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The Knoevenagel Reaction between Hydroxybenzaldehydes and Ethyl Cyanoacetate

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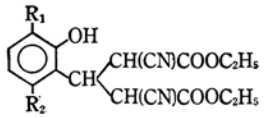
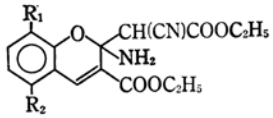
Substituted 2-hydroxybenzaldehydes react with two equivalents of ethyl cyanoacetate to give α-amino-β-(substituted 3-coumarinyl)-β-cyano-β-ethoxycarbonylethylenes in the presence of piperidine. When equivalent aldehyde and the cyanoacetate are used, substituted 2-imino-3-ethoxycarbonyl-2*H*-chromenes result, without the isolation of arylidenecyanoacetates. In *o*-hydroxyaryls, salicylic and *o*-thymotinic aldehydes, which give benzopyrane derivatives, are exceptional cases. 5-Phenylazo- and 5-nitro-2-hydroxybenzaldehydes result in the formation of coumarin derivatives. An abnormal condensation is also shown in the cases of 3, 5-dibromo-2, 4-dihydroxy-, 2-hydroxy-3-methoxy- and 2-hydroxy-4-methoxybenzaldehydes; i. e., the first one yields a 1 : 1-condensation product, while the last two give 3-cyanocoumarin derivatives, even with an excess of ethyl cyanoacetate. The condensation of *m*- and *p*-hydroxybenzaldehydes with ethyl cyanoacetate give the normally-expected arylidenecyanoacetates, even in the presence of a large excess of the cyanoacetate.

The base-catalyzed condensation of salicylaldehyde with ethyl cyanoacetate has already been described by Bechart[1] and by Knoevenagel et al.,[2] as giving an abnormal condensation product. They assigned the product to diethyl α, γ-dicyano-β-(2-hydroxyphenyl)-glutarate (Ia). Recently, however, Matsumura[3] established that this product has the structure of 2-amino-2-(cyano-ethoxycarbonylmethyl)-3-ethoxycarbonyl-α-benzopyrane (IIa) and not Ia. Sastry et al.[4] reported that ethyl 3-cyano-3, 4-dihydrocoumarin-4-cyanoacetate (III) was formed when Ia was refluxed in ethanol containing piperidine, but Matsumura gave the structure of α-amino-α-(3-coumarinyl)-β-cyano-β-ethoxycarbonylethylene (IV) instead of III.

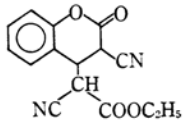
The present investigation will be concerned with the condensation of various *o*-hydroxyaromatic aldehydes with ethyl cyanoacetate in the presence of piperidine. In addition, *m*- and *p*-hydroxyaryls will also be investigated.



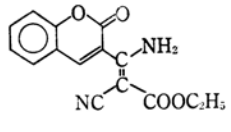
Ia, $R_1=R_2=H$
Ib, $R_1=i\text{-}C_3H_7$ $R_2=CH_3$



IIa, $R_1=R_2=H$
IIb, $R_1=i\text{-}C_3H_7$ $R_2=CH_3$



III



IV

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Results and Discussion

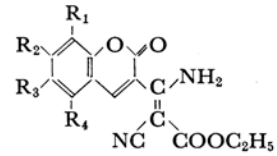
The condensation between salicylaldehyde and ethyl cyanoacetate was re-investigated. The condensation was attempted by heating the aldehyde with an equivalent amount of the cyanoacetate in ethanol containing piperidine or by letting the reactants stand; however, the required condensations could not be effected, and only negligible products were obtained.

The condensation was positive only with two equivalent amounts of the cyanoacetate; that is, only when the reaction mixture was heated for a short time at the boiling point of the solvent, two compounds (m. p. 239—240°C and m. p. 137.5—138.5°C) could be readily isolated.

