droxide, and extracted with ether. Distillation at 0.3 mm. gave 9.7 g. of mono-oxide, m.p. 38–39°. Experiments using two equivalents of hydrogen peroxide, or at higher temperatures gave the same mono-oxide in poorer yields. A solution in chloroform showed strong absorption at 1325 cm.$^{-1}$

Anal. Calcd. for $C_4H_4N_2O$: C, 50.0; H, 4.2; N, 29.2' Found: C, 50.4; H, 4.1; N, 29.0.

Pyridazine mono-oxide reacted vigorously with phosphorus oxychloride, but no pure product could be isolated.

MINNEAPOLIS, MINN.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Condensation of 3-Acetylcoumarin with Acetone and Amines[1]

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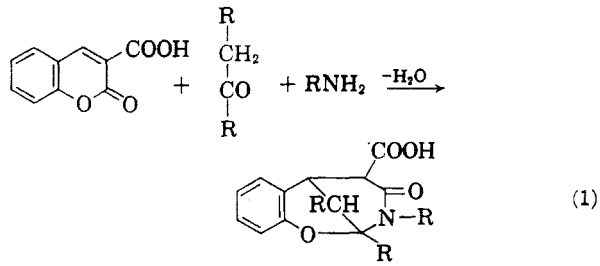
Received May 26, 1958

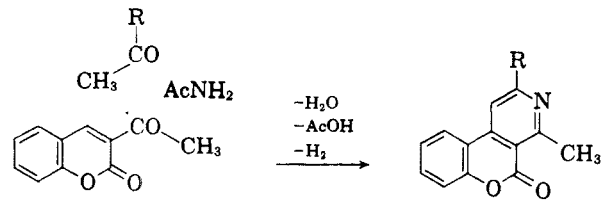
3-Acetylcoumarin reacts with acetone and certain primary amines to form *N*-substituted derivatives of 9-amino-7-methyl-6-dibenzo[*bd*]pyrone, I, in yields of 10–47%.

It has been shown that condensation of 3-coumarincarboxylic acid with ketones and amines yields bridged 8-membered ring compounds.[2]



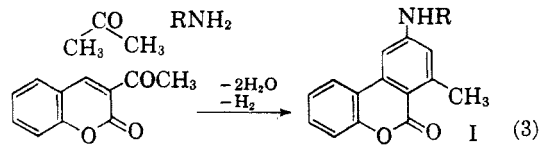
(1)

Further, the reaction of 3-acetylcoumarin with ketones and amides yields pyridocoumarins.[3]



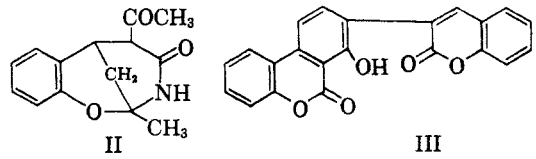
(2)

It has now been found that 3-acetylcoumarin reacts with acetone and amines to form aminobenzocoumarins, I.

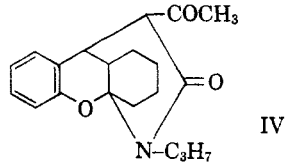


(3)

The amines used were aniline (yield 12.6%), *p*-chloroaniline (15.8%), *n*-butylamine (10.5%), isopropylamine (47%), and cyclohexylamine (40%). Other bases, *t*-butyl, benzyl, and hydroxyethylamine, gave no crystalline products. Ammonia reacted according to (1) forming II, and piperidine yielded III, the self-condensation product of 3-acetylcoumarin.[4]

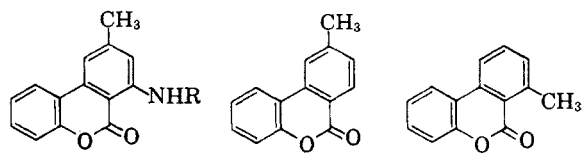


Ketones other than acetone were not thoroughly studied. Diethylketone with isopropylamine gave no crystalline product, whereas cyclohexanone, sterically prevented from forming a compound like I, reacted according to (1) forming IV.



The structures of the products were established by analysis and chemical properties. Although the substances were generally insoluble in dilute aqueous hydrochloric acid, crystalline hydrobromides and acetyl derivatives were formed. The lactone ring in I (R = C_6H_5) was opened when the compound was boiled with alcoholic alkali; acidification of the resulting solution regenerated I, whereas treatment with methyl sulfate gave a methoxy acid and a methoxy ester. Saponification of the ester was difficult but led to the methoxy acid.

