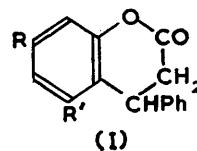


**280.** *The Reaction between Cinnamic Acid and Phenols in Presence of Hydrochloric Acid. A New Method for the Preparation of 3:4-Dihydro-4-phenylcoumarins.*

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Reaction between cinnamic acid and phenols in the presence of hydrochloric acid provides a new method for the preparation of 3:4-dihydro-4-phenylcoumarins in good yields. Crotonic acid does not react with phenols under similar conditions.

THE production of 3:4-dihydro-4-phenylcoumarins from cinnamic acid and phenols in presence of concentrated sulphuric acid has been reported,<sup>1</sup> but the yields were low, probably owing to sulphonation of the products. It has now been found that phenols react readily with cinnamic acid in presence of concentrated hydrochloric acid: if the phenol has free *ortho*- and *para*-positions the product is a mixture; e.g., from phenol, 3:4-dihydro-4-phenylcoumarin (I; R = R' = H) and  $\beta$ -*p*-hydroxyphenyl- $\beta$ -phenylpropionic acid are obtained; where the *para*-position is occupied the coumarin only is obtained. The yields in each case were good.



Orcinol yields the isomeric dihydrocoumarins (I; R = Me, R' = OH; and *vice versa*). The latter was also obtained by reduction of 7-hydroxy-5-methyl-4-phenylcoumarin with sodium amalgam. No product was obtained from catechol and cinnamic acid, and phloroglucinol yielded "phloroglucid" (2:4:6:3':5'-pentahydroxydiphenyl) by condensation of two mols. of phloroglucinol.<sup>2</sup> The present investigation has shown that no reaction takes place between crotonic acid and phenols in presence of hydrochloric acid.

## EXPERIMENTAL

The following general procedure was applicable to the preparation of all coumarins. A slow stream of hydrogen chloride was passed through a boiling mixture of cinnamic acid (1 mol.), concentrated hydrochloric acid (25 c.c. per g. of cinnamic acid), and the phenol (1 mol.). The reaction was complete when the mixture became clear; the oil which separated solidified when cooled. The solid was triturated with cold sodium hydrogen carbonate solution, filtered off, washed repeatedly with cold water, dried, and crystallised from ethanol. The alkaline filtrate and washings on acidification yielded, when possible, the corresponding  $\beta$ -aryl- $\beta$ -*p*-hydroxyphenylpropionic acid. Cinnamic acid with resorcinol monomethyl ether gives 3:4-dihydro-7-hydroxy-4-phenylcoumarin (7.5%) and 3:4-dihydro-7-methoxy-4-phenylcoumarin (87%); with resorcinol dimethyl ether it gives  $\beta$ -(2:4-dimethoxyphenyl)- $\beta$ -phenylpropionic acid (76%), 3:4-dihydro-7-hydroxy-4-phenylcoumarin (5%), and 3:4-dihydro-7-methoxy-4-phenylcoumarin (11%).

*Methylation of Coumarins.*—(a) The following method<sup>3</sup> avoids opening the lactone ring and is applicable to the hydroxycoumarins derived from di- and tri-hydric phenols. The coumarin (1 mol.) in dry xylene was heated with powdered anhydrous potassium carbonate (2.5 mol.) and methyl sulphate (2.5 mol.) at 140° for 4 hr. with occasional shaking. The hot solution was decanted and the residue twice extracted with boiling xylene which was added to the main bulk; removal of the xylene in steam left the methylated coumarin.

(b) To a solution of coumarin (1 mol.) in 10% aqueous sodium hydroxide (4 mol.) at room temperature, methyl sulphate (2.5 mol.) was added in small portions with vigorous shaking. The clear solution was then heated at 80° for 30 min., cooled, and on acidification yielded the methoxy-acid. The phenylhydrazides were prepared by the action of phenylhydrazine on coumarins according to Fischer and Nouri's directions.<sup>4</sup> The coumarins and hydroxy-acids were acetylated by heating them with acetic anhydride and fused sodium acetate for 2 hr.