On investigation, the product melting at 239—240°C was found to be devoid of saturated nitriles. This was confirmed by the infrared absorption spectrum, which showed no characteristic bands for the nitriles. However, two medium bands were shown near 3400 and near 3300 cm^{-1}, indicating a primary amino group; also, the spectrum exhibited an absorption near 2200 cm^{-1} for α, β-unsaturated nitrile. These facts, together with the analytical results, were in full agreement with the IV structure originally proposed by Matsumura. On the other hand, the spectrum of the compound melting at 137.5—138.5°C revealed two relatively intense bands near 3460

1) C. Bechart, *J. prakt. Chem.*, (2), **50**, 1 (1894).
2) E. Knoevenagel and R. Ornot., *Ber.*, **37**, 4496 (1904).
3) S. Matsumura, This Bulletin, **34**, 995 (1961).
4) V. D. N. Sastry and T. R. Seshadri, *Proc. Indian Acad. Sci.*, **16A**, 29 (1942).

TABLE I. α-AMINO-α-(SUBSTITUTED 3-COUMARINYL)-β-CYANO-β-ETHOXYCARBONYLETHYLENES



Compound	R_1	R_2	R_3	R_4	M.p. °C	Appearance[a]	Yield[b] %	Formula	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	N, % Calcd.	N, % Found
Va	H	H	Br	H	272—3 (decomp.)	SY Needles	53	$C_{15}H_{11}O_4N_2Br$	49.56	49.62	3.03	2.95	7.71	7.43
Vb	H	H	Cl	H	265—6	Y Needles	48	$C_{15}H_{11}O_4N_2Cl$	56.51	56.21	3.45	3.46	8.79	8.63
Vc	H	H	NO_2	H	238—9	Y Crystals	31	$C_{15}H_{11}O_6N_3$	54.71	54.30	3.37	3.36	12.76	12.89
Vd	H	H	H	CH_3	238—9	SY Needles	20	$C_{16}H_{14}O_4N_2$	64.42	64.59	4.73	4.58	9.39	9.28
Ve	H	OH	H	H	277—8 (decomp.)	Y Needles	49	$C_{15}H_{12}O_5N_2$	60.00	59.71	4.03	4.06	9.33	9.04
Vf	OCH_3	H	H	H	240—1	SY Needles	51	$C_{16}H_{14}O_5N_2$	61.14	60.85	4.49	4.43	8.91	8.80

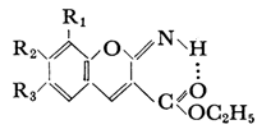
a) S, Slightly; Y, Yellow.
b) Overall yield from the aldehyde used, and recrystallized from *n*-butanol.

TABLE II. INFRARED DATA OF α-AMINO-α-(SUBSTITUTED 3-COUMARINYL)-β-CYANO-β-ETHOXYCARBONYLETHYLENES (in KBr disk)

Compound	Bonded NH_2 str.	NH_2 str.	C≡N str.	Ester C=O str.	Lactone C=O str.	C=C and NH_2 def.	(cm^{-1})
Va	3470m	3340m,br	2220 s	1720 s	1700 s	1620 s	
Vb	3470m	3330m	2220 s	1720 s	1700 s	1615m,sh	
Vc	3460m	3310m,br	2220 s	1715 s	1690 s	1615 s ,sh	
Vd	3420m	3290m,br	2220 s	1715 s	1695m	1615 s	
Ve	3460m	3300m,br	2220 s	1715 s	1700m	1635 s	
Vf	3440m	3370m	2220 s	1725 s,sh	1700 s	1620 s 1635 s	

Abbreviations: s, strong; m, medium; sh, shoulder; br, broad; str, stretching; def, deformation.

TABLE III. SUBSTITUTED 2-IMINO-3-ETHOXYCARBONYL-2*H*-CHROMENES



Compound	R_1	R_2	R_3	M. p. °C	Crystn. solvent	Appearance[a]	Yield[b] %
VIa	H	H	Cl	119—120	EtOH	YO Crystals	35
VIb	OH	H	H	179—180 (decomp.)	*n*-BuOH	Y Crystals	73
VIc	H	OH	H	182—183	*n*-BuOH	Y Needles	82
VId	H	H	OH	200—201	EtOH-H_2O	GY Crystals	84
VIe	Br	OH	Br	245—246 (decomp.)	*n*-BuOH	YO Needles	62
VIf	H	OH	NO_2	over 300	*n*-BuOH	YO Crystals	68

