200. *Synthesis of Some Bicoumarinyl and 8-Phenylcoumarin Derivatives.*

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Several 3,3′- and 8,8′-bicoumarinyls have been synthesised by the Ullmann reaction on iodocoumarins; and 8-phenylcoumarins have been synthesised by the crossed Ullmann reaction between iodocoumarins and iodobenzene.

DEY and ROW [1] prepared 4,3′-bicoumarinyls by condensation of various phenolic aldehydes with 4-coumarinylacetic acids. Huebner and Link [2] reported the formation of the bicoumarinyl derivative from 3-bromo-4-methoxycoumarin by the Ullmann reaction. No other work on the synthesis of bicoumarinyls appears to have been reported. Further, 8-phenylcoumarins have not hitherto been prepared. The present paper reports the synthesis of several bicoumarinyl and 8-phenylcoumarin derivatives from the monoiodocoumarins by the Ullmann reaction.

Methyl 8-iodocoumarin-6-carboxylates (Ia and b), (IIa and b) and (IIIb), when treated with copper bronze in boiling diphenyl ether, yielded the corresponding bicoumarinyl esters (IV—VI), and these on hydrolysis and decarboxylation gave the compounds (IVc and d), (Vc and d), and (VId), respectively, identical with those obtained from the Ullmann reaction on iodocoumarins (Ic and d), (IIc and d), and (IIId). These bicoumarinyls were demethylated to the corresponding hydroxy-derivatives.

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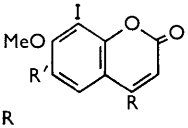

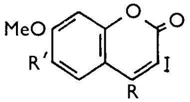

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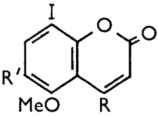

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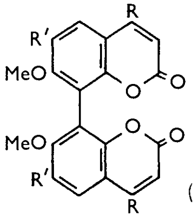

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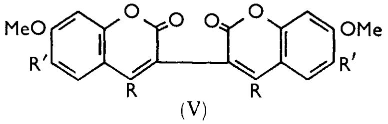

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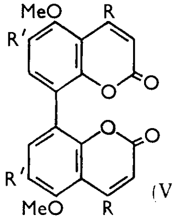

(VI)

	a	b	c	d
R	H	Me	H	Me
R′	CO_2Me	CO_2Me	H	H

Attempts to prepare the (—)-brucine salt of the acids from the bicoumarinyl esters (IVa and b), to see if they could be resolved into optical isomers, did not succeed on account of the sparing solubility of the acids in various solvents.

Crossed Ullmann reaction between iodobenzene and the iodocoumarin esters (Ia and b) yielded mixtures from which the corresponding 8-phenylcoumarin derivatives were isolated by fractional crystallisation. The esters were hydrolysed and decarboxylated to the simple 8-phenylcoumarin derivatives, which were also obtained by Ullmann reaction between iodobenzene and the iodocoumarins (Ic and d) respectively.

5-Methoxy-4-methyl-8-phenylcoumarin was similarly obtained from the iodocoumarin (IIId).

EXPERIMENTAL

Synthesis of Bicoumarinyls (*Table* 1).—The iodocoumarin [3] (0·01 mole) was refluxed in diphenyl ether with copper bronze (0·03 mole) for 2 hr. The mixture was then filtered. The

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[1] Dey and Row, *J. Indian Chem. Soc.*, 1924, **1**, 107.

[2] Huebner and Link, *J. Amer. Chem. Soc.*, 1945, **67**, 99.

[3] Lele and Sethna, *J. Org. Chem.*, 1958, **23**, 1731; Lele, Patel, and Sethna, *J. Indian Chem. Soc.*, in the press.

product which separated on dilution of the filtrate with light petroleum was dissolved in hot glacial acetic acid and allowed to cool. The sparingly soluble bicoumarinyl derivative separated and was further crystallised from the same solvent. The mother-liquor yielded the original but de-iodinated coumarin. The *bicoumarinyl derivatives* were very sparingly soluble in common solvents such as alcohols, acetone, acetic acid, benzene, and ether.

