soluble salts from acetone solutions of the initial product of the reaction.

Reaction of Tetrakis(dimethylamino)ethylene with Nitryl Perchlorate or Nitrosyl Tetrafluoroborate.—A solution containing 3.20 g of tetrakis(dimethylamino)ethylene in *n*-hexane was stirred for 6 hr with 2.20 g of nitryl perchlorate in a dry nitrogen atmosphere. The resulting solid, 4.54 g (84% yield), was a mixture of the dinitrate and diperchlorate salts and after recrystallization from water 2.50 g of the diperchlorate salt (95% yield) was recovered. This material had an infrared spectrum identical with that of an authentic sample of the diperchlorate salt and melted with decomposition at 277–279° (lit.[10] 279°).

Anal. Calcd for $C_{10}H_{24}Cl_2N_4O_8$: C, 30.08; H, 6.06; Cl, 14.04; N, 17.76. Found: C, 30.34; H, 6.09; Cl, 14.09; N, 17.64.

In the same way, 4.50 g of tetrakis(dimethylamino)ethylene and 3.00 g of nitrosyl tetrafluoroborate produced 4.35 g of solid (58% yield) which was recrystallized from methanol–water to give 2.03 g of the bis(tetrafluoroborate) salt (62% yield), mp 280–282° dec (lit.[11] 273°).

Anal. Calcd for $C_{10}H_{24}B_2F_8N_4$: C, 32.12; H, 6.47; N, 14.98. Found: C, 32.45; H, 6.70; N, 15.24.

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Synthetic Furocoumarins. VIII. The Pechmann Condensation of 2-Alkylhydroquinones

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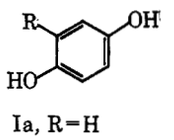
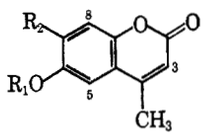
Earlier syntheses of furocoumarins have involved the use of the Pechmann condensation of hydroquinone (Ia) with acetoacetic ester to obtain 6-hydroxy-4-methylcoumarin (IIa).[1] As an extension of the earlier work, the present paper describes the preparation of two new furocoumarins from 2-methylhydroquinone (Ib). To establish their structures, it was necessary to reinvestigate the Pechmann condensation of acetoacetic ester with mono-substituted hydroquinones. Desai and Mavani[2] have studied that reaction, using 2-methyl- and 2-ethylhydroquinone. They assumed that condensation occurred at the 5 position to produce 7-alkyl-6-hydroxy-4-methylcoumarins (II, R_1 = H), but obtained no experimental evidence to exclude the isomeric 5-alkyl or 8-alkyl possibilities. Other workers[3] have made the same assumption in similar reactions. A contrary result has recently been reported[1] when 2-allylhydroquinone (Id) was treated with acetoacetic ester in the presence of concentrated sulfuric acid. It was shown that the Pechmann condensation occurred in the 3 position followed by cyclization of an intermediate *o*-allylhydroxycoumarin to produce the angular dihydrofurocoumarin (IV), although the yield was only 18% and the rest of the reaction mixture was not identified.

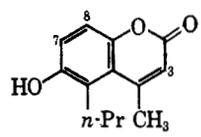
Experimental evidence has now been obtained to establish that acetoacetic ester undergoes sulfuric acid catalyzed Pechmann condensation with 2-methylhydroquinone (Ib) in the 5 position to produce 4,7-dimethyl-6-hydroxycoumarin (IIb) as originally assumed. Similar results were obtained with 2-*n*-propylhydroquinone (Ic).



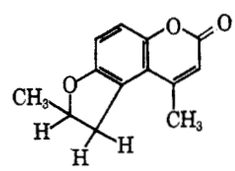
Ia, R=H
b, R=CH_3
c, R=*n*-C_3H_7
d, R=allyl



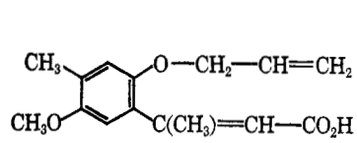
IIa, $R_1=R_2=H$
b, $R_1=H$; $R_2=CH_3$
c, $R_1=H$; $R_2=n$-C_3H_7
d, $R_1=R_2=CH_3$