<sup>1</sup> Liebermann and Hartmann, *Ber.*, 1891, **24**, 2582; 1892, **25**, 957, 2130; cf Simpson and Israelstam, *J. S. African Chem. Inst.*, 1949, **2**, 165.

<sup>2</sup> Herzig and Pollak, *Monatsh.*, 1894, **15**, 703.

<sup>3</sup> Stephen and Weizmann, *J.*, 1914, **105**, 1049.

<sup>4</sup> Fischer and Nouri, *Ber.*, 1917, **50**, 693.

The Tables give details of compounds prepared. In addition were obtained *phenylhydrazides* from:  $\beta$ -*o*-hydroxyphenyl- $\beta$ -phenylpropionic acid, yellow needles, m. p. 159° (Found: N, 8.4.  $C_{21}H_{20}O_2N_2$  requires N, 8.4%),  $\beta$ -(2-hydroxy-3-methylphenyl)- $\beta$ -phenylpropionic acid, yellow needles (from aqueous ethanol), m. p. 163° (Found: N, 8.2.  $C_{22}H_{22}O_2N_2$  requires N, 8.1%),  $\beta$ -(2-hydroxy-4-methylphenyl)- $\beta$ -phenylpropionic acid, needles (from aqueous methanol) (Found: N, 8.0%),  $\beta$ -(2-hydroxy-5-methylphenyl)- $\beta$ -phenylpropionic acid, needles (from aqueous

*Substituted 3 : 4-dihydro-4-phenylcoumarins.*

Subst.	Yield (%)	M. p.	Form	Solvent	Found (%)		Formula	Required (%)	
					C	H		C	H
— <sup>a</sup>	53	83°	Plates	Aq. EtOH	80.3	5.4	$C_{15}H_{12}O_2$	80.4	5.4
8-Me <sup>a</sup>	64	106	Needles	"	80.6	5.9	$C_{16}H_{14}O_2$	80.6	5.9
7-Me <sup>a</sup>	46	121	"	"	80.7	6.0			
6-Me <sup>a</sup>	—	83	"	"	80.6	6.0			
7 : 8-Benzo <sup>a</sup>	74	111.5	" <sup>b</sup>	MeOH	83.0	5.1	$C_{19}H_{14}O_2$	83.2	5.1
5 : 6-Benzo <sup>c</sup>	98	115	" <sup>b</sup>	EtOH	83.1	5.1			
7-OH <sup>a</sup>	99	140	"	Aq. EtOH	74.9	5.3	$C_{15}H_{12}O_3$	75.0	5.0
7-OMe	87	112	"	Aq. MeOH	75.6	5.7	$C_{16}H_{14}O_3$	75.5	5.5
7-OAc	—	89	Cubes	Aq. MeOH	72.3	5.1	$C_{17}H_{14}O_4$	72.3	5.0
7-OBz <sup>d</sup>	—	153	Needles	MeOH	73.05	5.4	$C_{22}H_{16}O_4 \cdot H_2O$	72.9	5.4
—	—	122	"	$C_6H_6$	76.7	4.8	$C_{22}H_{16}O_4$	76.7	4.7
6-OH <sup>a</sup>	98	133	"	Aq. EtOH	75.1	5.2	$C_{15}H_{12}O_3$	75.0	5.0
6-OMe	—	108	Cubes	MeOH	75.5	5.5	$C_{16}H_{14}O_3$	75.6	5.5
6-OAc	—	93	"	EtOH	72.3	5.1	$C_{17}H_{14}O_4$	72.3	5.0
5-OH-7-Me <sup>e</sup>	87	218	"	MeOH	75.5	5.6	$C_{16}H_{14}O_3$	75.6	5.5
7-OH-5-Me <sup>e</sup>	7.5	163	Needles	50% MeOH	75.6	5.7			
5-OMe-7-Me	—	147	"	MeOH	76.1	6.1	$C_{17}H_{16}O_3$	76.1	6.0
5-OAc-7-Me	—	160	"	—	72.9	5.5	$C_{18}H_{18}O_4$	73.0	5.4
7 : 8-(OH) <sub>2</sub>	98	147	"	Aq. EtOH	70.1	4.8	$C_{15}H_{12}O_4$	70.3	4.7
7 : 8-(OMe) <sub>2</sub>	—	112	"	"	67.6	6.0	$C_{17}H_{16}O_4 \cdot H_2O$	67.5	6.0
7 : 8-(OAc) <sub>2</sub>	—	168	"	EtOH	66.9	4.7	$C_{19}H_{18}O_6$	67.0	4.7
7 : 8-(OH) <sub>2</sub> -5-CO <sub>2</sub> H	96	248 <sup>f</sup>	"	EtOH	63.9	4.0	$C_{16}H_{12}O_6$	64.0	4.0
7 : 8-(OMe) <sub>2</sub> -5-CO <sub>2</sub> Me <sup>g</sup>	—	191	Cubes	MeOH	66.6	5.4	$C_{19}H_{18}O_6$	66.6	5.4
7 : 8-(OAc) <sub>2</sub> -5-CO <sub>2</sub> H <sup>h</sup>	—	243	—	MeOH	62.5	4.2	$C_{20}H_{18}O_8$	62.5	4.2
7-OH-3-Ph	52	175	Needles	Aq. MeOH	79.7	5.1	$C_{21}H_{16}O_3$	79.6	5.1
7-OMe-3-Ph	—	83	—	—	80.0	5.6	$C_{22}H_{18}O_3$	80.0	5.5

