Acetylation of Methyl Methoxycoumarilates and the Synthesis of 7-Methyl-9H-furo[3,2-*f*][1]benzopyran-9-one[1]

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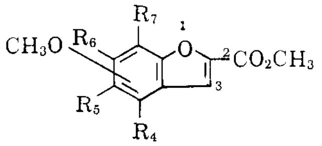
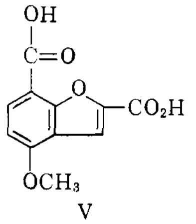
In an effort to synthesize those furanochromone ring systems not at this time known to occur in nature, 7-methyl-9H-furo[3,2-*f*][1]benzopyran-9-one (XII) has been made. Boron trifluoride–acetic acid-catalyzed acetylation of methyl 4- and 7-methoxycoumarilates occurred *para* to the methoxyl group; in the 5-methoxy isomer, attack took place at the 4-position; in the 6-methoxy isomer, 5- and 7-acetyl-6-hydroxycoumarilates were obtained.

Electrophilic attack on methyl or ethyl coumarilates takes place at the 5-position in chloromethylation[2] and nitration.[3] In the search for approaches to as yet unknown furanochrome ring systems[4] we have undertaken the investigation of the point of attack in the acetylation of methyl 4-, 5-, 6-, and 7-methoxycoumarilates (I–IV). Only in the case of II and III did acetylation occur *ortho* to the methoxyl group so as to allow the preparation of furanochromones.

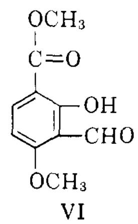


I. $4\text{-}CH_3O$; $R = H$
II. $5\text{-}CH_3O$; $R = H$
III. $6\text{-}CH_3O$; $R = H$
IV. $7\text{-}CH_3O$; $R = H$

Methyl 4-methoxycoumarilate (I), on acetylation in boron trifluoride-acetic acid[5] gave I ($R_7 = CH_3CO$) in 88% yield. The structure of I ($R_7 = CH_3CO$) was established by oxidation to a dicarboxylic acid V which was obtained in an independent synthesis by conversion of VI to methyl 5-methoxycoumarin-8-carboxylate.



V

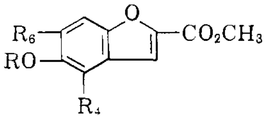


VI

Bromination of the coumarin and alkaline treatment of the bromocoumarin gave V, identical to the dicarboxylic acid previously obtained in the oxidation of I ($R_7 = CH_3CO$). The dimethyl esters from the two sources were also shown to be identical.

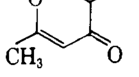
The Beckmann rearrangement of the oxime of I ($R_7 = CH_3CO$) gave methyl 7-acetylamino-4-methoxycoumarilate which was hydrolyzed and then esterified to produce methyl 7-amino-4-methoxycoumarilate.

The acetylation of II in boron trifluoride–acetic acid–acetic anhydride at room temperature for eighty hours gave a product (96%) which contained a free hydroxyl group. This behavior suggested that the position of attack was 4- or 6-, *ortho* to the methoxyl position, to yield either VII or VIII. Further, it was demonstrated that acetylation with retention of the methoxyl group was possible if the reaction was terminated after nine hours (73% yield of IX or its 6-acetyl isomer). The phenolic product VII on methylation produced IX. That acetylation occurred at position 4 was established by catalytic reduction of IX to X and its conversion to 4-ethyl-5-methoxybenzofuran. The synthesis of 6-ethyl-5-methoxybenzofuran provided material clearly not identical to the ethyl compound derived from the above acetylation. This isomeric 6-ethyl compound was obtained by acetylation of 1,4-dimethoxy-2-ethylbenzene to yield 4-ethyl-2-hydroxy-5-methoxyacetophenone which was brominated to a phenacyl bromide. Cyclization then gave 6-ethyl-5-methoxycoumaran-3-one. Lithium aluminum hydride reduced the latter to 6-ethyl-5-methoxybenzofuran.



VII. $R = H$; $R_4 = CH_3CO$; $R_6 = H$
VIII. $R = H$; $R_4 = H$; $R_6 = CH_3CO$
IX. $R = CH_3$; $R_4 = CH_3CO$; $R_6 = H$
X. $R = CH_3$; $R_4 = C_2H_5$; $R_6 = H$
XI. $R = CH_2$; $R_4 = H$; $R_6 = C_2H_5$

By saponification and decarboxylation of VII followed by condensation of the product with ethyl acetate, the new furanochromone XII was obtained. It represents the first reported example of a 9H-furo[3,2-*f*][1]benzopyran-9-one ring system.



XII

The boron trifluoride acetylation of III required a modification of the procedure[5] due to the formation of isomeric nonphenolic compounds which were not easily separable. If the reaction temperature was allowed to rise and remain at 80° during the introduction of the boron trifluoride, the acetylation occurred with cleavage to XIII and XIV, which were separable due to the insolubility of XIII in hot methanol. The structure assigned to these isomers rests on the saponification and decarboxylation of the less soluble product to XVII,

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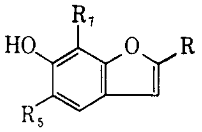
[1] This investigation was supported by a Public Health Service grant CY-4817 from the National Cancer Institute, Public Health Service.

[2] A. L. Mndzhoyan and A. A. Aroyan, *Izv. Akad. Nauk Arm. SSR, Khim. Nauki*, **11**, 45 (1958); *Chem. Abstr.*, **53**, 3185 (1959). E. L. Martin, U. S. Patent 2,754,286; *Chem. Abstr.*, **51**, 920 (1957). E. I. du Pont de Nemours and Co., British Patent 705,950; *Chem. Abstr.*, **49**, 2233 (1955).

[3] S. Tanaka, *J. Chem. Soc. Japan*, **73**, 282 (1952).

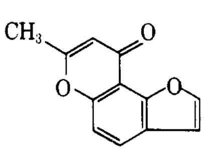
[4] Three of the six possible isomeric furanochromone ring systems are presently found in the literature due to their occurrence in natural products.

[5] W. J. Horton and M. G. Stout, *J. Org. Chem.*, **26**, 1221 (1961).

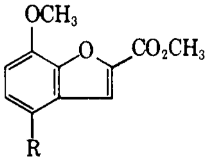


XIII. R = CO_2CH_3; R_5 = CH_3CO; R_7 = H
XIV. R = CO_2CH_3; R_5 = H; R_7 = CH_3CO
XV. R = CO_2H; R_5 = CH_3CO; R_7 = H
XVI. R = CO_2H; R_5 = H, R_7 = CH_3CO
XVII. R = H; R_5 = CH_3CO; R_7 = H
XVIII. R = H; R_5 = H; R_7 = CH_3CO

m.p. 95°. This compound is reported to melt at 96°.[6] Analogous treatment of the methanol-soluble isomer XIV gave a benzofuran XVIII, m.p. 117–118°. The condensation of XVIII with ethyl acetate and cyclization of the acetoacetyl compound with sulfuric acid gave the furanochromone XIX.