That the products were secondary amines of structure I rather than V was proved by degrada-



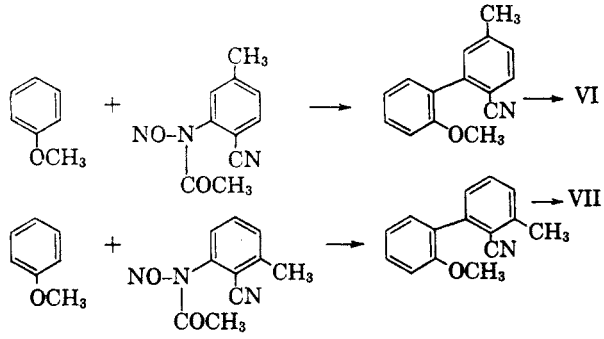
(1) From the Ph.D. Thesis of H. D. Embree, July 1952.

(2) C. F. Koelsch and M. C. Freerks, *J. Org. Chem.*, **18**, 1538 (1953).

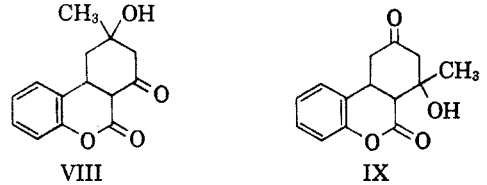
(3) C. F. Koelsch and S. A. Sundet, *J. Am. Chem. Soc.*, **72**, 168 (1950).

(4) C. F. Koelsch and S. A. Sundet, *J. Am. Chem. Soc.*, **72**, 1844 (1950).

tion to VII. This was accomplished by pyrolysis of the hydrobromide of I (R = C_3H_7 and C_6H_{11}), giving I (R = H). The primary amine was then deaminated (HNO_2, H_3PO_2) to VII. For comparison VI and VII were synthesized by standard methods.



In a previous study[4] it was shown that reaction of acetone with 3-acetocoumarin involved a Michael reaction and an aldol cyclization, and the product was formulated as VIII. This product has now been found to react with isopropylamine to form I, R = C_3H_7. Although not conclusive evidence against VIII, this indicates that the aldol cyclization took place in a different way, and that the compound formerly represented as VIII is actually IX.



EXPERIMENTAL

9-Anilino-7-methyl-6-dibenzo[bd]pyrone. I, R = C_6H_5. A mixture of 94 g. of 3-acetylcoumarin, 91 ml. of aniline, 57 ml. of acetic acid, and 500 ml. of acetone was stirred at room temperature for 24 hr. The orange precipitate was then removed, washed with acetone and alcohol, and dried. This material, 25 g., m.p. 220–246°, could not be purified. To convert it into I, 5 g. of it was stirred with 20 ml. of acetic acid at 80–100° for 3 hr. while a slow stream of air was passed through. Cooling to room temperature then gave 3.8 g. of product, m.p. 266–270°. A sample distilled (b.p. 318–320° at 9 mm.) and recrystallized from pyridine had m.p. 271.5–272.5°.

Anal. Calcd. for $C_{20}H_{15}NO_2$: C, 79.8; H, 5.0; N, 4.65. Found: C, 79.7; H, 5.3; N, 4.4.

The compound was nearly insoluble in common organic solvents, in hot aqueous alkali or 10% hydrochloric acid. It was moderately soluble in chloroform or ethyl acetate, and quite soluble in hot dioxan, acetic acid, or pyridine. It dissolved in alcoholic sodium hydroxide giving a water-soluble salt from which the original compound was precipitated by acids.

9-(p-Chloroanilino)-7-methyl-6-dibenzo[bd]pyrone was obtained from 9.4 g. of acetylcoumarin, 12.8 g. of *p*-chloroaniline, 5.7 ml. of acetic acid, and 50 ml. of acetone. The intermediate dihydro compound (3.4 g., m.p. 296–310°) was aerated in hot acetic acid. The product formed colorless needles from pyridine, m.p. 314–316° with darkening.

Anal. Calcd. for $C_{20}H_{14}ClNO_2$: C, 71.6; H, 4.2; N, 4.2. Found: C, 71.3; H, 4.1; N, 4.2.

9-n-Butylamino-7-methyl-6-dibenzo[bd]pyrone. I, R = C_4H_9. A mixture of 9.4 g. of 3-acetylcoumarin, 7.3 g. of butylamine, 5.7 ml. of acetic acid, and 50 ml. of acetone kept for 24 hr. gave 1.8 g. of solid product. Extraction of this with 100 ml. of warm acetone left 0.1 g. of III, the self-condensation product of acetylcoumarin, and concentration of the extract gave 1.63 g., m.p. 163–167°. A portion of this (0.56 g.) in 7 ml. of alcohol containing 0.23 g. of quinone was boiled for 30 min. Cooling gave 0.51 g. of nearly pure product, crystals from dilute acetic acid, m.p. 169–170°.