Compound	Formula	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	N, % Calcd.	N, % Found
VIa	$C_{12}H_{10}O_3NCl$	57.26	56.85	3.98	4.01	5.57	5.47
VIb	$C_{12}H_{11}O_4N$	61.80	61.79	4.75	4.72	6.01	5.95
VIc	$C_{12}H_{11}O_4N$	61.80	61.47	4.75	4.92	6.01	6.05
VId	$C_{12}H_{11}O_4N$	61.80	61.66	4.75	4.74	6.01	5.86
VIe	$C_{12}H_9O_4NBr_2$	36.83	36.61	2.30	2.36	3.58	3.59
VIf	$C_{12}H_{10}O_6N_2$	51.80	51.42	3.60	3.47	10.07	9.96

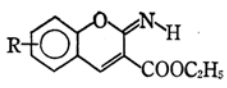
a) Y, Yellow; O, Orange; G, Green. b) Overall yield from the aldehyde used.

and near 3300 cm^{-1}; these were attributed to a primary amino group. The infrared and analytical data are in essential agreement with the IIa structure formulated by Matsumura.

The investigation was then extended to the action of the ethyl cyanoacetate on substituted 2-hydroxybenzaldehydes with the view of obtaining the IIa and/or the IV type. Using a 2 : 1 molar ratio of the aldehydes to the cyanoacetate, α-amino-α-(substituted 3-coumarinyl)-β-cyano-β-ethoxycarbonylethylenes (Va—Vf) (see Tables I and II), which very closely resemble the IV type, were regularly obtained, but the expected α-benzopyrane derivatives (the IIa type) could not be isolated; with a molar ratio of the aldehydes and the cyanoacetate, only the 1 : 1-condensation products were obtained.

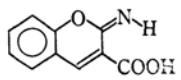
The 1 : 1-condensation products mentioned above did not exhibit the characteristic C≡N stretching vibration in each infrared spectrum examined; therefore, the following structure, VI, was considered to hold for the products concerned.

Apparently, the spectrum of the 1 : 1-product obtained from 5-chlorosalicylaldehyde and ethyl cyanoacetate, for example, supported the structure



VI

of 2-imino-3-ethoxycarbonyl-6-chloro-2*H*-chromene (VIa), since three recognizable bands, at 3380, 1710 and 1635 cm^{-1} which due to an N–H, an α, β-unsaturated ester C=O and a C=N stretching vibrations respectively, were detected. A medium band at 1615 cm^{-1} attributable to the C=C stretching mode adjacent to the ester residue was also observed. Baker and Howea[5] have already inferred that, in the conversion of 2-hydroxybenzylidenecyanoacetic acid into 3-coumarincarboxylic acid in boiling water, an imino-lactone (VII) is the intermediate.



VII

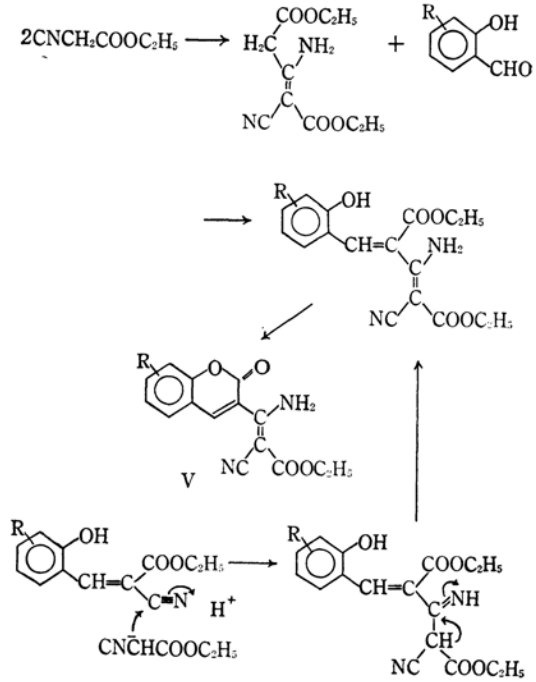
The 1 : 1-products investigated, accordingly, were considered to have the structure of 2-imino-3-ethoxycarbonyl-2*H*-chromenes (VIa—VIf) and not substituted arylidenecyanoacetates (see Tables III and IV). As may be seen in Table IV, α, β-unsaturated ester C=O bands of all the compounds measured in KBr disk are shifted to lower frequencies as compared with the normal spectral region of ester carbonyls vicinal to α, β-unsaturation. It is likely, judging from the infrared results, that these 2*H*-chromenes have the hydrogen-bonded chelate form in the solid state.