XIX



XX. R = CH_3CO
XXI. R = C_2H_5
XXII. R = NH_2

A boron trifluoride-catalyzed acetylation of IV at 30° with standing at room temperature overnight, gave an acetyl compound XX in 75% yield and similar acetylation of methyl 7-hydroxycoumarilate gave methyl 4-aceto-7-hydroxycoumarilate (79%) since methylation of the latter gave XX. The choice of the 4-position as the point of attack arose from the elimination of position 6 due to the retention of the methoxyl in the acetylation reaction. Further, the infrared spectra indicated the absence of a hydrogen bond in the acetyl-7-hydroxybenzofuran obtained from the hydroxycoumarilate ester. Position 5 was eliminated by the synthesis of 5-ethyl-7-methoxycoumarilic acid (m.p. 205–206°) whereas catalytic reduction of XX and saponification gave 4-ethyl-7-methoxycoumarilic acid (m.p. 187–188°).

The synthesis of 5-ethyl-7-methoxycoumarilic acid required the preparation of 4-ethyl-2-methoxyphenol from acetovanillone by Clemmensen reduction. This phenol, by a modification of the Duff reaction,[7] gave 5-ethyl-2-hydroxy-3-methoxybenzaldehyde (39%) which was converted to 5-ethyl-7-methoxycoumarilic acid by reaction with sodium ethoxide–methyl bromoacetate and saponification.

Unsuspected support for the structure XX came, during the course of our work, from a publication[8] in which XXII was reported. We obtained XXII by a Beckmann rearrangement of the oxime of XX, followed by hydrolysis. The similarity in the melting points supports the contention that XX represents the acylation product.

Saponification and decarboxylation of XX gave 4-acetyl-7-methoxybenzofuran. The oxidation of this to 7-methoxybenzofuran-4-carboxylic acid was desired so as to establish the structure of the reported 7-methoxybenzofuran-x-carboxylic acid.[9] However, oxidation of our compound with sodium hypochlorite unexpectedly gave 2-(?)chloro-7-methoxybenzofuran-4-carboxylic acid.

Experimental[10]

Methyl β-resorcylate was formylated according to Shah[11] and the product was selectively methylated[12] to yield VI. After saponification, the benzoic acid was decarboxylated to 2-hydroxy-6-methoxybenzaldehyde in 97% yield by heating 1.2 g. in 30 ml. of water at 150° for 5 hr. in a sealed tube. The aldehyde melted at 71–74° and at 74–75° after crystallization from ethanol–water; reported[12] m.p. 75°.

4-Methoxycoumarilic Acid.—A solution of 1.5 g. of sodium in 40 ml. of anhydrous ethanol was added dropwise over a 3.5-hr. period to a refluxing solution containing 5.3 g. of the above aldehyde and 3.5 ml. of methyl bromoacetate in 20 ml. of absolute ethanol. After a total of 7 hr. of refluxing followed by standing overnight, a solution of 1.5 g. of potassium hydroxide in 20 ml. of water was added and the alcohol was removed at once by distillation. After acidification of the residue and standing overnight, the solid was filtered, washed with water, and dissolved in excess sodium bicarbonate. The bicarbonate solution was washed with ether and the aqueous layer was then acidified. The 4-methoxycoumarilic acid weighed 6.0 g. (90%), m.p. 175–185°. Recrystallization from aqueous alcohol gave material, m.p. 204–205°; reported[13] m.p. 203–204°.

Methanolic hydrogen chloride esterification gave I (75%), m.p. 75–82° raised to m.p. 97–99° by recrystallization from alcohol; reported[12] m.p. 99–100°.

Methyl 7-Acetyl-4-methoxycoumarilate (I. R_7 = CH_3CO).—A solution containing 2 g. of I in 70 ml. of acetic acid was treated with boron trifluoride (58 g.) with occasional cooling so as to hold the temperature below 30°. After standing for 48 hr. at room temperature, the solution was poured into ice and water, the solid which separated was filtered and washed with cold water and then dissolved in 60 ml. of hot ethanol. On addition of 100 ml. of water and cooling, 2 g. (88%) of solid, m.p. 179–182°, was obtained. This was recrystallized from aqueous ethanol to yield light tan needles, m.p. 188–189° (Kofl.); $\lambda_{\max}^{\text{alc}}$ 228, 268.5, 292 mμ (ε 15,000, 21,200, 17,600) $\lambda_{\text{infl}}^{\text{alc}}$ 306 mμ (ε 14,800).

Anal. Calcd. for $C_{13}H_{12}O_5$: C, 62.90; H, 4.88. Found: C, 63.00; H, 5.12.

The oxime melted at 183.4–184.8° after crystallization from ethanol.

Anal. Calcd. for $C_{13}H_{13}NO_5$: C, 59.31; H, 4.98. Found: C, 59.35; H, 5.04.

Saponification gave 7-acetyl-4-methoxycoumarilic acid (90%), m.p. 237–244°. Recrystallization from alcohol–water gave light tan needles, m.p. 248–249° (Kofl.); $\lambda_{\max}^{\text{alc}}$ 227.5, 264, 295.5 mμ (ε 13,600, 18,100, 16,000).

Anal. Calcd. for $C_{12}H_{10}O_5$: C, 61.56; H, 4.31. Found: C, 61.75; H, 4.44.

7-Carboxy-4-methoxycoumarilic Acid (V).—A 200-ml. portion of commercial bleach (5.24% sodium hypochlorite) was treated with 4 g. of sodium hydroxide. One-half gram of 7-acetyl-4-methoxycoumarilic acid was dissolved in 180 ml. of the hypochlorite solution and heated to 85° for 10 min. followed by 20 min. at 80°. The solution was cooled and the excess oxidant was removed by the addition of sodium bisulfite. On acidification, 0.38 g. (75%) of material, m.p. 280–340°, was obtained. Recrystallization from aqueous ethanol gave needles, m.p. 360° (sealed tube; dec.).

Anal. Calcd. for $C_{11}H_8O_6$: C, 55.93; H, 3.39. Found: C, 55.78; H, 3.51.

The dimethyl ester of V, by esterification of V in methanolic hydrogen chloride, melted at 168.6–169.4° after several crystallizations from alcohol.

Anal. Calcd. for $C_{13}H_{12}O_6$: C, 59.09; H, 4.58. Found: C, 59.17; H, 5.08.

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[6] J. S. H. Davies, P. A. McCrea, W. L. Norris, and G. R. Ramage, *J. Chem. Soc.*, 3206 (1950).

[7] L. M. Liggett and H. Diehl, *Proc. Iowa Acad. Sci.*, **52**, 191 (1945); *Chem. Abstr.*, **41**, 110 (1947).

[8] G. Rodighiero and U. Fornasiero, *Gazz. chim. ital.*, **91**, 90 (1961).