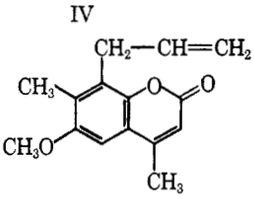
III



IV



V



VI

The nmr spectrum of 4,7-dimethyl-6-hydroxycoumarin shows two aromatic hydrogens as singlets (δ 7.02 and 7.07) The aromatic hydrogen spectrum of the coumarin from 2-*n*-propylhydroquinone is quite similar (δ 7.12 and 7.15). For comparison, the spectrum of 6-hydroxy-4-methyl-5-*n*-propylcoumarin[1] (III) was obtained and its aromatic hydrogen absorption appears as an AB multiplet (J = 9 cps, δ 7.15 and 7.17) because the two *ortho* hydrogens (7 and 8) split each other by spin coupling.[4] Since no splitting was observed in the spectra of the Pechmann condensation products, they were judged to be 7-alkylcoumarins (IIb and c), although the unknown 8-alkyl isomers could not be completely ruled out (*meta* hydrogens give weak couplings of 1–3 cps[4] which are not always seen).

Additional evidence, to eliminate the 8-alkyl possibility, was obtained from 4,7-dimethyl-6-hydroxycoumarin (IIb) by carrying out a synthetic sequence which requires that the 8 position be unsubstituted. It was converted to a methyl ether (IId), which was treated with allyl bromide and sodium hydroxide to obtain the allyloxycinnamic acid (V). When heated in boiling diethylaniline, V produced a compound ($C_{15}H_{16}O_3$) with an ultraviolet spectrum typical of 6-methoxycoumarins.[5] It must be 8-allyl-4,7-dimethyl-6-methoxycoumarin (VI) formed by *ortho* Claisen rearrangement and lactonization.

With its structure established, 4,7-dimethyl-6-hydroxycoumarin (IIb) was converted to its allyl ether (VIIa), which underwent the Claisen rearrangement in boiling diethylaniline to produce 5-allyl-4,7-dimethyl-6-hydroxycoumarin (VIIb) Ozonization, followed by catalytic hydrogenation, gave the hemiacetal (VIII)

(1) K. D. Kaufman, J. F. W. Keana, R. C. Kelly, D. W. McBride, and G. Slomp, *J. Org. Chem.*, **27**, 2567 (1962).
(2) R. D. Desai and C. K. Mavani, *Proc. Indian Acad. Sci.*, **15A**, 11 (1942).
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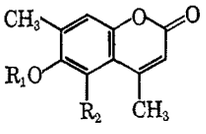
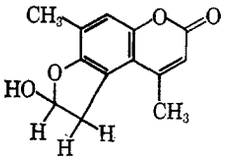
(4) H. S. Gutowsky, C. H. Holm, A. Saika, and G. A. Williams, *J. Am. Chem. Soc.*, **79**, 4596 (1957).
(5) A. Mangini and R. Passerini, *Gazz. Chim. Ital.*, **87**, 243 (1957).

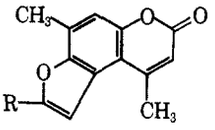
which was dehydrated to a furocoumarin (IXa) with hot 85% *o*-phosphoric acid. In another sequence, VIIb was acetylated and brominated to obtain 6-acetoxy-5-(2′,3′-dibromopropyl)-4,7-dimethylcoumarin (VIId), which was converted to a trimethylfurocoumarin (IXb) by treatment with sodium ethoxide in boiling ethanol. Both of these furocoumarins were evaluated for psoralene-like photosensitizing activity and were found to be inactive. The biological data will be included in a later publication.[6]



VIIa, R_1 = allyl; R_2 = H
b, R_1 = H; R_2 = allyl
c, R_1 = acetyl; R_2 = allyl
d, R_1 = acetyl; R_2 = $CH_2CHBrCH_2Br$



VIII



IXa, R = H
b, R = CH_3

Experimental Section

All melting points are corrected and were determined on a Fisher-Johns apparatus. Nmr spectra were observed on a Varian DP-60 spectrometer operating at 60 Mc on solutions (*ca.* 0.3 ml, *ca.* 0.15 M) of the samples in d_6-dimethyl sulfoxide. The spectra were calibrated against internal tetramethylsilane using the audio frequency side-band technique.

2-*n*-Propylhydroquinone (Ic).—Hydrogenation of 2-allylhydroquinone[1] (10.0 g) in ethyl acetate, using 5% Pd–C (1.0 g), gave colorless needles (9.4 g, 93%), mp 88–90° (lit.[7] mp 90°), after recrystallization from benzene.