TABLE IV. INFRARED DATA OF SUBSTITUTED 2-IMINO-3-ETHOXYCARBONYL-2*H*-CHROMENES
(in KBr disk)

Compound	Bonded OH and NH str.	Ester C=O str.	C=N str.	C=C str. (cm^{-1})
VIa	3380 m	1710 s	1635 m	1615 m
VIb	3380 m	1700 s	1620 m	1610 s, sh
VIc	3310 m	1705 s	1630 s	1620 s, sh
VId	3320 m	1715 s	1620 m, sh	1610 m
VIe	3340 w	1715 s	1625 m, sh	1615 m
VIf	3390 m	1715 s	1645 s	1620 s, sh

Abbreviation: s, strong; m, medium; w, week; sh, shoulder; str, stretching

The problem of the mechanism of the formation of the β-ethoxycarbonylethylenes (Va—Vf) is reduced to the question of whether the condensation involves a self-condensation of the cyanoacetate forming an enamine-type dimer via a ketimine-type dimer following the dehydration reaction between the dimer and the aldehydes, or, alternatively, the formation of normal dehydration products without cyclization and a nucleophilic addition reaction by the cyanoacetate on the dehydration products. The two possibilities are illustrated in Scheme 1.

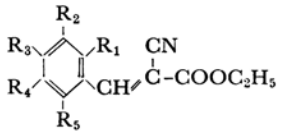


Scheme 1

When the *o*-hydroxyaryls were treated with an equivalent ethyl cyanoacetate, no β-ethoxycarbonylethylene derivatives occurred; only 1 : 1-products

5) W. Baker and C. S. Howea, *J. Chem. Soc.*, **1953**, 119.

TABLE V. SUBSTITUTED ETHYL *m*- OR *p*-HYDROXY-*α*-CYANOCINNAMATES



Compound	R_1	R_2	R_3	R_4	R_5	M. p. °C	Appearance[a]	Yield[b] %
IX	H	OH	H	H	H	91—92[c]	SY Needles	61
X	H	H	OH	H	H	171—172[d]	Y Needles	86
XI	H	OCH_3	OH	H	H	106—107[e]	YF Needles	79
XII	H	OC_2H_5	OH	H	H	76—77	Y Needles	82
XIII	H	CH_3	OH	H	H	220—221	SY Needles	78
XIV	H	CH_3	OH	CH_3	H	124—125	YM Crystals	95
XV	H	*i*-C_3H_7	OH	H	CH_3	190—191	Y Needles	80
XVI	H	Cl	OH	H	H	199—200	SY Needles	81
XVII	OCH_3	H	OCH_3	H	H	138—139[f]	Y Needles	89

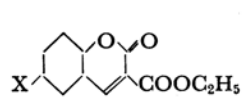
Compound	Formula	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	N, % Calcd.	N, % Found
IX	$C_{11}H_{12}O_3N$					6.45	6.43
X							
XI							
XII	$C_{14}H_{15}O_4N$	64.36	64.47	5.79	5.63	5.36	5.37
XIII	$C_{13}H_{13}O_3N$	67.53	67.08	5.63	5.52	6.06	6.08
XIV	$C_{14}H_{15}O_3N$	68.55	68.06	6.16	6.09	5.71	5.60
XV	$C_{16}H_{19}O_3N$	70.33	69.77	6.96	6.74	5.13	5.07
XVI	$C_{12}H_{10}O_3NCl$	57.26	57.43	3.98	3.97	5.57	5.35
XVII							

a) F, Flattened; M, Micro; S, Slightly; Y, Yellow.
b) Overall yield from the aldehyde used, and recrystallized from ethanol-water.
c) Reported m. p. 98°C, K. P. Dave and K. S. Nargund, *J. Univ. Bombay*, **7**, 196 (1938); *Chem. Abstr.*, **33**, 3779 (1939).
d) Reported m. p. 173—174°C, F. D. Popp, *J. Org. Chem.*, **25**, 646 (1960).
e) Reported m. p. 108—109°C, reference as footnote d.
f) Reported m. p. 142—143°C, reference as footnote 5.