[9] W. B. Whalley, *J. Chem. Soc.*, 3479 (1953).

[10] Melting points of analytically pure materials are corrected.

[11] R. C. Shah and M. C. Laiwalla, *J. Chem. Soc.*, 1828 (1938).

[12] D. B. Limaye, *Rasayanam*, **1**, 1 (1936); *Chem. Abstr.*, **31**, 2206 (1937).

[13] A. Roedig and S. Schödel, *Chem. Ber.*, **91**, 330 (1958).

Methyl 5-Methoxycoumarin-8-carboxylate.—The ester VI (1.3 g.) was heated at 180° with 1.5 g. of fused sodium acetate in 2 ml. of acetic anhydride for 8 hr. Acidification of the cooled solution with dilute hydrochloric acid gave 1.2 g. (72%), m.p. 170–175°. Crystallization from ethanol–water gave light yellow needles, m.p. 181.2–181.9°; $\lambda^{\text{alc}}_{\text{max}}$ 217, 255, 297.5 mμ (ϵ 21,500, 14,900, 13,400).

Anal. Calcd. for $C_{12}H_{10}O_5$: C, 61.56; H, 4.31. Found: C, 61.29; H, 4.40.

Methyl 3-Bromo-5-methoxycoumarin-8-carboxylate.—A solution containing 1.16 g. of the above coumarin in 30 ml. of acetic acid was treated with 4 ml. of 1.25 *M* bromine–acetic acid solution with shaking. The solution was heated in a sealed tube for 2 hr. at 120°. After cooling to 0°, some suspended matter was removed by filtration and discarded. Water was added until the solution was turbid and after standing at 0° for 5 hr., 1.08 g. (69%) of crystals was obtained. These formed colorless needles from methanol, m.p. 197.6–198.4°; $\lambda^{\text{alc}}_{\text{max}}$ 217, 258, 310 mμ (ϵ 22,800, 16,200, 17,000).

Anal. Calcd. for $C_{12}H_9BrO_5$: C, 46.03; H, 2.90. Found: C, 46.23; H, 3.25.

Methyl 7-Carbomethoxy-4-methoxycoumarilate.—One-half gram of the above crude bromocoumarin was heated for 2 hr. on the steam bath with 10 ml. of 20% sodium hydroxide. Cooling and acidification with hydrochloric acid gave material melting above 300°. Esterification of the diacid with methanolic hydrogen chloride gave 0.45 g. (84%) of diester which was recrystallized from methanol, m.p. 168.0–169.3° undepressed when mixed with the diester obtained from 7-acetyl-4-methoxycoumarilic acid. The infrared spectra of the two esters were identical; $\lambda^{\text{alc}}_{\text{max}}$ 229, 261, 285 mμ (ϵ 25,800, 12,400, 18,700).

Anal. Calcd. for $C_{13}H_{12}O_6$: C, 59.09; H, 4.58. Found: C, 58.91; H, 4.94.

Methyl 7-Amino-4-methoxycoumarilate.—The oxime of I (R_7 = CH_3CO) (500 mg.) in 300 ml. of benzene was combined with 500 mg. of phosphorus pentachloride and shaken vigorously for 10 min. followed by refluxing for 45 min. The residue, after distillation of the benzene, was combined with water. The solid methyl 7-acetylamino-4-methoxycoumarilate (480 mg., m.p. 185–200°) gave colorless needles from aqueous alcohol, m.p. 200.8–201.4°.

Anal. Calcd. for $C_{13}H_{13}NO_5$: C, 59.31; H, 4.98. Found: C, 59.26; H, 4.91.

Hydrolysis of the acetylamino compound (350 mg.) in 40 ml. of hydrochloric acid–ethanol (1:1) by refluxing for 4 hr. followed by esterification with 5% methanolic hydrogen chloride gave 320 mg. of the hydrochloride of methyl 7-amino-4-methoxycoumarilate, m.p. 156–162°. From benzene–alcohol, colorless needles, m.p. 166.5–168° (Kofl.), were obtained.

Anal. Calcd. for $C_{11}H_{12}ClNO_4$: C, 51.27; H, 4.70. Found: C, 51.32; H, 4.97.

The free amine from 250 mg. of hydrochloride, by careful neutralization with 5% sodium hydroxide, weighed 200 mg., m.p. 129–132°. Recrystallization from 25% ethanol gave yellow needles, m.p. 134.0–134.8°.

Anal. Calcd. for $C_{11}H_{11}NO_4$: C, 59.72; H, 5.01. Found: C, 59.46; H, 5.20.

Methyl 5-Methoxycoumarilate (II).—2-Hydroxy-5-methoxybenzaldehyde was prepared as reported[14] in 35% yield. It was converted to 5-methoxycoumarilic acid,[15] m.p. 215–217°; reported m.p. 212–213°[15] and 217°.[9] Esterification of 19.2 g. of the acid in methanolic hydrogen chloride gave 18 g. (87.5%) of II, m.p. 76–78°. From aqueous methanol, material melting at 77.8–78.6° was obtained; $\lambda^{\text{alc}}_{\text{max}}$ 271, 316.5 mμ (ϵ 19,500, 5610).

Anal. Calcd. for $C_{11}H_{10}O_4$: C, 64.07; H, 4.89. Found: C, 63.97; H, 5.00.

Methyl 4-Acetyl-5-hydroxycoumarilate (VII).—The boron trifluoride acetylation of 8.24 g. of the above ester in acetic acid–acetic anhydride[5] with 237 g. of boron trifluoride and standing for 80 hr. gave a yellow, water-insoluble complex which was decomposed by boiling in 850 ml. of ethanol for 30 min. Addition of an equal volume of water and cooling gave 9.0 g. (96%) of a slightly yellow solid, m.p. 195–199°. Repeated crystallization from benzene gave colorless prisms, m.p. 196.2–197.8°. The color with ferric chloride was dark brown; λ^{CHCl_3} 5.78, 6.13 μ; $\lambda^{\text{alc}}_{\text{max}}$ 231, 296, 351 mμ (ϵ 12,400, 17,500, 8440).

Anal. Calcd. for $C_{12}H_{10}O_5$: C, 61.56; H, 4.31. Found: C, 61.44; H, 4.33.

From the mother liquors in the purification of VII, an isomeric compound, presumed to be methyl 6-acetyl-5-hydroxycoumarilate (VIII), was obtained in small amount. After numerous crystallizations from ethanol, yellow prisms melting at 133–135° (Kofl.) were obtained. These gave a deep brown ferric chloride test.

Anal. Calcd. for $C_{12}H_{10}O_5$: C, 61.56; H, 4.31. Found: C, 61.56; H, 4.89.

When the above acetylation was repeated on 4.12 g. with 96.5 g. of boron trifluoride and standing for 9 hr., a colorless complex appeared when the reaction mixture was poured into water. This on treatment as before with 240 ml. of 1:1 ethanol–water gave 3.6 g. of IX (72.6%), m.p. 135–138°. Colorless needles formed from ethanol, m.p. 144.5–145.5°; $\lambda^{\text{alc}}_{\text{max}}$ 231, 293, 338 mμ (ϵ 13,600, 14,900, 8290).