6-Hydroxy-4-methyl-7-*n*-propylcoumarin (IIc).—Concentrated sulfuric acid (10 ml) was added slowly to a stirred, chilled (ice–salt bath), solution of 2-*n*-propylhydroquinone (5.0 g, 0.033 mole) in ethyl acetoacetate (5.0 g, 0.038 mole). Ice and water (*ca.* 150 g) were added to the solidified reaction mixture, after it had stood at room temperature for 25 hr. A brown solid was collected, dissolved in sodium hydroxide (5%), reprecipitated, and recrystallized three times from xylene to obtain off-white needles (6.0 g, 83%), mp 180–183°.

Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.20; H, 6.22.

4,7-Dimethyl-6-hydroxycoumarin (IIb).—A similar condensation of 2-methylhydroquinone with ethyl acetoacetate gave a quantitative yield of a red solid, mp 204–207°, suitable for use in subsequent syntheses. Recrystallization from 95% ethanol gave a sample, mp 207–208° (lit.[2] mp 208°), for spectral studies.

4,7-Dimethyl-6-methoxycoumarin (IId).—A solution of 4,7-dimethyl-6-hydroxycoumarin (29.3 g, 0.154 mole) and methyl iodide (54 ml, 0.87 mole) in acetone (1.5 l.) was stirred and heated under reflux with anhydrous potassium carbonate (92 g, 0.67 mole) for 15 hr. More methyl iodide (11 ml, 0.18 mole) was added and, after 3 more hr of reflux, the cooled reaction mixture was filtered and the filtrate was concentrated to a residue, which crystallized from benzene as colorless prisms (26 g, 83%), mp 165.5–166°. An ultraviolet spectrum in 95% ethanol showed peaks at 225 mμ (log ε 4.07), 278 (3.93), and 340 (3.81).

Anal. Calcd for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92. Found: C, 70.84; H, 5.64.

(6) The biological evaluation technique was similar to that used in M. A. Pathak, J. H. Fellman, and K. D. Kaufman, *J. Invest. Dermatol.*, **35**, 165 (1960).

(7) G. Baddely and J. Kenner, *J. Chem. Soc.*, 633 (1934).

2-Allyloxy-β,4-dimethyl-5-methoxycinnamic Acid (V).—A solution of 4,7-dimethyl-6-methoxycoumarin (2.50 g, 0.012 mole), 20% aqueous sodium hydroxide (50 ml), and 95% ethanol (100 ml) was heated in a nitrogen atmosphere under reflux for 1 hr. Allyl bromide (15 ml, 0.17 mole) was added and, after 4 more hr of reflux under nitrogen, the reaction was acidified with 10% hydrochloric acid. An oil, obtained by ether extraction, was heated under reflux (nitrogen atmosphere) with potassium hydroxide (8 g) in 75% aqueous ethanol (60 ml) for 90 min. An ether extract of the acidified reaction mixture was extracted with 5% aqueous sodium hydroxide which gave, after acidification, a brown solid that crystallized from water as yellow prisms (0.74 g, 24%), mp 87.5–88°. Additional recrystallizations from water gave an analytical sample, mp 89.5–90°. An ultraviolet spectrum in 95% ethanol showed one peak at 294 mμ (log ε 3.52).

Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.68; H, 6.91.

8-Allyl-4,7-dimethyl-6-methoxycoumarin (VI).—A solution of the cinnamic acid (V, 0.50 g) in diethylaniline (10 ml) was heated under reflux in a nitrogen atmosphere for 90 min. The solution was diluted with petroleum ether (bp 30–60°), washed repeatedly with 5% hydrochloric acid and once with 5% aqueous sodium hydroxide, and concentrated to an oil that crystallized from ligroin (*d* 0.67–0.69). Recrystallization from ligroin gave colorless needles (0.19 g, 41%), mp 80–81°. An ultraviolet spectrum in 95% ethanol showed peaks at 228 mμ (log ε 4.37), 283 (4.05), and 344 (3.86).

Anal. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.39; H, 6.47.

6-Allyloxy-4,7-dimethylcoumarin (VIIa).—A mixture of 4,7-dimethyl-6-hydroxycoumarin (100 g, 0.53 mole), allyl bromide (400 g, 3.3 moles), anhydrous potassium carbonate (300 g, 2.17 moles), and acetone (3.6 l.) was heated under reflux for 20 hr, filtered, and concentrated to a residue which crystallized from methanol as tan flakes (71.0 g, 59%), mp 148–151°. Recrystallization gave nearly colorless prisms, mp 151.5–153°, for analysis.

Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.02; H, 6.13. Found: C, 73.09; H, 6.24.

5-Allyl-4,7-dimethyl-6-hydroxycoumarin (VIIb).—A solution of 6-allyloxy-4,7-dimethylcoumarin (57.0 g) in boiling diethylaniline (600 ml) was allowed to reflux for 2 hr. Petroleum ether (3 l.) was added to the cooled solution and filtration gave tan flakes (53.0 g, 93%), mp 169–173°, a sample of which was completely soluble in 5% aqueous sodium hydroxide. Recrystallization from 95% ethanol gave off-white prisms, mp 171–173°.

Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.02; H, 6.13. Found: C, 72.81; H, 6.15.

2,3-Dihydro-4,9-dimethyl-2-hydroxy-7H-furo[3,2-*f*][1]benzopyran-7-one (VIII).—An ice-cold solution of 5-allyl-4,7-dimethyl-6-hydroxycoumarin (3.08 g, 0.0134 mole) in ethyl acetate (880 ml) was treated with ozonized (10% excess) oxygen and then hydrogenated, using 5% Pd–C (6 g). The filtered solution was concentrated to *ca.* 50 ml and cooling caused the separation of a solid, which crystallized from 95% ethanol as yellow needles (1.80 g, 58%), mp 240–242°.

Anal. Calcd for $C_{13}H_{12}O_4$: C, 67.23; H, 5.21. Found: C, 67.06; H, 4.79.

4,9-Dimethyl-7H-furo[3,2-*f*][1]benzopyran-7-one (IXa).—A mixture of VIII (1.00 g, 0.0043 mole) and 85% *o*-phosphoric acid (50 ml) was heated on a steam bath for 45 min and poured into water (400 ml). Filtration gave a solid which was washed with 5% aqueous sodium hydroxide and recrystallized from 95% ethanol to obtain colorless needles (0.877 g, 95%), mp 204–215°. Another recrystallization gave an analytical sample, mp 216.5–217°.

Anal. Calcd for $C_{13}H_{10}O_3$: C, 72.89; H, 4.71. Found: C, 72.84; H, 4.47.

6-Acetoxy-5-allyl-4,7-dimethylcoumarin (VIIc).—A solution of 5-allyl-4,7-dimethyl-6-hydroxycoumarin (35.0 g, 0.152 mole), acetic anhydride (31.2 g, 0.306 mole), and pyridine (350 ml) was stirred for 1 hr and diluted with water (*ca.* 1 l.) to obtain a colorless solid (39.6 g, 96%), mp 160–162°. Recrystallization from 95% ethanol did not change the melting point.

Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.57; H, 5.88.

6-Acetoxy-5-(2′,3′-dibromopropyl)-4,7-dimethylcoumarin (VIId).—A solution of bromine (23.3 g, 0.146 mole) in chloroform (100 ml) was added slowly to a stirred solution of 6-acetoxy-5-allyl-4,7-dimethylcoumarin (39.6 g, 0.145 mole) in chloroform

(400 ml). The solution was concentrated on a steam bath to a residue that crystallized from glacial acetic acid as colorless prisms (50.6 g, 81%), mp 167.5–169.5°.

Anal. Calcd for $C_{16}H_{16}Br_2O_4$: C, 44.47; H, 3.73; Br, 36.99. Found: C, 44.64; H, 3.81; Br, 37.08.

2,4,9-Trimethyl-7H-furo[3,2-*f*][1]benzopyran-7-one (IXb).—6-Acetoxy-5-(2′,3′-dibromopropyl)4,7-dimethylcoumarin (50.6 g, 0.117 mole) was heated under reflux for 105 min with a solution of sodium (15.0 g) in absolute ethanol (1 l.). The cooled solution was poured into a mixture of ice (*ca.* 2 kg) and 5% hydrochloric acid (*ca.* 1.5 l.) and the precipitate was washed with 5% aqueous sodium hydroxide and recrystallized from 95% ethanol to obtain colorless prisms (16.3 g, 61%), mp 218–220°.

Anal. Calcd for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30. Found: C, 73.26; H, 5.75.