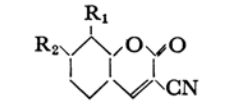
via intermediate arylidenecyanoacetates were obtained, as has been described above. These facts indicate that the latter mechanism, which involves the carbanion of the cyanoacetate attacking the possibly-polarized nitrile carbon atom of the resulting intermediates, may be more possible than the former mechanism. However, salicylaldehyde condensed with the dimer of ethyl cyanoacetate to give the *β*-ethoxycarbonylethylene (IV), as has been reported earlier.[3]

A definitive proof for the latter mechanism is lacking. Attempts to obtain the IV type by treating the appropriate 2*H*-chromene derivatives with ethyl cyanoacetate in boiling ethanol containing piperidine were unsuccessful.

5-Phenylazo-2-hydroxy- and 3, 5-dibromo-2, 4-dihydroxybenzaldehydes behaved "abnormally" in the condensation with an excess of ethyl cyanoacetate, giving ethyl 6-phenylazo-3-coumarincarboxylate (VIIa) and the 2*H*-chromene derivative (VIe) (see Table III), respectively. 5-Nitrosalicylaldehyde reacted with an equimolar ethyl cyanoacetate to yield an unexpected product, ethyl 6-nitro-3-coumarincarboxylate (VIIb); also, 2-hydroxy-3-methoxy- and 2-hydroxy-4-methoxybenzaldehydes resulted in the formation of 8-methoxy-3-cyanocoumarin (VIIIa) (C≡N stretching 2220 cm^{-1} in KBr disk) and 7-methoxy-3-cyanocoumarin (VIIIb) (C≡N 2220 cm^{-1}) respectively when an equimolar ethyl cyanoacetate was used. These were exceptional cases in the *o*-hydroxyaryl series.



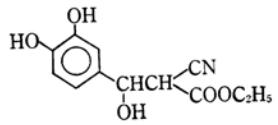
VIIa, X=Ph-N=N-
VIIb, X=NO_2



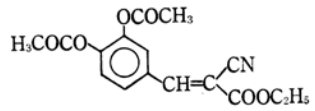
VIIIa, R_1=OCH_3 R_2=H
VIIIb, R_1=H R_2=OCH_3

The condensation of *m*- and *p*-hydroxybenzaldehydes with ethyl cyanoacetate gave the normally expected products, substituted ethyl *m*- and *p*-hydroxy-*α*-cyanocinnamates (IX—XVII), even with a large excess of the cyanoacetate. The results obtained are listed in Table V.

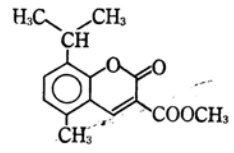
3, 4-Dihydroxybenzaldehyde reacted with an equivalent ethyl cyanoacetate to form ethyl α-cyano - β - hydroxy -β- (3, 4-dihydroxyphenyl)-propionate (XVIII); on subsequent treatment with acetic anhydride, this yielded ethyl α-cyano-3, 4-diacetyloxycinnamate (XIX). On the other hand, 2-imino-3-ethoxycarbonyl-7-hydroxy -2*H*- chromene (VIb), when refluxed with acetic anhydride, was converted into ethyl 7-acetyloxy-3-coumarincarboxylate (XX).



XVIII



XIX



XXI

Previously, one of the present authors[6] has reported that the condensation between 2-hydroxy-3-isopropyl - 6 - methylbenzaldehyde, *o*-thymotinic aldehyde, gave mainly diethyl β, γ-dicyano-β-(2-hydroxy -3- isopropyl -6- methyl)-glutarate (Ib). The present infrared study shows that the condensation product formulated as Ib has the structure of 2-amino-2- (cyanoethoxycarbonylmethyl) -3- ethoxycarbonyl-5-methyl-8-isopropyl-α-benzopyrane (IIb). The infrared spectrum of Compound IIb exhibited characteristic absorption bands at 3460 and at 3380 cm^{-1} for the primary amino group; at 2245 cm^{-1} for the non-conjugated C≡N; at 1746 cm^{-1} for the saturated ester C=O; at 1645 cm^{-1} for the ester C=O conjugated with the unstauration bond and at 1640 cm^{-1} for an absorption attributable to NH_2 deformation vibration. This compound afforded methyl 5-methyl-8-isopropyl-3-coumarincarboxylate (XXI) in boiling methanol containing concentrated sulfuric acid.