Anal. Calcd. for $C_{13}H_{12}O_5$: C, 62.90; H, 4.88. Found: C, 63.20; H, 5.11.

The ethylene thioketal of IX was prepared[16] by dissolving 1.85 g. of the compound in 8 ml. of acetic acid by warming on the steam bath. To this warm solution was added 2 ml. of distilled boron trifluoride etherate and 2 ml. of ethane dithiol. The solution was stirred at room temperature for 22 hr. and poured into 100 ml. of ice–water. The precipitate, after crystallization from ethanol, weighed 1.85 g., m.p. 100–104°. Further crystallization gave thioketal, m.p. 111.4–112.6°; $\lambda^{\text{alc}}_{\text{max}}$ 205.5, 278 mμ (ϵ 24,300, 23,300); $\lambda^{\text{alc}}_{\text{infl}}$ 316 mμ (ϵ 4960).

Anal. Calcd. for $C_{15}H_{16}O_4S_2$: C, 55.53; H, 4.97. Found: C, 55.19; H, 5.13.

Attempted reduction of this thioketal using Raney nickel (not modified) and ethanol[17] with refluxing for 21 hr. gave only an oil. This after saponification gave a small amount of a solid which did not depress the melting point of 4-ethyl-5-methoxycoumarilic acid obtained below.

4-Acetyl-5-methoxycoumarilic Acid.—(a) Potassium hydroxide saponification of IX gave the colorless acid (91%), m.p. 220–225°. The sample for analysis formed colorless needles from ethanol, m.p. 236.5–238.0°; $\lambda^{\text{alc}}_{\text{max}}$ 235.5, 293.5, 336 mμ (ϵ 16,800, 15,400, 9440).

Anal. Calcd. for $C_{12}H_{10}O_5$: C, 61.56; H, 4.31. Found: C, 61.62; H, 4.38.

(b) A solution containing 2.3 g. of VII in 20 ml. of water with 1.0 g. of sodium hydroxide was treated below 35° with 1 ml. of methyl sulfate. To the reaction mixture was then added a solution of 0.5 g. of sodium hydroxide in 5 ml. of water. After stirring for 8 hr. and heating on the water bath for 1 hr. the acid was precipitated by acidification. It melted at 220–225° and, on crystallization from ethanol, at 234–236°, not depressed when mixed with material from (a).

Methyl 4-Ethyl-5-methoxycoumarilate (X).—Hydrogenation[18] of 2 g. of IX with 400 mg. of 10% palladium–carbon in 50 ml. of acetic acid at room temperature and a pressure slightly above atmospheric, proceeded slowly over a 2-hr. period (271 ml. of hydrogen absorbed). The hydrogenation rate was then accelerated by the addition of 1 drop of 70% perchloric acid[19] (240 ml. of hydrogen over 3.25 hr.). The catalyst was filtered and washed with acetic acid. Addition of 200 ml. of water to the filtrate gave crystals on standing, m.p. 67–69°. These were crystallized from petroleum ether (b.p. 30–60°) for analysis, m.p. 71.4–72.4°. The tests with ferric chloride and with 2,4-dinitrophenylhydrazine were negative; $\lambda^{\text{alc}}_{\text{max}}$ 279 mμ (ϵ 22,300); $\lambda^{\text{alc}}_{\text{infl}}$ 318 mμ (ϵ 3520).

Anal. Calcd. for $C_{13}H_{14}O_4$: C, 66.65; H, 6.02. Found: C, 66.35; H, 6.05.

Saponification of this ester gave 4-ethyl-5-methoxycoumarilic acid (92%) which formed colorless needles from aqueous methanol (2:1), m.p. 163.0–164.4°; $\lambda^{\text{alc}}_{\text{max}}$ 203, 275.5 mμ (ϵ 22,800, 22,300); $\lambda^{\text{alc}}_{\text{infl}}$ 311 mμ (ϵ 3480).

Anal. Calcd. for $C_{12}H_{12}O_4$: C, 65.44; H, 5.50. Found: C, 65.50; H, 5.55.

4-Ethyl-5-methoxybenzofuran.—The above coumarilic acid (500 mg.) with 250 ml. of copper powder in 15 ml. of quinoline was heated at 230–240° for 30 min. The filtered quinoline was combined with 100 ml. of ether and washed three times with 5% hydrochloric acid and with water. After drying over sodium sulfate, the ether was distilled leaving a deep brown oil which crystallized on cooling. This on sublimation at 40–70° (0.08

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(14) L. Rubenstein, *J. Chem. Soc.*, **127**, 1999 (1925).

(15) S. Tanaka, *J. Am. Chem. Soc.*, **73**, 872 (1951).

(16) L. F. Fieser, *ibid.*, **76**, 1945 (1954).

(17) S. Bernstein and L. Dorfman, *ibid.*, **68**, 1152 (1946).

(18) R. T. Foster and A. Robertson, *J. Chem. Soc.*, 921 (1939).

(19) K. W. Rosenmund and E. Karg, *Ber.*, **75B**, 1850 (1942).

mm.)(sublimer temp.) gave 200 mg., m.p. 53.6–55.8°. A second sublimation gave colorless crystals with a naphthalene-like odor, m.p. 56.8–57.8°; $\lambda_{\max}^{\text{alc}}$ 248.5, 292 mμ (ϵ 12,800, 3380).

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.87. Found: C, 74.90; H, 6.89.

4′-Ethyl-2′-hydroxy-5′-methoxyacetophenone.—The Clemmensen reduction of 2′,5′-dimethoxyacetophenone[20] gave 1,4-dimethoxy-2-ethylbenzene in 90% yield, b.p. 80° (2 mm.); reported[21] b.p. 232°. The boron trifluoride-catalyzed acetylation of this ethylbenzene, with omission of acetic anhydride, produced a reddish precipitate when the reaction was poured into water. This boron complex was dissolved in 25 ml. of hot ethanol, cooled, and diluted with water. An oil separated which was extracted with ether. The ether was then washed with 5% sodium hydroxide and the basic washes acidified yielding 2.8 g. (55%) of 4′-ethyl-2′-hydroxy-5′-methoxyacetophenone, m.p. 60.4–61° after crystallization from ethanol; reported m.p. 60°.[21] The ferric chloride test produced a violet color. The compound had $\lambda_{\max}^{\text{alc}}$ 265, 353 mμ (ϵ 12,600, 10,000).

The colorless acetate from petroleum ether (b.p. 80–120°) melted at 82.6–83°.

Anal. Calcd. for $C_{13}H_{16}O_4$: C, 66.08, H, 6.82. Found: C, 66.14; H, 6.71.

The oxime from aqueous methanol melted at 128–129°.