Acknowledgment.—The authors are grateful for the assistance of the Upjohn Co., Kalamazoo, Mich., particularly Dr. R. C. Anderson, who provided the microcombustion analyses, and Dr. George Slomp, who provided the nmr spectra. A portion of this work was carried out under a research grant from the National Science Foundation (G-5795).

The Addition of N-Sulfinylaniline to Bicycloalkenes

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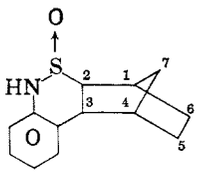
Received June 24, 1966

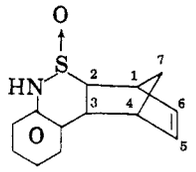
The reaction between N-sulfinylaniline[2,3] and norbornene has been reported[4] to yield adduct **1**. It was not possible however to assign an *exo* or *endo* configura-



1

tion to adduct **1** based on its nmr spectrum. It has been well established that *exo* adducts are formed exclusively when norbornene is treated with suitable reagents such as aryl azides,[5] or nitrosyl chloride.[6] The *exo* configuration for **1** is therefore likely *a priori;* definite proof of this configuration will be presented below.

Refluxing equimolar quantities of N-sulfinylaniline and norbornadiene yielded two products, adduct **2** with mp 186–187° (42% yield), and an adduct **3**, mp 306–307° (22% yield). Elemental analyses indicated that the former compound was a 1:1 adduct, and the latter a 2:1 adduct. The infrared spectra of both adducts exhibited N–H and S–O stretching frequencies.



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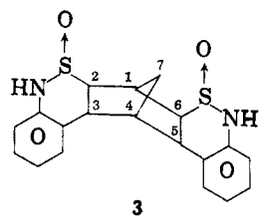
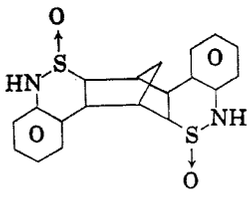


3

The hydrogenation of **2** at room temperature with palladium-over-carbon catalyst yielded **1** which established that compounds **1** and **2** have either both the *exo* configuration or both the *endo* configuration. That **2**, and consequently **1**, is the *exo* adduct may be concluded by examining its nmr spectrum,[7] which may be interpreted as follows: a multiplet from 2.65 to 3.20, which integrated for four phenyl protons; $H_{5,6}$, signal at 3.49; $H_{2,3}$ at 6.65–6.68; H_1 at 6.70; H_4 at 6.99; $H_{7\,syn}$ at 7.90; and $H_{7\,anti}$ at 8.45. The signal at 6.70 was designated for H_1 since the presence of sulfur was considered to effect the bridgehead proton H_1 more so than the phenyl group effects the bridgehead proton H_4.

Consistent values for the major coupling constants between various protons of norbornane derivatives have been reported.[8–10] The coupling constant for H_1 and $H_{2\,exo}$ was reported to fall in the range 3.8–5.6 cps, while the J value for H_1 and $H_{2\,endo}$ was approximately 1 cps. The presence of an *exo* proton in compound **2** should thus cause quite noticeable splitting with the bridgehead proton. In the observed spectrum however the bridgehead protons ($H_{1,4}$) are only very slightly split, $J < 1$ cps, indicative of the presence of an *endo* proton on C-2. It is clear then that compound **2** has the *exo* configuration. This also holds true for adduct **1** since it may be formed by the hydrogenation of **2**.

For compound **3** the nmr spectrum may be interpreted as follows: a multiplet from 2.45 to 3.10 which integrates for eight phenyl protons; $H_{2,3,5,6}$ signal at 6.02; H, at 6.69; H_4 at 7.42; and $H_{7\,anti}$, $H_{7\,syn}$ at 7.90. The bridgehead protons ($H_{1,4}$) are very slightly split, $J < 1$ cps, and thus indicative of *exo* addition. The nonequivalence of H_1 and H_4 confirmed the structure of the adduct as **3**, since in the alternate possibility (**4**) the bridgehead protons become equivalent.



4

Treatment of adducts **1**, **2**, and **3** with lithium aluminum hydride in tetrahydrofuran at room temperature or at reflux led to essentially quantitative recovery of the starting materials. Adduct **2** when treated with 30% hydrogen peroxide in acetic acid yielded the epoxy

(1) Abstracted from the Ph.D. dissertation of A. Macaluso presented to Tulane University, 1965.

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