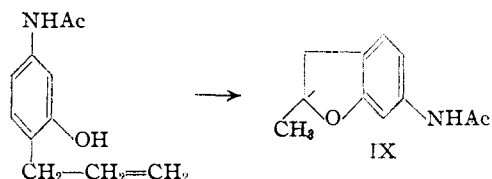
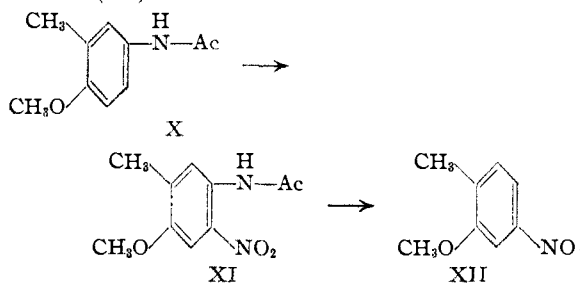


tration of IV would lead to substitution at the C₆ position. Nitration of the acetanilide (IV) gave excellent yields of a mononitro derivative (V) which could be transformed readily into a steam volatile nitrophenol. The volatility of the nitrophenol (VI) proves that the hydroxyl and nitro groups are ortho to each other. The nitroamine from V was diazotized and the diazonium salt reduced by hypophosphite³ to a mononitro-coumaran (VII). This substance on reduction and acetylation gave an acetanilide (VIII) which proved to be different from 6-acetamido-2-methylcoumaran (IX). The acetanilide (VIII) must then be 4-acetamido-2-methylcoumaran.

Compound IX was obtained by treating 4-allyl-3-hydroxyacetanilide⁴ with hydrobromic acid.



The orientation found in V became all the more surprising when it was shown that 4-acetamido-2-methylanisole (X) on nitration gave the 5-nitro isomer (XI).



The structure of XI was determined by replacing the acetamido group with hydrogen⁵ to give 5-nitro-2-methylanisole (XII).

Experimental

4-Allyloxyacetophenone.—A mixture consisting of 4-hydroxyacetophenone (27.2 g.), allyl bromide (25 g.), potassium carbonate, and acetone (30 cc.) was heated for eight hours on a steam cone. The reaction mixture was then worked up according to the general procedure of Claisen.⁶ The allyl ether (27.8 g.) was obtained as a liquid; b. p. 146–147° (10 mm.). The oxime, m. p. 115.5–116.5°, was purified by recrystallization from dilute ethanol.

Anal. Calcd. for C₁₁H₁₃O₂N: C, 69.1; H, 6.80. Found: C, 68.85; H, 7.29.

(3) Adams and Kornblum, *This Journal*, **63**, 197 (1941).

(4) Arnold, McCool and Schultz, *ibid.*, **64**, 1023 (1942).

(5) Hodgson and Marsden, *J. Chem. Soc.*, 207 (1940).

(6) Claisen, *Ber.*, **45**, 3157 (1912).

3-Allyl-4-hydroxyacetophenone.—4-Allyloxyacetophenone (16.5 g.) was heated at 200–210° in a carbon dioxide atmosphere for five hours. The reaction mixture was dissolved in ether and extracted with dilute alkali. On acidification of the basic solution a solid precipitated. Recrystallization from dilute methanol gave 12.8 g.; m. p. 115–116°.

5-Aceto-2-methylcoumaran.—(a) Six grams of 3-allyl-4-hydroxyacetophenone was refluxed with hydrobromic acid (12 cc.; 40%) and acetic acid (40 cc.) for three hours. The mixture was poured into cold water and ether extracted. After washing the ether layer with dilute alkali, it was dried and fractionated. The acetocoumaran (2.7 g.) was obtained as a liquid; b. p. 148–150° (8 mm.). The oxime melted at 85–86°.

(b) 2-Methylcoumaran (32 g.), nitrobenzene (190 cc.) and acetic anhydride were placed in a 500-cc. three-necked flask equipped with an efficient stirrer, a gas exit tube, and a rubber connection to a flask containing aluminum chloride (80 g.). The aluminum chloride was added to the solution during the course of one hour. At no time in this operation was the temperature inside the flask allowed to exceed 10°. After the addition, the reaction flask was removed from the ice-bath and the mixture was stirred for an additional ninety minutes. Decomposition of the reaction mixture with ice and dilute hydrochloric acid in the usual manner followed by ether extraction and fractionation of the ether layer gave 30.4 g. of ketone, b. p. 145–146° (6 mm.).