Anal. Calcd. for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23. Found: C, 62.91; H, 7.25.

On evaporation of the washed and dried ether layer, 1.4 g. (25%) of 2′,5′-dimethoxy-4′-ethylacetophenone was obtained. After crystallization from ethanol, the needle-shaped crystals melted at 76.4–76.8°; $\lambda_{\max}^{\text{alc}}$ 260, 330 mμ (ϵ 9500, 5400).

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.20; H, 7.74. Found: C, 69.29; H, 7.73.

The reaction of 1.2 g. of the dimethoxy compound with 6% hydrogen bromide–acetic acid at room temperature for 4.5 hr. gave 100 mg. (9%) of the above 2-hydroxyacetophenone. A yield of this order would be predicted under these reaction conditions for 2-methoxyacetophenones lacking a substituent in the 3-position.[20]

Methylation of the cleaved product of the boron trifluoride acetylation above gave 2′,5′-dimethoxy-4′-ethylacetophenone, m.p. 76–78° undepressed when mixed with the sample analyzed above.

2-Bromo-4′-ethyl-2′-hydroxy-5′-methoxyacetophenone.—To 1.2 g. of the hydroxyacetophenone above in 50 ml. of acetic acid a solution of 0.36 g. of bromine in 10 ml. of acetic acid was added slowly with continuous stirring over the course of 2 hr. After 5 hr. stirring at room temperature, the mixture was poured into ice–water and extracted with chloroform. A solid (1 g.) was obtained on evaporation of the chloroform. From methanol, the phenacyl bromide was obtained as yellowish crystals, m.p. 75.0–76.0°; $\lambda_{\max}^{\text{alc}}$ 220.5, 266, 361.5 mμ (ϵ 12,900, 8160, 4920).

Anal. Calcd. for $C_{11}H_{13}BrO_3$: C, 48.37; H, 4.80. Found: C, 48.35; H, 4.97.

The addition of 0.5 ml. of bromine to 1.9 g. of the hydroxyacetophenone in 10 ml. of anhydrous ether containing a trace of aluminum chloride gave 3′-bromo-4′-ethyl-2′-hydroxy-5′-methoxyacetophenone which formed pale yellow needles from methanol, m.p. 83°.

Anal. Calcd. for $C_{11}H_{13}BrO_3$: C, 48.37; H, 4.80. Found: C, 48.27; H, 4.95.

6-Ethyl-5-methoxycoumaran-3-one.—Sodium acetate cyclization[22] of 1.1 g. of the phenacyl bromide gave 1 g. of the coumaranone. From a small amount of methanol, yellow crystals, m.p. 121.6–122.0°, were obtained; $\lambda_{\max}^{\text{alc}}$ 258 mμ (ϵ 13,400) λ^{CHCl_3} 5.85 μ.

Anal. Calcd. for $C_{11}H_{12}O_3$: C, 68.73; H, 6.29. Found: C, 68.43; H, 6.25.

6-Ethyl-5-methoxybenzofuran.—A solution of 1 g. of the above coumaranone in 25 ml. of anhydrous ether was added slowly to a suspension of 0.5 g. of lithium aluminum hydride in ether. After refluxing for 4 hr. the excess reagent was decomposed by the addition of ethyl acetate. Dilute hydrochloric acid was added, the product, in ether, was washed with water, dried, and distilled, b.p. 55–60° (0.2 mm.). The yellow oil gave $\lambda_{\max}^{\text{alc}}$ 246, 290 mμ (ϵ 11,800, 5420) and had no carbonyl band in the infrared region. The liquid was seeded with a crystal of the 4-ethyl-5-methoxy isomer but this did not induce crystallization. The infrared spectra was not identical to the 4-ethyl-5-methoxy isomer.

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.91; H, 6.87. Found: C, 75.30; H, 6.89.

4-Acetyl-5-hydroxycoumarilic Acid.—Saponification of VII gave slightly brownish acid (90.5%), m.p. 263–265°. Crystallization from aqueous ethanol produced colorless material, m.p. 267.5–269.0°; $\lambda_{\max}^{\text{alc}}$ 230, 297, 352 mμ (ϵ 11,200, 13,000, 6910).

Anal. Calcd. for $C_{11}H_8O_5$: C, 60.00; 3.66. Found: C, 60.08; H, 3.56.

4-Acetyl-5-hydroxybenzofuran.—Three grams of the acid was decarboxylated in quinoline as described above. The quinoline-free ether was washed ten times with 8% sodium hydroxide which produced on acidification 2.2 g. (92%) of brown solid, m.p. 94–97°. This formed yellow plates from alcohol–water, m.p. 103.5–104.5°; $\lambda_{\max}^{\text{CCl}_4}$ 6.15 μ (no band at 2.3 μ); $\lambda_{\max}^{\text{alc}}$ 217, 295, 347 mμ (ϵ 13,100, 10,100, 4770).

Anal. Calcd. for $C_{10}H_8O_3$: C, 68.18; H, 4.58. Found: C, 68.37; H, 4.71.

7-Methyl-9H-furo[3,2-*f*][1]benzopyran-9-one (XII).—The portionwise addition of 3.5 g. of sodium hydride to 2.25 g. of 4-acetyl-5-hydroxybenzofuran in 22.5 ml. of dry ethyl acetate gave a yellowish brown color and the mixture became solid after 3 hr. After standing overnight, ice and dilute hydrochloric acid were added. The resulting brown viscous oil was extracted three times with ether, the extract was dried over sodium sulfate, and the ether distilled. The resultant brown oil was dissolved in 100 ml. of ethanol containing 24 ml. of concentrated sulfuric acid and the solution refluxed for 1 hr. on the steam bath. The cooled solution was then poured into 300 ml. of ice–water, the precipitated solid was collected and crystallized from ethanol–water (1:2). The brown-colored furanochromone XII (2.3 g.)(82%) melted at 165–170° and, after further crystallization from the same solvent, colorless needles, m.p. 172.4–173.6°, were obtained; $\lambda_{\max}^{\text{alc}}$ 262, 289, 315 mμ (ϵ 11,400, 13,800, 13,600); $\lambda_{\text{infl}}^{\text{alc}}$ 282 mμ (ϵ 12,700).

Anal. Calcd. for $C_{12}H_8O_3$: C, 72.00; H, 4.03. Found: C, 71.95; H, 4.23.

2-Hydroxy-4-methoxybenzaldehyde.—To a suspension of 20.9 g. of 2,4-dimethoxybenzaldehyde in 50 ml. of anhydrous toluene was added slowly with swirling 20 g. of aluminum chloride and the mixture was refluxed by heating in a bath at 150° for 5 min. The mixture was cooled at once and the aluminum chloride complex hydrolyzed in the usual manner. The product was collected by ether extraction and the ether solution was washed five times with 10% sodium hydroxide. After acidification of the alkaline washes and extraction of these with ether, the product distilled at 116–126° (6 mm.) (11.4 g.), m.p. 36–40°. By distillation of the alkali-washed ether solution, 5.8 g. of starting material, b.p. 136–148° (0.2 mm.), m.p. 58–67°, was recovered.