Anal. Calcd. for $C_{18}H_{19}NO_2$: C, 76.8; H, 6.8; N, 5.0. Found: C, 76.5; H, 6.5; N, 4.9.

The compound was insoluble in 10% sodium hydroxide or 10% hydrochloric acid.

9-Isopropylamino-7-methyl-6-dibenzo[bd]pyrone. I, R = C_3H_7. A mixture of 9.4 g. of 3-acetylcoumarin 5.9 g. of isopropylamine, 5.7 ml. of acetic acid, and 50 ml. of acetone gave 6.8 g. of solid, m.p. 186–193°; concentration of the mother liquor gave 0.8 g. more. The melting point of this material often varied in similar experiments sometimes being as low as 175–181°. This had little significance in the ultimate quantity of product, and probably depended on the proportion of aromatized substance formed by accidental dehydrogenation. Two grams of the solid and 0.84 g. of quinone heated in 60 ml. of alcohol for 1 hr. gave 1.65 g. of product, colorless needles from alcohol, m.p. 196–197°.

Anal. Calcd. for $C_{17}H_{17}NO_2$: C, 76.4; H, 6.4; N, 5.2. Found: C, 76.3; H, 6.4; N, 5.6.

Although the amine was insoluble in aqueous hydrochloric acid, treatment of an alcoholic solution with hydrogen bromide and ether converted it quantitatively into its *hydrobromide*, colorless needles, m.p. 251–252° dec.

Anal. Calcd. for $C_{17}H_{18}BrNO_2$: Br, 23.0. Found: Br, 23.3.

When the amine was warmed with acetic anhydride containing potassium acetate it was converted into its *acetyl derivative*, colorless prisms from benzene-ligroin, m.p. 188–189°.

Anal. Calcd. for $C_{19}H_{19}NO_3$: C, 73.8; H, 6.2; N, 4.5. Found: C, 74.0; H, 6.2; N, 4.6.

9-Cyclohexylamino-7-methyl-6-dibenzo[bd]pyrone. I, R = C_6H_{11}. When acetic acid was used as in the previous condensations, only about 4% of product was obtained. The low yield was due mainly to insolubility of cyclohexylamine acetate, and was greatly improved by use of butyric acid. Use of butyric acid in the previous condensations gave results no better, and in some cases worse than acetic acid.

A mixture of 9.4 g. of 3-acetylcoumarin, 9.9 g. of cyclohexylamine, 8.8 g. of butyric acid, and 50 ml. of acetone kept for 22 hr. gave 9.2 g., m.p. 190–197°. Two grams of this and 0.7 g. of quinone in 50 ml. of alcohol heated for 30 min. gave 1.33 g., m.p. 168–169° (dehydrogenation by aeration in hot acetic acid or benzene was not effective). Recrystallized from alcohol, the product had m.p. 168.5–169.3°.

Anal. Calcd. for $C_{20}H_{20}NO_2$: C, 78.4; H, 6.6; N, 4.6. Found: C, 78.2; H, 7.0; N, 4.8.

The compound was insoluble in aqueous hydrochloric acid; but alcoholic hydrogen bromide gave the *hydrobromide*, fine colorless needles from alcohol-ether, m.p. 238–239.5° dec.

Anal. Calcd. for $C_{20}H_{21}BrNO_2$: Br, 20.6. Found: Br, 21.1.

The *acetyl derivative* formed colorless prisms from benzene-ligroin or alcohol, m.p. 182–183°.

Anal. Calcd. for $C_{22}H_{23}NO_3$: C, 75.7; H, 6.6; N, 4.0. Found: C, 75.4; H, 6.9; N, 4.2.

Methylation of I, R = C_6H_5. A solution of 2 g. of sodium hydroxide and 3.25 g. of I, R = C_6H_5 in 90 ml. of alcohol was heated for 45 min. and then diluted with 30 ml. of water and distilled. The residue was dissolved in 20 ml. of water, treated with 3.2 g. of methyl sulfate, and stirred for 1 hr. The mixture was centrifuged to remove ester, and then acidified. The precipitate (2.7 g.) was extracted with 10% sodium bicarbonate, leaving 1.3 g. of I. Acidification of the extract gave 1.7 g. of crude *5-anilino-3-methyl 2'-methoxybiphenyl-2-carboxylic acid*, m.p. 174–176° dec. Recrystallization from dilute alcohol and then dilute acetic acid gave colorless needles, m.p. 181–182° dec.