<sup>a</sup> For previous preparations see ref. 1. <sup>b</sup> Yellow; others are colourless. <sup>c</sup> For previous preparation see Koelsch, *J. Amer. Chem. Soc.*, 1936, **58**, 1326. <sup>d</sup> Prepared by the Schotten-Baumann method. <sup>e</sup> Obtained from orcinol as a mixture, separated by dissolution in the minimum amount of methanol, from which the main component separated; the minor component was obtained on dilution of the mother-liquor with water. <sup>f</sup> Decomp.; blue colour with aqueous  $FeCl_3$ . <sup>g</sup> Prepared by methyl sulphate and potassium carbonate in xylene. <sup>h</sup> Ag salt: Found: Ag, 21.7; Reqd.: Ag, 21.9%.

*$\beta$ -Aryl- $\beta$ -phenylpropionic acids.*

Aryl	M. p.	Form	Solvent	Found (%)		Formula	Required (%)		Ag (%) in Ag salt	
				C	H		C	H	Found	Reqd.
Ph <sup>a, b, 1</sup>	153°	Needles	Aq. EtOH	74.3	5.9	$C_{15}H_{14}O_3$	74.4	5.8	30.7	30.4
<i>o</i> -MeO-C <sub>6</sub> H <sub>4</sub> <sup>a</sup>	135	"	"	75.1	6.4	$C_{16}H_{16}O_3$	75.0	6.3	29.4	29.7
<i>p</i> -MeO-C <sub>6</sub> H <sub>4</sub> <sup>a</sup>	123	"	MeOH	74.9	6.2					
<i>p</i> -AcO-C <sub>6</sub> H <sub>4</sub> <sup>a</sup>	125	Cubes	Aq. EtOH	71.8	5.7				$C_{17}H_{16}O_4$	
4 : 3-HO-C <sub>6</sub> H <sub>3</sub> Me <sup>b, 2</sup>	96	Needles	H <sub>2</sub> O	75.0	6.3	$C_{16}H_{16}O_3$	75.0	6.3	29.6	29.7
2 : 3-MeO-C <sub>6</sub> H <sub>3</sub> Me	127	Plates	MeOH	75.5	6.7	$C_{17}H_{16}O_3$	75.5	6.7	28.8	28.6
4 : 3-MeO-C <sub>6</sub> H <sub>3</sub> Me	120	Needles	Aq. MeOH	75.6	6.7					
4 : 3-AcO-C <sub>6</sub> H <sub>3</sub> Me	98	"	Aq. AcOH	72.5	6.1	$C_{18}H_{18}O_4$	72.5	6.0	26.5	26.6
4 : 2-HO-C <sub>6</sub> H <sub>3</sub> Me <sup>b, 3</sup>	126	"	Aq. EtOH	75.0	6.4	$C_{16}H_{16}O_3$	75.0	6.3	29.8	29.7
2 : 4-MeO-C <sub>6</sub> H <sub>3</sub> Me	133	Plates	MeOH	75.5	6.7	$C_{17}H_{16}O_3$	75.5	6.7	28.4	28.6
4 : 2-MeO-C <sub>6</sub> H <sub>3</sub> Me	121	Cubes	Aq. MeOH	75.5	6.8					
4 : 2-AcO-C <sub>6</sub> H <sub>3</sub> Me	90	Needles	Aq. AcOH	72.4	6.1	$C_{18}H_{18}O_4$	72.5	6.1	26.6	26.6
2 : 5-MeO-C <sub>6</sub> H <sub>3</sub> Me	132	Cubes	Aq. EtOH	75.4	6.8	$C_{17}H_{16}O_3$	75.5	6.7	28.8	28.6
4 : 1-HO-C <sub>10</sub> H <sub>6</sub> <sup>4</sup>	171	Needles <sup>e</sup>	—	77.9	5.6	$C_{19}H_{16}O_3$	78.8	5.5	—	—