Methyl 6-Methoxycoumarilate (III).—From the above aldehyde, 6-methoxycoumarilic acid, m.p. 199–202°, was obtained as described[3]; reported[3] m.p. 206°. Methanolic hydrogen chloride esterification of 4.6 g. of the acid gave the methyl ester in quantitative yield, m.p. 92–95°. By crystallization from aqueous methanol, the melting point was brought to 94.2–95.2°; $\lambda_{\max}^{\text{alc}}$ 240, 281, 310 mμ (ϵ 6490, 11,700, 23,000).

Anal. Calcd. for $C_{11}H_{10}O_4$: C, 64.07; H, 4.89. Found: C, 63.99; H, 5.11.

Acetylation of Methyl 6-Methoxycoumarilate.—Boron trifluoride was passed into a solution containing 3.6 g. of III in 80 ml. of acetic acid. The temperature, on reaching 80° was held at this point until 86 g. of boron trifluoride had been added. The dark-colored solution was then allowed to come to room temperature and stand overnight. It was then poured into cold water and after standing for 1 hr. in an ice–water bath, the brownish precipitate was filtered. The moist precipitate was suspended in 400 ml. of methanol and boiled for 5 min. (not completely soluble). This suspension was cooled and treated with 800 ml. of water. The solid so obtained was again boiled with 100 ml. of methanol for 2 min. and filtered while hot. The methanol-insoluble material was again extracted with hot methanol and then crystallized twice from ethyl acetate. The crystalline methyl 5-acetyl-6-hydroxycoumarilate (XIII) (1.1 g.) melted at 231–232° (Kofl.). It was soluble in sodium hydroxide and gave a strong green color with dilute alcoholic ferric chloride; $\lambda_{\max}^{\text{alc}}$ 229.5, 254, 290, 341.5 mμ (ϵ 16,200, 34,500, 13,000, 8520).

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(21) G. R. Ramage and C. V. Stead, *J. Chem. Soc.*, 3602 (1953).

(22) R. L. Shriner, E. J. Matson, and R. E. Damschroder, *J. Am. Chem. Soc.*, **61**, 2322 (1939).

Anal. Calcd. for $C_{12}H_{10}O_5$: C, 61.56; H, 4.31. Found: C, 61.54; H, 4.38.

The reaction of XIII with hydroxylamine hydrochloride in pyridine–absolute ethanol gave the oxime of ethyl 5-acetyl-6-hydroxycoumarilate, m.p. 247–248.5°, after crystallization from methanol.

Anal. Calcd. for $C_{13}H_{13}NO_5$: C, 59.31; H, 4.98. Found: C, 58.84; H, 4.56.

The filtrates obtained in the above hot methanolic extractions were evaporated and gave 600 mg. of the isomer methyl 7-acetyl-6-hydroxycoumarilate (XIV) which was crystallized three times from methanol, m.p. 135°. A sample for analysis, crystallized three times from aqueous ethanol, m.p. 134.5–135.4°, was soluble in aqueous sodium hydroxide and gave a purple-black ferric chloride test; $\lambda_{\max}^{\text{alc}}$ 231, 279.5, 342.5 mμ (ϵ 11,300, 26,700, 7920).

Anal. Calcd. for $C_{12}H_{10}O_5$: C, 61.56; H, 4.31. Found: C, 61.89; H, 4.43.

As with XIII, the oxime of XIV was prepared in pyridine–ethanol with ester exchange. The oxime of the ethyl ester melted at 220.1–220.9° after crystallization from methanol.

Anal. Calcd. for $C_{13}H_{13}NO_5$: C, 59.31; H, 4.98. Found: C, 59.68; H, 5.07.

5-Acetyl-6-hydroxybenzofuran.—The methanol-insoluble compound above was saponified in alcoholic sodium hydroxide and the acid obtained decarboxylated as previously described. The product, 5-acetyl-6-hydroxybenzofuran (XVII), melted at 95°; reported m.p. 96°[6]; λ^{CCl_4} 6.10 μ (no bands at 5.85, 2.3 μ); $\lambda_{\max}^{\text{alc}}$ 234, 341 mμ (ϵ 41,900, 2910).

7-Acetyl-6-hydroxybenzofuran (XVIII).—Saponification of the methanol-soluble isomer above and decarboxylation of the acid obtained gave material which, after three crystallizations from methanol, formed yellowish needles, m.p. 117.2–118.0°; λ^{CCl_4} 6.12 μ (no bands at 5.85, 2.3 μ); $\lambda_{\max}^{\text{alc}}$ 232, 280 mμ (ϵ 8980, 3520).

Anal. Calcd. for $C_{10}H_8O_3$: C, 68.18; H, 4.58. Found: C, 68.11; H, 4.66.

7-Methyl-9H-furo[2,3-*f*][1]benzopyran-9-one (XIX).—To the 7-acetyl compound above (500 mg.) in 5 ml. of anhydrous ethyl acetate, 600 mg. of sodium hydride was added in three portions with continuous stirring. The reaction solidified after 2 hr. to a brown mass and was allowed to stand overnight. After treatment with ice and dilute hydrochloric acid, the solution was extracted with ether, the dried ether solution was evaporated and the residue heated with 4 ml. of sulfuric acid and 16 ml. of ethanol for 1 hr. on the steam bath. A part of the alcohol was distilled and the solution was poured into water. The filtered product (230 mg.), from methanol gave pale brown crystals, m.p. 226.4–227.8°. The ultraviolet spectra gave $\lambda_{\max}^{\text{alc}}$ 240, 314 mμ (ϵ 27,500, 5380).

Anal. Calcd. for $C_{12}H_8O_3$: C, 72.00; H, 4.03. Found: C, 71.60; H, 4.14.

The isomeric 7-methyl-5H-furo[3,2-*g*][1]benzopyran-5-one is reported[6] as colorless needles from ethanol, m.p. 186°; $\lambda_{\max}$ 236, 280, 317 mμ (log ϵ 4.34, 3.74, 3.83) taken from a graph.

Methyl 7-Methoxycoumarilate (IV).—The reported procedure[23] gave reproducible results if the ester obtained was saponified immediately. The yield was 70%, m.p. 191–201° softening at 185°; reported m.p. 219.5–220.5°[23]; 213.5–215.5°.[24] A sample from aqueous alcohol melted at 220.2–222.0°; $\lambda_{\max}^{\text{alc}}$ 231, 270 mμ (ϵ 20,900, 14,800), reported[24] $\lambda_{\max}$ 228, 269 mμ.

