2-Bromo-3,5-dinitrobenzoic Acid.[8]—A solution of 30 g. of 2-bromo-3-nitrobenzoic acid in 125 cc. of concentrated sulfuric acid was prepared by warming in a beaker on a steam-bath. To this, while still warm, was added slowly with continuous stirring, a mixture of 20 cc. of fuming nitric acid, and 20 cc. of concentrated sulfuric acid. The solution became pasty after a few minutes and was then warmed for fifteen minutes on a steam-bath. After cooling, it was poured onto ice. The product was filtered, dissolved in dilute aqueous sodium hydroxide, reprecipitated with dilute hydrochloric acid and then purified by recrystallization from 50% ethanol. The product was nearly white; m. p. 215–216°; yield 33 g. (93% theory). Meisenheimer[9] gives a m. p. of 213°.

Methyl 2-Bromo-3,5-dinitrobenzoate.—A solution of 33 g. of 2-bromo-3,5-dinitrobenzoic acid in 200 cc. of absolute methanol containing 3% by weight of dry hydrogen chloride was refluxed for four hours, cooled and poured into ice and aqueous sodium hydroxide. The product was purified by recrystallization from ethanol, m. p. 106–108°.

Anal. Calcd. for $C_8H_5O_6N_2Br$: N, 9.18; Br, 26.20. Found: N, 9.16; Br, 26.15.

***dl*-2,4-Dinitro-6-carboxy-2′-methoxybiphenyl.**—The procedure for condensing methyl 2-iodo-3-nitro-5-bromobenzoate and *o*-iodoanisole with copper was used with 25 g. of methyl 2-bromo-3,5-dinitrobenzoate, 50 g. of *o*-iodoanisole and 75 g. of copper. In the hydrolysis sodium carbonate in dilute alcohol was used in place of sodium hydroxide. The yield of 2,4-dinitro-6-carboxy-2′-methoxybiphenyl was 6 g. (23%). It was purified from 70% ethanol; yellow crystals, m. p. 185°.

Anal. Calcd. for $C_{14}H_{10}O_7N_2$: C, 52.83; H, 3.17; N, 8.81; neut. equiv., 318. Found: C, 53.01; H, 3.34; N, 8.92; neut. equiv., 320.

Strychnine Salt of *l*-2,4-Dinitro-6-carboxy-2′-methoxybiphenyl.—To a hot solution of 2.0 g. of the acid in 75 cc. of 95% ethanol and 37.5 cc. of water was added 2.1 g. of strychnine. The clear solution that resulted was cooled overnight at 5° and 3.95 g. of yellow crystals separated, m. p. 136° (dec.). Recrystallization from 95% ethanol did not change the melting point.

Anal. Calcd. for $C_{35}H_{32}O_9N_4$: C, 64.37; H, 4.95; N, 8.58. Found: C, 63.92; H, 5.19; N, 8.51.

If the strychnine salt was prepared in absolute ethanol by the method used for the previous salts, a product, m. p. 206–208°, with decomposition, was obtained which showed no mutarotation.

Rotation.—0.1054 g. made up to 10 cc. in chloroform at 28° gave α_D $-0.30°$; $l = 1$; unchanged after fifty-one minutes, $[\alpha]^{28}_D$ $-28.4°$.

Anal. Calcd. for $C_{35}H_{32}O_9N_4$: N, 8.5. Found: N, 8.5.

***l*-2,4-Dinitro-6-carboxy-2′-methoxybiphenyl.**—The active acid was obtained by hydrolysis as previously described for other salts: yellowish crystals; m. p. 182–185°.

Summary

Four derivatives of 2-nitro-6-carboxy-2′-methoxybiphenyl have been prepared, namely, those with a NO_2, Br, Cl, and CH_3 group in the 4-position. The rates of mutarotation of the salts and the rates of racemization of the active acids were determined.