1 : 2-MeO-C <sub>10</sub> H <sub>6</sub> <sup>a</sup>	114.5	Needles	EtOH	78.3	5.9	$C_{20}H_{16}O_3$	78.4	5.9	—	—
4 : 1-AcO-C <sub>10</sub> H <sub>6</sub> <sup>a</sup>	93	Needles <sup>c</sup>	"	75.4	5.5	$C_{21}H_{18}O_4$	75.4	5.5	—	—
2 : 1-MeO-C <sub>10</sub> H <sub>6</sub> <sup>d</sup>	170	"	Aq. MeOH	78.4	5.9	$C_{20}H_{16}O_3$	78.4	5.9	26.0	26.1
2 : 4-(MeO) <sub>2</sub> C <sub>6</sub> H <sub>3</sub> <sup>e, 5</sup>	123	"	"	71.4	6.6	$C_{17}H_{16}O_4$	71.3	6.3	27.3	27.4
2 : 5-(MeO) <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	127	"	"	71.2	6.2					

<sup>a</sup> For previous preparations see ref. 1. <sup>b</sup> No colour with  $FeCl_3$ . <sup>c</sup> Yellow; others are colourless. <sup>d</sup> As footnote *c* to previous Table. <sup>e</sup> Also obtained by methylating 3 : 4-dihydro-7-hydroxy-4-methylcoumarin in alkali.

Yields: <sup>1</sup> 45, <sup>2</sup> 34, <sup>3</sup> 52, <sup>4</sup> 10, <sup>5</sup> 76%.

ethanol), m. p. 173° (decomp.) (Found: N, 8.2%), and  $\beta$ -(2-hydroxy-1-naphthyl)- $\beta$ -phenylpropionic acid, cubes (from dilute methanol), m. p. 148° (Found: N, 7.2.  $C_{25}H_{22}O_2N_2$  requires N, 7.3%).

$\beta$ -(2-Hydroxy-5-methylphenyl)- $\beta$ -phenylpropionamide was obtained by saturating a solution of 3:4-dihydro-4-phenyl-6-methylcoumarin (2 g.) in methanol (20 c.c.) at -5° with ammonia, heating the solution in a pressure vessel at 80° for 4 hr., and removing the solvent and excess of ammonia in a vacuum. The residue crystallised from methanol containing ammonia, as needles, m. p. 162° (decomp.) (Found: N, 5.5.  $C_{16}H_{17}O_2N$  requires N, 5.5%).

Methyl- $\beta$ -(2:4-dimethoxyphenyl)- $\beta$ -phenylpropionate was obtained by saturating a solution of  $\beta$ -(2:4-dimethoxyphenyl)- $\beta$ -phenylpropionic acid (1 g.) in methanol (10 c.c.) at 0° with hydrogen chloride; after 12 hr. at 0°, the solution was boiled for 1 hr., and the methanol distilled off, leaving the ester which solidified in ice. Crystallisation from aqueous methanol gave needles, m. p. 75° (Found: C, 72.0; H, 6.7.  $C_{18}H_{20}O_4$  requires C, 72.0; H, 6.7%).

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