Methanolic hydrogen chloride esterification gave the ester, m.p. 77.2–78.6° after crystallization from alcohol–water; $\lambda_{\max}^{\text{alc}}$ 234.5, 278 mμ (ϵ 22,100, 17,000). The reported melting point is 78°.[23]

Methyl 4-Acetyl-7-methoxycoumarilate (XX).—(a) The above methyl ester (8.8 g.) in 228 ml. of acetic acid was treated below 30° with 221 g. of boron trifluoride and allowed to stand overnight. The nearly colorless gelatinous precipitate obtained by pouring the reaction mixture into 1.5 l. of water was dissolved in 120 ml. of hot ethanol and concentrated to 100 ml. On cooling, 7.9 g. (75%) of colorless material, m.p. 138–142°, was obtained. It melted at 141–144° when mixed with the analytically pure compound prepared below.

(b) 7-Hydroxycoumarilic acid was obtained from 7-methoxycoumarilic acid (89%) as reported[3] and esterified with methanolic hydrogen chloride to give the methyl ester (90%), m.p. 154–163°; reported m.p. 166–167°.[23] On acetylation of 3.38 g. of the ester with boron trifluoride–acetic acid as above, light gray crystals were obtained after pouring the complex into water. These were not completely soluble in 70 ml. of hot alcohol and did not dissolve on addition of 70 ml. of water. On cooling, light sandy crystals (3.26 g. 79%) softening at 160°, m.p. 197–236°, were obtained. From acetic acid, long thin colorless prisms, m.p. 240.5–243° (Kofl.), appeared; $\lambda_{\max}^{\text{alc}}$ 210 253, 311 mμ (ϵ 10,800, 25,700, 18,300).

Anal. Calcd. for $C_{12}H_{10}O_5$: C, 61.54; H, 4.30. Found: C, 61.12; H, 4.44.

The acid obtained on saponification was purified by means of benzene–ethanol, m.p. 299.5–300.5° (Kofl.); $\lambda_{\max}^{\text{alc}}$ 250.5, 312 mμ (ϵ 21,100, 16,100).

Anal. Calcd. for $C_{11}H_8O_5$: C, 60.00; H, 3.66. Found: C, 59.94; H, 3.62.

Diazomethane converted 0.67 g. of the acid to 0.72 g. of XX, m.p. 133–138°. After five crystallizations from benzene, this melted at 142.0–142.2°; $\lambda_{\max}^{\text{alc}}$ 251.5, 305 mμ (ϵ 27,900, 19,100).

Anal. Calcd. for $C_{13}H_{12}O_5$: C, 62.90; H, 4.88. Found: C, 62.68; H, 4.89.

The oxime of XX was crystallized five times from alcohol, m.p. 180.6–182.4°.

Anal. Calcd. for $C_{13}H_{13}NO_5$: C, 59.31; H, 4.98. Found: C, 59.00; H, 5.03.

Saponification of XX gave 4-acetyl-7-methoxycoumarilic acid which was purified using acetic acid. It melted at 271–280° (dec. Kofl.); $\lambda_{\max}^{\text{alc}}$ 210, 249.5, 306 mμ (ϵ 11,600, 25,100, 17,500).

Anal. Calcd. for $C_{12}H_{10}O_5$: C, 61.56; H, 4.31. Found: C, 61.70; H, 4.53.

The ethylene dithiol mercaptal prepared from XX using boron trifluoride etherate[16] melted at 130.4–131.6° after extensive crystallization from ethyl acetate–alcohol; $\lambda_{\max}^{\text{alc}}$ 239, 281.5 mμ (ϵ 26,700, 13,900).

Anal. Calcd. for $C_{15}H_{16}O_4S_2$: C, 55.53; H, 4.97. Found: C, 55.45; H, 4.99.

Saponification gave the ethylene dithiol mercaptal of 4-acetyl-7-methoxycoumarilic acid, m.p. 227.0–227.5° (Kofl.); $\lambda_{\max}^{\text{alc}}$ 235.5, 278 mμ (ϵ 26,100, 13,700) $\lambda_{\text{infl}}^{\text{alc}}$ 311 mμ (ϵ 4700).

Anal. Calcd. for $C_{14}H_{14}O_4S_2$: C, 54.17; H, 4.55. Found: C, 53.88; H, 4.60.

A suspension of 9 teaspoons of W-2 Raney nickel (not modified) in 250 ml. of alcohol containing 1.83 g. of the ethylene dithiol mercaptal of XX was refluxed for 14 hr. The oil obtained was saponified with aqueous alcoholic potassium hydroxide to 1.06 g. of pale yellow crystals, m.p. 158–170°. Recrystallization from aqueous ethanol gave material melting at 188–189.5°, which was soluble in sodium bicarbonate and did not depress the melting point of 4-ethyl-7-methoxycoumarilic acid prepared below by catalytic reduction.

4-Acetyl-7-hydroxybenzofuran.—The reaction of 2.5 g. of XX in 50 ml. of chlorobenzene with 6.0 g. of aluminum chloride at the reflux temperature for 1 hr. gave material soluble in 5% sodium hydroxide. This was recrystallized from methanol, saponified and decarboxylated as described previously. The benzofuran (0.45 g.), crystallized from methanol (carbon), formed tan-colored needles, m.p. 203.2–204.0°; λ^{CHCl_3} 2.35, 6.00μ; $\lambda_{\max}^{\text{alc}}$ 235, 302 mμ (ϵ 11,000, 9830).

Anal. Calcd. for $C_{10}H_8O_3$: C, 68.18; H, 4.58. Found: C, 68.27; H, 4.50.

Methyl 4-Amino-7-methoxycoumarilate.—The oxime of XX (1.2 g.), m.p. 180–182°, in 20 ml. of dry benzene with 1.2 g. of phosphorus pentachloride was refluxed for 25 min. Distillation of the benzene and addition of ice–water gave 1.2 g. of light brown solid, m.p. 199–207°. Crystallization from ethanol gave short colorless needles of the acetylamino compound, m.p. 212.7–213.4°.

Anal. Calcd. for $C_{13}H_{13}NO_5$: C, 59.31; H, 4.98. Found: C, 59.48; H, 4.95.

The use of less pure oxime gave a product which could be purified or used in the subsequent step.

The above 4-acetylamino product (3.0 g., m.p. 180–202°) was refluxed in 120 ml. of alcohol and 120 ml. of concentrated hydrochloric acid under nitrogen for 2.5 hr. The ethanol and part of the hydrochloric acid were distilled *in vacuo*. Filtration gave 2.1 g., m.p. 260° (dec. from 210°). A 1-g. sample of the amine hydrochloride in 140 ml. of 10% methanolic hydrogen chloride was refluxed for 24 hr. The solvent was removed by distillation and the residue was cautiously treated with aqueous sodium bicarbonate. The product (0.69 g.) melted at 180–183°

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(23) T. Reichstein, *Helv. Chim. Acta*, **18**, 816 (1935).

(24) H. Richtzenhain and B. Alfredsson, *Acta Chem. Scand.*, **8**, 1519 (1954).

