A Synthesis of Coumaron-2,3-dicarboxylic Acids

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Coumaron-2,3-dicarboxylic acid should be of considerable value in studies of coumaron chemistry, but no simple method has been described for its preparation. The only reported synthesis[1] is lengthy and requires isatin, until recently an expensive substance, as a starting material.

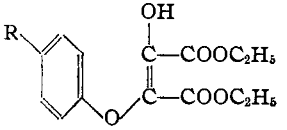
Table I

Cyclization Experiments

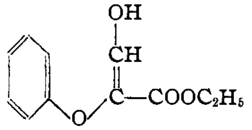
Starting material, g.	Reaction medium H_2SO_4, ml.	AcOH, ml.	Conditions	Isolated compd.	Yield, %[a]
I 8.3	15	15	*b*	Acid ester	15
I 5.0	15	0	*c*	Diester (?)	45
I 5.0	4	16	*d*	Tar	
I 6.2	4	16	*b*	Acid ester	15
I 5.2	15 (83%)	0	*e*	Tar	
I 5.0	10	10	*f*	Acid ester	25
I 5.3	10	10	*g*	Acid ester	52
I 20.0	40	40	*g*	Diacid	43
I 6.0	10	10	*g*	Diacid	44
III 5.0	10	10	*g*	Diacid	55
III 20.0	40	40	*g*	Diacid	66
III 5.0	10	10	*g*	Diacid	64
III 20.0	40	40	*g*	Acid ester	43
V 18.0	20	80	*c*	Acid	27

[a] Assuming pure starting material. [b] Steam-bath, thirty minutes. [c] Room temperature, ninety minutes. [d] Boil twenty minutes. [e] Steam-bath, one hour. [f] Room temperature, twelve hours. [g] Room temperature, twelve hours, then steam-bath, fifteen minutes.

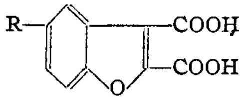
It is shown in the present paper that coumaron-2,3-dicarboxylic acid can be obtained readily through reactions analogous to those used by Bougault[2] for the preparation of indenedicarboxylic acid. Ethyl phenoxyacetate is condensed with ethyl oxalate, and the resulting ester (I) is cyclized with sulfuric–acetic acid. The synthesis can be applied also to the preparation of certain substituted coumaronedicarboxylic acids, for example the 5-methyl derivative (IV). And similarly ethyl formylphenoxyacetate (V) can be cyclized, yielding coumaron-2-carboxylic acid (coumarilic acid).



I, R = H
III, R = CH_3



V



II, R = H
IV, R = CH_3

Experimental

Sodium ethoxide was prepared by allowing powdered sodium (7.6 g.) to react with ethanol (15.2 g.) in ether (50 ml.). After twelve hours a solution of ethyl oxalate (66.6 g.) in ether (100 ml.) was added, and after this mixture had stood for thirty minutes, ethyl phenoxyacetate (54 g.) in ether (100 ml.) was added. The resulting solution was boiled for twenty-four hours, during which time it became dark red, and then it was poured into ice water. The aqueous layer was separated and acidified, and the precipitated oxalo compound was taken up in ether. It was washed and finally dried under a vacuum. There was obtained 86 g. (102%) of crude ethyl α-hydroxy-α′-phenoxymaleate (I), a yellow oil which was used without purification in the cyclization experiments.

Ethyl α-hydroxy-α′-*p*-cresoxymaleate (III), prepared in a similar way using ethyl *p*-cresoxyacetate, was likewise an oil which was not purified completely before cyclization.

Table II

Melting Points and Analyses

Coumarone	M. p., °C.	Formula	Calcd., % C	Calcd., % H	Found, % C	Found, % H
3-Carbethoxy-2-carboxy-	186–187	$C_{12}H_{10}O_5$[a]	61.5	4.3	61.7	4.5
2,3-Dicarboxy-	249–250[b]	$C_{10}H_6O_5$	58.3	2.9	58.0	3.2
3-Carbethoxy-2-carboxy-5-methyl-	147–148	$C_{13}H_{12}O_5$	62.9	4.8	63.1	5.1
2,3-Dicarboxy-5-methyl-	282[c]	$C_{11}H_8O_5$	60.0	3.6	60.0	3.9
2,3-Dicarbomethoxy-5-methyl-[d]	62.5–63.5	$C_{13}H_{12}O_5$	62.9	4.8	63.0	4.9
2-Carboxy-	188–192[e]	$C_9H_6O_3$				

[a] Neut. equiv., calcd., 234; found, 217, 219. [b] Literature, 259–260°. [c] Copper block; sublimes slowly. [d] From the diacid with methanol and sulfuric acid. [e] Perkin [*J. Chem. Soc.*, **24**, 45 (1871)] reported m. p. 192–193°.

The results of a number of cyclization experiments are given in Table I. In all cases the reaction mixtures were worked up by pouring on ice. Crystallization of the resulting precipitates from benzene gave the acid esters. In most cases the crude precipitates were dissolved in 5% sodium hydroxide and allowed to stand for fifteen minutes; acidification then gave the diacids, which were purified by crystallization from acetic acid. Descriptions of the compounds prepared are given in Table II.

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Received April 3, 1941

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[1] Titoff, Müller and Reichstein, *Helv. Chim. Acta*, **20**, 883 (1937).

[2] Bougault, *Compt. rend.*, **159**, 745 (1914).