The chlorinated acid racemizes a little more slowly, the brominated at about the same rate, and the methyl and nitro compounds more rapidly than 2-nitro-6-carboxy-2′-methoxybiphenyl itself. The influence of a substituent in the 4-position is much less than in the 3′-, 4′- or 5′-position.

URBANA, ILLINOIS RECEIVED APRIL 6, 1938

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(8) This compound and its derivatives described below were prepared first by Dr. D. B. Holmes (Ph.D. thesis, University of Illinois, 1934).

(9) Meisenheimer, *Ann.*, **446**, 205 (1925).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

Derivatives of Coumaran. II. Condensation of Aliphatic Aldehydes and Ketones with 6-Methoxycoumaran-3-one. Reduction of 2-Isopropylidene-6-methoxycoumaran-3-one

BY R. L. SHRINER AND JOHN ANDERSON

Since coumaran-3-ones condense readily with aromatic aldehydes to give 2-benzalcoumaran-3-ones,[1] it seemed reasonable that similar condensations involving aliphatic aldehydes and ketones should take place providing favorable experimental conditions could be found. In the present work a study of the condensation of simple aldehydes and ketones with 6-methoxycoumaran-3-one was made.

It has been found that aliphatic ketones and aldehydes do react with the active methylene group in coumaran-3-ones in a manner analogous to the well-known Knoevenagel condensation,[2] although a previous report on this reaction had been unfavorable.[3] In glacial acetic acid solution, with hydrochloric acid as the condensing agent, 6-methoxycoumaran-3-one (I) combined with ketones to give 2,2′-*bis*-(6-methoxycoumaran-3-one)-dialkylmethanes (II). Three ke-

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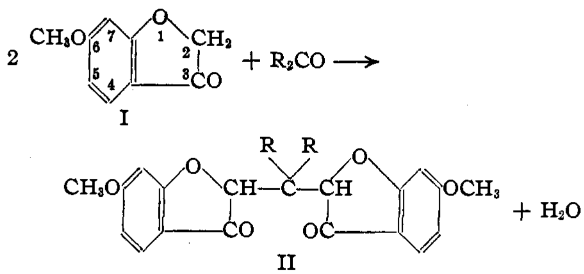
(1) Von Auwers and Pohl, *Ann.*, **405**, 243 (1914).

(2) Knoevenagel, *Ber.*, **31**, 2585 (1898).

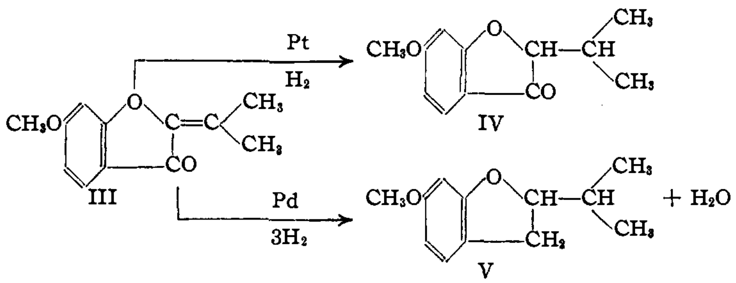
(3) Feist and Siebenlist, *Arch. Pharm.*, **265**, 196 (1927).



tones were used, acetone, ethyl methyl ketone and diethyl ketone. It was found that the yields decreased as the size of the alkyl groups increased (see Table I in Experimental). A similar condensation took place, in methanol solution, between the coumaranone and formaldehyde, acetaldehyde, propionaldehyde and *n*-butyraldehyde, providing a zinc chloride–hydrochloric acid mixture was used as the condensing agent.

In absolute ethanol as the solvent, in the presence of zinc chloride, 6-methoxycoumaran-3-one combined with acetone in a one-to-one ratio to yield the alkylidene derivative (III). Cyclohexanone gave a similar product but the higher aliphatic ketones did not condense under these conditions.