Experimental*

Condensation of Salicylaldehyde and Ethyl Cyanoacetate.—Three grams (0.0246 mol.) of the aldehyde was dissolved in 15 ml. of ethanol containing 5.6 g. (0.0496 mol.) of the ester. To the refluxing solution was added one drop of piperidine. The solution was refluxed for an additional one hour and allowed to stand overnight at room temperature. The crude α-amino-α- (3-coumarinyl) -β- cyano - β - ethoxycarbonylethylene (IV) separated was collected, washed with ethanol and weighed 1.3 g. One recrystallization from ethanol gave slightly yellowish micro crystals melting at 245—246°C (Lit.,[3] 245—246°C). The initial filtrate and washings from crude IV were combined and diluted with water. An oily matter was extracted with ether, and ethreal extract was dried over sodium sulfate. The residual oil, on removal of the ether, was shaken with methanol, and the crude 2-amino-2-(cyanoethoxycarbonylmethyl) - 3 - ethoxycarbonyl - α - benzopyrane (IIa) was recrystallized from ethanol-water in almost colorless plates melting at 137.5—138.5°C, and which weighed 3.3 g. Lit.,[3] m. p. 137°C.

Synthesis of α-Amino-α-(6-bromo-3-coumarinyl)-β-cyano-β-ethoxycarbonylethylene (Va).—The preparation of this compound is typical of the preparation of the substituted β-ethoxycarbonylethylenes and is described in detail.

Two grams (0.01 mol.) of 5-bromo-2-hydroxybenzaldehyde was dissolved in 20 ml. of ethanol containing 2.3 g. (0.02 mol.) of ethyl cyanoacetate and one drop of piperidine. The mixture was warmed on a water-bath for 1 hr., and being allowed to stand overnight. The precipitates were collected, washed with ethanol and recrystallized from *n*-butanol, giving the required compound melting at 272—273°C with decomposition. The melting points and analytical data of the β-ethoxycarbonylethylenes are summarized in Table I.

Synthesis of 2-Imino-3-ethoxycarbonyl-6-chloro-2*H*-chromene (VIa).—The 2*H*-chromenes synthesized in this study are listed in Table III. All of these were prepared from ethyl cyanoacetate and the corresponding aldehyde. The physical properties are also included in Table III.

An example of the preparation of the 2*H*-chromenes is described.

5-Chloro-2-hydroxybenzaldehyde (0.18 g., 0.00115 mol.) and 0.13 g. (0.00115 mol.) of ethyl cyanoacetate were dissolved in 2 ml. of hot ethanol containing one drop of piperidine. The solution was allowed to stand overnight at room temperature. The precipitates were collected, washed with methanol and recrystallized from ethanol in yellowish micro crystals melting at 119—120°C. The resulting VIa weighed 0.1 g.

Synthesis of Ethyl 6-Phenylazo-3-coumarincarboxylate (VIIa).—5-Phenylazo-2-hydroxybenzaldehyde (0.5 g., 0.0022 mol.) and ethyl cyanoacetate (0.25 g., 0.0022 mol.) were mixed in 10 ml. of ethanol containing one drop of piperidine. The mixture was warmed on a water-bath for 1 hr., and being allowed to stand overnight. The crystals separated were collected, washed with ethanol and recrystallized from dioxane-water in lustrous yellowish brown needles melting at 153—154°C, and which weighed 0.2 g.

Found: C, 67.07; H, 4.48; N, 8.77. Calcd. for $C_{18}H_{14}O_4N_2$: C, 67.07; H, 4.38; N, 8.69%.

Synthesis of Ethyl 6-Nitro-3-coumarincarboxylate (VIIb).—To a solution of 0.24 g. of 5-nitro-2-hydroxybenzaldehyde and 0.16 g. of ethyl cyanoacetate in 2 ml. of ethanol was added one drop of piperidine. The solution was allowed to stand overnight at room temperature. The crude VIIb separated as a crystalline

6) H. Yasuda, *Sci. Papers Inst. Phys. Chem Res.* (*Tokyo*), **52**, 83 (1958).

* All melting points are uncorrected.

product was collected, washed with ethanol and recrystallized from *n*-butanol, giving almost colorless lustrous short needles melting at 193—194°C, and which weighed 0.27 g.

Found: C, 54.44; H, 3.49; N, 5.54. Calcd. for $C_{12}H_9O_6N$: C, 54.76; H, 3.45; N, 5.32%.

