and the suspension was boiled under reflux for 20 min. and filtered hot. To the cooled filtrate, 44 ml. of concentrated ammonia was added, and the whitish suspension was immediately extracted with six successive portions of ether. The ether extracts were combined, dried with anhydrous sodium sulfate, filtered, and the filtrate was evaporated to dryness, affording 4.4 g. of a brown syrup (A). This was dissolved in 100 ml. of absolute ethanol and concentrated hydrochloric acid was added dropwise, with gentle swirling, until the solution was faintly acid to Methyl Orange. The solution was evaporated to dryness under diminished pressure, and a further 100 ml. of absolute ethanol was added and evaporated off, affording a mass of colorless crystals which were stirred with 25 ml. of absolute ethanol and filtered off. A total of 6.5 g. of base A, treated in this way, gave (in 3 successive crops) 6.7 g. of colorless, crystalline hydrochloride monohydrate; m.p. 218–227° (dec.). Recrystallized from boiling absolute ethanol (10 vol.) by cooling, it had m.p. 232–235°. Its infrared absorption spectrum agreed with the proposed structure.

Anal. Calcd. for $C_{12}H_{15}Cl_2N_3.HCl.H_2O$: C, 44.12; H, 5.55; Cl, 32.56; N, 12.86. Found: C, 44.16; H, 5.57; Cl, 33.33; N, 12.32.

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Condensation of 4,6,7-Trimethyl-5-hydroxyisocoumaranone with Carbonyl Compounds

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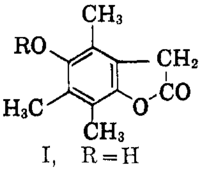
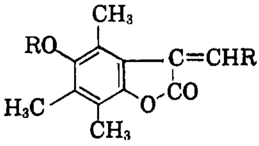
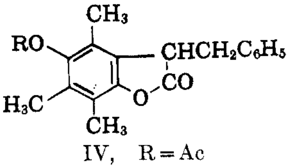
In connection with other work, some experiments have been made upon the condensation of the isocoumaranone I (R = H)[2] with aldehydes and ketones, leading to products having structure II. It was found that I could be condensed with aromatic aldehydes (benzaldehyde, anisaldehyde), and with cinnamaldehyde, although in the latter case the product was a mixture which could not be separated into pure compounds. Two ketones (2-pentanone and acetophenone) failed to give any reaction, and the one aliphatic aldehyde tried, butyraldehyde, gave a very low yield of the product derived from one mole of the aldehyde and two of the isocoumaranone.



I, R=H



II, R=H; R′=C_6H_5
III, R=Ac; R′=C_6H_5



IV, R=Ac
V, R=H

The reaction between I (R = H) and benzaldehyde was investigated in some detail. The product II (R = H; R′ = C_6H_5) resulted in 43% yield when aniline was used as condensing agent, and in 81% yield when piperidine was used. This material was converted into the monoacetate III by action of acetic anhydride. Catalytic reduction of III gave the benzyl derivative IV, and IV was also prepared by acetylation of V, prepared by catalytic hydrogenation of II. Hydrogenation of II gave a mixture of products which could not be separated by crystallization, but from which, after acetylation, IV could be isolated. The yellow alcoholic solution of II became colorless as reduction was completed, but when this colorless solution was exposed to air, it rapidly acquired a yellow color. Doubtless reduction of II proceeded beyond the stage of V, with opening of the coumaranone ring and formation of a hydroquinone. A pure specimen of V, however, could not be obtained, either by reduction of II, or by hydrolysis of IV.

Originally it was hoped that I could be condensed with glyoxal in such a way that two molecules of I would be connected by a butadiene chain. However, all attempts in this direction met with failure—use of glyoxal in aqueous alcoholic solution, or of glyoxal bisulfite compound as a source of anhydrous glyoxal, in air or under nitrogen led to dark, opaque solutions from which only dark, high-melting, insoluble solids could be isolated in small yields. No better success was had with benzil as the dicarbonyl compound. In this case, there was apparently no reaction at all, for most of the starting materials could be isolated unchanged from the reaction mixture.

