*Anal.* Calcd. for $C_{12}H_{11}NO_2$: C, 73.2; H, 5.8; N, 4.7. Found: C, 73.5; H, 5.9; N, 4.9.

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## Synthetic Furocoumarins. III.[1] 8-Acetyl-4,5′-dimethylpsoralene

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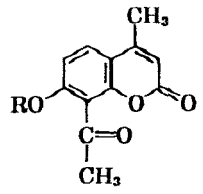
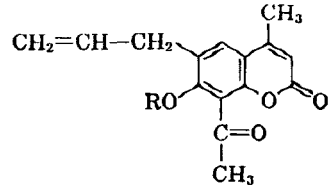
The method, described in earlier papers of this series[1] and developed for the synthesis of alkyl-substituted psoralenes, has been successfully applied to the synthesis of an acetylpsoralene. Samples of 8-acetyl-4,5′-dimethylpsoralene (VI) and its semicarbazone have thereby been made available for comparison of their photosensitizing activity with the very active 4,5′,8-trimethylpsoralene.[2] Details of the biological study are described elsewhere,[3] but it can be stated here that replacement of the 8-methyl group of 4,5′,8-trimethylpsoralene with an acetyl group or an acetylsemicarbazone group greatly reduces photosensitizing activity.

8-Acetyl-4-methyl-7-hydroxycoumarin[4] (I) was easily converted to 8-acetyl-7-allyloxy-4-methylcoumarin (II) by treatment with allyl bromide and anhydrous potassium carbonate in boiling acetone. Claisen rearrangement of II in boiling diethylaniline gave a 50% yield of 8-acetyl-6-allyl-7-hydroxy-4-methylcoumarin (III), which was characterized by the formation of an acetate (IV) with acetic anhydride and pyridine. Previous experiments[1] have shown that acetylation of 6-allyl-7-hydroxy coumarins is essential, to accomplish addition of bromine to the allyl double bond without simultaneous nuclear bromination. Acetylation was found to be unnecessary in this case, since 8-acetyl-6-allyl-7-hydroxy-4-methylcoumarin (III) smoothly added one molar equivalent of bromine to give a good yield of 8-acetyl-6-(2′,3′-dibromopropyl)-7-hydroxy-4-methylcoumarin (V). Presumably, the deactivating effect of the 8-acetyl group is sufficient to avoid nuclear bromination.

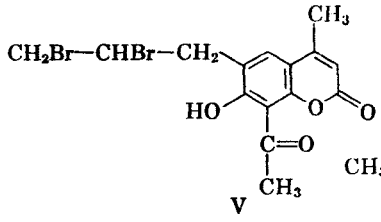
The final cyclization step presented difficulties not encountered in the synthesis of alkylpsoralenes[1,2] by this method. Treatment of V with sodium ethoxide in ethyl alcohol followed by acidification, gave a mixture of products, from which 8-acetyl-4,5′-dimethylpsoralene (VI), m.p. 165–165.5°, was



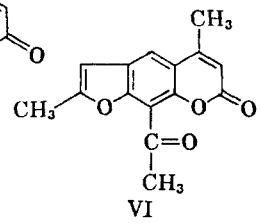
I. R = H
II. R = allyl



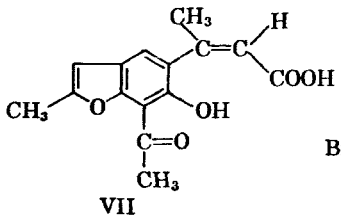
III. R = H
IV. R = acetyl



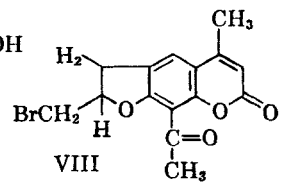
V



VI



VII



VIII

isolated in 23% yield. In addition, 46% yield of a compound having the formula $C_{15}H_{14}O_5$, m.p. 159–160°, was obtained by alkaline extraction of the mixed products. The structure of *cis*-7-acetyl-6-hydroxy-2-methylbenzofuran-5-β-methylacrylic acid (VII) appears reasonable for this compound, since coumarinic acids with a chelating group (such as acetyl) *ortho* to the hydroxyl group have been shown to be stable.[5] Its infrared spectrum was consistent with structure VII, and treatment with three milliliters of glacial acetic acid, containing one drop of concentrated hydrochloric acid at room temperature, converted it to 8-acetyl-4,5′-dimethylpsoralene (VI).