A second phase of the present investigation was concerned with the reduction of the alkylidene coumaranones, since a previous study indicated that arylidene coumaranones could be hydrogenated.[4] 2-Isopropylidene-6-methoxycoumaran-3-one (III) was reduced catalytically to 2-isopropyl-6-methoxycoumaran-3-one (IV) with hydrogen and platinum catalyst. With palladium deposited on Norite as the catalyst, reduction both of the double bond and of the ketone group took place, resulting in the formation of 2-isopropyl-6-methoxycoumaran (V). The reduction of the isopropylidene derivative (III) to the isopropylcoumaranone (IV) offers a new method for the synthesis of 2-alkylcoumaran-3-ones which heretofore have been prepared only by ring closure of *o*-hydroxy-ω-haloacetophenones.[5] Complete reduction of the isopropylidene coumaranone (III) to the 2-isopropylcoumaran (V) constitutes a simple synthesis of this type of molecule, which is of especial interest because such ring systems constitute a portion of the dihydrorotenone molecule.



Experimental

6-Methoxycoumaran-3-one.—A 75% yield of this compound was obtained from 2-hydroxy-4-methoxy-ω-chloroacetophenone according to the method of von Auwers and Pohl.[6]

2,2′-*bis*-(6-Methoxycoumaran-3-one)-dialkylmethanes. General Procedure.—In 150 cc. of glacial acetic acid there were dissolved 0.05 mole of 6-methoxycoumaran-3-one, 0.03 mole of the appropriate ketone and 3 cc. of concentrated hydrochloric acid. This solution was shaken at room temperature for forty-eight hours, at the end of which time the crude material which had separated was removed by filtration.

The products so obtained were recrystallized from the solvents indicated in Table I, which also summarizes their properties.

2,2′-*bis*-(6-Methoxycoumaran-3-one)-monoalkylmethanes. General Procedure.—A solution of 0.05 mole of 6-methoxycoumaran-3-one, 0.05 mole of the appropriate aldehyde, 2 cc. of concentrated hydrochloric acid and 0.5 g. of zinc chloride in 60 cc. of methanol was refluxed for twenty-four hours. The reaction mixture was allowed to cool and the crude product was removed by filtration. Additional amounts of the product were obtained by partial evaporation of the solvent.

The products so obtained were recrystallized from ethanol and their properties are also summarized in Table I.

2-Isopropylidene-6-methoxycoumaran-3-one.—A solution of 10 g. of 6-methoxycoumaran-3-one, 10 cc. of acetone and 2 g. of zinc chloride in 100 cc. of absolute ethanol was refluxed for three hours. The mixture was cooled, the crude product removed by filtration and purified by recrystallization from ethanol. The pure compound, consisting of yellow needles which melted at 141–142° (corr.), was isolated in 84% yield.

Anal. Calcd. for $C_{12}H_{12}O_3$: C, 70.57; H, 5.92. Found: C, 70.69; H, 5.82.

2-Isopropyl-6-methoxycoumaran-3-one.—A solution of 4 g. of 2-isopropylidene-6-methoxycoumaran-3-one in 50 cc. of absolute ethanol was reduced with hydrogen at a pressure of 2 to 3 atmospheres in the presence of 0.1 g. of platinum oxide. One mole of hydrogen was absorbed in two hours. The reduction mixture was filtered and the solvent was removed by evaporation to leave the product as an oily residue which soon solidified. It was recrystallized from ethanol to give white needles which melted at 75–75.5° (corr.). The yield of pure product was 3.5 g. or 87%.

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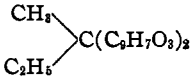
(4) Shriner and Damschroder, This Journal, 60, 894 (1938).

(5) Von Auwers and Wegener, *J. prakt. Chem.*, 108, 244 (1923); Arima and Okamoto, *J. Chem. Soc. Japan.*, 50, 344 (1929).

(6) Von Auwers and Pohl, *Ann.*, 405, 264 (1914).