EXPERIMENTAL[3]

3-Benzal-4,6,7-trimethyl-5-hydroxyisocoumaranone (II). A solution of I (5.6 g., 0.029 mole), benzaldehyde (freshly distilled, 2.9 cc., 0.029 mole) and piperidine (8 drops) in dry ethanol (130 cc.) was heated at 55–60° under a nitrogen atmosphere for 3 days. The cooled reaction mixture deposited II (6.6 g., 81%) melting at 182.5–184.5°. The analytical sample, recrystallized three times from aqueous ethanol, formed yellow needles which melted at 184.0–184.7°.

Anal. Calcd. for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75. Found: C, 77.33; H, 5.95.

Substitution of aniline for piperidine in the above experiment resulted in a much lower yield (43%) of II; failure to provide an atmosphere of nitrogen, or to use anhydrous conditions, also resulted in a lower yield. The use of sodium ethoxide in place of piperidine resulted in complete failure; the product consisted of tars and unchanged starting materials.

3-Benzal-4,6,7-trimethyl-5-acetoxyisocoumaranone (III). The isocoumaranone II (1.0 g.) was added to acetic anhy-

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[1] From the Ph.D. thesis of Richard N. Hurd, University of Minnesota, September 1956.

[2] L. I. Smith and C. W. MacMullen, *J. Am. Chem. Soc.*, **58**, 629 (1936).

[3] Microanalyses by the Microanalytical Laboratory of the University of Minnesota.

dride (50 cc.) containing sulfuric acid (4 drops). The apparatus was flushed with nitrogen and the solution was heated for 12 hr. at 60°. The product (1.14 g.), isolated in the usual way and recrystallized twice from ethyl acetate, melted at 198.5–199.5°.

Anal. Calcd. for $C_{20}H_{18}O_4$: C, 74.51; H, 5.62. Found: C, 74.39; H, 5.61.

3-Benzyl-4,6,7-trimethyl-5-acetoxyisocoumaranone (IV). A solution of III (0.5 g.) in ethyl acetate (150 cc., distilled over phosphorus pentoxide) was subjected at room temperature to action of hydrogen (29 lb.) in the presence of a platinum oxide catalyst (0.1 g.). In an hour the yellow color disappeared and the absorption of hydrogen ceased. The catalyst was removed and ethyl acetate was removed from the filtrate by distillation. The residual yellow oil (0.44 g.) solidified and then melted at 116–119°. The analytical sample, recrystallized twice from ethanol, melted at 118.5–120°.

Anal. Calcd. for $C_{20}H_{20}O_4$: C, 74.05; H, 6.21. Found: C, 74.40; H, 6.41.

3-Benzyl-4,6,7-trimethyl-5-hydroxyisocoumaranone (V). A solution of II (4.4 g.) in dry ethanol (150 cc.) was subjected at room temperature to the action of hydrogen (36 lb.) in the presence of a platinum oxide catalyst (0.22 g.). The amber solution became yellow in 30 min., pale green in an hour, and colorless after 6 hr. After 22 hr., the catalyst was removed by filtration; the filtrate immediately acquired a yellow color in the air. Most of the solvent (142 cc.) was removed, and the dark residue on standing for some time at 0°, deposited an orange solid (2.22 g.). Most of this material melted at 112–121° to a yellow liquid, but complete melting occurred only when the temperature reached 142°. No pure material could be isolated from this solid by repeated crystallization, but when the material (0.4 g.) was acetylated in the usual way by the action of acetic anhydride, there resulted a solid (0.3 g.) which could be separated into two components by crystallization from absolute ethanol. The major component (0.25 g.) was the acetate IV, m.p., and mixed m.p., 119–120°. The other component (0.01 g.) was insoluble in ethanol and melted at 219–220.5° to a yellow liquid. It was not investigated further. Hydrolysis of the acetate V (0.87 g.) by action of a solution of potassium hydroxide (1.25 g.) in ethanol (25 cc.) for 5 hr. at the boiling point led to a minute amount of brown infusible solid, and a dark oil (0.45 g.) which, by crystallization, gave a small amount of orange solid melting indefinitely at 120–140°. No better results were obtained when V (0.3 g.) was subjected to action of sodium methoxide (from sodium, 0.05 g., and dry methanol, 30 cc.) in an atmosphere of nitrogen.

3-Anisal-4,6,7-trimethyl-5-hydroxyisocoumaranone (II, $R=H$; $R' = p\text{-}CH_3OC_6H_4$). A solution of I (1.0 g., 0.005 mole), anisaldehyde (0.63 cc., 0.005 mole), and piperidine (5 drops) in dry ethanol (25 cc.) was processed under nitrogen as described above for preparation of II. The product (1.16 g.) formed bright yellow needles which, after crystallization from ethanol, melted at 170.5–172°.