In an effort to increase the yield of VI in the cyclization, 8-acetyl-6-(2′,3′-dibromopropyl)-7-hydroxy-4-methylcoumarin (V) was refluxed in *sym*-collidine for two hours. As before, a mixture of products was obtained but, in this case, 49% yield of a bromo compound $C_{15}H_{13}O_4Br$, m.p. 134.5–135.5°, was isolated. Its ultraviolet spectrum was quite similar to that of 8-acetyl-7-allyloxy-4-methylcoumarin (II) and did not shift in basic solution. It was insoluble in aqueous 5% sodium hydroxide and no OH absorption band could be found in its infrared spectrum. Although other structures are theoretically possible, 8-acetyl-5′-bromomethyl-4′,5′-dihydro-4-methylpsoralene (VIII) appears most likely for this substance. Additional evidence is required for a definite assignment.

(1) Part II: K. D. Kaufman, F. J. Gaiser, T. D. Leth, and L. R. Worden, *J. Org. Chem., in press.*

(2) K. D. Kaufman, *J. Org. Chem.*, 26, 117 (1961).

(3) M. A. Pathak, J. B. Fellman, and K. D. Kaufman, *J. Invest. Dermatol.*, 35, 165 (1960).

(4) A. Russell and J. R. Frye, *Org. Syntheses*, 21, 25 (1941).

(5) M. Crawford and J. W. Rasburn, *J. Chem. Soc.*, 2155 (1956) and R. M. Naik and V. M. Thakor, *J. Org. Chem.*, 22, 1240 (1957).

## EXPERIMENTAL[6]

*8-Acetyl-7-allyloxy-4-methylcoumarin* (II). A mixture of 8-acetyl-7-hydroxy-4-methylcoumarin[4] (I; 58.0 g., 0.266 mole), anhydrous potassium carbonate (161 g.), allyl bromide (116 ml., 1.33 moles), and acetone (1 l.) was stirred and refluxed for 7 hr. The acetone was removed under reduced pressure, and water (3 l.) was added. An insoluble residue was collected, washed with 5% aqueus sodium hydroxide followed by water, and dried. Crystallization from ethyl acetate, using Norit, gave a colorless solid (55.4 g., 80% yield), m.p. 119.5°.

*Anal.* Calcd. for $C_{15}H_{14}O_4$: C, 69.75; H, 5.46. Found: C, 69.70; H, 5.50.

*8-Acetyl-6-allyl-7-hydroxy-4-methylcoumarin* (III). A mixture of 8-acetyl-7-allyloxy-4-methylcoumarin (48.6 g.) and diethylaniline (110 ml.) was refluxed for 1 hr. The next day, yellow needles, which had crystallized from the solution, were collected by filtration and dissolved in chloroform. Extraction with 5% aqueous sodium hydroxide followed by acidification of the alkaline solution gave a yellow solid which crystallized from ethanol as light yellow needles (16.72 g.), m.p. 134°. The diethylaniline filtrate was diluted with 5% hydrochloric acid and the solution was extracted with chloroform. Extraction with 5% aqueous sodium hydroxide followed by acidification and several crystallizations from ethanol gave an additional 6.22 g. of product. The total yield was 22.94 g. (47%).

*Anal.* Calcd. for $C_{15}H_{14}O_4$: C, 69.75; H, 5.46. Found: C, 69.90; H, 5.64.

*7-Acetoxy-8-acetyl-6-allyl-4-methylcoumarin* (IV). Acetic anhydride (2.92 ml., 0.031 mole) was added to a chilled, stirred solution of 8-acetyl-6-allyl-7-hydroxy-4-methylcoumarin (4.00 g., 0.0155 mole) in pyridine (45 ml.) at such a rate as to keep the temperature below 20°. After standing overnight at room temperature, the reaction mixture was poured into a mixture of ice and 5% hydrochloric acid (370 ml.) and a colorless solid (4.64 g., quantitative yield), m.p. 125.3–125.5°, was collected by filtration. Recrystallization from ligroin (b.p. 90–120°) did not change the melting point but gave an analytical sample of colorless felted needles.

*Anal.* Calcd. for $C_{17}H_{16}O_5$: C, 67.99; H, 5.37. Found: C, 68.40; H, 5.46.