Synthesis of 8-*Phenylcoumarins* (*Table* 2).—A mixture of iodocoumarin (0·01 mole), iodobenzene (0·02 mole), and copper bronze (0·04 mole) was heated at the temperature mentioned in Table 2 for 3 hr., then extracted with light petroleum (to remove biphenyl) and then several times with boiling acetone. The products obtained on removal of acetone from the extracts and fractional crystallisation were the 8-*phenylcoumarin derivatives*. For the esters (Ia and b) nitrobenzene was used as solvent, and the 8-phenylcoumarin derivatives were isolated by

TABLE 1. *Bicoumarinyl derivatives.*

		Yield	Found (%)			Required (%)	
Bicoumarinyl	M. p.	(%)	C	H	Formula	C	H
IVc	376°	48	68·1	4·4	$C_{20}H_{14}O_6$	68·6	4·1
Vc	295	25	68·3	4·2	$C_{20}H_{14}O_6$	68·6	4·1
IVa	268	63	61·7	4·2	$C_{24}H_{18}O_{10}$	61·8	3·9
Va	326	16	61·3	4·3	$C_{24}H_{18}O_{10}$	61·8	3·9
IVd	358	68	69·5	4·9	$C_{22}H_{18}O_6$	69·8	4·8
Vd	268	17	69·8	4·8	$C_{22}H_{18}O_6$	69·8	4·8
IVb	250	64	63·0	4·5	$C_{26}H_{22}O_{10}$	63·2	4·4
Vb	286	20	63·2	4·2	$C_{26}H_{22}O_{10}$	63·2	4·4
VId	>400	8	69·4	5·2	$C_{22}H_{18}O_6$	69·8	4·8
VIb	353	12	63·2	4·6	$C_{26}H_{22}O_{10}$	63·2	4·4

TABLE 2. 8-*Phenylcoumarin derivatives.*

Reaction			Found (%)			Required (%)	
temp.	8-Phenylcoumarin	M. p.	C	H	Formula	C	H
220—225°	7-OMe	128—130°	75·6	4·9	$C_{16}H_{12}O_3$	76·2	4·8
*	7-OMe-6-CO_2Me	120—121	69·9	4·7	$C_{18}H_{14}O_5$	69·7	4·5
220—225	7-OMe-4-Me	158	76·3	4·9	$C_{17}H_{14}O_3$	76·7	5·3
*	7-OMe 4-Me-6-CO_2Me	168	70·5	5·0	$C_{19}H_{16}O_5$	70·4	4·9
260—265	5-OMe-4-Me	156—158	76·8	5·1	$C_{17}H_{14}O_3$	76·7	5·3

* In boiling nitrobenzene for 3 hr.

TABLE 3. *Demethylation products.*

Cpd.* but with		Found (%)			Required (%)	
OH replacing OMe	M. p.	C	H	Formula	C	H
IVc	390°	66·9	3·2	$C_{18}H_{10}O_6$	67·1	3·1
Vc	>400	67·3	3·5	$C_{18}H_{10}O_6$	67·1	3·1
IVd	366	68·7	4·3	$C_{20}H_{14}O_6$	68·6	4·0
Vd	>400	68·7	4·4	$C_{20}H_{14}O_6$	68·6	4·0
VId	>400	68·5	4·2	$C_{20}H_{14}O_6$	68·6	4·0
†	184	76·6	4·9	$C_{16}H_{12}O_3$	76·2	4·8

* In alkaline solution, the first four compounds show no fluorescence, the fifth gives a deep yellow colour, and the sixth shows intense blue fluorescence. † 7-Hydroxy-4-methyl-8-phenylcoumarin.

TABLE 4. *Hydrolysis products.*

Cpd.* but with		Found (%)			Required (%)	
CO_2H replacing CO_2Me	M. p.*	C	H	Formula	C	H
IVa	310°	60·8	3·6	$C_{22}H_{14}O_{10}$	60·3	3·2
Va	365	60·1	3·5	$C_{22}H_{14}O_{10}$	60·3	3·2
IVb	306	61·6	4·3	$C_{24}H_{18}O_{10}$	61·8	3·9
Vb	338	61·7	4·2	$C_{24}H_{18}O_{10}$	61·8	3·9
VIb	>400	61·6	3·7	$C_{24}H_{18}O_{10}$	61·8	3·9
†	237—238	68·5	4·3	$C_{17}H_{12}O_5$	68·9	4·1
‡	258	69·6	4·9	$C_{18}H_{14}O_5$	69·7	4·5

* All the acids dissolve in sodium hydrogen carbonate solution with effervescence and melt with effervescence. † 7-Methoxy-8-phenylcoumarin-6-carboxylic acid. ‡ 7-Methoxy-4-methyl-8-phenylcoumarin-6-carboxylic acid.

fractional crystallisations of the residue remaining on removal of nitrobenzene by steam-distillation.

Demethylations.—Demethylations were carried out by refluxing the compounds in acetic anhydride with hydriodic acid (*d* 1·7) at 120—130° for 2 hr. The *products* are listed in Table 3.

Hydrolyses.—The esters were hydrolysed by refluxing 10% alcoholic potassium hydroxide in 2 hr. The *acids* are listed in Table 4.

Decarboxylations.—The bicoumarinyl acids were decarboxylated by refluxing them in quinoline with copper powder for 0·5 hr. The 8-phenylcoumarincarboxylic acids were heated in quinoline with copper powder at 200°.

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