From 30 g. of the ketone, hydroxylamine hydrochloride (20.5 g.) and pyridine (150 cc.) there was obtained 27.5 g. of oxime; m. p. 85–86°. A mixed melting point determination established the identity of this product with that described in part (a).

Anal. Calcd. for C₁₁H₁₃O₂N: C, 69.11; H, 6.80. Found: C, 68.94; H, 6.78.

5-Acetamido-2-methylcoumaran.—Eighteen grams of the oxime from 5-aceto-2-methylcoumaran was dissolved in acetic acid (36 cc.) and acetic anhydride (67.5 cc.) and the solution was saturated with dry hydrogen chloride. The reaction was exothermic and the mixture was allowed to stand until the temperature dropped to 30°. The contents of the flask was poured into an excess of cold water and neutralized with sodium hydroxide. The precipitate was filtered and dried at 110°; the yield was practically quantitative. After recrystallization from benzene-petroleum ether the substance melted at 127–128° (Claisen⁷) reports 127–127.5°.

5-Amino-2-methylcoumaran Hydrochloride.—The acetanilide (IV) (15 g.) was refluxed with 78 cc. of 1:1 hydrochloric acid for seventy-five minutes. The solution was then boiled in the presence of Norite and filtered while hot. The cooled solution deposited 12.4 g. of amine hydrochloride.

4-Nitro-5-acetamido-2-methylcoumaran.—5-Acetamido-2-methylcoumaran (20 g.) in acetic acid (70 cc.) was cooled to 10°. Nitric acid (6 cc. sp. gr. 1.5) in 3 cc. of acetic acid was added dropwise with stirring and the reaction allowed to proceed for an additional forty-five minutes. The solid nitro compound precipitated when the reaction mixture was poured into water; wt. 22 g.; m. p. 134–135°. Re-

(7) Claisen, Eisleb and Kremer, *Ann.*, **418**, 100 (1919).

crystallization from methanol gave short yellow crystals; m. p. 135–136°.

Anal. Calcd. for $C_{11}H_{12}O_4N_2$: C, 55.93; H, 5.09. Found: C, 55.70; H, 5.13.

4-Nitro-5-amino-2-methylcoumaran.—The nitro-acetanilide (V) (8.14 g.) was refluxed for forty minutes with 1:1 hydrochloric acid (100 cc.) and then cooled. The nitroamine separated from the acid solution. An additional quantity was obtained by neutralizing the hydrolyzate solution with alkali. Recrystallization from methanol (40%) gave red needles (5.44 g.) melting at 104–104.5°.

Anal. Calcd. for $C_9H_{10}O_3N_2$: N, 14.43. Found: N, 14.77.

4-Nitro-5-hydroxy-2-methylcoumaran.—A suspension of the nitroamine (2.8 g.), sulfuric acid (30 cc.) and water (30 cc.) was warmed to effect solution and filtered through glass wool. The solution was cooled in an ice-bath and sodium nitrite (1.0 g. in water) was added slowly. After standing fifteen minutes the diazonium solution was decomposed by adding it to dropwise into a boiling copper sulfate solution (50%). The steam-volatile nitrophenol melted at 75–76° after recrystallization from methanol.

Anal. Calcd. for $C_9H_9O_4N$: C, 55.38; H, 4.62. Found: C, 55.79; H, 4.60.

4-Nitro-2-methylcoumaran.—A solution of 5-amino-4-nitro-2-methylcoumaran (1.9 g.), sulfuric acid (17 cc.) and water (50 cc.) was diazotized with sodium nitrite (0.7 g.) in the usual manner and allowed to stand for twenty minutes. A solution of hypophosphorous acid was prepared from calcium hypophosphite (11 g.), water (35 cc.) and sulfuric acid (6 g.). After filtering, the hypophosphorous acid solution was added to the solution of diazonium salt and allowed to stand at 0° for twenty-four hours and at 30° for an additional forty-eight hours. The solution was made alkaline and steam distilled. The white solid which was volatile with steam was recrystallized from methanol; m. p. 67.5–68°.