*8-Acetyl-6-(2',3'-dibromopropyl)-7-hydroy-4-methylcoumarin* (V). A solution of bromine (3.20 g., 0.020 mole) in chloroform (15 ml.) was added slowly to a stirred solution of 8-acetyl-6-allyl-7-hydroxy-4-methylcoumarin (III; 5.17 g., 0.020 mole) in chloroform (45 ml.). Evaporation of the solvent under reduced pressure on a steam bath gave a reddish residue which crystallized from ethyl acetate as light yellow needles (6.45 g., 77% yield), m.p. 146–147.5°.

*Anal.* Calcd. for $C_{15}H_{14}O_2Br_2$: C, 43.09; H, 3.38; Br, 38.23. Found: C, 43.37; H, 3.42; Br, 38.47.

*8-Acetyl-4,5'-dimethylpsoralene* (VI). To a solution of sodium (0.575 g., 0.025 mole) in absolute ethanol (25 ml., magnesium dried) was added 8-acetyl-6-(2',3'-dibromopropyl)-7-hydroxy-4-methylcoumarin (V; 2.09 g., 0.005 mole) and the clear solution was refluxed for 1.75 hr. After cooling for 15 min., the solution was poured into a mixture (*ca.* 125 ml.) of ice and 5% hydrochloric acid (80 ml.). A yellow precipitate was collected, washed with 5% sodium hydroxide (75 ml.) in three portions followed by water, and dried to obtain an alkali-insoluble residue (0.292 g., 23% yield), m.p. 160–163.5°. Two recrystallizations from 95% ethanol gave pale yellow needles (0.216 g.), m.p. 165–165.5°.

*Anal.* Calcd. for $C_{15}H_{12}O_4$: C, 70.30; H, 4.72. Found: C, 70.05; H, 4.89.

(6) All melting points are corrected and were determined in open capillary tubes. Ultraviolet and infrared spectra were determined for all compounds and are consistent with the structures proposed.

*cis-7-Acetyl-6-hydroxy-2-methylbenzofuran-5-β-methylacrylic acid* (VII). Ice was added to the combined sodium hydroxide wash solutions (75 ml.) from above and the mixture was carefully acidified with hydrochloric acid to give a yellow precipitate. A cloudy solution of the yellow precipitate in 5% sodium bicarbonate was clarified with Norit and acidified to give a pale yellow precipitate (0.63 g., 46% yield), m.p. 159–160°. Crystallization from 95% ethanol did not change the m.p. but gave an analytical sample of yellow prisms.

*Anal.* Calcd. for $C_{15}H_{14}O_5$: C, 65.69; H, 5.14. Found: C, 66.23; H, 4.73.

A small amount of the acrylic acid (VII) was dissolved in glacial acetic acid (3 ml.) containing 1 drop of concd. hydrochloric acid at room temperature. The next day, the solution was diluted with water to obtain a precipitate, which crystallized from 95% ethanol as pale yellow needles, m.p. 165–165.5°, which did not depress the melting point of 8 acetyl-4,5'-dimethylpsoralene (VI).

*8-Acetyl-5'-bromomethyl-4',5'-dihydro-4-methylpsoralene* (VIII) (?). A suspension of 8-acetyl-6-(2',3'-dibromopropyl)-7-hydroxy-4-methylcoumarin (2.09 g., 0.005 mole) in *sym*-collidine was refluxed for 2 hr., during which time a white solid precipitated. The entire reaction mixture was poured into 5% hydrochloric acid (*ca.* 100 ml.) and an insoluble gum was taken up in chloroform. After washing the chloroform extract with 5% sodium hydroxide and water, followed by drying, the solvent was removed to leave a residue, which crystallized from 95% ethanol as yellow prisms (0.83 g., 49% yield), m.p. 131.5–133°. Another recrystallization gave an analytical sample (0.68 g.), m.p. 134–135°.

*Anal.* Calcd. for $C_{15}H_{13}O_4Br$: C, 53.43; H, 3.88; Br, 23.70. Found: C, 53.88; H, 3.98; Br, 23.61.

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## Preparation of 2-(2,2,2-Trifluoroethoxy)-1,3-butadiene

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As part of a program on the preparation of fluorine-containing dienes, we became interested in the synthesis of alkoxybutadienes.

Kadesch[1] has shown that 3,4-epoxy-1-butene reacts with methanol in the presence of sulfuric acid to give the primary alcohol, 2-methoxy-but-3-ene-1-ol and the isomeric secondary alcohol in the presence of a basic catalyst. Yields of the primary alcohol varied from 40 to 63%.

(1) R. G. Kadesch, *J. Am. Chem. Soc.*, **68**, 411 (1946).