Anal. Calcd. for $C_{21}H_{19}NO_3$: C, 75.6; H, 5.8; N, 4.2; N.E. 333. Found: C, 75.4; H, 5.8; N, 4.4; Neut. Equiv. 335.

When the methylation was carried out in alcohol using a 3-fold excess of methyl sulfate the product was the *methyl ester*, colorless needles from alcohol or benzene—ligroin, m.p. 127–128°.

Anal. Calcd. for $C_{22}H_{21}NO_3$: C, 76.0; H, 6.1; N, 4.0. Found: C, 75.8; H, 6.3; N, 4.4.

The ester was resistant to saponification; 0.4 g. of it heated for 8 hr. with excess 10% alcoholic potash gave only 0.1 g. of the acid.

Dealkylation of I, R = cyclohexyl or isopropyl. When 2 g. of the hydrobromide of I, R = C_6H_{11} was heated for 1 hr. in a bath at 255–260°, cyclohexene was evolved. The residue was dissolved in 60 ml. of hot alcohol, filtered, and treated with aqueous sodium carbonate, giving 1.1 g. of *9-amino-7-methyl-6-dibenzo[b.d]pyrone, I, R=H*, faintly tan needles from alcohol, m.p. 192–193°.

Anal. Calcd. for $C_{14}H_{11}NO_2$: C, 74.7; H, 4.9; N, 6.2. Found: C, 75.0; H, 5.0; N, 6.5.

Pyrolysis of the iso-propyl analog gave the same product in a yield of 95%.

Deamination of I, R = H. A suspension of 3.7 g. of the hydrobromide of I, R = H in 30 ml. of 18% hydrochloric acid was stirred at 0° and treated with 0.83 g. of sodium nitrite in a little water. The diazonium salt separated and the mixture became pasty. After 30 min., 16 g. of 50% hypophosphorus acid in an equal volume of water was added. Nitrogen evolution caused severe foaming requiring the use of a large flask for the preparation. After 12 hr. at 0°, the mixture was diluted and extracted with chloroform. Colored impurities were removed by passing the chloroform solution through a short column of alumina. Crystallization from benzene-ligroin gave 1.7 g. of 7-methyl-6-dibenzo (b,d) pyrone (VII), m.p. 101–102° alone or mixed with a sample synthesized as described below.

Anal. Calcd. for $C_{14}H_{10}O_2$: C, 80.0; H, 4.8. Found: C, 80.1; 80.4; H, 4.7, 5.1.

7-Methyl-6-dibenzo[bd]pyrone (VII). A mixture of 16.3 of 3-amino-2-cyanotoluene,[5] 145 ml. of acetic acid, 70 ml. of acetic anhydride, and 11 g. of potassium acetate was boiled for 20 min. and then cooled to 0°. One gram of phosphorus pentoxide was added, followed by a solution of 8.5 g. of nitrosyl chloride in 50 ml. of acetic anhydride. The mixture was kept at 0° for 30 min., then poured into one liter of ice water. The oily nitroso compound was extracted with 250 + 150 ml. of anisole. The anisole extract was washed with water, 75 ml. of anisole being used to rinse the funnel. Addition of 40 g. of sodium sulfate and 20 g. of potassium carbonate brought about evolution of nitrogen and change to a deep red color. The mixture was kept for 12 hr. at room temperature, then filtered and distilled. After anisole had been removed, the main fraction came over at 133–136° at 0.15 mm. as a pale yellow oil. When a solution of this oil in ether-ligroin was kept for two days at room temperature, it deposited colorless prisms, 1.5 g., m.p. 152–153° or 154–155° after sublimation and recrystallization. This was a by-product of unknown structure that gave only resins when treated with hot hydrobromic acid.

Anal. Calcd. for $C_{14}H_{15}N_3O$: C, 69.7; H, 6.24; N, 17.4. Found: C, 69.7; H, 6.1; N, 16.3.

The main product was a yellow oil. A mixture of 1.5 g. of it with 20 ml. of concentrated hydrochloric acid was heated at 180° for 3 hr. Dilution with water, extraction with chloroform, and distillation gave 0.7 g., b.p. 170–174° at 1 mm. Crystallization from alcohol and then benzene-ligroin gave colorless needles (0.4 g.), m.p. 101–102°, identical with the previously described substance.