Anal. Calcd. for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85. Found: C, 72.94; H, 5.96.

3-Anisal-4,6,7-trimethyl-5-acetoxyisocoumaranone (III, $R' = p\text{-}CH_3OC_6H_4$) was prepared as described above for III. The analytical sample was recrystallized from acetone, when it melted at 222–223° with some sublimation. The compound held water tenaciously and required a long period of drying under vacuum in a pistol before it became anhydrous.

Anal. Calcd. for $C_{21}H_{20}O_5$: C, 71.57; H, 5.72. Found: C, 71.70; H, 5.91.

Reaction of cinnamaldehyde with I. A solution of I (3 g., 0.015 mole), cinnamaldehyde (1.78 cc., 0.015 mole), and piperidine (5 drops) in dry ethanol (75 cc.) was processed under nitrogen as described above for II. The product (4.38 g.) when dried was a reddish solid melting at 155–175°. Recrystallization of this material from 1:1 ethanol-ligroin (b.p. 30–60°) gave three crops of solid materials: (A) rust colored, melting at 196–206°; (B) brownish, melting at 195–205°; (C) yellow, melting at 170–180°. No pure materials could be obtained from (B) or (C), but (A), after crystallization four times from acetone-ethanol, yielded small yellow needles melting at 271–273° to a red liquid. This material decomposed when heated slowly—even at 150–170° for 10 min.

Anal. Found: C, 73.61, 74.52; H, 6.93, 6.21.

Reaction of butyraldehyde with I. The above procedure was applied to the reaction of I (1 g.), butyraldehyde (0.44 cc.), and piperidine (12 drops) in dry ethanol (25 cc.). The reaction mixture, when poured into water, deposited an oil which later solidified. Recrystallization of this material several times from ethanol yielded I (0.17 g.) and a yellow solid (0.01 g.) melting at 218.5–221°; which was formed from two moles of I and one mole of isobutyraldehyde.

Anal. Calcd. for $C_{26}H_{30}O_6$: C, 71.24; H, 6.85. Found: C, 71.34; H, 6.79.

Reactions of ketones with I. When either 2-pentanone or acetophenone was used with I and piperidine, the only product isolated was recovered I plus a minute amount of infusible dark solid.

Reaction of glyoxal with I. (A) Solution of I (1 g.), aqueous glyoxal (33%, 0.46 g.), and piperidine (3 drops) in ethanol (25 cc.) was processed as described. A black powder (0.55 g.) and tar were the only products. The black material did not melt below 350°; when extracted with ethanol in a Soxhlet apparatus, only a little I was obtained. (B) Substitution of aniline for piperidine gave essentially the same results—recovery of I (0.56 g. from 1 g.) and production of a dark infusible powder. (C) Glyoxal bisulfite (1.035 g.) was dissolved in hydrochloric acid (5%, 53 cc.), the solution was evaporated to dryness, and the residue was extracted with dry ethanol (50 cc.). To this extract, I (1.5 g.) and pyridine (2 drops) were added and the reaction mixture was processed as above. The product consisted of recovered I (0.53 g.) and a small amount (0.02 g.) of dark infusible material. In a duplicate experiment, except that glyoxal was prepared from the bisulfite compound by action of potassium carbonate, I (2.0 g.) yielded only a black solid in small amount, and 0.92 g. of I was recovered.

Reaction of benzil with I. A solution of I (1 g.), benzil (0.52 g.), acetic acid (3 drops), and piperidine (9 drops) in dry ethanol (40 cc.) was processed as above. The cooled solution deposited a small amount of black infusible material, and the filtrate from this, when concentrated, gave 0.67 g. of solid. The rest of the product was a black tar. The solid, extracted with hexane, gave only I (insoluble) and benzil (soluble).

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Convenient Synthesis of Pyrrocoline[1]

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Although pyrrocoline is one of the fundamental aromatic heterocycles, its chemistry has not been extensively investigated nor has a satisfactory synthesis for the parent compound been devised. The most general method of synthesis for this class of compounds is that developed by Chichibabin[2] and

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(1) This investigation was aided by a grant from the National Science Foundation.

(2) A. E. Chichibabin, *Ber.*, **60**, 1607 (1927).