Synthesis of 8-Methoxy-3-cyanocoumarin (VIIIa).—A solution of 0.5 g. of 2-hydroxy-3-methoxybenzaldehyde and 0.4 g. of ethyl cyanoacetate in 5 ml. of ethanol containing one drop of piperidine was warmed on a water-bath for 20 min. The precipitates, on cooling, was collected, washed with ethanol and weighed 0.4 g. One recrystallization from *n*-butanol gave yellowish short needles melting at 222—223°C.

Found: C, 64.99; H, 3.48; N, 7.05. Calcd. for $C_{11}H_7O_3N$: C, 65.67; H, 3.51; N, 6.96%.

Synthesis of 7-Methoxy-3-cyanocoumarin (VIIIb).—2-Hydroxy-4-methoxybenzaldehyde (0.38 g.) was dissolved in 5 ml. of ethanol containing 0.28 g. of ethyl cyanoacetate and one drop of piperidine. The solution was allowed to stand overnight at room temperature. The solid separated was collected, washed with ethanol and recrystallized from *n*-butanol in slightly yellowish short needles melting at 218—219°C.

Found; C, 65.38; H, 3.72; N, 6.79. Calcd. for $C_{11}H_7O_3N$: C, 65.67; H, 3.51; N, 6.96%.

Synthesis of Ethyl *m*- or *p*-Hydroxy-α-cyanocinnamates (IX—XVII).—The method for the preparation of this series is illustrated by the synthesis of ethyl *m*-hydroxy-α-cyanocinnamate (IX). To a solution of 0.001 mol. of *m*-hydroxybenzaldehyde and 0.001 mol. of ethyl cyanoacetate in 5 ml. of ethanol was added one drop of piperidine. The solution was warmed on a water-bath for a few minutes, and being allowed to stand overnight at room temperature. The solid separated was collected, and recrystallized from ethanol-water. See Table V for the melting point and the analysis.

Condensation of 3, 4-Dihydroxybenzaldehyde and Ethyl Cyanoacetate.—To a solution of 1.0 g. of the aldehyde and 0.81 g. of the ester in 5 ml. of ethanol was added three drops of piperidine. After standing overnight, the solution was diluted with water, and the precipitates were recrystallized from ethanol-water to give yellowish needles melting at 166—167°C, and which weighed 1.5 g. The analytical values were identical with that of ethyl α-cyano-β-hydroxy-β-(3, 4-dihydroxyphenyl)-propionate (XVIII).

Found: C, 57.97; H, 5.08; N, 5.58. Calcd. for $C_{12}H_{13}O_5N$: C, 57.37; H, 5.22; N, 5.58%.

Reaction of XVIII and Acetic Anhydride to Ethyl α-Cyano-3, 4-diacetyloxycinnamate (XIX).—An appropriate amount of XVIII was refluxed with an appropriate amount of the anhydride for two hours, and then acetic acid and the anhydride were recovered under water-pump pressure. The residual solid was recrystallized from ethanol-water in colorless plates melting at 103—104°C. The analytical data were identical with that of XIX.

Found: C, 60.28; H, 4.74; N, 4.39. Calcd. for $C_{16}H_{15}O_6N$: C, 60.50; H, 4.77; N, 4.41%.

Conversion of 2-Imino-3-ethoxycarbonyl-7-hydroxy-2*H*-chromene (VIb) into Ethyl 7-Acetyloxy-3-coumarincarboxylate (XX).—An appropriate amount of VIb was heated to reflux with an appropriate amount of acetic anhydride for 1 hr. The residual solid, after removal of the anhydride, was recrystallized from methanol-water in slightly brownish needles melting at 147—148°C.

Found: C, 60.16; H, 4.46. Calcd. for $C_{14}H_{12}O_6$: C, 60.87; H, 4.38%.

Conversion of 2-Amino-2-(cyano-ethoxycarbonylmethyl)-3-ethoxycarbonyl-5-methyl-8-isopropyl-α-benzopyrane (IIb) into Methyl 5-Methyl-8-isopropyl-3-coumarincarboxylate (XXI).—One gram of IIb was refluxed with 10 ml. of ethanol containing 1 ml. of concentrated sulfuric acid for 1 hr. after which colorless crystals separated, on cooling, were collected, washed with water and recrystallized from methanol-water to give lustrous colorless needles melting at 120—120.5°C.

Found: C, 69.14; H, 6.23. Calcd. for $C_{15}H_{16}O_4$: C, 69.21; H, 6.20%.

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