TABLE I

2,2′-*bis*-(6-METHOXYCOUMARAN-3-ONE)-ALKYLMETHANES

Compound	Solvent for recrystallization	M. p., corr., °C.	Yield, %	Analyses, %			
				Calcd.		Found	
				C	H	C	H
$(CH_3)_2C(C_9H_7O_3)_2$	Acetic acid	209–210	65	68.47	5.47	68.53	5.41
 $(CH_3)(C_2H_5)C(C_9H_7O_3)_2$	Dioxane	194	52	69.09	5.80	68.91	5.76
$(C_2H_5)_2C(C_9H_7O_3)_2$	Cellosolve	231.5–232.5	44	69.68	6.10	69.81	6.16
$H_2C(C_9H_7O_3)_2$	Acetone	169–170	27[7]	67.06	4.73	67.37	4.70
$CH_3CH(C_9H_7O_3)_2$	Ethanol	167–168	35[8]	67.79	5.12	68.04	5.34
$C_2H_5CH(C_9H_7O_3)_2$	Ethanol	135–136	33	68.47	5.47	68.54	5.53
n-$C_3H_7CH(C_9H_7O_3)_2$	Ethanol	141–142	60	69.09	5.80	69.21	5.85

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.88; H, 6.85. Found: C, 70.06; H, 6.97.

2-Isopropyl-6-methoxycoumaran.—A solution of 4 g. of 2-isopropylidene-6-methoxycoumaran-3-one in 50 cc. of absolute ethanol was reduced with hydrogen at a pressure of 2 to 3 atmospheres in the presence of 0.1 g. of colloidal palladium supported on 1.0 g. of Norite. The first mole of hydrogen was absorbed in a few minutes and the second and third over a period of twenty-four hours. After completion of the reduction, the mixture was filtered and the solvent was removed by distillation to leave a liquid residue. The pure product, a colorless liquid, was obtained in 45% yield by fractionation of this residue. The purified product gave the following constants: b. p. 149° (19 mm.), n^{16}_D 1.5215, d^{20}_{20} 1.0458; M_D calcd., 55.1; M_D found, 56.1.

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.95; H, 8.41. Found: C, 74.44; H, 8.49.

2 - Cyclohexylidene - 6 - methoxycoumaran - 3 - one.—This compound was prepared from 5.0 g. of 6-methoxycoumaran-3-one, 10.0 g. of cyclohexanone and 1.0 g. of zinc chloride by the method used for the preparation of 2-isopropylidene-6-methoxycoumaran-3-one. In this case the ethanol solution was refluxed for twenty-four hours and the product, consisting of white needles which melted at 146.5–147.5° (corr.), was isolated in 46% yield.

Anal. Calcd. for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.66; H, 6.68.

2 - Cyclohexyl - 6 - methoxycoumaran - 3 - one.—Catalytic hydrogenation of 2-cyclohexylidene-6-methoxycoumaran-3-one by the method indicated above for the preparation of 2-isopropyl-6-methoxycoumaran-3-one gave a 68% yield of white needles which melted at 86.5–87.5° (corr.).

Anal. Calcd. for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37. Found: C, 73.26; H, 7.40.

Summary

Aliphatic aldehydes and ketones condense with 6-methoxycoumaran-3-one to give 2,2′-*bis*-(6-methoxycoumaran-3-one)-alkylmethanes. In the case of acetone and cyclohexanone, condensation also was effected in a one-to-one ratio to yield alkylidene coumaranones.

Catalytic reduction of the alkylidene coumaranones with platinum and hydrogen yielded the 2-alkyl-6-methoxycoumaran-3-ones. With a palladium catalyst the reduction of 2-isopropylidene-6-methoxycoumaran-3-one to 2-isopropyl-6-methoxycoumaran was accomplished.

URBANA, ILLINOIS RECEIVED MARCH 18, 1938

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[7] Formalin (40%) was used in this experiment. No product could be obtained when paraformaldehyde was used.

[8] This yield was obtained when freshly prepared acetaldehyde was the reactant. When paraldehyde was used, a 91% yield of the *bis*-condensation product resulted since the hydrochloric acid depolymerized the paraldehyde to acetaldehyde and the latter then reacted with the coumaranone.