Anal. Calcd. for $C_9H_9O_3N$: C, 60.33; H, 5.03. Found: C, 60.25; H, 4.85.

4-Acetamido-2-methylcoumaran.—The 4-nitrocoumaran (0.36 g.) was reduced in acetic acid (0.1 cc.) and water (3 cc.) with iron filings. After the reduction was completed the solution was made alkaline and ether extracted. Evaporation of the ether gave the amine as a brown oil which was directly acetylated with acetic anhydride to 4-acetamido-2-methylcoumaran; m. p. 96–97°. When admixed with a sample of 6-acetamido-2-methylcoumaran (m. p. 126–126.5°) the melting point of the sample was lowered to below 86°.

6-Acetamido-2-methylcoumaran.—Two grams of 3-acetoxy-4-allylacetanilide was mixed with fuming hydrobromic acid (10 cc.) and allowed to stand in a glass-stoppered bottle for two days at room temperature. The mixture was poured into an excess of sodium hydroxide (10%) and allowed to stand in the refrigerator for several days. The solid was filtered and the aqueous solution extracted with benzene. The solid was dissolved in this benzene

layer and one-half of the benzene removed by distillation. The addition of low boiling petroleum ether to the cooled benzene solution caused the precipitation of the acetamidocoumaran; m. p. 124–126°. Recrystallization from water yielded white needles; m. p. 126–126.5°.

Anal. Calcd. for $C_{11}H_{13}O_2N$: C, 69.11; H, 6.80. Found: C, 69.32; H, 6.79.

5-Nitro-4-acetamido-2-methylanisole.—4-Acetamido-2-methylanisole (10 g.) was dissolved in acetic acid (35 cc.) and cooled while stirring to 10°. Nitric acid (3 cc.) was slowly added during which time the temperature rose to 20°. When the nitro compound began to crystallize the mixture was poured into water and filtered. After recrystallization from methanol the nitroacetanilide (10.8 g.) was obtained as long yellow needles; m. p. 144°.

Anal. Calcd. for $C_{10}H_{13}O_4N_2$: C, 53.57; H, 5.36. Found: C, 53.70; H, 5.23.

5-Nitro-4-amino-2-methylanisole.—This compound was prepared by hydrolyzing the corresponding acetanilide with sodium hydroxide and ethanol. The amine was obtained as red needles, m. p. 117.5–118.5°, after recrystallization from ethanol and water.

Anal. Calcd. for $C_8H_9O_2N_2$: N, 15.38. Found: N, 15.09.

5-Nitro-2-methylanisole.—A solution of 5-nitro-4-amino-2-methylanisole (1.44 g.), sulfuric acid (23 cc.) and water was cooled to 0°. Sodium nitrite (1 g.) in 10 cc. of cold water was added slowly to this solution. To the solution of diazonium salt was added a suspension prepared from sodium 1,5-naphthalene disulfonate (2.5 g.), sulfuric acid (2.5 cc.), and water (12.5 cc.). In forty minutes the diazonium naphthalene disulfonate was filtered and decomposed in ethanol in the presence of copper powder.⁵ 5-Nitro-2-methylanisole, m. p. 71.5–72.5°, was obtained as light tan crystals. Ullmann and Fitzenkam report 71°.⁸

5-Nitro-4-hydroxy-2-methylanisole.—This phenol was obtained from 5-nitro-4-amino-2-methylanisole by decomposition of the diazonium salt. The solution of nitroamine (2.5 g.), sulfuric acid (40 cc.), and water (70 cc.) was cooled to 0° and then diazotized with 1.5 g. of sodium nitrite in 15 cc. of water. After standing several hours the solution was decomposed by adding it dropwise to a boiling solution of copper sulfate (50%). The steam volatile nitrophenol weighed 1.55 g.; m. p. 98–99°.

Anal. Calcd. for $C_8H_9O_4N$: C, 52.46; H, 4.92. Found: C, 52.63; H, 4.86.

Summary

Several substitution reactions in the coumaran and *o*-methylanisole series have been studied in order to determine group orientations. It has been found that the orientations in these two series are not comparable.

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(8) Ullmann and Fitzenkam, *Ber.*, **38**, 3790 (1905).