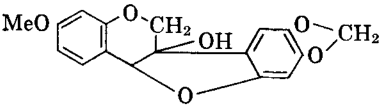
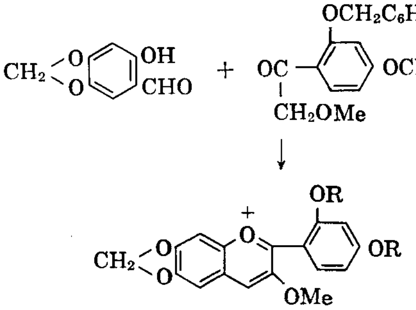


III



IV

It has been reported that peroxide oxidation of substituted flavylium salts yields 2-phenylbenzofurans (7–9). In the synthesis of medicagol, 6-hydroxypiperonal and ω-methoxy-2,4-dibenzyloxyacetophenone were condensed in acid solution to yield the dibenzyloxyflavylium salt (V*a*). This



V*a*, $R = CH_2C_6H_5$
V*b*, $R = H$

was debenzylated to give 3-methoxy-6,7-methylenedioxy-2′,4′-dihydroxyflavylium chloride (V*b*). Oxidation of V*b* with hydrogen peroxide then gave I*a*, which proved to be identical (2) with the product obtained by Livingston and his co-workers. Methylation of I*a* gave the methyl ether I*b*, whose properties are identical with those described by the Japanese authors.

EXPERIMENTAL

3 - Methoxy - 6,7 - methylenedioxy - 2′,4′ - dibenzyloxyflavylium Chloride (Va).—A solution of 6-hydroxypiperonal (1.66 Gm.) (10) and ω-methoxy-2,4-dibenzyloxyacetophenone (3.62 Gm.) (9) in ethyl acetate (25 ml.) and ether (100 ml.) was cooled in an ice bath and saturated with hydrogen chloride gas during 15 min. The flavylium salt separated as orange crystals. The mixture was maintained at 0° for 3 hr., and V*a*, m.p. 167° dec., was collected (5.40 Gm.).

3 - Methoxy - 6,7 - methylenedioxy - 2′,4′ - dihydroxyflavylium Chloride (Vb).—V*a* (3.0 Gm.) was dissolved in warm glacial acetic acid (15.0 ml.), treated with concentrated hydrochloric acid (8.0 ml.), and heated on a steam bath for 1 hr. A mass of orange-red needles separated during this period. Ten per cent aqueous hydrochloric acid (50 ml.) was added, and the flavylium salt was collected and washed with ether. Recrystallized from aqueous methanolic hydrochloric acid, V*b* separated as orange-red needles; $\lambda_{max.}$ 503, 298, 236 mμ (in ethanol containing 0.5% HCl).

7 - Acetoxy - 5′,6′ - methylenedioxybenzofurano (3′,2′:3,4) Coumarin.—Thirty per cent hydrogen peroxide (2.0 ml.) was added to a warm solution of V*b* (1.2 Gm.) in methanol (25.0 ml.) and water (12.0 ml.). The solution was allowed to stand for 30 min., diluted with water, and extracted with ether. The ether extract was washed successively with water, saturated aqueous sodium bicarbonate, and 10% aqueous hydrochloric acid, dried (Na_2SO_4), and evaporated. The oily residue was dissolved in 50% aqueous methanol (20.0 ml.), warmed, and treated with concentrated sulfuric acid (2.0 ml.). Almost colorless crystals separated at once. After 5 min., the mixture was cooled, and the product was collected. Recrystallized from a large volume of acetone–methanol, I*a* was obtained as slightly pink needles (0.32 Gm.). Although this product was chromatographically homogeneous, it was purified *via* its acetate. A solution of the product in acetic anhydride (10 ml.) and sodium acetate (0.5 Gm.) was heated to boiling for 3 min. and diluted with water. The solid acetate was recrystallized from tetrahydrofuran–methanol. 7-Acetoxy-5′,6′-methylenedioxybenzofurano (3′,2′:3,4) coumarin separated as colorless felted needles, m.p. 271°; $\lambda_{max.}$ 344, 308, 295, 281, 245 mμ (ethanol).

Anal.—Calcd. for $C_{18}H_{10}O_7$: C, 63.9; H, 2.98; 1 CH_3CO-, 12.7. Found: C, 64.0; H, 3.16; CH_3CO-, 12.9.

Medicagol (Ia).—A suspension of the above acetate (0.20 Gm.) in 50% acetone–methanol (20 ml.) was warmed with 10% aqueous sodium hydroxide (4.0 ml.) for 10 min., diluted with 10% aqueous hydrochloric acid (10.0 ml.), and warmed for a further 5 min. The crystalline product was collected and recrystallized from tetrahydrofuran–methanol. I*a* separated as cream-colored needles, m.p. 326–327° dec.; $\lambda_{max.}$ 347, 309, 245 mμ (ethanol); $\lambda_{max.}$ 365, 318, 247 mμ (ethanolic sodium acetate), $\lambda_{max.}$ 381, 318, 249 mμ (ethanolic sodium ethylate).

Anal.—Calcd. for $C_{16}H_8O_6$: C, 64.9; H, 2.72. Found: C, 65.1; H, 2.88.

Medicagol Methyl Ether (Ib).—I*a* (0.05 Gm.) was heated under reflux with dimethyl sulfate (2.0 ml.), anhydrous potassium carbonate (2.0 Gm.), and acetone (50 ml.) for 3 hr. The filtered acetone solution was concentrated and diluted with methanol. Colorless crystals separated. Recrystallized from acetone–methanol, I*b* was obtained as colorless needles, m.p. 269–270° [lit. (3) m.p. 269–270°]; $\lambda_{max.}$ 346, 308, 296, 282, 245 mμ (ethanol).

Anal.—Calcd. for $C_{17}H_{10}O_6$: C, 65.8; H, 3.25. Found: C, 65.6; H, 3.34.

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