9-Methyl-6-dibenzo[bd]pyrone (VI). A mixture of 28.5 g. of 3-amino-4-cyanotoluene,[6] 250 ml. of acetic acid, 120 ml. of acetic anhydride, and 20 g. of potassium acetate was boiled for 20 min., then cooled to 5°. One gram of phosphorus pentoxide was added, followed by 15.4 g. of nitrosyl chloride in 90 ml. of cold acetic anhydride. After one hour, the mixture was poured into 2.5 liters of ice water. The crystalline nitroso compound was collected, washed with water, and pressed as dry as possible (35 g., m.p. 70–72° dec.). It was then dissolved in 800 ml. of anisole containing a little potassium carbonate, and kept at room temperature for 12 hr. or until nitrogen evolution ceased. Filtration and distillation gave anisole and then 21 g. of crude product, b.p. 150–155° at 0.6 mm. Crystallization from ether-ligroin and then alcohol gave 7.7 g., m.p. 94–95°. Sublimation and recrystallization from alcohol gave pure *2-cyano-2'-methoxy-3-methylbiphenyl*, m.p. 96–97°.

Anal. Calcd. for $C_{15}H_{13}NO$: C, 80.7; H, 5.9; N, 6.3. Found: C, 80.7; H, 6.1; N, 6.3.

A mixture of 4 ml. of acetic acid, 4 ml. of 48% hydrobromic acid, and 0.75 g. of the cyano compound was boiled for 4 hr. and then diluted with water, giving 0.54 g. of crude product, m.p. 101–102°. The material was dissolved in hot alcoholic sodium hydroxide, treated with charcoal, precipitated by acidification, and recrystallized from alcohol giving colorless needles, m.p. 102.5–103°. A mixture with the isomeric 7-methyl derivative had m.p. 62–65°.

Anal. Calcd. for $C_{14}H_{10}O_2$: C, 80.0; H, 4.8. Found: C, 80.2; H, 4.8.

Condensation of acetylcoumarin with acetone and ammonia. A mixture of 9.4 g. of acetylcoumarin, 7.7 g. of ammonium acetate, and 50 ml. of acetone was stirred at room temperature for 16 hr. The white precipitate was removed, washed with acetone, alcohol, and water and then dried; yield 7.2 g., m.p. 222–226°. In another preparation 7.0 g. of product was obtained after only 4 hr. Again, 7 g. of product was obtained when only 7.3 ml. of acetone was used and the mixture was heated on a water bath for 20 min. Crystallization from acetic acid gave colorless prisms, m.p. 226–227°. The compound gave a deep purple color with alcoholic ferric chloride; it was not affected by aeration in hot acetic acid. It was insoluble in 10% hydrochloric acid or 20% sulfuric acid. Hot 10% sodium hydroxide slowly dissolved it. These properties suggest that the compound is II, *2-amino-2-methylchroman-4,α-acetoacetic acid lactam.*

Anal. Calcd. for $C_{14}H_{15}NO_3$: C, 68.6; H, 6.1; N, 5.7. Found: C, 68.6; H, 6.4; N, 5.4.

Condensation of acetylcoumarin with cyclohexanone and isopropylamine. A mixture of 9.4 g. of 3-acetylcoumarin, 5.9 g. of isopropylamine, 8.8 g. of butyric acid, and 50 ml. of cyclohexanone was stirred at room temperature for 24 hr. About 10 mg. of III was removed by filtration and most of the cyclohexanone by distillation under reduced pressure. The residue was dissolved in ether, washed with bicarbonate, concentrated and cooled for six days, giving 5.7 g. of crude crystalline product. Recrystallization from alcohol gave nearly colorless plates, m.p. 137.5–138.5°. The properties of the compound, insolubility in dilute acid and deep green color with alcoholic ferric chloride, indicate structure IV, *2-isopropylamino-2,3-tetramethylenechroman-4,α-acetoacetic acid lactam.*

Anal. Calcd. for $C_{20}H_{24}NO_3$: C, 73.6: H, 7.4: N, 4.3. Found: C, 73.6: H, 7.7: N, 4.4.

Reaction of the aldol IX *with Isopropylamine.* A mixture of 0.5 g. of the aldol prepared by Sundet,[4] 1 g. of isopropylamine, 1 ml. of acetic acid, and 15 ml. of acetone was stirred at room temperature for 22 hr., then filtered and concentrated. The resulting crystals were boiled in 6 ml. of alcohol with 0.2 g. of quinone for 30 min. The crystalline product was washed with alcohol, giving 0.3 g. of 7-methyl-9-isopropylamino-6-dibenzo[bd]pyrone, m.p. 195–196.5°.

MINNEAPOLIS, MINN.

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(6) S. Niementowski, *Ber.*, **21**, 1535 (1888); G. Glock, *Ber.*, **21**, 2662 (1888); G. T. Morgan and E. A. Coulson, *J. Chem. Soc.*, 2551 (1929).