(dec. sharply at 182°). Further crystallization from ethanol–benzene produced yellow plates, m.p. 182.2–183.6°; reported m.p. 185°.[8]

4-Acetyl-7-methoxybenzofuran.—By the quinoline–copper decarboxylation procedure above, 1.81 g. of the coumarilic acid gave 1 g. of the benzofuran, m.p. 87–95°. Repeated sublimation, finally at 80–100° (0.35 mm.) (bath temp.) gave colorless material, m.p. 92.8–95.2°; λ_{max}^{alc} 235, 293.5 mμ (ε 17,500, 16,100).

Anal. Calcd. for $C_{11}H_{10}O_3$: C, 69.46; H, 5.30. Found: C, 69.69; H, 5.31.

2-(?)Chloro-7-methoxybenzofuran-4-carboxylic Acid.—One-half gram of the sublimed benzofuran above (m.p. 94–97°) and 60 ml. of dioxane were added to 180 ml. of alkaline commercial bleach solution and treated as described above. The dioxane was distilled, the cooled solution was treated with a small portion of sodium bisulfite and acidified. The colorless product weighed 0.51 g., m.p. 236–240°. By sublimation at 150–170° (0.06 mm.) long thin colorless prisms were obtained, m.p. 249.0–252.5° (Kofl.). The presence of chlorine was shown by a sodium fusion test; λ_{max}^{alc} 228, 273 mμ (ε 31,300, 12,300).

Anal. Calcd. for $C_{10}H_7ClO_4$: C, 53.00; H, 3.11. Found: C, 52.74; H, 3.18.

Methyl 4-Ethyl-7-methoxycoumarilate (XXI).—One gram of XX was hydrogenated using 200 mg. of 10% palladium–carbon in 25 ml. of acetic acid containing 1 drop of 70% perchloric acid. In 65 min., 254 ml. of hydrogen was absorbed. Dilution with water gave 0.7 g. of product which was brought to a melting point of 74.3–74.5° by crystallization from aqueous ethanol; λ_{max}^{alc} 238.5, 283 mμ (ε 22,600, 16,400), λ_{infl}^{alc} 311 mμ (ε 3860).

Anal. Calcd. for $C_{13}H_{14}O_4$: C, 66.65; H, 6.02. Found: C, 66.90; H, 6.11.

Saponification gave the acid, crystallized from benzene, m.p. 187.3–188.1°; λ_{max}^{alc} 235, 276 mμ (ε 24,700, 16,500).

Anal. Calcd. for $C_{12}H_{12}O_4$: C, 65.44; H, 5.50. Found: C, 65.23; H, 5.23.

5-Ethyl-2-hydroxy-3-methoxybenzaldehyde.—Clemmensen reduction of acetovanillone, m.p. 97–112°, gave 4-ethyl-2-methoxyphenol (64%), b.p. 140–146° (46 mm.).

The benzoate melted at 57–60° after crystallization from alcohol; reported[25] m.p. 58–59°.

The 2,4-dinitrophenyl ether from alcohol melted at 87.0–88.6°.

Anal. Calcd. for $C_{15}H_{14}N_2O_6$: C, 56.60: H, 4.43. Found: C, 56.21; H, 4.30.

The Duff reaction[7] on 20 g. of the above phenol with steam distillation and extraction of the distillate with ether gave 5-ethyl-2-hydroxy-3-methoxybenzaldehyde, a light yellow oil (9.3 g. 39%), b.p. 98° (0.37 mm.). The sample submitted for analysis boiled at 120° (2 mm.); λ_{max}^{alc} 224, 269, 351 mμ (ε 21,000, 11,200, 2830).

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.72. Found: C, 66.73; H, 6.75.

The semicarbazone formed fluffy, pale yellow, microscopic prisms from 1:1 aqueous ethanol, m.p. 186–189° (Kofl.).

Anal. Calcd. for $C_{11}H_{15}N_3O_3$: C, 55.68; H, 6.37. Found: C, 55.57; H, 6.68.

The aldehyde (7.2 g.) was treated with malonic acid and aniline[26] to produce 6.51 g. (66%) of 6-ethyl-8-methoxycoumarin-3-carboxylic acid, m.p. 156–170°. Five crystallizations from alcohol gave light yellow crystals, m.p. 175.6–177.8°; λ_{max}^{alc} 208, 254.5, 307.5 mμ (ε 34,300, 8750, 14,700).

Anal. Calcd. for $C_{13}H_{12}O_5$: C, 62.90; H, 4.88. Found: C, 62.75; H, 4.93.

5-Ethyl-7-methoxycoumarilic Acid.—The sodium ethoxide condensation of the above aldehyde (4.1 g.) with methyl bromoacetate followed by saponification as previously described gave 4.12 g. of tacky brown solid soluble in sodium bicarbonate. Sublimation at 150° (0.13 mm.) gave 1.24 g. of colorless crystals contaminated with a yellow oil. Three crystallizations from methanol–water gave colorless needles, m.p. 205.4–206.6°; λ_{max}^{alc} 234.5, 274 mμ (ε 21,800, 16,800).

Anal. Calcd. for $C_{12}H_{12}O_4$: C, 65.44; H, 5.49. Found: C, 65.30; H, 5.36.

The amide melted at 182.0–183.6° after crystallization from aqueous methanol.

Anal. Calcd. for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98. Found: C, 65.72; H, 6.19.

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[26] W. Borsche and P. Hahn-Weinheimer, *Chem. Ber.*, **85**, 198 (1952).

Pyrolysis Studies. VII.[1,2] Rates of Thermal Decomposition of Substituted Ethyl Benzoates

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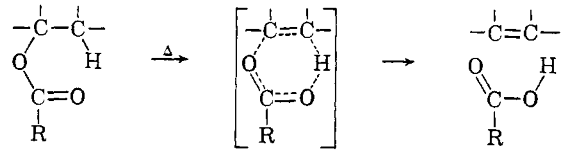
Relative rates of elimination in the pyrolysis of a series of *meta-* and *para-*substituted ethyl benzoates together with infrared data are shown to confirm that heterolytic breakage of the alkoxy C—O bond is of paramount importance in ester pyrolysis. The relative rates are best correlated using Taft's σ^0 values.

The pyrolytic decomposition of esters containing at least one β-hydrogen atom to olefins and acids is generally considered to proceed *via* a cyclic concerted mechanism.

In the transition state (I), the C—H bond and the alkoxy C—O bond are partially broken, and the olefinic C=C bond and the O—H bond are partially formed.[4]



I

Previous work[5] has shown that the C—O bond breakage is *heterolytic* and that the α-carbon atom develops some carbonium ion character in the transition state. Thus relative rate data for the vapor phase pyrolysis of a series of *meta-* and *para-* substituted 1-phenylethyl acetates show a σ^+ correlation.[5] It also appears that for a given ester at a fixed temperature, the rate of decomposition is determined more by the stability of the

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[1] Part VI: R. Taylor and G. G. Smith, *Tetrahedron*, submitted for publication.

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